

# Applications and Prospects for Triplet–Triplet Annihilation Photon Upconversion

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**Abstract:** Triplet–triplet annihilation photon upconversion (TTA-UC) is a photophysical process in which the energy of two photons are combined into a single photon of higher energy. While this strategy has been recognized in applications ranging from bioimaging to solar energy conversion, its uses in synthetic organic chemistry have not been extensively developed. Here, we present a short tutorial on the theoretical underpinnings and the design principles of TTA-UC systems. Selected applications are then discussed to highlight key features of the TTA mechanism, along with a prospective discussion of the potential of these mechanisms to enable innovation in photocatalysis, methods development, and synthetic organic chemistry.

**Keywords:** Excited state · Photochemistry · Triplet–triplet annihilation · Upconversion



Born in Denver, Pennsylvania, **Martin Rauch** received his B.S. in Chemistry from the Pennsylvania State University in 2014. Currently, he is a PhD candidate at Princeton in Robert Knowles' group and is engaged in developing new applications of TTA-UC to organic synthesis.



A native of Virginia's Shenandoah Valley, **Robert Knowles** received a B.S. in chemistry from the College of William and Mary in 2003. He went on to receive his PhD in synthetic organic chemistry from Caltech in 2008 for his work on natural product synthesis in the labs of Dave MacMillan. Following his doctoral work, Rob moved to Eric Jacobsen's lab at Harvard University as a NIH postdoctoral fellow, where his work focused on asymmetric catalysis and new reaction development. Rob moved to Princeton in the summer of 2011, where his group's work has focused primarily on the applications of proton-coupled electron transfer (PCET) in organic synthesis. In 2017 he was promoted to Professor of Chemistry.

## 1. Background

Luminescent materials play a central role in applications ranging from LEDs and solar cells,<sup>[1]</sup> to fluorescent tags in bioimaging,<sup>[2]</sup> and transition metal complexes in photoredox catalysis.<sup>[3]</sup> Most luminescent materials exhibit a Stokes shift, emitting photons lower in energy than the incident light. However recent years have witnessed an increased interest in photon

upconversion (UC), an anti-Stokes process wherein the energies from multiple lower energy photons are consolidated to produce a single photon of higher energy. Within this context one area of significant growth has been in upconversion based on triplet–triplet annihilation (TTA), a multi-photon process wherein two triplet excited state species combine their energies to produce a higher-energy singlet excited state.<sup>[4]</sup> Distinct from other upconversion approaches that typically require the use of lasers, TTA-UC can upconvert light from low-power, incoherent excitation sources, making it appealing for practical applications.<sup>[5]</sup> Moreover, numerous molecular TTA systems have been identified, enabling UC across a wide range of both excitation and emission wavelengths. Building on recent advances in multi-photon synthetic methods,<sup>[6–10]</sup> we envision TTA-UC will continue to expand and enable advances in a wide range of disciplines, including synthetic organic chemistry. In the following, we provide a tutorial review on the TTA-UC mechanistic process, as well as selected set of instructive examples demonstrating the feasibility of TTA-UC to affect synthetically relevant transformations and elementary steps.

### 1.1 Generalized Mechanism

TTA was first described in the early 1960s by Parker and Hatchard, who observed delayed fluorescence in solutions containing anthracene, phenanthrene, pyrene, or naphthalene.<sup>[11–13]</sup> The spectral features of this unexpected delayed phenomenon were identical with that of prompt fluorescence from each arene. However, the intensity of the fluorescence varied with the square of the excitation light in-

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tensity. These observations led to the suggestion that the observed luminescence was occurring through a two-photon triplet–triplet quenching mechanism that produced an excited singlet state and ground state molecule. Further work demonstrated that TTA could also be sensitized by an external chromophore, further expanding the range of triplet species that could potentially serve as TTA substrates, or annihilators.<sup>[14]</sup> A generalized mechanism for sensitized TTA is outlined in Fig. 1. The process begins with the long-wavelength excitation of a sensitizer chromophore to its singlet excited state. From here, intersystem crossing (ISC) converts the sensitizer into its triplet state. The sensitizer then undergoes triplet–triplet energy transfer (TTET) *via* a Dexter-type mechanism to an annihilator, regenerating the ground state of the sensitizer. Annihilators with long triplet lifetimes can persist to reach sufficient concentrations that allow for bimolecular collisional interactions between triplets. In principle, these interactions can produce nine different spin eigenstates.<sup>[15]</sup> TTA then occurs as a spin-allowed process to disproportionate the triplet annihilator pair into a higher energy singlet excited state localized on one annihilator while the other returns to the singlet ground state. Emission from this nascent singlet excited state is characteristically blue-shifted relative to the incident light, serving as confirmation of the upconversion process.

An advantage of TTA-UC is that a variety of sensitizers and annihilators covering a broad spectral range have been shown to be viable reaction partners.<sup>[4]</sup> The most commonly used sensitizers are transition metal complexes that undergo efficient ISC and exhibit long triplet lifetimes. However, common organic triplet photosensitizers like biacetyl and 1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicyano-benzene (4CzIPN) have similarly been used in this role. The annihilator components have also been extensively studied. A sample list of representative TTA-UC systems is presented in Table 1. Recently, a number of optimized and efficient systems within the visible spectrum have been shown, including platinum(II) tetraphenyltetrabenzoporphyrin (PtTPBP)/perylene and tris(4,4'-dimethyl-2,2'-bipyridine)ruthenium(II)/9,10-diphenylanthracene (Ru(dmb)<sub>3</sub><sup>2+</sup>/DPA), which constitute red-to-blue and green-to-blue transitions, respectively.<sup>[16,17]</sup> Also noted are upconversions that bridge two distinct regions of the electromagnetic spectrum. For example, palladium(II) tetraanthraporphyrin (PdTAP)/rubrene can convert near-IR light into visible yellow light.<sup>[18]</sup> On the opposite end, sensitizers such as biacetyl and 4CzIPN can convert visible blue light into the near-UV with annihilators like 2,5-diphenyloxazole (PPO) and *para*-terphenyl.<sup>[19,20]</sup>

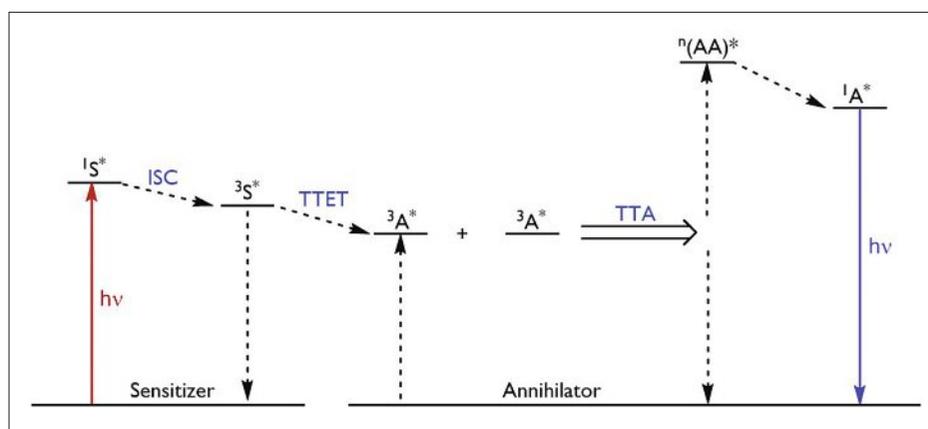


Fig. 1. Energy diagram illustrating the mechanism of TTA-UC as described in the text.

Notably, some of the pairs in Table 1 were found to enable anti-Stokes shifts of greater than 0.8 eV, including osmium(II) 4-bromophenylterpyridine/2,5,8,11-tetra-*tert*-butylperylene (Os(btpy)<sub>2</sub><sup>2+</sup>/TTBP) which approaches 1 eV of upconversion.<sup>[21]</sup>

## 1.2 Optimization of TTA Systems

While the identity of the sensitizer and annihilator allows for control over excitation and emission wavelengths, their properties can also play a role in optimizing the efficiency of the overall upconversion process. To maximize upconversion, one must optimize the quantum efficiency of each elementary step in the mechanism and minimize the amount of energy lost during each transition. Considering each step individually, the quantum yield of ISC for many metal sensitizers can approach unity. This beneficial feature can often be coupled to small singlet–triplet energy gaps to minimize energy loss during this transition. Next, bimolecular TTET can also approach unity quantum efficiencies in favorable cases; however, this efficiency usually results from a more exergonic energy transfer leading to larger energy losses. The TTA process itself is perhaps the

least intuitive step to optimize. Limited by a nominal efficiency of 50% and an even lower practical limit enforced by spin statistics (*vide supra*), TTA is often the least efficient elementary step in the upconversion process.<sup>[15,22]</sup> The two main factors that affect TTA efficiency include: (1) the rate at which the triplets decay through bimolecular TTA relative to unimolecular decay, such as phosphorescence; and (2) the likelihood that such a bimolecular event will lead to productive singlet formation. The first factor is primarily optimized by increasing the concentration of triplet excited annihilator in solution through increased sensitizer concentration, increased photon flux, or increased triplet monomer lifetimes. The second factor is inherent to the annihilator of choice, but it has been shown that inaccessibly high T<sub>2</sub> states may inhibit TTA, ending in the unproductive triplet eigenstates.<sup>[22]</sup> TTA is also frequently impaired by a loss of potential energy.<sup>[23]</sup> While it is a requirement that the resultant singlet state cannot exceed twice the triplet energy, a small singlet–triplet gap translates to greater energy losses. For example, high-energy annihilators like PPO (E<sub>s</sub> = 79 kcal/mol, E<sub>T</sub> = 53 kcal/mol)<sup>[19]</sup>

Table 1. Illustrative list of TTA-UC systems that encompass a broad range of wavelengths.

Sensitizer	Annihilator	Excitation λ [nm]	Emission λ [nm]	ΔE [eV]
phenanthrene	naphthalene	345	324	0.23
PtTPBP	perylene	635	451	0.80
Ru(dmb) <sub>3</sub>	DPA	515	445	0.38
PdTAP	rubrene	780	560	0.62
biacetyl	PPO	442	360	0.64
4CzIPN	<i>p</i> -terphenyl	445	345	0.81
Os(btpy) <sub>2</sub> <sup>2+</sup>	TTBP	724	462	0.97

or *p*-terphenyl ( $E_s = 83$  kcal/mol,  $E_T = 58$  kcal/mol)<sup>[24]</sup> exceed the energetic requirement by over 25 kcal/mol. Additionally, TTA may be enhanced by covalently connecting the annihilators in a copolymer.<sup>[25]</sup> Such polymers increase the proximity of annihilators, leading to more total annihilation events. And lastly, following upconversion, a high fluorescence quantum yield is desired to most efficiently extract the upconverted energy.

### 1.3 Experimental Characterization of TTA Processes

A number of simple experiments can be used to investigate whether a TTA-mediated upconversion process is operative. As a two-photon process, a log-log plot of upconverted luminescence vs. incident light power has a slope of 2, indicating its quadratic dependence to the incident power density.<sup>[26]</sup> Overall, this method has been one of the most practical methods for identifying TTA given its operational simplicity. Another characteristic of TTA is its delayed fluorescence, which exhibits a lifetime that is roughly half that of the lifetime of the triplet annihilator species.<sup>[14]</sup> This is particularly useful in distinguishing TTA-UC from prompt fluorescence of any singlet states generated by direct excitation. TTA is also perturbed by external magnetic fields that can affect the spin character of the various eigenstates the correlated pair proceeds through.<sup>[27]</sup> The field may either dilute the singlet character across many eigenstates or further concentrate this character into only a few of the states, leading to observable positive and negative magnetic field effects, respectively.<sup>[28]</sup> While less frequently employed, several studies have confirmed this effect across multiple annihilators and further validate a bimolecular triplet quenching mechanism.<sup>[29,30]</sup>

## 2. Bioimaging Applications

Studies into the mechanism and optimization of TTA-based upconversion have elucidated unique applications of this process.<sup>[5]</sup> The upconverted fluorescence has been studied for its applications in lighting and imaging materials using its visual response directly. In this manner, photon upconversion has found use as a promising new avenue in bioimaging. One of the most important parameters to optimize in bioimaging techniques is the signal-to-noise ratio, which is usually hampered by the problem of autofluorescence of tissues. However, by its nature of being an anti-Stokes process, TTA-UC removes this complication. The rarity of anti-Stokes shifts ensures that light at the wavelengths being monitored should only arise from TTA-based processes. Furthermore, the

long wavelengths used in excitation have greater penetration into tissue.

Given these advantages, many groups have developed technologies using upconversion materials for bioimaging.<sup>[5]</sup> First, a TTA system is typically chosen based on its efficiency and the wavelengths of interest. From there, the components are encapsulated in the form of a biocompatible nanostructure. In 2012, the Li group showed<sup>[31]</sup> that preparing a palladium porphyrin complex and diphenylanthracene in a silica nanoparticle led to high luminescence quantum yields of 4.5% in aqueous solution. Due to their photostability, low cytotoxicity, and high signal-to-noise ratios, these nanoparticles were excellent candidates for imaging of biological samples. Indeed, they were able to successfully image a lymph node in a living mouse using low-power 532 nm lasers. In 2018, the Li group further expanded this technology with a new system capable of upconverting near-IR light to yellow light and in nanocapsules containing reductive solvents.<sup>[32]</sup> The reductive solvents, such as dimethyl sulfoxide or linoleic acid, enhance the photostability of these particles in aerobic conditions by scavenging singlet oxygen. Furthermore, the use of near-IR light expands its utility by allowing for greater tissue penetration. These results are illustrated in Fig. 2 with the *in vivo* imaging of the liver of a mouse.

## 3. Photodynamic Therapy

### 3.1 Photodissociation of Ruthenium Complexes

While many applications employ the visual response of TTA, another area of research is focused on the capture and utilization of the increased output energy formed in the upconversion process. Similar to its application in bioimaging, TTA has found a presence in the field of photodynamic therapy because of the promising increases in light penetration.<sup>[33]</sup> In 2014, work by

the Bonnet group demonstrated the feasibility of an energy transfer event following TTA-UC to harvest the upconverted energy to drive further chemical processes.<sup>[34]</sup> In this study, Bonnet first demonstrated that liposomes containing palladium(II) tetraphenyltetra-benzoporphyrin and perylene can perform TTA-UC to convert red light (630 nm) to blue light (445 nm) with an overall quantum yield of 0.5%. Next, they further demonstrated that this light can be radiatively transferred in solution to neighboring liposomes containing a light-activatable prodrug,  $[\text{Ru}(\text{tpy})(\text{bpy})(\text{SRR}')]\text{]}^{2+}$ , which possesses a weak Ru-S bond that cleaves upon blue light excitation produced by TTA-UC. These authors further showed that the ruthenium complex can be directly attached to the upconverting liposome allowing for a more efficient Förster radiative energy transfer (FRET) process (Fig. 3) to occur in contrast to emission/reabsorption.<sup>[35]</sup> These results show a promising future for the development of *in vivo* photodissociative drug release using long wavelengths of light and demonstrate the ability of upconverted light to promote bond-breaking reactions. Current challenges lie in the development of these technologies to work *in vivo* and in the presence of oxygen and other quenchers.

### 3.2 Photocontrolled Cellular Binding

Along these lines, the Kohane group have also demonstrated the photocontrolled binding of cells to micellar nanoparticles using incident green light.<sup>[36]</sup> This study used micelles that were self-assembled from the block copolymer poly(D,L-lactic acid)-poly(ethylene glycol) (PLA-PEG) that contained components that could be activated toward cellular binding. Particularly they chose the peptide cyclo-(RGDFK) known to bind preferentially to  $\alpha_v\beta_3$  integrin, which is overexpressed in cells that contribute to tumor growth. As a way to activate this peptide, they chose to cage it using (7-diethylaminocoumarin-4-yl)methyl (DEACM) as a photocleav-

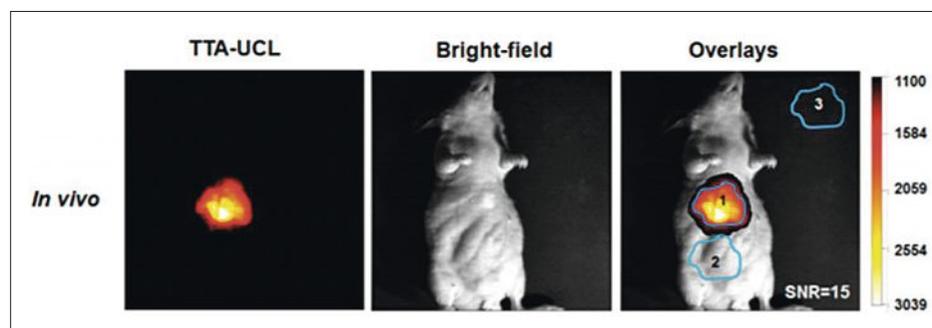


Fig. 2. *In vivo* bioimaging using TTA-UC nanocapsules in the liver 1 of a mouse compared to its spleen 2 and the *ex vivo* kidney 3. Reprinted (adapted) with permission from Q. Liu, M. Xu, T. Yang, B. Tian, X. Zhang, F. Li, *ACS Appl. Mater. Interfaces* 2018, 10, 9883. Copyright 2018 American Chemical Society.

able group. Upon cleavage, the hydrophilic peptide traverses to the micelle surface where it can become involved in cellular binding (Fig. 4). While DEACM is readily cleaved by blue light, Kohane noted that blue light has low penetration in tissue and so it would be advantageous to incorporate a TTA-UC system within the nanoparticle to activate the peptide with longer wavelength light therefore allowing more practical *in vivo* applications. Palladium(II) octaethylporphyrin and DPA as sensitizer and annihilator, respectively, were chosen, as they are well known to undergo green-to-blue upconversion efficiently. Both molecules sit within the core of the nanoparticle and were independently verified to undergo upconversion in the absence of the photocaging groups. Then, being adjacent to the DEACM group, the upconverted DPA singlet can efficiently undergo FRET to transfer its energy and promote the photocleavage reaction. This example demonstrates the capture of upconverted light to further enable a chemical bond cleavage.

#### 4. Photocatalysis

Semiconductors have been used both to convert light to electrical energy in solar cells, as well as transform it into chemical energy to perform photocatalytic reactions. While desirable for practical applications, the use of broad-spectrum visible light, such as sunlight, is problematic because many photons sit below the band-gap of the semiconductor and cannot be used for productive chemistry. TTA-UC offers the ability to capture these unused photons and convert them into higher energy light capable of sensitizing semiconductor photocatalysts.<sup>[37,38]</sup> In 2011, the Castellano group achieved this by combining a PdOEP/DPA system with nanostructured tungsten oxide photoanodes to generate a photocurrent using sub-band-gap green light.<sup>[39]</sup> A serious limitation still existed, however, because this work was carried out with complete physical separation of the semiconductor from the TTA-UC system. While the  $\text{WO}_3$  particles were suspended in an aqueous solution, the sensitizer and annihilator were both only soluble in organic solvents and required complete anaerobic conditions. This is problematic because the upconverted light has no directional preference for emission leading to many lost photons scattering in directions opposite the semiconductor. A year later, the Kim group published a study attempting to bypass these limitations by encapsulating a platinum porphyrin complex and DPA in a polymeric shell.<sup>[40]</sup> These microcapsules could be dispersed in the same aqueous solution as the semiconductors, and they also

contained an inner solvent system devoid of oxygen, eliminating the need for anaerobic conditions. It was further shown that not only were the microcapsules capable of efficient TTA-UC luminescence, but were also able to sensitize the  $\text{WO}_3/\text{Pt}$  photocatalysts in water leading to the multi-electron reduction of molecular oxygen to hydroxy

radical (Fig. 5). To monitor the formation of hydroxy radical, coumarin was added as a scavenger, leading to the production of 7-hydroxycoumarin. The characteristic fluorescence of 7-hydroxycoumarin at 460 nm was used to confirm the production of hydroxy radical, with control reactions ensuring its production only through TTA

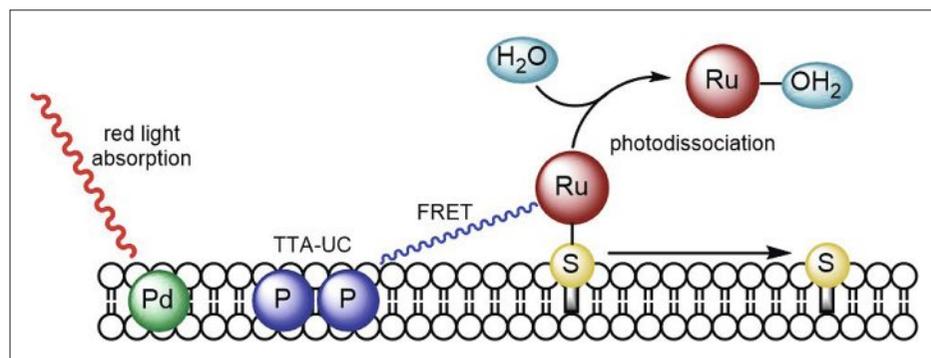


Fig. 3. TTA-UC followed by FRET to promote photodissociation of Ru prodrugs. P - perylene

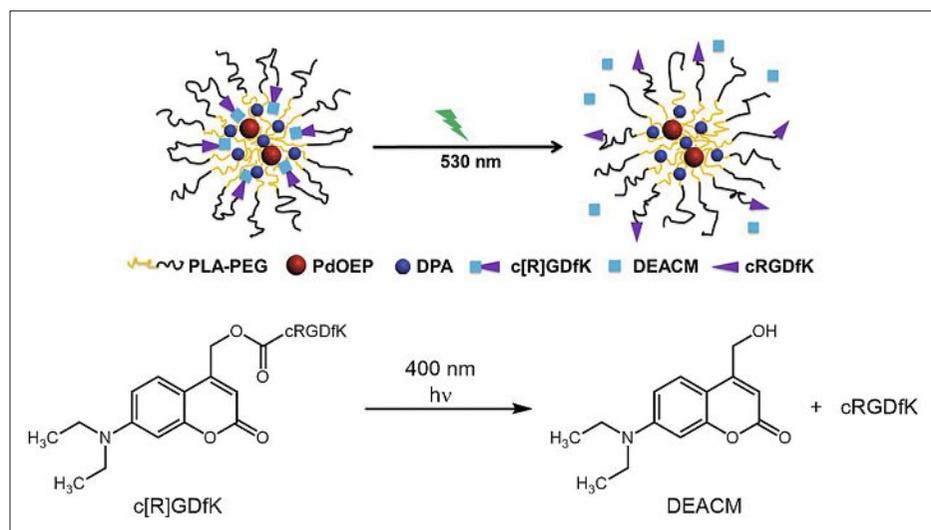


Fig. 4. Cell-targeting nanoparticles activated through TTA-UC. Reprinted (adapted) with permission from W. Wang, Q. Liu, C. Zhan, A. Barhoumi, T. Yang, R. Wylie, P. Armstrong, D. Kohane, *Nano Lett.* **2015**, *15*, 6332. Copyright 2015 American Chemical Society.

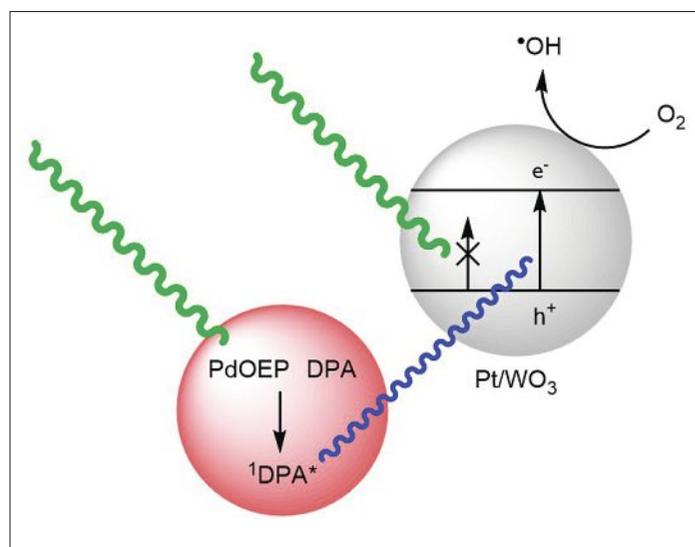


Fig. 5. Hydroxyl radical formation with sub-band-gap photons.

sensitization. These results suggest great potential for upconversion to photoexcite semiconductors as a means of energy storage or chemical transformations.

#### 4.1 Photoisomerization of Materials

In 2013, Jiang *et al.* saw the potential of TTA-UC to control light-driven soft actuators converting light energy into mechanical work.<sup>[41]</sup> Photodeformable cross-linked liquid crystal polymers (CLCPs) have been utilized as soft actuators in plastic motors,<sup>[42]</sup> flexible microrobots,<sup>[43]</sup> and artificial cilia,<sup>[44]</sup> among other uses. In this report, it was shown that, while blue light sources can deform the azobenzene moiety in the cross-linked polymer, the same polymer is also deformed by red light if first upconverted by passing through a TTA-UC film containing platinum(II) tetraphenyltetraabenzoporphyrin and DPA as a red-to-blue TTA system. Upon excitation of these films with 635 nm light, a bending of the CLCP film occurred after only 20 seconds. Images displaying this effect are shown in Fig. 6 and demonstrate that the direction of curvature is uniformly in the direction of the light source. Control experiments confirmed a TTA-UC mechanism of action. Most importantly, when a 150  $\mu\text{m}$  thick glass layer was used to separate the two films, photodeformation still occurred. This outcome precludes the viability of thermal reaction pathways and suggests that an emission–reabsorption mechanism is likely operative. To demonstrate potential *in vivo* applications of this work, it was also demonstrated that this chemistry works through a barrier of 3 mm thick pork tissue. This work was the first of its kind to demonstrate the ability of TTA-UC to promote an isomerization reaction and convert light into mechanical work.

#### 5. Synthetic Organic Catalysis

The above examples display the use of upconversion to enable photodissociations, sensitizations, and photoisomerizations, all of which are well known classical photochemical reactions. This raises the question whether it is feasible to harness the upconverted energy of TTA to drive synthetically relevant transformations. Such reactions would present a complementary approach to many other multiphoton catalyzed reactions that have been reported in the literature.<sup>[6–10]</sup> As detailed below, TTA-UC provides access to high-energy singlet species that act as electron donors and acceptors. The potential reach of these transient singlets can further expand the scope of substrates amenable to activation in photoredox catalysis. Alternatively, though less well studied, it should be possible to mediate energy transfer from the excited singlet generated in

the TTA process to a substrate in solution, potentially enabling high energy (UV) excited state photochemistry to be promoted using low-energy (visible) light. This type of transformation would rely on the key singlet intermediate to transfer its energy either radiatively or through FRET to an acceptor chromophore, though such behavior has yet to be reported in the context of synthetic method development. Below we survey the use of TTA-based UC catalysis for synthetic methods and highlight the prospects for future developments in this area.

#### 5.1 Photoreduction of Aryl Bromides

In 2015, the Jacobi von Wangelin group first reported the use of TTA as the basis for a synthetic method using the previously established biacetyl/PPO system to promote the photo-driven reduction of aryl bromides.<sup>[45]</sup> The authors postulated that such a reaction could operate under a mechanism wherein singlet PPO generated from TTA acts as a strong reductant ( $-2.14$  V vs. SCE) that can undergo electron transfer to aryl bromides (Fig. 7). The corresponding aryl radical anion can then undergo mesolytic bond cleavage followed by hydrogen atom transfer from the solvent to produce the desired reduced arene. Given a sufficiently negative substrate reduction potential, the reaction should only

proceed through the more reducing singlet excited PPO and not that of the triplet species ( $-0.84$  V vs. SCE). The feasibility of such a mechanism was probed by measuring the transient fluorescence of a DMF solution containing biacetyl (0.04 M) and PPO (0.013 M) following 430 nm laser excitation. The time-resolved signal at the fluorescence maximum of PPO at 360 nm was fit to a monoexponential decay to provide a delayed lifetime of 2.3  $\mu\text{s}$ . They then measured the decay of steady-state PPO fluorescence in the presence of different aryl bromide substrates acting as quenchers. The Stern–Volmer constant trends with the reduction potential of the substrates, consistent with an electron transfer mechanism. Furthermore, significant yields (18%) were only obtained with 4-bromoacetophenone, the only substrate in the study that was calculated to undergo exergonic electron transfer with singlet PPO. While the relatively low yields and use of laser light sources limit the practicality of this method, this work is conceptually significant in marking the first example of TTA-UC applied to catalytic method of synthetic significance.

This study was followed by an additional report in which the photoreduction of aryl halides was also achieved through TTA-UC in an intragel matrix utilizing PtOEP and DPA as a green-to-blue sys-

Fig. 6. Photo-deformable films activated by red light through TTA-UC. Reprinted (adapted) with permission from Z. Jiang, M. Xu, F. Li, Y. Yu, *J. Am. Chem. Soc.* **2013**, *135*, 16446. Copyright 2013 American Chemical Society.

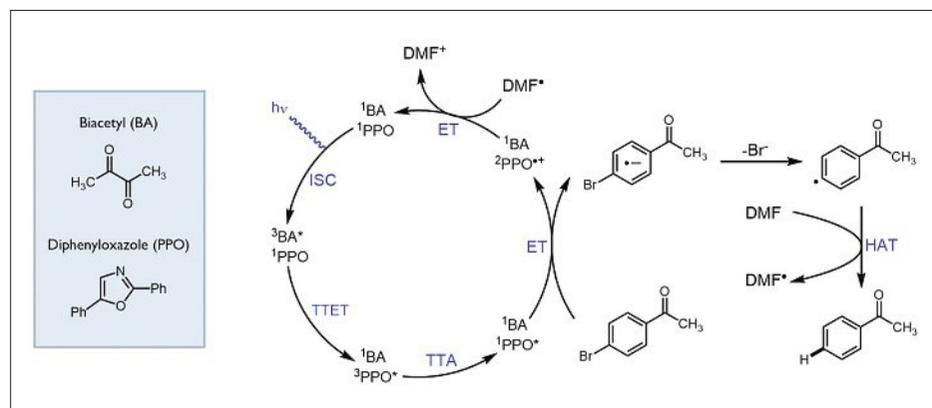
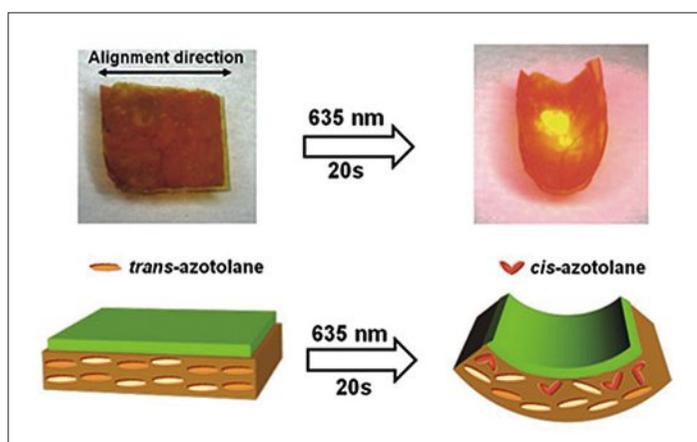


Fig. 7. Proposed catalytic cycle for photoreduction of aryl halides.

tem.<sup>[46]</sup> In this study, a similar mechanism was proposed using DPA as a strong reducing agent only in its singlet excited state. In contrast to the previous study, this work is enabled by lower energy light and contains a wider scope of substrates (Fig. 8); however, most significantly, confining the TTA system to within a supramolecular gel network of *N,N'*-bis(octadecyl)-*L*-Boc-glutamic diamide allows this reaction to proceed under aerobic conditions. Given the propensity of oxygen to quench triplet excited states, performing TTA-UC under aerobic conditions remains a challenge, but the use of a gel framework mitigates this issue.

## 5.2 Proposed TTA Mechanism

To the best of our knowledge, there have been no reports since 2015 explicitly evoking a TTA-UC based mechanism in a synthetic organic method. In 2017, one report by the König group on reductive coupling reactions with aryl halides, however, has recently been suggested to involve a TTA process. The original report proposed a catalytic cycle (Fig. 9) wherein photoexcited  $\text{Ru}(\text{bpy})_3^{2+}$  transfers its energy to a pyrene acceptor.<sup>[47]</sup> The triplet excited pyrene then oxidizes *N,N*-diisopropylethylamine (DIPEA) (+0.90 V vs. SCE) to generate pyrene radical anion. The reduction potential of the pyrene radical (−2.10 V vs. SCE) is sufficient to reduce aryl halide substrates while regenerating neutral ground-state pyrene. The resulting aryl radical anion will fragment *via* mesolytic cleavage into the halide anion and the aryl radical, which can be intercepted by a variety of coupling partners (heteroarenes, alkenes, and phosphites) to furnish a diverse scope of products. Later, Ceroni and Balzani proposed an alternative mechanism, in which a TTA-UC based mechanism may be operative.<sup>[48]</sup> In their proposal  $\text{Ru}(\text{bpy})_3^{2+}$  and pyrene constitute a sensitizer–annihilator system that can produce the higher energy singlet excited state of pyrene. This was favored over the initially suggested mechanism involving triplet pyrene, as the reduction potential of triplet pyrene was proposed to not be sufficiently oxidizing (−0.1 V vs. SCE) to undergo electron transfer with DIPEA.

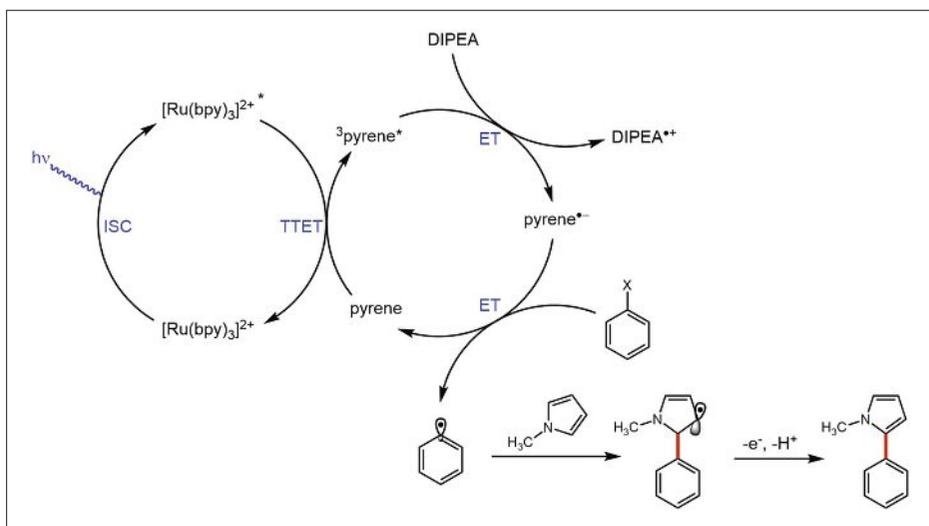


Fig. 9. Catalytic cycle proposed by König<sup>[49]</sup> for the sensitization-induced electron transfer reaction.

However, the electron transfer oxidation of DIPEA would be highly favorable if the singlet pyrene intermediate (+1.2 V vs. SCE) were to serve as the oxidant, leading to the generation of the key pyrene radical anion intermediate. This pyrene radical anion was proposed to then continue through the catalytic cycle as originally envisioned by König. A response later published by König also provided several other plausible mechanisms, including the reduction of triplet pyrene with *in situ* generated  $\text{Ru}(\text{bpy})_3^+$  or the direct reduction of the aryl bromides from TTA-generated singlet pyrene.<sup>[49]</sup> To date, the mechanism has yet to be fully elucidated. Regardless, these examples provide a conceptual framework for the potential use of TTA in synthetic organic reactions by harnessing the unconverted energy to drive challenging electron transfer reactions.

## 5.3 Prospects and Conclusions

Along with improving the strategies for using TTA partners as redox agents, TTA-UC is potentially well-suited to promote high-energy photochemical reactions. There is currently a wealth of classical photochemical reactions that remain underutilized in the field of organic synthesis, including the Paternò-Büchi oxetane formation, [2+2] cyclobutane ring forma-

tions, Norrish-type reactions of carbonyls, and the photolysis of weak E–X bonds.<sup>[50]</sup> Given the many examples highlighted above that invoke either FRET or emission–reabsorption following TTA, one can envision using this same process to drive synthetically important UV photochemical reactions through the generation of high energy singlet excited state species using incoherent and low energy visible light sources, which may offer significant practical benefits. We anticipate that interest in TTA-UC will continue to expand in coming years and provide a new avenue for the use of two-photon chemistries to access high energy intermediates for use in organic transformations.

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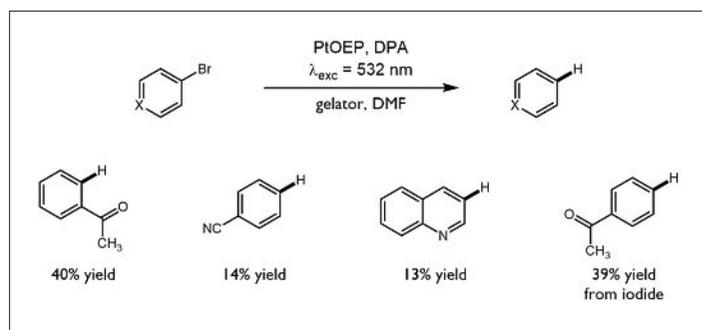


Fig. 8. Substrate scope of intragel photoreduction of aryl halides.

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