

Article

Beckmann Rearrangement of Ketoxime Catalyzed by *N*-methyl-imidazolium Hydrosulfate

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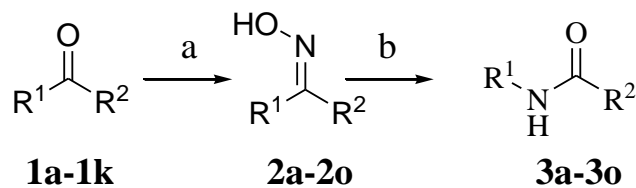
Abstract: Beckmann rearrangement of ketoxime catalyzed by acidic ionic liquid-*N*-methyl-imidazolium hydrosulfate was studied. Rearrangement of benzophenone oxime gave the desirable product with 45% yield at 90 °C. When co-catalyst P₂O₅ was added, the yield could be improved to 91%. The catalyst could be reused three cycles with the same efficiency. Finally, reactions of other ketoximes were also investigated.

Keywords: Beckmann rearrangement; ketoxime; acidic ionic liquid; catalysis

1. Introduction

Over the past years, amide derivatives have received much attention owing to their broad range of applications in many fields such as the pharmaceutical industry, chemical biology, the agrochemical industry, engineering plastics, and so on [1–6]. Various approaches have been developed for the synthesis of amide compounds including nucleophilic acyl substitution reactions with amines [7], Staudinger ligation [8], Schmidt reaction [9] and Beckmann rearrangement [10]. However, generations of large amounts of undesired by-products and corrosive phenomenon associated with common acid (H₂SO₄ and SOCl₂) based on liquid phase protocols provide a challenging task for chemists to develop alternative methods [11,12]. A variety of alternative routes [13–16] based on organic and inorganic solid acids were developed. However, traditional methods often suffer from some drawbacks such as poor selectivity, harsh conditions, are not atom economic, or are not environmentally friendly.

From the point of view of atom conversion efficiency, Beckmann rearrangement is a perfect way for construction of amides, in general sulfuric acid is most commonly used rearrangement catalyst in commercial production of amides. However, it brings equipment corrosion and environmental pollution problems. Recently, ionic liquids [17] have emerged as potential green alternatives to organic solvents due to their unique properties of low volatility, high polarity, good thermal stability, and excellent solubility [18–20]. Further, there are more potential capabilities as effective catalysts and reagents [13], as chemical transformations have also been explored. In order to develop a green pathway of amide synthesis, we report here a Beckmann rearrangement reaction catalyzed by *N*-methyl-imidazolium hydrosulfate ([HMI_m]⁺HSO₄⁻) [21] under solvent free conditions (Scheme 1).



Scheme 1. Synthesis of amides. Reagents and conditions: (a) $\text{NH}_2\text{OH}\cdot\text{HCl}$, NaOH , EtOH , H_2O , reflux; (b) acidic ionic liquid, P_2O_5 , N_2 , 90°C , 6 h.

2. Results

Beckmann rearrangement of benzophenone oxime catalyzed by $[\text{HMIm}]\text{HSO}_4$ was carried out at 120°C over 6 h without any solvent, the desired product, benzanilide, was obtained in moderate yield (45%). The co-catalysts such as P_2O_5 , FeCl_3 , ZnCl_2 , $\text{CuCl}_2\cdot 2\text{H}_2\text{O}$, and AlCl_3 were investigated in this reaction system, the yield was improved significantly to 91% with P_2O_5 . However, it has been shown in the literature that the conversion is around 20% only when P_2O_5 is used as the sole catalyst of Beckmann rearrangement [15]. When $\text{CuCl}_2\cdot 2\text{H}_2\text{O}$ was added, the yield was reduced to 14%, and the reverse reaction of benzophenone oxime was observed, benzophenone was regenerated. The results are presented in Table 1.

Table 1. Effect of co-catalyst on Beckmann rearrangement in ionic liquid systems.

Entry	Co-Catalyst	Yield (%)
1	a	45
2	P_2O_5	91
3	FeCl_3	47
4	AlCl_3	50
5	ZnCl_2	53
6	$\text{CuCl}_2\cdot 2\text{H}_2\text{O}$	14 ^b

Reaction conditions: Benzophenone oxime (9.5 mmol), $[\text{HMIm}]\text{HSO}_4$ (11.4 mmol), and co-catalyst (8%), 90°C , 6 h; ^a without co-catalyst; ^b benzophenone(%) was obtained.

The effect of the amount of co-catalyst P_2O_5 on reaction was investigated. The reaction yield was improved when more co-catalyst was added, and the best yield was around 90% when the amount of P_2O_5 was higher than 8 mol %. The results are presented in Figure 1.

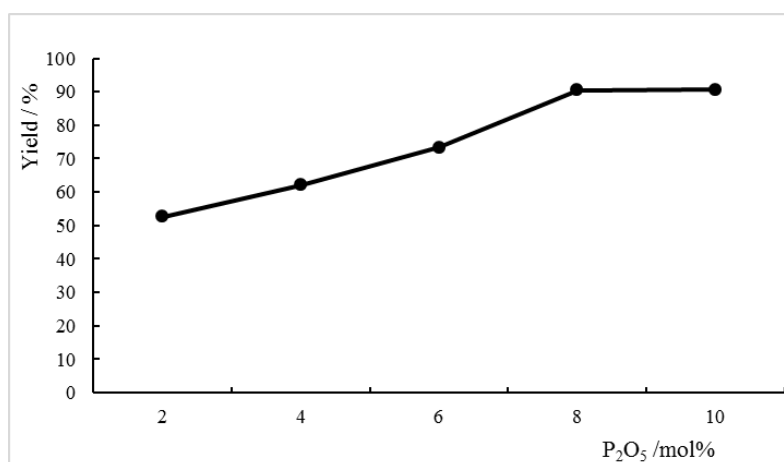


Figure 1. Effect of the amount of co-catalyst P_2O_5 on Beckmann rearrangement of benzophenone oxime. Reaction conditions: Benzophenone oxime (9.5 mmol), $[\text{HMIm}]\text{HSO}_4$ (11.4 mmol), 90°C , 6 h.

The influence of the reaction temperature on the yield was investigated subsequently. It was found that 90 °C is the best reaction temperature. The results are presented in Figure 2.

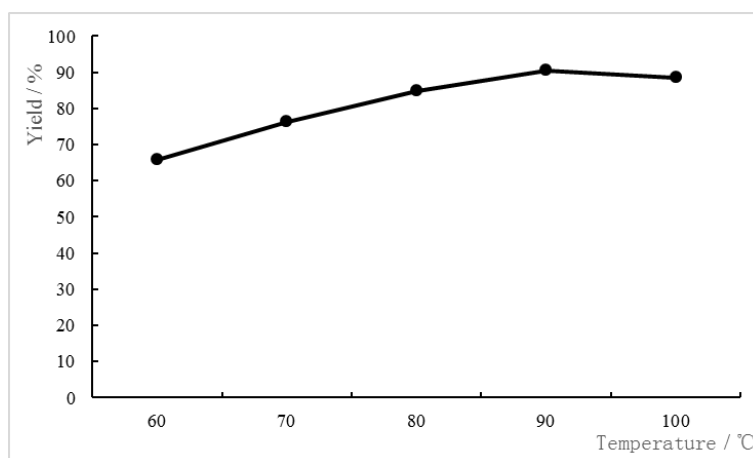


Figure 2. Influence of the reaction temperature on Beckmann rearrangement of benzophenone oxime. Reaction conditions: Benzophenone oxime (9.5 mmol), [HMIm]HSO₄ (11.4 mmol), 6 h, co-catalyst (P₂O₅ 8%).

The recycling performance of ionic liquid has the most benefits from the point of view of environmental protection. During the reaction workup, the white product was precipitated out when ice water was added, after filtration, the mother liquid was evaporated in a vacuum, and ionic liquid was recovered and could be reused for three times. The results are presented in Table 2.

Table 2. Effect of ionic liquid recycling on Beckmann rearrangement.

Reaction Turn	P ₂ O ₅ /%	Conversion/%	Yield/%
1	8	91	91
2	1	91	90
3	0.5	90	88

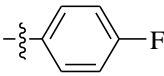
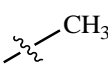
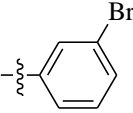
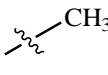
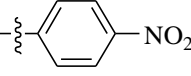
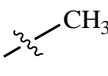
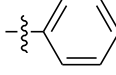
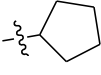
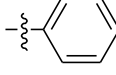
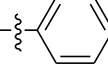
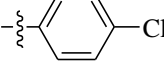
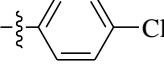


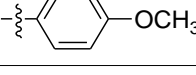
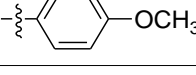
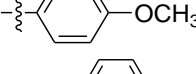
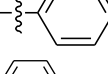
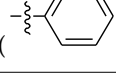
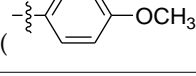
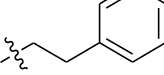

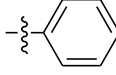

Reaction conditions: Benzophenone oxime (9.5 mmol), [HMIm]HSO₄ (11.4 mmol), 90 °C, 6 h; Conversion was determined by Gas Chromatography (GC) using internal standard method.

In order to explore the scope and limitations of this reaction, we extended the procedure to various aryl-substituted and alkyl-substituted ketoximes. In general, the reaction proceeded easily under the best conditions and the amide products were isolated in excellent yields and high purity. The results are presented in Table 3.

Table 3. Formation of amides (3a–3o) from ketoxime (2a–2o) in the presence of ionic liquid and co-catalyst P₂O₅.

Compd.	R ¹	R ²	Yield %
3a			91
3b			90
3c			90

Table 3. Cont.

3d			89
3e			88
3f			86
3g			91
3h			89
3i			85
3j			84
3k			90
3l(3l')			52
			28
3m			89
3n			82
3o	Caprolactam		85

Reaction conditions: Benzophenone oxime (9.5 mmol), [HMIm]HSO₄ (11.4 mmol), catalyst (P₂O₅ 8%), 90 °C, 6 h.

3. Experimental Section

All melting points were determined using a YRT-3 Digital Melting Point Apparatus (Tianjin, China). All melting points were uncorrected. All new compounds were characterized by HRMS-EI(M+), ¹H and ¹³C-NMR spectra were recorded in CDCl₃ or DMSO-d₆ on a Bruker AV 600 MHz or Bruker AV 400 MHz instrument. HRMS spectra were obtained on an Agilent 6230 mass spectrometer.

3.1. Synthesis of N-methyl-imidazolium Hydrosulfate ([HMIm]HSO₄)

N-Methylimidazole (8.2 g, 0.10 mol) was cooled down to 0 °C and concentrated sulfuric acid (10.0 g) was added dropwise. After addition, the solution was stirred 24 h at room temperature, a transparent viscous liquid (17.6 g) was obtained. Yield: 99%; IR (cm⁻¹): 3345, 3150, 2870, 1447, 1337, 1221, 1048, 1082, 887.

3.2. General Procedures for Synthesis of Oxime Substrates 2a–2o

Ketone (0.027 mol) and hydroxylamine hydrochloride (3.0 g, 0.043 mol) were dissolved in EtOH (10 mL) and H₂O (20 mL). To the mixture was added NaOH (5.5 g, 0.137 mol). The reaction mixture was heated under reflux and the reaction was monitored by thin layer chromatography (TLC). After completion of the reaction, the reaction mixture was cooled down to room temperature, to the reaction mixture were added concentrated hydrochloric acid (15 mL) and water (100 mL). The solid was filtered off and recrystallized from EtOH, affording the products 2a–2o.

2a: White solid, Yield: 91%. m.p.: 87.6–88.7 °C; ¹H-NMR (400 MHz, CDCl₃) δ 7.60 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 3.85 (s, 3H), 2.30 (s, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 160.5, 155.6, 129.0, 127.4, 113.9, 55.3, 13.3.

2b: White solid, Yield: 93%. m.p.: 88.0–89.0 °C; ¹H-NMR (400 MHz, CDCl₃) δ 7.55 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 2.39 (s, 3H), 2.31 (s, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 156.0, 139.3, 133.7, 129.3, 126.0, 21.3, 12.3.

2c: White solid, Yield: 90%. m.p.: 51.7–53.0 °C; ¹H-NMR (600 MHz, CDCl₃) δ 7.68–7.64 (m, 2H), 7.44–7.40 (m, 3H), 2.35 (s, 3H); ¹³C-NMR (150 MHz, CDCl₃) δ 156.1, 136.5, 129.3, 128.5, 126.1, 12.3.

2d: White solid, Yield: 70%. m.p.: 74.0–76.0 °C; ¹H-NMR (600 MHz, DMSO-*d*₆) δ 11.21 (s, 1H), 7.76–7.59 (m, 2H), 7.22–7.19 (m, 2H), 2.14 (s, 3H); ¹³C-NMR (150 MHz, DMSO-*d*₆) δ 162.4 (d, ¹*J*_{CF} = 245.5 Hz), 152.1, 133.5 (d, ⁴*J*_{CF} = 3.0 Hz), 127.6 (d, ³*J*_{CF} = 8.3 Hz), 115.2 (d, ²*J*_{CF} = 21.5 Hz), 11.9.

2e: White solid, Yield: 91%. m.p.: 141.0–142.0 °C; ¹H-NMR (600 MHz, DMSO-*d*₆) δ 11.40 (s, 1H), 7.80 (t, *J* = 1.8 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.34 (dd, *J* = 11.1, 4.6 Hz, 1H), 2.14 (s, 3H); ¹³C-NMR (150 MHz, DMSO-*d*₆) δ 151.9, 139.3, 131.3, 130.6, 128.1, 124.6, 121.8, 11.4.

2f: Yellow solid, Yield: 90%. m.p.: 172.0–173.0 °C; ¹H-NMR (400 MHz, DMSO-*d*₆) δ 11.78 (s, 1H), 8.28–8.18 (m, 2H), 7.96–7.88 (m, 2H), 2.21 (s, 3H); ¹³C-NMR (100 MHz, DMSO-*d*₆) δ 157.1, 152.5, 148.3, 131.9, 131.8, 16.6.

2g: White solid, Yield: 95.6%. m.p.: 129.6–131.0 °C; ¹H-NMR (600 MHz, DMSO-*d*₆) δ 10.49 (s, 1H), 7.42–7.27 (m, 5H), 3.04–2.85 (m, 1H), 1.75–1.66 (m, 2H), 1.64–1.50 (m, 6H); ¹³C-NMR (150 MHz, DMSO-*d*₆) δ 158.6, 135.8, 128.3, 128.2, 128.1, 45.2, 30.3, 24.9.

2h: White solid, Yield: 60%. m.p.: 92.0–93.0 °C; ¹H-NMR (600 MHz, DMSO-*d*₆) δ 11.40 (s, 1H), 7.48–7.44 (m, 2H), 7.43–7.40 (m, 1H), 7.387.37 (m, 5H), 7.30–7.25 (m, 2H); ¹³C-NMR (150 MHz, DMSO-*d*₆) δ 155.2, 136.8, 133.5, 128.88, 128.86, 128.40, 128.36, 128.2, 127.0.

2i: White solid, Yield: 87.5%. m.p.: 134.0–136.0 °C; ¹H-NMR (600 MHz, CDCl₃) δ 7.48 (d, *J* = 8.6 Hz, 2H), 7.43–7.37 (m, 4H), 7.36–7.31 (m, 2H); ¹³C-NMR (150 MHz, CDCl₃) δ 156.1, 135.9, 135.5, 134.3, 130.8, 130.4, 129.1, 128.8, 128.7.

2j: White solid, Yield: 88.5%. m.p.: 131.0–132.0 °C; ¹H-NMR (600 MHz, DMSO-*d*₆) δ 11.45 (s, 1H), 7.43–7.38 (m, 2H), 7.38–7.32 (m, 2H), 7.28 (dd, *J* = 12.3, 5.4 Hz, 2H), 7.19 (dd, *J* = 12.3, 5.4 Hz, 2H); ¹³C-NMR (150 MHz, DMSO-*d*₆) δ 162.6 (d, ¹*J*_{CF} = 244.6 Hz), 161.9 (d, ¹*J*_{CF} = 244.6 Hz), 153.4, 133.2, 131.3 (d, ³*J*_{CF} = 8.2 Hz), 129.5, 129.1 (d, ³*J*_{CF} = 8.2 Hz), 115.4 (d, ²*J*_{CF} = 22.6 Hz), 115.2 (d, ²*J*_{CF} = 22.3 Hz).

2k: White solid, Yield: 87.5%. m.p.: 129.0–130.0 °C; ¹H-NMR (400 MHz, DMSO-*d*₆) δ 11.1 (s, 1H), 7.31 (d, *J* = 8.8 Hz, 2H), 7.24 (d, *J* = 8.8 Hz, 2H), 6.99 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H), 3.76 (s, 3H); ¹³C-NMR (100 MHz, DMSO-*d*₆) δ 159.8, 159.1, 154.4, 130.7, 129.7, 128.6, 125.6, 113.7, 113.4, 55.2, 55.1.

2l: Light yellow solid, Yield: 87.9%. m.p.: 155.0–160.0 °C; (*isomer 1*): ¹H-NMR (600 MHz, DMSO-*d*₆) δ 11.27 (s, 1H), 7.38–7.34 (m, 4H), 7.29–7.24 (m, 3H), 7.00 (d, *J* = 8.7 Hz, 2H), 3.79 (s, 3H); (*isomer 2*): ¹H-NMR (600 MHz, DMSO-*d*₆) δ 11.09 (s, 1H), 7.46–7.43 (m, 2H), 7.42–7.38 (m, 3H), 7.30 (d, *J* = 8.8 Hz,

2H), 6.92 (d, $J = 8.8$ Hz, 2H), 3.75 (s, 3H); (isomer 1): $^{13}\text{C-NMR}$ (100 MHz, $\text{DMSO-}d_6$) δ 159.85, 154.85, 137.32, 130.74, 129.22, 128.32, 128.29, 128.12, 113.80, 55.20; (isomer 2): $^{13}\text{C-NMR}$ (100 MHz, $\text{DMSO-}d_6$) δ 159.20, 154.80, 133.82, 128.87, 128.76, 128.29, 127.32, 125.37, 113.46, 55.15.

2m: Yield: 94.0%. m.p.: 84–86 °C; $^1\text{H-NMR}$ (600 MHz, $\text{DMSO-}d_6$) δ 8.81 (brs, 1H), 7.30–7.18 (m, 5H), 2.83 (t, $J = 8.2$ Hz, 2H), 2.51 (t, $J = 8.2$ Hz, 2H), 1.91 (s, 3H); $^{13}\text{C-NMR}$ (150 MHz, $\text{DMSO-}d_6$) δ 157.9, 141.0, 128.4, 128.3, 126.1, 37.7, 32.6, 13.8.

2n: Yield: 90.0%. m.p.: 79–81 °C; $^1\text{H-NMR}$ (600 MHz, $\text{DMSO-}d_6$) δ 12.74 (s, 1H), 7.73–7.16 (m, 5H); $^{13}\text{C-NMR}$ (150 MHz, $\text{DMSO-}d_6$) δ 145.2 (q, $^2J_{\text{CF}} = 30.0$), 130.6, 129.0, 128.9, 127.2, 121.6 (q, $^1J_{\text{CF}_3} = 271.5$).

2o: Yield: 85.5%. m.p.: 89–91 °C; $^1\text{H-NMR}$ (600 MHz, $\text{DMSO-}d_6$) δ 2.48 (dd, $J = 6.8, 5.3$, 2H), 2.48 (m, 2H), 1.76–1.45 (m, 6H); $^{13}\text{C-NMR}$ (150 MHz, $\text{DMSO-}d_6$) δ 157.1, 31.6, 26.6, 25.4, 25.2, 23.8.

3.3. General Procedures for the Synthesis of Amides **3a–3o**

To a solution of the oxime substrates **2a–2o** (9.50 mmol) in (HMIm) HSO_4 (2.05 g, 11.4 mmol), the co-catalyst P_2O_5 (0.15 g, 1.0 mmol) was added. Then the solution was heated to 90 °C and the reaction was monitored by TLC. After completion of the reaction, the mixture was extracted with ethyl acetate (50 mL) twice, and the combined organic phase was washed with the aqueous solution of sodium bicarbonate and brine, dried over anhydrous Na_2SO_4 and concentrated in vacuo to afford a residue, which was purified by column (ethyl acetate: petroleum ether = 1:4) to afford the products **3a–3o**.

3a [22]: White solid, Yield: 91%. m.p.: 127.0–128.0 °C; $^1\text{H-NMR}$ (600 MHz, $\text{DMSO-}d_6$) δ 9.80 (brs, 1H), 7.51–7.46 (m, 2H), 7.20 (d, $J = 7.9$ Hz, 1H), 6.89–6.84 (m, 2H), 3.71 (s, 3H), 2.01 (s, 3H); $^{13}\text{C-NMR}$ (150 MHz, $\text{DMSO-}d_6$) δ 168.2, 155.5, 133.0, 121.0, 114.2, 55.6, 24.3; HRMS(+): calcd. for $\text{C}_9\text{H}_{11}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 166.0863, found 166.0859; calcd. for $\text{C}_9\text{H}_{11}\text{NO}_2\text{Na}$ $[\text{M} + \text{Na}]^+$ 188.0682, found 188.0682.

3b [22]: White solid, Yield: 90%. m.p.: 149.0–150.0 °C; $^1\text{H-NMR}$ (600 MHz, $\text{DMSO-}d_6$) δ 9.84 (s, 1H), 7.46 (d, $J = 8.3$ Hz, 2H), 7.09 (d, $J = 8.3$ Hz, 2H), 2.24 (s, 3H), 2.02 (s, 3H); $^{13}\text{C-NMR}$ (150 MHz, $\text{DMSO-}d_6$) δ 173.2, 142.1, 137.0, 134.1, 124.2, 29.2, 25.6; HRMS(+): calcd. for $\text{C}_9\text{H}_{11}\text{NO}$ $[\text{M} + \text{H}]^+$ 150.0913, found 150.0912; calcd. for $\text{C}_9\text{H}_{11}\text{NONa}$ $[\text{M} + \text{Na}]^+$ 172.0733, found 172.0741.

3c [23]: White solid, Yield: 90%. m.p.: 108.5–110.0 °C; $^1\text{H-NMR}$ (600 MHz, $\text{DMSO-}d_6$) δ 9.93 (brs, 1H), 7.58 (dd, $J = 1.0, 8.5$ Hz, 2H), 7.29 (dd, $J = 7.5, 8.4$ Hz, 2H), 7.08–6.91 (m, 1H), 2.05 (s, 3H); $^{13}\text{C-NMR}$ (150 MHz, $\text{DMSO-}d_6$) δ 168.7, 139.8, 129.1, 123.4, 119.4, 24.5; HRMS(+): calcd. for $\text{C}_8\text{H}_9\text{NO}$ $[\text{M} + \text{H}]^+$ 136.0757, found 136.0755; calcd. for $\text{C}_8\text{H}_9\text{NONa}$ $[\text{M} + \text{Na}]^+$ 158.0576, found 158.0572.

3d [24]: Light yellow solid, Yield: 89%. m.p.: 153–155 °C; $^1\text{H-NMR}$ (600 MHz, $\text{DMSO-}d_6$) δ 9.99 (brs, 1H), 7.87–7.47 (m, 2H), 7.12 (t, $J = 8.99$ Hz, 2H), 2.04 (s, 3H); $^{13}\text{C-NMR}$ (150 MHz, $\text{DMSO-}d_6$) δ 168.6, 158.3.8 (d, $^1J_{\text{CF}} = 237.0$ Hz), 136.2 (d, $^4J_{\text{CF}} = 1.5$ Hz), 121.1 (d, $^3J_{\text{CF}} = 7.5$ Hz), 115.2 (d, $^2J_{\text{CF}} = 22.5$ Hz), 24.3; HRMS(+): calcd. for $\text{C}_8\text{H}_8\text{FNO}$ $[\text{M} + \text{H}]^+$ 154.0663, found 154.0665; calcd. for $\text{C}_8\text{H}_8\text{FNONa}$ $[\text{M} + \text{Na}]^+$ 176.0482, found 176.0481.

3e [25]: White solid, Yield: 88%. m.p.: 87.0–89.0 °C; $^1\text{H-NMR}$ (600 MHz, $\text{DMSO-}d_6$) δ 10.11 (brs, 1H), 7.95 (s, 1H), 7.47 (d, $J = 7.9$ Hz, 1H), 7.27–7.23 (m, 1H), 7.22–7.19 (m, 1H), 2.05 (s, 3H); $^{13}\text{C-NMR}$ (150 MHz, CDCl_3) δ 169.1, 141.3, 131.1, 126.0, 122.0, 121.7, 118.1, 24.5; HRMS(+): calcd. for $\text{C}_8\text{H}_8\text{BrNO}$ $[\text{M} + \text{H}]^+$ 213.9862, found 213.9860; calcd. for $\text{C}_8\text{H}_8\text{BrNONa}$ $[\text{M} + \text{Na}]^+$ 235.9681, found 235.9681.

3f [25]: Yellow solid, Yield: 86%. m.p.: 214.0–215.0 °C; $^1\text{H-NMR}$ (600 MHz, $\text{DMSO-}d_6$) δ 10.57 (s, 1H), 8.21 (d, $J = 9.2$ Hz, 2H), 7.82 (d, $J = 9.4$ Hz, 2H), 2.12 (s, 3H); $^{13}\text{C-NMR}$ (150 MHz, $\text{DMSO-}d_6$) δ 169.8, 145.9, 142.3, 125.4, 119.0, 24.7; HRMS(+): calcd. for $\text{C}_8\text{H}_8\text{N}_2\text{O}_3$ $[\text{M} + \text{H}]^+$ 181.0608, found 181.0610; Calcd. for $\text{C}_8\text{H}_8\text{N}_2\text{O}_3\text{Na}$ $[\text{M} + \text{Na}]^+$ 203.0433, found 203.0437.

3g: White solid, Yield: 91%. m.p.: 160.0–161.0 °C; $^1\text{H-NMR}$ (600 MHz, $\text{DMSO-}d_6$) δ 8.29 (d, $J = 7.0$ Hz, 1H), 7.88–7.80 (m, 2H), 7.54–7.49 (m, 1H), 7.48–7.42 (m, 2H), 4.46–3.96 (m, 1H), 1.96–1.81 (m, 2H),

1.74–1.64 (m, 2H), 1.60–1.43 (m, 4H); ^{13}C -NMR (150 MHz, DMSO- d_6) δ 166.4, 135.3, 131.4, 128.6, 127.7, 51.4, 32.6, 24.1; HRMS(+): calcd. for $\text{C}_{12}\text{H}_{15}\text{NO}$ $[\text{M} + \text{H}]^+$ 190.1226, found 190.1228; calcd. for $\text{C}_{12}\text{H}_{15}\text{NO Na}$ $[\text{M} + \text{Na}]^+$ 212.1046, found 212.1044.

3h [23]: White solid, Yield: 89%. m.p.: 162.6–163.0 °C; ^1H -NMR (400 MHz, DMSO- d_6) δ 10.25 (s, 1H), 7.99–7.92 (m, 2H), 7.78 (d, $J = 7.6$ Hz, 2H), 7.63–7.58 (m, 1H), 7.57–7.51 (m, 2H), 7.36 (t, $J = 7.9$ Hz, 2H), 7.15–7.07 (m, 1H); ^{13}C -NMR (100 MHz, DMSO- d_6) δ 166.0, 139.6, 135.5, 132.0, 129.1, 128.9, 128.1, 124.1, 120.8; HRMS(+): calcd. for $\text{C}_{13}\text{H}_{11}\text{NO}$ $[\text{M} + \text{H}]^+$ 198.0913, found 198.0913; calcd. for $\text{C}_{13}\text{H}_{11}\text{NONa}$ $[\text{M} + \text{Na}]^+$ 220.0733, found 220.0733.

3i [25]: White solid, Yield: 85%. m.p.: 210.0–212.0 °C; ^1H -NMR (600 MHz, DMSO- d_6) δ 10.45 (s, 1H), 8.02–7.96 (m, 2H), 7.86–7.79 (m, 2H), 7.66–7.59 (m, 2H), 7.45–7.39 (m, 2H); ^{13}C -NMR (150 MHz, DMSO- d_6) δ 165.0, 138.4, 137.0, 133.8, 130.1, 129.0, 127.9, 122.4; HRMS(+): calcd. for $\text{C}_{13}\text{H}_9\text{C}_{12}\text{NO}$ $[\text{M} + \text{H}]^+$ 266.0134, found 266.0129; calcd. for $\text{C}_{13}\text{H}_9\text{C}_{12}\text{NONa}$ $[\text{M} + \text{Na}]^+$ 287.9953, found 287.9951.

3j [26]: Light yellow solid, Yield: 84%. m.p.: 183–185.0 °C; ^1H -NMR (600 MHz, DMSO- d_6) δ 10.31 (s, 1H), 8.04–8.02 (m, 2H), 7.82–7.72 (m, 2H), 7.37 (t, $J = 8.8$ Hz, 2H), 7.19 (t, $J = 8.8$ Hz, 2H); ^{13}C -NMR (150 MHz, DMSO- d_6) δ 164.3, 164.1 (d, $^1J_{\text{CF}} = 249.5$ Hz), 158.3 (d, $^1J_{\text{CF}} = 240.3$ Hz), 135.4, 131.2, 130.4 (d, $^3J_{\text{CF}} = 9.0$ Hz), 122.2 (d, $^3J_{\text{CF}} = 7.8$ Hz), 115.3 (d, $^2J_{\text{CF}} = 22.4$ Hz), 115.2 (d, $^2J_{\text{CF}} = 22.8$ Hz); HRMS(+): calcd. for $\text{C}_{13}\text{H}_9\text{F}_2\text{NO}$ $[\text{M} + \text{H}]^+$ 234.0725, found 234.0727; calcd. for $\text{C}_{13}\text{H}_9\text{F}_2\text{NONa}$ $[\text{M} + \text{Na}]^+$ 256.0544, found 256.0546.

3k [26]: Light yellow solid, Yield: 90%. m.p.: 204.0–205.0 °C; ^1H -NMR (600 MHz, CDCl_3) δ 7.83 (d, $J = 8.8$ Hz, 2H), 7.65 (s, 1H), 7.52 (d, $J = 9.0$ Hz, 2H), 6.97 (d, $J = 8.8$ Hz, 2H), 6.91 (d, $J = 9.0$ Hz, 2H), 3.87 (s, 3H), 3.81 (s, 3H); ^{13}C -NMR (150 MHz, DMSO- d_6) δ 164.5, 161.7, 155.4, 132.4, 129.4, 127.1, 121.9, 113.7, 113.5, 55.4, 55.2; HRMS(+): calcd. for $\text{C}_{15}\text{H}_{15}\text{NO}_3$ $[\text{M} + \text{H}]^+$ 258.1125, found 258.1127; calcd. for $\text{C}_{15}\text{H}_{15}\text{NO}_3\text{Na}$ $[\text{M} + \text{Na}]^+$ 280.0944, found 280.0946.

3l [25] (*N*-(4-Methoxyphenyl)benzamide): Light yellow solid, Yield: 52%. M.p.: 156.5–159.5 °C; ^1H -NMR (600 MHz, DMSO- d_6) δ 10.07 (s, 1H), 7.95 (d, $J = 9.2$ Hz, 2H), 7.74 (d, $J = 7.6$ Hz, 2H), 7.51 (t, $J = 7.6$ Hz, 1H), 7.33 (t, $J = 7.9$ Hz, 2H), 7.05 (d, $J = 9.2$ Hz, 2H), 3.84 (s, 3H); ^{13}C -NMR (100 MHz, DMSO- d_6) δ 164.94, 161.91, 139.36, 131.40, 129.61, 128.58, 123.45, 120.37, 113.62, 55.45; HRMS(+): calcd. for $\text{C}_{14}\text{H}_{13}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 228.1019, found 228.1020; calcd. for $\text{C}_{14}\text{H}_{13}\text{NO}_2\text{Na}$ $[\text{M} + \text{Na}]^+$ 250.0838, found 250.0838; (*4*-Methoxy-*N*-phenylbenzamide): Light yellow solid, Yield: 28% ^1H -NMR (600 MHz, DMSO- d_6) δ 10.12 (s, 1H), 7.94 (d, $J = 7.2$ Hz, 2H), 7.67 (d, $J = 9.0$ Hz, 2H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.09 (t, $J = 8.8$ Hz, 2H), 6.93 (d, $J = 9.0$ Hz, 2H), 3.74 (s, 3H); ^{13}C -NMR (100 MHz, DMSO- d_6) δ 165.14, 155.58, 135.07, 132.24, 128.37, 127.56, 127.00, 122.02, 113.76, 55.20. HRMS(+): calcd. for $\text{C}_{14}\text{H}_{13}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 228.1019, found 228.1020; calcd. for $\text{C}_{14}\text{H}_{13}\text{NO}_2\text{Na}$ $[\text{M} + \text{Na}]^+$ 250.0838, found 250.0838.

3m [27]: Yield: 89%. m.p.: 113–114 °C; ^1H -NMR (600 MHz, DMSO- d_6) δ 7.34–7.30 (m, 2H), 7.26–7.21 (m, 3H), 3.85–3.77 (m, 2H), 2.84–2.74 (m, 2H), 2.29 (s, 3H); ^{13}C -NMR (150 MHz, DMSO- d_6) δ 173.4, 139.0, 129.3, 129.0, 126.9, 46.4, 34.8, 26.6. HRMS(+): calcd. for $\text{C}_{10}\text{H}_{13}\text{NO}$ $[\text{M} + \text{H}]^+$ 164.1070, found 164.1071; calcd. for $\text{C}_{10}\text{H}_{13}\text{NONa}$ $[\text{M} + \text{Na}]^+$ 186.0889, found 186.0884.

3n [28]: Yield: 82%. m.p.: 84–87 °C; ^1H -NMR (600 MHz, DMSO- d_6) δ 11.26 (brs, 1H), 7.70 (dd, $J = 0.83, 8.53$ Hz, 2H), 7.43–7.38 (m, 2H), 7.24–7.20 (m, 1H), ^{13}C -NMR (150 MHz, DMSO- d_6) δ 155.0 (q, $^2J_{\text{CF}} = 36.0$), 136.8, 129.4, 126.0, 121.5, 116.3 (q, $^1J_{\text{CF}3} = 286.5$). HRMS(+): calcd. for $\text{C}_8\text{H}_6\text{F}_3\text{NO}$ $[\text{M} + \text{H}]^+$ 190.0474, found 190.0472; calcd. for $\text{C}_8\text{H}_6\text{F}_3\text{NONa}$ $[\text{M} + \text{Na}]^+$ 212.0294, found 212.0296.

3o [29]: Yield: 85%. m.p.: 68–71 °C; ^1H -NMR (600 MHz, DMSO- d_6) δ 7.41 (brs, 1H), 3.05 (dd, $J = 5.87, 10.09$ Hz, 2H), 2.38–2.13 (m, 2H), 1.66 (q, $J = 5.87$ Hz, 2H), 1.56–1.46 (m, 4H); ^{13}C -NMR (150 MHz, DMSO- d_6) δ 177.4, 41.9, 36.9, 30.5, 30.3, 23.4. HRMS(+): calcd. for $\text{C}_6\text{H}_{11}\text{NO}$ $[\text{M} + \text{H}]^+$ 114.0913, found 114.0910; calcd. for $\text{C}_6\text{H}_{11}\text{NONa}$ $[\text{M} + \text{Na}]^+$ 136.0733, found 136.0734.

4. Conclusions

In conclusion, we successfully demonstrated an efficient approach for the synthesis of amide derivatives via Beckmann rearrangement of ketoxime by using Brønsted acidic ionic liquid *N*-methyl-imidazolium hydrosulfate as an environmental friendly catalyst and solvent. The best reaction condition is: reaction temperature 90 °C, reaction time 6 h, solvent *N*-methyl-imidazolium hydrosulfate 10 grams, co-catalyst P₂O₅ 8 mol %. Ionic liquid can be reused three times. The procedure can be extended to various symmetrical and unsymmetrical aryl-substituted and alkyl-substituted ketoxime substrates. The aryl group migration products are sole products for unsymmetrical aryl alkyl substituted amides.

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Sample Availability: Samples of the compounds are available from the authors.



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