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Solid-phase Synthesis of α-Haloaldehydes from Polymer-supported 4-(Phenylseleno)morpholine

Shou Ri SHENG[1, 2], Lu Ling WU[1], Xian HUANG[1]*

[1]Department of Chemistry, Zhejiang University (Xixi Campus), Hangzhou 310028
[2]Department of Chemistry, Jiangxi Normal University, Nanchang 330027

Abstract: Polystyrene-supported 4-(phenylseleno)morpholine was synthesized and could be used as an efficient α-selenenylating agent for saturated aldehydes. α-Haloaldehydes were prepared by reaction of polystyrene-supported α-selenoaldehydes with bromine or sulfuryl chloride in good yield and high purity.

Keywords: Solid phase organic synthesis, (4-phenylseleno) morpholine, α-selenoaldehyde, α-haloaldehyde.

Polymer-supported reagents for organic synthesis are enjoying a renewed popularity with the emergence of combinatorial chemistry in recent years[1]. 4-(Arylseleno)morpholines formed *in situ* are useful α-seleno-introducing reagents for saturated aldehydes[2]. α-Selenoaldehydes, as a frequently used intermediates, can be converted into α-haloaldehydes by halogenating reaction[3]. However, organic selenium reagents always have a foul smell and are quite toxic, which is often problematic in organic synthesis. With the successful synthesis of carbonyl compounds from resin-bound vinylic selenides[4], we here wish to report the very simple preparation of polystyrene-supported (4-phenylseleno) morpholine and its application as a powerful reagent for α- selenenylation of saturated aldehydes and deselenenylation reaction by halogenation on solid-phase (**Scheme 1**).

A remarkable advantage of these new polymer-supported selenium reagents is the convenience of handling and totally odorless nature as compared to the non-bound reagents. Furthermore, simple work-up procedures take the place of the time-consuming isolation and purification steps in the corresponding solution-phase synthesis.

Simply stirring polymer-supported selenium bromide **1**[5] with morpholine resulted in nearly quantitative conversion to the polymer-supported (4-phenylseleno) morpholine (1.12 mmol / g) by elemental analysis of nitrogen. Treatment of resin **2** with saturated aldehydes gave the corresponding α-phenylselenoaldehyde resins **3**, which were indicated by IR spectra showing strong carbonyl absorption at 1700-1710 cm^{-1} and disappearance of Se-N absorption at 1252 cm^{-1}. The minimum degree of functionalization of resins **3** could be calculated from the nitrogen analysis of their corresponding

*E-mail: huangx@mail.hz.zj.cn

Scheme 1

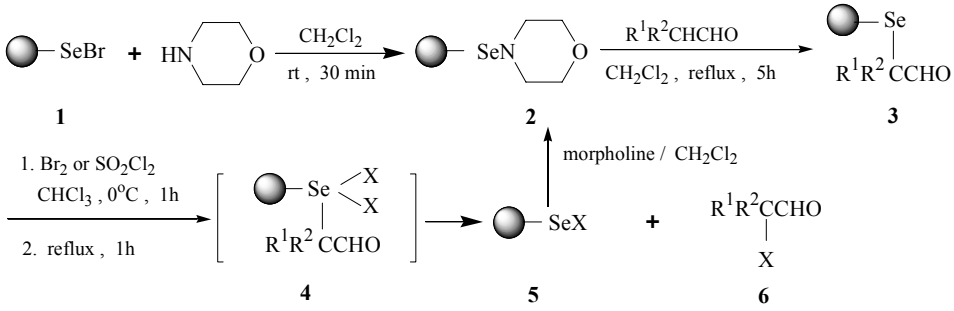

Table 1 Preparation of α-haloaldehydes

Entry	R^1	R^2	X	Product	Yield (%) [a]	Purity (%) [b]
1	CH_3CH_2	H	Br	**6a**	78	>95
2	C_6H_5	H	Br	**6b**	85	>95
3	C_6H_5	H	Cl	**6c**	74	>95
4	C_6H_5	CH_3	Br	**6d**	92	>95
5	C_6H_5	CH_3	Cl	**6e**	90	>95
6	C_6H_5	H	Br	**6b**	80	90 [c]
7	C_6H_5	H	Cl	**6c**	70	91 [c]

a. Overall yields based on polymer-supported 4-(phenylseleno)morpholine.
b. Determined by ^{1}H NMR (400 MHz) of the crude cleavage product.
c. Using recovered resin **2** (the 4th run).

aldoximes and corresponded to 1.02-1.10 mequiv of aldehyde functional group per gram. Treatment of resins **3** with the equimolar quantity of bromine or sulfuryl chloride furnish solid adduct **4** in $CHCl_3$ at 0°C. At more elevated temperature, these adducts decompose to give resin **5** upon simple filtration and α-haloaldehydes in good yield and high purity (**Table 1**) by evaporating the solvent. However, we can not obtain the corresponding compounds using iodine under the same conditions. Resin **2** can be regenerated by treatment of resin **5** with morpholine and reused several times without significant loss of activity, even after the fourth use.

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