Supporting Information

Reaction Calorimetry in Microreactor Environments – Measuring Heat of Reaction by Isothermal Heat Flux Calorimetry

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Mixing Enthalpy of Water and Ethylene Glycol. Mixing was performed at 60°C in the Dolomite glass static mixer (GSM) in the setup as shown in Figure S1. For the mixing experiment the flow rate of EG was set to 0.900 mL/min (P1) and the flow rate of water at 0.300 mL/min (P2). A 1:1 molar ratio of EG and water was kept constant (35.2 mmol) for both EG and water; the mixture was subsequently collected in a receiver flask. Mixing was conducted for 30 min subsequent to the cooling experiment being conducted for 30 min as well with a pre-prepared mixture of EG and water, which was left standing at room temperature for 24 h before use. The mixture was divided in two flasks and the experiment was performed with the same flow rates as in the initial mixing experiment, affording a total flow rate of 1.20 mL/min. The experimental data for true heat flow and reactor and reference temperature is presented in Figure 3.



Figure S1. Flow setup for mixing experiment (only GSM used).

Hydrolysis of Acetic Anhydride. The reaction was conducted in the setup shown in Figure S2 at a temperature of 60 °C. Feeds were consisting of acetic anhydride and 5M hydrochloric acid. Acetic anhydride was pumped with a flowrate of 0.5 mL/min (P1), and the hydrochloric acid solution with a flow rate of 1.0 mL/min (P2). The reaction was performed using the glass static mixer (GSM) with a total internal volume of 0.25 mL/min for 30 min. For measuring the cooling effect a mixture of acetic anhydride and hydrochloric acid (5M) was prepared and left for 24h at room temperature and was then pumped with flow rates of 0.5 mL/min and 1.0 mL/min respectively using 2 feeds, affording a total flow of 1.5 mL/min. The experimental data are presented in Figure S3.



Figure S2. Experimental setup for hydrolysis of acetic anhydride (only GSM used).



Figure S3. Experimental data for the hydrolysis of acetic anhydride. Event point 1 represents the start of the flow for both acetic anhydride and hydrochloric acid. Event point 3 represents the flow of a mixture of acetic anhydride and hydrochloric acid. The baseline for the system is provided before event point 1.

Nitration of Phenol. The experiment was performed in the setup shown in Figure S4 at a temperature of 50 °C. The reaction mixture was prepared in the following manner: 23g of phenol was dissolved in a mixture of 7g acetic acid and 71g of water thus obtaining a 23% phenol solution as feed one (P1) and pumped with flow rate of 0.2 mL/min. The second feed was concentrated nitric acid (65%), pumped with a flow rate of 0.6 mL/min (P2). After 30 min of pumping the reaction mixture was collected in a receiver flask and the composition of the reaction mixture was analyzed by HPLC (at 255 nm wavelength). The absolute amounts were determined by calibration with reference samples of 2-nitrophenol, 4-nitrophenol and 2,4-dinitrophenol. After the reaction, instead of the phenol solution, water was pumped with a flow rate of 0.2 mL/min (P1) and 65% nitric acid as feed 2 (P2) in order to determine the heat of dilution of nitric acid (30min). The experimental data for the nitration reaction are presented in Figure S5. The product was purified in following manner: after addition of water the obtained solid was filtered, washed with water and once with 20 mL of cold ethanol. The solid material was recrystallized from water/methanol (1:1) to produced 2,4-dinitrophenol as yellow crystals, mp 107-108 °C (lit.^{S1} mp 108 °C) in 80% yield. ¹H NMR (300 MHz, CDCl₃): δ 8.90 (d, 1H) 8.43 (dd, 2H J = 9.3 Hz) 7.34 (d, 1H), 11.09 (s, OH). MS (EI): m/z : 183 [M]⁺. The spectral data are in agreement with the previously published values.^{S2}



Figure S4. Experimental setup for nitration of phenol (a T-mixer was used for mixing plus a 5.2 mL residence time coil).



Figure S5. Nitration of phenol with 65% nitric acid. Event point 1 represents the start point of flow P1 and P2. Event point 3 represents the start of flow for phenol dissolved in a mixture of water and acetic acid (0.200 mL/min) and water (0.600 mL/min). Event point 5 represents the start of flow for water (0.200 mL/min) and (0.600 mL/min) nitric acid (for determining of the nitric acid dilution enthalpy).

Reduction of Nitrobenzene. The experiment was performed in the setup shown in Figure S6 at a temperature of 130° C. The reaction mixture was prepared from nitrobenzene (3.075 mL, 30 mmol), 1.2 equiv of hydrazine hydrate (1.75 mL, 36 mmol) and 0.5 mol% of Fe acetylacetonate (52.8 mg) in 25.18 mL of methanol. The solution was pumped for 30 min with a flow rate of 1.0 mL/min (P1). After the reaction the conversion of nitrobenzene was confirmed to be >99% by GC-MS and HPLC (215 nm). For the cooling effect experiment, a solution of nitrobenzene and hydrazine hydrate in the same amounts as with the reaction mixture but without catalyst was prepared. The mixture was pumped with a flow rate of 1.0 mL/min (P1). After the conversion of product was confirmed to be 0% by GC-MS. After solvent evaporation under reduced pressure the residue was filtered

through a plug of silica gel to furnish aniline in >99% purity (HPLC at 215 nm) in 99% yield. ¹H NMR (300 MHz, CDCl₃): δ 7.23 – 7.16 (m, 2H), 6.82 – 6.77 (m, 1H), 6.72 (dd, J = 8.5, 1.0 Hz, 2H), 3.52 (brs, 2H). MS (EI): m/z : 93 [M]⁺. The spectral data are in agreement with the previously published values.^{S3} The experimental data are presented in Figure 4.



Figure S6. Experimental setup for reduction of nitrobenzene (no mixing, 5.2 mL residence time coil).

Oxidation of 1-Phenyl-1-propanol. The experiment was performed in the setup shown in Figure S7 at a temperature of 130 °C. Feed one (P1) was prepared from racemic 1-phenyl-1-propanol (13.7 mL, 0.1 mol) and 1 mol% of PTC (465 mg). The second feed (P2) was a 25% solution of hydrogen peroxide (65.24 mL) and 1 mol% sodium tungstate dihydrate (329 mg). The reaction mixtures were pumped with flow rates of 0.1 mL/min and 0.467 mL/min, respectively, for 30 min. After the reaction was completed the organic layer of the mixture was checked for conversion by HPLC (215 nm area%) and GC-MS to provide 92.3 %. For the cooling effect only 1-phenyl-1-propanol (P1) and a 25% solution of hydrogen peroxide (P2) were pumped with flow rates of 0.1 mL/min and 0.467 mL/min, respectively, leading to 0% conversion. The experimental data are presented in Figure S8. 1-Phenyl-1-propanon, was separated together with the starting material from reaction mixture by extraction with DCM followed by column chromatography with petroleum ether, ethyl acetate (PE:EA, 95:5) to provide an 89% isolated yield, ¹H NMR (300 MHz, CDCl₃) δ 8.00–7.97 (m, 2H), 7.60–7.54 (m, 1H), 7.50–7.44 (m, 2H), 3.02 (q, J = 7.2 Hz, 2H), 1.24 (t, J = 7.2 Hz, 3H). MS (EI): m/z: 134 [M]⁺. The spectral data are in agreement with the previously published values.^{S4}



Figure S7. Experimental setup for oxidation of 1-phenyl-1-propanol (GSM and 2.11 mL residence time coil).



Figure S8. Experimental data for the oxidation of 1-phenyl-1-propanol. Before event point 1 is the cooling effect experiment with flow of only 1-phenyl-1-propanol and 25% hydrogen peroxide solution. Event point 1 represents the starting point of the reaction, the total flow rate was 0.576 mL/min, and the residence time ca. 4 min. The noisy signal is derived from the fact that during the reaction there is gas evolving. Event point 2 represents the stop of the experiment.

Reduction of Allylbenzene. The experiment was performed in the setup shown in Figure S9 at a temperature of 100 °C. The liquid feed consisted of allylbenzene (1.58 ml, 12 mmol) and 6 equiv of hydrazine hydrate (3.48 mL, 72 mmol) dissolved in 6.94 mL of 1-propanol. The liquid feed (P1) is pumped with a flow rate of 0.4 mL/min and oxygen is introduced by means of a calibrated mass flow control with a flow rate of 4 mL/min (the reaction was conducted for 25 min). After the reaction was completed the conversion was determined by GC—MS to be 99%. For the cooling effect experiment a solution of hydrazine hydrate (3.48 mL, 72 mmol) in 1-propanol (8.52 mL) was pumped with a flow rate of 0.4 mL/min and oxygen is introduced with flow rate of 4 mL/min for 20 min. For workup the solvent was evaporated under reduced pressure to produce propylbenzene in 98% yield (after drying overnight using a desiccator with CaCl₂). ¹H NMR (300 MHz, CDCl₃) δ 2.49 (t, 2H, CH₂), δ 2.0-1.8 (m, 2H, CH₂), δ 0.9 (t, 3H, CH₃); δ 23.65 (CH₂), MS (EI): m/z : 119 [M]⁺. The spectral data are in agreement with the previously published values.⁸⁵



Figure S9. Experimental setup for the reduction of allylbenzene with hydrazine hydrate and oxygen (GSM and residence time coil of 4.95 mL)



Figure S10. Experimental data for hydrogenation of allylbenzene with hydrazine hydrate and oxygen. Event point 3 represents start of the flow of reaction mixture and oxygen. Event point 4 represents stop of the reaction and start of the cooling experiment.

References

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