Study of Photochemistry and Mechanisms of Photoactivatable Compounds

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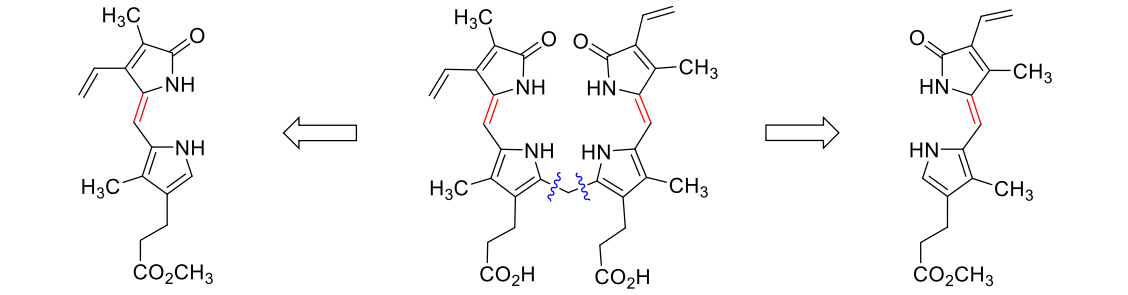
The work consist of two separate projects. In the first project, synthesis, optical properties and study of the sensing mechanism of Nile-red Pd-based carbon monoxide (CO) chemosensors,[1] structurally modified by core and bridge substituents, in methanol and aqueous solutions are reported. CO is a cell-signaling molecule (gasotransmitter)[2] produced endogenously by oxidative catabolism of heme, and its spatial and temporal sensing at the cellular level is still an open challenge.[3] The fluorescence of the "off-on" palladacycle-based sensors 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.[4]

In the second project, the photochemistry of bilirubin (BR) dipyrrinone subunits (**1** and **2**, prepared as the corresponding methyl esters) were studied by steady-state and transient spectroscopies.[5,6,7] Bilirubin is an essential metabolite formed by the catabolism of heme. Phototherapy with blue-green light can be applied to reduce high concentrations of BR in blood,

especially in the neonatal period.[8] Bilirubin subunits represent useful models to study the complex photochemistry of bilirubin. Both subunits undergo efficient reversible photoisomerization (Φ_{ZE} ~ Φ_{EZ} ~ 0.15–0.30), furthermore, *E*-**1** undergo lumirubin-type photorearrangement to form a seven-membered ring system. The cyclization process is significantly less efficient (Φ_c ~ 0.001–0.07), but is strongly wavelength-dependent. The photochemistry of bilirubin dipyrrinone subunits and its biological properties are discussed and compared to those of bilirubin.



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

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

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

[4] Madea, D.; Martínek, M.; Muchová, L.; Vítek, L.; Klán, P. *J. Org. Chem.* **2020**, *85*, 3473-3489.

[5] Madea, D. *et. al. J. Org. Chem.* **2020,** *85*, 13015.

[6] Janoš, J.; Madea, D. *et. al. J. Phys. Chem. A.* **2020**, *124*, 10457.

[7] Madea, D. *et. al.* (submitted to *J. Org. Chem.*)

[8] Vítek, L.; Ostrow, J. D. *Curr. Pharm. Des.* **2009**, *15*, 2869.