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# 1 General Remarks

- <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on JEOL JMN-LA500 or 600 spectrometers operating at 500 MHz or 600 MHz (<sup>1</sup>H) respectively. Chemical shifts are reported in parts per million ( $\delta$ ) and are reported relative to internal references of the deuterated solvent (CDCl<sub>3</sub> 7.24/77.0 ppm, DMSO-d<sub>6</sub> 2.50/39.5 ppm) or tetramethylsilane (0 ppm). Structures of known compounds were confirmed by comparison with commercially available compounds or data obtained from literature. Multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.
- IR spectra were recorded on JASCO FT/IR-6100 spectrometer.
- Direct Analysis in Real Time (DART) mass spectra were recorded on JEOL JMS-T100TD mass spectrometer.
- Inductively coupled plasma (ICP) analysis was performed with Shimadzu ICPS-7510 equipment.
- Melting point was determined on a standard melting point apparatus and is uncorrected.
- STEM/EDS images were obtained using a JEOL JEM-2100F instrument operating at 200 kV. All STEM specimens were prepared by placing a drop of the suspension on carbon-coated Cu grids and dried in air (without staining).
- GC analysis was performed with Shimadzu GC-2010 instrument. Column = J & W SCIENTIFIC DB-1 0.25 mm ID, 0.25 m, 60.0 m; Gas pressure: 157.5 kPa, Total flow: 41.3 mL/min, Column flow: 0.93 mL/min, Velocity: 21.1 cm/sec; Purge flow: 3.0 mL/min; Split ratio: 40.1; Injector: 300 °C, FID: 300 °C; Column program: starting from 100 °C, 10 min hold, then 10 °C/min to 300 °C, 15 min hold.
- GCMS analysis was performed with Shimadzu GCMS-QP2010 Ultra instrument. Column = J & W SCIENTIFIC DB-1 0.25 mm ID, 0.25 m, 60.0 m; Gas pressure: 157.5 kPa, Total flow: 48.3 mL/min, Column flow: 1.10 mL/min, Velocity: 27.6 cm/sec; Purge flow: 3.0 mL/min; Split ratio: 40.1; Injector: 300 °C, FID: 300 °C; Column program: starting from 100 °C, 10 min hold, then 10 °C/min to 300 °C, 70 min hold.
- AuClPPh<sub>3</sub> and Pd(OAc)<sub>2</sub> were purchased from Strem Chemical Inc.
- NaBH<sub>4</sub> was purchased from Wako Pure Chemical Industries, recrystallised with diglyme by heating according to the literature<sup>1</sup> and stored in an argon-filled glove box. The entire recrystallisation process was carried out under argon atmosphere.
- Ketjenblack (carbon black) EC300J was purchased from Lion Corporation.
- Aqua regia for ICP sample preparation was made by mixing concentrated hydrochloric acid and concentrated nitric acid in a volume ratio of 3:1.
- Thin layer chromatography (TLC) was performed on TLC plates (TLC Silica gel 60 F<sub>254</sub> glass plate) purchased from Merck KGaA and was visualised by UV light or by staining with 5–10% phosphomolybdic acid in ethanol followed by heating.
- Silica gel 60 from Merck KGaA was used for flash column chromatography with technical grade solvents.
- Preparative TLC (PTLC) was performed using Wakogel<sup>®</sup> B-5F from Wako Pure Chemical Industries.
- Dry and deoxidized toluene was purchased from Wako Pure Chemical Industries.
- Amides used in substrate scope were recrystallised before use.
- Benzyl alcohol and benzyl alcohol analogs were distilled before use.
- MgSO<sub>4</sub> was dried by heating it with over a Bunsen burner for at least 5 minutes before it was put under reduced pressure immediately. Afterwards, it was stored under argon until used.
- All other reagents were either purchased from Tokyo Chemical Industry (TCI), Sigma-Aldrich, Kanto Chemicals or Wako Pure Chemical Industries, and used as is without further purification.

Unless otherwise stated, all reactions were carried out under argon atmosphere.

#### 2 Preparation of PI/CB-Au/Pd

#### 2-1 Preparation of co-polymer used in the fabrication of PI/CB-Au/Pd



2,2'-Azobis(4-methoxy)-2,4-dimethylvaleronitrile (V-70, 212.5 mg) was added to a stirred solution of styrene (2.4 g, 23.0 mmol), 4-vinylbenzyl glycidyl ether (4.4 g, 23.1 mmol) and 2-(2-(2-(2-(4-vinylbenzyloxy)ethoxy)ethoxy)ethoxy)ethoxy)ethanol (7.0 g, 22.6 mmol) in chloroform (12 mL). The mixture was then degassed by sonication under argon. After stirring for 48 hours at room temperature, the resulting viscous polymer solution was slowly poured into diethyl ether. The solvent layer was then decanted and the remaining precipitated polymer was

washed with diethyl ether several times. The polymer was then dissolved in THF and the same precipitation, decantation and washing procedure was repeated two more times before being dried *in vacuo* to afford the co-polymer as a colourless viscous liquid (7.4 g, 54%).<sup>2</sup> The molar ratio of the components was determined by <sup>1</sup>H NMR analysis in CDCl<sub>3</sub> (*x*: *y*: *z* = 32 : 34 : 34). Note: The stabilisers in commercially available styrene were removed by passing it through a short column of basic alumina before use.

#### 2-2 PI/CB-Au/Pd

Fabrication:



Diglyme (30 mL) and Ketjenblack EC300J (500.0 mg) were added to a 200 mL round bottom flask charged with the co-polymer (500.0 mg) and a stirring bar. Then, a diglyme solution of NaBH<sub>4</sub> (107.0 mg, 2.82 mmol) was added. The suspension was cooled in an ice-bath and stirred under open-air until the Ketjenblack was evenly dispersed. To this suspension was slowly added a diglyme solution (6 mL) of AuClPPh<sub>3</sub> (138.4 mg, 0.28 mmol) and Pd(OAc)<sub>2</sub> (63.0 mg, 0.28 mmol) mixed together. The ice-bath was removed and the mixture was allowed to stir overnight at 30 °C. Diethyl ether (200 mL) was then added dropwise over one hour and the resulting mixture was vacuum-filtered. The black solid cake obtained at the top of the funnel was rinsed carefully with diethyl ether. The solid was crushed lightly with a mortar and pestle before being transferred to a 100 mL round bottom flask. The flask was flushed with argon and then placed in an oil bath (pre-heated to 170 °C) for 4 h. After allowing the flask to cool to room temperature, THF and water (100 mL respectively) were added and the suspension was stirred vigorously overnight to remove boron. The suspension was then vacuum-filtered and the residue on top of the filter funnel was rinsed with water, THF and DCM in that order two times. The residue was then ground with a mortar and pestle before being dried *in vacuo* overnight to afford PI/CB-Au/Pd (1.01 g). Au loading: 0.240 mmol/g, Pd loading: 0.214 mmol/g.

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# Procedure for the preparation of the sample for ICP analysis:

Approximately 10 mg of PI/CB-Au/Pd measured carefully (amount measured was recorded) and heated to 200 °C in H<sub>2</sub>SO<sub>4</sub> (1 mL). HNO<sub>3</sub> was added dropwise until all solid had dissolved and no more brown fumes were observed. The mixture was cooled to room temperature and aqua regia (1 mL) was added slowly. The resulting mixture was made up to 50 mL with water in a volumetric flask and the resulting solution was subjected to ICP analysis.

# STEM/EDS analysis:

STEM analysis indicated that metal nanoparticle size distribution was good and EDS mapping analysis indicated that alloyed bimetallic Au/Pd nanoparticles had formed.







⊐ 200 nm

An M - 200 nm IMG1

I h9

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EDS Line analysis indicated that the ratio of Au:Pd within the bimetallic nanoparticles is approximately 1:1.



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# 3 Procedure for the *N*-alkylation of primary amides and characterisation of products

# 3-1 General procedure for the *N*-benzylation of benzamide (GC analysis)



A Carousel® tube (image on the left) was charged with benzamide (30.3 mg, 0.25 mmol), PI/CB-Au/Pd (11.1 mg, 0.0025 mmol wrt Au) and a stirring bar. The carousel tube was then placed in an argon-filled glovebox. In the glovebox, additives, if any, were added (e.g.  $Ca(OTf)_2$  (4.2 mg, 0.0125 mmol)) and the tube was sealed tightly with a septum. The septum was also taped tightly to the tube and the tube was then removed from the glovebox. Benzyl alcohol (81.1 mg, 0.75 mmol) and toluene (0.5 mL) were added, and then the part of the septum where the syringe needle went through was covered with tape. The tube was then placed on a Carousel® (parallel synthesiser from Radleys) that had been preheated to 150 °C and it was left to stir for 18 hours, after which it was allowed to cool to room temperature. Ethyl acetate was added to dilute the mixture and the GC internal standard (dodecane) was added. An aliquot was passed through Celite into a GC phial and the clear solution was subjected to GC analysis.

# **3-2** N-Alkylation of primary amides and characterisation of products

General procedure as exemplified using benzamide and benzyl alcohol:



A Carousel® tube was charged with benzamide (1a, 30.5 mg, 0.25 mmol), PI/CB-Au/Pd (10.6 mg, 0.0025 mmol wrt Au) and a stirring bar. The carousel tube was then placed in an argon-filled glovebox. In the glovebox,  $Ba(OTf)_2$  (5.1 mg, 0.0117 mmol) was added and the tube was sealed tightly with a septum. The septum was also taped tightly to the tube and the tube was then removed from the glovebox. Benzyl alcohol (2a, 81.0 mg, 0.75 mmol) and deoxidised toluene (0.5 mL) were added, and then the part of the septum where the syringe needle went through was covered with tape. The tube was then placed on a Carousel® (parallel synthesiser from Radleys) that had been preheated to 150 °C and it was left to stir for 18 hours, after which it was allowed to cool to room temperature. Ethyl acetate was added to dilute the mixture and the catalyst was filtered off via vacuum filtration. The filtrate was concentrated and the crude obtained was purified by preparative TLC. After eluting with ethyl acetate, the solvent was removed via reduced pressure and then the pure product was dried under high vacuum for more than 1 day. White solid obtained (3aa, 50.5 mg, 95%).

# <u>*N*-benzylbenzamide (**3aa**)<sup>3</sup></u>

120.9, 44.1.

<u>*N*-benzyl-4-methylbenzamide (**3ba**)<sup>3</sup></u>

Used: 33.7 mg (0.25 mmol) of **1b**. Obtained: 54.8 mg (98%) of **3ba** as a white solid. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  7.69 (d, J = 7.8 Hz, 2H), 7.37–7.34 (m, 4H), , 7.30–7.28 (m, 1H), 7.22 (d, J = 7.7 Hz, 2H), 6.44 (br s, 1H), 4.63 (d, J = 5.4 Hz, 2H), 2.39 (s, 3H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  167.3, 141.9, 138.3, 131.5, 129.2, 128.7, 127.9, 127.5, 126.9, 44.0, 21.4.

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#### <u>N-benzyl-4-methoxybenzamide $(3ca)^4$ </u>

Used: 37.8 mg (0.25 mmol) of 1c. Obtained: 60.9 mg (quant) of 3ca as a white solid. <sup>1</sup>H **NMR (600 MHz, CDCl<sub>3</sub>):**  $\delta$  7.76 (d, J = 8.3 Hz, 2H), 7.34–7.29 (m, 4H), 7.31–7.28 (m, 1H), 6.91 (d, J = 8.3 Hz, 2H), 6.40 (br s, 1H), 4.63 (d, J = 5.6 Hz, 2H), 3.84 (s, 3H); <sup>13</sup>C **NMR** (150 MHz, CDCl<sub>3</sub>): δ 166.8, 162.2, 138.4, 128.7, 127.9, 127.5, 126.6, 113.7, 55.4, 44.0.

# *N*-benzyl-2-ethoxybenzamide (**3da**)

Used: 41.1 mg (0.25 mmol) of 1d. Obtained: 56.5 mg (89%) of 3da as a colourless oil.  $^{1}$ H **NMR** (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.34 (br s, 1H), 8.25 (dd, J = 7.8, 1.9 Hz, 1H), 7.42–7.34 (m, 5H), 7.29–7.26 (m, 1H), 7.06 (t, J = 7.5 Hz, 1H), 6.91 (d, J = 8.3 Hz, 1H), 4.66 (d, J = 5.4 Hz, 2H), 4.10 (q, J = 7.0 Hz, 2H), 1.31 (t, J = 7.0 Hz, 3H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$ 165.1, 156.9, 138.4, 132.6, 132.2, 128.5, 127.7, 127.3, 121.2, 121.1, 112.1, 64.5, 43.9, 14.5; HRMS

(**DART**): calculated for  $C_{16}H_{18}NO_2^+$  [*M*+H<sup>+</sup>] 256.13375, found 256.13403; **IR (neat)**: 3388, 2980, 1654, 1601, 1531, 1452, 1297, 1235, 1162, 1116, 1035, 755, 700 cm<sup>-1</sup>.

# *N*-benzyl-salicylamide $(3ea)^5$



Used: 34.5 mg (0.25 mmol) of 1e. Obtained: 30.2 mg (53%) of 3ea as a white solid. <sup>1</sup>H **NMR** (500 MHz, CDCl<sub>3</sub>):  $\delta$  12.31 (s, 1H), 7.42–7.32 (m, 7H), 7.00 (dd, J = 8.4, 0.7 Hz, 1H), 6.83 (ddd, J = 8.1, 7.0, 0.9 Hz, 1H), 6.57 (br s, 1H), 4.63 (d, J = 5.7 Hz, 2H); <sup>13</sup>C NMR (**125 MHz, CDCl**<sub>3</sub>): δ 169.8, 161.6, 137.4, 134.3, 128.9, 127.9, 125.3, 118.6, 114.0, 43.6.

<u>N-benzyl-4-fluorobenzamide (**3fa**)<sup>6</sup></u>

Used: 34.6 mg of 1f. Obtained: 51.3 mg (90%) of 3fa as a white solid. <sup>1</sup>H NMR (600 **MHz, CDCl<sub>3</sub>**):  $\delta$  7.81–7.79 (m, 2H), 7.38–7.30 (m, 5H), 7.10 (t, J = 8.5 Hz, 2H), 6.37 (br s, 1H), 4.64 (d, J = 5.6 Hz, 2H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  166.3, 164.7 (d, J =248.3 Hz), 138.0, 130.51, 129.3 (d, J = 8.5 Hz), 128.8, 128.0, 127.7, 115.6 (d, J = 21.7 Hz), 44.2; <sup>19</sup>F NMR (**600 MHz, CDCl<sub>3</sub>**): *δ*-108.0.

# <u>*N*-benzylpicolinamide $(3ga)^4$ </u>

Used: 30.8 mg (0.25 mmol) of 1g and 135.1 mg (1.25 mmol) of 2a. Obtained: 33.6 mg (63%) of **3ga** as an off-white solid. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  8.52 (d, J = 4.8 Hz, 1H), 8.40 (br s, 1H), 8.24 (d, J = 7.8 Hz, 1H), 7.85 (td, J = 7.7, 1.7 Hz, 1H), 7.42 (ddd, J = 7.6, 4.7, 1.1 Hz, 1H), 7.38–7.26 (m, 5H), 4.68 (d, J = 6.1 Hz, 2H); <sup>13</sup>C NMR (125 MHz, **CDCl**<sub>3</sub>): δ 164.2, 149.8, 148.0, 138.2, 137.3, 128.7, 127.8, 127.4, 126.2, 122.3, 43.4.

# N-benzylnicotinamide (**3ha**)<sup>7</sup>

Used: 30.8 mg (0.25 mmol) of 1h with twice the amount of catalyst and Ba(OTf)<sub>2</sub>. Obtained: 28.1 mg (52%) of **3ha** as a white solid. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.94 (br s, 1H), 8.63 (br s, 1H), 8.13 (d, J = 7.9 Hz, 1H), 7.35–7.27 (m, 6H), 7.09 (br s, 1H), 4.62 (d, J = 5.5 Hz, 2H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  165.4, 151.9, 147.8, 137.7, 135.4, 130.1, 128.7, 127.9, 127.7, 123.5, 44.1.

# <u>*N*-benzylacetamide $(3ia)^4$ </u>

Used: 14.9 mg (0.25 mmol) of 1i and 134.3 mg (1.24 mmol) of 2a. Obtained: 28.8 mg (77%) of **3ia** as a white solid. <sup>1</sup>H NMR (**500** MHz, CDCl<sub>3</sub>):  $\delta$  7.34–7.26 (m, 5H), 6.10 (br s, 1H), 4.40 (d, J = 5.7 Hz, 2H), 1.99 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  170.0, 138.2, 128.6, 127.8, 127.4, 43.6, 23.1.

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#### <u>N-benzylhexanamide</u> $(3ja)^8$

Used: 28.7 mg (0.25 mmol) of 1j. Obtained: 48.8 mg (95%) of 3ja as a white solid. <sup>1</sup>H **NMR (500 MHz, CDCl<sub>3</sub>):**  $\delta$  7.33–7.24 (m, 5H), 6.14 (br s, 1H), 4.39 (d, J = 5.8 Hz, 2H), 2.18 (t, *J* = 7.7 Hz, 2H), 1.66–1.60 (m, 2H), 1.33–1.26 (m, 4H), 0.88 (t, *J* = 6.7 Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 173.1, 138.4, 128.5, 127.6, 127.3, 43.4, 36.6, 31.4, 25.4, 22.3, 13.9.

# N-benzylisobutyramide (**3ka**)<sup>9</sup>

Used: 21.5 mg (0.25 mmol) of 1k. Obtained: 41.1 mg (94%) of 3ka as a white solid. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.32–7.24 (m, 5H), 6.08 (br s, 1H), 4.40 (d, J = 5.7 Hz, 2H), 2.39 (m, J= 6.8 Hz, 1H), 1.16 (d, J = 6.9 Hz, 6H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  176.8, 138.5, 128.6, 127.6, 127.3, 43.3, 35.5, 19.5.

# *N*-benzylpivalamide $(3la)^{10}$

Used: 25.6 mg (0.25 mmol) of 11. Obtained: 43.6 mg (90%) of 3la as a white solid. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.35–7.25 (m, 5H), 5.96 (br s, 1H), 4.44 (d, J = 5.6 Hz, 2H), 1.23 (s, 9H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 178.3, 138.6, 128.7, 127.6, 127.4, 43.5, 38.7, 27.6.

# *N*-benzyl-2-phenylacetamide $(3ma)^8$

Used: 33.9 mg (0.25 mmol) of 1m. Obtained: 51.6 mg (91%) of 3ma as a white solid. <sup>1</sup>H **NMR (500 MHz, CDCl<sub>3</sub>):**  $\delta$  7.34–7.22 (m, 8H), 7.16 (d, J = 7.4 Hz, 2H), 5.88 (br s, 1H), 4.39 (d, J = 5.8 Hz, 2H), 3.59 (s, 2H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  170.8, 138.1, 134.7, 129.4, 129.0, 128.6, 127.4, 127.33, 127.30, 43.7, 43.5.

# *N*-benzylcyclohexanecarboxamide $(3na)^4$

Used: 32.1 mg (0.25 mmol) of 1n. Obtained: 57.1 mg (quant) of 3na as a white solid. <sup>1</sup>H **NMR** (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.33–7.23 (m, 5H), 6.04 (br s, 1H), 4.40 (d, J = 5.8 Hz, 2H), 2.11 (tt, J = 11.9, 3.6 Hz, 1H), 1.88–1.85 (m, 2H), 1.80–1.76 (m, 2H), 1.67–1.64 (m, 1H), 1.49–1.41 (m, 2H), 1.29–1.18 (m, 3H);<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 175.9, 138.5, 128.5, 127.6, 127.3, 45.4, 43.2, 29.6, 25.6.

# N-(4-methylbenzyl)benzamide (**3ab**)<sup>7</sup>

Used: 30.3 mg (0.25 mmol) of 1a and 91.2 mg (0.75 mmol) of 2b. Obtained: 56.9 mg (quant) of **3ab** as a white solid. <sup>1</sup>**H** NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.78 (d, J = 7.8 Hz, 2H), 7.50–7.47 (m, 1H), 7.42–7.39 (m, 2H), 7.24 (d, J = 7.7 Hz, 2H), 7.15 (d, J = 7.7 Hz, 2H), 6.50 (br s, 1H), 4.58 (d, J = 5.6 Hz), 2.34 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  167.3, 137.3, 135.1, 134.4, 131.4, 129.4, 128.5, 127.9, 126.9, 43.8, 21.1.

# *N*-((methyl 4-carboxylate)benzyl)benzamide (**3ad**)

Used: 30.6 mg (0.25 mmol) of **1a** and 124.2 mg (0.75 mmol) of **2d**. Obtained: 41.1 mg (61%) of 3ad as a white solid after two purifications. However, a small amount (ratio of impurity to product is 0.065 : 1) of 2d still remained in the product as an impurity. <sup>1</sup>**H NMR (500 MHz, CDCl<sub>3</sub>):**  $\delta$  7.98 (d, J = 8.1 Hz, 2H), 7.81 (d, J = 7.8

Hz, 2H), 7.51–7.49 (m, 1H), 7.43–7.37 (m, 4H), 6.83 (br s, 1H), 4.67 (d, J = 5.9 Hz, 2H), 3.90 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 167.5, 166.8, 143.5, 134.0, 131.7, 130.0, 129.3, 128.6, 127.5, 127.0, 52.1, 43.6; **HRMS (DART):** calculated for C<sub>16</sub>H<sub>16</sub>NO<sub>3</sub><sup>+</sup> [*M*+H<sup>+</sup>] 270.11302, found 270.11295; **IR (KBr):** 3298, 1713,  $1639, 1543, 1317, 1283, 1113, 754, 698 \text{ cm}^{-1}; \text{ m.p.} = 142-146 \text{ }^{\circ}\text{C}.$ 

# N-(4-methylbenzyl)hexanamide (3jb)

Used: 28.6 (0.25 mmol) of **1j** and 91.9 mg (0.75 mmol) of **2b**. Obtained: 47.1 mg (86%) of **3jb** as a white solid. <sup>1</sup>H NMR (**500** MHz, CDCl<sub>3</sub>):  $\delta$  7.15 (q, *J* = 7.8 Hz, 4H), 5.83 (br s, 1H), 4.38 (d, *J* = 5.6 Hz, 2H), 2.33 (s, 3H), 2.18 (t, *J* = 7.7 Hz, 2H), 1.64 (m, *J* = 7.3 Hz, 2H), 1.33–1.28 (m, 4H), 0.89 (t, *J* = 6.7 Hz, 3H); <sup>13</sup>C NMR (**125** MHz, CDCl<sub>3</sub>):  $\delta$  172.9, 137.1, 135.4, 129.3, 127.8, 43.3, 36.7, 31.4, 25.4, 22.3, 21.0, 13.9; HRMS (DART): calculated for C<sub>14</sub>H<sub>22</sub>NO<sup>+</sup> [*M*+H<sup>+</sup>] 220.17014, found 220.16931; **IR** (**KBr**): 3291, 2953, 2928, 2869, 1634, 1545, 1462, 1422, 1214, 803, 719 cm<sup>-1</sup>; **m.p.** = 63–65 °C.

# N-(4-methoxybenzyl)hexanamide (3jc)



Used: 29.0 mg (0.25 mmol) of **1j** and 104.1 (0.75 mmol) of **2c**. Obtained: 26.0 mg (44%) of **3jc** as a white solid. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.20 (d, J = 8.4 Hz, 2H), 6.86 (d, J = 8.4 Hz, 2H), 5.78 (br s, 1H), 4.36 (d, J = 5.6 Hz, 2H),

3.79 (s, 3H), 2.18 (t, J = 7.6 Hz, 2H), 1.64 (m, J = 7.3 Hz, 2H), 1.34–1.28 (m, 4H), 0.89 (t, J = 6.7 Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  172.9, 158.9, 130.5, 129.1, 114.0, 55.2, 43.0, 36.7, 31.4, 25.4, 22.4, 13.9; HRMS (DART): calculated for C<sub>14</sub>H<sub>22</sub>NO<sub>2</sub><sup>+</sup> [*M*+H<sup>+</sup>] 236.16505, found 236.16484; **IR (KBr):** 3290, 2954, 2930, 2855, 1632, 1554, 1513, 1435, 1255, 1174, 1110, 1031, 814, 758 cm<sup>-1</sup>; **m.p.** = 86–89 °C.

# <u>N-((methyl 4-carboxylate)benzyl)hexanamide (3jd)</u>



Used: 28.9 mg (0.25 mmol) of **1j** and 124.5 (0.75 mmol) of **2d**. Obtained: 45.1 mg (68%) of **3jd** as a white solid. <sup>1</sup>**H NMR (500 MHz, CDCl<sub>3</sub>):**  $\delta$  7.96 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 6.28 (br s, 1H), 4.46 (d, J = 6.0 Hz, 2H), 3.90 (s, 3H), 2.22 (t, J = 7.4 Hz, 2H), 1.65 (m, J = 7.7 Hz, 2H), 1.32–1.28 (m,

4H), 0.89 (t, J = 6.6 Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  173.3, 166.8, 143.8, 129.8, 129.1, 127.4, 52.0, 43.0, 36.5, 31.4, 25.4, 22.3, 13.9; HRMS (DART): calculated for C<sub>15</sub>H<sub>22</sub>NO<sub>3</sub><sup>+</sup> [*M*+H<sup>+</sup>] 264.15997, found 264.15866; **IR (KBr)**: 3289, 2954, 2929, 2869, 1719, 1639, 1548, 1433, 1284, 1221, 1191, 1117, 1021, 851, 758, 699 cm<sup>-1</sup>; **m.p.** = 87–90 °C.

# 3-3 Recovery and reuse of catalyst & leaching test

At the end of the reaction, the Carousel<sup>®</sup> tube was removed from the Carousel<sup>®</sup> parallel synthesiser and allowed to cool to room temperature. The crude (with catalyst) was then diluted with ethyl acetate and spiked with dodecane (GC internal standard). An aliquot was passed through a thin pad of Celite into a GC vial for GC analysis. The remaining solution/suspension was vacuum filtered carefully with 8 mm filter paper (made for the Kiriyama funnel) to separate the catalyst from the organic compounds. The catalyst was then washed carefully with ethyl acetate on top of the funnel (with the vacuum still turned on) and then dried *in vacuo* while it was still on the filter paper and funnel. After 1 day, the recovered catalyst was transferred carefully to a new Carousel<sup>®</sup> tube for the next run. In the case of  $Ba(OTf)_2$ , an appropriate amount of additional  $Ba(OTf)_2$  was added in each run. On the other hand, in the case of  $Ca(OTf)_2$ , no additional  $Ca(OTf)_2$  was added in the subsequent runs after the first.

For the reactivation of the catalyst, after the transfer of the recovered catalyst to a new Carousel® tube, the catalyst was heated by lowering the tube (unsealed) into a 170 °C oil bath for 5 hours and then cooled to room temperature before reagents were added.

The scale of the reaction was changed according to the amount of catalyst recovered from each run.

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<sup>[a]</sup> Determined by GC analysis with dodecane as the internal standard. <sup>[b]</sup> No leaching of Au or Pd was detected (under detection limit; determined by ICP analysis). <sup>[c]</sup> The recovered catalyst from the previous run was reactivated before use. <sup>[d]</sup> Recovered catalyst was treated with DCM and no additional Lewis acid was added for the new run.

# Work-up procedures using only dichloromethane:

The crude mixture (with catalyst) was diluted with dichloromethane and dodecane (GC internal standard) was added. An aliquot was passed through a thin pad of Celite into a GC vial for GC analysis. The remaining solution/suspension was vacuum-filtered carefully with 8 mm filter paper (made for the Kiriyama funnel) to separate the catalyst from the organic compounds. The catalyst was then washed carefully with dichloromethane on top of the funnel (with the vacuum still turned on) and then dried *in vacuo* while it was still on the filter paper and funnel. The subsequent procedures are the same as those described above.

# Determination of metal(s) leaching during reaction

The filtrate obtained from each run was concentrated and then diluted with a small amount of MeOH. The methanol solution was then passed through a membrane filter (0.25 or 0.45  $\mu$ m) into a new test tube. The solvent was then removed under reduced pressure. The solid obtained in the test tube was then heated to 200 °C and 0.2 mL of concentrated H<sub>2</sub>SO<sub>4</sub> was added. After further heating for 1 hour, drops of concentrated HNO<sub>3</sub> were added at regular intervals (45~60 min) until the resulting solution was lightly coloured (yellow or orange, not brown) and clear. Brown fumes should not be observed at this point when addition HNO<sub>3</sub> is added. If brown fumes are still observed, the addition of HNO<sub>3</sub> at regular intervals should be continued. To the cooled clear solution obtained, 0.2 mL of aqua regia was added and the resulting mixture was shaken

Io the cooled clear solution obtained, 0.2 mL of aqua regia was added and the resulting mixture was shaken lightly at first and then more vigorously. It was then made up to 10 mL with water and the resulting diluted solution was filtered into a vial to remove any remaining solids. The clear solution was then subjected to ICP analysis.

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# 4 Additional data

# 4-1 Screening of PI/CB catalysts

O Ph → NH <sub>2</sub> + HO → Ph <b>1a</b> (0.25 mmol) <b>2a</b> (1 mL)	PI/CB-M catalyst additive neat, 150 °C, Ar, 18 h Ph	N ^ Ph H aa
M <sup>[a]</sup>	additive	yield <sup>[b]</sup> [%]
Ir, Ru, Rh, Ni or Co	_	n.d. <sup>[c]</sup>
Au	_	$n.d.^{[c]}$
Pd	_	trace <sup>[c]</sup>
Au	_	0
Pd	_	7
Au (2 mol%) + Pd (2 mol%)	_	24
Au/Pd ( $Au:Pd = 1:1$ )	_	43
Au/Pd (Au:Pd = 1:1)	MgSO <sub>4</sub> (50 mg)	89
_	$MgSO_4$ (50 mg)	0
_	_	0
	$\begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \begin{array}{c} \end{array} \\ \begin{array}{c} \end{array} \\ \begin{array}{c} \end{array} \\ \begin{array}{c} \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \end{array} \\ $	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$

[a] Catalyst loading was set to 2 mol%. In the case of bimetallic catalysts, the catalyst loading was set to 2 mol% with respect to the first metal stated. [b] Determined by GC analysis with dodecane as the internal standard. [c] Determined by GCMS analysis of crude after the stipulated reaction time (n.d. = not detected).[d] Deoxidised benzyl alcohol was used.

# 4-2 Optimisation with MgSO<sub>4</sub>

	0	P	I/CB-Au/Pd (y mol% Au) MgSO <sub>4</sub>	O II	
	Ph <sup></sup> NH <sub>2</sub> <b>1a</b> (0.25 mmol)	+ HO Ph 2a (x eq)	toluene (C = z M) 150 °C (reflux), Ar, 18 h	Ph <sup>M</sup> N <sup>Ph</sup> H <b>3aa</b>	
entry	X	у	MgSO <sub>4</sub>	Z	yield <sup>[a]</sup> [%]
1 <sup>[b]</sup>	4	2	50 mg	0.25	90
2	4	1	50 mg	0.25	76
3	4	2	25 mg	0.25	75
4	4	2	10 mg	0.25	55
5 <sup>[c]</sup>	4	2	50 mg	0.25	95
6	4	2	50 mg	0.5	quant
7 <sup>[d]</sup>	4	1	50 mg	0.5	quant
8	3	1	50 mg	0.5	91
9	2	1	50 mg	0.5	59
10	1.1	1	50 mg	0.5	33

[a] Determined by GC analysis with dodecane as the internal standard. [b] Average of 3 experiments. [c] Reaction time = 24 hours. [d] Average of 2 experiments.

#### 4-3 Screening of additives

		0	PI/CB-Au/Pd (1 mol% Au) additive	0 U
		Ph NH <sub>2</sub> + HO Ph	toluene (C = 0.5 M)	Ph N Ph
		1a 2a	reflux, Ar, 18 h	⊣ 3aa
		(0.25 mmol) (X eq)		
ontry	additivo	amount	<b>Y</b> – $\lambda^{[a]}$	<b>Y</b> - 2 <sup>[a]</sup>
entry	addilive	anount	<b>X</b> - 4	<b>X - 5</b> <sup>-1</sup>
1 <sup>10</sup>	MgSO₄	1.66 eq	quant	91
2	$MgX_2$ (X = FI, CI, Br)	1.66 eq	1–17	-
3	MgO	1.66 eq	31	-
4	Mg(OH) <sub>2</sub>	1.66 eq	31	-
5	Mg(OTf) <sub>2</sub>	1.66 eq	97	-
6	Mg(OTf) <sub>2</sub>	0.5 eq	quant	-
7	Mg(OTf) <sub>2</sub>	5 mol%	quant	quant (64) <sup>[d]</sup>
8	Ca(OTf) <sub>2</sub>	5 mol%	99	quant (63) <sup>[d]</sup>
9	Ba(OTf) <sub>2</sub>	5 mol%	98	quant (95) <sup>[c]</sup> (85) <sup>[d]</sup> (94) <sup>[e]</sup>
10	LiOTf	5 mol%	quant	90
11	NaOTf	5 mol%	98	-
12	KOTf	5 mol%	73	-
13	Sc(OTf)₃	5 mol%	98	92
14	Yb(OTf) <sub>3</sub>	5 mol%	quant	quant
15	TfOH	5 mol%	70	-
16 <sup>[f]</sup>	MS 3A or MS 4A	20 mg	<10	-
17 <sup>[f]</sup>	MS 5A	20 mg	87	-
18	-	-	50	-

[a] Yield was determined by GC analysis with dodecane as the internal standard. [b] Average of 2 experiments. [c] 2.5 eq of benzyl alcohol were used. [d] GC yields obtained when the reaction was conducted at 120 °C (hot plate temperature), [e] 4-Methylbenzyl alcohol used as the substrate; a 5:1 ratio of toluene: $H_2O$  was used as the solvent, [f] Catalyst loading: 2 mol% Au; solvent: xylene (C = 0.25 M).

#### 4-4 Possible disproportionation-like reaction during the initiation stages of the reaction

 $HO \frown Ph + HO \frown Ph \longrightarrow O \frown Ph + Me_{Ph} + H_2O$ 

# 4-5 Control experiment (1) – Reaction with water



A Carousel® tube was charged with PI/CB-Au/Pd (12.0 mg, 0.0025 mmol wrt Au), 4-Methylbenzyl alcohol (99.6 mg, 0.84 mmol), benzamide (33.8 mg, 0.28 mmol) and a stirring bar. The carousel tube was then placed in an argon-filled glovebox. In the glovebox,  $Ba(OTf)_2$  (5.7 mg, 0.013 mmol) was added and the tube was sealed tightly with a septum. The septum was also taped tightly to the tube and the tube was then removed from the glovebox. Deoxidized toluene (0.5 mL) and water (0.1 mL) were added, and then the part of the septum where the syringe needle went through was covered with tape. The tube was then placed on a Carousel® (parallel synthesiser from Radleys) that had been preheated to 150 °C and it was left to stir for 18 hours, after which it was allowed to cool to room temperature. Ethyl acetate was added to dilute the mixture and the GC internal standard (dodecane) was added. An aliquot was passed through Celite into a GC phial and the clear solution was subjected to GC analysis.

<u>4-6 Control experiment (2) – Reductive amidation (Formation of  $N_*N'$ -(*p*-methylphenylmethylene)dibenzamide ( $N_*N'$ -diamide))</u>



A Carousel® tube was charged with PI/CB-Au/Pd (12.5 mg, 0.0025 mmol wrt Au), benzamide (31.3 mg, 0.26 mmol) and a stirring bar. The carousel tube was then placed in an argon-filled glovebox. In the glovebox, Ba(OTf)<sub>2</sub> (6.2 mg, 0.014 mmol) was added. Deoxidised toluene (0.5 mL) and 4-methylbenzaldehyde (119.6 mg, 0.98 mmol) was added, and then a three-way cock was attached to the tube. A balloon filled with H<sub>2</sub> was attached and the tube was flushed with hydrogen gas 10 times. The tube was then placed on a Carousel® (parallel synthesiser from Radleys) that had been preheated to 150 °C and it was left to stir for 18 hours, after which it was allowed to cool to room temperature. 10 mL of 1 to 1 mixture of ethyl acetate and hexane was added to dilute the mixture and a suspension of a white solid was obtained. The suspension was then vacuum-filtered and the residue on top of the filter funnel was rinsed with 1 to 1 mixture of ethyl acetate and hexane. The residue was collected and dried under vacuum. N,N'-(p-Tolylmethylene)dibenzamide (**5a**) was obtained as white solid (35.9 mg, 81%). No N-(4-methylbenzyl)benzamide (**3ab**) was obtained.

<sup>1</sup>**H NMR (600 MHz, DMSO-d<sub>6</sub>):** δ 8.94 (d, J = 7.8 Hz, 2H), 7.90 (d, J = 7.7 Hz, 4H), 7.56 (t, J = 7.3 Hz, 2H), 7.48 (t, J = 7.7 Hz, 4H), 7.36 (d, J = 7.8 Hz, 2H), 7.19 (d, J = 7.8 Hz, 2H), 7.01 (t, J = 8.0 Hz, 1H), 2.30 (s, 3H); <sup>13</sup>**C NMR (150 MHz, DMSO-d<sub>6</sub>):** δ 165.4, 137.4, 136.8, 133.9, 131.5, 128.8, 128.3, 127.4, 126.3, 58.5, 20.6.<sup>11</sup>

# <u>4-7</u> Control experiment (3) –Formation of $N_*N'$ -(*p*-methylphenylmethylene)dibenzamide ( $N_*N'$ diamide)



A Carousel® tube was charged with benzamide (31.5 mg, 0.26 mmol) and a stirring bar. The carousel tube was then placed in an argon-filled glovebox. In the glovebox,  $Ba(OTf)_2$  (6.0 mg, 0.014 mmol) was added and the tube was sealed tightly with a septum. The septum was also taped tightly to the tube and the tube was then removed from the glovebox. 4-Methylbenzaldehyde (28.6 mg, 0.24 mmol) and deoxidized toluene (0.5 mL) were added, and then the part of the septum where the syringe needle went through was covered with tape. The tube was then placed on a Carousel® (parallel synthesiser from Radleys) that had been preheated to 150 °C and it was left to stir for 18 hours, after which it was allowed to cool to room temperature. 10 mL of 1 to 1 mixture of ethyl acetate and hexane was added to dilute the mixture and white solid suspension was obtained. The suspension was then vacuum-filtered and the residue on top of the filter funnel was rinsed with 1 to 1 mixture of ethyl acetate and hexane. The residue was collected and dried under vacuum. N,N'-(p-methylphenylmethylene)dibenzamide (N,N'-diamide) (**5a**) was obtained as white solid (35.4 mg, 79% based on the amount of benzamide).

# <u>4-8</u> Control experiment (4) –Formation of N,N'-(p-methylphenylmethylene)dibenzamide (<math>N,N'-<u>diamide</u>)



A Carousel® tube was charged with benzamide (31.8 mg, 0.26 mmol) and a stirring bar. The carousel tube was then placed in an argon-filled glovebox. In the glovebox,  $Ca(OTf)_2$  (4.0 mg, 0.012 mmol) was added and the tube was sealed tightly with a septum. The septum was also taped tightly to the tube and the tube was then removed from the glovebox. 4-Methylbenzaldehyde (28.6 mg, 0.24 mmol) and deoxidized toluene (0.5 mL) were added, and then the part of the septum where the syringe needle went through was covered with tape. The tube was then placed on a Carousel® (parallel synthesiser from Radleys) that had been preheated to 150 °C and it was left to stir for 18 hours, after which it was allowed to cool to room temperature. 10 mL of 1 to 1 mixture of ethyl acetate and hexane was added to dilute the mixture and a white solid suspension was obtained. The suspension was then vacuum-filtered and the residue on top of the filter funnel was rinsed with 1 to 1 mixture of ethyl acetate and hexane. The residue was collected and dried under vacuum. N,N'-(p-methylphenylmethylene)dibenzamide (N,N'-diamide) (**5a**) was obtained as white solid (40.1 mg, 89% based on the amount of benzamide).

# <u>4-9</u> Control experiment (5) –Formation of $N_*N'$ -(*p*-methylphenylmethylene)dibenzamide ( $N_*N'$ diamide)



A Carousel® tube was charged with benzamide (31.3 mg, 0.26 mmol) and a stirring bar. The carousel tube was then placed in an argon-filled glovebox. In the glovebox, the tube was sealed tightly with a septum. The septum was also taped tightly to the tube and the tube was then removed from the glovebox. 4-Methylbenzaldehyde (28.6 mg, 0.24 mmol) and deoxidized toluene (0.5 mL) were added, and then the part of the septum where the syringe needle went through was covered with tape. The tube was then placed on a Carousel® (parallel synthesiser from Radleys) that had been preheated to 150 °C and it was left to stir for 18 hours, after which it was allowed to cool to room temperature. 10 mL of 1 to 1 mixture of ethyl acetate and hexane was added to dilute the mixture and a white solid suspension was obtained. The suspension was then vacuum-filtered and the residue on top of the filter funnel was rinsed with 1 to 1 mixture of ethyl acetate and hexane. The residue was collected and dried under vacuum. N,N'-(p-methylphenylmethylene)dibenzamide (N,N'-diamide) (**5a**) was obtained as white solid (34.7 mg, 78% based on the amount of benzamide).

#### 4-10 Control experiment (6) – Transfer hydrogenation from the N<sub>N</sub>'-diamide



A Carousel® tube was charged with PI/CB-Au/Pd (10.3 mg, 0.0025 mmol wrt Au), 4-Methylbenzyl alcohol (86.0 mg, 0.70 mmol), N,N'-(p-Tolylmethylene)dibenzamide (45.0 mg, 0.13 mmol) and a stirring bar. The carousel tube was then placed in an argon-filled glovebox. In the glovebox, Ba(OTf)<sub>2</sub> (7.7 mg, 0.017 mmol) was added and the tube was sealed tightly with a septum. The septum was also taped tightly to the tube and the tube was then removed from the glovebox. Deoxidized toluene (0.5 mL) were added, and then the part of

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the septum where the syringe needle went through was covered with tape. The tube was then placed on a Carousel® (parallel synthesiser from Radleys) that had been preheated to 150 °C and it was left to stir for 18 hours, after which it was allowed to cool to room temperature. Ethyl acetate was added to dilute the mixture and the GC internal standard (dodecane) was added. An aliquot was passed through Celite into a GC phial and the clear solution was subjected to GC analysis.

# <u>4-11</u> Control experiment (7) – Transfer hydrogenation from *N*,*N*'-diamide derived from aliphatic <u>aldehyde</u>



Similar procedure as elaborated in Section "4-10 Control experiment (6) – Transfer hydrogenation from the N,N'-diamide". The crude mixture obtained was concentrated and then purified using preparative TLC. However, the two products were inseparable and we determined the yields by <sup>1</sup>H NMR analysis.

# Preparation of N,N-(3-phenylpropane-1,1-diyl)dibenzamide (5b)



and 3-phenylpropanal as the starting materials. <sup>1</sup>**H NMR (600 MHz, DMSO-d<sub>6</sub>):**  $\delta$  8.61 (d, J = 7.5 Hz, 2H), 7.87 (d, J = 7.7 Hz, 4H), 7.54 (t, J = 7.2 Hz, 2H), 7.47 (t, J = 7.5 Hz, 4H), 7.29–7.25 (m, 4H), 7.18 (t, J = 7.0 Hz,

This compound was prepared using the method shown in Section 4-9 with benzamide

11), 5.85 (quint, J = 7.3 Hz, 1H), 2.69 (t, J = 7.9 Hz, 2H), 2.17 (q, J = 7.8 Hz, 2H); <sup>13</sup>C NMR (150 MHz, DMSO-d<sub>6</sub>): δ 165.6, 141.4, 134.3, 131.2, 128.24, 128.20, 128.1, 127.3, 125.7, 57.0, 35.7, 31.2. HRMS (DART): calculated for C<sub>23</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub><sup>+</sup> [*M*+H<sup>+</sup>] 359.17595, found 359.17523.

# N-(3-Phenylpropyl)benzamide (3af)<sup>12</sup>



<sup>1</sup>**H** NMR (**500** MHz, CDCl<sub>3</sub>):  $\delta$  7.65 (d, J = 7.7 Hz, 2H), 7.47–7.18 (m, 8H), 6.19 (br s, 1H), 3.48 (dt, J = 7.1, 7.1 Hz, 2H), 2.71 (t, J = 7.4 Hz, 2H), 1.95 (dq, J = 7.0, 7.0 Hz, 2H); <sup>13</sup>C NMR (**150** MHz, CHCl<sub>3</sub>):  $\delta$  167.4, 141.4, 134.6, 131.3, 128.52, 128.46, 128.4, 126.8, 126.0, 39.8, 33.5, 31.1.

# 4-12 Control experiment (8) - Disproportionation reaction



A Carousel® tube was charged with 4-methylbenzylalcohol (**1b**, 113.9 mg, 0.93 mmol), PI/CB-Au/Pd (12.0 mg, 0.0025 mmol wrt Au) and a stirring bar. The carousel tube was then placed in an argon-filled glovebox. In the glovebox, the tube was sealed tightly with a septum. The septum was also taped tightly to the tube and the tube was then removed from the glovebox. Deoxidised toluene (0.5 mL) were added, and then the part of the septum where the syringe needle went through was covered with tape. The tube was then placed on a Carousel® (parallel synthesiser from Radleys) that had been preheated to 150 °C and it was left to stir for 18 hours, after which it was allowed to cool to room temperature. Ethyl acetate was added to dilute the mixture and dodecane (GC internal standard) was added. An aliquot was passed through a thin pad of Celite into a GC vial for GC analysis. Yields of products were determined by GC analysis.

#### **<u>4-13</u>** Control experiment (9) – Disproportionation reaction with Ba(OTf)<sub>2</sub>



A Carousel® tube was charged with PI/CB-Au/Pd (11.8 mg, 0.0025 mmol wrt Au) and a stirring bar. The carousel tube was then placed in an argon-filled glovebox. In the glovebox,  $Ba(OTf)_2$  (12.0 mg, 0.0275 mmol) was added and the tube was sealed tightly with a septum. The septum was also taped tightly to the tube and the tube was then removed from the glovebox. 4-Methylbenzyl alcohol (125.3 mg, 1.03 mmol) and deoxidized toluene (0.5 mL) were added, and then the part of the septum where the syringe needle went through was covered with tape. The tube was then placed on a Carousel® (parallel synthesiser from Radleys) that had been preheated to 150 °C and it was left to stir for 18 hours, after which it was allowed to cool to room temperature. Ethyl acetate was added to dilute the mixture and the GC internal standard (dodecane) was added. An aliquot was passed through Celite into a GC phial and the clear solution was subjected to GC analysis.

#### 4-14 Control experiment (10) – Hydrogenation of aldehyde



A Carousel® tube was charged with 4-methylbenzaldehyde (123.8 mg, 1.03 mmol), PI/CB-Au/Pd (11.6 mg, 0.0025 mmol wrt Au) and a stirring bar. Deoxidised toluene (0.5 mL) was added, and a three-way cock was attached to the tube. A balloon filled with  $H_2$  was attached and the tube was flushed with hydrogen gas 10 times. The tube was then placed on a Carousel® (parallel synthesiser from Radleys) that had been preheated to 150 °C and it was left to stir for 18 hours, after which it was allowed to cool to room temperature. Ethyl acetate was added to dilute the mixture and dodecane (GC internal standard) was added. An aliquot was passed through a thin pad of Celite into a GC vial for GC analysis. Yields of products were determined by GC analysis.

#### 4-15 Control experiment (11) – Hydrogenation of alcohol



A Carousel® tube was charged with 4-methylbenzaldehyde (118.4 mg, 0.97 mmol), PI/CB-Au/Pd (11.9 mg, 0.0025 mmol wrt Au) and a stirring bar. Deoxidised toluene (0.5 mL) was added, and a three-way cock was attached to the tube. A balloon filled with  $H_2$  was attached and the tube was flushed with hydrogen gas 10 times. The tube was then placed on a Carousel® (parallel synthesiser from Radleys) that had been preheated to 150 °C and it was left to stir for 18 hours, after which it was allowed to cool to room temperature. Ethyl acetate was added to dilute the mixture and dodecane (GC internal standard) was added. An aliquot was passed through a thin pad of Celite into a GC vial for GC analysis. Yields of products were determined by GC analysis.

#### **4-16** Control experiment (12) – Hydrogenation of ether



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A Carousel® tube was charged with 4,4'-(oxybis(methylene))bis(methylbenzene) (116.1 mg, 0.51 mmol), PI/CB-Au/Pd (11.2 mg, 0.0025 mmol wrt Au) and a stirring bar. Deoxidised toluene (0.5 mL) was added, and a three-way cock was attached to the tube. A balloon filled with H<sub>2</sub> was attached and the tube was flushed with hydrogen gas 10 times. The tube was then placed on a Carousel® (parallel synthesiser from Radleys) that had been preheated to 150 °C and it was left to stir for 18 hours, after which it was allowed to cool to room temperature. Ethyl acetate was added to dilute the mixture and dodecane (GC internal standard) was added. An aliquot was passed through a thin pad of Celite into a GC vial for GC analysis. Yields of products were determined by GC analysis.

# 4-17 Control experiment (13) – Transfer hydrogenation of ether



A Carousel® tube was charged with 4,4'-(oxybis(methylene))bis(methylbenzene) (70.3 mg, 0.31 mmol), PI/CB-Au/Pd (10.3 mg, 0.0025 mmol wrt Au) and a stirring bar. Deoxidised toluene (0.5 mL) was added, and a three-way cock was attached to the tube. A balloon filled with Ar was attached and the tube was flushed with argon gas 10 times. The tube was then placed on a Carousel® (parallel synthesiser from Radleys) that had been preheated to 150 °C and it was left to stir for 18 hours, after which it was allowed to cool to room temperature. Ethyl acetate was added to dilute the mixture and dodecane (GC internal standard) was added. An aliquot was passed through a thin pad of Celite into a GC vial for GC analysis. Yields of products were determined by GC analysis.

#### 4-18 Procedure for profiling of reaction

Each data point at a particular time on the reaction profile represents the data obtained from *one independent experiment*. In other words a number of reactions were set up at the same time with exactly the same conditions. The amount of catalyst and substrate used were the same as well. Each reaction was then removed from the heating plate after the stipulated time for that particular reaction. The reaction mixture was allowed to cool to room temperature. Ethyl acetate was then added to dilute the mixture and the GC internal standard (dodecane) was added. An aliquot was passed through Celite into a GC phial and the clear solution was subjected to GC analysis.

# 4-19 Reaction profile without Ba(OTf)<sub>2</sub>



Yield was calculated based	on the amount of benzamide.	i.e. $0.25 \text{ mmol} = 100\%$
Tield was calculated based	i on the amount of benzamide.	1.0., 0.25 mmol = 10070

time (h)	<b>2b</b> (%)	<b>3ab</b> (%)	5a (%)	4 (%)	6 (%)	7 (%)
0.167	351	0	0	28	8	0
0.5	325	0	0	56	10	0
1	304	2	0	80	16	0
2	255	6	0.3	88	28	1
3	210	12	0.5	117	34	3
6	186	20	0.5	110	41	4



# 4-20 Reaction profile with Ba(OTf)<sub>2</sub>



Yield was calculated based on the amount of benzamide. ie. 0.25 mmol = 100%

time (h)	<b>2b</b> (%)	<b>3ab</b> (%)	5a (%)	4 (%)	6 (%)	7 (%)
0.167	343	4	4	18	23	2
0.5	244	23	12	38	49	7
1	166	49	13	49	63	15
2	79	72	12	53	84	25
3	45	87	3	60	87	25
6	17	96	0	50	101	27



# 4-21 Reaction profile when MgSO<sub>4</sub> was employed with benzamide and benzyl alcohol



# 4-22 Reaction profile when Ba(OTf)<sub>2</sub> was employed with benzamide and benzyl alcohol



	Ba(OTf) <sub>2</sub>	MgSO <sub>4</sub>
time taken for consumption of half of benzyl alcohol	1 h	3 h
time taken to reach steady state for benzaldehyde	1 h	3 h
amount of benzaldehyde at steady state	0.5 eq	1 eq
time taken for reaction to reach completion	6 h	24 h
amount of alcohol left at the end of the reaction	0.5 eq	0 eq

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# **4-23** Comparison of reaction profiles (MgSO<sub>4</sub> and Ba(OTf)<sub>2</sub>)



Even at the same concentration of benzaldehyde (approx. 0.55 eq, 1 h), the rate of product formation was significantly faster when  $Ba(OTf)_2$  was used, as compared to when  $MgSO_4$  was used.

# 4-24 Full consumption of alcohol when benzamide is present



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# 5 NMR Spectra















































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