

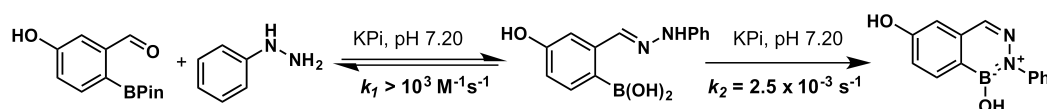
Boronic Acids Facilitate Oxime and Hydrazone Formation, Leading to a Fluorogenic Variant

C. Stress¹, D. G. Gillingham^{1*}

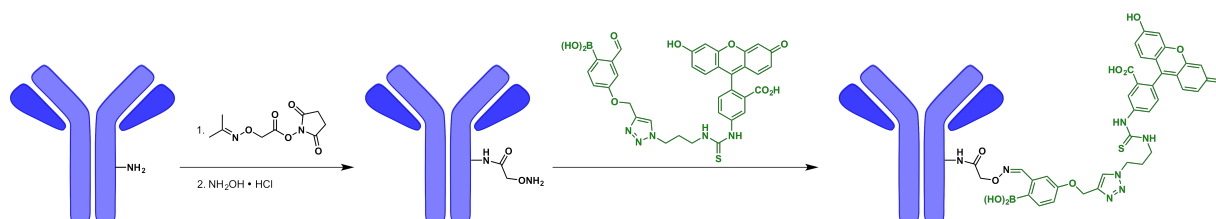
¹University of Basel, Department of Chemistry, St. Johanns-Ring 19, CH-4056 Basel

The reaction between α -effect amines (e.g. hydrazines, hydroxylamines) and carbonyls is a very well known method for bioconjugation. The main drawbacks of this reaction is the slow kinetics at neutral pH and the reversibility in aqueous systems. We have recently shown that the incorporation of a boronic acid, which acts as Lewis acid, in close proximity to the carbonyl (aldehyde in our case) greatly enhances the reaction rates under neutral aqueous conditions. We investigated the mechanism for this transformation by HPLC and NMR experiments.

Hydroxylamines and hydrazines show equal efficiency for oxime/hydrazone formations but the latter undergoes a second, much slower intramolecular reaction. The formed boron-containing heteroaromatic compounds (Borazaroisoquinolines, BIQ) were found to be very stable and no reversibility could be detected. Modification of the extended aromatic ring system led to the discovery of a new turn-on fluorophore.



With these results in hand we could create a guidebook for the different α -effect amine condensations. We furthermore used oxime formation for the labeling of an antibody as well as we are currently exploring the scope of these condensation reactions within biological systems.



[1] C. J. Stress, P. J. Schmidt, D. G. Gillingham, *Org. Biomol. Chem.* **2016**, *14*, 5529–5533.

[2] P. Schmidt, C. Stress, D. Gillingham, *Chem. Sci.* **2015**, *6*, 3329–3333.