

Note

Stereoselective Synthesis of (*E*)- and (*Z*)-1,2-Disubstituted Ethene from Polymer-Supported Vinylic Selenide

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This letter describes a method for the stereoselective synthesis of polymer-supported vinylic selenides and their applications to synthesis of (*E*)- and (*Z*)-1,2-disubstituted ethenes on solid-phase by the coupling reaction with Grignard reagents under the catalysis of NiCl₂(PPh₃)₂.

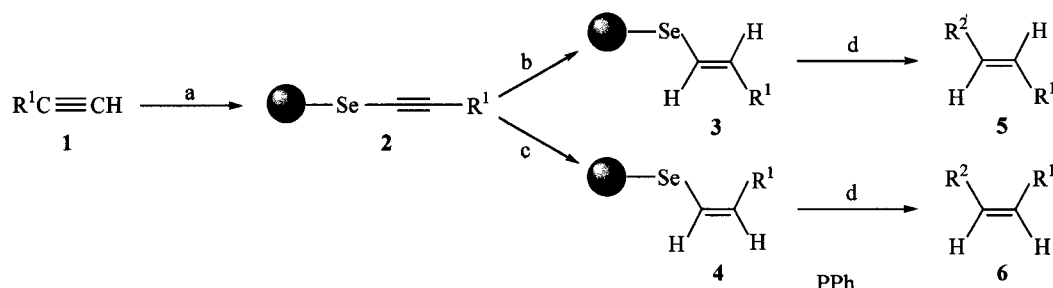
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The area of organic synthesis on polymeric supports has witnessed a great resurgence in recent years.¹ A current trend is the extension of feasibility of organic reactions known to take place in homogeneous phases to analogous reactions on solid supports. Organoselenium compounds have attracted considerable interest as reagents and intermediates in organic synthesis.² Among them, vinyl selenides are important precursors of alkenes because the seleno groups can be easily substituted by various reagents. There have been many reports about the stereoselective synthesis of vinyl selenide³ and its utilization in the synthesis of alkene.⁴ For example, the reaction of selenoacetylene with LiAlH₄ in refluxing THF afforded (*E*)-vinylic selenide,⁵ and with dicyclohexylborane followed by protonolysis with HOAc gave (*Z*)-vinylic selenide.⁶

Treatment of (*E*)- and (*Z*)-vinylic selenide with Grignard reagents using NiCl₂(PPh₃)₂ as catalyst afforded corresponding products with retention of configuration.^{7,8} However, organic selenium reagents always have a foul smell and are quite toxic, which is often problematic in organic synthesis. We previously described the preparation of carbonyl compounds by reaction of polymer-supported selenoalkylidetriphenylphosphoranes with aldehydes.⁹ Herein, we wish to report the stereoselective synthesis of polymer-supported vinylic selenide and its application to synthesis of the (*E*)- and (*Z*)-1,2-disubstituted ethene on solid supports (Scheme 1). An important advantage of these new polymer-supported selenium reagents is the convenience of handling and their totally odorless nature as compared to the non-bound reagents.

In our synthesis, treatment of polystyrene-supported selenium bromide¹⁰ with acetylenic lithium afforded the expected resin **2** as evidenced by alkyne group absorption in the FT-IR spectra (2159—2169 cm⁻¹). The resin **2** was then reduced to vinylic selenide resins **3** or **4** under different conditions, which were monitored by FT-IR for complete disappearance of alkyne group absorption. Resins **3** and **4** are quite stable and can be stored in the air at room temperature. The coupling

Scheme 1



Reagents and conditions: (a) (i) *n*-BuLi, THF, 0 °C, 15 min; (ii) —SeBr, r.t., 1 h; (b) LiAlH₄, THF, reflux, 4 h; (c) (i) (C₆H₁₁)₂BH, 0 °C → 25 °C, r.t., 4; (ii) HOAc, r.t., 1 h; (d) R²MgX, THF, NiCl₂(PPh₃)₂, r.t., 48 h.

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reaction of resin **3** or **4** with Grignard reagents would be the key for the success of this methodology. Thus, the coupling reaction of resin **3a** with PhMgBr was investigated (Table 1). When Et₂O was used as the solvent, the yield of **5a** was low. However, better results were obtained when THF was used instead of Et₂O. This may be due to the fact that THF swells cross-linked polystyrene resin adequately. It should be noted that while the reaction was carried out in THF at a refluxing temperature, the yield of **5a** was just the same as that at room temperature. On the other hand, both catalysts, NiCl₂(PPh₃)₂ and NiCl₂(dppe) were highly effective for the coupling reaction between resin **3** or **4** and Grignard reagents, but NiCl₂(PPh₃)₂ seems to show higher catalytic activity in the reaction than NiCl₂(dppe). (*Z*)-1,2-Disubstituted ethenes **6a–6e** were also obtained under the same conditions as above. Here, ten representative examples were randomly selected and their isolated yields are summarized in Table 1.

In summary, we have developed a solid-phase organic synthesis (SPOS) route to (*E*)- and (*Z*)-1,2-disubstituted ethenes in good yields from polymer-supported vinylic selenide. Although an excess of reagents is required, simple work-up procedures replace the time-consuming isolation and purification steps in the corresponding solution-phase reaction. Further work on the synthesis of isoxazoles from polymer-supported vinylic selenide resins is in progress.

Experimental

¹H NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer in CDCl₃ with TMS as internal standard. IR spectra were taken on a Bruker Vector-22 instrument. Melting points were not corrected. THF was newly distilled from sodium/benzophenone before use. Polystyrene for the preparation of polystyrene-supported selenium bromide according to the procedure described by Nicolaou¹⁰ was purchased from Aldrich (HC1001—2, 100—200 mesh, cross-linked with 1% divinylbenzene).

General procedure for the synthesis of the polymer-supported vinylic selenide resins **3** and **4**

To a solution of the terminal acetylene (1.2 mmol) (0 °C, nitrogen atmosphere, magnetic stirring) in THF (10 mL) was added *n*-butyllithium (in hexane, 1.2 mmol). After stirring for 15 min at 0 °C, the polymer-supported selenium bromide (1.0 g) was added, and the mixture was allowed to reach the room temperature. The stirring was maintained for 1 h and then treated with saturated solution of ammonium chloride. The reaction mixture was filtered, and the resin was washed successively with THF, methanol, CH₂Cl₂, ether (2 × 5 mL of each) and then dried under vacuum to afford resin

Table 1 Preparation of (*E*)- and (*Z*)-1,2-disubstituted ethenes^a

R ¹ (Resin 3 or 4)	R ² MgBr (mmol)	Cat. ^b	Solvent	Time (h)	Products	Yield ^d (%)
C ₆ H ₅ (Resin 3a)	C ₆ H ₅ MgBr (4.0)	—	Et ₂ O	24	5a	0
C ₆ H ₅ (Resin 3a)	C ₆ H ₅ MgBr (4.0)	A	Et ₂ O	24	5a	35
C ₆ H ₅ (Resin 3a)	C ₆ H ₅ MgBr (4.0)	A	Et ₂ O	48	5a	40
C ₆ H ₅ (Resin 3a)	C ₆ H ₅ MgBr (4.0)	A	THF	12	5a	55
C ₆ H ₅ (Resin 3a)	C ₆ H ₅ MgBr (4.0)	A	THF	24	5a	72
C ₆ H ₅ (Resin 3a)	C ₆ H ₅ MgBr (4.0)	A	THF	48	5a	77
C ₆ H ₅ (Resin 3a)	C ₆ H ₅ MgBr (4.0)	B	THF	48	5a	74
C ₆ H ₅ (Resin 3a)	C ₆ H ₅ MgBr (3.5)	A	THF	48	5a	70
C ₆ H ₅ (Resin 3a)	C ₆ H ₅ MgBr (5.0)	A	THF	48	5a	78
C ₆ H ₅ (Resin 3a)	C ₆ H ₅ MgBr (4.0)	A	THF ^c	24	5a	70
C ₆ H ₅ (Resin 3a)	C ₆ H ₅ MgBr (4.0)	A	THF ^c	48	5a	77
C ₆ H ₅ (Resin 3a)	<i>n</i> -C ₄ H ₉ MgBr (4.0)	A	THF	48	5b	80
C ₆ H ₅ (Resin 3a)	<i>n</i> -C ₄ H ₉ MgBr (4.0)	B	THF	48	5b	75
C ₆ H ₅ (Resin 3a)	<i>p</i> -ClC ₆ H ₄ MgBr (4.0)	A	THF	48	5c	75
<i>n</i> -C ₅ H ₁₁ (Resin 3b)	C ₆ H ₅ MgBr (4.0)	A	THF	48	5d	74
CH ₃ OCH ₂ (Resin 3c)	C ₆ H ₅ MgBr (4.0)	A	THF	48	5e	72
C ₆ H ₅ (Resin 4a)	C ₆ H ₅ MgBr (4.0)	A	THF	48	6a	78
C ₆ H ₅ (Resin 4a)	CH ₂ CH ₃ MgBr (4.0)	A	THF	48	6b	80
C ₆ H ₅ (Resin 4b)	<i>n</i> -C ₄ H ₉ MgBr (4.0)	A	THF	48	6c	75
<i>n</i> -C ₄ H ₉ (Resin 4c)	<i>n</i> -C ₄ H ₉ MgBr (4.0)	A	THF	48	6d	72
<i>n</i> -C ₅ H ₁₁ (Resin 4d)	CH ₃ MgBr (4.0)	A	THF	48	6e	79

^a All reactions were carried out at room temperature in the presence of catalyst (3 mol% of loading of selenium bromide resin), unless otherwise noted. ^b A: NiCl₂(PPh₃)₂, B: NiCl₂(dppe). ^c The reactions were carried out at a refluxing temperature. ^d Isolated yield based on selenium bromide resin (1.18 mmol/g).

2. This resin was pre-swollen in THF (10 mL) for 30 min followed by the addition of LiAlH_4 (0.1 g, 2.4 mmol). The mixture was refluxed for 4 h, treated with water, 15% NaOH, water, and then filtered. The resin was washed successively with THF, methanol, CH_2Cl_2 , ether, and then dried under vacuum to give resin 3.

Resin 4 was prepared from resin 2 by hydroboration followed by protonolysis with HOAc using the solution synthetic method.⁶

General procedure for the solid-phase synthesis of (E)- and (Z)-1,2-disubstituted ethenes

A solution of Grignard reagent (4.0 mmol) in THF (7.0 mL) was added to the stirred suspension of resin 3 or 4 swollen in THF (5.0 mL) containing $\text{NiCl}_2(\text{PPh}_3)_2$ (3% \times 1.18 mmol). The mixture was stirred for 48 h at room temperature under a nitrogen atmosphere, then quenched with saturated aqueous NH_4Cl . The residual solids were filtered off and washed with ether (3 \times 10 mL). The combined extracts were washed with water, dried over Na_2SO_4 and evaporated to give a crude product, which was purified by preparative TLC on silica gel or crystallization affording the final product.

(E)-Stilbene (5a)⁸ M.p. 121.5–123 °C (lit. 122–123 °C); ¹H NMR δ : 7.12 (s, 2H), 7.18–7.21 (m, 2H), 7.38–7.43 (m, 4H), 7.45–7.48 (m, 4H); IR (KBr) ν : 3019, 1579, 1468, 1072, 962, 910, 765, 693 cm^{-1} .

(E)-1-Phenyl-1-hexene (5b)¹¹ Colorless oil; ¹H NMR δ : 0.92 (t, $J = 7.0$ Hz, 3H), 1.11–1.36 (m, 4H), 1.85–1.98 (m, 2H), 6.20 (dt, $J = 16.1, 6.0$ Hz, 1H, CH = CHCH₂), 6.40 (d, $J = 16.1$ Hz, 1H, CH = CHCH₂), 7.20–7.29 (m, 5H); IR (neat) ν : 3015, 2946, 2850, 1590, 1374, 965, 912 cm^{-1} .

(E)-1-Phenyl-2-(4-chlorophenyl) ethylene (5c)⁸ M.p. 127–128 °C (lit. 126–127 °C); ¹H NMR δ : 7.02 (d, $J = 15.7$ Hz, 1H, PhCH = CH), 7.06 (d, $J = 15.7$ Hz, 1H, PhCH = CH), 7.28–7.50 (m, 9H); IR (KBr) ν : 3016, 1560, 1465, 965, 821 cm^{-1} .

(E)-1-Phenyl-1-heptene (5d)¹¹ Colorless oil; ¹H NMR δ : 0.90 (t, $J = 7.1$ Hz, 3H), 1.10–1.52 (m, 6H), 2.11–2.19 (m, 2H), 6.12 (dt, $J = 15.9, 6.5$ Hz, 1H, CH = CHCH₂), 6.24 (d, $J = 15.9$ Hz, 1H, CH = CHCH₂), 7.08–7.35 (m, 5H); IR (neat) ν : 3018, 2944, 2851, 1592, 1375, 963, 910 cm^{-1} .

(E)-1-Phenyl-3-methoxyl-1-propene (5e)¹¹ Colorless oil; ¹H NMR δ : 2.20 (s, 3H), 3.24 (d, $J = 6.2$ Hz, 2H), 6.12 (dt, $J = 15.6, 6.4$ Hz, 1H, CH = CHCH₂), 6.28 (d, $J = 15.6$ Hz, 1H, CH = CHCH₂), 7.01–7.30 (m, 5H); IR (neat) ν : 3012, 2945, 2848, 1590, 1372, 1026, 960, 912 cm^{-1} .

(Z)-Stilbene (6a)⁷ Colorless oil; ¹H NMR δ : 6.58 (s, 2H), 7.15–7.20 (m, 2H), 7.31–7.40 (m, 4H), 7.43–7.47 (m, 4H); IR (neat) ν : 3020, 1600, 1495, 1440, 920, 780, 700 cm^{-1} .

(Z)-1-Phenyl-1-butene (6b)¹² Colorless oil; ¹H NMR δ : 1.08 (t, $J = 6.9$ Hz, 3H), 2.16–2.35 (m, 2H), 5.64 (dt, $J = 12, 7.5$ Hz, 1H, CH = CHCH₂), 6.40 (dt, $J = 12, 2.2$ Hz, 1H, CH = CHCH₂), 7.16–7.42 (m, 5H); IR (neat) ν : 3018, 2941, 2847, 1608, 1490, 1445, 923, 740, 691 cm^{-1} .

(Z)-1-Phenyl-1-hexene (6c)⁷ Colorless oil; ¹H NMR δ : 0.93 (t, $J = 6.9$ Hz, 3H), 1.34–1.60 (m, 4H), 2.01–2.11 (m, 2H), 5.62 (dt, $J = 11.6, 7.3$ Hz, 1H, CH = CHCH₂), 6.33 (dt, $J = 11.6, 2.5$ Hz, 1H, CH = CHCH₂), 7.08–7.31 (m, 5H); IR (neat) ν : 3018, 2937, 2837, 1602, 1497, 1448, 924, 741, 690 cm^{-1} .

(Z)-5-Decene (6d)¹³ Colorless oil; ¹H NMR δ : 0.92 (t, $J = 7.0$ Hz, 6H), 1.10–1.58 (m, 8H), 2.05–2.21 (m, 4H), 5.50–5.52 (m, 2H); IR (neat) ν : 3010, 2936, 2842, 1626, 1442, 1376, 736 cm^{-1} .

(Z)-2-Octene (6e)¹⁴ Colorless oil; ¹H NMR δ : 0.90 (t, $J = 7.1$ Hz, 3H), 1.10–1.62 (m, 6H), 1.70–1.80 (m, 3H), 2.01–2.10 (m, 2H), 5.30–5.41 (m, 1H), 5.49–5.58 (m, 1H); IR (neat) ν : 3012, 2940, 2842, 1628, 1373, 738 cm^{-1} .

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