continued exploration of the [4 + 2] cycloaddition reactions of β,γ-unsaturated α-keto esters and their applications are in progress and will be reported in due course.

Acknowledgment. We gratefully acknowledge the financial support of the National Institutes of Health (CA 41986, 42056), the Alfred P. Sloan Foundation, and Molecular Design, Ltd. (software). We thank Dan Severance for his assistance with computational studies.

Supplementary Material Available: Representative experimental procedures, full spectral and physical characterizations of **1**, **2**, **5–8**, **10–14**, **16–18**, **20–23**, **25–28**, and a summary of the semiempirical computational (MOPAC, AM1 Hamiltonian) comparison of **1** and *trans*-3-methoxypropenal including HOMO and LUMO three-dimensional molecular orbital plots (21 pages). Ordering information is given on any current masthead page.

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(19) National Institutes of Health research career development award recipient, 1983–1988 (CA 01134). Alfred P. Sloan research fellow, 1985–1989.

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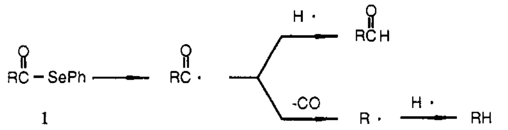
Acyl Radicals: Functionalized Free Radicals for Intramolecular Cyclization Reactions

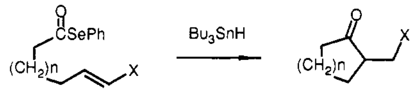
Summary: A study describing the use of phenyl selenoesters as direct precursors to acyl radicals suitable for the initiation of intramolecular free-radical cyclization reactions is detailed.

Sir: The rapid emergence of intramolecular free-radical cyclization reactions as a means of constructing carbocyclic systems can be attributed largely to the compatibility of most functional groups to the reaction conditions relative to the corresponding ionic reactions.[1,2] The required reaction conditions permit useful functionality to be employed at the reaction centers (initiator, terminator groups) without the need for protection or masking of proximal or distal functionality. Consequently, a wide variety of functionalized precursors suitable for initiation of intramolecular free-radical cyclization reactions have been introduced and include α-acylamino sulfides and selenides,[3] β-bromo acetals,[4] vinyl bromides/iodides,[5] and α-bromo or α-seleno ketones and esters.[6] Surprisingly, only selected and isolated reports of the intramolecular free-radical cyclization reactions of acyl derivatives have been described[7] despite their synthetic potential as fundamental functionalized free radicals. Herein we report that phenyl selenoesters serve as excellent precursors to acyl radicals suitable for use in intramolecular free-radical cyclization reactions.

Phenyl selenoesters **1**, readily available from the corresponding carboxylic acids,[8] have been reported to undergo reduction to the corresponding aldehydes and alkanes (decarbonylation and reduction) in the presence of trialkyltin hydrides and a free-radical initiator through generation of acyl radicals, eq 1.[9] This observation and the report that the free-radical generated from phenyl selenocarbonates effectively participate in intramolecular free-radical cyclization reactions[7c,d] suggested that in the presence of a proximal, unsaturated functionality (C=C, C≡C) the acyl radicals generated under such conditions possess the capability to cyclize directly to ketones **2**, eq 2, competitive with intermolecular reduction and intramolecular decarbonylation.[10]



(1)



(2)

The results summarized in Table I illustrate that the intramolecular free-radical cyclization reactions of acyl radicals generated from phenyl selenoesters proceed efficiently and in most cases with little or no competing reduction or decarbonylation.[11] This contrasts the comparable attempts to productively generate and trap acyl radicals in intramolecular free-radical cyclization reactions employing the corresponding acid chlorides[7a] and phenyl thioesters as precursors; Table I, entries 2 and 3.

The productive participation of acyl radicals generated from phenyl selenoesters in intramolecular free-radical cyclization reactions has proven independent of the free-radical acceptor group and both activated ($C{=}CCO_2R$) and unactivated (C=C) π-systems serve as suitable intramolecular acceptors. In the absence of directing functionality (e.g., $C{=}CCO_2R$) the intramolecular acyl radical–alkene cyclization reactions follow the anticipated mode of cyclization:[2] 5-*Exo-Trig* > 6-*Exo-Trig*, 5-*Exo-Trig*

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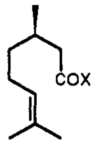
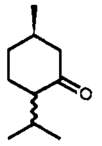
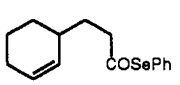
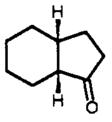
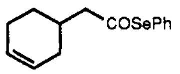
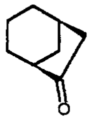
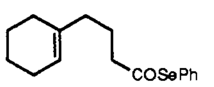
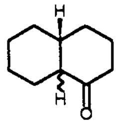
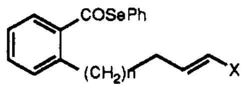
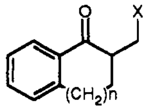
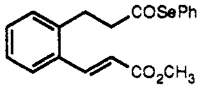
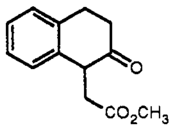
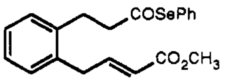
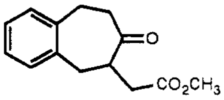
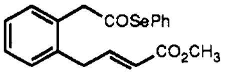
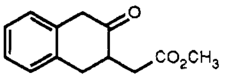
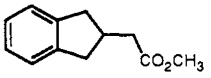
(9) Acid chlorides: (a) Kuivila, H. G.; Walsh, E. J., Jr. *J. Am. Chem. Soc.* **1966**, *88*, 571, 576. (b) Kuivila, H. G. *Synthesis* **1970**, 499. (c) Kupchik, E. J.; Kiesel, R. J. *J. Org. Chem.* **1966**, *31*, 456. (d) Kaplan, L. *J. Am. Chem. Soc.* **1966**, *88*, 1833, 4970. Selenoesters: (e) Pfenninger, J.; Heuberger, C.; Graf, W. *Helv. Chim. Acta* **1980**, *63*, 2328.

(10) In a typical procedure, a solution of the phenyl selenoester **1** (0.007–0.010 M) and α,α'-azobis(isobutyronitrile) (AIBN, ca. 0.05 equiv) in refluxing benzene was treated dropwise (syringe pump, 2 h) with a solution of tri-*n*-butyltin hydride (Bu_3SnH, 1.2 equiv) in benzene, and the solution was warmed at reflux for an additional 0.5–1.0 h.

(11) At present only one instance (Table I, entry 15) of competitive decarbonylation has been observed and presumably is the direct result of generation (and cyclization) of a stabilized benzylic radical.

Table I Generation and Intramolecular Free-Radical Cyclization Reactions of Acyl Radicals[a]

entry	selenoester[b]	product[c]	% yield[d]
1	 **1a** X=SePh	 **2a**	84[e]
2	**1b** X=SPh		--[f]
3	**1c** X=Cl		59 (43)[g]
4	 **1d**	 **2d**	86
5	 **1e**	 **2e**	69
6	 **1f**	 **2f**	82[h]
7	 **1g** X=H, n=0	 **2g** X=H, n=0	81
8	**1h** n=1	**2h** n=1	76
9	**1i** n=2	**2i** n=2	74
10	**1j** X=CO_2CH_3, n=0	**2j** X=CO_2CH_3, n=0	88
11	**1k** n=1	**2k** n=1	84
12	**1l** n=2	**2l** n=2	92
13	 **1m**	 **2m**	83
14	 **1n**	 **2n**	71
15	 **1o**	 **2o**  **2p**	37 42

[a] 1.2 equiv of Bu_3SnH and 0.05 equiv of AIBN, benzene, reflux, 2.5–3 h. [b] Full details for phenyl selenoester formation and characterization are provided in supplementary material. [c] All products exhibited the expected or previously reported ^1H NMR, IR, and MS characteristic of the assigned structure. [d] All yields are based on pure material isolated by chromatography (SiO_2) or sublimation (entry 5). [e] 56:44 trans:cis ratio determined by gas chromatography. [f] No reaction. [g] Taken from ref 7a. [h] 62:38 trans:cis ratio by gas chromatography.

> 6-*Endo-Trig*, 6-*Exo-Trig* > 7-*Endo-Trig*, 7-*Exo-Trig* > 8-*Endo-Trig*. The exception represents the predictable instance where the extent of alkyl substitution decelerates the preferred mode of cyclization; Table I, entry 6.

The effective generation of acyl radicals from phenyl selenoesters and their productive participation in intramolecular free-radical cyclization reactions provides direct access to a fundamental free radical comparable in synthetic utility to its ionic counterparts—the acylium ion,[12] the acyl anion,[13,14] and its synthetic equivalents.[14] The continued exploration of the scope of the participation of acyl radicals in free-radical reactions and their application are in progress and will be described in due course.

Acknowledgment. We gratefully acknowledge the financial support of the National Institutes of Health (CA 42056) and the Alfred P. Sloan Foundation.

Supplementary Material Available: Full details of the preparation and characterization of phenyl selenoesters **1a**,**d**–**o** and comparative or full spectroscopic and physical characterization of the free-radical cyclization products **2d**–**p** (9 pages). Ordering information is given on any current masthead page.

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[12] Groves, J. K. *Chem. Soc. Rev.* **1972**, *1*, 73.

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[15] National Institutes of Health Research Career Development Award recipient, 1983–88 (CA 01134). Recipient of an Alfred P. Sloan Foundation research fellowship, 1985–89.

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Vibrational Circular Dichroism and Absolute Configuration of 1-Substituted Indans[1]

Summary: Vibrational circular dichroism (VCD) spectra of (*R*)- and (*S*)-1-aminoindan, (*S*)-1-methylindan, and (*R*)-1-methylindan-*1-d* were measured in the 800–1600 cm^{-1} region. The VCD feature associated with the C*–H bending mode at about 1350 cm^{-1} is found to correlate with their absolute configurations. This correlation is in agreement with one found for (*S*)-methyloxirane and (*R*)-methylthiirane and reflects the potential importance of VCD measurements in stereochemical analysis of chiral rings systems.

Sir: Vibrational circular dichroism[2,3] (VCD) is a new spectroscopic technique developed in the last decade. As part of this activity, we have found that the C*–H bending vibration gives, for a series of related compounds, a VCD sign correlating with their absolute configurations.[4-7] To expand the general validity of such correlations, we have now measured[8] the VCD spectra for the first time in the 800–1600 cm^{-1} region of chiral 1-substituted indans.

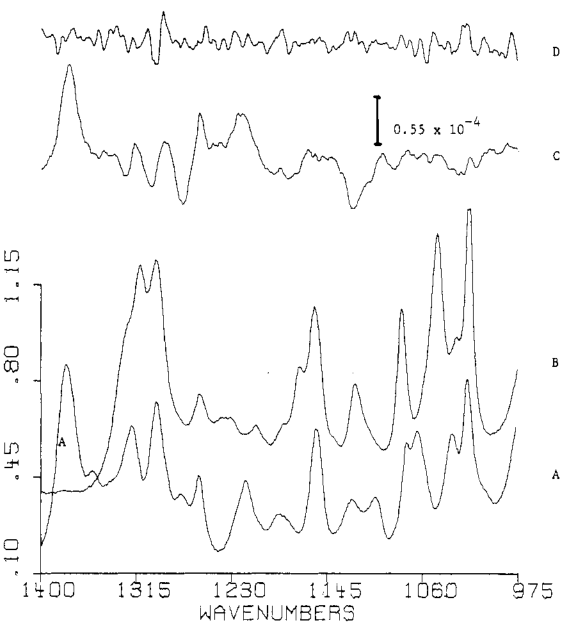
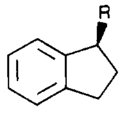
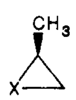


Figure 1. Fourier transform infrared absorption spectra of (*R*)-1-aminoindan [(*R*)-**1a**] (trace A) and (±)-1-aminoindan-*1-d* [(±)-**1a**-*1-d*] (trace B) and vibrational circular dichroism (VCD) spectrum of (*R*)-**1a** (trace C) for the neat liquids with a path lengths of ~60 μm. The absorption spectrum of (±)-**1a**-*1-d* (trace B) is moved upward in the figure for clarity. Trace D is the difference between two individual VCD observations for (*R*)-**1a** and provides an estimate of spectral reproducibility. The scale shown on the VCD spectrum is for $\Delta A = A_l - A_r$, the differential dichroic absorption for left versus right circularly polarized light.

(*R*)- and (*S*)-1-aminoindan[10,11] [(*R*)- and (*S*)-**1a**] were prepared by resolution of (±)-**1a** with *N*-acetyl-D- and -L-leucine,[13] while (±)-1-aminoindan-*1-d*[14] [(±)-**1a**-*1-d*] was obtained by reduction of 1-indanoxime with lithium aluminum deuteride. (±)- and (*S*)-1-Methylindane[15,16] (±)- and (*S*)-**1b**] were synthesized by Friedal–Crafts cyclization of (±)- and (*S*)-3-phenylbutanoic acid to (±)- and (*S*)-3-methyl-1-indanone and subsequent Clemmensen reduction of these latter two ketones.[15] (±)- and (*R*)-1-methyl-



(*S*)-**1a**, R = NH$_2$
(*S*)-**1b**, R = CH$_3$



(*S*)-**2a**, X = O
(*S*)-**2b**, X = S

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[1] Taken in part from the Ph.D. Dissertation of L.P.F., Vanderbilt University, December 1986.

[2] Holzwarth, G.; Hsu, E. C.; Mosher, H. S.; Faulkner, T. R.; Moscowitz, A. *J. Am. Chem. Soc.* **1974**, *96*, 251–252.

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[4] Polavarapu, P. L.; Michalska, D. F.; Neergaard, J. R.; Smith, H. E. *J. Am. Chem. Soc.* **1984**, *106*, 3378–3380.

[5] Polavarapu, P. L.; Fontana, L. P.; Smith, H. E. *J. Am. Chem. Soc.* **1986**, *108*, 94–99.

[6] Polavarapu, P. L.; Hess, B. A., Jr.; Schaad, L. J. *J. Chem. Phys.* **1985**, *82*, 1705–1710.

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[8] Infrared absorption and VCD measurements were made with the neat liquids on a Nicolet 6000C FTIR spectrometer as described in ref 9. The raw VCD spectra of the racemic mixtures were subtracted from the corresponding enantiomers to eliminate base-line artifacts. Noise in the VCD spectra was estimated from the difference in the two halves of the VCD scans.

[9] Polavarapu, P. L. In *Fourier Transform Infrared Spectroscopy*; Ferraro, J. R., Basile, L. J., Eds.; Academic Press: New York, 1985; Vol. 4, pp 61–96.

[10] Brewster, J. H.; Buta, J. G. *J. Am. Chem. Soc.* **1966**, *88*, 2233–2240.

[11] (*R*)- and (*S*)-1-aminoindan had $\alpha^{25}{}_D$ −25.0° (neat, 1 dm) and +13.2° (neat, 0.5 dm), respectively. Comparison of these values with the maximum reported, $\alpha^{22}{}_D$ +31.2° (neat, 1 dm), for (*S*)-**1a** in ref 12 gives for our samples of (*R*)- and (*S*)-**1a** 80% and 85% ee, respectively.

[12] Ghislandi, V.; La Manna, A.; Vercesi, D. *Farmaco, Ed. Sci.* **1976**, *31*, 561–571.

[13] Smith, H. E.; Willis, T. C. *Tetrahedron* **1970**, *26*, 107–118.

[14] Greater than 95% deuterium incorporation as inferred by ^{1}H NMR measurement.