A mild highly efficient and green protocol for preparation of *N*-alk-2'-enoyl cyclic imides using basic ionic liquid [bmIm]OH as base and reaction medium

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An efficient and green protocol for the preparation of *N*-alk-2'-enoyl cyclic imides at room temperature was developed using a basic ionic liquid, 1-methyl-3-butylimidazolium hydroxide, [bmIm]OH, as a base and a reaction medium.

Keywords: *N*-alk-2'-enoyl cyclic imides, 1-methyl-3-butylimidazolium hydroxide

N-Alk-2'-enoyl cyclic imides are of considerable interest, they have found increasing applications as important intermediates in organic synthesis.[1-5] However, reports concerning the synthesis of these compounds are rare, the main route to the α,β-unsaturated carboxylic acid derivatives involve reactions of activated carbonyl compound such as an acid chloride with cyclic imides using BuLi as a base under the temperature of –78 °C in THF.[1-2] In the past, we have delineated the utility of pyridine as base and medium in the reaction and *N*-alk-2'-enoyl cyclic imides has been prepared at room temperature,[4] but it suffered from major shortcomings such as environmentally hazardous residues, low yields in most examples, and troublesome chemical managing processes. Recently we successfully synthesised the target molecular using NaH as base at room temperature and the yields were raised apparently, but NaH was too dangerous to come into use in large scale.[5] For these reasons, the development of convenient, general, efficient and green methodologies for the synthesis of *N*-alk-2'-enoyl cyclic imides is highly desirable.

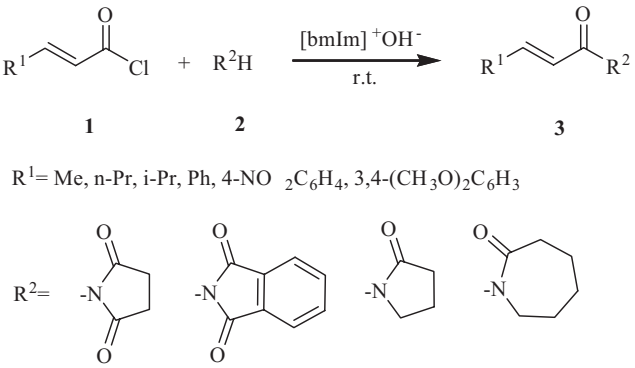
In recent times room temperature ionic liquids (RTLs) have attracted increasing interest in the area of green chemistry. RTLs containing imidazolium cations can act as a powerful medium in some organic reactions to accelerate the reaction.[6-12] RTLs include acidic, neutral and basic ionic liquids. The acidic and neutral ionic liquids have been well recognised and successfully applied in many organic reactions.[13-17] However, the related report about the basic ionic liquids was rare.

We now report the preparation of *N*-alk-2'-enoyl cyclic imides from acid chloride with cyclic imides in basic ionic liquids at room temperature. We chose $[bmIm]^+[OH]^-$ (1-methyl-3-butylimidazolium hydroxide) as base and reaction media and obtained high yield of products (Scheme 1). Compared with the method proposed before, the protocol was efficient and green, the products were readily separated from the ionic liquids and the yields of *N*-alk-2'-enoyl cyclic imides were satisfactory(see Table 1).

In summary, we have developed a new protocol for the preparation of the *N*-alk-2'-enoyl cyclic imides directly from α,β-unsaturated carboxylic acid chlorides with cyclic imides using a basic ionic liquid, $[bmIm]^+OH^-$, as base and reaction media. Further studies of possible applications of the moisture stable room temperature ionic liquids in the synthesis of acyl derivatives are being actively pursued.

Experimental

Reactions were carried out in a 10 ml flask equipped with a magnetic stirrer with no special precaution in the fume cupboard. Melting points were uncorrected. IR spectra were recorded on a Bruker Vector 22 spectrometer with absorption in cm^{-1}. ^1H NMR spectra were determined on a Bruker AC-400 (400 MHz) spectrometer with $CDCl_3$ as the solutions. Chemical shifts were expressed in ppm downfield from the internal standard tetramethylsilane. Mass spectra were recorded on a HP 5989B mass spectrometer. Elemental analyses were carried out on a VarioEL III instrument.



Scheme 1

General procedure for the preparation of (**3a**): To RTLs, $[bmIm]^+OH^-$, (364.0 mg, 2.0 mmol) was added succinimide (99.0 mg, 1.0 mmol), then the reaction mixture was stirred at room temperature for 1 h and crotonoyl chloride(104.5 mg, 1.0 mmol) was added dropwise over 15 min. After that, the reaction mixture was stirred for 2 h. The reaction mixture was extracted with ether (3 × 10 ml). The ether layer was separated and the product was further purified by column chromatography (3:1, petroleum ether/ethyl acetate), yield: 87%.

N-crotonoylsuccinimide (**3a**): White solid, m.p.109–111 °C (lit[2].108–109 °C); IR (KBr) 1731, 1692, 1440, 1416, 1331, 969 cm^{-1}; ^1H NMR ($CDCl_3$) δ:1.99 (dd, *J* = 1.7, 7.2 Hz, 3H), 2.82 (t, 4H), 6.42 (dd, *J* = 1.7, 15.4 Hz, 1H), 7.22–7.26 (m, 1H); ^{13}C NMR ($CDCl_3$): δ:19.1, 29.0, 125.0, 150.6, 164.4, 174.3, 175.0; MS *m/z*: 168 (M^+ + 1, 6.66%), 69 (Base peak); Anal. Calcd for $C_8H_9NO_3$: C, 57.48; H, 5.43; N, 8.38. Found: C,57.54; H,5.26; N, 8.45%.

N-crotonoylphthalimide (**3b**): White solid, m.p.124–126 °C; IR (KBr) 1744, 1685, 1638, 1466, 1446, 958 cm^{-1}; ^1H NMR ($CDCl_3$): δ:1.95 (d, *J* = 7.0 Hz, 3H), 6.68 (d, *J* = 15.2 Hz, 1H), 7.20–7.27(m, 1H), 7.77 (dd, *J* = 2.6, 5.2 Hz, 2H), 7.91 (dd, *J* = 2.8, 5.2 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ:168.4,168.2,141.7, 134.0, 130.9,128.7,128.0, 123.7, 123.3,18.8; MS *m/z*: 215 (M^+, 6.72%), 69 (Base peak); Anal. Calcd for $C_{12}H_9NO_3$: C, 66.97; H, 4.22; N, 6.51. Found: C,67.01; H, 4.20; N, 6.57%.

N-crotonoylpyrrolidin-2-one (**3c**): IR (film) 1736, 1680, 1639 cm^{-1}; ^1H NMR($CDCl_3$) δ:1.94 (d, *J* = 6.6 Hz, 3H), 2.03 (m, 2H), 2.61 (t, *J* = 8.1 Hz, 2H), 3.85 (t, *J* = 7.2 Hz, 2H), 7.11 (d, *J* = 15.5 Hz, 1H), 7.25 (m,1H); ^{13}C NMR ($CDCl_3$): δ: 175.4, 166.0, 145.7, 123.4, 45.5,33.7, 18.2, 17.0; MS *m/z*: 153 (M^+, 6.65%); Anal**.** Calcd for $C_8H_{11}NO_2$: C, 62.73; H, 7.24; N, 9.14. Found: C, 62.47; H, 7.51; N, 9.20%.

N-crotonoylazepan-2-one (**3d**): IR (film) 1703, 1655, 1515, 1463, 968 cm^{-1}; ^1H NMR ($CDCl_3$): δ:1.71, 1.82 (m, 6H), 1.90 (dd, *J* = 1.3, 6.6 Hz, 3H), 2.70–2.73 (m, 2H), 3.90 (t, *J* = 5.4 Hz, 2H), 6.70–6.73 (m, 1H), 6.94–7.02 (m, 1H); ^{13}C NMR ($CDCl_3$), δ:178.1, 168.7, 142.9, 122.5, 43.6, 39.5, 29.3, 28.8, 23.8, 18.3; MS *m/z*:181 (M^+, 20.65), 166 (base peak); Anal. Calcd for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N,7.73. Found: C,66.19; H, 8.35; N, 7.84%.

N-hex-2-enoylsuccinimide (**3e**): IR (film) 1803, 1734, 1695, 1632 cm^{-1}; ^1H NMR ($CDCl_3$): δ:0.94 (t, *J* = 7.5 Hz, 3H), 1.52 (m, 2H), 2.26 (m,

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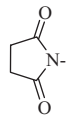
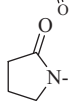
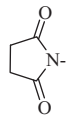
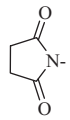
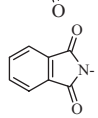
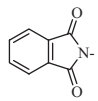
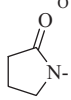
Table 1 N-alk-2'-enoyl cyclic imides products and the yields

Entry	R^1	R^2	Products	Time/h	Yield[a,b]/%
1	Me		**3a**	3	87
2	Me		**3b**	3	78
3	Me		**3c**	3	86
4	Me		**3d**	3	83
5	n-Pr		**3e**	3	84
6	n-Pr		**3f**	3	85
7	n-Pr		**3g**	3	79
8	i-Pr		**3h**	3	81
9	Ph		**3i**	5	85
10	Ph		**3j**	5	66
11	Ph		**3k**	5	70
12	4-$NO_2C_6H_4$		**3l**	5	64
13	3,4-$(CH_3O)_2C_6H_3$		**3m**	5	57

[a]All products were fully characterised by spectroscopic data(IR; ^{1}HNMR; ^{13}CNMR; MS).
[b]Isolated yield.

2H), 2.80 (s, 4H), 6.37 (d, J = 15.4 Hz, 1H), 7.21(dt, J = 15.9, 7.1 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ: 14.2, 21.6,29.2, 35.3, 123.8, 155.4, 164.7, 175.2; MS *m/z*: 195 (M^+, 24.2%); Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N, 7.18. Found: C, 61.60; H, 6.61; N, 7.21%.

N-hex-2-enoylpyrrolidin-2-one (**3f**): IR (film) 1737, 1679, 1634, 1357, 981 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 0.94 (t, J = 7.4 Hz, 3H), 1.52 (m, 2H), 2.04 (m, 2H), 2.25 (m, 2H), 2.61(t, J = 8.1 Hz, 2H), 3.85 (t, J = 7.2 Hz, 2H), 7.08–7.15 (m, 1H), 7.22–7.29 (m, 1H); ^{13}C NMR ($CDCl_3$) δ:175.6, 166.2, 150.5, 122.0, 45.6, 34.1, 33.8, 21.0, 17.0, 13.5; MS *m/z*: 181 (M^+, 9.59%); Anal. Calcd for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N,7.73. Found: C,66.17; H, 8.41; N, 7.79%.

N-hex-2-enoylazepan-2-one (**3g**): IR (film) 1787, 1729, 1646, 1462, 1378, 977 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 0.95 (t, J = 7.4 Hz, 3H), 1.49–1.53 (m, 2H), 1.70–1.79 (m, 6H), 2.17–2.22 (m, 2H), 2.72 (t, J = 6.4 Hz, 2H), 3.90 (t, J = 5.4 Hz, 2H), 6.70(dd, J = 1.4, 15.6 Hz, 1H), 6.94–7.01 (m, 1H); ^{13}C NMR ($CDCl_3$) δ: 178.0, 169.0, 147.9, 124.9, 43.6, 39.6, 34.5, 29.3, 28.6, 23.7, 21.4, 13.7; MS *m/z*: 209 (M^+, 23.54), 166 (base peak); Anal. Calcd for $C_{12}H_{19}NO_2$: C, 68.87; H, 9.15; N, 6.69. Found: C,68.77; H, 9.20; N, 6.83%.

N-(4-methylpent-2-enoyl)pyrrolidin-2-one (**3h**): IR (film)1742, 1674, 1634 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ:1.08(d, J = 3.2 Hz, 3H), 1.09(d, J = 2.8 Hz, 3H), 2.08–2.00(m, 2H), 2.54–2.51(m, 1H), 2.62 (t, J = 8.0 Hz, 2H) 3.86(t, J = 7.6 Hz, 2H), 7.09 (dd, J = 6.8, 15.4 Hz, 1H), 7.21(d, J = 16.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ:175.4, 166.5, 156.7, 119.3, 45.6, 33.8, 31.2, 21.2, 17.0; MS *m/z*: 182(M^+ + 1,44.4%), 96(base peak); Anal. Calcd for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N,7.73. Found: C, 66.17; H, 8.31; N, 7.48%.

N-cinnamoylsuccinimide (**3i**): White solid, m.p.118–119 °C (lit[2].119–120 °C); IR(KBr): 1794, 1728, 1684, 1663, 1447, 1442, 995 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ: 2.87 (s, 4H), 7.03 (d, J = 15.6 Hz, 1H), 7.38–7.46 (m, 3H), 7.59–7.63 (m, 2H), 7.92 (d, J = 15.6 Hz,1H); ^{13}C NMR($CDCl_3$): δ: 176.2, 166.0, 147.7, 134.2, 131.9, 129.5, 129.2, 128.7, 128.5, 121.2, 29.4; MS *m/z*: 229 (M^+, 9.89%). Anal. Calcd for $C_{13}H_{11}NO_3$: C, 68.11; H, 4.84; N, 6.11 Found: C, 67.80; H, 4.70; N, 6.10%.

N-cinnamoylphthalimide (**3j**): White solid, m.p.119–120 °C (lit[18].101–102 °C); IR(KBr): 1794, 1739, 1677, 1614, 1505, 986 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ: 7.38–7.44 (m, 4H), 7.64–7.66 (m, 2H), 7.85–7.87 (m, 2H), 7.97–8.01 (m, 3H); ^{13}C NMR($CDCl_3$): δ:165.5,

163.6, 147.7, 135.3, 134.0, 131.1, 131.0, 128.8, 128.7, 124.3, 119.3; MS *m/z*: 277(M^+, 9.54%); Anal**.** Calcd for $C_{17}H_{11}NO_3$: C, 73.64; H, 3.99; N, 5.05. Found: C,73.48; H, 3.88; N, 5.07%.

N-cinnamoylpyrrolidin-2-one (**3k**): White solid, m.p.101–102 °C (lit.[2] 101–102 °C); IR (KBr): 1769, 1701, 1631, 1495, 1450, 1422 cm^{-1}; ^1H NMR ($CDCl_3$): δ: 2.08 (tt, *J* = 6.8 Hz, 7.2 Hz, 2H), 2.66 (t, *J* = 6.8 Hz, 2H), 3.93 (t, *J* = 7.2 Hz, 2H), 7.38–7.41 (m, 3H), 7.61–7.64 (2H, m), 7.84, 7.95 (AB, *J* = 15.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ:17.2, 34.0, 45.9,119.0, 128.5, 128.8, 130.3, 134.9, 145.5, 166.3, 175.7; MS *m/z*: 215 (M^+, 9.59%); Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C,72.47; H, 6.11; N, 6.62%.

N-(3-(4-nitrophenyl)acryloyl)phthalimide (**3l**): Pale yellow solid, m.p. 215–217 °C; IR (KBr): 1797, 1739, 1619, 1593, 1516, 1412, 1342, 863 cm^{-1}; ^1H NMR ($CDCl_3$): δ: 7.57(d, *J* = 15.6 Hz, 1H), 7.80 (d, *J* = 8.3 Hz, 2H), 7.89 (t, *J* = 2.6 Hz, 2H), 7.98(d, *J* = 15.9 Hz, 1H), 8.02(d, *J* = 3.1 Hz, 2H), 8.29(d, *J* = 8.1 Hz, 2H); ^{13}C NMR($CDCl_3$): δ:165.9, 163.7, 148.7, 143.0, 140.8, 136.1, 131.6, 130.0, 125.2, 124.6, 124.5, 124.3; MS *m/z:* 322 (M^+, 28.28%), 102 (Base peak); Anal. Calcd for $C_{17}H_{10}N_2O_5$: C, 63.36; H, 3.13; N, 8.69. Found: C,63.27; H, 3.17; N, 8.74%.

N-(3-(3,4-dimethoxyphenyl)acryloyl)pyrrolidin-2-one (**3m**): White solid, m.p.147–148 °C; IR(KBr): 1638, 1597, 1513, 1445, 1349 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 2.05–2.10(m, 2H), 2.66(t, *J* = 8.0 Hz, 2H), 3.95–3.90(m, 8H), 6.87(d, *J* = 8.2 Hz, 1H), 7.14(d, *J* = 1.2 Hz, 1H), 7.19 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.80 (s, 1H), 7.81 (s, 1H); ^{13}C NMR ($CDCl_3$) δ:175.8, 166.4, 151.2, 149.0, 145.6, 127.9, 123.2, 116.6, 110.8, 109.9, 55.9, 55.8, 45.9, 34.0, 17.1; MS *m/z*: 275 (M^+, 52.8), 191(base peak); Anal. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.29; H, 6.22; N, 5.20%.

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