Stereoselective Preparation of α -Heteroatom Substituted α , β -Unsaturated Ketones

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Abstract: (*E*)- α -Selanylvinylzirconium and (*E*)- α -silylvinylzirconium complexes **2** were prepared conveniently via hydrozirconation of the alkynylselenides and the alkynylsilanes **1**, respectively. Intermediates **2** were reacted with acyl chlorides **3** via Zr-Cu transmetallation with retention of the configuration to afford α -seleno or α silyl α , β -unsaturated ketones **4** in good yield.

Key words: alkynylselenides, alkynylsilanes, hydrozirconation, Zr-Cu transmetallation, α -heteroatom substituted α , β -unsaturated ketones, acylations

Many biologically active compounds occurring in nature possess the structural skeleton of trisubstituted alkenes.¹⁻³ Because both disubstituted alkenylselenides and alkenylsilanes can be stereospecifically converted to trisubstituted alkenes by reactions with nucleophiles⁴ or electrophiles,⁵ the high-yield, stereoselective synthesis of disubstituted alkenylselenides or alkenylsilanes is a highly desirable goal. Hydrozirconation has emerged as a unique hydrometallation with some attractive features,⁶ such as the high regioselectivity and stereoselectivity observed with alkynes.⁷ However, to date, hydrozirconation of alkynylselenides and alkynylsilanes has received less attention.^{8,9} We now wish to report that α -seleno- or α -silyl-substituted α , β -unsaturated ketones could be synthesized by hydrozirconation of the alkynylselenides or the alkynylsilanes, followed by treatment with acyl halides via Zr-Cu transmetallation.¹⁰

Alkynylselenides and alkynylsilanes **1** were prepared according to the literature procedure.^{11,12} Hydrozirconation of alkynylselenides and alkynylsilanes at room temperature in CH₂Cl₂ gave (*E*)- α -selanylvinylzirconiums and (*E*)- α -silylvinylzirconiums **2**, which were reacted with acyl halides in the presence of 15mol% CuBr•SMe₂ to afford α -seleno or α -silyl α , β -unsaturated ketones **4**. Transmetallation from Zr to Cu proceeded predominantly with retention of configuration at carbon.¹³ The yields were 70–89% (Scheme 1).



le Synthesis of	Seleno or α -Sily	yl α , β -Unsaturated Ketones
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Entry	R	Х	R'	Product ^a	Yield ^b (%)
A	Pr	SeEt	Ph	4a	82
В	Pr	SeEt	C ₅ H ₁₁	4b	80
С	MeOCH ₂	SeEt	Ph	4c	80
D	$MeOCH_2$	SeEt	C ₅ H ₁₁	4d	78
Е	EtSe	SeEt	Ph	4 e	75
F	EtSe	SeEt	Bu	4f	70
G	Pr	SiMe ₃	C ₅ H ₁₁	4g	79
Н	Pr	SiMe ₃	Ph	4h	81
Ι	Pr	SiMe ₃	$4-ClC_6H_4$	4i	85
J	MeOCH ₂	SiMe ₃	$2,3-(NO_2)_2C_6H_3$	4j	89
K	$MeOCH_2$	SiMe ₃	Bu	4k	83
L	MeOCH ₂	SiMe ₃	Ph	41	85
М	$MeOCH_2$	SiMe ₃	4-ClC ₆ H ₄	4m	87
N	MeOCH ₂	SiMe ₃	$3,4-(NO_2)_2C_6H_3$	4n	89

^a All the compounds were characterized using ¹H NMR, IR, MS or elemental analyses.

^b Isolated yield based on the alkynylselenides or alkynylsilanes used.

Investigations of the crude products **4** by ¹H NMR spectroscopy (300 MHz) showed isomeric purities of more than 97%. One olefinic proton signal of **4** was characteristically split into one triplet with coupling constant J = 7.0 Hz, which indicated that the hydrozirconation of the alkynylselenides or alkynylsilanes had taken place with strong preference for the addition of the zirconium atom at the carbon adjacent to the alkylseleno or alkylsilyl group. The results of the reaction are summarized in the Table.

We have also carried out the coupling reaction of the compound **41** with aroyl halides in the presence of AlCl₃ (1 equiv) at 0 °C in CH₂Cl₂ for an hour to give the unsaturated α , γ -diketones **5** with high sterereoselectivity (Scheme 2).



Scheme 2

In summary, our results showed that the hydrozirconation-acylation sequence of the alkynylselenides and the alkynylsilanes has the advantages of readily available starting materials, straightforward and simple procedures, mild reaction conditions and high yields. The investigation on the synthetic applications of these α -seleno and α silyl α , β -unsaturated ketones is in progress.

¹H NMR spectra were recorded on an AZ-300 MHz spectrometer with TMS as an internal standard. Mass spectra were determined using a Finnigan 8230 mass spectrometer. IR spectra were obtained by use of neat capillary cells on a Shimadzu IR-408 instrument. The reactions were carried out in pre-dried (150 °C, 4 h) glassware and cooled under a stream of dry N₂. All solvents were dried, deoxygenated and freshly distilled before use

α-Seleno- or α-Silyl-α,β-unsaturated Ketones 4a–n; General Procedure

To a suspension of hydridozirconocene chloride (310 mg, 1.2 mmol) in CH_2Cl_2 (2 mL) was added a solution of alkynylselenide or alkynylsilane 1 (1.0 mmol) in CH_2Cl_2 at r.t. with stirring. After about 30 min, the mixture turned to a clear green solution. CuBr•SMe₂ (25 mg) was then added, followed by the appropriate acyl chloride (1.8 mmol). The mixture was stirred at 35 °C for about 20 min, quenched with sat. aq NaHCO₃ (25 mL) and extracted with wet Et₂O (2 × 10 mL). The organic layer was dried (MgSO₄), and concentrated in vacuo. The oily residue was purified by flash column chromatography silica gel (EtOAc/hexanes, 1:8) to give 4a–n as oils.

4a

¹H NMR (CDCl₃): δ = 7.90–7.75 (m, 2 H), 7.45–7.20 (m, 3 H), 6.35 (t, *J* = 6.9 Hz, 1 H, =CH), 2.52 (q, *J* = 7.5 Hz, 2 H, SeCH₂), 1.97–2.26 (m, 2 H), 1.49 (t, *J* = 7.5 Hz, 3 H, SeCH₂CH₃), 1.18–1.47 (m, 2 H), 0.75 (t, *J* = 5.3 Hz, 3 H, CH₂CH₃).

IR (film): v = 1720, 1665, 1100, 892 cm⁻¹.

MS: m/z = 281 (M⁺).

Anal. calcd for C₁₄H₁₈OSe: C, 59.60; H, 6.43. Found: C, 59.43; H, 6.22.

4b

¹H NMR (CDCl₃): $\delta = 6.32$ (t, J = 7.0 Hz, 1 H, =CH), 2.64 (t, J = 7.1 Hz, 2 H, O=CCH₂CH₂), 2.53 (q, J = 7.5 Hz, 2 H, SeCH₂), 2.26–1.98 (m, 2 H), 1.48 (t, J = 7.5 Hz, 3 H, SeCH₂CH₃), 1.43–1.10 (m, 2 H), 1.02–0.84 (m, 12 H).

IR (film): v = 1725, 1645, 1102, 910 cm⁻¹.

MS:
$$m/z = 275 (M^+)$$

Anal. calcd for $C_{13}H_{24}OSe: C$, 56.54; H, 8.76. Found: C, 56.32; H, 8.45.

4c

¹H NMR (CDCl₃): δ = 7.92-7.74 (m, 2 H), 7.60–7.35 (m, 3 H), 6.34 (t, *J* = 7.1 Hz, 1 H, =CH), 4.15 (d, *J* = 7.1 Hz, 2 H, CH₃OCH₂), 3.34 (s, 3 H), 2.55 (q, *J* = 7.4 Hz, 2 H, SeCH₂), 1.53 (t, *J* = 7.4 Hz, 3 H, SeCH₂CH₃).

IR (film): v = 1698, 1650, 1202, 890 cm⁻¹.

MS: m/z = 283 (M⁺).

Anal. calcd for $C_{13}H_{16}O_2Se: C, 54.97; H, 5.68$. Found: C, 55.01; H, 5.76.

4d

¹H NMR (CDCl₃): $\delta = 6.32$ (t, J = 7.0 Hz, 1 H, =CH), 3.95 (d, J = 7.0 Hz, 2 H, CH₃OCH₂), 3.35 (s, 3 H), 2.65 (t, J = 7.2 Hz, 2 H, O=CCH₂CH₂), 2.57 (q, J = 7.4 Hz, 2 H, SeCH₂), 1.52 (t, J = 7.4 Hz, 3 H, SeCH₂CH₃), 1.38–1.02 (m, 6 H), 0.84 (t, J = 5.4 Hz, 3 H, CH₂CH₃).

IR (film): v = 1730, 1670, 1201, 905 cm⁻¹.

MS: m/z = 277 (M⁺).

Anal. calcd for $C_{12}H_{22}O_2Se: C, 51.83; H, 7.97$. Found: C, 51.49; H, 7.65.

4e

¹H NMR (CDCl₃): $\delta = 8.09-7.09$ (m, 2 H), 7.55-7.45 (m, 3 H), 6.25 (s, 1 H), 2.65 (q, J = 7.4 Hz, 4 H, SeCH₂), 1.40 (t, J = 7.4 Hz, 6 H, SeCH₂CH₃).

IR (film): v = 1735, 1683, 1210, 850 cm⁻¹.

MS: m/z = 346 (M⁺).

Anal. calcd for $C_{13}H_{16}OSe_2$: C, 44.87; H, 4.64. Found: C, 44.98; H, 4.78.

4f

¹H NMR (CDCl₃): $\delta = 6.50$ (s, 1 H), 2.68 (t, J = 7.1 Hz, 2 H, O=CCH₂CH₂), 2.57 (q, J = 7.4 Hz, 4 H, SeCH₂), 1.58 (t, J = 7.4 Hz, 6 H, SeCH₂CH₃), 1.45–1.23 (m, 4 H), 0.92 (t, J = 5.3 Hz, 3 H, CH₂CH₃).

IR (film): v = 1722, 1683, 1318, 865 cm⁻¹.

MS: m/z = 326 (M⁺).

Anal. calcd for $C_{11}H_{20}OSe_2$: C, 40.29; H, 6.15. Found: C, 40.42; H, 6.32.

4g

¹H NMR (CDCl₃): $\delta = 6.33$ (t, J = 7.1 Hz, 1 H, =CH), 2.64 (t, J = 7.1 Hz, 2 H, O=CCH₂CH₂), 2.26–1.97 (m, 2 H), 1.43–1.11 (m, 2 H), 1.03–0.83 (m, 12 H), 0.15 (s, 9 H).

IR (film): v = 1710, 1665 cm⁻¹.

MS: $m/z = 239 (M^+ - 1)$.

Anal. calcd for $C_{14}H_{28}OSi: C, 70.00; H, 11.67$. Found: C, 70.39; H, 11.42.

4h

¹H NMR (CDCl₃): δ = 8.15–7.21 (m, 5 H), 6.34 (t, *J* = 7.0 Hz, 1 H, =CH), 2.24–1.98 (m, 2 H), 1.42–1.30 (m, 2 H), 0.85 (t, *J* = 5.3 Hz, 3 H, CH₂CH₃), 0.15 (s, 9 H).

IR (film): v = 1710, 1660, 700 cm⁻¹.

MS: $m/z = 245 (M^+ - 1)$.

Anal. calcd for $C_{15}H_{22}OSi: C, 73.17; H, 8.94$. Found: C, 73.25; H, 8.88.

4i

¹H NMR (CDCl₃): δ = 7.93–7.86 (m, 2 H), 7.42–7.35 (m, 2 H), 6.33 (t, *J* = 7.2 Hz, 1 H, =CH), 2.25–1.97 (m, 2 H), 1.33 (m, 2 H), 0.89 (t, *J* = 5.3 Hz, 3 H, CH₂CH₃), 0.15 (s, 9 H).

IR (film): v = 1715, 1670, 750 cm⁻¹.

MS: $m/z = 280 (M^+ - 1)$.

Anal. calcd for $C_{15}H_{21}$ ClOSi: C, 64.06; H, 7.47. Found: C, 64.32; H, 7.27.

4j

¹H NMR (CDCl₃): $\delta = 9.10$ (s, 3 H), 6.29 (t, J = 7.2 Hz, 1 H, =CH), 3.85 (d, J = 7.2 Hz, 2 H, CH₃OCH₂), 3.28 (s, 3 H), 0.16 (s, 9 H).

IR (film): v = 1720, 1665, 715 cm⁻¹.

MS: $m/z = 321 (M^+ - 1)$.

Anal. calcd for $C_{14}H_{18}N_2O_5Si$: C, 52.34; H, 5.61. Found: C, 52.52; H, 5.56.

4k

¹H NMR (CDCl₃): $\delta = 6.32$ (t, J = 7.0 Hz, 1 H, =CH), 3.85 (d, J = 7.0 Hz, 2 H, CH₃OCH₂), 3.28 (s, 3 H), 2.66 (t, J = 7.2 Hz, 2 H, O=CCH₂CH₂), 1.37–1.03 (m, 4 H), 0.85 (t, J = 5.3 Hz, 3 H,CH₂CH₃), 0.16 (s, 9 H).

IR (film): v = 1715, 1666 cm⁻¹.

MS: $m/z = 227 (M^+ - 1)$.

Anal. calcd for $C_{12}H_{24}O_2Si$: C, 63.16; H, 10.53. Found: C, 63.27; H, 10.46.

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¹H NMR (CDCl₃): $\delta = 8.12-7.23$ (m, 5 H), 6.32 (t, J = 7.0 Hz, 1 H, =CH), 4.05 (d, J = 7.0 Hz, 2 H, CH₃OCH₂), 3.25 (s, 3 H), 0.20 (s, 9 H).

IR (film): v = 1713, 1670, 720 cm⁻¹.

MS: $m/z = 247 (M^+ - 1)$.

Anal. calcd for $C_{14}H_{20}O_2Si: C$, 67.74; H, 8.06. Found: C, 67.53; H, 8.18.

4m

¹H NMR (CDCl₃): δ = 7.93–7.86 (m, 2 H), 7.42–7.35 (m, 2 H), 6.34 (t, *J* = 7.1 Hz, 1 H, =CH), 3.98 (d, *J* = 7.1 Hz, 2 H, CH₃OCH₂), 3.26 (s, 3 H), 0.15 (s, 9 H).

IR (film): v = 1715, 1680, 750 cm⁻¹.

MS: $m/z = 284 (M^+ - 1)$.

Anal. calcd for $C_{14}H_{21}SiClO_2$: C, 58.95; H, 7.37. Found: C, 58.76; H, 7.48.

4n

¹H NMR (CDCl₃): δ = 9.10 (s, 3 H), 6.32 (t, *J* = 7.2 Hz, 1 H, =CH), 3.95 (d, *J* = 7.2 Hz, 2H, CH₃OCH₂), 3.27 (s, 3 H), 0.17 (s, 9 H).

IR (film): v = 1720, 1685, 720 cm⁻¹.

MS: $m/z = 337 (M^+ - 1)$.

Anal. calcd for $C_{14}H_{18}N_2O_6Si:$ C, 49.70; H, 5.33. Found: C, 49.86; H, 5.29.

α,γ-Diketones 5; General Procedure

To a stirred suspension of AlCl₃ (133 mg, 1.0 mmol) and freshly prepared α -silyl α , β -unsaturated ketone **4l** (1.0 mmol) in CH₂Cl₂ (2

mL) was added a solution of the appropriate aroyl halide (1.0 mmol) in CH_2Cl_2 (2 mL) at r.t. and the mixture was stirred for 1 h. After the usual workup (see above), the residue was purified by flash column chromatography on silica gel (EtOAc/hexanes, 1:5) to give **51** and **51**' as oils.

51

¹H NMR (CDCl₃): δ = 8.12–7.23 (m, 11 H), 4.05 (d, *J* = 7.5 Hz, 2 H), 3.25 (s, 3 H).

IR (film: v = 1718, 1670, 720 cm⁻¹.

MS: m/z = 280 (M-1).

Anal. calcd for $C_{18}H_{16}O_3$: C, 77.14; H, 5.71. Found: C, 77.33; H, 5.65.

5I'

¹H NMR (CDCl₃): δ = 8.01–7.86 (m, 3 H), 7.42–7.35 (m, 2 H), 3.98 (d, *J* = 7.6 Hz, 2 H), 3.26 (s, 3 H).

IR (film): v = 1715, 1690, 750 cm⁻¹.

MS: $m/z = 315 (M^+ - 1)$.

Anal. calcd for $C_{18}H_{15}ClO_3$: C, 68.57; H, 4.76. Found: C, 68.78; H, 4.42.

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