An Efficient Protocol for the Synthesis of *N*-Alkyl- and *N*-Arylimides Using the Lewis Acidic Ionic Liquid Choline Chloride·2$ZnCl_2$

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Lewis acidic ionic liquid choline chloride·2$ZnCl_2$ is shown to be for the first time an excellent medium and efficient catalyst for the synthesis of *N*-alkyl- and *N*-arylimides in good yields under mild conditions.

Keywords: Choline chloride·2$ZnCl_2$; Succinic anhydride; Phthalic anhydride; Ionic liquid.

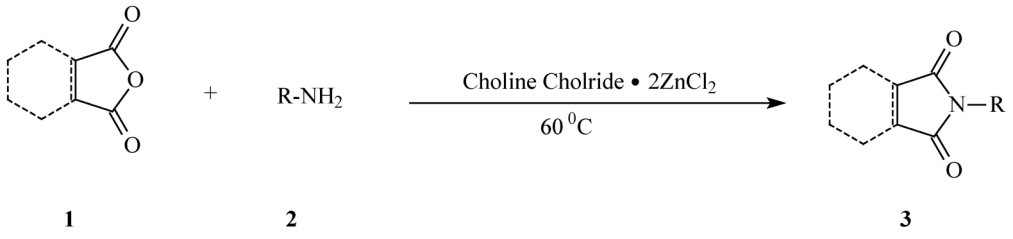
INTRODUCTION

Imide derivatives are an important class of substrates for biological and chemical applications.[1] Accordingly, extensive progress toward the synthesis of these derivatives has been made in recent years. Well known methods include (1) dehydrative condensation of anhydride and amine catalyzed by conc. H_2SO_4 in acetic anhydride under reflux conditions,[2] (2) Direct *N*-alkylation of phthaloyl dichloride with azide in the presence of PPh_3 in CH_2Cl_2,[3] (3) *N*-alkylation of imides using of alcohol promoted by PPh_3 and DIAP in THF,[4] etc. These methods have not been entirely satisfactory owing to the drawbacks such as using of organic solvents. It is necessary to develop an alterative solvent for the synthesis of imides under mild and environmentally benign conditions.

Ionic liquids have been the subject of consideeable interest in the context of green synthesis because of their wide acceptability as alternative green reaction media.[5] Recently, the alkylimidazolium-aluminium chloride mixtures have been studied extensively for use in acid-catalysed reactions, particularly in Friedel-Crafts reactions.[6] However, for practical utilization, these imidazolium-based ionic liquids still suffer from the relatively expensive cost. In the case of chloroaluminate ionic liquid, its poor stability toward moisture can lead to undesired side reactions. More recently, a series of inexpensive and moisture-stable Lewis acidic ionic liquids have been prepared from choline chloride and $ZnCl_2$,[7] and been used in Diels–Alder reactions[8] and Fischer indole synthesis.[9] We have reported an efficient protocol for the Friedländer quinoline synthesis using Lewis acidic ionic liquid choline chloride·2$ZnCl_2$.[10] In this paper, we report the use of choline chloride·2$ZnCl_2$ as a solvent and catalyst for the synthesis of *N*-alkyl- and *N*-arylimides (Scheme I).

First, we found that the reaction of succinic anhydride with aniline in ionic liquid choline chloride·2$ZnCl_2$ at 60 °C for 1 h to gave *N*-phenylsuccinimide (**3a**) in 90% yield. In a similar fashion, the reaction of phthalic anhydride with

Scheme I



1 **2** **3**

a variety of amines also underwent smooth dehydrative condensation to afford the respective imides in good yields. As can be seen from Table 1, the reaction is general and applicable to aliphatic and aromatic amines bearing different functionalities such as methyl, methoxy, chloro, nitro and cyano groups. When the reaction was conducted in ionic liquid 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF_6]), however, the preparation of *N*-phenylphthalimide (**3f**) required 8 h at 80 °C to go to completion.[11]

The ionic liquid choline chloride·2$ZnCl_2$ can typically be recovered by extracting it from the reaction mixtures and next by vacuum drying. The recovered solvent can be reused with no appreciable decrease in yields. The representative results are summarized in Table 2. The present method has many advantages including high efficiency, operational simplicity, environmentally benign character and ability to be recycled.

In conclusion, we describe a mild and efficient route for the synthesis of *N*-alkyl- and *N*-arylimides utilizing choline chloride·2$ZnCl_2$ as a solvent and catalyst in good yields under mild conditions. Compared to imidazolium-based ionic liquids, choline chloride·2$ZnCl_2$ is easier to the prepared, less moisture-sensitive and cheaper.

EXPERIMENTAL SECTION

All melting points are uncorrected. The IR spectra were recorded on a Shimadzu IR-27 G spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Unity Plus 400 MHz. Chemical shifts (δ) were measured in ppm with respect to TMS. MS were obtained on a JEOL JMS D-300 instrument. Elemental analyses were performed on an EA-1110 instrument.

N-Phenylsuccinimide (3a); Typical procedure

A mixture of succinic anhydride (100 mg, 1.0 mmol) and aniline (93 mg, 1.0 mmol) in ionic liquid choline chloride·2$ZnCl_2$ (0.5 mL) was stirred for 1 h at 60 °C. The reaction mixture was extracted with ethyl acetate. The remaining ionic liquid was reused after drying in vacuum. The extract was dried ($MgSO_4$) and concentrated under reduced pressure and the residue was purified by chromatography on a silica gel column eluting with *n*-hexane-ethyl acetate (1:1) to give **3a**, mp 152-154 °C (lit.[12] mp 156-167 °C), yield 90%. IR (KBr) ν: 3054, 2935, 1708, 1500, 1390, 1187, 764, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 2.90 (s, 4H), 7.28 (d, J = 7.2 Hz, 2H), 7.39-7.40 (m, 1H), 7.49-7.50 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 28.4, 126.4, 128.6, 129.2, 131.8, 176.2; EI-MS *m/z* (relative intensity) 175 (M^+), 147,

Table 1. The synthesis of *N*-alkyl- and *N*-arylimides using ionic liquid choline chloride·2$ZnCl_2$

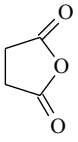
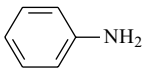
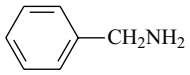
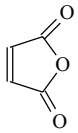
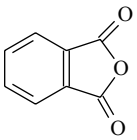
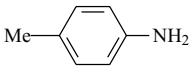
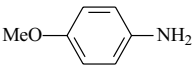
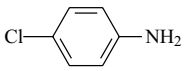
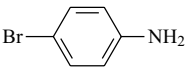
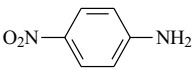
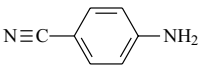
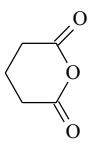
Entry	Anhydride	Amine	Product	Yield (%)
1	 **1a**	 **2a**	**3a**	90
2	**1a**	 **2b**	**3b**	86
3	**1a**	n-$C_4H_9NH_2$ **2c**	**3c**	84
4	 **1b**	**2a**	**3d**	88
5	**1b**	**2b**	**3e**	92
6	 **1c**	**2a**	**3f**	87
7	**1c**	 **2d**	**3g**	89
8	**1c**	 **2e**	**3h**	82
9	**1c**	 **2f**	**3i**	84
10	**1c**	 **2g**	**3j**	87
11	**1c**	 **2h**	**3k**	90
12	**1c**	 **2i**	**3l**	85
13	**1c**	**2b**	**3m**	83
14	 **1d**	**2b**	**3n**	87

Table 2. Results obtained using recycled ionic liquid choline chloride·2$ZnCl_2$

Entry	Product	Cycle	Yield (%)
1	**3a**	1	90
2	**3a**	2	91
3	**3a**	3	89

120, 119, 118, 93.

***N*-Benzylsuccinimide (3b)**

mp 99-100 °C (lit.[12] mp 98-99 °C). IR (KBr) ν: 3307, 3036, 1695, 1431, 1307, 713, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 2.67 (s, 4H), 4.64 (s, 2H), 7.26-7.32 (m, 3H), 7.38 (d, *J* = 6.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 28.1, 42.3, 127.9, 128.5, 128.8, 135.7, 176.8; EI-MS *m/z* (relative intensity) 189 (M^+), 161, 160, 132, 119, 104.

***N*-Butylsuccinimide (3c)**

Oily compound (lit.[13] oily compound). IR (neat) ν: 2957, 1767, 1697, 1403, 875, 731 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 0.85 (t, *J* = 7.6 Hz, 3H), 1.47 (m, 2H), 1.25 (m, 2H), 2.64 (s, 4H), 3.43 (t, *J* = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 13.4, 19.9, 28.0, 29.6, 38.4, 177.2; EI-MS *m/z* (relative intensity) 156 (M^+), 113, 100, 84.

***N*-Phenylmaleimide (3d)**

mp 86-87 °C (lit.[12] mp 89-90 °C). IR (KBr) ν: 3158, 3092, 1709, 1594, 1503, 1391, 1144, 831, 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 6.86 (s, 2H), 7.33-7.39 (m, 3H), 7.47 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 126.1, 128.0, 129.2, 131.1, 134.2, 169.5; EI-MS *m/z* (relative intensity) 173 (M^+), 129.

***N*-Benzylmaleimide (3e)**

mp 83-84 °C (lit.[12] mp 69-70 °C). IR (KBr) ν: 3092, 3062, 3033, 1700, 1576, 1497, 1342, 1308, 1136, 841, 781, 724, 693 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 4.67 (s, 2H), 6.70 (s, 2H), 7.25-7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 41.3, 127.8, 128.3, 128.6, 134.1, 136.1, 170.4; EI-MS *m/z* (relative intensity) 187 (M^+), 169, 130, 106.

***N*-Phenylphthalimide (3f)**

mp 206-208 °C (lit.[12] mp 208-209 °C). IR (KBr) ν: 3047, 1771, 1699, 1495, 1380, 1109, 755, 703 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.39-7.53 (m, 5H), 7.80 (dd, *J* = 5.4, 2.8 Hz, 2H), 7.96 (dd, *J* = 5.6, 3.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 123.7, 126.5, 128.1, 129.1, 131.7, 134.4, 167.3; EI-MS *m/z* (relative intensity) 223 (M^+), 179, 178, 76.

***N*-(4-Methylphenyl)phthalimide (3g)**

mp 200-202 °C (lit.[11] mp 203-204 °C). IR (KBr) ν: 3033, 1771, 1713, 1513, 1382, 1116, 792, 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 2.41 (s, 3H), 7.31 (s, 4H), 7.80 (dd, *J* = 5.2, 3.2 Hz, 2H), 7.95 (dd, *J* = 5.4, 2.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.1, 123.7, 126.4, 128.9, 129.7, 131.7, 134.3, 138.2, 167.4; EI-MS *m/z* (relative intensity) 237 (M^+), 194, 193, 192, 165, 76.

***N*-(4-Methoxyphenyl)phthalimide (3h)**

mp 164-166 °C. IR (KBr) ν: 3064, 1715, 1516, 1387, 1102, 784, 713 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 3.83 (s, 3H), 7.01 (dt, *J* = 9.6, 2.4 Hz, 2H), 7.33 (dt, *J* = 9.6, 2.4 Hz, 2H), 7.76 (dd, *J* = 5.4, 2.8 Hz, 2H), 7.92 (dd, *J* = 5.6, 2.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 55.4, 114.4, 123.5, 124.1, 127.8, 131.6, 134.2, 159.1, 167.5; EI-MS *m/z* (relative intensity) 253 (M^+), 238, 210, 130. Anal. Calcd for $C_{15}H_{11}NO_3$: C, 71.14; H, 4.38; N, 5.53. Found: C, 71.32; H, 4.15; N, 5.78.

***N*-(4-Chlorophenyl)phthalimide (3i)**

mp 202-204 °C (lit.[11] mp 192-194 °C). IR (KBr) ν: 3060, 1789, 1711, 1494, 1389, 1118, 789, 715 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.39-7.49 (m, 4H), 7.80 (dd, *J* = 5.4, 2.8 Hz, 2H), 7.95 (dd, *J* = 5.4, 2.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 123.8, 127.6, 129.3, 130.1, 131.5, 133.8, 134.5, 167.0; EI-MS *m/z* (relative intensity) 259 (M^++2) 257 (M^+), 178, 76.

***N*-(4-Bromophenyl)phthalimide (3j)**

mp 205-206 °C (lit.[11] mp 202-204 °C). IR (KBr) ν: 3060, 1787, 1710, 1491, 1386, 1118, 789, 715 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.36 (dt, *J* = 9.2, 2.2 Hz, 2H), 7.61-7.64 (m, 2H), 7.80 (dd, *J* = 5.6, 3.2 Hz, 2H), 7.95 (dd, *J* = 5.6, 2.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 121.8, 123.8, 127.9, 130.7, 131.6, 132.3, 134.5, 166.9; EI-MS *m/z* (relative intensity) 303 (M^++2), 301 (M^+), 259, 257, 178.

***N*-(4-Nitrophenyl)phthalimide (3k)**

mp 266-267 °C (lit.[11] mp 264-266 °C). IR (KBr) ν: 3061, 1782, 1732, 1520, 1343, 1077, 747, 709 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.75-7.79 (m, 2H), 7.84-7.86 (m, 2H), 8.01 (dd, *J* = 5.6, 3.2 Hz, 2H), 8.38 (dt, *J* = 9.6, 2.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 24.1, 124.4, 126.3, 131.3, 135.0, 137.5, 146.4, 166.4; EI-MS *m/z* (relative intensity) 268 (M^+), 238, 178, 166, 76.

***N*-(4-Cyanophenyl)phthalimide (3l)**

mp 184-186 °C. IR (KBr) ν: 3063, 1781, 1720, 1508, 1377, 1079, 785, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.67-7.70 (m, 2H), 7.78-7.81 (m, 2H), 7.82-7.84 (m, 2H), 7.98 (dd, *J* = 5.6, 2.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 111.3, 118.2, 124.1, 126.4, 131.3, 132.9, 134.9, 135.9, 166.4; EI-MS *m/z* (relative intensity) 248 (M^+), 205, 204, 177.

Anal. Calcd for $C_{15}H_8N_2O_2$: C, 72.58; H, 3.25; N, 11.28. Found: C, 72.63; H, 3.46; N, 11.37.

***N*-Benzylphthalimide (3m)**

mp 118-119 °C (lit.[12] mp 118-119 °C). IR (KBr) ν: 3055, 1767, 1701, 1392, 1106, 951, 787, 722 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 4.83 (s, 2H), 7.24-7.31 (m, 3H), 7.41 (d, *J* = 6.8 Hz, 2H), 7.65-7.67 (m, 2H), 7.80-7.82 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 41.5, 123.2, 127.7, 128.5, 128.6, 132.0, 134.0, 136.2, 167.9; EI-MS *m/z* (relative intensity) 237 (M^+), 219, 208, 130, 105, 104, 78, 77.

***N*-Benzylglutarimide (3n)**

Oily compound (lit.[1(e)] oily compound). IR (neat) ν: 3025, 2924, 1723, 1457, 1355, 755, 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.94 (q, *J* = 6.8 Hz, 3H), 2.68 (q, *J* = 6.8 Hz, 4H), 4.95 (s, 2H), 7.23-7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 17.0, 32.8, 42.6, 127.4, 128.3, 128.8, 137.2, 172.4; EI-MS *m/z* (relative intensity) 203 (M^+), 175, 146, 118, 104, 92, 84.

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