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A Novel Non-phosgene Process for the Synthesis of Methyl *N*-Phenyl Carbamate from Methanol and Phenylurea: Effect of Solvent and Catalyst

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A novel environmentally benign process for the synthesis of methyl *N*-phenyl carbamate (MPC) from methanol and phenylurea was studied. Effect of solvent and catalyst on the reaction behavior was investigated. The IR spectra of methanol and phenylurea dissolved in different solvents were also recorded. Compared with use of methanol as both a reactant and a solvent, phenylurea conversion and selectivity to MPC increased by using toluene, benzene or anisole as a solvent, while phenylurea conversion decreased slightly by using *n*-octane as a solvent. The phenylurea conversion declined nearly 50% when dimethyl sulfoxide (DMSO) was used as a reaction media, and MPC selectivity decreased as well. The catalytic reaction tests showed that a basic catalyst enhanced the selectivity to MPC while an acidic catalyst promoted the formation of methyl carbamate and aniline. Moderate degree of basicity showed the best catalytic performance in the cases studied.

Keywords methyl *N*-phenyl carbamate synthesis, phenylurea, phosgene-free, solvent effect, acid-base catalyst

Introduction

Isocyanate compound as an important raw material in organic and polymer chemistry has been produced commercially by a reaction between amine and phosgene, in which toxic reagent of phosgene was used and a stoichiometric amount of hydrogen chloride was co-produced as a by-product that causes serious corrosion. Replacement of this process by an environmentally benign phosgene-free process is of great significance. Methyl *N*-phenyl carbamate (MPC) is an important precursor for preparing isocyanates since it produces isocyanates and alcohols in good yields by thermal decomposition.[1] Several methods for preparing *N*-phenyl carbamates without using phosgene have been reported, including reductive carbonylation of nitro aromatics,[2] oxidative carbonylation of amines,[3] methoxycarbonylation of aniline with dimethyl carbonate (DMC),[4,5] and alcoholysis of diphenylurea.[6] Some of these methods, however, have some limitations. For example, the carbonylation reaction should be carried out under high pressures in the presence of noble metal such as Pt, Pd, Ru and Rh catalysts; 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. The synthesis of MPC by alcoholysis of diphenylurea will be accompanied by the formation of equimolar amount of aniline. The separation of MPC from aniline is quite difficult due to their very close boiling points. Phenylurea as an asymmetric urea that can be prepared in good yield by a non-catalytic reaction between urea and aniline hydrochloride[7] is a compound inexpensive and readily available for the synthesis of MPC compared with dialkyl carbonates. But the relevant study has not been found in the literature. Here we report the effect of solvent and catalyst on the reaction between phenylurea and methanol for the synthesis of MPC.

Experimental

The reaction between methanol and phenylurea was carried out in a 100 mL 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 (A.R., Shanghai Zhenxing Chemical Plant), 0.3 g of catalyst and 40 mL of solvent (A.R.) were charged into the reactor. The catalyst used was commercially available reagent with A.R. purity as-obtained without further treatment unless otherwise noted. The reactor was

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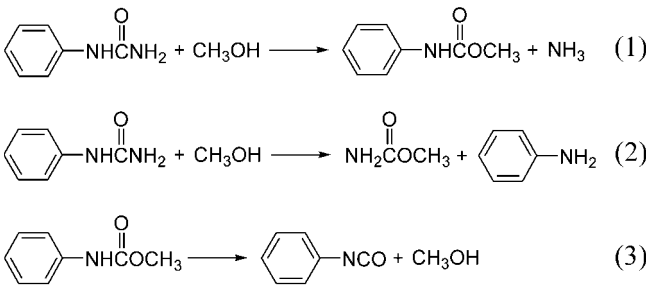
purged 5 times with argon at 0.6 MPa, and then heated at the rate of 7 K/min to 433 K under vigorous stirring. After reaction at 433 K for 4.5 h, the reactor was cooled quickly to 333 K and depressurized. A certain amount of biphenyl as an internal standard was added into the reaction mixture. The reaction mixture was analyzed by using GC-MS for qualification and by a temperature programmable gas chromatograph equipped with a flame ionization detector and an OV-1701 capillary column (50 m×0.32 mm) for quantification.

FTIR absorption spectra of the samples were measured by KBr disc method at room temperature on a Bruker Vector 22 FTIR spectrometer over the range of 4000—400 cm^{-1}. The phenylurea sample was prepared by mixing phenylurea with dry KBr fine powders and pressing the resultant mixture into a disc. The liquid samples were prepared by dropping the liquid onto a pretreated KBr disc to form a thin film.

Results and discussion

Effect of solvent

From the GC-MS data, it is found that methyl carbamate (MC), methyl *N*-phenyl carbamate (MPC), phenyl isocyanate (PIC) and aniline are all products detected in solvent in all cases studied. Based on the reaction products it is deduced that the reactions taking place in the system may include the followings:



The reaction results of methanol with phenylurea in different solvents in the absence of catalyst are listed in Table 1. The phenylurea conversion was 73.7% with MPC being the main product when methanol was used as both a reactant and a solvent. Meanwhile, MPC decomposition product of phenyl isocyanate (PIC) was also formed. When toluene, benzene or anisole was used as a solvent, the phenylurea conversion and MPC selectivity increased obviously. While phenylurea conversion and MPC selectivity decreased markedly when the reaction was carried out in dimethyl sulfoxide (DMSO). The phenylurea conversion decreased slightly when *n*-octane was used as a solvent. Moreover, for the reactions performed in a solvent other than methanol the selectivity to decomposition product of phenyl isocyanate was higher than that in methanol solvent.

In order to get an insight into the mechanism of reaction and of the solvent effect, FT-IR spectra of methanol, phenylurea, and phenylurea dissolved in methanol and in different solvents such as anisole, toluene, DMSO were recorded. Figure 1a shows the FT-IR spectra of methanol, phenylurea and phenylurea dissolved in methanol. In the FT-IR spectra of methanol a broad absorption band in 3100—3600 cm^{-1} region which was assigned to the associated O—H stretching vibrations, absorption bands at 2833 and 2946 cm^{-1} ascribable to C—H stretching mode as well as a band at 1031 cm^{-1} attributable to C—O stretching mode appeared. In the spectra of phenylurea, C=O stretching vibration band at 1657 cm^{-1}, N—H stretching vibration of terminal NH_2 at 3433, 3317 cm^{-1}, N—H stretching vibration of NH attached to benzene ring at 3215 cm^{-1}, and N—H bending vibration at 1615 cm^{-1}, the N—C=O symmetric stretching vibrations at 1556 cm^{-1} and the C=C, C—H in benzene ring at 1593 cm^{-1} and 3039 cm^{-1}, respectively were observed.[8] When phenylurea was dissolved in methanol, the absorption of C=O stretching mode was shifted to 1670 cm^{-1}, and half-width of the band was broadened. Meanwhile, absorptions of NH_2, NH, N—C=O modes were also shifted to lower wavenumbers, which means that there exist hydrogen bond and dipole-dipole interactions between methanol and phenylurea molecules. When phenylurea and methanol were dissolved into different solvents such as toluene, anisole and DMSO, the FT-IR spectra (Figure 1b) changed noticeably. When phenylurea and methanol were dissolved in toluene or anisole, the broad band in 3100—3600 cm^{-1} region ascribable to associative OH disappeared and two separate bands at 3427 and 3313 cm^{-1} attributable to N—H and free O—H vibrations appeared, indicating that the intermolecular hydrogen bond of methanol was absent. Meanwhile, the half width of C=O absorption was narrowed compared to that of phenylurea in methanol, quite similar to that of free phenylurea, indicating that the electrophilicity of phenylurea had little changed due to the solvation by toluene and anisole. When phenylurea and methanol were dissolved in a strongly polar solvent of DMSO, the half-width of the C=O absorption band was increased greatly and the band maximum downward shifted. Meanwhile, the intensity and wavenum-

Table 1 Effect of solvent on the reaction between methanol and phenylurea [a]

Solvent	Phenylurea conv./%	Selectivity [b]/mol%		
		MPC	Aniline	PIC
Methanol	73.7	65.1	34.3	0.6
DMSO	43.2	49.6	47.7	2.7
Benzene	83.7	76.1	21.8	2.1
Toluene	85.0	79.7	16.1	4.2
Anisole	78.1	66.4	31.1	2.5
n-Octane	70.2	72.2	25.2	2.6

[a] Reaction conditions: T=160 ℃, reaction time: 4.5 h, except using methanol as solvent, the molar ratio of methanol to phenylurea is 7.5. [b] MPC: methyl *N*-phenyl carbamate; PIC: phenyl isocyanate.

bers of NH_2, NH, N—C═O absorption were changed remarkably, indicating the strong interaction between the carbonyl group and the solvent. The broad band in 3100—3600 cm^{-1} still appeared, indicating existence of OH association in DMSO.

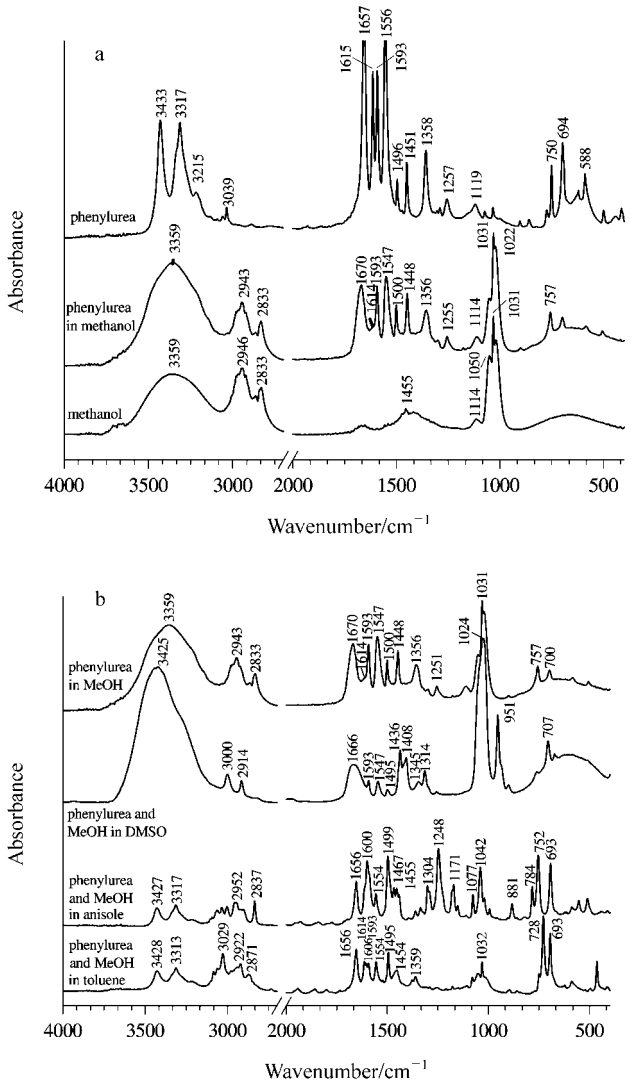


Figure 1 FT-IR spectra of the samples: (a) methanol , phenylurea and phenylurea dissolved in methanol; (b) methanol and phenylurea dissolved in different solvents.

Based on the reaction results and FT-IR spectra, solvent effect can be explained. Phenylurea is a derivative of carbonic acid. The reaction between phenylurea and methanol is a nucleophilic substitution, which may proceed via an addition-elimination mechanism as that for the reaction of carboxylic acid derivatives.[9] The initial step involves a nucleophilic attack of methanol on the carbonyl carbon of phenylurea, forming a tetrahedral intermediate, followed by the proton transfer from OH group to one of the nitrogens attached to the carbonyl carbon and ejecting a leaving group, as illustrated in Figure 2. 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.[9] In the formed tetrahedral intermediate, 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.

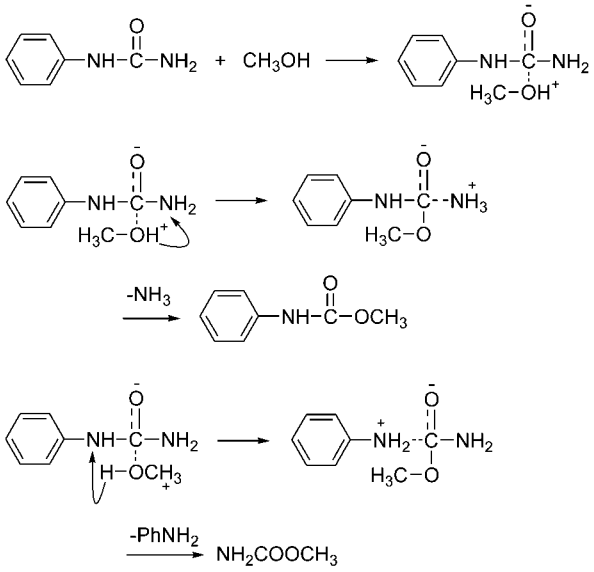


Figure 2 Proposed reaction scheme of methanol with phenylurea.

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 was 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. When the reaction was carried out in different solvents, due to the different solvation of methanol and phenylurea, their reactivities are different. When protic methanol was used as both a solvent and a reactant, the nucleophilic reactivity of methanol was reduced by the intermolecular hydrogen bond. When the reaction was carried out in toluene, benzene or anisole, the intermolecular hydrogen bond was absent as observed in IR spectra, and the interaction between methanol and the solvent was a weak electron pair donor/electron pair acceptor (EPD/EPA) one which makes methanol a more active nucleophile. Meanwhile, the electrophilic reactivity of carbonyl carbon was not influenced by the solvation of toluene, benzene or anisole. Consequently, an increase in phenylurea conversion was observed. When

the reaction was performed in a strongly polar solvent like DMSO, strong interactions between carbonyl group of phenylurea and solvent as observed in FT-IR spectra inhibited the interaction of phenylurea with methanol. Meanwhile, the association of methanol still existed as observed in FT-IR, which reduced its nucleophilicity, and the phenylurea conversion was decreased consequently. The declined selectivity to MPC in DMSO solvent may be related to the weak acidity (or protic character) of DMSO[10] which may interact with —NH_2 and decrease the electron density of —NH_2 and resultantly reduce the transferring possibility of proton to —NH_2. As for the non-polar *n*-octane, due to the poor miscibility of methanol with *n*-octane and relatively good solubility of phenylurea in octane, the interaction between solvent and solute was very weak. When *n*-octane was used as a reaction media, the phenylurea was partially dissolved in methanol and partially in *n*-octane. During reaction, methanol in *n*-octane might form small micelles under vigorous stirring, so the reaction was taking place within methanol droplets or at inter-phase between methanol and *n*-octane. Due to the concentration of phenylurea contacting with methanol decreased, the phenylurea conversion was decreased naturally.

Effect of catalyst

Table 2 lists the reaction results of methanol with phenylurea in the presence of a catalyst using toluene as a solvent. MPC selectivity was increased by using basic compound such as MgO, ZnO or ZrO_2 as a catalyst. Whereas the MPC selectivity was decreased by using acidic compound such as $ZnCl_2$ or $Pb(NO_3)_2$ as a catalyst. As discussed above, the product selectivity depends upon the leaving tendency of —NH_2 and PhNH— that is determined by their basicity and influenced by the direction of proton transfer in the formed tetrahedral intermediate. In the cases of non-catalytic reactions, proton is preferably transferred to —NH_2 to form —NH_3^+ and consequently NH_3 and MPC are given as the main products. In catalytic reactions, the catalyst may interact with the reactants and influences their electron density and reactivity. In the presence of an acidic catalyst, such as $ZnCl_2$ or $Pb(NO_3)_2$, 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, and aniline and methyl carbamate are formed. As a result, 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 is 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.[11] Another important information in Table 2 is that the phenylurea conversion and MPC selectivity using strongly basic catalyst like KOH and $NaOCH_3$ are not as high as those using a weak base like Na_2CO_3 or TiO_2, which means that moderate degree of base is favorable 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 is geometrically not favorable for the proton transfer, and hence the phenylurea conversion and MPC selectivity are not as high as those for moderate-strength base. The further research is under going to correlate the strength of basicity of a catalyst with its reaction behavior and to a detailed functioning mechanism.

Table 2 Reaction results of methanol with phenylurea using different catalysts[a]

Catalyst	Phenylurea Conv./%	Selectivity/mol%		
		MPC	Aniline	PIC
Non-catalytic	85.1	64.4	34.1	1.5
$CuCl_2 \cdot 2H_2O$	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
Cu_2O	74.0	61.1	37.1	1.7
ZnO	88.6	71.4	27.3	1.2
TiO_2 (anatase)	71.2	78.8	17.9	3.2
$NaOCH_3$	77.1	71.7	22.9	5.3
Na_2CO_3 (anhydrous)	81.1	79.9	17.8	2.3
KOH	83.5	68.6	30.1	1.3

[a] Toluene was used as a solvent, molar ratio of methanol to phenylurea: 5, reaction temperature: 160 ℃, amount of the catalyst charged: 0.3 g.

Summaries

A novel phosgene-free process for the synthesis of methyl *N*-phenyl carbamate (MPC) from methanol and phenylurea was studied. It was found that when toluene, benzene or anisole was used as a solvent, its solvation reduced the intermolecular associative hydrogen bond of methanol and made it more active as a nucleophile but had little influence on carbonyl carbon, hence the phenylurea conversion increased. When reaction took place in DMSO, the strong interactions between solvent and reactants reduced electrophilicity reactivity of carbonyl carbon and the nucleophilicity of methanol, as a result, a remarkable decrease in phenylurea conversion was observed. The catalytic reaction results indicated

that 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.

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