Electronic Supplementary Information for Dalton Transactions

Electronic Supplementary Information

A New Mechanistic Pathway under Sonogashira Reaction Protocol Involving Multiple Acetylene Insertions

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Introductory Experimental Section

All manipulations were carried out under argon using standard Schlenk techniques. Toluene was dried and anhydrous acetone was purchased from ACROS chemicals. The complexes $PdCl_2(phen)$,[1] $PdCl_2(PPh_3)_2$,[2] $PdCl_2(dppe)$,[3] $PdCl_2(bipy)$,[4] $PdCl_2(pyCH_2SMe)$,[5] and $PdI(C_6H_4\text{-}NO_2\text{-}4)(tmeda)$[6] were obtained as reported, 4-methyl-3-nitroiodobenzene was obtained from Alpha Aesar and recrystallised before use, and other reagents were obtained from the Aldrich Chemical Co. and were used as received unless specified. ^{n}BuLi was standardised[5] before use and 4-nitroiodobenzene was recrystallised before use. Ultra high purity argon was purchased from BOC Gases. ^{1}H NMR spectra were recorded on a Varian Mercury Plus 300 NMR Spectrometer at 299.9 MHz at ambient temperature Microanalyses were performed by Dr. Thomas Rodemann of the Central Science Laboratory (CSL), University of Tasmania using a ThermoFinnigan Flash EA 1112 Series Elemental Analyser. Mass spectrometry was conducted by Dr. Noel Davies and Dr. Marshall Hughes of the CSL. The EI (Electron Ionisation) were carried out using a Kratos ISQ mass spectrometer with a liquid matrix of nitrobenzyl alcohol using 10 kV Cs ions and a 5.3kV accelerating voltage. Gas chromatographic-mass spectrometry was conducted using a Varian 1200 triple quadrupole benchtop GC-MS.

Synthesis of 1-(4-nitrophenyl)-2,4,6-triphenylbenzene (5)

The title compound was obtained on reaction of 4-nitro-iodobenzene[7] with 2,4,6-triphenylphenylboronic acid[8] under slightly modified Suzuki catalysis conditions.[9]

1,3,5-Triphenylbenzene (6.0 g, 1.96 mmol) and bromine (1 mL) were dissolved in carbon disulfide (25 mL) and left to react for 12 h without stirring. Methanol (75 mL) was added and the mixture is left to stand until the solvents had evaporated. The product was recrystallised from hot ethanol to give a quantitative yield of 2,4,6-triphenylbromobenzene, m.p. 129-131°C.

^{n}BuLi (7.30 mL, 1.6 M in hexanes, 1.5 eq.) was added to a suspension of 2,4,6-triphenylbromobenzene (3.00 g, 7.79 mmol) in dry diethyl ether at 0 °C under argon, and the resulting solution was stirred at room temperature for 2 h. The resulting yellow solution was added dropwise to a rapidly stirred solution of $B(OMe)_3$ (8.68 mL, 10 eq.) in dry diethyl ether at -65 °C. Upon completion of the addition the resulting pale yellow solution was allowed to warm slowly to room temperature and stirred for 24 h. Aqueous 2M HCl solution was added

to the solution until acidic (pH 4 – 5) and the resulting biphasic solution was stirred rapidly for 2 h after which the organic layer was extracted with diethyl ether (3 x 30 mL), washed with brine, dried over $MgSO_4$ and the solvent removed under vacuum to obtain a pale yellow solid. The yellow colouration was removed by adding CH_2Cl_2 (5 mL), followed by hexane (40 mL) to precipitate the desired white boronic acid which was collected by filtration (2.26 g, 83%). The desired boronic acid was used in the next step without further purification.

Using a slightly modified procedure developed by Buchwald and co-workers,[9] an oven-dried Schlenk flask containing a magnetic stir bar was charged with 4-nitro-iodobenzene (0.062 g), 2,4,6-triphenylphenylboronic acid (0.131 g, 1.5 eq.), $Pd(dba)_2$ (5.74 mg, 4 mol%), 2-(2',6'-dimethoxybiphenyl)dicyclohexylphosphine (SPhos) (8.21 mg, 8 mol%), and powdered, anhydrous K_3PO_4 (0.153 g, 3.0 eq.). The flask was stoppered and the contents evacuated and backfilled with argon (repeated three times). Dry toluene (20 mL) was added to the flask and the resulting dark red solution was heated to 100 ^oC with vigorous stirring for 48 h. After 24 h another 0.5 eq. of 2,4,6-triphenylphenylboronic acid and a further 1 mol% of catalyst and 2 mol% of SPhos was added to the solution. After 48 h the solution was cooled to room temperature and diluted with diethyl ether (10 mL), filtered through a thin pad of silica gel and concentrated under vacuum. The crude yellow solid product was then obtained by removal of the solvent under vacuum, after which CH_2Cl_2 (2.5 mL) was added followed by hexanes (30 mL) to give a yellow solution and white precipitate. The precipitate was removed by filtration and the solvent removed in a vacuum to give an yellow solid which was further purified by column chromatography on silica gel using 1:10 CH_2Cl_2:hexanes to remove impurities, and the desired product eluted with 3:10 CH_2Cl_2:hexanes as an off white solid (0.087 g, 81 %) ^1H NMR (25 °C, ($CDCl_3$): δ 7.86 (d, ^3J = 9 Hz, 2H), 7.70 (m, 4H), 7.48-7.40 (m, 3H), 7.20 (m, 6H), 7.09 (m, 4H), 7.03 (d, ^3J = 9 Hz, 2H). EI *m/z* 427 $[M]^+$, $[^{12}C_{30}{}^1H_{21}{}^{14}N^{16}O_2$ 427]. M.S. High res. Calcd for "$[C_{30}H_{21}NO_2]^+$" = 427.15723 amu: Found M^+ = 427.15754 amu by EI.

Synthesis of iodo(4-nitrophenyl)(2-methylthiomethylpyridine)palladium(II) (7)

Recrystallised $PdI(C_6H_4\text{-}NO_2\text{-}4)(tmeda)$[10] (0.15 g, 0.32 mmol) was added to a solution of 2-methylthiomethylpyridine[11] (0.68 g, 15.0 eq.) in anhydrous acetone (20 mL) under argon. The resulting brown solution was stirred for 24 h at room temperature where upon a further 0.23 g (5.0 eq.) of 2-methylthiomethylpyridine was added to the solution. Further stirring at room temperature for another 24 resulted in a pale yellow which was subsequently

dried under reduced pressure. The solid residue was dissolved in CH_2Cl_2 (10 mL), treated with activated charcoal, and filtered through Celite. Reduction of the volume ~3 mL under reduced pressure followed by addition of diethyl ether yielded the desired complex as a pink-white powder (0.13 g, 81 %). ^{1}H NMR (25 °C, $(CD_3)_2CO$): δ 9.53 (d, ^3J = 7.8 Hz, 1H), 8.07 ("dt", ^3J = 7.8, 1.5 Hz, 1H), 7.81 (d, ^3J = 7.8 Hz, 1H), 7.77 ("dd", ^3J = 8.7, 1.8 Hz, 2H), 7.60-7.53 (m, 3H), 4.86-4.64 (broad d, CH_2), 2.84 (s, CH_3), Anal. Found: C, 31.62; H, 2.70; N, 5.59. Calc. for $C_{13}H_{13}N_2O_2IPd$: C, 31.57; H, 2.65; N, 5.66.

Synthesis of 1-(4-methyl-3-nitrophenyl)-2,4,6-triphenylbenzene

An oven-dried Schlenk flask containing a magnetic stir bar was charged with 4-methyl-3-nitro-iodobenzene (0.396 g), 2,4,6-triphenylphenylboronic acid (0.791 g, 1.5 eq.), $Pd(dba)_2$ (0.035 g, 4 mol%), SPhos (0.049 g, 8 mol%), and powdered, anhydrous K_3PO_4 (0.959 g, 3.0 eq.). The Schlenk flask was stoppered and the contents evacuated and backfilled with argon (repeated three times). Dry toluene (20 mL) was then added to the flask and the resulting dark red solution was heated to 100 ^{o}C with vigorous stirring for 48 h. After 24 h another 0.5 eq. of 2,4,6-triphenylphenylboronic acid and a further 1 mol% of catalyst and 2 mol% of SPhos was added to the solution. After 48 h the solution was cooled to room temperature and diluted with diethyl ether (10 mL) and filtered through a thin pad of silica gel and concentrated under vacuum. The crude yellow solid product was then obtained by removal of the solvent under vacuum after which CH_2Cl_2 (2.5 mL) was added followed by hexanes (30 mL) to give a yellow solution and white precipitate. The precipitate was removed by filtration and the solvent removed in a vacuum to give a yellow solid. The solid was further purified by column chromatography on silica gel by using 1:10 CH_2Cl_2:hexanes to remove impurities, and 1:5 CH_2Cl_2:hexanes to obtain the desired product as a off-white solid (0.531 g, 80 %) ^{1}H NMR (25 °C, $(CDCl_3)$: δ 7.70 (m, 4H), 7.50-7.40 (m, 4H), 7.22 (m, 6H), 7.11 (m, 4H), 7.60-6.96 (m, 2H), 2.45 (s, CH_3). EI *m/z* 441 $[M]^+$, $[^{12}C_{31}{}^1H_{23}{}^{14}N^{16}O_2$ 441]. M.S. High res. Calcd for "$[C_{31}H_{23}NO_2]^+$" = 441.17288 amu: Found M^+ = 441.17285 amu by EI.

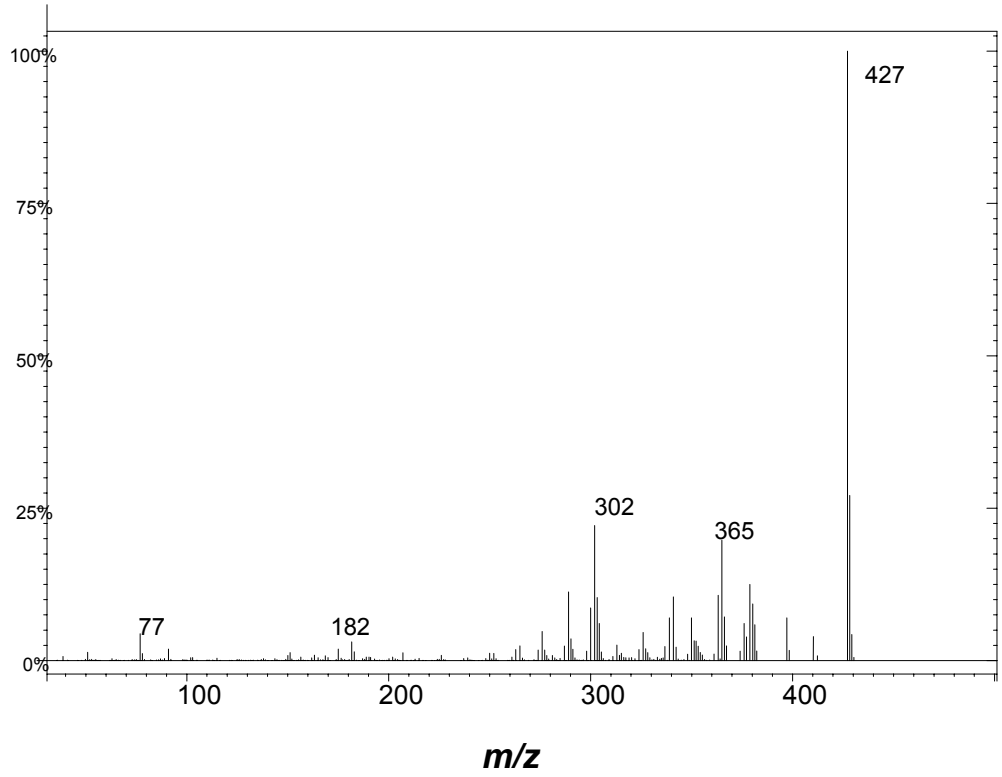
HPLC and GC-MS procedures

Preparative scale HPLC runs were carried out using a Waters Alliance 2690 HPLC and Waters 996 Diode Array Detector, using a Waters PrepLC 25mm Radial Compression Module column fitted with a 25 × 100 mm Prep Nova-Pak HR C18 *6*μm 60Å cartridge and a

Guard-Pak guard column of the same material. The mobile phase was a mixture of 92% methanol and 8% n-hexane at a flow rate of 5 mL min^{-1}. The absorbance at 250 nm was monitored in real time, and the major peak eluting between 7.4 and 8.4 min was automatically collected from multiple 50 μL injections of a concentrated solution of the crude product.

GC-MS data was acquired on a Varian 3800 GC coupled to a Varian 1200 triple quadrupole mass spectrometer. Samples were injected in split mode into a Varian 1177 injector at 270°C using a split ratio of 60:1. The column was a Varian VF-5ms (30m x 0.25mm i.d. x 0.25 micron film), using helium as carrier gas at a flow rate of 3.0 ml min^{-1}. The column oven was programmed from 100°C to 300°C at 8°C min^{-1}, with a final hold of 15 min. The transfer line was held at 300°C and the ion source was at 230°C. Electron ionisation mass spectra at 70 eV were collected over the range m/z 35 to 700 at 3 scans per sec.

EI-MS data of peak 427



427(100%), 428(27), 381(6), 380(9), 379(12), 377(4) 376 (7), 365(20), 363(11), 352(3), 351(3), 350(7), 341(10), 339(7), 326(5), 313(3), 304(6), 303(10), 302(22), 300(9), 290(4), 289(11), 276(5), 182(3), 77(4)

Catalysis procedure

4-Nitro-iodobenzene (0.374 g, 1.5 mmol) was added to a solution of phenylacetylene (0.25 mL, 2.25 mmol), Na_2CO_3 (0.318 g, 3.0 mmol), pre-catalyst (5 mg 0.015 mmol) and Bu^n_4NCl (0.625 g, 1.5 mmol) in anhydrous *N,N*-dimethylacetamide (5 mL) under argon. The mixture was stirred at 120 °C for 24 h under Ar. On cooling to room temperature an aliquot (1.50 mL) was diluted with CH_2Cl_2 (1.5 mL) and washed with an aqueous solution saturated with NaCl (3 x 1.5 mL). The organic layer was extracted, dried over $MgSO_4$, filtered and the sample analysed by GC-MS with yields calculated using 1-(4-methyl-3-nitrophenyl)-2,4,6-triphenylbenzene as an internal standard.

Reactions of iodo(4-nitrophenyl)(2-methylthiomethylpyridine)palladium(II) (7) with phenyl acetylene

Iodo(4-nitrophenyl)(2-methylthiomethylpyridine)palladium(II) (8) (40.0 mg, 8.1×10^{-5} mol) was added to a solution of phenylacetylene (31.1 μL, 3.5 eq.), Na_2CO_3 (17.1 mg, 2.0 eq.), Bu^n_4NCl (33.7 mg, 1.5 eq.) and if used, bis-substituted alkyne (1.5 eq., 0.12 mmol) in anhydrous *N,N*-dimethylacetamide (5 mL) under argon. The mixture was stirred at 120 °C for 24 h under Ar. On cooling to room temperature an aliquot (1.50 mL) was diluted with CH_2Cl_2 (1.5 mL) and washed with an aqueous solution saturated with NaCl (3 x 1.5 mL). The organic layer was extracted, dried over $MgSO_4$, filtered and the sample analysed by GC-MS with yields calculated using 1-(4-methyl-3-nitrophenyl)-2,4,6-triphenylbenzene as an internal standard.

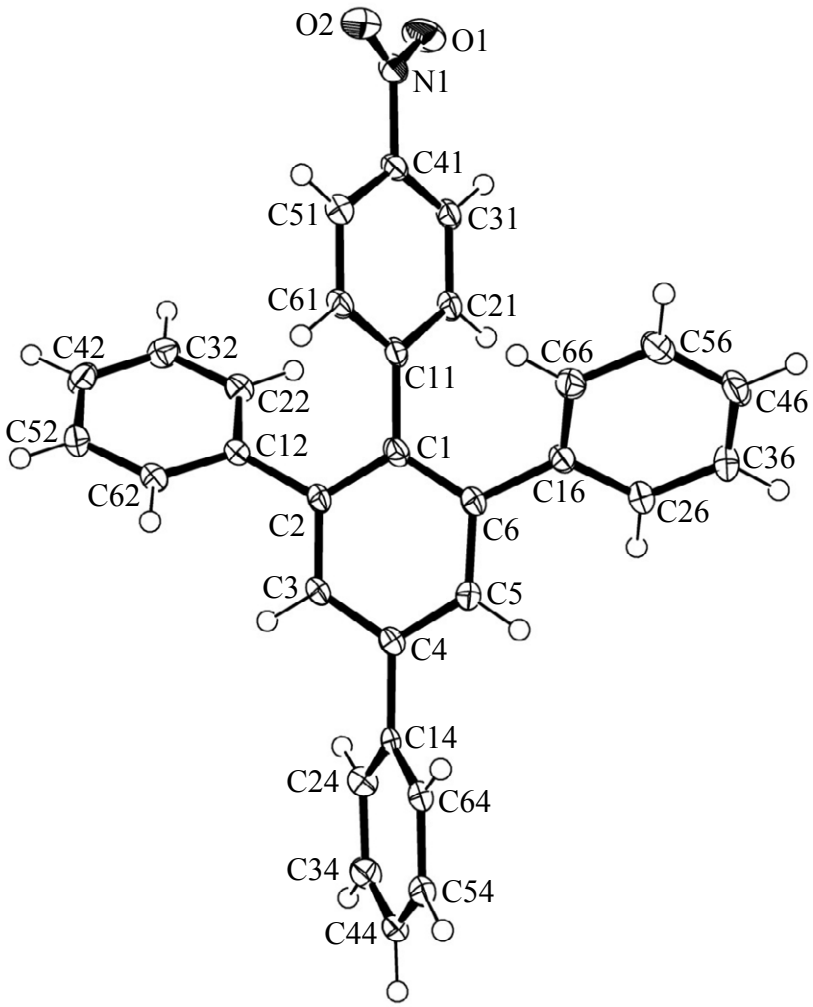
Structural determinations and crystallographic data

Data were collected at 100(2) K for crystals of **5** mounted on a Hampton Scientific cryoloop at the PX2 beamline of the Australian Synchrotron (λ = 0.76207 Å) by Dr. Thomas Caradoc-Davies using Blue Ice[12] software. The structure was solved by direct methods with SHELXS-97, refined using full-matrix least squares routines against F^2 with SHELXL-97,[13] and visualised using X-SEED.[14] All non-hydrogen atoms were refined anisotropically, and hydrogen atoms were placed in calculated positions and refined using a riding model with fixed C-H distances of 0.95 Å (sp^2C-H) and 0.98 Å (CH_3), and $U_{iso}(H) = 1.2U_{eq}(C)$ (sp^2) and

$1.5U_{eq}$(C) (sp^3). A summary of crystallographic data and views of the structure are given below.

Crystal data: $C_{30}H_{21}NO_2$, M = 427.48, triclinic, space group *P-1*, a = 10.588(4), b = 10.867(5), c = 10.920(4)Å, α = 87.032(11), β = 77.218(13), γ = 66.155(17)°, V = 1119.7(8)Å^3, Z = 2, D_c = 1.268 g cm^{-3}, specimen: pale yellow rod, 0.05 x 0.01 x 0.01 mm, 7122 measured reflections, R_{int} = 0.0579, R = 0.0604 for 3084 observed data ((I) >2σ(I)), wR = 0.1607, and GOOF = 1.055 for all data (3728).

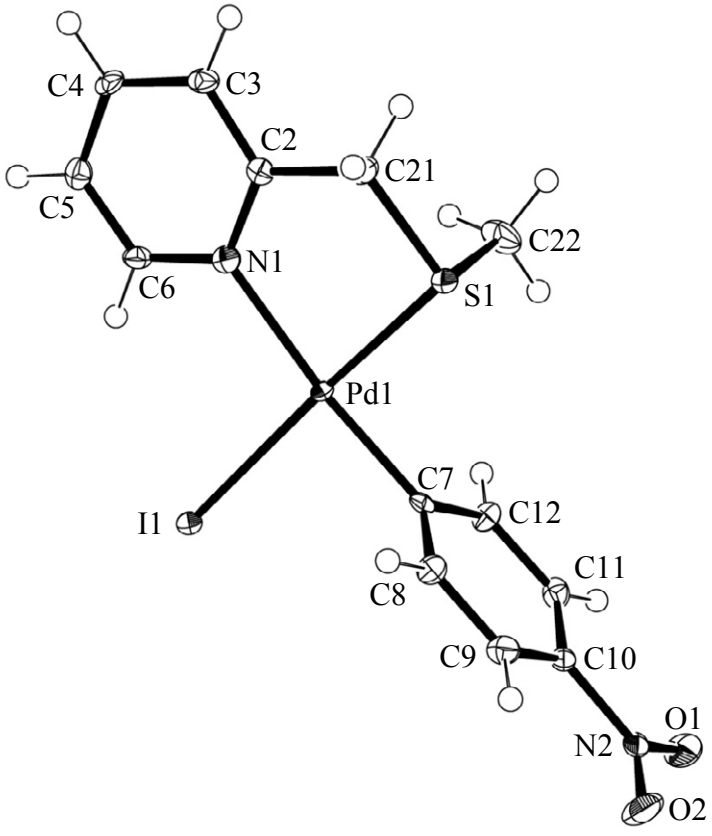
ORTEP representation of the structure of $C_{30}H_{21}NO_2$ (**5**). Displacement ellipsoids are drawn at the 50 % probability level.



Data were collected at 100(2) K for crystals of **7** mounted on a Hampton Scientific cryoloop at the PX1 beamline of the Australian Synchrotron (λ = 0.77487 Å) using Blue Ice[12] software. The structure was solved by direct methods with SHELXS-97, refined using full-matrix least squares routines against F^2 with SHELXL-97,[13] and visualised using X-SEED.[14] All non-hydrogen atoms were refined anisotropically, and hydrogen atoms were placed in calculated positions and refined using a riding model with fixed C-H distances of 0.95 Å (sp^2CH_2), 0.98 Å (CH_3), and $U_{iso}(H) = 1.2U_{eq}(C)$ (sp^2), and $1.5U_{eq}(C)$ (sp^3). A summary of crystallographic data and views of the structure are given below.

Crystal data: $PdC_{13}H_{13}N_2O_2IS$, M = 494.61, monoclinic, space group $P2_1/n$, a = 7.7510(10), b = 11.9940(13), c = 16.0450(12)Å, β = 95.476(6) °, V = 1484.8(3)Å^3, Z = 4, Dc = 2.213 g cm^{-3}, specimen: orange plate, 0.03 x 0.03 x 0.03 mm, 15675 measured reflections, R_{int} = 0.0995, R = 0.0363 for 2190 observed data ((I) >2σ(I)), wR = 0.0887, and GOOF = 1.087 for all data (2262).

ORTEP representation of the structure of $PdC_{13}H_{13}N_2O_2IS$ (**7**). Displacement ellipsoids are drawn at the 50 % probability level.



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