

Alkylation of Ammonium Salts Catalyzed by Imidazolium-Based Ionic Liquid Catalysts

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Abstract: Quaternary ammonium salts were synthesized from ammonium salts and dialkyl carbonates over imidazolium ionic liquid catalysts. The reaction gave almost stoichiometric amounts of the quaternary ammonium salts for halides and nitrates. It was found that the electron-donating property of the alkyl moieties of ammonium cations, the electrophilic nature of the alkyl group of the carbonate, the acidity of the acid that the anion of the ammonium salt corresponds to, and the steric hindrance of the ammonium salts and the dialkyl carbonates are the

key factors that influence the yields of quaternary ammonium salts. Strong electron-donating alkyl groups on the nitrogen atom of the ammonium salt, electron-withdrawing groups on the methylene carbon of dialkyl carbonate, and weaker steric hindrance of the starting ammonium salts and dialkyl carbonates favor the alkylation reaction of ammonium salts.

Keywords: alkylation; ammonium salts; dialkyl carbonates; ionic liquid; quaternary ammonium salts

Introduction

Ionic liquids (ILs) or room-temperature molten salts have attracted a lot of attention of chemists in recent years.^[1-21] Representing a new class of non-molecular ionic compounds, ionic liquids were extensively investigated as reaction media (solvents),^[14] phase-transfer catalysts,^[17] surfactants,^[18] molecular probes and ionic channel blockers,^[19] synthesis templates,^[20] and IL crystal applications.^[21] The reason why ionic liquids attract the increasing attention of chemists is that they have found potential applications in chemical reactions as solvents and/or catalysts. 1-Ethyl-3-methylimidazolium bromide ([EMIM]Br), which can be readily prepared from 1-methylimidazole and ethyl bromide,^[22] has found applications as reaction media and/or catalysts for organic reactions. Hence, in the current study, we explore the possibility of using [EMIM]Br as a catalyst in the synthesis of quaternary ammonium salts.

Since quaternary ammonium salts are widely used as surfactants, phase-transfer catalysts, ionic liquid solvents, and liquid-crystalline amphiphiles,^[21,23] there are many investigations devoted to their synthesis. Quaternary ammonium salts are generally synthesized

by reacting tertiary amines with alkyl halides. Wang et al.^[24] reported a facile method to synthesize quaternary ammonium salts by the direct reaction of amines with alcohols over acidic zeolites, such as H-Y and HZSM-5. When synthesizing quaternary ammonium salts by these methods, the anions of the quaternary ammonium salts are usually limited to halides. Among them, quaternary ammonium chlorides and quaternary ammonium bromides were the most commonly reported. In the case of synthesizing quaternary ammonium salts with anions other than halides, an anion-exchange process is necessary.^[25-27] In order to avoid this problem, Mori et al.^[27] patented a process for their synthesis by reacting a tertiary amine with a dialkyl carbonate to obtain a quaternary ammonium methyl carbonate, and then reacting the quaternary ammonium methyl carbonate with the corresponding acid to obtain the quaternary ammonium salt with the right anion. Compared to the anion-exchange process (from quaternary ammonium halides), Mori et al.'s method is more efficient.

In the current work, various quaternary ammonium salts were synthesized from ammonium salts and dialkyl carbonates in imidazolium ionic liquids. On comparing the current method with the previously re-

ported ones, it is remarkable with respect to the use of ammonium salts and dialkyl carbonates^[28,29] as feed stocks, which are less volatile and toxic than amines, amides, alkyl halides, and alkyl sulfates. Although there have also been reports to synthesize quaternary ammonium salts by employing dialkyl carbonates as alkylation reagents,^[27,30] these methods are limited to those cases where tertiary amines are used as reactants. In the current studies, all kinds of salts of amines, such as tertiary, primary, secondary amines, and even ammonia can be alkylated by dialkyl carbonates to furnish quaternary ammonium salts.

Results and Discussion

The alkylation results of ammonium bromide with dimethyl carbonate (DMC) as alkylation reagent are listed in Table 1. When the reaction was carried out in the absence of catalyst, only a trace of tetramethylammonium bromide (yield: 0.4%) was formed. Among the tested catalysts, an almost quantitative yield (96.5%) of tetramethylammonium bromide was obtained over 1-ethyl-3-methylimidazolium ([EMIM]) bromide. When 1-butyl-3-methylimidazolium ([BMIM]) bromide, [EMIM]CH₃CO₂, and [BMIM]CH₃CO₂ were used as catalysts, the yields decreased to 84.7%, 72.5%, and 74.3%, respectively. Even lower yields were obtained over [EMIM]BF₄ and [EMIM]₂SO₄. Obviously, the alkylation reaction of ammonium salts is accelerated by the IL catalysts, but the catalytic activity is strongly dependent upon the nature of the imidazolium cations and the counteranions of the imidazolium ion. In the cases of imidazolium bromides, the more bulky *n*-butyl-substituted imidazolium ring is relatively less active to the alkylation reaction of ammonium salts than the ethyl-substituted ring.

When ammonium salts having different N-substituent groups and different anions are reacted with DMC in the presence of [EMIM]Br catalyst, the results listed in Table 2 are obtained. In those cases

Table 1. Reactions of ammonium bromide with dimethyl carbonate over different imidazolium ionic liquid catalysts.^[a]

Entry	Reactants	Catalyst	Yield [%]
1	NH ₄ Br/DMC	[EMIM]Br	96.5
2	NH ₄ Br/DMC	[BMIM]Br	84.7
3	NH ₄ Br/DMC	[EMIM]CH ₃ CO ₂	72.5
4	NH ₄ Br/DMC	[BMIM]CH ₃ CO ₂	74.3
5	NH ₄ Br/DMC	[EMIM]BF ₄	41.6
6	NH ₄ Br/DMC	[BMIM]BF ₄	52.4
7	NH ₄ Br/DMC	[EMIM] ₂ SO ₄	11.3
8	NH ₄ Br/DMC	No catalyst	0.4

^[a] Reaction conditions: ammonium bromide (2.0 mmol), DMC (8.0 mmol), catalyst (0.8 mmol), 443 K, 8 h.

Table 2. Reactions of dimethyl carbonate with ammonium salts bearing different anions over [EMIM]Br catalyst.^[a]

Entry	Reactants	Product	Yield [%]
1	NH ₄ Cl/DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H}_3\text{C} \end{array} \right] \text{Cl}$	96.0
2	NH ₄ Br/DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H}_3\text{C} \end{array} \right] \text{Br}$	96.5
3	NH ₄ NO ₃ /DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H}_3\text{C} \end{array} \right] \text{NO}_3$	96.4
4	(NH ₄) ₂ SO ₄ /DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H}_3\text{C} \end{array} \right]_2 \text{SO}_4$	70.4
5	(NH ₄) ₂ C ₂ O ₄ /DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H}_3\text{C} \end{array} \right]_2 \text{C}_2\text{O}_4$	47.6
6	NH ₄ CH ₃ CO ₂ /DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H}_3\text{C} \end{array} \right] \text{OAc}$	44.3
7	(NH ₄) ₂ CO ₃ /DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H}_3\text{C} \end{array} \right]_2 \text{CO}_3$	44.8
8	(NH ₄) ₃ PO ₄ ·3H ₂ O/DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H}_3\text{C} \end{array} \right]_3 \text{PO}_4$	43.1
9	[(CH ₃) ₃ HN]Cl/DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H}_3\text{C} \end{array} \right] \text{Cl}$	> 99
10	[(CH ₃) ₃ HN]Br/DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H}_3\text{C} \end{array} \right] \text{Br}$	> 99
11	[(CH ₃) ₃ HN]NO ₃ /DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H}_3\text{C} \end{array} \right] \text{NO}_3$	> 99
12	[(CH ₂ CH ₃) ₂ H ₂ N]Cl/DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5 \end{array} \right] \text{Cl}$	97.4
13	[(CH ₂ CH ₃) ₂ H ₂ N]Br/DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5 \end{array} \right] \text{Br}$	> 99
14	[(CH ₂ CH ₃) ₂ H ₂ N]NO ₃ /DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5 \end{array} \right] \text{NO}_3$	98.3
15	[(CH ₂ CH ₃) ₂ H ₂ N] ₂ SO ₄ /DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5 \end{array} \right]_2 \text{SO}_4$	54.7
16	[(CH ₂ CH ₃) ₂ H ₂ N] ₂ C ₂ O ₄ /DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5 \end{array} \right]_2 \text{C}_2\text{O}_4$	73.2
17	[(CH ₂ CH ₃) ₂ H ₂ N]CH ₃ CO ₂ /DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5 \end{array} \right] \text{OAc}$	78.2
18	[(CH ₂ CH ₃) ₂ H ₂ N] ₃ PO ₄ /DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5 \end{array} \right]_3 \text{PO}_4$	48.6
19	[(CH ₂ CH ₃) ₃ HN]Cl/DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5 \end{array} \right] \text{Cl}$	> 99
20	[(CH ₂ CH ₃) ₃ HN]Br/DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5 \end{array} \right] \text{Br}$	96.9
21	[(CH ₂ CH ₃) ₃ HN]NO ₃ /DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5 \end{array} \right] \text{NO}_3$	98.2
22	[(CH ₂ CH ₃) ₃ HN] ₂ SO ₄ /DMC	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5 \end{array} \right]_2 \text{SO}_4$	62.2

Table 2. (Continued)

Entry	Reactants	Product	Yield [%]
23	$[(\text{CH}_2\text{CH}_3)_3\text{HN}]_2\text{C}_2\text{O}_4/\text{DMC}$	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \text{C}_2\text{H}_5 \end{array} \text{N} \begin{array}{c} \text{C}_2\text{H}_5 \\ \text{C}_2\text{H}_5 \end{array} \right]_2\text{C}_2\text{O}_4$	73.3
24	$[\text{NH}_3(n\text{-C}_{12}\text{H}_{25})]\text{Cl}/\text{DMC}$	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \text{H}_3\text{C} \end{array} \text{N} \begin{array}{c} \text{CH}_3 \\ n\text{-C}_{12}\text{H}_{25} \end{array} \right] \text{Cl}$	> 99
25	$[\text{NH}_3(n\text{-C}_{12}\text{H}_{25})]\text{Br}/\text{DMC}$	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \text{H}_3\text{C} \end{array} \text{N} \begin{array}{c} \text{CH}_3 \\ n\text{-C}_{12}\text{H}_{25} \end{array} \right] \text{Br}$	> 99
26	$[\text{NH}_3(n\text{-C}_{12}\text{H}_{25})]\text{NO}_3/\text{DMC}$	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \text{H}_3\text{C} \end{array} \text{N} \begin{array}{c} \text{CH}_3 \\ n\text{-C}_{12}\text{H}_{25} \end{array} \right] \text{NO}_3$	> 99
27	$[\text{NH}_3(n\text{-C}_{12}\text{H}_{25})]_2\text{SO}_4/\text{DMC}$	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \text{H}_3\text{C} \end{array} \text{N} \begin{array}{c} \text{CH}_3 \\ n\text{-C}_{12}\text{H}_{25} \end{array} \right]_2\text{SO}_4$	97.3
28	$[\text{NH}_3(n\text{-C}_{12}\text{H}_{25})]\text{CH}_3\text{CO}_2/\text{DMC}$	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \text{H}_3\text{C} \end{array} \text{N} \begin{array}{c} \text{CH}_3 \\ n\text{-C}_{12}\text{H}_{25} \end{array} \right] \text{OAc}$	84.4
29	$[\text{NH}_3(n\text{-C}_{12}\text{H}_{25})]_3\text{PO}_4/\text{DMC}$	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \text{H}_3\text{C} \end{array} \text{N} \begin{array}{c} \text{CH}_3 \\ n\text{-C}_{12}\text{H}_{25} \end{array} \right]_3\text{PO}_4$	88.7
30	$\left[\text{C}_6\text{H}_{11}\text{NH}_2 \right] \text{Cl}/\text{DMC}$	$\left[\text{C}_6\text{H}_{11}\text{N} \begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} \right] \text{Cl}$	> 99
31	$\left[\text{C}_6\text{H}_{11}\text{NH}_2 \right] \text{Br}/\text{DMC}$	$\left[\text{C}_6\text{H}_{11}\text{N} \begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} \right] \text{Br}$	> 99
32	$\left[\text{C}_6\text{H}_{11}\text{NH}_2 \right] \text{NO}_3/\text{DMC}$	$\left[\text{C}_6\text{H}_{11}\text{N} \begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} \right] \text{NO}_3$	> 99
33	$\left[\text{C}_6\text{H}_{11}\text{NH}_2 \right]_2\text{SO}_4/\text{DMC}$	$\left[\text{C}_6\text{H}_{11}\text{N} \begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} \right]_2\text{SO}_4$	> 99
34	$\left[\text{C}_6\text{H}_{11}\text{NH}_2 \right]_2\text{C}_2\text{O}_4/\text{DMC}$	$\left[\text{C}_6\text{H}_{11}\text{N} \begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} \right]_2\text{C}_2\text{O}_4$	92.3
35	$\left[\text{C}_6\text{H}_{11}\text{NH}_2 \right] \text{OAc}/\text{DMC}$	$\left[\text{C}_6\text{H}_{11}\text{N} \begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} \right] \text{OAc}$	95.7
36	$\left[\text{C}_6\text{H}_{11}\text{NH}_2 \right]_2\text{CO}_3/\text{DMC}$	$\left[\text{C}_6\text{H}_{11}\text{N} \begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} \right]_2\text{CO}_3$	91.5
37	$\left[\text{C}_6\text{H}_{11}\text{NH}_2 \right]_3\text{PO}_4/\text{DMC}$	$\left[\text{C}_6\text{H}_{11}\text{N} \begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} \right]_3\text{PO}_4$	95.8
38	$\left[\text{C}_6\text{H}_5\text{NH}_2 \right] \text{Cl}$	$\left[\text{C}_6\text{H}_5\text{N} \begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} \right] \text{Cl}$	0
39	$\left[\text{C}_6\text{H}_5\text{CH}_2\text{NH}_2 \right] \text{Cl}$	$\left[\begin{array}{c} \text{H}_3\text{C} \\ \text{H}_3\text{C} \end{array} \text{N} \begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array} \right] \text{Cl}$	> 99

^[a] Reaction conditions: entries 1–8, ammonium cations (2.0 mmol), entries 9–39, hydrogen atoms on the nitrogen atom of each kind of the ammonium salts (4.0 mmol), DMC (8.0 mmol), [EMIM]Br (0.8 mmol), 443 K, 8 h.

where an ammonium salt bearing Cl^- , Br^- , or NO_3^- anions was alkylated by DMC, a yield in excess of 96.0% of the quaternary ammonium salt was obtained. However, in the cases of DMC reacting with the sulfates, oxalates, acetates, and phosphates of ammonia, diethylamine, or triethylamine (Table 2 entries 4 to 8, 15 to 18, 22 to 23), relatively lower yields of the quaternary ammonium salts were obtained. For even bulkier alkyl-substituted ammonium salts, such as those with $n\text{-C}_{12}\text{H}_{25}$ and cyclohexyl substituents (Table 2, entries 27 to 29 and 33 to 37) even when the anions were SO_4^{2-} , CH_3CO_2^- , $\text{C}_2\text{O}_4^{2-}$, and PO_4^{3-} , the reaction still gave high yields of the quaternary ammonium salts (from 84.4 to 99.0%). Except for the cases of tertiary ammonium salts, carbamates were formed as by-products in our reactions. In Deng et al.'s work^[31] (also at 443 K), by employing imidazolium ILs as solvents and catalysts, primary and secondary aliphatic amines could react with DMC to give alkyl carbamates in good yields. What is worth mention is that in the current work, the methylation of ammonium halides and nitrates by DMC gave almost stoichiometric amounts of quaternary ammonium salts.

Comparing the yields of quaternary ammonium salt obtained from the reactions of DMC with $(\text{NH}_4)_2\text{C}_2\text{O}_4$, $\text{NH}_4\text{CH}_3\text{CO}_2$, or $(\text{NH}_4)_3\text{PO}_4$ to those obtained from the reactions of DMC with the alkyl-substituted ammonium oxalates, acetates, or phosphates (Table 2 entries 5, 6, 8, 16, 17, 18, 23, 28, 29, 34, 35 and 37), it was found that the substituted ammonium salts gave higher yields of quaternary ammonium salt yields than the simple NH_4^+ salts. This might be attributed to the fact that alkyl-substituted amines are better nucleophilic attacking reagents than ammonia. It also explains the higher yields in the cases of ammonium salts bearing stronger donor groups, such as $n\text{-C}_{12}\text{H}_{25}$ and cyclohexyl. On the other hand, the ammonium salt could be deactivated by substitution with electron-withdrawing group. For instance, aniline chloride (Table 2 entry 38) cannot be alkylated by DMC. Based on these results, we suggest that the alkylation of ammonium salts is realized through nucleophilic attack of the ammonium nitrogen on the methyl group of DMC. Among all of the tested ammonium salts, the behavior of sulfates is intricate. Research work in this aspect is still in progress.

Based on the results of the current investigation, there is no doubt that [EMIM]Br is an active catalyst for the alkylation of ammonium salts, although in some cases the product yields are still lower than 60%. Nevertheless, since that the catalyst bears Br^- anions, these could contaminate the final quaternary ammonium salt products. There are two approaches to resolve this problem. One approach is to use the traditional anion-exchange resin to clear out Br^- anions (since Br^- anions in our cases are impurities

introduced from the relatively small amount of catalyst, the current synthesis pathway still shows advantages over the traditional methods that need to use an anion-exchange resin to remove a large amount of halogen anions). The other approach is to use the imidazolium catalyst bearing the same anion as that of the final quaternary ammonium salt. In order to test the second approach, some the experiments were performed and the results are presented in Table 3. These investigations confirmed that it is possible to avoid the anion contamination introduced from the

catalyst. However, for some reactions, such as the cases of quaternary ammonium sulfates and acetates, the yields were low. Further research work for the optimization of the reaction conditions to improve product yield is needed.

In order to explore the impact of the higher homologues of DMC on the reaction, diethyl carbonate, dibenzyl carbonate, and diphenyl carbonate were tested as the alkylation or arylation reagents for ammonium salts. As shown in Table 4, the reactivity of the carbonates decreases in the order dimethyl carbonate

Table 3. Reactions of dimethyl carbonate with ammonium salts having the same anions as that of catalysts.^[a]

Entry	Ammonium salt	Catalyst	Product	Yield [%]
1		[EIM]Cl		> 99
2	$[(\text{CH}_3)_2\text{NH}(n\text{-C}_{12}\text{H}_{25})]\text{Br}$	[EMIM]Br		> 99
3		[EIM] ₂ SO ₄		21.6
4	$[\text{NH}_3(n\text{-C}_{12}\text{H}_{25})]\text{CH}_3\text{CO}_2$	[BMIM]CH ₃ CO ₂		52.6
5		[EMIM]CH ₃ CO ₂		59.8

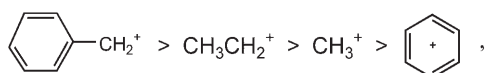
^[a] *Reaction conditions:* the hydrogen atoms on nitrogen atom of each kind of ammonium salt (4.0 mmol), DMC (8.0 mmol), catalyst (0.8 mmol), 443 K, 8 h. [EIM] refers to 1-ethyl-3-hydrogen imidazolium cation.

Table 4. Reactions of ammonium salts with dialkyl carbonates substituted by different groups.^[a]

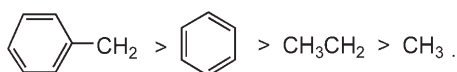
Entry	Ammonium salt	Carbonate	Product	Yield (%)
1	$[(\text{CH}_3)_3\text{HN}]\text{Cl}$	DBC		71.3
2	$[(\text{CH}_3)_3\text{HN}]\text{Br}$	DBC		72.0
3	$[(\text{CH}_3)_3\text{HN}]\text{NO}_3$	DBC		90.1
4	$[(\text{CH}_3)_3\text{HN}]\text{Cl}$	DEC		42.9
5	$[(\text{CH}_3)_3\text{HN}]\text{Br}$	DEC		53.6
6	$[(\text{CH}_3)_3\text{HN}]\text{Cl}$	DPC		0

^[a] *Reaction conditions:* the hydrogen atoms on nitrogen atom of each kind of ammonium salts (4.0 mmol), dialkyl carbonate (8.0 mmol, for DBC 4.0 mmol), [EMIM]Br (0.8 mmol), 443 K, 8 h. DBC denotes dibenzyl carbonate, DEC denotes diethyl carbonate and DPC denotes diphenyl carbonate.

(DMC) > dibenzyl carbonate (DBC) > diethyl carbonate (DEC) > diphenyl carbonate (DPC). We predict that there are two possible reasons that lead to this result. One is the stability of carbon cations, the other is the steric hindrance of the substituent groups of the carbonates. The stability of carbon cations follows the order:



and the strength of the steric hindrance of the substituent groups of the carbonates follows order:



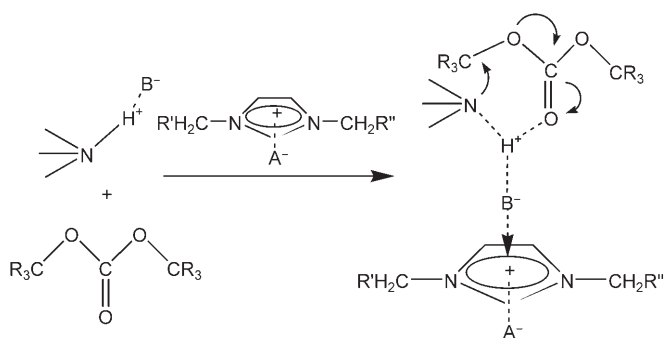
Concerning the stability of carbon cations, dibenzyl carbonate should give the highest yield of quaternary ammonium salt. However, from the steric hindrance point of view, dimethyl carbonate should give the highest yield of quaternary ammonium salt. As a result of both of the factors, some change in the yields of quaternary ammonium salts with these carbonates is expected. Hence, the reactivity order dimethyl carbonate > dibenzyl carbonate > diethyl carbonate > diphenyl carbonate is reasonable. Again, the results further verified that the reaction is a nucleophilic substitution of ammonium nitrogen on the alkyl group of the dialkyl carbonate.

From the results of our investigation, a possible reaction mechanism is suggested (Scheme 1). It is supposed that, at the reaction temperature (443 K), the ammonium salt might release free ammonia or amine, which could attack the alkyl group of the dialkyl carbonate. The suggested mechanism can explain most of the reaction results. If the ammonium cations bear electron-donating alkyl moieties, the carbonates bear good leaving groups (i.e., benzyl), and the geometrical hindrance of both of the reactants is weak, the reaction should give high yields of quaternary ammoni-

um salts, such as those listed in Table 2. It becomes complicated when one applies this mechanism to explain the behavior of the anions of ammonium salts. In the case of strong acid salts, such as chloride, bromide, and nitrate, the protons might be able to effectively polarize the oxygen atoms of the ester as shown in Scheme 1, which results in easier alkylation of the ammonium ions. In the reactions of DMC with ammonium sulfate and ammonium phosphate, the lower yields of quaternary ammonium salts might be attributed to the reason that there are two or three cations surrounding each anion, so the strong steric hindrance around the ammonium sulfate or phosphate might impair the access of the dialkyl carbonate to the ammonium ions. In the case of ammonium acetates, ammonium oxalates, and ammonium carbonates, one reason for the relatively lower yield of quaternary ammonium salts might be that they are weak acid salts and the proton shown in Scheme 1 cannot effectively protonize the oxygen of the ester; the other reason could be that, in the ammonium oxalate and ammonium carbonate cases, the strong steric hindrance around the ammonium ions might also retard the reaction and lead to low yields of quaternary ammonium salt.

Conclusions

In summary, we have developed a new method for the synthesis of quaternary ammonium salts. Quaternary ammonium salts having different anions could be directly synthesized by reacting ammonium salts with dialkyl carbonates over imidazolium IL catalysts. Our results show that the yield of the quaternary ammonium salt is correlated to the electron-donating property of the alkyl moieties of the ammonium ions, the nature of the anions, and the nature of the alkyl chains of the dialkyl carbonate. In the case that DMC reacts with strong acid ammonium salts, such as ammonium halides and nitrates, almost stoichiometric yields of quaternary ammonium salts were reached (not including the cases where the ammonium nitrogen atoms bear phenyl groups). For ammonium salts bearing bulky alkyl groups on the nitrogen atoms, such as cyclohexyl and $n\text{-C}_{12}\text{H}_{25}$, even when the ammonium salts are weak acid salts, high yields of quaternary ammonium salts were achievable. The current synthesis of quaternary ammonium salts, in contrast to the reported methods^[27,30] which work only in the case of tertiary amines, works for almost all kinds of ammonium salts (not including ammonium ions bearing phenyl groups on the nitrogen atom). In the current synthesis reaction, alcohol and carbon dioxide are formed as by-products, which could be converted back to dialkyl carbonate through a reported process.^[32]



Scheme 1. Possible reaction mechanism.

Experimental Section

General Remarks

The dialkyl carbonates were commercial products. Some of the ammonium salts were purchased and some were prepared by neutralizing amines with a stoichiometric amount of the corresponding acids, and then dried at room temperature in vacuum. The *N,N*-dialkylimidazolium ionic liquids were prepared according to the procedure described in literature.^[22,33]

Reactions and Product Analysis

In a typical reaction, ammonium salt, dialkyl carbonate, and the catalyst (the amount of every reagent is described in the corresponding sections) were charged into a stainless steel autoclave (inside volume 3.0 mL), and then the reactor was heated to 443 K in an oven and kept at this temperature for 8 h (without stirring).

For product quantification, in most cases, we did not separate the products for every reaction mixture. The mixture was directly dissolved in D₂O to prepare a solution and analyzed on an NMR spectrometer. Si(CH₃)₄ was used as reference. Calculations of the quaternary ammonium salt yield were based on the peak areas of the hydrogen atoms of the product and then calibrated by using standard samples, as indicated below.

¹H NMR Quantification of Quaternary Ammonium Salts

As an example, Figure 1 a shows one of the ¹H NMR spectra from the reaction mixture of ammonium bromide with DMC in the presence of [EMIM]Br. The peak a with a chemical shift at 1.42 ppm is assigned to the hydrogen of the methyl group on the ethyl group of [EMIM]Br. The peak b, which shows the same chemical shift of 3.12 ppm as that of the standard tetramethylammonium bromide (Figure 1 b), is assigned to the hydrogen atoms of the methyl groups on the tetramethylammonium cation. Since [EMIM]Br acts as a catalyst in the reaction system, the amount (*M_{IL}*) of [EMIM]Br should remain constant before and after the re-

action, thus the amount of tetramethylammonium cation (*M_{TC}*) can be calculated based on the ratio of the peak areas of peak a (*A_{H^a}*) to that of peak b (*A_{H^b}*) according to Eq. (1) below:

$$M_{TC} = A_{H^a} / A_{H^b} \times M_{IL} \times 1/4 \quad (1)$$

Product Isolation

In some of the scale-up reactions, the product quaternary ammonium salts were purified. Since both of the catalyst and product are ionic compounds, the complete isolation of the quaternary ammonium salt from the catalyst could be a challenge. Based on the differences in solubility of the catalyst and the product (quaternary ammonium salt) in acetone, quaternary ammonium salts of high purity can be recovered by an acetone washing process as follows: 1) after the reaction, alcohol and dialkyl carbonate were removed from the reaction mixture by distillation, 2) acetone was added and stirred for 2 h, 3) the mixture was filtrated to obtain the solid quaternary ammonium salt, and 4) the solid quaternary ammonium salt was washed two times with acetone, and then dried under vacuum.

Typical Reactions

DMC (3.600 g, 40.0 mmol) was reacted with trimethylammonium bromide (2.800 g, 20.0 mmol) over [EMIM]Br (0.764 g, 4.0 mmol) in a stainless steel autoclave lined with polytetrafluoroethylene (inside volume 50 mL) at 443 K for 8 h. The product tetramethylammonium bromide was purified according to the above described process; yield: 2.973 g (19.3 mmol, 96.5%). The ¹H NMR analysis did not show any [EMIM]⁺ contamination.

In another example, DMC (10.507 g, 116.6 mmol) was reacted with *N*-cyclohexylammonium bromide (3.584 g, 19.9 mmol) over [EMIM]Br (2.027 g, 10.6 mmol) in an autoclave (inside volume 75 mL) under the same reaction conditions as described in the previous example. After methanol and the unreacted dimethyl carbonate had been removed by distillation, the product was washed with acetone (150 mL of acetone were used in the first washing and 10 mL of acetone were used in the second and the third washings, respec-

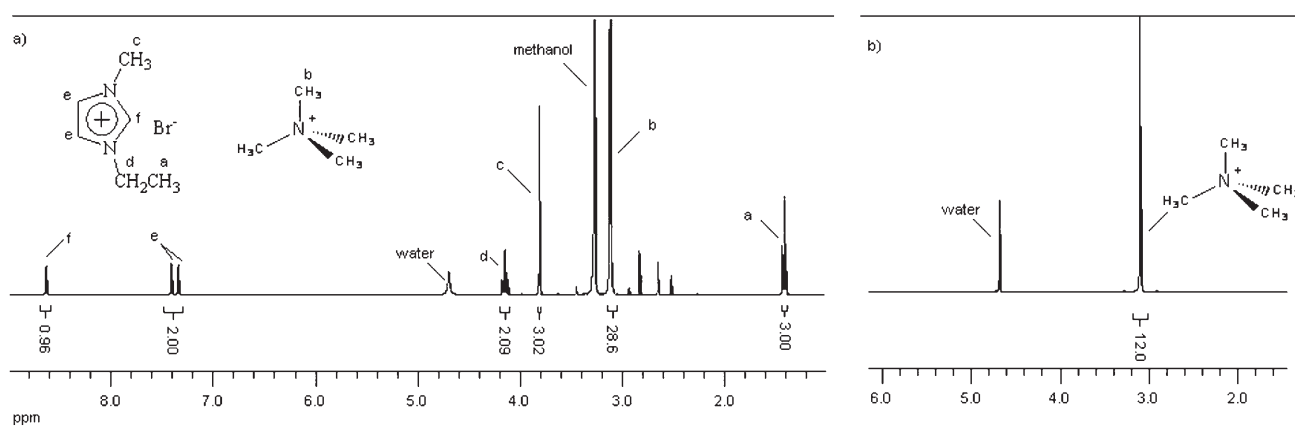


Figure 1. a) The ¹H NMR spectrum of the mixture from the reaction of NH₄Br and dimethyl carbonate in the presence of [EMIM]Br. b) The ¹H NMR spectrum of the standard sample tetramethylammonium bromide.

tively) to obtain the solid *N*-cyclohexyl-*N,N,N*-trimethyl ammonium bromide product which was dried under vacuum; yield 4.084 g (18.4 mmol, 92.4%). The ¹H NMR analysis did not show any [EMIM]Br contamination.

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