

A Novel Ionic Liquid/water Biphasic System for the Preparation of Oximes

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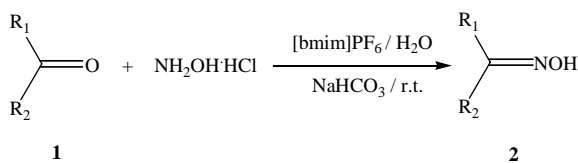
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Abstract: A variety of carbonyl compounds can be converted into oximes efficiently and conveniently in a novel ionic liquid/water bi-phasic system in the presence of sodium bicarbonate at ambient temperature. The ionic liquid 1-butyl-3-methyl imidazolium hexafluorophosphate [bmim]PF₆ is immiscible with water or diethyl ether and can be easily recycled for reuse without noticeable dropping in activity after separation of the products. The protocol is rapid, the yields are excellent, the method is simple and the ionic liquid can be reused.

Keywords: Oximes, synthesis, ionic liquid, bi-phasic system.

Oximes are useful intermediates in the organic synthesis. It is used not only for protecting, purification and characterization of carbonyl groups, but also for various function group transformation such as into nitriles¹, amides², nitro compounds³ and amines⁴ *etc.* Conventionally, oximes are prepared from carbonyl compounds with hydroxylamine hydrochloride in the presence of base in refluxing alcoholic solution⁵. The method has some drawbacks such as low yields, long reaction time and effluent pollution caused by used organic solvent. More recently, alumina⁶, silica gel⁷ and TiO₂/SO₄²⁻⁸ coupled with microwave irradiation without solvent has been proven to be an efficient method for the preparation of oximes. However, problems of generation of polluting HCl, high reaction temperature and occasionally low yields still present. Consequently, there is a need for developing an efficient, convenient and non-polluting method for the preparation of oximes. Ren *et al.*⁹ reported a green protocol for formation of the cyclohexanone oxime from cyclohexone using hydrophilic ionic liquid 1-butyl-3-methyl imidazolium tetrafluoroborate ([bmim]BF₄) solution as reaction media. The merit of the protocol is that the reaction process in mono-phase and the ionic liquid

Scheme 1



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can be recovered for recyclable use and the shortcoming is that the substrate is limited on cyclohexanone only.

The development of environmentally friendly solvents for organic chemistry is an area of considerable importance. From both economical and environmental points of view, the use of ionic liquids as solvents has attracted much interest recently, partly due to their polar nature, phase behavior and lack of vapour pressure. In our continuous studies of ionic liquids as recyclable media, we described herein the preparation of oximes based on the use of the hydrophobic ionic liquid 1-butyl-3-methyl imidazolium hexafluorophosphate [bmim]PF₆ as a replacement for classic organic solvents. The reaction conducted in ionic liquid/water bi-phasic system to afford the corresponding oximes (**Scheme 1**).

Twelve common carbonyl compounds were transformed into corresponding oximes in the ionic liquid/water bi-phasic system. The results are summarized in **Table 1**.

As shown in **Table 1**, the isolated yields of the products are excellent in all cases. The substrate containing the hydroxy moiety can be tolerance in this system. Additionally, the electron withdrawing group or electron donor group on the aromatic ring did not have significant effect on the yields. The reaction process for the preparation of oximes may be occurred in the ionic liquid phase. The free hydroxylamine was produced *in situ* in the water phase due to the reaction of the hydroxylamine hydrochloride and sodium bicarbonate, and then it subsequently was transferred into ionic liquid phase from water phase by the extraction of the hydrophobic ionic liquid [bmim]PF₆. After the completion of the reaction, the resulting product existed in ionic phase was easily separated by extraction with immiscible diethyl ether, and the inorganic salt as by-product dissolved in water phase was also conveniently removed. The separated ionic liquid could be reused directly without further purification with no diminution of the yields. The protocol has the merit of benignancy to environment, simple operation, convenient work-up and good yield.

In conclusion, the ionic liquid [bmim]PF₆ acts as an excellent alternative solvent for the synthesis of oximes. To our best knowledge, this is the first report of using ionic liquid/water bi-phase system for preparation of oximes at room temperature.

Experimental







IR was recorded on the Bruke Equinox 55 using KBr pellet. Benzaldehyde was purified by distillation. All other chemicals used were of commercial grade without further purification. [bmim]PF₆ was prepared according to the literature¹⁰.

General procedure for the preparation of oximes

A mixture of the carbonyl compound (5 mmol), hydroxylamine hydrochloride (6 mmol) and sodium bicarbonate (7.5 mmol) was introduced into a vigorous stirred [bmim]PF₆ and water mixture solvent (ionic liquid /water = 3 mL / 0.5 mL) at room temperature.

The course of the reaction was followed by TLC. After completion, the reaction was quenched with water (5 mL) and the immiscible ionic liquid [bmim]PF₆ layer was separated from the water phase and extracted with diethyl ether (10 mL×3). The organic extracts were dried over anhydrous MgSO₄ and then concentrated in *vacuo* to afford pure product. The recycled ionic liquid can be reused for the next run without noticeable effect on the reaction.

Table 1 Preparation of oximes in the ionic liquid [bmim]PF₆/water bi-phase system

Entry	Substrate (1)	Product ^a (2)	E/Z ^b	Yields ^c (%)
1	3-HO-4-MeO-C ₆ H ₃ CHO	3-HO-4-MeO-C ₆ H ₃ CH=NOH	0:100	90
2	2-HO-C ₆ H ₄ CHO	2-HO-C ₆ H ₄ CH=NOH	0:100	98
3	4-HO-C ₆ H ₄ CHO	4-HO-C ₆ H ₄ CH=NOH	20:80	94
4	2-MeO-C ₆ H ₄ CHO	2-MeO-C ₆ H ₄ CH=NOH	0:100	97
5	4-MeO-C ₆ H ₄ CHO	4-MeO-C ₆ H ₄ CH=NOH	14:86	90
6	4-Me ₂ N-C ₆ H ₄ CHO	4-Me ₂ N-C ₆ H ₄ CH=NOH	0:100	92
7	C ₆ H ₅ CHO	C ₆ H ₅ CH=NOH	22:78	88
8	4-Cl-C ₆ H ₄ CHO	4-Cl-C ₆ H ₄ CH=NOH	24:76	96(94) ^d
9	3-NO ₂ -C ₆ H ₄ CHO	3-NO ₂ -C ₆ H ₄ CH=NOH	22:78	89
10			/	91
11			/	88
12			/	98

^aAll compounds are characterized by m.p. and IR and also compared with the authentic sample; ^bE/Z ratio are confirmed by Shimadzu CS-9301 PC dual wavelength flying spot scanning densitometer; ^cIsolated yields; ^dYield in parenthesis obtained from the ionic liquid in the case of the forth run.

Acknowledgment

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References

- (a) H. M. S. Kumar, T. P. Reddy, J. S. Yadave, *Synthesis*, **1999**, 586.
(b) P. Das B. Madhusudhan, B. Venkataiah, *Synlett*, **1999**, 1569.
- A. I. Bosch, P. Greez, E. Diez-Barra, A. Loupy, F. Langa, *Synlett*, **1995**, 1259.
- (a) P. R. Dave, F. Forshar, *J. Org. Chem.*, **1996**, *61*, 8897.
(b) F. P. Ballistreni, E. Barbuzzi, G. A. Tomaselli, R. M. Toscano, *Synlett*, **1996**, 1093.
- (a) S. Sasatani, T. Miyazak, K. Maruoka, H. Yamamoto, *Tetrahedron Lett.*, **1983**, *24*, 4711.
(b) S. Negi, M. Matsukura, M. Mizuno, K. Miyake, *Synlett*, **1996**, 991.
- T. W. Greene, P. G. M. Wuts, *Protective Groups in Organic Synthesis*, John Wiley & Sons, Inc., New York, **1991**, 2nd Ed., p214.
- G. L. Kad, M. Bhandari, J. Kaur, R. Rathee, J. Singh, *Green Chem.*, **2001**, 275.
- A. R. Hajipour, S. E. Mallakpour, G. Imanzadeh, *J. Chem. Res(S)*, **1999**, 228.
- J. J. Guo, T. S. Jin, S. L. Zhang, T. S. Li, *Green Chem.*, **2001**, 193.
- R. X. Ren, W. Ou, *Tetrahedron Lett.*, **2001**, *42*, 8445.
- J. G. Huddleston, H. D. Willauer, R. P. Swatloski, *et al.*, *Chem. Commun.*, **1998**, 1765.

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