C5-DISUBSTITUTED MELDRUM'S ACID DERIVATIVES AS PLATFORM FOR THE ORGANOCATALYTIC SYNTHESIS OF C3-ALKYLATED DIHYDROCOUMARINS

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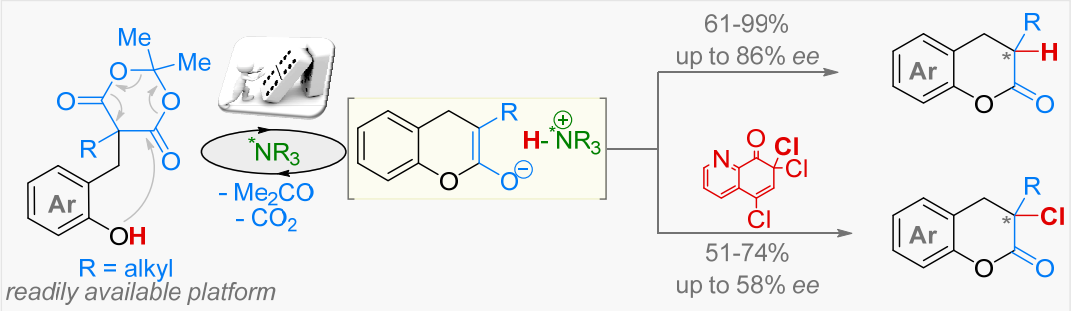
Amongst the privileged coumarin scaffolds in medicinal chemistry, the dihydrocoumarin derivatives are widely distributed within naturally occurring molecules and bioactive compounds. Consequently, several groups have developed catalytic enantioselective syntheses of 3,4-disubstituted chroman-2-ones and, to a much lesser extent, 3,3-disubstituted homologues. Nevertheless, the construction of enantioenriched 3-substituted derivatives turned out to be more challenging [1].



Based on recent observations [2], we will described hereby the use C5-disubstituted Meldrum's acid precursors as a useful platform for the synthesis of an array of 3-alkylated coumarins upon an organocatalyzed decarboxylative protonation or chlorination reactions [3].

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[1] (a) Lee, J.-W.; List, B. *J. Am. Chem. Soc.* **2012**, *134*, 18245. (b) Lee, A.; Scheidt, K. A. *Chem. Commun.* **2015**, *51*, 3407. (c) Liu, Y.-K.; Li, Z.-L.; Li, J.-Y.; Feng, H.-X.; Tong, Z.-P. *Org. Lett.* **2015**, *17*, 2022. (d) Sun, X.-L.; Chen, Y.-H.; Zhu, D.-Y.; Zhang, Y.; Liu, Y.-K. *Org. Lett.* **2016**, *18*, 864. (d) Zhou, D.; Mao, K.; Zhang, J.; Yan, B.; Wang, W.; Xie, H. *Tetrahedron Lett.* **2016**, *57*, 5649. Chen, Y.-H.; Sun, X.-L.; Guan, H.-S.; Liu, Y.-K. *J. Org. Chem.* **2017**, *82*, 4774. (e) Zhou, D.; Yu, X.; Zhang, J.; Wang, W.; Xie, H. *Org. Lett.* **2018**, *20*, 174.

[2] Legros, F.; Martzel, T.; Brière, J.-F.; Oudeyer, S.; Levacher, V. *Eur. J. Org. Chem.* **2018**, 1975.

[3] Martzel, T.; Annibaletto, J.; Levacher, V.; Brière, J.-F.; Oudeyer, S. *Adv. Synth. Catal.* **2018**, *361*, 995.