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Formation of Intermediate and By-products in Synthesis of 4,4′-Methylenedimethyldiphenylcarbamate

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Abstract The formation of intermediate and by-products in the synthesis of 4,4′-methylenedimethyldiphenylcarbamate (MDC) by the reaction of 4,4′-methylenedianiline (MDA) and dimethyl carbonate (DMC) over $Zn(CH_3COO)_2$ catalyst was studied in this paper. The work would be of importance to deeply understand the reaction mechanism and to further improve the yield of aimed product. The intermediate and by-products were isolated from the reaction mixture and identified. The effects of reaction variables upon the formation of the compounds were examined. The mechanism on formation of the intermediate and by-products was proposed based on the experimental results.

Keywords Intermediate · By-product · N-Methylation · Dimethyl carbonate · 4,4′-Methylenedimethyldiphenylcarbamate

1 Introduction

4,4′-Methylenediphenyl diisocyanate, hereinafter referred to as MDI, is one of the major polyisocyanates for the polyurethane production. To date, MDI is commercially manufactured by the phosgenation of primary amine [1, 2]. Due to the increasing environmental concern, plentiful efforts have been made to develop the non-phosgene ways for the purpose [3–7]. Among the routes proposed, methoxycarbonylation of 4,4′-methylenedianiline (MDA) with dimethyl carbonate (DMC) to yield 4,4′-methylenedimethyldiphenylcarbamate (MDC), followed by the thermal decomposition to offer MDI is thought to be one of the promising non-phosgene ways and has attracted much attention. Moreover, the realization of commercial production of DMC via the oxidative carbonylation of methanol instead of phosgene method endows the route with better prospect [8, 9].

In this route, MDC synthesis through the reaction of MDA and DMC is a crucial step. Several studies have been devoted to exploring new catalyst and to optimizing reaction condition for the step [10–14], which are necessary to consummate the process. However, few reports have dealt with the research on formation of the intermediate and by-products in the reaction. In fact, the research in these aspects would be of importance to deeply understand the reaction mechanism and to further improve the yield of aimed product. The present investigation was therefore undertaken with such objective. In this work, the intermediate methyl 4[(4′-aminophenyl)methylene]phenylcarbamate (MMC) and the major by-products produced were isolated and identified. Their formation rules were studied, and a possible reaction mechanism was proposed based on the experimental results.

2 Experimental

2.1 Chemicals

4,4′-Methylenedianiline (MDA) was commercially available and used without further treatment. DMC of analytically pure grade was purified by distillation before use. $Zn(CH_3COO)_2$ was obtained by heating $Zn(CH_3COO)_2 \cdot 2H_2O$ at 383 K,

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while $Pb(CH_3COO)_2$ was obtained by heating Pb $(CH_3COO)_2 \cdot 3H_2O$ at 303 K, the other catalysts were commercial products and used as received.

2.2 Analytical Equipment

^1H NMR spectra were recorded on a Bruker drx-300 instrument (Germany), IR spectra were obtained with a Thermo Nicolet 380 FT-IR (USA), Mass spectroscopy (MS) analysis was run on Waters micromass ZQ-4000 (USA) and Elemental analysis was performed on an Elementar Vario EL (Germany). High performance liquid chromatography (HPLC) analysis was conducted on a Shimadzu LC (Japan) equipped with SPD-10Avp detector. A Shim-pack Vp-ODS column (150 × 4.6 mm) and a mobile phase of CH_3OH/H_2O = 60/40 (volume) were used. HPLC coupled with tandem mass spectrometry (HPLC-MS/MS) was run on a Q-Trap LC (Agilent1100 series)/ MS/MS system with a turbo ionspray source (Applied Biosystem/MDS Sciex, USA) and a Zorbax SB-C18 column (2.1 × 150 mm). The mobile phase of CH_3OH/H_2O = 60/40 (volume) was used at flow rate 0.3 mL/min. Parameters of electrospray ionization were: ion spray voltage 5,500 V, source temperature 623 K, Cur Gas 25, Gas1 55, Gas2 45, DP 90 V, respectively.

2.3 Reaction and Analysis

All the reactions were carried out in a 100 mL stainless autoclave with a magnetic stirrer. The reactants and the catalyst were charged into the reactor. The mixture was then stirred constantly and heated to a selected temperature for certain hours after the air in the autoclave was fully replaced with nitrogen. When the reaction was completed, the autoclave was cooled down to room temperature. The solid-liquid mixture obtained was separated into two parts by filtration: a white solid and a clear filtrate containing all of products. The former was further purified by recrystallization to obtain MDC or MMC, while the latter was analyzed by HPLC-MS/MS to identify the structures of the by-products. The conversion of MDA, the selectivity of MMC, MDC and by-products were calculated by HPLC.

Characterization data of MDC and MMC were listed as follows.

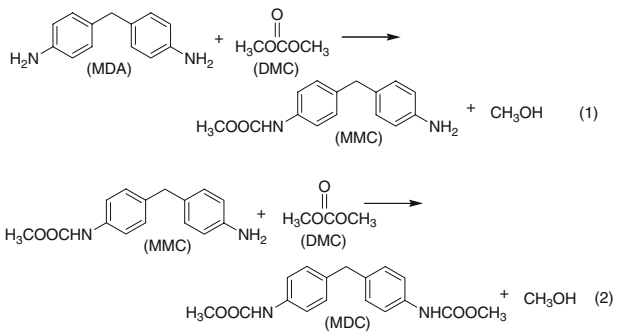
4,4′-Methylenedimethyldiphenylcarbamate (MDC): ^1H NMR ($CDCl_3$, 300 MHz) δ: 3.78 (s, 6H, OCH_3), 3.91 (s, 2H, CH_2), 6.58 (s, 2H, NH), 7.11–7.14 (m, 4H), 7.28–7.31 (m, 4H); IR (KBr) v: 3331 (m, br), 3281 (m, br), 2946 (w), 1708 (vs), 1689 (vs), 1600 (m), 1550 (vs), 1533 (m), 1437 (w), 1413 (w), 1318 (m), 1242 (vs), 1080 (m), 821 (w), 769 (w), 680 (w, br), 511 (w) cm^{-1}; MS m/z (relative intensity): 315 (M + H, 63.1); Anal. Calcd for $C_{17}H_{18}N_2O_4$: C 64.95, H 5.77, N 8.96; found C 64.99, H 5.53, N 8.86.

Methyl 4[(4′-aminophenyl)methylene] phenylcarbamate (MMC): ^1H NMR ($CDCl_3$, 300 MHz) δ: 3.56 (s, br, 2H, NH_2), 3.75 (s, 3H, OCH_3), 3.82 (s, 2H, CH_2), 6.52–6.62 (m, 2H), 6.93–6.95 (m, 2H), 7.08–7.11 (m, 2H), 7.25–727 (m, 2H); IR (KBr) v: 3405 (s, br), 3331 (m, br), 3224 (mw), 3170 (w), 3095 (w), 3029 (mw), 3005 (mw), 2955 (w), 1708 (vs), 1615 (ms), 1601 (ms), 1546 (s), 1515 (s), 1435 (ms), 1412 (ms), 1364 (w), 1310 (ms), 1279 (w), 1247 (vs), 1190 (w), 1179 (mw), 1117 (w), 1079 (s), 1013 (w), 951 (vw), 914 (w), 856 (mw), 836 (m), 814 (m), 771 (ms), 722 (m), 605 (mw), 533 (m), 512 (m), 495 (w) cm^{-1}; MS m/z (relative intensity): 257 (M + H, 9.9). Anal. Calcd for $C_{15}H_{16}N_2O_2$: C 70.29, H 6.29, N 10.93; found C 70.62, H 6.27, N 10.08.

3 Results and Discussion

3.1 Catalyst Function

Recently, zinc, lead, tin containing compounds have been reported to be effective catalysts for the methoxycarbonylation of various amines and DMC yielding corresponding carbamates, and some of them also exhibited good activity for the present reaction [14–16]. In this work, the formation of intermediate and byproducts during the synthesis of MDC from MDA and DMC over these catalysts were studied.



Scheme 1 Methoxycarbonylation reaction of MDA with DMC

Table 1 MDC synthesis over various catalysts

Catalysts	Conversion (%)	Selectivity (%)					
	MDA	MDC	MMC	**1**	**2**	**3**	Unknown
None	61.2	5.6	29.9	5.8	3.1	0.8	54.8
$Zn(CH_3COO)_2$	100	97.6	1.0	0.8	0.3	0.3	None
$Pb(CH_3COO)_2$	100	95.9	1.0	0.9	1.4	0.7	0.1
Pb_3O_4	98	63.2	20.3	11.4	0.3	2.5	2.3
$Sn(C_7H_{15}COO)_2$	98.2	49.1	16.9	13.6	0.9	2.9	16.6

Reaction conditions: MDA 0.02 mol, DMC 0.60 mol, catalyst 0.001 mol, reaction temperature 453 K, reaction time 2 h

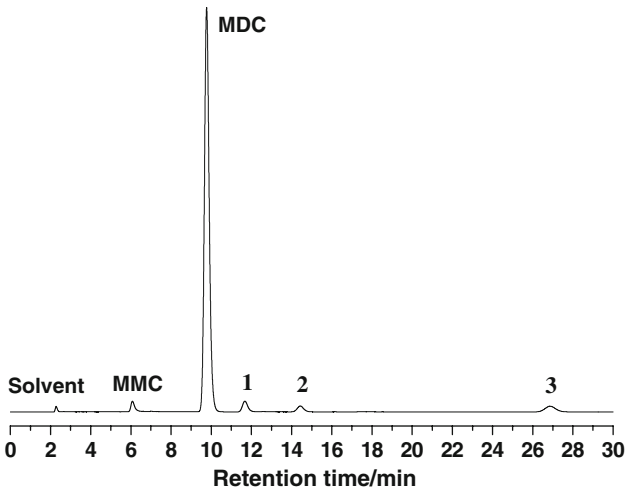


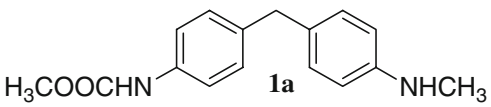
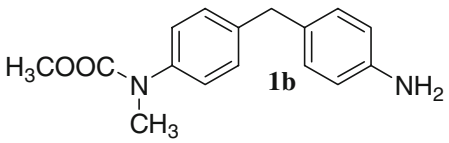
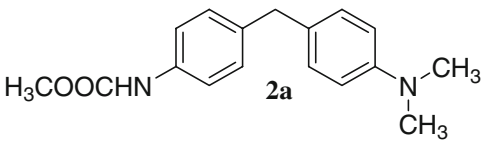
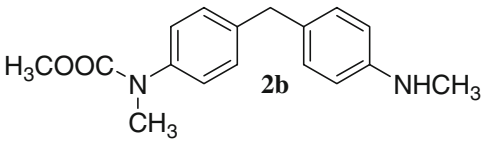
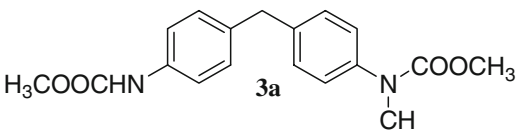
Fig. 1 The liquid chromatograms of the filtrates obtained after the reactions of MDA with DMC over $Zn(CH_3COO)_2$. Reaction conditions: MDA 0.02 mol, DMC 0.60 mol, catalyst 0.001 mol, reaction temperature 453 K, reaction time 2 h

The methoxycarbonylation reaction of MDA with DMC toward MDC is illustrated in Scheme 1.

The reaction could be regarded as a process consisting of two steps: MDA first reacts with DMC to provide MMC (1), and the monocarbamate formed then reacts with DMC to give dicarbamate product, MDC (2). Obviously, MMC is produced as the intermediate. In addition to MMC, some by-products were also found in the filtrates obtained by the reaction of MDA and DMC over these catalysts.

Table 1 shows such results in the absence, or presence of the catalysts. For the non-catalytic reaction, low MDA conversion (61.2%) and high by-products selectivity (total 64.5%) were registered. This suggested that catalyst is needed to implement the reaction and the formation of MMC is much easier than that of MDC in this case. When various catalysts were introduced, disparate catalytic behaviors were observed. Compared with other catalysts listed in Table 1, both Pb_3O_4 and $Sn(C_7H_{15}COO)_2$

Table 2 The molecular weights and structures of **1**, **2** and **3**

Compounds	m/z $[M + H]^+$	Molecular weights	Possible structures	Actual structures
1	271.40	270.39	 **1a**	**1a**
			 **1b**	
2	285.40	284.39	 **2a**	**2a**
			 **2b**	
3	329.40	328.39	 **3a**	**3a**

exhibited unwanted selectivity for MMC and by-products in spite of high MDA conversion. In contrast, $Zn(CH_3COO)_2$ and $Pb(CH_3COO)_2$ showed outstanding performance for MDC formation, in particular, the former possessed the highest MDC yield and the lowest by-product selectivity among the catalysts tested. Furthermore, the lowest MMC selectivity and the highest MDC selectivity over the catalyst implied that the main function of $Zn(CH_3COO)_2$ may promote the transformation of MMC toward MDC, besides the role facilitating conversion of MDA. This is of great importance to commendably conduct the reaction. Therefore, $Zn(CH_3COO)_2$ was selected as the model catalyst, over which the further investigation with respect to the formation of by-products was performed.

3.2 Identification of the Intermediate and By-products

The by-products coded as **1**, **2**, and **3** (Fig. 1) formed by the reaction of MDA and DMC over $Zn(CH_3COO)_2$ catalyst were identified in this section. Their configurations were first sketched by excluding other imaginable structures based on the molecular weights measured by MS^1 (Table 2). This method is feasible to recognize **3**, however, it is not enough to judge **1** and **2** because they may have structures **1a**, **1b** and **2a**, **2b,** respectively. The fragments in the MS^2 spectra (Fig. 2) were therefore used for this purpose.

Most of the fragment ions in Fig. 2a should be ascribed to compound **1a**. Moreover, the formation of the ion **4** at *m/z* 120.2 (Fig. 2a) was also related to the structure of **1a**, because **1b** could not generate an ion with such *m/z* value. Thus, byproduct **1** was confirmed to be **1a**. Similarly, byproduct **2** was testified as **2a** due to the formation of the ion **5** at *m/z* 134.2 (Fig. 2b) which is impossibly produced from **2b**. By analyzing Fig. 2c, the structure of **3** was again validated. So far, the by-products **1**, **2** and **3** were finally identified as three *N*-methylated derivatives, as shown in Table 2.

3.3 The Effects of Reaction Conditions

3.3.1 Effect of Catalyst Amount

The relationship between $Zn(CH_3COO)_2$ amount and the selectivity of intermediate and byproducts was shown in Fig. 3. It is found that the MDA was completely converted

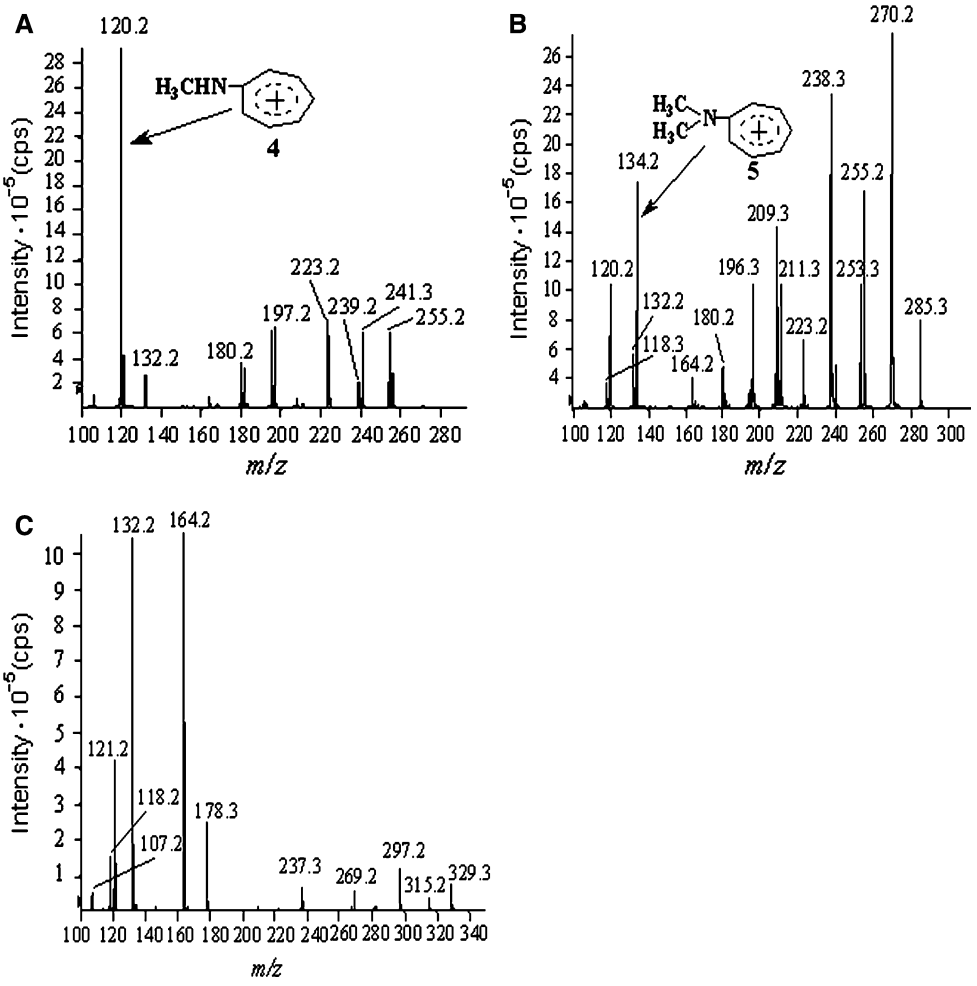


Fig. 2 MS^2 spectra of the pseudomolecular ions of compounds **1**, **2** and **3**. Subfigures (**a**), (**b**) and (**c**) present the MS^2 spectra of the pseudomolecular ions of compounds **1**, **2** and **3**, respectively. **4** stands for the ion with an *m/z* value of 120.2 and **5** represents the ion with an *m/z* value of 134.2

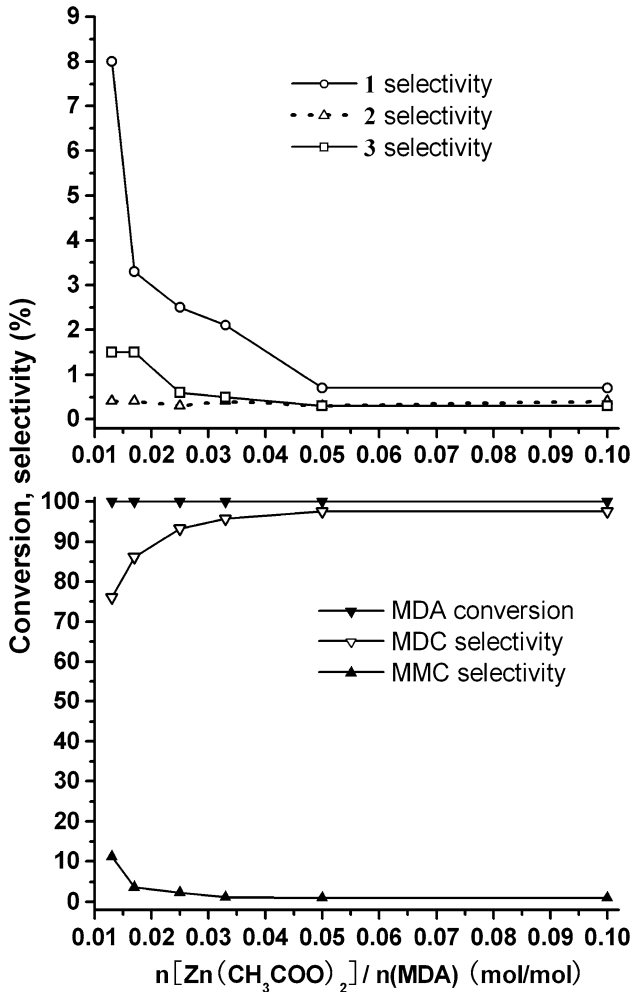


Fig. 3 The formation of MMC and by-products using different amounts of $Zn(CH_3COO)_2$. Reaction conditions: MDA 0.02 mol, DMC 0.60 mol, reaction temperature 453 K, reaction time 2 h

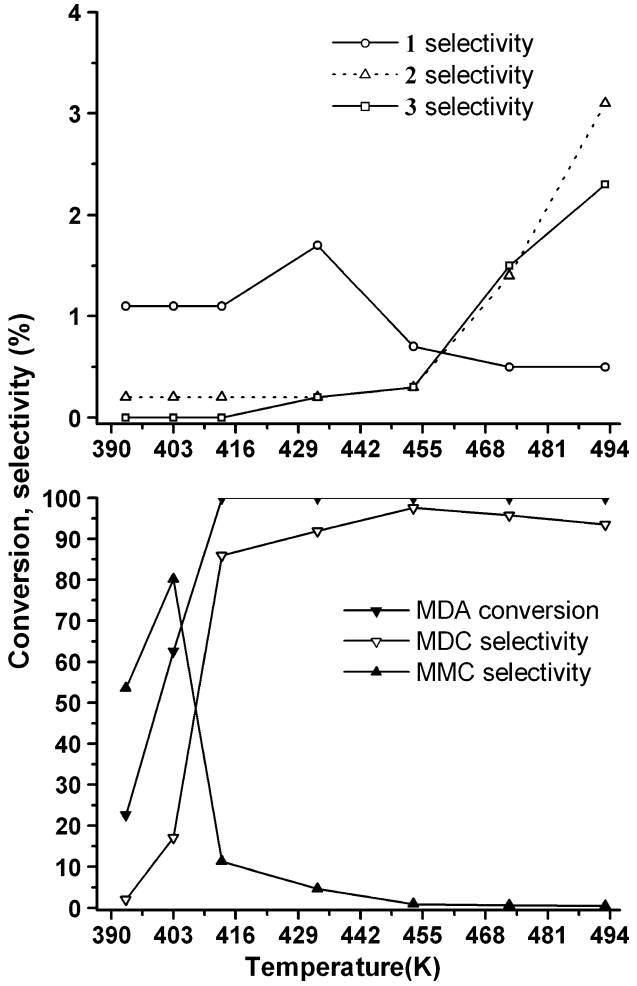


Fig. 4 The formation of MMC and by-products under different reaction temperatures. Reaction conditions: MDA 0.02 mol, DMC 0.60 mol, $Zn(CH_3COO)_2$ 0.001 mol, reaction time 2 h

in the examined range of catalyst amount. With increasing the amount, the selectivity of MMC and overall selectivity of by-products decreased. At the same time, the selectivity of MDC ascended until a plateau corresponding to 97.6%. This indicated that the increase of $Zn(CH_3COO)_2$ amount promoted the transformation of MMC to MDC and depressed the creation of the by-products, thereby benefiting the MDC formation. The proper molar ratio of the catalyst to MDA to achieve this purpose should be around 0.05. Overmuch catalyst is practically unnecessary from the viewpoint of economics.

3.3.2 Effect of Reaction Temperature

The effect of reaction temperature on the formation of MMC and by-products appeared to be rather complicated, as shown in Fig. 4. When the reaction was carried out at temperature ≤413 K, the selectivity of all by-products kept intact while the MMC selectivity first went through a maximum (around 80.1%) at 403 K and then dropped to 11.3% at 413 K. This suggested that lower temperature went against the conversion of MDA to MMC and higher temperature benefited the transformation. As the reaction temperature was increased up to 453 K, MMC selectivity gradually decreased while MDC selectivity was ceaselessly improved. This again indicated that MMC produced mainly contributed to MDC formation. The reason for the unexpectedly high selectivity of **1** at 433 K may be that the temperature is appropriate for the creation of the N-methylated compound. This speculation needs to be corroborated by further work. When the temperature attained 453 K, the best MDC selectivity of 97.6% with the lowest MMC selectivity of 1.0% was registered. At the same time, the selectivity of by-products also held the lowest level. However, the temperature higher than 453 K led to the attenuation of MDC selectivity caused by the augment in

by-products. The results above demonstrated that the reaction temperature played a key role deciding the production of MMC and the side-reactions in the synthetic reaction. The lower temperatures biased the formation of MMC, while exorbitant temperatures (> 453 K) favoured the formation of by-products **2** and **3.** The optimum reaction temperature should be controlled around 453 K to ensure the lowest yields of MMC and by-products.

3.3.3 Effect of DMC/MDA Molar Ratios

In this work, DMC serves as reactant and solvent. Based on our preliminary examination, the molar ratios of DMC to MDA at or higher than 10 were therefore adopted to study the effect of the ratio upon formation of MMC and by-products. Although the MDA conversion always kept 100% at 453 K regardless of the ratio (Fig. 5), the selectivity of MMC and by-products varied with the ratio. For example, when the molar ratio was 10, somewhat high selectivity of MMC and quite high selectivity of by-products were observed. Correspondingly, lower selectivity of MDC was found in this case. However, the molar ratio of DMC/MDA at 15 minimized these unwanted compounds to very small amount. Further increasing the ratio, the improvement was not obvious. It appeared that the molar ratio of DMC/MDA at 15 is suitable to obtain high selectivity of aimed product. Excess DMC is not necessary and would increase the recovery burden of unreacted DMC.

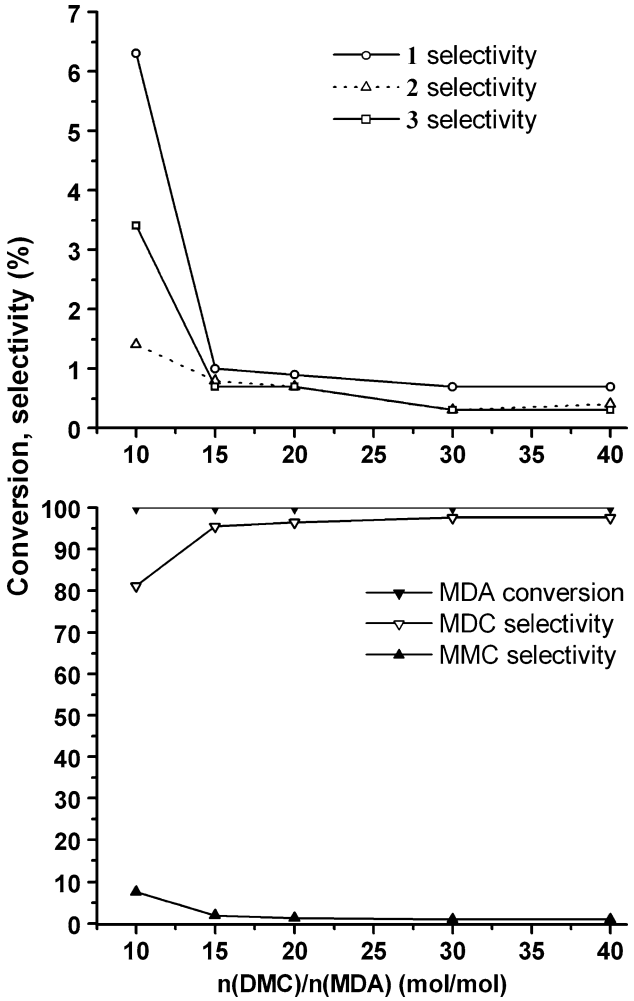


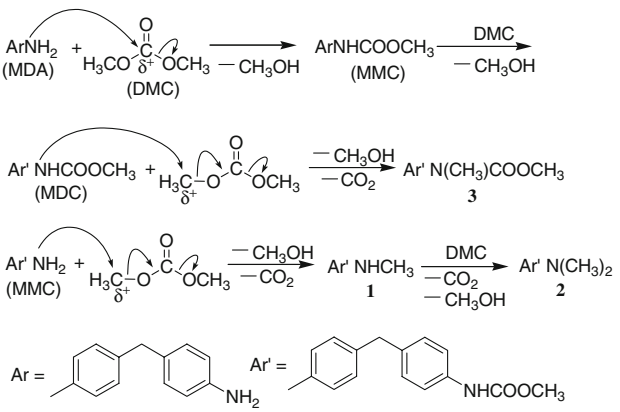
Fig. 5 The formation of MMC and by-products under different DMC/MDA molar ratios. Reaction conditions: MDA 0.02 mol, $Zn(CH_3COO)_2$ 0.001 mol, reaction temperature 453 K, reaction time 2 h

3.4 Mechanism on the Formation of MMC and By-products **1**, **2** and **3**

Based on the results mentioned above, the mechanism on the formation of MMC and N-methylated derivatives **1**, **2** and **3** could be represented as shown in Scheme 2. MMC is formed by the direct attack of one amino group of MDA on the carbonyl carbon of DMC, followed by the abstraction of methanol. The further reaction of amino group of MMC produced with DMC leads to MDC formation, eliminating methanol. The attack of amino group of MMC and MDC on methoxy group of DMC would generate by-products **1** and **3,** respectively. By-product **2** is created by the further reaction of amino group of **1** with DMC.

4 Conclusions

Formation of intermediate and by-products in the methoxycarbonylation of MDA with DMC over $Zn(CH_3COO)_2$ catalyst was studied in this work. Besides MMC, the by-products produced were identified as N-methylated derivatives by various techniques. The experimental results revealed that reaction conditions including catalyst amount,



Scheme 2 The mechanisms on the formation of MDC, MMC and by-products **1**, **2** and **3**

reaction temperature and molar ratio of starting materials evidently influenced the formation of the compounds. It was found that improved yield of aimed product could be warranted by optimization of the reaction conditions.

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