



# Selective *N,N*-dimethylation of primary aromatic amines with dimethyl carbonate in the presence of diphenylammonium triflate

Zhen Lu Shen, Xuan Zhen Jiang\*

Department of Chemistry, Zhejiang University, Hangzhou, Zhejiang 310027, China

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## Abstract

A facile synthesis of *N,N*-dimethylanilines (NNDMA) from primary aromatic amines and dimethyl carbonate (DMC) has been achieved for the first time in the presence of diphenylammonium triflate. *N,N*-Dimethylanilines were selectively obtained in high yields. All the reaction parameters, viz. reaction temperature, time, molar ratio of the reactants, and catalyst amount were examined in the reaction of aniline and dimethyl carbonate. The conversion of aniline and the selectivity to *N,N*-dimethylaniline were 99.9 and 99.6%, respectively, at 180 °C in 160 min.

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## 1. Introduction

The industrially important *N,N*-dimethyl aromatic amines, of which *N,N*-dimethylaniline (NNDMA) is the simplest form, are widely used as raw materials in organic syntheses and intermediates for the manufacture of dyes, pharmaceuticals, and agrochemicals [1,2]. The *N,N*-dimethylation of primary aromatic amines can be conducted with methyl halides or dimethyl sulfate, but the products are mixtures of secondary and tertiary aromatic amines [3,4]. Moreover, these methods require not only harmful reagents but also a stoichiometric amount of a strong base to neutralize acid by-products. The *N*-methylation of aniline with methanol in the presence of a strong acid catalyst [5] or a heterogeneous catalyst in gas-phase at high temperature has been extensively studied [6–11]. In most of these reactions, the conversions of aniline were low and the methylation of aniline gave toluidine, *N*-methylaniline (NMA), and *N,N*-dimethylaniline as major products.

Considering the environmental impact of methyl halides and dimethyl sulfate or the poor performance of methanol, dimethyl carbonate (DMC) has been used as a substitute for these reagents because of its low toxicity and high performance [12–15].

*N*-Methylation of primary aromatic amines with DMC has been previously studied using several different catalysts. Under gas–liquid phase-transfer (PT) conditions in a continuous-flow process, in the presence of  $K_2CO_3$  and polyethylene glycol (PEG) as a phase-transfer agents, the primary aromatic amines were selectively mono-*N*-methylated [16,17]. In that case, by-products, methyl *N*-methyl-*N*-aryl carbamates and methyl *N*-aryl carbamates were formed and the primary aromatic amines conversions were 45–90%. Over calcined Mg–Al hydrotalcites, 100% selectivity for mono-*N*- and *N,N*-dimethylation (NMA + NNDMA) in the vapor-phase reaction of aniline DMC was obtained [18]. Over  $AlPO_4$ -based catalysts, DMC was found to be a better methylation agent than methanol in *N*-methylation of aniline [19]. V- $AlPO_4$  showed 100% selectivity for mono-*N*-methylation of aniline though the conversion of aniline was low. Alkali-ion exchanged zeolite has been reported as effective catalyst in *N*-methylation of aniline in vapor-phase [20–22]. NMA and NNDMA were formed exclusively and the ratio of the two products depends on the reaction conditions and the used zeolites. Over NaX and KX, NNDMA was selectively obtained.

A batch synthesis of mono-*N*-methylanilines has been developed in the presence of  $K_2CO_3$  and PT agent (onium salts and crown ethers) [23]. In an autoclave, primary aromatic amines were mono-*N*-methylated by DMC in the presence of Y- or X-type zeolites [24,25]. But *N,N*-dimethylanilines, methyl *N*-aryl carbamates and methyl

\* Corresponding author. Tel.: +86-571-8795-1611; fax: +86-571-8795-1895.

E-mail address: [chejiang@public.zju.edu.cn](mailto:chejiang@public.zju.edu.cn) (X.Z. Jiang).



Scheme 1.

*N*-methyl-*N*-aryl carbamates were formed as by-products. In the reaction between aniline and DMC in liquid-phase over V–AlPO<sub>4</sub> or Co–AlPO<sub>4</sub>, biphenyl urea was obtained as one of the major products [26]. *N,N*-Dimethylation of primary aromatic amines by dimethyl carbonate under batch conditions is yet not extensively studied.

We report herein an effective process for highly selective *N,N*-dimethylation of primary aromatic amines with DMC (Scheme 1). The batch-wise reaction is carried out in an autoclave and in the presence of diphenylammonium triflate (DPAT), which is for the first time to be utilized in such reactions.

## 2. Experimental

### 2.1. Reagents

DMC (Shanghai Chemical Reagent Company) was fractionally distilled and stored in molecular sieve (4A). Aniline (Shanghai Chemical Reagent Company) was of laboratory reagent grade and subjected to purifying and drying by standard procedure. Tetrabutylammonium bromide (TBAB), tetrabutylammonium iodide (TBAI), 4-(dimethylamino)pyridine (DMAP, furnished by ACROS), K<sub>2</sub>CO<sub>3</sub>, *m*-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>, *p*-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>, *m*-OCH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>, *p*-OCH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>, *o*-OCH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>, *m*-ClC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>, *p*-ClC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>, and *o*-ClC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub> were of analytic grade and used as received.

DPAT was prepared in an improved method according to literature [27]: trifluoromethanesulfonic acid (15.0 g, 0.1 mol) was added to a stirred solution of diphenylamino (16.9 g, 0.1 mol) in toluene (100 ml) dropwise at room temperature. The mixture was stirred for 20 min and then filtered to obtain the crude product, which was washed with hexane (50 ml) for three times. The white crystals DPAT (31.6 g, 99% yield) was obtained after drying.

Tributylammonium triflate (TBAT) was prepared from tributyl amine and trifluoromethanesulfonic acid in a similar procedure as described above.

### 2.2. Analysis

The reaction was monitored by gas chromatography (HP-1102) equipped with a 30 m capillary column (OV-101). The injector and FID detector temperatures were 220 and 260 °C, respectively. The temperature of the program: started at 100 °C and ended at 230 °C, with a heating rate of 20 °C/min. The products obtained were purified before identified by <sup>1</sup>H NMR spectroscopy (Bruker AVANCE DMX500) and GC–MS (HP6890/5973). Thermogravimetry

was performed in a NETZSCH STA 409 PG/PC thermogravimetric analyzer.

### 2.3. Reaction procedure

The reaction was conducted in a stainless-steel autoclave (100 ml) equipped with a stirrer, a purging valve and a thermometer. A mixture of primary aromatic amine, DMC and catalyst were fed into the autoclave. Before reaction, air was replaced by purging with a stream of N<sub>2</sub>. Then the autoclave was heated to 120–200 °C. Once the reaction was completed, the reaction mixture was cooled down to room temperature and analyzed by GC. *N,N*-Dimethylanilines were isolated by distilling under reduced pressure. Then methanol and hexane was added to the residue. After separation, DPAT was recovered in the methanol layer and could be reused.

### 2.4. Typical example

Aniline (50 mmol), DMC (110 mmol), and DPAT (1.5 mmol) were loaded into the autoclave. This mixture was heated to 180 °C after air was replaced by N<sub>2</sub>, and the reaction was carried out under stirring for 160 min. After cooling down to room temperature, methanol as well as the excess of DMC was withdrawn from the reaction mixture with rotavapor. NNDMA was obtained by distillation under reduced pressure (76–78 °C, 10 mmHg). Then 20 ml methanol and 60 ml hexane were added to the residue. After separating the methanol layer from the hexane, DPAT in the methanol layer could be recovered.

## 3. Results and discussion

In order to understand the influence of different factors on the reactions, detailed studies have been performed using aniline as a substrate.

### 3.1. Effect of catalysts

The reaction of aniline with DMC was carried out at 180 °C for 160 min in the presence of various catalysts. The results are given in Table 1. In the absence of catalyst, the conversion of aniline was 20.3%, and the selectivity to NNDMA was 23.3% only. The other products were NMA, methyl *N*-phenyl carbamate (MNPC) and methyl *N*-phenyl-*N*-methyl carbamate (MNPNC). Both MNPC and MNPNC were produced by *N*-methoxycarbonylation of aniline with DMC.

The conversion of aniline and the selectivity to NNDMA was remarkably improved in the presence of catalysts. The catalysts promoted the *N*-methylation and suppressed the *N*-methoxycarbonylation. DPAT was the most efficient catalyst and gave the highest yield of NNDMA (99.5%) and highest selectivity (99.6%). Moreover, no MNPC was detected in the presence of DPAT as the catalyst only. TBAT

Table 1  
Reaction of aniline with dimethyl carbonate in the presence of different catalysts<sup>a</sup>

Catalysts	Conversion of aniline (%)	Selectivity (%)				Yield of NNDMA (%)
		NMA	NNDMA	MNPC	MNPNMC	
DPAT	99.9	0.3	99.6	–	0.1	99.5
TBAT	96.3	2.4	96.9	0.2	0.5	93.3
DMAP	86.7	26.0	66.8	2.4	4.8	57.9
TBAB	99.9	2.7	81.3	6.3	9.7	81.2
TBAI	97.6	3.6	79.3	8.7	8.4	77.4
K <sub>2</sub> CO <sub>3</sub> <sup>b</sup>	40.7	43.8	46.5	3.6	6.4	18.9
Without	20.3	54.1	23.3	18.3	12.5	4.7

<sup>a</sup> Reaction conditions: aniline 50 mmol, DMC 110 mmol, catalyst 3 mmol, reaction temperature 180 °C, reaction time 160 min.

<sup>b</sup> K<sub>2</sub>CO<sub>3</sub>: 2 g.

also performed a high catalytic activity. The selectivity to NNDMA and the yield of NNDMA were 96.9 and 93.3%, respectively. The conversion of aniline was greater than 97% when using TBAB or TBAI as the catalyst. However, the selectivity to NNDMA was about 80% and the selectivity to MNPC or MNPNMC was higher than that DPAT as the catalyst. DMAP presented lower catalytic activity than the other catalyst though it was an efficient catalyst for *O*-methylation in the reaction of phenols and DMC [28]. K<sub>2</sub>CO<sub>3</sub> showed the lowest catalytic activity. The selectivity to NNDMA was 46.5% only.

### 3.2. Effect of DMC/aniline molar ratio

Effect of DMC/aniline molar ratio on aniline conversion and product yields at 180 °C is presented in Fig. 1. The results show that the conversion of aniline and the yield of NNDMA increase with DMC/aniline molar ratio. Aniline was almost completely converted at DMC/aniline molar ratio of 1.7:1. The yield of NNDMA reached 99.5% at a molar ratio of 2.2:1 with a few side products. It was noteworthy that the yield of MNPNMC was always lower than 0.1%

in spite of varying DMC/aniline molar ratio. Thus, as the reaction temperature maintained at 180 °C, a DMC/aniline molar ratio of 2.2:1 was regarded as optimum.

### 3.3. Effect of reaction temperature

The reactions were carried out in autoclave. Therefore, the reaction temperature higher than the boiling point of DMC (89 °C) was able to be obtained. Fig. 2 shows the effect of reaction temperature on the aniline conversion and products distribution at a DMC/aniline molar ratio of 2.2.

From Fig. 2 one can see that the optimum reaction temperature was 180 °C, at which the conversion of aniline (99.9%) and the selectivity to NNDMA (99.6%) were obtained. Obviously, with the reaction temperature increased from 120 to 180 °C, the conversion of aniline and the selectivity to NNDMA increased, while the selectivity to NMA and methyl *N*-phenyl-*N*-methyl carbamate decreased. No MNPNMC was obtained at reaction temperature of 200 °C. Thus, it can be concluded that low reaction temperature is beneficial to *N*-carboxymethylation. In fact, we have found that MNPNMC was achieved with high yield (83%) in the

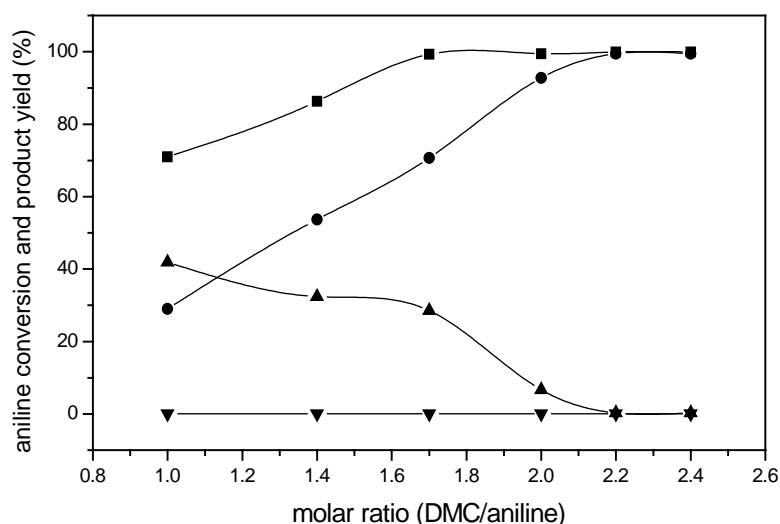


Fig. 1. Effect of DMC/aniline molar ratio on aniline conversion and product yields. Reaction conditions: aniline 50 mmol, catalyst 1.5 mmol, reaction temperature: 180 °C, reaction time, 160 min. (■) Conversion of aniline; (●) yield of NNDMA; (▲) yield of NMA; (▼) yield of MNPNMC.

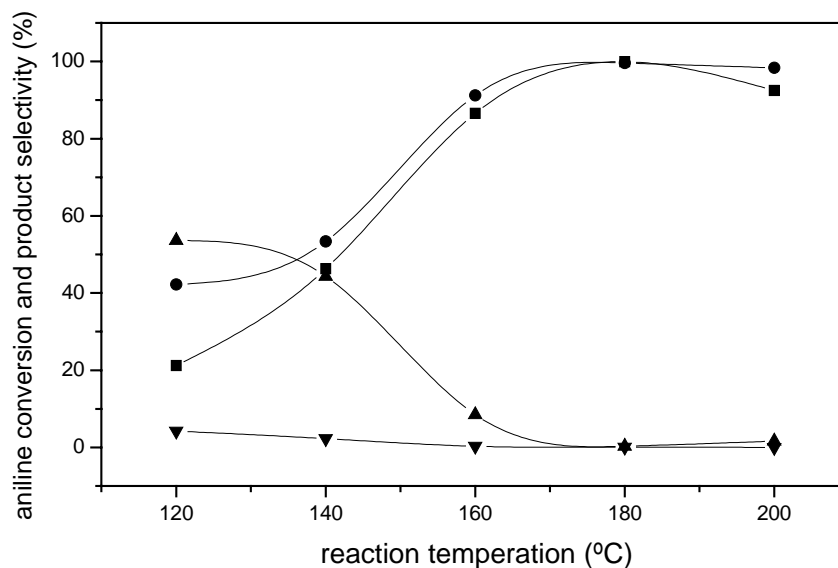


Fig. 2. Effect of reaction temperature on aniline conversion and product selectivity. Reaction conditions: aniline 50 mmol, DMC 110 mmol, catalyst 1.5 mmol, reaction time: 160 min. (■) Conversion of aniline; (●) selectivity to NNDMA; (▲) selectivity to NMA; (▼) selectivity to MNPnMC.

presence of  $\text{Bu}_4\text{NBr}/\text{K}_2\text{CO}_3$  at  $92^\circ\text{C}$  [29]. At  $200^\circ\text{C}$ , the conversion of aniline (92.5%), which was lower than that of at  $180^\circ\text{C}$  (99.9%) and the selectivity to NNDMA slightly decreased to 98.4%. It may be due to the partial degradation of DPAT. The thermogravimetric analysis shows that DPAT begins to decompose at ca.  $200^\circ\text{C}$ .

### 3.4. Effect of DPAT/aniline molar ratio

Effect of the molar ratio of DPAT/aniline on the selectivity to NNDMA is shown in Fig. 3. The reaction of aniline and DMC was carried out at  $180^\circ\text{C}$  for 160 min,

and the aniline/DMC molar ratio is 2.2. The conversion of aniline and the selectivity to NNDMA increased with DPAT/aniline molar ratio, and reached close to 100 and 99.6%, respectively, at DPAT/aniline molar ratio of 0.03.

As mentioned before, the *N*-methoxycarbonylated compounds (MNPC and MNPnMC) were formed in the absence of a catalyst. The yields of these compounds decreased with DPAT/aniline molar ratio and they were almost not observed at DPAT/aniline molar ratio of 0.03. This indicates that a certain amount of DPAT is necessary to obtain a very high selectivity to NNDMA.

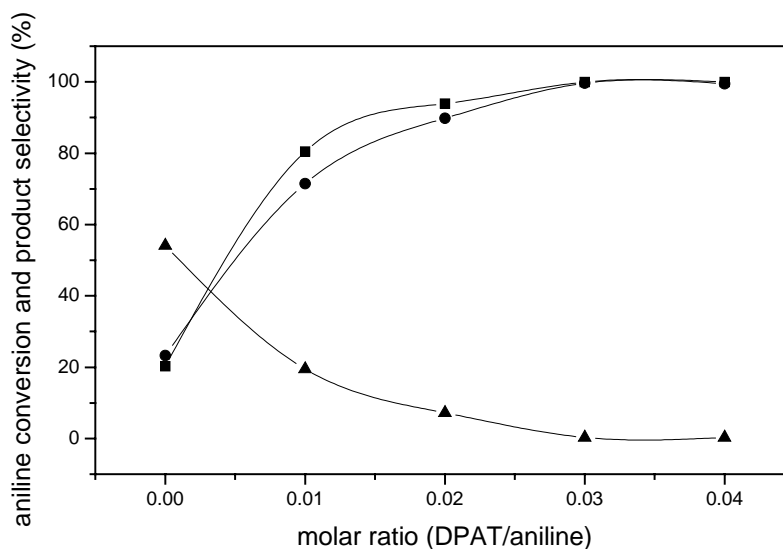


Fig. 3. Effect of molar ratio of DPAT/aniline on aniline conversion and product selectivity. Reaction conditions: aniline 50 mmol, DMC 110 mmol, reaction temperature:  $180^\circ\text{C}$ , reaction time: 160 min. (■) Conversion of aniline; (●) selectivity to NNDMA; (▲) selectivity to NMA.

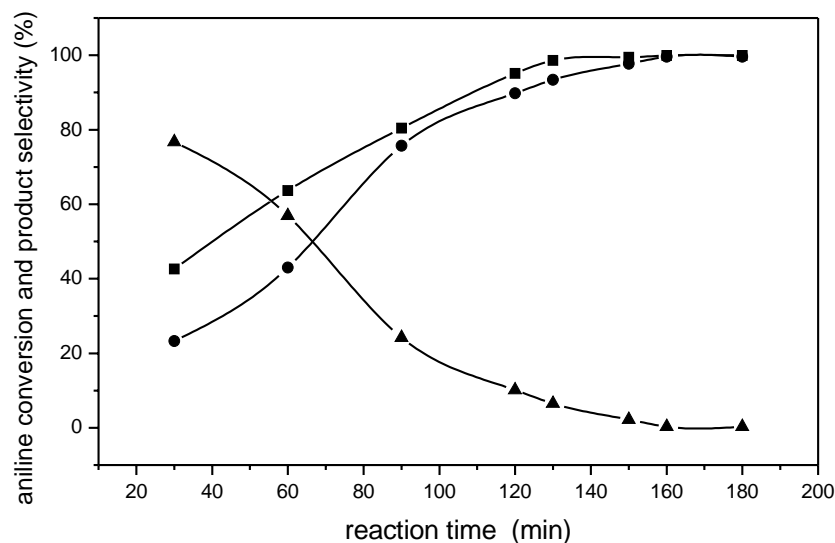


Fig. 4. Effect of reaction time on aniline conversion and product selectivity. Reaction conditions: aniline 50 mmol, DMC 110 mmol, catalyst 1.5 mmol, DMC/aniline molar ratio: 2.2; reaction temperature: 180 °C. (■) Conversion of aniline; (●) selectivity to NNDMA; (▲) selectivity to NMA.

### 3.5. Influence of reaction time

Influence of reaction time on aniline conversion and products distribution in the reaction of aniline *N,N*-dimethylation with DMC at 180 °C and molar ratio of DMC to aniline of 2.2 for a period of 180 min is depicted in Fig. 4. The increase in reaction time resulted in increase in the conversion of aniline and the selectivity to NNDMA with concomitant decrease in the selectivity of NMA. Aniline was almost completely converted at a reaction time of 130 min. After a period of 160 min, the selectivity to NNDMA reached the maximum value.

### 3.6. *N,N*-Dimethylation of primary aromatic amines

DPAT can catalyze not only the *N,N*-dimethylation of aniline, but also that of other primary aromatic amines. The results are summarized in Table 2. In all cases, the

*N,N*-dimethylated anilines [ArN(CH<sub>3</sub>)<sub>2</sub>] are obtained with high selectivities. The yields of *N,N*,3-trimethylaniline and *N,N*,4-trimethylaniline were 98.5 and 98.1% at 180 °C in 160 min when *m*-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub> and *p*-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub> were used as substrates. The yields of 3-methoxy-*N,N*-dimethylaniline and 4-methoxy-*N,N*-dimethylaniline were 97.9 and 99.5%, respectively, at 180 °C in 160 min, while the yield of 2-methoxy-*N,N*-dimethylaniline was 34.7% only. The low activity of 2-methoxyaniline was due to steric hindrance. Longer reaction time will improve the yield of 2-methoxy-*N,N*-dimethylaniline as presented in Table 2.

The presence of electron-withdrawing group (–Cl) on the benzene ring would decrease the activity of Cl–C<sub>6</sub>H<sub>5</sub>NH<sub>2</sub>. The yield of *N,N*-dimethyl-3-chloroaniline was only 29.4% at 180 °C in 160 min in the reaction of *m*-chloroaniline and dimethyl carbonate. Low activity substrates required much longer reaction times compared with aniline. The yields of *N,N*-dimethyl-3-chloroaniline

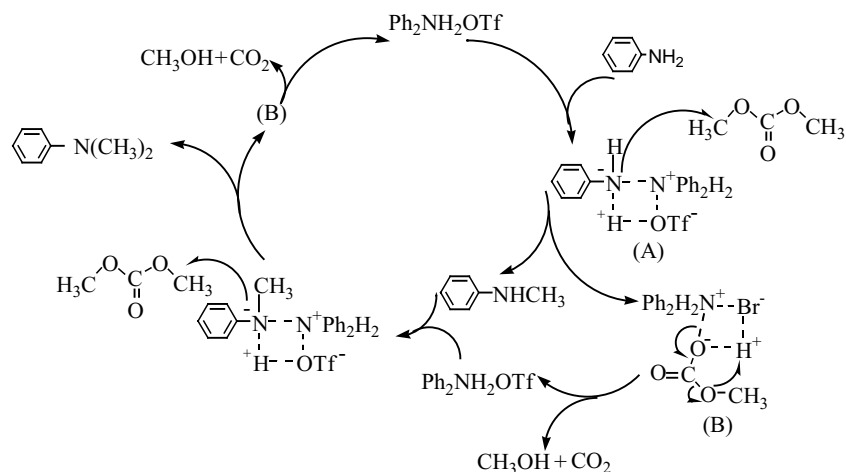
Table 2  
*N,N*-Dimethylation of primary aromatic amines with dimethyl carbonate in the presence DPAT<sup>a</sup>

Substrate: ArNH <sub>2</sub>	Conversion (%)	Selectivity (%)				Yield of ArN(CH <sub>3</sub> ) <sub>2</sub> (%)
		ArNHCH <sub>3</sub>	ArN(CH <sub>3</sub> ) <sub>2</sub>	ArNHCOOCH <sub>3</sub>	ArN(Me)COOCH <sub>3</sub>	
Ar: <i>m</i> -CH <sub>3</sub>	99.4	0.3	99.1	–	0.6	98.5
Ar: <i>p</i> -CH <sub>3</sub>	99.6	0.2	98.5	0.1	1.2	98.1
Ar: <i>m</i> -OCH <sub>3</sub>	99.9	1.7	98.0	–	0.3	97.9
Ar: <i>p</i> -OCH <sub>3</sub>	100	0.4	99.5	–	0.1	99.5
Ar: <i>o</i> -OCH <sub>3</sub>	53.4	35.1	64.9	–	–	34.7
Ar: <i>o</i> -OCH <sub>3</sub> <sup>b</sup>	98.7	1.5	98.5	–	–	97.2
Ar: <i>m</i> -Cl	63.6	53.5	46.3	–	0.2	29.4
Ar: <i>m</i> -Cl <sup>c</sup>	97.7	2.3	97.4	–	0.3	95.2
Ar: <i>p</i> -Cl <sup>c</sup>	98.4	1.1	98.8	0.1	–	97.2
Ar: <i>o</i> -Cl <sup>c</sup>	86.5	48.2	48.7	3.1	–	42.1

<sup>a</sup> Reaction conditions: primary aromatic amines 50 mmol, DMC 250 mmol, catalyst 5 mmol, reaction temperature 180 °C, reaction time 160 min.

<sup>b</sup> Reaction time 230 min.

<sup>c</sup> Reaction time 300 min.



Scheme 2. Plausible reaction mechanism.

and *N,N*-dimethyl-4-chloroaniline were 95.2 and 97.2%, respectively, after 300 min at 180 °C, while the yield of *N,N*-dimethylaniline was 99.5% after only 160 min. The yield of *N,N*-dimethyl-2-chloroaniline was fairly low (42.1%) after 300 min at 180 °C, which was due to the presence of steric hindrance and electron-withdrawing group on the benzene ring.

### 3.7. Plausible mechanism

In the reaction, aniline would react with DPAT to form a complex (A) containing nucleophilic anion (PhNH<sup>-</sup>). This intermediate (A) can react with DMC via direct B<sub>A1</sub>2 displacement to generate *N*-methylaniline and an intermediate (B). DPAT, methanol, and carbon dioxide were formed from the intermediate (B). *N*-Methylaniline undergoes the same B<sub>A1</sub>2 displacement to generate *N,N*-dimethylaniline (see Scheme 2).

## 4. Conclusion

The *N,N*-dimethylation of aniline with dimethyl carbonate was studied in the presence of various catalysts. Diphenylammonium triflate was the most active catalyst in the *N,N*-dimethylation of aniline with DMC. Primary aromatic amines can be converted into their corresponding *N,N*-dimethylanilines in high selectivity and yield using diphenylammonium triflate as a catalyst and no *C*-methylation product was obtained. The reaction also has remarkable environmentally benign features: it uses the non-toxic DMC, no hazardous wasters are produced, no solvents are required and no disposal problems are involved.

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