



# Phenanthridine derivatives via palladium catalyzed intramolecular functionalization of C(sp<sup>2</sup>)-H bonds.

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## INTRODUCTION

The biaryl structural motif is found in many natural and synthetic products of which phenanthridine derivatives are a specific heterocyclic system.<sup>1</sup>

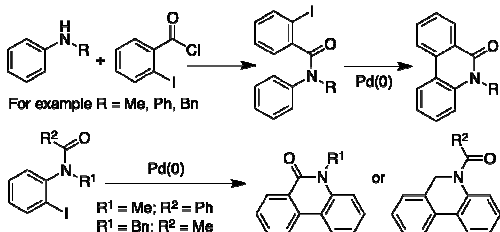
Biaryl bond formation is an important aspect in the synthesis of these compounds. As a result, organic chemists have sought to develop new and more efficient biaryl bond forming methods such as C-H direct arylation.<sup>2</sup>

## RESULTS AND DISCUSSION

In developing upon our original methodology (**M1**),<sup>3</sup> and that of others (**M2**),<sup>4</sup> we have discovered a more robust method (**M3**) for the intramolecular C-H functionalization of *N*-alkyl- and *N*-aroyl- anilines to give phenanthridine derivatives (Figures 1 and 2).

### Methodologies tested for biaryl bond formation.

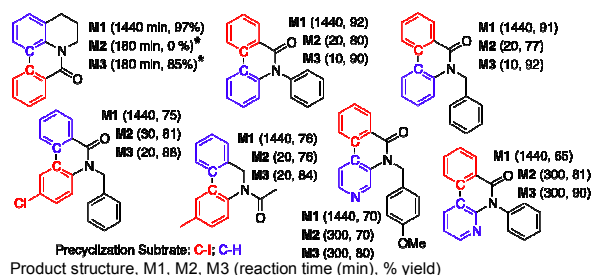
**All methods:** Substrate (1 mmol), DMF (5 mL) and stirring at 120°C. **M1** - 10 mol% Pd(OAc)<sub>2</sub>, Bu<sub>4</sub>NBr (1.1 mmol), KOAc (5 mmol). **M2** - 5 mol% Pd(OAc)<sub>2</sub>, 5 mol% dppe, K<sub>2</sub>CO<sub>3</sub> (5 mmol) an argon atmosphere. **M3** - 5 mol% Pd(OAc)<sub>2</sub>, 5 mol% dppe, 5 mol% hydroquinone (HQ), Bu<sub>4</sub>NBr (1.1 mmol), KOAc (5 mmol), an argon atmosphere.



**Figure 1.** Biaryl bond formation in the preparation of phenanthridine derivatives via C-H functionalization.

Substrates for investigation of the C-H functionalization reaction were prepared by the acylation of appropriately functionalized aniline derivatives. Reaction methods **M2** and **M3** (absence of HQ) were found to have long induction periods when virgin glass vials and stirrer bars were used and gave principally products resulting from reduction of the C-I bond. However, the addition of HQ in **M3** resulted in “instantaneous” reactions to give

the desired products. HQ had no effect upon **M2**. However, **M2** gave results comparable to **M3** when using glassware previously used for palladium catalyzed reactions. All products were spectroscopically characterized.



**Figure 2.** Illustrative results for catalytic intramolecular C-H functionalization. \* The reaction times for **M2** and **M3** were determined by GC-MS analysis of reaction aliquotes. \* In the case of **M2** no cyclized product was formed and substrate was consumed due to reduction of the C-I bond.

## CONCLUSION

The palladium catalyzed functionalization of a C-H bond allowed the satisfactory synthesis of phenanthridine derivatives. **M3** was found to be as good as or better than **M2** and both methods are a phenomenal advance upon our original method **M1**. Reaction times have been reduced from 12-24 hours to 10-300 minutes and catalyst loading has been halved, the overall result being similar or better product yields.

## ACKNOWLEDGEMENTS

CAPES, CNPQ, FAPERJ and PGQu-IQ-UFRJ

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