stirred and refluxed for 2.5 h. Most of the ethanol was removed in vacuo, and the residue was treated with 75 mL of water and 75 mL of saturated brine and worked up in the usual manner with ether. This afforded 10.25 g (99.5%) of (4*R*,8*R*)-4,8,12-trimethyltridecanenitrile as a yellow oil. GC analysis revealed a purity of 95.2%: $[\alpha]^{25}_D$ +3.93° (*c*, 2, hexanes); IR 2249 cm^{-1} (CN); ^1H NMR δ 2.34 ppm (m, 2, CH_2CN); ^{13}C NMR (400 MHz, $CDCl_3$) 120.02 (CN), 39.36, 37.22 (2 CH_2), 36.26, 32.78 (CH), 32.27, 32.08 (CH), 28.01 (CH), 24.80, 24.20, 22.74 (CH_3), 22.58 (CH_3), 19.73 (CH_3), 18.88 (CH_3), 14.95 (CH_2CN) ppm; EIHRMS *m/z* 238.2535 ($M + H^+$) ($C_{16}H_{31}N + H^+$ requires 238.2535).

A mixture of this nitrile (43.25 mmol) and 18.4 g (0.33 mol) of potassium hydroxide in 162 mL of ethylene glycol and 13.5 mL of water was stirred in a 150 °C oil bath for 4 h and then cooled to 0–5 °C and poured into 300 mL of 6 N HCl. The mixture was worked up with ethyl acetate in the usual manner, giving 11.1 g (100%) of (4*R*,8*R*)-4,8,12-trimethyltridecanoic acid as an oil.

A solution of this acid in 50 mL of toluene was stirred at room temperature while 25 mL of Red-Al in toluene (Aldrich, 3.4 M) was added dropwise. After being stirred for 3 h at room temperature, the reaction mixture was decomposed by the cautious addition of 5 mL of ethanol. The mixture was then treated with 300 mL of 6 N HCl and worked up with ethyl acetate in the usual manner. Kugelrohr distillation (160 °C bath temperature, 1 mmHg) of the residue gave 7.0 g of (4*R*,8*R*)-4,8,12-trimethyltridecanol (**12**) as a colorless liquid having a GC purity of 94.5%. The distillation residue contained starting acid and was re-reduced with 6 mL of Red-Al as described above. This provided an additional 1.8 g (total yield 8.8 g; 84.2%) of alcohol **12** having a GC purity of 95.8%. A 1.67-g sample of this material was further purified by chromatography on 50 g of silica gel. Elution with 9:1 and 4:1 hexanes–ether gave 1.53 g of alcohol **12**: $[\alpha]^{25}_D$ +1.67° (*c* 2, hexanes); IR 3623 cm^{-1} (OH); ^1H NMR δ 3.63 ppm (t, 2, *J* = 6.5 Hz, CH_2OH); ^{13}C NMR (400 MHz, $CDCl_3$) 63.55 (CH_2OH), 39.42, 37.34 (3 CH_2), 32.94, 32.84 (CH), 32.67 (CH), 30.42, 28.04 (CH), 24.82, 24.47, 22.71 (CH_3), 22.62 (CH_3), 19.75 (2 CH_3) ppm; FABHRMS *m/z* 241.2541 (M – H) ($C_{16}H_{34}O$ – H requires 241.2531).

To a solution of 9.6 g (39.6 mmol) of **12** in 30 mL of anhyd DMF was added 10.7 g (40.84 mmol) of triphenylphosphine. The solution was stirred in an acetone–ice bath (–10 °C) while 2.1 mL (41 mmol) of bromine was added dropwise. The temperature rose to 5 °C. The reaction mixture was stirred at room temperature for 1 h and then poured into 100 mL of water and 150 mL of hexanes. After filtration, the layers were separated and the aqueous phase was extracted twice with hexanes. The hexanes layers were combined, washed with saturated sodium bicarbonate solution, dried, filtered through a plug of silica gel, and concentrated in vacuo. Kugelrohr distillation (150–160 °C bath temperature, 1 mmHg) of the residue gave bromide **13** in two fractions: 5.15 g of 95.8% GC purity and 3.55 g of 97.9% GC purity (72.2% yield). Redistillation of the larger fraction gave a colorless liquid, bp 120 °C (0.15 mm) having a GC purity of 97.9%; $[\alpha]^{25}_D$ –3.01° (*c* 2, hexanes); ^1H NMR δ 3.40 ppm (t, *J* = 7 Hz, 2, CH_2Br); ^{13}C NMR (400 MHz, $CDCl_3$) 39.40, 37.39, 32.94, 37.29, 35.48, 34.32, 32.82 (CH), 32.25 (CH), 30.56, 28.01 (CH), 24.79, 24.38, 22.68 (CH_3), 22.58 (CH_3), 19.76 (CH_3), 19.63 (CH_3) ppm; EIMS *m/z* 304, 306 (M^+, ca. equal intensities); EIHRMS *m/z* 304.1756 (M^+) ($C_{16}H_{33}Br$ requires 304.1766).

(2*RS*,4′*R*,8′*R*)-α-Tocopheryl Benzyl Ether (1). A Grignard (**14**) solution was prepared from 0.28 g (11.2 mmol) of magnesium and 3.4 g (11.2 mmol) of bromide **13** in 25 mL of anhyd ether. Grignard formation was induced with a few drops of 1,2-dibromoethane, and the mixture was stirred and refluxed for 3.5 h. To a stirred solution of 2.6 g (7.87 mmol) of 2-chlorochroman **4** in 25 mL of anhyd ether, cooled to –10 °C (ice–acetone bath), was added the Grignard solution dropwise. The resulting mixture was stirred at 0 °C for 18 h and then treated with 100 mL of saturated ammonium chloride solution. Workup with ether in the usual manner gave 4.95 g of an oil which was dissolved in 50 mL of methanol and 30 mL of ether containing 200 mg of *p*-toluenesulfonic acid monohydrate. After being stirred at room temperature for 24 h, the solution was concentrated in vacuo and the residue was chromatographed on 200 g of silica gel. Elution with 40:1 hexanes–ether gave 1.82 g (44.5%) of **1** as a viscous oil. The identity of this material was confirmed by spectral and TLC comparison with an authentic sample of (2*R*,4′*R*,8′*R*)-α-tocopheryl benzyl ether.

6-(Phenylmethoxy)-2,5,7,8-tetramethyl-4*H*-1-benzopyran (10). An authentic sample of this chromene was best prepared as follows: The 2-methoxychroman **2**, in toluene (8 mL/g) was treated with 0.2 parts by weight of phosphorus pentoxide at room temperature. The orange-red suspension was stirred in an oil bath at 110 °C for 10 min and then approximately 25% of the solvent was slowly distilled off during 1 h. After being cooled, the supernatant toluene solution was decanted onto sodium carbonate (0.13 g/mmol substrate) and the mixture was stirred vigorously for 0.5 h and filtered through Celite, and the filtrate was concentrated in vacuo. Recrystallization of the residue from acetone afforded the chromene **10**, in 73% yield, as an off-white solid: mp 73–77 °C. EIMS *m/z* 294 (M^+), 203, 188, 91; ^1H NMR (C_6D_6) δ 7.40–7.50 (m, 2 Ph), 7.10–7.25 (m, 3, Ph), 4.58 (s, 2 $PhCH_2O$), 4.46 (m, 1, CH=), 3.05 (br s, 2, CH_2CH=), 2.20 (s, 3, CH_3), 2.15 (s, 3, CH_3), 2.02 (s, 3, CH_3), 1.78 ppm (d, 3, *J* = 1.1 Hz, CH_3C=). Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.30; H, 7.80.

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Mechanism for the Reaction of Tributyltin Radicals with Aldehydes

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The mechanism for the tributyltin hydride-initiated reaction of ketones with alkenes can be exemplified by the cyclization of δ,ε-alkenyl ketones (**1**, Scheme I).[1] This mechanism involves tin radical addition to the carbonyl oxygen followed by carbon radical cyclization. The same mechanism could apply as well to δ,ε-alkenyl aldehydes (**1**, R = H)[2] or to the addition of tributyltin radicals to other aldehydes.[3] However, it is well-known that radical abstraction of aldehydic hydrogen atoms is a facile process.[4] Consequently, an alternative mechanism to that shown in Scheme I for the cyclization of δ,ε-alkenyl aldehydes can be envisioned (Scheme II). This mechanism has precedence in the tributyltin radical reaction of methyl selenol esters of δ,ε-alkenyl acids.[5] Previously reported examples of tributyltin radical additions to aldehydes could be rationalized by either mechanism shown in Schemes I and II. In order to differentiate these two mechanistic pathways we have examined the reaction of tributyltin deuteride with various aldehydes. The results of these experiments are described in this note.

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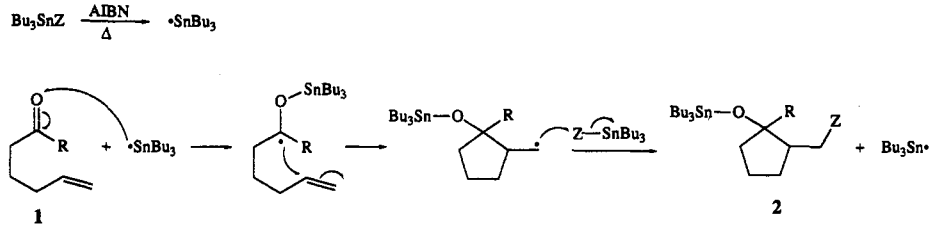
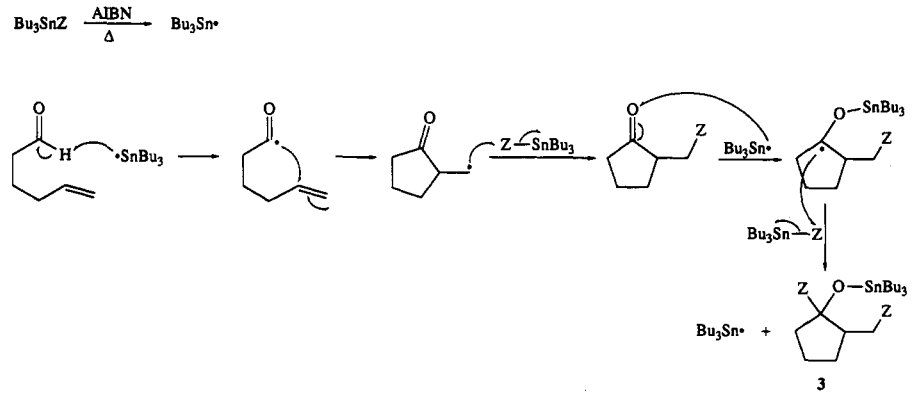
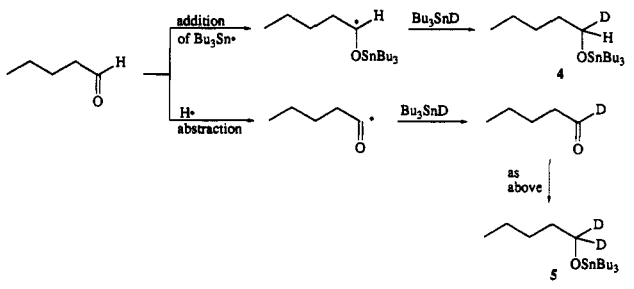
Scheme I. Mechanism for the Tributyltin Hydride-Initiated Cyclization of δ,ε-Alkenyl Ketones



Scheme II. Alternative Mechanism for the Tributyltin Hydride-Initiated Cyclization of δ,ε-Alkenyl Aldehydes



Scheme III. Deuterium Labeling during Reduction of Pentanal



Results and Discussion

Three experiments were carried out, all of which led to the conclusion that the mechanism in Scheme I is the relevant one. First, in order to determine if tributyltin radical abstracts the hydrogen atom from aldehydes in preference to addition to the carbonyl oxygen, pentanal was treated with tributyltin deuteride and AIBN. If there is initial addition of the tributyltin radical to the carbonyl oxygen, then the pentanol that is formed will be monodeuterated (4, Scheme III), but if there is hydrogen abstraction prior to tributyltin radical addition, then the pentanol will be dideuterated (5). Reduction of pentanal with tributyltin deuteride gave a ratio of ions in the mass spectrum corresponding to the monodeuterated–dideuterated products (after ^{13}C natural abundance is taken into account) of 99.3:0.7, indicating that prior hydrogen atom abstraction occurs to a negligible extent, if at all. Treatment of benzaldehyde and cinnamaldehyde with tributyltin deuteride and a metal catalyst was reported previously to give benzyl alcohol and cinnamyl alcohol, respectively, with formation of a C–D bond, as observed by IR spectroscopy.[3]

The decomposition of the cyclopropylcarbinyl radical to the homoallyl radical occurs[6] with a rate constant of about 10^8 s^{-1}. Previously, it had been shown that the reaction of tributyltin radical with the less reactive system, cyclopropanecarboxaldehyde, led to cyclopropyl ring opening.[7] The cyclopropane cleavage rate can be increased by 3 orders of magnitude when (2-phenylcyclopropyl)carbinyl radical is generated.[8] In order to attempt to identify the nature of the radical that is generated when tributyltin radical reacts with an aldehyde, 2-phenylcyclopropanecarboxaldehyde was treated with tributyltin hydride with a catalytic amount of AIBN as initiator. If there is an initial hydrogen atom abstraction, then the ring-cleaved product will be ethyl 4-phenylbutanoate after ethanol quench (Scheme IV, pathway a). If the tributyltin radical adds to the carbonyl, then a mixture of (2-phenylcyclopropyl)carbinol and 4-phenylbutanal would result (Scheme IV, pathway b). No ethyl 4-phenylbutanoate was detected by gas chromatography; only 4-phenylbutanal and (2-phenylcyclopropyl)carbinol (in the ratio 2.5:1) were detected, again indicating that aldehydic hydrogen atom abstraction is not important.

The third experiment was the reaction of hex-5-enal with tributyltin deuteride. As in the case of the first experiment, prior hydrogen atom abstraction leads to the dideuterated cyclopentane (Scheme II, 3, Z = D), but carbonyl addition directly gives the monodeuterated cyclopentane (Scheme I, 2, Z = D). This reaction produced at least three different products, none of which were isolated, but GC/mass spectrometry showed that none was dideuterated.

All three of these experiments are consistent with addition of tributyltin radicals to the aldehyde carbonyl without prior aldehydic hydrogen atom abstraction as shown in Scheme I. A similar longstanding debate regarding the mechanism of deoxygenation of secondary alcohols (the tributyltin hydride reduction of methyl xanthates) was resolved by Barton et al.[9] In this case the two questionable mechanisms were either tributyltin radical addition to the xanthate carbon–sulfur double bond (related to Scheme I) or tributyltin radical abstraction of

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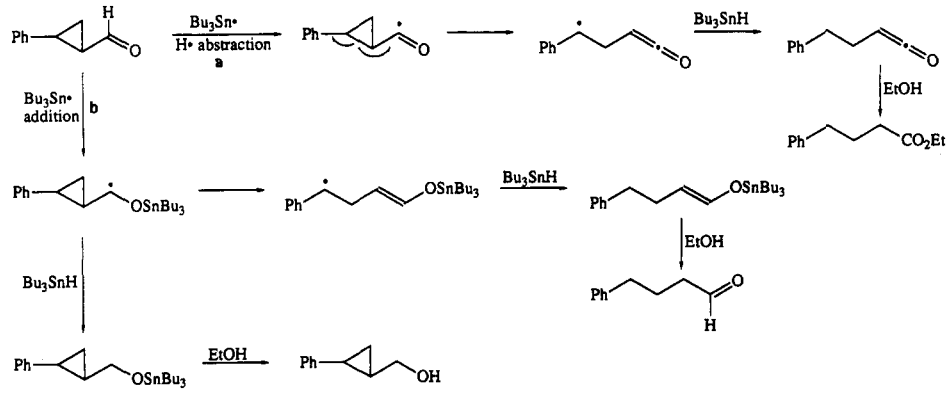
Scheme IV. Potential Pathways for the Reaction of 2-Phenylcyclopropanecarboxaldehyde with Tributyltin Radicals



the xanthate methylthio radical (related to Scheme II). ^{119}Sn NMR was used to confirm that the addition mechanism was correct in this case as well.

Experimental Section

NMR spectra were recorded either on a Varian XLA-400 (400 MHz) spectrometer or a Varian Gemini-300 (300-MHz) spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. Electron impact mass spectra were obtained at 70 eV on a V6 70-250SE chromatomass spectrometer with a HP cross-linked methyl silicone capillary column. All reagents were from Aldrich Chemical Co., Inc., and were used without further purification.

Reduction of Aldehydes with Tributyltin Hydride or Deuteride (General Procedure). Equimolar amounts of the reagents (5 mmol) in benzene (15 mL) and a catalytic amount of AIBN (5 mol %) were heated in a bath at 80 °C for 4 h. The mixture was cooled and passed through a short silica gel column (elution with ethanol), and the eluent was analyzed by GC or GC-mass.

***trans*-(2-Phenylcyclopropyl)carbinol.** The procedure of Sneen et al.[10] was followed starting from *trans*-2-phenylcyclopropanecarboxylic acid, and the product was obtained as a colorless oil: bp 140–141 °C (13.5 mmHg) (lit.[11] 144 °C (14 mmHg); lit.[10] bp 90 °C (0.3 mmHg)); ^1H NMR ($CDCl_3$) δ 0.70–0.90 (m, 2 H), 1.15–1.50 (m, 1 H), 1.55–1.85 (m, 1 H), 2.80 (s, OH), 3.45 (d, 2 H), 6.80–7.35 (m, 5 H).

***trans*-(2-Phenylcyclopropyl)carboxaldehyde.** The alcohol (5.9 g, 40 mmol) was oxidized with pyridinium chlorochromate (15.1 g, 70 mmol) in CH_2Cl_2 (100 mL) at room temperature (1.5 h) by the method of Corey and Suggs.[12] The aldehyde was extracted with ether from the reaction mixture and distilled to give the product as a colorless oil (3.5 g, 60%), 93–95 °C (5 mmHg), 2,4-dinitrophenylhydrazone, mp 181–182 °C (from alcohol) (lit.[11] mp 179–180 °C (from benzene)): ^1H NMR ($CDCl_3$) δ 1.25–1.80 (m, 2 H), 1.95–2.25 (m, 1 H), 2.35–2.75 (m, 1 H), 6.90–7.40 (m, 5 H), 9.27 (d, 1 H) (same as lit.[13]); HRMS (EI) calcd for $C_{10}H_{10}O$ 146.0732, found 146.0737. This product was readily oxidized in air to the corresponding carboxylic acid.

Hex-5-enal. 5-Hexenol (3.0 g, 30 mmol) was oxidized by pyridinium chlorochromate (9.5 g, 45 mmol) by the method of Corey and Suggs.[12] A colorless liquid (1.8 g, 60%) was obtained after distillation at 48–50 °C (50 mmHg) (lit.[14] distillation 118–118.5 °C): ^1H NMR δ 1.60–2.50 (m, 6 H), 4.80–5.10 (m, 2 H), 5.50–5.95 (m, 1 H), 9.78 (t, J = 1.4, 1 H) (same as ref 15).

4-Phenylbutanal. 4-Phenyl-1-butanol (1.5 g, 10 mmol) was oxidized by pyridinium chlorochromate (3.5 g, 16 mmol) by the method of Corey and Suggs.[12] A colorless liquid was obtained (0.8 g, 57%) after distillation at 65–67 °C (3 mmHg). The product oxidized rapidly to the carboxylic acid upon exposure to air: ^1H NMR δ 2.00–2.11 (m, 2 H), 2.45–2.55 (m, 2 H), 2.73 (t, J = 7.6 Hz, 2 H), 7.25–7.40 (m, 5 H), 9.80 (t, J = 1.4 Hz, 1 H); ^{13}C NMR δ 24.1, 35.4, 43.5, 126.5, 128.8, 128.9, 141.7, 202.8. Anal. Calcd for $C_{10}H_{12}O$: C, 81.08; H, 8.27. Found: C, 80.90; H, 8.27. 2,4-Dinitrophenylhydrazone, mp 105–107 °C (lit.[16] mp 106–107 °C). Anal. Calcd for $C_{16}H_{16}N_4O_4$: C, 58.53; H, 4.87; N, 17.07. Found: C, 58.48; H, 4.88; N, 17.03.

Ethyl 4-Phenylbutanoate. 4-Phenylbutanoic acid (3.28 g, 20 mmol) was heated to reflux for 10 h in ethyl alcohol (10 mL) with a catalytic amount of sulfuric acid. After distillation at 105–106 °C (3 mmHg) (lit.[17] distillation 139 °C (15 mmHg), 80 °C (0.5 mmHg)) the product was obtained as a colorless liquid (3.1 g, 80%): ^1H NMR δ 1.23 (t, 3 H), 1.90–2.00 (m, 2 H), 2.30 (t, 2 H), 2.65 (t, 2 H), 4.10 (q, 2 H), 7.13–7.25 (m, 5 H); ^{13}C NMR δ 14.7, 27.0, 34.1, 35.6, 60.7, 126.4, 128.8, 128.9, 141.9, 173.9. Anal. Calcd for $C_{12}H_{16}O_2$: C, 75.00; H, 8.33. Found: C, 75.13; H, 8.29.

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Silver(I)/Peroxydisulfate-Induced Oxidative Decarboxylation of Amino Acids. A Chemical Model for a Possible Intermediate in the Monoamine Oxidase-Catalyzed Oxidation of Amines

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Amino acids are known to undergo oxidative decarboxylation to give (after hydrolysis) the corresponding aldehyde by reaction with potassium peroxydisulfate ($K_2S_2O_8$) and catalytic silver(I)[1] or with silver(II) picolinate.[2] The mechanisms of these reactions, however, are not clear. In the case of the stoichiometric silver(II) reactions, where a cyclic complex can form, a concerted (electrocyclic) mechanism (Scheme I, 1) has been suggested, although a radical mechanism was not excluded.[2] The mechanism for

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