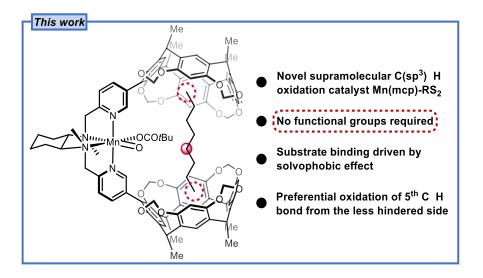
Site-Selective C(sp³)–H Oxidation of Aliphatic Substrates Devoid of Functional Handles¹

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Although tremendous progress in the field of C(sp³)–H oxidation has been achieved over the past decades, the selective oxidation of non-activated positions on hydrocarbon skeletons is still highly challenging. It usually requires the presence of a suitable functional group in proximity to the desired oxidation site or to use it to hold and orientate the substrate.²⁻⁴ Here we present a novel approach for catalyst-directed C– H oxidation that relies on substrate binding via the solvophobic effect in fluorinated alcohols, and thus is independent of functional groups on the substrate. Enabled by the novel supramolecular catalyst Mn(mcp)-RS₂, the preferential oxidation at the fifth position on aliphatic substrates was observed.



- Lu, Y.; Knezevic M.; Prescimone A.; Goldfuss B.; Tiefenbacher K. Site-Selective C(sp3)–H Oxidation of Aliphatic Substrates Devoid of Functional Groups. *ChemRxiv.* 2024; doi:10.26434/chemrxiv-2024-5gv6d.
- [2] Simmons, E. M.; Hartwig, J. F. Catalytic Functionalization of Unactivated Primary C–H Bonds Directed by an Alcohol. *Nature* **2012**, *483* (7387), 70–73. https://doi.org/10.1038/nature10785.
- [3] Bigi, M. A.; Reed, S. A.; White, M. C. Directed Metal (Oxo) Aliphatic C–H Hydroxylations: Overriding Substrate Bias. J. Am. Chem. Soc. **2012**, 134 (23), 9721–9726. https://doi.org/10.1021/ja301685r.
- [4] Olivo, G.; Farinelli, G.; Barbieri, A.; Lanzalunga, O.; Di Stefano, S.; Costas, M. Supramolecular Recognition Allows Remote, Site-Selective C–H Oxidation of Methylenic Sites in Linear Amines. *Angew. Chem. Int. Ed.* 2017, 56 (51), 16347–16351. https://doi.org/10.1002/anie.201709280.