



## A metal-catalyst-free oxidative coupling of anilines to aromatic azo compounds in water using bleach

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### Abstract

A simple route toward the synthesis of symmetrical and unsymmetrical aromatic azo compounds through oxidative coupling of anilines using widely available NaOCl is presented. This metal catalyst-free protocol is performed in water and affords the desired products in high yields.

### Key words:

Anilines, Oxidative coupling, Aromatic azo compounds.

### Introduction

Aromatic azo compounds have proven to be a relevant class of building blocks in chemical synthesis. Because of its synthetic versatility, azo chemistry has been successfully applied to various fields<sup>1</sup>. The majority of aromatic azo compounds are synthesized by conventional methods that are hampered by the use of environmentally unfriendly transition-metals and intricate challenges still remain in the synthesis of unsymmetrical aromatic azo compounds. Herein, we demonstrate the realization of our water-based approach, which resulted in the development of an operationally simple and scalable protocol to convert a broad range of anilines into symmetrical and unsymmetrical aromatic azo compounds.

### Results and Discussion

As an initial study, we selected the oxidative homocoupling of aniline as a representative transformation. By using 5.0 equiv. of NaOCl (6% active chlorine aqueous solution) as the oxidant, at room temperature, only 10% of (E)-azobenzene was obtained after 3 h along with several by products. To our delight, adding 1.0 equiv. of concentrated HCl to the reaction medium gave access to 2a in 95% yield. Also, under these conditions, we did not observe aniline polymerization. Other oxidants such as O<sub>2</sub> (dioxygen atmosphere), H<sub>2</sub>O<sub>2</sub> and K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> failed to provide the targeted product in acceptable yields. We then tried to decrease the amount of HCl employed in this transformation. Using 0.25 equiv. or 0.50 equiv. of HCl delivered product 2a in inferior yields (30% and 70%), thus confirming the necessity of 1.0 equiv. of HCl in this protocol. Decreasing the amount of NaOCl also led to inferior results. As an excess of oxidant was employed, we tried to reuse the aqueous solution for another reaction. Unfortunately, we could not obtain any product, thus evidencing decomposition of the oxidant. Gratifyingly, we observed that commercial bleach furnished product 2<sup>a</sup> with no deleterious effect on yield (5 equiv. 95%). With the optimized conditions in hand, we explored the substrate scope of the oxidative homocoupling reaction. Aniline derivatives having electron-withdrawing and -donating substituents were all tolerated giving access to products in high yields. Electron-poor aromatic amines reacted smoothly to furnish the corresponding azobenzenes in good yields,

albeit with longer reaction times when compared to electron-rich anilines. Interestingly, we did not detect lateral ring chlorination products under these conditions. This observation suggests the oxidative homocoupling reaction is faster than chlorination and once the azobenzene is formed, it is not prone to electrophilic substitution anymore. The outstanding reactivity of the hypochlorite-mediated oxidative homocoupling of anilines inspired us to evaluate our approach for the synthesis of unsymmetrical azobenzenes. Hence, for the heterocoupling reaction, an excess of the more electron-deficient aniline (molar ratio 3:1) was employed to improve the yield of the targeted products. Indeed, using our approach, we were able to achieve the unsymmetrical azobenzenes as a major product. The formation of only a small amount of homocoupling product was observed. After flash chromatography purification, we could recover around 70% of the remaining aniline used in excess.

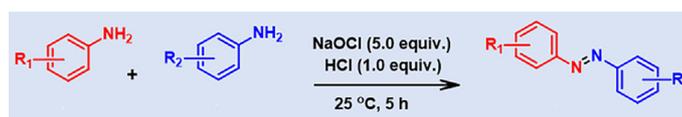


Image 1. Oxidative heterocoupling of substituted anilines.

### Conclusions

In summary, we have developed a metal-catalyst-free oxidative coupling of anilines in water to deliver symmetrical and unsymmetrical azo compounds using a very straightforward experimental protocol. Bleach is the suitable oxidant for this transformation and the execution of the reaction at room temperature allows its scaleup with no safety concerns. Despite the use of an excess of one aniline, it is recovered after purification and is prone to be reused. We believe our approach can be a suitable alternative to obtain azocompounds in large scale using low-cost reagents and energyinput.

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<sup>1</sup>Merino, E. *Chem. Soc. Rev.* **2011**, *40*, 3835–3853.