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Mn(III)-Based Oxidative Free-Radical 6-endo Cyclizations of Z-Trisubstituted Alkenes

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Abstract

Oxidative free-radical cyclization of Z-trisubstituted alkene **6a** gave the expected octahydrophenanthrenes **9** (11%) and **10** (24%), lactone **17** (10%), and octahydrophenanthrene **4** (25%), which was obtained from *E*-trisubstituted alkene **1a**. Cyclization of **6b** provided the expected hydrindane **11** (25%), cyclopentane **18b** (10%) formed by 5exo cyclization, and hydrindane **5** (13%), which was obtained from *E*-trisubstituted alkene **1b**. These results provide valuable information on the mechanism of Mn(III)-based oxidative radical cyclizations and indicate the profound effect of alkene geometry on the stereochemistry of radical cyclizations.

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Introduction

We have found that tandem $Mn(OAc)_3$ -based oxidative free-radical cyclization¹ of unsaturated β -keto esters provides a very efficient and stereospecific route to polycyclic systems as exemplified by the synthesis of **4** from **1a**, which proceeds stereospecifically in 50-80% yield depending on the substituents on the aromatic ring.²⁻⁷ We have established that these reactions proceed by formation of free radical **2a**, which cyclizes through a chair transition state with an axial ester to give **3a**. Tertiary radical **3a** reacts further to give **4**, either by 6*endo* radical cyclization followed by oxidation, or by oxidation to the cation followed by Friedel-Crafts cyclization. Similarly, oxidative free-radical cyclization of **1b** with Mn(OAc)₃



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0040-4020/98/\$ - see front matter © 1998 Elsevier Science Ltd. All rights reserved. *PII:* S0040-4020(98)00612-7 and $Cu(OAc)_2$ affords 33% of 5 stereospecifically. Radical 2b cyclizes through a chair transition state with an axial ester to give 3b, which undergoes a 5-*exo* cyclization to the terminal double bond to give a *cis*-hydrindane with a primary radical, which is oxidized by Cu(II) to yield 5.⁸ Zoretic has extended this approach to triple and quadruple cyclizations.⁹ *E*-Trisubstituted double bonds have been used in all of these studies, which invariably lead to the monocyclic tertiary radical with the stereochemistry shown in 3. Further cyclization leads to *trans*-decalins such as 4 or *cis*-hydrindanes such as 5.

We expected that use of Z-trisubstituted double bonds would provide a practical route to isomers of 4 and 5. For instance, 6a should be oxidized to radical 7a, which should cyclize to cyclohexyl radical 8a with an axial ester, which should cyclize to give octahydrophenanthrenes 9 and/or 10. Similarly, 6b should be oxidized to radical 7b, which should cyclize to cyclohexyl radical 8b, which should cyclize to provide hydrindane 11.



To the best of our knowledge, there is only a single study of the effect of double bond geometry on the cyclization of 5,6-disubstituted 5-hexenyl radicals.¹⁰ Julia and co-workers reported in 1975 that reduction of 7-bromo-3-methyl-2*E*-heptene with Bu₃SnH gave 13% of the 6-*endo* cyclization products *cis*- and *trans*-1,2-dimethylcyclohexane and 7.5% of the 5-*exo* cyclization product 1-ethyl-1-methylcyclopentane and acyclic material (eq 1). On the other hand, the Z-isomer gave none of the 6-*endo* cyclization products and 12% of the 5-*exo* cyclization product and acyclic material (eq 2). The shift from mainly 6-*endo* cyclization with the *E*-isomer to exclusively 5-*exo* cyclization with the Z-isomer hinted that **6a** and **6b** might not cyclize analogously to **1a** and **1b**. In contrast, the effect of double bond geometry



in cation-olefin cyclizations is more straightforward with *E*-double bonds leading to *trans*decalins (eq 3) and Z-double bonds leading to *cis*-decalins (eq 4).¹¹

Results and Discussion

The crucial step in the preparation of **6a** and **6b** was the Z-selective Horner-Emmons Wittig reaction using Still's procedure¹² [(EtO)₂POCH(CH₃)CO₂Et, KHMDS, 18-crown-6], which gave 45% of **13a** and 56% of **13b**. Reduction of **13a** with LAH gave 99% of alcohol **14a**,¹³ which was treated with MsCl, Et₃N, and LiBr to give 74% of bromide **15a**. Alkylation of the dianion of ethyl methylacetoacetate with **15a** provided 92% of **6a**. Similarly, reduction of **13b** afforded 71% of alcohol **14b**,¹⁴ which was converted to bromide **15b** with PBr₃. Because of its volatility, crude **15b** was converted to **6b** in 53% unoptimized yield.



To our surprise, oxidative cyclization of **6a** with 2.3 equiv of $Mn(OAc)_3 \cdot 2H_2O$ in AcOH at 25 °C for 2 h gave a complex mixture containing 24% of the expected product **10**, 11% of a compound tentatively assigned structure **9**, 22% of **4**, the only product from the cyclization of **1a**, 2% of alkenes **16**, and 10% of lactone **17**. The spectral data for **10** correspond closely to those reported for analogues with a methoxy group on the aromatic ring.^{15,16} The stereo-chemistry was confirmed by NOE experiments. Irradiation of the 4a-methyl group at δ 1.35 enhanced H_{3ax} at δ 2.77, H_{10ax} at δ 1.89, H_{4eq} at δ 2.56, and H_5 . Irradiation of the 1-methyl group enhanced H_{3ax} at δ 2.77 and H_{10ax} at δ 1.89. NOE enhancements cannot be observed between the two methyl groups because their absorptions are too close together. Octahydrophenanthrenes **4** and **9** were obtained as an inseparable mixture. The structure of **4** was



4. The cyclization of **3a** and **19a** should be slow since 4-phenylbutyl radicals cyclize with a rate constant of $\approx 10^3 \text{ s}^{-1.17}$ The cyclization of stabilized radicals such as **2** and **7** is known to be reversible and we have previously demonstrated that equilibration of double bond geometry can occur by ring opening of cyclic radicals in the 6-*exo* cyclization of analogous radicals to 1,2-disubstituted double bonds if the termination step is slow.¹⁸



Other possible explanations for the formation of 4 seem less likely. For instance, 7a could cyclize to give monocyclic radical 20a with an equatorial ester, which could flip to give 3a, which will cyclize to give 4. However, there is no apparent reason why the double bond geometry should affect the preference for an axial ester and equatorial methyl group observed in all other Mn(III)-based 6-*endo* cyclizations.¹

The formation of 5 from 6b probably results from a similar sequence in which monocyclic radical 8b undergoes chair-chair interconversion to give 19b, which opens to give acyclic radical 2b, which cyclizes to give 5. If this is the reaction pathway, the 5-*exo* cyclization of 8b to 11 must be relatively slow, so that ring opening to give 2b can occur. The formation of a 5-*exo* cyclization product (18b) from 6b but not from 6a, results from the need to use Cu(OAc)₂ as a co-oxidant with 6b to oxidize the primary bicyclic radical to the exomethylene double bond of 5 and 11. If Cu(OAc)₂ is not used as a co-oxidant, as in the cyclization of 6a, any secondary cyclopentyl alkyl radical 21a that is formed cannot be oxidized and will open to give acyclic radicals 2a and 7a. As expected, oxidative cyclization of 6a with Mn(OAc)₃·2H₂O and Cu(OAc)₂ provided a few percent of 18a as determined by the characteristic pattern of PhCH₂CH=CHR in the ¹H NMR spectrum.

In conclusion, the mixtures of products obtained from oxidative cyclization of Z-trisubstituted alkenes 6a and 6b provide valuable information about the mechanism and relative rates of the individual steps of Mn(III)-based oxidative radical cyclizations and indicate the profound effect of alkene geometry on the stereochemistry of radical cyclization products that will be valuable in synthetic planning.

Experimental Section

General. NMR spectra were recorded in $CDCl_3$ at 300 and 400 MHz (¹H), and 75 and 100 MHz (¹³C) unless otherwise indicated. Chemical shifts are reported in δ ; coupling constants are reported in Hz. $Mn(OAc)_3 \cdot 2H_2O$ was prepared as described by Heiba and Dessau.¹⁹

Ethyl 2-Methyl-5-phenyl-2Z-pentenoate (13a). KHMDS (7.6 mL, 3.78 mmol of 0.5 M solution in toluene) was added to a solution of triethyl 2-phosphonopropionate (901 mg, 3.78 mmol) and 18-crown-6 ether (5.0 g, 18.9 mmol) in THF (76 mL) at -78 °C under nitrogen. Hydrocinnamaldehyde (12a) (508 mg, 3.78 mmol) was added and the reaction was stirred at -78 °C for 40 min and quenched with saturated NH₄Cl solution. The mixture was warmed to rt and extracted with ether (3×75 mL). The combined organic layers were washed with water and brine, dried (MgSO₄) and concentrated giving a 4:1 Z/E mixture of isomers. Purification by flash chromatography on silica gel (25:1 hexane/EtOAc) afforded 366 mg (45%) of pure 13a¹³ followed by the *E*-isomer: ¹H NMR 7.31-7.15 (m, 5), 5.96 (br dt, 1, J = 1.3, 7.1), 4.19 (q, 2, J = 7.1), 2.82-2.70 (m, 4), 1.89 (br s, 3), 1.3 (t, 3, J = 7.1); ¹³C NMR 168.0, 141.6, 141.5, 128.4, 128.3, 127.8, 125.9, 60.1, 35.5, 31.1, 20.6, 14.3; IR (neat) 1713, 1647, 1603 cm⁻¹.

Ethyl 2-methyl-2Z,6-heptadienoate (13b). KHMDS (4.8 mL, 2.4 mmol of 0.5 M solution in toluene) was added to a solution of triethyl 2-phosphonopropionate (0.5 mL, 2.4 mmol) and 18-crown-6 ether (3.1 g, 12 mmol) in THF (50 mL) at -78 °C under nitrogen. 4-Pentenal (12b) (200 mg, 2.4 mmol) was added and the reaction was stirred at -78 °C for 40 min and quenched with saturated NH₄Cl solution. The mixture was warmed to rt and extracted with ether (3×100 mL). The combined organic layers were washed with water and brine, dried (MgSO₄) and concentrated giving a 5:1 Z/E mixture of isomers. Purification by flash chromatography on silica gel (25:1 hexane/EtOAc) afforded 224 mg (56%) of pure 13b followed by the *E*-isomer: ¹H NMR 5.93 (tq, 1, J = 7.3, 1.3), 5.81 (ddt, 1, J = 10.2, 17.0, 6.6), 5.03 (ddd, 1, J = 1.3, 1.3, 17.0), 4.98 (br d, 1, J = 10.2), 4.20 (q, 2, J = 7.1), 2.56 (ddt, 2, J = 1.3, 7.3, 7.3), 2.17 (dtt, 2, J = 6.6, 1.3, 7.3), 1.90 (d, 3, J = 1.3), 1.30 (t, 3, J = 7.1); ¹³C NMR 167.9, 141.8, 137.8, 127.5, 114.8, 59.9, 33.3, 28.7, 20.5, 14.2; IR (neat) 1715, 1641 cm⁻¹.

2-Methyl-5-phenyl-2Z-penten-1-ol (14a). LAH (200 mg, 5.3 mmol) was added to a solution of **13a** (366 mg, 1.68 mmol) in ether (20 mL) at 0 °C. The mixture was stirred for 2 h at room temperature and then quenched by sequential addition of H₂O (0.2 mL), 15% NaOH (0.2 mL), and H₂O (0.6 mL). Filtration and removal of the solvent afforded 292 mg (99%) of alcohol **14a**:¹³ ¹H NMR 7.32-7.14 (m, 5), 5.33 (br t, 1, J = 7.7), 3.93 (d, 2, J = 6.0), 2.66 (t, 2, J = 7.3), 2.37 (dt, 2, J = 7.7, 7.3), 1.76 (d, 3, J = 1.1); ¹³C NMR 141.8, 135.4, 128.7, 128.3, 127.1, 126.0, 61.5, 36.1, 29.6, 21.2; IR (CCl₄) 3622, 3570 cm⁻¹.

2-Methyl-2Z,6-heptadien-1-ol (14b). LAH (130 mg, 3.6 mmol) was added to a solution of 13b (200 mg, 1.2 mmol) in ether (20 mL) at 0 °C. The reaction was stirred for 2 h at rt and quenched by sequential addition of H_2O (0.13 mL), 15% aq.NaOH (0.13 mL), and H_2O (0.4 mL). Filtration and removal of the solvent gave 152 mg of crude 14b. Purification by flash chromatography on silica gel (4:1 hexane/EtOAc) afforded 108 mg (71%) of pure 14b:¹⁴ ¹H NMR 5.80 (ddt, 1, J = 10.2, 16.7, 6.6), 5.30 (br t, 1, J = 7.3), 5.02 (br d, 1, J = 16.7), 4.98 (br d, 1, J = 10.2), 4.12 (br s, 2), 2.19-2.06 (m, 4), 1.80 (s, 3) 1.39 (br s, 1); ¹³C NMR 138.2, 134.8, 127.6, 114.9, 61.5, 33.9, 27.0, 21.2; IR (neat) 3330 cm⁻¹.

1-Bromo-2-methyl-5-phenyl-2Z-pentene (15a). Et₃N (0.46 mL, 3.3 mmol) was added dropwise to a solution of alcohol 14a (292 mg, 1.66 mmol) and MsCl (0.2 mL, 2.6 mmol) in THF (10 mL) at -45 °C. The reaction was stirred for 1 h and warmed to 0 °C. A solution of LiBr (600 mg, 7.0 mmol) in THF (2 mL) was added. The reaction was stirred for 30 min and quenched with saturated NH₄Cl solution. The resulting mixture was extracted with CH₂Cl₂ (3 × 20 mL), and the combined organic layers were washed with water and brine, and dried (MgSO₄). Removal of the solvent afforded 412 mg of crude product. Purification by flash chromatography on silica gel (25:1 hexane/EtOAc) gave 295 mg (74%) of pure 15a: ¹H NMR 7.35-7.12 (m, 5), 5.43 (br tq, 1, J = 7.3, 1.3), 3.89 (s, 2), 2.69 (t, 2, J = 7.7), 2.38 (dt, 2, J = 7.3, 7.7), 1.82 (d, 3, J = 1.3); ¹³C NMR 141.4, 132.2, 130.5, 128.4, 128.3, 125.9, 33.4, 32.1, 29.9, 21.9; IR (neat) 3026, 2933, 2857, 1603 cm⁻¹.

1-Bromo-2-methyl-2Z,6-heptadiene (15b). PBr₃ (0.6 mL, 5.9 mmol) was added in one portion to a solution of crude alcohol 14b (prepared from 500 mg (5.95 mmol) of 12b) and pyridine (40 μ L, 0.5 mmol) in ether (20 mL) at rt. The reaction was stirred for 5 h and diluted with pentane. The organic phase was washed with saturated NaHCO₃ solution, water and brine, and dried (MgSO₄). Evaporation of the solvent afforded crude 15b that was used without purification because of its volatility: ¹H NMR 5.86-5.75 (m, 1), 5.41-5.37 (m, 1), 5.04 (br d, 1, J = 17.2), 4.89 (br d, 1, J = 10.2), 3.98 (s, 2), 2.22-2.10 (m, 4), 1.84 (d, 1, J = 1.5); ¹³C NMR

137.8, 131.9, 130.8, 115.0, 33.2, 32.2, 27.4, 21.8.

Ethyl 2,6-Dimethyl-3-oxo-9-phenyl-6Z-nonenoate (6a). Ethyl 2-methylacetoacetate (711 mg, 4.93 mmol) was added dropwise to a solution of NaH (208 mg, 5.2 mmol) and HMPA (0.52 mL, 3.0 mmol) in THF (20 mL) at 0 °C. The reaction was stirred for 1 h and then treated with *n*-BuLi (2.1 mL, 5.2 mmol of 2.5 M solution in hexane). The resulting mixture was stirred for 1 h and a solution of bromide **15a** (295 mg, 1.2 mmol) in THF (5 mL) was transferred to the reaction via cannula. The reaction mixture was stirred for 45 min, quenched with saturated NH₄Cl solution, and extracted with Et₂O (3 × 20 mL). The combined organic layers were washed with water and brine, and dried (MgSO₄). Purification by flash chromatography on silica gel (25:1 hexane/EtOAc) gave 345 mg (92%) of pure **6a**: ¹H NMR 7.31-7.14 (m, 5), 5.21 (br t, 1, *J* = 7.3), 4.19 (q, 2, *J* = 7.1), 3.46 (q, 1, *J* = 7.1), 2.63 (t, 2, *J* = 7.8), 2.54-2.21 (m, 6), 1.65 (br s, 3), 1.32 (d, 3, *J* = 7.1), 1.25 (t, 3, *J* = 7.1); ¹³C NMR 205.0, 170.2, 141.8, 133.9, 128.3, 128.0, 125.5, 125.3, 61.0, 52.6, 39.4, 35.9, 29.6, 25.5, 22.9, 13.8, 12.4; IR (neat) 1743, 1715 cm⁻¹.

Ethyl 2,6-Dimethyl-3-oxo-6Z,10-undecenoate (6b). Ethyl 2-methylacetoacetate (1.27 g, 8.8 mmol) was added dropwise to a solution of NaH (370 mg, 9.2 mmol) and HMPA (0.6 mL, 5.3 mmol) in THF (40 mL) in THF (20 mL) at 0 °C. The reaction was stirred for 1 h and then treated with *n*-BuLi (3.7 mL, 9.2 mmol of 2.5 M solution in hexane). The resulting mixture was stirred for 1 h and a solution of crude bromide 15b in THF (3 mL) was transferred to the reaction via cannula. The reaction mixture was stirred for 45 min, quenched with saturated NH₄Cl solution, and extracted with ether (3×50 mL). The combined organic layers were washed with water and brine, and dried (MgSO₄). Purification by flash chromatography on silica gel (25:1 hexane/EtOAc) gave 322 mg (21% from 12b) of pure 6b: ¹H NMR 5.80 (ddt, 1, *J* = 10.2, 17.0, 6.6), 5.16 (br t, 1, *J* = 6.2), 5.01 (d, 1, *J* = 17.0), 4.95 (d, 1, *J* = 10.2), 4.19 (q, 2, *J* = 7.1), 3.52 (q, 1, *J* = 7.1), 2.64 (dt, 1, *J* = 17.4, 7.8), 2.55 (dt, 1, *J* = 17.4, 7.8), 2.30 (dd, 2, *J* = 7.8, 7.8), 2.10-2.03 (m, 4), 1.67 (s, 3), 1.34 (d, 3, *J* = 7.1), 1.27 (t, 3, *J* = 7.1); ¹³C NMR 205.4, 170.4, 138.3, 133.7, 125.6, 114.5, 61.2, 52.8, 39.7, 33.9, 27.1, 25.7, 23.0, 14.0, 12.6; IR (neat) 1745, 1715 cm⁻¹.

Oxidative Cyclization of 6a. A solution of β -keto ester **6a** (98.5 mg, 0.33 mmol) in AcOH (3 mL) was added to a solution of Mn(OAc)₃•2H₂O (197 mg, 0.73 mmol) in AcOH (7 mL) and the resulting mixture was stirred for 2 h at rt, at which time it became clear. The reaction was diluted with water and extracted with CH₂Cl₂ (3 × 40 mL). The combined organic layers were washed with saturated NaHCO₃ solution, water, and brine, and dried (MgSO₄). Evaporation of the solvent under reduced pressure afforded 84.8 mg of crude product. Flash chromatography on silica gel (50:1 hexane/EtOAc) gave 6 mg of recovered **6a**, followed by 5 mg of a 2.3:3.6:1 mixture of **4**, **16**, and **6a**, 31 mg of a 1.8:1 mixture of **4** and **9**, 23 mg of **10**, and 9 mg of **17**. The calculated yields are 6.6 mg (7%) of recovered **6a**, 22 mg (22%) of **4**, 11 mg (11%) of **9**, 23 mg (24%) of **10**, 2.4 mg (2%) of **16**, and 8.9 mg (10%) of **17**.

Data for ethyl $(1\alpha,4\alpha\alpha,10\alpha\beta)$ -1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-2-oxophenanthrene-1-carboxylate (4) were determined from cyclization of **1a**:³ mp 109.5-110.5; ¹H NMR 7.30-7.05 (m, 4), 4.17 (q, 2, J = 7.1), 3.13 (ddd, 1, J = 6.8, 15.1, 15.1), 2.95 (ddd, 1, J = 3.5, 3.5, 16.8), 2.83 (ddd, 1, J = 10.0, 10.0, 16.8), 2.64-2.52 (m, 2), 2.22-2.12 (m, 2), 1.85-1.75 (m, 2), 1.46 (s, 3), 1.35 (s, 3), 1.27 (t, 3, J = 7.1); ¹³C NMR 207.9, 173.5, 146.0, 134.9, 129.2, 126.0, 126.0, 125.4, 61.2, 57.6, 53.8, 39.0, 38.0, 37.4, 31.7, 22.8, 21.3, 20.9, 13.9; IR (CHCl₃) 1748, 1708 cm⁻¹. Anal. Calcd for C₁₉H₂₄O₃: C, 75.97; H, 8.05. Found: C, 75.57; H, 8.00.

Partial data for ethyl $(1\alpha,4a\alpha,10a\alpha)$ -1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-2-oxophenanthrene-1carboxylate (9) were determined from the mixture: ¹H NMR 4.30-4.15 (m, 2), 2.78-2.71 (m, 2), 2.06-1.94 (m, 2), 1.50 (s, 3), 1.29 (s, 3), 1.28 (t, 3, J = 7.3).

Data for ethyl $(1\alpha,4\alpha\beta,10\alpha\alpha)$ -1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-2-oxo-phenanthrene-1-carboxylate (**10**): ¹H NMR 7.32-7.05 (m, 5), 4.27-4.10 (m, 2), 3.00-2.84 (m, 2), 2.81 (dd, 1, J = 2.2, 12.4), 2.77 (ddd, 1, J = 7.1, 11.5, 16.6), 2.66 (ddd, 1, J = 3.3, 6.6, 16.6), 2.56 (ddd, 1, J = 3.3, 7.1, 13.4), 2.05 (ddd, 1, J = 6.6, 11.5, 13.4), 1.89 (dddd, 1, J = 7.1, 11.1, 12.4, 13.2), 1.54 (dddd, 1, J = 2.2, 2.4, 6.2, 13.2), 1.45 (s, 3), 1.35 (s, 3), 1.23 (t, 3, J = 7.1); ¹³C NMR 210.2, 172.9, 146.7, 134.7, 129.2, 126.2, 126.0, 125.2, 61.4, 60.8, 46.6, 36.7, 36.6, 35.2, 30.4, 24.3, 21.2, 16.7, 14.0; IR (neat) 1733, 1706 cm⁻¹.

Partial data for 16 were determined from the mixture: ¹H NMR (endocyclic isomer) 5.49 (m, 1), 1.86 (m, 3); (exocyclic isomer) 5.10 (br s, 1), 4.98 (br s, 1).

Data for *syn*-1,5-dimethyl-8-(2-phenylethyl)-6-oxobicyclo[3.2.1]octane-2,7-dione (17): ¹H NMR 7.30-7.10 (m, 5), 2.74 (ddd, 1, J = 6.2, 9.5, 13.7), 2.63 (ddd, 1, J = 7.0, 9.5, 13.7), 2.57 (ddd, 1, J = 9.0, 10.1, 17.4), 2.50 (ddd, 1, J = 1.5, 8.1, 17.4), 2.38 (ddd, 1, J = 1.8, 7.5, 7.5), 2.27 (dddd, 1, J = 1.5, 1.8, 9.0, 14.5), 2.08 (ddd, 1, J = 8.1, 10.1, 14.5), 1.67-1.55 (m, 1), 1.53 (s, 3), 1.32 (s, 3), 1.32-1.22 (m, 1); ¹³C

NMR 201.8, 174.3, 140.2, 128.7, 128.2, 126.5, 85.2, 61.9, 56.6, 35.0, 34.1, 31.6, 28.4, 23.3, 13.4; IR (CCl₄) 1787, 1726 cm⁻¹.

Oxidative Cyclization of 6b. A solution of β -keto ester **6b** (80 mg, 0.32 mmol) in AcOH (3 mL) was added to a degassed mixture of Mn(OAc)₃•2H₂O (170 mg, 0.63 mmol) and Cu(OAc)₂ (58 mg, 0.32 mmol) in AcOH (5 mL). The resulting mixture was stirred for 2 h at rt. The reaction was diluted with water and extracted with CH₂Cl₂ (3 × 40 mL). The combined organic layers were washed with saturated NaHCO₃ solution, water, and brine, and dried (MgSO₄). Evaporation of the solvent under reduced pressure afforded 76 mg of crude product. Flash chromatography on silica gel (50:1 hexane/EtOAc) gave 12 mg of recovered **6b**, followed by 5 mg of a 1:6.7 mixture of **6b** and **11**, 9 mg of **11**, 6 mg of a 4:1 mixture of **11** and **5**, 19 mg of a 1:4:4.5 mixture of **11**, **18b** and **5**. The calculated yields are 13 mg (16%) of recovered **6b**, 20 mg (25%) of **11**, 10 mg (13%) of **5**⁸ and 8.0 mg (10%) of **18b**.

Data for ethyl $(3\alpha\alpha,4\alpha,7\alpha\alpha)$ -4,7a-dimethyl-1-methylene-5-oxo-2,3,3a,4,5,6,7,7a-octahydro-1*H*-indene-4carboxylate (**11**): ¹H NMR 4.87 (br s, 1), 4.76 (br s, 1), 4.29-4.13 (m, 2), 2.73 (dd, 1, J = 7.5, 12.3), 2.61 (ddd, 1, J = 4.8, 7.5, 16.5), 2.41-2.32 (m, 2), 2.20 (ddd, 1, J = 4.4, 9.0, 16.5), 1.93-1.82 (m, 2), 1.63 (ddd, 1, J = 4.4, 9.0, 19.2), 1.28 (t, 3, J = 7.1), 1.25 (s, 3), 1.24 (s, 3), 1.09-0.93 (m, 1); ¹³C NMR 209.4, 173.5, 159.2, 103.7, 61.4, 57.3, 53.4, 43.6, 36.2, 33.4, 30.9, 27.8, 26.7, 19.6, 14.0; IR (neat) 1714, 1655 cm⁻¹.

Partial data for **18b** were determined from the mixture: ¹H NMR 5.79 (ddt, 1, J = 10.4, 17.1, 6.4), 5.57-5.46 (m, 2), 5.06-4.98 (m, 2), 4.15-3.95 (m, 2), 2.78 (br dd, 2, J = 5.5, 5.5), 2.47-2.28 (m, 2), 1.80-1.72 (m, 1), 1.40 (s, 3), 1.01 (s, 3); ¹³C NMR 216.5, 171.0, 136.6, 134.8, 126.8, 115.3, 63.4, 60.9, 43.8, 36.7, 35.8, 31.6, 22.8, 14.1, 13.6.

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