Control of the Regioselectivity of Oxidative Free-Radical Cyclizations by Addition to Haloalkenes

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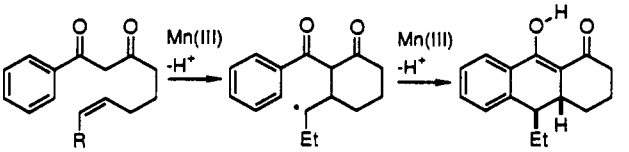
Chlorine substituents on the alkene control the regioselectivity of the cyclization of 5-hexenyl or 6-heptenyl radicals generated by oxidation of an acetoacetate ester or 1,3-diketone with $Mn(OAc)_3 \cdot 2H_2O$. 6-Exo-cyclization of the radicals obtained by oxidation of benzoylacetone derivatives **10** and **13**, containing a chlorine on the terminal double bond carbon, gives α-chloroalkyl radicals that add to the aromatic ring to give **11** and **16**, respectively. Loss of HCl leads to naphthols **8** and **17** indicating that this reaction may be useful for aureolic acid synthesis. Exo-cyclization is the exclusive process with acetoacetates **28b**, **44**, **55b**, and **59** containing a chlorine on the terminal double bond carbon. 6-Endo-cyclization is the exclusive process with acetoacetates **18c** and **51b** containing a chlorine on the internal double bond carbon. Intra- and intermolecular competition experiments indicate that these effects are primarily steric. The chlorine substituent controls the regioselectivity of the cyclization by sterically hindering attack of the radical on the chlorine bearing double bond carbon thereby retarding formation of the β-chloroalkyl radical. The chlorine substituent does not electronically accelerate attack on the other end of the double bond to give the α-chloroalkyl radical.

Introduction

Free-radical cyclizations have become a valuable and general method for the synthesis of cyclopentanes and cyclohexanes.[1] Most 5-hexenyl and 6-heptenyl radicals undergo regioselective exo-cyclizations to give cyclopentanemethyl and cyclohexanemethyl radicals, respectively. However, 5-hexenyl and 6-heptenyl α-keto radicals, in which the carbonyl is in the ring being formed, cyclize preferentially endo to give cyclohexyl and cycloheptyl radicals, respectively.[2] Alkyl substituents on the double bond influence the regioselectivity of the cyclization. Alkyl and aryl substituents on the terminal end of the double bond accelerate exo-cyclization and retard endo-substitution, while substituents on the internal end of the double bond accelerate endo-cyclization and retard exo-cyclization. Unfortunately, alkyl and aryl substituents usually cannot be used to control the regioselectivity of radical cyclization, since they cannot be removed easily after the cyclization has been carried out. We thought that chlorine substituents on the double bond might control the regioselectivity of the cyclization without modification of the carbon skeleton. Furthermore, the chlorine would also introduce additional functionality into the product.

We have recently developed an efficient oxidative free-radical cyclization using $Mn(OAc)_3$[2] to oxidize an unsaturated β-keto ester, 1,3-diketone, or 1,3-diester to an α-keto radical that cyclizes.[3] The reaction is terminated by oxidation of the cyclic radical with $Cu(OAc)_2$ or $Mn(OAc)_3$. Mono, tandem and triple cyclizations can be carried out in high yield. Since these reactions are initiated by oxidation of a 1,3-dicarbonyl compound rather than by halogen atom abstraction,[4] they should be readily compatible with the use of chloro- or bromoalkenes as substrates.

Several years ago, we reported that oxidation of **1a** with $Mn(OAc)_3 \cdot 2H_2O$ in acetic acid at rt gives **3a** (58%) as the sole isolable product.[3c] Enolization of **1a**, oxidation to the α-keto radical, and exo-cyclization give monocyclic radical **2a**. Cyclization of the monocyclic radical **2a** to the aromatic ring gives **3a** after oxidation and tautomerization. This oxidative cyclization forms two rings and leads to a highly functionalized product. This reaction might be useful for the synthesis of anthracycline and aureolic acid antibiotics if the reaction can be carried out without the ethyl substituent on the side chain to provide products such as **8** and **17**. To our disappointment, but as expected, no tricyclic products can be obtained from either the terminal alkene **1b** or the terminal alkyne **4a**. We believe



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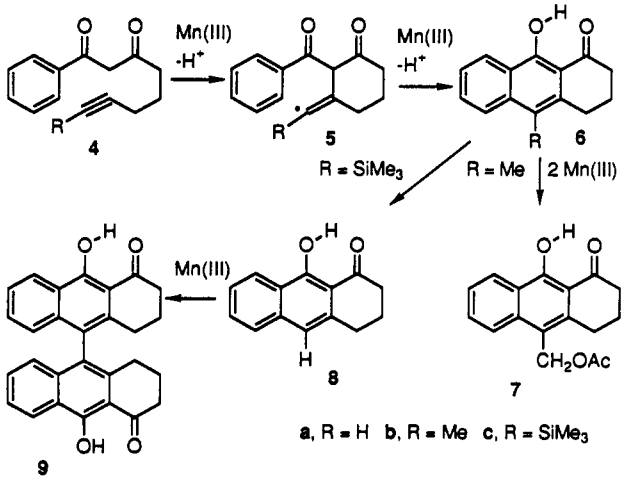
that these substrates undergo 7-endo-cyclizations to give products that are oxidized further.[3k] We therefore turned our attention to substrates with removable substituents on the terminal end of the double bond, which should favor 6-exo-cyclization.

Results and Discussion

Preparation of Dicarbonyl Compounds. The substrates were prepared in one step by standard dianion alkylations. Alkylation of the dianion of the appropriate dicarbonyl compound with 5-bromo-2-pentyne,[5a] 4-bromo-1-(trimethylsilyl)-1-butyne,[5b] 4-bromo-1-chloro-1-butene[6] (2:1 *E–Z* mixture), crotyl bromide, 1,2-dichloropropene, or 1,3-dichloropropene affords **4b** (60%), **4c** (48%), **10** (57%), **13** (68%), **28a** (45%), **44** (40%), **51b** (35%), **55b** (40%), and **59** (41%). 2,4-Dimethoxybenzoyl acetone (**12**)[7] was prepared by acylation of the enolate of acetone[8] with 2,4-dimethoxybenzoyl chloride in 75% yield. Allylation of methyl 7-chloro-3-oxo-6-heptenoate[3f] affords 50% of **28b**.

Synthesis of Dihydroanthracenes 8 and 17. We investigated the cyclizations of acetylenic radicals initially since these reactions will lead directly to products at the phenol oxidation state, i.e., **8**. Since the reaction fails with the terminal alkyne **4a** we examined the readily available methyl-substituted alkyne **4b** to demonstrate that acetylenic radicals do undergo this tandem cyclization. Oxidative cyclization of **4b** with 4.4 equiv of $Mn(OAc)_3 \cdot 2H_2O$ in AcOH for 17 h at 35 °C affords 81% of **7**. Oxidation

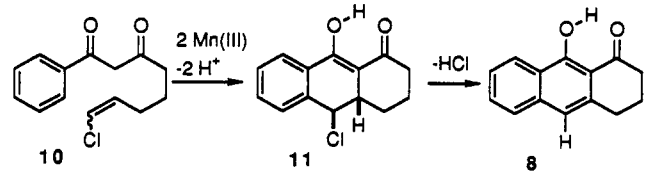


and 6-exo-cyclization form the expected radical **5b**, which cyclizes to give phenol **6b** after oxidation and tautomerization. Further oxidation of phenol **6b** by $Mn(OAc)_3 \cdot 2H_2O$ affords the quinone methide, which reacts with acetic acid to give acetoxy phenol **7**.[9] Oxidation of phenol **6b** is faster than oxidative cyclization of **4b**, since only recovered **4b** and **7** are isolated when only 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ are used. The isolation of **7** in high yield indicates that terminally substituted acetylenic radicals undergo facile 6-exo-cyclization. Unfortunately, the phenol **6** produced in this reaction is oxidized more rapidly than diketone **4b**, so this reaction will not be useful for the preparation of *p*-methylphenols.

We turned our attention to oxidative cyclization of silylalkyne **4c** since the anticipated product, phenol **6c**, cannot be oxidized to a quinone methide and protodesilylation of **6c** should give the desired phenol **8**. We were disappointed to find that reaction of **4c** with 4.5 equiv of $Mn(OAc)_3 \cdot 2H_2O$ in AcOH for 17 h at 35 °C provides 71% of binaphthol **9**. Presumably, oxidation and tandem cyclization proceed as expected to provide (trimethylsilyl)naphthol **6c**. Protodesilylation of **6c** gives naphthol **8**, which is oxidized to form binaphthol **9**. There is ample precedent for the oxidative dimerization of naphthols by $Mn(acac)_3$[10a] and other oxidants.[10b]

Since the protodesilylation of **6c** is acid catalyzed we examined buffered reaction mixtures and less acidic solvents for the oxidative cyclization. Reaction of **4c** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ in AcOH containing KOAc as a buffer leads to a 7:1:2 mixture of recovered **4c**, **8**, and **9**, confirming that **8** is an intermediate in the formation of **9**. The absence of **6c** indicates that protodesilylation is rapid even in the buffered solution. The formation of a 1:2 mixture of **8** and **9** at low conversion demonstrates that oxidation of **8** is faster than oxidation of **4c**. Oxidation of **4c** in EtOH[3j] gives a complex mixture. The oxidative cyclization of silylalkyne **4c** does not provide a route to **8**; this procedure should be useful for the synthesis of the natural product setomimycin, which has the cyclic framework of **9**.[11]

Since we could not produce naphthols **6** or **8** from alkynes we turned our attention to chloroalkenes. We were delighted to find that oxidative cyclization of **10** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ in AcOH for 15 h at 35 °C gives 79% of naphthol **8**[12] and a trace of binaphthol **9**. The chlorine substituent directs the initial cyclization 6-exo. Benzylic chloride **11** is obtained after the second cyclization and oxidation; loss of HCl from **11** leads to naphthol **8**.



The isolation of **8** in high yield from the oxidative cyclization of **10**, but not from **4c**, is puzzling. Oxidation of naphthol **8** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ in AcOH for 24 h at 35 °C gives 86% of binaphthol **9** confirming the proposed pathway for the formation of **9** from **4c**. Protodesilylation of **6c** must be much faster than oxidation of diketone **4c** since phenol **8** derived from protodesilylation of **6c** is oxidized to **9**. Conversely, loss of HCl from **11** must be slower than oxidation of diketone **10** since phenol **8** derived from loss of HCl from **11** is not oxidized to **9**.

Having established that oxidative cyclization of **10** provides phenol **8** in high yield, we considered the suitability of this reaction for the synthesis of olivin, the aglycon of aureolic acid antitumor antibiotic olivomycin.[13] Olivin

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(6) Hill, E. A. *J. Am. Chem. Soc.* **1972**, *94*, 7462. A 2:1 *E/Z* mixture of 1,3-dichloropropane isomers gives a 15% overall yield of a 1:2 *Z/E* mixture of 4-bromo-1-chloro-1-butene isomers. The initial S_N2 reaction with cyanide proceeds in much higher yield with (*E*)-1,3-dichloropropane.

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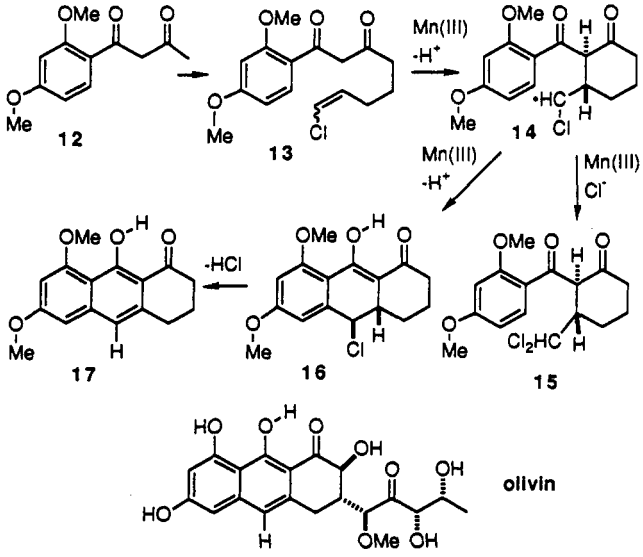
has the ring system of 8 with two hydroxy groups on the left-hand ring and additional functionality on the cyclohexanone ring. Dimethoxynaphthol 17 was chosen as the target for initial model studies since it has the oxygen functionality present in the left hand ring of olivomycin. We were concerned that the electron-rich naphthol 17 might be even more susceptible to oxidative dimerization than 8.

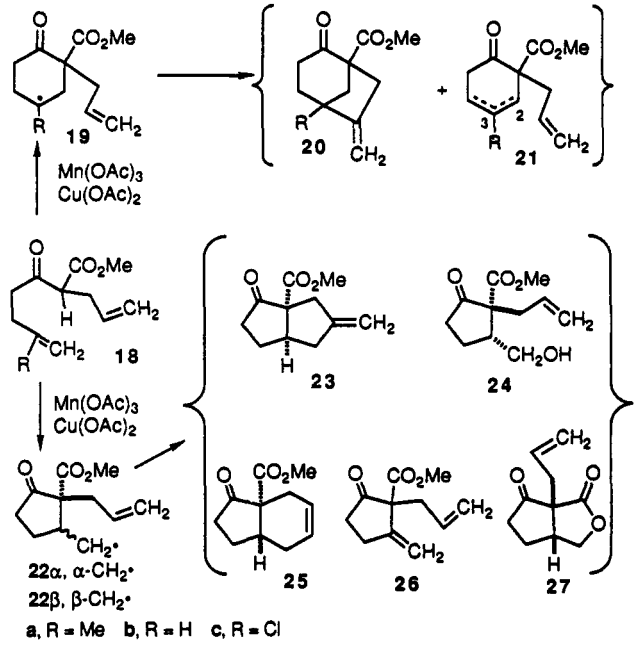


We were disappointed to find that oxidative cyclization of 13 with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ in AcOH for 8 h at 35 °C gives 20% of recovered 13, only 12% of the desired naphthol 17, 19% of dichloride 15, and 19% of dihydronaphthol 16. Oxidative cyclization of 13 gives the expected dihydronaphthol 16 that slowly loses HCl to give naphthol 17. The chloride ion liberated in the elimination that forms 17 reacts with α-chloroalkyl radical 14 to give dichloride 15.[14]

It is not clear why the analogous dichloride is not formed in the oxidation of 10. The most likely explanation is that the two methoxy groups slow down the cyclization of 14 to give 16 so that formation of the dichloride occurs at a competitive rate. Formation of 15 becomes the major process in the presence of excess chloride ion. Oxidation of 13 with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 4 equiv of LiCl[14] in AcOH for 17 h at rt provides 68% of 15. The dichloride 15 cannot be hydrolyzed to the aldehyde with $AgNO_3$ in aqueous dioxane at 50 °C.[15]

The pH of the solution affects the ratio of products in the oxidative cyclization. Oxidation of 13 with $Mn(OAc)_3 \cdot 2H_2O$ in 1:1 AcOH–TFA for 13 h at rt affords 30% of 17, and only 5% of 15 and 5% of 16. On the other hand, a similar reaction in KOAc–AcOH provides 31% of 16 and only 5% of 17 and 5% of 15. The elimination of HCl from 16 in AcOH is probably acid catalyzed since 17 is the major product in AcOH–TFA and 16 is the major product in KOAc–AcOH. Elimination of HCl from 16 can also be accomplished in high yield by treatment with K_2CO_3 in MeOH. The most efficient procedure for the preparation of naphthol 17 involves oxidative cyclization of 13 in KOAc–AcOH and treatment of the crude product with K_2CO_3 in MeOH to convert 16 to 17. This two-step procedure affords 43% of 17 from 13 suggesting that oxidative cyclization of chloroalkenes may be a viable route to aureolic acid aglycones.

Oxidative Cyclization of α-Allyl Acetoacetates 28 and 44. Oxidative cyclization of **18a** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc) \cdot H_2O$ gives **20a** in 86% isolated yield.[3i] Oxidation of **18a** by Mn(III) affords the α-keto radical, which cyclizes to the 1,1-disubstituted double bond exclusively 6-endo to give **19a**. On the other hand, oxidative cyclization of **18b** gives a complex mixture containing **20b** (55%), **21b** (5%), **23** (6%), **24** (15%), **25** (6%), **26** (1%), and **27** (12%).[3j] The α-keto radical cyclizes to the monosubstituted double bond to give a 1.7:1 mixture of cyclohexyl radical **19b** and cyclopentylmethyl radicals **22**. The cyclohexyl radical **19b** cyclizes to give **20b** after Cu(II) oxidation. 5-exo-Cyclization of the α-keto radical gives mainly **22α** that does not cyclize to give the strained trans-fused bicyclo[3.3.0]octane. 6-Endo-cyclization of **22α** gives **25**; oxidation of **22α** by Cu(II) gives **24**, **26**, and **27**. The cyclization can be directed exclusively 6-endo by placement of a chlorine on the internal carbon. Oxidative cyclization of **18c** forms exclusively **20c** in 72% yield.[3i]



The cyclization can be directed exclusively 5-exo by placement of a chlorine or methyl group on the terminal carbon of the double bond. Oxidative cyclization of **28a** gives 41% of vinylcyclopentane **34** and 6% of a 3:3:2 mixture of **30a**, **35a**, and **32a**. 5-exo-Cyclization to give **31αa** is the predominant reaction of the α-keto radical generated by oxidation of **28a**. Only 2% of **30a** resulting from 6-endo-cyclization is obtained. Oxidation of radical **31αa** by Cu(II) to give diene **34** is the major pathway since 5-exo-cyclization of **31αa** would give a highly strained trans-fused bicyclo[3.3.0]octane.[16] 6-Endo-cyclization of **31αa** to give a secondary cyclohexyl radical that is oxidized by Cu(II) to **32a** is a minor pathway. The minor radicals **31βa** and **29a** undergo the expected cyclizations to give **35a** and **30a**, respectively.

The monocyclic secondary radical **31αa** reacts very differently than the analogous monocyclic primary radical **22α** obtained from **18b**. Oxidation of primary radical **22α**

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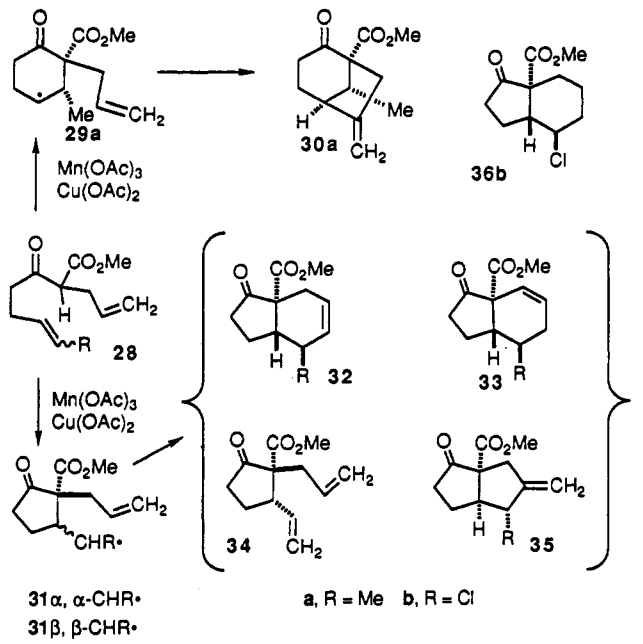
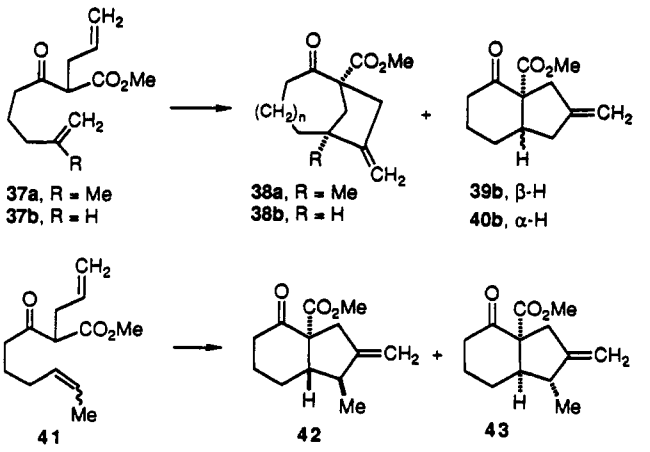


by Cu(II) gives mainly lactone **27** and alcohol **24a** in a process that involves the ester group; diene **26** is a minor product.[3j] On the other hand, oxidation of secondary radical **31αa** by Cu(II) gives only diene **34**; none of the ethylidenecyclopentane is formed.

The monocyclic α-chloroalkyl radical **31αb** reacts very differently than the monocyclic secondary radical **31αa**. Oxidative cyclization of chloroalkene **28b** gives 53% of a 1:1 inseparable mixture of hydrindanes **32b** and **33b**, 2% of a 4.4:2.5:1 mixture of a stereoisomer of **33b** and two stereoisomers of **35b**, and 3% of a ca. 1:1:1 mixture of two stereoisomers of **32b** and bicyclo[3.3.0]octane **35b**. The α-keto radical obtained from oxidation of **28b** undergoes exclusively 5-exo-cyclization and gives mainly **31αb** with the radical and the propenyl substituent trans to each other. Radical **31αb** cyclizes predominantly 6-endo to give a cyclohexyl radical that is oxidized by Cu(II) to give **32b** and **33b**, since 5-exo-cyclization would lead to a trans-fused bicyclo[3.3.0]octane[16] and Cu(II) does not oxidize the α-chloroalkyl radical.[17] The chlorine is equatorial in **32b** and **33b** to avoid a 1,3-diaxial interaction with the ester group. Hydrogenation of the mixture of **32b** and **33b** over Rh/C affords an 8:1 mixture of **36b** and the deschloro compound establishing that the alkenes are double bond position isomers.

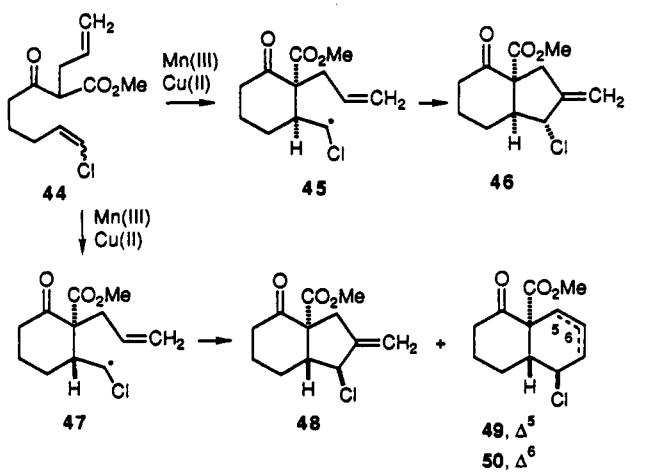
The substituents on the radical centers of **22α**, **31αa**, and **31αb** have a remarkable effect on the reactivity of the radical. Primary radical **22α** is oxidized by Cu(II) mainly to lactone **27** and alcohol **24** while secondary radical **31αa** is oxidized by Cu(II) to alkene **34**. Chloroalkyl radical **31βb** is too electron deficient to be oxidized rapidly by Cu(II).[17] Instead, it undergoes a 6-endo-cyclizaton to give **32b** and **33b** since strain prevents a 5-exo cyclization.[16]

Oxidative Cyclization of α-Allyl Acetoacetate 44. A chlorine substituent can also be used to direct the cyclizations of 6-heptenyl radicals to give exclusively 6-exo products. Oxidative cyclization of 1,1-disubstituted alkene **37a** affords 68% of **38a** from initial 7-endo-cyclization as the only product.[3k] Oxidative cyclization of the terminal alkene **37b** affords 32% of **38b** from 7-endo-cyclization and 12% of a 2:1 mixture of **39b** and **40b** from 6-exo-cyclization.[3k] The cyclization can be directed exclusively 6-exo by a terminal alkyl substituent.[3i] Oxidative cyclization of **41*Z*** affords 67% of a 25:1 mixture of **42** and **43** while **41*E*** gives 46% of a 2:1 mixture of **42** and **43**.



All the products obtained from chloroalkene **44** are formed from 6-exo-cyclization of the α-keto radical. Oxidative cyclization of **44** gives 66% of a 2:4:1:1 mixture of **46**, **48**, **49**, and **50**. The radical obtained from **44*E*** should cyclize to a 2:1 mixture of α-chloroalkyl radicals **47** and **45** since the cyclization of **41*E*** gives a 2:1 mixture of **42** and **43**.[3i,l] The radical obtained from **44*Z*** should give mainly **47**, although the selectivity should not be as high as the 25:1 ratio observed with **41*Z***[3i,l] since chlorine is smaller than an ethyl group. The observed 3:1 ratio of adducts (**48**–**50**):**46** derived from **47** and **45**, respectively, is identical to that predicted for the 2:1 *E*/*Z* mixture of **44**.

The chlorine substituent also perturbs the regioselectivity of the cyclization of α-chloroalkyl radical **47**. α-Chloroalkyl radical **45** cyclizes 5-exo, as expected, to give indanone **46** whose spectral data are analogous to those of **43**. To our surprise, α-chloroalkyl radical **47** cyclizes



both 5-exo to give indanone **48**, whose spectral data are analogous to those of **42** and 6-endo to give octalones **49** and **50**, whose spectral data are similar to those of **33b** and **32b**. On the basis of the yield data given above, 5-exo-cyclization of α-chloroalkyl radical **47** to give **48** is only twice as fast as 6-endo cyclization to give **49** and **50** while the analogous methyl substituted radical cyclizes exclusively 5-exo to give **42**.

Oxidative Cyclization of α-Benzyl Acetoacetates 51b, 55b, and 59. Oxidative free-radical cyclization of β-keto ester **51a** gives 50% of a 9:3:1 of 6-endo-cyclization product **52a** and 5-exo-cyclization products **53a** and **54a**.[3c] From this data, 6-endo-cyclization of the α-keto radical to

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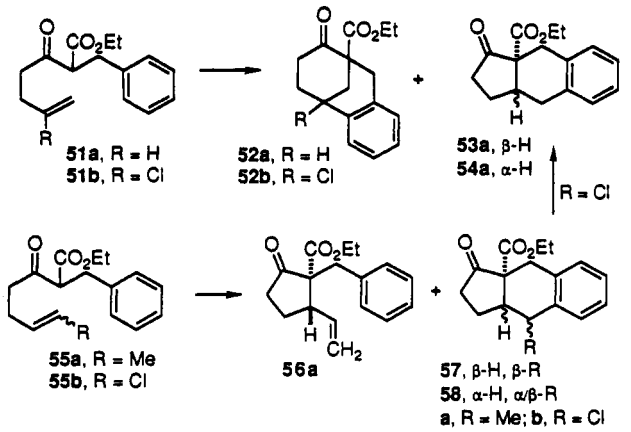
the terminal double bond is calculated to be 2.25 times faster than 5-exo cyclization.



The α-keto radical obtained from **51b**, with a chlorine substituent on the internal carbon of the double bond, undergoes exclusively 6-endo-cyclization. Oxidative cyclization of β-keto ester **51b** with $Mn(OAc)_3 \cdot 2H_2O$ gives 64% of tricyclic chloride **52b** as the only isolable product.

The α-keto radicals obtained from **55a** or **55b**, with a methyl group or chlorine on the terminal carbon of the double bond, undergo exclusively 5-exo-cyclization. Oxidative cyclization of (*E*)-**55a** with $Mn(OAc)_3 \cdot 2H_2O$ gives 9% of **56a**, 47% of **57a**, and 16% of **58a**.[31] Oxidative cyclization of **55b** gives 66% of a 5:1 mixture of trans-fused hydrindane **57b** and one of the diastereomers of cis-fused hydrindane **58b**, and 6% of the other diastereomer of **58b**. Hydrogenolysis of the 5:1 mixture over Pd/C gives a 5:1 mixture of **53a** and **54a**. Hydrogenolysis of the pure diastereomer of **58b** gives **54a**.

A chlorine substituent can also be used to direct the 6-exo-cyclization of 6-heptenyl α-keto radicals leading to anthracene derivatives. Oxidative cyclization of **59** for 28 h at 35 °C affords only traces of the expected products **60–63**. The major products are obtained from **60–63** by solvolysis to give acetate **64** (54%) and by elimination to give alkene **65** (15%). MM2 calculations suggest that solvolysis of the expected major product **60** should be much more facile than solvolysis of **57a**. The trans-fused cyclopentane of **57a** is calculated to increase the steric energy of the sp^2-hybridized benzylic cation obtained from **57a**, making ΔH for solvolysis of chloroindane **57a** 2.4 kcal/mol more endothermic than solvolysis of chlorodecalin **60**.[18]

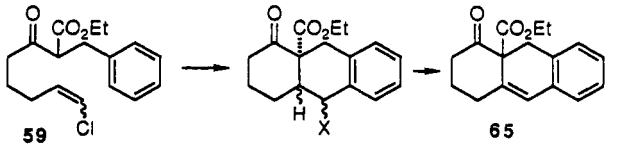
We carried out the oxidative cyclization for a shorter time at a lower temperature in an attempt to isolate **60–63**. Oxidative cyclization of **59** for 17 h at 25 °C provides 16% of **60**, 1% of **61**, 4% of **62**, 6% of **63**, 32% of **64**, and 10% of **65**. As discussed above for the cyclization of **44**, the 2:1 *E*/*Z* mixture of **49** should give a 3:1 mixture of trans- and cis-fused isomers **60–63**. The formation of significant amounts of alkene **65** and the possibility that **64** is formed by addition of acetic acid to **65** makes analysis of the stereoselectivity of the cyclization impossible.

Structure and Stereochemistry of the Cyclization Products. The gross structures of the products were established by analysis of the olefinic region in the ^1H NMR spectra. The ketone carbonyl stretch was used to establish the presence of a cyclopentanone or a cyclohexanone. The stereochemical assignments are based largely on analysis of the coupling constants. For instance, large vicinal coupling constants between the methine hydrogens indicate that the chloride is equatorial in **16** and that the benzoyl and dichloromethyl groups are equatorial in **15**.

The stereochemistry of **34** was assigned based on the absorption of the methine hydrogen at δ 2.94. The stereoisomer with the ester group cis to the hydrogen should absorb near δ 3.5.[3h,19] The chemical shifts of the olefinic protons of **30a** (δ Hz 5.10, br t, J = 2.5 Hz) and **35a** (δ 4.86, dd, J = 1.8, 3.8 Hz and δ 4.79, dd, J = 1.8, 4.1 Hz) are analogous to those of **20a** and **23**, respectively. The structure of **32a** is assigned based on absorptions at δ 5.68 (ddt, J = 4.8, 9.9, 2.1 Hz) and at δ 5.52 (ddt, J = 3.0, 9.9, 1.5 Hz) that are indicative of a cis double bond with two allylic hydrogens on one end and one on the other end.

The CHCl of **36b** absorbs at δ 4.57 (ddd, J = 5.3, 10.1, 10.1 Hz). The two large coupling constants indicate that the H is axial and the Cl equatorial. In C_6D_6, the alkene hydrogens of **32b** absorb at δ 5.60 (br d, J = 9.9 Hz) and 5.38 (ddt, J = 5.3, 9.9, 1.8 Hz) and the CHCl absorbs at δ 4.78 (br d, J = 10.0 Hz) indicating that **32b** is an allylic chloride with a cis double bond and an equatorial chloride. In C_6D_6, the alkene hydrogens of **33b** absorb at δ 6.12 (dt, J = 9.6, 2.1 Hz) and 5.22 (ddd, J = 3.8, 3.9, 9.6 Hz) and the CHCl absorbs at δ 4.88 (ddd, J = 6.6, 8.8, 11.5 Hz) indicating that **33b** is a homoallylic chloride with a cis double bond and an equatorial chloride.

The bicyclo[3.3.1]nonane structure of adduct **52b** was established based on the presence of only two benzylic hydrogen resonances at δ 3.48 and 3.15 in the ^1H NMR spectrum, the absorbtion of the ketone carbonyl carbon at δ 203.1, a value consistent with a cyclohexanone but not with a cyclopentanone,[20] and the IR absorption of the cyclohexanone at 1715 cm^{-1}. The stereochemistry of **57b** was assigned based on the doublet for the benzylic methine hydrogen at δ 5.40 (J = 10.3 Hz), which indicates that the hydrogen and adjacent ring fusion hydrogen are in a trans diaxial relationship to one another so that the chlorine must be equatorial. The coupling constants for the benzylic methine hydrogen of the cis-fused stereoisomers of **58b** of 4.8 and 2.9 Hz do not permit assignment of stereochemistry. The coupling constants between the methine hydrogens are 10.3, 9.5, and 8.8 Hz in **60**, **63**, and **64**, respectively, in which the hydrogens are trans diaxial and 4.6 and 4.5 Hz in **61** and **62**, respectively, in which the hydrogens are cis.



60, β-H, X = β-Cl
61, β-H, X = α-Cl
62, α-H, X = β-Cl
63, α-H, X = α-Cl
64, β-H, X = β-OAc

Relative Reactivity of Alkenes to Acetoacetate Radicals. The presence of the chlorine substituent on the double bond controls the regioselectivity of the reaction. However, from the cyclizations we have examined we

(18) MMX, obtained from Serena Software, 489 Serena Lane, Bloomington, IN 47401 was used on a VAX 8650. Updated versions of MODEL obtained from Prof. Midland, University of California, Riverside, and Prof. Steliou, University of Montreal, were used for structure input and analysis. NMR coupling constants were calculated using MODEL on structures minimized with MMX.

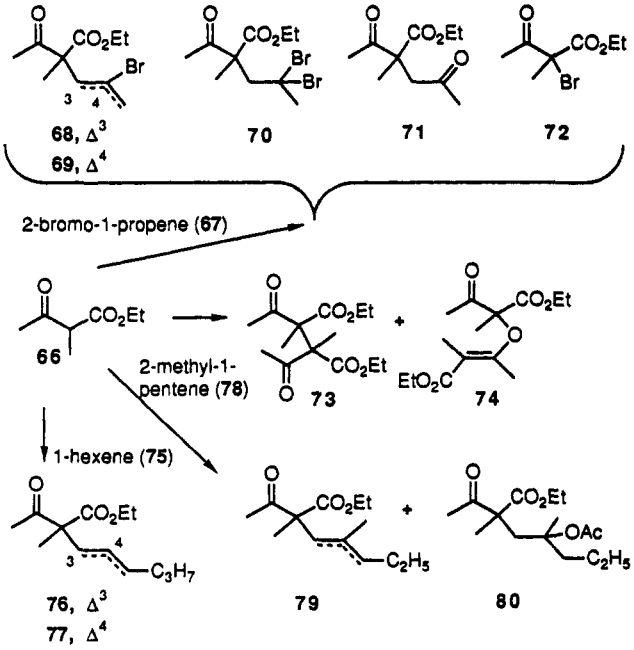
(19) Doerffel, V. K.; Kaspar, H.; Zimmerman, G. *J. Prakt. Chem.* **1974**, *316*, 645.

(20) Abraham, R. J.; Loftus, P. *Proton and Carbon-13 NMR Spectroscopy*, John Wiley & Sons: New York, 1985. Derome, A. E. *Modern NMR Techniques for Chemistry and Research*; Pergamon Press: Oxford and New York, 1987.

cannot determine whether this is due to acceleration of the pathway that gives the α-chloroalkyl radical or steric hindrance by the chlorine retarding the pathway that would give the β-chloroalkyl radical. These questions can be answered by determining the effect of a halide substituent on the rate of addition to the double bond. The rates of reactions of radicals with alkenes depend on the substituents on the radical center as well as the double bond. Although these reactions have been extensively studied,[21] there are only a few studies[22] using very electrophilic radicals bearing two carbonyl groups on the radical center and the addition of these radicals to haloalkenes has not been examined.

We have carried out intramolecular competition experiments in the oxidative cyclization of γ,γ-bis(allylic) acetoacetates.[3m] These indicate that 1,1-disubstituted alkenes are much more reactive than monosubstituted double bonds and that monosubstituted and 1,1-(chloro)alkyl disubstituted double bonds react at the same rate in 6-endo-cyclizations. These results suggest that a chlorine substituent controls the regioselectivity of α-keto radical cyclizations by sterically retarding addition of the radical to the chlorine bearing double-bond carbon.

We determined the relative rates of addition of the α-keto radical derived from ethyl 2-methylacetoacetate (**66**) to 2-bromo-1-propene (**67**), 1-hexene (**75**), and 2-methyl-1-pentene (**78**) to confirm this observation. Oxidation of



66 with $Mn(OAc)_3 \cdot 2H_2O$ and $Cu(OAc)_2 \cdot H_2O$ in the presence of 2-bromo-1-propene (**67**), which was used since simple 2-chloro-1-alkenes are inaccessible, affords 33% of a 1:3 mixture of **68*E*** and **68*Z***, 16% of **69**, 8% of **71**, 24% of **72**, and a trace of **70**, **73**, and **74**. The α-keto radical adds to **67** to give the α-bromoalkyl radical that is oxidized to **68** and **69**. Oxidation of the radical to a cation leads to ketone **71**. The bromide liberated in the formation of **71** can react with the α-keto radical to give **72** and with the α-bromoalkyl radical to give **71**. Oxidation of **66** with $Mn(OAc)_3 \cdot 2H_2O$ and LiBr in the presence of 2-bromo-1-propene (**67**) gives a 29:1 mixture of **72** and **70** as the only products.

Oxidation of **66** in the presence of 1-hexene gives 82% of a 2:1 mixture of **76** and **77**, 8% of **73**, and 7% of **74**. We have previously reported that oxidation of **66** in the absence of an alkene gives **73** and **74** while oxidation in the presence of 2-methyl-1-pentene (**78**) gives **79** as a mixture of isomers and a trace of acetate **80**.[3d]

Competition reactions were carried out by oxidation of **66** in the presence of 5 equiv of two of the three alkenes to ensure that the alkenes were present in large excess. The product mixtures were examined by capillary GC and ^1H NMR spectroscopy. We found that 2-methyl-1-pentene is about four times more reactive than 2-bromo-1-propene and 2.8 times more reactive than 1-hexene. 1-Hexene is about 1.3 times more reactive than 2-bromo-1-propene. These results indicate that a bromine substituent slightly retards the addition of the electrophilic α-keto radical to the alkene so that the selectivity observed in the cyclization reactions is probably due to steric retardation of addition to the chlorine bearing double-bond carbon. An electron-donating methyl substituent acclerates addition of the α-keto radical to the alkene by only a factor of 4, which is significantly smaller than the factor of 15 observed with the malononitrile radical.[22b]

Conclusion

The results described above indicate that a chlorine substituent on the double bond controls the regioselectivity of the radical cyclization. Substituents on the internal end of the double bond hinder exo-cyclization thereby favoring endo-cyclization. Conversely, substituents on the terminal end of the double bond hinder endo-cyclization thereby favoring exo-cyclization. The products contain chlorine that can be eliminated to introduce unsaturation as in the synthesis of naphthols **8** and **17** or reductively cleaved as in the preparation of **53a** and **54a**. We expect that use of haloalkenes will be a generally useful approach for controlling the regioselectivity of free-radical cyclizations.

Experimental Section

NMR spectra were recorded at 300 MHz in $CDCl_3$ unless otherwise indicated. Chemical shifts are reported in δ and coupling constants in Hz. ^{13}C NMR multiplicities were determined using APT or DEPT experiments. IR spectra are recorded in cm^{-1}. Analytical GC was performed on a Perkin-Elmer 8310 fitted with a flame ionization detector. A 30 m × 0.25 mm fused silica column containing RSL 150 was used at a helium flow rate of 25 mL/min. A temperature program starting at 60 °C, increasing to 150 °C at a rate of 10 °C/min, holding at 150 °C for 5 min, increasing to 190 °C at a rate of 20 °C/min, and holding at 190 °C for 8 min was used. The injector temperature was 240 °C. The detector temperature was 280 °C. Combustion analyses were performed by Spang Microanalytical Laboratory. $Mn(OAc)_3 \cdot 2H_2O$ was purchased from Aldrich. All alkylations and oxidative cyclizations were run under N_2.

Preparation of 1-Phenyl-7(*Z*)-decene-1,3-dione (1a). To a solution of LDA (6.8 mmol of diisopropylamine and 6.8 mmol of *n*-BuLi in 20 mL of THF) at 0 °C was added dropwise benzoylacetone (0.500 g, 3.1 mmol) in 10 mL of THF. The mixture was stirred for 1 h at 0 °C, and a solution of 1-bromo-3(*Z*)-hexene (0.552 g, 3.4 mmol) in 10 mL of THF was added dropwise. The mixture was stirred at 0 °C for 1 h and at rt for 16 h. Workup as described below for **4b** gave 650 mg of crude **1a**. Flash chromatography on silica gel (4:1 hexane–ether) gave 0.623 g (80%) of **1a** as a 20:1 mixture of enol and keto tautomers: ^1H NMR 7.87 (d, 2, J = 7.1), 7.42–7.52 (m, 3), 6.18 (s, 1), 5.33–5.46 (m, 2), 2.44 (t, 2, J = 7.7), 2.00–2.16 (m, 4), 1.73–1.80 (m, 2), 0.97 (t, 3, J = 7.2); ^{13}C NMR 196.8, 183.5, 135.1, 132.8, 132.3, 128.6, 127.9, 127.0, 96.1, 38.6, 26.6, 25.8, 20.6, 14.4; IR ($CDCl_3$) 1609. Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.76; H, 8.31.

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(22) (a) Giese, B.; Horler, H.; Leising, M. *Chem. Ber.* **1986**, *119*, 444. (b) Riemenschneider, K.; Bartels, H. M.; Dornow, R.; Drechsel-Grau, E.; Eichel, W.; Luthe, H.; Matter, Y. M.; Michaelis, W.; Boldt, P. *J. Org. Chem.* **1987**, *52*, 205. (c) Baciocchi, E.; Giese, B.; Farshchi, H.; Ruzziconi, R. *J. Org. Chem.* **1990**, *55*, 5688. (d) Gleicher, G. J.; Mahiou, B.; Aretakis, A. J. *J. Org. Chem.* **1989**, *54*, 308.

Preparation of (4aα,10α)-3,4,4a,10-Tetrahydro-10-ethyl-9-hydroxy-1(2*H*)-anthracenone (3a). To a solution of $Mn(OAc)_3 \cdot 2H_2O$ (219 mg, 0.82 mmol) in 4 mL of glacial acetic acid was added **1a** (0.100 g, 0.41 mmol). The mixture was stirred for 20 h at rt at which time the solution color had changed from dark brown to off-white. The reaction mixture was poured into water (100 mL), which was extracted with ether (3 × 100 mL). The combined ether layers were washed with saturated $NaHCO_3$ solution, dried ($MgSO_4$) and evaporated in vacuo to afford 96 mg (99%) of crude **3a**. Flash chromatography on silica gel (10:1 hexane–EtOAc) gave 57 mg (58%) of **3a** as a light yellow solid: mp 82–83 °C; ^1H NMR 8.01 (dd, 1, J = 7.0, 2.0), 7.49 (ddd, 1, J = 7.0, 7.0, 2.0), 7.34–7.38 (m, 2), 2.68 (ddd, 1, J = 13.5, 3.6, 3.6, H_{10}), 2.58 (ddd, 1, J = 13.5, 13.5, 5.0, H_{4a}), 2.44–2.50 (m, 2), 2.12–2.26 (m, 2), 1.88–2.06 (m, 2), 1.55–1.71 (m, 1), 1.22–1.38 (m, 1), 0.93 (t, 3, J = 7.7); ^{13}C NMR 189.0, 182.1, 143.3, 132.5, 132.3, 126.7, 126.5, 125.1, 108.2, 42.4, 34.4, 32.6, 27.7, 21.0, 18.6, 7.7; IR ($CDCl_3$) 1594. Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.16; H, 7.41.

Preparation of 1-Phenyl-7-nonyne-1,3-dione (4b). To a solution of LDA (22 mmol of diisopropylamine and 22 mmol of *n*-BuLi in 20 mL of THF) at 0 °C was added dropwise benzoylacetone (1.78 g, 11 mmol) in 5 mL of THF. The mixture was stirred for 30 min at 0 °C, at which time DMPU (2.5 mL, 22 mmol) and 5-bromo-2-pentyne[5a] (1.6 g, 11 mmol) were added. The mixture was stirred at 0 °C for 1.0 h and then warmed to 25 °C for 2.0 h. The reaction was quenched by the addition of 150 mL of water. The mixture was acidified with 40 mL of 10% HCl and extracted with 3 × 70 mL of ether. The combined organic layers were washed with 40 mL of saturated $NaHCO_3$ and 80 mL of brine and dried ($MgSO_4$). Removal of solvent in vacuo gave 2.53 g of crude product. Flash chromatography on silica gel (20:1 hexane–EtOAc) gave 1.51 g (60%) of **4b** as a 20:1 mixture of enol and keto tautomers: ^1H NMR (enol) 16.16 (s, 1), 7.88 (m, 2), 7.46 (m, 3), 6.19 (s, 1), 2.54 (t, 2, J = 7.5), 2.23 (m, 2), 1.86 (tt, 2, J = 7.5, 7.0), 1.78 (t, 3, J = 2.6); (keto) 7.40–7.90 (m, 5), 4.10 (s, 2), 2.71 (t, 2, J = 7.2), 2.15 (m, 2), 1.80 (m, 2), 1.75 (t, 3, J = 2.5); ^{13}C NMR (enol) 196.4, 183.1, 134.9, 132.2, 128.5, 126.9, 96.2, 78.0, 76.5, 38.1, 24.9, 18.3, 3.4; (keto) 133.7, 128.7, 127.1, 53.9, 42.1, 22.5, 18.0, 6 C not observed; IR (neat) 3070, 2960, 2920, 1610 (br), 1455, 1265, 760, 690. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 79.17; H, 7.18.

1-Phenyl-8-(trimethylsilyl)-7-octyne-1,3-dione (4c) was prepared as described for **4b** from LDA (4.6 mmol), benzoylacetone (472 mg, 2.3 mmol), DMPU (0.52 mL, 4.6 mmol), and 4-bromo-1-(trimethylsilyl)-1-butyne[5b] (373 mg, 2.3 mmol) in 8 mL of THF. Flash chromatography of 500 mg of 666 mg of crude product on silica gel (25:1 hexane–EtOAc) gave 236 mg (48%) of **4c** as a 20:1 mixture of enol and keto tautomers: mp 42.0–42.5 °C; ^1H NMR (enol) 16.12 (s, 1), 7.85 (m, 2), 7.46 (m, 3), 6.20 (s, 1), 2.50 (t, 2, J = 7.4), 2.34 (t, 2, J = 7.0), 1.91 (tt, 2, J = 7.4, 7.0), 0.17 (s, 9); (keto) 7.40–7.90 (m, 5), 4.11 (s, 2), 2.74 (t, 2, J = 7.0), 2.25 (t, 2, J = 6.8), 1.82 (tt, 2, J = 6.8, 7.0), 0.19 (s, 9); ^{13}C NMR (enol) 196.1, 183.1, 134.9, 132.3, 128.6, 127.0, 106.1, 96.3, 85.6, 37.9, 24.4, 19.4, 0.1; (keto) 132.2, 128.4, 127.2, 54.0, 41.9, 22.2, 19.0, 0.2, 5 C not observed; IR (neat) 2960, 2900, 2170, 1610 (br), 835, 755, 690. Anal. Calcd for $C_{17}H_{22}O_2Si$: C, 71.28; H, 7.74. Found: C, 71.21; H, 7.62.

Preparation of 3,4-Dihydro-9-hydroxy-10-(acetoxymethyl)-1(2*H*)-anthracenone (7). To a solution of $Mn(OAc)_3 \cdot 2H_2O$ (600 mg, 2.2 mmol) in 10 mL of glacial acetic acid was added **4b** (114 mg, 0.5 mmol). The mixture was stirred for 17 h at 35 °C and worked up to give 150.0 mg of crude product. Flash chromatography on silica gel (10:1 hexane–EtOAc) gave 115.0 mg (81%) of yellow crystalline **7**: mp 143.0–143.5 °C; ^1H NMR 14.68 (s, 1), 8.47 (br d, 1, J = 8.5), 7.95 (br d, 1, J = 8.5), 7.69 (ddd, 1, J = 8.5, 6.9, 1.4), 7.50 (ddd, 1, J = 8.5, 6.9, 1.0), 5.53 (s, 2), 3.18 (t, 2, J = 6.2), 2.76 (t, 2, J = 6.5), 2.15 (tt, 2, J = 6.5, 6.2), 2.07 (s, 3); ^{13}C NMR 205.4, 171.2, 164.4, 138.9, 136.7, 131.1, 125.2, 124.9, 124.1, 123.4, 117.9, 111.1, 59.4, 38.5, 26.8, 22.3, 21.0; IR (KBr) 3080, 3020, 2960, 2880, 1740, 1630, 1595, 1500, 1015, 945, 765. Anal. Calcd for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 71.72; H, 5.66.

Preparation of 3,4,3′,4′-Tetrahydro-9,9′-dihydroxy-[10,10′-bianthracene]-1,1′(2*H*,2′*H*)-dione (9). To a solution of $Mn(OAc)_3 \cdot H_2O$ (245 mg, 0.9 mmol) in 6 mL of glacial acetic acid was added **4c** (57 mg, 0.2 mmol). The reaction was stirred for 24 h at 35 °C and worked up to give 60.0 mg of crude product. Flash chromatography of 30.0 mg on silica gel (20:1 hexane–EtOAc) gave 15.0 mg (71%) of **9** as a yellow solid: mp 253 °C dec; ^1H NMR 14.52 (s, 2), 8.54 (dd, 2, J = 1.5, 8.0), 7.48 (ddd, 2, J = 1.5, 8.0, 6.9), 7.40 (ddd, 2, J = 1.5, 8.3, 6.9), 7.00 (br d, 2, J = 8.3), 2.76 (t, 4, J = 6.5), 2.53 (dt, 2, J = 16.6, 6.4), 2.44 (dt, 2, J = 16.6, 6.2), 1.97 (m, 4); ^{13}C NMR 205.6, 163.3, 137.1, 137.0, 130.9, 125.3, 125.2, 124.7, 124.2, 123.3, 111.5, 38.9, 27.7, 22.6; IR (KBr) 3080, 2950, 2880, 1630, 1595, 1500, 1415, 1380, 1350, 1335, 1315, 765; MS (m/z) 422 (100, M^+), 423 (30.2). Anal. Calcd for $C_{28}H_{22}O_4$: C, 79.60; H, 5.25. Found: C, 77.64; H, 5.85.

Reaction of **4c** (15 mg, 0.05 mmol) with $Mn(OAc)_3 \cdot 2H_2O$ (27 mg, 0.1 mmol) in a buffered solution of HOAc and KOAc (1 mL and 300 mg, 5.6:1 mole ratio) for 3 h at 25 °C gave 15.0 mg of a 7:1:2 mixture of **4c**, **8**, **9** as determined by analysis of the ^1H NMR spectrum.

8-Chloro-1-phenyl-7-octene-1,3-dione (10*E* and 10*Z*) was prepared as described for **4b** from LDA (7.5 mmol), benzoylacetone (600 mg, 3.7 mmol), DMPU (0.85 mL, 7.5 mmol), and 4-bromo-1-chloro-1-butene[6] (*E*/*Z* (2:1), 635 mg, 3.75 mmol) in 10 mL of THF. Flash chromatography of 435 mg of the 820 mg of crude product on silica gel (20:1 hexane–EtOAc) gave 284.0 mg (57%) of a 2:1 mixture of **10*E*** and **10*Z*** as a 20:1 mixture of enol and keto tautomers: ^1H NMR (*E*, enol) 16.14 (s, 1), 7.84 (m, 2), 7.45 (m, 3), 6.16 (s, 1), 6.00 (dt, 1, J = 13.2, 0.9), 5.90 (dt, 1, J = 13.2, 6.9), 2.44 (t, 2, J = 7.5), 2.15 (ddt, 2, J = 0.9, 6.9, 7.2), 1.80 (m, 2); (*E*, keto) 7.42–7.91 (m, 5), 5.72–6.18 (m, 2), 4.08 (s, 2), 2.60 (t, 2, J = 7.2), 2.06 (m, 2), 1.72 (m, 2); (*Z*, enol) 16.14 (s, 1), 7.85 (m, 2), 7.47 (m, 3), 6.19 (s, 1), 6.08 (dt, 1, J = 7.0, 1.5), 5.78 (dt, 1, J = 7.0, 7.2), 2.47 (t, 2, J = 7.5), 2.32 (ddt, 2, J = 1.5, 7.2, 6.5), 1.84 (m, 2); (*Z*, keto) 7.40–7.90 (m, 5), 5.70–6.20 (m, 2), 4.10 (s, 2), 2.62 (t, 2, J = 7.2), 2.26 (ddt, 2, J = 1.5, 7.1, 6.6), 1.73 (m, 2); ^{13}C NMR (*E*, enol) 196.1, 183.3, 134.8, 132.3, 130.6, 128.6, 127.0, 117.8, 96.2, 38.2, 30.2, 24.7; (*E*, keto) 132.5, 130.5, 128.7, 127.1, 118.9, 53.8, 42.2, 29.9, 22.4, 3 C not observed; (*Z*, enol) 196.2, 183.2, 134.9, 132.2, 130.6, 128.6, 127.0, 119.0, 96.2, 38.5, 26.5, 24.4; IR (neat) mixture: 3060, 2940, 1600 (br), 1455, 760, 690. Anal. Calcd for $C_{14}H_{15}ClO_2$: C, 67.07; H, 6.03. Found: C, 67.21; H, 5.99.

Preparation of 3,4-Dihydro-9-hydroxy-1(2*H*)-anthracenone (8). To a solution of $Mn(OAc)_3 \cdot 2H_2O$ (50 mg, 0.19 mmol) in 2 mL of glacial acetic acid was added **10*E*** and **10*Z*** (2:1, 22.5 mg, 0.09 mmol). The reaction was stirred at 35 °C for 15 h and worked up to give 21.9 mg of crude product containing **8** and a trace of **9** as determined by ^1H NMR. Flash chromatography of 20.0 mg on silica gel (20:1 hexane–EtOAc) gave 13.8 mg (79%) of **8** as a yellow solid: mp 93.0–94.0 °C (lit.[12] mp 93.5–94.0 °C); ^1H NMR 14.19 (s, 1), 8.38 (br d, 1, J = 8.3), 7.65 (br d, 1, J = 7.9), 7.59 (ddd, 1, J = 1.3, 6.6, 7.9), 7.44 (ddd, 1, J = 1.5, 6.6, 8.3), 7.05 (s, 1), 3.03 (t, 2, J = 6.2), 2.76 (t, 2, J = 6.5), 2.14 (tt, 2, J = 6.2, 6.5); ^{13}C NMR 205.1, 163.2, 138.3, 137.4, 130.3, 126.8, 125.0, 124.4, 123.8, 116.2, 111.5, 39.0, 30.2, 23.0; IR (neat) 2950, 1630, 1600, 1580, 1495, 1460, 1415, 1385, 1355, 1340, 1320, 840, 760.

Dimerization of 8. To a solution of $Mn(OAc)_3 \cdot 2H_2O$ (15.0 mg, 0.055 mmol) in 0.5 mL of glacial acetic acid was added **8** (10.6 mg, 0.05 mmol) in 0.1 mL of HOAc. The reaction was stirred at 35 °C for 24 h and worked up to give 10.5 mg of crude product. Flash chromatography gave 9.0 mg (86%) of **9**.

Preparation of 1-(2,4-Dimethoxyphenyl)-1,3-butanedione (12). To a solution of 2,4-dimethoxybenzoic acid (5.0 g, 27.0 mmol) in 20 mL of anhydrous ether was added oxalyl chloride (5.0 mL, 56.7 mmol). The solution was heated at reflux for 2 h, and the solvent was removed in vacuo to give the acid chloride (5.50 g) as a white powder. To a solution of this acid chloride in 30 mL of THF at −78 °C was added dropwise a solution of the enolate of acetone (prepared from 55.0 mmol of LDA and 55.0 mmol of acetone in 100 mL of THF at −78 °C) over 20 min. The solution was stirred at −78 °C to −60 °C for 1 h. The solvent was removed, and the residue was diluted with 200 mL of ether. The ether solution was washed with 40 mL of 10% HCl solution, 40 mL of saturated $NaHCO_3$ solution, and 40 mL of brine, dried ($MgSO_4$), and concentrated in vacuo to afford crude **12** (7.17 g). Flash chromatography (6:1 hexane–EtOAc) on silica gel gave 4.50 g (75%) of pure **12** as a 3:1 mixture of enol and keto tautomers: mp 67.0–68.0 °C (lit.[7] mp 68.0–69.0 °C); ^1H NMR (enol) 16.49 (s, 1), 7.91 (d, 1, J = 8.8), 6.55 (dd, 1, J = 8.8, 2.3), 6.46 (d, 1, J

= 2.3), 6.45 (s, 1), 3.88 (s, 3), 3.84 (s, 3), 2.16 (s, 3); ^{13}C NMR 193.5, 181.0, 163.8, 160.2, 131.8, 116.7, 105.1, 100.7, 98.5, 55.5, 55.4, 25.8; (keto) ^{1}H NMR 7.90 (d, 1, J = 8.8), 6.54 (dd, 1, J = 8.8, 2.3), 6.42 (d, 1, J = 2.3), 4.00 (s, 2), 3.85 (s, 3), 3.84 (s, 3), 2.23 (s, 3); ^{13}C NMR 203.1, 192.7, 165.2, 160.9, 133.0, 119.7, 105.7, 98.1, 58.8, 55.5, 55.3, 30.2; IR (KBr) 3010, 2960, 2850, 1610, 825, 790.

Dione **12** was also prepared in 40% yield by Seebach's procedure.[8]

8-Chloro-1-(2,4-dimethoxyphenyl)-7-octene-1,3-dione (13*E* and 13*Z*) was prepared as described for **4b** from LDA (1.2 mmol), **12** (125.0 mg, 0.56 mmol), DMPU (0.14 mL, 1.2 mmol), and 4-bromo-1-chloro-1-butene[6] (*E*/*Z* (2:1), 96.6 mg, 0.56 mmol) in 5 mL of THF. Flash chromatography (6:1 hexane–EtOAc) of the crude product on silica gel gave 118.6 mg (68%) of a 2:1 mixture of **13*E*** and **13*Z*** as a 3:1 mixture of enol and keto tautomers: mp 49.0–50.0 °C; ^{1}H NMR 16.45 (s, 1 × 0.75), 7.93 (d, 1 × 0.75, J = 8.7), 7.90 (d, 1 × 0.25, J = 8.7), 6.57 (dd, 1 × 0.75, J = 8.7, 2.4), 6.55 (dd, 1 × 0.25, J = 8.7, 2.4), 6.47 (d, 1 × 0.75, J = 2.4), 6.46 (s, enol/*E*, 1 × 0.5), 6.45 (s, enol/*Z*, 1 × 0.25, J = 2.4), 6.43 (d, 1 × 0.25, J = 2.4), 6.06–5.72 (m, 2), 4.01 (s, 2 × 0.08 keto/*Z*), 4.00 (s, 2 × 0.17 keto/*E*), 3.90 (br s, 3), 3.86 (br s, 3), 2.52 (t, 2 × 0.25, J = 7.2), 2.40 (t, 2 × 0.75, J = 7.7), 2.27–2.07 (m, 2), 1.82–1.65 (m, 2); ^{13}C NMR 204.6 (keto), 195.6 (enol), 192.9 (keto), 181.3 (enol), 165.2 (keto), 163.9 (enol), 160.9 (keto), 160.3 (enol), 133.1 (keto/*E*), 133.0 (keto/*E* + enol/*E*), 132.9 (enol/*Z*), 132.0 (enol/*E*), 130.8 (enol/*Z*), 118.7 (keto/*E*), 117.7 (enol/*Z*), 117.63 (enol/*E*), 117.57 (keto/*Z*), 116.9 (enol/*E*), 105.7 (keto/*E*), 105.6 (enol/*Z*), 105.1 (enol/*E*), 100.44 (enol/*E*), 100.37 (enol/*Z*), 98.6 (enol/*E*), 98.5 (enol/*Z*), 98.2 (keto/*E*), 58.2 (keto/*E*), 55.7 (enol/*Z*), 55.6 (enol + keto), 55.5 (enol/*E*), 55.4 (keto/*E*), 41.8 (keto/*E*), 38.5 (enol/*Z*), 38.1 (enol/*E*), 30.2 (enol/*E*), 30.0 (keto/*E*), 26.5 (enol/*Z*), 24.9 (enol/*E*), 24.5 (enol/*Z*), 22.4 (keto/*E*); IR (KBr) 2940, 1615, 1210, 825, 790. Anal. Calcd for $C_{16}H_{19}ClO_4$: C, 61.84; H, 6.16; Cl, 11.41. Found: C, 61.66; H, 6.10; Cl, 11.46.

Preparation of 15–17. To a solution of $Mn(OAc)_3{\cdot}2H_2O$ (75.0 mg, 0.27 mmol) in 4 mL of glacial acetic acid was added **13*E*** and **13*Z*** (2:1, 42.0 mg, 0.135 mmol). The reaction was stirred at 35 °C for 8 h and worked up to give 44.0 mg of crude product. Flash chromatography (12:1 hexane–EtOAc) on silica gel gave 8.4 mg (20%) of recovered **13** followed by 4.3 mg (12%) of pure **17** and 16.7 mg (38%) of a 1:1 mixture of **15** and **16**.

The data for **17**: mp 125.0–126.0 °C; ^{1}H NMR 15.25 (s, 1), 6.85 (s, 1), 6.55 (d, 1, J = 2.2), 6.42 (d, 1, J = 2.2), 3.99 (s, 3), 3.91 (s, 3), 2.95 (t, 2, J = 6.1), 2.73 (t, 2, J = 6.5), 2.09 (tt, 2, J = 6.1, 6.5); ^{13}C NMR 203.9, 166.0, 164.1, 161.2, 141.8, 139.9, 115.7, 110.8, 105.8, 98.8, 97.7, 56.1, 55.4, 38.8, 30.2, 22.8; IR (KBr) 2950, 1610, 1260, 820, 795. Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.40; H, 6.05.

Reaction of 0.05 mmol of **13** and 0.1 mmol of $Mn(OAc)_3{\cdot}2H_2O$ in 0.5 mL of HOAc and 0.5 mL of CF_3COOH at 25 °C for 13 h gave, after flash chromatography, 30% of **17** and 10% of a 1:1 mixture of **15** and **16**.

Reaction of 0.05 mmol of **13**, 0.2 mmol of LiCl, and 0.1 mmol of $Mn(OAc)_3{\cdot}2H_2O$ in 1 mL of HOAc at 25 °C for 17 h gave 68% of pure **15** after flash chromatography: ^{1}H NMR 7.97 (d, 1, J = 8.9), 6.57 (dd, 1, J = 2.3, 8.9), 6.41 (d, 1, J = 2.3), 5.99 (d, 1, J = 2.5), 4.69 (d, 1, J = 11.5), 3.86 (s, 3), 3.84 (s, 3), 3.02 (dddd, 1, J = 2.5, 3.7, 11.7, 11.5), 2.52 (m, 2), 2.45 (m, 1), 2.23 (m, 1), 1.96 (dddd, 1, J = 3.7, 13.2, 11.6, 13.4), 1.76 (m, 1); ^{13}C NMR 206.9, 194.3, 165.3, 160.8, 133.3, 117.0, 105.9, 98.6, 75.5, 65.3, 55.8, 55.6, 49.6, 41.9, 24.4, 22.8; IR (neat) 2980, 2940, 2870, 1725, 1660. Anal. Calcd for $C_{16}H_{18}Cl_2O_4$: C, 55.67; H, 5.26. Found: C, 54.97; H, 5.32.

Reaction of 0.05 mmol of **13**, 0.1 mmol $Mn(OAc)_3{\cdot}2H_2O$ and 300 mg of KOAc in 1 mL of HOAc at 25 °C for 18 h gave, after flash chromatography, 5% of **17**, 31% of **16**, and 5% of **15**. The above reaction was repeated, and the crude product was dissolved in 1 mL of MeOH containing 5 equiv of K_2CO_3. The solution was stirred at 25 °C for 3 h, worked up, and purified by flash chromatography to give 43% of pure **17**.

The data for **16**: mp 147.0–148.0 °C; ^{1}H NMR 16.42 (s, 1), 7.05 (dd, 1, J = 1.0, 2.3), 6.49 (d, 1, J = 2.3), 4.73 (dd, 1, J = 1.0, 11.6), 3.93 (s, 3), 3.91 (s, 3), 2.83 (ddd, 1, J = 11.6, 4.7, 11.8), 2.52 (m, 1), 2.45 (m, 2), 2.00 (m, 1), 1.62 (m, 1), 1.36 (m, 1); ^{13}C NMR 209.4, 168.3, 164.2, 162.0, 145.2, 138.7, 118.1, 104.1, 98.7, 64.8, 56.3, 55.6, 41.1, 31.1, 28.8, 20.2; IR (KBr) 2950, 2860, 1630. Anal. Calcd for $C_{16}H_{17}ClO_4$: C, 62.24; H, 5.55. Found: C, 61.98; H, 5.52.

Attempted Hydrolysis of 15.[15] To a solution of **15** (3.6 mg, 0.01 mmol) in 0.4 mL of dioxane and 0.2 mL of H_2O was added $AgNO_3$ (16.0 mg, 0.1 mmol). The solution was stirred at 50 °C for 14 h. Workup gave 3.6 mg of recovered **15**.

Methyl 3-oxo-2-(2-propenyl)oct-6-enoate (28a*E* and 28a*Z*) was prepared as previously described[3i] from diisopropylamine (1.79 mL, 0.013 mol), *n*-butyllithium (2.5 M in hexanes, 5.12 mL, 0.013 mol), methyl 2-allylacetoacetate (1.00 g, 0.006 mol), HMPA (2.23 mL, 0.013 mol), and crotyl bromide (a 4:1 mixture of *E* and *Z* isomers, 0.66 mL, 0.006 mol) in THF (21 mL). Purification of the crude product (1.423 g) by flash chromatography on silica gel (10:1 hexane–EtOAc) gave 0.601 g (45%) of a 4:1 mixture of **28a*E*** and **28a*Z***: ^{1}H NMR (**28a*E***) 5.73 (ddt, 1, J = 10.0, 17.0, 7.1), 5.52–5.28 (m, 2), 5.09 (br d, 1, J = 17.0), 5.04 (br d, 1, J = 10.0), 3.73 (s, 3), 3.55 (t, 1, J = 7.5), 2.68–2.48 (m, 4), 2.26 (dt, 2, J = 6.6, 7.5), 1.65–1.60 (m, 3); (**28a*Z***) 5.73 (ddt, 1, J = 10.0, 17.0, 6.9), 5.52–5.28 (m, 2), 5.09 (br d, 1, J = 17.0), 5.04 (br d, 1, J = 10.2), 3.73 (s, 3), 3.56 (t, 1, J = 7.4), 2.68–2.48 (m, 4), 2.30 (dt, 2, J = 7.2, 7.2), 1.65–1.60 (m, 3); ^{13}C NMR (**28a*E***) 204.0, 169.7, 134.2, 129.1, 126.4, 117.4, 58.4, 52.4, 42.0, 32.2, 26.3, 17.8; IR (neat) 3080, 1745, 1715, 1640. Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 7.93. Found: C, 68.60; H, 7.74.

Oxidative cyclization of 28a*E* and 28a*Z* (301 mg of a 4:1 mixture, 1.43 mmol) with $Mn(OAc)_3{\cdot}2H_2O$ (768 mg, 2.86 mmol) and $Cu(OAc)_2{\cdot}H_2O$ (286 mg, 1.43 mmol) in glacial acetic acid (17 mL) for 11.5 h at rt followed by normal workup gave 269 mg of crude product. Flash chromatography of 252 mg (10:1 hexane–EtOAc) on silica gel gave 116 mg (41%) of methyl 5β-ethenyl-3-oxo-1α-(2-propenyl)cyclopentane-1β-carboxylate (**34**), followed by 18 mg (6%) of a complex mixture of 13 products, containing **30a**, **35a**, and **32a** as the major constituents in a 1.6:1.6:1 ratio.

The data for **34**: ^{1}H NMR 5.69 (ddd, 1, J = 7.5, 10.2, 17.6), 5.59 (dddd, 1, J = 5.8, 8.9, 10.0, 17.0), 5.19–5.10 (m, 4), 3.67 (s, 3), 2.94 (br dt, 1, J = 7.5, 8.4), 2.73 (ddt, 1, J = 5.8, 14.2, 1.4), 2.65–2.56 (m, 1), 2.52 (dd, 1, J = 8.9, 14.2), 2.32–2.02 (m, 3); ^{13}C NMR 214.2 (CO), 170.2 (CO_2), 135.8 (CH), 132.7 (CH), 120.0 (CH_2), 117.4 (CH_2), 62.8 (C), 52.0 (CH_3), 45.7 (CH), 38.6 (CH_2), 35.6 (CH_2), 25.6 (CH_2). Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.75. Found: C, 69.40; H, 7.74.

Partial spectral data of the minor components were determined from the mixture: ^{1}H NMR (**30a**) 5.10 (br t, 1, J = 2.5), 3.71 (s, 3), 1.13 (d, 3, J = 6.8), (**35a**) 4.86 (dd, 1, J = 1.8, 3.8), 4.79 (dd, 1, J = 1.8, 4.1), 3.74 (s, 3), 1.15 (d, 3, J = 6.3); (**32a**) 5.68 (ddt, 1, J = 4.8, 9.9, 2.1), 5.52 (ddt, 1, J = 3.0, 9.9, 1.5), 3.67 (s, 3), 1.06 (d, 3, J = 6.9).

Preparation of Methyl 7-Chloro-3-oxo-2-(2-propenyl)-hept-6-enoate (28b*Z* and 28b*E*). Methyl 7-chloro-3-oxohept-6-enoate[3f] (0.495 g of a 2:1 mixture of *Z* and *E* isomers, 0.003 mol) in THF (2 mL) was added dropwise to a stirred suspension of NaH (0.108 g of a 60% dispersion in mineral oil, 0.003 mol) in THF (20 mL). After hydrogen evolution had ceased, the mixture was heated to reflux and allyl bromide (0.22 mL, 0.003 mol) was added over a period of 5 min. The resulting mixture was refluxed for 24 h, cooled to rt and poured into 200 mL of water. The aqueous solution was acidified with 10% HCl and extracted with ether (3 × 25 mL). The organic layers were combined, washed with saturated $NaHCO_3$ solution, and dried over $MgSO_4$. Removal of the solvent in vacuo gave 0.631 g of crude product. Flash chromatography of 0.631 g (9:1 hexane–EtOAc) on silica gel gave 0.301 g (50%) of a 2:1 mixture of **28b*Z*** and **28b*E***: ^{1}H NMR (**28b*Z***) 6.04 (dt, 1, J = 7.0, 1.3), 5.77 (q, 1, J = 7.0), 5.80–5.65 (m, 1), 5.09 (br d, 1, J = 16.4), 5.05 (br d, 1, J = 9.6), 3.72 (s, 3), 3.57 (t, 1, J = 7.5), 2.77–2.55 (m, 4), 2.50 (br dt, 2, J = 7.0, 7.5); (**28b*E***) 6.00 (dt, 1, J = 13.3, 1.3), 5.85 (dt, 1, J = 13.3, 6.9), 5.80–5.65 (m, 1), 5.09 (br d, 1, J = 16.4), 5.05 (br d, 1, J = 9.6), 3.72 (s, 3), 3.55 (t, 1, J = 7.4), 2.77–2.55 (m, 4), 2.34 (dq, 2, J = 1.3, 7.0); ^{13}C NMR (**28b*Z***) 203.4, 169.5, 134.0, 129.6, 119.2, 117.6, 58.1, 52.4, 40.5, 32.2, 20.9; (**28b*E***) 203.0, 169.4, 134.0, 131.6, 118.4, 117.6, 58.3, 52.4, 41.1, 32.1, 24.6; IR (neat) 3080, 1749, 1715, 1641. Anal. Calcd for $C_{11}H_{15}ClO_3$: C, 57.27; H, 6.55. Found: C, 57.44; H. 6.32.

Oxidative cyclization of 28b*Z* and 28a*E* (400 mg of a 2:1 mixture, 1.73 mmol) with $Mn(OAc)_3{\cdot}2H_2O$ (930 mg, 3.47 mmol) and $Cu(OAc)_2{\cdot}H_2O$ (346 mg, 1.73 mmol) in glacial acetic acid (17 mL) for 20 h at rt followed by normal workup gave 405 mg of crude product. Flash chromatography of 400 mg (10:1 hexane–EtOAc)

on silica gel gave 208 mg (53%) of a 1.1:1 mixture of **32b** and **33b** (53%), followed by 7 mg of a complex mixture of products containing a 4.4:2.5:1 ratio of one stereoisomer of **33b** and two stereoisomers of **35b**, followed by 12 mg of a complex mixture of containing a 1.4:1.1:1 ratio of two stereoisomers of **32b** and **35b**.

The data for **32b** and **33b**: ^{1}H NMR (C_6D_6) (**33b**) 6.12 (br dt, 1, J = 9.6, 2.1), 5.22 (ddd, 1, J = 3.8, 3.9, 9.6), 4.88 (ddd, 1, J = 6.6, 8.8, 11.5), 3.04 (s, 3), 2.52 (dddd, 1, J = 2.1, 3.9, 6.6, 18.6), 2.27–1.65 (m, 6); (**32b**) 5.60 (br d, 1, J = 9.9), 5.38 (ddt, 1, J = 5.3, 9.9, 1.8), 4.78 (br d, 1, J = 10.0), 3.02 (s, 3), 2.72 (dddd, 1, J = 5.3, 17.6, 1.6, 1.6), 2.27–1.65 (m, 6); ^{13}C NMR 210.9 (CO), 207.6 (CO), 168.6 (CO_2), 168.4 (CO_2), 130.4 (CH), 130.1 (CH), 127.8 (CH), 123.3 (CH), 63.1 (C), 60.6 (C), 58.2 (CH), 55.4 (CH), 52.9 (CH), 52.7 (CH), 51.4 (CH_3), 51.1 (CH_3), 38.4 (CH_2), 37.3 (CH_2), 36.8 (CH_2), 30.4 (CH_2), 23.0 (CH_2), 22.5 (CH_2); IR (neat) 3039, 1760, 1730, 1637. Anal. Calcd for $C_{11}H_{13}ClO_3$: C, 57.77; H, 5.73. Found: C, 57.68; H, 5.85. C_6D_6 was used for the ^{1}H NMR spectrum since the downfield peaks overlapped in $CDCl_3$.

Partial data for the minor components were determined from the mixture. ^{1}H NMR (isomer of **33b**) 5.85 (ddt, 1, J = 4.7, 10.4, 1.6), 5.78 (br d, 1, J = 10.4), 4.88–4.82 (m, 1), 3.68 (s, 3); (isomer of **35b**) 5.29 (br s, 1), 5.12 (dd, 1, J = 1.5, 3.8), 4.88–4.77 (m, 1), 3.74 (s, 3); (isomer of **33b**) 5.43 (br s, 1), 5.29 (br s, 1), 4.88–4.77 (m, 1), 3.73 (s, 3); (**35b**) 5.30 (br s, 1), 5.13 (br s, 1), 4.38 (br s, 1), 3.76 (s, 3), 3.57 (br d, 1, J = 18.3), 3.38 (dt, 1, J = 2.9, 9.2); (isomer of **32b**) 6.22 (dt, 1, J = 9.6, 1.9), 5.77 (dt, 1, J = 9.6, 3.6), 4.60 (dd, 1, J = 1.9, 5.8), 3.66 (s, 3); (isomer of **32b**) 6.06 (br ddd, 1, J = 2.4, 5.3, 10.1), 5.89 (br dt, 1, J = 10.1, 4.3), 4.76–4.73 (m, 1), 3.72 (s, 3).

Hydrogenation of 32b and 33b. A solution of **32b** and **33b** (0.025 g, 0.15 mmol and 5% Rh on carbon (approximately 0.02 g) in ether (5 mL) was stirred under a hydrogen atmosphere for 2 h. Filtration and removal of the solvent in vacuo gave 0.023 g of an inseparable 8:1 mixture of **36b** and the deschloro compound: ^{1}H NMR 4.57 (ddd, 1, J = 5.3, 10.1, 10.1), 3.70 (s, 3), 2.61–2.48 (m, 1), 2.40–2.09 (m, 5), 1.87–1.78 (m, 2), 1.59–1.50 (m, 2), 1.30 (ddd, 1, J = 4.8, 10.1, 14.4); ^{13}C NMR 168.8, 58.6 (CH), 54.1 (CH), 52.6 (CH_3), 37.4 (CH_2), 36.2 (CH_2), 29.6 (CH_2), 23.1 (CH_2), 22.9 (CH_2), 1 C not observed.

Methyl 8-chloro-3-oxo-2-(2-propenyl)-7-octenoate (44*E* and 44*Z*) was prepared as previously described[3i] from LDA (4 mmol), methyl 2-allylacetoacetate (312 mg, 2 mmol), DMPU (0.47 mL, 4 mmol), and 4-bromo-1-chloro-1-butene[6] (*E*/*Z* (2:1), 339 mg, 2 mmol) in 8 mL of THF. The reaction gave 490 mg of crude product. Flash chromatography on silica gel (25:1 hexane–EtOAc) gave 196.0 mg (40%) of a 2:1 mixture of **44*E*** and **44*Z***: ^{1}H NMR (**44*E***) 5.96 (br d, 1, J = 13.2), 5.85 (dt, 1, J = 13.2, 6.8), 5.72 (m, 1), 5.10 (br d, 1, J = 16.5), 5.05 (br d, 1, J = 9.5), 3.73 (s, 3), 3.54 (t, 1, J = 7.3), 2.20–2.70 (m, 6), 1.72 (m, 2); (**44*Z***) 6.03 (dt, 1, J = 7.0, 1.2), 5.75 (dt, 1, J = 7.0, 7.0), 5.70 (m, 1), 5.10 (br d, 1, J = 16.5), 5.05 (br d, 1, J = 9.5), 3.73 (s, 3), 3.55 (t, 1, J = 7.3), 2.21–2.77 (m, 6), 2.06 (m, 2); ^{13}C NMR (**44*E***) 203.9, 169.6, 134.1, 132.8, 117.7, 117.52, 58.26, 52.38, 41.0, 32.2, 29.8, 22.3; (**44*Z***) 204.1, 169.7, 134.2, 132.8, 117.6, 117.48, 58.31, 52.44, 41.1, 32.1, 29.8, 23.3; IR (neat) 1745, 1715. Anal. Calcd for $C_{12}H_{17}ClO_3$: C, 58.90; H, 7.00. Found: C, 59.09; H, 7.09.

Oxidative Cyclization of 44*E* and 44*Z*. To a solution of $Mn(OAc)_3{\cdot}2H_2O$ (143 mg, 0.53 mmol), $Cu(OAc)_2{\cdot}H_2O$ (53 mg, 0.265 mmol) in 4 mL of glacial acetic acid was added **44*E*** and **44*Z*** (2:1, 65.0 mg, 0.265 mmol). The reaction was stirred at 25 °C for 12 h. Normal workup gave 65.0 mg of a 4:1:1:2.5 mixture of **48**, **49**, **50**, and **46**. Flash chromatography of 60.0 mg on silica gel (50:1 hexane–EtOAc) gave 4.7 mg of a 4:2:1 mixture of **48** (4.5%), **49** (2.2%), and **50** (1.1%) followed by 4.4 mg of a 5:2:1:1 mixture of **48** (4.1%), **49** (1.6%), **50** (0.8%), and **46** (0.8%), 4.9 mg of a 6:3:2:2.5 mixture of **48** (3.6%), **49** (1.8%), **50** (1.2%), and **46** (1.5%), 6.4 mg of a 2.5:1:1:1 mixture of **48** (4.8%), **49** (1.9%), **50** (1.9%), and **46** (1.9%), 7.7 mg of a 4:1:2 mixture of **48** (7.9%), **50** (2.0%), and **46** (4.0%), and 8.9 mg of a 3:1:8 mixture of **48** (3.7%), **50** (1.2%), and **46** (9.9%): (first three column fractions) IR (neat) 1720 (br). Anal. Calcd for $C_{12}H_{15}ClO_3$: C, 59.39; H, 6.23. Found: C, 59.30; H, 6.30.

The data for **46** were determined from the mixture: ^{1}H NMR 5.34 (dt, 1, J = 2.4, 2.4), 5.21 (dt, 1, J = 2.4, 2.4), 4.25 (ddt, 1, J = 10.7, 1.8, 2.4), 3.75 (s, 3), 3.39 (br d, 1, J = 17.1), 3.09 (m, 1), 2.71 (br d, 1, J = 17.1), 2.45–2.53 (m, 2), 1.90–2.20 (m, 4); ^{13}C NMR 205.1, 171.1, 145.8, 112.3, 61.3, 60.1, 54.6, 53.0, 40.0, 35.3, 22.6, 22.5.

The data for **48** were determined from the mixture: ^{1}H NMR 5.42 (br s, 1), 5.28 (br s, 1), 5.04 (br d, 1, J = 10.8), 3.72 (s, 3), 3.06 (br d, 1, J = 17.4), 2.58 (br d, 1, J = 17.4), 2.47 (m, 2), 2.12 (m, 2), 1.92 (m, 2), 1.70 (m, 1); ^{13}C NMR 203.6, 170.9, 146.3, 113.6, 64.0, 61.1, 58.9, 52.6, 39.7, 35.3, 26.2, 22.5.

The data for **49** were determined from the mixture: ^{1}H NMR 6.12 (br dt, 1, J = 9.5, 2.2), 5.76 (ddd, 1, J = 3.3, 4.0, 9.6), 4.85 (ddd, 1, J = 11.9, 6.6, 8.7), 3.71 (s, 3), 2.97 (dddd, 1, J = 2.0, 4.0, 6.6, 18.7), 1.65–2.30 (m, 8); ^{13}C NMR 130.4, 123.3, 55.4, 53.0, 51.4, 38.5, 37.4, 22.7, 22.6; 3 C not observed.

The data for **50** was determined from the mixture: ^{1}H NMR 5.81 (ddt, 1, J = 4.7, 9.8, 1.6), 5.77 (br d, 1, J = 9.9), 4.85 (br d, 1, J = 10.0), 3.69 (s, 3), 2.81 (br dd, 1, J = 18.3, 4.7), 1.60–2.40 (m, 8); ^{13}C NMR 130.2, 127.8, 58.2, 52.7, 51.1, 36.8, 30.5, 23.1, 22.4; 3 C not observed.

Ethyl 2-benzyl-6-chloro-3-oxohept-6-enoate (51b) was prepared as described earlier[3i] from diisopropylamine (1.91 mL, 0.014 mol), *n*-butyllithium (2.6 M in hexanes, 5.45 mL, 0.014 mol) ethyl 2-benzylacetoacetate (1.45 mL, 0.007 mol), DMPU (1.65 mL, 0.014 mol), and 2,3-dichloropropane (0.63 mL, 0.007 mol) in THF (20 mL). Purification of 1.877 g of crude product by flash chromatography (9:1 hexane–EtOAc) on silica gel gave 0.706 g (35%) of **51b**: ^{1}H NMR 7.31–7.14 (m, 5), 5.11 (br s, 2), 4.15 (q, 2, J = 7.0), 3.80 (t, 1, J = 7.8), 3.17 (d, 2, J = 7.8), 2.92–2.78 (m, 1), 2.64–2.50 (m, 3), 1.21 (t, 3, J = 7.0); ^{13}C NMR 202.9, 168.8, 140.8, 138.0, 128.7 (2), 128.6 (2), 126.7, 113.2, 61.6, 60.6, 40.4, 33.9, 32.8, 14.0; IR (neat) 1742, 1711, 1633, 1599, 1580, 1490. Anal. Calcd for $C_{16}H_{19}ClO_3$: C, 65.19; H, 6.50. Found: C, 64.94; H, 6.33.

Preparation of Ethyl 6,7-Benzo-5-chloro-2-oxobicyclo-[3.3.1]nonane-1-carboxylate (52b). To a stirred solution of $Mn(OAc)_3{\cdot}2H_2O$ (473 mg, 1.76 mmol) in 8 mL of glacial acetic acid was added *β*-keto ester **51b** (260 mg, 0.88 mmol) in 3 mL of glacial acetic acid. The reaction mixture was stirred at rt for 20 h and worked up to give 275 mg of crude product. Purification of 228 mg by flash chromatography (9:1 hexane–EtOAc) on silica gel gave 135 mg (64%) of **52b**: ^{1}H NMR 7.82 (dd, 1, J = 1.8, 7.8), 7.36–7.26 (m, 2), 7.16 (br d, 1, J = 7.0), 4.19 (q, 2, J = 7.3), 3.48 (d, 1, J = 18.3), 3.15 (dd, 1, J = 2.0, 18.3), 3.13 (dd, 1, J = 2.0, 12.5), 2.68 (ddd, 1, J = 5.5, 13.0, 13.8), 2.66 (dd, 1, J = 3.7, 12.5), 2.48–2.28 (m, 2), 2.00 (ddd, 1, J = 6.9, 13.1, 16.4), 1.23 (t, 3, J = 7.3); ^{13}C NMR 203.1, 170.6, 137.6, 133.0, 128.5, 128.3, 127.5, 127.2, 67.4, 61.7, 58.6, 44.5, 44.1, 38.0, 35.5, 14.1; IR (neat) 1735, 1715. Anal. Calcd for $C_{16}H_{17}ClO_3$: C, 65.64; H, 5.85. Found: C, 65.60; H, 5.64.

Ethyl 2-benzyl-7-chloro-3-oxohept-7-enoate (55b*Z* and 55b*E*) was prepared as described earlier[3i] from diisopropylamine (1.91 mL, 0.014 mol), *n*-butyllithium (2.6 M in hexanes, 5.45 mL, 0.014 mol), ethyl 2-benzylacetoacetate (1.45 mL, 0.007 mol), DMPU (1.65 mL, 0.014 mol), and 1,3-dichloropropene (a 2:1 mixture of *Z* and *E* isomers, 0.756 g, 0.007 mol) in THF (20 mL). Purification of 1.983 g of the 2.011 g of crude product by flash chromatography (9:1 hexane–EtOAc) on silica gel gave 0.793 g (40%) of a 2:1 mixture of **55b*Z*** and **55b*E***: ^{1}H NMR (*Z*) 7.31–7.14 (m, 5), 5.93 (dt, 1, J = 13.2, 1.7), 5.74 (dt, 1, J = 13.2, 7.5), 4.40 (q, 2, J = 7.3), 3.77 (t, 1, J = 7.4), 3.16 (d, 2, J = 7.4), 2.48–2.36 (m, 2), 2.36–2.22 (m, 2), 1.21 (t, 3, J = 7.3); (*E*) 7.31–7.14 (m, 5), 5.99 (dt, 1, J = 7.7, 1.4), 5.67 (dt, 1, J = 7.7, 7.5), 4.39 (q, 2, J = 7.3), 3.78 (t, 1, J = 7.4), 3.16 (d, 2, J = 7.4, 2.76–2.60 (m, 2), 2.48–2.36 (m, 2), 1.20 (t, 3, J = 7.3); ^{13}C NMR (*Z*) 203.3, 168.8, 137.9, 131.6, 128.8 (2), 128.5 (2), 126.7, 118.3, 61.5, 60.4, 41.8, 34.0, 20.9, 14.0; (*E*) 203.6, 168.9, 138.0, 129.6, 128.7 (2), 128.5 (2), 126.6, 119.2, 61.5, 60.3, 41.2, 34.0, 24.4, 14.0; IR (neat) 1742, 1715, 1632, 1606, 1498. Anal. Calcd for $C_{16}H_{19}ClO_3$: C, 65.19; H, 6.50. Found: C, 65.01; H, 6.45.

Oxidative free-radical cyclization of 55b as described previously with $Mn(OAc)_3{\cdot}2H_2O$ (570 mg, 2.13 mmol) and **55b*Z*** and **55b*E*** (313 mg of a 2:1 mixture, 1.06 mmol) in glacial acetic acid (13 mL) for 20 h at rt gave 318 mg of crude product. Flash chromatography of 278 mg (9:1 hexane–EtOAc) on silica gel gave 184 mg (66%) of a 4.9:1 mixture of **57b** and one diastereomer of **58b**, followed by 15.3 mg (6%) of the other diastereomer of **58b**.

The data for **57b** were determined from the mixture: ^{1}H NMR 7.65 (dd, 1, J = 2.5, 7.2), 7.29–7.13 (m, 3), 5.40 (d, 1, J = 10.3), 4.04 (q, 2, J = 7.0), 3.45 (d, 1, J = 16.9), 2.88 (d, 1, J = 16.9), 2.75

(ddd, 1, J = 7.3, 10.4, 16.2), 2.57–2.24 (m, 4), 1.10 (t, 3, J = 7.0); ^{13}C NMR 211.2, 168.0, 136.1, 134.7, 129.5, 129.3, 128.2, 126.7, 61.7 (CH_2), 60.8 (C), 60.6 (CH), 51.9 (CH), 37.2 (CH_2), 34.8 (CH_2), 23.7 (CH_2), 13.8 (CH_3); IR (neat) 3070, 1755, 1725, 1600, 1572. Anal. Calcd for $C_{16}H_{17}ClO_3$: C, 65.64; H, 5.85. Found: C, 65.75; H, 5.72.

The data for the less polar diastereomer of **58b** were determined from the mixture: ^{1}H NMR 7.45 (dd, 1, J = 4.2, 5.7), 7.29–7.12 (m, 3), 5.25 (d, 1, J = 4.8), 4.17 (q, 2, J = 7.0), 3.46–3.38 (m, 1, H_5), 3.32 (d, 1, J = 15.9), 3.22 (d, 1, J = 15.9), 2.57–2.24 (m, 4), 1.26 (t, 3, J = 7.0); ^{13}C NMR 135.4, 128.7, 128.3, 127.0, 126.3, 62.0 (CH), 60.6 (CH_2), 47.4 (CH), 37.4 (CH_2), 31.5 (CH_2), 22.6 (CH_2), 14.0 (CH_3), 4 C not observed.

The data for the less polar diastereomer of **58b**: ^{1}H NMR 7.32 (m, 4), 5.04 (d, 1, J = 2.9), 4.23 (q, 2, J = 7.1), 3.74 (ddd, 1, J = 2.9, 8.6, 9.0, H_5), 3.69 (d, 1, J = 15.8), 3.18 (d, 1, J = 15.8), 2.52 (ddd, 1, J = 9.6, 11.2, 17.4, H_3), 2.28 (dddd, 1, J = 3.4, 8.6, 9.6, 12.7, H_4), 2.08 (ddd, 1, J = 3.4, 8.6, 17.4, H_3), 1.27 (t, 3, J = 7.1), 1.19 (dddd, 1, J = 8.6, 9.0, 11.2, 12.7, H_4); ^{13}C NMR 213.1 (CO), 170.9 (CO_2), 134.7 (C), 134.5 (C), 129.4 (CH), 129.0 (CH), 128.2 (CH), 127.1 (CH), 62.1 (CH_2), 60.4 (CH), 48.9 (CH), 37.8 (CH_2), 30.8 (CH_2), 25.4 (CH_2), 14.0 (CH_3); IR (neat) 1750, 1717.

Hydrogenation of 57b and the Less Polar Diastereomer of 58b. A mixture of 10% Pd on carbon (approximately 0.02 g) in ether (5 mL) was charged with hydrogen for 5 min, and **57b** and **58b** (0.029 g of a 4.9:1 mixture) were added as a solution in ether (1 mL). The system was charged with hydrogen for an additional 2 min, fitted with a hydrogen reservoir, and stirred for 2 h. The mixture was filtered through Celite and the solvent removed in vacuo to give 0.031 g of a 4.9:1 mixture of **53a** and **54a**.

The data for **53a** were determined from the mixture: ^{1}H NMR 7.22–7.08 (m, 4), 4.07 (q, 2, J = 7.0), 3.42 (d, 1, J = 16.5), 3.08–2.88 (m, 2), 2.86–2.61 (m, 2), 2.49–2.15 (m, 4), 1.12 (t, 3, J = 7.0); ^{13}C NMR 213.5, 169.1, 135.2, 134.9, 129.7, 129.2, 128.2, 125.7, 61.1 (CH_2), 44.4 (CH), 37.9 (CH_2), 34.4 (CH_2), 32.4 (CH_2), 25.1 (CH_2), 14.1 (CH_3); IR (neat) 1755, 1730.

Hydrogenation of the more polar diastereomer 58b (0.005 g) was carried out analogously with 10% Pd on carbon (approx. 0.02 g) in ether (5 mL) to give a quantitative yield of **54a**: ^{1}H NMR 7.12 (br s, 4), 4.16 (q, 2, J = 7.7), 3.21–3.10 (m, 1, H_5), 3.19 (d, 1, J = 14.9), 3.00 (d, 1, J = 14.9), 2.94 (dd, 1, J = 5.8, 14.9), 2.63 (dd, 1, J = 4.8, 14.9), 2.47 (dt, 1, J = 17.4, 9.1), 2.29–2.18 (m, 1), 2.06 (ddd, 1, J = 4.8, 8.7, 17.4), 1.43 (dddd, 1, J = 7.2, 9, 9, 13), 1.24 (t, 3, J = 7.7); IR (neat) 1755, 1735.

Ethyl 2-benzyl-8-chloro-3-oxo-7-octenoate (59*E* and *59Z*) was prepared as previously described[3i] from LDA (3 mmol), ethyl 2-benzylacetoacetate (0.227 mL, 1.5 mmol), DMPU (0.35 mL, 3 mmol), and 4-bromo-1-chloro-1-butene[6] (E/Z (2:1); 255 mg, 1.5 mmol) in 4 mL of THF. Flash chromatography of 456 mg of crude product on silica gel (20:1 hexane–EtOAc) gave 190.0 mg (41%) of a 2:1 mixture of **59*E*** and **59*Z***: ^{1}H NMR (*E*) 7.20 (m, 5), 5.87 (br d, 1, J = 13.5), 5.77 (dt, 1, J = 13.5, 6.8), 4.15 (q, 2, J = 7.1), 3.78 (t, 1, J = 7.7), 3.16 (d, 2, J = 7.7), 2.54 (dt, 1, J = 17.7, 7.0), 2.30 (dt, 1, J = 17.7, 7.0), 1.97 (dt, 2, J = 6.8, 7.3), 1.61 (m, 2), 1.21 (t, 3, J = 7.1); (*Z*) 7.20 (m, 5), 6.03 (dt, 1, J = 7.1, 1.4), 5.65 (dt, 1, J = 7.1, 7.0), 4.16 (q, 2, J = 7.1), 3.77 (t, 1, J = 7.7), 3.16 (d, 2, J = 7.7), 2.65 (dt, 1, J = 17.7, 7.0), 2.37 (dt, 1, J = 17.7, 7.0), 2.15 (ddt, 2, J = 1.4, 7.0, 7.3), 1.62 (m, 2), 1.21 (t, 3, J = 7.1); ^{13}C NMR (*E*) 204.2, 169.0, 138.1, 132.8, 128.8, 128.5, 126.7, 117.7, 61.5, 60.5, 41.7, 34.1, 29.8, 22.2, 14.0; (*Z*) 203.3, 168.8, 137.9, 130.6, 128.8, 128.5, 126.7, 118.4, 61.5, 60.6, 41.8, 34.1, 29.8, 24.5, 14.0; IR (neat) 1745, 1715, 795, 695. Anal. Calcd for $C_{17}H_{21}ClO_3$: C, 66.12; H, 6.85. Found: C, 66.21; H, 6.74.

Oxidative Cyclization of 59*E* and 59*Z*. To a solution of $Mn(OAc)_3 \cdot 2H_2O$ (91 mg, 0.336 mmol) in 4 mL of glacial acetic acid was added **59*E*** and **59*Z*** (2:1, 52.0 mg, 0.168 mmol). The reaction was stirred for 28 h at 35 °C and worked up to give 55.0 mg of crude product. Flash chromatography of 44.8 mg on silica gel (30:1 hexane–EtOAc) gave 6.6 mg (15%) of **65**, followed by 28.0 mg (54%) of **64**. Traces of **60**–**63** were observed in the ^{1}H NMR spectrum of the crude product.

The data for **64**: ^{1}H NMR 7.13 (m, 4), 6.67 (d, 1, J = 8.8), 4.09 (q, 2, J = 7.1), 3.27 (d, 1, J = 17.3), 3.21 (d, 1, J = 17.3), 2.56 (m, 2), 2.16 (s, 3), 2.04–2.19 (m, 3), 1.89 (m, 1), 1.70 (m, 1), 1.06 (t, 3, J = 7.1); ^{13}C NMR 205.2, 171.3, 169.3, 134.2, 133.6, 128.8, 127.9, 127.7, 126.9, 73.6, 61.82, 61.76, 48.7, 40.0, 34.9, 25.8, 25.1, 21.5, 14.0; IR (neat) 1730 (br). Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.58; H, 6.29.

The data for **65**: ^{1}H NMR 7.00–7.20 (m, 4), 6.43 (br s, 1), 4.06 (q, 2, J = 7.1), 3.45 (d, 1, J = 17.0), 3.16 (d, 1, J = 17.0), 2.81 (m, 2), 2.62 (m, 2), 2.12 (m, 1), 1.70 (m, 1), 1.13 (t, 3, J = 7.1); ^{13}C NMR 205.0, 171.6, 137.2, 132.7, 132.3, 127.6, 127.3, 126.7, 125.9, 125.8, 61.8, 61.2, 40.2, 33.4, 31.8, 23.6, 13.9; IR (neat) 1760, 1720, 750; MS (m/z) 270 (17.2, M^+), 197 (100, M-CO_2Et).

Reaction of **59*E*** and **59*Z*** (2:1, 92.5 mg, 0.3 mmol) with $Mn(OAc)_3 \cdot 2H_2O$ (160 mg, 0.6 mmol) at for 17 h at 25 °C followed by normal workup gave 95.0 mg of crude product that contained **63**, **60**, **65**, **61**, **62**, **64** in a 7:15:15:3:1:30 ratio as determined by ^{1}H NMR. Flash chromatography (20:1 hexane–EtOAc) of 70.0 mg gave 3.6 mg of a 4:1 mixture of **63** (4.0%) and **60** (1.0%), 4.1 mg of a 1:2 mixture of **63** (2%) and **60** (4%) and a trace of **65**, 14.4 mg of a 4:3:1 mixture of **60** (11.2%), **65** (9%), and **61** (2.8%), and 2.3 mg of a 1:1:1 mixture of **65** (1%), **61** (1%), and **62** (1%), followed by 28.1 mg (32%) of **64**.

The data for **60** were determined from the mixture: ^{1}H NMR 7.64 (dd, 1, J = 2.4, 6.6), 7.15–7.28 (m, 3), 5.41 (d, 1, J = 10.3), 4.06 (q, 2, J = 7.1), 3.46 (d, 1, J = 16.4), 2.91 (d, 1, J = 16.4), 2.76 (m, 1), 2.25–2.55 (m, 6), 1.12 (t, 3, J = 7.1).

Partial spectral data for **61** were determined from the mixture: ^{1}H NMR 7.45 (dd, 1, J = 4.1, 5.6), 7.12–7.28 (m, 3), 5.25 (d, 1, J = 4.6), 4.18 (q, 2, J = 7.1), 3.28 (d, 1, J = 15.8), 1.27 (t, 3, J = 7.1).

Partial spectral data for **62** were determined from the mixture: ^{1}H NMR 7.51 (dd, 1, J = 4.0, 5.8), 7.13–7.27 (m, 3), 5.14 (d, 1, J = 4.5), 4.22 (q, 2, J = 7.1), 3.42 (d, 1, J = 15.7), 1.28 (t, 3, J = 7.1).

The data for **63** were determined from the mixture: ^{1}H NMR 7.53 (d, 1, J = 7.5), 7.15–7.28 (m, 2), 7.09 (d, 1, J = 7.5), 5.78 (d, 1, J = 9.5), 4.03 (q, 2, J = 7.1), 3.22 (br s, 2), 1.70–2.55 (m, 7), 1.06 (t, 3, J = 7.1).

Oxidative Addition of Ethyl 2-Methylacetoacetate (66) to 2-Bromo-1-propene (67). Reaction of **66** (145 mg, 1 mmol), **67** (240 mg, 2 mmol), $Mn(OAc)_3 \cdot 2H_2O$ (545 mg, 2 mmol), and $Cu(OAc)_2 \cdot H_2O$ (200 mg, 1 mmol) in 10 mL of glacial acetic acid for 48 h at 40 °C followed by normal workup gave 277.1 mg of a mixture of **72** (24%), **68*E*** and **68*Z*** (1:3, 33%), **69** (16%), **71** (8%), a trace of **70**, and a trace of **73** and **74** by ^{1}H NMR and GC. Flash chromatography (25:1 hexane/EtOAc) of 60.0 mg gave 11.1 mg (23.8%) of pure **72** followed by 9.3 mg (16.3%) of a 1:1 mixture of **68*E*** and **68*Z***, 18.7 mg (32.8%) of a 1:1 mixture of **68*Z*** and **69**, and 3.6 mg (8.3%) of **71**.

The data for **68*E*** and **68*Z***: (**68*E***) ^{1}H NMR 6.58 (d, 1, J = 1.3), 4.23 (q, 2, J = 7.1), 2.17 (s, 3), 2.14 (d, 3, J = 1.3), 1.51 (s, 3), 1.28 (t, 3, J = 7.1); ^{13}C NMR 171.0, 129.7 (CH), 124.8 (C), 62.12, 62.06, 26.4, 24.7, 20.7, 13.9, C=O not observed; t_R = 6.80; (**68*Z***) ^{1}H NMR 6.61 (d, 1, J = 1.3), 4.21 (q, 2, J = 7.1), 2.37 (d, 3, J = 1.3), 2.20 (s, 3), 1.59 (s, 3), 1.28 (t, 3, J = 7.1); ^{13}C NMR 201.6, 171.2, 127.6 (CH), 124.1 (C), 62.12, 62.08, 30.3, 26.6, 19.5, 13.9; IR (neat) 2980, 2940, 2870, 1740, 1720, 1645, 1445, 1375, 1355, 1240, 1015; t_R = 6.69. Anal. Calcd for $C_{10}H_{15}BrO_3$: C, 45.65; H, 5.78. Found: C, 45.77; H, 5.66. The stereochemistry is assigned based on the shift of the methyl carbon at δ 24.7 in **68*E*** and δ 30.3 in **68*Z***.[23]

The data for **69** were determined from the mixture: ^{1}H NMR 5.64 (dt, 1, J = 1.6, 0.8), 5.56 (d, 1, J = 1.6), 4.23 (q, 3, J = 7.1), 3.17 (d, 1, J = 15.2, 0.8), 3.03 (d, 1, J = 15.2, 0.8), 2.20 (s, 3), 1.45 (s, 3), 1.28 (t, 3, J = 7.1); ^{13}C NMR 204.0, 171.8, 127.9 (C), 121.5 (CH), 61.8, 59.0 (C), 45.2, 26.0, 18.4, 13.9; t_R = 6.76.

The data for **71**: ^{1}H NMR 4.21 (q, 2, J = 7.1), 3.15 (d, 1, J = 18.2), 3.05 (d, 1, J = 18.2), 2.28 (s, 3), 2.17 (s, 3), 1.50 (s, 3), 1.28 (t, 3, J = 7.1); ^{13}C NMR 205.6, 203.4, 172.1, 61.6, 57.2, 48.9, 30.2, 26.4, 20.6, 13.9; IR (neat) 2990, 2940, 1740, 1730, 1720, 1455, 1425, 1365; t_R = 5.18. The data are identical to those previously reported.[24]

The data for **72**: ^{1}H NMR 4.28 (t, 2, J = 7.1), 2.44 (s, 3), 1.98 (s, 3), 1.33 (t, J = 7.1); ^{13}C NMR 198.1, 169.8, 63.1, 62.6, 25.7, 25.2, 13.8; IR (neat) 2980, 2930, 1740, 1720, 1440, 1370, 1350; t_R = 3.21. The data are identical to those previously reported.[25]

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The same reaction carried out without 1.0 equiv of $Cu(OAc)_2 \cdot H_2O$ gave 17.3% of **72** followed by 33.6% of a 1:1 mixture of **69** and **70**, 5% of **76**, 5% of **77**, and 15.4% of **71**.

The data for **70** were determined from the mixture: ^1H NMR 4.25 (q, 3, J = 7.1), 3.37 (d, 1, J = 15.9), 3.27 (d, 1, J = 15.9), 2.60 (s, 3), 2.21 (s, 3), 1.70 (s, 3), 1.30 (t, 3, J = 7.1); ^{13}C NMR 205.2, 171.1, 64.1, 62.1, 61.0, 53.7, 43.6, 25.5, 19.0, 14.0; t_R = 9.54.

Reaction of Ethyl 2-Methylacetoacetate (66) with $Mn(OAc)_3 \cdot 2H_2O$ and LiBr. A solution of **66** (175.0 mg, 1.2 mmol), $Mn(OAc)_3 \cdot 2H_2O$ (545 mg, 2 mmol), and LiBr (260 mg, 3 mmol) in 10 mL of glacial acetic acid was stirred for 17 h at 40 °C. Normal workup gave 269.0 mg (100%) of pure **72** as determined by GC and ^1H and ^{13}C NMR.

The same reaction carried out with 2.0 equiv of **67** gave an 86:3 mixture of **67** and **70** as determined by GC analysis.

Oxidative Addition of Ethyl 2-Methylacetoacetate (66) to 1-Hexene (75). Reaction of β-keto ester **76** (145 mg, 1 mmol), **75** (170 mg, 2 mmol), $Mn(OAc)_3 \cdot 2H_2O$ (545 mg, 2 mmol), and $Cu(OAc)_2 \cdot H_2O$ (200 mg, 1 mmol) in 10 mL of acetic acid for 48 h at 40 °C followed by normal workup afforded 238.3 mg of a 2:1 mixture of **76** and **77** and a mixture of **73** and **74**. Flash chromatography on silica gel (20:1 hexane-EtOAc) of 56.0 mg gave 43.4 mg (82%) of a 2:1 mixture of **76** and **77**, followed by 2.6 mg (7.9%) of **73** and 2.3 mg (6.8%) of **74**.

The data for **76** and **77**: ^1H NMR (**76**) 5.97 (dt, 1, J = 15.9, 1.4), 5.55 (dt, 1, J = 15.9, 6.8), 4.23 (q, 2, J = 7.1), 2.15 (s, 3), 2.09 (ddt, 2, J = 1.4, 6.8, 6.8), 1.45 (s, 3), 1.27 (t, 3, J = 7.1), 1.25–1.35 (m, 4), 0.89 (t, 3, J = 7.0); (**77**) 5.50 (dtt, 1, J = 15.0, 7.0, 1.3), 5.24 (dtt, 1, J = 15.0, 7.4, 1.3), 4.18 (q, 2, J = 7.1), 2.60 (ddd, 1, J = 7.4, 1.3, 14.2), 2.44 (ddd, 1, J = 7.4, 1.3, 14.2), 2.14 (s, 3), 1.95 (br dt, 2, J = 7.0, 7.0), 1.33 (m, 2), 1.31 (s, 3), 1.26 (t, 3, J = 7.1), 0.87 (t, 3, J = 7.0); ^{13}C NMR (**76**) 203.8, 172.1, 133.3, 127.6, 61.3, 61.1, 32.3, 31.0, 26.3, 22.0, 19.6, 13.9, 13.7; t_R = 7.73; (**77**) 205.2, 172.6, 135.1, 123.7, 61.5, 59.6, 38.1, 34.5, 26.2, 22.4, 18.8, 14.0, 13.5; IR (neat) 960, 2930, 2870, 2860, 1745, 1715, 1460, 1370, 1355, 1240, 1020, 970; t_R = 7.73. Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 69.05; H, 9.92.

The data for **73** and **74** are identical to those previously described:[1] t_R = 11.66 (**73**); t_R = 9.97 and 10.07 (**74**).

Competition Reactions. Reaction of **66** (145 mg, 1 mmol), **75** (430 mg, 5 mmol), **78** (430 mg, 5 mmol), $Mn(OAc)_3 \cdot 2H_2O$ (540 mg, 2 mmol), and $Cu(OAc)_2 \cdot H_2O$ (200 mg, 1 mmol) in 10 mL of glacial acetic acid for 48 h at 40 °C followed by normal workup gave 247.4 mg of crude product. GC analysis of the crude product indicated that **79** (75.3%), (**76** + **77**) (24.4%), and a trace of **73**, **74**, and **80** were present. ^1H NMR analysis of the crude product showed that **79** and (**76** + **77**) were formed in a 2.3:1 ratio. The data for **79** and **80** are identical to those previously described:[1] t_R = 5.77, 5.91, 7.09, 7.17, 7.38 (**79**); t_R = 10.26, 10.35 (**80**).

Reaction of 1 mmol of **66**, 5 mmol of **67**, 5 mmol of **75**, 2 mmol of $Mn(OAc)_3 \cdot 2H_2O$, and 1 mmol of $Cu(OAc)_2 \cdot H_2O$ as described above gave (**76** + **77**) (46.4%), (**68E** + **68Z** + **69**) (34.2%), **72** (19.4%), and a trace of **71**, **73**, **74**, **70** as determined by GC. ^1H NMR analysis of the crude product showed that (**76** + **77**) and (**68E** + **68Z** + **69**) were formed in a 1.3:1 ratio.

Reaction of 1 mmol of **66**, 5 mmol of **67**, 5 mmol of **78**, 2 mmol of $Mn(OAc)_3 \cdot 2H_2O$, and 1 mmol of $Cu(OAc)_2 \cdot H_2O$ as described above gave **79** (73%), (**68E** + **68Z** + **69**) (17%), **72** (7%), and a trace of **70**, **73**, **74**, **71** as determined by GC. ^1H NMR analysis of the crude product showed that **79** and (**68E** + **68Z** + **69**) were formed in a 4:1 ratio.

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Registry No. 1a, 112292-93-0; **3a**, 141726-23-0; **4b**, 141726-24-1; **4c**, 141726-25-2; **7**, 141726-26-3; **8**, 79482-36-3; **9**, 141726-27-4; (*E*)-**10**, 141726-28-5; (*Z*)-**10**, 141726-29-6; **12**, 65547-54-8; (*Z*)-**13**, 141726-30-9; (*E*)-**13**, 141726-31-0; **15**, 141726-32-1; **16**, 141726-33-2; **17**, 141726-34-3; (*E*)-**28a**, 141726-35-4; (*Z*)-**28a**, 141726-36-5; (*Z*)-**28b**, 141726-37-6; (*E*)-**28b**, 141726-38-7; **30a**, 141726-39-8; **32a**, 141726-40-1; **32b** (isomer 1), 141726-41-2; **32b** (isomer 2), 141726-42-3; **33b** (isomer 1), 141726-43-4; **33b** (isomer 2), 141726-44-5; **34**, 141726-45-6; **35a**, 141726-46-7; **35b** (isomer 1), 141726-47-8; **35b** (isomer 2), 141726-48-9; **36b**, 141726-49-0; **36b** deschloro derivative, 141726-50-3; (*E*)-**44**, 141753-23-3; (*Z*)-**44**, 141726-51-4; **46**, 141753-24-4; **48**, 141726-52-5; **49**, 141726-53-6; **50**, 141726-54-7; **51b**, 141726-55-8; **52b**, 141726-56-9; **53a**, 112293-00-2; **54a**, 112292-99-6; (*Z*)-**55b**, 141726-57-0; (*E*)-**55b**, 141726-58-1; **57b**, 141726-59-2; **58b** (isomer 1), 141726-60-5; **58b** (isomer 2), 141726-61-6; (*E*)-**59**, 141752-92-3; (*Z*)-**59**, 141726-62-7; **60**, 141726-63-8; **61**, 141726-64-9; **62**, 141726-65-0; **63**, 141726-66-1; **64**, 141726-67-2; **65**, 141726-68-3; **66**, 609-14-3; **67**, 557-93-7; (*E*)-**68**, 141726-69-4; (*Z*)-**68**, 141726-70-7; **69**, 141726-71-8; **70**, 141726-72-9; **71**, 111400-47-6; **72**, 32116-05-5; **73**, 21954-89-2; **74**, 141726-73-0; **75**, 592-41-6; **76**, 141726-74-1; **77**, 141726-75-2; **78**, 763-29-1; **79** (isomer 1), 141726-76-3; **79** (isomer 2), 113704-09-9; **80**, 141726-77-4; $CH_3COCH_2^- \cdot Zi^+$, 62415-84-3; $Mn(OAc)_3 \cdot 2H_2O$, 993-02-2; $Cu(OAc)_2 \cdot H_2O$, 142-71-2; benzoylacetone, 93-91-4; 1-bromo-3(*Z*)-hexene, 5009-31-4; 5-bromo-2-pentyne, 18719-27-2; 4-bromo-1-(trimethylsilyl)-1-butyne, 69361-41-7; (*E*)-4-bromo-1-chloro-1-butene, 40529-08-6; (*Z*)-4-bromo-1-chloro-1-butene, 40529-07-5; 2,4-dimethoxybenzoic acid, 91-52-1; 2,4-dimethoxybenzoyl chloride, 39828-35-8; methyl 2-allylacetoacetate, 3897-04-9; (*E*)-crotyl bromide, 29576-14-5; (*Z*)-crotyl bromide, 39616-19-8; allyl bromide, 106-95-6; (*Z*)-methyl 7-chloro-3-oxohept-6-enoate, 141726-78-5; (*E*)-methyl 7-chloro-3-oxohept-6-enoate, 141726-79-6; ethyl 2-benzylacetoacetate, 620-79-1; 2,3-dichloropropene, 78-88-6; 1,3-dichloropropene, 542-75-6.