[Nd(OTf)$_3$] mediated facile conversion of ketoximes to amides

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A variety of ketoximes, easily prepared from the corresponding ketones, undergo the Beckmann rearrangement upon treatment with [Nb(OTf)$_3$] to afford the corresponding amides in excellent yields.

Keywords: [Nd(OTf)$_3$], ketoximes, amides, lactams

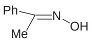
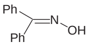
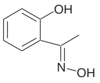
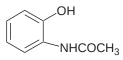
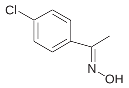
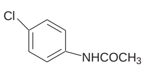
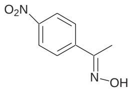
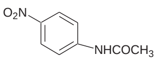
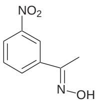
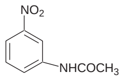
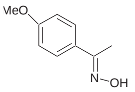
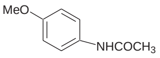
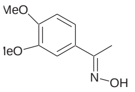
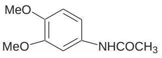
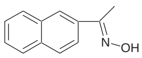
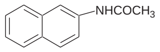
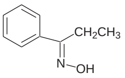
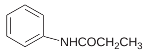
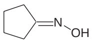
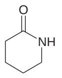
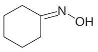
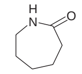
The rearrangement of ketoximes to the corresponding amides, known as the Beckmann reaction is an important reaction in organic chemistry.[1] The classical Beckmann rearrangement[2] requires excess amount of strong protic acids such as sulfuric acid, phosphoric acid which cause a large amount of by-products and serious corrosion problems.[1] Recently, this reaction has been studied by various modified reagents,[3] solid acid catalysts such as metal oxides, clay[4] and zeolites.[5] However, most of these reactions are under vapour phase conditions and they proceed in rather sluggish manner. The preparation procedures for these reagents often involve various tedious steps, such as precipitation, ion-exchange, hypothermal treatment, and prolonged activation time at higher temperature and reproducible is a another problem. On these bases, milder conditions were tried and several variants such as chloral,[6] solid metaboric acid[7] developed but these reactions were performed at higher temperature. Nevertheless, until now only a few methods are reported under mild conditions.[8] Therefore, there is still a need to develop a convenient and mild procedure for preparation amides from ketoximes.

Recently, there has been growing considerable interest in use of lanthanide triflate in organic synthesis[9] as they are water tolerable and reusable. The reagent [Nd(OTf)$_3$] is commercially available and can be used for preparation of amides and lactams from the corresponding ketoximes due to its high activity, greater selectivity, reusability and operation simplicity. Several aryl ketoximes undergo Beckmann rearrangement upon treatment with this reagent in refluxing acetonitrile to afford corresponding amides with high selectivity. In all cases only one of the two possible amides were obtained. Generally, migration of an aryl group predominates over that of an alky group. However, the results obtained suggest that the stereochemistry of oximes has very little effect as in other Beckmann rearrangements.[10] Possibly the *E* and *Z* oximes interconverted under the the reaction conditions as all oximes used were prepared by standard procedure and no separation of *E* and *Z* was made.

Table 1 shows that simple and electron rich ketoximes undergo a short reaction time but electron poor ketoximes took longer to complete. Cyclic oximes require longer reaction times and high temperature (110 °C) compared to aryl ketoximes, to give the corresponding lactams in good yields. This fact may be explained by steric or electronic factors, since it is known that substitution of an electron donating group on the aromatic ring facilitates the reaction. However, the reaction is reasonably fast and method has ability to tolerate a variety of substrates. This method can be applied on a large scale reaction. The conversions were clean and no deoximation of ketoximes to ketones were observed. The catalyst was recovered from the aqueous layer during work up and reused twice without any loss of activity.

In conclusion, I have developed a very simple, mild and efficient method for conversion of ketoximes to the corresponding amides in excellent yields with high selectivity.

Table 1 Nd(OTf)$_3$ mediated conversion of ketoximes to amides

Entry	Ketoximes	Amides	Time/h	Yield[a]/%
1		PhNHCOCH$_3$	2	94
2		PhNHCOPh	1.5	91
3			2	84
4			1.5	94
5			5	81
6			8	74
7			1	92
8			1	94
9			4	85
10			1.5	88
11			8	85[b]
12			9	79[b]

[a] Yields refer to pure isolated products, characterised by IR, ^{1}H NMR and MS.

[b] Refluxed in toluene.

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Experimental

All the products were known and characterised by ^{1}H NMR, IR and MS and were identical to data reported in the literature.[11]

Conversion of ketoximes to amides (general procedure): A mixture of ketoxime (5 mmol) and Nd(OTf)$_3$ (2.5 mmol) in acetonitrile (25 ml) was refluxed for indicated time(Table 1). After completion of the reaction (TLC monitored), the reaction mixture was diluted with water (25 ml) and extracted with ethyl acetate, dried (MgSO$_4$) and concentrated *in vacuo*. The residue was chromatographed over silica gel (eluted hexane-ethyl acetate, 8/2 to 6/4) to give pure product.

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References

1 (a) R.E Gowley, *Org. React*., 1988, **35**, 1; (b) M.B. Smith and J. Macrh, *Advanced Organic Chemistry*, 5th edn. Wiley and Sons, New York, 2001, 1415.

2 (a) E. Beckmann, *Chem. Ber*., 1886, **19**, 988; (b) Y. Izumi, S. Sato and K. Urabe, *Chem. Lett*., 1983, 1649.

3 (a) M.E. Jung and L.M. Zeng, *Tetrahedron Lett.*, 1983, 24, 4533; (b) T. Imamato, H. Yokoyama and M. Yokoyama, *Tetrahedron Lett*., 1981, **22**, 1803; (c) T. Kamijo, H. Harada and K. Lizuka, *Chem. Pharm. Bull*., 1984, **32**, 2560.

4 (a) S.G. Pai, A.R. Bajpai, A.B. Deshpande and S.D. Samant, *Synth. Commun*., 1997, **27**, 379; (b) H.M. Meshram, *Synth. Commun*., 1990, **20**, 3253.

5 (a) H. Kath, R. Glaser and J. Wietkam, *J. Chem. Eng. Technol*., 2001, **24**, 2; (b) M.A. Camblor, A. Corma and U.P. Garquimica, *J. Catal*., 1988, **177**, 267.

6 S. Chandrasekhar and K. Gopalaiah, *Tetrahedron Lett*., 2003, **44**, 2455

7 S. Chandrasekhar and K. Gopalaiah, *Tetrahedron Lett*., 2002, **43**, 6272.

8 (a) L. DeLuca, G. Giacomelli and A Porcheddu, *J.Org. Chem*., 2002, **67**, 6272; (b) J. Peng and Y. Deng, *Tetrahedron lett*., 2001, **42**, 403; (b) R.X. Ren, L.D. Zueva and W. Ou, *Tetrahedron Lett*., 2001, **42**, 8441.

9 (a) S. Kobayashi, *Eur. J. Org. Chem*., 1999, 15; (b) S. Kobayashi, *Synlett*, 1994, 689.

10 J.K. Chakraborti and T.M. Hotten, *J.Chem. Soc., Chem. Commun*., 1972, 1226.

11 (a) *Dictionary of Organic compounds*, 6th edn. Chapman & Hall, New York; (b) *Handbook of Data on Common Organic Compounds*, D.R. Lide and G.W.A. Milne, CRC press, London.