A One-Pot Trifunctionalization of Olefins with Benzeneseleninic and Trifluoroacetic Anhydrides Using a Commonly Undesirable Side Reaction as a Key Step[1]

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Summary: A multistep reaction of olefins with benzeneseleninyl trifluoroacetate (1) (generated in situ from benzeneseleninic and trifluoroacetic anhydrides) has been found to be a simple and effective one-pot synthesis of 2-(phenylseleno)-1,3-alkanediols.

Ever since syn elimination of selenoxides[2] became a popular synthetic procedure for introducing a carbon–carbon double bond, numerous attempts have been made to reduce or eliminate a "persistent side reaction" that is frequently an irritating complication in such reactions.[3] This is the formation of β-hydroxy selenides by addition of benzeneselenenic acid (also formed in the syn elimination) to the newly formed alkene double bond.

Because of its rapid disproportionation into diphenyl diselenide and benzeneseleninic acid, benzeneselenenic acid is actually present in only very low concentration at equilibrium in such solutions. Recently, we have shown[4] that PhSeSePh and PhSe(O)OSe(O)Ph (benzeneseleninic anhydride) undergo a facile and *complete* comproportionation into highly reactive selenium(II) electrophiles in the presence of triflic or trifluoroacetic anhydride (eq 1).

$$\mathrm{2PhSeSePh + PhSe(O)OSe(O)Ph + 3(CF_3CO)_2O \rightarrow 6PhSeOC(O)CF_3} \quad (1)$$

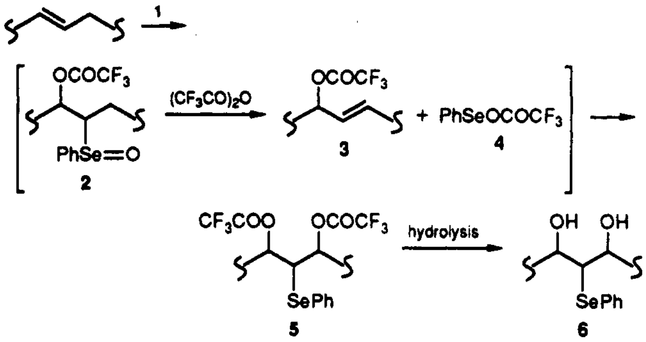
This suggested that if selenoxide elimination were to occur in the presence of trifluoroacetic anhydride it might lead to the formation of the very reactive electrophile $\mathrm{PhSeOC(O)CF_3}$ in high concentration. This would then be able to add readily to the previously formed olefinic double bond. This would create a situation where the "persistent side reaction" accompanying the selenoxide elimination could become a principal reaction path.

On the basis of such considerations we have developed and now report in this paper an effective new, one-pot method for olefin *tri*functionalization. It involves the following reaction sequence: (a) electrophilic addition of benzeneseleninyl trifluoroacetate ($\mathrm{PhSe(O)OC(O)CF_3}$) to the alkene; (b) syn elimination of PhSeOH from the resulting adduct to give a β,γ-unsaturated trifluoroacetate; and (c) regiospecific addition of $\mathrm{PhSeOC(O)CF_3}$ to this unsaturated trifluoroacetate to give a 2-(phenylseleno)-1,3-bis(trifluoroacetate). The diester can be easily hydrolyzed to afford the corresponding 2-(phenylseleno)-1,3-alkanediol. Note that a key step in the sequence is the aforementioned "undesirable" side reaction—addition of an Se(II) electrophile to the carbon–carbon double bond formed as a result of elimination of the selenoxide.

We have found that in dry methylene chloride (or chloroform) benzeneseleninic anhydride reacts with trifluoroacetic anhydride to give a species whose NMR and chemical behavior allow us to believe that it is the mixed anhydride 1 (eq 2).[5]

$$\mathrm{PhSe(O)OSe(O)Ph + (CF_3CO)_2O \rightleftarrows \underset{1}{PhSe(O)OC(O)CF_3}} \quad (2)$$

This Se(IV) electrophile reacts readily with alkenes at room temperature (and even at −78 °C), presumably giving β-trifluoroacetoxy selenoxides 2. The selenoxides 2 then undergo elimination to give allylic trifluoroacetates 3 and a mixture of $\mathrm{Ph_2Se_2}$ and $\mathrm{PhSeO_2H}$, which in the presence of an excess of trifluoroacetic anhydride comproportionate into $\mathrm{PhSeOCOCF_3}$, 4. Benzeneselenenyl trifluoroacetate (4) is known to be a reactive electrophile (see ref 3 and references cited therein). It adds readily and regiospecifically across the allylic double bond of trifluoroacetate 3 to give a 2-(phenylseleno)-1,3-alkanediol bis(trifluoroacetate) 5.[6] As one might expect, bis(trifluoroacetates) 5 easily undergo hydrolysis to furnish phenylseleno-substituted 1,3-diols 6.



Isolated yields of the reaction products are summarized in Table I. It is important to stress that in all cases addition of 4 to 3 was regiospecific and gave only the 2-(phenylseleno) 1,3-diols and bis(trifluoroacetates). There was no indication of the formation of regioisomeric 3-(phenyl-

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[2] For the first publication recognizing syn elimination of selenoxides see: Jones, D. N.; Mundy, D.; Whitehouse, R. D. *Chem. Commun.* 1970, 86.

[3] See, for example: Reich, H.; Wollowitz, S.; Trend, J. E.; Chow, F.; Wendelborn, D. *J. Org. Chem.* 1978, *43*, 1697.

[4] Kutateladze, A. G.; Kice, J. L.; Kutateladze, T. G.; Zefirov, N. S.; Zyk, N. V. *Tetrahedron Lett.* 1992, *33*, 1949.

[5] The ^{1}H NMR spectrum (CDCl$_3$) showed two multiplets at δ 8.08–7.97 ppm (2 H) and 7.85–7.69 ppm (3 H). The ^{13}C NMR was also consistent with formulation of the formed reagent as $\mathrm{PhSe(O)OC(O)CF_3}$: ($\delta$, ppm) 135.26, 130.72, and 128.05.

[6] Bis(trifluoroacetates) 5a–e were characterized by ^{1}H and ^{13}C NMR spectroscopy without additional purification.

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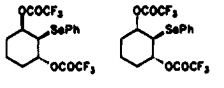
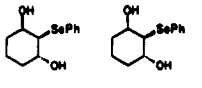
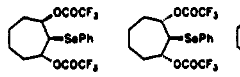
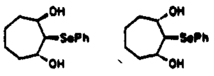
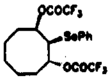
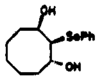
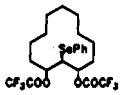
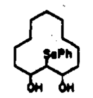
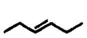
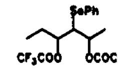
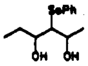
Table I. Reaction of Olefins with $(CF_3CO)_2O/PhSe(O)OSe(O)Ph$[a]

entry	olefin	trifluoroacetate(s) (5a–e)	diol(s) (6a–e)
a		 6 : 1	 6 : 1 (89 %)
b		 7 : 1	 7 : 1 (82 %)
c			 (96 %)
d			 (88 %)
e			 (a mixture of diastereomers) (76 %)

[a] Olefin (1 mmol) added to dry CH_2Cl_2 containing 6 mmol of $(CF_3CO)_2O$ and 2 mmol of benzeneseleninic anhydride at room temperature, and reaction allowed to proceed for 1 day (2 days for cyclohexene). Diols isolated after alkaline hydrolysis of trifluoroacetates.

seleno) 1,2-diols and/or bis(trifluoroacetates). This regiochemical result is in good agreement with previously reported data on addition of some selenenic electrophiles to allyl acetates.[7] The regiochemistry of the elimination of selenoxide **2** to form allylic trifluoroacetate **3** is consistent with the regiochemistry observed[8] in the elimination of β-acetoxy selenoxides.

Unfortunately, the initial addition (to form **2**) of the Se(IV) electrophile to *unsymmetrical* olefins is not generally completely regiospecific and leads to a mixture of regioisomers of **2**. This means that the described trifunctionalization technique is uniformly applicable only to symmetrical alkenes.

With cycloalkenes the trifunctionalization process was found to be stereoselective. The ^1H and ^{13}C NMR spectra of the bis(trifluoroacetates) **5c** and **5d**, derived from cyclooctene and cyclododecene, respectively, showed that the stereochemistry of the product of addition of $PhSeOCOCF_3$ to the allylic trifluoroacetate **3** was trans–cis. This is the same stereochemical outcome seen in the addition of benzeneselenenyl acetate (PhSeOAc) to 2-cyclohexen-1-yl acetate.[9] In that addition, it was postulated[9] that $PhSe^+$ prefers to attack the double bond from the same side as the acetate group. The actual addition itself was stereospecific trans. Subsequent hydrolysis of the bis(trifluoroacetate) results in the formation of the single regio- and stereoisomer of **6c** or **6d** shown. With cycloheptene or cyclohexene formation of some trans-trans isomer was observed, but the trans-cis isomer was still the major product of the reaction. It is possible that there is an isomerization of the trans-cis isomer into the thermodynamically more stable trans-trans isomer during the reaction. We assume that the lack of stereoselectivity in the case of the open-chain alkene, 3-hexene, is due to a free rotation around the C^1–C^2 single bond in the noncyclic allyl trifluoroacetate **3**.

Thus, trifunctionalization of olefins employing a multistep reaction with benzeneseleninic and trifluoroacetic anhydrides is shown to be a simple and yet useful tool in organic synthesis. In view of the synthetic potential provided by the phenylseleno moiety in the resulting diols, future applications of the reported method can be anticipated. For example, reaction of **6** with tributyltin hydride should lead to the replacement of the PhSe group with a hydrogen,[10] thereby affording *trans*-1,3-diols, a structural moiety important in some natural products. The PhSe group is also known to be a good radical precursor for other intra-[11a,b] and intermolecular[11c,d] radical reactions, which, in contrast to anionic chemistry, would be safely compatible with vicinal OR groups.

Supplementary Material Available: ^1H and ^{13}C NMR spectra of **6a–e**, experimental procedures, and characterization data (5 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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