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# Preparation of Functionalized Imidazolium Salts under Microwave Irradiation

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# Preparation of Functionalized Imidazolium Salts under Microwave Irradiation

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**Abstract:** A direct alkylation of a substituted imidazole to prepare the corresponding functionalized ionic liquid has been developed in excellent yields under microwave irradiation.

**Keywords:** Imidazolium, ionic liquid, microwave irridiation

From an environmental perspective, ionic liquids provide an alternative reaction medium for chemical reactions.[1] Among various ionic liquids, simple alkyl substituted 1,3-dialkyl-imidazolium cations associated with weakly coordinating anions are the most popular used in biphasic catalysis because of their distinct physical–chemical properties.[1,2] More recently, developments of the presence of appropriate functional groups as part of ionic liquid molecules to increase the immobilization of catalysts or facilitate the separation process represent a new area of interest.[3] Thus, a few of this type of ionic liquids, such as imidazolium-based ones with amine,[4] amido,[5] hydroxy,[6] carboxylate,[7] urea,[8] perfluoro-chains,[9] and nitriles,[3] are known.

Conventional heating in refluxing solvents is a typical way to prepare 1,3-dialkylimidazolium halides. Compared to the time-consuming processes of conventional methods, a microwave-assisted chemical reaction has been applied to synthesize ionic liquids.[10,11] In the past two decades, the use of microwave ovens in chemical synthesis and analysis has grown because of the advantages in reducing reaction times, improving yield, and simplifying procedures. The preparation of functionalized ionic liquids using a solvent-free approach has not reported in literature.[4–9]

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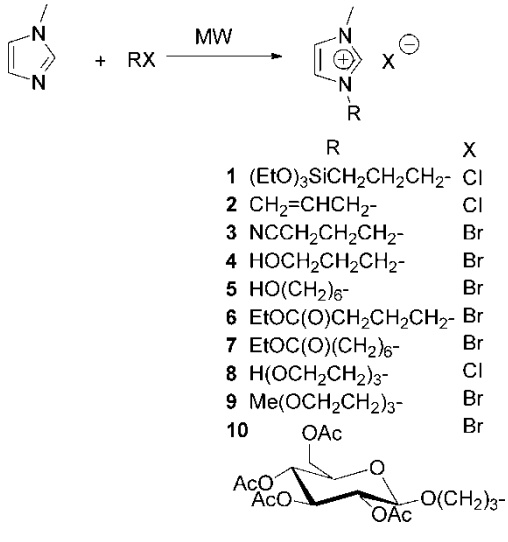
## RESULTS AND DISCUSSION

The microwave-assisted reaction was conducted in a round-bottom flask using a Discovery microwave heating apparatus with a thermal controller (CEM Corp., Matthews, NC). This apparatus allows the reaction flask to be equipped with condenser fitted into a microwave-irradiation chamber (see the experimental section). Typically, a mixture of equal molar amounts (6.5 mmol) of 1-methylimidazole and $\gamma$-bromobutyonitrile in a 20-mL flask was irradiated at 180 W at 180°C for 30 s. Upon completion of the reaction, the pale yellow, viscous oil was washed with dichloromethane (20 mL × 2) to remove the unreacted starting materials. The residue was dried under vacuum overnight, and the obtained material was analytical pure.

All reactions studied in this work are shown in Scheme 1. As a starting point, we studied the microwave-assisted coupling of 1-methylimidazole with 3-triethoxysilylpropyl chloride. Entries 1–5 of Table 1 show the results of this optimization. It appeared that the period of irradiation and reaction temperature were critical for the reaction. The best conditions for the preparation of **1** is irradiation at microwave power of 245 W for 40 s. Either a higher or a lower power of irradiation in this reaction gave decomposition or poorer yield. The scale for the reaction is irrelevant to the irradiation period employed. Because of the moisture sensitivity of the triethoxy silyl group, the reaction had to be carried out under a dry nitrogen atmosphere; otherwise the condensation leading to Si-O-Si took place, which caused a decrease in the yield of **1**. However, it can be carried out under aerobic




***Scheme 1.*** Preparation of functionalized 1,3-disubstituted imidazolium–based ionic liquids.

***Table 1.*** Results for the reactions of 1-methylimidazole with various alkyl halides[a]

| Entry | Quantity of reactant (mmol) | Product | Power of MW (W) | T (s) | Temp. (°C) | Atm. | Yield[b] | Physical property | Ref. |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 6.5 | **1** | 245 | 40 | 245 | $N_2$ | 95% | Pale yellow liquid | [12] |
| 2 | 60 | **1** | 245 | 40 | 245 | air | 49% | Pale yellow liquid | |
| 3 | 6.5 | **1** | 245 | 25 | 140 | $N_2$ | trace | — | |
| 4 | 6.5 | **1** | 185 | 40 | 145 | $N_2$ | trace | — | |
| 5 | 6.5 | **1** | 245 | 40 | 185 | $N_2$ | 93% | Pale yellow liquid | |
| 6 | 11.3 | **2** | 185 | 25 | 180 | air | 90% | Pale yellow liquid | [13] |
| 7 | 6.5 | **3** | 180 | 30 | 180 | air | 95% | Pale yellow liquid | [3] |
| 8 | 6.5 | **4** | 100 | 25 | 175 | air | 92% | Lemon yellow liquid | [14] |
| 9 | 6.5 | **5** | 100 | 35 | 180 | air | 90% | Colorless liquid | [15] |
| 10 | 3.4 | **6** | 100 | 35 | 168 | air | 90% | Pale yellow liquid | [16] |
| 11 | 4.6 | **7** | 180 | 30 | 180 | air | 81% | Lemon yellow liquid | |
| 12 | 5.0 | **8** | 250 | 90 | 185 | air | 90% | Colorless liquid | |
| 13 | 2.9 | **9** | 250 | 90 | 185 | air | 85% | Colorless liquid | |
| 14 | 1.5 | **10** | 30 | 20 | 110 | air | 45% | White powder solid | |
| 15 | 1.5 | **10** | 100 | 20 | 170 | air | dec. | — | |
| 16 | 1.5 | **10** | 5 | 20 | 170 | air | 0 | — | |

[a]Reaction conditions: an equal molar amount of 1-methylimidazole and RX in flask without using any solvent.
[b]Isolated yield and characterized by $^1$H NMR.

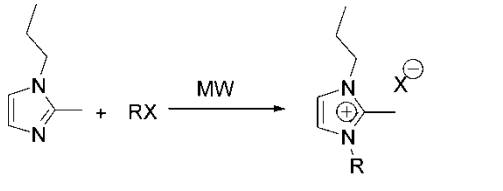
conditions for other substrates. All products were characterized by $^1$H NMR and elemental analysis. The optimum reaction conditions for reactions of 1-methylimidazole with various alkyl halides are summarized in Table 1.

As shown in Table 1, various alkyl halides were able to react with imidazole to give the corresponding ionic liquid in excellent yields (entries 6–13). For example, the production of **10** was achieved by adopting 30 W at 110°C, whereas the compound **8** was with 250 W at 185°C. For the acetylated glucose derivative, the reaction provided a moderate yield by using 30 W of microwave at 110°C. Attempts to improve the yield by varying the microwave powers and temperatures failed, indicating an intrinsic property of this substrate.

All functionalized imidazolium halides except **10** are in liquid phase at room temperature. Compound **10** is in a solid form, which becomes liquid at temperatures greater than 90–93°C. As for solubility, those containing —OH of polyether groups are water- and methanol-soluble materials. In fact, compound **8** is completely miscible with water. Of course, the halide anions of this series of ionic liquids also increase their solubility toward water. Similarly, the alkylation of 1-propyl-2-methylimidazole proceeded smoothly to give the corresponding ionic liquid in excellent yield (Scheme 2). The reaction conditions employed are comparable to the preparation of the related 1,3-disubstituted imidazolium-based ionic liquids (Table 2).

Reaction of 1-bromo-3-chloropropane with 1-methylimidazole under microwave irradiation yielded a mixture of **14**, **15**,[17] and **16**[18] (Scheme 3). It shows that the poor selectivity of nucleophilic substitution of imidazole toward alkyl bromide versus chloride under microwave-assisted conditions even with a lower power irradiation. Even under mild conditions with lower power (30 W), this reaction still provided a mixture of products. However, the reaction proceeded poorly at the temperature lower than 100°C. All these compounds were not able to be obtained in pure form because of the anion.

3-Aminopropyl chloride was also tested as a substrate for the alkylation. A mixture of an equalmolar amount of 3-aminopropyl chloride hydrochloride



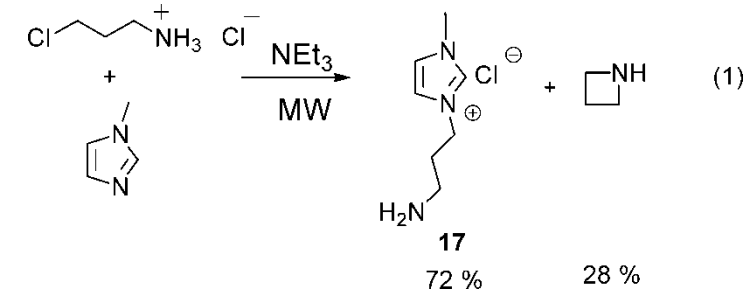

| | R | X |
|---|---|---|
| **11** | $(EtO)_3SiCH_2CH_2CH_2$- | Cl |
| **12** | $H(OCH_2CH_2)_3$- | Cl |
| **13** | $EtOC(O)CH_2CH_2CH_2$- | Br |

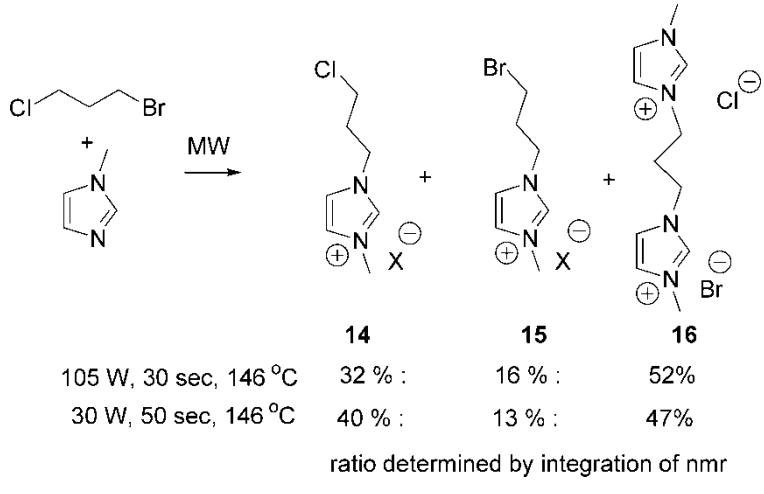
***Scheme 2.*** Preparation of functionalized 1,2,3-trisubstituted imidazolium–based ionic liquids.

***Table 2.*** Results for preparation of 1,2,3-trisubstituted imidazolium–based ionic liquids

| Product | Power (W) | T (s) | Temp. (°C) | Yield (%) | Physical property |
|---|---|---|---|---|---|
| **11** | 235 | 40 | 185 | 75 | Pale yellow liquid |
| **12** | 180 | 50 | 180 | 89 | Pale yellow liquid |
| **13** | 105 | 30 | 180 | 85 | Pale yellow liquid |

salt, 1-methylimidazole, and triethylamine was irradiated at 170°C with the power setting of 180 W for 90 s to provide the desired ionic liquid **17** in 65% yield accompanied by the formation of azetidine Eq. (1). This outcome shows that the alkylation takes place with imidazole nitrogen superior to the amine site. However, the use of excess 3-aminopropyl chloride salt can provide **17** in a high yield.




***Scheme 3.*** Reaction of imidazole with 3-chloro-1-bromopropane.

In summary, we have demonstrated a much faster and more efficient method for the preparation of functionalized imidazolium-based ionic liquid in high yields. Work on these functionalized ionic liquids continues and is expected to illustrate interesting new results.

## EXPERIMENTAL

Nuclear magnetic resonance spectra were recorded in $CDCl_3$ or acetone-$d_6$ on either a Bruker AM-300 or Avance 400 spectrometer. Chemical shifts are given in parts per million relative to $Me_4S$ for $^1H$ and $^{13}C$ NMR. Infrared spectra were measured on a Nicolet Magna-IR 550 spectrometer (series-II) as KBr pallets, unless otherwise noted. Microwave irradiation was carried out in a Discovery microwave heating apparatus with temperature controller (CEM Corp., Matthews, NC). The reaction temperature reported was based on this readout. Chemicals and solvents were of analytical grade and used as received unless otherwise stated. $\alpha$-Bromotetraacetyl-L-glucose was prepared from the earlier reported procedures.[19]

### General Procedure

An equal molar amount of 1-methylimidazole and alkyl halides in a 20-mL flask was set up as shown in Fig. 1 and was irradiated at a certain level of power with programming the temperature for a certain period of reaction time. Upon completion of the reaction, the pale yellow, viscous oil was washed with dichloromethane (20 mL $\times$ 2) to remove the unreacted starting materials and was dried under vacuum overnight. Spectroscopic data of the obtained compounds **1**–**6** are essentially identical to the literature reported.[3,12–16]

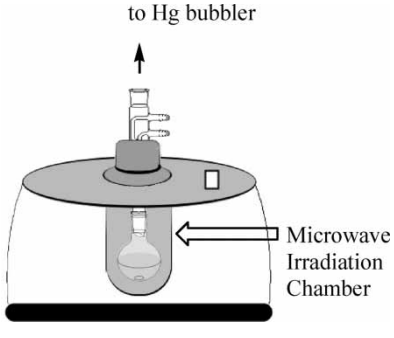



***Figure 1.*** Microwave-assisted heating apparatus.

## Data

**Compound 7**. $\upsilon_{max}$ KBr/cm$^{-1}$ 3164, 2952, 2866, 1726 ($\upsilon_{C=O}$), 1653 ($\upsilon_{C=C}$), 1573; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 9.99 (s, 1H), 7.53 (s, 1H), 7.47 (s, 1H), 4.20 (t, 2H, $J = 7.31$ Hz), 3.93 (s, 3H), 3.91 (q, 2H, $J = 7.05$ Hz), 2.16 (t, $J = 7.29$ Hz), 1.80 (m, 2H), 1.50 (m, 2H), 1.24 (m, 2H), 1.07 (t, 3H, $J = 7.18$ Hz). MS found [M-Br]$^+$ 239 for $C_{13}H_{23}N_2O_2$; anal. calcd. for $C_{13}H_{23}BrN_2O_2$: C, 48.91; H, 7.26; N, 8.78. Found for C, 45.45; H, 7.15; N, 9.46.

**Compound 8**. $\upsilon_{max}$ KBr/cm$^{-1}$ 3552 ($\upsilon_{O-H}$), 3164, 2872, 1653 ($\upsilon_{C=C}$), 1587, 1116; $^1$H NMR (300 MHz, $D_2O$): $\delta$ 8.75 (s, 1H), 7.52 (s, 1H), 7.45 (s, 1H), 4.39 (t, 2H, $J = 4.6$ Hz), 3.91 (s, 3H), 3.89 (m, 2H), 3.72 (m, 6H), 3.60 (m, 2H). MS found [M-Cl]$^+$ 215 for $C_{10}H_{19}N_2O_3$; anal. calcd. for $C_{10}H_{19}ClN_2O_3$: C, 47.9; H, 7.64; N, 11.19. Found: C, 47.21; H, 7.83; N, 11.37.

**Compound 9**. $\upsilon_{max}$ KBr/cm$^{-1}$ 3164, 2873, 1646, 1566, 1103; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 9.81 (s, 1H), 7.66 (s, 1H), 7.47 (s, 1H), 3.97 (s, 3H), 3.79 (t, 2H, $J = 4.58$ Hz), 3.52 (m, 8H), 3.25 (s, 3H). MS found [M-Br]$^+$ 229 for $C_{11}H_{21}N_2O_3$; anal. calcd. for $C_{11}H_{21}BrN_2O_3$: C, 42.73; H, 6.85; N, 9.06. Found: C, 42.59; H, 7.19; N, 8.98.

**Compound 10**. Mp: 90–93°C; $\upsilon_{max}$ KBr/cm$^{-1}$ 3171, 2939, 2879, 1726 ($\upsilon_{C=O}$), 1653, 1587, 1089; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 10.05 (s, 1H), 7.38 (s, 1H), 7.31 (s, 1H), 5.15 (t, 1H, $J = 9.6$ Hz), 5.02 (t, 1H, $J = 9.9$ Hz), 4.85 (t, 1H, $J = 8.0$ Hz), 4.50 (d, 1H, $J = 8.0$ Hz), 4.39 (m, 2H), 4.20 (m, 1H), 4.06 (s, 3H), 3.71 (m, 2H), 3.62 (m, 2H), 2.20 (m, 2H), 2.05 (s, 1H), 2.02 (s, 1H), 2.00 (s, 1H), 1.95 (s, 1H). MS found [M-Br]$^+$ 472 for $C_{20}H_{29}N_2O_{10}$; anal. calcd. for $C_{20}H_{29}BrN_2O_{10}$: C, 44.70; H, 5.44; N, 5.21. Found: C, 44.26; H, 5.45; N, 4.99.

**Compound 11**. $\upsilon_{max}$ KBr/cm$^{-1}$ 3144, 2980, 2933, 2849, 1640, 1586, 1076; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.66 (s, 1H), 7.51 (s, 1H), 4.27 (t, 2H, $J = 7.3$ Hz), 4.08 (t, 6H, $J = 7.3$ Hz), 3.92 (q, 2H, $J = 7.2$ Hz), 2.65 (s, 3H), 2.34 (t, 2H, $J = 7.2$ Hz), 1.97 (m, 2H), 1.72 (m, 2H), 0.82 (t, 9H, $J = 7.3$ Hz). MS found [M-Cl]$^+$ 287 for $C_{13}H_{27}N_2O_3Si$; anal. calcd. for $C_{13}H_{27}ClN_2O_3Si$: C, 48.35; H, 8.43; N, 8.68. Found: C, 47.21; H, 7.83; N, 11.37.

**Compound 12**. $\upsilon_{max}$ KBr/cm$^{-1}$ 3403 ($\upsilon_{O-H}$), 3144, 2952, 2886, 1653, 1593, 1129; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.81 (s, 1H), 7.49 (s, 1H), 4.43 (t, 2H, $J = 4.5$ Hz), 4.10 (t, 2H, $J = 7.2$ Hz), 3.81 (t, 2H, $J = 4.5$ Hz), 3.52 (m, 8H), 2.65 (s, 3H), 1.75 (m, 2H), 0.88 (t, 3H, $J = 5.2$ Hz). MS found [M-Cl]$^+$ 257 for $C_{13}H_{25}ClN_2O_3$; anal. calcd. for $C_{13}H_{25}ClN_2O_3$: C, 53.33; H, 8.61; N, 9.57. Found: C, 53.18; H, 8.98; N, 9.44.

**Compound 13**. $\upsilon_{max}$ KBr/cm$^{-1}$ 3139, 2974, 2883, 1727, 1640, 1587; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.65 (s, 1H), 7.54 (s, 1H), 4.19 (t, 2H, $J = 11.2$ Hz), 3.43 (s, 9H), 2.72 (s, 3H), 1.79 (m, 2H), 0.84 (t, 3H, $J = 18.4$ Hz), 0.54 (t, 3H, $J = 12.6$ Hz). MS found $[M\text{-}Br]^+$ 239 for $C_{13}H_{23}BrN_2O_2$; anal. calcd. for $C_{13}H_{23}BrN_2O_2$: C, 48.91; H, 7.26; N, 8.78. Found for C, 48.96; H, 7.93; N, 8.96.

**Compound 17**. $\upsilon_{max}$ KBr/cm$^{-1}$ 3455 ($\upsilon_{N-H}$), 3157, 2963, 2753, 1634, 1579; $^1$H NMR (300 MHz, $D_2O$): $\delta$ 8.65 (s, 1H), 7.39 (s, 1H), 7.32 (s, 1H), 4.19 (t, 2 H, $J = 7.3$ Hz), 3.75 (s, 3H), 2.93 (m, 2H), 2.16 (m, 2H). MS found $[M-Cl]^+$ 140 for $C_7H_{14}N_3$; anal. calcd. for $C_7H_{14}ClN_3$: C, 47.86; H, 8.03. Found for C, 47.66; H, 7.83.

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