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Hybrid Organometallic and Enzymatic Tandem Catalysis for Oxyfunctionalisation Reactions

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PURPOSE OF THE ABSTRACT
The biocatalytic insertion of oxygen into non-activated organic molecules is attracting an increasing interest in pharmaceutical and industrial chemistry.[1] Particularly, enzyme-mediated oxyfunctionalisation reactions usually reach high regio- and enantioselectivity representing alternative routes to the challenging conventional chemical methods. Although heme-containing monooxygenases (P450s) are widely used in this context, their reaction mechanisms via reductive activation of the molecular oxygen[2] poses several difficulties such as dependence on costly nicotinamide cofactors, intricate electron transport chains as well as the so-called Oxygen Dilemma.[3] This ampers the large-scale usage of P450s. Beside P450s, peroxygenases (UPOs) are receiving increased attention as selective oxyfuctionalisation catalysts as a consequence of the simpler reaction mechanism that enables the access to the same wide array of reactions and products, as they are considered the Swiss Army Knife of the oxyfunctionalisation chemistry.[4] However, the H2O2-dependence of UPOs also bears the challenges of irreversible oxidative enzymatic inactivation.[5] Thus, continuous low-level supply or in situ generation of hydrogen peroxide (H2O2) is essential for the stability of peroxygenases. A class of organometallic compounds potentially exploitable for H2O2 supply from formate, molecular oxygen and FMN as cocatalyst is constituted by Cp* iridium pyridincarboxyamidate complexes. They are extremely stable and water-soluble, and already used successfully as catalysts for hydrogenation reactions,[6] formic acid dehydrogenation,[7] water oxidation,[8] reductive amination of ketons[9] and hydrogen peroxide generation.[10]
In this contribution, we report that the organometallic complex [Cp*Ir(H-Pica)NO3] {pica = picolinamidate =κ2-pyridine-2-carboxamide ion (–1)} 1 (Scheme 1) is indeed a good catalyst for the H2O2-regeneration using simple flavin mononucleotide as co-catalyst and formate as hydride source. Furthermore, we show that 1 can successfully cooperate with rAaeUPO, which takes advantage by the in situ produced H2O2. Thus, we disclosed for the first time the chemoenzymatic tandem combining 1 and rAaeUPO to catalyse oxyfunctionalisation reactions. The feasibility of the proposed hybrid system is demonstrated by the wide portfolio of the reactions it can perform, including aromatic and (cyclo)aliphatic hydroxylation, epoxidation and sulfoxidation.

FIGURES

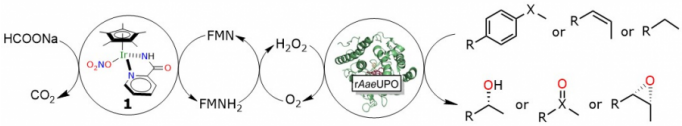

FIGURE 1

Scheme 1

Scheme of the chemoenzymatic tandem reaction combining 1 with rAaeUPO to catalyse oxyfunctionalisation reactions.

FIGURE 2

KEYWORDS

chemoenzymatic tandem | iridium FMN reduction | peroxygenases | oxyfunctionalisation

BIBLIOGRAPHY

(1) J. Dong, E. Fern?ndez-Fueyo, F. Hollmann, C. Paul, M. Pesic, S. Schmidt, Y. Wang, S. Younes, W. Zhang, Angew. Chem., 2018, 130, 9380-9404, Angew. Chem. Int. Ed. 2018, 57, 9238-9261.

(2) V. B. Urlacher, M. Girhard, Trends Biotechnol. 2019, 37, 882-897.

(3) D. Holtmann, F. Hollmann, ChemBioChem 2016, 17, 1391-1398.

(4) M. Hobisch, D. Holtmann, P. G. de Santos, M. Alcalde, F. Hollmann, S. Kara, Biotechnol. Adv. 2021, 51, 107615.

(5) B. Valderrama, M. Ayala, R. Vazquez-Duhalt, Chem. Biol. 2002, 9, 555-565.

(6) a) R. Kanega, N. Onishi, S. Tanaka, H. Kishimoto, Y. Himeda, J. Am. Chem. Soc. 2021, 143, 1570-1576; b) L. Tensi, A. V. Yakimov, C. Trotta, C. Domestici, J. De Jesus Silva, S. R. Docherty, C. Zuccaccia, C. Cop?ret, A. Macchioni, Inorg.
Chem. 2022, 61, 10575-10586.

(7) G. Menendez Rodriguez, C. Domestici, A. Bucci, M. Valentini, C. Zuccaccia, A. Macchioni, Eur. J. Inorg. Chem. 2018, 2018, 2247-2250.

(8) A. Bucci, S. Dunn, G. Bellachioma, G. Menendez Rodriguez, C. Zuccaccia, C. Nervi, A. Macchioni, ACS Catal. 2017, 11, 7788-7796.

(9) K. Tanaka, T. Miki, K. Murata, A. Yamaguchi, Y. Kayaki, S. Kuwata, T. Ikariya, M. Watanabe, J. Org. Chem. 2019, 84, 10962-10977.

(10) H. T. H. Nguyen, L. H. Do, Chem. Commun. 2020, 56, 13381-13384.