A novel route to obtain a xanthonic building block for the synthesis of potential antitumor pyranoxanthone derivatives

Introduction and Aims

Pyranoxanthones bear in common a pyran or a dihydropyran ring fused in a linear or angular way to the xanthone scaffold. Pyranoxanthones can be found in nature as secondary metabolites or can be obtained by laboratory synthesis. Many of them exhibit important biological activities, including antitumor activity. Pyranoxanthones 1 and 2 have exhibited promising antitumor potential. 4-Methoxyxanthone is a building block of 4-hydroxyxanthone, a key precursor of these pyranoxanthones. In this work, two synthetic routes for 4-methoxyxanthone were explored: a classical pathway based on the Ullmann coupling and a novel pathway based on a palladium-catalyzed carbonylative Suzuki coupling.

Results and Discussion

Classic pathway: Ullmann coupling

Novel pathway: Pd-catalyzed carbonylative Suzuki coupling

Reaction optimization

Conclusions

4-methoxyxanthone was synthesized using two methods: the classical pathway based on an Ullmann coupling and a novel synthetic route based on a Pd-catalyzed carbonylative Suzuki coupling. Pd-catalyzed carbonylative Suzuki coupling was able to yield the desired xanthone as well as a useful benzophenone precursor. Further reaction optimization is undergoing, considering the base, the CO source, and the catalyst loadings.

References


Acknowledgments

This research was supported by national funds by FCT – Foundation for Science and Technology through the projects UID/Multi/04423/2019 and UID/QUI/04423/2020. Support for this work was provided by the Strategic Funding UID/Multi/04423/2019 and under the project PTDC/SAU-PUB/28736/2017 (reference POCI-01-0145-FEDER- 028736), co-funded by COMPETE 2020, Portugal 2020 and the European Union through the ERDF and by FCT through national funds, as well as CHIRALBIOACTIVE-P IIF/IF (002021/2009). DRL thanks FCT for her PhD grant (SFRH/BD/146940/2019). JDS thanks for the FCT PhD Programme, specifically by the BiotechHealth Programme (PD/000162/2012), and for the grants (SFRH/BD/98105/2013 and SFRH/BD/110167/2015).