Electronic Supplementary Material (ESI) for Catalysis Science & Technology.

Supporting information

Direct Liquid-Phase Phenol-to-Aniline Amination Using Pd/C

Thomas Cuypers[†], Patrick Tomkins[†] and Dirk E. De Vos*[,†]

[†] Centre for Surface Chemistry and Catalysis, Department of Microbial and Molecular Systems, KU Leuven – University of Leuven, Leuven Chem&Tech, Celestijnenlaan 200F, Post Box 2461, 3001 Heverlee, Belgium

*E-mail: dirk.devos@kuleuven.be

1. Chemicals and catalyst

All chemicals used in reactions and/or analysis were obtained from commercial sources and were used without further purification: toluene (>99.8%, Acros Organics), phenol (>99%, Sigma Aldrich), NH_3 (gas, 99.98%, Air Liquide), *n*-nonane (99%, Acros Organics), cyclohexanone (>99%, TCI Europe), cyclohexylamine (>99%, TCI Europe), aniline (>98%, TCI Europe), dicyclohexylamine (>99%, Acros Organics), *N*-cyclohexylaniline (97%, Acros Organics), diphenylamine (99%, Acros Organics), *o*-cresol (≥99%, Sigma Aldrich), *m*-cresol (99%, Sigma Aldrich), *p*-cresol (99%, Alfa Aesar), 2-methylcyclohexanone (99%, Sigma Aldrich), 3-methylcyclohexanone (97%, Sigma Aldrich), 4-methylcyclohexanone (99%, Sigma Aldrich). All tested catalysts, loaded with 5 wt% metal, were obtained from commercial sources: Pd/C (Johnson Matthey), Pt/C (Johnson Matthey), Rh/C (Alfa Aesar), Ru/C (Alfa Aesar).

2. Amination reactions

All amination reactions were performed in a 60 mL high-pressure stainless steel Premex Vivor batch reactor equipped with a digital pressure sensor. In a standard reaction, the reactor was loaded with phenol (2 mmol) in toluene (20 mL), catalyst (5 mol% metal relative to phenol) and a magnetic stirring rod. After purging three times with N_2, the reactor was subsequently pressurized with 3.5 bar N_2, 0.5 bar H_2 and 2 bar NH_3 at room temperature. Next, the reactor was heated at an internal temperature of 200 °C under continuous agitation (530 rpm) for 24 h. After the reaction, the reactor was cooled down in ice and the solid catalyst was separated from the reaction mixture via centrifugation (3250 rpm). Finally, the liquid phase of the reaction mixtures were analyzed by GC-FID with *n*-nonane as external standard and GC-MS. For the recycling experiments, the catalyst was separated from the reaction products by centrifugation, washed thoroughly with ethanol and dried in an oven at 60 °C for 24 h. Approximately 97% of the original catalyst mass could be recovered and was replenished with new catalyst in the recycle run.

3. Product analysis and identification

3.1. GC-FID

The reaction products were analyzed using a Shimadzu GC-2010 gas chromatograph instrument equipped with a AOC-20s Autosampler and AOC-20i Auto-injector. For every analysis, 1 mL of the reaction mixture was transferred together with *n*-nonane as external standard into a GC-vial (1.8 mL). The various reaction products were separated after 1 µL of the sample was injected via split-injection (30:1) at 315 °C on an Agilent CP-Sil 5 CB capillary column (length: 60 m; internal diameter: 0.32 mm and film thickness: 0.25 µm). The volatile components were carried through the column by a constant N_2 flow of 2.39 mL/min, before it reached a FID detector (Flame Ionisation Detector) at 325 °C. The temperature profile of the column is shown in the table below:

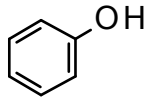
Step	Rate [°C/min]	Temperature [°C]	Hold-time [min]
1	-	70	7
2	1.5	100	-
3	20	320	5
Total time = 43 min			

The concentrations of different reaction products were obtained by the effective carbon number (ECN) concept, as described in a prior report,[1] with *n*-nonane as external standard. Conversion (X), yield (Y) and selectivity (S) of the products in all the reaction mixtures were calculated by normalizing the concentration of each product to the initial phenol concentration.

3.2. GC-MS

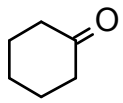
The different reaction products were identified using a Agilent 6890 gas chromatograph equipped with a HP-1 MS column (length: 30 m; internal diameter: 0.25 mm and film thickness: 0.25 μm) connected to a 5973 MSD mass spectrometer. The used instrumental parameters were identical to those for GC-FID analysis. The resulting fragmentation spectra were matched to those in databases, such as the database of the National Institute of Standards and Technology (NIST), resulting in the identification of all compounds in the reaction mixtures.

Phenol (MW = 94.11 g/mol)



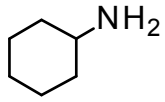
GC/MS (EI, 70 eV): m/z (rel. int., %): 55 (5), 62 (5), 63 (8), 65 (27), 66 (46), 94 (100), 95 (7).

Cyclohexanone (MW = 98.15 g/mol)



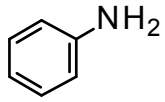
GC/MS (EI, 70 eV): m/z (rel. int., %): 51 (7), 53 (10), 54 (11), 55 (100), 56 (16), 57 (25), 67 (14), 69 (38), 70 (29), 80 (9), 82 (20), 83 (19), 91 (10), 98 (91), 99 (7).

Cyclohexylamine (MW = 99.17 g/mol)



GC/MS (EI, 70 eV): m/z (rel. int., %): 56 100), 57 (7), 70 (12), 99 (18).

Aniline (MW = 93.13 g/mol)



GC/MS (EI, 70 eV): m/z (rel. int., %): 52 (5), 63 (6), 65 (16), 66 (36), 67 (5), 92 (14), 93 (100), 94 (7).

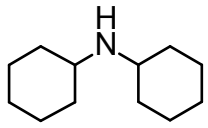
Cyclohexane (MW = 84.16g/mol)

GC/MS (EI, 70 eV): m/z (rel. int., %): 55 (37), 56 (100), 57 (11), 69 (25), 84 (75), 85 (6).

Benzene (MW = 78.11 g/mol)

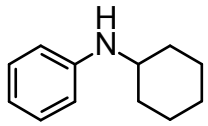
GC/MS (EI, 70 eV): m/z (rel. int., %): 51 (9), 52 (13), 77 (19), 78 (100), 79 (5).

Dicyclohexylamine (MW = 181.32 g/mol)



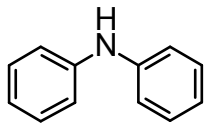
GC/MS (EI, 70 eV): m/z (rel. int., %): 55 (7), 56 (12), 138 (100), 139 (11), 152 (5), 181 (16).

***N*-Cyclohexylaniline** (MW = 175.27 g/mol)



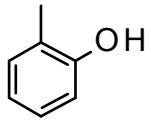
GC/MS (EI, 70 eV): m/z (rel. int., %): 51 (5), 55 (5), 65 (8), 66 (5), 77 (12), 79 (7), 91 (17), 92 (14), 93 (16), 104 (9), 106 (9), 118 (18), 119 (18), 132 (100), 133 (11), 152 (6), 153 (5), 174 (7), 175 (33), 176 (5).

Diphenylamine (MW = 169.23 g/mol)



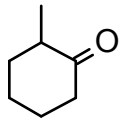
GC/MS (EI, 70 eV): m/z (rel. int., %): 50 (6), 51 (15), 52 (11), 65 (9), 66 (12), 77 (14), 83 (9), 84 (5), 104 (5), 115 (15), 140 (7), 141 (5), 142 (7), 154 (7), 166 (17), 167 (50), 168 (86), 169 (100), 170 (15).

***o*-Cresol** (MW = 108.14 g/mol)



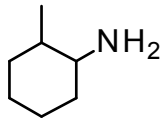
GC/MS (EI, 70 eV): m/z (rel. int., %): 51 (13), 52 (6), 53 (10), 63 (9), 77 (44), 78 (13), 79 (47), 80 (22), 89 (14), 90 (23), 91 (7), 107 (92), 108 (100), 109 (8).

***2*-Methylcyclohexanone** (MW = 112.17 g/mol)



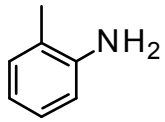
GC/MS (EI, 70 eV): m/z (rel. int., %): 51 (6), 53 (10), 54 (5), 55 (65), 56 (56), 57 (5), 67 (18), 68 (93), 69 (57), 70 (11), 79 (7), 83 (21), 84 (41), 94 (5), 97 (17), 112 (100), 113 (9).

2-Methylcyclohexylamine (MW = 113.20 g/mol)



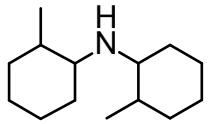
GC/MS (EI, 70 eV): m/z (rel. int., %): 54 (5), 56 (100), 57 (15), 67 (6), 70 (60), 84 (8), 113 (36).

***o*-Toluidine** (MW = 107.15 g/mol)



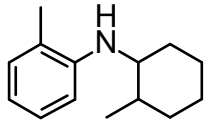
GC/MS (EI, 70 eV): m/z (rel. int., %): 51 (8), 52 (6), 53 (5), 63 (5), 77 (20), 78 (8), 79 (16), 80 (9), 89 (7), 90 (6), 106 (100), 107 (75), 108 (13).

Di(2-methylcyclohexyl)amine (MW = 209.37 g/mol)



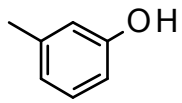
GC/MS (EI, 70 eV): m/z (rel. int., %): 55 (14), 56 (12), 70 (9), 82 (6), 96 (7), 97 (7), 112 (6), 114 (10), 124 (7), 152 (100), 153 (11), 166 (69), 167 (8), 180 (5), 209 (25).

***N*-(2-methylcyclohexyl)-*o*-toluidine** (MW = 203.32 g/mol)



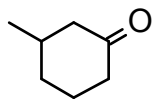
GC/MS (EI, 70 eV): m/z (rel. int., %): 54 (8), 63 (5), 77 (7), 81 (7), 89 (5), 91 (24), 92 (5), 103 (9), 106 (21), 107 (10), 108 (8), 117 (13), 118 (44), 119 (13), 120 (9), 125 (8), 128 (5), 130 (31), 131 (13), 132 (14), 133 (9), 134 (8), 144 (16), 145 (6), 146 (100), 147 (14), 160 (34), 174 (10), 188 (9), 203 (71), 204 (11).

***m*-Cresol** (MW = 108.14 g/mol)



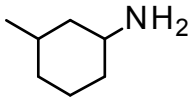
GC/MS (EI, 70 eV): m/z (rel. int., %): 51 (10), 52 (5), 53 (8), 63 (8), 77 (39), 78 (10), 79 (40), 80 (16), 89 (6), 90 (11), 91 (7), 107 (100), 108 (100), 109 (7).

3-Methylcyclohexanone (MW = 112.17 g/mol)



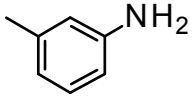
GC/MS (EI, 70 eV): m/z (rel. int., %): 53 (7), 55 (33), 56 (39), 67 (6), 68 (11), 69 (100), 70 (10), 79 (9), 84 (6), 94 (8), 97 (21), 112 (64), 113 (6).

3-Methylcyclohexylamine (MW = 113.20 g/mol)



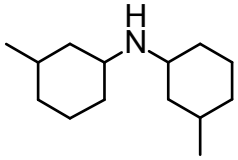
GC/MS (EI, 70 eV): m/z (rel. int., %): 53 (5), 56 (65), 57 (6), 70 (100), 71 (5), 81 (12), 96 (22), 98 (9), 113 (12).

***m*-Toluidine** (MW = 107.15 g/mol)



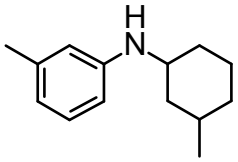
GC/MS (EI, 70 eV): m/z (rel. int., %): 51 (5), 52 (5), 77 (15), 78 (7), 79 (16), 80 (10), 106 (100), 107 (93), 108 (7).

Di(3-methylcyclohexyl)amine (MW = 209.37 g/mol)



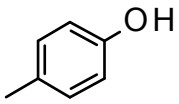
GC/MS (EI, 70 eV): m/z (rel. int., %): 55 (12), 56 (8), 70 (10), 96 (6), 152 (45), 153 (5), 166 (100), 167 (13), 194 (9), 209 (15).

***N*-(2-methylcyclohexyl)-*m*-toluidine** (MW = 203.32 g/mol)



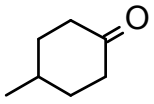
GC/MS (EI, 70 eV): m/z (rel. int., %): 65 (6), 77 (6), 91 (17), 106 (9), 107 (23), 117 (12), 118 (17), 120 (13), 130 (11), 131 (16), 132 (28), 133 (22), 144 (8), 145 (8), 146 (71), 147 (12), 160 (100), 161 (14), 203 (69), 204 (11).

***p*-Cresol** (MW = 108.14 g/mol)



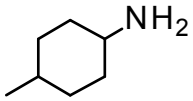
GC/MS (EI, 70 eV): m/z (rel. int., %): 51 (11), 53 (8), 63 (6), 77 (33), 78 (8), 79 (26), 80 (13), 90 (7), 107 (100), 108 (80), 109 (7).

4-Methylcyclohexanone (MW = 112.17 g/mol)



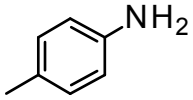
GC/MS (EI, 70 eV): m/z (rel. int., %): 51 (7), 53 (11), 55 (100), 56 (51), 57 (17), 67 (7), 68 (7), 69 (22), 70 (19), 79 (14), 83 (43), 84 (28), 94 (12), 97 (13), 112 (79), 113 (7).

4-Methylcyclohexylamine (MW = 113.20 g/mol)



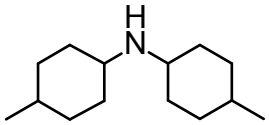
GC/MS (EI, 70 eV): m/z (rel. int., %): 56 (100), 57 (6), 67 (5), 81 (5), 84 (5), 113 (19).

***p*-Toluidine** (MW = 107.15 g/mol)



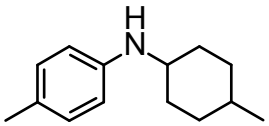
GC/MS (EI, 70 eV): m/z (rel. int., %): 51 (5), 52 (5), 77 (13), 78 (6), 79 (10), 80 (7),

Di(4-methylcyclohexyl)amine (MW = 209.37 g/mol)



GC/MS (EI, 70 eV): m/z (rel. int., %): 55 (6), 56 (10), 152 (100), 153 (12).

***N*-(2-methylcyclohexyl)-*p*-toluidine** (MW = 203.32 g/mol)



GC/MS (EI, 70 eV): m/z (rel. int., %): 90 (9), 106 (6), 107 (6), 117 (5), 118 (7), 120 (5), 130 (8), 131 (12), 132 (13), 133 (12), 144 (5), 146 (100), 147 (12), 203 (39), 204 (6).

3.3. ICP-OES

The leaching of Pd into the solution was investigated by ICP-OES at 340.458 nm using a Varian 720-ES equipped with a double-pass glass cyclonic spray chamber, a Sea Spray concentric glass nebulizer and a high solids torch; and applying the calibration curve method. For this, the organic solvent was removed from the supernatant of the reaction mixture (1 mL) by rotary evaporation. Next, 1.5 mL of aqua regia was added to dissolve the Pd in the sample overnight. The resulting reaction mixture was diluted with 8.5 mL of 0.42 N HNO_3 in Milli-Q water.

4. Determination of NH_3 solubility in phenol-toluene mixture

In order to determine the ammonia concentration in the liquid phase at a certain NH_3 partial pressure, a calibration curve was made. For this, the reactor was loaded with 5 mol% catalyst, phenol (2 mmol) in 20 mL toluene as solvent and a magnetic stirring rod, analogous to the procedure described in section 2 of supporting information (amination reactions). After purging three times with N_2, the reactor was pressurized with 1 bar of N_2 and weighed, m(N_2). Next, the reactor was loaded with different NH_3 partial pressures and weighed again, m(N_2 + xNH_3). Finally, the ammonia concentration can be obtained by subtracting the weight of NH_3 in the gas phase (determined by the ideal gas law) from the total NH_3 weight, m(N_2 + xNH_3).

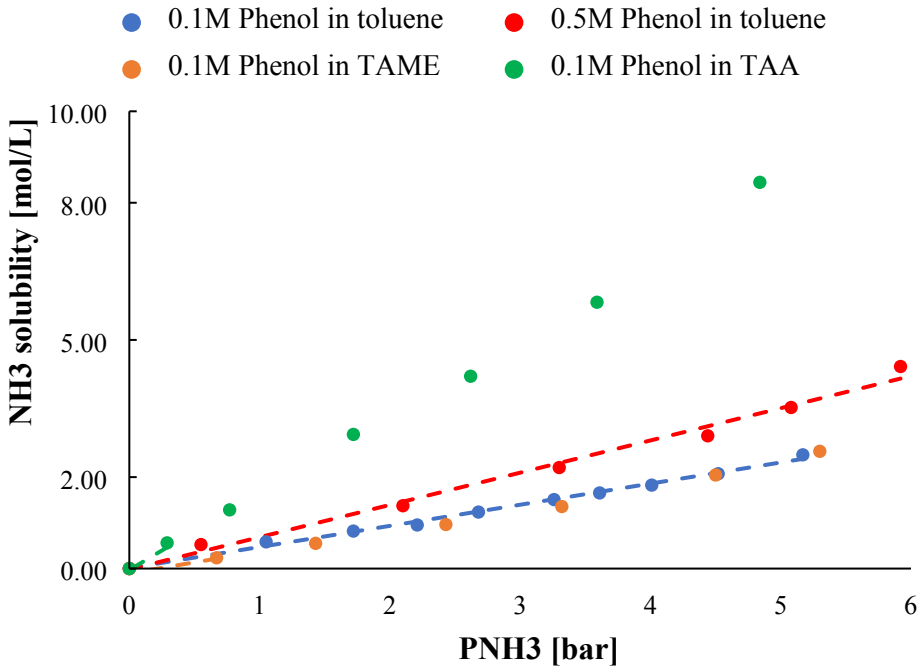


Figure S1. Solubility of ammonia in the solution. Conditions: • 0.1M phenol in toluene (20 mL), • 0.5M phenol in toluene (20 mL), • 0.1M phenol in TAME (20 mL) or • 0.1M phenol in TAME (20 mL), 5 mol% Pd/C at room temperature.

5. Supplementary experiments

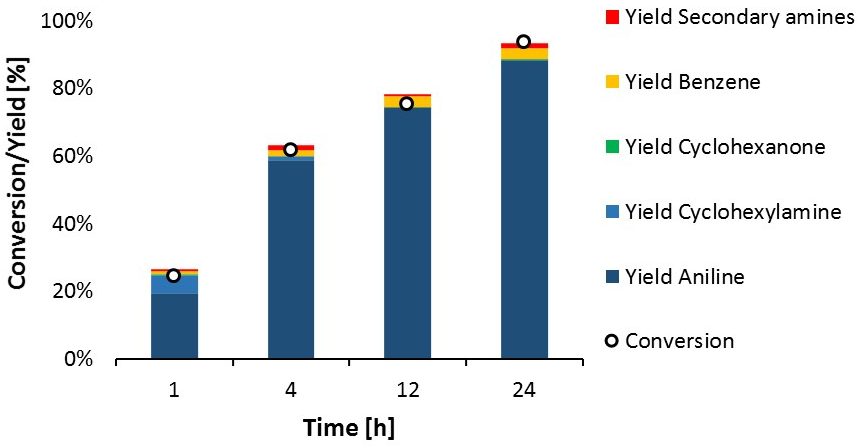


Figure S2. Kinetic profile for the direct phenol-to-aniline amination with ammonia using commercial Pd/C. Reaction conditions: phenol (2 mmol) in toluene (20 mL), 5 mol% Pd/C, 200 °C, 0.5 bar H_2 and 2 bar NH_3.

Table S1. Experiments on intermediates or in the absence of reagents.[a]

Entry	Substrate	P (H_2) [bar]	P (NH_3) [bar]	Conversion [%][b]	Y_{AN} [%][b]	Y_{SEC} [%][b]	Y_{CHO} [%][b]	Y_{CHOL} [%][b]
1	Cyclohexylamine	0.5	2	>99	94	3	-	-
2	Cyclohexylamine	0.5	0	99	39	57	-	-
3[c]	Phenol	1	0	11	-	-	10	1
4[c]	Phenol	0	4	0	-	-	-	-

[a] Reaction conditions: substrate (2 mmol) in toluene (20 mL), 5 mol% Pd/C, at 200 °C for 24 h. [b] Conversions and yields (Y) were determined by GC analysis with *n*-nonane as external standard. Observed products: Cyclohexanone (CHO), cyclohexanol (CHOL), aniline (AN), secondary amines (SEC). [c] 2.5 mol% Pd/C.

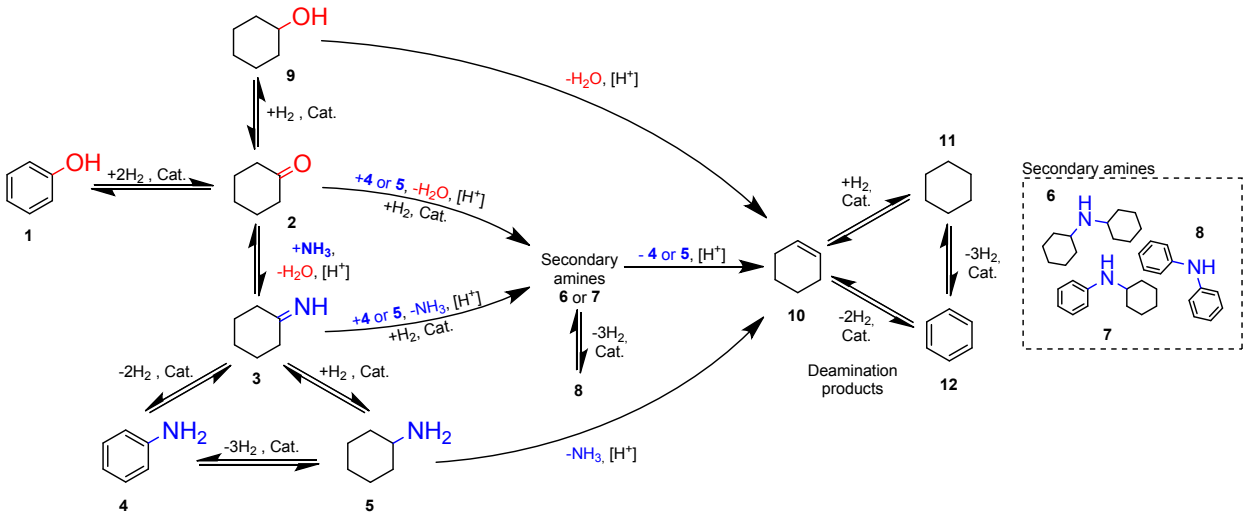
Table S2. Investigation of the substituent effect on the conversion of cyclohexanones.[a]

Entry	Substrate	P(H_2) [bar]	P(NH_3) [bar]	Conversion [%]	Y_{CHA} [%]	Y_{AN} [%]	Y_{SEC} [%]
1	Cyclohexanone	1	4	>99	66	16	19
2	Cyclohexanone	4	2	>99	73	6	21
3	2-Methylcyclohexanone	1	4	61	37	21	4
4	2-Methylcyclohexanone	4	2	57	49	4	7
5	3-Methylcyclohexanone	1	4	80	37	27	15
6	3-Methylcyclohexanone	4	2	77	51	5	22
7	4-Methylcyclohexanone	1	4	77	43	20	14
8	4-Methylcyclohexanone	4	2	74	53	4	20

[a] Reaction conditions: substrate (2 mmol) in toluene (20 mL), 2.5 mol% Pd/C, at 200 °C for 1 h. [b] Conversions and yields (Y) were determined by GC analysis with *n*-nonane as external standard. Observed products: corresponding cyclohexylamine (CHA), aniline (AN), secondary amines (SEC).

6. Detailed reaction scheme

Scheme S1. Detailed tentative reaction scheme for the noble metal catalyzed amination of phenol with ammonia.



Products: phenol (**1**), cyclohexanone (**2**), cyclohexanimine (**3**), cyclohexylamine (**4**), aniline (**5**), dicyclohexylamine (**6**), *N*-cyclohexylamine (**7**), diphenylamine (**8**), cyclohexanol (**9**), cyclohexene (**10**), cyclohexane (**11**) and benzene (**12**).

7. References

(1) Scanlon, J. T.; Willis, D. E. J. Chromatogr. Sci. 1985, 23 (8), 333–340.