

Electrochemical C–H/C–H Cross-Coupling of Aromatic Compounds Using Radical Cation Pools

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Direct oxidative C–H/C–H cross-coupling (cross-dehydrogenative-coupling)^[1] of aromatic compounds has fascinated many chemists because it does not need prefunctionalization of starting aromatic compounds and serves as a straightforward, atom- and step-economical method for connecting two aromatic rings by a single C–C bond.

Electrochemical oxidation serves as an efficient method for activating aromatic compounds without using metal catalysts and chemical oxidants. In fact, the electrochemical oxidation of a mixture of two aromatic compounds give the cross-coupling products, although yields are usually low.^[2] Recently, Waldvogel reported a selective electrochemical phenol–arene cross-coupling reaction using boron-doped diamond electrodes.^[3] This method, however, cannot be applied to aromatic compounds that do not have an OH group because the phenoxy radical intermediate plays a crucial role.

In general, the oxidative C–H/C–H cross-coupling of two aromatic compounds suffers from the formation of homocoupling products derived from the nonselective oxidation of the starting materials (Figure 1a). Based on statistics, the yield of the cross-coupling product will be, at most, moderate because of the formation of products derived from homocoupling. Overoxidation is also unavoidable because the biaryl products have lower oxidation potentials than those of the corresponding starting materials owing to the extended π conjugation of the biaryl products. Therefore, the development of methods for direct anodic cross-coupling is very challenging. To avoid nonselective oxidation of starting materials and the oxidation of products we have developed a method using “radical-cation pools” (Figure 1b). Thus, an aromatic compound is allowed to react with a radical cation of another aromatic compound, which is generated and accumulated by low-temperature electrolysis. This new method serves as a powerful and selective method for synthesizing unsymmetrical biaryl compounds from unactivated electron-rich aromatic compounds in a straightforward and efficient way.

General procedure for oxidative cross-coupling of Ar¹ and Ar² is as follows. The electrochemical oxidation of Ar² (0.66 mmol) was carried out in 0.1 M Bu₄NB(C₆F₅)₄/CH₂Cl₂ in an H-type divided cell equipped with a graphite felt anode and a platinum plate cathode at –78 °C in the absence of Ar¹. After 0.30 mF of electricity was consumed, Ar¹ (0.10 mmol) and 1,2-dimethoxyethane were added. The mixture was stirred at –90 °C for 3 h. The desired cross-coupling product was obtained in good yield (Table 1).

The regioselectivity of the reaction is notable, because only single regioisomer was obtained in most cases. Another point to be mentioned is that halo-substituted aromatic compounds are effective (entries 2, 3 and 4) and that the unchanged halo-functionality in the cross-coupling products can be used for further transformations such as halogen/metal exchange and transition-metal catalyzed coupling reactions. Therefore, we anticipate that

this new tactic will provide access to a wide range of chemical processes for making organic compounds with aromatic rings.

In conclusion, we have developed an efficient method for C–H/C–H cross-coupling of aromatic compounds using “radical cation pools”.^[4] Because the present method consists of two sequential processes; the oxidative generation of a radical cation of an aromatic compounds and then coupling with a substrate under non-oxidative conditions, nonselective oxidation and overoxidation of products are avoided. Thus, the present method serves as selective technique for C–H/C–H cross-coupling of aromatic compounds. The absence of metal complexes and chemical oxidants are also advantageous.

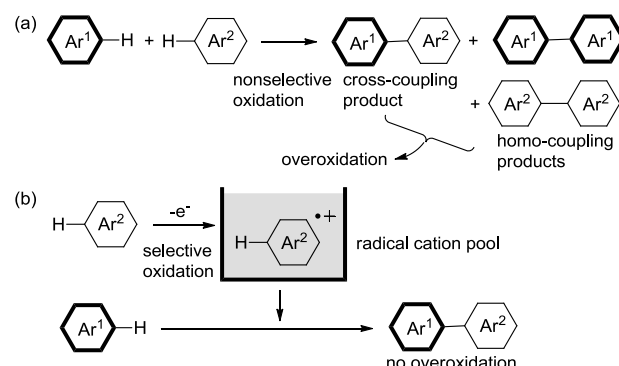


Figure 1. Oxidative C–H/C–H cross-coupling of aromatic compounds. (a) A conventional approach. (b) An approach based on the “radical cation pool” method.

Table 1. Direct oxidative cross-coupling of two unactivated arenes based on the “radical cation pool” method.

Entry	Ar ¹ H	Ar ² H	Product	Yield (%)
1				87
2				73
3				86
4				84
5				71
6				70

References

- [1] C.-J. Li, *Acc. Chem. Res.* **2009**, *42*, 335–344.
- [2] K. Nyberg, *Acta Chem. Scand.* **1971**, *25*, 3770–3776.
- [3] a) A. Kirste, G. Schnakenburg, F. Stecker, A. Fischer, S. R. Waldvogel, *Angew. Chem. Int. Ed.* **2010**, *49*, 971–975. b) A. Kirste, B. Elsler, G. Schnakenburg, S. R. Waldvogel, *J. Am. Chem. Soc.* **2012**, *134*, 3571–3576.
- [4] T. Morofuji, A. Shimizu, J. Yoshida, *Angew. Chem. Int. Ed.* **2012**, *51*, 7259–7262.