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Article

Stereoselective Synthesis of 1,3-Enynylstannanes via Palladium Catalyzed Cross-Coupling Reactions of (*Z*)-*α*-Bromovinylstannanes

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Based on the different reactivity of stannyl and bromo groups, (*Z*)-*α*-bromovinylstannanes can undergo the cross-coupling reaction with alkynyl Grignard reagents in the presence of tetrakis(triphenylphosphine)palladium(0) catalyst in THF at room temperature to afford stereoselectively 1,3-enynylstannanes in good yields.

Keywords (*Z*)-*α*-bromovinylstannane, 1,3-enynylstannane, palladium, cross-coupling reaction, stereoselective synthesis

Introduction

The chemistry of enynes[1] is currently attracting great interest because 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.[2,3] 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 many useful functional group transformations can be achieved by introduction and removal of metal or heteroatom functions. Many methods can be used for the synthesis of chalcogenoenynes, such as the addition of organotellurolates[6] or thiols[7] to diynes, the coupling reactions of halovinylic chalcogenides with alkynyl Grignard reagents[8] or ethynyltributylstannane,[9] the coupling reactions of bromovinylic chalcogenides with terminal alkynes[10] and the cross-coupling of (*E*)-*α*-selanylvinylstannanes with 1-haloalkynes.[11] The stereoselective synthesis of 1,3-enynylsilanes has also been described in the literature.[12] However, so far, the stereoselective synthesis of 1,3-enynylstannanes has received less attention.[13] Herein we wish to report that 1,3-enynylstannanes could be synthesized via a cross-coupling reaction of (*Z*)-*α*-bromovinylstannanes with alkynyl Grignard reagents in the presence of $Pd(PPh_3)_4$ catalyst (Scheme 1).

Results and discussion

The required starting (*Z*)-*α*-bromovinylstannanes (**1**) were prepared in good yields with high stereoselectivity by the hydrozirconation of alkynylstannanes and successive reaction with NBS.[14] It was observed that when (*Z*)-*α*-bromovinylstannanes (**1**) were allowed to react with alkynyl Grignard reagents **2** in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium(0) in THF at room temperature for 6 h, 1,3-enynylstannanes **3** were obtained in good yields. The typical results are summarized in Table 1.

Scheme 1

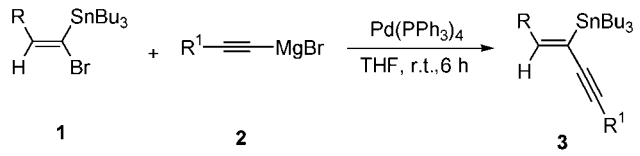

Table 1 1,3-Enynylstannanes **3** prepared according to Scheme 1

Entry	R	R^1	Product	Yield [a]/%
1	*n*-C_4H_9	*n*-C_4H_9	**3a**	82
2	*n*-C_4H_9	Ph	**3b**	88
3	*n*-C_4H_9	CH_3OCH_2	**3c**	74
4	Ph	*n*-C_4H_9	**3d**	86
5	Ph	Ph	**3e**	81
6	Ph	CH_3OCH_2	**3f**	72
7	CH_3OCH_2	*n*-C_4H_9	**3g**	78
8	CH_3OCH_2	Ph	**3h**	84
9	CH_3OCH_2	CH_3OCH_2	**3i**	73
10	*n*-C_6H_{13}	Ph	**3j**	85

[a] Isolated yield based on **1** used.

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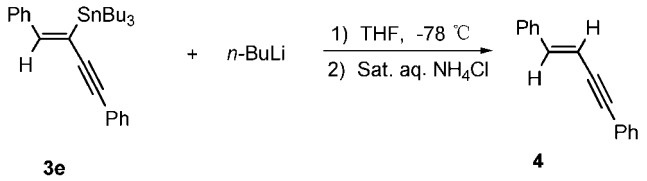
The products **3** were identified by ^{1}H NMR, IR, MS spectra and elemental analyses. The double bond geometries of the products **3** were determined by the treatment of (*Z*)-1-phenyl-2-tributylstannyl-4-phenyl-1-buten-3-yne (**3e**) at −78 ℃ with butyllithium in THF followed by hydrolysis with sat. aq. NH_4Cl to produce (*E*)-1,4-diphenyl-1-buten-3-yne **4** (Scheme 2).[15] The stereochemistry of product **4** was easily established, since the ^{1}H NMR spectrum of the product **4** gives rise to two doublets at δ 6.30 and δ 7.01 with coupling constant of 16 Hz, typical of *trans* positioned protons. The experimental results showed that the palladium-catalyzed cross-coupling reaction of (*Z*)-α-bromovinylstannanes with alkynyl Grignard reagents occurred with total retention of configuration.

Scheme 2



3e **4**

In conclusion, we have developed a novel approach to the stereoselective synthesis of 1,3-enynylstannanes by the cross-coupling reaction of (*Z*)-α-bromovinylstannanes with alkynyl Grignard reagents in the presence of $Pd(PPh_3)_4$. The present method has the advantages of readily available starting materials, straightforward and simple procedures, mild reaction conditions and good yields.

Experimental

Tetrahydrofuran (THF) was freshly distilled from sodium-benzophenone prior to its use. $Cp_2Zr(H)Cl$,[16] alkynylstannanes[17] and $Pd(PPh_3)_4$[18] were prepared according to the literature procedures. IR spectra were obtained on a Perkin-Elmer 683 instrument as neat films. ^{1}H NMR spectra were recorded on a Bruker AC-300 (300 MHz) spectrometer using $CDCl_3$ as solvent. ^{1}H chemical shifts are reported relative to TMS. Mass spectra were obtained on a Finigan 8230 mass spectrometer. Elemental analyses were carried out on a Carlo Erba EA 1110 instrument.

General procedure for synthesis of (*Z*)-α-bromovinylstannanes 1a—1d

A mixture of $Cp_2Zr(H)Cl$ (1 mmol) and alkynylstannane (1 mmol) in THF (5 mL) was stirred at room temperature for 40 min to yield a clear solution. Into the resulting solution was added NBS (1 mmol) at 0 ℃, and the mixture was stirred for 30 min, then at room temperature for 30 min. The solvent was removed by rotary evaporator under reduced pressure. The residue was extracted with light petroleum (3×10 mL) and filtered through a short plug of silica gel. After evaporation of the filtrate, the residue was purified by column chromatography on silica gel eluting with light petroleum.

(*Z*)-1-Bromo-1-tributylstannyl-1-hexene (**1a**): Yield 83%; Oil; ^{1}H NMR δ: 6.85 (t, J=7.8 Hz, 1H), 2.12—1.93 (m, 2H), 1.67—0.85 (m, 34H); IR (film) ν: 2957, 2928, 2872, 2855, 1596, 1463, 1377, 1073, 693 cm^{-1}. Anal. calcd for $C_{18}H_{37}SnBr$: C 47.79, H 8.19; found C 47.54, H 8.03.

(*Z*)-1-Bromo-1-tributylstannyl-2-phenylethene (**1b**): Yield 76%; Oil; ^{1}H NMR δ: 8.18 (s, 1H), 7.46—7.11 (m, 5H), 1.47—0.79 (m, 27H); IR (film) ν: 3058, 3023, 2956, 2921, 2871, 2853, 1600, 1489, 1463, 1376, 1072, 754, 722, 695 cm^{-1}. Anal. calcd for $C_{20}H_{33}SnBr$: C 50.85, H 6.99; found C 50.60, H 6.83.

(*Z*)-1-Bromo-1-tributylstannyl-3-methoxy-1-propene (**1c**): Yield 82%; Oil; ^{1}H NMR δ: 7.00 (t, J=6.5 Hz, 1H), 3.79 (d, J=6.4 Hz, 2H), 3.33 (s, 3H), 1.65—0.76 (m, 27H); IR (film) ν: 2957, 2922, 2872, 2853, 1606, 1464, 1377, 1117 cm^{-1}. Anal. calcd for $C_{16}H_{33}OSnBr$: C 43.64, H 7.50; found C 43.42, H 7.37.

(*Z*)-1-Bromo-1-tributylstannyl-1-octene (**1d**): Yield 79%; Oil; ^{1}H NMR δ: 6.82 (t, J = 7.8 Hz, 1H), 2.13—1.94 (m, 2H), 1.50—0.75 (m, 38H); IR (film) ν: 2958, 2926, 2871, 2856, 1597, 1463, 1377 cm^{-1}. Anal. calcd for $C_{20}H_{41}SnBr$: C 50.00, H 8.54; found C 49.82, H 8.42.

General procedure for synthesis of 1,3-enynylstannanes 3a—3j

To a solution of ethylmagnesium bromide (2 mmol) in THF (3 mL) was added terminal alkyne (2 mmol) in THF (1 mL) at 0 ℃ under nitrogen. After stirring the mixture for 30 min, it was continued at 30 ℃ for another 3 h. (*Z*)-α-Bromovinylstannane **1** (1 mmol) and $Pd(PPh_3)_4$ (0.02 mmol) were then added to the resulting THF solution of alkynyl Grignard reagent **2** and the mixture was stirred at room temperature for 6 h. Then a saturated aqueous NH_4Cl solution (20 mL) was added and the mixture was stirred for 10 min, and extracted with diethyl ether (2×30 mL). The ethereal solution was washed with water (3×30 mL), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel eluting with light petroleum.

(*Z*)-6-Tributylstannyl-5-dodecen-7-yne (**3a**): Oil; ^{1}H NMR δ: 6.36 (t, J=7.0 Hz, 1H), 2.48—2.04 (m, 4H), 1.73—0.67 (m, 41H); IR (film) ν: 2958, 2929, 2194, 1464 cm^{-1}; MS (70 eV) *m/z* (%): 453 (M^+, 2.4), 397 (27.5), 291 (16.3), 177 (41.2), 82 (24.2), 57 (100). Anal. calcd for $C_{24}H_{46}Sn$: C 63.58, H 10.15; found C 63.35, H 10.21.

(*Z*)-1-Butyl-2-tributylstannyl-4-phenyl-1-buten-3-yne (**3b**): Oil; ^{1}H NMR δ: 7.42—6.95 (m, 5H), 6.56 (t, J=7.0 Hz, 1H), 2.29—2.06 (m, 2H), 1.75—0.68 (m, 34H); IR (film) ν: 3031, 2927, 2178, 1583, 1488, 1463 cm^{-1}; MS (70 eV) *m/z* (%): 473 (M^+, 1.7), 417 (33.6), 291 (20.4), 177 (38.5), 102 (11.6), 77 (46.3), 57 (100). Anal. calcd for $C_{26}H_{42}Sn$: C 65.96, H 8.88; found C

65.71, H 8.69.

(*Z*)-1-Butyl-2-tributylstannyl-5-methoxy-1-penten-3-yne (**3c**): Oil; ^{1}H NMR δ: 6.48 (t, J=7.0 Hz, 1H), 4.28 (s, 2H), 3.24 (s, 3H), 2.28—2.08 (m, 2H), 1.71—0.67 (m, 34H); IR (film) v: 2957, 2927, 2175, 1463, 1189 cm^{-1}; MS (70 eV) *m/z* (%): 441 (M^+, 3.1), 411 (8.7), 384 (9.8), 291 (14.7), 177 (56.2), 57 (51.4), 45 (100). Anal. calcd for $C_{22}H_{42}OSn$: C 59.86, H 9.52; found C 59.98, H 9.71.

(*Z*)-1-Phenyl-2-tributylstannyl-4-butyl-1-buten-3-yne (**3d**): Oil; ^{1}H NMR δ: 7.45—7.01 (m, 6H), 2.40—0.65 (m, 36H); IR (film) v: 3023, 2927, 2307, 1597, 1488, 1463 cm^{-1}; MS (70 eV) *m/z* (%): 473 (M^+, 1.4), 416 (20.3), 291 (18.6), 177 (47.3), 102 (19.2), 77 (34.7), 57 (100). Anal. calcd for $C_{26}H_{42}Sn$: C 65.96, H 8.88; found C 65.72, H 8.73.

(*Z*)-1-Phenyl-2-tributylstannyl-4-phenyl-1-buten-3-yne (**3e**): Oil; ^{1}H NMR δ: 7.54—7.01 (m, 11H), 1.68—0.66 (m, 27H); IR (film) v: 3022, 2924, 2175, 1596, 1487, 1463 cm^{-1}; MS (70 eV) *m/z* (%): 493 (M^+, 1.6), 436 (17.5), 291 (14.8), 202 (33.5), 77 (54.2), 57 (100). Anal. calcd for $C_{28}H_{38}Sn$: C 68.15, H 7.71; found C 68.27, H 7.84.

(*Z*)-1-Phenyl-2-tributylstannyl-5-methoxy-1-penten-3-yne (**3f**): Oil; ^{1}H NMR δ: 7.52—7.02 (m, 6H), 4.15 (s, 2H), 3.27 (s, 3H), 1.71—0.67 (m, 27H); IR (film) v: 3023, 2925, 2183, 1598, 1488, 1463 cm^{-1}; MS (70 eV) *m/z* (%): 461 (M^+, 2.3), 404 (14.6), 291 (22.3), 147 (100), 77 (38.3), 45 (76.3). Anal. calcd for $C_{24}H_{38}OSn$: C 62.47, H 8.24; found C 62.24, H 8.06.

(*Z*)-1-Methoxy-3-tributylstannyl-2-nonen-4-yne (**3g**): Oil; ^{1}H NMR δ: 6.45 (t, J=6.8 Hz, 1H), 3.83 (d, J=6.4 Hz, 2H), 3.22 (s, 3H), 2.42—0.67 (m, 36H); IR (film) v: 2928, 2872, 2195, 1463, 1122 cm^{-1}; MS (70 eV) *m/z* (%): 441 (M^+, 2.8), 385 (11.7), 291 (16.8), 177 (45.4), 57 (49.1), 45 (100). Anal. calcd for $C_{22}H_{42}OSn$: C 59.86, H 9.52; found C 59.71, H 9.45.

(*Z*)-1-Methoxy-3-tributylstannyl-5-phenyl-2-penten-4-yne (**3h**): Oil; ^{1}H NMR δ: 7.42—7.01 (m, 5H), 6.04 (t, J=6.8 Hz, 1H), 3.91 (d, J=6.4 Hz, 2H), 3.32 (s, 3H), 1.75—0.66 (m, 27H); IR (film) v: 3021, 2922, 2359, 1596, 1488, 1463, 1122 cm^{-1}; MS (70 eV) *m/z* (%): 461 (M^+, 1.8), 405 (17.4), 291 (14.4), 147 (100), 77 (28.6), 57 (39.5), 45 (67.3). Anal. calcd for $C_{24}H_{38}OSn$: C 62.47, H 8.24; found C 62.19, H 8.11.

***(Z)*-1,6-Dimethoxy-3-tributylstannyl-2-hexen-4-yne** (**3i**): Oil; ^{1}H NMR δ: 6.56 (t, J=6.8 Hz, 1H), 4.13 (s, 2H), 3.87 (d, J=6.4 Hz, 2H), 3.28 (s, 3H), 3.24 (s, 3H), 1.72—0.66 (m, 27H); IR (film) v: 2924, 2872, 2189, 1463, 1122 cm^{-1}; MS (70 eV) *m/z* (%): 429 (M^+, 3.8), 399 (43.4), 372 (19.6), 291 (11.2), 57 (69.8), 45 (100). Anal. calcd for $C_{20}H_{38}O_2Sn$: C 55.94, H 8.86; found C 55.71, H 8.69.

(*Z*)-1-Hexyl-2-tributylstannyl-4-phenyl-1-buten-3-yne (**3j**): Oil; ^{1}H NMR δ: 7.50—6.94 (m, 5H), 6.53 (t, J=7.0 Hz, 1H), 2.45—2.02 (m, 2H), 1.77—0.69 (m, 38H); IR (film) v: 3024, 2957, 2928, 2183, 1594, 1492, 1464 cm^{-1}; MS (70 eV) *m/z* (%): 501 (M^+, 1.2), 444 (15.8), 291 (23.2), 177 (38.5), 77 (34.4), 57 (100). Anal. calcd for $C_{28}H_{46}Sn$: C 67.07, H 9.18; found C 66.84, H 9.02.

Synthesis of (*E*)-1,4-diphenyl-1-buten-3-yne (4)

To a solution of (*Z*)-1-phenyl-2-tributylstannyl-4-phenyl-1-buten-3-yne (**3e**, 1 mmol) in THF (5 mL) was added BuLi (1.6 mol/L hexane solution, 1.1 mmol) at −78 ℃. After being stirred for 1 h, the mixture was hydrolyzed with sat. aq. NH_4Cl and extracted with Et_2O (2×30 mL). The ethereal solution was washed with water (2×15 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (light petroleum) to afford enyne **4** (0.173 g, 75%); m.p. 95—96 ℃ (lit.[19] 96—97 ℃); ^{1}H NMR ($CDCl_3$) δ: 7.72—7.10 (m, 10 H), 7.01 (d, J=16 Hz, 1H), 6.30 (d, J=16 Hz, 1H).

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