

Supplementary Information

A solid-supported phenylboronic acid-based catalyst for direct amidation

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General experimental

All the reactions were performed under air unless otherwise specified. The reagents were purchased directly from standard chemical suppliers and used as received from the supplier without further purification. All solvents were used as received from the supplier, except THF, MeOH and *i*PrOH which were stored over dehydrating agent and deoxygenated before use. Molecular Sieves with 4 Å 1-2 mm beads, were supplied from Alfa Aesar, and stored at 220 C (>48 h), Mortmorillonite K10 powder, 250 m²/g, was supplied from Sigma Aldrich and stored at 80 C (>48 h) and heated under vacuum before use. The purification of the reaction crudes was performed using flash-column chromatography, which was carried out using different supports as supplied from Sigma Aldrich; Silica gel (230-400 mesh, 40-63 µm, 60 Å); activated magnesium silicate FLORISIL[®] (100-200 mesh, 289 m²·g⁻¹) and monitored in both cases by TLC analysis using POLYGRAM[®] SIL G/UV254 (40 x 80 mm) TLC plates or activated neutral aluminum oxide aluminium-backed TLC-PET plates with 254 nm (40 x 80 mm) fluorescent indicator. In all cases the TLC plates were visualized under a UV lamp operating at short (254 nm) and long (365 nm) wavelength ranges. Visualization was aided by dipping the plates into an alkaline potassium permanganate solution or a *p*-anisaldehyde solution.

Parallel reactions looking at catalytic reaction timescales were carried out using a Radleys[®] Carousel 6 Plus Parallel Reaction Station, equipped with six Radley's 100 mL azeotropic distillation heads and matching two-neck flasks.

Low pressure distillation was carried out using a Büchi B-585 glass oven (Kügelrohr). Pressures were not controlled, and the values reported are the operating pressure of the vacuum pump used, as indicated by a separate pressure gauge. Solution state NMR spectra were recorded on a Bruker Advance spectrometer, operating at 400 MHz for ¹H and 100 MHz for ¹³C. Deuterated chloroform (CDCl₃) was used as solvent for routine NMR measurements, otherwise stated. ¹H NMR spectra were recorded on a Varian-Mercury 400 MHz spectrometer, operating at ambient probe temperature unless specified elsewhere. Coupling constants (*J*) are given in Hz, and the multiplicity of the NMR signals is described as singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). ¹³C NMR spectra were recorded on Varian Bruker Advance 100 MHz. ¹H NMR and ¹³C NMR chemical shifts are reported in ppm (δ) referencing the chemical shifts of residual solvent resonances. ¹¹B NMR spectra were recorded on a Varian Bruker Advance 400 MHz operating at a frequency of 128 MHz and the chemical shifts are reported in ppm (δ) relative to BF₃(CH₃)₂O.

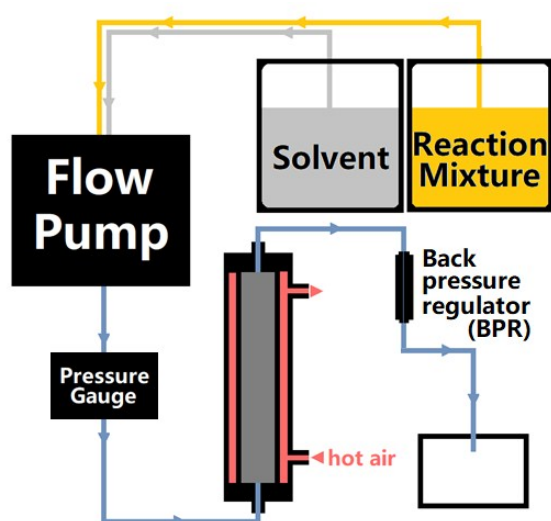
Mass spectra for liquid chromatography mass spectrometry (LCMS) were obtained using a Waters (UK) TQD mass spectrometer (low resolution ESI+, electrospray in positive ion mode, ES+) unless stated elsewhere. Accurate mass spectrometry was obtained on a Finnigan LTQ-FT.

IR spectra were recorded on a Perkin Elmer Paragon 1000 FT-IR spectrometer with an ATR attachment.

In situ infrared spectroscopy

Reactions monitored by *in situ* IR spectroscopy were carried out using a Mettler-Toledo ReactIR 4000 equipped with an MCT detector (ConcIRT, window 1900–900 cm⁻¹; Advanced setting, Laser WN 7901–415 cm⁻¹; Apodization Happ General; Probe, Prob A DiComp (Diamond) connected *via* K6 Conduit (16 mm probe); Sampling 4000–6500 at 8 cm⁻¹ resolution; Scan option auto select, gain 2×.

Flow reactor system setup



The Vapourtec R2+/R4 unit is a commercially available flow synthesis platform available from Vapourtec Ltd, Bury St Edmunds, U.K. The Vapourtec system has twin pump heads with an independently controlled four-channel air-circulated heating module. A low-pressure input valve is used to route either solvent or bulk stock solutions directly to the self-regulating HPLC pumps. Two additional mounted Rheodyne 6-port-2-position switching valves can be used to introduce reagents or substrates into the main flow line through individual sample loop arrangements of user-defined variable volumes. A positive system pressure was maintained by using an in-line 75 psi back-pressure regulator. The use of an appropriate back-pressure regulator allows superheating of solvents as required. An additional in-line bespoke custom made pressure detector was placed in line to monitor the system pressure after the column reactor. Mixing of the reagent streams is achieved with a simple T-piece and the combined output is then directed through perfluoroalkoxy (PFA) tubing to the packed bed reactor (Omnifit glass reactor 10 x 100 mm), which can be precisely heated to 150 °C. Upon exiting the flow column, the fluidic stream is rapidly cooled and is then directed to a Gilson FC 203B Fraction Collector which was set in timing mode for sample collection. A rapid screening of reaction parameters was performed, which included reaction temperature, residence time (flow rate), internal pressure, solubility, reagent concentrations and stoichiometry.

Synthesis of polymer catalyst.

To a mixture of styrene (1.20 g, 12 wt. %), divinylbenzene (1.80 g, mixed isomers, 18 wt. %), 4-vinylphenylboronic acid (1.20 g, 12 wt. %) and 1-dodecanol (5.70 g, 57 wt. %) was added. AIBN (0.10 g, 1 wt. %). The solution was decanted into two Omnifit glass tubes (each 12.37 ml) which were sealed at both ends with PTFE caps. These were placed in the Vapourtec column heating zone and heated to 80 °C for 20 hrs. The polymer monoliths were cooled, removed from the tubes, combined and submerged in methanol (100 ml) for 6 hrs, then DCM (100 ml) for another 6 hrs to remove the dodecanol solvent, before drying in an oven at approximately 100 °C overnight. The monoliths were crushed into a powder (particle size approx. 1-3 mm) and then ground more finely (<1 mm) before use. ¹¹B solid state (MAS) NMR (128.3 MHz): δ before use 16; δ after use 13 and 0. After washing and drying (removal of 1-dodecanol) the polymer comprised of 28% catalytically active monomer by mass, and as such this factor was used when calculating the required mass for reactions. In order to prepare larger amounts of the catalysts, this procedure was readily scaled by increasing the number of columns used to prepare the polymer.

Soxhlet Extraction of Polymer catalyst.

To a dry extraction thimble (25 mm x 100 mm) in a Soxhlet extractor, ground polymer catalyst (10 g) was added, followed by 200 mL of toluene added in the round bottom flask. The Soxhlet extraction was left for 72 hrs before drying in a desiccator.

Activation of heterogeneous catalyst 1 through reaction with carboxylic acid, followed by amine reaction

Polymer catalyst (3.03 g, 5.72 mmol, 1 equiv.) and toluene (50 mL) were added to a 100 mL Radley's azeotropic round-bottom flask with a built-in Dean-Stark trap. The probe for the React-IR experiment was submerged in the reaction solution. A React-IR experimental schedule was set and the probe started collecting data. The mixture was maintained at reflux and a stoichiometric amount of phenylacetic acid (5.72 mmol, 1 equiv.) was added, and the resulting mixture was stirred for 50 min. Then benzylamine (5.72 mmol, 1 equiv.) was added and reaction was stirred for a further 21 hrs. After cooling the polymer catalyst was filtered, washed with toluene, and dried overnight before being analysed. The filtrate solvent was removed *in vacuo* and the resulting crude solid was redissolved in DCM (50 mL), washed with 5% HCl (3 × 50 mL), saturated NaHCO₃ (3 × 50 mL), brine (3 × 50 mL), and finally water (50 mL). Solvent was removed under reduced pressure to give the crude amide product. Purifications were then carried out by low pressure distillation (Kugelrohr).

General procedure A for the heterogeneous catalytic direct amide formations.

Carboxylic acid (2.86 mmol), polymer catalyst **1** (75.8 mg, 0.143 mmol, 5 mol%), and toluene (20 mL) were added to a 50 mL round-bottom flask. Amine (2.86 mmol, 1 equiv.) was then added and the resulting mixture stirred at a vigorous reflux using a Dean-Stark trap for 24 hrs.* After cooling to rt, the solvent was removed *in vacuo*. The resulting crude solid was redissolved in DCM or chloroform (50 mL), filtered to remove the catalyst, and the filtrate washed with 5% HCl (3 × 20 mL), saturated NaHCO₃ (3 × 20 mL), brine (3 × 20 mL), and finally water (20 mL). The solvent was removed *in vacuo* to give the crude amide product which was purified by low pressure distillation (Kugelrohr).

*Upon addition of the amine, many of the initially formed ammonium carboxylate salts crystallised out of solution. In most cases these redissolved upon heating.

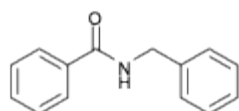
General procedure B for the heterogeneous catalytic direct amide formations.

Carboxylic acid (5.72 mmol), polymer catalyst **1** (151.6 mg, 0.286 mmol, 5 mol %), and toluene (40 mL) were added to a 100 mL Radley's azeotropic round-bottom flask with a built in Dean-Stark trap. Amine (5.72 mmol, 1 equiv.) was then added and the resulting mixture stirred for the prescribed length of time. The reaction mixture was allowed to cool to rt, and the solvent was removed *in vacuo*. The resulting crude solid was redissolved in DCM or chloroform (50 mL), filtered to remove catalyst **1**, and the filtrate washed with 5% HCl (3 × 50 mL), saturated NaHCO₃ (3 × 50 mL), brine (3 × 50 mL), and finally water (50 mL). The solvent was removed under reduced pressure to give the crude amide product which was purified by low pressure distillation (Kugelrohr).

General procedure C for the homogeneous catalytic direct amide formations.

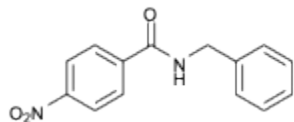
Carboxylic acid (5.72 mmol), phenylboronic acid (34.9 mg, 0.286 mmol, 5 mol %), and toluene (40 mL) were added to a 100 mL Radley's azeotropic round-bottom flask with a built in Dean-Stark trap. Amine (5.72 mmol, 1 equiv.) was then added and the resulting mixture stirred for the prescribed period of time. The reaction mixture was then allowed to cool to rt, and the solvent was removed *in vacuo*. The resulting crude solid was redissolved in DCM or chloroform (50 mL), washed with 5% HCl (3 × 50 mL), saturated NaHCO₃ (3 × 50 mL), brine (3 × 50 mL), and finally water (50 mL). The solvent was removed under reduced pressure to give the crude amide product which was purified by low pressure distillation (Kugelrohr).

N-Benzylbenzamide.



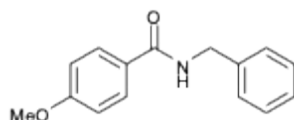
Prepared according to the general procedure A, with benzoic acid (0.34 g) and benzylamine (0.31 mL). Kugelrohr distillation (175-185 °C, 0.4 torr) yielded 0.55 g (90%) as a white crystalline solid: Mpt. 104.5-105.5 °C (Lit.^[1] 105.0-105.5). All spectroscopic and analytical data were consistent with those reported in the literature.^[2]

N-Benzyl-4-nitrobenzamide.



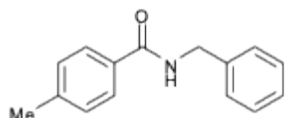
Prepared according to the general procedure A, with 4-nitrobenzoic acid (0.48 g) and benzylamine (0.31 mL). Kugelrohr distillation (195-200 °C, 0.4 torr) yielded 0.038 g (5%) as a pale yellow powder: Mpt. 141.0-142.0 °C (Lit.^[1] 141-142 °C). All spectroscopic and analytical data were consistent with those reported in the literature.^[3]

N-Benzyl-4-methoxybenzamide.



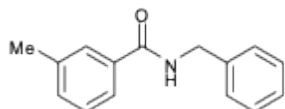
Prepared according to the general procedure A, with 4-methoxybenzoic acid (0.44 g) and benzylamine (0.31 mL). Kugelrohr distillation (175-190 °C, 0.2-0.3 torr) yielded 0.265 g (38%) as a white crystalline solid: Mpt. 129.5-130.0 °C (Lit.^[1] 131.0-132.5 °C). All spectroscopic and analytical data were consistent with those reported in the literature.^[2]

N-Benzyl-4-methylbenzamide.



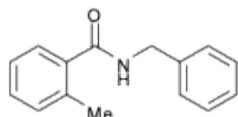
Prepared according to the general procedure A, with 4-methylbenzoic acid (0.39 g) and benzylamine (0.312 mL). Kugelrohr distillation (155-160 °C, 0.3 torr) yielded 0.122 g (19%) as a white crystalline mass: Mpt. 133.0-134.0 °C (Lit.^[1] 133 °C). All spectroscopic and analytical data were consistent with those reported in the literature.^[2]

N-Benzyl-3-methylbenzamide.



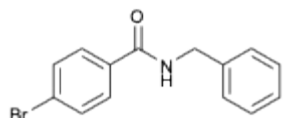
Prepared according to the general procedure A, with 3-methylbenzoic acid (0.39 g) and benzylamine (0.31 mL). Kugelrohr distillation (155-160 °C, 0.3 torr) yielded 0.294 g (46%) as a white crystalline solid: Mpt. 84.5-85.5 °C (Lit.^[1] 74.5-75.5 °C). All spectroscopic and analytical data were consistent with those reported in the literature.^[4]

N-Benzyl-2-methylbenzamide.



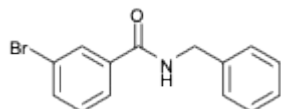
Prepared according to the general procedure A, with 2-methylbenzoic acid (0.39 g) and benzylamine (0.31 mL). Kugelrohr distillation (175-180 °C, 0.3 torr) yielded 0.130 g (20%) as a white crystalline solid: Mpt. 102.5-104.0 °C (Lit.^[2] 105 °C). All spectroscopic and analytical data were consistent with those reported in the literature.^[5]

N-Benzyl-4-bromobenzamide.



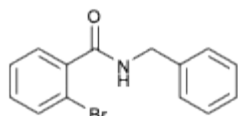
Prepared according to the general procedure A, with 4-bromobenzoic acid (0.58 g) and benzylamine (0.31 mL). Kugelrohr distillation (175-180 °C, 0.3 torr) yielded 0.203 g (25%) as an off-white crystalline solid: Mpt. 168-169 °C. All spectroscopic and analytical data were consistent with those reported in the literature.^[6]

N-Benzyl-3-bromobenzamide.



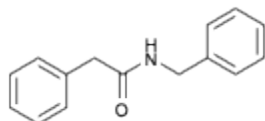
Prepared according to the general procedure A, with 3-bromobenzoic acid (0.58 g) and benzylamine (0.31 mL). Kugelrohr distillation (165 °C, 0.3-0.4 torr) yielded 0.244 g (30%) as an off-white crystalline solid: Mpt. 96.0-97.0 °C (Lit.^[2] 87.0-88.0 °C). All spectroscopic and analytical data were consistent with those reported in the literature.^[2]

N-Benzyl-2-bromobenzamide



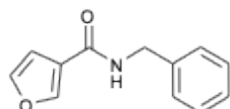
Prepared according to the general procedure A, with 2-Bromobenzoic acid (0.57 g) and benzylamine (0.31 mL) were added for amidation. Kugelrohr distillation carried (160-170 °C, 0.4 torr) and yielded 0.15 g (27%) of pure amide product as a white solid: ¹H NMR (400 MHz, CDCl₃) δ 4.69 (d, *J* 5.6, 2H), 6.26 (br, s, 1H), 7.26-7.44 (m, 7H), 7.64-7.57 (m, 2H). All the other spectroscopic and analytical data were consistent with those reported in the literature^[6].

N-Benzyl-2-phenylacetamide.



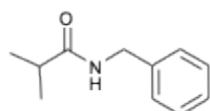
Prepared according to the general procedure A, with phenylacetic acid (0.39 g) and benzylamine (0.31 mL). Kugelrohr distillation (170 °C, 0.2 torr) yielded 0.590 g (92%) as a white crystalline solid: Mpt. 121.0-122.5 °C (Lit.^[1] 121.0-122.0 °C). All spectroscopic and analytical data were consistent with those reported in the literature^[7], although the reported ¹³C NMR data was consistently 30 ppm lower than observed here.

N-Benzyl-3-furamide.



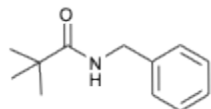
Prepared according to the general procedure A, with 3-furoic acid (0.32 g) and benzylamine (0.31 mL). Kugelrohr distillation (140-145 °C, 0.2-0.3 torr) yielded 0.387 g (67%) as a white crystalline mass: Mpt. 124.5-126.0 °C. All spectroscopic and analytical data were consistent with those reported in the literature.^[8]

N-Benzylisobutyramide.



Prepared according to the standard procedure with isobutyric acid (0.26 mL) and benzylamine (0.31 mL). Kugelrohr distillation (120-130 °C, 0.4 torr) yielded 0.385 g (76.%) as a white crystalline solid: Mpt. 88.0-89.5 °C (Lit.^[1] 86.5-87.5 °C). All spectroscopic and analytical data were consistent with those reported in the literature.^[9]

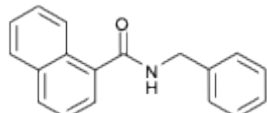
N-Benzylpivalamide.



Prepared according to the general procedure A, with pivalic acid (0.29 g) and benzylamine (0.31 mL). Kugelrohr distillation (130-140 °C, 0.4 torr) yielded 0.227 g (42%) as a colourless oil which crystallised upon standing to large colourless crystals: Mpt. 80.5-81.5 °C (Lit.^[1] <35 °C).^{*} All spectroscopic and analytical data were consistent with those reported in the literature.^[10]

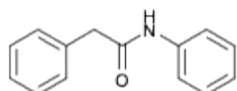
^{*}The crystallisation only occurring on standing could explain the reported melting point of <35 °C.

N-Benzyl-1-naphthamide.



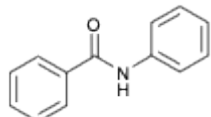
Prepared according to the general procedure A, with 1-naphthoic acid (0.49 g) and benzylamine (0.31 mL). Kugelrohr distillation (190-200 °C, 0.3-0.4 torr) yielded 0.0036 g (5%) as a white powder: Mpt. 124.0-125.0 °C. All spectroscopic and analytical data were consistent with those reported in the literature.^[11]

N-Phenyl-2-phenylacetamide.



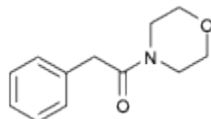
Prepared according to the general procedure A, with phenylacetic acid (0.39 g) and aniline (0.26 mL). Kugelrohr distillation (160-165°C, 0.3 torr) yielded 0.450 g (75%) as a white crystalline solid. Mpt. 116.5-118.0 °C. All spectroscopic and analytical data were consistent with those reported in the literature.^[8]

N-Phenylbenzamide.



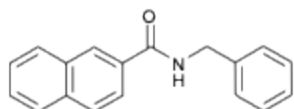
Prepared according to the general procedure A, with benzoic acid (0.34 g) and aniline (0.26 mL). Kugelrohr distillation (165-175 °C, 0.4 torr) yielded 0.083 g (15%) as a white crystalline solid: Mpt. 159.0-160.0°C (Lit.^[12] 160.0-161.0 °C). All spectroscopic and analytical data were consistent with those reported in the literature.^[13]

1-Morpholino-2-phenylethanone.



Prepared according to the general procedure A, with phenylacetic acid (0.39 g) and morpholine (0.25 mL). Kugelrohr distillation (145-160 °C, 0.3 torr) yielded 0.465 g (79%) as a white crystalline solid: Mpt. 65.0-66.0 °C. All spectroscopic and analytical data were consistent with those reported in the literature.^[14]

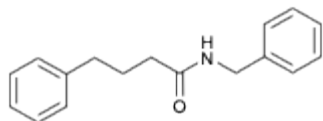
N-Benzyl-2-naphthamide



Prepared according to the general procedure A, with 2-naphthoic acid (0.49 g) and benzylamine (0.31 ml) were added for amidation. Kugelrohr distillation (190-200 °C, 0.3-0.4 torr) yielded 0.50 g (68%) as a white powder: ¹H NMR (400 MHz, CDCl₃) δ 4.72 (d, *J* 5.7, 2H), 6.54 (br s, 1H), 7.24-7.47 (m, 6H), 7.56 (p, *J* 7.2, 2H), 7.88 (m,

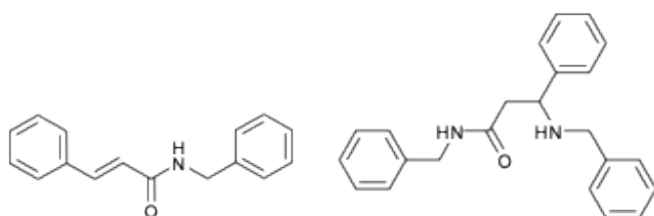
4H), 8.33 (s, 1H). All the other spectroscopic and analytical data were consistent with those reported in the literature.^[11]

N-Benzyl-4-phenylbutanamide



Prepared according to the general procedure A, with phenylbutyric acid (0.47 g) and benzylamine (0.31 ml) were added for amidation. Kugelrohr distillation (200-210 °C, 0.4 torr) yielded 0.59 g (82%) as a white solid: ¹H NMR (400 MHz, CDCl₃) δ 1.99-2.08 (m, 2H), δ 2.24 (dd, *J* 8.5, 6.8, 2H), δ 2.69 (t, *J* 7.5, 2H), δ 4.46 (d, *J* 5.7, 2H), 5.66 (br. s, 1H), 7.16-7.24 (m, 3H), 7.27-7.33 (m, 5H), 7.33-7.39 (m, 2H). All the other spectroscopic and analytical data were consistent with those reported in the literature.^[15]

N-Benzylcinnamamide and N-benzyl-3-(benzylamino)-3-phenylpropanamide



Trans-cinnamic acid (0.42 g, 2.86 mmol), polymer catalyst (75.8 mg, 5 mol%) and toluene (20 ml) were added to a 50 ml round-bottom flask. Benzylamine (0.62 ml, 5.76 mmol) was added and the resulting mixture stirred at a vigorous reflux using a Dean-Stark trap for 24 hrs. After cooling to rt, solvent was removed *in vacuo*. The resulting crude solid was redissolved in DCM or chloroform (50 ml), filtered to remove catalyst, washed with 5% HCl (3 × 20 ml), saturated NaHCO₃ (3 × 20 ml), brine (3 × 20 ml), and finally water (20 ml). Solvent was removed under reduced pressure to give the crude amide product. Kugelrohr distillation afforded two fractions:

Fraction 1 (175-185 °C, 0.3-0.4 torr); 0.37 g (55%) as a white powder; ¹H NMR (400 MHz, CDCl₃) δ 4.61 (d, *J* 5.7, 2H), 5.93 (br s, 1H), 6.43 (d, *J* 15.6, 1H), 7.30-7.42 (m, 8H), 7.48-7.56 (m, 2H), 7.71 (d, *J* 15.6, 1H). All the other spectroscopic and analytical data were consistent with those reported in the literature.^[16]

Fraction 2 (190-200 °C, 0.3-0.4 torr); 0.19 g (28%) as a pale yellow oil; ¹H NMR (400 MHz, CDCl₃) δ 1.68 (br. s, 1H), δ 2.55 (dd, *J* 15.6, 3.8, 1H), δ 2.66 (dd, *J* 15.7, 9.7, 1H), δ 3.52 (d, *J* 12.7, 1H), δ 3.65 (d, *J* 12.7, 1H), δ 4.06 (dd, *J* 9.8, 3.8, 1H), δ 4.43 (qd, *J* 14.6, 5.5, 2H), δ 7.10 (dd, *J* 6.6, 2.9, 2H), δ 7.22-7.43 (m, 13H), δ 7.52 (br. s, 1H). All the other spectroscopic and analytical data were consistent with those reported in the literature.^[17]

Stoichiometric Catalysis with React-IR Equipment monitoring.

The React-IR probe was placed in a 100 mL round-bottom azeotropic flask with a built-in Dean-stark trap. Stoichiometric loading of polymer catalyst (3.0 g, 1 equiv.) and toluene (50 mL) were added before heating up and refluxing. Then phenylacetic acid (0.78 g, 5.72 mmol, 1 equiv.) and benzylamine (0.62 mL, 5.72 mmol, 1 equiv.) were added in order, and the resulting mixture stirred for 21 hrs. After cooling to rt, the probe was removed and the solvent was removed *in vacuo*. The resulting crude solid was redissolved in DCM (50 mL), filtered to remove catalyst, washed with 5% HCl (3 × 40 mL), saturated NaHCO₃ (3 × 40 mL), brine (3 × 40 mL), and finally water (40 mL). Solvent was removed under reduced pressure to give the crude amide product. Kugelrohr distillation (170 °C, 0.2 torr) yielded 0.89 g (69%) as a white crystalline mass: Mpt. 121.0-122.5 °C (Lit.^[1] 121.0-122.0 °C). All spectroscopic and analytical data were consistent with those reported in the literature.^[7]

Recycling test of the heterogeneous catalyst 1.

To a 100 mL Radley's azeotropic round-bottom flask with a built-in Dean-Stark trap, was added carboxylic acid (1 equiv.), polymer catalyst **1** (5 mol%), and toluene (50 mL), followed by amine (1 equiv.) before the reaction

mixture stirred at a vigorous reflux for 24 hrs. After cooling to rt, the solvent was removed *in vacuo*. The resulting crude solid was redissolved in DCM (50 mL), filtered to remove the catalyst **1** (which was washed several times with toluene and dried *in vacuo* ready to reuse in the next reactions), and the filtrate washed with 5% HCl (3 × 30 mL), saturated NaHCO₃ (3 × 30 mL), brine (3 × 30 mL) and finally water (30 mL). The organic solvent was evaporated to give the crude amide product. Purifications was carried out by low pressure distillation (Kugelrohr).

Results for batch recycling of Catalyst **1**

In the first batch of reaction, an equivalent of 7.15 mmol substrates were added, with polymer catalyst **1** (189.5 mg, 0.358 mmol, 5 mol %). Catalyst **1** was isolated 185.7 mg (98% recovery) as pale yellow solid.

In the second batch of reaction, an equivalent of 7.01 mmol substrates were added, with polymer catalyst **1** (185.7 mg, 0.5351 mmol, 5 mol %). Catalyst **1** was isolated 176.4 mg (95% recovery) as pale yellow solid.

In the third batch of reaction, an equivalent of 6.66 mmol substrates were added, with polymer catalyst **1** (176.4 mg, 0.340 mmol, 5 mol %). Catalyst **1** was isolated 174.6 mg (99% recovery) as pale yellow solid.

In the fourth batch of reaction, an equivalent of 6.59 mmol substrates were added, with polymer catalyst **1** (174.6 mg, 0.337 mmol, 5 mol %). Catalyst **1** was isolated 129.2 mg (74% recovery) as pale yellow solid.

In the fifth batch of reaction, an equivalent of 4.88 mmol substrates were added, with polymer catalyst **1** (129.2 mg, 0.249 mmol, 5 mol %). Catalyst **1** was isolated 90.4 mg (70% recovery) as pale yellow solid.

Kinetic studies on the heterogeneous catalytic direct amide formation.

According to General Procedure B, up to 6 identical reactions were performed in the parallel reactor and reactions stopped individually after the prescribed reaction time. Yields were determined by the ¹H NMR analysis of the crude product isolated after work up. 10 reactions of phenylacetic acid with benzylamine were conducted which gave the following results:

Entry	Reaction Time (h)	Yield (%)
1	0.5	17
2	1	28
3	3	66
4	6	69
5	9	70
6	12	71
7	15	75
8	18	76
9	21	79
10	24	80

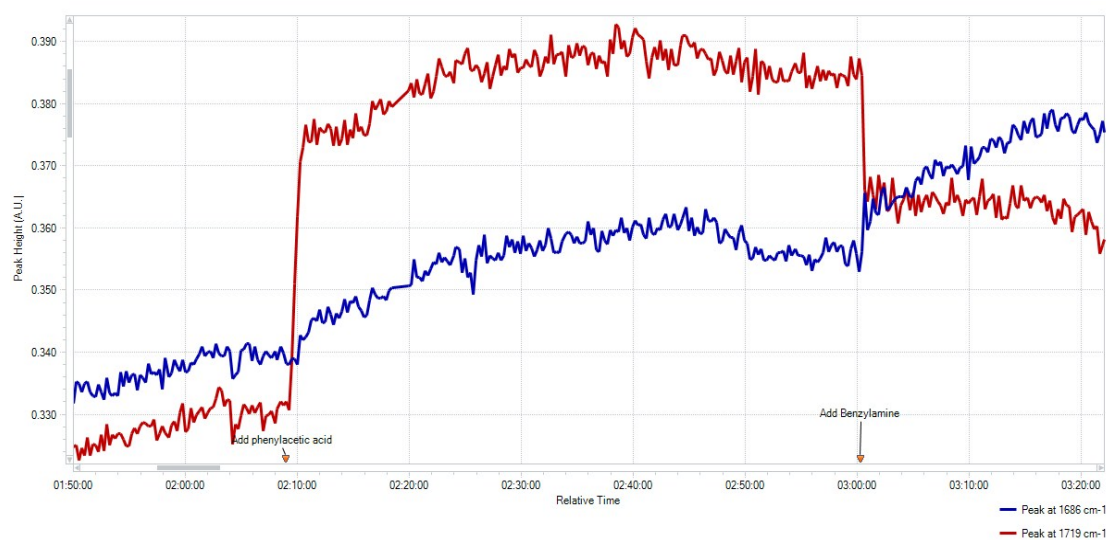
General Procedure for Flow system test

An Omnifit glass column (10 x 100 mm) was filled with a mixture of polymer catalyst **1** (6.0 g) and Celite (1.0 g), after packing adjustable end-pieces were attached and the reactor was flushed with toluene at 0.100 mL/min for 1 h before heating up to 130 °C. A solution of the carboxylic acid (14.30 mmol 1 equiv.) and amine (14.30 mmol, 1 equiv.) in toluene (250 mL) was then pumped through the column reactor at a flow rate of 0.100 mL/min and collected by an automatic sample collector based upon a setting of 100 min per fraction. The flow system was left running in automated mode overnight, and 12 fractions were collected. All the fractions were then evaporated *in vacuo* to remove the solvent before analysis of ¹H NMR which indicated the substrate conversion.

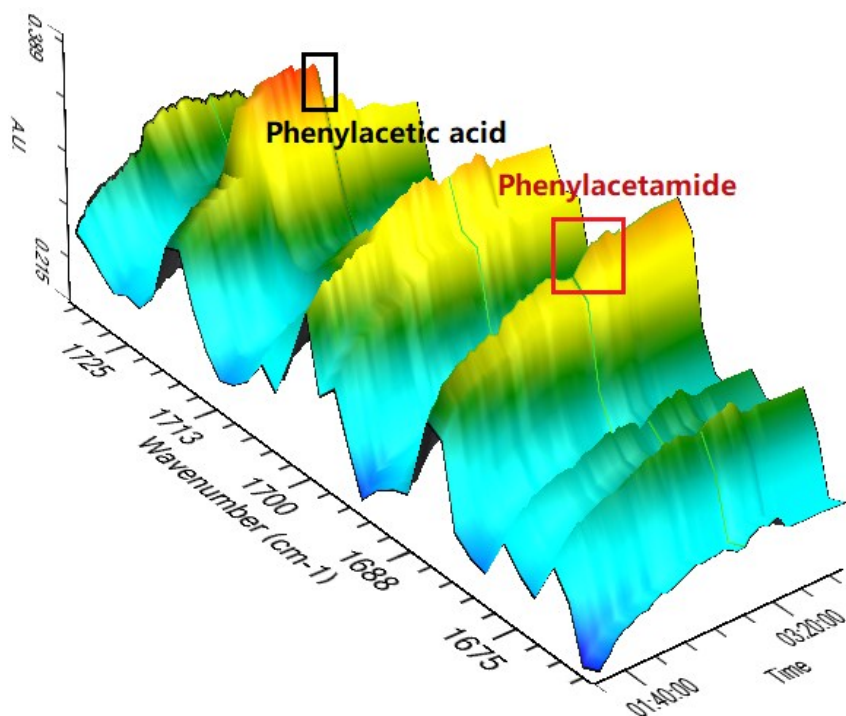
Studies on the reaction of phenylbutyric acid with benzylamine in flow

Based on the general flow procedure a 57.2 mmol/L reaction mixture was used in the test. All the conversions and throughput were determined by analysis of ^1H NMR of the crude reaction mixture.

Entry	Fraction No.	Reaction Time (min)	Conversion (%)
1	1	0-100	13
2	2	100-200	19
3	3	200-300	32
4	4	300-400	35
5	5	400-500	24
6	6	500-600	17
7	7	600-700	14
8	8	700-800	13
9	9	800-900	12
10	10	900-1000	13
11	11	1000-1100	12
12	12	1100-1200	12

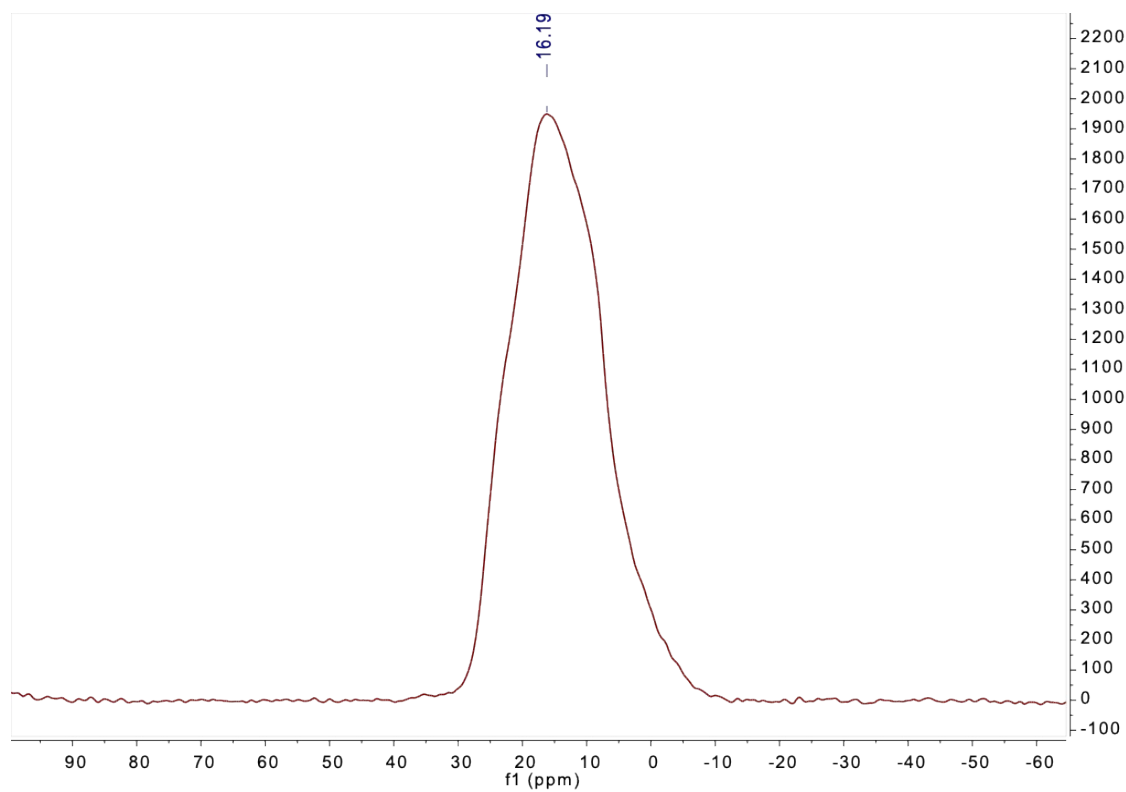


React-IR data for the reaction the reaction of phenylacetic acid with benzylamine using stoichiometric catalyst **1** in toluene at reflux

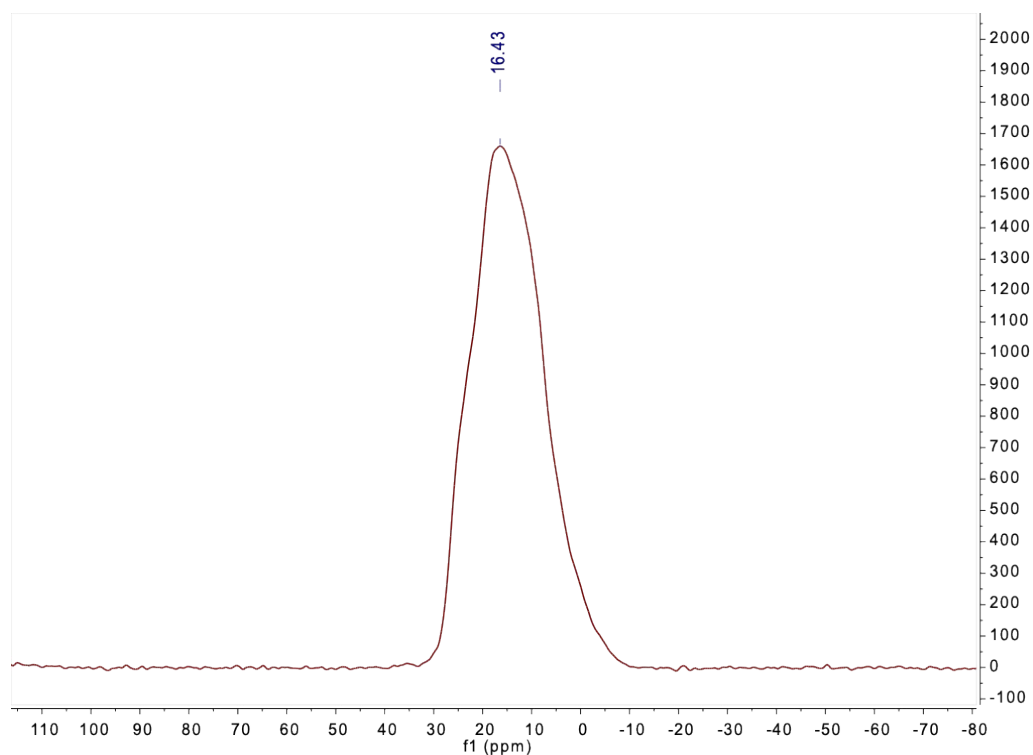


React-IR data for the reaction the reaction of phenylacetic acid with benzylamine using stoichiometric catalyst **1** in toluene at reflux.

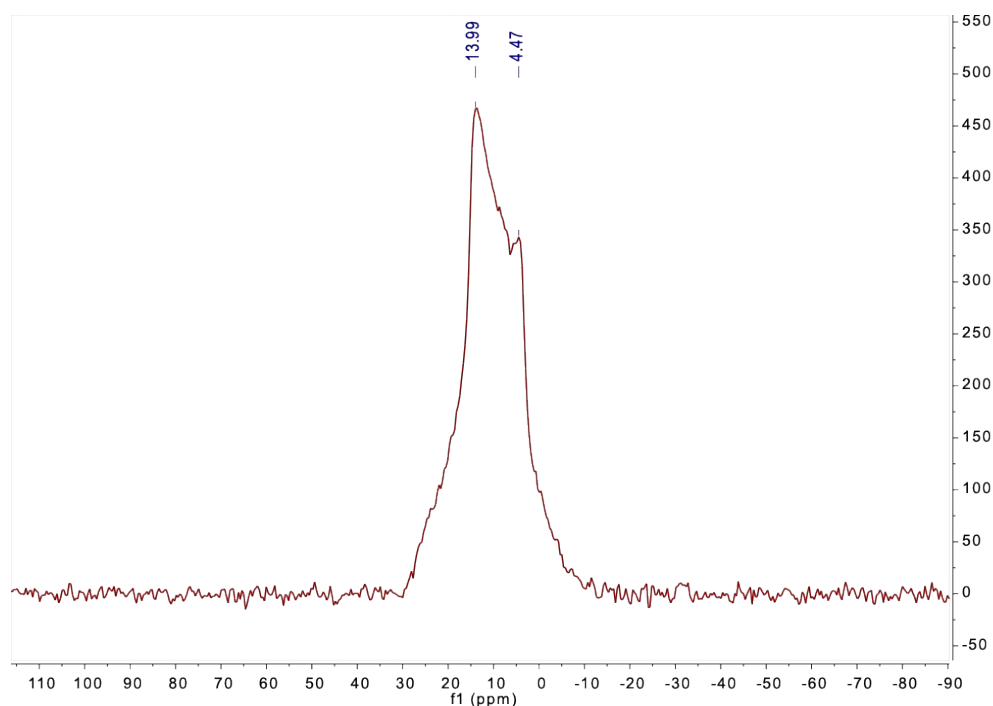
Solid-State ^{11}B NMR of polymer catalyst **1**



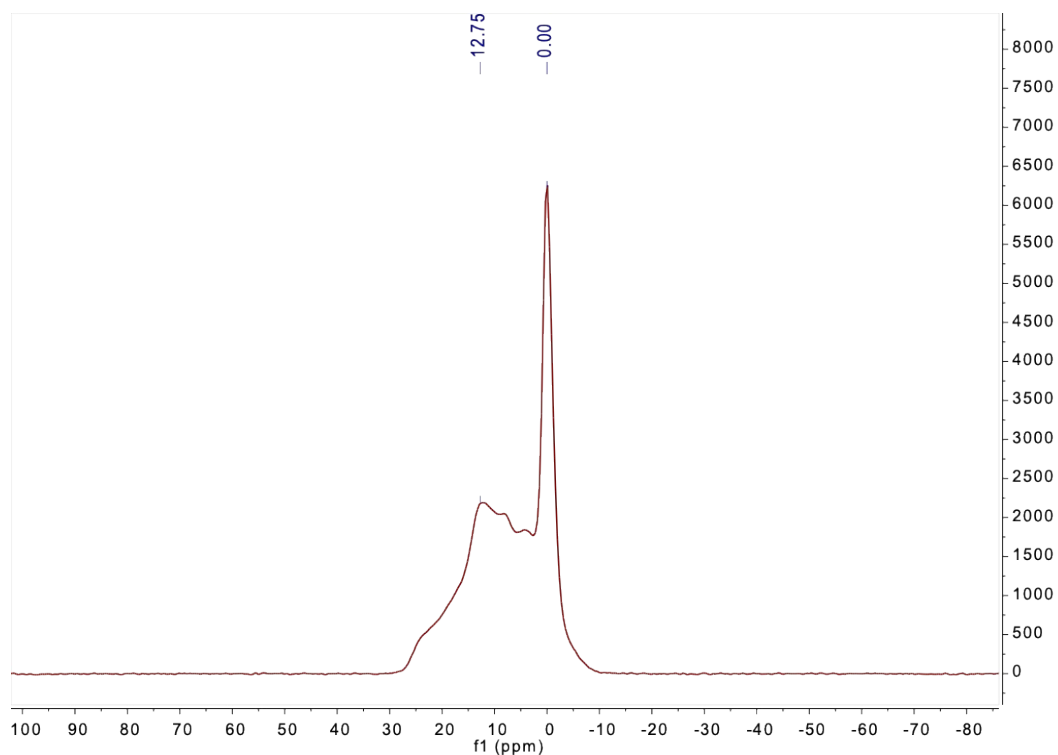
^{11}B NMR of initial polymer catalyst **1** after preparation.



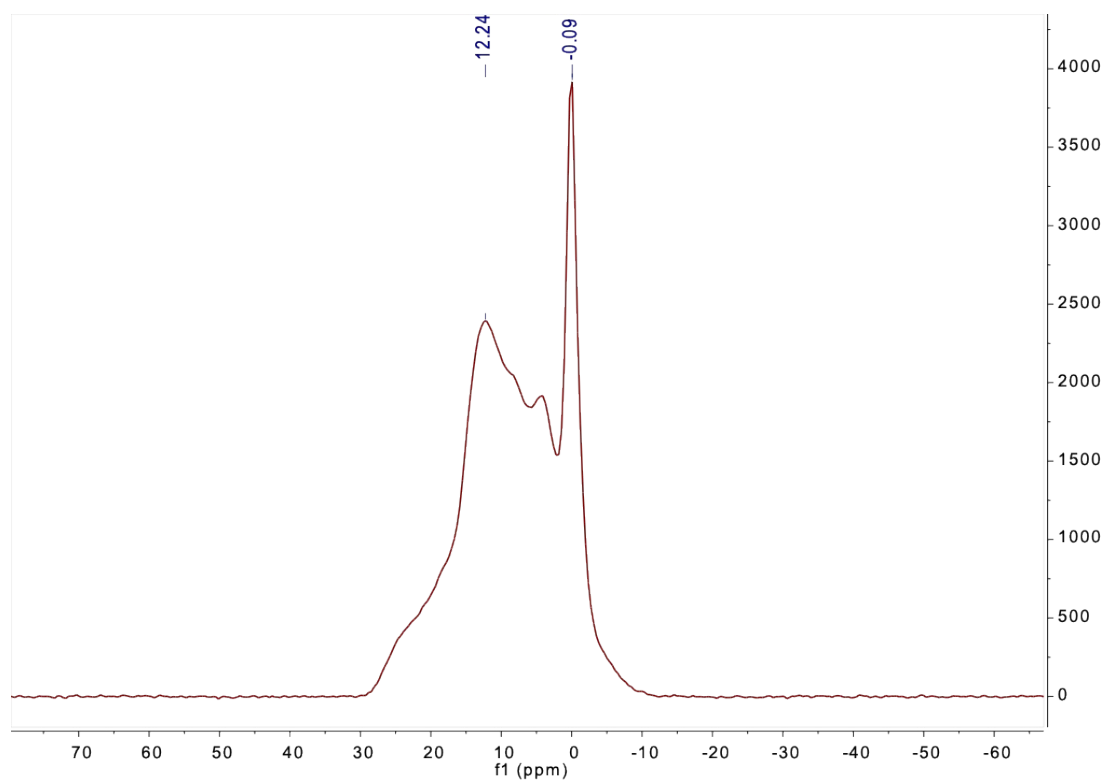
^{11}B NMR of catalyst **1** after Soxhlet extraction showing a range of boron species though centered at δ 16, ranging from 30--5 ppm, and including a boronate/boroxine shoulder around δ 25.



^{11}B NMR of recovered catalyst **1** after refluxing with phenylacetic acid in toluene, again showing a range of boron species from δ 28 to -5, but with a reduction in the boronate/boroxine shoulder around δ 25, and a considerable increase in tetrahedral boronate species centered at 5 ppm.

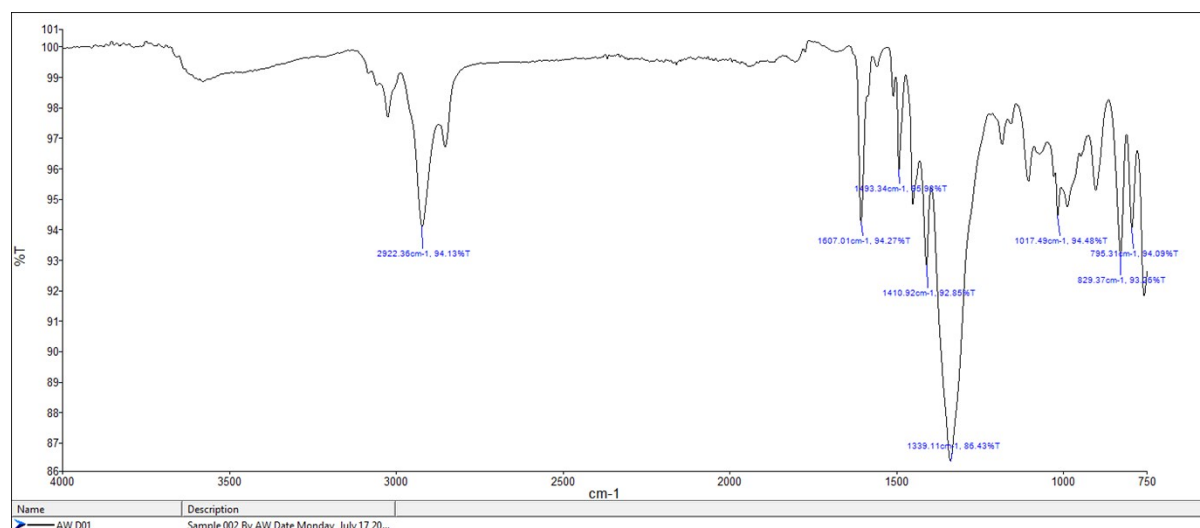


^{11}B NMR of recovered catalyst **1** after 10 min reflux with benzylamine and phenylacetic acid in toluene, with several boron species ranging from 28 to -5 ppm, with the major peak being a tetrahedral boron "ate"-complex species centered at δ 0.

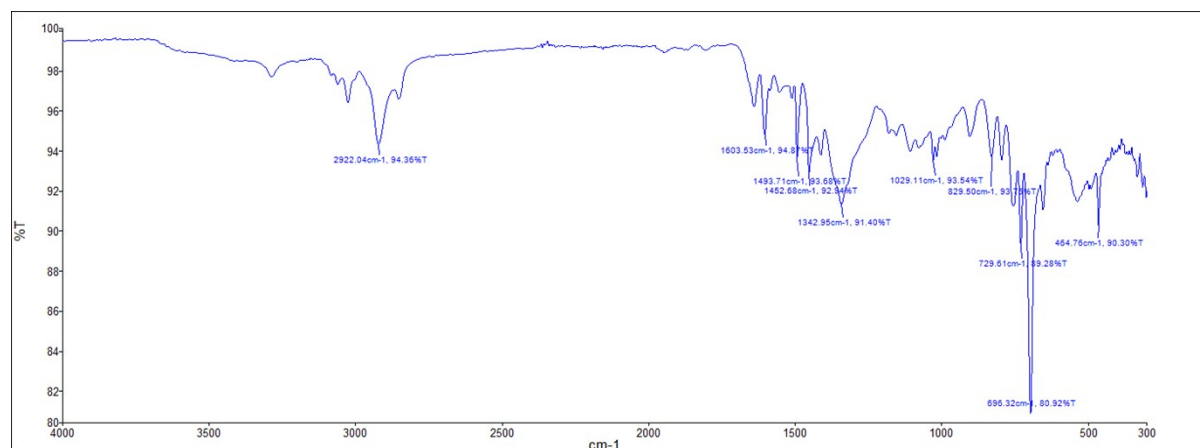


^{11}B NMR of recovered catalyst **1** after 21 h reflux with benzylamine and phenylacetic acid in toluene.

IR Spectra



Recovered catalyst **1** after Soxhlet extraction

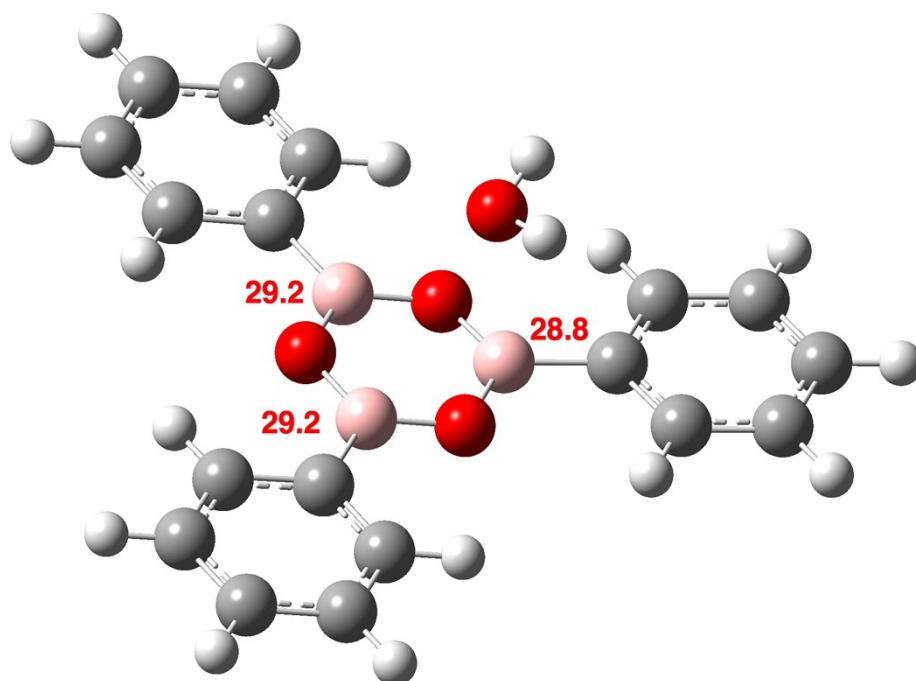


Recovered catalyst **1** after amidation

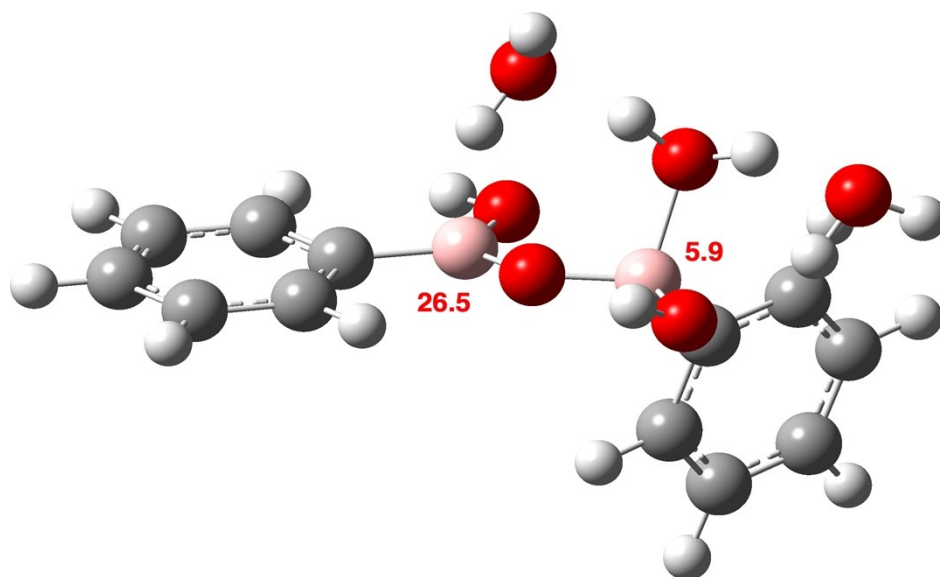
^{11}B NMR theoretical calculations

^{11}B shifts were calculated for a wB97XD/aug-cc-pvdz scrf=(cpcm,solvent=water) model according to recent procedures.¹⁸ Full data for calculations carried out to estimate the ^{11}B NMR shifts for the solid phase dehydrated catalyst system can be found at DOI: 10.14469/hpc/5030. The structural results and ^{11}B NMR shifts are shown for a single water complex of: a) phenylboronic acid derived boroxine which indicates only a weak dispersion complex with a long B-O bond of 2.77 Å, as demonstrated by calculated shifts of δ 29.8-29.3 chemical shifts for this system; and b) phenylboronic acid derived dimeric anhydride which similarly forms a weak (3.28 Å) single water complex with δ 27.1-29.1 ppm. Only if the model is enlarged to three waters does a boron-bound isomer (B-O 1.65 Å) appear as a minimum in the potential surface, with the four-coordinate boron at δ 6 and the other trigonal boron at δ 26.5. However, this isomer is 6.4 kcal/mol higher in free energy than a purely hydrogen bonded form containing only weak water-B interactions, B-O lengths 3.35 Å, δ 28.0-28.2 ppm.

a)



b)



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