Polystyrene-Supported Selenosulfonates: Efficient Reagents for Regio- and Stereocontrolled Synthesis of Vinyl Sulfones

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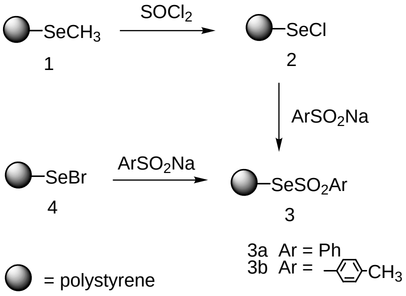
Abstract: Two novel polystyrene-supported selenosulfonates reagents have been developed. As reagents for boron trifluoride catalyzed or AIBN catalyzed addition to olefins were successfully demonstrated and have been used for regioselective synthesis of vinyl sulfones.

Key words: solid-phase synthesis, selenosulfonate, polymer reagent, vinyl sulfone

Solid-phase reactions play an important role in parallel synthesis and combinatorial chemistry, particularly in the area of medicinal chemistry, where their potential has emerged as a result of the possibility of automation.[1] Vinyl sulfones (α,β-unsaturated sulfones) have now become generally accepted useful intermediates in organic synthesis. Thus vinyl sulfones serve efficiently as both Michael acceptors and π partners in cycloaddition reaction.

Many methods for preparing vinyl sulfones have been developed.[2] Among these methods the method for ionic and radical addition of selenosulfonate to alkenes and alkynes is more important.[3] This convenient method can introduce two synthetically versatile functionalities, sulfone and selenide, into a given unsaturated substrate in one step. Organoselenium reagents, however, typically have a foul smell and are quite toxic, which is often problematic in organic synthesis.

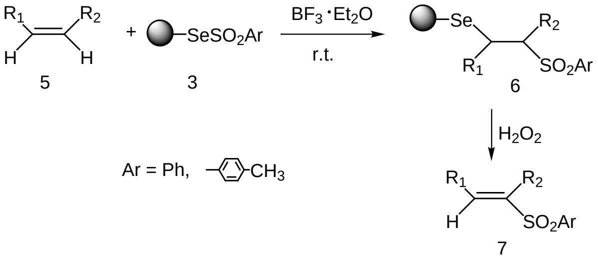
Our research group has been interested in the application of organo- selenium reagents in the organic synthesis for many years. Now we wish to report the preparation of polystyrene-supported selenosufonates and their application for regio and stereocontrolled synthesis of vinyl sulfones. A distinct advantage of the new polymer reagents is the convenience of handling and odorless nature as compared to the non-polymer-supported reagents. The preparation of the polystyrene-supported benzeneselenosulfonate and tolueneseleno-sulfonate is described in Scheme 1.



Scheme 1

Resin **1,** prepared by literature route,[4] reacted with thionylchloride to give resin **2** (elemental analysis Cl, 1.8 mmol/g),[5] which was treated with sodium benzenesulfinate or sodium toluenesulfinate in DMF at room temperature to afford resin **3** (elemental analysis S, 1.12 mmol/g).[6] Resin **3** can also been prepared by reaction of resin **4** (elemental analysis Br, 1.71 mmol/g)[4] with sodium benzenesulfinate or sodium toluenesulfinate in DMF at room temperature (elemental analysis S, 1.33 mmol/g).

Back and co-workers reported[3] that the selenosulfonation of unsymmetrical olefins catalyzed by boron trifluoride evidently results chiefly or exclusively in Markovnikov addition. We first examined the selenosulfonation of olefins by the resin **3** in the presence of the boron trifluoride at room temperature (Scheme 2). Thus the resin **3**, cyclohexene and a catalytic amount of boron trifluoride etherate were stirred at room temperature for 40 h, then the mixture was filtered. The obtained resin **6** may be converted to 1-*p*-toluenesulfonylcyclohexene by hydrogen peroxide in good yield.[7] Results are shown in Table 1.



Scheme 2

In contrast to the selenosulfonation of olefins by ionic addition, radical additions of resin **3** to olefins performed by AIBN catalyasis led to the highly regioselective formation

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1437-2096,E;2001,0,12,1913,1916,ftx,en;Y19101ST.pdf.

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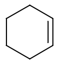
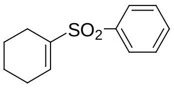
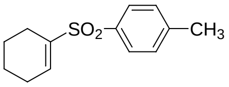
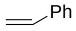
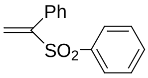
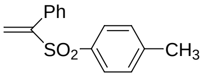
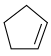
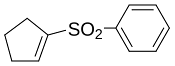
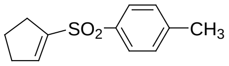
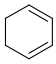
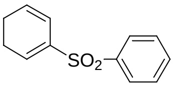
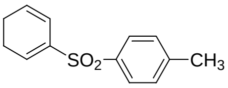
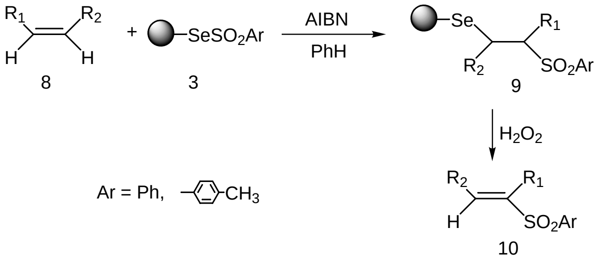
Table 1 Boron Trifluoride Catalyzed Selenosulfonation of Olefins

Entry	Olefin	Resin **3**	Product	Yield (%)[a]	Purity (%)[b]
1	 **5a**	**3a**		86	>95
2	**5a**	**3b**		87	>95
3	 **5b**	**3a**		78	>90
4	**5b**	**3b**		82	>90
5	 **5c**	**3a**		85	>95
6	**5c**	**3b**		86	>95
7	 **5d**	**3a**		87	>95
8	**5d**	**3b**		87	>95

[a] Yields of products based on the loading of the resin **3** and the products were identified by mp and ^{1}H NMR, MS, IR spectra.
[b] Determined by ^{1}H NMR (400 MHz).

of anti-Markovnikov products (Scheme 3). The resin **3**, styrene and a catalytic amount of AIBN were stirred in benzene at reflux for 20 h. The reaction mixture was filtered and the obtained resin **9** may be converted to (*E*)-1-phenyl-2-(*p*-toluenesulfonyl)ethene by hydrogen peroxide in good yield.[8] In the absence of AIBN, the yield of the vinyl sulfone is only 32%. Results are summarized in Table 2.



Scheme 3

In conclusion, we have developed two novel polystyrene-supported selenosulfonates reagents, which were readily prepared from polystyrene-supported selenenyl chloride or polystyrene-supported selenenyl bromide. We successfully demonstrated the viability of polystyrene-supported selenosulfonates as reagents for boron trifluoride or AIBN catalyzed addition to olefins and had been used for regiocontrolled synthesis of vinyl sulfones.

Acknowledgement

We are grateful to the National Natural Science Foundation of China (Project No.29932020) for the financial support.

References

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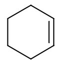
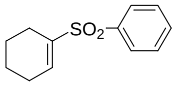
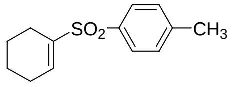
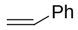
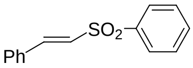
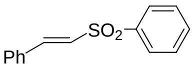
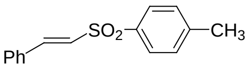
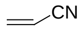
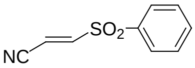
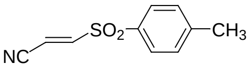
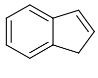
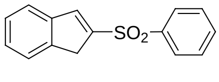
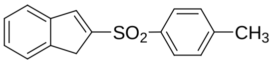
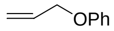
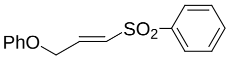
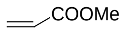
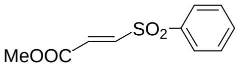
Table 2 AIBN Catalyzed Selenosulfonation of Olefins

Entry	Olefin	Resin **3**	Product	Yield (%)[a]	Purity (%)[b]
1	 **8a**	**3a**		89	>95
2	**8a**	**3b**		90	>95
3	 **8b**	**3a**		92	>90
4	**8b**	**3a**		32 [c]	
5	**8b**	**3b**		92	>90
6	 **8c**	**3a**		71	>95
7	**8c**	**3b**		73	>95
8	 **8d**	**3a**		89	>95
9	**8d**	**3b**		90	>95
10	 **8e**	**3a**		74	>90
11	 **8f**	**3a**		70	>90

[a] Yields of products based on the loading of the resin **3** and the products were identified by mp and ^{1}H NMR, MS, IR spectra.
[b] Determined by ^{1}H NMR (400 MHz).
[c] Without AIBN.

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(4) Nicolaou, K. C.; Pastor, J.; Barluenga, S.; Winssinger, N. *Chem. Commun.* **1998**, 1947.

(5) Preparation of polystyrene supported selenenyl chloride **2**: Polystyrene supported methylselenide **1** (1.96 mmol/g, Se, 2 g), prepared from 1% cross-linked polystyrene beads as ref. 4 describes, was swelled in CH_2Cl_2 (30 mL) overnight. Thionyl chloride (20 mL) was added to the mixture and the mixture was refluxed for 24 h. The IR spectrum of the reacted resin **2** exhibited no absorption at 1274 cm^{-1} which is ascribable to methyl group ($SeCH_3$). Then the mixture was cooled to room temperature and filtered. The resin was washed successively with CH_2Cl_2 (15 mL × 2), MeOH (20 mL × 2), THF (15 mL × 2), CH_2Cl_2 (15 mL × 2) and finally dried in vacuum. Elemental analysis: Cl, 1.8 mmol/g. IR (KBr): 3024, 2921, 1600, 1492, 1452, 1028, 758, 698 cm^{-1}.

(6) A typical procedure for preparation of polystyrene supported phenyl selenosulfonate **3**: Under a nitrogen atmosphene, resin **2** (2 g) was swelled in DMF (20 mL) over night. To the mixture was added sodium benzenethiosulfonate (12 mmol)

and stirred at room temperature for 6 h. The resin **3** was collected on a filter and washed with DMF (15 mL), H_2O (20 mL × 4), EtOH (15 mL × 2), MeOH (15 mL), THF (15 mL × 2), CH_2Cl_2 (15 mL × 2), and dried in vacuum. **3a.** (S, 1.12 mmol/g), IR (KBr): 3024, 2921, 1600, 1492, 1446, 1320, 1134, 1073, 823, 753, 697, 579, 527 cm^{-1}. **3b**. (S, 1.33 mmol /g), IR (KBr): 3024, 2921, 1600, 1492, 1457, 1452, 1320, 1134, 1075, 811, 757, 698, 645, 572, 512 cm^{-1}.

(7) A typical experimental procedure: Under a nitrogen atmosphere, to a suspension of the swelled resin **3b** (0.5 g) in dry CH_2Cl_2 (8 mL) was added cyclohexene (3 mmol, 0.3 mL) and 3 drops of boron trifluoride etherate. The mixture was stirred at room temperature for 40 h. The resin **6** was collected by a filter and washed with CH_2Cl_2 (10 mL × 2), MeOH (10 mL × 2), THF (10 mL × 2), CH_2Cl_2 (10 mL × 2). Then the washed resin **6** was suspended in THF (15 mL). To the mixture was added 30% H_2O_2 (2 mL) at 0 °C and stirred for 2 h at room temperature. The mixture was filtered, the resin was washed with CH_2Cl_2 (15 mL × 3). The filtrate was washed with H_2O (30 mL × 2) and dried over $MgSO_4$, and evaporated to dryness in vacuo to afford 135 mg (86%) of the pure 1-*p*-toluenesulfonylcyclohexene.

(8) A typical experimental procedure: Under a nitrogen atmosphere, to a suspension of the swelled resin **3b** (0.5 g) in dry benzene (8 mL) was added styrene (3 mmol, 312 mg) and AIBN (0.15 mmol, 24 mg). The mixture was refluxed for 20 h. The resin **9** was collected by a filter and washed with benzene (10 mL × 2), MeOH (10 mL × 2), THF (10 mL × 2), CH_2Cl_2 (10 mL × 2). Then the washed resin **9** was suspended in THF (15 mL). To the mixture was added 30% H_2O_2 (2 mL) at 0 °C and stirred for 2 h at room temperature. The mixture was filtered, the resin was washed with CH_2Cl_2 (15 mL × 3). The filtrate was washed with H_2O (30 mL × 2) and dried over $MgSO_4$, and evaporated to dryness in vacuo to afford 149 mg (87%) of the pure (*E*)-1-phenyl-2-(*p*-toluenesulfonyl)ethene.