Can Superoxide-responsive CO Delivery Molecules be Developed?

NIH (R15GM124596)

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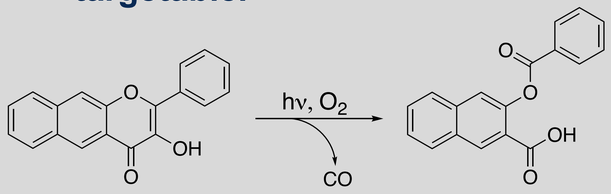
Introduction

CO delivery molecules:

- Carbon monoxide (CO) has a reputation as a toxic molecule.
- CO produces therapeutic effects including anti-inflammatory effects.
- We are especially interested in CO delivery molecules that are **triggerable, trackable, and targetable.**

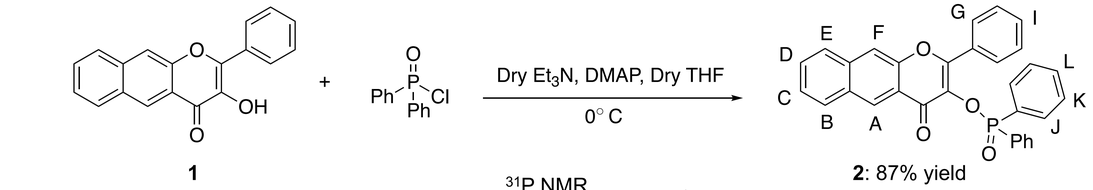


Reactive Oxygen Species (ROS):

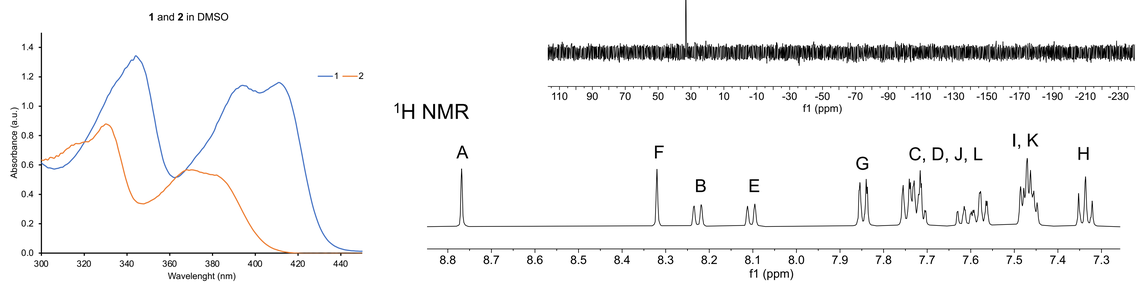
$$O_2 + e^- \rightleftharpoons O_2^{\bullet -} \text{ (superoxide)}$$

- Generated in the mitochondria
- Overproduction of ROS causes oxidative stress

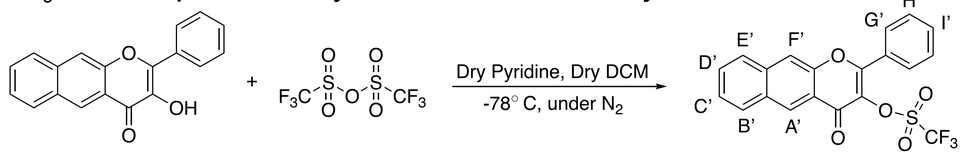
Goal: Combine superoxide detecting groups with Flav-1 (**1**) to act as potential trigger for precise CO release.



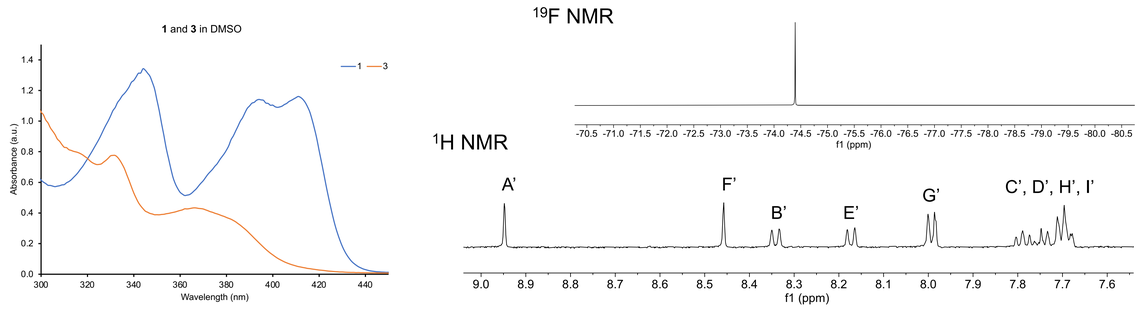
1 **2**: 87% yield



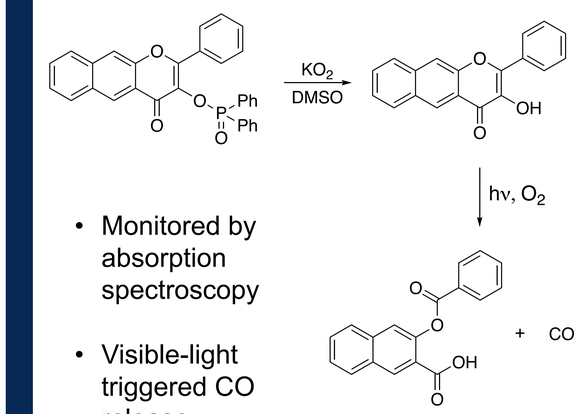
Compounds **2** and **3** characterized by: ^{1}H, ^{13}C{^{1}H}, ^{31}P, and ^{19}F NMR in DMSO-d_6, mass spectrometry, and elemental analysis.



1 **3**: 75% yield



Proposed reaction with addition of KO_2:



- Monitored by absorption spectroscopy
- Visible-light triggered CO release

Conclusion

- We have synthesized and characterized potential superoxide responsive CO delivery molecules.
- Their response to superoxide can be monitored by the addition of potassium superoxide (KO_2) via absorption spectroscopy.

Future Work:

- Characterize end products after addition of KO_2 by ^{1}H NMR and ^{31}P/^{19}F NMR.
- Illumination after addition of KO_2 to observe CO release.

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