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Palladium-catalysed hydrostannylations of 1-bromoalkynes. A practical synthesis of (*E*)-1-stannylalk-1-enes

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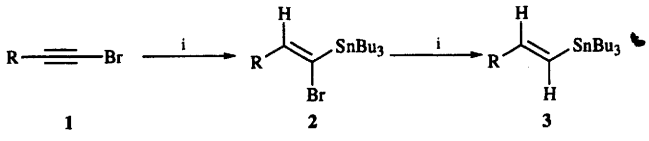
A practical synthesis of (*E*)-1-stannylalk-1-enes containing a range of oxygen and nitrogen functionality is highlighted, involving hydrostannylation followed by palladium-catalysed carbon–bromine bond cleavage reactions of 1-bromoalkynes.

Vinylstannanes are pivotal intermediates in a wide range of carbon–carbon bond forming reactions involving electrophiles,[1] frequently under palladium catalysis.[2] As a result of their central importance, considerable effort has been expended towards the regio- and stereo-controlled synthesis of geometrically defined (*E*)- and (*Z*)-, 1- and 2-vinylstannanes. The most popular and commonly employed synthetic routes to vinylstannanes involve hydrostannylations[3–12] or stannylmetallations[13–20] of monosubstituted alkynes. Whilst there have been several developments in controlling both the regio- and stereo-chemistry of hydrostannylations of alkynes, unfortunately mixtures of isomers are commonly observed. Recently Hodgson *et al.*[21] described an approach to (*E*)-1-vinylstannanes which uses a modified Takai reaction between an aldehyde and $Bu_3SnCHBr_2$ in the presence of $CrCl_2$.

In contemporaneous investigations of the scope of the intramolecular Stille coupling reaction between vinylstannanes and vinyl halides in the elaboration of polyene macrolides, *e.g.* macrolactin A,[22] and polyene macrolactams, *e.g.* leinamycin[23] and virginiamycins,[24] we have evaluated a range of methods for the stereocontrolled synthesis of several (*E*)-1-vinylstannanes, including those methods highlighted above. In many instances either poor yields or poor stereocontrol, or both, resulted. In 1990, Zhang *et al.*[10] revealed that 1-bromoalkynes can be converted into (*E*)-1-vinylstannanes in a regioselective manner using two equivalents of tributylstannane in the presence of $PdCl_2(PPh_3)_2$. The corresponding chloroalkynes did not react in an analogous manner, and the reactions were thought to occur *via* an alkylidene carbenoid intermediate, *viz* **2**, and involve palladium-catalysed carbon–bromine bond cleavage (Scheme 1). Surprisingly, this method has not been developed or



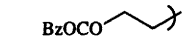
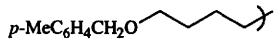
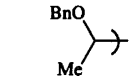
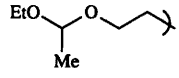
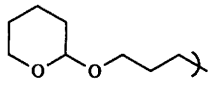
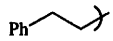
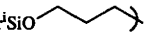
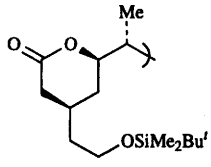
1 2 3

Scheme 1 *Reagents:* i, Bu_3SnH, Pd^0

exploited in synthesis by other researchers. To highlight the scope for this method, we now report the concise synthesis of a range of sensitive heteroatom-functionalised (*E*)-1-vinylstannanes from hydrostannylations of appropriate 1-bromoalkynes under palladium catalysis.

1-Bromoalkynes can be simply prepared from the corresponding alkyne by reaction with *N*-bromosuccinimide in the presence of a catalytic amount of silver nitrate.[25] They can also be elaborated from aldehydes *via* 1,1-dibromoalkene intermediates, using Grandjean's modification[26] of the Corey–Fuchs procedure. In this manner a variety of oxygen- and nitrogen-

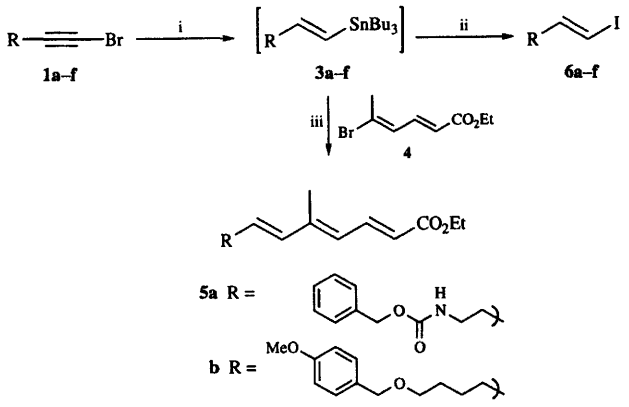
Table 1 Hydrostannylations of bromoalkynes **1** to give **3**

1	R	Isolated yield of 3[a] (%)
a		78
b		77
c		80
d		74
e		74
f		82
g		72
h		86
i		70

[a] *E*:*Z* > 95:5 in all cases.

substituted 1-bromoalkynes were synthesised (Table 1). When solutions of the 1-bromoalkynes in THF were treated with 2.2 equiv. of tributylstannane at room temperature in the presence of *in situ* generated catalytic tetrakis(triphenylphosphine)-palladium(0), they were smoothly converted into the corresponding (*E*)-1-vinylstannanes in reproducible yields of 72–86% (Table 1). Analysis of the NMR spectroscopic data of the vinylstannane products showed that the hydrostannylation–palladium-catalysed C–Br bond cleavage is essentially regiospecific and highly stereoselective (>95% *E*-alkene). We have evaluated a wide range of methods for the synthesis of vinylstannanes over the past few years, and we commend this particular method for the synthesis of (*E*)-1-vinylstannanes. It is convenient, clean, efficient to operate and highly stereoselective in our hands.

As a corollary, we also examined the scope for *in situ* generation of vinyl iodides and for *in situ* Stille reactions from the crude vinylstannanes generated in this study. Thus, treatment of the vinylstannanes *in situ* at −78 °C with *N*-iodosuccinimide (NIS) followed by warming to 0 °C and work-up with saturated aqueous KF (to remove Bu_3SnBr and Bu_3SnI) led to the corresponding *E*-vinyl iodides (>93%) in 75–84% yield (Scheme 2, Table 2); these yields and stereoselectivities are similar to those



Scheme 2 *Reagents:* i, PPh_3, $Pd_2(dba)_3$, THF, Bu_3SnH (2.2 equiv.); ii, NIS, THF; iii, PPh_3, $Pd_2(dba)_3$

Table 2 Formation *in situ* of vinyl iodides **6** from **1**

1	R	Isolated yield of vinyl iodide **6** (%)	Ratio *trans*:*cis*
a	BzOCONH	84	12:1
b	*p*-$MeC_6H_4CH_2O$	80	16:1
c	BnO, Me	82	13:1
d	EtO, O, Me	75	13:1
e	O, O	77	11:1
f	Ph	83	13:1

obtained using the procedures developed by Takai *et al.*[27] and Stork *et al.*[28] Furthermore, when the crude products from hydrostannylation–palladium-catalysed C–Br cleavage of the bromoalkynes **1a** and **1b** were treated *in situ* with the vinyl bromide **4** and $Pd_2(dba)_3$–PPh_3† under standard Stille conditions, satisfactory yields (*ca.* 60% overall) of the all-*E*-trienoates **5a** and **5b**, respectively, were realised (Scheme 2).

Experimental

Preparation of 1-bromoalkynes 1

(i) Silver nitrate (15 mg) was added to a suspension of the alkyne (1 mmol) and *N*-bromosuccinimide (1.1 mmol) in acetone (4 ml), and the mixture was stirred at room temperature until the bromination was complete (TLC monitoring; < 1 h). The mixture was diluted with light petroleum (20 ml) and then washed with water (2 × 5 ml). The separated aqueous layer was extracted with diethyl ether–light petroleum (bp 40–60 °C) (1:1; 10 ml), and the combined organic extracts were then dried ($MgSO_4$) and filtered through a pad of silica gel. Evaporation of the solvent left the 1-bromoalkyne (> 90%) in a high state of purity which was used directly in the next stage.

(ii) A solution of the homologous aldehyde (1 equiv.) and triethylamine (1 equiv.) in dry dichloromethane (10 ml) was added dropwise over 0.5 h to a stirred solution of carbon tetrabromide (2 equiv.) and triphenylphosphine (4 equiv.) in dry dichloromethane (20 ml) at −60 °C under argon. The mixture was stirred at −60 °C for 15 min and then allowed to warm to room temperature. Light petroleum (40 ml) was added and the mixture was then filtered through silica gel and evaporated to dryness *in vacuo* to leave the corresponding 1,1-dibromoalkene. A solution of sodium hexamethyldisilazide (1.2 equiv.) in THF (10 ml) was added dropwise over 10 min to a stirred solution of the 1,1-dibromoalkene (1 equiv.) in THF (10 ml) at −78 °C under argon, and the mixture was stirred at −78 °C for 2 h. The mixture was diluted with saturated aqueous ammonium chloride (20 ml) and extracted with diethyl ether (3 × 25 ml). Evaporation of the solvent left an oil which was purified by chromatography on silica using diethyl ether–light petroleum (1:9) as eluent to give the 1-bromoalkyne (> 85%) as a colourless oil. Representative data for **1e**: δ_H 4.50 (1 H, m), 3.72 (2 H, m), 3.39 (2 H, m), 2.25 (2 H, t, *J* 7.1 Hz), 1.72 (3 H, m), 1.59–1.65 (1 H, m), 1.41–1.52 (4 H, m); δ_C 98.42 (CH), 79.14 (C), 65.41 (CH_2), 61.76 (CH_2), 37.72 (C), 30.38 (CH_2), 28.27 (CH_2), 25.24 (CH_2), 19.22 (CH_2), 16.36 (CH_2).

Preparation of (*E*)-1-stannyl-1-alkenes 3

Freshly distilled tributyltin hydride (2.2 mmol) was added dropwise over 0.5 h to a stirred solution of the 1-bromoalkyne (1 mmol), triphenylphosphine (0.04 mmol) and tris(dibenzylideneacetone)dipalladium(0) (0.005 mmol) in THF (5 ml) under nitrogen at room temperature. The mixture was stirred at room temperature for a further 2 h, then quenched with saturated aqueous KF (7 ml) and stirred vigorously overnight. Light petroleum (50 ml) was added, and the separated organic layer was then washed with water (40 ml) and brine (40 ml). The organic layer was evaporated to dryness to leave a residue which was purified by chromatography on silica using diethyl ether–light petroleum (5:95) as eluent to give the vinylstannane as a colourless oil. Representative data for **3e**: δ_H 5.98 (1 H, dt, *J* 18.9, 5.4 Hz), 5.90 (1 H, d, *J* 18.9 Hz), 4.58 (1 H, m), 3.87 (1 H, m), 3.75 (1 H, m), 3.49 (1 H, m), 3.39 (1 H, m), 2.22 (2 H, m), 1.84 (1 H, m), 1.71 (3 H, m), 1.41–1.58 (10 H, m), 1.26–1.39 (6 H, m), 0.83–0.90 (15 H, m); δ_C 148.73 (CH), 127.62 (CH), 98.76 (CH), 66.96 (CH_2), 62.16 (CH_2), 34.34 (CH_2), 30.71 (CH_2), 29.08 (CH_2), 28.92 (CH_2), 27.23 (CH_2), 25.48 (CH_2), 19.59 (CH_2), 13.68 (CH_3), 9.33 (CH_2); *m/z* 403 (5.0, $M^+ - C_4H_9$), 85 (32.6) (Found: $M^+ - C_4H_9$, 403.1664. $C_{18}H_{35}O_2Sn$ requires 403.1659).

Palladium-catalysed hydrostannylations of 1-bromoalkynes and *in situ* Stille reactions

The 1-bromoalkynes were treated with Bu_3SnH–PPh_3–$Pd_2(dba)_3$ as described previously. In the same flask the crude vinylstannane product was then treated with the vinyl bromide **4** (1 mmol) and a further quantity of PPh_3–$Pd_2(dba)_3$ (0.005 mmol). The mixture was heated under reflux for 2 h (TLC monitoring), then cooled and diluted with an equal volume of saturated aqueous KF. The two-phase mixture was stirred vigorously overnight then diluted with diethyl ether. The separated organic layer was washed with saturated ammonium chloride (50 ml) and brine (50 ml), then dried and evaporated to dryness. The residue was purified by chromatography on silica gel, using ethyl acetate–light petroleum (1:9) as eluent, to give the trienoates **5** as colourless oils. Representative data for **5b**: δ_H 7.67 (CH, dd, *J* 15.1, 12.0 Hz), 6.98 (2 × ArH, d, *J* 8.6 Hz), 6.87 (2 × ArH, d, *J* 8.6 Hz), 6.14 (CH, d, *J* 15.7 Hz), 6.08 (CH, d, *J* 12.0 Hz), 5.93 (CH, dt, *J* 15.7, 7.1 Hz), 5.85 (CH, d, *J* 15.1 Hz), 4.42 (CH_2, s), 4.20 (CH_2, q, *J* 7.1 Hz), 3.79 (CH_3, s), 3.44 (CH_2, t, *J* 6.4 Hz), 2.17 (CH_2, app. q, *J* 7.0 Hz), 1.96 (CH_3, s), 1.62 (CH_2, m), 1.50 (CH_2, m), 1.29 (CH_3, t, *J* 7.1 Hz); δ_C 167.36 (C), 159.06 (C), 143.82 (C), 140.51 (CH), 134.30 (CH), 133.99 (CH), 130.61 (C), 129.11 (CH), 126.60 (CH), 120.09 (CH), 113.67 (CH), 72.48 (CH_2), 69.75 (CH_2), 60.06 (CH_2), 55.15 (CH_3), 32.79 (CH_2), 29.23 (CH_2), 25.82 (CH_2), 14.26 (CH_3), 13.11 (CH_3); *m/z* 358 (0.38, M^+), 121 (100), 29 (4.4) (Found: M^+, 358.2145. $C_{22}H_{30}O_4$ requires 358.2144).

† dba = dibenzylideneacetone.

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References

1 M. Pereyre, J. P. Quintard and A. Rahm, *Tin in Organic Synthesis*, Butterworths, London, 1987.
2 (*a*) J. K. Stille, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 508; (*b*) T. N. Mitchell, *Synthesis*, 1992, 801.
3 A. J. Leusink, H. A. Budding and J. W. Marsman, *J. Organomet. Chem.*, 1967, **9**, 285.
4 A. J. Leusink, H. A. Budding and W. Drenth, *J. Organomet. Chem.*, 1968, **11**, 541.
5 E. J. Corey and R. H. Wollenberg, *J. Org. Chem.*, 1975, **40**, 2265.
6 M. E. Jung and L. A. Light, *Tetrahedron Lett.*, 1982, **23**, 3851.
7 G. A. Tolstikov, M. S. Miftakhov, N. A. Danilova and Y. L. Vel'der, *Synthesis*, 1986, 496.
8 Y. Ichinose, H. Oda, K. Oshima and K. Utimoto, *Bull. Chem. Soc. Jpn.*, 1987, **60**, 3468.
9 K. Kikukawa, H. Umekawa, F. Wada and T. Matsuda, *Chem. Lett.*, 1988, 881.
10 H. X. Zhang, F. Guibé and G. Balavoine, *J. Org. Chem.*, 1990, **55**, 1857.
11 N. Greeves and J. S. Torode, *Synlett*, 1994, 537.
12 G. T. Crisp and P. T. Glink, *Tetrahedron*, 1994, **50**, 3213.
13 V. S. Zavgorodnii, V. B. Simin, T. P. Zubova and A. A. Petrov, *Zh. Obshch. Khim.*, 1976, **46**, 197.
14 J.-I. Hibino, S. Matsubara, Y. Morizawa, K. Oshima and H. Nozaki, *Tetrahedron Lett.*, 1984, **25**, 2151.
15 E. Piers and H. E. Morton, *J. Org. Chem.*, 1980, **45**, 4264.
16 K. Nozaki, K. Wakamatsu, T. Nonaka, W. Tückmantel, K. Oshima and K. Utimoto, *Tetrahedron Lett.*, 1986, **27**, 2007.
17 S. Sharma and A. C. Oehlschlager, *Tetrahedron Lett.*, 1986, **27**, 6161.
18 L. Capella, A. Degl'Innocenti, A. Mordini, G. Reginato, A. Ricci and G. Seconi, *Synthesis*, 1991, 1201.
19 A. Barbero, P. Cuadrado, I. Fleming, A. M. González, F. J. Pulido and R. Rubio, *J. Chem. Soc., Perkin Trans. 1*, 1993, 1657.
20 P. Le Ménez, I. Berque, V. Fargeas, J. Ardisson and A. Pancrazi, *Synlett*, 1994, 998.
21 D. M. Hodgson, L. T. Boulton and G. N. Maw, *Tetrahedron*, 1995, **51**, 3713.
22 R. J. Boyce and G. Pattenden, *Tetrahedron Lett.*, 1996, **37**, 3501.
23 G. Pattenden and S. M. Thom, *Synlett*, 1993, 215.
24 D. A. Entwistle, S. I. Jordan, J. Montgomery and G. Pattenden, *J. Chem. Soc., Perkin Trans. 1*, 1996, 1315.
25 H. Hofmeister, K. Annen, H. Laurent and R. Weichert, *Angew. Chem., Int. Ed. Engl.*, 1984, 727.
26 D. Grandjean, P. Pale and J. Chuche, *Tetrahedron Lett.*, 1994, **35**, 3529.
27 K. Takai, K. Nitta and K. Utimoto, *J. Am. Chem. Soc.*, 1986, **108**, 7408.
28 G. Stork and K. Zhao, *Tetrahedron Lett.*, 1989, **30**, 2173.

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