

# Reply to “Photoredox Catalysis: The Need to Elucidate the Photochemical Mechanism”

Indrajit Ghosh, Javier I. Bardagi, and Burkhard König\*

electron transfer · photocatalysis · pyrene · reaction mechanism

We have reported in our recent Communication<sup>[1a]</sup> the advantages of combining the best features of visible light absorbing tris(2,2'-bipyridine)ruthenium(II), Ru(bpy)<sub>3</sub><sup>2+</sup>, and visible light transparent, however, strongly reducing, polycyclic aromatic hydrocarbons via a simple triplet–triplet energy transfer process in synthetic photoredox catalysis. The key conceptual message is the sensitization of pyrene (Py) by Ru(bpy)<sub>3</sub><sup>2+</sup> in order to engage and thus to utilize its superior reduction potential for visible light photoredox catalytic transformations. Under the reaction conditions, which comprise the presence of a base as an electron donor, aryl halides as substrates, excess radical trapping reagents, and light irradiation, we observed highly efficient C–C and C–P bond formation reactions. Compared to previous photoredox systems, reaction times are short with broad synthetic utility.

Balzani, Ceroni et al. question in their Correspondence<sup>[1b]</sup> the formation of a pyrene radical anion as proposed reactive intermediate, as the electron transfer from the amine to a pyrene triplet state is endothermic based on the estimated values derived from literature redox potentials. They propose the formation of singlet pyrene as an additional reactive intermediate, generated via a triplet–triplet annihilation process, which under the photoredox catalytic reaction condition eventually leads to a pyrene radical anion upon quenching by DIPEA (*N,N*-diisopropylethylamine).

Our proposed reaction mechanism was intended as a minimalistic model. The complexity of the conditions of synthetic organic reaction mixtures under LED illumination make detailed mechanistic investigations extremely challenging. We do agree with Balzani, Ceroni et al. that all efforts should be undertaken towards a more detailed mechanistic understanding of complex reactions, but we disagree with their approach in criticizing our photoredox catalytic reaction model, and their proposed only possible alternative.

1. We report in our publication and in the Supporting Information a series of control experiments that confirm the

role of the ruthenium catalyst as sensitizer, pyrene as triplet acceptor, and the necessary presence of suitable sacrificial electron donors (e.g., DIPEA) and visible light irradiation for the described synthetic transformations to take place (see the control reactions in Ref. [1a]). Our proposed mechanism is in accordance with all above-mentioned facts. Being aware of the complexity of the reaction system (i.e., taking all plausible electron transfer events under photoredox catalytic conditions in account, see below and Figure 1), we did not refer to the pyrene triplet state as the exclusive redox reaction partner in our manuscript. The determination of the exact nature of the involved pyrene species generating its radical anion and respective kinetics requires sophisticated spectroscopic investigations under non-idealized conditions, which was beyond the scope of the manuscript.

2. Balzani, Ceroni et al. base their criticism on our proposed model on the estimated value for electron transfer to a triplet state pyrene from DIPEA [Eq. (VI)]. The sensitization-initiated electron transfer photoredox catalytic protocol is a multicomponent system, and many electron transfer events of the key catalytic components are plausible. We provide some of these together with the reported reduction potentials (cf. Ref. [2,3]) below.


Ru(bpy)<sub>3</sub><sup>2+</sup> is known to be reduced in the presence of amine donors forming Ru(bpy)<sub>3</sub><sup>+</sup> [Eq. (III)].<sup>[4]</sup> Under the reported reaction conditions, this is a feasible process competing with the energy transfer event to pyrene. The Ru(bpy)<sub>3</sub><sup>+</sup> species is not able to activate aryl halides, such as 2-bromobenzonitrile, via single electron transfers (see control chemical reactions in Ref. [1a]) and therefore may accumulate in the reaction mixture. With a reduction potential value of ca. –1.33 vs. SCE<sup>[3]</sup> an electron transfer to triplet excited state pyrene is thermodynamically highly exergonic.

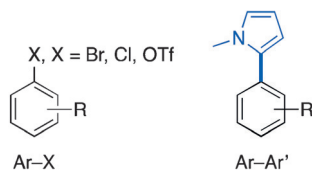
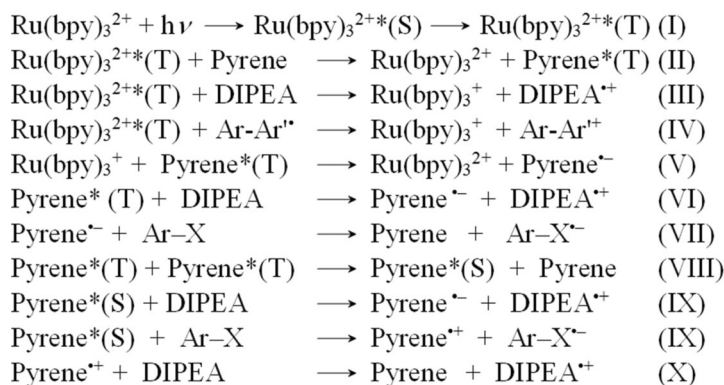
$$\Delta E = E(*\text{Py}(\text{T})/\text{Py}^{\cdot-}) - E(\text{Ru}(\text{bpy})_3^{2+}/\text{Ru}(\text{bpy})_3^+) \cong +1.23 \text{ V} \Rightarrow \Delta G < 0$$

This exemplarily illustrates that under the photoredox catalytic reaction condition the conversion of pyrene(T) to its radical anion is feasible in an overall exergonic redox reaction, in which DIPEA is the parent and only source of electrons under visible light photoirradiation.

3. Balzani, Ceroni et al.'s alternative mechanistic proposal included an additional step involving triplet–triplet annihilation of pyrene generating pyrene in its singlet-excited state.

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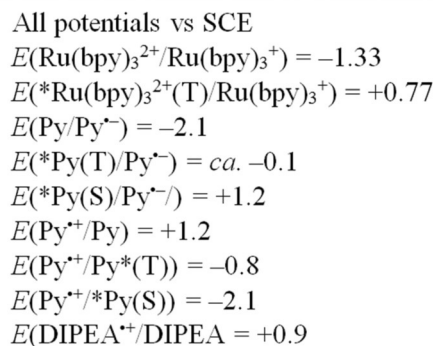
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Their proposal is based on earlier publications reporting the  $\text{Ru}(\text{bpy})_3^{2+}$  sensitized triplet–triplet annihilation of a pyrene derivative (in supramolecular assemblies<sup>[5]</sup>), and applications of triplet–triplet annihilated excited singlet species, generated under laser irradiation, for photoredox applications.<sup>[6,7]</sup> We would like to emphasize that the same papers (see Refs. [6, 7]) also report that the reactions failed to yield any<sup>[6]</sup> (or negligible under confined gel microenvironment<sup>[7]</sup>) photoredox products under irradiations with LEDs.<sup>[8]</sup> For instance, the butane-2,3-dione/2,5-diphenyloxazole pair shows low power visible-to-UV upconversion, but the same system, despite having a suitable reduction potential to activate substituted aryl halides, failed to yield any photoreduction product under LED irradiation and requires a laser to be productive.<sup>[6]</sup> The coherence and intensity of photoirradiation under the photoredox catalytic conditions seems to play a significant role for a productive synthetic reaction based on triplet–triplet annihilation.

The spectroscopic experiment reported by Balzani, Ceroni et al. was performed in the absence of any additives and devoid of any reactive intermediates. Hence, the result cannot directly be connected to our reported reaction. In addition, singlet pyrene with its estimated reduction potential of  $-2.1$  V vs. SCE is capable of direct electron transfer to aryl halides. The reaction should therefore proceed without an added electron donor (see Figure 1). However, under our reported reaction conditions the desired products were only obtained in notable amounts in the presence of DIPEA.

4. The electron transfer from DIPEA to  $^*\text{pyrene}(\text{T})$  under the “idealized” electron transfer conditions is endergonic. We would like to remind that such estimations, in particular for complex reaction mixtures, must be taken with care.<sup>[9]</sup> Redox potentials are sensitive to the experimental conditions and photoredox reaction conditions often deviate significantly from conditions of spectroscopic or electrochemical experiments. To illustrate this we refer to reports in the literature that  $\text{Ru}(\text{bpy})_3\text{Cl}_2$  and  $\text{Ru}(\text{bpm})_3\text{Cl}_2$  are able to slowly activate



strong C–F bonds in pentafluoro pyridine with a reduction potential of  $-2.12$  vs. SCE despite their reported ground state reduction potential value of  $-1.33$  and  $-0.91$  vs. SCE, respectively.<sup>[10]</sup> Frequently, it has also been reported that the excited state of *fac*- $\text{Ir}(\text{ppy})_3$  (possessing a reduction potential value of  $-1.73$ )<sup>[3]</sup> could be quenched by compounds with reduction potentials that have been reported to be more negative than  $-2.1$  V vs. SCE.<sup>[11]</sup>  $[\text{Ir}(\text{ppy})_2(\text{dtbbpy})]^+$  with an estimated excited state oxidation potential of  $+0.66$  is also reported to be quenched by amines under visible light irradiation.<sup>[12]</sup> Significant amounts of base, substrates and radical trapping reagents change the solvent properties (e.g., polarity) and microsolvation of the components of the photocatalytic system. In addition, photochemically or photoredox chemically generated reactive intermediates in the reaction mixture with mostly unknown redox properties may actively participate in electron transfer events.

The discussed experimental and reported facts therefore do not single out a triplet–triplet annihilation followed by electron transfer from DIPEA to the  $^*\text{pyrene}(\text{S})$  as the only mechanistic alternative for our reported reaction as proposed by Balzani, Ceroni et al. Other pathways are thermodynamically feasible and likely to occur under the reaction conditions used for synthesis. We summarize potential pathways of a SenI-ET reaction in Figure 1. In order to determine which of the pathways are exclusively or simultaneously operative for a given substrate a very detailed mechanistic study is required. A distinction based only on thermodynamic literature values may not be valid.

In summary, we agree that detailed spectroscopic studies are important to gain a better insight into the reaction mechanisms of visible light photoredox catalytic reactions. We do this extensively and collaborate for the more sophisticated experiments with many colleagues in chemistry and physics (for example, see our previous collaborative work (Ref. [13, 14]) on visible light photoredox catalysis). However, we strongly disagree with the approach of the authors to this issue, which ignores the complexity of synthetic reaction mixtures/conditions and the challenges of performing spectroscopic and electrochemical experiments under non-idealized conditions. Such conditions result from the systematic variation of solvents, additives, reactant concentrations and reactant ratios, which is an essential part in the development of practically useful organic transformations. Relative reac-

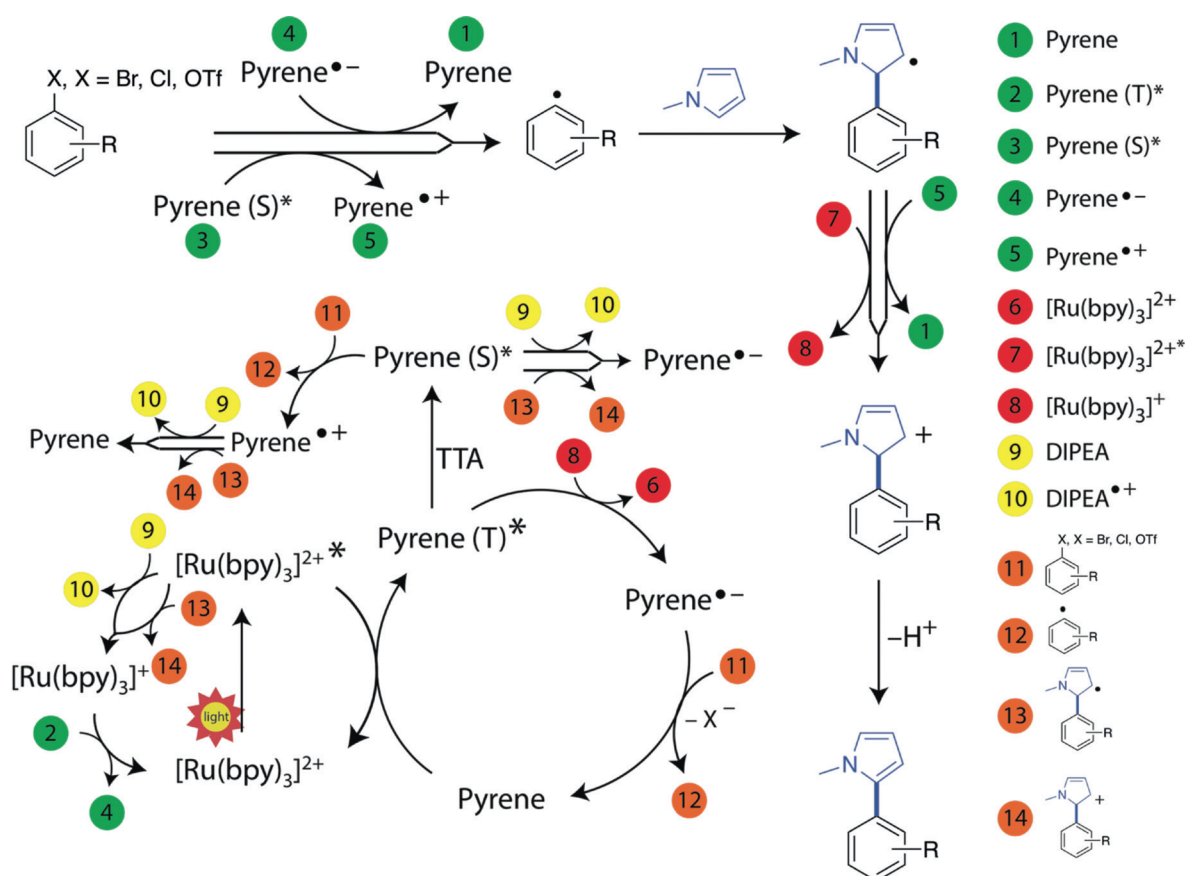


Figure 1. Plausible energy- and electron-transfer events for a SenI-ET photoredox catalytic reaction.

tion rates and, in part, lifetimes and properties of reactive intermediates are empirically adjusted to obtain the desired product in the highest yield and minimal time. Thermodynamic and kinetic values, determined under idealized conditions, can guide such optimizations in synthetic chemistry, but at the current level of our mechanistic understanding, surely not replace them.

We believe it is a future challenge to develop methods combining spectroscopic and electrochemical techniques, reaction kinetics, and theoretical approaches to investigate photoinduced reaction mechanisms under such realistic conditions of synthesis. For this, experts from the different fields should collaborate, and adapt and develop in a joined effort current methods to become applicable to complex reaction mixtures.

### Conflict of interest

The authors declare no conflict of interest.

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