Stille Cross-Coupling Reactions Using Vinylcyclopropylstannanes

Gerald Pattenden,* Davey A. Stoker

School of Chemistry, The University of Nottingham, Nottingham, NG7 2RD, UK
Fax +44(115)9513535; E-mail: gp@nottingham.ac.uk

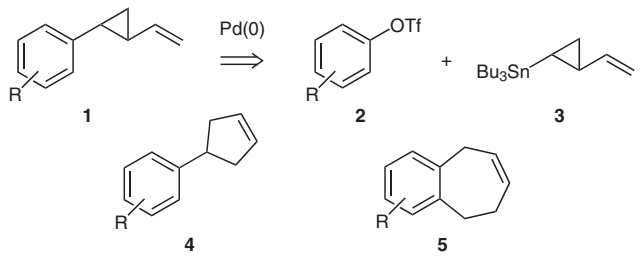
Received 3 February 2009

Abstract: The Stille cross-coupling reaction between a vinylcyclopropylstannane and iodobenzene or phenol triflate provides an expedious route to 1,2-phenylvinylcyclopropanes. However, similar coupling reactions using *ortho*-substituted aromatic substrates also lead to butylaromatic products, resulting from competitive sp^3–sp^2 coupling reactions.

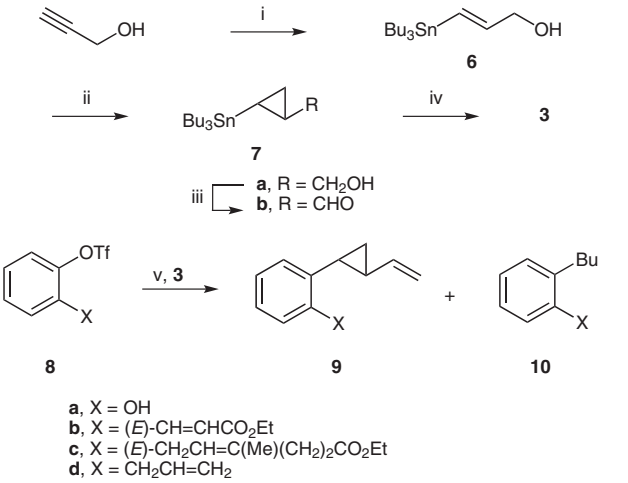
Key words: Stille reaction, cross-coupling, arylations, vinyl cyclopropanes, sp^3–sp^2 coupling

Palladium-catalysed cross-coupling reactions involving a wide variety of saturated and unsaturated organostannane precursors are ubiquitous in organic synthesis.[1] In connection with a specific synthetic objective, that is, the synthesis of 1,2-arylvinyl-substituted cyclopropanes **1**, it came as a surprise to us therefore that the Stille coupling reaction between vinylcyclopropylstannanes, for example, **3** and aryl derivatives **2** (Scheme 1), had not been described.[2–4] We surmise that the absence of such a description in the literature may have its origins in the propensity for vinylcyclopropanes to undergo Pd(II)-catalysed ring-opening reactions, and/or for the arylvinylcyclopropane products to undergo 6π-electrocyclisation in situ, leading, in both cases, to cyclic byproducts, namely **4** and **5**, respectively. We have therefore evaluated the scope for cross-coupling reactions involving the vinylcyclopropylstannane **3** and a series of substituted aryl triflate and halides. Here we present the outcome of this study and draw attention to an interesting dichotomous reaction pathway followed by the stannane **3**.

The *trans*-vinylcyclopropylstannane **3** was easily accessible from propargyl alcohol using four straightforward steps (Scheme 2). Thus, treatment of propargyl alcohol with Bu_3SnH–AIBN first led to the known (*E*)-vinylstannane **6** in 89% yield.[5] A Simmons–Smith reaction between **6** and diiodomethane in the presence of diethylzinc at –50 °C next gave the cyclopropane methanol **7a** (74%). Oxidation of **7a** to the corresponding aldehyde **7b**, using IBX and DMSO, followed by a straightforward Wittig reaction with methyltriphenylphosphoranylid then gave the *trans*-vinylcyclopropylstannane **3**.[6]



Scheme 1



Scheme 2 *Reagents and conditions*: i, Bu_3SnH, AIBN, 100 °C, 5 h, 89%; ii, CH_2I_2, Et_2Zn, CH_2Cl_2, –50 °C, 74%; iii, IBX, DMSO, 25 °C, 20 h, 96%; iv, $MePPh_3Br$, NaHMDS, –78 °C, 97%; v, $Pd(OAc)_2$, Ph_3As, CuI, LiCl, NMP, 24 h, 40–70%, ratios of **9/10** = ~ 1:2.

After examining a range of reaction conditions and catalytic systems, we found that when a solution of the vinylcyclopropylstannane **3** and phenoltriflate in NMP was added to palladium acetate (10 mol%) which had been premixed with triphenylarsine (60 mol%), and the resulting mixture was stirred and heated at 80 °C for 24 hours in the presence of CuI (20 mol%) and LiCl (6 equiv), a reproducible 70% yield of the phenylvinylcyclopropane **1** (R = H) could be realised. A similar outcome was seen using iodobenzene in place of phenoltriflate.[7] What came as a surprise to us was that when we examined the cross-coupling reactions between **3** and the phenoltriflates **8**, substituted at their *ortho* positions with oxy and carbon groups, we obtained the corresponding *n*-butylaromatic compounds **10** as major products.

Thus, a palladium-catalysed coupling reaction between the vinylcyclopropylstannane **3** and catechol monotriflate (**8a**) led to a 2:1 mixture of *o*-butylphenol (**10a**) and the phenolvinylcyclopropane (**9a**). Likewise, separate similar coupling reactions between **3** and the *ortho*-substituted triflates **8b**, **8c**, and **8d** gave approximately 2:1 mixtures

SYNLETT 2009, No. 11, pp 1800–1802
Advanced online publication: 02.06.2009
DOI: 10.1055/s-0029-1217327; Art ID: D04109ST

of the corresponding substituted butylbenzenes **10b**, **10c**, and **10d**, and phenylvinylcyclopropanes **9b**, **9c**, and **9d**, respectively, in combined yields of approximately 40%.

Although deliberate sp^3–sp^2 cross-coupling reactions between butylstannanes and aryl iodides/triflates have been used in synthesis,[8] the preferential migration of the sp^3-butyl group within vinyl- and aryltributylstannanes in Stille cross-coupling reactions is quite rare.[9] This feature, of course, is the main reason why the Stille sp^2–sp^2 cross-coupling reaction has been so revered in synthesis! In the specific cases of the coupling reactions involving the vinylcyclopropylstannanes **3** and the *ortho*-substituted triflates **8**, the Stille reaction is clearly limited. We suggest that this limitation is associated with steric impedance between the stannane **3** and the *ortho* substituents within the arylpalladium species at the stage of triflate–cyclopropyl/butyl exchange in the catalytic cycle, favouring butyl group over cyclopropane ring migration.

Acknowledgment

We thank the EPSRC (Studentship to D.A.S.) and AstraZeneca for support.

References and Notes

(1) (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508. (b) Farina, V.; Krishnamurthy, V.; Scott, W. K. In *Organic Reactions*, Vol. 50; Wiley: New York, **1997**. (c) Mitchell, T. N. In *Metal-Catalyzed Cross-Coupling Reactions*; de Meijere, A.; Diederich, F., Eds.; Wiley-VCH: Weinheim, **2004**, Chapt. 3.

(2) For a Negishi cross-coupling involving a vinylcyclopropylstannane and a vinyl iodide, see: Piers, E.; Jean, M.; Marrs, P. S. *Tetrahedron Lett.* **1987**, *43*, 5075.

(3) For zirconium-catalysed and Negishi cross-coupling reactions using vinylcyclopropyl halides and vinyl substrates, see: (a) Thomas, E.; Kasatkin, A. N.; Whitby, R. J. *Tetrahedron Lett.* **2006**, *52*, 9181. (b) Piers, E.; Coish, P. D. G. *Synthesis* **2001**, 251.

(4) For some Suzuki cross-coupling reactions using cyclopropyl boronic acids, see: (a) Baba, D.; Yang, Y.-J.; Uang, B.-J.; Fuchigami, T. *J. Fluorine Chem.* **2003**, *1*, 93. (b) Rubina, M.; Rubin, M.; Gevorgyan, V. *J. Am. Chem. Soc.* **2003**, *24*, 7198. (c) Wallace, D. J.; Chen, C.-Y. *Tetrahedron Lett.* **2002**, *39*, 6987. (d) Zhou, S.-M.; Deng, M.-Z.; Xia, L.-J.; Tang, M.-H. *Angew. Chem. Int. Ed.* **1998**, *20*, 2845.

(5) Oda, H.; Kobayashi, T.; Kosugi, M.; Migita, T. *Tetrahedron* **1995**, *51*, 695.

(6) The vinylcyclopropylstannane **3** was obtained as a colourless oil. IR ($CHCl_3$): ν_{max} = 3083, 1631 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.11 (1 H, ddd, *J* = 10.5, 8.5, 5.5 Hz, $CHSnBu_3$), 0.70–0.76 (2 H, m, $CHCH_2CH$), 0.81 (6 H, t, *J* = 8.0 Hz, $SnCH_2$), 0.89 (9 H, t, *J* = 7.5 Hz, CH_2CH_3), 1.25–1.36 (6 H, m, CH_3CH_2), 1.36–1.44 (1 H, m, CH_2=CHCH), 1.44–1.56 (6 H, m, $SnCH_2CH_2$), 4.80 (1 H, dd, *J* = 10.0, 1.5 Hz, HHC=CH), 5.05 (1 H, dd, *J* = 17.0, 1.5 Hz, HHC=CH), 5.29 (1 H, ddd, *J* = 17.0, 10.0, 9.0 Hz, CH_2=CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 2.6 (CH), 8.7 (CH_2), 11.5 (CH_2), 13.7 (CH_3), 19.4 (CH), 27.3 (CH_2), 29.1 (CH_2), 110.5 (CH_2), 144.6 (CH) ppm. MS (EI): *m/z* $C_{13}H_{25}Sn$ [M^+ – Bu]: 301.0978; 301.0986.

(7) **Typical Stille Coupling Procedure**: $Pd(OAc)_2$ (10 mol%), Ph_3As (60 mol%), CuI (20 mol%), and LiCl (6 equiv) were dissolved in NMP, and the mixture was then stirred at r.t. under an argon atmosphere for 10 min. A soln of the aryltriflate or aryliodide (1.0 equiv.) and the stannane **3** (1.05 equiv) in NMP was added dropwise over 1 min, and the mixture was then degassed and heated to 80 °C for 24 h. The cooled mixture was poured onto H_2O (50 mL) and EtOAc (50 mL), and the separated aqueous extract was extracted with EtOAc (3 × 100 mL). The combined organic extracts were washed successively with H_2O (3 × 20 mL), 2 M aq HCl (10 mL) and brine (50 mL), then dried (Na_2SO_4) and concentrated in vacuo to leave the coupled product (s) as a colourless oil. Chromatographic separation and purification was carried out on SiO_2, using PE (bp 40–60 °C), then 1–6% EtOAc in PE as eluant. The *o*-butylphenol (**10a**) showed identical spectroscopic data to those reported in the literature.[10]

Butylcinnamate 10b

IR ($CHCl_3$): ν_{max} = 1727cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$): δ = 0.94 (3 H, t, *J* = 7.0 Hz, CH_2CH_3), 1.35 (3 H, t, *J* = 7.0 Hz, OCH_2CH_3), 1.60–1.70 (4 H, m, CH_2CH_2), 2.75 (2 H, t, *J* = 7.0 Hz, $ArCH_2$), 4.28 (2 H, t, *J* = 7.0 Hz, OCH_2CH_3), 6.40 (1 H, d, *J* = 15.0 Hz, COCH=), 7.10–7.70 (4 H, m, ArH), 8.04 (1 H, d, *J* = 15.0 Hz, ArCH=) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 13.9 (CH_3), 14.3 (CH_3), 22.5 (CH_2), 25.6 (CH_2), 33.8 (CH_2), 60.5 (CH_2), 119.3 (CH), 126.5 (CH), 127.3 (CH), 128.6 (CH), 130.0 (CH), 133.7 (C), 134.0 (C), 142.3 (CH), 168.0 (C) ppm.

Butylaromatic Compound 10c

^1H NMR (360 MHz, $CDCl_3$): δ = 0.96 [3 H, t, *J* = 7.0 Hz, $(CH_2)_2CH_3$], 1.30 (3 H, t, *J* = 7.5 Hz, OCH_2CH_3), 1.33 (2 H, m, $CH_2CH_2CH_3$), 1.62 (2 H, app. pent., *J* = ca. 7 Hz, $CH_2CH_2CH_2$) 1.71 (3 H, s, CH=CCH), 2.20–2.40 (4 H, m, $CH_2CH_2CO_2Et$), 2.55 (2 H, t, *J* = 7.0 Hz, $ArCH_2$), 3.22 (2 H, d, *J* = 6.0 Hz, $ArCH_2CH$=), 4.12 (2 H, q, *J* = 7.5 Hz, OCH_2CH_3), 5.80 (1 H, t, *J* = 6.0 Hz, =CHCH), 6.90–7.05 (4 H, m, ArH) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 14.1 (2 × CH_3), 17.1 (CH_3), 22.4 (CH_2), 29.6 (CH_2), 31.9 (CH_2), 33.8 (CH_2), 34.6 (CH_2), 35.2 (CH_2), 61.3 (CH_2), 122.8 (CH), 125.6 (CH), 125.9 (CH), 128.1 (CH), 128.9 (CH), 135.5 (C), 136.5 (C), 136.6 (C), 173.1 (C) ppm.

Arylvinylcyclopropane 9b

^1H NMR (360 MHz, $CDCl_3$): δ = 1.15–1.30 (2 H, m, $CHCH_2CH$), 1.60 (3 H, t, *J* = 7.0 Hz, CH_2CH_3), 1.60–1.75 (1 H, m, $CHCH_2CH$), 2.10–2.20 (1 H, m, $CHCH_2CH$), 4.30 (2 H, q, *J* = 7.0 Hz, CH_2CH_3), 5.10 (1 H, d, *J* = 11.0 Hz, CH=CHH), 5.20 (1 H, d, *J* = 16.0 Hz, CH=CHH), 5.70 (1 H, ddd, *J* = 16.0, 11.0, 8.0 Hz, CH=CH_2), 6.40 (1 H, d, *J* = 15.0 Hz, ArCH=CH), 7.00–7.60 (4 H, m, ArH), 8.30 (1 H, d, *J* = 15.0 Hz, ArCH=CH) ppm.

Vinylcyclopropane 9c

IR ($CHCl_3$): ν_{max} = 3011 (s), 1727 (s), 1634 (m), 1602 (w) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.05 (1 H, app dt, *J* = 8.5, 5.0Hz, ArCHCHH), 1.22 (3 H, t, *J* = 7.0 Hz, OCH_2CH_3), 1.24–1.27 (1 H, m, ArCHCHH), 1.54–1.59 (1 H, m, H_2C=CHCH), 1.72 (3 H, app s, C=CCH_3), 1.96 (1 H, ddd, *J* = 8.5, 5.5, 5.0 Hz, ArCH), 2.36 (2 H, t, *J* = 7.0Hz, O=CCH_2CH_2), 2.43 (2 H, t, *J* = 7.0 Hz, O=CCH_2CH_2), 3.43 (1 H, dd, *J* = 16.0, 7.0 Hz, ArCHH), 3.49 (1 H, dd, *J* = 16.0, 7.0 Hz, ArCHH), 4.10 (2 H, q, *J* = 7.0 Hz, OCH_2CH_3), 4.96 (1 H, dd, *J* = 10.0, 1.5 Hz, HC=CHH), 5.13 (1 H, dd, *J* = 17.0, 1.5 Hz, HC=CHH), 5.34 (1 H, app tq, *J* = 7.0, 1.5 Hz, C=CH), 5.58 (1 H, ddd, *J* = 17.0, 10.0, 8.5 Hz, H_2C=CH), 6.99 (1 H, dd, *J* = 6.0, 2.0 Hz, ArH), 7.12–7.15 (3 H, m, 3 × ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (CH_3), 14.6 (CH_2), 16.2 (CH_3), 23.0 (CH), 25.7 (CH), 31.6

(CH_2), 33.2 (CH_2), 34.7 (CH_2), 60.3 (CH_2), 112.4 (CH_2), 123.6 (CH), 125.7, 126.0, 126.1 (3 × CH), 128.4 (CH), 134.4 (C), 139.5 (C), 140.9 (C), 141.0 (CH), 173.4 (C) ppm. MS (ES): *m/z* $C_{20}H_{26}O_2Na$ [M + Na^+]: 321.1825; found: 321.1817.

(8) For some examples, see: (a) Allegretti, M.; Bertini, R.; Cesta, M. C.; Bizzarri, C.; Di Bitondo, R.; Di Cioccio, V.; Galliera, E.; Berdini, V.; Topai, A.; Zampella, G.; Russo, V.; Di Bello, N.; Nano, G.; Nicolini, L.; Locati, M.; Fantucci, P.; Florio, S.; Colotta, F. *J. Med. Chem.* **2005**, *13*, 4312. (b) Tamayo, N.; Echavarren, A. M.; Paredes, M. C.; Fariña, F.; Noheda, P. *Tetrahedron Lett.* **1990**, *36*, 5189. (c) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *18*, 5478.

(9) For examples of some competitive alkyl *vs* aryl couplings involving aryltributylstannane precursors, see: (a) Yasuda, N.; Yang, C.; Wells, K. M.; Jensen, M. S.; Hughes, D. L. *Tetrahedron Lett.* **1999**, *3*, 427. (b) O'Neill, D. J.; Shen, L.; Prouty, C.; Conway, B. R.; Westover, L.; Wu, J. Z.; Zhang, H. C.; Maryanoff, B. E.; Murray, W. V.; Demarest, K. T.; Kuo, G. H. *Bioorg. Med. Chem.* **2004**, *12*, 3167. (c) Paintner, F. F.; Gorler, K.; Voelter, W. *Synlett* **2003**, 522. (d) Ito, S.; Okujima, T.; Morita, N. *J. Chem. Soc., Perkin Trans. 1* **2002**, *16*, 1896.

(10) Ohe, K.; Yokoi, T.; Miki, K.; Nishino, F.; Uemura, S. *J. Am. Chem. Soc.* **2002**, *124*, 526.