International Journal of Sustainable Progress
Volume 3, Issue 1, June 2024
https://ijsp.globalpublisher.org/

Introducing a novel, interesting, attractiveness, profitable and environmental friendly method in accordance with microwave-assisted, one-pot three component conditions

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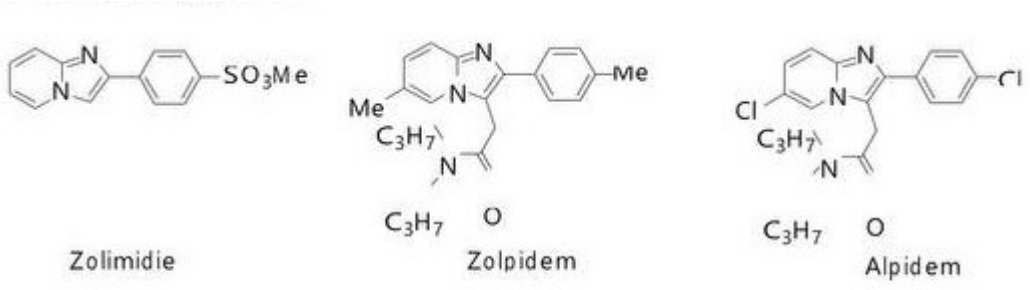
ABSTRACT
In this study, a new synthesis style of 2-phenylH-imidazo[1,2-a] pyridine is, acquired from a one-pot, three-component reaction between pyridine, urea (or guanidine) and a-iodoketone under microwave irradiation circumstances by watching the fulfilled principles of fluid mechanics and without solvent situation in excellent yields. Also, in this work, one-pot multicomponent reactions have been indicated as an effective facility for fluid mechanics accomplished synthesis principles with regards to their convergence, productivity, and generation of highly diverse and complex products from simple accessible beginner reagents.
The green chemistry in relationship with fluid mechanics possible principles outlines the necessity for environmentally clean and safe synthesis, that comprises high atom effectiveness, going out of dangerous reagents, and simple separation with recovery and reapply of reagents. In this manner, the utility of microwave energy in synthetic organic chemistry has been increasingly recognized as compared with conventional heating. Reactions evolved by the microwave irradiation (MWI) have indicated an environmentally friendly nature, larger selectivity, and improved reaction rate. In other words, the MWI-mediated multicomponent reaction has made a particular effective synthetic pattern for the fast and effective library manufacturing.

Keywords: synthetic method, Pyridine, Microwave-assisted reaction , fluid, manufacturing, environment

1. INTRODUCTION

In recent years, Imidazo [1,2-α] pyridines have got noticeable attention from the drug industry because of their interesting therapeutic properties (1-3), including antibacterial (5) antifungal (6) , antiviral (7), antiulcer (8) and anti-inflammatory behaviour (9) . The recent drug chemists have also been characterized as selective cyclin-dependent kinase inhibitors (10) , calcium channel blockers (11), β -amyloid formation inhibitors (12) and benzodiazepine receptor agonists (13). Drug formulations comprising imidazo [1,2-α] pyridines such as alpidem (anxiolytic), zolpidem (hypnotic), and zolimidine (antiulcer) are currently available (Scheme 1). various synthetic styles have been performed to synthesize substituted imidazo [1,2-α] pyridines, either from the imidazole or from the pyridine nucleus (14). any progressing in selectivity, high atom effectiveness, being evolved and exited and then elimination of dangerous reagents, and simple separation with recovery and reperform of reagents (2). In this way, the utility of microwave energy in synthetic organic chemistry has been increasingly known as compared with conventional heating (4). Reactions promoted by microwave irradiation (MWI) have indicated an environmentally friendly nature, greater selectivity, and advanced reaction rate (11,12). Thus, the MWI-mediated multicomponent reaction has made a specific attractive synthetic drawing style for the fast and efficient library generation (3).

Imidazo[1,2-α] pyridine has acquired noticeable interest from the drug industry because of their interesting therapeutic properties (4), including antibacterial (5), antifungal (6), antiviral (7) antiulcer (8), and anti-inflammatory behavior (9). They have also been characterized as selective cyclin-dependent kinase inhibitors (10), calcium route blockers (11), β-amyloid formation inhibitors,(12) and benzodiazepine receptor agonists (13). Drug formulations containing imidazo [1,2-α] pyridines such as alpidem (anxiolytic), zolpidem (hypnotic), and zolimidine (antiulcer) are currently available (Scheme 1). various synthetic sideways have been performed to synthesize displaced imidazo [1,2-α] pyridines, either from the imidazole or from the pyridine nucleus (14). Moreover, they have been acquired by cyclocondensation of 2-minopyridines with displaced phenacylbromides of α-bromoacetophenones in weak yields (15). 2-substituted-imidazo[1,2-α] pyridines have been prepared by cyclocondensation of alkynyl(phenyl)iodonium salts with 2-aminopyridine simply in CHCl3 under reflux current in the presence of K2CO3 (16). Other techniques concluded reacting 2-aminopyridines with α-tosyloxy ketones (17) a polymer shielded [hydroxy (sulfonyloxy)iodo] benzene with ketones or alcohols (18) α-diazoketones (19) and propargyl iodide (20). Although, these methods are suitable for obvious synthetic conditions. Sometimes, however, some of these procedures are associated with one or more disadvantages such as high cost, performance stoichiometric and even excess amounts of chemicals or catalysts, long reaction time, dangerous organic solvents, weak yield, which leaves scope for further advancement of new environmentally clean syntheses (22). Thus, there is an increasingly essential for progressed and newer pathways of synthesis of imidazo[1,2-α] pyridines (21).



Scheme 1. Biologically related formulas imidazo[1,2-a]pyridines

Figure 1. Talks about the reagent formulas imidazo [1,2-a]pyridine based upon biological scenes.

In this article, we are decided to introduce a novel and effective pathway for the synthesis of 2-phenylH- imidazo [1,2-α] pyridine 4 via the pairing of pyridine 1, phenacyl iodide 2 and guanidine (urea or thiourea) 3 under microwave irradiation based upon the fundamentals of fluid mechanics (21). (Scheme 2).

2. EXPERIMENTAL

Reagents and solvents were acquired from Merck (Germany) and Fluka (Switzerland) and were used without further purification. Microwave assisted reactions were performed in microwave oven (ETHOS 1600, Milestone) with a power of 600 W particularly designed for organic synthesis. Column chromatography were established upon silica Gel (0.019-0.06 mm, mesh-size 67) and TLC upon precoated plastic sheets (25 DCUV-254), respectively. Melting points were measured on Barnstead Electrothermal melting point apparatus and were not corrected. IR spectra were done on Shimadzu FT-IR-4300 spectrophotometer as KBr discs. 1H NMR and 13C NMR spectra were determined in CDCl3 upon a Brucker 500 spectrophotometer and chemical shifts were expressed in ppm downfield from tetramethyl lsilane.

GENERAL PROCEDURE

A mixture of pyridine (1, 0.24 g, 3 mmole) and phenacyl iodide (2, 0.738 g, 3 mmole) was irradiated with microwaves at 160 °C for 2 minutes. After nearly complete conversion to N-Phenacyl pyridinium iodides, as was shown by TLC, urea hydrochloride (3, 0.34 g, 3 mmole) was added to reaction mixture and it was irradiated at 158 °C for a further 6-8 minutes with a power of 600 W (ETHOS 1600, Milestone). Then, the reaction mixture was cooled to room temperature and the residue was purified by column chromatography (1:2 n- hexane–EtOAc as eluent, Merck silica gel 70 mesh).

2-Phenylimidazo[1,2-a]pyridine (4a)
White powder; mp 135-137 °C (lit. 131-133)19; νmax (KBr): 2928, 2856, 1743, 1627, 1515,

1467, 1372, 1269, 1205, 1145, 1082, 1034, 692 cm-1; δH (500 MHz, CDCl3): 8.11 (d, J = 6.78 Hz, 1H), 7.96 (d, J = 7.80 Hz, 2H), 7.86 (s, 1H), 7.65 (d, J = 9.18 Hz, 1H), 7.43 (t, J = 7.36 Hz, 2H), 7.33 (d, J = 7.6 Hz, 1H), 7.20 (t, J = 7.21 Hz, 1H), 6.78 (t, J = 6.77 Hz, 1H); δc (125 MHz, CDCl3): 146.0, 145.9, 134.0, 129.8, 129, 126.3, 125.8, 124.8, 117.8, 114.5, 108.4.

2-(4-Chlorophenyl)imidazo[1,2-a]pyridine (4d)
White powder; mp 209-210 (lit. 208) [18]; νmax (KBr): 2923, 1652, 1472, 1373, 1262, 1202, 1085, 1015, 952, 842, 742, 602, 516; cm-1; δH (500 MHz, CDCl3): 8.11 (d, J = 6.78 Hz, 1H), 7.91 (d, J = 8.19 Hz, 2H), 7.85 (s, 1H), 7.61 (d, J = 9.13 Hz, 1H), 7.41 (d, J = 8.19 Hz, 2H), 7.21 (t, J = 7.16 Hz, 1H), 6.79 (t, J = 6.71 Hz, 1H); δc (125 MHz, CDCl3): 145.8, 144.7, 133.9, 132, 129, 127, 125.2, 127, 120, 112.8, 108.4.

3. RESULTS AND DISCUSSION

The used solvent free reaction progressed in 9-11 minutes to provide products with excellent yields. The scope and generality of this reaction is explained with respect to different phenacyl iodides and pyridines. The results are brought in Table 1. The structures of the products were drawn by 1H NMR, 13C NMR spectroscopy technique and by comparison of their spectral data and melting point data with those of the genuine samples mentioned in the literature.

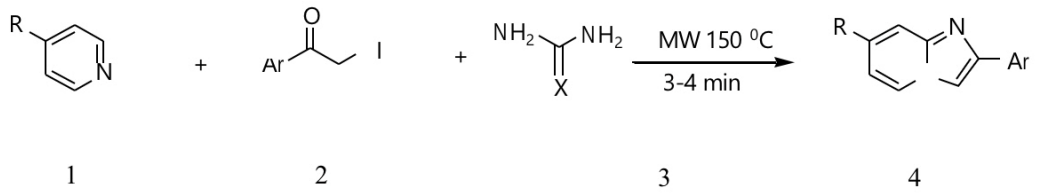


Figure 2. A chemical reaction under microwave irradiation based upon the fundamentals of fluid mechanics

The proposed mechanism of the cyclization step has been inserted in Scheme 3. In accordance with that, nucleophilic attack of pyridine 1 to phenacyl iodide 2 products charged species of that subsequently reacts with urea 3 to produce adduct 4 that undergoes cyclization by elimination of HI to product 5. Finally, product 6 is acquired by omitting of formamide.

Table 1. Synthesis of product 4 under microwave irradiation.

4	Ar	R	X	Time (min)	Yield (%)	M.P (°C)	Lit mp(°C)
a	C_6H_5	H	O	7	79	133-134	131-133[19]
b	C_6H_5	H	S	9	75		
c	4-$MeOC_6H_4$	H	O	5	80	134-135	133-134[17]
d	4-ClC_6H_4	H	O	6	82	208-209	208[18]
e	2,4-$Cl_2C_6H_3$	H	S	7	85	182-184	181-182[22]
f	4-FC_6H_4	H	O	7	80	170-172	169[24]
g	4-$NO_2C_6H_4$	H	O	6	82	267-269	269[24]
h	4-MeC_6H_4	H	S	8	85	137-138	137[23]
i	C_6H_5	CH_3	O	5	85	169-171	172-173[25], 163[24]
j	4-ClC_6H_4	CH_3	S	5	78	242-244	240-242[23]
k	4-ClC_6H_4	CH_3	O	8	85		
l	4-BrC_6H_4	CH_3	S	8	80	215-217	216-217[25]

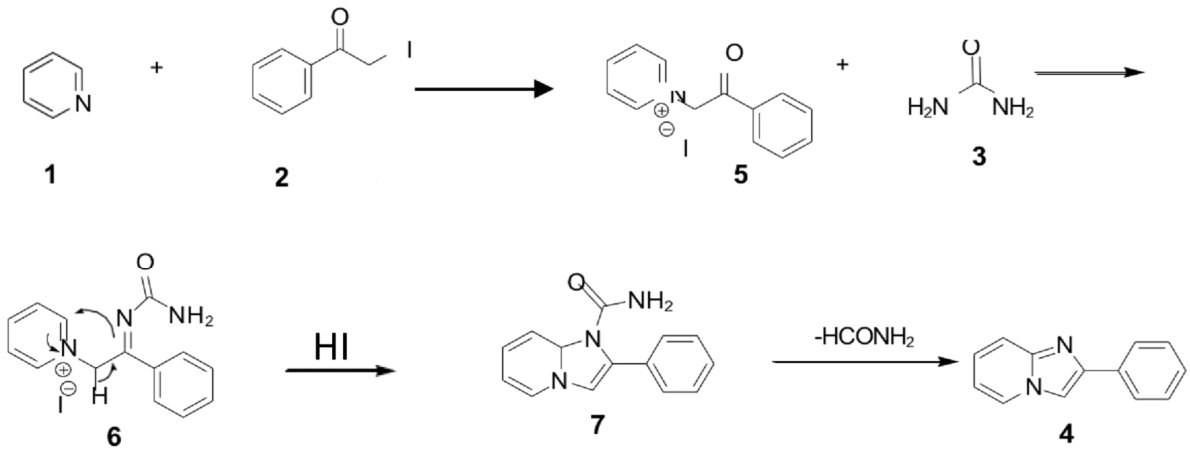


Figure 3. The proposed mechanism of the cyclization step

4. CONCLUSION

In conclusion, we have yielded a novel and effiective and suitable one-pot synthesis method of the 2-phenyl H- imidazo[1,2-α] pyridine ring systems in acceptable yields. In addition to its simplicity and solvent free conditions, this pathway makes high yields of products changing the circumstances as a helpful and interesting strategy for the synthesis of biologically relating to imidazo [1,2-α]pyridines in a single step method.

ACKNOWLEDGMENTS

Acurate support of this work by the Islamic Azad University Tehran south branch through grant is thankfully acknowledged.

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