Preparation of amides mediated by isopropylmagnesium bromide under continuous flow conditions.

Experimental.

The GC measurement was performed using a 6890 Series Gas Chromatograph (Agilent Technologies) system comprising a 7683 Series injector and autosampler, J&W HP-5MS column (20 m x 0.18 mm, 0.18 μm) from Agilent Technologies coupled to a 5973N MSD Mass Selective Detector (single quadrupole, Agilent Technologies). The MS detector was configured with an electronic impact ionization source / chemical ionization source (EI/CI). EI low-resolution mass spectra were acquired by scanning from 50 to 550 at a rate of 14.29 scan. The source temperature was maintained at 230°C. Helium was used as the nebulizer gas. Data acquisition was performed with Chemstation-Open Action software. Thin layer chromatography (TLC) was carried out on silica gel 60 F254 plates (Merck) using reagent grade solvents. Unless otherwise specified, reagents were obtained from commercial sources and used without further purification.

General flow procedure.

Two solutions, amine (1.5 equiv) in THF and isopropylmagnesium chloride lithium chloride complex solution 1.3 M in THF (3 equiv) were pumped at 0.1 mL/min (each one) using a syringe pump through Sigma-Aldrich microreactor. At the same time a third solution of ester (1 equiv) in THF was pumped at 0.2 mL/min with a second syringe pump and mixed with the previous solution in a Sigma-Aldrich microreactor and then pass through a coil of 5 mL (Rt= 14 min). The outlet solution was poured into HCl 1M and extracted with ether. The organic layer was separated, dried (MgSO4), filtered and the solvents evaporated in vacuo to yield the product.

Work-up on-line.
The output of the coil was then directed into a 10 mm diameter Omnifit column filled with Amberlyst A-15 (2 g). The solution collected was evaporated to dryness to yield the product.

**General batch procedure.**

A solution of isopropylmagnesium chloride lithium chloride complex solution 1.3 M (3 equiv) in THF was added to a stirred solution of amine (1.5 equiv) in THF in a sealed tube under nitrogen at rt. The mixture was stirred for 1 hour. Then a solution of ester (1 equiv) in THF was added to the previous one at room temperature for 1 hour (at 14min the reaction was not completed). The mixture was quenched with HCl 1M and extracted with eter. The organic layer was separated, dried (MgSO4), filtered and the solvents evaporated in vacuo to yield the product.
GCMS spectra of representative reactions crude.

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\text{O} \quad \text{NH}_2 \quad \text{F} \text{F} \\
\text{O} \quad \text{iPrMgCl} \quad \text{THF} \\
\text{O} \quad \text{iPrMgCl} \quad \text{THF}
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Electronic Supplementary Material (ESI) for Green Chemistry
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GCMS spectra of selectively reactions.

Flow reaction

Batch reaction
Flow reaction

Batch reaction
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