Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in
Green and Sustainable Chemistry

Recent advances toward sustainable flow photochemistry

Jason D. Williams[1,2] and C. Oliver Kappe[1,2]

Although flow photochemistry has significant potential in advancing sustainable processing, there are substantial hurdles to attaining this. Development in three key areas over the past 3 years are discussed here: 1) light source technology; 2) reactor design; and 3) process understanding and intensification. A small number of illustrative examples provide an insight on the benefits that can be accessed through advances in these areas. More in-depth knowledge and experimentation around wavelength dependence can enhance efficiency and selectivity in transformations. Reactors capable of handling solid–liquid reactions can allow reliable processing of metal-free and recyclable catalyst systems. Concentrating and accelerating transition-metal/photoredox coupling methodologies make these processes increasingly attractive. Continuation of these trends will undoubtedly lead to future large-scale applications, carried out in a sustainable manner.

Addresses
[1] Center for Continuous Flow Synthesis and Processing (CC FLOW), Research Center Pharmaceutical Engineering GmbH (RCPE), Inffeldgasse 13, 8010 Graz, Austria
[2] Institute of Chemistry, University of Graz, NAWI Graz, Heinrichstrasse 28, 8010 Graz, Austria

Corresponding author: Kappe, C. Oliver (oliver.kappe@uni-graz.at)

Current Opinion in Green and Sustainable Chemistry 2020, **25:**100351

This review comes from a themed issue on **Flow Chemistry**

Edited by **Francesca Paradisi** and **John Woodley**

Available online 19 May 2020

For complete overview of the section, please refer the article collection - Flow Chemistry 2020

https://doi.org/10.1016/j.cogsc.2020.05.001

Introduction

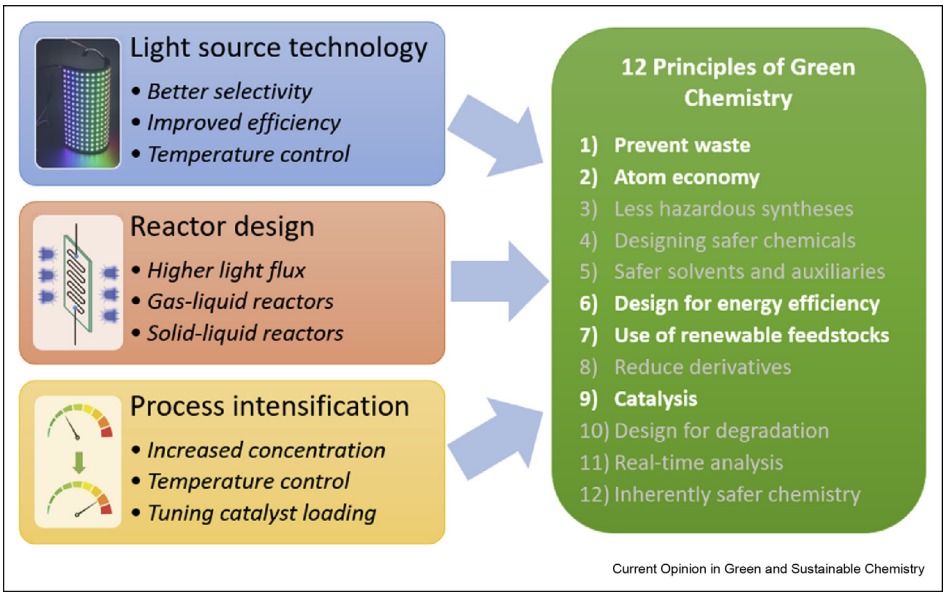
Within the organic chemistry community, photochemistry has made significant recent impact, by introducing a plethora of novel synthetic methods, which are driven by irradiation of a component in the reaction mixture. This can be the substrate itself, a metal [1] or organic [2] photocatalyst, or an *in situ*–generated charge transfer complex [3]. The implementation of synthetic photochemistry can already begin to meet the aims of green chemistry [4,5] through two main principles. Many known disconnections can be achieved under milder conditions, by using photons as a traceless reagent to activate otherwise benign starting materials. Alternatively, entirely new disconnections can be facilitated, which can complete target-oriented syntheses in fewer steps, for significant savings in resources, time, energy, and waste.

Photochemistry in batch is generally limited by poor light penetration, therefore, scaling up to larger batch reactors is generally impractical. Performing photochemistry in continuous flow has been demonstrated as a widely suitable method to carry out photochemical reactions on larger scales. Consequently, there are numerous reviews on flow photochemistry [6–9], including more specific focuses on reactions toward active pharmaceutical ingredient (API) synthesis [10,11], reactor technology [12], and dual catalysis methodologies [13].

This review will focus specifically on the developments made over the past 3 years toward sustainable photochemical processing in flow. The general benefits of flow chemistry with respect to sustainable processing are discussed in detail elsewhere [14,15], so will be avoided here. It is also noteworthy that recently developed photoredox methodologies have not yet reached the stage of production in the pharmaceutical industry. Although long process development cycles and a lack of photochemical retrosynthetic experience [16] may be partly responsible, it is also likely that scale-up and engineering issues are to blame. In particular, poor sustainability profiles (e.g. low reaction concentrations and the use of precious metal catalysts) render most photochemical routes undesirable. Accordingly, there are very few published examples of modern flow photochemical processes on large scales. As a result, this article will focus on laboratory-scale examples, and the reader must bear in mind that these are often not fully optimized for sustainable processing.

Within this article, the impact of three key elements of flow photochemical processing will be considered: 1) new light source technologies; 2) development of reactor design; and 3) reaction understanding and optimization for process intensification (Figure 1). Owing to its short length, it is not possible to be exhaustive in examples, so each of these points will be illustrated with a small selection of case studies, which demonstrate the key principles and their potential environmental impact. The continuing developments in these fields will increase the likelihood of flow photochemistry being incorporated into production-scale

Figure 1



A summary of the topics discussed here and their potential impact on the 12 Principles of Green Chemistry.

synthetic routes in the coming years, allowing the enhanced sustainability profiles of photochemical transformations to be fully realized.

Toward sustainable flow photochemistry

Light source improvements

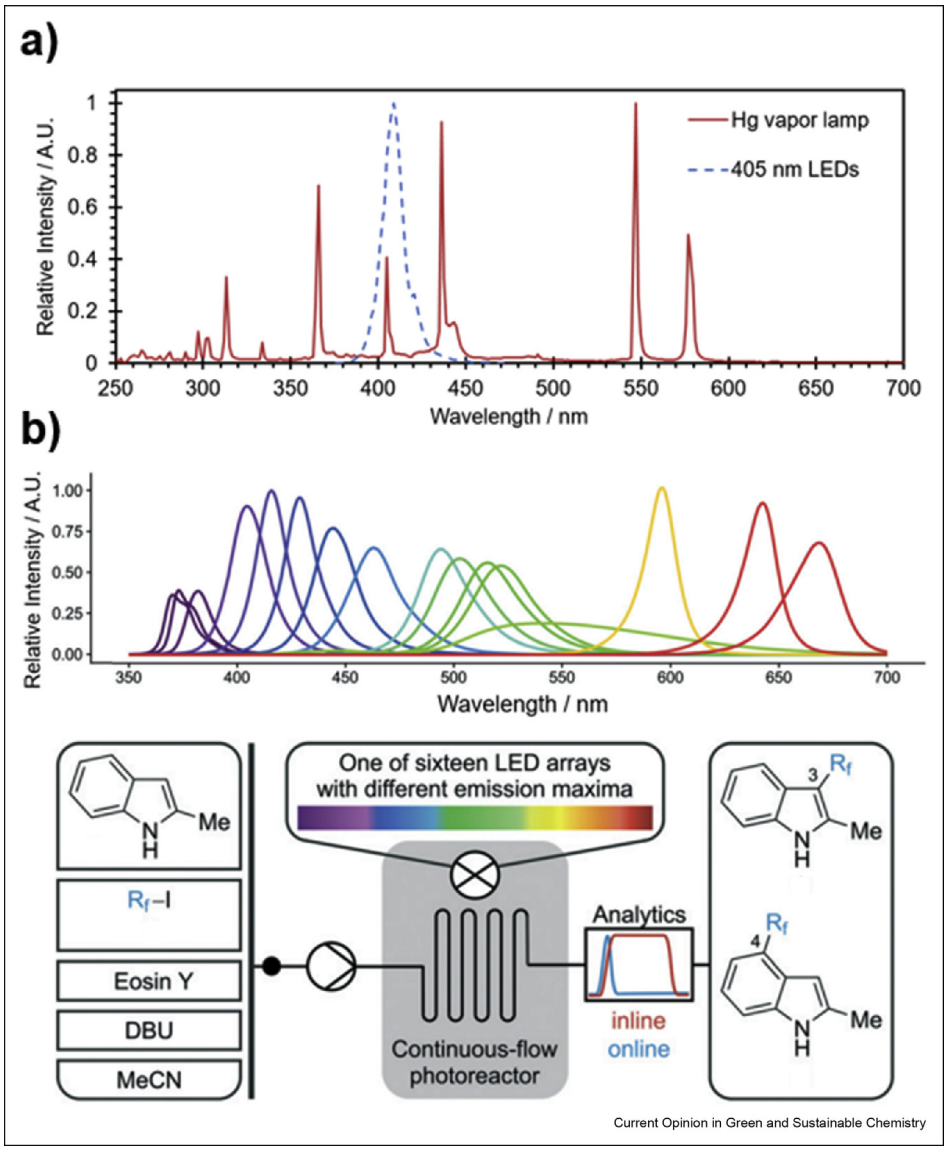
Although often overlooked, especially by synthetic chemists developing new methodologies, the light source is, in many cases, the most important reactor component. As highlighted by a recent synthetic photochemistry commentary [17], many reactions developed on small scales inevitably use suboptimal light sources. In simple cases, UV/vis characterization of the reaction substrate or photosensitizer can easily determine the most suitable wavelength. Deeper understanding, however, can occasionally reveal mechanistic considerations, which lead to improved reaction conditions or alternative pathways.

Advances in light-emitting diode (LED) technology confers that pseudo-monochromatic light sources in a wide range of wavelengths are now available with good efficiencies (~25–60% for wavelengths 365–525 nm) [18]. This approach is far more energy-efficient than the traditionally used polychromatic light sources (e.g. pressurized mercury vapor lamps; Figure 2a) [18]. Using an efficient monochromatic light source minimizes energy losses in nonabsorbed light and, more importantly, in heat. When considering larger-scale processing, light source cooling can potentially require more energy than powering the light source itself. It has been estimated that every decade, the cost per lumen from an LED light source has been falling by a factor of 10 as the amount of light generated increases by a factor of 20. An upward trend in efficiency is set to continue in coming years, leading to further improvements in energy efficiency [19].

In consequence, many traditional photochemical transformations have now benefited from being performed using LED light sources in place of pressurized mercury vapor lamps. A prime example is benzylic bromination, where efficient irradiation of Br_2 ($\lambda_{max} \approx 395$ nm) can be targeted without also applying extraneous wavelengths [20–22]. Improvements in LED materials (e.g. gallium-nitride) mean that shorter wavelength LEDs, currently down to 365 nm, are available with high efficiencies [23]. Therefore, an increasing variety of UV photochemistries can now also be performed using LEDs. This trend is set to continue, eventually allowing access to high power deep UV LEDs for direct-excitation photochemistries (e.g. singlet state rearrangements) [24].

The use of pseudo-monochromatic light sources has allowed changes in reaction mechanism at different wavelengths to be discerned. For example Tallarek et al. [25] reported the wavelength-dependent perfluoroalkylation of an indole. A flow reactor was used in combination with LED arrays of 16 different wavelengths, whereby different mechanisms could be distinguished: eosin Y single electron catalysis, versus activation via an EDA (electron donor–acceptor) complex with either the substrate or an added base

Figure 2



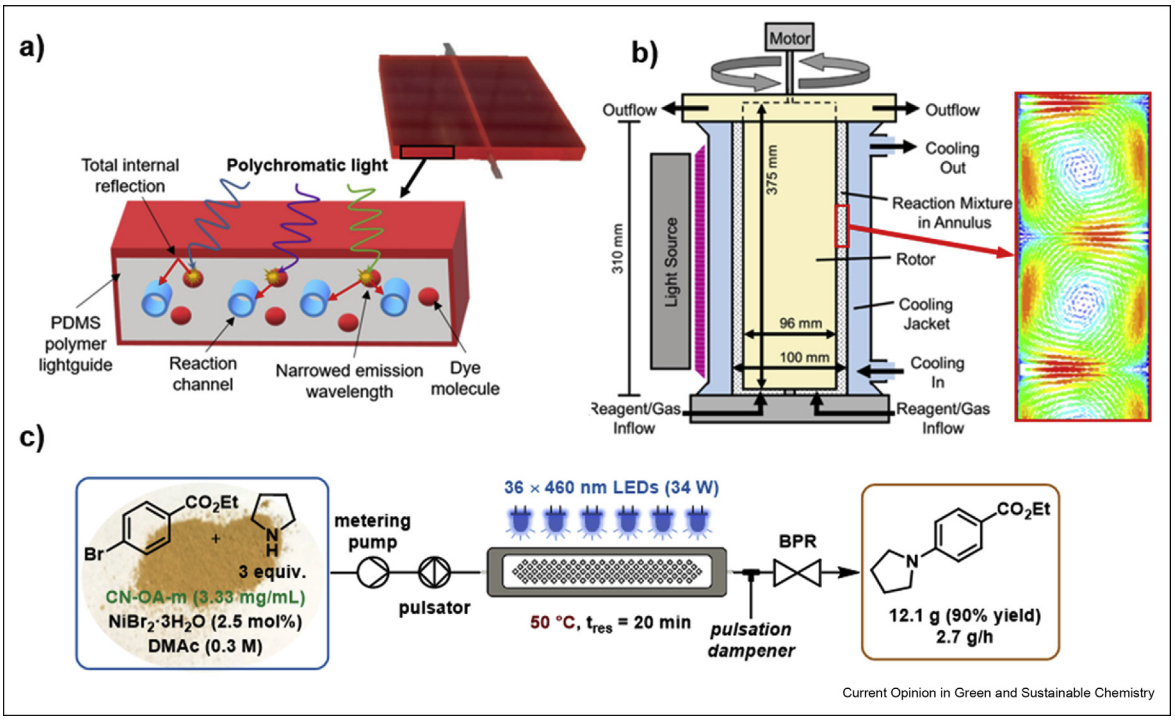
Comparison of light sources used in flow photochemistry. **a)** Overlapping (relativized) emission spectra of a medium pressure mercury vapor lamp, with a 405 nm pseudo-monochromatic LED. **(b)** Overview of the experimental setup and LED wavelengths examined for the wavelength-dependent perfluoroalkylation of an indole [25]. Adapted from Ref. [25] with permission from The Royal Society of Chemistry.

(Figure 2b). This in-depth study allowed discrimination between multiple different reported mechanisms, toward the most energy- and mass-efficient solution for this specific case. A similar report by our group also showed that the photocatalyst can be removed from an iodoperfluoroalkylation reaction when operating with wavelengths <420 nm [26].

Reactor design

Alongside the light source, flow reactor design plays a vital role, and has also seen significant progress [12,27]. The impact of 3D printing has been of some note, but generally limited to 'homemade' laboratory-scale reactors, allowing fast design and production of parts to hold and support lamps, tubing-based reactors, and so on [28]. However, dye-doped polymers have played an important role in the development of luminescent solar concentrators (LSCs), which act to harvest broad spectrum light and release it as the desired wavelength toward the flow reaction channel [29–31]. This allows significantly improved efficiency and the opportunity to easily convert sunlight [32,33] to the desired wavelength (Figure 3a).

Figure 3



Representative examples of reactor technologies at work in flow photochemistry. **(a)** Photoemissive dye encapsulated in plastic, forming the channels of an LSC. **(b)** Vortex fluidic reactor used for photochemical oxidation, showing the reactor principle and the mixing within small vortices, calculated using computational fluid dynamics (CFD). Adapted with permission from Ref. [38]. Copyright 2020 American Chemical Society. **(c)** A pulsator-assisted oscillatory plug flow reactor, used to maintain and pump a reaction mixture containing a carbon nitride heterogeneous photocatalyst.

Gases can often act as incredibly atom efficient reagents and are well suited to flow processing [34]. In the realm of photochemistry, oxygen is particularly prevalent, because of its easily accessible singlet state, when combined with a photosensitizer. Performing aerobic reactions in flow is considered to be a far safer option than batch, because of the low reactive inventory and high explosive pressure tolerance [35,36]. As a result, aerobic photochemistry in flow has been proven to be an excellent match.

Indeed, many reports have taken advantage of aerobic oxidation chemistry to demonstrate new reactor designs. For example, in a vortex reactor, a central rotor is positioned within a sleeve, providing a small annulus, which the reaction mixture is pumped through. As the central rotor spins, small Taylor vortices are generated, imparting intensive mixing as the material moves through the reactor (Figure 3b).

Recent reports have demonstrated this on small scale (1 mm annulus, 8 mL reactor volume) [37], before increasing to a larger reactor (2 mm annulus, 280 mL reactor volume) [38]. The initial report was limited to using air drawn in from the laboratory, but when performed in the larger reactor, oxygen was delivered directly using a mass flow controller, which significantly increased the throughput, providing productivity up to almost 2 kg/day (Figure 3b). Owing to complex moving parts, this type of reactor is limited to working at low pressure, where oxygen solubility in the organic solvent (ethanol) is low. It is yet to be seen, however, whether this approach offers an improvement versus highly pressurized reactors.

Another substantial goal toward greener photochemistry is to circumvent the use of noble metal catalysts, such as the commonly used iridium and ruthenium complexes. Use of precious metals with very low abundance is wasteful and detrimental to the Earth's reserves. Although organic photocatalysis has shown significant promise [3,39], higher loadings are often required and photobleaching during the reaction can be problematic. Alternatively, semiconductor catalysis has also emerged as a prominent field [40]. In particular, nanodots, such as CdSe, and organic polymers, such as carbon nitrides [41,42], have shown tremendous promise.

The implementation of these heterogeneous catalysts presents further challenges for flow processing—which is often considered by organic chemists to be incompatible with solids. The first carbon nitride-catalyzed

flow photochemical process was achieved using a highly viscous reaction medium, combined with gas flow, to set up a slug flow regime with internal mixing of the solid photocatalyst [43].

We recently described the first use of an oscillatory plug flow photoreactor to provide a stable suspension of carbon nitride photocatalyst as it progresses through the photoreactor (Figure 3c) [44]. Stable operation was demonstrated over 5 h, yielding to 2.7 g/h of the desired product. Furthermore, complete recyclability of the carbon nitride photocatalyst was observed over ten experimental cycles, reinforcing the enhanced sustainability of this strategy. In a similar vein, a small continuous stirred-tank reactor (CSTR) cascade has also been reported for handling solids in flow photochemical reactions. However, this application focused on the use of an insoluble inorganic base, which avoids requirements for an expensive and unsustainable organic alternative [45]. It must be noted, however, that handling of solids in flow reactors requires optimization for each specific system, because the properties of solvent and solids (e.g. particle size, suspendability) varies significantly.

Process intensification

A key contributor to the aim of sustainable manufacturing is that of process intensification. By successfully intensifying a process, it is possible to produce far more of a desired product using less solvent, energy, space, and/or time [46]. A significant focus of process intensification has been on reactor engineering [47]; however, the development of novel chemistries has urged further attention to be directed to the reaction conditions themselves.

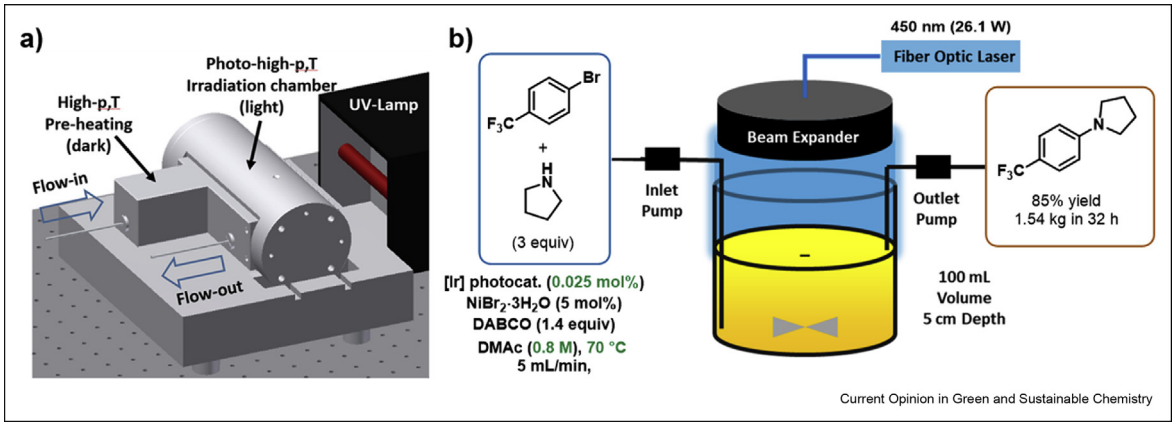
In photochemical processes, solvent use is a particular issue, because a significant proportion of these reactions must be run at very low concentrations (in the millimolar range) to achieve selectivity for the desired product. Adaptation of reaction conditions to a specific flow reactor can facilitate this, because of shorter irradiated path lengths allowing homogeneous reaction mixture irradiation. For example, recent work on the flow photochemical rearrangement of provitamin D has further developed high temperature and pressure conditions to facilitate an increase in reaction concentration from 30 [48] to 220 mM, corresponding to a sevenfold decrease in solvent usage (Figure 4a) [49].

Another field of photochemistry that has recently been the subject of intensive research is that of transition-metal/photoredox dual catalytic methods [13,50]. Being a relatively new class of reactions, with multiple catalytic species, the initially used reaction conditions have generally been very poor from a sustainability perspective. However, as the corresponding mechanistic knowledge continues to grow, these transformations can become increasingly intensified.

A process chemistry group from Abbvie demonstrated the tuning of catalyst loading to enhance reaction rate in an irradiated CSTR for a nickel/ iridium-catalyzed aryl amination. By decreasing the loading of photocatalyst, homogeneous irradiation of the solution was achieved, leading to a maximized reaction rate. The optimal catalyst loading was found to be 0.025 mol% whereby 1.54 kg of the desired product could be isolated using only 2.2 g of iridium catalyst (Figure 4b) [51]. Although the use of precious metal catalysts should be eliminated where possible, this approach at least allowed a significant reduction of wastage.

In addition to an optimized catalyst loading, increases in the reaction temperature and concentration were also

Figure 4



Illustrated examples of intensified flow photochemical processes. **(a)** High pressure and temperature vitamin D3 production, facilitating higher reaction concentration. Adapted with permission from Ref. [49]. Copyright 2018 American Chemical Society. **(b)** Laser CSTR reactor used for high temperature and concentration nickel/photoredox dual catalytic C–N coupling, with an exceptionally low photocatalyst loading. Adapted with permission from Ref. [51]. Copyright 2019 American Chemical Society.

found to have a profound positive effect on reaction rate. In general, photochemical transformations are assumed to be light-limited, yet dual-catalytic protocols appear, in some cases, to be accelerated using methods analogous to standard process intensification techniques. This was also exemplified by Buchwald et al. [52], who demonstrated that increasing the reaction temperature to 80 °C allowed complete reaction in residence times as short as 10 min. Intensification of these, and related protocols, will inevitably lead to increased adoption for larger-scale processing.

Summary and outlook

It must be reiterated that the current state of flow photochemistry is far from reaching maturity, particularly at production scale. Although significant advances are required before the Green benefits of synthetic photochemistry can be fully exploited, progress has undoubtedly been made in recent years. As the interest of the synthetic and process chemistry communities continue to grow, it is inevitable that further opportunities will present themselves. This will allow flow photochemistry to become an indispensable tool in the Green chemist's synthetic arsenal.

The three main topics covered here demonstrate that flow photochemistry is heavily reliant on other disciplines. Material scientists contribute through development of light source technologies and chemical engineering principles are invoked in the design of improved reactors. The most significant input by the chemist concerns the development of new chemistries and optimization toward the most efficient operating conditions. The enhanced understanding that underpins this development will arguably be the area of greatest impact in the coming years. With even more new transformations, and enhanced understanding of current ones, flow photochemistry will undoubtedly begin to influence sustainable manufacture.

Funding sources

The CCFLOW Project (Austrian Research Promotion Agency FFG Austria Grant number: 862766) is funded through the Austrian COMET Program by the Austrian Federal Ministry of Transport, Innovation and Technology (BMVIT), the Austrian Federal Ministry for Digital and Economic Affairs (BMDW), and by the State of Styria (Styrian Funding Agency SFG).

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Papers of particular interest, published within the period of review, have been highlighted as:

* of special interest
** of outstanding interest

1. Prier CK, Rankic DA, MacMillan DWC: **Visible light photoredox catalysis with transition metal complexes: applications in organic synthesis**. *Chem Rev* 2013, **113**:5322–5363.

2. Romero NA, Nicewicz DA: **Organic photoredox catalysis**. *Chem Rev* 2016, **116**:10075–10166.

3. Lima CGS, Lima TDM, Duarte M, Jurberg ID, Paixão MW: **Organic synthesis enabled by light-irradiation of EDA complexes: theoretical background and synthetic applications**. *ACS Catal* 2016, **6**:1389–1407.

4. Anastas P, Eghbali N: **Green chemistry: principles and practice**. *Chem Soc Rev* 2010, **39**:301–312.

5. Erythropel HC, Zimmerman JB, de Winter TM, Petitjean L, Melnikov F, Lam CH, Lounsbury AW, Mellor KE, Janković NZ, Tu Q, Pincus LN, Falinski MM, Shi W, Coish P, Plata DL, Anastas PT: **The Green ChemisTREE: 20 years after taking root with the 12 principles**. *Green Chem* 2018, **20**:1929–1961.

6. Knowles JP, Elliott LD, Booker-Milburn KI: **Flow photochemistry: old light through new windows**. *Beilstein J Org Chem* 2012, **8**: 2025–2052.

7. Noël T: **A personal perspective on the future of flow photochemistry**. *J Flow Chem* 2017, **7**:87–93.

8. Cambié D, Bottecchia C, Straathof NJW, Hessel V, Noël T: **Applications of continuous-flow photochemistry in organic synthesis, material science, and water treatment**. *Chem Rev* 2016, **116**:10276–10341.

9. Sambiagio C, Noel T: **Flow photochemistry: shine some light on those tubes!** *Trends Chem* 2020, **2**:92–106.

10. Politano F, Oksdath-Mansilla G: **Light on the horizon: current research and future perspectives in flow photochemistry**. *Org Process Res Dev* 2018, **22**:1045–1062.

11. Filippo M Di, Bracken C, Baumann M: **Continuous flow photochemistry for the preparation of bioactive molecules**. *Molecules* 2020, **25**:356–368.

12. Rehm TH: **Reactor technology concepts for flow photochemistry**. *ChemPhotoChem* 2019, **3**:1–21.

13. Kim SD, Lee J, Kim NJ, Park BY: **Visible-light-mediated cross-couplings and C–H activation via dual photoredox/transition-metal catalysis in continuous-flow processes.** *Asian J Org Chem* 2019, **8**:1578–1587.

14. Dallinger D, Kappe CO: **Why flow means green – evaluating the merits of continuous processing in the context of sustainability**. *Curr Opin Green Sustain Chem* 2017, **7**:6–12.

15. Rogers L, Jensen KF: **Continuous manufacturing-the green chemistry promise?** *Green Chem* 2019, **21**:3481–3498.

16. * Petzold D, Giedyk M, Chatterjee A, König B: **A retrosynthetic approach for photocatalysis**. *Eur J Org Chem* 2020, **2020**: 1193–1244.
This review looks at photochemical transformations from a retrosynthetic perspective, which is likely to assist in targetting specific transformations which could shorten synthetic routes.

17. * Bonfield HE, Knauber T, Lévesque F, Moschetta EG, Susanne F, Edwards LJ: **Photons as a 21st century reagent**. *Nat Commun* 2020, **11**:804.
A short commentary, authored by process chemists in the pharmaceutical industry, which highlights the importance of light source and reactor characterization for reproducible photochemistry.

18. ** Sender M, Ziegenbalg D: **Light sources for photochemical processes – estimation of technological potentials**. *Chem Ing Tech* 2017, **89**:1159–1173.
A detailed review of different light sources for application to photochemical processes, including assessment of light output, efficiencies, and cost per mole of photons.

19. Soht MY, Teo TH, Ngt WX, Yeo KS: **Review of high efficiency integrated LED lighting**. *Proc Int Conf Power Electron Drive Syst* 2017, **2017**:93–97.

20. Chen Y, de Frutos O, Mateos C, Rincon JA, Cantillo D, Kappe CO: **Continuous flow photochemical benzylic bromination of a key intermediate in the synthesis of a 2-oxazolidinone**. *ChemPhotoChem* 2018, **2**:906–912.

21. Steiner A, Williams JD, de Frutos O, Rincón JA, Mateos C, Kappe CO: **Continuous photochemical benzylic bromination using in situ generated Br 2: process intensification towards optimal PMI and throughput**. *Green Chem* 2020, **22**:448–454.

22. Manabe Y, Kitawaki Y, Nagasaki M, Fukase K, Matsubara H, Hino Y, Fukuyama T, Ryu I: **Revisiting the bromination of C-H bonds with molecular bromine by using a photo-microflow system**. *Chem Eur J* 2014, **20**:12750–12753.

23. Hölz K, Lietard J, Somoza MM: **High-power 365 nm UV LED mercury arc lamp replacement for photochemistry and chemical photolithography**. *ACS Sustain Chem Eng* 2017, **5**:828–834.

24. Davies DME, Murray C, Berry M, Orr-Ewing AJ, Booker-Milburn KI: **Reaction optimization and mechanism in maleimide [5 + 2] photocycloaddition: a dual approach using tunable UV lasers and time-dependent DFT**. *J Org Chem* 2007, **72**:1449–1457.

25. ** Haas CP, Roider T, Hoffmann RW, Tallarek U: **Light as a reaction parameter – systematic wavelength screening in photochemical synthesis**. *React Chem Eng* 2019, **4**: 1912–1916.
The authors demonstrate the influence of wavelength on reaction mechanism, using a flow reactor equipped with 16 different LED wavelengths. Some difference in selectivity is observed through these different mechanisms.

26. Rosso C, Williams JD, Filippini G, Prato M, Kappe CO: **Visible-light-mediated iodoperfluoroalkylation of alkenes in flow and its application to the synthesis of a key iintermediate**. *Org Lett* 2019, **21**:5341–5345.

27. André JC, Viriot ML, Villermaux J: **New developments in photochemical technology**. *Pure Appl Chem* 1986, **58**:907–916.

28. Guba F, Tastan Ü, Gugeler K, Buntrock M, Rommel T, Ziegenbalg D: **Rapid prototyping for photochemical reaction engineering**. *Chem Ing Tech* 2018, **91**:17–29.

29. * Cambié D, Dobbelaar J, Riente P, Vanderspikken J, Shen C, Seeberger PH, Gilmore K, Debije MG, Noël T: **Energy-efficient solar photochemistry with luminescent solar concentrator based photomicroreactors**. *Angew Chem Int Ed* 2019, **58**: 14374–14378.
This describes the latest iteration of the luminescent solar concentrator theme, which is demonstrated to be compatible and has benefits for multiple different chemistries.

30. Cambié D, Zhao F, Hessel V, Debije MG, Noël T: **A leaf-iinspired luminescent solar concentrator for energy-efficient continuous-flow photochemistry**. *Angew Chem Int Ed* 2017, **56**: 1050–1054.

31. Cambié D, Zhao F, Hessel V, Debije MG, Noël T: **Every photon counts: understanding and optimizing photon paths in luminescent solar concentrator-based photomicroreactors (LSC-PMs)**. *React Chem Eng* 2017, **2**:561–566.

32. Cambié D, Noël T: **Solar photochemistry in flow**. *Top Curr Chem* 2018, **376**:1–27.

33. Oelgemöller M: **Solar photochemical synthesis: from the beginnings of organic photochemistry to the solar manufacturing of commodity chemicals**. *Chem Rev* 2016, **116**: 9664–9682.

34. Mallia CJ, Baxendale IR: **The use of gases in flow synthesis**. *Org Process Res Dev* 2016, **20**:327–360.

35. Hone CA, Roberge DM, Kappe CO: **The use of molecular oxygen in pharmaceutical manufacturing: is flow the way to go?** *ChemSusChem* 2017, **10**:32–41.

36. Hone CA, Kappe CO: **The use of molecular oxygen for liquid phase aerobic oxidations in continuous flow**. *Top Curr Chem* 2019, **377**:67–110.

37. Lee DS, Amara Z, Clark CA, Xu Z, Kakimpa B, Morvan HP, Pickering SJ, Poliakoff M, George MW: **Continuous photooxidation in a vortex reactor: efficient operations using air drawn from the laboratory**. *Org Process Res Dev* 2017, **21**: 1042–1050.

38. * Lee DS, Sharabi M, Jefferson-Loveday R, Pickering SJ, Poliakoff M, George MW: **Scalable continuous vortex reactor for gram to kilo scale for UV and visible photochemistry**. *Org Process Res Dev* 2020, **24**:201–206.
The vortex reactor described in this publication builds upon the previous work (2017), demonstrating a larger-scale reactor. This reactor has capability to reach kg/day productivities, using oxygen with no applied back pressure.

39. Kudisch M, Lim C-H, Thordarson P, Miyake GM: **Energy transfer to Ni-amine complexes in dual catalytic, light-driven C–N cross-coupling reactions**. *J Am Chem Soc* 2019, **141**: 19479–19486.

40. Gisbertz S, Pieber B: **Heterogeneous photocatalysis in organic synthesis**. *ChemPhotoChem* 2020. https://doi.org/10.1002/cptc.202000014.

41. * Antonietti M, Savateev A, Ghosh I, König B: **Photoredox catalytic organic transformations using heterogeneous carbon nitrides**. *Angew Chem Int Ed* 2018, **57**:15936–15947.
A review of carbon nitrides as photocatalysts. This summarizes some of the excellent potential for this sustainable class of photocatalyst.

42. Ghosh I, Khamrai J, Savateev A, Shlapakov N, Antonietti M, König B: **Organic semiconductor photocatalyst can bifunctionalize arenes and heteroarenes**. *Science* 2019, **365**:360–366.

43. Pieber B, Shalom M, Antonietti M, Seeberger PH, Gilmore K: **Continuous heterogeneous photocatalysis in serial microbatch reactors**. *Angew Chem Int Ed* 2018, **57**:9976–9979.

44. ** Rosso C, Gisbertz S, Williams J, Gemoets H, Debrouwer W, Pieber B, Kappe CO: **An oscillatory plug flow photoreactor facilitates semi-heterogeneous dual nickel/carbon nitride photocatalytic C-N couplings**. *React Chem Eng* 2020, **5**: 597–604.
The first use of an oscillatory plug flow reactor for photochemical reactions. Excellent results in scalability and productivity are achieved, demonstrating the benefits of this type of reactor.

45. Pomberger A, Mo Y, Nandiwale KY, Schultz VL, Duvadie R, Robinson RI, Altinoglu EI, Jensen KF: **A continuous stirred-tank reactor (CSTR) cascade for handling solid-containing photochemical reactions**. *Org Process Res Dev* 2019, **23**: 2699–2706.

46. Grützner T, Ziegenbalg D, Güttel R: **Process intensification – an unbroken trend in chemical engineering**. *Chem Ing Tech* 2018, **90**:1823–1831.

47. Van Gerven T, Mul G, Moulijn J, Stankiewicz A: **A review of intensification of photocatalytic processes**. *Chem Eng Process* 2007, **46**:781–789.

48. Fuse S, Tanabe N, Yoshida M, Yoshida H, Doi T, Takahashi T: **Continuous-flow synthesis of vitamin D3**. *Chem Commun* 2010, **46**:8722–8724.

49. Escribà-Gelonch M, Noël T, Hessel V: **Microflow high-p,T intensification of vitamin D3 synthesis using an ultraviolet lamp**. *Org Process Res Dev* 2018, **22**:147–155.

50. De Abreu M, Belmont P, Brachet E: **Synergistic photoredox/transition-metal catalysis for carbon–carbon bond formation reactions**. *Eur J Org Chem* 2019:1327–1378.

51. ** Harper KC, Moschetta EG, Bordawekar SV, Wittenberger SJ: **A laser driven flow chemistry platform for scaling photochemical reactions with visible light**. *ACS Cent Sci* 2019, **5**: 109–115.
This publication demonstrates the scalability of transition-metal/photoredox dual catalysis methodology, by process intensification. Very impressive throughput is demonstrated in a relatively simple reactor.

52. Park BY, Pirnot MT, Buchwald SL: **Visible light-mediated (hetero)aryl amination using Ni(II) salts and photoredox catalysis in flow: a synthesis of tetracaine**. *J Org Chem* 2020, **85**:3234–3244.