

Polystyrene-supported Selenomethyl-sulfonates: Efficient Reagents for Stereocontrolled Synthesis of Substituted Vinyl Sulfones

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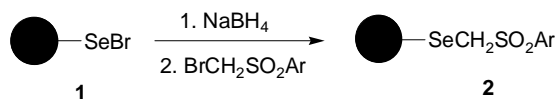
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Abstract: Polystyrene-supported selenomethyl-sulfonates have been prepared. These novel reagents were treated with LDA to produce selenium stabilized carbanions, which reacted with alkyl halide and epoxides, followed by selenoxide *syn*-elimination, to give *E*-vinyl sulfones and γ -hydroxy-substituted-*E*-vinyl sulfones respectively.

Keywords: Solid phase synthesis, polystyrene-supported selenomethyl-sulfonates, vinyl sulfones.

Solid-phase methodology has been rapidly and extensively applied to the preparation of small organic molecules recently¹. Organic selenides are of considerable interest in academia because of their wide involvement as key intermediates in organic synthesis. However, organic selenides are highly malodorous and generally unpleasant and difficult to handle, especially because of their toxicity. Since the first organoselenium resin² was reported in 1976, several groups have developed some organoselenium resins as convenient linkers³. Recently, our research group has been interested in the application of organic selenium resins in organic synthesis⁴. Since vinyl sulfones⁵ have now become generally accepted useful intermediates in organic synthesis, we report here a novel preparation of polystyrene-supported selenomethyl-sulfonates and its application for highly stereocontrolled syntheses of *E*-vinyl sulfones and γ -hydroxy-substituted *E*-vinyl sulfones, which have significant advantages of easy operation, freedom from odors, and good purities of products.

Scheme 1



2a Ar = Ph, **2b** *p*-CH₃C₆H₄

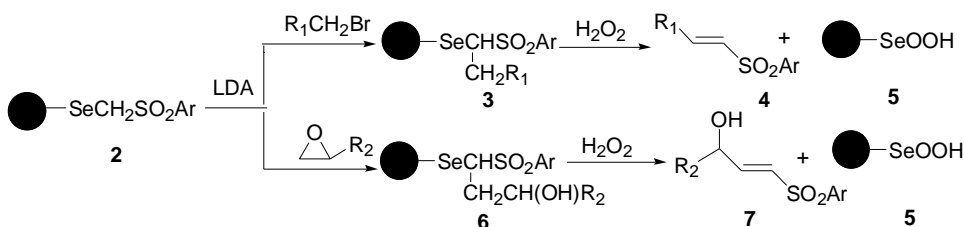
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We have developed a novel method to prepare polystyrene-supported selenomethyl-sulfonates. They reacted with LDA then alkyl halide and epoxides, followed by oxidation and stereospecific selenoxide *syn*-elimination, to provide vinyl sulfones and γ -hydroxy-substituted *-E*-vinyl sulfones. The novel polystyrene-supported selenomethyl-sulfonates can be regenerated and reused.

The preparation of polystyrene-supported selenomethyl-sulfonates (**Scheme 1**) is as follows: To a suspension of the swollen resin **1**³ (2 g) in dry THF /DMF (V/V=5:1) (30 mL) was added NaBH₄ (0.185 g) under nitrogen atmosphere at 45°C. After stirring for 12 h at 45°C, bromomethyl-sulfonates (8 mmol) were added dropwise, stirring for another 5 h. The resin **2** was collected by filtration, washed and dried in vacuum. Resin **2a** (S: 1.21 mmol/g), IR (KBr): 3444, 3058, 2922, 1600, 1566, 1449, 1318, 1301, 1149, 905, 823, 787, 757, 697, 540 cm⁻¹. Resin **2b** (S: 1.18 mmol/g), IR (KBr): 3445, 3058, 2921, 1599, 1567, 1451, 1318, 1301, 1145, 905, 816, 757, 698, 540 cm⁻¹.

Resin **2** reacted smoothly with LDA followed by substitution with alkyl halides to give resin **3**. The resin **3** was converted to vinyl sulfones **4** and resin **5** through selenoxide-elimination using hydrogen peroxide (**Scheme 2**). The use of epoxides in the place of alkyl halides gave γ -hydroxy-substituted-*E*-vinyl sulfones **7** using the same procedure. The results are summarized in **Table 1**. Resin **5** could be regenerated^{5a}.

Scheme 2

**Table 1** Reagents, yields and purities of substituted vinyl sulfones

Products	Resin	R ₁	R ₂	Yield (%) ^a	Purity (%) ^b
4a	2a	-Ph		84	95
4b	2b	-Ph		85	96
4c	2b	-CH ₃		87	95
4d	2a	-CH=CH ₂		89	96
4e^c	2a	-CH=CH ₂		88	96
7a	2a		-CH ₃	83	94
7b	2b		-CH ₃	85	92
7c	2b		<i>m</i> -CH ₃ -C ₆ H ₄ OCH ₂ -	79	92

a. Yields of products based on the loading of the resin **2**, the products were identified by NMR, MS and IR spectra. b. Determined by ¹H NMR (400MHz). c. Using regenerated resin **2a**.

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References

1. (a) R. E. Dolle, *J. Comb. Chem.*, **2001**, 3, (6), 1. (b) *Handbook of Combinatorial Chemistry* (Eds.: K. C. Nicolaou, R. Hanco, W. Hartwig), Wiley-VCH, Weinheim, **2002**.
2. R. Michels, M. Kato, W. Heitz, *Makromol. Chem.*, **1976**, 177, 2311.
3. (a) K. C. Nicolaou, J. Pastor, S. Barluenga, N. Winssinger, *Chem. Commun.*, **1998**, 1947. (b) Zaragoza, F. *Angew. Chem., Int. Ed. Engl.*, **2000**, 39, 2077.
4. Simpkins, N. S. *Sulphones in Organic Synthesis*, Pergamon Press: Oxford, **1993**.
5. (a) X. Huang, W. M. Xu *Tetrahedron Lett.*, **2002**, 43, 5495. (b) W. M. Xu, L. M. Yu, X. Huang, *Chin. Chem. Lett.*, **2003**, 4, 335. (c) X. Huang, S. R. Sheng, *J. Comb. Chem.*, **2003**, 5, 273. (d) H. Qian, X. Huang, *Tetrahedron Lett.*, **2002**, 43, 1063.

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