β-Phenylselenoethanol, an efficient reagent for the one-pot synthesis of aryl vinyl ethers

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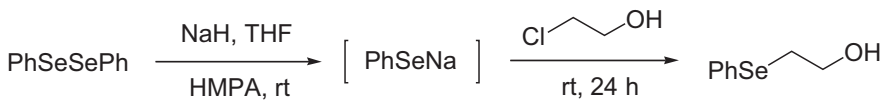
β-Phenylselenoethanol was treated with phenols under Mitsunobu conditions and subsequent oxidation-elimination with 30% hydrogen peroxide furnished aryl vinyl ethers with good yields (85–90%) in a one-pot, two-step transformation.

Keywords: aryl vinyl ether, β-phenylselenoethanol, phenol, Mitsunobu reaction, oxidation–elimination

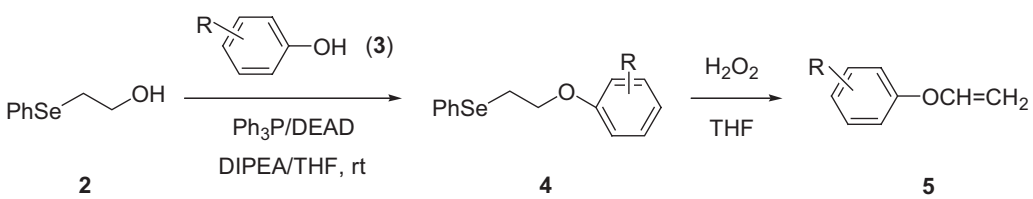
Aryl vinyl ethers with unsubstituted vinyl moiety, have many synthetic applications[1] and are employed as key intermediates for the generation of new polymeric materials,[2] as dienophiles for cycloaddition reactions such as [2 + 2],[3] [2 + 4][4] and 1,3-dipolar cycloadditons,[5] in cyclopropanations,[6] in hydroformylations,[7] and in natural product analogue synthesis.[8] Aryl vinyl ethers are usually prepared by the dehydrohalogenation of aryl 2-haloethyl ethers,[9–13] the addition of phenols to acetylene[14,15] or the copper(II)-promoted coupling of arylboronic acids with phenols.[16] Recently, the use of vinyl acetate in an iridium-catalysed reaction with phenols,[17] and the transformations with copper(II) acetate mediated coupling of 2,4,6-trivinylcyclotriboroxane as a vinylboronic acid equivalent,[18] and tributy(vinyl)tin[19] with phenols have also been reported. However, most of these methods involved difficulties such as harsh reactions, laborious manipulation and low overall yields. In some cases the reactions are unsuitable for sensitive substrates, vigorous toxic compounds are used and some reagents are not readily available. Therefore, exploring more efficient, experimentally simple methodology is still interesting. Selenium-based methods have been developed rapidly over the past few years and are now a very important tool for introducing new functional groups into organic substrates under extremely mild conditions.[20] For example, the phenylseleno group is readily converted to a leaving group giving access to a carbon–carbon double bond *via* oxidation followed by β-elimination.[21] β-Hydroxyalkyl selenides can be converted to allylic alcohols, olefins, bromohydrins and vinyl selenides and epoxide.[22] They can be used to prepare tetrahydrofuran derivatives[23] and some important nature products, such as sphingosine, pancratistatin, schweinfurthin B, spirotryprostatin B and siastatin B.[24] Additionally, the Mitsunobu reaction of alcohols has been extensively used in organic synthesis for the preparation of esters, alcohols, aryl ethers, amine, and thioethers.[25] Based on these, we designed a novel, convenient, and efficient one-pot, two-step route for the preparation of aryl vinyl ethers from β-phenylselenoethanol (Scheme 1). This was treated with phenols under Mitsunobu conditions followed by oxidation-elimination with 30% hydrogen peroxide (Scheme 2). The present method has advantages such as mild reaction condition, convenient manipulation and good yields.

In general, β-hydroxyalkyl phenyl selenides were prepared by the ring-opening of epoxides with benzeneselenolate ions in ethanol at ambient temperature.[26] However, the required β-phenylselenoethanol was only obtained in 50% yield by the reaction of sodium borohydride with an ethylene epoxide in our trial. Interestingly, 2-chloroethanol was reacted with phenylselenium anion to give the corresponding β-phenylselenoethanol **(2)** in excellent yield (Scheme 1). With **2** in hand, the preparation of intermediate 2-phenylselenoethyl aryl ethers **4**, was investigated from **2** with phenol (**3a**). Firstly, the etherification reaction was carried out with dicyclohexylcarbodiimide (DCC), but the yield of corresponding product **4a** was about 60%, and a large excess of both DCC and substrate **3a** were required. In addition, forcing conditions were required involving heating to reflux temperature in a solution of THF and triethylamine. This prompted the search for a mild coupling reaction that would consistently produce high yields. The alkylation of phenols with alcohols effected by the triphenylphosphine/diethyl azodicarboxylate (TPP/DEAD) system is well-documented in the literature.[27] Treatment of β-phenylselenoethanol **(2)** with phenol (**3a**) with both standard reagents (TPP and DEAD) afforded the corresponding 2-phenylselenoethyl phenyl ether **(4a)** in 85% yield. After a series of experiments, the best result with 94% yield of **4a** was obtained when the *N, N*-diisopropylethylamine (DIPEA) was added to the above



1 **2**

Scheme 1



2 **4** **5**

Scheme 2

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Table 1 Yields of aryl vinyl ethers **5a–5k**

Entry	Phenol	R	Product	Yield/%[a]
1	**3a**	H	**3a**	89
2	**3b**	3-CH_3	**3b**	90
3	**3c**	4-*t*-C_4H_9	**3c**	88
4	**3d**	4-C_6H_5	**3d**	87
5	**3e**	4-Cl	**3e**	86
6	**3f**	2-Br	**3f**	86
7	**3g**	4-NO_2	**3g**	90
8	**3h**	4-CN	**3h**	88
9	**3i**	4-CO_2CH_3	**3i**	86
10	**3j**	4-$NHCOCH_3$	**3j**	88
11	**3k**	1-naphthol	**3k**	85

[a]Isolated yield based on β-phenyselenoethanol **(2)**.

Mitsunobu reaction system. Subsequent oxidation–elimination of **4a** with 30% hydrogen peroxide afforded phenyl vinyl ether (**5a**) in 90% yield. In fact, although selenated intermediate **4a** can be isolated and purified by chromatography, we have found it most convenient to carry out the oxidation of the material in one-pot. Mild oxidation of the selenide **4a** and elimination of the selenoxide provided **5a** in 89% yield.

After successfully completing the initial studies on the preparation of **5a**, extension of this method to the synthesis of other analogues in good yields was investigated (Table 1). As seen from the Table 1, phenolic substrates having either an electron-withdrawing or an electron-donating substituent on the aromatic ring resulted in no obvious effect on the reaction yields.The phenylseleno moiety, introduced in the starting material is eliminated as benzeneseleninic acid in the oxidation step. Diphenyl diselenide can be recovered in 60% yield by the addition of hydrazine monohydrate to the aqueous extract.

In summary, we have developed a novel and convenient method for the preparation of aryl vinyl ethers in good yield in a one-pot, two-step transformation employing the Mitsunobu reaction of β-phenylselenoethanol with phenols followed by oxidation-elimination.

Experimental

Melting points were uncorrected. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker Avance (400 MHz) spectrometer, using $CDCl_3$ as the solvent and TMS as internal standard. FT-IR spectra were recorded on a Perkin-Elmer SP One FT-IR spectrophotometer. All reagents were purchased from commercial suppliers and used without further purification. THF was distilled from sodium-benzophenone immediately prior to use.

Preparation of β-phenylselenoethanol (**2**):
Sodium hydride (0.14 g, 6.0 mmol) was added to a solution of diphenyl disselenide (0.96 g, 3.0 mmol), in anhydrous THF (30 ml), The suspension was refluxed for 2 h and then allowed to cool to 40 °C. HMPA (6 ml) was then added. 2-Chloroethanol (0.48 g, 6.0 mmol) was added to the resulting orange-coloured solution, After 24 h the reaction was quenched with a 10% solution of NH_4Cl (10 ml). The reaction mixture was extracted with Et_2O (3 × 30 ml) and the combined organic layers were dried over anhydrous Na_2SO_4 and evaporated to give the crude product. This was purified by column chromatography on a silica gel column using a mixture of Et_2O and light petroleum (4:6) as eluent to afford pure compound **2** (1.13 g) as a pale yellow oil in 94%. ^{1}H NMR: δ = 7.24–7.23 (m, 3 H), 7.06–7.04 (m, 2 H), 4.10–3.99 (m, 2 H), 3.18–3.12 (m, 2 H), 2.85 (br s, 1H). ^{13}C NMR: δ = 135.1, 128.3, 128.2, 127.6, 65.1, 51.0. IR (neat): ν = IR (neat): 3400, 3052, 2921, 1580, 1475, 1060, 941, 730, 688 cm^{-1}.

Preparation of aryl vinyl ethers (**5**); *general procedure*
Phenols **(3)** (2.0 mmol) and DIPEA (1.0 ml, 6.0 mmol) in dry THF (20 ml), DEAD (316 μl, 2.0 mmol) were added dropwise under ice-cooling. To the stirred mixture of β-phenylselenoethanol **(2)** (2.01 g, 1.0 mmol), TPP (525 mg, 2.0 mmol), under nitrogen. The reaction mixture was stirred at room temperature until TLC analysis showed that the starting selenide was completely converted into the corresponding selenated intermediates **4** (5–6 h). The mixture was cooled to 0 °C, the 30% hydrogen peroxide (1.0 ml, 11.6 mmol) was added and. stirred until the reaction was finished as determined by TLC (2–2.5 h). Powered K_2CO_3 (0.53 g, 5 mol) was then added to the reaction mixture and stirred at room temperature and the mixture was extracted with ether (20 × 3 ml). The combined organic layers were washed with saturated $NaHCO_3$ solution, brine and twice with water and then dried over magnesium sulfate. The solvent was removed *in vacuo* and the residue was purified by column chromatography on silica gel using chloroform/hexane (10 : 90) as eluent to give pure products **5a–k**.

Phenyl vinyl ether (**5a**): Colourless oil (Lit.[10] oil); ^{1}H NMR: δ = 7.15–7.02 (m, 5H), 6.58 (dd, *J* = 14.0, 6.0 Hz, 1H), 4.70 (dd, *J* = 14.0, 1.5 Hz, 1H), 4.34 (dd, *J* = 6.0, 1.5 Hz, 1H); ^{13}C NMR: δ = 154.0, 144.4, 133.1, 120.5, 115.3, 95.3; IR (neat): ν = 3045, 1640, 1623, 1600, 1495, 1230, 1212, 1165, 1155, 1145, 956, 942 cm^{-1}.

3-Methylphenyl vinyl ether (**5b**): Colourless oil (Lit.[14] oil); ^{1}H NMR: δ = 6.83–7.20 (m, 4H), 6.50 (dd, *J* = 14.2, 6.5 Hz, 1H), 4.32 (dd, *J* = 14.2, 1.8 Hz, 1H), 4.04 (dd, *J* = 6.5, 1.8 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR: δ = 154.6, 140.4, 132.1, 123.7, 122.6, 119.5, 115.3, 95.6, 21.5; IR (neat): ν = 3050, 1640, 1622, 1600, 1500, 1380, 1230, 1160, 1149, 960, 822 cm^{-1}.

4-t-Butylphenyl vinyl ether (**5c**): Colourless oil (Lit.[19] oil); ^{1}H NMR: δ = 6.80 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 8.2 Hz, 2H), 6.51 (dd, *J* = 14.0, 6.2 Hz, 1H), 4.28 (dd, *J* = 14.0, 1.6 Hz, 1H), 4.24 (dd, *J* = 6.2, 1.6 Hz, 1H), 1.31 (s, 9H); ^{13}C NMR: δ = 157.1, 145.5, 133.7, 120.0, 117.3, 95.8, 38.0, 28.5; IR (neat): ν = 3045, 2940, 1640, 1600, 1600, 1500, 1378, 1240, 1180, 1149, 825 cm^{-1}.

4-Vinyloxybiphenyl (**5d**): White solid, 52–53 °C. (Lit.[19] 52–53 °C); ^{1}H NMR: δ = 7.66–7.34 (m, 7 H), 7.12–7.06 (m, 2 H), 6.80 (dd, *J* = 13.5, 6.0 Hz, 1 H), 4.72 (dd, *J* = 13.5, 1.5 Hz, 1 H), 4.47 (dd, *J* = 6.0, 1.5 Hz, 1 H); ^{13}C NMR: δ = 156.6, 148.2, 140.6, 136.3, 129.0, 128.5, 127.2, 126.8, 117.5, 95.5; IR (KBr): ν = 3050, 3021, 1636, 1595, 1509, 1476, 1240, 1136, 826, 755 cm^{-1}.

4-Chlorophenyl vinyl ether (**5e**): Colourless oil (Lit.[10] oil); ^{1}H NMR: δ = 7.43 (d, *J* = 8.4 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.63 (dd, *J* = 13.7, 6.1 Hz, 1H), 4.80 (dd, *J* = 13.7, 1.8 Hz, 1H), 4.51 (dd, *J* = 6.1, 1.8 Hz, 1H); ^{13}C NMR: δ = 156.2, 148.1, 132.8, 119.1, 116.1, 95.8; IR (neat): ν = 3048, 1635, 1595, 1475, 1232, 1165, 1142, 1058, 1002, 955, 834 cm^{-1}.

2-Bromophenyl vinyl ether (**5f**): Colourless oil (Lit.[18] oil); ^{1}H NMR: δ = 7.67–7.65 (m, 1H), 7.42–7.36 (m, 1H), 7.21–7.18 (m, 1H), 7.10–7.06 (m, 1H), 6.80 (dd, *J* = 6.3, 13.5 Hz, 1H), 4.68 (dd, *J* = 1.8, 13.5 Hz, 1H), 4.53 (dd, *J* = 1.8, 6.3 Hz, 1H); ^{13}C NMR: δ = 153.5, 148.7, 133.7, 129.7, 125.3, 118.5, 113.6, 96.2; IR (neat): ν = 3043, 1640, 1595, 1472, 1232, 1164, 1142, 1063, 1005, 953, 765 cm^{-1}.

4-Nitrophenyl vinyl ether (**5g**): Pale yellow oil (Lit.[19] oil); ^{1}H NMR: δ = 8.25 (d, *J* = 8.9 Hz, 2H), 7.10 (d, *J* = 8.9 Hz, 2H), 6.68 (dd, *J* = 13.6, 6.0 Hz, 1H), 5.01 (dd, *J* = 13.6, 1.9 Hz, 1H), 4.70 (dd, *J* = 6.0, 1.9 Hz, 1H); ^{13}C NMR: δ = 161.3, 145.5, 142.8, 125.7, 116.3, 99.1; IR (neat): ν = 3060, 1638, 1600, 1580, 1498, 1481, 1330, 1230, 1160, 1120, 1100, 945, 840 cm^{-1}.

4-Cyanophenyl vinyl ether (**5h**): Colourless oil (Lit.[19] oil); ^{1}H NMR: δ = 7.70 (d, *J* = 8.6 Hz, 2H), 7.10 (d, *J* = 8.6 Hz, 2H), 6.66 (dd, *J* = 13.7, 6.1 Hz, 1H), 4.98 (dd, *J* = 13.7, 2.0 Hz, 1H), 4.68 (dd, *J* = 6.1, 2.0 Hz, 1H); ^{13}C NMR: δ = 159.8, 145.8, 134.1, 118.6, 117.1, 106.1, 98.6; IR (neat): ν = 3050, 2200, 1635, 1595, 1492, 1300, 1235, 1160, 1125, 950, 824 cm^{-1}.

Methyl 4-(vinyloxy)benzoate (**5i**): Colourless oil (Lit.[19] oil); ^{1}H NMR: δ = 8.00 (d, *J* = 8.3 Hz, 2H), 7.15 (d, *J* = 8.3 Hz, 2H), 6.88 (dd, *J* = 13.6, 6.0 Hz, 1H), 4.85 (dd, *J* = 13.6, 1.6 Hz, 1H), 4.55 (dd, *J* = 6.0, 1.6 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR: δ = 166.5, 160.2, 146.6, 131.5, 124.5, 116.1, 97.3, 51.8; IR (neat): ν = 3050, 2985, 2940, 1710, 1635, 1596, 1498, 1425, 1300, 1272, 1235, 1156, 1132, 1100, 840 cm^{-1}.

N-[4-(Vinyloxy)phenyl]acetamide (**5j**): White solid, m.p. 102–103 °C (Lit.[19] 103–103.5 °C) ^{1}H NMR: δ = 7.40–7.50 (m, 2H), 7.26 (br s, 1H), 6.95–7.05 (m, 2H), 6.63 (dd, *J* = 13.7, 6.1 Hz, 1H), 4.75 (dd, *J* = 13.7, 1.7 Hz, 1H), 4.55 (dd, *J* = 6.1, 1.7 Hz, 1H), 2.18 (s, 3H). ^{13}C NMR: δ = 169.2, 153.2, 148.5, 133.4, 122.1, 117.3, 94.6, 24.1. IR: ν = 3258, 3188, 3130, 3055, 1650, 1600, 1495, 1300, 1235, 1210, 1162, 1145, 940, 830 cm^{-1}. Anal. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.87; H, 6.36; N, 7.96.

1-Naphthyl vinyl ether (**5k**): White solid, 31–32 °C (Lit.[28] 32 °C); ^{1}H NMR: δ = 7.00–7.50 (m, 7H), 6.71 (dd, *J* = 14.1, 6.0 Hz, 1H), 4.81 (dd, *J* = 14.1, 1.6 Hz, 1H), 4.45 (dd, *J* = 6.0, 1.6 Hz, 1H); ^{13}C NMR: δ = 152.7, 144.9, 133.9, 132.6, 128.9, 128.7, 128.3, 126.7, 125.9, 123.5, 115.8, 95.7; IR (KBr): ν = 3050, 1630, 1600, 1495, 1255, 1226, 1172, 1152, 1142, 942 cm^{-1}.

Recovery of diphenyl diselenide

Hydrazine monohydrate (3.5 mmol, 0.16 ml) was added gradually to the aqueous extract containing the benzeneseleninic acid from the oxidation procedure. Stirring was continued until diphenyl diselenide was formed, as indicated by the yellow colour. The mixture was then concentrated *in vacuo*, poured into water (30 ml) and extracted with Et_2O (3 × 20 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated. Diphenyl diselenide was recovered as a pure compound in 60% yield.

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