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Journal of Applied Chemical Research, 11, 4, 18-27 (2017)

Application of Acidic Ionic Liquid as a Solvent/Catalyst for Preparation of α-Oximinoketones from β-Dicarbonyl Compounds

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(Received 14 Mar. 2017; Final version received 17 Jun. 2017)

Abstract

The selective nitrosation of β-dicarbonyl compounds with sodium nitrite was carried out under1-methyl-3-carboxymethylimidazolium chloride, prepared from N-methylimidazole and chloroacetic acid, as an acidic ionic liquid. The reaction was found to proceed under relatively mild conditions with excellent conversion and selectivity. The ionic liquid was recycled and reused.

***Keywords*:** *β-Dicarbonyl compounds, α-Oximinoketones, Acidic ionic liquid, Nitrosation.*

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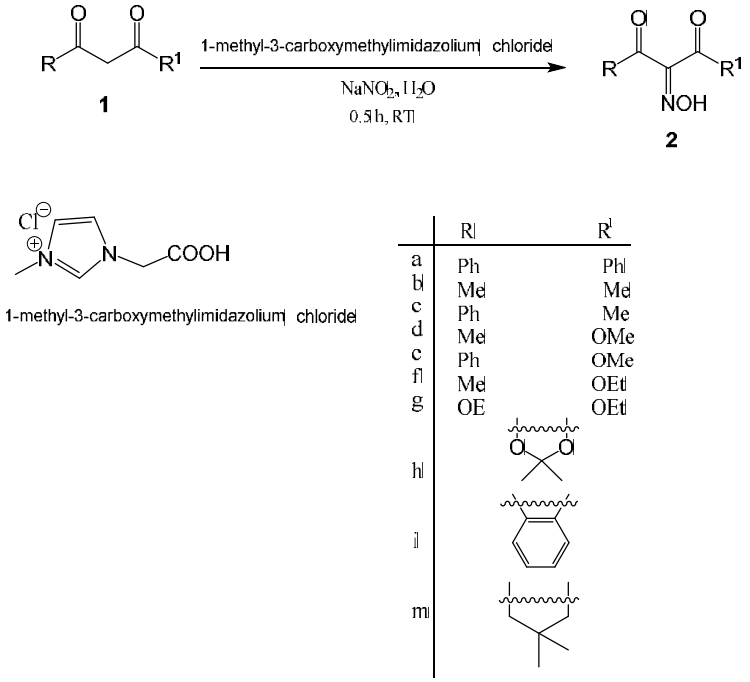
Introduction

α-Oximinoketones are important organic compounds because of their applications in various fields, for example in agricultural industry as herbicides [1-3]. Also α-oximinoketones attached to heterocyclic compounds are used as useful pharmaceuticals [4-6]. Some *α*-oximinoketones derivatives are key intermediates for the synthesis of important compounds such as amino acids [7], *α*-diketones[8], nylon[9], nitrosopyrazoles[10]. Therefore, synthetic organic chemists are interested in the facilitation of oxime synthesis. The formation of oximes is usually catalyzed by both acids and bases. Several methods for their preparation have been reported in the literature including the reaction of carbonyl compounds with hydroxylamine hydrochloride in the presence of sodium nitrite and a mineral acid [11] as a nitrosonium source [12] and using a solid support such as silica gel in the presence of a base [13]. Moreover, there are reports of using CaO as an efficient catalyst for the preparation of oximes at 130 ^{0}C under mild conditions [14] and TSIL-ONO as a heterogeneous catalyst and effective nitrosonium source for the synthesis of oximinoketones [15].

Although various synthetic methods have been reported for the synthesis of these compounds, in most of these methods one environmentally-harmful mineral acid was used as a catalyst. In order to avoid these limitations, many alternative strategies have recently been developed. For example, using solid catalysts such as basic Al_2O_3 [16], resin (Amberlyst A-21) in ethanol [17], $FeCl_3$ [18] and TiO_2/SO_4^{2-} without solvent [19]. Ionic liquids (ILs) have attracted considerable attention as a novel media in recent years due to their unique properties, such as lack of measurable vapor pressure, immiscibility with both organic compounds and water, high thermal stability, non-flammability, and recyclability [20-23].Acidic ionic liquids (AILs) are an important branch of this category. The combination of acidic and ionic liquid properties into a single molecule has opened new opportunities. This may be due to organic soluble nature and interactions of charged intermediates with cation/anion in AIL that allows facile proton or electron transfers with acidic ionic liquids [24].

To our best knowledge, there is no report of using the ionic liquid 1-methyl-3-imidazolium acetic acid, as a catalyst for the preparation of oximes under mild reaction. In this paper and in the continuity of our work [25-28] we wish to report a new, simple, and green method for the green synthesis of oximes (Scheme1).



Scheme 1. Nitrosation of *β*-dicarbonyl compounds with sodium nitrite using acidic ionic liquid.

Experimental

Sodium nitrite, *β*-dicarbonyl compounds were obtained from fluka and were used without further purification. The ILs used in this study was 1-metyl-3-carboxymethylimidazolium chloride synthesized according to the procedure reported in the literature [29]; M.P.: Electrothermal-9100apparatus; IR Spectra: *Shimadzu IR-460* spectrometer.^{1}H and ^{13}C NMR spectra: *Bruker DRX-300 AVANCE* instrument; in $CDCl_3$ at 300 and 75 MHz, respectively; *δ*in ppm, *J* in Hz; EI-MS (70 eV): Elemental analyses(C, H, N) were performed with a *Heraeus CHN-Orapid* an alyzer. The results agreed favorably with the calculated values.

General procedure for the preparation of AIL:

1-Methylimidazole (7.92 mL, 0.1 mol) and monochloroacetic acid (9.45 g, 0.1mol) were refluxed in acetonitrile (50 mL) for 5–6 h under stirring. After completion of the reaction (5-6 h; TLC (AcOEt/hexane 1:1)) and evaporation of the solvent, the AIL was appeared to solid form and used in the next step without further purification; yield: 16.7 g (95%).

1-metyl-3-carboxymethylimidazolium chloride (AIL)

White viscous oil, 16.7 g, yield 95%.$C_6H_9N_2O_2$, IR (KBr) (ν_{max}/cm^{-1}): 2500-3340, 1725, 1607, 1520, 1230. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.40 (3 H, s, *Me*), 4.70 (2 H, s, CH_2), 7.03 (1 H, d, ^3J = 1.6 Hz, CH), 7.08 (1 H, d, ^3J = 1.6 Hz, CH),8.42 (1 H, s, NCHN), 11.83 (1 H, br-s, COOH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.8 (Me), 54.8 (CH_2), 118.9 (CH), 122.3 (CH), 134.6 (CH), 174.2 (C=O) ppm.

*General procedure for the preparation of compounds **2:***

To a stirred solution of 1mmol of β-dicarbonyl compounds **1** in 1ml 1-metyl-3-carboxymethylimidazolium chloride, $NaNO_2$(1mmol in 1ml of water) was added dropwise. The reaction mixture was further stirred at room temperature for 0.5 h. The mixture was extracted with EtOAc (2×10 ml) and after evaporation of solvent, was purified by column chromatography (silica gel (230-400 mesh; *Merck*), hexane/AcOEt2:1) to afford the oximes**2**. The ionic liquid can be reused after extraction from the aqueous phase.

2-(Hydroxyimino)-1,3-diphenylpropane-1,3-dione (**2a**)

Cream powder, 0.24 g, yields 95%, mp 145-146 ºC. IR (KBr) (ν_{max}/cm^{-1}): 3448, 1735, 1667, 941. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.51 (2 H, t, ^3J =7.3Hz, 2 CH), 7.54 (2 H, t, ^3J = 7.0Hz, 2 CH), 7.65 (1 H, t, ^3J = 7.3Hz, CH), 7.67 (1 H, t, ^3J = 7.0 Hz, CH). 7.94 (2 H, d, ^3J = 7.0Hz, 2 CH), 8.13 (2 H, d, ^3J = 7.3Hz, 2 CH), 8.35 (1 H, br-s, NOH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 127.8 (2 CH), 128.1 (2 CH), 129.9 (2 CH), 130.1 (2 CH), 130.6 (CH), 132.1 (CH), 135.9 (C), 136.2 (C), 139.7 (C=N),183.6 (C=O), 185.1 (C=O).Anal.Calc. for $C_{15}H_{11}NO_3$ (253.25): C, 71.14; H, 4.38; N, 5.53.Found:C, 71.43; H, 4.14; N, 5.34.

*3-(Hydroxyimino) pentane-2,4-dione (***2b***)*

White powder, 0.11g,yields 87%, mp 120-123 ºC. IR (KBr) (ν_{max}/cm^{-1}): 3448, 1735, 1667, 941. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.36 (3 H, s, Me), 2.45 (3 H, s, Me), 8.39(1 H, br-s, NOH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.3 (Me), 28.5 (Me), 137.5 (C=N), 186.9 (C=O), 189.2 (C=O).Anal.Calc. for $C_5H_7NO_3$(129.12): C, 46.51; H, 5.46; N, 10.85.Found:C, 46.76; H, 5.34; N, 10.76.

*2-(Hydroxyimino)-1-phenylbutane-1,3-dione (***2c***)*

White powder, 0.16g, yields 86%, mp 125-126 ºC. IR (KBr) (ν_{max}/cm^{-1}): 3444, 1734, 1660, 940. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.36 (3 H, s, Me), δ = 7.51 (2 H, t, ^3J =7.3 Hz, 2 CH), 7.54 (2 H, t, ^3J = 7.0Hz, 2 CH), 7.65 (1 H, t, ^3J = 7.3Hz, CH), 7.67 (1 H, t, ^3J = 7.0Hz, CH). 7.94 (2 H, d, ^3J = 7.0Hz, 2 CH), 8.13 (2 H, d, ^3J = 7.3Hz, 2 CH), 8.39(1 H, br-s, NOH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.3 (Me), δ = 127.8 (2 CH), 128.1 (2 CH), 129.9 (2 CH), 130.1 (2 CH), 130.6 (CH), 132.1 (CH), 135.9 (C), 136.2 (C), 137.5 (C=N), 186.9 (C=O), 189.2 (C=O).Anal.Calc. for $C_{10}H_9NO_3$ (191.19): C, 62.82; H, 4.74; N, 7.33.Found:C, 62.55; H, 4.54; N, 7.43.

Methyl 2-(hydroximino)-3-oxobutanoate(**2d**)

Pale yellow oil, 0.12g, yields 85%. IR (KBr) (ν_{max}/cm^{-1}): 3278, 1754, 1624, 1249, 839. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 2.34 (3 H, s, Me), δ = 3.83 (3 H, s, Me), 8.23 (1 H, br-s, NOH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.2 (Me), δ56.2 (Me), 141.5 (C=N), 166.9 (C=O), 169.2 (C=O).Anal. Calc. for $C_5H_7NO_4$ (145.11):C, 41.38; H, 4.86; N, 9.65.Found:C, 41.54; H, 4.86; N, 9.15;

*Ethyl 2-(hydroximino)-3- oxo-3-phenylpropanoate (***2e***)*

White powder, 0.18g, yields 80%, mp128-130 ºC. IR (KBr) (ν_{max}/cm^{-1}): 3302, 1731, 1673, 1443, 1298, 939.^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22(3 H, t, ^3J = 7.3 Hz,CH_3), 4.26(2H, q, ^3J = 7.3 Hz,OCH_2), 7.49 (2 H, t, ^{3}J =8.1 Hz, 2 CH), 7.62 (H, t, ^3J = 8.1 Hz, CH), 7.86(2 H, d, ^{3}J = 8.1 Hz, 2CH), 8.12 (1 H, br-s, NOH).^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.3 (Me), 52.4 (OCH_2), 128.1 (2 CH), 129.9 (2 CH),130.6 (CH), 136.2 (C), 139.5 (C=N), 186.9 (C=O), 189.2 (C=O).Anal.Calc. for $C_{11}H_{11}NO_4$ (221.21): C, 59.73; H, 5.01; N, 6.33.Found:C, 59.67; H, 5.11; N, 6.12.

*Diethyl 2-(hydroxyimino) malonate (***2g***)*

Viscose oil, 0.16g, yields 85%. IR (KBr) (ν_{max}/cm^{-1}): 3448, 1735, 1667, 941. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.36 (3 H, t, ^{3}J = 7.0 Hz, Me), 1.38 (3 H, t, ^{3}J = 6.6Hz, Me), 4.38 (2 H, q, ^{3}J = 7.0Hz, CH_2), 4.40 (2 H, q, ^{3}J = 6.6Hz, CH_2), 8.21 (1 H, br-s, NOH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6 (Me), 14.2 (Me), 52.3 (CH_2), 52.9 (CH_2), 141.5 (C=N), 166.9 (C=O), 169.2 (C=O).Anal. Calc. for $C_7H_{11}NO_5$ (189.17):C, 44.45; H, 5.86; N, 7.40.Found:C, 44.43; H, 5.72; N, 7.23.

*5-(Hydroxyimino)-2,2-dimethyl-1,3-dioxane-4,6-dione (***2h***)*

Viscose oil, 0.14g, yields 80%. IR (KBr) (ν_{max}/cm^{-1}): 3419, 1671, 1655, 1609, 919. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.84 (3 H, s, Me), 1.86 (3 H, s, Me), 8.59 (1 H, br-s, NOH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.4 (Me), 30.1 (Me), 108.3 (C), 134.1 (C=N), 156.2 (C=O), 158.4 (C=O), Anal.Calc. for $C_6H_7NO_5$ (173.12):C, 41.63; H, 4.08; N, 8.09.Found:C, 41.55; H, 4.13; N, 8.11.

*2-(Hydroxyimino)-2H-indene-1,3-dione(***2i***)*

White powder, 0.13g, yields 75%, mp 128-129 ºC.IR (KBr) (ν_{max}/cm^{-1}): 3361, 1727, 1711, 1629, 959. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.51-7.54(2 H, m, 2 CH), 7.67-7.69 (2 H, m, 2 CH), 8.68 (1 H, br-s, NOH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 127.4 (CH),127.8 (CH), 128.1 (2 CH),128.7 (CH),135.9 (C), 136.2 (C), 139.7 (C=N),183.6 (C=O), 185.1 (C=O).Anal.Calc. for $C_9H_5NO_3$(175.14):C, 61.72; H, 2.88; N, 8.00. Found:C, 61.56; H, 2.86; N, 8.09.

*2-(Hydroxyimino)-5,5- dimethylcyclohexane-1,3-dione (***2m***)*

White powder, 0.12g, yields 70%, mp 123-125 ºC.IR (KBr) (ν_{max}/cm^{-1}): 3361, 1727, 1711, 1629, 959. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 (3 H, s, Me), 1.06 (3 H, s, Me), 2.67 (2H, s, CH_2), 2.45 (2H, s, CH_2), 8.68 (1 H, br-s, NOH) ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3 (Me), 14.6 (Me), 28.9 (C), 29.2 (CH_2), 30.1 (CH_2), 138.4 (C=N), 195.2 (C=O), 195.6 (C=O). Anal. Calc. for $C_8H_{11}NO_3$(169.18):C, 56.80; H, 6.55; N, 8.28.Found: C, 56.43; H, 6.43; N, 8.15.

Results and discussion

The essential structures of compounds **2a–m** were deduced from their elemental analyses and their ^{1}H and ^{13}C NMR spectra as well as from the IR spectra. The ^{1}H NMR spectrum of **2a** displayed six distinct signals for the aromatic protons, along with a fairly broad band for the NOH group at δ = 8.34. The ^{13}CNMR spectrum of **2a** indicated eight signals for phenyl groups at δ= 127.8, 128.1, 129.9, 130.1, 130.6, 132.1, 135.9, 136.2 and C=N group at δ = 139.7 ppm. The two signals for carbonyl groups appeared at δ = 183.6 and 185.1 ppm. The ^{1}H and ^{13}C NMR spectra of **2b-2m** were similar to those of **2a**, except for the side chains, which exhibited characteristic signals with appropriate chemical shifts (See Experimental Section).

In addition, we examined the nitrosation of β-dicarbonyl compounds within sodium nitriteusing various conditions about the product **2a** (Table 1).

Table 1. Screening of different catalysts for the preparation of α-oximinoketonederivatives[a].

Entry	Reaction conditions	Timereaction (h)	Yield(%)[b]
1	Methyl acetoacetate + H_2O +$NaNO_2$ + HCl(10%)	4	80
2	Methyl acetoacetate + H_2O +$NaNO_2$ + HCl(10%) + Neutral IL	1	83
3	Methyl acetoacetate + H_2O +$NaNO_2$ + Neutral IL	No reaction	-
4	Methyl acetoacetate + H_2O +$NaNO_2$ + Alum catalyst ($KAl(SO_4)_2.12H_2O$)	2	65
5	Methyl acetoacetate + H_2O +$NaNO_2$	No reaction	-
6	Methyl acetoacetate + H_2O +$NaNO_2$+ 1-methyl-3-imidazolium acetic acid	0.5	88

[a] *All reactions were carried out using metylacetoacetat (1 mmol), $NaNO_2$ (1 mmol) and H_2O (1 mL).*
[b] *Isolated yields*

The use of hydrochloric acid (HCl) 10% (entry 1, Table 1), neutral ionic liquid and hydrochloric acid (HCl) 10% (entry 2, Table 1), neutral ionic liquid(entry 3, Table 1), and acidic Alum catalyst (entry 4, Table 1) were examined and the best result was obtained using acidic ionic liquid (entry 6, Table 1). The use 1-methyl-3-imidazolium acetic acid (as an AIL) increased the product yield to 88% and decreased reaction time to 0.5 h. However in the absence of the catalyst (entry 5, Table 1), no product was obtained. This reaction was also studied in various solvents like dichloromethane, acetonitrile, *N,N*-dimethylformamide and tetrahydrofuran but with a reduced yield of desired product.

A good feature of this method is that the IL can be regenerated and reused several times without considerable loss of activity. To regenerate the ILs, after completion of the reaction, the mixture was successively washed with water. After evaporation of the water under reduced pressure, the residue was identical in all aspects of the parent ILs. This process was repeated for three cycles in the preparation of oxime and the yield of oxime did not change significantly (Table 2). The decrease in conversion can be attributed to the loss of the small amount of ILs during recycling process. These results clearly show the stability of ILs in the reaction media as well as its recovery and recycling without any appreciable decrease in its activity.

Table 2. Recycling studies of preparation of 2-(hydroxyimino)-1,3-diphenylpropane-1,3-dione (**2a**) with 1-methyl-3-imidazolium acetic acid.

Entry	Cycle	Time(min)	Yield%[a]
1	Fresh	30	95
2	1	30	95
3	2	32	93
4	3	32	93

[a]*Yields refer to isolated products.*

Conclusion

In conclusion, we have developed an efficient, economical and eco-friendly approach for the synthesis of diketoximes using an acidic ionic liquid as a catalytic green solvent. Easy work-up, substantially good to high yields, and synthesis of polyfunctional compounds, which are ready for further reactions, are advantages of this new method. The use of an easily accessible and recyclable ionic liquid makes this procedure convenient and reaction times were dramatically reduced.

Acknowledgement

We are grateful to Yadegar-e-Imam Khomeini (RAH) Shahre-rey Branch, IslamicAzad University Research Council for the financial support of this research.

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