Exploration of the Photocatalytic Activity of Eosin Y in Benzylic Peroxidation Reactions

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Abstract

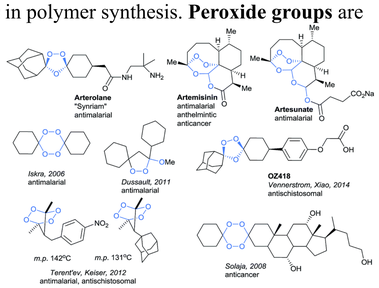
The use of photoredox catalysis for functionalization reactions is a novel approach in synthetic organic chemistry. Synthetic efforts in our lab focus on halogenation and benzylic peroxidation reactions. Peroxides are prevalent in drug molecules, commonly part of pharmacophores. Eosin Y is a low-cost, long-known dye molecule used for photocatalysis. Successful benzylic peroxidation reactions of 2-phenethylbromide, 3-methylacetophenone, and other phenylic compounds using the photocatalyst Eosin Y were confirmed via NMR analyses. The mechanism of photocatalysis by Eosin Y is being explored computationally using the General Atomic and Molecular Electronic Structure System (GAMESS) software. Through the application of several different levels of theory, ground- and excited-state potential energy surfaces may be investigated to uncover insights into the mechanistic action of Eosin Y as a photoredox catalyst.

Background

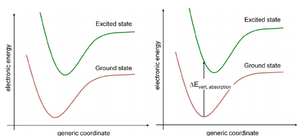
Peroxides are used as radical initiators in polymer synthesis. **Peroxide groups** are also prevalent in drug molecules.

Benzylic peroxidation reactions are carried out via photoredox catalysis.

Photoredox catalysis is a method whereby light is used to energize an organic dye to catalyze a redox reaction.



Gomes, G. D. P.; Vil, V.; Terentev, A.; Alabugin, I. V. *Chemical Science* **2015**, 6 (12), 6783–6791.



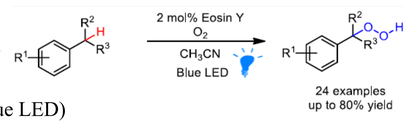
To support the proposed reaction mechanism, uncovering the **potential energy surfaces** of ground and excited states of the photocatalyst is useful.

Potential energy surfaces of ground and excited states tell about the absorbance and fluorescence of molecules by providing insight into the energy gap between the two states.

Methods

Benzylic Peroxidation Reaction

- ✓ metal-free organocatalyst (Eosin Y)
- ✓ sustainable oxidant (O_2)
- ✓ energy-economical light source (blue LED)



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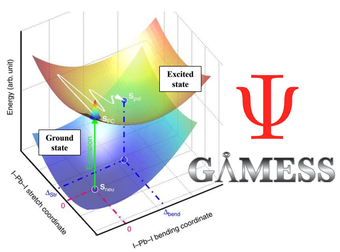
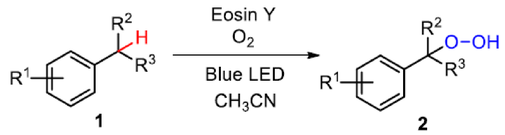
GAMESS for Potential Energy Surfaces

Equilibrium geometries are calculated using the General Atomic and Molecular Electronic Structure Software (GAMESS) to generate PES of ground and excited states of Eosin Y. They provide insight into energy gaps, as well as UV absorption and fluorescence signals typical of each species.



Proposed Mechanism

The proposed mechanism refers to the visible-light-induced benzylic hydroperoxidation reaction represented by the following scheme reproduced from recently published JOC paper *(2)*:



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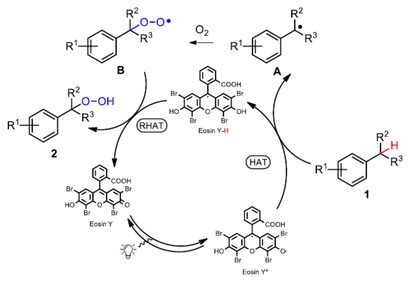


1. Eosin Y is excited upon light irradiation to produce Eosin Y*, which abstracts a H atom from a benzylic C-H bond to generate benzylic radical A and Eosin Y-H.

2. Molecular oxygen (O_2) traps radical A to produce peroxy radical B.

3. A retro-HAT from eosin Y-H to peroxy radical B finally forms hydroperoxide product 2 and regenerates eosin Y back to catalytic cycle.

Results/Conclusions

Table 1. Optimization of the Reaction Condition[a]

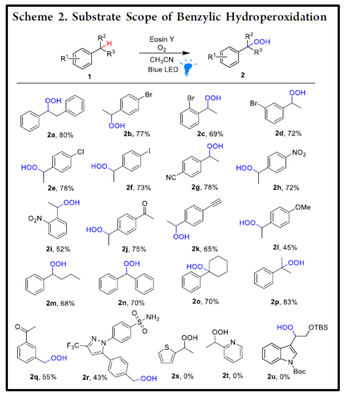
entry	*t*-BuOOH equiv	solvent	catalyst	LED	base[b]	yield[c]
1	4	CH_3CN	eosin Y	blue	N/A	80%
2	4	CH_3CN	Ir(III)[d]	blue	N/A	60%
3	4	CH_3CN	rose Bengal	blue	N/A	15%
4	4	CH_3CN	$[Mes–Acr]^+ClO^{4-}$	blue	N/A	70%
5	4	CH_3CN	eosin Y	green	N/A	50%
6	4	CH_3CN	eosin Y	white	N/A	56%
7	4	CH_2Cl_2	eosin Y	blue	N/A	70%
8	4	DCE	eosin Y	blue	N/A	72%
9	4	CH_3CN	eosin Y	blue	DBU	35%
10	4	CH_3CN	eosin Y	blue	Et_3N	40%
11	2	CH_3CN	eosin Y	blue	N/A	78%
12	1	CH_3CN	eosin Y	blue	N/A	80%
13	0	CH_3CN	eosin Y	blue	N/A	79%

[a]Reaction conditions: 1,2-diphenylethane (1 mmol), *t*-BuOOH (0–4 mol), and photocatalyst (2% mmol) were added to solvent (5 mL) under light in the presence of an oxygen balloon at room temperature. [b]1 mmol of DBU or Et_3N was used; N/A, not applicable. [c]Yields of isolated product. [d]Ir(III): $(Ir[dF(CF_3)ppy]_2(dtbpy))PF_6$

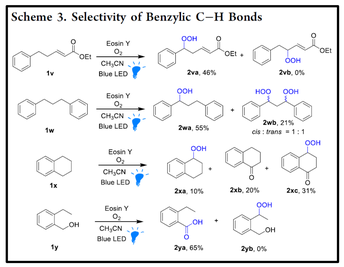
Benzylic Peroxidation Reaction

The reaction conditions were optimized (**Table 1**), where entry 13 represents the optimal reaction conditions. The substrate scope was explored (**Scheme 2**), and the reaction selectivity was illustrated using substrates with more than one potential oxidation site (**Scheme 3**). These figures were reproduced from recently published JOC paper *(2)*.

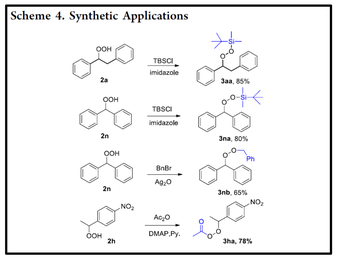
Scheme 2. Substrate Scope of Benzylic Hydroperoxidation



Scheme 3. Selectivity of Benzylic C–H Bonds



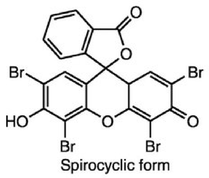
Scheme 4. Synthetic Applications

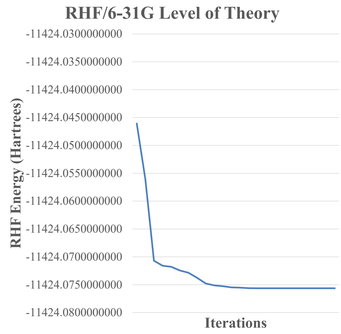


Finally, silyl, benzyl, and acyl peroxides were successfully synthesized with good yields using this reaction. (**Scheme 4**). This figure is reproduced from recently published JOC paper *(2)*.

Potential Energy of Geometries of Eosin Y

The **equilibrium geometry** of the ground state has been located.





Future Directions

Benzylic Peroxidation Reaction

- Applications of the benzylic hydroperoxidation reaction will be explored and expanded.
- Reactions of benzylic substrates with TEMPO will be conducted to support the proposed reaction mechanism.
- Other confirmatory reactions may be explored.

Potential Energy of Geometries of Eosin Y

- Using electronic structure theories, the equilibrium geometries of excited states of the Spirocyclic form will be determined.
- Equilibrium geometries of the Spirocyclic form will be determined using higher levels of theory. Equilibrium geometries of the Neutral form, which is in equilibrium with the Spirocyclic form, will also be determined.

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References

(1) Gomes, G. D. P.; Vil, V.; Terentev, A.; Alabugin, I. V. Stereoelectronic Source of the Anomalous Stability of Bis-Peroxides. *Chemical Science* **2015**, 6 (12), 6783–6791.
(2) Inoa, J.; Patel, M.; Dominici, G.; Eldabagh, R.; Patel, A.; Lee, J.; Xing, Y. Benzylic Hydroperoxidation via Visible-Light-Induced Csp3–H Activation. *The Journal of Organic Chemistry* **2020**.