論 文 の 要 旨

題　目　Development of a New Series of Chromophores with Nitrobiphenylamines for Application to Photoremovable Protecting Groups
（ニトロビフェニルアミン骨格をもつ新しい光アンテナ部位の開発とフォトケージへの応用）

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Spatiotemporal control of bioactive substances by caging and uncaging using photoremovable protecting groups (PPGs) (Figure 1a) is an efficient method to investigate the functional mechanisms of bioactive molecules in physiological studies[1]. Since bioactive molecules can be released from caged compounds by light irradiation, this caging and uncaging method enables concentration jumps of bioactive substances under mild conditions with high spatiotemporal control to efficiently stimulate biological processes. Irradiation with high-energy UV light effectively releases bioactive molecules. However, UV light cannot penetrate deep areas of biological samples and may cause cytotoxicity due to high-energy photons. In contrast, near-infrared (NIR) light (650–1050 nm) has significantly better bio-permeability and less cytotoxicity, although its low energy challenges the efficient release of biologically active substances. To solve this problem, two-photon (2P) excitation has been introduced[2] (Figure 1b). This process enables the excitation of molecules to the same electronic excited state as that given in 1P excitation by simultaneous absorption of two lower-energy photons. In addition, it is possible to limit the excitation to molecules at the focal point of the laser in 2P excitation and achieve the three-dimensional control of photo-deprotection reactions. The 2P uncaging efficiency (δ_u) of a caged compound is determined by the equation $\delta_u = \sigma_2 \times \Phi_u$, in which Φ_u is the quantum yield of the uncaging reaction, and σ_2 is the 2P absorption cross-section measured in GM (1 GM = 10^{-50} cm^4 s photon^{-2} molecule^{-1}). The growing popularity of 2P excitation has created a demand for developing organic molecules that demonstrate improved 2P absorption characteristics.

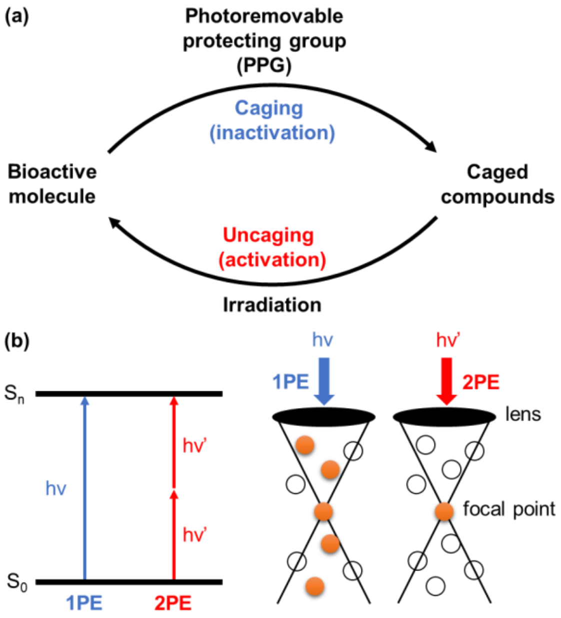

Figure 1. (a) Photoremovable protecting groups; (b) 1P excitation (1PE) and 2P excitation (2PE).

Octupolar systems with triangular or star-shaped structures have been found to exhibit exceptional 2P absorption performance[3]. However, the large molecular sizes and strong aromaticity of these chromophores could hinder the compatibility with biological samples. Therefore, there is a high demand for designing compounds that can balance optical properties and biocompatibility. In Chapter 2, we introduced a novel and simple octupolar molecule, tris(4'-nitrobiphenyl)amine, which contains three nitro moieties connected to the central nitrogen atom via biphenylene bridges (Figure 2). The 2P absorption spectrum of the octupolar molecule obtained in toluene using the 2P excitation fluorescence method revealed two 2P absorption maxima at 730 nm (σ_2 = 1330 GM) and 820 nm (σ_2 = 900 GM). These σ_2 values showed considerable improvement compared to those of similar-size triphenylamine derivatives and are equivalent to those of molecules with much larger π-conjugation. Subsequently, we develop EGTA-substituted derivatives with octupolar nature, which serve as photolabile Ca^{2+} chelators. The release of Ca^{2+} was verified by observing the fluorescence emission from fluo-3, a Ca^{2+}-sensitive fluorescence dye. The rise in the fluorescence intensity upon irradiation confirmed the release of Ca^{2+} from these calcium chelators by 2P excitation.

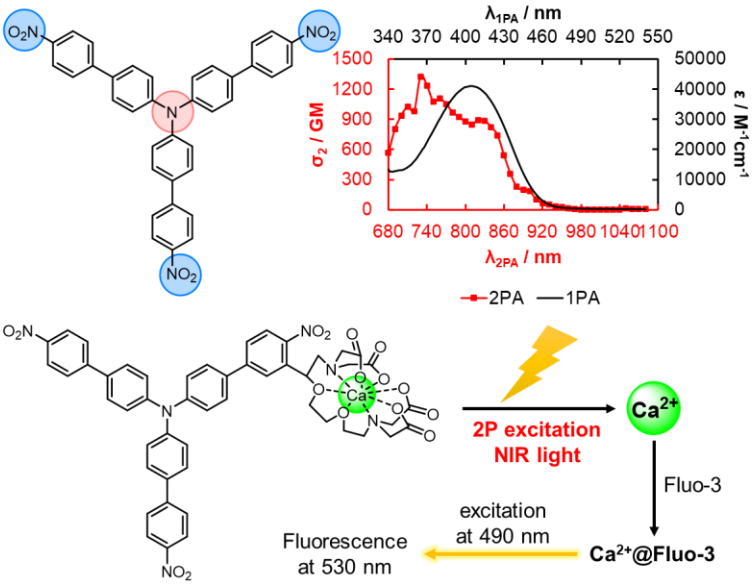

Figure 2. Octupolar system and uncaging of Ca^{2+} using NIR light.

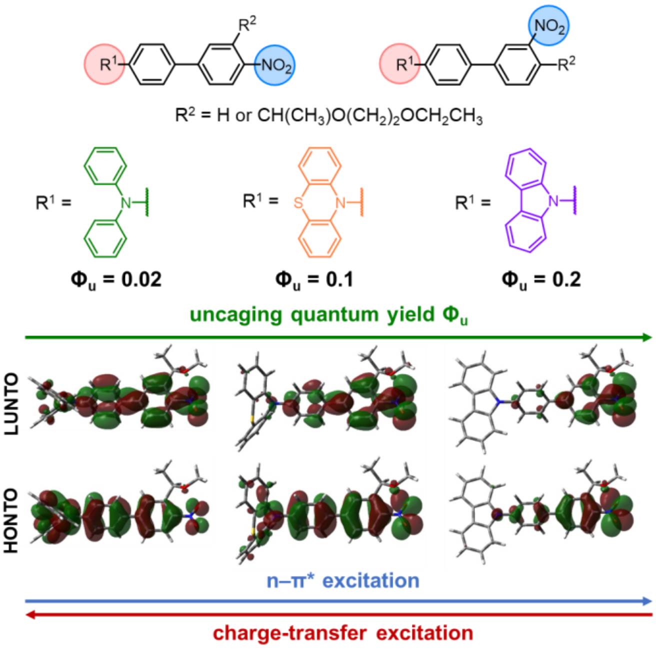

Figure 3. Effect of amino substituents on uncaging quantum yield of nitrobiphenyl units.

Although an exceptional 2P absorption cross-section was revealed for the parent octupolar chromophore, low uncaging quantum yields of the caged derivatives prevent further applications in biological studies. Therefore, in Chapter 3, we attempted to shed light on factors that govern the uncaging quantum yield for the nitrobiphenyl scaffolds with varying amino substituents (Figure 3). Among the newly developed compounds, those substituted by carbazole and phenothiazine units showed significantly increased uncaging quantum yields (0.2 and 0.1, respectively). The cyclic structure of the donor destabilized the charge-transfer transition and preserved the local n–π* excitation at the lowest excited state, which is necessary to trigger the intramolecular hydrogen abstraction process in the photo-uncaging of *ortho*-nitrobenzyl (oNB) PPGs[4]. Quantum chemical calculations, which predict the character of lowest excited states, can serve as a useful tool to predict quantum efficiencies. This study can contribute to improving the understanding of the need to balance optical properties and quantum efficiencies to accelerate the evolution of proficient PPGs for applications in physiological and therapeutic research.

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