

An Efficient Method for the Production of Cyclohexylamine from Cyclohexanone and Ammonia over Cu-Cr-La/ γ -Al₂O₃

Shuanglin Qin[†], Pan Wang[‡], Shuangping Huang[†], Shuai Liu^{†,§}, Gaopeng Wang[†], Liping Wang[†], Meng Sun^{†,*} and Xiaoji Wang^{†,*}

[†]School of Pharmacy, Jiangxi Science and Technology Normal University, Nanchang, China, 330013.

*E-mail: professorwxj@163.com

[‡]First Teaching Hospital of Tianjin University of Traditional Chinese Medicine, AnShan Xi Road 314, Nankai District, Tianjin, China, 300193

[§]Shaoxing Xingxin Chemical Co., Ltd., Shangyu, Zhejiang, China, 312369

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ABSTRACT. The reductive amination of cyclohexanone with ammonia over Cu-Cr-La/ γ -Al₂O₃ was investigated. It was found that a proper solvent with high solubility of ammonia and 4Å molecular sieves for the elimination of generated water contributed to the formation of cyclohexylamine in the premixing process. In addition, the addition of ammonia in the fixed-bed reactor could obviously improve the conversion of cyclohexanone to cyclohexylamine. Finally, reaction conditions including reaction temperature, hydrogen pressure and charging rate of the premix were optimized. Under the optimized conditions, cyclohexylamine was obtained in 83.06% yield.

Key words: Reductive amination, Cyclohexylamine, Cyclohexanone, Cu-Cr-La/ γ -Al₂O₃, Premixing process

INTRODUCTION

Amines and their derivatives served as one of the most important raw materials and always were employed for the synthesis of herbicides, insecticides, pharmaceuticals, corrosion inhibitors, plastics and rubber chemicals.¹⁻⁴ Recently, the reductive amination of appropriate carbonyl compounds was the most environmental benign method to yield amines and thus attracted tremendous attentions. Accordingly, the related reports kept emerging as well. As a common industrial intermediate, the production of cyclohexylamine (CyNH₂) was also a hotpot.⁵⁻¹² It was traditionally produced by amination of cyclohexanol or cyclohexanone. For example, Poppe *et al.*¹³ have reported the production of cyclohexylamine with ammonium formate as ammonia source over Pd/C and 68% of yield was obtained. Ramachandran *et al.*¹⁴ and Burkhardt *et al.*¹⁵ respectively employed 5-ethyl-2-methylpyridine and ammonia borane for the reductive amination of cyclohexanone. Though the yield of cyclohexylamine was above 75%, the recycling of these catalysts was also an obstacle. H₂ or H β was applied for this reductive amination as well. However, only 19% of cyclohexylamine yield was achieved.¹⁶ Undoubtedly, these tedious work-up procedures or the poor selectivity restricted the development of CyNH₂. It was very imperative to further improve the CyNH₂ selectivity.

In this work, a serial of catalysts are employed for the reaction of cyclohexanone and ammonia in a fixed-bed reactor, and Cu-Cr-La/ γ -Al₂O₃ exhibited the excellent performance. Meanwhile, in order to improve the selectivity of CyNH₂, reaction conditions and premixing process were investigated. Based on aforementioned results, the possible reaction mechanisms were proposed.

EXPERIMENTAL

4Å molecular sieves were provided by The Catalyst Plant of Nankai University, Tianjin, PR China. Commercially available reagents and solvents were used without further purification.

The Preparation of Catalysts

Cu-Cr-La/ γ -Al₂O₃ catalysts in this study were prepared by coprecipitation-kneading method. The details were briefly described as follows. Cu(NO₃)₂·3H₂O (38.05 g), Cr(NO₃)₃·9H₂O (19.23 g) and La(NO₃)₃·6H₂O (7.79 g) were all dissolved in 400 ml of deionized water. In addition, Na₂CO₃ (29.38 g) was dissolved in 400 ml of deionized water. These two aqueous solutions were added simultaneously into a beaker containing 200 ml of deionized water under mechanical stirring. In this period, the pH of the suspension was maintained around 7.5-8.0. After aging for another

1 h, the mixture was filtered and the residue was washed with deionized water until no nitrate anion was left. Then, the samples were dried at 110 °C for 6 h and grind up into powders. Afterwards, the powders were kneaded with a mixture of pseudo-boehmite (57.55 g) and 50 ml, 2 wt % nitric acid. The mixture was molded into $\Phi 3$ bars by an extruder. The obtained catalysts were dried at 110 °C for 6 h, calcined at 500 °C for 4 h and activated at 240 °C for 4 h in a hydrogen steam (1.0 MPa) for later use.^{17–19} Other catalysts such as Ni/ γ -Al₂O₃, Co/ γ -Al₂O₃, Cu/ γ -Al₂O₃, Cu-Cr/ γ -Al₂O₃, Cu-Cr-Fe/ γ -Al₂O₃, Cu-Cr-Mn/ γ -Al₂O₃ and Cu-Cr-Zn/ γ -Al₂O₃ were prepared as a similar approach.

4A molecular sieves were activated by calcination at 400 °C for 4 h in a muffle furnace. Afterwards, they were cooled down to ambient temperature and transferred to a drier before use.

Catalytic Reaction

The reductive amination of cyclohexanone with ammonia was carried out in a fixed-bed reactor consisting of a stainless steel tube with an inner diameter of 15 mm and a length of 660 mm inside a vertical furnace with a temperature controller. 40 ml of catalysts were placed in the middle of the tube. A solution of 10 wt % cyclohexanone in methanol and a certain amount of 4A molecular sieves were placed in a 100 ml one-necked flask fitted with magnetic stirrer. Cooled by ice bath, ammonia was dissolved into the mixture as much as possible. The resulting mixture was stirred for another 2 h at 0–5 °C. Then the supernatant was pumped into the fixed-bed reactor at a speed of 0.2 ml/min. The obtained reaction mixture were analyzed every 3 h by GC equipped with a 30 m SE-54 capillary column and the components were confirmed on a GC-MS instrument equipped with a 30 m HP-5 capillary column.

RESULTS AND DISCUSSION

Catalyst Selection

Initially, a series of catalysts including Ni/ γ -Al₂O₃, Co/ γ -Al₂O₃, Cu/ γ -Al₂O₃, Cu-Cr/ γ -Al₂O₃, Cu-Cr-Fe/ γ -Al₂O₃, Cu-Cr-Mn/ γ -Al₂O₃, Cu-Cr-Zn/ γ -Al₂O₃ and Cu-Cr-La/ γ -Al₂O₃ were employed for the reductive amination of cyclohexanone with ammonia and the results were summarized in Table 1. It was found that Cu-Cr-La/ γ -Al₂O₃ displayed the best catalytic performance, which was accordance with the results Sun *et al.* reported²⁰ (Sun *et al.*, 2011), so this catalyst was used for the following research.

Reaction Mechanism

Subsequently, the reaction mechanism was investigated. When this reaction was proceeded using Cu-Cr-La/ γ -Al₂O₃, a range of byproducts, including cyclohexanol (Cyol), 2-cyclohexylcyclohexanol (Cy-cyol) and dicyclohexylamine (Dicy) were detected except for CyNH₂. So the improvement of CyNH₂ selectivity was still an obstacle.

Referring to the mechanism for reductive amination of cyclohexanone with 1,6-diaminohexane,²¹ we proposed the possible reaction route for this reaction (Fig. 1). Initially, the nucleophilic addition of ammonia to cyclohexanone was carried out and then followed by the dehydration to yield cyclohexylimine, reversibly. Subsequently, CyNH₂ could be obtained through the hydrogenation of cyclohexylimine. The formed CyNH₂ would react with cyclohexanone to produce *N*-cyclohexylcyclohexylimine (Cy-N-cy), which was further hydrogenated to form Dicy. Meanwhile, cyclohexanol (Cyol) was produced with the direct hydrogenation of cyclohexanone. It also lowered the selectivity of CyNH₂. Besides, the aldol condensation of cyclohexanone was preceeded on the acid sites of Cu-Cr-La/ γ -Al₂O₃ and Cy-cyol might be generated. Therefore, the selectivity of CyNH₂ would be further decreased. More-

Table 1. Reductive amination of cyclohexanone with ammonia over various catalysts

Catalyst	Conversion/%	Selectivity/%			
		Cyol	Cy-cyol	Dicy	CyNH ₂
Ni/ γ -Al ₂ O ₃	82.7	28.65	2.56	29.86	38.93
Co/ γ -Al ₂ O ₃	89.6	31.56	2.37	30.46	35.61
Cu/ γ -Al ₂ O ₃	85.4	29.43	2.49	27.19	40.89
Cu-Cr/ γ -Al ₂ O ₃	94.1	29.48	2.31	24.68	43.53
Cu-Cr-La/ γ -Al ₂ O ₃	99.0	29.76	2.25	21.73	46.26
Cu-Cr-Fe/ γ -Al ₂ O ₃	89.7	28.21	2.69	25.89	43.21
Cu-Cr-Mn/ γ -Al ₂ O ₃	99.2	26.85	2.28	26.12	44.75
Cu-Cr-Zn/ γ -Al ₂ O ₃	99.7	28.52	2.29	26.33	42.86

Reaction conditions: 180 °C, 3.0 MPa H₂, Charging rate: 0.2 ml/min of the premix, solvent: methanol.

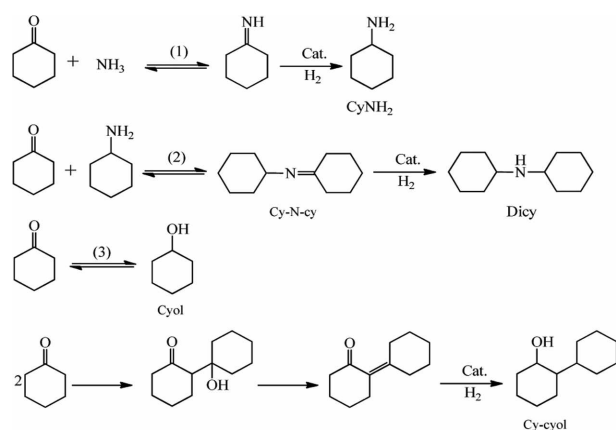


Figure 1. Possible reaction route of amination of cyclohexanone with ammonia.

over, two other byproducts, aniline and N-cyclohexylaniline, reported by Becker *et al.* (2000) were not detected in our study. This was probably due to different catalysts and reaction conditions in our work.

Influences of Reaction Parameters in the Premixing Process

As indicated in Fig. 1, the reaction of cyclohexanone and ammonia to form cyclohexylimine was crucial to enhance the selectivity of CyNH₂. As this reaction was reversible, the increase of cyclohexanone would undoubtedly improve the formation of cyclohexylimine. However, the excess cyclohexanone would also suffer from amination with the obtained CyNH₂ direct hydrogenation or aldol condensation. The corresponding by-products were followed as well. So it was important to convert cyclohexanone into cyclohexylimine for the improvement of CyNH₂ selectivity and a premixing process prior to this reaction in the fixed-bed reactor was investigated.

Solvent: Since the aforementioned reaction is reversible, the addition of ammonia would certainly prompt this reaction to shift right. The proper solvent with satisfied ammonia solubility was required. Therefore, three solvents including cyclohexanone, dioxane and methanol were employed for this reaction and the results were summarized in Table 2.

As shown in Table 1, when this reaction was carried out

in cyclohexanone, only 1.46% of CyNH₂ selectivity was obtained. Obviously, the poor ammonia solubility in cyclohexanone inhibited the formation of CyNH₂ and excess cyclohexanone would be directly hydrogenated into Cycl. It was the reason why the poor CyNH₂ selectivity was obtained with cyclohexanone.

When dioxane and methanol were employed, the selectivity of CyNH₂ were 28.21% and 46.26%, respectively. The conversion of cyclohexanone basically kept consistent. Meanwhile, methanol also resulted into 21.73% of Dicy selectivity, which was lower compared with dioxane. We speculated that the excellent ammonia solubility in methanol always contributed to the conversion of cyclohexanone into CyNH₂. Thus, methanol was selected as the solvent for amination of cyclohexanone with ammonia.

Molecular sieves: It was well known that the reaction of cyclohexanone with ammonia to produce cyclohexylimine was followed by the formation of H₂O. So the removal of H₂O would be in favor of right shift of this equilibrium.

During the synthesis of Schiff base, the generated water is normally removed by azeotropic distillation or vacuum distillation. However, both ammonia and cyclohexanone would be removed as well by these two methods. Therefore, commercially available 4Å molecular sieves were picked out for this dehydration. The obtained results were summarized in Table 3.

With the increase of molecular sieves amount, the quantity of Cycl and Dicy presented an obvious decrease. However, the selectivity of CyNH₂ dramatically increased. The reason might be attributed to the right shift of this equilibrium for the removal of H₂O. When 4Å molecular sieves came up to 30 wt % of cyclohexanone, the selectivity of CyNH₂ reached a high level, and continuously increasing 4Å molecular sieves did not have obvious impact on this reaction. Thus, 30 wt % of molecular sieves (based on cyclohexanone) were used in the premixing process.

Influences of Reaction Conditions in the Fixed-bed Reactor

Reaction temperature: Fig. 2 clearly indicated that

Table 2. Influence of solvent on amination of cyclohexanone with ammonia

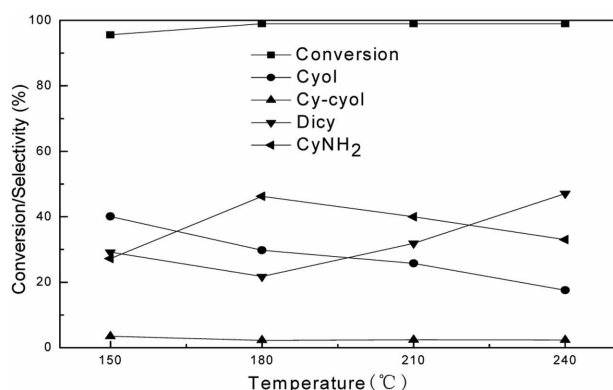
Solvent	Conversion/%	Selectivity/%			
		Cycl	Cy-cycl	Dicy	CyNH ₂
Cyclohexanone	99.2	90.48	2.82	5.24	1.46
Dioxane	98.6	27.05	2.53	42.21	28.21
Methanol	99.0	29.76	2.25	21.73	46.26

Reaction conditions: 180 °C, 3.0 MPa H₂, Charging rate: 0.2 ml/min of the premix.

Table 3. Influence of molecular sieves on amination of cyclohexanone with ammonia

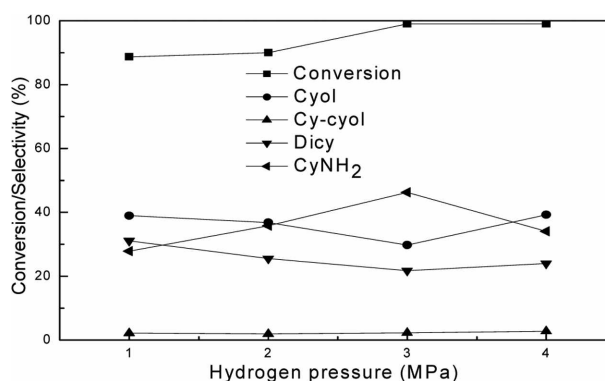
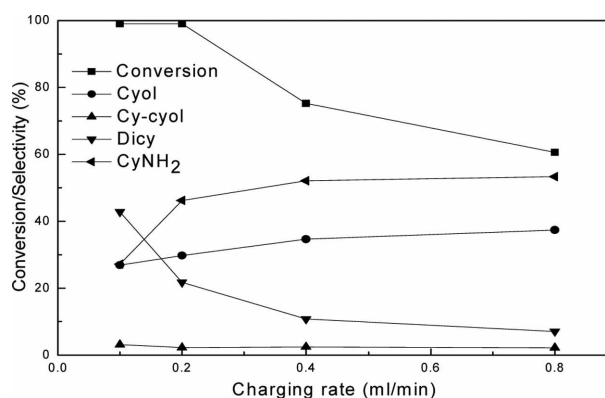
Molecular sieves/wt%	Conversion/%	Selectivity/%			
		Cyol	Cy-cyol	Dicy	CyNH ₂
0	99.0	30.70	2.25	16.37	50.68
15	99.0	19.83	2.45	12.23	65.49
30	99.0	12.71	2.03	6.60	78.66
45	99.0	13.23	2.24	6.39	78.14

Reaction conditions: 180 °C, 3.0 MPa H₂, Charging rate: 0.2 ml/min of the premix, ammonia in the fixed-bed reactor: 8 L/h.

**Figure 2.** Influence of temperature on amination of cyclohexanone with ammonia.

with the increase of reaction temperature, the conversion of cyclohexanone basically kept unchanged. However, the selectivity of CyNH₂ went up at first, and then lowered down after 180 °C, which were exactly opposite to the selectivity of Dicy. So it could be concluded that the enhanced temperature might facilitated the reaction between CyNH₂ and cyclohexanone. This results were in accordance with the report by Becker *et al.* Thus, 180 °C was selected as the optimum reaction temperature.

Hydrogen pressure: As shown in Fig. 3, the hydrogen pressure played a noticeable role on the reaction. With the enhancement of hydrogen pressure, the conversion of cyclohexanone rose from 88.7% to 99.0%. In contrast to Cyol and Dicy, the selectivity of CyNH₂ increased firstly with a peak at 3.0 MPa and then decreased. We speculated that the high hydrogen pressure might be in favor of reaction (1) compared with reaction (2) and (3). The majority of cyclohexanone was consumed in reaction (1) to yield CyNH₂. Correspondingly, the selectivity of Cyol and Dicy both decreased. But when hydrogen pressure increased to 4.0 MPa, parts of cyclohexanone would be directly hydrogenated into Cyol. In addition, Cy-N-cy obtained from cyclohexanone and CyNH₂ was similarly converted into Dicy. Therefore, the selectivity of CyNH₂ would be decreased. On the basis of the analysis above, 3.0 MPa was selected as the optimum hydrogen pressure.

**Figure 3.** Influence of hydrogen pressure on amination of cyclohexanone with ammonia.**Figure 4.** Influence of charging rate of the premix on amination of cyclohexanone with ammonia.

Charging rate of the premix: Subsequently, the different charging rate of the premix was used to enhance the conversion of cyclohexanone and the selectivity of CyNH₂. It was found that when the charging rate rose from 0.1 ml/min to 0.8 ml/min, the conversion of cyclohexanone decreased from 99.0% to 60.6%. The increase of weight hourly space velocity (WHSV) of cyclohexanone shortened the residence time, so that the obtained CyNH₂ did not have enough time to be consumed to produce Dicy and the selectivity of CyNH₂ would be increased. Considering the conversion of cyclohexanone and the selectivity of CyNH₂, 0.2 ml/min was chosen as the optimum charging rate of the premix.

Table 4. Influence of ammonia in the fixed-bed reactor on amination of cyclohexanone with ammonia

Speed/L · h ⁻¹	Conversion/%	Selectivity/%			
		Cyol	Cy-cyol	Dicy	CyNH ₂
0	99.0	29.76	2.25	21.73	46.26
8	99.0	12.71	2.03	6.60	78.66
10	99.0	9.17	1.92	5.01	83.90

Reaction conditions: 180 °C, 3.0 MPa H₂, Charging rate: 0.2 ml/min of the premix.

Ammonia in the Fixed-bed Reactor

It was obvious from Table 2 that although NH₃ was added to the solution of cyclohexanone in methol as much as possible, quite high proportion of Cyol and Dicy remained in the product. It implied that more ammonia was required in the fixed-bed reactor. The obtained results were summarized in Table 4.

With the addition of ammonia in the fixed-bed reactor, the selectivity of CyNH₂ increased. In contrast, the selectivity of Cyol and Dicy both decreased. The reason had been illustrated in our previous analysis. However, further increase of ammonia would give rise to the difficulty for operation, so ammonia was pumped into the fixed-bed reactor at a speed of 10 L/h.

CONCLUSIONS

The premixing process had an important effect on the reductive amination of cyclohexanone with ammonia over Cu-Cr-La/ γ -Al₂O₃ catalyst. The application of methanol could efficiently dissolve NH₃ and the addition of 4A molecular sieves could tremendously facilitated the formation of cyclohexylimine though removal of H₂O, which would improve the conversion of cyclohexanone and the selectivity of cyclohexylamine. Beside, the addition of ammonia in the fixed-bed reactor also contributed to the formation of cyclohexylamine. Meanwhile, reaction conditions including reaction temperature, hydrogen pressure and charging rate of the premix, were investigated. Under optimum conditions, the conversion of cyclohexanone was 99.0% and the selectivity of CyNH₂ reached 83.90%.

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