

AFRL-ML-TY-TP-2006-4574

PREPRINT



PROBING THE ROLE OF PROMOTERS IN ZINC REDUCTION OF NITROBENZENE: CONTINUOUS PRODUCTION OF HYDROXYLAMINO BENZENE

Lixiong Li, Theodore V. Marolla
Applied Research Associates, Inc
430 West 5th Street, Suite 700
Panama City, FL 32401

Lloyd Nadeau
Air Force Research Laboratory
Tyndall AFB, FL 32403-5323

Jim C. Spain
School of Civil & Environmental Engineering
Georgia Institute of Technology
Atlanta, GA 30332

Interim Paper, September 2006

**DISTRIBUTION STATEMENT A: Approved for public release;
distribution unlimited.**

Submitted for publication in Industrial and Engineering Chemistry Research.

**Air Force Research Laboratory
Materials and Manufacturing Directorate
Airbase Technologies Division
139 Barnes Drive, Suite 2
Tyndall AFB, FL 32403-5323**

REPORT DOCUMENTATION PAGE

*Form Approved
OMB No. 0704-0188*

The public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden, to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number.

PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.

1. REPORT DATE (DD-MM-YYYY)	2. REPORT TYPE	3. DATES COVERED (From - To)
------------------------------------	-----------------------	-------------------------------------

4. TITLE AND SUBTITLE	5a. CONTRACT NUMBER
	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)	5d. PROJECT NUMBER
	5e. TASK NUMBER
	5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)	8. PERFORMING ORGANIZATION REPORT NUMBER
---	---

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER (Include area code)

Probing the Role of Promoters in Zinc Reduction of Nitrobenzene: Continuous Production of Hydroxylaminobenzene

Lixiong Li,^{*,1} Theodore V. Marolla,¹ Lloyd Nadeau,² and Jim C. Spain³

¹ Applied Research Associates, Inc., 430 West 5th Street, Suite 700, Panama City, Florida 32401

² Air Force Research Laboratory, Tyndall Air Force Base, Florida 32403

³ School of Civil & Environmental Engineering, Georgia Institute of Technology, Atlanta, Georgia 30332

Production of hydroxylaminobenzene (HAB) via zinc reduction of nitrobenzene (NB) is an established batch process based on aqueous electrolytic reactions involving an electrolyte as the promoter. This experimental study explored continuous production of HAB that is needed as an intermediate in a novel zinc/biocatalyst processing train to obtain aminophenols. Experiments were conducted using a Zn packed bed to probe the role of promoters under continuous-flow conditions at a temperature of 60°C and promoter/NB molar ratios of 0.75, 1.15, and 1.5. In addition to the conventional NH₄Cl, ammonium formate and acetate were used as promoters. The best HAB yield was 95%, as compared to the batch yield of 68%. The formation of oxidized zinc species caused the packed bed to build back pressure, which appeared to enhance the selectivity of HAB/aniline. *In situ* voltammetric measurements provided evidence of the formation of NB and ammonium/zinc complexes, based on which reaction pathways were proposed. These findings can be used to further improve performance of continuous-flow reactors for HAB production.

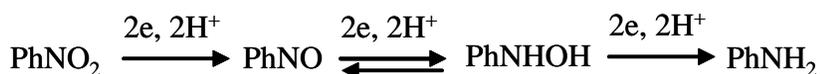
Key Words: zinc reduction, nitrobenzene (NB), hydroxylaminobenzene (HAB), promoters, continuous-flow processing, packed-bed reactor

Introduction

Reduction of nitrobenzene (NB) and its analogs to the corresponding hydroxylaminobenzenes (HAB) and its analogs is a reaction of considerable industrial importance. HAB is an intermediate in the synthesis of aminophenols (particularly *ortho*- and *para*-aminophenols) that are used as precursors for synthesis of high-performance polymers, biologically active compounds, pharmaceuticals, dyestuffs, photoprocessing agents, and specialty additives. HAB can be obtained either from selective hydrogenation of NB using catalysts in organic solvents or aqueous-phase metal-promoted reduction of NB. Karwa and Rajadhyaksha (1987) reported selective catalytic hydrogenation of NB with an optimum HAB yield of 76% using 18 wt% aqueous methanol solvent and 0.3 wt% dimethyl sulfoxide as a catalyst promoter at a

temperature of 60°C and reaction time of one hour. HAB synthesis is traditionally accomplished by zinc reduction of NB in aqueous phase (Vogel, 1954; Blatt, 1956). Zinc reduction of NB is an electrolytic reaction in the aqueous phase, wherein an electrolyte is required to serve as the promoter. The traditional batch method uses ammonium chloride (NH₄Cl) as a promoter and the reaction is carried out at a temperature of 50°C – 65°C. The batch process can achieve nearly 100% conversion of NB and 62 – 68% yield of HAB, with aniline being the major byproduct. However, little information has been provided about the mechanism of ammonium chloride as a promoter, or the basis for selecting the type and concentration of promoters. Chloride is generally known to promote the metal corrosion process, which has certain similarities with zinc reduction of NB. Klausen et al. (2001) demonstrated that reduction of nitroaromatic compounds by zero-valent iron was enhanced in the presence of chloride (NaCl).

Although the Vogel method has been used exclusively for batch production of HAB, attempts have been made over the years to improve the yield of HAB by probing the role of promoters for zinc reduction of NB. There are two general areas of experimental efforts involving mechanistic studies by electrolytic techniques, and screening studies in search of more effective promoters and/or alternative solvents to carry out zinc reduction of NB. Most studies in the area of electrolytic chemistry involving zinc reduction of NB have focused on elucidating reaction mechanisms. Specifically, the reduction of NB (PhNO₂) is proposed to occur by a succession of two-electron steps as shown below. The second step of this sequential reaction train (i.e., from nitrosobenzene (NSB) to HAB) has been reported as a reversible reaction (Zuman and Shah, 1994).



The reduction has been studied using a number of different metal electrodes. Molybdenum (Mo) is also an effective electrocatalyst for the reduction of NB over a wide range of pH (4.4 – 13). Under mildly alkaline and alkaline conditions, the reduction is terminated at the formation of HAB (Seshadri and Kelber, 1999). Under acidic conditions, the reaction proceeds further to form aniline (Zuman and Shah, 1994).

In the second area, zinc reduction of NB has been shown to be promoted by several other salts including ammonium formate (Ram and Ehrenkauffer, 1984; Gowda et al., 2001; Abiraj et al., 2004), ammonium sulfate (Khan et al., 2003), and ammonium acetate (Tsukinoki and Tsuzuki, 2001). However, when ammonium nitrate was present, the zinc reduction of NB did not proceed at all (Tsukinoki and Tsuzuki, 2001). In addition to ammonium salts, formic acid has also been used as a promoter. Gowda et al. (2001) conducted a comparative study on zinc reduction of 27 nitroaromatic compounds using formic acid and ammonium formate as promoters, respectively. For 12 of the 27 compounds, the rates of zinc reduction were the same for both promoters, while for the remaining 15, formic acid was a less active promoter than ammonium formate. Since the use of a buffer solution was not discussed by Gowda et al., it is likely that the

difference in reactivity between these two promoters was due to variation in pH in these solutions. Zinc salts ($ZnCl_2$ and $ZnSO_4$) and amines (L-alanine and L-glutamine) have also shown certain promoting effect to the zinc reduction of NB (Tsukinoki and Tsuzuki, 2001).

These studies show that the role of the promoters is critical in two aspects. First, without a promoter, the zinc reduction of NB does not proceed at a measurable rate within commonly reported temperatures ranging from $40^\circ C$ to $80^\circ C$. Second, the types of the promoter as well as the metal can affect product selectivity among HAB, aniline, and azoxybenzene, and azobenzene in the reduction of NB (Dunlap, 1998). In addition, temperature can also be a key factor affecting the product spectrum. Recently, it has been shown that zinc reduction of NB can take place in high-temperature water (*i.e.*, near-critical water) without the presence of typical electrolyte promoters. However, because HAB is unstable at elevated temperatures, this reaction leads to the formation of aniline as the recoverable product. For example, aniline yields of 98% can be achieved at a reaction temperature of $250^\circ C$ (Boix and Poliakoff, 1999). It is postulated that the reaction of Zn with high-temperature water generates H_2 followed by hydrogenation of the NO_2 group catalyzed by residual traces of zinc. The use of ionic liquids as the solvent for zinc reduction of NB has also been explored. However, the results reported by Khan et al. (2003) show that the products were either anilines using Zn/NH_4Cl in 1-*n*-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF₆]) or hydrazobenzenes with Zn/HCO_2NH_4 (aq.) in recyclable 1-*n*-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF₄]).

Luckarift et al. (2005) demonstrated the continuous synthesis of aminophenols from nitroaromatic compounds by sequential reactions involving zinc and biocatalyst in two continuous-flow reactors connected in series. The first reactor was a packed-bed filled with zinc powder for reduction of NB to form the intermediate product, HAB. The second reactor was a packed-bed filled with biomimetically-derived silica to increase the mechanical stability of the immobilized enzyme (HAB mutase B) for the conversion of HAB to *ortho*-aminophenol. When the mutase reactor was used alone with HAB as the feedstock, the HAB conversion efficiency was relatively low and quantification of the conversion efficiency was difficult, since HAB was unstable due to auto-oxidation. The flow-through reactor system demonstrated by Luckarift et al. (2005) offers a number of advantages over conventional chemical synthesis, including high efficiency and regiospecificity, simplicity for transforming antibiotics with nitro functional groups to the corresponding aminophenols (novel antibiotic analogs), and recovery of the immobilized enzyme. However, back pressure build-up in the zinc packed bed was encountered, typically after 5 to 8 hours of operation due to the formation of oxidized zinc species.

To enhance the effectiveness of this novel continuous synthesis method, several process/reactor design areas should be explored. They include (1) the role of promoters in terms of reactivity and selectivity enhancement; (2) reactor design; and (3) electrolytic chemistry. The purpose of this experimental study was to probe the role of promoters for zinc reduction of NB to produce HAB using a continuous-flow, packed-bed reactor at selected test conditions similar to those used in the conventional batch operations.

Experimental Section

Materials. Zinc powder (assay: 100.6 g/mol, -100+200 mesh) was obtained from Fisher Scientific. HAB was prepared according to Vogel (1954) by S. F. Nishino. NB (99%), NSB (99.99%), and ammonium chloride (99.9%) were obtained from SIGMA. Aniline (99.5%) was obtained from Aldrich. Ammonium formate (99.995%) and ammonium acetate (99.99%) were obtained from SIGMA-Aldrich. All chemicals were used as received.

Test Apparatus. All continuous-flow experiments were conducted using a packed-bed reactor. Figure 1 shows the schematic of the test apparatus (A) and the packed-bed reactor setup (B). The feed solution was delivered by a Waters HPLC pump (Model 510). The reactor assembly was housed in a NESLAB water bath (Model RTE-110). The pressure at the upstream of the packed bed was monitored using an Ashcroft pressure indicator (Model 1009, 4.5-inch dial size) with 0 – 60 psig full scale and accuracy of $\pm 1.0\%$ full scale. Details of the packed-bed reactor are illustrated in Figure 1B. The reactor tube was modified from a 5-mL Baxter glass pipette (Sterile Plugged Borosilicate). The top part of the pipette was cut off at the 2.50-mL marker. The remaining part of pipette was used as the reactor tube, and was packed in the fashion illustrated in Figure 1B. The amount of zinc loaded for each experiment was 0.5 ± 0.01 g, which corresponded to a volume of 0.2 mL. A new reactor tube was prepared and used for each experiment.

HPLC Measurement. Aqueous effluent samples were analyzed using a Hewlett Packard (HP) HPLC (Model 1050) equipped with HP 1040A Detector and HP 1050 HPLC Auto Sampler, and operated by HP Chem Station software. The column was a 25-cm long SUPELCO SIL ABZ+PLUS (spherical silica, Cat. No. 59197-C30). The HPLC method called for an eluent comprising 40% acetonitrile and 60% water, and sample injection volume of 50.0 μ L. Instrument settings included a flowrate of 1.00 mL/min; signals of 210 nm, 4 nm band width (BW), with reference at 550 nm, 100 nm BW; peak width of 0.100 minute; and (4) threshold of 2.0 mAU. More details of the method have been reported in the literature (Luckarift et al., 2005).

Voltammetry Measurement. A Brinkmann (Metrohm 757 VA Comutrace) voltammeter equipped with a DME electrode was used for detection of various species in the zinc reduction reaction. The instrument was operated in differential pulse mode and the scan typically ranged from -5 V to 5 V for 1.5 minutes. During each scan, mercury droplets were automatically introduced at the tip of the electrode into the sample solution at a selected pulse rate. The current response signal was recorded into an interfacing computer, which also displayed the scan plot in real time on the screen.

Procedures.

Nitrobenzene (NB) Solution: All experiments were conducted using 5 mM NB aqueous solution. Promoter dosages were as follows:

NH_4Cl = 3.75, 5.75, and 7.5 mM (0.75, 1.15, 1.5 molar ratios, respectively);
 HCOONH_4 (formic acid) = 5.75 mM (1.15 molar ratio); and
 $\text{CH}_3\text{COONH}_4$ (acetic acid) = 5.75 mM (1.15 molar ratio).

Packed-bed reactor: The zinc powder was loaded in the reactor according to the illustration in Figure 1B. The zinc loading of 0.5 gram occupied a volume of 0.2 mL. A 0.1-mL head space was left to allow bed expansion. A few drops of water were added from the top of the reactor to wet the zinc powder. The reactor was then installed in the water bath, which had been stabilized at $60^\circ\text{C} \pm 0.5^\circ\text{C}$. The feed pump was started immediately to deliver the NB solution at a predetermined flowrate. Assuming a porosity of 0.4 for the zinc powder, the void space for the packed bed was 0.08 mL. At the feed flow rate of 0.25 ml/min, the contact time of the fluid in the packed-bed was 0.32 minute.

Sampling and HPLC analysis: Reactor effluent samples were collected with a syringe and a 3-inch-long needle near the cotton packing at the top of the reactor. The three-way valve was typically set to direct the flow to the effluent tank. During sampling, the three-way valve was turned 90° so that the syringe needle could pass through the valve body, and reach the region adjacent to the packed-bed to ensure the collection of representative samples. About 1 mL of liquid effluent was withdrawn downstream of the packed bed located at the top of the reactor, as indicated in Figure 1B. A portion (*i.e.*, 0.5 mL) of the sample in the syringe was immediately transferred into a 2-mL glass vial, and diluted with 0.5 mL of acetonitrile prior to analysis by HPLC. The vial was sealed and placed in the Auto Sampler for analysis.

Sampling for each experiment began about two hours after the feed solution was pumped into the reactor system. Since the fluid contact time in the packed bed was only about one-third of a minute, five minutes was considered to be adequate to displace the fluid in the system with a sufficient number of bed volume. Preliminary tests were conducted by collecting samples from five minutes up to two hours, and the results indicated that the system reached a steady state, and NB conversion and HAB yield increased steadily.

Voltammeter: The sample cup (with 50-ml capacity) was first filled with 20 mL of 5 mM NB containing corresponding promoters at 1:1 molar ratio of promoter to NB. After the system was scanned to register the baseline response, 0.1 gram of the zinc powder was added, and the run time was set at zero. The system was scanned at five-minute intervals during the first 30 minutes, and then every half-hour. The solution was stirred quickly, before each scan to improve the uniformity of the solution since the reaction took place at the bottom of the cup in the vicinity of the zinc powder.

Method. The role of promoters in zinc reduction of NB under continuous-flow conditions was explored in terms of promoter/NB molar ratio and type of promoters. Whenever possible, process conditions similar to the batch method were selected. First, the reported batch temperature of 60°C was chosen for the continuous-flow experiments. Second, baseline tests were conducted using the ammonium chloride to NB molar ratio of 1.15 as shown in Table 1. In addition, a lower level (0.75) and a higher level (1.5) of the

$\text{NH}_4\text{Cl}/\text{NB}$ molar ratio were tested. Third, metal-promoted NB reduction would also be affected by the $p\text{H}$ of the aqueous solution due to the $p\text{H}$ dependence of reduction potential of the reaction $\text{Zn}^0 - 2e = \text{Zn}^{2+}$. Mu et al. (2004) studied the effect of $p\text{H}$, in the range from 3 to 12, on reduction of NB in aqueous solution by zero-valent iron. The removal of NB decreased 400% when $p\text{H}$ was changed from 3 to 12. However, the NB reduction was least affected by $p\text{H}$ in the range from 5 and 6.5. The $p\text{H}$ value of each feed solution with the promoter measured in this study fell within the range from 5 to 6.5. Several flowrates were initially experimented ranging from 0.25, 0.5, 1.0 and 2.0 mL/min. Eventually, the flowrate of 0.25 mL/min was chosen because good flow characteristics for the given packed-bed reactor was observed without causing excessive back pressure or requiring an excessively long duration of the experiment. The reactions were also monitored in real time using voltammetric measurements. Comparative evaluations were made for ammonium chloride, formate and acetate as promoters at promoter/NB molar ratio of 1.15. The NB conversion, HAB yield, and selectivity of HAB vs. aniline as function of time were derived from samples collected over a period of several days and analyzed by HPLC.

Results and Discussion

Four sets of tests using the ammonium chloride to NB molar ratio of 1.15 were first conducted to establish a baseline for reactor performance. The NB conversion reached 99+% within two hours, and stayed at this level for at least 35 hours before showing a slight reduction over time, Figure 2. The HAB yield reached a plateau of around 85% after 4 – 6 hours, and the yield remained at this level for about 30 hours.

The amount of zinc loading calculated for 1 L of 5 mM NB solution corresponds to a Zn/NB molar ratio of 1.53, which is slightly lower than the value (2.0) used in the batch method (Table 1). At a flowrate of 0.25 mL/min, 1 L of NB solution was processed in 66.7 hours. The time-averaged HAB yield over 66.7 hours was 82.7%. This is 15 – 20% higher than the previous reported yield of 62 – 68% (Vogel, 1954; Blatt, 1956). Furthermore, the highest HAB yield found in this study was about 95%, typically occurring between 10 and 30 hours from the start of a given experiment. The selectivity of HAB over aniline (*i.e.*, HAB/AN molar ratio) typically ranged from 15 to 50, after the packed-bed reactor reached its peak performance for each test.

Since one of the motives for this study was to address the problem of pressure build-up encountered previously (Luckarift et al., 2005), the pressure drop across the packed-bed reactor was monitored during each experiment. In the baseline tests (Figure 3), the averaged back pressure in the packed bed rose to about 8 psig after 80 hours. Since zinc acts as an auxiliary reducing agent (electron source) in the packed bed, the pressure build-up is likely due to the formation of zinc oxide (ZnO). The zinc powder in the packed bed started as a grayish color, and became progressively whiter over time. Since ZnO has a lower density than zinc and is practically insoluble in water, the packed bed expands as the reaction proceeds, resulting in fluid flow restriction as reflected by the

back pressure build-up. At later stages of the experiment, certain regions of the packed bed may be shifted due to increased pressure. The bed shift could open up new channels and reduce flow resistance for a short period time, which could explain the noticeably increased fluctuation in pressure starting from around 60 hours.

Effect of NH₄Cl/NB Molar Ratios.

The second series of tests determined the effect of varying the molar ratio of NH₄Cl/NB. As shown in Figure 4, the maximum HAB yields (~78%) at the NH₄Cl/NB molar ratios of 0.75 and 1.5 were lower than those obtained from the baseline test (~90%). The test with the NH₄Cl/NB molar ratio of 0.75 showed no pressure build-up, but the HAB yield dropped sharply to less than 10% after about 20 hours. On the other hand, the test with the NH₄Cl/NB molar ratio of 1.5 resulted in higher pressure build-up as compared to the baseline tests. These test results demonstrated the importance of the “stoichiometric” ratio of promoter to NB in the zinc reduction reaction. Furthermore, the NH₄Cl/NB molar ratio of 1.15 used in the classical batch method appears to be optimal.

Effect of Promoters.

Both ammonium formate (Gowda et al., 2001; Abiraj et al., 2004) and ammonium acetate (Tsukinoki and Tsuzuki, 2001) have been used as the promoters for zinc reduction of nitroaromatic compounds. However, all of the studies reported in the literature involved batch operating conditions. When ammonium formate was used in the continuous-flow experiments, the HAB yield reached the maximum level of 75% at about 8 hours from the start, and dropped sharply to less than 3% at about 30 hours (Figure 5). The reactor back pressure was less than 2 psig, which was the lowest among the three promoters. However, the NB conversion remained above 97% between 2 hours and 31 hours from the start of this experiment. Both aniline and nitrosobenzene, the other products in the reaction mixture, were less than 0.1 mM, respectively. This means there were other primary products that were not identified by the HPLC method used for the effluent analysis. Furthermore, the lack of usual back pressure was probably due to the presence of formate. The reason for the rapid decline in HAB yield was not clear.

Compared to the NH₄Cl baseline tests, the use of ammonium acetate caused a slower rise initially in the HAB yield, and reached the highest HAB yield of 95% at about 24 hours from the start of the experiment. However, the reactor back pressure in the ammonium acetate test rose much faster than in tests involving the other two promoters. These experimental observations led to further probing of the zinc reduction of NB using the voltammetric technique.

Voltammetric Evidence of Reaction Pathways.

Voltammetric measurements were conducted in the batch mode with all three promoters. The NB scan, Figure 6, shows a very slight peak at -0.9 V, while the NH_4Cl scan displays the characteristic peaks at -2.2 V and 0.2 V for NH_4^+ and Cl^- , respectively. However, in the scan for the solution of NB + NH_4Cl , a peak with peak height comparable to that of NH_4^+ appears at about -1.0 V, while the Cl^- peak at -0.2 V remains the same. This indicates the formation of a stable complex (**1**) between NB and NH_4^+ , since the peak at about -0.9 V is the characteristic location for NB and the NH_4^+ peak at -2.2 V completely disappeared before zinc was added to the solution. Voltammetric scans of all three promoters and their solutions with NB, Figure 7, reveal that patterns in the region above voltage = 0 V vary slightly, since the anions are different. The key shift of the NH_4^+ peak at -2.2 V to about -0.9 V was consistent among all three promoters. Of the data not shown, the zinc cation in zinc acetate displays its characteristic peak at -1.1 V.

A series of voltammetric scans of NH_4Cl -promoted Zn reduction of NB provides a qualitative display of the time course of Zn reduction of NB with disappearance of the reactants and appearance of intermediates and products (Figure 8). The appearance of a series of small peaks at about -1.5 V that shifted to -1.1 V provides strong evidence of the presence of zinc complex and/or cations. The series of peaks at about -0.2 V is clearly indicative of HAB. The decrease in the peak intensity confirms that HAB is further converted to aniline. The peaks for nitrosobenzene (NSB) and aniline were apparent at -0.5 V and 0.2 V, respectively. At 16 hours after the reaction started, the conversion of NB was complete, and nearly all of the HAB was converted into aniline. The key characteristics of the voltammetric response for $\text{CH}_3\text{COONH}_4$ -promoted reactions, Figure 9, are similar to those observed for the conventional NH_4Cl -promoted Zn reduction of NB.

According to the reaction pathways reported by Lavine et al. (2001) and Bieber et al. (2000) for similar reaction systems, and reaction pathways for ammonium-salt-promoted zinc reduction of NB to HAB were proposed. As shown in

Figure 10 shows proposed reaction pathways for ammonium-salt-promoted zinc reduction of NB to HAB. Based on the voltammetric analysis from this study, it appears that the formation of NB-ammonium complex (**1**) identified as the peak at -0.9 V in Figure 7, is the prerequisite the Zn reduction reaction. Upon addition of zinc into the NB-ammonium salt solution, the complex (**1**) establishes an adsorption and desorption equilibrium with a second complex (**2**) involving zinc surface and water molecules. Once the complex (**2**) is formed, the chemical potential, similar to that encountered in the iron corrosion process (Deng et al., 1997), would drive zinc to transfer an electron to NB to produce an intermediate (**3**) containing a chemical bond between zinc and nitrogen. The intermediate (**3**) proceeds with a proton transfer step to form another intermediate (**4**) and $\text{Zn}^+(\text{OH})$. The former proceeds to repeat the electron and proton transfer steps to form the next intermediate (**5**), which after dehydration becomes nitrosobenzene (**6**). $\text{Zn}^+(\text{OH})$ goes through rapid hydration and dehydration to form ZnO, which has been identified as the main byproduct from the zinc reduction process. Nitrosobenzene (**6**) proceeds

through the similar electron and proton transfer steps involving several five-member ring intermediates (7 – 10), before materializing as HAB (11). In this pathway presentation, the ammonium cation is left in the complex with nitrobenzene and its reducing derivatives in each step for illustration purposes, although voltammetric scans indicate that the complex becomes significantly weaker as the reaction proceeds. The reaction pathways from NB to NSB (6) and from NSB (6) to HAB (11), respectively, are typically presented as two-electron reactions (Zuman and Shah, 1994), and are consistent with those for similar reaction systems reported by Lavine et al. (2001) and Bieber et al. (2000).

According to Zuman and Shah (1994), the two-electron reduction of NSB (6) to HAB (11) rapidly reaches equilibrium, and the reaction is reversible. The observed shifts of about 0.06 V/pH in the potentiometrical measurement are not sufficient evidence to distinguish whether the proton transfer occurs before, during, or after electron transfers. The reduction of HAB to form aniline, which is not shown in Figure 10, follows similar reaction pathways, but at a lower rate under typical experimental conditions for HAB production. As shown in Figure 9, aniline becomes the dominating product if given sufficient time for the reduction reaction to completion.

Implications on Flow-Through Reactor Design.

There are two key design features for the continuous-flow operation that may have contributed to the observed high HAB yield and high selectivity. First, a high Zn/NB molar ratio can be maintained under the continuous-flow operation. This is because the zinc loading in the reactor is based on the amount of NB in a given solution, which is pumped through the reactor at a specific NB concentration and flow rate. Therefore, NB that passes through the packed bed at any given time, is exposed to excess stoichiometric amounts of Zn. According to the reaction pathways presented in Figure 10, two moles of zinc are consumed in the conversion process to produce one mole of HAB from NB. This is the same molar ratio that is employed in the conventional batch operation (Table 1). Using 0.08 mL as the estimated void volume in the packed bed and 5 mM as the concentration of NB solution, the Zn/NB molar ratio encountered in the packed bed used in this study was 19,125. As the reaction proceeds, this ratio linearly decreases proportional to the accumulative amount of NB pumped through the reactor.

Second, the HAB produced quickly leaves the packed bed without further contact with the zinc surfaces. Without zinc, further reduction of HAB is effectively halted. If HAB is immediately consumed as an intermediate for subsequent reactions, the loss of HAB should be minimal. As a result, the continuous-flow operation can generate much higher HAB yield and higher selectivity of HAB/aniline than what is expected in the batch operation where zinc and HAB are in full contact throughout the reaction duration.

Since HAB is an intermediate product from Zn reduction of NB, the selectivity of HAB over the end product, aniline, is one of the important performance criteria for evaluating reactor designs. In the traditional batch operation, the NB conversion is nearly

100%, while the HAB yield is 68% (Table 1). Assuming aniline is the predominant product other than HAB, the selectivity of HAB/aniline would be 2.10. In the continuous-flow operation, the NB conversion drops off as the reaction time increases, as shown in Figure 2. Using the data set given in Table 1 for $\text{NH}_4\text{Cl}/\text{NB}$ ratio of 1.15, the time-averaged NB conversion and HAB yield are 93.7% and 82.7%, respectively. Using the same assumption as that for the batch operation, the calculated selectivity of HAB/aniline for the continuous-flow operation is 7.50. This is one of the inherited benefits of flow-through reactor systems for Zn reduction of NB.

The selectivity data derived from the continuous-flow, packed-bed reactor appear to be correlated with system pressure. Figure 11 shows the plot of the molar ratio of HAB/aniline against the packed-bed back pressure. There were several extremely high selectivity data points corresponding to HAB/aniline molar ratio ranging from 800 to 8000, which are excluded from this plot. However, the measured data do suggest the potential for reactor design improvement to achieve high HAB selectivity. The correlation appears to be linear, and generally independent of the types and concentrations of promoters for all experiments with promoter/NB ratios greater than 1. The selectivity of HAB/aniline reaches 50 at 20 psig, rendering a pressure-dependency coefficient of $2.5 (\text{psig})^{-1}$. The exception was observed for the data obtained from NH_4Cl -promoted Zn reduction of NB with the $\text{NH}_4\text{Cl}/\text{NB}$ ratio of 0.75, for which the back pressure of the packed bed was less than 0.5 psig.

Unlike the pressure dependency of the selectivity, the best HAB yield corresponds to a low level of the back pressure. As shown in Figures 4 and 5, the maximum HAB yield for each system corresponds to about 2 psig pressure drop across the packed bed. This implies the excess amount of zinc at the early stages of the reaction may be a critical factor to maintain a high HAB yield. Since pressure is directly related to the driving force to help the fluid penetrate into pores at zinc and/or oxidized zinc surface, the pressure dependence of HAB/aniline selectivity and HAB yield may also imply that Zn reduction of NB is a diffusion-controlled reaction, particularly after the surface layer of active zinc has been consumed.

Experimental findings from this study suggest that one of the potential design options may involve employing fluidized-bed design operated under a low level of system pressure. In addition to pressure, there are other options available for further improving reactor performance under continuous-flow conditions. The process parameters that may be further evaluated include temperature, reactor residence time, mixed metals (*i.e.*, Zn + other metals), and mixed promoters.

Conclusion

Since conversion of NB to HAB is a model reaction system for many commercially important syntheses involving nitroaromatics, production of HAB via zinc reduction of NB under flow-through conditions offers a valuable processing tool for developing new synthetic approaches in biotechnology as well as traditional chemical

technology areas. This study demonstrated that reduction of NB using zinc powder under continuous-flow conditions has the potential to achieve high HAB yield (>90%) and high HAB/aniline selectivity (>50). Promoters, traditionally ammonium chloride, serve as electrolytes and complex forming agents to enable zinc reduction of NB to proceed at near ambient temperatures. Voltammetric evidence suggests the presence of ammonium complexes with NB and with NB + Zn in an aqueous composition. Therefore, other ammonium salts, such as ammonium formate and acetate, can also be used for zinc reduction. The option that allows for selecting promoters with different anions, inorganic as well as organic, in zinc reduction of NB could offer new opportunities for synergetic reaction schemes where the anions may play a multi-functional role.

As an unexpected finding, increasing process pressure significantly improved both HAB yield and HAB/aniline selectivity. Formation of ZnO as the oxidation product of Zn in a packed-bed setting results in raising fluid flow resistance, and in turn building up reactor back pressure, which must be addressed in the reactor design and process development. The beneficial effect of pressure on the HAB production observed in this experimental study should help develop continuous-flow reactor systems, as well as further understanding of reaction pathways and the role of promoters in zinc reduction of NB.

Acknowledgement

The authors thank Shirley Nishino for providing the HAB standard; Dr. Matthew Eby for providing instructions associated with the HPLC analysis; Robert Diltz for setting up the voltammeter and providing operational instructions; Janet Davis for assisting in literature search; Dr. Joe Wander for discussions and comments regarding zinc reduction chemistry and reaction pathways; and Dr. Jean Renard and Carrie Delcomyn for reviewing the manuscript.

References

- Abiraj, K.; Srinivasa, G.R.; Gowda, D.C. Facile Synthesis of Symmetrical Functionalized Biaryls from Aryl Halides Catalyzed by Commercial Zinc Dust using Ammonium Formate. *Tetrahedron Lett.* **2004**, 45, 2081.
- Berman, A.; Epstein, M. The Kinetics of Hydrogen Production in the Oxidation of Liquid Zinc with Water Vapor.” *International J. of Hydrogen Energy* **2000**, 25, 957.
- Bieber, L.W.; da Costa, R. C.; da Silva, M. F. Reductive Alkylation of Nitrobenzene Promoted by Zinc and Tin in Protic Solvents. *Tetrahedron Lett.* **2000**, 41, 4827.
- Blatt, G. *Organic Synthesis Collection*, V 1, 445, John Wiley & Sons, Inc., 2nd Ed., London, 1956.

- Boix, C.; Poliakoff, M. Selective Reductions of Nitroarenes to Anilines using Metallic Zinc in Near-Critical Water. *J. Chem. Soc., Perkin Trans.* **1999**, 1, 1487.
- Deng, B.; Campbell, T.J.; Burris, D.R. Hydrocarbon Formation in Metallic Iron/Water Systems. *Environ. Sci. and Technol.* **1997**, 31, 1185.
- Karwa, S.L.; Rajadhyaksha, R.A. Selective Catalytic Hydrogenation of Nitrobenzene to Phenylhydroxylamine. *Ind. Eng. Chem. Res.* **1987**, 26, 1746.
- Khan, F.A.; Dash, J.; Sudheer, C.; Gupta, R.K. Chemoselective Reduction of Aromatic Nitro and Azo Compounds in Ionic Liquids using Zinc and Ammonium Salts. *Tetrahedron Lett.* **2003**, 44, 7783.
- Klausen, J.; Ranke, J.; Schwarzenbach, R.P. Influence of Solution Composition and Column Aging on the Reduction of Nitroaromatic Compounds by Zero-Valent Iron. *Chemosphere* **2001**, 44, 511.
- Gowda, D.; Mahesh, B.; Shankare, G. Zinc-Catalyzed Ammonium Formate Reductions: Reduction of Nitro Compounds. *Ind. J. Chem.* **2001**, Sect. B, 40, 75.
- Dunlap, K.L. Nitrobenzene and Nitrotoluenes. Kirk-Othmer Encyclopedia of Chemical Technology, 17, 135, John Wiley & Sons, 4th Ed., New York, 1998.
- Lavine, B.K.; Auslander, G.; Ritter, J. Polarographic Studies of Zero Valent Iron as a Reductant for Remediation of Nitroaromatics in the Environment. *Microchemical Journal* **2001**, 70, 69.
- Luckarift, H.R.; Nadeau, L.J.; Spain, J.C. Continuous Synthesis of Aminophenols from Nitroaromatic Compounds by Combination of Metal and Biocatalyst. *Chemical Communications* **2005**, 3, 383.
- Mu, Y.; Yu, H-Q; Zheng, J-C; Zhang, S-J; Sheng, G-P. Reductive Degradation of Nitrobenzene in Aqueous Solution by Zero-Valent Iron. *Chemosphere* **2004**, 54, 789.
- Ram, S.; Ehrenkaufner, R.E. A General Procedure for Mild and Rapid Reduction of Aliphatic and Aromatic Nitro Compounds using Ammonium Formate as a Catalytic Transfer Agent. *Tetrahedron Lett.* **1984**, 25(32), 3415.
- Seshadri, G.; Kelber, J.A. A Study of the Electrochemical Reduction of Nitrobenzene at Molybdenum Electrodes. *J. Electrochemical Society* **1999**, 146(10), 3762.
- Vogel, A. I. *Practical Organic Chemistry*, 602, Longman, 2nd Ed., London, 1954.
- Zuman, P.; Shah, B. Addition, Reduction and Oxidation Reactions of Nitrosobenzene. *Chemical Review* **1994**, 94, 1621.

List of Tables

Table 1. Comparison of Batch and Continuous-Flow Processes for Zinc Reduction of NB

List of Figures

Figure 1. Schematic of test apparatus.

Figure 2. Zn Reduction of NB in a continuous-flow, packed-bed reactor.
The data points are averaged over those derived from four separate experiments, and the error bars show one standard deviation ($\pm \sigma$).

Figure 3. Pressure drop across the packed-bed reactor

Figure 4. Effect of $\text{NH}_4\text{Cl}/\text{NB}$ ratio on HAB yield and packed-bed back pressure

Figure 5. Effect of promoters on HAB yield and packed-bed back pressure

Figure 6. Effect of NH_4Cl on voltammetric response for NB

Figure 7. Voltammetric responses for NB using different promoters

Figure 8. Voltammetric time-plot for NH_4Cl -promoted Zn reduction of NB

Figure 9. Voltammetric time-plot for $\text{CH}_3\text{COONH}_4$ -promoted Zn reduction of NB

Figure 10. Proposed reaction pathways for NH_4Cl -promoted Zn reduction of NB

Figure 11. HAB/Aniline selectivity as a function of process pressure

Table 1. Comparison of Batch and Continuous-Flow Processes for Zinc Reduction of Nitrobenzene

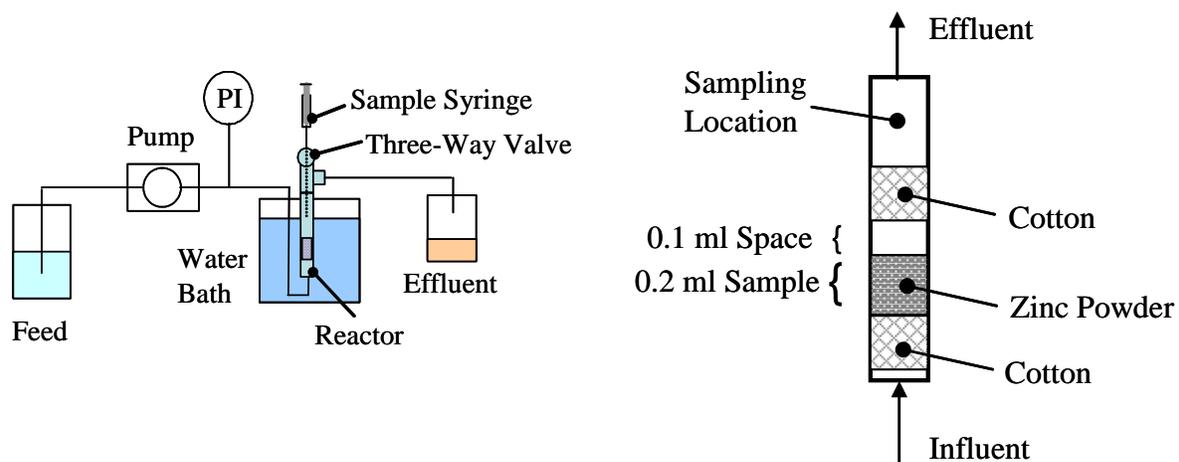
<u>NH₄Cl</u>			<u>NB</u>			<u>Zn Powder</u>			<u>H₂O</u>		<u>NH₄Cl</u>	<u>Zn</u>	<u>HAB</u>		<u>HAB</u>	<u>NB</u>	<u>Reference</u>
(g)	(mmol)	(mM)	(g)	(mmol)	(mM)	(g)	(%)	(mmol)	(L)	(mol)	<u>/NB</u>	<u>/NB</u>	<u>Theo.</u>	<u>Actual</u>	<u>Yield</u>	<u>Conv.</u>	
<u>Batch Operation</u>																	
250	4670	580	500	4100	510	620	85	8060	8.0	444	1.15	1.98	443	300	67.8	~100	Blatt, 1956
25	470	580	50	400	510	59	90	810	0.8	44.4	1.15	2.00	44.3	29	65.5	~100	Vogel, 1954
<u>Continuous-Flow Operation</u>																	
<u>Ammonium Chloride</u>																	
0.308	5.75	5.75	0.616	5	5	0.5	99.9	7.65	1.0	55.6	1.15	1.53	0.545*	0.451	82.7	93.7	This work
0.401	7.5	7.5	0.616	5	5	0.5	99.9	7.65	1.0	55.6	1.5	1.53	0.545*	0.327	60.0	97.4	This work
0.201	3.75	3.75	0.616	5	5	0.5	99.9	7.65	1.0	55.6	0.75	1.53	**		16.6	72.7	This work
<u>Ammonium Acetate</u>																	
0.442	5.75	5.75	0.616	5	5	0.5	99.9	7.65	1.0	55.6	1.15	1.53	**		85.1	99.4	This work
<u>Ammonium Formate</u>																	
0.363	5.75	5.75	0.616	5	5	0.5	99.9	7.65	1.0	55.6	1.15	1.53	**		32.8	98.7	This work

Test Procedure/Conditions (Batch Operation):

1. Add NH₄Cl to H₂O, and add NB to the solution;
2. Add Zn in 15 minutes while stirred; and continue to stir for 15 minutes after Zn is added;
3. Temperature rises to 60 – 65°C, and ceases to rise when reaction is completed;
4. Filter the solution to remove zinc oxide;
5. Saturate the filtrate with common salt and cool to 0°C; and
6. HAB crystallizes out in long, light yellow needles.

* Theoretical yield per one liter of 5 mM NB solution. ** Tests terminated before consuming one liter of 5 mM NB solution.

*** Percent of theoretical yield for the continuous-flow operation is based on time-averaged HAB yield or NB conv over 66.7 hours.



A. Process flow diagram

B. Packed-bed reactor setup

Figure 1. Schematic of test apparatus.

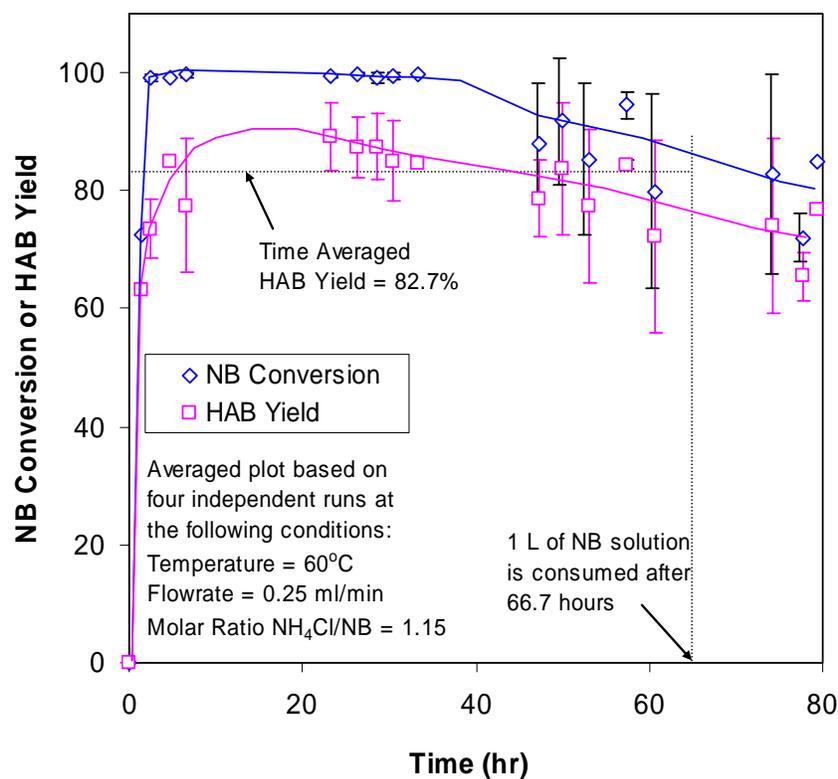


Figure 2. Zn Reduction of NB in a continuous-flow, packed-bed reactor.

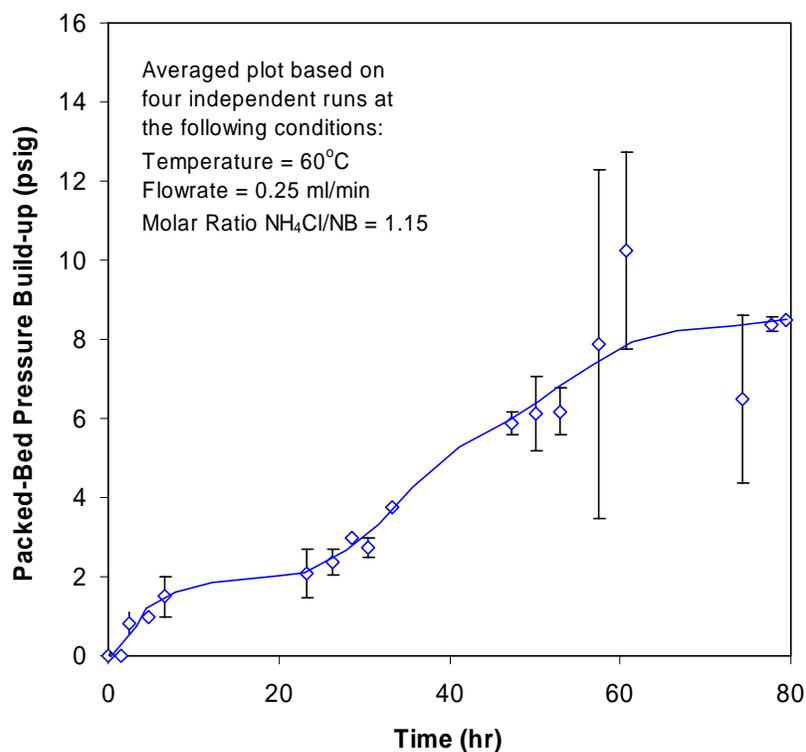


Figure 3. Pressure drop across the packed-bed reactor.

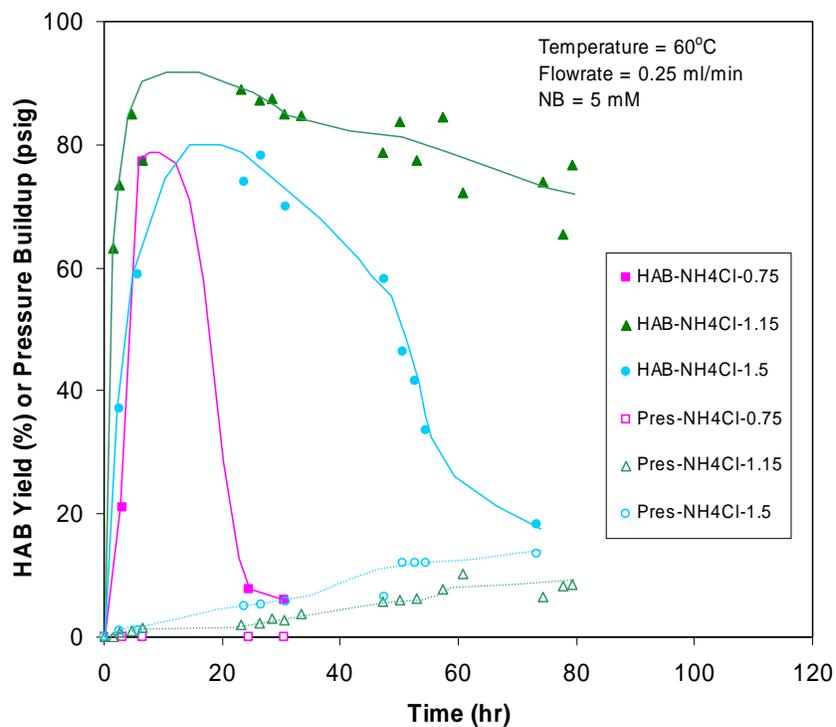


Figure 4. Effect of $\text{NH}_4\text{Cl}/\text{NB}$ ratio on HAB yield and packed bed back pressure.

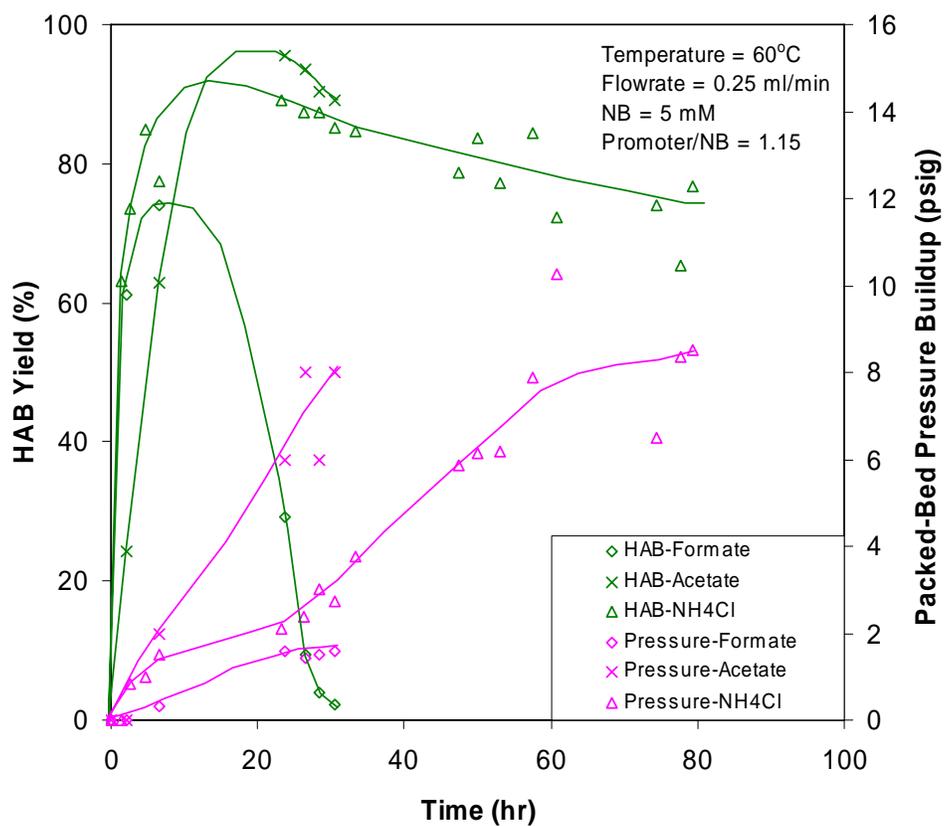


Figure 5. Effect of promoters on HAB yield and packed bed back pressure.

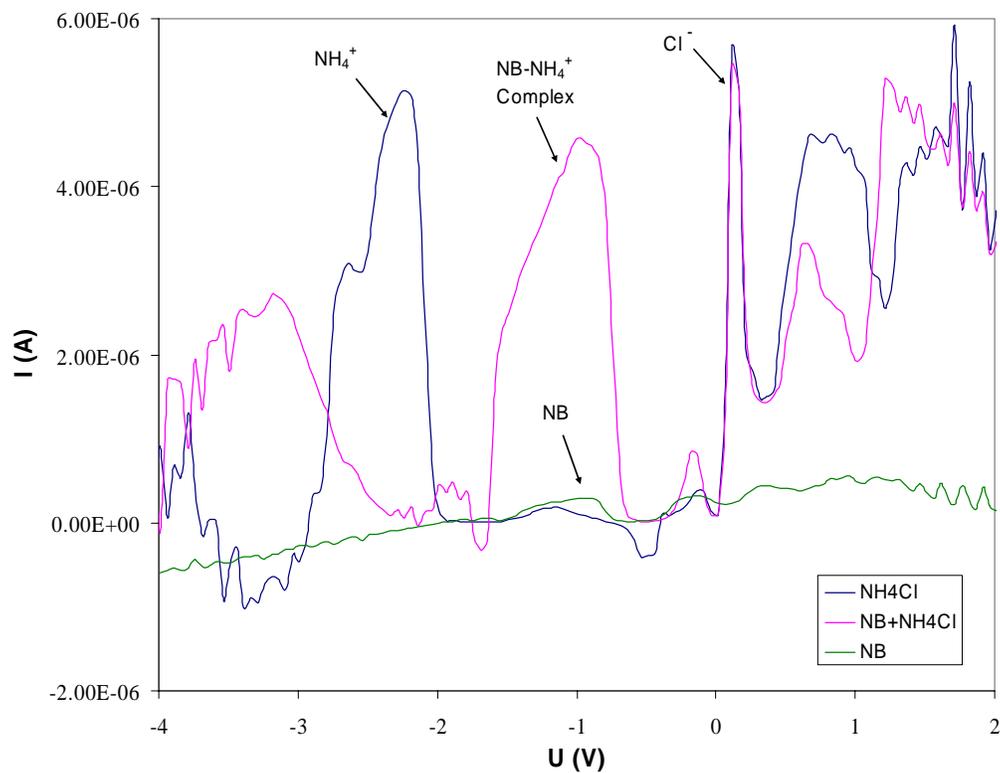


Figure 6. Effect of NH_4Cl on voltammetric response for NB.

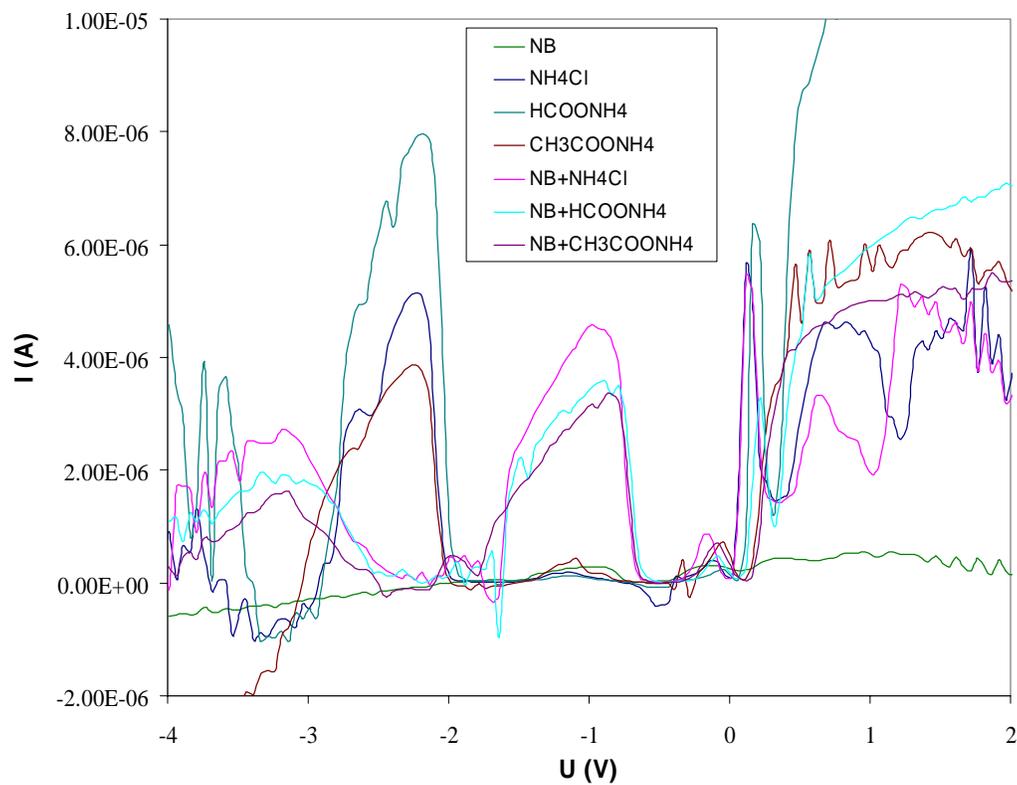


Figure 7. Voltammetric responses for NB using different promoters.

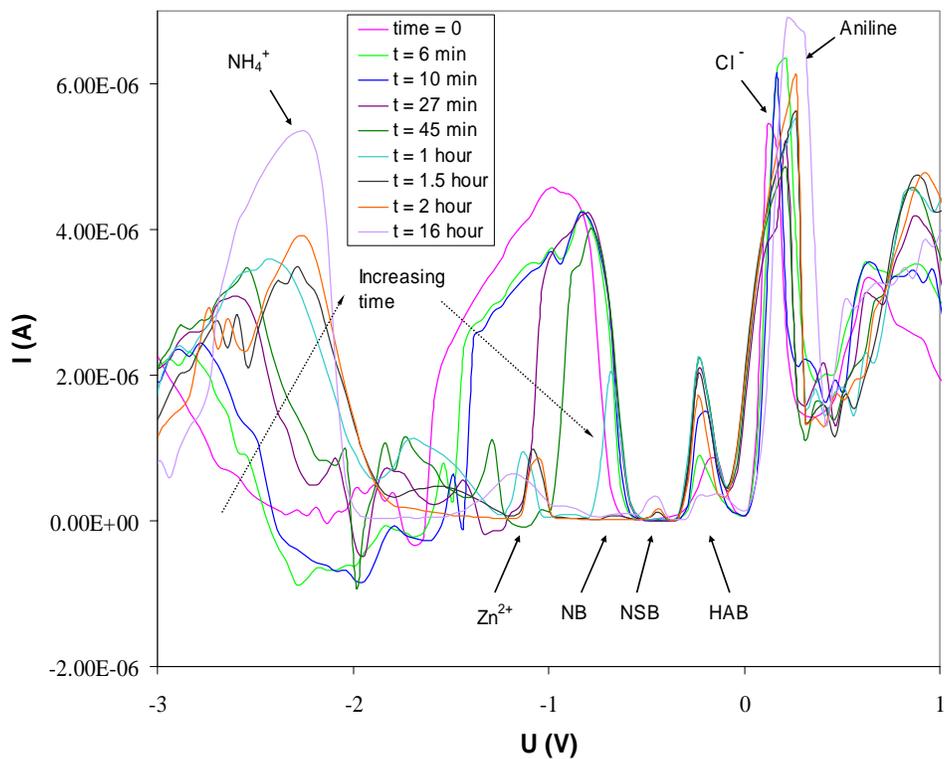


Figure 8. Voltammetric time-plot for NH_4Cl -promoted Zn reduction of NB.

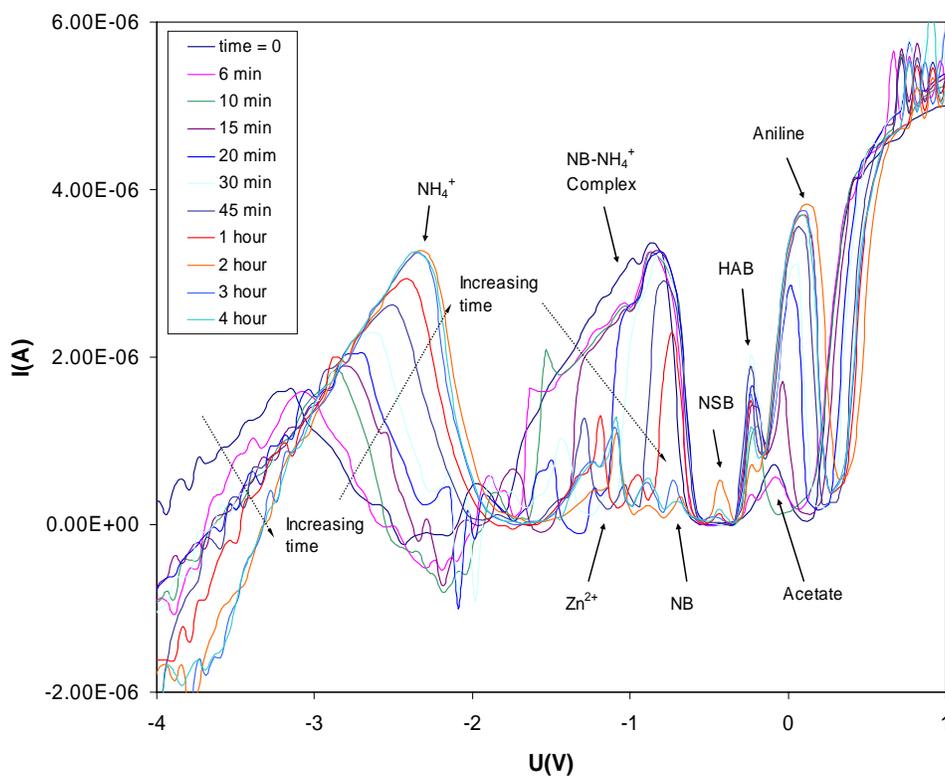


Figure 9. Voltammetric time-plot for $\text{CH}_3\text{COONH}_4$ -promoted Zn reduction of NB.

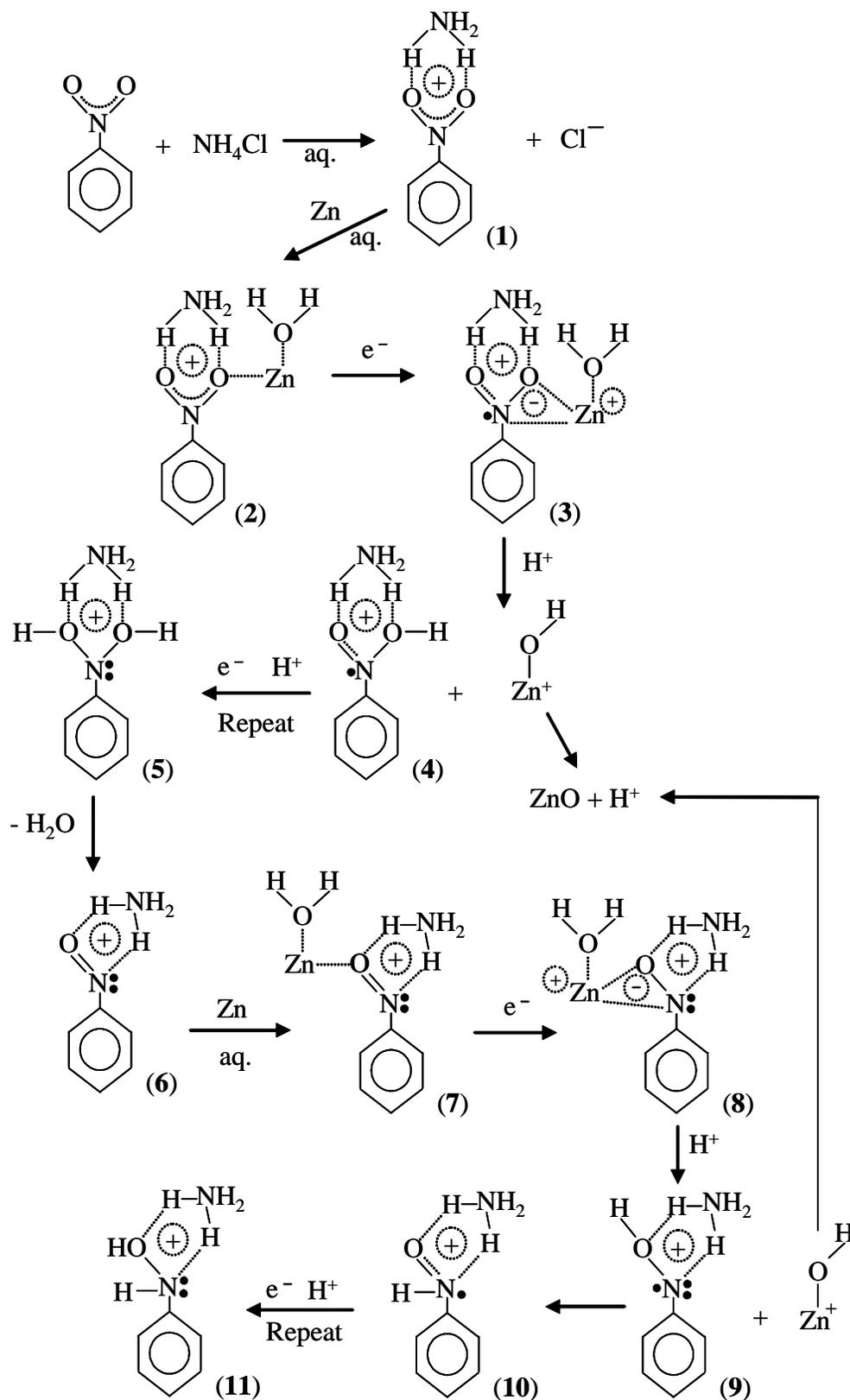


Figure 10. Proposed reaction pathways for NH_4Cl -promoted Zn reduction of NB.

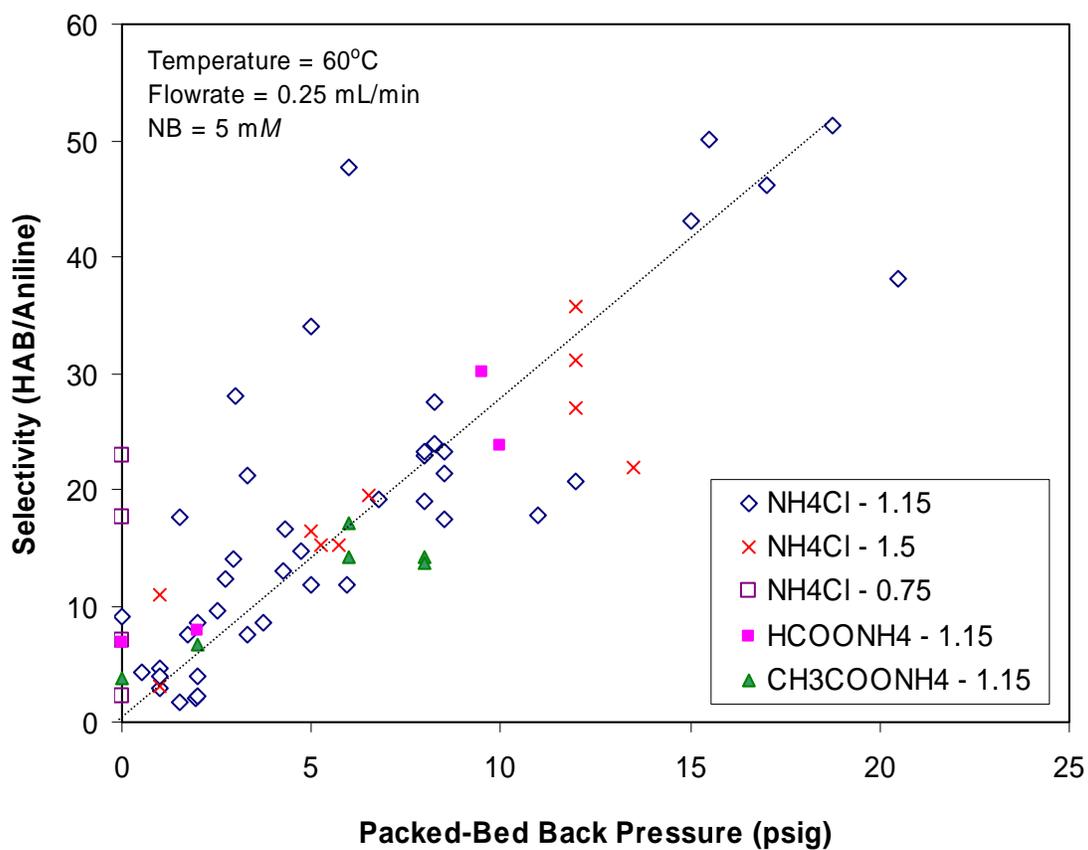


Figure 11. HAB/Aniline selectivity as a function of process pressure.