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Effects of Light Intensity and Reaction Temperature on Photoreactions in Commercial Photoreactors

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In the last decade, visible-light photoredox catalysis has evolved into a versatile tool in organic synthesis. However, most reports have used homemade photoreactors in their design and optimisation of new methods, complicating the reproducibility of some transformations. To improve reproducibility and efficiency, laboratory photoreactors have been developed and commercialized. Herein we report a comparison of four commercially available photoreactors in six mechanistically distinct photoredox reactions focusing on the difference in product yields and kinetics as well as the factors which lead to these differences, including reaction temperature and light intensity.

1. Introduction

Over the past decade, researchers in both academia and industry sectors have used visible light (400–700 nm) to solve synthetic challenges by photoredox catalysis.[1,2] The research activities focused on the invention of novel reactions, exploration of reaction mechanisms and improving classic radical reactions.[3] Despite rapid progress, photoredox catalysis still faces several challenges, such as reproducibility, scalability and better standardized light sources.

The challenges are often a result of a scarcity of detailed instructions regarding the photoreactor set-up. Crucial information such as the light intensity is often absent in reported procedures, particularly when reactions are performed in custom-made lab equipment or vaguely specified household lamps are used as the irradiation source. This issue has improved overtime, with more and more labs using high-power LEDs or commercial LED lamps (e.g., EvoluChem or Kessil) where specifications of the emitted light are documented.

Developing standardized operating protocols to improve reproducibility and scalability will facilitate a broader use of the new methods e.g. in pharmaceutical research and drug development. Thus it is vital to understand and control the key parameters affecting photochemical transformations.[4,5] Important parameters that are often considered when optimising a photoreactor are: light source, light uniformity, reactor geometry, agitation intensity (flow rate/stirring rate) and temperature control. These factors are not just taken into greater consideration within large scale industrial settings, but are also important in continuous flow photochemistry, for organic synthesis, material science, water treatment and polymer or nanoparticle manufacturing.[6,7] Research articles utilising continuous flow for photochemical transformations typically report their reaction set-up and conditions in great detail to ensure reproducibility, while the same level of detailed reporting of reaction conditions is rare for small scale organic synthetic methods reported in the literature. Recently, standardized purpose-built reactors were developed to address these aforementioned issues with some success. A single-well photoreactor (PennOC/PennPhD photoreactor M1 and M2) was commercialized by PennOC in collaboration with MSD and the MacMillan group.[8] They have shown that the increased photon flux available in the photoreactor improved yields and decreased reaction times of photocatalysed N-arylations, alkyl decarboxylative coupling reactions, fluorinations, trifluoromethylations, and other reactions in comparison to previous literature reports using non-standardised equipment.

The need to run several reactions in parallel in standardized conditions led to the development of an adaptor to the PennOC allowing up to 5-vials to be run simultaneously while photoreactors developed by HepatoChem, HK Testsysteme and other systems have this as standard. While all these photoreactors individually ensure constant reaction conditions within a single set-up, these set-ups differ in variety of ways such as: the number of reaction vessels that can be used simultaneously, the distance of the reaction vessel from the light source, capability of the built-in cooling system, the reaction vessel stirring system and light pollution protection for the operator. Therefore, significant variations in the reaction outcome from published data and also between the different photoreactors are to be expected.

One particularly important parameter in photoredox catalysis is the reaction temperature, which has often been ignored

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or at best been given as a rough estimate despite having a potentially significant effect on a photocatalytic transformations outcome.[9–11] Despite this, an increasing number of photoredox reactions are now being reported as requiring a narrow temperature range for optimum results, it stands to reason that many previously reported photocatalysed transformations would benefit from closer temperature control.[12,13] While manufacturers have provided a steady increase in intensity and power of light sources available, adequate temperature control will become an increasingly important factor and challenge in photoredox catalysis.

In this paper, we compare the performance of four commercially available photoreactors in literature-reported photoredox-catalysed reactions: PennOC Photoreactor M1, HepatoChem EvoluChem™PhotoRedOx Box and the photoreactor TAK120, available with either air-cooling or liquid-cooling. The aim of the comparison is to illustrate that different photoreactors will lead to different reaction performance dependent on the reaction performed and to highlight that light intensity should not be the only factor considered when optimising the yield and reaction times of photoredox catalysed transformations.

We are aware that a holistic description and control of a photocatalytic reaction set-up would require considering more parameters than we can address here, such as temperature dependent light emission spectra, the photon flux depending on the intensity setting determined *via* actinometry, and the light uniformity in the reaction vessel derived e.g. *via* simulations. This would be of particular importance for deeper mechanistic investigations and achieving best possible efficiency. A standardized and widely available set-up addressing all these parameters is, to the best of our knowledge, not available yet, but our comparison and discussion of set-ups in current use may help to identify points of improvement for the next generation of standardized reaction set-ups for photocatalytic organic synthesis.

1.1. Reactor Comparison

While all commercial photoreactors tested are standardized pieces of equipment, they have different features, with some requiring additional equipment in order to function. The features of the different photoreactors are highlighted here (Figure 1).

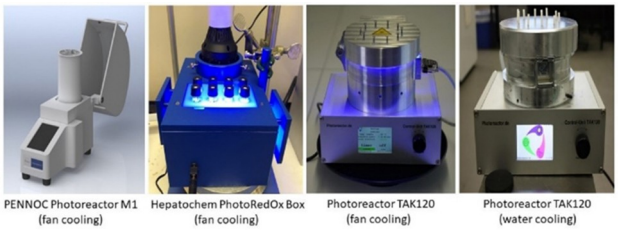

Figure 1. Photoreactors used in this study.

1.1.1. PennOC PhotoreactorM1 (PennOC)

The PennOC (https://www.pennphd.com/product/1)[8] is an all-in-one photoreactor requiring no external equipment, featuring a built-in magnetic stirring system, a variable-speed fan for cooling and is compatible with three different LED modules (365, 420 or 450 nm). The light intensity, reaction time and fan speed are tunable to fit the reaction needs and all settings controlled by a touch-screen panel. While it was initially designed as a single slot reactor, adaptors are also available to allow for up to 4×8 mL vials or 5×4 mL vials. The distance between vial and light-source is adjustable by using different height adaptors with a reflective coating to ensure maximum reaction illumination. The light is blocked from sight with a light shield with interlock to prevent harmful light rays escaping. Average optical irradiation power output: 2.1 W (see supporting information for details of the measurement).

1.1.2. HepatoChem EvoluChem PhotoRedOx Box (HepatoChem Box)

The HepatoChem Box (https://www.hepatochem.com/photochemistry/photoredox-box/) is a modular photoreactor, which requires an external stirring plate and light source in order to operate (light intensity is thus only controllable if the external light source is capable of it). It is compatible with most vial formats (0.3, 2, 4, 8 and 20 mL) and can run up to 32 vials simultaneously depending on vial size. This photoreactor is cooled by a single-speed case fan and the reactions are indirectly illuminated via a mirror system to ensure all reactions are illuminated equally. A liquid cooled system is available from HepatoChem, which we have not tested. Average Power output: 1.8 W (see supporting information for details of the measurement).

1.1.3. TAK120 Air cooled System (TAK120 (AC))

The TAK120 photoreactor (http://wppr.photoreactor.de/tak120/) is a modular system requiring an external magnetic stirrer to operate and is available in 365, 455, 521 and 850 nm wavelengths (a dual-colour option is also available). The reactor consists of 10 reaction slots with each slot being irradiated individually by 4 LEDs (7 W per slot). The temperature is controlled by a fan-based air-cooling system for both the LEDs and reaction vessels. An integrated sensor allows for monitoring of the reaction temperature. Light intensity, irradiation time and other parameters are adjustable by an electronic control unit. The photoreactor has a lid to minimize light pollution as well as resealable holes above each of the reaction slots to allow easy sampling from reaction vessels during irradiation removing the need to open the system. Average Power output: 2.8 W (see supporting information for details of the measurement).

1.1.4. TAK120 Liquid Cooled System (TAK120 (LC))

In this variation (http://wppr.photoreactor.de/announcement) of the TAK120 photoreactor, the air cooling of LEDs and reactions is replaced by a recirculated liquid cooling system which may be connected to any recirculated chiller, this also circulates around the reaction vessels for better temperature control. The reactor consists of 4 reaction slots with each slot being irradiated individually by 4 LEDs (up to 14 W per slot). This purportedly allows for a more precise temperature control and with the use of a cryostat, photoreactions may be performed below room temperature. Parameters of the reaction can be set and monitored by an electronic control unit. Average Power output: 2.8 W (see supporting information for details of the measurement).

1.2. Reaction Comparison

Six published photocatalytic reactions of varying complexity that were reported for "homemade" non-standardized photoredox set-ups were selected for comparison. Each reaction is mechanistically distinct, either generating a different radical species, having a different coupling partner or multiple catalytic cycles are involved. We chose reactions of particular interest for medicinal chemistry as the new synthetic avenues of photoredox catalysis has raised interest in this area.[14] The selected reactions were performed in the four aforementioned photoreactors and initial reaction rates, time to reaction completion, final yields and reaction temperature were monitored. The reactions were replicated at least three times to ensure that the obtained results were reproducible and consistent. All reactions were run at the same scale as described in literature and in the same volume of solvent (1.0–4.0 mL) as stated in literature (see the Supporting Information for exact volumes for each transformation) In the TAK120 photoreactors, light intensity was set to 7 W to allow for a more accurate temperature control comparison. In the PennOC the light intensity and fan speeds were set to maximum (see SI for the complete photoreactor power measurements).

2. Results and Discussion

2.1. Brønsted Acid Photocatalytic Radical Addition of α-Amino C–H Bonds Across Michael Acceptors

The first reaction investigated was the α-alkylation of amines with Michael acceptors reported by Yoon and co-workers (Figure 2).[15] In this transformation the photocatalyst is proposed to initiate a reductive photoredox cycle, leading to the oxidation of the amine forming an α-amino radical. This nucleophilic radical adds to a Michael acceptor forming a carbon-centered radical, which may be reduced and subsequently protonated to form the desired product. In their report, the authors observed a significant increase in the rate of the reactivity with a temperature increase from room temperature

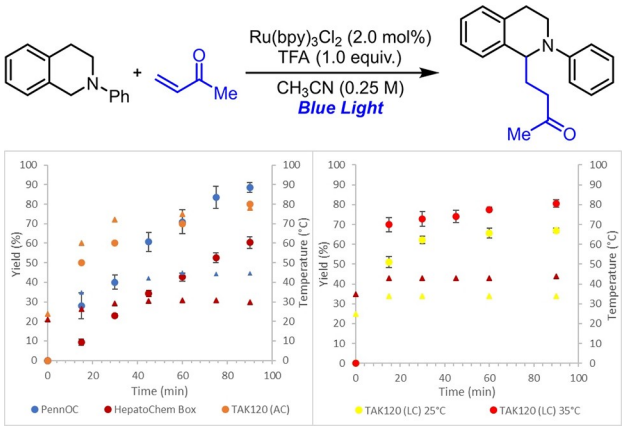

Figure 2. Photoredox mediated α-functionalization of amines; solid dots represent yields (%) and small triangles represent temperature (°C). Left: difference in reaction yields (%) and temperature (°C) over time in the air-cooled photoreactors. Right: difference in reaction yields (%) and temperature (°C) over time in in the TAK120 (LC) photoreactor.

to 50 °C. In the reactor comparison the TAK120 (LC) was operated with a 25 °C and 35 °C recirculated cooling set-up.

All photoreactors showed an improvement in yield (> 50 %, 90 min) compared with literature results (35 %, 90 min), which may be attributed to the use of high intensity blue-LEDs instead of the literature reported fluorescent lamp. The high light intensity photoreactors (PennOC, TAK120 (AC & LC) obtained higher product yields faster than the Hepatochem system. Temperatures also varied between the four reactors; the TAK120(AC) reached 75 °C reaction temperature, PennOC operating in the range of 40–45 °C, and the TAK120(LC) and the HepatoChem Box reached between 30–35 °C. Initial reaction rate was highest in the TAK120 systems. Difference in reaction temperature affects the initial rate of the reaction significantly as shown by the rates at 25 °C and 35 °C in the TAK120(LC) photoreactor. While the slightly higher temperature proved beneficial to reaction rates (70 % after 15 minutes at 35 °C whereas only 51 % was seen at 15 minutes at 25 °C), higher temperatures seem to be detrimental with the TAK120 (AC) only reaching 50 % and hitting 60 °C. The results confirm that the reaction is positively affected by higher temperature (up to a certain point), achieving higher yields in a shorter time. This is supported by the extensive mechanistic investigations by the authors as they suggest that the rate limiting step in this transformation is a chain-propagating hydrogen atom abstraction. This hydrogen atom abstraction process is independent of light intensity, indicating that light intensity is not the major factor in the initial kinetic rate of this transformation. Reactors which were maintained at similar temperatures throughout did not exhibit the same initial rate of reactivity as seen in the case of the TAK120 (LC, 35 °C) and PennOC photoreactors with the TAK120(LC) having a far greater initial reaction rate. This was also observed when comparing the TAK120 (LC, 25 °C) and the HepatoChem Box. These discrepancies are likely due to the higher irradiation intensity available in the TAK120 photoreactors.

2.2. Regioselective Amination of Arenes Using Alkyl Amines

The next reaction we explored was the photoredox mediated amination of arenes using alkylamines reported by Leonori and co-workers (Figure 3).[12] N-chlorosuccinimide is used to generate an N-chloramine; upon visible light excitation the photocatalyst reduces N-chloramine to form an aminium radical cation under the strongly acidic conditions. This aminium radical cation can rapidly react with electron rich or neutral arenes, leading to direct C–H amination and upon deprotonation and rearomatisation gives the corresponding arylamine. This transformation is reported to require low reaction temperatures (0 °C) for optimum results. In this reactor comparison, the TAK120 (LC) was operated with a 0 °C and −3 °C recirculated cooling set-up. Although sub-ambient temperatures cannot be obtained with air cooling, we investigated this transformation using pre-cooled reaction mixtures in the different air-cooled photoreactors. In our experiments all air-cooled photoreactors failed to achieve yields greater than 10%, despite pre-cooling the reactions to 0 °C beforehand. All reactions performed within air-cooled photoreactors reached temperatures far above the recommended temperature for this reaction, indicating a more effective form of cooling was required for maintaining temperatures that lead to the correct reactivity. Initial results with the liquid cooled TAK120 set-up were slightly better, with yields approaching 35% after 2 h and the reactions being maintained at ~5 °C (when recirculated fluid was set to −3 °C). The conversion to the desired product in all cases however, was significantly lower than the reported literature yield (62% for the *para*-functionalised product in MeCN) and this is obviously due to reaction temperatures rising above 0 °C in all photoreactors. This significant drop in yield may be attributed to an increasing rate of competing undesirable reactivity that occurs at higher temperatures. Leonori and co-workers demonstrated that higher temperatures lead to competition between nitrogen radical addition to the arene and electrophilic aromatic halogenation/substitution of the arene with chloride anions present in the reaction mixture. This mechanistic understanding also provides an explanation why the large discrepancies in yields occur and also explains why light intensity has no correlation to yield in this case.

The reaction illustrates an experimental limitation of the photoreactors for transformations requiring sub-ambient reaction temperatures. Due to the increasingly powerful light sources used in photoredox, photoreactors with cooling fluids up to 20 °C below the desired reaction temperature may be required to sufficiently maintain the correct reaction temperatures.

2.3. Trifluoromethylation of Arenes and Heteroarenes by Photoredox Catalysis

The trifluoromethylation of arenes reported by MacMillan and co-workers is a methodology of particular interest to medicinal chemists as facile introduction of fluorinated groups is a highly desirable transformation.[16] After visible light excitation of the Ir photocatalyst an oxidative photoredox cycle leads to the reduction of triflyl chloride, to give a highly electrophilic carbon-centered CF_3 radical. This CF_3 radical may attack an arene and the following species is oxidized and subsequently deprotonated leading to rearomatisation and formation of the desired trifluoromethylated product (Figure 4).

These trifluoromethylations were reported as requiring a reaction time of 24–72 h in the general procedure and in the case of lidocaine the reported time required was 48 h. The reaction was replicated in all three air-cooled photoreactors and monitored over 18 h, but the reported yield of 78% was not reached after 18 h and yields on average did not increase further after 3 h. The TAK120 (AC) gave 58% product after 3 h, the PennOC 39% in 3 h and the HepatoChem box 32% after 3 h. The liquid cooled TAK120 gave a 64% yield after 3 h at

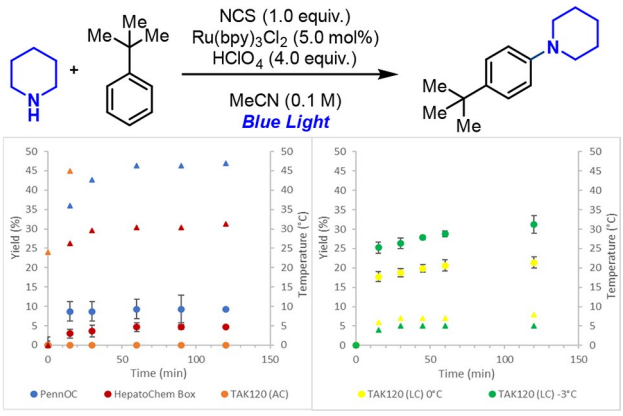

Figure 3. Photoredox mediated Minisci amination of tert-butylbenzene with piperidine; solid dots represent yields (%) and small triangles represent temperature (°C). Left: difference in reaction yields (%) and temperature (°C) over time in the air-cooled photoreactors. Right: difference in reaction yields (%) and temperature (°C) over time in in the TAK120 (LC) photoreactor.

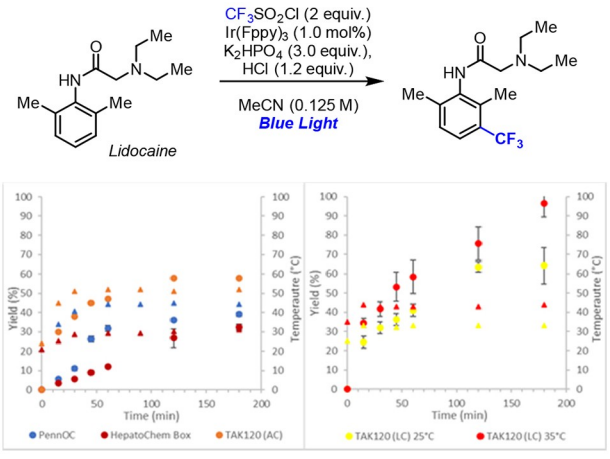

Figure 4. Photoredox trifluoromethylation of lidocaine; solid dots represent yields (%) and small triangles represent temperature (°C). Left: difference in reaction yields (%) and temperature (°C) over time in the air-cooled photoreactors. Right: difference in reaction yields (%) and temperature (°C) over time in in the TAK120 (LC) photoreactor.

25 °C and performed exceptionally well at 35 °C achieving a near complete conversion (97%) after 3 h. Initial reaction rate was highest in the TAK120 reactors, followed by the PennOC and finally the Hepatochem Box indicating that the reaction rate is dependent on light intensity. Increased reaction temperature also appears to directly correlate with reaction rates with the hotter reactions converting faster. However, in the case of the TAK120 (AC) reactor, as the temperature of the reaction continues to ascend the rate of reactivity slows and the final yield falls short of its liquid cooled counterpart. No in depth mechanistic studies have been carried out on this transformation that would allow to explain the observation. Despite only a moderate temperature difference between the TAK120 (AC) (~55 °C) and TAK120 (LC, 35 °C) (45 °C) a large difference in yield is observed, highlighting the importance of temperature control. In contrast to the complex temperature dependence of this reaction, the effect of varying the light intensity is simple: the photoreactors with the highest light intensity perform best in this reaction. The literature reports that the reaction was performed at ambient temperature although the procedure does not report an internal reaction mixture temperature. The results we obtained highlight the challenge in reproducing literature results, especially if other equipment is employed and only part of the reaction parameters are available.

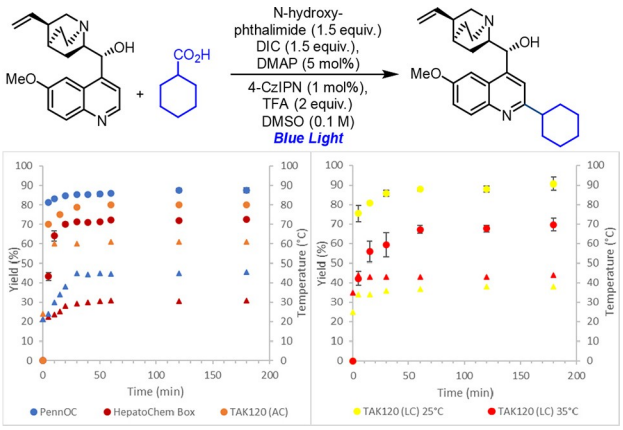

Figure 5. Radical addition of a cyclohexyl radical to quinine via a photoredox Minisci alkylation; solid dots represent yields (%) and small triangles represent temperature (°C). Left: difference in reaction yields (%) and temperature (°C) over time in the air-cooled photoreactors. Right: difference in reaction yields (%) and temperature (°C) over time in in the TAK120 (LC) photoreactor.

2.4. Organo-Photoredox Minisci Reaction Using N-(Acyloxy) phthalimides

The Minisci-alkylation is a classical radical transformation and is particularly useful in functionalizing basic N-heterocycles. A photoredox mediated variation of the Minisci alkylation was reported by Sherwood at Bristol-Myers Squibb.[17] This methodology relies on pre-formation of the redox active ester (RAE), allowing for a large variety of alkyl radicals to be accessed due to the broad availability of carboxylic acids. Upon visible-light excitation the photocatalyst undergoes an oxidative redox cycle leading to the reduction of the RAE, which subsequently fragments into a phthalimide anion and the alkyl radical. These electron rich carbon-centered radicals may undergo Minisci alkylation of protonated N-heterocycles, leading to C–C bond formation and upon subsequent rearomatisation (by oxidation and deprotonation of the arene radical) yielding the desired alkylated N-heterocycles (Figure 5).

All photoreactors gave the product in yields exceeding the literature reported values for the C–H alkylation of *Quinine* with a cyclohexyl radical (48%) within a shorter reaction time than the literature reported 3 h. While all reactors achieved excellent yields, the kinetic profiles of the various reactors was noticeably different: the PennOC, TAK120 (AC) and (LC, 25 °C) reactors achieved product yields of more than 70% within 10 min of illumination, whereas the HepatoChem box reached 70% after 30 min and the TAK120 (LC, 35 °C) taking 3 hrs. With the exception of the TAK120 (LC, 35 °C) all the initial reaction temperatures were between 20–25 °C and all had very fast initial reaction rates (with the exception of the Hepatochem Box, which is likely due to lower light intensity) relative to the hotter reaction run at 35 °C. This inverse temperature dependence on rate for this reaction allows for the cooler reactions to rapidly react initially and then slow down significantly after a mere 10 °C increase in temperature, explaining why the typically hotter TAK120 (AC) reactor outperforms the TAK120 (LC, 35 °C). The literature procedure used no active cooling, while illuminating the reactions with two blue Kessil brand KSH150B Grow Light LED 34 W lamps with reactions reaching between 40–48 °C by their measurements. While, both the TAK120 (AC) (61 °C) and PennOC (45°) systems exceeded reaction mixture temperatures of 40 °C, these temperatures were reached after the reactions had essentially gone to completion (while in the 25–35 °C range), exemplifying how important temperature control can be.

2.5. Silyl Radical Activation of Alkyl Halides in Metallaphotoredox Catalysis

Next, we investigated a metallaphotoredox-catalyzed cross coupling developed by MacMillan and co-workers.[18] This methodology allows the coupling of two different electrophiles, in this case 4-bromotetrahydropyrane and 4-bromo methylbenzoate (Figure 6). This reaction utilizes the oxidative addition of the aryllbromide to Ni(0) and the propensity of nickel complexes in higher oxidation states to undergo reductive elimination. Photoredox catalysis allows for room temperature formation of an alkyl radical and catalytically adjusts the nickel's oxidation state to allow for the desired reductive elimination.

All photoreactors gave yields higher than the literature reported yield of 64% after 6 h. The PennOC and TAK120 photoreactors had the fastest initial conversion. The conversion in the TAK120 (AC) reactor slowed significantly down beyond 30 minutes, coinciding with an increase in reaction temperature, reaching completion after 6 hours-significantly slower

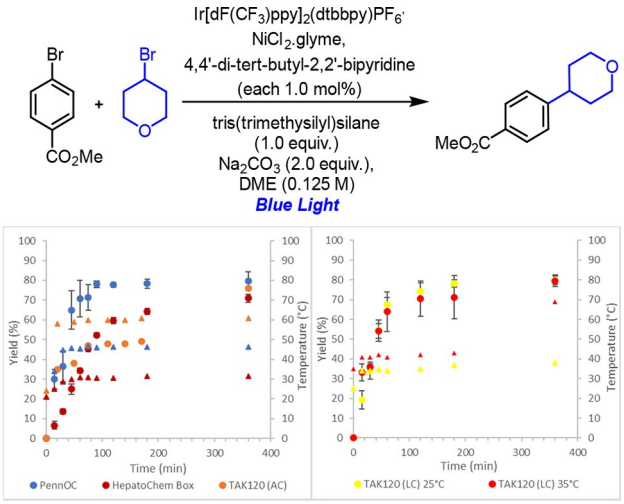

Figure 6. Cross-electrophile coupling of 4-Bromotetrahydropyran and methyl 4-bromobenzoate via metallaphotoredox; solid dots represent yields (%) and small triangles represent temperature (°C). Left: difference in reaction yields (%) and temperature (°C) over time in the air-cooled photoreactors. Right: difference in reaction yields (%) and temperature (°C) over time in in the TAK120 (LC) photoreactor.

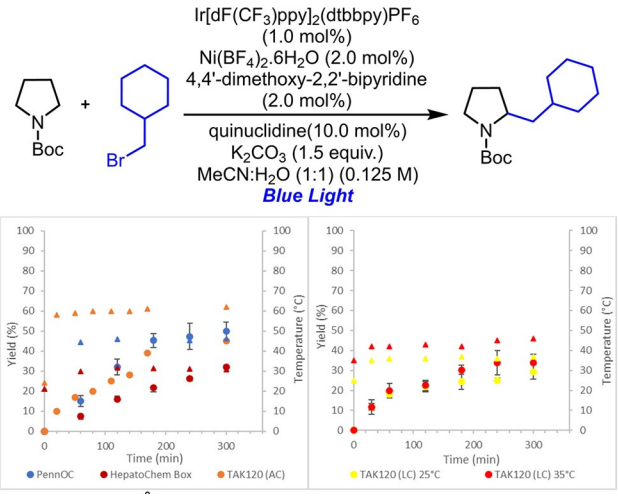

Figure 7. sp^3 C–H alkylation of N-boc pyrrolidine with (bromomethyl) cyclohexane via polarity-match cross-coupling; solid dots represent yields (%) and small triangles represent temperature (°C). Left: difference in reaction yields (%) and temperature (°C) over time in the air-cooled photoreactors. Right: difference in reaction yields (%) and temperature (°C) over time in in the TAK120 (LC) photoreactor.

than its liquid cooled counterpart (~2-3 hrs). The Heptaochem Box also was significantly slower than the other photoreactors despite maintaining a lower temperature. All photoreactors reached similar yields (+/−10%) within 6 h reaction time, despite the difference in light intensity and reaction mixture temperatures varying from 30 °C to 60 °C. The reaction kinetics in the TAK120 (LC) at 25 °C and 35 °C are almost identical. The results indicate that this reaction, to some extent, tolerates a larger range of reaction temperatures, but insufficient temperature control can affect reaction times.

2.6. Selective sp^3 C–H Alkylation Via Polarity-Match Cross-Coupling

Finally, another transformation using metallaphotoredox chemistry was explored. The sp^3-sp^3 C–C bond formation between alkyl C–H and alkyl bromides was developed by MacMillan and co-workers, utilizing a triple catalytic system. Here, the photocatalyst is used to oxidize quinuclidine, which upon oxidation is a potent hydrogen atom transfer (HAT) agent for hydridic alkyl hydrogen atoms (Figure 7).[19] The alkyl radical is trapped by a Ni(II) species as described in the previous example, and the reduced photocatalyst is proposed to reduce the formed Ni(III) intermediate to allow for reductive elimination of the product.

The reactions in all three air-cooled photoreactors proceeded with good yields of the desired product. The TAK120 (AC) and PennOC reached 58% yield after 6 h despite the difference in reaction temperature and light intensity; the reaction in the HepatoChem box was slower initially relative to all the other photoreactors. The reactions in the TAK120 (LC) when cooled with 25 °C and 35 °C cooling solutions maintained a reaction temperature below 50 °C and gave a lower product yield. It remains unclear whether the light intensity and reaction temperature are significantly affecting the rate and product formation of this reaction without further mechanistic investigations. The kinetic profile of the reaction run in the PennOC and TAK120 (AC) are similar despite the differences in these parameters.

3. Conclusion

We have investigated the performance of six reported photocatalytic reactions in four commercially available photoreactors. Our results show that standardization of photoreactors may help to improve reaction reproducibility and accessibility to novel transformations. All reactions showed very little variance in yield within a single reactor, with multiple repetitions of a reaction giving very similar results with only minor deviations. Our investigation shows that improvements in product yield and reaction times in the majority of tested reactions are possible when using high light intensity standardized setups and in many cases, the lower powered Hepatochem box had significantly slower initial reaction rates due to this. Reactions which originally were reported using broad-wavelength CFL as the light source were improved when run in the photoreactors using blue LEDs. Increased light intensity clearly enhanced the rate of reaction in most of the tested reactions, such as the radical trifluoromethylation of arenes, the Minisci alkylation of arenes and the cross electrophile coupling of organohalides. Some reactions benefited from more efficient temperature control and a clear decrease in reactivity was seen in some reactions upon heating up; in the case of the amination of arenes, almost no product formation was seen in the air-cooled photoreactors. Overall, irradiation intensity and temperature are important parameters affecting the rate and yield of a

reaction. However, to truly understand how they each affect specific reactions further mechanistic studies are often required. For photoredox catalysis to be successfully implemented in medicinal chemistry on substrates beyond the scope of the initial publication, better reporting of reaction conditions and set-ups will be essential. As such, details pertaining to reaction set-ups must also take into account light intensity and reaction temperatures. While major progress in the design and implementation of photoreactors has been made, for the next generation of standardized photoreactors an accurate control of light intensity and reaction temperature will be highly desirable for clearer separation of thermal and photo-chemical effects on photocatalyzed reactions. This feature would be greatly appreciated by those developing new methods and those applying them in industrial research and development.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: light intensity · photoredox catalysis · photoreactor · reaction temperature · reproducibility

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