A facile stereoselective synthesis of (*E*)-1-arylseleno-2-aryl-sulfanylethenes *via* hydrozirconation of arylselenoethynes

Ming-Zhong Cai*, Min-Hua Jiang and Hai-Gen Li

School of Chemistry and Chemical Engineering, Jiangxi Normal University, Nanchang 330027, P. R. China

Hydrozirconation of arylselenoethynes **1** gave (*E*)-2-arylselenovinylzirconium(IV) complexes **2**, which reacted with arylsulfenyl chlorides **3** stereoselectively to afford (*E*)-1-arylseleno-2-arylsulfanylethenes **4** in good yields. (*E*)-1-Arylseleno-2-arylsulfanylethenes **4** could undergo a cross-coupling reaction with Grignard reagents stereoselectively in the presence of a nickel-phosphine complex to give (*E*)-vinylic sulfides **5**.

Keywords: hydrozirconation, (*E*)-1-arylseleno-2-arylsulfanylethene, arylsulfenyl chloride, cross-coupling reaction, stereoselective synthesis

The stereoselective synthesis of multifunctional alkenes is an important goal in organic synthesis and is still being actively explored because of the fact that many biologically active compounds have the structure of substituted alkenes.[1] Difunctional reagents, which have two different functional groups linked to the olefinic carbon atoms, for example S–Cu,[2] S–B,[3] S–Sn,[4] Se–Zr,[5] Se–Sn,[6] Se–Si,[7] and Se–Te[8] combinations, play an important role in organic synthesis, especially in developing many convenient methods for the stereoselective synthesis of substituted alkenes. These reagents and their synthetic applications have been reported. Vinyl selenides are important synthetic intermediates owing to the versatile reactivity of the selanyl group and the carbon–carbon double bond.[9] Vinyl sulfides have been widely used as building blocks in organic synthesis.[10] However, to the best of our knowledge, the difunctional reagent containing sulfur and selenium has rarely aroused much attention and there has been no report of the stereoselective synthesis of (*E*)-1-arylseleno-2-arylsulfanylethenes to date. Hydrozirconation has emerged as a unique hydrometallation with some attractive features such as the high regioselectivity and stereoselectivity observed with alkynes[11] and heteroatom-substituted alkynes.[12] Herein, we report that (*E*)-1-arylseleno-2- arylsulfanylethenes could be conveniently synthesised by hydrozirconation of arylselenoethynes, followed by a reaction with arylsulfenyl chlorides.

Recently, it has become popular to transform alkenylzirconium(IV) complexes to products with other functional groups with a high level of stereochemical purity.[13] For example, vinylzirconium complexes react with phenyltellurenyl iodide, arylselenenyl bromides, acid chlorides or sulfonyl chlorides readily to afford (*E*)-vinylic tellurides,[14] (*E*)-vinylic selenides,[15] (*E*)-vinylic ketones[16] or (*E*)-vinylic sulfones[17] respectively. However, the sulfidation of (*E*)-2-arylselenovinylzirconium(IV) complexes has not been reported. Considering the electrophility of arylsulfenyl chlorides, we tried to react them with the (*E*)-2-arylselenovinylzirconium complexes (**2**) produced by hydrozirconation of arylselenoethynes (**1**) (Scheme 1). The experimental results show that, $Cp_2Zr(H)Cl$[18] adds to arylselenoethynes (**1**) in THF at 0°C with high regioselectivity to yield (*E*)-2-arylseleno-vinylzirconium(IV) complexes (**2**), which react with arylsulfenyl chlorides (**3**) at room temperature to afford (*E*)-1-arylseleno-2-arylsulfanylethenes (**4**) in good yields. Typical results are summarised in Table 1. We found that the optimum molar ratio of $Cp_2Zr(H)Cl$ to **1** was 1 : 1 and that the hydrozirconation of arylselenoethynes (**1**) must be carried out at 0°C. When $Cp_2Zr(H)Cl$ was in an excess, a side reaction occurred giving undesired yellow diaryldiselenides.

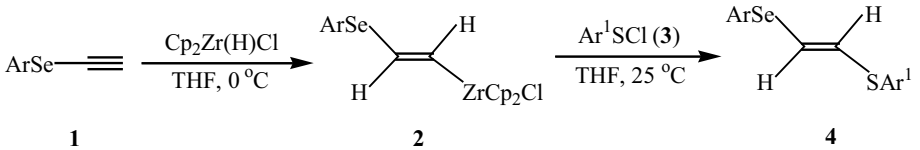
Table 1 Synthesis of compounds **4a–h**

Ar	Ar[1]	Product	Yield (%)[a]
Ph	Ph	**4a**	78
Ph	4-ClC_6H_4	**4b**	79
4-ClC_6H_4	4-$CH_3C_6H_4$	**4c**	81
4-$CH_3C_6H_4$	4-ClC_6H_4	**4d**	86
4-ClC_6H_4	Ph	**4e**	80
4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	**4f**	83
4-$CH_3C_6H_4$	Ph	**4g**	85
4-ClC_6H_4	4-ClC_6H_4	**4h**	84

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

All the compounds **4** were purified by preparative TLC on silica gel and fully characterised by IR, ^1H NMR, ^{13}C NMR, MS and elemental analyses. The stereochemistry of the (*E*)-1-arylseleno-2-arylsulfanylethenes (**4**) was easily established, since the ^1H NMR spectra of products (**4a–h**) give rise to two doublets at δ = 6.40–6.80 with a coupling constant of 14.8–15.2 Hz (J_{HH}) typical of *trans*-positioned protons.

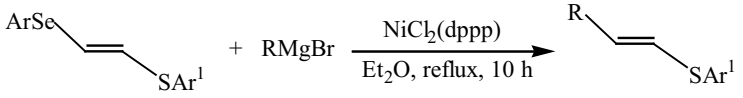
(*E*)-1-Arylseleno-2-arylsulfanylethenes **4** are difunctional reagents in which two synthetically versatile groups are linked to the olefinic carbon atoms and can be considered both as vinylselenides and vinylsulfides. Both vinylselenides and vinylsulfides have been employed to effect Ni(0)-catalysed cross-coupling reactions with Grignard reagents.[19] Takei and coworkers[19a] reported that the reactivity order of coupling reaction with BuMgBr catalysed by $NiCl_2$(dppp) was PhSeMe >> PhCl > PhSMe, determined by competitive reactions. Based on this different reactivity of selanyl and sulfanyl groups, compounds **4** should undergo the cross-coupling reaction with Grignard reagents stereoselectively in the presence of the $NiCl_2$(dppp) catalyst to give (*E*)-vinylic sulfides. Therefore, we carried out the Ni-catalysed cross-coupling reaction of (*E*)-1-arylseleno-2-arylsulfanylethenes **4** with Grignard reagents in diethyl ether (Scheme 2).



1 **2** **4**

Scheme 1

* Correspondent. E-mail: caimzhong@163.com



4 **5**

Scheme 2

Table 2 Synthesis of (*E*)-vinylic sulfides **5**

Ar	Ar[1]	R	Product	Yield/%[a]
Ph	Ph	*n*-C_4H_9	**5a**	76
4-ClC_6H_4	4-$CH_3C_6H_4$	Ph	**5b**	82
Ph	Ph	CH_3OCH_2	**5c**	68
4-$CH_3C_6H_4$	Ph	*n*-$C_4H_9C{\equiv}C$	**5d**	75

[a]Isolated yield based on (*E*)-1-arylseleno-2-arylsulfanylethene **4** used.

The experimental results showed that, in the presence of 3 mol% $NiCl_2$(dppp), the cross-coupling reaction of **4** with Grignard reagents in diethyl ether at 35°C proceeded smoothly to afford the corresponding selenium free (*E*)-vinylic sulfides **5** with retention of configuration and in good yields (see Table 2).

In summary, the hydrozirconation/sulfidation strategy provides a direct route to (*E*)-1-arylseleno-2-arylsulfanylethenes from arylselenoethynes. The method has some attractive advantages such as readily available starting materials, good yields, mild reaction conditions and straightforward access to the exclusively (*E*)-configuration product.

Experimental

^{1}H NMR spectra were recorded on a Bruker AC-P400 (400 MHz) spectrometer with TMS as an internal standard using $CDCl_3$ as the solvent. ^{13}C NMR (100 MHz) spectra were recorded on a Bruker AC-P400 (400 MHz) spectrometer using $CDCl_3$ as the solvent. IR spectra were determined on an FTS-185 instrument as neat films. Mass spectra were obtained on a Finigan 8230 mass spectrometer. Microanalyses were determined using a Yanaco MT-3 CHN microelemental analyser. All reactions were carried out in predried glassware (150°C, 4 h) and cooled under a stream of dry N_2. THF was freshly distilled from sodium-benzophenone prior to use. Diethyl ether was treated with lithium aluminum hydride and distilled before use.

General procedure for the synthesis of (E)-1-arylseleno-2-arylsulfanylethenes **4a–h**: A dry 10 ml round-bottomed flask was charged with $Cp_2Zr(H)Cl$ (1 mmol). THF (4 ml) was injected, followed by addition of arylselenoethyne **1** (1 mmol) at 0°C. The mixture was stirred at 0°C for 40 min to yield a clear solution. It was then added arylsulfenyl chloride **3** (1 mmol) and stirred at room temperature for 40 min. The mixture was diluted with diethyl ether (20 ml) and the mixture was filtered through a short plug of silica gel and concentrated to give a residue. The residue was purified by preparative TLC on silica gel eluting with light petroleum ether (b.p. 30–60°C). (For some AA'XX' systems in ^{1}H NMR $J^* = J_{23} + J_{25}$).

(E)-1-Phenylseleno-2-phenylsulfanylethene **(4a)**: IR (film): 3060, 1724, 1579, 1477, 1439, 1023, 926 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.47–7.21 (m, 10H), 6.74 (d, J = 14.8 Hz, 1H), 6.63 (d, J = 14.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 134.7, 132.1, 130.3, 129.8, 129.5, 129.3, 128.4, 127.5, 127.2, 119.6; MS: *m/z* 292 (M^+, 84), 183 (100), 157 (62), 135 (82), 134 (76), 109 (61); Anal. Calcd. for $C_{14}H_{12}SSe$: C, 57.7; H, 4.15. Found: C, 57.5; H, 3.9.

(E)-1-Phenylseleno-2-(4-chlorophenyl)sulfanylethene **(4b)**: IR (film): 3059, 1723, 1578, 1475, 1438, 1094, 925 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.54–7.22 (m, 9H), 6.79 (d, J = 14.8 Hz, 1H), 6.52 (d, J = 14.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 133.3, 133.1, 132.4, 130.9, 129.8, 129.5, 129.4, 127.7, 126.7, 121.4; MS: *m/z* 328 (M^+, 25, ^{37}Cl), 326 (M^+, 41, ^{35}Cl), 183 (100), 157 (63), 143 (36), 134 (43), 108 (52); Anal. Calcd. for $C_{14}H_{11}ClSSe$: C, 51.6; H, 3.4. Found: C, 51.4; H, 3.2.

(E)-1-(4-Chlorophenyl)seleno-2-(4-methylphenyl)sulfanylethene **(4c)**: IR (film): 3024, 1716, 1492, 1474, 1091, 1012, 925 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.34 (m, J^* = 8.4 Hz, 2H), 7.27 (m, J^* = 8.0 Hz, 2H), 7.23 (m, J^* = 8.4 Hz, 2H), 7.13 (m, J^* = 8.0 Hz, 2H), 6.68 (d, J = 15.0 Hz, 1H), 6.51 (d, J = 15.0 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 138.0, 133.6, 133.1, 132.9, 130.6, 130.3, 129.3, 125.5, 124.9, 122.9, 21.2; MS: *m/z* 342 (M^+, 49, ^{37}Cl), 340 (M^+, 100, ^{35}Cl), 216 (36), 191 (29), 182 (62), 156 (43), 134 (86), 123 (93); Anal. Calcd. for $C_{15}H_{13}ClSSe$: C, 53.0; H, 3.9. Found: C, 52.7; H, 3.7.

(E)-1-(4-Methylphenyl)seleno-2-(4-chlorophenyl)sulfanylethene **(4d)**: IR (film): 3022, 1714, 1489, 1476, 1095, 1013, 924, 793 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.39 (m, J^* = 7.6 Hz, 2H), 7.27–7.20 (m, 4H), 7.11 (m, J^* = 7.6 Hz, 2H), 6.80 (d, J = 14.8 Hz, 1H), 6.42 (d, J = 14.8 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 138.0, 133.7, 133.1, 132.9, 130.8, 130.6, 130.3, 129.3, 124.9, 122.9, 21.2; MS: *m/z* 342 (M^+, 46, ^{37}Cl), 340 (M^+, 86, ^{35}Cl), 216 (54), 191 (38), 183 (86), 156 (57), 143 (76), 109 (100); Anal. Calcd. for $C_{15}H_{13}ClSSe$: C, 53.0; H, 3.9. Found: C, 52.7; H, 3.7.

(E)-1-(4-Chlorophenyl)seleno-2-phenylsulfanylethene **(4e)**: IR (film): 3059, 1724, 1582, 1473, 1439, 1090, 925 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.36–7.23 (m, 9H), 6.73–6.65 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 134.2, 133.6, 133.2, 130.2, 130.1, 129.6, 129.4, 128.7, 127.4, 117.9; MS: *m/z* 328 (M^+, 43, ^{37}Cl), 326 (M^+, 94, ^{35}Cl), 246 (31), 216 (83), 191 (37), 182 (85), 156 (45), 134 (96), 109 (100); Anal. Calcd. for $C_{14}H_{11}ClSSe$: C, 51.6; H, 3.4. Found: C, 51.35; H, 3.2.

(E)-1-(4-Methylphenyl)seleno-2-(4-methylphenyl)sulfanylethene **(4f)**: IR (film): 3021, 2921, 1716, 1491, 923, 786 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.35 (m, J^* = 7.6 Hz, 2H), 7.23 (m, J^* = 7.6 Hz, 2H), 7.11–7.06 (m, 4H), 6.63 (d, J = 14.8 Hz, 1H), 6.53 (d, J = 14.8 Hz, 1H), 2.30 (s, 6H); ^{13}C NMR ($CDCl_3$): δ 137.5, 137.4, 132.6, 130.8, 130.5, 130.3, 130.1, 128.4, 126.3, 118.9, 21.2; MS: *m/z* 320 (M^+, 57), 216 (39), 182 (100), 157 (74), 143 (54), 109 (82); Anal. Calcd. for $C_{16}H_{16}SSe$: C, 60.2; H, 5.05. Found: C, 59.9; H, 4.8.

(E)-1-(4-Methylphenyl)seleno-2-phenylsulfanylethene **(4g)**: IR (film): 3021, 2922, 1717, 1582, 1488, 1439, 925, 794 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.39–7.07 (m, 9H), 6.76 (d, J = 15.2 Hz, 1H), 6.53 (d, J = 15.2 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 137.7, 135.0, 132.9, 130.3, 129.6, 129.3, 127.0, 126.6, 126.0, 121.1, 21.2; MS: *m/z* 306 (M^+, 64), 183 (100), 157 (74), 134 (81), 109 (74); Anal. Calcd. for $C_{15}H_{14}SSe$: C, 59.0; H, 4.6. Found: C, 58.8; H, 4.3.

(E)-1-(4-Chlorophenyl)seleno-2-(4-chlorophenyl)sulfanylethene **(4h)**: IR (film): 3027, 1897, 1714, 1640, 1573, 1473, 1388, 1092, 1011, 924 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.39–7.19 (m, 8H), 6.69 (d, J = 14.8 Hz, 1H), 6.57 (d, J = 14.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 133.8, 133.6, 132.8, 131.2, 129.6, 129.5, 129.4, 128.3, 128.2, 119.7; MS: *m/z* 364 (M^+, 11, ^{37}Cl), 362 (M^+, 39, ^{35} ^{37}Cl), 360 (M^+, 63, ^{35}Cl), 216 (72), 191 (61), 182 (100), 156 (54), 143 (74), 134 (82), 108 (91); Anal. Calcd. for $C_{14}H_{10}SSeCl_2$: C, 46.7; H, 2.8. Found: C, 46.4; H, 2.6.

General procedure for the synthesis of (E)-vinylic sulfides **5a–d:** To a mixture of (*E*)-1-arylseleno-2-arylsulfanylethene **4** (1.0 mmol) and $NiCl_2$(dppp) (0.03 mmol) in diethyl ether (8 ml) was added RMgBr (2.5 mmol) in diethyl ether (4 ml) under nitrogen at room temperature with stirring. The resulting mixture was heated to reflux for 10 h. The mixture was treated with saturated aqueous NH_4Cl solution (15 ml) at 0°C and extracted with diethyl ether (2 × 20 ml). The ethereal solution was washed with water (2 × 20 ml) and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave an oil, which was purified by preparative TLC on silica gel eluting with light petroleum ether (b.p. 30–60°C).

(E)-1-Phenylsulfanylhex-1-ene[20] **(5a)**: IR (film): 3073, 2956, 2925, 1716, 1582, 1471, 1439, 1089, 952, 812, 738 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.30–7.18 (m, 5H), 6.13 (d, J = 14.8 Hz, 1H), 6.05–5.93 (m, 1H), 2.21–2.15 (m, 2H), 1.44–1.23 (m, 4H), 0.92 (t, J = 7.2 Hz, 3H); Anal. Calcd. for $C_{12}H_{16}S$: C, 74.9; H, 8.4. Found: C, 74.7; H, 8.5.

(E)-1-Phenyl-2-(4-methylphenyl)sulfanylethene[20] **(5b)**: IR (film): 3070, 1610, 1581, 1498, 950, 776, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.41–7.06 (m, 9H), 6.79 (d, J = 15.2 Hz, 1H), 6.61 (d, J = 15.2 Hz, 1H), 2.24(s, 3H); Anal. Calcd. for $C_{15}H_{14}S$: C, 79.6; H, 6.2. Found: C, 79.4; H, 6.1.

(E)-1-Phenylsulfanyl-3-methoxypropene[20] **(5c)**: IR (film): 3076, 1597, 1488, 1089, 950, 736, 695 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.44–7.05 (m, 5H), 6.31 (d, *J* = 15.2 Hz, 1H), 5.79–5.68 (m, 1H), 3.83 (d, *J* = 6.2 Hz, 2H), 3.22(s, 3H); Anal. Calcd. for $C_{10}H_{12}OS$: C, 66.6; H, 6.7. Found: C, 66.4; H, 6.8.

(E)-1-Phenylsulfanyloct-1-en-3-yne **(5d)**: IR (film): 3059, 2957, 2925, 2221, 1596, 1487, 954, 696 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.40–7.25 (m, 5H), 6.69 (d, *J* = 15.2 Hz, 1H), 5.65 (d, *J* = 15.2 Hz, 1H), 2.31 (t, *J* = 7.2 Hz, 2H), 1.54–1.32 (m, 4H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 135.5, 133.7, 130.7, 129.3, 127.5, 110.4, 92.0, 78.3, 30.8, 22.0, 19.2, 13.6; Anal. Calcd. for $C_{14}H_{16}S$: C, 77.7; H, 7.45. Found: C, 77.5; H, 7.3.

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