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Luke D. Elliott,*[†] Malcolm Berry,[§] Bashir Harji,[#] David Klauber,[¥] John Leonard,[¥] and Kevin I. Booker-Milburn*[†]
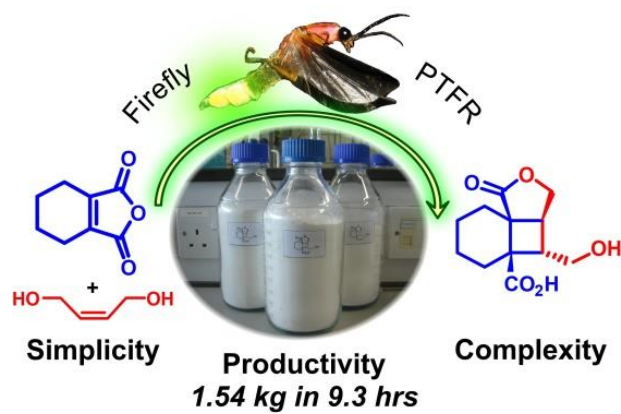
[†]School of Chemistry, University of Bristol, Cantock's Close, Bristol, UK, BS8 1TS

[§]GlaxoSmithKline, Gunnels Wood Road, Stevenage, UK, SG1 2NY

[¥]Pharmaceutical Sciences, AstraZeneca, Silk Road Business Park, Macclesfield, UK, SK10 2NA

[#]Cambridge Reactor Design Ltd, Unit D2 Brookfield Business Centre, Twentypence Road, Cottenham, UK, CB24 8PS

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ABSTRACT

The development of a highly compact and powerful reactor for synthetic organic photochemistry is described enabling a 10 fold reduction in reaction times, with up to 30% more power efficiency than previous FEP tube reactors. Two reactions gave over 1kg of product in 24 hours. Two other reactions had productivities of 4 and 8 kg in 24h. The reactor consists of a succession of quartz tubes connected together in series and arranged axially around a variable power mercury lamp. This compact and relatively simple device can be safely operated in a standard fumehood.

Keyword

Flow reactor; photochemistry; ultra-violet; scale-up; kilogram productivity; cycloaddition; cyclobutane

Introduction

Over the last ten years there has been a very significant increase in the use of continuous flow reactors in organic synthesis.[1] A variety of reactors have been developed for numerous organic reactions in both academic and industrial labs. In many cases these offer an alternative to classic batch reactors and can often display significant advantages in heat and mass transfer, efficient mixing, scale-up, safety and cost. In 2005 we reported[2] the development of a practical flow reactor for photochemical synthesis on scales of up to a few hundred grams per day. This reactor consisted of a single length of UV transparent fluorinated ethylene propylene (FEP) tubing wrapped closely around a high power UV source. One to three layers of FEP could be coiled around the UV source to give a reactor of high surface area and excellent UV capture (Figure

1a). Many labs worldwide[3,4] have adopted this reactor and variants thereof and a commercial version[5] is now available based on the original concept. Key to the success of the FEP reactor is its ability to totally encapsulate the UV emitting source and as such photon capture by the circulating substrate is near optimal.

A key brief of a recent collaboration[6] was to design a higher capacity reactor to enable photochemistry to be carried out on the kg/day scale. Initially we considered building larger FEP reactors with more powerful UV sources. However, this raised some issues that would be exacerbated by simply 'scaling-up'. For example, although FEP is a versatile material it is not completely UV transparent and any kinks or abrasions leads to weak spots that can rupture under pressure requiring the whole length of FEP tubing to be replaced. Neither is FEP immune to foul-up and blockage. In our experience a blocked FEP tube can sometimes be reversed by a short flush of solvent. On other occasions, especially if there is photochemical damage to the FEP, the whole tubing has to be replaced and the reactor rewound (see SI, Fig. 1-3 for examples).

With this experience behind us we set out to design a higher capacity flow reactor meeting the following specifications:

- Capable of delivering ≥ 1kg per day productivity

- Encapsulate UV as effectively as in FEP reactors

- Small footprint to fit within a standard fumehood

- Replace FEP with durable and more UV transparent tubing

- Safe containment of high-power (1-5 kW) UV source
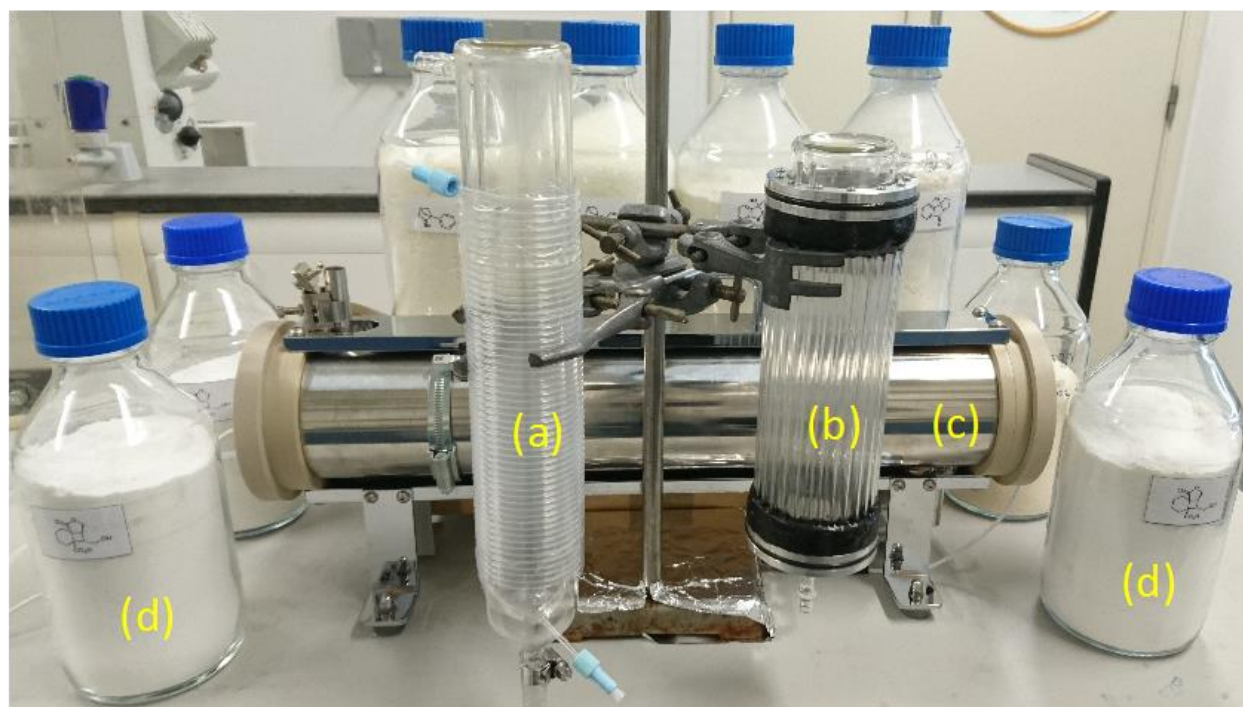
Figure 1. Comparison of reactor types: (a) FEP photoreactor for 400W Hg-lamp; (b) prototype

parallel tube flow reactor (PTFR) for 400W Hg-lamp; (c) final design of PTFR for 1.5-5 kW Hg-

lamp (Firefly reactor); (d) kilogram quantities of product from Firefly reactor.

Results & Discussion

Replacing FEP with a more durable material, with at least equal performance characteristics,

was non-trivial. Although a spiral quartz reactor would be ideal, and have been described[7],

obtaining the necessary compact, multi-layer coiled quartz device on the scale required for this

project was not feasible. A multi-tube reactor system has been reported[8a,b] but in these designs

the reactor tubes were isolated from each other and acting independently and no synthetic

photochemistry was described. We therefore designed a modular reactor comprised of an array

of quartz tubes linked in series and arranged axially around a high power UV source so that they

effectively operate as one single tube with a large surface area. We proposed that such a reactor

could encapsulate light just as effectively as the previous FEP reactors. At the centre of the

concentric reactor array would be placed a standard, high power medium pressure Hg-lamp,

although this would be able to accommodate different types of lamps and light sources (eg

LEDs) to suite a broad range of photochemistry. The reaction solution would enter through an

end-cap, flow through one tube, into the opposite end-cap, then back through the adjacent tube in

the opposite direction. Thus a relatively thin profile of solution would get high UV exposure by

the time it had passed through the entire reactor assembly. Any UV that passes through or

between the tubes would be reflected back in very close proximity to the reaction solution.

Initially we built a prototype for a 400 W Hg-lamp contained in a water-cooled jacket (Fig 2).
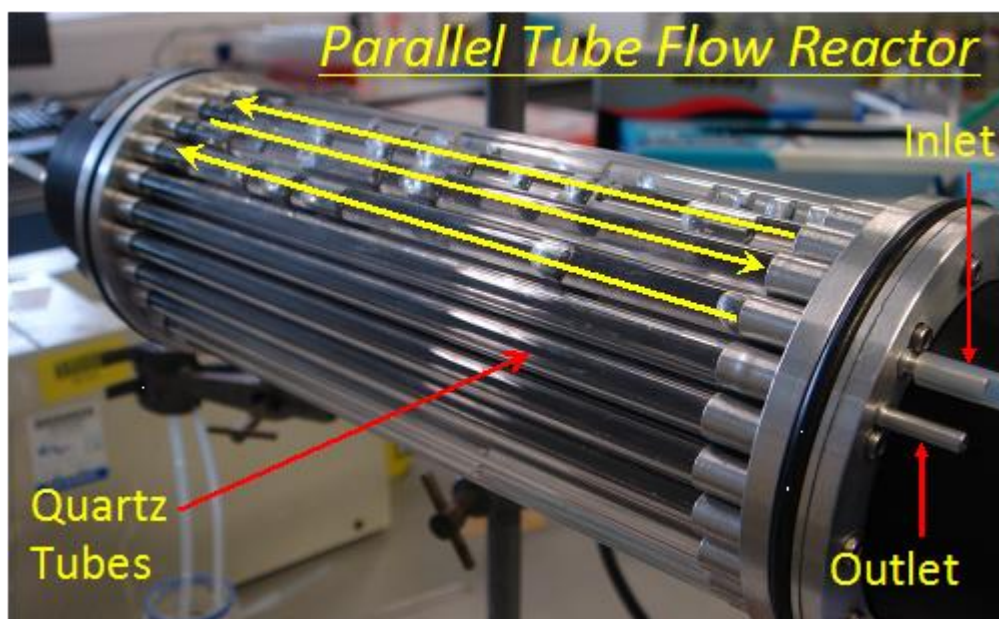

Figure 2. A Parallel Tube Flow Reactor (PTFR), 20 cm (l) x 7 cm (d)

Initial screening with a [2+2] reaction between N-methyl maleimide and hex-1-yne gave a

productivity of 3.41g/h, which approached that of an optimized 3-layer FEP reactor[2d] (3.62 g/h).

Similarly maleimide and propargyl alcohol gave a productivity of 2.13 g/h vs 2.35 g/h for the

FEP reactor (Table 1). These were surprising initial results, especially considering that they were

obtained using the reactor without the metal reflector. However, when the metal reflector was

placed around the reactor significant overheating was encountered. It was clear that the stagnant

hot air between the water jacket and the reactor tubing was overheating. It was conceived that

this could be prevented by encapsulating the reactor tubes within a fluid-cooled annular cavity.

In addition, a fan installed at one end of the reactor would simultaneously remove the stagnant

hot air. This dual mode of cooling should be effective at negating the heating effects produced by

the powerful UV source (Figure 3a). The lamp would not require containment within a cooling

jacket, thus simplifying the design. The inner boundary could also serve as an exchangeable UV

filter. A highly polished and earthed outer metal tube would serve to reflect any transmitted UV

back into the reactor tubes and to protect the user from intense radiant energy.

Table 1. Comparison of maleimide [2+2] in 400 W FEP and PTFR reactors
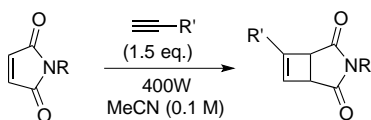
Reactor	R/R'	mL/min	Yield [%]	g/h
3-layer FEP	Me/^{n}Bu	6	52	3.62
400W PTFR[a]	Me/^{n}Bu	6	49	3.41
3-layer FEP	H/CH$_2$OH	4	64	2.35
400W PTFR[a]	H/CH$_2$OH	4	58	2.13

[a]Results obtained without metal reflector

The reactor (Fig. 3b) was constructed to these specifications, with interlocks put in place to

protect against overheating, electrical and coolant failures. A sophisticated variable power supply

meant that the lamp could be run at powers ranging from 1.5 - 5 kW to match the photochemical reaction productivity. The footprint of this reactor was not much larger than a rotary-evaporator condenser, which is remarkable considering the power of the device. Although mains water could be used for cooling, our results were obtained using a commercial recirculating chiller (water/glycol - see SI). The final operational design[9] of the reactor was named The Firefly.
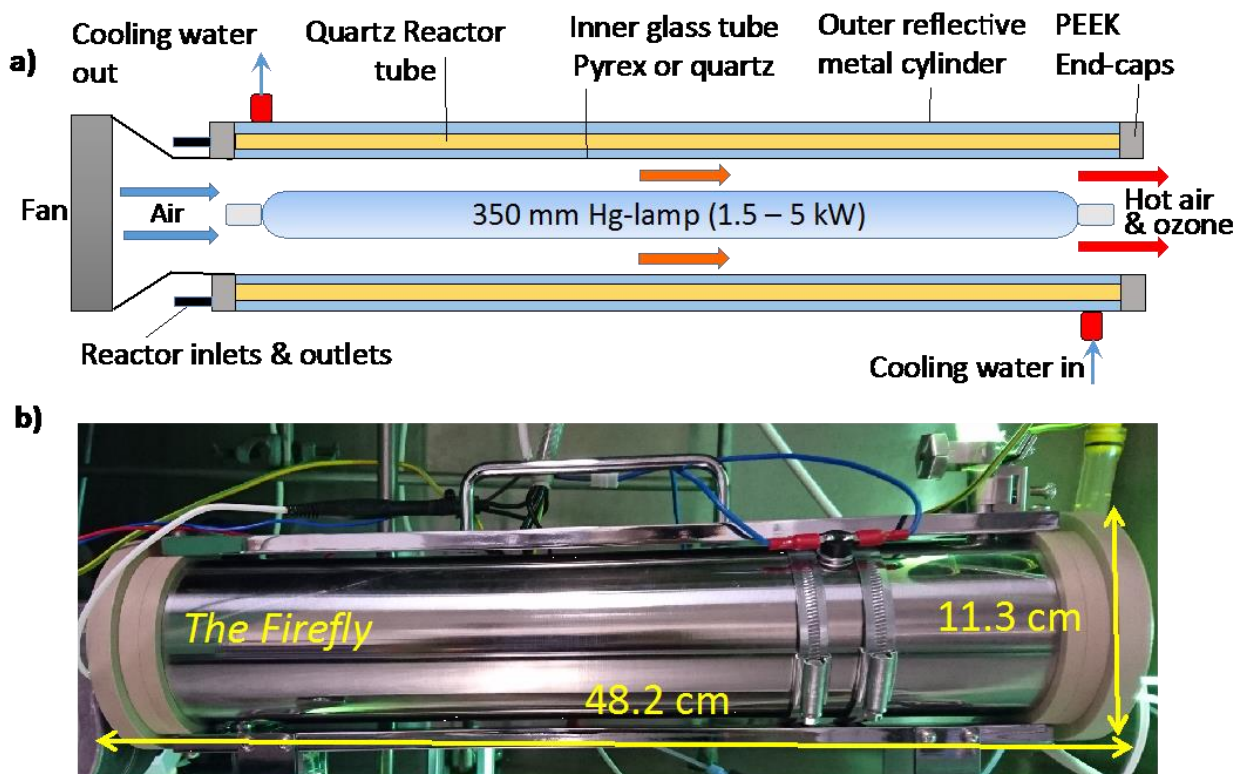
Figure 3: Schematics and operational pictures of an Immersion-Cooled Parallel Tube Flow Reactor - The Firefly: a) Diagram of reactor; b) Firefly reactor in operation. Internal volume of the reactor = 120 mL.

After trialing a few reactions we soon found 3 kW to be a convenient power setting. At this power the reactor gave approximately 10 times greater productivity than the corresponding three-layer FEP flow reactor with a 400 W lamp. For example, the [2+2] cycloaddition of N-methyl

maleimide and trichloroethene [2d] (Table 2, entry 2) gave 2.85 g/h (68%) in a 400 W FEP reactor. At 3 kW the Firefly reactor gave a productivity of 28.8 g/h (66%), enabling the isolation of 64 g of product in just 2 h 10 min (400 W FEP, 62 g in 22 h).

The [2+2] cycloaddition of maleimide and propargyl alcohol[2d] (Table 2, entry 3) can be problematic on account of formation of insoluble by-products (see SI). When using the quartz tube reactor at 3 kW, we were able to process 2.5 L of a 0.1 M solution at 36 ml/min and still maintain almost complete conversion with a productivity of 24.6 g in 70 min (64%, 21.2 g/h). We believe the high flow rate in this case prevents significant foul-up.
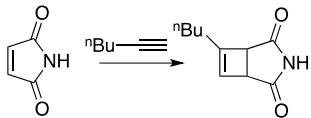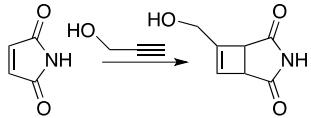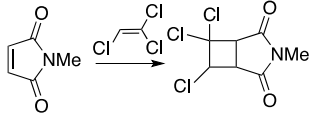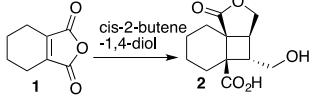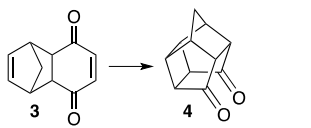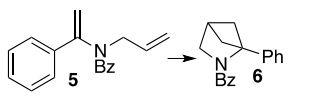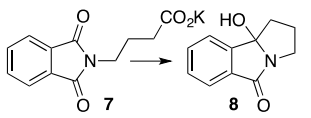
Entries 1-3 were invaluable benchmarks for testing the Firefly reactor as their performances were well understood. However, in terms of scale-up to kg quantities they were limited as the starting maleimides were relatively expensive and chromatography was required. We therefore sought to test the Firefly with low-cost readily available starting materials that produced complex, structurally diverse molecules that could be easily purified on kg scales.

Previously[10] we had shown that 3,4,5,6-tetrahydrophthalic anhydride (THPA, **1**) and cis-2-butene-1,4-diol undergo an efficient batch [2+2] cycloaddition-lactonisation sequence to tricyclic lactone **2** upon direct UV irradiation. Repeating the batch irradiation at 0.4 M with just 1% of isopropythioxanthone (*i*THX) as sensitizer gave an impressive *15-fold increase* in productivity. Use of the parent THX[4p,q] led to equally good productivity, however due to the insoluble nature of THX it was more difficult to remove from the crystallized product **2**. This demonstrates how previously optimized, but scale-limited reactions can be made dramatically more productive by judicious choice of sensitizer and solvent. Transferring these newly optimized conditions to the Firefly (0.4 M @ 36 mL/min) gave a staggering 1,538 g of pure **2** in

just 9.26 h of irradiation, with the product crystalizing out in the receiving flask. In a 24 hour run this productivity would enable the synthesis of almost 4 kg of **2** at this power setting.

'Cookson's Dione' **4**[11] (table 2, entry 5) is produced by an intramolecular [2+2] of the ene-dione **3**, and was previously shown to be highly productive in our FEP reactors with a UVA lamp.[2d] In the Firefly we found that at just 1.5 kW a single 140 min run of a 0.5M solution (5 L, 36 mL/min) gave 387g of pure **4** (89%). Increasing the concentration to 1.0 M and power to 3kW gave 385g (8 kg/24 h) in just 1.16 h (36 mL/min) - the product crystalizing in the receiving flask. Using these conditions we carried out a 'kilo-run' and were able to produce 1,165g of pure **4** in a single 3.5 h run. It is important to highlight that these three results demonstrate complete linearity in productivity with respect to power as might be expected *e.g.* doubling the power from 1.5 kW to 3 kW gave an exact doubling in productivity. In a certified process lab it can be confidently predicted that at the full 5 kW power rating the Firefly could deliver over 13 kg of **4** in 24 h.

Table 2. Scale-up of synthetic organic photochemistry in a Parallel Tube Flow Reactor (The Firefly)

entry	reaction	run time[a] (h)	lamp power (kW)	M	flow rate (mL/min)	yield (%)	g/h[h]	isolated (g)	g/24h (projected)
1		1.16	3	0.1[b]	36	65	25.2	29.3	605
2		1.16	3	0.1[b]	36	64	21.2	24.6	509
3		2.22	3	0.2[b]	15	66	28.8	64.0	691
4[g]		9.26	3	0.4[c]	36	80	166	1,538	3984
5		2.31	1.5	0.5[c]	36	89	167	387	4,008
		1.16	3	1.0	36	88	331	385	7,944
		3.47	3	1.0[d]	36	89	335	1,165	8,058
6[g]		22.22	3	0.4[e]	9	86	48.9	1,082	1,174
7		17.78	3	0.2[f]	30	85	57.9	1,032	1,390

[a]Total reaction volume/flow rate, [b]MeCN; [c]EtOAc; [d]10% MeCN in EtOAc; [e]10% H_2O in MeCN; [f]50% H_2O in MeCN; [g]1% isopropyl thioxanthone (iTHX); [h]Hourly productivity (g/h) = Conc. (M) x Flow Rate (L/h) x MW x Yield (%) /100.
Note:

Following the work of Piotrowski[12] we developed a highly scalable route to the bridged pyrrolidine **6** by a 'crossed' [2+2] cycloaddition of the enamine **5** (table 2, entry 6). After extensive screening in batch, we again found iTHX a most productive sensitizer. In batch (400W, 0.4 M) the reaction proceeded with a productivity of 17 mmol/h with just 1% iTHX. Using these optimized conditions a total of 4.8 moles of **5** in 12 L of MeCN was irradiated in the

Firefly at 9 ml/min to give 1,082 g (86% yield) of pure **6** in 22.2 h. This represents an 11-fold increase in productivity over the batch reactor.

Griesbeck and Oelgemöller[13] had previously reported the useful photo-decarboxylative cyclisation of the phthalimide-potassium salt **7** to the hydroxy lactam **8** in the presence of acetone as a triplet sensitizer. When a 3 kW excimer lamp (XeCl, 308 nm) was employed within a falling film reactor[14] the reaction proceeded with a productivity of 7 g/hr. More recently Oelgemöller reported[15] a 4.56 mmol/h (2.89 g, 3.3h, 76%) productivity of **8** using the Vapourtec-UV150 (10 ml/min, 0.01M, 82 W lamp power). This reaction was attractive to us to test on kg scales as **7** was readily available in large quantities. Interestingly we found that the acetone solvent sensitizer was not necessary and acetonitrile was a more convenient alternative co-solvent with water. Thus irradiation of a 0.2 M solution of **7** in a 150 ml quartz batch reactor (125 W) gave full conversion to **8** in just 2 h (4.6 g, 81%, 12.2 mmol/h). By increasing the concentration 20-fold, purification of **8** was made considerably more efficient as the product precipitated on solvent evaporation. This enabled us to test, for the first time, the exchangeable inner glass filter (Fig. 2a), by simply swapping the pyrex inner tube for quartz. Ultimately a total of 6.4 moles of **7** in 32 L of MeCN/H_2O was irradiated over a total of 18 h at 3kW @ 30 ml/min, giving 1,032 g of pure **8** in 85% overall yield with a productivity of 57.9 g/h (Table 2, entry 7)

Entries 4-7 have all proved to be excellent low-cost reactions with greater than 1-kilogram productivities in a 24 h processing period. It is perhaps surprising that with the high-powers and concentrations involved that foul-up of the reactor was much less than expected in long runs. In general, we found that as long as the starting material was pure, and the reactor clean to start-with, then foul-up proved not to be an issue for the examples studied. For example, in entry 5 colored impurities carried over from the preparation of a particular batch of **3** had a

deleterious effect on productivity and product quality as well as resulting in minor fouling of the reactor. These unidentified impurities were likely chromophoric quinone derivatives from the previous Diels-Alder step. Although in this specific case substrate **3** was ≥ 95% pure by NMR it does highlight that in photochemistry it is important that substrates are not contaminated with small quantities of compounds that may act as quenchers of the reaction or sensitizers of undesired side reactions. For all other reactions in this study substrate quality of ≥ 95% purity was tolerated without issue.

The Firefly reactor would appear to be significantly more efficient than any of the FEP reactors that we have previously designed. For example entry 2 gave 10.1 times the productivity of the 400W FEP result using only 7.5 times the UV power, making the Firefly almost 30% more power efficient. Although we can only speculate at this stage, this performance enhancement is likely due to the superior UV transparency of the quartz tubing vs. FEP combined with the efficiency of UV capture and reflection of the device.

Conclusions

In summary, we have developed a powerful new flow reactor that enables complex photochemical synthesis to be carried out on a variety of scales whilst reducing reaction times 10-fold compared to previous FEP reactors. The fact that such a small photo-reactor can routinely produce over a kilogram of product, and more, in a 24 h processing period is unprecedented. The small footprint enables the device to be operated in a standard (1.5 m) research lab fumehood. The versatility of the device was demonstrated by successful scale-up of reactions at UVA (Table 2, entry 4-6), UVB (entries 1-3) and UVB/UVC (entry 7) - all using the same Hg-lamp. As the UV lamp is not an integral part of the reactor, it could easily be removed

and replaced with sources of different wavelengths such as visible light LEDs to match other types of photochemistry. As UV LED's continue to develop, we expect high-power, compact devices to eventually exceed the productivity and efficiency of the medium pressure lamp presented and such UV sources will be easily accommodated within the Firefly reactor. We hope these formidable capabilities can make significant contributions to synthetic photochemistry in research and process labs within universities and industry and encourage others to use this technology as an enabling synthetic tool. Current work is concerned with developing a commercial version of the prototype Firefly reactor in order to realize these ambitious goals.

Experimental Section

General

For photolysis, standard reagent grade solvents were used without further purification. For all photochemical reactions, solvents were "degassed" by evacuating under vacuum and re-filling with N_2. For the duration of the reaction, N_2 was bubbled through the solution in the holding flask. When photochemical reactions were followed for their duration by NMR, 1,3,5-trimethoxybenzene was used as an internal standard. In all cases, a stock solution of this was added to aliquots of the reaction mixture prior to NMR sample preparation.

For flow reactions, when the full volume of solution had been taken up, the reactor was flushed out with a reactor volume of neat solvent and the reactor cleaned with recirculating DMSO/water (ca. 10 mins) prior to irradiating the next volume. The 5 kW variable power supply (JA5000 VPXi) and the 350 mm mercury lamp were purchased from Jenton International, Whitchurch. For the Firefly reactor, an FMI Q-series valveless piston pump was used along with an FMI pulse dampener (Cole-Parmer). The reactor was cooled with a Huber Unichiller 025-MPC,

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purchased from Radleys, Saffron Walden. Large-scale evaporations were assisted using a Heidolph Distimatic automatic module in conjunction with a standard rotary evaporator.

Flow procedure: Table1, Entry 1

A solution of maleimide CAS: 541-59-3 (24.3 g, 250 mmol) and 1-hexyne CAS: 693-02-7 (43 ml, 374 mmol) in degassed MeCN (2.5 L) was irradiated with the Firefly reactor fitted with a Pyrex inner filter and lamp at 3 kW at 36 ml/min. The mixture was concentrated *in vacuo* and chromatography on silica (30% EtOAc in hexane) yielded the product as a pale yellow oil (29.3 g, 65%). Analytical data as previously reported.[2d]

Flow procedure: Table1, Entry 2

A solution of maleimide (24.3 g, 250 mmol) and propargyl alcohol CAS: 107-19-7 (22 ml, 378 mmol) in degassed MeCN (2.5 L) was irradiated with the Firefly reactor fitted with a Pyrex inner filter and lamp at 3 kW at 36 ml/min. The mixture was concentrated *in vacuo* and chromatography on silica (100% EtOAc) yielded the product as an off white solid (24.6 g, 64%). Analytical data as previously reported.[2d]

Flow procedure: Table1, Entry 3

A solution of NMe maleimide CAS: 930-88-1 (44.4 g, 400 mmol) and trichloroethene CAS: 79-01-6 (180 ml, 2 mol) in degassed MeCN (0.2 M) was irradiated with the Firefly reactor fitted with a Pyrex inner filter and lamp at 3 kW at 15 ml/min. The mixture was concentrated *in vacuo* and chromatography on silica (10% Et_2O in DCM) yielded the product as a mixture of diastereomers (64.0 g, 66%). Analytical data as previously reported.[2d]

Representative Procedure: Table1, Entry 4

 A solution of THPA[16] **1** CAS: 2426-02-0 (608 g, 4 mol), *cis*-2-butene-1,4-diol CAS: 6117-80-2 (500 ml, 6.1 mol) and isopropylthioxanthone CAS: 75081-21-9 (10.2 g, 40 mmol) in degassed EtOAc (0.4 M) was irradiated with the firefly reactor fitted with a Pyrex inner filter and lamp at 3 kW at 36 ml/min. The mixture was concentrated *in vacuo* to a slurry which was filtered, washing with EtOAc and Et_2O and dried to give product **2** as a colourless crystalline solid (769 g, 80%): m.p. 188 -189°C (MeOH); ^{1}H NMR (400 MHz, DMSO) δ 12.25 (br. s, 1H), 4.45 (br. s, 1H), 4.21 (dd, J = 9.2, 4.8 Hz, 1H), 4.13 (d, J = 9.2 Hz, 1H), 3.54 – 3.44 (m, 2H), 2.83 (dd, J = 8.5, 4.8 Hz, 1H), 2.64 (dt, J = 8.5, 7.2 Hz, 1H), 1.94 – 1.25 (m, 8H) ppm; ^{13}C NMR (100 MHz, DMSO) δ 179.9, 174.4, 70.3, 59.4, 48.4, 45.7, 42.7, 37.3, 26.1, 26.1, 21.5, 20.9 ppm

Two additional runs yielded 577g (3.47 hr) and 192g (1.16 hr) of **2** (Total = 1,538g in 9.26 h). Although no drop off in productivity was observed during each run, the reactor was flushed with DMSO/water as a precaution before the next run was commenced. This allowed for safe evaporation of three successive volumes of solvent in a research lab setting. All three runs were completed in a single working day. This strategy was adopted for other reactions where large volumes of flammable solvents were involved. In a certified process lab, where real-time evaporation of bulk solvent is routine, it is likely that the Firefly could be run continuously with continuous evaporation of solvent. Any drop in productivity detected by online monitoring could initiate a brief automated shutdown of the reactor, flush with DMSO/water followed by start-up of the reactor.

Representative flow procedure: Table1, Entry 5

A solution of Diels-Alder adduct[17] **3** CAS: 51175-59-8 (1,307 g, 7.5 mol) in degassed solvent (10% MeCN in EtOAc, 1.0 M) was irradiated with the firefly reactor fitted with a Pyrex inner

filter and lamp at 3.0 kW at 36 ml/min. The mixture was concentrated *in vacuo* to a slurry to

which was added hexane. The mixture was filtered, washing with petroleum ether and the solid

dried to give pure Cookson's dione **4** CAS: 2958-72-7 as a colourless crystalline solid (1,165 g,

89%): m.p. 242 - 243°C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.19 – 3.14 (m, 2H), 2.95 – 2.90 (m,

2H), 2.82 – 2.78 (m, 2H), 2.72 – 2.68 (m, 2H), 2.04 (app. d, *J* = 11.4 Hz, 1H), 1.88 (app. d, *J* =

11.4 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) 212. 2, 54.9, 44.8, 43.9, 40.6, 38.9 ppm

Representative flow procedure: Table1, Entry 6

  To a solution of enamine **5**[12] (421 g, 1.6 mol) and isopropylthioxanthone (4.1 g, 16 mol) in

degassed MeCN (3 L) was added water (380 ml) and further MeCN to make up to 4 L (0.4 M).

The solution was irradiated with the firefly reactor fitted with a Pyrex inner filter and lamp at 3

kW at 9 ml/min. The photolysate was concentrated to a slurry which was triturated with hexane

and filtered, washing with hexane then cold Et$_2$O to give pyrrolidine **6** as a white crystalline

granular solid (367.3 g, 87%): m.p. 101 – 103 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.63 – 7.03 (m,

10H), 3.70 (br. s, 2H), 2.93 – 2.89 (m, 1H), 2.21 – 2.14 (m, 2H), 2.05 – 1.99 (m, 2H) ppm; [13]C

NMR (126 MHz, DMSO, 80°C) δ 171.8, 139.2, 136.4, 129.6, 127.5, 127.3, 127.1, 125.9, 125.7,

73.9, 54.9, 42.9, 34.2 ppm; HRMS (CI) calcd [M + H]$^+$ for C$_{18}$H$_{18}$NO 264.1388, found

264.1380

Three additional runs yielded 361.7g (7.41 hr), 177g (3.7hr) and 176.2g (3.7h hr) of **6** (Total =

1,082g in 22.22 h). As a slight (~2%) drop in productivity was observed towards the end of some

runs, the reactor was flushed with DMSO/water as a precaution before the next run was

commenced.

Representative flow procedure: Table1, Entry 7

A mixture of carboxylic acid **7**[18] CAS: 3130-75-4 (233 g, 1.0 mol) and K_2CO_3 (69 g, 0.5 mol) was sonicated in deionised water (1 L) until fully dissolved. The solution was diluted to 2.5 L with more water then made up to 5 L with degassed MeCN (0.2 M). The solution was irradiated with the firefly reactor fitted with a quartz inner filter and lamp at 3 kW at 30 ml/min. The MeCN was removed *in vacuo* to give a white slurry which was washed (water), filtered and the aqueous filtrate extracted with $CHCl_3$ (4×400 ml). Into the combined organic extracts was dissolved the wet residue which was separated, dried ($MgSO_4$), filtered through Celite and evaporated to give product **8** as white solid (167 g, 88%), m.p. 128-130˚C: ^{1}H NMR (400 MHz, DMSO) δ 7.66 – 7.57 (m, 3H), 7.54 – 7.49 (m, 1H), 6.35 (d, J = 1.6 Hz, 1H), 3.52 (app. dt, J = 11.2, 8.4 Hz, 1H), 3.29 (ddd, J = 11.2, 9.2, 2.9 Hz, 1H), 2.53 – 2.40 (m, 1H), 2.27 – 2.12 (m, 2H), 1.49 – 1.38 (m, 1H) ppm; ^{13}C NMR (100 MHz, DMSO) δ 169.1, 148.3, 132.5, 131.5, 129.3, 122.8, 122.7, 95.6, 41.1, 35.2, 27.4 ppm

Four additional runs yielded 335g (5.56 hr), 317g (5.56 hr), 147g (2.78 hr) and 66g (1.12 hr) of **8** (Total = 1,032 g in 17.78 hr). Due to the relatively dilute nature of this reaction (0.2 M) it was split into 5 runs in order to make product extraction and solvent evaporation more manageable. After one run a small residue build-up on the quartz tubes resulted in 13% drop in yield over the run. Before the subsequent run 30% water/DMSO was circulated for ca. 10 min (36 ml/min) and no significant drop in conversion was observed for the next 20 L of reaction solution (see table in SI).

Corresponding Authors

*E-mail: k.booker-milburn@bristol.ac.uk; luke.elliott@bristol.ac.uk

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Supporting Information

^{1}H & ^{13}C spectral data for all photochemically prepared compounds, experimental and optimisation procedures for photoreactions, sensitizer screens, pictures of FEP tubing (PDF).

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