

Photocatalysis

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# The Impact of Boron Hybridisation on Photocatalytic Processes

Alessandro Marotta<sup>+</sup>, Callum E. Adams<sup>+</sup>, and John J. Molloy\*



**Abstract:** Recently the fruitful merger of organoboron chemistry and photocatalysis has come to the forefront of organic synthesis, resulting in the development of new technologies to access complex (non)borylated frameworks. Central to the success of this combination is control of boron hybridisation. Contingent on the photoactivation mode, boron as its neutral planar form or tetrahedral boronate can be used to regulate reactivity. This Minireview highlights the current state of the art in photocatalytic processes utilising organoboron compounds, paying particular attention to the role of boron hybridisation for the target transformation.

## 1. Introduction

The selective introduction of organoboron motifs to modulate function and provide traceless reactivity handles is an expansive concept in the chemical sciences.<sup>[1]</sup> Paramount to the success of these functional groups is the capacity of boron to exist in solution in discrete hybridised forms as a neutral trigonal planar species or as the negatively charged, tetrahedral boronate (Figure 1).<sup>[2]</sup>

Although this change in ligand coordination may appear subtle, it enables stark differences in reactivity to be leveraged at the practitioner's discretion: a phenomenon that continues to be utilised in contemporary reaction development. In addition to their role in enabling technologies, boronic and borinic acids are finding increasing application in modern medicinal chemistry by enhancing potency through improved physicochemical performance. Pertinent examples include Bortezomib and Vaborbactam as shown in Figure 2.<sup>[3]</sup> Often the vacant p-orbital provides a docking site for Lewis basic components of target proteins enabling strong dative covalent binding,<sup>[4]</sup> while the hydroxyl ligand can be tuned to mimic hydrogen bonding of carboxylic acids.<sup>[5]</sup> Similar distinctions in hybridisation have been harnessed in materials science, enabling the rational design of boron molecules for conductive materials<sup>[6,7]</sup> and hydrogen activation.<sup>[8]</sup> Boron speciation also plays a critical role in sensors (Figure 2, bottom).<sup>[1c]</sup> In such scenarios, the boron species serves as a molecular antenna enabling detection of sugars and fluoride as their spectroscopically distinct boronates through speciation events.<sup>[9]</sup>

It is, however, in contemporary organic synthesis that organoboron compounds are at the forefront. With a multitude of classic and modern approaches which enable their facile installation and subsequent manipulation, the organoboron motif can truly be considered as the chameleon functionality of the organic chemists repertoire. Well-established transformations including hydroboration<sup>[10]</sup> and transition metal catalysed borylation<sup>[11]</sup> allow simple trans-

lation of abundant feedstock molecules to desirable borylated building blocks such as boronic acids, esters, and organoboranes (Figure 3, top). Utilising these linchpins in subsequent reactions, such as the venerable Suzuki–Miyaura<sup>[12]</sup> and Chan–Lam<sup>[13]</sup> cross-coupling, enables a platform for diversity-oriented-synthesis to rapidly generate chemical libraries from a common precursor, a vital technology for 3D fragment, hit-to-lead campaigns in drug discovery.<sup>[14]</sup> Again, intrinsic reactivity is governed by boron hybridisation and solution speciation events (Figure 3, middle), where boronate formation and subsequent stereospecific 1,2 rearrangement is the core foundation of oxidation/amination protocols<sup>[15]</sup> and stereoselective homologation chemistry to access complex polyketides as seen in assembly-line synthesis.<sup>[16]</sup> The introduction of boron protecting groups as a design concept to render the p-orbital inert to conventional ground state reactivity paradigms remains a crucial advance in the field (Figure 3, bottom). Trifluoroborates,<sup>[17]</sup> boronamides,<sup>[18]</sup> and N-coordinated boronates such as BMIDA<sup>[19]</sup> and BTIDA<sup>[20]</sup> have been

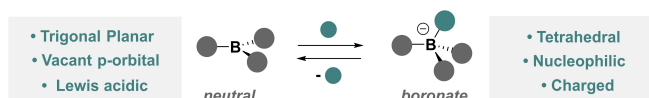
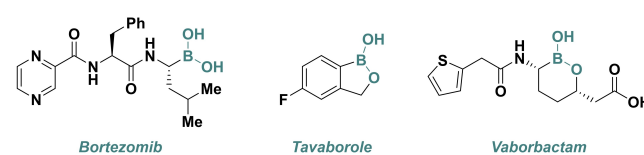


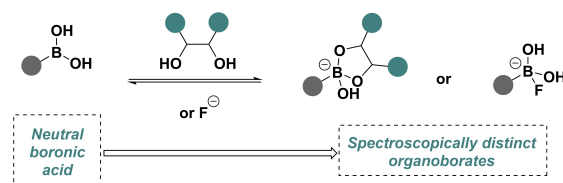
Figure 1. Boron hybridisation and solution speciation.

### Organoboron Compounds in Drug-discovery



- Covalent binders
- Tunable pKa
- Potent CO<sub>2</sub>H bioisosteres

### Organoboron Residues for Sensing and Drug Delivery



- Sugar sensing
- Fluoride sensing
- Insulin delivery

Figure 2. The prominent role of organoboron compounds

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strategically employed to enable chemoselective manipulation of organoboron species leading to seminal advances in the iterative synthesis of complex molecules.<sup>[21]</sup> A key milestone is the strategic use of boron protecting groups in automation platforms by Burke and co-workers allowing access to complex molecules at “the touch of a button”.<sup>[22]</sup>

Recent advances in catalyst design and method development have enhanced photocatalytic platforms in contemporary organic synthesis. Contingent on the modus operandi, differing key factors govern reactivity (Figure 4). Photo-induced electron transfer (PET) typically relies on redox properties and feasible electron transfer between the target substrate and photocatalyst, enabling reductive and oxidative quenching cycles to initiate subsequent reactivity.<sup>[23]</sup> Alternatively, excited state energy transfer (EnT) catalysis is reliant on triplet energies and efficient orbital overlap between substrate and photocatalyst.<sup>[24]</sup> As the abstraction of a hydrogen atom constitutes the main mechanistic step in photocatalysed hydrogen-atom transfer (HAT) reactions, bond dissociation energies of the target C–H bond play a vital role in governing reactivity in both direct and indirect HAT.<sup>[25]</sup>

It serves as no great surprise that the surge in methodological advances in photocatalysis has coincided with inherent progress in organoboron chemistry. While many reviews primarily focus on new photocatalytic strategies at hand, this Minireview serves to highlight the recent development of strategies using organoboron species, paying specific attention to the hybridisation of boron and its importance for tuning desired reactivity (Figure 5). Highlighted methods will include both reactions activating and retaining the C–B bond. Photocatalytic reactions that enable the formation of

a C–B bond will not be discussed as these have been extensively discussed elsewhere.<sup>[26]</sup>

## 2. Photocatalytic Activation of the C–B Bond

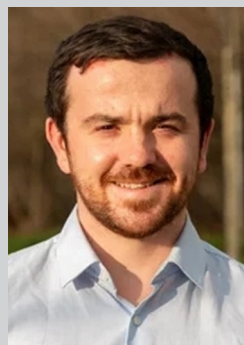
Operationally simple approaches that permit functional group interconversion of an organoboron motif to an alternate functionality are being intensively pursued.<sup>[27]</sup> While a rich palette of methods exist in ground state reactivity paradigms, the recent surge in light-enabled technologies has presented an often milder and cost-effective alternative to generate key intermediates. Of these technologies, photoredox catalysis is perhaps the most profound, where reactivity is contingent on properties of the target functional group.<sup>[23]</sup> Here, the above-mentioned structural dichotomy of organoboron compounds plays a prominent role, with both discrete hybrid forms displaying significant differences in redox properties (Figure 6). Common trigonal-planar boron motifs such as boronic acids and esters are electron deficient in nature, resulting in prohibitively high oxidation potentials that require powerful photocatalysts for activation, limiting functional group tolerance.<sup>[28]</sup> However, a simple switch via occupation of the p-orbital increases electron density of the C–B bond, lowering oxidation potentials. The resultant boronate can efficiently interact with various reductants, most notably excited state photocatalysts, to generate reactive radical derivatives via C–B bond scission. Intriguingly, this logic contradicts ground state reactivity paradigms where p-orbital occupation renders the organoboron motif inert.<sup>[1a]</sup> This section serves to highlight the importance of hybrid-



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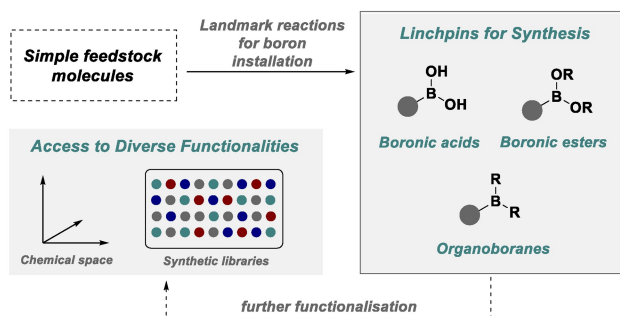


*Callum E. Adams was born in Oxford (UK), and obtained his MChem degree at Cardiff University under the supervision of Dr. Louis C. Morrill (2019), spending a year abroad working with Assoc. Prof. Kellie Tuck at Monash University (Australia). He began his doctoral studies with Dr. Craig P. Johnston at the University of St Andrews (2019). He was awarded an RSE Saltire Early Career Fellowship in his third year to support work at the Max Planck Institute of Colloids and Interfaces with Dr. John J. Molloy.*

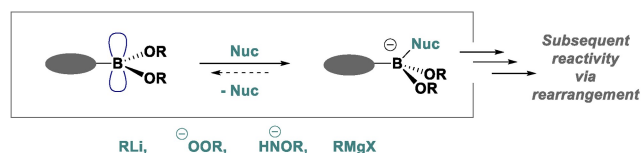


*Born in Glasgow (Scotland), John J. Molloy carried out his MChem (2014) and doctoral studies (2018) at the University of Strathclyde with Prof. Allan J. B. Watson. After a secondment to the University of St Andrews he joined the group of Prof. Ryan Gilmour as an Alexander von Humboldt Post-doctoral Research Fellow. He started his independent career at the Max Planck Institute of Colloids and Interfaces in the Biomolecular Systems department (2021) supported by a Liebig Stipendium from VCI.*

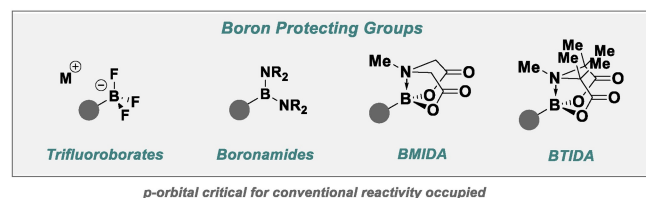
## The Utility of Organoboron Reagents in Organic Synthesis



## Importance of the Boron p-Orbital in Ground State Reactivity



## Boron Protecting Groups as Synthetic Tools in Organic Synthesis



## Platform for Automation and Iterative Synthesis of Complex Molecules

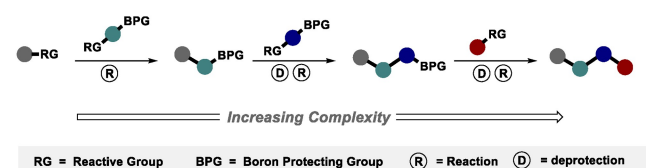


Figure 3. The ground state reactivity of organoboron compounds.

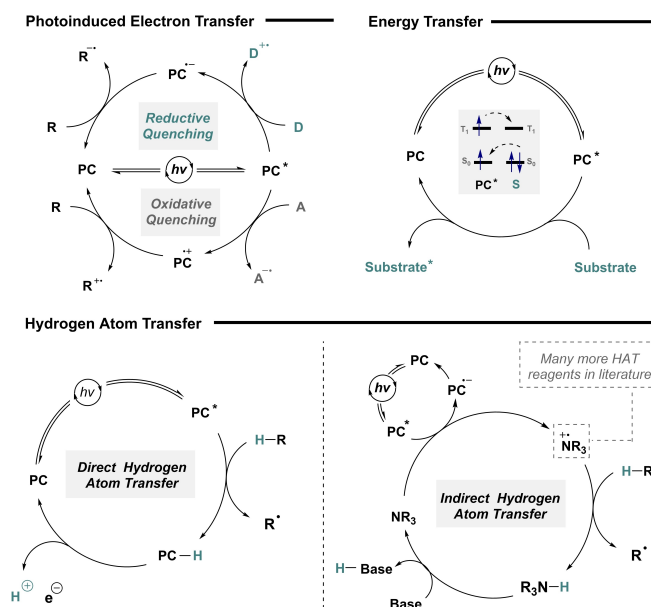


Figure 4. Prominent reaction manifolds in photocatalysis.

## The Critical Role of Boron Hybridisation in Emerging Photocatalytic Strategies

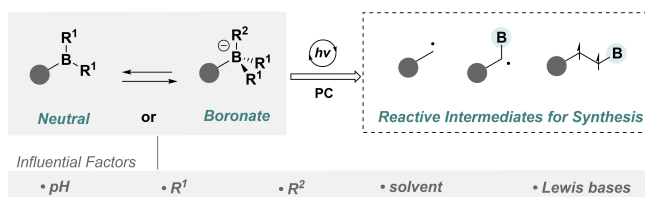
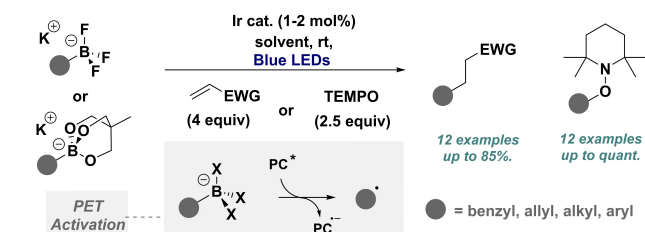


Figure 5. Exploring the impact of boron hybridisation on photocatalytic reactions.

## Trifluoroborates and Triolborates as Radical Precursors

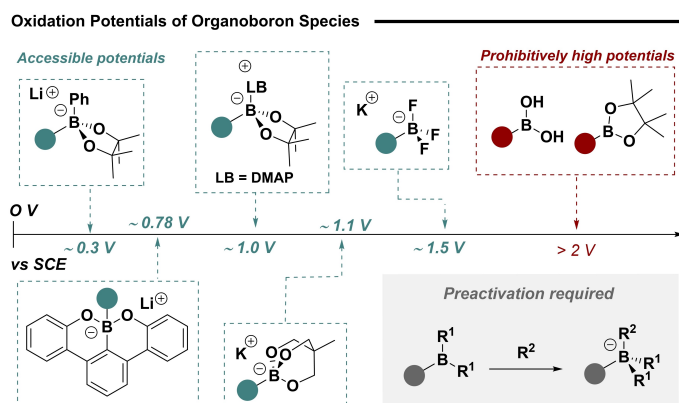
Scheme 1. Photocatalytic activation of potassium trifluoroborates and triolborates. Ir cat. = [Ir(dF(CF<sub>3</sub>)ppy)<sub>2</sub>(bpy)](PF<sub>6</sub>).

isation and solution speciation for the photocatalytic activation of the C–B bond.

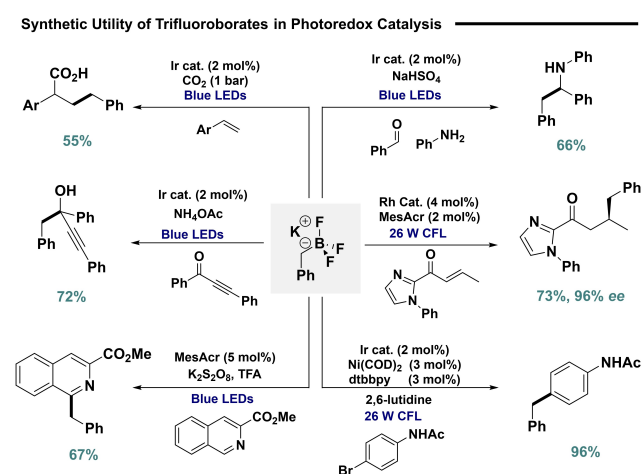
## 2.1. Photoredox Activation of Preformed Tetracoordinated Borates

The merger of organoboron and photochemistry has a rich history in synthetic chemistry, with the direct excitation of tetraphenylboronate<sup>[29]</sup> by Williams and co-workers in 1967 serving as a blueprint for future catalytic strategies involving boronates.<sup>[30]</sup> Building on these seminal contributions, in 2012, Akita and co-workers demonstrated the synthetic potential of potassium trifluoroborates and triolborates as radical precursors in photoredox catalysis (Scheme 1).<sup>[31]</sup> Gathered knowledge on redox potentials by cyclic voltammetry enabled strategic reaction design, employing [Ir(dF(CF<sub>3</sub>)ppy)<sub>2</sub>(bpy)](PF<sub>6</sub>) as a suitable catalyst under blue light irradiation to reductively quench the boronates to form alkyl and aryl radicals. Interception of the resultant radicals by a Giese acceptor or TEMPO enabled the rapid construction of C–C and C–O bonds. A key highlight of this discovery was the inversion of conventional ground state chemoselectivity, as boronic esters were retained under model reaction conditions, further reiterating the requirement of boronate formation as a prerequisite for photoactivation. This landmark study would lay the foundation for what was to be a surge in method development employing trifluoroborates as radical precursors.<sup>[32]</sup>

Their ease of isolation and long-term storage has ensured that trifluoroborates enjoy broad use as radical precursors in a plenum of transformations (Scheme 2). Pertinent examples include the carbo-functionalisation of



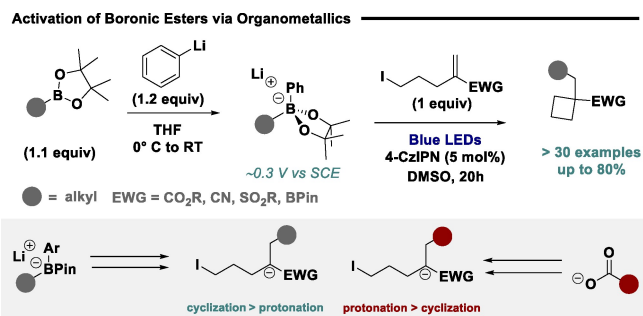
**Figure 6.** A comparison of oxidation potentials of organoboron species. DMAP = 4-(dimethylamino)pyridine.



**Scheme 2.** Synthetic utility of trifluoroborates as radical precursors.

styrenes (Scheme 2, top left),<sup>[33]</sup> radical addition to activated electrophiles (Scheme 2, top right),<sup>[34]</sup> and Minisci-type addition to heteroarenes (Scheme 2, bottom left),<sup>[28],[35]</sup> among others.<sup>[36]</sup> However, trifluoroborates are perhaps most celebrated for their role as coupling partners in metallophotoredox processes (Scheme 2, bottom right), pioneered by Molander and co-workers.<sup>[37]</sup> This platform enables the construction of C(sp<sup>3</sup>)-C(sp<sup>2</sup>) bonds under mild reaction conditions, which was previously considered to be a persistent challenge for conventional transition metal catalysis.

A prominent feature that has contributed to the popularity of trifluoroborates as radical precursors is the irreversibility of C-B bond scission. As a result, single-electron-transfer (SET) reactions, although occasionally slightly endergonic in nature, remain feasible. Despite this, trifluoroborates span a vast range of oxidation potentials (1.1 V to 1.83 V, benzyl vs. primary or aryl) providing a degree of unpredictability with substrate specificity.<sup>[38]</sup> To address this, boronate precursors with a lower oxidation potential, achievable by increasing electron density at boron, are required.



**Scheme 3.** Activation of boronic esters via nucleophilic addition to the p-orbital with organometallic reagents.

In 2019, Aggarwal and co-workers demonstrated the synthetic utility of organolithium-derived organoborates as radical precursors (Scheme 3).<sup>[39]</sup> Simple alkyl boronic esters could be rapidly transformed to the redox-active boronate, creating a boron species with a significantly reduced oxidation potential ( $E_{p/2} = 0.31$  V vs. SCE). The key activation involved a highly exergonic SET between the boronate and 4-CzIPN photocatalyst ( $E_{1/2} [\text{PC}^*/\text{PC}^-] = 1.35$  V vs. SCE in MeCN). Addition of the generated radical to an electron-deficient alkene, followed by SET with the reduced state of the photocatalyst resulted in an anion primed for intramolecular cyclisation (Scheme 3, bottom). Here, boronate precursors play a pivotal role in cyclobutane formation, allowing fully aprotic conditions. Comparable precursors, such as carboxylates, led to undesired protonation of the intermediate anion.<sup>[40]</sup> The same group has also demonstrated the versatility of this activation mode through a remarkable activation/rearrangement protocol involving 1,2 bis-boryl systems.<sup>[41]</sup> In this case, the arylboronate is formed on the less hindered primary boronic ester, but, after radical generation, a boryl rearrangement occurs, affording the more stable secondary radical for subsequent reactivity. Recently, organolithium-derived organoborates have also seen utility in photoredox-catalysed protodeboronation<sup>[42]</sup> and styrene carbofunctionalisation protocols.<sup>[43]</sup> While these boronates are typically formed in situ under stringently dry conditions, it is believed the enhancement of redox proper-

ties will lead to new synthetic endeavors and future discoveries.

## 2.2. In Situ Activation of Trigonal-Planar Organoboron Species

Often employed in ground state activation modes, the utility of boronic acids and esters has been comparatively underexplored in excited state reactivity paradigms involving direct C–B bond scission. Cognizant of their prohibitively high oxidation potentials,<sup>[28]</sup> users typically favour prefunctionalisation to access boronate motifs, a prerequisite for photoredox activation.<sup>[32]</sup> As this often requires direct formation via organometallics, or an additional synthetic step, protocols that permit the in situ activation of a neutral organoboron species through a dative interaction, or boron speciation, provide a complementary platform to existing technologies.

While designing a continuous flow protocol for the venerable Ir/Ni-catalysed cross-coupling of organoboron compounds,<sup>[37c]</sup> Ley and co-workers experienced solubility issues using trifluoroborates in sustainable solvents.<sup>[44]</sup> Through thoughtful reaction design, the group were able to overcome this obstacle by in situ activation of boronic esters using DMAP as a nucleophilic Lewis base additive (Scheme 4, top). The ensuing boronate ( $E_{1/2} = +0.81$  V vs. SCE) could then engage with the photocatalyst ( $E_{1/2}[\text{PC}^*/\text{PC}^{\bullet-}] = 1.2$  V vs. SCE) enabling reductive quenching to generate an alkyl radical. Harnessing this activation mode, the authors developed metallophotoredox cross-coupling and radical addition to cyanoarenes (Scheme 4, top). This method has also been complemented by a protocol that is catalytic in Lewis base through the simple use of methanol

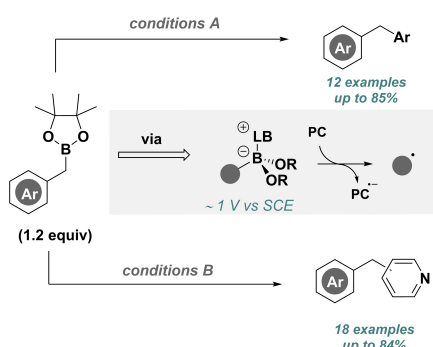
as a co-solvent (Scheme 4, bottom).<sup>[45]</sup> This field has vastly expanded, with many research groups making use of various additives such as organic and inorganic bases for the in situ activation of boronic esters and acids alike.<sup>[46]</sup>

Contingent on reaction media, boronic acids can exist in solution in many discrete forms through a series of complex equilibria.<sup>[2]</sup> While this is often reliant on the Lewis acidity of the boron p-orbital, external factors such as pH, solvent, and additives can distort this equilibria to favour one hybridised form over another. Recently, several studies have capitalised on this phenomenon to prompt the formation of photoredox-active boronates in solution. In 2020, Bloom and co-workers delivered a striking example harnessing water as a co-solvent to activate a boronic acid towards reductive quenching with Lumiflavin (Scheme 5, top).<sup>[47]</sup> The consequent radical could be trapped via Giese addition to form desirable C–C bonds. A key highlight is the use of heteroaryl boronic acids, notoriously prone to proto-deboration in aqueous media.<sup>[48]</sup>

In 2021, Sharma and co-workers disclosed a powerful solution to previously troublesome alkyl substrates (Scheme 5, bottom).<sup>[49]</sup> In this case, DMA was employed as a dative solvent for in situ activation of the trigonal-planar boronic acid. The solvent-assisted tetrahedral boronate (1.13 V vs. SCE in MeCN) could undergo reductive quenching with the photocatalyst (4-CzIPN, 1.35 V vs. SCE in MeCN) to extrude an alkyl radical which engaged SOMO-philic such as Giese acceptors, vinyltrifluoromethyls, and allylsulfones. Remarkably, the authors demonstrated chemoselectivity of boronic acids in the presence of boronic esters, highlighting the importance of the boronic acid functionality for suitable boronate formation.<sup>[50]</sup>

### Activation of Boronic Acids/Esters via Lewis Bases

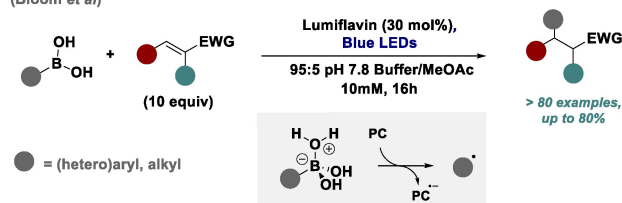
#### Cross-coupling Reactions



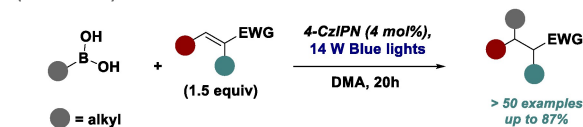
**Scheme 4.** In situ activation of neutral boronic esters and acids. Ir cat. = [Ir(dF(CF<sub>3</sub>)ppy)<sub>2</sub>(dtbbpy)](PF<sub>6</sub>).

### Activation of Boronic Acids via in situ Solvent Interactions

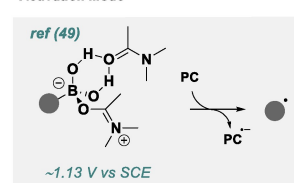
#### (Bloom et al)



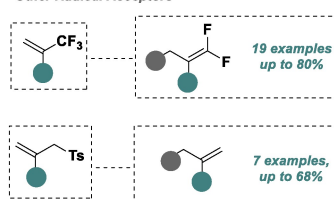
#### (Sharma et al)



#### Activation Mode



#### Other Radical Acceptors



**Scheme 5.** Activation of trigonal-planar boronic acids.

### 2.3. Emerging Concepts for Photocatalyst-Free Activation

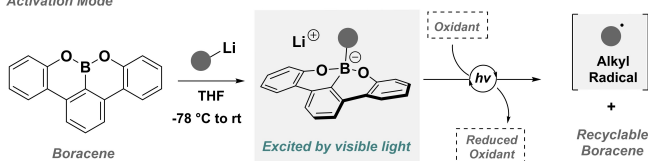
Photocatalysis has become a prominent force in modern synthetic chemistry. Its target, among others, was to address the inability of organic molecules to absorb light irradiation outwith the UV region ( $>400$  nm). However, photocatalysis, while still in its prime, has subtle drawbacks that continue to hinder its uptake in many aspects of synthesis, such as the continuous use of prohibitively expensive precious metal catalysts.<sup>[51]</sup> As such, catalyst-free photochemical activation is often pursued. To achieve such a feat, chemists rely on reagent or method design to elicit bathochromic shifts in the visible light spectrum to enable efficient photon absorption of the target molecule with a desirable light source.<sup>[52]</sup>

Through elegant ligand design, Ohmiya and co-workers developed an efficient catalyst-free activation of an organoboron species (Scheme 6).<sup>[53]</sup> Easily accessible boracene, when exposed to organolithium reagents, can generate a boronate which absorbs visible light. The direct excitation in the presence of a suitable oxidant permits the efficient generation of the target radical, mitigating the requirement for catalyst activation. The applicability of this activation mode has been demonstrated in many reactions including addition to heteroarenes, Giese-type addition, and cross-coupling.<sup>[53]</sup> Since these seminal studies, the group have made further advances in ligand design improving synthesis and absorption properties,<sup>[54]</sup> while the boronate has also been strategically aligned in NHC-catalysed methods.<sup>[55]</sup>

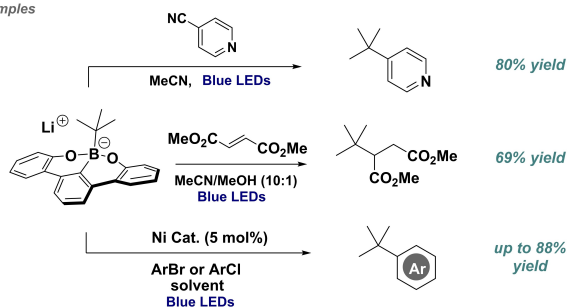
In addition to photocatalysis-based strategies, the formation of electron donor/acceptor (EDA) complexes has had a visible impact in recent years.<sup>[56]</sup> The field of C–B bond activation has been positively impacted by this development as is evident from the prominent work by Aggarwal and co-workers (Scheme 7, top).<sup>[57]</sup> Again, boron hybridisation is key to success, with the electron-rich boronate species forming a noncovalent interaction with the

#### C–B Bond Activation via Direct Excitation of Borates

Activation Mode



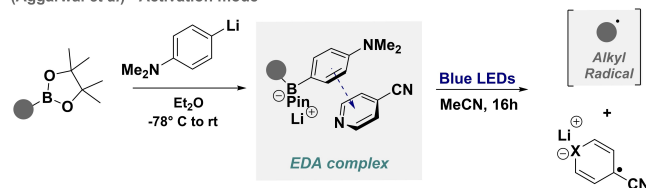
Examples



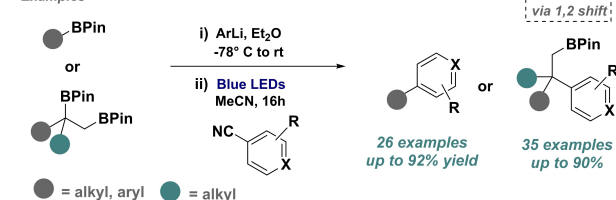
**Scheme 6.** Activation of boronates via direct excitation using visible light.

#### Activation of Boronic Acids/Esters via EDA complex formation

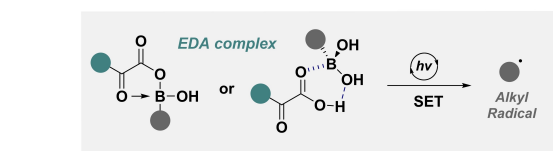
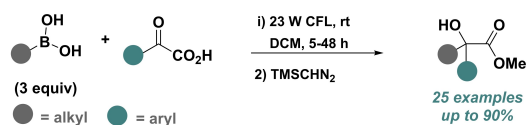
(Aggarwal *et al.*) - Activation mode



Examples



(Chen *et al.*)

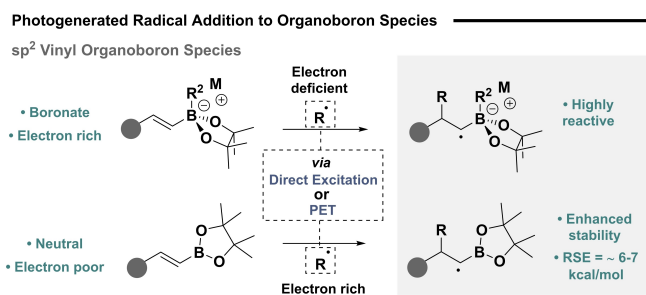


**Scheme 7.** Activation of organoboron species via EDA complexation.

electron-deficient 4-cyanopyridine. Excitation initiates electron transfer to afford the alkyl radical which can subsequently recombine with the transient 4-cyanopyridine radical. Not limited to boronates, an EDA complex was proposed directly with the neutral boronic acid by Chen and co-workers in 2019 (Scheme 7, bottom). It is foreseen that these seminal studies will lay the foundations for future development of photocatalyst-free protocols.<sup>[58]</sup>

### 3. Photochemical Strategies Retaining the C–B Bond

The ubiquity of organoboron residues in contemporary synthesis is arguably a consequence of the variety of transformative downstream synthetic manipulations which can supersede their installation. As such, methods which enable the rapid construction of complex boron-containing scaffolds are being intensively pursued. Unsurprisingly, recent advances in photochemistry have afforded a rich palette of methods to access borylated frameworks. Critical to the success of these protocols is the key consideration of boron hybridisation. While in the preceding section, this phenomenon influenced the interaction between light, photocatalyst, and the C–B bond, here hybridisation attenuates reactivity of starting materials and high-energy intermediates (Scheme 8). Photoinduced radical addition to vinyl organo-



**Scheme 8.** Photogenerated radical addition to organoboron species. RSE = Radical stabilisation energy.

boron species serves as a pertinent example,<sup>[59]</sup> where a subtle variance in electronic properties leads to stark differences in reactivity. Radical philicity plays a prominent role,<sup>[60]</sup> so too does consideration for the photoactivation mode, to mitigate undesired C–B bond activation (vide supra). Selected examples of landmark photochemical strategies on organoboron molecules in which the C–B bond is retained will be the subject of Section 3.

### 3.1. Photoinduced Radical Addition to Organoboron Species

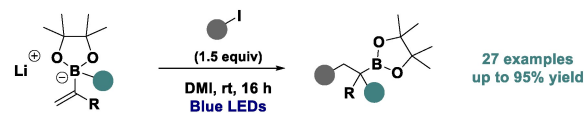
#### 3.1.1. Boronates

Organoboronates have a rich history in contemporary synthesis, most prominently in 1,2-rearrangement chemistry, where the additional ligand at boron serves as a nucleophilic reservoir for C–C bond formation.<sup>[61]</sup> Recently, this phenomenon was extended to facilitate an open-shell activation mode. Pioneering studies by the Studer group (BET<sub>3</sub>/O<sub>2</sub> radical initiation)<sup>[62]</sup> and Aggarwal group (light-driven homolysis, Scheme 9, top)<sup>[63]</sup> identified radical polar crossover driven 1,2 rearrangements of organolithium-derived organoboronates, enabling 1,2-difunctionalisation of vinyl boronates.<sup>[64]</sup> Initial studies by Aggarwal revealed a wide range of radical precursor that could be initiated by light-driven homolysis, including  $\alpha$ -iodo ketones, perfluoroalkyl iodides, and  $\alpha$ -fluorinated halo-acetate esters.<sup>[63]</sup> This reactivity mode enables chain propagation and circumvents the use of a photocatalyst that can lead to undesired activation of the C–B bond, which possesses a relatively low oxidation potential. Since these seminal contributions there has been remarkable advances, with dienyl boronates<sup>[65]</sup> and bicyclobutylboronates (Scheme 9, middle)<sup>[66]</sup> serving as radical acceptors to afford allylic and cyclobutyl boronic esters, respectively. Stereodefined starting materials have also been shown to undergo stereospecific 1,2-rearrangements.<sup>[67]</sup> Recently a prominent example by Studer and co-workers enabled the 1,2-carboamination of vinyl boronates using chloroamines as a light-labile amido-radical precursor (Scheme 9, middle).<sup>[68]</sup>

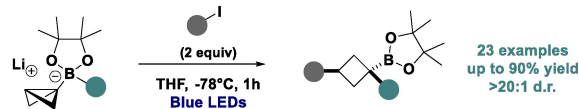
Despite advances in reaction development, the mechanistic dichotomy of radical polar crossover reactions remains a topic of debate.<sup>[69]</sup> Focussing on photochemical

### Radical Addition to Vinyl and Strained Boronates Initiated by Light

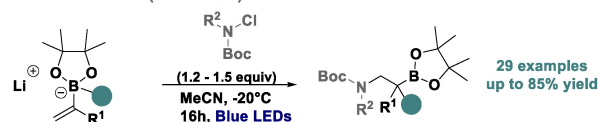
Addition to Vinyl Boronates (Aggarwal *et al*)



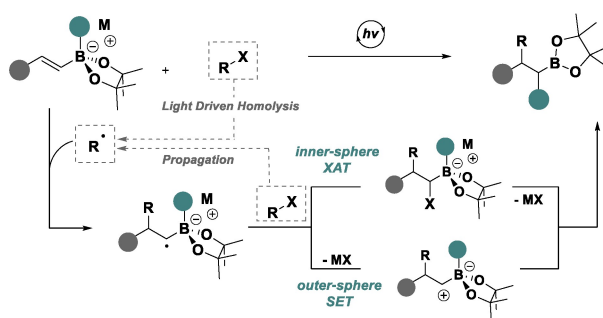
Addition to Strained  $\sigma$  Bond (Aggarwal *et al*)



C–N Bond Formation (Studer *et al*)



Mechanistic Dichotomy



**Scheme 9.** Radical addition to vinyl and strained boronates.

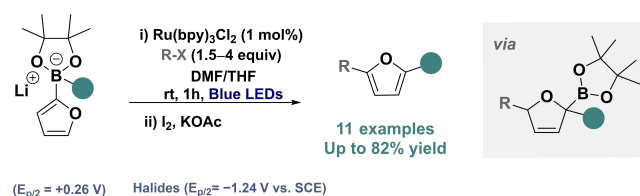
activation (Scheme 9, bottom), light-driven homolysis generates a radical electrophilic in nature which can engage with the nucleophilic boronate via Giese-type  $\beta$ -addition, creating an  $\alpha$ -boryl radical. Subsequent steps are still a matter of discussion and the mechanism has been proposed to go through two possible pathways. The first involves an inner-sphere XAT/ATRA process, whereby a halogen is abstracted from the halide precursor by the  $\alpha$ -boryl radical, producing the  $\alpha$ -halogenated boronate species and a radical for chain propagation. Alternatively, an outer-sphere mechanism has been supported by many seminal studies in which the  $\alpha$ -boryl radical undergoes a single-electron oxidation with the radical precursor to afford an  $\alpha$ -cation. Both intermediates undergo a 1,2-rearrangement with the boronate nucleophilic reservoir to afford 1,2-difunctionalisation of the vinyl boronate.

A landmark study by Orr-Ewing, Aggarwal, and co-workers recently provided evidence to support an inner-sphere mechanism as operational.<sup>[69]</sup> Revisiting their work on bicyclobutylboronates, in-depth analysis by time-resolved infrared (TRIR) absorption spectroscopy and DFT calculations revealed reaction kinetics favouring an inner-sphere reaction mechanism. The study was extended to vinyl boronates identifying the transient  $\alpha$ -iodo boryl species (specific to an inner-sphere mechanism) to be involved in the rate-determining step.

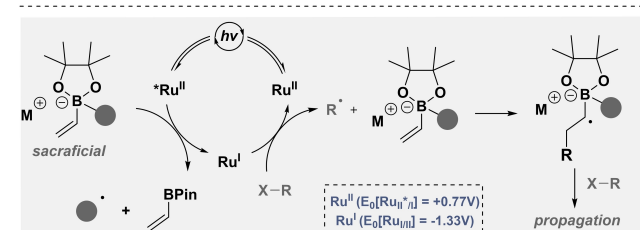
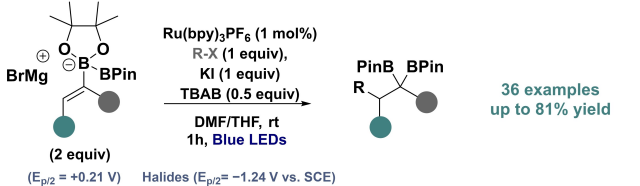


While most strategies for radical addition to boronates are contingent on external initiators or homolysis of weak bonds, recent studies have demonstrated that boronates can serve a dual role under photoredox conditions. Run in the absence of a catalyst, little to no product was observed in studies by the Aggarwal and Shi groups,<sup>[70,71]</sup> suggesting direct excitation and chain propagation was inefficient (Scheme 10, top). Judicious choice of a photoredox catalyst enabled “smart initiation” where the boronate plays a dual role to permit the synthesis of functionalised furans and geminal boronic esters, respectively. Initially considered an undesired reaction (Scheme 10, bottom), reductive quenching of the aryl/vinyl boronate ( $E_{p/2} = +0.26$  and  $+0.21$  V) with the excited state photocatalyst  $\text{Ru}^{\text{II}}$  ( $E^0[\text{Ru}^{\text{II}*}] = +0.77$  V) delivers the reduced state of the ruthenium catalyst  $\text{Ru}^{\text{I}}$  ( $E^0[\text{Ru}^{\text{I}}] = -1.33$  V). The resulting reduced state of the catalyst can then oxidatively quench the alkyl halide ( $\text{R-X}$ ,  $E_{p/2} = -1.24$  V) to generate a radical which undergoes Giese-type addition to the boronate. Successive propagation results in a chain process, meaning the photoredox event is only required for initiation. The merger of photoredox activation with vinyl boronates has also been employed in the use of MIDA boronates as well as multicomponent reactions using trifluoroborates.<sup>[72,73]</sup>

#### Radical Addition to Aryl and Vinyl Boronates Initiated via Photoredox Coupling with Heteroarenes (Aggarwal *et al*)



#### Photoredox Initiated Access to Geminal Boron Systems (Shi *et al*)



**Scheme 10.** The use of organoborates as initiators via photoredox catalysis.

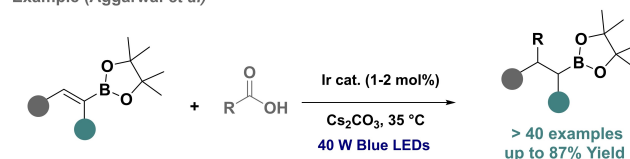
### 3.1.2. Trigonal-Planar Boronic Esters

The hybridisation of boron is key in attenuating radical reactivity. When considering vinyl organoboron species, a simple exchange of a boronate for a neutral boronic ester uncovers new reactivity paradigms. Electron deficient in nature, these SOMOphiles preferentially engage with electron-rich radicals to generate a comparatively more stable  $\alpha$ -boryl radical due to stabilisation via the adjacent boron p-orbital (Scheme 8, bottom).<sup>[74]</sup> The use of trigonal-planar-hybridised boronic esters and stringent control over reaction media precludes the formation of redox-active boronates, allowing photoredox catalysis to be employed once again with ease. In 2018, Aggarwal and co-workers provided a striking example using carboxylic acids as radical precursors to afford  $\gamma$ -amino boronic esters (Scheme 11, top).<sup>[75]</sup> The excited state photocatalyst undergoes reductive quenching with the carboxylate, generated via deprotonation of the parent acid, to afford a radical primed for decarboxylation (Scheme 11, bottom). Following decarboxylation, the electron-rich  $\alpha$ -amino radical can undergo  $\beta$ -radical addition to the neutral vinyl boron species to create a stabilized  $\alpha$ -boryl radical ( $E_{1/2}^{\text{red}} = -1.25$  V vs SCE by DFT). A thermodynamically favoured SET with the reduced photocatalyst ( $E_{1/2}[\text{Ir}^{\text{III}}/\text{Ir}^{\text{II}}] = -1.51$  V vs. SCE in MeCN) generates an  $\alpha$ -boryl anion which is subsequently protonated. By a simple modification of the boron SOMOphile, the same researchers were able to furnish densely functionalised cyclopropanes containing a boron handle.<sup>[40]</sup> However, this chemistry is not restricted to the use of carboxylic acids,<sup>[76]</sup> with many other examples using silicates and redox active esters among others.<sup>[77-79]</sup>

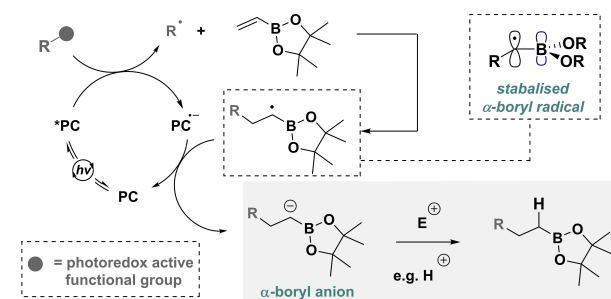
The elegant amalgamation of this activation platform with nickel catalysis has enabled expedient access to complex organoboron scaffolds via metallaphotoredox multicomponent reactions (Scheme 12). Various precursors

#### Radical Addition to Neutral Vinyl Boronic Esters via Photoredox Catalysis

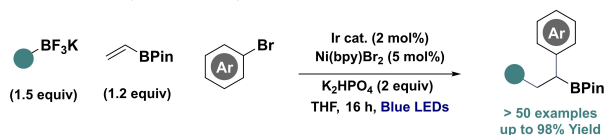
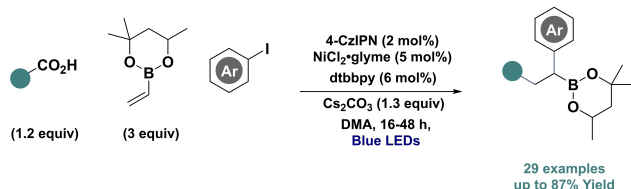
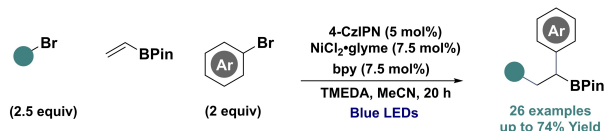
Example (Aggarwal *et al*)



#### Photoredox Activation



**Scheme 11.** Radical addition to neutral vinyl boronic esters via photoredox catalysis. Ir cat. =  $[\text{Ir}(\text{dF}(\text{CF}_3)\text{ppy})_2(\text{dtbbpy})](\text{PF}_6)$  or  $[\text{Ir}(\text{ppy})_2(\text{dtbbpy})](\text{PF}_6)$ .

Interception of  $\alpha$ -Boryl Radical with Nickel - MetallaphotoredoxTrifluoroborates - (Molander *et al*)Carboxylic Acids - (Aggarwal *et al*)Alkyl Bromides - (Martin *et al*)

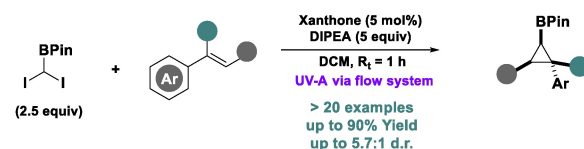
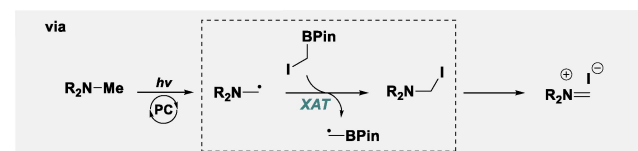
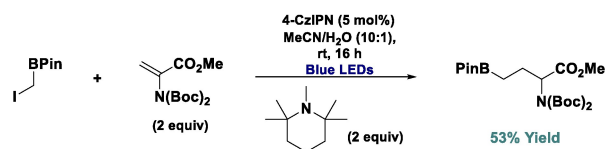
**Scheme 12.** Interception of  $\alpha$ -boryl radicals with nickel. Ir cat. = [Ir(dF(CF<sub>3</sub>)ppy)<sub>2</sub>(bpy)](PF<sub>6</sub>).

could be readily employed including trifluoroborates,<sup>[80]</sup> carboxylic acids,<sup>[81]</sup> and alkyl bromides<sup>[82]</sup> to generate the stabilised  $\alpha$ -boryl radical intermediate after addition to vinyl BPin, which is intercepted by a ArNi<sup>II</sup> complex to enable efficient cross-coupling after reductive elimination. A key highlight is the system developed by Molander and co-workers observing chemoselective activation of trifluoroborates in the presence of their neutral boronic ester counterparts.<sup>[80]</sup>

3.2. Photoinduced  $\alpha$ -Activation of Organoboron Species3.2.1.  $\alpha$ -Halo Boronic Esters

The synthetic potential of  $\alpha$ -boryl radicals as reactive intermediates is abundantly clear. Cognizant of this fact, many research groups have focussed on alternate photocatalytic methods to form these species in solution without relying on initial conjugate radical addition to a vinyl organoboron. Accessed via classical Matteson-type homologation methods,  $\alpha$ -iodo boronic esters have been employed with great effect due to their propensity for selective activation of the C–X bond.<sup>[83,84]</sup> Charette and co-workers showed how simple small building blocks can be translated to complex 3D frameworks in a single step (Scheme 13, top).<sup>[85]</sup>

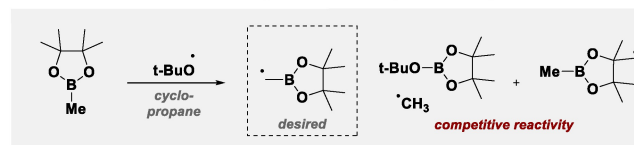
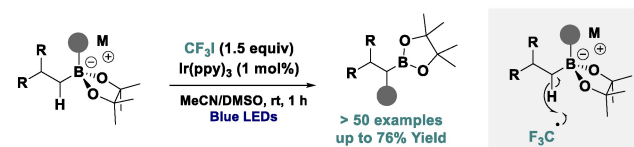
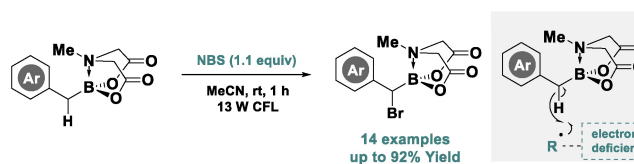
The arsenal of strategies to directly access  $\alpha$ -boryl radicals was extended by Leonori and co-workers in 2020 (Scheme 13, bottom).<sup>[86]</sup> The group developed conditions which enabled the in situ generation of  $\alpha$ -amino radicals. In-depth mechanistic analysis using flash laser photolysis and DFT calculations revealed the  $\alpha$ -amino radical behaves as an XAT reagent abstracting halides to reveal alkyl radicals.

Photo-catalysed Activation of  $\alpha$ -Iodo Organoboron SpeciesSynthesis of Cyclopropyl Boronic Esters (Charette *et al*)Halogen Atom Transfer Activation of  $\alpha$ -Iodo Organoboron Species (Leonori *et al*)

**Scheme 13.** Photocatalysed activation of  $\alpha$ -iodo organoboron species.

## 3.2.2. Hydrogen-Atom Transfer (HAT)

In modern organic synthesis, atom economy is a key consideration in reaction design.<sup>[87]</sup> To address this, protocols in which a hydrogen atom is abstracted to produce a radical have also been explored. However, this task also presents many challenges, as demonstrated by Walton and Carboni (Scheme 14, top).<sup>[74]</sup> Exposing methyl BPin to a *tert*-butoxide radical, formed via homolysis of *tert*-butyl peroxide, led to the generation of three distinct radical species by EPR. The desired hydrogen-atom abstraction of methyl BPin, a methane radical as a result of homolytic substitution and a cyclopropyl radical from H-atom abstrac-

Indirect  $\alpha$ -HAT of  $sp^3$  Hybridised BoronatesCurrent Limitations in HAT with Alkyl Boronic Esters (Carboni *et al*)Hydrogen Atom Transfer Using Trifluoromethyl Iodide (Studer *et al*)Hydrogen Atom Transfer of Benzylic BMIDAS (Wang *et al*)

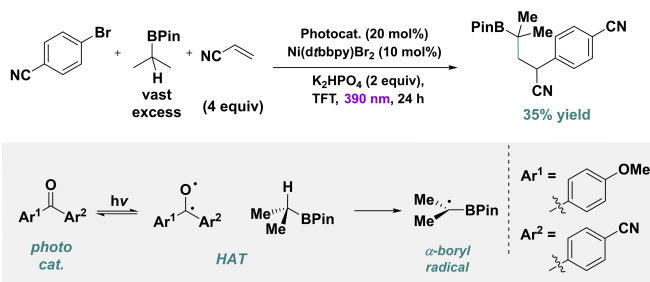
**Scheme 14.** Indirect hydrogen-atom transfer approaches.

tion of the solvent. Interestingly, at elevated temperatures ( $T > 230$  K) H-atom abstraction of the methyl backbone was also observed, cementing the challenges of HAT on classic boronic esters. In 2019, Studer and co-workers were able to overcome these challenges in a landmark study (Scheme 14, middle).<sup>[88]</sup> Altering the hybridisation state of the boron species to a boronate mitigated concerns of homolytic substitution while concomitantly modulating the bond dissociation energy of the adjacent C–H bond. The group identified trifluoromethyl iodide as an electrophilic radical source capable of selective HAT to generate an  $\alpha$ -boryl radical, as supported by DFT calculations. Further oxidation and 1,2-rearrangement, akin to radical polar crossover (vide infra), permits access to complex borylated frameworks without the requirement of a redox-active functionality as a prerequisite for activation. The same group have advanced this platform to include intramolecular abstraction and boryl migration to form geminal boronic esters.<sup>[89,90]</sup>

The generation of an  $\alpha$ -boryl radical enabled by indirect H-atom abstraction was also achieved by Wang and co-workers, utilising benzylic MIDA boronates in C–H halogenation reactions (Scheme 14, bottom).<sup>[91]</sup> Photoactivation of NBS generates a radical which can effectively elicit C–H abstraction adjacent to boron. The intramolecular dative interaction of the MIDA nitrogen backbone mitigates homolytic substitution while weakening the C–H bond.

The vast majority of photoinduced H-atom abstraction methods to furnish  $\alpha$ -boryl radicals are contingent on reagent-based (indirect) activation modes. Recently, Molander and co-workers made use of diarylketones as direct HAT catalysts to develop a dual nickel-catalysed difunctionalisation of olefins.<sup>[92]</sup> A standout example was the use of isopropyl BPin as a radical precursor (Scheme 15). Upon excitation of the diarylketone photocatalyst, the ketyl radical could efficiently abstract an  $\alpha$ -hydrogen atom from the neutral organoboron precursor to form an  $\alpha$ -boryl radical. Giese addition to acrylonitrile and subsequent participation in a nickel cross-coupling cycle afforded the borylated product in 35% yield. Despite a moderate yield and the use of a vast excess of boron precursor, this reaction serves as a benchmark as one of the first of its kind.

#### Direct HAT Example on Neutral Organoboron Species



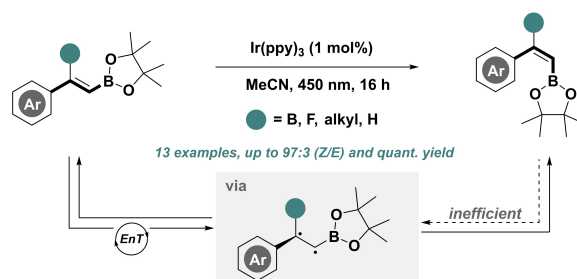
**Scheme 15.** Direct hydrogen-atom transfer of a neutral boronic ester.

### 3.3. Energy Transfer Catalysis of Alkenyl Organoboron Species

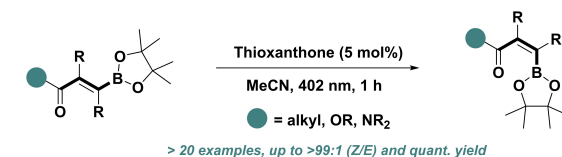
Photochemistry via direct excitation is often plagued by inefficient absorption of organic molecules in the visible light region. The use of ultraviolet light provides a temporary solution but often jeopardises reaction selectivity due to the use of high-energy shorter wavelengths. The inception of energy transfer catalysis has afforded a mild solution where a photocatalyst can harness light of a longer wavelength. The excited state photocatalyst can then undergo the simultaneous exchange of electrons with the target organic molecule (typically in the triplet state via Dexter EnT) to generate a high-energy intermediate (Figure 4). Recently, this reaction manifold has come to the forefront of organic chemistry with many developments uncovered using alkenyl organoboron species.

The spatiotemporal control of alkene geometry has been a challenge in contemporary synthesis for many years. While synthetic methods, under the auspices of thermodynamic control, typically favour the *E*-isomer, protocols enabling access to the *Z*-isomer are less well developed. To address this conundrum, selective energy transfer catalysis has been harnessed to permit the contra-thermodynamic *E*→*Z* isomerisation of alkenes.<sup>[93]</sup> In 2018, this phenomenon was extended to tolerate styrenyl boronic esters using an Ir(ppy)<sub>3</sub> catalyst by Gilmour, Watson, and co-workers (Scheme 16, top).<sup>[94]</sup> Here, efficient sensitisation of the *E*-isomer leads to the formation of a biradical intermediate which can recombine to form the *E*-isomer or the *Z*-isomer. Formation of the *E*-isomer ultimately leads to reexcitation via EnT, whereas, formation of the *Z*-isomer results in a styrene chromophore twisted in geometry leading to inefficient EnT with the photocatalyst. As a result, the *Z*-isomer accumu-

#### Photocatalytic Isomerisation of Styrenyl Boron Species (Gilmour *et al.*)



#### Photocatalytic Isomerisation of $\beta$ -Borylacrylates (Gilmour *et al.*)



- Neutral boron
  - Extended chromophore
  - Efficient EnT
- 
- p-orbital occupied
  - Deconjugated
  - Inefficient EnT

**Scheme 16.** Photocatalytic contra-thermodynamic isomerisation of alkenes.

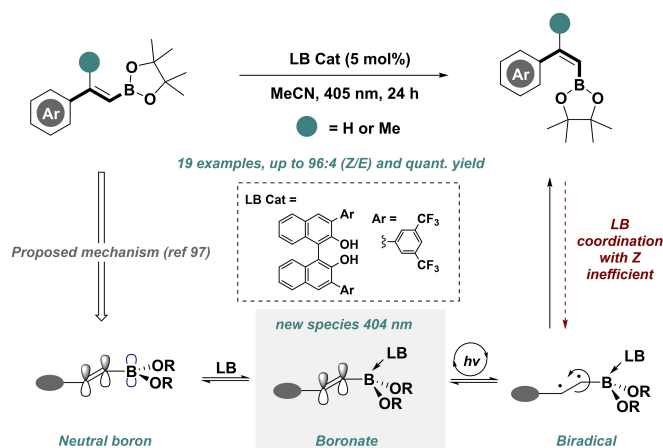
lates over time. Successful EnT is contingent on a suitable chromophore with a low-lying triplet energy, and thus examples are typically limited to styrenyl motifs. In 2020, Gilmour and co-workers addressed this limitation with the development of the contra-thermodynamic geometric isomerisation of  $\beta$ -boryl acrylates (Scheme 16 bottom).<sup>[95]</sup> Ground state X-ray crystallography revealed a boron-gated mechanism highlighting the pivotal role of boron in regulating directionality. In its *E*-isomeric form the system is planar with the boron p-orbital in conjugation with the acrylate core. However, EnT-enabled isomerisation reveals a *Z*-isomer twisted in conformation with the p-orbital occupied from an intramolecular dative interaction by the oxygen of the adjacent carbonyl (Scheme 16, bottom). This study highlights the importance of boron hybridisation in regulating excited state reactions.

The geometric isomerisation of alkenyl boron systems is not limited to EnT, with many studies using direct excitation.<sup>[96]</sup> A pertinent example was disclosed by Poisson and co-workers in 2021 using catalytic amounts of a binaphthol derivative to enable the contra-thermodynamic *E*→*Z* isomerisation of styrenyl boronic esters (Scheme 17).<sup>[97]</sup> Boron hybridisation plays a pivotal role in regulating the double bond geometry. The authors propose the BINOL catalyst acts as a Lewis base forming a dative interaction with the boron p-orbital resulting in a new species with a bathochromic shift in the absorption spectra (404 nm). Efficient direct excitation enables access to a high-energy biradical intermediate akin to that of Gilmour and co-workers. The origin of selectivity stems from inefficient Lewis base formation with the product *Z*-isomer. To further compound this hypothesis the authors demonstrated BMIDAs, containing an already occupied p-orbital, were inefficient under model reaction conditions.

The rapid translation of easily accessible 2D building blocks into complex 3D architectures is a desirable feat for drug discovery in the continuous drive to “escape from flatland”.<sup>[14b]</sup> Photocatalysed [2+2] cycloaddition serves as a

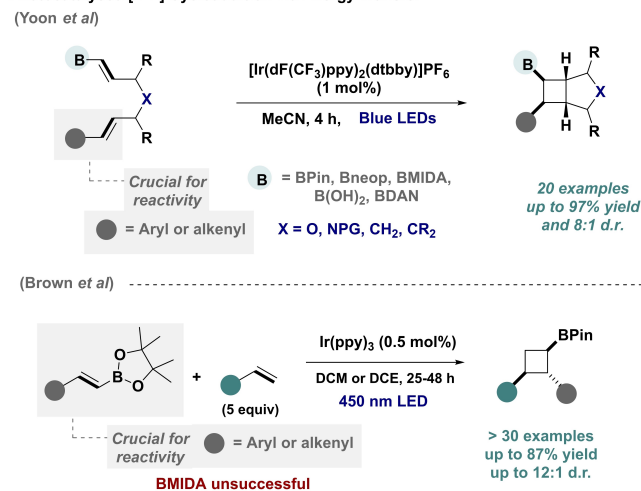
powerful platform to readily convert alkene precursors into cyclobutanes under mild, operationally simple conditions.<sup>[98]</sup> Given the synthetic utility of a boron handle for downstream synthetic manipulations, it comes as no great surprise that uptake of alkenyl boron species in this platform has been prominent.<sup>[99]</sup> Pertinent examples include the enantioselective intermolecular [2+2] cycloaddition of vinyl BPin with quinolones by Bach and co-workers using a chiral templated photocatalyst.<sup>[100]</sup> Also Knowles and co-workers have demonstrated an elegant photocatalysed [2+2] reaction manifold to access borylated oxaspiro[3.3]heptanes.<sup>[101]</sup> However, both landmark studies are contingent on excitation of another chromophore followed by a bimolecular quench with the vinyl boron species; direct EnT to the alkenyl boron is not anticipated. In 2021, Yoon and co-workers provided strong evidence to support this phenomenon (Scheme 18, top).<sup>[102]</sup> In the development of their photocatalysed synthesis of complex borylated architectures a strategic control reaction, removing the conjugated system, resulted in no cyclisation. Interestingly, while geometric isomerisation of the alkenyl boron was observed, suggesting sensitisation, intramolecular quench with the pendant alkene was not detected. It is pertinent to note this allowed a series of boron functionalities of different hybridisation states to be compatible with model reaction conditions. Recently Brown and co-workers provided a striking example demonstrating EnT-catalysed intermolecular [2+2] cycloaddition of alkenyl boronic esters (Scheme 18, bottom).<sup>[103]</sup> Mechanistic studies identified a triplet energy transfer mechanism highlighting that energy is transferred to the alkenyl (styrene or diene) organoboron species. Modifying the boron motif to BMIDA resulted in a loss of reactivity under model reaction conditions.

Photocatalytic Isomerisation of Styrenyl Boron Species (Poisson *et al.*)



**Scheme 17.** Photocatalytic isomerisation of styrenyl boronic esters using a BINOL-derived ligand. LB = Lewis base.

Photocatalysed [2+2] Cycloaddition via Energy Transfer



**Scheme 18.** Photocatalysed [2+2] cycloaddition via EnT.

#### 4. Conclusion

The uptake of organoboron motifs in new photocatalytic technologies continues at an accelerating pace. Central to this surge is the fundamental understanding of boron hybridisation and its profound effect on modulating reactivity in excited state reactivity paradigms. While platforms which involve the activation of the C–B bond can be considered comparatively mature, photocatalytic manifolds, which retain the boron motif while concomitantly increasing molecular complexity, continue to progress. Exciting developments in EDA activation,<sup>[57]</sup> precursor-free technologies using HAT,<sup>[88–90]</sup> and the recent discovery of efficient energy transfer reactions<sup>[95,103]</sup> lay the foundations for this already fruitful merger of two iconic research areas of organic synthesis.

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#### Conflict of Interest

The authors declare no conflict of interest.

**Keywords:** Boron · Energy Transfer · Hybridization · Photocatalysis · Reaction Mechanisms

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