Supporting Information

Multistep synthesis of amides from alcohols and amines in continuous flow microreactor systems using oxygen and urea hydrogen peroxide as oxidants

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Construction of microreactor systems

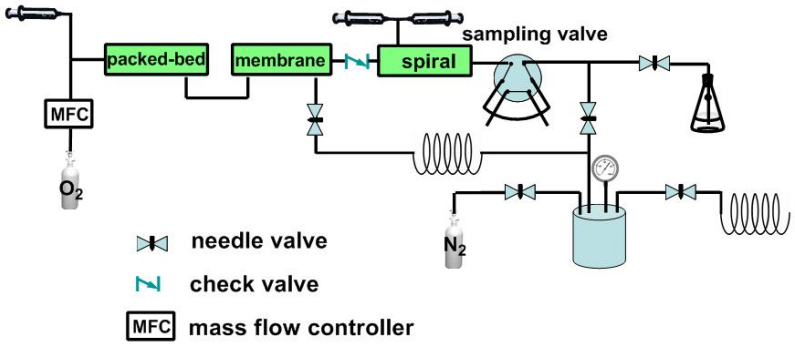

Figure S1 Diagram of the experimental setup for multistep synthesis of amides from alcohols and amines.

The experimental setup (Figure S1) consists of three micro-system devices (Figure S2): a packed-bed microreactor, a membrane separator, and a spiral-channel microreactor. The first reactor is a silicon-Pyrex microreactor with a single-channel (27×8×0.6 mm^3). An array of pillars was fabricated downstream of the reactor with 25 μm intervals as a weir to hold the catalytic materials inside the channel. The stainless steel packaging chuck allows the device to be heated and pressurized. The separator is constructed of two stainless steel chucks with a single channel (20×2×1 mm^3) on each piece. A piece of Zefluor membrane is sandwiched between the two pieces that are compressed together. The third device is a silicon-Pyrex microreactor (220 μL in total volume) with a spiral channel. The mixing and reaction zones are separated by a halo etched region.

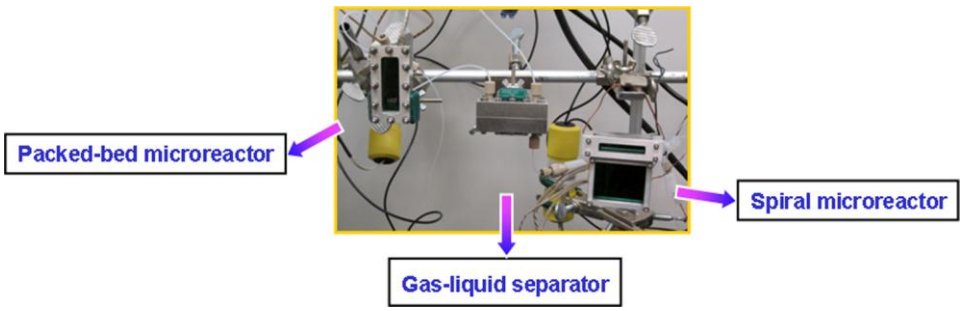

Figure S2 Photo of the three micro-system devices forming a continuous network.

Product isolation

The product (Table 1, Entry 3), 4-(4-chlorobenzoyl)morpholine, was isolated following a procedure described below. The reaction mixture was collected by combining 32 samples from the same stock solutions running continuously for a total reaction time of 24 h. Water was then added followed by extraction using dichloromethane for 4 times. The organic layers were combined and concentrated under vacuum. Purification was performed with column chromatography (silica gel, dichloromethane:ethyl acetate 5:1 for first column and hexane:ethyl acetate 4:5 for second column) and the solvent was removed under vacuum to give light yellow crystals. Nuclear Magnetic Resonance spectra were obtained on a Bruker 400 MHz instrument with deuterated chloroform as the solvent. Chemical shifts of ^{1}H were relative to the residual chloroform and those of ^{13}C to deuterated chloroform. ^{1}H NMR: δ 3.30-3.90 (m, 8H), 7.30-7.39 (m, 4H); ^{13}C NMR: δ 67.0, 128.9, 129.1, 133.8, 136.2, 169.6.