

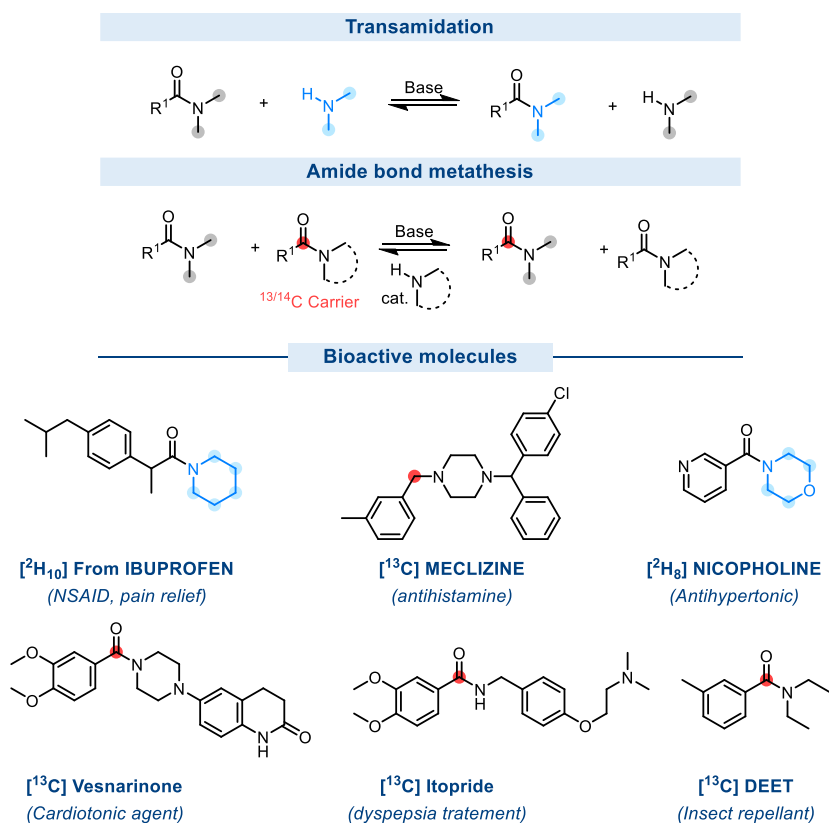


EXPLORING BASE PROMOTED DYNAMIC PROCESSES TO ACCESS ISOTOPICALLY LABELED TERTIARY AMIDES

Rémi Blicck, Quentin Lemesre, Antoine Sallustrau, Timothé D'Anfray, Frédéric Taran, Davide Audisio*

CEA-Saclay, DRF-JOLIOT-Service de Chimie Bio-organique et de Marquage, Gif-sur-Yvette, France

The amide bond is a fundamental molecular linkage omnipresent in nature, materials and drugs (such as: Nylon, Kevlar, Proteins, 66% of drug candidates)¹. Radioactive labelling is essential when comes the study of Absorption, Distribution, Metabolism and Excretion (ADME) of drug candidates². However, classical ways of amide labelling requires a costly and environmentally harmful multi-step radiosynthesis. Based on recent report on amide bond activation^{3,4}, we demonstrate a novel, direct and late-stage way of amide labelling. Two approaches have been investigated: the trans-amidation for deuterium labelling and the amide bond metathesis for carbon-13. Both methods were extensively applied (51 examples) and used on bioactive scaffolds with good isotopic incorporation.



References:

- ¹R. M. De Figueiredo, J.-S. Suppo, J.-M. Campagne, *Chem. Rev.* 2016, 116, 12029–12122.
- ²V. Babin, F. Taran, D. Audisio, *JACS Au* 2022, 2, 1234–1251.
- ³G. Li, C.-L. Ji, X. Hong, M. Szostak, *J. Am. Chem. Soc.* 2019, 141, 11161–11172.
- ⁴J. M. Hoerter, K. M. Otte, S. H. Gellman, Q. Cui, S. S. Stahl, *J. Am. Chem. Soc.* 2008, 130, 647–654.