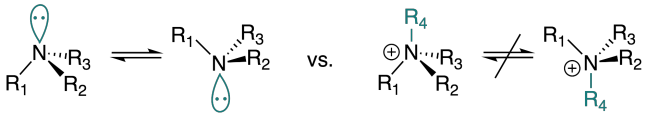
Dynamic kinetic resolution of racemic amines with stereogenic nitrogen centers

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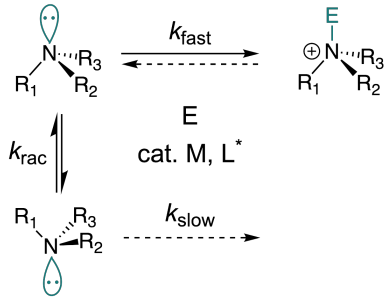
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Within the last decades, much attention from the chemical community has been directed at the development of asymmetric reactions. Just as a tetrahedral carbon atom, nitrogen with three different substituents can be a stereogenic centre. Such tertiary amines, however, usually do not show optical activity due to a low lying transition state for nitrogen inversion, which results in a rapid equilibrium between the enantiomers. This inversion can be prevented by conformational strain such as the one observed in Tröger's base[1], or by a quaternization of the nitrogen atom.[2]



Chiral ammonium salts are widely used as phase-transfer catalysts[3] and recently also as stereo-controlling cations[4]; they can be found in nature[5] and some exhibit pharmacological activity.[6] Current strategies for the synthesis of such compounds are based on the resolution techniques of diastereoselective adducts or salts.[7]

Recently we published the first example of the Pd-catalyzed enantioselective allylation of tertiary amines, where we could realize excellent conversions and significant stereoselectivities.[8] Hence, our research is focused on the dynamic kinetic resolution of racemic amines with stereogenic nitrogen centers via TM-catalyzed transformations.



[1] Vladimir Prelog, Peter Wieland, *Helv. Chim. Acta*, **1944**, 27, 1127-1134.

[2] William J. Pope, Stanley J. Peachey, *J. Chem. Soc., Trans.* **1899**, 75, 1127-1131.

[3] Elias J. Corey, Feng Xu, Mark C. Noe, *J. Am. Chem. Soc.* **1997**, 119, 12414-12415.

[4] Alexander Fanourakis, Benjamin D. Williams, Kieran J. Paterson, Robert J. Phipps, *J. Am. Chem. Soc.* **2021**, 143, 10070-10076.

[5] Robert H. Burnell, A. Chapelle, M. F. Khalil, Peter H. Bird, *J. Chem. Soc. D,* **1970**, 12, 772-773.

[6] R. Hughes, *Br. J. Anaesth.* **1986**, 58, 2S-5S.

[7] a) Mark P. Walsh, Joseph M. Phelps, Marc E. Lennon, Dmitry S. Yufit, Matthew O. Kitching, *Nature,* **2021**, 597, 70-82; b) Frank B. Buckney, Humphrey O. Jones, *J. Chem. Soc., Trans.* **1907**, 91, 1821-1826.

[8] Snizhana Zaitseva, Alessandro Prescimone, Valentin Köhler, *Org. Lett.* **2023**, 25, 1649–1654.