A new modified synthetic method for preparation of \(N,N\)-dichlorocarbamates

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A rapid, efficient, economic and easy to scale method for the effective conversion of carbamates to corresponding \(N,N\)-dichlorocarbamates by using calcium hypochlorite in acidic medium has been described. The transformation has been carried out at room temperature with high yield and purity with reduced reaction time.

Keywords: Substituted \(N,N\)-dichlorocarbamates, calcium hypochlorite, acidic medium

\(N\)-chloro compounds have been extensively exploited, both for fundamental research and a wide range of industrial applications, owing to their easy handling, commercial availability and high storage stability. As a result, intensive research and studies have been carried out over a long period of time on their chlorination, oxidation, water disinfection and some other applications\(^{1-8}\) in synthetic organic chemistry\(^{9}\). \(N\)-Chloro compounds have also been employed for decontamination of chemical warfare agents\(^{10,11}\). \(N\), \(N\)-Dichlorocarbamate was prepared by Dutta and Gupta\(^{12}\) and subsequently by Houben\(^{13}\) and by Chabrier\(^{14}\) but explicit details concerning yield, methods of isolation and purity and physical characteristics of products was not reported. A major drawback of the Foglia and Swern\(^{15}\) method was passage of chlorine gas for an extended period at RT, which can result in inhalation toxicity. White and Kovaic\(^{16}\) have also reported low yields and time consuming processes for the synthesis of \(N\), \(N\)-dichlorocarbamate and also difficulties in isolation of pure \(N\), \(N\)-dichlorocarbamate.

These limitations prompted the development of a rapid and efficient synthetic procedure for \(N\), \(N\)-dichlorocarbamate that involves easy work-up and quantitative yields with shorter reaction times by making use of calcium hypochlorite. In this paper is reported an improved method, which results in high yield in shorter time to give pure \(N\), \(N\)-dichlorocarbamate in acidic medium without using any volatile solvents for extraction. Calcium hypochlorite is a versatile and very safe reagent for \(N\)-chlorination of substituted carbamates as compared to other reagents like sodium hypochlorite and chlorine gas. This reagent is commercially available, cheap, has high chlorine content and storage stability. Synthesis of all other hypochlorites involve passage of chlorine gas either into aqueous solution of sodium hydroxide or \(\text{tert}\)-butyl alcohol for extended periods, which result in inhalation toxicity and difficulties in handling and work-up procedures.

Due to the high chlorine content of \(\text{Ca(OCl)}_2\) (60-70%) as compared to \(\text{NaOCl}\) (4-12%), a lesser quantity of the reagent is able to convert a larger portion of the substituted carbamates into \(N\), \(N\)-dichlorocarbamates with high yields in less time.

Calcium hypochlorite is a commercially available compound that produces positive chlorine in aqueous medium for \(N\)-chlorination of carbamate. It was found that for chlorination of carbamates, an acidic medium is required to avoid the formation of salt of monochlorocarbamates. In this procedure, the carbamates was first suspended in acetic acid and the reaction mixture cooled to 0-5°C with stirring till the starting material dissolved completely. To this mixture, an aqueous solution of calcium hypochlorite was added slowly in 10 min with stirring. Acetic acid was added in portions to bring the \(pH\) of the mixture to acidic condition. After 15 min, a translucent yellow organic layer was well separated in aqueous medium. Acetic acid was used for complete dissolution of calcium hypochlorite in aqueous medium and also used as a solvent and to maintain acidic \(pH\) of the reaction mixture.

The reaction of various substituted alkyl and aryl carbamates (Entry 1-8) with calcium hypochlorite afforded corresponding \(N\), \(N\)-dichlorocarbamates in

**Scheme I**
15-20 min with excellent yields. The reaction and yield of *N,N*-dichlorocarbamates is depicted in Scheme I and Table I. This method has allowed the achievement of quantitative yields of the products with reduced reaction time. The important advantage of this reaction is that there is no inhalation of chlorine (industrially important due to reduced pollution) at RT, low cost, and simplicity in process and handling. Completion of the reaction is self-indicated by separation of pure product in organic phase (golden yellow colour) in the bottom of the flask within 15 min. The crude product in all cases did not require to be purified anymore as it had sufficient purity. Pure products were obtained in high yield as summarized in Table I. Active chlorine of all products was determined by iodometric titration using sodium thiosulphate, which was comparable with theoretical values.

In conclusion, herein is described an efficient, convenient and rapid one pot conversion of carbamates to *N,N*-dichlorocarbamates in excellent yield by making use of calcium hypochlorite in acidic medium.

### Experimental Section

All starting materials such as calcium hypochlorite, carbamates (entry 1-4 and 6) and acetic acid were purchased from Aldrich and Qualigen. Remaining carbamates (entry 5, 7, and 8) were synthesized from NaOCN and corresponding alcohol or phenol by using silica sulfuric acid (SSA) according to procedures reported in literature.

The IR spectra were obtained on a Perkin-Elmer BX-2 instrument as KBr disk. 1H NMR spectra were recorded on a Bruker DPX Avance FT-NMR instrument in CDCl3 using tetramethylsilane as an internal standard at 400 MHz.

### Table I — Synthesis of *N,N*-dichlorocarbamates

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Time (min)</th>
<th>Yield&lt;sup&gt;a&lt;/sup&gt; (%)</th>
<th>b.p. °C/(mm Hg)</th>
<th>Active Chlorine&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Obsd. %</th>
<th>Calcd. %</th>
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<tbody>
<tr>
<td>1</td>
<td>-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>15</td>
<td>94</td>
<td>49-50/7.5</td>
<td>49.27</td>
<td>49.31</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>-C&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>15</td>
<td>95</td>
<td>44-45/6.0</td>
<td>44.46</td>
<td>44.90</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>-CH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>15</td>
<td>81</td>
<td>46.0/0.3</td>
<td>37.79</td>
<td>38.17</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>-C(CH&lt;sub&gt;3&lt;/sub&gt;)&lt;sub&gt;3&lt;/sub&gt;</td>
<td>16</td>
<td>86</td>
<td>44-45/2.6</td>
<td>38.25</td>
<td>38.17</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>16</td>
<td>87</td>
<td>122/3.0</td>
<td>33.12</td>
<td>33.49</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>20</td>
<td>89</td>
<td>120/1.0</td>
<td>34.31</td>
<td>34.46</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>20</td>
<td>88</td>
<td>124/1.5</td>
<td>32.11</td>
<td>32.27</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>20</td>
<td>78</td>
<td>126/5.0</td>
<td>29.41</td>
<td>30.34</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Isolated yield.

<sup>b</sup> Active chlorine of products was determined by iodometric titration.

A mixture of ethyl carbamate (8.9 g, 0.1 mol) and acetic acid (30 mL) were taken in a two neck round bottom flask equipped with condenser and dropping funnel mounted on a magnetic stirrer. The reaction mixture was cooled to 5°C in an ice-bath and calcium hypochlorite (60-70%, 30 g in 90 mL of water) was added slowly with the help of a dropping funnel within 10 min with stirring. Acetic acid (5-10 mL) was added in portions to bring down the pH of the mixture to acidic. After 15 min a translucent yellow layer of the product was separated from aqueous layer. The organic phase was washed with water and dried over anhydrous sodium sulphate. Yield was 95% (16.8 g) as a yellow oil b.p. 44-45°C at 6.0 mm Hg. The positive chlorine of *N,N*-dichloroethylcarbamates were checked by standard iodometric titration. Yields of all compounds were found to be...
quantitative. The products formed were characterized by FT-IR and $^1$H NMR.

**N,N-Dichloro methyl carbamate, 1**

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 3.86 (s, 3H, CH$_3$); IR (KBr): 2960 (C-H), 1759 (C=O), 1438 (CH$_2$ scissoring), 1244 (C-O), 1048 (C-N), 763 cm$^{-1}$ (N-Cl). Anal. (Iodometric Titration) Calcd for C$_5$H$_6$Cl$_2$NO$_2$: Cl, 49.31. Found: Cl, 49.27%.

**N,N-Dichloro ethyl carbamate, 2**

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 1.39 (t, 3H, CH$_3$), 4.37 (q, 2H, CH$_2$); IR (KBr): 2986 (C-H), 1757 (C=O), 1458 (CH$_2$ scissoring), 1232 (C-O), 1064 (C-N), 762 cm$^{-1}$ (N-Cl). Anal. (Iodometric Titration) Calcd for C$_5$H$_6$Cl$_2$NO$_2$: Cl, 44.9%. Found: Cl, 44.5%.

**N,N-Dichloro n-butyl carbamate, 3**

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 1.39-1.47 (m, 2H, CH$_2$), 1.61-1.68 (m, 2H, CH$_2$), 4.13-4.25 (t, 2H, CH$_2$); IR (KBr): 2963 (C-H), 1761 (C=O), 1465 (CH$_2$ scissoring), 1224 (C-O), 1064 (C-N), 762 cm$^{-1}$ (N-Cl). Anal. (Iodometric Titration) Calcd for C$_7$H$_8$Cl$_2$NO$_2$: Cl, 38.17. Found: Cl, 37.79%.

**N,N-Dichloro t-butyl carbamate, 4**

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 1.53 (s, 3H, CH$_3$); IR (KBr): 2983 (C-H), 1759 (C=O), 1458 (CH$_2$ scissoring), 1240 (C-O), 1040 (C-N), 755 cm$^{-1}$ (N-Cl). Anal. (Iodometric Titration) Calcd for C$_7$H$_8$Cl$_2$NO$_2$: Cl, 38.17. Found: Cl, 38.25%.

**N,N-Dichloro cyclohexyl carbamate, 5**

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 1.54-1.64 (m, 6H, CH$_2$), 1.72-1.79 (m, 4H, CH$_2$), 3.9 (m, 1H, CH); IR (KBr): 2937 (C-H), 1695 (C=O), 1458 (CH$_2$ scissoring), 1247 (C-O), 1063 (C-N), 759 cm$^{-1}$ (N-Cl). Anal. (Iodometric Titration) Calcd for C$_8$H$_{11}$Cl$_2$NO$_2$: Cl, 33.49. Found: Cl, 33.12%.

**N,N-Dichloro phenyl carbamate, 6**

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.12-7.39 (m, 5H, Ph); IR (KBr): 3020 (aromatic C-H), 2970 (C-H), 1740 (C=O), 1250 (C-O), 1055 (C-N), 765 cm$^{-1}$ (N-Cl). Anal. (Iodometric Titration) Calcd for C$_7$H$_6$Cl$_2$NO$_2$: Cl, 34.46. Found: Cl, 34.31%.

**N,N-Dichloro benzyl carbamate, 7**

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 5.2 (s, 2H, CH$_2$), 7.24-7.36 (m, 5H, Ph); IR (KBr): 3023 (aromatic C-H), 2968 (C-H), 1739 (C=O), 1453 (CH$_2$ scissoring), 1229 (C-O), 1048 (C-N), 766 cm$^{-1}$ (N-Cl). Anal. (Iodometric Titration) Calcd for C$_7$H$_6$Cl$_2$NO$_2$: Cl, 32.27. Found: Cl, 32.11%.

**N,N-Dichloro phenethyl carbamate, 8**

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 2.92-2.95 (t, 2H, CH$_2$), 4.27-4.30 (t, 2H, CH$_2$), 7.21-7.32 (m, 5H, Ph); IR (KBr): 3029 (aromatic C-H), 2978 (C-H), 1747 (C=O), 1458 (CH$_2$ scissoring), 1224 (C-O), 1048 (C-N), 762 cm$^{-1}$ (N-Cl). Anal. (Iodometric Titration) Calcd for C$_8$H$_9$Cl$_2$NO$_2$: Cl, 30.34. Found: Cl, 29.41%.

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**References**