Supplementary Material (ESI) for Chemical Communications

Supporting Information

A Dynamic Micromixer for Arbitrary Control of Disguised Chemical Selectivity

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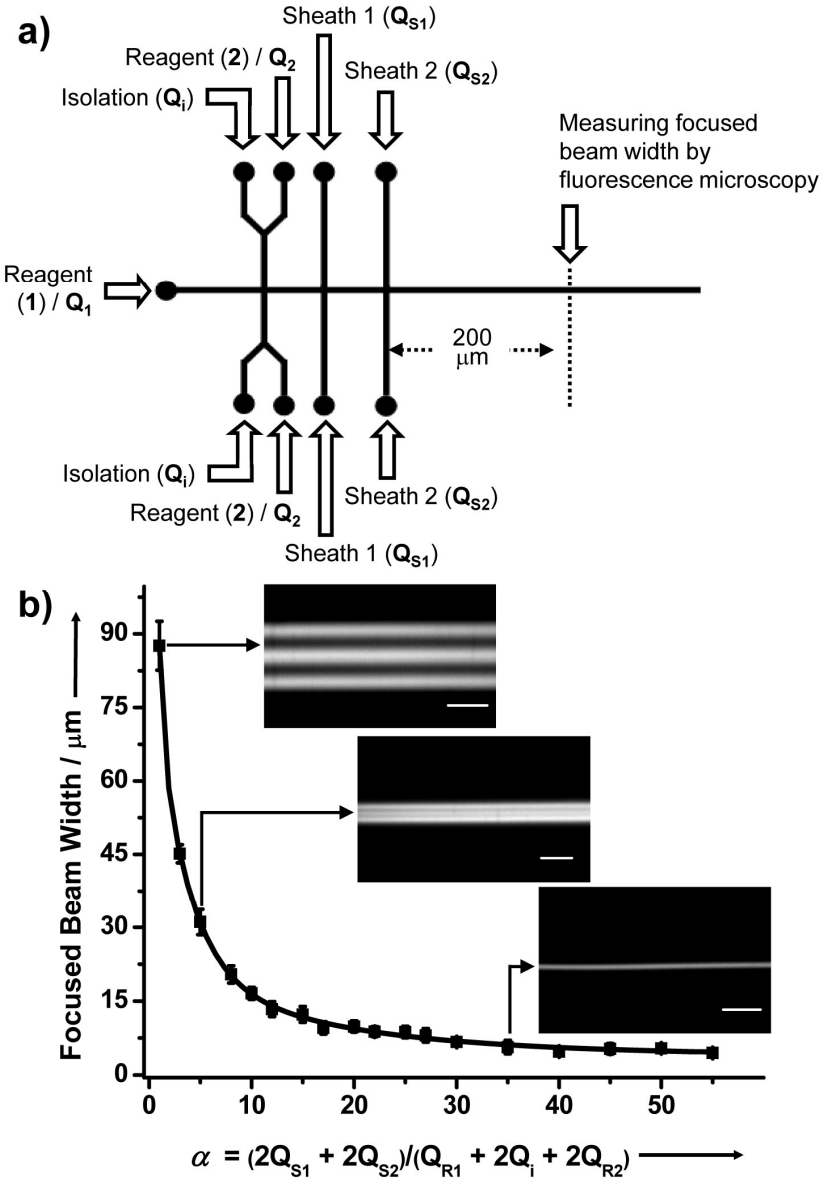

Figure S1 a) Schematic presentation of the experimental setting for measuring dynamic focused beam widths in the dynamic microreactor. Herein, the stream compression ratio α is the ratio between the four sheath flows ($2Q_{s1} + 2Q_{s2}$) and the five focused streams ($Q_1 + 2Q_i + 2Q_2$). b) A plot summarizes the relationship between dynamic focused beam widths (measured by fluorescence microscopy) and flow compression ratio α. Inset: micrographs of the focused streams at α = 1, 5 and 35. The scale bars in the micrographs are 50 μm.

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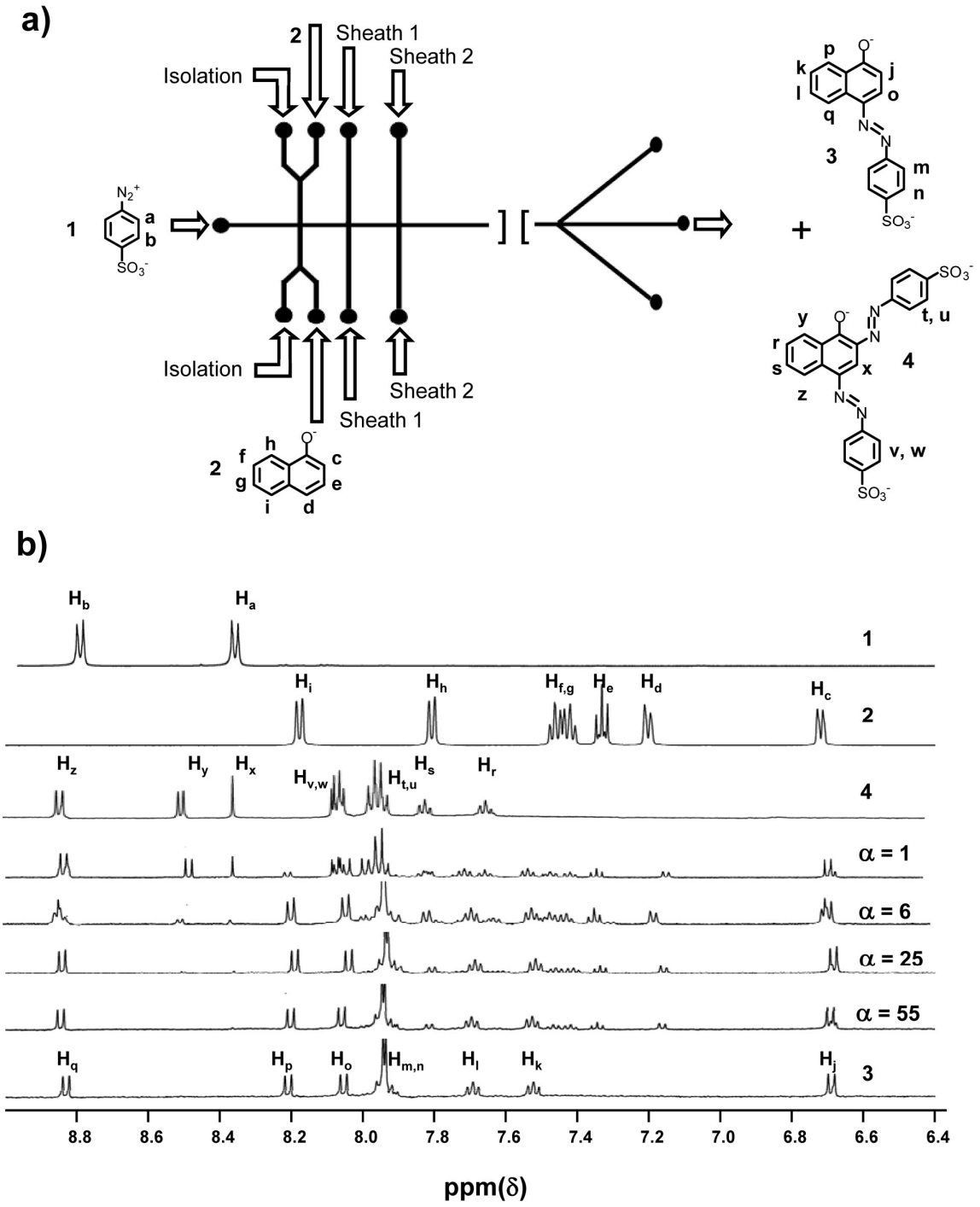

Figure S2. a) Competitive-consecutive diazo-coupling reaction between 4-sulfono-1-phenyldiazonium tetrafluoroborate (**1**) and 1-naphthol (**2**) were carried out in the dynamic reactor at different stream compression ratios (α). b) Representative ^{1}H-NMR spectra of reaction mixtures collected at α = 1, 6, 25

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and 55 are shown along with those obtained for starting materials **1** and **2** and products **3** and **4**.

General Sulfanilic acid, calcium chloride, sodium nitrite, tris-HCl, 1-naphthol, 4-(4-sulfonophenyldiazo)-1-naphthol (Compound **3),** deuterium oxide and DMSO-d_6 were obtained from Sigma-Aldrich and Fluka (St Louis, MI), and used without further purification. Tetrafluoroboric acid (48%) was purchased from Alfa Aesar (Ward Hill, MA). 5-Carboxyfluorescein was purchased from molecular probes (Carlsbad, CA). Fluorescence micrographs were obtained using an Eclipse TE 2000-E Nikon inverted fluorescence microscope (MetaMorph Software®). All ^{1}H-NMR spectra were recorded in a Bruker DRX 500 MHz spectrometer in a deuterated mixture solution (DMSO-d_6:D_2O, 8:2, v/v, 10 mM Na_2CO_3/$NaHCO_3$, pH 10, referred to as DMSO-D_2O-buffer) and the residual solvent peak of D_2O was used as the internal standard.

Synthesis.

Synthesis of 4-sulfono-1-phenyldiazonium tetrafluoroborate (1). To prepare 4-sulfono-1-phenyldiazonium tetrafluoroborate (**1**),[1] sulfanilic acid (3.0 g , 17.3 mmol) and sodium nitrite (1.2 g, 17.3 mmol) were dissolved in hydrochloric acid (5.1 g, 51.9 mmol) at 0 ^{o}C for 5 h. The resulting reaction mixture was warmed to 5 ^{o}C and a 48 % aqueous solution of tetrafluoroboric acid was added to crystallize **1**. The precipitate was washed with anhydrous ether to yield a white solid (3.39 g, 60 %). ^{1}H-NMR (500 MHz, DMSO-D_2O-buffer) 8.78 (d, J = 8.5 Hz, 2H) and 8.30 (d, J = 8.5 Hz, 2H).

Synthesis of 2,4-Di-(4-sulfonophenyldiazo)-1-naphthol (4). Compound **4** was prepared according to literature.[2] The crude mixture was purified by prepared aluminum oxide thin layer chromatography with 4:1 *n*-hexane: ethyl acetate as elute. ^{1}H-NMR (500 MHz, DMSO-D_2O-buffer, and agreed with literature) 8.82 (d, J = 7.0 Hz, 1H), 8.38 (d, J = 8.0 Hz, 1H), 8.35 (s, 1H), 8.02 – 7.07 (m, 4H), 7.94– 7.90 (m, 4H), 7.83 – 7.81 (t, J = 7.0, 8.0 Hz, 1H), 7.64 – 7.62 (t, J = 7.0, 8.0 Hz, 1H).

Fabrication of dynamic microreactors.

The dynamic microreactors were fabricated from PDMS and poly(methyl methacrylate) (PMMA) using soft lithography method[3] and laser engraving, respectively.

PDMS chip fabrication. The silicon master for the fluidic channels was made by introducing an 80 μm-thin negative photoresist (SU8-2050, Microchem, Newton, MA) pattern on a silicon wafer (Silicon Quest Inc., Santa Clara, CA). After UV exposure and development, a square-profiled pattern was obtained (channel width: 200 μm, channel height: 80 μm). Before fabricating the chemical reactors, the silicon masters were exposed to trimethylchlorosilane vapor for 5 minutes. A well-mixed PDMS pre-polymer (GE, RTV 615 A and B in 10 to 1 ratio) was poured onto the silicon master located in a Petri dish to give a 5 mm-thick fluidic layer. The pre-polymer was then cured in an 80 ^{o}C oven for overnight. After oven baking, the PDMS was peeled off the master and holes were introduced into the PDMS replicas for

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solution inlets and outlets. The PDMS was bonded onto glass slides after oxygen plasma treatment (PDC-32G, Harrick Scientific Products, Inc.) for 30 s prior to contacting. The microreactors were ready for use after baking at 80 ^{o}C overnight.

PMMA chip fabrication. The microchannel structures with the same configuration as that of PDMS chips were engraved on PMMA plates (length: 4 cm, width: 2 cm, thickness: 1.10 mm) using CO_2 laser (HB-1290 laser engraving/cutting machine, 3w). The patterned micro-channel PMMA and blank PMMA substrates were bonded together through thermal bonding[4] with at 120 ^{o}C without pressure control.

Characterizing fluid behavior in the dynamic micromixer by fluorescence microscopy. All of the experiments were performed at room temperature; the fluids were driven by syringe pump at constant flow rate. The reactant and isolation flow rates were kept at 1 μl/min and the sheath flow streams were systematically changed to vary the hydrodynamic focused widths (from 4 μm to 88 μm) [5]. To visualize the flow behavior in the micromixer, 5-carboxyfluorescein (50 nM, pH 8.5 adjusted with 10 mM Tris-HCl buffer) was introduced into the three reactant inlets and Tris-HCl buffer was introduced into the isolation streams, while 18-MΩ water was used as the sheath streams. For Figure 1a and b, α = 20, which corresponds to a focused beam width of 9.8 μm were recorded using MetaMorph Software®.

Determining the relationship between hydrodynamically focused beam width and α with fluorescence microscopy. The same device configuration and set-up as that for the characterization of the fluid behavior in the microreactor was used for measuring the hydrodynamic focused beam widths. The sheath flow rates were systematically changed (from 1.25 to 68.75 μL/min) while the fluorescent and isolation streams were kept at 1 μL/min, corresponding to hydrodynamic focused beam widths of 88 μm to 4 μm. The micrographs were captured using the best bit range to ensure the best focused and highest intensity fluorescence for the focused beam width. Before measuring the focused beam widths, however, the bit range for all micrographs was changed to 300-4000 (within a 12-bit range) bits to reduce the pixels from the scattered fluorescence. The focused beam widths were then measured directly from the fluorescent micrographs using MetaMorph Software®. The average of 9 data measurements for the focused beam widths were then plotted as a function of their corresponding α and shown in figure S1b. The error bars represent the standard deviation of each measurement from the average value.

Diazo coupling reaction of 1 and 2 in the dynamic micromixer. All the solutions were prepared in DMSO-D_2O-buffer. Compound **1** (30 mM) and **2** (16 mM) as well as the isolation streams were introduced into their respective inlets at 1 μL/min. For each α value, the flow rate of the sheath flows was

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changed accordingly; the collected reaction mixture was kept at -78 ^{o}C to avoid any possible further reaction between **1** and **2,** until it was analyzed by ^{1}H-NMR spectroscopy. The product distribution of **3** and **4** was determined by the integration of the characteristic signals located at δ = 6.77 and 8.35 ppm corresponding to *ortho* proton of the naphthol ring H_j and *meta* proton of the naphthol ring H_x of **3** and **4**, respectively, and plotted as a function of α and focused beam width as described in the main text.

References:

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[5] It is noticeable that this system can be used for the residence times between 0.2 s and 3.2 min. If the flow rate lowers than 0.1 μl/min, the streams become instable.

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