Regio- and stereo-selective synthesis of tetrasubstituted olefins by the three-component tandem reaction of phenylselenomagnesium bromide, acetylenic sulfones and allylic bromides

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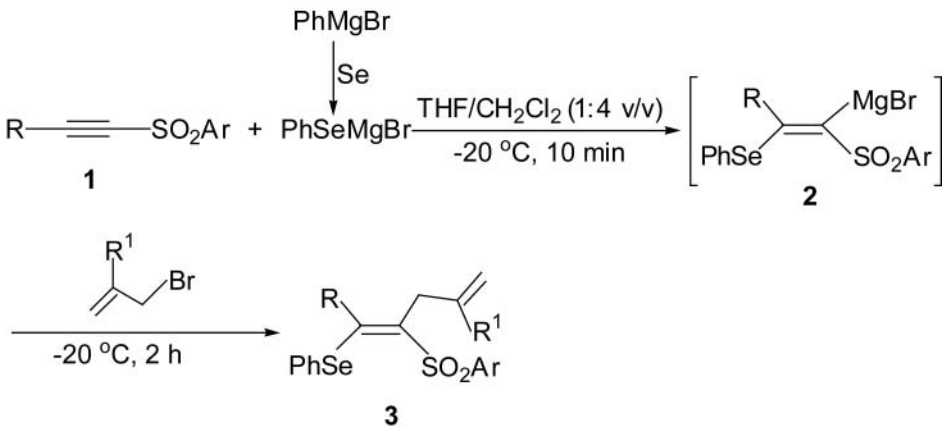
Tetrasubstituted olefins containing a 1,4-diene structural unit can be regio- and stereo-selectively synthesised in good yields under mild conditions, in one pot, by Michael addition of phenylselenomagnesium bromide to acetylenic sulfones, followed by coupling with allylic bromides.

Keywords: acetylenic sulfone, Michael addition, vinyl sulfone, vinyl selenide, tetrasubstituted olefin

The stereo-selective synthesis of multifunctional alkenes remains a challenging problem in organic synthesis and is still being actively explored because many useful functional group transformations can be achieved by introduction and removal of metal or heteroatom functions.[1–3] Difunctional group reagents, which have two different functional groups linked to the olefinic carbon atoms (such as Sn–Si,[4] Sn–Mg,[5] Sn–Zr,[6] Sn–Se,[7] Se–Zr,[8] Se–Al,[9] and Se–Cu[10]), are useful intermediates in developing convenient methods for the stereocontrolled synthesis of various substituted alkenes. Organomagnesium reagents[11,12] and vinyl selenides[13] have been widely used as building blocks in organic synthesis. However, the synthesis of functionalised alkenes from Se–Mg difunctional reagents has received less attention. Acetylenic sulfones are known as electrophiles,[14] whereas selenolate and its analogues are good nucleophiles for Michael addition.[15] The tandem reaction has recently been of interest for organic synthesis because it offers a convenient and economical method to prepare desired organic molecules.[16–19] Huang and Xie reported the stereo-selective Michael–aldol tandem reaction of phenylselenomagnesium bromide with acetylenic sulfones and carbonyl compounds, providing a simple and efficient one-pot protocol for the synthesis of difunctionalised tetrasubstituted alkenes.[20] Recently, we investigated the Michael addition of magnesium selenolate to acetylenic sulfones to prepare Se–Mg difunctional reagents which were captured by allylic bromides. Herein, we wish to report that tetrasubstituted olefins containing a 1,4-diene structural unit can be regio- and stereo-selectively synthesised in good yields under mild conditions, in one pot, by Michael addition of phenylselenomagnesium bromide to acetylenic sulfones, followed by coupling with allylic bromides.

Acetylenic sulfones **1** were prepared according to a literature procedure.[21] It is well known that the conjugate addition of phenylselenomagnesium bromide to acetylenic sulfones **1** in THF/CH_2Cl_2 (1:4 v/v) at –20 °C proceeds highly regio- and stereo-selectively to generate (*Z*)-α-arylsulfonyl-β-phenylselenovinylmagnesium bromides **2**. The Michael addition of phenylselenomagnesium bromide to acetylenic sulfones has been shown to take place in an *anti*-fashion.[20] To extend the application of the conjugate addition of phenylselenomagnesium bromide to acetylenic sulfones, considering the fact that allylic bromides are efficient electrophiles and can undergo cross-coupling reactions with organometallic reagents under mild conditions, we investigated the cross-coupling reaction of allylic bromides with (*Z*)-α-arylsulfonyl-β-phenylselenovinylmagnesium bromides **2** obtained by the conjugate addition of phenylselenomagnesium bromide to acetylenic sulfones **1** in THF/CH_2Cl_2 (1:4 v/v) (Scheme 1).

At –20 °C, 1-phenylsulfonylhex-1-yne (**1a**) was added to the solution of phenylselenomagnesium bromide in THF/CH_2Cl_2 (1:4 v/v), which was prepared *in situ* from phenylmagnesium bromide and selenium powder. When the Michael addition was complete (monitored by TLC), an allyl bromide was added to the reaction mixture and the reaction mixture was stirred at –20 °C for 2 h. The desired (4*Z*)-4-phenylsulfonyl-5-phenylseleno-1,4-nonadiene (**3a**) was obtained in 84% yield stereo-selectively. A series of acetylenic sulfones **1** were subjected to the above reaction conditions and the results are summarised in Table 1. From Table 1, we can see that the Michael addition reactions of phenylselenomagnesium bromide to a variety of acetylenic sulfones proceeded smoothly in THF/CH_2Cl_2 (1:4 v/v) at –20 °C to afford the corresponding



Scheme 1

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Table 1 Synthesis of tetrasubstituted olefins containing a 1,4-diene structural unit[a]

Entry	R	Ar	R^1	Product	Yield[b]/%
1	n-C_4H_9	Ph	H	**3a**	84
2	n-C_4H_9	Ph	CH_3	**3b**	81
3	n-C_4H_9	4-$CH_3C_6H_4$	H	**3c**	79
4	Ph	4-$CH_3C_6H_4$	H	**3d**	83
5	Ph	Ph	CH_3	**3e**	78
6	Ph	4-$CH_3C_6H_4$	CH_3	**3f**	75
7	n-C_6H_{13}	4-$CH_3C_6H_4$	H	**3g**	80
8	n-C_6H_{13}	Ph	H	**3h**	82

[a] The reaction was performed with 0.5 mmol of acetylenic sulfone **1**, 0.6 mmol of phenylselenomagnesium bromide, and 0.5 mmol of allylic bromide in THF/CH_2Cl_2 (1/4 v/v) at –20 °C for 2 h.
[b] Isolated yield based on **1** used.

intermediates **2**, which were captured by allylic bromides to give stereo-selectively tetrasubstituted olefins containing a 1,4-diene structural unit in good yields. However, when allylic chlorides were used as the electrophiles, the cross-coupling reactions of intermediates **2** did not occur and none of the desired products were obtained.

The (4*Z*)-configuration of compound **3c** was confirmed by NOESY NMR experiments. There was a correlation between the allylic protons (δ = 2.84 ppm) of the butyl group and the allylic protons (δ = 3.51 ppm) of the allyl group. No correlation between the allylic protons (δ = 2.84 ppm) of the butyl group and the aromatic protons (δ = 7.88 ppm) of the *p*-tolylsulfonyl group was observed. The NOE results indicate that **3c** has the expected (4*Z*)-configuration and the cross-coupling reaction of the intermediates **2** with allylic bromides occurs with retention of configuration of the starting intermediates **2**.

In summary, an efficient and stereo-selective one-pot synthetic method for tetrasubstituted olefins containing a 1,4-diene structural unit has been developed by Michael addition of phenylselenomagnesium bromide to acetylenic sulfones, followed by coupling with allylic bromides. The present method has the advantages of readily conditions and good yields. These tetrasubstituted olefins may be potential precursors in the synthesis of natural products and in other synthetic transformations.

Experimental

IR spectra were obtained using a Perkin-Elmer 683 instrument. ^{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 spectra were recorded on a Bruker AC-P400 (100 MHz) spectrometer using $CDCl_3$ as the solvent. Mass spectra (EI) were determined with a Finnigan 8230 mass spectrometer. Microanalyses were obtained using a Perkin-Elmer 240 elemental analyzer. THF was distilled from sodium-benzophenone immediately prior to use and CH_2Cl_2 was distilled from P_2O_5 immediately prior to use. Other reagents were used as received without further purification.

General procedure for the synthesis of tetrasubstituted olefins containing a 1,4-diene structural unit

To a colourless solution of phenylselenomagnesium bromide (0.6 mmol) in THF/CH_2Cl_2 (v/v = 1:4, 5 mL) was added acetylenic sulfone (0.5 mmol) at –20 °C. The reaction mixture was stirred at –20 °C for 10 min, then allylic bromide (0.5 mmol) was added and the resulting mixture was stirred at –20 °C for 2 h and room temperature for 1h, quenched with a saturated NH_4Cl solution (10 mL) and extracted with diethyl ether (3 × 20 mL). The organic layer was combined, washed with water (3 × 10 mL), and dried over $MgSO_4$. After filtration and removal of solvent under reduced pressure, the residue was purified by column chromatography on silica gel (eluent: light petroleum ether/Et_2O, 5:1).

(4Z)-4-Phenylsulfonyl-5-phenylselenonona-1,4-diene (**3a**): Oil. IR (film): ν (cm^{-1}) 3059, 2926, 1634, 1577, 1477, 1305, 1148, 1084, 723, 687; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99–8.01 (m, 2H), 7.53–7.34 (m, 3H), 7.13–7.08 (m, 5H), 5.88 (m, 1H), 5.23 (m, 1H), 5.14 (d, *J* = 9.6 Hz, 1H), 3.52 (d, *J* = 7.2 Hz, 2H), 2.84 (t, *J* = 8.0 Hz, 2H), 1.49–1.25 (m, 4H), 0.86 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 140.0, 137.4, 133.3, 132.8, 132.2, 129.3, 129.1, 128.5, 128.4, 126.8, 119.2, 39.6, 32.5, 30.0, 22.4, 13.8; MS (EI): *m/z* 419 (M$^+$, 1.4), 157 (44), 115 (75), 77 (100); Anal. Calcd for $C_{21}H_{24}O_2SSe$: C, 60.13; H, 5.77. Found: C, 59.85; H, 5.53%.

(4Z)-2-Methyl-4-phenylsulfonyl-5-phenylselenonona-1,4-diene (**3b**): Oil. IR (film): ν (cm^{-1}) 3067, 2929, 1644, 1577, 1477, 1307, 1149, 1084, 723, 687; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01–7.99 (m, 2H), 7.53–7.36 (m, 3H), 7.13–7.08 (m, 5H), 4.96 (s, 1H), 4.92 (d, *J* = 1.2 Hz, 1H), 3.52 (s, 2H), 2.85 (t, *J* = 8.0 Hz, 2H), 1.85 (s, 3H), 1.47–1.23 (m, 4H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 140.5, 133.9, 133.2, 132.3, 129.3, 129.1, 128.5, 128.3, 127.2, 126.7, 115.4, 39.6, 34.8, 32.6, 22.4, 22.0, 13.8; MS (EI): *m/z* 433 (M$^+$, 1.1), 157 (26), 115 (63), 77 (100); Anal. Calcd for $C_{22}H_{26}O_2SSe$: C, 60.95; H, 6.05. Found: C, 60.70; H, 6.21%.

(4Z)-4-(p-Tolylsulfonyl)-5-phenylseleno-1,4-nonadiene (**3c**): Oil. IR (film): ν (cm^{-1}) 3058, 2927, 1633, 1596, 1477, 1302, 1148, 1084, 736, 676; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 7.6 Hz, 2H), 7.18–7.07 (m, 7H), 5.87 (m, 1H), 5.23 (m, 1H), 5.13 (d, *J* = 10.0 Hz, 1H), 3.51 (d, *J* = 7.2 Hz, 2H), 2.84 (t, *J* = 8.0 Hz, 2H), 2.36 (s, 3H), 1.48-1.24 (m, 4H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 144.2, 137.5, 137.0, 132.9, 132.3, 129.3, 129.1, 129.0, 128.5, 126.6, 119.2, 39.6, 32.5, 30.0, 22.4, 21.6, 13.8; MS (EI): *m/z* 433 (M$^+$, 1.5), 157 (46), 139 (54), 115 (68), 91 (100), 77 (51); Anal. Calcd for $C_{22}H_{26}O_2SSe$: C, 60.95; H, 6.05. Found: C, 60.68; H, 6.13%.

(1Z)-1-Phenyl-1-phenylseleno-2-(p-tolylsulfonyl)penta-1,4-diene (**3d**): Oil. IR (film): ν (cm^{-1}) 3057, 1636, 1597, 1313, 1146, 1084, 810, 690; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.13–7.06 (m, 3H), 6.96–6.91 (m, 5H), 6.69–6.67 (m, 2H), 5.54 (m, 1H), 5.01 (m, 1H), 4.93 (d, *J* = 10.0 Hz, 1H), 3.33 (d, *J* = 8.0 Hz, 2H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.5, 144.5, 139.4, 137.4, 137.2, 133.5, 129.8, 129.4, 128.5, 128.4, 128.3, 128.2, 127.4, 127.1, 122.8, 117.9, 34.5, 21.8; MS (EI): *m/z* 453 (M$^+$, 1.2), 361 (15), 269 (22), 220 (100), 91 (46); Anal. Calcd for $C_{24}H_{22}O_2SSe$: C, 63.56; H, 4.89. Found: C, 63.29; H, 5.07%.

(1Z)-1-Phenyl-1-phenylseleno-2-phenylsulfonyl-4-methylpenta-1,4-diene (**3e**): Oil. IR (film): ν (cm^{-1}) 3056, 1644, 1577, 1315, 1146, 1085, 816, 687; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12–8.10 (m, 2H), 7.51–7.46 (m, 2H), 7.25–6.84 (m, 11H), 4.71 (d, *J* = 1.2 Hz, 1H), 4.60 (s, 1H), 2.73 (s, 2H), 1.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.3, 140.1, 139.5, 133.5, 132.4, 131.0, 129.6, 128.8, 128.7, 128.6, 128.1, 128.0, 127.4, 127.2, 127.0, 115.1, 37.2, 21.7; MS (EI): *m/z* 453 (M$^+$, 2.1), 178 (53), 155 (62), 105 (100), 97 (69), 77 (52); Anal. Calcd for $C_{24}H_{22}O_2SSe$: C, 63.56; H, 4.89. Found: C, 63.35; H, 4.61%.

(1Z)-1-Phenyl-1-phenylseleno-2-(p-tolylsulfonyl)-4-methylpenta-1,4-diene (**3f**): Oil. IR (film): ν (cm^{-1}) 3058, 1642, 1597, 1318, 1140, 1085, 811, 669; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, *J* = 8.4 Hz, 2H), 7.28–6.83 (m, 12H), 4.71 (t, *J* = 1.2 Hz, 1H), 4.60 (s, 1H), 2.72 (s, 2H), 2.42 (s, 3H), 1.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.6, 144.5, 140.2, 139.6, 137.1, 132.6, 130.9, 129.3, 128.8, 128.5, 128.1, 128.0, 127.9, 127.3, 126.9, 115.0, 37.1, 21.8, 21.7; MS (EI): *m/z* 467 (M$^+$, 1.2), 314 (36), 178 (97), 155 (99), 91 (100), 77 (96); Anal. Calcd for $C_{25}H_{24}O_2SSe$: C, 64.23; H, 5.17. Found: C, 64.38; H, 5.41%.

*(4Z)-4-(p-Tolylsulfonyl)-5-phenylselenoundeca-1,4-diene (**3g**):* Oil. IR (film): ν (cm^{-1}) 3057, 2926, 1635, 1597, 1478, 1305, 1146, 1081, 737, 679; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, *J* = 8.0 Hz, 2H), 7.19–7.08 (m, 7H), 5.86 (m, 1H), 5.22 (m, 1H), 5.13 (d, *J* = 10.0 Hz, 1H), 3.52 (d, *J* = 7.2 Hz, 2H), 2.85 (t, *J* = 8.0 Hz, 2H), 2.35 (s, 3H), 1.49–1.23 (m, 8H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 144.3, 137.3, 137.1, 132.8, 132.2, 129.4, 129.2, 129.1, 128.4, 126.5, 119.3, 39.7, 35.7, 31.6, 29.3, 29.0, 22.6, 21.6, 14.0; MS (EI): *m/z* 461 (M$^+$, 1.3), 157 (37), 115 (63), 91 (100), 77 (82); Anal. Calcd for $C_{24}H_{30}O_2SSe$: C, 62.45; H, 6.55. Found: C, 62.19; H, 6.33%.

*(4Z)-4-Phenylsulfonyl-5-phenylselenoundeca-1,4-diene (**3h**):* Oil. IR (film): ν (cm^{-1}) 3057, 2928, 1631, 1579, 1475, 1307, 1149, 1085, 725, 689; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00–8.02 (m, 2H), 7.54–7.35 (m, 3H), 7.14–7.09 (m, 5H), 5.89 (m, 1H), 5.22 (m, 1H), 5.14 (d, *J* = 9.6 Hz, 1H), 3.53 (d, *J* = 7.2 Hz, 2H), 2.85 (t, *J* = 8.0 Hz, 2H), 1.50–1.24 (m, 8H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 140.1, 137.3, 133.4, 132.9, 132.3, 129.4, 129.2, 128.6, 128.5, 126.9, 119.1, 39.5, 35.6, 31.78, 29.3, 29.1, 22.7, 14.1;

MS (EI): *m/z* 447 (M^+, 1.5), 157 (49), 115 (70), 77 (100); Anal. Calcd for $C_{23}H_{28}O_2SSe$: C, 61.73; H, 6.31. Found: C, 61.97; H, 6.48%.

We thank the National Natural Science Foundation of China (Project No. 20862008) and the Natural Science Foundation of Jiangxi Province in China (Project No.2007GZW0172) for financial support.

Received 24 October 2009; accepted 27 January 2010
Paper 090839 doi: 10.3184/030823410X12670432614319
Published online: 22 March 2010

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