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Low-valent Titanium Induced Reductive Coupling of Diaryl Diselenides with Acid Chlorides or Acid Anhydrides: Facile Synthesis of Selenoesters†

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Selenoesters have been prepared in good yield by reaction of diaryl diselenides with acid chlorides or acid anhydrides induced by the $TiCl_4$–Sm–THF system under mild reaction conditions.

Organoselenium and organotellurium compounds have attracted considerable interest as reagents and intermediates in organic synthesis.[1] In contrast to their O-analogs, selenoesters frequently exhibit a higher and more selective reactivity towards nucleophiles. These properties make selenoesters valuable acyl transfer agents and permit selective transformations in complex molecules. In particular, the total synthesis of macrolide antibiotics and cytochalasanes, and the synthesis of acyl-coenzyme A and naturally occurring macrocyclic lactones and lactams demand activated selenoesters as acyl transfer agents and simple, mild and general methods for the preparation of selenoesters.[2]

A number of synthetic methods have been devised to prepare organoselenium and organotellurium derivatives. A convenient and general method to introduce a selenium or tellurium group into organic molecules is the reaction of a metal selenoate or telluroate with appropriate electrophiles such as organic halides, epoxides and α,β-enones.

Diaryl diselenides and diaryl ditellurides are important intermediates due to their air and water stability. When they are reduced, the nucleophilic selenoates and telluroates are obtained. Reaction of diselenide or ditelluride usually requires alkali metals (such as Li, Na) or hydride reducing agents (such as $NaBH_4$).[3] Recently, reductive cleavage of Se–Se and Te–Te bonds by SmI_2 has been investigated and there have been numerous reports on its application to synthesis.[4]

Low-valent titanium reagents are excellent at promoting reductive coupling of carbonyl compounds and are attracting increasing interest for organic synthesis. Various other functional groups can also be reduced.[5] Recently, we reported the reduction of sulfoxides to sulfides and reductive coupling of nitriles with nitro compounds using the $TiCl_4$–Sm–THF system.[6] To our knowledge, the reductive cleavage of Se–Se and Te–Te bonds induced by low-valent titanium has not been reported in the literature. Recently, we reported an effective method for synthesis of β-selenium and β-tellurium carbonyl compounds *via* reaction of diaryl diselenides or diaryl ditellurides with α,β-unsaturated carbonyl compounds induced by low-valent titanium.[7] Here we describe a new method for reducing diaryl diselenides using the $TiCl_4$–Sm–THF system and its use in the synthesis of selenoesters.

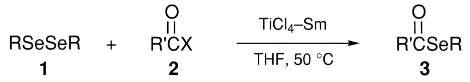
When diaryl diselenides **1** and acid chlorides or acid anhydrides **2** were treated with low-valent titanium, prepared from titanium tetrachloride and samarium powder in anhydrous tetrahydrofuran, the selenoesters **3** were obtained in good yields. The results are summarized in Table 1. The yield using acid anhydrides is higher than that using acid chlorides.

There are many methods for preparing selenoesters.[8] However, most of these methods have disadvantages such as harsh reaction conditions, laborious manipulation or low yields. The present method has the advantage of accessible starting materials, simple and mild reaction conditions, convenient manipulation and good yields. Further studies to develop other new uses of the $TiCl_4$–Sm system are now in progress.

Experimental

Tetrahydrofuran (THF) was distilled from sodium–benzophenone immediately prior to use. All reactions were conducted under a nitrogen atmosphere. Infrared spectra were recorded on a Perkin-Elmer 683 spectrometer. ^1H NMR spectra were determined using a JEOL PMX-60 spectrometer with CCl_4 as solvent and Me_4Si as an internal standard. *J* values are in Hz. Diaryl diselenides were prepared by the literature procedure.[9]

Table 1 Synthesis of selenoesters



$$\underset{\mathbf{1}}{\text{RSeSeR}} + \underset{\mathbf{2}}{\overset{\overset{\text{O}}{\|}}{\text{R'CX}}} \xrightarrow[\text{THF, 50 °C}]{\text{TiCl}_4\text{–Sm}} \underset{\mathbf{3}}{\overset{\overset{\text{O}}{\|}}{\text{R'CSeR}}}$$

Product	R	R′	X	Reaction time/h	Yield (%)[a,b]
3a	C_6H_5	C_6H_5	Cl	10	58
3b	C_6H_5	CH_3	Cl	5	65
3b	C_6H_5	CH_3	CH_3COO	6	81
3c	C_6H_5	CH_3CH_2	Cl	8	56
3c	C_6H_5	CH_3CH_2	CH_3CH_2COO	8	80
3d	C_6H_5	$CH_3CH_2CH_2$	Cl	5	65
3d	C_6H_5	$CH_3CH_2CH_2$	n-C_3H_7COO	5	79
3e	C_6H_5	$CH_3(CH_2)_4$	Cl	6	63
3f	p-$CH_3OC_6H_4$	CH_3	CH_3COO	5	75
3g	p-$CH_3C_6H_4$	CH_3	CH_3COO	5	81
3h	n-C_4H_9	C_6H_5	Cl	12	54

[a] Yield of isolated pure product based on **1**. [b] 0.5 mmol **1** and 1.5 mmol **2** were used.

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General Procedure for the Synthesis of Selenoesters **3**.—$TiCl_4$ (0.11 ml, 1 mmol), was added dropwise using a syringe to a stirred suspension of Sm powder (0.15 g, 1 mmol) in freshly distilled dry THF (7 ml) at room temperature under a N_2 atmosphere. On completion the mixture was refluxed for 2 h. The suspension of the low-valent titanium reagent formed was cooled to room temp. and a solution of diaryl diselenides **1** (0.5 mmol) and acid chlorides or acid anhydrides **2** (1.5 mmol) in THF (2 ml) was added dropwise. The mixture was stirred at 50 °C under a N_2 atmosphere. On completion, the reaction mixture was quenched with 5% HCl (20 ml) and extracted with diethyl ether (3 × 30 ml). The combined extracts were washed with saturated solution of $Na_2S_2O_3$ (15 ml), a saturated solution of K_2CO_3 (15 ml), and a saturated solution of NaCl (15 ml), and dried over anhydrous Na_2SO_4. After evaporating the solvent under reduced pressure, the crude product was purified by preparative TLC on silica gel using ethyl acetate–cyclohexane (1:20) as eluent.

3a: light yellow crystals. Mp: 39–40 °C (lit[10] 37–38 °C); ν_{max}/cm^{-1} 3080, 1700, 1600, 1590, 1480, 1450, 1410, 1200, 1185, 1020, 1000, 870, 760, 735, 680; δ_H 7.20–7.65 (8 H, m, ArH), 7.75–8.05 (2 H, m, ArH).

3b: yellow oil.[10] ν_{max}/cm^{-1} 3080, 2940, 1740, 1590, 1480, 1445, 1350, 1240, 1105, 1070, 1020, 1000, 935, 730, 680; δ_H 2.35 (3 H, s, CH_3CO), 7.06–7.65 (5 H, m, ArH).

3c: yellow oil.[11] ν_{max}/cm^{-1} 3080, 2940, 1740, 1590, 1480, 1440, 1380, 1000, 900, 780, 730, 680; δ_H 1.20 (3 H, t, *J* 7.2, CH_3), 2.77 (2 H, q, *J* 7.2, CH_2CO), 7.10–7.70 (5 H, m, ArH).

3d: yellow oil.[12] ν_{max}/cm^{-1} 3085, 2980, 2950, 2890, 1735, 1590, 1485, 1445, 1405, 1105, 1065, 1020, 980, 955, 875, 790, 730, 680; δ_H 0.95 (3 H, t, *J* 7.0, CH_3), 1.40–2.05 (2 H, m, CH_2), 2.67 (2 H, t, *J* 7.2, OCH_2), 7.03–7.65 (5 H, m, ArH).

3e: yellow oil.[13] ν_{max}/cm^{-1} 2980, 2940, 1740, 1590, 1485, 1440, 1410, 1120, 1020, 1000, 730, 690; δ_H 0.70–1.90 (9 H, m, $CH_2CH_2CH_2CH_3$), 2.50 (2 H, t, *J* 7.0, CH_2CO), 7.10–7.63 (5 H, m, ArH).

3f: yellow oil.[14] ν_{max}/cm^{-1} 2980, 1745, 1600, 1580, 1500, 1465, 1370, 1290, 1175, 1100, 1040, 940, 820; δ_H 2.38 (3 H, s, CH_3CO), 3.78 (3 H, s, OCH_3), 6.60–6.95 (2 H, m, ArH), 7.25–7.53 (2 H, m, ArH).

3g: light-yellow oil.[15] ν_{max}/cm^{-1} 3040, 2940, 1740, 1595, 1495, 1350, 1210, 1180, 1100, 1015, 935, 800; δ_H 2.28 (3 H, s, CH_3), 2.36 (3 H, s, CH_3), 6.90–7.53 (5 H, m, ArH).

3h: yellow oil.[16] ν_{max}/cm^{-1} 2975, 2940, 2880, 1735, 1590, 1450, 1280, 1200, 1175, 1880, 760; δ_H 0.80–1.90 (7 H, m, $CH_2CH_2CH_3$), 3.05 (2 H, t, *J* 7.0, CH_2Se), 7.25–7.60 (3 H, m, ArH), 7.80–8.05 (2 H, m, ArH).

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