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Synthesis of *p*-Aminophenol by Catalytic Hydrogenation of Nitrobenzene

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Abstract:

The present work describes the preparation of *p*-aminophenol via single-step catalytic hydrogenation of nitrobenzene in acid medium. A conventional method of synthesis of *p*-aminophenol is a two-step reaction involving iron−acid reduction of *p*-nitrophenol. This method causes serious effluent disposal problems due to the stoichiometric use of iron−acid, which leads to the formation of Fe−FeO sludge (≅1.2 kg/kg of product) in the process, which cannot be recycled. The single-step hydrogenation of nitrobenzene was carried out using platinum catalyst, and the process conditions were optimized. Complete conversion of nitrobenzene was achieved with selectivity to *p*-aminophenol as high as 75% under the best set of conditions. Furthermore, the catalyst can be easily recovered and efficiently recycled giving the TON as high as $1.38 \times 10.^{5}$ This paper presents studies on the effect of various process parameters such as temperature, hydrogen pressure, and substrate and acid concentration on the rate of reaction and selectivity to *p*-aminophenol.

Introduction

p-Aminophenol is of great commercial importance as an intermediate for the manufacture of paracetamol, acetanilide, phenacetin—all analgesic and antipyretic drugs.[1] It is also used as a developer in photography under trade names activol and azol and in chemical dye industries.[2] Conventionally, *p*-aminophenol is synthesized by the following methods:[1]

(i) From *p*-chloronitrobenzene: this is the most commonly used multistep process starting from chlorobenzene.

(ii) From phenol: this is also a two-step process starting from phenol.

Both of these multistep routes involve an important step of reduction of *p*-nitrophenol using stoichiometric quantities of Fe−HCl reagents. These routes have several drawbacks and lead to a poor overall yield. The major disadvantages of iron−acid reduction process are:[1,3] (1) The quantity of iron required is very large, and hence the subsequent production of Fe−FeO sludge is large (1.2 kg/kg of product), posing serious effluent problems. (2) Workup of reaction crude for separation of *p*-aminophenol from Fe−FeO sludge is cumbersome. (3) The rate of reduction varies in a single batch, sometimes leading to a violent reaction. (4) Erosion of the reactor takes place due to Fe particles. Now, with a change in the scenario in chemical industry, pertaining to the efficient and ecofriendly processes demanded by the statutory authorities, the conventional iron−acid reduction process needs to be replaced by a catalytic hydrogenation route. The catalytic route will minimize the effluent disposal problems to a great extent and is also expected to improve the overall process economics as well as the product quality.

The catalytic route involves hydrogenation of nitrobenzene in a single step to *p*-aminophenol using supported noble metal catalysis in the presence of an acid like H_2SO_4 (7%). At present, Mallinckrodt Inc. (U.S.A.) is the only company producing PAP by this route.[4] The process involves initial reduction of nitrobenzene to give β-phenylhydroxylamine as an intermediate (Scheme 1) which then rearranges in situ to *p*-aminophenol in the presence of an acid (Bamberger's rearrangement).[5] Formation of aniline is the main competing side reaction in this process.

The preparation of *p*-aminophenol (PAP) by hydrogenation of nitrobenzene using Pt/C catalyst in the presence of a mineral acid was originally discovered in 1940.[6] Other catalysts mentioned in the literature are PtO_2, Pd, Mo,[7−9] etc. The use of surfactants for increasing the rate of reaction has been mentioned in some other patents.[10] Attempts have been made to replace mineral acid by other solid acids in order to eliminate the corrosion problems. However, the yield of PAP in such reactions was found to be very low.[11] The use of formic acid or acetic acid is mentioned in other patents.[12] Most of the information regarding this industrially important reaction is available in the form of patents except for a few reports in the open literature.[13,14] In the present work, effects of various process parameters such as catalyst loading, substrate loading, hydrogen partial pressure, organic phase hold up on the rate of the reaction and selectivity to *p*-aminophenol were investigated. Also, the catalyst recycle was successfully carried out in up to three experiments and the catalyst turnover number (TON) was found to be much higher than the literature value.

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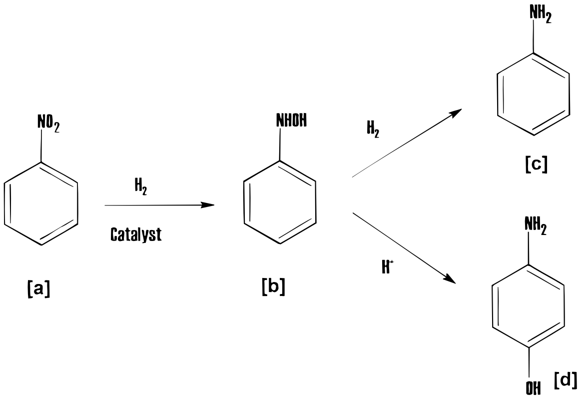
Scheme 1: **Schematic of hydrogenation of nitrobenzene**



[a] Nitrobenzene [b] β-Phenylhydroxylamine
[c] Aniline [d] *p*-Aminophenol

Experimental Section

Materials. Nitrobenzene, aniline, and H_2SO_4 (98%) were procured from SD Fine Chemicals Ltd. (India). Catalyst (3%Pt/C) and *p*-aminophenol were Aldrich products.

Experimental Setup. The reactions were carried out in a 300 cm^3 capacity high-pressure Hastelloy reactor supplied by Parr Instruments Co., U.S.A. The reactor was connected to a hydrogen reservoir held at a pressure higher than that of the reactor, through a constant pressure regulator. Hydrogen gas was supplied from this reservoir to the reactor through a nonreturn valve. The gas consumed during the course of the reaction was monitored by pressure drop in the reservoir vessel using a transducer.

A Hewlett-Packard model 1050 liquid chromatograph equipped with an ultraviolet detector was employed for the analysis. The analytical column, lichrospher RP 18 (125 × 4 mm), supplied by Hewlett-Packard was used for analysis. The separation of nitrobenzene hydrogenation products was achieved with 30% acetonitrile−water as mobile phase at 25 °C and flow rate of 1 mL/minute. Samples of 10 μL were injected into the column through the septum.

Procedure. In a typical hydrogenation experiment, 23 gm (1.86 $kmol/m^3$) of nitrobenzene, 35 mg of 3% Pt/C catalyst, and 6 mL of sulfuric acid were charged, and the total reaction volume was made to 1×10^{-4} m^3 with water. The contents were first flushed with nitrogen and then with hydrogen. After the desired temperature was attained, the system was pressurized with hydrogen to a level required for the experiment, and the reaction was started by switching the stirrer on. The progress of the reaction was monitored by the observed pressure drop in the reservoir vessel as a function of time. The contents were cooled to room temperature and discharged after completion of the reaction. The resultant reaction crude product was filtered to separate the solid catalyst. The filtrate was extracted with toluene (2 × 30 mL) to remove the byproduct aniline and traces (<0.1%) of any unconverted nitrobenzene. The pH of the aqueous layer after extraction was made to 8 by the addition of aqueous ammonia leading to the complete precipitation of solid PAP. The solid PAP was filtered under vacuum and washed with toluene and distilled water twice, vacuum-dried, and weighed. The amount of *p*-aminophenol obtained was 11.8 gm (yield, 58.2%).

Table 1: **Range of operating conditions**

1	hydrogen pressure	0.68−6.80 MPa
2	sulfuric acid concentration	5−20% w/w
3	substrate concentration	0.54−3.73 $kmol/m^3$
4	catalyst loading	0.175−0.70 kg/m^3
5	speed of agitation	500−1000 rpm
6	organic phase hold up	0.1−0.4
7	temperature	323−373 K
8	total reaction volume	1×10^{-4} m^3

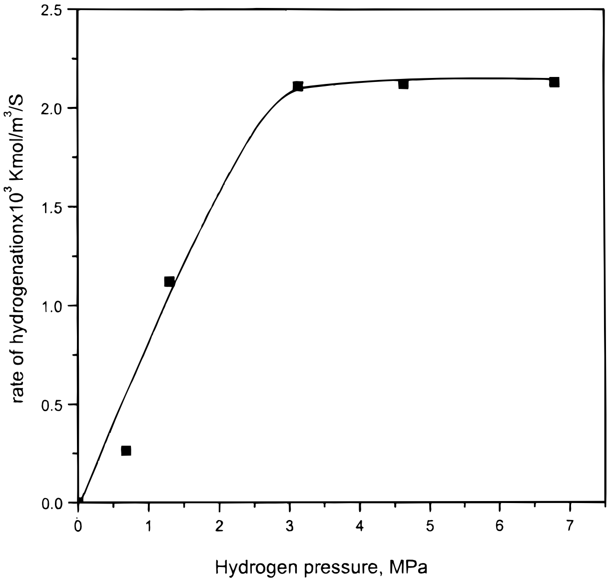


Figure 1. **Effect of hydrogen pressure on initial rate of hydrogenation of nitrobenzene to *p*-aminophenol. Reaction conditions: nitrobenzene, 1.86 $kmol/m^3$; catalyst, 0.35 kg/m^3; water, 70 × 10^{-6} m^3; acid, 10% w/w; temperature, 353 K; agitation, 700 rpm; total reaction volume, 1 × 10^{-4} m^3.**

Results and Discussion

The effects of various process parameters were studied on the hydrogenation of nitrobenzene to *p*-aminophenol using 3% Pt/C catalyst and sulfuric acid (aqueous) medium. In each experiment, a final sample was analyzed by HPLC to calculate the conversion of nitrobenzene and selectivity to *p*-aminophenol, which agreed well with the hydrogen absorption data and recovered PAP. In each experiment, complete conversion of nitrobenzene was observed. Initial rates of hydrogenation were also calculated from the slope of hydrogen absorbed vs time plots, essentially under low conversion (<20%) conditions. Table 1 presents the range of various process parameters studied in this work.

Effect of Hydrogen Pressure. The effect of hydrogen partial pressure on the initial rate of hydrogenation was studied in the range of 0.68−6.80 MPa at 353 K. The initial rate of reaction increased linearly with increase in pressure up to 2.72 MPa, beyond which the rate was constant as shown in Figure 1. The selectivity to *p*-aminophenol showed maxima at 2.72 MPa, and it decreased on further increase in hydrogen pressure. The results are shown in Figure 2. The increase in hydrogen pressure retards the desorption of

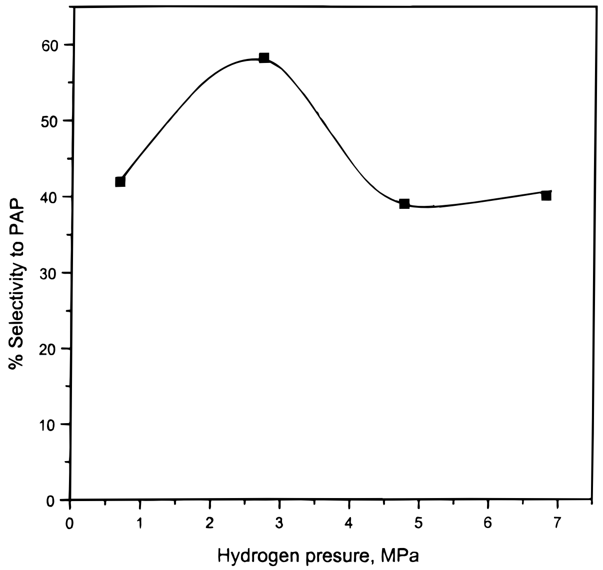


Figure 2. **Effect of hydrogen pressure on selectivity to *p*-aminophenol by hydrogenation of nitrobenzene. Reaction conditions: nitrobenzene, 1.86 kmol/m^3; catalyst, 0.35 kg/m^3; water, 70×10^{-6} m^3; acid, 10% w/w; temperature, 353 K; agitation, 700 rpm; total reaction volume, 1×10^{-4} m^3.**

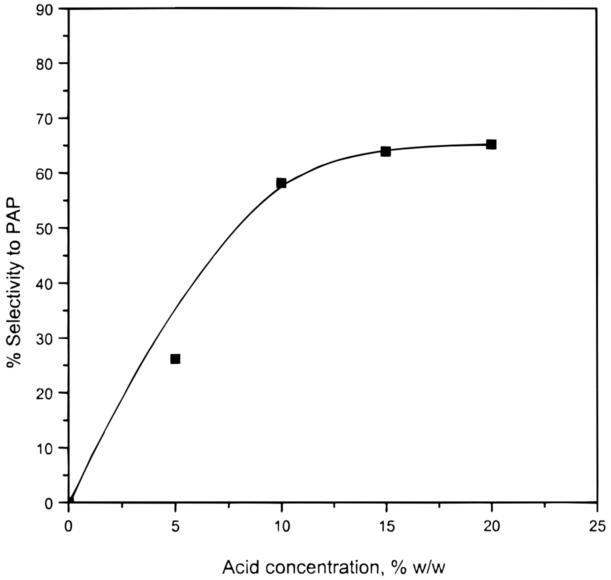


Figure 3. **Effect of acid concentration on selectivity to *p*-aminophenol by hydrogenation of nitrobenzene. Reaction conditions: nitrobenzene, 1.86 kmol/m^3; catalyst, 0.35 kg/m^3; water, 70×10^{-6} m^3; temperature, 353 K; agitation, 700 rpm total reaction volume, 1×10^{-4} m^3.**

the intermediate phenylhydroxylamine from the catalyst surface, facilitating further hydrogenation of phenylhydroxylamine and leading to the formation of aniline and decrease in selectivity to *p*-aminophenol.

Effect of Sulfuric Acid Concentration. In situ rearrangement of an intermediate phenylhydroxylamine to *p*-aminophenol is acid-catalyzed, and hence it is necessary to study the effect of acid concentration on the selectivity of *p*-aminophenol. The effect of acid concentration on selectivity of PAP was studied in the range of 5−20% w/w, keeping other reaction conditions constant, and the results are shown in Figure 3. It was observed that the selectivity to *p*-aminophenol first increased with increase in acid concentration up to 15% w/w beyond which it was almost constant. This may be due to the fact that the mobility of protons is more at lower concentration than at higher acid concentration. The results also suggest that the optimum acid strength of sulfuric acid to be about 15% (w/w). However, the initial rate of hydrogenation remained unaffected with change in acid concentration. This observation supports the assumption that the second step, that is, the rearrangement step, in the mechanism is not a rate-determining step. This is also in agreement with the observation made by Juang et al.[13]

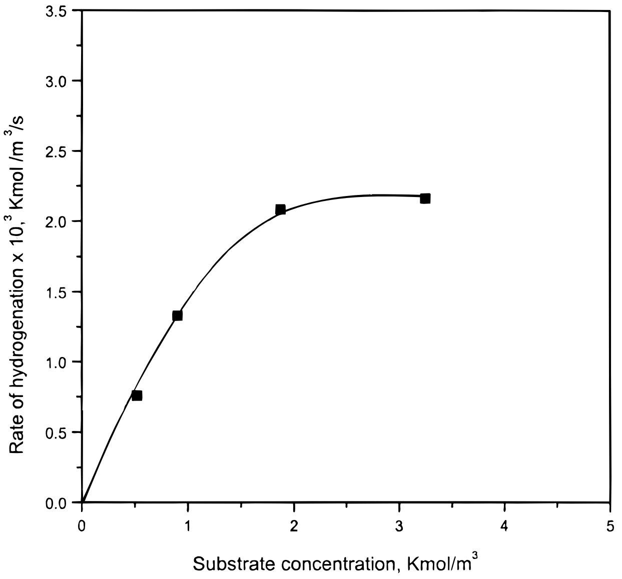


Figure 4. **Effect of substrate concentration on initial rate of hydrogenation of nitrobenzene to *p*-aminophenol. Reaction conditions: catalyst, 0.35 kg/m^3; acid, 10% w/w; temperature, 353 K; pressure, 2.72 MPa; agitation, 700 rpm. total reaction volume, 1×10^{-4} m^3.**

Table 2: **Effect of substrate concentration on selectivity to *p*-aminophenol**

substrate concn (kmol/m^3)	selectivity (%)
0.54	70.66
0.90	70.06
1.86	58.20
3.73	42.19

Reaction conditions: catalyst, 0.35 kg/m^3 acid, 10% w/w; temperature, 353 K; pressure, 2.72 MPa; agitation, 700 rpm; total volume, 1×10^{-4} m.^{3}

Effect of Substrate Concentration. Typical results of the effect of initial concentration of substrate in the range from 0.548 to 3.73 kmol/m^3 at 353 K are shown in Figure 4. It was found that the initial rate of reaction increased up to 1.86 kmol/m^3, beyond which the rate increased only marginally with further increase in substrate concentration. The results indicate a first-order tending to zero-order dependence at higher concentration of nitrobenzene. The selectivity to *p*-aminophenol was found to be almost constant at lower substrate concentration up to 0.90 kmol/m^3 (Table 2) but decreased with further increase in substrate concentration.

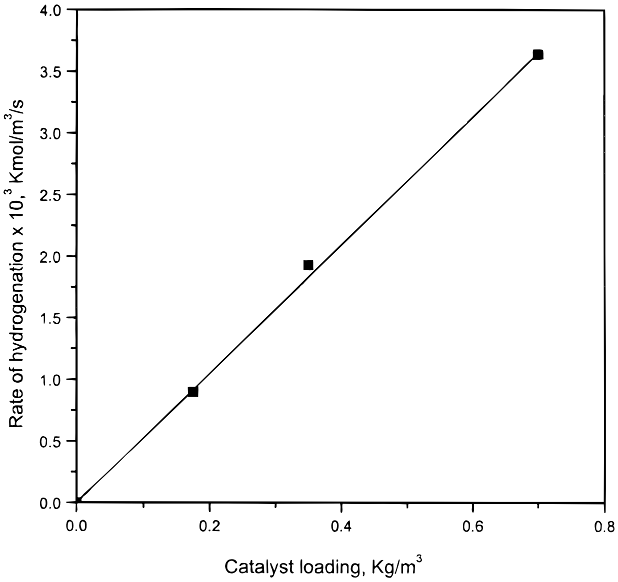


Figure 5. **Effect of catalyst loading on initial rate of hydrogenation of nitrobenzene to *p*-aminophenol. Reaction conditions: nitrobenzene, 1.86 kmol/m^3; acid, 10% w/w; water, 70 × 10^{-6} m^3; temperature, 353 K; pressure, 2.72 MPa; agitation, 700 rpm; total volume, 1 × 10^{-4} m^3.**

Effect of Catalyst Loading. The effect of catalyst loading on the initial rate of reaction was studied in the range of 0.175−0.70 kg/m^3 at 353 K and 2.72 MPa of hydrogen pressure and the results are presented in Figure 5. The initial rate was found to increase by 4.5 times when catalyst loading was increased from 0.175 to 0.70 kg/m.^{3} A linear dependence with respect to the catalyst loading indicates that the external gas−liquid mass transfer resistance may not be significant.[15] A plot of selectivity of *p*-aminophenol vs catalyst loading for the same range of conditions is also shown in Figure 6. It can be seen from this figure that the selectivity increased up to a catalyst loading of 0.35 kg/m^3 beyond which it decreased. This may be due to the fact that increase in catalyst loading mainly increases the rate of hydrogenation of the intermediate, phenylhydroxylamine, leading to the formation of more of aniline, which is a major byproduct in this reaction.

Effect of Speed of Agitation. The effect of speed of agitation on the selectivity and rate of reaction was studied between 500 and 1000 rpm at 353 K and at hydrogen pressure of 2.72 MPa, and the results on the selectivity pattern are presented in Figure 7. The selectivity of PAP was found to increase with increase in speed of agitation from 500 to 1000 rpm. This indicates that the phase-transfer catalysis may be an important aspect, since the present system involves two immiscible liquids. More work needs to be done to understand this phenomenon. However, as shown in Figure 8, it was observed that the initial rate of reaction remained unchanged beyond 700 rpm speed of agitation.

Effect of Organic Phase Hold Up. Since the present system involved two immiscible phases, aqueous and organic and the catalyst mainly stays in the organic phase, it was essential to study the effect of organic phase hold up on the rate of reaction and selectivity to *p*-aminophenol. The organic phase hold up is the ratio of the weight of organic phase to the total weight of charge. In these experiments, ratios of concentration of substrate to that of catalyst and acid were kept constant. The total reaction volume, that is, 1 × 10^{-4} m^3, was kept constant in each experiment. It can be seen from Figure 9 that selectivity to *p*-aminophenol increased with increase in organic phase hold up. Initial rate of hydrogenation was also found to increase with increase in organic phase hold up. The increase in organic phase hold up causes an increase in interfacial area and subsequently

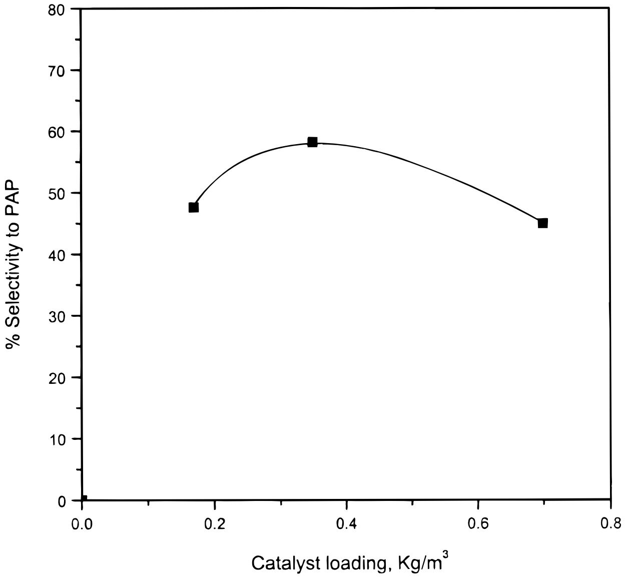


Figure 6. **Effect of catalyst loading on selectivity to *p*-aminophenol by hydrogenation of nitrobenzene. Reaction conditions: nitrobenzene, 1.86 kmol/m^3; acid, 10% w/w; water, 70 × 10^{-6} m^3; temperature, 353 K; pressure, 2.72 MPa; agitation, 700 rpm; total volume, 1 × 10^{-4} m^3.**

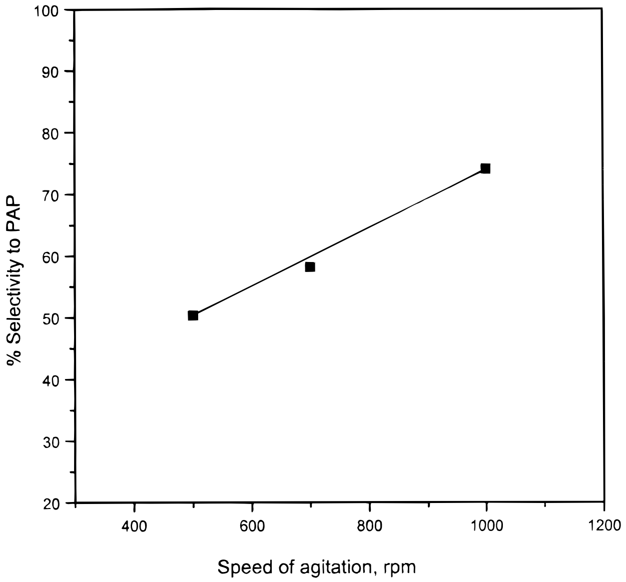


Figure 7. **Effect of speed of agitation on selectivity to *p*-aminophenol by hydrogenation of nitrobenzene. Reaction conditions: nitrobenzene, 1.86 kmol/m^3; catalyst, 0.35 kg/m^3; water, 70 × 10^{-6} m^3; acid, 10% w/w; temperature, 353 K; pressure, 2.72 MPa; total volume, 1 × 10^{-4} m^3.**

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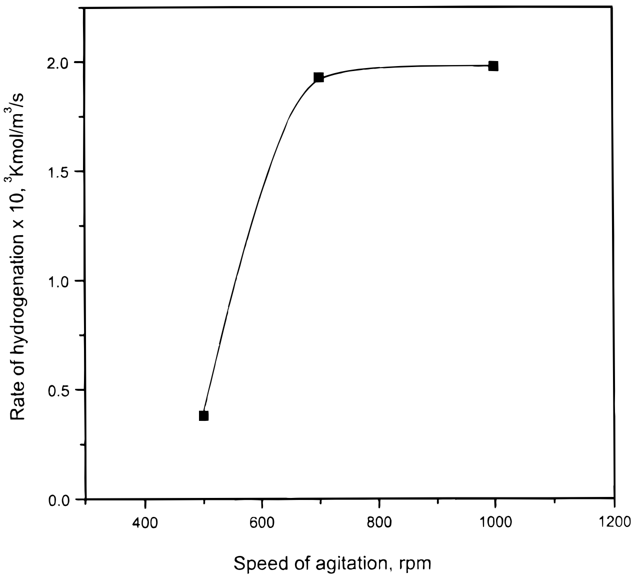

Figure 8. **Effect of speed of agitation on initial rate of hydrogenation of nitrobenzene to *p*-aminophenol. Reaction conditions: nitrobenzene, 1.86 kmol/m^3; catalyst, 0.35 kg/m^3; water, 70 × 10^{-6} m^3; acid, 10% w/w; temperature, 353 K; pressure, 2.72 MPa; total volume, 1 × 10^{-4} m^3.**

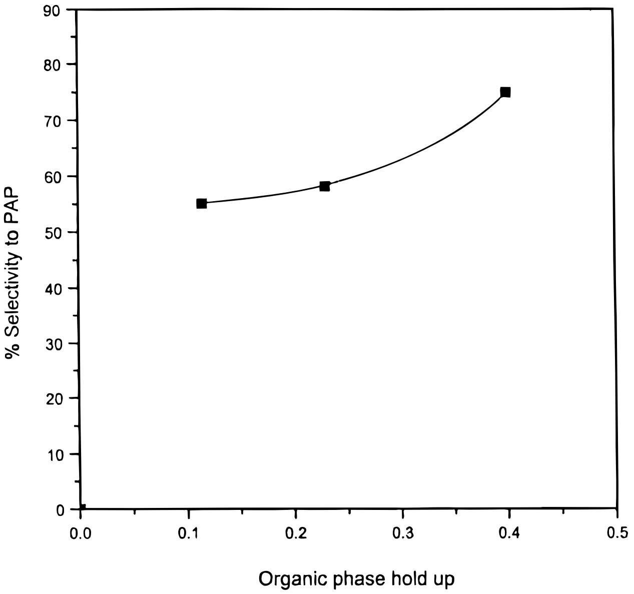

Figure 9. **Effect of organic phase hold up on selectivity to *p*-aminophenol. Reaction Conditions: pressure, 2.72 MPa; temperature, 353 K; agitation, 700 rpm; total volume, 1 × 10^{-4} m^3.**

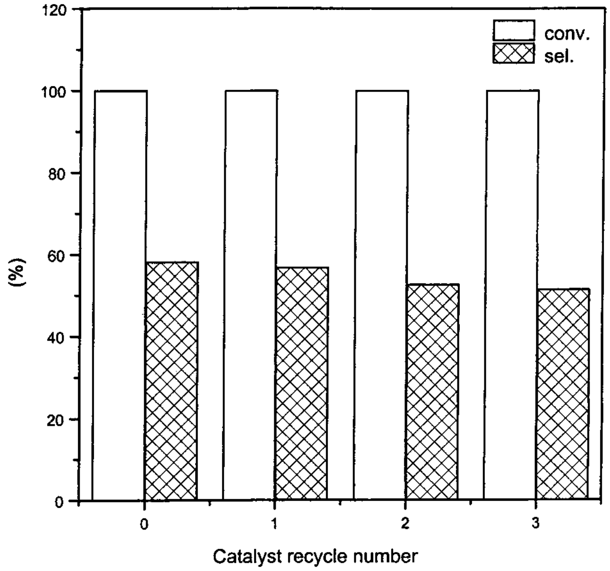

Figure 10. **Effect of catalyst recycle on conversion of nitrobenzene and selectivity to *p*-aminophenol. Reaction conditions: nitrobenzene, 1.86 kmol/m^3; acid, 10% w/w; water, 70 × 10^{-6} m^3; temperature, 353 K; pressure, 2.72 MPa; total volume, 1 × 10^{-4} m^3.**

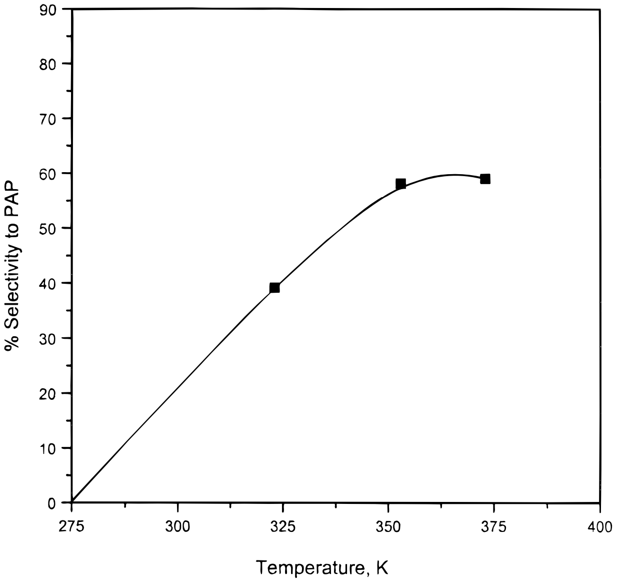

Figure 11. **Effect of temperature on selectivity to *p*-aminophenol by hydrdogenation of nitrobenzene. Reaction conditions: nitrobenzene, 1.86 kmol/m^3; catalyst, 0.35 kg/m^3; water, 70 × 10^{-6} m^3; acid, 10% w/w; temperature, 353 K; pressure, 2.72 MPa; total volume, 1 × 10^{-4} m^3.**

higher hydrogenation rates under the mass-transfer controlling conditions.

Catalyst Recycle. Since the catalyst used in this reaction was a noble metal catalyst, it was important to study the recycle of this catalyst. In these experiments, the catalyst charged for the first reaction was filtered out and again recharged to the reactor for subsequent runs. The catalyst recycle experiments were performed at 353 K and hydrogen partial pressure of 2.72 MPa with acid concentration of 10% w/w and the results are shown in Figure 10. The catalyst was found to retain its activity even after fourth recycle without affecting the conversion of nitrobenzene; however, selectivity for PAP decreased by 5−7%. This lowering of selectivity could be due to the handling losses of catalyst transfer in the subsequent recycle runs. The overall turnover number (TON) for the catalyst was found to be 1.38 × 10^5 which is more than the literature value[4] of 1.34 × 10.[3]

Effect of Temperature. The effect of temperature on both selectivity of PAP and the rate of reaction was studied in the temperature range of 323−373 K and the results are presented in Figures 11 and 12, respectively. The selectivity to PAP was found to increase from 40 to 58% with an increase in temperature up to 353 K, while it remained constant with further increase in temperature from 353 to

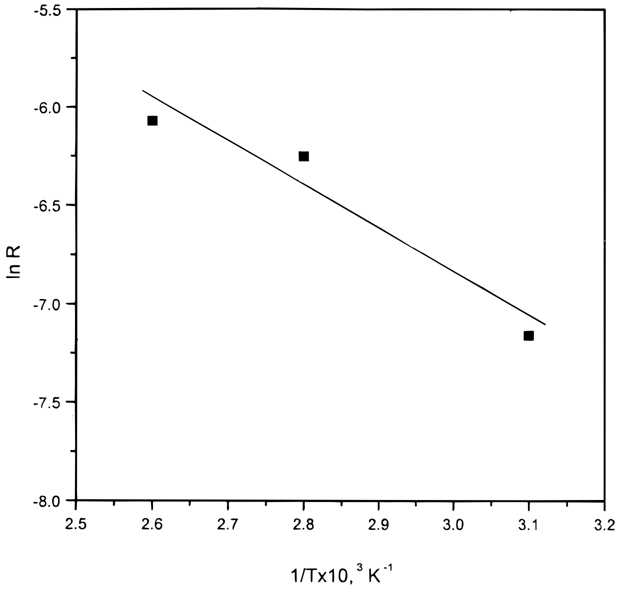

Figure 12. **Effect of temperature on hydrogenation of nitrobenzene to *p*-aminophenol (Arrhenius plot). Reaction conditions: nitrobenzene, 1.86 kmol/m^3; catalyst, 0.35 kg/m^3; water, 70 × 10^{-6} m^3; acid, 10% w/w; pressure, 2.72 MPa; agitation, 700 rpm; total volume, 1 × 10^{-4} m^3.**

373 K. The initial rate of reaction increased with increase in temperature and the activation energy evaluated from the Arrhenius plot (Figure 12) was found to be 10.3 kcal/mol.

Conclusion

Hydrogenation of nitrobenzene was carried out using 3% Pt/C as a catalyst in the presence of sulfuric acid medium to give *p*-aminophenol as a major product and aniline as a byproduct. Under suitable reaction conditions (nitrobenzene: 3.73 kmol/m^3; 3% Pt/C catalyst: 0.70 kg/m^3; sulfuric acid: 15% w/w; water: 0.4 × 10^{-4} m^3; total reaction volume: 1 × 10^{-4} m^3; temperature: 353 K; hydrogen pressure: 2.72 MPa; speed of agitation: 1000 rpm) complete conversion of nitrobenzene was achieved with 75% selectivity to *p*-aminophenol. Both the initial rate of hydrogenation and selectivity of *p*-aminophenol increased linearly with the increase in the hydrogen pressure up to 2.72 MPa, beyond which the rate of reaction was constant, while selectivity of PAP decreased with further increase in hydrogen pressure. The selectivity of PAP was found to be strongly dependent on acid concentration, catalyst loading, organic phase hold up, and speed of agitation. The catalyst was successfully used for three recycle experiments giving a total TON of 1.38 × 10^5, which is 2 orders of magnitude higher than the literature value.

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