A Visible-Light-Powered Polymerization Method for the Immobilization of Enantioselective Organocatalysts into Microreactors

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## Chemicals

### Chemicals for the synthesis of Monomer-HJ

| Chemical                      | Purity   | Supplier                                      |
|-------------------------------|----------|-----------------------------------------------|
| Propargyl-HJ                  | Pure     | Synthesized (see General experimental procedure) |
| 1-(azidomethyl)-4-vinylbenzene| Pure     | Synthesized (see General experimental procedure) |
| Cu                            | >99%     | Sigma Aldrich, Steinheim, Germany              |
| N,N-Diisopropylethylamine (DIPEA)| >99%  | Sigma Aldrich, Steinheim, Germany              |
| Toluene                       | >99%     | Sigma Aldrich, Steinheim, Germany              |
| N,N-Dimethylformamide (DMF)   | 99%      | Sigma Aldrich, Steinheim, Germany              |

### Chemicals for the synthesis of Monolith-HJ

| Chemical                              | Purity  | Supplier                                      |
|---------------------------------------|---------|-----------------------------------------------|
| 1-decanol                             | 99%     | Sigma Aldrich, Steinheim, Germany              |
| 2-propanol                            | HPLC grade | VWR International, Dresden, Germany             |
| ACN                                   | >99%    | Carl Roth GmbH + Co. KG, Karlsruhe, Germany    |
| Divinylbenzene                        | techn. grade 80% | Sigma Aldrich, Steinheim, Germany              |
| Ethyl-N-dimethylbenzoate (EDAB)       | >99%    | Sigma Aldrich, Steinheim, Germany              |
| (1S)-(+-)-Camphorquinone              | 99%     | Sigma Aldrich, Steinheim, Germany              |
| Monomer-HJ                            | pure    | Synthesized (see Photopolymerization procedure and polymer characterization) |
| N-methoxy-phenyl-pyridinium tetrafluoroborate, NMPPT | pure | Synthesized (see General experimental procedure) |
| Styrene                               | >99%    | Sigma Aldrich, Steinheim, Germany              |
| THF                                   | HPLC grade | Carl Roth GmbH + Co. KG, Karlsruhe, Germany    |

### Chemicals for on-chip flow-experiments

| Chemical                              | Purity  | Supplier                                      |
|---------------------------------------|---------|-----------------------------------------------|
| Acetic acid                           | 100%    | Merck KGaA, Darmstadt, Germany                 |
| ACN                                   | >99%    | Carl Roth GmbH + Co. KG, Karlsruhe, Germany    |
| Benzoic acid                          | >99.5%  | Sigma Aldrich, Steinheim, Germany              |
| Butyraldehyde                         | >99%    | Sigma Aldrich, Steinheim, Germany              |
| Dibenzyl azodicarboxylate (DBAD)      | 90%     | Sigma Aldrich, Steinheim, Germany              |
| Formic acid (FA)                      | 98%     | Carl Roth GmbH + Co. KG, Karlsruhe, Germany    |
| Hydrocinnamaldehyde                   | 95%     | Sigma Aldrich, Steinheim, Germany              |
| Propionaldehyde                       | 97%     | Sigma Aldrich, Steinheim, Germany              |
| Trans-4-Chloro-β-nitrostyrene         | 97%     | Sigma Aldrich, Steinheim, Germany              |
| Trans-4-Methyl-β-nitrostyrene         | 98%     | Sigma Aldrich, Steinheim, Germany              |
| Trans-β-nitrostyrene                  | 99%     | Sigma Aldrich, Steinheim, Germany              |
| Water                                 | pure    | Smart2Pure water purifying system (18.2 MΩ·cm), TKA Wasseraufarbeitungssysteme GmbH, Niedereilbert, Germany |

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**SUPPORTING INFORMATION**

**Materials, equipment and software**

**List of devices used for experiments**

| Device Description                                           | Source Details                                      |
|--------------------------------------------------------------|-----------------------------------------------------|
| 10-port valve, Cheminert C2H-2000                            | VICI AG International, Schenkon, Switzerland        |
| 473 nm laser, 50 mW                                           | Cobolt AB, Solna, Sweden                            |
| 40-fold objective lens                                       | Olympus, Tokyo, Japan                               |
| Agilent 1260 infinity binary LC-System                       | Agilent Technologies Inc., Santa Clara, United States|
| base module (NEM-B100-01)                                    | cetoni GmbH, Korbussen, Germany                     |
| Bruker amaZonSL ion trap (with integrated 6-port valve)      | BrukerDaltonik GmbH, Bremen, Germany                |
| Chiralpak IG-3, 3 µm, 4.6x50 mm column                        | Chiral Technologies Europe, Daicel Corp., Osaka, Japan|
| Chiralpak IG-3, 3 µm, 4.6x250 mm column                      | Chiral Technologies Europe, Daicel Corp., Osaka, Japan|
| High pressure syringe pump (NEM-B207-01, 2.5 mL)             | cetoni GmbH, Korbussen, Germany                     |
| Inverted IX71 epifluorescence microscope                     | Olympus, Tokyo, Japan                               |
| (2x) LED-array, Oslon SSL 80, 470 nm                         | OSRAM GmbH, Munich, Germany                         |

**List of software used for instrument control and data evaluation**

| Software Description                           | Source                                             |
|------------------------------------------------|----------------------------------------------------|
| Data analysis 4.2                              | BrukerDaltonik GmbH, Germany                       |
| ESI Compass 1.7 for amaZon                      | BrukerDaltonik GmbH, Germany                       |
| Microsoft Office 2016                          | Microsoft Corporation, Redmond, USA                |
| Origin Pro 8G                                   | OriginLab Corporation, Northampton, USA            |
| trapControl 7.2                                 | BrukerDaltonik GmbH, Germany                       |
| Qmix Elements (syringe pump control and pressure sensing) | cetoni GmbH, Korbussen, Germany                     |

**General experimental procedure**

All reactions were run under Argon atmosphere, using freshly distilled solvents under anhydrous conditions. Reactions were monitored by TLC on silica gel 60 F254 with detection by charring with sulfuric acid and/or ninhydrin or by UV light. Flash column chromatography was performed on silica gel 60 (230-400 mesh), using reagent grade solvents. Optical rotations were measured at 22 ± 2 °C in CHCl₃; [α]D values are given in 10⁻¹ deg cm² g⁻¹ (concentration c given as g/100 mL). ¹H (300 MHz) and ¹³C (101 MHz) spectra were recorded respectively in CDCl₃, at room temperature. The chemical shifts in ¹H and ¹³C NMR spectra were referenced to trimethylsilane (TMS). Peak assignments were aided by ¹H-¹H COSY and gradient-HMQC experiments. For high resolution mass spectrometry (HRMS) the compounds were analysed in positive ion mode using an Agilent 6520 HPLC-Chip Q/TOF-MS (nanospray) with a quadrupole, a hexapole, and a time of flight unit to produce the spectra. The capillary source voltage was set at 1700 V; the gas temperature and drying gas were kept at 350 °C and 5 L min⁻¹, respectively. The MS analyzer was externally calibrated with ESI-L low concentration tuning mix from m/z 118 to 2700 to yield accuracy below 5 ppm. Accurate mass data were collected by directly infusing samples in 40/60 H₂O/ACN 0.1% TFA into the system at a flow rate of 0.4 µL min⁻¹. Illumination was performed using two 470 nm LED arrays (Oslon SSL 80, 48 V, Osram GmbH). Elemental analyses were performed with Elementar Vario EL CHNS/O analyzer (Elementar Analysensysteme GmbH). FT-IR analyses were performed with the Jasco Instrument FT/IR-4100. Parameter f represents the catalyst loading on Monolith-HJ and is calculated by elemental analysis using nitrogen as the reference atom [N(%) = (f × 14 × 4 /10)]. SEM imaging was performed using a Nova NanoLab 200 instrument (FEI Company). Racemic amino aldehydes[1] and Michael addition products[2] were obtained performing reactions using DL-proline following literature procedures. Propargyl-HJ[3] and 7[4] were synthesized following the literature procedure. All monomers, porogens, and photoinitiators were commercially available except for Monomer-HJ (see Synthesis of Monomer-HJ, SI) and N-methoxy-phenyl-pyridinium tetrafluoroborate (NMPPT) that was synthesized following literature procedure.[5]
Synthesis of Monomer-HJ

4-(((3R,5S)-5-(diphenyl((trimethylsilyl)oxy)methyl)pyrrolidin-3-yl)(oxy)methyl)-1-(4-vinylbenzyl)-1H-1,2,3-triazole (Monomer-HJ)

To a stirred mixture of 7 (26 mg, 0.16 mmol), Propargyl-HJ (100 mg, 0.26 mmol), toluene (1.7 mL), and DMF (0.17 mL), DIPEA (115 μL, 0.66 mmol) and CuI (6 mg, 0.03 mmol) were sequentially added. The resulting mixture was stirred for at room temperature. After 16 h, complete conversion of starting material was detected by TLC. The reaction was then cooled to room temperature, quenched with water (2 mL), and extracted with EtOAc (2 × 5 mL). The combined organic phases were dried over Na2SO4, concentrated, and eluted from a column of silica with the suitable elution system (Cyclohexane-EtOAc 1:1 + 1% NEt3) to give Monomer-HJ (67 mg, 75%) as a pale orange oil.

$[\alpha]_{D}^{22} = -12.0 \ (c = 1.0, \text{CHCl}_3)$. 1H NMR (300 MHz, CDCl3) δ = 7.48–7.45 (m, 2H), 7.44–7.40 (m, 3H), 7.36–7.31 (m, 2H), 7.29–7.21 (m, 8H), 6.72 (dd, J = 17.6, 10.9 Hz, 1H), 5.78 (dd, J = 17.6, 0.7 Hz, 1H), 5.50 (s, 2H), 5.31 (dd, J = 10.9, 0.7 Hz, 1H), 4.55–4.45 (m, 2H), 4.34–4.27 (m, 1H), 3.88–3.79 (m, 1H), 2.94 (dd, J = 11.7, 2.1 Hz, 1H), 2.83 (dd, J = 11.7, 5.0 Hz, 1H), 1.80 (bs, 1H), 1.75–1.64 (m, 2H), -0.11 (s, 9H); 13C NMR (101 MHz, CDCl3) δ = 146.2, 145.8, 145.0, 138.1, 136.0, 133.9, 128.4 (4X), 127.7 (2X), 127.6 (2X), 127.5 (2X), 127.1, 126.9, 126.9 (2X), 122.3, 114.9, 82.8, 79.4, 63.8, 62.5, 53.9, 52.6, 34.2, 2.2 (3X). HRMS (ESI/Q-TOF) calcld for C32H39N4O2Si+ ([M + H]+) 539.2837, found 539.2816.

Photopolymerization procedure and polymer characterization

Procedure for the photoinitiated Monolith-HJ synthesis

In detail, a solution containing photoinitiators was prepared in a small brown glass reaction vial (A) by dissolving S-camphorquinone (1.6 mg; 0.01 mmol), ethyl-N,N-dimethylbenzoate (8 mg; 0.042 mmol) and N-methoxy-phenyl-pyridinium tetrafluoroborate (11.7 mg; 0.043 mmol) in acetonitrile (62.5 µL).

In another brown glass vial (B), isopropanol (20 µL), 1-decanol (24 µL), styrene (14 µL, 0.121 mmol), divinylbenzene (7.5 µL, 0.051 mmol) crosslinker and Monomer-HJ (10.35 mg, 0.019 mmol) were added. Then, 10 µL of the photoinitiators solution (A) previously prepared were added to vial (B), and the reaction mixture was stirred (by using a vortex mixer), duly degassed by a gentle N2 stream, and finally sonicated for 20 min. The resulting pre-polymer mix was transferred to the chip by pipetting.

Afterwards, the chip was sealed at both ends with adhesive tape and placed 2 cm in front of the 470 nm LED source with similar size as the chip (2x LED array, 70 mm x 20 mm, 2x 126 lm). First polymerized Material was visible inside the channel after half an hour. To assure complete polymerization, the chip was turned around every half an hour for a total illumination time of 2 h. In addition, the chip was cooled by a fan and temperature hold at 25-30 °C. After polymerization was completed, the chip was connected to a high pressure syringe pump and duly flushed with THF at a flow rate of 0.5 µL·min⁻¹ for 2 hours to remove the porogens from the polymer and create the classical porous monolithic structure.
Photoinitiated Monolith-HJ synthesis using an inverted epifluorescence microscope

The pre-polymer mix was prepared according to the previous section and transferred to the chip by pipetting. Afterwards, the chip was sealed with adhesive tape and placed onto an inverted IX71 epifluorescence microscope (Olympus, Japan). A 473 nm laser (50 mW, Cobolt, Sweden) was focused inside the microfluidic channel using a 40-fold objective lens (Olympus, Japan). Irradiation of 1 minute resulted in the formation of a polymeric particle about the size of 1-2 µm. Applying this polymerization several times, a polymeric structure with a ring-like shape was crafted as shown in Figure 1C (main text).

Used chips /chip-layouts

A – Used for the initial proof of concept α-amination. B – Used in Michael addition reaction screening. C – Commercial microreactor (R300.500.2, Micronit GmbH) used for the long-term stability experiment. Chips of Layouts A and B contained polymeric retaining structures (acrylate-based, photopolymerized as presented before)\(^3\) whereas these were not included in Chip C. As an approximation, we assumed an exception volume of 50% of the initial empty microreactor volumes.

A 0.30 µL (volume, empty) 0.15 µL (volume, with monolith)
B 1.98 µL (volume, empty) 0.99 µL (volume, with monolith)
C 1.98 µL (volume, empty) 0.99 µL (volume, with monolith)

Figure S-3 Layouts of the Chips used in the flow experiments
Elemental analysis – Catalyst loading

A solution containing photoinitiators was prepared in a small brown glass reaction vial (A) by dissolving S-camphorquinone (3.2 mg; 0.02 mmol), ethyl-N-dimethylbenzoate (16 mg; 0.083 mmol) and N-methoxy-phenyl-pyridinium tetrafluoroborate (23.5 mg; 0.086 mmol) in acetonitrile (125 µL).

In another white glass vial (B), isopropanol (40 µL), 1-decanol (48 µL), styrene (28 µL, 0.242 mmol), divinylbenzene (15 µL, 0.103 mmol) crosslinker and Monomer-HJ (20.7 mg, 0.038 mmol) were added.

Now, 20 µL of the photoinitiators solution (A), previously prepared, were added to the vial (B), and the reaction mixture was stirred (by using a vortex mixer), duly degassed by a gentle N₂ stream, and finally sonicated for 30 min.

For mixing, a small stirring bar was put inside the vial and it was placed the same distance (2 cm, compared to the polymerization inside the chips) above the light source (fixed on the magnetic stirrer).

The vial was illuminated for a total of 30 hours with the above-mentioned light source (same as for the chip). The remaining solvent was evaporated and the white/brownish polymer was washed two times with THF and subsequently dried over a stream of nitrogen for 20 hours. Approximately 25 mg were obtained as a result of this polymerization in batch.

FT-IR (KBr): ν 3443, 3024, 2923, 1602, 1450, 1064, 760, 700 cm⁻¹.

A part of this white/brownish powder (11 mg, dried) was used for CHN-Analysis.

| Sample    | weight in mg | N-%  | C-%  | H-%  |
|-----------|--------------|------|------|------|
| Monolith-HJ | 3.221         | 3.61 | 82.96| 7.14 |
|           | 3.726         | 3.51 | 82.72| 7.51 |
|           | 3.138         | 3.29 | 82.89| 7.63 |

With the measured amounts of N inside the sample, a loading of 0.63 mmol·g⁻¹ can be calculated.
Part of the previously described synthesized polymer (batch) was sputtered with gold and used for first SEM images:

Figure S-5 SEM images of the synthesized co-polymer particles containing Hayashi-Jørgensen catalyst.
In order to have an idea about the structure inside the chips, two microreactors (which were applied to the exact polymerization procedure as mentioned above) were cut into pieces with a glasscutter made of diamond material. The pieces were covered with aluminum foil at the side, and SEM images were taken:

![SEM images of microreactor chips cross sections.](image)

It is visible that the pores are in the range of macropores (>50 nm). This is also explaining the low pressures needed for pumping through the microflow reactor (between 1 and 3 bar for almost all chips at a flow rate of 0.2 µL·min⁻¹). Comparing chip1 and chip2 (SEM measurements), it can be stated that the polymerization is reproducible.
Monolith Removal

Removal of the monolithic structure without damaging the microfluidic chips could be achieved by applying a heating temperature program:

![Figure S-7 Temperature program for monolith removal](image)

For complete removal of monolith debris, the chip was flushed and stored with piranha acid (equal amounts of concentrated H₂SO₄ and H₂O₂) for a total of 1 hour.

![Figure S-8 Photographs of the meandering channel of the commercial microreactor (layout C). Top – empty reactor channel (grey texture due to channel surface roughness), Bottom – reactor channel filled with Monolith-HJ](image)
Microflow experiments

The fluidic setup

As depicted: A syringe pump connected to the 10-port, 2-position switching valve A bearing a loop of 300 μL filled with reactant solution (starting materials). Switching valve A, the solution could flow into the microreactor. The microreactors effluent was sampled by utilizing a 6-port, 2-position switching valve B with a 2 μL sample loop. By switching valve B into the "injection position (not depicted), the sample of the effluent is transferred and analysed by chiral HPLC with subsequent mass spectrometric detection (ESI-MS).

Figure S-9 Setup for on-line analysis of the microreactor effluent. X as plug and W as waste container.
As first proof, the α-amination reaction was conducted in 2 different glass chip microreactors (Design A, straight channel, further described in Fig. S-3), one filled with a plain polystyrene-divinylbenzene monolith (same photopolymerization procedure but without Monomer-HJ) and one containing Monolith-HJ as catalytic species.

Figure S-10 Extracted ion chromatograms (EICs) after on-line chiral HPLC-ESI-MS analysis of the microreactor effluent. Red – EIC of the starting material DBAD 2. Black – EIC of the α-amination product adduct 3 ([M+Na]+). Reaction mixture: Hydrocinnamaldehyde (6.25 mmol·L⁻¹), DBAD (1.25 mmol·L⁻¹) and CH₃COOH (0.62 mmol·L⁻¹) as co-catalyst in pure CH₃CN with an overall flow rate of 0.2 µL·min⁻¹.

Left – Analysis after microflow reaction (5 hours on stream) using a microreactor filled with monolith without catalytic HJ-sites. (HPLC: Chiralpak IG-3, 50 mm, 4.6 mm i.d. Mobile phase: 0.4 mL·min⁻¹, ACN/H₂O, 60/40 vol% with 0.1 mM sodium formate) ESI-source: 60 psi nebulizer, 9 L·min⁻¹ dry gas, 340°C dry heater.

Right – Analysis after microflow reaction (2 hours on stream) using a microreactor filled with Monolith-HJ. (HPLC: Chiralpak IG-3, 250 mm, 4.6 mm i.d. Mobile phase: 0.5 mL·min⁻¹, ACN/H₂O, 70/30 vol% with 0.1 mM sodium formate) ESI-source: 60 psi nebulizer, 9 L·min⁻¹ dry gas, 340°C dry heater.
Flow reaction: Aldehyde 4 (0.30 mmol·L⁻¹), nitro-styrene 5 (0.03 mmol·L⁻¹), PhCOOH (0.013 mmol·L⁻¹) in pure CH₃CN. A flow rate of 0.1 µL·min⁻¹, room temperature, and a residence time of about 10 min was applied. For on-line analysis, 2 µL of the reactors effluent were injected onto the HPLC-MS setup using a two-position switching valve after an approx. Microreactor runtime of 2 hours.

In the following, the extracted ion chromatograms (EICs) of the respective products from the on-line analysis are shown (left). In comparison, the EIC of the racemic mix of the respective compound is shown (right). Respective HPLC-ESI parameters are shown in the labels of the figures.:

**Table S-1** Peak analysis of Figure S-11

| peak | tᵣ [min] | area [counts] | area [%] |
|------|----------|---------------|----------|
| 1    | 5.8      | 282187        | 12       |
| 2    | 6.0      | 1606499       | 69       |
| 3    | 6.4      | 117451        | 5        |
| 4    | 7.0      | 335953        | 14       |

**Figure S-11** EIC of 6a (m/z 230, 15 points Savitzky Golay smooth) from microreactor effluent (Monolith-HJ). HPLC: Chiralpak IG-3, 250 mm, 4.6 mm i.d. Mobile phase: 1 mL·min⁻¹, ACN/H₂O (60/40 vol% with 0.1 mM sodium formate). ESI-source: 50 psi nebulizer, 8 L·min⁻¹ dry gas, 340°C dry heater.

**Figure S-12** EIC of 6a (m/z 230, 15 points Savitzky Golay smooth) from racemic sample. HPLC: Chiralpak IG-3, 250 mm, 4.6 mm i.d. Mobile phase: 1 mL·min⁻¹, ACN/H₂O (60/40 vol% with 0.1 mM sodium formate). ESI-source: 50 psi nebulizer, 8 L·min⁻¹ dry gas, 340°C dry heater.
Table S-2 Peak analysis of Figure S-13

| peak | \( t_R \) [min] | area [counts] | area [%] |
|------|----------------|--------------|---------|
| 1    | 7.5            | 97361        | 6       |
| 2    | 7.7            | 1243011      | 74      |
| 3    | 8.1            | 185377       | 11      |
| 4    | 9.8            | 152205       | 9       |

d.r. 84:16
e.r. 89:11

Figure S-13 EIC of 6b (m/z 244) from microreactor effluent (Monolith-HJ). HPLC: Chiralpak IG-3, 250 mm, 4.6 mm i.d. Mobile phase: 1 mL·min\(^{-1}\), ACN/H\(_2\)O (60/40 vol% with 0.1 mM sodium formate). ESI-source: 50 psi nebulizer, 8 L·min\(^{-1}\) dry gas, 340°C dry heater.

Figure S-14 EIC of 6b (m/z 244, 15 points Savitzky Golay smooth) from racemic sample. HPLC: Chiralpak IG-3, 250 mm, 4.6 mm i.d. Mobile phase: 1 mL·min\(^{-1}\), ACN/H\(_2\)O (60/40 vol% with 0.1 mM sodium formate). ESI-source: 50 psi nebulizer, 8 L·min\(^{-1}\) dry gas, 340°C dry heater.
Table S-3 Peak analysis of Figure S-15

| peak | $t_R$ [min] | area [counts] | area [%] |
|------|-------------|---------------|----------|
| 1    | 8.7         | 159658        | 7        |
| 2    | 9.4         | 1842524       | 81       |
| 3    | 10.7        | 210382        | 9        |
| 4    | 11.3        | 50762         | 2        |

d.r. 91:9
e.r. 90:10

Figure S-15 EIC of 6c (m/z 264, 20 points Savitzky Golay smooth) from microreactor effluent (Monolith-HJ). HPLC: Chiralpak IG-3, 250 mm, 4.6 mm i.d. Mobile phase: 1 mL·min$^{-1}$, ACN/H$_2$O (60/40 vol%) with 0.1 mM sodium formate). ESI-source: 50 psi nebulizer, 8 L·min$^{-1}$ dry gas, 340°C dry heater.

Figure S-16 EIC of 6c (m/z 264, 20 points Savitzky Golay smooth) from racemic sample. HPLC: Chiralpak IG-3, 250 mm, 4.6 mm i.d. Mobile phase: 1 mL·min$^{-1}$, ACN/H$_2$O (60/40 vol%) with 0.1 mM sodium formate). ESI-source: 50 psi nebulizer, 8 L·min$^{-1}$ dry gas, 340°C dry heater.
Table S-4 Peak analysis of Figure S-17

| peak | $t_R$ [min] | area [counts] | area [%] |
|------|-------------|---------------|---------|
| 1    | 7.3         | 196484        | 7       |
| 2    | 7.7         | 2343598       | 80      |
| 3    | 8.9         | 118619        | 4       |
| 4    | 10.8        | 272881        | 9       |

**Analysis from microreactor (Monolith-HJ) effluent**

**Analysis of the corresponding racemic sample**

**Figure S-17** EIC of 6d (m/z 278, 20 points Savitzky Golay smooth) from microreactor effluent (Monolith-HJ). HPLC: Chiralpak IG-3, 250 mm, 4.6 mm i.d. Mobile phase: 1 mL·min$^{-1}$, ACN/H$_2$O (60/40 vol% with 0.1 mM sodium formate). ESI-source: 50 psi nebulizer, 8 L·min$^{-1}$ dry gas, 340°C dry heater.

**Figure S-18** EIC of 6d (m/z 278, 20 points Savitzky Golay smooth) from racemic sample. HPLC: Chiralpak IG-3, 50 mm, 4.6 mm i.d. Mobile phase: 0.4 mL·min$^{-1}$, ACN/H$_2$O (60/40 vol% with 0.1 mM sodium formate). ESI-source: 50 psi nebulizer, 8 L·min$^{-1}$ dry gas, 340°C dry heater.

$d.r.$ 89:11

$e.r.$ 90:10
Table S-5 Peak analysis of Figure S-19

| peak | t_R [min] | area [counts] | area [%] |
|------|-----------|---------------|---------|
| 1    | 7.0       | 227318        | 11      |
| 2    | 7.9       | 77035         | 4       |
| 3    | 8.2       | 1683973       | 81      |
| 4    | 9.2       | 90691         | 4       |

**d.r.** 85:15
**e.r.** 94:6

Figure S-19 EIC of 6e (m/z 244, 30 points Savitzky Golay smooth) from microreactor effluent (Monolith-HJ). HPLC: Chiralpak IG-3, 250 mm, 4.6 mm i.d. Mobile phase: 1 mL·min⁻¹, ACN/H₂O (60/40 vol%) with 0.1 mM sodium formate). ESI-source: 50 psi nebulizer, 8 L·min⁻¹ dry gas, 340°C dry heater.

Figure S-20 EIC of 6e (m/z 244, 15 points Savitzky Golay smooth) from racemic sample. HPLC: Chiralpak IG-3, 250 mm, 4.6 mm i.d. Mobile phase: 1 mL·min⁻¹, ACN/H₂O (60/40 vol%) with 0.1 mM sodium formate). ESI-source: 50 psi nebulizer, 8 L·min⁻¹ dry gas, 340°C dry heater.
Table S-6 Peak analysis of Figure S-21

| peak | t_R [min] | area [counts] | area [%] |
|------|----------|--------------|----------|
| 1    | 7.6      | 139780       | 4        |
| 2    | 8.1      | 2770145      | 85       |
| 3    | 8.6      | 181845       | 6        |
| 4    | 11.0     | 151397       | 5        |

d.r. 90:10
e.r. 95:5
Calibration of Michael addition product (commercial chip)

For the determination of the resulting yields from the flow experiment using the commercial microreactor, an external calibration was carried out using an authentic sample of the product (6f).

Figure S-23 External calibration of product 6f of the Michael addition using HPLC-ESI-MS.

\[ y = 4 \times 10^7 x \]

\[ R^2 = 0.9585 \]
NMR spectra of Monomer-HJ

$^1$H (300 MHz) and $^{13}$C (101 MHz) spectra (CDCl$_3$) of Monomer-HJ
FT-IR spectra of Monolith-HJ

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