Palladium-catalyzed cross-coupling between vinyl halides and *tert*-butyl carbazate: First general synthesis of the unusual *N*-Boc-*N*-alkenylhydrazines

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SUPPORTING INFORMATION

General considerations: All reactions were carried out under nitrogen atmosphere in a RR98030 12 place Carousel Reaction StationTM from Radleys Discovery Technologies, equipped with gas-tight threaded caps with a valve, cooling reflux head system, and digital temperature controller. DMF, dichloromethane and hexanes were dehydrated using the procedures described in D. Perrin *Purification of Laboratory Chemicals*, Pergamon Press Ltd. 1980, 2nd Ed. Pd₂(dba)₃ was purchased from Strem Chemical co. and used without further purification. All ligands used are commercially available from Strem Chemical co. or Aldrich Chemical co. and were used without further purification. Cs₂CO₃ was purchased from Aldrich Chemical co., stored in a flask purged with nitrogen and weighted in the air. *tert*-Butyl carbazate is commercially available from Acros Organics and was used without further purification. β-bromostyrene is commercially available from Aldrich Chemical co. and was used after being distilled. GC analysis were performed with a GC Agilent Technologies 6890N instrument. NMR spectra were recorded at 400, 300 or 200 MHz for ¹H and 100, 75 or 50 MHz for ¹³C, with tetramethylsilane as internal standard for ¹H and the residual solvent signals as standard for ¹³C. Chemical shifts are given in ppm. Mass spectra were obtained by EI (70 eV) or FAB-LR.

Preparation of bromoalkenes 2b, 2c and 2i:

To the stirred suspension of 24 mmol of $\text{Cp}_2\text{Zr(H)Cl}$ in 30 mL THF under N_2 atmosphere, and in a flask protected from the sun light, were added dropwise 20 mmol of the corresponding alkyne dissolved in 10 mL of THF. The mixture was stirred at room temperature for 3 hours. The solution was cooled to 0°C and then 20 mmol of bromine were added dropwise. After stirring for 10 min, the reaction was quenched with 20 mL of saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution. The organics were extracted with diethyl ether (2x30mL), the organic layers were combined, washed with brine and dried over Na_2SO_4 . Removal of the solvent under reduced pressure afforded the bromoalkenes as nearly pure materials, which were further purified by filtration through a short chromatographic column.

Preparation of bromoalkenes 2d, 2e, 2f and 2g: These bromoalkenes were prepared following the procedure described in S. Abbas, C. J. Hayes, S. Worden, *Tetrahedron Lett.* **2000**, 41, 3215-3219.

Preparation of bromoalkene 2h: This bromoalkene was prepared following the procedure described in E.-i Negishi, M. Hata, C. Xu, *Org. Lett.* **2000**, 2, 3687-3689.

Preparation of chlorodienes 2j and 2k: These chlorodienes were prepared according to the procedure described in J. Barluenga, P. Moriel, F. Aznar, C. Valdés, *Adv. Synth. Cat.* **2006**, 348, 347-353.

General procedure for the cross-coupling of *tert*-butyl carbazate 1 with alkenyl halides 2a-j. A carousel reaction tube under nitrogen atmosphere was charged with JOHNPHOS (0.08 mmol, 8 mol%), tris(dibenzylideneacetone)dipalladium (0) (0.02 mmol, 4 mol% Pd), cesium carbonate (1.4 mmol), *tert*-butyl carbazate **1** (1.2 mmol) and DMF (2 mL). After stirring the mixture for a minute, the haloalkene **2a-j** (1 mmol) was added. The system was heated at 110°C (90°C for **2d**) with stirring until the starting halide had been completely consumed as judged by GC analysis. The mixture was

allowed to cool to room temperature, taken up in dry dichloromethane (15 mL), and filtered through Celite. The solvents were removed under reduced pressure. The residue was purified by flash chromatography.

Using this procedure were prepared the following compounds:

***N*-tert-butoxycarbonyl-*N*-[(*E*)-2-phenylethenyl]hydrazine (3a):**

HRMS (EI): calcd. for $C_{13}H_{18}N_2O_2$: 234.1368; found: 234.1369; 1H NMR ($CDCl_3$, 200 MHz): δ = 1.58 (s, 9H), 4.16 (br. s, 2H), 6.39 (d, $^3J_{trans}$ = 14.1 Hz, 1H), 7.12–7.21 (m, 1H), 7.26–7.33 (m, 5H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 28.2 (CH_3), 82.4 (C), 109.2 (CH), 125.3 (CH), 125.72 (CH), 127.2 (CH), 128.5 (CH), 137.0 (C), 153.2 (C).

***N*-tert-butoxycarbonyl-*N*-[(*E*)-2-(*p*-tolyl)ethenyl]hydrazine (3b):**

HRMS (EI): calcd. for $C_{14}H_{20}N_2O_2$: 248.1519; found: 248.1526; 1H NMR ($CDCl_3$, 300 MHz): δ = 1.59 (s, 9H), 2.37 (s, 3H), 3.80 (br. s, 2H), 6.35 (d, $^3J_{trans}$ = 14.1 Hz, 1H), 7.00–7.26 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): 21.0 (CH_3), 28.2 (CH_3), 82.3 (C), 109.2 (CH), 125.2 (CH), 126.5 (CH), 129.0 (CH), 134.1 (C), 135.4 (C), 153.2 (C).

***N*-tert-butoxycarbonyl-*N*-[(*E*)-2-(*p*-methoxyphenyl)ethenyl]hydrazine (3c):**

HRMS (EI): calcd. for $C_{14}H_{20}N_2O_3$: 264.1468; found: 264.1463; 1H NMR ($CDCl_3$, 300 MHz): δ = 1.59 (s, 9H), 3.83 (br. s, 5H), 6.37 (d, $^3J_{trans}$ = 14.0 Hz, 1H), 6.88 (d, 3J = 8.7 Hz, 2H), 7.27–7.31 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 28.2 (CH_3), 55.2 (CH_3), 82.3 (C), 109.0 (CH), 114.0 (CH), 125.7 (CH), 126.4 (CH), 129.7 (C), 153.3 (C), 157.9 (C).

***N*-tert-butoxycarbonyl-*N*-[(*E*)-2-(*p*-methoxycarbonylphenyl)ethenyl]hydrazine (3d):**

HRMS (EI): calcd. for C₁₅H₂₀N₂O₄: 292.1418; found: 292.1414; ¹H NMR (CDCl₃, 300 MHz): δ = 1.55 (s, 9H), 3.88 (br. s, 5H), 6.38 (d, ³J_{trans} = 14.2 Hz, 1H), 7.25–7.34 (m, 3H), 7.92 (d, ³J = 8.2 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz): δ = 28.1 (CH₃), 51.8 (CH₃), 82.9 (C), 108.4 (CH), 124.9 (CH), 126.8 (C), 126.9 (CH), 129.9 (CH), 142.0 (C), 153.0 (C), 166.9 (C).

***N*-tert-butoxycarbonyl-*N*-[(*E*)-2-(*p*-chlorophenyl)ethenyl]hydrazine (3e):**

HRMS (FAB) (M+1)⁺: calcd. for C₁₃H₁₈ClN₂O₂: 269.1057; found: 269.1064; ¹H NMR (CDCl₃, 400 MHz): δ = 1.56 (s, 9H), 3.98 (br. s, 2H), 6.33 (d, ³J_{trans} = 14.1 Hz, 1H), 7.24–7.32 (m, 5H); ¹³C NMR (CDCl₃, 100 MHz): δ = 28.3 (CH₃), 82.8 (C), 108.2 (CH), 126.6 (CH), 127.8 (C), 128.7 (CH), 131.2 (C), 135.8 (CH), 153.3 (C).

***N*-tert-butoxycarbonyl-*N*-[(*E*)-2-(*o*-bromophenyl)ethenyl]hydrazine (3f):**

HRMS (EI): calcd. for C₁₃H₁₇BrN₂O₂: 312.0468; found: 312.0456; ¹H NMR (CDCl₃, 300 MHz): δ = 1.55 (s, 9H), 4.16 (br. s, 2H), 6.66 (d, ³J_{trans} = 14.1 Hz, 1H), 7.01 (t, ³J = 7.6 Hz, 1H), 7.23 (t, ³J = 7.6 Hz, 1H), 7.40–7.43 (m, 2H), 7.53 (d, ³J = 8.0 Hz, 1H); ¹³C NMR (CDCl₃, 75 MHz): δ = 28.2 (CH₃), 82.7 (C), 108.4 (CH), 123.2 (C), 125.7 (CH), 127.1 (CH), 127.3 (CH), 129.4 (CH), 132.9 (CH), 137.0 (C), 153.1 (C).

***N*-tert-butoxycarbonyl-*N*-[(1*E*,3*E*)-4-phenyl-1,3-butadienyl]hydrazine (3g):**

HRMS (EI): calcd. for C₁₅H₂₀N₂O₂: 260.1519; found: 260.1512; ¹H NMR (CDCl₃, 300 MHz): δ = 1.54 (s, 9H), 3.99 (br. s, 2H), 6.25 (dd, ³J_{trans} = 13.4 Hz, ³J = 10.8 Hz, 1H), 6.46 (d, ³J_{trans} = 15.7 Hz, 1H), 6.81 (dd, ³J_{trans} = 15.7 Hz, ³J = 10.8 Hz, 1H), 7.18 (d, ³J = 7.1 Hz, 1H), 7.27–7.39 (m, 5H); ¹³C NMR (CDCl₃, 75 MHz): δ = 30.7 (CH₃), 85.1 (C), 113.0 (CH), 128.2 (CH), 129.0 (CH), 129.8 (CH), 131.0 (2xCH), 133.1 (CH), 140.4 (C), 155.4 (C).

***N*-tert-butoxycarbonyl-*N*-[(*E*)-1-(dodec-1-en-3-ynyl)]hydrazine (3h):**

HRMS (EI): calcd. for C₁₇H₃₀N₂O₂: 294.2302; found: 294.2298; ¹H NMR (CDCl₃, 400 MHz): δ = 0.88 (t, ³J = 6.8 Hz, 3H), 1.25–1.35 (m, 9H), 1.36–1.40 (m, 1H), 1.50 (s, 11H), 2.30 (t, ³J = 7.0 Hz, 2H), 4.00 (br. s, 2H), 5.42 (dt, ³J = 13.7 Hz, ⁵J = 2.3 Hz, 1H), 7.19 (d, ³J = 13.7 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ = 14.0 (CH₃), 19.5 (CH₂), 22.6 (CH₂), 28.1 (CH₃), 28.8 (CH₂), 28.9 (CH₂), 29.0 (CH₂), 29.1 (CH₂), 31.7 (CH₂), 77.7 (C), 82.7 (C), 88.7 (CH), 89.2 (C), 136.4 (CH), 152.5 (C).

***N*-tert-butoxycarbonyl-*N*-[(*E*)-1-hexenyl]hydrazine (3i):**

HRMS (EI): calcd. for C₁₁H₂₂N₂O₂: 214.1681; found: 214.1685; ¹H NMR (CDCl₃, 300 MHz): δ = 0.85–0.90 (m, 3H), 1.32–1.33 (m, 4H), 1.48 (s, 9H), 2.00–2.03 (m, 2H), 3.98 (br. s, 2H), 5.28 (dt, ³J_{trans} = 14.1 Hz, ³J = 7.3 Hz, 1H), 6.65–6.70 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz): δ = 13.8 (CH₃), 22.1 (CH₂), 28.2 (CH₃), 29.4 (CH₂), 32.5 (CH₂), 81.6 (C), 109.4 (CH), 126.5 (CH), 153.2 (C).

***N*-tert-butoxycarbonyl-*N*-[(1*E*,3*E*)-deca-1,3-dienyl]hydrazine (3j):**

HRMS (EI): calcd. for C₁₅H₂₈N₂O₂: 268.2145; found: 268.2144; ¹H NMR (CDCl₃, 400 MHz): δ = 0.88 (t, ³*J* = 6.7 Hz, 3H), 1.26-1.38 (m, 8H), 1.50 (s, 9H), 2.06 (c, ³*J* = 7.0 Hz, 2H), 3.97 (br. s, 2H), 5.57 (dt, ³*J*_{trans} = 13.8 Hz, ³*J* = 7.0 Hz, 1H), 5.97-6.06 (m, 2H), 6.78-7.07 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz): 14.0 (CH₃), 22.5 (CH₂), 28.1 (CH₃), 28.7 (CH₂), 29.4 (CH₂), 31.6 (CH₂), 32.7 (CH₂), 82.0 (C), 110.4 (CH), 127.6 (CH), 127.9 (CH), 131.2 (CH), 153.2 (C).

***N*-tert-butoxycarbonyl-*N*-[(1*E*,3*E*)-4-(4-chlorophenyl)buta-1,3-dienyl]hydrazine (3k):**

HRMS (EI): calcd. for C₁₅H₁₉ClN₂O₂: 294.1129; found: 294.1125; ¹H NMR (CDCl₃, 400 MHz): δ = 1.52 (s, 9H), 4.09 (br. s, 2H), 6.21 (dd, ³*J*_{trans} = 13.2 Hz, ³*J*_{cis} = 11.0 Hz, 1H), 6.36 (d, ³*J*_{trans} = 15.5 Hz, 1H), 6.74 (dd, ³*J*_{trans} = 15.5 Hz, ³*J*_{cis} = 11.0 Hz, 1H), 7.21-7.28 (m, 5H); ¹³C NMR (CDCl₃, 100 MHz): 28.1 (CH₃), 82.6 (C), 110.1 (CH), 126.8 (CH), 126.9 (CH), 128.0 (CH), 128.5 (CH), 131.1 (CH), 131.8 (C), 136.5 (C), 153.0 (C).

General procedure for the homocoupling of alkenyl bromides 2a, 2b, 2d and 2g. A carousel reaction tube under nitrogen atmosphere was charged with Verkade's proazaphosphatane **9** (0.08 mmol, 8 mol%), tris(dibenzylideneacetone)dipalladium (0) (0.02 mmol, 4 mol% Pd), cesium carbonate (0.7 mmol), and DMF (1 mL). After stirring the mixture for a minute, the bromoalkene **2a**, **2b**, **2d** and **2g** (1 mmol) was added. The system was heated at 110 °C (90 °C for **2d**) with stirring until the starting halide had been completely consumed as judged by GC analysis. The mixture was allowed to cool to room temperature, taken up in dry hexanes (15 mL), and filtered through Celite. The solvents were evaporated under reduced pressure. The residue was purified by flash chromatography.

Using this procedure were prepared the following compounds:

(1*E*,3*E*)-1,4-diphenylbuta-1,3-diene (4a):

HRMS (EI): calcd. for C₁₆H₁₄: 206.1096; found: 206.1097; ¹H NMR (CDCl₃, 300 MHz): δ = 6.70 (m, 2H), 6.98 (m, 2H), 7.23 (m, 2H), 7.29 (m, 4H), 7.37 (m, 4H); ¹³C NMR (CDCl₃, 75 MHz): δ = 126.3 (CH), 127.5 (CH), 128.6 (CH), 129.2 (CH), 132.7 (CH), 137.2 (C).

(1*E*,3*E*)-1,4-di-*p*-tolylbuta-1,3-diene (4b):

HRMS (EI): calcd. for C₁₈H₁₈: 234.1409; found: 234.1920; ¹H NMR (CDCl₃, 400 MHz): δ = 2.37 (s, 6H), 6.66–6.73 (m, 2H), 6.91–6.95 (m, 2H), 7.16 (d, ³*J* = 8.1 Hz, 4H), 7.36 (d, ³*J* = 8.1 Hz, 4H); ¹³C NMR (CDCl₃, 100 MHz): δ = 21.2 (CH₃), 126.2 (CH), 128.4 (CH), 129.3 (CH), 132.2 (CH), 134.6 (C), 137.3 (C).

(1*E*,3*E*)-1,4-di(*p*-methoxycarbonylphenyl)buta-1,3-diene (4d):

HRMS (EI): calcd. for C₂₀H₁₈O₄: 322.1199; found: 322.1196; ¹H NMR (CDCl₃, 300 MHz): δ = 3.92 (s, 6H), 6.72–6.80 (m, 2H), 7.01–7.11 (m, 2H), 7.50 (d, ³*J* = 8.5 Hz, 4H), 8.00 (d, ³*J* = 8.5 Hz, 4H); ¹³C NMR (CDCl₃, 100 MHz): δ = 52.0 (CH₃), 126.3 (CH), 129.1 (C), 130.0 (CH), 131.2 (CH), 133.1 (CH), 141.4 (C), 166.7 (C).

(1*E*,3*E*,5*E*,7*E*)-1,8-diphenylocta-1,3,5,7-tetraene (4g):

HRMS (EI): calcd. for C₂₀H₁₈: 258.1403; found: 258.1407; ¹H NMR (CDCl₃, 400 MHz): δ = 6.47-6.48 (m, 4H), 6.60 (d, ³J_{trans} = 15.5 Hz, 2H), 6.86-6.91 (m, 2H); 7.23 (t, ³J = 7.2 Hz, 2H), 7.33 (t, ³J = 7.2 Hz, 4H), 7.43 (d, ³J = 7.2 Hz, 4H); ¹³C NMR (CDCl₃, 100 MHz): δ = 126.3 (CH), 127.5 (CH), 128.6 (CH), 129.1 (CH), 132.6 (CH), 133.4 (CH), 137.3 (C).

¹H and ¹³C NMR spectra of all the compounds 3 and 4 prepared: