

## Solid-Phase Synthesis of Acrylamide Using Polymer-Supported $\beta$ -Selenopropionic Acid

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**Abstract:** A novel polystyrene-supported  $\beta$ -selenopropionic acid has been developed and applied to facile synthesis of acrylamides.

**Keywords:** Solid phase organic synthesis,  $\beta$ -selenopropionic acid, acrylamide.

Polymer-supported reagents have found increasing applications for the preparation of small organic molecules during the past few years<sup>1</sup>. The purification of the organic products has been greatly simplified through the use of polymer-supported reagents. Acrylamides, useful monomers for polyacrylamides and intermediates in organic synthesis, have been known to chemists for a long time. Several solid-phase synthesis of amides have already been reported, but to the best of our knowledge, all previous reports for related solid-phase synthesis of acrylamides have paid no attention to the use of phenylseleno group as leaving group. Polymer-bound selenides have proven to be versatile traceless linkers, which give access to alkenes by oxidation followed by  $\beta$ -elimination<sup>2</sup>. Meanwhile, the use of the selenium reagents immobilized on polymer-resin has provided significant advantages, including decrease volatility and simplification of product work-up. With the successful synthesis of carbonyl compounds from polymer-bound vinylic selenides,<sup>3</sup> we here wish to report a facile solid-phase synthetic approach to acrylamides based on a novel polystyrene-supported  $\beta$ -selenopropionic acid (**Scheme 1**).

Treatment of polystyrene-supported selenium bromide **1**<sup>2</sup> with NaBH<sub>4</sub>,<sup>4</sup> followed with  $\beta$ -bromopropionic acid to afforded polystyrene-supported  $\beta$ -selenopropionic acid **3**. The minimum loading of COOH of resin **3** verified by their FT-IR spectra exhibiting a strong carbonyl absorption at 1708 cm<sup>-1</sup> was determined by acid-base titration<sup>5</sup> to be 1.23 mmol COOH/g. Reaction of resin **3** with excess thionyl chloride in anhydrous 1,2-dichloroethane under reflux for 10 h gave polystyrene-supported  $\beta$ -selenopropanoyl chloride **4**, which showed a single strong carbonyl absorption at 1768 cm<sup>-1</sup> in FT-IR. After removing excess thionyl chloride, and without further isolation, it was allowed to react with corresponding primary or secondary amines in the presence of anhydrous

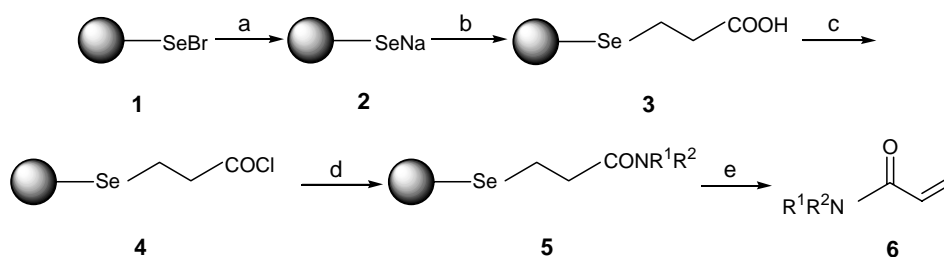
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triethylamine to form  $\beta$ -selenopropanamide resins **5** as evidenced by FT-IR with appearance of carbonyl absorption at 1645-1665  $\text{cm}^{-1}$  and complete disappearance of peak at 1708  $\text{cm}^{-1}$ .

As expected, oxidation-elimination of resin **5** was very rapid and efficient with excess of 30% hydrogen peroxide at room temperature to produce the corresponding acrylamides **6** in good yields (85-93 %) and with high purity of crude materials in all cases (>95 % by  $^1\text{H}$  NMR analysis). A summary of these results is given in **Table 1**. The residual resin with no residual carbonyl absorption in FT-IR shown the oxidative cleavage was complete.

Scheme 1



Reagents and conditions: (a)  $\text{NaBH}_4$ , DMF/THF, rt, 6 h; (b)  $\text{Br}(\text{CH}_2)_2\text{COOH}$ , rt, 10 h; (c)  $\text{SOCl}_2$ ,  $\text{ClCH}_2\text{CH}_2\text{Cl}$ , reflux, 10 h; (d)  $\text{R}^1\text{R}^2\text{NH}$ ,  $\text{Et}_3\text{N}$ , rt, 2 h; (e)  $\text{H}_2\text{O}_2$ ,  $\text{CH}_2\text{Cl}_2$ , rt, 30 min.

**Table 1** Yields and purities of acrylamides

Product	$\text{R}^1$	$\text{R}^2$	Yield (%) <sup>a</sup>	Purity (%) <sup>b</sup>
<b>6a</b>	$\text{C}_6\text{H}_5$	H	90	>95
<b>6b</b>	4- $\text{CH}_3\text{C}_6\text{H}_4$	H	93	>95
<b>6c</b>	4- $\text{ClC}_6\text{H}_4$	H	92	>95
<b>6d</b>	$\text{C}_6\text{H}_5\text{CH}_2$	H	89	>95
<b>6e</b>	<i>i</i> - $\text{C}_3\text{H}_7$	<i>i</i> - $\text{C}_3\text{H}_7$	88	>95

a) Overall yields based on the loading of resin **3**. b) Determined by  $^1\text{H}$  NMR (400 MHz).

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