



A Novel Method for Beckmann Rearrangement Catalyzed by Potassium Dihydrogen Phosphate Under Microwave-Irradiation

KEYWORDS

Beckmann rearrangement, oximes, Microwave Irradiation, Potassium dihydrogen phosphate.

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ABSTRACT Potassium dihydrogen phosphate (KH_2PO_4) is found to be a new efficient medium for the Beckmann rearrangement in solvent-free conditions under microwave irradiation. The present method is simple, efficient, cost-effective and the yields are good to excellent.

Introduction:-

The rearrangement of ketoximes to the amides, known as the Beckmann reaction, is a common method in organic chemistry, and is a topic of current interest[1,2]. The classical Beckmann rearrangement[3] requires excess or stoichiometric amounts of strong protic acids such as concentrated sulfuric acid or phosphoric acid which cause a large amount of byproducts and serious corrosion problems[1]. The reaction generally requires relatively high reaction temperature for long reaction times. On these bases, milder conditions were tried and investigations on clean, simple, environmentally benign, and highly efficient processes became the chemists interesting undertaking[4,5]. Several improved procedures have been reported using modified reagents[6] and solid acids like clay[7] and zeolites[8]. However, most of these procedures involve vapor phase reactions[9]. Low selectivity of the migrating group and rapid decay of catalyst activity, generally resulted because of high reaction temperature[3,9]. Furthermore, the reactions are sluggish when they are performed in the liquid phase[5a,10]. Relatively few solid phase methods have been developed[11] and fewer methods are available for one-pot Beckmann rearrangement of ketones[12-15].

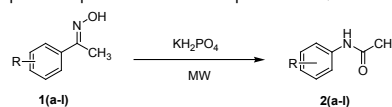
The coupling of microwave irradiation with the use of catalysts on mineral supported reagents, under solvent-free conditions, provide unique chemical processes with special attributes such as enhanced reaction rates, higher yields, greater selectivity, and ease of manipulation. Various improvements for this reaction were also developed using K-10[16] or alumina[17] in dry media under microwave irradiation.

Now a day, it is shown that the use of solid acidic catalysts has gained importance in organic synthesis due to several advantages such as, operational simplicity, no toxicity and ease of isolation after completion of the reaction. In the current study, the commercially available catalyst potassium dihydrogen phosphate having pH 4.2–4.7 is used as a catalyst but its scope has not been fully explored. Potassium dihydrogen phosphate can be used as buffer, neutralizing agent, sequester, yeast food and also as an efficient heterogeneous acid catalyst[18]. Recently, Gill & his co-workers have reported the synthesis of α -hydroxyphosphonates using potassium dihydrogen phosphate[19] under solvent-free condition. Owing to the numerous advantages associated with this cheap and non hazardous catalyst, we have considered Potassium dihydrogen phosphate to be an ideal heterogeneous acid catalyst for Beckmann rearrangement. Herein, we would like to report the facile and eco-friendly methodology for the synthesis of amides under solvent-free condition and microwave-irradiation.

Results and discussion:-

In continuation of our research work on the development of novel synthetic methodologies, using solid acid cata-

lyst[20-25] and microwave irradiation techniques[26-28] herein, we have developed methodology for the synthesis of amides using Potassium dihydrogen phosphate which makes use of mild catalyst under solvent-free condition over the reported procedure as depicted in (Scheme 1).



Initially, the acetophenone oxime has been used as a substrate for the model reaction using Potassium dihydrogen phosphate as a catalyst for the Beckmann rearrangement under solvent-free conditions and microwave-irradiation.

In the next examination, we have performed the same reaction with various powers of microwave and we found that 400W is good enough to carry out reaction over other powers. The optimization of reaction results with various power of microwave irradiation summarized in Table 1. We have found that, if reaction was carried out without microwave irradiation it takes more reaction time (2h) with negligible yield (40%). As increase in the power of microwave, there is increase in yield with decrease in reaction time still at 400 W, but future that there is no significant change observed at 600 W. Hence, we satisfied over 400W and done all derivatization at 400 W.

After optimizing the conditions, the generality of this method was examined by the reaction of several substituted ketoximes with Potassium dihydrogen phosphate under microwave-irradiation, the results are shown in Table 2. Here, we found that electron-donating substituents (-OH, -OMe) on the aromatic ring were found to reduce the reaction time (Table 2, entries 7) in comparison with the unsubstituted oxime (Table 2, entry 1). In contrast, the rearrangement reaction was slower with the electron-withdrawing groups (-NO₂ and -Cl) (Table 2, entries 6 and 8). All the synthesized compounds were characterised by spectral data and compared (MS, NMR, and IR) with authentic sample. This comparison revealed that the compounds synthesized by this newly developed method were exactly similar in all aspects to the reference compounds.

Table1: Screening of various powers of MW for synthesis of compound (2a)

Entry	MW (Watts)	Time(min.)	Yield(%) ^a
1	-	120	40
2	100	80	50
3	200	65	75
4	300	50	80
5	400	25	93
6	600	25	93

^aIsolated yields.

Table 2: Synthesis of anilides by Beckmann rearrangement^a

Entry	Compounds	R	Time (min.)	Yield ^a (%)	M.P. (°C)
1	2a	H	7	93	114-115
2	2b	4-CH ₃	7	87	150-152
3	2c	3-CH ₃	6	88	65-66
4	2d	2-CH ₃	5	86	110-112
5	2e	4-Cl	10	80	173-175
6	2f	4-NO ₂	8	80	218-219
7	2g	4-OCH ₃	5	85	130-131
8	2h	2-Cl	8	81	85-87
9	2i	4-F	9	80	140-142
10	2j	4-OC ₂ H ₅	5	87	135-136
11	2k	2-Br	8	83	165-166
12	2l	2-OH,5-Cl	9	84	160-162

^aReaction conditions: KH₂PO₄ (2 mmol), Ketoxime 1(a-l) (1.0 mmol). ^bIsolated yield. All the compounds were characterised by ¹H NMR, MS spectral data and were compared with the reference compounds

Experimental:- All melting points were recorded in open capillary and are uncorrected. Microwave oven (LG Smart Chef MS-255R operating at 2450 MHz having maximum out put power of 960 W) was used for microwave irradiation. ¹H NMR spectra were recorded on Mercury plus Varian at 400 MHz in CDCl₃ as a solvent and TMS as an internal standard. IR spectra were recorded on a Perkin Elmer FTIR using KBr discs.

General procedure for synthesis of compounds (2a-l):

A mixture of ketoxime (1 mmol), Potassium dihydrogen phosphate (2 mmol) was irradiated in a domestic Microwave oven (2450 MHz, 400 W) for the time indicated in Table 1.

The progress of the reaction was monitored by TLC (ethyl acetate: hexane, 7:3). After completion of reaction, dichloromethane (15 cm³) was added and washed with water (10 cm³) and dried over anhydrous CaCl₂. The solvent was removed under vacuum and the crude product was obtained. The purification of products was achieved by crystallization from EtOH. The products are known and are characterized by comparison of their spectral data (IR, ¹H-NMR) and physical properties with those reported in the literature.

Spectral data of principal compounds

Compound (2j): IR (KBr, cm⁻¹): 3300, 1670, ¹H NMR (CDCl₃, 400 MHz, δ ppm): 2.0 (s, 3H), 4.0 (q, 2H), 1.3 (t, 3H), 6.8 (d, J = 9Hz, 2H), 7.8 (d, J = 9Hz, 2H), 9.8 (s, 1H, -NH); MS m/z 180 (M+1).

Compound (2k): IR (KBr, cm⁻¹): 3250, 1665, ¹H NMR (CDCl₃, 400 MHz, δ ppm): 2.0 (s, 3H), 7.0-7.6 (m, 4H), 9.4 (s, 1H, -NH); MS m/z 215 (M+1).

Compound (2l) : IR (KBr, cm⁻¹) 3387, 3081, 1664, ¹H NMR (CDCl₃, 400 MHz, δ ppm.): 2.25 (s, 3H), 6.88 (d, J = 8Hz, 1H), 7.08 (d, J = 8Hz, 2H), 7.44 (bs, 1H, -OH), 8.42 (s, 1H, -NH) ; MS m/z 186 (M+1).

Conclusion:-

In conclusion this method presents a mild and 'green' protocol for obtaining amides from the corresponding ketoximes under microwave-irradiation. The Potassium dihydrogen phosphate revealed a cheap and effective catalyst and no additional cocatalysts were necessary to promote the rearrangement. It is expected that the present methodology will find application in organic synthesis.

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