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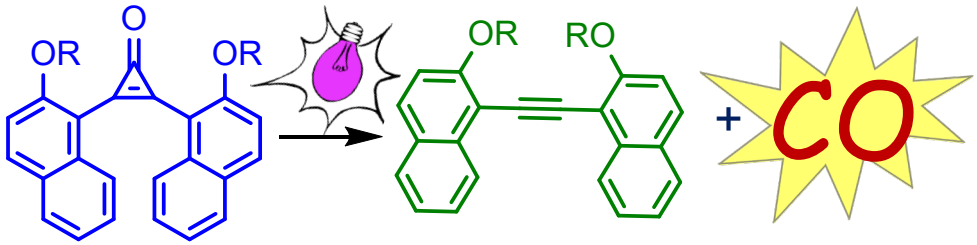
Cyclopropenone-based Platform for Light-directed Drug Delivery, Photo-medicine, and Bio-imaging



Efficient and non-toxic water-soluble light-activated carbon monoxide releasing molecule (photo-CORM). CO released is triggered by UVA or blue LED, or NIR laser.

Quantum efficiency of CO release in nanocrystalline suspension increases to 330%

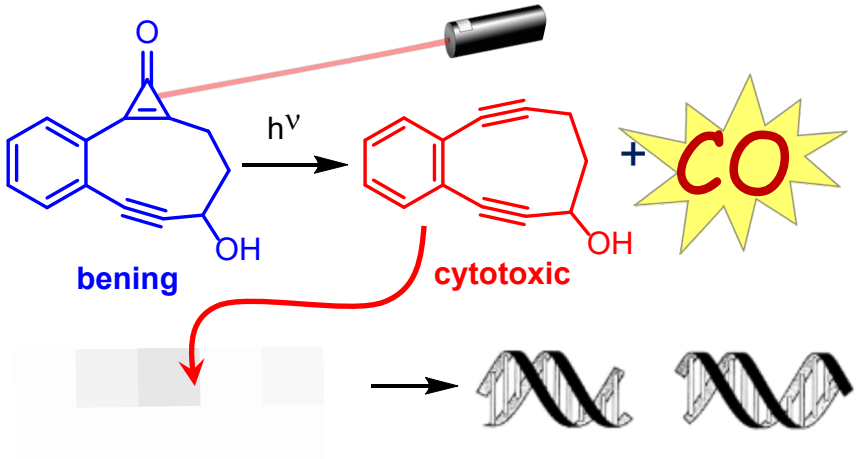


Photo-activatable enediyne antibiotics permit simultaneous release of highly cytotoxic enediyne compounds and carbon monoxide. Enediynes cause double strand DNA scission, while CO sensitizes cancerous cells to this damage.

Efficient light-activated carbon monoxide releasing compounds have been developed. The exposure of these photo-CORMs to UVA or blue light, as well as IR radiation, generates CO with high quantum efficiency. The modification of the substituents (R) in the core structure allows for the controlling of aqueous solubility and/or targeting various parts of the cell.

The quantum efficiency of the CO generation (the ratio of photons absorbed to molecules produced) can be dramatically enhanced in nanocrystalline suspension (from 42% to 330%).

Cyclopropenone-caged analogs of natural enediyne antitumor antibiotics allows for simultaneous release of highly cytotoxic enediyne and CO. The latter induces thousand-fold enhancement of tumor cells antibiotic sensitivity.

Carbon monoxide is one of the important endogenous gaso-transmitters. It is known to reduce inflammation, cause vasodilation and smooth muscle relaxation, as well as sensitize cancerous cell to antibiotics. The toxicity of CO, however, hampers its medical applications. Therefore, the selective and controlled delivery of CO is an important goal of modern pharmacology. Photo-CORMs developed with NSF support allows for the selective release of CO by light-controlled decarbonylation of cyclopropenones.

Harnessing the quantum yield amplification in crystalline state might benefit many areas of technology, e.g., sensing, photo-polymerization and lithography, signal amplification, etc. Due to highly absorbing nature of mammalian tissues, this effect would find many applications in photo-medicine.

This project is currently supported by an award from the Chemistry Division of the Directorate for Mathematical & Physical Sciences. The science behind this project has been developed with the support of previous awards from the Chemistry Division. The interdisciplinary experiments in these projects proved to be an excellent training vehicle for undergraduate and graduate students. In addition, high school students are conducting internships via the UGA Young Dawgs Program.