

Accelerating radicals generation by photoredox catalysis from organoborates in continuous microflow reactor

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Abstract: During the last decade, continuous microflow processes have received an increasing amount of attention to facilitate photoredox catalyzed reactions. Indeed, under continuous flow conditions, more sustainable, safer and easier scalable processes could be developed with respect to conventional batch procedures. In such reactors, improved irradiation of the reaction medium impacts the photoredox catalyzed process. The generation of carbon-centered radical *via* oxidation of benzylborates by photoredox catalysis under UV irradiation was significantly faster in continuous flow microreactors. The generated radicals smoothly react with TEMPO to afford coupling products.

Keywords: Continuous microflow system – Photoredox catalysis – Organoborate

Introduction

Flow chemistry based on microfluidic technology has currently gained a lot of interest due to its significant advancement over the classical batch processes with respect to reduced consumption of chemicals, solvents, time and thus energy along with enhanced yields, selectivity and control over reaction [1]. Moreover, microfluidic systems usually occupy very limited spaces and can be designed using simple and cost effective material. Thus, flow chemistry is considered the greener approach that can be used in a wide range of applications including photoredox catalysis. However, light penetration through the reaction media is limited which restrains the productivity of photochemistry processes in batch reactors. These drawbacks can be circumvented with continuous microflow reactors since their high surface-to-volume ratio (small channel depth) improve sample irradiation and also enhance heat and mass transfer [2]. Herein, the obvious benefits of this technology prompted us to investigate the influence of microreactors on generation of radicals from organoborates by photoredox catalysis. Recently, organoborates and

notably benzyl trifluoroborates proved to be effective precursors as C-centered radicals easily generated by single electron transfer (SET) oxidative processes under photocatalytic conditions [3]. This methodology represents a sustainable alternative to the traditional use of tin reagents as a radical initiator.

Materials and Methods

Description of the designed microfluidic system/LEDs

A microreactor (dwell device manufactured by Mikroglass Chemtech Mainz, Germany) with a rectangular shape of dimensions 115 mm × 2 mm × 0.5 mm was used as photo-microreactor (Figure 1). The relatively small depth (500 micron) ensures homogeneous illumination of the reaction mixture which, in contrary to batch conditions, prevents the formation of hot spots and exhibits better efficiency as the desired product is formed without the need of the usage of high power mercury lamps. Moreover this microreactor is made up of glass that is transparent up to 300 nm allowing to work at a wide range of wavelengths (UV & visible) where all of the photons delivered by the lamp are strictly absorbed by the reaction mixture. In order to control the temperature cooling channel was connected to a MultiTemp III thermostatic circulator (Amersham Biosciences).

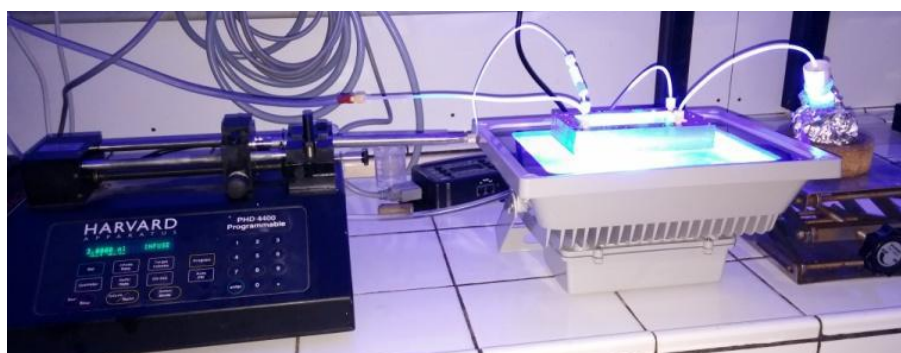


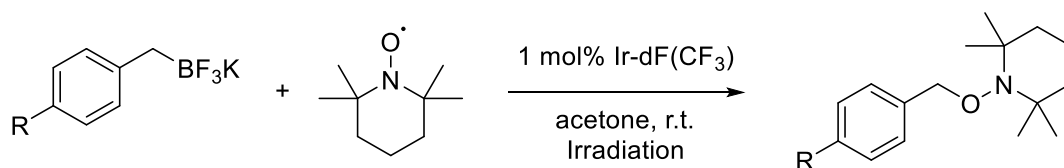
Figure 1: Reaction set-up incorporating dwell device photomicroreactor

UV LEDs (365 nm, irradiance up to 3 W.cm⁻²) AC475 model from Lumen Dynamics (Mississauga, Canada) and blue high power spots (50 W electrical power, 4500 lumen, 0.02 W.cm⁻²) LED from Bridgelux (Livermore, CA, USA) were used. The irradiation time was regulated by varying the flow rate of the reaction mixture using a Harvard PHD ULTRA CP syringe pump.

Results and Discussion

Organotrifluoroborates salts are known as air- and water-stable reagents and thus can be stored and handled easily. They can be readily prepared by simple treatment of the corresponding boronic acid pinacol ester derivatives with an aqueous solution of KHF₂ obtained by Suzuki-Miyaura coupling [4]. The efficiency of this microreactor vs classical batch reactor was then assessed using the photocatalytic C-O bond formation of

potassium benzyltrifluoroborate with TEMPO as the radical scavenger in the presence of Ir-dF(CF₃) as photoredox catalyst (Scheme 1).



Scheme 1: Photocatalytic C-O bond formation. Ir-dF(CF₃): [Ir(dF(CF₃))₂(ppy)₂(bpy)](PF₆)

When realized in a batch reactor with condition reported by Akita [3a], the reaction needed 4 h for completion. However, the use of the previously described microfluidic system has remarkably accelerated the rate of the reaction (full conversion after 2 hours) with only 1.0 mol% of catalyst (Table 1). This can be explained using Beer-Lambert Law $A = \epsilon \times c \times l$; for a given ϵ and c , the quantity of light that traverses the system decreases with the increase in the optical length. For a flow system, this problem is excluded as the optical length is around few mms (in our case it's 0.5 mm). In contrast, the optical length of a batch system is around 4 cm, so light reaches only a small part of the reactor leading to reagent and energy loss and thus lower yields. Consequently, the small optical length provided by the microfluidic system has a great impact on the increase in the rate of the reaction.

The microreactor was then used for assessing the reaction in the UV range since the iridium catalyst absorbs more within this range. Interestingly, the reaction needed around 20 min to get a complete conversion in batch conditions. Using the microreactor has dramatically diminished the irradiation time to only 3.5 min. This clearly demonstrates the superiority of the flow conditions as compared to batch transformation. Note that throughout the assessment the kinetic studies gave straight lines of slopes with a good correlation coefficient ($R^2 > 0.99$) that is less likely to be obtained in batch conditions. The scope of the reaction was then explored. Benzyltrifluoroborates could be substituted with electron donating group and with electron withdrawing group on the benzene ring to smoothly produce the corresponding C-O product with excellent yield (Table 1).

Table 1: Flow vs Batch

Entry	Substituent R	Irradiation	System	Time	Yield ^{a)}
1	OMe	Blue	Flow	2h	99%
2	OMe	Blue	Batch	4h	99%
3	OMe	UV	Flow	3.5 min	99%
4	OMe	UV	Batch	20 min	99%
5	H	UV	Flow	1h20	99%
6	Me	UV	Flow	17 min	99%
7	Cl	UV	Flow	4h	99%

a) Yield was determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal solvent

Conclusion

We show here that the combination of micrometric microreactors with low depth channel with UV or visible LED light source led to very simple kinetics which allow easy optimization and reduce side-reactions which affords better yields than batch. In conclusion, micrometric microreactors are effective tools to reduce time and reagent usage.

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