BIOMIMETIC SITE- AND ENANTIOSELECTIVE C–H OXYGENATION OF QUINOLONE ANALOGUES MEDIATED BY HYDROGEN BONDING

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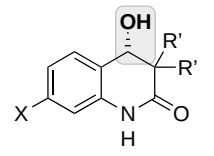
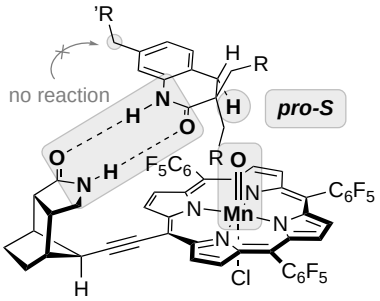
Site- and enantioselective C-H oxygenation of unfunctionalized sp^3-carbon atoms is unambiguously among the most coveted chemical transformations in modern organic synthesis. Among those, the oxygenation of prochiral methylene groups to their corresponding secondary alcohols remains particularly challenging as overoxidation to the respective ketone commonly diminishes yield and enantioselectivity.

Inspired by nature's cytochrome P450 unique capability to catalyze highly selective oxygen insertion into C–H bonds, we discovered that a chiral manganese porphyrin complex equipped with a remote hydrogen bonding site is effective in the enantioselective oxygenation of quinolone analogues [1].



up to 97% conversion
87-99% *ee*



Substantial progress was made regarding reactivity (up to 97% conversion), chemoselectivity (alcohol to ketone ratio >3:1) and most importantly the enantioselectivity was extraordinarily high (up to 99% *ee*). Remarkably even in the presence of a potentially more reactive benzylic position at C7 the reaction exclusively proceeds at position C4 of the heterocyclic skeleton. Our detailed kinetic and mechanistic data (*e.g.* KIE studies, X-ray) corroborate the hypothesis that the reaction occurs *via* a radical oxygen rebound mechanism from a Mn^V-Oxo species whose active site is directed to a specific C–H bond by hydrogen bonding.

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[1] F. Burg, M. Gicquel, S. Breitenlechner, A. Pöthig, T. Bach *Angew. Chem. In. Ed.* **2018**, *57*, 2953-2957.