SHORT PAPER

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One-step Beckmann rearrangement from carbonyl compounds and hydroxylamine hydrochloride in Al_2O_3/CH_3SO_3H (AMA) as a new reagent†

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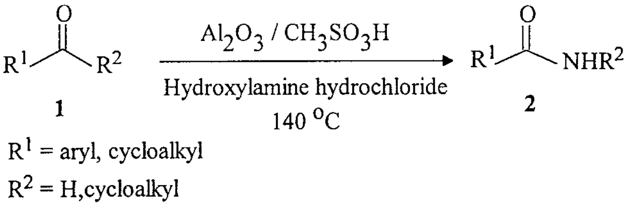
A facile and efficient synthetic procedure, for one-step Beckmann rearrangement of aldehydes and ketones with hydroxylamine hydrochloride and Al_2O_3/CH_3SO_3H (AMA) has been developed; cyclohexanone has been converted into ε-caprolactam in a quantitative yield.

Keywords: one-step Beckmann rearrangement, carbonyl compounds, hydroxylamine hydrochloride, $A1_2O_3/CH_3SO_3H$

It is well known that the most common media for Beckmann rearrangements are excess or stoichiometric amounts of strong Bronsted acids or Lewis acids. Recent methods include reagents such as zeolite,[1] $FeCl_3$ impregnated montmorillonite K10,[2] $AlCl_3$ in the solid state,[3] clay minerals,[4] trialkyloxonium salts,[5] antimony(V) salt,[6] aluminium iodide,[7] tetrabutylammonium per-rhenate(VII)(Bu_4NReO_4),[8] trifluoromethanesulfonic acid[8] and ionic liquids.[9] Amongst other reagents used have been concentrated H_2SO_4, formic acid,[10] liquid SO_2, HMPA,[11] $SOCl_2$,[12] silica gel,[13] P_2O_5-methanesulfonic acid,[14] HCl-HOAc, Ac_2O,[15] polyphosphoric acid,[16] and PCl_5,[17] causing large amounts of by-products and serious corrosion problems.[18] Although a great number of the vapour-phase Beckmann rearrangement processes have been reported, low selectivity for ε-caprolactam and rapid decline of acidity generally resulted partially because of high reaction temperatures.[18–21] However, liquid-phase rearrangements are generally sluggish and in all cases the previous preparation of the corresponding aldoximes and ketoximes are required, which constitutes a particular inconvenience.

Our new approach reported herein involves the use of Al_2O_3/CH_3SO_3H (AMA) for the Beckmann rearrangement of several aldehydes and ketones. Satisfactory conversion and selectivity were obtained for the transformation of cyclohexanone into ε-caprolactam.

For the Beckmann rearrangement reaction, ketones and aldehydes (1 mmol) in a mixture of CH_3SO_3H (2 ml) and Al_2O_3 (3 mmol) were heated in an oil bath at 140°C. Then the hydroxylamine hydrochloride (3 mmol) was added , there was no requirement for any other additional solvent. The experimental results are summarised in Table 1, Scheme 1.



Scheme 1

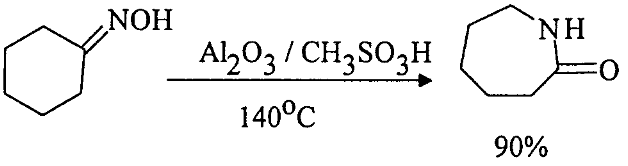
Firstly, the Beckmann rearrangement of aromatic aldehydes was carried out in AMA and the transformation proceeded effectively when both electron donating and electron withdrawing groups at the *ortho* and *para* position were used. According to Table 1, aromatic aldehydes gave only the primary amides. The Beckmann rearrangement is generally suggested to proceed through *anti* migration, and the Z forms of oximes are expected to give the corresponding amides. Indeed, various types of aldehydes in the presence of AMA were cleanly, rapidly and selectively condensed with hydroxylamine hydrochloride at 80°C in 5–10 min giving the corresponding *Z*-isomer of oximes (OH *syn* to aryl) in excellent yields. These results are summarised in Table 2.

Further, *meta* substituted aromatic aldehydes have not afforded the corresponding rearranged product in similar reaction conditions (140°C, 6 h; entries 8–13, Table 1). Schofield and his co-workers[22] have shown that the rates of rearrangement for *meta* substituted aromatic oximes were lower than the *para* and *ortho* substituted compounds in 98.2% sulfuric acid at 80°C.

Finally, AMA showed the highest activity and selectivity for preparation of ε-caprolactam from cyclohexanone (entry 16, Table 1) and Beckmann rearrangement of cyclopentanone and cycloheptanone (entries 17,18, Table 1).

The experimental results showed that the Beckmann rearrangements of several oximes in AMA media could be proceed with high conversion and selectivity, while the Beckmann rearrangement of *meta* substituted aromatic aldoximes were not observed in the same system (Table 3). In addition, cyclohexanone oxime could be converted into ε-caprolactam in AMA in 90% yield (Scheme 2). Although there was no difference in conversion between cyclohexanone and cyclohexanone oxime to yield ε-caprolactam.

In conclusion, the method described presents the advantages to be able to prepare directly amides in good yields from the corresponding aldehydes and ketones without previous need to prepare the corresponding aldo- and ketoximes. Easy work-up and high yields of amides are other advantages of this method.



Scheme 2

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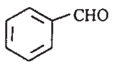
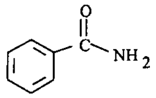
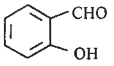
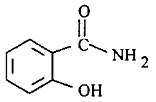
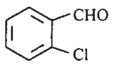
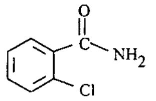
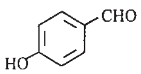
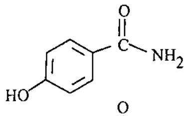
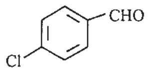
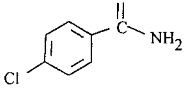
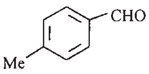
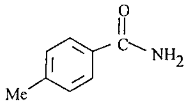
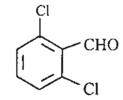
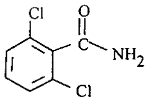
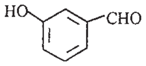
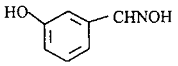
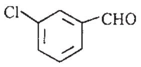
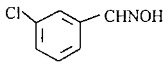
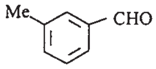
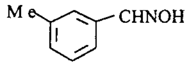
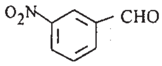
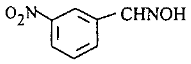
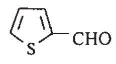
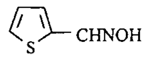
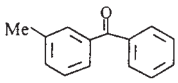
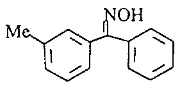
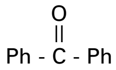
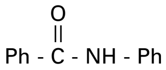
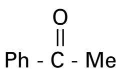
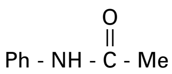
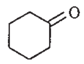
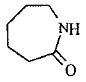
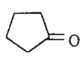
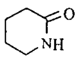
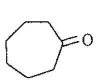
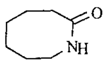
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

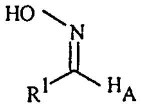
Table 1 Beckmann rearrangement of aldehydes and ketones

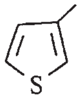
Entry	Substrate	Time/h	Products	^{1}H-NMR chemical shift of H amide (lit.)	IR (KBr) (lit.)	Yield[a] /%
1		3		6.26 (7.4[23])[b]	3385, 3190 (NH_2), 1665 (C = O) (3369, 3191, 1665[23])	95
2		2.5		6.02 (7.0[24])[b]	3420, 3210 (NH_2), 1685 (C = O) (3397, 3191, 1653[23])	80
3		3		6.45–6.49 (6.5[23])	3340, 3140 (NH_2), 1640 (C = O) (3369, 3191, 1638[23])	95
4		3.5		5.85 (7.12, 7.76[23])[b]	3140, 3210 (NH_2), 1650 (C = O) (3627, 3417, 1651[23])	75
5		3.5		5.97 (7.5[24])[b]	3333, 3226 (NH_2), 1650 (C = O) (333, 3226, 1667[24])	90
6		3.5		6.12 (7.5[24])[b]	3343, 3168 (NH_2), 1671 (C = O) (3343, 3168, 1670[23])	80
7		2		5.83–6.14	3450, 3190 (NH_2), 1650 (C = O) (3432, 3280, 1652[23])	90
8		6		—	—	95
9		6		—	—	95
10		6		—	—	95
11		6		—	—	90
12		4		—	—	80
13		6		—	—	70
14	 $Ph-\overset{O}{\overset{\|}{C}}-Ph$	0.7	 $Ph-\overset{O}{\overset{\|}{C}}-NH-Ph$	8.1 (10.3[23])[b]	3345 (NH), 1657 (C = O) (3346, 1657[23])	98
15	 $Ph-\overset{O}{\overset{\|}{C}}-Me$	2.5	 $Ph-NH-\overset{O}{\overset{\|}{C}}-Me$	7.79 (7.79[23])	3297 (NH), 1665 (C = O) (3294, 1665[23])	65
16		2		7.4 (7.0[23])	3212 (NH), 1658 (C = O) (3212, 1658[23])	90
17		2		7.00 (7.0[23])	3219 (NH), 1660 (C = O)	90
18		2		6.9 (6.9[23])	3231 (NH), 1663 (C = O) (3231, 1663[23])	90

[a] Yields were determined by ^{1}H NMR spectrometry.

[b] ^{1}H-NMR was obtained in DMSO-d_6

Table 2 Convertion of aldehydes to *Z*-isomer oximes using AMA



Entry	R^1	Time /min	M.p. (lit.)	^1H NMR Chemical[29] shift of H_A	Yields[a,b] /%
1	*p*-MeC_6H_4	5	72 (80^{24})	8.49	85
2	*p*-OHC_6H_4	5	94 (72^{24})	8.07	85
3	*p*-ClC_6H_4	5	146 (145^{25})	8.12	85
4	*p*-$NO_2C_6H_4$	10	100 (129^{26})	8.21	80
5	*p*-$MeOC_6H_4$	10	132 (133^{25})	8.00	80
6	*m*-MeC_6H_4	10	56 (60^{24})	8.13	80
7	*m*-OHC_6H_4	10	90 (90^{24})	8.09	85
8	*m*-ClC_6H_4	10	100 (100^{24})	8.11	85
9	*m*-$MeOC_6H_4$	10	110 (112^{24})	8.10	85
10	*o*-OHC_6H_4	5	63 (63^{24})	8.22	95
11	*o*-ClC_6H_4	5	103 (100^{27})	8.57	95
12	Ph	5	120 (128^{25})	8.17	85
13	2,6-diClC_6H_3	5	132 (150^{28})	8.40	95
14		10	130 (133^{24})	7.73	90

[a] ^1H NMR yields.

[b] Only a small amount of *E*-isomer, *i.e.* 5–20% was obtained.

Experimental

Starting materials were obtained from Fluka company. Melting points were determined by Buchi 510 apparatus and are uncorrected. IR spectra recorded on Perkin-Elmer spectrometer. Proton NMR spectra were recorded on Bruker Advance DPX FT 250 MHz instrument, in $CDCl_3$. Acidic alumina (Al_2O_3) type 540 C was purchased from the Fluka-company.

Amides from carbonyl compounds: CH_3SO_3H (2 ml, 0.03 mol) and Al_2O_3 (0.3 g, 3 mmol) were charged into a 5 ml round-bottomed flask equipped with a magnetic stirrer and thermometer. Then the aldehyde or ketone (1 mmol) was added with vigorous stirring in an oil bath at 100°C. After a few minutes, hydroxylamine hydrochloride (0.21 g, 3 mmol) was added in small portions and temperature was kept at 140°C for the periods indicated in the Table 1. At the end of the reaction the resulting mixture was mixed with 40 ml of water, extracted twice with dichloromethane (2 × 10 ml), and then dried with anhydrous sodium sulfate. The resulting products were characterised by melting points, NMR and IR spectra.

Amides from aldoximes and ketoximes: Z-aldoxime or ketoxime (1 mmol) was added to a stirred mixture of CH_3SO_3H (2 ml, 0.03 mol) and Al_2O_3 (0.3 g, 3 mmol) at 140°C in an oil bath. The progress of reaction was monitored by TLC. After appropriate time (Table 3), the reaction mixture was washed with water (40 ml) and extracted with dichloromethane (2 × 30 ml). The organic solution was dried over Na_2SO_4 and evaporated to give the corresponding amide.

Oximes from aldehydes and ketones: The aldehyde or ketone (1 mmol) was added to a stirred mixture of CH_3SO_3H (2 ml, 0.03 mol) and Al_2O_3 (0.3 g, 3 mmol) in an oil bath at 80°C. Then hydroxylamine hydrochloride (0.21 g, 3 mmol) was added. After the periods of time reported in Table 2 the reaction mixture was washed with water (2 × 50 ml) and extract with dichloromethane (2 × 10 ml). The organic layer was dried over Na_2SO_4 and evaporated to give the crude oxime.

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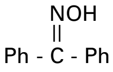
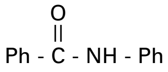
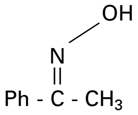
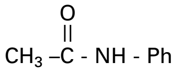
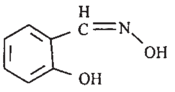
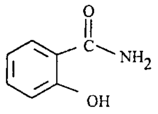
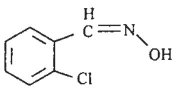
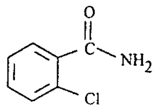
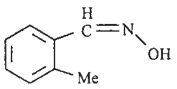
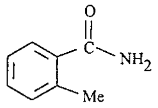
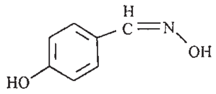
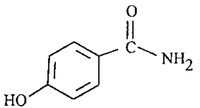
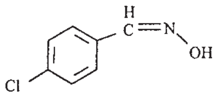
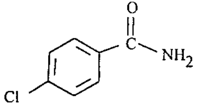
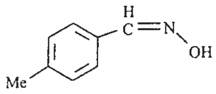
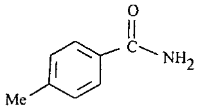
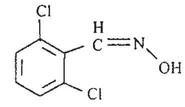
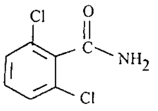
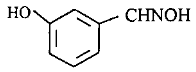
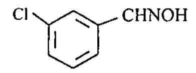
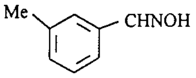
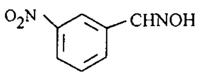
Table 3 Beckmann rearrangement of some oximes

Entry	Substrate	Time /h	Product	M.P. (lit.)	Yield[a] /%
1	 $\mathrm{Ph{-}C({=}NOH){-}Ph}$	2.5	 $\mathrm{Ph{-}C({=}O){-}NH{-}Ph}$	156 (163[24])	80
2		2.5	 $\mathrm{CH_3{-}C({=}O){-}NH{-}Ph}$	153 (157[24])	60
3		2.5		139 (142[24])	80
4		3		140 (142.4[24])	95
5		3		142 (147[24])	90
6		4.5		160 (162[24])	75
7		4.5		178 (179[24])	90
8		4.5		160 (160[24])	80
9		2		146 (144[24])	90

Entry	Starting material	Time/h	Products	Yield/%[a]
10		6	Not rearranged	
11		6	Not rearranged	
12		6	Not rearranged	
13		6	Not rearranged	

[a] Yields refer to pure isolated products.

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