Synthetic applications of eosin Y in photoredox catalysis

Durga Prasad Hari and Burkhard König*

Eosin Y, a long known dye molecule, has recently been widely applied as a photoredox catalyst in organic synthesis. Low cost and good availability make eosin Y an attractive alternative to typical inorganic transition metal photocatalysts. We summarize the key photophysical properties of the dye and the recent synthetic applications in photoredox catalysis.

1. Introduction

Visible light photoredox processes have recently found many applications in organic synthesis, but the general interest in the field started much earlier. Unlike thermal reactions, photoredox processes occur under mild conditions and do not require radical initiators or stoichiometric chemical oxidants or reductants. Typical irradiation sources are LEDs or household lamps, which are cheaper and easier to apply than specialized UV reactors used in classical photochemistry. Ruthenium and iridium polypyridyl complexes are commonly employed visible light photocatalysts and their chemistry and application in organic synthesis has recently been summarized.

Despite the excellent photophysical properties of ruthenium and iridium polypyridyl complexes in visible light photocatalysis, the compounds are expensive and potentially toxic, causing disadvantages on a larger scale. Organic dyes have been used as an attractive alternative to transition metal complexes in photoredox catalysis. They are typically less expensive and less toxic, easy to handle and even outperform organometallic and inorganic catalysts in some cases. Particularly eosin Y was widely used as an organo-photocatalyst in synthetic transformations. The classic dye has been known for a long time and finds application in cell staining, as a pH indicator, as an indicator in the analytical halide determination by Fajans and as a dye pigment. In this article, we discuss recent applications of eosin Y as a visible light photocatalyst in organic synthesis.

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2. Photochemistry of eosin Y

The photochemistry of eosin Y is well investigated: upon excitation by visible light, eosin Y undergoes rapid intersystem crossing to the lowest energy triplet state, which has a lifetime of 24 μs. Eosin Y absorbs green light; the UV-Vis spectrum shows a characteristic peak at 539 nm with a molar extinction coefficient ε = 60 803 M⁻¹ cm⁻¹. Upon excitation eosin Y becomes more reducing and more oxidizing compared to in its ground state. The redox potentials of the excited state can be estimated from the standard redox potentials of the ground state, determined by cyclic voltammetry, and the triplet excited state energy. The measured ground state and the estimated excited state oxidation and reduction potentials are given in Scheme 1. In addition, the photoexcited state of eosin Y may also undergo energy transfer.

3. Reduction reactions

The first reaction demonstrating the use of eosin Y photocatalysis in organic synthesis was the photoreduction of sulfonium salts.

3.1. Reduction of phenacyl sulfonium salts

In 1978, Kellogg and coworkers reported the visible light induced reduction of phenacyl sulfonium salts by 1,4 dihydropyridines (Scheme 2). Irradiation of a mixture of 1 and 2 in CD₃CN or CD₃COCD₃ without any photosensitizer provided the reduced product 3 in quantitative yield after 48 h using normal room light (neon fluorescent lamp at ca. 2 m distance) at 25 °C. Addition of 1 mol% of Na₂-eosin Y accelerated the reaction resulting in complete conversion within 1 h of irradiation. The authors speculated that light induced single electron transfer (SET) steps are responsible for the formation of the reduced product and suggested an acceleration effect upon addition of the photocatalyst. However, the exact role of the photocatalyst in the reaction mechanism remains undisclosed.

3.2. Reduction of nitrobenzene

Tung and coworkers utilized eosin Y as a photocatalyst and triethanolamine (TEOA) as a sacrificial reducing agent for the efficient photocatalytic reduction of nitrobenzene under green light irradiation (Scheme 3). The reaction is chemoselective and tolerates the presence of other functional groups, such as carbonyls, halogen atoms, and nitriles. The nitro group is a better electron acceptor. Important factors to achieve the optimal reaction yield are the pH value of the reaction mixture in the deoxygenated ethanol-water (3:2, v/v) mixture and the amount of added TEOA. Nitro groups of substrates bearing either electron donating or electron withdrawing substituents are smoothly reduced.

Based on quenching experiments and a flash photolysis study, the authors proposed a tentative mechanism for the photocatalytic reduction of nitrobenzene as shown in Scheme 4. A SET from eosin Y* to nitrobenzene generates 6 and the radical cation of eosin Y, which is reduced by TEOA to close the catalytic cycle and produce the radical cation of TEOA. The reaction of the radical anion 6 with the TEOA cation radical in the presence of water gives glycolaldehyde, diethanolamine and the further reduced intermediates, which are again reduced in a similar fashion to finally yield aniline.
3.3. Desulfonylation

The use of sulfones as auxiliary groups is an efficient synthetic strategy to generate a wide range of important products. Commonly the sulfone group is removed using metal containing reducing agents, such as Bu₃SnH, Al(Hg), or Sm/HgCl₂. Recently environmentally friendly desulfonylation reactions were reported by Wu and coworkers using eosin Y bis-tetrabutylammonium salt (TBA-eosin Y) as a photocatalyst and diisopropylethylamine (iPr₂EtN) as a reducing agent (Scheme 5).39

Irradiation of a mixture of 7, TBA-eosin Y and diisopropylethylamine under an inert atmosphere using a 3 W blue LED in CH₃CN furnishes the desired product 8 in good yields. Sulfonylated aliphatic ketones give no reaction yield due to their very negative reduction potential of \(-1.94 \text{ V vs. SCE}\) not accessible by the excited state of TBA-eosin Y.

The mechanism for the desulfonylation reaction is proposed in Scheme 6. Irradiation of TBA-eosin Y generates its excited state, which is oxidatively quenched by \(\beta\)-arylketosulfones resulting in the formation of the cation radical of TBA-eosin Y and the radical anion of 9. A SET from diisopropylethylamine to the radical cation of TBA-eosin Y regenerates the photocatalyst and closes the cycle. Finally, the radical anion 10 undergoes desulfonylation to produce a ketone radical which abstracts a hydrogen atom from the radical cation of diisopropylethylamine affording the desired ketone 11. The radical cation of the TBA-eosin Y was identified in the presence of \(\beta\)-arylketosulfones by laser-flash photolysis. The observed absorption at 460 nm corresponds to the reported value for the eosin Y radical cation.

4. Oxidation reactions

Eosin Y has been used to mediate photooxidation reactions in the presence of stoichiometric amounts of electron acceptors. The reported reactions include the oxidation of amines, thioamides, and enol ethers.

4.1. Oxidative iminium ion formation

The construction of C–C and C–P bonds by C–H activation is an emerging research area in organic synthesis.40–48 Our group reported an efficient visible light mediated method for the formation of C–C and C–P bonds using eosin Y as a photo redox catalyst under visible light (Scheme 7).49 Nitroalkanes, dialkyl phosphonates, dialkyl malonates, and malononitrile were used as nucleophiles to trap the iminium ion leading to the formation of a new bond at the \(\alpha\)-position of tetrahydroisoquinolines. The reaction does not require the addition of stoichiometric oxidants and uses molecular oxygen from air as the terminal oxidant.

The proposed mechanism for the reaction is depicted in Scheme 8. A single electron transfer from tetrahydroisoquinoline 12 to the excited state of eosin Y furnishes the aminyl radical cation 14 and the radical anion of eosin Y, which then transfers an electron to oxygen present in the reaction. The superoxide radical anion may abstract a hydrogen atom from 14 to generate the iminium ion 15, which is finally trapped by a nucleophile resulting in the desired product 13. H₂O₂ has been obtained as the by-product.17
Later, Wu and coworkers reported the photocatalytic oxidative Mannich reaction under aerobic conditions using molecular oxygen (Scheme 9).\(^{50}\) Irradiation of TBA-eosin Y, 1-proline, tetrahydroisoquinoline 16, and acetone produces the synthetically important product 17 in moderate yields. The catalyst system consists only of organic compounds, which can be an advantage.

Wu and coworkers combined eosin Y as a photosensitizer with graphene-supported RuO\(_2\) nanocomposites as a catalyst for C–C bond formation without external oxidants. Hydrogen is generated in good to excellent yield as the only byproduct (Scheme 10).\(^ {51}\) Eosin Y initiates the coupling reaction of the tetrahydroisoquinoline line with the nucleophile via visible light photoredox catalysis and at the same time RuO\(_2\) is used to capture the excess electron and proton from the C–H bonds of the substrates. Irradiation of eosin Y, graphene–RuO\(_2\), tetrahydroisoquinoline 12, and indole 18 at room temperature affords the desired cross coupling product 19 in good yield. The products containing halogen atoms may serve as important intermediates for further synthetic transformations. The cross coupling reaction occurs exclusively at the 3-position of indole 18 irrespective of the substitution on the indole moiety.

In the reactions described so far, the iminium ion and the nucleophile react intermolecularly. Recently, Xiao and coworkers reported the synthesis of isoquinol[2,1-\(a\)]pyrimidine 21 via intramolecular trapping of the iminium ion with a pendant N-tosyl moiety using Na\(_2\)-eosin Y as a photoredox catalyst (Scheme 11).\(^ {52}\) Irradiation of Na\(_2\)-eosin Y, tBuOK, and 4-methyl-N-(2-(7-methyl-3,4-dihydroisoquinolin-2(1H)-yl)benzyl)-benzene sulfonamide 20 in MeOH–dichloromethane affords 3-methyl-5-tosyl-4,5,12,13-tetrahydro-6H-isoquinolino[2,1-\(a\)]quinazoline 21 in 85% yield after 25 h.

### 4.2. Bromination

Selective bromination of C–H bonds under ambient conditions is an important synthetic method in organic synthesis. Recently, Tan and coworkers reported a selective method for the bromination of aliphatic and benzylic C–H bonds via visible light photoredox catalysis using eosin Y (Scheme 12).\(^ {53}\) The reaction was performed under mild conditions using CBr\(_4\) as the bromine source and morpholine as the reducing agent. The amount of water is essential for the reaction: a higher ratio of water to dichloromethane is important for the formation of the brominated product 23. The authors conducted experimental and computational studies on the mechanism and suggest that an N-morpholino radical is responsible for the C–H activation step during the reaction. The reaction tolerates ester, ether, and ketone functional groups. Synthetic applications of the method are the selective bromination of (+)-sclareolide and of acetate protected estrone.

### 4.3. Hydroxylation

Xiao and coworkers reported a highly efficient method for the hydroxylation of arylboronic acids to aryl alcohols using visible light photoredox catalysis under aerobic oxidative conditions (Scheme 13).\(^ {54}\) Typical reaction conditions used transition metal photocatalysts, but in a single example Na\(_2\)-eosin Y was successfully adopted. Irradiation of a mixture of 2 mol% Na\(_2\)-eosin Y, arylboronic acid 24 (0.5 mmol), iPr\(_2\)NEt (2.0 equiv.) in DMF provided the hydroxylated product 25 in 90% yield after 96 h.
The superoxide radical anion, which is generated in the photo-redox cycle, reacts with arylboronic acid 24. Its Lewis acidity arises from the vacant boron p-orbital. A subsequent series of rearrangements and hydrolysis affords the desired aryl alcohol 25.

4.4. Cyclization of thioamides

1,2,4-Thiadiazoles have found applications in biology and pharmaceutical sciences. An example is the clinically used antibiotic cefozopram, which contains a 1,2,4-thiadiazole moiety. Elegant methods have been reported for synthesis of the privileged structure, but most of them require oxidizing agents. Yadav and coworkers recently reported a metal free synthesis of 1,2,4-thiadiazole avoiding stoichiometric oxidants and using instead visible light and molecular oxygen in the presence of eosin Y as a photoredox catalyst.\textsuperscript{55} This reaction involves the oxidative cyclization of thioamides via the sequential formation of C–N and C–S bonds to afford 1,2,4-thiadiazole in very good yields. Irradiation of benzothioamide 26 under aerobic conditions in the presence of 2 mol% eosin Y in DMF gave the desired product 27 in good yield (Scheme 14). A wide range of aliphatic, aromatic, and heteroaromatic primary amides underwent this reaction smoothly.

The suggested mechanism for the formation of 1,2,4-thiadiazole is depicted in Scheme 15. A single electron transfer from the thiolic form 28 to eosin Y\textsuperscript{*} generates the radical anion of eosin Y and the radical cation 29, which undergoes deprotonation to a sulfur radical intermediate 30. The cyclodesulfurization of intermediate 30 furnishes 31, which gives another sulfur radical 32 by photooxidation as described before. The intermediate radical 32 is further oxidized by the anion radical of O\textsubscript{2}, which is produced in the photocatalytic cycle of eosin Y, to give peroxysulfenate 33. Finally, an intermolecular nucleophilic attack of the imino nitrogen on the SO\textsubscript{2}− substituted carbon affords the desired product 27 with loss of SO\textsubscript{2}−\textsubscript{2}.\textsuperscript{36}

4.5. Desulfurization

Aerobic desulfurization of thioamides to amides has been achieved by Yadav and coworkers via visible light photoredox catalysis using eosin Y as a photocatalyst (Scheme 16).\textsuperscript{57} Green light irradiation of 2 mol% eosin Y, thioamide 34 in DMF under an air atmosphere affords the desired product 35 in very good yield. Control experiments demonstrated that there was no significant product formation in the absence of either light or eosin Y. The photoreaction tolerates a wide range of functional groups including nitro, bromo, and methoxy groups. Thioamides bearing electron donating groups on the aromatic ring reacted faster and gave higher yields in comparison to those bearing

![Scheme 15](image1.png)

**Scheme 15** Proposed mechanism for the cyclization of thioamides.

![Scheme 16](image2.png)

**Scheme 16** Desulfurization of thioamides via eosin Y photocatalysis.
electron withdrawing groups. The reaction was not applicable to primary thioamides, which form dimers under identical reaction conditions.

The mechanism for the desulfurization of thioamides to amides is shown in Scheme 17. Initial SET from 34 to eosin Y* produces the radical anion of eosin Y and the radical cation 36. This is oxidized to intermediate 37 which converts to the desired product 35 along with the formation of elemental sulfur as the byproduct. The authors ruled out a singlet oxygen mechanism for this reaction by performing several control experiments. The use of O₂ (balloon) instead of open air did not increase the reaction yield and the reaction was not affected by singlet oxygen quenchers like 1,4-diazabicyclo[2.2.2]octane (DABCO) or 2,3-dimethyl-2-butene.

### 4.6. Aldoximes and primary amides into nitriles

An efficient method for the transformation of aldoximes and primary amides into nitriles has been reported by Yadav and coworkers (Scheme 18). The photoreaction involves the visible light initiated in situ generation of the Vilsmeier Haack reagent from DMF and CBr₄, which is the electrophilic reagent responsible for the conversion of primary amides and aldoximes into the corresponding nitriles. A mixture of aldoxime (1 mmol), 2 mol% eosin Y, 2 equiv. of CBr₄, and 20 mol% DMF was irradiated in CH₃CN for 14–18 h affording the desired product in good yields. A wide range of aromatic, heteroaromatic, aliphatic aldoximes, and primary amides reacted smoothly under these conditions. The reaction yield was higher in the presence of electron donating groups in the aryl moiety of the oxime.

### 4.7. Oxidation of silyl enol ethers

α,β-Unsaturated carbonyl compounds are essential structural motifs for the construction of a variety of natural products. Elegant methods have been reported for their synthesis, but most of them require either metal catalysts or stoichiometric oxidants. Huang and coworkers utilized the photoredox chemistry of Na₂-eosin Y under aerobic oxidative conditions (Scheme 19). Polar protic solvents like MeOH and EtOH as well as the polar aprotic solvent DMSO were identified as suitable for this reaction. The major side product of the reaction was the oxidative cleavage of the enol ether double bond.

The authors proposed a singlet oxygen mechanism for this transformation based on radical clock experiments and literature reports (Scheme 20). First, singlet oxygen is generated from sensitization by Na₂-eosin Y. An one reaction between the silyl enol ether 41 and singlet oxygen produces the intermediate 43, which is further converted into a hydroperoxy silyl hemiacetal 44. The intermediate 44 undergoes an intramolecular silyl transfer to afford the desired product 42 along with hydroperoxysilane 45, which further undergoes decomposition to give O₂ and silanol.

### 5. Arylation reactions

Aryl radicals can be generated from aryl diazonium salts via visible light photocatalysis. The method is an efficient alternative...
to reported procedures. We have used eosin Y as a photoredox catalyst for the direct arylation of heteroarenes with aryl diazonium salts in green light (Scheme 21).\(^5^9\) The reaction tolerates a wide range of functional groups, such as nitro, ester, cyano, and hydroxyl groups, and has a broad scope with respect to both aryl diazonium salts and the heteroarenes. In addition to aryl diazonium salt \(46\), thienyl diazonium salts also react providing the corresponding products in good yields. External base decreased the reaction yield due to the direct reaction between the aryl diazonium salt and the base. This metal free reaction represents an efficient alternative to transition metal catalyzed C–H arylation reactions and avoids the use of copper salts required in the classical Meerwein arylation protocol.

The proposed mechanism for the photocatalytic direct C–H arylation reaction is shown in Scheme 22. Initial reduction of the aryl diazonium salt \(46\) by eosin Y\(^*\) gives aryl radical \(49\) and the radical cation of eosin Y. The aryl radical \(49\) adds to heteroarene \(47\) yielding radical intermediate \(50\), which is oxidized by the radical cation of eosin Y to carbenium ion \(51\) while regenerating the neutral form of the photocatalyst eosin Y.

Finally, carbenium ion \(51\) is deprotonated to the desired product \(48\). The oxidation of intermediate \(50\) is also possible by the aryl diazonium salt \(46\) directly via a radical chain mechanism. However, monitoring of the reaction progress after shutting off the irradiation indicates that the radical chains undergo only few turnovers. The radical intermediates \(49\) and \(50\) were trapped with (2,2,6,6-tetramethyl-piperidin-1-yl)oxyl (TEMPO) and the corresponding adducts \(52\) and \(53\) were confirmed by mass spectrometry.

Substituted benzothiophenes find applications in biology, pharmaceutical and materials science. We applied the direct C–H arylation method for the arylation of benzothiophenes, but unfortunately a mixture of regioisomers was obtained in low yields. To obtain a single regioisomer, we decided to explore a radical annulation for the synthesis of the benzothiophene moiety (Scheme 23).\(^6^0\)
Irradiation of a mixture of 5 mol% eosin Y, o-methylthio benzenediazonium salt 54 (0.25 mmol), and alkyne 55 (5 equiv.) in DMSO afforded the desired product 56 in moderate to good yield after 14 h using a 530 nm LED. The scope of the reaction is wide, and halogen substituted benzothiophenes are available by this route. We utilized the reaction for the synthesis of the drug intermediate Raloxifene 57.

The proposed mechanism for the radical annihilation is shown in Scheme 24. Initially, eosin Y* is oxidatively quenched by the diazonium salt 54 to generate the reactive aryl radical 57 and the radical cation of eosin Y. Upon addition of the aryl radical 57 to alkyne 55 the radical intermediate 58 is obtained, which undergoes cyclization to give sulphuranyl radical 59. Subsequent oxidation of 59 by the cation radical of eosin Y followed by transfer of the methyl group to nucleophiles present in the reaction, e.g. the solvent DMSO, yields the product 56. The radical intermediate 59 may also be oxidized by the diazonium salt 54 through a radical chain transfer mechanism. TEMPO adducts of radical intermediates 57 and 58 were identified, which supports the proposed reaction mechanism.

A visible light induced [4+2] benzannulation method for the synthesis of phenanthrenes was reported by Zhou et al. using eosin Y as a photocatalyst under mild conditions (Scheme 25). Eosin Y (1 mol%), biphenyl diazonium salt 61 (0.2 mmol), and an alkyne (3 equiv.) were dissolved in CH₃CN and irradiated with a 24 W fluorescent bulb at room temperature giving the corresponding product 62 in very good yield. The reaction proceeds smoothly in polar solvents. In non-polar solvents the solubility of the diazonium salt 61 is poor. Additions of bases, such as tBuOLi or NEt₃, decrease the yield due to the direct reaction of the diazonium salt 61 and the base. The photoreaction tolerates many functional groups and has a broad scope of alkynes and biphenyldiazonium salts.

The proposed reaction mechanism for the [4+2] photobenzannulation is similar to the other diazonium salt reactions (Scheme 26). Initial SET from eosin Y* to biphenyl diazonium salt 61 generates the radical cation of eosin Y and biphenyl radical 63, which upon addition to alkyne 55 furnishes vinyl radical 64. Subsequent intramolecular radical cyclization affords the cyclized radical intermediate 65. Oxidation of 65 by the eosin Y radical cation closes the catalytic cycle and produces the carbenium intermediate 66. Finally, cation 66 is deprotonated to afford the desired phenanthrene 62.

Photoredox catalysis with eosin Y has been discussed so far, for the formation of C–C and C–P bonds. Recently, the Yan group utilized eosin Y for the borylation of aryl diazonium salts (Scheme 27). Acetonitrile was found to be a suitable solvent to promote the reaction with good yields. Irradiation of a mixture of 5 mol% eosin Y, B₂Pin₂ 67 (0.3 mmol), and aryl diazonium salt 46 (1.5 equiv.) in acetonitrile at room temperature affords the desired product 68 in good yields. Aryl diazonium salts bearing electron withdrawing groups showed higher reactivity than those bearing electron donating groups. The photoreaction tolerates a range of functional groups including acetyl, nitro, alkyl, halo, and alkoxy groups. Heteroaromatic diazonium salts are not suitable substrates for this reaction.

The proposed mechanism for the borylation of aryl diazonium salts is depicted in Scheme 28. Initially, a SET from eosin Y* to the diazonium salt 46 generates the radical cation of eosin Y and aryl radical 65, which upon addition to alkyne 55 furnishes vinyl radical 64. Subsequent intramolecular radical cyclization affords the cyclized radical intermediate 65. Oxidation of 65 by the eosin Y radical cation closes the catalytic cycle and produces the carbenium intermediate 66. Finally, cation 66 is deprotonated to afford the desired phenanthrene 62.

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Y* to the aryl diazonium salt 46 gives the aryl radical 49 and the radical cation of eosin Y. Addition of the aryl radical 49 to the tetracoordinated complex 69, which was generated in situ from the interaction between B2Pin2 and the counter anion BF4−/C0, affords the target borylated product 68 and the radical anion intermediate 70. Finally, intermediate 70 was oxidized by the radical cation of eosin Y to complete the catalytic cycle.

Arylsulfides are important structural motifs in synthetic and natural molecules and they are usually prepared by treatment of aryl diazonium salts with thiols under basic or neutral conditions. The intermediate diazosulfide, which is formed during the reaction, is a potent explosive. The recently reported method by Jacobi and coworkers avoids the risk by utilizing eosin Y as a photoredox catalyst for the synthesis of arylsulfide 73 from aryl diazonium salt 46 and disulfide 72 under green light irradiation (Scheme 29). DMSO was found to be a very good solvent for this reaction. Without eosin Y and without irradiation no product formation is observed, but irradiating the reaction mixture without eosin Y gave very low product yields. The observation is explained by formation of a charge transfer complex between DMSO and the aryl diazonium salt, which absorbs in the visible range. In addition, the authors also prepared unsymmetrical diaryl diselenides from aryl diazonium salts and diphenyl diselenide.

The suggested mechanism for the photocatalytic thiolation reaction is shown in Scheme 30. A SET reduction of aryl diazonium salt 46 by eosin Y* generates aryl radical 49 and the radical cation of eosin Y. The nucleophilic disulfide 72 attacks the aryl radical giving a trivalent sulfur radical 74, which is stabilized by the adjacent aryl and sulfur groups. Oxidation of the intermediate 74 by the radical cation of eosin Y furnishes an electrophilic species 75 and completes the photocatalytic cycle. Finally, the cation intermediate 75 undergoes substitution with DMSO to give the desired product 73.

6. Cooperative catalysis

A dual catalytic combination of photocatalysis with organocatalysis was reported by Zeitler and coworkers for the enantioselective α-alkylation of aldehydes. Eosin Y and imidazolidinone were found to be capable of alkylating aldehydes with electron deficient alkyl halides to provide the corresponding products in good yields with high enantiomeric excess (Scheme 31). Eosin Y catalyzed reactions require a little longer reaction times compared to the ruthenium-trisbipyridine catalyzed MacMillan reaction, but did not result in any product racemization. The photo reaction allows the stereospecific incorporation of fluorinated alkyl moieties, which are important structural units in drugs, to modulate their properties.
Following mainly the mechanism proposed by MacMillan and coworkers, the authors suggested a mechanism for the eosin Y reaction, which is shown in Scheme 32. Initially, a catalytic amount of enamine is oxidized by eosin Y* to generate the radical anion of eosin Y that reduces the halide to give the electron deficient radical species. Addition of radical to the enamine furnishes a -amino radical. Subsequent oxidation of the amino radical to the iminium ion provides the electron for the reductive quenching of eosin Y*. Finally, iminium ion undergoes hydrolysis to afford the desired alkylated product.

Another dual catalytic mode of hydrogen bond promoted organophotoredox catalysis was applied for highly diastereoselective reductive enone cyclization by Zeitler et al. These reactions proceed smoothly at ambient temperature using Na<sub>2</sub>-eosin Y as a photocatalyst and thiourea or a,a,a',a'-tetraphenyl-1,3-di-oxolan-4,5-dimethanol (TADDOL) as organocatalysts (Scheme 33). The combination of Hantzsch ester and diisopropylethyl amine (DIPEA) was found to be a very good reductive quencher as well as a hydrogen donor. Aryl bisenones bearing electron donating and electron withdrawing substituents undergo reductive enone cyclization to give the desired trans-cyclopentanes in good yields. However, aliphatic enones are not converted in this reaction due to their more negative potential compared to the eosin Y radical anion. In addition, heterocycles and cyclohexanes were also obtained in good yields, while cycloheptanes were not accessible.

The proposed mechanism for the reaction starts with the reductive quenching of Na<sub>2</sub>-eosin Y* by either the Hantzsch ester or DIPEA to generate the radical anion of Na<sub>2</sub>-eosin Y and (Scheme 34). Subsequent reduction of 87 by the radical anion of Na<sub>2</sub>-eosin Y closes the photocatalytic cycle and yields the 1,4-distonic radical anion, which undergoes a 5-exo-trig cyclization to give a-carbonyl radical. The radical abstracts a hydrogen atom from the radical cation following by a proton transfer to give the final product and a pyridine derivative. An alternative mechanism is the oxidation of radical followed by hydride transfer to give compound.
Scheme 35 α-Trifluoromethylation of ketones.

7. Trifluoromethylation

α-Trifluoromethylation of ketones has been reported by Kappe and coworkers via a continuous flow visible light photoredox catalysis with eosin Y (Scheme 35). The reaction proceeds in two steps: in the first step the ketones are converted into their respective silyl enol ethers by reaction with trimethylsilyl trifluoromethanesulfonate (TMSOTf) and DIPEA. The in situ formed silyl enol ethers are then converted in a visible light mediated trifluoromethylation process. The two step procedure is faster compared to reported reactions. Several ketones including acetophenones, heteroaromatic ketones, and aliphatic ketones were successfully trifluoromethylated.

8. Conclusions

Visible light photoredox catalysis with metal complexes, such as Ru(bipy)_3^2+ or Ir(ppy)_3, has already received a lot of attention as a tool for organic synthetic transformations. For several applications eosin Y serves as an attractive alternative to redox active metal complexes and even outperforms them in some cases. Eosin Y photocatalysis has been applied to generate reactive intermediates including electrophilic α-carbonyl radicals, aryl radicals, iminium ions, trifluoromethyl radicals, and enone radical anions, which are utilized in arene C–H functionalization, [2+2] cyclo addition, amine α-functionalization, hydroxylation, reduction, and oxidation reactions.

In addition, eosin Y catalysis has been merged with other modes of catalysis, such as enamine catalysis and hydrogen bond promoted catalysis, to achieve enantioselective reactions. The use of eosin Y photocatalysis in continuous flow technology has been described. Overall, the good availability, strong absorption in the visible part of the spectrum and suitable redox potential values for a variety of organic transformations make eosin Y an appealing and green photocatalyst for organic synthesis.

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