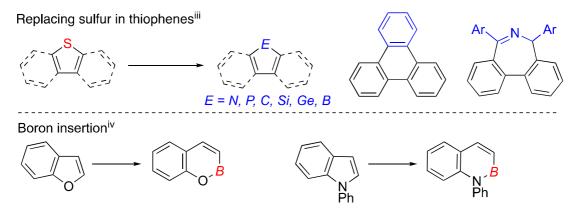
Aromatic Metamorphosis

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Aromatic rings hold a central position in organic chemistry and govern the fundamental nature of numerous useful compounds. Aromatic rings are stable due to their aromatic resonance energy and thus usually considered as being unbreakable. Compared with exocyclic modifications of aromatic compounds, little is known about endocyclic modifications such as substitutions of endocyclic atoms and atom insertions into the rings through partial disassembly of the cyclic skeletons and subsequent ring reconstruction. For the last decade, we have been interested in developing a series of new synthetic methods to achieve endocyclic modifications of heteroarenes as a game-changing strategy in organic synthesis. I will talk about our endeavors to establish 'aromatic metamorphosis',ⁱ in other words 'skeletal editingⁱⁱ of aromatic rings', focusing on the transformations of heteroaromatic skeletons.^{iii,iv}



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ⁱ a) H. Yorimitsu, D. Vasu, M. Bhanuchandra, K. Murakami, A. Osuka, *Synlett* **2016**, *27*, 1765-1774; b) K. Nogi, H. Yorimitsu, *Chem. Commun.* **2017**, *53*, 4055-4065.

ⁱⁱ a) J. Jurczyk, J. Woo, S. F. Kim, B. D. Dherange, R. Sarpong, M. D. Levin, *Nat. Synth.* **2022**, *1*, 352-364; b) B. W. Joynson, L. T. Ball, *Helv. Chim. Acta* **2023**, *106*, e202200182.

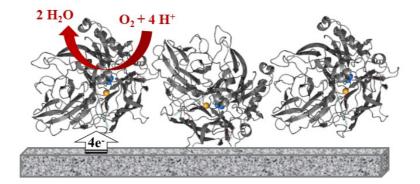
ⁱⁱⁱ a) D. Vasu, H. Yorimitsu, A. Osuka, *Angew. Chem. Int. Ed.* 2015, *54*, 7162-7166; b) M. Bhanuchandra, K. Murakami, D. Vasu, H. Yorimitsu, A. Osuka, *Angew. Chem. Int. Ed.* 2015, *54*, 10234-10238; c) A. Kaga, K. Nogi, H. Yorimitsu, *Chem. Eur. J.* 2019, *25*, 14780-14784; d) M. Bhanuchandra, H. Yorimitsu, A. Osuka, *Org. Lett.* 2016, *18*, 384-387; e) M. Onoda, Y. Koyanagi, H. Saito, M. Bhanuchandra, Y. Matano, H. Yorimitsu, *Asian J. Org. Chem.* 2017, *6*, 257-261; f) T. Furukawa, T. Yanagi, A. Kaga, H. Saito, H. Yorimitsu, *Helv. Chim. Acta* 2021, *104*, e202100195; g) T. Yanagi, T. Tanaka, H. Yorimitsu, *Chem. Sci.* 2021, *12*, 2784-2793.

^{iv} a) H. Saito, S. Otsuka, K. Nogi, H. Yorimitsu, J. Am. Chem. Soc. **2016**, 138, 15315-15318; b) S. Tsuchiya, H. Saito, K. Nogi, H. Yorimitsu, Org. Lett. **2017**, 19, 5557-5560; c) S. Tsuchiya, H. Saito, K. Nogi, H. Yorimitsu, Org. Lett. **2019**, 21, 3855-3860.

Biodiversity as an amazing source of enzymes for electrocatalysis

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Enzymes, that catalyze a diversity of key reactions in living organisms, are very promising eco-friendly catalysts. Among them, metalloenzymes involved in electron transfer reactions can be envisioned for sensing applications, fine-product synthesis as well as for sustainable energy conversion [1]. Biodiversity offers a tremendous source of such biomolecules presenting structural properties that allow them to operate in various environments including in extreme conditions. In this context, one of the most significant challenges is to achieve stable and efficient electron transfer for electrocatalysis once these enzymes are immobilized on conductive surfaces [2]. During this conference, we will especially consider a major reaction, namely O₂ reduction (ORR) catalyzed by multicopper oxidases (MCO). We will discuss the molecular basis for the functional immobilization of the enzymes on planar and nanostructured electrodes. We will show how in situ and in operando tools that are currently experiencing a great development allow obtaining intercorrelated relationships between enzymatic currents and loading/localization/conformation/orientation of the enzyme on the electrode [4]. We will open the discussion to new electroenzymatic reactions related to copper homeostasis, specially highlighting the role of specific enzyme domains on electrocatalysis [5].

[1] X. Xiao et al. Chem. Rev. 119 (2019) 9509-9558.

[2] I. Mazurenko et al., Curr. Op. Electrochem. 19 (2020) 113-121.

[3] I. Mazurenko et al. Energy & Environmental Science 10 (2017) 1966; S. Hardt et al. Nat. Catal. 4 (2021) 251-258.

[4] V. Pratap Hitaishi et al., ACS Catal. 8 (2018) 12004-12014; B. Tassy et al. Anal. Chem. 92 (2020) 7249-7256; H. Man et al. Anal. Chem. (2022).

[5] V. Hitaishi et al. JACS 142 (2020) 1394-1405; I. Mazurenko et al; Curr. Op. Electrochem. 32 (2022) 100919.

Acknowledgments:

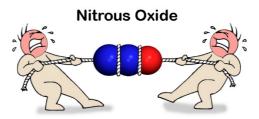
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Synthetic Chemistry with Laughing Gas

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Nitrous oxide (N₂O, 'laughing gas') is rarely used as a reagent in synthetic chemistry. On the contrary, industrially produced N₂O is destroyed by catalytic decomposition into the elements. In the lecture, I will discuss the use of nitrous oxide as an oxidant in homogeneous catalysis.^[1] Furthermore, I will show that N₂O can be employed as a nitrogen-atom donor for the synthesis of diazoolefins,^[2] organic reducing agents,^[3] azo dyes,^[4] and alkynyl triazenes.^[5] The latter display an ynamide-like reactivity, enabling diverse application in synthetic chemistry.



References:

- [1] Review: K. Severin, Trends Chem. 2023, 5, 574..
- [2] P. Varava, Z. Dong, R. Scopelliti, F. Fadaei-Tirani, K. Severin, *Nature Chem.* 2021, 13, 1055.
- [3] L. Eymann, P. Varava, A. M. Shved, B. F. E. Curchod, Y. Liu, O. M. Planes, A. Sienkiewicz, R. Scopelliti, F. Fadaei Tirani, K. Severin, *J. Am. Chem. Soc.* **2019**, *141*, 17112.
- [4] A. G. Tskhovrebov, L. C. E. Neasted, E. Solari, R. Scopelliti, K. Severin, Angew. Chem. Int. Ed. 2015, 54, 1289.
- [5] Review: A. A. Suleymanov, K. Severin, Angew. Chem. Int. Ed. 2021, 60, 6879.

Design and Synthesis of Chemical Biology Tools to unravel biological functions of

G-quadruplex structures

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Nucleic acid sequences containing runs of 3 or 4 adjacent guanines may spontaneously arrange into fourstranded DNA or RNA supramolecular structures called G-quadruplexes (G4s).ⁱ These non-canonical structures are likely to form in G-rich regions throughout the genome and thus are assumed to have functional roles in key biological processes, such as replication, transcription, repair, and recombination,ⁱⁱ and thereby they represent potential barriers for all the enzymatic machineries involved in these pathways. However, the dynamic nature of these structures makes their identification in live cells extremely challenging; therefore, G4 actual formation in vivo is still a matter of debate. G4s can be stabilized by small synthetic molecules (G4 ligands),ⁱⁱⁱ hence, the latter represent a new family of DNA drugs assumed to act region selectively at specific genomic G-rich loci including telomeres, oncogene promoters, tandem mini satellites that have higher propensity to generate quadruplexes.^{iv} In general, G4 ligands do not display acute cytotoxicity and produce diverse cellular effects, suggesting that targeting of genomic G4 is characterized by different accessibility. Consequently, it is highly important to follow G4 ligand distribution in cells and identify precisely their binding sites genome-wide; this knowledge will enhance understanding in regard to characterization and exploitation of drug responses. These objectives will be achieved by the construction of specifically tagged G4 selective small molecules that will act as molecular reporters enabling visualization of G4 in cells^v and photoactivatable covalent agents.^{vi}

Acknowledgments:

- ⁱ J. Spiegel, S. Adhikari, S. Balasubramanian, *Trends Chem.* 2020, 2, 123-136.
- ⁱⁱ H. J. Lipps, D. Rhodes, *Trends Cell Biol.* 2009; 19, 414-422.

ⁱⁱⁱ a) D. Monchaud, M.-P. Teulade-Fichou, Org. Biomol. Chem. 2008, 6, 627-636; b) D. Verga, F. Hamon, F. Poyer, S. Bombard, M.-P. Teulade-Fichou, Angew. Chem. Int. Ed. 2014, 53, 994-998.

^{iv} S. Balasubramanian, L. H. Hurley, S. Neidle, *Nature drug discov.* 2011; 10, 261-275.

^v a) D. Verga, F. Hamon, C. Nicoleau, C. Guetta, T.-D. Wu, J.-L. Guerquin-Kern, S. Marco, M.-P. Teulade-Fichou, *J. Mol. Biol. & Mol. Imaging* **2017**, 4(1); T. Masson, C. Landras Guetta, E. Laigre, A. Cucchiarini, P. Duchambon, M.-P. Teulade-Fichou, D. Verga, *Nucleic Acids Res.* **2021**, *49*, 12644-12660.

^{vi} A. Lena, A. Benassi, M. Stasi, C. Saint-Pierre, M. Freccero, D. Gasparutto, S. Bombard, F. Doria, D. Verga, *Chem. Eur. J.* **2022**, 28, e20220073.