

# A facile synthesis of 2-stannyl-1,3-enynes via palladium catalysed coupling reactions

Mingzhong Cai\* and Haigen Li

Institute of Chemistry, Jiangxi Normal University, Nanchang 330027, P. R. China

$\alpha$ -Iodoethenylstannanes undergo a direct coupling reaction with terminal alkynes in the presence of 5 mol% of tetrakis(triphenylphosphine)palladium(0) and 10 mol% of CuI in piperidine at room temperature to afford 2-stannyl-1,3-enynes in good yields.

**Keywords:**  $\alpha$ -iodoethenylstannane, 2-stannyl-1,3-enyne, palladium, coupling reaction

The discovery of strong antifungal agents<sup>1</sup> and new powerful antitumor antibiotics<sup>2</sup> has stimulated intense interest in the chemistry of enynes,<sup>3</sup> which is at the origin of the biological properties of these substances. The conjugated enynes are also important synthetic intermediates since the conjugated enyne moiety can be readily converted in a stereospecific manner into the corresponding diene system.<sup>4</sup> The metal or heteroatom-containing enynes will also be useful as building blocks in organic synthesis because many useful functional group transformations can be achieved by the introduction and removal of metal or heteroatom functions. Recently, the synthesis of 1,3-enynylsulfides,<sup>5</sup> 1,3-enynylselenides,<sup>6</sup> 1,3-enynytellurides,<sup>7</sup> 1,3-enynylsilanes<sup>8</sup> has been described in the literature. However, so far, the synthesis of 1,3-enynylstannanes has received less attention.<sup>9</sup>

The transition metal-catalysed cross-coupling reaction is a highly versatile method for carbon–carbon bond formation and has been widely used as a synthetic tool.<sup>10</sup> The palladium-catalysed coupling reaction of alkenyl halides with terminal alkynes (Sonogashira reaction) provides a direct route to 1,3-enynes.<sup>11</sup> In this paper, we report that 2-stannyl-1,3-enynes can be conveniently synthesised by the coupling reaction of  $\alpha$ -iodoethenylstannanes with terminal alkynes in the presence of Pd(PPh<sub>3</sub>)<sub>4</sub> and CuI catalysts (Scheme 1).

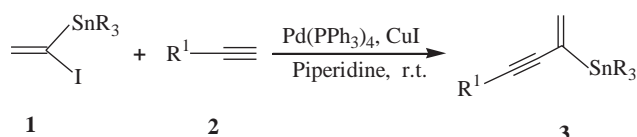
The required starting  $\alpha$ -iodoethenylstannanes **1** were prepared in good yields by the hydrozirconation of ethynyltrialkylstannanes and successive reaction with iodine.<sup>12</sup> We observed that when  $\alpha$ -iodoethenylstannanes **1** were allowed to react directly with terminal alkynes **2** in the presence of 5 mol% of Pd(PPh<sub>3</sub>)<sub>4</sub> and 10 mol% of CuI in piperidine at room temperature for 4h, 2-stannyl-1,3-enynes **3** were obtained in good yields. The typical results are summarised in Table 1. The products **3** were identified by <sup>1</sup>H NMR, IR spectra and elemental analysis.

In conclusion, we have developed a facile route for the synthesis of 2-stannyl-1,3-enynes by the direct coupling reaction of  $\alpha$ -iodoethenylstannanes with terminal alkynes in the presence of Pd(PPh<sub>3</sub>)<sub>4</sub> and CuI catalysts. The reactions have the advantages of mild conditions, short reaction times, simple manipulation and good yields. Investigations on the synthetic applications of 2-stannyl-1,3-enynes are in progress.

## Experimental

Cp<sub>2</sub>Zr(H)Cl and ethynyltrialkylstannanes were prepared according to the literature.<sup>13,14</sup> <sup>1</sup>H NMR spectra were recorded on a Bruker AC-400 (400 MHz) spectrometer with TMS as an internal standard. IR spectra were obtained on a Perkin-Elmer 683 instrument as neat films. Microanalyses were carried out using a Yanaco MT-3 CHN microelemental analyser. Tetrahydrofuran (THF) was freshly distilled from sodium-benzophenone prior to its use. Piperidine was dried, deoxygenated and freshly distilled before use.

**General procedure for the synthesis of  $\alpha$ -iodoethenylstannanes 1:** A mixture of Cp<sub>2</sub>Zr(H)Cl (5 mmol) and ethynyltrialkylstannane



**Scheme 1**

**Table 1** Synthesis of 2-stannyl-1,3-enynes **3a–i**

Entry	R	R <sup>1</sup>	Product	Yield <sup>a</sup> /%
1	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	Ph	<b>3a</b>	74
2	CH <sub>3</sub>	Ph	<b>3b</b>	82
3	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	<b>3c</b>	86
4	CH <sub>3</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	<b>3d</b>	81
5	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	Me <sub>3</sub> Si	<b>3e</b>	87
6	CH <sub>3</sub>	Me <sub>3</sub> Si	<b>3f</b>	79
7	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub>	<b>3g</b>	78
8	CH <sub>3</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub>	<b>3h</b>	73
9	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	CH <sub>3</sub> OCH <sub>2</sub>	<b>3i</b>	84

<sup>a</sup>Isolated yield based on the  $\alpha$ -iodoethenylstannane **1** used.

(5 mmol) in THF (25 ml) was stirred under Ar at room temperature for 40 min to yield a clear solution. Iodine (5 mmol) was added to the resulting solution at 0°C and the mixture was stirred for 30 min and then at room temperature for 30 min. The mixture was diluted with diethyl ether (90 ml), filtered through a short plug of silica gel, and concentrated to give a residue. The residue was purified by column chromatography on silica gel, eluting with hexane.

**1-Iodo-1-tributylstannylethene:** yield 78%; IR (film)/cm<sup>-1</sup> 2954, 2873, 1580, 1464, 1376;  $\delta_{\text{H}}$ (CDCl<sub>3</sub>) 7.00(d, 1H, *J* = 1.6 Hz), 6.77(d, 1H, *J* = 1.6 Hz), 1.59–1.51 (m, 6H), 1.38–1.28 (m, 6H), 1.02 (t, 6H, *J* = 8.2 Hz), 0.91 (t, 9H, *J* = 7.4 Hz); Anal. Calcd for C<sub>14</sub>H<sub>29</sub>SnI: C, 37.92; H, 6.55. Found: C, 37.68; H, 6.37.

**1-Iodo-1-trimethylstannylethene:** yield 73%; IR (film)/cm<sup>-1</sup> 2955, 2871, 1585, 1463, 1378;  $\delta_{\text{H}}$ (CDCl<sub>3</sub>) 6.95 (d, 1H, *J* = 2.0 Hz), 6.77 (d, 1H, *J* = 2.0 Hz), 0.25 (s, 9H); Anal. Calcd for C<sub>5</sub>H<sub>11</sub>SnI: C, 18.93; H, 3.47. Found: C, 18.75; H, 3.36.

**General procedure for the synthesis of 2-stannyl-1-en-3-ynes 3a–i:** To a solution of Pd(PPh<sub>3</sub>)<sub>4</sub> (0.05 mmol, 0.058g) and CuI (0.1 mmol, 0.019g) in piperidine (2 ml) at 0°C under Ar, was added the terminal alkyne (2.0 mmol) and after stirring at r.t. for 10 min, a solution of  $\alpha$ -iodoethenylstannane (1.0 mmol) in piperidine (1 ml) was added dropwise over 30 min with stirring. The reaction mixture was stirred at r.t. for another 2 h, hydrolysed with sat. aq. NH<sub>4</sub>Cl (10 ml) and extracted with Et<sub>2</sub>O (2×20ml). The organic layer was washed with sat. aq. NH<sub>4</sub>Cl (15 ml) and water (2×15ml) and dried (MgSO<sub>4</sub>). Removal of solvent under reduced pressure gave an oil, which was purified by column chromatography on silica gel using hexane or hexane/ether(20:1) (for entry 9) as eluent.

**2-Tributylstannyl-4-phenylbut-1-en-3-yne (3a):** IR (film)/cm<sup>-1</sup> 3056, 2927, 2172, 1598, 1488, 1464, 913, 754, 690;  $\delta_{\text{H}}$ (CDCl<sub>3</sub>) 7.43–7.28 (m, 5H), 6.32 (d, 1H, *J* = 3.6 Hz), 5.63 (d, 1H, *J* = 3.6 Hz), 1.63–1.51 (m, 6H), 1.40–1.34 (m, 6H), 1.08 (t, 6H, *J* = 8.0 Hz), 0.92 (t, 9H, *J* = 7.2 Hz); Anal. Calcd for C<sub>22</sub>H<sub>34</sub>Sn: C, 63.31; H, 8.15. Found: C, 63.08; H, 8.17.

**2-Trimethylstannyl-4-phenylbut-1-en-3-yne (3b):** IR (film)/cm<sup>-1</sup> 3056, 3032, 2981, 2916, 2202, 1676, 1598, 1570, 1489, 1442, 915, 755, 690;  $\delta_{\text{H}}$ (CDCl<sub>3</sub>) 7.43–7.26 (m, 5H), 6.28 (d, 1H, *J* = 3.2 Hz), 5.64 (d, 1H, *J* = 3.2 Hz), 0.29 (s, 9H); Anal. Calcd for C<sub>13</sub>H<sub>16</sub>Sn: C, 53.61; H, 5.50. Found: C, 53.38; H, 5.32.

\* Correspondence.

*2-Tributylstannyloct-1-en-3-yne (3c)*: IR (film)/cm<sup>-1</sup> 3054, 2928, 2196, 1681, 1568, 1464, 1377, 1072, 910, 875, 691;  $\delta_{\text{H}}(\text{CDCl}_3)$  6.13 (d, 1H,  $J = 3.6$  Hz), 5.44 (d, 1H,  $J = 3.6$  Hz), 2.36 (t, 2H,  $J = 6.8$  Hz), 1.56–1.30 (m, 16H), 1.00–0.87 (m, 18H); Anal. Calcd for C<sub>20</sub>H<sub>38</sub>Sn: C, 60.45; H, 9.57. Found: C, 60.19; H, 9.42.

*2-Trimethylstannyloct-1-en-3-yne (3d)*: IR (film)/cm<sup>-1</sup> 2959, 2933, 2172, 1594, 1465, 1287, 795;  $\delta_{\text{H}}(\text{CDCl}_3)$  6.12 (d, 1H,  $J = 3.2$  Hz), 5.46 (d, 1H,  $J = 3.2$  Hz), 2.37 (t, 2H,  $J = 6.8$  Hz), 1.52–1.25 (m, 4H), 0.90 (t, 3H,  $J = 7.2$  Hz), 0.21 (s, 9H); Anal. Calcd for C<sub>11</sub>H<sub>20</sub>Sn: C, 48.71; H, 7.38. Found: C, 48.50; H, 7.17.

*2-Tributylstannyl-4-trimethylsilylbut-1-en-3-yne (3e)*: IR (film)/cm<sup>-1</sup> 2957, 2926, 2109, 1563, 1464, 1377, 1249, 842, 759;  $\delta_{\text{H}}(\text{CDCl}_3)$  6.26 (d, 1H,  $J = 3.2$  Hz), 5.56 (d, 1H,  $J = 3.2$  Hz), 1.57–1.51 (m, 6H), 1.36–1.30 (m, 6H), 1.03–0.98 (m, 6H), 0.90 (t, 9H,  $J = 7.2$  Hz), 0.19 (s, 9H); Anal. Calcd for C<sub>19</sub>H<sub>38</sub>SiSn: C, 55.21; H, 9.20. Found: C, 54.95; H, 9.03.

*2-Trimethylstannyl-4-trimethylsilylbut-1-en-3-yne (3f)*: IR (film)/cm<sup>-1</sup> 2960, 2929, 2873, 2108, 1666, 1598, 1465, 1287, 1074, 844, 787, 761;  $\delta_{\text{H}}(\text{CDCl}_3)$  6.24 (d, 1H,  $J = 3.2$  Hz), 5.59 (d, 1H,  $J = 3.2$  Hz), 0.24 (s, 9H), 0.18 (s, 9H); Anal. Calcd for C<sub>10</sub>H<sub>20</sub>SiSn: C, 41.81; H, 6.97. Found: C, 41.63; H, 6.78.

*2-Tributylstannyldec-1-en-3-yne (3g)*: IR (film)/cm<sup>-1</sup> 2929, 2856, 2178, 1464, 1377, 1072, 910, 875, 691;  $\delta_{\text{H}}(\text{CDCl}_3)$  6.13 (d, 1H,  $J = 3.2$  Hz), 5.44 (d, 1H,  $J = 3.2$  Hz), 2.35 (t, 2H,  $J = 6.8$  Hz), 1.57–1.26 (m, 20H), 1.00–0.88 (m, 18H); Anal. Calcd for C<sub>22</sub>H<sub>42</sub>Sn: C, 62.12; H, 9.88. Found: C, 61.93; H, 9.75.

*2-Trimethylstannyldec-1-en-3-yne (3h)*: IR (film)/cm<sup>-1</sup> 2932, 2859, 2164, 1678, 1570, 1466, 1427, 1378, 771, 725;  $\delta_{\text{H}}(\text{CDCl}_3)$  6.10 (d, 1H,  $J = 3.2$  Hz), 5.47 (d, 1H,  $J = 3.2$  Hz), 2.35 (t, 2H,  $J = 6.8$  Hz), 1.47–1.22 (m, 8H), 0.88 (t, 3H,  $J = 7.2$  Hz), 0.21 (s, 9H); Anal. Calcd for C<sub>13</sub>H<sub>24</sub>Sn: C, 52.17; H, 8.03. Found: C, 51.89; H, 7.89.

*2-Tributylstannyl-5-methoxy-pent-1-en-3-yne (3i)*: IR (film)/cm<sup>-1</sup> 2956, 2923, 2206, 1636, 1526, 1464, 1376, 1102, 743, 696;  $\delta_{\text{H}}(\text{CDCl}_3)$  6.38 (d, 1H,  $J = 3.2$  Hz), 5.71 (d, 1H,  $J = 3.2$  Hz), 4.12 (s, 2H), 3.39 (s, 3H), 1.58–1.52 (m, 6H), 1.37–1.30 (m, 6H), 1.00 (t, 6H,  $J = 8.0$  Hz), 0.90 (t, 9H,  $J = 7.2$  Hz); Anal. Calcd for C<sub>18</sub>H<sub>34</sub>O<sub>2</sub>Sn: C, 56.10; H, 8.83. Found: C, 55.92; H, 8.61.

We thank the National Natural Science Foundation of China (Project No. 20062002) and the Natural Science Foundation of Jiangxi Province for financial support.

Received 12 June 2004; accepted 3 August 2004  
Paper 04/2568

## References

- 1 A. Stutz, *Angew. Chem., Int. Ed. Engl.*, 1987, **26**, 320; P. Nussbaumer, L. Leitner, K. Mráz and A. Stutz, *J. Med. Chem.*, 1995, **38**, 1831.
- 2 A.G. Myers, P.J. Proteau and T.M. Handel, *J. Am. Chem. Soc.*, 1988, **110**, 7212.
- 3 R. Aksela and A.C. Oehlschlager, *Tetrahedron*, 1991, **47**, 1163; P. Magnus, A. Hirokazo and J. Harling, *J. Org. Chem.*, 1990, **55**, 1709; S. Ikeda and Y. Sato, *J. Am. Chem. Soc.*, 1994, **116**, 5975; M. Alami, S. Gueugnot, E. Domingues and G. Linstrumelle, *Tetrahedron*, 1995, **51**, 1209.
- 4 P.A. Magriotis and K.D. Kim, *J. Am. Chem. Soc.*, 1993, **115**, 2972; J.A. Miller and G. Zweifel, *J. Am. Chem. Soc.*, 1983, **105**, 1383; E.J. Corey and A. Tramontano, *J. Am. Chem. Soc.*, 1984, **106**, 462.
- 5 M. Koreeda and W. Yang, *Synlett*, 1994, 201.
- 6 A. L. Braga, G. Zeni, L. H. Andrade, C. C. Silveira and H. A. Stefani, *Synthesis*, 1998, 39; Y. Ma and X. Huang, *Synth. Commun.*, 1997, **27**, 3441; M.Z. Cai, C.Y. Peng, H. Zhao and J.D. Huang, *J. Chem. Res.*, 2002, 376.
- 7 M.J. Dabdoub, V. Dabdoub and J.V. Comasseto, *Tetrahedron Lett.*, 1992, **33**, 2261; J.P. Marino, F. Tucci and J.V. Comasseto, *Synlett*, 1993, 761.
- 8 N. Chatani, N. Amishiro and S. Murai, *J. Am. Chem. Soc.*, 1991, **113**, 7778; M. Cai, W. Hao, H. Zhao and C. Song, *J. Chem. Res. (S)*, 2003, 485.
- 9 X. Huang and P. Zhong, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1543.
- 10 A. Suzuki, *Pure Appl. Chem.*, 1985, **57**, 1749; T. N. Mitchell, *Synthesis*, 1992, 803.
- 11 K. Sonogashira, Y. Tohda and N. Hagihara, *Tetrahedron Lett.*, 1975, 4467; M. Alami and G. Linstrumelle, *Tetrahedron Lett.*, 1991, **32**, 6109.
- 12 B. H. Lipshutz, R. Keil and J. C. Barton, *Tetrahedron Lett.*, 1992, **33**, 5861.
- 13 J. Schwartz and J. A. Labinger, *Angew. Chem., Int. Ed. Engl.*, 1976, **15**, 333.
- 14 L. Brandsma and H. D. Verkruisje, *Synthesis*, 1999, 1727.