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Polystyrene-supported selenosulfonates: efficient reagents for the synthesis of acetylenic sulfones

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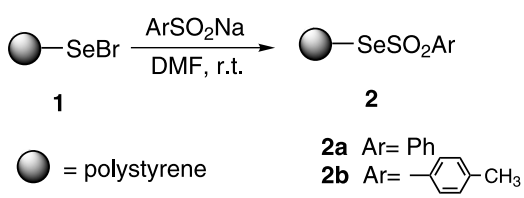
Abstract—Two novel polystyrene-supported selenosulfonate reagents have been developed for AIBN-catalyzed addition to acetylenes and have been used for the synthesis of acetylenic sulfones.

During the last few years, solid-phase methodology 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 solid-phase synthesis.[1] Acetylenic sulfones have become generally accepted as useful intermediates in organic synthesis. The chemistry of acetylenic sulfones has been extensively studied and widely exploited in organic synthesis for several years.

Many methods have been developed for preparing acetylenic sulfones.[2] Among these methods, an important method involves radical addition of selenosulfonates to acetylenes.[2c,3] However, organic selenium reagents always have a foul smell and are quite toxic, which is often problematic in organic synthesis. Although polymers with selenium functionalities have been known for a long time, there remains high interest in this kind of solid-phase organic chemistry. Recently, selenium-based approaches for solid-phase chemistry have been reported from different research groups.[4,5] Our research group has been interested in the applications of organic selenium reagents in organic synthesis for many years. We now wish to report a preparation of polystyrene-supported selenosulfonates and their application for the synthesis of acetylenic sulfones. An advantage of the novel polymer reagents is their convenience of handling and their odorless nature when compared with non-polymer-supported reagents.

The preparation of the polystyrene-supported benzene selenosulfonate and toluene selenosulfonate is described in Scheme 1.

Resin **1** prepared by a literature procedure[5] (elemental analysis Br, 1.71 mmol/g) was reacted with sodium benzenesulfinate or sodium toluenesulfinate in DMF at room temperature to afford resin **2** in nearly quantitative yield (elemental analysis S, 1.33 mmol/g). Back and co-workers[3] reported the selenosulfonation of acetylene, the reaction being highly regioselective and stereoselective. So we examined the selenosulfonation of acetylenes by resin **2** under AIBN catalysis (Scheme 2). The resin **2**, the acetylenes and a little AIBN were mixed and the mixture refluxed for 20 h in benzene. The reaction mixture was filtered and washed. The resins **4** obtained were converted to acetylenic sulfones and resin **6**[6,7] using hydrogen peroxide in good yield. The products do not require purification and show good purity (>95%) by ^{1}H NMR (400 MHz). Resin **2** can be regenerated by reacting resin **6** with



Scheme 1.

Keywords: solid-phase synthesis; polystyrene-supported; selenosulfonate; acetylenic sulfone.

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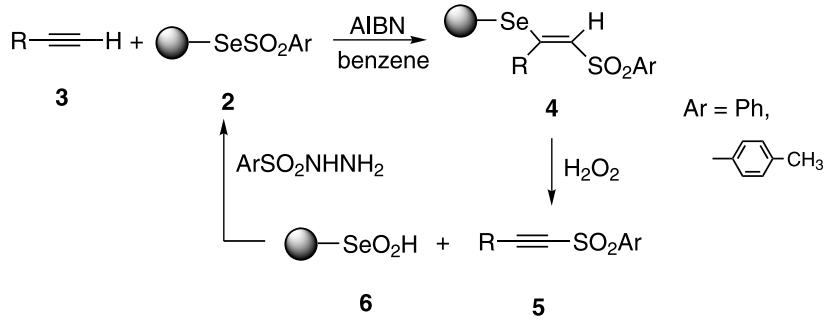

Scheme 2.

sulfonylhydrazides[8] and can be reused. The results are summarized in Table 1.

Typical procedure for the preparation of polystyrene supported phenyl selenosulfonate: Under a nitrogen atmosphere, resin **1** (2 g) was swelled in DMF (20 ml) overnight. To the mixture was added sodium benzenethiosulfonate (12 mmol) and the mixture was stirred at room temperature for 6 h. Resin **2** was collected by filtration and washed alternately 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 under vacuum. **2a**. (S, 1.33 mmol/g), IR *v* (KBr): 3024, 2921, 1600, 1492, 1446, 1320, 1134, 1073, 823, 753, 697, 579 and 527 cm^{-1}. **2b**. (S, 1.30 mmol /g), IR *v* (KBr): 3024, 2921, 1600, 1492, 1457, 1452, 1320, 1134, 1075, 811, 757, 698, 645, 572 and 512 cm^{-1}.

Typical procedure for the synthesis of acetylenic sulfones: To a suspension of the swelled resin **2b** (0.5 g) in dry benzene (8 ml) was added phenylacetylene (3 mmol, 306 mg) and AIBN (0.15 mmol, 24 mg) under a nitrogen atmosphere. The mixture was refluxed for 20 h. The resin **4** was collected by filtration and washed with benzene (10 ml×2), MeOH (10 ml×2), THF (10 ml×2) and CH_2Cl_2 (10 ml×2). The washed resin **4** was suspended in THF (15 ml). To the mixture was added 30% H_2O_2 (2 ml) at room temperature and the mixture was stirred for 2 h at 60°C. The mixture was filtered and the resin was washed with CH_2Cl_2 (15 ml×3). The filtrate was washed with H_2O (30 ml×2), dried over $MgSO_4$, and evaporated to dryness in a vacuum to afford 140 mg (84%) of the pure 1-phenyl-2-(*p*-toluenesulfonyl)-ethyne.

Typical procedure for regeneration of the polystyrene supported phenyl selenosulfonate: The resin **6** (1 g) was swelled in THF (20 ml) overnight. To the mixture was added benzenesulfonylhydrazide (5 mmol) at 0°C and the mixture was stirred at room temperature for 20 h. The regenerated resin **2** was collected by filtration and washed alternately with THF (15 ml×2), MeOH (15 ml×2), CH_2Cl_2 (15 ml×2), and then dried under vacuum.

In summary, we have developed two novel polystyrene-supported selenosulfonate reagents which were readily prepared from polystyrene-supported selenenyl bromide. The selenosulfonation of acetylenes with the polystyrene-supported selenosulfonate reagents, followed by oxidation and stereospecific selenoxide *syn* elimination, provides a convenient method for the synthesis of acetylenic sulfones.

Table 1. Synthesis of acetylenic sulfones by AIBN-catalyzed selenosulfonation of acetylene and oxidation–elimination

Products	R	Ar	Yield (%)[a]	Purity (%)[b]
5a	Ph-	*p*-$CH_3C_6H_4$-	84	>95
5b	Ph-	Ph-	86	>95
5c[7]	$PhOCH_2$-	*p*-$CH_3C_6H_4$-	84	>95
5d[7]	$PhOCH_2$-	Ph-	82	>95
5e	*n*-C_4H_9-	*p*-$CH_3C_6H_4$-	69	>95
5f	*n*-C_4H_9-	Ph-	72	>95
5g	$MeOC_6H_4$-	*p*-$CH_3C_6H_4$-	76	>95
5h	*p*-$CH_3C_6H_4$-	*p*-$CH_3C_6H_4$-	86	>95
5i	*p*-$CH_3C_6H_4$-	Ph-	88	>95
5j	*p*-BrC_6H_4-	*p*-$CH_3C_6H_4$-	89	>95
5k[7]	*p*-BrC_6H_4-	Ph-	90	>95
5l[c]	Ph-	Ph-	82	>95
5m[c]	Ph-	*p*-$CH_3C_6H_4$-	82	>95

[a] Yields of products based on the loading of resin **2**, the products were identified by mp, ^1H NMR, MS and IR spectra.[9]
[b] Determined by ^1H NMR (400 MHz)
[c] Using regenerated resin **2**.

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9. Spectral data for new products: **5c**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, 2H), 7.36 (d, 2H), 7.26 (m, 2H), 7.02 (m, 1H), 6.87 (m, 2H), 4.80 (s, 2H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 157.1, 145.8, 138.2, 130.0, 129.7, 127.6, 122.3, 115.0, 88.7, 83.8, 55.5, 21.8; MS (EI) m/z: 286 (M^+), 221, 179, 139, 131, 91, 77; IR ν (KBr): 3064, 3042, 2924, 2855, 2206, 1597, 1495, 1337, 1212, 1162, 1088, 1050, 814, 708, 690, 590 cm^{-1}; anal. calcd for $C_{16}H_{14}O_3S$: C, 67.11; H, 4.93. Found: C, 66.94; H, 4.95. **5d**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (m, 2H), 7.68 (t, 1H), 7.56 (m, 2H), 7.27 (m, 2H), 7.02 (t, 1H), 6.87 (m, 2H), 4.80 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 157.0, 141.4, 134.5, 129.7, 129.4, 127.5, 122.4, 115.0, 89.2, 83.5, 55.5; MS (EI) m/z: 272 (M^+), 207, 179, 131, 103, 97, 91, 77; IR ν (KBr): 3065, 2920, 2853, 2206, 1598, 1494, 1448, 1335, 1212, 1165, 1088, 1050, 755, 732, 687, 598, 570 cm^{-1}; anal. calcd for $C_{15}H_{12}O_3S$: C, 66.16; H, 4.44. Found: C, 66.36; H, 4.45. **5k**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (m, 2H), 7.69 (m, 1H), 7.61 (m, 2H), 7.52 (m, 2H), 7.39 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 141.6, 134.3, 134.0, 132.2, 129.5, 127.5, 126.6, 116.8, 92.1, 86.3; MS (EI) m/z: 322 (M^+, ^{81}Br), 320 (M^+, ^{79}Br), 258, 256, 229, 227, 199, 197, 185, 183, 176, 125, 91, 77; IR ν (KBr): 3063, 2184, 1582, 1483, 1448, 1395, 1330, 1161, 1086, 1071, 1010, 841, 761, 690, 584, 557 cm^{-1}; anal. calcd for $C_{14}H_9BrO_2S$: C, 52.35; H, 2.82. Found: C, 52.21; H, 2.82.
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