The free-radical addition of phenyl trichloromethyl selenide to alkenes: a new method for the regioselective carboxylation of alkenes

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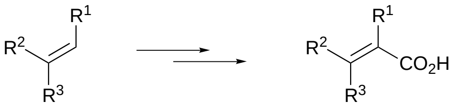
The free-radical addition of phenyl trichloromethyl selenide to alkenes affords 2-phenylseleno-1-trichloromethylalkanes, which can be converted into α,β-unsaturated carboxylic acids or amides by base-promoted dehydrochlorination, followed by [2,3]sigmatropic rearrangement of the corresponding selenoxides in the presence of water or diethylamine, respectively.

Free-radical 1,2-additions of selenium compounds of general structure PhSeX to alkenes and alkynes[1] provide a synthetically useful means for introducing the versatile phenylseleno group, as well as an additional functionality [*e.g.* X = SO_2Ar,[2] SePh,[3] C(=O)R,[4] SC(=O)Ph,[5] and CHZ_2,[6] where Z is an electron-withdrawing group] into the substrates. Free-radical additions of perhaloalkanes such as bromotrichloromethane are also well known.[7] Moreover, PhSe group transfers to alkyl radicals occur with rates comparable to those of bromine atom transfers,[8] suggesting that phenyl trichloromethyl selenide **1**[9] should undergo free-radical additions similar to those of bromotrichloromethane. We now report the novel photo-initiated or thermally initiated radical additions of **1** to alkenes, followed by some illustrative further transformations of the trichloromethyl and phenylseleno moieties that permit the overall conversion of the alkene into the corresponding α,β-unsaturated carboxylic acid (or amide), as shown in Scheme 1. Other methods for the carboxylation of alkenes generally require the presence of activating substituents to permit deprotonation of the alkene, or an existing functionality (*e.g.* halide, stannane) that provides a site for metallation, followed by reaction with carbon dioxide or



Scheme 1

$$PhSeSePh + CHCl_3 \xrightarrow[77\%]{i} PhSeCCl_3$$

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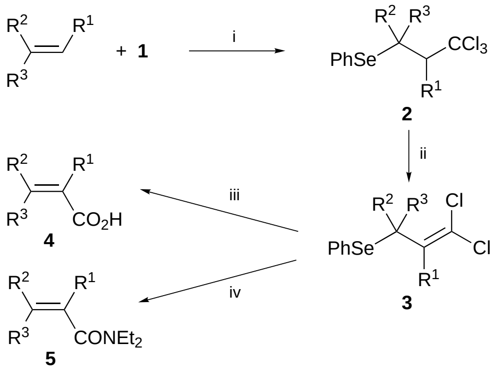
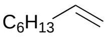
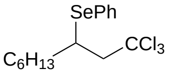
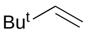
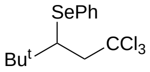
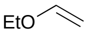
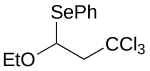
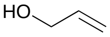
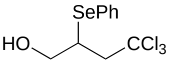
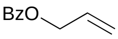
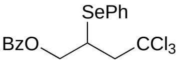
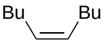
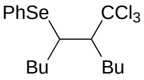
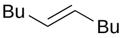
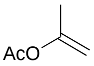
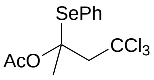
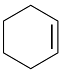
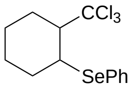
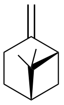
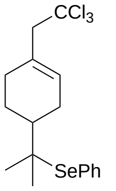
Scheme 2 *Reagents and conditions*: i, 50% NaOH–H_2O, Adogen 464®, O_2, 15–20 °C



Scheme 3 *Reagents and conditions*: i, *hν* or heat, AIBN; ii, Bu^tOK–THF, −30 or 10 °C; iii, 30% H_2O_2 H_2O, −30 °C; iv, MCPBA, CH_2Cl_2, −30 °C, then Et_2NH, room temp.

Table 1 Addition of **1** to alkenes[a]

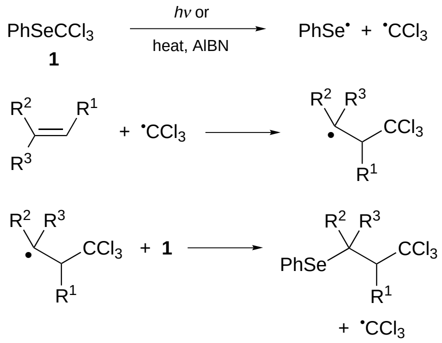
Alkene	Product	Yield (%)	*t*/h
	 **2a**	88 62[b] 78[c]	12 60 25
	 **2b**	75	13
	 **2c**	81	5
	 **2d**	65	13
	 **2e**	69	12
	 **2f**	60[d]	19
	**2f**	54[e]	12
	 **2g**	43	17
	 **2h**	63[f]	24
	 **2i**	87	19

[a] All reactions were performed neat using photo-initiation and 5 equiv. of the alkene unless otherwise noted; isolated yields are reported. [b] Only 1.5 equiv. of the alkene was used. [c] Performed in benzene at 80 °C with 10 mol% of AIBN. [d] The diastereomeric ratio was 3.8 : 1, as determined by NMR integration. [e] The diastereomeric ratio was 4.2 : 1, as determined by NMR integration. [f] The *cis* : *trans* ratio was 1 : 1.8, as determined by NMR integration.

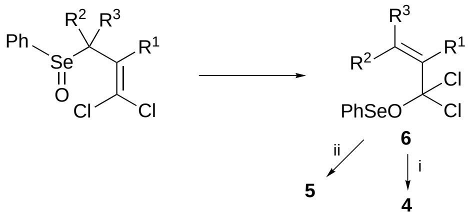
one of its synthetic equivalents.[10] The present method permits the use of unactivated olefins.

Selenide **1** was conveniently prepared by a new method from the base-catalysed reaction of diphenyl diselenide with $CHCl_3$ (Scheme 2). Thus, a mixture of the diselenide, a catalytic amount of Adogen 464® (methyltrialkylammonium chloride), 50% aqueous NaOH and $CHCl_3$ was stirred for 9 h at 15–20 °C, while air was bubbled through the reaction mixture to recycle the byproduct selenolate ($PhSe^-$). The product was isolated in 77% yield by flash chromatography.

The free-radical 1,2-addition of **1** to various alkenes to give **2** was then effected as shown in Scheme 3 and Table 1. Monosubstituted alkenes afforded adducts **2a–e** with only traces (< 5%) of their corresponding regioisomers, as indicated by NMR analysis. Both *cis*- and *trans*-dec-5-ene produced **2f** as the same *ca*. 4 : 1 mixture of diastereomers. Cyclohexene furnished a mixture of *cis* and *trans*-adducts **2h** in a ratio of 1 : 1.8. Thus, the additions are highly regioselective, but only moderately stereoselective. β-Pinene underwent ring-opening during the addition to afford the rearranged 1,6-adduct **2i**. In general, the reactions were performed by irradiation of the reaction mixture, either neat or in benzene solution, containing an excess (usually five-fold) of the alkene with a 300 W incandescent lamp. The use of a smaller excess of the alkene resulted in lower yields and required longer reaction times. The reaction was also performed in the case of **2a** in benzene at 80 °C in the presence of 10 mol% of the radical initiator AIBN. These results suggest a free-radical chain process in which cleavage of the Se–CCl_3 bond initiates the reaction, followed by addition of the trichloromethyl radical to the less substituted alkenic atom, and finally transfer of the PhSe group from **1** to the resulting 2-alkyl radical (Scheme 4).



Scheme 4



Scheme 5 *Reagents and conditions*: i, H_2O; ii, Et_2NH, then H_2O

Table 2 Preparation of allylic selenides **3**, carboxylic acids **4** and amides **5** from **2**

				Isolated yields (%)		
Adduct	R^1	R^2	R^3	**3**	**4**	**5**
2a	H	C_6H_{13}	H	92	91	73
2b	H	Bu^t	H	90	84	50
2f	Bu^n	Bu^n	H	92	81	59
2g	$–[CH_2]_4–$		H	86	60	50

Several of the adducts **2** were then transformed into allylic selenides **3** by dehydrochlorination with $KOBu^t$ in THF at −30 °C (except for **3f**, which required 6 h at 10 °C), and finally into α,β-unsaturated carboxylic acids **4** by oxidation and *in situ* [2,3]sigmatropic rearrangement (Scheme 3) of the resulting selenoxides.[11] Products **4a**, **4b** and **4f** were obtained as the *E*-isomers with high stereoselectivity. When Et_2NH was present during the latter step, the corresponding diethylamides were obtained instead. These results are shown in Table 2. Presumably, the sigmatropic rearrangement produces **6** initially, which then hydrolyses to the carboxylic acid **4** (Scheme 5). On the other hand, **6** reacts preferentially by aminolysis in the presence of diethylamine to afford the amide **5** instead of **4** after aqueous workup.

All new compounds reported here gave IR, ^1H NMR, ^{13}C NMR and low and high resolution mass spectra consistent with their structures.

These results demonstrate that the free-radical additions of readily available selenide **1** to alkenes occur efficiently and with high regioselectivity. Moreover, when the above process was used in conjunction with base-promoted dehydrochlorination and [2,3]sigmatropic rearrangement of the corresponding selenoxides, a novel method for the overall regioselective carboxylation of alkenes was achieved.

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Footnote and References

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