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ORIGINAL PAPER

Amination of aliphatic alcohols catalyzed by CuO–NiO/γ–Al_2O_3

Jia-min Huang · Chao Qian · Lie Feng ·
Yun-bin Chen · Xin-zhi Chen

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Abstract The amination of aliphatic alcohols in the gas–solid phase was investigated in a fixed-bed reactor in the presence of CuO–NiO/γ–Al_2O_3 as the catalyst. This catalytic system was successfully applied for both the N-methylation of aliphatic amines and N-alkylation of piperidine with primary or secondary alcohols. N-Alkylation of piperidine with low-carbon alcohols resulted in high conversions and selectivities, and the conversion of piperidine and the selectivities toward the desired products declined gradually with the increase of the carbon number of aliphatic alcohols. The influence of varied conditions on the N-cyclohexylation of piperidine was also evaluated, including liquid hourly space velocity (LHSV), temperature and the catalyst; especially the catalyst had the greatest impact. Finally, the test of the catalyst's stability was performed.

Keywords Fix-bed reactor · Piperidine · N-Alkylation · Catalyst

Introduction

The development of general and efficient methods for the synthesis of amines is of fundamental importance in synthetic organic chemistry [1], because a large number of amines have been utilized as synthetic intermediates for pharmaceuticals, agricultural chemicals and bioactive compounds [2]. With the applications widening, the reactions of amines are still an active area of research.

The alkylation with aryl/alkyl halides is a well-known procedure, and an article about this procedure has reported a chemoselective protocol for the mono-N-alkylation of primary amines [3]. However, the procedure is limited because of the use of the toxic aryl/alkyl halides and the generation of undesired waste salts [4]. With the rise of green chemistry, the atom efficiency of the process has become particularly important [5]. There are only a few methods for the synthesis of amines that take into account the atom efficiency factor. One of them is the hydroamination of olefins and alkynes [6, 7], although the procedure cannot generate the products of the methylation, benzylation, etc., and the regioselectivity of the addition is also a difficult problem. Another attractive protocol is the catalytic amination of alcohols, the so-called "hydrogen autotransfer process," in which the by-product is only water, and alcohols are friendlier to the environment than the corresponding halides [8, 9].

The catalytic systems for the amination of alcohols can be divided into heterogeneous and homogeneous catalysts [10]. Many homogeneous transition metal catalysts, especially ruthenium complexes [11] and iridium complexes [12], have been extensively used in the catalytic amination of alcohols. However, the disadvantages of these systems lie in their non-recoverability and high cost. Compared with the reactions catalyzed by the homogeneous catalysts, the catalytic amination of alcohols with the heterogeneous one allows the separation of catalysts and products easily [13, 14]. There are many different heterogeneous catalysts that have been reported, such as silicon and aluminum

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J. Huang · C. Qian · X. Chen (✉)
State Key Laboratory of Chemical Engineering,
Zhejiang University, Hangzhou,
People's Republic of China
e-mail: chemtec@163.com

J. Huang
e-mail: gavinhjm@163.com

L. Feng · Y. Chen
Zhejiang Jianye Chemical Co., Ltd, Hangzhou,
People's Republic of China

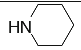
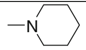
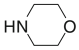
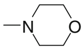
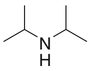
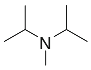
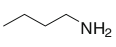
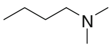
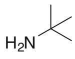
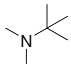
oxides [15–17], nickel catalysts [18–20], copper catalysts [21–23] and platinum catalysts [24]. The catalytic activity of silicon and aluminum oxides is low and requires a high reaction temperature. Although nickel catalysts have high catalytic activity, the catalytic selectivity is not good. Due to the short lifetime of the copper catalysts and the high cost of the platinum catalysts, their applications are limited. Until now, there have been no reports on the CuO-NiO/γ-Al_2O_3 catalyst for the N-methylation of aliphatic amines and N-alkylation of piperidine with different alcohols, which has the advantages of good selectivity, high activity, a long lifetime and low cost.

In this article, we show that the CuO-NiO/γ-Al_2O_3 catalyst, prepared by the impregnation method, can act as an efficient heterogeneous catalyst for the N-methylation of aliphatic amines and N-alkylation of piperidine with different kinds of alcohols as alkylating agents in a fixed-bed reactor. Furthermore, the influence of varied conditions, especially the catalyst, on the N-alkylation of piperidine was also studied.

Results and discussion

Initially, methanol was treated as a substrate to give different amines in the presence of CuO-NiO/γ-Al_2O_3 as the catalyst. The reactions were carried out at a 3:1 mol ratio of methanol to amine, 0.18 h^{-1} liquid hourly space velocity (LHSV), 150 °C temperature and 1.0 MPa. Results are summarized in Table 1. Piperidine and morpholine reacted with an excess of methanol to give methylated amines with high conversions and selectivities (entries 1, 2). Diisopropylamine gave a poor conversion, probably because of the steric effect of the diisopropylamine molecule (entry 3). The reaction using butylamine had a good conversion, but the selectivity of the product was unsatisfactory. This might be the self-disproportionation of butylamine (entry 4). *Tert*-butylamine was also successfully applied under the same conditions (entry 5).

Table 1 Amination of methanol with different amines

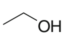
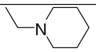
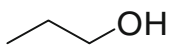
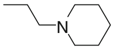
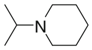
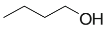
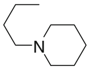
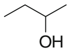
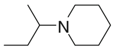
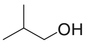
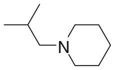
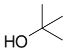
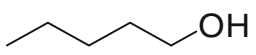
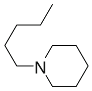
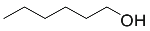
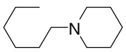
Entry	Amine	Product	Conversion/%[a]	Selectivity/%
1			>99	>99
2			96	92
3			81	90
4			97	83
5			99	98

Reaction conditions: Cu content of the catalyst 17.2 wt%; Ni content of the catalyst 4.5 wt%; mole ratio of methanol/amine = 3:1, $T = 150$ °C, LHSV = 0.18 h^{-1}

$P = 1.0$ MPa

[a] Conversion of amines

Table 2 N-alkylation of piperidine with different alcohols

Entry	Alcohol	Product	Conversion/%[a]	Selectivity/%
1			99	99
2			99	99
3			92	94
4			95	96
5			87	90
6			89	90
7		--------	----	----
8			88	84
9			84	81

Reaction conditions: Cu content of the catalyst 17.2 wt%; Ni content of the catalyst 4.5 wt%; mole ratio of methanol/amine = 3:1, $T = 150$ °C, LHSV = 0.18 h^{-1}

$P = 1.0$ MPa

[a] Conversion of piperidine

Results of N-alkylation of piperidine with different aliphatic alcohols are listed in Table 2. In general, the good conversion of piperidine and high selectivities of products were obtained, except for the reaction using *tert*-butyl alcohol (entry 7). It is demonstrated in Table 2 that the conversion of piperidine and the selectivities of the desired products declined gradually with the increase of the carbon number of aliphatic alcohols (entries 1, 2, 4, 8, 9). Nevertheless, applications of ethanol and 1-propanol afforded ideal results (entries 1, 2). When the reactions of piperidine with secondary alcohols were carried out under the same conditions, the results were slightly worse than those of the reactions using primary alcohols, but the conversions and selectivities were also considerably high (entries 2–5). This indicates that both primary and secondary alcohols are good alkylating reagents. Besides the kind of alcohol, the molecular volume of the alcohol also influences the result, for example, the result of N-alkylation of piperidine with isobutanol was worse than that obtained using N-butyl alcohol (entries 4, 6).

To determine how the varied reaction conditions and the catalyst influence the N-alkylation of piperidine, several related experiments were done in the model reaction between piperidine and cyclohexanol, and the results are summarized in Table 3. The conversion and product selectivity are strongly affected by the LHSV, because it determines the contact time with the catalyst. Low LHSV prolongs the contact time, promoting the piperidine conversion, but lowering the product selectivity. On the contrary, at high LHSV, the short contact time led to the reduction of the piperidine conversion, but the desired product selectivity slightly increased (entries 1–3). In addition, the reaction temperature is also an important factor. Low temperature lowered the piperidine conversion, but the selectivity toward the formation of the desired product was enhanced. On the other hand, raising the temperature gave a sufficient conversion but a low selectivity instead (entries 1, 4, 5). Moreover, the influence of the catalyst was also explored. When the supported metal content was reduced, decreases in both conversion and selectivity were recorded (entry 6). The worse result was obtained for the non-calcined carrier Al_2O_3 before the preparation (entry 7). Raising the Ni content of the catalyst led to an increase in conversion up to 88 %, but the selectivity decreased (entry 8).

The test of the catalyst's stability was also performed in the model reaction between piperidine and cyclohexanol over a period of 300 h through product analysis at irregular time intervals, and the results are summarized in Fig. 1. Only trivial turbulence could be found in the result so as to conclude the constant stability of the catalyst.

Table 3 The influence of varied conditions on the N-cyclohexylation of piperidine

Entry	Cu content/%	Ni content/%	LHSV/ h^{-1}	Conversion/ %^{e}	Selectivity/ %
1^a	17.2	4.5	0.18	78	87
2^a	17.2	4.5	0.3	72	89
3^a	17.2	4.5	0.12	81	82
4^b	17.2	4.5	0.18	65	88
5^c	17.2	4.5	0.18	83	75
6^a	11.5	3.0	0.18	56	72
7^{a,d}	17.2	4.5	0.18	26	54
8^e	17.2	9.0	0.18	88	62

The reactions were carried out at a 3:1 mol ratio of cyclohexanol to piperidine, and the product was *N*-cyclohexylpiperidine

$P = 1.0$ MPa

[a] $T = 150$ °C

[b] $T = 120$ °C

[c] $T = 180$ °C

[d] The carrier Al_2O_3 of the catalyst was not calcined before the impregnation

[e] Conversion of piperidine

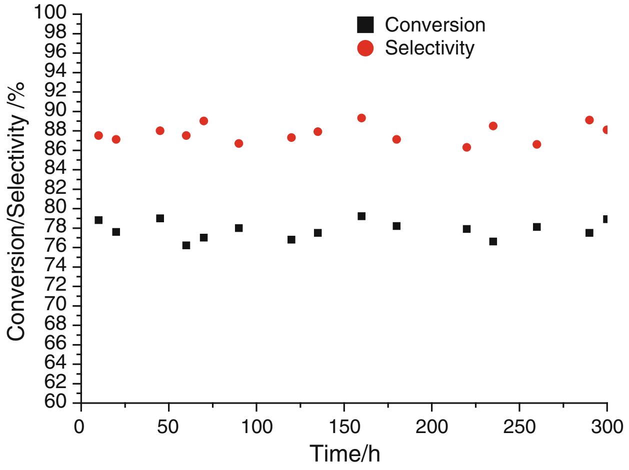


Fig. 1 The test of the catalyst's stability. Reaction conditions: 3:1 mol ratio of cyclohexanol to piperidine; $P = 1.0$ MPa; $T = 150$ °C; LHSV = 0.18 h^{-1}; Cu content of the catalyst 17.2 wt%; Ni content of the catalyst 4.5 wt%

Experimental

Catalyst preparation

The CuO-NiO/γ-Al_2O_3 catalyst was prepared using the impregnation method at a fixed Cu/Ni ratio. A solution of copper nitrate and nickel nitrate was prepared to obtain a Cu and Ni concentration of 14.5 and 3.8 wt%, respectively. The carrier γ-Al_2O_3 with particle radius 2–3 mm was calcined for 4 h at 400 °C and for 5 h at 800 °C in a muffle furnace to get $S_{BET} = 200-230\ m^2g^{-1}$. Then, the calcined γ-Al_2O_3 was impregnated with the above-mentioned solution for 36 h, filtrated and dried at 60 °C for 2 h, and the filtrate was collected at the same time. The filtrated catalyst was calcined at 350 °C for 6 h in a muffle furnace and then cooled. The cooled catalyst was repeated as in the above-described concrete steps including impregnation, filtration, evaporation, calcination and cooling until the filtrate was absorbed entirely.

Catalyst characterization

The XRD analysis of CuO-NiO/γ-Al_2O_3 catalyst after catalyst preparation is shown in Fig. 2. The crystallite diameters of the copper oxide and nickel oxide were estimated by the Scherrer formula, and both diameters were 5–6 nm.

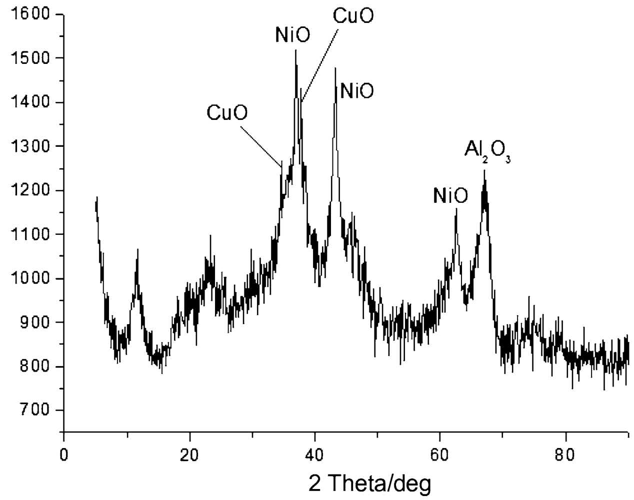


Fig. 2 XRD patterns of CuO-NiO/γ-Al_2O_3 catalyst

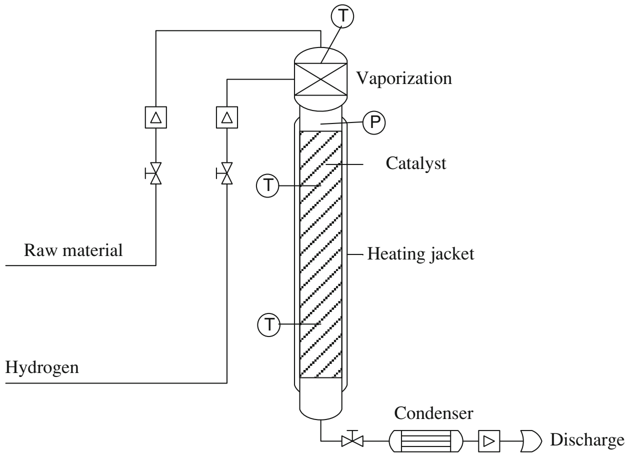


Fig. 3 The fixed-bed reactor

Reaction procedure

The reaction was performed in a stainless-steel reactor tube filled with catalyst and surrounded by a jacket filled with molten salt bath to control the temperature of the fixed bed. Total height of the reactor was 60 cm, and the effective length was 40 cm. Ceramic rings were placed on the top and at the bottom. The effective radius of the reactor was 15 mm. The figure of the fixed-bed reactor is shown in Fig. 3.

The reaction product analysis was done by GC and GC–MS. An external standard method was employed to determine the conversion and selectivity, and the concrete steps were as follows:

1. On the basis of the analyte's probable concentration, standard samples prepared at seven different concentrations were analyzed by GC at the same injection volume.
2. A scatter plot was made with a regression line, of which the abscissa and ordinate were the concentration of standard sample and the peak area, respectively.
3. Finally, the reaction mixture was analyzed by GC at the same injection volume as the standard samples, then based on the peak area, the expected product's concentration was obtained.

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