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Stereoselective Synthesis of (E)-1, 3-Enynyl Bromides *via* Pd/Cu-catalyzed Cross-coupling Reaction of (Z)-α-Bromovinylstannanes

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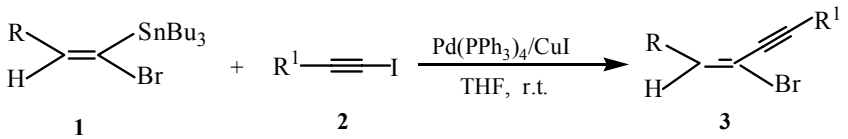
Abstract: (Z)-α-Bromovinylstannanes undergo the cross-coupling reaction with alkynyl iodides in the presence of $Pd(PPh_3)_4$ and CuI in THF at room temperature to afford stereoselectively (E)-1, 3-enynyl bromides in good yields.

Keywords: (Z)-α-Bromovinylstannane, palladium, cross-coupling, stereoselective synthesis.

The conjugated enyne moiety is incorporated in a number of natural products and it can be readily converted in a stereospecific manner into the corresponding diene system[1-3]. Recently, the discovery of strong antifungal agents[4] and new powerful antitumor antibiotics[5] has stimulated intense interest in the chemistry of enynes, which is at the origin of the biological properties of these substances. The metal or heteroatom- containing enynes will also be useful as building blocks for this purpose, since a lot of useful functional group transformations can be achieved by introduction and removal of metal or heteroatom functions. The synthesis of 1,3-enynes containing functional groups is of considerable interest in recent years. The stereoselective synthesis of 1,3-enynylsilanes[6], 1,3-enynylsulfides[7], 1,3-enynylselenides[8], 1,3-enynyltellurides[9], 1,3-enynylstannanes[10] has already been described in the literature. However, to date, the synthesis of 1,3-enynyl halides has not been reported yet. The transition metal- catalyzed cross-coupling reaction is a highly versatile method for carbon-carbon bond formation and has been widely used as synthetic tool[11]. In this paper, we wish to report that (E)-1,3-enynyl bromides could be synthesized by the cross-coupling reaction of (Z)-α-bromovinylstannanes with alkynyl iodides in the presence of $Pd(PPh_3)_4$ and CuI (**Scheme 1**).

Scheme 1



1 **2** **3**

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The required starting (Z)-α-bromovinylstannanes **1** were prepared in good yields with high stereoselectivity by the hydrozirconation of alkynylstannanes and the successive reaction with NBS[12]. The palladium copper cocatalyzed cross coupling reaction of (E)-α-selanylvinylstannanes with haloalkynes has been described[8b]. We observed that when (Z)-α-bromovinylstannanes **1** were allowed to react with alkynyl iodides **2** in the presence of catalytic amounts of $Pd(PPh_3)_4$ and CuI in THF at room temperature for 48 h, (E)-1,3-enynyl bromides **3** were obtained in good yields. The typical results are summarized in **Table 1**. The products were identified by ^1H NMR, IR spectra and elemental analysis. The double bond geometries of the products **3** were determined by the treatment of **3a** with *n*-butyllithium in THF followed by hydrolysis to produce compound **4**, a reaction which occurs stereoselectively (**Scheme 2**)[13]. The stereochemistry of compound **4** was easily established, since ^1H NMR spectrum of **4** gives rise to a doublet at δ 5.74 with a coupling constant of 11.8Hz, which is consistent with a (Z)-configuration.

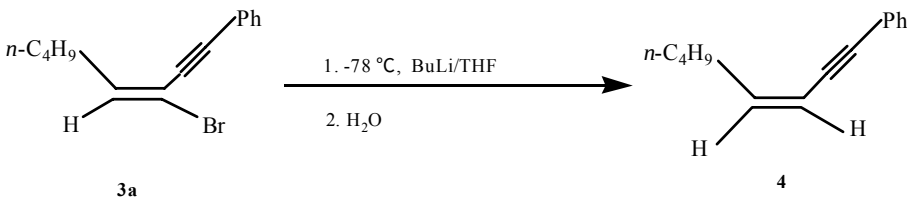
In conclusion, we have described a direct route to the stereoselective synthesis of (E)-1,3-enynyl bromides by the palladium catalyzed cross-coupling reaction of (Z)-α-bromovinylstannanes with alkynyl iodides. The method has the advantages of mild reaction conditions, straightforward, simple procedure and good yield. Investigation on the synthetic applications of (E)-1,3-enynyl bromides is in progress.

Table 1 Synthesis of (E)-1,3-enynyl bromides **3**

Entry	R	R^1	Product[a]	Yield[b](%)
1	*n*-C_4H_9	Ph	**3a**	64
2	*n*-C_4H_9	*n*-C_4H_9	**3b**	73
3	*n*-C_4H_9	CH_3OCH_2	**3c**	54
4	Ph	Ph	**3d**	61
5	Ph	*n*-C_4H_9	**3e**	67
6	Ph	*i*-C_5H_{11}	**3f**	65
7	*n*-C_6H_{13}	Ph	**3g**	62
8	*n*-C_6H_{13}	*i*-C_5H_{11}	**3h**	71

[a] All the compounds were characterized by IR、^1H NMR and elemental analyses.
[b] Isolated yield based on the (Z)-α-bromovinylstannane used.

Scheme 2



3a **4**

Experimental

^{1}H NMR spectra were recorded on a Bruker AC-P300 (300 MHz) spectrometer with TMS as an internal standard (δ in ppm). IR spectra were obtained on a Perkin-Elmer 683 instrument as neat films. Elemental analysis was measured using a Yanaco MT-3 CHN microelemental analyzer. THF was distilled from sodium-benzophenone ketyl before use. $Pd(PPh_3)_4$ and alkynyl iodides were prepared according to literature[14,15].

*General procedure for the synthesis of (E)-1,3-enynyl bromides **3a-3h***

To a stirred suspension of alkynyl iodide **2** (1.2 mmol), $Pd(PPh_3)_4$ (58 mg, 0.05 mmol) and CuI (19 mg, 0.1 mmol) in THF (5 mL) was added a solution of (Z)-α-bromo-vinylstannane **1** (1 mmol) in THF (1 mL) under Ar. The reaction mixture was stirred at room temperature for 48 h, treated with sat. aq NH_4Cl (10 mL) and extracted with CH_2Cl_2 (2×15 mL). The organic layer was washed with sat. aq NH_4Cl (2×10 mL), water (3×20 mL) and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography on silica gel eluting with light petroleum (30-60°C).

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References and Notes

1. P. A. Magriotis, K. D. Kim, *J. Am. Chem. Soc.*, **1993**, *115*, 2972.
2. M. F. Shostakovskii, A. V. Bogdanova, *The Chemistry of Diacetylenes*, Wiley J., New York, **1974**, 242.
3. (a) J. A. Miller, G. Zweifel, *J. Am. Chem. Soc.*, **1983**, *105*, 1383.
   (b) E. J. Corey, A. Tramontano, *J. Am. Chem. Soc*., **1984**, *106*, 462.
4. (a) A. Stutz, *Angew. Chem., Int. Ed. Engl.*, **1987**, *26*, 320.
   (b) P. Nussbaumer, L. Leitner, K. Mraz, A. Stutz, *J. Med. Chem.*, **1995**, *38*, 1831.
5. (a) M. D. Lee, T. S. Dunne, C. C. Chang, *et al*., *J. Am. Chem. Soc.*, **1987**, *109*, 3466.
   (b) A. G. Myers, P. J. Proteau, T. M. Handel, *J. Am. Chem. Soc.*, **1988**, *110*, 7212.
6. N. Chatani, N. Amishiro, S. Murai, *J. Am. Chem. Soc*., **1991**, *114*, 7779.
7. M. Koreeda, W. Yang, *Synlett,* **1994**, 201.
8. (a) A. L. Braga, G. Zeni, L. H. Andrade, C. C. Silveira, H. A. Stefani, *Synthesis*, **1998**, 39.
   (b) Y. Ma, X. Huang, *Synth. Commun.*, **1997**, *27*, 3441.
   (c) M. Z. Cai, C. Y. Peng, H. Zhao, J. D. Huang, *J. Chem. Res*., **2002**, 376.
9. (a) M. J. Dabdoub, V. Dabdoub, J. V. Comasseto, *Tetrahedron Lett*., **1992**, *33*, 2261.
   (b) J. P. Marino, F. Tucci, J. V. Comasseto, *Synlett,* **1993**, 761.
10. X. Huang, P. Zhong, *J. Chem. Soc., Perkin Trans. 1*, **1999**, 1543.
11. (a) A. Suzuki, *Pure Appl. Chem*., **1985**, *57*, 1749.
    (b) T. N. Mitchell, *Synthesis,* **1992**, 803.
12. B. H. Lipshutz, R. Keil, J. C. Barton, *Tetrahedron Lett.*, **1992**, *33*, 5861.
13. G. Cahiez, *Synthesis*, **1976**, 245.
14. D. R. Coulson, *Inorg. Synth*., **1972**, *13*, 121.
15. M. Lakshmi, N. Rao, M. Periasamy, *Synth. Commun*., **1995**, *25*, 2295.
16. Data of the compounds **3**:
    Compound **3a**: colorless oil; IR (film) 3065, 3025, 2958, 2929, 2220, 1594, 1570, 1486, 1442

cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.54-7.23 (m, 5H), 6.50 (t, 1H, *J* = 7.0 Hz), 2.18 (m, 2H), 1.56-1.22 (m, 4H), 0.89 (t, 3H, *J* = 5.4 Hz); Anal. Calcd. for $C_{14}H_{15}Br$: C, 63.88; H, 5.70. Found: C, 63.61; H, 5.57.

Compound **3b**: colorless oil; IR (film) 2956, 2926, 2326, 1605, 1463, 1378, 1124 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.45 (t, 1H, *J* = 7.3 Hz), 2.03-1.89 (m, 4H), 1.51-1.25 (m, 8H), 1.06-0.78 (m, 6H); Anal. Calcd. for $C_{12}H_{19}Br$: C, 59.26; H, 7.82. Found: C, 59.04; H, 7.57.

Compound **3c**: colorless oil; IR (film) 2928, 2213, 1608, 1455, 1090 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.39 (t, 1H, *J* = 7.1 Hz), 4.23 (s, 2H), 3.22 (s, 3H), 2.04 (m, 2H), 1.52-1.26 (m, 4H), 0.89 (t, 3H, *J* = 5.4 Hz); Anal. Calcd. for $C_{10}H_{15}OBr$: C, 51.95; H, 6.49. Found: C, 51.78; H, 6.58.

Compound **3d**: colorless oil; IR (film) 3056, 3023, 2953, 2923, 2201, 1599, 1573, 1489, 855, 692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.68 (s, 1H), 7.49-7.26 (m, 10H); Anal. Calcd. for $C_{16}H_{11}Br$: C, 67.84; H, 3.89. Found: C, 67.59; H, 3.70.

Compound **3e**: colorless oil; IR (film) 3057, 3024, 2956, 2931, 2256, 1601, 1573, 1490, 1443, 854, 692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.69 (s, 1H), 7.48-7.27 (m, 5H), 2.26 (t, 2H, *J* = 6.8 Hz), 1.57-1.31 (m, 4H), 0.91 (t, 3H, *J* = 7.2 Hz); Anal. Calcd. for $C_{14}H_{15}Br$: C, 63.88; H, 5.70. Found: C, 63.67; H, 5.73.

Compound **3f**: colorless oil; IR (film) 3058, 3023, 2956, 2930, 2254, 1602, 1574, 1491, 1443, 1384, 1367, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.68 (s, 1H), 7.49-7.27 (m, 5H), 2.25 (t, 2H, *J* = 6.8 Hz), 1.64-1.18 (m, 3H), 0.88 (d, 6H, *J* = 6.7 Hz); Anal. Calcd. for $C_{15}H_{17}Br$: C, 64.98; H, 6.14. Found: C, 64.75; H, 5.90.

Compound **3g**: colorless oil; IR (film) 3059, 3021, 2957, 2926, 2223, 1596, 1571, 1490, 1444 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.55-7.22 (m, 5H), 6.49 (t, 1H, *J* = 7.1 Hz), 2.19 (m, 2H), 1.57-1.21 (m, 8H), 0.90 (t, 3H, *J* = 5.4 Hz); Anal. Calcd. for $C_{16}H_{19}Br$: C, 65.98; H, 6.53. Found: C, 65.79; H, 6.31.

Compound **3h**: colorless oil; IR (film) 2957, 2927, 2325, 1604, 1464, 1384, 1367 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.46 (t, 1H, *J* = 7.2 Hz), 2.05-1.88 (m, 4H), 1.54-1.24 (m, 11H), 1.07-0.76 (m, 9H); Anal. Calcd. for $C_{15}H_{25}Br$: C, 63.16; H, 8.77. Found: C, 62.88; H, 8.56.

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