Dual Gold Photoredox $C(sp^2)$-$C(sp^2)$ Cross Couplings – Development and Mechanistic Studies

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ELECTRONIC SUPPORTING INFORMATION

1 - General Experimental Section

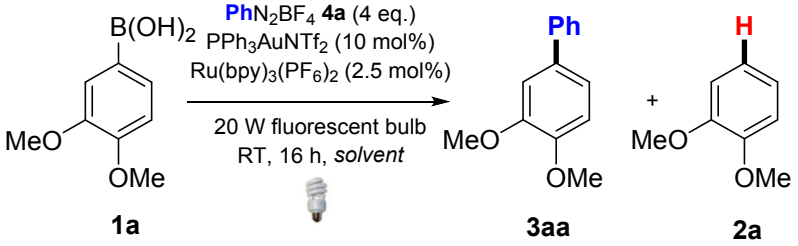
Unless otherwise stated, all reagents were obtained commercially and used without further purification. Unless otherwise stated, all reactions were carried out under inert atmosphere using Schlenk techniques. Prior to each catalytic run, the reaction vessel was wrapped in aluminium foil and the mixture was degassed in the dark through three freeze-thaw (1 min)-pump cycles. The foil was then removed, and light irradiation was performed using a desk lamp fitted with a 20 W spiral fluorescent bulb. The light source was placed *ca* 10 cm from the reaction vessel, to prevent excess heating. TLC analysis was performed on Merck 60 F254 Silica aluminium sheets, and visualised by UV (254 nm) and/or stained by the use of aqueous acidic $KMnO_4$. Dry solvents were obtained from a solvent purification system, and solvents used for purification by chromatography were obtained from Fisher Scientific.

^{1}H, ^{13}C and ^{31}P NMR spectra were recorded at ambient temperatures on Bruker AV-300 and AV-400 MHz spectrometers, and chemical shifts (δ in ppm) were referenced to residual solvent peaks. *J* values are given in Hz and s, d, dd, ddd, dt, t, td, tt, q, qn, sext and m abbreviations correspond to singlet, broad singlet, doublet, doublet of doublet, doublet of doublet of doublets, doublet of triplets, triplet, triplet of doublets, triplet of triplets, quartet, quintet, sextet and multiplet. Mass Spectra were obtained at the EPSRC National Mass Spectrometry Facility in Swansea, and spectra were recorded on a Thermo Scientific LTQ Orbitrap XL, Xevo G2-S or Waters CGT Premier spectrometers.

2-Optimisation of the reactions conditions

2.1-Solvent Screen

Table S1: Solvent Screen



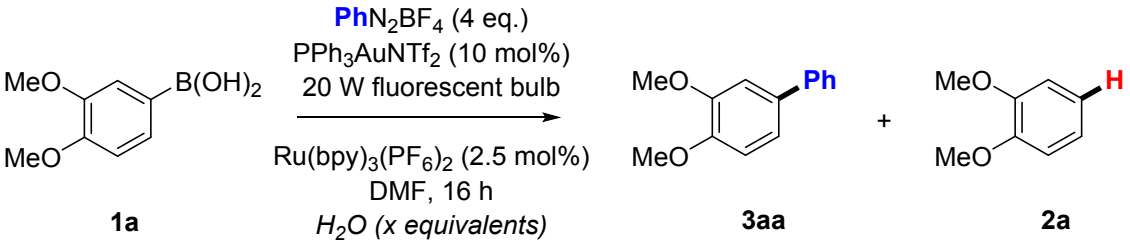
Entry[a]	Solvent	**3aa**:**2a**[b]	Yield **3aa** (%)[b]	Yield **2a** (%)[b]
1	CH_2Cl_2	0.6 : 1	24	38
2	THF	0.1 : 1	13	87
3	DMF	1 : 1	45	48
4	CH_3CN	0.7 : 1	16	20
5	Toluene	>0.1 : 1	5	80
6	MeOH	0.7 : 1	34	51
7	Dimethylcarbonate	**2a** only	-	31

[a]Reaction carried out on 0.1 mmol scale in 1 mL of degassed solvent. [b]Determined by ^{1}H NMR analysis using dimethylsulfone as internal standard.

While the undesired protodeboronated product **2a** was major in all cases, some solvents provided promising results. In particular, this screen initially identified DMF as the most suitable solvent (1:1 of **3aa**:**2a**, Entry 3), while dimethylcarbonate, our solvent of choice for the protodeboronation reaction,[1] was predictably the worst as it favoured protodeboronation **2a** exclusively (Entry 7). However, further optimisation using DMF as solvent failed to significantly improve the ratio of **3aa**:**2a** (see Table S2), so acetonitrile (Entry 4) was taken forward for further optimisation (see Table S3).

2.2-Initial Screening using DMF as solvent

Table S2: Water screening using DMF as solvent



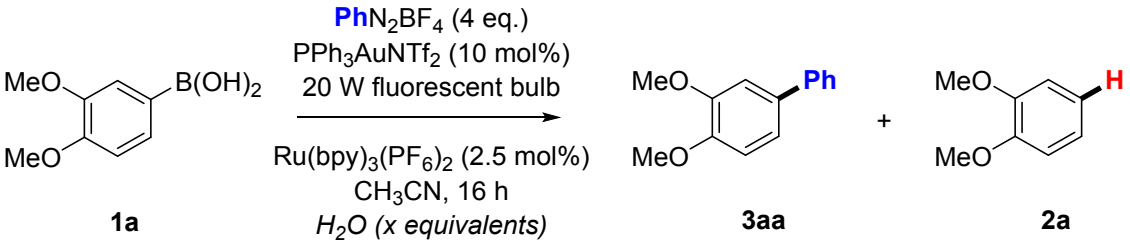
1a **3aa** **2a**

Entry	H_2O equivalents	Ratio 3aa : 2a	NMR Yield[a]
1	0.5	**0.9 :** 1	41%
2	1	**1.2 :** 1	37%
3	2	**0.8 :** 1	34%
4	5	**4.4 :** 1	50%
5	10	**3.2** : 1	68%
6	25	**2.4 :** 1	46%
7	50	**1.7 :** 1	52%

Reaction carried out on 0.1 mmol scale in 1 ml DMF. [a]Dimethylsulfone was used as an internal standard.

2.3-Full water content screening in MeCN

Table S3: Complete water screening



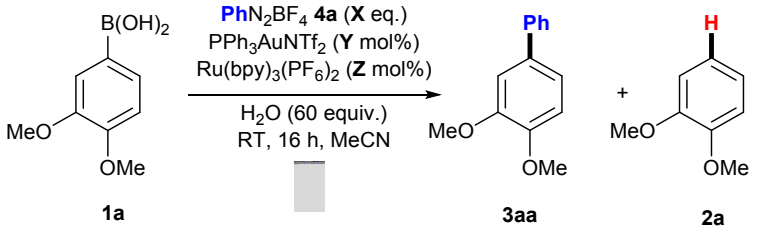
1a **3aa** **2a**

Entry	H_2O equivalents	Ratio 3aa : 2a	NMR Yield[a]
1	1	**1.7 :** 1	41%
2	2	**1.7 :** 1	38%
3	5	**0.6 :** 1	18%
4	10	**2.7 :** 1	42%
5	20	**2.5** : 1	43%
6	25	**4.3 :** 1	68%
7	30	**2.8** : 1	56%
8	35	**2.6** : 1	62%
9	40	**3.3** : 1	51%
10	50	**4.2** : 1	70%
11	60	**10** : 1	71% (70%)[b]
12	75	**3.5** : 1	66%
13	100	**2.7** : 1	56%
14	250	**1.4** : 1	-

Reaction carried out on 0.1 mmol scale; V_{MeCN}= 1 ml. [a] Dimethylsulfone was used as an internal standard. [b]Isolated yield in parentheses.

2.4-Further optimisation

Table S4: Further optimisation – equivalents screens



1a **3aa** **2a**

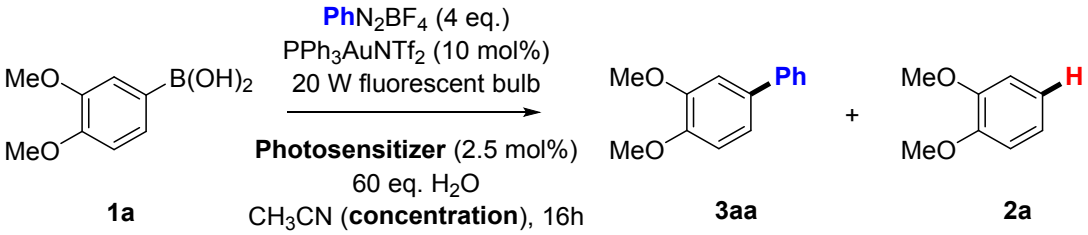
Entry[a]	**X** (equiv.)	**Y** (mol%)	**Z** (mol%)	**3aa** : **2a**[b]	Yield (%)[b]
1	1	10	2.5	3.1:1	50
2	2	10	2.5	11.5:1	90
3	4	10	2.5	10:1	71
4	6	10	2.5	3.3:1	57
5	4	10	1	2.1:1	55
6	4	10	5	4.2:1	66
7	4	5	2.5	18:1	61
8	**2**	**5**	**2.5**	**>20:1**	**83**

[a]Reaction carried out on 0.1 mmol scale in 1 mL of degassed solvent. [b]Determined by ^{1}H NMR analysis using dimethylsulfone as internal standard.

In further attempts to finely tune and increase the overall efficiency of our system, we were pleased to observe a noticeable increase in conversion when reducing the quantity of diazonium salt **4a** in the reaction from 4 to 2 equivalents (Table S4, Entry 2). In parallel, decreasing the gold catalyst loading from 10 mol% to 5 mol% provided very good results in terms of product distribution (18:1 **3aa**:**2a**, Entry 7). Pleasingly, the combination of these new conditions afforded our best results, with the desired biaryl product **3aa** now formed exclusively in 83% NMR yield and 82% isolated yield (Entry 8).

2.5-Photosensitizer and concentration screen

Table S5: Fine optimisation of the system

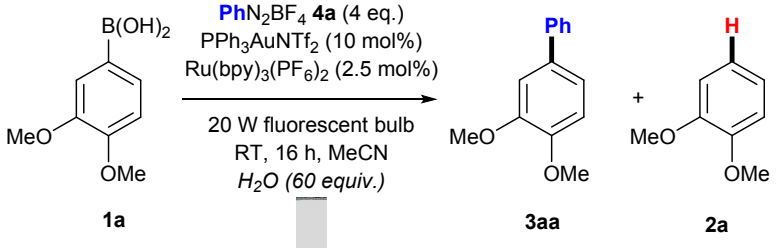


Entry	Changing Parameter	Ratio X : X	NMR Yield[a]
2	[Ru] –> Eosin Y	**1.5** : 1	54%
3	[Ru] –> Fluorescein	**2.2** : 1	28%
4	Conc : 0.2 M	**1.7** : 1	55%
5	Conc : 0.05 M	**7** : 1	57%

Reaction carried out on 0.1 mmol scale. [a] Dimethylsulfone was used as an internal standard.

2.6-Control Reactions

Table S6: Control Reactions



Entry[a]	Variation	Yield 3aa (%)[b]	Yield 2a (%)[b]
1	Normal reaction	83[c]	-
2	No gold catalyst	-	22
3	No Ru catalyst	<15	22
4	No light	6	49
5	Under air, non-degassed solvent	50	6

[a]Reaction carried out on 0.1 mmol scale in 1 mL of degassed MeCN. [b]Determined by ^{1}H NMR

3 - Mechanistic studies

3.1 – Preparation of the NMR samples

All monitored reactions were carried out in 3 ml vials, in deuterated solvents. At an indicated time, an aliquot was taken out from the reaction vial and directly transferred into an NMR tube. ^{1}H and ^{31}P NMR experiments were recorded on a Bruker AV 400 MHz spectrometer. Upon completion of the analyses, the sample was immediately transferred back into the reaction vial.

3.1.1 – Control reactions.

Transmetallation with PPh_3AuNTf_2: A vial was loaded with PPh_3AuNTf_2 (10 mg, 0.014 mmol, 1 equiv.) and 3,4-dimethoxybenzeneboronic acid **1a** (2.5 mg, 1 equiv.). CD_3CN (1 ml) and D_2O (108 µl) were added and the reaction mixture was stirred at room temperature for 14 h. Aliquots were taken, analysed and returned to the reaction mixture at indicated times.

Transmetallation with PPh_3AuCl: A vial was loaded with PPh_3AuCl (6.7 mg, 0.014 mmol, 1 equiv.) and 3,4-dimethoxybenzeneboronic acid **1a** (2.5 mg, 1 equiv.). CD_3CN (1 ml) and D_2O (108 µl) were added and the reaction mixture was stirred at room temperature for 14 h. Aliquots were taken, analysed and returned to the reaction mixture at indicated times.

Reaction of PhN_2BF_4 with PPh_3AuNTf_2: A vial was loaded with PPh_3AuNTf_2 (10 mg, 0.014 mmol, 1 equiv.), $Ru(bpy)_3(PF_6)_2$ (2.5 mol %) and PhN_2BF_4 **4a** (2.6 mg, 1 equiv.). CD_3CN (1 ml) and D_2O (108 µl) were added and the reaction mixture was stirred at room temperature under light for 14 h. Aliquots were taken, analysed and returned to the reaction mixture at indicated times.

3.1.2 – Gold- and photoredox-catalysed reactions.

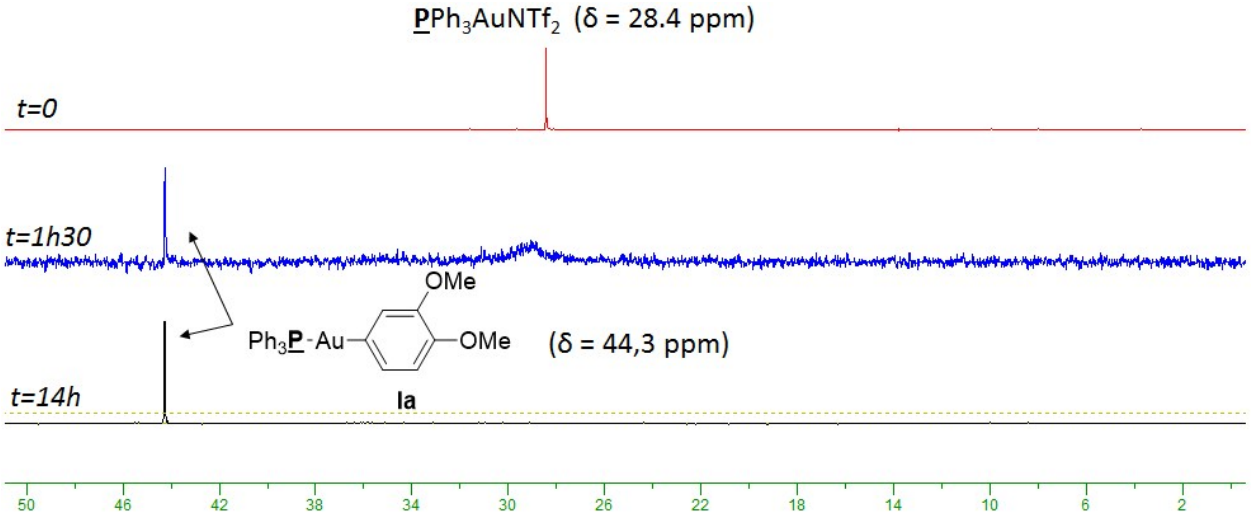
PPh_3AuNTf_2 as the catalyst: A vial was loaded with PPh_3AuNTf_2 (10 mg, 0.014 mmol, 1 equiv.), $Ru(bpy)_3(PF_6)_2$ (2.5 mol%), PhN_2BF_4 **4a** (2.6 mg, 1 equiv.) and 3,4-dimethoxybenzeneboronic acid **1a** (2.5 mg, 1 equiv.). CD_3CN (1 ml) and D_2O (108 µl) were added and the reaction mixture was stirred at room temperature under light for 14 h. Aliquots were taken, analysed and returned to the reaction mixture at indicated times.

PPh_3AuCl as the catalyst: A vial was loaded with PPh_3AuCl (6.7 mg, 0.014 mmol, 1 equiv.), $Ru(bpy)_3(PF_6)_2$ (2.5 mol %), PhN_2BF_4 **4a** (2.6 mg, 1 equiv.) and 3,4-dimethoxybenzeneboronic acid **1a** (2.5 mg, 1 equiv.). CD_3CN (1 ml) and D_2O (108 µl) were added and the reaction mixture was stirred at room temperature under light for 14 h. Aliquots were taken, analysed and returned to the reaction mixture at indicated times.

3.2 – Relevant ^{1}H and ^{31}P NMR spectra

3.2.1 - *Transmetallation with PPh_3AuNTf_2*

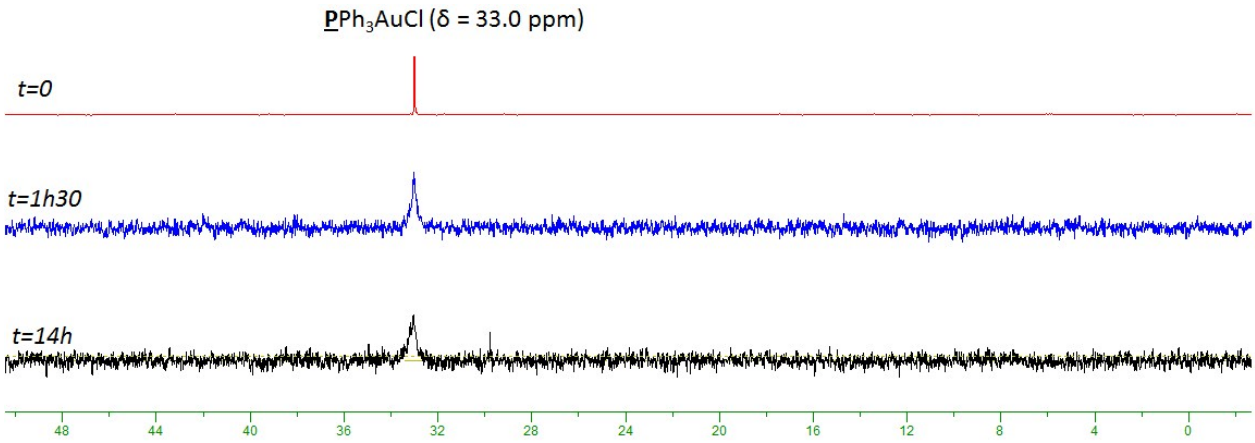
Figure S1: ^{31}P NMR spectra



Evidence of transmetallation is observed here as the Gagosz catalyst PPh_3AuNTf_2 signal (28.4 ppm) disappeared over time upon reaction with 3,4-dimethoxybenzeneboronic acid. The peak at 44.3 ppm was identified as the transmetallated species **Ia**.[2] In order to confirm this observation, compound **Ia** was prepared according to literature.[3] Full characterisation of **Ia** and copies of spectra can be be found in sections 5 and 6.

3.2.2 - *Transmetallation with PPh_3AuCl*

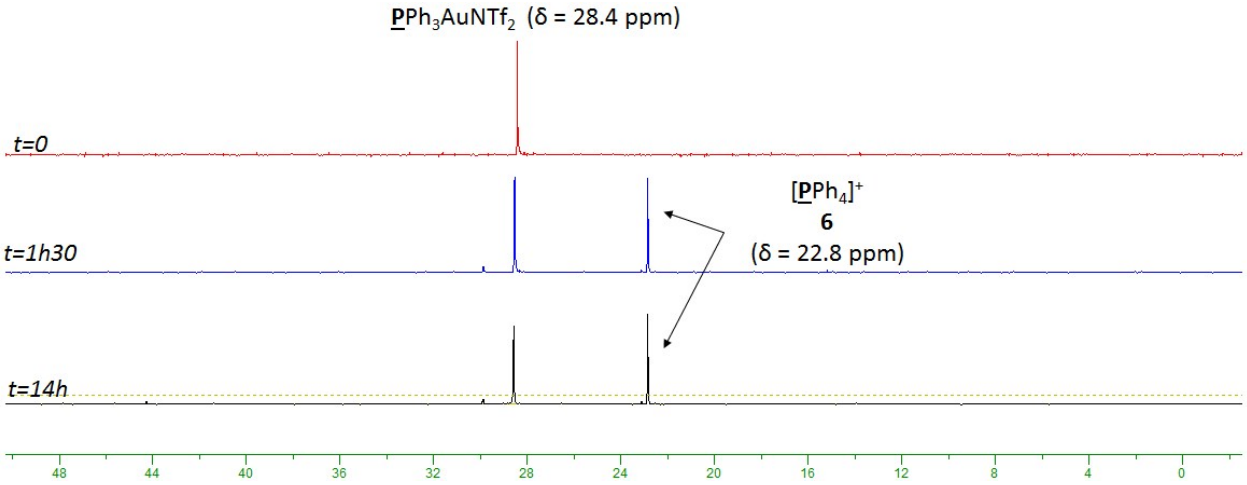
Figure S2: ^{31}P NMR spectra



Absence of a peak around 44.3 ppm indicates that no transmetallation is taking place with this catalyst, in accordance with previous reports.[4]

3.2.3 - *Reaction of PhN_2BF_4 with PPh_3AuNTf_2*

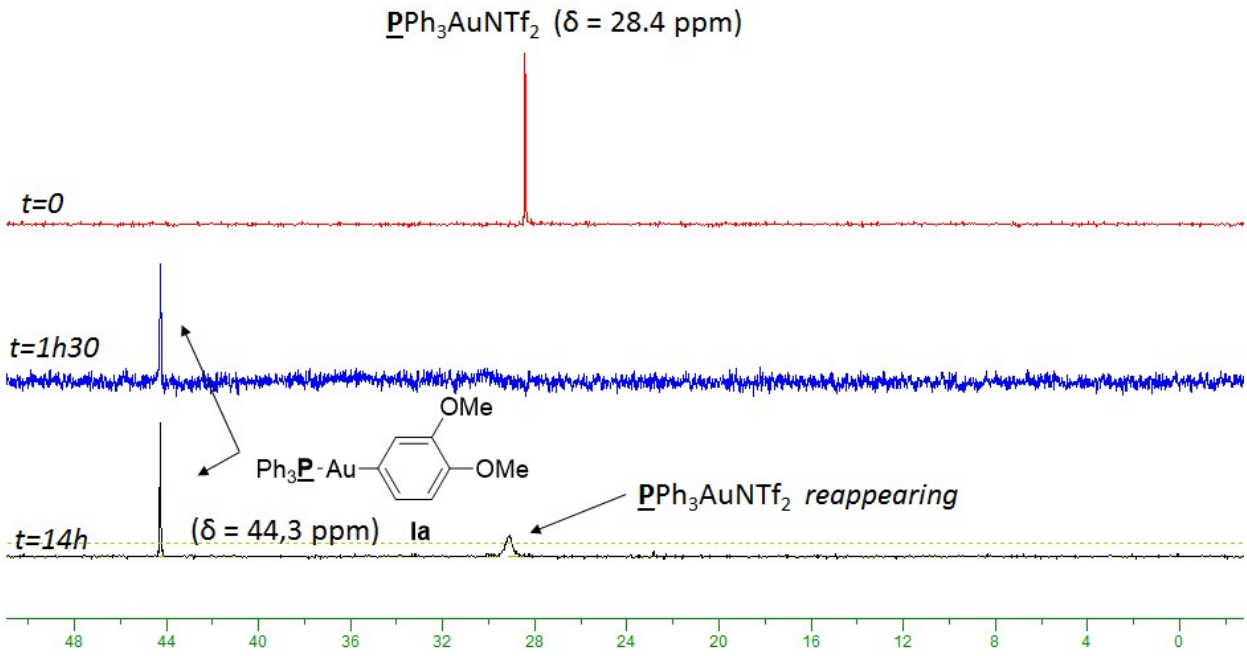
Figure S3: ^{31}P NMR spectra



A new peak appears over time at 22.8 ppm, which corresponds to tetraphenylphosphonium **6**. As shown by Toste *et al*, **6** can be formed through reductive elimination of gold(III) species **V**.[5] This strongly implies the possibility of another mechanism, where gold oxidation through a radical addition/SET sequence would occur prior to transmetallation. This hypothesis is substantiated by a control experiment carried out with the same conditions, in the dark. In the dark, only the original catalyst signal was observed, and no additional signal was present after 14 h.

3.2.4 - *Gold/photoredox catalytic reaction with PPh_3AuNTf_2*

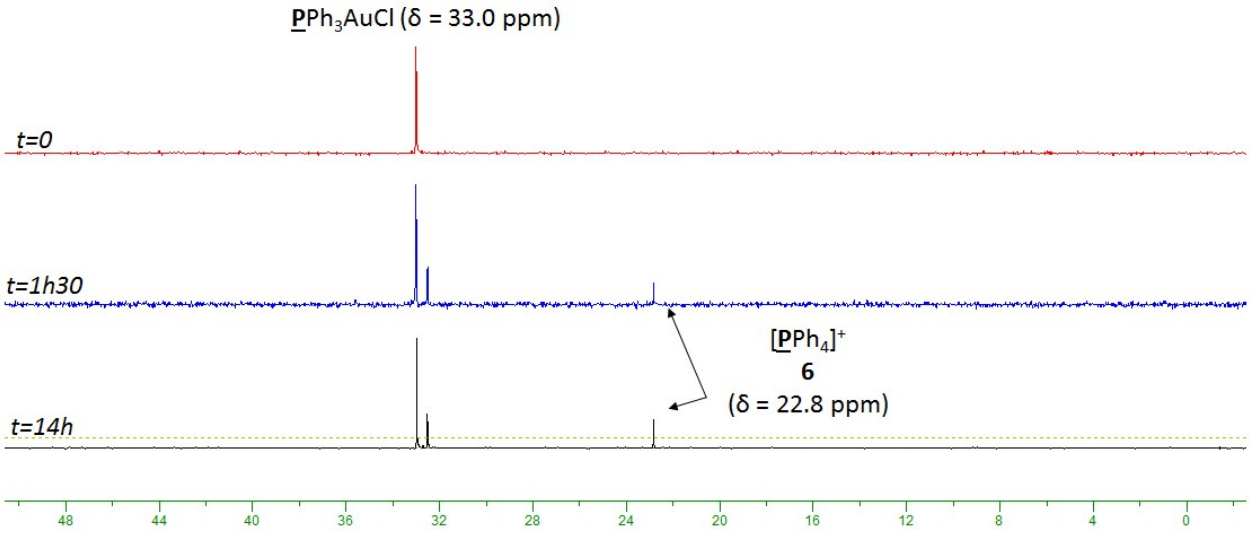
Figure S4: ^{31}P NMR spectra



When the reaction is catalysed by PPh_3AuNTf_2, the transmetallation peak previously identified in 3.2.1 appears here as the sole observable species (**Ia**), clearly indicating that transmetallation does occur with cationic Au(I). The absence of any peak around 22.8 ppm strongly suggest that the radical addition/SET sequence does *not* occur with PPh_3Au^+ in presence of the arylboronic acid, since **6** (and by implication **V**) is not detected. While short-lived phosphorus-based species such as **III** and **II** should exist during the reaction, their lifetimes are too short to be observed on the NMR timescale (reductive elimination steps involving Au(III) can be extremely fast, see: W. J. Wolf, M. S. Winston and F. D. Toste, *Nat. Chem.*, 2014, **6**, 159). Concurrently, ^{1}H NMR reveals the formation of the coupling product **3aa**, supporting the aforementioned *transmetallation first* hypothesis. After 16 h, the catalyst peak (28.4 ppm) started to reappear. (The reaction did not go to completion on the timescale of the NMR experiment due to the higher dilution of the stoichiometric reaction.)

3.2.5 – Gold/photoredox catalytic reaction with PPh_3AuCl

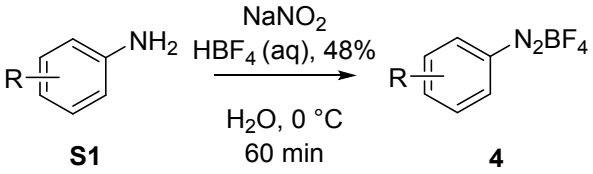
Figure S5: ^{31}P NMR spectra



When the reaction is catalysed by PPh_3AuCl, the absence of a peak at 44.3 ppm reveals that the Au(I) transmetallated species **Ia** is *not* formed during the reaction. However, the presence of the peak at 22.8 ppm, accounting for the formation of tetraphenylphosphonium **6** indicates that the transformation occurs through an oxidation/transmetallation sequence, as opposed to 3.2.4 (Figure S4). Indeed, ^1H NMR indicates the formation of the coupling product over time.

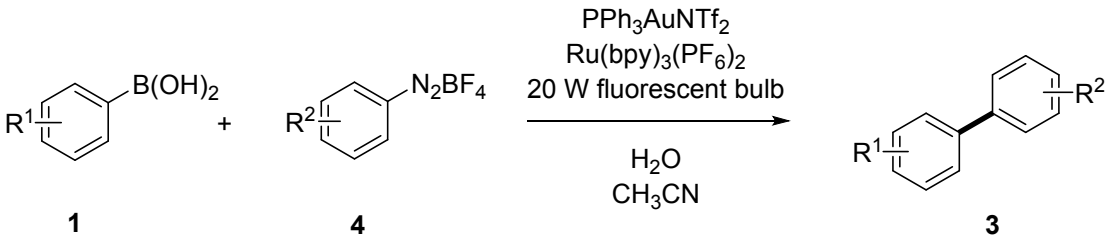
Based on these observations, it is clear that the cationic and neutral Au(I) catalysts follow distinct mechanistic pathways. These divergent pathways make sense in light of the fact that unlike PPh_3AuNTf_2, the neutral PPh_3AuCl is unable to transmetallate with arylboronic acids,[6] so radical addition and SET to the reactive Au(III) species **V** occurs first to allow subsequent transmetallation. In contrast, transmetallation can occur prior to radical addition and SET when the more active cationic PPh_3AuNTf_2 catalyst is used.

4-General procedure for the preparation of diazonium salts



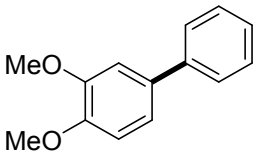
Diazonium salts were prepared according to literature procedures.[5] Under air, in a round-bottom flask, the corresponding aniline **S1** (3 mmol) was suspended in an aqueous solution of HBF_4 (1 ml) and cooled to 0 °C. A solution of sodium nitrate (207 mg, 3 mmol, 1 equiv.) in water (1 ml) was then added dropwise and the reaction mixture was stirred for 60 minutes at 0 °C. Upon completion of the reaction, the mixture was filtered and the residue washed once with cold water. The residual solid was then dissolved in a minimum amount of acetone, and precipitation of the diazonium salt was induced by addition of diethyl ether. The solid was filtered and dried under vacuum to afford the corresponding diazonium salt **4**. All salts were used without further purification.

5-General procedure for the dual-catalysed preparation of biaryls compounds



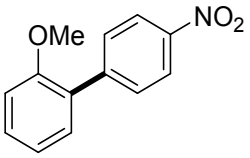
A Schlenk tube was loaded with the diazonium salt **4** (0.2 mmol, 2 equiv.), PPh_3AuNTf_2 (3.9 mg, $5x10^{-3}$ mmol, 5 mol%) and $Ru(bpy)_3(PF_6)_2$ (2.2 mg, $2.5x10^{-3}$ mmol). The reaction vessel was wrapped in aluminium foil before distilled water (108 µl, 60 eq.) and CH_3CN (1 ml) were added, and the mixture was degassed using 3 freeze-pump-thaw cycles. The mixture was allowed to warm up to room temperature and the arylboronic acid **1** (0.1 mmol, 1 equiv.) was added to the reaction vessel. The foil was removed and the reaction mixture was stirred for 16 h at room temperature, using a desk lamp fitted with a 20 W fluorescent bulb as the light source. The mixture was then diluted with EtOAc (10 ml) and the organic phase was washed with distilled water once. The aqueous phase was re-extracted once; the combined organic phases were washed with brine, dried over magnesium sulfate and evaporated *in vacuo*. The residue was subsequently purified by chromatography on silica gel using petroleum ether and ethyl acetate to yield the coupled product **3**. Spectral data for all known compound matched the literature. Spectra for new compounds can be found in Section 6.

Compound 3aa[7]



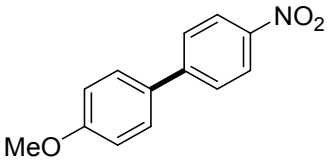
Yield : 17.8 mg, 0.083 mmol, 83%; **^{1}H NMR** : ($CDCl_3$,300 MHz): δ =7.57 - 7.62 (m, 2 H), 7.42 - 7.50 (m, 2 H), 7.31 - 7.39 (m, 1 H), 7.13 - 7.21 (m, 2 H), 6.99 (d, J=8.4 Hz, 1 H), 3.99 (s, 3 H), 3.96 ppm (s, 3 H); **^{13}C NMR** : $CDCl_3$,75 MHz): δ = 149.2, 148.6, 141.1, 134.3, 128.7, 126.9, 126.8, 119.4, 111.5, 110.5, 56.0, 55.9 ppm; **HRMS:** (FTMS + p NSI) $[M + H]^+$ found 215.1064, $C_{14}H_{15}O_2$ requires 215.1067.

Compound 3bb[8]



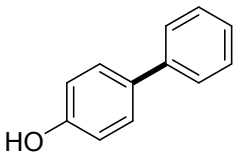
Yield : 20.9 mg, 0.091 mmol, 91%; **^{1}H NMR** : ($CDCl_3$,300 MHz): δ = 8.29 (d, J=9.0 Hz, 2 H), 7.73 (d, J=9.0 Hz, 2 H), 7.33 - 7.49 (m, 2 H), 7.02 - 7.15 (m, 2 H), 3.87 ppm (s, 3 H); **^{13}C NMR** : ($CDCl_3$,75 MHz): δ = 156.4, 146.7, 145.5, 130.7, 130.4, 130.2, 128.3, 123.2, 121.1, 111.4, 55.6 ppm; **HRMS**: (ASAP+) $[M+H]^+$ found 230.0817, $C_{13}H_{12}NO_3$ requires 230.0816.

Compound 3cb[8]



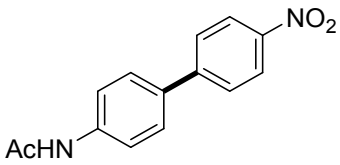
Yield : 21.1 mg, 0.092 mmol, 92%; **^{1}H NMR** : ($CDCl_3$,300 MHz): δ = 8.31 (d, J=8.9 Hz, 2 H), 7.73 (d, J=9.0 Hz, 2 H), 7.61 (d, J=8.9 Hz, 2 H), 7.06 (d, J=8.9 Hz, 2 H), 3.91 ppm (s, 3 H); **^{13}C NMR** : ($CDCl_3$,75 MHz): δ = 160.5, 147.3, 146.6, 131.1, 128.6, 127.1, 124.2, 114.6, 55.5 ppm; **HRMS**: (ASAP+) $[M+H]^+$ found 230.0817, $C_{13}H_{12}NO_3$ requires 230.0819.

Compound 3da[7]



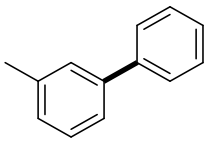
Yield : 12.4 mg, 0.073 mmol, 73%; **^{1}H NMR** : ($CDCl_3$,300 MHz): δ = 7.41 - 7.61 (m, 6 H), 7.30 - 7.37 (m, 1 H), 6.90 - 6.98 ppm (m, 2 H); **^{13}C NMR** : ($CDCl_3$,75 MHz): δ = 155.2, 140.8, 134.1, 128.7, 128.4, 126.7, 115.6 ppm; **HRMS:** (ASAP) $[M]^+$ found 170.0732, $C_{12}H_{10}O$ requires 170.0729.

Compound 3eb[9]



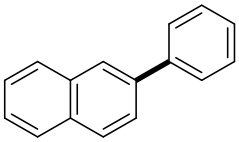
Yield : 22.8 mg, 0.089 mmol, 89%; **^{1}H NMR** : ($CDCl_3$,300 MHz): δ = 8.24 - 8.38 (m, 2 H), 7.55 - 7.82 (m, 6 H), 2.26 ppm (s, 3 H); **^{13}C NMR** : ($CDCl_3$,75 MHz): δ = 168.3, 147.0, 146.8, 138.7, 134.5, 128.0, 127.4, 124.2, 120.2, 24.7 ppm; **HRMS:** (ASAP+) $[M+H]^+$ found 257.0926, $C_{14}H_{12}N_2O_3$ requires 257.0928.

Compound 3fa[10]



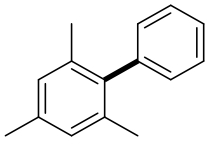
Yield : 14.5 mg, 0.086 mmol, 86%; **^{1}H NMR** : ($CDCl_3$,300 MHz): δ = 7.57 - 7.64 (m, 2 H), 7.39 - 7.49 (m, 4 H), 7.31 - 7.38 (m, 2 H), 7.16 - 7.21 (m, 1 H), 2.44 ppm (s, 3 H); **^{13}C NMR** : ($CDCl_3$,75 MHz): δ = 141.3, 141.2, 138.3, 128.8, 128.7, 128.7, 128, 127.9, 127.2, 124.3, 21.5 ppm; **HRMS**: (EI+) $[M]^+$ found 168.0939, $C_{13}H_{12}$ requires 168.0932.

Compound 3ga[10]



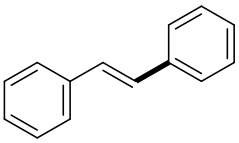
Yield : 14.3 mg, 0.07 mmol, 70%; **^{1}H NMR** : ($CDCl_3$,300 MHz): δ = 8.09 (d, J=1.8 Hz, 1 H), 7.88 - 8.00 (m, 3 H), 7.74 - 7.84 (m, 3 H), 7.49 - 7.60 (m, 4 H), 7.39 - 7.47 ppm (m, 1 H); **^{13}C NMR** : ($CDCl_3$,75 MHz): δ = 141.1, 138.6, 133.7, 132.6, 128.9, 128.4, 128.2, 127.7, 127.5, 127.4, 126.3, 126,0, 125.8, 125.6 ppm; **HRMS**:(EI+) $[M]^+$ found 204.0931, $C_{16}H_{12}$ requires 204.0939.

Compound 3ha[11]



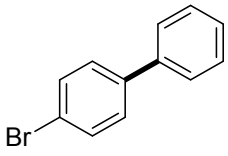
Yield : 77% (NMR yield, dimethylsulfone used as the internal standard); **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 7.32 - 7.50 (m, 4 H), 7.13 - 7.22 (m, 2 H), 6.98 (s, 2 H), 2.37 (s, 3 H), 2.04 ppm (s, 6 H); **^{13}C NMR** : ($CDCl_3$,75 MHz): δ = 141.1, 129.3, 128.8, 128.4, 128.0, 127.3, 127.2, 126.5, 21.0, 20.8 ppm; **HRMS**: (EI+) $[M]^+$ found 196.1252, $C_{15}H_{16}$ requires 196.1245.

Compound 3ja[12]



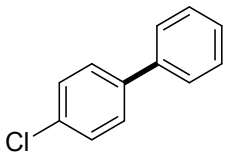
Yield : 7.1 mg, 0.039 mmol, 39%; **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 7.18 - 7.31 (m, 10 H), 6.64 ppm (s, 2 H); **^{13}C NMR** : ($CDCl_3$, 75 MHz): δ = 136.2, 129.2, 127.8, 127.2, 126.1 ppm; **HRMS:** (EI+) $[M]^+$ found 180.0939, $C_{14}H_{12}$ requires 180.0931.

Compound 3ka[13]



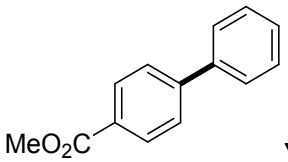
Yield : 19.9 mg, 0.085 mmol, 85%; **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 7.56 - 7.64 (m, 4 H), 7.44 - 7.55 (m, 4 H), 7.35 - 7.44 ppm (m, 1 H)**^{13}C NMR** : ($CDCl_3$, 75 MHz): δ = 140.2, 140, 131.9, 128.9, 128.8, 127.7, 127, 121.6 ppm; **HRMS:** (EI+) $[M]^+$ found 231.9880, $C_{12}H_9Br$ requires 231.9882.

Compound 3la[14]



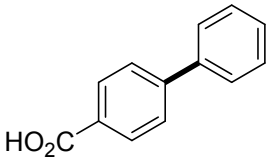
Yield : 16.6 mg, 0.088 mmol, 88%; **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 7.52 - 7.66 (m, 4 H), 7.36 - 7.52 ppm (m, 5 H); **^{13}C NMR** : ($CDCl_3$, 75 MHz): δ = 140, 139.7, 133.4, 128.9, 128.9, 128.4, 127.6, 127.0 ppm; **HRMS**: (EI+) $[M]^+$ found 188.0383, $C_{12}H_9Cl$ requires 188.0387.

Compound 3ma[11]



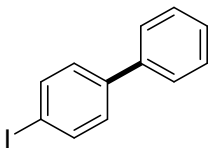
Yield : 55%; **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 8.10 - 8.18 (m, 2 H), 7.62 - 7.75 (m, 4 H), 7.38 - 7.55 (m, 3 H), 3.98 ppm (s, 3 H); **^{13}C NMR** : ($CDCl_3$,75 MHz): δ = 167.0, 145.7, 140.0, 130.1, 128.9, 128.9, 128.1, 127.3, 127.1, 52.2 ppm; **HRMS**: (FTMS + p NSI) $[M + H]^+$ found 213.0911, $C_{14}H_{13}O_2$ requires 213.0915.

Compound 3na[11]



Purification of this product was carried out in a slightly different manner. The crude reaction mixture was filtered through a silica plug, using CH_2Cl_2 as the eluent. All volatiles were removed, and the residue was re-dissolved in a minimum amount of CH_2Cl_2. Precipitation was induced by petroleum ether, and the resulting solid was filtered to afford compound **3ja**. **Yield** : 12.1 mg, 0.061 mmol, 61%; **^{1}H NMR** : ($CDCl_3$,300 MHz): δ = 8.19 - 8.27 (m, 2 H), 7.72 - 7.77 (m, 2 H), 7.64 - 7.71 (m, 2 H), 7.41 - 7.55 ppm (m, 3 H); **^{13}C NMR** : ($CDCl_3$,75 MHz): δ = 171.2, 146.5, 139.9, 130.8, 129.0, 128.3, 127.9, 127.3, 127.2 ppm; **HRMS:** (FTMS – p NSI) $[M-H]^-$ found 197.0610, $C_{13}H_{12}NO_3$ requires 197.0608.

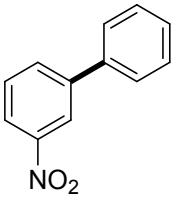
Compound 3oa[15]



Yield : 905 mg, 0.034 mmol, 34%; **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 7.80 (d, J=8.4 Hz, 2 H), 7.57 (m, 2 H), 7.47 (m, 2 H), 7.36 ppm (m, 3 H); **^{13}C NMR** : ($CDCl_3$, 75 MHz): δ =

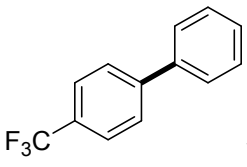
140.7, 140.1, 137.8, 129.0, 128.9, 127.7, 126.9, 93.0 ppm; **HRMS:** (ASAP+) $[M]^+$ found 279.9749, $C_{12}H_{19}I$ requires 279.9748.

Compound 3pa[14]



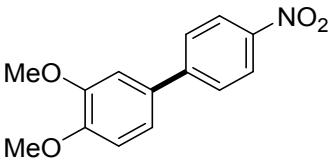
Yield : 9.4 mg, 0.047 mmol, 47% **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 8.50 (t, J=1.8 Hz, 1 H), 8.24 (ddd, J=8.2, 2.4, 1.0 Hz, 1 H), 7.91 - 8.00 (m, 1 H), 7.63 - 7.73 (m, 3 H), 7.42 - 7.60 ppm (m, 3 H)**^{13}C NMR** : ($CDCl_3$,75 MHz): δ = 143, 138.7, 133.1, 129.7, 129.2, 128.6, 127.2, 122.1, 122.0 ppm; **HRMS:** (ASAP+) $[M + H]^+$ found 200.0714 $C_{13}H_9NO_2$ requires 200.0633.

Compound 3qa[16]



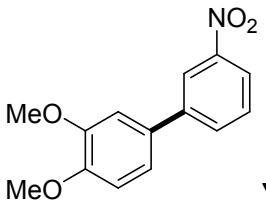
Yield : 7.6 mg, 0.034 mmol, 34%; **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 7.73 (s, 4 H), 7.60 - 7.67 (m, 2 H), 7.40 - 7.55 ppm (m, 3 H); **^{13}C NMR** : ($CDCl_3$, 75 MHz): δ = 144.8, 139.8, 129.0, 128.2, 127.4, 127.3, 125.7 (q, J=3.7 Hz) ppm; **HRMS**: (EI+) $[M]^+$ found 222.0656, $C_{13}H_9F_3$ requires 222.0650.

Compound 3ab[17]



Yield : 21.3 mg, 0.082 mmol, 82%; **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 8.31 (dt, J=8.8, 3.0 Hz, 2 H), 7.73 (dt, J=9.0, 3.0 Hz, 2 H), 7.12 - 7.28 (m, 2 H), 7.02 (d, J=8.4 Hz, 1 H), 4.01 (s, 3 H), 3.98 ppm (s, 3 H); **^{13}C NMR** : ($CDCl_3$, 75 MHz): δ = 150.0, 149.5, 147.4, 146.7, 131.5, 127.3, 124.1, 120.1, 111.6, 110.4, 56.1, 56.1 ppm; **HRMS:** (ASAP+) $[M + H]^+$ found 260.0923, $C_{14}H_{14}NO_4$ requires 260.0923.

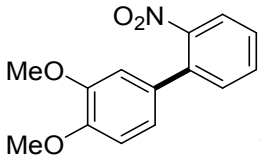
Compound 3ac



Yield : 18.7 mg, 0.072 mmol, 72%; **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 8.44 (t, J=3.1 Hz, 1 H), 8.19 (ddd, J=8.1, 2.2, 1.1 Hz, 1 H), 7.91 (ddd, J=8.1, 2.1, 1.1 Hz, 1 H), 7.62 (t, J=8.1 Hz, 1 H), 7.13 - 7.25 (m, 2 H), 7.02 (d, J=8.4 Hz, 1 H), 4.01 (s, 3 H), 3.98 ppm (s, 3 H); **^{13}C**

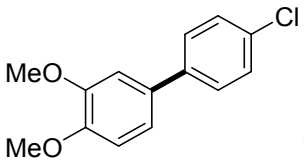
NMR : ($CDCl_3$,75 MHz): δ = 149.6, 148.7, 142.7, 134.1, 132.7, 129.7, 129.3, 129.2, 121.6, 117.7, 111.6, 110.2, 56.1, 56.0 ppm; **HRMS**: (ASAP+) $[M + H]^+$ found 260.0923, $C_{14}H_{14}NO_4$ requires 260.0922.

Compound 3ad[18]



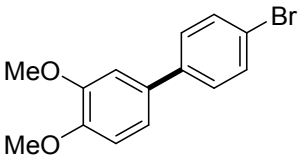
Yield : 10.1 mg, 0.039 mmol, 39%; **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 7.83 (dd, J=9.0, 2.9 Hz, 1 H), 7.60 - 7.67 (m, 1 H), 7.46 - 7.52 (m, 2 H), 6.94 - 6.97 (m, 1 H), 6.84 - 6.94 (m, 2 H), 3.95 (s, 3 H), 3.92 ppm (s, 3 H); **^{13}C NMR** : ($CDCl_3$, 75 MHz): δ = 149.2, 149.1, 140.0, 135.9, 132.1, 131.9, 129.7, 127.9, 123.9, 120.4, 111.3, 111.1, 56.0, 55.9 ppm; **HRMS:** (FTMS + p NSI) $[M + NH_4]^+$ found 277.1184, $C_{14}H_{13}NO_4$ requires 277.1183.

Compound 3ae[7]



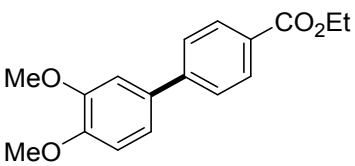
Yield : 19.1 mg, 0.077 mmol, 77%; **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ =7.51 (dt, J=8.9, 2.9 Hz, 2 H), 7.42 (dt, J=9.0, 2.9 Hz, 2 H), 7.07 - 7.17 (m, 2 H), 6.97 (d, J=8.1 Hz, 1 H), 3.98 (s, 3 H), 3.96 ppm (s, 3 H); **^{13}C NMR** : ($CDCl_3$, 75 MHz): δ = 148.2, 147.8, 138.5, 131.9, 131.8, 127.8, 127.0, 118.3, 110.5, 109.2, 54.0, 54.0 ppm; **HRMS:** (FTMS + p NSI) $[M + Na]^+$ found 271.0499, $C_{14}H_{13}ClO_2Na$ requires 271.0496.

Compound 3af[7]



Yield :22 mg, 0.075 mmol, 75%; **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 7.57 (dt, J=9.1, 2.8 Hz, 2 H), 7.45 (dd, J=9.0, 2.9 Hz, 2 H), 7.08 - 7.17 (m, 2 H), 6.97 (d, J=8.4 Hz, 1 H), 3.98 (s, 3 H), 3.96 ppm (s, 3 H); **^{13}C NMR** : ($CDCl_3$, 75 MHz): δ = 149.3, 148.9, 140.0, 133.0, 131.8, 128.4, 121, 119.3, 111.6, 110.2, 56.0, 56.0 ppm; **HRMS:** (FTMS + p NSI) $[M + Na]^+$ found 314.9993, $C_{14}H_{13}BrO_2Na$ requires 314.9991.

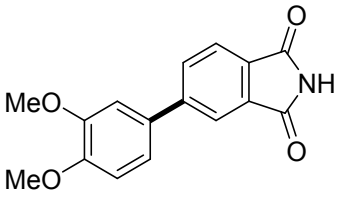
Compound 3ah[7]



Yield : 23.7 mg, 0.083 mmol, 83%; **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 8.12 (dt, J=8.9, 3.0 Hz, 2 H), 7.65 (dt, J=9.0, 3.1 Hz, 2 H), 7.15 - 7.27 (m, 2 H), 7.00 (d, J=8.1 Hz,

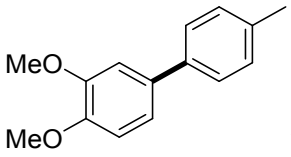
1 H), 4.43 (q, J=8.8 Hz, 2 H), 4.00 (s, 3 H), 3.97 (s, 3 H), 1.45 ppm (t, J=9.0 Hz, 3 H); **^{13}C NMR** : ($CDCl_3$, 75 MHz): δ = 166.6, 149.3, 149.3, 145.3, 133.0, 130.1, 128.8, 126.6, 119.8, 111.5, 110.4, 61.0, 56.0, 56.0, 14.4 ppm; **HRMS:** (FTMS + p NSI) $[M + H]^+$ found 287.1278, $C_{17}H_{19}O_4$ requires 287.1278.

Compound 3ai



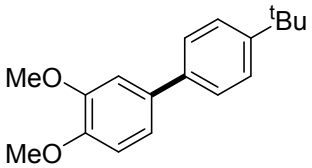
Yield : 16.4 mg, 0.058 mmol, 58%; **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 8.08 (s, 1 H), 7.89 - 8.00 (m, 2 H), 7.55 (br. s., 1 H), 7.14 - 7.28 (m, 2 H), 7.03 (d, J=8.1 Hz, 1 H), 4.01 (s, 3 H), 3.99 ppm (s, 3 H); **^{13}C NMR** : ($CDCl_3$, 100 MHz): δ = 167.8, 167.6, 150.1, 149.6, 147.7, 133.5, 132.4, 131.7, 130.4, 124.1, 121.7, 120.1, 111.7, 110.4, 56.1, 56.0 ppm; **HRMS**: (ASAP+) $[M + H]^+$ found 284.0923, $C_{18}H_{23}O_2$ requires 284.0923.

Compound 3aj[19]



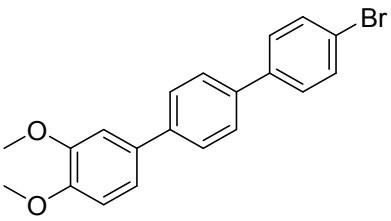
Yield : 16.4 mg, 0.072 mmol, 72%; **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 7.48 (d, J=8.2 Hz, 2 H), 7.27 (d, J=7.7 Hz, 2 H), 7.11 - 7.19 (m, 2 H), 6.97 (d, J=8.4 Hz, 1 H), 3.98 (s, 3 H), 3.95 (s, 3 H), 2.42 ppm (s, 3 H); **^{13}C NMR** : ($CDCl_3$, 75 MHz): δ = 149.2, 148.4, 138.2, 136.5, 134.3, 129.5, 129.7, 119.2, 111.5, 110.4, 56.0, 55.9, 21.1 ppm; **HRMS:** (FTMS + p NSI) $[M + H]^+$ found 229.1221, $C_{15}H_{17}O_2$ requires 229.1223.

Compound 3ak



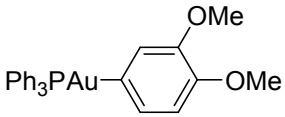
Yield : 10.3 mg, 0.038 mmol, 38%; **^{1}H NMR** : ($CDCl_3$, 300 MHz): δ = 7.46 - 7.57 (m, 4 H), 7.13 - 7.20 (m, 2 H), 6.97 (d, J=8.1 Hz, 1 H), 3.98 (s, 3 H), 3.96 (s, 3 H), 1.40 ppm (s, 9 H); **^{13}C NMR** : ($CDCl_3$, 75 MHz): δ = 149.9, 149.1, 148.4, 138.2, 134.2, 126.5, 125.7, 119.2, 111.5, 110.4, 56.0, 55.9, 34.5, 31.4 ppm; **HRMS**: (FTMS + p NSI) $[M + H]^+$ found 271.1691, $C_{18}H_{23}O_2$ requires 271.1693.

Compound 5[20]



This compound was prepared according to literature procedure, using crude **3ag** as the starting material. **Yield** : 15.9 mg, 0.043mmol, 83% from **3ag**, (43% over two steps); **^{1}H NMR** : ($CDCl_3$,400 MHz): δ = 7.58 - 7.70 (m, 6 H), 7.51 - 7.56 (m, 2 H), 7.16 - 7.26 (m, 2 H), 7.01 (d, J=8.5 Hz, 1 H), 4.01 (s, 3 H), 3.97 ppm (s, 3 H); **^{13}C NMR** : ($CDCl_3$,75 MHz): δ = 149.3, 148.9, 140.4, 139.7, 138.5, 133.6, 131.9, 128.6, 127.3, 127.3, 121.6, 119.4, 111.6, 110.4, 56.1, 56.0 ppm; **HRMS**: (FTMS + p NSI) $[M + H]^+$ found 369.0488, $C_{20}H_{18}BrO_2$ requires 369.0485.

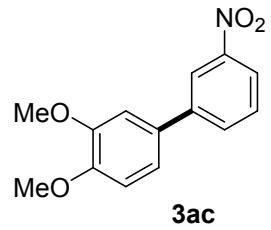
Compound Ia



This compound was prepared according to literature.[3] In a Schlenk tube, 3,4-dimethoxyphenylboronic acid (40mg, 0.22 mmol) and cesium carbonate (71.7 mg, 0.22 mmol) were suspended in dry isopropanol (1 ml). Ph_3PAuCl (49.5 mg, 0.1 mmol) was added to the suspension and the mixture was heated to 50 °C for 24 h. Volatiles were removed via rotary evaporation, the residue was taken in 20 ml of benzene and filtered through Celite®. The filtrate was evaporated *in vacuo* and the residual solid was recrystallized from benzene/hexanes to yield **Ia** as a white solid. **Yield** : 44.7 mg, 0.075 mmol, 75% **^{1}H NMR** : (C_6D_6, 400 MHz): δ = 7.65 - 7.77 (m, 2 H), 7.38 - 7.54 (m, 6 H), 7.04 (d, J=7.6 Hz, 1 H), 6.88 - 7.01 (m, 9 H), 3.65 (s, 3 H), 3.55 ppm (s, 3 H); **^{13}C NMR** : (C_6D_6 ,75 MHz): δ = 149.9 (s), 149.0 (s), 134.5 (d, J_{C-P}= 13.4 Hz), 132.5 (s), 131.9 (s), 131.4 (s), 130.8 (d, J_{C-P}= 2.20 Hz), 129.0 (d, J_{C-P}= 10.7 Hz), 124.4 (s), 112.6 (s), 55.9 (s), 55.7 (s) ppm. **^{31}P NMR**: (C_6D_6, 162 MHz): δ = 43.4 ppm; **HRMS**: (ASAP+) $[M + H]^+$ found 597.1257, $C_{26}H_{24}AuO_2PH$ requires 597.1258.

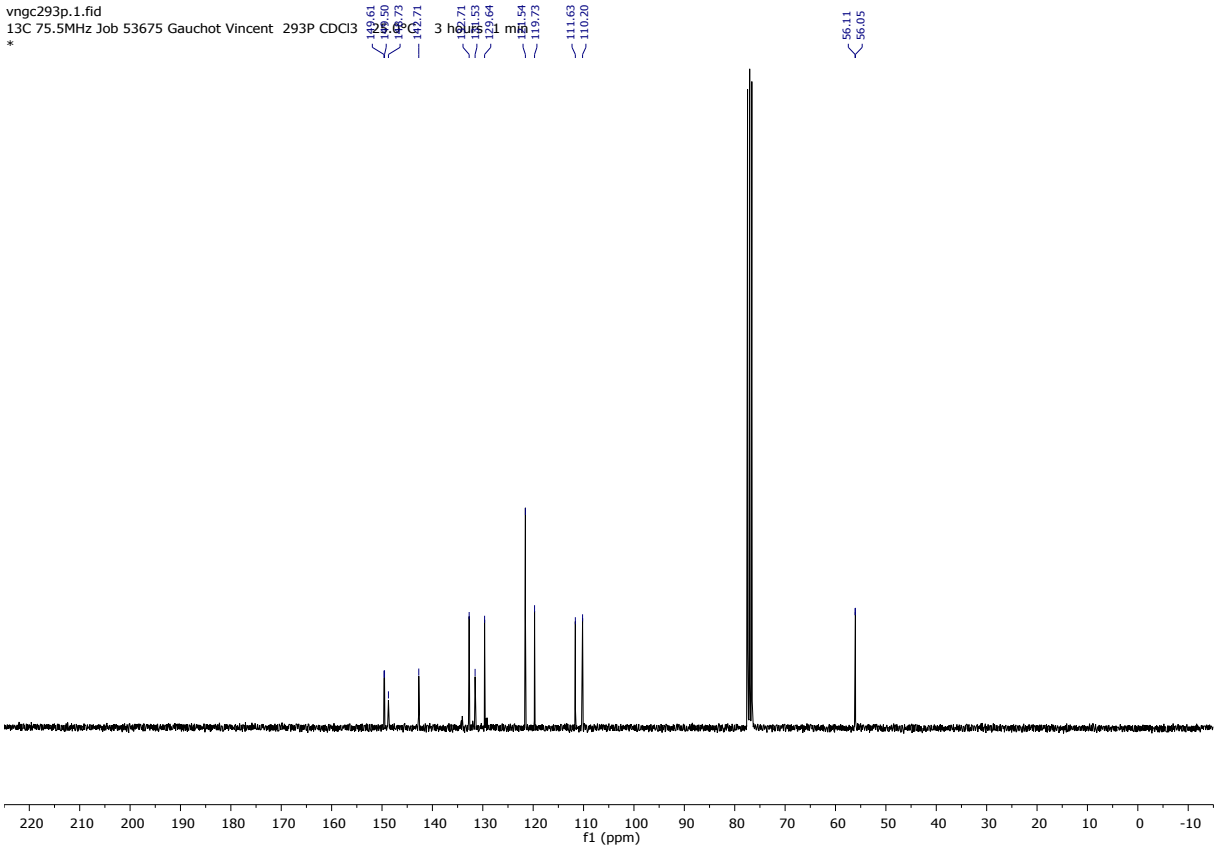
6-Relevant NMR Spectra

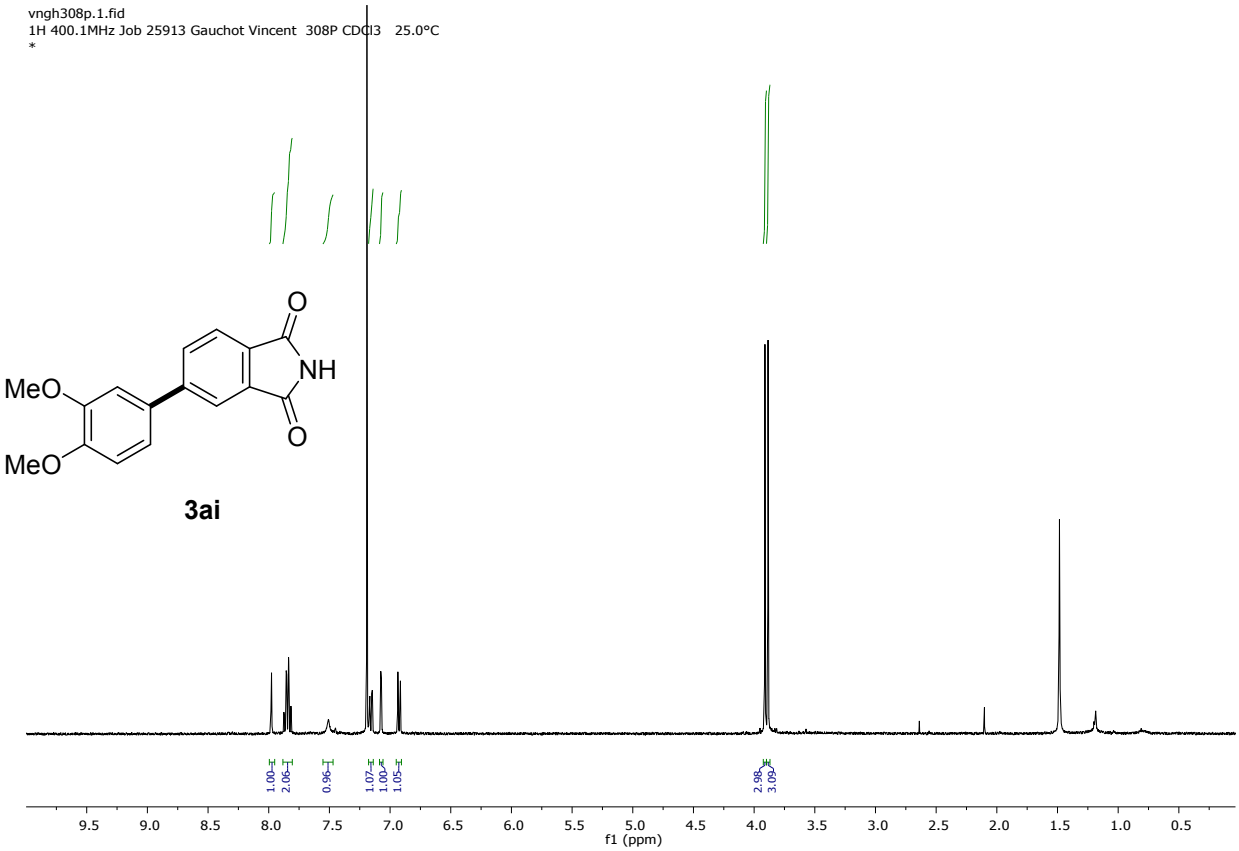
vngh293p.1.fid
1H 300.1MHz Job 53618 Gauchot Vincent 293P CDCl3 25.1°C
*

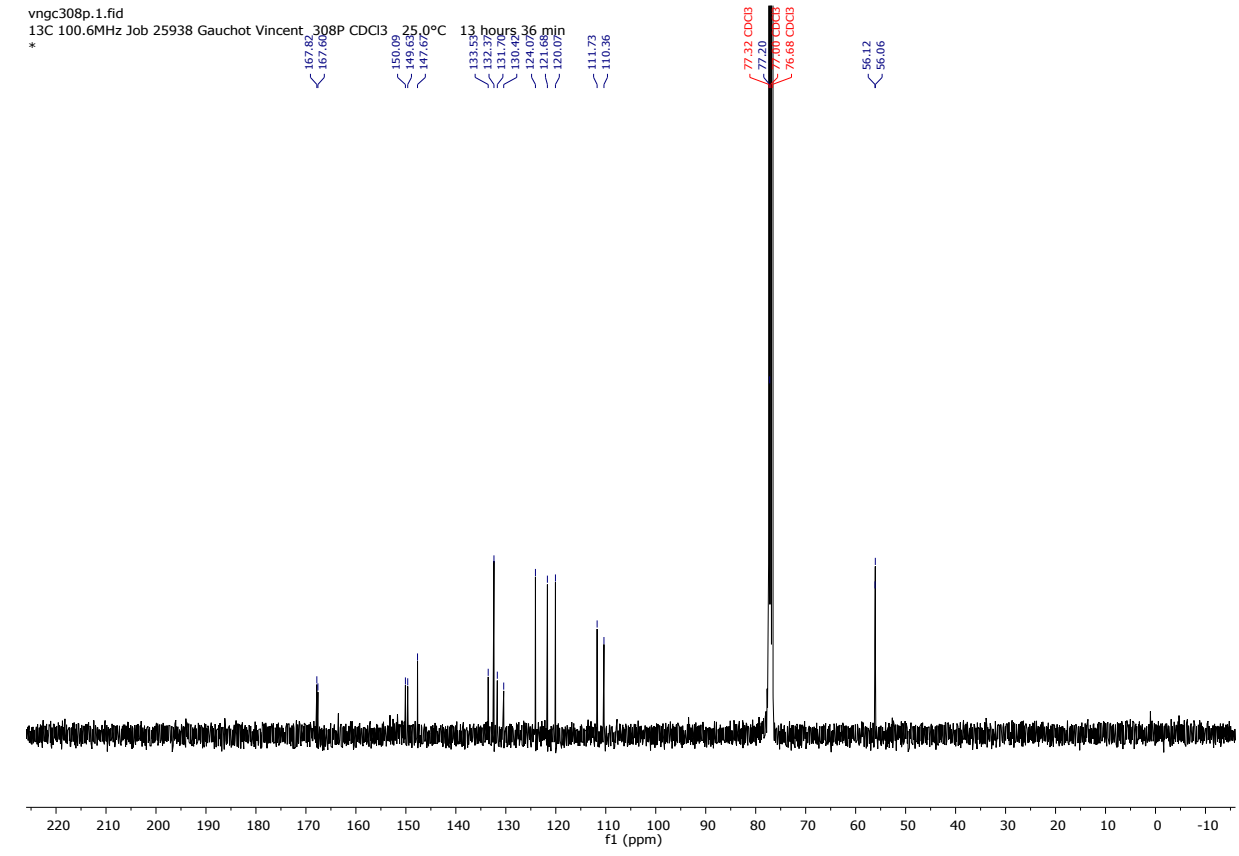


3ac

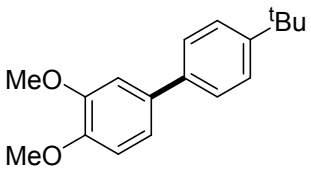
vngc293p.1.fid
13C 75.5MHz Job 53675 Gauchot Vincent 293P CDCl3 25.6°C 3 hours 21 min
*




vngh308p.1.fid
1H 400.1MHz Job 25913 Gauchot Vincent 308P CDCl3 25.0°C
*
O
NH
O
MeO
MeO
3ai
1.00
2.06
0.96
1.07
1.00
1.05
2.98
3.09
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

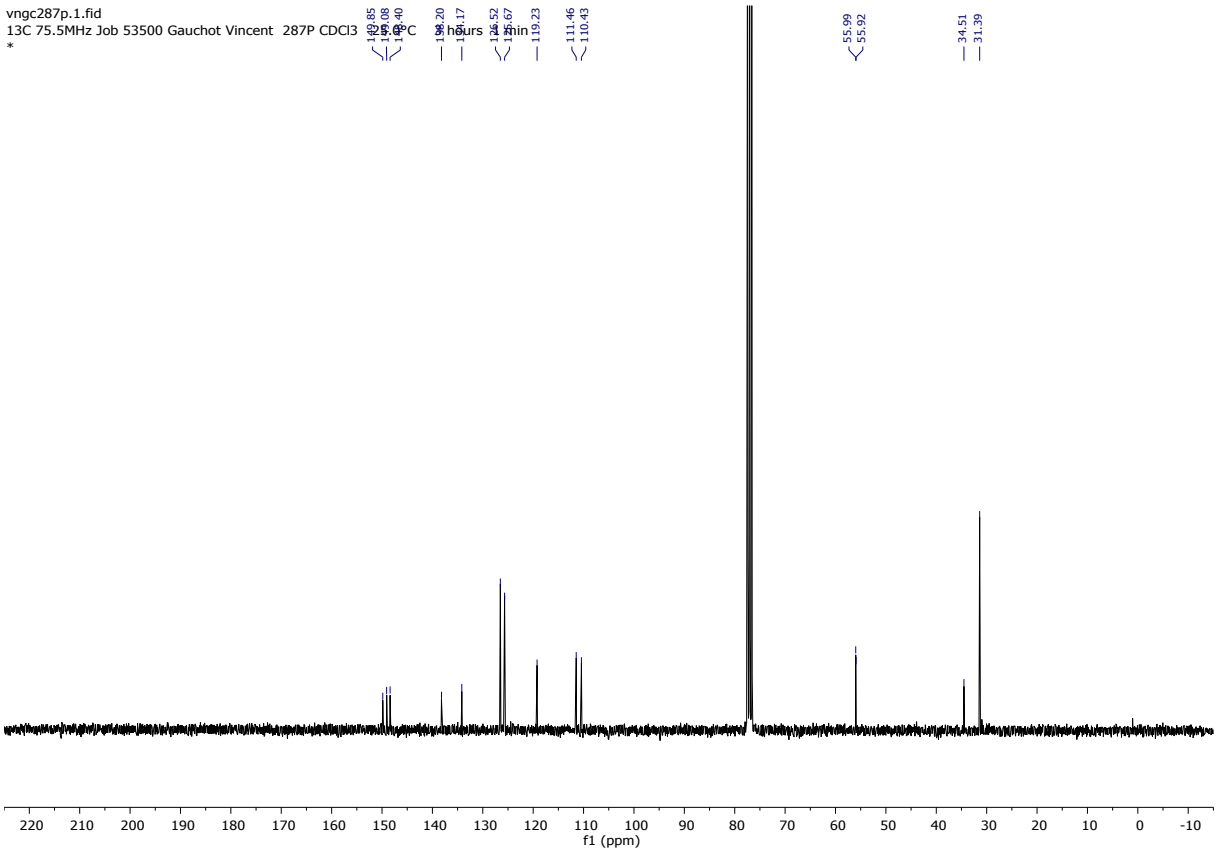

vngc308p.1.fid
13C 100.6MHz Job 25938 Gauchot Vincent 308P CDCl3 25.0°C 13 hours 36 min
*
167.82
167.60
150.09
149.63
147.67
133.53
132.37
131.70
130.42
124.07
121.68
120.07
111.73
110.36
77.32 CDCl3
77.20
77.00 CDCl3
76.68 CDCl3
56.12
56.06
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

vngh287p.1.fid
1H 300.1MHz Job 53459 Gauchot Vincent 287P CDCl3 25.0°C
*

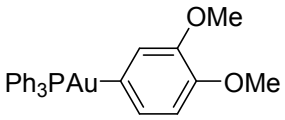


3ak

vngc287p.1.fid
13C 75.5MHz Job 53500 Gauchot Vincent 287P CDCl3 25.0°C 14 hours 5 min
*

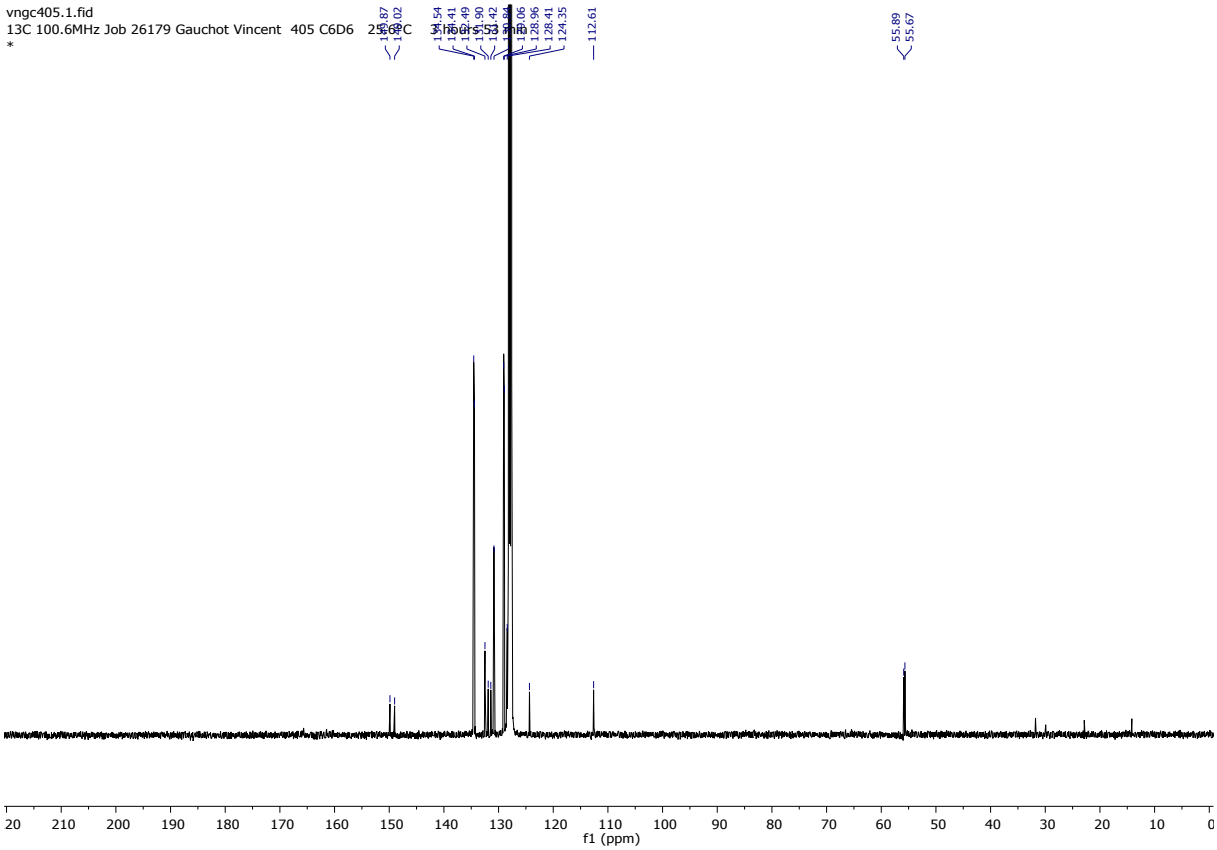


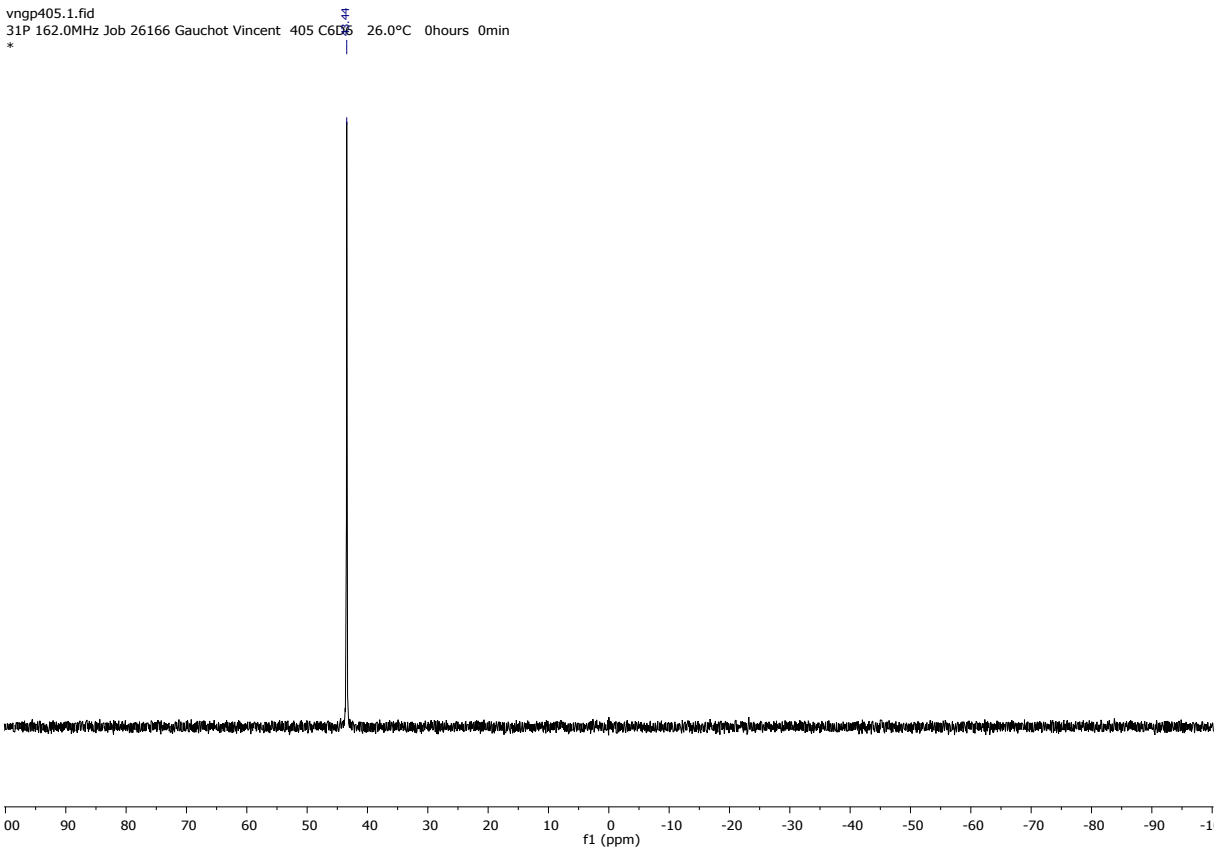
vngh405.1.fid
1H 400.1MHz Job 26165 Gauchot Vincent 405 C6D6 25.0°C
*



Ia

vngc405.1.fid
13C 100.6MHz Job 26179 Gauchot Vincent 405 C6D6 25.0°C
*




vngp405.1.fid
31P 162.0MHz Job 26166 Gauchot Vincent 405 C6D6 26.0°C 0hours 0min
*
36.44
00 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -1
f1 (ppm)

7-REFERENCES

1. G. Barker, S. Webster, D. G. Johnson, R. Curley, M. Andrews, P. C. Young, S. A. Macgregor and A.-L. Lee, *J. Org. Chem.*, 2015, **80**, 9807-9816.
2. D. Weber, T. D. Jones, L. L. Adduci and M. R. Gagne, *Angew. Chem. Int. Ed.*, 2012, **51**, 2452-2456.
3. S. Pankajakshan and T. P. Loh, *Chem - Asian J.*, 2011, **6**, 2291-2295.
4. E. Tkatchouk, N. P. Mankad, D. Benitez, W. A. Goddard, 3rd and F. D. Toste, *J. Am. Chem. Soc.*, 2011, **133**, 14293-14300.
5. X. Z. Shu, M. Zhang, Y. He, H. Frei and F. D. Toste, *J. Am. Chem. Soc.*, 2014, **136**, 5844-5847.
6. E. Tkatchouk, N. P. Mankad, D. Benitez, W. A. Goddard and F. D. Toste, *J. Am. Chem. Soc.*, 2011, **133**, 14293-14300.
7. C. L. Ciana, R. J. Phipps, J. R. Brandt, F. M. Meyer and M. J. Gaunt, *Angew. Chem. Int. Ed.*, 2011, **50**, 458-462.
8. W. Yang, C. Liu and J. Qiu, *Chem. Commun.*, 2010, **46**, 2659.
9. H. Tye, M. Whittaker and S. Ramdeehul, *Comb. Chem. & High Throughput Screen.*, 2006, **9**, 703-710.
10. P. D. Stevens, J. Fan, H. M. Gardimalla, M. Yen and Y. Gao, *Org. Lett.*, 2005, **7**, 2085-2088.
11. J. Wen, J. Zhang, S. Y. Chen, J. Li and X. Q. Yu, *Angew. Chem. Int. Ed.*, 2008, **47**, 8897-8900.
12. R. Bandari, T. Hoche, A. Prager, K. Dirnberger and M. R. Buchmeiser, *Chem. - Eur. J.*, 2010, **16**, 4650-4658.
13. F.-X. Felpin and E. Fouquet, *Adv. Synth. & Catal.*, 2008, **350**, 863-868.
14. L. Bai and J.-X. Wang, *Adv. Synth. & Catal.*, 2008, **350**, 315-320.
15. H. Bonin, D. Delbrayelle, P. Demonchaux and E. Gras, *Chem. Commun.*, 2010, **46**, 2677-2679.
16. X. Bei, H. W. Turner, W. H. Weinberg, A. S. Guram and J. L. Petersen, *J. Org. Chem.*, 1999, **64**, 6797-6803.
17. L. Keller, M. V. Sanchez, D. Prim, F. Couty, G. Evano and J. Marrot, *J. Organomet. Chem.*, 2005, **690**, 2306-2311.
18. M. J. Lai, H. Y. Lee, H. Y. Chuang, L. H. Chang, A. C. Tsai, M. C. Chen, H. L. Huang, Y. W. Wu, C. M. Teng, S. L. Pan, Y. M. Liu, S. Mehndiratta and J. P. Liou, *J. Med. Chem.*, 2015, **58**, 6549-6558.
19. D. Wu and Z. X. Wang, *Org. Biomol. Chem.*, 2014, **12**, 6414-6424.
20. A. Lützen, M. Schiek and K. Al-Shamery, *Synthesis*, 2007, **2007**, 613-621.