SHORT PAPER

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Preparation of selanyl-substituted conjugated enynes by copper-catalysed coupling reaction of (*E*)-γ-selanyl vinylzirconocene with acetylenic bromide†

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A stereoselective synthesis of conjugated enynes containing allyl selenide unit is reported. Selanyl-substituted conjugated enynes were obtained by the coupling reaction of (*E*)-γ-selanyl vinylzirconocene with acetylenic bromide in the presence of CuCl.

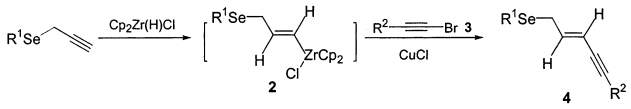
Keywords: selanyl-substituted conjugated enynes

The conjugated enyne framwork is the typical structural fragment of many natural compounds[1] and is also an important unit in organic chemistry.[2] Recently, the discovery of strong antifungal agents[3] and new powerful antitumor antibiotics[4] has stimulated intense interest in the chemistry of enynes,[5] which is at the origin of the biological properties of these substances. There exist many synthetic approaches to this structural unit, most of which include the coupling procedures of haloalkynes with vinyl metals such as vinyl boron,[6] vinyl copper,[7,8] vinyl zinc,[9] or vinyl magnesium reagents.[10]

On the other hand, allyl selenide is an important intermediate in organic synthesis. Allyl selenide can undergo substitution reaction with a variety of typical electrophiles.[11] It can also cause reductive allylic homocoupling in the presence of catalyst[12] and the facile oxidative conversion of allyl selenides to alcohols accompanied by [2,3]-sigmatropic rearrangement is a useful synthetic transformation.[13] Therefore the synthesis of allyl selenides is of interest in organic synthesis. We recently reported the stereoselective synthesis of functionalised allyl selenides from the reaction of 1,3-difunctional reagents – (*E*)-γ-selsnyl vinylzirconocene (**2**) with aldehydes or acyl chlorides.[14] However, to the best of our knowledge, the synthesis of conjugated enynes containing a structural unit of allyl selenide has not been reported before. Considering the importance of conjugated enynes as well as the versatile reactivity of allyl selenides, we wish to report herein the stereoselective synthesis of conjugated enynes containing the structural unit of allyl selenides by the coupling reaction of 1, 3-difunctional reagent **2** with acetylenic bromide.

Hydrozirconation of propargyl selenides at room temperature in THF gave (*E*)-γ-selanyl vinylzirconocene **2** stereospecifically, which further reacted with acetylenic bromide in THF at room temperature in the presence of CuCl to afford selanyl-substituted conjugated enynes **4** in good yields (Scheme 1). The results are summarised in Table 1.

The coupling reaction of (*E*)-γ-selanyl vinylzirconocene with acetylenic bromide gave **4a**–**4f** with retention of the configuration. The (*E*)-configuration of the products **4a**–**4f** was confirmed by the coupling constants of the vinylic protons (15.04 – 15.76 Hz).



Scheme 1

Table 1 Preparation of selanyl-substituted conjugated enynes **4a–4f**

Entry	R^1	R^3	Product	Yield/% [a]
1	C_6H_5-	C_6H_5-	**4a**	74
2	C_6H_5-	*n*-C_4H_9-	**4b**	72
3	C_6H_5-	CH_3OCH_2-	**4c**	80
4	Et	C_6H_5-	**4d**	68
5	Et	*n*-C_4H_9-	**4e**	72
6	Et	CH_3OCH_2-	**4f**	78

[a] Isolated yield based on the propargyl selenides 1 used.

In conclusion, hydrozirconation of propargyl selenides and its further reaction with acetylenic bromide provide a convenient method for the synthesis of selanyl-substituted conjugated enynes. The present procedure has the advantages of readily available starting materials, simple procedures, mild reaction conditions and regio- and stereoselectivity. Due to the versatile reactivity of allyl selenide, the obtained compounds **4** can be the useful precursors of various substituted conjugated enynes. Efforts are made in our laboraotry to study the further transformation of the selanyl-substituted conjugated enynes.

Experimental

All ^{1}H NMR spectra were measured in $CDCl_3$ and recorded on Brucker Avance – 400 (400MHz) spectrometer with TMS as the internal standard, chemical shifts are expressed in ppm and *J* values are given in Hz. IR spectra were run on Shimadzu IR-408 spectrometer. EIMS were determined with a HP5989B mass spectrometer. All the reactions in this paper were performed under nitrogen atmosphere. THF was freshly distilled from sodium/benzophenone ketyl prior to use. Propargyl selenides [15] and hydrozirconocene chloride [16] were prepared according to literature procedure.

General procedure for the synthesis of 4a–4f: A mixture of hydrozirconocene chloride (1.2mmol) and propargyl selenide (**1**) (1.0mmol) in THF was stirred at room temperature for 20min. To the resulting clear solution was added acetylenic bromide **3** (1.5mmol) followed by CuCl (1.5mmol). The reaction mixture was stirred for 2–3h and then quenched with saturated $NaHCO_3$ aqueous solution. Extractive workup (EtOAc) followed by purification with flash chromatography (hexanes as eluent) gave selanyl-substituted conjugated enynes **4a**–**4f**.

(2E)-1-phenylseleno-5-phenyl-pent-2-en-4-yne (**4a**): yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) 7.53–7.51 (m, 2H), 7.41–7.38 (m, 2H), 7.29–7.26 (m, 6H), 6.35–6.27 (m, 1H), 5.55 (d, *J* = 15.56Hz, 1H),

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3.58 (dd, *J* = 7.94Hz, 0.73Hz, 2H). IR (film) 3050, 2958, 2210, 1590 cm^{-1}. MS (EI) *m/z* 298 (M^+, 3.5), 141 (M^+–SePh, 100). Anal. Calcd. For $C_{17}H_{14}Se$: C, 68.69; H, 4.75. Found: C, 68.55; H, 4.83.

(2E)-1-phenylseleno-non-2-en-4-yne (**4b**): yellow oil. ^1H NMR (400 MHz, $CDCl_3$) 7.51–7.48 (m, 2H), 7.29–7.24 (m, 3H), 6.16–6.08 (m, 1H), 5.35 (dd, *J* = 15.53Hz, 0.40Hz, 1H), 3.52 (dd, *J* = 7.88Hz, 0.45Hz, 2H), 2.29–2.25 (m, 2H), 1.50–1.36 (m, 4H), 0.90 (t, *J* = 7.31Hz, 3H). IR (film) 3044, 2958, 2220, 1590 cm^{-1}. MS (EI) *m/z* 278 (M^+, 5.4), 121 (M^+–SePh, 100). Anal. Calcd. For $C_{15}H_{18}Se$: C, 64.98; H, 6.54. Found: C, 64.88; H, 6.58.

(2E)-1-phenylseleno-6-methoxy-hex-2-en-4-yne (**4c**): yellow oil. ^1H NMR (400 MHz, $CDCl_3$) 7.51–7.48 (m, 2H), 7.28–7.26 (m, 3H), 6.28–6.20 (m, 1H), 5.35 (d, *J* = 15.64Hz, 1H), 4.18 (d, *J* = 1.87Hz, 2H), 3.52 (dd, *J* = 7.91Hz, 0.98Hz, 2H), 3.36 (s, 3H). IR (film) 3048, 2925, 2215, 1590 cm^{-1}. MS (EI) *m/z* 266 (M^+, 9.9), 109 (M^+–SePh, 14.8), 77 ($C_6H_5^+$, 100). Anal. Calcd. For $C_{13}H_{14}OSe$: C, 58.87; H, 5.32. Found: C, 58.92; H, 5.35.

(2E)-1-ethylseleno-5-phenyl-pent-2-en-4-yne (**4d**): yellow oil. ^1H NMR (400 MHz, $CDCl_3$) 7.44–7.41 (m, 2H), 7.32–7.28 (m, 3H), 6.31–6.23 (m, 1H), 5.67 (d, *J* = 15.53Hz, 1H), 3.27 (dd, *J* = 8.01Hz, 1.12Hz, 2H), 2.56 (q, *J* = 7.49Hz, 2H), 1.39 (t, *J* = 7.5Hz, 3H). IR (film) 3057, 2958, 2216, 1600 cm^{-1}. MS (EI) *m/z* 250 (M^+, 4.5), 141 (M^+–SeEt, 100). Anal. Calcd. For $C_{13}H_{14}Se$: C, 62.65; H, 5.66. Found: C, 62.52; H, 5.80.

(2E)-1-ethylseleno-non-2-en-4-yne (**4e**): yellow oil. ^1H NMR (400 MHz, $CDCl_3$) 6.12–6.04 (m, 1H), 5.44 (d, *J* = 15.54Hz, 1H), 3.20 (d, *J* = 7.89Hz, 2H), 2.53 (q, J = 7.48Hz, 2H), 2.30–2.28 (m, 2H), 1.53–1.36 (m, 7H), 0.91 (t, *J* = 7.29Hz, 3H). IR (film) 3045, 2955, 2220, 1590 cm^{-1}. MS (EI) *m/z* 230 (M^+, 3.7), 121 (M^+–SeEt, 100). Anal. Calcd. For $C_{11}H_{18}Se$: C, 57.64; H, 7.92. Found: C, 57.50; H, 7.88.

(2E)-1-ethylseleno-6-methoxy-hex-2-en-4-yne (**4f**): yellow oil. ^1H NMR (400 MHz, $CDCl_3$) 6.24–6.17 (m, 1H), 5.49 (d, *J* = 15.60Hz, 1H), 4.21 (d, *J* = 1.85Hz, 2H), 3.39 (s, 3H), 3.22 (dd, *J* = 7.96Hz, 0.92Hz, 2H), 2.53 (q, *J* = 7.49Hz, 2H), 1.38 (t, *J* = 7.48Hz, 3H). IR (film) 3050, 2925, 2210, 1598 cm^{-1}. MS (EI) *m/z* 218 (M^+, 3.1), 109 (M^+–SeEt, 100). Anal. Calcd. For $C_9H_{14}OSe$: C, 49.77; H, 6.50. Found: C, 49.71; H, 6.58.

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