

Titanium oxide (TiO₂) catalysed one-Step Beckmann rearrangement of aldehydes and ketones in solvent free conditions[†]

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In the presence of titanium oxide (TiO₂) and without any additional organic solvents, Beckmann rearrangement of several ketones and aldehydes was performed in good yield.

Keywords: titanium oxide, Beckmann rearrangement, aldehydes, ketones

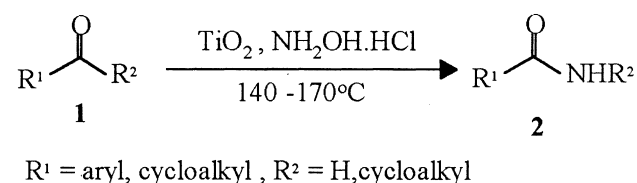
Since the original observation by Beckmann¹ that benzophenone oxime is converted into benzanilide in the presence of acidic dehydrating agents, extensive investigations of this rearrangement have been carried out. Applications of the rearrangement have been important in both theoretical and preparative chemistry, and a variety of conditions have been developed for effecting the reaction.

The conventional Beckmann rearrangement usually requires the use of strong Brønsted or Lewis acids, e.g. concentrated sulfuric acid, phosphorus pentachloride in ether, hydrogen chloride in a mixture of acetic anhydride, causing large amounts of by-products and serious corrosion problems.²

Although, a large number of vapour-phase Beckmann rearrangement processes have been reported, low selectivity (e.g. for ϵ -caprolactam) and rapid decay of activity generally resulted because of high reaction temperatures.²⁻⁵ Liquid-phase catalytic rearrangement under milder conditions, can afford high selectivity, in which the solvent plays an important role.⁶ A relatively large amount of an organic solvent such as DMF,^{7,8} however, was needed, which would cause environmental problems due to volatility and toxicity. Relatively few solid-phase methods have been developed⁹ and very few methods are available for one-step Beckmann rearrangement of aldehydes and ketones.¹⁰

In connection with our interest in solid-state reactions, the use of TiO₂ for this rearrangement was examined and it was found that NH₂OH.HCl reacts with various types of aldehydes and ketones using TiO₂ as a catalyst to give the corresponding amides in one step and quantitative yields without the previous preparation of the corresponding oximes.

For each Beckmann rearrangement reaction, the ketone or aldehyde, hydroxylamine hydrochloride and TiO₂ were mixed thoroughly. The reaction mixture was charged into a 10 ml round-bottomed flask equipped with a magnetic stirrer and thermometer and heated in an oil bath at 140–170°C, there was no requirement for any additional solvent (Scheme 1).



Scheme 1

The experimental results are summarised in Table 1. The Beckmann rearrangement of symmetrical ketones proceeds effectively to afford the corresponding amides in good to excellent yields (entries 1,2, Table 1). In the case of unsymmetrical ketones the reaction was selective and one of the two possible amides produced (entries 3,4, Table 1).

As shown in Table 1, aromatic aldehydes with both electron donating and withdrawing substituted were converted into the corresponding amides in good yields. According to Table 1, aldehydes gave only the primary amides. We have also found that in the presence of TiO₂ the corresponding *Z*-isomer of the benzaldoximes (OH *syn* to aryl) were obtained (Table 2). The Beckmann rearrangement is generally suggested to proceed through *anti* migration, wherein the *Z* forms of oximes are expected to give the corresponding amides.

It is interesting to note that the yields were obviously reduced when *meta* substituted aromatic aldehydes were used (entries 13,14 and 15, Table 1). Schofield and his co-workers¹¹ have shown that the rates of rearrangement of *meta* substituted aromatic oximes were lower than the *para* and *ortho* substituted ones in 98.2% sulfuric acid at 80°C.

In conclusion, the present procedure of solvent free Beckmann rearrangement of aldehydes and ketones on TiO₂ catalyst provides a general methodology for the preparation of amides. Solvent free condition, simple work-up, use of commercial, available and inexpensive catalyst and high yields, can make this procedure a useful and attractive alternative to the currently available methods.

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 CDCl₃.



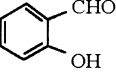
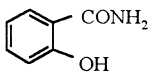
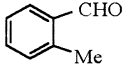
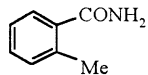
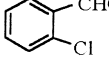
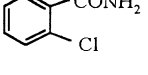
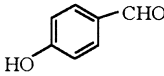
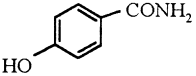
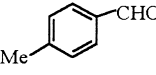
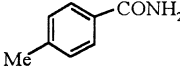
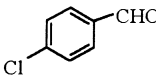
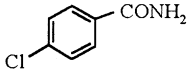

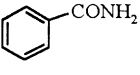
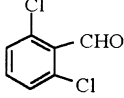
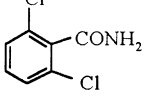
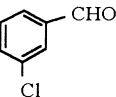
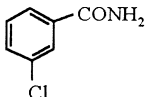
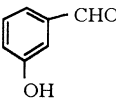
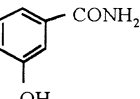
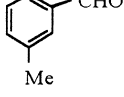
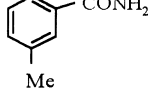
Typical procedure for preparation of amides from carbonyl compounds: Ketone or aldehyde (1 mmol), hydroxylamine hydrochloride (0.3 g, 4.3 mmol) and TiO₂ (2 mmol) were mixed sufficiently. Then the mixture was charged into a 10 ml round-bottomed flask equipped with a magnetic stirrer and heated in an oil bath at 140–170°C, there was no requirement for any additional solvent. At the end of the reaction (see Table 1) the resulting mixture was mixed with ethyl acetate (2×5ml) and filtered to remove TiO₂. The solvent was removed *in vacuo* to give the product which was recrystallized from a suitable solvent or purified by column chromatography (ethyl acetate-hexane). All of the products are known and gave satisfactory physical data compared with those of authentic samples.

Typical procedure for preparation of aldoximes in the presence of TiO₂: Hydroxylamine hydrochloride (0.3 g, 4.3 mmol) was added to a stirred mixture of TiO₂ (0.16 g, 2 mmol) and aldehyde (1 mmol) at 80°C in an oil bath. The progress of reaction was monitored by TLC. After complete disappearance of the starting material (see Table 2), the reaction mixture was washed with CH₂Cl₂ (2 × 10 ml) and water (2 × 50 ml). The organic layer was dried over Na₂SO₄ and evaporated

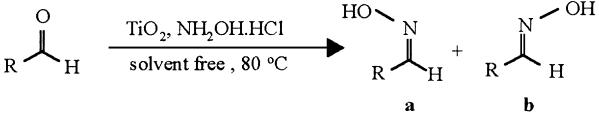
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[†] This is a Short Paper, there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 1 Beckmann rearrangement of ketones and aldehydes into amides by TiO₂

Entry	Substrate	Time/Temp. h/°C	Product	¹ H NMR chemical shift of H amide (lit.)	IR (KBr)/cm ⁻¹ (lit.)	M.P./°C (lit.) ¹⁵ /% ^a	yield (lit.) ¹⁵ /%
1		2.5/150		7.4 (7.4 ¹²)	3212 (NH), 1658 (C=O) (3212, 1658 ¹²)	30 (30)	78
2	Ph - C(=O) - Ph	1/150	Ph - C(=O) - NH - Ph	8.1 (10.3 ¹⁴) ^b	3345 (NH), 1657 (C=O) (3346, 1657 ¹⁴)	156 (163)	90
3	Ph - NH - C(=O) - Me	1.5/150	Ph - NH - C(=O) - Me	7.79 (7.79 ^{12,14})	3297 (NH), 1665 (C=O) (3294, 1665 ¹⁴)	156 (157)	86
4	<i>p</i> MePh - NH - C(=O) - Me	1/150	<i>p</i> MePh - NH - C(=O) - Me	7.0 (7.8 ¹⁴)	3296 (NH), 1662 (C=O) (3298, 1664 ¹⁴)	150 (151)	85
5		3/140		6.02 (7.0 ¹⁵) ^b	3420, 3210 (NH ₂), 1685 (C=O) (3397, 3191, 1653 ¹⁴)	140 (142)	80
6		3/150		7.0 (7.5 ¹⁵) ^b	3420, 3210 (NH ₂), 1685 (C=O) (3443, 3168, 1671 ¹⁵)	142 (147)	60
7		3.5/140		6.45 (6.5 ¹⁴)	3340, 3140 (NH ₂), 1640 (C=O) (3369, 3191, 1638 ¹⁴)	140 (142.4)	58
8		2/140		5.85 (7.12 ¹⁴) ^b	3140, 3210 (NH ₂), 1650 (C=O) (3627, 3417, 1651 ¹⁴)	162 (162)	70
9		2.5/150		6.12 (7.15 ¹⁵) ^b	3343, 3168 (NH ₂), 1671 (C=O) (3343, 3168, 1670 ¹²)	160 (160)	84
10		1/140		5.97 (7.5 ¹⁵) ^b	3333, 3226 (NH ₂), 1650 (C=O) (3333, 3226, 1667 ¹⁵)	178 (179)	85
11		2/140		6.2 (6.26 ¹²)	3385, 3190 (NH ₂), 1665 (C=O) (3385, 3190, 1665 ¹²)	132 (132.5)	86
12		3/150		5.8 (6.1 ¹²)	3350, 3190 (NH ₂), 1650 (C=O) (3432, 3280, 1652 ¹⁴)	146 (146)	80
13		9/170		6.4 (7.6 ¹⁴) ^b	3340, 3180 (NH ₂), 1550 (C=O) (3361, 3182, 1550 ¹⁴)	135 (135.5)	65
14		9.5/170		6.4 (7.6 ¹⁵) ^b	3340, 3180 (NH ₂), 1550 (C=O) (3361, 3182, 1550 ¹⁵)	170 (170)	70
15		9/170		7.22 (6.6 ¹⁴)	3377, 3197 (NH ₂), 1651 (C=O) (3377, 3197, 1651 ¹⁴)	95 (97)	70

^a Isolated yields.^b ¹H NMR was obtained in DMSO-d₆.

Table 2 Conversion of aldehydes into oximes using TiO₂


Entry	R	Time /min	Yields/% ^a		M.p. of a (lit.) /°C
			a	b	
1	<i>p</i> -MeC ₆ H ₄	5	85	15	72 (80 ¹⁵)
2	<i>o</i> -OHC ₆ H ₄	5	>98	Trace	63 (63 ¹⁵)
3	<i>p</i> -ClC ₆ H ₄	15	85	15	146(145 ^{16a})
4	<i>m</i> -ClC ₆ H ₄	15	80	20	100 (100 ¹⁵)
5	<i>o</i> -ClC ₆ H ₄	5	>98	Trace	103 (100 ^{16b})
6	2,6-di-ClC ₆ H ₃	10	>98	Trace	132 (150 ¹⁵)
7	Ph	5	85	15	125 (128 ¹⁵)

^aIsolated yields.

to give the oxime. The products were recrystallised from a suitable solvent and identified by comparison of their physical data with those prepared in accordance with the literature procedures.¹⁶

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

Received 25 May 2002; accepted 17 October 2002
Paper 02/1411

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