A Convenient Synthesis of β-Phenylselenocarbonyl Compounds by In-TMSCl Promoted Cleavage of Diphenyl Diselenide and Subsequent Michael Addition

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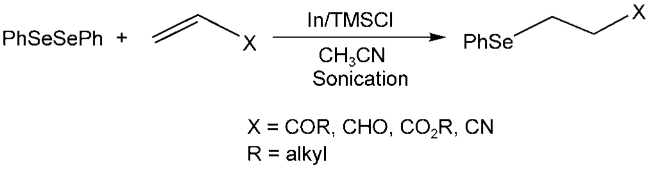
Abstract: A simple and convenient procedure has been developed for the synthesis of β-phenylselenocarbonyl compounds by a one-pot reaction of diphenyl diselenide and α,β-unsaturated ketones, aldehydes, esters and nitriles in the presence of indium metal-trimethylsilyl chloride under sonication. Presumably, the In-TMSCl reagent system reacts with diphenyl diselenide to form an intermediate, $PhSeSiMe_3$, which then undergoes Michael addition with the α,β-unsaturated carbonyl compounds to produce the products.

Keywords: indium; Michael addition; β-selenocarbonyl compound; trimethylsilyl chloride; ultrasound

The interest in organoselenium compounds for organic synthesis is growing because of their facile participation as key intermediates in various reactions.[1] Although the importance of β-selenocarbonyl compounds as potential enone β-anion equivalents has been well established,[2] the methods for their synthesis are very limited.[3] In general, these methods are not very satisfactory and they suffer from low yields of products, poor generality and the disadvantage of handling of selenium reagents such as benzeneselenol, used as selenium sources because of their instability towards air and moisture. Thus, the development of efficient synthetic methods using a stable and user-friendly selenium reagent under mild conditions would have significant synthetic value.

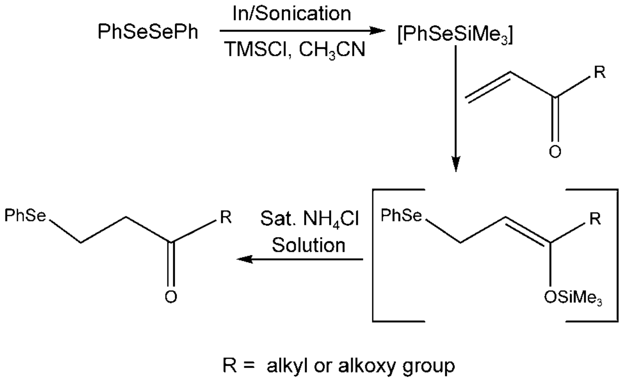
Indium metal and its derivatives have made a tremendous impact in organic synthesis in recent times because of their successful applications in a variety of organic transformations.[4] As a part of our interest in indium chemistry,[4e,5] we are in constant search for new indium reagents with novel applications in chemical reactions. We report here the use of the indium metal-trimethylchlorosilane reagent system for the cleavage of diphenyl diselenide and *in situ* Michael addition of selenoate anion to α,β-unsaturated carbonyl compounds and nitriles leading to the synthesis of β-phenylselenocarbonyl compounds and nitriles (Scheme 1).



Scheme 1.

The experimental procedure is very simple. A solution of diphenyl diselenide and a conjugated alkene in acetonitrile was sonicated in the presence of indium metal (finely cut) and trimethylchlorosilane and the product was isolated by usual work-up. Several α,β-unsaturated ketones, aldehydes, carboxylic esters, and nitriles underwent facile Michael additions with selenate anions to provide the corresponding β-phenylseleno adducts. The results are summarized in Table 1.

Other indium reagents, such as indium metal, indium(III) chloride and indium(I) iodide which promote similar reactions with diphenyl disulfide,[5k] are not successful for this selenium Michael addition. Although the exact role of In-TMSCl in this reaction is not very clear to us at this moment, it is speculated that diphenyl dise-



Scheme 2.

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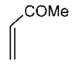
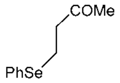
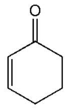
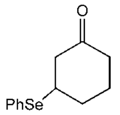
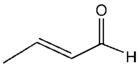
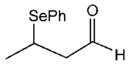
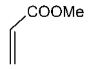
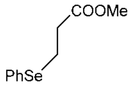
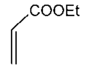
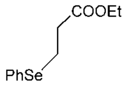
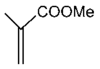
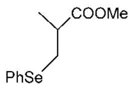
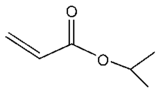
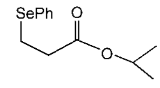
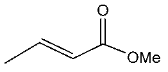
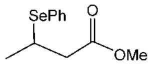
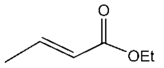
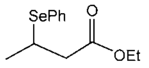
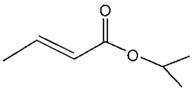
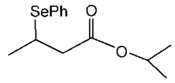
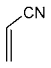
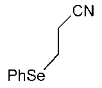
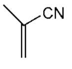
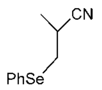
Table 1. In-TMSCl-promoted cleavage of diphenyl diselenide and addition to conjugated alkenes.

Entry	Alkenes	Time [h]	Product	Yield [%][a]	Ref
1		4.00		72	[3e]
2		5.00		71	[3e]
3		4.00		70	[3d]
4		3.10		83	[3f]
5		3.10		82	[3c]
6		3.20		82	
7		3.30		80	
8		4.00		70	
9		4.10		72	
10		4.2		70	
11		3.10		82	[3f]
12		3.20		81	[6]

[a] Yields refer to pure isolated products characterized by spectroscopic data (IR, ^{1}H and ^{13}C NMR).

lenide forms an intermediate, $PhSeSiMe_3$ with trimethylsilyl chloride in presence of indium metal[7] which facilitates the transfer of phenylselenate to the conjugated alkene.

The effect of ultrasound to carry out this reaction is also important. Without ultrasound and under room temperature stirring only a marginal reaction (10%) was observed. Under reflux for a prolonged period the reaction was found to proceed; however, it was not very clean being associated with undesirable side products.

In conclusion, this In-TMSCl-promoted one-pot procedure for the Michael addition of diphenyl diselenide to conjugated alkenes in the presence of indium metal and trimethylsilyl chloride provides an efficient methodology for the synthesis of β-phenylseleno carbonyl compounds and nitriles. Certainly this method offers significant advantages with regard to operation, yield, time and handling of reagents and thus presents a practical alternative to the existing procedures.[3] Moreover, this procedure demonstrates the synthetic potential of the indium-trimethylsilyl chloride reagent system which has not been explored to a great extent.

Experimental Section

General Experimental Procedure. Representative Example for the Michael Addition of Diphenyl Diselenide to Methyl Acrylate (entry 4)

A solution of diphenyl diselenide (344 mg, 1.1 mmol) and methyl acrylate (172 mg, 2 mmol) in dry acetonitrile (3 mL) was sonicated in an ultrasonic bath (Eyela, Japan) in the presence of indium metal (138 mg, 1.2 mmol, finely cut into small pieces) and freshly distilled trimethylchlorosilane (540 mg, 2.5 mmol) for 3 h (monitored by TLC). The reaction mixture was then quenched with water or saturated ammonium chloride solution and extracted with Et_2O (3×10 mL). The ether extract was washed with brine and dried (Na_2SO_4). Evaporation of solvent left the crude product which was purified by column chromatography (hexane:Et_2O, 95:5) to provide the pure addition product, *3-phenylselenomethyl propanoate*, as a pale yellow oil; yield: 403 mg (83%). The product was easily identified by comparison of its spectroscopic data (IR, ^{1}H and ^{13}C NMR) with those reported.[3f]

This procedure was followed for all the reactions listed in Table 1. All the products are adequately characterized by their spectroscopic data (IR, ^{1}H and ^{13}C NMR). These values for the known compounds are in good agreement with those reported (Table 1). The spectroscopic data for new compounds which are not available in the literature are provided here.

Methyl 2-methyl-3-phenylselenopropanoate (entry 6): Colorless oil; $R_f=0.60$; IR (neat): $\nu=1735, 1434, 1207, 736\ cm^{-1}$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1,27$ (d, $J=6.99$ Hz, 3 H), 2.71–2.78 (m, 1H), 2.90–2.96 (m, 1H), 3.17–3.23 (m, 1H), 3.64 (s, 3H), 7.24–7.28 (m, 3H), 7.50–7.53 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=18.0$, 31.2, 40.7, 52.1, 127.5, 129.4 (2C), 129.5, 133.5 (2C), 175.8; anal. calcd. for $C_{11}H_{14}O_2Se$: C 51.37, H 5.49; found: C 51.29, H 5.56.

Isopropyl 3-phenylselenopropanoate (entry 7): Colorless oil; $R_f=0.65$; IR (neat): $\nu=736, 1107, 1222, 1732\ cm^{-1}$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.24$ (d, $J=6.39$ Hz, 6H), 2.69 (t, $J=7.43$ Hz, 2H), 3.11 (t, $J=7.43$ Hz, 2H), 4.99–5.07 (m, 1H), 7.26–7.29 (m, 3H), 7.52–7.55 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=22.1$ (2C), 22.2, 35.9, 68.5, 127.6, 129.4 (2C), 129.5, 133.6 (2C), 172.0; anal. calcd. for $C_{12}H_{16}O_2Se$: C 53.14, H 5.95; found: C 53.11, H 5.99.

Methyl 3-phenylselenolbutanoate (entry 8): Yellowish oil; $R_f=0.65$; IR (neat): $\nu=1735, 1434, 1211, 736\ cm^{-1}$; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.44$ (d, $J=6.82$ Hz, 3H), 2.53–2.61

(m, 1H), 2.67–2.74 (m, 1H), 3.59–3.70 (m, 1H), 3.66 (s, 3H), 7.24–7.31 (m, 3H), 7.56–7.64 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.8$, 33.7, 42.6, 51.7, 127.9, 128.9 (2C), 129.0, 135.5 (2C), 172.0; anal. calcd. for $C_{11}H_{14}O_2Se$: C 51.37, H 5.49; found: C 51.30, H 5.56.

Ethyl 3-phenylselenobutanoate (entry 9): Colorless oil; $R_f = 0.62$; IR (neat): $\nu = 736$, 1022, 1473, 1732 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.25$ (t, $J = 7.11$ Hz, 3H), 1.44 (d, $J = 7.11$ Hz, 3H), 2.52–2.60 (m, 1H), 2.63–2.73 (m, 1H), 3.61–3.68 (m, 1H), 4.13 (q, $J = 7.11$ Hz, 2H), 7.25–7.31 (m, 3H), 7.57–7.63 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.5$, 22.2, 34.2, 43.1, 60.9, 128.0, 129.3 (2C), 129.4, 135.9 (2C), 171.9; anal. calcd. for $C_{12}H_{16}O_2Se$: C 53.14, H 5.95; found: C 53.10, H 5.98.

Isopropyl 3-phenylselenobutanoate (entry 10): Colorless oil; $R_f = 0.55$; IR (neat): $\nu = 740$, 1107, 1728 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.26$ (d, $J = 5.99$ Hz, 6H), 1.43 (d, $J = 6.93$ Hz, 3H), 2.48–2.56 (m, 1H), 2.62–2.69 (m, 1H), 3.57–3.67 (m, 1H), 4.98–5.06 (m, 1H), 7.25–7.33 (m, 3H), 7.57–7.62 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 22.1$ (2C), 22.2, 34.2, 43.4, 68.3, 128.2, 129.3 (2C), 129.5, 135.9 (2C), 171.4; anal. calcd. for $C_{13}H_{18}O_2Se$: C 54.74, H 6.36; found: C 54.70, H 6.40.

Acknowledgements

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[7] Although the formation of $PhSeSiMe_3$ by the reaction of PhSeSePh with Me_3SiCl under sonication in the presence of In metal is indicated by TLC (compared with that of authentic sample) we failed to isolate the pure compound after work-up. Probably, the $PhSeSiMe_3$ formed is not very stable under the reaction conditions and reacts instantaneously with the conjugated alkene.