Structural Modifications of Nile Red Carbon Monoxide Fluorescent Probe: Sensing Mechanism and Applications

Dominik Madea,[1)] Marek Martínek,[1)] Lucie Muchová,[2)] Jiří Váňa,[3)] Libor Vítek,[2)] Petr Klán[1)]

[1)] Department of Chemistry and RECETOX, Faculty of Science, Masaryk University, Kamenice 5/A8, 625 00 Brno, Czech Republic, email: dominik.madea@seznam.cz

[2)] Institute of Medical Biochemistry and Laboratory Diagnostics, 1st Faculty of Medicine, Charles University, Na Bojišti 3, 121 08 Praha 2, Czech Republic [3)] Institute of Organic Chemistry and Technology, Faculty of Chemical Technology, University of Pardubice, Studentská 573, 532 10 Pardubice, Czech Republic

Carbon monoxide (CO) is a cell-signaling molecule (gasotransmitter)[1] produced endogenously by oxidative catabolism of heme, and its spatial and temporal sensing at the cellular level is still an open challenge.[2]

Synthesis, optical properties and study of the sensing mechanism of Nile-red Pd-based CO chemosensors,[3] structurally modified by core and bridge substituents, in methanol and aqueous solutions are reported in this work. The sensing fluorescence "off-on" response of palladacycle-based sensors possessing low background fluorescence arises from their reaction with CO to release the corresponding highly fluorescent Nile red derivatives in the final step. Our kinetic study showed that electron-withdrawing and electron-donating core substituents affect a rate-determining step of the reaction. More importantly, the substituents were found to have a substantial effect on the Nile red sensor fluorescence quantum yields, hereby defining the sensing detection limit.

The highest overall fluorescence and sensing rate enhancements were found for a 2-hydroxy palladacycle derivative, which was used in subsequent biological studies on mouse hepatoma cells as it easily crosses the cell membrane and qualitatively traces localization of CO within the intracellular compartment with the linear quantitative response to increasing CO concentrations.

[1] Ryter, S. W.; Alam, J.; Choi, A. M. K. *Physiol. Rev.* **2006**, *86*, 583-650.

[2] Wu, L.; Wang, R. *Pharmacol. Rev.* **2005**, *57*, 585-630.

[3] Liu, K. Y.; Kong, X. Q.; Ma, Y. Y.; Lin, W. Y. *Angew. Chem. Int. Ed.* **2017**, *56*, 13489-13492.