Thesis Summary

2-(4-Nitrophenyl)-1*H*-indole: A Versatile Chromophore in Photoreaction
(2‐(4‐ニトロフェニル)‐1*H*‐インドール：光反応で多様性を持つ発色団)

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The "caging and uncaging" of bioactive compounds is an elegant strategy to investigate biochemical processes and mechanisms and involves the temporal masking (caging) with a photoremovable protecting group (PPG) and the subsequent unmasking (uncaging) by photolysis (Figure 1a). Importantly, this method can spatiotemporally achieve a concentration increment in bioactive compounds. Because the biological responses induced by concentration spikes occur on the micro to the millisecond time scales, spatiotemporal control in the release of bioactive molecules by "uncaging" is an effective tool in physiological studies.[1]

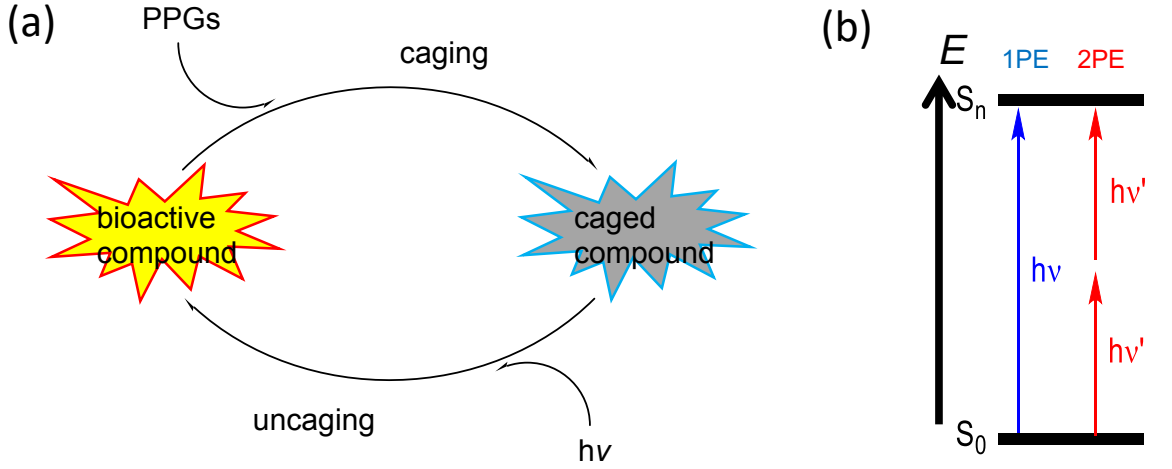

Figure 1. (a) Elucidation of caging and uncaging process; (b) One-Photon (1P) and Two-photon (2P) excitation.

To avoid cell damage of UV light during "uncaging" process, a clever strategy of 2P excitation was applied (Figure 1b). In this study, we designed the related 2-(4-nitrophenyl)-1*H*-indole (NPI) chromophore as PPG to explore the 2P responsive contribution from strongly electron-donating character of the indole nitrogen atom, and to exploit the possibilities for improving the water solubility of the probe by introducing water-soluble groups at the nitrogen atom. Caged benzoic acid was prepared, and its photochemical uncaging reaction was examined. Benzoic acid was released in a moderate chemical yield of 40–60%. In addition to the formation of benzoic acid, an unexpected aldehyde was isolated during product analysis (Figure 2a). The identification of the aldehyde product prompted us to investigate the mechanism of the transformation and the excited-state dynamics. Based on the TA spectroscopy and TD-DFT computational results, the intramolecular electron transfer to the excited state was proposed for the initial step of the chemical transformation to generate the intramolecular zwitterion intermediate. The successive CO_2 elimination and absorption of O_2 (breathing reaction) produced the hydroperoxide together with its photoinduced decomposition products, alcohol and aldehyde (Figure 2b).[2]

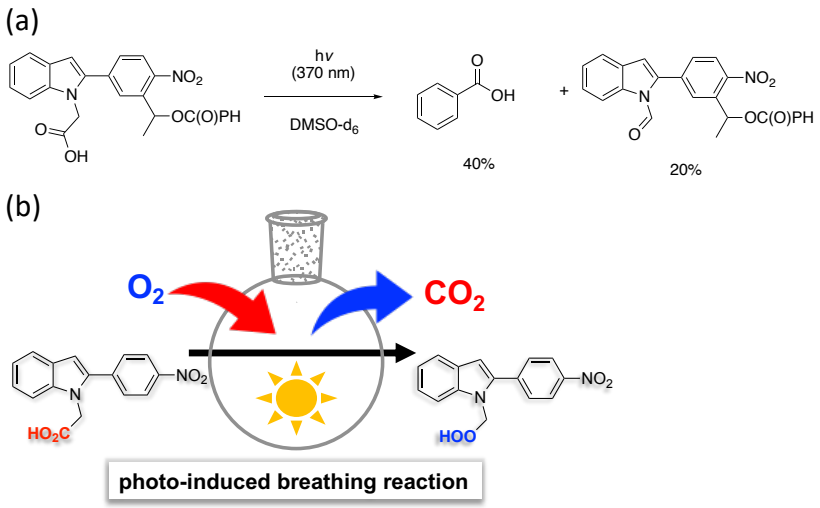

Figure 2. (a) Uncaging reaction of NPI chromophore; (b) breathing reaction.

Inspired by such results, we moved leaving group from *o*-nitrobenzene to 3-indole to chase a better performance of NPI in uncaging reaction. To test the uncaging performance of NPI caged compounds, we have linked NPI with typical LGs: Acid, Alcohol and Amine. As results, NPI can conduct a clean uncaging by releasing different types of LGs with high chemical yields and the remained chromophore was detected as aldehyde products, which was formed by oxygen quenched methyl radical. Surprisingly, we found NPI can not only release acids but also poor leaving groups: alcohols and free amines directly. Suffered from the low efficiency of alcohols and amines elimination, normally such uncaging will attach through a carbonate or carbamate linkage to have similar leaving group properties to that of a carboxylate and undergoes decarboxylation after photolysis to generate targets. Benefiting from homolytic cleavage, NPI can release leaving groups more efficient and such direct release of alcohols and amines make NPI has potential to play an active role in biological study.

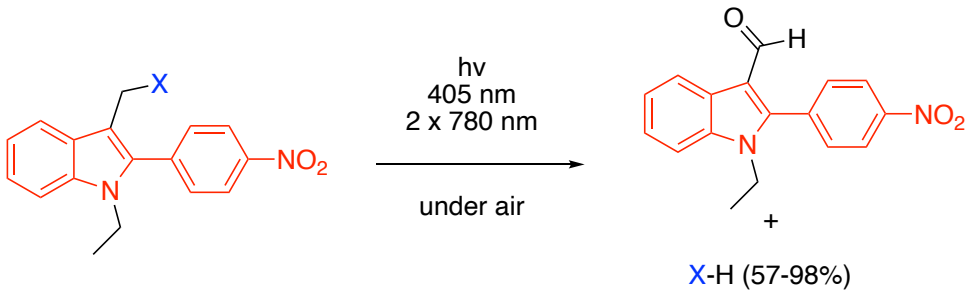

Figure 3. 1P and 2P uncaging of novel NPI chromophore.

1 M. Abe, Y. Chitose, S. Jakkampudi, P. Thuy, Q. Lin, B. Van, A. Yamada, R. Oyama, M. Sasaki, C. Katan, *Synthesis (Stuttg).* **2017**, *49*, 3337.
2 Q. Lin, M. Abe, *Photochem. Photobiol. Sci.* **2021**, *20*, 421.