A 3D-Printed Open Access Photoreactor Designed for Versatile Applications in Photoredox- & Photoelectrochemical Synthesis

Florian Schiel, Christoph Peinsipp, Stefan Kornigg, Dietrich Böse

Submitted date: 04/12/2020 • Posted date: 07/12/2020

Licence: CC BY-NC 4.0

Citation information: Schiel, Florian; Peinsipp, Christoph; Kornigg, Stefan; Böse, Dietrich (2020): A 3D-Printed Open Access Photoreactor Designed for Versatile Applications in Photoredox- & Photoelectrochemical Synthesis. ChemRxiv. Preprint. https://doi.org/10.26434/chemrxiv.13302539.v2

Most published photochemical reactions are still not performed under standardized conditions. It is well known that the control of light intensity, the exact reaction temperature and other parameters are crucial for the success of a photochemical reaction. However, for most reactions reported in the literature, these parameters are not precisely controlled and recorded. As a result, the reproduction of these reactions is difficult and the progress in the field of photoredox chemistry is hampered by this limitation. To address this problem, a 3D-printed photoreactor was designed which can be easily replicated with a small number of inexpensive and easily available components. Equipped with thermoelectric coolers, the reactor can access and precisely control the temperature in the range of -17 °C to 80 °C, while reactions under high-intensity irradiation are performed with LED lamps from Kessil or HepatoChem. The practical design of the vial holder allows a versatile use of different reaction vessels - in addition to fast reaction optimization with up to eight vials simultaneously, upscaling in batch and flow is easily possible. Due to the high light intensity, the catalyst loading can be reduced to 0.1 mol% for large-scale reactions. The flexibility of the vial holder is demonstrated by combining IKA’s ElectraSyn 2.0 with the photoreactor to perform photoelectrochemical reactions in a reproducible manner.

File list (4)

- 3D-printed photoreactor.pdf (764.56 KiB)
- Supporting Information.pdf (1.38 MiB)
- photoreactor printing files.zip (3.40 MiB)
- Photoreactor_Arduino program.ino (7.31 KiB)
A 3D-printed open access photoreactor designed for versatile applications in photoredox- & photoelectrochemical synthesis

Florian Schiel,*[a][b] Christoph Peinsipp,[a] Stefan Kornigg,[a], Dietrich Böse[a][c]

Abstract: Most published photochemical reactions are still not performed under standardized conditions. It is well known that the control of light intensity, the exact reaction temperature and other parameters are crucial for the success of a photochemical reaction. However, for most reactions reported in the literature, these parameters are not precisely controlled and recorded. As a result, the reproduction of these reactions is difficult and the progress in the field of photoredox chemistry is hampered by this limitation. To address this problem, a 3D-printed photoreactor was designed which can be easily replicated with a small number of inexpensive and easily available components. Equipped with thermoelectric coolers, the reactor can access and precisely control the temperature in the range of -17 °C to 80 °C, while reactions under high-intensity irradiation are performed with LED lamps from Kessil or HepatoChem. The practical design of the vial holder allows a versatile use of different reaction vessels - in addition to fast reaction optimization with up to eight vials simultaneously, upscaling in batch and flow is easily possible. Due to the high light intensity, the catalyst loading can be reduced to 0.1 mol% for large-scale reactions. The flexibility of the vial holder is demonstrated by combining IKA’s ElectraSyn 2.0 with the photoreactor to perform photoelectrochemical reactions in a reproducible manner.

Introduction

The use of visible light as an alternative energy source to drive chemical reactions has enabled the development of novel and unique transformations over the last decade. With the growing interest, many groups have diversified their research to the field of synthetic photochemistry and numerous experimental setups were created. However, the large variety of setups and light sources are problematic with regards to reproducibility, since the outcome of the reaction depends on many factors of which some are not fully understood.[1] Oftentimes, little or no reactor/setup details are reported and therefore it may be challenging to reproduce the published experimental results.[2] To address this issue a standardized set of equipment is needed, which must meet several requirements to be used on a broad basis (Figure 1).

1) Fixed vial and lamp position: A set distance between the light sources and the reaction vials enables constant light intensity in the reaction medium to ensure reproducibility.
2) Variable light intensity: Photochemical reactions are initiated by the absorption of photons and the effectiveness of the processes is determined by quantum yields. The kinetics of those processes are light intensity-dependent and therefore the reaction rate is affected by a change in the number of photons. Reactions with a low photoredox catalyst concentration are saturated already at lower irradiation while for higher catalyst loadings, or for direct irradiation of the reactants higher intensities are required.[3] In several photoredox reactions a high photon flux showed a significant improvement in the transformation compared to the unsaturated variant, but sometimes it can cause a diminished yield and reproducibility problems.[4] In some cases the chemoselectivity can be altered by changing the number of photons which are absorbed.[5] Furthermore, according to the Beer-Lambert law, the light intensity decreases exponentially with depth of the reaction medium, which may decrease the efficiency of the process, especially for larger scale reactions.[6]
3) Exchangeable and defined light source: In terms of selectivity and reproducibility, it is important to know and control the wavelength that drives the reactions. Light sources such as CFL or medium pressure Hg lamp cover a broad range of different emission bands and therefore the use of LEDs are currently the preferred choice due to the narrower emission bands.[5, 3b, 6] On
the other hand, the choice of the wavelength is also crucial to obtain an effective irradiation of the chromophore and to avoid side-reactions.[7]

4) Broad, controllable temperature range: Most photochemical reactions are carried out at ambient temperature since energy is introduced by the absorbed photons and often no or little temperature influence is observed. But if the photon absorption process is no longer the rate determining step, which is achieved at high light intensity, then the reaction is affected by the temperature.[3] In addition, the generated intermediates are normally in the ground state, and temperature effects may arise due to the intrinsic activation barriers.[8] On the other hand, some reactions require temperatures below 0 °C.[9] This shows that a widely accessible temperature range is essential for the best possible reaction optimization and the reproduction of literature examples.

5) Flexibility in the use of different types of vials and the possibility of upscaling (batch or flow): Different chemistries require different reaction vessels and therefore the vial holder should be easily adaptable to ensure that the reactions are reproducible.

6) Performing several reactions simultaneously: Allows a rapid screening of reaction conditions and parallel synthesis.

7) Practicality in terms of size, accessories and safety: A frequently used device is preferably small, and no external devices are required. It should also be well sealed to avoid exposure of the environment to high energetic radiation.

8) Price: The device should be affordable, since most research groups require several reactors.

Several companies have already addressed the problem of standardization and created commercially available photoreactors. At least five different companies offer them, with prices ranging from 1.800 € to over 20.000 €. [4a, 7b, 10] However, none of the commercial reactors fulfill all criteria discussed. The more features a reactor covers, the more expensive it becomes. Their main field of application is in the chemical industry and a standardized design is rarely found in recent publications. Therefore, we have decided to design an open-access photoreactor to ensure that more photochemical reactions are performed in a standardized reactor. This assumes that the reactor is suitable for many different applications (i.e. it should cover all points mentioned above) and at the same time the cost and size should be reduced to a minimum (about 450 € without lamps). In addition, the barrier to reproduction must be minimized by a simple and robust construction.

## Results and Discussion

### Reactor design

We mainly focused on three parts: 1) 3D-printing[11] to quickly design prototypes at low cost, 2) air as cooling medium to ensure high light intensity and 3) thermoelectric cooling elements (TECs) as inexpensive and precise temperature control units. TECs are heat pumps consisting of P-type (holes) and N-type (electrons) semiconductors which are able to transport heat from the cooler to the hotter side by applying current.[12] They are well suited for this purpose due to their small size and inexpensive availability.

A reactor was then designed and 3D-printed with TECs inserted into the chamber walls (Figure 3). On the outside, the heat of the TECs is removed by an additional water-cooling circuit. Inside the reactor, heat transfer is achieved by heat sinks with a large surface area and by additional fans, which ensure optimal cooling of the entire chamber. The TECs are automatically switched off when the desired temperature is reached, the LED lamps heat up the chamber and the TECs switch on again. This process ensures that the temperature fluctuation of the air is kept within ±1-3 °C. The fluctuation range inside of the reaction vessels is even smaller. The temperature range that can be used with this setup is between -20 °C and +80 °C. The lower limit is determined by four factors: The thermal insulation, the efficiency of the TECs, the power of the fans and the light intensity. The thermal insulation is achieved by printing the reactor with 2 cm thick walls with 10% grid filling. This value indicates that the empty space is filled with 10% filament in 3D printing. However, the most important cooling factor is the efficiency of the TECs (including quality and performance). The chamber is cooled by two high-tech 8.5 A TECs to -20°C without light. A temperature gradient is created in the reactor, with the coolest parts being the heat sinks, while the hottest area is in the beam of the lamps. How well the heat is dissipated is determined by the power of the fans. The most effective cooling is achieved by using high-speed fans at a voltage of 5-7 V (higher voltage reduces cooling efficiency and the noise level increases significantly)

![Figure 2. All electronic components that are required (except power supply unit and TECs). Upper picture (from left to right): Power plug, 2 x connector clamp, 3 x resistor, 2 x pushbutton, XT60, On/Off switch, veroboard. Lower picture (from left to right): Temperature sensor, display, step down converter, motor driver, Arduino microchip.](image-url)
The effective working temperature is strongly dependent on the light intensity. While -17 °C is obtained with one Kessil PR160L 45 W 440 nm at 25% light intensity, -2 °C can be reached with two Kessil PR160L 45 W 440 nm lamps at 100% light intensity each. On the other hand, the upper temperature limit is defined by the glass transition point of the filament, which is 80 °C for the used PETG. At this point a deformation of the reactor can occur. When working at temperatures below or near 0 °C, the potential problem of water condensation had to be addressed. Fortunately, it was found that no water condensation occurs on the reaction vessels. Instead, the water freezes on the heat sinks, which is reduced to a minimum when the reactor is sealed almost airtight. The closed system has the additional advantage that there is no light pollution of the environment, which allows a safe handling of the reactor environment with UV and intense blue light (Figure 3).

The electronic control unit is based on an Arduino microchip and a motor driver, to ensure that the reactor remains small, practical and easy to rebuild (Figure 2). The microchip controls the temperature in the chamber while the motor driver is responsible for switching the TECs on and off. The water-cooling for the TECs alone is sufficient to maintain the chamber around 40 °C (with two Kessil PR160L 45 W 440 nm lamps, 100% light intensity each) and to increase the temperature range the microchip is necessary. It enables a change in the current flow, which reverses the mode of action of the TECs, where the chamber is heated while the outside is cooled. In addition, safety related functions are added, such as an emergency shutdown of the thermoelectric coolers in case of overheating if the water-cooling is not turned on (for a complete list of safety features see SI).

To ensure that the reactor is easily rebuilt, the commercially available LED lamps from Kessil and HepatoChem were chosen as light sources. Both companies provide LED lamps at different wavelengths (365 – 740 nm) with a narrow and well-defined emission band. Additionally, the light intensity of the Kessil lamps is dimmable. The two independent lamp positions enable the possibility of using two different wavelengths at the same time. The exchangeable vial holder allows the use of a variety of vessels to perform reactions in different scales. Due to the simple design it can be easily adjusted if different vessels are required (e.g. a Schlenk flask). Holders are provided for 1 ml vials (HPLC vials), 4 ml and 8 ml vials, so that several reactions can be performed simultaneously.
Six positions are available for the 4 and 8 ml vials and eight for the 1 ml vials, all of which perform with the same efficiency using the Kessil PR160 45 W 440 nm lamps (Figure 4). The benchmark reaction was the sp² – sp³ cross-electrophile coupling method from the MacMillan group with optimized conditions. The vials can easily be removed from the reactor during the reaction (e.g. for taking a reaction control) while the LED lamps are still running, light exposure to the environment is minimal. Since reproducibility depends on the identical light intensity in each vial, all positions of the 4 ml vial holder were tested with different lamps (Kessil PR160L 45 W 440 nm and HepatoChem 450 nm 18 & 30 W, Figure 4). The Kessil PR160 45 W 440 nm, PR160L 45 W 440 nm and the HepatoChem 30 W 450 nm can be used without any restrictions. Only with the HepatoChem 18 W 450 nm lamp the positions 3 and 4 were faster than the other four, probably due to the more focused beam.

For larger scales, a holder for 50 ml and 100 ml NS 25 flasks and a flow unit (~ 7 ml capacity) are available (Figure 5). The batch version benefits from the simple design, but it suffers from a lower light penetration, according to the Beer-Lambert law, especially in heterogeneous mixtures. Additionally, temperature gradients in the flask may arise due to a lower heat transfer.

On the other hand, flow chemistry has a better scalability due to the small reaction volume, but the set-up is usually more complex. Since most photochemical reactions do not proceed in the absence of light, no complex mixing procedure has to be taken into account. This simplifies the process: All components are combined beforehand and only a normal syringe pump is necessary (Figure 6).
Evaluating literature reactions

The reactor was tested on several photoredox reactions, including batch, flow and photoelectrochemistry.

**Batch:** The arylation of aryl halides by a C-H activation (Scheme 2) by the König group[14] was carried out by a custom-made aluminum block setup with blue LED irradiation of the bottom side of the vials. They achieved a yield of 87% after 3 h, whereas with the 3D-printed photoreactor the reaction time was reduced to only 15 min (14-fold increase) with an isolated yield of 78%. In contrast to the reported conditions, low yields were obtained when the reaction mixture was carefully degassed and complete conversion was observed only in the presence of oxygen.

**Flow:** The flow unit was tested using the sp² – sp³ cross coupling method using trifluoroborates and aryl bromides (Scheme 5) from the Boyd lab at Vertex Pharmaceuticals Incorporated.[17] They used the Vapourtec E-series UV-150 device with a capacity of 10 ml. At a flow rate of 0.25 ml/min the residue time was 40 min and a yield of 62% was achieved. At higher light intensity the flow rate in the 7 cm long tube was increased to 0.35 ml/min, reducing the residue time to 20 min with a yield of 66%. The reaction was carried out using a syringe pump (Figure 6).

The deaminative sp²-sp³ alkylation (Scheme 4) was reported using a classical reaction setup (Kessil lamps with fan) and with the integrated photoreactor from Merck & Co by the MacMillan group.[16] With the 3D-printed photoreactor the same results as with the integrated photoreactor were obtained with a yield of 86% after 8.5 h.
Photoelectrochemistry: A new research field that has gained interest over recent years is the combination of synthetic photochemistry with synthetic electrochemistry to expand the spectrum of possible chemical transformations.\textsuperscript{[18]} In terms of reproducibility, this is quite a challenge, since electrochemistry also suffers from a lack of standardized equipment. However, this problem was already addressed by a collaboration between Prof. Phil Baran and IKA, to design the ElectraSyn 2.0.\textsuperscript{[19]} They also provide a module (ElectraSyn GOGO module) which allows the user to perform reactions outside the ElectraSyn (e.g. to perform reactions at different temperatures). As a result, a cover for this module was designed (Figure 7) to provide a possibility to perform photoelectrochemical transformations in a standardized manner. With the combination of both standardized reactors it was possible to reproduce the decarboxylative C-H functionalization reaction (Scheme 6) from the Xu group.\textsuperscript{[20]} With their custom-made LED/electrode setup a yield of 85% after 3.9 F/mol was isolated using both standardized reactors. However, to obtain a full conversion the loading of the oxamic acid had to be increased from 2.5 to 4 equivalents.

![Scheme 6. Reaction conditions for the decarboxylative C-H functionalization reaction.](image)

**Figure 7.** Performing photoelectrochemistry with the GoGo module insert.

**Conclusion**

A simple and easily reproducible 3D-printed photoreactor was developed, which solves various problems of photochemical setups. It allows the user to perform reactions in a standardized way at high light intensity with well-defined, commercially available LED lamps of different wavelengths. Complete temperature control over a wide range (-20 °C to +80 °C) has been achieved by integrating TECs into the reactor.

The flexible vial holder allows up to eight reactions to be performed simultaneously and can be easily adapted to different vial types (such as the ElectraSyn GOGO module holder). This ensures that reproducibility is not limited to a few provided vial holders. It is also designed for performing reactions on a larger scale with a flask or the 3D-printed flow unit. The reactor combines all these features while remaining small, practical and cost effective. The closed system prevents exposure to ambient light and allows safe handling without additional protective equipment.

**Acknowledgment**

We are grateful for the support of Dr. Stephan Zahn, Dr. Harald Weinstabl, Dr. Andreas Gollner and Prof. Nuno Maulide for valuable discussions and their ongoing support which helped to realize this project.

**Keywords:** Photochemistry • Electrochemistry • Photoreactor • 3D-printing • Flow chemistry

---

[1] M. Baker, Nature 2016, 533, 452-454.
[2] H. E. Bonfield, T. Knauber, F. Levesque, E. G. Moschetta, F. Susanne, L. J. Edwards, Nat. Commun. 2020, 11, 804.
[3] a) J. Z. Bish, Front. Chem. 2019, 7, 128; b) L. Buzzetti, G. E. M. Grispen, P. Melchiorre, Angew. Chem. Int. Ed. 2019, 58, 3730-3747.
[4] a) C. C. Le, M. K. Wismer, Z. C. Shi, R. Zhang, D. V. Conway, G. Li, P. Vachali, I. W. Davies, D. W. C. MacMillan, ACS Cent. Sci. 2017, 3, 647-653; b) M. N. Lavagnino, T. Liang, D. W. C. MacMillan, Proc. Natl. Acad. Sci. 2020, 117, 21058-21064.
[5] C. Kerzig, O. S. Wenger, Chem. Sci. 2018, 10, 11023-11029.
[6] M. Sender, D. Ziegenbalg, Chem. Eng. Tech. 2017, 39, 1159-1173.
[7] a) C. P. Haas, T. Roeder, R. W. Hoffmann, U. Tallarek, React. Chem. Eng. 2019, 4, 1912-1916; b) H. E. Bonfield, K. Mercer, A. Diaz-Rodriguez, G. C. Cook, B. S. J. McKay, P. Slade, G. M. Taylor, W. X. Ooi, J. D. Williams, J. A. Murphy, L. Schermmer, W. Kroull, T. Meike, J. Cartwright, G. Grogan, L. J. Edwards, ChemPhotoChem 2020, 4, 45-51; c) S. Prati, D. Raveli, M. Fagnoni, photochemphotobiol.com, 2019, 18, 2094-2101; d) F. Glaser, C. Kerzig, O. S. Wenger, Angew. Chem. Int. Ed. 2020, 59, 10266-10284.
[8] a) B. Y. Park, M. T. Pirnot, S. L. Buchwald, J. Org. Chem. 2020, 85, 3234-3244; b) H. A. Sakai, W. Liu, C. C. Le, D. W. C. MacMillan, J. Am. Chem. Soc. 2020, 142, 11691-11697; c) X. Zhang, D. W. C. MacMillan, J. Am. Chem. Soc. 2016, 138, 13862-13865.
[9] a) G. Goli, B. Bieszczad, A. Vega-Penalosa, P. Melchiorre, Angew. Chem. Int. Ed. 2019, 58, 1213-1217; b) C. Verrier, N. Alandini, C. Pezzetta, M. Moliterno, L. Buzzetti, H. B. Hepburn, A. Vega-Penalosa, M. Silvi, P. Melchiorre, ACS Catal. 2018, 8, 1062-1066.
[10] a) http://www.penphd.com/product5/5, 29.11.2020; b) http://www.hepatochem.com/photoreactors- leds-accessories/29.11.2020; c) http://www.thalesiano.com/products-and-services/phototube/, 29.11.2020; d) http://www.pacer.co.uk/case-studies/medical-case-studies/led-illuminator.html, 29.11.2020; e) http://www.luzchem.com/ProductList.php?product_line_ID=1, 29.11.2020; f) http://www.luzchem.com/ProductList.php?product_line_ID=11, 29.11.2020.
[19] a) M. Yan, Y. Kawamata, P. S. Baran, Angew. Chem. Int. Ed. 2018, 57, 4149–4155. b) http://www.ika.com/de/Produkte-Lab-Eq/Electrochemistry-Kit-csp-516/, 29.11.2020.

[20] X. L. Lai, X. M. Shu, J. Song, H. C. Xu, Angew. Chem. Int. Ed. 2020, 59, 10626–10632.
A 3D-printed open access photoreactor designed for versatile applications in photoredox- & photoelectrochemical synthesis

Florian Schiel,*[a][b] Christoph Peinsipp,[a] Stefan Kornigg,[a] Dietrich Böse[b][c]
[a] Boehringer Ingelheim RCV GmbH & Co KG, Dr.-Boehringer-Gasse 5-11, 1121 Vienna, Austria.
[b] Institute of Organic Chemistry, Faculty of Chemistry, University of Vienna, Währinger Straße 38, 1090 Vienna, Austria.
[c] Current adress: Merck Healthcare KGaA, Frankfurter Strasse 250, Darmstadt, 64293, Germany.

Table of Contents
1. 3D Printer Equipment ......................................................................................................................................................... 2
  1.1 3D Printed Parts ................................................................................................................................................................. 3
  1.2 Equipment .............................................................................................................................................................................. 4
  1.3 Purchase List – Reactor ............................................................................................................................................................ 4
  1.4 Purchase List – Electronic Components .............................................................................................................................. 5
2. Construction Manual .................................................................................................................................................................. 6
  2.1 Reactor ...................................................................................................................................................................................... 6
  2.2 Electronics ............................................................................................................................................................................... 8
  2.3 Program .................................................................................................................................................................................. 12
3. Safety Features .......................................................................................................................................................................... 12
4. User’s Guide .............................................................................................................................................................................. 13
5. Tips and Tricks ............................................................................................................................................................................ 14
6. General Information - Chemistry .............................................................................................................................................. 15
7. Experimental Part ....................................................................................................................................................................... 15
8. HPLC Calibration Curves ......................................................................................................................................................... 19
9. NMR spectra ............................................................................................................................................................................ 20
1. 3D Printer Equipment

An original Prusa i3 MK3S was used for all 3D-printings, all parts were designed in the program Fusion 360 and for slicing the Prusa slicer 2.0 was used. All parts were printed with PETG and TPU, unless otherwise stated PETG was the standard filament.

Filament details:

PETG: https://www.herz-filament.at/PETG
- Manufacturer: Herz
- Type: PETG – metallic blau
- Size: 1.75 mm
- Print settings:
  ➢ 0.2 mm SPEED @MK3, change contact Z distance for supports to 0.15 mm
  ➢ 3 perimeters
  ➢ 0.2 mm layer height
  ➢ 20% grid infill, unless otherwise stated
  ➢ More changes, see table 3D printed parts
- Filament settings: Pursament PETG
  ➢ No custom changes
- Printer settings:
  ➢ Original Prusa i3 MK3S MMU2S Single, no custom changes

TPU: https://fillamentum.com/TPU
- Manufacturer: Fillamentum
- Type: Flexfill TPU 98A “Sky Blue”
- Size: 1.75 mm
- Print settings:
  ➢ Custom profile – based on 0.2 mm SPEED @MK3
  ➢ Change all speeds to 25 mm/s (leave travel move speed at 180 mm/s)
  ➢ Change contact Z distance for supports to 0.15 mm
  ➢ 3 perimeters
  ➢ 0.2 mm layer height
  ➢ 20% grid infill, unless otherwise stated
- Filament settings:
  ➢ Custom profile – based on SemiFlex or Flexfill 98A
  ➢ Change cooling settings to: Keep fan always on, enable auto cooling, disable fan for first layer.
  ➢ Fan speed: min. 70%, max: 90%
- Printer settings:
  ➢ Custom profile – based on original Prusa i3 MK3S MMU2S Single
  ➢ Change retraction speed to 25 mm/s
# 1.1 3D Printed Parts

| Part name                        | Quantity | Recommended print settings                                                                 | File name              |
|----------------------------------|----------|-------------------------------------------------------------------------------------------|------------------------|
| Reactor                          | 1 x      | 10% grid infill                                                                            | reactor.stl            |
|                                  |          | 1 solid layer every 10 mm                                                                  |                        |
|                                  |          | Use support                                                                                |                        |
|                                  |          | Pause print at 5 3 mm and insert 4 M3 nuts                                                 |                        |
|                                  |          | Pause print at 103.2 mm and insert 4 M3 nuts                                               |                        |
|                                  |          | Pause print at 117.4 mm and insert 4 M3 nuts                                               |                        |
| Clamp                            | 2 x      |                                                                                           | clamp.stl              |
| Lid                              | 1 x      | 10% grid infill                                                                            | lid.stl                |
|                                  |          | Pause print at 4.8 mm and insert 4 magnets                                                 |                        |
|                                  |          | (d = 6 mm)                                                                                 |                        |
| Lamp holder left                 | 1 x      |                                                                                           | lamp holder left.stl    |
| Lamp holder right                | 1 x      |                                                                                           | lamp holder right.stl   |
| Lamp holder adapter              | 2 x      |                                                                                           | lamp holder adapter.stl|
| *optional for Kessil lamp        |          |                                                                                           |                        |
| Magnetic stirrer adapter         | 1 x      | Use support and optional a brim                                                            | magnetic stirrer adapter.stl|
| *for ika magnetic stirrer        |          | (20 cm diameter)                                                                           |                        |
| Electronics case                 | 1 x      | Use support and optional a brim                                                            | electronics case.stl    |
| Electronics lid                  | 1 x      | Use support and optional a brim                                                            | electronics lid.stl     |
| Electronics cover                | 1 x      | Use support                                                                                | electronics cover.stl   |
| 4 ml vial insert                 | 1 x      | Use support                                                                                | insert – 4 ml vials.stl|
| *optional                        |          | Pause print at 35.2 mm and insert 4 magnets                                                 |                        |
|                                  |          | (d = 6 mm)                                                                                 |                        |
| 4 ml vial insert cap             | 6 x      | Best printed in semiflex TPU                                                               | cap – 4 ml vial.stl    |
| *optional                        |          |                                                                                           |                        |
| 8 ml vial insert                 | 1 x      | Use support                                                                                | insert – 8 ml vials.stl|
| *optional                        |          | Pause print at 35.2 mm and insert 4 magnets                                                 |                        |
|                                  |          | (d = 6 mm)                                                                                 |                        |
| 8 ml vial insert cap             | 6 x      | Best printed in semiflex TPU                                                               | cap – 8 ml vial.stl    |
| *optional                        |          |                                                                                           |                        |
| HPLC vial insert                 | 1 x      | Use support                                                                                | insert – HPLC vials.stl|
| *optional                        |          | Pause print at 45.4 mm and insert 4 magnets                                                 |                        |
|                                  |          | (d = 6 mm)                                                                                 |                        |
| HPLC vial insert cap             | 8 x      | Best printed in semiflex TPU                                                               | cap – HPLC vial.stl    |
| *optional                        |          |                                                                                           |                        |
| Flow unit insert                 | 1 x      | Pause print at 4.6 mm and insert 4 magnets                                                 | insert – flow unit.stl |
| *optional                        |          | (d = 6 mm)                                                                                 |                        |
| Flask holder – main part         | 1 x      | Pause print at 4.4 mm and insert 4 magnets                                                 | flask holder – main part.stl|
| *optional                        |          | (d = 6 mm)                                                                                 |                        |
| Flask holder – slider left       | 1 x      | Pause print at 5.6 mm and insert 4 magnets                                                 | flask holder – slider left.stl|
| *optional                        |          | (d = 4 mm)                                                                                 |                        |
| Flask holder – slider right      | 1 x      | Pause print at 5.6 mm and insert 4 magnets                                                 | flask holder – slider right.stl|
| *optional                        |          | (d = 4 mm)                                                                                 |                        |
| Flask holder – stopper           | 2 x      |                                                                                           | flask holder – stopper.stl|
| *optional                        |          |                                                                                           |                        |
| Flask holder – cover             | 2 x      | Use support                                                                                | flask holder – cover.stl|
| *optional                        |          |                                                                                           |                        |
| Ika- GoGo module lid             | 1 x      | Use support                                                                                | lid – GoGo module.stl   |
| *optional                        |          |                                                                                           |                        |

**Construction manual for the flask holder:** Insert the right and left slider into the main part and stick both stoppers with super glue behind the sliders.

**General note:**
- The use of magnets is optional but the nuts in the reactor are essential.
- Fix the magnets with super glue to the filament, otherwise it may stick to the 3D printer.
1.2 Equipment
- Screwdrivers
- Soldering-iron
- Tin solder (best with a flux)
- Wire stripper
- Hot gun
- Multimeter
- Cutter

1.3 Purchase List – Reactor

| Part name                          | Quantity | Specification                                                                 | Link                                                                 |
|-----------------------------------|----------|-------------------------------------------------------------------------------|----------------------------------------------------------------------|
| Fan                               | 2x       | High speed fan¹, 40 x 40 x 28 mm                                              | http://www.mercateo.at/Fan Sunon                                      |
|                                   |          | Sunon PF40281B1-000U-A99 used at 7 V                                           | https://www.amazon.de/Fan Sunon                                       |
|                                   |          | or Delta TFB0412EHN used at 5 V                                                | https://www.amazon.de/Fan Delta                                        |
| Thermoelectric cooler             | 2x       | 15.5 V, 8.5 A, 72 W, 40 x 40 x 3.4 mm                                          | http://www.mercateo.at/8.5 A TEC                                      |
|                                   |          | Quick-Cool High-Tech                                                            | https://www.amazon.de/8.5 A TEC                                       |
|                                   |          | *amazon: search for DIY thermoelectric cooler                                  | https://www.quick-cool-shop.de/8.5 A TEC                              |
| Heatsink, air & water cooling     | 2x       | since the air heatsink is not available as a single product use a kit like this | https://www.amazon.de/Heat sink                                        |
|                                   |          | Note: TECs & fans of this set are too weak                                     |                                                                       |
| Thermal conductive paste          | 4g       | 5 W/(m*K) or better                                                            | http://www.mercateo.at/Paste                                          |
| PA screws (nylon)                 | 4        | M3, 30 mm                                                                      | http://www.mercateo.at/Nylon screw                                    |
|                                   |          | could be longer                                                                | https://www.amazon.de/Nylon screw                                      |
| PA nuts (nylon)                   | 4        | M3                                                                             | http://www.mercateo.at/Nylon nuts                                     |
|                                   |          | **Note:**                                                                        | https://www.amazon.de/Nylon nuts                                      |
| Reflecting foil                   | 1 roll   | shiny finish                                                                     | http://www.mercateo.at/Foil                                          |
| Screws                            | 4        | M3, 10 mm                                                                      | http://www.mercateo.at/M3x10 screw                                    |
|                                   |          | for fan mount                                                                   | https://www.amazon.de/M3x10 screw                                     |
| Screws                            | 12       | M3, 20 mm                                                                      | http://www.mercateo.at/M3x20 screw                                    |
|                                   |          | cylinder head                                                                   | https://www.amazon.de/M3x20 screw                                     |
|                                   |          | for lid and lamp holder                                                         |                                                                       |
| Nuts                              | 12       | M3                                                                             | http://www.mercateo.at/M3 nuts                                       |
|                                   |          | for lid and lamp holder                                                         | https://www.amazon.de/M3 nuts                                         |
| Sheet of glass                    | 2        | min. 70 x 70 mm                                                                 |                                                                       |
| Double-sided tape                 |          |                                                                                |                                                                       |
| Neodymium magnets                 | 2 + 4 for every insert                                                         | d = 6 mm                                                           | http://www.mercateo.at/Magnet                                       |
|                                   |          |                                                                                   | h = 3 mm                                                           | https://www.amazon.de/Magnet                                       |
| Neodymium magnets                 | 8        |                                                                                   | d = 4 mm                                                           | http://www.mercateo.at/Magnet                                       |
|                                   |          |                                                                                   | h = 4 mm                                                           | https://www.amazon.de/Magnet                                       |
| Super glue                        |          | If the reflecting foil doesn’t stick on PETG                                    | https://www.amazon.de/Glue                                             |
| PFA tube for flow insert          | >5m      | outer d = 3 mm; inner d = 1.5 mm                                                 | https://www.bola.de/PFA tube                                          |
| Luer adapter for flow tube        | 1        | 1/16, female luer                                                                | https://www.coleparmer.com/Luer adapter                               |
|                                   |          |                                                                                   | https://www.amazon.com/Luer adapter                                   |

¹ Other high speed fans can be use as well but the optimal voltage has to be determined.

All links were accessed on 27.11.2020.
### 1.4 Purchase List – Electronic Components

| Part name                                | Quantity | Specification                                                                 | Link                                                                 |
|------------------------------------------|----------|-------------------------------------------------------------------------------|----------------------------------------------------------------------|
| Arduino nano                             | 1x       | V3 Atmega 328P                                                                | [http://www.mercateo.at/Arduino](http://www.mercateo.at/Arduino)    |
| Motor driver (full bridge)²              | 1x       | BTS7960B 42 A High Power min. 25 A constant output current                    | [https://www.amazon.de/Motordriver](https://www.amazon.de/Motordriver) |
| Step-Down converter                      | 1x       | adjustable DC-DC Buck Converter LM2596S 12 V to 5 V                           | [https://www.amazon.de/Converter](https://www.amazon.de/Converter)    |
| OLED display                             | 1x       | 128 x 64 px with I2C interface                                                | [https://www.amazon.de/Display](https://www.amazon.de/Display)        |
| Temperature sensor                       | 1x       | DS18b20 with 1-wire interface                                                 | [http://www.mercateo.at/Sensor](http://www.mercateo.at/Sensor)       |
| Power supply                             | 1x       | 12 V DC output 264 W min. 22 A output current IP67 e.g. HLG-320H-12A         | [http://www.mercateo.at/Power supply](http://www.mercateo.at/Power supply) |
| XT60 connector                           | 1x       | for soldered                                                                  | [http://www.mercateo.at/Connector](http://www.mercateo.at/Connector) |
| On/Off switch                            | 1x       | min. 25 A                                                                    | [http://www.mercateo.at/On/Off switch](http://www.mercateo.at/On/Off switch) |
| Pushbutton                               | 2x       | 6 x 6 x 5 mm micro pushbutton                                                | [https://www.amazon.de//Button](https://www.amazon.de//Button)       |
| Resistor, 10 k                           | 2x       | ¼ W                                                                          | [https://www.amazon.de/Resistor](https://www.amazon.de/Resistor)      |
| Resistor, 4.7 k                          | 1x       | ¼ W                                                                          | [https://www.amazon.de/Resistor](https://www.amazon.de/Resistor)      |
| Wire                                     | ~1m      | rated for min. 20 A ~2 mm diameter (14 AWG) multiple colors preferable       | [http://www.mercateo.at/Wire black](http://www.mercateo.at/Wire black) and [http://www.amazon.de/Wire black](http://www.amazon.de/Wire black) |
| Wire *optional                           | ~0.75 mm diameter, working on the breadboard is easier with smaller wires   | [http://www.mercateo.at/Wire red](http://www.mercateo.at/Wire red)     |
| Connector clamps                         | 2        |                                                                              | [http://www.mercateo.at/Clamps](http://www.mercateo.at/Clamps)        |
| Vero board                               | 1        | ~ 80 x 50 mm                                                                 | [http://www.mercateo.at/Veroboard](http://www.mercateo.at/Veroboard) |
| Power plug                               | 1        | IP44                                                                         | [https://www.mercateo.at/Power plug](https://www.mercateo.at/Power plug) |
| Heat shrink tubing for XT60 Connector    | 1        | ~12 mm                                                                       | [http://www.mercateo.at/Heat shrink tubing](http://www.mercateo.at/Heat shrink tubing) |
| Heat shrink tubing for 2 mm wire (TECs)  | ~10      |                                                                              | [http://www.mercateo.at/Heat shrink tubing](http://www.mercateo.at/Heat shrink tubing) |
| Heat shrink tubing *optional              |          |                                                                              | [http://www.mercateo.at/Heat shrink tubing](http://www.mercateo.at/Heat shrink tubing) |
| Screws                                   | 4        | M2, 10 mm for Display mount                                                  | [https://www.amazon.de/M2x10 screw](https://www.amazon.de/M2x10 screw) |
| Screws                                   | 2        | M3, 10 or 20 mm for motor driver mount                                       | [https://www.amazon.de/M3x20 screw](https://www.amazon.de/M3x20 screw) |
| Nuts                                      | 2        | M3 for motor driver mount                                                    | [https://www.amazon.de/M3 nuts](https://www.amazon.de/M3 nuts)        |

All links were accessed on 27.11.2020.

² The motor driver may be defect due to manufacturing errors. If the electronics don’t work, then replace the motor driver with a new one (use connector clamps to connect the new motor driver with the veroboard, to avoid additional soldering on the veroboard).
2. Construction Manual
2.1 Reactor

1) Remove all supporting materials from the 3D prints.
2) Expand the cables of one TEC (the cables from the other should be long enough) and insert the TECs into the reactor wall (the labelling on the TEC is inside). If the hole for the TEC is too tight (depends on the filament), then scratch the filament a little bit away.

![TEC Insertion](image1.png)

3) Prepare two aluminum foil pieces (10 x 19 cm and 10 x 20 cm) for the reactor wall, stick them onto the wall (use super glue if they don’t stick well) and cut out the lamp holes.
4) Expand the cable of the fans if needed and mount them on the heat sink (2 screws for each fan are enough).

![Fan Mounting](image2.png)

5) Put the thermal conductive paste on both sides of each TEC and mount the heat sinks with the nylon screws & nuts. The water-cooling heat sink is fixed with the 3D printed clamp (both water cooling heat sinks should point to the right).

![TEC Cooling](image3.png)

6) Place all cables in the cable channel (may use a glue or a doubled sided tape to fix them).
7) Stick the aluminum foil on the reactor floor (use super glue if it doesn’t stick well).

![Foil on Floor](image4.png)
8) Remove the protecting foil on the aluminum foil and stick the glass plates with double sided tape onto the reactor wall (the top should be free of tape – it prevents water condensation on the outside of the glass).

9) Mount the electronic case and connect the TECs with the motor driver and the fans with the clamps of the step-down converter (construction manual is found in the next section).

10) Fix the motor driver with screws, mount the display onto the cover of the case (do not screw it tightly to the cover, due to the resistors on the back of the display), put the temperature sensor through the hole, place the pushbuttons onto their positions and glue them to the cover.

11) Push the cover and lid onto the case (once it sticks to the case it is hard to remove again!).

12) Stick the aluminum foil onto the reactor cover and mount it with 4 screws.

13) Mount the lamp holder with 4 screws each.

14) Mount the magnetic stirrer holder.
2.2 Electronics

Figure 1: Required components for the photoreactor.

Figure 2: Circuit diagramm of the electronic components.
1. Connect the input of the power supply unit with the power plug and close the power plug.

2. Solder the output of the power supply unit with the XT60 (male), the cables are isolated with heat shrink tubing. If necessary the cable can be expanded but only on the output side – do not expand the 240 V cable (input)! Note: The metal of the XT60 has to be hot enough to get a proper soldering result, therefore the plastic cover will also be very hot.

3. The XT60 (female) is soldered with two cables (14 AWG; ~15 cm) and isolated with heat shrink tubing.

4. The display and motor driver are soldered with four (~15 cm) and six cables (~15 cm) (see circuit diagram) and the pins are isolated with heat shrink tubing. Two cables (~25 cm) from the On/Off switch are fixed in the green clamps.

5. The pushbuttons are soldered with two cables (be careful to pick the right pins, ~12 cm), the pins are isolated with heat shrink tubing and the remaining pins are cut off.
6. The Arduino chip is soldered onto the veroboard, a cable (~5 cm) connects the 5 V pin with the two 10 k and the 4.7 k resistor. The overlapping wire of the resistors is cut off (keep the wire, it is needed later).

7. The display and the motor driver are connected with the Arduino chip (see circuit diagramm).

8. Approximately 2 cm of the heat shrink tubing of the temperature sensor is removed (makes it easier to work) and it is connected with the Arduino chip. The yellow cable is also connected with the 4.7 k resistor (see circuit diagramm).

9. The pushbuttons are connected with the Arduino chip and the red cables are connected with the 10 k resistors (they can be connected with tin solder or with the wire which was cut off from the resistors).
10. The motor driver is connected with the 5 V pin and the GND pin on the Arduino.

11. All 12 V cables are connected with each other (1 from the Arduino chip (~2-3 cm), 1 from the step-down converter (~10 cm) and 1 from the On/Off switch (~20 cm). The same is done with the mass from all three components.

12. The step-down converter is soldered at the “In” holes with the red and black cable from the veroboard and at the “Out” holes with cables connected to the clamps.

13. The female XT60 is placed into the 3D-printed case and the ends of the cables are placed outside of the On/Off switch hole. The motor driver is also placed into the case (do not mount it with the screws yet) and the four cables (2 from the motor driver and 2 from the veroboard) are placed outside of the On/Off switch hole.

14. The 2 red and black cables are soldered together (don’t forget do place the heat shrink tubing onto the cables before starting to solder the cable onto the On/Off switch). Then the red cable from the XT60 is connected with the power. The red one from the motor driver and veroboard are connected with the ACC and all black one are connected with the ground. Isolate all cables with the heat shrink tubing.

15. Place the On/Off switch into the case.
16. Adjust the step-down converter to 7 V (for the Sunon fans) or 5 V (for the Delta fans) output with the multimeter.

Note: If a component is defect, cut the cable and connect them with connector clamps with the new unit to avoid extra soldering work.

2.3 Program

1) Download Arduino IDE
2) Open Sketch → Include library → Library Manager
3) Install Library: (Note: location of libraries should be /User/<username>/Documents/Arduino/libraries/)
   - Adafruit BusIO
   - Adafruit GFX Library
   - Adafruit SSD1306
   - OneWire
4) Settings:
   - Board: Arduino Nano
   - Processor ATmega328P (for Joy-It Arduino: Processor ATmega328P (Old Bootloader))
   - Programmer: AVRISP mkll
5) Connect the Arduino Nano with a mini USB cable with the computer.
6) Upload the program “Photoreactor_Arduino program.ino”.

3. Safety Features

- There are two main safety features:
  1) The controller checks if the temperature is within the limits. If not, it will turn off the TECs and enter error mode (e.g. overheating of the TECs if not cooled by water).
  2) The controller measures the heating and cooling time. If the set temperature is not reached within a certain time (max. cooling time = 1 h; max heating time = 3 min) it will turn off the TECs and enter the error mode (e.g. if the temperature sensor is not in the reactor).
- Once in error mode the photoreactor will stay in error mode until a button is pressed. The display will show error.
- After powering the photoreactor, it will be in a safe condition. Only after pressing a button, the reactor will start heating/cooling.
- Temperature limits, cooling and heating time can be set in the script.
  - Default values:
    - max. temperature: 60 °C
    - min. temperature: -10 °C
    - max. heating time: 3 min (only above 25 °C the TECs starts heating)
    - max. cooling time: 60 min
- Unfortunately, the photoreactor is not able to detect if the water cooling is running. Please make sure to turn it on before using the reactor - otherwise the TECs will overheat.
4. **User’s Guide**

a) **General** - make sure that:
   - The water cooling is running (otherwise TECs will overheat).
   - The temperature sensor is in the reactor.
   - The temperature sensor is in the lamp beam (important only with the flask holder, flow unit and Ika GoGo module lid; fix the sensor with parafilm).
   - The reactor is sealed nearly airtight (otherwise too much water will condensate on the heat sinks):
     ➔ Vial holder: All positions must be closed with a vial or a lid.
     ➔ Flask holder: Temperature hole and the empty space around the flask is sealed with the 3D-printed cover lid or parafilm.
     ➔ Flow unit: Temperature hole is sealed with parafilm.
     ➔ Ika GoGo module lid: Temperature hole is sealed with parafilm.

b) **Below 0 °C**:
   - The reactor has to be sealed nearly airtight (if too much water freezes on the heat sinks the fans will stop working).
   - Adjust to a temperature the reactor is able to reach (see Table 2Table 3 - the motor driver produces a lot of heat if it is continuously running. After 60 min the reactor will enter the error mode if the desired temperature is not reached (max. cooling time).
   - Water may condensate outside of the glass plate due to the small area of air between the glass and the lamp – this is prevented by a gap of the tape at the top of the glass plate.

c) **With UV light**:
   - Use UV stable glue or tape for fixing the glass plate, make sure that the glass plate is not sealed airtight at the top (to prevent water condensation on the outside).
   - Use a tube for the flow unit that is UV stable.

| Table 1: Temperature dependence on the power of the Sunon fan (with two Kessil PR160L lamps at 100% light intensity). |
|-------------------------------------------------------------|
| 5 V | 7 V | 8 V | 9 V | 12 V |
|-----|-----|-----|-----|-----|
| 10 °C | -2 °C | -1.9 °C | -1.7 °C | +1 °C |

| Table 2: Temperature dependence on the light intensity (with two Kessil PR160L lamps; Sunon fans used at 7 V). |
|-------------------------------------------------------------|
| 100% | 75% | 50% | 25% | 25% (only 1 lamp) | 0% |
|-----|-----|-----|-----|-----------------|-----|
| -2 °C | -5 °C | -9 °C | -15 °C | -17 °C | -20 °C |

| Table 3: Temperature dependence on the lamp. |
|---------------------------------------------|
| Kessil PR160L (100%) | HepatoChem 30 W | HepatoChem 18 W |
|------------------------|-----------------|-----------------|
| -2 °C | -3 °C | -6 °C |

**Is further cooling possible?** Yes, but it requires:
1) A stronger power supply unit → The TECs are designed for 14.5 V but are only operated at 12 V.
2) An external cooling device → with a 0 °C cold water cooling a temperature of -26 °C (without light) was obtained.
3) A better thermal insulation.
5. **Trouble Shooting**

| Problem | Reason | Solution |
|---------|--------|----------|
| Display enters continuously the error mode | • Loose connection of the temperature sensor.  
• Power supply unit is of poor quality and has a voltage fluctuation. Temperature sensor receives not enough voltage and stops working for a moment. | • Check connection of the sensor with the Arduino.  
• Replace the power supply unit with one from a trusted supplier. |
| TECs don't cool or don't stop cooling | • Arduino chip may be defect.  
• Motor driver may be defect: TECs receives no current or the motor driver is not able to stop the current flow. | • Check if the Arduino chip can be connected to the computer. If not, replace it.  
• Replace the motor driver. |
| Displays enters error mode after 1 h | • Temperature sensor is not in the reactor.  
• The set temperature is not reached and the TECs are switched off due to the safety features (e.g. set temperature is 10 °C but the actual temperature cannot be lower than -2 °C at 100% light intensity). | • Place the sensor in the reactor.  
• Use a set temperature that can be reached at the certain light intensity. |
| Displays enters error mode after 3 min or faster | • Temperature sensor is not in the reactor.  
• Overheating of the TECs, as there is no water-cooling. | • Place the sensor in the reactor.  
• Switch on the water-cooling. |
| After a time period the reactor heats up although a low set temperature is used | • Reactor is not well sealed - fans don’t work anymore due to ice frozen on the heat sinks. | • Make sure the reactor is sealed almost airtight. |

6. **Tips and Tricks**

- High quality TECs are more effective compared to cheap TECs.
- Variation of the lowest possible temperature is possible, since its value is also determined by the temperature of the cooling water.
- Rapid defrost of the heat sinks is managed by setting higher temperatures (the vial holder should be open).
- Vials can be taken out of the reactor while it is running.
- Due to the height of the reactor, stirring problems in the ElectraSyn 2.0 vial may occur at higher rpm. It is avoided by using cross stir bars.
- Tips for TEC: [https://www.heat-management.info/know-how.html](https://www.heat-management.info/know-how.html).
7. General Information - Chemistry
All reagents and solvents were purchased from a commercial supplier and were used without further purification, except benzyl-4-bromopiperidine-1-carboxylate was purified by normal phase column chromatography if stabilizers were added. For all reactions dry solvents were used. All photochemical reactions were performed in the 3DP photoreactor and the photoelectrochemistry was carried out using the ElectraSyn 2.0 from Ika with the GoGo module adapter. The calibration curves and all reaction controls were performed using an Agilent Technologies Series 1200; Agilent 6130 Quadrupole LC/MS with a Waters X-Bridge C18 X (30 x 2.1 mm, 2 μm particle size). The HPLC/MS method was basic H2O (0.1% NH4HCO3/NH3, pH = 9)/ACN with a gradient 15% – 95% ACN (1.4 ml/min). Flash column chromatography was performed using a Combi Flash Companion Rf provided by Teledyne Isco with Chromabond Flash columns (40 – 63 μm particle size). NMR spectra were recorded on Bruker Advance 400 and 500 FT – NMR instruments and were calibrated using residual undeuterated solvent as an internal reference (CDCl3: 7.26 ppm 1H – NMR, 77.16 ppm 13C – NMR). The following abbreviations were used to explain NMR peak multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad). High-resolution mass spectra (HRMS) were recorded on an Agilent LCMS TOF mass spectrometer using electrospray ionization time of flight (ESI – TOF) reflectron experiments.

8. Experimental Part

Cross electrophile sp2 – sp3 cross coupling

In a separate vial NiCl2·glyme (0.02 eq.) and dtbbpy (0.02 eq.) were dissolved in DMA (7.2 eq.). The reaction vial/flask equipped with a stir bar was charged with Na2CO3 (2.0 eq.), Ir[dF(CF3)ppy]2(dtbbpy)PF6 (0.02 eq.), the pre-catalyst solution, methyl-4-bromobenzoate (1.0 eq.), benzyl-4-bromopiperidine-1-carboxylate (2.0 eq.) and TTMSS (1.0 eq.). The compounds were dissolved in ACN (114 eq.), the reaction was purged with argon for 2 min via an inlet needle (5 min for the 5.0 mmol scale) and irradiated with two Kessil PR160L 440 nm lamps (100% light intensity) at 20 °C in the photoreactor for 2 h (3 h for the 5.0 mmol scale). The yields of the small scale reactions were calculated using the calibration curve.

Work up for the 5.0 mmol batch: The solvent was removed under reduced pressure, the mixture was diluted with water and extracted with DCM three times. The org. layer was dried with MgSO4, filtered and the solvent was removed. After purification by normal phase column chromatography (cyclohexane/EtOAc, 0-30% EtOAc in 30 min, 120 g column) the product (1.43 g, 4.1 mmol, 81% yield) was obtained as a colourless oil (which crystalized over time).

Scale:
1 ml vial: 0.08 mmol of methyl-4-bromobenzoate
4 ml vial: 0.30 mmol of methyl-4-bromobenzoate
8 ml vial: 0.60 mmol of methyl-4-bromobenzoate
100 ml flask: 5.00 mmol of methyl-4-bromobenzoate

Upscaling with 0.1 mol% Ir cat
In a separate vial NiCl2·glyme (11 mg, 50 μmol, 0.01 eq.) and dtbbpy (13 mg, 50 μmol, 0.01 eq.) were dissolved in DMA (1.7 ml). A 50 ml flask equipped with a stir bar was charged with Na2CO3 (1.1 g, 10 mmol, 2.0 eq.), Ir[dF(CF3)ppy]2(dtbbpy)PF6 (5.6 mg, 5 μmol, 0.001 eq.), the pre-catalyst solution, methyl-4-bromobenzoate (1.1 g, 5.0 mmol, 1.0 eq.), benzyl-4-bromopiperidine-1-carboxylate (3 g, 10 mmol, 2.0 eq.) and TTMSS (1.2 g, 1.5 ml, 5 mmol, 1.0 eq.). The compounds were dissolved in ACN (15 ml), the reaction was purged with argon for 5 min via an inlet needle and irradiated with two Kessil PR160L 440 nm lamps (100% light intensity) at 40 °C in the photoreactor for 16 h. The solvent was removed under reduced pressure, the mixture was diluted with water and extracted with DCM three times. The org. layer was dried with MgSO4, filtered and the solvent was removed. After purification by normal phase column chromatography (cyclohexane/EtOAc, 0-30% EtOAc in 30 min, 120 g column) the product (1.27 g, 3.6 mmol, 72% yield) was obtained as a colourless oil (which crystalized over time).
1H NMR (400 MHz, CDCl₃): δ = 7.99 (d, J = 8.4 Hz, 2H), 7.41 – 7.30 (m, 5H), 7.29 – 7.25 (m, 2H), 5.17 (s, 2H), 4.36 (br d, J = 11.7 Hz, 2H), 3.91 (s, 3H), 2.90 (br t, J = 12.4 Hz, 2H), 2.75 (tt, J = 3.5, 12.1 Hz, 1H), 1.86 (br d, J = 12.9 Hz, 2H), 1.67 (dq, J = 3.9, 12.6 Hz, 2H).

13C NMR (126 MHz, CDCl₃): δ = 166.96, 155.25, 150.74, 136.80, 129.91, 128.50, 128.40, 128.00, 127.92, 126.81, 67.14, 52.04, 44.46, 42.68, 32.80.

HRMS m/z (ESI): [C₈₂H₆₂NO₄ + H⁺]: calcd. for 354.1700; found 354.1700.

**Aryl-Aryl cross coupling via a C-H activation**

![Aryl-Aryl cross coupling](image)

A 4 ml vial equipped with a stir bar was charged with 2-chlorobenzonitrile (28 mg, 0.2 mmol, 1 eq.), pyrene (2.0 mg, 0.01 mmol, 0.05 eq.), Ru(bpy)₂Cl₂·6 H₂O (1.5 mg, 0.002 mmol, 0.01 eq.) and DMSO (1.0 ml). N-methylpyrrole (180 µl, 2.0 mmol, 10 eq.) and DIPEA (53 µl, 0.28 mmol, 1.4 eq.) were added and the mixture was purged with argon via an argon balloon for 1 min. The reaction was irradiated with two Kessil PR160L 440 nm lamps (100% light intensity) at 25 °C for 15 min. The mixture was diluted with water and extracted with DCM three times. The org. layer was dried with MgSO₄, filtered and the solvent was removed. After purification by normal phase column chromatography (cyclohexane/EtOAc, 0-30% EtOAc in 10 min, 4 g column) the product (28 mg, 0.15 mmol, 78% yield) was obtained as a white solid.

1H NMR (400 MHz, CDCl₃): δ = 7.75 (dd, J = 7.7, 0.9 Hz, 1H), 7.62 (td, J = 7.7, 1.3 Hz, 1H), 7.46 – 7.39 (m, 2H), 6.82 – 6.79 (m, 1H), 6.42 (dd, J = 3.5, 1.8 Hz, 1H), 6.26 (dd, J = 3.5, 2.8 Hz, 1H), 3.63 (s, 3H).

**Deaminative sp²-sp³ cross coupling reaction**

![Deaminative sp²-sp³ cross coupling](image)

In a separate vial NiBr₂glyme (8 mg, 0.025 mmol, 0.1 eq.) and dtbbpy (7 mg, 0.025 mmol, 0.1 eq.) were dissolved in THF (1 ml). A 8 ml vial equipped with a stir bar was charged with 4CzIPN (12 mg, 0.015 mmol, 0.03 eq.), the pre-catalyst solution, the alkylpyridinium salt (378 mg, 0.75 mmol, 1.5 eq.), methyl 4-bromobenzoate (108 mg, 0.5 mmol, 1 eq.) and THF (4 ml). The vial was sealed and purged with argon for 10 minutes via an inlet needle and Et₃N (0.2 ml, 1.5 mmol, 3 eq.) was added via a syringe. The reaction was irradiated with two Kessil PR160L 440 nm lamps (100% light intensity) at 25 °C for 6 h. The solvent was removed under reduced pressure and the crude product was purified by normal phase column chromatography (cyclohexane/EtOAc, 0-5% EtOAc in 15 min, 24 g column). The product (97 mg, 0.44 mmol, 88% yield) was obtained as a white solid.

1H NMR (400 MHz, CDCl₃): δ = 7.98 (d, J = 8.4 Hz, 1H), 7.28 (d, J = 8.4 Hz, 2H), 4.12 – 4.05 (m, 2H), 3.89 (s, 3H), 3.52 (td, J = 11.6, 2.7 Hz, 2H), 2.80 (tt, J = 11.4, 4.3 Hz, 1H), 1.92 – 1.71 (m, 4H).

**Decarboxylative sp²-sp³ alkylation**

![Decarboxylative sp²-sp³ alkylation](image)

A 8 mL vial equipped with a stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (11 mg, 0.01 mmol, 0.02 eq.), NiCl₂glyme (11 mg, 0.05 mmol, 0.1 eq.), 4,4’-dimethoxy-2,2’-bipyridine (11 mg, 0.05 mmol, 0.1 eq.), 1-[(tert-butoxy)carbonyl]pyrrolidine-2-carboxylic acid (161 mg, 0.75 mmol, 1.5 eq.), K₂CO₃ (138 mg, 1 mmol, 2 eq.) and ACN (5 ml). The vial was sealed and purged with nitrogen for 15 minutes via an inlet needle. Afterwards water (180 µl, 10
mmol, 20 eq.) and benzy1 chloride (58 µl, 0.5 mmol, 1 eq.) were added via a syringe and the reaction was irradiated with two Kessil PR160L 440 nm lamps (100% light intensity) at 25 °C for 8.5 h. The solvent was removed under reduced pressure and the crude product was purified by normal phase column chromatography (cyclohexane/acetone, 0-20% acetone in 15 min, 15 g column). The product (116 mg, 0.44 mmol, 86% yield) was obtained as a colorless oil.

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.26 - 7.17\) (m, 1H), 7.17 – 7.05 (m, 1H), 4.05 – 3.81 (m, 1H), 3.38 – 3.15 (m, 2H), 3.14 – 2.92 (m, 1H), 2.54 – 2.39 (m, 1H), 1.67 (br s, 4H), 1.44 (s, 9H).

**Decarboxylative C-H functionalization reaction**

![Decarboxylative C-H functionalization reaction](image)

A 10 ml ElectraSyn vial equipped with a cross-stir bar was charged with lepidine (26 µl, 0.2 mmol, 1 eq.), (isopropylamino)(oxo)acetic acid (105 mg, 0.8 mmol, 4 eq.), 4CzIPN (2 mg, 0.002 mmol, 0.01 eq.) and tetraethylammonium p-toluenesulfonate (18 mg, 0.06 mmol, 0.3 eq.). The vial was sealed with the ElectraSyn cap, equipped with RCV (Anode) and Pt (Cathode) and the vial was evacuated and back-filled with argon for three times. ACN (6.0 ml) was added via syringe and the solution was purged with argon for 15 min via an inlet needle. The reaction was irradiated with two Kessil PR160L 440 nm lamps (100% light intensity) under constant current of 2 mA at 55 °C until 3 F/mol (~ 8 h) was reached (with the Ika ElectraSyn GoGo module). The electrodes were washed with ACN, the solvent was removed under reduced pressure and the crude product was purified by normal phase column chromatography (cyclohexane/acetone, 0-30% acetone in 10 min, 15 g column). The product (38 mg, 0.17 mmol, 83% yield) was obtained as a colorless oil.

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 8.16\) (s, 1H), 8.14 – 8.07 (m, 2H), 8.03 (d, \(J = 8.4\) Hz, 1H), 7.74 (ddd, \(J = 8.3, 6.9, 1.3\) Hz, 1H), 7.62 (ddd, \(J = 8.2, 7.0, 1.0\) Hz, 1H), 4.40 – 4.27 (m, 1H), 2.77 (s, 3H), 1.34 (d, \(J = 6.6\) Hz, 6H).

**sp\(^2\) – sp\(^3\) cross coupling in flow**

![sp\(^2\) – sp\(^3\) cross coupling in flow](image)

A 50 ml flask equipped with a stir bar was charged with NiCl\(_2\)-glyme (27 mg, 0.12 mmol, 0.12 eq.), dbbpy (32 mg, 0.12 mmol, 0.12 eq.) and DMA (4.0 ml). It was sealed with a septum and the solution was stirred for 5 min while purging it with nitrogen via an inlet needle. 5-bromo-2-methylpyrimidine (173 mg, 1 mmol, 1 eq.), potassium trifluoro(oxan-4-yl)boranuide (288 mg, 1.5 mmol, 1.5 eq.), 2,6-lutidine (190 µl, 1.6 mmol, 1.6 eq.) and [Ir(dFCDppy)\(_2\)(bppy)]PF\(_6\) (30 mg, 0.03 mmol, 0.03 eq.) were added. Then the solution was diluted with 1,4-dioxane (16 ml) and the mixture was purged again with nitrogen via an inlet needle for 10 min. Afterwards it was transferred into a 24 ml syringe which was fixed on the syringe pump. The flow unit was pre-equilibrated with 1,4-dioxane at 30 °C. The reaction was irradiated with two Kessil PR160L 440 nm lamps (100% light intensity) in the photoreactor at a flow rate of 0.35 ml/min. After everything was injected into the flow unit, the syringe was exchanged with one containing a 1,4-dioxane and the reaction was continued at a flow rate of 0.35 ml/min. The solvent was removed under reduced pressure, the crude product was dissolved in water and extracted with DCM three times. The org. layer was dried with MgSO\(_4\) filtered and the solvent was removed. After purification by normal phase column chromatography (cyclohexane/EtOAc, 0-80% EtOAc in 15 min, 15 g column) the product (118 mg, 0.66 mmol, 66% yield) was obtained as a yellow solid.

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 8.52\) (s, 1H), 4.16 – 4.06 (m, 2H), 3.54 (td, \(J = 11.5, 2.9\) Hz, 2H), 2.83 – 2.75 (m, 1H), 2.73 (s, 3H), 1.91 – 1.74 (m, 4H).
**Optimization Upscaling:**

![Chemical Reaction](image)

| Entry | Ir cat [mol%] | Ni cat [mol%] | ACN/DMA [ml] | Temp [°C] | Yield [%] |
|-------|---------------|---------------|---------------|-----------|-----------|
| 1     | 0.1           | 0.1           | 30 / 3.3      | 20        | 19        |
| 2     | 0.1           | 0.1           | 15 / 1.7      | 20        | 26        |
| 3     | 0.1           | 1             | 15 / 1.7      | 20        | 52        |
| 4     | 0.1           | 1             | 5 / 0.55      | 20        | 28        |
| 5     | 0.1           | 2             | 15 / 1.7      | 20        | 45        |
| 6     | 0.1           | 1             | 15 / 1.7      | 40        | 72        |

**Entry 1:**

![HPLC Chromatogram](image)

- Dehal. Aryl-Br
- Aryl-Br
- Product

**Entry 2:**

![HPLC Chromatogram](image)

**Entry 3:**

![HPLC Chromatogram](image)

**Entry 4:**

![HPLC Chromatogram](image)

**Entry 5:**

![HPLC Chromatogram](image)

**Entry 6:**

![HPLC Chromatogram](image)
9. HPLC Calibration Curves

The calibration curve was measured at three wavelengths and the yield of the cross-electrophile sp\(^2\)-sp\(^3\) coupling reaction was calculated by using the mean value of all three wavelengths with o-terphenyl as internal standard.

**214 nm**

\[ y = 0.0084x + 0.0361 \]
\[ R^2 = 0.9989 \]

**230 nm**

\[ y = 0.0144x + 0.0353 \]
\[ R^2 = 0.9973 \]

**254 nm**

\[ y = 0.0175x + 0.0428 \]
\[ R^2 = 0.9979 \]
10. NMR spectra
| Other files                              |                          |
|-----------------------------------------|--------------------------|
| photoreactor printing files.zip (3.40 MiB) | [view on ChemRxiv](#) » [download file](#) |
| Photoreactor_Arduino program.ino (7.31 KiB) | [view on ChemRxiv](#) » [download file](#) |