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Eosin: a versatile organic dye whose synthetic uses keep expanding

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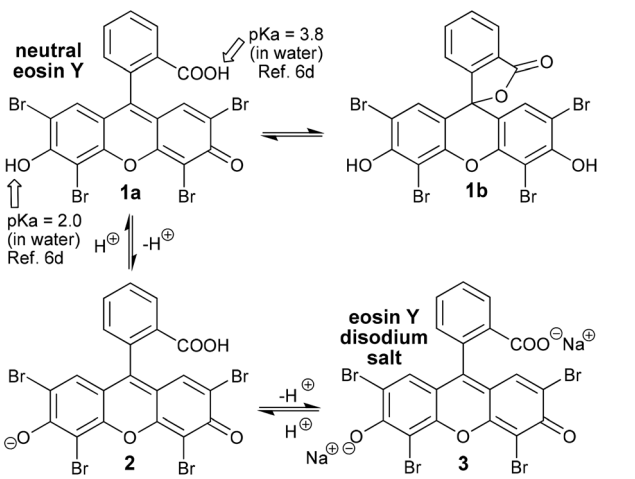
Organic dyes, which absorb light in the visible region of the electromagnetic spectrum, offer a lower cost, greener alternative to precious metals in photocatalysis. In this context, the organic dye eosin's uses are currently expanding at a significant rate. For a long time, its action as an energy transfer agent dominated, more recently, however, there has been a growing interest in its potential as an electron transfer agent. In this short review, we highlight some recent (from 2016 onwards) contributions to the field with a focus on the breadth of the reactions eosin can catalyse.

1 Introduction

The synthetic organic dye eosin was named -albeit, indirectly- after the Titaness Eos who was the bringer of light at Dawn and it has now graced the shelves of chemical laboratories for almost 150 years.[1] Van Gogh was an early user of eosin; indeed, his famous irises were originally a unique purple colour due to the red eosin he had included in his paint.[2] Eosin was invented in a time when dyes could make chemists rich and were driving the growth of the nascent chemical industry,[3] but, for over a century eosin languished in obscurity being used in synthetic chemistry only sporadically as a photosensitizer for generating singlet oxygen[4] (an energy transfer process). However, with the explosive resurgence of interest in photocatalysis that has occurred over the last decade and a half,[5] eosin too has seen a very rapid expansion in its uses (now including both energy and electron transfer processes). There have been a number of excellent reviews focusing on eosin in synthetic chemistry published already[6] (particularly worthy of note are those from Hari and König in 2014[6a] and from Srivastava and Singh in 2017[6b]), but, the true extent of its versatility is, nonetheless, only just beginning to come to light, and, with this review of some of the most recent contributions to the field (after 2016), we hope to highlight this fact.

Before we begin to review recently published eosin-catalysed reactions, some of eosin's basic features and characteristic behaviours need to be established. These issues are very comprehensively dealt with in the superb review on *Organic Photoredox Catalysis* by Romero and Nicewicz.[5b] Instead of regurgitating all the material here, we will try, to highlight some of the most important take home messages. Firstly, it is eosin Y, the most commonly used photocatalyst from the eosin family, which will be discussed throughout this review. Secondly, eosin Y commonly comes in either its neutral form or as the disodium salt, and, unfortunately, it is not always clearly indicated which of the two has been employed in the experimental protocols that have been published (Scheme 1). Thirdly, understanding of the whole fluorescein family of dyes[5b] is complicated by both the complex tautomermism and the acid–base equilibria which exist with these compounds (Scheme 1). For example, the closed lactone ring tautomer **1b** does not absorb visible light. A corollary of the existence of these equilibria is that the absorption wavelength and intensity are both pH and solvent dependent for eosin. In contrast, the redox potentials, however, do not vary significantly.[5b]



Scheme 1 Relevant tautomeric and acid–base equilibria for eosin Y.

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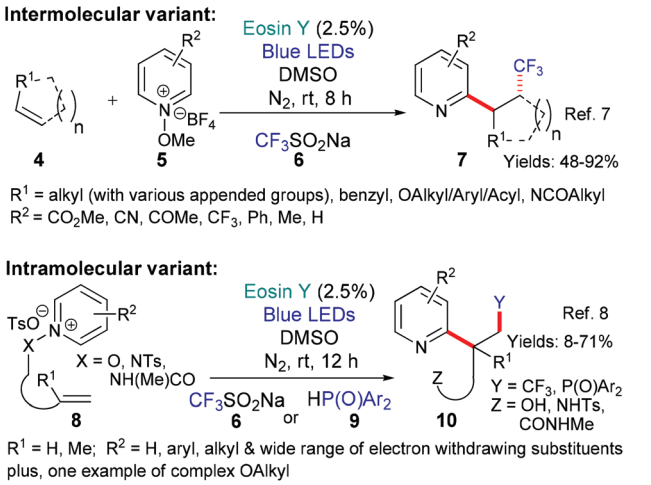
Eosin undergoes very fast intersystem crossing (ISC, ^{1}[EY] – $h\nu$ → ^{1}[EY]* – ISC → ^{3}[EY]*), so the initially formed singlet excited state(^{1}[EY]*) has a very short lifetime and it is, therefore, the triplet excited state (^{3}[EY]*) that is considered to be the most relevant. Triplet excited state eosin is both a moderate oxidant and reductant in single electron transfer (SET) pathways (redox potentials: for ^{3}EY* → EY$^{\bullet-}$ = +0.83 V *vs.* SCE and for ^{3}EY* → EY$^{\bullet+}$ = +1.15 V *vs.* SCE),[5b] but it is also an adept energy transfer agent (including; for the generation of singlet oxygen = its historical use[4]). It is of note that Romero and Nicewicz[5b] assert that eosin along with the other fluorescein dyes (fluorescein itself, rose Bengal and erythrosine) are the most analogous of all the organic dyes in their photoredox activity to the commonly used precious transition metal photocatalysts. They should, therefore, always be considered as alternatives because they are not only lower in cost, but their use is also more sustainable.



Scheme 2 Synthesis of substituted pyridines (**7** and **10**) using an eosin-catalyzed domino sequence.

2 Eosin-catalysed reactions

We have categorised the examples of eosin-catalysed reactions that will be presented in this review, firstly, by the type of bond (s) formed, and, then, within these categories, by the role eosin is proposed (by each of the work's authors) to have played mechanistically. In the schemes, the newly formed bonds are highlighted in bold (this does not indicate relative stereochemistry).

2.1 Eosin-catalyzed C–C bond forming reactions (no ring formed)

2.1.1 Excited state eosin initially acting as an oxidant (*EY → EY$^{\bullet-}$). In this section, the introduction into various substrates of highly sought-after alkyl fluoride groups dominates. We will start the survey with an elegant domino sequence yielding substituted pyridines that was developed in Hong's group (Scheme 2).[7,8] Here, an eosin/blue light combination is used to generate the trifluoromethyl radical ($^{\bullet}CF_3$), or, in a few examples,[8] a $^{\bullet}P(O)Ar_2$ radical, which adds selectively to an alkene substrate to form a new nucleophilic alkyl radical. This radical then adds exclusively to the *ortho* position of the pyridinium salt. Both inter-[7] and intramolecular[8] variants were explored. The sequences were shown to have broad scope. Endocyclic alkenes (**4**) could be used as substrates, tertiary centres could be formed ($R^1 \neq H$ in **10**) and various pyridinium salts with alternative heteroatoms (**X** in **8**, Scheme 2) adjacent

From left to right in the photo: Artemis Bosveli, Dr Tamsyn Montagnon, Dr Dimitris Kalaitzakis, Prof. Georgios Vassilikogiannakis

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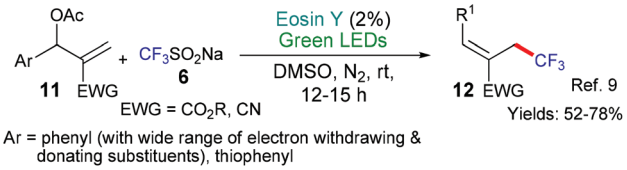
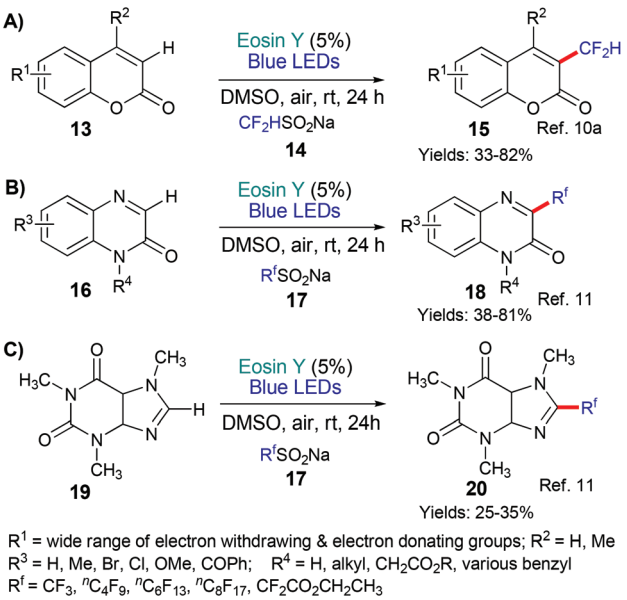
The research interests of the authors are in the field of sustainable synthetic organic chemistry with a particular focus on the development and application of new photocatalytic synthetic methodologies.

to the pyridyl nitrogen could be used as substrates, as well as, two different initiating radicals (*vide supra*). A triflouromethyl radical is also generated from sodium triflinate (Langois' reagent) using a similar eosin-light (this time, green LEDs) combination in the next example from Yadav, Sharma and Singh (Scheme 3).[9] In this case, in the mechanism proposed by the authors, regioselective addition of the CF_3 radical to the alkene substrate **11** generates a new alkyl radical stabilized by being positioned alpha to an ester group. The radical is then reduced to the corresponding anion which eliminates the adjacent acetate to form a new (*E*)-double bond (**12**). In this way, useful fluorinated building blocks can be easily accessed.

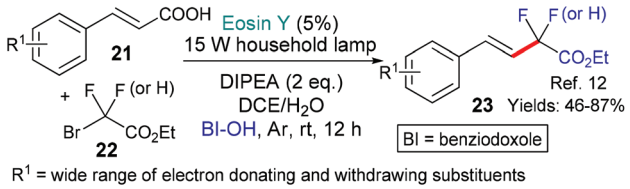
This general strategy is not limited to triflurometyl radical additions; alongside Hong's work there are two reports wherein various fluorinated alkyl radicals are added to aromatic heterocycles from families that exhibit a broad range of biological activities. In 2018, Zhang, Deng and coworkers presented the difluoromethylation of courmarins in pursuit of new antifungal agents (Scheme 4A).[10a] This work was followed by a report from Wei *et al.* showcasing the addition, using the same conditions, of a variety of fluorinated alkyl groups to quinoxalinones and xanthines (Scheme 4B and C, respectively).[11] Difluoromethylation (or monofluoromethylation) of a different



Scheme 3 Eosin-light catalyzed addition of trifluoromethyl radicals to allylic acetates **11**.



Scheme 4 Addition of various fluorinated alkyl radicals to aromatic heterocycles of interest.

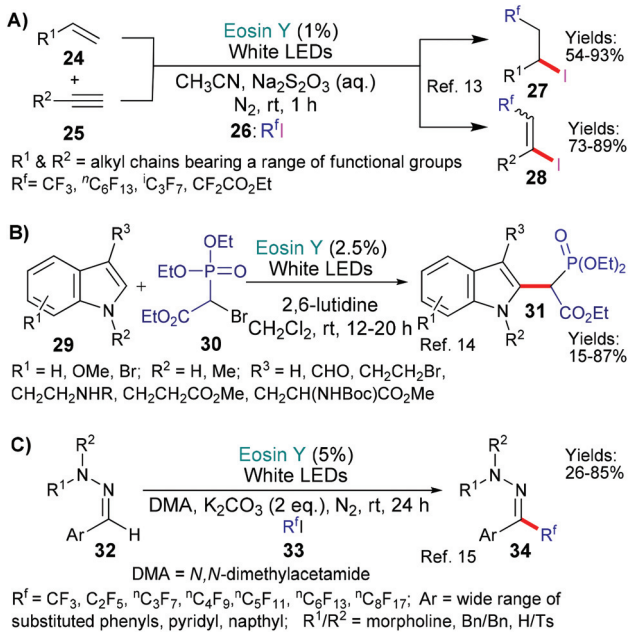


Scheme 5 (Di)Fluoromethylation of various cinnamic acids **21**.

type was investigated by Feng, Xu and coworkers (Scheme 5).[12] The authors propose that DIPEA acts as a sacrificial electron donor reducing excited state eosin to the corresponding radical anion (***EY → EY$^{\bullet-}$**); this species, in turn, donates an electron to the bromoacetate substrate **22** which fragments to give the halide anion (Br^-) and the corresponding fluorinated alkyl radical. The fluorinated radical adds regioselectivity to a cinnamic acid derivative (formed *in situ* by reaction of the cinnamic acid **21** with BI-OH). This intermediate then fragments to yield the desired product **23**.

2.1.2 Excited state eosin initially acting as a reductant (*EY → EY$^{\bullet+}$). There are a large number of examples wherein excited state eosin donates an electron to a substrate causing heterolytic cleavage of a suitable electronegative heteroatom bond to yield a stable anion (*e.g.* a halide anion) and a radical (*e.g.* $^{\bullet}$R). The latter can then add to an appropriate functionality in the starting material to form a new carbon–carbon bond. The most common example of this process involves the cleavage of C–X bonds (where X = halide) to generate carbon-centered radicals (Scheme 6).[13–15]

In the first of these examples from Yajima and Ikegami (Scheme 6A),[13] two generalised iodoperfluoroalkylation reac-

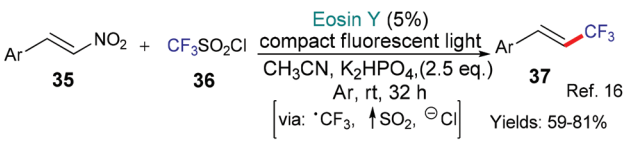


Scheme 6 Examples where heterolytic cleavage of a carbon-halide bond generates a C-centered radical for addition to a suitable substrate.

tions are presented wherein an iodide and a perfluoroalkyl group have been regioselectively added across either a terminal unactivated double or triple bond (**24** or **25** → **27** or **28**, respectively). The developed methodology showed good functional group tolerance and may be used to provide important fluorinated building blocks for use in synthesis. In the second example (Scheme 6B), from the group of Opatz,[14] indoles **31** bearing the necessary functionality for onward elaboration *via* a Horner–Wadsworth–Emmons reaction were successfully targeted. Once again wide functional group tolerance was seen as a big advantage of the metal-free method. In the final and most recent example of the three from Zhou, Li and coworkers (Scheme 6C),[15] fluorinated alkyl groups were successfully added to aromatic hydrazone substrates (**32** → **34**, Scheme 6C).

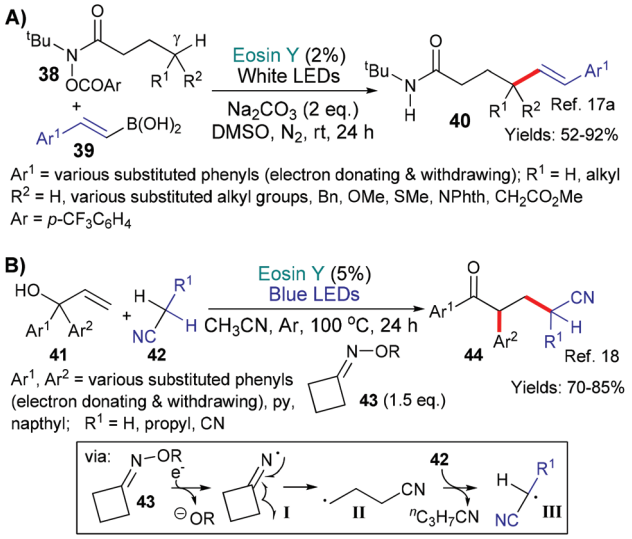
Earlier, we saw excited state eosin operating as an oxidant to generate trifluoromethyl radicals (Schemes 2 and 3); in Scheme 7, an alternative means to generate the same trifluoromethyl radical is shown by the group of Balaraman that uses excited state eosin as a reductant (***EY** → **EY$^{\bullet+}$**) and CF_3SO_2Cl.[16] The susbstrates are aromatic nitroalkenes and after addition of the trifluoromethyl radical it is proposed that NO_2 is eliminated to yield the *trans* 1-trifluoromethylalkenes, selectively.

In the next examples,[17,18] the inherent weakness and reducibility of N–O bonds has been exploited (Scheme 8). In 2018, Chen, Guo and Yu presented a new method for synthesizing δ-alkenyl amides (**40**, Scheme 8A).[17a] The reaction sequence was initiated by the reduction of the N–O bond (by ***EY** → **EY$^{\bullet+}$**) in substrates **38** to yield the corresponding aromatic carboxylate anion and an amidyl radical. This radical then undergoes 1,5-hydrogen atom transfer (HAT) to shift the position of the radical to the carbon at the γ-position (relative to the carbonyl group) on the side chain. This new carbon-centred radical then reacts with an alkenyl boronic acid **39** to eventually yield the desired δ-alkenyl amides **40**. Increasing steric hindrance (increasing substitution) at the carbon centre γ to the amide led to better *trans*-selectivity when the product's (**40**) double bond was formed. In the second example from the group of Liu and Zhou,[18] a strained oxime additive (**43**) was used to generate the desired radicals and initiate the sequence (Scheme 8B). Specifically, excited state eosin is proposed to reduce the N–O bond of **43** generating the corresponding alkoxide anion and *N*-centred imine radical (**I**), which, in turn, fragments opening the cyclobutyl ring to form a cyano-functionality and a primary alkyl radical (**II**). It is proposed that



Ar = PhX (X = H, Me, OMe, SMe, F, Cl, Br, Ph, NO_2), (substituted)napthyl, (substituted)thiophenyl

Scheme 7 Addition of trifluoromethyl radical to aromatic nitroalkenes **35**.



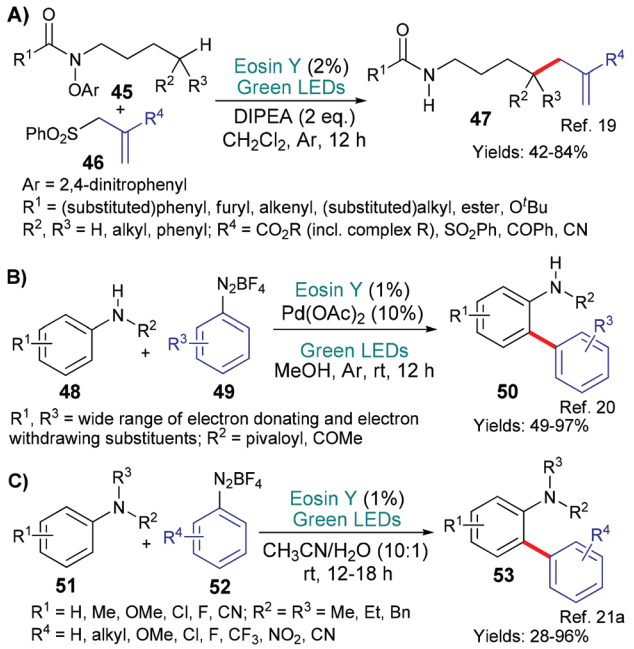
Scheme 8 Exploiting the weakness of N–O bonds to generate radicals for further reaction.

this radical abstracts an H atom from **42** to generate yet another radical intermediate (**III**) which adds to the double bond of **41**. Next after *ipso*-addition of the resulting homobenzylic radical to an adjacent aromatic residue, a 1,2-migration-oxidation sequence is completed to afford the final product **44**.

Our next example shares some characteristics with the one shown in Scheme 8A, but, in this case, it is proposed by the group of Flechsig and Wang that the aromatic functionality (of N-OAr in **45**) first accepts an electron from excited state eosin (***EY** → **EY$^{\bullet+}$**, Scheme 9A).[19] This initial reduction of the aromatic ring is followed by cleavage of the N–O bond to yield the corresponding phenoxide anion and amidyl radical. The fate of the latter mirrors the previous example (Scheme 8A); thus, a 1,5-HAT relocates the radical to the δ-position of the side chain and the resulting carbon-centred radical reacts with allyl sulfones **46** to form the adducts **47**.

Aromatic diazonium salts have also proven to be easily reducible substrates (Scheme 9B and C).[20,21] In both instances, excited state eosin donates an electron (***EY** → **EY$^{\bullet+}$**) to the aromatic diazonium salt (**49** or **52**) which then fragments to release nitrogen gas and the corresponding nucleophilic aromatic carbon-centred radical (an aryl radical). In the older of the two examples from group of Balaraman (2017),[20] this aryl radical reacts with a complex formed between the palladium catalyst and substrate **48**. After several steps standard to palladium chemistry, the biaryl products **50** are produced. In the later (2019), metal-free, example from Kapoor, Chawla and Yadav,[21a] the aryl radical produced adds directly to the *ortho*-position of the aniline substrate **51**. Only, an oxidation and deprotonation step are then required to afford the biaryl products **53**.

In our final example of this section from the groups of An and Li, we return again to the generation of trifluoromethyl



Scheme 9 Examples where excited state eosin reduces an aromatic functionality to initiate a reaction sequence.

radicals (Scheme 10).[22] In this example, a third way of generating these radicals is presented (for the two previous methods; see, Schemes 2, 3 and 7). In this instance, the authors propose that excited state eosin reduces the peroxydisulfate anion ($S_2O_8^{2-}$) to form a sulfate anion (SO_4^{2-}) and a $SO_4^{\bullet-}$ radical. This radical, in turn, reacts with sodium triflinate (CF_3SO_2Na also known as Langois' reagent) to generate the trifluoromethyl radical which then adds regioselectively to the 8-amino quinoline substrate **54**.

2.1.3 Excited state eosin abstracts a hydrogen atom (HAT process *EY → ˙EY–H). Eosin has also been used to form C–C bonds by acting as a transfer agent within HAT processes (hydrogen atom transfer processes). Here, excited state eosin can abstract a hydrogen atom with a low bond dissociation enthalpy (BDE) from one substrate to furnish a radical (usually, stabilised by an adjacent heteroatom or conjugating functionality – hence the lower BDE). This radical then reacts with a second substrate to give the desired adduct. In this section, two useful and general methods will be presented that use just such a strategy.

Scheme 10 Addition of trifluoromethyl radical to 8-amino quinolines **54**.

The first example, from the group of Wu in 2018,[23] represents a very wide ranging study into the successful addition of a variety of radicals (derived from **56**), formed through the mechanism described above, to electron deficient double bonds (**56** + **57** → **58**, Scheme 11A). This methodology is an effective and sustainable way of generating important building blocks (**58**) for synthetic applications.

The second contribution comes from Srivastava, Singh and Singh who showed that a similar strategy could be used to add a variety of α-amino alkyl radicals (derived from **59**, Scheme 11B) to styrenes **60**.[24]

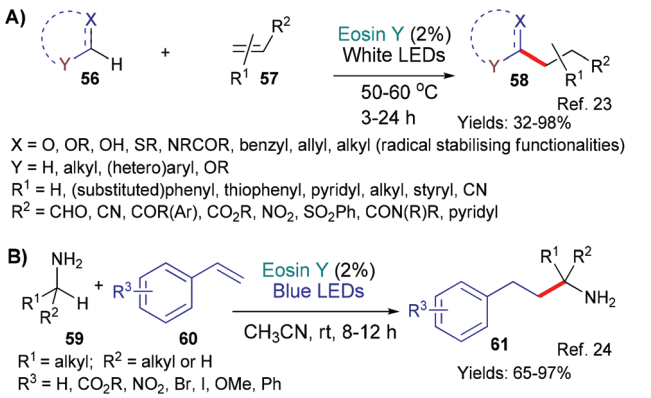
2.2 Eosin-catalyzed cyclization reactions (C–C and/or C–X bond forming reactions)

This section of the review contains really diverse examples because it encompasses not only C–C bond forming reactions, but also C–X (X = a heteroatom) bond forming reactions. Additionally, the number of bonds formed in each example varies from one to three. As such, the section forms a bridge between the preceding one, where a single C–C bond was formed in each case, and the next, where C–X bonds become the focus.

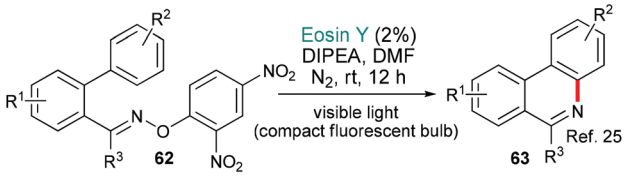
2.2.1 Excited state eosin initially acting as an oxidant (*EY → EY$^{\bullet-}$) in cyclization reactions. With cyclic compounds making up the vast majority of target compounds for synthesis, new ways to form rings are always of value.

In the first example, phenanthridines are targeted. These alkaloids exhibit a very wide range of biological activities. They were made by the group of Xie in 2016 using an eosin-mediated cyclization (Scheme 12).[25] More specifically, DIPEA acts as a sacrificial electron donor to generate **EY**$^{\bullet-}$, which, in turn, donates an electron to the 2,4-dinitrophenyl oxime group of the substrates **62**. A fragmentation then occurs to generate an iminyl radical, which cyclizes onto the proximal pendent phenyl group to yield the products **63**.

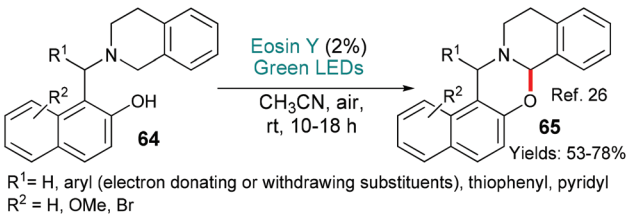
1,3-Oxazines also exhibit a wide variety of activities and can be made using an eosin-mediated cyclization (Scheme 13).[26] In this investigation, from the Borpatra, Deb and Baruah, the substrates **64** contain an internal electron donor (the tertiary



Scheme 11 Examples where excited state eosin abstracts a hydrogen atom.



Scheme 12 Synthesis of phenanthridines **63** using eosin-mediated cyclization.



Scheme 13 Synthesis of 1,3-oxazines **65** using eosin-mediated cyclization.

amine) which cedes an electron to excited state eosin (***EY** → **EY**$^{\bullet-}$). H-Atom abstraction from the intermediate then yields an imminium ion which is attacked by the nucleophilic phenol to give the products **65**. This methodology may be said to be greener than previous variants that used copper salts to achieve the same overall transformation.

Oxazoles make up a large and very popular class of synthetic targets often having interesting biological activities. In 2019, a new eosin-mediated method for their synthesis was published by the group of Gu and Li starting from α-bromoketones **66** and primary amines (**67**, Scheme 14).[27] In this instance, two new bonds are formed in the key eosin-mediated reaction. A complex multi-component mechanism is proposed for this new synthesis of oxazoles.

Another reaction that forms two new bonds was reported in 2018 by Kshirsagar's group (Scheme 15).[28a] In this case, sulfenylindoles **71** are formed from 2-alkynyl-azidoarenes **69**. It is proposed that the thiol partner initiates the process by donating an electron to excited state eosin (***EY** → **EY**$^{\bullet-}$). After a proton transfer from the thiol radical cation, a thiol radical ($R^3S^{\bullet}$) is generated that adds to the alkyne forming a vinyl radical, which, in turn, adds onto the azide ejecting nitrogen gas to form the products **71**. This work builds on an earlier

Scheme 14 Synthesis of oxazoles **68** using eosin-mediated cyclization.

Scheme 15 Synthesis of sulfenylindoles **71** using eosin-mediated cyclization.

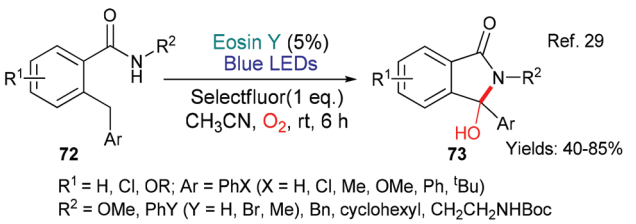
example from Gu *et al.*[28b] that made 2,3-disubstituted indoles from similar substrates using eosin Y.

The next example from the groups of Chen and Xiao (2018) is particularly interesting mechanistically (Scheme 16).[29] In this synthesis of 3-hydroxyisoindolinones **73**, it was proposed, following mechanistic investigations supported by DFT calculations, that ground state eosin donates an electron to Selectfluor initiating the first stages of the sequence which involve abstraction of a benzylic hydrogen atom from the substrate **72**. In the latter stages of the sequence, eosin fulfills a second more classical role when in its excited state it accepts an electron (***EY** → **EY**$^{\bullet-}$) to participate in the final benzylic oxidation.

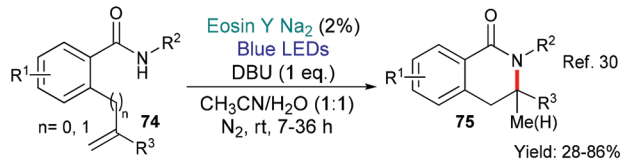
Huang's group published an eosin-mediated synthesis of dihydroisoquinolinones **75** in 2019 (Scheme 17).[30] These compounds were targeted due to previously reported biological activities. The authors propose that DBU deprotonates the amide in the starting benzamide **74**. The so-formed anion then donates an electron to excited state eosin (***EY** → **EY**$^{\bullet-}$) generating the *N*-centred amidyl radical which cyclises onto the proximal double bond to give the products **75**.

2.2.2 Excited state eosin initially acting as a reductant (*EY → EY$^{\bullet+}$) in cyclization reactions. The cyclization reactions wherein eosin acts initially as a reductant are very varied in their nature with the vast majority yielding one specific type of hetereocycle.

The first example in this section, from Leonori's group, uses classic concepts to give versatile access to a wide range of high value *N*-containing 5-membered ring products (Scheme 18).[31] Excited state eosin donates an electron (***EY** → **EY**$^{\bullet+}$) to the 2,4-dinitrophenylhydroxylamine moiety which fragments to generate the amidyl radical (compare with other examples that also form an amidyl radical, Schemes 9A and

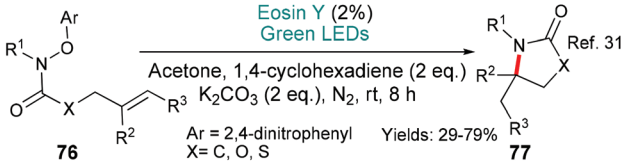


Scheme 16 Synthesis of 3-hydroxyisoindolinones **73** using dual role eosin-mediated reactions.



R^1 = H, Me, OMe, F, Cl; R^2 = OAlkyl, OBnX (X = H, OMe, F)
R^3 = H, Me (there is also an example where the alkene is replaced with an alkyne and one where the alkene is part of a cyclohexenyl unit)

Scheme 17 Synthesis of dihydroisoquinolinones **75** using eosin-mediated reactions.



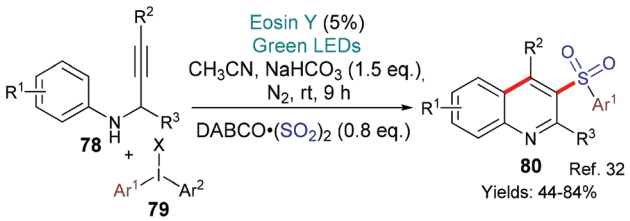
R^1 = alkyl, alkylsufone, Bn, Boc, Cbz, phenyl; R^2 = H, alkyl, F
R^3 = (cyclo)alkyl, F, H

Scheme 18 Synthesis of high value heterocycles **77** using eosin-mediated cyclization.

17). This radical then undergoes 5-*exo* cyclization with 1,4-cyclohexadiene acting as the requisite hydrogen atom source to complete the transformation into the product 77 (Scheme 18).

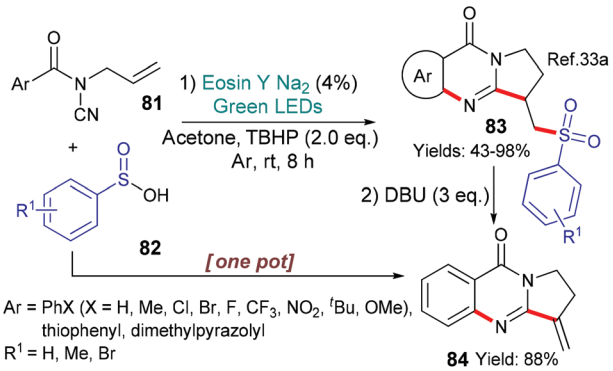
In 2018, Sun, Yin and Zhang published an eosin-mediated synthesis of 3-arylsulfonylquinolines **80** (Scheme 19).[32] Here it is proposed that excited state eosin donates an electron (***EY** → **EY**$^{\bullet+}$) to the diaryliodonium salt **79** which then fragments to generate the aromatic radical (Ar$^{\bullet}$). This radical reacts with DABSO (DABCO$(SO_2)_2$) to form the arylsulfonyl radical (Ar$SO_2^{\bullet}$) which adds to the alkyne (in **78**) giving a vinyl radical. The vinyl radical cyclizes onto the aromatic ring to afford the products **80**.

In 2017, Qian *et al.* reported a new synthesis of sulfonated quinazolines **83** mediated by eosin (Scheme 20).[33a] Quinazolines can be found in many bioactive natural products, and, additionally, sulfonyl modifications are becoming



R^1 = H, F, Cl, Br, OMe, CN, ^{t}Bu, Me
R^2 = PhY (Y = H, Me, OMe, F, Cl, Br, CN, CO_2Me, NO_2), thiophenyl, H
R^3 = H, Ph
Ar^1 = PhZ (Z = H, F, Cl, Br, Me, CF_3, CH_2OH, CO_2Me, CN), py-Cl
Ar^2 = 2,4,6-trimethoxyphenyl, Ph
X = OTf, BF_4, OTs

Scheme 19 Synthesis of quinolines **80** using eosin-mediated cyclization.

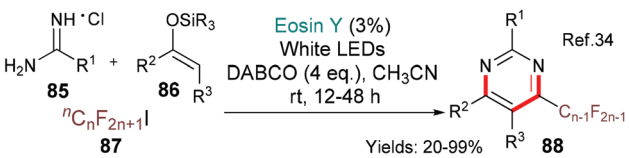


Ar = PhX (X = H, Me, Cl, Br, F, CF_3, NO_2, ^{t}Bu, OMe), thiophenyl, dimethylpyrazolyl
R^1 = H, Me, Br

Scheme 20 Synthesis of quinazolines **83** and **84** using eosin-mediated cyclization.

common in drugs; thus, these sulfonated quinazolines **83** are attractive targets. It is proposed that excited state eosin helps to generate a butoxide radical (^{t}BuO$^{\bullet}$) from tertiary-butylhydroperoxide (TBHP) by donation of an electron (***EY** → **EY**$^{\bullet+}$). This radical then abstracts a hydrogen atom from the arylsulfinc acid **82** (ArSOOH → ArS$^{\bullet}$OO) to form a new radical which adds to the terminal double bond of substrate **81**. 5-Exo cyclization onto the cyano moiety is followed by a second cyclization onto the aromatic ring yielding the final compounds **83**. The combination of eosin with an arylsulfinic acid (*c.f.* **82**) and a peroxide, to generate an ArS$^{\bullet}$OO radical, was also used to make certain sulfonylated benzofurans.[33b] In a curious twist, the same radical (ArS$^{\bullet}$OO) was also generated from the sodium salt of the corresponding arylsulfinic acid ($ArSO_2Na$) upon donation of an electron to excited state eosin (in this case, ***EY** → **EY**$^{\bullet-}$) and then used to make a set of sulfonylated isoquinolinediones.[33c]

The importance of pyrimidines (such as; **88**, Scheme 21) in nature and their wide occurrence in drugs (for example, nucleotides & nucleotide analogues) make them highly attractive targets for synthesis. The groups of Shen and Loh chose to investigate including fluorinated side chains in a new regioselective multicomponent synthesis of pyrimidines (using eosin) in order to be able to modify the lipophilicity, solubility and metabolic stability profiles of pyrimidine drug candidates.[34] In this case, it is proposed that excited state eosin donates an electron to the fluorinated iodide **87** to generate the alkyl fluoride radical ($^{\bullet}R^f$) which adds to the silyl enol



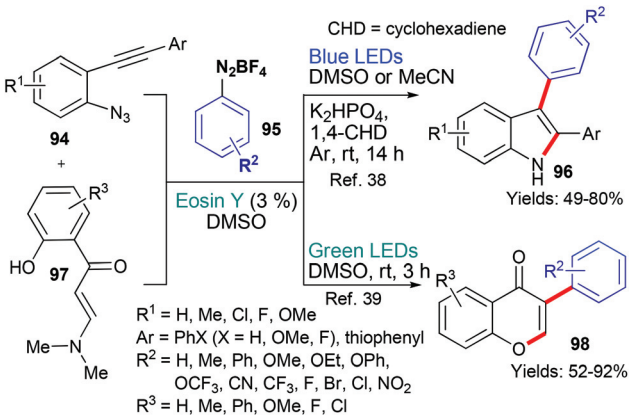
R^1 = PhX (X = H, Br, Cl, F, Me, OEt, NO_2), py, pyrimidine, NH_2
R^2 = PhY (Y = H, OMe, alkyl, Cl, Br, I, CN, NO_2), napthyl, bezothiophenyl, ^{t}Bu
R^3 = H, CO_2Et, Bn, alkyl

Scheme 21 Synthesis of pyrimidines **88** using eosin-mediated cyclization.

ether **86**. A single electron oxidation followed by elimination of hydrogen fluoride yields the corresponding fluorinated α,β-unsaturated ketone which then condenses with the amidine **85** to furnish the target pyrimidine **88**. Yang and Tang used the same method for generating alkyl fluoride radicals ($^{\bullet}R^{f}$) in their synthesis of perfluoroalkylated oxindoles from *N*-arylacrylamides.[35]

In 2018 the group of Guo[36] and in 2020 the groups of Sarkar and Murarka,[37] published new methods that used phthalimide derivatives **90** as a source of alkyl radicals (Scheme 22). In both cases, it is proposed that excited state eosin donates an electron (***EY → EY$^{\bullet+}$**) to the phthalamide **90** which subsequently fragments to generate alkyl radicals ($^{\bullet}R^{3}$). Again in both cases this alkyl radical adds to the double bond in the substrate (either **89** or **92**). After this addition, the two methods diverge mechanistically. Where the intermediate contains an azide (from **89**), an iminyl radical is formed as nitrogen is released and this iminyl radical cyclizes onto the biaryl core to yield the products **91**.[36] In the other example, the radical formed after the addition of $^{\bullet}R^{3}$ to the double bond of **92**, cyclizes onto the aldehyde residue affording the products of type **93**.[37] The phenanthridine **91** and chroman-4-one **93** products were targeted due to their potential for having biological activities of interest.

In 2017 and 2020, the groups of Jin/Cheng[38] and Mkrtchyan/Iaroshenko,[39] respectively, published new methods that used aryldiazonium tetrafluoroborates **95** as a source of aryl radicals (Scheme 23). In both cases, it is proposed that excited state eosin donates an electron (***EY → EY$^{\bullet+}$**) to the aryldiazonium tetrafluoroborate **95** which subsequently fragments to generate the aryl radical ($^{\bullet}$Ar). In the first instance, it is proposed that this aryl radical adds to the triple bond in substrate **94** and the resulting vinyl radical cyclizes onto the azide residue with loss of nitrogen to give the indole product **96**.[38] In the other example, it is proposed that the aryl radical adds to the α,β-unsaturated ketone's double bond to form an intermediate radical adjacent to the amine group. This radical is oxidized to give the imminium cation which is attacked by

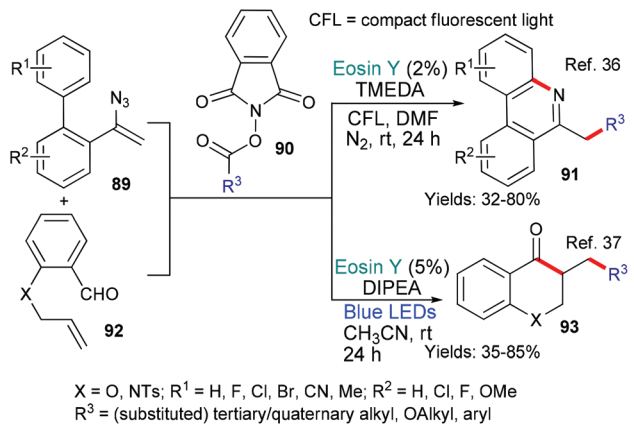


Scheme 23 Synthesis of products **96** and **98** using eosin-mediated cyclizations.

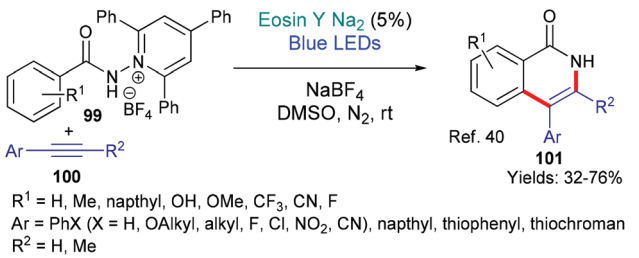
the proximal phenol to afford the cyclized product. Finally, elimination of Me_2NH yields the product **98**.[39] In both cases, the products were targeted due to their ubiquity; firstly, it is well-known that indoles are extremely common in bioactive natural products and synthetic compounds. Chromones are also privileged heterocycles abundant not only in nature, but in synthetic compounds with a range of applications (from use in the life sciences to uses in the food industry).

Recently (in 2020), the groups of Zhao and Xia published a new methodology for synthesizing isoquinolones **101** from *N*-substituted pyridinium salts **99** using eosin catalysis (Scheme 24).[40] The authors targeted isoquinolones not only for their potential biological activities, but also because they may be used in organic light emitting diodes (LEDs) and as organocatalysts. It is proposed that excited state eosin donates an electron to the pyridinium salt **99** which fragments to afford the corresponding amidyl radical. This radical adds regioselectively to the alkyne **100**, with the resulting vinyl radical cyclizing onto the aromatic amide core to furnish the isoquinolone product **101**.

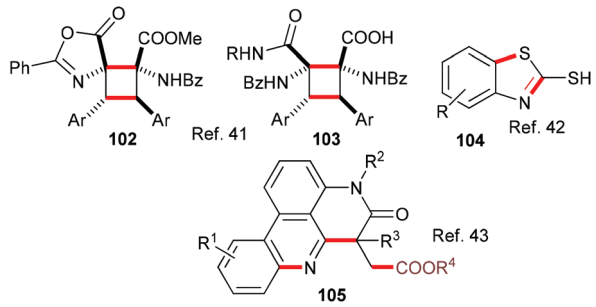
Also belonging to this section are reports of an eosin-mediated head-to-head dimerisation of Erlenmeyer azlactones to yield highly functionalized cyclobutanes **102** and **103**;[41] an eosin-mediated synthesis of 2-mercaptobenzothiazoles **104** from 2-azidoarenediazonium salts and carbon disulfide[42] and an eosin-mediated synthesis of phenanthradine derivatives



Scheme 22 Synthesis of products **91** and **93** using eosin-mediated cyclizations.



Scheme 24 Synthesis of isoquinolones **101** using eosin-mediated cyclization.



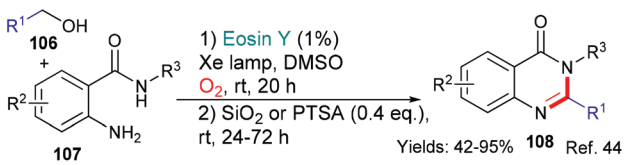
Scheme 25 Synthesis of products **102–105** using eosin-mediated cyclizations.

105 from *N*-arylacrylamides and alkyl carbazates (Scheme 25).[43]

2.2.3 Excited state eosin abstracts a hydrogen atom (HAT process *EY → ˙EY–H) in cyclization reactions. One to three new bonds are formed in these more rarely reported reactions wherein eosin abstracts a hydrogen atom during a cyclization sequence.

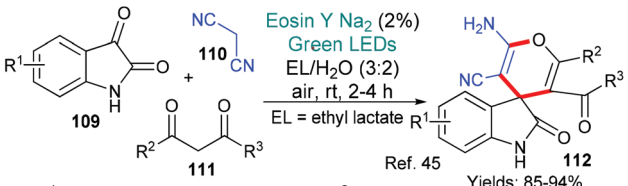
In 2019, Xia *et al.* published a novel methodology for the synthesis of quinazolinones of type **108** (Scheme 26).[44] Quinazolinones are common in both natural products and drugs, indeed, two drugs are synthesized in the paper. In a process with broad scope, it is proposed that eosin initiates the reaction sequence by abstracting one of the hydrogen atoms (***EY → ˙EY–H**) from adjacent to the alcohol functionality in **106**. Oxidation of the resulting radical to give the corresponding aldehyde (using O_2 and eosin) is followed by acid-catalyzed condensation with the *o*-aminobenzamide **107** to furnish the final products **108**.

Spirooxindoles are complex structures that have been found in natural products and are being included in biologically active synthetic compounds. Recently, the group of Mo and Zhang presented a simple synthesis of a specific group of spirooxindoles of type **112** (Scheme 27).[45] In this methodology, it is proposed that excited state eosin abstracts a hydrogen atom from the 1,3-dicarbonyl compound **111**. The resulting radical adds to a previously formed adduct of malononitrile **110** and isatin **109**. A final cyclization (*via* a two electron mechanism) unites the ketone and a cyano group to form the pyran ring in the product **112**.



R^1 = PhX (X = H, Me, F, Br, Cl, OMe, OH), alkyl, thiophenyl
R^2 = H, NO_2, Cl, Br, OMe
R^3 = alkyl, PhY (Y = H, Me, Cl)

Scheme 26 Synthesis of quinazolinones **108** using eosin-mediated cyclization.



R^1= H, Me, F, Cl, Br, NO_2, CF_3, OMe; R^2= Me, Et
R^3= Me, OMe, OEt, $OCH_2CH(CH_3)_2$, OCH_2CH_2OMe, $OCH_2CH{=}CH_2$

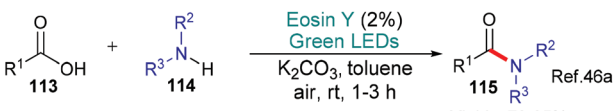
Scheme 27 Synthesis of spirooxindoles **112** using eosin-mediated cyclization.

2.3 Eosin-catalyzed C–X bond forming reactions (no ring formed)

Eosin's versatility continues to be seen in this section where we discuss the formation of carbon-heteroatom bonds; excluding, cases where it is part of a cyclization step which were discussed in the previous section (above). The mechanistic roles of eosin are not separated in the section, instead, the reactions are categorized using the hetereoatom's identity. Particularly in this area, this review is not exhaustive as very many minor investigations exist.

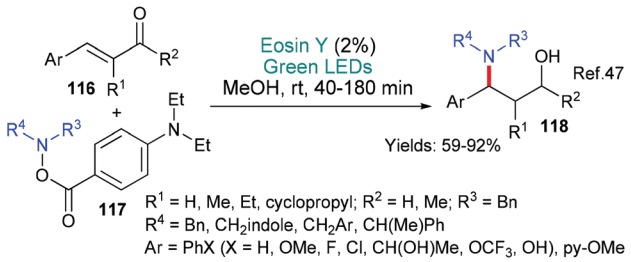
2.3.1 Eosin-catalyzed C–N bond forming reactions. In the first example in this sub-section, one of the most important bonds of all -the amide bond- is made in an eosin-mediated reaction (Scheme 28).[46a] This fundamental transformation which takes carboxylic acids **113** (albeit only ones with either a quarterny centre or an aromatic group adjacent to the carboxylate) and unites them with primary or secondary amines **114** was published by Singh's group in 2019. It is proposed that the carboxylate anion donates an electron to excited state eosin (***EY → EY˙⁻**) to generate the carboxyl radical which then dimerizes to give a peroxyanhydride. It is then proposed that this peroxyanhydride reacts with the amine to yield the final products **115**. Another example of amide bond formation (in water) was published recently.[46b]

Our second example in this section also involves a new methodology for making a fundamentally important motif, in this case it is 1,3-amino alcohols **118** (Scheme 29).[47] The method may be said to be particularly useful because it starts from a common substrate class, namely, α,β-unsaturated ketones **116**. The authors propose that excited state eosin donates an electron (***EY → EY˙⁺**) to the α,β-unsaturated ketone of substrates **116** to yield the corresponding radical anion. It is proposed that the resulting eosin radical cation

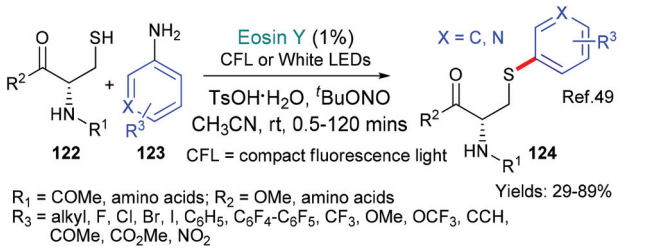


R^1 = quarterny alkyl, PhX (X = H, OMe, Me, Cl), indole, thiophenyl, quinoline
R^2 = H, alkyl
R^3 = alkyl, CH_2CHF_2, Bn, CH_2py, CH_2CH_2PhY (Y = H, NH_2), CH_2CH_2indole

Scheme 28 Synthesis of amides **115** using eosin.



Scheme 29 Synthesis of 1,3 amino alcohols **118** using eosin.



Scheme 31 Biocompatible conditions for the arylation of cysteines **122** → **124** in either batch or flow.

assists in the fragmentation of the aminating agent **117** to afford an aminyl radical which combines with the radical anion formed from the α,β-unsaturated ketone yielding, after an additional reduction (enol to alcohol), the product **118**.

In 2018, the groups of Wei and Zhao reported a new metal-free way of aminating quinoxalinones (**119** → **121**, Scheme 30).[48] The authors propose that this simple procedure occurs when the primary or secondary amine **120** donates an electron to excited state eosin (***EY** → **EY**$^{\bullet-}$) and the resulting radical cation loses a proton to generate the aminyl radical which adds to the quinoxalinone substrate **119**. Following an oxidation (N$^{\bullet}$ → N^{+}) facilitated by oxygen, subsequent elimination of an adjacent proton yields the aminated quinoxolinone **121** product.

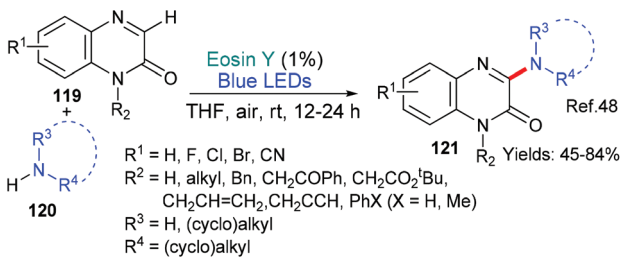
2.3.2 Eosin-catalyzed C–S bond forming reactions. Formation of C–S bonds using eosin catalyzed reactions are interesting because all the oxidation states of sulfur are represented in the examples (SH, SO, SO_2).

The first example from the groups of Noël and Madder is a biocompatible cysteine modification reaction that can be conducted in batch or in microflow; with the latter accelerating the reaction and leading to consistently higher yields (Scheme 31).[49] Aryldiazonium salts are formed *in situ* from readily available anilines **123**. The aryldiazonium salts then fragment to form the corresponding aryl radicals (Ar$^{\bullet}$) in an eosin-catalzyed process (*via* ***EY** → **EY**$^{\bullet+}$ as we have already seen in many examples in this review, see; Schemes 9B, C and 23) and go on to arylate the cysteine residues in small peptide units (**122** → **124**).

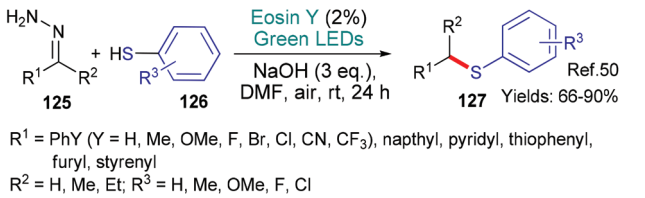
In 2019, the group of Singh published a new methodology for the synthesis of aromatic thioethers **127** from hydrazones **125** (Scheme 32).[50] The authors propose that the transformation begins when excited state eosin accepts an electron (***EY** → **EY**$^{\bullet-}$) from the thiol substrate **126**. Following loss of a proton, the RS$^{\bullet}$ radical is formed. Two alternative pathways are proposed for the reaction of this radical with the hydrazones **125** with evolution of nitrogen gas to ultimately yield the thioether product **127**. Another example of thioether formation was published recently in the form of a protocol for the oxathiacetalization of aldehydes & ketones.[51]

Earlier, in 2017, the group of Fraile and Alemán published a synthesis of sulfoxides **130** through an eosin-mediated addition of RS$^{\bullet}$ radicals to alkenes **129** (Scheme 33).[52] In this case, the mechanism proposed by the authors has eosin fulfilling two distinct roles; firstly, excited state eosin accepts an electron from the thiol **128** which, after loss of a proton, generates the RS$^{\bullet}$ radical. This radical adds regioselectively to the alkene substrate **129**. In a final step, the sulfur atom is oxidized by singlet oxygen generated through eosin photosensitization.

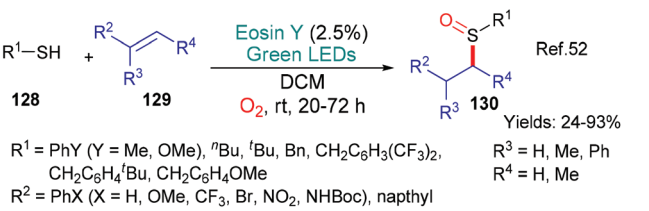
Sulfones were targeted by Chawla and Yadav in 2019 because they represent a common motif within drug candidates (Scheme 34).[53] Diazonium salts **131** were used to generate aryl radicals (Ar$^{\bullet}$ *via* ***EY** → **EY**$^{\bullet+}$ as we have already seen in many examples in this review, see; Schemes 9B, C, 23 and 31) that added to the sodium sulfinate substrates **132** to afford the desired sulfone products **133**. The authors showed that the diazo-



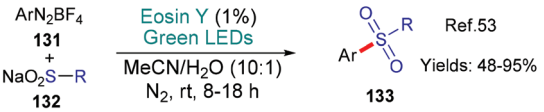
Scheme 30 Amination of quinoxalinones **119** using eosin.



Scheme 32 Synthesis of aromatic thioethers **127** using eosin.



Scheme 33 Synthesis of sulfoxides **130** using eosin.



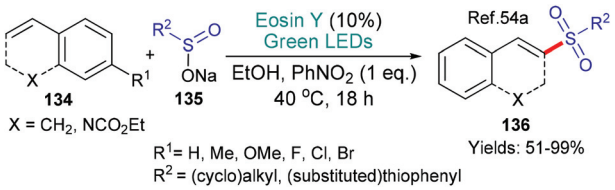
Scheme 34 Synthesis of unsymmetrical sulfones **133** using eosin.

nium salts could be formed *in situ* directly from anilines as had been previously achieved in other protocols (*c.f.* Scheme 31 [49]).

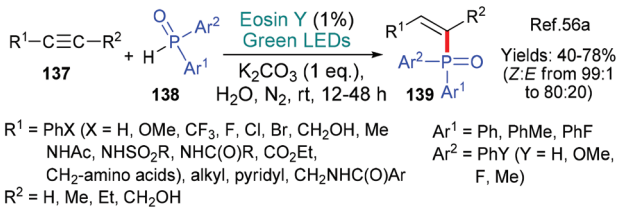
Sulfones had also been made earlier, in 2016, in a methodology using eosin that was published by König *et al.* (Scheme 35).[54a] In this example, excited state eosin is used to generate a sulfinyl radical by accepting an electron (*EY + R^2SO_2Na → $EY^{\bullet-}$ + $R^2SO_2^{\bullet}$). This radical then adds to the substrate **134**, ultimately, yielding the products **136**. Sulfinyl radicals generated through a variety of eosin-mediated mechanisms[54b–d] have also been added to double[54c,d] or triple bonds.[54b] Yet another interesting example of sulfinyl radical formation was published very recently in a new procedure for the synthesis of enaminosulfones[55] which builds on earlier protocols such as the one shown in Scheme 22.[36]

2.3.3 Eosin-catalyzed C–P bond forming reactions. Formation of C–P bonds is seen more rarely than the previous carbon-heteroatom bond forming reactions, but that it can be done, once again, underlines the versatility eosin exhibits as a catalyst.

A mechanistically interesting example of the addition phosphinyl radicals ($^{\bullet}P(O)Ar^1Ar^2$) to alkynes **137** was published by the group of Lei in 2018 (Scheme 36).[56a] The addition is overwhelmingly *Z*-selective with substrates where R^1 is an aryl group showing the highest selectivity; this enhancement is attributed to π–π stabilization between R^1 and Ar^2. The authors propose that the reaction proceeds through a proton coupled electron transfer (PCET) mechanism. Thus, the base additive



Scheme 35 Synthesis of sulfones **136** using eosin.



Scheme 36 Synthesis of *Z*-alkenylphosphine oxides **139** using eosin.

removes a proton from the diarylphosphine oxide **138** at the same time as excited state eosin removes an electron (***EY → EY$^{\bullet-}$**) generating the phosphinoyl radical that subsequently adds to the radical acceptor alkyne **137**. Phosphinyl radicals generated using eosin have also been added to coumarins[56b] and benzothiazoles.[56c]

2.4 Cooperative catalysis: eosin plus a transition metal-based catalyst

Eosin's versatility is very well showcased in this section about cooperative catalysis being used for the synthesis of privileged scaffolds. In these examples that are summarized in Scheme 37,[57–63] eosin is acting in consort with a transition metal to complete the requisite catalytic cycles. Eosin facilitates the use of mild conditions and can widen functional group tolerance. Here, excited state eosin most frequently acts as an oxidant (***EY → EY$^{\bullet-}$**, Scheme 37A–E),[57–61] but there is also an example where it is acting as a reductant (***EY → EY$^{\bullet+}$**, Scheme 37F)[62] and one where it acts as an energy transfer agent to generate singlet oxygen (Scheme 37G).[63] An important application of this concept within the critical fields of green chemistry and clean energy chemistry (hydrogen production) was recently reported by the group of Kim.[64] In this investigation, a bio- inspired nickel catalyst with eosin as co-oxidant was used to fix carbon dioxide to produce formate ions. The same catalyst system was examined for hydrogen production.

2.5 Oxidation and dehydrogenation protocols

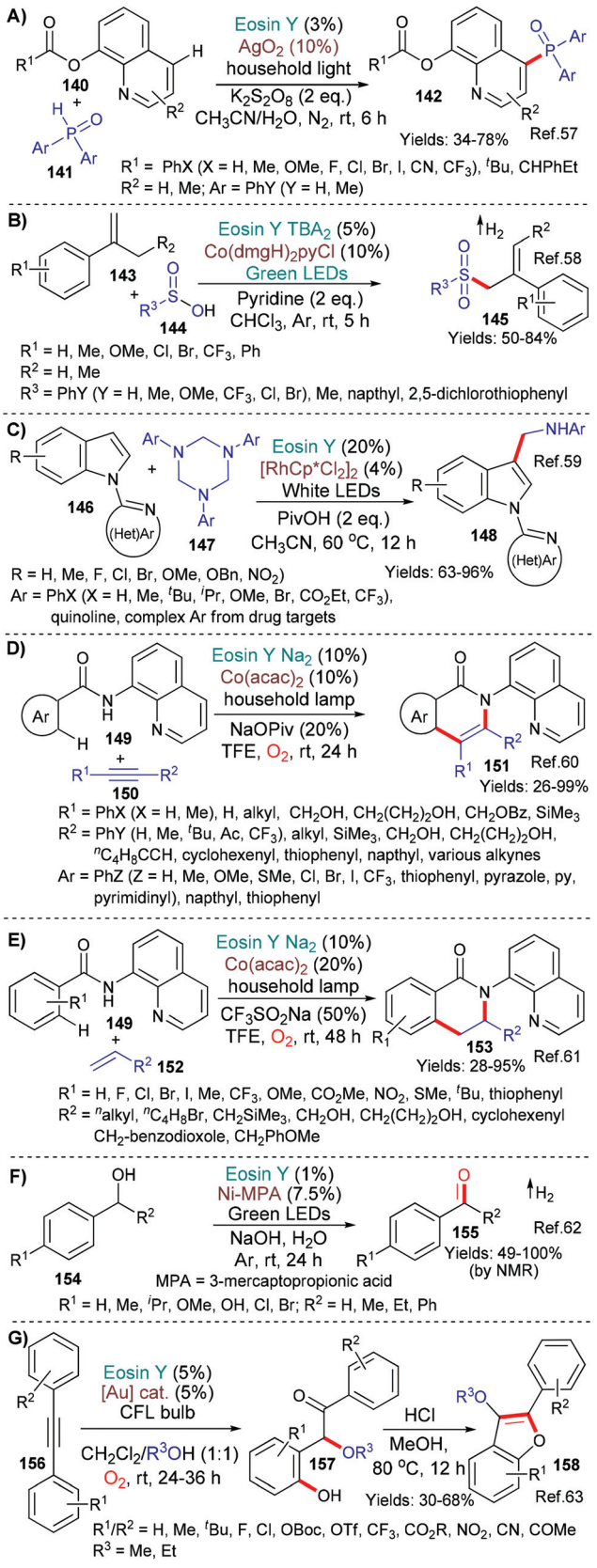
Building on precedents, the benzylic oxidation of various benzylamine-containing scaffolds has been shown to be facile using eosin (Scheme 38).[65,66] Mechanistically, the reactions are said to proceed *via* excited state eosin acting as an oxidant (***EY → EY$^{\bullet-}$**) with the resulting benzylic radical being trapped by a reactive oxygen species (ROS) to afford, ultimately, the oxidized products, dihydroisoquinolones **160**[65] or picolinamides **162**.[66]

In 2018, the group of Das published an investigation into the dehydrogenation of a wide range of activated amines (substrates **163–166** afford products **167–170**) using excited state eosin (Scheme 39).[67] The protocol uses the bases 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) and requires a carbon dioxide atmosphere. The authors propose a mechanism which includes formation of a DBN-CO_2 adduct and excited state eosin acting as an oxidant (***EY → EY$^{\bullet-}$**).

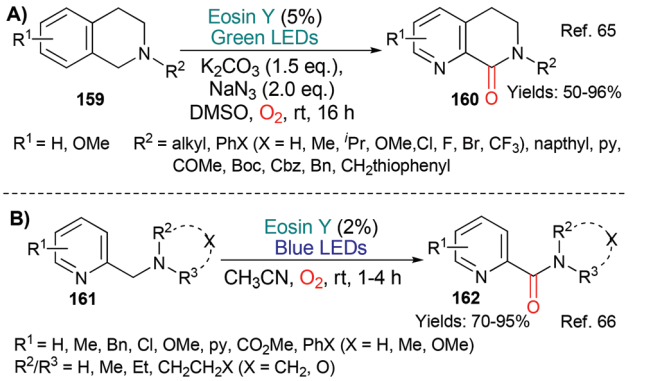
2.6 Unusual uses of eosin

2.6.1 Reactions of Eosin in the dark. If one examines the heteroatom rich, highly conjugated structures of many of the organic dyes, it is not altogether surprising that there are also examples of them acting as redox agents in the ground state without the further activation afforded by exposing them to visible spectrum light. For example, methylene blue has been shown to act as a redox agent in the dark.[68]

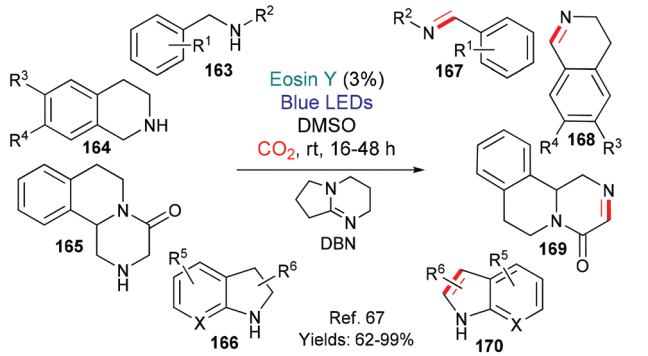
In 2018, the group of Liu published a new method for the synthesis of 4-pyrrolin-2-ones **173** which uses a catalyst combination of eosin and copper acetate in the dark (Scheme 40).[69]



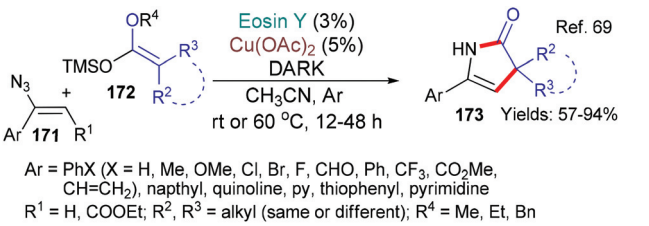
Scheme 37 Examples of cooperative catalysis between transition metals and eosin for the synthesis of various privileged scaffolds.



Scheme 38 Synthesis of dihydroisoquinolones **160** and picolinamides **162** using eosin.



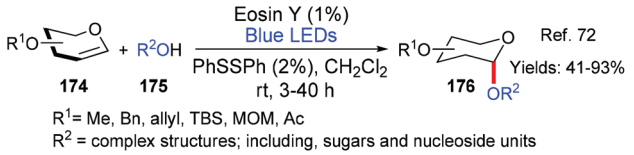
Scheme 39 Dehydrogenation of activated amines **163–166** to give privileged structures **167–170** using eosin.



Scheme 40 Synthesis of 4-pyrrolin-2-ones **173** using eosin in the dark.

The authors propose that eosin acts as an electron donor (a reductant) for the transformation of Cu(II) to Cu(I) (**EY** → **EY**$^{\bullet+}$) and also as an oxidant by accepting an electron from the ketene acetal **172** (**EY**$^{\bullet+}$ → **EY**) to return to its neutral state. The 4-pyrrolin-2-one products **173** are interesting compounds with many uses.[70]

2.6.2 Miscellaneous uses of eosin. Beyond all the uses of eosin that have been discussed in the preceding sections, eosin has also been employed in a number of other miscellaneous reaction types, such as, cleavages[71] or as a photoacid.[72] In the former case,[71] a wide range of aryl, heteroaryl and alkyl dithianes were cleaved to afford the corresponding ketone or aldehyde using a simple eosin, light and water combination.



Scheme 41 Synthesis of 2-deoxyglycosides **176** using eosin as a photoacid.

Yields were generally high (61–97%) and the methodology, thus, presents a viable deprotection protocol for dithianes. In the second example, a range of differentially protected galactals, L-rhamnals and glucals (**174**) were coupled with primary alcohols (including complex ones) to form deoxyglycosides **176**.[72] The authors, Zhao and Wang, suggest that excited state eosin is acting as a photoacid to facilitate this reaction (Scheme 41).

3 Conclusion

Here ends our survey of the recent uses of eosin in synthesis. It is not possible for the review to be an exhaustive compilation of works published, not least because with every week that passes new papers appear that add to the body of literature building up around eosin. The main message we would like to convey is the extraordinary versatility of eosin. Eosin has moved far beyond its traditional role as a photosensitizer (energy transfer agent) to encompass so much more. In this review, we have seen eosin act as an oxidant (electron acceptor), as a reductant (electron donor), as an H-atom abstractor, as a photoacid, in cooperative catalysis, in the light and in the dark. We have seen it catalyze the formation of single bonds, multiple bonds, carbon–carbon bonds and many different types of carbon-heteroatom bonds. It is hard to think of another reagent that can mediate so many different types of reaction and fulfill so many different mechanistic roles while at the same time offering excellent functional group tolerance and mild reaction conditions. For these reasons and many more, eosin certainly offers a promising alternative to precious metal catalysis and should be considered as a possible catalyst for new transformations. We expect to see an expansion in the groups that can be oxidized by eosin and in the bonds that can be reduced by eosin to initiate reaction sequences. We also anticipate that the number of radical cascades initiated by eosin will increase significantly in the near future. Thus, eosin's story will continue to develop at a significant pace.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

1 A. S. Travis, in *Tech and Culture*, John Hopkins University Press, 1998, vol. 39, issue 1, pp. 105–115.
2 M. Geldof, A. N. P. Gaibor, F. Ligterink, E. Hendriks and E. Kirchner, *Heritage Sci.*, 2018, **6**, 17.
3 K. C. Nicoloau and T. Montagnon in *Molecules that Changed the World*, Weinheim, Germany, 2008, pp. 49–56.
4 For a classic example, see: (*a*) E. J. Corey, D. N. Crouse and J. E. Anderson, *J. Org. Chem.*, 1975, **40**, 2140–2141; For a review containing many examples, see: (*b*) T. Montagnon, D. Kalaitzakis, M. Triantafyllakis, M. Stratakis and G. Vassilikogiannakis, *Chem. Commun.*, 2014, **50**, 15480–15498.
5 (*a*) C. R. J. Stephenson, T. P. Yoon and D. W. C. MacMillan, *Visible Light Photocatalysis in Organic Chemistry*, Wiley-VCH, Weinheim, Germany, 2018; (*b*) N. A. Romero and D. A. Nicewicz, *Chem. Rev.*, 2016, **116**, 10075–10166.
6 (*a*) D. P. Hari and B. König, *Chem. Commun.*, 2014, **50**, 6688–6699; (*b*) V. Srivastava and P. P. Singh, *RSC Adv.*, 2017, **7**, 31377–31392; (*c*) F. Herbrik, P. C. González, M. Krstic, A. Puglisi, M. Benaglia, M. A. Sanz and S. Rossi, *Appl. Sci.*, 2020, **10**, 5596; For important mechanistic discussion, see: (*d*) M. Majek, F. Filace and A. Jacobi von Wangelin, *Beilstein J. Org. Chem.*, 2014, **10**, 981–989; For a useful review on metal free C–X bond formation containing many eosin-mediated reactions, see: (*e*) L. Ren, M. Ran, J. He, Y. Qian and Q. Yao, *Chin. J. Org. Chem.*, 2019, **39**, 1583–1595.
7 Y.-T. He, D. Kang, I. Kim and S. Hong, *Green Chem.*, 2018, **20**, 5209–5214.
8 J. Jeon, Y.-T. He, S. Shin and S. Hong, *Angew. Chem., Int. Ed.*, 2020, **59**, 281–285.
9 A. K. Yadav, A. K. Sharma and K. N. Singh, *Org. Chem. Front.*, 2019, **6**, 989–993.
10 (*a*) P. Dai, X. Yu, P. Teng, W. H. Zhang and C. Deng, *Org. Lett.*, 2018, **20**, 6901–6905; For a further example where Langois' reagent is used, see: (*b*) J. Fang, W.-G. Shen, G.-Z. Ao and F. Liu, *Org. Chem. Front.*, 2017, **4**, 2049–2053.
11 Z. Wei, S. Qi, Y. Xu, H. Liu, J. Wu, H. Li, C. Xia and G. Duan, *Adv. Synth. Catal.*, 2019, **361**, 5490–5498.
12 W.-K. Tang, Y.-S. Feng, Z.-W. Xu, Z.-F. Cheng, J. Xu, J.-J. Dai and H.-J. Xu, *Org. Lett.*, 2017, **19**, 5501–5504.
13 T. Yajima and M. Ikegami, *Eur. J. Org. Chem.*, 2017, 2126–2129.
14 M. M. Nebe, D. Loeper, F. Fürmeyer and T. Opatz, *Eur. J. Org. Chem.*, 2018, 2471–2476.
15 M.-D. Zhou, Z. Peng, L. Li and H. Wang, *Tetrahedron Lett.*, 2019, **60**, 151124.

16 S. P. Midya, J. Rana, T. Abraham, B. Aswin and E. Balaraman, *Chem. Commun.*, 2017, **53**, 6760–6763.
17 (*a*) H. Chen, L. Guo and S. Yu, *Org. Lett.*, 2018, **20**, 6255–6259; For a related *N*-(acyloxy)phthalimide with eosin as an oxidant example, see: (*b*) Y.-L. Zhang, L. Yang, J. Wu, C. Zhu and P. Wang, *Org. Lett.*, 2020, **22**, 7768–7772.
18 Q.-L. Wang, Z. Chen, C.-S. Zhou, B.-Q. Xiong, P.-L. Zhang, C.-A. Yang, Y. Liu and Q. Zhou, *Tetrahedron Lett.*, 2018, **59**, 4551–4556.
19 K. Wu, L. Wang, S. Colón-Rodríguez, G.-U. Flechsig and T. Wang, *Angew. Chem., Int. Ed.*, 2019, **58**, 1774–1778.
20 M. K. Sahoo, S. P. Midya, V. G. Landge and E. Balaraman, *Green Chem.*, 2017, **19**, 2111–2117.
21 (*a*) R. Kapoor, R. Chawla and L. D. S. Yadav, *Tetrahedron Lett.*, 2019, **60**, 805–809; For other examples using diazonium salts and eosin, see: (*b*) T. Adak, C. Hu, M. Ruldoph, J. Li and A. S. K. Hashmi, *Org. Lett.*, 2020, **22**, 5640–5644; (*c*) T. Meyer, J.-X. Xu, J. Rabeah, A. Brückner and X.-F. Wu, *ChemPhotoChem*, 2020, **4**, 713–720.
22 C. Tian, L.-M. Yang, H.-T. Tian, G.-H. An and G.-M. Li, *J. Fluor. Chem.*, 2019, **219**, 23–28.
23 X.-Z. Fan, J.-W. Rong, H.-L. Wu, Q. Zhou, H.-P. Deng, J. D. Tan, C.-W. Xue, L.-Z. Wu, H.-R. Tao and J. Wu, *Angew. Chem., Int. Ed.*, 2018, **57**, 8514–8518.
24 V. Srivastava, P. K. Singh and P. P. Singh, *Tetrahedron Lett.*, 2019, **60**, 1333–1336.
25 X. Liu, Z. Qing, P. Cheng, X. Zheng, J. Zeng and H. Xie, *Molecules*, 2016, **21**, 1690.
26 P. J. Borpatra, M. L. Deb and P. K. Baruah, *Tetrahedron Lett.*, 2017, **58**, 4006–4010.
27 X. Zhang, Y. He, J. Li, R. Wang, L. Gu and G. Li, *J. Org. Chem.*, 2019, **84**, 8225–8231.
28 (*a*) S. D. Tambe, R. S. Rohokale and U. A. Kshirsagar, *Eur. J. Org. Chem.*, 2018, 2117–2121; (*b*) l. Gu, C. Jin, W. Wang, Y. He, G. Yang and G. Li, *Chem. Commun.*, 2017, **53**, 4203–4206.
29 D.-M. Yan, Q.-Q. Zhao, L. Rao, J.-R. Chen and W.-J. Xiao, *Chem. – Eur. J.*, 2018, **24**, 16895–16901.
30 S. Zou, S. Geng, L. Chen, H. Wang and F. Huang, *Org. Biomol. Chem.*, 2019, **17**, 380–387.
31 J. Davies, T. D. Svejstrup, D. F. Reina, N. S. Sheikh and D. Leonori, *J. Am. Chem. Soc.*, 2016, **138**, 8092–8095.
32 D. Sun, K. Yin and R. Zhang, *Chem. Commun.*, 2018, **54**, 1335–1338.
33 (*a*) P. Qian, Y. Deng, H. Mei, J. Han, J. Zhou and Y. Pan, *Org. Lett.*, 2017, **19**, 4798–4801; (*b*) L. Wan, M. Zhang, Y. Zhang, Q. Liu, X. Zhao, J.-S. Li, Z. Luo and W. Wei, *Chin. Chem. Lett.*, 2020, **31**, 67–70; (*c*) K.-L. Zuo, Y.-H. He and Z. Guan, *Eur. J. Org. Chem.*, 2019, 939–948.
34 X.-Q. Chu, T. Xie, L. Li, D. Ge, Z.-L. Shen and T.-P. Loh, *Org. Lett.*, 2018, **20**, 2749–2752.
35 Z. Yang and A. Tang, *Synlett*, 2019, **30**, 1061–1066.
36 J.-C. Yang, J.-Y. Zhang, J.-J. Zhang, X.-H. Duan and L.-N. Guo, *J. Org. Chem.*, 2018, **83**, 1598–1605.
37 S. Das, S. K. Parida, T. Mandal, L. Sing, S. De Sarkar and S. Murarka, *Chem. – Asian J.*, 2020, **15**, 568–572.
38 C. Jin, L. Su, D. Ma and M. Cheng, *New J. Chem.*, 2017, **41**, 14053–14056.
39 S. Mkrtchyan and V. O. Iaroshenko, *Chem. Commun.*, 2020, **56**, 2606–2609.
40 Y. Zhao, C. Shi, X. Su and W. Xia, *Chem. Commun.*, 2020, **56**, 5259–5262.
41 I. F. S. Marra, A. M. de Almeida, L. P. Silva, P. P. de Castro, C. C. Corrêa and G. W. Amarante, *J. Org. Chem.*, 2018, **83**, 15144–15154.
42 P. Natarajan, N. Kumar and Priya, *ChemistrySelect*, 2020, **5**, 4862–4865.
43 X. Li, X. Fang, S. Zhuang, P. Liu and P. Sun, *Org. Lett.*, 2017, **19**, 3580–3583.
44 Q. Xia, Z. Shi, J. Yuan, Q. Bian, Y. Xu, B. Liu, Y. Huang, X. Yang and H. Xu, *Asian J. Org. Chem.*, 2019, **8**, 1933–1941.
45 M.-N. Chen, J.-Q. Di, J.-M. Li, L.-P. Mo and Z.-H. Zhang, *Tetrahedron*, 2020, **76**, 131059.
46 (*a*) V. Srivastava, P. K. Singh and P. P. Singh, *Tetrahedron Lett.*, 2019, **60**, 40–43; (*b*) Y. Xu, X. Xu, B. Wu, C. Gan, X. Lin, J. Wang and F. Ke, *Asian J. Org. Chem.*, 2020, **9**, 1032–1035.
47 V. Srivastava, P. K. Singh, S. Kanaujia and P. P. Singh, *New J. Chem.*, 2018, **42**, 688–691.
48 W. Wei, L. Wang, P. Bao, Y. Shao, H. Yue, D. Yang, X. Yang, X. Zhao and H. Wang, *Org. Lett.*, 2018, **20**, 7125–7130.
49 C. Bottecchia, M. Rubens, S. B. Gunnoo, V. Hessel, A. Madder and T. Noël, *Angew. Chem., Int. Ed.*, 2017, **56**, 12702–12707.
50 S. Chand, A. K. Pandey, R. Singh, S. Kumar and K. N. Singh, *Chem. – Asian J.*, 2019, **14**, 4712–4716.
51 Y.-C. Liu, D. M. Reddy, X.-A. Chen, Y.-C. Shieh and C.-F. Lee, *Eur. J. Org. Chem.*, 2020, 2542–2552.
52 A. Guerrero-Corella, A. M. Martinez-Gualda, F. Ahmadi, E. Ming, A. Fraile and J. Alemán, *Chem. Commun.*, 2017, **53**, 10463–10466.
53 R. Chawla and L. D. S. Yadav, *Org. Biomol. Chem.*, 2019, **17**, 4761–4766.
54 (*a*) A. U. Meyer, K. Straková, T. Slanina and B. König, *Chem. – Eur. J.*, 2016, **22**, 8694–8699; (*b*) D. Yang, B. Huang, W. Wei, J. Li, G. Lin, Y. Liu, J. Ding, P. Sun and H. Wang, *Green Chem.*, 2016, **18**, 5630–5634; (*c*) H. Wang, Q. Lu, C.-W. Chiang, Y. Luo, J. Zhou, G. Wang and A. Lei, *Angew. Chem., Int. Ed.*, 2017, **56**, 595–599; (*d*) S. Cai, Y. Xu, D. Chen, L. Li, Q. Chen, M. Huang and W. Weng, *Org. Lett.*, 2016, **18**, 2990–2993.
55 O. M. Mulina, A. I. Ilovaisky, T. Opatz and A. O. Terent'ev, *Tetrahedron Lett.*, 2021, **64**, 152737.
56 (*a*) H. Wang, Y. Li, Z. Tang, S. Wang, H. Zhang, H. Cong and A. Lei, *ACS Catal.*, 2018, **8**, 10599–10605; (*b*) Q. Li, X. Zhao, Y. Li, M. Huang, J. K. Kim and Y. Wu, *Org. Biomol. Chem.*, 2017, **15**, 9775–9778; (*c*) P. Peng, L. Peng, G. Wang, F. Wang, Y. Luo and A. Lei, *Org. Chem. Front.*, 2016, **3**, 749–752.
57 X. Su, F. Yang, Y. Wu and Y. Wu, *Org. Biomol. Chem.*, 2018, **16**, 2753–2756.

58 G. Zhang, L. Zhang, H. Yi, Y. Luo, X. Qi, C.-H. Tung, L.-Z. Wu and A. Lei, *Chem. Commun.*, 2016, **52**, 10407–10410.
59 R. Liu, J. Liu, Y. Wei and M. Shi, *Org. Lett.*, 2019, **21**, 4077–4081.
60 D. Kalsi, S. Dutta, N. Barsu, M. Rueping and B. Sundararajua, *ACS Catal.*, 2018, **8**, 8115–8120.
61 D. Kalsi, N. Barsu, S. Chakrabarti, P. Dahiya, M. Rueping and B. Sundararajua, *Chem. Commun.*, 2019, **55**, 11626–11629.
62 X.-J. Yang, Y.-W. Zheng, L.-Q. Zheng, L.-Z. Wu, C.-H. Tung and B. Chen, *Green Chem.*, 2019, **21**, 1401–1405.
63 S. P. Sancheti, M. O. Akram, R. Roy, V. Bedi, S. Kundu and N. T. Patil, *Chem. – Asian J.*, 2019, **14**, 4601–4606.
64 S. E. Lee, A. Nasirian, Y. E. Kim, P. T. Fard, Y. Kim, B. Jeong, S.-J. Kim, J.-O. Baeg and J. Kim, *J. Am. Chem. Soc.*, 2020, **142**, 19142–19149.
65 K. C. C. Aganda, B. Hong and A. Lee, *Adv. Synth. Catal.*, 2019, **361**, 1124–1129.
66 V. Srivastava, P. K. Singh and P. P. Singh, *Tetrahedron Lett.*, 2019, **60**, 151041.
67 D. Riemer, W. Schilling, A. Goetz, Y. Zhang, S. Gehrke, I. Tkach, O. Hollóczki and S. Das, *ACS Catal.*, 2018, **8**, 11679–11687.
68 (*a*) D. Kalaitzakis, A. Kouridaki, D. Noutsias, T. Montagnon and G. Vassilikogiannakis, *Angew. Chem., Int. Ed.*, 2015, **54**, 6283–6287; (*b*) D. Kalaitzakis, D. Noutsias and G. Vassilikogiannakis, *Org. Lett.*, 2015, **17**, 3596–3599; (*c*) D. Kalaitzakis, M. Triantafyllakis, M. Sofiadis, D. Noutsias and G. Vassilikogiannakis, *Angew. Chem., Int. Ed.*, 2016, **55**, 4605–4609; (*d*) M. Sofiadis, J. Sarris, T. Montagnon, D. Kalaitzakis and G. Vassilikogiannakis, *Eur. J. Org. Chem.*, 2018, 4523–4526; (*e*) D. Kalaitzakis, K. Daskalakis, M. Triantafyllakis, M. Sofiadis and G. Vassilikogiannakis, *Org. Lett.*, 2019, **21**, 5467–5470.
69 W.-L. Lei, K.-W. Feng, T. Wang, L.-Z. Wu and Q. Liu, *Org. Lett.*, 2018, **20**, 7220–7224.
70 T. Montagnon, D. Kalaitzakis, M. Sofiadis and G. Vassilikogiannakis, *Org. Biomol. Chem.*, 2020, **18**, 180–190.
71 P. D. Dharpure, A. Bhowmick, P. K. Warghude and R. G. Bhat, *Tetrahedron Lett.*, 2020, **61**, 151407.
72 G. Zhao and T. Wang, *Angew. Chem., Int. Ed.*, 2018, **57**, 6120–6124.