Photo-controllable bioorthogonal reactions and biomolecules

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Photo-driven bioorthogonal reactions add spatial-temporal resolution to bioorthogonal reactions using photo-irradiaiton, which may provide photo-controllable molecular tools in chemical biological studies. We have established the visible-light driven bioorthogonal DVPC reaction of the *o*-dione (9,10-phenanthrenequinone) with the electron-rich alkene (vinyl ether), which proceeded via the single electron transfer (SET) from the vinyl ether to the photo-excited state of *o*-dione as the first bioorthogonal bond-forming step[1]. The presence of water in biological system was used to "polar solvent cages" of the excited state to block side reactions and realize bioorthogonality. Spatial-temporal labeling of antibodies on live cells was achieved using DVPC. DVPC was also orthogonal to the strain-promoted azide alkyne click reaction (SPAAC), which enabled orthogonal labeling of two proteins in one batch. Further exploration on the cycloaddition reactions between *o*-diones and other electron-rich C=C bonds led to the discovery of the bioorthgonal DFC reaction[2], which was the first anionic cycloaddend-promoted bioorthogonal cycloaddition reaction. With the water-mediated formation of the highly electron-rich anionic cycloaddend from furan-2(3H)-one derivatives, which is stabilized in water with high polarity, DFC reaction with ground state *o*-diones proceeds rapidly in aqueous solution and on live cells. The combined utilization of this reaction together with the two other widely used bioorthogonal reactions SPAAC and IEDDA allows for mutually orthogonal labelling of three types of proteins or three groups of living cells in one batch without cross-talking. Using bioorthogonal reactions, we were able to build various bio-active molecules to visualize or regulate biological systems with spatial and temporal resolution.[3-5]

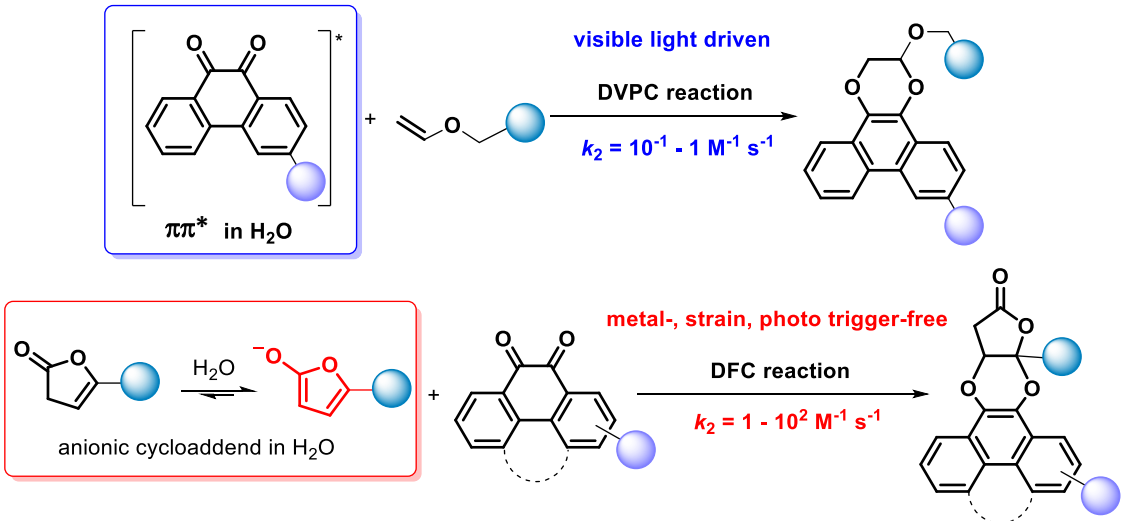

Figure 1. Bioorthogonal cycloaddition reactions of o-diones driven by visible light or by water.

References

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