Tandem Free-Radical Alkene Addition Reactions of Acyl Radicals

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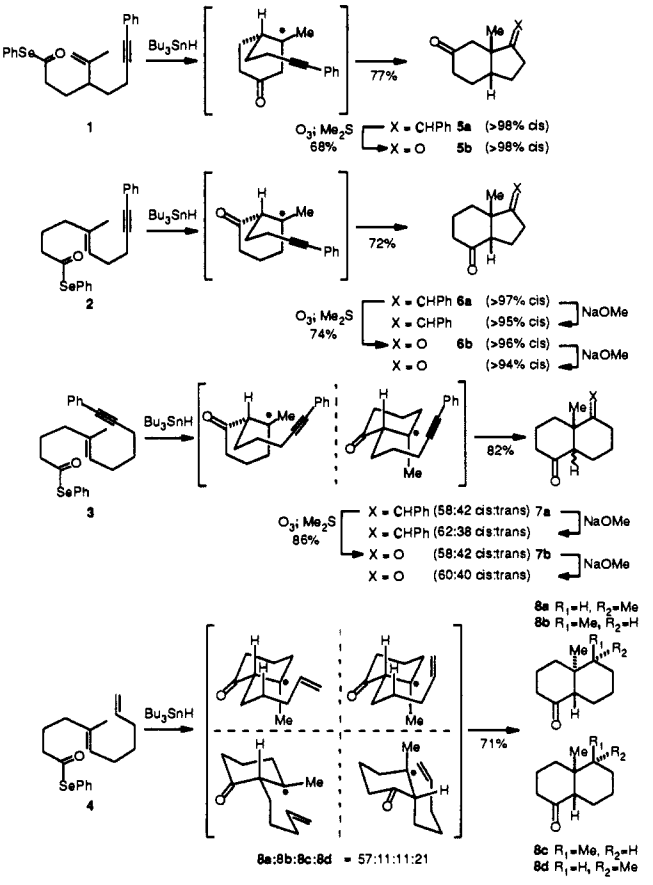
Abstract: The generation of acyl radicals from phenyl selenoesters and the scope of their participation in tandem free-radical alkene addition reactions including intramolecular polycyclization reactions, tandem intramolecular cyclization–intermolecular addition reactions, and tandem intermolecular addition–intramolecular cyclization reactions are detailed.

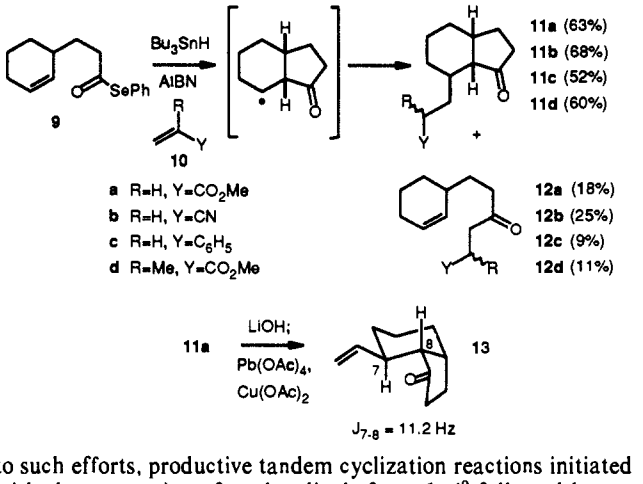
A majority of the synthetically useful free-radical alkene addition reactions depend on the trapping of intermediate adduct radicals by hydrogen atom donors. However, the increased understanding of the reactivity and selectivity of organic free radicals has resulted in the introduction of synthetic methods based on the participation of intermediate free radicals in subsequent inter- and intramolecular alkene addition reactions.[2] Recently, we have shown that acyl radicals generated from phenyl selenoesters participate in effective intramolecular[3] and intermolecular[4] alkene addition reactions at rates greater than that of the potentially competitive tri-*n*-butyltin hydride hydrogen atom abstraction[5] and decarbonylation.[6] Herein, we report that acyl radicals[7] generated in this manner effectively participate in each of the fundamental tandem free radical alkene addition reactions with predictable regio- and diastereoselectivity and with the introduction of useful functionality at the radical initiator site.

Tandem Polycyclization Reactions. A range of intramolecular polycyclization reactions of alkyl radicals have been detailed and have focused principally on the preparation of fused polycyclopentanoids through the use of a combination of extraannular and/or transannular free-radical cyclizations.[8] Complementary

Scheme I. Polycyclization Reactions



Scheme II. Cyclization–Addition Reactions



to such efforts, productive tandem cyclization reactions initiated with the generation of acyl radicals from **1**–**4**[9] followed by se-

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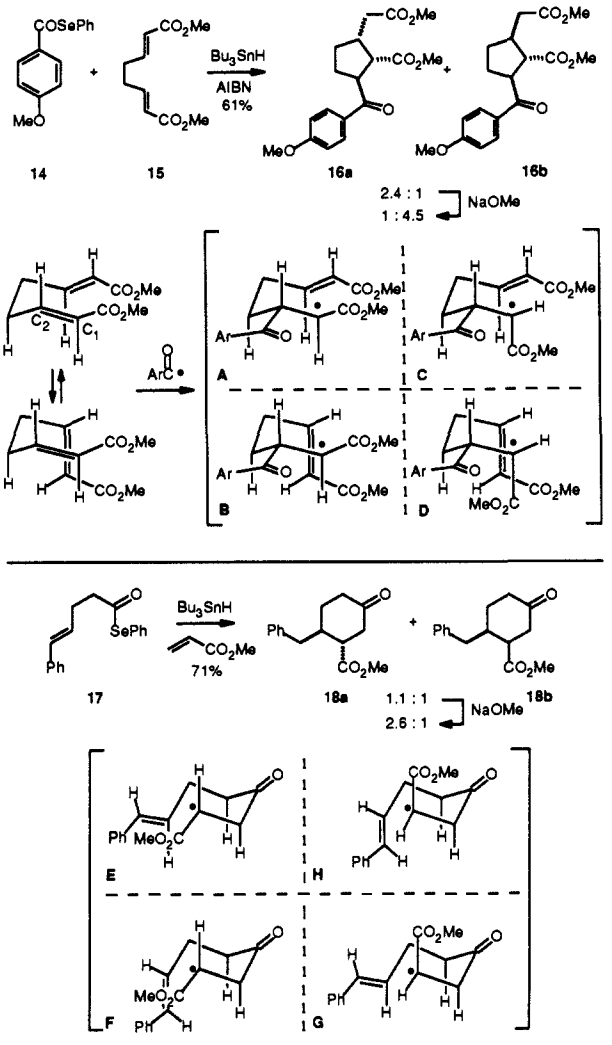
Scheme III. Addition-Cyclization Reactions



quential 6-endo-trig/5-exo-dig, 6-endo-trig/6-exo-dig, or 6-endo-trig/6-exo-trig free-radical cyclizations provided **5a–8**,[10] respectively (Scheme I). In each instance, the polycyclization reaction was initiated with clean 6-endo-trig versus 5-exo-trig free-radical cyclization that may be attributed to the extent of substitution at the proximal alkene. The preference for 6-endo-trig cyclization and the facility with which it proceeds may arise from kinetic deceleration of 5-exo-trig cyclization,[2d] acceleration of 6-endo-trig cyclization (radical stability),[2d] and/or thermodynamic equilibration of initial cyclization products (5-exo-trig → 6-endo-trig).[2d,11-12] The subsequent 5-exo-dig (**1–2** → **5a–6a**, respectively), 6-exo-dig (**3** → **7a**), or 6-exo-trig (**4** → **8**) cyclization provided products reflecting the relative thermodynamic stability of the reaction products with loss of the stereochemical integrity of the central carbon–carbon double bond. Thus, the subsequent free-radical cyclization reactions proceed through intermediate radical conformations that reflect the relative destabilizing torsional and steric interactions present in the potential reaction products. In the case of **1** and **2**, free-radical cyclization followed by ozonolysis permits the preparation of **5b** and **6b**[13] (>20:1 cis:trans), useful hydrindandiones that complement systems available through conventional methodology.

Cyclization–Intermolecular Addition Reactions. Relatively few reports of successful tandem free-radical cyclization–intermolecular addition reactions have been detailed despite their potential for the stereocontrolled construction of functionalized carbon frameworks.[14] Treatment of **9** with tri-*n*-butyltin hydride in the

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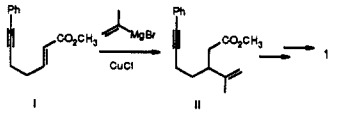
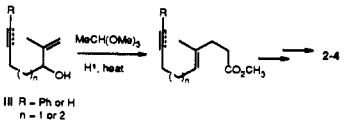
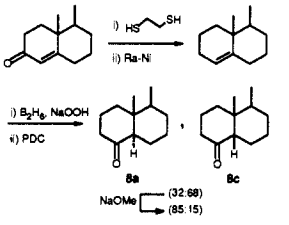
(9) (a) Phenyl selenoester **1** was prepared from i by Cu(I)-catalyzed conjugate addition of isopropenylmagnesium bromide followed by standard one-carbon homologation of ii. Full details are provided in the supplementary material. (b) Phenyl selenoesters **2–4** were prepared from the corresponding



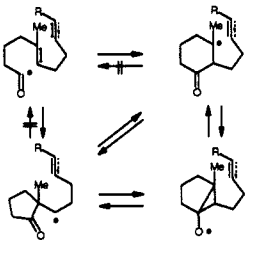
allylic alcohols iii by ortho ester Claisen rearrangement (c.f., Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brocksom, T. J.; Li, T.-t.; Faulkner, D. J.; Petersen, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741) followed by standard one-carbon homologation methods.



(10) Assignment of the stereochemistry of **8a–8d** was tentatively made on the basis of molecular mechanics relative energies of **8a–d** (MacroModel V2.5, MM2 forcefield). Calculation of a Boltzmann distribution (80 °C) based on the relative energies of **8a–d** resulted in a predicted equilibrium ratio **8a**:**8b**:**8c**:**8d** = 66:7:18:9 (trans–cis ring fusion, 73:27) that corresponds closely to the experimental product ratio of 57:11:11:21 (trans–cis ring fusion, 68:32). The initial assignments were supported by base-catalyzed equilibration of the reaction products that resulted in little change (60:10:10:20; trans–cis ring fusion, 70:30) from the initial product ratios (trans–cis ring fusion, 68:32) and confirmed upon the preparation and comparison with authentic **8a** and **8c** as detailed below and in the supplementary material.



(11) A thermodynamic equilibration (5-exo-trig → 6-endo-trig) is not likely to occur through reversible acyl radical–alkene addition but may occur by intramolecular rearrangement (cf. Julia, M.; Maumy, M. *Bull. Soc. Chim. Fr.* **1969**, 2415, 2427 and ref 2d, p 156). Recent studies (R.J.M., unpublished observations) indicate that although the 5-exo-trig → 6-endo-trig rearrangement may be operationally viable for the observed **2** → **6a** cyclization, it is not operationally viable for the conversion of **3** → **7a**. These observations coupled with additional unpublished observations (RJM) of the *lack* of observation of a reversible acyl radical–alkene addition reaction suggest the observation of a direct kinetically *and* thermodynamically preferred 6-endo-trig free-radical cyclization. Full details of this work will be published in due course.



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presence of acceptor alkenes **10a–d** (0.01 M **9**, C_6H_6, 3–5 equiv of alkene, 80 °C, 1–1.5 h addition of Bu_3SnH) provided the 7-substituted-*cis*-1-hydrindanones **11a–d** as single diastereomers accompanied by small amounts of the corresponding simple alkene addition products **12a–d** (Scheme II). The stereochemistry of the bicyclic adducts was established through ester hydrolysis of **11a** (LiOH, THF–MeOH–H_2O) and oxidative decarboxylation[15] of the corresponding carboxylic acid (1.6 equiv of $Pb(OAc)_4$, 0.2 equiv of $Cu(OAc)_2$, 1.2 equiv of pyridine, benzene, 80 °C) to provide the vinyl ketone **13**, which exhibited a C7-H/C8-H coupling constant (J = 11.2 Hz) consistent with the assigned trans-diaxial relationship. Thus, the initial and clean 5-exo-trig acyl radical–alkene cyclization[3] to provide the intermediate cis-fused 1-hydrindanone radical is followed by efficient free-radical addition to the acceptor alkene exclusively from the less hindered face without evidence of significant acyl or alkyl free-radical reduction.

Intermolecular Addition–Cyclization Reactions. Complementary to the tandem cyclization–addition free-radical reactions, two fundamentally different types of tandem intermolecular addition–cyclization reactions[16] provided useful approaches to the preparation of functionalized carbocyclic systems. Aryl acyl radical generation through tri-*n*-butyltin hydride treatment of aryl phenyl selenoester **14** in the presence of the acceptor alkene **15**[17] possessing a pendant, proximal alkene proceeded with intermolecular acyl radical–alkene addition, intramolecular 5-exo-trig free radical–alkene cyclization, and subsequent reduction to provide **16** (61%) as a mixture of diastereomers (**16a**:**16b**, 2.4:1) (Scheme III). The major and minor diastereomers arise from cyclization through the radical conformations A and B, respectively, with predominate and well-precedented hex-5-enyl radical 1,5-cis diastereoselectivity[18] and an apparent exclusive hex-5-enyl 1,2-trans diastereoselectivity.[19] As established in prior studies of hex-5-enyl radical cyclizations, it is not likely that destabilizing steric interactions would prove sufficient to prevent cyclization through radical conformation C (1,2-*cis* diastereoselectivity),[18] and, thus, the product distribution must reflect the initial trans olefin configuration of **15** and an intramolecular 5-exo-trig cyclization that proceeds at a rate that exceeds C1–C2 bond rotation.

In a complementary tandem addition–cyclization reaction, treatment of acyl radical precursor **17** with tri-*n*-butyltin hydride in the presence of methyl acrylate (4 equiv) proceeded with acyl radical generation, effective intermolecular acyl radical–alkene addition, 6-exo-trig intramolecular cyclization, and subsequent reduction to provide **18** (71%) (Scheme III). Although the diastereoselectivity of the addition–cyclization reaction is not high, it does qualitatively reflect the relative destabilizing torsional and steric interactions present in the final reaction products and may be rationalized as proceeding preferentially through the radical conformations E–G (E > G > F ≫ H).[20]

These observations illustrate that acyl radicals generated from phenyl selenoesters serve as productive functionalized free radicals useful in the initiation of each of the fundamental tandem inter- and intramolecular free radical alkene-addition reactions with inherent introduction of useful functionality at the radical initiation site. Thus, the participation of acyl radicals generated from phenyl selenoesters in effective regio- and diastereoselective tandem free radical alkene reactions may serve to complement related cationic,[21] anionic,[22] and transition-metal-mediated[23] tandem addition reactions employed in the preparation of carbocycles. Such applications are in progress and will be reported in due course.

Experimental Section[24]

General Procedure for Tandem Polycyclization Reactions. 1-Benzylidene-8β-methyl-9β-hydrindan-6-one (5a). A solution of phenyl selenoester **1** (297 mg, 0.75 mmol) and AIBN (15 mg) in 60 mL of dry benzene was warmed at reflux and treated dropwise (syringe pump) with a solution of tri-*n*-butyltin hydride (0.26 mL, 274 mg, 0.94 mmol, 1.25 equiv) in benzene (5 mL) over a period of 1 h. After warming at reflux for an additional 30 min, the mixture was cooled to room temperature and concentrated, providing an oily residue containing a mixture of two bicyclic ketones. Flash chromatography (2 × 13 cm SiO_2, 12% EtOAc–hexane eluant) afforded 109 mg (180 mg theoretical, 61%) of pure *E*-**5a** and 31 mg (16%) of a 2.9:1 mixture (GLC, oven temperature 190 °C) of *Z*- and *E*-**5a** (>98% purity). *E*-**5a**: colorless oil; (t_R = 8.8 min); ^{1}H NMR ($CDCl_3$, 300 MHz, ppm) 0.94 (3 H, s, CH_3), 1.69–1.95 (5 H, m), 2.18 (2 H, overlapping 1 H, m, and 1 H, d, J = 13.8 Hz, 1 × C7-H), 2.34 (1 H, m), 2.49 (1 H, d, J = 13.8 Hz, 1 × C7-H), 2.63 (2 H, m), 6.47 (1 H, s, C=C*H*Ph), 7.08–7.32 (5 H, m, 5 × ArH); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) 25.9 (e), 26.2 (o), 27.2 (e), 33.2 (e), 37.1 (e), 46.8 (o), 48.1 (e), 49.2 (e), 122.7 (o), 126.2 (o), 127.7 (o), 128.8 (o), 138.0 (e), 151.2 (e), 211.8 (e); IR (neat) ν_{max} 2952, 1712, 1598, 1492, 1464, 1442, 1286, 1234, 750, 702 cm^{-1}; EIMS *m/e* (relative intensity) 240 (81, M^+), 225 (22), 183 (79), 167 (52), 131 (39), 115 (42), 91 (base, $C_7H_7^+$), 77 (29), 55 (69); CIMS (isobutane) *m/e* 241 (base, $M^+ + H$); EIHRMS *m/e* 240.1513 ($C_{17}H_{20}O$ requires 240.1514).

Z-**5a**: colorless oil; (t_R = 10.4 min); ^{1}H NMR ($CDCl_3$, 300 MHz, ppm) 1.19 (3 H, s, CH_3), 1.73–2.42 (8 H, m), 2.58 (1 H, d, J = 14.3 Hz), 2.70–2.83 (2 H, m), 6.17 (1 H, s, C=C*H*Ph), 7.11–7.38 (5 H, m, 5 ×

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(24) (a) Proton nuclear magnetic resonance spectra (^{1}H NMR) and carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded on a General Electric QE-300 spectrometer and chemical shifts are reported in parts per million (ppm) relative to internal tetramethylsilane (0.00 ppm). ^{1}H NMR data (300 MHz) are reported as follows: chemical shift (number of hydrogens, multiplicity, coupling constant(s) in hertz). For APT ^{13}C NMR, e = even and o = odd number of attached protons. Infrared spectra (IR) were recorded on a Perkin Elmer 1420 or Perkin-Elmer Model 1800 FTIR spectrometer. Melting points (mp) were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. Electron-impact mass spectra (EIMS) and chemical-ionization mass spectra (CIMS) were recorded on a Finnigan 4000 spectrometer. Electron-impact (EI) and chemical-ionization (CI) high-resolution mass spectra were recorded on a Kratos MS-50 spectrometer. Capillary GLC analyses were performed on a Varian 3700 chromatograph equipped with a 30 m × 0.25 μm (film thickness) RSL-150 capillary column. Helium was used as the carrier gas (flow rate 1 mL/min) and peak area integrations are uncorrected for flame ionization detector response. Ozonolyses were carried out on a Welsbach ozonator. Flash chromatography[24b] was performed on 230–400-mesh silica gel. Benzene and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl. Dichloromethane (CH_2Cl_2) was distilled from phosphorus pentoxide. Methanol (MeOH) was distilled from magnesium methoxide. All extraction and chromatographic solvents (diethyl ether, ethyl acetate (EtOAc), and hexane) were distilled prior to use. All other solvents and reagents were used as received from commercial sources. All reactions were carried out under an atmosphere of nitrogen or argon. (b) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

ArH); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) 26.6 (o), 26.8 (e), 27.4 (e), 28.9 (e), 37.9 (e), 43.9 (o), 49.4 (e), 50.6 (e), 120.5 (o), 126.1 (o), 128.1 (o), 128.3 (o), 137.9 (e), 151.3 (e), 211.2 (e); IR (neat) ν_{max} 2952, 1712, 1596, 1492, 1448, 1288, 754 cm^{-1}; EIMS *m/e* (relative intensity) 240 (73, M$^+$), 225 (21), 183 (76), 167 (48), 141 (39), 115 (45), 91 (base, $C_7H_7^+$), 77 (27), 55 (68); CIMS (isobutane) *m/e* 241 (base, M$^+$ + H); EIHRMS *m/e* 240.1517 ($C_{17}H_{20}O$ requires 240.1514).

General Procedure of Ozonolysis of Bicyclic Enones. 8β-Methyl-9β-hydrindan-1,6-dione (5b). A solution of ketone **5a** (90 mg, 0,38 mmol; 5.0:1 *E*:*Z* mixture of olefin isomers) in 10 mL of CH_2Cl_2 was cooled to −78 °C, and ozone was bubbled into the solution until a blue color developed. After the blue color was discharged with a stream of nitrogen, dimethyl sulfide (0.12 mL, 4 equiv) was added dropwise, and the reaction mixture was allowed to warm to room temperature over a period of 14 h. The solvent and excess dimethyl sulfide were removed under reduced pressure; and the residue was dissolved in 20 mL of ether and was washed with 5 mL of water and 5 mL of saturated aqueous sodium chloride. The organic layer was dried ($MgSO_4$) and concentrated in vacuo, and the residue was purified by flash chromatography (20% EtOAc–hexane eluant) to afford 43 mg (63 mg theoretical, 68%) of diketone **5b** as a light yellow oil: ^{1}H NMR ($CDCl_3$, 300 MHz, ppm) 1.00 (3 H, s, CH_3), 1.68–2,41 (8 H, m), 2.46 (1 H, d, *J* = 13.4 Hz, 1 × C7-H), 2.54 (2 H, m); IR (neat) ν_{max} 2948, 1742, 1710 cm^{-1}; EIMS *m/e* (relative intensity) 166 (45, M$^+$), 151 (57, M$^+$ − CH_3), 123 (43, M$^+$ − CH_3CO), 111 (53), 82 (base, $C_5H_6O^+$), 67 (99), 55 (68); CIMS (isobutane) *m/e* 167 (base, M$^+$ + H); EIHRMS *m/e* 166,0994 ($C_{10}H_{14}O_2$ requires 166.0994). Capillary GLC analysis (oven temperature 110 °C) indicated the presence of one component (t_R = 7.8 min, >98% purity).

1-Benzylidene-8β-methyl-9β-hydrindan-4-one (6a). Phenyl selenoester **2** (594 mg, 1.50 mmol) was treated with tri-*n*-butyltin hydride (0.48 mL, 524 mg, 1.80 mmol) and AIBN (20 mg) as described in the general procedure. Flash chromatography (3 × 12 cm SiO_2, 10% EtOAc–hexane eluant) gave 260 mg (360 mg theoretical, 72%) of **6a** as a colorless, viscous oil. GLC analysis (oven temperature 170 °C) indicated the presence of a single component (t_R = 7.6 min; >97% purity): ^{1}H NMR ($CDCl_3$, 300 MHz, ppm) 1.12 (3 H, s, CH_3), 1.48–1.72 (3 H, m), 1.78 (2 H, m), 2.18 (2 H, m), 2,34 (2 H, m), 2.60 (2 H, apparent t), 6.44 (1 H, s), 7.11–7.29 (5 H, m, 5 × ArH); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) 22,3 (e), 24,2 (e), 27.4 (o), 33.0 (e), 33.7 (e), 39.3 (e), 50.2 (e), 62.7 (o), 122.3 (o), 126.2 (o), 127.6 (o), 128.7 (o), 138.3 (e), 149.5 (e), 212.9 (e); IR (neat) ν_{max} 2948, 2863, 1711, 1602, 1112, 982, 741 cm^{-1}; EIMS *m/e* (relative intensity) 240 (base, M$^+$), 225 (39), 197 (26), 169 (16), 141 (19), 128 (18), 115 (27), 107 (18), 91 (63), 77 (16); CIMS (isobutane) *m/e* 241 (base, M$^+$ + H); EIHRMS *m/e* 240.1518 ($C_{17}H_{20}O$ requires 240.1514). Base equilibration (catalytic NaOMe, MeOH, reflux, 28 h) provided **6a** in >95% (GLC) purity.

8β-Methyl-9β-hydrindan-1,4-dione (6b). A 240-mg (1.0 mmol) sample of ketone **6a** was subjected to ozonolysis (CH_2Cl_2, −78 °C, 5 min; 4 equiv of Me_2S, 25 °C, 14 h) to give 123 mg (166 mg theoretical, 74%) of a single diketone **6b** by GLC analysis (t_R = 6.7 min, oven temperature 170 °C; 96.5% purity): ^{1}H NMR (300 MHz, $CDCl_3$, ppm) 1.13 (3 H, s, CH_3) (lit. value[13] 1.17 ppm for *cis*-**6b**); IR (neat) ν_{max} 2953, 1740, 1706 cm^{-1}. Base equilibration (catalytic NaOMe, MeOH, reflux, 39 h) returned **6b** in >94% (GLC) purity.

1-Benzylidene-9β-methyl-10β-decalin-5-one (*cis*-7a) and 1-Benzylidene-9β-methyl-10α-decalin-5-one (*trans*-7a). Treatment of phenyl selenoester **3** (356 mg, 0.868 mmol) with tri-*n*-butyltin hydride (0.32 mL, 341 mg, 1.17 mmol, 1.3 equiv) and AIBN (20 mg) in 100 mL of benzene according to the general procedure gave 64 mg (220 mg theoretical, 29%) of pure *cis*-**7a** and 117 mg (53%) of a 38:62 *cis*-**7a**:*trans*-**7a** mixture. *cis*-**7a**: oil; ^{1}H NMR ($CDCl_3$, 300 MHz, ppm) 1.05 (3 H, s, CH_3), 1,34–1.77 (7 H, m), 1.88 (1 H, m), 2.20 (3 H, m), 2.35 (1 H, dd, *J* = 12.0 and 3.6 Hz), 2.47 (1 H, m), 6.43 (1 H, s, C=CHPh), 7.10–7.29 (5 H, m, 5 × ArH); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) 19.7 (o), 20.9 (e), 22.6 (e), 26.3 (e), 35.6 (e), 38.4 (e), 41.3 (e), 46.9 (e), 58.4 (o), 124.1 (o), 125.9 (o), 127.5 (o), 128.8 (o), 140.8 (e), 146.6 (e), 212.3 (e); IR (neat) ν_{max} 2938, 2858, 1712, 1596, 1444, 1070, 946, 832, 746 cm^{-1}; EIMS *m/e* (relative intensity) 254 (base, M$^+$), 129 (51), 115 (49), 91 (87), 77 (24), 55 (37); CIMS (isobutane) *m/e* 255 (base, M$^+$ + H); EIHRMS, *m/e* 254.1668 ($C_{18}H_{22}O$ requires 254.1670). Base equilibration (catalytic NaOMe, MeOH, reflux, 37 h) of pure *cis*-**7a** gave a 68:32 *cis*-**7a** (t_R = 8,8 min):*trans*-**7a** (t_R = 9.3 min) ratio (GLC; oven temperature 200 °C).

9β-Methyl-10β-decalin-1,5-dione (*cis*-7b) and 9β-Methyl-10α-decalin-1,5-dione (*trans*-7b). Ozonolysis of a sample of pure *cis*-**7a** (46 mg; >98% pure by GLC analysis) gave a single diketone (*cis*-**7b**) as a colorless oil (22 mg, 67% yield): ^{1}H NMR ($CDCl_3$, 300 MHz, ppm), 1.00 (3 H, s, CH_3), 1.51–2.32 (11 H, m), 2.48 (1 H, dd, *J* = 15.6 and 8.2 Hz), 2.57 (1 H, dd, *J* = 15.6 and 6.7 Hz); IR (neat) ν_{max} 2953, 1718, 1711 cm^{-1}; EIMS *m/e* (relative intensity) 180 (36, M$^+$), 165 (59, M$^+$ − CH_3), 137 (48), 125 (59), 96 (base, $C_6H_8O^+$), 55 (81); CIMS (isobutane) *m/e* 181 (base, M$^+$ + H); EIHRMS *m/e* 180.1154 ($C_{11}H_{16}O_2$ requires 180.1151). Base equilibration (catalytic NaOMe, MeOH, reflux, 28 h) of *cis*-**7b** (t_R = 9.7 min) gave a 60:40 *cis*-**7b**:*trans*-**7b** mixture (GLC, oven temperature 130 °C) ratio of which the minor component (t_R = 8.6 min) was identified as *trans*-**7b** on the basis of the ^{1}H NMR chemical shift of the angular methyl singlet (1.19 ppm; lit. value[25] for trans isomer = 1.20 ppm).

Ozonolysis of a sample (254 mg, 1.0 mmol) of the crude mixture of bicyclic ketones **7a** from a separate cyclization experiment gave a 58:42 *cis*-**7b**:*trans*-**7b** ratio (GLC, oven temperature 130 °C). Base equilibration (NaOMe, MeOH, reflux, 30 h) provided a 60:40 *cis*-**7b**:*trans*-**7b** ratio (GLC).

5,10-Dimethyldecalin-1-one (8a-d). Free-radical cyclization of **4** (240 mg, 0.714 mmol) with tri-*n*-butyltin hydride (0,24 mL, 262 mg, 0,90 mmol, 1,25 equiv) and AIBN (15 mg) in 60 mL of benzene was performed as described for the cyclization of **1**. Flash chromatography (2 × 12 cm SiO_2, 0% then 7% EtOAc–hexane eluant) gave 92 mg (128 mg theoretical, 72%) of a mixture of **8a–d** as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz, ppm) 0.68 and 0.89 (3 H, two s, **8a** and **8c** C10-CH_3), 0.85 and 1.08 (3 H, two d, *J* = 6.6 Hz, **8a** and **8c** C5-CH_3), 1.21–2.42 (14 H, m); IR (neat) ν_{max} 2940, 1716 (C=O), 1448, 1377, 1312 cm^{-1}; EIMS *m/e* (relative intensity) 180 (55, M$^+$), 165 (82, M$^+$ − CH_3), 137 (26), 111 (83), 98 (base, $C_7H_8O^+$), 81 (60), 67 (85), 55 (71); CIMS (isobutane) *m/e* 181 (base, M$^+$ + H); EIHRMS *m/e* 180.1515 ($C_{12}H_{20}O$ requires 180.1514).

GLC analysis (oven temperature 130 °C) of the crude reaction mixture indicated the presence of the four diastereomers in the ratio **8a**:**8b**:**8c**:**8d** = 57:11:11:21 (t_R = 8.1, 8.7, 7.4, and 9.2 min, respectively). Coinjection of the mixture of **8a–d** with an authentic, independently prepared[10] sample of a 32:68 **8a**:**8c** mixture unambiguously identified the major component (**8a**; t_R = 8.1 min) and one minor component (**8c**; t_R = 7.4 min) in the mixture.

General Procedure for Cyclization–Addition Reactions of 9. Methyl 3′-[7β-(1-Oxo-8β,9β-hydrindan)]propionate (11a) and Methyl 6-(3′-Cyclohexenyl)-4-oxohexanoate (12a). A solution of phenyl selenoester **9** (220 mg, 0.75 mmol), methyl acrylate (0.34 mL, 323 mg, 3.75 mmol, 5 equiv), and AIBN (15 mg) in 70 mL of dry benzene was warmed at reflux while a solution of tri-*n*-butyltin hydride (0.26 mL, 281 mg, 0.98 mmol, 1.3 equiv) in 5 mL of benzene was added dropwise (syringe pump) over a period of 1.0 h. The solution was warmed at reflux for an additional 1.0 h, cooled to room temperature, and concentrated under reduced pressure. The residual oil was purified by flash chromatography (2 × 12 cm SiO_2, 20% EtOAc–hexane eluant) to give 105 mg (168 mg theoretical, 63%) of **11a** as a colorless oil and 30 mg (168 mg theoretical, 18%) of **12a** as a colorless oil. For **11a**: ^{1}H NMR ($CDCl_3$, 300 MHz, ppm) 1.08–1.49 (7 H, m), 1.62–1.97 (6 H, m), 2.21–2.43 (4 H, m), 3,67 (3 H, s, OCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) 19.2 (e), 25.2 (e), 26.9 (e), 27.7 (2e), 30,8 (o), 31.9 (e), 33.9 (o), 34.9 (e), 51.3 (o), 54.2 (o), 173.7 (e), 219.0 (e); IR (neat) ν_{max} 2930, 1736 (br, ester and ketone C=O), 1456, 1438, 1200, 1166, 1106 cm^{-1}; EIMS *m/e* (relative intensity) 224 (4, M$^+$), 206 (16, M$^+$ − H_2O), 192 (12, M$^+$ − CH_3OH), 164 (7, M$^+$ − $HCOOCH_3$), 137 (base, M$^+$ − $CH_2CH_2COOCH_3$), 109 (33), 91 (40), 79 (61), 67 (56), 55 (55); CIMS (isobutane) *m/e* 225 (base, M$^+$ + H); EIHRMS *m/e* 224.1410 ($C_{13}H_{20}O_3$ requires 224.1412).

For **12a**: ^{1}H NMR ($CDCl_3$, 300 MHz, ppm) 1,15–1.82 (6 H, m, 3 × CH_2), 1.95 (2 H, m, C6′-H_2), 2.08 (1 H, m, C3′-H), 2.50 (2 H, t, *J* = 7.8 Hz, C5-H_2), 2.59 (2 H, t, *J* = 6.5 Hz, C3-H_2), 2.74 (2 H, t, *J* = 6.5 Hz, C2-H_2), 3.68 (3 H, s, OCH_3), 5.53 (1 H, m, C*H*=CH), 5.68 (1 H, m, CH=C*H*); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) 21.2 (e), 25.2 (e), 27.6 (e), 28.6 (e), 29.8 (e), 34.5 (o), 36.9 (e), 40.0 (e), 51.7 (o), 127.5 (o), 130.9 (o), 173.2 (e), 209.0 (e); IR (neat) ν_{max} 2926, 1735 (br, ester and ketone C=O), 1410, 1362, 1202 cm^{-1}; EIMS *m/e* (relative intensity) 224 (6, M$^+$), 192 (24, M$^+$ − $HOCH_3$), 164 (24, M$^+$ − HCO_2CH_3), 129 (71), 81 (base, $C_6H_9^+$), 55 (70); CIMS (isobutane) *m/e* 225 (base, M$^+$ + H); EIHRMS *m/e* 224.1416 ($C_{13}H_{20}O_3$ requires 224.1412).

3′-[7β-(1-Oxo-8β,9β-hydrindan)]propionitrile (11b) and 6-(3′-Cyclohexenyl)-4-oxohexanenitrile (12b). According to the general procedure, phenyl selenoester **9** (0.75 mmol) and acrylonitrile (1.88 mmol, 2.5 equiv) gave 97 mg (143 mg theoretical, 68%) of **11b** as a colorless oil and 36 mg (143 mg theoretical, 25%) of **12b** as an oil after purification by flash chromatography (2 × 11 cm SiO_2, 25% EtOAc–hexane eluant). For **11b**: ^{1}H NMR ($CDCl_3$, 300 MHz, ppm) 1.21 (2 H, m), 1.46 (3 H, m), 1.66 (2 H, m), 1.78–1.99 (5 H, m), 2.23–2.40 (5 H, m); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) 14.8 (e), 19.2 (e), 24.9 (e), 26.8 (e), 27.2 (e), 28.3 (e), 30.7 (o), 34.1 (o), 35.2 (e), 53.6 (o), 119.4 (e), 218.6 (e); IR (neat) ν_{max} 2930, 2244 (C≡N), 1736 (C=O), 1458, 1166, 1106 cm^{-1}; EIMS *m/e*

(25) Reichel, C. J.; Bryson, T. A. *Heterocycles* **1982**, *18*, 277.

(relative intensity) 191 (25, M^+), 162 (22), 109 (51), 93 (27), 83 (base, $C_6H_{11}^+$), 68 (62), 55 (77); CIMS (isobutane) *m/e* 192 (base, $M^+ + H$); EIHRMS *m/e* 191.1309 ($C_{12}H_{17}NO$ requires 191.1310).

For **12b**: ^1H NMR ($CDCl_3$, 300 MHz, ppm), 1.17–1.84 (6 H, m), 1.99 (2 H, m, C6′-H_2), 2.07 (1 H, m, C3′-H) 2.50 (2 H, t, J = 7.7 Hz, C5-H_2), 2.58 (2 H, t, J = 7.0 Hz, C3-H_2), 2.82 (2 H, t, J = 7.0 Hz, C2-H_2), 5.51 (1 H, m, C*H*=CH), 5.69 (1 H, m, CH=C*H*); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) 11.2 (e), 21.1 (e), 25.0 (e), 28.4 (e), 29.5 (e), 34.2 (o), 37.4 (e), 39.6 (e), 119.0 (e), 127.7 (o), 130.5 (o), 206.2 (e); IR (neat) ν_{max} 3016, 2928, 2248 (C≡N), 1718 (C=O), 1450, 1414, 1374, 1104, 724 cm^{-1}; EIMS *m/e* (relative intensity) 191 (1, M^+), 109 (6), 94 (93, $C_7H_{10}^+$), 79 (base, $C_6H_7^+$), 67 (26), 54 (42); CIMS (isobutane) *m/e* 192 (base, $M^+ + H$); CIHRMS *m/e* 192.1388 ($C_{12}H_{17}NO$ requires 192.1388).

7β-(2′-Phenylethyl)-8β,9β-hydrindan-1-one (11c) and 5-(3′-Cyclohexenyl)-1-phenyl-3-pentanone (12c). According to the general procedure, phenyl selenoester **9** (0.75 mmol) and styrene (1.88 mmol, 2.5 equiv) afforded 95 mg (182 mg theoretical, 52%) of **11c** as an oil and 15 mg (182 mg theoretical, 9%) of **12c** as an oil. For **11c**: ^1H NMR ($CDCl_3$, 300 MHz, ppm), 1.04–1.23 (2 H, m,), 1.38 (2 H, m), 1.51–2.05 (9 H, m), 2.23 (2 H, m), 2.36 (1 H, m, 1 × C2-H), 2.60 (1 H, ddd, J = 24.6, 5.1, and 4.6 Hz, 1 × C2-H), 7.06–7.34 (5 H, m, 5 × ArH); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) 19.5 (e), 22.5 (e), 25.3 (e), 27.5 (e), 31.2 (o), 33.7 (e), 34.2 (o), 34.8 (e), 35.2 (e), 54.6 (o), 125.6 (o), 128.2 (2o), 142.4 (e), 219.6 (e); IR (neat) ν_{max} 2928, 2858, 1738 (C=O), 1496, 1454, 1166, 750, 700 cm^{-1}; EIMS *m/e* (relative intensity) 242 (6, M^+), 137 (68, $M^+ - C_8H_9$), 105 (37), 91 (base, $C_7H_7^+$), 79 (50), 67 (72); CIMS (isobutane) *m/e* 243 ($M^+ + H$), 139 (base, $M^+ + H - C_8H_8$); EIHRMS *m/e* 242.1675 ($C_{17}H_{22}O$ requires 242.1670).

For **12c**: ^1H NMR ($CDCl_3$, 300 MHz, ppm) 1.15–2.15 (9 H, m), 2.25 (2 H, t, J = 7.4 Hz, C5-H_2), 2.52 (2 H, t, J = 7.6 Hz, C2-H_2), 2.61 (2 H, t, J = 7.4 Hz, C4-H_2), 5.51 (1 H, m, C*H*=CH), 5.70 (1 H, m, CH=C*H*), 7.14–7.29 (5 H, m, 5 × ArH); IR (neat) ν_{max} 2922, 1716 (C=O), 1461, 1408, 1168, 749, 694 cm^{-1}; EIMS *m/e* (relative intensity) 242 (10, M^+), 161 (34), 137 (28), 91 (77, $C_7H_7^+$) 81 (base, $C_6H_9^+$), 79 (61), 55 (71); CIMS (isobutane) *m/e* 243 (base, $M^+ + H$); EIHRMS *m/e* 242.1674 ($C_{17}H_{22}O$ requires 242.1670).

Methyl 3′-[7β-(1-Oxo-8β,9β-hydrindan)]-2′-methylpropionate (11d) and Methyl 6-(3′-Cyclohexenyl)-2-methyl-4-oxohexanoate (12d). According to the general procedure, **9** (0.75 mmol) and methyl methacrylate (1.88 mmol, 2.5 equiv) gave 108 mg (179 mg theoretical, 60%) of **11d** as a colorless oil and 19 mg (179 mg theoretical, 11%) of **12d** as an oil after purification by flash chromatography (2 × 11 cm, SiO_2, 20% EtOAc–hexane eluant). For **11d**; ^1H NMR ($CDCl_3$, 300 MHz, ppm) 1.15 (4 H, overlapping 3 H, apparent t, 2 × diastereomeric C2′-CH_3, and 1 H, m), 1,20–1.44 (5 H, m), 1.48–2.03 (7 H, m), 2.21 (1 H, dd, J = 11.4 and 6.8 Hz, C8-H), 2.34 (1 H, m), 2.46 (1 H, m), 3.67 (3 H, s, OCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) 16.8 and 17.7 (o), 19.2 and 19.4 (e), 25.3 and 25.4 (e), 26.8 and 27.5 (e), 27.8 and 27.9 (e), 28.9 and 29.1 (o), 33.9 (o), 35.0 (e), 36.5 and 36.9 (e), 37.1 and 37.2 (o), 42.8 and 44.0 (o), 51.5 (o), 54.4 and 54.8 (o), 177.2 (e), 219.0 and 219.1 (e); IR (neat) ν_{max} 2934, 1736 (ester and ketone C=O), 1460, 1200, 1168 cm^{-1}; EIMS *m/e* (relative intensity) 238 (5, M^+), 220 (6, $M^+ - H_2O$), 206 (25, $M^+ - CH_3OH$), 151 (79), 137 (98), 109 (67), 83 (base, $C_6H_{11}^+$), 79 (66), 67 (80), 55 (91); CIMS (isobutane), *m/e* 239 (base, $M^+ + H$); EIHRMS *m/e* 238.1589 ($C_{14}H_{22}O_3$ requires 238.1584).

For **12d**: ^1H NMR ($CDCl_3$, 300 MHz, ppm) 1.13 (3 H, d, J = 7.2 Hz, C2-CH_3), 1.44–1.83 (6 H, m), 1.95 (3 H, m), 2.30 (1 H, dd, J = 16.8 and 5.2 Hz, 1 × C3-H), 2,54 (2 H, m, C5-H_2), 2.78 (1 H, dd, J = 16.8 and 8.7 Hz, 1 × C3-H), 3.01 (1 H, m, C2-H), 3.65 and 3.66 (3 H, two s, diastereomeric OCH_3), 5.51 (1 H, m, C*H*=CH), 5.68 (1 H, m, CH=C*H*); IR (neat) ν_{max} 2930, 1736 (ester C=O), 1716 (ketone C=O), 1438, 1272, 1200, 1178, 1006, 722 cm^{-1}; EIMS *m/e* (relative intensity) 238 (4, M^+), 207 (3), 144 (27), 129 (79), 112 (51), 94 (52), 81 (73), 59 (base, $CO_2CH_3^+$); CIMS (isobutane) *m/e* 239 (base, $M^+ + H$); EIHRMS *m/e* 238.1574 ($C_{14}H_{22}O_3$ requires 238.1584).

7β-Vinyl-8β,9β-hydrindan-1-one (13). A solution of **11a** (350 mg, 1.56 mmol) in 8 mL of 3:2:1 THF–MeOH–H_2O was treated with lithium hydroxide monohydrate (131 mg, 3.12 mmol, 2.0 equiv), and the mixture was stirred at room temperature for 1.0 h. After diluting with 20 mL of water and washing with 20 mL of ether, the aqueous solution was acidified with concentrated hydrochloric acid and extracted with ether (2 × 20 mL). The combined ether extracts were washed with water, saturated sodium chloride, dried ($MgSO_4$), and concentrated to afford 320 mg (328 mg theoretical, 97%) of crude carboxylic acid as a pale yellow, viscous oil. The crude acid (300 mg, 1.43 mmol) was dissolved in benzene (2.0 mL) and treated with cupric acetate monohydrate (10 mg) and pyridine (0.14 mL, 1.72 mmol, 1.2 equiv). After the mixture was stirred room temperature for 1 h, lead tetraacetate (1.01 g, 2.29 mmol, 1.6 equiv) and benzene (8 mL) were added, and the mixture was degassed with a flow of argon before it was warmed at reflux for 3 h. After cooling to room temperature, the mixture was diluted with 30 mL ether, washed with 5% aqueous sodium hydroxide, saturated sodium chloride, dried ($MgSO_4$), and concentrated to a yellow oil (440 mg). Flash chromatography (2 × 12 cm SiO_2, 5% EtOAc–hexane eluant) gave 101 mg (234 mg theoretical, 43%) of pure **13** as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz, ppm) 1.15 (1 H, m), 1.43 (4 H, m), 1.60–1.71 (1 H, m), 1.74–1.94 (2 H, m), 2.16 (1 H, dd, J = 11.2 and 6.3 Hz, C8-H; irradiation at 2.67 ppm causes collapse to a doublet, J = 6.3 Hz), 2.21–2.34 (2 H, m, C2-H_2), 2.41 (1 H, m, C9-H), 2.67 (1 H, m, C7-H), 5.06 (2 H, m, CH=CH_2), 5.90 (1 H, m, C*H*=CH_2; irradiation at 2.67 ppm causes collapse to dd, J = 14.6 and 10.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) 19.7 (e), 25.3 (e), 27.7 (e), 28.4 (e), 34.3 (o), 35.0 (e), 35.5 (o), 53.8 (o), 113.9 (e), 141.3 (o), 218.9 (e); IR (neat) ν_{max} 2930, 2860, 1742 (C=O), 1638 (C=C), 1448, 1410, 1166, 1104, 912 cm^{-1}; EIMS *m/e* (relative intensity) 164 (19, M^+), 120 (47), 108 (22), 93 (49), 79 (base, $C_6H_7^+$), 67 (46); CIMS (isobutane) *m/e* 165 (base, $M^+ + H$); EIHRMS *m/e* 164.1203 ($C_{11}H_{16}O$ requires 164.1201).

Methyl 2-[(1*S,2*S**,3*R**)-3-(4′-Methoxybenzoyl)-2-(methoxycarbonyl)cyclopentyl]acetate (16a) and Methyl 2-[(1*S**,2*S**,3*S**)-3-(4′-Methoxybenzoyl)-2-(methoxycarbonyl)cyclopentyl]acetate (16b).** A solution of phenyl selenoester **14**[4] (292 mg, 1.0 mmol), diester **15**[17] (396 mg, 2.0 mmol, 2 equiv), and AIBN (16 mg) in 10 mL of dry benzene was warmed at reflux and treated dropwise (syringe pump, 2.5 h) with a solution of tri-*n*-butyltin hydride (0.35 mL, 378 mg, 1.3 mmol) in dry benzene (5 mL). After an additional 60 min at reflux, the solution was cooled to room temperature and concentrated in vacuo. The residual oil was purified by flash chromatography (25% EtOAc–hexane eluant) to give 204 mg (334 mg theoretical, 61%) of **16** as a mixture of diastereomers: ^1H NMR ($CDCl_3$, 300 MHz, ppm) 1.55–2.49 (4 H, m), 2.58–2.86 (3 H, m), 3.17 and 3.49 (2 H, two apparent t, trans and cis C2-H, respectively), 3.56 and 3.57 (3 H, two s, trans and cis ester OCH_3 respectively), 3.60 (3 H, s, cis and trans ester OCH_3), 3.79 (3 H, s, cis and trans ArOCH_3), 6.86 (2 H, d, J = 8,6 Hz, 2 × ArH), 7.87 (2 H, d, J = 8.6 Hz, 2 × ArH); IR (neat) ν_{max} 2954, 1736 (br), 1674, 1600, 1576, 1260, 1198, 1170 cm^{-1}; EIMS *m/e* (relative intensity) 334 (1, M^+), 303 (2, $M^+ - OCH_3$), 275 (2), 163 (7), 135 (base, $ArCO^+$), 107 (6), 92 (8), 77 (14, $M^+ - CO_2CH_3$); CIMS (isobutane) *m/e* 335 (base, $M^+ + H$); EIHRMS *m/e* 334.1420 ($C_{18}H_{22}O_6$ requires 334.1416); GLC analysis (oven temperature 240 °C) indicated the presence of **16a** (t_R = 7.9 min) and **16b** (t_R = 7.6 min) in a ratio of 2.4;1. Base equilibration (catalytic NaOMe, MeOH, reflux, 3 days) gave a 1:4.5 **16a**:**16b** GLC ratio.

***trans*- and *cis*-3-(Methoxycarbonyl)-4-(phenylmethyl)cyclohexanone (18a and 18b).** A solution of the phenyl selenoester **17** (316 mg, 1.0 mmol), methyl acrylate (0.36 mL, 344 mg, 4.0 mmol, 4 equiv), and AIBN (20 mg) in 50 mL of benzene was degassed and subsequently warmed to reflux. A solution of tri-*n*-butyltin hydride (0.32 mL, 350 mg, 1.2 mmol) and AIBN (10 mg) in 10 mL of benzene was added dropwise (syringe pump) over a period of 3 h. After the reaction solution was warmed for an additional 1.0 h and cooled to room temperature, the solvent was removed. The residual oil was purified by flash chromatography (20% EtOAc–hexane eluant) to give 96 mg (246 mg theoretical, 39%) of **18a** (trans) and 78 mg (32%) of **18b** (cis). For **18a**: white solid, mp 73.5–75°C (ether–hexane); ^1H NMR ($CDCl_3$, 300 MHz, ppm) 1.32 (1 H, m, 1 × C5-H), 1.82 (1 H, m, 1 × C5-H), 2.17–2.64 (7 H, m), 2.77 (1 H, rough d, J = 9.5 Hz), 3.62 (3 H, s, CO_2CH_3), 7.06–7.29 (5 H, m, 5 × ArH); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) 29.2 (e), 39.4 (o), 39.6 (e), 39.8 (e), 42.5 (e), 48.6 (o), 51.9 (o), 126.3 (o), 128.3 (o), 129.0 (o), 139.0 (e), 174.0 (e), 208.6 (e); IR (neat) ν_{max} 2952, 1736 (two C=O), 1494, 1454, 1436, 1276, 1164, 746, 702 cm^{-1}; EIMS *m/e* (relative intensity) 246 (25, M^+), 215 (5), 187 (25, $M^+ - CO_2CH_3$), 117 (24), 91 (base, $C_7H_7^+$), 87 (52); CIMS (isobutane) *m/e* 247 (base, $M^+ + H$); EIHRMS *m/e* 246.1255 ($C_{15}H_{18}O_3$ requires 246.1255).

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.45; H, 7.45.

For **18b**: colorless oil; ^1H NMR ($CDCl_3$, 300 MHz, ppm) 1.86 (2 H, m, C5-H_2), 2.18–2.62 (6 H, m), 2.76 (1 H, dd, J = 13.6 and 6.6 Hz, C2-axial H), 3.05 (1 H, m, C3-H; irradiation at 2.76 ppm causes collapse to dd, J = 9.4 and 4.9 Hz), 3.73 (3 H, s, CO_2CH_3), 7.18–7.43 (5 H, m, 5 × ArH); ^{13}C NMR ($CDCl_3$, 75 MHz, ppm) 27.3 (e), 37.9 (e), 38,8 (e), 39.4 (o), 41.8 (e), 45.4 (o), 51.7 (o), 126.3 (o), 128.4 (o), 128.9 (o), 139.7 (e), 173.4 (e), 208.8 (e); IR (neat) ν_{max} 2952, 1732 (C=O), 1454, 1436, 1194, 740, 702 cm^{-1}; EIMS *m/e* (relative intensity) 246 (33, M^+), 215 (8), 187 (36, $M^+ - CO_2CH_3$), 117 (25), 91 (base, $C_7H_7^+$), 87 (91), 55 (38); CIMS (isobutane) *m/e* 247 (base, $M^+ + H$); EIHRMS *m/e* 246.1255 ($C_{15}H_{18}O_3$ requires 246.1255).

GLC analysis (oven temperature 170 °C) of the crude reaction mixture indicated the presence of **18a** and **18b** (t_R = 12.2 and 13.4 min, respectively) in a ratio of 1.14:1. Base-catalyzed equilibration (NaOMe, MeOH, reflux, 24-30 h) provided a 2.6:1 **18a**:**18b** ratio by GLC analysis.

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Supplementary Material Available: Full experimental details of the preparation and characterization of phenyl selenoesters **1-4**, **9**, **14**, and **17** and details of the experimental assignment of the stereochemistry of **8a-d** (18 pages). Ordering information is given on any current masthead page.

Intramolecular Acyl Radical-Alkene Addition Reactions: Macrocyclization Reactions

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Abstract: The generation of acyl radicals from phenyl selenoesters and the scope of their participation in macrocyclization free-radical alkene addition reactions are detailed. The studies illustrate that large ring ω-acryloyl radical cyclizations proceed at rates competitive with those of 5-*exo*-*trig* cyclization of 5-hexenoyl radicals and that exceed those of 6-*exo*- or 7-*endo*-*trig* cyclization of 6-heptenoyl radicals, thus providing an effective macrocyclization technique that proceeds through carbon-carbon bond formation and with introduction of useful functionality at the ring-closure site.

In recent years, the development and application of numerous techniques suitable for conducting effective macrocyclization reactions have been introduced. Most prominent among the approaches are macrolactonization[1] and macrolactamization[2] techniques, and few useful macrocyclization procedures that rely on carbon-carbon bond formation have been introduced.[3] In recent studies, we have shown that acyl radicals generated from phenyl selenoesters participate in effective intramolecular,[4] intermolecular,[5] and tandem[6] alkene addition reactions at rates greater than that of the potentially competitive tri-*n*-butyltin hydride hydrogen abstraction (reduction)[7] and decarbonylation[8] reactions. Herein, we report that acyl radicals[9] generated in this manner effectively participate in macrocyclization alkene addition reactions with the introduction of useful functionality at the radical initiator site.

Macrocyclization Reactions. Recent studies of Porter and co-workers have defined the structural requirements for successful application of alkyl radical macrocyclization reactions.[10] Acyl radicals exhibit nucleophilic character and reactivity comparable to that of alkyl radicals,[4,5] thus substrates containing an electron-deficient and terminally unsubstituted alkene acceptor group were chosen to test the viability of acyl radical participation in macrocyclization alkene addition reactions. Phenyl selenoesters **1a-e** were prepared from the corresponding ω-hydroxy acids by phenyl selenoesters formation (diethyl phosphorochloridate, Et_3N, THF; NaSePh, THF) and acylation (acryloyl chloride, pyridine, ether, 0 °C).[11] Free-radical cyclization of **1a-e** under high-dilution conditions (5-6 mM in benzene, cat. AIBN, 80 °C, slow addition of 1.2 equiv of tri-*n*-butyltin hydride over 1 h) provided good yields of macrolides **2a-e** (eq 1, Table I) with no evidence of formation of products derived from direct reduction or decarbonylation of the intermediate acyl radicals.[12,13] Thus, macrocyclization reactions involving the addition of acyl radicals to activated alkenes serve as an efficient method for the preparation of large-ring compounds of various sizes with the introduction of additional, useful functionality at the initial radical-bearing center.

Competitive Cyclizations: Macrocyclization versus Seven- to Five-Membered-Ring Cyclizations. With the viability of the acyl radical cyclization for the preparation of saturated macrolides demonstrated, the free-radical cyclization reactions of substrates possessing additional internal sites of unsaturation were examined

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