A one-pot, stereoselective synthesis of (*Z*)-1,2-disubstituted vinyl sulfides by sequential hydrostannylation and Stille reaction of acetylenic sulfides with tributyltin hydride and then with aryl iodides

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(*Z*)-1,2-Disubstituted vinyl sulfides can be stereoselectively synthesised in one pot under mild conditions, in good yields, by the palladium-catalysed hydrostannylation of acetylenic sulfides, followed by Stille coupling with aryl iodides.

Keywords: acetylenic sulfide, hydrostannylation, (*Z*)-1,2-disubstituted vinylsulfide, Stille coupling, stereoselective synthesis

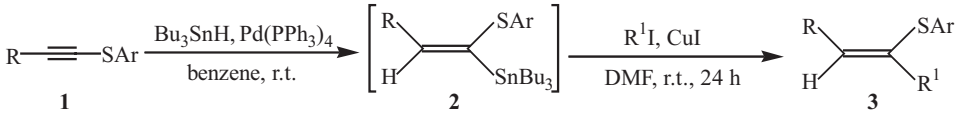
Many biologically active compounds occurring in nature possess the structural skeleton of trisubstituted alkenes.[1-5] Because disubstituted vinylsulfides can be stereospecifically converted into trisubstituted alkenes by Ni-catalysed cross-coupling reactions with nucleophiles,[6] the high-yield, stereoselective synthesis of disubstituted vinyl sulfides is a highly desirable goal. The palladium-catalysed hydrostannylation of alkynes and the Stille reaction are acknowledged as useful tools for constructing complex organic molecules. However, there has been no report on the palladium-catalysed sequential hydrostannylation and Stille reaction of alkynes with Bu_3SnH and then with organic halides to date. Herein we report that (*Z*)-1,2-disubstituted vinyl sulfides can be stereoselectively synthesised in one pot under mild conditions in good yields by the palladium-catalysed hydrostannylation of acetylenic sulfides, followed by Stille coupling with aryl iodides.

Palladium-catalysed hydrostannylation of alkynes provides a simple general route for the synthesis of vinylstannanes.[7] In 1991, Magriotis *et al.* reported that the palladium-catalysed hydrostannylation of phenylthioalkynes with Bu_3SnH was highly regio- and stereoselective, giving (*E*)-α-stannylvinyl sulfides in high yields.[8] (*E*)-α-Stannylvinyl sulfides are difunctional group reagents, in which two synthetically versatile groups are linked to the same olefinic carbon atom, and can be considered both as vinylstannanes and vinyl sulfides. The palladium-catalysed coupling reaction of organostannanes with organic halides known as Stille coupling has already been established as an efficient stereospecific method for the formation of carbon–carbon bonds under mild conditions.[9] Considering the fact that both the hydrostannylation and Stille reactions are catalysed by $Pd(PPh_3)_4$, we tried to combine the two reactions, in one pot, to prepare stereoselectively (*Z*)-1,2-disubstituted vinyl sulfides (Scheme 1).

We found that hydrostannylation of acetylenic sulfides **1** with tributyltin hydride using 5 mol% $Pd(PPh_3)_4$ in benzene, followed by solvent change (to DMF) and subsequent reaction with aryl iodides and 75 mol% CuI, gave the (*Z*)-1,2-disubstituted vinylsulfides in good yields. The experimental results are summarised in Table 1. As shown in Table 1, the hydrostannylation-Stille sequential reaction of Bu_3SnH with a variety of acetylenic sulfides and the aryl iodides proceeded smoothly under very mild conditions to afford the corresponding (*Z*)-1,2-disubstituted vinyl sulfides **3** stereoselectively. The Stille coupling reaction of the intermediates **2** with aryl bromides was very slow under the same reaction conditions, only traces of coupling products were obtained after 48 h. The Stille coupling reaction of the intermediates **2** with aryl chlorides did not occur at all.

(*Z*)-1,2-Disubstituted vinyl sulfides **3** are effective precursors for preparing stereodefined trisubstituted alkenes. In the presence of the catalyst bis(triphenylphosphine)nickel (II) chloride they can easily undergo cross-coupling reactions with Grignard reagents providing an effective method for synthesis of trisubstituted alkenes. Thus, compounds **3a** and **3h** afford the sulfur-free trisubstituted alkenes **5a** and **5b** in 61 and 65% yield, respectively (Scheme 2).

In conclusion, we have developed an efficient and stereoselective one-pot method for the synthesis of (*Z*)-1,2-disubstituted vinyl sulfides. The present method has the advantages of readily available starting materials, a straightforward and simple procedure, mild reaction conditions and good yields.



Scheme 1

Table 1 Synthesis of (*Z*)-1,2-disubstituted vinyl sulfides **3a–h**

Entry	R	Ar	R^1	Product	Yield[a]/%
1	*n*-C_4H_9	4-ClC_6H_4	Ph	**3a**	82
2	*n*-C_4H_9	4-ClC_6H_4	4-ClC_6H_4	**3b**	80
3	*n*-C_4H_9	4-ClC_6H_4	4-$CH_3C_6H_4$	**3c**	74
4	*n*-C_4H_9	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	**3d**	79
5	CH_3OCH_2	Ph	Ph	**3e**	76
6	CH_3OCH_2	Ph	4-$CH_3C_6H_4$	**3f**	78
7	Ph	Ph	4-$CH_3C_6H_4$	**3g**	79
8	Ph	Ph	Ph	**3h**	81

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

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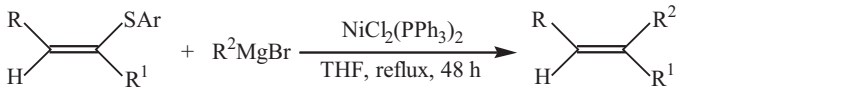

3 **4**

5a R = Bu, R^1= Ph, R^2= Me, 61%
5b R = R^1= Ph, R^2= Me, 65%

Scheme 2

Experimental

THF and benzene were distilled from sodium-benzophenone immediately prior to use. DMF was dried and distilled before use. IR spectra were obtained on a Perkin-Elmer 683 instrument as neat films. ^{1}H NMR spectra were recorded on a Bruker AC-300 (300 MHz) spectrometer using $CDCl_3$ as solvent. ^{13}C NMR spectra were recorded on a Bruker AC-300 (75 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 analyser. Methylmagnesium bromide was purchased from Aldrich and $Ni(PPh_3)_2Cl_2$ was prepared according to the procedure described by Venanzi.[10]

General procedure for the synthesis of (Z)-1,2-disubstituted vinyl sulfides **3a–h**

A 25 ml, two-necked, round-bottom flask equipped with a magnetic stirring bar, was charged sequentially with acetylenic sulfide **1** (1 mmol), benzene (4 ml), $Pd(PPh_3)_4$ (0.05 mmol) and Bu_3SnH (1.05 mmol) under argon. The mixture was stirred at room temperature for 8 h. The solvent was removed under reduced pressure and the residue was dissolved in DMF (10 ml). Then aryl iodide (1.1 mmol) and CuI (0.75 mmol) were added and the mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with Et_2O (30 ml), filtered and then treated with 20% aqueous KF (10 ml) for 30 min before the organic layer was taken, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography on silica gel using light petroleum ether as eluent.

For ^{1}H NMR AA'XX' systems, $J^* = J_{23} + J_{25}$.

Compound **3a**: IR (film): ν (cm^{-1}) 3057, 2957, 2856, 1595, 1475, 1389, 1093, 1012, 813, 759, 696; ^{1}H NMR: δ 7.51 (m, J^* = 7.6 Hz, 2H), 7.24–7.02 (m, 7H), 6.42 (t, J = 7.2 Hz, 1H), 2.56–2.50 (m, 2H), 1.50–1.34 (m, 4H), 0.92 (t, J = 7.6 Hz, 3H); ^{13}C NMR: δ 140.6, 140.1, 134.7, 133.0, 131.2, 129.4, 128.8, 128.3, 127.6, 127.4, 31.5, 30.8, 22.5, 14.0; MS: *m/z* 302 (M^+, ^{35}Cl, 76), 259 (27), 159 (36), 147 (39), 117 (64), 91 (100); Anal. Calcd. for $C_{18}H_{19}SCl$: C, 71.39; H, 6.32. Found: C, 71.1; H, 6.1.

Compound **3b**: IR (film): ν (cm^{-1}) 2957, 2857, 1718, 1591, 1475, 1390, 1093, 1012, 814, 743; ^{1}H NMR: δ 7.44 (m, J^* = 8.8 Hz, 2H), 7.18 (m, J^* = 8.8 Hz, 2H), 7.09 (m, J^* = 8.4 Hz, 2H), 7.03 (m, J^* = 8.4 Hz, 2H), 6.38 (t, J = 7.2 Hz, 1H), 2.55–2.49 (m, 2H), 1.50–1.35 (m, 4H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR: δ 140.9, 138.6, 134.2, 133.4, 132.2, 131.6, 129.6, 128.9, 128.7, 128.4, 31.5, 30.8, 22.5, 14.0; MS: *m/z* 336 (M^+, ^{35}Cl, 45), 293 (23), 181 (25), 151 (94), 125 (100), 81 (36), 55 (79); Anal. Calcd. for $C_{18}H_{18}SCl_2$: C, 64.09; H, 5.38. Found: C, 63.8; H, 5.2.

Compound **3c**: IR (film): ν (cm^{-1}) 2957, 2926, 1712, 1610, 1475, 1389, 1093, 1012, 814, 743; ^{1}H NMR: δ 7.41 (m, J^* = 8.0 Hz, 2H), 7.09–7.01 (m, 6H), 6.39 (t, J = 7.2 Hz, 1H), 2.54–2.48 (m, 2H), 2.27 (s, 3H), 1.49–1.35 (m, 4H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR: δ 139.8, 137.4, 137.2, 134.9, 132.8, 131.1, 129.3, 129.0, 128.8, 127.3, 31.6, 30.8, 22.5, 21.1, 14.0; MS: *m/z* 316 (M^+, ^{35}Cl, 34), 173 (21), 131 (63), 115 (36), 105 (100), 91 (31), 81 (68); Anal. Calcd. for $C_{19}H_{21}SCl$: C, 72.02; H, 6.68. Found: C, 71.8; H, 6.6.

Compound **3d**: IR (film): ν (cm^{-1}) 2957, 2925, 1713, 1492, 1455, 1089, 1018, 803; ^{1}H NMR: δ 7.43 (m, J^* = 8.0 Hz, 2H), 7.05–7.00 (m, 4H), 6.92 (m, J^* = 8.0 Hz, 2H), 6.34 (t, J = 7.2 Hz, 1H), 2.54–2.49 (m, 2H), 2.25 (s, 3H), 2.19 (s, 3H), 1.49–1.36 (m, 4H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR: δ 139.1, 137.8, 137.1, 135.0, 133.5, 132.6, 129.4, 128.8, 128.3, 127.4, 31.6, 30.7, 22.5, 21.1, 20.9, 14.0; MS: *m/z* 296 (M^+, 32), 173 (12), 131 (46), 115 (21), 105 (100), 91 (26); Anal. Calcd. for $C_{20}H_{24}S$: C, 81.03; H, 8.16. Found: C, 80.8; H, 7.9.

Compound **3e**: IR (film): ν (cm^{-1}) 3058, 2925, 1722, 1582, 1478, 1440, 1119, 1024, 740; ^{1}H NMR: δ 7.48 (d, J = 7.6 Hz, 2H), 7.14–6.94 (m, 8H), 6.38 (t, J = 6.0 Hz, 1H), 4.31 (d, J = 5.6 Hz, 2H), 3.32 (s, 3H); ^{13}C NMR: δ 139.2, 136.4, 134.9, 134.7, 128.9, 128.8, 128.3, 128.1, 127.7, 125.9, 70.8, 58.4; MS: *m/z* 256 (M^+, 18), 147 (27), 121 (83), 103 (36), 91 (13), 77 (45), 45 (100); Anal. Calcd. for $C_{16}H_{16}OS$: C, 74.96; H, 6.29. Found: C, 74.7; H, 6.1.

Compound **3f**: IR (film): ν (cm^{-1}) 3056, 2922, 1719, 1582, 1478, 1368, 1119, 1024, 809, 740; ^{1}H NMR: δ 7.46 (m, J^* = 8.0 Hz, 2H), 7.15–7.01 (m, 7H), 6.44 (t, J = 6.0 Hz, 1H), 4.38 (d, J = 6.0 Hz, 2H), 3.40 (s, 3H), 2.25 (s, 3H); ^{13}C NMR: δ 138.0, 136.4, 136.2, 135.2, 134.1, 129.0, 128.8, 128.7, 127.6, 125.8, 70.9, 58.4, 21.1; MS: *m/z* 270 (M^+, 28), 136 (37), 119 (63), 91 (42), 77 (11), 45 (100); Anal. Calcd. for $C_{17}H_{18}OS$: C, 75.52; H, 6.71. Found: C, 75.3; H, 6.5.

Compound **3g**: IR (film): ν (cm^{-1}) 3021, 2925, 1725, 1582, 1478, 1440, 1180, 1024, 739; ^{1}H NMR: δ 7.71 (m, J^* = 7.6 Hz, 2H), 7.54 (d, J = 8.0 Hz, 2H), 7.36–7.00 (m, 11H), 2.27 (s, 3H); ^{13}C NMR: δ 138.1, 137.9, 136.9, 135.6, 135.3, 134.4, 129.5, 129.0, 128.9, 128.7, 128.2, 127.9, 127.8, 125.7, 21.2; MS: *m/z* 302 (M^+, 100), 193 (77), 178 (67), 135 (79), 115 (49), 91 (21), 77 (18); Anal. Calcd. for $C_{21}H_{18}S$: C, 83.40; H, 5.99. Found: C, 83.2; H, 5.7.

Compound **3h**: IR (film): ν (cm^{-1}) 3057, 3021, 1724, 1582, 1478, 1445, 1075, 1025, 762, 691; ^{1}H NMR: δ 7.73 (d, J = 7.6 Hz, 2H), 7.63 (d, J = 7.6 Hz, 2H), 7.38–7.00 (m, 12H); ^{13}C NMR: δ 141.0, 136.8, 135.7, 135.3, 134.7, 129.6, 129.2, 128.7, 128.2, 128.1, 127.9, 127.8, 125.9; MS: *m/z* 288 (M^+, 100), 178 (97), 121 (53), 77 (28); Anal. Calcd. for $C_{20}H_{16}S$: C, 83.29; H, 5.59. Found: C, 83.1; H, 5.4.

General procedure for the synthesis of stereodefined trisubstituted alkenes **5a–b**

To a stirred suspension of $NiCl_2(PPh_3)_2$ (0.05 mmol) and the (*Z*)-1,2-disubstituted vinyl sulfide **3** (1 mmol) in THF (6 ml) was added a 3.0 M THF solution of Me MgBr (15 mmol) at room temperature under argon. The mixture was stirred at reflux temperature for 48 h. After being cooled to room temperature, the mixture was quenched with sat. aq NH_4Cl (15 ml) and extracted with Et_2O (2 × 30 ml). The organic layer was washed with water (3 × 10 ml) and dried ($MgSO_4$). Removal of solvent under reduced pressure gave an oil, which was purified by column chromatography on silica gel using light petroleum ether as eluent.

(E)-2-Phenylhept-2-ene (**5a**): IR (film): ν (cm^{-1}) 3021, 2957, 2928, 1646, 1597, 851, 753; ^{1}H NMR: δ 7.37–7.10 (m, 5H), 5.71 (t, J = 6.4 Hz, 1H), 2.24–2.05 (m, 2H), 2.02 (s, 3H), 1.47–1.21 (m, 4H), 0.89 (t, J = 7.2 Hz, 3H); Anal. Calcd. for $C_{13}H_{18}$: C, 89.59; H, 10.41. Found: C, 89.3; H, 10.3.

(E)-1-Methyl-1,2-diphenylethene (**5b**): IR (film): ν (cm^{-1}) 3057, 2925, 1651, 1528, 1422; ^{1}H NMR: δ 7.52–7.03 (m, 10H), 6.71 (m, 1H), 2.15 (d, J = 1.3 Hz, 3H); Anal. Calcd. for $C_{15}H_{14}$: C, 92.74; H, 7.26. Found: C, 92.5; H, 7.0.

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