



New insight on the mechanism of the catalytic hydrogenation of nitrobenzene to 4-aminophenol in $\text{CH}_3\text{CN}-\text{H}_2\text{O}-\text{CF}_3\text{COOH}$ as a reusable solvent system. Hydrogenation of nitrobenzene catalyzed by precious metals supported on carbon

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ARTICLE INFO

Article history:

Received 14 November 2013
Received in revised form 9 January 2014
Accepted 13 January 2014
Available online 22 January 2014

Paper dedicated to Prof. Luigi Toniolo for celebrating his long research and teaching activity in the field of Catalysis and Industrial Chemistry after his mandatory retirement.

Keywords:

Nitrobenzene hydrogenation
4-aminophenol
Trifluoroacetic acid
Reusable solvent
Hydrogenation mechanism

ABSTRACT

The preparation of 4-aminophenol via hydrogenation of nitrobenzene in a single liquid phase has been carried in the presence of different precious metal catalysts. The liquid phase is composed of $\text{CH}_3\text{CN}-\text{H}_2\text{O}-\text{CF}_3\text{COOH}$, which can be easily distilled at low temperature, thus avoiding work-up operation. The yield of 4-aminophenol is in the range 45% and in the presence of sulfolane as promoter reaches almost 50%. The best result has been obtained in the presence of Pt/C as hydrogenation catalyst. The role of the solvent is strictly related to the selectivity to 4-aminophenol, since CH_3CN decreases the hydrogenation activity compared to other solvent, CF_3COOH promotes the formation of the desired product both via Bamberger rearrangement in solution as well by a surface catalyzed reaction, while H_2O is responsible for 4-aminophenol formation in both reactions. Even though, nitrosobenzene and phenylhydroxylamine have not been observed, their reactivity suggest a complex pattern of reactions occurring either on the catalyst surface or in the solution. Indeed, formation of 4-aminophenol may occur both in solution, via acid catalyzed Bamberger rearrangement and on the catalyst surface by the formation of a surface Pt-nitrenium complex, which undergoes surface nucleophilic attack by H_2O .

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1. Introduction

4-Aminophenol is an important raw material for several products in the field of dyes, polymer and pharmaceuticals [1–3]. For instance, paracetamol (*N*-acetyl-4-aminophenol) is a widely employed analgesic and antipyretic whose production is in continuous growth, particularly in the Far East region [4–9]. Industrial synthesis of paracetamol is based on 4-aminophenol, which is obtained through four different routes: (i) nucleophilic substitution of the chlorine of the 4-chloronitrobenzene, (ii) reduction of 4-nitrophenol, (iii) selective hydrogenation of nitrobenzene, (iv) Beckmann rearrangement of 4-hydroxyacetophenone oxime.

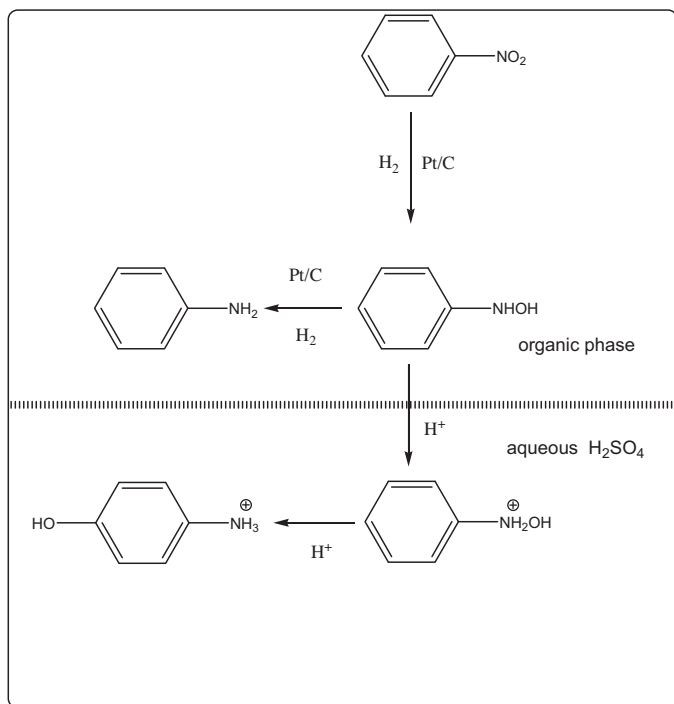
Till now, the selective hydrogenation of nitrobenzene is likely to be the most convenient from both economical and environmental point of view [1,2,4–9]. The major concern of this process is, however, the use of H_2SO_4 , which poses corrosion, safety, purification and environmental problems. The reaction is carried out

in continuous stirred tank reactor in which the biphasic reaction medium is used to accomplish simultaneously the Pt catalyzed hydrogenation of nitrobenzene and the acid catalyzed Bamberger rearrangement of the intermediate *N*-phenylhydroxylamine (see Scheme 1) [4–6,8,9]. The aqueous solution of H_2SO_4 is the key for obtaining high selectivity to the 4-aminophenol. The success is due to the easy protonation of the phenylhydroxylamine ($pK_a = 1.9$ [10]), which is extracted from the organic phase. In the acid solution (H_2SO_4 concentration $0.6\text{--}1\text{ mol L}^{-1}$), the sulfate of the *N*-phenylhydroxylamine is formed and it undergoes fast rearrangement to the corresponding 4-aminophenol salt [11]. Moreover, in aqueous phase, the competitive hydrogenation of the phenylhydroxylamine is negligible, being the hydrogenation catalyst hydrophobic. In fact, only the fraction present in the organic phase is hydrogenated to aniline [12].

From an environmental point of view, the major drawback of the process is the neutralization of the acidic phase, with the consequent by-production of sulfate salts, which are undesired low values products and/or wastes. In addition, diluted sulfuric acid causes huge corrosion concern, with the consequent increased costs [1,2,4–6,8,9].

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Scheme 1. Hydrogenation of nitrobenzene in biphasic liquid system.

Therefore, removal of H_2SO_4 use is likely to be the most important target for the improvement of the process. Several researchers have recently proposed the use of a biphasic liquid system (water-nitrobenzene) employing Pt supported on solid acid in the presence of surfactant and promoters, which, however, cause problems in the recycle and/or disposal of the aqueous phase [13–15].

Besides, gas phase reaction catalyzed by bifunctional Pt-zeolites catalysts has been proposed. The yields to the 4-aminophenol are interesting for practical purposes, however extensive catalyst deactivation limits its synthetic utility [16].

Starting from these considerations, a single liquid phase process could be a catwalk to a more sustainable process by using easily reusable solvents and catalysts [17–20]. When products are solids or high boiling point liquids the use of a much lower boiling point solvent can be the key to improve the environmental sustainability of the whole process, because of products separation, catalyst and solvents reuse is made easy by filtration and evaporation. In this way, the high cost of CF_3COOH is counter balanced by its recycling, making the process sustainable also from an economical point of view.

The bases of the present research are the results in the Beckmann rearrangement of ketoximes to the corresponding amides in $\text{CH}_3\text{CN}-\text{CF}_3\text{COOH}$ as solvent catalytic system [17–20]. The analogy between the Beckmann rearrangement with the process to 4-aminophenol via nitrobenzene hydrogenation originates from the idea that the *N*-phenylhydroxylamine (the intermediate of the process) (see Scheme 1) may undergo acid Bamberger rearrangement very easily in non-aqueous CF_3COOH system.

The rearrangement is well known from long time and the commonly accepted mechanism is via nitrenium ion intermediate followed by nucleophilic attack of a water molecule (Scheme 2) [11,21,22].

Several solvents can be used for the hydrogenation reaction, but those to be considered in this research possess low nucleophilicity in order to avoid side reaction in the Bamberger rearrangement [21,22]. In addition, suitable solvents (for instance CH_3CN and $(\text{CH}_3)_2\text{SO}$) have to lower the hydrogenation activity of

the precious metal catalyst in order to depress the reduction of *N*-phenylhydroxylamine to aniline [23].

Here, we present some new results on the hydrogenation of nitrobenzene to 4-aminophenol in a single liquid phase composed of solvent- $\text{H}_2\text{O}-\text{CF}_3\text{COOH}$ and in the presence a precious metal hydrogenation catalyst. Furthermore, we propose a reaction path, which allows an explanation for the several features of this reaction.

2. Experimental

2.1. Materials

Nitrobenzene, aniline, 4-aminophenol, 2-aminophenol, trifluoroacetic acid, sulfolane were all Aldrich products, their purity were checked by the usual methods (melting point, TLC, HPLC, GC and GC-MS) and employed without any purification, acetonitrile HPLC gradient grade was supplied by BDH, 1,4-dioxane, methanol, nitromethane, dimethylformamide and dimethyl sulfoxide are ACS reagent supplied by Aldrich.

Catalysts used were commercial materials supplied by Engelhard (now Basf Catalysts): Pd/C 5%: Escat 10, Pt/C 3%, Ru/C 5% Escat 40 and Rh/C 5%.

2.2. Equipment

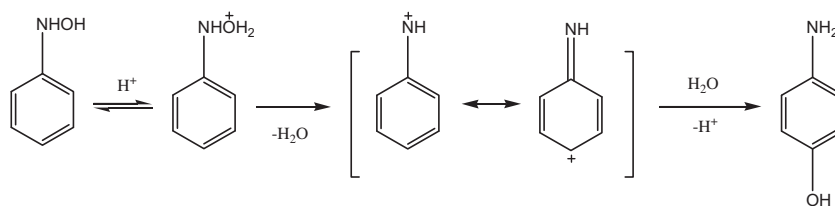
Products were identified by gas chromatography (GC), gas chromatography coupled mass spectrometry (GC-MS) and high performance liquid chromatography (HPLC). GC and GC-MS analysis were carried out with a Agilent 7890A equipped with FID or MS detector (Agilent 5975 C and a HP 5 column (I.D. 320 μm 30 m long), helium was employed as carrier under the following conditions: injector 523 K, detector 543 K, flow 1 mL min^{-1} , oven 333 K for 3 min 523 K 15 K min^{-1} and 523 K for 15 min. Due to the thermal instability of the products, routine analysis were carried out by HPLC (PerkinElmer 250 pump, LC 235 diode array detector and a C 8, 5 μm , 4 mm i.d. 25 cm long column) analysis were carried out with $\text{CH}_3\text{CN}-\text{H}_2\text{O}$ as mobile phase in isocratic 70% of CH_3CN at 1 mL min^{-1} . Conversion yield and selectivity are calculated by the calibration with standard solutions of the pure products. N_2 physisorption and CO chemisorption has been carried out with a Micromeritics ASAP 2010C automatic adsorption analyzer.

2.3. Catalyst characterization

Chemisorption of carbon monoxide was carried at 308 K with the double isotherm method and 1 min of equilibration time [24]. The chemisorption stoichiometry was set 1 (1 molecule of CO for 1 surface atom of metal) only for comparative purpose. Before the analysis, the catalyst was pretreated in a flow of hydrogen (20 mL min^{-1}) at 473 K for 3 h and for 5 h under vacuum at the same temperature in order to ensure total reduction of the precious metal particles average diameter of catalyst particles (40 μm) and apparent density (0.54 g mL^{-1}) were given by the supplier and are the same for all the catalysts (see Table 1).

2.4. Hydrogenation of nitrobenzene

Some preliminary reactions have been carried out in several solvents (1,4-dioxane CH_3NO_2 , $(\text{CH}_3)_2\text{NCHO}$ and $(\text{CH}_3)_2\text{SO}$ CH_3OH). The kinetic runs were carried out in a well stirred glass reactor thermostatted by circulation bath in the range 323–353 K, using $\text{CH}_3\text{CN}-\text{H}_2\text{O}$ as a solvent, CF_3COOH as an acid catalyst and a precious metal catalyst (Pt, Pd, Rh, Ru) supported on carbon. Hydrogen was fed continuously at constant pressure (c.a. 0.12 MPa) by a gum balloon (see supplementary information). Blank reactions in the absence of nitrobenzene have been carried out in order to verify



Scheme 2. Bamberger rearrangement of phenylhydroxylamine.

Table 1

Properties of precious metal catalysts supported on carbon black: metal dispersion, total surface area.

Catalyst	Metal dispersion (%)	CO uptake (mL g _{cat} ⁻¹)	BET surface area (m ² g _{cat} ⁻¹)
Pt/C 3%	65	2.5	920
Pd/C 5%	27	3.2	880
Rh/C 5%	24	2.9	890
Ru/C 5%	23	2.8	910

the stability of the solvent. All the solvents employed did not show any products of reduction at GC analysis.

In a typical experiment 2.5 mL of acetonitrile, with suspended the Pd/C catalyst (typically 50 mg), was introduced into the reactor. After that the reactor was closed, purged before with nitrogen and then with hydrogen, pressurized at 121 kPa, finally heated at 353 K under stirring for 2 h in order to activate the catalyst. The temperature of reaction (range 323–363 K) was left to stabilize, than the preheated solution of acetonitrile water trifluoroacetic acid and nitrobenzene (*c.a.* 22.5 mL, concentration nitrobenzene 0.075 mol L⁻¹, CF₃COOH 0.2–0.8 mol L⁻¹) was added to reactor. After the addition of this solution, the computing of the reaction time starts and the liquid phase is periodically sampled and analyzed by GC, GC-MS and HPLC, during reaction course. Nitrobenzene at a concentration of 0.075 mol L⁻¹ is completely soluble in the H₂O–CH₃CN–TFA till 5 g of water in 25 mL of solution.

3. Results and discussion

3.1. Influence of the solvent system on the activity and selectivity

The type of solvent and the acidity of the system are parameters of paramount importance for activity, selectivity and resistance to deactivation of the precious metal phase in a catalyzed reaction. This is especially true in the nitrobenzene conversion to 4-aminophenol, since both reactions of the process (consecutive hydrogenation and Bamberger rearrangement) are sensitive to the nature of the solvent [23,25]. For this reason a screening of various solvents is important in order to select the best one for the reaction. We tested several solvents in the presence of Pt/C, however, CH₃CN gives the best results (see Table 2 and supplementary materials). The reason of the higher yield in 4-aminophenol by using CH₃CN as a solvent is likely due to a simultaneous and synergic effect of CH₃CN in deactivating the stage of hydrogenation and in promoting the rearrangement of the *N*-phenylhydroxylamine. As a matter of fact, in single phase reactions when CH₃CN is not the solvent much lower yield in 4-aminophenol is obtained. For instance, in the presence of 1,4-dioxane, methanol and nitromethane the reaction is selective to aniline, while it shows a complex mixture of products in dimethylformamide. On the contrary, the reactions are practically inhibited by using dimethyl sulfoxide or sulfolane as solvents, since they are both deactivating substances for hydrogenation precious metal catalysts [26]. Moreover, the reaction has been tested in the presence of HCl and CH₃SO₃H as acid systems. In the presence of HCl, as expected, the reaction proceed to the formation of aniline

and chloroanilines, while in the presence CH₃SO₃H we observe aniline and a complex mixtures of not identified products. In addition, we found the formation of two liquid phases and precipitation of salts in both reactions.

3.2. Influence of the catalyst type on reaction rate and selectivity

The results in the previous section suggest that the best solvent is CH₃CN, coupled with CF₃COOH as acid catalyst. Because of these evidences we will exclusively show results of experiments carried out in the mixture CF₃COOH–CH₃CN, which is actually a CF₃COOH–H₂O–CH₃CN system since H₂O is contained either in the solvent or in the reagent. In addition, H₂O is a reagent in the Bamberger rearrangement for this reason its role in the reaction path will be studied.

The comparison of various precious metal catalysts is reported in Table 2. It is noteworthy that the best performing one, in terms of both catalytic activity and yield to 4-aminophenol, is Pt/C. This gives the best results also with the biphasic sulfuric acid nitrobenzene system [1–6]. Both Pd/C and Rh/C show high hydrogenation activity, but 4-aminophenol yields (in both cases) is lower than that observed in the presence of Pt/C. Ru/C shows both poor hydrogenation activity and negligible 4-aminophenol yield, because of its intrinsic low hydrogenation activity observed in these reactions (Table 3).

Fig. 1 shows that the trends of 4-aminophenol yield vs. time are similar in the presence of different metal catalysts. These trends show that the formation of 4-aminophenol decreases as the reaction proceeds suggesting an influence of the products on the 4-aminophenol yield. As a matter of fact, amines reduce the overall acidity of the solution, thus likely decreasing the rate of rearrangement of the *N*-phenylhydroxylamine and the overall yield in 4-aminophenol. Besides, it is likely that the better performance

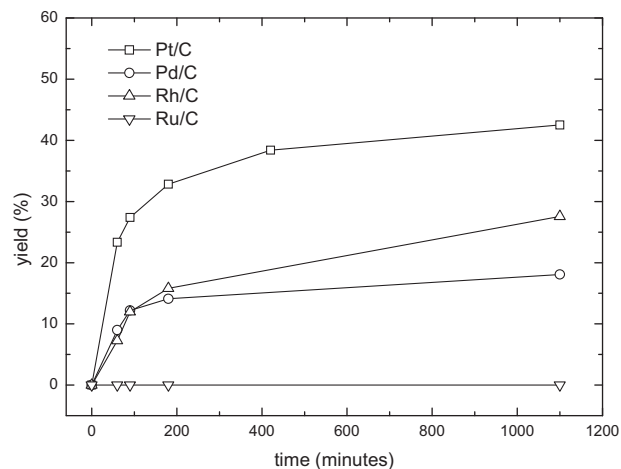


Fig. 1. Influence of the catalyst type on 4-aminophenol yield. Run conditions: T: 353 K, kPa, PH₂ 121 kPa, nitrobenzene 0.075 mol L⁻¹, CF₃COOH 0.6 mol L⁻¹, H₂O 0.2 g, CH₃CN 22 g, catalyst 50 mg.

Table 2
Influence of the solvent on 4-aminophenol and aniline yield after 20 h. Run conditions: T : 353 K, P_{H_2} 121 kPa, nitrobenzene 0.075 mol L^{-1} , acid catalyst 0.6 mol L^{-1} , H_2O 2.2 g, solvent 22 g, catalyst Pt/C 3% 50 mg.

Solvent-acid	Conversion (%)	Yield 4-AP ^a (%)	Yield AN ^b (%)	Yield others (%)	Notes
CH_3CN-CF_3COOH	65	42	13	10	Azoxy - azo benzene
$CH_3CN-HCl$	20	traces	10	10	Azoxy - azo benzene, chloroanilines
$CH_3CN-CH_3SO_3H$	20	traces	12	8	Azoxy - azo benzene
$C_4H_4O_2^c-CF_3COOH$	98	5	90	3	trifluoroacetanilide
$CH_3NO_2-CF_3COOH$	88	15	60	13	Azoxy - azo benzene, 2-EtO-aniline and anilides
$(CH_3)_2NCHO-CF_3COOH$	92	10 ^d	40	42	Unidentified products
$(CH_3)_2SO-CF_3COOH$	<1	-	-	Traces	At 378 K 1 MPa reaction does not proceed
$(CH_2)_4SO_2^e-CF_3COOH$	<1	Traces	Traces	Traces	Practically no reaction
CH_3OH-CF_3COOH	96	5	60	31	Trifluoroacetanilides, 2-EtO-aniline and anilides, Azoxy - azo benzene

^a 4-AP = 4-aminophenol.

^b AN = aniline.

^c 1,4-Dioxane.

^d mainly *N*-trifluoroacetyl-4-aminophenol.

^e Sulfolane.

Table 3
Influence of the catalyst type on nitrobenzene conversion, 4-aminophenol yield minutes and initial reaction rate after 180 min. Run conditions: T : 353 K, P_{H_2} 121 kPa, nitrobenzene 0.075 mol L^{-1} , CF_3COOH 0.6 mol L^{-1} , H_2O 2.2 g, CH_3CN 22 g, catalyst 50 mg.

Catalyst	Conversion (%)	Yield 4-AP ^a (%)	Yield AN (%)	Yield others (%)	r_0 ($\text{mol L}^{-1} \text{ min}^{-1} \text{ g}_{\text{met}}^{-1}$)
Pt/C 3%	41	26	2	12	0.13
Pd/C 5%	42	14	26	1	0.078
Rh/C 5%	46	16	29	1	0.080
Ru/C 5%	0.4	Traces	0.19	0.2	0.0007

^a These products are a mixture of 4-aminophenol and trifluoroacetylated compounds of 4-aminophenol.

of Pt/C catalyst is due to a specific selectivity of the catalyst to 4-aminophenol.

3.3. Time vs. concentration profiles

In Fig. 2 reaction shows time vs. concentration profiles of the species observed in the hydrogenation of nitrobenzene in $CH_3CN-H_2O-CF_3COOH$. The concentration of 4-aminophenol increases smoothly with the time, on the contrary, the yield to aniline has a significant increase only after a long time. Other products have been identified, but not precisely quantified and are signed as “other”. The main side products (in agreement with the Haber reduction scheme of nitrobenzene [27]) are azoxybenzene and azo-benzene, which are hydrogenated to aniline after a longer time. Besides, there are traces of *N*-phenylhydroxylamine

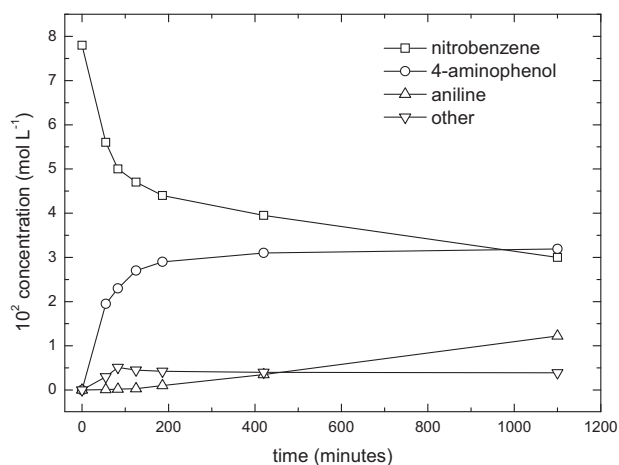


Fig. 2. Time concentration profile of nitrobenzene hydrogenation to 4-aminophenol. Run conditions: T : 353 K, P_{H_2} 121 kPa, nitrobenzene 0.75 mol L^{-1} , CF_3COOH 0.6 mol L^{-1} , H_2O 2.2 g, CH_3CN 22 g, catalyst Pt/C 50 mg.

and nitrosobenzene, but these products are present in very small amount and only after few minutes of reaction. It is noteworthy that the products “other” pass through a maximum and their decrease is accompanied with the steepest aniline increase. This behavior is consistent with the Haber reduction scheme of nitrobenzene where azobenzene and azoxybenzene are intermediates to aniline [27].

3.4. Influence of catalyst amount on the initial reaction rate

Fig. 3 shows the influence of the catalyst amount on the initial reaction rate and on the yield of 4-aminophenol. It appears (Fig. 3a) that external mass transfer poorly influences the reaction kinetics because of the small value of the intercept [28]. However, a complete evaluation of the influence of rate of diffusion of reagents and products on the reaction kinetics is beyond the scope of the present work, in which initial reaction rate data are given only for comparative purpose. The yield of 4-aminophenol seems to be faintly influenced by the catalyst amount (Fig. 3b), furthermore, catalyst deactivation affects the overall reaction kinetics, being reached a plateau, in any case.

3.5. Influence of temperature on reaction rate and selectivity

The Arrhenius plot of the initial reaction rate (see supplementary materials) presents an almost linear trend, with a temperature coefficient (or apparent activation energy) of 91 kJ mol^{-1} . Even though, kinetic data are referred to initial reaction rate, the value of the apparent activation energy together with the results of the previous section suggest the kinetic of reaction is poorly influenced by external diffusion limitation [28]. In additions, the inspection of Wheeler–Weisz criterion implies little influence of the internal diffusion, since values in the range of 0.05–0.11 are calculated for hydrogen and nitrobenzene, respectively [28]. These results are in agreement with other hydrogenation reaction carried out under similar conditions by using Pd/C catalysts with similar porosity and granulometry [24].

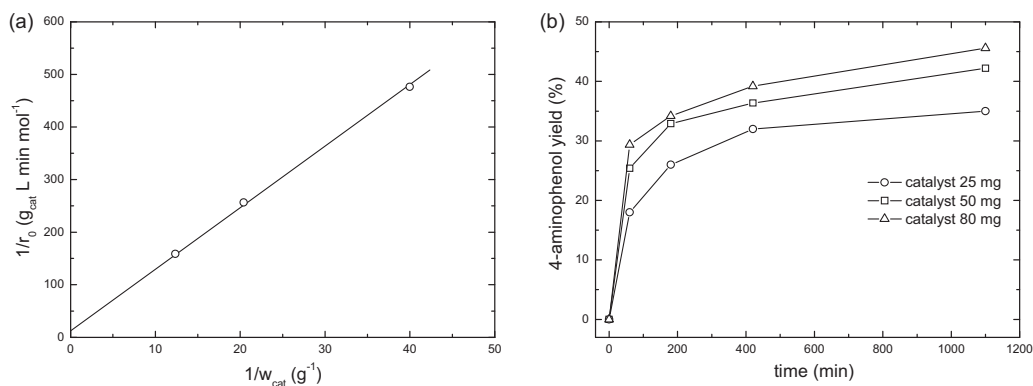


Fig. 3. Influence of catalyst loading on the initial reaction (a) rate and 4-aminophenol yield (b): T : 353 K, P_{H_2} 121 kPa, nitrobenzene 0.75 mol L⁻¹, CF_3COOH 0.6 mol L⁻¹, H_2O 2.2 g, CH_3CN 22 g, catalyst Pt/C 25–80 mg.

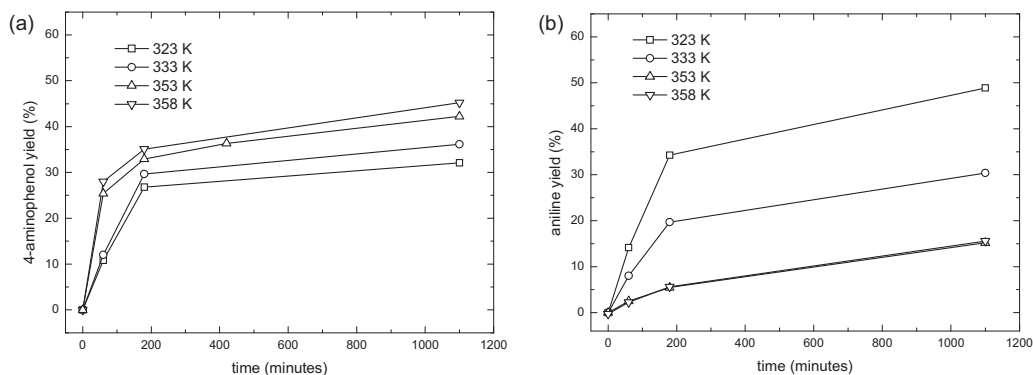


Fig. 4. Influence of temperature on 4-aminophenol (a) and aniline (b) yield. Run conditions: T : 323–358 K, P_{H_2} 121 kPa, nitrobenzene 0.075 mol L⁻¹, CF_3COOH 0.6 mol L⁻¹, H_2O 2.2 g, CH_3CN 22 g, catalyst Pt/C 50 mg.

The trends of 4-aminophenol and aniline yield (observed at different temperature and reported in Fig. 4) show that high temperatures favor the formation of 4-aminophenol, while aniline is the preferred product at the lower ones. This behavior suggests intermediates whose reactivity is strongly influenced by temperature and the kinetics of formation of 4-aminophenol has an activation energy higher than that of aniline.

3.6. Influence of CF_3COOH concentration on reaction rate and selectivity

The influence of the concentration of CF_3COOH on the reaction rate is reported in Fig. 5. The increase of the acid concentration corresponds to a small increase of the initial rate of reaction both at 333 K and at 353 K, thus suggesting the acid concentration slightly influences the overall kinetics of reaction. It is likely that the first step of nitrobenzene hydrogenation is the rate determining step, for which the influence of the acid is negligible. The small increase of the initial rate with acid concentration could be interpreted as a solvent effect of the acid on the polarity of the solvent [23,29].

On the contrary, Fig. 6 shows that the selectivity is strongly influenced by the CF_3COOH concentration. The increase of the acid concentration causes an increase of 4-aminophenol yield and a decrease of the yield in aniline. Such a behavior is in agreement with the formation of an intermediate whose reactivity is sensitive to the acid concentration. Besides, it is likely that the practically negligible concentration of *N*-phenylhydroxylamine (only traces), observed during the reaction course, is due to all the simultaneous reactions involved both in solution and on the catalyst surface.

3.7. Influence of water concentration on initial rate of reaction and 4-aminophenol yield

In Table 4 the influence of water concentration after 180 min of reaction is reported. The sensitivity of the reaction to water concentration is noteworthy, since only in a narrow range of concentration (c.a. 10 wt.%) both high initial reaction rate and high yield in 4-aminophenol is achieved. The reasons of such a behavior are not straightforward because of the large number of

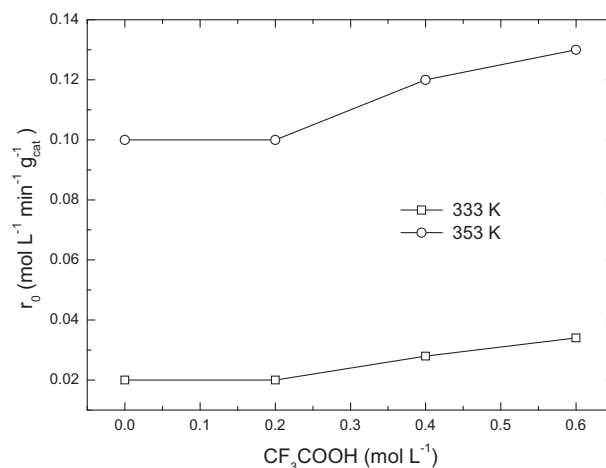


Fig. 5. Influence of CF_3COOH concentration on initial reaction rate. Run conditions: T : 353 K, P_{H_2} 121 kPa, nitrobenzene 0.075 mol L⁻¹, CF_3COOH 0–0.6 mol L⁻¹, H_2O 2.2 g, CH_3CN 22 g, catalyst Pt/C 50 mg.

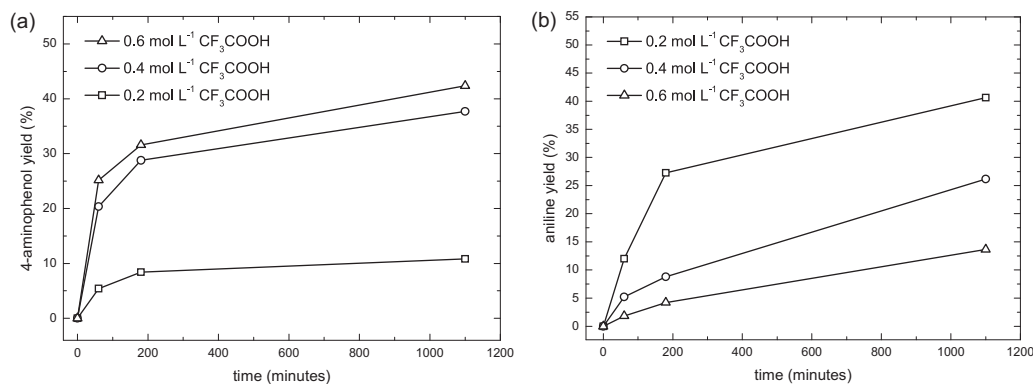


Fig. 6. Influence of CF_3COOH concentration on 4-aminophenol (a) and aniline (b) yield. Run conditions: T : 353 K, PH_2 121 kPa, nitrobenzene 0.075 mol L^{-1} , CF_3COOH 0–0.6 mol L^{-1} , H_2O 2.2 g, CH_3CN 22 g, catalyst Pt/C 50 mg.

equilibria in which water is involved. Indeed, water may compete with the reagents for the adsorption on Pt surface and may reduce the protonation ability of the trifluoroacetic acid, which is likely to be related to *N*-phenylhydroxylamine rearrangement to 4-aminophenol [11,20,21]. On the other hand, water is involved in the formation of 4-aminophenol, being the required nucleophile for obtaining the product [11,20,21].

3.8. Influence of sulfolane and dimethyl sulfoxide as promoters in 4-aminophenols formation

The influence of sulfolane and dimethyl sulfoxide as promoters for 4-aminophenols formation is reported in Fig. 7. In the preliminary study on the solvent effect (Section 3.1) both sulfolane and dimethyl sulfoxide used as the solvent inhibit the reaction completely. Such a strongly deactivating effect of these sulfur compounds as solvent towards the Pt catalyst, suggests their potential use as selective modifier of the platinum surface, in order to try an enhancement of the selectivity to 4-aminophenol [8,26]. As a matter of fact, the presence of sulfolane increases both reaction

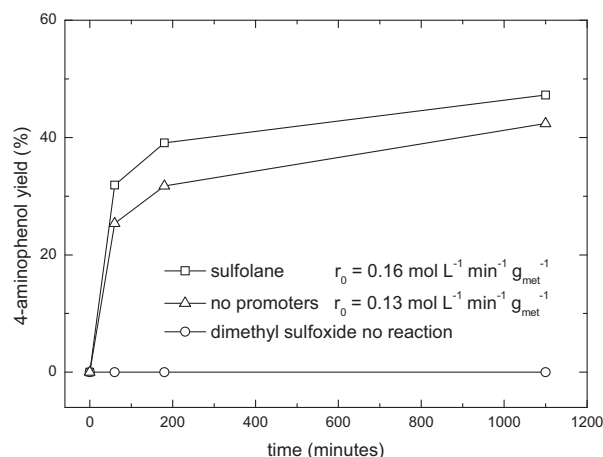


Fig. 7. Influence of promoters on 4-aminophenol yield. Run conditions: T : 353 K, PH_2 121 kPa, nitrobenzene 0.075 mol L^{-1} , CF_3COOH 0.6 mol L^{-1} , H_2O 2.2 g, CH_3CN 22 g, catalyst Pt/C 50 mg, sulfolane and dimethyl sulfoxide concentration 0.03 mol L^{-1} .

Table 4
Influence of water on nitrobenzene hydrogenation. Run conditions: T : 353 K, PH_2 121 kPa, nitrobenzene 0.075 mol L^{-1} , CF_3COOH 0.6 mol L^{-1} , CH_3CN 22 g, catalyst Pt/C 3% 50 mg.

Water (mg)	Conversion (%)	Yield 4-AP ^a (%)	Yield AN ^b (%)	Yield others (%)	r_0 ($\text{mol L}^{-1} \text{ min}^{-1} \text{ g}_{\text{met}}^{-1}$)
20 ^c	10	6 ^d	2	2 ^e	0.02
1300	60	10 ^d	3	40 ^e	0.18
2200	42	26 ^d	3	12 ^e	0.13
3400	16	6 ^d	2	8 ^e	0.03
4000	1	–	Traces	1 ^e	0.001

^a 4-AP = 4-aminophenol.

^b AN = aniline.

^c H_2O contained in the CH_3CN measured by HPLC analysis [30].

^d These products are a mixture of 4-AP and trifluoroacetylated compounds of 4-AP.

^e These products are mainly recognized as azobenzene and azoxybenzene and trifluoroacetanilide.

Table 5
Reactivity of nitrosobenzene in the presence of phenylhydroxylamine and aniline under N_2 after 120 min of reaction. Run conditions T : 353 K, nitrosobenzene 0.02 mol L^{-1} , H_2O 2.2 g, CH_3CN 22 g.

Hydrogen donor	Pt/C 3% (mg)	CF_3COOH (mol L^{-1})	Conversion (%)	Yield azoxybenzene + azobenzene (%)
Phenylhydroxylamine ^a	–	0.6	99	95
Phenylhydroxylamine ^a	50	0.6	99	95
Phenylhydroxylamine	–	–	99	95
Aniline	–	0.6	97	95
Aniline	50	0.6	99	95
Aniline	–	–	2	Traces
–	–	0.6	–	–
–	50	0.6	–	–

^a The reaction is quantitative in few minutes at 298 K, and the rest of the mass balance is recognized by GC–MS analysis as condensation products mainly benzidine and its oxidation products.

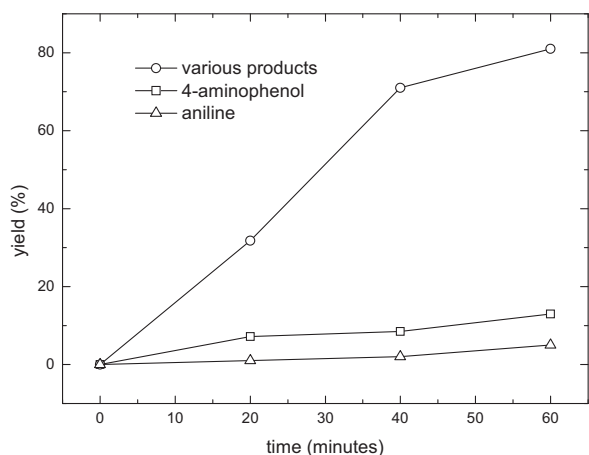


Fig. 8. Hydrogenation of nitrosobenzene, initial reaction: $r_0 = 0.28 \text{ mol L}^{-1} \text{ min}^{-1} \text{ g}_{\text{met}}^{-1}$. Run conditions: $T: 353 \text{ K}$, $P_{\text{H}_2} 121 \text{ kPa}$, nitrosobenzene 0.06 mol L^{-1} , CF_3COOH 0.6 mol L^{-1} , H_2O 2.2 g , CH_3CN 22 g , catalyst Pt/C 3% 50 mg.

rate and yield in 4-aminophenol, while dimethyl sulfoxide inhibits the reaction completely. It is likely that the effect of the dimethyl sulfoxide is due to its reduction to dimethyl sulfide (stench of sulfides when reaction is ended), which is known to be a strong poison for Pt catalysts [8,26]. On the contrary, sulfolane is quite strongly adsorbed on catalyst surface, thus inhibiting the reaction when used as a solvent, but it is not hydrogenated to sulfide, which is the actual poison of the catalyst in the presence of dimethyl sulfoxide.

This is confirmed by an evident stench of sulfides clearly smelt only in the presence of dimethyl sulfoxide and not with sulfolane. The higher initial rate of reaction, in the presence of sulfolane could be related with adsorption equilibria of the species in contact with the catalyst. In particular, Pt surface can be modified by sulfolane adsorption thus increasing both reaction rate and selectivity, but these are conjectures needing further investigations. Despite of the higher reaction rate and yield to 4-aminophenol compared to the reactions carried out in the absence of sulfolane, the presence of small amount of this high boiling point compounds, is a problem both for solvent recovery and for product purification, thus suggesting to avoid its use for practical purposes.

3.9. Reactivity of nitrosobenzene and *N*-phenylhydroxylamine

Fig. 8 reports the hydrogenation of nitrosobenzene in $\text{CH}_3\text{CN}-\text{H}_2\text{O}-\text{CF}_3\text{COOH}$ in the presence of Pt/C catalyst. At difference of what is found by Jackson and coworkers [31,32], the reaction proceed faster ($r_0 = 0.27 \text{ mol L}^{-1} \text{ min}^{-1} \text{ g}_{\text{met}}^{-1}$ and conversion is almost quantitative after 1 h) than that of nitrobenzene hydrogenation, but the yield to 4-aminophenol and aniline is 10% and 5%, respectively, the rest is a complex mixture of products, mainly azoxybenzene, azobenzene and several unidentified products. As a matter of fact, several reactions occur between nitrosobenzene and the products of hydrogenation (for instance *N*-phenylhydroxylamine and aniline) thus diminishing the selectivity to 4-aminophenol and aniline. This is confirmed by the data of Table 5 where the reactivity of nitrosobenzene is checked under different conditions. Nitrosobenzene is

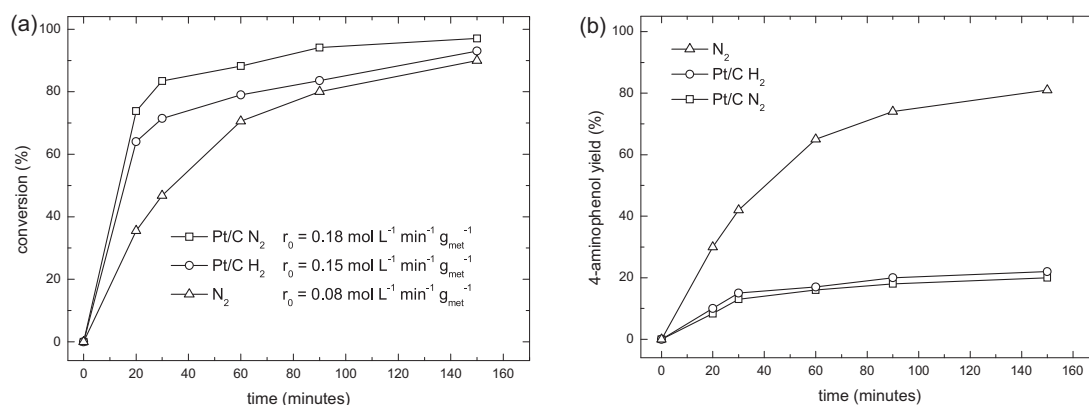


Fig. 9. *N*-phenylhydroxylamine rearrangement, conversion (a) and yield (b) of 4-aminophenol vs. time in the presence of Pt/C-N₂, Pt/C-H₂ and N₂. Run conditions: $T: 353 \text{ K}$, $P_{\text{H}_2} 121 \text{ kPa}$, *N*-phenylhydroxylamine 0.02 mol L^{-1} , CF_3COOH 0.6 mol L^{-1} , H_2O 2.2 g , CH_3CN 22 g , catalyst Pt/C 3% 50 mg.

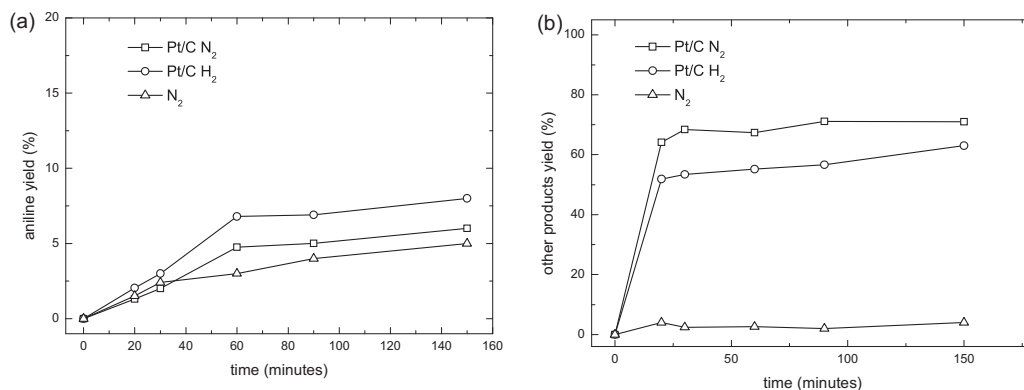
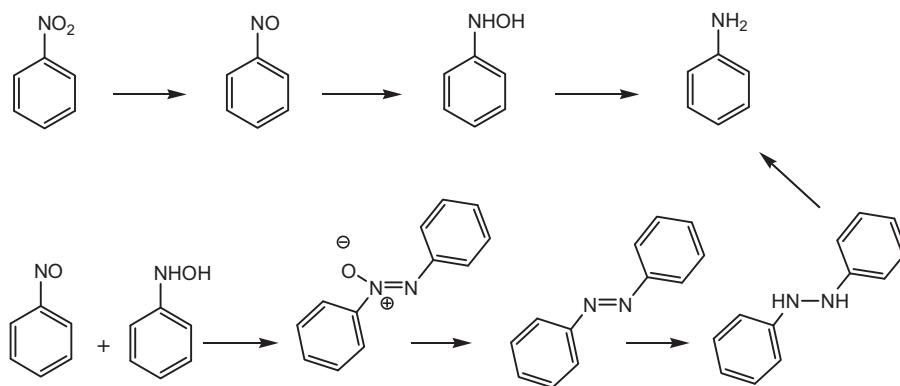


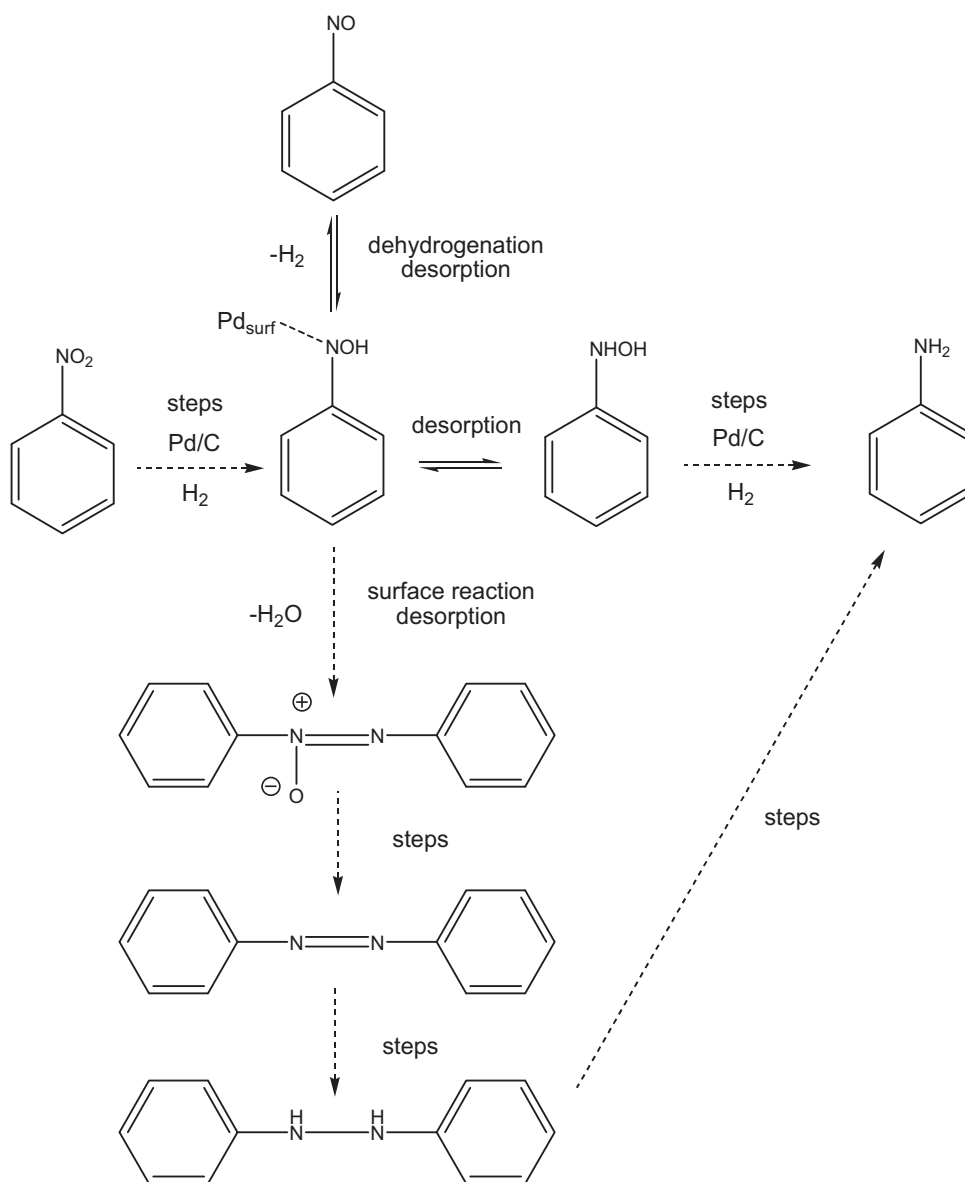
Fig. 10. *N*-phenylhydroxylamine rearrangement, yield of aniline (a) and other byproducts (b) vs. time in the presence of Pt/C-N₂, Pt/C-H₂ and N₂. Run conditions: $T: 353 \text{ K}$, $P_{\text{H}_2} 121 \text{ kPa}$, *N*-phenylhydroxylamine 0.02 mol L^{-1} , CF_3COOH 0.6 mol L^{-1} , H_2O 2.2 g , CH_3CN 22 g , catalyst Pt/C 3% 50 mg.



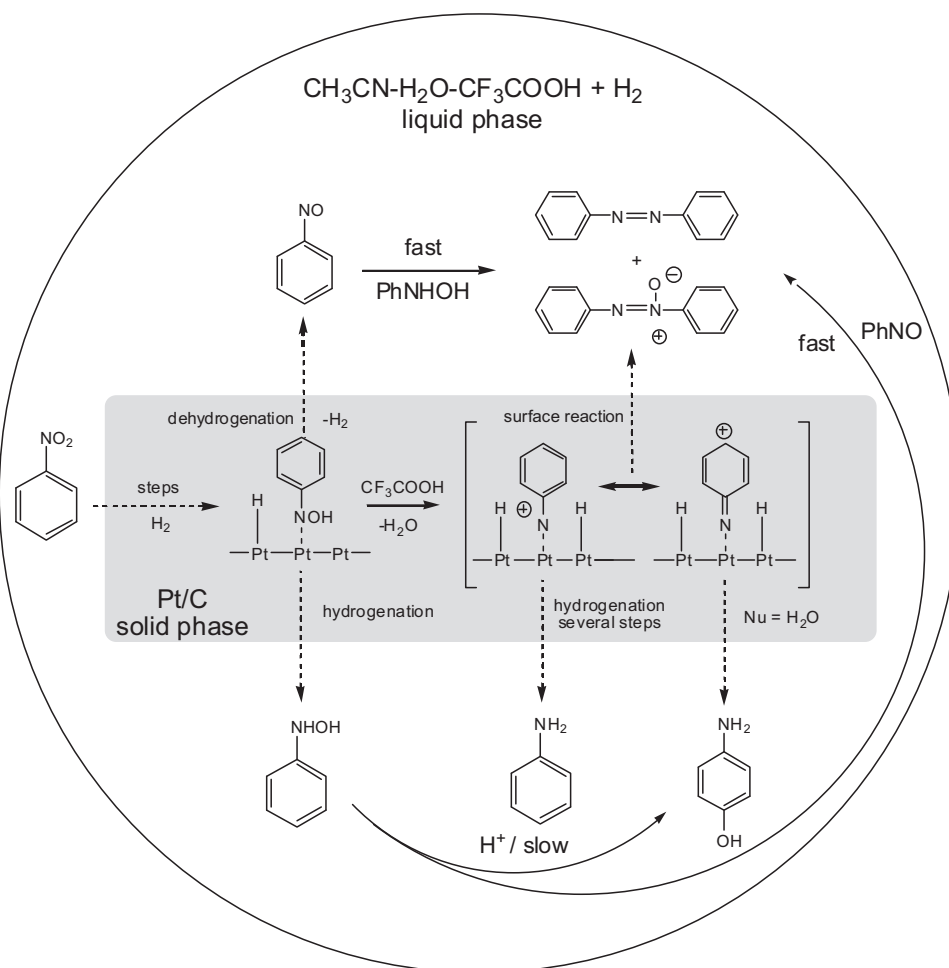
Scheme 3. Haber reaction path for nitrobenzene reduction.

stable in $\text{CH}_3\text{CN}-\text{H}_2\text{O}-\text{CF}_3\text{COOH}$ and $\text{CH}_3\text{CN}-\text{H}_2\text{O}-\text{CF}_3\text{COOH}$ Pt/C at 358 K, but when aniline or *N*-phenylhydroxylamine are present, it reacts almost instantaneously (particularly fast reaction occurs in the presence of *N*-phenylhydroxylamine, also without any

catalyst), giving mainly azoxybenzene and azobenzene [31]. In fact, both *N*-phenylhydroxylamine and aniline are reductants toward nitrosobenzene, but *N*-phenylhydroxylamine is much more reactive.



Scheme 4. Jackson reaction path for nitrobenzene hydrogenation. Pd_{surf} : metallic surface of the Pd/C catalyst.



Scheme 5. Proposed reaction path for nitrobenzene hydrogenation in $\text{CH}_3\text{CN}-\text{H}_2\text{O}-\text{CF}_3\text{COOH}$. Species outside the rectangle are in liquid phase with the relative homogeneous reactions, those inside are adsorbed on Pt/C catalyst with the relative surface reaction, dotted lines indicate adsorption and desorption steps.

As mentioned above, the reaction rate of nitrosobenzene hydrogenation is higher than that observed in nitrobenzene, this could be ascribed to a solvent effect, which competes with nitrobenzene and nitrosobenzene in the adsorption on Pt sites (CH_3CN is a coordinating solvent). In this case, it is likely that nitrosobenzene could be favored in the first step of hydrogenation because of its ability to form Pt-nitroso complexes more stable than the nitrobenzene ones [33].

Figs. 9 and 10 show the reactivity of *N*-phenylhydroxylamine under different reaction conditions. The initial reaction rate is comparable to that of nitrobenzene hydrogenation, even though substrate concentration is about 4 times lower than in nitrobenzene hydrogenation. It is noteworthy that the highest reaction rate is observed in the presence of Pt/C 3% and in the absence of H_2 , while the slowest one occurs without the Pt catalyst (see Fig. 9a). The highest yield to 4-aminophenol is achieved in the presence of CF_3COOH without Pt catalyst (Fig. 9b). On the contrary, the yield of aniline in various systems (see Fig. 10a) is poorly influenced by the type of reaction environment, thus suggesting that its formation occurs through a parallel path, which does not directly involve the catalysis of the Pt during the first 160 min of reaction. *N*-phenylhydroxylamine in the presence Pt/C catalyst gives in small amount 4-aminophenol and mainly condensation products, such as azoxybenzene and azobenzene (compare Fig. 9b and Fig. 10b). Starting from these evidences, it is likely that the homogeneous acid catalyzed Bamberger rearrangement is not the only responsible for 4-aminophenol formation (or at least it is not the main way)

during the direct hydrogenation of nitrobenzene. This suggests an alternative path for 4-aminophenol formation in the hydrogenation reactions involving species generated step by step on the Pt surface, directly. On the contrary, desorption of nitrosobenzene and *N*-phenylhydroxylamine will cause reactions of condensation and decomposition giving mainly byproducts. Besides, this is in agreement with the evidence that, except during the first minutes, neither nitrosobenzene nor *N*-phenylhydroxylamine is detected during nitrobenzene hydrogenation.

3.10. Discussion on the reaction mechanism

Taking into account the results shown in the previous sections, we will attempt a discussion on the whole reaction path for nitrobenzene hydrogenation catalyzed by Pt/C in the presence of $\text{CH}_3\text{CN}-\text{H}_2\text{O}-\text{CF}_3\text{COOH}$ solvent acid system.

The generally accepted Haber mechanism for nitrobenzenes reduction consists in a multistep reaction path (Scheme 3), which comprises the step of reduction of nitro-group to nitroso-, hydroxyamino- and amino-, as well as the condensation of the intermediates to azoxybenzenes and azobenzenes, being, in turn, reduced to hydrazine and finally to aniline [27].

The mechanism [27] has been generally accepted for long time but recently several authors have criticized some aspects, which do not explain the reactivity of the intermediates and of the specificity of different type of catalyst [31,32,34–38]. In particular, Jackson and co-workers showed that the hydrogenation rate of

nitrobenzene is higher than that of nitrosobenzene, and no nitrosobenzene accumulation is observed. In addition, a large isotopic effect is evidenced, when D₂ is used instead of H₂, for nitrobenzene while for nitrosobenzene this effect is not observed [31]. On the basis of these results they suggested a reaction path involving a surface Pd-hydroxyamino species from that starts several parallel reactions as exemplified in Scheme 4 [31].

The results of the present research do not exclude the formation of all intermediates of the Haber Scheme, but suggest that reactivity of the catalyst surface may play the major role, being in agreement with Jackson path, too. In fact, it is likely that reaction steps are influenced by all the intermediates of the Haber mechanism, but it is also probable that a Pt-hydroxyamino surface complex, similar to that suggested by Jackson and co-workers, may play a fundamental role for 4-aminophenol formation. Indeed, the results, discussed in Section 3.9, on the reactivity of nitrosobenzene and *N*-phenylhydroxylamine, support a mechanism mediated by Pt-surface species, as reported in Scheme 5. The Pt-hydroxyamino surface complex is protonated by CF₃COOH giving a Pt-nitrenium surface complex that reacts with a nucleophile to give the substituted aniline, if H₂O is present 4-aminophenol is the product. Formation of 4-aminophenol by a Pt-nitrenium intermediate explains the high yield obtained by nitrobenzene hydrogenation compared to the much lower yield observed when *N*-phenylhydroxylamine or nitrosobenzene are used instead of nitrobenzene. This is in agreement, with the research of Jackson and coworkers on substituted nitroacetophenones hydrogenation, in which Pd-nitrenium species has been identified as an intermediate [32]. As a matter of fact, homogeneous acid catalyzed Bamberger rearrangement is not the preferred reaction of *N*-phenylhydroxylamine if Pt catalysts are present, since its decomposition and condensation reactions are faster than the acid catalyzed rearrangement. In addition, this reaction scheme allows the explanation of the relevant concentration of azobenzene and azoxybenzene observed during hydrogenation reaction being formed by fast homogeneous reaction between nitrosobenzene and *N*-phenylhydroxylamine desorbed from Pt/C.

4. Conclusions

The main results of the present work can be divided in two main parts:

- I) the reaction, which gives to 4-aminophenol in good yield;
- II) the mechanism.

Concerning the first point, we develop a single liquid phase methodology, which allows quite high yield in the 4-aminophenol avoiding the work-up operation of the biphasic process. Moreover, the single phase process may allow complete recovery of the system CF₃CN–H₂O–CF₃COOH, by evaporation at low pressure, thus allowing an almost complete reuse of the solvent. The employment of sulfolane as a promoter shows an increase in the yield of the 4-aminophenol, but not sufficient to justify its use for practical purposes.

The new proposed mechanism accounts for the reactivity of all the species observed in solution as well as the reactivity of the species observed by the electrochemical reduction proposed by Haber. The evidences suggest the coexistence of reactions occurring both in solution and on the Pt surface, the latter are likely those affecting the selectivity to 4-aminophenol for the most part. The role of the acid is strictly connected with the selectivity to 4-aminophenol, because of its involvement both on the Bamberger

rearrangement in solution, as well as on promoting the formation of a Pt-nitrenium complex on the catalysts surface, which gives 4-aminophenol.

Acknowledgements

Financial support by Ca' Foscari University of Venice is gratefully acknowledged (ADIR fund 2011). A special thank to Mr. Claudio Tortato for the helpful discussions and the valuable suggestions.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.apcata.2014.01.033>.

References

- [1] S. Mitchell, R. Waring, Kirk Ohtmer Aminophenols, 2, fourth ed., John Wiley & Sons, 1999.
- [2] S.K. Tanielyan, J.J. Nair, N. Marin, G. Alvez, R.J. McNair, D. Wang, R.L. Augustine, Org. Proc. Res. Dev. 11 (2007) 681–688.
- [3] K. Hunger, Industrial Dyes, 25 WILEY-VCH, Weinheim (2003).
- [4] C.V. Rode, M.J. Vaidya, R. Jaganathan, R.V. Chaudhari, Chem. Eng. Sci. 56 (2001) 1299–1304.
- [5] C.V. Rode, M.J. Vaidya, R.V. Chaudhari, Org. Proc. Res. Dev. 3 (1999) 465–470.
- [6] <http://www.dsir.gov.in/reports/techreps/tsr131.pdf>.
- [7] J. R. Fritch, O. S. Fruchney, T., Horlenko, D.A., Aguilar, C. B. Hilton, P. S. Snyder, W. J. Seelinger, U.S. Patent 5,155,273 to Hechst-Celanese Co. (1992).
- [8] Y. Gao, F. Wang, S. Liao, D. Yu, React. Kinet. Catal. Lett. 64 (1998) 351–357.
- [9] K. Min, J. Choi, Y. Chung, W. Ahn, R. Ryoo, P.K. Lim, Appl. Catal. A: Gen. 337 (2008) 97–104.
- [10] I.M.C. Brighente, L.R. Vottero, A.J. Terezani, R.A. Yunes, J. Phys. Org. Chem. 4 (1991) 107–111.
- [11] T. Sone, Y. Tokuda, T. Sakai, S. Shinkai, O. Manabe, J. Chem. Soc. Perkin Trans. 2 (1981) 298–301.
- [12] F. Coloma, J. Narciso-Romero, A. Sepúlveda-Escribano, F. Rodríguez-Reinoso, Carbon 36 (1998) 1011–1019.
- [13] S. Wang, Y. Ma, Y. Wang, W. Xue, X. Zhao, J. Chem. Technol. Biotechnol. 83 (2008) 1466–1471.
- [14] A. Deshpande, F. Figueras, M.L. Kantam, K.J. Ratnam, R.S. Reddy, N.S. Sekhar, J. Catal. 275 (2010) 250–256.
- [15] S. Wang, B. He, Y. Wang, X. Zhao, Catal. Commun. 24 (2012) 109–113.
- [16] T. Komatsu, T. Hirose, Appl. Catal. A: Gen. 276 (2004) 95–102.
- [17] L. Ronchin, A. Vavasori, M. Bortoluzzi, Catal. Commun. 10 (2008) 251–256.
- [18] L. Ronchin, A. Vavasori, J. Mol. Catal. A: Chem. 313 (2009) 22–30.
- [19] L. Ronchin, M. Bortoluzzi, A. Vavasori, J. Mol. Struct.: Theochem 858 (2008) 46–51.
- [20] G. Quartarone, E., Rancan, L., Ronchin, A. Vavasori, Appl. Catal. A: Gen. (DOI information: 10.1016/j.apcata.2013.12.026).
- [21] G. Kohnstam, W.A. Petch, D.L.H. Williams, J. Chem. Soc. Perkin II (1984) 423–427.
- [22] T. Sone, K. Hamamoto, Y. Siji, S. Shinkai, O. Manabe, J. Chem. Soc. Perkin II (1984) 1596–1598.
- [23] N.M. Bertero, A.F. Trasarti, C.R. Apesteguía, A.J. Marchi, Appl. Catal. A: Gen. 394 (2011) 228–238.
- [24] L. Ronchin, A. Vavasori, D. Bernardi, G. Cavinato, L. Toniolo, Appl. Catal. A: Gen. 355 (2009) 50–60.
- [25] N.C. Marziano, L. Ronchin, C. Tortato, A. Vavasori, C. Badetti, J. Mol. Catal. A: Chem. 277 (2007) 221–232.
- [26] A. Li-Dun, D.Y. Quan, Appl. Catal. 66 (1990) 219–234.
- [27] F. Haber, Z. Elektrochem. 22 (1898) 506–512.
- [28] G.W. Roberts, in: P.N. Rylander, H. Greenfield (Eds.), Catalysis in Organic Synthesis, Academic Press, NY, 1976, pp. 1–48.
- [29] C. Reichardt, Solvents and Solvent Effects in Organic Chemistry, 2nd ed., VCH, Weinheim, 1988.
- [30] B. Joerqvist, H. Toivonen, J. Chromatogr. 178 (1979) 271–276.
- [31] E. A. Gelder, S. D. Jackson, C. M. Lok, Chem. Commun. (2005) 522–524.
- [32] S.D. Jackson, R. McEwan, R.R. Spence, Hydrogenation of nitro-substituted acetophenones, in: M. Prunier (Ed.), Catalysis of Organic Reactions, Taylor & Francis, Boca Raton, 2008, pp. 79–86.
- [33] D. Groskova, M. Stolcova, M. Hronec, Catal. Lett. 69 (2000) 113–116.
- [34] M. Pizzotti, F. Porta, S. Cenini, F. Demartin, N. Masciocchi, J. Organomet. Chem. 330 (1987) 265–278.
- [35] F. Figueras, B. Coq, J. Molec. Catal. A: Chem. 173 (2001) 223–230.
- [36] A. Corma, P. Serna, Science 313 (2006) 332.
- [37] H.U. Blaser, Science 313 (2006) 312.
- [38] A. Corma, P. Concepcion, P. Serna, Angew. Chem. Int. Ed. 46 (2007) 7266–7269.