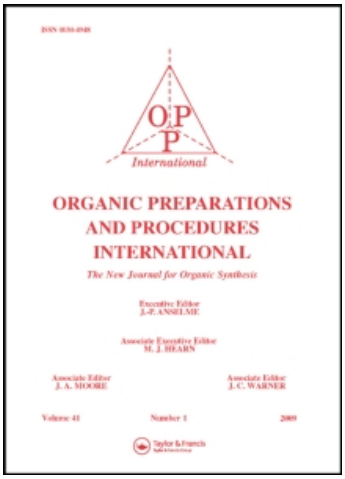

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FACILE BECKMANN REARRANGEMENT OF KETOXIMES MEDIATED BY YTTRIUM TRIFLATE

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poured into crushed ice (200 g) and extracted with three portions of ether (150 mL x 3). The combined organic extract was dried over magnesium sulfate and concentrated under vacuum to give the crude products. The crude products were purified through column chromatography; wherever possible the product was recrystallized from hexane.

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FACILE BECKMANN REARRANGEMENT OF KETOXIMES MEDIATED BY YTTRIUM TRIFLATE

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(06/01/04)

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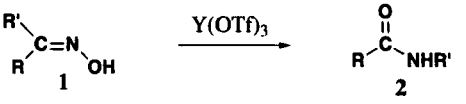
The Beckmann rearrangement of ketoximes to the corresponding amide is a common method in organic chemistry and is a topic of current interest.[1] The rearrangement proceeds through *anti*-migration and is usually stereospecific.[2] Generally, this reaction requires an excess amount of a strong protic acid, such as conc. sulfuric or phosphoric acid which can lead a large

amount of by-products and cause serious corrosion problems.[1] Various modified reagents[3], such as metal oxides, clay[4] and zeolites[5] have been investigated for this conversion. However, most of these reactions proceed under vapor phase conditions and in a rather sluggish manner. Furthermore, the procedures to obtain these reagents often involve various tedious steps, such as precipitation, ion-exchange chromatography, hypothermal treatment and prolonged activation time at higher temperature and are not always reproducible. As a result, milder conditions were tried and several variants such as chloral[6] and solid metaboric acid[7] have been developed but these reactions also required higher temperatures. Therefore, there is still a need to develop a new and milder procedure for the Beckmann rearrangement.



a) R = Me, R' = C_6H_5; b) R = R' = C_6H_5; c) R = Me, R' = *o*-HOC_6H_4; d) R = Me, R' = *p*-ClC_6H_4;
e) R = Me, R' = *p*-$NO_2C_6H_4$; f) R = Me, R' = *m*-$NO_2C_6H_4$; g) R = Me, R' = *p*-$CH_3OC_6H_4$;
h) R = Me, R' = 2-naphthyl; i) R = CH_2CH_3, R' = C_6H_5; j) R = R' = -$(CH_2)_4$- k) R = R' = -$(CH_2)_5$-

Recently, there has been growing interest in use of lanthanide and group III metal trifluoromethanesulfonates in various organic reactions[8] as they are relatively stable, easy to handle solids that are insensitive to small amounts of moisture and air and may be recovered and reused. The reagent yttrium trifluoromethanesulfonate [$Y(OTf)_3$] is commercially available and may be used for preparation of amides (**2**) from the corresponding ketoximes (**1**). Examination of *Table 1* indicates that generally, migration of an aryl group predominates over an alkyl group and the

Table 1. Conversion of Ketoximes to Amides Mediated by $Y(OTf)_3$

Cmpd	Yield (%)	Time (hr)	mp(°C)	*lit.* mp (°C)[a]
2a	90	2.5	114-115	112-113
2b	93	1.5	164-166	161-165
2c	80	2	209-210	208-209
2d	91	1.5	178-179	175-176
2e	80	5	215-216	217-218
2f	72	8	147-149	147-148
2g	92	1.5	125-126	128-129
2h	85	4	132-134	133-135
2I	87	1.5	104-106	103-105
2j	80	8[b]	37-39	39-40
2k	79	9[b]	70-72	71-73

a) All the amides are known and commercially available from Aldrich Chemical Co. b) Carried out in toluene as solvent

yields ranged from 72% to 93%. The nature of the substituent on the aromatic ring showed some

effect on this rearrangement. Simple and electron-rich ketoximes **1a**, **1b**, **1g**, **1i** gave excellent yields in a short reaction time whereas nitro-substituted acetophenone oximes **1e**, **1f** took longer (this may be rationalized in terms of steric and/or electronic factors since it is known that electron-donating substituents facilitate the reaction). Cyclic ketoximes require longer reaction times and higher temperature (110°C) compared to aryl ketoximes. However, the reaction is reasonably rapid and the method tolerates a variety of substrates. The experimental procedure is very simple and can be successfully applied on grams scale. Moreover, the results obtained suggest that the stereochemistry of the oximes has very little effect as in other Beckmann rearrangements.[9] Possibly the *E*-and *Z*-oximes interconverted under the reaction conditions, since all of the oximes used were prepared by standard procedure and no separation of *E* and *Z* was made. The conversions were clean and no deoximation of the ketoximes to the ketones were observed. The catalyst was recovered from the aqueous layer during work-up and reused twice without loss of activity.

In summary, a novel and practical method has been developed for the conversion of ketoximes to the corresponding amides in excellent yields with high selectivity. The method also has the advantage compared with conventional Lewis-acid mediated reactions requiring dry organic solvents, because tedious procedures to remove water from the solvents, substrates, and catalysts are not necessary.

EXPERIMENTAL SECTION

Mps were determined on a Mel-temp apparatus and are uncorrected. All solvents and reagents were purchased from Aldrich and used without purification. All the products are known and characterized by ^{1}H NMR, IR, and MS and were identical with data reported in the literature.[10]

Conversion of Ketoximes to Amides. General Procedure.- A mixture of ketoxime (5 mmol) and $Y(OTf)_3$ (2.5 mmol) in acetonitrile (25 mL) was refluxed for specified time (*Table 1*). After completion of the reaction (monitored by TLC), the reaction mixture was quenched with water (30 mL), and extracted with ethyl acetate (100 mL). After drying ($MgSO_4$) and concentration *in vacuo*, the residue was chromatographed over silica gel (eluted hexane-ethyl acetate, 8:2 to 6:4) to give the pure products. The aqueous layer containing catalyst was evaporated under reduced pressure to give a white solid which was reused for two additional times without any loss of activity.

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AN IMPROVED SYNTHESIS OF NEOCRYPTOLEPINE

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The plant *Cryptolepis sanguinolenta* has been used in traditional West African medicine (Ghana, Congo) for the treatment of various disorders such as malaria, infections of the respiratory, urogenital and urinary tracts, colic, and rheumatism. For this reason, many research workers have focused on the isolation and identification of the active compounds in this plant, which include complex molecules such as **1** and **7a**.[1-3] One of these, neocryptolepine, also named cryptotackieine (**7a**), has considerable structural resemblance to the highly potent alkaloid ellip-