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Mechanism of Manganese(III)-Based Oxidation of β-Keto Esters

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The rate-determining step in the oxidation of 2-substituted acetoacetate esters such as **10b** by $Mn(OAc)_3 \cdot 2H_2O$ is the loss of a proton from the **10b**–Mn(III) complex **17b** to form **18b**. The rate-determining step in the oxidation of 2-unsubstituted acetoacetate esters such as **10a** by $Mn(OAc)_3 \cdot 2H_2O$ in the presence of an alkene is the oxidation of Mn(III)–**10a**–alkene complex **20a** to give the addition product **21a**. In the absence of alkene, a much slower electron transfer from the enolate to the oxo-centered metal system to give **19a** is the rate-determining step. Oxidative cyclization of **1b** produces oxocyclopentanecarboxylates such as **4b** in poor yield since overoxidation of the product occurs at a rate comparable to that of the initial cyclization. Oxidative cyclization of **1a** produces oxocyclohexanecarboxylates such as **4a** in good yield since the oxidation of **1a** is much faster than the oxidation of **1b**. Overoxidation can be prevented by oxidative cyclization of 2-chloroacetoacetates such as **30a** and **36a** followed by zinc reduction to give **32c** and **39c** in good overall yield.

Introduction

We[1] and others[2a,3d] have recently shown that the manganese(III)-based oxidative free-radical cyclizations of β-keto esters to alkenes is an attractive method for the formation of cyclic and polycyclic products.[4] Treatment of β-keto ester **1a** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ gave a 75% yield of **4a**. The available evidence[1c,5] suggests that oxidative cyclization occurs to give **2a**, which reacts rapidly with $Cu(OAc)_2 \cdot H_2O$ to give **3a**. β-Hydride elimination then occurs rapidly to give **4a** and cuprous acetate, which is reoxidized by $Mn(OAc)_3 \cdot 2H_2O$. Oxidative cyclization of β-keto ester **1b** was much less effective. Similar treatment of **1b** gave only a 36% yield of **4b**, a 10% yield of **5b**, and other overoxidation products.

The formation of **5b** was not surprising, since β-keto ester **4b** still contains an enolizable hydrogen and is therefore susceptible to further oxidation. Overoxidation has previously been observed in intermolecular oxidative coupling reactions of carbonyl compounds with alkenes.[2b,3c,4] In these cases the problem can be partially overcome by the use of a large excess of carbonyl compound. However, this approach is not applicable to oxidative cyclizations. The formation of overoxidized products from oxocyclopentanecarboxylates such as **4b** but not from oxocyclohexanecarboxylates such as **4a** indicated that overoxidation was not inevitable and prompted a study of the mechanism of the oxidation reaction in an attempt to learn how to prevent overoxidation.

The mechanism of oxidation of monocarbonyl substrates with $Mn(OAc)_3 \cdot 2H_2O$ has been extensively studied.[3,6] Fristad and co-workers showed that the rate-determining step in oxidation of acetic acid by $Mn(OAc)_3 \cdot 2H_2O$, which

(1) (a) Snider, B. B.; Mohan, R. M.; Kates, S. A. *J. Org. Chem.* **1985**, *50*, 3659. (b) Snider, B. B.; Mohan, R. M.; Kates, S. A. *Tetrahedron Lett.* **1987**, *28*, 841. (c) Mohan, R.; Kates, S. A.; Dombroski, M.; Snider, B. B. *Tetrahedron Lett.* **1987**, *28*, 845.

(2) (a) Corey, E. J.; Kang, M.-C. *J. Am. Chem. Soc.* **1984**, *106*, 5384. (b) Corey, E. J.; Gross, A. W. *Tetrahedron Lett.* **1985**, *26*, 4291. (c) Corey, E. J.; Ghosh, A. K. *Tetrahedron Lett.* **1987**, *28*, 175.

(3) (a) Fristad, W. E.; Peterson, J. R. *J. Org. Chem.* **1985**, *50*, 10. (b) Fristad, W. E.; Hershberger, S. S. *J. Org. Chem.* **1985**, *50*, 1026. (c) Fristad, W. E.; Peterson, J. R.; Ernst, A. B. *J. Org. Chem.* **1985**, *50*, 3143. (d) Ernst, A. B.; Fristad, W. E. *Tetrahedron Lett.* **1985**, *26*, 3761. (e) Fristad, W. E.; Peterson, J. R.; Ernst, A. B.; Urbi, G. B. *Tetrahedron* **1986**, *42*, 3429.

(4) For earlier studies of the oxidative addition of acetic acid and β-dicarbonyl compounds to alkenes, see: (a) Bush, J. B., Jr.; Finkbeiner, H. *J. Am. Chem. Soc.* **1968**, *90*, 5903. (b) Heiba, E. I.; Dessau, R. M.; Koehl, W. J., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 5905. (c) Heiba, E. I.; Dessau, R. M. *J. Am. Chem. Soc.* **1971**, *93*, 524. (d) Heiba, E. I.; Dessau, R. M. *J. Am. Chem. Soc.* **1972**, *94*, 2888. (e) Heiba, E. I.; Dessau, R. M.; Rodewald, P. G. *J. Am. Chem. Soc.* **1974**, *96*, 7977. (f) Heiba, E. I.; Dessau, R. M. *J. Org. Chem.* **1974**, *39*, 3456. (g) Heiba, E. I.; Dessau, R. M.; Williams, A. L.; Rodewald, P. G. *Org. Synth.* **1983**, *61*, 22. (h) Nikishin, G. I.; Vinogradov, M. G.; Fedorova, T. M. *J. Chem. Soc., Chem. Commun.* **1973**, 693. (i) Vinogradov, M. G.; Petrenko, O. N.; Verenchikov, S. P.; Nikishin, G. I. *Izv. Akad. Nauk SSSR. Ser. Khim.* **1979**, 1916.

(5) Kochi, J. K.; Bemis, A.; Jenkins, C. L. *J. Am. Chem. Soc.* **1968**, *90*, 4616. Kochi, J. K.; Bacha, J. D. *J. Org. Chem.* **1968**, *33*, 2746.

(6) (a) van der Ploeg, R. E.; de Korte, R. W.; Kooyman, E. C. *J. Catal.* **1968**, *10*, 52. (b) Vinogradov, M. G.; Verenchikov, S. P.; Nikishin, G. I. *J. Org. Chem. USSR (Engl. Transl.)* **1976**, *12*, 2245; *Zh. Org. Khim.* **1976**, *12*, 2313. (c) Vinogradov, M. G.; Dolinko, V. I.; Nikishin, G. I. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1982**, 2036; *Izv. Akad. Nauk SSSR, Ser. Khim.* **1982**, 2313. (d) Vinogradov, M. G.; Kovalev, I. P.; Nikishin, G. I. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1984**, 342; *Izv. Akad. Nauk SSSR, Ser. Khim.* **1984**, 384. (e) Vinogradov, M. G.; Fedorova, T. M.; Nikishin, G. I. *J. Org. Chem. USSR (Engl. Transl.)* **1976**, *12*, 1183; *Zh. Org. Khim.* **1976**, *12*, 1175.

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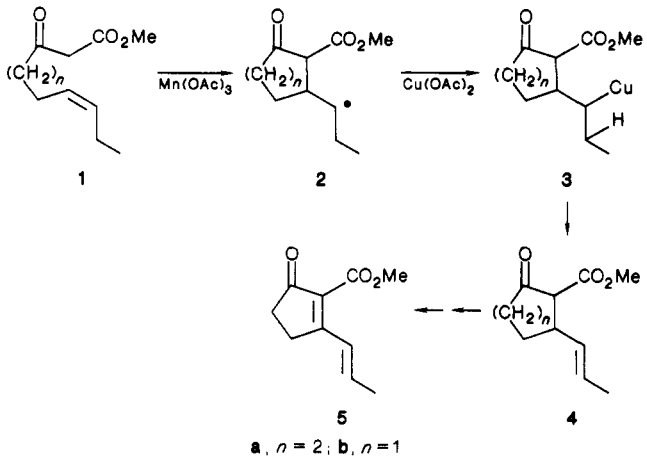
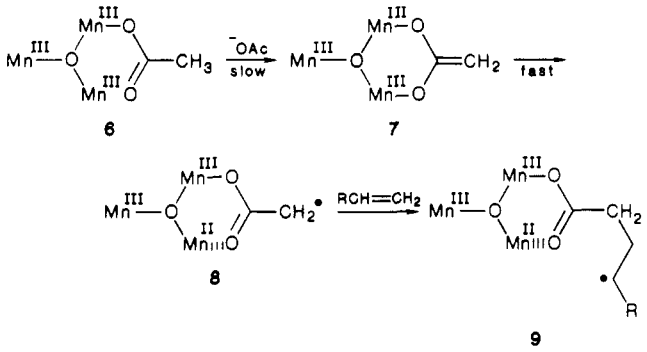


is actually an oxo-centered triangle of Mn(III), is the loss of a proton from a complexed acetate such as **6** to give **7**, which rapidly suffers electron loss to the oxo-centered metal system to give **8**.[3a,3e] The resulting radical **8** then adds to the alkene to give **9** prior to dissociation from the manganese. The rate of reaction is independent of alkene concentration since the alkene is not involved in the rate-determining step. The rate of reaction increases with the increasing acidity of an α-proton. Fristad found that the log of the rate of oxidation relative to acetic acid equals 0.344 (ΔpK_a) for five monosubstituted acetic acids covering an acidity range for the α-proton of 16 pK_a units.[3a]



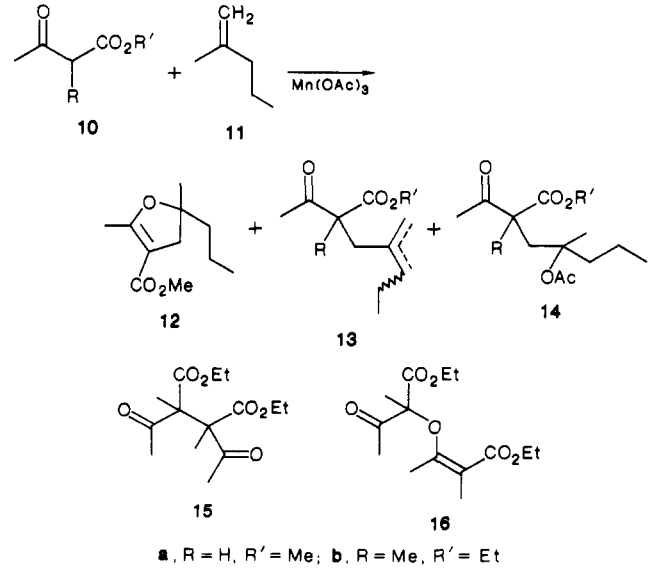
Results and Discussion

Mechanism of Oxidation of β-Keto Esters. In order to determine the validity of this mechanism for the oxidation of β-keto esters, we determined the rates of manganese(III) oxidation of several β-keto esters in the presence and absence of an alkene. Qualitative data was obtained by addition of 1 equiv of $Mn(OAc)_3 \cdot 2H_2O$ to 5 equiv of β-keto ester and 0–5 equiv of alkene in acetic acid at 40 °C. Studies were carried out by using 2-methyl-1-pentene (**11**) since the resulting tertiary radicals are rapidly oxidized to cations while secondary radicals undergo intermolecular hydrogen atom transfer reactions unless $Cu(OAc)_2$ is present.[1,4]

The reaction rate was determined by measuring the time for decolorization of the solution as brown $Mn(OAc)_3 \cdot 2H_2O$ was reduced to colorless $Mn(OAc)_2$. This indicates the time for complete consumption of $Mn(OAc)_3 \cdot 2H_2O$, which provides useful information on the rate of the reaction if all other reagents are present in excess. This approach has obvious limitations since it only indicates the time required for complete reaction and does not give any information on the rate of the reaction. Precise studies of the rate of oxidation of monocarbonyl substrates with $Mn(OAc)_3 \cdot 2H_2O$ have been carried out by monitoring the change in Mn(III) concentration at 465 nm. Because of the strong absorbance of Mn(III), only concentrations of Mn(III) below 10^{-3} M can be followed. These studies suggested a complicated mechanism that was 0.25 order in Mn(III) and −1 order in Mn(II).[6b-e] We chose not to use this approach to study the rate of oxidation of β-keto esters since the low concentrations of Mn(III) that can be monitored do not resemble synthetically useful reaction conditions. Monitoring of product formation is not possible since complex mixtures are produced.

Our results indicate that $Mn(OAc)_3 \cdot 2H_2O$ was fully reduced in 6–8 h, as evidenced by decolorization of the solution, by methyl acetoacetate (**10a**), ethyl 2-methylacetoacetate (**10b**), ethyl 2-chloroacetoacetate, ethyl 2-oxocyclohexanecarboxylate, ethyl 2-oxocyclopentanecarboxylate, and ethyl 2-benzylacetoacetate if an excess of **11** was present. Furthermore, $Mn(OAc)_3 \cdot 2H_2O$ was fully reduced in 6–8 h by **10b**, ethyl 2-chloroacetoacetate, ethyl 2-oxocyclohexanecarboxylate, ethyl 2-oxocyclopentanecarboxylate, and ethyl 2-benzylacetoacetate even if no alkene was present. On the other hand, **10a** was oxidized very slowly if no alkene was present; complete reduction of $Mn(OAc)_3 \cdot 2H_2O$ occurred after 56 h. Oxidation of **10a** was complete in 6–8 h if 0.5 or more equiv of alkene was present, occurred at the same rate with 0.5 and 5 equiv of **11**, and occurred at the same rate with either **11**, 1-hexene, or 2,3-dimethyl-2-butene.

The products of the oxidation of **10a** and **10b** by $Mn(OAc)_3 \cdot 2H_2O$ with and without added **11** were determined. Oxidation of **10a** in the presence of **11** gave furanone **12** in 30% yield, a mixture of unsaturated esters **13a** in 16% yield, and acetoxy ester **14a** in 13% yield as reported by Heiba and Dessau in closely related systems.[4f] Oxidation of **10b** in the presence of **11** gave a mixture of unsaturated esters **13b** in 35% yield, acetoxy ester **14b** in ≈5% yield, and dimers **15** and **16** in ≈5% yield each. Oxidation of **10b** in the absence of alkene gave the dimer **15** in 34% yield as a mixture of diastereomers, dimer **16** in 36% yield, and uncharacterizable polymer in 25% yield. Dimer **15** and the decarboethoxylation product from **16** have been obtained from lead dioxide oxidation of **10b**.[7] Oxidation of **10a** in the absence of alkene led only to volatile products.



These results suggest that the rate-determining step in the oxidation of **10a** is different from that of the oxidation of β-keto esters containing only one enolizable hydrogen. The rates of oxidation of **10b** and other β-keto esters containing only one enolizable hydrogen are independent

(7) Brettle, R.; Seddon, D. *J. Chem. Soc. C* **1970**, 1320.

of alkene concentration as is the oxidation of acetic acid.[3,6] On the other hand, the rate of oxidation of **10a** is very slow unless at least 0.5 equiv of alkene is present. Since the oxidation of **10a** to give **12a**, **13a**, and **14a** consumes 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$, 0.5 equiv of alkene corresponds to the amount of **10a** consumed.

The rate of oxidation of **10a** in the absence of alkene is 8 times slower than the oxidation of **10b**, even though **10a** (pK_a 10.7) is more acidic than **10b** (pK_a 12.5).[8] The relationship between ΔpK_a and the rate of oxidation developed by Fristad[3a] clearly does not hold in these cases; enolization is not the rate-limiting step for the oxidation of **10a**.

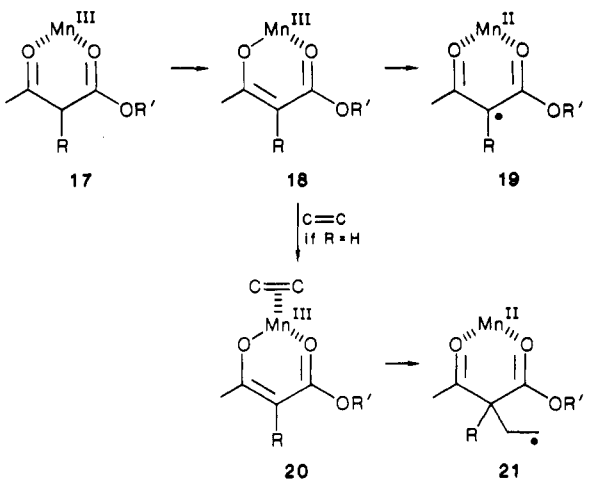
The rates of enolization of **10a** and **10b** in acetic acid-d_4 were determined by NMR analysis of deuterium incorporation. **10a** exchanged completely within 2 h at 25 °C, clearly indicating that enolization is not the rate-determining step. **10b** exchanged relatively slowly; incorporation of deuterium was only 50% complete after 10 h at 40 °C. This suggests that enolization of a Mn(III) complex of **10b** is the rate-determining step for oxidation of **10b**. In order to compare the rate of enolization with the rate of oxidation, we carried out the oxidative dimerization reaction of **10b** in acetic acid-d_1 at 40 °C and aliquots were examined by NMR. The results indicate that deuterium incorporation in unreacted **10b** occurs at a rate comparable to that which occurred in the absence of $Mn(OAc)_3 \cdot 2H_2O$ and that oxidation is much faster than deuterium incorporation.

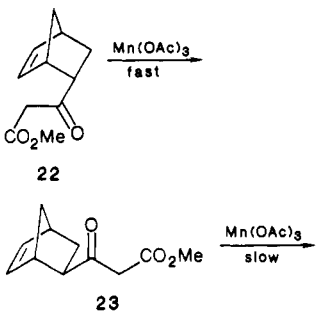
These results establish that the rate-determining step in oxidation of **10b** by $Mn(OAc)_3 \cdot 2H_2O$ is the loss of a proton from the **10b**–Mn(III) complex **17b** to form **18b**. The coupling reaction to form dimers **15** and **16** must occur after the rate-determining step since only ≈10% of these dimers are formed in the presence of alkene 11 and the oxidation occurs at the same rate in the presence or absence of alkene 11.

The rate-determining step in the oxidation of **10a** by $Mn(OAc)_3 \cdot 2H_2O$ in the absence of alkenes cannot be the formation of the complex **18a**, since **18a** should be formed faster than **18b** and the rate of proton exchange is much faster than oxidation. Presumably, electron transfer from the enolate to the oxo-centered metal system to give **19a** is the rate-determining step in the absence of alkene.

The rate-determining step in the oxidation of **10a** by $Mn(OAc)_3 \cdot 2H_2O$ in the presence of an alkene must involve the alkene since the reaction is much faster than in the absence of alkene. Formation of **20a** is probably not the rate-determining step since the rate appears to be independent of alkene concentration as long as the required amount of alkene is present. The rate-determining step could be the oxidation of Mn(III)–**10a**–alkene complex **20a** to give the addition product **21a**. Although the alkene should not be a good ligand for the Mn(III), similar intermediates have been suggested in related $Mn(OAc)_3 \cdot 2H_2O$ oxidations.[6c-d,9a] A rate-determining step involving the alkene has also been observed in $Mn(OAc)_3 \cdot 2H_2O$ oxidative cyclization of unsaturated β-keto acids.[2a]

Independent evidence indicating double-bond participation in the rate-determining step in the oxidation of unsubstituted acetoacetates was obtained with **22** and **23**. Oxidation of the endo isomer **22** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ was complete in 2 days at 25 °C, as determined by decolorization of the solution. Only polymer derived from overoxidation of the initially formed oxocyclopentanecarboxylate was isolated. On the other hand, oxidation of the exo isomer **23**, in which the double bond cannot coordinate to the Mn or approach the acetoacetate, was very slow. $Mn(OAc)_3 \cdot 2H_2O$ was still present after 14 days at 25 °C; an additional 18 h at 60 °C was required for decolorization of the solution.





Why does the 2-methyl group accelerate the oxidation? The methyl group should slow down the formation of **18b** relative to **18a** since it is electron donating and decreases the acidity of the α-proton. On the other hand, the methyl group should facilitate the oxidation of 18 to **19** since it will stabilize the radical. Confirmation of this hypothesis can be obtained by examining electrochemical data for the oxidation of enolates of β-dicarbonyl compounds to the radical in DMSO.[10] The presence of a methyl group facilitates the oxidation of the enolate of β-dicarbonyl compounds by 0.25–0.4 V. Therefore it is plausible for formation of **18b** and **19a** to be the rate-determining steps in the absence of alkene and formation of **18b** and **21a** to be the rate-determining steps in the presence of alkene.

Effect of Ring Size on the Rate of Oxidative Cyclization. These results indicate why overoxidation of **4b** is a problem and provide a basis for examination of the effect of ring size on the amount of overoxidation products. Alkene-assisted oxidation of 2-unsubstituted acetoacetates such as 1 occurs at a rate similar to that of the alkene-independent oxidation of 2-substituted acetoacetates such as **4b**. Overoxidation products are therefore expected from both **1a** and **1b**, but are formed in significant amount only from **1b**.

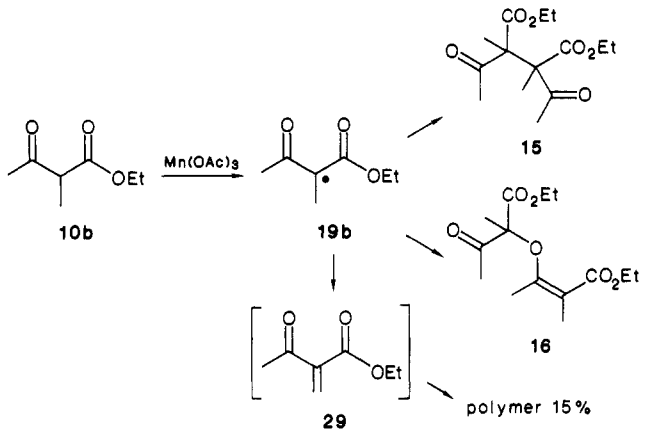
There are two possible explanations for this observation. Firstly, overoxidation of **4b** may be much faster than ov-

(8) Rumpf, P.; Reynaud, R. *C. R. Hebd. Seances Acad. Sci.* **1960**, *250*, 1501.

(9) (a) Vinogradov, M. G.; Dolinko, V. I.; Nikishin, G. I. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1984**, 1884; *Izv. Akad. Nauk SSSR, Ser. Khim.* **1984**, 2065. (b) Vinogradov, M. G.; Dolinko, V. I.; Nikishin, G. I. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1984**, 334; *Izv. Akad. Nauk SSSR, Ser. Khim.* **1984**, 375.

(10) Kern, J. M.; Federlin, P. *Tetrahedron Lett.* **1977**, 837. Kern, J. M.; Federlin, P. *Tetrahedron* **1978**, *34*, 661.

Scheme I

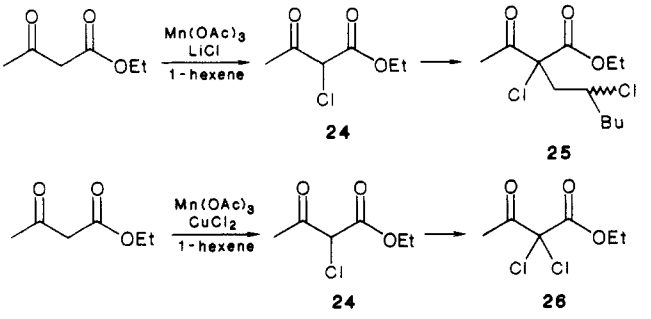


eroxidaton of **4a**. Secondly, oxidative cyclization of **1a** may be faster than oxidative cyclization of **1b**. We have obtained evidence that suggests that both of these possible explanations are correct.

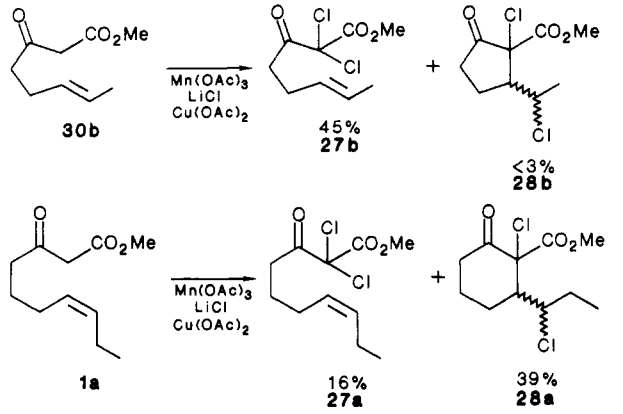
Oxidation of **4b** with $Mn(OAc)_3 \cdot 2H_2O$ and $Cu(OAc)_2 \cdot H_2O$ under standard conditions for 18 h at 25 °C gave a 1:1 mixture of **5** and recovered **4b**. Similar oxidation of **4a** for 6 days gave only recovered **4a**. These qualitative results make it clear that **4b** is oxidized much more rapidly than **4a**. The reason for the difference in reactivity is obscure, but may be related to the fact that 2-oxocyclohexanecarboxylate esters are largely enolic while 2-oxocyclopentanecarboxylate esters are largely ketonic.[11]

We have also explored the rates of cyclization of **1a** and **1b**. It is possible that the alkene–acetoacetate–Mn(III) complex **20** would be converted to **21** (i.e., **2**) more readily with the longer three-carbon tether of **1a** than the shorter two-carbon tether of **1b**. If formation of **4b** is slower than formation of **4a**, overoxidation will be more of a problem. We have been able to demonstrate that this is the case.

Vinogradov et al. have explored the oxidation of ethyl acetoacetate by $Mn(OAc)_3 \cdot 2H_2O$ in the presence of LiCl and 1-hexene.[9] They found that ethyl chloroacetoacetate (**24**) was initially formed. Further oxidation gave the dichloride **25** in 61% yield. If the oxidation was carried out with $CuCl_2$, instead of LiCl, ethyl 2,2-dichloroacetoacetate (**26**) was the major product.[6c] Only traces of **25** were formed.



We have carried out similar oxidations of **1a** and **30b**. Reaction of either **1a** or **30b** with $Mn(OAc)_3 \cdot 2H_2O$ and LiCl gave the cyclic dichloro esters **28a** and **28b** in good yield as a complex mixture of stereoisomers. More significantly, reaction of either **1a** or **30b** with $Mn(OAc)_3 \cdot 2H_2O$, LiCl, and $Cu(OAc)_2 \cdot H_2O$ gave mixtures of **28** and the unsaturated acyclic dichloro ester **27** since addition of $Cu(OAc)_2 \cdot H_2O$ and LiCl is equivalent to adding $CuCl_2$. The ratios of products varied markedly with ring size. Oxidation of **1a** gave a 39% yield of **28a** and a 16% yield of **27a**. Oxidation of **30b** gave a <3% yield of **28b** and a 45% yield of **27b**. Since **27a** and **27b** should be formed at the same rate, these results establish that **28a** is formed much faster than **28b**, indicating that the longer tether of **1a** substantially accelerates the rate of the oxidation.[12]



Structure of Overoxidation Products. We have been able to isolate a monomeric overoxidation product from an oxidative cyclization in only a single case, i.e., **5**, although we have often isolated polar, presumably polymeric, material which we believe results from overoxidation of the initial cyclic product. These results appear to be inconsistent with the oxidation of ethyl methylacetoacetate (**10b**), which gave only a 24% yield of polar polymeric material and gave dimers **15** and **16** in a combined yield of 70%. No dimers have ever been observed as overoxidation products of cyclization reactions. What is the origin of this dichotomy in reactivity?

Oxidation of 2-monosubstituted acetoacetates will give radicals, e.g., **19**. These radicals can react to give dimers, e.g., **15** and **16**, or lose a proton and be oxidized to give alkenes, e.g. **29**, which will polymerize readily. (See Scheme I.) The dimers need not be formed by coupling of two molecules of **19** but can also be formed by reaction of **19** with unoxidized acetoacetate followed by a second oxidation step. In the case of **10b**, the sterically unencumbered radical **19b** will dimerize readily and lose a proton slowly to give the unstable alkene **29**, which will polymerize. The radical derived from oxidation of **4b** is sterically hindered so that dimerization is slow. Formation of **5** on the other hand is rapid since a conjugated diene is formed and the proton that is lost is allylic. Confirmation of this analysis was obtained by oxidation of ethyl 2-allylacetoacetate, which gave only polymeric products and no dimers analogous to **15** and **16**.[13]

Prevention of Overoxidation. To prevent overoxidation, one of the hydrogens on the 2-position of **1b** must

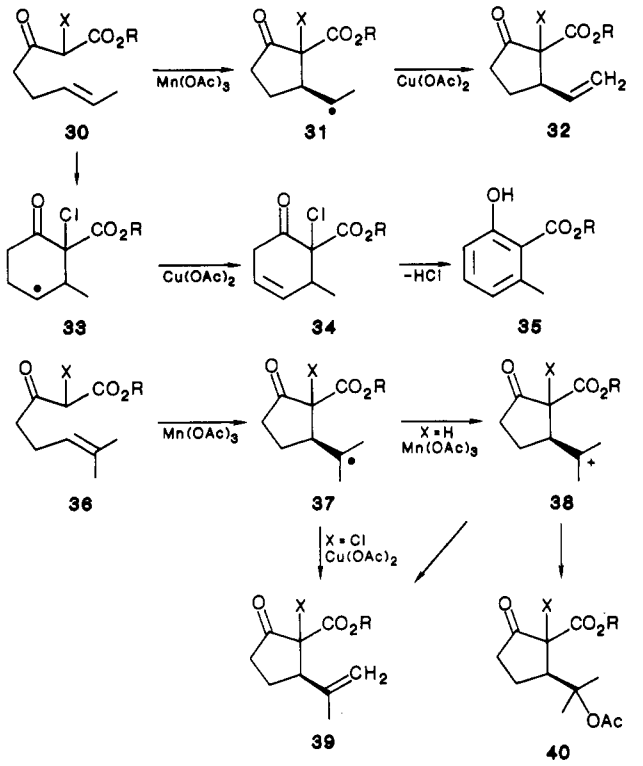
(11) Rhoads, S. J. *J. Org. Chem.* **1966**, *31*, 171. Kol'tsov, A. I.; Kheifets, G. M. *Russ. Chem. Rev. (Engl. Transl.)* **1971**, *40*, 773.

(12) A referee has suggested that the relative yields of **27** and **28** could depend on the relative stabilities of the acyclic and cyclic radicals since these cyclizations are reversible. If this were the case, the observed formation of **28a** but not **28b** with LiCl and $Cu(OAc)_2 \cdot H_2O$ would reflect the greater stability of the six-membered ring rather than faster cyclization to form **28a**. Although we cannot rigorously exclude this possibility, the exclusive trapping of the cyclic radicals to give both **28a** and **28b** when only LiCl is used suggests that the different behavior in the presence of $Cu(OAc)_2 \cdot H_2O$ is due to kinetic and not thermodynamic factors.

(13) Oxidation of ethyl 2-benzylacetoacetate with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ gave 24% of C–C dimer, 46% of C–O dimer, and 28% of polymer. Ethyl 2-oxocyclopentanecarboxylate gave 16% of C–C dimer, 29% of C–O dimer, and 38% of polymer. Ethyl 2-oxocyclohexanecarboxylate gave 13% of C–C dimer, 28% of C–O dimer, and 42% of polymer. Ethyl 2-chloroacetoacetate gave 44% of C–C dimer, 23% of C–O dimer, and no polymer.

be replaced with a substituent such as chlorine,[2b,9] which is stable to oxidation but can be easily removed. Alkylation of the dianion of ethyl 2-chloroacetoacetate with crotyl bromide and prenyl bromide gave **30a** and **36a** in 39% and 43% yield, respectively. No attempt was made to optimize the yield of the alkylation. Oxidative cyclization of **30a** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ in acetic acid gave a 10% yield of ethyl 6-methylsalicylate (**35**) and a 48% yield of a 3:2 mixture of **32a** and **32b**. Reduction of this mixture with zinc in acetic acid gave an 81% yield of **32c**. Alternatively, oxidation of **30a** as described above followed by addition of zinc dust to the reaction mixture gave **35** in 16% yield and **32c** in 51% overall yield. Since direct oxidation of **30c** gave only a 21% yield of **32c**,[1a] introduction of a chlorine effectively serves to prevent overoxidation.

The formation of salicylate **35** as a minor product in the oxidative cyclization of **30a** results from cyclization to give the cyclohexyl radical **33**. $Cu(OAc)_2 \cdot H_2O$ oxidation of **33** gave **34**, which aromatized by dehydrochlorination to give **35**. Oxidative cyclization of **30c** led to similar amounts of **35** and the corresponding dihydro compounds.[1a]



a, X = α-Cl; **b**, X = β-Cl; **c**, X = H

Oxidative cyclization of **36a** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ in acetic acid gave a 49% yield of a 3:2 mixture of **39a** and **39b**. Oxidation in the absence of Cu(II) gave a complex mixture of products. This is a marked improvement over the $Mn(OAc)_3 \cdot 2H_2O$ oxidation of **36c**, which gave an 8% yield of **39c** and a 10% yield of **40c**, both with and without the use of $Cu(OAc)_2 \cdot H_2O$ as a cooxidant.[1a] Tertiary radicals such as **37c** are readily oxidized by Mn(III) to cations such as **38c** which lose a proton to give **39c** or react with solvent to give **40c**.[1b] Secondary radicals such as **31c** are not oxidized by Mn(III) but are converted to the alkene by Cu(II) without the intermediacy of a cation.[1c,4] Since the oxidation of **36a** required the presence of Cu(II) for the formation of **39a,b** and since no **40a,b** was formed, we believe that the electron-withdrawing chlorine group prevents the oxidation of **37a** to the cation **38a,b** by Mn(III), allowing clean conversion to **39a,b** by Cu(II) oxidation.

The stereochemistry of **32** and **39** was established by analysis of the ^1H NMR absorptions of the methine hydrogen. The shifts caused by vicinal cis and trans ester and chlorine substituents in a variety of norbornanes have been determined.[14] These values suggest that a hydrogen cis to a chlorine and trans to an ester will absorb 0.49 ppm upfield from the diastereomer with a hydrogen cis to an ester and trans to a chlorine. Structures **32a** and **39a** are therefore assigned to the major isomers in which the methine hydrogen absorbs at δ 3.12 and 3.10, respectively. Structures **32b** and **39b** are assigned to the minor isomers in which the methine hydrogen absorbs at δ 3.46 and 3.40, respectively.

Conclusion

These results indicate that oxidation of β-keto esters by $Mn(OAc)_3 \cdot 2H_2O$ can occur by two different mechanisms. The rate-determining step in the oxidation of 2-substituted acetoacetate esters, the loss of a proton from the **10b**–Mn(III) complex **17b** to form **18b**, does not involve the alkene. The rate-determining step in the oxidation of 2-unsubstituted acetoacetate esters in the presence of an alkene is the oxidation of Mn(III)–**10a**–alkene complex **20a** to give the addition product **21a**. In the absence of alkene, a much slower electron transfer from the enolate to the oxo-centered metal system to give **19a** is the rate-determining step.

Oxidative cyclization of unsubstituted acetoacetate esters will occur at variable rates depending on the length of the tether since the alkene is involved in the rate-determining step. Overoxidation of the product, which is a monosubstituted β-keto ester, occurs more rapidly for oxocyclopentanecarboxylates than for oxocyclohexanecarboxylates. Oxidative cyclization produces oxocyclopentanecarboxylates such as **4b** in poor yield since overoxidation of the product occurs at a rate comparable to that of the initial cyclization. Oxidative cyclization produces oxocyclohexanecarboxylates such as **4a** in good yield since the oxidation of **1a** is much faster than the oxidation of **1b**.

Overoxidation can be efficiently prevented by oxidative cyclization of 2-chloroacetoacetates such as **30a** and **36a** followed by addition of zinc to the reaction mixture to give **32c** and **39c** in good overall yield.

Experimental Section

General Procedures. $Mn(OAc)_3 \cdot 2H_2O$ was purchased from Aldrich Chemical Co. and used without purification. NMR spectra were recorded on a Varian XL-300 NMR spectrometer in $CDCl_3$ solution. Chemical shifts are reported in δ, and coupling constants are reported in hertz.

General Procedure for Determination of Rate of Oxidation of β-Keto Esters. The β-keto ester (5 mmol) and alkene (0–5 mmol) were dissolved in 10 mL of glacial acetic acid in a flame-dried flask under nitrogen. The solution was heated to 40 °C in a thermostated oil bath. One millimole of $Mn(OAc)_3 \cdot 2H_2O$ was then added to the solution, and the color of the solution was carefully monitored. The dark brown solution became lighter as the Mn(III) was reduced. When the reaction was complete, the solution was colorless to light yellow with variable amounts of white precipitate present.

Oxidative Addition of Methyl Acetoacetate (10a) to 2-Methyl-1-pentene (11). β-Keto ester **10a** (119 mg, 1 mmol), **11** (171 mg, 2 mmol), and $Mn(OAc)_3 \cdot 2H_2O$ (545 mg, 2 mmol) were dissolved in 10 mL of glacial acetic acid. The solution was stirred for 24 h at 40 °C, at which time the solution was colorless and

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

contained a white precipitate. Water was added to give a single cloudy phase in which the precipitate had dissolved. The solution was extracted with three portions of methylene chloride. The combined organic layers were washed several times with saturated $NaHCO_3$ solution and then water and then dried ($MgSO_4$). Evaporation of the solvent gave 203 mg of crude product. Flash chromatography on silica gel (9:1 hexane–EtOAc) gave 61 mg (30%) of **12**, followed by 32 mg (16%) of **13a** as a mixture of alkene isomers and 34 mg (13%) of **14a** as a mixture of diastereomers.

The data for **12**: ^{1}H NMR 3.69 (s, 3), 2.74 (d, 1, J = 14.1), 2.47 (d, 1, J = 14.1), 2.17 (s, 3), 1.60 (t, 2, J = 8.3), 1.43–1.32 (m, 2), 1.33 (s, 3), 0.93 (t, 3, J = 7.2); ^{13}C NMR 167.2, 166.8, 100.6, 88.4, 50.6, 43.4, 40.6, 26.5, 17.0, 14.3, 14.2; IR (neat) 1702, 1646 cm^{-1}. Anal. Calcd for $C_{11}H_{18}O_3$: 198.1256. Found: 198.1250.

The data for **13a**: ^{1}H NMR 5.26–5.15 (m, 1, =CH), 4.79 (br s, 1, $=CH_2$), 4.71 (br s, 1, $=CH_2$); IR (neat) 1745, 1720 cm^{-1}. Anal. Calcd for $C_{11}H_{18}O_3$: 198.1256. Found: 198.1254.

The data for **14a**: ^{1}H NMR 3.75 (s, 3), 3.65 (m, 1), 2.26 (s, 3), 1.3–2.5 (m, 6), 1.94 (s, 3), 1.42 (s, 3), 0.91 (t, 3, J = 7.3); ^{13}C NMR 170.4 (2), 170.0 (2), 83.3, 55.4 and 55.3, 52.6 and 52.5, 40.5 and 40.2, 36.8 and 36.6, 28.6 (2), 23.6 and 23.2, 22.1 (2), 17.0 (2), 14.3 (2), the ketone carbonyl was not observed; IR (neat) 1750–1730 cm^{-1}.

Oxidative Addition of Ethyl 2-Methylacetoacetate (10b) to 2-Methyl-1-pentene (11). Reaction of **10b** (145 mg, 1 mmol), **11** (171 mg, 2 mmol), and $Mn(OAc)_3$·$2H_2O$ (545 mg, 2 mmol) in 10 mL of glacial acetic acid for 55 h at 40 °C followed by normal workup as described above gave 225 mg of crude product. Flash chromatography on silica gel (9:1 hexane–ethyl acetate) gave 81 mg (35%) of **13b** as a mixture of alkene isomers, followed by 13 mg of a mixed fraction containing ca. 7 mg (5%) of **16**, followed by 27 mg of a mixed fraction containing ca. 14 mg (5%) of **14b** as a mixture of diastereomers, followed by 50 mg of a mixed fraction containing ca. 7 mg of **15**.

The data for **13b**: ^{1}H NMR 5.29 (t, 1, J = 4.3), 5.17 (t, 1, J = 4.3), 4.85 (br s, 1), 4.71 (br s, 1); IR (neat) 1744, 1726 cm^{-1}. Anal. Calcd for $C_{13}H_{22}O_3$: 226.1570. Found: 226.1575.

Oxidative Dimerization of Ethyl 2-Methylacetoacetate. Reaction of **10b** (290 mg, 2 mmol) and $Mn(OAc)_3$·$2H_2O$ (1.0838 g, 4 mmol, 2 equiv) in 10 mL of glacial acetic acid for 87 h at 40 °C as described above gave 288 mg of crude product. Flash chromatography on silica gel (4:1 hexane–EtOAc) gave 104 mg (36%) of **16** followed by 98 mg (34% yield) of **15** as a 1:1 mixture of diastereomers and 74 mg (25%) of polar material.

The data for **15**: ^{1}H NMR 4.26–4.20 (m, 4), 2.29 (s, 0.5 × 3), 2.28 (s, 0.5 × 3), 1.57 (s, 0.5 × 3), 1.55 (s, 0.5 × 3), 1.30 (t, 0.5 × 3, J = 7.2), 1.30 (t, 0.5 × 3, J = 7.2); ^{13}C NMR 205.2, 172.6, 172.4, 61.6, 28.41, 28.36, 18.83, 18.79, 13.77; IR (neat) 1735, 1717 cm^{-1}. The data are identical with those previously described.[7]

The data for **16**: ^{1}H NMR 4.27 (q, 2, J = 7.1), 4.18 (q, 2, J = 7.1), 2.41 (s, 3), 2.15 (q, 3, J = 1.5), 1.92 (q, 3, J = 1.5), 1.58 (s, 3), 1.30 (t, 3, J = 7), 1.30 (t, 3, J = 7); ^{13}C NMR 204.1, 169.5, 168.8, 159.2, 114.6, 86.6, 62.3, 60.2, 25.4, 19.1, 17.8, 14.2, 13.8, 12.9; IR (neat) 1753, 1730, 1712, 1639 cm^{-1}. Anal. Calcd for $C_{14}H_{22}O_6$: 286.1417. Found: 286.1413.

Oxidative Cyclization of Keto Ester 1a with Mn(OAc)$_3$·$2H_2O$ and LiCl. A solution of keto ester **1a** (140 mg, 0.7 mmol), $Mn(OAc)_3$·$2H_2O$ (752 mg, 2.8 mmol), and LiCl (120 mg, 2.8 mmol) in 7 mL of glacial acetic acid was stirred at 25 °C overnight. Normal workup of the light brown heterogeneous mixture gave 162 mg of crude product. Flash chromatography of 144 mg on silica gel (10:1 hexane–EtOAc) gave 8 mg (5%) of a 3:1 mixture of the two minor diastereomers of **28a**, followed by 47 mg (28%) of one diastereomer of **28a**, followed by 52 mg (31%) of a second diastereomer of **28a**.

The data for the less polar isomer of **28a**: ^{1}H NMR 4.48 (dd, 1, J = 5.9, 5.4), 3.80 (s, 3), 3.19 (ddd, 1, J = 6.8, 13.7, 15), 2.74 (dddd, 1, J = 2.1, 2.3, 4.6, 15.6), 2.37–2.13 (m, 3), 1.99–1.63 (m, 4), 1.07 (t, 3, J = 7.2); ^{13}C NMR 198.4, 165.8, 79.9, 63.7, 57.0, 54.0, 40.1, 31.6, 23.4, 23.0, 11.7; IR (neat) 1760, 1725 cm^{-1}. Anal. Calcd for $C_{11}H_{16}Cl_2O_3$: 266.0478. Found: 266.0477.

The data for the more polar isomer of **28a**: ^{1}H NMR 4.44 (ddd, 1, J = 9.8, 3.2, 1.6), 3.79 (s, 3), 2.93 (ddd, 1, J = 6.6, 13.1, 14.5), 2.79–2.59 (m, 2), 2.30–1.56 (m, 6), 1.08 (t, 3, J = 6.6); ^{13}C NMR 79.1, 64.8, 59.3, 53.7, 40.0, 27.6, 23.8, 22.7, 12.4, the carbonyl carbons were not observed; IR (neat) 1740 (br) cm^{-1}.

Oxidative Cyclization of Keto Ester 30b with Mn(OAc)$_3$·$2H_2O$ and LiCl. A solution of keto ester **30b** (85 mg, 0.5 mmol), $Mn(OAc)_3$·$2H_2O$ (537 mg, 2.0 mmol), and LiCl (85 mg, 2.0 mmol) in 4 mL of glacial acetic acid was stirred at 50 °C overnight. Normal workup of the light brown heterogeneous mixture gave 88 mg of crude product. The NMR spectrum indicated that a complex mixture of all four diastereomers of **28b** as present: 4.6–4.10 (m, 1), 3.65–3.70 (4 s, 3).

Oxidative Cyclization of Keto Ester 1a with Mn(OAc)$_3$·$2H_2O$, LiCl, and Cu(OAc)$_2$·H_2O. A solution of keto ester **1a** (89 mg, 0.45 mmol), $Mn(OAc)_3$·$2H_2O$ (484 mg, 1.8 mmol), $Cu(OAc)_2$·H_2O (92 mg, 0.45 mmol), and LiCl (77 mg, 1.8 mmol) in 5 mL of glacial acetic acid was stirred at 25 °C overnight. Normal workup gave 102 mg of crude product. Flash chromatography of 96 mg on silica gel (15:1 hexane–EtOAc) gave 20 mg (16%) of **27a**, followed by 5 mg (4%) of a 3:1 mixture of two minor diastereomers of **28a**, followed by 19 mg (16%) of one diastereomer of **28a**, followed by 22 mg (18%) of a second diastereomer of **28a**. The spectral data for the two major diastereomers of **28a** are as described above.

The data for **27a**: ^{1}H NMR 5.44 (dtt, 1, J = 9.6, 8.2, 1.4), 5.29 (dtt, 1, J = 9.6, 7.0, 1.5), 3.92 (s, 3), 2.85 (t, 2, J = 7.2), 2.12–1.98 (m, 4), 1.74 (dq, 2, J = 7.0, 7.2), 0.96 (t, 3, J = 7.2); ^{13}C NMR 194.3, 133.2, 127.3, 62.0, 54.9, 35.1, 26.0, 24.2, 20.5, 14.3, the ester carbonyl was not observed; IR (neat) 1785, 1750 cm^{-1}.

Oxidative Cyclization of Keto Ester 30b with Mn(OAc)$_3$·$2H_2O$, LiCl, and Cu(OAc)$_2$·H_2O. A solution of keto ester **30b** (61 mg, 0.35 mmol), $Mn(OAc)_3$·$2H_2O$ (382 mg, 1.43 mmol), $Cu(OAc)_2$·H_2O (73 mg, 0.36 mmol), and LiCl (60 mg, 1.4 mmol) in 4 mL of glacial acetic acid was stirred at 25 °C overnight. Normal workup gave 71 mg of crude product. Flash chromatography of 43 mg on silica gel (5:1 hexane–EtOAc) gave 11 mg (21%, 43% based on recovered **30b**) of **27b** followed by 19 mg of recovered **30b**: ^{1}H NMR 5.59–5.32 (m, 2), 3.92 (s, 3), 2.90 (t, 2, J = 7.3), 2.45–2.32 (m, 2), 1.65 (d, 3, J = 6.2); ^{13}C NMR 128.3, 126.9, 54.9, 35.8, 27.1, 17.9, the carbonyl carbons and quaternary carbons were not observed; IR (neat) 1770, 1750 cm^{-1}.

Preparation of Ethyl (*E*)-2-Chloro-3-oxo-6-octenoate (30a). The dianion of ethyl 2-chloroacetoacetate (823 mg, 5 mmol) was prepared from sodium hydride (217 mg, 60% dispersion in mineral oil, 5.3 mmol) and butyllithium (3.0 mL of 1.8 M in hexane, 5.33 mmol) in 7 mL of THF by the literature procedure used for formation of the dianion of ethyl acetoacetate.[15] Crotyl bromide (743 mg, 5.5 mmol) was added to this solution at 0 °C, and the resulting solution was stirred for 2 h at 25 °C followed by normal workup to give 1.338 g of crude product. Flash chromatography on silica gel (25:1 hexane–EtOAc) gave 427 mg (39%) of **30a** as a ca. 5:1 mixture of keto and enol tautomers: ^{1}H NMR 12.46 (s, 0.16 × 1, enol H), 5.54–5.30 (m, 2), 4.78 (s, 0.83 × 1), 4.29 (q, 2, J = 7.0), 2.80–2.74 (m, 2), 2.45–2.25 (m, 2), 1.64 (d, 3, J = 5.8), 1.32 (t, 3, J = 7.0); ^{13}C NMR 198.4, 165.0, 128.5, 126.6, 63.1, 61.0, 38.8, 26.4, 17.8, 13.9; IR (neat) 1730 (br) cm^{-1}. Anal. Calcd for $C_{10}H_{15}ClO_3$: C, 54.92; H, 6.91. Found: C, 54.99; H, 7.01.

Preparation of Ethyl 1-Chloro-2-ethenyl-5-oxocyclopentanecarboxylate (32a,b). β-Keto ester **30a** (120 mg, 0.55 mmol) in 2 mL of glacial acetic acid was added to a solution of $Mn(OAc)_3$·$2H_2O$ (294 mg, 1.1 mmol) and $Cu(OAc)_2$·H_2O (110 mg, 0.55 mmol) in 3 mL of glacial acetic acid. The resulting dark brownish-green solution was stirred at room temperature until it turned light bluish-green (≈36 h). The solution was worked up in the usual manner to give 93 mg of crude product. Flash chromatography on silica gel (15:1 hexane–ethyl acetate) gave 9.3 mg (9.5%) of ethyl 6-methylsalicylate (**35**) followed by 10.5 mg (9%) of **32b** and 41.5 mg (35%) of a 4:1 mixture of **32a** and **32b**.

The data for **35**: ^{1}H NMR 11.37 (s, 1, OH), 7.26 (dd, 1, J = 8.5, 8.5), 6.84 (d, 1, J = 8.5), 6.71 (d, 1, J = 8.5), 4.44 (q, 2, J = 7.1), 2.56 (s, 3), 1.44 (t, 3, J = 7.1). The ^{13}C NMR spectral data are identical with those previously described.[16]

The data for **32b**: ^{1}H NMR 5.87 (ddd, 1, J = 17.3, 9.8, 6.5), 5.24 (ddd, 1, J = 17.3, 1.3, 1.3), 5.21 (ddd, 1, J = 9.8, 1.3, 1.3), 4.34–4.26 (m, 2), 3.46 (ddd, 1, J = 11.7, 6.5, 6.5), 2.69 (ddd, 1, J = 18.3, 8.4, 2.4), 2.49–2.35 (m, 1), 2.24–2.00 (m, 2), 1.31 (t, 3, J

(15) Huckin, S. N.; Weiler, L. *J. Am. Chem. Soc.* **1974**, *96*, 1082.
(16) Hauser, F. M.; Pogany, S. A. *Synthesis* **1980**, 814. Weller, D. D.; Haber, A.; Rinehart, K. L., Jr.; Wiley, P. F. *J. Antibiot.* **1978**, *31*, 997.

= 7.0); ^{13}C NMR 133.5, 119.1, 74.2, 63.1, 50.6, 35.2, 24.8, 14.1, the carbonyl carbons were not observed; IR (neat) 1765, 1725, 1645 cm^{-1}.

The data for **32a** were determined from a mixture with **32b**: ^1H NMR 5.86 (ddd, 1, J = 17.2, 10.6, 6.8), 5.30 (ddd, 1, J = 17.2, 1.3, 1.3), 5.26 (ddd, 1, J = 10.6, 1.2, 1.2), 4.35–4.18 (m, 2), 3.12 (ddd, 1, J = 9.5, 6.8, 6.5), 2.72 (ddd, 1, J = 19.2, 7.4, 3.7), 2.58–2.41 (m, 1), 2.25–2.09 (m, 2), 1.28 (t, 3, J = 7.4); ^{13}C NMR 206.6, 165.5, 133.1, 118.8, 74.1, 62.9, 54.8, 35.8, 24.3, 14.1; IR (neat) 1770, 1755, 1715 cm^{-1}.

Anal. Calcd for $C_{10}H_{13}ClO_3$ (**32a** and **32b**): 216.0554. Found: 216.0557.

Preparation of Ethyl 2-Ethenyl-5-oxocyclopentanecarboxylate (32c) by Reduction of 32a,b. Zinc dust (89 mg, 1.36 mmol) was added to a solution of **32a,b** (21 mg, 0.1 mmol) in 0.6 mL of glacial acetic acid. The resulting mixture was stirred for 5 h at 25 °C and filtered to remove unreacted zinc. The residue was washed well with water and CH_2Cl_2. The aqueous layer was separated and extracted with several portions of CH_2Cl_2. The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution, dried ($MgSO_4$), and evaporated to give 15 mg (81%) of pure **32c**: ^1H NMR 5.85 (ddd, 1, J = 17.0, 10.3, 6.9), 5.16 (ddd, 1, J = 17.0, 1.3, 1.3), 5.10 (ddd, 1, J = 10.3, 1.3, 1.3), 4.21 (q, 2, J = 7.0), 3.22 (dddd, 1, J = 11.5, 11.5, 6.5, 6.5), 3.00 (d, 1, J = 11.5), 2.53–2.21 (m, 3), 1.77–1.65 (m, 1), 1.29 (t, 3, J = 7.0); ^{13}C NMR 210.9, 168.7, 138.2, 115.9, 61.4, 60.9, 44.9, 38.1, 27.2, 14.2; IR (neat) 1755, 1725 cm^{-1}. The data correspond closely to those reported for the methyl ester.[17]

Preparation of Ethyl 2-Ethenyl-5-oxocyclopentanecarboxylate (32c) from 30a without the Isolation of 32a,b. β-Keto ester **30a** (120 mg, 0.55 mmol) in 2 mL of glacial acetic acid was added to a solution of $Mn(OAc)_3 \cdot 2H_2O$ (300 mg, 1.12 mmol) and $Cu(OAc)_2 \cdot H_2O$ (110 mg, 0.55 mmol) in 3 mL of glacial acetic acid. The resulting dark brownish-green solution was stirred at room temperature for 48 h. Zinc dust (695 mg, 10.6 mmol) was added to the light bluish-green solution. The resulting mixture was stirred at 25 °C for 5 h and worked up as described above for the preparation of **32c** from **32a,b** to give 79 mg of crude product. Flash chromatography on silica gel (6:1 hexane–EtOAc) gave 16 mg (16%) of **35** followed by 51 mg (51%) of pure **32c**.

Preparation of Ethyl 2-Chloro-7-methyl-3-oxo-6-octenoate (36a,b). The dianion of ethyl 2-chloroacetoacetate (823 mg, 5 mmol) was prepared as described above and treated with prenyl bromide (849 mg, 5.7 mmol) at 0 °C. The resulting solution was stirred for 2 h at 25 °C followed by normal workup to give 1.404 g of crude product. Flash chromatography on silica gel (25:1 hexane–EtOAc) gave 497 mg (43%) of **36a** as a 9:1 mixture of keto and enol tautomers: ^1H NMR 12.41 (s, 0.1 × 1, enol H), 5.06 (br t, 1, J = 7.2), 4.80 (s, 0.9 × 1), 4.29 (q, 2, J = 7.5), 2.73 (m, 2), 2.31 (dt, 2, J = 7, 7.4), 1.68 (br s, 3), 1.62 (br s, 3), 1.32 (t, 3, J = 7.5); ^{13}C NMR 198.5, 164.9, 133.3, 121.7, 63.0, 60.9, 39.0, 25.5, 22.2, 17.5, 13.8; IR (neat) 1730 (br) cm^{-1}. Anal. Calcd for $C_{11}H_{17}ClO_3$: C, 56.77; H, 7.36; Cl, 15.23. Found: C, 56.62; H, 7.43; Cl, 15.11.

Preparation of Ethyl 1-Chloro-2-(1-methylethenyl)-5-oxocyclopentanecarboxylate (39a,b). β-Keto ester **36a** (79 mg, 0.34 mmol) in 1 mL of glacial acetic acid was added to a solution of $Mn(OAc)_3 \cdot 2H_2O$ (183 mg, 0.68 mmol) and $Cu(OAc)_2 \cdot H_2O$ (68 mg, 0.34 mmol) in 3 mL of glacial acetic acid. The resulting dark brownish-green solution was stirred at room temperature until it turned light bluish-green (≈18 h). The solution was worked up in the usual manner to give 65 mg of crude product. Flash chromatography on silica gel (25:1 hexane–ethyl acetate) gave 38 mg (49%) of **39a** and **39b** as a 3:2 mixture of diastereomers: (**39a**) ^1H NMR 4.89 (br s, 1), 4.80 (br s, 1), 4.07 (q, 2, J = 7.0), 3.00 (dd, 1, J = 11.7, 6.0), 2.68–1.95 (m, 4), 1.82 (s, 3), 1.15 (t, 3, J = 7.0); ^{13}C NMR 206.9, 165.7, 140.6, 113.3, 73.8 or 73.0, 62.8, 56.8, 36.1, 23.6, one of 23.2, 23.1, and 22.4, 14.0; (**39b**) ^1H NMR 4.93 (br s, 1), 4.76 (br s, 1), 4.22 (q, 2, J = 7.0), 3.40 (dd, 1, J = 9.3, 6.0), 2.68–1.95 (m, 4), 1.62 (s, 3), 1.22 (t, 3, J = 7.0); ^{13}C NMR 205.3, 167.5, 141.4, 114.3, 73.8 or 73.0, 63.2, 52.7, 35.6, two of 23.2, 23.1, and 22.4, 14.1; IR (neat) 1765, 1750, 1715, 1645 cm^{-1}. Anal. Calcd for $C_{11}H_{15}ClO_3$: C, 57.27; H, 6.55. Found: C, 57.27; H, 6.64.

Preparation of Ethyl 2-(1-Methylethenyl)-5-oxocyclopentanecarboxylate (39c). Zinc dust (42 mg, 0.64 mmol) was added to a solution of **39a,b** (11 mg, 0.05 mmol) in 0.6 mL of glacial acetic acid. The resulting mixture was stirred for 5 h at 25 °C and worked up as described above to give 6 mg (70%) of pure **39c**. The spectral data are identical with those previously described.[18]

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Registry No. **1a**, 71203-73-1; **10a**, 105-45-3; **10b**, 609-14-3; **11**, 763-29-1; **12**, 113704-03-3; **13a** (4-ene isomer), 113704-05-5; **13a** (4-methylene isomer), 113704-04-4; **13b** (4-ene isomer), 113704-09-9; **13b** (4-methylene isomer), 113704-08-8; **14a** (isomer 1), 113704-06-6; **14a** (isomer 2), 113704-07-7; **14b** (isomer 1), 113704-11-3; **14b** (isomer 2), 113704-12-4; **15** (isomer 1), 113704-13-5; **15** (isomer 2), 113704-14-6; **16**, 113704-10-2; **27a**, 113704-17-9; **27b**, 113704-18-0; **28a** (isomer 1), 113704-15-7; **28a** (isomer 2), 113774-51-9; **28a** (isomer 3), 113774-55-3; **28a** (isomer 4), 113774-56-4; **28b** (isomer 1), 113704-16-8; **28b** (isomer 2), 113774-52-0; **28b** (isomer 3), 113774-53-1; **28b** (isomer 4), 113774-54-2; **30a**, 113704-19-1; **30b** (enol), 113704-20-4; **30b**, 62344-14-3; **32a**, 113704-21-5; **32b**, 113704-22-6; **32c**, 67695-10-7; **35**, 6555-40-4; **36a**, 113704-23-7; **36a** (enol), 113704-24-8; **39a**, 113704-25-9; **39b**, 113704-26-0; **39c**, 113704-27-1; $Mn(OAc)_3$, 993-02-2; $Cu(OAc)_2$, 142-71-2; $EtO_2CCHClCOCH_3$, 609-15-4; $BrCH_2CH{=}CHCH_3$, 4784-77-4; $BrCH_2CH{=}C(CH_3)_2$, 870-63-3.

(17) Nugent, W. A.; Hobbs, F. W., Jr. *J. Org. Chem.* **1986**, *51*, 3376. Taber, D. F.; Petty, E. H. *J. Org. Chem.* **1982**, *47*, 4808.

(18) Trost, B. M.; Runge, T. A. *J. Am. Chem. Soc.* **1981**, *103*, 7550.