

A Novel Non-phosgene Approach to the Synthesis of Methyl N-phenyl Carbamate by a Reaction of Methanol with Phenylurea

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Abstract—A novel non-phosgene process for the synthesis of methyl N-phenyl carbamate (MPC) by a reaction of phenylurea with methanol was studied. The reaction between phenylurea and methanol was found to be a spontaneous reaction that took place in the absence of catalyst and gave MPC as the main product. Addition of a catalyst markedly influenced the reaction behavior. A basic catalyst greatly enhanced the yield of MPC, whereas an acidic catalyst promoted the formation of aniline and methyl carbamate. Moderate strength of basicity showed the best catalytic performance in the cases studied. The mechanism of reaction and catalyst functioning was discussed.

Key words: Phenylurea, Methyl N-phenyl Carbamate, Acid-base Catalyst, Non-phosgene

INTRODUCTION

Isocyanate compounds as important raw materials in organic chemistry have been produced commercially by reaction between amines and toxic reagent phosgene; however, this causes serious environmental problems. Clearly, the replacement of this process by an environmentally benign process is of great significance; thus the production of isocyanate via carbamate decomposition has received extensive attention [Smith, 1995; Katada, 2002]. Several methods have been reported for preparing phenyl carbamates without using phosgene, including one-step routes such as reductive carbonylation of nitro aromatics [Ikariya, 1989; Lee, 1990; Yang, 1999; Paul, 2000], oxidative carbonylation of amines [Wan, 1999; Kim, 1999], and methoxycarbonylation of aniline with dimethyl carbonate (DMC) [Fu, 1994; Baba, 2002; Arthur, 1981; Floro, 1985] and two step route which involves synthesis of N,N'-diphenylurea from nitrobenzene, aniline and carbon monoxide followed by alcoholysis of diphenylurea to give MPC and equimolar of aniline [Giannoccaro, 1988; Oh, 1991]. Some of these methods, however, have some limitations. For example, the carbonylation reactions should be carried out under high pressures in the presence of noble metal such as Pt, Pd, Ru and Rh catalysts [Chen, 2003; Ikariya, 1989; Paul, 2000]; the methoxycarbonylation of aniline gives high selectivity to MPC under mild conditions in the presence of Pb-based catalysts, which seems promising, but it involves a difficult process of separation of methanol from DMC azeotrope, and DMC is relatively expensive. Phenylurea as an asymmetric urea that can be prepared by a non-catalytic reaction between urea and aniline hydrochloride (Davis) is a compound that is inexpensive and readily available for the synthesis of methyl N-phenyl carbamate (MPC). But a relevant study has not been found in the literature. As a part of our ongoing studies on exploration of a novel non-phosgene process for the synthesis of MPC from methanol, aniline hydrochloride and urea via phenyl-

urea intermediate, we here report for the first time the reaction behavior of phenylurea with methanol in the presence of a catalyst to synthesize MPC.

EXPERIMENTAL

The reaction was performed in a 100ml autoclave. In a typical experiment, 6.81 g (0.05 mol) of phenylurea (C.P., Beijing Chemical Plant), 12.02 g (0.375 mol) of methanol (AR, Shanghai Zhenxing Chemical Plant), 0.3 gram of the catalyst and 36 ml of toluene (AR) as a solvent were charged into the reactor. The catalyst used was commercially available reagent as-obtained without further treatment. After purging with argon for a few minutes, the reactor was sealed and then ramped at the rate of 7 K/min to 433 K under vigorous stirring. After reaction at 433 K under vigorous stirring for 4.5 hrs, the reactor was cooled quickly to 333 K and depressurized. A known amount of biphenyl as an internal standard was added into the reaction mixture. The products were identified by using GC-MAS. A quantitative analysis of the products was conducted over a Shangfen GC122 gas chromatograph equipped with a flame ionization detector (FID) and an OV-1701 capillary column (50 m × 0.32 mm). The yield of MPC is expressed based on the phenylurea.

RESULTS AND DISCUSSION

From the reaction results presented in Table 1 it is found that the reaction of phenylurea with methanol was a spontaneous reaction that took place in the absence of catalyst giving MPC as the main product, and the MPC decomposition product of phenyl isocyanate was also formed. The reaction behavior was significantly affected by the incorporation of catalyst and its acid-base properties. It was found that MPC yield was increased obviously by using a basic compound such as MgO, ZnO or ZrO₂ as catalyst, whereas the yield of MPC was decreased markedly by using an acidic compound such as ZnCl₂, CuCl₂ or Pb(NO₃)₂ as catalyst.

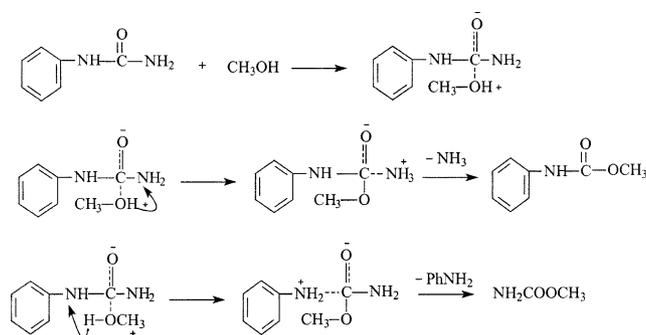
As a derivative of carbonic acid, the reaction of phenylurea with

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Table 1. Reaction results of methanol with phenylurea over different catalysts

Catalyst	Phenylurea conv. (%)	Selectivity (mol%)		
		MPC	Aniline	PhNCO
Non-catalytic	82.1	64.4	34.1	1.5
CuCl ₂	84.6	51.7	47.8	0.5
ZnCl ₂	76.5	41.6	56.7	1.6
Pb(NO ₃) ₂	84.5	58.3	40.8	0.9
MgO	86.3	73.3	21.4	5.2
ZrO ₂	80.1	80.4	14.7	4.9
ZnO	88.6	71.4	27.3	1.2
NaOCH ₃	77.1	71.7	22.9	5.3
Na ₂ CO ₃	81.1	79.9	17.8	2.3
KOH	83.5	68.6	30.1	1.3

**Fig. 1. Proposed reaction scheme of methanol with phenylurea.**

methanol should be a nucleophilic substitution, which may proceed via an addition-elimination mechanism [Solomons Graham, 1983]. The reaction begins with a nucleophilic attack of methanol on the carbonyl carbon of phenylurea to give a tetrahedral intermediate, followed by the proton transfer from OH group to one of the two adjacent nitrogens and ejecting a leaving group, as illustrated in Fig. 1. Hence the conversion of phenylurea depends on not only the rate of addition reaction, but also the leaving easiness of the leaving group. The product selectivity is dependent upon the leaving tendency of the two groups attached to carbonyl carbon. If -NH_2 is the leaving group, MPC and ammonia are formed. On the contrary, if PhNH- is the leaving group, aniline and methyl carbamate are formed. The leaving tendency of the group attached to carbonyl carbon is determined by its basicity [Solomons Graham, 1983]. In the tetrahedral intermediate formed, the direction of proton transfer is dependent upon the charge (electron density) of the adjacent nitrogen atom, which, in turn, influences the basicity of the group attached.

In order to get an in-depth understanding of the direction of proton transfer during the reaction, the charge of each atom in phenylurea molecule was studied by quantum chemical calculation using density functional theory/Hartree-Fock hybrid method B3LYP. It is found from calculation that the natural bond orbital charge of nitrogen in -NH_2 is -0.8402 and in PhNH- -0.6504 . Therefore, the proton is preferably transferred to -NH_2 to form NH_3^+ which is a weaker base and a better leaving group compared to the PhNH- group. After losing NH_3 , MPC is formed as the product. This is the case of reaction in the absence of catalyst. In the catalytic reactions, the cata-

lyst may interact with the reactants and influence their electron density. In the presence of acidic catalyst, such as ZnCl_2 or $\text{Pb(NO}_3)_2$, the catalyst may preferentially interact with the terminal NH_2 that has the highest electron density in phenylurea molecule to form a kind of complex. As a result, the electron density of NH_2 is decreased after interaction with the catalyst and hence the driving force for the proton transfer to -NH_2 is decreased. If the proton is transferred to PhNH- , it becomes a better leaving group; aniline and methyl carbamate are formed. Resultantly, MPC selectivity is decreased. In the presence of a base catalyst such as MgO or ZnO , the catalyst may preferentially activate the methanol that is an acidic compound, increase its nucleophilicity and facilitate the proton transfer to -NH_2 . As a consequence, MPC selectivity was increased. ZrO_2 is frequently classified into the amphoteric oxide, but some researchers in heterogeneous catalysis consider it as weakly basic oxide based on the adsorption behavior of acid compound. It is reported that zirconia strongly adsorbs the benzoate anion and is therefore classified into the weakly basic material [Niwa, 1991]. Other important information in Table 1 is that MPC yield over strong base like KOH and NaOCH_3 is not as high as that over mild base like Na_2CO_3 or ZnO , which means that high strength of basicity is unfavorable to the reaction. The possible reason might be that the strong base may react with acidic methanol to form CH_3O^- which has the higher electron density and nucleophilicity but geometrically is not favorable for the proton transfer, and hence the phenylurea conversion and MPC selectivity were not as high as that for moderate-strength base. Further investigations are needed to correlate the strength of basicity of a catalyst with its reaction behavior and the detailed functioning mechanism.

CONCLUSIONS

A novel non-phosgene approach to the synthesis of MPC by a catalytic reaction between phenylurea and methanol was studied for the first time. The reaction results showed that reaction between phenylurea and methanol was a spontaneous reaction taking place in the absence of catalyst and giving MPC as the main product. Addition of a catalyst markedly influenced the reaction behavior. A basic catalyst greatly enhanced the yield of MPC, whereas an acidic catalyst promoted the formation of aniline and methyl carbamate. In terms of MPC yield, moderate strength of basicity showed the best catalytic performance in the cases studied. The present work provides a new route for the synthesis of MPC from methanol urea and aniline hydrochloride via phenylurea intermediate.

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