Preparation of Epoxides by Oxidative Decarboxylation of β-Hydroxy Acids. Stereo- and Regiochemistry of Oxidative Elimination of Secondary Radicals with Cupric Acetate

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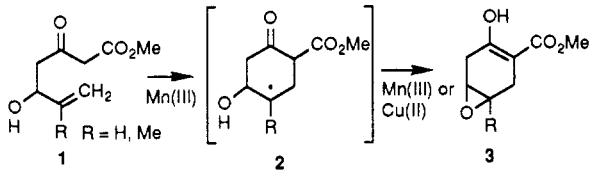
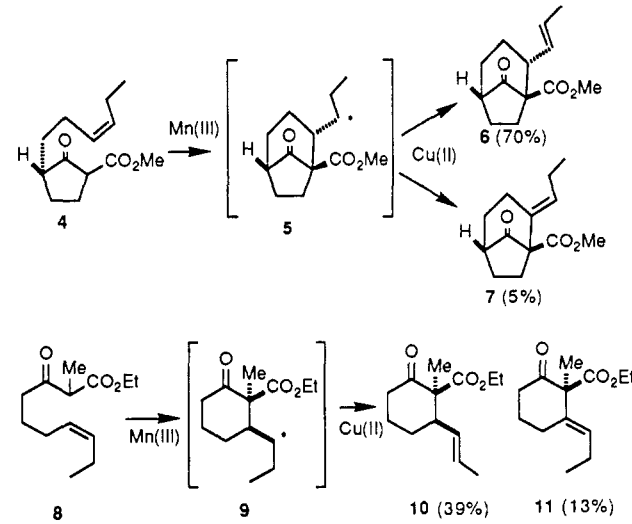
Introduction

During our studies of manganese(III)-based oxidative free-radical cyclizations[1-10] we observed to our surprise that the β-hydroxy radical **2**, prepared by oxidation of the β-keto ester **1** with manganese triacetate in acetic acid, was oxidized by manganese(III) to epoxide **3** in 30–50% yield.[7] There are isolated reports that transition-metal oxidants will convert β-hydroxy radicals to epoxides. Copper(II) has been shown to oxidize β-hydroxy radicals to epoxides with a second order rate constant of $\approx 10^7$ M^{-1} S^{-1}.[11-13] Corey found that oxidative decarboxylation of a β-hydroxy acid with lead tetraacetate gave a compound tentatively identified as an epoxide.[14,15] Oxidation of β-hydroxy radicals has also been implicated in the biosynthesis of epoxides from alkenes.[16] We report here studies on the generality, mechanism, and stereochemistry of epoxide formation from β-hydroxy radicals generated by the decarboxylation of β-hydroxy acids with lead tetraacetate.[17]



We also observed to our surprise that secondary radical **5**, prepared by oxidation of the β-keto ester **4** with manganese triacetate and cupric acetate in acetic acid, was oxidized by copper(II) to give a 14:1 mixture of the *E* Hofmann elimination product **6** and the Zaitsev elimination product **7**. Similarly, secondary radical **9**, prepared by oxidation of the β-keto ester **8** with manganese triacetate and cupric acetate in acetic acid, was oxidized by copper(II) to give a 3:1 mixture of the *E* Hofmann elimination product **10** and the Zaitsev elimination product **11**. The oxidation of secondary radicals to alkenes by cupric acetate is well-known.[18-22] The selective formation of the Hofmann isomer and the exclusive formation of the *E* isomer[23] was unanticipated since Kochi has reported that oxidation of the 3-pentyl radical by cupric acetate gave both (*E*)-2-pentene (45%) and (*Z*)-2-pentene (27%),[21] and that oxidation of the 2-butyl radical gave 1-butene (35%), (*E*)-2-butene (24%), and (*Z*)-2-butene (25%).[22] Mixtures of *Z* and *E* isomers have also been observed in lead tetraacetate and cupric acetate decarboxylation of diacids and acetoxy acids.[24,25]



There is limited precedent for the selective formation of Hofmann and *E* isomers in oxidation of secondary radicals with cupric acetate. Collum reported a selective Hofmann oxidative elimination of a 1-cyclohexylethyl radical to a vinylcyclohexane in his phyllanthoside synthesis.[26] Čeković found that oxidation of the 5-hydroxy-2-hexyl radical with cupric acetate gave a 6:1 mixture of 5-hexen-2-ol and 4-hexen-2-ol, while oxidation of the 6-hydroxy-3-hexyl radical gave a 4:1 mixture of 4-hexen-1-ol (90% *E*) and 3-hexen-1-ol.[27] They suggested that the

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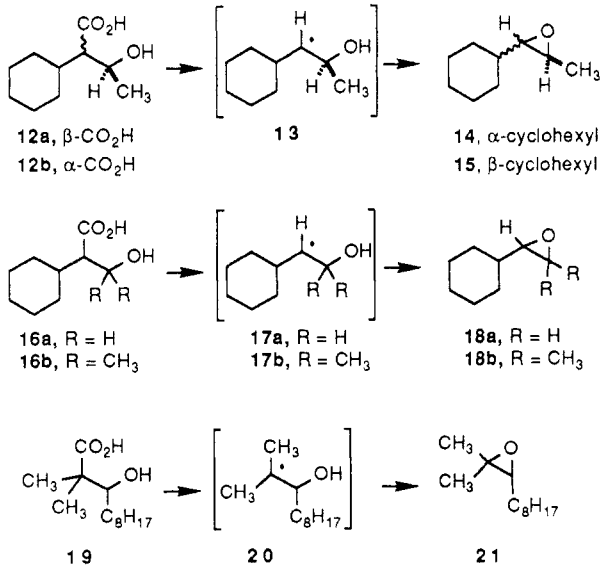
control resulted from coordination of the copper to the hydroxyl group. In some, but not all, cases, Schreiber has observed selective formation of the *E* isomer in cupric acetate oxidation of secondary radicals generated by fragmentation of α-alkoxy hydroperoxides.[28-30]

We decided to briefly examine the regio- and stereoselectivity of alkene formation in oxidative decarboxylation of secondary acids with $Pb(OAc)_4$ and $Cu(OAc)_2$. Substrates were chosen to provide radicals analogous to those obtained in the oxidative free-radical cyclizations of **4** and **8** to determine whether the Hofmann and *E* selectivity observed in the oxidation of **5** and **9** results from the proximity of the ketone and ester groups to the radical center.

Results and Discussion

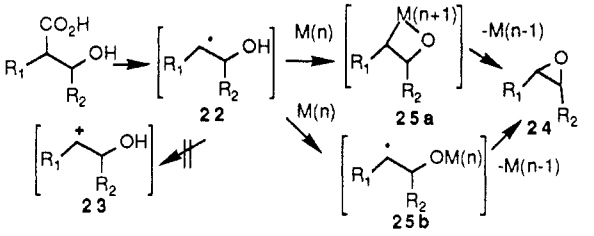
Epoxide Formation. A mixture of hydroxy acids **12a** and **12b**[31] (88%) was prepared by addition of acetaldehyde to the lithium enolate of ethyl cyclohexaneacetate in THF/HMPA at −78 °C followed by hydrolysis.[32] Separation of the esters prior to hydrolysis gave pure samples of **12a** and **12b**.[33] Hydroxy acids **16a**[31] (88%) and **16b**[31] (85%) were prepared by reaction of the dianion of cyclohexaneacetic acid in THF/HMPA at 0 °C with formaldehyde and acetone, respectively. Addition of nonanal to the dianion of isobutyric acid in THF/HMPA at 0 °C gave hydroxy acid **19** (90%).[34]



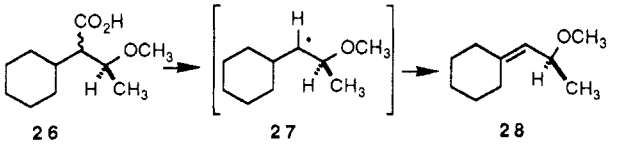
Formation of epoxides in oxidative decarboxylation of secondary β-hydroxy acids is a general reaction. Oxidative decarboxylation of a mixture of **12a** and **12b** with 1 equiv each of lead tetraacetate and pyridine in benzene at reflux for 5 h gave 50% of a 10:1 mixture of **14**[35] and **15**. An identical mixture of **14** and **15** was obtained from either pure diastereomer, **12a** or **12b**. A similar reaction with 1 equiv of both lead tetraacetate and cupric acetate gave 47% of a 4:1 mixture of **14** and **15**. Apparently, oxidative cyclization of **13** is more stereoselective with lead than with copper. Oxidative decarboxylation of **16a** and **16b** with 1 equiv of lead tetraacetate in benzene at reflux gave **18a**[36] (31%) and **18b** (68%), respectively.

Oxidative decarboxylation of primary and tertiary β-hydroxy acids was less successful. Reaction of **19** with 1 equiv of $Pb(OAc)_4$ and pyridine in benzene at reflux gives only 16% of **21**.[37] The low yield may be due to competing oxidation of the tertiary radical **20** to the cation. No epoxide could be isolated from the reaction of 4-*tert*-butyl-1-hydroxycyclohexaneacetic acid with lead tetraacetate in benzene at reflux.

These results demonstrate that lead tetraacetate, manganese triacetate, or cupric acetate will oxidize β-hydroxy radicals to epoxides. The presence of radical intermediates such as **22** are implicated by the mechanism of lead tetraacetate decarboxylation[15] and the formation of identical mixtures of epoxides from either diastereomer of **12**. Oxidation of radical **22** to cation **23** and collapse to epoxide **24** is precluded since lead tetraacetate does not oxidize secondary radicals to cations.[15] The most likely mechanisms involve either formation of the metallooxetane **25a** and reductive elimination to give epoxide **24** or formation of the β-metallooxy radical **25b** followed by attack of the carbon radical on the oxygen center and elimination of the reduced metal.



We have demonstrated that the proton on the hydroxyl group is necessary for epoxide formation. Methylation of the methyl ester of **12** with KOH and methyl iodide in DMSO followed by hydrolysis with sodium iodide in DMF at reflux gave 32% of methoxy acid **26**. Reaction of **26** with lead tetraacetate gave a complex mixture of products. Oxidative decarboxylation with 1 equiv each of lead tetraacetate, cupric acetate, and pyridine in benzene at reflux gave 51% of allylic ether **28**. Decarboxylation of **26** gives radical **27** which, as expected,[15] is not oxidized by lead tetraacetate. Radical **27** undergoes oxidative elimination on reaction with cupric acetate to give allylic ether **28**. The methoxy group does effect the direction of the elimination (see below).



Alkene Formation. Secondary radicals can be easily generated in the presence of cupric acetate by oxidative decarboxylation by Kochi's procedure with lead tetraacetate and cupric acetate.[15] Acids **31a**[38] (90%) and **31b**[39]

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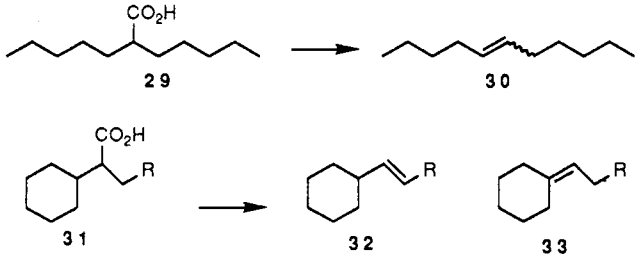
(97%) were prepared by alkylation of the enolate of ethyl cyclohexaneacetate followed by hydrolysis. Oxidative decarboxylation of acid **29** with 1 equiv of lead tetraacetate and 1 equiv of cupric acetate in benzene containing 1% pyridine gave 96% of a 4:1 mixture of (*E*)- and (*Z*)-5-undecene (**30**).[40] A similar reaction using only 0.02 equiv of cupric acetate gave 99% of a 5:1:2 mixture of (*E*)- and (*Z*)-5-undecene (**30**) and 6-undecanyl acetate. Oxidative decarboxylation of acid **31a** with 1 equiv of cupric acetate gave 98% of a 4:1 mixture of (*E*)-alkene **32a**[41] and **33a**.[42] The *Z* isomer of **32a** was not formed. Use of only 0.02 equiv of cupric acetate gave 26% of the acetate and 68% of a 4:1 mixture of (*E*)-alkene **32a** and **33a**. Oxidative decarboxylation of acid **31b** with 1 equiv of cupric acetate gave a 2.7:1 mixture of alkenes **32b** and **33b**.



These results demonstrate that oxidative elimination of secondary radicals with cupric acetate is modestly selective for the Hofmann and *E* isomer. The exceptional Hofmann selectivity observed by Collum[26] in a single case is probably a result of substituent effects. The formation of a 4:1 mixture of **32a** and **33a** corresponds closely to the 3:1 ratio of **10** and **11** obtained from radical **9**, suggesting that the oxidative elimination steps in these two reactions are similar. The exclusive formation of *E* isomer **32a**, the formation of 20% of the *Z* isomer of **30** and the formation of 50% of (*Z*)-2-butene[22] suggests that oxidative elimination will be stereospecific when one of the two substituents on the alkene is α-branched, selective for the *E* isomer when both substituents are primary, and stereorandom when both substituents are methyl groups.

Experimental Section

General. NMR spectra were recorded on Varian EM-390 and XL-300 NMR spectrometers in $CDCl_3$. Chemical shifts are reported in δ, and coupling constants in hertz. IR spectra were obtained on a Perkin-Elmer 683 spectrometer. All air-sensitive reactions were run under nitrogen in flame-dried glassware with magnetic stirring. Reagents were added via oven-dried syringes through septa. All solvents for moisture-sensitive reactions were dried by standard procedures.

Synthesis of 2-Cyclohexyl-3-hydroxybutanoic Acid (12). *n*-Butyllithium in hexane (2.4 M, 4.0 mL, 9.3 mmol) was added dropwise to a solution of diisopropylamine (1.3 mL, 9.3 mmol) in 7 mL of THF at 0 °C under nitrogen. The solution was stirred for 0.5 h and treated with HMPA (3.2 mL, 9.3 mmol). The solution was stirred for an additional 0.5 h and cooled to −78 °C. Ethyl cyclohexaneacetate (1.58 g, 9.30 mmol) in 10 mL of THF was added dropwise to the LDA solution. The resulting solution was stirred under N_2 for 0.5 h at −78 °C and then treated with acetaldehyde (3.9 mL, 70 mmol). The reaction mixture was stirred at −78 °C under N_2 for 0.5 h and for 1.5 h at 0 °C, acidified with aqueous 5% HCl solution, and extracted twice with ether (20 mL). The ether solution was washed with saturated aqueous NaCl solution, dried ($MgSO_4$), and concentrated in vacuo to give 1.90 g (96%) of ethyl 2-cyclohexyl-3-hydroxybutanoate as a mixture of diastereomers, which was hydrolyzed without further purification.

A solution of crude ester (1.17 g, 5.47 mmol) and lithium hydroxide (2.12 g, 88 mmol) in DME–water (70 mL/100 mL) was heated at reflux for 2 days. The solution was cooled to room temperature, acidified with 5% aqueous HCl solution, and extracted with ether. The ether layer was washed with saturated aqueous NaCl solution, dried over anhydrous $MgSO_4$, and concentrated in vacuo to give 940 mg (88%) of a mixture of **12a** and **12b**.

The diastereomers of the ethyl ester were separated by flash column chromatography (3:1 hexane/ether) on silica gel. The less polar isomer was hydrolyzed to **12a**. The more polar isomer was hydrolyzed to **12b**.

The data for **12a**:[33] mp 140–141 °C (lit.[31] mp 140–142 °C); ^{1}H NMR 4.12 (dq, 1, J = 4.3, 6.5), 2.19 (dd, 1, J = 4.3, 8.7), 1.28 (d, 3, J = 6.5), 0.90–2.00 (m, 11); ^{13}C NMR 180.0, 65.2, 58.0, 36.9, 31.0, 30.9, 26.2, 26.1 (2 C), 22.1; IR (neat) 3000–3500, 2930, 1708 cm^{-1}.

The data for **12b**:[33] mp 133–134 °C; ^{1}H NMR 4.16 (dq, 1, J = 6.6, 6.5), 2.40 (dd, 1, J = 6.6, 6.6), 1.29 (d, 3, J = 6.5), 0.90–2.00 (m, 11); ^{13}C NMR 179.0, 66.2, 58.0, 36.4, 31.3, 30.3, 26.4, 26.2, 26.1, 20.0; IR (neat) 3000–3500, 2930, 1708 cm^{-1}.

Reaction of 12 with Lead Tetraacetate. A solution of **12** (200 mg, 1.07 mmol), $Pb(OAc)_4$ (476 mg, 1.07 mmol), and pyridine (0.086 mL, 1.07 mmol) in 10 mL of benzene was heated at reflux for 5 h. A few drops of ethylene glycol were added to destroy the remaining lead tetraacetate, and 20 mL of water was added to the reaction mixture. The layers were separated, the aqueous layer was extracted with ether (5 mL × 2), and the combined organic layers were washed with saturated aqueous $NaHCO_3$ solution, 5% aqueous HCl solution, and saturated aqueous NaCl solution and dried over anhydrous $MgSO_4$. Evaporation of the solvent in vacuo gave 140 mg of yellow oil, which was purified by bulb-to-bulb distillation to give 75.7 mg (50%) of a 10:1 mixture of *trans*- and *cis*-2-cyclohexyl-3-methyloxiranes (**14** and **15**),[35] respectively: ^{1}H NMR (**14**) 2.80 (dq, 1, J = 2.2, 5.2), 2.42 (dd, 1, J = 2.3, 6.4), 1.29 (d, 3, J = 5.2), 0.50–2.00 (m, 11); (**15**) 3.05 (dq, 1, J = 4.4, 5.6), 2.60 (dd, 1, J = 4.4, 8.3), 1.27 (d, 3, J = 5.6), 0.50–2.00 (m, 11); ^{13}C NMR (**14**) 64.1, 53.2, 39.9, 29.5, 28.9, 26.2, 25.6, 25.4, 17.7; (**15**) 61.4, 52.5, 36.2, 30.5, 28.7, 26.1, 25.3, 12.6, one carbon in the 25.0–27.0 region is masked by the major isomer; IR (neat) 2930 cm^{-1}.

Synthesis of 2-Cyclohexyl-3-hydroxypropanoic Acid (16a). A solution of cyclohexaneacetic acid (1.39 g, 9.21 mmol) was added at 0 °C to a solution of LDA made from diisopropylamine (2.6 mL, 18.5 mmol), *n*-butyllithium (2.5 M, 7.6 mL, 19 mmol), and HMPA (1.61 mL, 9.26 mmol) in 15 mL of THF. The solution was stirred at 0 °C for 1 h and treated at 0 °C with gaseous formaldehyde (generated from the thermal decomposition at 180–200 °C of 2.5 g of paraformaldehyde which had been dried 2 days over P_2O_5 in vacuo) and stirred at 0 °C for 1 h and at room temperature overnight. To this reaction mixture was added 10 mL of water, and the organic layer was separated and washed with 5 mL of water. The combined aqueous layer was washed twice with ether (10 mL), acidified with 5% aqueous HCl solution, and extracted twice with ether (10 mL). The combined ether layers were washed three times with saturated aqueous NaCl solution (10 mL), dried over anhydrous $MgSO_4$, and evaporated in vacuo to give 1.39 g (88%) of **16a**: mp 88–89 °C (lit.[31] mp 89–90 °C); ^{1}H NMR 3.88 (dd, 1, J = 8.7, 11.0), 3.80 (dd, 1, J = 4.2, 11.0), 2.43 (ddd, 1, J = 4.2, 6.6, 8.7), 0.6–2.1 (m, 11); ^{13}C NMR 180.1, 61.2, 53.6, 37.2, 31.0, 30.4, 28.2 (2 C), 26.1; IR (neat) 3000–3700, 2930, 1708 cm^{-1}.

Reaction of 16a with Lead Tetraacetate. Reaction of acid **16a** (300 mg, 1.76 mmol) with $Pb(OAc)_4$ (781 mg, 1.76 mmol) in benzene (10 mL) as described above for **12** gave 68 mg (31%) of cyclohexyloxirane (**18a**):[36] ^{1}H NMR 2.52 (dd, 1, J = 3.4, 4.4), 2.68–2.74 (m, 2), 0.60–2.10 (m, 11); ^{13}C NMR 56.6, 45.9, 40.3, 29.7, 28.8, 26.3, 25.6, 25.5; IR (neat) 3050, 2930 cm^{-1}.

Synthesis of 2-Cyclohexyl-3-hydroxy-3-methylbutanoic Acid (16b). Cyclohexaneacetic acid (1.31 mg, 9.21 mmol) was converted to the dianion with LDA as described above and treated with acetone (0.67 mL, 9.21 mmol). Workup as above gave 1.58 g (85%) of **16b**: mp 104–105 °C (lit.[31] mp 107–108 °C); ^{1}H NMR

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2.28 (d, 1, J = 5.1), 1.33 (s, 3), 1.31 (s, 3), 0.90–2.10 (m, 11); ^{13}C NMR 180.0, 71.9, 60.2, 36.7, 34.2, 30.2, 30.0, 27.0, 26.9, 26.5, 26.0; IR (neat) 3000–3700, 2930, 1708 cm^{-1}.

Reaction of 16b with Lead Tetraacetate. Reaction of **16b** (349 mg, 1.74 mmol) with $Pb(OAc)_4$ (772 mg, 1.74 mmol) in 10 mL of benzene as described above gave 147 mg (68%) of 2-cyclohexyl-3,3-dimethyloxirane (**18b**): ^{1}H NMR 2.45 (d, 1, J = 9.7), 1.30 (s, 3), 1.28 (s, 3), 0.90–2.10 (m, 11); ^{13}C NMR 68.9, 58.2, 37.6, 30.4, 28.9, 26.2, 25.5, 25.3, 25.0, 18.7; IR (neat) 2930 cm^{-1}. Anal. Calcd for $C_{10}H_{18}O$: C, 77.92; H, 11.68. Found: C, 77.61; H, 11.87.

Synthesis of 2,2-Dimethyl-3-hydroxyundecanoic Acid (19). Isobutyric acid (1.28 mL, 27.8 mmol) was converted to the dianion with LDA as described above and treated with nonanal (2.37 mL, 13.8 mmol). Workup as above gave 2.87 g (90%) of **19**:[34] ^{1}H NMR 3.65 (dd, 1, J = 2.0, 10.0), 1.19 (s, 3), 1.23 (s, 3), 0.9–1.7 (m, 14), 0.88 (t, 3, J = 6.8); ^{13}C NMR 183.4, 76.6, 47.0, 31.8, 31.5, 29.6, 29.5, 29.3, 26.6, 22.6, 22.4, 20.1, 14.1; IR (neat) 2300–3700, 1708 cm^{-1}.

Reaction of 19 with Lead Tetraacetate. Reaction of acid **19** (334 mg, 1.45 mmol), $Pb(OAc)_4$ (643 mg, 1.45 mmol), and pyridine (0.116 mL) as described above in 10 mL of benzene gave 281 mg of yellow oil, which was purified by flash column chromatography on silica gel (6:1 hexane/ether) to give 42.5 mg (16%) of 2,2-dimethyl-3-octyloxirane (**21**):[37] ^{1}H NMR 2.72 (t, 1, J = 7.1), 1.32 (s, 3), 1.25 (s, 3), 0.9–1.75 (m, 14), 0.88 (t, 3, J = 6.8); ^{13}C NMR 64.6, 58.2, 31.8, 29.6, 29.5, 29.2, 28.8, 26.5, 24.9, 22.6, 18.7, 14.1; IR (neat) 2930 cm^{-1}.

Synthesis of α-(1-Methoxyethyl)cyclohexaneacetic Acid (26). Iodomethane (0.56 mL, 9.00 mmol) was added to a solution of potassium hydroxide (1.14 g, 10.85 mmol) and the methyl ester of **12** (828 mg, 4.44 mmol) in 9 mL of DMSO. This reaction mixture was stirred at room temperature for 0.5 h, poured into 75 mL of water, and extracted with ether (25 mL × 3). The combined ether solution was washed with water, dried over anhydrous $MgSO_4$, and evaporated in vacuo to give 381 mg (42%) of methyl α-(1-methoxyethyl)cyclohexaneacetate, which was hydrolyzed without further purification.

A solution of crude ester (309 mg, 1.53 mmol) and NaI (1.80 g, 12.0 mmol) in 10 mL of DMF was heated at reflux overnight. This reaction mixture was cooled, poured into 20 mL of water, and extracted with ether. The ether solution was washed with 5% aqueous HCl solution and saturated aqueous NaCl solution, dried over anhydrous $MgSO_4$, and evaporated in vacuo to give 321 mg of crude acid, which was purified by flash column chromatography on silica gel (9:1 hexane/ether) to give 225 mg (77%) of **26** as a 6:1 mixture of diastereomers: (major diastereomer) ^{1}H NMR 3.66 (dq, 1, J = 6.5, 6.2), 3.35 (s, 3), 2.30 (dd, 1, J = 6.5, 7.3), 1.21 (d, 3, J = 6.2), 0.70–2.00 (m, 11); ^{13}C NMR 178.7, 75.1, 58.0, 56.5, 36.5, 31.4, 28.9, 26.3, 26.2, 26.1, 16.2; IR (neat) 2300–3700, 1708 cm^{-1}.

Reaction of 26 with Lead Tetraacetate. A solution of **26** (132 mg, 0.66 mmol), $Pb(OAc)_4$ (292 mg, 0.66 mmol), pyridine (0.50 mL, 0.66 mmol), and $Cu(OAc)_2 \cdot H_2O$ (131 mg, 0.66 mmol) in 10 mL of benzene was heated at reflux under nitrogen for 4 h. Workup as described above gave 93.2 mg of yellow oil, which was purified by column chromatography on silica gel (9:1 hexane/ether) to give 36.8 mg (51%) of (2-methoxypropylidene)cyclohexane (**28**): ^{1}H NMR 4.98 (br d, 1, J = 9.0), 4.07 (dq, 1, J = 9.0, 6.3), 3.35 (s, 3), 2.00–2.40 (m, 4), 1.40–1.90 (m, 6), 1.19 (d, 3, J = 6.3); ^{13}C NMR 143.1, 123.8, 72.3, 55.4, 37.1, 29.2, 28.6, 27.9, 26.7, 21.7; IR (neat) 2930, 1670 cm^{-1}.

Reaction of 2-Pentylheptanoic Acid (29) with Lead Tetraacetate. $Pb(OAc)_4$ (589 mg, 1.33 mmol) was added to a solution of **29** (250 mg, 1.25 mmol), $Cu(OAc)_2 \cdot H_2O$ (265 mg, 1.33 mmol), and pyridine (0.125 mL) in 10 mL of dry benzene at reflux under nitrogen. The reaction mixture was stirred at reflux for 3 h. A few drops of ethylene glycol was added to destroy the remaining lead tetraacetate, and water was added. The layers were separated, and the aqueous layer was extracted three times with ether. The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution, 5% aqueous HCl solution, and saturated aqueous NaCl solution and dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give 185 mg (96%) of a 4:1 mixture of (*E*)- and (*Z*)-5-undecene (**30**)[40] as determined by analysis of the ^{1}H and ^{13}C NMR spectra: ^{1}H NMR 5.30–5.45 (m, 2), 1.90–2.10 (m, 4), 1.00–1.70 (m, 10), 0.90 (t, 6, J = 6.6); ^{13}C NMR (*E*) 130.4, 130.3, 32.6, 32.3, 31.9, 31.5, 29.4, 22.6, 22.2, 14.0, 13.9; (*Z*) 129.9, 129.8, 32.0, 31.8, 29.5, 27.2, 27.0, 22.5, 22.4, 14.0, 13.9; IR (neat) 2930 cm^{-1}.

Synthesis of α-Pentylcyclohexaneacetic Acid (31a). 1-Bromopentane (5.17 g, 34.2 mmol) in 10 mL of THF was added to the lithium enolate of ethyl cyclohexaneacetate (4.75 g, 27.9 mmol) in THF/HMPA at −78 °C prepared as described above. The reaction mixture was stirred under nitrogen for 2 h at −78 °C and for 1 h at 0 °C, quenched with water (20 mL), and extracted twice with ether (10 mL). The combined ether layers were washed with 5% aqueous HCl solution and saturated aqueous NaCl solution, dried over anhydrous $MgSO_4$, and concentrated in vacuo to give 7.17 g of ethyl α-pentylcyclohexaneacetate as a clear yellow oil, which was hydrolyzed without further purification.

A solution of crude ester (341 mg, 1.42 mmol) and potassium *tert*-butoxide (240 mg, 2.14 mmol) in 7 mL of dry DMSO was stirred at room temperature for 12 h under nitrogen and heated at 130 °C for an additional 2 h. The reaction mixture was poured into water, acidified with 5% aqueous HCl solution, and extracted with ether. The organic layer was washed with saturated aqueous NaCl solution, dried over anhydrous $MgSO_4$, and concentrated in vacuo to give 300 mg of brown oil. Flash column chromatography on silica gel (6:1 hexane/ether) gave 270 mg (90%) of **31a**:[38] ^{1}H NMR 2.14 (dt, 1, J = 6.6, 7.6), 0.9–1.9 (m, 19), 0.88 (t, 3, J = 6.6); ^{13}C NMR 182.7, 52.0, 40.0, 31.8, 31.0, 30.5, 29.1, 27.4, 26.4, 26.3, 26.2, 22.5, 14.0; IR (neat) 2930, 1710 cm^{-1}.

Reaction of 31a with Lead Tetraacetate. A solution of **31a** (222 mg, 1.05 mmol) and $Pb(OAc)_4$ (465 mg, 1.05 mmol), $Cu(OAc)_2 \cdot H_2O$ (210 mg, 1.05 mmol), and pyridine (0.1 mL, 1.25 mmol) in 10 mL of benzene was heated at reflux for 4 h. Workup as described above gave 171 mg (98%) of a 4:1 mixture of (*E*)-1-hexenylcyclohexane (**32a**)[41] and hexylidenecyclohexane (**33a**)[42] as determined by analysis of the ^{1}H and ^{13}C NMR spectra: ^{1}H NMR 5.35–5.45 (m, 2, **32a**), 5.07 (br t, 1, J = 8.6, **33a**), 0.95–2.35 (m), 0.8–0.95 (m, 3); ^{13}C NMR (**32a**) 136.3, 127.7, 40.7, 33.3 (2 C), 32.4, 31.9, 26.3, 26.2 (2 C), 22.2, 14.0; (**33a**) 139.3, 121.5, 37.2, 31.9, 31.6, 30.0, 28.8, 28.7, 27.9, 27.1, 22.7, 14.1; IR (neat) 2930 cm^{-1}.

Synthesis of α-Methylcyclohexaneacetic Acid (31b). A solution of iodomethane (0.58 mL, 9.32 mmol) in 3 mL of THF was added to the lithium enolate of ethyl cyclohexaneacetate (1.58 g, 9.30 mmol) in THF/HMPA at −78 °C prepared as described above. The reactiom mixture was stirred under nitrogen for 3 h at −78 °C and for 1 h at 0 °C and was quenched with water. Workup as described above gave 1.89 g of ethyl α-methylcyclohexaneacetate as a yellow oil, which was hydrolyzed without further purification.

A solution of the crude ester and potassium *tert*-butoxide (1.73 g, 15.4 mmol) in 30 mL of dry DMSO was heated at 130 °C under nitrogen for 2.5 h. Workup as described above gave 1.41 g (97%) of **31b**: mp 60–61 °C (lit.[39a] mp 62 °C); ^{1}H NMR 2.27 (dq, 1, J = 7.0, 7.0), 1.14 (d, 3, J = 7.0), 0.8–1.90 (m, 11); IR (neat) 2930, 1710 cm^{-1}.

Reaction of 31b with Lead Tetraacetate. A solution of **31b** (200 mg, 1.28 mmol), $Pb(OAc)_4$ (568 mg, 1.28 mmol), $Cu(OAc)_2 \cdot H_2O$ (255 mg, 1.28 mmol), and pyridine (0.102 mL, 1.28 mmol) in 10 mL of benzene was heated at reflux for 4 h. Workup as described above gave a benzene–ether solution of **32b** and **33b**. Capillary GC (OV 225B) at 30 °C indicated that a 2.7:1 mixture of vinylcyclohexane (**32b**) and ethylidenecyclohexane (**33b**) was present.

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Registry No. **12a**, 124781-91-5; **12a** ethyl ester, 124781-97-1; **12a** methyl ester, 124782-02-1; **12b**, 124781-92-6; **12b** ethyl ester, 124781-98-2; **12b** methyl ester, 124782-03-2; **14**, 77262-42-1; **15**, 124781-93-7; **16a**, 6051-09-8; **16b**, 92058-00-9; **18a**, 3483-39-4; **18b**, 124781-94-8; **19**, 56888-79-0; **21**, 79092-24-3; **26** (isomer 1), 124781-95-9; **26** (isomer), 124781-99-3; **26** ester (isomer 1), 124782-00-9; **26** ester (isomer 2), 124782-01-0; **28**, 124781-96-0; **29**, 5422-52-6; (*E*)-**30**, 764-97-6; (*Z*)-**30**, 764-96-5; **31a**, 37457-31-1; **31b**, 6051-13-4; **32a**, 16538-48-0; **32b**, 695-12-5; **33a**, 10201-62-4; **33b**, 1003-64-1; ethyl cyclohexaneacetate, 5452-75-5; cyclohexaneacetic acid, 5292-21-7; 1-bromopentane, 110-53-2; isobutyric acid, 79-31-2; nonanal, 124-19-6.