Solid-phase synthesis of aryl vinyl ethers based on polystyrene-supported β-phenylselenoethanol

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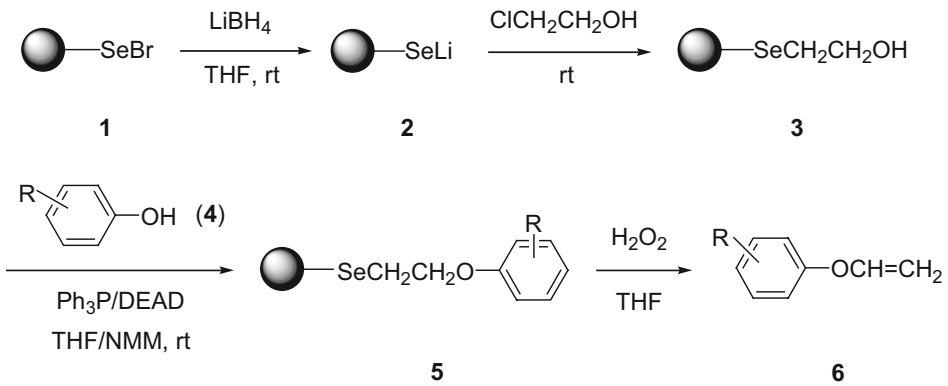
A novel facile solid-phase organic synthesis of aryl vinyl ethers by reaction of polystyrene-supported β-phenylselenoethanol with phenols under Mitsunobu conditions and subsequent oxidation-elimination with 30% hydrogen peroxide has been developed. The advantages of this method include straightforward operation, lack of odour, good yield and high purity of the products.

Keywords: solid-phase organic synthesis, polystyrene-supported β-phenylselenoethanol, aryl vinyl ether

Vinyl ethers are valuable intermediates that can be used in a wide array of chemical transformations.[1] More specifically, aryl vinyl ethers with unsubstituted vinyl moiety, have wide synthetic applications 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 according to the following procedures: the dehydrohalogenation of aryl 2-haloethyl ethers,[9] the addition of phenols to acetylene[10] and the copper (II)-promoted coupling of arylboronic acids with phenols.[11] Recently, the use of vinyl acetate in an iridium-catalysed reaction with phenols,[12] and the transformations with copper (II) acetate mediated coupling of 2, 4, 6-trivinyl-cyclotriboroxane as a vinylboronic acid equivalent,[13] and tributy(vinyl)tin[14] with phenols have also been reported. However, most of these methods involved difficulties such as harsh reactions, laborious manipulation and low overall yields, or in some cases, reactions are unsuitable for sensitive substrates, vigorous toxic compounds are used or some reagents are not readily available. It is well known that phenylseleno group is readily converted to a leaving group giving access to carbon–carbon double bond *via* oxidation followed by β-elimination under extremely mild conditions.[15] Moreover, the polymeric selenium reagents[16] have been now developed for solid-phase organic synthesis (SPOS) with a combined advantage of decrease volatility and simplification of product work-up. In continuation of our interest in solid-phase organoselenium chemistry,[17] describe here a new simple and efficient SPOS approach to aryl vinyl ethers based on a novel polystyrene-supported β-phenylselenoethanol reagent (Scheme 1).

Polymer-supported β-phenylselenoethanol (**3**) was readily prepared by treatment of a THF-swollen suspension of cross-linked (1%) polystyrene-bound selenium bromide (**1**)[16] with $LiBH_4$, followed by treatment with 2-chloroethanol. The IR spectrum of resin **3** showed a large hydroxyl absorption at 3400 cm^{-1}, and band at 1060 cm^{-1} (C–O). Resin **3** can be stored at room temperature for a long time without diminution of capacity or the liberation of disagreeable odors. With the resin **3** in hand, the etherification reaction was investigated from resin **3** with phenol (**4a**) under Mitsunobu reaction conditions [triphenylphosphine/diethyl azodicarboxylate] in 4-methylmorpholine to afford polystyrene-supported 2-phenoxyethyl selenide(**5a**) efficiently, which could not be reliably analysed with FT-IR. Hence we carried out next cleavage reaction directly after washing the resin **5a** using solvents. Treatment of resin **5a** with 30% hydrogen peroxide at 0 °C and then at room temperature afforded the corresponding phenyl vinyl ether (**6a**) in good yields (90%) and with good purities of crude material (95%). The residual resin, polystyrene-supported phenylseleninic acid, was obtained as a by-product, whose IR data were identical to the previously reported data.[18] The polystyrene-supported phenylseleninic acid could be converted to polymer-supported selenium lithium for recycle by treatment of it with $KI/Na_2S_2O_3$[19,20] followed by bromine.[16] For example, phenyl vinyl ether (**6a**) was obtained in 88% yield under the same reaction condition using the recovered selenium lithium resin (second run), and in 85% yield after second recycle (*i.e.* third run). It was shown that recycling 2–3 times led to a gradual deterioration of the resin. After successfully preparation of **6a**, extension of this method to the synthesis of other analogues in good yields and good purities was investigated (Table 1). As seen from the Table 1, for substrates phenols, with substitution of an



Scheme 1

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Table 1 The yields and purities of aryl vinyl ethers (**6a–6m**)

Entry	R (Phenol)	Product	Yield[a]/%	Purity[b]/%
1	H (**4a**)	**6a**	90	95
2	3-CH_3 (**4b**)	**6b**	89	94
3	4-CH_3O (**4c**)	**6c**	90	97
4	4-*t*-C_4H_9 (**4d**)	**6d**	88	95
5	4-C_6H_5 (**4e**)	**6e**	86	96
6	4-Cl(**4f**)	**6f**	83	95
7	4-Br (**4g**)	**6g**	88	95
8	2-Br (**4h**)	**6h**	86	94
9	4-NO_2 (**4i**)	**6i**	90	96
10	4-CN (**4j**)	**6j**	88	95
11	4-CO_2CH_3 (**4k**)	**6k**	86	94
12	4-$NHCOCH_3$ (**4l**)	**6l**	88	96
13	1-Naphthol (**4m**)	**6m**	84	95

[a]Overall yields based on polystyrene-supported selenium bromide **1** (1.18 mmol Br/g).
[b]Determined by HPLC of crude cleavage product (λ = 254 nm).

electron-withdrawing group or an electron-donating group on the aromatic ring resulted in no obvious effect on the reaction yields.

In summary, we have developed a novel, efficient and convenient method for the SPOS of aryl vinyl ethers employing polymer-supported β-phenylselenoethanol. The advantages of this method include straightforward operation, lack of odour, good yield and high purity of the products.

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 taken on a Perkin–Elmer SP One FT-IR spectrophotometer. HPLC analysis was performed on Agilent 1100 automated system having a PDA detector using a gradient with CH_3CN/H_2O (1 mL min^{-1}) on a RP-18e column (150 × 4.6 mm). Polystyrene (H 1000, 100–200 mesh, cross-linked with 1% divinylbenzene) for preparation of selenium bromide resin[16] was purchased from Nankai University, and the other starting materials were purchased from commercial suppliers and used without further purification. THF was stilled from sodium benzophenone immediately prior to use.

Preparation of polystyrene-supported β-*phenylselenoethanol* (**3**)
Under a nitrogen atmosphere, to deep red coloured polystyrene-supported selenium bromide **1** (1.0 g, 1.18 mmol Br/g, the loading of functional Br was analysed by elementary analysis) swollen in THF (10 mL) for 30 min was added $LiBH_4$ (3.0 mmol). After 1 h with shaking at room temperature, 2-chloroethanol (3.0 mmol) in 2 mL of THF was added slowly and the mixture was shaken for 6 h. The resin was collected on a filter and washed successively with H_2O (2 × 20 mL), THF (3 × 5 mL) and CH_2Cl_2 (3 × 5 mL), and then dried under vacuum overnight to afford 950 mg of resin **3**, which was calculated to have a loading of 1.20 mmol g^{-1}, assuming the etherification reaction went to completion. IR (KBr): ν = 3400, 3052, 2925, 1595, 1475, 1060, 940, 732, 688 cm^{-1}.

Preparation of aryl vinyl ethers(**6a–m**); *general procedure*
The resin **3** (1.0 g, 1.20 mmol) was swollen in THF (10 mL) at room temperature for 30 min and then a solution of triphenylphosphine (1.57 g, 6.0 mmol) and phenols (**4a–m**) (5.0 mmol) in 4-methylmorpholine (5 mL) was added. Neat diethyl azodicarboxylate (790 μL, 5.0 mmol) was added in small portions over a period of 20 min at room temperture After the suspension was shaken for 12 h at room temperture, the resin (**5a–m**) was filtered and subsequently washed with THF (3 × 5 mL), DMSO (2 × 10 mL), THF (3 × 5 mL), water (2 × 10 mL), MeOH (2 × 10 mL) and CH_2Cl_2 (3 × 5 mL). To a suspension of the swollen resin **5a–m** in CH_2Cl_2 (10 mL) and 0.5 mL of 30% H_2O_2 (5.8 mmol) was added at 0 °C. The suspension was shaken at 0 °C for 0.5 h and then at room temperature for 1.0 h, the residual resin was collected by filtration and washed with CH_2Cl_2 (2 × 10 mL). The filtrate was treated with saturated $NaHCO_3$ (20 mL) and washed with water, dried over magnesium sulfate and evaporated to give crude products **6a–m** with 94–97% purity determined by HPLC, which were further purified by column chromatography on silica gel using chloroform/hexane (10:90) as eluent to give pure products **6a–m** for ^{1}H NMR and IR analyses.

Phenyl vinyl ether (**6a**): Colourless oil. (lit.[14] oil); ^{1}H NMR: δ = 7.15–7.02 (m, 5 H), 6.58 (dd, *J* = 14.0, 6.0 Hz, 1 H), 4.70 (dd, *J* = 14.0, 1.5 Hz, 1 H), 4.34 (dd, *J* = 6.0, 1.5 Hz, 1 H); ^{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 (**6b**): Colourless oil (lit.[10] oil); ^{1}H NMR: δ = 6.83–7.20 (m, 4 H), 6.50 (dd, *J* = 14.2, 6.5 Hz, 1 H), 4.32 (dd, *J* = 14.2, 1.8 Hz, 1 H), 4.04 (dd, *J* = 6.5, 1.8 Hz, 1 H), 2.30 (s, 3 H); ^{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-Methoxyphenyl vinyl ether (**6c**): Colourless oil (lit.[21] oil); ^{1}H NMR: δ = 6.95 (d, *J* = 8.2 Hz, 2 H), 6.86 (d, *J* = 8.2 Hz, 2 H), 6.58 (dd, *J* = 14.1, 6.3 Hz, 1 H), 4.65 (dd, *J* = 14.1, 2.0 Hz, 1 H), 4.35 (dd, *J* = 6.3, 2.0 Hz, 1 H), 3.78 (s, 3 H); ^{13}C NMR: δ = 155.4, 145.8, 134.1, 120.5, 118.0, 115.5, 95.5, 55.2; IR (neat): ν = 3045, 1638, 1620, 1600, 1495, 1379, 1230, 1162, 1145, 958, 825 cm^{-1}.

4-t-Butylphenyl vinyl ether (**6d**): Colourless oil (lit.[9] oil); ^{1}H NMR: δ = 6.80 (d, *J* = 8.2 Hz, 2 H), 7.18 (d, *J* = 8.2 Hz, 2 H), 6.51 (dd, *J* = 14.0, 6.2 Hz, 1 H), 4.28 (dd, *J* = 14.0, 1.6 Hz, 1 H), 4.24 (dd, *J* = 6.2, 1.6 Hz, 1 H), 1.31 (s, 9 H); ^{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-Phenylphenyl vinyl ether (**6e**): White solid, m.p. 72–73 °C. (lit.[14] m.p. 71–72 °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 (**6f**): Colourless oil (lit.[22] oil); ^{1}H NMR: δ = 7.43 (d, *J* = 8.4 Hz, 2 H), 7.01 (d, *J* = 8.4 Hz, 2 H), 6.63 (dd, *J* = 13.7, 6.1 Hz, 1 H), 4.80 (dd, *J* = 13.7, 1.8 Hz, 1 H), 4.51 (dd, *J* = 6.1, 1.8 Hz, 1 H); ^{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}.

4-Bromophenyl vinyl ether (**6g**): Colourless oil (lit.[14] oil); ^{1}H NMR: δ = 7.40 (d, *J* = 8.5 Hz, 2 H), 6.95 (d, *J* = 8.5 Hz, 2 H), 6.60 (dd, *J* = 13.8, 6.1 Hz, 1 H), 4.78 (dd, *J* = 13.8, 1.8 Hz, 1 H), 4.48 (dd, *J* = 6.1, 1.8 Hz, 1 H); ^{13}C NMR: δ = 155.9, 147.7, 132.6, 118.5, 115.7, 96.0; IR (neat): ν = 3050, 1636, 1578, 1475, 1230, 1160, 1140, 1060, 1000, 950, 820 cm^{-1}.

2-Bromophenyl vinyl ether (**6h**): Colourless oil (lit.[13] oil); ^{1}H NMR: δ = 7.67–7.65 (m, 1 H), 7.42–7.36 (m, 1 H), 7.21–7.18 (m, 1 H), 7.10–7.06 (m, 1 H), 6.80 (dd, *J* = 6.3, 13.5 Hz, 1 H), 4.68 (dd, *J* = 1.8, 13.5 Hz, 1 H), 4.53 (dd, *J* = 1.8, 6.3 Hz, 1 H); ^{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 (**6i**): Colourless oil (lit.[14] oil); ^{1}H NMR: δ = 8.25 (d, *J* = 8.9 Hz, 2 H), 7.10 (d, *J* = 8.9 Hz, 2 H), 6.68 (dd, *J* = 13.6, 6.0 Hz, 1 H), 5.01 (dd, *J* = 13.6, 1.9 Hz, 1 H), 4.70 (dd, *J* = 6.0, 1.9 Hz, 1 H); ^{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 (**6j**): Colourless oil (lit.[14] oil); ^{1}H NMR: δ = 7.70 (d, *J* = 8.6 Hz, 2 H), 7.10 (d, *J* = 8.6 Hz, 2 H), 6.66 (dd, *J* = 13.7, 6.1 Hz, 1 H), 4.98 (dd, *J* = 13.7, 2.0 Hz, 1 H), 4.68 (dd, *J* = 6.1, 2.0 Hz, 1 H); ^{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}.

4-Methoxycarbonylphenyl vinyl ether (**6k**): Colourless oil (lit.[14] oil); ^{1}H NMR: δ = 8.00 (d, *J* = 8.3 Hz, 2 H), 7.15 (d, *J* = 8.3 Hz, 2 H), 6.88 (dd, *J* = 13.6, 6.0 Hz, 1 H), 4.85 (dd, *J* = 13.6, 1.6 Hz, 1 H), 4.55 (dd, *J* = 6.0, 1.6 Hz, 1 H), 3.84 (s, 3 H); ^{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}.

4-Acetaminophenyl vinyl ether (**6l**): White solid, m.p. 102–103 °C. (lit.[14] m.p. 103–103.5 °C); ^{1}H NMR: δ = 7.40–7.50 (m, 2 H), 7.26 (br s, 1 H), 6.95–7.05 (m, 2 H), 6.63 (dd, *J* = 13.7, 6.1 Hz, 1 H), 4.75 (dd, *J* = 13.7, 1.7 Hz, 1 H), 4.55 (dd, *J* = 6.1, 1.7 Hz, 1 H), 2.18 (s, 3 H); ^{13}C NMR: δ = 169.2, 153.2, 148.5, 133.4, 122.1, 117.3, 94.6, 24.1; IR (KBr): ν = 3258, 3188, 3130, 3055, 1650, 1600, 1495, 1300, 1235, 1210, 1162, 1145, 940, 830 cm^{-1}.

1-Naphthyl vinyl ether (**6m**): White solid, m.p. 31–32 °C. (lit.[23] m.p. 32 °C); ^{1}H NMR: δ = 7.00–7.50 (m, 7 H), 6.71 (dd, *J* = 14.1, 6.0 Hz, 1 H), 4.81 (dd, *J* = 14.1, 1.6 Hz, 1 H), 4.45 (dd, *J* = 6.0, 1.6 Hz,

1 H); ^{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}.

We gratefully acknowledge financial support from the Natural Science Foundation of Jiangxi Province of P. R. China (No. 2007GZH839 and No. 2008GZH0029) and the Research Program of Jiangxi Province Department of Education (GJJ08165).

Received 26 December 2008; accepted 6 March 2009
Paper 08/0352 doi: 10.3184/030823409X447682
Published online: 20 May 2009

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