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A dual visible light photoredox and gold-catalysed $C(sp^2)$ – $C(sp^2)$ cross coupling is described. The success of this mild, oxidant- and base-free cross coupling is highly dependent on the amount of water added. Mechanistic studies show two distinct pathways depending on the gold catalyst employed: transmetallation of the arylboronic acid with gold(i) occurs prior to oxidation of gold(i) to gold(iii) using cationic gold(i) catalysts, whereas oxidation of gold(i) to gold(iii) precedes transmetallation using neutral gold(i) catalysts.

Over the past two decades, homogenous gold catalysis has emerged as a powerful and versatile tool for C–C and C–heteroatom bond formation. By virtue of its excellent carbophilicity, gold(i) complexes have traditionally been used to activate unsaturated C–C bonds towards nucleophilic attack, whereby the gold species typically does not change oxidation states throughout the catalytic cycle.¹ Nevertheless, in order to significantly expand the repertoire of gold-catalysed processes, there has been intense recent interest in developing Au(i)/Au(iii) catalytic processes.² However, unlike the readily accessible Pd(0)/Pd(II) cycle, the high redox potential of the Au(i)/Au(iii) redox couple ($E_0 = 1.41$ V)³ means that strong oxidative conditions are usually required to access Au(i)/Au(iii) catalytic processes. While these seminal works⁴ have proven that Au(i)/Au(iii) catalytic cycles are accessible and can be used as powerful cross-coupling strategies, the use of typically super-stoichiometric, strong external oxidants negates one of the attractive features of gold-catalysis: mild reaction conditions and functional group tolerance. In order to circumvent the use of strong oxidants, the groups of Glorius⁵ and Toste^{6,7} have recently demonstrated the elegant use of dual gold and photoredox⁸ catalytic systems:⁹ a photosensitiser and an aryl radical source combined with visible light irradiation to access the Au(i)/Au(iii) catalytic cycles under mild conditions.¹⁰

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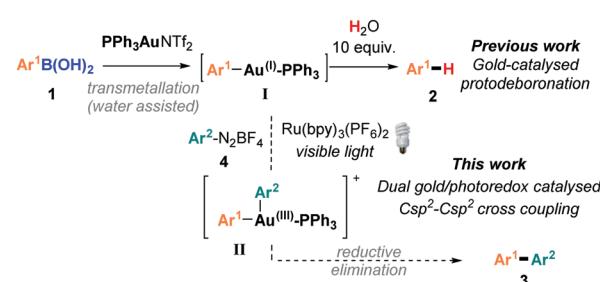
† Electronic supplementary information (ESI) available: Experimental procedures, full optimisation and control studies, mechanistic studies, characterisation data and copies of NMR spectra of new compounds. See DOI: 10.1039/c6cc05078f

Dual gold photoredox $C(sp^2)$ – $C(sp^2)$ cross couplings – development and mechanistic studies†

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While visible light-mediated gold-catalysed $C(sp^2)$ – $C(sp^2)$ cross couplings to form aryl-alkynes have been very recently reported,^{5c,6b} there are, to the best of our knowledge, no examples of $C(sp^2)$ – $C(sp^2)$ biaryl couplings using dual gold/photoredox catalysts.^{11,12} Since we recently disclosed that arylboronic acids **1** readily transmetallate with $\text{PPh}_3\text{AuNTf}_2$ to form the arylgold species **I**,^{13–15} which regenerates the gold(i) catalyst upon protodeauration, we hypothesised that it should be possible to trap the arylgold intermediate **I** using photoredox catalysis and diazonium salts **4**, in order to achieve the first dual/photoredox catalysed $C(sp^2)$ – $C(sp^2)$ biaryl couplings (Scheme 1). Upon addition of an aryl radical onto the Au(i) catalyst and the subsequent SET, the resulting Au(iii) species **II** should undergo reductive elimination¹⁶ to yield **3**. However, a significant challenge lies in the propensity for **I** to protodeaurate in the presence of water, and our previous mechanistic studies showed that water is necessary for the transmetallation step to form **I**. Despite this conundrum, we herein disclose our successful attempts at overcoming this challenge to develop the first dual gold/photoredox catalysed $C(sp^2)$ – $C(sp^2)$ cross-couplings, along with our mechanistic studies.

We initiated our studies using **1a** and **4a**, with $\text{PPh}_3\text{AuNTf}_2$ as the gold(i) catalyst¹⁷ and $\text{Ru}(\text{bpy})_3(\text{PF}_6)_2$ as the photocatalyst (Table 1). As expected, a significant amount of the unwanted protodeboronated product **2a** was initially observed alongside **3aa**. A solvent screen identified MeCN as the most promising



Scheme 1 Dual gold/photoredox coupling between arylboronic acids and aryl diazonium salts.



Table 1 Significant impact of water content

Entry ^a	H ₂ O ^b (equiv.)	3aa : 2a ^c	Yield 3aa ^c (%)	Reaction conditions	
				PhN ₂ BF ₄ 4a (4 equiv.)	PPh ₃ AuNTf ₂ (10 mol%)
1	—	0.7 : 1	16	PPh ₃ AuNTf ₂ (10 mol%)	Ru(bpy) ₃ (PF ₆) ₂ (2.5 mol%)
2	1	1.7 : 1	41	20 W fluorescent bulb	
3	5	0.6 : 1	18	RT, 16 h, MeCN	
4	10	2.7 : 1	42	H ₂ O (x equivalents)	
5	50	4.2 : 1	70		
6	60	10 : 1	71 (70) ^d		
7	75	3.5 : 1	66		
8	60	>20 : 1	83 ^{d,e}		

^a 0.1 mmol scale in degassed MeCN (1 mL). ^b With respect to **1a**.

^c Determined by ¹H NMR analysis using dimethylsulfone as internal standard. ^d Isolated yield. ^e **4a** (2 equiv.), PPh₃AuNTf₂ (5 mol%), Ru(bpy)₃(PF₆)₂ (2.5 mol%).

solvent (see the ESI†), but the most significant change to improve the **3aa** : **2a** ratio proved to be the impact of water (Table 1).

As shown in Table 1, addition of 1 equiv. of water instantly increases the amount of coupling product (1.7 : 1 **3aa** : **2a**, entries 1 and 2). However, this trend is non-linear: 5 equiv. of water produces a poor result (entry 3). Interestingly, when 10 or more equiv. of water are added, the reaction mixture becomes homogeneous, thus allowing for better light irradiation through the reaction mixture. This translates into a significant increase in yield observed in favour of the coupling product **3aa** (entries 4–7). Surprisingly, this increase is once again non-linear. Our best results in this screen were obtained with 60 equiv. of water, yielding 70% **3aa** (entry 6). However, going above 60 equiv. leads to a significant drop in the product ratio (entry 7, see the ESI† for full study). We believe that this double-edged effect of water, as well as the non-linearity of the effect, can be attributed to three factors. Firstly, water is involved in aiding the transmetalation step (**1** → **I**, Scheme 1),¹³ which explains its beneficial effect. Working against this is the fact that water also promotes the undesired competing protodeboronation (**I** → **2**, Scheme 1). Thirdly, water affects the homogeneity of the reaction mixture, and therefore the ability of light to efficiently penetrate the mixture to promote photoredox coupling. Therefore, a delicate balance needs to be struck between all three factors. Finally, further optimisation (see the ESI†) improved the yield to 83% with >20 : 1 **3aa** : **2a** (entry 8). Control reactions show that only a trace amount of **3aa** is produced in the absence of the gold catalyst, the Ru catalyst, or light, confirming that the reaction is dual gold/photoredox catalysed (see the ESI†).

With these optimised conditions in hand, we commenced our substrate scope studies by investigating a range of arylboronic acids (Table 2). Since the system is base-free and mild, we expected the reaction to be tolerant to a range of different functional groups. Electron-rich aryl boronic acids are ideal coupling partners for this system, yielding the desired products with good to excellent yields (70–92%, **3aa**–**3ha**). The substitution pattern seems to have little effect, with electron-rich *ortho*-, *meta*- and *para*-substituted aryls all

Table 2 Substrate scope: arylboronic acids

ArN ₂ BF ₄ (2 equiv.)	1	PPh ₃ AuNTf ₂ (5 mol%)	Ru(bpy) ₃ (PF ₆) ₂ (2.5 mol%)	20 W fluorescent bulb	H ₂ O (60 equiv.)	MeCN, r.t., 16 h	3a
1a	1a						3aa
3aa (83%)	3bb (90%)	3cb (91%)	3da (73%)				Ar ¹ = <i>p</i> O ₂ NC ₆ H ₅
3eb (92%)	3fa (86%)	3ga (70%)	3ha (77%) ^b				
3ia' (73%) ^c deprotected only	3ja (39%)	3ka (85%)	3la (88%)				
3ma (55%)							
3na (61%)	3oa (34%)	3pa (47%)	3qa (34%)				

^a Isolated yields. ^b NMR yield. ^c Deprotected product **3ia'** = **3da**.

providing good yields (**3aa**–**3ha**). Furthermore, steric hindrance seems to be well tolerated as exemplified by the formation of **3ha** in 77% yield. In terms of functional group tolerance, we were pleased to see that phenols (**3da**), amides (**3eb**), esters (**3ma**) and carboxylic acids (**3na**) are compatible. However, the acid-sensitive THP group is cleaved during the reaction, producing the deprotected product **3ia'**. The performance of electron-poor arylboronic acids is slightly more variable. While the presence of mildly electron-withdrawing *p*-bromo- and *p*-chloro substituents provide coupling products **3ka** and **3la**, respectively, in high yields (85–88%), the yields are more moderate with *p*-ester (**3ka**, 55%) and carboxylic acid (**3la**, 61%) substituted arylboronic acids. Noticeably lower yields are achieved with strongly electron-withdrawing substituents: nitro- (**3pa**, 47%) and CF₃- (**3qa**, 34%), as well as with iodoboronic acid (**3oa**, 34%). Alkeneboronic acids are tolerated, albeit in a modest yield (39%, **3ja**).

Gratifyingly, the opposite trend is observed in the aryldiazonium substrate scope (Table 3), which means that good yields can generally be achieved by the judicious choice of coupling partners. While electron-rich arylboronic acid coupling partners generally perform better than very electron-poor ones, electron-withdrawing substituents on the aryldiazonium coupling partners now provide the best yields (**3ab**–**3ai**, up to 83%). *Para*- (**3ab**) and *meta*-substituted (**3ac**) substrates are tolerated well, but a drop in yield is observed for more hindered *ortho*-substituted substrates (**3ad**). Predictably,¹⁸ electron-rich aryldiazonium salts react more sluggishly, with the yields decreasing as the substituent gets progressively more electron-donating (72% **3aj**, 38% **3ak**, traces **3al**). Halogen substituted 4-chloro-, 4-bromo- and 4-iodophenyldiazonium salts once again perform well, producing the corresponding biaryls **3ae**, **3af** and **3ag** in 77%, 75% and 52%.



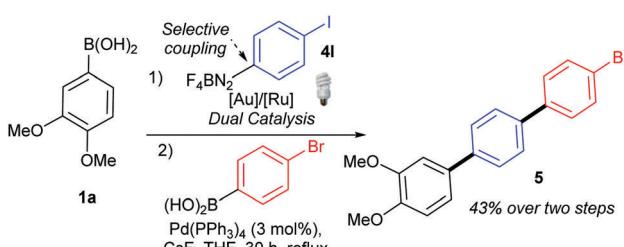
Table 3 Substrate scope: aryl diazonium salt

^a 2 equivalents. ^b Isolated yields. ^c NMR yield as co-elutes with 2.

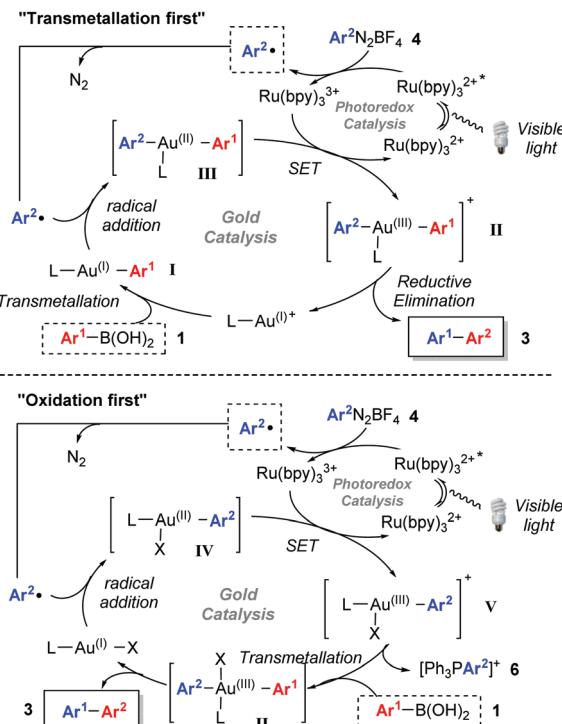
These results are of significance because the tolerance to C-halogen bonds¹⁹ renders the dual gold/photoredox coupling orthogonal to Pd(0)-catalysed reactions. The dual catalytic system can therefore be applicable to sequential cross-coupling reactions as exemplified by the reaction in Scheme 2. The cross coupling of **1a** and **4l** occurs without competitive cleavage of the C–I bond, which is then available for further Pd(0) cross-coupling. Subjecting the crude mixture of **3ag** to Suzuki coupling²⁰ subsequently produces triaryl **5** in 43% over the two steps.

Based on a combination of literature reports,^{5b,c,6c,21} we postulated that the reaction can proceed through two different mechanisms (Scheme 3). In the “transmetallation first” pathway, LAu(i)⁺ undergoes transmetallation with **1** to form **I** prior to radical addition and oxidation to Au(III) (**II**). The alternative involves oxidation of the Au(i) species to Au(III) **V** before transmetallation (“oxidation first” pathway). Mechanistic studies²¹ on Glorius’ dual gold/photoredox-catalysed oxyarylation of alkenes^{5b} as well as Toste’s elegant studies on arylative ring expansions^{6c} both point towards the oxidation first pathway. Nevertheless, as the reaction developed here involves a transmetallation rather than alkene activation with Au(i), we decided to carry out mechanistic studies.

We chose to study both cationic PPh₃AuNTf₂ as well as neutral PPh₃AuCl catalysts using ³¹P NMR analysis, as the latter successfully produces an appreciable amount of coupled



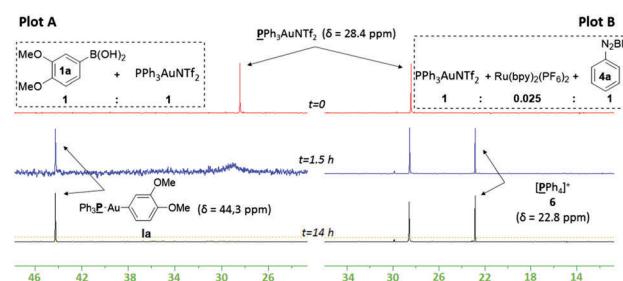
Scheme 2 Sequential cross-coupling.



Scheme 3 Postulated mechanistic pathways.

product **3aa** (37% conversion) even though previous reports have paradoxically shown that it is unable to undergo transmetallation with phenylboronic acid.²² Indeed, stirring stoichiometric amounts of PPh₃AuCl and **1a** in CD₃CN and D₂O revealed no transmetallation product (see the ESI†). In stark contrast, the same procedure using PPh₃AuNTf₂ gives the transmetallated Au(i) species **Ia** (Fig. 1, Plot A).²³ Next, stoichiometric amounts of PPh₃AuNTf₂ and **4a** with a catalytic amount of Ru(bpy)₃(PF₆)₂ were irradiated under visible-light to produce a new signal at 22.1 ppm, corresponding to **6** (Fig. 1, Plot B).^{21,24} **6** has been shown to arise from reductive elimination of gold(III) species **V** (Scheme 3),^{6c} therefore, the detection of **6** can be used to imply that intermediate **V** exists in solution. In the absence of light, only the original PPh₃AuNTf₂ signal at 28.4 ppm was present.

In light of these preliminary results, two separate gold/photoredox coupling experiments were carried out with stoichiometric amounts of PPh₃AuCl or PPh₃AuNTf₂ respectively (Fig. 2). As expected, no traces of the transmetallated product **Ia** were

Fig. 1 ³¹P NMR studies in CD₃CN:D₂O.

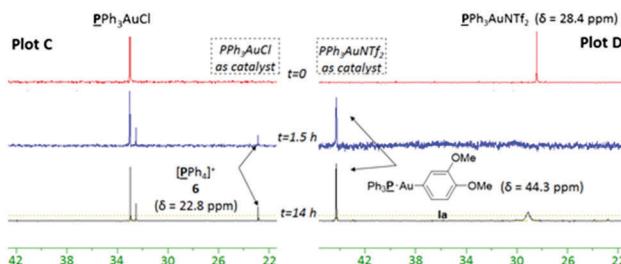


Fig. 2 ^{31}P NMR monitoring of PPh_3AuCl -catalysed reaction (plot C) and $\text{PPh}_3\text{AuNTf}_2$ -catalysed reaction (plot D).

observed using PPh_3AuCl as catalyst (Plot C). Instead, the upfield signal appearing at 22.8 ppm matches that of 6 observed during control reaction B (Fig. 1, Plot B), implying that intermediate **V** is formed during the reaction.²⁵ Concurrently, ^1H NMR analysis confirmed the formation of coupling product **3aa** after 14 h. These results suggest that the “oxidation first” catalytic cycle is the most plausible mechanism when neutral PPh_3AuCl is used as catalyst. In stark contrast, a single signal matching the chemical shift of organogold species **Ia** appeared over time and no signal corresponding to 6 (and by implication, no formation of **V**) was observed using $\text{PPh}_3\text{AuNTf}_2$ as catalyst (Plot D). Concurrently, ^1H NMR analysis clearly showed the formation of coupling product **3aa** over the same time period. These results suggest that the “transmetalation first” catalytic cycle is the most plausible mechanism when cationic $\text{PPh}_3\text{AuNTf}_2$ is used as catalyst.

In conclusion, we have developed the first application of dual gold/photoredox catalysis for $\text{C}(\text{sp}^2)\text{--C}(\text{sp}^2)$ coupling. The successful cross-coupling was found to significantly depend on the amount of water added. While studies have shown that oxidation of $\text{Au}(\text{i})$ to $\text{Au}(\text{m})$ species **V** is the first step in several dual gold/photoredox catalysed reactions, our mechanistic studies reveal that the mechanistic sequence is in fact highly catalyst dependent. Cationic $\text{PPh}_3\text{AuNTf}_2$ actually undergoes transmetalation with arylboronic acid prior to oxidation of $\text{Au}(\text{i})$ to $\text{Au}(\text{m})$, whereas neutral PPh_3AuCl undergoes the expected “oxidation first” pathway.

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