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Phase-transfer catalyzed stereoselective γ -C–C bond formation on the phthalide core

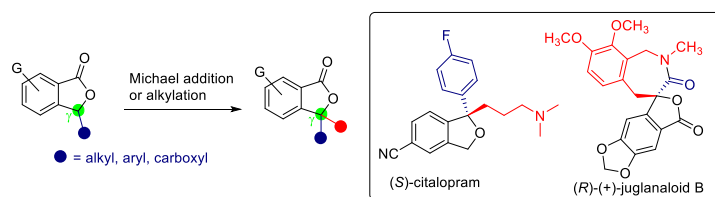
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The 1(3*H*)-isobenzofuranone core is incorporated in a huge number of biologically active natural products and analogs of pharmaceutical relevance, collectively known as phthalides.¹ The interest spawned by the wide array of biological activities exhibited by phthalides has stimulated continuous efforts devoted to the stereoselective synthesis of such compounds. While the most common approach for achieving this goal is the stereocontrolled closure of the lactone ring, the C–C bond formation at the γ -position of the isobenzofuranone has been so far largely unexplored, mainly because of the poor acidity of this site.² In this perspective, a promising tool was envisioned to be phase-transfer catalysis, which combines hyperbasic effect, mild conditions and excellent stereocontrolling ability. In this oral communication we will give an overview of our recent achievements in the development of phase-transfer catalyzed alkylation reactions and Michael additions involving the γ -site of phthalides, and their application to the enantioselective synthesis of biologically active natural products and derivatives. Some examples are the synthesis of the antidepressant Escitalopram, and the first synthesis of juglanaloids, phthalide alkaloids that proved to strongly inhibit the activity of arachidonate 5-lipoxygenase.



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References

- [1] Leon, A.; Del-Ángel, M.; Ávila, J. L.; Delgado, G. In Rinner, U.; Hudlicky, T. *In Progress in the Chemistry of Organic Natural Products*, vol. 104; Kinghorn, A. D.; Falk, H.; Gibbons, S.; Kobayashi, J., Eds.; Springer: Cham, 2017. [2] (a) Karmakar, R.; Pahari, P.; Mal, D. *Chem. Rev.* **2014**, *114*, 6213–6284. (b) Awasthi, A.; Singh, M.; Rathee, G.; Chandra, R. *RSC Adv.* 2020, *10*, 12626–12652.