

Microwave-assisted rapid Beckmann rearrangement of ketoximes using two acidic functional groups containing ionic liquids

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Abstract: An efficient microwave-assisted conversion of ketoximes into amides using Brønsted acidic task-specific ionic liquids, 3-methyl-1-sulfonic acid imidazolium chloride, 3-methyl-1-sulfonic acid imidazolium hydrogen sulfate and 1,3-disulfonic acid imidazolium chloride via the Beckmann rearrangement is described. This method offers significant advantages such as efficiency, solvent-free and mild reaction conditions with shorter reaction times.

Keywords: Microwave-assisted, Beckmann rearrangement, [Msim]HSO₄, Ketoxime, Solvent-free.

Introduction

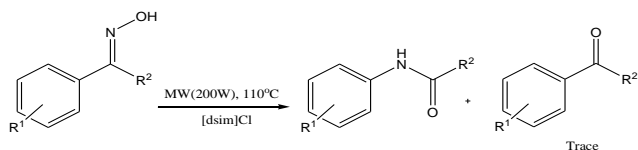
Amides are very important organic compounds which are used for the preparation of some chemically useful materials. Beckmann rearrangement, the well-known reaction in organic chemistry, is used for the synthesis of amides from the ketoximes. It also shows an important role in the chemical industry such as manufacturing of ϵ -Caprolactam from cyclohexanone oxime. This reaction generally carried out in high temperatures and in the presence of concentrated strong protic acids such as sulfuric acid and SOCl₂ [1]. But this process suffers from some drawbacks such as corrosion problems and large amount of by-products. Some milder conditions by using a variety of interesting catalysts were also reported [2-5]. Tatsumi and co-workers reported this rearrangement in gaseous phase [6]. Triphosphazene and some heterogeneous catalysts were found to be efficiently catalyzed this reaction [7-8].

Microwave irradiation (MWI) has a wide range of applications in the organic synthesis and is a very

efficient to accelerate the organic reactions [9-11]. Ionic liquids (ILs) have been investigated as an alternative attractive solvent in chemical processes [12,13]. ILs have favorable properties such as extremely low volatility, low flammability, ease of recovery, recycling, and applicability to catalytic processes [14,15]. ILs containing covalently bonded functional groups, known as task-specific ionic liquids (TSILs). TSILs are able to play multiple roles as solvent, catalyst and/or reagent [16-18]. Vilas et al. reported the Beckmann rearrangement of ketoximes in ionic liquids [19]. Brønsted acidic ILs, have been used as an efficient alternative catalyst in chemical reactions [20]. In continuation of our interest to use ionic liquids (IL's), in water or solventless systems as green reaction media [21], in this report, we wish to highlight our results on using the ionic liquids, [Msim]Cl, [Msim]HSO₄ or [Dsim]Cl as a catalyst for the Beckmann rearrangement of ketoximes to produce amides in good to excellent yields under MW-assisted solvent-free conditions (Scheme 1).

Results and discussion

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Scheme 1: MW-assisted Beckmann rearrangement catalyzed with acidic ionic liquids.

Brønsted acidic ionic liquids, [Bmim]Cl, [Msim]Cl, [Msim]HSO₄ and [Dsim]Cl were prepared according to the reported methods in the literature [22]. 4-Chloroacetophenone oxime has been used as a typical molecule to investigate the feasibility of Beckmann rearrangement reaction of oxime using these ionic liquids. We first, examined the reaction in [bmim]Cl at 90 °C in the absence of any acid under solvent-free conditions. The reaction failed and no significant change was observed. This reaction was then examined under MW irradiation and negligible amount (<7%) of the 4-chloroacetanilide was isolated. Good improvement in yield of the product (>25%) was achieved using the acidic ionic liquid, [Msim]Cl under the same conditions. This reaction was tested in organic solvents such as toluene, DMF, acetonitrile,

chloroform in the presence of the catalytic amount of [Msim]Cl and no significant changes in the yield of the product was observed. However, good improvement in the yield of 4-chloroacetanilide was observed when the ionic liquid, [Bmim]Cl was added to the reaction mixture as a solvent. 4-Chloroacetanilide was isolated in 35% yield under MW-irradiation (200W) at 110 °C after 3 min. The only MW confirmed by-product is a trace amount of 4-chloroacetophenone, which is derived from the deoxygenation of 4-chloroacetophenone oxime. Optimization of the reaction conditions were studied with different molar ratios of the 4-chloroacetophenone, [Bmim]Cl and [Msim]Cl. The best ratio was found to be 1:3:0.3. The effect of the other Brønsted acidic ionic liquids, [Msim]HSO₄ and [Dsim]Cl were also investigated and 4-chloroacetanilide were obtained in 82% and 88% yields using these ILs respectively. For comparison, this procedure was examined for the rearrangement of the three other ketoximes in the presence of acidic ILs, [Msim]Cl, [Msim]HSO₄ and [Dsim]Cl. The results are summarized in Table 1.

Table 1: Beckmann rearrangement of selected ketoximes in the presence of acidic ionic liquids in neutral [bmim]Cl under MW-irradiation.

Entry	Oxime	[Msim]Cl		[Msim]HSO ₄		[Dsim]Cl		
		[Bmim]Cl	Time (min)	Yield ^a (%)	Time (min)	Yield ^a (%)	Time (min)	Yield ^a (%)
1		-	4.5	28	3.5	79	3	85
2		-	3.5	35	3	82	2.5	88
3		-	3.5	30	3.5	80	2.5	87
4		-	4.5	25	4	76	3.5	82

^aIsolated yields after recrystallization.

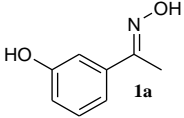
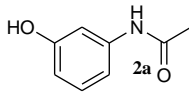
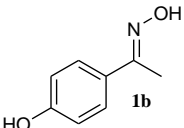
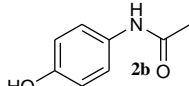
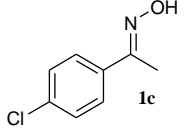
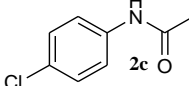
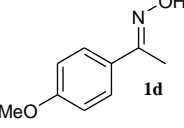
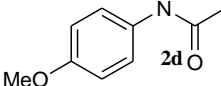
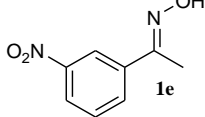
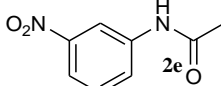
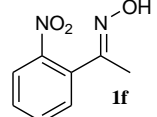
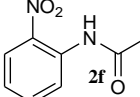
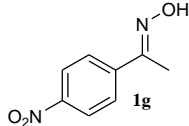
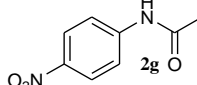
As it can be observed from Table 1, since there are double acidic functional groups in ILs [Msim]HSO₄ and [Dsim]Cl, compared to single acidic functional

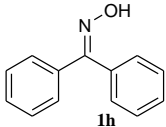
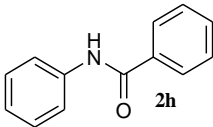
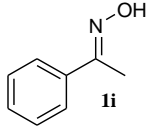
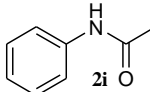
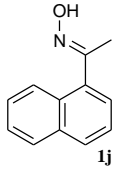
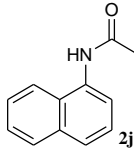
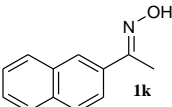
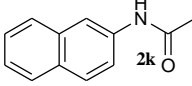
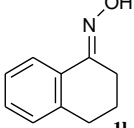
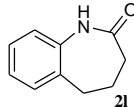
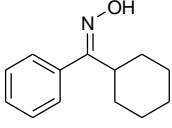
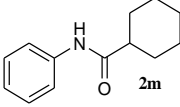
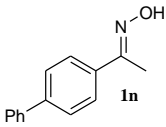
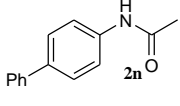
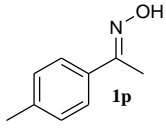
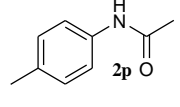
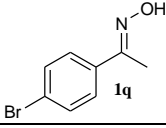
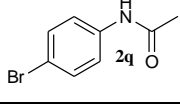
group in [Msim]Cl, higher yields of products in shorter reaction times were achieved using these two ionic liquids. As it was shown in Table 1, the products were

obtained in significantly higher yields in the presence of [Dsim]Cl in comparison with [Msim]HSO₄ under optimized conditions. To investigate the scope and applicability of this method, the Beckmann rearrangement of a variety of ketoximes were proceeded using the [Dsim]Cl, and the related amides

were isolated and characterized (Table 2). It was observed that aryl group migrate preferably over alkyl and cycloalkyl groups. When there is an electron withdrawing group in aromatic ring, especially in other or para position, the reaction proceeds in a shorter time and higher yields (entries 3, 5, 6, 7, 16, Table 2).

Table 2: MW assisted Beckmann rearrangement of a variety of ketoximes using [Dsim]Cl in neutral [Bmim]Cl.

Entry	Oximes (1a-1q)	Amides	Reaction times (min)	M.P (°C)	Yield ^a (%)
1			3	145-148	83
2			3	168-172	80
3			2.5	177-181	88
4			3	129-132	80
5			2.5	155-156	89
6			2	92-94	85
7			1.5	213-216	94

8			3.5	161-165	83
9			3	111-115	85
10			3.5	-	90
11			3.5	-	80
12			3	137-139	80
13			3.5	-	82
14			3	-	85
15			3	145-148	80
16			2.5	168	87

^aIsolated yields after recrystallization.

Conclusion

In conclusion, a mild, general and efficient conversion of oximes to corresponding amides under MW-irradiation has been developed. The key feature of this method is the use of acidic ionic liquid, [Dsim]Cl as a mild and efficient catalyst. This method seems to be convenient and very rapid with respect to other existing reports and can be used as an alternative.

Experimental

General information:

All reagents were purchased from Merck Company and used without further purification. Infrared spectra were recorded on a Perkin Elmer FT-IR spectrometer using KBr pellets. NMR spectra of samples in CDCl₃ and DMSO-d₆ solution were measured using a Bruker Avance AC-400 instrument (¹H at 300 MHz and ¹³C at 75 MHz). Mass spectra, using electron ionization (EI)-

mass spectrometry (MS), were recorded on a Shimadzu GCMS-QP-2000A mass spectrometer. Elemental analyses were conducted using the Perkin-Elmer 240C elemental analyzer, their results were found to be in good agreement with the calculated values. All melting points measured in open glass-capillaries using Stuart melting point apparatus. Microwave experiments were conducted in a Milestone MicroSYNTH apparatus.

Preparation of 3-methyl-1-sulfonic acid imidazolium chloride [Msim]Cl:

A round-bottom flask (100 ml) was charged with 1-methylimidazole (0.410 g, 5 mmol) in dry CH_2Cl_2 (50 ml), and then chlorosulfonic acid (0.583 g, 5 mmol) was added dropwise over a period of 5 min at room temperature. After the addition was completed, the reaction mixture was stirred for 20 min, stand for 5 min, and the CH_2Cl_2 was decanted. The residue was washed with dry CH_2Cl_2 (3×50 ml) and dried under vacuum to give [Msim]Cl as a viscous colorless oil.

Preparation of 1,3-disulfonic acid imidazolium chloride, [Msim]HSO₄:

To a round-bottom flask (100 ml) that was charged with [Msim]Cl (1.63 g, 10 mmol) in dry acetone (30 ml), NaHSO_4 (1.44 g, 12 mmol) was added. The reaction mixture was then stirred at room temperature for 24 h under nitrogen pressure (to remove produced HCl). The resulting mixture was filtered and evaporation of solvent under reduced pressure afforded yellow colored viscous liquid [Msim]HSO₄.

Preparation of 1,3-disulfonic acid imidazolium chloride, [Dsim]Cl:

To a round-bottom flask (100 ml) containing imidazole (0.340 g, 5 mmol) in CH_2Cl_2 (50 ml), was added chlorosulfonic acid (1.177 g, 10.2 mmol) dropwise over a period of 20 min at room temperature. After the addition was completed, the reaction mixture was stirred for 12 h under pressure of nitrogen, stand for 5 min, and then CH_2Cl_2 was decanted. The residue was washed with dry CH_2Cl_2 (3×50 ml) and dried under vacuum to give [Dsim]Cl as a viscous pale yellow oil.

Beckmann rearrangement of ketoxime in ILs: General procedure:

Ketoxime (10 mmol) was added to [Bmim]Cl (30 mmol) and subjected to microwave irradiation (200W) for a few seconds. Then, 30 mol% of acidic ionic liquid was added to the reaction mixture and irradiated with MW (200W) at 110 °C for a time as mentioned in Table

1. The completion of the reaction was concluded by TLC using EtOAc/petroleum ether as eluent and the product was isolated via thin layer chromatography using EtOAc/petroleum ether as eluent in good yields (Table 1).

Selected spectroscopic data:

N-(4-Chlorophenyl)acetamide (2c):

¹HNMR (DMSO-d₆, 300 MHz), δ : 2.04 (3H, s), 7.34 (2H, d, J = 8.7 Hz), 7.59 (2H, d, J =8.7 Hz), 10.06 (1H, s). ¹³CNMR (DMSO-d₆, 75 MHz), δ : 29.1, 125.6, 131.6, 133.7, 143.4, 173.6.

N-(4-Methoxyphenyl)acetamide (2d):

¹HNMR (DMSO-d₆, 300 MHz), δ : 1.99 (3H, s), 3.70(3H, s), 6.84 (2H, d, J =9 Hz), 7.45 (2H, d, J =15 Hz), 9.75 (1H, s). ¹³CNMR (CDCl₃, 75 MHz), δ : 23.9, 55.3, 113.8, 122.0, 131.1, 156.2, 168.9.

N-(4-Nitrophenyl)acetamide (2g):

¹HNMR (CDCl₃, 300 MHz), δ : 10.59 (1H, br s) 8.18 (d, 2H, J = 9Hz), 7.81 (2H, d, 9Hz), 2.1(1H, s). ¹³CNMR (CDCl₃, 75MHz), δ : 169.3, 145.46, 141.95, 124.97, 118.52, 24.23.

N-(2-Nitrophenyl)acetanilide (2f):

¹HNMR (CDCl₃, 300 MHz), δ : 9.94 (1H, s), 8.04 (d, 1H), 7.62(1H, d), 7.53 (1H, t), 7.38 (1H, d), 2.26 (3H, s); ¹³CNMR (CDCl₃, 75 MHz), δ : 170.4, 142.2, 134.8, 131.3, 130.3, 128.2, 124.2, 23.1.

N-Phenylbenzamide (2h):

¹HNMR (CDCl₃, 300 MHz), δ : 7.1 (1H, t, J = 7.5 Hz), 7.36 (2H, t, J = 7.5 Hz), 7.46 (2H, t, J = 7.5 Hz), 7.53 (1H, d, J = 7.5 Hz), 7.64 (2H, d, J = 7.8Hz), 7.86 (2H, d, J = 7.2 Hz), 7.93 (1H, s). ¹³CNMR (CDCl₃, 75 MHz), δ : 120.2, 124.5, 126.9, 128.8, 129.1, 131.8, 134.9, 137.9.

N-Phenylacetamide (2i):

¹HNMR (DMSO-d₆, 300 MHz), δ : 2.03 (3H, s), 7.55 (2H, d, J = 8.4 Hz), 9.9(1H, s). ¹³CNMR (CDCl₃, 75MHz), δ : 24.3, 120, 124.2, 128.8, 137.9, 169.0.

N-(3-Nitrophenyl)acetanilide (2e):

¹HNMR (DMSO-d₆, 300 MHz), δ : 8.82 (1H, s), 8.37 (1H, s), 8.08 (1H, t), 7.80 (1H, d), 7.47 (1H, d), 2.27 (3H, s). ¹³C NMR (CDCl₃, 75 MHz), δ : 170.0, 150.5, 140.8, 132.6, 129.5, 124.7, 121.4, 20.2.

4-(Trifluoromethoxy)benzamide (2k):

¹HNMR (DMSO-d₆, 300 MHz), δ: 8.08 (1H, s), 7.99 (2H, m), 7.51 (1H, s), 7.45 (2H, m). ¹³CNMR (DMSO-d₆, 75 MHz), δ: 166.7, 150.3, 133.4, 129.8, 121.7, 120.6.

N-p-Tolylacetamide (2p):

¹HNMR (CDCl₃, 300 MHz), δ: 8.28 (1H, br s), 7.40 (2H, d, *J*= 8.2 Hz), 7.09 (2H, d, *J*= 8.1 Hz), 2.30 (3H, s), 2.12 (3H, s); ¹³CNMR (CDCl₃, 75MHz), δ: 168.95, 135.53, 133.84, 129.36, 120.30, 24.28, 20.84.

Acknowledgement

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