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## GRAPHICAL ABSTRACT

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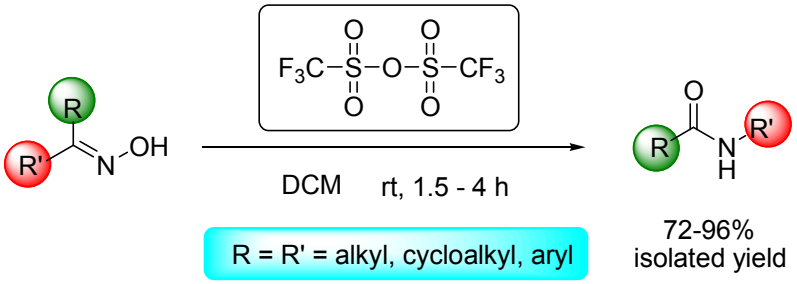
**Rajesh G. Kalkhambkar,[a*] Hemantkumar M. Savanur [a]**

*[a]Department of Chemistry, Karnatak University's Karnatak Science College, Dharwad Karnatak 580001, India*



# Highly efficient synthesis of amides from ketoximes using trifluoromethanesulphonic anhydride

**Rajesh G. Kalkhambkar,[a*] Hemantkumar M. Savanur [a]**

[a]*Department of Chemistry, Karnatak University's Karnatak Science College, Dharwad Karnatak 580001, India*

## ABSTRACT:

Trifluoromethanesulphonic anhydride (Triflic anhydride: TA) has been successfully used as a reagent for Beckmann rearrangement in the conversion of variety of ketoximes into amides without any additive or base. This reagent works well for the synthesis of library of amides with excellent yields.

**Keywords:** Triflic anhydride; Amides; Ketoximes; Beckmann rearrangement

## INTRODUCTION

Amides are highly significant precursors for the synthesis of various natural products and intermediates for large number of medicinally important compounds.[1] Out of number of methods reported for the synthesis of amides, Beckmann rearrangement is quite effective since it avoids the use of corrosive acid chlorides and has been employed in the industrial production of ω-caprolactam and laurolactam.[2] In many cases, this reaction requires strong bronsted acids (which acts as dehydrating agents),[3] there by restricting its application to acid sensitive substrates.

A survey of literature reveals application of various techniques and reagents for the synthesis of amides. Methods involving vapour phase,[4] solvent free conditions,[5] supercritical water,[6] ionic liquids,[7-9] liquid phase conditions,[10-12] and microwave irradiation on silica support have been reported.[13] Heterogeneous reaction conditions that are facilitated by supported reagents on solid surfaces have also been developed to bring about Beckmann rearrangement with certain limitations.[14]

Metal salts like $Ga(OTf)_3$,[15] $Sc(OTf)_3$,[16] $Cu(OAc)_2$,[17] $TiCl_4$,[18] and In/Zn cuple[19] have also been found to be effective in this reaction. Organic acids or reagents capable of acting as better leaving groups constitute a major group which includes sulfamic acid,[20] chlorosulfonic acid,[21] anhydrous oxalic acids,[22] *O*-alkyl DMF salt,[23] $CF_3COOH$,[24] trifluoromethanesulfonic acid,[25] and pivaloyl chloride-DMF complex.[26] However, some of these variants suffer from drawbacks such as toxicity, expensive reagents, and production of considerable amounts of by-products. In addition, these reactions also require longer reaction times, high temperature and produce low yields. Though, enzymatic methods are also available, their isolation costs and application to limited substrates can present challenges for their general applicability.[27] In spite of all these still there is a need for simpler and widely applicable method for the synthesis of amides.

Trifluoromethanesulfonic anhydride has been an effective reagent in a number of reactions.[28-31] We have demonstrated the applications of this reagent for the conversion of aldoximes into nitriles[32] and formation of amides from nitriles by Ritter reaction.[33] In continuation of our work, the present paper illustrate the utility of triflic anhydride in Beckmann transformations.

## RESULTS AND DISCUSSION

For optimization of reaction conditions benzophenone oxime was selected as the model substrate to study the effect of solvent, temperature and reaction time on the overall yield of the reaction (Table 1). Reaction of equimolar quantities of benzophenone oxime **12a** and TA was attempted in methanol under reflux conditions. The yield of the product was very low in this case (Table 1, entry 1). Solvents such as ethanol, acetonitrile and acetone, were suitable for this reagent but to our disappointment only 39-65% of product was isolated even after 8h under reflux conditions (Table 1, entries 2-4). Further, when we used $CCl_4$, reaction did not proceed even after 12h under reflux conditions (Table 1, entry 5) and very poor conversion of the product was observed in THF and in dioxane (Table 2, entries 6 and 7). Reaction in dipolar aprotic solvents and high boiling aromatic solvents were not effective which are reflected in low percentage of the transformation (Table 1, entries 8-10). Serendipitously, excellent isolated yield (96%,

Table 1, entry 11) at a shorter reaction time (2.5h) was realized when the reaction was carried out at room temperature in DCM. On the other hand, the same reaction was completed in 2h at reflux mode with 98% of isolated yield. In order to evaluate the influence of other chlorinated solvent in this reaction, ethylene dichloride (EDC) was tried. With EDC, 93% conversion and 81% isolated yield are achieved in 3h at rt while at reflux mode, conversion and isolated yield noticed are 98% and 87% respectively in 2.4h (Table 1, entry 12). On the grounds of obtained results and carcinogenic nature (class 2) with EDC, we have demonstrated the said Beckmann rearrangement in DCM as the only choice of the solvent for rest of the substrates.

Further, the effect of the reaction temperature and time has also been investigated. Based on the observations it shows that, increase in the reaction temperature and time is propitious to the increasing yield of product (Table 1, entries 11 and 12).

**Table 1:**

The successful synthesis of *N*-benzylbanzamide in DCM prompted us to investigate the applicability of this procedure for the synthesis of other amides via Beckmann rearrangement of variety of ketoximes (see **Scheme 1**).

**Scheme 1:**

A similar trend of reaction was observed in the Beckmann rearrangement of acetoxime to the corresponding *N*-methylacetamide (Table 2, entry 1). The reaction was completed in 2h with 72% isolated yield. Further, we have also carried out the synthesis of piperidine-2-one in 78% isolated yield by the ring enlargement of cyclopentanone oxime (Table 2, entry 2). In addition, we were also successful in synthesizing 2-azepanone (ω-caprolactam) by the ring enlargement of cyclohexanone oxime (Table 2, entry 3). Based on the qualitative analysis by GC and GC–MS (Table 1, optimization study), it could be known that their main by-products were the corresponding ketones and only trace amounts of dimeric oximes were observed (0.2 - 0.3%). Much better results

could be obtained if different substituted aryl ketoximes were used as substrates in Beckmann rearrangement.

To generalize the applicability of this method on the nature of substitution, we also carried out the Beckmann rearrangement of substituted acetophenone oximes to the corresponding amides (Table 2, entries 4-11). All the reactions were completed in 1.5 to 3.5h with 92% to 96% isolated yield and 99% selectivity. This showed the nature of substituent (either electron withdrawing or electron donating) has no effect on the reactivity of TA for the Beckmann rearrangement. Furthermore, we are successful to convert oxime of 2-acetyl thiophene to thiophene-2-yl acetamide in 4.5h with 86% isolated yield (Table 2, entry 19) via Beckmann rearrangement. But to our disappointment, reaction did not proceed with oxime of 3-acetyl coumarin even after 12h (Table 2, entry 20).

Thus, the Beckmann rearrangement of wide range of structurally varied ketoximes in the presence of TA was carried out under the optimized reaction conditions described above. The results (Table 2) show that a variety of structurally varied ketoximes rearranged smoothly in DCM to give the corresponding amides in excellent yields (72% to 96%).

However, under optimized reaction conditions, the reaction did not proceed when we subjected oximes of propiophenone, 2-methyl propiophenone, 1-(pyridine-2-yl)propanone, and 1-(pyridine-3-yl)propanone for Beckmann rearrangement even after 12h under reflux conditions (Table 2, entries 21-24).

**Table 2:**

The plausible mechanism of formation of various amides is depicted in Figure 1.

**Figure 1:**

A plausible explanation for reaction mechanism is discussed in Figure 1. The hydroxyl group of the oxime **1** reacts with TA results in the formation of *O*-Trifyloxime **2** which undergoes intramolecular rearrangement leading to the formation of reactive intermediate nitrile **3**. The conversion of 2–3 proceeds through a concerted 1,2 intramolecular shift.

The subsequent reaction of reactive intermediate **3** with *O*-Triflate (**OT**) affords the formation of *O*-Trifylimine **4** which upon hydrolysis losses triflic acid leading to the formation of amide **5**.

Under the optimized set of reaction conditions, different ketoximes (**1–19**) having varying structural features were reacted with TA to afford corresponding amides in excellent yields via Beckmann rearrangement.

In summary, we have identified new, convenient, and highly efficient reagent which rearrange various ketoximes into amides with good to excellent yields.

## EXPERIMENTAL

The reagents employed were of high purity commercial samples which were used as received (Fischer, Merck and Sigma Aldrich). Reactions were carried out in oven-dried RB flask. Column chromatography was performed on silica gel (200-400 mesh). TLC was performed on alumina silica gel $60F_{254}$ (Fischer) detected by UV light (254 nm) and iodine vapors. The melting points were determined by open capillaries on a Buchi apparatus and are uncorrected. The IR spectra were recorded on a Nicolet-Impact-410 FT-IR spectrometer, using KBr pellets. $^{1}H$ NMR and $^{13}C$ NMR spectra were recorded on a Bruker AC-300F, 300 MHz, spectrometer in DMSO-$d_6$ using TMS as an internal standard with $^{1}H$ resonance frequency of 300 MHz, $^{13}C$ resonance frequency of 75 MHz. GC analyses were performed on Nucon 5700 series Gas chromatograph. GC-MS analyses were performed on Shimadzu 2010 series mass selective detector instrument. Elemental analysis was carried out by using Heraus CHN rapid analyzer. All the compounds gave C, H and N analysis within ± 0.4% of the theoretical values. Dry DCM was obtained from commercial source by the standard procedure.

### Typical procedure for the synthesis of amides using triflic anhydride

The desired ketoxime (2.0 mmol) in 5 mL dry DCM was taken in an oven-dried RB flask. To the reaction mixture was added drop wise triflic anhydride (2.0 mmol) in DCM (5mL) under nitrogen for 10 to 15 minutes. The reaction mixture was stirred at RT and the progress of the reaction was monitored by TLC and GC-MS (Table 2). After completion of reaction, the contents were poured to crushed ice (100 mL) and neutralized

with 10% $NaHCO_3$ solution (20 mL) and extracted with DCM (15 mL x 3). The pure products were obtained by column chromatography with hexane-ethyl acetate and DCM-methanol mixture. All the amides were characterized by IR, GC-MS, $^1$H NMR, $^{13}$C NMR and by elemental analysis and the results are compared with authentic samples.

## Characterization data of various amides

**_N_-Methylacetamide (1)** [1, 2, 3, 4, 5, 6]

Yield: 170 mg (72%); colorless liquid, MP = 204-206 $^O$C; Rf: 0.48 (80:20 Hexane:EtOAc, Iodine vapors); IR (KBr): 3345, 1660, 1246, 1028, 822 cm$^{-1}$. $^1$H NMR (300MHz, DMSO-$d_6$): δ = 2.18 (s, 3H, $CH_3$), 2.83 (s, 3H, $CH_3$), 10.31 (s, 1H, NH). $^{13}$C NMR (75MHz, DMSO-$d_6$): δ = 168.2, 28.7, 23.4 GC-MS: m/z 73 $[M]^+$. Anal. Calc. For $C_3H_7NO$: C, 49.30; H, 9.65; N, 19.16% found: C, 49.28; H, 9.62; N, 19.15%.

**Piperidin-2-one (2)** [1, 2, 3, 5]

Yield: 190 mg (73%); colorless liquid, MP = 257-259 $^O$C; Rf: 0.37 (80:20 Hexane:EtOAc, Iodine vapors); IR (KBr): 3342, 1672, 1541, 1308, 1132, 796 cm$^{-1}$. $^1$H NMR (300MHz, DMSO-$d_6$): δ = 1.62 (m, 4H), 2.34 (m, 2H), 3.36 (m, 2H), 10.44 (s, 1H, NH). $^{13}$C NMR (75MHz, DMSO-$d_6$): δ = 169.1, 38.8, 36.2, 26.5, 24.2. GC-MS: m/z 99 $[M]^+$. Anal. Calc. For $C_5H_9NO$: C, 60.58; H, 9.15; N, 14.13% found: C, 60.57; H, 9.14; N, 14.13%.

**ω-Caprolactam (3)** [1, 2, 3, 4, 5, 6]

Yield: 230 mg; colorless solid, MP = 68-71 $^O$C; Rf: 0.51 (80:20, Hexane:EtOAc, Iodine vapors); $^1$H NMR (300MHz, DMSO-$d_6$): δ = 1.2 (m, 2H, $CH_2$), 1.55 (m, 2H, $CH_2$), 2.15 (m, 2H, $CH_2$), 2.44 (m, 2H, $CH_2$), 10.08 (s, 1H, NH). $^{13}$C NMR (75MHz, DMSO-$d_6$): δ = 179.2, 39.2, 35.8, 30.1, 29.6, 21.8. GC-MS: m/z 113 $[M]^+$. Anal. Calc. For $C_6H_{11}NO$: C, 63.68; H, 9.80; N, 12.38 % found; C, 63.70; H, 9.78; N, 12.35%

**_N_-Phenylacetamide (4)** [1, 2, 3, 4, 5, 6]

Yield: 288 mg (96%); colorless solid, MP = 114-116 $^O$C; Rf: 0.47 (95:5, DCM:MeOH, UV); IR (KBr): 3351, 3031, 1669, 1582, 1530, 1474, 1421, 1285, 1230, 698 cm$^{-1}$. $^1$H NMR (300MHz, DMSO-$d_6$): δ = 2.48 (s, 3H, $CH_3$), 7.75 (m, 5H), 10.15 (s, 1H, NH). $^{13}$C NMR (75MHz, DMSO-$d_6$): δ = 167.1, 138.8, 128.3, 127.6, 124.1, 121.9, 121.6, 22.9.

GC-MS: m/z 135 $[M]^+$. Anal. Calc. For $C_8H_9NO$: C, 71.09; H, 6.71; N, 10.36% found: C, 71.07; H, 6.70; N, 10.34%.

***N*-*p*-tolylacetamide (5)** [1, 2, 3, 4]

Yield: 245 mg (92%); colorless solid, MP = 145-148 $^O$C; Rf: 0.35 (98:2, DCM:MeOH, UV); IR (KBr): 3331, 1665, 1573, 1394, 1310, 921, 719 $cm^{-1}$. $^1$H NMR (300MHz, DMSO-$d_6$): δ = 2.32 (s, 3H, $CH_3$), 2.38 (s, 3H, $CH_3$), 6.87 (d, 2H, j = 8.5 Hz), 7.42 (d, 2H, j = 8.5 Hz), 10.34 (s, 1H, NH). $^{13}$C NMR (75MHz, DMSO-$d_6$): δ = 168.4, 142.5, 135.2, 129.6, 122.1, 22.8, 24.6. GC-MS: m/z 149 $[M]^+$. Anal. Calc. For $C_9H_{11}NO$: C, 72.46; H, 7.43; N, 9.39% found: C, 72.45; H, 7.41; N, 9.40%.

***N*-(4-Methoxyphenyl)acetamide (6)** [1, 3, 4]

Yield: 286 mg (96%); colorless solid, MP = 130-132 $^O$C; Rf: 0.48 (95:5 DCM:MeOH, UV); IR (KBr): 3341, 1669, 1576, 1343, 1320, 887, 689 $cm^{-1}$. $^1$H NMR (400MHz, DMSO-$d_6$): δ = 2.37 (s, 3H, $CH_3$), 3.86 (s, 3H, $OCH_3$), 6.89 (d, 2H, j = 8.5 Hz), 7.46 (d, 2H, j = 8.5 Hz), 9.97 (s, 1H, NH). $^{13}$C NMR (100MHz, DMSO-$d_6$): δ = 169.6, 154.5, 134.2, 130.2, 122.6, 56.4, 22.6. GC-MS: m/z 165 $[M]^+$. Anal. Calc. For $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48% found: C, 65.42; H, 6.70; N, 8.47%.

***N*-(4-Nitrophenyl)acetamide (7)** [1, 2, 3, 4]

Yield: 266 mg (94%); pale yellow solid, MP = 215-218 $^O$C; Rf: 0.25 (95:5, DCM:MeOH, UV); IR (KBr): 3320, 1667, 1565, 1380, 1302, 829, 834 $cm^{-1}$. $^1$H NMR (400MHz, DMSO-$d_6$): δ = 2.30 (s, 3H, $CH_3$), 7.84 (d, 2H, j = 9.0 Hz), 8.40 (d, 2H, j = 9.0 Hz), 10.12 (s, 1H, NH). $^{13}$C NMR (100MHz, DMSO-$d_6$): δ = 169.1, 145.7, 142.8, 124.6, 122.1, 22.2. GC-MS: m/z 180 $[M]^+$. Anal. Calc. For $C_8H_8N_2O_3$: C, 53.33; H, 4.48; N, 15.55% found: C, 53.32; H, 4.46; N, 15.54%.

***N*-(4-Aminophenyl)acetamide (8)** [1, 2, 4, 6]

Yield: 285 mg (94%); colorless solid, MP = 165-167 $^O$C; Rf: 0.34 (95:5, DCM:MeOH, UV); IR (KBr): 3340, 1672, 1580, 1323, 1314, 857, 670 $cm^{-1}$. $^1$H NMR (300MHz, DMSO-$d_6$): δ = 2.27 (s, 3H, $CH_3$), 6.68 (d, 2H, j = 8.5 Hz), 7.42 (d, 2H, j = 8.5 Hz), 10.18 (s, 1H, NH). $^{13}$C NMR (75MHz, DMSO-$d_6$): δ = 170.2, 142.5, 130.6, 122.8, 118.3, 22.8. GC-MS: m/z 150 $[M]^+$. Anal. Calc. For $C_8H_{10}N_2O$: C, 63.98; H, 6.71; N, 18.65% found: C, 63.97; H, 6.70; N, 18.66%.

***N*-(4-Chlorophenyl)acetamide (9)** [1, 2, 3]

Yield: 288 mg (95%); colorless solid, MP = 176-178 $^{O}$C; Rf: 0.33 (95:5, DCM:MeOH, UV); IR (KBr): 3342, 1670, 1590, 1353, 1322, 890, 667 cm$^{-1}$. $^{1}$H NMR (400MHz, DMSO-$d_6$): δ = 2.38 (s, 3H, $CH_3$), 7.42 (d, 2H, j = 9.0 Hz), 7.60 (d, 2H, j = 9.0 Hz), 10.28 (s, 1H, NH). $^{13}$C NMR (100MHz, DMSO-$d_6$): δ = 168.4, 138.8, 130.9, 129.4, 124.3, 23.4. GC-MS: m/z 169 $[M]^+$. Anal. Calc. For $C_8H_8ClNO$: C, 56.65; H, 4.75; N, 8.26% found: C, 56.66; H, 4.74; N, 8.25%.

***N*-(4-Bromophenyl)acetamide (10)** [1, 2]

Yield: 268 mg (90%); brown solid, MP = 163-165 $^{O}$C; Rf: 0.34 (95:5, DCM:MeOH, UV); IR (KBr): 3336, 1665, 1570, 1323, 1310, 812, 654 cm$^{-1}$. $^{1}$H NMR (400MHz, DMSO-$d_6$): δ = 2.18 (s, 3H, $CH_3$), 7.40 (d, 2H, j = 9.0 Hz), 7.68 (d, 2H, j = 9.0 Hz), 9.98 (s, 1H, NH). $^{13}$C NMR (100MHz, DMSO-$d_6$): δ = 169.2, 138.8, 131.2, 125.4, 121.3, 23.8. GC-MS: m/z 213 $[M-1]^+$, 215 $[M+1]^+$ Anal. Calc. For $C_8H_8BrNO$: C, 44.89; H, 3.77; N, 6.54% found: C, 44.88; H, 3.75; N, 6.55%.

***N*-(4-Fluorophenyl)acetamide (11)** [1, 2]

Yield: 280 mg (92%); colorless solid, MP = 153-155 $^{O}$C; Rf: 0.38 (95:5, DCM:MeOH, UV); IR (KBr): 3330, 1668, 1530, 1345, 1312, 845, 656 cm$^{-1}$. $^{1}$H NMR (400MHz, DMSO-$d_6$): δ = 2.10 (s, 3H, $CH_3$), 7.12 (d, 2H, j = 9.0 Hz), 7.80 (d, 2H, j = 9.0 Hz), 10.38 (s, 1H, NH). $^{13}$C NMR (100MHz, DMSO-$d_6$): δ = 169.2, 159.8 (C-F, $J$ = 245.20 Hz), 134.3, 124.3, 116.4, 22.8. GC-MS: m/z 153 $[M]^+$. Anal. Calc. For $C_8H_8FNO$: C, 62.74; H, 5.26; N, 9.15% found: C, 62.75; H, 5.24; N, 9.15%.

***N*-phenylbenzamide (12)** [1, 2, 3, 4, 5, 6]

Yield: 285 mg (96%); colorless solid, MP = 161-163 $^{O}$C; Rf: 0.52 (80:20, Hexane:EtOAc, UV); IR (KBr): 3359, 1660, 1580, 1530, 1478, 1420, 1320, 1285, 688 cm$^{-1}$. $^{1}$H NMR (300MHz, DMSO-$d_6$): δ = 7.35 (m, 2H), 7.62 (m, 3H), 7.86 (m, 2H), 8.10 (m, 3H), 10.32 (s, 1H, NH). $^{13}$C NMR (75MHz, DMSO-$d_6$): δ = 166.3, 136.8, 134.8, 132.3, 131.6, 129.1, 128.9, 128.4, 127.6, 122.9, 121.4, 120.6. GC-MS: m/z 197 $[M]^+$. Anal.Calc.for $C_{13}H_{11}NO$: C,79.16; H, 5.62; N, 7.10% found: C, 79.17; H, 5.60; N,7.10 %.

***N*-(4-Fluorophenyl)benzamide (13)** [1, 2, 4]

Yield: 260 mg (88%); colorless solid, MP = 169-172 $^{O}$C; Rf: 0.55 (80:20, Hexane:EtOAc, UV); IR (KBr): 3341, 1652, 1535, 1325, 1312, 845, 650 cm$^{-1}$. $^{1}$H NMR (300MHz, DMSO-$d_6$): δ = 7.05 (d, 2H, j = 9.0 Hz), 7.54 (m, 2H), 7.68 (d, 2H, j = 9.0 Hz), 7. 95 (m, 3H), 10.18 (s, 1H, NH). $^{13}$C NMR (75MHz, DMSO-$d_6$): δ = 166.6, 160.2, (C-F, $J$ = 246.12Hz), 135.2, 131.6, 130.7, 129.8, 129.3, 128.5, 128.0, 127.4, 124.6, 123.4, 116.8. GC-MS: m/z 215 $[M]^{+}$. Anal. Calc. For $C_{13}H_{10}FNO$: C, 72.55; H, 4.68; N, 6.51% found: C, 72.55; H, 4.66; N, 6.50%.

***N*-(4-Bromophenyl)benzamide (14)** [1, 2, 3]

Yield: 266 mg (90%); pale yellow solid, MP = 162-165 $^{O}$C; Rf: 0.67 (80:20, Hexane:EtOAc, UV); IR (KBr): 3334, 1656, 1540, 1320, 1332, 840, 760 cm$^{-1}$. $^{1}$H NMR (300MHz, DMSO-$d_6$): δ = 7.36 (d, 2H, j = 9.0 Hz), 7.58 (m, 2H), 7.72 (d, 2H, j = 9.0 Hz), 8.16 (m, 3H), 10.28 (s, 1H, NH). $^{13}$C NMR (75MHz, DMSO-$d_6$): δ = 164.5, 159.4, 136.2, 132.6, 130.7, 129.8, 129.0, 128.5, 128.1, 127.2, 123.8, 123.2, 118.4. GC-MS: m/z 275 $[M-1]^{+}$, 277 $[M+1]^{+2}$ Anal. Calc. For $C_{13}H_{10}BrNO$: C, 56.55; H, 3.65; N, 5.07% found: C, 56.53; H, 3.64; N, 5.05%.

***N*-(4-Nitrorophenyl)benzamide (15)** [1, 2]

Yield: 256 mg (87%); pale yellow solid, MP = 202-204 $^{O}$C; Rf: 0.611 (98:2, DCM:MeOH, UV); IR (KBr): 3333 1650, 1563, 1325, 1312, 1280, 945, 780, 694 cm$^{-1}$. $^{1}$H NMR (300MHz, DMSO-$d_6$): δ = 7.56 (m, 5H), 7.80 (d, 2H, j = 8.5 Hz), 8.34 (d, 2H, j = 8.5 Hz), 9.80 (s, 1H, NH). $^{13}$C NMR (75MHz, DMSO-$d_6$): δ = 164.6, 148.2, 142.2, 132.6, 131.1, 129.8, 129.3, 128.7, 128.1, 127.4, 124.6, 123.4, 121.2. GC-MS: m/z 242 $[M]^{+}$. Anal. Calc. For $C_{13}H_{10}N_2O_3$: C, 64.46; H, 4.16; N, 11.56% found: C, 64.45; H, 4.16; N, 11.54%.

***N*-(2-Methoxyphenyl)acetamide (16)** [1, 3, 4]

Yield: 248 mg (86%); colorless solid, MP = 87-90 $^{O}$C; Rf: 0.611 (98:2, DCM:MeOH, UV); IR (KBr): 3340, 3331, 1674, 1580, 1520, 1466, 1411, 1280, 1230, 792 cm$^{-1}$. $^{1}$H NMR (300MHz, DMSO-$d_6$): δ = 2.42 (s, 3H, $CH_3$), 3.86 (s, 3H, $OCH_3$), 6.96 (m, 4H), 10.25 (s, 1H, NH). $^{13}$C NMR (75MHz, DMSO-$d_6$): δ = 171.1, 153.2, 126.3, 124.1, 121.9, 121.6, 113.4, 56.8, 22.9. GC-MS: m/z 165 $[M]^{+}$. Anal. Calc. For $C_8H_9NO$: C, 71.09; H, 6.71; N, 10.36% found: C, 71.08; H, 6.71; N, 10.35 %.

***N*-(3-Methoxyphenyl)acetamide (17)** [3, 4]

Yield: 265 mg (90%); colorless solid, MP = 103-105 $^{O}$C; Rf: 0.514 (98:2, DCM:MeOH, UV); IR (KBr): 3338, 1670, 1540, 1530, 1468, 1421, 1230, 1218, 754 cm$^{-1}$. $^{1}$H NMR (300MHz, DMSO-$d_6$): δ = 2.36 (s, 3H, $CH_3$), 3.92 (s, 3H, $OCH_3$), 6.72 (d, 2H, j = 8.5 Hz), 7.76 (m, 2H), 10.15 (s, 1H, NH). $^{13}$C NMR (75MHz, DMSO-$d_6$): δ = 170.6, 161.5, 140.4, 131.6, 114.4, 110.3, 105.6, 55.4, 24.1. GC-MS: m/z 165 $[M]^+$. Anal. Calc. For $C_8H_9NO$: C, 71.09; H, 6.71; N, 10.36% found: C, 71.07; H, 6.71; N, 10.34%.

***N*-(Naphthalene-2-yl)acetamide (18)** [5]

Yield: 230 mg (85%); colorless solid, MP = 176-178 $^{O}$C; Rf: 0.36 (80:20, Hexane:EtOAc, UV); IR (KBr): 3331, 3020, 1668, 1584, 1530, 1424, 1410, 1235, 1250, 658 cm$^{-1}$. $^{1}$H NMR (300MHz, DMSO-$d_6$): δ = 2.18 (s, 3H, $CH_3$), 6.75 (m, 2H), 7.10 (m, 2H), 7.89 (m, 3H), 10.10 (s, 1H, NH). $^{13}$C NMR (75MHz, DMSO-$d_6$): δ = 170.2, 136.4, 132.4, 127.8, 126.4, 125.8, 124.6, 124.1, 121.9, 118.6, 110.3, 23.2. GC-MS: m/z 185 $[M]^+$. Anal. Calc. For $C_{12}H_{11}NO$: C, 77.81; H, 5.99; N, 7.56% found: C, 77.80; H, 5.98; N, 7.54%.

**N-(thiophen-2-yl)acetamide (19)**

Yield: 230 mg (85%); colorless solid, MP =159-161 $^{O}$C; Rf: 0.36 (97:3, DCM:MeOH , Iodine vapors); [1]. $^{1}$H NMR (300MHz, DMSO-$d_6$): δ = 2.08 (s, 3H, $CH_3$), 6.75 (m, 1H), 6.90 (m, 1H), 7.38 (m, 1H), 10.24 (s, 1H, NH). $^{13}$C NMR (75MHz, DMSO-$d_6$): δ = 171.3, 144.4, 126.6, 122.4, 112.8, 23.2. GC-MS: m/z 141 $[M]^+$. Anal. Calc. For $C_6H_7NOS$: C, 51.04; H, 5.00; N, 9.92% found; C, 51.01; H, 4.98; N, 9.90%

## CONCLUSIONS

In conclusion, we have successfully demonstrated the convenient method for the synthesis of wide variety of amides from variuos ketoximes using triflic anhydride. Further work, including the development of synthetic applications of aryl and heteroaryl oximes and exploration of the enormous potential of triflic anhydride as a triflyl source in organic synthesis is underway in our laboratory.

## ACKNOWLEDGEMENTS

The authors thank the University Sophisticated Instrument Center, KUD for IR, GC, GC-MS, $^{1}$H NMR and $^{13}$C NMR. Thanks are also due to Department of Science and Technology, Science and Engineering Research Board New Delhi (DST-SERB) Project No SB/FT/CS-175/2013 for financial assistance. Authors also thank Prof. M. V. Kulkarni for his useful discussion.

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**Scheme 1**. Synthesis of different substituted amides via Beckmann rearrangement

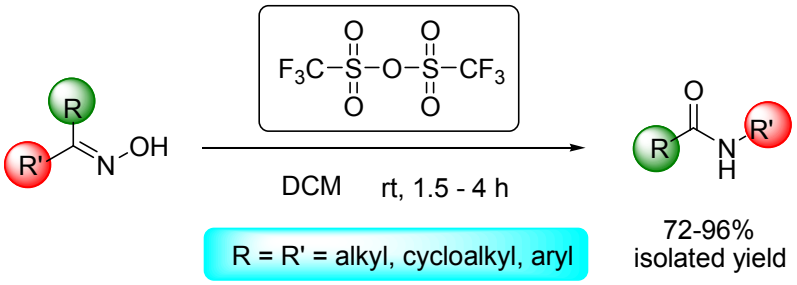
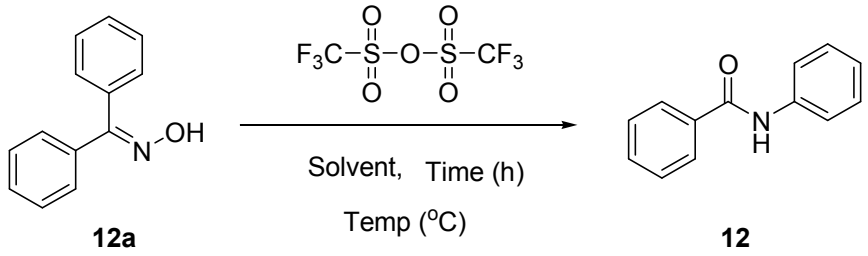


**Table 1:**
Optimization of the reaction conditions[a]




**12a** **12**

| Entry | Solvent | Time (h) | Temp ($^{o}$ C) | Conversion[b] (%) | Yield[c] (%) |
|---|---|---|---|---|---|
| 1 | MeOH | 9 | reflux | 38 | 27 |
| 2 | EtOH | 8 | reflux | 55 | 39 |
| 3 | MeCN | 7 | reflux | 62 | 54 |
| 4 | Acetone | 8 | reflux | 70 | 65 |
| 5 | $CCl_4$ | 12 | reflux | Nil | None |
| 6 | THF | 6 | reflux | 54 | 43 |
| 7 | Dioxane | 10 | 110 | 34 | 26 |
| 8 | PhMe | 8 | 110 | 28 | NI[g] |
| 9 | DMF | 5 | 140 | 35 | NI[g] |
| 10 | DMSO | 7 | 130 | 30 | NI[g] |
| 11 | DCM | 2.5, 2[d] | rt | 100 | 96, 98[f] |
| 12 | EDC | 3, 2.4[d] | rt | 93, 98[e] | 81, 87[f] |

[a] Reaction carried out using compound 11 (2.0 mmol) and Triflic anhydride (2.0 mmol) in 5 mL of solvent, unless otherwise stated.
[b] Conversion (%) of product based on GC analysis.
[c] Isolated yield of pure product.
[d] Reaction time in reflux condition.
[e] Conversion (%) of product in reflux condition.
[f] Isolated yield of pure product in reflux condition.
[g] Not isolated

**Table 2.** List of amides synthesized using TA

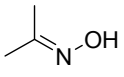
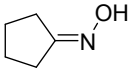
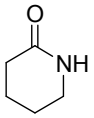
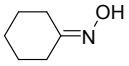
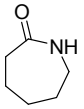
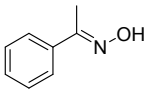
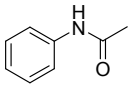
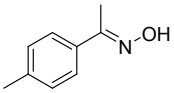
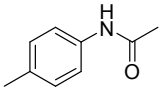
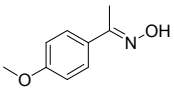
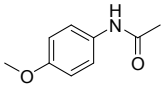
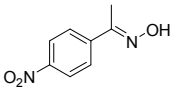
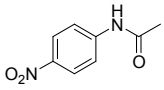
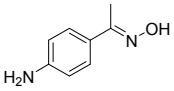
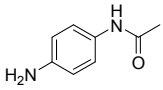
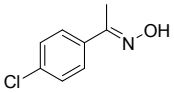
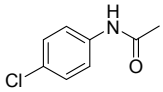
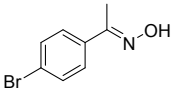
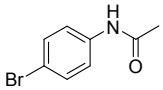
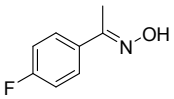
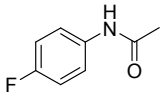
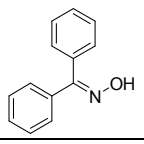
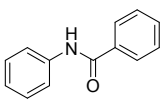
| Entry | Oximes | Product | Conversion (%) | Selectivity (%) | Time (h) | Yield* |
|---|---|---|---|---|---|---|
| 1 |  |  | 74 | 98 | 3 | 72 |
| 2 |  |  | 80 | 98 | 3 | 78 |
| 3 |  |  | 86 | 99 | 4 | 82 |
| 4 |  |  | 99 | 99 | 2.5 | 96 (87[a]) |
| 5 |  |  | 100 | 99 | 2.5 | 92 (81[a]) |
| 6 |  |  | 100 | 99 | 1.5 | 96 |
| 7 |  |  | 99 | 99 | 2 | 94 |
| 8 |  |  | 99 | 98 | 3 | 94 |
| 9 |  |  | 99 | 99 | 3.5 | 95 |
| 10 |  |  | 99 | 98 | 2.5 | 90 |
| 11 |  |  | 99 | 98 | 3.5 | 92 |
| 12 |  |  | 100 | 99 | 2.5 | 96 |

**Table 2. Continued…**

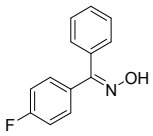
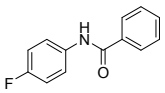
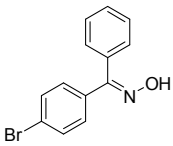
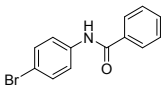
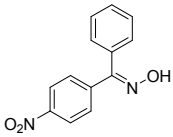
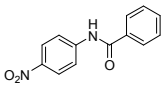
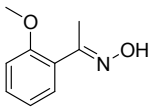
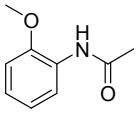
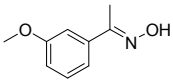
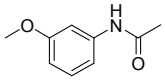
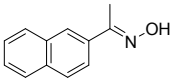
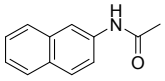
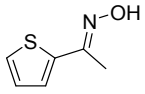
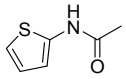
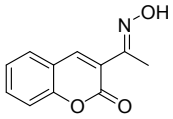
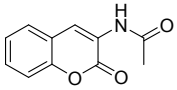
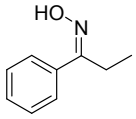
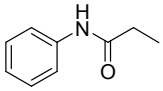
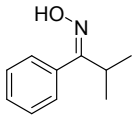
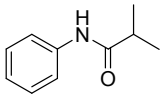
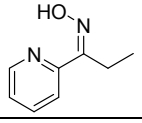
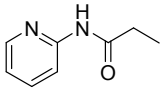
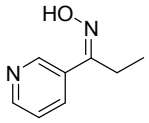
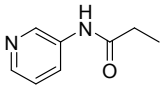
| Entry | Oximes | Product | Conversion (%) | Selectivity (%) | Time (h) | Yield* |
|---|---|---|---|---|---|---|
| 13 |  |  | 100 | 99 | 3 | 88 |
| 14 |  |  | 100 | 99 | 3 | 90 |
| 15 |  |  | 100 | 99 | 4 | 87 |
| 16 |  |  | 99 | 99 | 2.5 | 86 |
| 17 |  |  | 99 | 99 | 2 | 90 |
| 18 |  |  | 99 | 99 | 3 | 85 |
| 19 |  |  | 100 | 99 | 4.5 | 86 |
| 20 |  |  | ---- | ---- | 12 | NR[b] |
| 21 |  |  | ---- | ---- | 12 | NR[b] |
| 22 |  |  | ---- | ---- | 12 | NR[b] |
| 23 |  |  | ---- | ---- | 12 | NR[b] |

**Table 2. Continued…**

| Entry | Oximes | Product | Conversion (%) | Selectivity (%) | Time (h) | Yield* |
|---|---|---|---|---|---|---|
| 24 |  |  | ---- | ---- | 12 | NR[b] |

*****Isolated yield of pure product
[a]The reaction was carried out in EDC.
[b]No reaction

*Note:* 1. Identity of the products **4-11** was confirmed by acetylation of Corresponding amines except in the case of entry **7** which was confirmed By the nitration of acetanilide.

2. In the case of entry **13** and **14** migration of *p*-fluorophenyl and *p*-bromophenyl Moiety was confirmed by the IR Carbonyl frequency and melting point with The literature Reports.[34-37]

**Figure 1**. Plausible mechanism of formation of amides using TA via Beckmann rearrangement