A one-pot stereoselective synthesis of 2-selenenyl-substituted 1,3-dienes by hydrostannylation-Stille tandem reaction of Bu_3SnH with acetylenic selenides and alkenyl iodides

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2-Selenenyl-substituted 1,3-dienes can be stereoselectively synthesised in one pot under mild conditions in good yields by the palladium-catalysed hydrostannylation of acetylenic selenides, followed by Stille coupling with alkenyl iodides.

Keywords: acetylenic selenide, hydrostannylation, Stille coupling, 2-selenenyl-substituted 1,3-diene, stereoselective synthesis

The stereocontrolled synthesis of conjugated dienes has attracted considerable interest in organic chemistry because of their appearance in a wide variety of biologically active molecules and because they are key synthetic intermediates.[1] Conjugated dienes are usually prepared by utilising either a Wittig-type approach[2] or the transition metal-catalysed coupling reactions of stereodefined vinyl halides with vinyl organometallic compounds.[3] Recently, Kasatkin and Whitby reported the insertion of 1-lithio-1-halobutadiene into organozirconocenes providing a stereocontrolled synthesis of (*E,Z*)-1,3-dienes.[4] The stereoselective synthesis of 1,3-dienes containing metal or heteroatom functional groups is also of considerable interest in organic synthesis because many useful functional group transformations can be achieved by introduction and removal of metal or heteroatom functions. Heteroatom-substituted 1,3-dienes are also useful precursors for the construction of highly functionalised ring systems in Diels–Alder reactions.[5] The stereoselective synthesis of 1,3-dienylsilanes,[6] 1,3-dienylsulfides,[7] 1,3-dienylsulfones,[8] and 1,3-dienylstannanes[9] has already been described in the literature. 1,3-Dienylselenides are extensively used as intermediates in organic synthesis since vinyl selenides are synthetically equivalent to carbonyls and can be stereospecifically converted into alkenes by nickel-catalysed coupling reactions with Grignard reagents.[10] However, reports on the stereocontrolled synthesis of polysubstituted 1,3-dienyl selenides are limited.[11] The tandem reaction has recently been of interest for organic synthesis because it offers a convenient and economical method to prepare desired organic molecules.[12] 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 hydrostannylation-Stille tandem reaction of Bu_3SnH with alkynes and organic halides to date. Here we report that 2-selenenyl-substituted 1,3-dienes can be stereoselectively synthesised in one pot under mild conditions in good yields by the palladium-catalysed hydrostannylation of acetylenic selenides, followed by Stille coupling with alkenyl iodides.

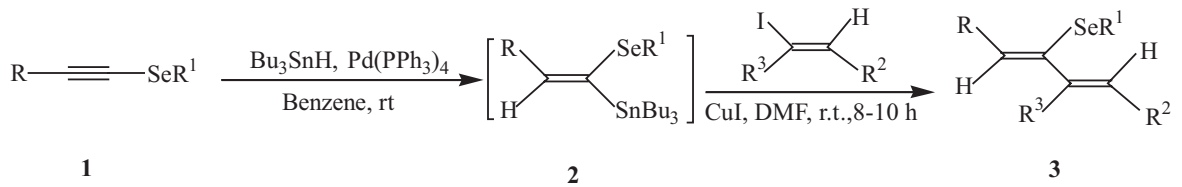
Palladium-catalysed hydrostannylation of alkynes provides a simple general route for the synthesis of vinylstannanes.[13] In 1991, Magriotis reported that the palladium-catalysed hydrostannylation of phenylthioalkynes with Bu_3SnH was highly regio- and stereoselective, giving (*E*)-α-stannylvinyl sulfides in high yields.[14] Paley *et al*. reported that the palladium-catalysed hydrostannylation of chiral alkynyl sulfoxides at –78°C was also highly regio- and stereoselective, affording chiral (*E*)-α-stannylvinyl sulfoxides in good yields.[15] Huang and Ma demonstrated that alkynyl selenides can also undergo palladium-catalysed hydrostannylation to afford stereoselectively (*E*)-α-stannylvinyl selenides.[16] (*E*)-α-Stannylvinyl selenides 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 as vinyl selenides. Vinylstannanes can undergo the Stille coupling reaction with organic halides.[17] Considering the fact that both the hydrostannylation and Stille reactions were catalysed by $Pd(PPh_3)_4$, we tried to combine the two reactions in one pot to prepare stereoselectively 2-selenenyl-substituted 1,3-dienes (Scheme 1).

We found that, after the hydrostannylation reaction of acetylenic selenides **1** with Bu_3SnH using 5 mol% $Pd(PPh_3)_4$ in benzene at room temperature for 5 h, solvent removal under reduced pressure and stirring of the residue with DMF, alkenyl iodides and 75 mol% CuI at room temperature for 8–10 h, 2-selenenyl-substituted 1,3-dienes **3** were obtained

Table 1 Synthesis of 2-selenenyl-substituted 1,3-dienes **3a–i**

R	R^1	R^2	R^3	Product	Yield/%[a]
n-Bu	Ph	Ph	H	**3a**	68
n-Bu	Ph	*n*-Bu	H	**3b**	65
n-Bu	Ph	$MeOCH_2$	H	**3c**	60
$MeOCH_2$	Me	—$(CH_2)_4$—	–	**3d**	61
$MeOCH_2$	Me	Ph	H	**3e**	65
$MeOCH_2$	Me	*n*-C_5H_{11}	H	**3f**	67
n-C_6H_{13}	Me	$MeOCH_2$	H	**3g**	59
$MeOCH_2$	Ph	Ph	H	**3h**	63
$MeOCH_2$	Ph	—$(CH_2)_4$—	–	**3i**	64

[a]Isolated yield based on the alkenyl iodide used.



1 **2** **3**

Scheme 1

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in good yields. The experimental results are summarised in Table 1. As shown in Table 1, the hydrostannylation-Stille tandem reaction of Bu_3SnH with a variety of acetylenic selenides and alkenyl iodides proceeded smoothly under very mild conditions to afford stereoselectively the corresponding 2-selenenyl-substituted 1,3-dienes **3**.

It is well documented that the Stille coupling reaction of vinylstannanes with organic halides in the presence of a palladium catalyst occurs with retention of configuration.[17,18] The *E*-configuration of the R^2 substituted double bond compounds **3a, 3c, 3e,** and **3h** has been proved by their ^{1}H NMR spectra which show a doublet at δ = 6.31–6.96 with a coupling constant of 15.2–16.4 Hz, and this is also the evidence of the retention of the *E*-configuration of the starting alkenyl iodides. In addition, the *Z*-configuration of the *n*-Bu and SePh groups of the compound **3c** was confirmed by the NOESY in the ^{1}H NMR spectrum. An enhancement of the allylic protons of the *n*-Bu graph was observed as the vinylic proton (δ = 6.24) of **3c** was irradiated. There was no correlation between the vinylic proton (δ = 6.24) and any aromatic protons. The correlation between the vinylic proton (δ = 6.24) and another vinylic proton (δ = 6.31) was also observed. The NOE results indicate that **3c** has the expected *Z*-configuration of the Se-substituted double bond and the cross-coupling reaction of (*E*)-α-stannylvinyl selenides with alkenyl iodides occurs with the configuration retention of both the starting compounds **2** and the alkenyl iodides.

In summary, we have developed an efficient and stereoselective one-pot method for the synthesis of 2-selenenyl-substituted 1,3-dienes. The present method has the advantages of readily available starting materials, straightforward and simple procedures, mild reaction conditions and good yields. The procedure should find wide application to the synthesis of a large array of naturally occurring substances having the 1,3-diene system.

Experimental

^{1}H NMR spectra were recorded on a Bruker AC-P300 (300 MHz) spectrometer with TMS as an internal standard 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 8239 mass spectrometer. Microanalyses were measured using a Yanaco MT-3 CHN microelemental analyser. All reactions were carried out in pre-dried glassware (150°C, 4 h) and cooled under a stream of dry Ar. Benzene was distilled from sodium prior to use. DMF was dried by distillation over calcium hydride.

General procedure for the synthesis of 2-selenenyl-substituted 1,3-dienes **3a–i**

A 25 ml, two-necked, round-bottom flask equipped with a magnetic stirring bar and under argon was charged sequentially with the acetylenic selenide **1** (1 mmol), benzene (4 ml), $Pd(PPh_3)_4$ (0.05 mmol) and Bu_3SnH (1.05 mmol). The mixture was stirred at room temperature for 5 h. The solvent was removed under reduced pressure and the residue was dissolved in DMF (10 ml). Then the alkenyl iodide (0.9 mmol) and CuI (0.7 mmol) were added and the mixture was stirred at room temperature for 8–10 h. The reaction mixture was diluted with diethyl ether (30 ml), filtered and then treated with 20% aqueous KF (10 ml) for 30 min before being dried and concentrated. The residue was purified by column chromatography on silica gel, eluting either a mixture of diethyl ether and petrol or just petrol.

Compound **3a:** Oil. IR (film): ν (cm^{-1}) 3058, 3024, 2956, 2870, 1623, 1578, 1493, 1476, 734, 689; ^{1}H NMR ($CDCl_3$): δ 7.47–7.14 (m, 11H), 6.83 (d, *J* = 16.2 Hz, 1H), 6.37 (t, *J* = 7.2 Hz, 1H), 2.47–2.40 (m, 2H), 1.49–1.27 (m, 4H), 0.90 (t, *J* = 7.2 Hz, 3H); MS: *m/z* 342 (M^+, 10), 129 (100), 77 (43), 57 (37); Anal. Calc. for $C_{20}H_{22}Se$: C, 70.36; H, 6.49. Found: C, 70.1; H, 6.5%.

Compound **3b**: Oil. IR (film): ν (cm^{-1}) 3058, 3015, 2942, 1578, 1476, 1438, 734, 689; ^{1}H NMR ($CDCl_3$): δ 7.54–7.15 (m, 5H), 6.53 (t, *J* = 7.6 Hz, 1H), 6.13–6.04 (m, 2H), 2.45–2.05 (m, 4H), 1.52–1.18 (m, 8H), 1.05–0.69 (m, 6H); MS: *m/z* 322 (M^+, 28), 81 (100), 77 (37), 57 (51); Anal. Calc. for $C_{18}H_{26}Se$: C, 67.27; H, 8.15. Found: C, 67.05; H, 7.9%.

Compound **3c**: Oil. IR (film): ν (cm^{-1}) 3057, 3038, 2924, 1644, 1578, 1476, 1438, 1123, 734, 689; ^{1}H NMR ($CDCl_3$): δ 7.39–7.14 (m, 5H), 6.31 (d, *J* = 15.2 Hz, 1H), 6.24 (t, *J* = 7.6 Hz, 1H), 6.18–6.09 (m, 1H), 3.94 (t, *J* = 5.8 Hz, 2H), 3.30 (s, 3H), 2.47–2.39 (m, 2H), 1.42–1.26 (m, 4H), 0.89 (t, *J* = 7.2 Hz, 3H); MS: *m/z* 310 (M^+, 41), 77 (28), 57 (33), 45 (100); Anal. Calc. for $C_{16}H_{22}OSe$: C, 62.12; H, 7.17. Found: C, 61.9; H, 7.1%.

Compound **3d**: Oil. IR (film): ν (cm^{-1}) 2980, 1583, 1457, 1114; ^{1}H NMR ($CDCl_3$): δ 6.37–6.33 (m, 1H), 5.65 (t, *J* = 5.8 Hz, 1H), 3.59 (d, *J* = 5.8 Hz, 2H), 3.39 (s, 3H), 2.08 (s, 3H), 2.20–2.01 (m, 4H), 1.61–1.46 (m, 4H); MS: *m/z* 246 (M^+, 18), 151 (43), 106 (5), 45 (100); Anal. Calc. for $C_{11}H_{18}OSe$: C, 53.87; H, 7.40. Found: C, 53.6; H, 7.1%.

Compound **3e**: Oil. IR (film): ν (cm^{-1}) 3052, 3024, 2996, 1578, 1477, 1118; ^{1}H NMR ($CDCl_3$): δ 7.47–7.04 (m, 6H), 6.78 (d, *J* = 16.4 Hz, 1H), 6.22 (t, *J* = 6.0 Hz, 1H), 4.37 (d, *J* = 6.0 Hz, 2H), 3.48 (s, 3H), 2.10 (s, 3H); MS: *m/z* 268 (M^+, 11), 173 (53), 141 (100), 45 (27); Anal. Calc. for $C_{13}H_{16}OSe$: C, 58.42; H, 6.03. Found: C, 58.55; H, 6.15%.

Compound **3f**: Oil. IR (film): ν (cm^{-1}) 2981, 1580, 1494, 1115; ^{1}H NMR ($CDCl_3$): δ 6.58–6.27 (m, 2H), 5.91 (t, *J* = 6.1 Hz, 1H), 3.77 (d, J = 6.1 Hz, 2H), 3.26 (s, 3H), 2.36–2.27 (m, 2H), 2.08 (s, 3H), 1.50–1.19 (m, 6H), 0.90 (t, *J* = 7.2 Hz, 3H); MS: *m/z* 261 (M^+, 26), 167 (34), 57 (100), 45 (26); Anal. Calc. for $C_{12}H_{22}OSe$: C, 55.16; H, 8.49. Found: C, 55.3; H, 8.5%.

Compound **3g**: Oil. IR (film): ν (cm^{-1}) 2928, 1601, 1466, 1120; ^{1}H NMR ($CDCl_3$): δ 6.07–6.01 (m, 2H), 5.92 (t, *J* = 5.8 Hz, 1H), 3.89 (m, 2H), 3.33 (s, 3H), 2.45–2.40 (m, 2H), 2.02 (s, 3H), 1.58–1.21 (m, 8H), 0.89 (t, *J* = 7.2 Hz, 3H); MS: *m/z* 276 (M^+, 38), 245 (11), 149 (35), 110 (100), 45 (39); Anal. Calc. for $C_{13}H_{24}OSe$: C, 56.71; H, 8.79. Found: C, 56.5; H, 8.6%.

Compound **3h**: Oil. IR (film): ν (cm^{-1}) 3082, 3059, 1601, 1577, 1494, 1118; ^{1}H NMR ($CDCl_3$): δ 7.39–7.16 (m, 10H), 6.96–6.79 (dd, *J* = 16.0 Hz, 2H), 6.18 (t, *J* = 5.9 Hz, 1H), 4.24 (d, *J* = 5.9 Hz, 2H), 3.29 (s, 3H); MS: *m/z* 330 (M^+, 12), 173 (50), 77 (100), 45 (70); Anal. Calc. for $C_{18}H_{18}OSe$: C, 65.65; H, 5.51. Found: C, 65.8; H, 5.5%.

Compound **3i**: Oil. IR (film): ν (cm^{-1}) 3090, 3045, 1580, 1477, 1116; ^{1}H NMR ($CDCl_3$): δ 7.68–7.17 (m, 5H), 6.38–6.32 (m, 1H), 5.90 (t, *J* = 5.8 Hz, 1H), 4.16 (d, *J* = 5.8 Hz, 2H), 3.33 (s, 3H), 2.58–2.40 (m, 4H), 1.67–1.15 (m, 4H); MS: *m/z* 308 (M^+, 72), 151 (85), 121 (100), 77 (27), 45 (59); Anal. Calc. for $C_{16}H_{20}OSe$: C, 62.53; H, 6.56. Found: C, 62.3; H, 6.3%.

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