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Study on the Selective Hydrogenation of Nitroaromatics to *N*-aryl hydroxylamines using a Supported Pt nanoparticle Catalyst

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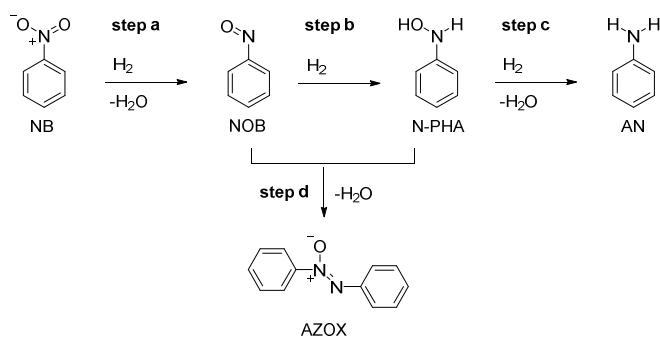
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A supported Pt nanoparticle-based catalyst was used in the chemoselective hydrogenation of nitroarenes to *N*-arylhydroxylamines (*N*-AHA). Optimization of NB hydrogenation conditions showed that substantially higher *N*-PHA yields can be obtained at low temperature. Especially, the influence of an increased hydrogen pressure on selectivity is remarkable. Maximum yields increase from 55% *N*-PHA at 4 bar H₂ to 80% at 23 bar H₂ in ethanol. Further optimization led to the use of small amounts of amine additive, TMEDA, with 50 bar H₂ raising the maximum yield to 97% *N*-PHA. The decreased *N*-PHA hydrogenation rate at high H₂ pressure and the presence of TMEDA allow for selective transformation of a range of other nitroarenes, containing electron withdrawing and donating (reducible) functional groups, to their *N*-AHAs in excellent (90%+) yields.

Introduction

Aniline derivatives are important chemical building blocks which are produced industrially on a large scale since the 19th century.¹ An important route is the hydrogenation of nitrobenzenes (NB) by solid precious metal catalysts (Cu, Pd, Pt) at high temperature. During the last decades catalyst development has been aimed at the chemo-selective hydrogenation of the nitro-group in the presence of other reducible groups on the substrate. This is of special interest for the production of pharmaceuticals. A common difficulty in the formation of aniline is the formation and built-up of intermediates. For nitrobenzene these are *N*-phenylhydroxylamine (*N*-PHA), nitrosobenzene (NOB) and their condensation product azoxybenzene (AZOXY), which is summarized in scheme 1.^{2,3} This is especially true when working under mild reaction conditions, namely, low temperature (<30°C) and H₂ pressure (<10 bar). Also, electron-withdrawing substituents on the phenyl ring enhance the formation of the *N*-arylhydroxylamine intermediate (*N*-AHA). Suppression of these intermediates is well looked into, and has been successful when metal salts that can adopt multiple oxidation states are used, such as vanadium and molybdenum oxides.³⁻⁵



Scheme 1. Reaction pathway in the Pt-catalysed hydrogenation of nitrobenzene with intermediates.

Even though considered unwanted in aniline production, arylhydroxylamines are versatile compounds with multiple synthetic applications. For example, in the presence of sulphuric acid *N*-PHA can rearrange into aminophenols, called the Bamberger rearrangement.⁶ The hydroxylamine group can add to double and triple bonds in a gold-catalysed addition reaction.⁷ Furthermore, *N*-PHA is suggested as the active

intermediate in biologically active substances,^{8,9} and has been reported as polymerization inhibitor.¹⁰

In the literature a couple of synthetic routes towards *N*-PHA are reported, but these procedures have limitations related to ease of application, scale-up and fundamental understanding. Firstly, the oldest synthetic procedure is a non-catalytic reduction using Zn in water saturated with ammonium chloride, which results in an isolated yield of 65%.¹¹ In the presence of catalysts, one example shows the selective conversion of nitrobenzene using a novel nitroreductase system giving excellent selectivities but a poor 60% *N*-PHA isolated yield.¹² Alternatively, stoichiometric transfer hydrogenation with hydrazine over a rhodium on carbon catalyst gave an 80% *N*-PHA yield.¹³ For the catalytic reduction with hydrogen gas, palladium and especially platinum are preferred due to their high activity and *N*-PHA selectivity compared to similarly carbon supported metallic Rh, Ir, Ru and Os catalysts.¹⁴⁻¹⁶ Moreover, Pt and Pd are far less prone to aromatic ring hydrogenation when compared with e.g. Ru.¹⁷ Platinum supported by silica has the highest reported *N*-PHA yield of 80% at 5°C in ethanol in absence of any additives.¹⁵ Metallic Pt as transition metal (over Ir, Pd and Rh) and the low reaction temperature were found to be crucial for the high *N*-PHA yield.

It is long known that the addition of dimethyl sulfoxide (DMSO) to Pt catalysts can increase selectivity in the three-phase hydrogenation of NB, but unfortunately it also decreased the hydrogenation rates.¹⁴ In one example, platinum supported on carbon is used in the hydrogenation of nitrobenzene with a reported selectivity increase from 26% without to 70% with DMSO additive at partial NB conversion.¹⁸ This trend was confirmed by Yasuda *et al.*. They found that the addition of amines (such as triethylamine) can increase the *N*-PHA yield even further to 99% with 1 bar H₂ at r.t.¹⁹ However, the catalyst poison DMSO is still required in order to obtain high selectivities.

In our catalyst development studies of supported Pt nanoparticles in the catalytic hydrogenation of nitrobenzene we found that *N*-PHA was formed in unusually high amounts (50+%) as intermediate in the preparation of anilines. This occurred when no molybdenum oxide promoter nor any other modifier was added.⁵ For this reason, instead of suppression of *N*-PHA, we were interested in its selective formation under catalytic hydrogenation conditions. Our goal was to devise a methodology for lab-scale preparative production of *N*-arylhydroxylamines (*N*-AHA) as easily accessible intermediates for organic syntheses.

In this paper, we report on the selective formation of *N*-AHAs in the activated carbon supported platinum nanoparticulate catalysed hydrogenation of nitrobenzene. Moreover, we will show how reaction conditions, such as hydrogen pressure, temperature and the choice of solvent have an influence on the formation of *N*-PHA and aniline.

Experimental

Nitrobenzene ACS reagent (>99%), 2-chloronitrobenzene (99%), 4-nitroanisole (97%), 4-nitrobenzotrile (98%), 4-bromonitrobenzene (99%), 1,3,5-trimethoxybenzene (≥99.0%) and absolute ethanol were purchased from Sigma-Aldrich and used as received. Hydrogen, at industrial grade (=99.995%), was supplied by BOC gases. All products were identified by comparison with authentic samples. NanoSelectTM nanoparticulate platinum 0.7% c-Pt/C (surface area BET: 1346 ± 8.5 m²/g) and palladium catalyst 0.6% c-Pd/C (BET: 485 ± 9.4 m²/g) were dried in an oven at 120°C for 3 hours before use. A complete catalyst characterisation can be found in the supplementary information for both catalysts. 5%Pt/C and 5%Pt/SiO₂ were purchased from STREM chemicals and used as received.

Strict reaction conditions have to be applied since *N*-phenylhydroxylamine thermally disproportionates into nitrosobenzene and aniline. Moreover, *N*-PHA self-condensates in the presence of oxygen forming the strongly coloured azoxybenzene.

All measurements were performed in the kinetic regime by vigorous stirring at 1500 rpm with an overhead stirrer. Varying the stirring speed between 500 and 3000 rpm did not affect the reaction rate. Catalysts of the NanoSelectTM type prepared via reduction-deposition (0.7% c-Pt/C and 0.6% c-Pd/C) have the Pt and Pd crystallites deposited in an egg-shell fashion^{20,21} on the activated carbon support, so that internal diffusion limitations and heat transfer constraints were not considered.

Autoclave catalytic hydrogenation of nitrobenzene

62 mg 0.7% c-Pt/C, 2.75 g (22.3 mmol) nitrobenzene (S/Pt=10 x 10³) and 80 mL absolute ethanol were added to a 100 mL stainless steel autoclave equipped with a heating jacket, a hydrogen supply system, a sampling unit, and a mechanical stirrer. This mixture was heated to 30°C after which the reactor was flushed with hydrogen and pressurized to the desired absolute pressure. The reaction was initiated by switching on the mechanical stirrer at 1500 rpm. The pressure was kept constant with a mass-flow controller (which also logs the total gas consumption) and the temperature was kept at 30°C during the reaction. The reaction was stopped at the required hydrogen uptake (600 mL), after which the hydrogen pressure was released. The reactor was opened and 10 % 1,3,5-trimethoxybenzene was added as internal standard. A ¹H NMR spectrum of the reaction mixture was obtained within 1 hour by placing three drops of the reaction mixture into an NMR tube with 0.6 mL of methanol-d⁴. Reaction profiles were measured from samples which were withdrawn from the autoclave during the reaction and analysed by ¹H NMR spectroscopy and/or by GLC measurements, without any further sample treatment.

Schlenk tube catalytic hydrogenation of nitrobenzene

62 mg 0.7% c-Pt/C was added to a 100 mL Schlenk flask and an inert atmosphere was created by repetitive evacuation and argon introduction and 40 mL solvent was gently added under a stream of argon. This solution was stirred at 600 rpm with a magnetic PTFE stirring bar for 5 minutes, after which 22.3 mmol nitrobenzene was slowly added to the reaction mixture. The flask cap was replaced by a septum and the mixture was degassed three times replacing argon for hydrogen via introduction of a hydrogen-filled balloon (connected to a needle). This resulted in a total hydrogen pressure of about 1

bar at the start. While stirring at room temperature, the balloon was left connected to the flask overnight. Full reduction of nitrobenzene equals 1 L of hydrogen consumption at standard conditions. After 16 hours (overnight), the reaction was stopped and the catalyst was filtered off over a funnel with paper filter. Samples were withdrawn from the crude reaction mixture and analysed by GLC and ^1H NMR after addition of 10 % 1,3,5-trimethoxybenzene as internal standard.

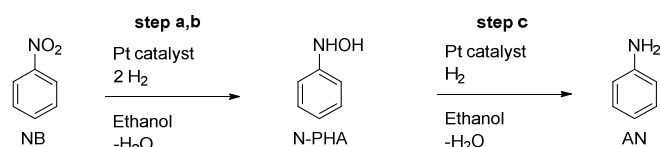
!Important: all products were kept at room temperature or lower at all times to prevent thermal decomposition forming byproducts such as nitrosobenzene, aniline and azoxybenzene. Furthermore, *N*-arylhydroxylamines are (potentially) carcinogenic and should be handled with care in a well-ventilated hood at all times!

GLC-analysis was performed on a Shimadzu-2010 gas chromatograph equipped with FID detector and a 50m capillary column, the Agilent's HP-PONA with a dimethylpolysiloxane stationary phase. The injector inlet temperature (split) of the GC was set to 70°C at which most (thermal) decomposition of *N*-PHA can be avoided.

NMR spectroscopy was performed on a 500 MHz Bruker machine. All ^1H NMR spectra were obtained within 1 hour by addition of three drops of the reaction mixture into an NMR tube with 0.6 mL of methanol- d_4 . All conversion and selectivity data reported in percentages related to substrate and products in this work are molar percentages.

Results and discussion

The catalyst used in these examples was the NanoSelectTM nanoparticulate platinum solid catalyst, supported on activated carbon.²² Nanoparticles were determined to be 2.3 ± 0.3 nm in size by transmission electron microscopy (TEM). The TEM images can be found in the supplementary information. Scheme 2 represents the simplified reaction profile of the Pt-catalysed hydrogenation based on compounds observed in solution thus leaving out the elementary reaction **step a** to NOB.



Scheme 2. Pt-catalysed hydrogenation of nitrobenzene in ethanol forming *N*-Phenylhydroxylamine at an intermediate stage and aniline. Full conversion will leave aniline as the sole product.

Figure 1 shows the reaction profile for this reaction as analysed from solution compared with a Pd-catalysed analogous reaction at 4 bar H_2 and 30°C.

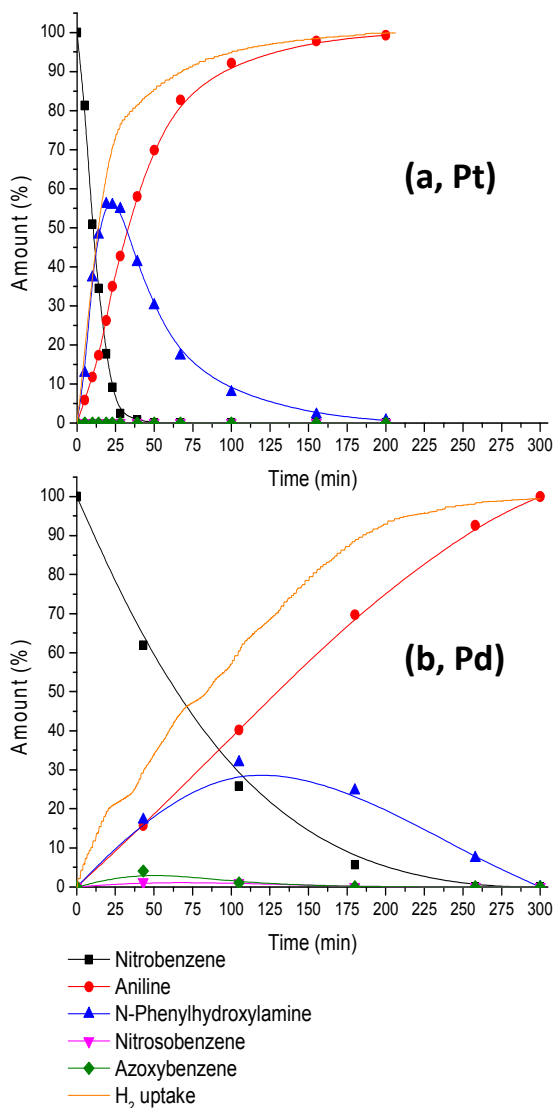


Figure 1. Reaction profile for nitrobenzene hydrogenation in the presence of platinum (a) and palladium (b). Conditions: 22.3 mmol nitrobenzene ($S/C=10 \times 10^3$), 80 mL EtOH and 4 bar H_2 (total pressure) at 30°C with (a) 62 mg 0.7% c-Pt/C and (b) 37.1 mg 0.6% c-Pd/C. Samples were withdrawn from the reactor for GLC and ^1H NMR analysis.

The initial reaction rate of the Pt system is fast in terms of nitrobenzene conversion and its corresponding H_2 uptake. After complete consumption of nitrobenzene the reaction slows down significantly and *N*-PHA, formed up to 55%, is left for hydrogenation. If aniline is the desired product it is evident that reactions have to be run longer until full hydrogen uptake is reached at 200 minutes. Nitrosobenzene (NOB) is formed on the catalyst's surface, but is not detected in solution under these reaction conditions.²³ Azoxybenzene (AZOX) formation is largely suppressed, because it is formed by the condensation of NOB and *N*-PHA. The trace amounts of AZOX that are observed by NMR and GLC analysis are probably formed after the samples have been withdrawn from the reactor exposing them to light and oxygen. A measurement of the samples a few days later revealed that all *N*-PHA had disappeared and AZOX became the main constituent. Therefore, to prevent measuring

decomposition products, all measurements were performed within 1 h after sampling.

Pd nanoparticles (15.2 ± 1.6 nm) supported on activated carbon were also used in a similar experiment under the same conditions and substrate to catalyst ratio (Figure 1, graph b). Notably, full conversion to aniline takes place within 300 minutes compared to 200 minutes for the Pt-catalysed hydrogenation. NB is consumed within 260 minutes whereas for Pt this is only 30 minutes. Consequently, the intermediate build-up of *N*-PHA is much lower for Pd (30%) as compared to Pt (55%). Therefore further investigation into the selective formation of *N*-PHA was focused only on Pt-nanoparticle catalysis.

One reason for the high selectivity compared to the literature values given in the introduction is the high substrate to catalyst ratio of 10,000. The fact that less catalyst and a low metal on support loading are beneficial for the *N*-PHA yield was already reported by Rylander *et al.* in 1970.¹⁴ In this work this S/C ratio was set at 10,000 to have reasonable conversion times, but still high *N*-PHA selectivity.

Reaction temperature and hydrogen pressure were varied to investigate the influence on *N*-PHA formation with the Pt nanoparticulate catalyst. The results are reported in Table 1 and Table 2 respectively. In table 2, the NB hydrogenation rates R_0 have also been included. Intermediates NOB and AZOX are not detected in ethanol under given reaction conditions, so aniline is the only by-product. NB conversion and *N*-PHA selectivity were determined at partial NB conversion (around 40% of total expected H_2 uptake). At this point, the reaction was completely stopped and samples were withdrawn for analysis. The time at which the sample is withdrawn is also reported in the tables and is related to the reaction rate of mainly NB/NOB hydrogenation (step a,b). The results in Table 1 clearly demonstrate that a decrease in reaction temperature increases the formation of *N*-PHA. Formation of *N*-PHA over AN in the early stage of the reaction is favoured at 7, 21 and 30°C whereas an increase in the reaction temperature results in a steep selectivity decrease. At 60°C, *N*-PHA is formed at almost the same rate as AN and at 100°C its formation becomes drastically suppressed with a selectivity of only 18.4%. These results seem to give a hint towards a higher activation barrier for the final hydrogenation step c to aniline. Lowering the temperature can therefore promote the built-up of the *N*-PHA intermediate.

Table 1. Effect of temperature on *N*-PHA selectivity. Conditions: 62 mg 0.7% c-Pt/C, 2.75 g (22.3 mmol) nitrobenzene (S/Pt=10 x 10³) in 80 mL ethanol at 4 bar H₂.

Temperature (°C)	7	21	30	41	60	100
Time (min)	32.5	13.5	15.9	5.0	3.5	3.0
NB conv. (%)	59.3	62.6	72.0	57.5	52.7	50.7
<i>N</i> -PHA select. (%)	92.6	86.9	79.1	75.3	57.7	18.4

Table 2. Effect of H₂ pressure on *N*-PHA selectivity. Conditions: 62 mg 0.7% c-Pt/C, 2.75 g (22.3 mmol) nitrobenzene (S/Pt=10 x 10³) in 80 mL ethanol at 30°C.

H ₂ Pressure (bar)	1.0	4.0	12.0	23.0	35	50.0
Time (min)	46.5	15.9	10.2	8.4	4.0	3.0
NB conv. (%)	53.0	72.0	65.1	66.2	51.2	51.7
<i>N</i> -PHA select. (%)	53.4	79.1	89.1	91.1	94.3	91.1
R_0 (M s ⁻¹ g _{Pt} ⁻¹)	0.12	0.47	0.66	0.82	1.3	1.8

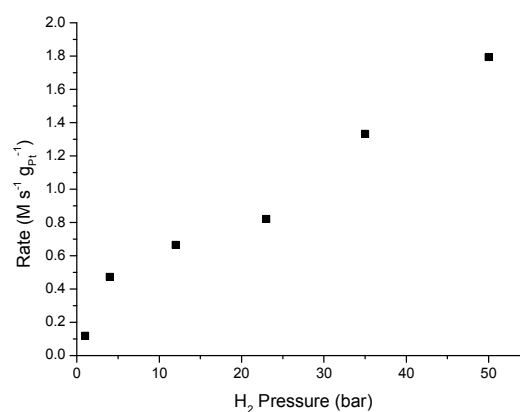


Figure 2. Pt-catalysed hydrogenation of nitrobenzene at 30°C as a function of H₂ pressure. Rate was determined at the data points reported in Table 2, expressed in M s⁻¹ g_{Pt}⁻¹.

As reported in Table 2, an increase in H₂ pressure at 30°C results in a steep increase in *N*-PHA formation. Selectivity increases from 53.4% at 1 bar to 91.1% at 50 bar H₂. Also the rate of *N*-PHA formation, $R_{a,b}$, increase, since the time to reach the specified conversion drops significantly and a first order rate dependence on H₂ is observed from 4 bar H₂ to 50 bar (see Figure 2). The remarkable lower activity at 1 bar H₂ is in line with previously reported work with supported Pt and Pd catalysts.^{24,25} When the pressure was increased from 23 to 50 bar, the *N*-PHA selectivity remains 91.1% with a 94.3% selectivity at 35 bar. An increased individual reaction rate $R_{a,b}$ (and the decreased rate R_c) results in the dominant *N*-PHA presence at an intermediate stage. Naturally, aniline will be the sole product at longer reaction times. This relationship between the pressure of molecular hydrogen and *N*-PHA selectivity has not been reported thus far in literature. Previously reported work shows that the intermediate *N*-PHA concentration does not change over supported Pt catalysts from

10 to 50 bar H₂.^{15,18} Moreover, a reported H₂ pressure screening from 0 to 1 bar showed a decrease in selectivity.²⁶

In order to elucidate why an increased H₂ pressure results in higher *N*-PHA yields, the full reaction profile was monitored for the reaction at 23 bar H₂ (Figure 3). In comparison, the reaction rate, $R_{a,b}$, was somewhat higher compared to the reaction rate at 4 bar H₂ (Figure 1). The relative rate of *N*-PHA formation ($R_{a,b}$) and *N*-PHA hydrogenation (R_c) is $R_{a,b}/R_c = 8.0/0.62 = 12.9$ at 23 bar and 30°C where at 4 bar H₂ this is $3.62/0.82 = 4.5$. At 23 bar H₂, a maximum *N*-PHA concentration was reached at 15 min and all NB was consumed within 20 min. At this H₂ pressure full conversion to aniline took 350 min. Surprisingly, the time to full conversion was only 200 minutes at 4 bar H₂. The *N*-PHA hydrogenation rate R_c is actually lower under 23 bar H₂ total pressure. This implies a negative order dependence in hydrogen on R_c , which is the reason for the increased selectivity to *N*-PHA. Mechanistically, when *N*-PHA is adsorbed on a metal surface via its oxygen atom, *N*-O hydrogenolysis would yield aniline and Pt-O bond hydrogenolysis yields *N*-PHA. At hydrogen concentrations reaching Pt surface saturation Pt-O bond dissociation becomes more dominant.¹⁵

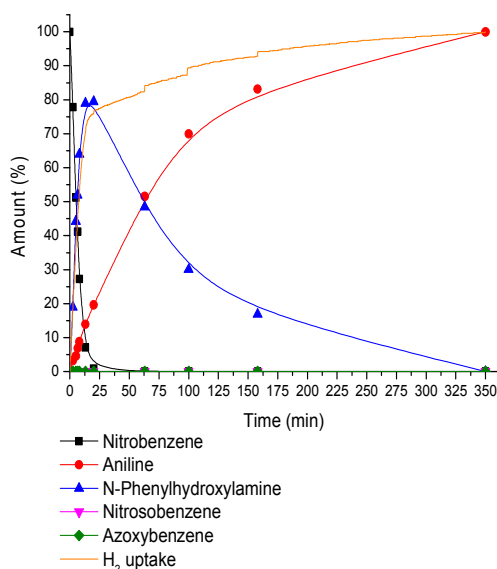


Figure 3. Reaction profile for the Pt-catalysed nitrobenzene hydrogenation at 23 bar H₂. Conditions: 62 mg 0.7% c-Pt/C, 2.75 g (22.3 mmol) nitrobenzene ($S/Pt=10 \times 10^3$) in 80 mL ethanol at 30°C.

From literature it is well-known that activity increases when more polar protic solvents are used, therefore methanol, ethanol, or isopropanol are typically the solvents of choice.²⁷ This higher activity could be explained by their ability to donate a proton besides activated hydrogen on the surface of the catalyst. Ethanol was chosen as solvent in the results shown above. However, since the results are slightly different compared to previously reported work, also the influence of solvent on the selectivity was investigated. After an initial screening, we found that in polar amine solvents, the reaction almost completely stops at 2/3 of total H₂ uptake. Figure 4 compares the H₂ uptake of two separate hydrogenation

experiments, one in ethanol and one in triethylamine. It appeared that the *N*-PHA hydrogenation is blocked, most probably by competitive adsorption of the strongly coordinating amine on the catalyst surface. In triethylamine, at the plateau, the *N*-PHA yield is 80 % with 10 % AN and 10 % AZOX. In ethanol, the *N*-PHA yield was 55 % at the transition point (20 min) with 10 % NB and 35 % AN.

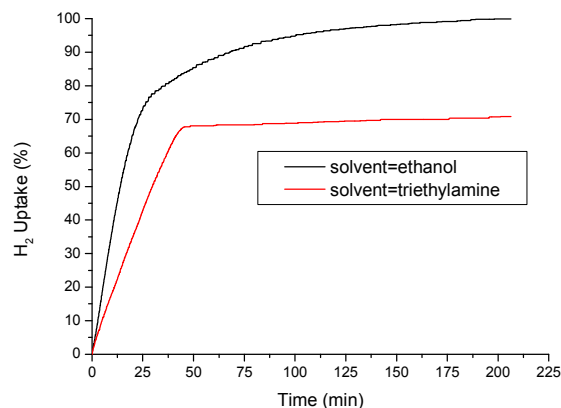
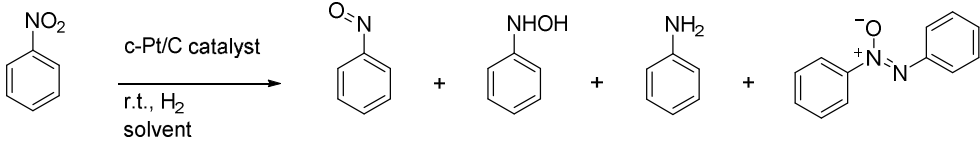


Figure 4. H₂-uptake plot for the Pt-catalysed nitrobenzene hydrogenation in 80 mL (a) ethanol and (b) triethylamine with 62 mg 0.7% c-Pt/C, 2.75 g (22.3 mmol) nitrobenzene ($S/Pt=10 \times 10^3$) and 4 bar H₂ at 30°C.

To test the influence of solvent, a range of Pt-catalyzed NB hydrogenation experiments were performed at room temperature in combination with H₂ supply from a balloon. Table 3 contains the results obtained after a reaction time of 16 h. Important when looking at high *N*-PHA selectivity is the formation of NOB. NOB formation seems to go along with more AZOX, since AZOX is formed from the reaction of NOB with *N*-PHA (Scheme 1). Self-condensation of *N*-PHA in comparison is much slower and appears to require oxygen, which is why entries 1-4 in Table 3 show no AZOX formation. Namely they do not release NOB into solution, thus *N*-PHA can be formed in significant amount without AZOX formation. Note that azobenzene was not detected in any of the reactions reported in this work. When NB was hydrogenated in triethylamine at 20 bar H₂, still 16.5 % AZOX was formed, meaning that NOB is still formed at elevated pressures.

Table 3. Pt-catalysed nitrobenzene hydrogenation in different solvents after 16 h of reaction.


Entry	Solvent	NB Conv. (%)	NOB (%)	N-PHA (%)	AN (%)	AZOX (%)	N-PHA Select. (%)
1	Ethanol	51.6	0	31.4	20.2	0	60.9
2	Isopropanol	58.1	0.9	34.7	22.6	0	59.6
3	Toluene	34.1	0	15.8	18.4	0	46.3
4	n-Hexane	31.8	0	1.3	30.6	0	4.1
5	Triethylamine	80.8	1.2	69.3	3.6	6.8	85.7
6 ^a	5% Pt/C	65.2	0.7	52.4	4.7	7.5	80.2
7 ^a	5% Pt/SiO ₂	91.9	4.1	30.3	50.6	6.9	33.0
8	Pyridine	30.3	0	29.9	0	0.4	98.7
9	Piperidine	19.1	3.3	12.9	0	2.9	67.5
10	n-Butylamine	56.1	2.5	28.7	0	24.9	51.2
11	Aniline	39.2	0	16.1	23.1	0	41.1

62mg of 0.7% c-Pt/C, 22.3 mmol nitrobenzene (mol ratio, S/Pt=10 x 10³), 40 mL solvent, 1 bar H₂ total pressure (balloon) at r.t.
¹H NMR yields, 10% 1,3,5-trimethoxybenzene used as internal standard.
^aS/Pt=1.0 x 10³

As reported in Table 3, ethanol and isopropanol show respectively 51.6% and 58.1% conversion in 16 hours. In comparison, *n*-hexane as non-polar solvent, showed a somewhat lower activity with a conversion of only 31.8% and the formation of *N*-PHA is largely suppressed. Among the amine solvents, triethylamine is most activating (high $R_{a,b}$) with a relatively high selectivity of 85.7% but with still considerable NB conversion in 16 h. Variation of the H₂ pressure in experiments performed at 1 bar and 23 bar H₂ in triethylamine showed that the overall yield was limited to 80% *N*-PHA due to NOB and AZOX formation. These yields of up to 80% *N*-PHA are the same as results obtained in ethanol at high H₂ pressure at 30°C, but in ethanol aniline is the only by-product.

Little is reported about the role of solvents and their individual performance in the three-phase hydrogenation of nitrobenzene. Quantum mechanical PM3 calculations of solvent-substrate adducts have been performed in literature to correlate empirical reaction rates with effective charges on NB/NOB/*N*-PHA atoms when dissolved in ethanol.²⁸ Naturally, ethanol can form hydrogen bonds with the atoms of the nitrogen group of all the NB hydrogenation intermediates presented in Scheme 1. Interestingly, the *N*-PHA-ethanol adduct showed a lowered effective positive charge of the nitrogen atom ($q_{er}=0.119$) compared to a solvent free environment ($q_{er}=0.127$). This was not the calculated result for NB and NOB ethanol adducts,

where the effective charge on nitrogen increased. This could indicate a stabilizing effect of *N*-PHA in alcoholic solvents.²⁸ Since hexane and toluene are not capable of forming hydrogen bonds with *N*-PHA, *N*-PHA is detected in much lower quantities during the course of the reaction. Besides nitrobenzene solubility, naturally also the hydrogen solubility is of importance. Especially, since an increase in the pressure of hydrogen resulted in an increase in *N*-PHA selectivity. However, the H₂ solubility in hexane is much higher than in ethanol, isopropanol and toluene, but the selectivity is substantially lower.²⁷ The different levels of hydrogen dissolved in the liquid seems to be of minor importance when comparing the solvents.

To investigate how the NanoSelectTM catalyst compares with other commercially available Pt catalysts, 5% Pt/C and 5% Pt/SiO₂ were used as reported in Table 3 entries 6 and 7. More Pt (S/Pt=1,000) was introduced, as much lower activities were observed. Besides being intrinsically less active, reasonable selectivities were obtained with 5% Pt/C and 5% Pt/SiO₂ yielding resp. 52.4% and 30.3% *N*-PHA. Comparison of hydrogenation activity and *N*-PHA selectivity between the 0.6% c-Pd, 0.7% c-Pt/C and 5% Pt/C at varied H₂ pressure are reported in the supplementary information in a separate table. It shows that the response when increasing H₂ pressure from 4 bar to 23 bar at 30°C is similar for the 5% Pt/C catalyst. However,

still at a much lower initial rate of $0.036 \text{ M s}^{-1} \text{ g}_{\text{Pt}}^{-1}$ compared with $0.82 \text{ M s}^{-1} \text{ g}_{\text{Pt}}^{-1}$ for the colloidal 0.7% c-Pt/C at 23 bar and 30°C .

When other nitroarenes were tested we combined both strategies so to obtain maximum yields of the corresponding *N*-AHAs using the NanoSelect™ Pt catalyst. This meant adding small amounts of amine to the reactions in EtOH at high pressure (50 bar H_2). As an amine derivative, *N,N,N',N'*-tetramethylethylenediamine (TMEDA) was found very efficient when added in small quantities to the reaction mixture. 1% TMEDA was sufficient, addition of more did not result in a further increased *N*-PHA yield. A solvent mixture of EtOH and THF (1/1, v/v) was chosen because of the poor solubility of some of the substituted nitrobenzene substrates tested, e.g. 4-nitroanisole in absolute ethanol. Experimental procedure is fully described in the supplementary information. When nitrobenzene was hydrogenated under these conditions, the *N*-PHA yield increased to 97.1% as reported in Table 4 entry 1.

Table 4. Pt-catalysed nitroarene hydrogenation. Conditions: 62 mg 0.7% c-Pt/C, 22.3 mmol nitroarene ($\text{S/Pt}=10 \times 10^3$), 0.223 mmol TMEDA, 80 mL EtOH/THF (1/1), 50 bar H_2 at r.t.

entry	R	t (min)	R-NB Conv. (%)	<i>N</i> -AHA yield (%)	R-AN (%)	<i>N</i> -AHA Select. (%)
1	H	43	>99.9	97.1 (95.0) ^a	2.9	97.1
2	2-Cl	30	98.6	97.2	1.4	98.6
3	4-Br	25	>99.9	98.6	1.4	98.6
4	4-CN	13	99.1	98.0	1.0	99.0
5	4-OMe	96	98.8	91.4	7.4	92.5
6	3-C=C	35	>99.9	89.3	3.2	89.3

^aIsolated yield.

2-Chloronitrobenzene was chosen as a substrate with an electron-withdrawing functional group. As expected, the selectivity for the hydrogenation of 2-chloronitrobenzene to *N*-2-chlorophenyl hydroxylamine is high with 97.2% (Table 4, entry 2). No hydrogenolysis of the C-Cl bond was observed, not even after 20 h of reaction. Notably, even the C-Br was retained at set hydrogenation conditions with a 98.6% maximum formation of 4-bromo-*N*-phenylhydroxylamine.

4-Nitrobenzotrile was chosen as it contains another electron withdrawing, but reducible substituent (Table 4, entry 4). Full conversion was reached in only 13 minutes with a maximum *N*-AHA yield of 98%.

4-Nitroanisole is more challenging due to the electron donating methoxy substituent, making the nitro functional group less electrophilic. A lowered electrophilicity means lower activity when hydrogenated with the strongly nucleophilic Pt-catalyst. For this reason 96 minutes were required for full conversion of 4-nitroanisole with a corresponding maximum yield of 91.4% 4-Methoxy-*N*-phenylhydroxylamine (Table 4, entry 5).

Entry 6 in Table 4 shows the high chemoselectivity for the nitro group in the hydrogenation of 3-nitrostyrene. An 89.3% yield of the corresponding *N*-AHA was obtained without much hydrogenation of the C=C bond (7.5% of 3-ethylaniline is formed).

This selected group of nitroaromatics was chosen but we believe that a much broader group of substituted *N*-Phenylhydroxylamines could be synthesized with high yields.

Finally, a “hot filtration” experiment was carried out to exclude possible leaching of large amounts of platinum into solution. At high pressure and in the presence of TMEDA, the reactivity in terms of nitrobenzene hydrogenation stopped completely after catalyst filtration from the reaction solution and no sign of any additional reactivity was observed (see supplementary information).

Conclusions

In the Pt-catalysed hydrogenation of nitrobenzenes using Pt nanoparticles of the NanoSelect™ type the selectivity towards the intermediate *N*-arylhydroxylamines has been optimized. Hydrogenation of nitrobenzene to aniline in ethanol at 4 bar H_2 pressure already showed reasonable 79.1% intermediate selectivity of *N*-PHA, with a maximum intermediate yield of 55%. Increasing the hydrogen pressure to 23 bar significantly increased the intermediate formation to 80% so that *N*-PHA can be obtained in good yields at an intermediate stage. This is explained by the negative order in H_2 concentration for the (over)hydrogenation rate of *N*-PHA. Performing the experiments in different solvents showed that polar solvents are more activating and selective towards *N*-PHA because they are capable of forming hydrogen bonds with the substrate. Moreover, amine solvents such as triethylamine and pyridine were found especially selective, because they suppress further *N*-PHA hydrogenation to a large extent (step c) by competitive adsorption. However, formation of AZOX side products makes using amine solvents undesired.

In summary, to obtain high yields of *N*-PHA in the Pt-catalysed hydrogenation of nitrobenzene, firstly a low temperature is favourable. Secondly, hydrogen bonding of *N*-PHA with the solvent and finally *N*-PHA substitution from the surface by amines and a high concentration of molecular hydrogen.

With this knowledge, the conditions were optimized in order to convert a variety of nitroarene substrates to *N*-AHAs. Experiments performed at high H_2 pressure (50 bar) with TMEDA as amine additive resulted in excellent 90+% *N*-AHA yields.

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Notes and references

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Electronic Supplementary Information (ESI) available: Results of the Pt leaching experiment, catalyst synthesis, detailed experimental procedure including NMR data of all the N-arylhydroxylamines, TEM images. See DOI: 10.1039/b000000x/

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