1265, 1098, 961 $cm^{-1}$. Anal. Calcd for $C_{24}H_{22}O_{10}$: C, 61.27, H, 4.72. Found: C, 61.59; H, 4.65.

**Tetramethyl 1,1,5,5-Tetracyano-1,1a,2,3,5a,5,6,7-octahydro-4,8-dimethylphenanthrene-2,2,6,6-tetracarboxylate (13, *m*-DIB and DDED).** Cycloaddition run in acetonitrile for 3 days. Adventitious polymerization occurred, leading to very low yield (<5%). Mp 182 °C. $^1H$ NMR ($CDCl_3$): $\delta$ 6.80 (dd, $H_{10}$, $J_{10,9}$ = 10 Hz, $J_{10,1a}$ = 3 Hz, 1 H), 6.10 (d, $H_9$, 1 H), 4.19 (s, $H_{5a}$, 1 H), 3.94 ($H_{1a}$, 1 H), 3.93, 3.91, 3.90 (3 s, Me esters, 12 H), 3.20 and 2.85 (2d each, $CH_2$ at $C_3$ and $C_7$, 4 H), 2.06 (d, 3 H), 1.98 (s, 3 H). IR (KBr): 2958, 1742 (s), 1435, 1380, 1266, 1217, 1112 $cm^{-1}$. Anal. Calcd for $C_{28}H_{26}N_4O_8$: C, 61.53; H, 4.80. Found: C, 61.55; H, 5.16.

**Dimethyl 4,4,5,5-Tetracyano-2,3,4,4a,5a,5,6,7-octahydro-1,8-dimethylphenanthrene-3,6-dicarboxylate (14, *p*-DIB and DCA).** Cycloaddition run in acetonitrile at 28 °C for 5 days. Filter off precipitated adduct 14. Yield: 10%. Mp >250 °C. $^1H$ NMR (acetone-$d_6$): $\delta$ 6.55 (s, $H_9$ and $H_{10}$, 2 H), 3.85 (s, Me ester, 6 H), 3.78 (dd, $H_3$ and $H_6$, $J$ = 9.6, 7.8 Hz, 2 H), 3.53 (br s, $H_{4a}$ and $H_{5a}$, 2 H), 2.73 (br d, $CH_2$ at $C_2$ and $C_7$, 4 H), 1.97 (s, Me at $C_1$ and $C_8$, 6 H). IR (KBr): 2960, 1740 (s), 1435, 1264, 1110 $cm^{-1}$. Anal. Calcd for $C_{24}H_{22}N_4O_4$: C, 66.96; H, 5.15; N, 13.02. Found: C, 66.98; H, 5.06; N, 13.08.

**Methyl 2,2-Dicyano-3-methyl-3-(*p*-isopropenylphenyl)-cyclobutane-1-carboxylate (15, *p*-DIB and CDA).** $ZnCl_2$ (0.67 g, 5 mmol) was placed under Ar in a round-bottomed flask and was dried by heating with a Bunsen burner until it melted. DCA (0.77 g, 5 mmol), dry $CHCl_3$ (30mL), and 5 mL of anhydrous ether were added, and the mixture was stirred at rt for 15 min. *p*-DIB (0.85 g, 5 mmol) was added, and a yellow CT complex could be observed. The mixture was stirred overnight at rt and extracted with water to remove $ZnCl_2$. Attempted recrystallizations failed. The cyclobutane adduct could be purified by running it very fast through a short silica gel column (15 cm), using $CHCl_3$ as eluent. After evaporation of the solvent, a sticky solid is obtained. NMR shows the presence of two isomers in a 60:40 ratio. The NMR data for the major isomer are listed, with the data for the minor isomer, if different, (between brackets). $^1H$ NMR ($CDCl_3$): $\delta$ 7.52 ($H_6$, $H_{10}$, *AB*, $J$ = 8.2 Hz, 2 H), 7.16 ($H_7$, $H_9$, *AB*, 2 H) [7.55, 7.27 (AB, $J$ = 8.3 Hz) 2 H], 5.4 (m, $H_{12}$, 1 H), 5.13 (m, $H_{12}$, 1 H), 3.85 (s, Me ester, 3 H) [3.89], 3.84 (dd, $H_1$, $J$ = 8.9, 11.1 Hz, 1 H) [3.63 (dd)], 3.18 (dd, $H_4$, $J$ = 11.1, 11.7 Hz, 1 H), 2.43 (dd, $H_4$, 1 H) [2.73 (dd)], 1.80 (s, Me on $C_3$, 3 H) [1.78 (s)] ppm.

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**Registry No.** 1, 134815-53-5; 2, 134782-06-2; 3, 129371-24-0; 4, 129534-35-6; 5, 13625-25-7; 6, 13592-50-2; 7, 134782-07-3; 8, 134782-08-4; 9, 97186-80-6; 10, 134782-09-5; 11, 134815-54-6; 12, 134815-55-7; 13, 134782-10-8; 14, 134782-11-9; 15, 134782-12-0; *m*-DVB, 108-57-6; TCNE, 670-54-2; *m*-DIB, 3748-13-8; *p*-DVB, 105-06-6; *p*-DIB, 1605-18-1; MA, 108-31-6; CMA, 69327-00-0; DDED, 82849-49-8; DCA, 82849-50-1.

**Supplementary Material Available:** Experimental procedures for *p*-divinylbenzene, *p*-diisopropenylbenzene, and *m*-divinylbenzene and $^1H$ NMR spectra for 5-7 and 15 (5 pages). Ordering information is given on any current masthead page.

# Solvent Effects on Manganese(III)-Based Oxidative Free-Radical Cyclizations: Ethanol and Acetic Acid

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Ethanol complements the typical solvent, acetic acid, for Mn(III)-based oxidative free-radical cyclizations. Cyclization of enol ether **1c** to give gibberellic acid intermediate **6c** is successful in ethanol, but not in acetic acid. Ethanol acts as a reducing agent for primary radicals, converting **13** and **33** to alkanes **17** and **32**. Acetylenes can be used as substrates since the vinyl radicals **24** and **25** are reduced by ethanol to alkenes **26-28**. The 1-hydroxyethyl radical obtained from ethanol is oxidized to acetaldehyde by Mn(III). The effect of solvent on the oxidative cyclization of unsaturated $\beta$-keto esters **35** and **48** was examined. A higher percentage of 5-exo product is obtained in ethanol. The primary cyclopentanemethyl radicals **40** and **53** are oxidized mainly to alkenes **43** and **57** in ethanol and mainly to the alcohols **42** and **55** and lactones **41** and **58** in acetic acid.

## Introduction

Free-radical cyclizations of alkenes provide a valuable method for the synthesis of cyclic compounds.[1] We have recently developed an efficient oxidative free-radical cyclization using $Mn(OAc)_3$[2] to oxidize a $\beta$-keto ester, 1,3-diketone, or 1,3-diester to an enol radical that undergoes efficient cyclization to a double bond.[3] The reaction is terminated by oxidation of the radical to an alkene with $Cu(OAc)_2$. Mono, tandem, and triple cyclizations can be carried out in high yield. Tandem oxidative cyclization of acetoacetate **1a** provides 86% of bicyclo[3.2.1]octanone **6a**. Acetic acid has been the solvent of choice of these reactions and earlier studies involving intermolecular addition reactions of radicals generated by $Mn(OAc)_3$, since acetic acid dissolves both organic compounds and Mn(O-

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(3) For previous papers in this series see: (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. *Ibid.* **1987**, *28*, 845. (d) Snider, B. B.; Patricia, J. J.; Kates, S. A. *J. Org. Chem.* **1988**, *53*, 2137. (e) Snider, B. B.; Dombroski, M. A. *J. Org. Chem.* **1987**, *52*, 5487. (f) Snider, B. B.; Patricia, J. J. *J. Org. Chem.* **1989**, *54*, 38. (g) Merritt, J. E.; Sasson, M.; Kates, S. A.; Snider, B. B. *Tetrahedron Lett.*, **1988**, *29*, 5209. (h) Kates, S. A.; Dombroski, M. A.; Snider, B. B. *J. Org. Chem.* **1990**, *55*, 2427. (i) Dombroski, M. A.; Kates, S. A.; Snider, B. B. *J. Am. Chem. Soc.* **1990**, *112*, 2759.

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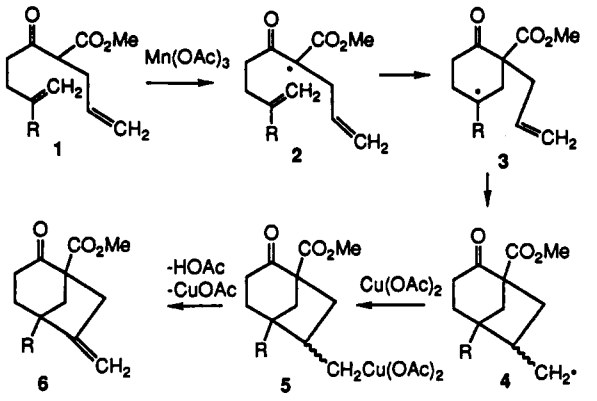
$Ac)_3$ and Mn(III) is unstable in solutions containing significant amounts of water.[2]

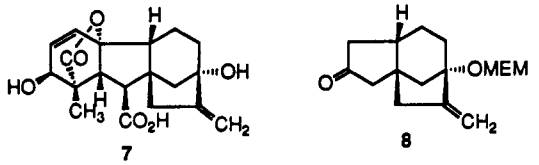



a, R = $CH_3$ b, R = $OPO(OCH_2CH_3)_2$ c R = $OCH_2OCH_2CH_2OCH_3$

We report here studies demonstrating that ethanol is an attractive alternative solvent for $Mn(OAc)_3$ oxidative free-radical cyclizations. Acid-sensitive enol ethers can be used in ethanol, but not in acetic acid.[4] Cyclization of 5-hexenyl radicals gives a higher percentage of 5-exo product in ethanol than in acetic acid. Oxidation of primary cyclopentanemethyl radicals with $Cu(OAc)_2$ gives predominantly alkene in ethanol and mainly alcohol and lactone in acetic acid. Finally, ethanol can act as a hydrogen atom donor efficiently reducing primary and vinyl radicals to alkanes and alkenes, respectively.

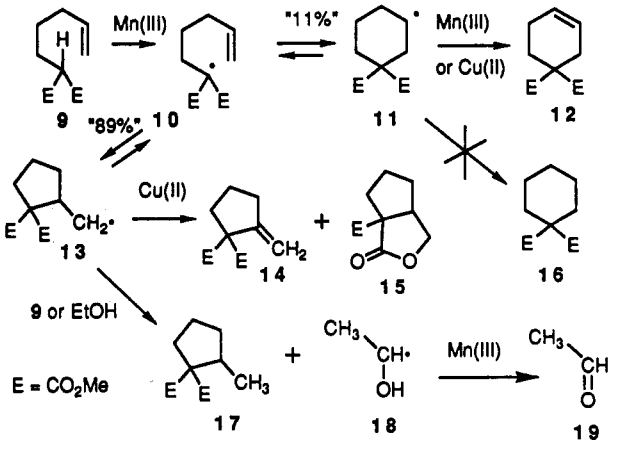
## Results and Discussion

**Preparation of Gibberellic Acid Intermediate 6c.** Methylenebicyclo[3.2.1]octane **6a** closely resembles the CD ring system of gibberellic acid (**7**); oxidative cyclization should provide an efficient route to synthetic intermediates for gibberellic acid synthesis. Corey and co-workers reported the first total synthesis of gibberellic acid, which proceeds through intermediate **8**.[5,6] The ketone and ester




groups of **6** provide functionality that will permit elaboration of the cyclopentanone of **8**. However, the allylic oxygen of **8** must be introduced by cyclization of an enol ether or ester. We have previously reported that alkylation of the dianion of methyl 2-allylacetoacetate with 3-chloro-2-((diethylphosphoryl)oxy)propene gives 55% of enol phosphate **1b**, which undergoes cyclization with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ in acetic acid to give 77% of **6b**.[3i] Unfortunately, hydrolysis of the phosphate ester has been problematic. We therefore chose to prepare and cyclize **1c**. Alkylation of the lithium dianion of methyl allylacetoacetate[7] in the presence of 2 equiv of HMPA with 3-chloro-2-((2-methoxyethoxy)-methoxy)propene, prepared by the literature procedure for the corresponding MOM ether,[8] affords 39% of **1c**. Attempted oxidative cyclization of **1c** in acetic acid at 25 °C was unsuccessful. The only isolable product is the ketone resulting from hydrolysis of the MEM enol ether. Use of lower reaction temperatures or KOAc as a buffer were also unsuccessful. Fortunately, oxidative cyclization in ethanol is successful. Reaction of **1c** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ in ethanol (0.2 M) for 13 h at 60 °C affords 52% of **6c**, which contains the fully functionalized CD ring system of gibberellic acid. Although the rate of oxidation in ethanol is considerably slower than in acetic acid, the enol ether is not hydrolyzed.

**Oxidative Cyclization of Dimethyl 4-Pentenylmalonate (9) in Acetic Acid.** In a collaborative study with Curran and co-workers we established that Mn(III)-based oxidative cyclizations and atom-transfer cyclizations give the same mixtures of stereoisomers in a variety of cases, strongly suggesting that Mn(III)-based oxidative cyclizations proceed through a manganese-free free radical such as **2** or **10**.[9] Oxidative cyclization of malonate ester **9** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ in acetic acid at 55 °C gives 48% of **15**, 20% of **14**, and 7% of **12**.[9] Oxidation of **9** gives radical **10**, which cyclizes to a 9:1 mixture of **13** and **11** as has been observed in atom-transfer cyclizations.[10] Oxidation of **13** with Cu(II) gives **14** and **15**. Oxidation of **11** with Mn(III) or Cu(II) gives **12**.




We examined the Mn(III)-based oxidative cyclization of **9**, without Cu(II) as a cooxidant, with the expectation that a greater percentage of products derived from the cyclohexyl radical **11** would be isolated. Julia has shown in the cyclizations of related cyanoacetates that 5-exo cyclization to give a cyclopentanemethyl radical is kinetically preferred. However, cyclohexanes, derived from reduction of the more stable secondary radical, are the major products. In Julia's examples the cyclization is readily reversible, since the acyclic radical is stabilized by two electron-withdrawing groups and reduction of the cyclic radical is slow.[11] Primary radicals such as **13** are not oxidized by Mn(III). In the absence of Cu(II) or an efficient hydrogen atom donor, we expected that ring opening of **13** to regenerate **10** might be faster than other reactions of **13**.

(4) Alkyl enol ethers have been used successfully in acetic acid in intermolecular additions: (a) Corey, E. J.; Ghosh, A. K. *Tetrahedron Lett.* **1987**, *28*, 175. (b) Corey, E. J.; Ghosh, A. K. *Chem. Lett.* **1987**, 223.

(5) Danheiser, R. L. In *Strategies and Tactics In Organic Synthesis*: Lindberg, T., Ed.; Academic Press: Orlando, FL, 1984; pp 21–70. Corey, E. J.; Munroe, J. E. *J. Am. Chem. Soc.* **1982**, *104*, 6129. Stork, G.; Boeckman, R. K., Jr.; Taber, D. F.; Still, W. C.; Singh, J. *J. Am. Chem. Soc.* **1979**, *101*, 7107.

(6) For a review of Gibberellic acid syntheses see: Mander, L. N. *Nat. Prod. Rep.* **1988**, *5*, 541.

(7) Huckin, S. N.; Weiler, L. *J. Am. Chem. Soc.* **1974**, *96*, 1082.

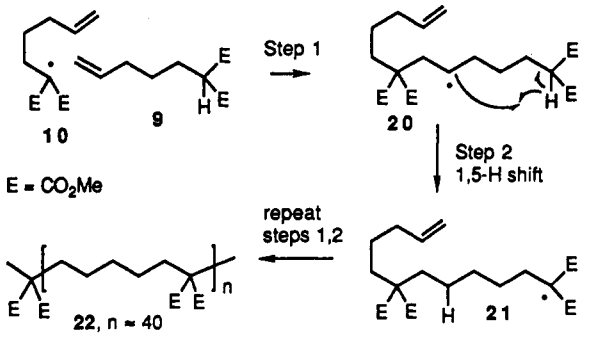
(8) Gu, X.-P.; Nishida, N.; Ikeda, I.; Okahara, M. *J. Org. Chem.* **1987**, *52*, 3192.

(9) Curran, D. P.; Morgan, T. M.; Schwartz, C. E.; Snider, B. B.; Dombroski, M. A. *J. Am. Chem. Soc.*, in press.

(10) Curran, D. P.; Chang, C.-T. *J. Org. Chem.* **1989**, *54*, 3140.

(11) Julia, M. *Acc. Chem. Res.* **1971**, *4*, 386.

Oxidative cyclization of **9** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ in acetic acid at 55 °C gives 16% of methylcyclopentane **17**, 4% of cyclohexene **12**, and 75% of a polar white polymer characterized as **22**. The $^{13}C$ NMR spectrum of **22** showed only the six peaks expected for this symmetrical structure. We confirmed that the product was not simply dimethyl 1,1-cyclohexanedicarboxylate (**16**), which could be formed by reduction of **11**, by comparison with an authentic sample.[12] The molecular weight of **22** was determined to be 8106 g/mol by vapor-phase osmometry, indicating that the number of units in the polymer is approximately 40. The polymeric structure of **22** is confirmed by $T_1$ measurements. In general, $T_1$ values decrease as the size of the molecule increases, since the increase in correlation time facilitates dipole–dipole relaxation.[13] The $T_1$ values of the carbons of **22** are 10 times smaller than of the monomer **16**. For instance, the $T_1$ values of the methylene carbons are 0.13–0.16 s for **22** and 1.6–1.8 s for **16**.




Oxidation of **9** gives **10**, which undergoes the expected cyclization to **11** and **13**. Cyclohexyl radical **11** is oxidized to cyclohexene **12** by Mn(III). Primary radical **13** is not oxidized; instead, it abstracts a hydrogen from a second molecule of **9** to give cyclopentane **17**.[10] This process is inefficient, and the major process is ring opening to regenerate **10**, which then adds to a second molecule of **9**, in the first step of a propagation sequence, to generate **20**. The second step in the propagation sequence is a 1,5-hydrogen atom shift to give stabilized radical **21**. Analogous 1,5-hydrogen shifts have been observed in the telomerization of dimethyl malonate and ethylene.[14] Cyclization of **20** by either a 7-exo or 8-endo pathway should be much slower than the 1,5-hydrogen shift. Polymer should be formed once radical **10** adds to **9** to give **20**, since cyclization is no longer possible. Many repetitions of these two propagation steps generate polymer **22**.

Only a catalytic quantity of $Mn(OAc)_3 \cdot 2H_2O$ should be required, if the structure of **22** and the mechanism proposed for its formation are correct, since Mn(III) is consumed only in the initial generation of **10**. Reaction of **9** with 0.5, rather than 2, equiv of $Mn(OAc)_3 \cdot 2H_2O$ affords 4% of **17**, 5% of **12**, and 81% of polymer **22**, indicating that the reaction is catalytic in Mn(III), as required by the proposed mechanism and structure of polymer **22**.

**Oxidative Cyclization of Dimethyl 4-Pentenylmalonate (9) in Ethanol.** We examined the oxidative cyclization of **9** with Mn(III) in ethanol to determine whether the solvent would affect the ratio of products or the nature of the termination process. To our surprise, treatment of **9** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ in ethanol at 55 °C gives 40% of methylcyclopentane **17** and 15% of recovered **9** as the only products. Reduction of primary radical **13** is apparently much more efficient in ethanol than in acetic acid.[15] Some of **17** may be formed by transfer of a hydrogen from another molecule of **9**. The major pathway is presumably transfer of a hydrogen atom from ethanol to **13** to give **17** and α-hydroxyethyl radical (**18**), which is rapidly oxidized by Mn(III) to acetaldehyde (**19**).[16]

Two equivalents of Mn(III) are required for the formation of **17** by this mechanism since Mn(III) is consumed in the formation of **10** and the oxidation of **18** to **19**. Oxidative cyclization of **9** with 0.5, rather than 2, equiv of $Mn(OAc)_3 \cdot 2H_2O$ in ethanol gives a 1:3 mixture of **17** and recovered **9** confirming that production of **17** in ethanol consumes 2 equiv of Mn(III) even though there is no net oxidation of substrate.

**Oxidative Cyclization of Acetylenic β-Keto Esters.** Cossy and Leblanc reported that allyl and propargyl β-keto amides undergo oxidative cyclization, with reduction of the cyclic radical, on treatment with Mn(III).[17,18] They found that better results were obtained in ethanol than in acetic acid or acetonitrile and that higher yields were obtained with anhydrous $Mn(OAc)_3$ than with $Mn(OAc)_3 \cdot 2H_2O$. Our results with malonate cyclizations in ethanol suggest that better yields are obtained in ethanol since it is able to function as an efficient hydrogen atom donor for the vinyl radical.[15] We chose to examine the effect of solvent on the oxidative cyclization of acetylenic β-keto ester **23**.

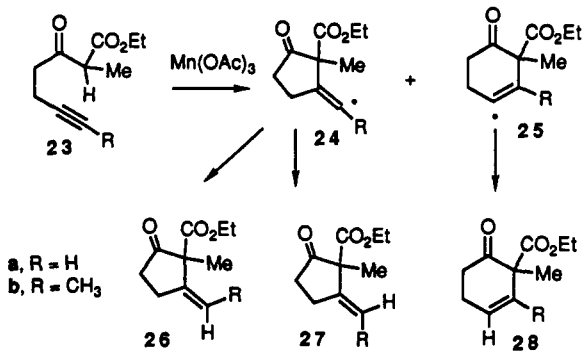
Treatment of **23a** with 2 equiv of anhyd $Mn(OAc)_3$ in ethanol for 21 h at 25 °C gives 32% of a 1.6:1 mixture of **27a** and **28a**. Similar product mixtures are obtained when $Cu(OAc)_2 \cdot H_2O$ is used as a cooxidant. Oxidation and cyclization affords a mixture of cyclic radicals **24a** and **25a**. Vinyl radicals are not efficiently oxidized by either Mn(III) or Cu(II). The only effective means of termination is hydrogen transfer from ethanol or substrate to give **27a** and **28a**. Preparation of cyclic products should consume 2 equiv of Mn(III), even though no net oxidation of substrate is taking place, since ethanol is oxidized to acetaldehyde. This was confirmed by oxidation with only 0.5 equiv of anhyd $Mn(OAc)_3$, which gives a 3:1 mixture of recovered **23a** and products (**27a** and **28a**). The role of the solvent in the reduction of **24a** and **25a** was confirmed by use of deuterium-labeled solvent. No deuterium was incorporated when ethanol-OD was used as solvent, indicating that exchange of the α-proton of acetoacetate **23a** is not important. Use of ethanol-$d_6$ as solvent resulted in quantitative, stereorandom deuterium incorporation into the methylene hydrogens of **27a** and 67% deuterium incorporation into the expected hydrogen of **28a** as shown by examination of the $^1H$ NMR spectra. Reaction in ethanol-$d_6$ proceeded in lower yield and gave more complex mixtures of products. This is expected since deuterium transfer will be much slower than hydrogen transfer ($k_H/k_D$ = 3–7 for related hydrogen transfers)[19] permitting reactive

(12) Wightman, W. A. *J. Chem. Soc.* **1926**, 2541.
(13) Breitmaier, E.; Voelter, W. *Carbon-13 NMR Spectroscopy*; VCH: Weinheim, FRG, 1987; pp 166–168.
(14) Freidlina, R. K.; Terent'ev, A. B. *Acc. Chem. Res.* **1977**, *10*, 9.
(15) The methyl radical abstracts a hydrogen atom slowly from acetic acid ($k = 2 \times 10^2$ $M^{-1}$ $s^{-1}$) and acetonitrile ($k < 3 \times 10^2$ $M^{-1}$ $s^{-1}$) and more rapidly from the hydroxyl-bearing carbon of 2-cyanoethanol ($k < 1.6 \times 10^3$ $M^{-1}$ $s^{-1}$): Gilbert, B. C.; Norman, R. O. C.; Placucci, G.; Sealy, R. C. *J. Chem. Soc., Perkin Trans. 2* **1975**, 885. The methyl radical abstracts a hydrogen atom from ethanol to give the 1-hydroxyethyl radical ($k = 5.9 \times 10^2$ $M^{-1}$ $s^{-1}$): Thomas, J. K. *J. Phys. Chem.* **1967**, *71*, 1919.
(16) The 1-hydroxyethyl radical is oxidized to acetaldehyde by a variety of metals with rate constants of $10^6$–$10^8$ $M^{-1}$ $s^{-1}$: Asmus, K.-D.; Bonifacic, M. In *Landolt-Börnstein New Series, Group 2*; Fischer, H., Ed.; Springer Verlag: Berlin, 1984; Vol. 13b, pp 311–313.
(17) Cossy, J.; Leblanc, C. *Tetrahedron Lett.* **1989**, *30*, 4531.
(18) Alkynes have been used with modest success in intermolecular additions.[2b]
(19) Burchill, C. E.; Thompson, G. F. *Can. J. Chem.* **1971**, *49*, 1305.

Table I. Oxidative Cyclization of 35

| substrate | solvent | 38 (%) | 39 (%) | 6-endo:5-exo | 41 (%) | 42 (%) | 43 (%) |
|---|---|---|---|---|---|---|---|
| 35a | ethanol | 17 | 17 | 1:1.9 | 0 | 5 | 61 |
| 35a | acetic acid | 43 | 9 | 1:0.9 | 5 | 25 | 18 |
| 35b | ethanol | 8 | 21 | 1:2.4 | 0 | 0 | 71 |
| 35b | acetic acid | 39 | 10 | 1:0.9 | 14 | 17 | 19 |

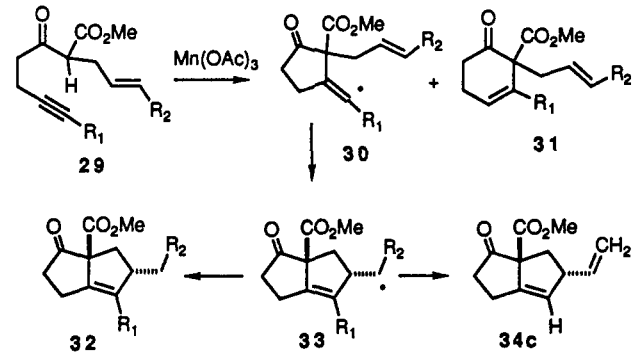
vinyl radicals **24a** and **25a** to undergo undesired side reactions.




Not surprisingly, since acetic acid is a weaker hydrogen donor,[15] cyclization of **23a** proceeds in low yield in acetic acid giving a 9% yield of a 1:6.3 mixture of **27a** and **28a**. Cyclization with $Mn(OAc)_3 \cdot 2H_2O$ in ethanol was slower than with the anhydrous reagent. Since **27a** decomposed at extended reaction times, lower yields of product mixtures richer in **28a** were isolated.

The oxidative cyclization of **23b** was investigated since introduction of a terminal methyl group should favor 5-exo cyclization at the expense of 6-endo cyclization.[1,20] Treatment of **23b** with 2 equiv of anhyd $Mn(OAc)_3$ in ethanol affords 66% of a 1:2.6 mixture of **26b** and **27b**. The assignment of stereochemistry follows from the $^{13}C$ NMR spectra. The ring methylene carbons of **26b** absorb at $\delta$ 37.9 and 28.5, close to the values of $\delta$ 37.5 and 28.0 for **27a**. The ring methylene carbons of **27b** absorb at $\delta$ 37.2 and 23.6; the allylic carbon is shifted upfield 4–5 ppm by the cis methyl group. Cyclization occurs exclusively to give the 5-exo radical **24b**. Hydrogen transfer occurs with modest selectivity from the more hindered side of the alkenyl radical to give the more stable product **27b**. The increase in yield in the cyclization of **23b** (66%) as compared to **23a** (32%) is probably due to the instability of methylenecyclopentane **27a**.

Tandem oxidative cyclizations of dienyl acetoacetates proceed in excellent yield.[3i] We therefore investigated the tandem cyclization of **29** in which the first cyclization is to an acetylene.[21] Treatment of **29a** with anhyd $Mn(OAc)_3$ and $Cu(OAc)_2 \cdot H_2O$ in ethanol affords a complex mixture of largely polymeric products. We believe that cyclization occurs to give mainly **30a**, which undergoes the expected cyclization to give **33a**. Oxidation of **33a** by Cu(II) will give a conjugated diene that is not stable to the reaction conditions. We therefore repeated the reaction under conditions designed to reduce radical **33**. Treatment of **29a** with anhyd $Mn(OAc)_3$ in ethanol, without $Cu(OAc)_2 \cdot H_2O$ as a cooxidant, provides 20% of a 2:1 mixture of **32a** and **31a**. In the absence of Cu(II) primary radical **33a** is reduced to a single stereoisomer of **32a**. Similar cyclization of **29b** afforded 35% of a single stereoisomer of **32b**. The first cyclization will now give exclusively the secondary 5-exo radical **30b**, which cyclizes to **33b** as a single stereoisomer.




a, $R_1 = R_2 = H$; b, $R_1 = CH_3$, $R_2 = H$; c, $R_1 = H$, $R_2 = CH_3$

The cyclization of **29c** was investigated in the presence of Cu(II) since oxidative cyclization of secondary radical **33c** should give the less substituted alkene **34c** selectivity.[22] Diene **34c** is not conjugated and should therefore be stable to the reaction conditions. Oxidative cyclization of **29c** with 2 equiv of anhyd $Mn(OAc)_3$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ in ethanol affords 32% of a single stereoisomer of vinylbicyclo[3.3.0]octene **34c** and 15% of cyclohexene **31c**.

The cyclization of **30** gives only a single side-chain stereoisomer of **33**, which is converted to **32a**, **32b**, and **34c**. MM2 calculations suggest that cyclization with the ester and side chains trans should be preferred by 0.97 kcal/mol for **32a** and 0.70 kcal/mol for **32b**.[23] The coupling constants also suggest that the ester and side chains are trans. MM2 calculations predict that the allylic methine hydrogen of **32b** will be coupled to the adjacent methylene group with $J$ = 8.2 and 1.0 Hz for the cis isomer and $J$ = 10.9 and 6.7 Hz for the trans isomer shown.[23] The actual values of 9.1 and 6.4 Hz fit closely with those predicted for the trans isomer.

**Solvent Effects on the Cyclization of 35.** Oxidative cyclization of **23a** gives a mixture rich in methylenecyclopentane **27a** in ethanol and a mixture rich in cyclohexene **28a** in acetic acid. Although the very low yield of products in acetic acid limits the significance of these observations, they raised the question of solvent effects on the regiochemistry of the cyclization. We therefore examined the oxidative cyclizations of **35** and **48** with 2 equiv of anhyd $Mn(OAc)_3$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ in both ethanol and acetic acid.

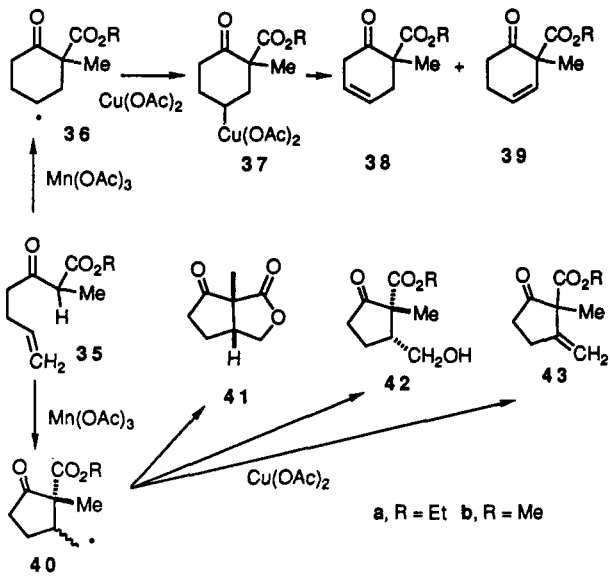
The results of the cyclization of **35** are shown in Table I. Oxidation and cyclization will give cyclohexyl radical

(20) (a) Beckwith, A. L. J. In *Landolt-Börnstein, New Series, Group 2*; Fischer, H., Ed.; Springer-Verlag: Berlin, 1984; Vol. 13a, pp 252–317. (b) Beckwith, A. L. J.; Blair, A. I.; Phillipou, G. *Tetrahedron Lett.* **1974**, 2251. (c) Beckwith, A. L. J.; Phillipou, G.; Serelis, A. K. *Tetrahedron Lett.* **1981**, *22*, 2811. (d) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925.

(21) For tandem cyclizations in which the first addition is to an acetylene see: Stork, G.; Mook, R., Jr. *J. Am. Chem. Soc.* **1983**, *105*, 3720. Journet, M.; Magnol, E.; Agnel, G.; Malacria, M. *Tetrahedron Lett.* **1990**, *31*, 4445.

(22) Kwon, T.; Snider, B. B. *J. Org. Chem.* **1990**, *55*, 1965.

(23) MMX, obtained from Serena Software, 489 Serena Lane, Bloomington, IN 47401 was used on a VAX 6420. 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.

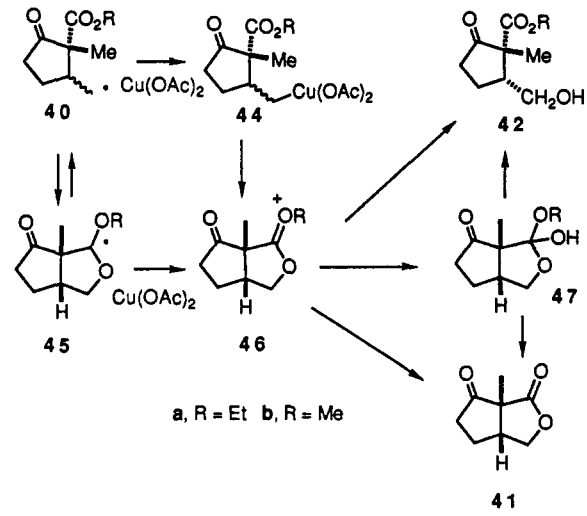



36, which is oxidized by Cu(II) to give cyclohexenes **38** and **39**, and cyclopentanemethyl radical **40**, which is oxidized by Cu(II) to give lactone **41**,[24] alcohol **42**, and methylenecyclopentane **43**. The ratio of products was determined by analysis of the $^1H$ and $^{13}C$ NMR spectra and GC analysis. The partial or complete lactonization of alcohols **42** and **55** during GC and silica gel chromatography complicated the analysis.

Cyclization of ethyl ester **35a** in acetic acid gives a 1:0.9 ratio of products derived from 6-endo and 5-exo cyclization. In ethanol, the ratio of 6-endo to 5-exo cyclization decreases to 1:1.9. There are other significant effects of the solvent on the products obtained. In ethanol, oxidation of cyclohexyl radical **36a** by Cu(II) gives a 1:1 mixture of **38a** and **39a**. In acetic acid, oxidation gives a 4.8:1 mixture of **38a** and **39a**. Even more remarkable is the effect of solvent on the products derived from cyclopentanemethyl radical **40a**.

In ethanol, methylenecyclopentane **43a** is formed almost exclusively from cyclopentanemethyl radical **40a**. In acetic acid, primary alcohol **42a** is the major product and lactone **41**[24] is also formed. The oxidation of **40** by Cu(II) in acetic acid is atypical since the ester participates in the reaction. Oxidation of the cyclopentanemethyl radical by $Cu(OAc)_2$ gives only methylenecyclopentane. Presumably radical **40a** reacts with Cu(II) in ethanol to give **44a**, which undergoes oxidative $\beta$-hydride elimination to give **43a**. The origin of **41** and **42a** in acetic acid is less clear. It is possible that **44a** cyclizes to **46a** with loss of Cu(I). Alternatively, **40a** could cyclize reversibly to **45a**, which could be oxidized by Cu(II) to **46a**. $S_N2$ attack of adventitious water on the methylene carbon of **46a** would give alcohol **42a**. $S_N2$ attack of any nucleophile on the R group would give lactone **41**. A more likely mechanism involves addition of adventitious water to the carbonyl group to give hemiortho ester **47**, which could lose ROH to give lactone **41** or open to give alcohol **42**.

If lactone **41** and alcohol **42** are formed from hemiortho ester **47**, the ratio of **41** to **42** should not depend on the nature of R. If lactone **41** or alcohol **42** are formed directly from **46**, the ratio of **41** to **42** should depend on the nature



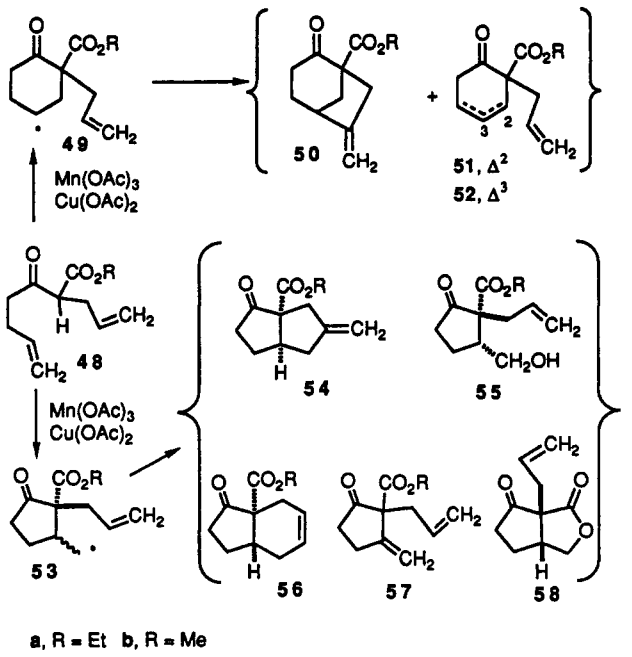

of R. We therefore examined the cyclization of methyl ester **35b**, which gives similar product ratios to ethyl ester **35a** as shown in Table I. The methyl ester gives slightly more 5-exo products in both solvent and more **39b** in ethanol. The one significant difference is the ratio of alcohol and lactone obtained in acetic acid. A 5:1 ratio of alcohol **42a** and lactone **41** are obtained from ethyl ester **35a**. A 1.3:1 mixture of alcohol **42b** and lactone **41** are obtained from methyl ester **35b**. Although lactone formation is favored with the methyl ester the effect is small, suggesting that hemiortho ester **47** is an intermediate.

Cyclopentanemethyl radical **40** should be formed as a mixture of diastereomers. Since the trans-fused stereoisomer of lactone **41** is very strained, only the isomer of **40** with the methylene group cis to the ester can form **41**. Since alcohol **42** cyclizes to lactone **41**, the hydroxymethyl group of alcohol **42** must also be cis to the ester. The formation of a single stereoisomer of **42** is expected if the alcohol is formed by hydrolysis of **46** or hemiortho ester **47**, because the trans-fused stereoisomers of **46** and **47** are very strained. On the basis of related cyclizations we expected that **40** would be formed as a 2–3:1 mixture of stereoisomers.[3h] The major isomer of **40** with the methylene group cis to the ester can give **41–43**. The minor isomer with the methylene group trans to the ester can only form methylenecyclopentane **43**. Since the ratio of **41** + **42**:**43** is $\approx$1.6:1 in acetic acid, the cyclization leading to **40** must give a >1.6:1 mixture of stereoisomers favoring the isomer with the methylene group cis to the ester.

**Oxidative Cyclization of 48.** The effect of solvent on the regiochemistry of the cyclization was also examined with acetoacetate **48**, which undergoes tandem cyclizations.[3i] Oxidative cyclization will give cyclohexyl radical **49**, which can either undergo a second cyclization, followed by oxidation to give **50**, or react with Cu(II) to give cyclohexenes **51** and **52**. Cyclopentanemethyl radical **53** will be oxidized to methylenecyclopentane **57**, alcohol **55**, and lactone **58**[24] as previously described. The minor isomer of **53**, with a $\beta$-methylene group, should cyclize rapidly to methylenebicyclo[3.3.0]octane **54**. The major isomer of **53**, with an $\alpha$-methylene group, should cyclize very slowly to a highly strained trans-fused bicyclo[3.3.0]octane; 6-endo cyclization to give indene **56** should occur at a moderate rate.

The results of these cyclizations are shown in Table II. A 1:0.6 ratio of 6-endo and 5-exo products is obtained in acetic acid; as in the cyclization of **35**, use of ethanol favors the 5-exo cyclization leading to a 1:1 mixture of 6-endo and 5-exo products. Replacement of the $\alpha$-methyl group of **35** with the allyl group of **48** increases the preference for the

(24) For the synthesis of related lactones see: Boeckman, R. K., Jr.; Naegely, P. C.; Arthur, S. D. *J. Org. Chem.* **1980**, *45*, 752. Goldsmith, D. J.; Thottathil, J. K. *Tetrahedron Lett.* **1981**, *22*, 2447. White, W. L.; Anzeveno, P. B.; Johnson, F. *J. Org. Chem.* **1982**, *47*, 2379. Boeckman, R. K., Jr.; Napier, J. J.; Thomas, E. W.; Sato, R. I. *J. Org. Chem.* **1983**, *48*, 4152.




a, R = Et b, R = Me

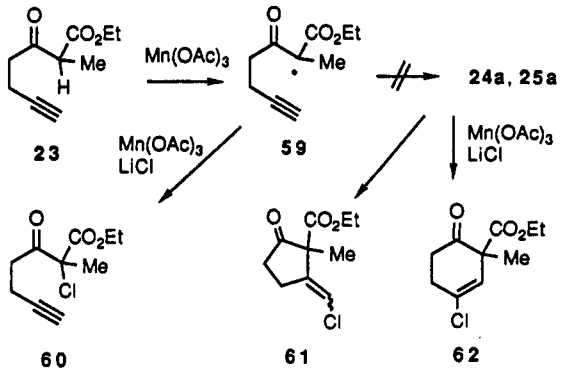
formation of 6-endo products in both solvents. Apparently, the 5-exo cyclization is more sensitive to steric hindrance; a larger $\alpha$-alkyl group favors 6-endo cyclization. The other solvent effects observed with **35** are also apparent here. Methylenecyclopentane **57** is formed in ethanol but not in acetic acid, and a greater percentage of lactone **58** is formed from the methyl ester than the ethyl ester.

The reasons for the increase in 5-exo cyclization in ethanol are not clear. However, the difference between a 1:1 and 1:0.6 mixture, while synthetically significant, is energetically quite small. Therefore, solvent effects on the regiochemistry will be observed only when the energetics of 5-exo and 6-endo cyclization are similar. Cyclization of radical **2c** gives only 6-endo radical **3c** in ethanol because of the directing effect of the ether.

The formation of small quantities of **51** and **52** by Cu(II) oxidation of **49** is surprising since the corresponding tertiary radical **3a** with a methyl group on the radical center cyclizes to the bicyclo[3.2.1]octane **6a** in quantitative yield. We have also observed that secondary, but not tertiary radicals, are oxidized prior to the second cyclization in the formation of bicyclo[4.2.1]nonanes and bicyclo[5.2.1]decanes.[3g] These observations are counterintuitive. Oxidation of the tertiary, rather than the secondary, radical should be electronically favored. Mn(III) oxidizes tertiary radicals rapidly to cations and oxidizes secondary radicals slowly. Furthermore, cyclization of the more hindered tertiary radical should not be faster than cyclization of the secondary radical. By a process of elimination, the oxidation of a secondary radical by Cu(II) must be faster than oxidation of a tertiary radical by either Mn(III) or Cu(II), presumably due to increased steric hindrance to oxidation of the tertiary radical. There is some precedent for this hypothesis. Oxidation of the primary 2-hydroxyethyl radical to ethylene oxide by Cu(II) proceeds with a rate constant of $2 \times 10^7$ $M^{-1}$ $s^{-1}$. Oxidation of the tertiary 3-hydroxy-2-methyl-2-propyl radical to isobutylene oxide by Cu(II) is almost 1 order of magnitude slower with a rate constant of $3 \times 10^6$ $M^{-1}$ $s^{-1}$.[25]

**Oxidative Cyclization of Malonate 9 in Ethanol with Cu(II).** Oxidation of cyclopentanemethyl radicals **40** and **53** with Cu(II) affords mainly methylenecyclopentanes **43** and **57** in ethanol and mainly alcohols **42** and **55** and lactones **41** and **58** in acetic acid. If this solvent effect is general, different mixtures of products should be obtained from the oxidation of cyclopentanemethyl radical **13** in ethanol and acetic acid. As indicated above, oxidation of malonate **9** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ in acetic acid affords a 2.4:1 mixture of lactone **15** and methylenecyclopentane **14**.[9] Oxidative cyclization of **9** for 6.5 d at 60 °C in ethanol affords 4% of cyclohexene **12**, 22% of methylenecyclopentane **14**, 14% of lactone **15**, and 26% of recovered malonate **9**. Oxidative cyclization is slower in ethanol, but, as anticipated, methylenecyclopentane **14** is now the major product from radical **13**.

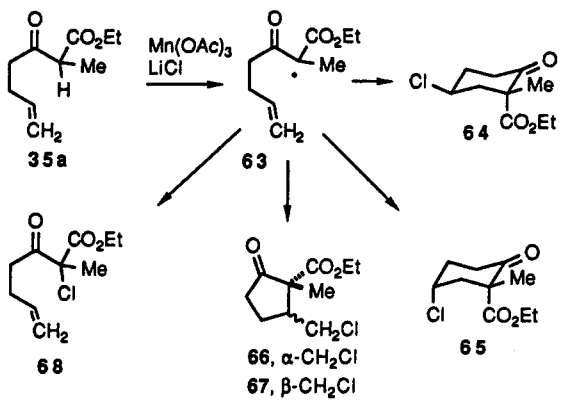
**Relative Rate of Cyclization of 5-Hexenyl and 5-Hexynyl Radicals.** Oxidative addition of 1,3-dicarbonyl compounds to alkenes with Mn(III) in the presence of LiCl results in trapping of the alkyl radical formed in the addition reaction as the chloride.[2b] We have previously shown that secondary and primary chlorides can be formed by carrying out oxidative cyclizations with $Mn(OAc)_3 \cdot 2H_2O$ and LiCl.[3d,i] We examined the reaction of **23a** under these conditions since alkenyl chlorides are produced in modest yield by intermolecular oxidative addition of 1,3-dicarbonyl compounds to alkynes with Mn(III) in the presence of LiCl.[2b] To our surprise, the only product, isolated in 77% yield, is the acyclic chloride **60**. Apparently, oxidation to radical **59** occurs normally. Reaction of **59** with chloride ion and oxidation to give **60** must be must faster than cyclization to give **24a** and **25a** since neither chlorides **61** or **62**, nor hydrocarbons **27a** or **28a** are present in the reaction mixture.




We were not sure whether the cyclization of **59** fails because of the decreased reactivity of the alkyne, the nature of the tether, or the methyl substituent on the $\beta$-keto ester. We therefore examined the reaction of the analogous alkene **35a** with $Mn(OAc)_3 \cdot 2H_2O$ and LiCl. In this case, cyclization of **63** occurs normally. We obtained a ≈7:3:7:3:1 mixture of 64–68. The acyclic chloride **68**, which is analogous to **60**, is a very minor product. An authentic sample of **68** was prepared in 85% yield by oxidation of **35a** with $Mn(OAc)_3 \cdot 2H_2O$ and $CuCl_2$.[3d] The ratio of **64–67** suggest that LiCl does not perturb the cyclization but simply traps the cyclic radicals **36a** and **40a**. The 1:1 ratio of 6-endo/5-exo cyclization products corresponds closely to the 1:0.9 mixture obtained with $Cu(OAc)_2 \cdot H_2O$. The 2.3:1 mixture of cyclopentane isomers corresponds closely to that observed in related reactions.[3h]

5-Hexenyl radical **63** cyclizes to **36a** and **40a** 20 times faster than it reacts with chloride ion to give **68**. On the other hand, 5-hexynyl radical **59** reacts with chloride ion to give **60** at least 20 times faster than it cyclizes to **24a** and **25a**. Since radicals **59** and **63** should react with chloride ion at the same rate, 5-hexenyl radical **63** must

(25) Buxton, G. V.; Green, J. C.; Higgins, R.; Kanji, S. *J. Chem. Soc., Chem. Commun.* **1976**, 158.




cyclize at least 400 times faster than 5-hexynyl radical **59**. This result is in marked contrast to that obtained with simpler radicals. Beckwith has reported that the parent 5-hexynyl radical cyclizes only 5 times slower than the parent 5-hexenyl radical.[26] Presumably, the electrophilic nature of the enol radical and the presence of the carbonyl group in the ring being formed have different effects on the rates of cyclization of 5-hexenyl and 5-hexynyl radicals.

## Conclusion

These results show that ethanol complements the typical solvent, acetic acid, for Mn(III)-based oxidative free-radical cyclizations. Cyclization of enol ether **1c** to give gibberellic acid intermediate **6c** is successful in ethanol, but not in acetic acid. Ethanol acts as a reducing agent for primary radicals, converting **13** and **33** to alkanes **17** and **32**. Acetylenes can be used as substrates since the vinyl radicals **24** and **25** are reduced to alkenes **27** and **28** by ethanol. Finally, a higher percentage of 5-exo cyclization products are obtained from **35** and **48** in ethanol than in acetic acid.

## Experimental Section

**Preparation of Starting Materials.** 3-Chloro-2-((2-methoxyethoxy)methoxy)propene was prepared by the literature procedure for the corresponding MOM ether.[8] Dimethyl 4-pentenylmalonate was prepared as previously described.[9,10] Acetylenic β-keto esters **23a** (33%), **23b** (48%), **29a** (55%), **29b** (33%), and **29c** (40%) were prepared by alkylation of the dianion[7] of the appropriate β-keto ester with 3-bromopropyne or 1-bromo-4-butyne as previously described.[3] Esters **35a** (61%), **35b** (56%), and **48b** (48%) were prepared by alkylation of the dianion[7] of ethyl and methyl 2-methylacetoacetate and methyl 2-allylacetoacetate with allyl bromide as previously described.[3h,i] Ethyl 3-oxo-2-(2-propenyl)-6-heptenoate **48a** (46%) was prepared by the Claisen condensation[27] of ethyl 4-pentenoate. Anhyd $Mn(OAc)_3$ was prepard by the literature procedure.[28] $Mn(OAc)_3 \cdot 2H_2O$ was purchased from Aldrich.

All oxidative cyclizations were run under $N_2$. Solutions were degassed by bubbling $N_2$ through the solution of the oxidant for 20 min prior to addition of the substrate. NMR spectra were recorded at 300 MHz in $CDCl_3$ and are reported in δ; $J$ values are reported in Hz. APT was used to assign $^{13}C$ NMR spectra whose multiplicities are indicated. Analytical GC was carried out on a capillary 0.25 mm × 25 m polydimethylsiloxane column. The oven temperature was increased from 60 to 90 °C at 2.5 °C/min and from 90 to 150 °C at 30 °C/min and then held at 150 °C.

**Methyl 6-((2-Methoxyethoxy)methoxy)-3-oxo-2-(2-propenyl)hept-6-enoate (1c).** To a stirred solution of diisopropylamine (2.18 mL, 0.016 mol) in THf (22 mL) at 0 °C was added dropwise *n*-butyllithium (2.5 M in hexanes, 6.22 mL, 0.016 mol). The mixture was stirred at 0 °C for 0.25 h at which time methyl 2-allylacetoacetate (1.213 g, 0.008 mol) in THF (2.5 mL) was added dropwise over 5 min. The resulting deep orange solution was stirred for 0.5 h at 0 °C. HMPA (2.70 mL, 0.016 mol) was then added, followed by 3-chloro-2-((2-methoxyethoxy)methoxy)propene[8] (1.404 g, 0.008 mol) in 2.5 mL of THF. The mixture was warmed to rt and stirred for 1.5 h. The reaction was quenched by the addition of water (50 mL) and diluted to a final volume of 200 mL with water. The mixture was acidified with saturated $NaH_2PO_4$ and extracted with three parts of ether. The combined organic phases were washed with saturated $NaHCO_3$ solution and dried ($MgSO_4$). Removal of the solvent in vacuo gave 2.34 g of crude material. Purification of 1.40 g by flash chromatography (3:1 hexane/EtOAc, deactivated silica gel) gave 0.56 g (39%) of **1c**: $^1H$ NMR 5.73 (ddt, 1, $J$ = 10.3, 17.0, 6.7), 5.09 (ddt, 1, $J$ = 1.5, 17.0, 1.4), 5.05 (s, 2), 5.04 (ddt, 1, $J$ = 1.5, 10.3, 1.1), 4.15 (br d, 1, $J$ = 2.3), 4.05 (br d, 1, $J$ = 2.3), 3.76–3.71 (m, 2), 3.73 (s, 3), 3.60–3.54 (m, 3), 3.39 (s, 3), 2.85–2.63 (m, 2), 2.60 (br t, 2, $J$ = 7.3), 2.39 (t, 2, $J$ = 7.3); $^{13}C$ NMR 203.4, 169.6, 159.0, 134.2, 117.5, 92.6, 85.0, 71.6, 67.8, 59.0, 58.3, 52.4, 39.9, 32.2, 28.8; IR (neat) 1745, 1717 $cm^{-1}$. Anal. Calcd for $C_{15}H_{24}O_6$: C, 59.98; H, 8.05. Found: C, 59.78; H, 7.94.

**Methyl 5-((2-Methoxyethoxy)methoxy)-6-methylene-2-oxobicyclo[3.2.1]octane-1-carboxylate (6c).** To a stirred solution of $Mn(OAc)_3 \cdot 2H_2O$ (328 mg, 1.22 mmol) and $Cu(OAc)_2 \cdot H_2O$ (122 mg, 0.61 mmol) in 3 mL of ethanol was added β-keto ester **1c** (184 mg, 0.61 mmol) in 3.5 mL of ethanol. The reaction mixture was heated to 60 °C and stirred for 13 h, at which time 50 mL of water was added. A solution of 10% $NaHSO_3$ was added dropwise to the mixture to decompose any residual $Mn(OAc)_3$. The resulting solution was extracted with three 30-mL portions of $CH_2Cl_2$. The combined organic extracts were washed with saturated NaCl solution and dried ($Na_2SO_4$). Removal of the solvent in vacuo gave 162 mg (89%) of a yellow oil. Purification of 152 mg by flash chromatography (3:1 hexane/ethyl acetate followed by 2:1 hexane/EtOAc) gave 84 mg (52%) of **6c**: $^1H$ NMR 5.25 (dd, 1, $J$ = 2.5, 2.9), 5.20 (br t, 1, $J$ = 2.5), 4.94 (d, 1, $J$ = 7.9, $OCH_2O$), 4.78 (d, 1, $J$ = 7.9, $OCH_2O$), 3.84 (ddd, 1, $J$ = 4.3, 4.9, 10.9, $OCH_2$), 3.78–3.58 (m, 2, $OCH_2$), 3.76 (s, 3, $CO_2CH_3$), 3.55 (ddd, 1, $J$ = 0.7, 3.6, 10.3, $OCH_2$), 3.39 (s, 3, $OCH_3$), 2.97 (br dt, 1, $J$ = 18.3, 2.5, H7), 2.79 (ddd, 1, $J$ = 2.5, 3.9, 18.3, H7), 2.64 (dd, 1, $J$ = 3.9, 12.1, H8 anti), 2.53 (dddd, 1, $J$ = 0.7, 8.4, 11.4, 16.4, H3 endo), 2.47 (ddd, 1, $J$ = 2.3, 7.5, 16.4, H3 exo), 2.31 (dd, 1, $J$ = 1.9, 12.1, H8 syn), 2.19 (ddd, 1, $J$ = 7.5, 11.4, 11.6, H4 exo), 1.96–1.87 (m, 1); $^{13}C$ NMR 206.0 (C2), 170.9, (OC=O), 148.0 (C6), 108.4 (=$CH_2$), 91.1 ($OCH_2O$), 82.7 (C5), 71.7 ($OCH_2$), 67.2 ($OCH_2$), 60.4 (C1), 58.9 ($OCH_3$), 52.2 (O=$COCH_3$), 42.0 (C4), 37.9 (C8), 37.3 (C7), 34.9 (C3); IR (neat) 1750, 1710 $cm^{-1}$. Anal. Calcd for $C_{15}H_{22}O_6$: C, 60.39; H, 7.43. Found: C, 60.35; H, 7.20.

**Oxidative Free-Radical Cyclization of 9 with $Mn(OAc)_3 \cdot 2H_2O$ in Acetic Acid. Preparation of 12, 17, and Polymer 22.** Reaction of $Mn(OAc)_3 \cdot 2H_2O$ (803 mg, 3.00 mmol) and **9** (300 mg, 1.50 mmol) in glacial acetic acid (15 mL) at 55 °C for 28 h, followed by normal workup,[3i] gave 345 mg of crude product. Flash chromatography of 282 mg (19:1 hexane/EtOAc) gave 39 mg (16%) of dimethyl 2-methylcyclopentane-1,1-dicarboxylate (**17**), followed by 11 mg (4%) of dimethyl 3-cyclohexene-1,1-dicarboxylate (**12**). Elution with $CH_2Cl_2$ gave 213 mg (75%) of polymer **22**.

The spectral data for **17**: $^1H$ NMR 3.72 (s, 3, $OCH_3$), 3.70 (s, 3, $OCH_3$), 2.67 (ddq, 1, $J$ = 6.5, 8.8, 7.1, H2), 2.44 (ddd, 1, $J$ = 7.6, 8.5, 13.7, H5), 2.03 (ddd, 1, $J$ = 4.5, 9.3, 13.7, H5), 1.92–1.76 (m, 2, H3), 1.65–1.49 (m, 1, H4), 1.41 (ddd, 1, $J$ = 3.8, 8.6, 12.3, H4), 0.97 (d, 3, $J$ = 7.1, $CH_3$); $^{13}C$ NMR 173.0 (C=O), 171.8 (C=O), 63.6 (C1), 52.3 ($OCH_3$), 51.9 ($OCH_3$), 40.8 (C2), 33.9 (C5), 33.4 (C3), 22.8 (C4), 16.4 ($CH_3$); IR (neat) 2959, 2879, 1732, 1379 $cm^{-1}$. The data are identical with those previously described.[10]

The spectral data for **12**: $^1H$ NMR 5.67 (br t, 2, $J$ = 2.0, H3 and H4), 3.72 (s, 6, $OCH_3$), 2.57 (br s, 2, H2), 2.20–2.00 (m, 4, H5 and H6); $^{13}C$ NMR 172.0 (2 × C=O), 126.1 (CH=), 123.9 (=CH), 52.6 (2 × $OCH_3$), 30.5 (C2), 27.5 (C5), 22.3 (C6), C1 was not observed; IR (neat) 3080, 1760, 1737, 1641 $cm^{-1}$. The data are identical with those previously described.[9,10]

The spectral data for **22**: $^1H$ NMR 3.69 (br s, n × 6), 1.86–1.74 (br m, n × 4), 1.34–1.20 (br m, n × 2), 1.20–1.04 (br m, n × 4); $^{13}C$ NMR 172.2 (C=O, n × 2, $T_1$ = 3.04 s), 57.6 (C1, n × 1, $T_1$ = 2.42 s), 52.3 ($OCH_3$, n × 2, $T_1$ = 0.86 s), 32.7 (C2, C6, n × 2,

(26) Reference 1e, page 202.
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Table II. Oxidative Cyclization of 48

| substrate | solvent | 50 (%) | 51, 52 (%) | 6-endo:5-exo | 54 (%) | 55 (%) | 56 (%) | 57 (%) | 58 (%) |
|---|---|---|---|---|---|---|---|---|---|
| 48a | ethanol | 44 | 7 | 1:1 | 7 | 14 | 7 | 19 | 2 |
| 48a | acetic acid | 55 | 6 | 1:0.6 | 7 | 18 | 7 | 1 | 6 |
| 48b | ethanol | 42 | 5 | 1:1 | 5 | 11 | 5 | 27 | 5 |
| 48b | acetic acid | 55 | 5 | 1:0.6 | 6 | 15 | 6 | 1 | 12 |

$T_1$ = 0.13 s), 30.1 (C4, n × 1, $T_1$ = 0.16 s), 24.0 (C3, C5, n × 2, $T_1$ = 0.15 s); IR (neat) 3005, 2960, 2870, 1737 cm$^{-1}$. The average molecular weight was found to be 8106 g/mol by vapor-pressure osmometry.

The spectral data for dimethyl cyclohexane-1,1-dicarboxylate (16):[12] $^1$H NMR 3.72 (s, 6, $OCH_3$), 2.01–1.94 (m, 4, H2 and H6), 1.56–1.38 (m, 6, H3, H4, H5); $^{13}$C NMR 172.3 (2, OC=O, $T_1$ = 29.02 s), 54.9 (C1, $T_1$ = 25.44 s), 52.3 (2, $OCH_3$, $T_1$ = 6.27 s), 31.3 (2, C2, C6, $T_1$ = 1.77 s), 25.0 (C4, $T_1$ = 1.62 s), 22.6 (2, C3, C5, $T_1$ = 1.84 s); IR (neat) 2945, 2860, 1739 cm$^{-1}$.

**Oxidative Cyclization of 23a in Ethanol.** To a stirred solution of anhyd $Mn(OAc)_3$ (222.2 mg, 0.96 mmol) in 1.7 mL of degassed ethanol was added β-keto ester **23a** (86.4 mg, 0.47 mmol) in 3.0 mL of degassed ethanol via cannula. The reaction mixture was stirred for 21 h at 25 °C. Normal workup afforded 70.7 mg of a yellow oil. Bulb to bulb distillation (90–100 °C (16 Torr)) of the crude material (59.1 mg) gave 22.8 mg (32%) of a 1.6:1 mixture of ethyl 1-methyl-2-methylene-5-oxocyclopentanecarboxylate (**27a**) and ethyl 1-methyl-6-oxo-2-cyclohexenecarboxylate (**28a**).

The data for **27a** were determined from the mixture: GC $t_R$ = 8.6 min; $^1$H NMR 5.18 (dd, 1, $J$ = 2.3, 2.3), 5.10 (dd, 1, $J$ = 1.4, 2.4), 4.14 (q, 2, $J$ = 7.1), 2.96–2.81 (m, 1), 2.70–2.65 (m, 1), 2.56–2.40 (m, 2), 1.41 (s, 3), 1.21 (t, 3, $J$ = 7.1); $^{13}$C NMR 214.1 (C=O), 170.0 (OC=O), 150.0 (C2), 110.2 (=$CH_2$), 61.4 ($OCH_2$), 59.6 (C1), 37.5 (C4), 28.0 (C3), 18.6 ($CH_3$), 13.8 ($CH_3$).

The data for **28a** are identical with those previously reported:[29] GC $t_R$ = 10.5 min; $^1$H NMR 5.97 (ddd, 1, $J$ = 4.2, 4.2, 9.7, H3), 5.70 (ddd, 1, $J$ = 1.7, 1.7, 9.7, H2), 4.16 (q, 2, $J$ = 7.1), 2.83–2.71 (m, 1), 2.64–2.41 (m, 3), 1.41 (s, 3), 1.24 (t, 3, $J$ = 7.1); $^{13}$C NMR 207.5 (C=O), 170.0 (OC=O), 130.3 (HC=), 128.0 (HC=), 61.2 ($OCH_2$), 56.1 (C1), 37.0 ($CH_2$), 25.9 ($CH_2$), 20.9 ($CH_3$), 13.7 ($CH_3$).

**Cyclization of 23a in Ethanol-$d_6$.** To a stirred solution of anhyd $Mn(OAc)_3$ (57.0 mg, 0.25 mmol) in 0.2 mL of degassed ethanol-$d_6$ was added β-keto ester **23a** (21.6 mg, 0.12 mmol) in 0.8 mL of degassed ethanol-$d_6$ via cannula. The reaction mixture was stirred for 6 h at 25 °C. Normal workup afforded 19.7 mg of a viscous yellow oil. Bulb to bulb distillation (100 °C (16 Torr)) afforded 2.7 mg (15%) of a mixture containing ca. 50% of a 1.3:1 mixture of **27a** and **28a** as determined by GC and NMR analysis: 5.97 (ddd, 1, **28a**, $J$ = 4.2, 4.2, 9.7, relative area ≈0.33), 5.70 (br s, 1, and ddd, 1, **28a**, $J$ = 1.7, 1.7, 9.7, relative area ≈1.0), 5.18 (dd, 1, **27a**, $J$ = 2.3, 2.3, relative area ≈0.5), 5.10 (dd, 1, **27a**, $J$ = 1.4, 2.4, relative area ≈0.5). The peak at δ 5.70 consists of the broad doublet from **28a** superimposed on a broad singlet from **28a**-$d_1$. The other peaks are the same shape as in **27a** and **28a**.

Deuterium cannot be incorporated into $H_2$ of **28a** since this was the acetylene hydrogen of **23a**. Therefore, the integration of the absorption of this hydrogen at δ 5.70 can be used as a standard. Since the ratio of areas of the peaks at δ 5.70 and δ 5.97 is 3:1, **28a** contains ≈67% of **28a**-$d_1$. The ratio of the peaks at δ 5.10 and δ 5.18 is 1:1, indicating that deuterium is incorporated equally in both positions of the exomethylene group. Since the GC ratio of **27a** to **28a** is 1.3:1 and the ratio of combined areas at both δ 5.18 and δ 5.10 to δ 5.70 is 1:1, **27a** contains 90–100% **27a**-$d_1$.

**Oxidative Cyclization of 23b.** To a stirred solution of anhyd $Mn(OAc)_3$ (284.6 mg, 1.23 mmol) in 3.0 mL of ethanol was added β-keto ester **23b** (118.4 mg, 0.60 mmol) in 3.0 mL of ethanol via cannula. The reaction mixture was stirred for 4.5 h at 25 °C. Normal workup afforded 106.8 mg of a yellow oil. Flash chromatography of the crude material (93.5 mg) on silica gel (19:1 hexane/EtOAc) gave 68.1 mg (66%) of a 2.6:1 mixture of the *E* isomer **27b** and *Z* isomer **26b** of ethyl 1-methyl-2-ethylidene-5-oxocyclopentane-1-carboxylate: IR (neat) 2985–2860, 1760, 1735, 1455–1443, 1403 cm$^{-1}$. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.54; H, 8.02.

The data for **27b** were determined from the mixture: $^1$H NMR 5.56 (ddq, 1, $J$ = 2.3, 2.3, 6.9), 4.12 (q, 2, $J$ = 7.2), 2.78–2.36 (m, 4), 1.69 (ddd, 3, $J$ = 1.4, 1.4, 6.9), 1.36 (s, 3), 1.21 (t, 3, $J$ = 7.2); $^{13}$C NMR 170.8 (OC=O), 141.1 (C2), 120.3 (=CH), 61.3 ($OCH_2$), 59.4 (C1), 37.2 (C4), 23.6 (C3), 19.2 ($CH_3$), 13.9 ($CH_3$), 13.6 ($CH_3$); the ketone carbon was not observed.

The data for **26b** were determined from the mixture: $^1$H NMR 5.59–5.50 (m, 1), 4.17 (q, 2, $J$ = 7.2), 2.78–2.36 (m, 4), 1.61 (ddd, 3, $J$ = 1.6, 1.6, 7.0), 1.43 (s, 3), 1.23 (t, 3, $J$ = 7.2); $^{13}$C NMR 170.8 (OC=O), 140.7 (C2), 121.4 (=CH), 61.4 ($CH_2$), 58.5 (C1), 37.9 (C4), 28.5 (C3), 18.9 ($CH_3$), 14.0 ($CH_3$), 13.5 ($CH_3$); the ketone carbon was not observed.

**Oxidative Cyclization of 29a.** To a stirred solution of anhyd $Mn(OAc)_3$ (271.5 mg, 1.17 mmol) in 3.0 mL of ethanol was added β-keto ester **29a** (113.6 mg, 0.58 mmol) in 2.8 mL of ethanol via cannula. The reaction mixture was stirred for 8 h at 25 °C. Normal workup afforded 86.6 mg of a yellow oil. Flash chromatography of the crude material (79.2 mg) on silica gel (19:1 hexane/EtOAc) gave 20.4 mg (20%) of a 2:1 mixture of methyl (3a$\alpha$,5$\beta$)-1,2,4,5-tetrahydro-3-oxo-5-methyl-3a-(3*H*)-pentalenecarboxylate (**32a**) and methyl 1-(2-propenyl)-6-oxo-2-cyclohexenecarboxylate (**31a**).

The data for **32a** were determined from the mixture: $^1$H NMR 5.54 (br s, 1), 3.76 (s, 3), 3.36–3.25 (m, 1), 2.91–2.41 (m, 4), 2.79 (dd, 1, $J$ = 5.0, 12.9), 1.43 (dd, 1, $J$ = 8.9, 12.9), 1.05 (d, 3, $J$ = 7.0); $^{13}$C NMR 170.5, 144.5, 132.8, 58.2, 52.5, 43.5, 41.3, 40.8, 23.1, 20.6; the ketone carbon was not observed; IR (neat) 3025, 2953, 2920, 2865, 1755, 1730, 1433 cm$^{-1}$.

The data for **31a** were determined from the mixture: $^1$H NMR 6.08 (ddd, 1, $J$ = 4.2, 4.2, 9.7), 5.70 (ddd, 1, $J$ = 1.7, 1.7, 9.7), 5.72–5.57 (m, 1), 5.12–5.04 (m, 2), 3.70 (s, 3); no other protons were identifiable in the mixture; $^{13}$C NMR 132.7, 129.5, 128.3, 119.0, 52.7, 39.2, 38.0, 25.5; the ketone, ester, and quaternary carbons were not observed.

**Oxidative Cyclization of 29b.** To a stirred solution of anhyd $Mn(OAc)_3$ (317.4 mg, 1.37 mmol) in 3.8 mL of ethanol was added β-keto ester **29b** (141.9 mg, 0.68 mmol) in 3.0 mL of ethanol via cannula. The reaction mixture was stirred for 27 h at 25 °C. Normal workup afforded 108.5 mg of a yellow oil. Flash chromatography of the crude material (98.6 mg) on silica gel (9:1 hexane/EtOAc) gave 45.7 mg (35%) of methyl (3a$\alpha$,5$\beta$)-1,2,4,5-tetrahydro-3-oxo-5,6-dimethyl-3a(3*H*)-pentalenecarboxylate (**32b**): $^1$H NMR 3.70 (s, 3), 3.25–3.13 (m, 1), 2.83 (ddd, 1, $J$ = 3.5, 8.0, 18.0), 2.73 (dd, 1, $J$ = 6.2, 12.9), 2.65–2.57 (m, 2), 2.52–2.40 (m, 1), 1.66 (s, 3), 1.40 (dd, 1, $J$ = 9.2, 12.9), 1.01 (d, 3, $J$ = 7.1); $^{13}$C NMR 212.5 (C=O), 171.0 (OC=O), 139.8 (=C), 136.8 (=C), 69.4 (C), 52.3 ($OCH_3$), 45.7 (CH), 41.0 ($CH_2$), 39.7 ($CH_2$), 21.3 ($CH_2$), 18.8 ($CH_3$), 11.6 ($CH_3$); IR (neat) 2958, 2928, 2870, 1755, 1735, 1643–1570, 1440 cm$^{-1}$. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.38; H, 7.76.

**Oxidative Cyclization of 29c.** To a stirred solution of anhyd $Mn(OAc)_3$ (327.1 mg, 1.41 mmol) and $Cu(OAc)_2{\cdot}H_2O$ (141.1 mg, 0.71 mmol) in 4.0 mL of ethanol was added β-keto ester **29c** (119.4 mg, 0.70 mmol) in 3.0 mL of ethanol via cannula. The reaction mixture was stirred for 23 h at 25 °C. Normal workup afforded 156.0 mg of a viscous yellow oil containing solvent. Flash chromatography of the crude material (146.4 mg) on silica gel (9:1 hexane/EtOAc) gave 40.3 mg (28%) of a 1.5:1.9:1 mixture of methyl (3a$\alpha$,5$\beta$)-1,2,4,5-tetrahydro-3-oxo-5-ethenyl-3a-(3*H*)-pentalenecarboxylate (**34c**), methyl (*E*)-1-(2-butenyl)-6-oxocyclohex-2-ene-1-carboxylate (**31c**), and recovered starting material, and 36.9 mg (25%) of a 8.5:1 mixture of **34c** and **31c**.

The data for **34c** were determined from the mixture: $^1$H NMR 5.71 (ddd, 1, $J$ = 7.8, 10.1, 17.3), 5.58 (br s, 1), 5.07 (ddd, 1, $J$ =

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1.4, 1.4, 17.3), 4.98 (ddd, 1, $J$ = 1.0, 1.4, 10.1), 3.88–3.86 (m, 1), 3.73 (s, 3), 2.89 (ddd, 1, $J$ = 2.0, 9.5, 17.7), 2.83–2.40 (m, 3), 2.78 (dd, 1, $J$ = 6.4, 13.1), 1.69 (dd, 1, $J$ = 9.1, 13.1); $^{13}$C NMR 211.7, 170.7, 146.2, 140.8, 130.2, 115.0, 71.1, 53.0, 52.9, 41.8, 39.2, 23.4; IR (neat) 3290–2860, 1757, 1735, 1670, 1643, 1435, 1403 cm$^{-1}$.

The data for **31c** were determined from the mixture: $^1$H NMR 6.07 (ddd, 1, $J$ = 4.1, 4.1, 9.9), 5.68 (ddd, 1, $J$ = 1.7, 1.7, 9.9), 5.59–5.42 (m, 1), 5.38–5.20 (m, 1), 3.69 (s, 3). No other protons were identifiable in the mixture.

**Oxidative Cyclization of 35a in Ethanol.** To a stirred solution of anhyd $Mn(OAc)_3$ (261.6 mg, 1.13 mmol) and $Cu(OAc)_2 \cdot H_2O$ (111.8 mg, 0.56 mmol) in 2.5 mL of ethanol was added β-keto ester **35a** (102.0 mg, 0.55 mmol) in 3.0 mL of ethanol via cannula. The reaction mixture was stirred for 3.5 h at 25 °C. Normal workup afforded 103.7 mg of a yellow oil. The crude reaction mixture was found by $^1$H and $^{13}$C NMR and GC analysis to contain (based on 90% reacted starting material) 61% of ethyl 1-methyl-2-methylene-5-oxocyclopentane-1-carboxylate (**43a**), 5% of ethyl 1-methyl-2-(hydroxymethyl)-5-oxocyclopentane-1-carboxylate (**42a**), 0% of tetrahydro-6a-methyl-1*H*-cyclopenta[*c*]furan-1,6(3*H*)-dione (**41**), 17% of ethyl 1-methyl-6-oxocyclohex-3-ene-1-carboxylate (**38a**), and 17% of ethyl 1-methyl-6-oxocyclohex-2-ene-1-carboxylate (**39a**). During GC analysis **42a** cyclizes to lactone **41** and **38a** partially isomerizes to ethyl 1-methyl-2-oxocyclohex-3-ene-1-carboxylate. During flash column chromatography **42a** cyclizes partially to lactone **41**.

Flash chromatography on silica gel (9:1 hexane/ethyl acetate to ethyl acetate) of a reaction carried out in acetic acid affords 45% of a ≈4:2:1 mixture of **39a**, **43a**, and **38a** followed by 20% of a ≈2:1 mixture of **42a** and **41**. The data given below were determined from these and related mixtures.

The data for **43a** are identical with those described above for **27a**.

The data for **42a**: $^1$H NMR 4.17 (q, 2, $J$ = 7.1), 3.74 (d, 2, $J$ = 7.0), 2.68–2.04 (m, 6), 1.38 (s, 3), 1.26 (t, 3, $J$ = 7.2); $^{13}$C NMR 171.3 (OC=O), 63.3 ($CH_2OH$), 61.3 ($OCH_2$), 57.8 (C), 51.1 (CH), 37.2 ($CH_2$), 23.0 ($CH_2$), 19.6 ($CH_3$), 14.0 ($CH_3$); the ketone carbon was not observed.

The data for **41**: GC $t_R$ = 13.6 min; $^1$H NMR 4.54 (dd, 1, $J$ = 7.2, 9.5), 4.13 (dd, 1, $J$ = 4.4, 9.5), 3.01 (dddd, 1, $J$ = 4.4, 5.7, 7.2, 7.2), 2.50–2.44 (m, 1), 2.40–2.23 (m, 2), 1.90 (dddd, 1, $J$ = 5.8, 6.8, 7.2, 13.4), 1.42 (s, 3); $^{13}$C NMR 70.2 (C3), 56.7 (C6a), 44.6 (C3a), 36.2 ($CH_2$), 23.6 ($CH_2$), 18.2 ($CH_3$); the ketone and ester carbons were not observed. The data correspond closely to that reported for related lactones.[31,24]

The data for **38a**: GC $t_R$ = 10.1 min; $^1$H NMR 5.82 (dddd, 1, $J$ = 2.6, 3.2, 5.3, 9.7), 5.71 (dddd, 1, $J$ = 2.4, 3.2, 5.9, 9.7), 4.18 (q, 2, $J$ = 7.1), 3.25–3.14 (m, 1), 3.05 (dd, 1, $J$ = 5.9, 17.4), 2.93–2.83 (m, 1), 2.25 (ddd, 1, $J$ = 2.4, 2.4, 17.4), 1.38 (s, 3), 1.24 (t, 3, $J$ = 7.1); $^{13}$C NMR 206.3 (C=O), 172.6 (OC=O), 125.6 (HC=), 124.5 (HC=), 61.3 ($OCH_2$), 55.6 (C1), 39.0 ($CH_2$), 37.2 ($CH_2$), 19.6 ($CH_3$), 13.9 ($CH_3$). The data are analogous to those reported for the methyl ester.[30]

The data for **39a** are identical with those described above for **28a**.

**Oxidative Cyclization of 48b in Ethanol.** To a stirred solution of anhyd $Mn(OAc)_3$ (309.5 mg, 1.33 mmol) and $Cu(OAc)_2 \cdot H_2O$ (134.7 mg, 0.67 mmol) in 4.0 mL of ethanol was added β-keto ester **48b** (129.6 mg, 0.66 mmol) in 2.6 mL of ethanol via cannula. The reaction mixture was stirred for 10 h at 25 °C. Normal workup afforded 114.4 mg of a yellow oil. The crude reaction mixture was found by NMR analysis (based on 75% reacted starting material) to contain 27% of methyl 1-(2-propenyl)-2-methylene-5-oxocyclopentane-1-carboxylate (**57b**), 11% of methyl 1-(2-propenyl)-2-(hydroxymethyl)-5-oxocyclopentane-1-carboxylate (**55b**), 5% of tetrahydro-6a-(2-propenyl)-1*H*-cyclopenta[*c*]furan-1,6(3*H*)-dione (**58**), 5% of methyl *trans*-3-oxo-1,2,3,4,7,7a-hexahydro-3a*H*-indene-3a-carboxylate (**56b**), 5% of methyl 1,2,4,5-tetrahydro-3-oxo-5-methylene-3a-(3*H*)-pentalenecarboxylate (**54b**), 42% of methyl 6-methylene-2-oxobicyclo[3.2.1]octane-1-carboxylate (**50b**), 2.5% of methyl 1-(2-propenyl)-6-oxocyclohex-3-ene-1-carboxylate (**52b**), and 2.5% of methyl 1-(2-propenyl)-6-oxocyclohex-2-ene-1-carboxylate (**51b**).

The identification of minor products was facilitated by the partial separation of the mixture by flash chromatography on silica gel (9:1 and then 1:1 hexane/EtOAc). For instance, cyclization of **48a** in acetic acid followed by chromatography afforded 6% of a mixture of consisting mainly of **52a** with a trace of **51a** and **57a** followed by 17% of a mixture of a 2:1:1 mixture of **50a**, **54a**, and **56a**, 35% of **50a**, and 24% of a mixture of **55a** and **58**. The structure assignments of the minor products **54** and **56** are tentative. The data given below were determined from these and related mixtures.

The data for **57b**: $^1$H NMR 5.29 (dd, 1, $J$ = 2.0, 2.0), 3.68 (s, 3); no other protons were identifiable in the mixture; $^{13}$C NMR 147.4, 132.0, 119.4, 111.5, 52.6, 38.6, 38.0, 28.4; the ketone, ester, and quaternary carbons were not observed.

The data for **55b**: $^1$H NMR 5.73–5.55 (m, 1), 5.24–5.11 (m, 2), 3.73 (s, 3), 3.72 (apparent d, 2, $J_{app}$ = 7.1), 2.78–1.80 (m, 8); $^{13}$C NMR 132.7, 120.0, 63.3, 59.4, 52.6, 44.7, 40.0, 37.2, 22.9. The ketone and ester carbons were not observed.

The data for **56b**: $^1$H NMR 5.74–5.70 (m, 2), 3.72 (s, 3); no other protons were identifiable in the mixture; $^{13}$C NMR 126.9, 125.4; no other carbons were observed in the mixture.

The data for **54b**: $^1$H NMR 4.89 (m, 2), 3.69 (s, 3); no other protons were identifiable in the mixture; $^{13}$C NMR 148.1, 107.8; no other carbons were observed in the mixture.

The isolation of **50b** and **58** from this reaction have been previously described.[3i] The data for **51b** are identical with those reported for **31a**.

The data for **52b**: $^1$H NMR 5.73–5.58 (m, 3), 5.20–5.00 (m, 2), 3.75 (s, 3), 2.85–1.81 (m, 6); $^{13}$C NMR 125.5, 124.3; no other carbons were observed in the mixture.

**Ethyl 2-Chloro-2-methyl-3-oxo-6-heptynoate (60).** To a stirred suspension of anhydrous $Mn(OAc)_3$ (106.2 mg, 0.40 mmol) and LiCl (36.0 mg, 0.85 mmol) in 0.9 mL of glacial acetic acid was added β-keto ester **23a** (34.4 mg, 0.19 mmol) in 1.0 mL of glacial acetic acid via cannula. The reaction mixture was stirred for 19 h at 25 °C. Normal workup afforded 31.3 mg (77%) of **60**: $^1$H NMR 4.28 (q, 2, $J$ = 7.1), 3.10 (dt, 1, $J$ = 18.3, 7.2), 2.94 (dt, 1, $J$ = 18.3, 7.2), 2.51 (dt, 2, $J$ = 2.7, 7.2), 1.97 (t, 1, $J$ = 2.7), 1.85 (s, 3), 1.31 (t, 3, $J$ = 7.1); $^{13}$C NMR 199.5, 167.8, 82.3, 70.3, 69.0, 63.1, 36.7, 24.3, 13.9, 13.4; IR (neat) 3308, 1755, 1734 cm$^{-1}$.

**Ethyl *cis*- and *trans*-5-Chloro-1-methyl-2-oxocyclohexane-1-carboxylate (64 and 65), Ethyl *cis*- and *trans*-5-(Chloromethyl)-1-methyl-2-oxocyclopentane-1-carboxylate (66 and 67), and Ethyl 2-Chloro-2-methyl-3-oxo-6-heptenoate (68).** A solution of **35a** (0.208 g, 1.13 mmol), $Mn(OAc)_3 \cdot 2H_2O$ (0.605 g, 2.26 mmol), and LiCl (0.1913 g, 4.51 mmol) in 11 mL of acetic acid was stirred at 25 °C for 22 h. Workup afforded 0.182 g (74%) of a ≈7:3:7:3:1 mixture of **64** through **68**, respectively, as determined by analysis of the $^1$H NMR spectra. Flash chromatography on silica gel (30:1 hexane/EtOAc) afforded 0.005 g (2%) of **68**, followed by 0.048 g (20%) of **64**, followed by 0.034 (14%) of **66**, followed by 0.003 g (1%) of a 5:1 mixture of **65** and **67**, followed by 0.016 g (7%) of a 5:1 mixture of **67** and **65**.

The data for **64**: $^1$H NMR 4.34 (dddd, 1, $J$ = 4.2, 4.2, 11.9, 11.9), 4.21 (m, 2, $J$ = 7.2), 2.94 (ddd, 1, $J$ = 3.4, 4.2, 13.5), 2.63–2.40 (m, 3), 2.00 (dddd, 1, $J$ = 4.9, 11.9, 13, 13.5), 1.82 (dd, 1, $J$ = 11.9, 13.5), 1.31 (s, 3), 1.27 (t, 3, $J$ = 7.2); $^{13}$C NMR 204.6, 171.8, 61.8, 56.5, 53.3, 46.6, 38.9, 36.6, 21.0, 14.0; IR (neat) 1740, 1720 cm$^{-1}$. Anal. Calcd for $C_{10}H_{15}ClO_3$: C, 54.92; H, 6.91; Cl, 16.21. Found: C, 55.01; H, 7.02; Cl, 16.26.

The data for **65** were determined from the mixture: $^1$H NMR 4.48 (br dddd, 1, $J$ = 3.7, 4, 5, 5.1), 4.30–4.10 (m, 2), 3.09 (ddd, 1, $J$ = 6.1, 10.7, 14.8), 2.95 (ddd, 1, $J$ = 2.3, 5.1, 14.8), 2.48 (ddd, 1, $J$ = 2.3, 5.1, 14.8), 2.38–2.18 (m, 2), 2.07 (ddd, 1, $J$ = 0.7, 3.7, 14.8), 1.35 (s, 3), 1.29 (t, 3, $J$ = 7.1); $^{13}$C NMR 206.7, 172.9, 61.7, 55.0, 54.6, 44.9, 35.8, 35.4, 21.8, 13.8.

The data for **66**: $^1$H NMR 4.23–4.08 (m, 2), 3.76 (dd, 1, $J$ = 4.9, 11), 3.43 (dd, 1, $J$ = 9.1, 11), 2.63 (m, 1), 2.40–2.23 (m, 3), 1.99–1.82 (m, 1), 1.37 (s, 3), 1.26 (t, 3, $J$ = 7.1); $^{13}$C NMR 214.4, 169.8, 61.5, 58.8, 50.9, 44.7, 37.1, 24.9, 19.1, 14.1; IR (neat) 1760, 1735 cm$^{-1}$. Anal. Calcd for $C_{10}H_{15}ClO_3$: C, 54.92; H, 6.91; Cl, 16.21. Found: C, 54.93; H, 7.09; Cl, 16.30.

The data for **67** were determined from the mixture: $^1$H NMR 4.31–4.10 (m, 2), 3.58 (br d, 2, $J$ = 8), 3.19 (br dddd, 1, $J$ = 7, 7, 12, 12), 2.51–2.42 (m, 1), 2.32–2.22 (m, 1), 1.61 (m, 2), 1.26 (t, 3,

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$J$ = 7), 1.25 (s, 3); $^{13}$C NMR 213.9, 171.6, 61.6, 58.8, 46.9, 44.0, 37.4, 24.3, 14.0, 12.8.

The data for **68**: $^1$H NMR 5.80 (tdd, 1, $J$ = 6.6, 10.3, 17), 5.06 (br d, 1, $J$ = 17), 5.01 (br d, 1, $J$ = 10.3), 4.27 (q, 2, $J$ = 7.2), 2.97 (td, 1, $J$ = 7.4, 18), 2.68 (td, 1, $J$ = 7.4, 18), 2.38 (br dt, 2, $J$ = 7.4, 7.4), 1.83 (s, 3), 1.30 (t, 3, $J$ = 7.2); $^{13}$C NMR 200.5, 168.0, 136.4, 115.6, 70.7, 62.9, 36.8, 27.9, 24.4, 18.8; IR (neat) 1760, 1740 cm$^{-1}$. Anal. Calcd for $C_{10}H_{15}ClO_3$: C, 54.92; H, 6.91; Cl, 16.21. Found: C, 54.83; H, 6.81; Cl, 16.32.

**Ethyl 2-Chloro-2-methyl-3-oxo-6-heptenoate (68).** A solution of **35a** (0.058 g, 0.313 mmol), $Mn(OAc)_3 \cdot 2H_2O$ (0.168 g, 0.626 mmol), and $CuCl_2$ (0.042 g, 0.313 mmol) in 3 mL of acetic acid was stirred at 25 °C for 22 h. Workup afforded 0.059 g (85%) of crude **68**.

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**Registry No.** **1c**, 134906-06-2; **6c**, 134906-08-4; **9**, 93185-10-5; **12**, 41079-58-7; **17**, 120790-38-7; **22**, 134906-38-0; **23a**, 134906-09-5; **23b**, 134906-14-2; **26b**, 134906-16-4; **27a**, 134906-10-8; **27a-$d_1$**, 134906-13-1; **27b**, 134906-15-3; **28a**, 134906-11-9; **28a-$d_1$**, 134906-12-0; **29a**, 134906-17-5; **29b**, 134906-20-0; **29c**, 134906-22-2; **31a**, 134906-18-6; **31c**, 134906-24-4; **32a**, 134906-19-7; **32b**, 134906-21-1; **34c**, 134906-23-3; **35a**, 87027-59-6; **38a**, 134906-27-7; **39a**, 134906-11-9; **41**, 134906-26-6; **42a**, 134906-25-5; **43a**, 134906-10-8; **48b**, 111086-20-5; **50b**, 111086-22-7; **51b**, 134906-18-6; **52b**, 134906-31-3; **54b**, 134906-30-2; **55b**, 134906-29-9; **56b**, 134906-32-4; **57b**, 134906-28-8; **58**, 111086-21-6; **60**, 134906-33-5; **64**, 134906-34-6; **65**, 134938-20-8; **66**, 134906-35-7; **67**, 134906-36-8; **68**, 134906-37-9; $Mn(OAc)_3$, 993-02-2; ethanol, 64-17-5; acetic acid, 64-19-7; methyl 2-allylacetoacetate, 3897-04-9; 3-chloro-2-((2-methoxyethoxy)methoxy)propene, 134906-07-3.

**Supplementary Material Available:** $^1$H and $^{13}$C NMR spectra of **27a** and **28a**, **31a** and **32a**, **31c** and **34c**, **38a**, **39a** and **43a**, **41** and **42a**, **51a**, **52a** and **57a**, **50a**, **54a** and **56a**, **55a** and **58**, and **60** (17 pages). Ordering information is given on any current masthead page.

# π-Selective Dichlorocyclopropanation and Epoxidation of 9-Chloro-1,4,5,8-tetrahydro-4a,6a-methanonaphthalene. Controlled Synthesis of the C9 Epimers of (1aα,2aα,6aα,7aα)-1,8,8-Trichloro-1a,2,3,6,7,7a-hexahydro-2a,6a-methanocyclopropa[*b*]naphthalene

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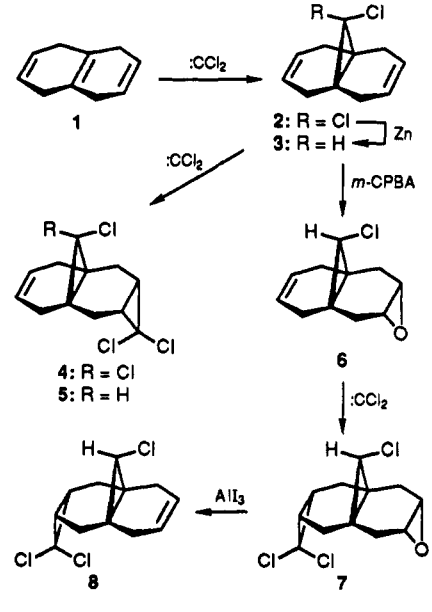
Dichlorocarbene addition to the 9-chloromethanonaphthalene **3** shows remarkable π-selectivity; syn trichloride **5** is the only monoadduct isolated (72%). Epoxidation likewise yields the syn epoxide **6** (78%), which, on dichlorocyclopropanation and deoxygenation, gives the epimeric trichloride **8**. The regioselectivities are in accord with PM3-derived molecular electrostatic potentials.

In connection with our ongoing program on cyclopropanarene chemistry,[1] we had need[2] of the epimeric tetracyclic trichlorides **5** and **8** as well as the known[3] tetrachloro homologue **4**. Our strategy was based upon dichlorocyclopropanation and half-reduction protocols commencing with isotetralin (**1**), and in bringing this work to fruition we have discovered remarkably high π-selectivity in additions to the unsymmetrical diene **3** (Scheme I). The results are compatible with depletion of electron density from the π-bond remote from the chloro substituent such that addition is to the syn double bond; the expected[4-6] high stereoselection of addition to the α-face of the molecule is observed.

Dichlorocarbene addition to **1** affords **2**[3,4] which when separately subjected to further controlled addition gives **4** in 80% (optimized) yield (Scheme I). In our hands this procedure minimizes the amount of unwanted **9** from addition to the three double bonds and is an improvement

Scheme I




on the published[4] method. Half-reduction of **2** affords chloropropelladiene **3** almost quantitatively (Zn/EtOH/KOH is superior to $Bu_3SnH$). When dichlorocarbene is added to **3**, syn trichloride **5** (72%) and the diadduct **10** (23%) are the only products isolated. Although the NMR

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