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Sunflow: Sunlight Drives Fast and Green Photochemical Flow Reactions in Simple Micro Capillary Reactors — Application to Photoredox- and H-Atom Transfer Chemistry

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Abstract: "Sunflow" — The combination of a micro capillary reactor in continuous flow mode with sunlight as the most sustainable energy source imaginable was applied to a range of photoredox and H-atom transfer reactions turning them both fast and green.

Introduction

Photoredox catalysis has attracted tremendous interest within the scientific community and is currently one of the most active research areas in the field of organic chemistry.^[11] After the absorption of a photon, the electronically excited photoredox catalyst is converted back to its ground state via two successive redox reactions. By engaging in these electron transfer reactions, substrates of the reaction mixture can be oxidized or reduced depending on the conditions. This opens up the possibility to perform net redox neutral transformations involving unique bond-forming events in a one-pot fashion using light as a sustainable energy source.^[2] A large variety of photoredox catalysts including transition metal complexes (based on Ru,^[3] Ir^[4] or Au^[5])^[6], organic dyes (rose bengal,^[7] eosin Y,^[8] TPP,^[9] DAP²⁺ ^[10])^[11] or semiconductors (TiO₂^[12]) have been employed for this purpose.

Nowadays, the aspects of eco-friendliness and environmental sustainability are becoming increasingly important. The growing field of green chemistry strives for reactions that combine high yields with a good atom economy, are devoid of heavy metals or other toxic agents, use renewable starting materials and are not energy intensive.^[13] Even though many photoreactions fulfill these requirements, the ultimate approach to green chemistry would be the use of sunlight as sole energy source for a chemical transformation. It is therefore not surprising that this idea has been appealing to chemists for a long time, leading to the development of a large variety of sunlight driven reactions cycloadditions,[14] including for example [2+2] photooxygenations,[15] photoalkylations^[16] and dehydratisations.^[17] The solar spectrum covers all wavelengths needed for photoredox catalysis down to about 330 nm. Furthermore, the human eye is adapted to the solar emission

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Supporting information for this article is given via a link at the end of the document spectrum which overcomes the hazards of working with mercury lamps or other UV-light sources, the emissions of which may not induce a blink reflex.

Since the pioneering works of Giacomo Luigi Ciamician, Max Dennstedt and Günther Otto Schenk, much progress has been made in optimizing reaction setups to achieve more efficient sunlight-driven reactions.^[18] Special photo macro reactors like the SOLFIN,^[19] the CPC^[14a] or flatbed reactors^[20] were designed. The hearts of the SOLFIN and the CPC are relatively big tubes in parabolic mirrors which focus the solar light and increase the light flux in the tubes. These reactors are cyclic flow reactors, in which the reaction medium is circulated repeatedly between the reaction tubes and the reservoirs leading to a constant mixing of irradiated and non-irradiated solution. This is particularly troublesome if the products of a photoreaction are unstable upon prolonged exposure to light or to components of the reaction mixture. Moreover, such macro reactors are not easy to build and are therefore not suitable for most laboratories. Furthermore, these setups require relatively long irradiation times. Due to the day/night cycle, the efficient use of day time is essential when using sunlight as sole energy source. An efficient and fast photon absorption by the photoredox catalyst or by the photosensitizer is crucial for achieving a rapid reactant turnover. According to the Lambert-Beer law, a higher irradiated surface to volume ratio correlates with a higher average photon number in the solution and therefore with a higher turnover with the same light intensity. This higher ratio can be accomplished by using micro capillary reactors in a continuous flow mode.^[21] The significant acceleration of photoredox reactions by using micro capillary flow reactors with artificial light sources has been demonstrated repeatedly.^[22] In 2015. Kim et al. reported a sunlight-induced radical bromination of toluene derivatives in an FEP capillary flow reactor within short reaction times.[23]

The beneficial influence of a flow setup on the speed of photo(redox) transformations as well as the potential use of sunlight as an entirely eco-friendly light source are two well-known principles of photochemistry. However, the application of a micro capillary continuous "sunflow" system to photoredox and H-atom transfer reactions has, to the best of our knowledge, not been described. This might be due to the widespread belief that expensive equipment is required to obtain satisfactory results.

Results and Discussion

Therefore, the aim of this study was to combine the advantages of a simple and inexpensive micro capillary reactor with the use

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of sunlight to accomplish green and fast photoredox and H-atom transfer reactions in a continuous flow mode. To exemplify the utility of this "sunflow" approach, we chose a range of photoreactions which have recently been investigated by our group, including a benzophenone mediated C–C coupling of 2-chlorobenzazoles with alcohols, ethers and carbamates, an oxidative cyanation of tertiary amines as well as a phenanthrene catalyzed Minisci type cross coupling reaction (scheme 1).^[7a, 24]



Scheme 1. Overview of reactions used to exemplify the utility of the presented "sunflow" approach.

As a first example, the benzophenone mediated C-C coupling protocol developed recently by our group was investigated (A, scheme 1) which is an example of a UV-A-driven photoreaction. The combination of tetrahydrofuran and 2-chlorobenzoxazole was chosen as the benchmark system.^[24a] Performing the reaction under typical batch conditions yielded 21% of the coupled product after three hours of exposure to sunlight (60 mL stock solution in a 100 mL round bottom flask). In order to confirm the anticipated acceleration of the reaction by increasing the surface-to-volumeratio, the same reaction was performed in an NMR tube, resulting in an almost doubled yield (38.8%) in the same time period. In order to further accelerate the reaction, a capillary reactor was constructed for harvesting sunlight. This reactor was built out of an aviary fence, a wooden plank and a 25 m FEP tube (OD: 1.59 mm / ID: 1.0 mm) with fittings resulting in an acquisition value below 80 € / 90 US-\$ (see SI). The first kinetic studies showed a remarkably fast reaction as highlighted in figure 1. After only 20 minutes, high yields (61%) comparable to those achieved by irradiation with an UV-A spotlight for 24 h could be obtained.^[24a]



Figure 1. Kinetic investigation of the benzophenone mediated C–C coupling of tetrahydrofuran with 2-chlorobenzoxazole in the "sunflow" reactor. For each data point, 5 mL of the stock solution (described in the SI) were injected into the "sunflow" reactor and withdrawn after the indicated time period. [a] Yields were calculated by ¹H-NMR spectroscopy using 1,4-bis(trimethylsilyl)benzene as internal standard.

In order to demonstrate the applicability of these "sunflow" conditions for various substrates such as alcohols, ethers and carbamates, the reaction protocol was applied to ethanol, diethyl ether as well as Boc-azepane (table 1). In all cases, the use of the micro capillary flow reactor led to a significant acceleration of the reaction as judged by the direct comparison with the analogous batch reactions. Moderate to good yields could be obtained which were in most cases close to those reported in the literature under batch conditions (UV-A).^[24a] Individual kinetic studies and optimization of each of these systems might have allowed a further increase of the yields.

Since visible light represents a large part of the solar emission, we next focused on catalyst systems with absorption maxima in this wavelength region. The oxidative α -cyanation of tertiary amines to the corresponding α -aminonitriles was chosen as model reaction (B, scheme 1). A kinetic study using several organic (rose bengal and eosin Y) and transition metal ([Ru(bpy)₃]²⁺) based catalysts in combination with oxygen as terminal oxidant was performed (figure 2). Furthermore, a catalyst-free approach using bromotrichloromethane as reported by the group of Kirsten Zeitler was investigated (figure 3).^[25] Additional figures and tables for turnovers as well as yield to turnover ratios are provided in the SI. In all cases, high to excellent yields could be obtained after very short reaction times.

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 Table 1. Comparison of the investigated reaction type A under "sunflow" and batch conditions with sunlight.

Compound	"Sunflow"		batch with sunlight		Literature (UV-lamp) ^{24a}	
	Yield ^[a]	Time	Yield ^[b]	Time	Yield	Time
	68%	20 min	21% ^[c] / 39% ^[d]	180 min	70%	1440 min
\texttt{P}_{N}^{O}	59%	30 min	24% ^[c]	30 min	68%	1440 min
	54%	30 min	8% ^[c]	30 min	59%	1440 min
	38%	30 min	15% ^[c]	30 min	74%	2160 min

For each substrate, the stock solution (described in the SI) was either pumped through the "sunflow" reactor or placed in a round bottom flask in the sun. [a] Isolated yield, [b] yields were calculated based on ¹H-NMR spectroscopy using 1,4-bis(trimethylsilyl)benzene as internal standard, [c] 60 mL stock solution in a 100 mL flask, [d] 1.1 mL stock solution in a NMR tube.



Figure 2. Kinetic investigation of the photocyanation with $[Ru(bpy)_3]Cl_2$ (blue), rose bengal (orange) and eosin Y (gray) in the "sunflow" reactor. For each data point, 20 mL of the stock solution (described in the SI) and oxygen were pumped through the reactor in the stated residence time. [a] Yields were calculated by ¹H-NMR spectroscopy using pyridine as internal standard.





Figure 3. Kinetic investigation of the photocyanation with BrCCl₃ in the "sunflow" reactor. For each data point, 5 mL of the stock solution (described in the SI) were injected into the reactor and withdrawn after a specific time period. [a] Yields were calculated based on ¹H-NMR spectroscopy using 1,4-bis(trimethylsilyl)benzene as internal standard.

To further demonstrate the utility of this "sunflow" approach for the α -cyanation of aliphatic as well as benzylic substrates, a series of amines, comprising tri-*n*-butylamine, atropine as well as 6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline was investigated (figure 4). The decrease of the yield for elevated reaction times can be explained by decomposition of the formed α -aminonitriles.



Figure 4. Kinetic investigation of the rose bengal catalyzed photocyanation of three exemplary amines in the "sunflow" reactor. For each substrate, the stock solution (described in the SI) and oxygen were pumped through the "sunflow" reactor in the stated residence time. Yields were calculated by ¹H-NMR spectroscopy using pyridine as internal standard. For the data points marked in red, isolated yields were determined as well. Tabulated data is provided in the SI.

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Table 2 shows a comparison of the isolated yields for various α -aminonitriles prepared under "sunflow" conditions with the ones reported in the literature.^[7a] In all cases, the green "sunflow" protocol afforded higher yields within shorter reaction times compared to batch photoreactions using a household CFL bulb or a blue LED.

 Table 2. Comparison of investigated reaction type B under "sunflow" and batch conditions.

	"Sun	flow"	Literature		
Compound	Yield ^[a]	Time	Yield	Time	
	93%	5 min	80% ^{7a}	180 min	
	99%	10 min	85% ^{[d]26} , 98% ^{[e]25}	180 min	
H ₃ CO H ₃ CO CN	97%	5 min	80% ^{7a}	180 min	
	94%	2 min	89% ^{7a}	180 min	
CN (b)	73%	3 min	65% ^{7a}	960 min	

For each substrate, the stock solution (described in the SI) and oxygen were pumped through the "sunflow" reactor. [a] Isolated yield, [b] with rose bengal as catalyst, [c] with bromotrichloromethane, [d] literature reaction uses additional 1 mol% [Ru(bpy)₃]Cl₂, [e] literature yield and reaction time only for oxidation to the iminium ion with BrCCl₃.

Finally, the "sunflow" approach was extended to the mostly UV-B driven phenanthrene-catalyzed Minisci type reaction of carboxylic acids with aromatic nitriles (C, scheme 1).^[24b] Boc-L-valine and 4-cyanopyridine were chosen as a model system for kinetic investigations (figure 5). Since sunlight comprises only a small fraction of UV-B, this reaction is generally much slower than the visible light-driven cyanations mentioned above (compare reaction times in figure 2–5). Again, high yields could be obtained in relatively short reaction times compared to the literature.^[24b] The small fraction of solar UV-B makes the photon absorption and excitation of phenanthrene the rate determining step. Assumption of a constant photon flux results in a zero order kinetics leading to a linear increase of yield and turnover with time.

The concept of "sunflow" could also be used to prepare an alkaloid-like structure as well as a C-arylated dipeptide derivative in reasonable yields and within short reaction times using the same photoredox cross-coupling reaction (Table 3).



Figure 5. Kinetic investigation of the phenanthrene catalyzed Minisci type reaction of Boc-L-valine with 4-cyanopyridine in the "sunflow" reactor. For each data point, 5 mL of the stock solution (described in the SI) were injected into the "sunflow" reactor and withdrawn after a specific time period. [a] Yields were calculated based on ¹H-NMR spectroscopy using 1,4-bis(trimethylsilyl)benzene

Table 3. Comparison of the investigated reaction type C under "sunflow" and batch conditions.



For each substrate, the stock solution (described in the SI) was pumped through the "sunflow" reactor. [a] Isolated yield.

Conclusions

In the present study, sunlight as the most sustainable light source was combined with a micro capillary reactor to achieve fast and environmentally benign photoreactions in continuous flow. To

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exemplify the utility of this "sunflow" approach, a range of reactions and catalysts with absorption maxima in various regions of the solar spectrum were investigated in terms of their kinetic behavior. The optimized conditions were applied to a range of exemplary reactions, highlighting the applicability of this method for various transformations. The used "sunflow" reactor is easy to build and readily affordable for every research group interested in eco-friendly flow photochemistry.

Experimental Section

All reactions were performed in the "sunflow" reactor, which was constructed as described in the *Supporting Information* (SI). The reactor was placed outside, oriented directly towards the sun and repositioned every hour.

Homogenous reactions: For homogeneous reactions, the stock solutions were pumped through the capillary reactor using a syringe pump and the reaction mixture was collected in a round bottom flask, which was kept under an argon atmosphere and wrapped in aluminium foil.

Heterogeneous reactions: For heterogeneous reactions consisting of a liquid and a gaseous phase, both phases were pumped with syringe pumps in a volume ratio of 2:1 (gas:liquid) and mixed with a CTA-Union-Tee before entering the reaction capillary. The reaction mixture was collected in a round bottom flask, which was kept under an argon atmosphere and wrapped in aluminium foil.

A detailed description of the reactor setup, all experimental procedures as well as a complete list of analytical data and copies of NMR spectra can be found in the SI.

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