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Polystyrene-supported benzyl selenide: an efficient reagent for highly stereocontrolled synthesis of olefins and allylic alcohols

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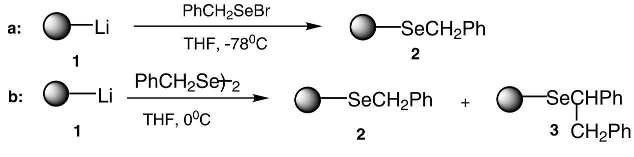
Abstract—Polystyrene-supported benzyl selenide has been prepared. This novel reagent was treated with LDA to produce a selenium-stabilized carbanion, which reacted with alkyl halide and epoxides, followed by selenoxide *syn*-elimination, to give olefins and allylic alcohols, respectively. © 2002 Elsevier Science Ltd. All rights reserved.

Solid-phase methodology has been rapidly and extensively applied to the preparation of small organic molecules recently. Polymer supported reagents have attracted growing interest because they can provide attractive and practical methods for combinatorial chemistry and solid-phase synthesis (SPS).[1]

α-Seleno alkyllithiums play an important role in organic synthesis because of their easy availability and high nucleophilicity, which allow the formation of new functionalized carbon–carbon bonds when they are used to react with carbon electrophiles.[2] It might be argued that selenoxide *syn*-elimination provided the principal impetus for the development of organoselenium chemistry. In addition, the required selenoxides are readily available from the oxidation of the corresponding selenides, which in turn can be prepared by the reaction of selenium-stabilized carbanions with various electrophilic substrates.[3] However, organic selenides are highly malodorous and generally unpleasant and difficult to handle, especially because of their toxicity. Several groups[4,5] have developed some organoselenium resins to solve this problem. Recently, our research group has been interested in the application of organic selenium resins in organic synthesis.[6] Since olefins and allylic alcohols are two important intermediates in organic synthesis, we report here a novel preparation of polystyrene-supported benzyl selenide and its application for a highly stereocontrolled synthesis of olefins[7] and allylic alcohols with significant advantages of easy operation, freedom from odors and good purities of products.



Scheme 1.

The preparation of polystyrene-supported benzyl selenide is described in Scheme 1a.

Dibenzyl diselenide did not react with resin **1** at −78°C. When the temperature was raised to 0°C, dibenzyl diselenide did react with resin **1**, but produced a mixture of resin **2** and resin **3**. So we adopted path **a** as the best method to prepare resin **2** in solid-phase synthesis.

Typical procedure for the preparation of polystyrene-supported benzyl selenide

To a suspension of the swelled resin **1** (2 g) in dry THF (30 mL), cooled to −78°C, was added dropwise benzylselenium bromide under nitrogen. After stirring for 0.5 h at −78°C, the resin **2** was collected by filtration and washed with THF (15 mL×2), ether (15 mL×2), THF/H_2O (3:1) (15 mL×2), H_2O (15 mL×2), benzene (15 mL×2), MeOH (15 mL×2), and CH_2Cl_2 (15 mL×2) and dried in vacuum. Resin **2** (Se: 1.01 mmol/g), IR

Keywords: solid-phase synthesis; polystyrene-supported benzyl selenide; allylic alcohol.

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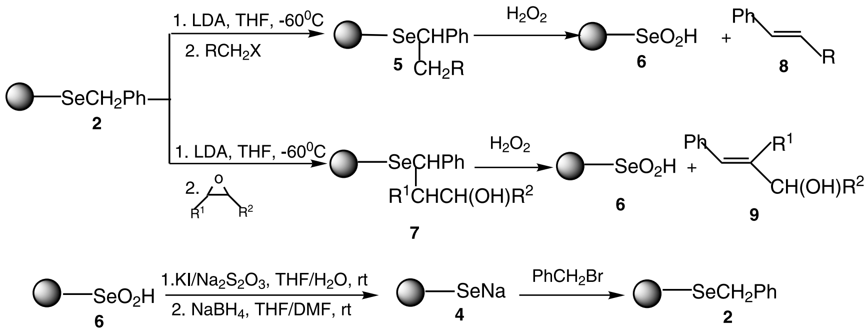


Scheme 2.

(KBr): 3024, 2921, 1601, 1492, 1451, 1180, 1069, 1028, 906, 864, 757, 697, 537 cm^{-1}.

Resin **2** reacted smoothly with LDA followed by substitution with alkyl halides to give resin **5**.[8] The resin **5** was converted to olefins **8** and resin **6** through oxide-elimination using hydrogen peroxide.[8] Resin **6** reacted with KI/$Na_2S_2O_3$[9] followed by $NaBH_4$ and benzyl bromide to regenerate resin **2**.[10] The use of epoxides in place of alkyl halides gave allylic alcohols using the same procedure (Scheme 2).[8] The results are summarized in Tables 1 and 2.

In summary, we have developed a novel method to prepare polystyrene-supported benzyl selenide. It was reacted with LDA and then with an alkyl halide or an epoxide, followed by oxidation and stereospecific selenoxide *syn*-elimination, to provide olefins and allylic alcohols, respectively. The novel polystyrene-supported benzyl selenide can be regenerated and reused.

Table 1. Yields and purities of olefins

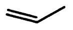
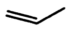
Products	R	X	Yield (%)[a]	Purity (%)[b]
8a	H-	I	81	95
8b	$(CH_3)_2CH$-	Br	79	97
8c	Ph-	Br	89	96
8d	*p*-$NO_2C_6H_4$	Cl	71	81
8e		Cl	87	94
8f		Br	91	93
8g[c]		Br	90	91

Table 2. Yields and purities of allylic alcohols

Products	R¹	R²	Yield (%)[a]	Purity (%)[b]
9a	H-	CH_3-	85	96
9b	H-	Ph-	88	95
9c[c]	H-	Ph-	86	95
9d	H-	$PhOCH_2$-	84	91
9e	$-CH_2CH_2CH_2CH_2-$		77	86

[a] Yields of products based on the loading of the resin **2**, the products were identified by ^1H NMR, MS and IR spectra.

[b] Determined by ^1H NMR (400 MHz).

[c] Using regenerated resin **2**.

Acknowledgements

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8. **Typical procedure for the preparation of olefins**: To a suspension of the swelled resin **2** (1 g) in dry THF, cooled to −60°C, was added dropwise LDA (2 M in THF/hexane, 0.75 mL) under nitrogen. After stirring for 0.5 h at −60°C, a solution of benzyl bromide (4 mmol) in 5 mL of dry THF was added. The suspension was stirred for another 0.5 h at −60°C. The resin **5** was collected by filtration and washed with THF (10 mL×2), MeOH (10 mL×2) and CH_2Cl_2 (10 mL×2). The washed resin was suspended in THF (15 mL). To the mixture was added 30% (aq.) H_2O_2 (1 mL) and stirred for 1 h at 0°C followed by 20 min at room temperature. The mixture was filtered and the resin was washed with CH_2Cl_2 (15 mL×2). The filtrate was washed with H_2O (30 mL×2), dried over $MgSO_4$, and evaporated to dryness in vacuo to afford 160 mg (89%) of pure (*E*)-1,2-diphenyl-ethene.
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10. **Typical procedure for the regeneration of polystyrene-supported benzyl selenide**: The resin **6** (2 g) was swelled in dry THF (30 mL) overnight. To the mixture was added a solution of KI/$Na_2S_2O_3$ (20 mmol, respectively) in 30 mL EtOH/H_2O (v/v = 1:1). The suspension was stirred at rt for 6 h. The resin was collected by filtration and washed with THF (10 mL×2), MeOH (10 mL×2) and CH_2Cl_2 (10 mL×2). The washed resin was suspended in 30 mL THF/DMF (v/v = 4:1). To the mixture was added $NaBH_4$ (0.19 g, 5.1 mmol). After stirring for 10 h at 40°C, benzyl bromide (8 mmol) was added. The suspension was stirred at 40°C for another 5 h. The resin **2** was isolated by filtration and washed with THF/H_2O (3:1) (15 mL×2), THF (15 mL×2), MeOH (15 mL×2), and CH_2Cl_2 (15 mL×2), and reused.