### PAPER

# Solvent-Free and One-Step Beckmann Rearrangement of Ketones and Aldehydes by Zinc Oxide

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**Abstract:** In the presence of zinc oxide and without any additional organic solvents, Beckmann rearrangement of several ketones and aldehydes were performed in good yields.

Key words: zinc oxide, Beckmann rearrangement, oxime, aldehyde, ketone

Recently considerable attention has been paid to solventfree reactions.<sup>1,2</sup> These reactions are not only of interest from an environmental point of view, but in many cases also offer considerable synthetic advantages in terms of yield, selectivity and simplicity of the reaction procedure.

The Beckmann rearrangement is a fundamental and useful reaction, long recognized as an extremely valuable and versatile method for the preparation of amides or lactams, and often employed even in industrial processes.<sup>3</sup> The conventional Beckmann rearrangement usually requires the use of strong Brönsted or Lewis acids, i.e. concentrated sulfuric acid, phosphorus pentachloride in diethyl ether, hydrogen chloride in acetic anhydride, causing large amounts of byproducts and serious corrosion problems.<sup>4</sup>

Although a large number of vapour-phase Beckmann rearrangement processes have been reported, low selectivity for  $\varepsilon$ -caprolactam and rapid decay of activity generally resulted because of high reaction temperatures.<sup>4–7</sup> Liquidphase catalytic rearrangement under milder conditions, can afford high selectivity, in which solvent plays an important role.<sup>8</sup> A relatively large amount of organic solvent such as DMF,<sup>9,10</sup> however, was needed, which would cause environmental problems due to volatility and toxicity. Relatively few solid-phase methods have been developed <sup>11</sup> and very few methods are available for one-step Beckmann rearrangement of aldehydes and ketones.<sup>12</sup>

Therefore, there still exists a need for novel and facile methods for efficient conversion of ketones and aldehydes into the corresponding amides via Beckmann rearrangement. Our new approach reported herein involves the use of the cheap and commercially available ZnO in the absence of solvent as catalyst for Beckmann rearrangement of several ketones and aldehydes. Satisfactory conversion and selectivity were obtained for the transformation of cyclohexanone into  $\varepsilon$ -caprolactam (Scheme).

$$R^{1} \xrightarrow{O} R^{2} \xrightarrow{ZnO, NH_{2}OH \cdot HCl} R^{1} \xrightarrow{O} R^{1} \xrightarrow{O} NHR^{2}$$

 $R^1$  = alkyl, aryl, cycloalkyl  $R^2$  = H, cycloalkyl

Scheme

For each Beckmann rearrangement reaction, the ketone or aldehyde, hydroxylamine hydrochloride and ZnO were mixed throughly. Then the mixture was heated in an oil bath at 140-170 °C; there was no requirement for any other additional solvent. The experimental results are summarized in Table 1.

The Beckmann rearrangement of symmetrical ketones proceed effectively to afford the corresponding amides in good to excellent yields (entries 1–3, Table 1). In the case of unsymmetrical ketones the reaction was selective and one of the two possible amides was produced (entries 4,5 Table 1).

In the present method, as shown in Table 1, aromatic and aliphatic aldehydes were converted to the corresponding amides in good yields. According to Table 1, aldehydes gave only the primary amides. The Beckmann rearrangement is generally suggested to proceed through *anti* migration, wherein, the *Z*-forms of oximes are expected to give the corresponding amides.

We have also found that various types of aldehydes in the presence of ZnO were condensed cleanly, rapidly and selectively with hydroxylamine hydrochloride at 80 °C in 5–15 min to afford the corresponding Z-isomer of the oximes (OH *syn* to aryl) in excellent yields. Only a small amount of *E*-isomer, i.e. ca. 10–20% was obtained. These results are summarized in Table 2 and can be compared with our previous work.<sup>13</sup>

It is interesting to note that the yield were obviously reduced when *meta*-substituted aromatic aldehydes were used (entries 11,14 and 17, Table 1). Schofield and his coworkers<sup>14</sup> have shown that the rates of rearrangement for *meta*-substituted aromatic oximes were lower than the *para*- and *ortho*-substituted ones in 98.2% sulfuric acid at 80 °C.

Synthesis 2002, No. 8, 04 06 2002. Article Identifier: 1437-210X,E;2002,0,08,1057,1060,ftx,en;Z02502SS.pdf. © Georg Thieme Verlag Stuttgart · New York ISSN 0039-7881

Table 1	Beckmann	Rearrangement	of Ketones an	nd Aldehydes	into Amides	by ZnO

	8						
Entry	Substrate	Time/Temp. (h/°C)	Product	<sup>1</sup> H NMR, δ <sup>a</sup> CONH (Lit.)	IR (KBr) (Lit.)	Mp (Lit. <sup>18,19</sup> )	Yield <sup>b</sup> (%)
1	O    Ph - C -Ph	1/140	O    Ph - C -NH-Ph	8.1 (8.1 <sup>19</sup> )	3346 (NH), 1657 (C=O) (3345, 1657 <sup>19</sup> )	156 (163)	95
2	$\bigcirc^{\circ}$	1/150	O NH	7.4 (7.4 <sup>19</sup> )	3212 (NH), 1658 (C=O) (3212, 1658 <sup>19</sup> )	30 (30)	85
3	<b>)</b> =0	1/150		6.9 (6.9 <sup>19</sup> )	3231 (NH), 1663 (C=O) (3231, 1663 <sup>19</sup> )	69 (67)	83
4	0    Ph - C - Me	1/140	O II Ph-NH - C - Me	7.79 (7.79 <sup>18,19</sup> )	3297 (NH), 1665 (C=O) (3297, 1665 <sup>19</sup> )	156 (157)	90
5	ме	1/140	Me	(7.8 <sup>18</sup> )	3296 (NH),1662 (C=O) (3298, 1664 <sup>18</sup> )	150 (151)	85
6	Ph-CH <sub>2</sub> COCH <sub>3</sub>	8/170	n.r. <sup>c</sup>	_	_	_	_
7	COCH3	8/170	n.r. <sup>c</sup>	_	_	_	_
8	СНО	1/140	CONH <sub>2</sub>	6.2 (6.26 <sup>19</sup> )	3385, 3190 (NH <sub>2</sub> ), 1665 (C=O) (3385, 3190, 1665 <sup>19</sup> )	132 (132.5)	86
9	СНО	3/140	CONH <sub>2</sub> Cl	6.45 (6.5 <sup>19</sup> )	3340, 3140 (NH <sub>2</sub> ), 1640 (C=O) (3340, 3140, 1640 <sup>19</sup> )	140 (142.4)	60
10	CI	1/140	CI CONH <sub>2</sub>	5.97 (7.5 <sup>15</sup> ) <sup>b</sup>	3333, 3226 (NH <sub>2</sub> ), 1660 (C=O) (3333, 3226, 1667 <sup>15</sup> )	178 (179)	90
11	CI CHO	8/170	CI CONH <sub>2</sub>	6.4 (7.6 <sup>18</sup> ) <sup>b</sup>	3340, 3180 (NH <sub>2</sub> ), 1550 (C=O) (3361, 3182, 1550 <sup>18</sup> )	135 (135.5)	70
12	носно	1/140	HO CONH <sub>2</sub>	5.85 (5.85 <sup>19</sup> )	3140, 3210 (NH <sub>2</sub> ), 1650 (C=O) (3140, 3210, 1650 <sup>19</sup> )	162 (162)	75
13	СНО	2/140	CONH <sub>2</sub> OH	6.02 (7.0 <sup>15</sup> ) <sup>b</sup>	3420,3210 (NH <sub>2</sub> ), 1685 (C=O) (3397, 3191, 1653 <sup>18</sup> )	140 (142)	80
14	ОН СНО	7/170	OH CONH <sub>2</sub>	6.4 (7.0 <sup>15</sup> )	3340, 3180 (NH <sub>2</sub> ), 1550 (C=O) (3361, 3182, 1550 <sup>15</sup> )	170 (170)	70
15	СНО	3/150	CONH <sub>2</sub> Me	7.00 (7.5 <sup>15</sup> )	3420, 3210 (NH <sub>2</sub> ), 1685 (C=O) (3443, 3168, 1671 <sup>15</sup> )	142 (147)	60

Entry	Substrate	Time/Temp. (h/°C)	Product	<sup>1</sup> H NMR, δ <sup>a</sup> CONH (Lit.)	IR (KBr) (Lit.)	Mp (Lit. <sup>18,19</sup> )	Yield <sup>b</sup> (%)
16	ме	1/140	Me CONH <sub>2</sub>	6.12 (7.5 <sup>15</sup> ) <sup>b</sup>	3343, 3168 (NH <sub>2</sub> ), 1671 (C=O) (3343, 3168, 1671 <sup>19</sup> )	160 (160)	90
17	CHO Me	9/170	Me CONH <sub>2</sub>	7.22 (6.6 <sup>18</sup> )	3377, 3197 (NH <sub>2</sub> ), 1651 (C=O) (3377, 3197, 1651 <sup>18</sup> )	95 (97)	70
18	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CHO	3/140	O ∥ CH₃CH₂CH₂CNH₂	5.34 (6.7 <sup>18</sup> ) <sup>b</sup>	3360, 3180 (NH <sub>2</sub> ), 1630 (C=O) (3366, 3184, 1634 <sup>18</sup> )	113 (114.8)	80

 Table 1
 Beckmann Rearrangement of Ketones and Aldehydes into Amides by ZnO (continued)

<sup>a</sup> Solvent: DMSO-*d*<sub>6</sub>–TMS.

<sup>b</sup> Isolated yields.

<sup>c</sup> n.r. = no reaction.

R H	ZnO, NH <sub>2</sub> OH·HCl solvent free , 80 °C		b OH					
Entry	R	Time (min)	Yield (%) <sup>a</sup>		<sup>1</sup> Η NMR, δ, Η <b>a</b>	<sup>13</sup> Mp of <b>a</b> (Lit.)	Lit.)	
			a	b				
1	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	5	90	10	8.49	72 (80 <sup>15</sup> )		
2	$p ext{-OHC}_6 ext{H}_4$	5	90	10	8.07	94 (72 <sup>15</sup> )		
3	p-ClC <sub>6</sub> H <sub>4</sub>	5	90	10	8.12	146 (145 <sup>16</sup> )		
4	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	10	90	10	8.00	132 (133 <sup>16</sup> )		
5	m-MeC <sub>6</sub> H <sub>4</sub>	15	80	20	8.13	56 (60 <sup>15</sup> )		
6	m-OHC <sub>6</sub> H <sub>4</sub>	15	80	20	8.09	90 (90 <sup>15</sup> )		
7	m-ClC <sub>6</sub> H <sub>4</sub>	15	80	20	8.11	100 (100 <sup>15</sup> )		
8	<i>m</i> -MeOC <sub>6</sub> H <sub>4</sub>	15	80	20	8.10	110 (112 <sup>15</sup> )		
9	$o ext{-OHC}_6 ext{H}_4$	5	>98	trace	8.22	63 (63 <sup>15</sup> )		
10	o-ClC <sub>6</sub> H <sub>4</sub>	5	>98	trace	8.57	103 (10017)		
11	Ph	5	85	15	8.17	125 (12816)		

 Table 2
 Convertion of Aldehydes to Oximes in the Presence of ZnO

<sup>a</sup> Isolated yields.

<sup>b</sup> Solvent: DMSO-*d*<sub>6</sub>-TMS.

Finally, ZnO as catalyst, is remarkably easy to use, nonhazardous, inexpensive for use in Beckmann rearrangement. Also, the present procedure not only has the chemical, economical and environmental advantages of solvent-free reactions but also constitutes a method to prepare directly amides in good yields from the corresponding aldehydes and ketones without the previous need to prepare the aldo- and ketoximes.

### **Beckmann Rearrangement; General Procedure**

The appropriate ketone or aldehyde (1 mmol), NH<sub>2</sub>OH·HCl (0.3 g, 4.3 mmol) and ZnO (0.16 g, 2 mmol) were mixed sufficiently. Then the mixture was charged into a 10 mL round-bottomed flask equipped with a magnetic stirrer and heated in an oil bath at 140–170 °C; there was no requirement for any other additional solvent. At the end of the reaction (see Table 1), the resulting mixture was extracted with EtOAc ( $2 \times 5$  mL) and filtered to remove ZnO. The solvent was removed in vacuo to give the product which was recrys-

tallized from a suitable solvent or purified by column chromatography (EtOAc-hexane). All of the products are known and gave satisfactory physical data compared with those of authentic samples (Table 1).

# Preparation of Aldoximes in the Presence of ZnO; General Procedure

NH<sub>2</sub>OH·HCl (0.3 g, 4.3 mmol) was added to a stirred mixture of ZnO (0.16 g, 2 mmol) and aldehyde (1 mmol) at 80 °C in an oil bath. The progress of the reaction was monitored by TLC. After complete disappearance of the starting material (see Table 2), the mixture was washed with CH<sub>2</sub>Cl<sub>2</sub> ( $2 \times 10$  mL) and H<sub>2</sub>O ( $2 \times 50$  mL). The organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated to give the oxime. The products were identified by comparison of their physical data with those prepared in accordance with the literature procedures (Table 2).

## Acknowledgement

We gratefully acknowledge the support of this work by the Shiraz University Research Council.

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