Free Radical-Mediated Ring Expansion Reactions: Endocyclic Cleavage of Cyclopropylcarbinyl Radicals

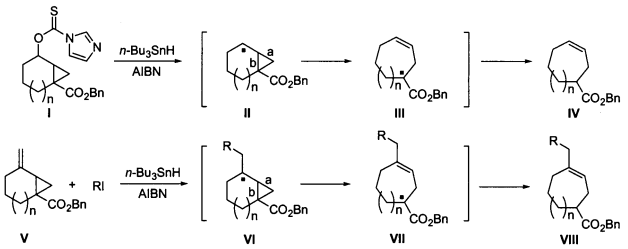
Phil Ho Lee,* Byungcheol Lee, Kooyeon Lee, Chang-Hee Lee, and Sukbok Chang†

Department of Chemistry, Kangwon National University, Chuncheon 200-701, Korea
†Department of Chemistry, Ewha Womans University, Seoul 120-750, Korea
Received March 21, 2000

Ring expansion reactions *via* endocyclic cleavage of cyclopropylcarbinyl radicals derived from the reaction of [1-benzyloxycarbonylbicyclo[n.1.0]alk-(n+1)-yl]-1-imidazolethiocarboxylates with tributyltin hydride/AIBN proceeded to produce 3-cycloalkenecarboxylates in good yields. Benzyl (5'-phenoxypentyl)-3-cyclohepten-1-carboxylate was obtained in 33% yield from the reaction of benzyl 5-methylenebicyclo[4.1.0]-1-carboxylates with 4-phenoxybutyl iodide under radical conditions. Selective cleavage of endocyclic bond in cyclopropane to the cyclohexane, results from stabilization of the resultant radical by the carbonyl groups, such as the benzyloxycarbonyl group, which lower the transition state energy for the final cyclopropane cleavage in the ring expansion.

Introduction

Radical based ring opening reactions have been successfully exploited in the development of a wide variety of useful synthetic transformations.[1] Especially, recent advances in the ring opening reactions of three-membered rings have led to the steadily increasing utilization of cyclopropyl derivatives as building blocks for organic synthesis.[2] In this respect, ring opening of the cyclopropylcarbinyl radicals and cyclopropyl alkoxy radicals has proved to be an useful strategy for ring expansion because cleavage of the three-membered ring takes place easily and the disfavored entropy effect usually associated with medium and large size ring formation can be avoided.[3] However, the literature on bicyclo[n.1.0] radicals reveals a preference for stereoelectronically controlled exocyclic radical ring opening as opposed to thermodynamically favored endocyclic ring opening.[4] The exocyclic cleavage has usually been achieved under reaction conditions such as electrolysis,[5] samarium iodide,[6] alkali metal[7] and photochemical electron transfer.[8] Ingold has studied the stereoelectronic requirements of the fragmentation of cyclopropylcarbinyl radicals.[9] In addition, Beckwith,[10] Dowd,[11] Baldwin[12] and Crimmins[13] have reported on some unusual radical based ring expansion reactions. Much of the attention in this area has focused on exocyclic cleavage of cycloalkylcarbinyl radicals and endocyclic cleavage of cyclopropyl alkoxy radicals generated *in situ* by the addition of carbon radical centers to an adjacent carbonyl group. Considerably less effort has been expended on the development of ring expansion reactions *via* endocyclic cleavage of cycloalkylcarbinyl radicals. In connection with our research interest in the synthetic utility of cyclopropane derivatives, we reported the convenient SmI_2-induced ring opening reactions of alkyl (n+1)-oxobicyclo[n.1.0]alkane-1-carboxylates *via* endocyclic cleavage.[14] We next studied the feasibility of ring expansion reactions *via* endocyclic cleavage of cyclopropylcarbinyl radicals derived from [1-benzyloxycarbonylbicyclo[n.1.0]alk-(n+1)-yl]-1-imidazolethiocarboxylates and benzyl (n+1)-methylenebicyclo[n.1.0]-1-carboxylates (Scheme 1).



Scheme 1

Experimental Section

Benzyl 3-oxocyclohexene-1-carboxylate (3). To a solution of triphenylphosphine (230.9 mg, 0.88 mmol) in THF (4 mL) were added 2-cyclohexen-1-one (84.6 mg, 0.88 mmol) and TBSOTf (244.2 mg, 0.92 mmol) at -30 °C. After being stirred at room temperature for 30 min, the reaction mixture was cooled to -78 °C and *n*-butyllithium (0.62 mL, 0.97 mmol) was added dropwise to give a black-colored ylide solution. The reaction mixture was stirred for 30 min at -78 °C and benzyl chloroformate (165.5 mg, 0.97 mmol) was added to the ylide solution. After being warmed to room temperature, TBAF (1.32 mL, 1.32 mmol) was added and stirred at room temperature for 2 h. The reaction mixture was then diluted with ether (2 × 20 mL) and washed with saturated $NaHCO_3$ solution (10 mL) and brine (10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexanes = 1/10) to give benzyl 3-oxocyclohexene-1-carboxylate (174.3 mg, 86%) as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (m, 5H), 6.80 (m, 1H), 5.26 (s, 2H), 2.60 (m, 2H), 2.45 (t, J = 6.73 Hz, 2H), 2.11 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.64, 165.83, 148.36, 134.73, 132.74, 128.19, 128.06, 127.80, 66.85, 37.20, 24.35, 21.63; IR (film) 3050, 2950, 1730, 1690, 1240 cm^{-1}.

Benzyl (*E*)-2-methyl-4-oxo-2-hexenoate (1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (s, 5H), 7.12 (s, 1H), 5.24 (s, 2H), 2.56 (q, J = 7.24 Hz, 2H), 2.25 (s, 3H), 1.1 (t, J = 7.31 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.68, 165.79, 143.38, 134.38, 134.25, 127.69, 127.56, 127.30, 126.55, 72.43, 66.57, 18.64, 14.02; IR (film) 3050, 2950, 1725, 1700 cm^{-1}.

Benzyl 3-oxocyclopentene-1-carboxylate (2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.34 (m, 5H), 6.8-6.78 (m, 1H), 5.3 (s, 2H), 2.90-2.83 (m, 2H), 2.55-2.5 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.35, 164.51, 164.28, 138.75, 135.55, 129.09, 129.00, 128.74, 67.64, 35.93, 27.88; IR (film) 3050, 2950, 1700, 1260 cm^{-1}.

Benzyl 4-methyl-3-oxocyclohexene-1-carboxylate (4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.25 (m, 5H), 6.7 (dd, J = 0.7, 0.66 Hz, 1H), 5.18 (s, 2H), 2.7-2.63 (m, 1H), 2.53-2.43 (m, 1H), 2.38-2.29 (m, 1H), 2.18-2.04 (m, 1H), 1.73-1.62 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.88, 166.75, 148.39, 135.67, 133.28, 129.08, 128.93, 128.68, 67.68, 41.88, 30.63, 25.02, 15.13; IR (film) 3050, 2950, 1730, 1680, 1260, 1240 cm^{-1}.

Benzyl 4,4-dimethyl-3-oxocyclohexene-1-carboxylate (5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 5H), 6.71 (s, 1H), 5.25 (s, 2H), 2.61 (t, J = 5.9 Hz, 2H), 1.87 (t, J = 5.64 Hz, 2H), 1.11 (s, 6H).

Benzyl 3-oxocycloheptene-1-carboxylate (6). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.25 (m, 5H), 6.84 (s, 1H), 5.13 (s, 2H), 2.65 (t, J = 5.47 Hz, 2H), 2.55 (t, J = 6.37 Hz, 2H), 1.76-1.73 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.67, 167.79, 145.08, 137.76, 135.77, 129.06, 128.88, 128.69, 67.87, 43.09, 28.13, 25.43, 21.91; IR (film) 3050, 2950, 1770, 1720, 1680, 1460, 1250 cm^{-1}.

Benzyl 3-hydroxycyclohexene-1-carboxylate (9). To a solution of benzyl 3-hydroxycyclohexene-1-carboxylate (322.4 mg, 1.4 mmol) and $CeCl \cdot 7H_2O$ (521.6 mg, 1.4 mmol) in MeOH (3.5 mL) was added dropwise a solution of sodium borohydride (52.9 mg, 1.4 mmol) in MeOH (1 mL) at room temperature under N_2. After 2 h, the reaction mixture was quenched with $NaHCO_3$ (sat. aq.). The aqueous layer was extracted with ether (3 × 15 mL), and combined organic layers were washed with water (15 mL), brine (15 mL), dried with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexenes=1/3) to give benzyl 3-hydroxycyclohexene-1-carboxylate (318.7 mg, 98%) as a colorless liquied: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (m, 5H), 6.93 (m, 1H), 5.18 (s, 2H), 4.35 (m, 1H), 2.98 (m, 2H), 1.93 (m, 2H), 1.84 (m, 1H), 1.58 (m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 167.02, 140.10, 136.00, 132.42, 128.55, 128.19, 128.10, 66.38, 65.98, 31.11, 24.21, 19.08.

Benzyl (*E*)-2-methyl-4-hydroxy-2-hexenoate (7). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 5H), 6.70 (d, J = 9.16 Hz, 1H), 5.20 (s, 2H), 4.42 (dt, J = 6.69, 1.84 Hz, 1H), 1.91 (s, 3H), 1.75-1.48 (m, 3H), 0.94 (t, J = 7.45, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 167.65, 143.26, 135.99, 128.48, 128.10, 128.03, 69.97, 66.50, 29.69, 12.94, 9.43; IR (film) 3400, 3050, 2950, 2900, 2850, 1700, 1640 cm^{-1}.

Benzyl 3-hydroxycycloheptene-1-carboxylate (12). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.31 (m, 5H), 7.11 (s, 1H), 5.17 (s, 2H), 4.57-4.52 (m, 1H), 2.9 (dd, J = 6.83, 6.83 Hz, 1H), 2.17-1.61 (m, 7H), 1.31-1.17 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.86, 150.14, 136.50, 133.21, 128.93, 128.53, 128.50, 72.38, 67.04, 36.13, 28.42, 27.81, 25.84; IR (film) 3400, 3050, 2950, 1720, 1660, 1260 cm^{-1}.

Benzyl 5-hydroxybicyclo[4.1.0]heptane-1-carboxylate (15). To a solution of benzyl 5-oxobicyclo[4.1.0.]heptane-1-carboxylate (134 mg, 0.55 mmol) and $CeCl \cdot 7H_2O$ (208 mg, 0.55 mmol) in MeOH (1.4 mL) was added dropwise a solution of sodium borohydride (22 mg, 0.55 mmol) in MeOH (1 mL) at room temperature under N_2. After 2 h, the reaction mixture was quenched with $NaHCO_3$ (sat. aq.). The aqueous layer was extracted with ether (3 × 15 mL), and combined organic layers were washed with water (15 mL), brine (15 mL), dried with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexenes=1/3) to give benzyl 5-hydroxybicyclo[4.1.0]heptane-1-carboxylate (113 mg, 89%) as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 5H), 5.12 (s, 2H), 4.10 (m, 1H), 2.55 (m, 1H), 1.42 (m, 8H), 0.60 (dd, J = 6.83, 4.48 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.31, 134.40, 126.81, 126.39, 126.16, 64.74, 63.67, 27.30, 26.49, 23.95, 21.89, 18.14, 16.31; IR (film) 3400, 3050, 2950, 2850, 1730 cm^{-1}.

Benzyl (E)-1-methyl-2-(1'-hydropropyl)cyclopropane-carboxylate (13). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (s, 5H), 5.10 (s, 2H), 3.31-3.21 (m, 1H), 1.74-1.55 (m, 4H), 1.44 (dd, J = 9.16, 3.97 Hz, 1H), 1.34 (s, 3H), 0.97 (t, J = 7.48 Hz, 3H), 0.72 (dd, J = 6.41, 3.97 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.52, 136.56, 128.93, 128.49, 128.16, 73.22, 66.83, 32.80, 31.16, 23.67, 20.62, 15.07, 10.06; IR (film) 3400, 3050, 2950, 2580, 1720 cm^{-1}.

Benzyl 4-hydroxybicyclo[3.1.0]hexane-1-carboxylate (14). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.22 (m, 5H), 5.03 (d, J = 1.35 Hz, 2H), 4.52-4.47 (m, 1H), 2.16-2.08 (m, 1H), 2.60-2.01 (m, 1H), 1.97-1.85 (m, 2H), 1.36-1.30 (m, 1H), 1.20-1.05 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.57, 135.83, 128.17, 127.72, 127.55, 73.06, 65.89, 65.51, 36.08, 31.01, 24.34, 16.35; IR (film) 3400, 3050, 2950, 1720, 1460 cm^{-1}.

Benzyl 4-methyl-5-hydroxybicyclo[4.1.0]heptane-1-carboxylate (16). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (s, 5H), 5.08 (s, 2H), 2.32-1.86 (m, 3H), 1.70-0.57 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.67, 134.91, 127.28, 126.83, 126.65, 73.90, 65.11, 36.43, 28.35, 24.48, 23.31, 22.44, 17.96, 15.29; IR (film) 3400, 3050, 2950, 2850, 1730, 1460 cm^{-1}.

Benzyl 4,4-dimethyl-5-hydroxybicyclo[4.1.0]heptane-1-carboxylate (17). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.31 (m, 5H), 5.07 (d, J = 3.36 Hz, 2H), 3.32 (s, 1H), 2.34 (ddd, J = 14.02, 7.63, 6.41 Hz, 1H), 1.84-1.71 (m, 2H), 1.52-1.21 (m, 4H), 0.86 (d, J = 15.87 Hz, 6H), 0.55-0.52 (m, 1H); IR (film) 3400, 3050, 2950, 2850, 1720, 1460 cm^{-1}.

Benzyl 6-hydroxybicyclo[5.1.0]octane-1-carboxylate (18). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.26 (m, 5H), 5.09 (s, 2H), 4.40-4.34 (m, 1H), 2.53-2.47 (m, 1H), 1.92-1.42 (m,

9H), 1.28 (dd, J = 9.65, 9.8 Hz, 1H), 1.17 (dd, J = 6.89, 6.83 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.29, 137.24, 129.45, 128.94, 128.69, 67.28, 66.80, 36.06, 33.42, 30.40, 28.88, 28.55, 25.25, 16.20; IR (film) 3450, 3050, 2950, 1720, 1460, 1160, 1100 cm^{-1}.

Methyl 8-hydroxytricyclo[5.4.0.0^{2,6}]undecane-1-carboxylate. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88-3.82 (m, 1H), 3.68 (s, 3H), 2.78-2.76 (m, 1H), 2.67 (t, J = 7.38 Hz, 1H), 2.44 (m, H), 2.23 (dt, J = 6.78, 3.68 Hz, 1H), 1.88-1.84 (m, 2H), 1.69-1.52 (m, 8H), 1.43-1.33 (m, 1H), 1.25-1.11 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.24, 67.98, 51.53, 48.85, 47.85, 41.87, 34.82, 33.75, 32.20, 30.85, 28.23, 26.77, 21.18; IR (film) 3400, 2950, 2850, 1720, 1710, 1450, 1180 cm^{-1}.

Benzyl 5-hydroxybicyclo[4.1.0]heptane-1-carboxylate (15). To a solution of samarium metal (5.1 g, 33.8 mmol) in THF (75 mL) were added a solution of mercuric chloride (0.92 g, 3.38 mmol) in THF (75 mL) at room temperature under N_2. After being stirred for 10 min at room temperature, Benzyl 3-hydroxy- cyclohexene-1-carboxylate (1.96 g, 8.46 mmol) was added to the reaction mixture. The reaction mixture was cooled to -78 °C, and diiodomethane (9.1 mg, 33.8 mmol) was added dropwise. The reaction mixture was warmed to room temperature and stirred at room temperature for 2 h. The reaction mixture was quenched with K_2CO_3 (sat. aq.). The aqueous layer was extrated with ether (3 × 50 mL), and the combined organic layers were washed with saturated K_2CO_3 solution (50 mL), brine (50 mL), dried with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexanes=1/2) to give benzyl 5-hydroxybicyclo[4.1.0] heptane-1-carboxylate (1.55 g, 74%) as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 5H), 5.12 (s, 2H), 4.10 (m, 1H), 2.55 (m, 1H), 1.42 (m, 8H), 0.60 (dd, J = 6.83, 4.48 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.31, 134.40, 126.81, 126.39, 126.16, 64.74, 63.67, 27.30, 26.49, 23.95, 21.89, 18.14, 16.31; IR (film) 3400, 3050, 2950, 2850, 1730 cm^{-1}.

[1-Benzyloxycarbonylbicyclo[4.1.0]het-5-yl]-1-imidazolethiocarboxylate (21). A solution of Benzyl 5-hydroxybicyclo[4.1.0]heptane-1-carboxylate (51 mg, 0.2 mmol), 1,1'-thiocarbonyldiimidazole (59 mg, 0.3 mmol) and 4-dimethylaminopyridine (5 mg, 0.04 mmol) in MC (1.2 mL) under N_2. After being stirred for 10 h at room temperature, the reaction mixture was quenched with water. The aqueous layer was extrated with ether (3 × 25 mL), and the combined organic layers were washed with saturated $NaHCO_3$ solution (20 mL), brine (20 mL), dried with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexanes=1/3) to give [1-Benzyloxycarbonylbicyclo[4.1.0]-het-5-yl]-1-imidazolethiocarboxylate (60 mg, 85%) as a yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 6.93 Hz, 1H), 7.57 (s, 1H), 7.28 (m, 5H), 6.69 (d, J = 2.30 Hz, 1H), 5.81 (t, J = 4.12 Hz, 1H), 5.05 (m, 2H), 2.63 (m, 1H), 1.90 (dd, J = 10.40, 6.83 Hz, 1H), 1.59 (m, 5H), 1.27 (m, 1H), 0.70 (dd, J = 6.54, 4.98 Hz, 1H); IR (film) 2950, 1720, 1470, 1400, 1330, 1290, 1250 cm^{-1}.

Cyclopropylthionoimidazolide (19). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.66 (s, 1H), 7.44-7.35 (m, 5H), 7.05 (s, 1H), 5.58-5.45 (m, 1H), 5.13 (s, 2H), 2.00-1.83 (m, 3H), 1.49-1.43 (m, 4H), 1.03-1.96 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.75, 136.28, 129.01, 128.67, 128.29, 86.08, 67.19, 29.36, 28.44, 24.35, 21.02, 15.45, 9.63; IR (film) 3050, 2950, 2300, 1720, 1460 cm^{-1}.

[1-Benzyloxycarbonylbicyclo[3.1.0]hex-4-yl]-1-imidazolethiocarboxylate (20). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.62 (s, 1H), 7.34 (s, 5H), 7.04 (s, 1H), 6.02-5.92 (m, 1H), 5.12 (d, J = 1.83 Hz, 2H), 2.53-2.26 (m, 3H), 2.16-2.30 (m, 1H), 1.60-1.43 (m, 2H), 1.39-1.24 (m, 1H); IR (film) 3050, 2950, 1730, 1480 cm^{-1}.

[4-Methyl-1-benzyloxycarbonylbicyclo[4.1.0]hept-5-yl]-1-imidazolethiocarboxylate (22). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.66 (s, 1H), 7.62-7.31 (m, 5H), 7.06 (s, 1H), 5.19-5.01 (m, 3H), 2.42-2.04 (m, 2H), 1.84-1.58 (m, 3H), 1.50-1.04 (m, 2H), 1.02-0.71 (m, 4H); IR (film) 3050, 2950, 1720, 1530, 1460 cm^{-1}.

[4,4-Dimethyl-1-benzyloxycarbonylbicyclo[4.1.0]hept-5-yl]-1-imidazolethiocarboxylate (23). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.64 (s, 1H), 7.39-7.31 (m, 5H), 7.07 (s, 1H), 5.18-5.00 (m, 3H), 2.53-2.35 (m, 1H), 1.93-1.83 (m, 1H), 1.57-0.67 (m, 11H); IR (film) 3050, 2950, 1720, 1460 cm^{-1}.

[1-Benzyloxycarbonylbicyclo[5.1.0]oct-6-yl]-1-imidazolethiocarboxylate (24). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.64 (s, 1H), 7.35 (s, 5H), 7.08 (s, 1H), 6.13-6.07 (m, 1H), 5.12 (s, 2H), 2.65-2.57 (m, 1H), 2.26-1.01 (m, 10H); IR (film) 3050, 2950, 1710, 1450 cm^{-1}.

Cyclobutylthionoimidazolide (29). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.61 (d, J = 1.16 Hz, 1H), 7.03 (d, J = 0.79 Hz, 1H), 5.67-5.61 (m, 1H), 3.72 (s, 3H), 3.02-2.98 (m, 1H), 2.92-2.87 (m, 1H), 2.55-2.51 (m, 1H), 2.36-2.33 (m, 1H), 2.32-2.22 (m, 1H), 1.81-1.26 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.17, 175.35, 136.59, 130.61, 117.88, 80.75, 51.78, 49.02, 47.93, 38.13, 35.84, 33.41, 31.61, 28.12, 26.71, 26.49, 20.51; IR (film) 3100, 2950, 2850, 1720, 1460 cm^{-1}.

Benzyl 5-oxobicyclo[4.1.0]heptane-1-carboxylate (26). A solution of dimethylsulfoxonium methylide was prepared from NaH (81.4 mg, 3.39 mmol) and trimethylsulfoxonium iodide (743.2 mg, 3.38 mmol) in DMSO (4.5 mL) under N_2. After 1 h, a solution of 3-benzyloxycarbonyl 2-cyclohexen-1-one (597.1 mg, 2.59 mmol) in DMSO (2 mL) was added dropwise over 20 min to a solution of dimethylsulfoxonium methylide. After being stirred for 10 h at room temperature, the solution was poured into ice-cold water (10 mL) and extracted with ether (3 × 50 mL). The combined organic layers were washed with brine (50 mL), dried with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexanes=1/5) to give benzyl 5-oxobicyclo-[4.1.0]heptane-1-carboxylate (240.5 mg, 38%) as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (m, 5H), 5.13 (s, 2H), 2.33 (m, 5H), 1.82 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 205.92, 172.49, 135.55, 128.63, 128.38, 128.08, 66.91, 36.52, 33.80, 28.67, 22.12, 17.74, 16.75; IR (film) 3050, 2950, 1710, 1690, 1280 cm^{-1}; MS (CI) calcd for $C_{15}H_{16}O_3$ $[M+H]^+$ 245, found 245.

Benzyl 4-oxobicyclo[3.1.0]hexane-1-carboxylate (25). ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 5H), 5.16 (s, 2H), 2.58 (m, 1H), 2.33 (dd, J = 4.34, 4.21 Hz, 1H), 2.21 (m, 3H), 2.0 (dd, J = 4.82, 4.55 Hz, 1H), 1.36 (t, J = 4.56 Hz, 1H); IR (film) 3050, 2950, 1740, 1280, 1160 cm^{-1}; MS (CI) calcd for $C_{14}H_{14}O_3$ $[M+H]^+$ 230, found 230.

Benzyl 4-methyl-5-oxobicyclo[4.1.0]heptane-1-carboxylate (27). ^1H NMR (400 MHz, $CDCl_3$) δ 7.3-7.24 (m, 5H), 5.06 (s, 2H), 2.29-2.21 (m, 3H), 1.93-1.9 (m, 1H), 1.77-1.75 (m, 1H), 1.55 (dd, J = 5.02, 5.02 Hz, 1H), 1.39 (dd, J = 5.53, 5.27 Hz, !H), 1.28-1.18 (m, 1H), 1.03 (d, J = 6.92 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.86, 173.00, 135.99, 129.01, 128.74, 128.45, 67.21, 42.48, 33.43, 27.99, 25.72, 22.70, 16.14, 15.75; IR (film) 3050, 2950, 1735, 1700, 1280 cm^{-1}.

Benzyl 4,4-dimethyl-5-oxobicyclo[4.1.0]heptane-1-carboxylate (28). ^1H NMR (400 MHz, $CDCl_3$) δ 7.32-7.24 (m, 5H), 5.06 (d, J = 3.51 Hz, 2H), 2.35-2.2 (m, 2H), 1.56 (dd, J = 4.95, 4.94 Hz, 2H), 1.47-1.41 (m, 2H), 1.37 (t, J = 5.37 Hz, 1H), 1.01 (s, 3H), 0.97 (s, 3H); IR (film) 3050, 2950, 1720, 1460, 1280, 1150 cm^{-1}.

Benzyl 5-oxobicyclo[4.1.0]heptane-1-carboxylate (26). To a solution of molecular sieves 5 Å (2.9 g) and pyridinium chlorochromate (1.74 g, 8.05 mmol) in MC (17 mL) was rapidly added a solution of benzyl 5-hydroxybicyclo[4.1.0]-heptane-1-carboxylate (1.32 g, 5.37 mmol) in MC (3 mL) at room temperature. After being stirred for 2 h at room temperature, the reaction mixture was quenched with $NaHCO_3$ (sat. aq.). The aqueous layer was extracted with ether (3 × 50 mL), and combined organic layers were washed with water (50 mL), brine (50 mL), dried with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexenes=1/5) to give benzyl 5-oxobicyclo[4.1.0]heptane-1-carboxylate (1.23 g, 94%) as a colorless liquid: ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (m, 5H), 5.13 (s, 2H), 2.33 (m, 5H), 1.82 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.92, 172.49, 135.55, 128.63, 128.38, 128.08, 66.91, 36.52, 33.80, 28.67, 22.12, 17.74, 16.75; IR (film) 3050, 2950, 1710, 1690, 1280 cm^{-1}; MS (CI) calcd for $C_{15}H_{16}O_3$ $[M+H]^+$ 245, found 245.

Benzyl 3-cycloheptenecarboxylate (32). The [1-Benzyloxycarbonylbicyclo[4.1.0]het-5-yl]-1-imidazolethiocarboxylate (35 mg, 0.1 mmol) was dissolved in dry, degssed benzene (1 mL) and heated to reflux. A solution of tributyltin hydride (34.9 mg, 0.12 mmol) and AIBN (3 mg, 0.02 mmol) in benzene (1 mL) was added over 4 h by syringe pump. When the addition was complete, the benzene was removed under reduced pressure and the residue was extracted with ether (3 × 25 mL). The combined organic layers were washed with saturated KF solution (20 mL) and brine (20 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexanes=1/30) to give benzyl 3-cycloheptenecarboxylate (18.9 mg, 82%) as a colorless liquid: ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 5H), 5.99 (m, 1H), 5.57 (m, 1H), 5.13 (s, 2H), 2.08 (m, 4H), 1.85 (m, 3H), 1.56 (m, 1H), 1.22 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.25, 174.58, 135.77, 132.95, 128.74, 128.02, 127.55, 127.35, 126.16, 124.22, 65.77, 65.57, 42.91, 33.75, 30.08, 27.94, 26.25, 24.80, 20.71, 20.68, 19.12, 18.37; IR (film) 3050, 2950, 1730, 1300 cm^{-1}; MS (CI) calcd for $C_{15}H_{18}O_2$ $[M-H]^-$ 231, found 231.

Benzyl (*E*)-2-methyl-4-heptenoate (30). ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (s, 5H), 5.53-5.17 (m, 2H), 5.11 (s, 2H), 2.59-1.90 (m, 5H), 1.16 (dd, J = 7.02, 6.72 Hz, 3H), 0.93 (t, J = 7.33 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.79, 135.90, 134.43, 128.17, 127.74, 125.18, 65.65, 39.48, 36.34, 25.20, 16.14, 13.44; IR (film) 3050, 2950, 2900, 1730, 1450 cm^{-1}; MS (CI) calcd for $C_{15}H_{20}O_2$ $[M-H]^+$ 233, found 233.

Benzyl 3-Cyclohexenecarboxylate (31). ^1H NMR (400 MHz, $CDCl_3$) δ 7.39-7.30 (m, 5H), 5.68 (s, 2H), 5.14 (s, 2H), 2.66-2.58 (m, 1H), 2.28 (d, J = 6.93 Hz, 2H), 2.12-2.01 (m, 3H), 1.74-1.71 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.96, 137.51, 129.84, 129.42, 129.29, 127.98, 126.45, 67.38, 40.65, 28.73, 26.37, 25.71; IR (film) 3050, 2950, 1730, 1460, 1320 cm^{-1}; MS (CI) calcd for $C_{14}H_{16}O_2$ $[M-H]^+$ 217, found 217.

Benzyl 4,4-dimethyl-3-cycloheptenecarboxylate (34). ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (s, 5H), 5.55-5.37 (m, 2H), 5.09 (s, 2H), 2.61-2.26 (m, 3H), 2.10-0.87 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.81, 142.66, 128.54, 128.13, 128.06, 124.78, 66.10, 44.31, 38.36, 36.62, 30.69, 29.71, 29.40, 28.77, 27.85; IR (film) 3050, 2950, 1720, 1450, 1140 cm^{-1}; MS (CI) calcd for $C_{17}H_{22}O_2$ $[M-H]^+$ 259, found 259.

Benzyl 3-Cyclooctenecarboxylate (35). ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (s, 5H), 5.82-5.59 (m, 2H), 5.11 (s, 2H), 2.55-2.05 (m, 5H), 1.83-1.10 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.68, 135.25, 131.12, 127.51, 127.07, 126.98, 126.37, 65.01, 44.07, 28.13, 27.20, 26.16, 24.86, 23.44; IR (film) 3050, 2950, 1720, 1140 cm^{-1}; MS (CI) calcd for $C_{16}H_{20}O_2$ $[M-H]^-$ 245, found 245.

Epoxyketone (43). To a solution of benzyl 3-oxocyclohexene-1-carboxylate (130 mg, 0.57 mmol) in 2-propanol (2 mL) was added 28% hydrogen peroxide (277 μL, 2.28 mmol) and 6 M NaOH (19 μL, 0.114 mmol) at 0 °C. After being stirred at room temperature for 6 h, the reaction mixture was quenched with $NaHCO_3$ (sat. aq.). The aqueous layer was extracted with ether (3 × 15 mL), and combined organic layers were washed with water (15 mL), brine (15 mL), dried with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexenes=1/5) to give epoxyketone (**43**) (116.8 mg, 83%) as a colorless liquid: ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 5H), 5.21 (m, 2H), 3.55 (s, 1H), 2.54 (m, 1H), 2.39 (m, 2H), 2.11 (m, 1H), 1.93 (m, 1H), 1.75 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.00, 168.01, 134.77, 128.71, 128.39, 67.76, 60.51, 59.19, 35.98, 22.91, 16.58; IR (film) 3050, 3000, 2950, 2850, 1720

cm^{-1}.

Epoxyalcohol (44). To a solution of epoxyketone (**43**) (55.5 mg, 0.225 mmol) and $CeCl \cdot 7H_2O$ (83.8 mg, 0.225 mmol) in 2-propanol (0.5 mL) was added dropwise a solution of sodium borohydride (8.5 mg, 0.225 mmol) in 2-propanol (0.5 mL) at room temperature under N_2. After 2 h, the reaction mixture was quenched with $NaHCO_3$ (sat. aq.). The aqueous layer was extracted with ether (3 × 10 mL), and combined organic layers were washed with water (10 mL), brine (10 mL), dried with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexenes=1/2) to give epoxyalcohol derivatives (**44**) (48.6 mg, 87%) as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (m, 5H), 5.26 (d, J = 1.12 Hz, 2H), 4.10 (m, 1H), 3.82 (m, 1H), 2.08 (m, 3H), 1.70 (m, 3H), 1.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.36, 134.54, 128.76, 128.71, 128.39, 78.22, 71.71, 68.30, 35.30, 31.63, 18.69; IR (film) 3400, 3050, 2950, 2850, 1730 cm^{-1}.

Epoxythionoimidazolide (45). A solution of epoxyalcohol drivatives (**44**) (27.4 mg, 0.11 mmol), 1,1'-thiocarbonyldiimidazole (29.4 mg, 0.17 mmol) and 4-dimethylaminopyridine (2.7 mg, 0.02 mmol) in MC (0.8 mL) under N_2. After being stirred for 10 h at room temperature, the reaction mixture was quenched with water. The aqueous layer was extrated with ether (3 × 10 mL), and the combined organic layers were washed with saturated $NaHCO_3$ solution (10 mL), brine (10 mL), dried with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexanes=1/1) to give epoxythionoimidazolide (**45**) (29.2 mg, 74 %) as a yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.63 (s, 1H), 7.41 (m, 5H), 7.05 (s, 1H), 6.03 (m, 1H), 5.31 (dd, J = 33.08, 11.94 Hz, 2H), 4.16 (d, J = 9.99 Hz, 1H), 2.44 (m, 1H), 2.15 (m, 1H), 1.81 (m, 3H), 1.54 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.06, 172.36, 137.17, 134.51, 130.68, 129.35, 129.22, 118.46, 83.11, 78.77, 69.31, 66.64, 35.65, 29.70, 19.16; IR (film) 3100, 2900, 1720, 1460, 1380 cm^{-1}.

Benzyl 1-hydroxy-2-cyclohexene-1-carboxylate (46). The epoxythionoimdazolide (**45**) (35 mg, 0.1 mmol) was dissolved in dry, degssed benzene (1 mL) and heated to reflux. A solution of tributyltin hydride (34.9 mg, 0.12 mmol) and AIBN (3 mg, 0.02 mmol) in benzene (1 mL) was added over 4 h by syringe pump. When the addition was complete, the benzene was removed under reduced pressure and the residue was extracted with ether (3 × 25 mL). The combined organic layers were washed with saturated KF solution (20 mL) and brine (20 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexanes=1/7) to give benzyl 1-hydroxy-2-cyclohexene-1-carboxylate (20 mg, 88%) as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 5H), 6.04 (m, 1H), 5.63 (d, J = 10.0 Hz, 1H), 5.21 (d, J = 5.40 Hz, 2H), 1.94 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.31, 135.37, 132.77, 128.60, 128.39, 127.96, 126.45, 71.61, 67.50, 33.85, 24.52, 18.25; IR (film) 3400, 3050, 2950, 1730, 1460, 1250 cm^{-1}.

Benzyl 5-methylenebicyclo[4.1.0]heptane-1-carboxylate (47). To A solution of zinc (0.86 g, 13.2 mol) in THF (14 mL) was added diiodomethane (1.95 g, 7.3 mmol) at room temperature under N_2. After being stirred for 30 min at room temperature, a dichloromethane solution of $TiCl_4$ (1.0 M, 1.46 mmol) was added at 0 and the reaction mixture was stirred at room temperature for 30 min. A solution of benzyl 5-oxobicyclo[4.1.0]heptane-1-carboxylate (0.36 g, 1.46 mmol) in THF (3 mL) was added dropwise at room temperature. After being stirred for 15 min at room temperature, the reaction mixture was diluted with ether (10 mL) and the organic layer was washed with 1 M HCl solution (20 mL), brine (20 mL), dried with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexenes=1/30) to give benzyl 5-methylenebicyclo[4.1.0]heptane-1-carboxylate (0.25 g, 70%) as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (m, 5H), 5.10 (s, 2H), 4.92 (s, 1H), 4.81 (d, J = 1.58 Hz, 1H), 2.50 (m, 1H), 2.29 (dd, J = 9.88, 6.33 Hz, 1H), 2.05 (m, 2H), 1.83 (m, 1H), 1.49 (m, 3H), 0.94 (dd, J = 6.31, 4.31 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.92, 144.15, 136.17, 128.52, 128.07, 127.90, 110.15, 66.41, 29.70, 28.80, 25.38, 23.83, 21.50, 21.01; IR (film) 3050, 3000, 2900, 2850, 1710, 1640 cm^{-1}; MS (CI) calcd for $C_{16}H_{18}O_2$ $[M+H]^+$ 243, found 243.

Benzyl 4-(tributyltin)methyl-3-cycloheptene-1-carboxylate (48). The benzyl 5-methylenebicyclo[4.1.0]heptane-1-carboxylate (76.3 mg, 0.31 mmol) was dissolved in dry, degssed benzene (4 mL) and heated to reflux. A solution of tributyltin hydride (110.7 mg, 0.38 mmol) and AIBN (5 mg, 0.03 mmol) in benzene (2.4 mL) was added over 1 h by syringe pump. When the addition was complete, the benzene was removed under reduced pressure and the residue was extracted with ether (3 × 25 mL). The combined organic layers were washed with saturated KF solution (20 mL) and brine (20 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexanes=1/40) to give benzyl 4-(tributyltin)methyl-3-cycloheptene-1-carboxylate (103.4 mg, 63%) as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 5H), 5.31 (t, J = 6.44 Hz, 1H), 5.10 (s, 2H), 2.36 (m, 1H), 2.30 (m, 2H), 2.13 (m, 2H), 1.94 (m, 1H), 1.79 (m, 2H), 1.72 (s, 2H), 1.47 (m, 6H), 1.30 (m, 7H), 0.86 (m, 15H); ^{13}C NMR 175.00, 145.28, 135.32, 127.48, 127.02, 126.97, 116.41, 64.90, 42.80, 33.96, 33.62, 29.28, 28.12, 26.36, 23.90, 21.78, 12.70, 8.52; IR (film) 3050, 2950, 2900, 2850, 1730, 1480 cm^{-1}.

Benzyl (5'-phenoxypentyl)-3-cycloheptene-1-carboxylate (50). The benzyl 5-methylenebicyclo[4.1.0]heptane-1-carboxylate (94.4 mg, 0.39 mmol) and 4-phenoxybutyl iodide (861.5 mg, 3.12 mmol) was dissolved in dry, degssed benzene (3 mL) and heated to reflux. A solution of tributyltin hydride (908 mg, 3.12 mmol) and AIBN (13 mg, 0.08 mmol) in benzene (2 mL) was added over 20 h by syringe pump. When the addition was complete, the benzene was removed under reduced pressure and the residue was

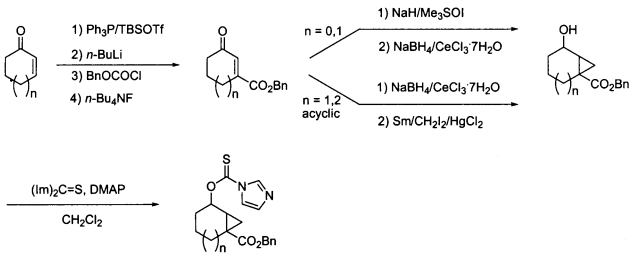
extracted with ether (3 × 25 mL). The combined organic layers were washed with saturated KF solution (20 mL) and brine (20 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (EtOAc/hexanes=1/30) to give Benzyl (5'-phenoxypentyl)-3-cycloheptene-1-carboxylate (50 mg, 33%) as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (m, 7H), 6.83 (m, 3H), 5.40 (t, J = 6.22 Hz, 1H), 5.02 (s, 2H), 3.87 (t, J = 6.53 Hz, 2H), 2.31 (m, 3H), 2.00 (m, 5H), 1.71 (m, 4H), 1.34 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.24, 159.46, 146.28, 136.67, 129.80, 128.92, 128.49, 128.44, 123.06, 120.86, 114.86, 68.12, 66.39, 43.65, 40.18, 35.06, 32.52, 30.45, 29.45, 29.55, 27.90, 26.06, 25.35; IR (film) 3050, 2900, 2850, 1720, 1600, 1500 cm^{-1}; MS (CI) calcd for $C_{26}H_{32}O_3$ $[M+H]^+$ 393, found 393.

Benzyl (5'-isopropyl)-3-cycloheptene-1-carboxylate (51). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (s, 5H), 5.45 (t, J = 6.11 Hz, 1H), 5.10 (s, 2H), 2.48-1.18 (m, 11H), 0.98-0.69 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.27, 145.21, 136.67, 128.93, 128.50, 128.46, 124.33, 66.42, 50.26, 43.72, 35.09, 32.52, 30.54, 26.30, 25.28, 23.01, 22.82.

Results and Discussion

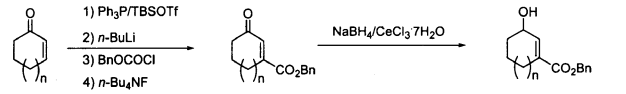
Precusors (I) of radical reactions were prepared from phosphoniosilylation,[15] 1,2-reduction,[16] cyclopropanation[17] followed by acylation[18] of α,β-enones (Scheme 2). We used many reagents (zinc-copper couple, ethylzinc iodide, and etc.) to obtain cyclopropane derivatives from benzyl 3-hydroxy-1-cycloalkenylcarboxylate and found that samarium and diiodomethane in the presence of mercury chloride gave the best results. Experimental results are shown in the Table 1 and Table 2. Also, some compounds (**14**, **15**, **16** and **17**) could be obtained from phosphoniosilylation, cyclopropanation, followed by 1,2-reduction (Table 3). Trimethyloxosulfoxonium iodide gave the best results for cyclopropanation of cyclopropyl ketones.

Initial studies were performed with thiocarbamate **21** (entry 3, Table 4). Slow addition of a solution of tributyltin hydride and AIBN to thiocarbamate **21** in benzene at 80 °C resulted in reductive cleavage of the cyclopropane to give an 82% yield of benzyl 3-cycloheptenecarboxylate (**32**). The tentative mechanism for this reaction is shown in Scheme 1. The cyclopropylcarbinyl radical (**II** and **VI**) fragments to produce the more stable *tertiary* radical (**III** and **VII**), which is reduced by tributyltin hydride. Selective cleavage of bond



Scheme 2

Table 1. β-Benzyloxycarbonylation and 1,2-Reduction of α,β-Unsaturated Ketones



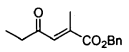
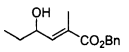
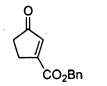
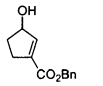
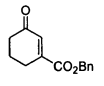
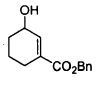
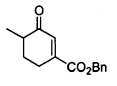
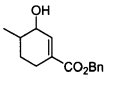
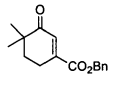
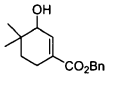
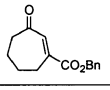
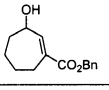
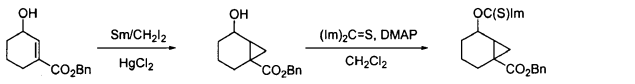
product		isolated yield/%	product		isolated yield/%
	1	58		7	87
	2	80		8	79
	3	86		9	98
	4	40		10	89
	5	43		11	72
	6	19		12	85

Table 2. Cyclopropanation and Thiocarbonylation of Allylic Alcohol Derivatives



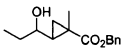
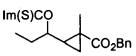
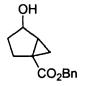
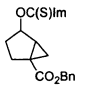
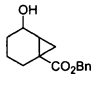
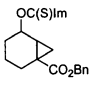
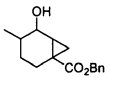
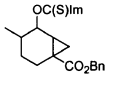
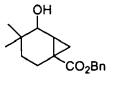
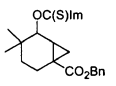
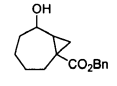
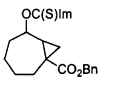
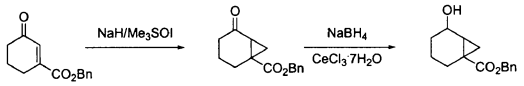
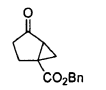
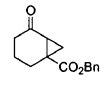
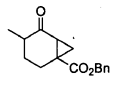
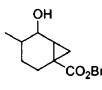
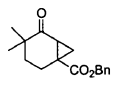
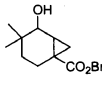
product		isolated yield/%	product		isolated yield/%
	13	27		19	85
	14	10		20	78
	15	74		21	85
	16	–		22	76
	17			23	61
	18	43		24	53

Table 3. Cyclopropanation and 1,2-Reduction of α,β-Unsaturated Ketones



product		isolated yield/%	product		isolated yield/%
	**25**	21		**14**	58
	**26**	35		**15**	89
	**27**	35		**16**	89
	**28**	62		**17**	72

"**b**" in cyclopropane, endocyclic to the cyclohexane, results from stabilization of the resultant radical by the carbonyl groups, such as the benzyloxycarbonyl group, which lowers the transition state energy for the final cyclopropane cleavage in the ring expansion. This result is compatible with the fact that thiocarbamate **21** lacking carbonyl group which can stabilize the produced radical undergoes simple exocyclic cleavage to give 3-methylcyclohexene **37** in 82% yield. To explain two contrasting results, we propose that stereoelectronic effects initially favor the cleavage of bond "a" in **21** because "a" σ-bond has better orbital overlap with the sp^2 orbital of the adjacent radical as seen in structure **38**. However, bond "b" is almost orthogonal to the sp^2 orbital of the radical.

Our observation means that both endo- and exo-bond cleavage involve cyclopropylmethyl radicals and potentially can involve a reversible ring-closure process; however, bond cleavage is highly favored because of the release of ring strain energy, as shown in Scheme 3. Reclosure could become more facile in **41** because no substituent is present and the center is less hindered. At this point, cleavage of bond "b" likely occurs, leading to the resonance-stabilized radical intermediate **42** in which the reverse reaction is possible, but less likely.[19]

The generality of this process was evaluated by preparing **20**, **23** and **24** exposing these to *n*-Bu_3SnH in benzene in 80 °C to produce ring expansion compounds in good yields (Table 4). Monocyclic compound **19** (entry 1, Table 4) reacted readily and gave a good yield of benzyl *trans*-2-methyl-4-

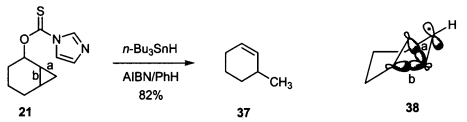
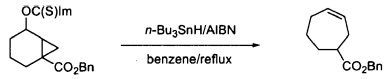
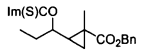
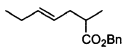
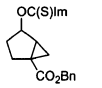
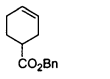
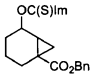
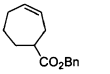
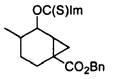
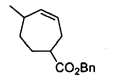
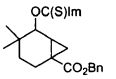
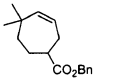
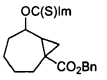
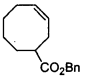
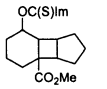
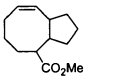


Figure 1

Table 4. Ring Expansion Reactions *via* Endocyclic Cleavage of Cycloalkylcarbinyl Radicals

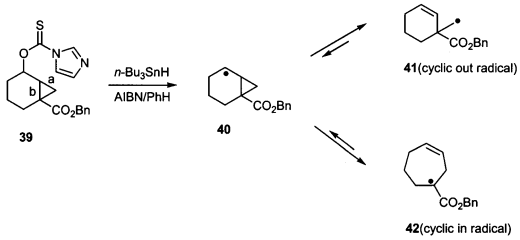


entry	starting material		product		isolated yield/%
1		**19**		**30**	82
2		**20**		**31**	83
3		**21**		**32**	82
4		**22**		**33**	65
5		**23**		**34**	65
6		**24**		**35**	71
7		**29**		**36**	30[a]

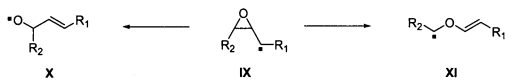
[a]The exocyclic cleavage and direct reduction product were produced in 13% and 7% yield, respectively.

heptenoate (**30**). The present method reaches a limit with **29** derived from [2+2]-photoaddition of α,β-enone and cyclopentene. In this case, the desired product **36** was obtained in only 30% yield together with the exocyclic ring opening and direct reduction products in 13% and 7% yield, respectively, which is consistent with Ranus and Beckwith's results on the kinetics of ring opening of radicals containing the cyclobutylcarbinyl system.[20]

It has been well established that ring opening of oxiranylcarbinyl radicals (**IX**) is dependent on the substituents R_2. When R_2=vinyl or aryl, C-C bond cleavage predominates to give (**X**) otherwise the C-O bond cleaves to afford the alkoxy radicals (**XI**),[21] although there are some reports of the oxiranylcarbinyl radicals being reluctant to cleave the oxirane



Scheme 3



Scheme 4

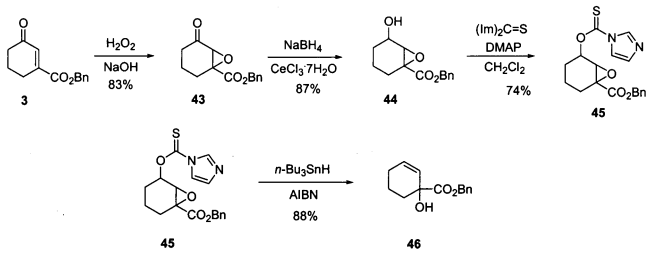
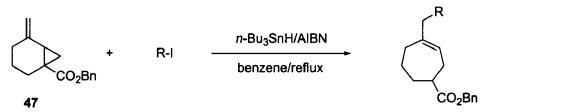
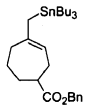
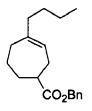
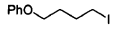
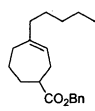
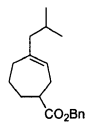


Figure 2

Table 5. Ring Expansion Reactions *via* Endocyclic Cleavage of Cyclopropylcarbinyl Radicals Derived from the Reaction of Benzyl (n+1)-methylenebicyclo[n.1.0]-1-carboxylates with Alkyl Iodide



entry	R-I	product		isolated yield/%
1	–		**48**	63
2			**49**	8
3			**50**	33
4			**51**	23

ring.[22] We have observed that the epoxycyclohexane thiocarbonylimidazolide **45** was treated with *n*-Bu_3SnH/AIBN in benzene to produce benzyl 1-hydroxy-2-cyclohexene-1-carboxylate (**46**) in 88% yield arising from the C-O bond cleavage of the oxiranyl radical.

We next studied ring expansion reactions *via* endocyclic cleavage of cyclopropylcarbinyl radicals derived from the reaction of benzyl (n+1)-methylenebicyclo[n.1.0]-1-carboxylates with alkyl iodide (Scheme 1). To find optimum conditions for radical-mediated ring opening reaction, initially the radical acceptor **47**[23] was reacted with *n*-Bu_3SnH/AIBN in benzene to produce benzyl 4-(tributylstannylmethyl)-3-cycloheptenecarboxylate (**48**) in 63% yield. On the basis of this result, 4-phenoxybutyl iodide was used as radical donor to yield benzyl 4-(5-phenoxybutyl)-3-cycloheptenecarboxylate (**50**) in 33% yield together with reduction and radical coupling compounds. Although 4-phenoxybutyl iodide was treated with $Bu_3SnSnBu_3$ (1.2 equiv), **47** (2.0 equiv) and acetone (5 equiv) as a sensitizer in benzene (0.3 M in iodide) at 300 nm for 4 h, **50** was obtained in 33% yield. Because **47** was decomposed under the reaction conditions, when 350 nm was used for ring opening reaction, a similar result was obtained (Table 5).

In summary, the free radical ring expansion reactions proceed *via* endocyclic cleavage of the bridged bond of cyclopropylcarbinyl radicals. Because the exocyclic cleavage of cyclopropylcarbinyl radicals was reported mainly in previous work, the present method contrasts with and complements the existing synthetic methods.

Acknowledgment. We thank the Korea Research Foundation (1998-015-D00173) and Research Center for Advanced Mineral Aggregate Composite Products for financial support.

References

1. (a) Dowd, P.; Zhang, W. *Chem. Rev.* **1993**, *93*, 2091. (b) Hesse, M. *Ring Enlargement in Organic Chemistry*; VCH: Weinheim, 1991. (c) Thebtaranonth, C.; Thebtaranonth, Y. *Cyclization Reactions*; CRC: Boca Raton, 1994.
2. (a) de Meijere, A. *Topics in Current Chemistry*; Springer-Verlag: New York, U.S.A., 1986; Vol. 133, 1987; Vol. 135, 1988; Vol. 144, 1990; Vol. 195. (b) Rappoport, Z. *The Chemisrty of the Cyclopropyl Group*; John Wiley & Sons: New York, U.S.A., 1995; Vol 2. (c) Danishefsky, S. *Acc. Chem. Res.* **1979**, *12*, 66. (d) de Meijere, A. *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 809.
3. (a) Roxburgh, C. J. *Tetrahedron* **1993**, *49*, 10749. (b) Stach, H.; Hesse, M. *Tetrahedron* **1988**, *44*, 1573. (c) Trost, B. M.; Fleming, I. *Comprehensive Organic Synthesis*; Pergamon: Oxford, 1991; Vol. 1, Chapter 3.3.
4. (a) Cristol, S.; Barbour, R. V. *J. Am. Chem. Soc.* **1968**, *90*, 2832. (b) Beckwith, A. L. J.; Phillipou, G. *J. Chem. Soc., Chem. Commun.* **1971**, 658. (c) Beckwith, A. L. J.; Phillipou, G. *Aust. J. Chem.* **1976**, *29*, 123. (d) Friedrich, E. C.; Holmstead, R. L. *J. Org. Chem.* **1971**, *36*, 971. (e) Ingold, K. U.; Walton, J. C. *Acc. Chem. Res.* **1986**, *19*, 72.
5. Robbins, R. J.; Falvey, D. E. *J. Org. Chem.* **1993**, *58*, 3616.
6. Batey, R. A.; Motherwell, W. B. *Tetrahedron Lett.* **1991**, *32*, 6649.
7. (a) Norin, T. *Acta Chem. Scan.* **1965**, *19*, 1020. (b) Imanishi, T.; Yamashita, M.; Matsui, M.; Ninbari, F.; Tanaka, T.; Iwate, C. *Chem. Pharm. Bull.* **1988**, *36*, 1351.
8. Cossy, J.; Furet, N.; BouzBouz, S. *Tetrahedron* **1995**, *51*, 11751.
9. (a) Griller, S. J.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317. (b) Effio, A.; Griller, S. J.; Ingold, K. U.; Beckwith, A. L. J.; Serelis, A. K. *J. Am. Chem. Soc.* **1980**, *102*, 1734.
10. (a) Beckwith, A. L. J.; Kazlauskas, R.; Syner-Lyons, M. R. *J. Org. Chem.* **1983**, *48*, 4718. (b) Beckwith, A. L. J.; O'Shea, D. M.; Gerba, S.; Westwood, S. W. *J. Chem. Soc., Chem. Commun.* **1987**, 666. (c) Beckwith, A. L. J.; O'Shea, D. M.; Westwood, S. W. *J. Am. Chem. Soc.* **1988**, *110*, 2565.

11. (a) Dowd, P.; Choi, S. C. *Tetrahedron* **1989**, *45*, 77. (b) Dowd, P.; Choi, S. C. *J. Am. Chem. Soc.* **1987**, *109*, 6548. (c) Dowd, P.; Choi, S. C. *J. Am. Chem. Soc.* **1987**, *109*, 3493. (d) Dowd, P.; Choi, S. C. *Tetrahedron Lett.* **1989**, *30*, 6129.
12. (a) Baldwin, J. E.; Adlington, R. M.; Robertson, J. *Tetrahedron* **1989**, *45*, 909. (b) Baldwin, J. E.; Adlington, R. M.; Robertson, J. *J. Chem. Soc., Chem. Commun.* **1988**, 1404.
13. Crimmins, M. T.; Dudek, C. M.; Cheungn, A. *Tetrahedron Lett.* **1992**, *33*, 181.
14. Lee, P. H.; Lee, J. *Tetrahedron Lett.* **1998**, *39*, 7889.
15. Kim, S.; Lee, P. H. *Tetrahedron Lett.* **1988**, *29*, 5413.
16. Luche, J-L. *J. Am. Chem. Soc.* **1978**, *100*, 2226.
17. (a) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1978**, *87*, 1353. (b) Molander, G. A.; Harring, L. S. *J. Org. Chem.* **1989**, *54*, 3525.
18. Batey, R. A.; Harling, J. D.; Motherwell, W. B. *Tetrahedron* **1992**, *37*, 8031.
19. (a) Enholm, E. J.; Jia, Z. J. *Tetrahedron Lett.* **1995**, *36*, 6819. (b) Enholm, E. J.; Jia, Z. J. *J. Org. Chem.* **1997**, *62*, 174.
20. (a) Ranu, B. C.; Das, A. R. *J. Chem. Soc., Perkin Trans. 1* **1994**, 921. (b) Beckwith, A. L. J.; Moad, G. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1083.
21. (a) Motherwell, W. B.; Circh, D. *Free Radical Chain Reactions in Organic Synthesis*: Academic Press: London, 1992; p 166. (b) Bowman, W. R.; Brown, D. S.; Burns, C. A.; Marples, B. A.; Zaidi, N. A. *Tetrahedron* **1992**, *48*, 6883.
22. (a) Thomas, A. F.; di Giorgio, R.; Guntern, O. *Helv. Chim. Acta* **1989**, *72*, 767. (b) Foster, R. W. G.; Imam, S. H.; Marples, B. A.; Stubbings, G. W. F. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2653. (c) Corser, D. A.; Marples, B. A.; Dart, R. K. *Synlett* **1992**, 987.
23. (a) Osima, K.; Takai, K.; Hotta, Y.; Nozaki, H. *Tetrahedron Lett.* **1978**, *19*, 2417. (b) Takai, K. *Tetrahedron Lett.* **1985**, *26*, 5579. (c) Takai, K.; Kataoka, Y.; Okazoe, T.; Utimoto, K. *Tetrahedron Lett.* **1988**, *29*, 1065.