# We are IntechOpen,
# the world's leading publisher of
# Open Access books
# Built by scientists, for scientists

## 6,900
Open access books available

## 186,000
International authors and editors

## 200M
Downloads

Our authors are among the

## 154
Countries delivered to

## TOP 1%
most cited scientists

## 12.2%
Contributors from top 500 universities

CLARIVATE ANALYTICS
**BOOK CITATION INDEX**
INDEXED

**WEB OF SCIENCE**™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

# Interested in publishing with us?
# Contact book.department@intechopen.com

# Photo-Organocatalysis, Photo-Redox, and Electro-Organocatalysis Processes

Karolina Zalewska, Miguel M. Santos,
Hugo Cruz and Luis C. Branco

Additional information is available at the end of the chapter

## Abstract

The research involving photo-organocatalysis, photoredox, and electro-organocatalysis processes is revised in this chapter. Modern synthetic processes enable the formation of large arrays of organic molecules with precise control over their three-dimensional structure, which is important in a variety of fields ranging from pharmaceutical to materials science. Photochemical reactions may have a substantial impact on these fields by affording direct access to specific structural motifs that are difficult to construct otherwise. The conjugate structural feature shown by most of the photo-organocatalysts seems to enable the production of free radicals or radical ions in an easy fashion. Electro-organocatalysis has also received recent interest from both academia and industry. In this chapter, we mainly review recent remarkable advancements in organocatalysis involving photo-, photoredox, and electrochemical processes with particular emphasis on asymmetric protocols.

**Keywords:** photochemistry, photoredox, electrochemistry, organocatalysis, sustainable chemistry

## 1. Introduction

In general, organocatalysts are divided into two main classes according to the interaction, covalent or non-covalent (H-bonding, proton transfer, ion pair formation), with the organic substrate within the catalytic cycle. In this context, an organocatalyst reacts with an organic molecule in order to form a stable organic compound or a labile intermediate. At this stage, the activation induced by the organocatalyst enables the attack of the second reagent to form a

second adduct that releases the desired product with the concomitant regeneration of the organocatalyst.

Most of the common organocatalysts used for carbon-carbon bond formation reactions are based in chiral and achiral secondary amines, while reagents are electrophiles such as aldehydes, ketones, or α,β-unsaturated carbonyls. For these cases, the selected organocatalysts normally promote the generation of either an iminium ion or an enamine. *N*-heterocyclic carbenes have also been used as organocatalysts that promote the polarity inversion of an organic moiety for C—C bond formation.

Photocatalysis, where an electronically excited species acts as the catalyst, has gained increasing interest over the last years, with different organic transformations under such conditions being reported.

Recently, the catalytic activation of organic molecules by visible light photoredox catalysis that works under stereochemical control and provides chiral molecules in an asymmetric fashion has been largely reported. Generically, this approach relies on the ability of metal complexes and organic dyes to engage in single-electron transfer (SET) processes with organic substrates upon photoexcitation with visible light. Most common visible light photocatalysts are based on polypyridyl complexes of ruthenium, for example, tris(2,2′-bipyridine)ruthenium(II) or $[Ru(bpy)_3]^{2+}$, and iridium. These complexes absorb light in the visible region of the electromagnetic spectrum to give stable, long-living photoexcited states. The lifetime of the excited species is sufficiently long that it may engage in bimolecular electron transfer reactions in competition with deactivation pathways. Although these species are poor single-electron oxidants and reductants in the ground state, excitation of an electron affords excited states that are very potent single-electron transfer reagents. The ability of $[Ru(bpy)_3]^{2+}$ and related complexes to function as visible light photocatalysts has been recognized and currently applied to the electrolysis of water and the reduction in carbon dioxide to methane. These photocatalysts have also been employed in organic transformations including asymmetric approaches. Much of the excitement around visible light photoredox organocatalysis is due to the ability to achieve unique, if not exotic bond constructions that are not possible using the established protocols. For instance, photoredox organocatalysis can perform under overall redox neutral reactions where both oxidants and reductants are transiently generated in the same reaction vessel. This approach stands in contrast to methods requiring stoichiometric chemical oxidants and reductants, which are often incompatible with each other, as well as to electrochemical approaches, which are not amenable to redox neutral transformations.

Electro-organocatalysis has also received recent interest from both academia and industry. Electron transfer is one of the most important processes in organic chemistry in which one electron is added to or removed from an electroactive substrate. Such an electron transfer is reversible only when the resulting species are stable under those conditions. In other cases, an electron transfer generates subsequent chemical processes such as bond dissociation and bond formation. In general, radical cations and radical anions can be generated by electrochemical electron transfer reactions. Carbocations, carbon-free radicals, and carbanions can also be generated by subsequent bond dissociation or bond-forming processes. Several organic

synthetic transformations especially carbon-carbon bond formation reactions, oxidation, and reduction processes (electrocatalytic processes) have been reported.

# 2. Recent approaches in photo-organocatalysis

## 2.1. Asymmetric Photo-Organocatalysis

In the area of catalytic reactions, tremendous improvement has been made in the last decades, mostly upon the discovery of efficient transition metal catalysts. According to the variety of reactions, accessible, metal-catalyzed and enantioselective reactions have become significant tools in organic synthesis [1]. However, some disadvantages remain, such as the high cost and toxicity of the transition metal catalysts, employed and in some cases the problems that their residues, mainly in pharmaceutical products, can cause. Nonetheless, this transition metal catalysis will certainly continue to have an impact in synthetic organic chemistry in the future [2]. Alternatively, over the last years, a metal-free approach known as organocatalysis has reached a level of reliability that has allowed researchers to combine this procedure with other powerful techniques for molecule activation based on photochemical processes promoted by visible light. This green strategy has allowed previously unachievable synthetic issues to be solved and has rapidly progressed with application in both symmetric and asymmetric reactions (e.g., nucleophilic substitutions, Michael additions, cycloadditions, and aldol reactions) [3]. Generically, the organic catalysts can be categorized into two main classes according to the covalent or non-covalent (*viz.* H-bonding, proton transfer, ion pair formation) nature of the interaction established with the substrate within the catalytic cycle.
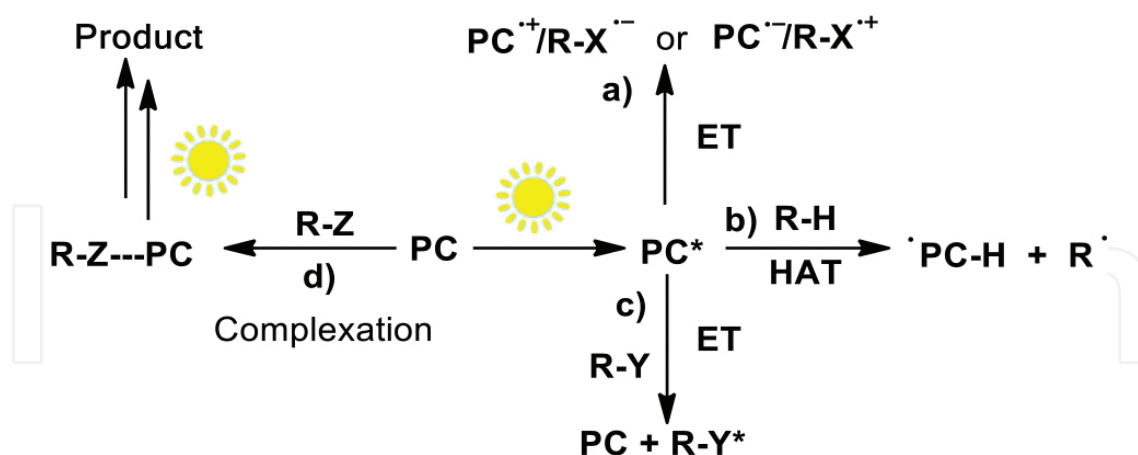


**Scheme 1.**

Homogeneous catalytic asymmetric transformations utilizing visible light photocatalysis include chiral and racemic photocatalysts with chiral organocatalysts, chiral Brønsted acids, or chiral Lewis acids [4]. In photo-organocatalytic processes, there are two main reaction models: the photocatalyst (PC) can act through an electron transfer (ET) process that causes an one-electron oxidation/reduction in the organic substrate R-X (**Scheme 1**, route a) or through

hydrogen atom transfer (HAT, route b) from a hydrogen donor R-H [5]. Most of the photo-organocatalysts are aromatic ketones, dyes, and (chiral) secondary amines, while R substrates are electrophiles, typically aldehydes, ketones, or $\alpha,\beta$-unsaturated carbonyls [5, 6]. Furthermore, photosensitization is known as an energy transfer between the excited photocatalyst (PC*) and substrate, which creates an excited state (R-Y*, from quenching of PC*), that is able to initiate a chemical reaction (route c). Sensitization can occurs by energy or electron transfer processes. The catalyst is transformed to act as a photosensitizer via photo-induced electron transfer (PET), hence leading the resulting photo-organocatalytic reaction to occur under stereoselective control [7].

Nowadays, a possible alternative can be considered in the photochemical activation step, in which the complexation of an organic reagent R-Z is controlled by a distinct, photostable chiral catalyst (route d) [8].

The aim of this subchapter was to point out the effective tools that the stereoselective ground-state processes offer to enantioselective photochemistry. The catalysts control the photoactivation of the substrates by inducing the transient formation of photon-absorbing chiral electron donor-acceptor (EDA) complexes. In addition, high stereocontrol in synthetically relevant intermolecular carbon-carbon bond-forming reactions driven by visible light can be provided by the inherent chirality of the catalysts.

The group of Bach focuses on catalytic processes, which allow previously unknown transformations employing both photochemical and conventional techniques. Their published papers concern photoredox organocatalysis, such as the first highly enantioselective (up to 90% *ee*) singlet oxygen [2+4] cycloaddition reactions [9], but also some related with the photo-organocatalysis. In 2005, Bach and co-workers presented an enantioselective photo-induced electron transfer (PET) sensitization with significant turnover and high enantioselectivity [10]. These PET-catalyzed conjugate additions of $\alpha$-amino alkyl radicals to enones have already been studied non-enantioselectively [11]. For the first time, an electron-accepting chiral organocatalyst was applied, in contrast to conventional complexing reagents. The (pyrrolidinylethyl) quinolone (**PC1**; 30 mol%) that induces a chiral environment on the substrate through hydrogen bonding at the bridgehead lactam, lead to the formation of the spirocyclic pyrrolizidine product in high enantiomeric excess and yields (*ee* up to 70%, yield 64%).

Four years later, the same group tested the intramolecular [2+2] photocycloaddition of prochiral 4-(3′-butenyloxy) quinolone to the desired products (**Scheme 2**) [12]. The previously characterized chiral organocatalyst-benzophenone **PC1** indeed caused a rate acceleration of the photocycloaddition, but low stereoselectivity was achieved. In contrast, a novel synthesized xanthone **PC2** proved to be a more active catalyst resulting in significant rate acceleration by triplet energy transfer and high enantiomeric excess values. After initial optimization using 20 mol% of chiral organocatalyst, it was possible to obtain the products in 94% *ee* (**Table 1**, entry 12). Bearing in mind these two catalysts as a potential prototype for synthetically relevant transformations of quinolones, in 2011 Bach and co-workers reported the synthesis of six 2-quinolones and their use in intramolecular [2+2] photocycloaddition [13].
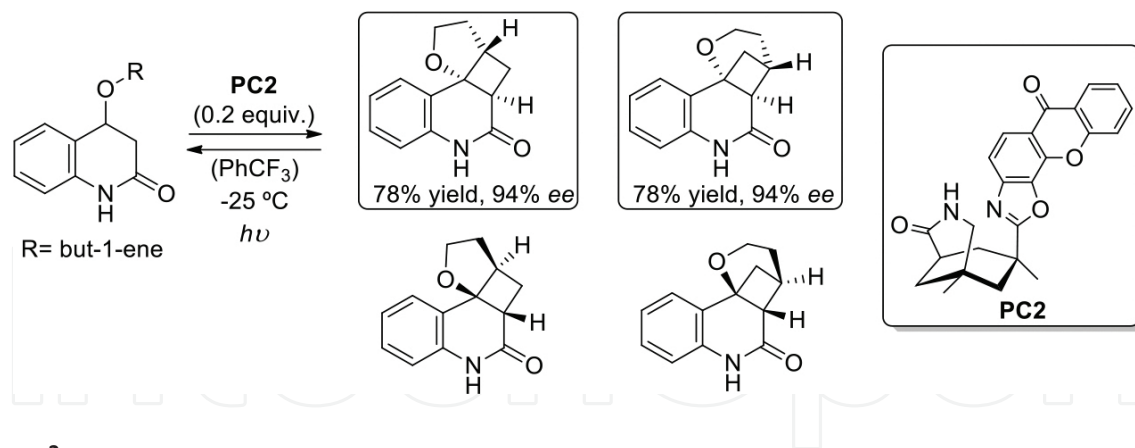
**Scheme 2.**

This photo-organocatalytic transformation was provided by applying a chiral, hydrogen-bonding template with an attached catalytically active sensitizing unit (benzophenone or xanthone). In all cases, it was possible to obtain high yields (78–99%) and enantioselectivities (83–94% *ee*) as shown in **Table 1**. These studies lead to a better understanding of stereoselective photo-organocatalytic processes, showing the importance of kinetic factors in creating an optimal catalytic cycle, as well as the activity range of different quinolones.

| Entry | Substrate | λ (nm) | Catalyst (mol%) | Yield (%)[a] | ee (%)[b] |
|-------|-----------|--------|-----------------|--------------|-----------|
| 1 | 1 | 300 | **PC3** 25 | 43 | 89 |
| 2 | 2 | 300 | **PC3** 25 | 87 | >90 |
| 3 | 3 | 300 | **PC3** 25 | 66 | 83 |
| 4 | 4 | 366 | **PC3** 25 | 89 | 89 |
| 5 | 5 | 366 | **PC3** 25 | 99 | 90 |
| 6 | 6 | 366 | **PC3** 25 | 99 | 94 |
| 7 | 4 | 366 | **PC2** 10 | 58 | 92 |
| 8 | 4 | 366 | **PC2** 10 | 75 | 90 |
| 9 | 4 | 366 | **PC2** 10 | 50 | 91 |
| 10 | 4 | 366 | **PC2** 10 | 46 | 89 |
| 11 | 4 | 366 | **PC2** 5 | 48 | 90 |
| 12 | 4 | 366 | **PC2** 20 | 53 | 94 |

[a] Yield of isolated product.
[b] The enantiomeric excess of the straight photocycloaddition products was determined by chiral HPLC analysis.

**Table 1.** Enantioselective photo-organocatalytic intramolecular [2+2]-photocycloaddition of quinolones.

In parallel, the group of Bach proposed an immobilization of earlier mentioned chiral photo-organocatalysts and their use in intramolecular [2+2] photocycloaddition of 4-allyloxyquinolone (**Scheme 3**) [14]. Under irradiation with light, the immobilized templates **PC4** and **PC5** allowed the substrate to undergo a [2+2] photocycloaddition to give the chiral products in high *ee* values and did not decrease even after the fourth use of recovered catalyst. Furthermore, the linking position of the catalyst at the C-6 carbon atom of the tetrahydronaphthalene was the one that rendered best results.
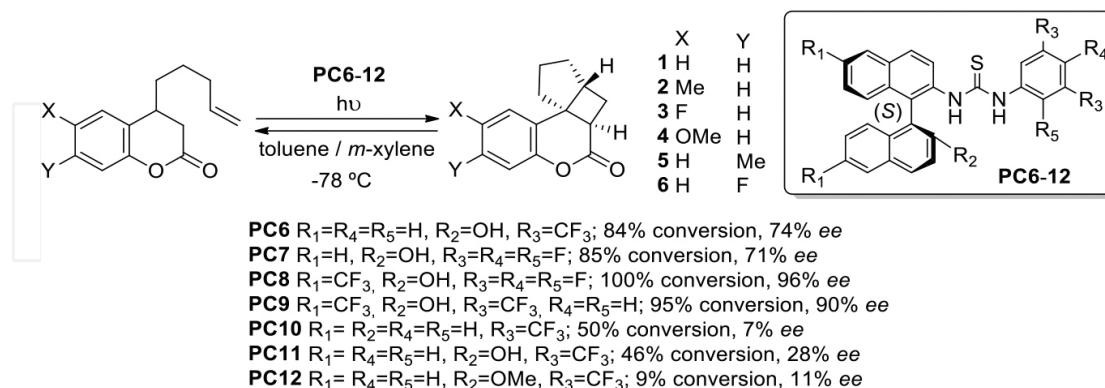
In different experiments, the group of Bach also investigated enantioselective photochemical reactions resorting on chiral Lewis acids as catalysts [15]. They reported the $AlBr_3$-activated chiral cationic oxazaborolidine catalyst for enantioselective intramolecular [2+2] photocycloaddition reactions of 4-alkenyl-substituted coumarins (78% *ee* were recorded with 20 mol % of catalyst). Nevertheless, the use of metals was inevitable.
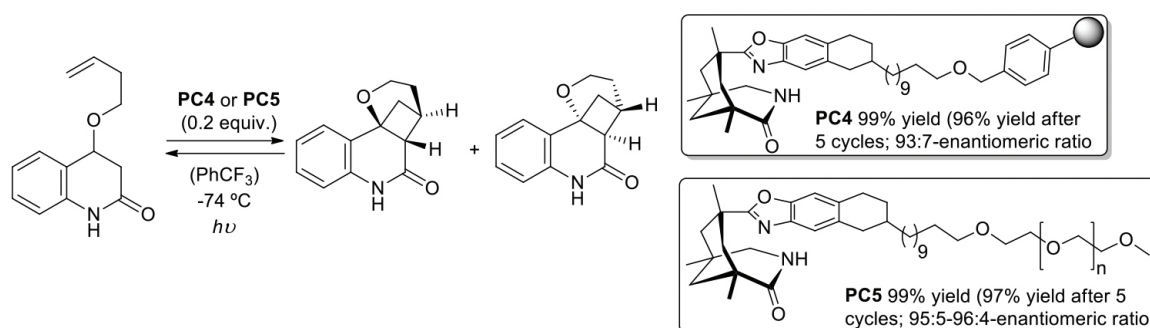


**Scheme 3.**

More recently, Vallavoju et al. [16] reported intramolecular [2+2] photocycloadditions of 4-alkenyl-substituted coumarins promoted by various atropisomeric binaphthyl-derived thioureas as photo-organocatalysts (**Scheme 4**). Thiourea catalysts are simple, environmentally benign, sustainable, and inexpensively synthesized from 'chiral pool', as well as easy to modulate and to handle. The photocatalytic cycle involves the formation of both static and dynamic complexes (exciplex formation) between the photo-organocatalyst and the reactive substrate, which are stabilized by hydrogen bonding. The corresponding products were achieved with high enantioselectivities (77–96% *ee* of product **1**, **Scheme 5**) with low catalyst loading (1–10 mol%). The authors tested the catalyst readily prepared in one step from commercially available, optically pure 2-amino-2'-hydroxy-1,1'-binaphthalene with different functional groups, in order to understand the interaction(s) between the catalyst and improve the stereoselectivity. It was discovered that using catalyst **PC6,** an excellent conversion and high enantioselectivity of the photoproduct would be obtained (84% conversion; 74% *ee* of product **1**). Nevertheless, the catalyst **PC8** showed a great potential as photo-organocatalyst for this transformation resulting in 100% product conversion and 96% *ee*. Additionally, it was proved that reducing the **PC8** catalyst loading from 100 to 30 to 10 mol% had a minimal impact on the enantioselectivity (94–96% *ee*; of product **1**) of the photoaddition product, and the reaction was completed in 30 min. By controlling the reactivity of the excited state through the formation of static and dynamic complexes, photocatalysts or sensitizers with higher excited-

state energies than the substrates can be completely avoided. This concept of catalysts may be a breakthrough in the discovery on new task-specific photo-organocatalysts.
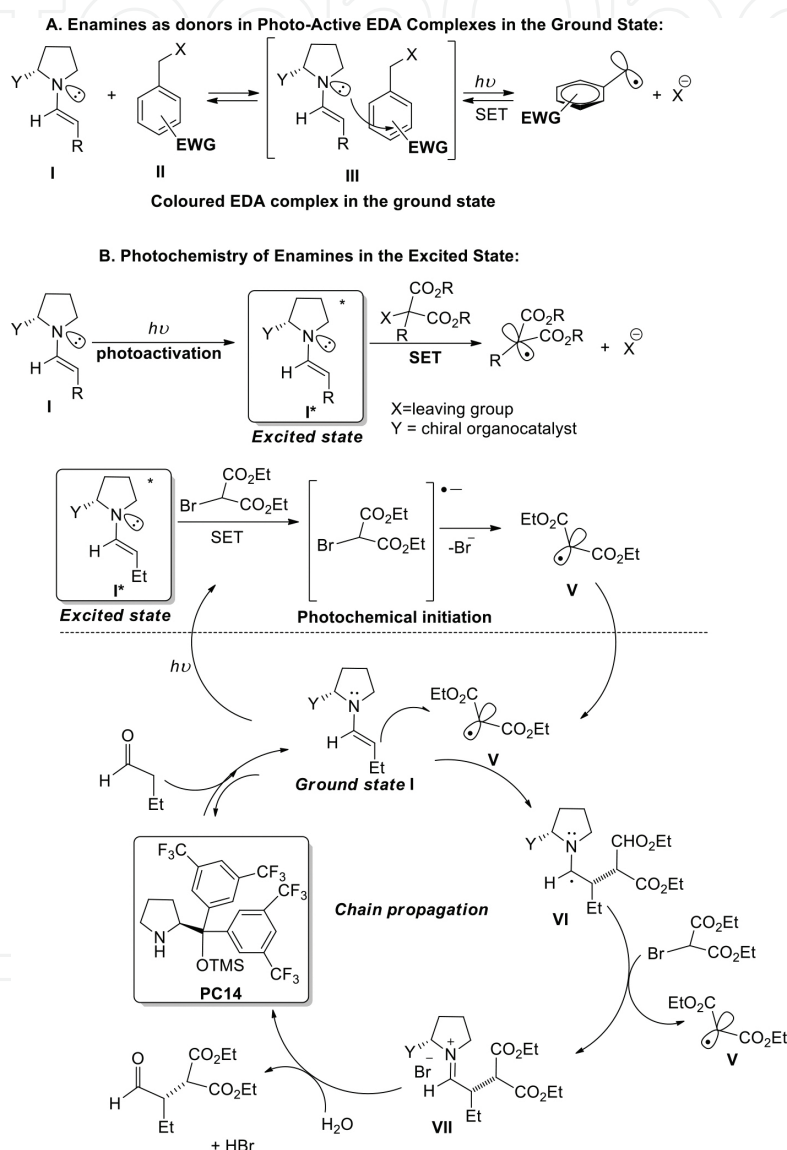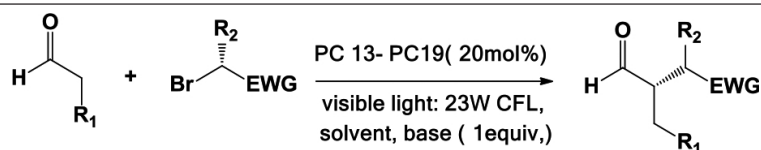


**PC6** $R_1=R_4=R_5=H$, $R_2=OH$, $R_3=CF_3$; 84% conversion, 74% *ee*
**PC7** $R_1=H$, $R_2=OH$, $R_3=R_4=R_5=F$; 85% conversion, 71% *ee*
**PC8** $R_1=CF_3$, $R_2=OH$, $R_3=R_4=R_5=F$; 100% conversion, 96% *ee*
**PC9** $R_1=CF_3$, $R_2=OH$, $R_3=CF_3$, $R_4=R_5=H$; 95% conversion, 90% *ee*
**PC10** $R_1=R_2=R_4=R_5=H$, $R_3=CF_3$; 50% conversion, 7% *ee*
**PC11** $R_1=R_4=R_5=H$, $R_2=OH$, $R_3=CF_3$; 46% conversion, 28% *ee*
**PC12** $R_1=R_4=R_5=H$, $R_2=OMe$, $R_3=CF_3$; 9% conversion, 11% *ee*

**Scheme 4.**

Melchiorre and co-workers presented the catalytic approach using a chiral organic catalyst with hydrogen-bonding motifs to bind a specific substrate selectively in synthetically relevant intermolecular carbon-carbon bond-forming reactions driven by visible light [7]. In the asymmetric $\alpha$-alkylation of aldehydes with alkyl halides, the commercially available diarylprolinol silyl ether catalysts [17] **PC13** and **PC14** were chosen due to their ability to induce high enantioselectivity in thermal reactions of aldehydes that carry on through enamine formation. The authors tested the possibility of EDA complex formation by addition of an excess of butanal (15 equiv.) and amines **PC13** and **PC14** (1 equiv.) in methyl *tert*-butyl ether (MTBE) with 2,4-dinitrobenzyl bromide (1 equiv.). Using either 2,6-lutidine or sodium acetate as bases, this model reaction provided the desired $\alpha$-benzylated product with high enantioselectivity (**Table 2**, entries 1 and 2, 83% *ee* with **PC14**). In its turn, the chiral organocatalyst **PC15** increased the *ee* value of the final product to 92%. The discovery of *in situ* created chiral EDA complexes from enamine intermediates which have the potential to participate actively in the photoexcitation of substrates without the required external photosensitizer, took the group of Melchiorre a step further.
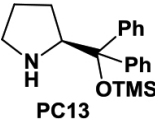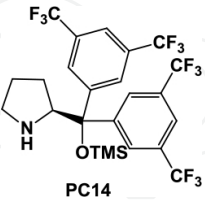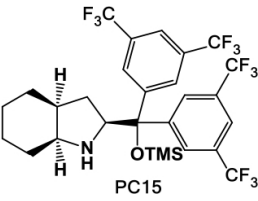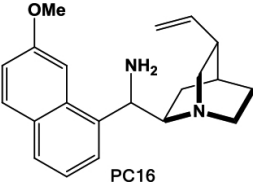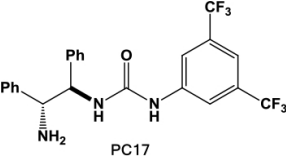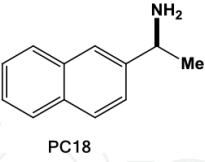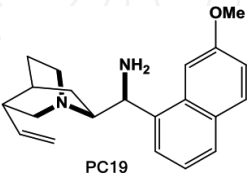
In 2014, the authors describe the first light-driven enantioselective organocatalytic alkylation of unmodified ketones with alkyl halides [18]. This correlates to the previously established mechanism, in which the chiral enamines are the key intermediates in ground-state organocatalytic asymmetric processes. A variety of chiral primary amines (20 mol%) to activate cyclohexanone towards benzylation with 2,4-dinitrobenzyl bromide were studied. A chiral secondary amine did not show any ability to catalyze the photochemical alkylation; nevertheless, the primary amines displayed promising (entries 4 and 5) or even excellent (entry 6) reactivity, but insufficient enantioselectivity. The primary cinchona-based amine catalyst **PC16** confirmed the formation of photon-absorbing chiral electron donor-acceptor complexes, thus the photoactivation of the substrates. The benzylation product was obtained under cryogenic conditions (0°C) in a good yield and with an improved optical purity (60% yield, 90% *ee*, entry 7). Based on these optimized experiments, Melchiorre and co-workers examined different

cyclic ketones in order to have an overview of the photochemical organocatalytic ketone alkylation approach. They discovered that a variety of N-Boc protected piperidine and dioxaspiro species can be readily active in this asymmetric alkylation reaction. Furthermore, the scope of the photochemical α-alkylation with diverse alkylating agents and cinchona-based amine catalyst led to the formation of α-alkylated products with high levels of regio-, diastereo-, and enantioselectivity.



**A. Enamines as donors in Photo-Active EDA Complexes in the Ground State:**

Coloured EDA complex in the ground state

**B. Photochemistry of Enamines in the Excited State:**

X=leaving group
Y = chiral organocatalyst

*Excited state*

*Photochemical initiation*

*Chain propagation*

**PC14**

**Scheme 5.**



PC 13- PC19( 20mol%)

visible light: 23W CFL,
solvent, base ( 1equiv,)

| Entry | Ketone or aldehyde | Alkyl halide substituted with EWG | Catalyst | Yield (%) | ee (%) | Ref. |
|---|---|---|---|---|---|---|
| 1 | -(CH$_2$)$_2$-CH$_3$ | 2,4-dinitrobenzyl bromide | PC13 | 98 | 75 | [7] |
| 2 | | | PC14 | 98 | 83 | [7] |
| 3 | | | PC15 | 87 | 92 | [7] |
| 4 | Cyclohexanone | | PC16 | 45 | 88 | [18] |
| 5 | | 2,4-dinitrobenzyl bromide | PC17 | 45 | 42 | [18] |
| 6 | | | PC18 | 90 | 18 | [18] |
| 7 | | | PC16 | 60 | 90 | [18] |
| 8 | | | PC19 | 50 | 90 | [18] |
| 9 | 4,4-dimethylcyclohexanone | | PC16 | 65 | 82 | [18] |
| 10 | 3,3-dimethylcyclohexanone | | PC16 | 57 | 94 | [18] |
| 11 | 4-methylcyclohexanone | | PC16 | 94 | 94 | [18] |
| 12 | 1,4-dioxaspiro[4.5]decan-8-one | | PC16 | 70 | 95 | [18] |
| 13 | -(CH$_2$)$_2$-CH$_3$ | Diethyl-2-bromomalonate | PC14 | 94 | 83 | [19] |

| Entry | Ketone or aldehyde | Alkyl halide substituted with EWG | Catalyst | Yield (%) | *ee* (%) | Ref. |
|---|---|---|---|---|---|---|
| 14 | -(CH$_2$)$_2$-CH$_3$ | diethyl 2-bromo-2 -methylmalonate | PC14 | 98 | 91 | [19] |
| 15 | -(CH$_2$)$_4$-TIPSO | diethyl 2-bromo-2 -methylmalonate | PC14 | 94 | 88 | [19] |

**Table 2.** Asymmetric α-alkylation of aldehydes and ketones with alkyl halides by photo-organocatalysis.

Last year, the group of Melchiorre reported the photo-organocatalytic enantioselective α- and γ-alkylation of aldehydes and enals with bromomalonates by a fluorescent light bulb without the need of any external photoredox catalyst [19]. The preliminary studies involved butanal and diethyl bromomalonate (**Table 2**) as substrates for this photo-organocatalytic reaction. The results showed that using the aminocatalyst **PC14** (20 mol%) in a MTBE solution under irradiation, the alkylation product was obtained in high yield and enantioselectivity after 4 h (94% yield, 83% *ee*; entry 13). The detailed photochemical studies using absorption and emission spectroscopy suggested that the direct photoexcitation of the enamine could trigger the radical generation from diethyl bromomalonate. Furthermore, no photoabsorbing ground-state EDA complex formation was observed. Accordingly, the photochemical reaction proceeds through a different mechanism. As previously described, the metal-free process depends on the creation of photon-absorbing electron donor-acceptor (EDA) complexes [18], generated in the ground state upon association of electron-deficient benzyl and phenacyl bromides **II** with the electron-rich enamine **I** (**Scheme 5A**). A single-electron transfer (SET) induced by visible light irradiation of the colored EDA complex **III** allows access to radical species under mild conditions. This reactivity allowed the expansion of a light-driven stereo-selective α-alkylation of carbonyl compounds [18]. In contrast to this, the authors suggest a novel photo-organocatalytic mechanism, in which enamines can use to drive the photochemical generation of radicals acting as a photosensitizer upon direct photoexcitation (**Scheme 5B**). The enamine **I**, under light absorption, reaches an electronically excited state (**I***) and to act as a photoinitiator causing the formation of the electron-deficient radical **V** through the reductive cleavage of the bromomalonate C—Br bond via a single-electron transfer (SET) mechanism (**Scheme 5B**) [19, 20]. Taking into consideration the capacity of **I** to infer high stereoselectivity in enamine-mediated polar reactions, adding the radical **V** to the ground-state **I** progresses in a stereocontrolled manner. Since α-aminoalkyl radicals known as strong reducing agents, the intermediate **VI** would induce the reductive cleavage of bromomalonate through an outer-sphere SET process, thus regenerating the radical **V**. This route affords a bromide iminium ion pair **VII**, which then hydrolyzes to release the desired product and the aminocatalyst **PC14**. Then, the scope of enantioselective organocatalytic alkylation of aldehydes and enals was examined. Differently substituted bromomalonates successfully contributed to the enantio-selective alkylation of butanal at room temperature (**Table 2**, entry 14). Aldehydes with a heteroatom moiety, long-alkyl chain, or an internal olefin, were also stereoselectively alkylated to give products with good enantioselectivity (**Table 2**, entry 15). Additionally, it was pre-

sented that enamine intermediates, synthesized from $\alpha$-branched enals, could trap the generated radical while locating a new stereocenter at a distant $\gamma$-position.

In parallel, the same group of researchers investigated the phase transfer catalyzed, enantioselective perfluoroalkylation and trifluoromethylation of cyclic $\beta$-ketoesters under visible light irradiation [21]. The photo-organocatalytic approach is again caused by the photochemical activity of EDA complexes generated *in situ* from the ground-state association of chiral enolates and perfluoroalkyl iodides. Irradiating the colored EDA complex induces a single-electron transfer (SET) allowing access to radical species at ambient temperature. Perfluoroalkyl iodides were selected as electrophiles due to their potential for facilitating EDA associations in the ground state. At the same time, chiral quaternary ammonium salts were used as phase transfer catalysts (PTC) that enabled the formation of a chiral ion pair after deprotonation of $\beta$-ketoesters by an inorganic base [22]. Perfluoroalkylation of one indanone methyl ester with perfluorohexyl iodide in chlorobenzene under visible light irradiation with PTC organocatalyst was chosen as model reaction. The best results were obtained using the *pseudo*-enantiomeric cinchonine **PC20** derivative catalysts, with an excess of perfluorohexyl iodide (3 equiv) for 64 h (59% yield, 93% *ee*) (**Scheme 6**) [21].

The above presented strategies of enantioselective photo-organocatalytic processes have a great potential for the sustainable preparation of chiral molecules, a rapidly developing area of modern chemical research.

In parallel to the efforts performed in the field of asymmetric photo-organocatalysis, some attempts were also performed in the non-enantioselective processes.
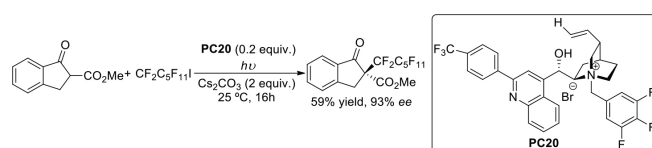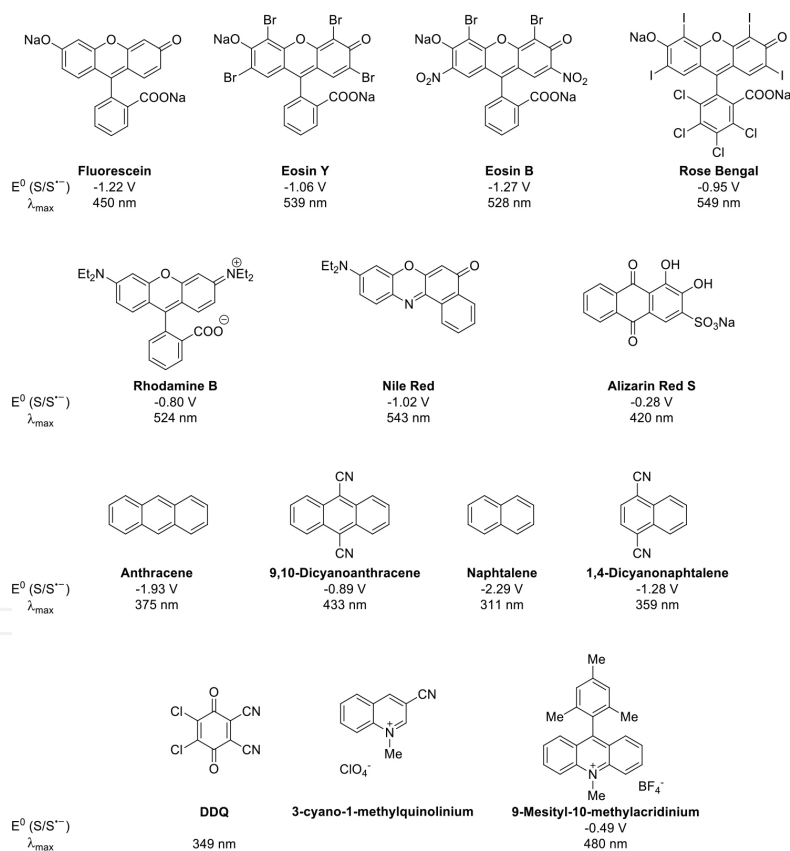


Scheme 6.

Non-asymmetric photocatalysis has gained a great deal of attention during the last decades [23, 24], and a remarkable and interesting case was recently described by the already cited group of Melchiorre, in which an aromatic aldehyde was involved in the intermolecular atom transfer radical additions (ATRA) of a variety of haloalkanes to alkenes, one of the essential carbon-carbon bond-forming processes in organic chemistry [25]. In an ATRA reaction, the addition of an organic halide across a carbon-carbon double-bond yields a new C—C and C—X bond (X = halogen) in a single operation. Once more, organic compounds known to be capable of high photoreactivity [25] could alternatively be used as an energy transfer photocatalyst. It is important to note that for the first time, aromatic aldehydes have been used as photoorganocatalysts in an effective and valuable process [26]. Recent exciting findings by Melchiorre and co-workers have also shown the metal-free photo-organocatalysis which allows the direct alkylation of 2- and 3-substituted 1*H*-indoles with electron-accepting benzyl and phenacyl bromides [27].

## 3. Recent approaches in photoredox organocatalysis

The term photoredox organocatalysis has its origin in the work by Nicewicz and MacMillan in 2008. They reported the enantioselective $\alpha$-alkylation of aldehydes using $[Ru(bpy)_3]Cl_2$ as a photoredox catalyst. This complex, alongside many others such as $[Ir(ppy)_2(dtb-bpy)]PF_6$ and *fac*-$[Ir(ppy)_3]$ that have been subsequently reported, acts as strong oxidizers in the excited state upon absorbing visible light. In general, different inorganic solid photocatalysts such as $TiO_2$ and ZnO have been largely explored as photoredox catalysts. The poor absorption of visible light by such inorganic photocatalysts is considered a limitation for application in organic synthetic processes using solar energies. In contrast, organic photocatalysts show some advantages regarding their low-cost, significant synthetic versatility, and the possibility to tune their redox properties. In this context, the organic photoredox dyes are usually selected according to their $\lambda_{max}$ and redox potential $E^0$.

**Scheme 7** depicts the most popular dyes investigated in photoredox catalysis procedures.
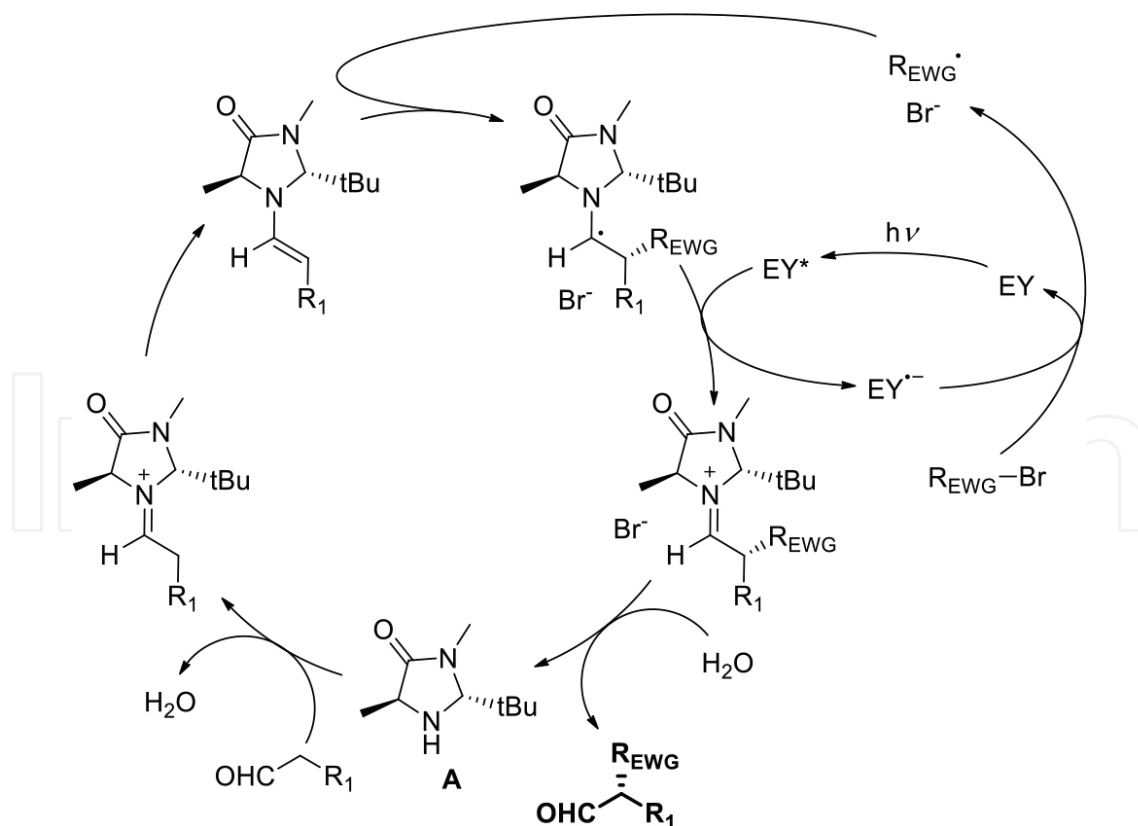


**Scheme 7.**

The photoactivation reveals the ability of the photosensitizer to absorb in the visible domain and to act both as a strong oxidant in the excited state S* and as an efficient reductant in its semi-reduced form $S^{\bullet-}$. In **Scheme 8**, a comparison between the general photoredox catalytic cycles of ruthenium-based catalysts and a photo-organocatalyst, *viz.* Eosin Y (EY), is presented.
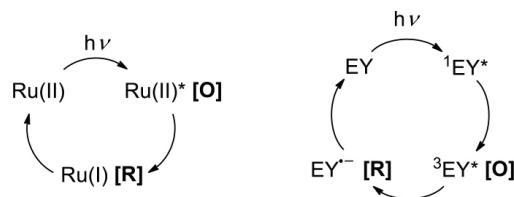
**Scheme 8.**

## 3.1. Asymmetric photoredox organocatalysis

One of the most explored aspects investigated in the field of enantioselective photoredox catalysis has been the use of organic dyes as photocatalysts. In the seminal work by Zeitler *et al.* [28], they reported the efficient cooperative asymmetric intermolecular α-alkylation of aldehydes catalyzed by Eosin Y under LED green light and in the presence of MacMillan's imidazolidinone catalyst **A** (see **Scheme 9** for a simplified proposed mechanism of the reaction). According to the electron-withdrawing groups of the substrates [diethylmalonate, *p*-nitrophenyl (PNP) and polyfluorinated alkane], the reactions performed better between −15 and +5°C with yields from 56 to 85% and enantiomeric excesses higher than 86%, despite the 18 h reaction time (see **Table 3**, entries 1–4).



**Scheme 9.**

Using the same conditions adapted to a microreactor flow regime, smaller reaction times were obtained with comparable results [29]. Rose Bengal was also applied as photoredox catalyst in this type of reaction (**Table 3**, entries 3–9). Again, imidazolinone **A** was employed as well as a Lewis acid such as LiCl to co-catalyze the photoreaction [30].

On the other hand, asymmetric α-amination of aldehydes has also been accomplished by means of photoredox chemistry [31]. By using an amine substrate bearing ODNs, photolabile groups that simultaneously work as the photoredox catalyst and also release the reactive carbamyl reagent that couples with the *in situ* formed enamines; sixteen α-amino aldehydes were successfully prepared in 67–79% yield and >86% *ee* (see **Table 4**).



| Entry | R$_1$ | R$_2$ | R$_3$ | Yield (%) | ee (%) | Ref. |
|---|---|---|---|---|---|---|
| 1 | *n*-Pentane | H | (CF$_2$)$_3$CF$_3$ | 56 | 96 | [28] |
| 2 | *n*-Pentane | H | PNP-CO | 82 | 95 | [28] |
| 3 | Ph | CO$_2$Et | H | 76 | 86 | [28] |
|   | Ph | CO$_2$Et | H | 89 | 83 | [30] |
| 4 | *n*-Pentane | CO$_2$Et | H | 85 | 88 | [28] |
|   | *n*-Pentane | CO$_2$Et | H | 88 | 80 | [30] |
| 5 | 4-*t*BuPh | CO$_2$Et | H | 51 | 83 | [30] |
| 6 | 3-ClPh | CO$_2$Et | H | 90 | 82 | [30] |
| 7 | 4-OMePh | CO$_2$Et | H | 94 | 80 | [30] |
| 8 | 2,4-(OMe)$_2$Ph | CO$_2$Et | H | 51 | 83 | [30] |
| 9 | (CH$_2$)$_2$CH=CHEt | CO$_2$Et | H | 56 | 85 | [30] |

**Table 3.** Asymmetric alkylation of aldehydes catalyzed by Eosin Y or Rose Bengal.
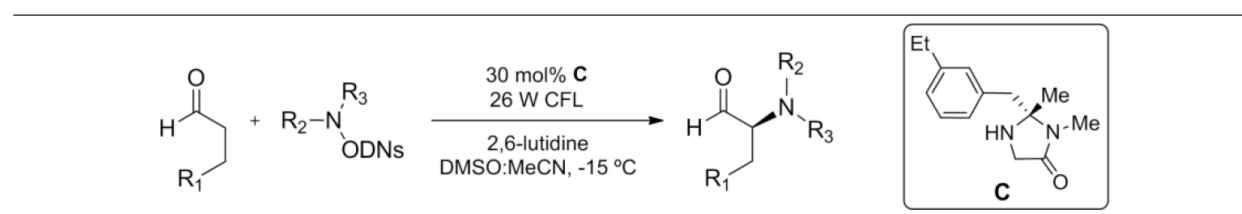
| Entry | R₁ | R₂ | R₃ | Yield (%) | ee (%) | Ref. |
|---|---|---|---|---|---|---|
| 1 | Ph | Me | Cbz | 77 | 89 | [31] |
| 2 | Ph | Me | Alloc | 75 | 90 | [31] |
| 3 | Ph | Me | Boc | 71 | 89 | [31] |
| 4 | Ph | Me | Fmoc | 73 | 89 | [31] |
| 5 | Ph | Bu | CO₂Me | 76 | 90 | [31] |
| 6 | Ph | MOM | CO₂Me | 75 | 94 | [31] |
| 7 | Ph | (CH₂)₃Ph | CO₂Me | 71 | 86 | [31] |
| 8 | Ph | Me | CO₂Me | 79 | 92 | [31] |
| 9 | n-pent | Me | CO₂Me | 71 | 90 | [31] |
| 10 | (CH₂)₂OBn | Me | CO₂Me | 73 | 88 | [31] |
| 11 | (CH₂)₂ONPhth | Me | CO₂Me | 77 | 90 | [31] |
| 12 | CH=CH₂ | Me | CO₂Me | 76 | 90 | [31] |
| 13 | (CH₂)₂CO₂Et | Me | CO₂Me | 71 | 90 | [31] |
| 14 | PMP | Me | CO₂Me | 79 | 91 | [31] |
| 15 | Cyclohexyl | Me | CO₂Me | 72 | 91 | [31] |
| 16 | Me₂ | Me | CO₂Me | 67 | 94 | [31] |

**Table 4.** Asymmetric α-amination of aldehydes by ODNs dual catalysis.



| Entry | R₁ | R₂ | Yield (%) | ee(%) | Ref. |
|---|---|---|---|---|---|
| 1 | 4-FPh | iPr | 72 | 83 | [32] |
| 2 | Ph | iPr | 75 | 97 | [32] |
| 3 | Ph | (CH₂)₂SCH₃ | 76 | 69 | [32] |
| 4 | Ph | Bn | 37 | 88 | [32] |

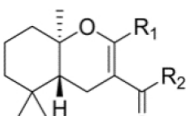**Table 5.** Decarboxylative reduction in 1-aryl-2,2,2-trifluoroethyl-substituted amino acids.
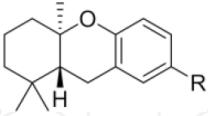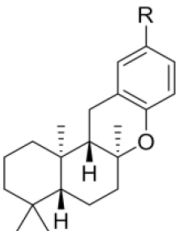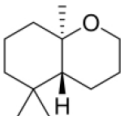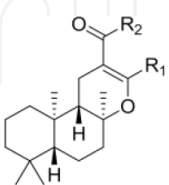
| Entry | Compounds | R | Yield (%) | d.r. (%) | Ref. |
|---|---|---|---|---|---|
| 1 | | Br | 93 | > 19:1 | [33] |
| 2 | | CO₂Me | 79 | > 19:1 | [33] |
| 3 | | F | 85 | > 19:1 | [33] |
| 4 |  | Cl | 85 | > 19:1 | [33] |
| 5 | | OCF₃ | 83 | > 19:1 | [33] |
| 6 | | I | 83 | > 19:1 | [33] |
| 7 | | OMe | 83 | | |
| 8 | | Br | 72 | > 19:1 | [33] |
| 9 |  | Cl | 40 | > 19:1 | [33] |
| 10 |  | – | 70 | > 19:1 | [33] |
| 11 |  | – | 65 | > 19:1 | [33] |
| 12 | | Ph | Ph | 88 | [33] |
| 13 | | Ph | OEt | 88 | [33] |
| 14 |  | Ph | Me | 87 | [33] |
| 15 | | Me | OEt | 91 | [33] |
| 16 |  | Ph | OEt | 60 | [33] |

**Table 6.** Cyclization of polyprenoids and 1,3-ketocabonyls catalyzed by Eosin Y.

Wallentin et al. [32] reported the photocatalyzed decarboxylative reduction in several classes of biologically relevant enantio-enriched 1-aryl-2,2,2-trifluoroethyl-substituted amino acids (see **Table 5**). A plausible redox-coupled hydrogen shuttle mechanism was proposed by using one of the strongest oxidizing organic dyes mesityl acridinium (Mes-Acr⁺BF₄⁻,

$E_{1/2}^{red}$ = +2.06 V *vs* SCE) as photoredox catalyst and bis(4-chlorophenyl)disulphide (DDDS) as a sacrificial hydrogen atom donor. This methodology was also applied to the synthesis of other achiral carboxylic acids, namely α-amino acids, α-hydroxy acids, and phenylacetic acids in moderate to quantitative yields.

A stereoselective radical cascade cyclization of polyprenoids through a photocatalytic mechanism has been reported yielding polyenes in moderate to very high yields with excellent diastereoselectivities (d.r. > 19:1) in HFIP and using Eosin Y as the photoredox catalyst (**Table 6**) [33]. The methodology was based on the cyclization by terminal OH groups of a large substrate array of aliphatic alcohols, phenols, or enols, which was tolerable to electron-rich or electron-poor substituents. In addition, the cyclization of 1,3-diketones required the use of LiBr as a weak Lewis acid. Stern-Volmer analysis reinforced that these reactions proceeded *via* a PET-induced radical mechanism.

The photoredox catalyst 2,4,6-*tris*(4-methoxyphenyl)pyrylium tetrafluoroborate (**D**) was used in the enantioselective ring opening metathesis polymerization (ROMP) of *endo*-DCPD to provide the corresponding linear polymer with conversion yields as high as 20% [34] (**Scheme 10**). The copolymerization of this monomer with norbornene was also accomplished. By using partially hydrogenated monomers, side reactions at the terminal positions were hindered which enabled higher degrees of polymerization to be obtained. By applying visible light, the polymerization can be turned on or off at will, bringing a dynamic nature to it by exposure to the stimulus.
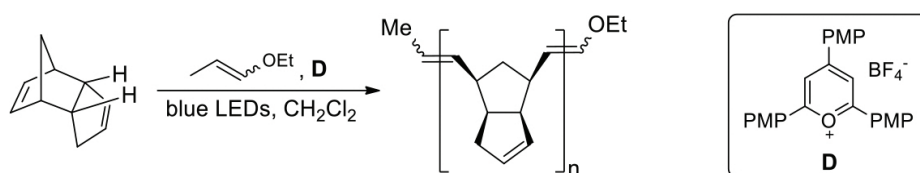


**Scheme 10.**

Over the last years, several publications involving non-asymmetric photoredox organocatalytic synthetic transformations mediated by metal-free organic photoredox catalysis under mild conditions have been reported [35].

From the industrial point of view, it is important to focus the recent developments on selective photocatalytic transformations of benzene, in particular the oxidation of benzene to phenol [36], alkoxylation of benzene [37], and monofluorination of benzene with fluoride and oxygen [38]. As an alternative to inorganic catalysts, the selective oxidation of benzene to phenol can be made under visible light irradiation of 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) in an oxygen-saturated acetonitrile solution of benzene and water [39]. In 2004, Fukuzumi *et al.* [40] reported the use of 9-mesityl-10-methylacridinium (Acr⁺-Mes) ion as an efficient photoredox catalyst due to its high oxidizing and reducing abilities of the long-lived electron transfer (ET) state. Acr⁺-Mes provides an efficient mediator to the formation of radical cations of

electron donors and radical anions of electron acceptors thus enabling coupling between electron donors and acceptors.
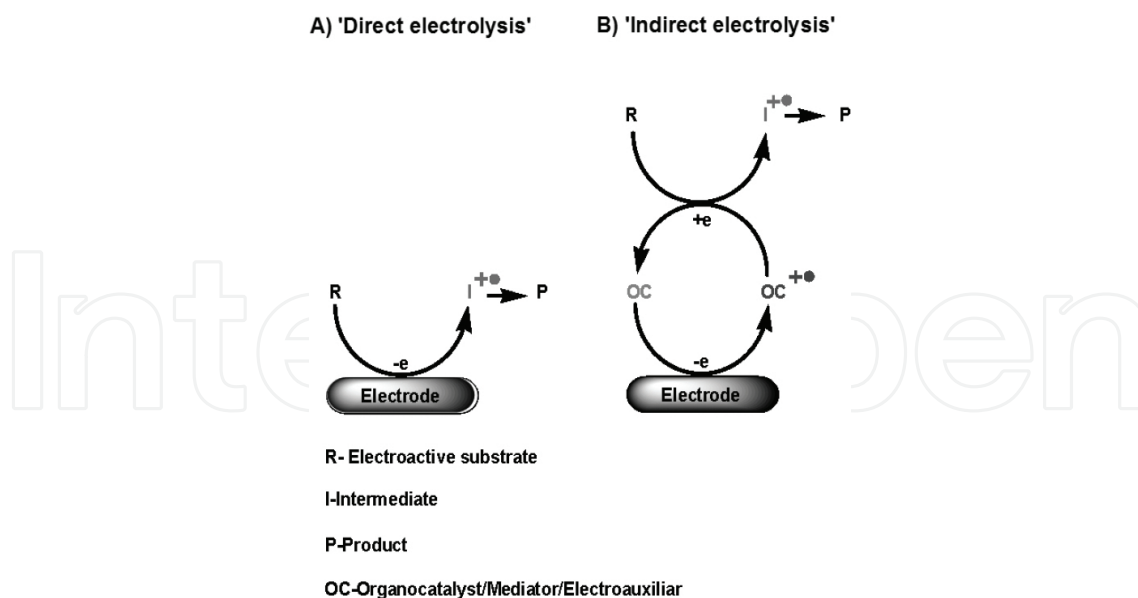
Photocatalytic [2+2] cycloaddition of dioxygen to tetraphenylethylene (TPE) *via* electron transfer reactions of TPE and oxygen with the ET state of Acr$^+$-Mes is one example of the strategies described before [41].

Eosin Y as a well-known low-cost organic dye that absorbs green light (characteristic peak at 539 nm) has been extensively investigated as photoredox catalyst for different organic transformations [42–49].

## 4. Recent approaches in electro-organocatalysis

As described in the previous sections, the electron transfer (ET) process is a crucial step in the organic chemistry field on which many organic reactions rely in order to occur [50, 51]. Essentially, an electron transfer process is based on the removal (or addition) of at least one electron from (or to) the electroactive substrate. This process is considered reversible only when the obtained products are stable under those experimental conditions. An electron transfer can generate intermediates which subsequently undergo chemical processes such as bond dissociation and bond formation. Basically, electroctrochemical techniques can be applied to establish the electrochemical oxidation and reduction mechanisms, that is the electron transfer reaction (formation and determination of the intermediates) and subsequent chemical reaction associated with the electrochemical generated process (formation of the reaction products). Thus, those formed intermediates are radical cations (or radical anions), and they can be generated by electrosynthetic processes using organic compounds. Carbon-free radicals (carbocations and carbanions) can also be generated by subsequent bond dissociation or bond formation process. Several electro-organic synthetic transformations, especially carbon-carbon, carbon-nitrogen, and carbon-phosphorous bond formation reactions, as well as oxidation and reduction processes have been reported [52]. Electrochemical processes are considered 'green' procedures for those synthetic transformations. The main advantage of the electrosynthetic approach is that electrons flow as current and are regard as one inexpensive reactant, thus making the route more environmentally friendly. Moreover, reactions take place in low-temperature conditions, reducing the local consumption of energy and the risk of corrosion, material failure, and accidental release. Finally, it is important to highlight that electrodes can be regarded as heterogeneous catalysts that are easily separated from the products. The low or even almost inexistent volatility of the reaction media is another factor to be taken into account. Therefore, electro-organocatalysis constitutes a valuable tool for the organic chemist with numerous applications in both academia [53, 54] and industry [55].

The electro-organocatalysis field can be divided into two main branches, depicted in **Scheme 11(A)** direct electrolysis, in which the redox process occurs between the electrode surface and the reactant without the addition of other compounds and (B) 'indirect electrolysis' where the redox process occurs between the electrode surface and an external redox catalyst (or 'mediator') which then performs the ET with the reactive species) [56].

A) 'Direct electrolysis'        B) 'Indirect electrolysis'

R- Electroactive substrate

I-Intermediate

P-Product

OC-Organocatalyst/Mediator/Electroauxiliar

**Scheme 11.**

## 4.1. Direct electro-organocatalysis'

In the direct electro-organocatalysis process, the electron transfer (ET) step occurs at the electrode surface. Due to its heterogeneous nature, the catalyst recycling can be performed easily by separating it from the reaction media after the formation of the desired organic product.

'Direct electro-organocatalysis' or electro-organic synthesis has recently gained increasing attention, which can be attributed to their sustainable and 'green' features when compared to the traditional ones.

In the literature, there are few reports concerning bond formation and bond dissociation reactions. Gallardo and co-workers reported the formation of C—C [52, 57, 58], C—N [58], C—P [59], and C—S [60] bonds by an electrochemical approach of nucleophilic aromatic substitution reactions ($S_N Ar$). The proposed new route for the electrochemical processes consists on the reaction between an electron-deficient, aromatic compound and a nucleophile, leading to the formation of a σ-complex or Meisenheimer complex intermediate. Then, this species undergoes an oxidation that leads to the departure of the leaving group (heteroatom radical [NASX] and/or hydride, two electrons and a proton [NASH]). This procedure was similarly conducted with other nucleophiles (hydride, cyanide, fluoride, methoxy, ethanethiolate, and n-butylamine) and aromatic compounds as starting materials. In addition, preparative electrolysis was also employed as means to promote the oxidation of the intermediate produced in the first step of the process [52, 58].

This technique allows determination, characterization, and quantification of the type and number of electrochemically produced complexes present in the reaction media. It is also

possible to assess if the reaction was successful once most classical $S_NAr$ reactions give lower yields.

The main drawbacks of the electrochemical approach are the use of solvent and the amount of tetraalkylammonium salt as electrolyte, which consequently have to be separated from the desired product. The use of ionic liquids (ILs) in particular room temperature ionic liquid (RTIL) as solvents may address this specific problem. They are considered non-flammable, non-volatile, and thermally stable over a wide range of temperatures, as well as good solvents for organic and inorganic compounds. In addition, they may be applied concomitantly as solvent and as electrolyte thereby enhancing the 'green' aspect of these procedures.

Gallardo and co-workers [61] adapted the electrochemical approach of nucleophilic aromatic substitution reactions to this 'greener' alternative family of solvents. The authors described the investigation of the electrocatalytic process as well as regioselectivity effects induced by the solvation properties of the RTILs (1-butyl-3-methylimidazolium [BMIM] combined with tetrafluoroborate [BF$_4$], hexafluorophosphate [PF$_6$], bis(trifluoromethylsulfonyl)imide [NTf$_2$], and acetate [AcO] as anions).

The use of electrochemical techniques such as cyclic voltammetry (CV) and controlled potential electrolysis allows the evaluation of the nature and stability of the electrochemically generated intermediate on the solvent, as well as the extension of the reaction.

Despite the successful reports on $S_NAr$ reactions, the 'direct electrolysis' approach requires the application of high potentials in order for the electrosynthetic process to occur. To address this issue, the redox process can be applied to organocatalysts which then lead to yield the desired products in the indirect electrocatalysis fashion.

## 4.2. Indirect electro-organocatalysis

In the indirect electro-organocatalysis process, the electron transfer (ET) step is shifted from a heterogeneous process occurring at the electrode surface (as described earlier as 'direct electrolysis') to homogeneous process that can provide an electrochemically generated substance which acts as a so-called organocatalyst (or 'mediator'). Usually triarylamines, triarylimidazoles and *N*-oxyl radicals [62] are employed as these electroauxiliary species. The group of R. D. Little has reported several environmentally friendly methodologies to obtain products *via* 'indirect electro-organocatalysis' in which no metal catalyst and external chemical oxidants were employed [63–65].

In order to explore and generalize this methodology, analogous organocatalysts with modified aromatic rings were also reported by the authors. The desired products were formed in good yields [63].

## 4.3. Asymmetric electro-organocatalysis

In this specific case of the 'indirect electro-organocatalysis', particular conditions of solvent and catalyst are employed in order to enhance the enantioselectivity of the formed products. It is considered as safer and 'green route' towards enantioselective reactions by combining

asymmetric organocatalysis with electrochemistry. The selected organocatalysts are stable, stereoselective organic compounds that can undergo the electrosynthetic process under unsuitable conditions for conventional catalysts. Asymmetric electro-organocatalysis methodologies have been successfully employed to produce several optically active compounds with application in life sciences. **Scheme 12** depicts the direct intermolecular α-arylation of aldehydes to produce meta-alkylated anilines using electron-rich aromatic compounds [66].
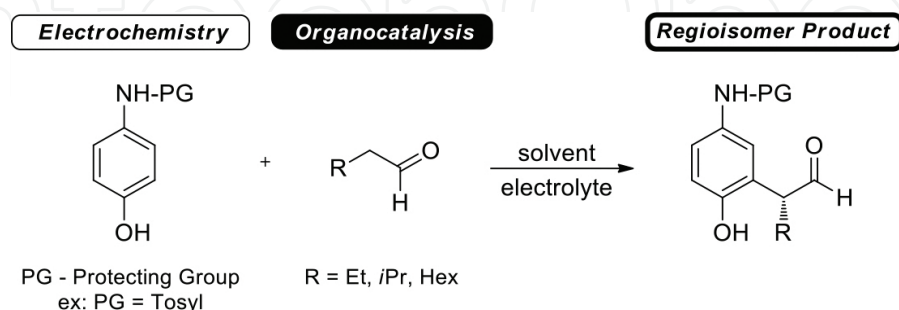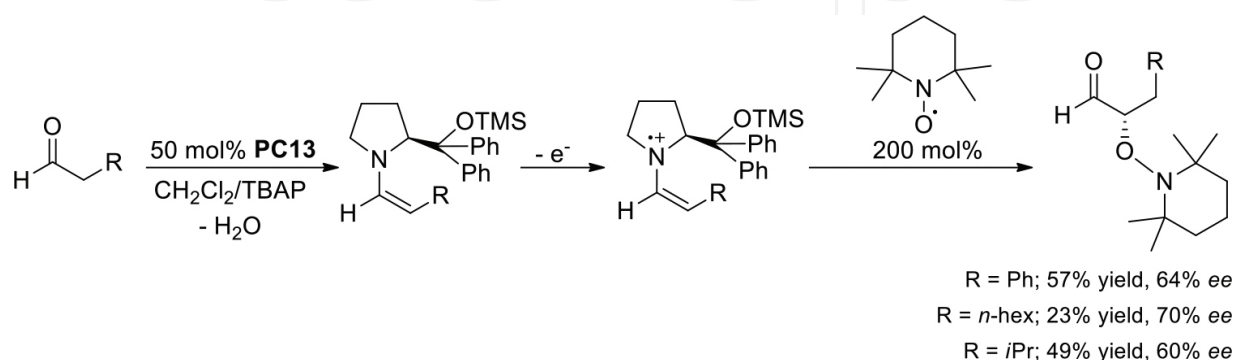


**Scheme 12.**
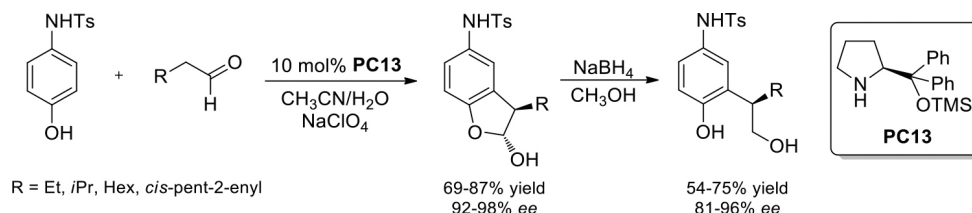


**Scheme 13.**

The described methodology for the regio- and stereoselective electroorganocatalyzed production of the *meta*-substituted anilines takes place in two steps: (1) firstly occurs the electrochemical activation of the aromatic compound that evolves to an electrophilic intermediate and (2) then an electron-rich enamine is generated by the condensation of the organocatalyst and the desired aldehyde, which subsequently undergoes a nucleophilic addition to the intermediate formed in step 1, giving rise to another intermediate that upon hydrolysis and proton transfer regenerates the organocatalyst and yields the corresponding product. The described reactions occur between the tosyl-protected reactant with a series of aldehydes catalyzed by [(S)-2-[diphenyl(trimethylsilyloxy)methyl]pyrrolidine] (**PC13**), which has also been reported for the photocatalyzed α-alkylation of aldehydes [7]. In these conditions, the *meta*-substituted aniline enantiomeric products were obtained in 54–75% yields and high enantiomeric excess between 81 and 96% (**Scheme 13**) [66].
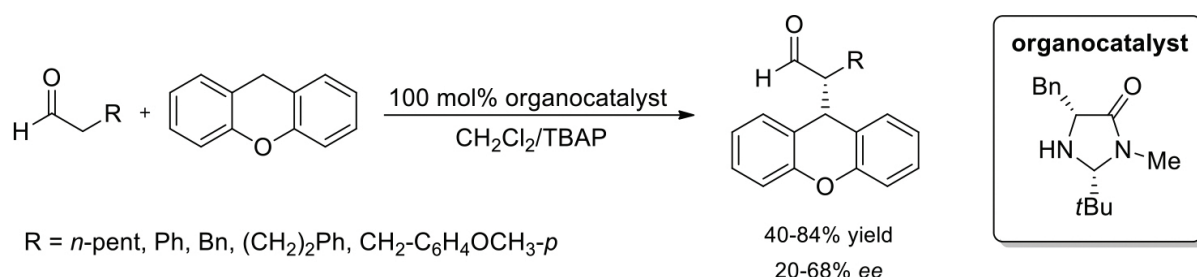
In 2005, Schäfer and co-workers [67] reported the reaction of enamines and mediated anodic oxidation of carbohydrates in the presence of 2,2,6,6-tetramethylpiperidine-1-oxoammonium cation ([TEMPO]) as organocatalyst. These species reacted with selected enaminoesters to form intermediate imidazolium cations, which selectively oxidize the primary hydroxy groups of

trisaccharides at the anode to give tricarboxylic acid sugars in 50–80% yields. The relative stability of the electrogenerated TEMPO cation in acetonitrile enables it to react as a selective oxidant, electrophile, and also catalyst.

Enantioselective α-oxyamination of aldehydes has been reported by the group of H.-J. Jang using a *sec*-amine as chiral catalyst (**Scheme 14**) [68]. An enamine intermediate is formed by anodic oxidation of the aldehydes that ultimately reacts with TEMPO leading to the formation of the desired products in reasonable yields. Once again using **PC13** as organocatalyst, α-oxyaldehydes were obtained in 23–57% yields and 60–70% *ee*.



R = Ph; 57% yield, 64% *ee*
R = *n*-hex; 23% yield, 70% *ee*
R = *i*Pr; 49% yield, 60% *ee*

**Scheme 14.**



R = *n*-pent, Ph, Bn, (CH₂)₂Ph, CH₂-C₆H₄OCH₃-*p*

40-84% yield
20-68% *ee*

**Scheme 15.**

An asymmetric electro-organocatalysis method for enantioselective α-alkylation of aldehydes with xanthene has also been devised by the group of Jang et al. [69]. **Scheme 15** depicts the best results using a chiral imidazole as organocatalyst, which was chosen from a plethora of differently substituted imidazole-based compounds [69]. According to electrochemical studies and control experiments, the reaction is probable to occur through the formation of an enamine intermediate. DFT calculations suggested that xanthene adds to the opposite side of the phenyl ring of the radical intermediate blue to stereochemical hindrance issues, thus enhancing the stereoselectivity of the reaction.

In 2014, Xu and co-workers [70] published an electrochemical intramolecular aminooxygenation reaction of unactivated alkenes based on the addition of N-centered radicals to alkenes (generated from electrochemical oxidation) followed by trapping of the cyclized radical

intermediate with TEMPO. This process allowed the preparation of different aminooxygenation products in high yields and excellent trans-selectivity for cyclic systems (d.r. up to > 20:1).

Very recent, Xu and collaborators [71] reported the first electrocatalytic method using ferrocene as a cheap redox catalyst to produce amidyl radicals from N-arylamides. The conventional methods for oxidative generation of amidyl radicals from N—H amides need to use a stoichiometric quantity of expensive noble-metal catalysts or strong oxidants. In this case, the authors showed an efficient radical-generating process based on intramolecular olefin hydroamidation reaction.

## Acknowledgements

## Author details

Karolina Zalewska, Miguel M. Santos, Hugo Cruz and Luis C. Branco[*]

*Address all correspondence to: l.branco@fct.unl.pt

Department of Chemistry, Faculty of Science and Technology, LAQV-REQUIMTE, New University of Lisbon, Caparica, Portugal

## References

[1]  Belle M, Bolm C, editors. Transition Metals for Organic Synthesis. 2nd ed. Weinheim: Wiley-VCH; 2004. doi: 10.1002/9783527619405

[2]  Wessig P. Organocatalytic enantioselective photoreaction. Angew. Chem. Int. Ed. 2006; 45:2168–2171. doi: 10.1002/anie.200503908

[3]  Ravelli D, Fagnoni M, Albini A. Photoorganocatalysis. What for?. Chem. Soc. Rev. 2013; 42:97–113. doi: 10.1039/C2CS35250H

[4]  Wang C, Lu Z. Catalytic enantioselective organic transformations via visible light photocatalysis. Org. Chem. Front. 2015; 2:179–190. doi: 10.1039/C4QO00306C

[5]  Fagnoni M, Dondi D, Ravelli D, Albini A. Photocatalysis for the formation of the C—C bond. Chem. Rev. 2007; 107:2725–2756. doi: 10.1021/cr068352x

[6]   Turro NJ, Ramamurthy V, Scaiano JC. Modern Molecular Photochemistry of Organic Molecules. USA: University Science Books; 2010.

[7]   Arceo E, Jurberg ID, Alvarez-Fernandez A, Melchiorre P. Photochemical activity of a key donor-acceptor complex can drive stereoselective catalytic-alkylation of aldehydes. Nat. Chem. 2013; 5:750–756. doi: 10.1038/nchem.1727

[8]   Nicewicz DA, MacMillan DWC. Merging photoredox catalysis with organocatalysis: the direct asymmetric alkylation of aldehydes. Science. 2008; 322:77–80. doi: 10.1126/science.1161976

[9]   Wiegand C, Herdtweck E, Bach T. Enantioselectivity in visible light-induced, singlet oxygen [2+4] cycloaddition reactions (type II photooxygenations) of 2-pyridones. Chem. Commun. 2012; 48:10195–10197. doi: 10.1039/C2CC35621J

[10]  Bauer A, Westkämper F, Grimme S, Bach T. Catalytic enantioselective reactions driven by photoinduced electron transfer. Nature. 2005; 436:1139–1140. doi: 10.1038/nature03955

[11]  Jeon YT, Lee CP, Mariano PS. Radical cyclization reactions of silyl amine $\alpha,\beta$-unsaturated ketone and ester systems promoted by single electron transfer photosensitization. J. Am. Chem. Soc. 1991; 113:8847–8863. doi: 10.1021/ja00023a038

[12]  Müller C, Bauer A, Bach T. Light-driven enantioselective organocatalysis. Angew. Chem. Int. Ed. 2009; 48:6640–6642. doi: 10.1002/anie.200901603

[13]  Müller C, Bauer A, Maturi MM, Cuquerella MC, Miranda MA, Bach T. Enantioselective intramolecular [2+2]-photocycloaddition reactions of 4-substituted quinolones catalyzed by a chiral sensitizer with a hydrogen-bonding motif. J. Am. Chem. Soc. 2011; 133:16689–16697. doi: 10.1021/ja207480q

[14]  Breitenlechner S, Bach T. A polymer-bound chiral template for enantioselective photochemical reactions. Angew. Chem. Int. Ed. 2008; 47:7957–7959. doi: 10.1002/anie.200802479

[15]  Guo H, Herdtweck E, Bach T. Enantioselective lewis acid catalysis in intramolecular [2+2] photocycloaddition reactions of coumarins. Angew. Chem. Int. Ed. 2010; 49:7782–7785. doi: 10.1002/anie.201003619

[16]  Vallavoju N, Selvakumar S, Jockusch S, Sibi MP, Sivaguru J. Enantioselective organo-photocatalysis mediated by atropisomeric thiourea derivatives. Angew. Chem. Int. Ed. 2014; 53:5604–5608. doi: 10.1002/anie.201310940

[17]  Jensen KL, Dickmeiss G, Jiang H, Albrecht Ł, Jørgensen KA. The diarylprolinol silyl ether system: a general organocatalyst. Acc. Chem. Res. 2012; 45:248–264. doi: 10.1021/ar200149w

[18] Arceo E, Bahamonde A, Bergonzinib G, Melchiorre P. Enantioselective direct $\alpha$-alkylation of cyclic ketones by means of photo-organocatalysis. Chem. Sci. 2014; 5:2438–2442. doi: 10.1039/C4SC00315B

[19] Silvi M, Arceo E, Jurberg ID, Cassani C, Melchiorre P. Enantioselective organocatalytic alkylation of aldehydes and enals driven by the direct photoexcitation of enamines. J. Am. Chem. Soc. 2015; 137:6120–6123. doi: 10.1021/jacs.5b01662

[20] Barata-Vallejo S, Flesia MM, Lantaño B, Argüello JE, Peñéñory AB, Postigo A. Heterogeneous photoinduced homolytic aromatic substitution of electron-rich arenes with perfluoroalkyl groups in water and aqueous media – a radical ion reaction. Eur. J. Org. Chem. 2013; 5:998–1008. doi: 10.1002/ejoc.201201271

[21] Woźniak Ł, Murphy JJ, Melchiorre P. Photo-organocatalytic enantioselective perfluoroalkylation of β-ketoesters. J. Am. Chem. Soc. 2015; 137:5678–5681. doi: 10.1021/jacs.5b03243

[22] Lian M, Li Z, Cai Y, Meng Q, Gao Z. Enantioselective photooxygenation of β-keto esters by chiral phase-transfer catalysis using molecular oxygen. Chem. Asian J. 2012; 7:2019–2023. doi: 10.1002/asia.201200358

[23] Schuster DI. The photochemistry of enones. In: Patai S, Rappoport Z, editors. The Chemistry of Enones. New York: Wiley. 1989. p. 623–756

[24] Chanon M, Eberson L, Conceptual basis. In: Fox MA, Chanon M, editors. Photoinduced Electron Transfer. New York: Elsevier. 1988.

[25] Arceo E, Montroni E, Melchiorre P. Photo-organocatalysis of atom-transfer radical additions to alkenes. Angew. Chem. Int. Ed. 2014; 53:12064–12068. doi: 10.1002/anie.201406450

[26] Ravelli D, Fagnoni M. Aromatic aldehydes as energy-transfer photoorganocatalysts. Chem. Cat. Chem. 2015; 7:735–737. doi: 10.1002/cctc.201403024

[27] Kandukuri SR, Bahamonde A, Chatterjee I, Jurberg ID, Escudero EC, Melchiorre P. X-ray characterization of an electron donor-acceptor complex that drives the photochemical alkylation of indoles. Angew. Chem. Int. Ed. 2015; 54:1485–1489. doi: 10.1002/anie.201409529

[28] Neumann M, Füldner S, König B, Zeitler K. Metal-free, cooperative asymmetric organophotoredox catalysis with visible light. Angew. Chem. Int. Ed. 2011; 50:951–954. doi: 10.1002/anie.201002992

[29] Neumann M, Zeitler K. Application of microflow conditions to visible light photoredox catalysis. Org. Lett. 2012; 14:2658–2661. doi: 10.1021/ol3005529

[30] Fidaly K, Ceballos C, Falguières A, Veitia MSI, Guy A, Ferroud C. Visible light photoredox organocatalysis: a fully transition metal-free direct asymmetric $\alpha$-alkylation of aldehydes. Green Chem. 2012; 14:1293–1297. doi: 10.1039/C2GC35118H

[31] Cecere G, König CM, Alleva JL, MacMillan DWC. Enantioselective direct $\alpha$-amination of aldehydes via a photoredox mechanism: a strategy for asymmetric amine fragment coupling. J. Am. Chem. Soc. 2013; 135:11521–11524. doi: 10.1021/ja406181e

[32] Cassani C, Bergonzini G, Wallentin CJ. Photocatalytic decarboxylative reduction of carboxylic acids and its application in asymmetric synthesis. Org. Lett. 2014; 16:4228–4231. doi: 10.1021/ol5019294

[33] Yang Z, Li H, Zhang L, Zhang MT, Cheng JP, Luo S. Organic photocatalytic cyclization of polyenes: a visible-light-mediated radical cascade approach. Chem. Eur. J. 2015; 21:14723–14727. doi: 10.1002/chem.201503118

[34] Goetz AE, Boydston AJ. Metal-free preparation of linear and cross-linked polydicyclopentadiene. J. Am. Chem. Soc. 2015; 137:7572–7575. doi: 10.1021/jacs.5b03665

[35] Fukuzumi S, Ohkubo K. Organic synthetic transformations using organic dyes as photoredox catalysts. Org. Biomol. Chem. 2014; 12:6059–6069. doi: 10.1039/C4OB00843J

[36] Weber M, Weber M, Kleine-Boymann M. Phenol. Ullmann's Encyclopedia of Industrial Chemistry, Weinheim: Wiley-VCH, 2004. doi: 10.1002/14356007.a19_299.pub2

[37] Ohkubo K, Kobayashi T, Fukuzumi S. Photocatalytic alkoxylation of benzene with 3-cyano-1-methylquinolinium ion. Opt. Express. 2012; 20:A360–A365. doi: 10.1364/OE. 20.00A360

[38] Furuya T, Adam S, Kamlet AS, Ritter T. Catalysis for fluorination and trifluoromethylation. Nature. 2011; 473:470–477. doi: 10.1038/nature10108

[39] Ohkubo K, Fujimoto A, Fukuzumi S. Visible-light-induced oxygenation of benzene by the triplet excited state of 2,3-dichloro-5,6-dicyano-p-benzoquinone. J. Am. Chem. Soc. 2013; 135:5368–5371. doi: 10.1021/ja402303k

[40] Fukuzumi S, Kotani H, Ohkubo K, Ogo S, Tkachenko NV, Lemmetyinen H. Electron-transfer state of 9-mesityl-10-methylacridinium ion with a much longer lifetime and higher energy than that of the natural photosynthetic reaction center. J. Am. Chem. Soc. 2004; 126:1600–1601. doi: 10.1021/ja038656q

[41] Ohkubo K, Nanjo T, Fukuzumi S. Efficient photocatalytic oxygenation of aromatic alkene to 1,2-dioxetane with oxygen via electron transfer. Org. Lett. 2005; 7:4265–4268. doi: 10.1021/ol051696+

[42] Hari DP, Konig B. Synthetic applications of eosin Y in photoredox catalysis. Chem. Commun. 2014; 50:6688–6699. doi: 10.1039/C4CC00751D

[43]  Hedstrand DM, Kruizinga WH, Kellogg RM. Light induced and dye accelerated reductions of phenacyl onium salts by 1,4-dihydropyridines. Tetrahedron Lett. 1978; 19:1255–1258. doi: 10.1016/S0040-4039(01)94515-0

[44]  Cantillo D, de Frutos O, Rincon JA, Mateos C, Kappe CO. Continuous flow $\alpha$-trifluoromethylation of ketones by metal-free visible light photoredox catalysis. Org. Lett. 2014; 16:896–899. doi: 10.1021/ol403650y

[45]  Yang XJ, Chen B, Zheng LQ, Wu LZ, Tung CH. Highly efficient and selective photocatalytic hydrogenation of functionalized nitrobenzenes. Green Chem. 2014; 16:1082–1086. doi: 10.1039/C3GC42042F

[46]  Yang DT, Meng QY, Zhong JJ, Xiang M, Liu Q, Wu LZ. Metal-free desulfonylation reaction through visible-light photoredox catalysis. Eur. J. Org. Chem. 2013; 33:7528–7532. doi: 10.1002/ejoc.201301105

[47]  Hari DP, Konig B. Eosin Y catalyzed visible light oxidative C—C and C—P bond formation. Org. Lett. 2011; 13:3852–3855. doi: 10.1021/ol201376v

[48]  Liu Q, Li YN, Zhang HH, Chen B, Tung CH, Wu LZ. Reactivity and mechanistic insight into visible-light-induced aerobic cross-dehydrogenative coupling reaction by organophotocatalysts. Chem. Eur. J. 2012; 18:620–627. doi: 10.1002/chem.201102299

[49]  Hari DP, Schroll P, König B. Metal-free, visible-light-mediated direct C—H arylation of heteroarenes with aryl diazonium salts. J. Am. Chem. Soc. 2012; 134:2958–2961. doi: 10.1021/ja212099r

[50]  Savéant JM. Molecular catalysis of electrochemical reactions. Mechanistic aspects. Chem. Rev. 2008; 108:2348–2378. doi: 10.1021/cr068079z

[51]  Yoshida J, Kataoka K, Horcajada R, Nagaki A. Modern strategies in electroorganic synthesis. Chem. Rev. 2008; 108:2265–2299. doi: 10.1021/cr0680843

[52]  Gallardo I, Guirado G. Thermodynamic study of $\sigma^H$-complexes in nucleophilic aromatic substitution reactions: relative stabilities of electrochemically generated radicals. Eur. J. Org. Chem. 2008; 14:2463–2472. doi: 10.1002/ejoc.200701098

[53]  Moeller KD. Synthetic applications of anodic electrochemistry. Tetrahedron. 2000; 56:9527–9554. doi: 10.1016/S0040-4020(00)00840-1

[54]  Sperry JB, Wright DL. The application of cathodic reductions and anodic oxidations in the synthesis of complex molecules. Chem. Soc. Rev. 2006; 35:605–621. doi: 10.1039/B512308A

[55]  Heinze J. Cathodic reactions of Hydrocarbons in Organic Electrochemistry. Ed. H. Lund, O. Hammerich. Marcel Dekker: New York. 2001.

[56] Francke R, Little RD. Redox catalysis in organic electrosynthesis: basic principles and recent developments. Chem. Soc. Rev. 2014; 43:2492–2521. doi: 10.1039/C3CS60464K

[57] Gallardo I. Nucleophilic aromatic substitution of hydrogen: a novel electrochemical approach to the cyanation of nitroarenes. Chem. Eur. J. 2001; 7:1759–1765 doi: 10.1002/1521-3765(20010417)7:8<1759::AID-CHEM17590>3.0.CO;2-F

[58] Cruz H, Gallardo I, Guirado G. Electrochemical synthesis of organophosphorus compounds through nucleophilic aromatic substitution: mechanistic investigations and synthetic scope. Eur. J. Org. Chem. 2011; 36:7378–7389. doi: 10.1002/ejoc.201101357

[59] Gallardo I, Guirado G, Marquet J. Nucleophilic aromatic substitution for heteroatoms: an oxidative electrochemical approach. J. Org. Chem. 2002; 67:2548–2555. doi: 10.1021/jo010847t

[60] Alfonso-Súarez P, Kolliopoulos VA, Smith JP, Banks CE, Jones AM. An experimentalist's guide to electrosynthesis: the Shono oxidation. Tetrahedron Lett. 2015; 56:6863–6867. doi: 10.1016/j.tetlet.2015.10.090

[61] Cruz H, Gallardo I, Guirado G. Electrochemically promoted nucleophilic aromatic substitution in room temperature ionic liquids—an environmentally benign way to functionalize nitroaromatic compounds. Green Chem. 2011; 13:2531–2542. doi: 10.1039/C1GC15303J

[62] Ogawa KA, Boydston AJ. Recent developments in organocatalyzed electroorganic chemistry. Chem. Lett. 2015; 44:10–16. doi: 10.1246/cl.140915

[63] Zeng CC, Zhang NT, Lam CM, Little RD. Novel triarylimidazole redox catalysts: synthesis, electrochemical properties, and applicability to electrooxidative C—H activation. Org. Lett. 2012; 14:1314–1317. doi: 10.1021/ol300195c

[64] Gao WJ, Li WC, Zeng CC, Tian HY, Hu LM, Little RD. Electrochemically initiated oxidative amination of benzoxazoles using tetraalkylammonium halides as redox catalysts. J. Org. Chem. 2014; 79:9613–9618. doi: 10.1021/jo501736w

[65] Chen J, Yan WQ, Lam CM, Zeng CC, Hu LM, Little RD. Electrocatalytic aziridination of alkenes mediated by n-Bu$_4$NI: a radical pathway. Org. Lett. 2015; 17:986–989. doi: 10.1021/acs.orglett.5b00083

[66] Jensen KL, Franke PT, Nielsen LT, Daasbjerg K, Jørgensen KA. Anodic oxidation and organocatalysis: direct regio- and stereoselective access to meta-substituted anilines by $\alpha$-arylation of aldehydes. Angew. Chem. Int. Ed. 2010; 49:129–133. doi: 10.1002/anie.200904754

[67] Schämann M, Schäfer HJ. Reaction of enamines and mediated anodic oxidation of carbohydrates with the 2,2,6,6-tetramethylpiperidine-1-oxoammonium ion (TEMPO$^+$). Electrochim. Acta. 2005; 50:4956–4972. doi: 10.1016/j.electacta.2005.02.077

[68] Bui NN, Ho XH, Mho S, Jang HY. Organocatalyzed $\alpha$-oxyamination of aldehydes using anodic oxidation. Eur. J. Org. Chem. 2009; 31:5309–5312. doi: 10.1002/ejoc.200900871

[69] Ho XH, Mho S, Kang H, Jang HY. Electro-organocatalysis: enantioselective $\alpha$-alkylation of aldehydes. Eur. J. Org. Chem. 2010; 23:4436–4441. doi: 10.1002/ejoc.201000453

[70] Xu F, Zhu L, Zhu S, Yan X, Xu HC. Electrochemical intramolecular aminooxygenation of unactivated alkenes. Chem. Eur. J. 2014; 20:12740–12744. doi: 10.1002/chem.201404078

[71] Zhu L, Xiong P, Mao ZY, Wang YH, Yan X, Lu X, Xu HC. Electrocatalytic generation of amidyl radicals for olefin hydroamidation: use of solvent effects to enable anilide oxidation. Angew. Chem. Int. Ed. 2016; 55:2226–2229. doi: 10.1002/anie.201510418