SHORT PAPER

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A convenient route to α,β-unsaturated aldehydes based on polymer-supported α-selenoaldehydes†

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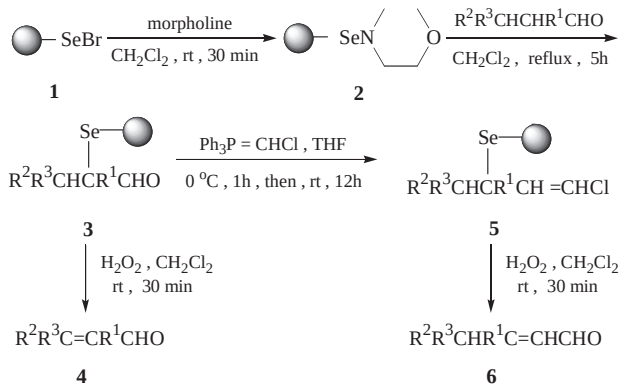
Polystyrene-supported (4-phenylseleno)morpholine was synthesised and could be used as an efficient α-selenenylating agent for saturated aldehydes; subsequent oxidation of polystyrene-supported α-selenoaldehydes and the products from the Wittig reaction of them with chloromethylidenetriphenylphosphorane with an excess of 30% hydrogen peroxide at room temperature afforded α,β-unsaturated aldehydes in good yields and purities.

Keywords: α,β-unsaturated aldehydes, polystyrene-supported (4-phenylseleno)morpholine, polystyrene-supported α-selenoaldehydes

During the last few years, solid-phase organic synthesis (SPOS) has been rapidly and extensively applied to the preparation of small organic molecules. Polymer-supported reagents have attracted growing interest because they can provide attractive and practical methods for combinatorial chemistry and SPOS.[1] α, β-Unsaturated aldehydes are a class of reagents useful in organic synthesis. Many methods are available for their synthesis and efforts are continuing for the development of more efficient methods with experimental simplicity. α-Selenoaldehydes, easily prepared from 4-(arylseleno)morpholines formed *in situ* with saturated aldehydes, [2a] are frequently used as important intermediates in organic synthesis.[3] For example, α-selenoaldehydes can be efficiently converted into α,β-unsaturated aldehydes by oxidation–elimination.[4] However, organoselenium reagents always have a foul smell and are quite toxic, which is often a problem in organic synthesis. With the successful synthesis of carbonyl compounds from polymer-bound vinylic selenides [5] and allylic ethers and esters [6] from polymer-bound selenium bromide in mind,[7] we wish to report here the very simple preparation of polystyrene-supported (4-phenylseleno)morpholine and its application as a powerful reagent for α-selenenylation of saturated aldehydes and the oxyselenenylation–deselenenylation reaction on solid-phase (Scheme 1). The use of these selenium reagents immobilised on polymer-resin has proved to provide significant advantages, including decreased volatility and simplification of product work-up.

Simple stirring of polymer-supported selenium bromide **1** with morpholine in CH_2Cl_2 resulted in nearly quantitative conversion into the polymer-supported (4-phenylseleno)morpholine **2**. Treatment of resin **2** with saturated aldehydes bearing an α-hydrogen gave the corresponding α-phenylselenoaldehyde resin **3**, as indicated by IR spectra showing a strong carbonyl absorption at 1700–1710 cm^{-1}, an aldehydic CH stretching absorption at 2720–2725 cm^{-1} and absence of the Se–N absorption at 1252 cm^{-1}. The minimum capacities of resins **3** were calculated to be 1.02–1.10 mmol CHO/g from the nitrogen elemental analysis of their corresponding aldoximes according to the method described in literature.[8] Oxidation–elimination of resin **3** was very rapid and efficient with an excess of 30% hydrogen peroxide at room temperature to afford the corresponding α,β-unsaturated aldehydes **4** in good yields (75–85%) and with high purities (>90%) (Table 1). The residual resin, polystyrene-supported phenylseleninic acid, was obtained as a by-product, the infrared data of which were identical to the previously reported data [9] and showed no residual carbonyl absorption. The polystyrene-supported phenylseleninic acid could be converted into resin **2** for recycling by treatment with $KI/Na_2S_2O_3$ [10,11] followed by Br_2 [5] and morpholine. On the other hand, treatment of resin **3** with chloromethylidenetriphenylphosphorane formed the resin **5** evidenced by the complete disappearance of the C=O absorption. Subsequent oxidation-rearrangement of resin **5** with hydrogen peroxide as above furnished another route for the preparation of α,β-unsaturated aldehydes **6** in good yields and purities. It is worthy of note that *E*-isomers of **4** and **6** are only formed from corresponding aldehydes, which are unsubstituted at C-2 except for **4d** (*E*/*Z* = 55:45). Resins **2, 3** and **5** are quite stable under the reaction conditions and can be stored in the air at room temperature for several months without loss of reactivity or the liberation of disagreeable odors.



Scheme 1

Table 1 Yield and purity of α, β-unsaturated aldehydes

Comp.	R^1		R^2	R^3	Yield/%[a]	Purity/%[b]
4a	H		H	CH_3	75	92
4b	H		H	C_2H_5	78	>95
4c	H		H	C_6H_5	85	>95
4d	H		CH_3	C_6H_5	80	>95
4e		$(CH_2)_4$		H	85	>95
6a	H		H	*n*-C_3H_7	81	90
6b	H		H	*n*-C_4H_9	75	92
6c	H		H	*n*-C_5H_{11}	77	93

[a]Overall yields based on polymer-supported 4-(phenylseleno)morpholine (1.12 mmol N/g).
[b]Determined by ^1H NMR (400 MHz) of the crude cleavage product.

In summary, we have developed novel polymer-supported 4-(phenylseleno)morpholine as an α-selenenylating agent for saturated aldehydes. Polymer-supported α-selenoaldehydes

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can efficiently be converted into α,β-unsaturated aldehydes in good yields and high purities. Although an excess amount of reagents was required, the considerably simplified workup procedure replaces the time-consuming isolation and purification steps in the corresponding solution-phase synthesis.

Experimental

^{1}H NMR spectra were recorded on a Bruker Avance 400 MHz instrument using $CDCl_3$ as the solvent and with TMS as an internal standard. Infrared spectra were obtained on a Bruker Vector-22 instrument. Polystyrene for the preparation of polymer-supported selenium bromide according to the procedure described in the literature [7] was purchased from Aldrich (H C100-2, 100–200 mesh, cross-linked with 1 % divinylbenzene).

Preparation of polymer-supported 4-(phenylseleno)morpholine ***2****:* Polystyrene-supported selenium bromide (1.0 g, 1.18 mmol Br/g) was swelled in CH_2Cl_2 (8 ml) for 30 min, and morpholine (2.40 mmol) was added. The mixture was stirred at room temperature for 30 min and filtered. After washing successively with H_2O, CH_3OH, CH_2Cl_2 (2×3 ml of each) and then drying in vacuum, the resin **2** containing 1.12 mmol N/g was obtained as a yellow beads. IR (KBr): 3058, 3024, 2920, 2849, 1600, 1584, 1492, 1449, 1275, 1252, 1108, 1067, 903, 755, 696 cm^{-1}. Anal Calcd for resin **2**: N, 1.64%. Found: N, 1.57%.

General procedure for preparation of α,β*-unsaturated aldehydes* **4** *(method A) and* **6** *(method B):*

Method A: Resin **2** (1.0 g, 1.12 mmol) was swelled in CH_2Cl_2 (8 ml) at room temperature for 30 min. The aldehyde (1.25 mmol) was then added, and the mixture was refluxed for 5 h, cooled, filtered and washed with CH_2Cl_2 (4×3 ml) to afford the resin **3**. The resin was swelled in CH_2Cl_2 (10 ml) at room temperature for 30 min. 30% Hydrogen peroxide (1 ml, 11.6 mmol) was added and the mixture was stirred at room temperature for 30 min. The resin was then filtered off and washed with CH_2Cl_2 (3×3 ml). The filtrate was treated with saturated $NaHCO_3$ solution and the organic extracts were washed with water, dried over magnesium sulfate and evaporated to give products **4**.

Method B: The dried resin **3** (1.0 g) was swelled in THF (8 ml) at room temperature for 30 min. After cooling 0°C, the solution of the chloromethylidenetriphenylphosphorane prepared from chloromethyltriphenylphosphonium chloride (1.5 mmol) and *n*–BuLi (in hexane 1.5 mmol) in 10 ml of THF was added under a nitrogen atmosphere and the mixture was stirred for 1 h at the same temperature. Then the reaction mixture was warmed up to room temperature and stirred for 12 h and filtered. After washing successively with H_2O, THF, CH_3OH, CH_2Cl_2 (2×3 ml of each), the resin **5** was obtained and treated with 30% hydrogen peroxide as above to afford the final products **6**.

(E)-But-2-enal (**4a**)[12] : oil , ^{1}H NMR δ2.05 (dd, *J* = 6.6, 1.7 Hz, 3H), 6.10 (ddq, *J* = 15.7, 7.5, 1.7 Hz, 1H), 6.87 (dq, *J* = 15.7, 6.6 Hz, 1H), 9.51 (d, *J* = 7.5 Hz, 1H); IR (film) 2733, 1694, 1641 cm^{-1}.

(E)-Pent-2-enal (**4b**)[12] : oil , ^{1}H NMR δ1.05 (t, *J* = 7.0 Hz, 3H), 2.15–2.22 (m, 2H), 6.05 (ddt, *J* = 16.0, 7.6, 1.5 Hz, 1H), 6.75 (dt, *J* = 16.0, 6.5 Hz,1H), 9.42 (d, *J* = 7.6 Hz, 1H); IR (film) 2731, 1680, 1634 cm^{-1}.

(E)-3-Phenylprop-2-enal (**4c**)[12] : oil , ^{1}H NMR δ 6.61 (dd, *J* = 16.1, 7.6 Hz, 1H), 6.85 (d, *J* = 16.1 Hz, 1H), 7.20–7.61 (m, 5H), 9.68 (d, *J* = 7.6 Hz, 1H); IR (film) 2743, 1677, 1626 cm^{-1}.

(E)- and (Z)-3-Phenylbut-2-enal (**4d**)[13] : oil , ^{1}H NMR δ 2.31, 2.55 (d, *J* = 1.7 Hz, 3H), 6.12, 6.35 (dq, *J* = 7.2, 1.7 Hz, 1H), 7.20–7.58 (m, 5H), 9.22, 9.45 (d, *J* = 7.2 Hz, 1H); IR (film) 2742, 1660 cm^{-1}.

Cyclohex-1-ene-1-carboxaldehyde (**4e**)[14] : oil , ^{1}H NMR δ 1.01–1.68 (m, 4H), 2.15–2.24 (m, 4H), 6.65 (dt, *J* = 6.9, 1.6 Hz,1H), 9.40 (d, *J* = 6.9 Hz, 1H); IR (film) 2722, 1680, 1630 cm^{-1}.

(E)-Hept-2-enal (**6a**)[14] : oil , ^{1}H NMR δ 0.98 (t, *J* = 7.1 Hz, 3H), 1.11–1.80 (m, 4H), 2.20–2.24 (m, 2H), 6.01 (ddt, *J* = 15.8, 7.6, 1.5 Hz, 1H), 6.75 (dt, *J* = 15.8, 6.5 Hz, 1H), 9.45 (d, *J* = 7.6 Hz, 1H); IR (film) 2720, 1684, 1633 cm^{-1}.

(E)-Oct-2-enal (**6b**)[15] : oil , ^{1}H NMR δ 0.95 (t, *J* = 7.0 Hz, 3H), 1.10–1.80 (m, 6H), 2.21–2.25 (m, 2H), 6.05 (ddt, *J* = 16.1, 7.6, 1.5 Hz, 1H), 6.77 (dt, *J* = 16.1, 6.5 Hz, 1H), 9.44 (d, *J* = 7.6 Hz, 1H); IR (film) 2722, 1690, 1635 cm^{-1}.

(E)-Non-2-enal (**6c**)[14] : oil , ^{1}HNMR σ 0.95 (t, *J* = 7.0 Hz, 3H), 1.13–1.78 (m, 8H), 2.23–2.27 (m, 2H), 6.05 (ddt, *J* = 16.1, 7.6, 1.5 Hz, 1H), 6.77 (dt, *J* = 16.1, 6.6 Hz, 1H), 9.44 (d, *J* = 7.6 Hz, 1H); IR (film) 2725, 1685, 1636 cm^{-1}.

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