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Synthesis of 1,3-enynes via Suzuki-type reaction of vinylic tellurides and potassium alkynyltrifluoroborate salts

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Abstract—The palladium-catalyzed cross-coupling reaction between potassium alkynyltrifluoroborate salts and vinylic tellurides proceeds readily to afford 1,3-enynes with moderate to good yields. © 2004 Elsevier Ltd. All rights reserved.

The interest for chemistry of organotellurium compounds has increased in the last 10 years, being the subject of many reviews¹ as well as books.² Among several classes of tellurium compounds, vinylic tellurides are one of the most useful. Several methods have been developed for their preparation,^{1,2} and among them, one of the most important is the hydrotelluration reaction of alkynes,³ which provide exclusively the (Z)-vinylic telluride. This kind of tellurium compound can be transmetallated with many organometallic reagents to generate the corresponding (Z)-vinyl organometallic with retention of the double bond geometry, which can react with several electrophiles like carbonyl compounds,⁴ enones⁵ and epoxides.⁶

Palladium-catalyzed cross-coupling reaction of vinylic tellurides with terminal alkynes was previously described.^{7,8} The symmetrical diorganotellurium dichlorides have also been used in cross-coupling reactions with organostannanes⁹ and iodonium salts.¹⁰

The Suzuki palladium-catalyzed cross-coupling reaction between arylboronic acids and aryl halides or triflates has proven to be a very popular and versatile method for forming carbon–carbon bonds.¹¹ An investigation

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of the palladium-catalyzed cross-coupling of diaryl and bis-vinyltellurium dichlorides with organoboronic acids has recently been reported.¹² However, to the best of our knowledge, organotrifluoroborates, still in their infancy as coupling reagents, have never been partnered with organotellurides in Suzuki-type reactions.

Herein we report an efficient protocol for the synthesis of 1,3-enynes from the potassium alkynyltrifluoroborate salts¹³ and vinylic tellurides¹⁴ as a useful alternative to the widely used organic halides. Our initial studies of this process focused on developing an optimum set of reaction conditions for the palladium-catalyzed

Table 1. Study of catalyst effect on cross-coupling reaction



Entry	Catalysts	Isolated yield (%)			
1	PdCl ₂	53			
2	$Pd(PPh_3)_4$	16			
3	Pd(OAc) ₂	55			
4	$Pd(acac)_2$	77			
5	Pd(dba) ₃	40			
6	[Pd(allyl)Cl] ₂	68			
7	PdCl ₂ (C ₆ H ₅ CN) ₂	66			

Keywords: 1,3-Enynes; Suzuki; Vinylic tellurides; Potassium alkynyl-trifluoroborate salts.

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coupling of potassium alkynyltrifluoroborate salts and vinylic tellurides as electrophilic partners. The reaction was optimized using potassium (phenylacetylene)trifluoroborate and vinylic telluride as standard substrates (Table 1). The cross-coupling in all studied reactions cases were performed in the presence of 3 equiv of base. Bases such as Cs_2CO_3 (39%), NaOH (35%), KOBu-*t* (34%) and KF (34%) led to similar yields. K_2CO_3 improved the yield to 49%. We have found that amine bases such as Et_3N



Table 2. Cross-coupling reaction of vinylic tellurides

Table 3. Cross-coupling of vinylic telluride with different potassium alkynyltrifluoroborate salts

(77%) in dry MeOH provided the best result in the crosscoupling reaction between potassium alkynyltrifluoroborate salts and vinylic tellurides.

Solvents such as THF (38%), 1,4-dioxane (31%), DME (31%), toluene (18%), isopropanol (37%) were also considered. Among the solvents tested, MeOH (77%) proved to be far the most effective.

The use of $Pd(acac)_2$ with 3 equiv of Et_3N in MeOH was employed to study the catalyst loading. These results indicate that the use of 15 mol % of $Pd(acac)_2$ produces the best yield.

Having established the viability of the presented methodology, general applicability as well as the reactivity of various potassium alkynyltrifluoroborate salts¹³ and vinylic tellurides were also tested (Table 2). To this end we have prepared a series of vinylic tellurides by hydrotelluration of alkynes with lithium butyl tellurolate generated by reaction of *n*-butyllithium with elemental tellurium.¹⁴

Although the method for cross-coupling proved to be general to prepare 1,3-enynes, no coupling occurred with some organotelluride compounds (Table 1, entries **5** and **6**). A probable explanation would be the suggested coordination of the nitrogen and tellurium atoms with the palladium forming a stable six-membered ring complex.¹⁵

In an attempt to broaden the scope of the methodology, the possibility of performing the reaction with other potassium alkynyltrifluoroborate salts were also investigated (Table 3). All compounds have had their structure confirmed by ¹H and ¹³C NMR, IR and mass analysis.¹⁶ The stereochemical outcome of the reaction shows that it proceeds in a stereoconservative way, resulting in only the (Z)-enyne. The stereochemistry was established by measuring the coupling constants of the vinylic hydrogens, showing a *cis* (J = 11.45 Hz) relationship between them.

In summary, we have demonstrated here a new transformation leading to the synthesis of 1,3-enynes. One feature of this protocol was the tolerance of a variety of functional groups such OH, OCH₃, EtO₂C and conjugated C=C double bond under the reaction conditions. No homocoupling products were observed, what is an advantage on comparison with the usual Suzuki reaction using organic halides. The use of potassium organotrifluoroborate salts, (Z)-vinylic tellurides and commercially Pd(II) catalyst makes this methodology useful and attractive for the synthesis of 1,3-enynes. Further studies of this methodology and the mechanism reaction are currently ongoing in our laboratory and will be reported in due course.

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- 16. Suzuki-type reaction

Representative experimental procedure (3a): To a twonecked 25 mL round-bottomed flask under N₂ atmosphere containing Pd(acac)₂ (0.045 g, 15 mol %), CuI (0,060 g, 30 mol %), Et₃N (0.5 mL) and dry methanol (8 mL) was added the vinylic telluride 1a (0,287 g, 1.0 mmol) and the potassium (1-phenylethynyl)trifluoroborate 2a (0,229 g, 1.1 mmol). The solution was heated at reflux for 8 h. After this time the mixture was cooled and 10 mL of brine was added to the flask. The resulting solution was then extracted with diethyl ether; the combined organic layers were dried over MgSO₄. After filtering off the solid the solvent was removed under reduced pressure to afford a brown oil. This oil was purified by flash chromatography silica gel (elution with 5% ethylacetate/hexane) to provide the product **3a** as a yellow oil in 77% yield (0.157 g). ¹H NMR (300 MHz, CDCl₃) δ 7.93–7.91 (m, 2H), 7.53–7.27 (m, 8H), 6.69 (d, J = 11.9 Hz; 1H), 5.91 (d, J = 11.9 Hz; 1H); ¹³ \tilde{C} NMR (75 MHz, CDCl₃) δ 138.6, 136.5, 131.5, 128.72, 128.49, 128.37, 128.33, 128.25, 126.26, 107.34, 95.82, 88.22. IR (neat): 729.27, 1264.96, 1426.52, 2305.50, 2986.40, 3054.73 cm⁻¹. CG/MS: *m/z* (relative, %) 204 $(100) [M^+], 203 (82) [M-1]^+, 101 (26), 77(9), 50(13).$

Compound **3b**: ¹H NMR (300 MHz, CDCl₃) δ 7.46–7.40 (m, 2H); 7.34–7.29 (m, 3H); 6.14 (dt, J = 10.9 Hz–6.40 Hz;

1H); 5.81 (dt, J = 10.90-1.44 Hz; 1H); 4.49 (d, J = 5.53 Hz; 2H); 1.94 (s, 1H). ¹³C NMR (75 MHz, CDCl₃) & 141.29, 131.44, 128.48, 128.37, 122.93, 110.63, 95.25, 84.87, 61.09. IR (neat): 1025, 1608, 2349, 3042, 3398 cm⁻¹. CG/MS: *m*/*z* (relative, %) 158 (42) [M⁺], 129 (100), 122 (38), 115 (71). Compound 3c: ¹H NMR (300 MHz, CDCl₃) δ 7.52–7.48 (m, 2H); 7.39–7.35 (m, 3H); 5.66–5.62 (m, 2H); 4.29 (s, 1H); 1.88 (b, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 130.64, 130.16, 127.48. 127.32, 121.70, 119.49, 89.90, 85.91, 64.38. IR (neat): 1051, 1613, 2205, 3056, 3359 cm⁻¹. CG/ MS: *m*/*z* (relative, %) 158 (83) [M⁺], 159 (10) [M+1]⁺, 127 (100).Compound **3d**: ¹H NMR (300 MHz, CDCl₃) δ 7.42–7.24 (m, 5H); 6.20 (d, J = 11.89 Hz; 1H); 6.00–5.96 (m, 1H); 5.51 (d, J = 11.93 Hz; 1H); 2.72–2.70 (m, 2H); 2.19–2.18 (m, 2H); 1.72–1.57 (m, 4H). ¹³C NMR (75 MHz, CDCl₃) δ 142.68, 137.24, 133.59, 130.98, 128.29, 127.89, 123.91, 103.42, 94.01, 89.20, 27.00, 26.17, 23.30, 22.20. IR (neat): 1596, 1712, 2196, 2939, 3056 cm^{-1} . CG/MS: *m/z* (relative, %) 208 (38) [M⁺], 180 (93), 165 (100), 127 (12). Compound 3g: ¹H NMR (300 MHz, CDCl₃) δ 7.46–7.41 (m, 2H); 7.33-7.26 (m, 3H); 6.09 (d, J = 11.85 Hz; 1H); 5.73 (d, J = 11.87 Hz; 1H); 3.00 (s, 1H); 1.79–1.36 (m, 10H). ¹³C NMR (75 MHz, CDCl₃) δ 138.96, 131.47, 128.75, 128.66, 125.16, 121.09, 97.38, 79.87, 55.11, 33.10, 24.88, 21.59. IR (neat): 1451, 1595, 2932, 3046, 3374 cm⁻ CG/MS: m/z (relative, %) 193 (5), 107 (100), 77 (18), 69 (8). Compound **3h**: ¹H NMR (300 MHz, DMSO– d_6) δ 7.47– 7.40 (m, 5H); 6.14 (t, J = 6.33 Hz; 1H); 5.25 (t, J = 5.94 Hz; 1H); 4.91 (t, J = 5.53 Hz; 1H); 4.27 (t, J = 5.86 Hz; 2H); 4.03 (d, J = 5.38 Hz; 2H). ¹³C NMR (75 MHz, DMSO-d₆) δ 136.72, 131.23, 128.75, 128.69, 123.16, 122.47, 94.63, 85.99, 63.31, 59.47. IR (neat): 1182, 1626, 2350, 2958, 3058, 33,328 cm⁻¹. CG/MS: *m/z* (relative, %) 188 (4) [M^+], 86 (15), 77 (100). Compound **3i**: ¹H NMR (300 MHz, CDCl₃) δ 7.55–7.52 (m, 2H); 7.36–7.26 (m, 3H); 6.02 (s, 1H); 4.23 (q, J = 7.13 Hz; 2H); 2.36 (t, J = 7.53 Hz; 2H); 1.67 (q, J = 7.2 Hz; 2H); 1.38–1.25 (m, 7H); 0.91 (t, J = 6.78 Hz; 3H). ¹³C NMR (75 MHz, CDCl₃) δ 165.27, 139.60, 132.04, 128.97, 128.34, 123.75, 122.88, 100.68, 87.73, 60.13, 38.84, 31.06, 27.76, 22.44, 14.36, 13.98. IR (neat): 1612, 1707, 2200, 2949, 3054 cm⁻¹. CG/MS: *m/z* (relative, %) 270 (16) $[M^+]$, 213 (34), 199 (48), 185 (100), 141 (60). Compound 3j: ¹H NMR (300 MHz, CDCl₃) δ 7.76–7.73 (m, 2H); 7.63–7.5 (m, 4H); 7.44–7.32 (m, 9H); 6.58 (s, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 136.69, 133.36, 131.76, 131.62, 128.86, 128.75, 128.61, 128.53, 128.44, 128.42, 127.98, 126.10, 125.87, 123.41, 123.09, 113.65, 89.00, 87.55. IR (KBr plate): 1546, 1594, 2179, 3045 cm⁻¹ Compound **3k**: ¹H NMR (300 MHz, CDCl₃) δ 7.87–7.85 (m, 2H); 7.35-7.20 (m, 3H); 6.53 (d, J = 11.9 Hz; 1H); 5.69(dt, J = 11.9-2.46 Hz; 1H); 2.42 (td, J = 7Hz-2.45 Hz; 2H); 1.64–1.28 (m, 12H); 0.88 (t, J = 7 Hz; 3H). ¹³C NMR (75 MHz, CDCl₃) δ 137.22, 136.70, 128.45, 128.13, 128.10, 108.21, 97.91, 79.20, 31.89, 29.27, 29.22, 29.05, 28.63, 22.70, 19.94, 14.13. IR (neat): 1694, 2199, 2931, 3022 cm⁻¹. CG/MS: *m/z* (relative, %) 240 (24) [M⁺], 183 (9), 169 (15), 155 (25), 141 (100). Compound 3I: ¹H NMR (300 MHz, CDCl₃) δ 8.15–8.12 (m, 2H); 7.41–7.28 (m, 3H); 6.68 (d, J = 12.00 Hz; 1H); 5.77 (dt, *J* = 12.00–2.03 Hz; 1H); 4.36 (d, *J* = 1.95 Hz; 2H); 3.47 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 139.52, 136.66, 129.01, 128.71, 126.31, 107.24, 92.21, 85.20, 61.03, 58.16. IR (neat): 1001, 1265, 1601, 2339, 2988 cm⁻¹. CG/MS: *m*/*z* (relative, %) 172 (51) [M⁺], 157 (30), 141 (63), 128 (100). Compound **3m**: ¹H NMR (300 MHz, CDCl₃) δ 7.89–7.86 (m, 2H); 7.36–7.21 (m, 3H); 6.53 (d, *J* = 11.80 Hz; 1H);

5.70 (d, $J = 11$.50 Hz;	1H); 1	1.31 (s,	9H).	^{13}C	NMR
(75 MI	Hz, CDC	Cl ₃) δ	137.16,	136.70	, 128.4	19,	128.08,
128.02	, 108.15,	105.49,	77.92,	30.73,	28.47.	IR	(neat):

1600, 2206, 2929, 2968, 3022 cm⁻¹. CG/MS: m/z (relative, %) 185 (15) [M-1]⁺, 184 (100) [M⁺], 169 (84), 154 (85), 127 (15).