The recent achievements of redox-neutral radical C–C cross-coupling enabled by visible-light

Jin Xie, Hongming Jin and A. Stephen K. Hashmi

Visible-light photoredox catalysis has been esteemed as one sustainable and attractive synthetic tool. In the past four years, a new yet challenging trend, visible-light-driven redox-neutral radical C–C cross-coupling involving putative radical intermediates, has been booming rapidly. Its advent brings a powerful platform to achieve non-classical C–C connections, and should lead to fundamental changes in retrosynthetic analysis. In this tutorial review, we highlight the recent achievements of visible-light-mediated redox-neutral radical C(sp³)–C(sp²), C(sp³)–C(sp), and C(sp³)–C(sp³) bond formation, opening a new window for C–C cross-coupling through the photoredox electron shuttling cycle between two coupling partners. While radical–radical coupling steered by the persistent radical effect was proposed as a rational explanation for the redox-neutral photoredox events, alternative kinetically driven chain propagation and radical addition pathways cannot be ruled out. This tutorial review aims to highlight the recent achievements of photoredox-neutral radical C–C coupling in synthetic chemistry.

Key learning points
(1) The significant advancements of redox-neutral C–C coupling by means of photoredox catalysis.
(2) The persistent radical effects for radical recombination.
(3) Redox-neutral construction of C(sp³)–C(sp²), C(sp³)–C(sp) and C(sp³)–C(sp³) bonds.
(4) Stereocontrolled C–C bond formation.
(5) Radical C(sp³)–H bond functionalization.

1 Introduction
Solar energy is a unique and renewable natural source of energy. Chemists aim at using sunlight or visible-light to drive chemical reactions, with the potential to decrease pollution and energy consumption to a greater extent and to develop new reaction modes. However, most organic compounds cannot directly absorb visible-light (λ > 400 nm) efficiently. Consequently, visible-light photoredox catalysis with a catalytic amount of photosensitizers has become particularly popular. In the past decade, we have witnessed a blooming development of visible-light photoredox catalysis for the concise construction of molecular architectures with different photosensitizers (Scheme 1). Inarguably, this emerging strategy is one of the most efficient and sustainable methods to generate radical intermediates from a great number of readily available starting materials, and can complement traditional radical chemistry which heavily depends on the use of toxic...
organotin reagents, radical initiators and UV light (λ < 300 nm). To date, several reviews have summarized the recent applications of visible-light photocatalysis in organic synthesis. In this tutorial review, we mainly discuss the achievements of visible-light-mediated redox-neutral radical C–C cross-coupling in the past four years. To the community it offers a new strategy to construct targeted molecules beyond transition-metal-catalyzed classical C–C coupling technologies.

A general mechanistic skeleton for light-induced redox-neutral C–C coupling is depicted in Scheme 2. In general, based on the redox potential of the excited state photocatalyst, either reductive quenching with electron donors (amines, thiols, carboxylates etc.) or oxidative quenching with electron acceptors (R-X, 1,4-dicyano-benzene, high valent metal complexes etc.) can initiate the photoredox cycle. In some cases, the combination of another catalytic cycle (organocatalysis or transition-metal catalysis) with photoredox catalysis is necessary for a successful coupling. In each case, double single electron transfer (SET) enables electron shuttling to photocatalysts. It is noteworthy that the photoredox electron shuttling can avoid using external sacrificial oxidants and reductants, offering a promising bond-forming strategy. To account for the photoredox cycle, a plausible radical–radical coupling based on the thermodynamic potentials of the ground and the excited state photocatalyst and putative radical intermediates was proposed for photoredox-neutral C–C coupling events. While these thermodynamic data sound reasonable for closed catalytic cycles, kinetically driven radical chain propagation or radical addition/elimination pathways may also play a determinative role. For example, the generation of

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Prof. Dr A. Stephen K. Hashmi studied chemistry at LMU Munich, where he obtained his diploma and PhD with Prof. G. Szeimies in the field of nickel- and iron-catalysed cross coupling of strained organic compounds. His postdoctoral research with Prof. B. M. Trost at Stanford University covered transition metal-catalysed enzyme metathesis. After his habilitation on enantiomerically pure organo-palladium compounds and palladium-catalysed conversions of allenes with Prof. J. Mulzer at the FU Berlin, the JWG-University Frankfurt and the University of Vienna, in 1998 he was awarded a Heisenberg fellowship of the DFG for a proposal on gold-catalysed reactions for organic synthesis – still a major focus of the group. His next stations were at the University of Tasmania in 1999, and Marburg University during 1999–2000; in 2001 he was appointed Professor for Organic Chemistry at Stuttgart University, and since 2007, he has occupied a chair for Organic Chemistry at Heidelberg University. Since 2013 he has been Vice President for Research and Structure, since 2016 Vice President for Research and Transfer at Heidelberg University.
nucleophilic radical B holds potential to add to electron acceptor AX (Path B), or the resulting intermediate can undergo radical propagation with the starting material BH to afford products and initiate another new catalytic cycle (Path C) or several competing pathways work concurrently. Herein, we ask the readers to be aware of the latter overlooked pathways. Of note, the visible-light-mediated redox-neutral C–C coupling inarguably represents a mild and efficient bond-formation kit-tool for synthetic manipulations. The future focus on the detailed mechanistic study of photoredox-neutral C–C coupling will further help the chemist to entirely predict a possible reaction.

Notoriously, owing to the high reactivity of open-shell radicals, controllable radical–radical heterocoupling is a highly challenging task in organic synthesis. With profuse efforts, the cross-coupling selectivity of two radicals can be steered by the persistent radical effect (PRE). The PRE is based on a kinetic effect; if one “persistent” (more long-lived, radical A) and one “transient” (more short-lived, radical B) species are generated at equal rates, the persistent radical A is less prone to undergo self-termination to form A–A but the transient radical B can undergo homo-coupling to form the dimer B–B. During the initial step, the concentrations of both radicals are very low (usually $<10^{-7}$ M), which enables the homo-coupling of transient radical B and the cross-coupling of radicals A and B unfavorable. After this period, the concentrations of persistent radical A and transient radical B increase gradually and then the high concentration of transient radical B makes its self-termination preferred. Along with the consumption of transient radical B, the concentration of persistent radical A continues to slowly increase. When the concentration of persistent radical A turns out to be much higher than that of transient radical B, the newly generated radical B is subjected to an increased concentration of persistent radical A and then rapid formation of A–B becomes much more favourable than the homo-coupling of radical B (Scheme 3). We would like to provide two comprehensive reviews for further reading about the PRE.16,17

Although the PRE principle was initially discovered with persistent radicals, this kinetic phenomenon may also be suitable for the selective heterocoupling between two transient radicals if they have significantly different lifetimes. Indeed, many visible-light-mediated redox-neutral C–C coupling reactions may proceed via other pathways (e.g., radical chain propagation) rather than the proposed radical–radical coupling. We would like to witness future work on possible mechanistic studies by combination of experiments and theoreticians.

### 2 Redox-neutral C(sp$^3$)–C(sp$^2$) coupling

In 2011, MacMillan’s group developed an early and rare example of visible-light-mediated radical–radical heterocoupling of ω-aminoalkyl radicals and arene radical anions.18 It represents the first redox-neutral ω-amino C(sp$^3$)–H arylation protocol with broad applications (Scheme 4). Both aromatic and aliphatic tertiary amines are uniformly ω-arylated. In particular, several different types of electron-deficient arenes and heteroaromatics can be applied. As illustrated in Scheme 4, oxidative quenching of *Ir(ppy)$_3$ produces a long-lived arene radical anion 7 and a strong oxidant Ir(IV) [$E_{1/2}$(Ir$^{IV}$/Ir$^{III}$) = +0.77 V versus SCE]. The formed Ir(IV) species then undergoes an SET from tertiary amines and subsequently generates transient ω-aminooalkyl radical 6 by deprotonation of radical cation 5. The cross-coupling of ω-aminooalkyl radical 6 with arene radical anion 7 leads to the desired product 4 by expulsion of a cyanide group. One major drawback of this protocol is the generation of toxic cyanide salts. However, this limitation can be addressed by dual photoredox and nickel catalysis,19 allowing for ω-arylation of amines with aromatic halides.

The benzylic amine is a privileged structural motif in biologically important reagents. To further enrich the access to this class of compounds, MacMillan and co-workers expanded this radical heterocoupling scope, by switching tertiary amines to commercially available ω-amino acids 9 (Scheme 5).20 The successful application of abundant and inexpensive ω-amino acids represents a practical route to many structurally diverse benzylic amines. Its excellent chemoselectivity was explained according to the PRE by the authors, in which ω-amino radical

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**Scheme 3** The general synopsis of radical–radical cross-coupling.

**Scheme 4** ω-Amino arylation with electron-deficient arenes.
12 is a highly reactive radical and arene radical anion 13 is a more stable radical.

The selective functionalization of C(sp^3)-H bonds constitutes the state-of-the-art in synthetic chemistry. However, visible light-mediated C(sp^3)-H bond functionalizations are usually limited to the α-C(sp^3)-H bond of amines. Therefore, the predictable C(sp^3)-H functionalization of other classes of substrates beyond amines is a worthwhile objective. On the basis of the bond dissociation energies (BDEs) of different kinds of C–H bonds (Scheme 6), selective functionalization of allylic and benzylic C–H bonds (relatively low C–H bond BDE) has been realized.

In 2013, a dual photoredox and organocatalytic arylation of benzylic C(sp^3)-H bonds was reported (Scheme 7). The main advance of this protocol is proton-coupled electron transfer (PCET) oxidation of a thiol organocatalyst with an excited-state photocatalyst to generate transient thiyl radical, which is highly reactive towards hydrogen atom abstraction from weak benzylic C–H bonds. The low C–H bond BDE and high hydrogen atom transfer (HAT) rate constant are two crucial factors for success. Under the standard conditions, both benzylic ethers and benzylic alcohols are efficient coupling partners, delivering the desired radical heterocoupling products in good yields. Intriguingly, for benzylic alcohol substrates, the additive octanal has two distinct functions: formation of a hemiacetal intermediate and sequestering of the CN/C0 anion. In the absence of octanal, benzylic alcohol was oxidized to benzaldehyde under the same conditions. This redox-neutral radical C–C coupling provides a new route to a series of important diarylmethylalkyl ethers.

The allylic C–H bond has a C–H BDE comparable to or even lower than that of the benzylic C–H bond (allylic C–H bond of cyclohexene at 83.2 kcal mol^-1 versus benzylic C–H of ethylbenzene at 85.4 kcal mol^-1). As a consequence, the photoredox C(sp^3)-H bond arylation was expanded to various allylic C–H bonds. The synergistic organocatalysis and photocatalysis completed a broad allylic C–H bond scope. As illustrated in Scheme 8, a wide array of useful functional groups was tolerated and moderate to good yields were achieved. In this redox-neutral cross-coupling reaction, the PRE was proposed to control its selectivity between the “persistent” arene radical anion and the “transient” allyl radical. Although ethylbenzene was a good coupling partner (69%), the competition experiment with equivalent ethylbenzene and cyclohexene gave a surprising result—only allylic arylation product. The authors envisioned that the weaker BDE and more hydridic allylic C(sp^3)-H bonds would benefit the H-atom abstraction to thiyl radicals.
In the past decade, organocatalysis with a catalytic amount of primary or secondary amines was established as a new opportunity to enantioselectively functionalize the α-C(sp^3)–H bonds of aldehydes and ketones. However, organocatalytic β-C(sp^3)–H bond functionalization of carbonyl compounds remains elusive. Based on their success with the α-arylation of tertiary amines, the MacMillan group introduced a novel 5π electron activation mode into carbonyl compounds, and β-C(sp^3)–H bond arylation of aliphatic aldehydes and cycloketones was accomplished with electron-deficient arenes (Scheme 9). It offers an intriguing β-monoarylation of aliphatic aldehydes and cycloketones under mild conditions via synergistic photocatalysis and aminocatalysis.

When irradiated with visible light, an oxidative quenching of excited state ^1Ir(ppy)_3 (a strong reductant, E_{1/2}(Ir^{IV}/Ir^{III}) = −1.73 V versus SCE) with electron-deficient arenes can produce Ir(IV) species [a strong oxidant, E_{1/2}(Ir^{IV}/Ir^{III}) = +0.77 V versus SCE] and an arene radical anion 32 (Scheme 10). The enamine intermediate 29, generated in situ from aldehydes and ketones, undergoes an SET process with the Ir(IV) species to produce radical cation 30, which can be deprotonated to give the 5π electron−intermediate 31. The radical–radical heterocoupling of 31 and 32 finally leads to the desired β-arylation products 27 or 28. Interestingly, only β-monoarylation products were formed.

The authors speculated that the produced adducts 27 and 28 failed to undergo the second β-arylation reaction mainly because the corresponding β-enaminyl radicals had lower nucleophilicity. With a chiral aminocatalyst (cinchona-derived organocatalyst), moderate enantioselectivity can be achieved (50% ee). The combination of organocatalysis and photoredox catalysis inarguably brings us a new radical–radical coupling blossom. It can be expected that the electron-withdrawing arene radical anions should selectively couple with a lot of transient carbon-centered radicals in line with the PRE principle.

The monofluoroalkenylation group is a very valuable structural motif for potential application in synthetic chemistry, medicinal chemistry and high-performance materials. Very recently, Hashmi and co-workers reported a photoredox-neutral strategy accessing α-monofluoroalkylated tertiary amines (Scheme 11). It represents the first dual C(sp^3)–H bond and C(sp^3)–F bond functionalization by visible-light photoredox catalysis. Aromatic and aliphatic tertiary amines and different gem-difluoroalkenes were applied to construct valuable tetra-substituted monofluoroalkenes.
with satisfactory results. Its mild reaction conditions, broad substrate scope, excellent functional group compatibility and good selectivity make this protocol very promising. Its synthetic robustness was convincingly established by late-stage monofluoroalkenylation of some top-selling drugs and complex molecules such as (+)-diltiazem, citalopram, rosiglitazone, venlafaxine and dihydroartemisinin (Scheme 11). Although a radical–radical coupling model was proposed for this monofluoroalkenylation according to initiatory mechanistic studies, alternative pathways cannot be ruled out.

Very recently, Jamison and co-workers developed an efficient amino acid synthesis protocol (Scheme 12).\(^\text{28}\) Owing to the higher reduction potential of CO\(_2\) (\(E^0 = -2.21\) V versus SCE) than typical photocatalysts, they finally used p-terphenyl 38 as a metal-free photosensitizer (\(E^0 = -2.63\) V vs. SCE), and designed a redox-neutral carboxylation of tertiary amines using a photoredox-catalysed continuous flow technique. A variety of amines can be directly converted into valuable \(\alpha\)-amino acids. The authors proposed a radical–radical coupling of an \(\alpha\)-aminoalkyl radical and a CO\(_2\) radical anion which is formed via single electron reduction of CO\(_2\) under photoredox conditions.

### 3 Redox-neutral C(sp\(^3\))–C(sp) coupling

In 2015, Hashmi and co-workers developed the first sunlight-mediated, gold-catalyzed \(\alpha\)-amino alkylation of tertiary aliphatic amines with 1-iodoalkynes.\(^\text{29}\) As shown in Scheme 13, it has a broad substrate scope with regard to both coupling partners. Although the known A3 coupling and oxidative \(\alpha\)-amino alkylation can get access to propargylic amine products, this developed redox-neutral C(sp\(^3\))–H alkylation protocol showcases its synthetic advantages. Some products bearing versatile functional groups such as –CHO, –PhCH\(_2\)O and –OH, cannot be obtained with the previously known alkylation methods. Moreover, using this strategy, the direct alkylation of important drug citalopram can be easily achieved.

### 4 Redox-neutral C(sp\(^3\))–C(sp\(^3\)) coupling

The previous routes to \(\beta\)-amino ethers usually need multiple steps with the use of sensitive organometallic reagents. As a follow-up work in dual photocatalysis and organocatalysis, visible-light-induced redox-neutral C–C coupling of benzyl ether and imines affords a compelling access to \(\beta\)-amino ethers which represent an important class of structural units in biologically important compounds (Scheme 14).\(^\text{30}\) Under the optimized reaction conditions, a diverse range of benzyl ethers and Schiff bases were examined. Its good functional group tolerance and simple operation delivers a mild and efficient protocol for the synthesis of \(\beta\)-amino ethers. It is no doubt that the development of enantioselective version will be of great importance in future.

Similarly, an unprecedented \(\beta\)-(sp\(^3\))-H aminoalkylation of cycloketones with Schiff base was developed (Scheme 15).\(^\text{31}\) Although the substrate scope of the \(\beta\)-Mannich reaction is limited to only cyclic ketones, it opens a new approach to construct 1,4-aminoketones under mild conditions. To further increase the viability of this new protocol, a three component coupling of cyclohexanone, benzaldehyde and anisidine was explored (Scheme 16). Interestingly, in the presence of DABCO, the

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**Scheme 12** Photoredox \(\alpha\)-amino acid synthesis.

**Scheme 13** Sunlight-driven, gold-catalyzed redox-neutral \(\alpha\)-amino alkylation (r.r. = regioisomeric ratio).

**Scheme 14** Benzyl C(sp\(^3\))–H bond aminoalkylation with Schiff bases.
\[\text{b-Mannich product 55 was exclusively formed in 70\% yield, while the classical } \alpha\text{-Mannich product 54 was obtained as the major product (54\%) along with minor b-Mannich product 55 (19\%) when DABCO was omitted from the standard reaction conditions. The corresponding asymmetric version allowing access to nitrogen-bearing tetrasubstituted carbon centers would be very attractive for medicinal applications.}\]

In early 2015 the \(\alpha\)-allylation of tertiary and secondary amines was reported by Xiao and Lu through dual photoredox and palladium catalysis (Scheme 17). 32 Both N-Ar tetrahydroisoquinolines and N-Ar \(\alpha\)-amino ketones were good coupling partners, while the other N-Ar tertiary amines exhibited less reactivity. The authors performed an electron paramagnetic resonance (EPR) spin trapping experiment with DMPO to determine \(\alpha\)-aminoalkyl radicals. Although \(\alpha\)-aminoalkyl radicals are proposed as important reactive intermediates in photoredox catalysis, to the best of our knowledge, this is the first case to directly verify it by EPR. Its practice was also underlined by the easy scale up to the gram scale.

As illustrated in Scheme 18, Xiao and co-workers applied this allylation strategy as a key step (61 to 62) to the formal synthesis of potential anticancer candidate 8-oxoprotoberberine derivative 65. Although the radical–radical coupling was proposed as a likely pathway for photoredox-neutral allylation, radical addition of \(\alpha\)-aminoalkyl radicals to organopalladium was also possible.

In 2014, Tunge and co-workers disclosed an interesting intramolecular redox-neutral decarboxylative allylation.33 As shown in Scheme 19, the dual photoredox and palladium catalysis combination make the decarboxylative allylation of intractable \(\alpha\)-amino and phenylacetic allyl ethers feasible without the use of any additives. To avoid the preparation of allylic esters, Tunge and co-workers also applied this dual catalysis tactic into the intermolecular radical decarboxylative allylation of phenylacetic acids with allyl methyl carbonates as allyl sources. From the perspective of one organic chemist, the moderate yields don’t compromise its synthetic value, because it offers a rare example of a site-specific decarboxylative radical allylation protocol, complementing Xiao’s \(\alpha\)-allylation of amines.32

In the next year, Tunge and co-workers thoroughly expanded the substrate scope of this dual photoredox and palladium catalysis system.34 Photoredox-neutral decarboxylative allylation of N-protected \(\alpha\)-amino allyl esters 70 were accomplished (Scheme 20).

Gratifyingly, the mechanistic study indicates that the reaction pathway is closely related to the stability of \(\alpha\)-aminoalkyl radicals.
It was found that the stable \( \alpha \)-aminoalkyl radical favours the radical–radical heterocoupling steered by the PRE principle, while the less stable \( \alpha \)-aminoalkyl radical would be prone to undergo a Pd(III)-mediated reductive elimination pathway. For example, as depicted in Scheme 21, among starting materials 70A–C, both 70A and 70B can form relatively more stable \( \alpha \)-amino radicals than 70C. Therefore, \( \alpha \)-amino radicals derived from 70A and 70B are preferable for the radical heterocoupling with allyl radicals, and the less stable radical derived from 70C prefers to add to the Pd(II)-\( \pi \)-allyl species to form a Pd(III)-complex 73. Furthermore, with a chiral palladium catalyst it was found that for the less stable radical, moderate enantioselectivity (50% ee) was achieved. Conversely, the more stable radicals led to only racemic products or very low enantioselectivity. Much better enantioselectivity for starting material 70C is evidence for the formation of Pd(III)-bound intermediate 73 which can be tuned by the chiral ligand.

At the end of 2015, Ooi and co-workers reported an unprecedented, visible-light-driven redox-neutral enantioselective C–C coupling of \( N \)-arylaminomethanes and \( N \)-sulfonyl aldimines, allowing for the synthesis of enantioenriched 1,2-diamines (Scheme 22).35 Under photoredox conditions, a single electron oxidation of \( N \)-arylaminomethanes 75 and a single electron reduction of aldimines 74 are known to generate \( \alpha \)-aminoalkyl radicals and aldimine radical anions, respectively. Based on their rich experience in chiral ionic Brønsted acid catalysis,36 they hypothesized that the chiral tetraaminophosphonium ion-type catalyst 77 would form a chiral ion-pair 78 with the photoredox-generated aldimine radical anion. Finally, the radical–radical heterocoupling of chiral ion pair 78 with \( \alpha \)-aminomethyl radical 79 delivers the coupling products in good yields with excellent enantioselectivities.

To demonstrate the synthetic value of this new strategy, a rapid synthesis of chiral benzopiperazine derivatives was illustrated (Scheme 23). First, a radical–radical heterocoupling and a subsequent intramolecular amination furnished 83 in 63% total yield (two steps) and with 97% ee. Although currently the substrate scope is limited to \( N \)-arylaminomethanes only, we believe that this piece of work represents a significant advance in the photoredox-neutral enantioselective C–C coupling and highlights the potential of visible-light photoredox catalysis in this area.

Almost simultaneously, Meggers et al. reported a similar process; a visible-light-induced, bifunctional chiral Ir(III)-type photocatalyst enabled redox-neutral stereocontrolled C–C cross-coupling of trifluoromethylated ketones and tertiary amines.37 This protocol allows for the direct construction of chiral 1,2-amino alcohols from easily available trifluoromethyl ketones and tertiary amines (Scheme 24). It is noteworthy that the other
commercially available photocatalysts (1a and 1d) are ineffective, thus stressing the unique property of this kind of bifunctional Ir-based photocatalyst. A variety of enantioenriched 1,2-amino alcohols were constructed under mild reaction conditions. The Ir-bound radical pair was regarded as one key combination for its successful asymmetric induction. Later, the employment of α-silylamines instead of tertiary amines allows for a broader amine scope.38 Interestingly, almost at the same time as those reported by Ooi and Megger, racemic but more general examples were documented by Rueping39 and Xiao40 respectively.

The robustness of visible-light-mediated redox-neutral intramolecular C–C coupling of ketones and α-C(sp3)–H of tertiary amines was achieved by Zhu and co-workers, providing a concise route to a wide range of 4–6-membered N-heterocycles 88 (Scheme 25).41 The reaction is brilliant with excellent selectivity and good synthetic yields. It enriches our toolbox for the mild synthesis of N-heterocycles bearing one quaternary carbon centre.

Much more recently, Cheng and co-workers developed an elegant photoredox-neutral C(sp3)–C(sp3) coupling accessing congested ketones (Scheme 26).42 A wide range of 4-alkyl Hantzsch esters 90 were used as efficient tertiary alkyl radical sources by means of visible-light photoredox catalysis. Its promising synthetic values were showcased by the concise connection of two contiguous quaternary carbon centres and the formal synthesis of hydroxysteroid dehydrogenase inhibitors. In the past four years, we have witnessed the rapid growth of redox-neutral C–C coupling in organic synthesis and some examples are not discussed in detail.43–46

5 Conclusions

In conclusion, the recent achievements of visible-light-induced redox-neutral radical C–C cross-coupling during the past four years have been summarized. Its advent offers a powerful C–C coupling strategy under mild reaction conditions, which is beyond what traditional coupling chemistry would bring to synthetic chemistry. Inarguably, it will lead to fundamental changes in non-classical C–C disconnection in retrosynthesis analysis. Perhaps more importantly, it should stimulate forward development of visible-light-driven, redox-neutral enantioselective C–C coupling, which is almost underdeveloped yet deceptively challenging. At the moment, reaction discovery is outpacing the exacting analysis of individual reaction mechanisms,15,47–50 and most literature reviewed in this tutorial review can only propose a tentative radical–radical coupling pathway based on the thermodynamic potentials of the ground and the excited state photocatalyst and putative radical intermediates. Accordingly, it is a good chance for the readers to reconsider the possible mechanism. Nonetheless, given the significant advances of photoredox-neutral radical C–C coupling in synthetic chemistry, we believe that this timely tutorial review will draw great enthusiasm of chemists in the near future.

Abbreviations

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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>PRE</td>
<td>Persistent radical effect</td>
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<tr>
<td>SET</td>
<td>Single electron transfer</td>
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<td>SSCE</td>
<td>Sodium saturated calomel electrode</td>
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<td>SCE</td>
<td>Saturated calomel electrode</td>
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<td>BDE</td>
<td>Bond dissociation energy</td>
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<td>Proton-coupled electron transfer</td>
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<td>DMA</td>
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<td>DABCO</td>
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Conflicts of interest

There are no conflicts of interest to declare.

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References