Generation of Acyl Radicals from Thiolesters by Intramolecular Homolytic Substitution at Sulfur

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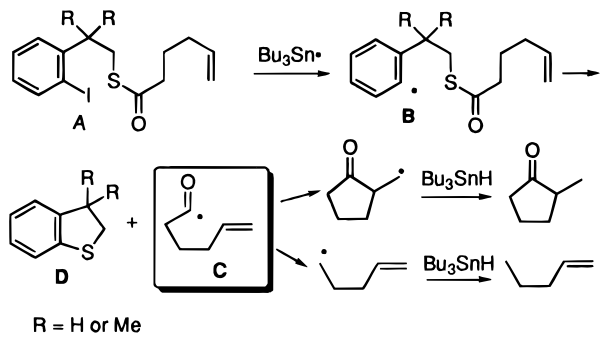
Introduction

Acyl radicals have considerable potential in organic synthesis in terms of both intra- and intermolecular carbon−carbon bond forming reactions.[1] In nonreductive or atom transfer processes, the acyl radical precursors may be selected from either the acyl tellurides,[2] the acylcobalt(III) derivatives,[3] or the *S*-acyl xanthates,[4] according to subsequent requirements. In stannane-mediated chain sequences the acyl aryl selenides are the precursors of choice owing to their ease of preparation, relative stability, and ability to participate smoothly in chain sequences.[5,6] The replacement of acyl selenides by thiolesters in these tributyltin hydride- and allyltributylstannane-mediated chain reactions would be attractive from a number of viewpoints, not least the enhanced stability under oxidizing conditions and ease of preparation. Unfortunately, to date it has not been possible to coax simple *S*-phenyl thiolesters into chain reactions propagated by trialkyltin radicals.[5d,k] The homolytic dissociation of *S*-2-naphthyl and other thiolesters as a means of entry into acyl radicals appears to be limited *inter alia* by low quantum yields.[7] Here, we report a solution to this problem based on the philosophy that one inefficent propagation step can often be replaced advantageously by two efficient ones.[8] Thus, we conceived a strategy wherein the sluggish reaction of stannyl radicals with thiolesters is substituted by two very efficient free radical reactions, namely, iodine abstraction by tributyltin or tris(trimethylsilyl)silyl radicals from an aryl iodide and intramolecular homolytic attack at sulfur[9] by aryl radicals, with release of the acyl radical.

Scheme 1



Results and Discussion

Homolytic substitution (S_H2) reactions, both intermolecular and intramolecular, on divalent as well as tetravalent sulfur centers[9] have been extensively studied by several groups.[10] The intramolecular S_H2 processes were found to proceed in the exo fashion,[9b,10f] with formation of radicals resulting from the cleavage of the exocyclic bond. The ring closure can be so efficient that even such reactive species as methyl and phenyl radicals can be formed. With this in mind, we elected to synthesize and investigate the tributyltin hydide-mediated reaction of substrates of the general type **A**. It was anticipated that a highly reactive, electrophilic aryl radical (**B**), formed by iodine atom abstraction from **A** by the stannyl radical, would rearrange with expulsion of the acyl radical (**C**) and concomitant formation of the five-membered heterocycle (**D**) (Scheme 1). *gem*-Dimethyl groups might be incorporated to speed up the cyclization (Scheme 1, R = Me) in the event that quenching of the intial, unsubstituted (Scheme 1, R = H) aryl radical by the stannane were a competing process.

Starting from commercially available 2-(2-bromophenyl)ethanol (**1**), thiol **4** was readily prepared in 70% overall yield through halogen/metal exchange and iodonation of its TMS ether, followed after deprotection by Mitsunobu thiolesterification[11] and, finally, DIBALH reduction (Scheme 2).

Preparation of a second, *gem*-dimethyl-substituted, thiol (**10**) was initiated by exhaustive methylation of **5**[12]

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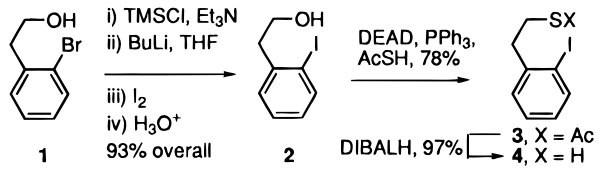
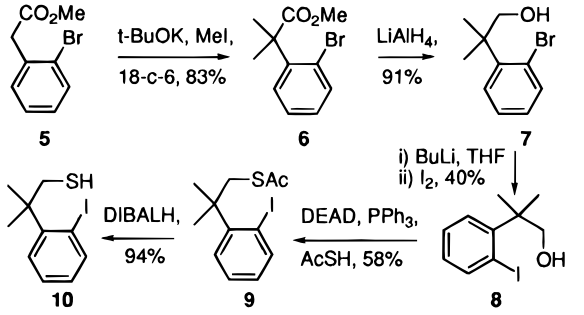
Scheme 2



Scheme 3



with MeI and potassium *tert*-butoxide in the presence of 18-crown-6 to give **6** in 83% yield. Lithium aluminum hydride reduction then afforded the bromo alcohol **7**, and direct bromine/lithium exchange with excess *n*-butyllithium[13] followed by quenching with I_2 gave the desired iodo alcohol **8**, albeit in only fair yield. Conversion of **8** to **10** was achieved uneventfully through Mitsunobu thiolesterification and DIBALH reduction (Scheme 3).

With the two thiols in hand, we prepared a number of thiolesters (**11**−**15**) either by reaction of acid chlorides with the thiols in the presence of DMAP or by direct coupling of the thiols and the carboxylic acids in the presence of DCC and DMAP. In all cases, the thiolesters were obtained in good to excellent yield (see the Experimental Section).

Reactions of thiolesters **11**−**15** (Chart 1) with the three most commonly used reagents, i.e. tri-*n*-butylstannane,[14] tris(trimethylsilyl)silane,[15] and allyltributylstannane[16] were conducted with AIBN initiation, and the results are listed in Table 1. The reaction of **11** with 1.3 equiv of *n*-Bu_3SnH in refluxing benzene with AIBN initiation for 1 h led to complete consumption of the substrate and clean formation of the cyclization and reduction products **16** and **17** in a ratio of 96:4 (Table 1, entry 1) as determined by the ^{1}H-NMR of the crude reaction mixture. As anticipated dihydrobenzothiophene **24** was also formed in this reaction. The efficient formation of **16** and **24** clearly establishes the validity of the concept set out in Scheme 1. It is noteworthy that **17**, identified with the aid of an authentic sample, was formed in only very low yield, suggesting the cyclization of the initial aryl radical to be fast relative to hydrogen atom abstraction from the stannane. As expected, use of the poorer hydrogen atom donor TMS_3SiH as the reducing agent completely eliminated the formation of **17** (Table 1, entry 2). Hydrogen transfer to the aryl radical could also be completely eliminated by use of thiol **10** with the cyclization-enhancing *gem*-dimethyl group (Table 1, entries 3 and 4) with no indication of the formation of the corresponding reduction products in the crude reaction mixtures. It should be noted that in the cyclization of **13** (Table 1, entry 4) a minor amount of the formal 6-endo product (**20**) was identified along with the 5-exo product (**19**), although it is not yet clear whether this is the result of direct 6-endo ring closure or the product of a Dowd type[17] ring expansion. Entry 5 of Table 1 illustrates the use of

Chart 1

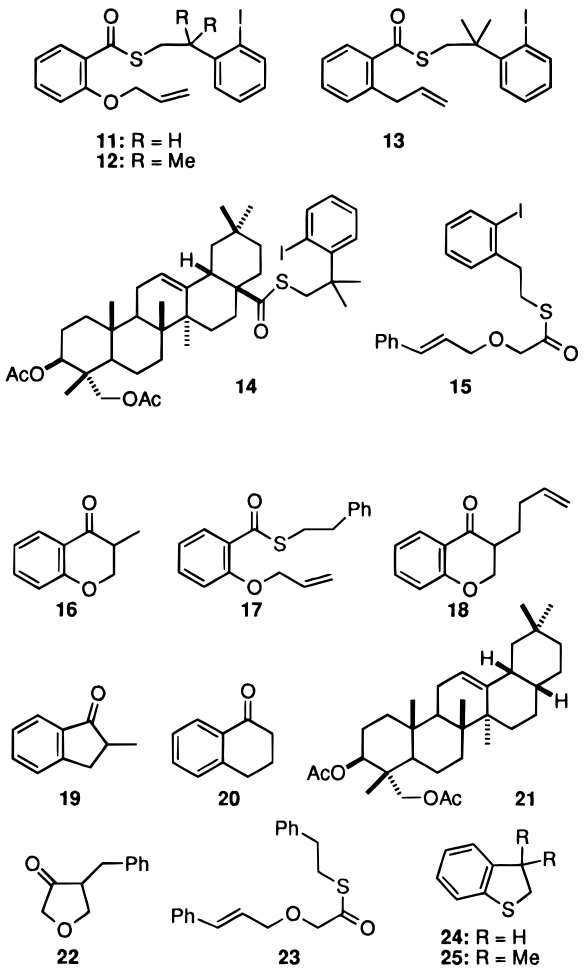


Table 1. Generation of Acyl Radicals from Thiolesters

entry	substrate (concn, M)	reagent (equiv)[a]	products (% yield)
1	**11** (2.4×10^{-2})	A (1.3)	**16** (96),[b] **17** (4),[b] **24** (94)[b]
2	**11** (2.4×10^{-2})	B (1.3)	**16** (100),[b] **17** (0),[b] **24** (100)[b]
3	**12** (2.5×10^{-2})	A (1.3)	**16** (100),[b] **17** (0),[b] **25** (100)[b]
4	**13** (2.5×10^{-2})	A (1.3)	**19** + **20** (82%, 94:6),[c] **25** (100)[b]
5	**12** (0.2)	C (4)	**16** (10), **18** (56), **25** (91)[b]
6	**14** (2.5×10^{-2})	A (1.3)	**21** (92), **25** (71)[b]
7	**15** (2.5×10^{-2})	A (1.3)	**22** (78) + **23** (8),[b] **24** (86)[b]

[a] A, Bu_3SnH; B, TMS_3SiH; C, allyltributylstannane. [b] Estimated by ^{1}H-NMR spectroscopy. [c] Inseparable mixture.

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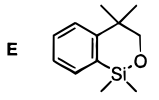
(13) TMS ether protection of the hydroxyl group in **7** followed by bromine/lithium exchange, iodination, and aqueous workup gave, not **8**, but rather a very nonpolar product assigned as **E** resulting from cyclization of the aryllithium onto the TMS group with expulsion of MeLi. **E**: ^{1}H-NMR δ 0.36 (s, 6H), 1.29 (s, 6H), 3.83 (s, 2H), 7.22−7.38 (m, 4H); ^{13}C-NMR δ −0.3, 27.0, 38.3, 73.4, 124.7, 125.5, 129.6, 132.6, 133.0, 154.8; MS *m*/*z* (relative intensity) 206 ($M^{+\bullet}$, 16), 191 ($M^{+\bullet}$−Me, 100). This unusual reaction, contrasted with that in Scheme 2, illustrates the pronounced effect of the *gem*-dimethyl group on ring closure reactions. For examples of related displacements at siloxanes, see: (a) Frye, C. L.; Salinger, R. M.; Fearon, F. W. G.; Klosowski, J. M.; DeYoung, T. *J. Org. Chem.* **1970**, *35*, 1308. (b) Sieburth, S. McN.; Fensterbank, L. *J. Org. Chem.* **1993**, *58*, 6314.



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allyltributylstannane as a chain transfer product, enabling the isolation of **18** in 56% yield. Interestingly, chromanone **16** was also isolated from this reaction in 10% yield, suggesting that hydrogen atom abstraction from the reagent competes with allyl transfer. This new entry into acyl radicals may also be used for the generation of tertiary alkyl radicals following decarbonylation. This is illustrated by entry 6 of Table 1 and the isolation of the known noroleanene derivative **21**[18] in excellent yield. Finally, it is interesting to note (Table 1, entry 7) that the acyl radical derived from **15** underwent cyclization more rapidly than decarbonylation.

In summary acyl radicals may be generated very cleanly from thiolesters by a means of intramolecular S_H2 at sulfur as outlined in Scheme 1. When the thiolester is derived from the *gem*-dimethyl-substituted thiol **10**, competing reduction of the aryl radical is not observed. However, the more straightforward preparation of the simple thiol **4** makes this the reagent of choice, especially as reduction of the aryl radical may be completely eliminated by use of TMS_3SiH as chain transfer agent. Finally, we note that although we have here generated the requisite aryl radical from aryl iodides with stannanes and silanes, almost any other entry into the appropriate aryl radical **B** (Scheme 1) should be applicable, rendering this chemistry potentially extremely versatile.

Experimental Section

General. See ref 8b for the general experimental protocol.

2-(2-Iodophenyl)ethanol (2). To a stirred solution of 2-(2-bromophenyl)ethanol (3.00 g, 14.9 mmol) and NEt_3 (3.07 mL, 22 mmol) in THF (150 mL) cooled to 0 °C was added by syringe TMSCl (2.43 mL, 19.3 mmol). The reaction mixture was stirred at room temperature for 2 h before water (200 mL) was added, the organic layer was extracted with EtOAc (3 × 100 mL), and the combined extracts were washed with saturated $NaHCO_3$ and brine and dried (Na_2SO_4). Removal of solvents under reduced pressure gave the crude silyl ether (4.08 g, 100%) as a colorless oil: ^{1}H-NMR δ 0.07 (s, 9 H), 2.99 (t, J = 7.2 Hz, 2 H), 3.80 (t, J = 7.2 Hz, 2 H), 7.07 (m, 1 H), 7.22−7.26 (m, 2 H), 7.53 (d, J = 8.3 Hz, 1 H). A solution of this silyl ether (4.08 g, 14.9 mmol) in THF (200 mL) was cooled to −78 °C under N_2 and treated with BuLi (10 mL, 2 M in pentane, 20 mmol). After the mixture was stirred at −78 °C for 0.5 h, I_2 (5.1 g, 20 mmol) was added in one portion and the reaction mixture brought to room temperature over 0.5 h before being quenched with dilute aqueous HCl (3 M, 50 mL). The resulting mixture was stirred for another 0.5 h and then extracted with EtOAc (3 × 100 mL). The organic extracts were washed with saturated $NaHCO_3$ and brine and dried (Na_2SO_4). Removal of solvents under reduced pressure followed by column chromatography on silica gel (eluent: CH_2Cl_2) gave the known alcohol **2**[19] (3.45 g, 93%) as an oil: ^{1}H-NMR δ 3.02 (t, J = 6.8 Hz, 2 H), 3.86 (t, J = 6.8 Hz, 2 H), 6.92 (dt, J = 2.4, 8.0 Hz, 1 H), 7.26−7.33 (m, 2 H), 7.84 (d, J = 7.7 Hz, 1 H).

***S*-2-(2-Iodophenyl)ethyl Thiolacetate (3).** To a mixture of **2** (2.30 g, 9.3 mmol) and PPh_3 (3.67 g, 14 mmol) in THF (70 mL) was added dropwise DEAD (2.44 g, 14 mmol). After 5 min of stirring, thioacetic acid (1.42 g, 18.6 mmol) was introduced and the reaction mixture was stirred at room temperature for 20 h. The reaction mixture was then concentrated under reduced pressure to ca. 10 mL, hexane (100 mL) was added, and resulting precipitate was removed by filtration. The filtrate was concentrated and the residue column chromatographed on silica gel (eluent: CH_2Cl_2/hexane, 1/3) to give **3** (2.22 g, 78%) as a colorless oil: ^{1}H-NMR δ 2.35 (s, 3 H), 2.96−3.14 (m, 4 H), 6.92 (m, 1 H), 7.26−7.32 (m, 2 H), 7.82 (d, J = 7.7 Hz, 1 H); ^{13}C-NMR δ 29.0, 30.6, 40.4, 100.3, 128.4, 129.9, 139.5, 142.4, 195.5; IR ($CDCl_3$, cm^{-1}) 1684. Anal. Calcd for $C_{10}H_{11}IOS$: C, 39.23; H, 3.62. Found: C, 39.54; H, 3.55.

2-(2-Iodophenyl)ethanethiol (4). A solution of **3** (1.73 g, 5.65 mmol) in Et_2O (50 mL) cooled at −78 °C was treated dropwise with DIBALH (14 mL, 1 M in CH_2Cl_2). The reaction was gradually warmed to 0 °C over 0.5 h and then quenched with dilute aqueous HCl (3 M, 10 mL). The organic layer was separated, washed with water and brine, and dried (Na_2SO_4). Removal of solvent followed by column chromatography on silica gel (eluent: hexane) gave **4** (1.46 g, 97%) as a colorless oil: ^{1}H-NMR δ 1.45 (t, J = 8.0 Hz, 1 H), 2.74−2.81 (m, 2 H), 3.01−3.05 (m, 2 H), 6.93 (dt, J = 1.9, 7.4 Hz, 1 H), 7.22−7.30 (m, 2 H), 7.83 (dd, J = 1.0, 8.0 Hz, 1 H); ^{13}C-NMR δ 24.5, 45.0, 100.3, 128.3, 128.4, 130.0, 139.6, 142.3. Anal. Calcd for C_8H_9IS: C, 36.38; H, 3.43. Found: C, 36.49; H, 3.44.

Methyl 2-(2-Bromophenyl)isobutyrate (6). A solution of **5** (6.9 g, 30 mmol), methyl iodide (12.8 g, 90 mmol), and 18-crown-6 (2.0 g, 7.5 mmol) in THF (250 mL) was treated, with caution, with potassium *tert*-butoxide (10.2 g, 90 mmol). The reaction mixture was stirred at room temperature for 24 h before NaH (1.2 g, 60% dispersion in mineral oil, 30 mmol) was added. After a further 12 h of stirring, the reaction mixture was diluted with water (300 mL) and extracted with EtOAc (3 × 100 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated to dryness under reduced pressure. Column chromatography on silica gel (eluent: EtOAc/hexane, 1/4) gave **6** (6.42 g, 83%) as a colorless oil: ^{1}H-NMR δ 1.64 (s, 6 H), 3.68 (s, 3 H), 7.12 (dt, J = 1.7, 7.6 Hz, 1 H), 7.32 (dt, J = 1.3, 7.6 Hz, 1 H), 7.42 (dd, J = 1.7, 7.9 Hz, 1 H), 7.56 (dd, J = 1.3, 7.9 Hz, 1 H); ^{13}C-NMR δ 26.4, 48.0, 52.5, 123.8, 127.1, 127.5, 128.3, 134.3, 143.7, 177.4. Anal. Calcd for $C_{11}H_{13}BrO_2$: C, 51.38; H, 5.10. Found: C, 51.50; H, 5.15.

2-(2-Bromophenyl)-2-methylpropanol (7). To a solution of **6** (5.04 g, 19.6 mmol) in Et_2O (150 mL) was added $LiAlH_4$ (800 mg, 21 mmol) in one portion at −20 °C. After 1 h of stirring at 0 °C, the reaction was quenched by addition of aqueous HCl (3 M, 20 mL) and the organic layer separated. The aqueous layer was extracted with EtOAc (3 × 50 mL), and the combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated to dryness under reduced pressure. Column chromatography on silica gel (eluent: EtOAc/hexane, 1/3) gave the **7** (4.09 g, 91%) as colorless oil: ^{1}H-NMR δ 1.51 (s, 6 H), 4.04 (s, 2 H), 7.07 (dt, J = 1.7, 7.7 Hz, 1 H), 7.28 (m, 1 H), 7.47 (dd, J = 1.7, 8.0 Hz, 1 H), 7.60 (dd, J = 1.4, 7.8 Hz, 1 H); ^{13}C-NMR δ 25.2, 42.2, 69.6, 122.3, 127.4, 128.1, 130.1, 135.9, 143.6. Anal. Calcd for $C_{10}H_{13}BrO$: C, 52.42; H, 5.72. Found: C, 52.61; H, 5.83.

2-(2-Iodophenyl)-2-methylpropanol (8). A solution of **7** (3.94 g, 17.2 mmol) in THF (200 mL) was cooled to −78 °C under N_2 and treated with BuLi (20 mL, 2 M in hexane, 40 mmol). After 0.5 h of stirring at this temperature, I_2 (11.4 g, 45 mmol) was added, and the reaction mixture was warmed to 0 °C over 2 h before water (200 mL) was added and the whole extracted with EtOAc (3 × 70 mL). The combined organic extracts were washed sequentially with 5% aqueous $Na_2S_2O_3$, water, and brine and dried (Na_2SO_4). Removal of solvents followed by column chromatography on silica gel (eluent: EtOAc/hexane, 1/3) gave 3.03 g of an inseparable mixture of the iodo alcohol **8** and 2-methyl-2-phenylpropanol. Removal of the latter by careful Kugelrohr distillation (80−90 °C, 0.7 mbar) gave pure **8** (1.90 g, 40%) as a colorless oil: ^{1}H-NMR δ 1.53 (s, 6 H), 4.04 (s, 2 H), 6.86 (dt, J = 1.8, 7.5 Hz, 1 H), 7.31 (dt, J = 1.4, 7.6 Hz, 1 H), 7.45 (dd, J = 1.7, 8.0 Hz, 1 H), 8.01 (dd, J = 1.4, 7.8 Hz, 1H); ^{13}C-NMR δ 25.3, 42.1, 69.3, 94.5, 128.0, 128.2, 129.8, 143.7, 146.0. Anal. Calcd for $C_{10}H_{13}IO$: C, 43.50; H, 4.75. Found: C, 43.72; H, 4.80.

***S*-2-(2-Iodophenyl)-2-methylpropyl Thiolacetate (9).** To a solution of **8** (1.28 g, 4.65 mmol) and PPh_3 (2.44 g, 9.3 mmol) in THF (50 mL) was added dropwise DEAD (1.47 mL, 9.3 mmol). After the addition was complete, the reaction mixture was stirred for 5 min before thioacetic acid (1.33 mL, 18.6 mmol) was slowly introduced. After 16 h of stirring, another portion of thioacetic acid (0.67 mL, 9.3 mmol) was added, and stirring was continued for a further 8 h. The reaction mixture was concentrated under reduced pressure to ca. 10 mL, hexane (100 mL) was added, and

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the resulting precipitate was removed by filtration. The filtrate was concentrated and the residue column chromatographed on silica gel (eluent: hexane/CH_2Cl_2, 1/1, then neat CH_2Cl_2) to give the title thiolester (907 mg, 58%) as a colorless oil and unreacted **10** (390 mg, 30%). **9:** ^{1}H-NMR δ 1.57 (s, 6 H), 2.28 (s, 3 H), 3.75 (s, 2 H), 6.87 (dt, J = 1.8, 7.4 Hz, 1 H), 7.30 (dt, J = 1.3, 7.5 Hz, 1H), 7.36 (dd, J = 1.9, 8.0 Hz, 1 H), 8.00 (dd, J = 1.3, 7.8 Hz, 1 H); ^{13}C-NMR δ 27.8, 30.5, 38.7, 40.2, 94.6, 127.9, 128.2, 128.7, 143.7, 146.6, 195.5; IR ($CDCl_3$, cm^{-1}) 1688. Anal. Calcd for $C_{12}H_{15}IOS$: C, 43.13; H, 4.52. Found: C, 43.27; H, 4.61.

2-(2-Iodophenyl)-2-methylpropanethiol (10). To a solution of **9** (710 mg, 2.13 mmol) in Et_2O (20 mL) cooled to −78 °C under N_2 was added dropwise DIBALH (5.3 mL, 1 M in CH_2Cl_2). After the addition was complete, the reaction mixture was slowly warmed to 0 °C over 0.5 h and then quenched with dilute aqueous HCl (3 M, 10 mL). The organic layer was separated, washed with water and brine, and dried (Na_2SO_4). Removal of solvent followed by column chromatography on silica gel (eluent: hexane/CH_2Cl_2, 9/1) gave **10** (587 mg, 94%) as a colorless oil: ^{1}H-NMR δ 0.95 (t, J = 8.8 Hz, 1 H), 1.59 (s, 6 H), 3.27 (d, J = 8.8 Hz, 2 H), 6.87 (dt, J = 1.8, 7.4 Hz, 1 H), 7.32 (dt, J = 1.3, 7.5 Hz, 1 H), 7.40 (dd, J = 1.8, 8.0 Hz, 1 H), 8.01 (dd, J = 1.3, 7.8 Hz, 1 H); ^{13}C-NMR δ 27.7, 34.5, 41.6, 94.4, 128.0, 128.2, 129.6, 143.6, 146.3. Anal. Calcd for $C_{10}H_{13}IS$: C, 41.11; H, 4.48. Found: C, 41.22; H, 4.46.

Preparation of Thiolesters 11−14, 17 and 23. General Procedure via Acyl Chlorides. A solution of the appropriate carboxylic acid (1.0 mmol) in benzene (10 mL) was treated at room temperature with oxalyl chloride (0.87 mL, 10 mmol) and a small drop of DMF. After 0.5 h, the solvent and excess reagent were removed *in vacuo* and the crude acid chloride was taken up with CH_2Cl_2 (15 mL). DMAP (159 mg, 1.3 mmol) was then added followed by the appropriate thiol (**4** or **10**). The resulting mixture was stirred at room temperature until the reaction was complete (0.5 to 16 h). Hexane (15 mL) was then added, and the precipitates were removed by filtration. The filtrate was concentrated to dryness and the product purified by column chromatography on silica gel.

***S*-2-(2-Iodophenyl)ethyl 2-(Allyloxy)thiobenzoate (11).** **11** was prepared from 2-allyloxybenzoic acid (178 mg, 1.0 mmol) and thiol **4** according to the general procedure. Column chromatography on silica gel (eluent: CH_2Cl_2/hexane, 1/2) gave **11** (400 mg, 94%) as a colorless oil: ^{1}H-NMR δ 3.06 −3.29 (m, 4 H), 4.67 (dt, J = 5.1, 1.5 Hz, 2 H), 5.31 (dquart, J = 10.5, 1.4 Hz, 1 H), 5.49 (dquart, J = 17.3, 1.5 Hz, 1 H), 6.04 −6.16 (m, 1 H), 6.89−7.03 (m, 3 H), 7.27 −7.41 (m, 3 H), 7.78 −7.83 (m, 2 H); ^{13}C-NMR δ 29.5, 40.4, 69.9, 100.4, 113.4, 118.0, 120.6, 127.3, 128.3, 128.4, 129.7, 130.1, 132.6, 133.4, 139.5, 142.9, 156.8, 190.7; IR ($CDCl_3$, cm^{-1}) 1672. Anal. Calcd for $C_{18}H_{17}IO_2S$: C, 50.95; H, 4.04. Found: C, 50.97; H, 4.00.

***S*-2-(2-Iodophenyl)-2-methylpropyl 2-(Allyloxy)thiobenzoate (12).** **12** was prepared from 2-(allyloxy)benzoic acid (178 mg, 1.0 mmol) and thiol **10** according to the general procedure. Column chromatography on silica gel (eluent: CH_2Cl_2/hexane, 1/2) gave **12** (430 mg, 95%) as a colorless oil: ^{1}H-NMR δ 1.64 (s, 6 H), 3.91 (s, 2 H), 4.58 (dt, J = 5.0, 1.6 Hz, 2 H), 5.23 (ddt, J = 10.7, 1.5, 1.5 Hz, 1 H), 5.41 (ddt, J = 17.3, 1.5, 1.8 Hz, 1 H), 5.98 (m, 1 H), 6.83 −6.97 (m, 3 H), 7.29 −7.42 (m, 3 H), 7.66 (dd, J = 1.7, 7.7 Hz, 1 H), 8.01 (dd, J = 1.4, 7.8 Hz, 1H): ^{13}C-NMR δ 28.0, 38.9, 40.5, 69.6, 94.8, 113.3, 117.6, 120.5, 127.8, 128.1, 128.9, 129.5, 132.5, 133.0, 143.7, 146.9, 156.3, 191.1. Anal. Calcd for $C_{20}H_{21}IO_2S$: C, 53.10; H, 4.68. Found: C, 53.13; H, 4.71.

Hederagenin Diacetate 2-(2-Iodophenyl)-2-methylpropanethiol Ester (14). **14** was prepared from hederagenin diacetate (128 mg, 0.23 mmol) and thiol **10** (73 mg, 0.25 mmol) according to the general procedure. Column chromatography on silica gel (eluent: EtOAc/hexane, 1/3) gave **14** (138 mg, 72%) as a crystalline solid and the starting acid (30 mg, 23%). **14**: mp 102 −103 °C (CH_2Cl_2); $[\alpha]_D$ = +24° (*c* 1.8, $CHCl_3$); ^{1}H-NMR δ 0.71 (s, 3 H), 0.83 (s, 3 H), 0.88 (s, 3 H), 0.89 (s, 3 H), 0.97 (s, 3 H), 1.09 (s, 3 H), 1.54 (s, 3 H), 1.56 (s, 3 H), 0.80−2.05 (m, 22 H), 2.02 (s, 3 H), 2.06 (s, 3 H), 2.88 (dd, J = 3.7, 13.2 Hz, 1 H), 3.62 (d, J = 13.5 Hz, 1 H), 3.68 (d, J = 13.5 Hz, 1 H), 3.69 (d, J = 11.7 Hz, 1 H), 3.88 (d, J = 11.6 Hz, 1 H), 4.78 (dd, J = 5.2, 11.1 Hz, 1 H), 5.24 (t, J = 3.3 Hz, 1 H), 6.84 (dt, J = 1.8, 7.6 Hz, 1 H), 7.24−7.35 (m, 2 H), 7.98 (dd, J = 1.3, 7.8 Hz, 1 H); ^{13}C-NMR δ 13.1, 15.9, 17.4, 17.9, 20.9, 21.2, 22.9, 23.4, 23.6 (2 × C), 25.6, 27.1, 27.9, 28.0, 30.6, 32.3, 32.9, 33.8, 34.1, 36.7, 37.7, 38.0, 39.4, 40.5, 40.6, 41.3, 41.5, 46.2, 47.6, 47.8, 54.3, 94.8, 122.8, 127.7, 128.0, 128.9, 143.2, 143.7, 147.0, 170.7, 171.0, 206.2. Anal. Calcd for $C_{44}H_{63}IO_5S$: C, 63.60; H, 7.64. Found: C, 63.48; H, 7.65.

***S*-2-(2-Iodophenyl)-2-methylpropyl 2-Allylthiobenzoate (13).** **13** was prepared from 2-allylbenzoic acid[2c] (97.5 mg, 0.6 mmol) and thiol **10** according to the general procedure. Column chromatography on silica gel (eluent: CH_2Cl_2/hexane, 1/4) gave **13** (254 mg, 97%) as a colorless oil: ^{1}H-NMR δ 1.65 (s, 6 H), 3.54 (d, J = 6.5 Hz, 2 H), 3.91 (s, 2 H), 4.97−5.04 (m, 2 H), 5.87−6.00 (m, 1 H), 6.86 (dt, J = 1.7, 7.5 Hz, 1 H), 7.18−7.41 (m, 5 H), 7.62 (d, J = 7.8 Hz, 1 H), 8.01 (dd, J = 1.3, 7.8 Hz, 1 H); ^{13}C-NMR δ 28.0, 37.4, 39.3, 40.53, 94.7, 115.9, 126.0, 127.9, 128.2, 128.3, 128.8, 130.5, 131.4, 136.8, 137.9, 138.0, 143.7, 146.6, 194.2; IR ($CDCl_3$, cm^{-1}) 1665. Anal. Calcd for $C_{20}H_{21}IOS$: C, 55.05; H, 4.85. Found: C, 55.30; H, 4.76.

***S*-2-(2-Iodophenyl)ethyl [(*(E)*-3-Phenylprop-2-enyl)oxy]-thioacetate (15): DCC/DMAP Method.** A mixture of (cinnamyloxy)acetic acid[20] (135 mg, 0.70 mmol), DMAP (17 mg, 0.14 mmol), and DCC (173 mg, 0.84 mmol) in DCM (10 mL) was stirred at room temperature for 5 min before thiol **4** (222 mg, 0.84 mmol) was added. After stirring at room temperature overnight the reaction mixture was concentrated to dryness. Column chromatography of the residue on silica gel (eluent: CH_2Cl_2/hexane, 1/1) gave **15** (289 mg, 94%) as a colorless oil: ^{1}H-NMR δ 2.98−3.18 (m, 4 H), 4.20 (s, 2 H), 4.29 (dd, J = 6.2, 1.3 Hz, 2 H), 6.30 (dt, J = 15.9, 6.2 Hz, 1 H), 6.86 (d, J = 15.9 Hz, 1 H), 6.92 (m, 1 H), 7.24−7.43 (m, 7 H), 7.82 (d, J = 7.7 Hz, 1 H); ^{13}C-NMR δ 27.8, 40.3, 72.6, 74.6, 100.3, 124.5, 126.5, 127.9, 128.3, 128.5, 129.9, 133.7, 136.2, 139.5, 142.4, 199.8; IR ($CDCl_3$, cm^{-1}) 1681. Anal. Calcd for $C_{19}H_{19}IO_2S$: C, 52.06; H, 4.37. Found: C, 51.88; H, 4.29.

***S*-2-Phenylethyl 2-(Allyloxy)thiobenzoate (17): Authentic Sample.** **17** was prepared from *O*-allylsalicylic acid (35.6 mg, 0.20 mmol) and 2-phenylethanethiol (35 mg, 0.25 mmol) according to the general procedure except that Et_3N (35 μL, 0.25 mmol) was used as the base. Column chromatography on silica gel (eluent: CH_2Cl_2/hexane, 1/1) gave **17** (58 mg, 97%) as a colorless oil: ^{1}H-NMR δ 2.95−3.00 (m, 2 H), 3.25−3.30 (m, 2 H), 4.67 (dt, J = 5.1, 1.6 Hz, 2 H), 5.31 (dq, J = 10.6, 1.4 Hz, 1 H), 5.49 (dq, J = 17.3, 1.6 Hz, 1 H), 6.03−6.16 (m, 1 H), 6.95−7.03 (m, 2 H), 7.21−7.49 (m, 6 H), 7.79 (dd J = 7.7, 1.7 Hz, 1 H); ^{13}C-NMR δ 30.9, 35.7, 69.6, 113.3, 117.9, 120.5, 126.3, 127.4, 128.4, 128.6, 129.7, 132.5, 133.3, 140.3, 158.7, 190.8; IR ($CDCl_3$, cm^{-1}) 1666. Anal. Calcd for $C_{18}H_{18}O_2S$: C, 72.45; H, 6.08. Found: C, 72.44; H, 6.18.

***S*-2-Phenylethyl [(*(E)*-3-Phenylprop-2-enyl)oxy]thioacetate (23): Authentic Sample.** **23** was prepared from (cinnamyloxy)acetic acid (38.6 mg, 0.20 mmol) in exactly the same way as for the preparation of **17**. Column chromatography on silica gel (eluent: CH_2Cl_2/hexane, 1/1, then neat CH_2Cl_2) gave **23** (58 mg, 93%) as a colorless oil: ^{1}H-NMR δ 2.87−2.92 (m, 2 H), 3.14−3.20 (m, 2 H), 4.19 (s, 2 H), 4.28 (dd, J = 6.2, 1.1 Hz, 2 H), 6.30 (dt, J = 15.9, 6.2 Hz, 1 H), 6.65 (d, J = 15.9 Hz, 1 H), 7.21−7.42 (m, 10 H); ^{13}C-NMR δ 29.2, 35.9, 72.6, 74.6, 124.5, 126.47, 126.53, 127.9, 128.4, 128.5 (2 × C), 133.7, 136.2, 139.9, 199.8; IR ($CDCl_3$, cm^{-1}) 1681. Anal. Calcd for $C_{19}H_{20}O_2S$: C, 73.04; H, 6.45. Found: C, 73.04; H, 6.56.

Reaction of 11 with Bu_3SnH and TMS_3SiH: General Procedures for the Generation of Acyl Radicals from Thioesters. A solution **11** (20 mg, 0.047 mmol), Bu_3SnH (18 mg, 1.3 equiv), and AIBN (1 mg, 10%) in degassed benzene (2.0 mL) was heated to reflux under Ar for 1 h. After the mixture was cooled to room temperature, the solvent was removed *in vacuo*. Examination of the crude reaction mixture by ^{1}H-NMR spectroscopy revealed complete consumption of **11** with the formation of the cyclized product **16**, the simple reduction product **17**, and dihydrobenzothiophene (**24**) in a ratio of **16**:**17**:**24** = 96:4:94. Replacement of Bu_3SnH with TMS_3SiH (15 mg, 1.3 equiv) under the same conditions gave **16** and **24** both quantitatively as determined from the ^{1}H-NMR spectrum of the crude reaction mixture.

Reaction of 12 with Bu_3SnH. **12** (45 mg, 0.10 mmol) was treated with Bu_3SnH under the standard conditions to give a

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crude reaction mixture consisting solely of a 1:1 mixture of **16** and **25** and organotin residues. Column chromatography on silica gel (eluent: hexane then CH_2Cl_2) gave **25** (12 mg, 73%) and **16** (14 mg, 86%).

Reaction of 12 with Allyltributylstannane: 3-(3-Butenyl)chromanone (18). A solution of **12** (136 mg, 0.30 mmol), allyltributylstannane (387 mg, 1.20 mmol), and AIBN (10 mg, 0.06 mmol) in benzene (1.5 mL) was heated to reflux under Ar. After 6 h another portion of AIBN (5 mg, 0.03 mmol) was added, and heating was continued for a total of 10 h. After the mixture was cooled to room temperature, the solvent was removed under reduced pressure and the residue taken up with CH_2Cl_2 (1 mL) and treated with Et_3N (50 μL). Column chromatography on silica gel (eluent: hexane/CH_2Cl_2, 1/1) gave **18** (34 mg, 56%), a colorless oil, and **16** (6 mg, 10%). **18**: ^{1}H-NMR δ 1.51−1.64 (m, 1 H), 1.96−2.08 (m, 1 H), 2.13−2.29 (m, 2 H), 2.66−2.75 (m, 1 H), 4.27 (dd, J = 11.4, 8.7 Hz, 1 H), 4.53 (dd, J = 11.4, 4.4 Hz, 1 H), 5.00−5.11 (m, 2 H), 5.81 (ddt, J = 17.0, 10.3, 6.6 Hz, 1 H), 6.95 (d, J = 8.2 Hz, 1 H), 7.02 (dt, J = 0.9, 7.5 Hz, 1 H), 7.47 (m, 1 H), 7.89 (dd, J = 1.8, 7.8 Hz, 1 H); ^{13}C-NMR δ 25.3, 30.9, 45.0, 70.2, 115.8, 117.6, 120.5, 121.3, 127.3, 135.5, 137.4, 161.3, 194.4. Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 76.89; H, 6.96.

3-Methylchromanone (16):[5e] ^{1}H-NMR δ 1.22 (d, J = 7.0 Hz, 3 H), 2.87 (m, 1 H), 4.15 (t, J = 11.1 Hz, 1 H), 4.50 (dd, J = 5.1, 11.3 Hz, 1 H), 6.96 (bd, J = 8.5 Hz, 1 H), 7.01 (dt, J = 1.0, 7.5 Hz, 1 H), 7.46 (m, 1 H), 7.90 (dd, J = 1.7, 7.9 Hz, 1 H).

2-Methylindanone (19):[21] ^{1}H-NMR δ 1.32 (d, J = 7.3 Hz, 3 H), 2.69−2.77 (m, 2 H), 3.41 (dd, J = 8.6, 17.8 Hz, 1 H), 7.37 (t, J = 7.4 Hz, 1 H), 7.45 (d, J = 7.7 Hz, 1 H), 7.59 (dt, J = 1.0, 7.4 Hz, 1 H), 7.76 (d, J = 7.6 Hz, 1 H).

3*β*,24-Diacetoxy-28-norolean-12-ene (21): mp 77−78 °C (MeOH); $[\alpha]_D$ = +79° (c = 1.2, $CHCl_3$) [lit.[18] mp 114−115 °C; $[\alpha]_D$ = +80° (c = 1)]. The ^{1}H-NMR spectrum was identical with that described in the literature.[18]

3-Benzyltetrahydrofuran-4-one (22): ^{1}H-NMR δ 2.65 (dd, J = 10.0, 13.8 Hz, 1 H), 2.78 (m, 1 H), 3.16 (dd, J = 3.9, 13.8 Hz, 1 H), 3.85 (d, J = 17.5 Hz, 1 H), 3.86 (d, J = 8.7 Hz, 1 H), 4.07 (d, J = 17.2 Hz, 1 H), 4.31 (t, J = 8.7 Hz, 1 H); ^{13}C-NMR δ 33.5, 48.8, 71.2, 71.8, 126.7, 128.6, 128.7, 138.5, 215.7; MS m/z 176 ($M^{\bullet+}$). This compound proved to be rather unstable, decomposing substantially within a matter of hours on standing at room temperature, preventing obtainment of microanalytical or HRMS data.

2,3-Dihydrobenzothiophene (24):[22] ^{1}H-NMR δ 3.27−3.38 (m, 4 H), 7.00 (t, J = 7.3 Hz, 1 H), 7.11 (t, J = 7.3 Hz, 1 H), 7.20 (t, J = 8.2 Hz, 2 H).

2,3-Dihydro-3,3-dimethylbenzothiophene (25):[23] ^{1}H-NMR δ 1.37 (s, 6 H), 3.17 (s, 2 H), 7.04−7.20 (m, 4 H).

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Supporting Information Available: Copies of ^{1}H- and ^{13}C-NMR spectra of **22** (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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