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A new type of palladium-catalysed aromatic cross-coupling combined with a Suzuki reaction: synthesis of selectively 2,3′-substituted 1,1′;2′,1″-terphenyl derivatives

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Dedicated to Prof. Renato Ugo in recognition of his outstanding contribution to catalysis and organometallic chemistry

Abstract

A one-pot catalytic synthesis of selectively substituted terphenyl derivatives is reported. The method is based on the combination of a new palladium- and norbornene-mediated aryl–aryl coupling of two molecules of an *ortho*-substituted aryl iodide with a Suzuki-type arylation. Under the reported conditions, the reaction follows a precisely ordered sequence of steps and the Suzuki coupling only occurs at the end of the sequence. While proposing a new pathway for C–C coupling, the process provides a simple and efficient tool for preparing an interesting class of *ortho*-substituted terphenyls catalytically and with satisfactory yields.

Keywords: Catalysis; Palladium; Palladacycles; Aryl coupling; Terphenyls

1. Introduction

In the course of our studies aimed at working out new selective procedures for the formation of C–C bonds through palladacycle-assisted reactions [1–3], we observed that aryl iodides reacted with norbornene in the presence of a palladium catalyst to afford methanotriphenylene derivatives [4]. Further studies performed stoichiometrically at room temperature in *N*,*N*-dimethylformamide (DMF) as solvent allowed us to established that the reaction occurred according to Scheme 1, which involves the formation of a palladacycle [5].

Complex **1** [6–9] readily forms palladacycle **2** [10,11] by electrophilic aromatic substitution [12]. The latter reacts with a molecule of iodobenzene at the norbornyl site (way a) and the resulting arylpalladium species **3** undergoes cyclisation in the presence of a base (K_2CO_3) to form the organic compound **4**. This behaviour was proved to be general for unsubstituted (R = H) as well as *meta*- and *para*-substituted complexes of type **1** [5]. By contrast, *ortho*-substituted complexes **1** behave in a dramatically different way (way b), with the aryl iodide attacking the aryl site of the palladacycle to give **5**. Formation of **6** follows through norbornene expulsion for steric reasons, as previously observed with similar complexes bearing two alkyl groups in *ortho*-position [5,13].

Since in the latter case, a new biphenylylpalladium complex (**6**) is formed stoichiometrically, we

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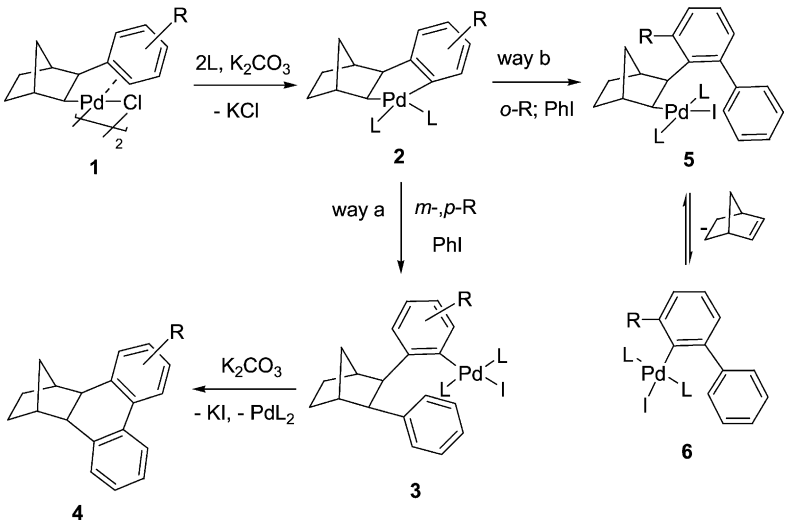


Scheme 1.

wondered whether a reaction leading to terphenyl derivatives could be obtained by coupling complex **6** with an arylboronic acid according to the well-known Suzuki reaction [14]. This reaction would make available the palladium(0) necessary for the generation of **1** from iodoarenes and norbornene, thus rendering the catalytic process as shown by us in other cases [15–18].

We now report that such a reaction has been successfully achieved in spite of the ability of the arylboronic acid to react with other palladium species present in the reaction medium [14,19].

2. Experimental

Starting materials were commercially available products and were used without further purification. *ortho*-R-substituted aryl iodides (R = *n*-Pr [20], *n*-Bu [21], *t*-Bu [22], NHMe [23], $MeCO_2$ [24]) were prepared by standard procedures. DMF was dried and stored over 4 Å molecular sieves under nitrogen. Identification of known compounds **8** (R = Me, OMe [25], Et, *i*-Pr, *n*-Bu [16], *t*-Bu [5]) was obtained by comparison with the data reported in the literature. Reactions were carried out under an atmosphere of nitrogen using standard Schlenk techniques. Flash chromatography was performed on silica gel 60 (Merck 70–230 mesh) and analytical TLC on pre-coated silica gel plates (Merck 60 F254, 0.25 mm). GC analyses were carried out with a Carlo Erba HRGC 5300 instrument equipped with a 30 m OV-101 capillary column and a Hewlett-Packard 3394 integrator. E.I. mass spectra (*m/z*, relative intensity (%)) were performed with a Finnigan Mat SSQ 710 instrument at 70 eV ionisation voltage. ^{1}H NMR (300.13 MHz) and ^{13}C NMR (75.41 MHz) spectra were recorded on Bruker AC300 and Bruker AVANCE 300 spectrometers in $CDCl_3$ using the solvent as internal reference (7.26 and 77.00 ppm, respectively, for ^{1}H and ^{13}C). The reported assignments are based on decoupling and 2D experiments: asterisks indicates interchangeable assignments. Elemental analyses were performed with a Carlo Erba EA 1108-Elemental Analyser. Satisfactory elemental analyses were obtained for all compounds: C ± 0.3, H ± 0.3.

2.1. Reaction of ortho-substituted aryl halides with arylboronic acids: general procedure

A DMF solution (8 ml) containing the aryl halide (1.6 mmol) and 2-norbornene (76 mg, 0.8 mmol) was introduced under nitrogen into a Schlenk-type flask containing $Pd(OAc)_2$ (1.8 mg, 0.008 mmol) and K_2CO_3 (420 mg, 3.2 mmol). The arylboronic acid (0.96 mmol) was then added as a solid. The resulting mixture was heated under stirring at 105 °C for 90 h. After cooling to room temperature the mixture was

diluted with CH_2Cl_2 and extracted three times with a 5% solution of H_2SO_4. The organic layer was washed with water and dried over anhydrous Na_2SO_4. The solvent was evaporated and the products were isolated by flash chromatography using hexane or mixtures of hexane–EtOAc as eluent. The yields of by-products were determined by GC analyses.

2.2. 2,3′-Dimethyl-1,1′;2′,1″-terphenyl (7) (R = Me; R′ = H)

Yield: 88%, conversion 100%. ^{1}H NMR: δ 7.32−7.28 (2H, m, H4′, H5′), 7.19−7.08 (4H, m, H3″, H5″, H4″, H6′), 7.06−6.98 (4H, m, H6, H3, H2″, H6″), 6.97−6.93 (2H, m, H4, H5), 2.18 (3H, s, CH_3(C3′)), 2.04 (3H, s, CH_3(C2)); ^{13}C NMR: δ 141.52 (C1), 141.24 (C2′), 140.90 (C1′), 140.08 (C1″), 136.29 (C3′), 135.49 (C2), 130.51 (C4), 130.42 (br s, C2″*), 129.34 (C3), 129.10 (br s, C6″*), 129.00 (C4′), 127.49 (C6′), 127.44 (br s, C3″**), 127.31 (br s, C5″**), 126.74 (C5′), 126.58 (C6), 126.21 (C4″), 124.60 (C5), 21.18 (CH_3(C3′)), 20.36 (CH_3(C2)); MS: 258 (100), 243 (67), 228 (34), 165 (37), 120 (23).

2.3. 2,3′-Diethyl-1,1′;2′,1″-terphenyl (7) (R = Et; R′ = H)

Yield: 77%, conversion 100%. ^{1}H NMR: δ 7.40−7.33 (2H, m), 7.19−6.95 (10H, m), 2.51 (2H, q, J = 7.5 Hz), 2.48−2.25 (2H, m), 1.11, 1.07 (6H, two partly overlapping t, J = 7.5 Hz); ^{13}C NMR: δ 142.29, 141.39, 141.14, 140.94, 140.45, 139.77, 130.57, 129.17, 127.42, 127.36, 127.27, 127.21, 127.13, 126.77, 126.75, 126.13, 124.36, 26.84, 26.08, 15.54, 15.07; MS: 286 (100), 257 (80), 241 (37), 229 (29), 165 (22).

2.4. 2,3′-Di-i-propyl-1,1′;2′,1″-terphenyl (7) (R = i-Pr; R′ = H)

Yield: 93%, conversion 98%. ^{1}H NMR: δ 7.43 (1H, dd, J = 7.8, 1.6 Hz, H4′), 7.38 (1H, dd, J = 7.8, 7.2 Hz, H5′), 7.19−7.01 (7H, m, H3″, H4″, H5″, H3, H6, H6′, H6″*), 7.01−6.91 (3H, m, H2″*, H4, H5), 2.86 (1H, hept., J = 6.8 Hz, CH(C3′)), 2.76 (1H, hept., J = 6.8 Hz, (CH(C2)), 1.21 (3H, d, J = 6.8 Hz, CH_3CH(C3′)), 1.15 (3H, d, J = 6.8 Hz, CH_3CH(C3′)), 1.07 (3H, d, J = 6.8 Hz, CH_3CH(C2)), 1.00 (3H, d, J = 6.8 Hz, CH_3CH(C2)); ^{13}C NMR: δ 146.92 (C3′), 146.14 (C2), 141.16 (C1′), 140.42 (C1), 139.88 (C2′), 139.80 (C1″), 130.65 (C4), 130.60 (C6″*), 129.56 (C2″*), 127.26 (C6′), 127.20 (C3″**), 127.13 (C5″**), 126.97 (C6), 126.82 (C5′), 126.13 (C4″), 124.67 (C3), 124.22 (C4′), 124.18 (C5), 29.96 (CH(C3′)), 29.84 (CH(C2)), 25.47 (CH_3CH(C2)), 24.39 (CH_3CH(C3′)), 24.16 (CH_3CH(C3′)), 22.49 (CH_3CH(C2)); MS: 314 (100), 299 (22), 271 (99), 257 (94), 242 (22), 241 (36), 239 (26), 229 (38).

2.5. 2,3′-Di-n-butyl-1,1′;2′,1″-terphenyl (7) (R = n-Bu; R′ = H)

Yield: 73%, conversion 93%. ^{1}H NMR: δ 7.33−7.28 (2H, m), 7.15−6.92 (10H, m), 2. 25−2.40 (2H, m), 2.40−2.18 (2H, m), 1.52−1.30 (4H, m), 1.29−1.11 (4H, m), 0.81, 0.77 (6H, 2 overlapping t, J = 7.2 Hz); ^{13}C NMR: δ 141.22, 141.15, 140.97, 140.60, 140.16, 139.81, 130.72, 130.67, 129.32, 128.00, 127.93, 127.45, 127.14, 127.04, 126.55, 126.53, 126.06, 124.31, 33.55, 33.37, 33.00, 32.81, 22.63, 22.52, 13.94, 13.81; MS: 342 (71), 299 (20), 285 (19), 243 (100), 229 (24), 165 (27), 91 (18).

2.6. 2,3′-Dimethoxy-1,1′;2′,1″-terphenyl (7) (R = OMe; R′ = H)

Yield: 82%, conversion 100%. ^{1}H NMR: δ 7.38 (1H, dd, J = 8.2, 7.6 Hz, H5′), 7.19−7.09 (6H, m, H4, H2″−H6″), 7.08 (1H, dd, J = 7.4, 1.8 Hz, H6), 7.04−6.98 (2H, m, H4′, H6′), 6.83 (1H, td, J = 7.4, 1.1 Hz, H5), 6.64 (1H, dd, J = 8.2, 0.8 Hz, H3), 3.78 (3H, s, CH_3O(C3′)), 3.44 (3H, s, CH_3O(C2)); ^{13}C NMR: δ 156.4 (q), 156.0 (q), 139.6 (q), 137.1 (q), 131.4 (C6), 130.6 (C2″, C6″), 130.4 (q), 128.3 (C4), 127.9 (C5′), 126.7 (C3″, C5″), 126.1 (C4″), 123.0 (C6′), 119.8 (C5), 110.1 (C3), 110.0 (C4′), 55.7 (CH_3O(C3′)), 54.9 (CH_3O(C2)); MS: 290 (100), 259 (29), 215 (55), 202 (42), 137 (42), 107 (58), 101 (60), 95 (43).

2.7. 2,3′-Dimethoxycarbonyl-1,1′;2′,1″-terphenyl (7) (R = CO_2Me; R′ = H)

Yield: 89%, conversion 100%. ^{1}H NMR: δ 7.83 (1H, dd, J = 7.5, 1.7 Hz, H4′), 7.72 (1H, dd, J = 7.7,

1.5 Hz, H3), 7.45 (1H, t, $J = 7.5$ Hz, H5′), 7.39 (1H, dd, $J = 7.6$, 1.7 Hz, H6′), 7.33 (1H, td, $J = 7.5$, 1.5 Hz, H5), 7.23 (1H, td, $J = 7.6$, 1.4 Hz, H4), 7.13−7.09 (3H, m, H3″, H4″, H5″), 7.07 (1H, dd, $J = 7.5$, 1.4 Hz, H6), 7.05−6.88 (2H, vbr s, H2″, H6″), 3.61 (3H, s, CH_3), 3.55 (3H, s, CH_3); ^{13}C NMR: δ 169.08 (q), 167.36 (q), 142.16 (q), 141.87 (q), 140.00 (q), 139.18 (q), 131.99 (C6′), 131.97 (q), 131.77 (C6), 130.98 (C5), 130.39 (q), 129.70 (C3), 129.38 (br s, C2″, C6″), 128.51 (C4′), 127.14 (C3″, C5″), 126.93 (C4), 126.75 (C5′), 126.57 (C4″), 51.84 (OCH_3), 51.80 (OCH_3); MS: 346 (15), 314 (51), 283 (55), 255 (100), 227 (41), 226 (73), 113 (27).

2.8. 2,3′-Di-n-butyl-4″-methyl-1,1′;2′,1″-terphenyl (7) (R = n-Bu; R′ = 4-Me)

Yield: 72%, conversion 91%. ^{1}H NMR: δ 7.32−7.28 (2H, m, H4′, H5′), 7.12−7.01 (3H, m, H6′, H6, H3), 7.00−6.95 (2H, m, H4, H5), 6.95−6.84 (4H, m, H3″, H5″, H2″, H6″), 2.55−2.39 (2H, m, CH_2(C3′)), 2.39−2.15 (5H, m, CH_2(C2), CH_3(C4″) at 2.24), 1.58−1.30 (4H, m, 2C$H_2$$CH_2CH_3$), 1.30−1.10 (4H, m, 2C$H_2$$CH_3$), 0.82, 0.72 (6H, two partly overlapping t, $J = 7.3$ Hz, 2CH_3); ^{13}C NMR: δ 141.44 (C1′), 141.24 (C2), 141.15 (C3′), 140.60 (C2′), 140.16 (C1), 136.72 (C1″), 135.36 (C4″), 130.68 (C4), 130.52 (C2″*), 129.14 (C6″*), 127.99 (C3), 127.87 (C4′), 127.86 (C3″**), 127.79 (C5″**), 127.48 (C6′), 126.44 (C6), 126.34 (C5′), 124.31 (C5), 33.59 ($CH_2$$CH_2$(C3′)), 33.37 ($CH_2$(C3′)), 32.97 ($CH_2$$CH_2$(C2)), 32.80 ($CH_2$(C2)), 22.64 ($CH_2$$CH_3$), 22.54 ($CH_2$$CH_3$), 21.12 ($CH_3$(C4″)), 13.94 ($CH_3$), 13.86 ($CH_3$); MS: 356 (100), 313 (20), 257 (77), 255 (22).

2.9. 2,3′-Di-n-butyl-4″-fluoro-1,1′;2′,1″-terphenyl (7) (R = n-Bu; R′ = 4-F)

Yield: 71%, conversion 95%. ^{1}H NMR: δ 7.35−7.27 (2H, m, H4′, H5′), 7.15−7.03 (3H, m, H6′, H6, H3), 7.00−6.90 (4H, m, H4, H5, H2″, H6″), 6.87−6.77 (2H, m, H3″, H5″), 2.54−2.38 (2H, m, CH_2(C3′)), 2.38−2.16 (2H, m, CH_2(C2)), 1.50−1.29 (4H, m, 2C$H_2$$CH_2CH_3$), 1.29−1.12 (4H, m, 2C$H_2$$CH_3$), 0.81, 0.78 (6H, two partly overlapping t, $J = 7.3$ Hz, 2CH_3); ^{13}C NMR: δ 161.02 (d, $J_{C,F} = 244.8$ Hz, C4″), 141.35 (C1′), 141.09 (C3′), 141.02 (C1), 140.07 (C2), 139.51 (C2′), 135.67 (d, $J_{C,F} = 3.4$ Hz, C1″), 132.22 (d, $J_{C,F} = 7.9$ Hz, C2″*), 130.77 (d, $J_{C,F} = 7.9$ Hz, C6″*), 130.56 (C4), 128.13 (C3), 128.03 (C4′), 127.51 (C6′), 126.78 (C5′), 126.69 (C6), 124.47 (C5), 114.10 (d, $J_{C,F} = 21.2$ Hz, C3″, C5″), 33.52 ($CH_2$$CH_2$(C3′)), 33.38 ($CH_2$(C3′)), 33.01 ($CH_2$$CH_2$(C2)), 32.80 ($CH_2$(C2)), 22.60 ($CH_2$$CH_3$), 22.53 ($CH_2$$CH_3$), 13.92 ($CH_3$(C2)), 13.80 ($CH_3$(C3′)); MS: 360 (81), 317 (18), 261 (100), 259 (25), 57 (23).

2.10. 2,3′-Di-n-propyl-2″-methyl-1,1′;2′, 1″-terphenyl (7) (R = n-Pr; R′ = 2-Me)

Yield: 73%, conversion 100%. ^{1}H NMR: δ 7.36−7.28 (2H, m), 7.17−6.87 (8H, m), 6.87−6.82 (1H, m), 2.48−2.32 (2H, m), 2.32−2.18 (2H, m), 2.04−1.89 (3H, 2s), 1.68−1.36 (4H, m), 0.94−0.74 (6H, overlapping t); ^{13}C NMR: δ 141.46, 141.27, 140.93, 140.91, 140.80, 140.51, 140.04, 139.99, 139.84, 139.57, 138.86, 135.85, 135.80, 131.73, 131.69, 129.41, 129.29, 129.19, 128.75, 128.16, 127.98, 127.70, 127.63, 127.58, 126.65, 126.64, 126.56, 126.47, 126.46, 126.29, 124.69, 124.37, 124.30, 124.00, 35.74, 35.46, 35.40, 35.06, 24.73, 24.13, 23.91, 23.79, 20.21, 19.72, 14.38, 14.22, 14.15, 14.08; MS: 328 (100), 299 (28), 285 (43), 257 (67), 241 (32), 239 (28).

2.11. 2,3′-Di-i-propyl-2″-methyl-1,1′;2′, 1″-terphenyl (7) (R = i-Pr; R′ = 2-Me)

Yield: 49%, conversion 57%. ^{1}H NMR: δ 7.45−7.33 (2H, m, H4′, H5′), 7.17−7.06 (3H, m, H3, H4, H6′), 7.06−7.00 (2H, m, H3″, H4″), 6.98−6.87 (3H, m, H5″, H5, H6), 6.87−6.82 (1H, m, H6″), 2.92−2.70 (1H, m, CH(C2)), 2.70−2.51 (1H, m, CH(C3′)), 2.09−1.99 (3H, 2s, CH_3(C2″)), 1.27−0.98 (12H, eight partly overlapping d, $J = 6.8$ Hz, CH_3); ^{13}C NMR: δ 147.49, 147.06, 146.25, 146.17, 140.87, 140.84, 140.59, 139.83, 139.49, 138.92, 138.90, 138.73, 135.93, 135.69, 131.79, 131.66, 129.64, 129.32, 129.18, 128.64, 127.95, 127.50, 127.07, 126.82, 126.81, 126.70, 126.60, 124.98, 124.75, 124.69, 124.40, 124.21, 124.06, 124.00, 123.89, 30.16, 29.97, 29.60, 25.98, 25.73, 25.16, 25.04, 23.16, 23.14, 22.99, 22.58, 20.39, 19.77. MS: 328 (100), 299 (21), 271 (43), 257 (69), 241 (29).

2.12. 5-n-Propyl-1,2,3,4,4a,8b-hexahydro-1,4-methanobiphenylene (**8**) (R = n-Pr)

Yield: 2%. ^{1}H NMR: δ 7.14 (1H, t, J = 7.5 Hz, H7), 7.00 (1H, d, J = 7.8 Hz, H6), 6.84 (1H, d, J = 7.2 Hz, H8), 3.19 (1H, d, J = 3.9 Hz, H4a), 3.16 (1H, d, J = 3.9 Hz, H8b), 2.26−2.48 (2H, m, CH_2(C5)), 2.32 (1H, m, H4), 2.28 (1H, m, H1), 1.74−1.49 (4H, m, CH_3CH_2 centred at 1.66. H2 *exo*, H3 *exo*), 1.26−1.16 (2H, m, H2 *endo*, H3 *endo*), 1.03−0.93 (4H, m, H9 *anti*, CH_3 centred at 0.97), 0.91 (1H, d quint., J = 10.2, 1.9 Hz, H9 *syn*); ^{13}C NMR: δ 146.24 C8a), 144.61 (C4b), 136.98 (C5), 127.49 (C7), 127.13 (C6), 119.12 (C8), 49.94 (C4a), 49.84 (C8b), 36.54 (C1), 36.36 (C4), 33.88 (CH_2(C5)), 31.96 (C9), 27.90 (C2, C3), 23.68 (CH_2CH_3), 14.05 (CH_3); MS: 212 (9), 171 (100), 141 (32), 129 (53), 128 (22), 115 (22).

2.13. 5-(Bicyclo[2.2.1]hept-2′-yl)-6-methyl-1,2,3,4,4a,8b-hexahydro-1,4-methanobiphenylene (**9**) (R = Me)

Yield: 6%; two diastereoisomers in 1:1 ratio (yield of **8** (R = Me) 1%) [25]. ^{1}H NMR: δ 7.02, 7.01 (2H, 2 overlapping d, J = 7.3 Hz), 6.71 (2H, br d, J = 7.3 Hz), 3.30−3.22 (2H, 2 overlapping d), 3.06−2.98 (2H, m), 2.80−2.69 (2H, m), 2.58−2.50 (1H, m), 2.45−2.19 (13H, m, CH_3 at 2.25), 2.11−1.99 (1H, m), 1.81−1.45 (13H, m), 1.45−1.09 (10H, m), 1.02−0.91 (4H, m); MS: 278 (10), 237 (100), 157 (15).

2.14. 5-(Bicyclo[2.2.1]hept-2′-yl)-6-ethyl-1,2,3,4,4a,8b-hexahydro-1,4-methanobiphenylene (**9**) (R = Et)

Yield: 9%; two diastereoisomers in 1:1 ratio indicated as A and B (yield of **8** (R = Et) 4%) [16]. ^{1}H NMR: δ 7.08, 7.07 (2H, 2 overlapping d, J = 7.4 Hz, H7 (A, B)), 6.80, 6.79 (2H, 2 overlapping d, J = 7.4 Hz, H8 (A, B)), 3.32−3.27 (2H, 2 overlapping d, H4a (A, B)), 3.06−3.02 (2H, m, H8b (A, B)), 2.89−2.80 (2H, m, H2′ (A, B)), 2.73−2.58 (4H, m, 2 overlapping quart., J = 7.4 Hz, CH_2(C6) (A, B), (H1′B)), 2.54−2.50 (1H, m, H1′B), 2.48−2.35 (3H, m, H4A, H4B, H4′A), 2.35−2.30 (1H, m, H4′B), 2.29−2.21 (3H, m, H1A, H1B, H1′A), 2.13−2.01 (1H, m, H3′ *exo* A), 1.79−1.72 (2H, m, H3′ *exo* B, H3′ *endo* B), 1.72−1.56 (11H, m, H2 *exo*, H3 *exo*, H5′ *exo*, H6′ *exo*, H7′ *syn*, (A, B), H3′ *endo* A), 1.45−1.13 (16H, m, H5′ *endo*, H6′ *endo*, H2 *endo*, H3 *endo*, H7′ *anti*, CH_3 (A, B), 1.05−0.95 (4H, m, H9 *syn*, H9 *anti*, (A, B)); ^{13}C NMR: δ 144.34, 144.30 (C8a; A, B), 142.84, 142.37 (C4b; A, B), 141.18, 141.14 (C6; A, B), 140.09, 139.81 (C5; A, B), 128.07 (C7; A, B), 119.06 (C8; A, B), 52.77, 52.64 (C4a; A, B), 48.92 (C8b; A, B), 44.41 (C1′A), 43.67, 43.08 (C2′; A, B), 41.68 (C1′B), 38.73 (C3′B), 38.19, 38.00 (C4; A, B), 37.00 (C3′A), 36.98, 36.96 (C1; A, B), 36.91 (C4′A), 36.79, 36.67 (C7′; A, B), 36.61 (C4′B), 31.79, 31.76 (C9; A, B), 30.85, 30.63 (C6′; A, B), 29.09, 28.89 (C5′; A, B), 28.14, 28.12 (C3; A, B), 28.10, 27.94 (C2; A, B), 26.62, 26.22 (CH_2(C6); A, B), 15.73, 15.67 (CH_3; A, B); MS: 292 (15), 251 (100), 171 (24), 165 (18).

2.15. 5-(Bicyclo[2.2.1]hept-2′-yl)-6-n-propyl-1,2,3,4,4a,8b-hexahydro-1,4-methanobiphenylene (**9**) (R = n-Pr)

Yield: 10%; two diastereoisomers in 1:1 ratio indicated as A and B. ^{1}H NMR: δ 7.07, 7.06 (2H, 2 overlapping d, J = 7.4 Hz, H7 (A, B)), 6.79, 6.78 (2H, 2 overlapping d, J = 7.4 Hz, H8 (A, B)), 3.34−3.28 (2H, 2 overlapping d, H4a (A, B)), 3.08−3.04 (2H, m, H8b (A, B)), 2.85 (2H, br dd, J = 7.9, 6.9 Hz, H2′ (A, B)), 2.75−2.50 (5H, m, CH_2(C6) (A, B), H1′B), 2.48−2.20 (7H, m, H4 (A, B), H4′A, H4′B, H1 (A, B), H1′A), 2.16−2.05 (1H, m, H3′ *exo* A), 1.80−1.75 (2H, m, H3′ *exo* B, H3′ *endo* B), 1.75−1.53 (15H, m, H2 *exo*, H3 *exo*, H5′ *exo*, H6′ *exo*, CH_3CH_2, H7′ *syn*, (A, B), H3′ *endo* A), 1.46−1.14 (10H, m, H5′ *endo*, H6′ *endo*, H2 *endo*, H3 *endo*, H7′ *anti* (A, B)), 1.08−0.98 (10H, m, H9 *syn*, H9 *anti*, CH_3 (A, B)); ^{13}C NMR: δ 144.37, 144.33 (C8a; A, B), 142.88, 142.42 (C4b; A, B), 140.24, 139.97 (C5; A, B), 139.74, 139.73 (C6; A, B), 129.00, 128.92 (C7; A, B), 118.93, 118.92 (C8; A, B), 52.83, 52.67 (C4a; A, B), 48.96 (C8b; A, B), 44.63, (C1′A), 43.74, 43.14 (C2′; A, B), 41.81 (C1′B), 38.76 (C3′B), 38.23, 38.07 (C4; A, B), 37.05, 37.03 (C1; A, B), 36.96 (C3′A), 36.93 (C4′A), 36.85, 36.67 (C7′; A, B), 36.67 (C4′B), 36.21, 35.78 (CH_2(C6); A, B), 31.83, 31.80 (C9; A, B), 30.98, 30.73 (C6′; A, B), 29.12, 28.92 (C5′; A, B), 28.18, 28.15 (C3; A,

B), 27.98, 27.95 (C2; A, B), 24.81, 24.77 (CH_2CH_3; A, B), 14.57, 14.52 (CH_3; A, B); MS: 306 (10), 265 (100), 185 (38), 165 (41), 141 (28), 95 (50), 67 (52).

2.16. 5-(Bicyclo[2.2.1]hept-2′-yl)-6-i-propyl-1,2,3,4,4a,8b-hexahydro-1,4-methanobiphenylene (**9**) (R = i-Pr)

Yield: 2% (run 3) and 10% (run 10); two diastereoisomers in 1:1 ratio indicated as A and B (yield of **8** (*R* = *i*-Pr) [16] 2% (run 3) and 1% (run 10)). ^{1}H NMR: δ 7.19, 7.18 (2H, 2 overlapping d, $J = 7.5$ Hz, H7 (A, B)), 6.85 (2H, br d, $J = 7.5$ Hz, H8 (A, B)), 3.35−3.31 (2H, 2 overlapping d, H4a (A, B)), 3.27, 3.25 (2H, 2 overlapping hept., $J = 6.8$ Hz, $CH(CH_3)_2$ (A, B)), 3.07−3.03 (2H, m, H8b (A, B)), 2.96−2.87 (2H, m, H2′ (A, B)), 2.58−2.54 (1H, m, H1′B), 2.48−2.37 (3H, m, H4′A, H4A, H4B), 2.37−2.31 (1H, m, H4′B), 2.31−2.24 (3H, m, H1A, H1B, H1′A), 2.21−2.11 (1H, m, H3′ *exo* A), 1.82−1.75 (2H, m, H3′ *exo* B, H3′ *endo* B), 1.74−1.52 (11H, m, H2 *exo*, H3 *exo*, H5′ *exo*, H6′ *exo*, H7′ *syn*, (A, B), H3′ *endo* A), 1.49−1.14 (22H, m, H5′ *endo*, H6′ *endo*, H2 *endo*, H3 *endo*, H7′ *anti*, $(CH_3)_2CH$ (4 overlapping d, $J = 6.8$ Hz, at 1.27, 1.26, 1.23, 1.21) (A, B)), 1.10−0.95 (4H, m, H9 *syn*, H9 *anti*, (A, B)); ^{13}C NMR: δ 146.13 (C6; A, B), 144. 09, 144.05 (C8a; A, B), 142.68, 142.18 (C4b; A, B), 139.24, 138.78 (C5; A, B), 125.28, 125.14 (C7; A, B), 119.24, 119.21 (C8; A, B), 53.01, 52.94 (C4a; A, B), 48.91, 48.88 (C8b; A, B), 44.65 (C1′A), 43.79, 43.17 (C2′; A, B), 41.71 (C1′B), 38.96 (C3′B), 38.27, 38.05 (C4; A, B), 37.03 (C1; A, B), 36.93, 36.60 (C7′; A, B), 36.83 (C4′A), 36.76 (C3′A), 36.70 (C4′B), 31.87, 31.81 (C9; A, B), 30.72, 30.51 (C6′; A, B), 29.23, 29.02 (C5′; A, B), 29.00, 28.94 (CH; A,B), 28.16, 28.14 (C2, C3; A, B), 25.00, 24.69, 24.55, 24.20 (CH_3; A, B); MS: 306 (15), 265 (100), 185 (17), 165 (14).

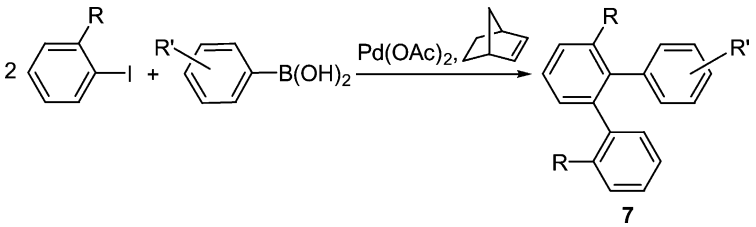
2.17. 5-(Bicyclo[2.2.1]hept-2′-yl)-6-n-butyl-1,2,3,4,4a,8b-hexahydro-1,4-methanobiphenylene (**9**) (R = n-Bu)

Yield: 9% (run 4), 6% (run 7) and 7% (run 8); two diastereoisomers in 1:1 ratio (yield of **8** (R = *n*-Bu) [16] 3% (runs 4 and 7) and 4% (run 8)). ^{1}H NMR: δ 7.06, 7.05 (2H, 2 overlapping d, $J = 7.4$ Hz), 6.78, 6.77 (2H, 2 overlapping d, $J = 7.4$ Hz), 3.34−3.26 (2H, m), 3.07−3.00 (2H, m), 2.84 (2H, br t, $J = 7.4$ Hz), 2.72−2.54 (4H, m), 2.54−2.20 (8H, m), 2.17−2.03 (1H, m), 1.81−1.72 (2H, m), 1.72−1.50 (15H, m), 1.50−1.12 (14H, m), 1.08−0.92 (10H, m); ^{13}C NMR: δ 144.29, 144.26, 142.88, 142.44, 140.14, 139.97, 139.94, 139.87, 128.94, 128.88, 118.93, 118.92, 52.80, 52.62, 48.93, 44.64, 43.70, 43.09, 41.87, 38.59, 38.17, 38.05, 37.01, 36.99, 36.85, 36.82, 36.63, 36.61, 33.98, 33.95, 33.71, 33.30, 31.80, 31.77, 30.90, 30.65, 29.10, 28.88, 28.14, 28.11, 27.94, 23.10, 23.06, 14.09, 14.08; MS: 320 (12), 279 (100), 197 (12), 179 (12), 157 (24), 95 (23), 67 (19).

3. Results and discussion

As shown in Scheme 2, the reaction of an *ortho*-substituted aryl iodide and an arylboronic acid in the presence of 2-norbornene, $Pd(OAc)_2$ and K_2CO_3 as a base, in DMF at 105 °C for 90 h under nitrogen, afforded the corresponding 2,3′-disubstituted-1,1′;2′,1″-terphenyl derivative (**7**).

As shown in Table 1, the reaction gives good results with aryl iodides containing primary and secondary *ortho*-alkyl groups (runs 1–4). Bulky substituents such as the *t*-butyl hinder the formation of



Scheme 2.

Table 1
Reaction of *ortho*-substituted aryl iodides and arylboronic acids in the presence of norbornene, $Pd(OAc)_2$ and K_2CO_3[a]

Run	R in aryl iodide	R′ in boronic acid	Terphenyl **7** yield (%)[b]
1	Me	H	88
2	Et	H	77
3	*i*-Pr	H	93
4	*n*-Bu	H	73
5	OMe	H	82
6	CO_2Me[c]	H	89
7	*n*-Bu	4-Me	72
8	*n*-Bu	4-F	71
9	*n*-Pr	2-Me	73
10	*i*-Pr	2-Me	49[d]

[a] Molar ratio of the reagents in the order reported in the title 200:120:100:1:400; 105 °C, 90 h, DMF as solvent, under nitrogen; 0.1×10^{-2} mmol $Pd(OAc)_2$/ml DMF.

[b] Isolated yield on the charged amount of the aryl iodide; conversion is over 91% unless otherwise noted.

[c] Similar results were also obtained using the corresponding aryl bromide or carrying out the reaction at 80 °C.

[d] 62% conversion.

the corresponding terphenyl derivative. Interestingly, the reaction can be carried out with good yields also using aryl iodides bearing *ortho*-functionalized groups such as the methoxy and methoxycarbonyl ones (runs 5 and 6). By contrast, *ortho*-functionalised groups that become reactive under the reaction conditions can impair the reaction. Among these groups are the monomethylamino and the hydroxy and acetoxy ones. The use of aryl bromides in place of iodides gives poor results, only with R = CO_2Me comparable yields being obtained. The process tolerates different substituents in the phenylboronic acid, even in the *ortho*-position (runs 7–10), thus allowing a simple, direct and efficient way to 1,1′;2′,1″-terphenyl derivatives. In most cases, by-products **8** and **9** (as a mixture of two diastereoisomes, one of which is shown in Fig. 1), containing one [25] or two [26] norbornyl units are also formed (1–10%). No result was obtained with *ortho*-disubstituted arylboronic acids.

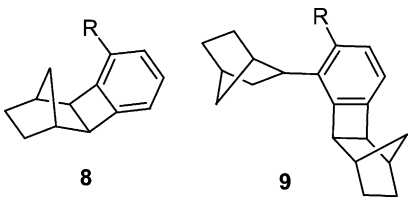


Fig. 1. Reaction by-products.

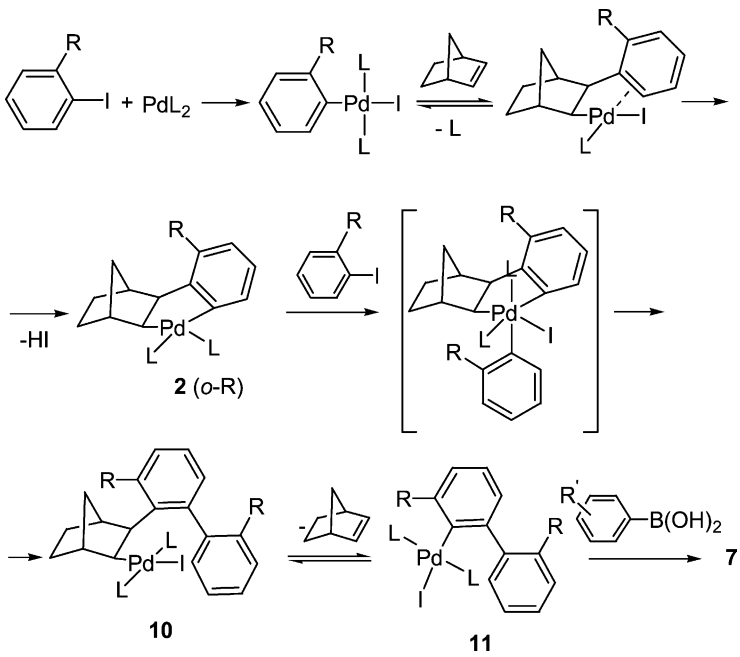
Interestingly, under the conditions adopted no product deriving from direct coupling of the arylboronic acid with one molecule of the *ortho*-substituted aryl iodide was formed. Also, contrary to what previously reported [27] and observed by us in the synthesis of *o,o'*-disubstituted biaryls [17], by-products resulting from aryl–aryl scrambling of the iodide and boronic acid were not observed. Likewise, biaryls resulting from homocoupling [28,29] were not found. Although higher substrate-to-catalyst ratios can be used, so far no optimisation work has been carried out; however, in some cases (*ortho*-CO_2Me, *ortho*-*i*-Pr) catalytic efficiency up to 200–300 mol/mol of catalyst has been attained.

The reaction can be interpreted according to the mechanism shown in Scheme 3 (L = solvent or coordinanting substrates).

The key intermediate, palladacycle **2** (*ortho*-R), is formed by oxidative addition of the aryl iodide to palladium(0) followed by norbornene insertion [6–9] and cyclisation [10,11]. The subsequent reaction of this complex with the *ortho*-substituted aryl iodide occurs through selective attack of the aryl group on the aromatic site of **2** (*ortho*-R) leading to complex **10** [5,18], likely through the intermediacy of a palladium(IV) species analogous to the one shown in Scheme 1, obtained by oxidative addition of an alkyl halide.[1] The reaction further proceeds by norbornene expulsion (for isobutene expulsion from a palladacycle see [36]) caused by the presence of two *ortho*-substituents [13,15–18] and terminates by coupling of the resulting biphenylylpalladium species (**11**) with the arylboronic acid according to a Suzuki-type process [14]. It is worth noting that the molecule of norbornene, inserted into the arylpalladium bond at the beginning of the catalytic cycle, is deinserted towards the end of the same cycle, thus acting as a catalyst. An excess, however, is generally used to favour the insertion step.

As anticipated, the success of the reaction essentially depends on the preference of the aryl iodide

[1] The presence of this species is assumed on the basis of isolation of palladium(IV) complexes, containing an allyl [30] or benzyl [31] group in place of the *ortho*-substituted aryl, and of the recent report of the aryl transfer to palladium(II) with concomitant oxidation to palladium(IV) by diphenyliodonium triflate [32]. For other references on palladium(IV) chemistry see [33–35].



Scheme 3.

to react with the aromatic rather than with the aliphatic carbon of the *ortho*-substituted palladacycle **2** (*ortho*-R) selectively [5] and on the delay of Suzuki coupling till the end of the stoichiometric process.

The present procedure, thus provides an efficient tool for the synthesis of substituted terphenyls starting from readily available *ortho*-substituted aryl iodides. It has to be noted in this context that *ortho*-terphenyls can be obtained from a Suzuki aryl coupling with *ortho*-iodobiphenyls, as recently reported for the unsubstituted *ortho*-iodobiphenyl [37]. However, the use of this method to obtain the selectively substituted *ortho*-terphenyls here described would require the synthesis of the corresponding *ortho*-iodobiphenyls.

Inspection of Scheme 3 also allows to account for the negative effect of the previously mentioned *ortho*-methylamino, *ortho*-hydroxy and *ortho*-acetoxy substituents: the latter interfere at the stage of the precursor of complex **2** (*ortho*-R) to give hexahydromethanocarbazole and hexahydromethanodibenzofuran, respectively, through five-membered ring closure as previously observed [38]. The formation of by-products **8** and **9** deserves some comments: both derive directly or indirectly from type **2** (*ortho*-R) palladacycle complexes, thus providing further support to the reaction mechanism. Product **8** is the result of direct reductive elimination from complex **2** (*ortho*-R), a process which is favoured by *ortho*-R substituents as we previously showed [25]. The formation of compound **9** implies hydrogenolysis at the norbornyl site of **2** (*ortho*-R) [39–42], which is followed by norbornene insertion and ring closure as for compound **8**.

Compound **8** is the only product obtained with R = *t*-Bu and its formation is likely due to both the negative effect exerted by the bulky *t*-butyl group on metallacycle **2** (*ortho*-R = *t*-Bu) and to the lack of reactivity of 2-*t*-BuC_6H_4I towards oxidative addition to the same palladium(II) metallacycle (Scheme 3). The expected negative effect of the *ortho*-substituent has been observed only with a tertiary group. In fact, when R = *i*-Pr, the reaction is very efficient and gives compound **7** (R = *i*-Pr; run 3) in 93% yield. Thus, while the bulky *t*-butyl group inhibits the reaction leading to **7**, the steric hindrance of the secondary alkyl group turns out to be the most appropriate to give the best yield: it is not too sterically demanding to prevent the reaction with palladacycle **2** (*ortho*-R) and in the same time it is sufficiently bulky to favour

norbornene deinsertion, which is the only step of Scheme 3 to benefit of the presence of a bulky group.

With R = Me in the starting aryl iodide, two additional by-products are formed (2 and 3%) which derive from activation of the benzylic C–H bond as previously reported [43].

Finally, it is worth noting that the presence of *ortho*-alkyl groups R in product **7** hinders phenyl rotation even in the absence of an *ortho*-R′ substituent, as evidenced by NMR spectroscopy. For example, the carbons of the unsubstituted phenyl ring of compound **7** (R = *i*-Pr; R′ = H) resonate at different chemical shifts (Section 2). With *ortho*-R′ substituents, the spectra are more complex due to the presence of additional conformational isomers. This subject is being currently addressed.

4. Conclusions

A catalytic process has been worked out, which offers a valuable tool for the one-pot synthesis of selectively substituted *ortho*-terphenyls not easily accessible by other ways. The process is based on a new type of aryl–aryl coupling of *ortho*-substituted aryl halides, followed by Suzuki's-type coupling.

The *ortho*-terphenyl class is particularly interesting for the molecular dynamics properties [44] which also are useful for electrochemical [45,46] and rheological [47] applications. Further study of the reaction scope is in progress.

Acknowledgements

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