A facile stereoselective synthesis of 1,4-dienyl sulfides via Stille coupling reactions of (*E*)-α-stannylvinyl sulfides with allylic bromides

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(*E*)-α-Stannylvinyl sulfides **1** underwent Stille coupling reactions with allylic bromides **2** in DMF at room temperature in the presence of $Pd(PPh_3)_4$ and CuI co-catalyst to afford stereoselectively 1,4-dienyl sulfides **3** in good yields.

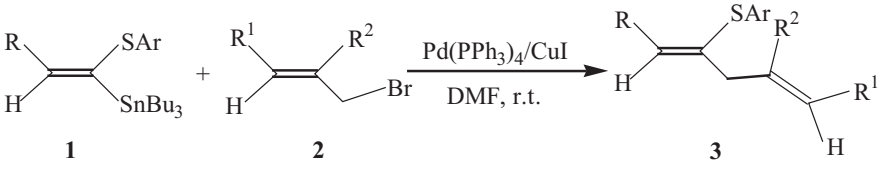
Keywords: (*E*)-α-stannylvinyl sulfide, 1,4-dienyl sulfide, stille coupling, allylic bromide, stereoselective synthesis

The 1,4-diene framework constitutes an important structural assembly in many molecules of biological importance[1] in addition to its application in organic synthesis[2] and so the synthesis of 1,4-dienes has attracted much interest.[3] Many methods can be used for this synthesis. The stereospecific reduction of 1,4-diynes by catalytic hydrogenation over Lindlar catalyst or reduction with sodium in liquid ammonia gives the *Z,Z*- or *E,E*-1,4-dienes, respectively.[4] The tandem alkylation-reduction of α, β, γ, δ-unsaturated ketones forms 1,4-dienes regiospecifically.[5] The methylcopper-induced cross-coupling of alkenylboranes with allylic halides affords 1,4-dienes stereoselectively.[6] The palladium-catalysed stereo- and regiospecific coupling of allylic derivatives with alkenylmetals also gives 1,4-dienes highly selectively.[7] Very recently, Kabalka and Al-Masum reported a new route to 1,4-pentadienes by microwave-enhanced palladium-catalysed cross-coupling reactions of potassium vinyltrifluoroborates and allyl acetates.[8]

The heteroatom-containing 1,4-dienes are also useful as building blocks since many useful functional group transformations can be achieved by introduction and removal of the heteroatom functions. The stereoselective synthesis of 1,4-dienylsilanes,[9] 1,4- dienyl selenides[10] and 1,4-dienyl sulfones[11] has been described in the literature. Herein, we wish to report that 1,4-dienyl sulfides can be conveniently synthesised by the Stille coupling reactions of (*E*)-α-stannylvinyl sulfides with allylic bromides.

(*E*)-α-Stannylvinyl sulfides **1** were conveniently prepared by the palladium-catalysed hydrostannylation reactions of alkynylsulfides according to the literature.[12] (*E*)-α-Stannylvinyl sulfides **1** are very useful 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 as vinyl sulfides. With a convenient route to the (*E*)-α-stannylvinyl sulfides **1** we decided to establish the feasibility of using **1** in cross-coupling reactions with allylic bromides **2**. Gratifyingly, when the cross-coupling reactions of **1** with a variety of allylic bromides **2** were conducted in DMF at room temperature using $Pd(PPh_3)_4$ and CuI as co-catalyst (Scheme 1), fairly rapid reactions occurred affording stereoselectively the desired coupling products **3** in good yields. The experimental results are summarised in Table 1. However, we found that when the cross-coupling reactions of (*E*)-α-stannylvinyl sulfides **1** with allylic chlorides were performed under the same conditions, only traces of coupling products were obtained.

It is well documented that the cross-coupling reaction (Stille coupling) of vinylstannanes with organic halides in the presence of a palladium catalyst occurs with retention of configuration.[13] The *E*-configuration of the compounds **3i** and **3j** has been proved by their ^{1}H NMR spectra which show doublets at δ = 6.27 or 6.28 with coupling constants of 16.0 Hz. In addition, the *Z*-configuration of the compound **3e** was confirmed by the NOESY in the ^{1}H NMR spectrum. An enhancement of the allylic protons was observed as the vinylic proton (δ = 5.92) of **3e** was irradiated. There was no correlation between the vinylic proton (δ = 5.92) and aromatic



Scheme 1

Table 1 Synthesis of 1,4-dienyl sulfides **3a–j**[a]

R	Ar	R^1	R^2	Product	Yield/%[b]
n-C_4H_9	Ph	H	H	**3a**	82
n-C_4H_9	4-$CH_3C_6H_4$	H	H	**3b**	84
CH_3OCH_2	Ph	H	H	**3c**	80
Ph	4-$CH_3C_6H_4$	H	H	**3d**	78
n-C_4H_9	Ph	H	CH_3	**3e**	88
n-C_4H_9	4-$CH_3C_6H_4$	H	CH_3	**3f**	87
Ph	4-$CH_3C_6H_4$	H	CH_3	**3g**	81
CH_3OCH_2	Ph	H	CH_3	**3h**	86
n-C_4H_9	Ph	Ph	H	**3i**	75
Ph	4-$CH_3C_6H_4$	Ph	H	**3j**	77

[a]Reactions were carried out with **1** (1.0 mmol), **2** (1.05 mmol), $Pd(PPh_3)_4$ (0.05 mmol), and CuI (0.75 mmol), using DMF (10 ml) as solvent at room temperature under Ar for 8 h.
[b]Isolated yield based on the **1** used.

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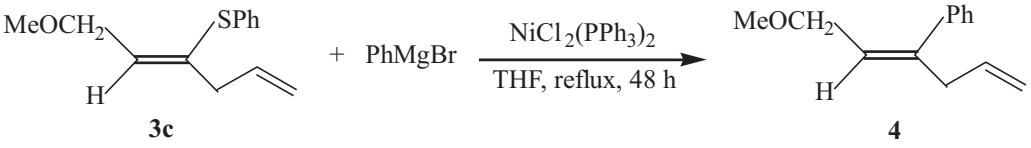

Scheme 2

protons. A correlation between the vinylic proton (δ = 5.92) and another allylic protons (δ = 2.84) was also observed. The NOE results indicate that **3e** has the expected *Z*-configuration and the cross-coupling reaction of (*E*)-α-stannylvinyl sulfides with allylic bromides occurs with retention of configuration.

Vinyl sulfides are important synthetic intermediates owing to the versatile reactivity of the sulfanyl group and the carbon-carbon double bond.[14] 1,4-Dienyl sulfides can undergo cross-coupling reactions with Grignard reagents easily to provide an effective method of stereoselective synthesis of 1,4-dienes (Scheme 2).

In summary, the present method has the advantage of simple starting materials, mild reaction conditions, convenient manipulation and stereoselectivity.

Experimental

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. ^{13}C NMR spectra were recorded on a Bruker AC-400 (100 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. All solvents were dried, deoxygenated and freshly distilled before use.

General procedure for the synthesis of 1,4-dienyl sulfides **3a–j**

(*E*)-α-Stannylvinyl sulfide **1** (1 mmol) and allylic bromide **2** (1.05 mmol) were dissolved in DMF (10 ml) under Ar at room temperature. The compounds $Pd(PPh_3)_4$ (0.05 mmol) and CuI (0.75 mmol) were then added. The mixture was stirred at room temperature and monitored by TLC for the disappearance of the starting organostannane. Then it was diluted with diethyl ether (40 ml) and the organic layer was washed with aqueous NH_4Cl (10 ml) and water (20 ml), and then dried with $MgSO_4$. The solvent was removed under reduced pressure and the residue purified by column chromatography on silica gel eluting with light petroleum ether.

Compound **3a**: IR (film): ν (cm^{-1}) 3074, 3023, 2957, 1715, 1639, 1583, 1477, 740, 690; ^{1}H NMR ($CDCl_3$): δ 7.37–7.10 (m, 5H), 5.91 (t, *J* = 7.2 Hz, 1H), 5.85–5.76 (m, 1H), 5.02–4.93 (m, 2H), 2.89 (d, *J* = 6.8 Hz, 2H), 2.37–2.32 (m, 2H), 1.43–1.26 (m, 4H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 137.4, 136.0, 135.3, 131.3, 129.7, 128.8, 126.0, 116.4, 41.8, 31.6, 29.7, 22.4, 14.0; MS: *m/z* 231 (M$^+$-1, 4.7), 57 (54), 43 (68), 41 (100); Anal. Found: C, 77.3; H, 8.5. $C_{15}H_{20}S$ Calc.: C, 77.53; H, 8.68%.

Compound **3b**: IR (film): ν (cm^{-1}) 3076, 2957, 1716, 1639, 1491, 1457, 913, 807; ^{1}H NMR ($CDCl_3$): δ 7.18 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 5.84 (t, *J* = 7.2 Hz, 1H), 5.81–5.77 (m, 1H), 5.01–4.93 (m, 2H), 2.85 (d, *J* = 6.8 Hz, 2H), 2.38–2.34 (m, 2H), 2.31 (s, 3H), 1.41–1.23 (m, 4H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 136.2, 136.1, 136.0, 131.9, 131.3, 130.4, 129.6, 116.2, 41.5, 31.6, 29.6, 22.4, 21.1, 14.0; MS: *m/z* 246 (M$^+$, 8.4), 244 (19), 124 (47), 91 (77), 57 (80), 41 (100); Anal. Found: C, 77.8; H, 8.8. $C_{16}H_{22}S$ Calc.: C, 77.99; H, 9.00%.

Compound **3c**: IR (film): ν (cm^{-1}) 3075, 2957, 1715, 1639, 1583, 1477, 1439, 1191, 1116, 742, 691; ^{1}H NMR ($CDCl_3$): δ 7.35–7.19 (m, 5H), 5.99 (t, *J* = 6.0 Hz, 1H), 5.84–5.75 (m, 1H), 5.05–4.94 (m, 2H), 4.23 (d, *J* = 6.0 Hz, 2H), 3.36 (s, 3H), 2.90 (d, *J* = 6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 135.8, 135.1, 133.9, 131.8, 130.7, 129.0, 126.8, 117.1, 70.1, 58.2, 41.3; MS: *m/z* 220 (M$^+$, 4.6), 176 (43), 147 (100), 109 (44), 77 (42), 45 (88); Anal. Found: C, 70.7; H, 7.0. $C_{13}H_{16}OS$ Calc.: C, 70.87; H, 7.32%.

Compound **3d**: IR (film): ν (cm^{-1}) 3077, 3021, 2956, 1715, 1638, 1598, 1491, 1444, 808, 693; ^{1}H NMR ($CDCl_3$): δ 7.56 (d, *J* = 7.6 Hz, 2H), 7.38–7.23 (m, 5H), 7.09 (d, *J* = 8.0 Hz, 2H), 6.72 (s, 1H), 5.89–5.83 (m, 1H), 5.08–4.98 (m, 2H), 2.97 (d, *J* = 6.8 Hz, 2H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 137.3, 136.7, 135.7, 134.6, 133.2, 132.1, 131.2, 129.7, 129.2, 128.0, 127.1, 116.8, 42.0, 21.1; MS: *m/z* 266 (M$^+$, 3.8), 265 (M$^+$-1, 11), 128 (36), 115 (56), 91 (100), 77 (46); Anal. Found: C, 80.9; H, 6.6. $C_{18}H_{18}S$ Calc.: C, 81.15; H, 6.81%.

Compound **3e**: IR (film): ν (cm^{-1}) 3074, 2957, 1713, 1651, 1583, 1477, 739, 690; ^{1}H NMR ($CDCl_3$): δ 7.28–7.14 (m, 5H), 5.92 (t, *J* = 7.2 Hz, 1H), 4.79 (s, 1H), 4.60 (s, 1H), 2.84 (s, 2H), 2.40–2.34 (m, 2H), 1.66 (s, 3H), 1.43–1.32 (m, 4H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 142.8, 138.1, 135.4, 130.7, 129.9, 128.8, 126.0, 112.9, 45.8, 31.6, 29.7, 22.4, 21.7, 14.0; MS: *m/z* 246 (M$^+$, 3.5), 229 (100), 228 (77), 186 (51), 110 (46), 77 (42); Anal. Found: C, 77.8; H, 8.8. $C_{16}H_{22}S$ Calc.: C, 77.99; H, 9.00%.

Compound **3f**: IR (film): ν (cm^{-1}) 3073, 3018, 2958, 1713, 1650, 1583, 1491, 1454, 890, 807; ^{1}H NMR ($CDCl_3$): δ 7.18 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 5.85 (t, *J* = 7.2 Hz, 1H), 4.79 (s, 1H), 4.59 (s, 1H), 2.80 (s, 2H), 2.40–2.34 (m, 2H), 2.32 (s, 3H), 1.65 (s, 3H), 1.42–1.31 (m, 4H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 142.9, 137.0, 136.1, 131.4, 131.2, 130.5, 129.5, 112.9, 45.5, 31.6, 29.6, 22.4, 21.7, 21.1, 14.0; MS: *m/z* 260 (M$^+$, 3.8), 259 (M$^+$-1, 10), 242 (98), 240 (67), 91 (100); Anal. Found: C, 78.1; H, 9.1. $C_{17}H_{24}S$ Calc.: C, 78.40; H, 9.29%.

Compound **3g**: IR (film): ν (cm^{-1}) 3075, 3021, 2957, 1713, 1650, 1598, 1492, 1444, 808, 693; ^{1}H NMR ($CDCl_3$): δ 7.58 (d, *J* = 7.6 Hz, 2H), 7.38–7.23 (m, 5H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.73 (s, 1H), 4.84 (s, 1H), 4.66 (s, 1H), 2.92 (s, 2H), 2.32 (s, 3H), 1.64 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 142.3, 136.8, 133.6, 131.9, 131.3, 130.1, 129.5, 129.1, 128.8, 127.6, 126.7, 112.9, 45.6, 21.4, 20.7; MS: *m/z* 280 (M$^+$, 100), 226 (23), 157 (47), 115 (37), 91 (35), 77 (22); Anal. Found: C, 81.2; H, 6.9. $C_{19}H_{20}S$ Calc.: C, 81.38; H, 7.19%.

Compound **3h**: IR (film): ν (cm^{-1}) 3074, 2957, 1716, 1650, 1583, 1476, 1439, 1194, 1121, 743, 691; ^{1}H NMR ($CDCl_3$): δ 7.32–7.19 (m, 5H), 6.00 (t, *J* = 6.0 Hz, 1H), 4.82 (s, 1H), 4.60 (s, 1H), 4.25 (d, *J* = 6.0 Hz, 2H), 3.38 (s, 3H), 2.86 (s, 2H), 1.66 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 142.1, 135.1, 133.9, 132.5, 130.9, 128.9, 126.8, 113.6, 70.2, 58.2, 45.3, 21.7; MS: *m/z* 234 (M$^+$, 7.8), 203 (25), 177 (27), 147 (57), 93 (100), 77 (54), 45 (24); Anal. Found: C, 71.5; H, 7.5. $C_{14}H_{18}OS$ Calc.: C, 71.75; H, 7.74%.

Compound **3i**: IR (film): ν (cm^{-1}) 3083, 3018, 2923, 1723, 1650, 1481, 1464, 963, 808, 694; ^{1}H NMR ($CDCl_3$): δ 7.37–7.15 (m, 10H), 6.27 (d, *J* = 16.0 Hz, 1H), 6.20 (dt, *J* = 16.0, 6.4 Hz, 1H), 5.97 (t, *J* = 7.2 Hz, 1H), 3.04 (d, *J* = 6.4 Hz, 2H), 2.41–2.34 (m, 2H), 1.42–1.25 (m, 4H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 139.3, 137.4, 135.2, 131.5, 129.8, 129.1, 128.9, 128.5, 127.7, 127.1, 126.1, 116.4, 41.0, 31.6, 29.7, 22.4, 14.0; MS: *m/z* 308 (M$^+$, 36), 218 (51), 115 (100), 109 (52), 77 (48); Anal. Found: C, 81.5; H, 7.7. $C_{21}H_{24}S$ Calc.: C, 81.76; H, 7.84%.

Compound **3j**: IR (film): ν (cm^{-1}) 3080, 3024, 2921, 1718, 1492, 1445, 965, 808, 693; ^{1}H NMR ($CDCl_3$): δ 7.59–7.56 (m, 2H), 7.38–7.16 (m, 10H), 7.12 (d, *J* = 8.0 Hz, 2H), 6.77 (s, 1H), 6.28 (d, *J* = 16.0 Hz, 1H), 6.22 (dt, *J* = 16.0, 5.6 Hz, 1H), 3.12 (d, *J* = 5.6 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 139.7, 137.4, 136.7, 135.0, 133.4, 132.4, 132.0, 131.2, 129.8, 129.3, 128.5, 128.1, 127.5, 127.2, 126.2, 116.9, 41.4, 21.2; MS: *m/z* 342 (M$^+$, 100), 225 (92), 210 (94), 115 (53), 91 (88), 77 (22); Anal. Found: C, 84.0; H, 6.2. $C_{24}H_{22}S$ Calc.: C, 84.16; H, 6.47%.

Reaction of the 1,4-dienyl sulfide **3c** *with Ph MgB*r: To a stirred suspension of $NiCl_2(PPh_3)_2$ (0.05 mmol) and 1,4-dienyl sulfide **3c** (1 mmol) in THF (5 ml) was added a solution of Ph MgBr (15 mmol) in THF (5 ml) at room temperature under Ar. 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. Yield 67%.

Compound **4:** IR (film): ν (cm^{-1}) 3087, 3021, 1613, 1589, 1454, 1119, 741, 690; ^{1}H NMR ($CDCl_3$): δ 7.36–7.12 (m, 5H), 6.08–6.01 (m, 1H), 5.89 (t, *J* = 6.0 Hz, 1H), 5.14–5.03 (m, 2H), 4.14 (d, *J* = 6.0 Hz, 2H), 3.38 (s, 3H), 3.13 (d, *J* = 5.6 Hz, 2H). Anal. Found: C, 82.7; H, 8.6. $C_{13}H_{16}O$ Calc.: C, 82.94; H, 8.57%.

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References

1 (a) S. Durand, J.-L. Parrain and M. Santelli, *J. Chem. Soc., Perkin Trans. 1,* 2000, 253; (b) O. Andrey, C. Glanzmann, Y. Landais and L. Parra-Rapado, *Tetrahedron,* 1997, **53**, 2835; (c) K.C. Nicolaou, J.Y. Ramphal, N.A. Petasis and C.N. Serhan, *Angew. Chem., Int. Ed. Engl.,* 1991, **30**, 1100.

2 (a) D. Basavaiah, D.S. Sharada, N. Kumaragurubaran and R.M. Reddy, *J. Org. Chem.,* 2002, **67**, 7135; (b) N. Tsukada, T. Sato and Y. Inoue, *Chem. Commun.,* 2001, 237; (c) E. Klaps and W. Schmid, *J. Org. Chem.,* 1999, **64**, 7537; (d) H. Matsushita and E. Negishi, *J. Am. Chem. Soc.,* 1981, **103**, 2882.

3 S. Okamoto, Y. Takayama, Y. Gao and F. Sato, *Synthesis,* 2000, 975.

4 K.C. Nicolaou, P.E. Hernandez, T. Ladduwhetty, J.L. Randall, S.E. Webber, W.S. Li and N.A. Petasis, *J. Org. Chem.*, 1983, **48**, 5404.

5 J.S.R. Zilenovski and S.S. Hall, *J. Org. Chem.*, 1979, **44**, 1159.

6 (a) Y. Yamamoto, H. Yatagai, A. Sonoda and S. Murahashi, *J. Chem. Soc., Chem. Commun.*, 1976, 452; (b) H. Yatagai, *J. Org. Chem.*, 1980, **45**, 1640.

7 H. Matsushita and E.I. Negishi, *J. Am. Chem. Soc.*, 1981, **103**, 2882.

8 G.W. Kabalka and M. Al-Masum, *Org. Lett.*, 2006, **8**, 11.

9 (a) E. Schaumann and A. Kirschning, *J. Chem. Soc., Perkin Trans. 1,* 1990, 419; (b) H. Zhao, W. Hao, M. Cai and Z. Zhou, *J. Chem. Res.*, 2003, 780.

10 Y. Ma and X. Huang, *J. Chem. Res.*, 1998, 312.

11 (a) M. Xie, L. Liu, J. Wang and S. Wang, *J. Organomet. Chem.*, 2005, **690**, 4058; (b) M. Xie, J. Wang, X. Gu, Y. Sun and S. Wang, *Org. Lett.*, 2006, **8**, 431.

12 P.A. Magriotis, J.T. Brown and M.E. Scott, *Tetrahedron Lett.*, 1991, **32**, 5047.

13 (a) J.K. Stille, *Angew. Chem. Int. Ed. Engl.*, 1986, **25**, 508; (b) T.N. Mitchell, *Synthesis*, 1992, 803.

14 (a) B.M. Trost, *Chem. Rev.,* 1978, **78**, 363; (b) S. Farhat, I. Zouev and I. Marek, *Tetrahedron*, 2004, **60**, 1329; (c) N. Muraoka, M. Mineno, K. Itami and J. Yoshida, *J. Org. Chem.*, 2005, **70**, 6933.