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Organic Photoredox Cycloadditions under Confinement

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A thesis submitted in partial fulfillment of the requirements for a baccalaureate degree in Chemistry with honors in Chemistry

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ABSTRACT

Inspired from the complexity and versatility of nature's catalysts: enzymes, artificial biocatalysts have been of large interest for their applicability to non-natural syntheses. However, the limitations of these systems, such as substrate specificity, selectivity, and solubility, call for novel approaches. The hypothesis is that, by designing modular polymer frameworks that are highly adaptable and functionalized, the supramolecular confinement can facilitate substrate-active site interactions, and substrate activation with enzyme-like features. [2+2] and [4+2] cycloadditions rank among the most important transformations in organic synthesis, as they enable high-yielding, stereospecific access to cyclobutane and six-membered ring scaffolds. Due to the ubiquity of these cyclic motifs in bioactive natural products, therapeutic agents, and relevant intermediates for organic synthesis, achieving optimized yields and product selectivity is an important challenge. The research herein outlines progress in this direction, with the development of a photocatalytic single-chain nanoparticle (SCNP) with 2,4,6-tri(4-methoxyphenyl)pyrylium tetrafluoroborate (*p*-MeO-TPT) pendants as the active site, and styrylpyrene units as visible-light cross-linking agents. The SCNP demonstrated enhanced reactivity on the dimerization of trans-anethole when compared to the small molecule catalysis. Additionally, progress for the design and development of SCNPs as selective photocatalysts for the [4+2] cycloadditions of electronically-mismatched partners is reported for three different model systems. Notably, quantitative yields were obtained for the photoinduced, p-MeO-TPT mediated Diels-Alder between trans-anethole and 1,3-cyclohexadiene. Overall, these results strive to contribute to the understanding and development of organic photoredox catalysts as versatile, modular platforms for visible-light-promoted organic transformations.

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Chapter 1 : Background Information

Cycloaddition reactions are some of the most important, fascinating, and powerful tools in organic synthesis. Molecular, stereochemical, and functional complexity can be rapidly achieved in these one-step processes, resulting in the formation of multiple bonds per reaction. The study of these pericyclic processes emerged with the revolutionary discovery of the [4+2] cycloaddition by Professor Otto Diels and his student Kurt Alder, in the regioselective reaction between cyclopentadiene and benzoquinone,¹ as illustrated in Figure 1.



Figure 1. The discovery of the Diels-Alder reaction and its regioselectivity

This remarkable transformation earned the founders the Nobel Prize in 1950, as it enabled significant advances in the synthesis of complex natural compounds and had fundamental applications to modern society. Subsequently, Woodward and Hoffman developed a theoretical treatment of all concerted reactions by establishing that orbital symmetry must be conserved in these types of transformations. Since then, the breadth of the Diels-Alder reaction scope, regioselectivity, and stereoselectivity has been largely diversified through intramolecular [4+2] cycloadditions, hetero Diels-Alder reactions, Lewis acid catalyzed and pressure accelerated Diels-Alder reactions¹⁶ More recently, the advancement of light-mediated catalysis of organic substrates

through single-electron transfer has enabled access to challenging transformations with unique selectivity, such as [2+2], [4+2], [2+2+2], and [3+2] cycloadditions.

1.1: Organic Photoredox Catalysis

Over the past few decades, there has been a resurgence in the interest in photochemical activation as a powerful means to construct new bonds. Drawing inspiration from nature's efficient conversion of light energy into chemical energy, chemists have been motivated to exploit and advance diverse photochemical methods, striving for sustainable synthesis. Among these, photoredox catalysis has grown substantially in the past years, providing new synthetical toolkits for facile assembly of complex organic structures. In particular, these strategies utilize the ability of organic dyes or transition metal complexes to absorb visible light and generate open-shell reactive intermediates that are otherwise inaccessible through traditional thermal activation. These advances have been invaluable to the development of green, sustainable methods in pharma production, drug discovery, biomedical chemistry, and feedstock valorization.²

Photoredox catalyzed reactions occur when the light-absorbing species or catalyst is promoted to an excited electronic state and is then quenched by a substrate or a secondary catalyst to afford unique reaction pathways. Specifically, upon absorption of energy in the form of light, an electron within the irradiated molecule is promoted from a ground-state singlet (S₀) to the first singlet excited state (S₁), which can then undergo intersystem crossing (ISC) to a longer-lived triplet excited state (T₁). Most bimolecular reactions proceed via S₁ and T₁ through either energy transfer or electron transfer pathways. This general process of excitation and electron transfer to a ground state molecule is commonly known as photoinduced electron transfer (PET).³ Photophysical properties of photoredox catalysts such as lifetime of fluorescence, quantum yield of fluorescence, quantum yield of intersystem crossing, and excited state redox potentials affect the modes of action and their efficiency. However, most PET processes can be categorized in either oxidative or reductive quenching cycles (Figure 2).



Figure 2: Oxidative and reductive quenching cycles of a photoredox catalyst. (Adapted with permission from Ref. 3 Copyright 2016 American Chemical Society)

While iridium and ruthenium complexes are prominent visible-light activated catalysts, vastly employed in organic synthesis for their ability to activate a broad range of substrates, their organic photoredox counterparts provide not only metal-free alternatives, but also much more potential for diversification and fine properties tuning through structural modifications. Methodologies that utilize visible-light organic photosensitizers are still narrow and focus only on specific transformations. Among these, photocycloadditions are some of the most important photoredox-catalyzed reactions, as they enable fast formation of multiple new bonds with high regio- and stereoselectivity. The next two sections will focus on the existing methods and photocatalysts commonly used to promote [2+2] and [4+2] cycloadditions.

1.2: [2+2] Cycloadditions

The [2+2] photocycloaddition reaction between olefins is one of the most important and widely used chemical transformations in organic synthesis. It provides not only a facile assembly of the cyclobutene scaffold, but it also enables fast access to structural complexity in highly regioand stereoselective fashion. Additionally, the products are ubiquitous motifs in many complex natural compounds, as they can also serve as substrates for ring enlargements, due to their inherent strain.⁴ Despite the fact that the [2+2] photocycloaddition has served as a key step in many syntheses of natural compounds, such as the ones listed in Figure 3, this reaction is currently an understudied avenue of research compared to its [4+2] and [3+2] counterparts.



Figure 3: Representative natural products prepared with [2+2] cycloaddition as a key step

One of the most common ways of forming cyclobutanes is the photocycloaddition between enones and olefins by direct irradiation or mediated by a photosensitizer (acetone, benzophenone). In this method, one of the olefins is promoted to its first excited singlet or triplet state, which then adds to a ground-state olefin to form the cycloadduct through a 1,4 biradical.^{4,5} Despite its apparent simplicity and viability, this method has significant limitations. Non-conjugated alkenes have high lying singlet and triplet states so their dimerization cannot be feasibly promoted with common sources of UV light. Unproductive deactivation pathways such as fluorescence and E/Z isomerization decrease the efficiency of these reactions. However, the use of transition metals, such as Cu(I) salts has proven useful in overcoming these issues.^{4, 5} Upon complexation with metals, non-conjugated alkenes can be easily promoted to their excited states and react to give the [2+2] photodimerization products. The main limitation of this largely employed alternative is that its use is strictly limited to intramolecular reactions or strained alkenes.

More recently, the development of environmentally-benign visible light photocatalysis has overcome the challenges associated with traditional ultraviolet light use. The reduced cost and energy demand of visible light sources, in addition to the possibility to selectively activate the catalysts without side reactions of functional groups on the substrates, have shifted the focus to new "greener" photocatalytic methods. Among these, Ru(bipy)₃²⁺ is a notable example of efficient photoredox catalyst that acts as an oxidant or reductant upon visible light irradiation and has a long living, chemically stable photoexcited state. In 2008, the Yoon group first demonstrated the excellent potential of Ru(bipy)₃²⁺ as a photoredox catalyst in intramolecular [2+2] cycloadditions of electron deficient enones (Figure 4a).⁶ Later, in 2009, they extended their method to [2+2] heterodimerizations between aryl enones and Michael acceptors, generating cycloadducts with excellent diastereoselectivity (Figure 4b).⁷ The emerging class of Ir and Ru photocatalysts proved to be successful in promoting [2+2] cycloadditions of electron rich olefins as well. In 2010, and 2012, the Yoon group disclosed the successful intramolecular, and crossed intermolecular oxidative dimerization of styrenes (Figure 4c, d).^{8,9}



Figure 4: Examples of photoredox catalysis in (a) [2+2] cycloaddition of enones (b) crossed [2+2] cycloaddition of enones, (c) [2+2] cycloaddition of styrenes, and (d) crossed [2+2] cycloaddition of styrenes as disclosed by the Yoon group.

These methods enabled access to the cyclobutane scaffold in a readily available, low energy, operationally convenient, selective, and high-yielding manner. Nonetheless, the scope of the substrates is still limited; olefins that are neither electron deficient, nor electron rich, such as simple, aliphatic alkenes, fail to react in these [2+2] cycloadditions. To circumvent this issue, the Yoon group developed a method that uses unsaturated 2-acylimidazole groups as redox auxiliaries for olefins.¹⁰ The advantage of this method is that, while the substrates still undergo efficient [2+2] cycloadditions, the cyclobutane products can be post-functionalized to access a variety of cyclobutane carboxylic acid derivatives that were otherwise difficult to synthesize.

Another key aspect of modern synthesis is focused on the development of green, environmentally benign methods. Thus far, transition metal catalysts have been largely employed for efficient [2+2] cycloaddition reactions, despite the associated drawbacks of toxicity, limited availability, and poor stability caused by photobleaching. Green, cheaper alternatives in visible light photocatalyzed cycloadditions are, however, underrepresented compared to the noble metal-

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containing catalysts, because of the latter's excellent selectivity and high-yielding transformations. Efforts in this direction are represented by electrochemical heterodimerizations,¹¹ heterogeneous polymer framework catalysis,¹² and visible light-activated organic photosensitizers.^{13, 14} Several limitations such as low yields and narrow substrate scope demand new approaches that overcome the rapid photobleaching of small molecules, unselective catalysis, and inaccessible experimental setup.

Notably, in 2013, Nicewicz group reported the dimerization of electron rich styrene derivatives using the organic photoredox catalyst *para*-methoxy-2,4,6-triphenylpyrylium tetrafluoroborate (*p*-OMeTPT) in conjunction with an electron relay.¹⁴ The rationale of this method is that the electron relay, which has an oxidation potential only slightly higher than that of the alkene, would be oxidized first to a cation radical, which can then only oxidize the starting material, thus minimizing the oxidation of the cycloadduct product. This concept is represented in Figure 5b, where the different potentials of organic photosensitizers are shown relative to that of the olefin substrates. The electron relay should have a lower oxidizing potential than the photocatalyst, just above that of the alkene and below that of the dimer, thus preferentially facilitating the forward reaction. Higher yields associated with the addition of naphthalene and anthracene suggested the important role of the electron relay in the inhibiting the unproductive



Figure 5: (a) The proposed mechanism of the [2+2] homodimerization of styrenes using *p*-OMeTPT as photocatalyst and an Electron Relay (Used with permission of Royal Society of Chemistry, from Ref. 14; permission conveyed through Copyright Clearance Center, Inc.) (b) A schematic diagram of the relative redox potential of different organic photosensitizers and electron rich olefin substrates to illustrate the role of the Electron Relay

cycloreversion pathway. The system was proposed to undergo successful reaction through the mechanism depicted in Figure 5a.

The main drawbacks of this procedure are long reaction times, modest yields, and limited substrate scope. In response to these issues, and using the findings of the Nicewicz group, our group has recently disclosed a TPT-based polymer that acts as an organic single-electron oxidant/ electron-relay (ER) nanoreactor.¹⁵ The polymer catalyst provided numerous advantages such as increased yields, solubility, and controlled catalyst loadings.

Considering the promising yields of the [2+2] system, we hypothesized that a similar method can be developed for [4+2] cycloadditions, which will be discussed in the next section.

1.3: [4+2] Cycloadditions

The [4+2] cycloaddition, also known as the Diels-Alder reaction is one of the most powerful carbon-carbon bond forming methods in organic synthesis, being widely employed in the total synthesis of bioactive natural products and pharmaceuticals. Even though the Diels-Alder reaction and its mechanistic underpinnings have been extensively studied and understood, the scope of the substrates is limited by rigid electronic requirements. Specifically, successful transformations occur between electron-rich (typically the diene) and electron-deficient (typically the dienophile) components. Diels-Alder reactions between electronically mismatched substrates are considerably understudied, since they usually require harsh conditions and long reaction times.¹⁶

More recently, photoinduced electron transfer (PET) processes have enabled access to the otherwise impractical [4+2] cycloadditions between either electron rich or electron poor partners. A notable example is the work of Steckhan, who reported the Diels-Alder reaction of indole (an electron rich dienophile) with electron rich dienes, using catalytic amounts of photoexcited triphenylpyrylium tetrafluoroborate (TPT) derivatives.^{17, 18} As illustrated in Figure 6, the indoles form [4+2] cycloadducts with electronically mismatched dienes in high yields, which are synthetically useful cores with post-functionalization potential (Figure 6).



Figure 6: Examples of electronically mismatched Diels-Alder reactions of indole as reported by Steckhan et al.

Recently, the growing interest in the ability of metal polypyridyl complexes to promote a broad range of organic transformations, and particularly in [2+2] cycloadditions, has motivated the Yoon group to further explore their use in electronically mismatched Diels-Alder reactions. In their reports, they have shown that Ru(bpz)₃(BArF)₂ in combination with atmospheric oxygen as a co-oxidant can generate high yields of the cycloadduct between electron rich *trans*-anethole and electron-rich isoprene upon irradiation with visible light. In the absence of the photocatalyst, the thermal reaction did not occur even after 24 hours of stirring at 200 °C.¹⁶ The scope of this radical cation Diels-Alder cycloaddition proved to be quite broad for the case of electron-rich dienes and dienophiles, which is consistent with the mechanism in Figure 7. Moreover, when the same reaction was ran using organic photoredox catalysts, such as Rose Bengal and TPT instead of the ruthenium complex, the yields were 0% and 28% respectively, significantly lower than the yield obtained for the standard conditions (98%).¹⁶



Figure 7: Radical cation Diels-Alder cycloaddition between trans-anethole and isoprene and its proposed mechanism (Adapted with permission from Ref. 16 Copyright 2011 American Chemical Society)

Building on the pioneering work by Bauld and others,¹⁹ the Yoon group also disclosed that gram-scale intramolecular radical-cation Diels-Alder cycloadditions can be performed using Ru(bpy)₃(PF₆)₂ with methyl viologen as a co-oxidant and ambient sunlight as source of irradiation.²⁰

At the other end of the spectrum, high yields and diastereoselectivity were obtained in the radical anion hetero-Diels-Alder cycloadditions between electronically mismatched bis(enones), also investigated by the Yoon group.²¹ Their findings illustrate, once again, the efficacy of $Ru(bpy)_{3}^{2+}$ as a visible light photocatalyst in constructing cycloadducts that cannot be generated using thermal activation. In this study, however, the addition of a Lewis acid and 10 equivalents of water was necessary for high reaction rates and yields. The mechanism proposed for this transformation (Figure 8) involves the reduction of the Lewis acid-activated enone by $Ru(bpy)_{3}^{+}$



Figure 8: Radical cation Diels-Alder cycloaddition of bis(enones) and its proposed mechanism (Adapted from Ref. 21, Copyright 2011, with permission from Elsevier)

to afford a radical anion intermediate that subsequently undergoes intramolecular β , β coupling, followed by the formation of the carbon-oxygen bond via two pathways. Moreover, it is apparent that the length of the tether in these bis(enones) was critical in determining the chemoselectivity between the competing [2+2] and the [4+2] cycloaddition pathways.

Despite the development of diverse, robust methodologies using visible light photocatalysis in [4+2] and [2+2] cycloadditions, many limitations such as narrow substrate scope, toxicity, and inaccessibility of expensive catalysts require further investigation and improved catalyst design. Specifically, the Diels-Alder reaction between electron neutral dienes and dienophiles is significantly understudied, given their low reactivity in either radical-cation or radical-anion cycloaddition pathways. However, given the mechanistic insights of these processes, and the exquisite properties of homogeneous polymeric materials, we can access novel, improved catalytic features through the use of rational and modular design. The next section will discuss the emerging applications of SCNPs in catalysis, and their advantages over traditional homogeneous small molecule photocatalysts.

1.4: Catalysis Under Confinement: Single Chain Polymer Nanoparticles as Photoredox Catalysts

Inspired from nature's structural design of enzyme catalysts, chemists have been motivated to mimic the complex cooperativity and substrate specificity of proteins by creating synthetic polymers with well-defined architectures. Single-chain nanoparticles (SCNP) are an emerging class of such responsive materials, assembled using intramolecular crosslinking of linear polymer chains bearing various reactive pendants.²² The resulting folded polymers are compact objects that feature architecturally defined nanostructures. Their unique compartmentalization triggered the development of controlled drug delivery capsules,²³ chemical sensors,²⁴ nanoreactors,²⁵ and biomimetic catalysis²².

Notably, SCNPs provide versatile alternatives for homogeneous catalysis that overcome issues of catalyst solubility and excessive amounts of chemical waste generated during workup in

typical industrial settings.²² Using polymer-based catalysts with tunable solubility of the backbone, can allow for facile separation of the catalyst from the reaction products, thus fostering recyclability as a step towards sustainable synthesis. Terashima *et al* demonstrated these unique properties by employing a ruthenium-based, water-soluble SCNP in the aqueous reduction of ketones via transfer hydrogenation at the catalytic site.²⁶ Solubility-tuned recyclability of SCNPs as catalysts was further illustrated by Barner-Kowollik when using Pt(PPh₃)₂ SCNPs to aminate allyl alcohol.²⁷

1.5: Thesis Overview

This thesis discusses the progress on the synthesis and applicability of functionalized single-chain nanoparticles as dual catalysts for [2+2] and [4+2] cycloadditions. The design, synthesis, and characterization of the pyrylium-based polymeric photocatalysts is outlined in Chapter 2. In Chapter 3, their use in the [2+2] dimerization of *trans*-anethole is described, along with a structure-property analysis of TPT-based catalysts. A *para*-methoxy-triphenylpyrylium-based SCNP is shown to have enhanced catalytic activity when compared to the small-molecule equivalent, as well as to the previously developed TPT-SCNP. Chapter 4 dives into the small-molecule TPT and SCNP catalysis on [4+2] cycloadditions between electronically mismatched dienes and dienophiles, by discussing catalysis results from three different systems. Optimized conditions lay the groundwork for broadening the reaction scope which is underway. Lastly, Chapter 5 describes future research avenues such as using the developed cooperative catalysts in [2+2+2] cycloadditions, expanding the scope of the SCNP-catalyzed [4+2] cycloadditions, and further derivatizing TPT catalysts for access to enhanced photoredox properties.

Chapter 2 : SCNPs and Small Molecule TPT Design and Synthesis

Based on the recent publication of our group in *ACS Catalysis*,¹⁵ we hypothesized that changing the substitution pattern on the triarylpyrylium salt will allow us to tune the photoreactivity of the resulting polymeric catalysts, by changing the excited-state redox potential of the catalyst. In order to determine the effect of confinement that was shown in previous reports,¹⁵ we compared the standard optimized conditions of the SCNP catalysis to the small molecule equivalent, in which TPT photocatalysts and the electron relay were separately added.

Triarylpyrylium (TPT) salts were chosen as single-electron photooxidants due to their excitation in the visible region (~ 400 nm)²⁸ and other advantages. Specifically, TPT is commercially available and affordable, and it can be readily prepared from benzaldehyde and acetophenone in the presence of a Lewis acid in one step.²⁹ Moreover, the use of TPT salts were found to enhance the escape of the radical ions from the catalyst after the single-electron transfer process due to the lack of Coulombic attraction that typically leads to unproductive back-electron transfer within the contact pair.²⁸ This, along with the absence of toxic, expensive transition metal catalysts such as Ru, or Ir, that are commonly used to facilitate cycloadditions, make TPT a tunable, efficient photocatalyst, well-suited for our proposed system.

A styrylpyrene comonomer was used because of its ability to dimerize upon visible-light irradiation to form the crosslink³⁰ as well as for its function as an electron relay for the TPT catalyst.³¹ The idea behind this design is that colocalization of TPT and pyrene in the confined environment of the polymer would enhance single-electron transfer.¹⁵ For the polymer backbone, methyl methacrylate (MMA) was selected to ensure solubility in organic solvents.

2.1: TPT Small Molecule Synthesis



Figure 9: Synthesis of Triarylpyrylium (TPT) salts

The small molecule triarylpyrylium salts were prepared by condensation of acetophenone derivatives with benzaldehyde derivatives, in the presence of boron trifluoride etherate as the Lewis acid (Figure 9). The low yields obtained for the methoxy and bromo-substituted TPT can be explained by the relatively short reaction times (24 hours), as well as the unoptimized workup which led to significant product loss in the form of a dark red viscous solution. However, due to the high accessibility of the starting materials, and the low amounts required for the catalysis experiments, the condensation reactions were not further optimized, and the products were used in all subsequent cycloaddition reactions.

2.2: Monomer Synthesis

The triphenylpyrylium methacrylate monomers were synthesized in two steps from 4hydroxybenzaldehyde and 4-substituted acetophenones (Figure 10). In the first step, 4hydroxybenzaldehyde was reacted with methacroloyl chloride, generating 4-formylphenyl methacrylate in 91% yield. Next, a Lewis acid mediated condensation with 4-substituted acetophenones produces the 4-substituted TPT methacrylates as yellow, orange, and bright red powders in various yields. Notably, the 4-methoxy TPT methacrylates were obtained in very low yields, most likely due to the favorable polymerization of the product under the reaction conditions. A metallic green, soft and insoluble solid was collected as a side product in all reaction trials.

The styrylpyrene comonomer was prepared in three steps, by first assembling the styryl pyrene component and the linker methacrylate separately, followed by coupling the two (Figure 11). The first steps involved the reaction of 1-bromopyrene with 4-vinylphenylacetate in a palladium mediated Heck cross-coupling, giving 1-(4-hydroxyvinylphenyl)pyrene in 21% yield as bright yellow powder. The hydrocarbon linker synthesized from 2was а hydroxyethylmethacrylate and 5-bromovaleryl chloride via nucleophilic acyl substitution in the presence of DMAP. The last step yielded the desired comonomer by nucleophilic substitution of 1-(4-hydroxyvinylphenyl)pyrene in the brominated site in a 98% yield in the form of a yellow powder.



Overall, the yield of the electron relay comonomer is limited by the Heck coupling outcome of the first step. However, given the catalytic amounts of the product required for catalysis experiments, the convergent nature of the route, and the high accessibility of the starting materials,

no further optimization was required for this step. For improved yields, the crude product could be submitted to column chromatography instead of recrystallization for a better recovery of the target monomer.



2.3: Polymer and SCNP Synthesis

Statistical copolymers of TPT methacrylate, styrylpyrene (SP) methacrylate, and MMA were obtained by reversible-addition-fragmentation chain-transfer (RAFT) polymerization (Figure 12). Targeting incorporations of [MMA]:[TPT]:[SP] = 90:5:5, and 25-35 kDa molecular weights, the polymers were obtained by mixing the TPT, SP, and methyl methacrylates in dimethylformamide using AIBN as a radical source and 4-cyano-4-[(dodecylsulfanylthiocarbonyl)sulfanyl]pentanoic acid as the chain transfer agent for RAFT. After

stirring the reaction at 80 °C for 24 hours, the crude products were purified by reprecipitation in cold methanol or diethyl ether. The incorporations of TPT and SP in the photocatalytic polymers were calculated from the ¹H-NMR spectra with respect to the MMA methyl group appearing as a singlet at 3.55 ppm, the methylene peaks from the SP linker at 4.26 ppm and 4.14 ppm, and the aromatic protons from TPT without the styrylpyrene aromatic peaks. The incorporation ratios are



Figure 12: Random copolymerization of TPT methacrylate with SP methacrylate and methyl methacrylate presented in Table 1. The polymers that were used in further catalysis studies were characterized by GPC and ¹H-NMR spectroscopy.

Polymer	Target Ratio [MMA]:[TPT]:[SP]	% TPT by NMR	% SP by NMR	Mn	$\mathbf{M}_{\mathbf{w}}$	Ð
TPT-co-SP-co-MMA*	[90]:[5]:[5]	2.17	1.3	14681	17635	1.201
OMe TPT-co-SP-co- MMA	[90]:[5]:[5]	1.88	1.07	13781	18410	1.336
Cl TPT-co-SP-co- MMA	[90]:[5]:[5]	2.05	0.93	18271	21964	1.202
Br TPT-co-SP-co- MMA	[90]:[5]:[5]	1.95	0.95	17500	21532	1.230
OMe TPT-co-MMA	[95]:[5]	1.69	N/A	15263	18845	1.235
OMe TPT SCNP**	N/A	N/A	N/A	14580	19818	1.359

Table 1: Characterization of TPT-co-SP-co-MMA polymers and of SCNP

Lastly, the nanoparticle was prepared by irradiation of the polymer samples for 1-6 hours with a white CFL lamp without stirring. Folding the linear polymers to obtain the photocatalytic nanoparticle occurs via a [2+2] dimerization of the styrylpyrene moieties within the chain (Figure

13).



Figure 13: Crosslinking of the TPT-co-SP-co-MMA polymers by light-mediated [2+2] cycloadditions

The degree of crosslinking was monitored via UV/vis spectroscopy, such as the one in Figure 14b. The disappearance of the styrenyl absorbance and concomitant appearance of the cyclobutane peaks on the spectrum suggest successful crosslinking. The Size Exclusion Chromatography (SEC) data confirms intramolecular folding due to a typical shift to lower molecular weights despite slightly higher dispersity values (Figure 14a). The SEC data was not collected for the chloro-, bromo, and methoxy-TPT nanoparticles due to time constraints. However, it can be assumed that, by following the same procedure as in previously characterized instances, the resulting nanoparticle will have similar properties.



Figure 14: (a) Model SEC data for TPT-SP-polymer overlaid with TPT-SCNP; (b) Model TPT-SP-polymer and SCNP overlaid UV/vis absorption spectra. (Adapted with permission from Ref. 15 Copyright 2020 American Chemical Society)

The small molecule and polymer-based TPT catalysts discussed herein will become the foundation of photoredox-mediated reactions in subsequent chapters. Their efficacy will be screened in net oxidative cycloadditions (e.g., [2+2] and [4+2] Diels-Alder reactions) using multiple substrate pairs based on *trans*-anethole, styrene, isoprene, and/or 1,3-cyclohexadiene.

Chapter 3 : Small Molecule TPT and SCNP Catalysis in [2+2] Dimerization of *Trans*-Anethole

The [2+2] cycloaddition of electron rich styrenes has been largely investigated in the realm of visible light photoredox catalysis. In previous reports, Nicewicz demonstrated that the use of an electron relay as a cocatalyst, along with the organic sensitizer, drastically improves the efficiency of the [2+2] reaction by inhibiting unproductive cycloreversion.¹⁴ Nevertheless, cooperative catalysis is often limited by the diffusion of reactants, and requires multiple catalyst interactions in dilute solutions.¹⁵ Recent developments by our group in this direction comprised of a modular, recyclable, confined dual-catalytic polymer that exhibits enhanced reaction rates and yields for the dimerization of electron rich olefins.

To further explore the modularity of the catalyst, and access new photooxidative properties by altering the excited state redox potential of the triarylyrylium component, we synthesized a series of polymers bearing various 4-substituted TPT pendants. Small-molecule and SCNP catalysis studies revealed that the nanoparticle's confined environment, generated using controlled crosslinking, contributes to accelerated, higher-yielding [2+2] dimerizations of styrenes when compared to the small molecule catalysis in the same conditions. In this chapter, we disclose insights into structure-property relationships of the TPT catalysts and their corresponding TPT-SP SCNPs, with an emphasis on the 4-methoxy-substituted variant.

3.1: Small Molecule TPT Catalysis

Triarylpyrylium salts have been long known for being efficient, visible light photosensitizers. Owing to easy accessibility, solubility in most organic solvents, and highly oxidative properties in its excited states, TPT has been largely studied and employed in cycloadditions, cycloreversions, rearrangements, oxygenations, and fragmentation reactions in the past decades.²⁸ Since the substitution of the triarylpyryliums can be diversified with ease, we sought to investigate the effect of structure on the photophysical properties and ultimately on the photocatalyst efficiency in cyclodimerizations.

The parent structure of this category, 2,4,6-triphenylpyrylium (TPT), has a strong oxidizing character in both the singlet and triplet excited states with potentials of 2.55 V and 2.02 V (vs. SCE), respectively.³ Given that the singlet state lifetime, τ_f , is very short (< 5 ns), Photoinduced Electron Transfer (PET) less likely to occur from this state. TPT also exhibits an Inter-System Crossing (ISC) quantum yield (ϕ_{ISC}) of 0.58, which provides good access to the highly oxidizing triplet state. If the oxidation potential of the substrates is low enough, PET has been considered to happen as a result of quenching of both singlet and triplet states.

It is important to mention that the highly oxidative properties of TPT are not always desirable, as they can lead to poor selectivity and side reactions. In the case of the [2+2] cycloadditions, an aldehydic peak around 10 ppm is typically observed in TPT or SCNP-catalyzed experiments, suggesting competitive oxidation of the substrate occurs. In order to mitigate this issue, *p*-OMe-TPT has been used as a milder excited state oxidant with only 1.84 V and 1.71 V (vs. SCE) singlet and triplet state potentials. Even though the ϕ_{ISC} is considerably lower (0.03) compared to the unsubstituted TPT, its quantum yield of fluorescence is significantly higher (0.95), corresponding to a greater chance for PET to arise in the relatively short-lived singlet state. Considering previous reports where *p*-OMe-TPT was employed in [2+2] dimerizations of electronrich styrenes, we aimed to explore the effect of the TPT substitution on the SCNP system recently developed in our laboratory.

Trans-anethole was selected as the model system for consistency with the results obtained with TPT-SCNPs in the Elacqua group. In a regular experiment, the olefin was added to a solution of the photocatalyst with or without pyrene (as an electron relay) in acetonitrile, sparged with nitrogen, and irradiated with 427 nm Kessil lamps under stirring for 24 hours. The yields were determined using ¹H-NMR spectroscopy against trioxane as an internal standard. Unreacted *trans*-anethole and dimer amounts were calculated from the integration of the highlighted peaks in Figure 15.



Figure 15: Annotated ¹H-NMR spectrum of crude reaction product from the dimerization of trans-Anethole As previously noted by Nicewicz et al.,¹⁴ the use of an electron relay has significant effects on the yield of the dimer. For instance, when using pyrene in conjunction with *p*-OMe-TPT, 63% of the cycloadduct is obtained, as compared to only 6% in the absence of ER. These trends were consistent when the reactions were conducted with 456 nm light, keeping all other conditions the same (Table 2).

Photocatalyst	Electron Relay	PC Equivalents	Wavelength (nm)	Yield in dimer (%)
OMe-TPT	Pyrene	1 mol %	427	63
OMe-TPT	Pyrene	5 mol %	427	10
OMe-TPT	none	1 mol %	427	6
OMe-TPT	Pyrene	1 mol %	456	48
OMe-TPT	none	1 mol %	456	8
Br-TPT	Pyrene	1 mol %	427	23

 Table 2: Comparison of small-molecule TPT-pyrene cocatalytic system with monocatalytic TPT in the dimerization of *trans*-Anethole

Surprisingly, increasing the catalyst loading to 5 mol % had an adverse effect on the dimerization yield, with the majority of *trans*-anethole still being present after 24 hours. This can be attributed to the fact that the ER was added in very small amounts compared to the PC, leading to more cycloreversion than in experiments where the ER to PC ratio is higher.

Lastly, the trend of photocatalyst structure-efficiency seems to be largely dependent on the oxidative power of the excited states. When subjecting *trans*-anethole to differently substituted TPTs, while keeping all other parameters constant, the yield varies from 23% in the case of p-Br-TPT, to 31% for TPT,¹⁵ and 63% when p-OMe-TPT is used. These results are in line with the predictions: electron-withdrawing groups (such as Br) increase the oxidation potential of TPT, while electron-donating ones (such as methoxy) lower it. The latter produces the most dimer presumably because of less unproductive side oxidations. This idea is also supported by the increasing ratio of oxidative product to dimer, when using Br-TPT instead of MeO-TPT.

Future investigations should focus on further derivatizing the photocatalyst and changing the substitution pattern for a comprehensive study of structure-property relationships. For instance, extending the conjugation system could provide more insight into the photophysical properties of small-molecule TPTs, which can then be used in designing more efficient SCNPs.



Figure 16: Deactivation pathways of triarylpyrylium salts. (Reprinted with permission from Ref. 3 Copyright 2016 American Chemical Society)

Additionally, given the susceptibility of the TPTs to catalyst deactivation via dimerization of the pyranyl radical, nucleophilic attack, or oxygen quenching (Figure 16), a 4-mesityl-2,6-diphenylpyrylium salt could be synthesized for further improvement to the stability and recyclability of SCNPs. The steric bulk of the mesityl group distorts the planarity of the TPT molecule, which then protects the catalyst from photobleaching. Previous reports have demonstrated that installing a mesityl group at the 4-position increases the stability of the TPT catalyst while maintaining its photooxidative properties.³²

3.2: SCNP Catalysis

The second stage of the study was focused on exploring the effect of the confinement and catalyst colocalization on the enhanced catalysis of SCNP. To do that, we continued using trans-

anethole as the model system, but used the MeO-TPT polymer for comparison with the previous study conducted in our group. The experiments were set up by adding the alkene substrate to a solution of crosslinked MeO-TPT-co-SP-co-MMA polymer (SCNP), sparging with nitrogen, and irradiating the reaction mixture with 427 or 456 nm Kessil lamps at 25% light intensity for 24 hours. Similar to the small-molecule experiments, the yields were calculated via ¹H-NMR spectroscopy, against trioxane as the internal standard.

Reactions conducted in the presence of unfolded MeO-TPT-co-SP-co-MMA polymer at 427 nm afforded very little of the product, compared to the crosslinked SCNP, and even the small-molecule equivalent from Table 3. This result supports the hypothesis that catalyst colocalization through confinement provides substantially increased product formation.

Photocatalyst	Electron Relay	PC Equivalents	Wavelength (nm)	Yield of dimer (%)
MeO-TPT-co-SP- co-MMA	SP	1 mol %	427	5
MeO-TPT-SP SCNP	SP	1 mol %	427	77
MeO-TPT-co-SP- co-MMA	SP	1 mol %	456	12
MeO-TPT-SP SCNP	SP	1 mol %	456	7
MeO-TPT-co- MMA	pyrene	1 mol %	427	10
Br-TPT-SP SCNP	SP	1 mol %	427	1

Table 3: Comparison of the catalytic SCNP with the non-crosslinked polymers

To further investigate the confinement contributions to catalysis, the reaction was conducted with a linear MeO-TPT-co-MMA polymer and pyrene as a small-molecule additive.

Not surprisingly, only 10% of the cycloadduct was obtained, similar to the outcome of the reaction with non-crosslinked polymer as the catalyst.

Changing the energy of the light source from 427 nm to 456 nm had negative effects on the efficiency of the nanoparticle, which gave a lower yield (7%) than its unfolded version (12%). This suggests that the photophysical properties of the polymer and SCNP catalyst may be affected by the energy of irradiation. Even though decreased yields are also observed in the small-molecule experiments when using the 456 nm lights, the separate addition of PC and ER in solution affords much more product (48%) than our proposed catalyst (7%). This discrepancy can be further investigated by irradiating the MeO-TPT-co-SP-co-MMA polymer and SCNP at 456 nm while monitoring the UV-vis of the solutions over time. These results will contribute to understanding how light energy affects photocatalysis at both small-molecule and nanoparticle levels.

As observed in the small-molecule studies in Chapter 3.1, the Br-TPT-SP SCNP gives only traces of the dimer, with majority of the trans-anethole being transformed into the oxidative aldehydic product. This supports the idea that the high oxidation potential of the Br-TPT photocatalyst decreases the selectivity for the [2+2] cycloaddition through cycloreversion and side oxidative processes.



Figure 17: Other [2+2] cycloadditions of styrenyl derivatives through MeO-TPT-SCNP photocatalysis
Further understanding of the structure-properties differences between the TPT-SCNP and MeO-TPT-SCNP motivated us to explore the reaction scope of this transformation with the proposed catalyst on styrenyl substrates with various reduction potentials (Figure 17). As previously noted in the catalysis with the TPT-SCNP,¹⁵ the electron-deficient olefin, (E)-3-(4-methoxyphenyl)acrylonitrile, fails to undergo dimerization in the reported conditions. Moreover, 4-methoxystyrene affords mostly polymeric product, and only traces of the cycloadduct with MeO-TPT-SCNP, whereas it gives 26% dimer with the regular TPT-SCNP. These results can be explained by the fact that olefins with higher potentials are less reactive in the presence of the less oxidizing MeO-TPT photocatalyst, while the alkenes with several electron-donating groups (therefore lower oxidation potentials) undergo slightly faster dimerizations with MeO-TPT-SCNP (52%) compared to normal TPT-SCNP (49%).

It should be noted that the procedure used to crosslink the MeO-TPT-co-SP-co-MMA requires 6 hours of exposure to CFL lamp. This can in turn decrease the activity of the photocatalyst component, which is quite susceptible to photobleaching. Shown in Figure 18 is the



Figure 18: Overlay of UV-vis absorption spectra of MeO-TPT-co-SP-co-MMA at different times of CFL exposure

overlay of the UV-vis spectra of the polymer at 0, 1, and 6 hours of exposure to light. Even after 6 hours of irradiation, some SP units are still unreacted (judging by the relative intensities of pyrene and crosslinker peaks). An important avenue of future study would therefore be optimizing the crosslinking of the MeO-TPT-co-SP-co-MMA at different light intensities and wavelengths. Minimizing the exposure of the catalyst to light before catalysis, while maximizing the crosslinking efficiency is desired for the improvement of the proposed system.

3.3: Conclusions

In summary, our studies on the effect of structure of TPT on photocatalysis revealed that electron-deficient substituents increase the oxidative potential of the catalyst, leading to lower selectivities for the PET-induced [2+2] cycloadditions. In this regard, a new polymeric dual catalyst, MeO-TPT-SCNP, was synthesized and used to promote the dimerization of *trans*-anethole with improved yields (75%) compared to the regular TPT-SCNP previously reported by our group.

Chapter 4 : Small Molecule TPT and SCNP Catalysis in [4+2] Cycloadditions

Given the previous reports from our group regarding the effective design and use of SCNP in organic photoredox cycloadditions and motivated by the mechanistic similarities between the photoinduced-electron transfer [4+2] and [2+2] pathways, we hypothesized that a novel SCNP could be designed to effectively promote [4+2] cycloadditions of electronically mismatched dienes and dienophiles.

Herein, we disclose optimized methods for Diels-Alder reactions of deactivated partners that have little to no precedent in the literature. The cycloadditions were first optimized using the small-molecule TPT salts and then with the TPT-based SCNPs as photocatalysts. Given the ease of preparation of the triarylpyrylium salts with various functionalities at the aryl positions, and the absence of toxic and expensive transition-metal catalysts that are typically used to promote mismatched Diels-Alder reactions, the proposed catalyst provides a modular platform for catalysis that could be adjusted to a broad range of substrates.

4.1: *Trans*-Anethole and Isoprene

Trans-anethole and isoprene were selected as a model system to study the [4+2] cycloaddition using small-molecule TPT and SCNP (Figure 19), considering previous reports by Yoon and coworkers of visible-light mediated, Ru(bpz)₃(BArF)₂-catalyzed radical cation Diels-



Figure 19: *trans*-Anethole and Isoprene reaction as model system for the TPT and SCNP-catalyzed Diels-Alder cycloadditions

Alder cycloadditions.¹⁶ Their results indicate that the use of triarylpyrylium salts as photocatalysts leads to a 28% yield in the [4+2] cycloadduct after 1 hour of stirring. Given this precedent and having the spectrum of the desired product at hand, we decided that the reaction between *trans*-anethole and isoprene would be a good starting point. Additionally, considering our results on the [2+2] dimerization of *trans*-anethole, we expected to observe competitive reaction pathways, where the radical cation could either react with isoprene to give the [4+2] cycloadduct, or with another ground-state olefin to give the dimer.

A typical experiment consists of adding the alkene and excess diene to a solution of smallmolecule TPT or SCNP in acetonitrile (usually containing 1 mol% of photocatalyst), sparging with nitrogen for 5-10 minutes, and irradiating the reaction mixture with 427 or 440 nm Kessil LED lamps for 24 hours under stirring. The yields in the [2+2] and [4+2] cycloadducts were determined using ¹H-NMR spectroscopy against trioxane peaks as the internal standard. The first set of experiments were run in similar conditions as the ones employed in the dimerization of *trans*anethole reported by our group:¹⁵ 0.2 M relative to the alkene, 1 mol % TPT and 0.67% of pyrene



Figure 20: NMR spectra overlay of (bottom to top): *trans*-anethole and isoprene products, with and without ER, pure *trans*-anethole dimer, and *trans*-anethole

as the electron relay. As shown in Figure 20, the crude reaction product NMR spectrum is overlaid with that of the starting material and the pure dimer of *trans*-anethole, in order to characterize the peaks.

The peaks highlighted in yellow are characteristic to the [2+2] product, while the green doublet region corresponds to the [4+2] cycloadduct. The blue range was used to determine the conversion of *trans*-anethole in each reaction. Based on these results, it appears that more of the [2+2] dimer is formed when electron relay is added to the reaction, which is consistent with our previous observations. In the case of no electron relay, however, less of the [4+2] cycloadduct is obtained which suggests that the ER may also facilitate the Diels-Alder pathway.

Further optimization experiments revealed that dilute reactions and 7 equivalents of isoprene provide the best yields of the Diels-Alder cycloadduct, while minimizing the [2+2] to [4+2] products ratio. In fact, the ratio is improved as more diene equivalents are used. An annotated ¹H-NMR spectrum of one attempt's crude product (Figure 21) revealed all the signals corresponding to the desired product, in accordance with the published results.¹⁶ In all



Figure 21: Annotated ¹H-NMR spectrum of the [4+2] cycloadduct from a crude reaction product

experiments, the peaks at 0.73 ppm and 5.46 ppm were used for integration against the internal standard for yield calculations. A summary of the optimization trials and their outcomes are presented in Table 4.

Photocatalyst	ER	Eq. PC	Eq. diene	λ (nm)	Solvent	Conc. (alkene)	Yield of [2+2] product (%)	Yield of [4+2] product (%)
OMe-TPT	Pyrene	1 mol %	3	440	MeCN	0.2 M	29	5
OMe-TPT	none	1 mol %	3	440	MeCN	0.2 M	18	5
OMe-TPT	none	1 mol %	3	440	MeCN	0.1 M	30	13
OMe-TPT	none	1 mol %	5	440	MeCN	0.1 M	25	22
OMe-TPT	none	1 mol %	7	440	MeCN	0.1 M	4	15
OMe-TPT SCNP	SCNP	1 mol %	5	440	MeCN	0.1 M	trace	trace
none	none	N/A	5	440	MeCN	0.1 M	none	none
none	none	N/A	5	440	MeCN	0.1 M	none	none
TPT-SPhen SCNP	SCNP	1 mol %	7	427	MeCN	0.1 M	2	10
TPT-SNap SCNP	SCNP	1 mol %	7	427	MeCN	0.1 M	12	8
TPT	none	5 mol %	10	427	MeCN	0.1 M	3	2
TPT	none	5 mol %	10	427	toluene	0.1 M	0	13
TPT	none	5 mol %	10	427	nitromethane	0.1 M	0	trace
TPT	none	5 mol %	10	427	DCM	0.1 M	0	0

 Table 4: Optimization experiments of [4+2] cycloaddition between *trans*-anethole and isoprene

Interestingly, when subjecting the reactants to SCNPs with styrylphenanthrene (SPhen) and styrylnaphthalene (SNap) moieties as electron relays, the [4+2] to [2+2] product ratio is

significantly lower in the latter case. This result is in line with previous reports from the Nicewicz group which indicate that naphthalene is a better electron relay than anthracene for [2+2] dimerizations of *trans*-anethole. Additionally, the absence of an electron relay in the optimized small-molecule experiments leads to lower [4+2] to [2+2] product ratio than in the SPhen-SCNP trial, suggesting that the confinement of the nanoparticle in conjuncture with a 'poor' ER may increase the selectivity of the photocatalyst for the Diels-Alder cycloadditions.

Control experiments with and without sparging confirmed that the reaction does not take place in the absence of photocatalyst, and that the alkene starting material does not escape the vial during sparging. Reactions conducted in the presence of the MeO-TPT-SCNP yielded trace cycloadducts, which can be attributed to low catalyst loadings, as well as possible prior photobleaching of the TPT photocatalytic component during the 6-hour CFL lamp exposure for crosslinking. For comparison, small-molecule co-catalysts MeO-TPT and pyrene gave 29% of the dimer and 5% of the Diels-Alder product. Solvent screening experiments (Figure 22) revealed that toluene gives the highest yields in the [4+2] cycloadduct with no traces of the dimer. In contrast, nitromethane and dichloromethane lead to no formation of either of the cycloaddition products. The NMR spectra for the DCM screen



Figure 22: Overlay of the ¹H-NMR data of the solvent screening experiments. The yellow regions correspond to the characteristic peaks of the [4+2] cycloadduct.

(wide, not well-defined) is similar to what is commonly seen in polymers, making DCM a poor solvent for this reaction.

Visible-light-organocatalyzed [4+2] cycloadditions typically proceed with low yields and slow rates, and are usually limited to narrow substrate scopes. In this section, we have disclosed the optimization progress on the photoredox, TPT-mediated Diels-Alder reaction of electron mismatched partners *trans*-anethole and isoprene that has only been previously enabled by noble metal iridium and ruthenium complexes. Further optimization studies with the SCNPs are underway.

4.2: Styrene and Isoprene

Given the fact that several methods have been developed to allow for the Diels-Alder reaction between electron rich dienes and dienophiles, we decided to shift our attention to understudied systems that are not covered in the scope of the aforementioned methods. In this regard, we selected styrene as the dienophile for our next round of experiments (Figure 23), particularly because its reaction with isoprene has only been synthetically useful in copolymerizations. The only precedents to describe a [4+2] cycloaddition between the two involve inaccessible chiral catalysts that are specific to these substrates. This reaction system is significantly understudied given that unsubstituted styrenes are extremely prone to polymerization when subjected to mild conditions such as light and photocatalysts.¹⁴ These substrates are also unreactive in the methods developed for radical cation Diels-Alder reactions by Yoon and others.¹⁶. ³³ We therefore aimed to investigate different reaction outcomes of styrene and isoprene using the SCNP and small-molecule TPT, to optimize the reaction, and to design a suitable polymeric catalyst for the [4+2] cycloaddition of electron-neutral partners.



Figure 23: Styrene and Isoprene as model system for electron-neutral Diels-Alder reactions

Considering the susceptibility of styrene to polymerization, and its high oxidation potential, little to no product was obtained in the first few trials, which were run with 1 mol% of the photocatalyst. In a typical experiment, styrene and isoprene were added to a solution of the TPT or SCNP in acetonitrile, sparged with nitrogen for 5-10 minutes, sealed with electric tape, and stirred under 427 nm Kessil lamps irradiation for 24 hours. The crude product was then concentrated under nitrogen flow and analyzed by ¹H-NMR spectroscopy. In order to assess the

outcomes of these reactions, ChemDraw-predicted ¹H-NMR spectra of the cycloadducts (Figure 24) were used for reference in parallel with NMR spectra of the starting materials.



Figure 24: ChemDraw ¹H-NMR prediction of the [4+2] cycloadducts from styrene and isoprene

Based on the predictions in Figure 24, and the reported spectra of the cycloadducts,^{34, 35} we expected well-defined, complex splitting in the upfield region (1.5-2.5 ppm), a multiplet between 2.5 and 3.5 ppm, and a new signal around 5.3-5.5 ppm corresponding to the olefinic proton. The first trials with TPT and SCNP as catalysts revealed that, while styrene is consumed in high



Figure 25: ¹H-NMR spectra overlay of different reaction outcomes (in red) against the starting materials and catalyst (in blue)

conversions, the cycloadduct is not observed among the products (Figure 25). Analyzing these results, it is evident that different products are obtained in the small-molecule TPT catalysis compared to the SCNP case. Additionally, the potential interference of SCNP signals with the desired product in the upfield region calls for new yield assessment methods. An alternative would be redissolving the concentrated crude mixture in methanol (which does not solubilize the polymer), reconcentrating the new solution, and then analyzing it by NMR.

In an attempt to understand the conditions and catalysts that alter the reaction products, we performed a set of control experiments and compared their ¹H-NMR spectra side-by-side. Surprisingly, the catalyst loading has a significant effect on the reaction outcome, as suggested by the overlayed ¹H-NMR spectra in Figure 26. While the outcome of the reaction between styrene



Figure 26: ¹H-NMR overlay of upfield region of control experiments with catalyst (in red) and without catalyst (in blue)

and isoprene with 2 mol % TPT is the same as the one where isoprene is irradiated with no catalyst, it appears that at 5 mol % TPT, the reaction product differs.

Changing the irradiation source's wavelength revealed that the cycloadduct is obtained in small amounts at 440 nm light. The clear peaks, integration values, and chemical shifts

demonstrate that the [4+2] cycloadduct of styrene and isoprene can be obtained with little to no polymeric side products (Figure 27). The aromatic signals of the target compounds were not



assigned due to the overlap of the product peaks with those of the catalyst in the downfield region. Increasing the catalyst loading had adverse effects on the product formation, so 5 mol% were used in subsequent experiments. Using 10 equivalents of the isoprene instead of 5 led to a very small yield increase from 5.5% to 5.7%, as well as a cleaner product spectrum. The yields were calculated using integration of the olefinic peak at 5.16 ppm against an internal standard (1,3,5-trimethoxybenzene).

In studies previously conducted by the Nicewicz group, methoxystyrene polymerization was avoided by addition of an electron relay along with the TPT photocatalyst, which led to 83% dimerization product.¹⁴ We thus hypothesized that, by adding pyrene or naphthalene as cocatalysts, the cycloreversion processes would be inhibited and higher yields of the cycloadduct will be obtained. Nevertheless, addition of ER did not inhibit polymerization when one equivalent with respect to the styrene was used. Moreover, adding only 0.5 equivalents of the naphthalene led to

the same product as the one obtained when isoprene is stirred without catalyst under visible light. Future optimization experiments with electron relay additives could be performed at cryogenic temperatures to circumvent styrene's and isoprene's susceptibility to polymerization.

Solvent screening experiments confirmed that acetonitrile is the best solvent for the [4+2] cycloaddition. Reactions conducted in toluene and dichloromethane seem to facilitate



Figure 28: Overlay of ¹H-NMR spectra from solvent screening experiments of styrene and isoprene

polymerization, as it is observed from the broad peaks in the highlighted upfield region of the ¹H-NMR spectra overlay (Figure 28).

Styrene has a higher oxidation potential compared to typical substrates used in photocatalytic Diels-Alder reactions due to the lack of *para* or *ortho* electron-donating substituents that facilitate radical cation formation. We hypothesized that using 4-substituted TPT salts with greater photooxidative power could facilitate substrate turnover. For comparison, the styrene-isoprene reaction was conducted in the optimized conditions (10 equivalents of isoprene, acetonitrile as solvent, 5 mol % photocatalyst, 0.1 M, 440 nm, 25 % light intensity for 24 hours) with OMe-TPT, TPT, and Br-TPT as catalysts. The outcomes of these reactions (Figure 29) suggest that Br-TPT might enhance product formation based on the appearance of a peak at 5.5 ppm. However, polymerization of isoprene and styrene are still observed in the broad upfield regions.



Figure 29: ¹H-NMR overlay of catalyst screening experiments

Overall, due to the low reactivity of unsubstituted styrenes towards single-electron transfer processes with TPT, as well as their high susceptibility to polymerize instead of forming productive [4+2] cycloaddition, the styrene-isoprene model system proved to be a challenging platform that still requires significant optimization. While the product is observed under optimized conditions, the yields obtained are still considerably low. Future experiments will address these issues of selectivity and reactivity by adjusting the reaction temperature, identity of the electron relay, and light intensity.

4.3: Trans-Anethole and 1,3-Cyclohexadiene

More recently, we redirected our attention toward *trans*-anethole as a dienophile, since previous reports from our group confirmed that the SCNP effectively initiates its homo and crossdimerizations via single-electron transfer. Despite the relatively low yields obtained for the *trans*anethole-isoprene system, we turned to a presumably more reactive diene, 1,3-cyclohexadiene, hoping to gain more meaningful insights into the SCNP catalysis effects.



Figure 30: Trans-Anethole and 1,3-Cyclohexadiene as model system for TPT and SCNP-catalyzed Diels-Alder

To this date, only a few methods have been developed towards the efficient catalysis of the Diels-Alder reaction between *trans*-anethole and 1,3-cyclohexadiene.³⁶⁻³⁸ Notably, the cycloadduct was previously obtained with an excellent 96% yield in a study that uses host-guest chemistry interactions by employing PdL₄ cages in conjunction with quinone.³⁷ Encapsulation within the cage activates the quinone, raising its oxidation potential by a good 1 V, making it a potent oxidant for radical cation cycloadditions. Nevertheless, these catalysts are synthetically inaccessible, contain noble metals, or require UV light for catalysis. Herein, we report preliminary

findings in the TPT-mediated [4+2] cycloadditions of *trans*-anethole and cyclohexadiene. Quantitative conversion to the Diels-Alder cycloadduct was observed in the presence of 5 mol% of small molecule MeO-TPT.

In these experiments, *trans*-anethole and the diene were added to a solution of the photocatalyst in dichloromethane or acetonitrile (0.1 M with respect to the olefin), sparged with nitrogen for 5 minutes, and irradiated with 440 nm Kessil lamps with 25% light intensity under stirring for 24 hours. The yields were determined using NMR spectroscopy with trioxane as an internal standard. The conditions for this first round of experiments were selected based on the optimized conditions from the styrene-isoprene system.

In these preliminary studies, only the catalyst and solvent were varied, while the rest of the parameters were kept constant. Considering our previous investigations of *trans*-anethole dimerization in the presence of TPT, it was reasonable to assume that [2+2] cycloaddition could be a competitive pathway, so no electron relay was added. The results are summarized in Table 5.

<i>trans-</i> Anethole eq.	Diene eq.	Photocatalyst	Solvent	Yield in [4+2] product (%)	Yield in [2+2] product (%)
1	5	TPT	MeCN	41	trace
1	5	OMe-TPT	MeCN	52	trace
1	5	Br-TPT	MeCN	31	trace
1	5	none	MeCN	0	0
1	5	TPT	DCM	96	0
1	5	OMe-TPT	DCM	>99	0
1	5	none	DCM	0	0
0	1	TPT	DCM	0	0

Table 5: Small-molecule TPT catalyzed [4+2] cycloaddition of trans-anethole and 1,3-cyclohexadiene

In order to adequately assess the outcomes of the reactions, a series of control experiments were conducted. As expected, in the absence of the catalyst, none of the cycloaddition products are observed. Additionally, the reaction proceeds with considerably lower yields in acetonitrile, presumably due to the low solubility of 1,3-cyclohexadiene in this solvent (it crashes out in the form of a white solid). However, quantitative yield is achieved when the substrates are reacted in dichloromethane in the presence of 5 mol % small molecule p-MeO-TPT. Similarly, excellent yield and selectivity for Diels-Alder reaction over dimerization are observed when 5 mol % TPT is used as the photocatalyst. The formation of the [4+2] cycloadduct is demonstrated via ¹H-NMR



Figure 31: Annotated ¹H-NMR spectrum of the trans-anethole-1,3-cyclohexadiene [4+2] cycloadduct

spectroscopy of the crude product (Figure 31). Yields were calculated based on the olefinic proton peak at 6.4 ppm.

Characterization of the product was done based on previous experimental spectra reported in the literature.³⁸ For a comprehensive understanding of the reaction outcome and the origin of other peaks in the spectrum, cyclohexadiene was submitted to the reaction conditions in the absence of the alkene. As shown in Figure 32, the peaks not attributed to the cycloadduct are most likely due to the reaction of the excess diene with itself in the presence of TPT.



Figure 32: Overlay of ¹H-NMR spectra of [4+2] cycloaddition outcomes against starting materials and control experiments

It is also important to note that the trend in yield versus oxidation potential of the TPT is in line with the results obtained for the [2+2] cycloaddition of *trans*-anethole. In the acetonitrile experiments, the Br-TPT affords the least cycloadduct, with the most unconsumed substrate, while the MeO-TPT gives the highest yields for that solvent system. This trend is consistent with the one discussed in Chapter 2, where the efficiency of the catalyst is correlated with its oxidative potential in the excited state. The more electron-deficient Br-TPT exhibits stronger oxidizing character, which leads to unproductive side transformations. This trend is, however, specific to the reduction potential of the olefin that undergoes PET. For electron neutral alkenes with higher oxidation potentials, such as styrene, regular TPT has proven to be ineffective, so better oxidants should be used in future experiments. Altogether, these preliminary results provide unprecedented efficiency for the Diels-Alder reaction between *trans*-anethole and 1,3-cyclohexadiene with the use of a tunable, synthetically-modular organic photoredox catalyst. Future studies will be focused on exploring the scope of the alkene substrate.

Chapter 5 : Conclusions and Future Outlook

This thesis reports the development and synthesis of versatile single-chain nanoparticle photocatalysts bearing different 4-substituted triarylpyrylium tetrafluoroborates and styrylpyrene units as pendants. Enhanced reaction rates for the [2+2] cycloadditions of *trans*-anethole were observed when using the cocatalytic *p*-MeO-TPT-SP-SCNP as compared to TPT-SP-SCNP, separate addition of small-molecule catalysts, or monocatalytic polymers.

In addition, dimerization yields of *trans*-anethole in the presence of the 4-substituted smallmolecule TPT in conjunction with pyrene as an electron relay have been shown to vary inverse proportionally with the oxidation potential of the photocatalyst, which can be tuned by varying substituents on the parent TPT molecule. Given the facile, convergent synthesis of TPT from acetophenones and benzaldehydes,²⁹ new derivatives should be obtained for a future, in-depth study of structure-property relationships of TPT. Understanding the effects of structure, connectivity, and molecule electron density on the photophysical properties of catalyst, will enable access to a diverse library of organophotoredox TPT catalysts with broad applications.³⁹ Overall, exploiting the potent reactivity of organic photocatalysts is an understudied yet promising avenue of research.

This thesis also reports the progress in optimizing the [4+2] cycloadditions of electronically mismatched dienes and dienophiles using small-molecule TPT and TPT-SCNP. In the case of *trans*-anethole and isoprene, the cycloaddition shows excellent selectivity for the [4+2] cycloadduct over the [2+2] one when a TPT-SPhen-SCNP is employed as the photocatalyst, as compared to TPT-SNap-SCNP and TPT-SP-SCNP. Hence, future work will investigate the effect of different electron relays on the reaction selectivity and yield in both small-molecule and SCNP catalysis. While the styrene-isoprene system presents significant challenges associated with the

substrates overall susceptibility to polymerization, lower reaction temperatures, using stronger oxidizing TPTs, and introducing small amounts of an electron relay constitute future directions that might circumvent this issue and enable the [4+2] cycloaddition. Additionally, the most recently studied model system, *trans*-anethole and 1,3-cyclohexadiene exhibits quantitative yields with small-molecule MeO-TPT photocatalysis. Ongoing and future work will focus on implementing SCNP as catalysts in this reaction, with the goal of expanding the reaction scope to electron-neutral and deficient olefins.

Building the results of the photocatalytic SCNPs developed, and their rate-accelerating properties in [2+2] and potentially [4+2] cycloadditions, we aim to expand the breadth of SCNP-catalyzed transformations. Specifically, further work will explore the effect of Cl-TPT-SCNP on [2+2+2] cyclizations of alkynes with nitriles to afford substituted pyridines.

Appendix A: Experimental Procedures



2,4,6-Tris(4-methoxyphenyl)pyrylium tetrafluoroborate (3) 2.5 mL (20.5 mmol) of **1** and 7.66 g (51 mmol) of **2** were dissolved in 40 mL DCM. Boron trifluoride diethyl etherate (6.3 mL, 51 mmol) was added dropwise to the solution upon stirring. The reaction mixture was heated to 50 °C under reflux for 24 hours. The resulting product was cooled to room temperature and precipitated in 100 mL of diethyl ether. The precipitate was collected via vacuum filtration and washed with diethyl ether (3 x 25 mL) which yielded 500 mg (6%) of **3** as an orange powder. ¹H NMR (400 MHz, CDCl₃) δ 8.25 (m, 6H), 8.14 (m, 1H), 7.97 (m, 1H), 7.16 (d, 2H), 6.99 (d, 3H), 3.95 (s, 6H), 3.78 (s, 3H).

2,4,6-Tris(4-bromophenyl)pyrylium tetrafluoroborate (6) 1.85 g (10 mmol) of **4** and 5.05 g (25 mmol) of **5** were dissolved in 15 mL DCM. Boron trifluoride diethyl etherate (3.2 mL, 26 mmol) was added dropwise to the solution upon stirring. The reaction mixture was heated to 50 °C under reflux for 24 hours. The resulting product was cooled to room temperature and precipitated in 50 mL of diethyl ether. The precipitate was collected via vacuum filtration and washed with diethyl ether (3 x 25 mL) which yielded 1.53 g (28%) of **6** as a yellow-orange powder. ¹H NMR (400

MHz, CDCl₃) δ 7.91 (m, 3H), 7.75 (s, 1H), 7.68 (m, 3H), 7.59 (m, 3H), 7.54 (s, 2H), 7.51 (m, 2H), 7.46 (m, 1H).

TPT monomer syntheses



4-formylphenyl methacrylate (9) 7 was dissolved in 50 mL of DCM. 7.7 mL (55 mmol) of triethylamine were added and the reaction was cooled down to 0 °C. **8** (5.4 mL, 55 mmol) was added dropwise to the solution, and the resulting mixture was stirred for 24 hours at room temperature. The crude product was extracted with water (3 x 25 mL) and brine (2 x 25 mL). The organic layer was dried over anhydrous Na₂SO₄ and concentrated in vacuo under mild heating (30 °C or less on the water bath to avoid polymerization). 9.44 g of crude product **9** was obtained as a clear gel. ¹H NMR (400 MHz, CDCl₃) δ 10.0 (s, 1H), 7.96 (d, J = 8.42 Hz, 2H), 7.34 (d, J = 8.42 Hz, 2H), 6.41 (s, 1H), 5.84 (s, 1H), 2.10 (s, 3H).

4-(4-(methacryloyloxy)phenyl)-2,6-diphenylpyrylium tetrafluoroborate (10) 4.18 g (22 mmol) of **9** and acetophenone (6.4 mL, 55 mmol) were dissolved in 22 mL of DCM. Boron trifluoride diethyl etherate (7.0 mL, 57 mmol) was added dropwise to the solution upon stirring. The reaction mixture was heated to 50 °C under reflux for 16 hours. The resulting solution was

cooled to room temperature and diluted with 200 mL of diethyl ether. The precipitate was collected via vacuum filtration and washed with diethyl ether (3 x 25 mL), yielding 4.73 g (45%) of bright yellow powder. ¹H NMR (400 MHz, CDCl₃) δ 8.62 (s, 2H), 8.39 (m, 6H), 7.75 (m, 6H), 7.38 (d, J = 8.35, 2H), 6.31 (s, 1H), 5.82 (s, 1H), 2.03 (s, 3H).

4-(4-(methacryloyloxy)phenyl)-2,6-di(4-methoxyphenyl)pyrylium tetrafluoroborate (11)

6.08 g (32 mmol) of **9** and 4-methoxyacetophenone (12.7 g, 80 mmol) were dissolved in 32 mL of DCM. Boron trifluoride diethyl etherate (10.2 mL, 83 mmol) was added dropwise to the solution upon stirring. The reaction mixture was heated to 50 °C under reflux for 24 hours. The resulting solution was cooled to room temperature and diluted with 200 mL of diethyl ether. The solution was stored in the refrigerator overnight. The precipitate was collected via vacuum filtration. The filtrate was concentrated, dissolved in minimal amount of acetone, and precipitated in diethyl ether. The resulting precipitate was also collected and yielded a total of 500 mg (3%) of bright red solid. ¹H NMR (400 MHz, CDCl₃) δ 8.32 (m, 8H), 7.41 (d, J = 8.66 Hz, 2H), 7.19 (d, 8.83 Hz, 4H), 6.36 (s, 1H), 5.84 (s, 1H), 3.97 (s, 6H), 2.08 (s, 3H).

4-(4-(methacryloyloxy)phenyl)-2,6-di(4-chlorophenyl)pyrylium tetrafluoroborate (12) 3.86 g (20 mmol) of **9** and 4-chloroacetophenone (6.7 mL, 50.7 mmol) were dissolved in 20 mL of DCM. Boron trifluoride diethyl etherate (6.5 mL, 52.8 mmol) was added dropwise to the solution upon stirring. The reaction mixture was heated to 50 °C under reflux for 23 hours. The resulting solution was cooled to room temperature and diluted with 150 mL of diethyl ether. The precipitate was collected via vacuum filtration and washed with diethyl ether (3 x 25 mL), yielding 3.19 g (29%) of yellow solid. ¹H NMR (400 MHz, CDCl₃) δ 8.56 (s, 1H), 8.31 (m, 4H), 7.92 (d, J = 8.0 Hz, 2H),

7.68 (d, J = 8.24 Hz, 2H), 7.47 (d, J= 8.28 Hz, 3H), 7.39 (d, J = 7.92 Hz, 2H), 6.38 (s, 1H), 5.88 (s, 1H), 2.20 (s, 3H).

4-(4-(methacryloyloxy)phenyl)-2,6-di(4-bromophenyl)pyrylium tetrafluoroborate (13) 2.85

g (15 mmol) of **9** and 4-bromoacetophenone (7.46 g, 37.5 mmol) were dissolved in 15 mL of DCM. Boron trifluoride diethyl etherate (4.8 mL, 39 mmol) was added dropwise to the solution upon stirring. The reaction mixture was heated to 50 °C under reflux for 24 hours. The resulting solution was cooled to room temperature and diluted with 50 mL of cold diethyl ether. The precipitate was collected via vacuum filtration and washed with diethyl ether (3 x 10 mL), yielding 3.16 g (33%) of yellow-orange solid. ¹H NMR (400 MHz, CDCl₃) δ 8.22 (s, 3H), 7.85 (d, J = 7.64 Hz, 5 Hz), 7.64 (d, J = 7.32 Hz, 6H), 6.23 (s, 1H), 5.71 (s, 1H), 1.99 (s, 3H).



Compounds 16, 19, and 22 were synthesized as previously reported in literature. (Piane, J. J.; Chamberlain, L. E.; Huss, S.; Alameda, L. T.; Hoover, A. C.; Elacqua, E., Organic Photoredox-Catalyzed Cycloadditions Under Single-Chain Polymer Confinement. *ACS Catalysis* **2020**, *10* (22), 13251-13256.)

(E)-4-(2-(pyren-1-yl)vinyl)phenol (16) 14 (4.05 g, 14.4 mmol) and Pd(OAc)₂ (0.135 g, 0.6 mmol) were dissolved in 60 mL of triethanolamine. 15 (1.82 mL, 12 mmol) was added and the reaction was stirred at 100 °C for 20 hours. The resulting mixture was cooled down to room temperature, diluted with 30 mL of water and 30 mL of EtOAc. The solution was filtered through a celite plug and extracted with EtOAc (3 x 30 mL), water (2 x 30 mL), and brine (30 mL). The organic layer

2-(methacryloyloxy)ethyl 5-bromopentanoate (19) DMAP (0.305 g, 2.5 mmol), **18** (2.43 mL, 20 mmol) and triethylamine (5.3 mL)were dissolved in 30 mL of THF and cooled to 0 °C. **17** (3.36 mL, 25 mmol) was dissolved in 10 mL of THF and added dropwise to the reaction mixture. The complete transfer of **17** was ensured with another 10 mL of THF. The reaction was stirred at 0 °C for an hour, warmed to room temperature, and then stirred for another 30 minutes. The resulting mixture was concentrated, diluted with 250 mL of EtOAc and washed with water (2 x 50 mL), NaHCO₃ (2 x 50 mL) and brine (50 mL). The organic layer was dried over anhydrous Na₂SO₄ and concentrated in vacuo. The crude product was purified via flash column chromatography (10-20-25-30 % EtOAc/Hex) to give 5.22 (99%) of **19** as a clear oil.

2-(methacryloyloxy)ethyl (E)-5-(4-(2-(pyren-1-yl)vinyl)phenoxy)pentanoate (22) 16 (1.037 g, 3.24 mmol) and **19** (1.54 g, 5.83 mmol) were dissolved in MeCN (50 mL). Cs₂CO₃ (1.90 g, 5.83 mmol) was added, the reaction mixture was sparged with N₂ for 20 min and stirred under N₂ at 45 °C for 23 hours. The resulting mixture was cooled to room temperature and filtered. The filtrate was diluted with MeOH (170 mL) and placed in the freezer overnight. The product was filtered off to yield 1.68 g (98 %) of 11 as a bright yellow powder.

Polymer Synthesis



Copolymer (21) TPT monomer **10** (341 mg, 0.74 mmol), ER monomer **20** (118 mg, 0.23 mmol), CTA (49.2 mg, 0.122 mmol) and AIBN (4 mg, 0.024 mmol) were dissolved in MMA (3.5 mL, 36.54 mmol) in the dark. DMF (5.3 mL) was added to the reaction mixture and it was sparged with N₂ for 20 minutes. The polymerization was stirred at 80°C for 24 hours under N₂. The reaction was cooled to room temperature and then precipitated into MeOH (150 mL). The polymer was filtered off and washed with methanol (2 x 30 mL) and diethyl ether (2 x 30 mL). The resulting polymer was dissolved in a minimal amount of DCM, reprecipitated in cold methanol and washed with diethyl ether to yield **21** as a yellow-green solid.

Copolymers (22-24) TPT monomer **11-13** (0.58 mmol), ER monomer **20** (93 mg, 0.18 mmol), CTA (38.4 mg, 0.095 mmol) and AIBN (3.2 mg, 0.019 mmol) were dissolved in MMA (3.5 mL, 36.54 mmol) in the dark. DMF (4.1 mL) was added to the reaction mixture which was then sparged with N₂ for 20 minutes. The polymerization was stirred at 80°C for 24 hours under N₂. The reaction was cooled to room temperature and then precipitated into cold MeOH (170 mL). The polymer was filtered off and washed with methanol (2 x 30 mL) and diethyl ether (2 x 30 mL). The resulting polymer was dissolved in a minimal amount of DCM, reprecipitated in cold methanol and washed with diethyl ether to yield a yellow (24), orange (22), or light green (23) solid.

Incorporations of TPT and SP in the copolymers were calculated from the ¹H-NMR spectra with respect to the MMA methyl group appearing as a singlet at 3.55 ppm, the methylene peaks from the SP linker at 4.26 ppm and 4.14 ppm, and the aromatic protons from TPT from which we subtracted the styrylpyrene aromatic peaks. Using the integration values, the actual over theoretical ratios were calculated for the TPT and MMA components, which were then used to determine the percent incorporations, as shown in the examples below.

MeO-TPT-co-SP-co-MMA (22) incorporations (representative example for polymers 22-24)

$$TPT \ ratio = \frac{23.10 + 14.62 - 13}{14} = 1.763 ; MMA \ ratio = \frac{272.80}{3} = 90.93$$

% $TPT = \frac{1.763 \times 100}{1.763 + 90.93 + 1} = 1.88 \% ; \% \ MMA = \frac{90.93 \times 100}{1.763 + 90.93 + 1} = 97.05 \%$
% $SP = 100 - 1.88 - 97.05 = 1.07\%$

TPT-co-SP-co-MMA (21) incorporations

$$TPT \ ratio = \frac{39.774 - 13}{16} = 1.673; MMA \ ratio = \frac{223.36}{3} = 74.45$$

% **TPT** = $\frac{1.673 \times 100}{1.673 + 74.45 + 1} = 2.17$ %; % $MMA = \frac{74.45 \times 100}{1.673 + 74.45 + 1} = 96.53$ %
% **SP** = 100 - 2.17 - 96.53 = **1.30** %

SCNP (general procedure): The copolymers were dissolved in MeCN (10 mg/mL) in a foil wrapped vial. The polymer was allowed to completely dissolve and then the foil was removed. The vial was placed about in front of a white CFL light (light-to-vial distance ~ 6 in.) with a cooling fan above it. The vial was irradiated without stirring for at least 1 hour and then immediately

wrapped in foil. The MeO-TPT-SCNP required at least 6 hours of irradiation for significant crosslinking to occur (as monitored by UV-vis). The Br-TPT-SCNP, and Cl-TPT-SCNP were not monitored by UV-vis and their crosslinking conditions are yet to be optimized.

Monocatalytic polymer synthesis



Copolymer (25) 11 (277 mg, 0.53 mmol) was combined with CTA (38.3 mg, 0.095 mmol) and AIBN (3.2 mg, 0.018 mmol) and dissolved in MMA (3.0 mL, 28.1 mmol) in the dark. DMF (4.1 mL) was added to the reaction mixture which was then sparged with N₂ for 20 minutes. The polymerization was stirred at 80 °C for 24 hours under N₂. The reaction was cooled to room temperature and then precipitated into MeOH (150 mL). The polymer was then filtered off and washed with MeOH (2 x 30 mL) and Et2O (2 x 30 mL) to yield the homopolymer **25** as a red solid.

MeO-TPT-co-MMA (24) incorporations

$$TPT \ ratio = \frac{157.92}{14} = 11.29 \ ; MMA \ ratio = \frac{1973.3}{3} = 657.8$$

% $TPT = \frac{11.29 \times 100}{11.29 + 657.8} = 1.69 \ \% \ ; \% \ MMA = \frac{657.8 \times 100}{11.29 + 657.8} = 98.3 \ \%$



The [2+2] cycloadditions procedures were conducted in the same conditions as previously reported in literature. (Piane, J. J.; Chamberlain, L. E.; Huss, S.; Alameda, L. T.; Hoover, A. C.; Elacqua, E., Organic Photoredox-Catalyzed Cycloadditions Under Single-Chain Polymer Confinement. *ACS Catalysis* **2020**, *10* (22), 13251-13256.). Two 440 nm (instead of 427 nm) Kessil lamps were used for the experiments involving MeO-TPT and MeO-TPT-SCNP.

[4+2] Cycloadditions of Trans-Anethole and Isoprene



Trans-anethole (1 equiv., 0.1 mmol), isoprene (10 equiv., 1 mmol), and the photocatalyst stock solution (1-2 mol % in TPT) were added to a scintillation vial in the dark. Acetonitrile was added to reach a concentration of 0.1 M in the alkene. The vial was then sealed with electrical tape and sparged with a nitrogen needle and a vent needle for 5 minutes. The needles were removed, and the top of the vial was promptly covered with electrical tape. The vial was then placed between two 427 nm or 440 nm Kessil lamps at 25% intensity and stirred for 24 hrs. The resulting mixture was concentrated on a N₂ flow and the crude product mixture was dissolved in CDCl₃ with a known amount of trioxane for yield calculations via ¹H-NMR spectroscopy.

[4+2] Cycloadditions of Styrene and Isoprene



Styrene (1 equiv., 0.1 mmol), isoprene (10 equiv., 1 mmol), and the photocatalyst stock solution (5 mol % in TPT) were added to a scintillation vial in the dark. Acetonitrile was added to reach a concentration of 0.1 M in the alkene. The vial was then sealed with electrical tape and sparged with a nitrogen needle and a vent needle for 5 minutes. The needles were removed, and the top of the vial was promptly covered with electrical tape. The vial was then placed between two 440 nm Kessil lamps at 25% intensity and stirred for 24 hrs. The resulting mixture was concentrated on a N₂ flow and the crude product mixture was dissolved in CDCl₃ with a known amount of trimethoxybenzene (TMB) for yield calculations via ¹H-NMR spectroscopy.

[4+2] Cycloadditions of Trans-Anethole and 1,3-Cyclohexadiene



Trans-Anethole (1 equiv., 0.1 mmol), 1,3-cyclohexadiene (5 equiv., 0.5 mmol), and the photocatalyst stock solution (5 mol % in TPT) were added to a scintillation vial in the dark. Acetonitrile was added to reach a concentration of 0.1 M in the alkene. The vial was then sealed with electrical tape and sparged with a nitrogen needle and a vent needle for 5 minutes. The needles

were removed, and the top of the vial was promptly covered with electrical tape. The vial was then placed between two 440 nm Kessil lamps at 25% intensity and stirred for 24 hrs. The resulting mixture was concentrated on a N₂ flow and the crude product mixture was dissolved in CDCl₃ with a known amount of trioxane for yield calculations via ¹H-NMR spectroscopy.



Appendix B: ¹H-NMR Data






















REFERENCES

1. Diels, O.; Alder, K., Synthesen in der hydroaromatischen Reihe. *Justus Liebigs Ann. Chem*. **1928**, (460), 98-122.

2. Crisenza, G. E. M.; Melchiorre, P., Chemistry glows green with photoredox catalysis. *Nature Communications* **2020**, *11* (1).

3. Romero, N. A.; Nicewicz, D. A., Organic Photoredox Catalysis. *Chemical Reviews* 2016, *116* (17), 10075-10166.

4. Sarkar, D.; Bera, N.; Ghosh, S., [2+2] Photochemical Cycloaddition in Organic Synthesis. *European Journal of Organic Chemistry* **2020**, *2020* (10), 1310-1326.

 Poplata, S.; Tröster, A.; Zou, Y.-Q.; Bach, T., Recent Advances in the Synthesis of Cyclobutanes by Olefin [2+2] Photocycloaddition Reactions. *Chemical Reviews* 2016, *116* (17), 9748-9815.

 Ischay, M. A.; Anzovino, M. E.; Du, J.; Yoon, T. P., Efficient Visible Light Photocatalysis of [2+2] Enone Cycloadditions. *Journal of the American Chemical Society* 2008, *130* (39), 12886-12887.

 Du, J.; Yoon, T. P., Crossed Intermolecular [2+2] Cycloadditions of Acyclic Enones via
 Visible Light Photocatalysis. *Journal of the American Chemical Society* 2009, *131* (41), 14604-14605.

8. Ischay, M. A.; Lu, Z.; Yoon, T. P., [2+2] Cycloadditions by Oxidative Visible Light Photocatalysis. *Journal of the American Chemical Society* **2010**, *132* (25), 8572-8574.

9. Lu, Z.; Yoon, T. P., Visible Light Photocatalysis of [2+2] Styrene Cycloadditions by Energy Transfer. *Angewandte Chemie* **2012**, *124* (41), 10475-10478.

10. Tyson, E. L.; Farney, E. P.; Yoon, T. P., Photocatalytic [2 + 2] Cycloadditions of Enones with Cleavable Redox Auxiliaries. *Organic Letters* **2012**, *14* (4), 1110-1113.

11. Okada, Y.; Nishimoto, A.; Akaba, R.; Chiba, K., Electron-Transfer-Induced Intermolecular [2+2] Cycloaddition Reactions Based on the Aromatic "Redox Tag" Strategy. *The Journal of Organic Chemistry* **2011**, *76* (9), 3470-3476.

Li, R.; Ma, B. C.; Huang, W.; Wang, L.; Wang, D.; Lu, H.; Landfester, K.; Zhang, K.
 A. I., Photocatalytic Regioselective and Stereoselective [2 + 2] Cycloaddition of Styrene Derivatives Using a Heterogeneous Organic Photocatalyst. *ACS Catalysis* 2017, *7* (5), 3097-3101.
 Wu, L.-L.; Yang, G. H.; Guan, Z.; He, Y.-H., Metal-free visible-light-promoted intermolecular [2+2]-cycloaddition of 3-ylideneoxindoles. *Tetrahedron* 2017, *73* (14), 1854-1860.

14. Riener, M.; Nicewicz, D. A., Synthesis of cyclobutane lignans via an organic single electron oxidant–electron relay system. *Chemical Science* **2013**, *4* (6), 2625.

15. Piane, J. J.; Chamberlain, L. E.; Huss, S.; Alameda, L. T.; Hoover, A. C.; Elacqua, E., Organic Photoredox-Catalyzed Cycloadditions Under Single-Chain Polymer Confinement. *ACS Catalysis* **2020**, *10* (22), 13251-13256.

 Lin, S.; Ischay, M. A.; Fry, C. G.; Yoon, T. P., Radical Cation Diels–Alder Cycloadditions by Visible Light Photocatalysis. *Journal of the American Chemical Society* 2011, *133* (48), 19350-19353.

17. Mlcoch, J.; Steckhan, E., Photochemically Initiated, Electron-Transfer-Catalyzed Diels-Alder Reactions of Electron-Rich Dienophiles. *Angewandte Chemie International Edition in English* **1985**, *24* (5), 412-414. Gieseler, A.; Steckhan, E.; Wiest, O.; Knoch, F., Photochemically induced radical-cation
 Diels-Alder reaction of indole and electron-rich dienes. *The Journal of Organic Chemistry* 1991, 56 (4), 1405-1411.

19. Harirchian, B.; Bauld, N. L., The intramolecular cation radical diels-alder reaction. *Tetrahedron Letters* **1987**, *28* (9), 927-930.

20. Lin, S.; Padilla, C. E.; Ischay, M. A.; Yoon, T. P., Visible light photocatalysis of intramolecular radical cation Diels–Alder cycloadditions. *Tetrahedron Letters* **2012**, *53* (24), 3073-3076.

21. Hurtley, A. E.; Cismesia, M. A.; Ischay, M. A.; Yoon, T. P., Visible light photocatalysis of radical anion hetero-Diels–Alder cycloadditions. *Tetrahedron* **2011**, *67* (24), 4442-4448.

22. Lyon, C. K.; Prasher, A.; Hanlon, A. M.; Tuten, B. T.; Tooley, C. A.; Frank, P. G.; Berda, E. B., A brief user's guide to single-chain nanoparticles. *Polymer Chemistry* **2015**, *6* (2), 181-197.

23. Kröger, A. P. P.; Hamelmann, N. M.; Juan, A.; Lindhoud, S.; Paulusse, J. M. J., Biocompatible Single-Chain Polymer Nanoparticles for Drug Delivery—A Dual Approach. *ACS Applied Materials & Interfaces* **2018**, *10* (37), 30946-30951.

24. Gillissen, M. A. J.; Voets, I. K.; Meijer, E. W.; Palmans, A. R. A., Single chain polymeric nanoparticles as compartmentalised sensors for metal ions. *Polymer Chemistry* **2012**, *3* (11), 3166.

25. Rothfuss, H.; Knöfel, N. D.; Roesky, P. W.; Barner-Kowollik, C., Single-Chain Nanoparticles as Catalytic Nanoreactors. *Journal of the American Chemical Society* **2018**, *140* (18), 5875-5881.

26. Terashima, T.; Mes, T.; De Greef, T. F. A.; Gillissen, M. A. J.; Besenius, P.; Palmans, A. R. A.; Meijer, E. W., Single-Chain Folding of Polymers for Catalytic Systems in Water. *Journal of the American Chemical Society* **2011**, *133* (13), 4742-4745.

27. Knöfel, N. D.; Rothfuss, H.; Willenbacher, J.; Barner-Kowollik, C.; Roesky, P. W., Platinum(II)-Crosslinked Single-Chain Nanoparticles: An Approach towards Recyclable Homogeneous Catalysts. *Angewandte Chemie International Edition* **2017**, *56* (18), 4950-4954.

28. Miranda, M. A.; Garcia, H., 2,4,6-Triphenylpyrylium Tetrafluoroborate as an Electron-Transfer Photosensitizer. *Chemical Reviews* **1994**, *94* (4), 1063-1089.

29. Fathimath Salfeena, C. T.; Basavaraja, B.; Ashitha, K. T.; Kumar, V. P.; Varughese, S.; Suresh, C. H.; Sasidhar, B. S., Synthesis of symmetrical and unsymmetrical triarylpyrylium ions via an inverse electron demand Diels–Alder reaction. *Chemical Communications* **2018**, *54* (88), 12463-12466.

30. Frisch, H.; Menzel, J. P.; Bloesser, F. R.; Marschner, D. E.; Mundsinger, K.; Barner-Kowollik, C., Photochemistry in Confined Environments for Single-Chain Nanoparticle Design. *Journal of the American Chemical Society* **2018**, *140* (30), 9551-9557.

31. Tamai, T.; Ichinose, N.; Tanaka, T.; Sasuga, T.; Hashida, I.; Mizuno, K., Generation of Polyphenylene Radical Cations and Their Cosensitization Ability in the 9,10-Dicyanoanthracene-Sensitized Photochemical Chain Reactions of 1,2-Bis(4-methoxyphenyl)cyclopropane. *The Journal of Organic Chemistry* **1998**, *63* (10), 3204-3212.

32. Alfonzo, E.; Alfonso, F. S.; Beeler, A. B., Redesign of a Pyrylium Photoredox Catalyst and Its Application to the Generation of Carbonyl Ylides. *Organic Letters* **2017**, *19* (11), 2989-2992.

33. Okada, Y.; Yamaguchi, Y.; Ozaki, A.; Chiba, K., Aromatic "Redox Tag"-assisted Diels– Alder reactions by electrocatalysis. *Chemical Science* **2016**, *7* (10), 6387-6393.

34. Liu, X.; Zhang, W.; Wang, Y.; Zhang, Z.-X.; Jiao, L.; Liu, Q., Cobalt-Catalyzed Regioselective Olefin Isomerization Under Kinetic Control. *Journal of the American Chemical Society* **2018**, *140* (22), 6873-6882.

35. Taarning, E.; Madsen, R., Unsaturated Aldehydes as Alkene Equivalents in the Diels– Alder Reaction. *Chemistry - A European Journal* **2008**, *14* (18), 5638-5644.

36. Stevenson, S. M.; Shores, M. P.; Ferreira, E. M., Photooxidizing Chromium Catalysts for Promoting Radical Cation Cycloadditions. *Angewandte Chemie International Edition* **2015**, *54* (22), 6506-6510.

37. Spicer, R. L.; Stergiou, A. D.; Young, T. A.; Duarte, F.; Symes, M. D.; Lusby, P. J., Host–Guest-Induced Electron Transfer Triggers Radical-Cation Catalysis. *Journal of the American Chemical Society* **2020**, *142* (5), 2134-2139.

38. Horibe, T.; Ohmura, S.; Ishihara, K., Structure and Reactivity of Aromatic Radical Cations Generated by FeCl3. *Journal of the American Chemical Society* **2019**, *141* (5), 1877-1881.

Mccarthy, B. G.; Pearson, R. M.; Lim, C.-H.; Sartor, S. M.; Damrauer, N. H.; Miyake,
G. M., Structure–Property Relationships for Tailoring Phenoxazines as Reducing Photoredox
Catalysts. *Journal of the American Chemical Society* 2018, *140* (15), 5088-5101.

ACADEMIC VITA

CRISTINA-VALENTINA CRAESCU

EDUCATION

The Pennsylvania State University, Schreyer Honors College University Park, PA **Major**: Bachelor of Science in Chemistry | **Graduation**: May 2021

RESEARCH EXPERIENCE

Research with Prof. Elizabeth Elacqua

Chemistry Department, The Pennsylvania State University

- Synthesized organic photocatalysts, polymers, and single-chain nanoparticles designed to catalyze organic cycloaddition reactions
- Conducted a variety of organic reactions such as polymerization, condensation, cross-coupling, dimerization, and nucleophilic substitution
- Received the Erickson Discovery Grant for research during the summer and fall semesters

Research with Prof. Ayusman Sen

Chemistry Department, The Pennsylvania State University

- Investigated the mobility of enzyme-bound lipid bilayers via confocal microscopy
- Collaborated with a team of graduate students in understanding the factors that affect mobility in celllike structures
- Received the Student Engagement Network Grant for research during the spring
- Utilized concepts across fields to analyze data and design relevant experiments

Research with Prof. Ahmed Nuriye (A.C.U.R.A)

Abington College Undergraduate Research Activities

- Collaborated with a faculty professor in the development of new and high-yielding synthesis pathways for natural compounds with potential biological activity
- Designed experiments, set up reactions and optimized yields for novel synthetic paths, processed spectroscopic analysis and identified new compounds
- Completed the total synthesis of the natural compound Cinncassin A₁ and devised a novel, general synthetic strategy for symmetric trans-2,3-disubstituted-gamma-butyrolatones
- Presented the project in 6 local and national chemistry meetings and research symposia

TEACHING AND LEADERSHIP

Learning Assistant for Analytical Chemistry (CHEM 227)

The Pennsylvania State University, University Park PA

August 2020 - Present

• Guided and managed weekly, socially-distanced laboratory sessions with 16 students

August 2018 – August 2019

October 2019 - May 2020

May 2020 - Present

- Collaborated closely with faculty to develop new protocols and teaching strategies suited for the ongoing pandemic
- Created instructional material that covers challenging topics in analytical chemistry such as statistics, • methods of quantitation, and competing equilibria
- Held weekly problem-solving sessions to engage students with the material learned in lectures and • laboratory
- Organized exam review sessions and one-on-one tutoring sessions with the students •
- Lectured and led a laboratory class session on creating Excel prediction models •

Teaching Assistant for Quantum Chemistry (CHEM 452)

The Pennsylvania State University, University Park PA

August 2020-Present

- Monitored and managed class questions daily on the online platform Piazza
- Maintained close communication with students through emails, office hours, and review sessions for a • class of 50 students
- Organized and led independent review sessions to reinforce the material and bolster problem-solving • skills
- Continued teaching a 90-students quantum chemistry class during the Fall 2020 semester

Learning Assistant for Organic Chemistry II (CHEM 212)

- The Pennsylvania State University, University Park PA
- Held office hours weekly to guide a class of 100+ students through the material •
- Collaborated with a team of instructors weekly to discuss teaching strategies, assignments, and resources available for students in the online format

Volunteer at U Haunt Science event

The Pennsylvania State University, University Park, PA

- Promoted STEM through chemistry demos integrated in a medieval-themed play for children in the • area
- Collaborated with a team of students to create the play and set up the décor for the young audience •
- Performed the barking dog, colored flames, and elephant toothpaste demos for the play •

Peer Tutor for Chemistry and Mathematics

The Pennsylvania State University, Abington PA

- Guided students through course material in one-on-one tutoring weekly sessions •
- Customized study strategies for students to improve their academic performance and understanding •
- Encouraged students of diverse backgrounds and ages to develop independent studying habits in STEM •

Tutor for Chemistry Olympiad Preparation

International Computer High School of Bucharest, Bucharest, Romania

- Organized weekly lectures on advanced topics in organic chemistry
- Designed relevant problem sets for the students and discussed their solutions and questions in class
- Presented problem-solving strategies in synthetic routes and determination of structures from spectra

PRESENTATIONS AND CONFERENCES

9th Annual Undergraduate Research Symposium, University Park, PA Presenter in Poster Session

September 2019

October 2018 - May 2019

October 2017 – May 2018

May 2020-June 2020

October 2019

May 2020- June 2020

ACS National Conference, San Diego, CA Presenter in Poster Session	August 2019
ACS Empowering Women in Organic Chemistry, Philadelphia, PA Presenter in Poster Session	June 2019
ACS Mid-Atlantic Regional Meeting, Baltimore, MA Presenter in Poster Session	May 2019
Sigma XI Research Symposium, Philadelphia, PA Presenter in Poster Session	April 2019
Abington College Undergraduate Research Activities Poster Fair, Abington, PA Presenter in Poster Session	April 2019
AWARDS AND HONORS	
The John and Elizabeth Holmes Teas Scholarship for academic achievement and chemistry interest to cover full tuition, room, and board for the 2020-2021 academic year awarded by the Chemistry Department of the Pennsylvania State University	July 2020
Peter Gold Memorial Award for service to the chemistry department awarded by the Chemistry Department of the Pennsylvania State University	May 2020
Erickson Discovery Grant for research over Summer and Fall 2020 with Dr. Elizabeth Elacqua	March 2020
Student Engagement Network Grant for research during Spring 2020 with Dr. Ayusman Sen	December 2020
Schreyer Honors College Scholar for academic achievement in the chemistry major	as of May 2019
President's Freshman Award for academic results awarded by the chancellor of the Pennsylvania State University Abington College	April 2019
"In honoris" diploma recipient for exceptional results in international chemistry olympiads awarded by the Romanian Ministry of Education	December 2017

PUBLICATIONS

1. Nuriye, A. Y.; Craescu, C. V. Total Synthesis of Cinncassin A1. J Heterocyclic Chem 2020. https://doi.org/10.1002/jhet.3973.