CH_3COONa as an effective catalyst for methoxycarbonylation of 1,6-hexanediamine by dimethyl carbonate to dimethylhexane-1,6-dicarbamate†

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Methoxycarbonylation of 1,6-hexanediamine (HDA) by dimethyl carbonate (DMC) was carried out, using, for the first time, CH_3COONa as catalyst. The effects of the solvent, reaction temperature, reaction time, and catalyst amount, were investigated. A yield as high as 99.0% of dimethylhexane-1,6-dicarbamate **2** has been obtained at a temperature of 348 K and a reaction time of 6 h. Mechanistic studies revealed that N-substituted acetamide, as the active intermediate product, and NaOH were first formed *via* the reaction between HDA and CH_3COONa. A further reaction between the N-substituted acetamide and DMC generated carbamates and methyl acetate, *via* a hexatomic ring intermediate. The CH_3COONa catalyst was finally recovered through the reaction between NaOH and methyl acetate, which thus completed the catalytic cycle.

1. Introduction

Organic carbamates, which are very important starting materials and/or intermediates, have found versatile applications in the production of fine and commodity chemicals[1,2] and in organic synthesis.[1] Currently, the commercial production of carbamates is based mainly on the reaction between alcohols and isocyanates.[3] However, this route is not environmentally friendly, because the industrial production of isocyanates is associated with a high energy input, toxic phosgene as a raw material, and the corrosive hydrochloric acid as a side product.[2] Several phosgene-free processes for the production of organic carbamates have been explored,[4-8] among which the alkoxycarbonylation of amines by alkyl carbonates,[4] particularly dimethyl carbonate (DMC),[5] have received considerable attention. This route appears to be promising, because on the one hand methanol is obtained as the main by-product and on the other hand DMC is non-toxic and can be prepared on a large scale by the oxidative carbonylation of methanol.[9,10] In addition, DMC can be easily handled and is cheap, non-toxic and clean. Thus, if the methoxycarbonylation reaction between an amine and DMC is combined with the oxidative carbonylation of methanol, a green process for the production of organic carbamates, with "zero emission", can be achieved.

In the synthesis of carbamates from amines and DMC, Lewis acidic catalysts, such as the acetates of Mn, Zr, Sn, Zn and Pb,[4,11-13] the nitrates of Bi and Pb,[14,15] the triflates of IIIB metals ($M(OTf)_3$ with M = Sc, La),[16,17] and even CO_2,[18] were often employed, providing appreciable yields of carbamates. Because they can be thermally or catalytically converted into diisocyanates, which are widely used as precursors in polymer preparation,[19] the dicarbamates are of particular industrial interest. Few papers have dealt with the synthesis of dicarbamate from DMC and diamines, especially the aliphatic ones, over catalysts such as $Bi(NO_3)_2$,[14] $M(OTf)_3$ (with M = Sc, La),[16,17] $NaOCH_3$[20] and ionic liquids $MIm(CH_2)_4SO_3HTfO$.[21] We have previously reported the synthesis of dimethylhexane-1,6-dicarbamate *via* the methoxycarbonylation of 1,6-hexanediamine (HDA) by DMC over a $ZnAlPO_4$ berlinite catalyst.[22] In the present paper, sodium acetate was employed, for the first time, as catalyst for this reaction and a yield as large as 99.0% of **2** (dimethylhexane-1,6-dicarbamate) under mild conditions has been obtained. The sodium acetate catalyst is superior to the other catalysts already reported in the literature, because it is cheaper, non-toxic, and much more efficient. In addition, the mechanism of methoxycarbonylation of HDA by DMC using sodium acetate as catalyst was examined.

2. Experimental

2.1 Reagents

The reagents involved are as follows: HDA (C.P., Shanghai Lingfeng Chemicals Company); CH_3OH (A.R., Shanghai Ludou Chemicals Company); CH_3CN (A.R., Tianjin Kemiou Chemicals Reagents Company); CH_3COONa, DMC, DMF, CH_3COOH, $(CH_3CO)_2O$, and acetamide (A.R., China National Medicines Chemicals Reagents Corporation Ltd.). Before use, all the agents were pretreated to remove the water they contained: CH_3COONa was dried at 373 K in a vacuum

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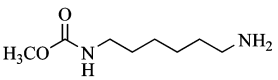
oven and the liquid agents were dehydrated using molecular sieves 4A.

2.2. Methoxycarbonylation of HDA by DMC

The methoxycarbonylation of HDA by DMC was performed under a N_2 atmosphere in a 250 ml three-neck flask equipped with a condenser and a magnetic stirrer. A solution was first prepared by mixing selected amounts of HDA, DMC, CH_3COONa and solvent (CH_3OH, CH_3CN, or DMC) with stirring at room temperature, until a small amount of white floccules appeared. Then, a flow of nitrogen was introduced to drive out the air contained in the three-neck flask, and the solution was heated to the desired temperature and kept at that temperature for the reaction to take place. The white floccules disappeared within the first 10 min of reaction, and by prolonging the reaction time, the clear solution turned gradually into a white emulsion. After a certain reaction time, a white viscous gel was generated. This gel was cooled to room temperature and then subjected to GC and GC-MS analysis.

2.3. Analysis of intermediates and products

The product mixtures of methoxycarbonylation of HDA by DMC were sampled, dissolved into methanol and analyzed using a Varian Saturn2200-CP3800 GC-MS spectrometer equipped with two 15 m × 0.32 mm CP-Wax 52CB fused silica capillary columns, which were linked to a mass detector for qualitative analysis and to a flame ionization detector (FID) for quantitative analysis. It was reported[14,17] that in the methoxycarbonylation of HDA by DMC, besides the desired product **2** (dimethylhexane-1,6-dicarbamate), a few by-products, such as, **1** (methyl-6-amino-hexyl-1-carbamate) and **3**–**6**, might be generated. In our work, the desired product **2**, the main by-product **1** and the minor by-product **7** have been identified (ESI: Fig. S1 and Tables S1 and S2) in all the runs. Occasionally, depending on reaction conditions, trace amounts of the by-products **3**–**6** could also be detected. Since the amounts of by-products **3**–**7** identified in our experiments were small, their selectivities are reported together in this paper. Unless otherwise



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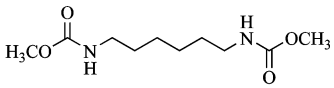

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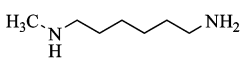

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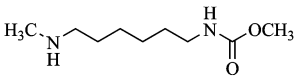

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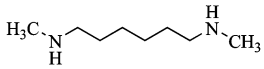

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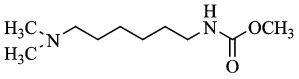

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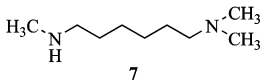

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mentioned, the conversion of HDA was calculated on the basis of the initial amount of HDA, the selectivities to products were calculated on the basis of the amount of HDA converted, and the yield of **2** was calculated by multiplying the conversion of HDA with the selectivity to **2** (ESI: Section 2). The thus-obtained yield of **2** is denoted as GC yield.

To identify the reaction intermediates and products, FT-IR and ^{1}H NMR spectroscopies were employed. The FT-IR spectrum was recorded on a Thermo Nicolet Nexus 670 FT-IR spectrometer equipped with a MCTA detector and a ZnSe single-bounce attenuated total reflectance (ATR) accessory, using a 32 scans at 4 cm^{-1} resolution. The specimen was prepared *via* a dip-coating procedure using a KBr disk as support. The ^{1}H NMR spectrum was recorded on a 400 MHz Varian INOVA-400 spectrometer, with tetramethylsilane (TMS) in deuterochloroform ($CDCl_3$) as internal standard.

2.4. Purification and identification of dimethylhexane-1,6-dicarbamate

After the methoxycarbonylation of HDA by DMC in the presence of CH_3COONa as catalyst, the product mixture was cooled to room temperature and an excess amount of dilute aqueous HCl solution was added with stirring. The resulting mixture was allowed to stand until two layers were formed. A hydrophilic layer contained mainly the catalyst (CH_3COONa), and a hydrophobic layer consisted mainly of the unconverted reactants and products. After the separation of the hydrophilic layer, the hydrophobic layer was vacuum-distilled to remove the DMC, the methanol, and, if any, solvent, yielding a white solid, *i.e.*, the crude **2**. Then, the crude **2** was subjected to re-crystallization, involving the steps of dissolution in water at *ca.* 353 K, aging at room temperature for 2 h, filtration and washing with cold water. The re-crystallization procedure was repeated five times, and after drying in vacuo, the purified **2** was finally obtained. The percentage of the weight of purified **2** relative to that of **2** predicted theoretically by the stoichiometry of the reaction was then obtained and denoted as isolated yield of **2**.

^{1}H NMR and GC-MS were employed to identify the purified **2** and the results are as follows: ^{1}H NMR (ESI: Fig. S2), δ = 1.33 (*m*, 4H; -$CH_2CH_2CH_2CH_2CH_2CH_2$-), 1.48 (*m*, 4H; -$CH_2CH_2CH_2CH_2CH_2CH_2$-), 3.14 (*q*, 4H; -$NHCH_2$-), 3.66 (*s*, 6H; -OCH_3) and 4.79 (broad, 2H; -$NHCO$-); GC-MS (ESI: Fig. S3 and Table S3), m/z = 232, 201, 173, 158, 144, 130, 116, 114, 102, 99, 88, 74, 59, 56 and 44.

3. Results and discussion

3.1 Methoxycarbonylation of HDA by DMC

Table 1 presents the results of methoxycarbonylation of HDA by DMC in the absence and presence of various solvents (methanol, DMC, or CH_3CN), using CH_3COONa as catalyst, a reaction time of 10 h and a reaction temperature of 348 K. All the batches consisted of 100 mmol HDA, 200 mmol (16.8 ml) DMC, 24.4 mmol (2 g) CH_3COONa and 50 ml solvent. Except the batch that employed DMC as solvent, all other batches had a stoichiometric molar ratio of DMC/HDA (= 2) required for the methoxycarbonylation of HDA by DMC. It was found that in the absence of solvent, the conversion of HDA, the selectivity to

Table 1 Effect of solvent on methoxycarbonylation of HDA by DMC using CH_3COONa as catalyst[a]

Solvent	χ_{HDA}[c] (%)	S_i[d] (%)			$Y_{2,GC}$[e] (%)	$Y_{2,isolated}$[f] (%)
		1	**2**	**3–7**		
CH_3OH	100	2.6	96.1	1.3	96.1	87.2
DMC	98	3.9	93.6	2.6	91.7	81.5
CH_3CN	97	20.4	80.7	2.0	78.3	62.8
None[b]	74	29.2	65.8	5.0	48.7	21.9

[a] HDA: 100 mmol; DMC: 200 mmol (16.8 ml); CH_3COONa: 2.0 g (24.4 mmol); solvent: 50 ml; reaction time: 10 h; reaction temperature: 348 K. [b] No solvent was employed. [c] χ_{HDA}: conversion of HDA. [d] S_i: selectivity to component i in the products mixture [e] $Y_{2,GC}$: GC yield of **2**. [f] $Y_{2,isolated}$: isolated yield of **2**.

2 and the yield of **2** were only 74.0, 65.8 and 48.7%, respectively. When a solvent was employed, the conversion of HDA, the selectivity to **2** and the yield of **2** increased to above 97.0, 80.7 and 78.3%, respectively. This indicates that the solvent stimulated the methoxycarbonylation of HDA by DMC. The stimulation by the solvent was in the order CH_3OH > DMC > CH_3CN > no solvent. Though the isolated yields of **2** were lower than the GC ones, due to the loss of **2** during re-crystallization, they still remained in the order CH_3OH > DMC > CH_3CN > no solvent. The above observation is useful, because DMC is, on the one hand, one of the main raw materials employed in the synthesis of **2**, and on the other hand, is currently manufactured *via* the reaction between methanol and CO_2.[9,10] Consequently, the product mixture (DMC + CH_3OH) obtained during the DMC synthesis can be directly employed in the synthesis of **2**. The use of DMC or methanol as solvent is consistent with the "green chemistry rule", to pursue a synthesis process using as little solvent and operational steps as possible.[23]

The above result reveals that both methanol and DMC are good solvents for the methoxycarbonylation of HDA by DMC. Since methanol is also a by-product and DMC is one of the reactants of the methoxycarbonylation of HDA by DMC, it is kinetically favorable for the amount of methanol to be reduced and that of DMC increased. Therefore, in the following experiments, as illustrated by Fig. 1–3, batches consisting of 50 mmol HDA, 200 mmol (16.8 ml) DMC and 20 ml CH_3OH, which have a higher molar ratio of DMC/HDA and a lower amount of methanol than those used in Table 1, were employed. One can consider that in these experiments the methoxycarbonylation of HDA by DMC takes place in the presence of DMC and methanol as co-solvents. These reactions were conducted at 348 K for 6 h, using 0.6 g (7.3 mmol) of CH_3COONa as catalyst. By changing the reaction temperature, reaction time and amount of CH_3COONa, the effects of these factors were investigated.

Fig. 1 presents the effect of reaction temperature. One can see that the selectivity to **3–7** is much lower than those to **1** and **2** at all temperatures tested. With increasing reaction temperature, the selectivity to **3–7** increases only slightly. This occurs because the activation energy for N-methylation is much larger than that for methoxycarbonylation.[17] The selectivity to **2** first increases, attains a maximum at 348 K, followed by a slight decrease, with increasing reaction temperature. The change of the selectivity to **1** with temperature exhibits the opposite trend, compared to that to **2**. This indicates that the activation energy for the formation of **2** is higher than that for **1**. The decrease in the selectivity to **2** and

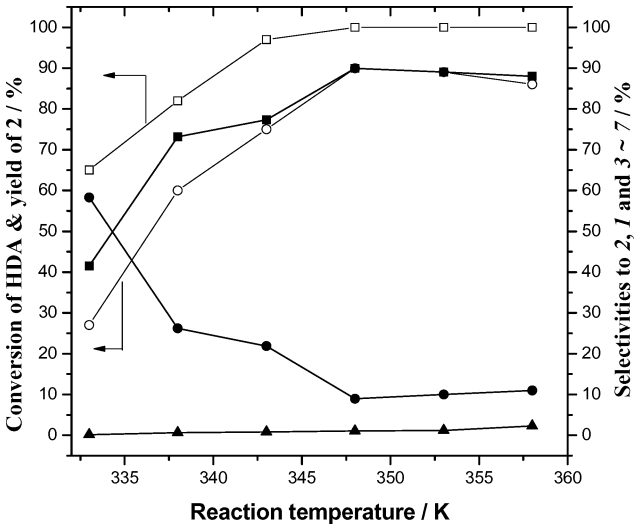


Fig. 1 Effect of reaction temperature on HDA conversion, yield of **2** and selectivities to reaction products. Reaction conditions: HDA, 50 mmol; CH_3COONa, 0.6 g; DMC, 200 mmol; time, 6 h; CH_3OH, 20 ml. (Legend: (□) HDA conversion; (○) yield of **2**; (■), (●) and (▲), selectivities to **2**, **1** and **3–7**, respectively.)

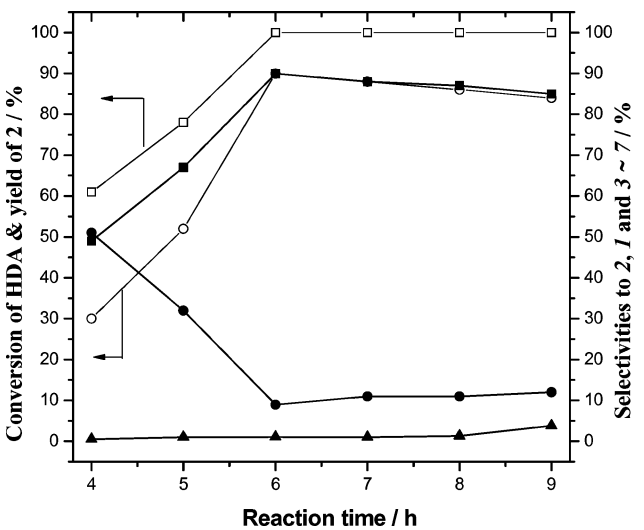


Fig. 2 Effect of reaction time on HDA conversion, yield of **2** and selectivities to reaction products. Reaction conditions: HDA, 50 mmol; CH_3COONa, 0.6 g; DMC, 200 mmol; temperature, 348 K; CH_3OH, 20 ml. (Legend: (□) HDA conversion; (○) yield of **2**; (■), (●) and (▲), selectivities to **2**, **1** and **3–7**, respectively.)

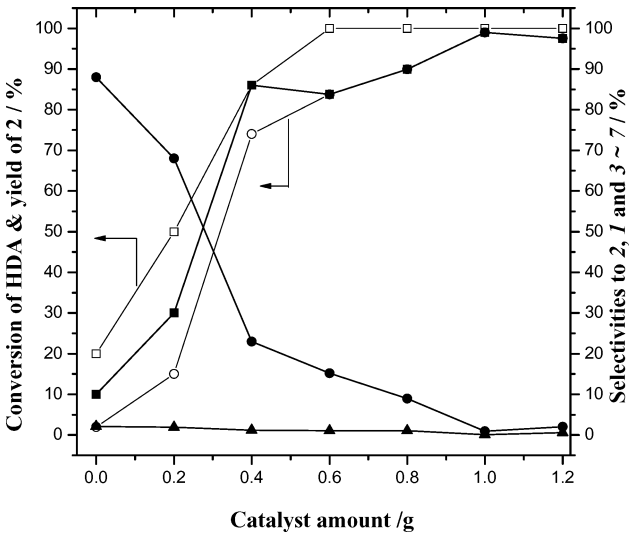


Fig. 3 Effect of amount of catalyst on HDA conversion, yield of **2** and selectivities to reaction products. Reaction conditions: HDA, 50 mmol; DMC, 200 mmol; time, 6 h; temperature, 348 K; CH_3OH, 20 ml. (Legend: (□) HDA conversion; (○) yield of **2**; (■), (●) and (▲), selectivities to **2**, **1** and **3**–**7**, respectively.)

the increase of that to **1** at temperatures higher than 348 K may be due to the decomposition of **2** to **1**, because **1** is the primary and **2** the secondary product in the methoxycarbonylation of HDA by DMC.[14] With increasing temperature, both the conversion of HDA and the yield of **2** increase. At temperatures ≥348 K, the conversion increases to and is maintained at 100%, however, the yield of **2** decreases, as a result of the decrease of the selectivity to **2**. Consequently, the optimum temperature for the production of **2** *via* the methoxycarbonylation of HDA by DMC is around 348 K.

Fig. 2 outlines the effect of reaction time. One can see that for all reaction times tested, the selectivity to **3**–**7**, which increases very slightly with increasing reaction time, was much lower than those to **1** and **2**. By prolonging the reaction time, the selectivity to **2** increases, attaining a maximum at 6 h, followed by a decrease. The selectivity to **1** exhibits, however, the inverse trend, compared to that to **2**, with increasing reaction time. This occurs because **2** is a secondary product formed *via* the further reaction of **1**. Both the conversion of HDA and the yield of **2** increase rapidly when the reaction time increases up to 6 h. The further increase of reaction time results in an approach towards a HDA conversion of 100%, but by a decrease of the yield of **2**, caused by the decomposition of **2** to **1**. Consequently, the optimum reaction time is 6 h.

Fig. 3 presents the effect of the amount of CH_3COONa. One can see that in the presence of this catalyst, the conversion of HDA, the yield of **2** and the selectivity to **2** increase but the selectivity to **1** decreases, compared to those in the absence of this catalyst. The selectivity to **3**–**7** is much lower than those to **1** and **2** and almost unchanged in the absence or in the presence of various amounts of catalyst. When 0.6 g (7.3 mmol) of catalyst is employed, a 100% conversion of HDA is achieved. With a further increase of the amount of catalyst in the range of 0.6 to 1.0 g (12.2 mmol), the conversion of HDA remains 100%, the selectivity to **2** increases and that to **1** decreases. These results indicate that the catalyst stimulates the formation of both **1** and **2**, with **1** as the primary product and **2** as the secondary one *via* the further reaction of **1**. After HDA was completely converted, the increase of the amount of catalyst stimulated the conversion of **1** to **2**, because HDA is no longer available for the formation of **1**. When the amount of catalyst is higher than 1.0 g, the selectivity to **2** decreases slightly and that to **1** increases. This occurs most likely because the decomposition of **2** to **1** becomes predominant, when **1** is no longer available for the formation of **2**. Consequently, the optimum amount of catalyst is 1.0 g (12.2 mmol).

Table 2 presents the results of methoxycarbonylation of HDA by DMC in the absence and in the presence of CH_3COONa as catalyst; for comparison, the results obtained with other catalysts reported in the literature are also included. One can see that both the conversion of HDA, the selectivity to **2** and the yield of **2** are small in the absence of the catalyst but large in its presence. CH_3COONa appears to be the most efficient catalyst for the methoxycarbonylation of HDA by DMC under comparable reaction conditions, exhibiting a 100.0% conversion of HDA and a 99% yield of **2** at 348 K in 6 h.

3.2. On the reaction mechanism

It is known that the methoxycarbonylation of amines by DMC is the result of a S_N2 nucleophilic attack by amines on the carbonyl

Table 2 Methoxycarbonylation of 1,6-hexanediamine by DMC with various catalysts

	Batch composition			Reaction conditions			S_i[b](%)			Y_2[c]
Catalyst and its quantity	HDA/mmol	DMC/mmol	CH_3OH/ml	T/K	Time/h	χ_{HDA}[a](%)	**1**	**2**	**3**–**7**	(%)
None	50.0	200.0	20.0	348	6	16.0	51.9	25.6	22.5	4.1
CH_3COONa (1.0 g/ 12.2 mmol)	50.0	200.0	20.0	348	6	100.0	0.9	99.0	0.1	99.0
$Bi(NO_3)_3$ (0.12 mmol)[14]	3.5	21.0	3.0	353	18	100.0	11.0	84.0	5.0	84.0
$NaOCH_3$ (28.2 mmol)[20]	392.0	2875.0	123.8	343	1	99.5	*N A*[d]	98.9	*N A*	98.4
$MIm(CH_2)_4SO_3HTfO$ (3.26 mmol 1 wt% ionic liquids)[21]	400.0	820.0	0	353	4	100.0	*N A*	95.0	*N A*	95.0
$Sc(OTf)_3$ (0.295 mmol)[17]	11.3	59.4	0	293	144	100.0	*N A*	88.0	*N A*	88.0
$ZnAlPO_4$ (1.0 g)[22]	200.0	1600.0	0	353	8	99.0	3.9	88.6	7.5	87.7

[a] χ_{HDA}: conversion of HDA. [b] S_i: selectivity to component i in products mixture. [c] Y_2: yield of **2**; all the rows in this column are GC yields, except the second row from bottom, which is isolated yield. [d] N. A.: not available.

carbon of DMC. Whereas a significantly higher basicity of the amine than that of the leaving group (methoxyl) is required,[4,24-26] methoxycarbonylation depends mostly upon the reactivity of DMC. The factors that increase the electrophilicity of carbonyl carbon promote this reaction. An electron-withdrawing effect exerted on the carbonyl group facilitates its reaction with a nucleophilic amine.[4,24,27] Lewis acidic catalysts were often employed to promote the methoxycarbonylation of amines by DMC. For example, over the Lewis acidic catalyst $ZnAlPO_4$,[22] dimethylhexane-1,6-dicarbamate is formed *via* a catalytic cycle, which involves the activation of DMC due to the coordination of the carbonyl oxygen with Zn(II) and the nucleophilic attack by the amino group of HDA on the carbonyl carbon of the activated DMC. The absence of acidity in the CH_3COONa catalyst suggests that a different mechanism may be involved in the methoxycarbonylation of HDA by DMC over this catalyst. Mason and Charles[19] found that the organic diisocyanate is formed *via* the reaction between diphenyl carbonate and an organic diformamide at temperatures higher than 473 K. The organic diformamide can be employed as such or can be generated *in situ* by reacting the corresponding diamine with formic acid. Besides the diisocyanate, byproducts such as dicarbamate, mixed isocyanate/carbamate and phenyl formiate are also obtained. While the mechanism was not provided by the authors, the carbamate was most likely the key intermediate in the formation of isocyanate from formamide and carbonate, because the thermolysis of the carbamate yields isocyanate. For the methoxycarbonylation of HDA by DMC, catalyzed by CH_3COONa, it is suggested that the N-substituted acetamide, $RNHCOCH_3$, is formed *in situ via* the reaction between HDA and CH_3COONa and further contributes to the formation of carbamate by reacting with DMC. The following experiments provide evidence in this direction.

Experiment A: Identification of reaction intermediates and products *via* a two-step reaction for the methoxycarbonylation of HAD by DMC using CH_3COONa as catalyst. A mixture of HDA (50 mmol), CH_3COONa (1.0 g/12.2 mmol) and CH_3OH (20 ml) was first subjected to reaction at 337 K for 1 h. Chemical analysis and FT-IR identified that N-substituted acetamide (ESI: Fig. S4 and Table S4) and NaOH (ESI: Section 5) were formed *via* this reaction. Then, 200 mmol (16.8 ml) of DMC were added to the above products mixture for further reaction. After heating to 348 K and being kept at this temperature for reaction for 5 h, the product mixture was analyzed by GC and GC-MS and the results revealed that the conversion of HDA was 100% and that the selectivities to **1**, **2** and **3**–**7** were 0.9%, 99% and 0.1%, respectively. The product mixture was also vacuum-distilled until a white powder was generated. The FT-IR characterization of the white powder indicated the presence of mainly **2**, much less **1** and very little **3**–**7** (ESI: Fig. S5 and Table S5). The above results indicate that both the N-substituted acetamide and NaOH were formed as intermediates, which were consumed during the formation of carbamates, by the reaction between HDA and CH_3COONa.

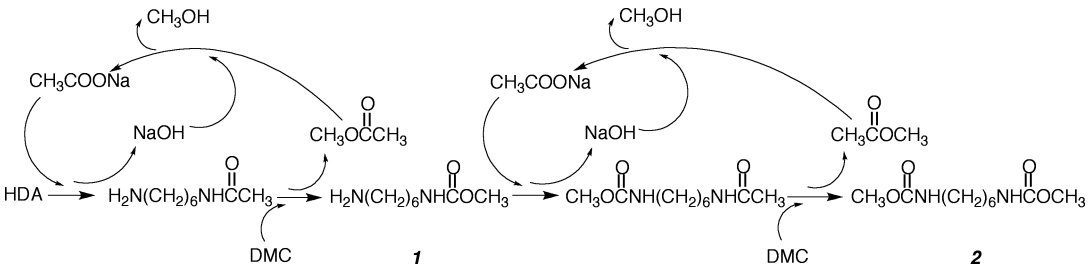
Experiment B: Role of the reaction intermediates N-substituted acetamide and NaOH. A mixture of HDA (10 mmol), CH_3COONa (0.8 g/9.8 mmol) and CH_3OH (20 ml) was first subjected to reaction at 337 K for 4 h. Then, the formed NaOH in the form of white floccules was removed by centrifugal separation. The supernatant liquid was characterized by FT-IR and the results indicated the presence of the N-substituted acetamide, HDA and acetate (the spectrum was similar to that of Fig. S4 in ESI and for this reason is not provided). To the above supernatant liquid, an excess amount of DMC was added. The resulted mixture was heated to 348 K for further reaction, and after 6 h, the product mixture was vacuum-distilled. A white powder was finally obtained and characterized by FT-IR, which indicated the presence of di-carbamate and mono-carbamate (the spectrum was similar to that of Fig. S5 in ESI and therefore is not given). The above results indicate that the N-substituted acetamide plays the role of an active intermediate and that NaOH is not a catalyst for the formation of carbamates during the methoxycarbonylation of HDA by DMC, since the separation of NaOH from the reaction system did not stop the formation of carbamate.

One may argue that a part of NaOH was dissolved into the above supernatant liquid, and after the addition of DMC to the supernatant liquid, this residual NaOH catalyzed the methoxycarbonylation reaction. To clarify this issue, we conducted an experiment, which can be described as follows. HDA (10 mmol), DMC (40 mmol) and NaOH (0.4 g/10 mmol) were dispersed into CH_3OH (20 ml) with stirring at room temperature. Then, the mixture was heated to 348 K and kept at that temperature for 6 h. After cooling to room temperature, a few white floccules appeared. The floccules were recovered by centrifugal separation and identified to be NaOH. The GC-MS analysis of the supernatant liquid indicated the presence of HDA, DMC and methanol; no other component could be identified. This result confirms the conclusion that NaOH is not a catalyst for the formation of carbamates *via* the methoxycarbonylation of HDA by DMC.

Experiment C: Methoxycarbonylation of acetamide by DMC in the absence of any catalyst. Acetamide (50 mmol) was mixed with DMC (200 mmol/16.8 ml) and methanol (20 ml) with stirring at room temperature, and then the temperature was raised to 348 K and kept at that temperature for reacting for 6 h. After that, the reaction mixture was vacuum-distilled, resulting in a white powder, which was characterized by FT-IR (ESI: Fig. S6 and Table S6). The results revealed the presence of methyl carbamate (CH_3OCONH_2), besides the unconverted acetamide. It indicates that an amide such as the acetamide can interact directly with DMC to generate carbamate.

Experiment D: Methoxycarbonylation of HDA by DMC using either CH_3COOH or $(CH_3CO)_2O$ as catalyst. DMC (200 mmol/16.8 ml) and methanol (20 ml) were first mixed and then HDA (50 mmol) was added with stirring at room temperature, resulting in a clear solution. After that, CH_3COOH (0.8 g/13.3 mmol) was added, and it was found that a white fume burst out and a few small white crystals appeared in the solution, releasing a large amount of heat. The crystals were sampled and identified to be N-substituted ammonium acetate, which is formed *via* the neutralization reaction of CH_3COOH with HDA, as shown by eqn (1):

$$CH_3COOH + H_2N(CH_2)_6NH_2 \rightarrow CH_3COOH_3N(CH_2)_6NH_2 \quad (1)$$



Scheme 1 Possible mechanism for the methoxycarbonylation of HDA by DMC using CH_3COONa as catalyst.

After the batch (HDA + DMC + CH_3COOH + CH_3OH) was heated to 348 K and kept at that temperature for 6 h, neither **1** nor **2** could be identified. When the CH_3COOH in the (HDA + DMC + CH_3COOH + CH_3OH) batch was replaced by $(CH_3CO)_2O$ and heated at 348 K for 6 h, again, neither **1** nor **2** could be identified. This occurred because though the N-substituted acetamide may be formed *via* the ammonolysis of $(CH_3CO)_2O$ by HDA (eqn (2)), this reaction is competing with both the alcoholysis of $(CH_3CO)_2O$ by methanol (eqn (3)) and the neutralization of HDA by CH_3COOH (eqn (1)):

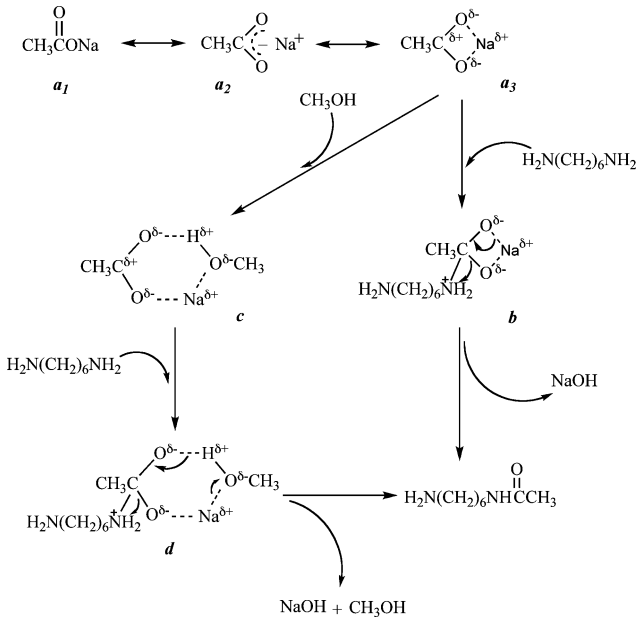
$$H_2N(CH_2)_6NH_2 + (CH_3CO)_2O \rightarrow CH_3COHN(CH_2)_6NH_2 + CH_3COOH \quad (2)$$

$$CH_3OH + (CH_3CO)_2O \rightarrow CH_3COOCH_3 + CH_3COOH \quad (3)$$

Reactions (1) and (3) proceed at much higher rates than reaction (2), thus transforming HDA mainly into the N-substituted ammonium acetate. Thus, not enough N-substituted acetamide remained available for the formation of carbamates (**1** and **2**). The above results indicate that, neither CH_3COOH nor $(CH_3CO)_2O$ play the role of catalyst in the methoxycarbonylation of HDA by DMC, since the acidic environment they provided rapidly transformed HDA into the N-substituted ammonium acetate instead of N-substituted acetamide.

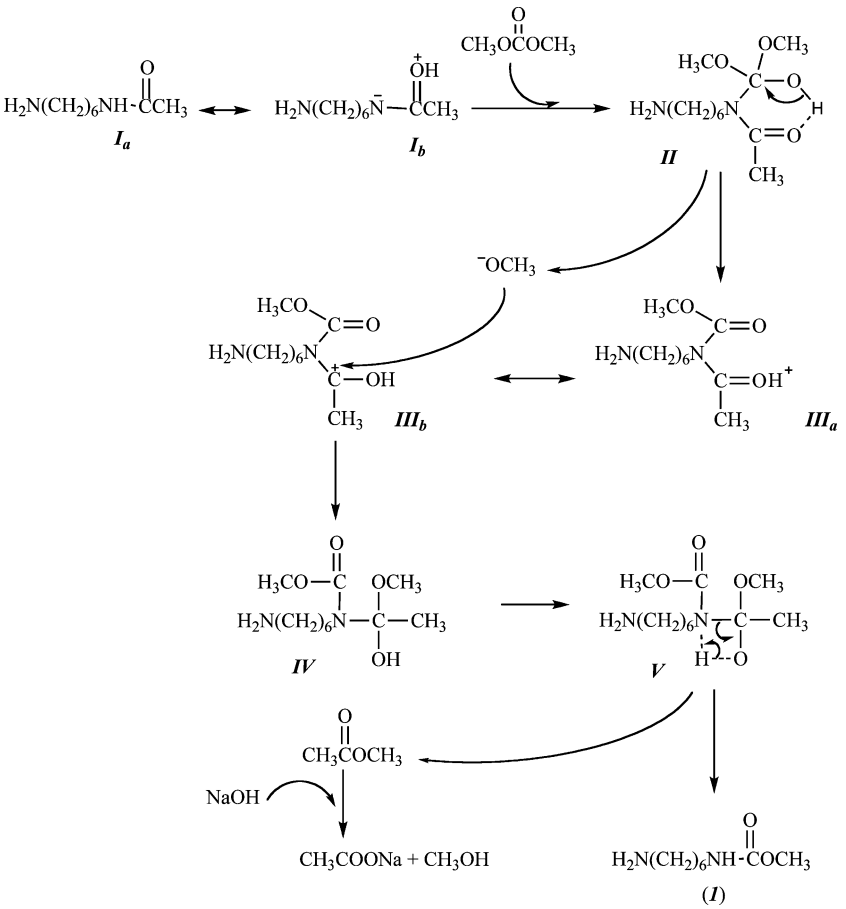
Summing up the results of experiments A to D, one can conclude that during the methoxycarbonylation of amines by DMC, CH_3COONa plays the role of a catalyst. The N-substituted acetamide, $RNHCOCH_3$, and NaOH are first formed *via* the reaction between HDA and CH_3COONa. NaOH does not play the role of a catalyst but provides an alkaline environment that ensures the conversion of HDA to N-substituted acetamide instead of N-substituted ammonium acetate. The observation that an alkaline environment is favorable to the methoxycarbonylation of amines by DMC has already been reported in the literature.[4,9] The N-substituted acetamide constitutes the key intermediate product and its further reaction with DMC results in the formation of the carbamates **1** and **2**. A possible mechanism, shown in Scheme 1, for the methoxycarbonylation of HDA by DMC, with CH_3COONa as catalyst, is proposed, and more details are provided in Schemes 2–4.

In the methoxycarbonylation of amines by DMC, an acidic catalyst was usually employed to activate the DMC. However, the nucleophilicity of the amine is potentially reduced by the interaction between the basic amine and the acidic catalyst. In the methoxycarbonylation of amines by DMC, in the presence of the basic CH_3COONa catalyst, N-substituted acetamide is first formed *via* the reaction between HDA and CH_3COONa.

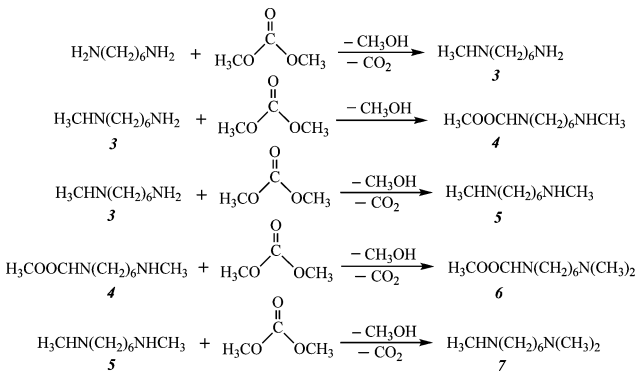


Scheme 2 Possible mechanism for the formation of N-substituted acetamide *via* the reaction between HDA and CH_3COONa.

As shown in Scheme 2, in the absence of a solvent, CH_3COONa may exist as an equilibrium among a few resonant structures, *e.g.*, $\mathbf{a_1}$, $\mathbf{a_2}$ and $\mathbf{a_3}$. The positively charged carbon of $\mathbf{a_3}$ is attacked by the nucleophilic HDA, generating the intermediate **b**. The ring-opening and rearrangement of **b** results in N-substituted acetamide and NaOH. Due to the large strain of the tetratomic ring, the equilibrium among $\mathbf{a_1}$, $\mathbf{a_2}$ and $\mathbf{a_3}$ may be displaced to $\mathbf{a_1}$ and $\mathbf{a_2}$, generating less $\mathbf{a_3}$ and in turn less **b** and N-substituted acetamide. While N-substituted acetamide has been identified as the active intermediate product for the formation of carbamates, a relatively low yield of carbamates is expected in the absence of a solvent. When a polar non-protic solvent, *e.g.*, CH_3CN, is employed, $\mathbf{a_3}$ can be stabilized by the dipole–dipole interactions between solvent and $\mathbf{a_3}$. As a result, the yield of carbamates is increased. When a non-polar non-protic solvent, *e.g.*, DMC, is employed, a higher yield of carbamates than for the polar non-protic solvent CH_3CN is obtained. This occurs because, whereas no stabilization of $\mathbf{a_3}$ is provided by the solvent, the increase in the amount of DMC, as one of the reactants of the methoxycarbonylation, promotes the reaction in the right direction. When a polar protic solvent is employed, *e.g.*, CH_3OH, a hexatom-ringed intermediate **c** may be formed between $\mathbf{a_3}$ and CH_3OH. The higher stability of **c** than $\mathbf{a_3}$ results in a higher yield



Scheme 3 Possible mechanism for the formation of carbamate *via* the reaction between N-substituted acetamide and DMC.



Scheme 4 Possible mechanism for the formation of **3**–**7** during the methoxycarbonylation of HDA by DMC using CH_3COONa as catalyst.

of carbamates when CH_3OH is employed as solvent rather than CH_3CN.

The formation of carbamates is a result of the reaction between the N-substituted acetamide and DMC. As shown in Scheme 3, the N-substituted acetamide is expected to exist as an equilibrium between the resonant structures $\mathbf{I_a}$ and $\mathbf{I_b}$. With the proton of $\mathbf{I_b}$ transferred to the carbonyl oxygen of DMC, the DMC becomes activated and the negatively charged N in the $\mathbf{I_b}$ becomes more active in the nucleophilic attack on the carbonyl carbon of the DMC. This results in the formation of a hexatomic ring intermediate **II**. The ring-opening and rearrangement of **II** generates the intermediate $\mathbf{III_a}$ and the methoxyl group (CH_3O^-), both driven by the resonance between $\mathbf{III_a}$ and $\mathbf{III_b}$. The positive charge of the carbon in $\mathbf{III_b}$ enables its attack by CH_3O^-, resulting in the intermediate **IV**. Due to the hydrogen bonding between N, O and H in **IV**, a tetratomic ring intermediate **V** is formed, and the ring-opening and rearrangement of **V** generates the carbamate **1** and the methyl acetate. The reaction between methyl acetate and NaOH, which occurs concomitantly with the formation of the N-substituted acetamide through the reaction between HDA and CH_3COONa, recovers the CH_3COONa catalyst and produces the byproduct CH_3OH. Similar steps and intermediates are expected to occur for the reaction between **1** and DMC, in the presence of CH_3COONa as catalyst, to produce the desired product **2**. We tried to react N,N′-dimethyl formamide (DMF) with DMC, but no carbamates (**1** and **2**) could be identified. This probably occurred because no hydrogen atom can be provided by DMF for the formation of a hexatomic ring intermediate, and for this reason, it cannot generate carbamates. This indicates that the formation of the intermediate **II** in the above steps is essential.

The formation of the N-alkylated byproducts **3**–**7**, identified in the present work, may be a result of a nucleophilic attack of the amino groups of the amines on the methoxyl carbon of DMC, as shown in Scheme 4. Because of the ambident electrophilicity, DMC may react with nucleophiles not only at the carbonyl group but also at the methyl moiety.[17] When a Lewis acidic

catalyst was employed in the methoxycarbonylation of amines by DMC, the carbonyl in DMC was activated by the catalyst, inducing a positive charge on the carbonyl carbon and further on the methoxyl carbon.[15] The nucleophilic attack of the amines on the positively charged carbons results in the formation of both carbamates and N-alkylated amines. High selectivities to N-alkylated amines were also achieved at relatively high reaction temperatures.[17] In the present work, the basic CH_3COONa catalyst promotes the methoxycarbonylation of amines by DMC *via* a mechanism very different from that of the Lewis acidic catalysts. Carbamates are formed as a result of the reaction between DMC and the N-substituted acetamides, which are generated by reacting amines with CH_3COONa. It is expected that the positive charge of the methoxyl carbon of DMC in the presence of a basic catalyst will be smaller than that for a Lewis acidic catalyst. This might be another reason for the extremely low selectivity to **3**–**7** observed in our work, besides the relatively low reaction temperature (lower than 360 K) employed compared with that used in the literature for N-alkylation of amines.

4. Conclusion

It is demonstrated, for the first time, that CH_3COONa is a very effective catalyst for the production of dimethylhexane-1,6-dicarbamate (**2**) *via* the methoxycarbonylation of HDA by DMC, when CH_3OH or even DMC itself is used as solvent. At a temperature of 348 K and reaction time of 6 h, a 100% conversion of HDA with a 99% selectivity to **2** could be achieved. It is shown that the catalytic cycle of the methoxycarbonylation of HDA by DMC with CH_3COONa as catalyst consists mainly of three steps: the formation of the N-substituted acetamide and NaOH *via* the reaction between HDA and CH_3COONa, the generation of carbamates and methyl acetate *via* the reaction between the N-substituted acetamide and DMC, and the regeneration of the CH_3COONa catalyst, releasing methanol as a byproduct, *via* the reaction between the NaOH and methyl acetate. The yield of carbamates is affected largely by the solvent, most likely due to the different stabilities of the reaction intermediates, which depend on the nature of the solvent.

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