

# Investigation of the Regioselectivity of the Singlet Oxygen Ene Reaction in Metal-Organic Frameworks

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## ABSTRACT

Regioselectivity of the Singlet Oxygen Ene-Reaction using Metal-Organic Frameworks

By

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Singlet oxygen is an extremely reactive molecule which has garnered attention over the years for its reactivity. Singlet oxygen reactions have seen applications in solar cells, drug synthesis, and in photodynamic treatment of cancer cells. In this study, we examine the controlled selectivity of the products from the singlet oxygen ene-reaction, resulting in allylic hydroperoxides. This reaction has been used in the total synthesis of various molecules and is the primary way to introduce oxygen functionality in organic molecules. Past works have used cagelike structures such as zeolites as photocatalytic sites to influence the selectivity. Instead, in this study, we report the use of metal-organic frameworks (MOFs) as a photocatalytic site to influence the selectivity of the reaction via Al-TCPP, NUPF-2Y, and DGIST-1 MOFs. Through these MOFs, controlled selectivity was observed as a result of the cage confinement effect.

## ACKNOWLEDGMENTS

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## CHAPTER 1

### Introduction and Overview

The photooxidation of olefins has various synthetic applications. It is used primarily to introduce oxygen functionality in organic molecules. The singlet oxygen ene-reaction produces two regioisomeric allylic hydroperoxides in a 50:50 mix. Due to the lack of selectivity, it is desirable to manipulate the selectivity of this reaction. Metal-organic frameworks are crystalline, porous frameworks with metal nodes and organic linkers. They have a tunable surface area, pore diameter, and stability. Therefore, to investigate the regioselectivity of the ene-reaction, metal-organic frameworks will be used as a catalyst.

#### Problem Statement

The singlet oxygen ene-reaction generates two regioisomeric products in a 50:50 mix. Since the photooxidation of olefins leading to allylic hydroperoxides has various synthetic applications, controlled selectivity is desirable.

#### Purpose/Goals of the Project

This project aims to use metal-organic frameworks as a catalyst for the singlet oxygen ene-reaction and to investigate the solvent effect on this reaction. As a result, the effect of different porphyrinic MOFs and solvent systems will be detailed. This project will highlight the photocatalytic function of MOFs and expand understanding of singlet oxygen reactions with olefins.

#### Approach

The MOFs used for this project are Al-TCPP, TCPP, and NUPF-2Y. These MOFs were synthesized and characterized using powder X-ray diffraction (PXRD) and gas

desorption. Photooxidation of 2-methyl-2-heptene in protic and aprotic solvents was performed. The yield and product distribution of the reaction was determined using  $^1\text{H}$  NMR.

### Significance

This project is significant due to the various synthetic applications of the singlet oxygen ene reaction in total synthesis of biomolecules. Namely, the total synthesis of Rhodonoids, a family of polycyclic meroterpenoids, utilized a singlet oxygen ene-reaction pathway. To improve the overall yield of a synthetic pathway, further investigation into the singlet oxygen ene-reaction pathway is necessary. Previous studies have illustrated how other catalysts, such as zeolites, influenced the regioselective outcomes through additional steric hindrance. This led to the favorable formation of the less sterically hindered product. Similarly, the pore diameter effect in MOFs may also result in the formation of the less sterically hindered product.

### Specific research questions

In this project, I am investigating whether the regioselectivity and solvent effect of the ene-reaction can be affected by MOFs. I hypothesize that the cage confinement of MOFs will affect the regioselectivity by favoring the less sterically hindered product similar to what is observed in zeolitic frameworks. It has also been hypothesized that the solvent effect has little effect on the reaction.

## CHAPTER 2

### Background

#### 2.1 Singlet Oxygen

Molecular oxygen, also known as the triplet state of oxygen, is the ground state of the dioxygen molecule in the environment. Triplet oxygen is unreactive due to being a diradical in its chemical environment<sup>1-2</sup>. Singlet oxygen, the first excited state of molecular oxygen, can be generated in the presence of light and a photosensitizer. This occurs through an energy transfer where a ground-state photosensitizer absorbs light and gets excited to a singlet photosensitizer. After intersystem crossing, singlet oxygen is generated by the excited photosensitizer and triplet oxygen collision<sup>3</sup>.

#### 2.2 Properties of Singlet Oxygen

Singlet oxygen is the lowest-lying excited state of molecular oxygen present at 22.5 kcal/mol above the triplet state<sup>2</sup>. The differences between the reactivity of singlet oxygen and molecular oxygen can be described in terms of the electronic structure. In singlet oxygen, the HOMO and LUMO are degenerate orbitals, causing singlet oxygen to be extremely reactive. From its excited state, singlet oxygen can return to its ground state by relaxing to the ground state or transferring its energy to another molecule without chemically changing that molecule (physical quenching).

#### 2.3 Types of Photosensitizers

Several groups of UV-vis absorbing molecules have been observed to exhibit singlet oxygen-generating ability. The most common photosensitizers for singlet oxygen are organic dyes and aromatics, porphyrins and other macrocycles, semiconductors, and

transition metal complexes<sup>1</sup>. In this project, we will look at the photosensitized generation of singlet oxygen through macrocycles, particularly tetraphenyl porphyrins.

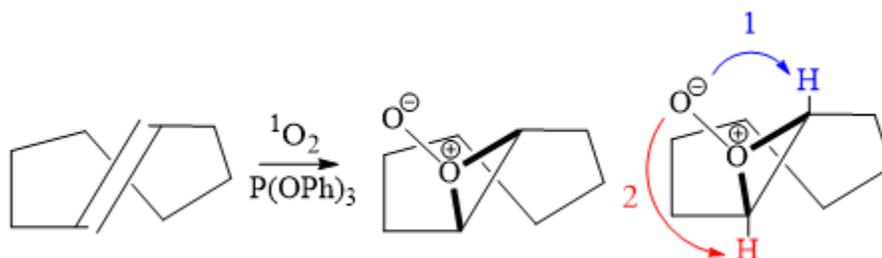
## 2.4 Applications of Singlet Oxygen

Photosensitized singlet oxygen has applications in photodynamic therapy of cancer, photooxidation, DNA damage, and small molecule synthesis<sup>2</sup>. Due to the electrophilic nature of singlet oxygen, it has been observed to participate in reactions with electron-rich molecules such as olefins and dienes. Particularly, we studied the singlet oxygen reaction with 2-methyl-2-heptene.

## 2.5 Singlet Oxygen Ene Reaction

The singlet oxygen ene-reaction with olefins yields allylic hydroperoxides. This reaction proceeds through a per-epoxide intermediate. The anionic oxygen abstracts hydrogen from the per-epoxide intermediate to form two regioisomers. This reaction then yields two products evenly<sup>4</sup>.

Scheme 1: Formation of per-epoxide intermediate and its hydrogen abstractions



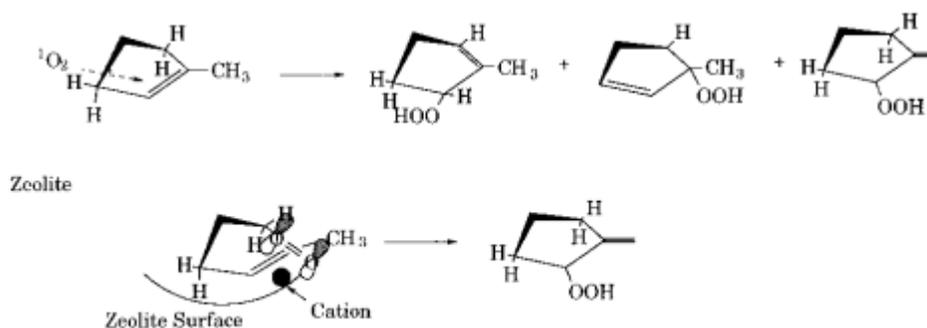
Foote and co-workers trapped the per-epoxide intermediate, confirming that the per-epoxide intermediate proceeds through a concerted pathway<sup>4</sup>.

Orfanopoulous et al. studied the photooxidation of 2-methyl-2-heptene with C<sub>60</sub> fullerene with aluminum or silicon supporting surfaces<sup>5</sup>. This further confirmed that the mechanism of the ene-reaction remained consistent in the presence of fullerene, rose

bengal, and fullerene (C<sub>60</sub>). The work done by Orfanopoulous et al. discovered that the conversion rate was higher in deuterated solvents due to higher lifetimes and that the selectivity of the reaction could be controlled by different surfaces<sup>5</sup>. Furthermore, the activity of C<sub>60</sub> was higher on aluminum over silicon surfaces. However, in the presence of C<sub>60</sub>, no selectivity was observed.

Li et al. reported the singlet oxygen-mediated oxidation of olefins within dye-exchanged X and Y zeolites<sup>6</sup>. The reaction of cyclic and acyclic olefins within zeolites resulted in the favoring of one product. The alkene was proposed to adsorb on the zeolite surface from the less sterically hindered side. As a result, the oxygen would attack the olefin from the side with a methyl and hydrogen. Due to the steric effects, an attack would not result in hydroperoxide formation from the allylic hydrogen's abstraction. Without a zeolitic framework, no change in selectivity was observed in either methylene blue or rose bengal on silica. One of the limitations of this work is that conversion percentage of the reactants to products was not calculated to determine reaction completion.

Scheme 2: Ene-reaction in the presence of dye-exchanged zeolites.



Adapted from Li et. al

## 2.6 Metal-Organic Frameworks

Metal-organic frameworks are a class of porous frameworks composed of a metal node and an organic linker<sup>7</sup>. Due to the amount of different metals and linkers that can be incorporated, many MOFs have been synthesized with versatile properties. MOFs have also been studied and observed to participate in a wide range of reactions. The porous framework of MOFs defines the reaction space and shape.

The confinement effect that MOFs exhibit refer to the structural and functional properties of the MOF cavity. The pore diameter affects the selectivity via size exclusion of substrate or products like the effect observed in zeolitic frameworks. To examine confinement effects, the pore size, neighboring group, and topology and active site effects should be considered.

MOFs were first reported to exhibit pore size effects on polymerization reactions. In this study, increased selectivity of the trans-polymerization product was observed due to the limitation of the reaction space<sup>7</sup>. This effect was further established in the polymerization of divinylbenzene where in small pore diameters, the formation of linear polymers was observed, but in larger pore diameters, cross-linked polymers were favored.

In this project, we will investigate MOFs with varying pore diameters to examine the cage confinement effect. Specifically, we will be looking at porphyrin MOFs for their ability to generate singlet oxygen. Particularly, we will look at three select MOFs: Al-TCPP, NUPF-2Y, and DGIST.

The linker used for all these MOFs will be tetrakis-carboxy-phenyl porphyrin (TCPP). Under irradiation, MOFs containing organic photosensitizers can promote the

formation of singlet oxygen species<sup>8</sup>. MOFs are well studied in the literature as photocatalysts for the degradation of 2-chloroethyl ethyl sulfide (CEES) to 2-chloroethyl ethyl sulfoxide (CEESO).

The Al-TCPP MOF will be synthesized under solvothermal conditions, resulting in a surface area of 1400 m<sup>2</sup>g<sup>-1</sup>. Two topologically elliptical channels are present in Al-TCPP, one channel forms in plane with the porphyrin linker resulting in a hourglass shaped pore as shown in Fig. 1.<sup>9</sup> The other elliptical channels forms a staggered arrangement with the porphyrin linker, leading to a S shaped pore. This MOF has shown to be a viable active site for visible light photocatalysis.

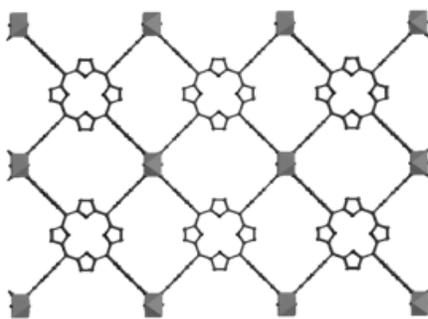


Fig. 1: Structure of Al-TCPP.

The NUPF-2Y MOF will be synthesized under solvothermal conditions and it had a surface area of 1718 m<sup>2</sup>g<sup>-1</sup>. The use of rare earth metals such as yttrium as the metal node, exhibits unique electronic and optical properties, making these MOFs multifunctional<sup>10</sup>. These frameworks were reported as having high chemical and thermal stability. The structure of NUPF-2Y resulted in a hexagonal structure with 4 TCPP linkers preserving their planarity. NUPF-2Y has also shown potential as heterogeneous catalysts for carbene insertion in N-H bonds.

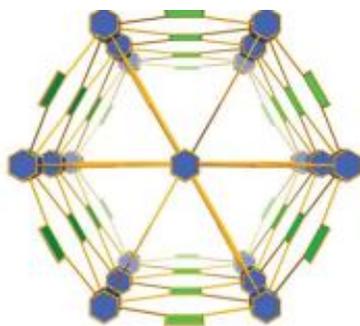


Fig. 2: Structure of NUPF-2Y.

## Methods and Approach

### Synthesis of Al-TCPP

Al-TCPP, NUPF-2Y, and DGIST-1 were synthesized according to the following procedure<sup>9-11</sup>. For characterization, powder x-ray diffraction (PXRD) and gas isotherm were performed to confirm MOF properties.

### Approach

To investigate the regioselectivity and the solvent effects of the ene-reaction, three MOFs with different pore diameters were investigated: Al-TCPP, NUPF-2Y, and DGIST-1. These three MOFs were selected for their singlet oxygen generation ability and potential as photocatalysts. The solvent effect was tested for using CD<sub>3</sub>OD and CD<sub>3</sub>CN. Free TCPP will be used as a negative control to ensure that selectivity is controlled through the MOF.

For the photooxidation of 2-methyl-2-heptene, 15% catalytic loading was used and the MOF or free TCPP was dissolved in 1 mL of solvent. After the addition of solvent, the mixture was sonicated for 20 minutes, followed by the bubbling of O<sub>2</sub> for 5 minutes. 2-methyl-2-heptene was then added and the sample was irradiated for 30 minutes. The conversion of reactants to product and the product distribution was analyzed by <sup>1</sup>H NMR. The corresponding <sup>1</sup>H NMR peaks are shown in Fig. 4-6.

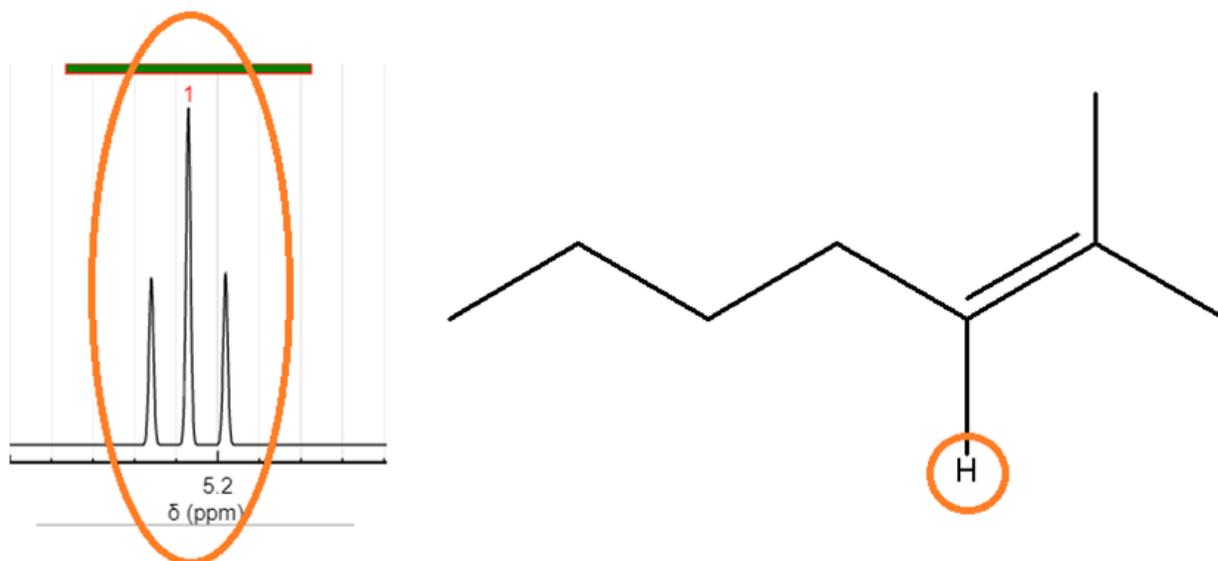


Figure 4:  $^1\text{H}$  NMR of reactant 1. The expected peak is a triplet near 5.2 ppm.

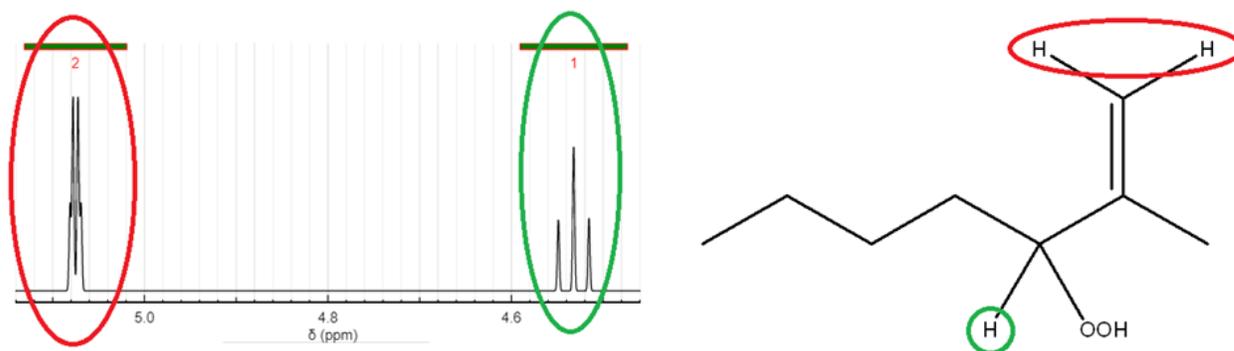


Figure 5:  $^1\text{H}$  NMR of product 2a. The expected peak area doublet near 5.1 ppm and a triplet at 4.5 ppm. The intensity of the doublet (red) should be twice that of the triplet (green).

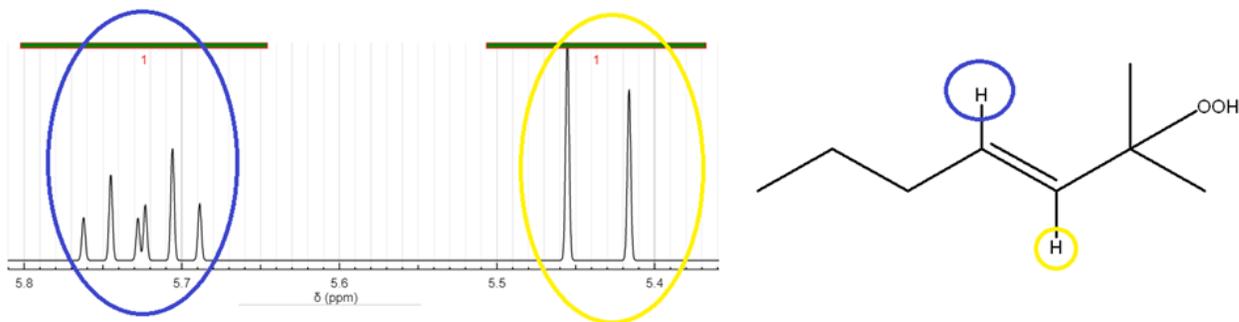


Figure 6:  $^1\text{H}$  NMR of product 2b. The expected peak is a doublet of triplet near 5.6 ppm. The large decoupling constant between the two peaks is representative of the trans double bond.

Furthermore, the conversion percentage and the product distribution will be calculated using the characteristic peaks of the product using Eq. 1 and 2.

**Equation 1.** The calculation of conversion percentage using the  $^1\text{H}$  NMR data.

$$100\% - \left( \frac{\text{Peak Intensity of Reactant (1)}}{\text{Peak Intensities of the Reactant and the Products (2a and 2b)}} \right) * 100\%$$

**Equation 2.** The calculation of yield ratio using the  $^1\text{H}$  NMR data.

$$\frac{\text{Peak Intensity of Product 2a}}{\text{Peak Intensities of Products (2a + 2b)}} * 100\%$$

## CHAPTER 4

## Results and Discussion

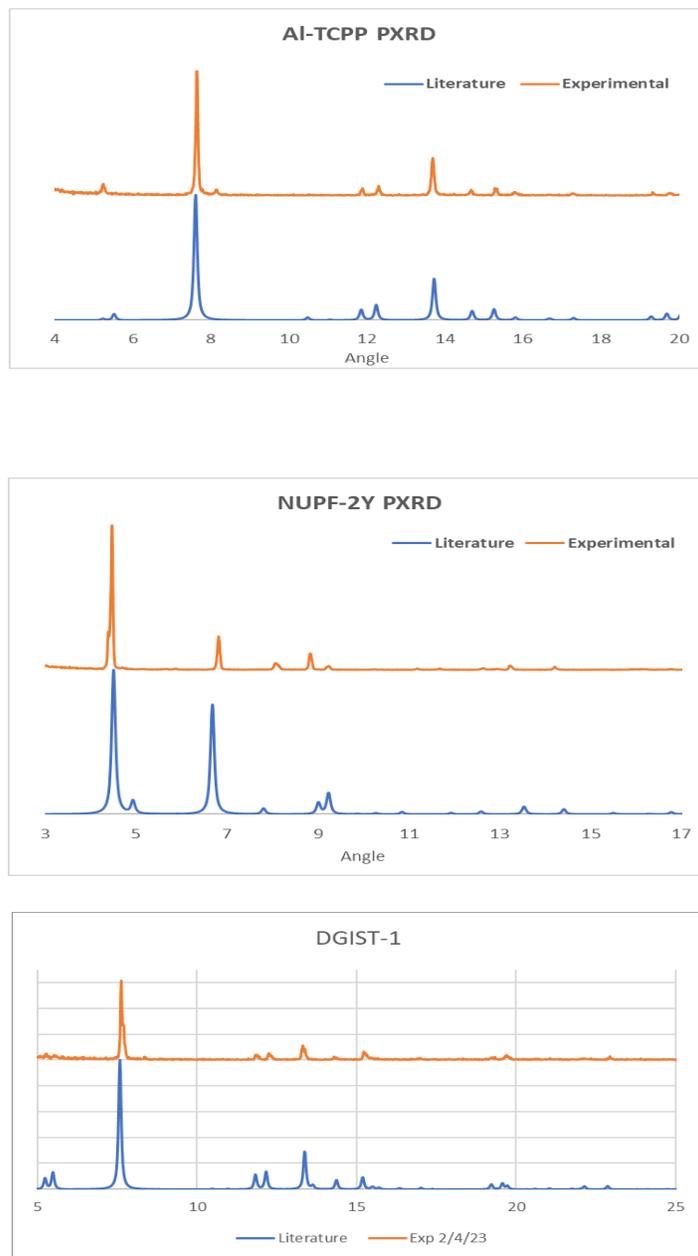


Fig. 7-9: PXRD characterization for Al-TCPP, NUPF-2Y, and DGIST-1.

The data closely aligns with the literature for the powder x-ray diffraction (PXRD) of the three MOFs. Isotherm characterization was done to confirm the porosity of the MOFs and followed very closely to the literature values.

Table 1: Photooxidation and Yield with Al-TCPP, NUPF-2Y, and TCPP

MOF	Pore Diameter Range(Å)	Surface Area	Solvent	Yield	A:B	Reaction Time
TCPP	NA	NA	CD <sub>3</sub> CN	100%	48/52	30 mins
Al-TCPP	8.49-11	1400m <sup>2</sup> /g	CD <sub>3</sub> CN	100%	48/52	30 mins
NUPF-2Y	6-8.47	1718m <sup>2</sup> /g	CD <sub>3</sub> CN	100%	29/71	150 mins
TCPP	NA	NA	CD <sub>3</sub> OD	100%	42/58	30 mins
Al-TCPP	8.49-11	1400m <sup>2</sup> /g	CD <sub>3</sub> OD	100%	42/58	30 mins
NUPF-2Y	6-8.47	1718m <sup>2</sup> /g	CD <sub>3</sub> OD	100%	25/75	150 mins

Initially, the TCPP was used to serve as a negative control and replicated the previous result in which no significant product selectivity was observed with 100% conversion with irradiation of 30 minutes. The solvent effect was studied using various polar and aprotic solvents, but the product selectivity was not affected. In the presence of larger pore size, Al-TCPP had little to no effect on the reaction outcome. Al-TCPP most likely did not show any selectivity since the reaction size due to having a big pore diameter. On the other hand, NUPF-2Y showed preference for the 2b product due to its smaller pore size, but irradiation of 150 minutes was necessary to achieve full conversion of the reactants to products.

For discussion of the pore diameter effect, we should consider the bond lengths of the substrate, particularly the O-O bond distance, C-C bond distance, the distance of O to a hydrogen available for abstraction, and the overall diameter of the molecule in angstroms. The bond distance from anionic oxygen to the less sterically hindered H was less than that of the more sterically hindered H. The distance from the two hydrogens that could be abstracted is 8.338 Å. The diameter of the molecule was 4.053 Å, small enough to fit inside the MOF. Based on these measurements, it is reasonable that Al-TCPP yielded no change in the selectivity because its pore size was more than large enough to

accommodate the entire molecule. On the other hand, NUPF-2Y exhibits selectivity since its pore diameter is 6-8 Å, smaller than the distance between the two hydrogens that could be abstracted. As a result, we observe some change in the selectivity favoring the less sterically hindered hydrogen was abstracted.

#### Conclusion

In this project, we observed regioselectivity of the ene-reaction in NUPF-2Y, a MOF with a small pore size. Because selectivity was only observed in NUPF-2Y and not Al-TCPP, selectivity occurs most likely as a result of pore diameter effect. To investigate this further, other MOFs with small pore sizes should be investigated. One candidate for a study of this nature would be DGIST-1, a MOF with small pore sizes and has shown potential as a photocatalyst. Furthermore, more studies on quantum yield measurement of MOFs would be necessary to increase our understanding.

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