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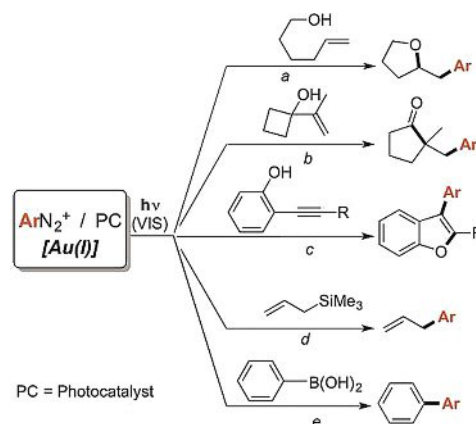
# Photocatalyst-free, Visible Light Driven, Gold Promoted Suzuki Synthesis of (Hetero)biaryls

Christopher Sauer,<sup>[a]</sup> Yang Liu,<sup>[a]</sup> Assunta De Nisi,<sup>[a]</sup> Stefano Protti,<sup>\*,[b]</sup> Maurizio Fagnoni,<sup>[b]</sup> and Marco Bandini<sup>\*,[a]</sup>

A visible-light driven Suzuki cross-coupling reaction was performed with colored and bench-stable arylazosulfones in the presence of  $\text{Ph}_3\text{PAuCl}$  (5 mol%) as the catalyst. The absence of a photocatalyst, along with the use of commercially available and easy-to-handle arylboronic acids underline the novelty and synthetic usefulness of the protocol. A reaction mechanism involving the generation of an aryl radical as the key intermediate has been proposed on the basis of experimental investigations.

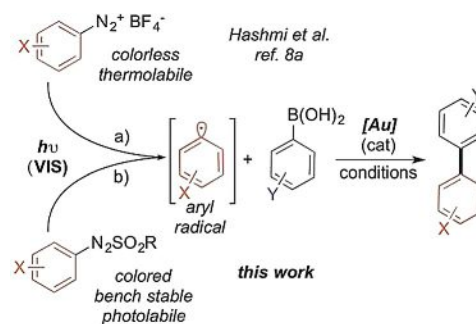
In recent decades, homogeneous gold catalysis has been applied to an impressive variety of synthetic protocols<sup>[1]</sup> with outstanding examples in the field of total synthesis<sup>[1d]</sup> and asymmetric catalysis.<sup>[1i]</sup> In particular, the  $[\text{Au}^{\text{I}}/\text{Au}^{\text{III}}]$  redox cycle was exploited in a wide range of cascade nucleophilic addition-oxidative coupling processes,<sup>[2]</sup> in which the formation of an alkyl- $[\text{Au}^{\text{III}}]$  intermediate is followed by its reaction with nucleophilic species such as alkynes or boronic acids, in Sonogashira and Suzuki protocols, respectively.<sup>[3]</sup> In these cases, different strategies have been proposed to facilitate the redox cycle, including the use of a strong external oxidant (e.g. Selectfluor,  $\text{PhI}(\text{OAc})_2$ ) or a dual Au/Pd transition metal system.<sup>[4a]</sup> In this regard, the development of innovative dual catalytic systems is currently a challenge<sup>[4b]</sup> and the pioneering works by Toste<sup>[5a]</sup> and Glorius<sup>[5b]</sup> prompted the rise of the combination of gold and visible light photoredox catalysis in dual catalytic arylation processes.<sup>[4b,6]</sup> Arenediazonium salts were considered as the substrates of choice, which were smoothly reduced by the photoexcited catalyst  $\text{PC}^*$  (a colored inorganic complex or an organic dye) to generate, after nitrogen loss, the corresponding aryl radical. The latter is then involved in the  $[\text{Au}^{\text{I}}/\text{Au}^{\text{III}}]$  redox catalytic cycle. Therefore, this strategy has been success-

fully applied to a plethora of synthetic protocols, including the oxy- and amino arylation of alkenes (Scheme 1, path a)<sup>[7a-c]</sup> the synthesis of cyclic ketones through the arylation of allyl alcohols (path b),<sup>[5b,c]</sup> the synthesis of oxygen- (path c)<sup>[7d]</sup> and nitrogen-based heterocycles<sup>[7e,f]</sup> via arylation of alkynes, as well as the synthesis of allyl- (path d)<sup>[7g]</sup> and vinylarenes,<sup>[7h]</sup> aryl alkynes<sup>[7i]</sup> and biaryls (path e).<sup>[7j-l]</sup>



**Scheme 1.** A selection of synthetic targets achieved through a dual gold/photoredox catalytic approach.

Moreover, this approach was recently implemented into a visible-light-driven photocatalyst-free cross-coupling of boronic acids and arenediazonium tetrafluoroborate salts by Hashmi and co-workers. ( $p\text{CF}_3\text{-C}_6\text{H}_4$ ) $\text{PAuCl}$  was used as the catalyst, with the isolation of biaryls in satisfactory yields (Scheme 2 path a).<sup>[8a]</sup>



**Scheme 2.** a) Light induced, photocatalyst-free Suzuki coupling described by Hashmi and co-workers (see ref. [8a]). b) Visible light promoted synthesis of substituted biaryls from arylazosulfones described in the present paper.

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Arenediazonium salts are rather unstable and colorless compounds, thus the visible light absorption was attributed to the species  $[LAu(III)](N_2Ar)^+$  generated in situ.<sup>[8]</sup>

A recent report by Crespi et al. focused on the wavelength-dependent photoreactivity of arylazosulfones, a class of compounds that can be readily prepared from the corresponding anilines in a two-step procedure.<sup>[9]</sup> Such molecules bear a colored photolabile moiety (i.e.  $-N_2SO_2CH_3$ )<sup>[10,11]</sup> which undergoes, upon visible light exposure, homolytic cleavage of the N–S bond and  $N_2$  loss, delivering the corresponding radicals. We report herein that such photo-triggered, bench-stable precursors of aryl radicals can be exploited satisfyingly in the visible light promoted photocatalyst-free Suzuki cross coupling under gold catalytic regime (Scheme 2, path b).

At the outset of our investigation, we considered *p*-CN-derivative **1a** and phenyl boronic acid **2a** as the model reactants for the cross-coupling event and a range of reaction parameters (including the nature of the base and its concentration, the solvent, the presence of additives, the stoichiometric ratio between **1a** and **2a** as well as the light source employed) were assessed to ascertain optimal reaction conditions. The optimization of the process has been described in detail in Tables S1–S7.

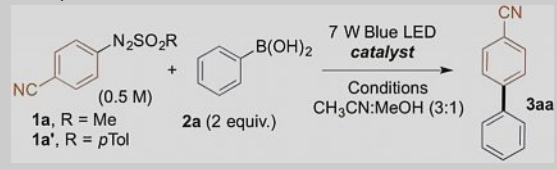
Thus, the conditions that emerged as optimal involved the irradiation of a mixture containing **1a** (0.5 M), **2a** (2 equiv),  $PPh_3AuCl$  (5 mol%), 2,2'-bipyridine (bpy, 20 mol%), NaOAc (2 equiv),  $CH_3CN/MeOH$  (degassed 3:1) using a 7 W Blue-LED as the light source. Under these conditions, biphenyl **3aa** was isolated in 61% yield along with a 20% of 4,4'-dicyanobiphenyl (**3a'**) arising from the homocoupling of **1a**.<sup>[12]</sup> Additionally, GC-MS analysis of the reaction crude revealed the presence of traces (overall < 10% yield) of *p*-cyanophenyl-methyl sulfone as well as of 4-(phenyldiazenyl)benzonitrile.

Any deviation from the above-described conditions caused either a marked drop in reaction performances or no significant changes (see Table 1). Indeed, the presence of the gold(I) complex as well as of a base proved to be mandatory for the success of the titled cross-coupling reaction (entries 1–3), whereas attempts to improve the efficiency of the process by catalytic modulation (i.e.  $PPh_3AuNTf_2$ , or higher loading) did not result in a significant change of the final outcomes (entries 4,5).<sup>[13]</sup> Finally, if the tosyl derivative **1a''** was employed instead of **1a**, no significant improvements were achieved (yield = 41%, entry 6).

The positive role played by the bpy (20 mol%) in aryl-gold-mediated coupling processes has been documented in literature.<sup>[14]</sup> This effect was also proven in our methodology, as the absence of bpy was detrimental to the final chemical outcome (entry 1 vs. entry 7). Although a conclusive explanation for this effect has not been offered yet, bpy could act as an acidity scavenger for the stabilization of organo-gold adducts (e.g. ligand assistance) during the catalytic cycle.

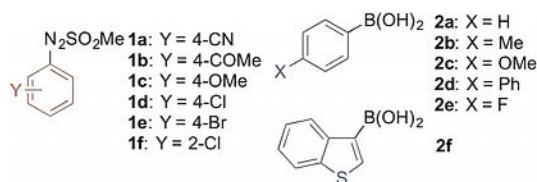
The scope of the photocatalyst-free, gold-catalyzed Suzuki-type cross coupling was then investigated by conducting the reaction of a range of arylazosulfones **1a–g** with aryl boronic acids **2a–f** (Figure 1) under the reaction conditions previously optimized. The obtained results are shown in Scheme 3.

**Table 1.** Optimization of the reaction conditions.



Entry	Conditions	<b>3aa</b> yield [%] <sup>[a]</sup>
1	<b>1a</b> , <b>2a</b> , $PPh_3AuCl$ (5 mol%), bpy (20 mol%), NaOAc (2 equiv)	61 <sup>[b]</sup>
2	<b>1a</b> , <b>2a</b> , $PPh_3AuCl$ (5 mol%), bpy (20 mol%)	— <sup>[c]</sup>
3	<b>1a</b> , <b>2a</b> , bpy (20 mol%), NaOAc (2 equiv)	— <sup>[c]</sup>
4	<b>1a</b> , <b>2a</b> , $PPh_3AuNTf_2$ (5 mol%), <sup>[d]</sup> bpy (20 mol%), NaOAc (2 equiv)	50
5	<b>1a</b> , <b>2a</b> , $PPh_3AuCl$ (20 mol%), bpy (20 mol%), NaOAc (2 equiv)	53
6	<b>1a''</b> , <b>2a</b> , $PPh_3AuCl$ (5 mol%), bpy (20 mol%), NaOAc (2 equiv)	41
7	<b>1a</b> , <b>2a</b> , $PPh_3AuCl$ (5 mol%), NaOAc (2 equiv)	17
8 <sup>[e]</sup>	<b>1a</b> , <b>2a</b> , $PPh_3AuCl$ (5 mol%), bpy (20 mol%), NaOAc (2 equiv)	15

[a] Isolated yield. A complete conversion of **1** was observed in all cases. [b] 20% of 4,4'-dicyanobiphenyl **3a''** was isolated. [c] No arylation observed. [d] Preformed gold complex was employed [e] Blank experiment in the absence of light, RT.



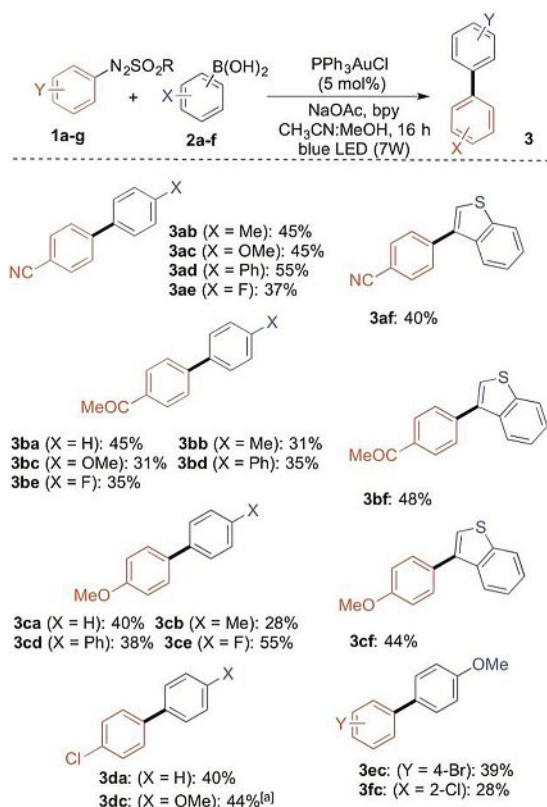
**Figure 1.** Substrates employed in the present work.

Isolated yields range from moderate to good, and no significant effect of the electronic properties of the aromatic substituents was observed. Interestingly, functionalized terphenyls (e.g. **3ad** and **3bd**) were obtained in satisfactory yields of up to 55%. *Ortho*-substitution on the arylazosulfone (**1f**) was also tolerated, though the desired compound (e.g. **3fc**) was isolated only in modest amounts (28% yield). Notably, heteroaromatic boronic acids such as C(3)-benzothiophene (**2f**) underwent arylation with diversely substituted arylazosulfones, providing the corresponding cross-coupling products **3af–3cf** in acceptable yields (40–48%).

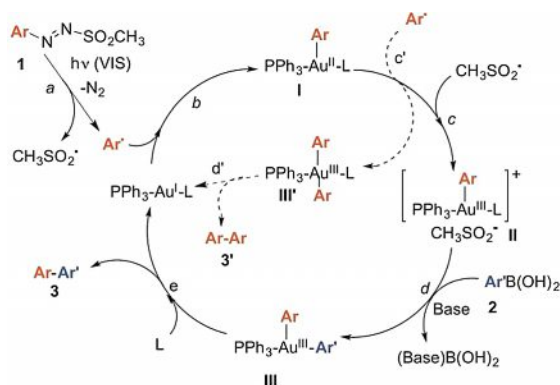
Remarkably, the protocol also allows the persistence in the final product of an aryl halide bond (see compounds **3da**, **3dc**, **3ec** and **3fc**), which enables further chemical manipulations under complementary reaction conditions.

A reaction mechanism was suggested on the basis of both the experimental data and the previous report by Fouquet and co-workers on dual photoredox/Au catalyzed arylation processes.<sup>[7]</sup>

In the first step (Scheme 4, path a), visible light irradiation of arylazosulfones **1** result in the generation of the corresponding aryl radical (Ar) via homolysis of the S–N bond from the  $1n\pi^*$  state of the arylazosulfone followed by dinitrogen loss.



**Scheme 3.** Scope of the photocatalyst-free gold catalyzed Suzuki reaction.<sup>[a]</sup> Blue led 1 W was used ( $\text{CH}_3\text{CN}:\text{H}_2\text{O} = 3:1$ ).



**Scheme 4.** Proposed mechanism for the visible light/[Au<sup>I</sup>] catalyzed Suzuki cross-coupling described herein.

Oxidative addition occurring on the [Au<sup>I</sup>] catalyst by the photogenerated aryl radical resulted in the formation of the [Au<sup>II</sup>] species I (path b), which is further oxidized by the methanesulfonyl radical ( $\text{CH}_3\text{SO}_2^\cdot$ ), thus forming the triphenylphosphine [Au<sup>III</sup>] species/methanesulfinate ion pair II. The activation of boronic acid 2 by a base allowed for an enhanced polarization of the boron-carbon bond, which facilitated the transmetalation with II (path d) to form the intermediate III. Following reductive elimination resulted in the release of the coupling products (3, path e) while affording the starting [Au<sup>I</sup>] catalyst.

In competition with path c, a second aryl radical might concur to the oxidation of the [Au<sup>II</sup>] intermediate I (path c'), re-

sulting in a [Au<sup>III</sup>] species III' that could release the side-product  $\text{Ar-Ar}'$  via reductive elimination.<sup>[15]</sup>

The key role of the aryl radical was confirmed through experiments conducted in the presence of 2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) as the radical trap.<sup>[10]</sup> In the present case, irradiation of 1a and 2a under the optimized conditions with 1.2 equiv of TEMPO resulted in a significant decrease in the efficiency of the desired cross-coupling reaction (See Table S5 for further details).

In conclusion, an unprecedented [Au<sup>I</sup>] catalyzed Suzuki cross-coupling between aryl azosulfones and boronic acids has been documented under visible-light assisted regime. The colored and photolabile properties of the sulfonyl partners enabled a photocatalyst-free protocol to be implemented under mild reaction conditions. Experimental evidences account for a dual metal-photoredox catalytic cycle involved in the  $\text{Ar-C}$  bond forming process.

## Experimental Section

**General procedures for the synthesis of (hetero)biaryls:** Boronic acid 2 (0.2 mmol, 2 equiv), NaOAc (0.2 mmol),  $\text{PPh}_3\text{AuCl}$  (5 mol%) and bpy (20 mol%) were added subsequently to a solution (200  $\mu\text{L}$ ,  $\text{CH}_3\text{CN}:\text{MeOH} = 3:1$ , reagent grade) of aryl azosulfone 1 (0.1 mmol, 0.5 M). The resulting mixture was then degassed by bubbling  $\text{N}_2$  gas and the vial exposed to blue LED (1 or 7 W) light until the complete consumption of 1 (TLC monitoring). The solvent was then removed under vacuum and the reaction crude purified by flash chromatography.

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## Conflict of interest

The authors declare no conflict of interest.

**Keywords:** aryl radicals • aryl azosulfones • gold • photoredox catalysis • Suzuki cross-coupling

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