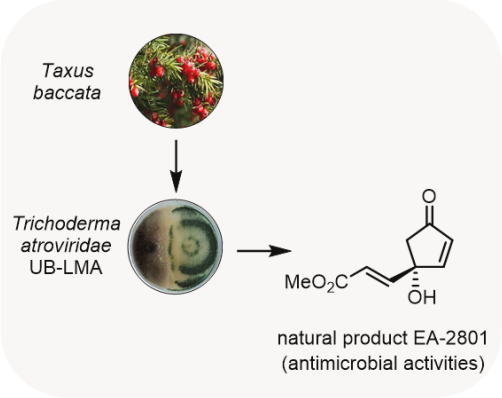
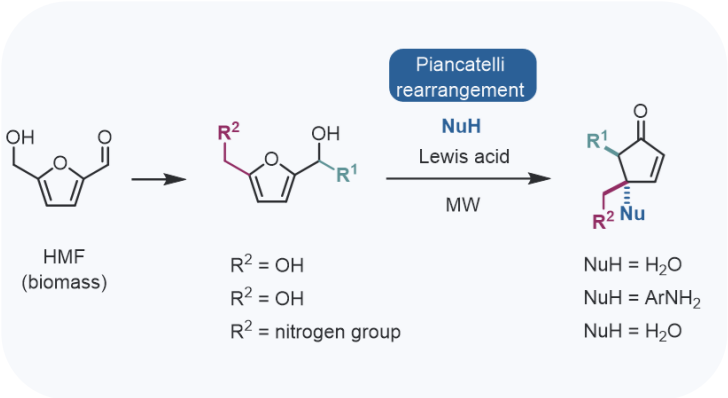
APPLICATION OF THE PIANCATELLI REARRANGEMENT FOR THE SYNTHESIS OF NITROGENOUS CYCLOPENTENONES

Clémentine Mayet[1], Jean-François Betzer[1]

[1]Université Paris-Saclay, CNRS, Institut de Chimie des Substances Naturelles, UPR 2301, 91190 Gif-sur-Yvette, France

In 2017, a new natural product, EA-2801, was isolated from an extract of a fungus (*Trichoderma atroviridae UB-LMA*) living in symbiosis with the *Taxus baccata* tree. This new compound was found to exhibit interesting antimicrobial activities, particularly against Gram-negative bacteria.[1,2] To form this substituted cyclopentenone, studies demonstrated that the target motif could be obtained in a single step through a Piancatelli rearrangement of non-symmetrical furan-2,5-dicarbinols, catalyzed by a Lewis acid. [3,4] This challenging methodology enabled the development of a general route for the synthesis of nitrogen-containing analogs from non-symmetrical 2,5-furyldicarbinol substrates, functionalized with aminomethyl (-CH_2-NR_1R_2) groups and in particularly the azido group, using bio-sourced hydroxymethylfurfural as the starting material. The Piancatelli rearrangement of these derivatives, catalyzed by $Dy(OTf)_3$ and under microwave activation, affords substituted cyclopentenones with two contiguous stereogenic centers, one of which is quaternary, with moderate to good yields and with excellent diastereoselectivities. Moreover, these 4-(azidomethyl)-cyclopentenones exhibited relevant cytotoxic activities against HCT116 and HL60 cancer cell lines with nanomolar IC_{50} values.[5]





Reference(s)

[1] Adelin, E.; Le Goff, G.; Retailleau, P.; Bonfill, M.; Ouazzani, J. *J. Antibiot*. **2017**, *70*, 1053-1056. doi: 10.1038/ja.2017.107.

[2] Le Goff, G.; Adelin, E.; Arcile, G.; Ouazzani, J. *Tetrahedron Lett.* **2017**, *58*, 2337-2339. doi: 10.1016/j.tetlet.2017.04.086

[3] Piancatelli, G.; Scettri, A.; Barbadoro, S. *Tetrahedron Lett*. **1976**, *17*, 3555-3558. doi: 10.1016/S0040-4039(00)71357-8.

[4] Cacheux, F.; Le Goff, G.; Ouazzani, J.; Bignon, J.; Retailleau, P.; Marinetti, A.; Voituriez, A.; Betzer, J.-F. *Org. Chem. Front*. **2021**, *8*, 2449-2455. doi: 10.1039/D1QO00268F

[5] Mayet, C.; Bignon, J.; Betzer, J.-F. *ChemRxiv*. **2024**, doi:10.26434/chemrxiv-2024-r98bn