Preparation of Polymer-Supported Selenocyanates and their Application to Solid-Phase Oxyselenenylation-Deselenenylation

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Received 28 August 1999

Abstract: Polymer-supported selenocyanates were readily prepared from substituted-polystyrene resins such as Merrifield resin and aminomethyl-polystyrene resin. Employing these polymer-supported selenocyanates, the corresponding oxyselenenylation-deselenenylation reactions proceeded in the solid-phase.

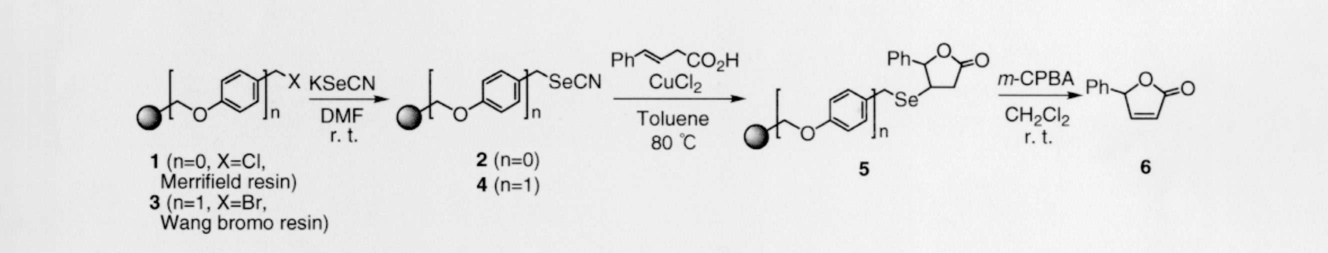
Key words: polymer-supported selenocyanate, solid-phase synthesis

Solid-phase organic synthesis is a powerful and rapid method for the preparation of large numbers of structurally distinct molecules.[1] In the case of this technique, the purification of organic molecules has been greatly simplified through the use of polymer-resins.

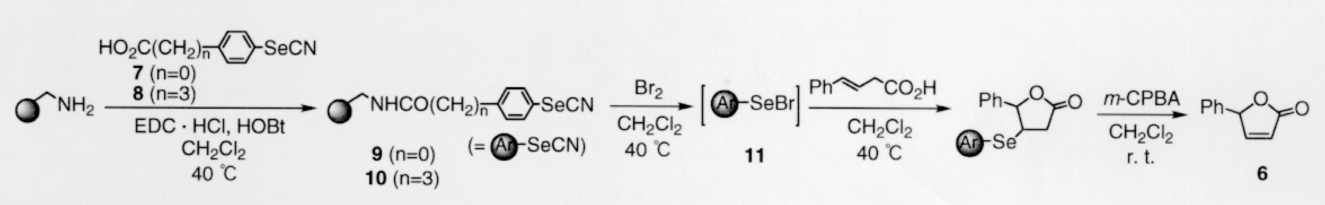
The use of organoselenium reagents in organic synthesis is now commonly accepted as a powerful tool for introducing new functional groups into organic substrates under extremely mild reaction condition.[2] Among them, selenocyanate is a useful seleno-introducing reagent that is employed as both an electrophilic and nucleophilic reagent.[3] Very recently, Nicolaou *et al.* have reported the preparation of polymer-supported selenenyl bromide from polystyrene resin and its application to organic synthesis.[4] Herein, we wish to report the very simple preparation of polymer-supported selenocyanates[5] from substituted-polystyrene resins such as the readily available Merrifield resin and aminomethyl-polystyrene resin, and their application as reagents to the oxyselenenylation-deselenenylation reaction in the solid-phase. A remarkable advantage of these polymer-supported selenocyanates is their easy handling and odorless nature, as compared with non-supported selenocyanates, whose toxicity and strong odor is often problematic in the laboratory.

Polymer-supported selenocyanates were prepared according to Scheme 1. Chloromethyl-polystyrene resin **1** (Merrifield resin, 4.3 mmol/g, crosslinked with 2 % divinylbenzene) was treated with potassium selenocyanate in *N*,*N*-dimethylformamide (DMF) at room temperature for overnight. Formation of polymer-supported selenocyanate **2** was indicated by IR spectra showing a strong stretching vibration of the cyano group at 2149 cm^{-1}. Elemental analysis of selenium showed that **2** was obtained in nearly quantitative yield.[6] Similarly, Wang bromo resin **3** (1.05 mmol/g, crosslinked with 1 % divinylbenzene), which possessed a phenoxymethyl linker, also afforded the corresponding polymer-supported selenocyanate **4** in nearly quantitative yield.[7]

In application to solid-phase synthesis, we have examined an electrophilic oxyselenenylation reaction,[2d] which proceeds exclusively by mechanism of *trans*-addition. First, through the addition of bromine to **2** in dichloromethane to produce the corresponding selenenylbromide,[8] elemental selenium was deposited *via* the decomposition of **2**, contrary to our expectation. Then, stirring **2** and (*E*)-4-phenyl-3-butenoic acid in the presence of copper chloride (II) in toluene at 80 °C,[9] the corresponding intramolecular oxyselenenylation (namely, selenolactonization) proceeded in the solid-phase to produce polymer-supported selenolactone **5**(n=0) (Scheme 1), indicated by a strong carbonyl stretching vibration at 1776 cm^{-1} in the IR spectrum. Moreover, through the oxidation of **5**(n=0) with *m*-chloroperbenzoic acid (*m*-CPBA),[2d] the deselenenylation product **6** was obtained in fair yield (56 % yield from **2**). However in the case of **4**, the corresponding solid-phase selenolactonization by use of copper chloride (II) did not proceed smoothly to afford a slight amount of **6**.



Scheme 1



Scheme 2

We also prepared polymer-supported arylselenocyanates, whose selenocyano groups are directly attached to the aromatic ring (Scheme 2). Stirring either arylselenocyanate **7** or **8**[10] and aminomethyl-polystyrene resin (2.0 mmol/g, crosslinked with 3 % divinylbenzene) in the presence of 3-ethyl-1-[3-(dimethylamino)propyl]carbodiimide hydrochloride (EDC·HCl) and 1-hydroxybenzotriazole (HOBt) in dichloromethane,[11] the corresponding polymer-supported arylselenocyanates **9** and **10** were obtained respectively in nearly quantitative yield.[12] In this type of polymer-supported selenocyanate, the corresponding selenenyl bromide **11**, which acted as an electrophilic reagent, was easily prepared by the addition of bromine. Furthermore, after the removal of excess bromine, the corresponding solid-phase selenolactonization of (*E*)-4-phenyl-3-butenoic acid proceeded in dichloromethane. Also in this case, subsequent deselenenylation reaction with *m*-CPBA proceeded smoothly to provide **6** in decent yield (33 % yield from **9**, 46 % yield from **10**).

Moreover, in the case of using **10** and 4-pentenoic acid, the corresponding solid-phase selenolactonization proceeded smoothly to afford **12** (Scheme 3). However, followed by reduction with triphenyltin hydride (Ph_3SnH),[13] the corresponding deselenenylation product **13** was obtained in low yield probably due to unexpected side-reaction of amide linker with Ph_3SnH (20 % yield from **10**).

We are currently trying to apply this method to other reactions and to the asymmetric version. The results will be reported in due course.

References and Notes

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(6) **2**: pale yellow beads; IR (KBr): 3025, 2922, 2149, 1707, 1510, 1451, 1422, 1190, 700, 596 cm^{-1}; Anal Calcd: C, 64.17; H, 5.05; N, 4.63; Se, 26.14 %. Found: C, 64.19; H, 4.96; N, 4.01; Se, 24.21 %.

(7) **4**: pale yellow beads; IR (KBr): 3027, 2924, 2149, 1605, 1510, 1248, 1175, 1017, 758 cm^{-1}; Anal Calcd: C, 82.16; H, 6.69; N, 1.43; Se, 8.08 %. Found: C, 81.51; H, 6.83; N, 1.30; Se, 7.74 %.

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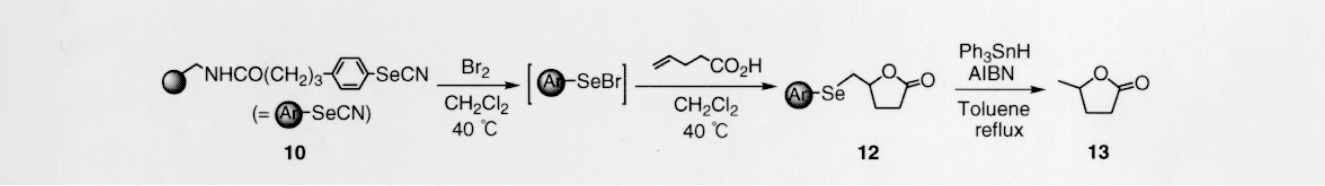

Scheme 3

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(10) **7** and **8** were prepared from the corresponding amino derivatives by diazotization followed by reaction with potassium selenocyanate.

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(12) **9**: pale yellow beads; IR (KBr): 3025, 2920, 2155, 1649, 1491, 1451, 1296, 754, 698 cm^{-1}; Anal Calcd: C, 76.64; H, 6.00; N, 3.95; Se, 11.14 %. Found: C, 75.46; H, 6.11; N, 4.02; Se, 10.61 %. **10**: pale yellow beads; IR (KBr): 3025, 2922, 2149, 1605, 1510, 1248, 1175, 1017, 758 cm^{-1}; Anal Calcd: C, 77.14; H, 6.47; N, 3.73; Se, 10.52 %. Found: C, 76.52; H, 6.68; N, 3.32; Se, 9.05 %.

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Article Identifier:
1437-2096,E;1999,0,11,1760,1762,ftx,en;Y16899ST.pdf