SHORT PAPER

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[Yb(OTf)$_3$] catalysed facile conversion of ketoximes to amides and lactams[†]

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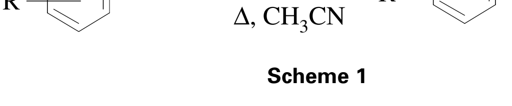
A variety of ketoximes undergo the Beckmann rearrangement upon treatment with a catalytic amount of [Yb (OTf)$_3$] in refluxing acetonitrile to afford the corresponding amides and lactams in excellent yields with high selectivity.

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

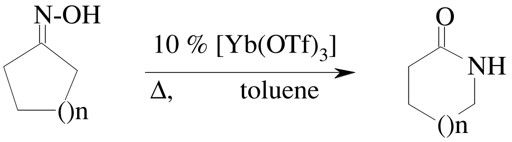
Beckmann rearrangement is an important transformation in organic synthesis for the preparation of amides and lactams from oximes.[1] Recently, more attention has been paid towards the Beckmann rearrangement of ketoximes because of its versatility and widespread applications in the synthesis of many biologically active natural products.[2] The rearrangement proceeds through anti-migration and is usually stereospecific. The classical Beckmann rearrangement[3] requires excess or stoichiometric amount of strong protic acids such as conc. H_2SO_4 or phosphoric acids which cause a large amount of by products and serious corrosion problems.[1] To circumvent some of these problems, several improved procedures have been reported using modified reagents[4] and solid acids like clays[5] and zeolites.[6] However, most of these procedures involve vapour phase reactions,[7] and they are carried out at very high temperatures for a long reaction time resulting in low yields of the products. Furthermore, the reactions are sluggish when they are performed in the liquid phase.[8] Therefore, there is a need to develop a convenient and potentially practical method for this transformation under mild conditions. Recently, there has been growing interest in the use of lanthanide triflates as potential Lewis acids in various organic transformations[9] because they are quite stable to water and reusable as well as highly efficient. Particularly, ytterbium salts have attracted much research interest due to their high catalytic activity, easy availability, economic viability, reusability, greater selectivity and operational simplicity. The unique catalytic properties of ytterbium triflate prompted us to investigate the use of this catalyst in the Beckmann rearrangement of ketoximes.

In continuation of our interest on the applications of lanthanide triflates for various transformations[10] we herein describe a novel and highly efficient protocol for the synthesis of amides and lactams from ketoximes using catalytic amount of ytterbium triflate (Scheme 1).

Acetophenone oxime, on treatment with a catalytic amount of ytterbium triflate in refluxing acetonitrile underwent Beckmann rearrangement to produce acetanilide in 92% yield. Similarly, several substituted ketoximes reacted well to give the corresponding amides in high yields. The rearrangement proceeded smoothly in refluxing acetonitrile with high selectivity and the products were obtained in high yields. The conversions were clean and no undesirable side products were observed. *o*-Hydroxy acetophenone oxime was selectively rearranged to *o*-hydroxyacetanilide without the formation of benzoxazole as has been reported by others.[11] The nature of substituent on the aromatic ring showed some effect on this conversion. Simple and electron-rich ketoximes gave excellent yields of products in a short reaction time, whereas nitro-substituted acetophenone oxime took a longer reaction time to attain yields comparable with those of their electron-rich counterparts. Further, cyclic oximes like cyclohexanone, cyclopentanone and tetralone oximes required longer reaction time (7–8 h) and high temperature (110°C) compared to acyclic oximes, to give the corresponding lactams in high yields (Scheme 2).



Scheme 1



Scheme 2

This may be explained by steric or electronic factors, since it is known that substitution of an electron donating group on the aromatic ring or in cyclic ketones facilitates the reaction. The experimental procedure is very simple, more convenient and also the method has ability to tolerate a variety of substrates. Acetonitrile is the solvent of choice as best results were obtained. All the products were characterised by ^{1}H NMR, IR and mass spectral data. The spectroscopic data was identical with data reported in the literature.[12] Among various metal triflates like yttrium triflate, ytterbium triflate and zinc triflate used for this transformation, ytterbium triflate was found to be more effective in terms of yields and reaction times. The catalyst was recovered from the aqueous layer during work-up and reused twice without any significant loss of activity.

In summary, we have demonstrated a novel and practical method for the conversion of ketoximes to amides and lactams using a catalytic amount of ytterbium triflate. In addition to its simplicity and milder reaction conditions, this method provides excellent yields of products with high selectivity.

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Experimental

Conversion of aryl ketoximes to amides: A mixture of ketoxime (5 mmol) and Yb(OTf)$_3$ (10 mol %) in acetonitrile (15 ml) was stirred at reflux temperature for an appropriate time (Table 1). After completion of the reaction, as indicated by TLC, the reaction mixture was

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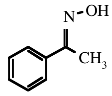
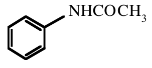
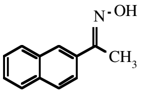
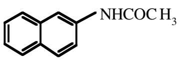
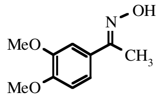
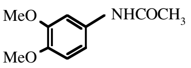
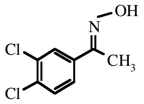
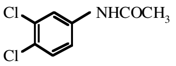
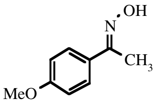
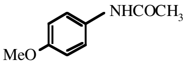
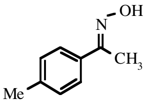
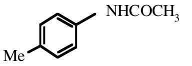
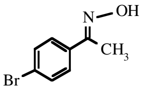
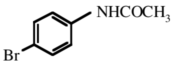
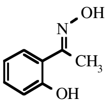
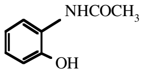
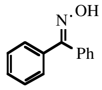
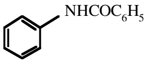
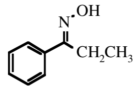
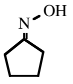
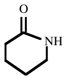
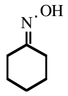
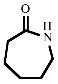
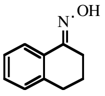
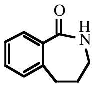
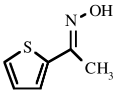
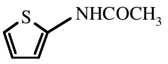
[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.

Table 1 Yb(OTf)$_3$ catalysed conversion of ketoximes to amides and lactams

Entry	Ketoxime	Amide[a]	Time/h	Yield/%[b]
a			5.0	90
b			8.0	81
c			4.5	88
d			7.0	84
e			5.0	90
f			6.5	87
g			6.0	82
h			7.5	78
i			8.0	71
j			6.0	89
k			8.0[c]	78
l			7.5[c]	83
m			8.0[c]	70
n			5.0	90

[a] All products were characterised by ^{1}H NMR, IR, and mass spectra.
[b] Isolated and unoptimised yield after purification.
[c] Refluxed in toluene.

quenched with water (15 ml) and extracted with ethyl acetate (2 × 15 ml). The combined organic layers was dried over anhydrous sodium sulfate, concentrated *in vacuo* and purified by column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate: hexane, 3:7) to afford pure amide.

Conversion of cyclic oximes to lactams: A mixture of cyclic oxime (5 mmol) and Yb(OTf)$_3$ (10 mol %) in toluene (15 ml) was stirred at reflux temperature for a specified time (Table 1). After completion of the reaction, as indicated by TLC, the solvent was removed *in vacuo*, diluted with water (10 ml) and extracted with ethyl acetate (2 × 15 ml). The combined organic layers were dried over anhydrous sodium sulfate, concentrated *in vacuo* and purified by column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate: hexane, 3:7) to afford pure lactam.

Spectral data for the products **2b:** ^{1}H NMR (CDCl$_3$) δ: 2.20 (s, 3H), 7.35–7.45 (m, 2H), 7.50 (brs, NH), 7.60–7.70 (m, 3H), 8.15 (s, 1H).

EIMS: *m/z*: 185 M$^+$. IR (KBr)ν: 3283, 3085, 1668, 1588, 1564, 1561, 1396, 1350, 1280, 1168, 1014, 858, 745.

2c: ^{1}H NMR ($CDCl_3$) δ: 2.25 (s, 3H), 3.85 (s, 6H), 6.80 (d, 1H, *J* = 6.9Hz), 7.10 (dd, 1H, *J* = 6.9 and 1.7 Hz), 7.30(d, 1H, *J* = 1.7 Hz), 8.60 (brs, NH). EIMS: *m*/*z*: 195 M^+. IR (KBr)ν: 3285, 3083, 1675, 1585, 1458, 1333,1271, 1148, 1016, 867.

2d: ^{1}H NMR ($CDCl_3$) δ: 2.20 (s, 3H) 7.35–7.45 (m, 2H),7.65 (brs, NH), 7.70 (m, 1H). EIMS: *m*/*z*: 203 $M^{+\cdot}$ IR (KBr)ν: 3295, 3185, 1668, 1597, 1534, 1484, 1389, 1308, 1006, 822.

2f: ^{1}H NMR ($CDCl_3$) δ: 2.18(s, 3H) , 2.30 (s, 3 H) 7.10 (d, 2H, *J* = 6.8 Hz), 7.25 (brs, NH), 7.38 (d, 2H, *J* = 6.8 Hz). EIMS: *m*/*z*: 149 $M^{+\cdot}$ IR (KBr) ν: 3292, 3188, 3065, 1664, 1604, 1552, 1452, 1320, 1263, 1040, 820.

2h: ^{1}H NMR ($CDCl_3$) δ: 2.10 (s, 3H), 6.80 (t, 1H, *J* = 7.0 Hz), 6.85 (d, 1H, *J* = 6.9 Hz) , 7.15 (t, 1H, *J* = 7.0 Hz), 7.25 (brs, NH), 7.40 (d, 1H, *J* = 6.9 Hz), 10.05 (brs, OH). . EIMS: *m*/*z*: 151 M^+. IR (KBr) ν: 3480, 3295, 3058, 1670, 1598, 1530, 1480, 1386, 1280, 1168, 1030, 855.

2k: ^{1}H NMR ($CDCl_3$) δ: 1.75 (m, 4H), 2.30 (m, 2H), 3.25(m, 2H), 7.50(brs, NH). EIMS: *m*/*z*: 99 $M^{+\cdot}$ IR (KBr) ν: 3296, 2935, 1664, 1531, 1480, 1448, 1250, 992, 898, 760.

2n: ^{1}H NMR ($CDCl_3$) δ: 2.20 (s, 3H), 6.60 (m, 1H), 6.70 (m, 2H), 7.80 (brs, NH). EIMS: *m*/*z*: 141 M^+. IR (KBr) ν: 3241, 3108, 1647, 1578, 1439, 1302, 1038, 802, 745, 674.

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