



Microwave-assisted Beckmann Rearrangement of Ketoximes using Lemon Juice as an efficient catalyst

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Abstract:

Beckmann rearrangement of a variety of ketoximes has been carried out in the presence of catalytic amount of Lemon Juice. This mild and 'green' procedure is highly regioselective affording the corresponding *N*-substituted amides in good to quantitative yields. This method provides several advantages such as environment benign, high yields and simple work-up procedure

Keywords: Beckmann rearrangement, Oximes, Amides, Lemon Juice

Introduction

An extremely significant commercial technique for the creation of raw materials for polyamides like nylon-6 and nylon-12 is the Beckmann rearrangement of oximes to amides/lactams. [1,2]. A stoichiometric amount of very acidic and dehydrating media, such as concentrated sulfuric acid, phosphorous pentachloride in diethyl ether, or hydrogen chloride in a mixture of acetic acid and acetic anhydride, are required for the reaction, which often calls for high temperatures (about 130°C). [3]. As a result, this reaction can produce a lot of byproducts and, more significantly, cannot be used on substrates that are sensitive to acid. Among the myriad ways that these reactions could manifest themselves under softer conditions [4], There have been reports of using ionic liquids (IL) at ambient temperature instead of polar media. [5].

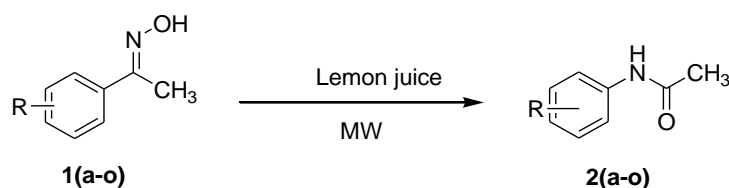
Citrus aurantium, Citrus indica, Citrus limonium are some important species of citrus family commonly known as lemon. The lemon is indigenous to the north-west regions of India. It is now widely grown in all tropical and subtropical countries. In India it is also cultivated in home gardens. The main constituent of lemon juice are moisture (85%), carbohydrates (11.2%), citric acid (5-7%), protein (1%), vitamin-C

(0.5 %), fat (0.9%), minerals (0.3 %), fibers (1.6 %) and some other organic acids. As lemon juice is acidic in nature (pH \approx 2-3) and percentage of citric acid (5-7%) is more than other acids, it worked as acid catalyst for various reactions such as Biginelli reaction[6], synthesis of Schiff Base[7], synthesis of Bis-, Tris-, Tetraindoles[8], synthesis of 3,4-dihydropyrimidine-2(1H)-one[9], Synthesis of Bis(indolyl)methanes[10] etc.

Microwave irradiation is a rapid means of material heating for domestic, industrial and medical purposes. Microwaves offer a number of advantages over conventional heating such as non-contact heating, energy transfer instead of heat transfer, material selective and volumetric heating, fast start-up and stopping. Moreover, the reduced time of processing under microwave conditions found for a great number of chemical reactions was the main reason that microwave techniques became so attractive for chemists, who, in the last two decades, have begun to apply this technique as a routine in their everyday practice. overview of application of microwaves in polymer synthesis can be found in the review articles and in the comprehensive review with over 600 references cited in the recently publish book and chapter. In

continuation of our previous work, we have developed the cheap and eco-friendly materials as catalysts for development of new synthetic methodologies [11]. In this paper, we would like to report a mild and high yielding method for the synthesis of 1,8-dioxo-octahydroxanthenes via cyclo-condensation of various aldehydes and 1,3-cyclohexenedione using Lemon Juice under microwave-irradiation.

The main advantages of MW irradiation usage are: very short reaction time and the solvent less procedures which are eco-friendly [12,13]. To the best of our knowledge MW irradiation has been mostly reported as a heating technique particularly for low molecular weight compounds for chemical modifications.



Scheme-1

Initially, we have carried out the model reaction by taking the ketoxime under Microwave-irradiation using Lemon Juice as a catalyst. We observed that, the model reaction was carried out in presence of 0.5 ml of Lemon Juice catalyst to give the product (2a) in modest 80% yield but when the concentration of catalyst have been increased

Microwave irradiation (MWI) has become an established tool in organic synthesis, because of the rate enhancements, higher yields, and often, improved selectivity, with respect to the conventional reaction conditions [14].

Results and Discussion

In the course of our work on the development of new methodologies, for the eco-friendly synthesis with microwave-irradiation[15,16] Herein, we have developed methodology for the Beckmann rearrangement using highly effective lemon juice as a catalyst under microwave-irradiation over the reported procedure as depicted in (Scheme 1).

to 1ml which results in accelerating the reaction yields to 92%. Use of 2 ml of catalyst is sufficient to push the reaction forward. Higher amount of the catalyst did not improve catalyst for this reaction, as shown in (Table 1).

Table 1: Optimization of catalyst(ml) for model reaction (2a).

Entry	Catalyst (ml)	Yield (%) ^a
1	0.5	80
2	1	92
3	2	92

^a Isolated yields.

In the next examination, We conducted the same reaction using other microwave powers and discovered that 400W is sufficient to carry out the reaction over other powers. Table 2 summarizes the optimization of reaction outcomes with various microwave irradiation powers. We discovered that the

reaction would take longer to complete (2 hours) with a significantly lower yield (only 50%). At 400 W, there is a gain in yield and a decrease in reaction time as microwave power increases, but at 600 W, no appreciable change is seen. We achieved above 400W as a result, and all derivatization was completed at 400 W.

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

Entry	MW (Watts)	Time(min.)	Yield(%) ^a
1	-	120	50
2	100	80	60
3	200	65	75
4	300	50	80
5	400	10	92
6	600	10	92

^aIsolated yields.

The findings of a reaction between different substituted ketoximes and lemon juice when exposed to microwave radiation after the circumstances had been optimized are displayed in Table 3. Here, we discovered that, when compared to the unsubstituted oxime (Table 3, entry 1), electron-donating substituents (-OH, -OMe) on the aromatic ring sped up the reaction time (Table 3, entries 7 and 15). In contrast, the electron-

withdrawing groups (-NO₂ and -Cl) slowed down the rearrangement reaction (Table 3, entries 6, 8 and 13). The spectral characteristics of every compounds were assessed and compared (MS, NMR, and IR) with authentic samples. This comparison showed that the compounds created using this novel technique were identical to the reference compounds in every way.

Table 3: Synthesis of anilides by Beckmann rearrangement^a

Entry	Compounds	R	Time (min.)	Yield ^a (%)	M.P. (°C)
1	2a	H	10	92	114-115
2	2b	4-CH ₃	10	88	150-152
3	2c	3-CH ₃	10	87	65-66
4	2d	2-CH ₃	8	85	110-112
5	2e	4-Cl	10	82	173-175
6	2f	4-NO ₂	8	80	218-219
7	2g	4-OCH ₃	8	84	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	8	87	135-136
11	2k	2-Br	8	83	165-166
12	2l	2-OH,5-Cl	9	84	160-162
13	2m	3,5-di Cl,2-OH	12	82	95-97
14	2n	3-Cl,4-F	9	76	81-82
15	2o	2-OH,4-CH ₃	10	87	118-120

^aReaction conditions: Lemon juice (1 ml), Ketoxime **1(a-o)** (1.0 mmol). ^bIsolated yield. All the compounds were characterised by ¹H NMR, MS spectral data and were compared with the reference compounds

Conclusion:-

In conclusion this method presents a mild and 'green' protocol for obtaining amides from the corresponding ketoximes in presence of lemon juice as a catalyst under microwave-irradiation. Lemon juice 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.

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-o):

A mixture of ketoxime (1 mmol), lemon juice (1 ml) was grounded thoroughly in a beaker. It was then irradiated in a domestic Microwave oven (2450 MHz, 400 W) for the time indicated in Table 2. The completion of reaction was monitored by TLC (Hexane: EtOAc 8:2). The reaction mixture was cooled at room temperature and the solid product was extracted with dichloromethane. The organic layer was evaporated under reduced pressure and the crude product was obtained. The crude products were purified by recrystallization from ethanol. 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).

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