Stereoselective synthesis of 1,3-enynyltellurides via palladium catalysed cross-coupling reaction of (E)-α-iodovinyltellurides

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(E)-α-Iodovinyltellurides undergo a direct coupling reaction with terminal alkynes in the presence of $[Pd(PPh_3)_4]$ and CuI catalysts in pyrrolidine at room temperature to give 1,3-enynyltellurides in good yields.

Keywords: 1,3-enynyltelluride, (E)-α-iodovinyltelluride, cross-coupling reaction, stereoselective synthesis

The discovery of strong antifungal agents[1] and new powerful antitumor antibiotics[2] has stimulated intense interest in the chemistry of enynes,[3] 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.[4] The synthesis of 1,3-enynes containing functional groups is of considerable interest in recent years. The stereoselective synthesis of 1,3-enynylsulfides,[5] 1,3-enynylselenides,[6] 1,3-enynylsilanes[7] and 1,3-enynylstannanes[8] has already been described in the literature. However, synthesis of 1,3-enynyltellurides has received less attention[9] and the 1,3-enynyltellurides with the tellurenyl group attached between the double and triple bonds has not been reported.

The transition metal-catalysed cross-coupling reaction is a highly versatile method for carbon–carbon bond formation and has been widely used as synthetic tool.[10] The palladium-catalysed coupling reaction of alkenyl halides with terminal alkynes (Sonogashira reaction) provides a direct route to 1,3-enynes.[11] Here, we report that 1,3-enynyltellurides could be conveniently synthesised by the coupling reaction of (E)-α-iodovinyltellurides with terminal alkynes in the presence of $[Pd(PPh_3)_4]$ and CuI catalysts (Scheme 1).

The required starting (E)-α-iodovinyltellurides **1** were prepared in good yields by the hydrozirconation of alkynyltellurides and successive reaction with iodine.[12] We observed that when (E)-α-iodovinyltellurides **1** were allowed to react directly with terminal alkynes **2** in the presence of 5 mol% of $[Pd(PPh_3)_4]$ and 10 mol% of CuI in pyrrolidine at room temperature for 2 h, 1,3-enynyltellurides **3** were obtained stereoselectively in good yields. The typical results are summarised in Table 1.

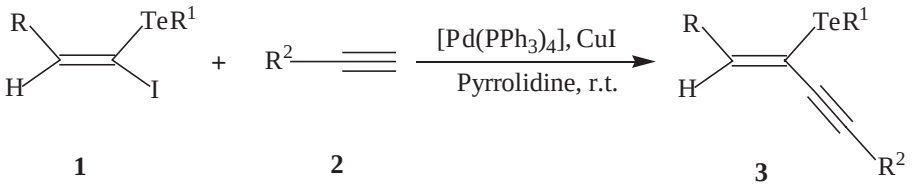
Table 1 Synthesis of 1,3-enynyltellurides **3a–i**

R	R^1	R^2	Product	Yield/%[a]
n-C_4H_9	*n*-C_4H_9	*n*-C_4H_9	**3a**	72
n-C_4H_9	*n*-C_4H_9	Ph	**3b**	81
n-C_4H_9	*n*-C_4H_9	CH_3OCH_2	**3c**	78
n-C_6H_{13}	*n*-C_4H_9	*n*-C_6H_{13}	**3d**	73
n-C_6H_{13}	*n*-C_4H_9	Ph	**3e**	68
n-C_6H_{13}	*n*-C_4H_9	CH_3OCH_2	**3f**	64
n-C_4H_9	Ph	CH_3OCH_2	**3g**	62
Ph	*n*-C_4H_9	*n*-C_4H_9	**3h**	65
Ph	*n*-C_4H_9	Ph	**3i**	87

[a]Isolated yield based on the (E)-α-iodovinyltelluride **1** used.

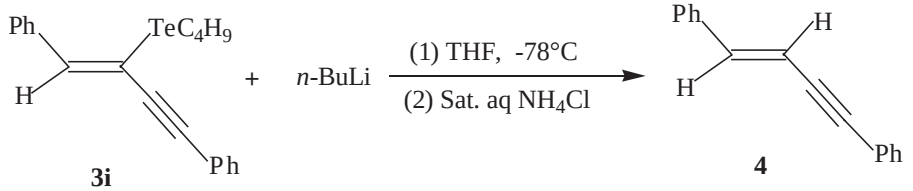
The products **3** were identified by ^1H NMR, IR spectra and elemental analyses. The double bond geometries of the products **3** were determined by the treatment of (Z)-1-phenyl-2-butyltelluro-4-phenyl-1-buten-3-yne at –78 °C with butyllithium in THF followed by hydrolysis with sat. aq. NH_4Cl to produce (E)-1,4-diphenyl- 1-buten-3-yne **4** (Scheme 2).[13] The stereochemistry of product **4** was easily established, since the ^1H NMR spectrum of 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 catalysed cross-coupling reaction of (E)-α-iodovinyltellurides with terminal alkynes occurred with total retention of configuration.

In conclusion, we have developed a novel approach to the stereoselective synthesis of 1,3-enynyltellurides by the cross-coupling reaction of (E)-α-iodovinyltellurides with terminal alkynes in the presence of $[Pd(PPh_3)_4]$ and CuI. The reactions have the advantages of mild conditions, short reaction times, simple manipulation and good yields.



1 **2** **3**

Scheme 1



3i **4**

Scheme 2

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Experimental

[$ZrCp_2$(H)Cl] and alkynyltellurides were prepared according to the literature, respectively.[14,15] ^{1}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 measured using a Yanaco MT-3 CHN microelemental analyzer. Tetrahydrofuran (THF) was freshly distilled from sodium-benzophenone prior to its use. Pyrrolidine was dried, deoxygenated and freshly distilled before use.

General procedure for the synthesis of (E)-α-iodovinyltellurides **1**: To a mixture of [$ZrCp_2$(H)Cl] (2.0 mmol) in THF (6.0 ml) under Ar, a solution of the corresponding alkynyltelluride (1.0 mmol) in THF (3.0 ml) was added *via* a syringe. The reaction mixture was stirred at room temperature for 30 min. Then, the resulting dark red mixture formed was treated at room temperature with a solution of iodine (3.0 mmol) in THF (5.0 ml), transferred *via* a syringe. The stirring was continued for an additional 30 min, the mixture was diluted with ethyl acetate (10 ml), 95% ethanol (10 ml) and water (5 ml) and finally $NaBH_4$ (3.0 mmol) was added to remove the electrophile excess and to perform the dehalogenation of the tellurium atom. After this treatment the product was extracted with ethyl acetate (5×30 ml) and washed with water (5×50 ml), the organic layer was dried over $MgSO_4$ and the solvent evaporated under reduced pressure. The residue was purified by flash chromatography using hexane as eluent.

(E)-1-Iodo-1-butyltelluro-1-hexene: yield 64%: IR (film)/cm^{-1} 2957, 2923, 2869, 2818, 1582, 1464, 1377; δ_H ($CDCl_3$) 7.02 (t, *J* = 7.2 Hz, 1H), 2.88 (t, *J* = 7.6 Hz, 2H), 2.08–1.96 (m, 2H), 1.87–1.75 (m, 2H), 1.48–1.29 (m, 6H), 0.97–0.87 (m, 6H); Anal. Calcd for $C_{10}H_{19}TeI$: C, 30.5; H, 4.9. Found: C, 30.8; H, 4.8.

(E)-1-Iodo-1-butyltelluro-1-octene: yield 66%: IR (film)/cm^{-1} 2958, 2922, 2870, 2819, 1580, 1463, 1378; δ_H ($CDCl_3$) 6.71 (t, *J* = 7.2 Hz, 1H), 2.79 (t, *J* = 7.2 Hz, 2H), 2.26–2.21 (m, 2H), 1.85–1.76 (m, 2H), 1.45–1.28 (m, 10H), 0.95–0.86 (m, 6H); Anal. Calcd for $C_{12}H_{23}TeI$: C, 34.2; H, 5.5. Found: C, 33.9; H, 5.6.

(E)-1-Iodo-1-butyltelluro-2-phenylethene: yield 71%: IR (film)/cm^{-1} 3057, 3021, 2956, 2872, 1598, 1487, 1463, 1377; δ_H ($CDCl_3$) 8.32 (s, 1H), 7.49–7.20 (m, 5H), 2.88 (t, *J* = 7.6 Hz, 2H), 1.83–1.76 (m, 2H), 1.43–1.32 (m, 2H), 0.91 (t, *J* = 7.2 Hz, 3H); Anal. Calcd for $C_{12}H_{15}TeI$: C, 34.8; H, 3.7. Found: C, 34.6; H, 3.5.

(E)-1-Iodo-1-phenyltelluro-1-hexene: yield 68%: IR (film)/cm^{-1} 3058, 3019, 2957, 2873, 1595, 1490, 1464, 1377; δ_H ($CDCl_3$) 7.77–7.67 (m, 2H), 7.40–7.21 (m, 3H), 7.10 (t, *J* = 7.2 Hz, 1H), 2.13–2.06 (m, 2H), 1.44–1.28 (m, 4H), 0.91 (t, *J* = 7.2 Hz, 3H); Anal. Calcd for $C_{12}H_{15}TeI$: C, 34.8; H, 3.7. Found: C, 35.0; H, 3.7.

General procedure for the synthesis of 1,3-enynyltellurides **3a–i**: To a solution of [$Pd(PPh_3)_4$] (0.05 mmol, 0.058g) and CuI (0.1 mmol, 0.019g) in pyrrolidine (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 α-iodovinyltelluride (1.0 mmol) in pyrrolidine (1 ml) was added with stirring. The reaction mixture was stirred at r.t. for another 2 h, hydrolysed with sat. aq. NH_4Cl (10 ml) and extracted with Et_2O (2×20 ml). The organic layer was washed with sat. aq NH_4Cl (15 ml) and water (2×15 ml) and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave an oil, which was purified by column chromatography on silica gel using hexane or hexane/ether (20:1)(for **3c**, **3f**, **3g**) as eluent.

(Z)-6-Butyltelluro-5-dodecen-7-yne (**3a**): IR (film)/cm^{-1} 2957, 2930, 2872, 2860, 2221, 1587, 1465, 1435, 1378,743, 696; δ_H ($CDCl_3$) 6.14 (t, *J* = 7.6 Hz, 1H), 2.91 (t, *J* = 7.6 Hz, 2H), 2.49 (t, *J* = 7.2 Hz, 2H), 2.13–2.04 (m, 2H), 1.88–1.79 (m, 2H), 1.56–1.21 (m, 10H), 0.97–0.82 (m, 9H); Anal. Calcd for $C_{16}H_{28}Te$: C, 55.2; H, 8.1. Found: C, 54.9; H, 7.9.

(Z)-1-Butyl-2-butyltelluro-4-phenyl-1-buten-3-yne (**3b**): IR (film)/cm^{-1} 3020, 2979, 2874, 2401, 1599, 1446, 1383, 1216, 909, 771, 669; δ_H ($CDCl_3$) 7.43–7.41 (m, 2H), 7.31–7.26 (m, 3H), 6.45 (t, *J* = 7.2 Hz, 1H), 3.01 (t, *J* = 7.6 Hz, 2H), 2.18–2.13 (m, 2H), 1.89–1.84 (m, 2H), 1.49–1.17 (m, 6H), 0.94–0.85 (m, 6H); Anal. Calcd for $C_{18}H_{24}Te$: C, 58.7; H, 6.5. Found: C, 58.4; H, 6.4.

(Z)-1-Butyl-2-butyltelluro-5-methoxy-1-penten-3-yne (**3c**): IR (film)/cm^{-1} 2957, 2927, 2872, 2249, 1689, 1464, 1376, 1186, 1098, 908, 733; δ_H ($CDCl_3$) 6.38 (t, *J* = 6.8 Hz, 1H), 4.29 (s, 2H), 3.39 (s, 3H), 2.92 (t, *J* = 7.6 Hz, 2H), 2.14–2.08 (m, 2H), 1.89–1.78 (m, 2H), 1.45–1.21 (m, 6H), 0.96–0.82 (m, 6H); Anal. Calcd for $C_{14}H_{24}OTe$: C, 50.0; H, 7.1. Found: C, 49. 8; H, 7.0.

(Z)-8-Butyltelluro-7-hexadecen-9-yne (**3d**): IR (film)/cm^{-1} 2956, 2924, 2855, 2205, 1590, 1462, 1435, 1377, 885, 723; δ_H ($CDCl_3$) 6.26 (t, *J* = 7.6 Hz, 1H), 2.91 (t, *J* = 7.6 Hz, 2H), 2.39 (t, *J* = 7.2 Hz, 2H), 2.10–2.02 (m, 2H), 1.87–1.78 (m, 2H), 1.58–1.20 (m, 18H), 0.97–0.78 (m, 9H); Anal. Calcd for $C_{20}H_{36}Te$: C, 59.4; H, 8.9. Found: C, 59.2; H, 8.8.

(Z)-1-Hexyl-2-butyltelluro-4-phenyl-1-buten-3-yne (**3e**): IR (film)/cm^{-1} 3064, 2958, 2927, 2872, 2856, 2318, 1667, 1594, 1487, 1464, 1442, 1378, 688; δ_H ($CDCl_3$) 7.53–7.29 (m, 5H), 6.45 (t, *J* = 7.2 Hz, 1H), 3.01 (t, *J* = 7.6 Hz, 2H), 2.17–2.10 (m, 2H), 1.89–1.81 (m, 2H), 1.47–1.19 (m, 10H), 0.92–0.82 (m, 6H); Anal. Calcd for $C_{20}H_{28}Te$: C, 60.6; H, 7.1. Found: C, 60.4; H, 6.9.

(Z)-1-Hexyl-2-butyltelluro-5-methoxy-1-penten-3-yne (**3f**): IR (film)/cm^{-1} 2956, 2925, 2871, 2855, 2202, 1463, 1377, 1353, 1186, 1098, 786; δ_H ($CDCl_3$) 6.38 (t, *J* = 7.2 Hz, 1H), 4.29 (s, 2H), 3.39 (s, 3H), 2.93 (t, *J* = 7.2 Hz, 2H), 2.15–2.04 (m, 2H), 1.86–1.77 (m, 2H), 1.45–1.18 (m, 10H), 0.94–0.83 (m, 6H); Anal. Calcd for $C_{16}H_{28}OTe$: C, 52.8; H, 7.7. Found: C, 52.45; H, 7.6.

(Z)-1-Butyl-2-phenyltelluro-5-methoxy-1-penten-3-yne (**3g**): IR (film)/cm^{-1} 3056, 3024, 2956, 2870, 2857, 2139, 1597, 1572, 1487, 1442, 1180, 1026, 754, 691; δ_H ($CDCl_3$) 7.38–7.24 (m, 5H), 6.43 (t, *J* = 7.2 Hz, 1H), 4.20 (s, 2H), 3.42 (s, 3H), 2.25–2.17 (m, 2H), 1.47–1.34 (m, 4H), 0.94 (t, *J* = 7.2 Hz, 3H); Anal. Calcd for $C_{16}H_{20}OTe$: C, 53.9; H, 5.6. Found: C, 53.7; H, 5.5.

(Z)-1-Phenyl-2-butyltelluro-1-octen-3-yne (**3h**): IR (film)/cm^{-1} 3065, 2923, 2818, 2317, 1599, 1574, 1473, 1371, 732, 691; δ_H ($CDCl_3$) 7.54–7.26 (m, 6H), 2.90 (t, *J* = 7.2 Hz, 2H), 2.49 (t, *J* = 7.6 Hz, 2H), 1.88–1.80 (m, 2H), 1.47–1.21 (m, 6H), 0.95–0.84 (m, 6H); Anal. Calcd for $C_{18}H_{24}Te$: C, 58.7; H, 6.5. Found: C, 58.5; H, 6.3.

(Z)-1,4-Diphenyl-2-butyltelluro-1-buten-3-yne (**3i**): IR (film)/cm^{-1} 3056, 3024, 2957, 2925, 2194, 1596, 1488, 1440, 754, 689; δ_H ($CDCl_3$) 7.53–7.23 (m, 10H), 7.17 (s, 1H), 3.08 (t, *J* = 7.6 Hz, 2H), 1.90–1.85 (m, 2H), 1.42–1.36 (m, 2H), 0.89 (t, *J* = 7.2 Hz, 3H); Anal. Calcd for $C_{20}H_{20}Te$: C, 61.9; H, 5.2. Found: C, 61.6; H, 5.0.

Synthesis of (E)-1,4-diphenyl-1-buten-3-yne (**4**): To a solution of (*Z*)-1,4-diphenyl-2-butyltelluro-1-buten-3-yne (**3i**) (1.0 mmol) in THF (5.0 ml) was added BuLi (1.6 M hexane solution, 1.1 mmol) at –78 °C. After stirring for 1 h, the mixture was hydrolysed 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 (hexane) and recrystallised (EtOH) to afford enyne **4** (0.168g, 82%); M.p. 96–97 °C (lit.[16] M.p. 96–97 °C); δ_H ($CDCl_3$) 7.67–7.11 (m, 10H), 7.01 (d, *J* = 16 Hz, 1H), 6.30 (d, *J* = 16 Hz, 1H).

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