Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Information
for
Photon Upconversion for the Enhancement of Microfluidic Photochemical Synthesis

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General Synthetic Methods

Synthetic reagents were purchased from Sigma Aldrich and Fisher Scientific, and used without further purification. Urethane monomers were purchased from Reynolds. NMR spectroscopy was performed with a Bruker DRX500 spectrometer with a BBO probe for ^{1}H NMR experiments. ^{13}C NMR was performed *via* Bruker DRX500 with a cryoprobe. All spectra were acquired at 298 K. ^{1}H NMR spectra were acquired at 500 MHz, ^{13}C NMR were acquired at 125 MHz. All NMR spectra were taken in $CDCl_3$. Chemical shifts are reported in ppm relative to NMR solvent. All gas chromatography was performed at UC Irvine's Mass Spectrometry Facility.

Synthesis of Dye- and Sensitizer-Doped Urethane Monomers and Polyurethane

Monomers were synthesized following Kim *et al.* with modifications.[1] A dye solution is made by dissolving 0.128 g diphenylanthracene in 1.8 mL degassed THF. A sensitizer solution is made by disolving 0.010 g palladium(II) octaethylporphryrin in 1.8 mL degassed THF, followed by sonication for 20 min. The dye solution is drawn up into a syringe and added to 7.8 mL Clearflex 50 Part A (Reynolds), which is then degassed with stirring by bubbling argon for 20 min. The sensitizer solution is drawn up into a syringe while the solution is stirred vigorously. The sensitizer solution is then added to 15.6 mL of Clearflex 50 part B, which is then degasses with argon bubbling and vigorous stirring for 20 min. Doped Clearflex A and B are then mixed, and the mixture is cast into the reactor mold (see below). The mold setup is degassed under vacuum in a bell jar for 20 min. The degassed reactor is then placed in a vacuum oven at 60 ºC for 24 h. After removal from the oven, the reactor is allowed to return to room temperature before use.

Reactor Fabrication

Reactors were fabricated using custom-milled or 3-D printed molds (**Fig S1 a** and **b**), with sides comprising custom-etched brass plates for the precise positioning of tubing (**Fig S1 c** and **d**). FEP-lined clear Versilon ultra chemical-resistant tubing 1/16" I.D., 1/8" O.D. (McMaster-Carr) was added to the mold by securing to the brass plates. The mold set up is then coated with mold release (Reynolds) and the monomer mixture is then poured (**Fig S1 e**). After curing, the brass plates are removed, and the finished reactor monolith is lifted from the mold. Fittings are added to connect the reactor interior to tubing from the reagent reservoirs.

Supplementary Discussion 1: Chemical Scope of Reactor Feedstock

The photochemical generation of $^{1}O_2$ *via* tris(bipyridine)ruthenium(II) chloride and subsequent addition to α-terpinene to create the antihelmenthic drug ascaridole was used to assay the reactor effectiveness. This reaction is kinetically rapid and lends itself to a short slug-flow reactor for which multiple prototypes can be easily fabricated in an academic setting. The current reactor is designed for fast, air- and water- tolerant reactions. Parameters will need to be adjusted for slower reactions (*e. g*. modify flow rate and inlet gas pressure if using gas-mixing flow methods), and reactions that are air- or water-sensitive (*e. g*. install purge valve in line with reactor). Research into the scope of this process is ongoing and is toward 3 main coupled groups of reactor/reaction families: (1) cooling processes to effect more sensitive photochemical $^{1}O_2$ additions such as that which occurs during Seeberger's artemisinin synthesis;[3] (2) closed loop reactors for photoredox

reactions that require 12-24 h; and (3) expansion of wavelength range. So far, extended residence times (based on the individual reaction's kinetics) and the lower end of irradiance (tolerated by the catalyst selected) trends to showing the most dramatic improvement in percent conversion with the upconversion reactor across the different conditions we are testing.

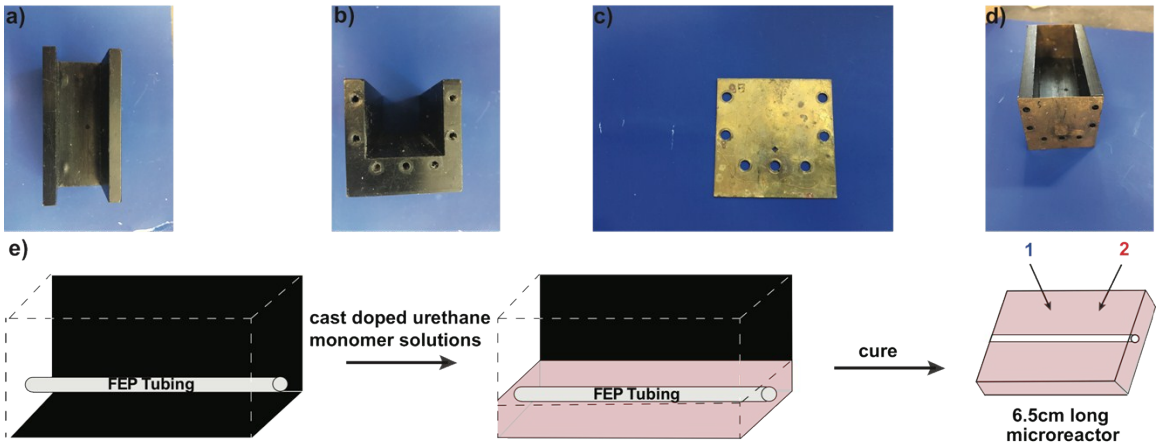


Fig S1. a) and b) Top and side views of the reactor mold; **c**) custom-made brass plate for positioning tubing; **d**) reactor mold with brass plate attached; **e**) casting and curing process for doped polyurethane.

Upconversion-Assisted Microfluidic Synthesis of Ascaridole

To a 25 mL round bottomed flask was added degassed methanol (7.5 mL), α-terpinene (0.18 mL, 1.6 mmol), and tris(bipyridine)ruthenium(II) chloride hexahydrate (28 mg, 37 μmol). The flask was wrapped in aluminum foil at all times, and the fume hood is darkened. The flask was stirred in the dark for 15 min. The reaction mixture is then loaded into a foil-wrapped syringe, and placed on a multi-port syringe pump (syringepumps.com) with a syringe of an equal volume of dioxygen. Gas and liquid reactants mix in a slug-flow manner–following passage through a Y junction, the mixture travels through a 7 cm mixing channel before entry into the upconversion reactor. Light is excluded from all portions of the set-up except for the upconversion monolith. The monolith was irradiated with a full-spectrum actinic solar simulator (Osram). Photon flux was measured using a solar light meter before each run. For a diagram of the set-up please see Main Text figure 3. After the reaction is complete, the mixture is concentrated under a stream of nitrogen, diluted in ~3 mL of diethyl ether, and passed over a small silica plug to remove the ruthenium catalyst. The plug is then washed with further portions of ether, and the combined fractions are concentrated under a stream of nitrogen. Ascaridole peak assignments match those reported.[2]

Flow Rate and Residence Time Studies

Flow rate studies were accomplished by altering the flow rate in microliters/min on the variable-speed multi-port syringe pump. Residence time was quantified by tracking the transit of individual boluses of reaction mixture as they passed through the illuminated upconversion reactor.

Photon Flux Studies Photon flux was monitored using a solar light meter (Extech). The solar simulator was positioned so the desired flux was achieved.

Reactor Upconversion Controls

Reactor controls were performed by synthesizing reactors in a method analgous to that on p. 2, but with modifications in composition. Specifically, reactors were fabricated with undoped A and B; doped A with undoped B; or undoped A and doped B. The percent conversion of ascaridole was monitored at a flow rate of 40 μL / min.

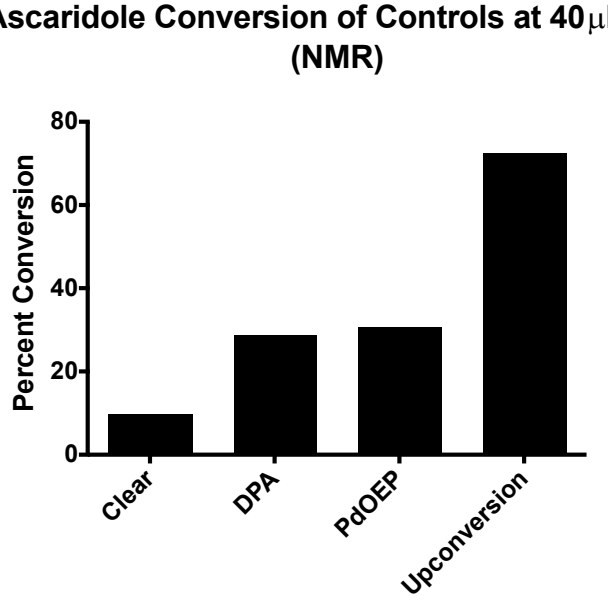


Fig. S2. Upconversion controls. Clear: undoped A and B; DPA: diphenyl anthracene doped only; PdOEP: palladium(II) octaethylporphryrin doped only; Upconversion: doped with both diphenyl anthracene and palladium(II) octaethylporphryrin.

Gas Chromatography

Reaction mixture effluent from the reactor was diluted to ~50 μg/mL in ethyl acetate. Gas chromatography was then performed on diluted samples using a Waters (Micromass) GCT premier. A DB-5 30 m × 0.25 mm × 0.25μ film column was used. The temperature program was 35 ºC starting temp, ramp rate of 10, and final temp 270 ºC. The carrier gas was helium. Chemical ionization (CI) with ammonia reagent gas was used to detect analytes. Standards of solvents, α-terpinene, and ascaridole were used to identify peaks, as well as referencing the GC/MS mass/retention time database on Xcalibur. Data were analyzed by integrating peaks with Xcalibur (ThermoFisher) and MassLynx (Waters) post-processing software.

Sample Gas Chromatography Data

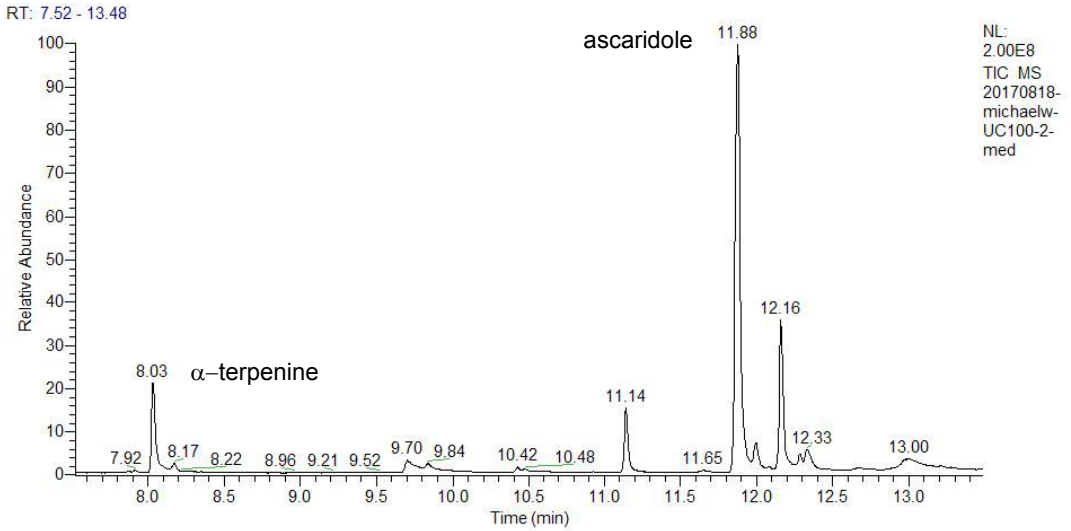
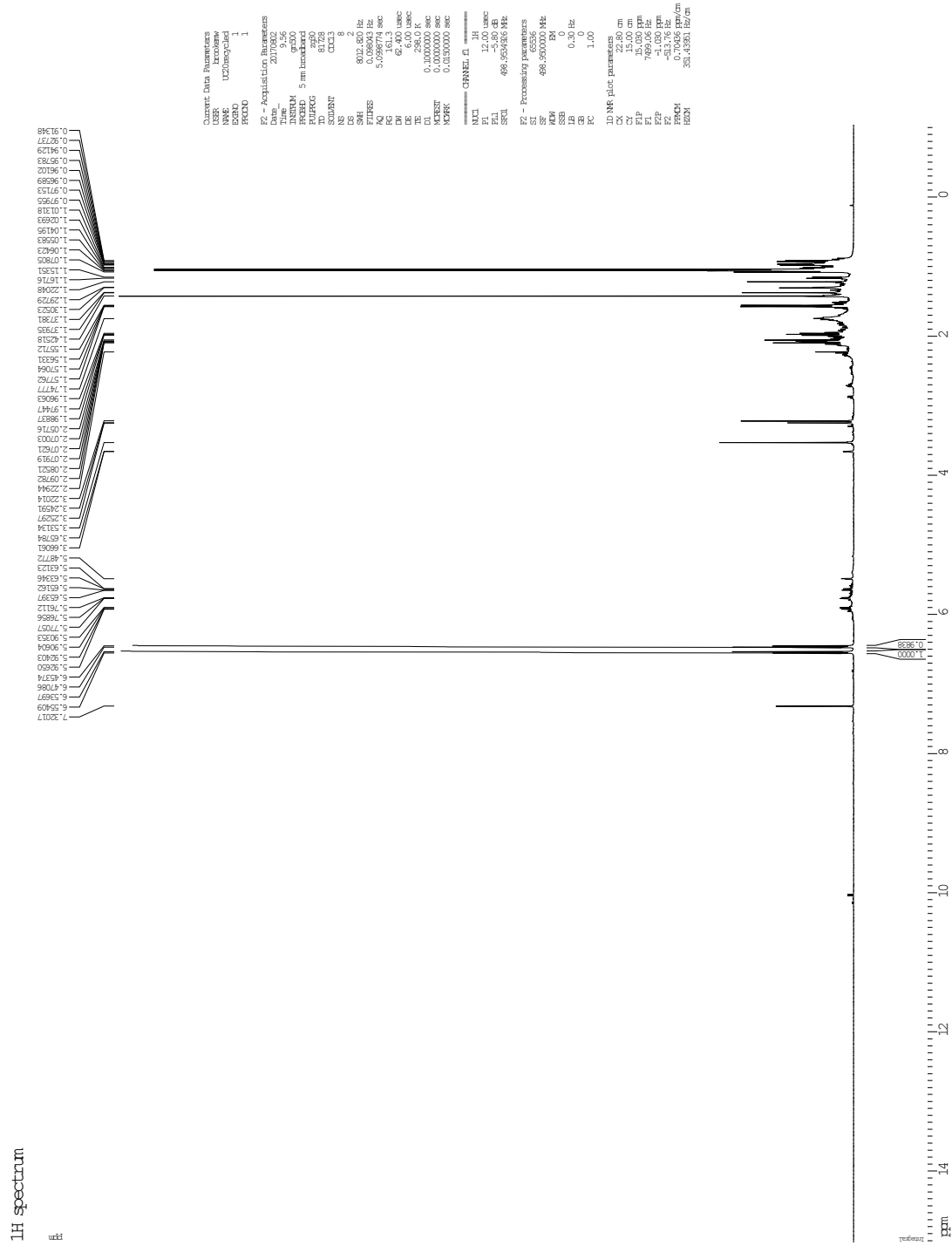


Figure S2. Sample GC data of a 100 μL/min run in the upconversion reactor.

Sample NMR Data



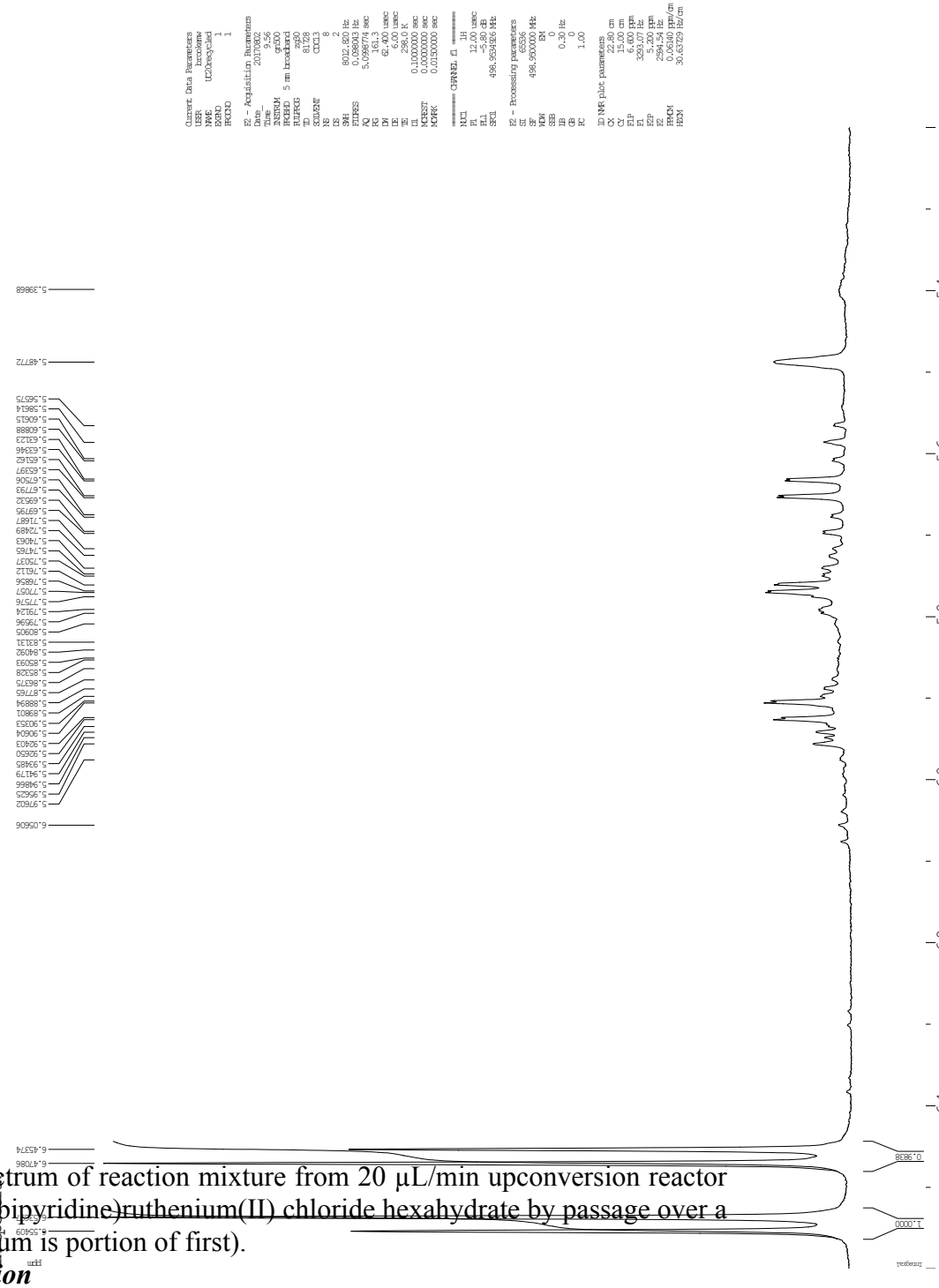


Figure S3. ^{1}H NMR spectrum of reaction mixture from 20 µL/min upconversion reactor run, after removal of tris(bipyridine)ruthenium(II) chloride hexahydrate by passage over a silica plug (second spectrum is portion of first).

UV-Vis Spectra Acquisition

Spectra were acquired on a Varian Cary Bio 50 UV-Vis spectrophotometer, and a Varian Cary Eclipse Fluorescence Spectrophotometer. Samples of PdOEP and DPA were weighed out, and added to a round-bottomed flask, which was then flushed with argon. To these samples were added anhydrous toluene, to a final concentration of 10 µM. Samples were aliquoted into argon-flushed cuvettes, and spectra were taken. For the $[Ru(bpy)]^{2+}$, a sample was made at a concentration of 10 µM in methanol, the solvent used for the endoperoxide synthesis.

References

1. J.-H. Kim; F. Deng; F. N. Castellano; J-H Kim. *Chem. Mater.* 2012, **24**, 2250.
2. J. R. Backhouse; H. M. Lowe; E. Sinn; S. Suzuki; S. Woodward. *J. Chem. Soc., Dalton Trans.* 1995, **9**, 1489.
3. Lévesque, F.; Seeberger, P. H. *Angew. Chem. Int. Ed.* 2012, **51**, 1706.