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A Facile Stereoselective Synthesis of (*E*)-1,2-Disubstituted Vinylic Selenides via Hydromagnesiation of Alkylarylacetylenes

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ABSTRACT: *Hydromagnesiation of alkylarylacetylenes* **1** *in diethyl ether gave (E)-α-arylvinyl Grignard reagents* **2**, *which reacted with arylselenenyl bromides* **3** *in THF to afford stereoselectively (E)-1,2-disubstituted vinylic selenides* **4** *in good yields.* © 2005 Wiley Periodicals, Inc. Heteroatom Chem 16: 65–68, 2005; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20066

INTRODUCTION

Vinylic selenides are promising synthetic intermediates because they can participate in highly stereoselective carbon–carbon bond formation processes [1,2]. Due to their synthetic utility, a variety of methods have been developed for their stereoselective preparation including those involving the addition of selenophenol to acetylenes [3], the radical hydroselenation of alkynes with triorganoselenoboranes [4], the reduction of acetylenic selenides with $LiAlH_4$ [5], and zirconium–selenium transmetalation [6]. Recently, Huang and Zhu have reported the stereoselective synthesis of (*E*)-vinylic selenides via hydrozirconation of arylselenoethynes followed by the cross coupling reaction with aryl halides in the presence of $Pd(PPh_3)_4$ [7].

Hydromagnesiation has emerged as a unique hydrometallation with some attractive features such as the high regioselectivity and stereoselectivity observed with alkylarylacetylenes [8] and alkynylsilanes [9]. Very recently, we have reported the stereoselective syntheses of (*E*)-allylic alcohols [10], (*E*)-α-selenenylvinylsilanes [11], 1,3-dienylsilanes [12], and (*E*)-α-aryltellurenylvinylsilanes [13]. Herein we wish to report that (*E*)-1,2-disubstituted vinylic selenides could be conveniently synthesized via the hydromagnesiation of alkylarylacetylenes, followed by the reaction with arylselenenyl bromides.

RESULTS AND DISCUSSION

Alkylarylacetylenes **1** were prepared according to the literature procedure [14]. Hydromagnesiation of alkylarylacetylenes **1** at 25°C in diethyl ether for 1 h gave (*E*)-α-arylvinyl Grignard reagents **2**, which reacted with arylselenenyl bromides **3** in THF to afford stereoselectively (*E*)-1,2-disubstituted vinylic selenides **4** in good yields (Scheme 1). The typical results are summarized in Table 1.

Investigations of the crude products **4** by ^{1}H-NMR spectroscopy (400 MHz) showed their isomeric purities of more than 97%. One olefinic proton signal of compounds **4a–m** splits characteristically into one triplet at $\delta = 6.09$–6.23 with coupling constant $J = 7.2$ or 7.6 Hz, which indicated that the hydromagnesiation to the alkylarylacetylenes had taken place with strong preference for the addition

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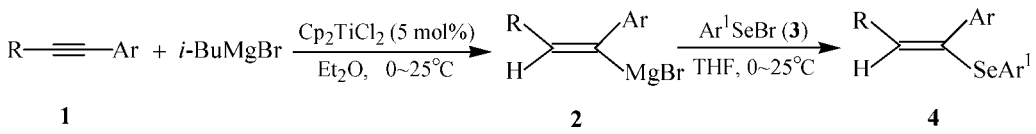


SCHEME 1

of the magnesium atom at the carbon adjacent to the aryl group. We observed that the Mg/Se exchange reaction on intermediates **2** occurs with total retention of the configuration. The configuration of compound **4a** could be confirmed from compound **5** that was obtained by treatment of **4a** with *n*-butyllithium in THF followed by hydrolysis, a reaction which occurs stereoselectively (Scheme 2). The stereochemistry of compound **5** was easily established, since ^{1}H-NMR spectrum (400 MHz) of **5** gives rise to a doublet at $\delta = 6.45$ with a coupling constant of 11.6 Hz, which is consistent with a *Z*-configuration.

In summary, our results showed that the hydromagnesiation-selenylation sequence of the alkylarylacetylenes has the advantages of readily available starting materials, straightforward and simple procedures, mild reaction conditions, and good yields.

EXPERIMENTAL

Diethyl ether was distilled from sodium immediately prior to use. IR spectra were obtained on a Perkin-Elmer 683 instrument as neat films. ^{1}H-NMR spectra were recorded on a Bruker AC-400 (400 MHz) spectrometer using $CDCl_3$ as solvent. Mass spectra were determined on a Finnigan 8230 mass spectrometer. Microanalyses were measured using a Yanaco MT-3 CHN microelemental analyzer.

General Procedure for the Synthesis of (E)-1,2-Disubstituted vinylic Selenides **4a–m**

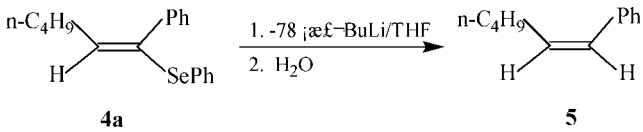
To a solution of isobutylmagnesium bromide (2.5 mmol) in diethyl ether (4 mL) was added Cp_2TiCl_2 (25 mg, 0.1 mmol) at 0°C under Ar, and the mixture was stirred for 30 min at that temperature. To this solution was added alkylarylacetylene **1** (2.0 mmol), and the mixture was stirred for 1 h at 25°C. After removal of the Et_2O under reduced pressure (2 h, r.t./2 Torr), the residue was dissolved in THF (3 mL), cooled to 0°C. Then a solution of arylselenenyl bromide **3** (2.0 mmol) in THF (3 mL) was added dropwise over 30 min with stirring at 0°C and the mixture was stirred for 6 h at 25°C, quenched with sat. aq. NH_4Cl (15 mL) and extracted with Et_2O (2×30 mL). The organic layer was washed with sat. aq. NH_4Cl (20 mL) and water (3×20 mL) and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave oil, which was purified by column chromatography on silica gel using light petroleum as eluent.

(E)-1-Phenyl-1-phenylseleno-1-hexene **4a**. IR (film): ν (cm^{-1}) 3057, 3017, 2923, 2856, 1596, 1578, 1488, 1464, 760, 736, 699; ^{1}H NMR ($CDCl_3$): δ 7.43–7.15 (m, 10H), 6.13 (t, $J = 7.6$ Hz, 1H), 2.10–2.05 (m, 2H), 1.36–1.20 (m, 4H), 0.84 (t, $J = 6.8$ Hz, 3H); MS: *m/z* 316 (M^+, 34), 159 (21), 117 (100), 91 (99), 81 (49), 77 (25), 41 (24); anal. found: C, 68.31; H, 6.16. $C_{18}H_{20}Se$ calc.: C, 68.57; H, 6.35%.

TABLE 1 Synthesis of (*E*)-1,2-Disubstituted Vinylic Selenides **4a–m**

Entry	*R*	*Ar*	*Ar^1*	*Product*	*Yield(%)*[a]
1	*n*-C_4H_9	Ph	Ph	**4a**	79
2	*n*-C_4H_9	Ph	4-ClC_6H_4	**4b**	66
3	*n*-C_4H_9	Ph	4-BrC_6H_4	**4c**	73
4	*n*-C_6H_{13}	Ph	Ph	**4d**	82
5	*n*-C_6H_{13}	Ph	4-ClC_6H_4	**4e**	72
6	*n*-C_6H_{13}	Ph	4-BrC_6H_4	**4f**	73
7	*n*-C_4H_9	4-ClC_6H_4	4-ClC_6H_4	**4g**	83
8	*n*-C_4H_9	4-ClC_6H_4	Ph	**4h**	85
9	*n*-C_4H_9	4-ClC_6H_4	4-BrC_6H_4	**4i**	77
10	*n*-C_6H_{13}	4-$CH_3OC_6H_4$	4-ClC_6H_4	**4j**	80
11	*n*-C_6H_{13}	4-$CH_3OC_6H_4$	Ph	**4k**	68
12	*n*-C_4H_9	4-$CH_3C_6H_4$	4-ClC_6H_4	**4l**	67
13	*n*-C_4H_9	4-$CH_3C_6H_4$	Ph	**4m**	70

[a]Isolated yield based on the alkylarylacetylene **1** used.



4a **5**

SCHEME 2

(E)-1-Phenyl-1-(4-chlorophenylseleno)-1-hexene **4b**. IR (film): ν (cm^{-1}) 3076, 3055, 3017, 2956, 2926, 1596, 1574, 1488, 1472, 1386, 812, 760; ^1H NMR ($CDCl_3$): δ 7.38–7.12 (m, 9H), 6.17 (t, $J = 7.6$ Hz, 1H), 2.11–2.05 (m, 2H), 1.37–1.21 (m, 4H), 0.83 (t, $J = 6.8$ Hz, 3H); MS: *m/z* 350 (M^+, 27.5), 159 (17), 117 (100), 91 (90), 81 (47), 55 (23), 41 (22); anal. found: C, 61.52; H, 5.24. $C_{18}H_{19}ClSe$ calc.: C, 61.71; H, 5.43%.

(E)-1-Phenyl-1-(4-bromophenylseleno)-1-hexene **4c**. IR (film): ν (cm^{-1}) 3055, 3017, 2956, 2857, 1597, 1565, 1488, 1466, 1380, 808, 760; ^1H NMR ($CDCl_3$): δ 7.29–7.08 (m, 9H), 6.18 (t, $J = 7.6$ Hz, 1H), 2.10–2.02 (m, 2H), 1.35–1.21 (m, 4H), 0.83 (t, $J = 7.2$ Hz, 3H); MS: *m/z* 394 (M^+, 17.4), 159 (28), 117 (100), 91 (76), 81 (59), 55 (18), 41 (19); anal. found: C, 54.60; H, 4.63. $C_{18}H_{19}BrSe$ calc.: C, 54.82; H, 4.82%.

(E)-1-Phenyl-1-phenylseleno-1-octene **4d**. IR (film): ν (cm^{-1}) 3057, 3017, 2924, 2854, 1577, 1489, 1438, 1377, 761, 736, 699; ^1H NMR ($CDCl_3$): δ 7.46–7.20 (m, 10H), 6.16 (t, $J = 7.6$ Hz, 1H), 2.18–2.04 (m, 2H), 1.40–1.20 (m, 8H), 0.87 (t, $J = 6.8$ Hz, 3H); MS: *m/z* 344 (M^+, 18.4), 117 (83), 91 (100), 77 (18), 55 (15), 41 (38); anal. found: C, 69.72; H, 6.82. $C_{20}H_{24}Se$ calc.: C, 69.97; H, 7.00%.

(E)-1-Phenyl-1-(4-chlorophenylseleno)-1-octene **4e**. IR (film): ν (cm^{-1}) 3077, 3056, 3018, 2925, 2855, 1597, 1575, 1489, 1442, 813, 761, 699; ^1H NMR ($CDCl_3$): δ 7.36–7.15 (m, 9H), 6.20 (t, $J = 7.6$ Hz, 1H), 2.14–2.08 (m, 2H), 1.41–1.20 (m, 8H), 0.88 (t, $J = 6.8$ Hz, 3H); MS: *m/z* 378 (M^+, 17.4), 117 (100), 105 (43), 91 (89), 41 (31); anal. found: C, 63.22; H, 5.89. $C_{20}H_{23}ClSe$ calc.: C, 63.49; H, 6.08%.

(E)-1-Phenyl-1-(4-bromophenylseleno)-1-octene **4f**. IR (film): ν (cm^{-1}) 3055, 3017, 2925, 2854, 1597, 1565, 1488, 1466, 1379, 808, 760, 699; ^1H NMR ($CDCl_3$): δ 7.38–7.15 (m, 9H), 6.21 (t, $J = 7.6$ Hz, 1H), 2.15–2.06 (m, 2H), 1.41–1.21 (m, 8H), 0.89 (t, $J = 6.8$ Hz, 3H); MS: *m/z* 422 (M^+, 13.4), 117 (100), 105 (47), 91 (82), 41 (30); anal. found: C, 56.64; H, 5.28. $C_{20}H_{23}BrSe$ calc.: C, 56.87; H, 5.45%.

(E)-1-(4-Chlorophenyl)-1-(4-chlorophenylseleno)-1-hexene **4g**. IR (film): ν (cm^{-1}) 2957, 2857, 1611, 1589, 1487, 1473, 1386, 1090, 870, 813, 729; ^1H NMR ($CDCl_3$): δ 7.32–7.13 (m, 8H), 6.23 (t, $J = 7.2$ Hz, 1H), 2.15–2.05 (m, 2H), 1.40–1.24 (m, 4H), 0.86 (t, $J = 6.8$ Hz, 3H); MS: *m/z* 384 (M^+, 35.3), 193 (29), 151 (94), 125 (100), 115 (75), 81 (67), 55 (72), 41 (47); anal. found: C, 56.04; H, 4.52. $C_{18}H_{18}Cl_2Se$ calc.: C, 56.25; H, 4.69%.

(E)-1-Phenylseleno-1-(4-chlorophenyl)-1-hexene **4h**. IR (film): ν (cm^{-1}) 3071, 2957, 2857, 1611, 1596, 1578, 1486, 1438, 870, 820, 737, 690; ^1H NMR ($CDCl_3$): δ 7.43–7.21 (m, 9H), 6.21 (t, $J = 7.6$ Hz, 1H), 2.11–2.05 (m, 2H), 1.40–1.25 (m, 4H), 0.86 (t, $J = 6.8$ Hz, 3H); MS: *m/z* 350 (M^+, 53.7), 193 (46), 151 (100), 125 (86), 115 (72), 81 (90), 77 (44), 55 (62), 41 (52); anal. found: C, 61.48; H, 5.26. $C_{18}H_{19}ClSe$ calc.: C, 61.71; H, 5.43%.

(E)-1-(4-Chlorophenyl)-1-(4-bromophenylseleno)-1-hexene **4i**. IR (film): ν (cm^{-1}) 2956, 2857, 1612, 1589, 1565, 1486, 1466, 1380, 870, 809, 709; ^1H NMR ($CDCl_3$): δ 7.42–7.14 (m, 8H), 6.22 (t, $J = 7.6$ Hz, 1H), 2.09–2.03 (m, 2H), 1.37–1.23 (m, 4H), 0.84 (t, $J = 6.8$ Hz, 3H); MS: *m/z* 428 (M^+, 20.3), 193 (23), 151 (86), 125 (100), 115 (74), 81 (66), 55 (79); anal. found: C, 50.17; H, 4.05. $C_{18}H_{18}ClBrSe$ calc.: C, 50.41; H, 4.20%.

(E)-1-(4-Methoxyphenyl)-1-(4-chlorophenylseleno)-1-octene **4j**. IR (film): ν (cm^{-1}) 2926, 2855, 1605, 1574, 1506, 1472, 813, 729; ^1H NMR ($CDCl_3$): δ 7.34–6.79 (m, 8H), 6.15 (t, $J = 7.2$ Hz, 1H), 3.80 (s, 3H), 2.18–2.05 (m, 2H), 1.39–1.20 (m, 8H), 0.88 (t, $J = 6.8$ Hz, 3H); MS: *m/z* 408 (M^+, 7.2), 217 (58), 147 (61), 121 (100); anal. found: C, 61.52; H, 5.98. $C_{21}H_{25}ClOSe$ calc.: C, 61.76; H, 6.13%.

(E)-1-Phenylseleno-1-(4-methoxyphenyl)-1-octene **4k**. IR (film): ν (cm^{-1}) 3057, 2926, 2854, 1603, 1577, 1506, 1475, 1464, 828, 736, 690; ^1H NMR ($CDCl_3$): δ 7.45–7.17 (m, 7H), 6.78 (d, $J = 8.8$ Hz, 2H), 6.09 (t, $J = 7.2$ Hz, 1H), 3.77 (s, 3H), 2.15–2.05 (m, 2H), 1.36–1.15 (m, 8H), 0.85 (t, $J = 6.8$ Hz, 3H); MS: *m/z* 374 (M^+, 10.8), 217 (70), 147 (61), 121 (100); anal. found: C, 67.30; H, 6.82. $C_{21}H_{26}OSe$ calc.: C, 67.56; H, 6.97%.

(E)-1-(4-Methylphenyl)-1-(4-chlorophenylseleno)-1-hexene **4l**. IR (film): ν (cm^{-1}) 3078, 3023, 2956, 2871, 1607, 1564, 1508, 1473, 814, 729; ^1H NMR ($CDCl_3$): δ 7.33–7.04 (m, 8H), 6.13 (t, $J = 7.2$ Hz, 1H), 2.30 (s, 3H), 2.15–2.06 (m, 2H), 1.35–1.23 (m, 4H), 0.83 (t, $J = 7.2$ Hz, 3H); MS: *m/z* 364 (M^+, 23),

362 (11), 173 (100), 131 (91), 105 (62), 81 (81); anal. found: C, 62.42; H, 5.56. $C_{19}H_{21}ClSe$ calc.: C, 62.64; H, 5.77%.

(E)-1-Phenylseleno-1-(4-methylphenyl)-1-hexene **4m**. IR (film): ν (cm^{-1}) 3055, 3021, 2955, 2924, 1607, 1578, 1506, 1476, 1438, 817, 736, 690; ^1H NMR ($CDCl_3$): δ 7.43–7.13 (m, 7H), 7.05 (d, $J = 7.6$ Hz, 2H), 6.10 (t, $J = 7.6$ Hz, 1H), 2.29 (s, 3H), 2.13–2.05 (m, 2H), 1.36–1.22 (m, 4H), 0.83 (t, $J = 7.2$ Hz, 3H); MS: *m/z* 330 (M^+, 31.5), 328 (17), 173 (100), 131 (79), 105 (52), 81 (62); anal. found: C, 69.12; H, 6.57. $C_{19}H_{22}Se$ calc.: C, 69.30; H, 6.69%.

The Synthesis of (Z)-1-Phenyl-1-hexene **5**

BuLi (1 mL, 1.1 M hexane solution) was added to a THF (5 mL) solution of **4a** (1.0 mmol) at −78°C. After stirring for 1 h, the mixture was hydrolyzed with saturated aq. NH_4Cl and extracted with Et_2O (2 × 30 mL). The organic extract was washed with water (2 × 10 mL), dried with $MgSO_4$, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel, eluting with light petroleum to give (*Z*)-1-phenyl-1-hexene **5** (yield: 76%) as a colorless oil. IR (film): ν (cm^{-1}) 2926, 2855, 1647, 1595, 1498, 1378. ^1H-NMR ($CDCl_3$): δ 7.34–7.20 (m, 5H), 6.45 (d, $J = 11.6$ Hz, 1H), 5.70 (dt, $J = 11.6$, 7.2 Hz, 1H), 2.36–2.29 (m, 2H), 1.46–1.32 (m, 4H), 0.93 (t, $J = 7.2$ Hz, 3H). Anal. found: C, 89.73; H, 9.84. $C_{12}H_{16}$ calc.: C, 90.00; H, 10.00%.

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