A new era for homolytic aromatic substitution: replacing Bu3SnH with efficient light-induced chain reactions

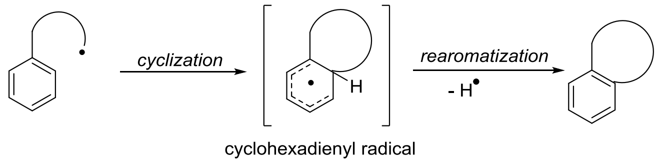
A new era for homolytic aromatic substitution: replacing Bu_3SnH with efficient light-induced chain reactions†

Michael Gurry, and Fawaz Aldabbagh*

Herein is a pertinent review of recent photochemical homolytic aromatic substitution (HAS) literature. Issues with using the reductant Bu_3SnH in an oxidative process where the net loss of a hydrogen atom occurs is discussed. Nowadays more efficient light-induced chain reactions are used resulting in HAS becoming a synthetic mechanism of choice rivaling organometallic, transition-metal and electrophilic aromatic substitution protocols. The review includes aromatic substitution as part of a tandem or cascade reaction, Pschorr reaction, as well as HAS facilitated by *ipso*-substitution, and Smiles rearrangement. Recently visible-light photoredox catalysis, which is carried out at room temperature has become one of the most important means of aromatic substitution. The main photoredox catalysts used are polypyridine complexes of Ru(II) and Ir(III), although eosin Y is an alternative allowing metal-free HAS. Other radical initiator-free aromatic substitutions have used 9-mesityl-10-methylacridinium ion and *N*,*N*-bis(2,6-diisopropylphenyl)perylene-3,4,9,10-bis(dicarboximide) as the photoredox catalyst, UV-light, photoinduced electron-transfer, zwitterionic semiquinone radical anions, and Barton ester intermediates.

1. Introduction

Homolytic aromatic substitution (HAS) is the radical analogue of the more facile electrophilic aromatic substitution (EAS). In contrast to EAS, HAS is traditionally thought of as being difficult, since re-aromatization requires the net loss of a hydrogen atom (H•), which is a poor leaving group (Scheme 1). The transformation can be facilitated by *ipso*-substitution, where a better leaving group than a hydrogen atom is involved, but these often require more elaborate radical precursors. Alternatively the radical intermediate can be oxidized to a cation, whereby re-aromatization occurs with the loss of proton (H^+).



Scheme 1. General intramolecular HAS.

School of Chemistry, National University of Ireland Galway, University Road, Galway, Ireland. SW4 NUI.
E-mail: Fawaz.Aldabbagh@nuigalway.ie

† Dedicated to the memory of Prof W. Russell Bowman: An inspirational teacher, friend and researcher in radical chemistry.

Michael Gurry

Michael Gurry obtained First Class Honours from National University of Ireland Galway in 2011 before commencing his PhD in synthetic heterocyclic chemistry under the direction of Dr Fawaz Aldabbagh. Michael completed a placement at the University of Reims-Champagne, France working on a collaborative project with Prof Janos Sapi.

Fawaz Aldabbagh

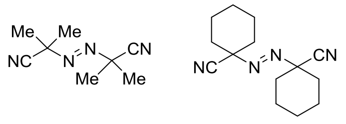
Fawaz Aldabbagh completed his PhD in 1997 with Prof Russ Bowman at Loughborough University, UK. He was postdoctoral fellow at Griffith University in Brisbane, Australia working with Profs Ken Busfield and Ian Jenkins. In 2000 Fawaz began his independent academic career at National University of Ireland Galway, where he remains as Senior Lecturer. Fawaz has diverse research interests, including heterocyclic, medicinal, and polymer chemistry with his research into radicals and homolytic aromatic substitution beginning with Russ Bowman.

1.1 Scope

The 2007 review by Bowman and Storey on HAS mainly reviewed the most widely used synthetic method of the time namely the accessing of heteroarenes and aromatics using Bu_3SnH or $(TMS)_3SiH$ with azo-initiator.[1] The difficulties in carrying out net oxidation in the presence of a Group 14 metal hydride reductant are rationalized along with an overview of recent synthetic examples. Over the last five years however there has been a renascence with more efficient and green chain reactions invented with the most prominent being visible light photoredox catalysis and base-promoted HAS. Studer and Curran provide an authoritative review on base-promoted HAS,[2] which is viewed as being catalyzed by an electron.[3] HAS reactions that combine photocatalysis with the latter, and photocatalysis that is used to regenerate the transition metal (e.g. Ni, Pd or Rh) involved in the aromatic substitution are not discussed herein. The many HAS reactions using oxidants, peroxides, and transition metals are also not reviewed. Here the subject is photochemical or light-induced HAS as alternatives to conventional Bu_3SnH-mediated HAS, in particular new chain reactions occurring in the absence of radical initiators. The review is not meant to be exhaustive, but an overview of recent literature.

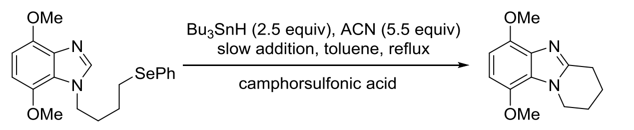
1.2 Use of Bu_3SnH for homolytic aromatic substitution

Despite intense research into alternatives, synthetically acceptable yields of novel heteroarenes and substituted aromatics continue to be reported using metal hydride-mediated HAS reactions.[1,4-28] It is now understood that careful choice of initiators and equivalents is required in order to optimize yields with generally greater than full equivalents of radical initiators required to support the non-chain reaction. For example higher yield of pyrido[1,2-*a*]benzimidazole **2** was obtained when 1,1'-azobis(cyclohexanecarbonitrile) ACN (Figure 1) is combined with Bu_3SnH, and added slowly to the phenylselenide substrate **1** rather than using 1,1'-azobis(isobutyronitrile) AIBN with Bu_3SnH under the same conditions (Scheme 2).[7] In toluene under reflux, ACN allows a slow generation of radicals for the rearomatization as well as giving further $Bu_3Sn^{\bullet}$ in the absence of propagation (ACN, $t_{1/2} \sim 40$ min, AIBN $t_{1/2} \sim 2$ min in at 110 °C).



AIBN **ACN**

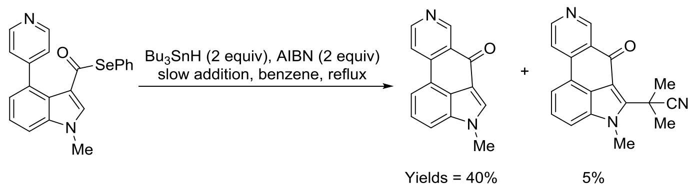
Figure 1. Structure of azo-initiators.



1 **2** (Yield = 70%)

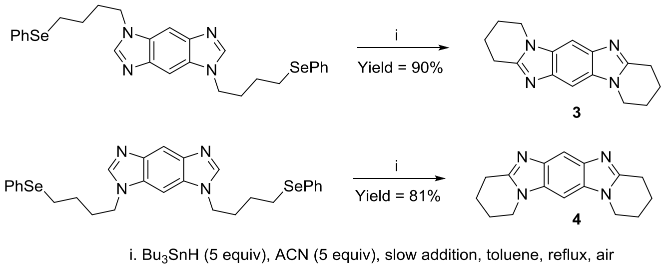
Scheme 2. Synthesis of pyrido[1,2-*a*]benzimidazole using Bu_3SnH.

Mechanistic studies have shown that azo-initiator derived radicals[7-12] and/or oxygen[12-14] may be involved in the hydrogen atom abstraction from the intermediate cyclohexadienyl radical (Scheme 1). It is thus tempting for researchers to add large amounts of azo-initiator however this can result in the incorporation of the initiator derived radicals into the aromatic substitution products[15-17] or through radical combination to give non-aromatic products.[11] HAS of 3-indolylacyl radical onto pyridine occurs in moderate yield, and is accompanied by the product of incorporation of the 2-cyano-2-propyl radical onto the 2-position of indole due the use of stoichiometric amounts of AIBN (Scheme 3).[16] However when aryl iodides are used as substrates single electron transfer (SET) chain mechanism may operate explaining the requirement for less than stoichiometric amounts of AIBN.[18,19]



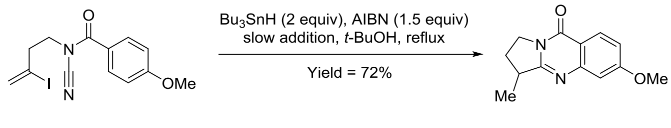
Scheme 3. Cyclizations of the 3-indolylacyl radical onto pyridine.

With an understanding of the requirements for the non-chain reaction, more than one C-C bond can be formed in one-pot, including double HAS to give alicyclic ring-fused imidazobenzimidazoles with the most facile being six-membered cyclizations giving pentacycles **3** and **4** in 90 and 81% yield (Scheme 4).[14]



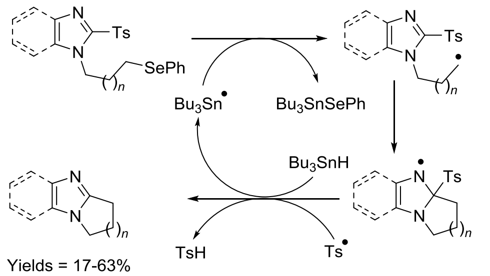
Scheme 4. One-pot double HAS mediated by Bu_3SnH.

There are examples of iminyl radicals undergoing HAS,[20] including cascades from *N*-acyl cyanamides with aromatic substitution facilitated by virtue of displacement of a substituent (hydrogen or alkyl) on the aromatic ring.[21-23] Although HAS is part of the cascade due to the migration of the hydrogen atom an overall reduction occurs (Scheme 5).[23]



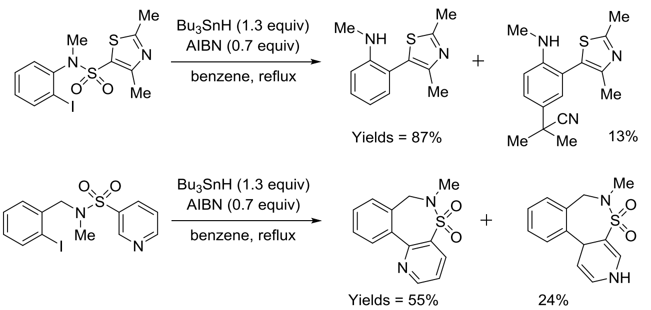
Scheme 5. Radical cascade involving *N*-acyl cyanamide.

A HAS chain reaction is possible using Bu_3SnH with azo-initiator if cyclization is accompanied by *ipso*-substitution.[17, 24-26] This is evidenced by the requirement for less than one equivalent of AIBN. The regeneration of the tin radical chain carrier using hydrogen atom abstraction from Bu_3SnH by the expelled tosyl group was proposed (Scheme 6).[26]



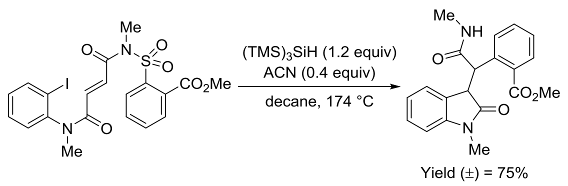
Scheme 6. HAS chain reaction using Bu_3SnH and *ipso*-substitution.

Smiles rearrangements usually proceed via a five-membered ring intermediate with a subsequent 8-*endo-trig* HAS reported.[27] The rearrangement can be facilitated by an *ipso*-substitution step.[17,24,28] AIBN fragment substitution and reduced dihydropyridine respectively accompanied the Smiles rearrangement and 7-membered aromatic substitution major products indicating inefficient propagation (Scheme 7).[17]



Scheme 7. Smiles rearrangement facilitated by *ipso*-substitution.

The Smiles rearrangement was incorporated into a cascade to give oxindole with reduction (Scheme 8).[28]

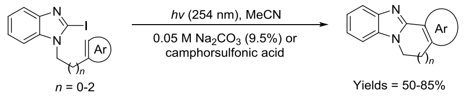


Scheme 8. Smiles rearrangement as part of a radical cascade.

2. Recent advances in light-induced homolytic aromatic substitution

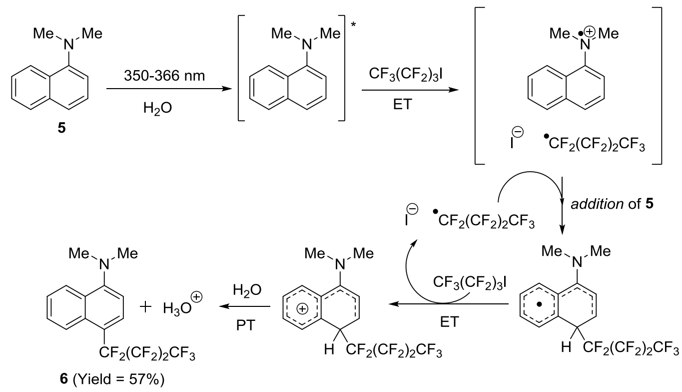
2.1 Use of UV light

It is well-established that UV-light can allow HAS to occur in the absence of radical initiators,[29-37] particularly aryl radical substitutions, which can be superior to those using Bu_3SnH.[36] Benzimidazol-2-yl radicals readily cyclize onto aromatics with best yields achieved in the presence of a small quantity of sodium carbonate required to quench HI (Scheme 9). Alternatively constrained cyclization was carried out under acidic conditions to allow for protonation of the basic 3-*N* to produce an electrophilic benzimidazol-2-yl radical,[37] which would be analogous to EAS, and the inverse of the Minisci reaction.[8,38]



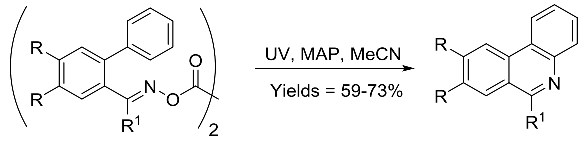
Scheme 9. Benzimidazol-2-yl radical cyclizations using UV-light.

Mechanistic studies for radical perfluoroalkylation of electron-rich aromatics demonstrated photoinduced electron-transfer (ET) with addition and proton transfer (PT) steps.[39,40] For example, *N*,*N*-dimethyl-1-naphthylamine **5** is converted to 4-substitution product **6** in water using a medium pressure Hg lamp (Scheme 10).[39]



Scheme 10. Heterogeneous photoinduced electron transfer.

UV-irradiation of dioxime oxalates generates iminyl radicals by decarboxylation. The iminyl radical undergoes intramolecular HAS to give phenanthridine in the presence of 4-methoxyacetophenone (MAP) in acetonitrile (Scheme 11).[41,42] The photosensitizer MAP improved the yield of the phenanthridine, and is proposed to be involved in the oxidative rearomatization.



Scheme 11. Decarboxylation of dioxime oxalates using UV-light.

2.2 Use of visible light photoredox with Ru(II) and Ir(III) catalysts

The last five years has seen the number of reports of HAS using visible light photoredox catalysis mushroom. It has now become one of the main pillars of aromatic substitution, which is understandable given it allows intricate carbon-carbon bond forming reactions to occur at room temperature. Moreover due to the lack of absorbance by organic molecules, side reactions associated with higher energy UV-light are avoided. There are several recent authoritative reviews on visible light photoredox catalysis,[43-49] but the present review is the first to focus on HAS. The most commonly used photoredox catalysts are Ru(II) and Ir(III) as $Ru(bpy)_3Cl_2$ and $Ir(ppy)_3$.

We believe the first report of visible light photoredox catalysis in HAS was made in 1984 reporting the conversion of stilbenediazonium salt into phenanthrene using the Pschorr reaction.[50] One of the drivers of the recent renaissance has been the work of Stephenson.[43,49] In 2010, visible light photoredox catalyzed HAS gave intramolecular five and six-membered cyclization of electrophilic alkyl radicals onto electron-rich indoles and pyrroles (Scheme 12).[51] The Ru(II) polypyridine complex ($Ru(bpy)_3Cl_2$ Figure 2) is excited by visible light via metal to ligand charge transfer leading to a species that is more easily reducible to Ru(I) using triethylamine.[52] Ru(I) acts as a reductant to give the cyclizing radical, and regenerating the catalyst with the source of the subsequent oxidation for the aromatic substitution less clear.

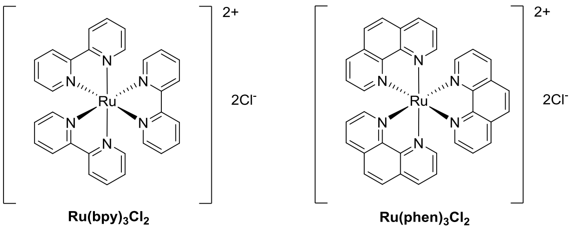
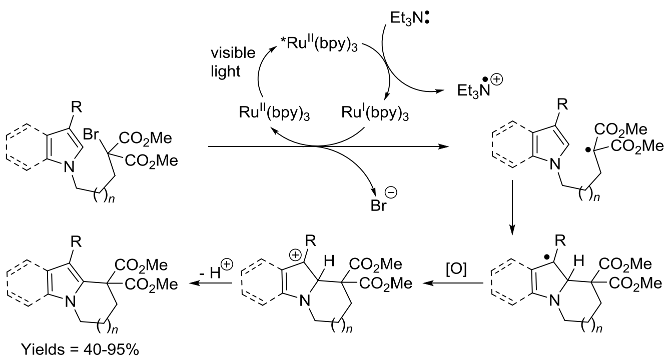
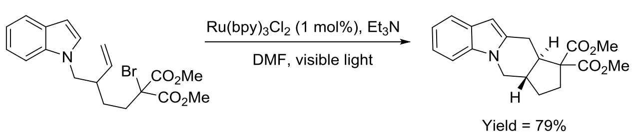


Figure 2. Structure of Ru(II)-photoredox catalysts.



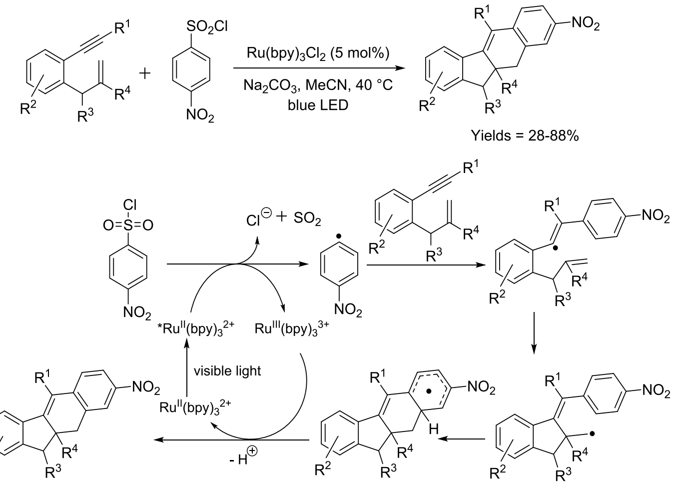
Scheme 12. One of the first synthetically useful HAS using visible light photoredox $Ru(bpy)_3Cl_2$ catalysis.

Impressive cascade radical cyclizations using visible light photoredox catalysis have since been reported,[51,53,54] with the first being a 5-*exo-trig* followed by six-membered substitution onto indole (Scheme 13).[51]



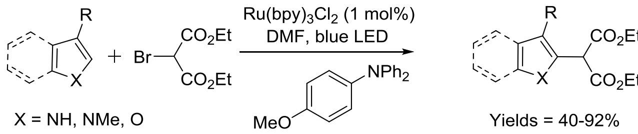
Scheme 13. Intramolecular cascade using Ru(II) photoredox catalysis.

Radical tandem 1,6-enyne cyclization was reported using the same catalyst with excited Ru(II) behaving as a reductant of 4-nitrophenylsulfonyl chloride (Scheme 14).[54] The substituent on the alkyne was important with the lowest yield of 28% obtained for the aliphatic alkyne (R^1 = hexyl), where 6-*exo* competed with 5-*exo* cyclization.



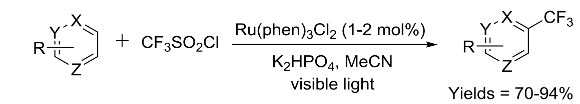
Scheme 14. Tandem Cyclization of 1,6-enyne.

Intermolecular HAS onto indoles, pyrroles and furans using diethyl bromomalonate is made possible by replacing the trialkylamine with an appropriate triarylamine of higher oxidation potential and that is unable to undergo competitive hydrogen atom transfer (Scheme 15).[55]



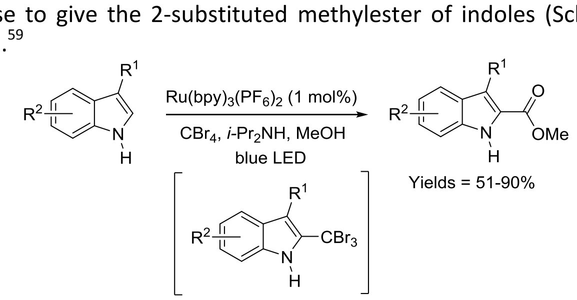
Scheme 15. Intermolecular substitution onto heterocycles.

Trifluoromethylation is essential in medicinal chemistry.[56] Nagib and MacMillan reported expedient trifluoromethylation of arenes and heteroarenes using photoredox catalysis whereby excited Ru(II) reduces triflyl chloride to give the trifluoromethyl radical (Scheme 16).[57] Trifluoromethylation of heterocycles can also occur when using trifluoroiodomethane as an electrophilic radical source.[58]



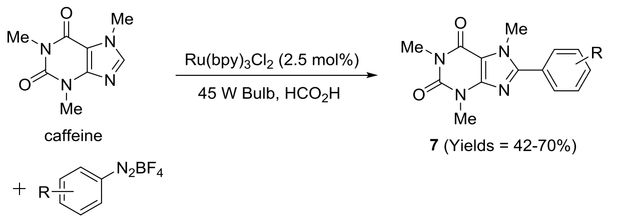
Scheme 16. Trifluoromethylation of aromatics.

Similarly, the tribromomethyl radical was generated from carbon tetrabromide using Ru(II)-photoredox catalysis, and undergoes substitution then methanolysis in the presence of base to give the 2-substituted methylester of indoles (Scheme 17).[59]



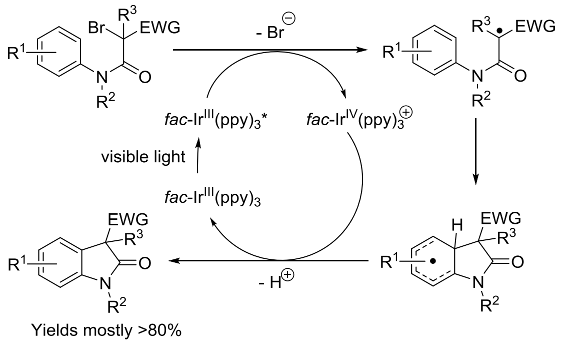
Scheme 17. Radical carboxylation of indoles.

Visible light Ru(II)-photoredox catalysis has been used to mediate the intermolecular coupling of aryldiazonium salts with arenes,[60] and *N*-heteroarenes,[61,62] including caffeine to give 8-aryl substituted derivatives **7** in moderate to good yields (Scheme 18).[62] The substitution of the nucleophilic aryl radical is facilitated by activating the *N*-heteroarene with formic acid in order to quaternize the basic *N*-atom of caffeine.



Scheme 18. Radical arylation of caffeine.

One of the earliest Ir(III)-photoredox catalyzed HAS reactions was the intramolecular non-enantioselective formation of 3,3-disubstituted oxindoles via five-membered cyclization of electrophilic *tert*-alkyl radicals (Scheme 19).[63] The intermediate Ir(IV) is proposed to facilitate the substitution by performing a SET oxidation of the π-cyclohexadienyl radical, which deprotonates to give the aromatic product to regenerate the catalyst.



Scheme 19. Synthesis of oxindoles using *fac*-Ir(ppy)$_3$ and 40 W lamp

Iridium (III) complexes (Figure 3) are widely used as visible light photocatalysts, including examples such as difluoromethylene-phosphonation, and difluoromethyleneacetamidation of aromatics by Liu and co-workers (Scheme 20).[64,65]

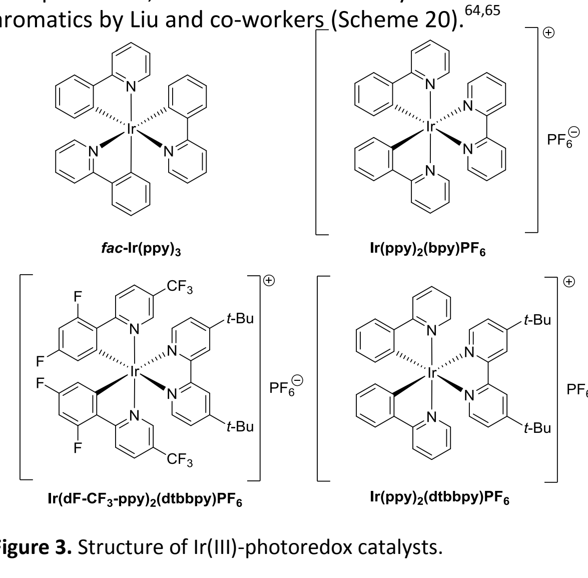
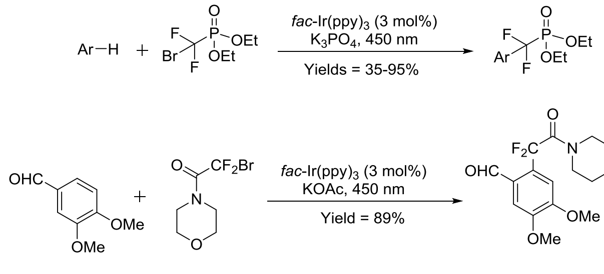
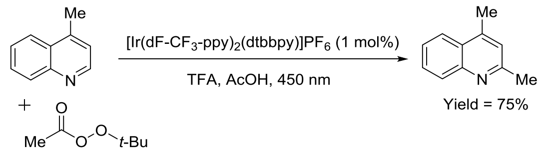


Figure 3. Structure of Ir(III)-photoredox catalysts.



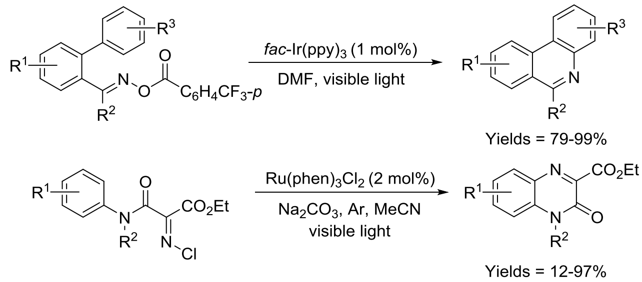
Scheme 20. Difluoromethyl radical aromatic substitution.

As part of a late stage functionalization of bioactive heterocycles, Minisci-style substitutions[8, 38] were demonstrated by methylation of quinoline under acidic conditions using acyl peroxide (Scheme 21).[66]



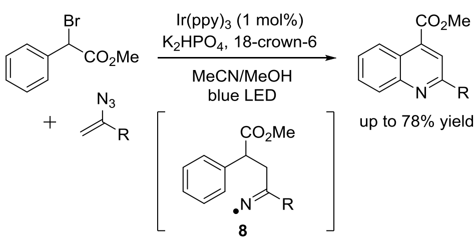
Scheme 21. Methylation of quinoline using acyl peroxide.

Iminyl radical intramolecular HAS using acyl oximes,[67] and chloroimines[68] allowed the respective formation of a variety of phenanthridines and quinoxalin-2-ones (Scheme 22). The generation of iminyl radicals from acyl oximes is reminiscent of earlier approaches by Walton using UV-light (Scheme 11),[41,42] and allow aldehydes to act as precursors for *in situ* generated acyl oximes.[69]



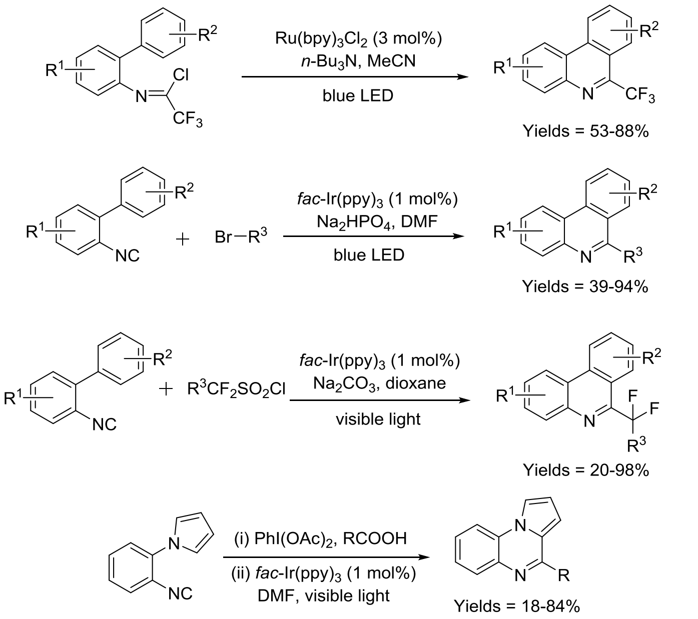
Scheme 22. Intramolecular iminyl radical aromatic substitutions.

Alternatively iminyl radicals were formed by addition of benzyl radicals onto vinyl azide precursors. The intermediate iminyl radical **8** underwent intramolecular substitution mediated by Ir(III) photoredox catalysis (Scheme 23).[70]



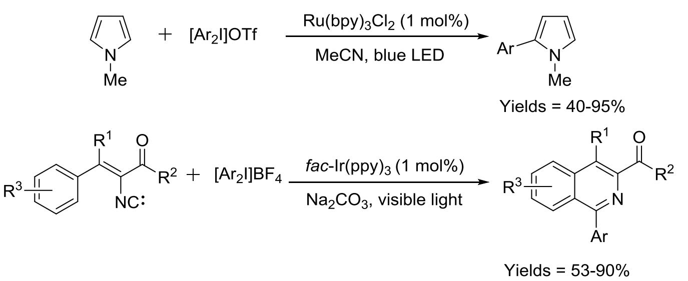
Scheme 23. Tandem iminyl radical formation and cyclization.

There are several reports on the synthesis of phenanthridines and quinoxalines from isocyanide precursors using visible light photoredox catalysis (Scheme 24).[71-74] Synthesis of 6-trifluoromethyl phenanthridine derivatives was achieved using intramolecular HAS using trifluoroacetimidoyl chlorides and Ru(II) catalyst.[71] 6-Substituted phenanthridine derivatives were synthesized using Ir(III) catalyst with intermolecular alkyl radical addition onto the isocyanide followed by radical cyclization.[72,73] Quinoxaline derivatives were prepared by photoinduced decarboxylation of phenyliodine (III) dicarboxylates with the generated alkyl radicals coupling with the isocyanide.[74]



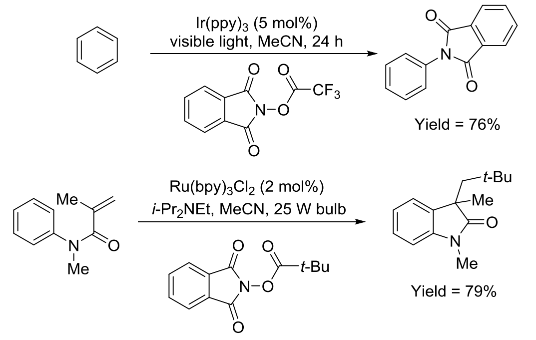
Scheme 24. Phenanthridines and quinoxalines from isocyanides.

Diaryliodonium salts are a source of aryl radicals substituting onto heterocycles; including pyrroles.[75] Isoquinolines were formed via the coupling of vinyl isocyanides with aryl radicals with subsequent HAS (Scheme 25).[76]



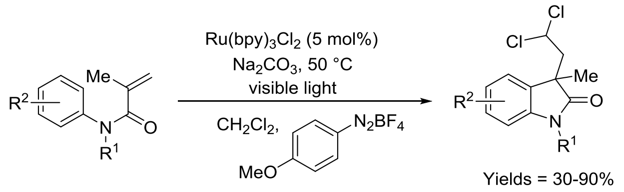
Scheme 25. Diaryliodonium salts as sources of aryl radicals for HAS.

N-(Acyloxy)phthalimides can be a source of nitrogen and carbon-centred radicals. Intermolecular substitution of the nitrogen of phthalimide,[77] and synthesis of 3,3-dialkyl substituted oxindoles via a tandem radical addition onto methacrylamide with subsequent intramolecular HAS of the tertiary adduct radical have been reported (Scheme 26).[78]



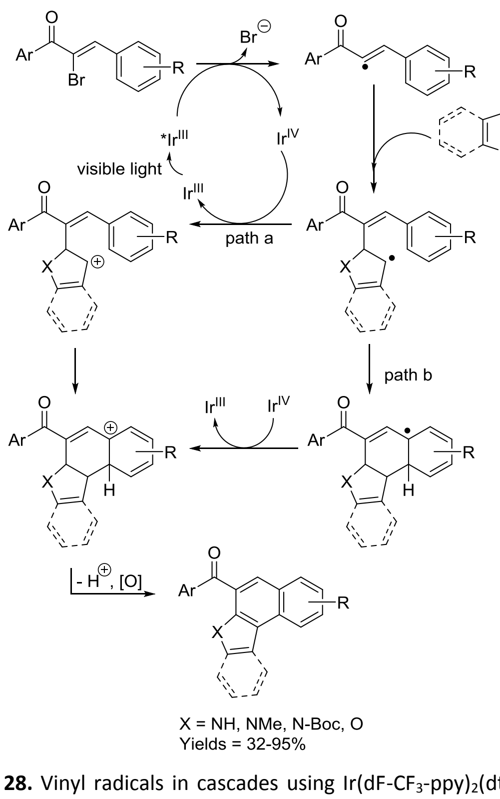
Scheme 26. *N*-(Acyloxy)phthalimides in photoredox catalysis.

Other tandem reactions using methacrylamide substrates to give oxindoles have been reported.[79] The aryl radical from the diazonium salt first abstracts a hydrogen atom from dichloromethane, which adds onto the methacrylamide with subsequent aromatic substitution of the tertiary alkyl radical (Scheme 27).



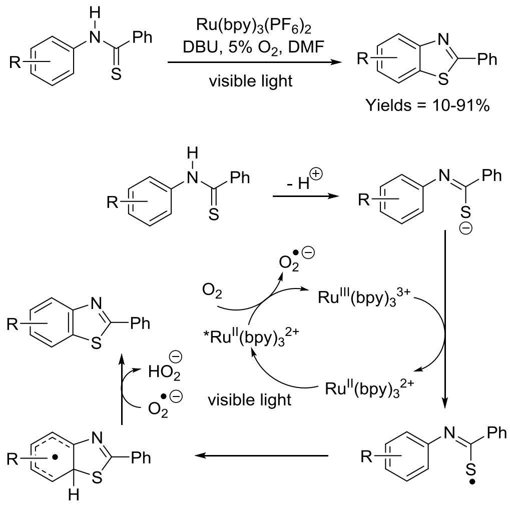
Scheme 27. Use of dichloromethane solvent as the radical source.

Photoredox catalysis cascades may involve radical or cationic cyclizations depending on the possibility of oxidation of the cyclizing radical to regenerate the catalyst (Scheme 28).[80]



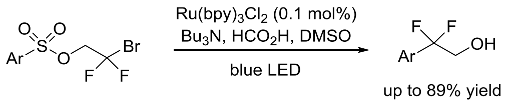
Scheme 28. Vinyl radicals in cascades using $Ir(dF\text{-}CF_3\text{-}ppy)_2(dtbbpy)PF_6$ photocatalysis.

Sulfur radicals were reported to undergo HAS to give 2-substituted benzothiazoles. The catalyst is thought to be involved in S-radical formation with oxygen proposed as the terminal oxidant for the cyclohexadienyl radical (Scheme 29).[81]



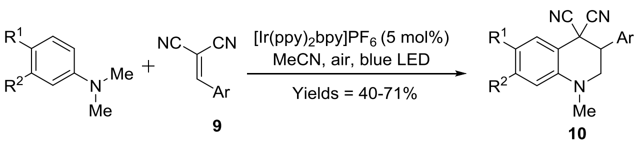
Scheme 29. Photoredox catalyzed HAS of sulfur radicals.

Smiles rearrangement using visible light photoredox catalysis has been achieved using aryl difluorobromosulfonates to give difluoroethanol substituted arenes (Scheme 30).[82]



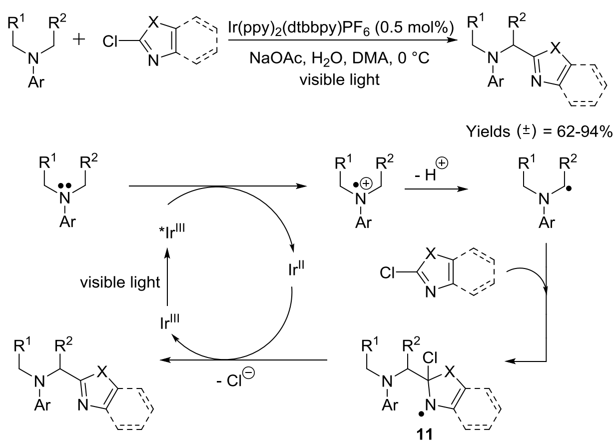
Scheme 30. Smiles rearrangement using photoredox catalysis.

Photoredox Ir(III)-catalysts can be used to generate nucleophilic α-amino alkyl radicals.[83-88] *N,N*-Dimethylanilines undergo addition onto electron-deficient alkenes **9** via α-amino radical intermediates and cyclization to give quinoline derivatives **10** (Scheme 31).[83]



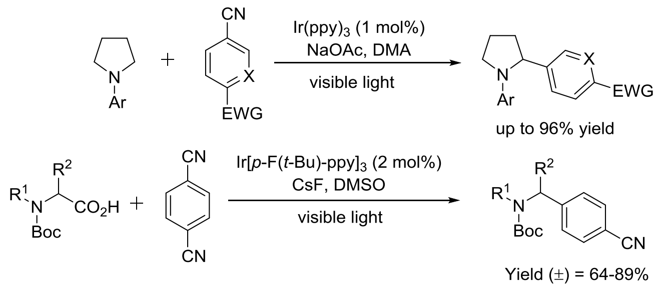
Scheme 31. α-Amino radicals in a tandem sequence.

The α-amino radical is formed via oxidation and deprotonation of tertiary amines. α-Heteroarylation of tertiary amines occurs through an aromatic *ipso*-substitution. Reduction of intermediate **11** regenerates the Ir(III) catalyst with loss of chloride to give the substitution product. (Scheme 32).[84]



Scheme 32. α-Amino radicals in an *ipso*-substitution.

MacMillian utilized nucleophilic α-amino radicals generated using visible light photoredox Ir(III) catalysis in substitutions onto electron-deficient dicyanobenzenes and heterocyclic variants, where the reductive loss of cyanide occurs (Scheme 33).[85,86] The α-amino radicals were also generated from α-amino acids via oxidative decarboxylation.[86] The choice of photocatalyst depends upon the required redox processes, and authors optimise the yield of the desired substitution product using several types of catalyst and conditions. HAS can work with both Ru(II) and Ir(III), but yields of the desired substitution product can vary.[83] In the case of the decarboxylative arylation α-amino acids low yields were obtained using Ir(ppy)$_3$, and highly oxidizing fluorinated Ir(III) photocatalyst alternatives.[86] The new catalyst Ir[*p*-F(*t*-Bu)-ppy]$_3$ (Figure 4) with electron-donating *tert*-butyl groups gave the best yields of substitution product by allowing electron-donation into the pyridine rings, so facilitating the reductive step of the catalytic cycle. CsF was found to be the most suitable base presumably due to its ability to increase the solubility of the carboxylate ion.



Scheme 33. Arylation of α-amino radicals using cyanide displacement.

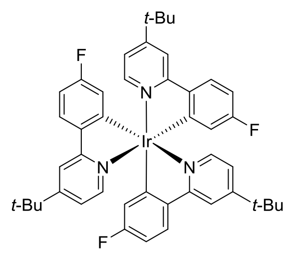
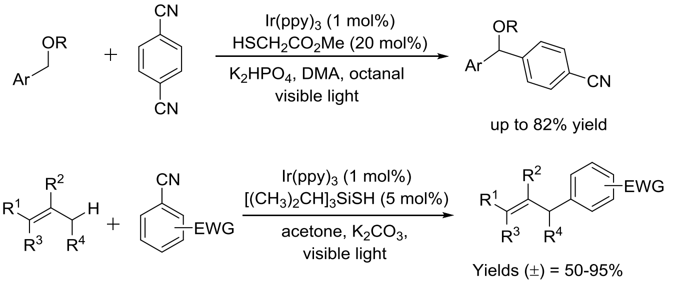


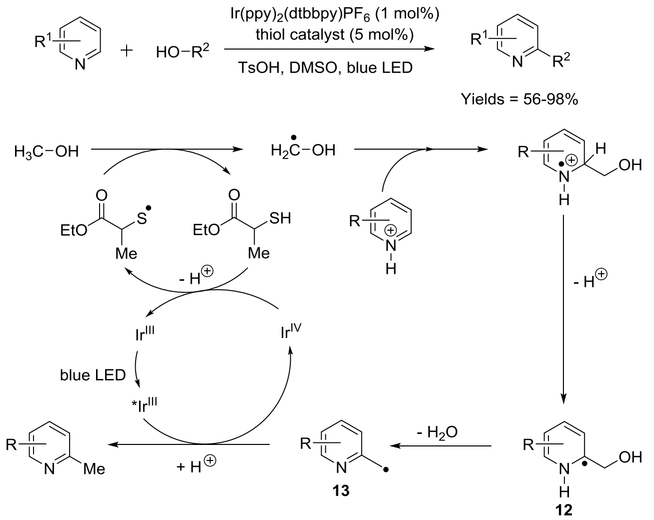
Figure 4. Structure of Ir[*p*-F(*t*-Bu)-ppy]$_3$

Couplings as a result of net loss of HCN under visible light photoredox $Ir(ppy)_3$ catalysis with cyanoarenes were reported for α-benzylic ethers and the sp^3-allylic carbon (Scheme 34).[89,90]



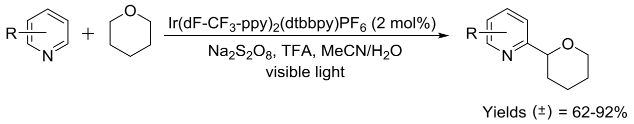
Scheme 34. Arylation of benzylic ether and sp^3-allylic substrates.

Alcohols can be used to alkylate electron-deficient arenes. The electrophilic thiyl radical was used to generate the reactive α-methyloxy radical by hydrogen atom abstraction from the alcohol through an organocatalytic cycle that accompanies the photoredox catalysis. (Scheme 35).[91] Elimination of water from the α-amino radical intermediate **12** generates a benzylic radical **13.** SET oxidation of the photocatalyst, and protonation of the reduced benzylic radical **13** gives 2-methylpyridines.



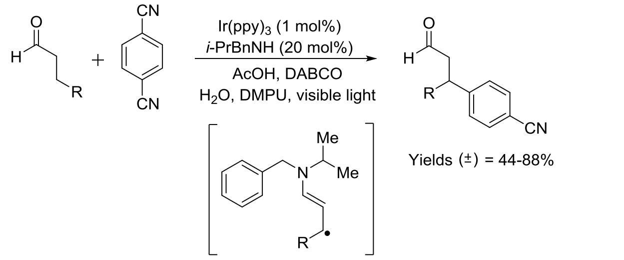
Scheme 35. Alcohol as a methylating agent via Minisci-type reaction.

α-Oxyalkyl radicals were generated from cyclic ethers using persulfate salt and Ir(III) photocatalyst.[92] Generation of the nucleophilic radical is facilitated by donation from the adjacent ethereal oxygen lone pair of electrons,[93,94] which allows for a Minisci-type reaction by substitution onto the 2-position of the pyridine ring (Scheme 36).[8,38]



Scheme 36. Arylation of THP using visible light photoredox catalysis.

β-Arylation of ketones and aldehydes with electron-deficient aromatics was achieved through β-enaminyl radical intermediates. The β-enaminyl radical was generated *in situ* using amine organocatalyst (Scheme 37).[95]



Scheme 37. Arylation through β-enaminyl radical intermediate.

2.3 Use of visible light photoredox with non-metal catalysts

Eosin Y (Figure 5) is an acidic fluorescent dye, which can be used for metal-free visible light photoredox catalysis.[96] Eosin Y has been reported to catalyze the arylation of furans, thiophenes and pyrroles using aryl and heteroaryl diazonium salts (Scheme 38).[97,98] The photocatalytic process is thought to involve SET reductive activation of the aryl diazonium salt with regeneration of the catalyst through SET oxidation of the intermediate π-radical **14**, as part of the rearomatization process.[97]

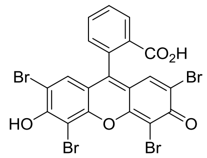
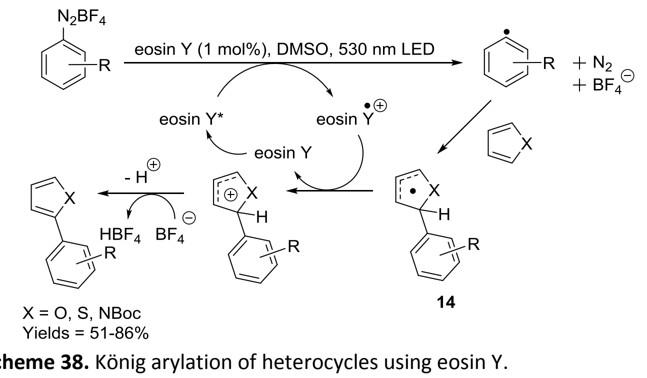
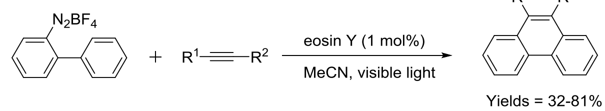


Figure 5. Structure of eosin Y.



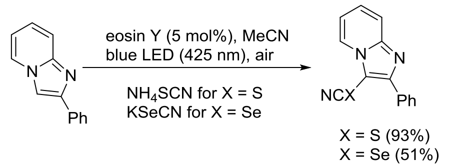
Scheme 38. König arylation of heterocycles using eosin Y.

Eosin Y catalyzes the [4+2] benzannulation of biaryldiazonium salts with alkynes to give phenanthrenes reminiscent of the Pschorr reaction.[50] The generated aryl radical adds onto the alkyne followed by vinyl radical cyclization (Scheme 39).[99]



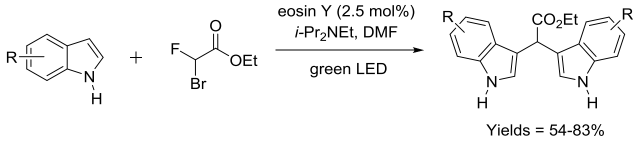
Scheme 39. Eosin Y [4+2] benzoannulation.

Recently thiocyanation and selenocyanation of imidazoheterocycles was reported using metal-free visible light photoredox catalysis (Scheme 40).[100]



Scheme 40. Thiocyanation and selenocyanation using eosin Y.

Eosin Y catalyzes the activation of ethyl bromofluoroacetate allowing for the one-pot double arylation of indoles (Scheme 41).[101] Arylation occurs at the indole 3-position by SET reduction and loss of bromine from the acetate. This is followed by a second arylation onto a second indole with the loss of fluorine.



Scheme 41. Synthesis of bisindolyl derivatives.

The photoredox catalyst PDI (Figure 6) catalyzes the reduction of aryl halides for substitution onto pyrroles (Scheme 42).[102] Mechanistic studies demonstrated the reduction of excited PDI to its radical anion using triethylamine. The PDI radical anion undergoes a second excitation to allow reduction of the aryl halide (Ar-X) substrate to its radical anion so regenerating neutral PDI. When compared to eosin Y which is limited to aryl precursors with weakly bound leaving groups, PDI has the capability to reduce aryl chlorides, as well as, bromides, and iodides under visible light.

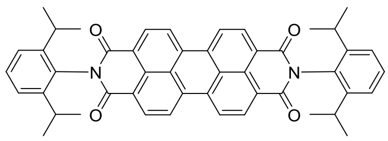
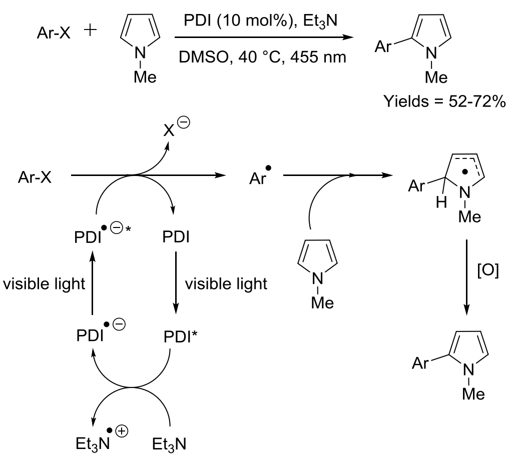


Figure 6. Structure of *N*,*N*-bis(2,6-diisopropylphenyl)perylene-3,4,9,10-bis(dicarboximide) (**PDI**).



Scheme 42. Arylation of pyrrole using PDI photoredox catalysis.

Dehydrogenative lactonization of 2-arylbenzoic acids to give benzo-3,4-coumarins is proposed to be HAS reaction via the cyclization of the benzoyloxy radical **15**. 9-Mesityl-10-methylacridinium ion is the photoredox catalyst ([Acr$^+$-Mes]) (Figure 7) and ammonium persulfate is used to regenerate the latter cationic species after SET with the substrate to give the benzoyloxy radical **15** (Scheme 43).[103]

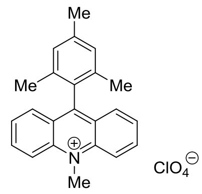
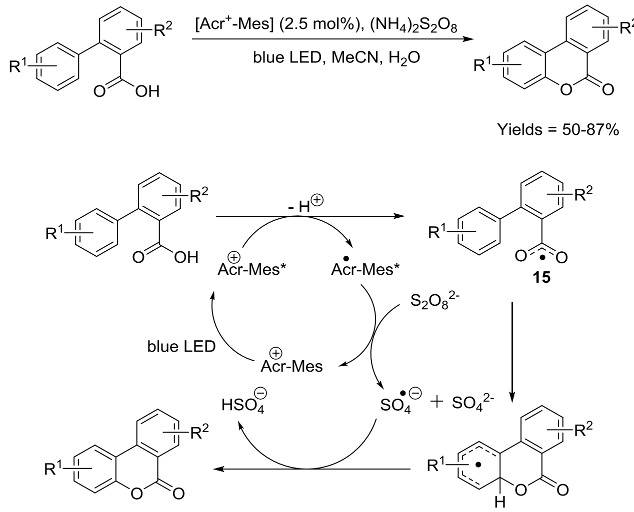


Figure 7. Structure of 9-mesityl-10-methylacridinium [Acr$^+$-Mes] perchlorate salt.



Scheme 43. Dehydrogenative lactonization of 2-arylbenzoic acids using [Acr$^+$-Mes] photoredox catalysis.

2.4 Other photoredox catalysis

HAS using UVA LED in combination with Au-photocatalyst $[Au_2(dppm)_2]Cl_2$ (Figure 8) has been used to obtain alicyclic ring-fused indoles (Scheme 44).[104]

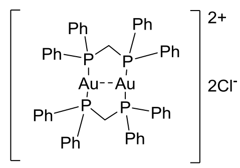
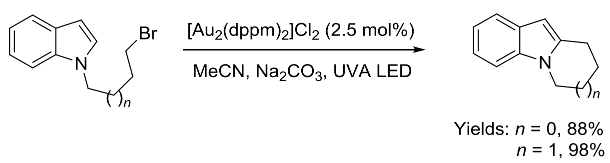
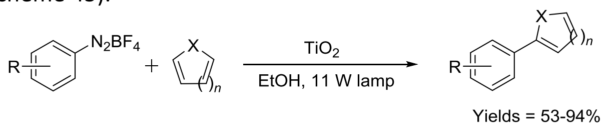


Figure 8. Structure of $[Au_2(dppm)_2]Cl_2$.



Scheme 44. Radical cyclizations onto indoles using Au-catalysis.

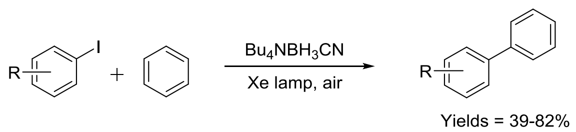
Analogous to Scheme 38, recyclable heterogeneous TiO_2-catalyst in place of eosin Y was shown capable of the photo-induced arylation of aromatics using aryldiazonium salts (Scheme 45).[105]



Scheme 45. Arylation of heterocycles using TiO_2-catalysis.

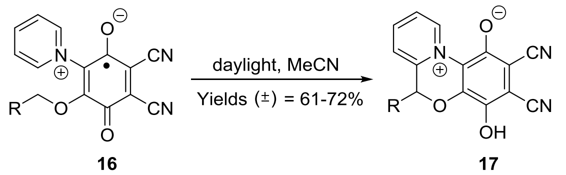
3. Miscellaneous homolytic aromatic substitutions

Irradiation using a Xe lamp allows for biaryl couplings using iodoarenes and benzene promoted by tetrabutylammonium cyanoborohydride in air (Scheme 46).[106]



Scheme 46. Cyanoborohydride-promoted arylation of benzene.

Zwitterionic hydroquinone-fused [1,4]oxazinium derivatives **17** were prepared via a photoinduced dehydrogenative coupling reaction. This involves the preparation of stable semiquinone radical anion substrates **16**, which are derived from DDQ. HAS occurs via cyclization of the nucleophilic α-alkyloxy radical onto the α-carbon of the quaternized heterocycle in the presence of an air atmosphere to facilitate the rearomatization (Scheme 47).[107]



Scheme 47. Use of stable zwitterionic radicals for HAS.

Light-sensitive Barton esters {pyridine-2-thione-*N*-oxycarbonyl (PTOC) or *O*-acyl thiohydroxamate ester} intermediates can be readily prepared *in situ* in the dark from robust carboxylic acids, and upon exposure to heat and/or visible light give cyclopropyl and alkyl radicals for five, six and seven-membered intramolecular HAS onto the indole or benzimidazole-2-position.[108] Commercial indole-1-propanoic acids **18** were converted into Barton esters **19** using *S*-(1-oxido-2-pyridinyl)-1,1,3,3-tetramethylthiouronium hexafluorophosphate (HOTT) (Figure 9) for tandem reactions upon thermal decomposition (Scheme 48). The tandem reaction involves fast addition of the intermediate ethyl radical **20** onto alkyl propiolates or phenylacetylene to give vinyl radicals that undergo substitution onto indole.[109] The cyclized (indol-3-yl) radical adduct is trapped by the 2-thiopyridinyl fragment from **19** returning chain carrier radical **20**. This is in agreement with Barton's radical chain proposal with rearomatization facilitated by elimination of 2-pyridinethiol.[110]

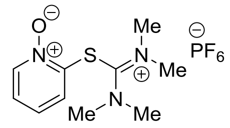
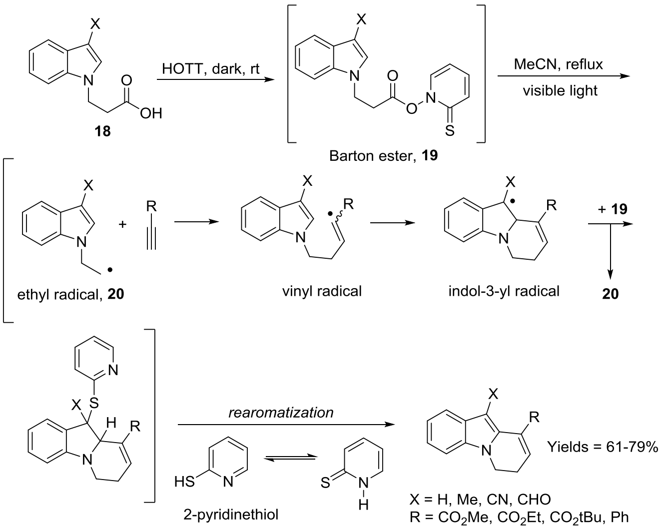


Figure 9. Structure of *S*-(1-oxido-2pyridinyl)-1,1,3,3-tetramethylthiouronium hexafluorophosphate (HOTT).



Scheme 48. Barton's esters for initiator-free tandem radical cyclizations.

4. Conclusions and outlook

Despite its synthetic utility, disadvantages with using Bu_3SnH include requirements for syringe pump addition in order minimize radical reduction, and more than stoichiometric amounts of azo-initiator in order to support the non-chain mechanism. HAS yields have been at best moderate to good, which meant that non-radical protocols for aromatic substitution were preferred. Over the past decade, the introduction of several radical initiator-free chain reaction protocols has resulted in HAS becoming a synthetic mechanism of choice rivaling organometallic, transition-metal and EAS protocols. In this review we have focused on photochemical techniques with seemingly the most widely used and promising being visible light photoredox catalysis, which allows HAS at room temperature. Visible is preferable to UV-light because the organic substrate and product cannot absorb, thus cannot become excited into performing unwanted side-reactions. The most widely used visible light photoredox catalysts are polypyridine complexes of Ru(II) and Ir(III). An alternative is the fluorescent dye called eosin Y, which has the distinct advantage of allowing HAS to occur under metal-free conditions. Our understanding of the mechanisms of HAS using visible light are however far from complete, including the oxidative aromatization step. Some authors use inert atmospheres, while others purposely add air or oxygen in order to facilitate the rearomatization.[81,83] Further the catalyst itself can undergo competitive HAS (at the aromatic ligands), which ultimately leads to its deactivation.[111] However recent reports of visible-light mediated syntheses of heterocycles demonstrate good yields can be achieved in the absence of an external catalyst including, the coupling of electron-deficient arenes onto indoles through electron donor-acceptor complexes,[112] and synthesis of polycyclic indolizines which themselves can act as photocatalysts.[113] Nevertheless careful optimization of photochemical conditions allows the interception of the substituting radical through reduction (as with Bu_3SnH) to be avoided, including in intermolecular HAS leading to high yields of aromatic substitution product. It is clear that light-induced chain reactions allow intricate carbon-carbon bond formation, including cascades with an aromatic substitution step, which would otherwise be prohibited or inefficient using Bu_3SnH. Therefore the recently invented efficient light-induced chain reactions have resulted in a dramatic decline in reports of aromatic substitution using Bu_3SnH.

Acknowledgments

The College of Science, National University of Ireland Galway is acknowledged for financial support.

References

1 W. R. Bowman and J. M. D. Storey, *Chem. Soc. Rev.*, 2007, **36**, 1803. DOI: 10.1039/b605183a
2 A. Studer and D. P. Curran, *Angew. Chem. Int. Ed.*, 2011, **50**, 5018. DOI: 10.1002 /anie.201101597
3 A. Studer and D. P. Curran, *Nature Chem.*, 2014, **6**, 765. DOI: 10.1038/nchem.2031
4 J. Coulomb, V. Certal, M.-H. Larraufie, C. Ollivier, J.-P. Corbet, G. Mignani, L. Fensterbank, E. Lacôte and M. Malacria, *Chem. Eur. J.*, 2009, **15**, 10225. DOI: 10.1002/chem.200900942
5 S. L. Kostiuk, T. Woodcock, L. F. Dudin, P. D. Howes and D. C. Harrowven, *Chem. Eur. J.*, 2011, **17**, 10906. DOI: 10.1002/chem.201101550
6 R. R. Castillo, C. Burgos, J. J. Vaquero and J. Alvarez-Builla, *Eur. J. Org. Chem.*, 2011, 619. DOI: 10.1002/ejoc.201001071
7 M. Lynch, S. Hehir, P. Kavanagh, D. Leech, J. O'Shaughnessy, M. P. Carty and F. Aldabbagh, *Chem. Eur. J.*, 2007, **13**, 3218. DOI: 10.1002/chem.200601450
8 F. Minisci, F. Fontana, G. Pianese and Y. M. Yan, *J. Org. Chem.*, 1993, **58**, 4207. DOI: 10.1021/jo00068a013
9 A. L. J. Beckwith, V. W. Bowry, W. R. Bowman, E. Mann, J. Parr and J. M. D. Storey, *Angew. Chem. Int. Ed.*, 2004, **43**, 95. DOI: 10.1002/anie.200352419
10 K. Fahey, R. Coyle, P. McArdle and F. Aldabbagh, *Arkivoc*, 2013, 401. DOI: 10.3998/ark.5550190.p008.208
11 P. T. F. McLoughlin, M. A. Clyne and F. Aldabbagh, *Tetrahedron*, 2004, **60**, 8065. DOI: 10.1016/j.tet.2004.06.120
12 D. P. Curran, H. Yu and H. Liu, *Tetrahedron,* 1994, **50**, 7343. DOI: 10.1016/S0040-4020(01)90466-1
13 D. P. Curran and A. I. Keller, *J. Am. Chem. Soc.*, 2006, **128**, 13706. DOI: 10.1021/ja066077q
14 V. Fagan, S. Bonham, M. P. Carty and F. Aldabbagh, *Org. Biomol. Chem.*, 2010, **8**, 3149. DOI: 10.1039/c003511d
15 D. Nanni, P. Pareschi, C. Rizzoli, P. Sgarabotto and A. Tundo, *Tetrahedron*, 1995, **51**, 9045. DOI: 10.1016/0040-4020(95)00348-C
16 M.-L. Bennasar and T. Roca, *J. Org. Chem.*, 2011, **76**, 4213. DOI: 10.1021/jo2006279
17 F. Ujjainwalla, M. L. E. N. Da Mata, A. M. K. Pennell, C. Escolano, W. B. Motherwell and S. Vázquez, *Tetrahedron,* 2015, **71**, 6701. DOI: 10.1016/j.tet.2015.07.048
18 D. C. Harrowven, B. J. Sutton and S. Coulton, *Tetrahedron*, 2002, **58**, 3387. DOI: 10.1016/S0040-4020(02)00295-8
19 D. C. Harrowven, I. L. Guy and L. Nanson, *Angew. Chem. Int. Ed.*, 2006, **45**, 2242. DOI: 10.1002/anie.200504287
20 G. Bencivenni, T. Lanza, R. Leardini, M. Minozzi, D. Nanni, P. Spagnolo and G. Zanardi, *J. Org. Chem.*, 2008, **73**, 4721. DOI: 10.1021/jo800453z
21 A. Beaume, C. Courillon, E. Derat and M. Malacria, *Chem. Eur. J.*, 2008, **14**, 1238. DOI: 10.1002/chem.200700884
22 M.-H. Larraufie, C. Ollivier, L. Fensterbank, M. Malacria and E. Lacôte, *Angew. Chem. Int. Ed.*, 2010, **49**, 2178. DOI: 10.1002/anie.200907237
23 M.-H. Larraufie, C. Courillon, C. Ollivier, E. Lacôte, M. Malacria and L. Fensterbank, *J. Am. Chem. Soc.*, 2010, **132**, 4381. DOI: 10.1021/ja910653k
24 W. B. Motherwell and A. M. K. Pennell, *J. Chem. Soc. Chem. Commun.*, 1991, 877. DOI: 10.1039/C39910000877
25 S. Caddick, K. Aboutayab and R. West, *Synlett* 1993, 231. DOI: 10.1055/s-1993-22414
26 F. Aldabbagh and W. R. Bowman, *Tetrahedron Lett.*, 1997, **38**, 3793. DOI: 10.1016/S0040-4039(97)00740-5
27 P. Lan, C. J. Jackson, M. G. Banwell and A. C. Willis, *J. Org. Chem.*, 2014, **79**, 6759. DOI: 10.1021/jo501255c
28 M. Pudlo, I. Allart-Simon, B. Tinant, S. Gérard and J. Sapi, *Chem. Commun.*, 2012, **48**, 2442. DOI: 10.1039/C2CC15670A
29 W. Wolf and N. Kharasch, *J. Org. Chem.*, 1965, **30**, 2493. DOI: 10.1021/jo01019a001
30 A. Fozard and C. K. Bradsher, *J. Org. Chem.*, 1967, **32**, 2966. DOI: 10.1021/jo01285a007
31 P. W. Jeffs, J. F. Hansen and G. A. Brine, *J. Org. Chem.*, 1975, **40**, 2883. DOI: 10.1021/jo00908a008
32 J. Grimshaw and A. P. De Silva, *J. Chem. Soc. Chem. Commun.*, 1979, 193. DOI: 10.1039/C39790000193
33 Y.-T. Park, C.-H. Jung, M.-S. Kim, K.-W. Kim, N. W. Song and D. Kim, *J. Org. Chem.*, 2001, **66**, 2197. DOI: 10.1021/jo001470e
34 A. M. Linsenmeier, C. M. Williams and S. Bräse, *J. Org. Chem.*, 2011, **76**, 9127. DOI: 10.1021/jo201542x
35 E. Campos-Gómez, P. J. Campos, H. F. González and M. A. Rodríguez, *Tetrahedron*, 2012, **68**, 4292. DOI:10.1016/j.tet.2012.03.056
36 M. A. Clyne and F. Aldabbagh, *Org. Biomol. Chem.*, 2006, **4**, 268. DOI: 10.1039/B512729G
37 J. M. O'Connell, E. Moriarty and F. Aldabbagh, *Synthesis*, 2012, **44**, 3371. DOI: 10.1055/s-0032-1316775
38 M. A. J. Duncton, *Med. Chem. Commun.*, 2011, **2**, 1135. DOI: 10.1039/C1MD00134E
39 S. Barata-Vallejo, M. M. Flesia, B. Lantaño, J. E. Argüello, A. B. Peñéñory and A. Postigo, *Eur. J. Org. Chem.*, 2013, 998. DOI: 10.1002/ejoc.201201271
40 B. Lantaño, S. Barata-Vallejo, M. R. Torviso, S. M. Bonesi, J. E. Argüello and A. Postigo, *J. Fluorine Chem.*, 2014, **161**, 149. doi:10.1016/j.jfluchem.2014.02.008
41 F. Portela-Cubillo, E. M. Scanlan, J. S. Scott and J. C. Walton, *Chem. Commun.*, 2008, 4189. DOI: 10.1039/B808625G
42 F. Portela-Cubillo, J. Lymer, E. M. Scanlan, J. S. Scott and J. C. Walton, *Tetrahedron*, 2008, **64**, 11908. DOI: 10.1016/j.tet.2008.08.112
43 J. M. R. Narayanam and C. R. J. Stephenson, *Chem. Soc. Rev.*, 2011, **40**, 102. DOI: 10.1039/b913880n
44 J. Xuan, L.-Q. Lu, J.-R. Chen and W.-J. Xiao, *Eur. J. Org. Chem.*, 2013, 6755. DOI: 10.1002/ejoc.201300596
45 D. P. Hari and B. König, *Angew. Chem. Int. Ed.*, 2013, **52**, 4734. DOI: 10.1002/anie.201210276
46 C. K. Prier, D. A. Rankic and D. W. C. MacMillan, *Chem. Rev.* 2013, **113**, 5322. DOI: 10.1021/cr300503r

47 M. N. Hopkinson, B. Sahoo, J.-L. Li and F. Glorius, *Chem. Eur. J.*, 2014, **20**, 3874. DOI: 10.1002/chem.201304823
48 R. A. Angnes, Z. Li, C. R. D. Correia and G. B. Hammond, *Org. Biomol. Chem.*, 2015, **13**, 9152. DOI: 10.1039/C5OB01349F
49 J. W. Beatty, and C. R. J. Stephenson, *Acc. Chem. Res.*, 2015, **48,** 1474. DOI: 10.1021/acs.accounts.5b00068
50 H. Cano-Yelo and A. Deronzier, *J. Chem. Soc., Perkin Trans. 2*, 1984, 1093. DOI: 10.1039/P29840001093
51 J. W. Tucker, J. M. R. Narayanam, S. W. Krabbe and C. R. J. Stephenson, *Org. Lett.*, 2010, **12**, 368. DOI: 10.1021/ol902703k
52 K. Monserrat, T. K. Foreman, M. Grätzel and D. G. Whitten, *J. Am. Chem. Soc.*, 1981, **103**, 6667. DOI: 10.1021/ja00412a022
53 J. W. Tucker and C. R. J. Stephenson, *Org. Lett.*, 2011, **13**, 5468. DOI: 10.1021/ol202178t
54 G.-B. Deng, Z.-Q. Wang, J.-D. Xia, P.-C. Qian, R.-J. Song, M. Hu, L.-B. Gong and J.-H. Li, *Angew. Chem. Int. Ed.*, 2013, **52**, 1535. DOI: 10.1002/anie.201208380
55 L. Furst, B. S. Matsuura, J. M. R. Narayanam, J. W. Tucker and C. R. J. Stephenson, *Org. Lett.*, 2010, **12**, 3104. DOI: 10.1021/ol101146f
56 A. Studer, *Angew. Chem. Int. Ed.*, 2012, **51**, 8950. DOI: 10.1002/anie.201202624
57 D. A. Nagib and D. W. C. MacMillan, *Nature*, 2011, **480**, 224. DOI: 10.1038/nature10647
58 N. Iqbal, S. Choi, E. Ko and E. J. Cho, *Tetrahedron Lett.*, 2012, **53**, 2005. DOI: 10.1016/j.tetlet.2012.02.032
59 Q.-Q. Yang, M. Marchini, W.-J. Xiao, P. Ceroni and M. Bandini, *Chem. Eur. J.*, 2015, **21**, 18052. DOI: 10.1002/chem.201503787
60 F. Gomes, V. Narbonne, F. Blanchard, G. Maestri and M. Malacria, *Org. Chem. Front.*, 2015, **2**, 464. DOI: 10.1039/C5QO00031A
61 J. Zhang, J. Chen, X. Zhang and X. Lei, *J. Org. Chem.*, 2014, **79**, 10682. DOI: 10.1021/jo5020432
62 D. Xue, Z.-H. Jia, C.-J. Zhao, Y.-Y. Zhang, C. Wang and J. Xiao, *Chem. Eur. J.*, 2014, **20**, 2960. DOI: 10.1002/chem.201304120
63 X. Ju, Y. Liang, P. Jia, W. Li, and W. Yu, *Org. Biomol. Chem.*, 2012, **10**, 498. DOI: 10.1039/C1OB06652H
64 L. Wang, X.-J. Wei, W.-L. Lei, H. Chen, L.-Z. Wu and Q. Liu, *Chem. Commun.*, 2014, **50**, 15916. DOI: 10.1039/C4CC07925F
65 L. Wang, X.-J. Wei, W.-L. Jia, J.-J. Zhong, L.-Z. Wu and Q. Liu, *Org. Lett.*, 2014, **16**, 5842. DOI: 10.1021/ol502676y
66 D. A. DiRocco, K. Dykstra, S. Krska, P. Vachal, D. V. Conway and M. Tudge, *Angew. Chem. Int. Ed.*, 2014, **53**, 4802. DOI: 10.1002/anie.201402023
67 H. Jiang, X. An, K. Tong, T. Zheng, Y. Zhang and S. Yu, *Angew. Chem. Int. Ed.*, 2015, **54**, 4055. DOI: 10.1002/anie.201411342
68 D. Li, H. Ma and W. Yu, *Adv. Synth. Catal.*, 2015, **357**, 3696. DOI: 10.1002/adsc.201500774
69 X.-D. An and S. Yu, *Org. Lett.*, 2015, **17**, 2692. DOI: 10.1021/acs.orglett.5b01096
70 Q. Wang, J. Huang and L. Zhou, *Adv. Synth. Catal*., 2015, **357**, 2479. DOI: 10.1002/adsc.201500141
71 W. Fu, M. Zhu, F. Xu, Y. Fu, C. Xu and D. Zou, *RSC Adv*., 2014, **4**, 17226. DOI: 10.1039/c4ra02384f
72 H. Jiang, Y. Cheng, R. Wang, M. Zheng, Y. Zhang and S. Yu, *Angew. Chem. Int. Ed.*, 2013, **52**, 13289. DOI: 10.1002/anie.201308376
73 Z. Zhang, X. Tang and W. R. Dolbier Jr, *Org. Lett.*, 2015, **17**, 4401. DOI: 10.1021/acs.orglett.5b02061
74 Z. He, M. Bae, J. Wu and T. F. Jamison, *Angew. Chem. Int. Ed.*, 2014, **53**, 14451. DOI: 10.1002/anie.201408522
75 Y.-X. Liu, D. Xue, J.-D. Wang, C.-J. Zhao, Q.-Z. Zou, C. Wang and J. Xiao, *Synlett*, 2013, **24**, 507. DOI: 10.1055/s-0032-1318155
76 H. Jiang, Y. Cheng, R. Wang, Y. Zhang, and S. Yu, *Chem. Commun.*, 2014, **50**, 6164. DOI: 10.1039/C4CC01122H
77 L. J. Allen, P. J. Cabrera, M. Lee and M. S. Sanford, *J. Am. Chem. Soc.*, 2014, **136**, 5607. DOI: 10.1021/ja501906x
78 Q. Tang, X. Liu, S. Liu, H. Xie, W. Liu, J. Zeng and P. Cheng, *RSC Adv*., 2015, **5**, 89009. DOI: 10.1039/C5RA17292F
79 Y. Liu, J.-L. Zhang, R.-J. Song and J.-H. Li, *Org. Chem. Front.*, 2014, **1**, 1289. DOI: 10.1039/c4qo00251b
80 S. Paria and O. Reiser, *Adv. Synth. Catal.*, 2014, **356**, 557. DOI: 10.1002/adsc.201301069
81 Y. Cheng, J. Yang, Y. Qu and P. Li, *Org. Lett.*, 2012, **14**, 98. DOI: 10.1021/ol2028866
82 J. J. Douglas, H. Albright, M. J. Sevrin, K. P. Cole and C. R. J. Stephenson, *Angew. Chem. Int. Ed.*, 2015, **54**, 14898. DOI: 10.1002/anie.201507369
83 S. Zhu, A. Das, L. Bui, H. Zhou, D. P. Curran and M. Rueping, *J. Am. Chem. Soc.*, 2013, **135**, 1823. DOI: 10.1021/ja309580a
84 C. K. Prier and D. W. C. MacMillan, *Chem. Sci.*, 2014, **5**, 4173. DOI: 10.1039/C4SC02155J
85 A. McNally, C. K. Prier and D. W. C. MacMillan, *Science,* 2011, **334**, 1114. DOI: 10.1126/science.1213920
86 Z. Zuo, and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2014, **136**, 5257. DOI: 10.1021/ja501621q
87 A. Singh, A. Arora and J. D. Weaver, *Org. Lett.*, 2013, **15**, 5390. DOI: 10.1021/ol402751j
88 J. J. Douglas, K. P. Cole and C. R. J. Stephenson, *J. Org. Chem.*, 2014, **79**, 11631. DOI: 10.1021/jo502288q
89 K. Qvortrup, D. A. Rankic and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2014, **136**, 626. DOI: 10.1021/ja411596q
90 J. D. Cuthbertson and D. W. C. MacMillan, *Nature*, 2015, **519**, 74. DOI: 10.1038/nature14255
91 J. Jin and D. W. C. MacMillan, *Nature,* 2015, **525**, 87. DOI: 10.1038/nature14885
92 J. Jin and D. W. C. MacMillan, *Angew. Chem. Int. Ed*., 2015, **54**, 1565. DOI: 10.1002/anie.201410432
93 W. K. Busfield, I. D. Grice and I. D. Jenkins, *J. Chem. Soc., Perkin Trans. 2*, 1994, 1079. DOI: 10.1039/P29940001079
94 I. D. Jenkins, *J. Chem. Soc., Chem. Commun.,* 1994, 1227. DOI: 10.1039/C39940001227
95 M. T. Pirnot, D. A. Rankic, D. B. C. Martin and D. W. C. MacMillan, *Science*, 2013, **339**, 1593. DOI: 10.1126/science.1232993
96 D. P. Hari and B. König, *Chem. Commun.*, 2014, **50**, 6688. DOI: 10.1039/c4cc00751d
97 D. P. Hari, P. Schroll and B. König, *J. Am. Chem. Soc.*, 2012, **134**, 2958. DOI: 10.1021/ja212099r
98 P. Maity, D. Kundu and B. C. Ranu, *Eur. J. Org. Chem.*, 2015, 1727. DOI: 10.1002/ejoc.201500006
99 T. Xiao, X. Dong, Y. Tang and L. Zhou, *Adv. Synth. Catal.*, 2012, **354**, 3195. DOI: 10.1002/adsc.201200569
100 S. Mitra, M. Ghosh, S. Mishra and A. Hajra, *J. Org. Chem.*, 2015, **80**, 8275. DOI: 10.1021/acs.joc.5b01369
101 S. D. Jadhav, D. Bakshi and A. Singh, *J. Org. Chem.*, 2015, **80**, 10187. DOI: 10.1021/acs.joc.5b01736
102 I. Ghosh, T. Ghosh, J. I. Bardagi and B. König, *Science*, 2014, **346**, 725. DOI: 10.1126/science.1258232
103 N. P. Ramirez, I. Bosque and J. C. Gonzalez-Gomez, *Org. Lett.*, 2015, **17**, 4550. DOI: 10.1021/acs.orglett.5b02269
104 S. J. Kaldas, A. Cannillo, T. McCallum and L. Barriault, *Org. Lett.*, 2015, **17**, 2864. DOI: 10.1021/acs.orglett.5b01260
105 J. Zoller, D. C. Fabry and M. Rueping, *ACS Catal*., 2015, **5**, 3900. DOI: 10.1021/acscatal.5b00668
106 T. Kawamoto, A. Sato and I. Ryu, *Org. Lett.*, 2014, **16**, 2111. DOI: 10.1021/ol500614q

107 C. Yi, S.-X. Liu, A. Neels, P. Renaud and S. Decurtins, *Org. Lett.*, 2009, **11**, 5530. DOI: 10.1021/ol902355b
108 R. Coyle, K. Fahey and F. Aldabbagh, *Org. Biomol. Chem.*, 2013, **11**, 1672. DOI: 10.1039/C3OB27313J
109 R. Coyle, P. McArdle and F. Aldabbagh, *J. Org. Chem.*, 2014, **79**, 5903. DOI: 10.1021/jo5008543
110 D. H. R. Barton, B. Garcia, H. Togo and S. Z. Zard, *Tetrahedron Lett.*, 1986, **27**, 1327. DOI: 10.1016/S0040-4039(00)84250-1
111 J. J. Devery III, J. J. Douglas, J. D. Nguyen, K. P. Cole, R. A. Flowers II and C. R. J. Stephenson, *Chem. Sci.*, 2015, **6**, 537. DOI: 10.1039/c4sc03064h
112 S. R. Kandukuri, A. Bahamonde, I. Chatterjee, I. D. Jurberg, E. C. Escudero-Adán and P. Melchiorre, *Angew. Chem. Int. Ed.,* 2015, **54**, 1485. DOI: 10.1002/anie.201409529
113 B. Sahoo, M. N. Hopkinson and F. Glorius, *Angew. Chem. Int. Ed.*, 2015, **54**, 15545. DOI: 10.1002/anie.201506868