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Microwave Irradiation Versus Conventional Method: Synthesis of Benzimidazolyl Chalcone Derivatives

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Abstract: Benzimidazole is synthesized by reaction between anthranillic acid and orthophenylene diamine. Further the acetylated product of benzimidazole undergoes Claisen-Schimdt condensation with aryl aldehyde to produce corresponding chalcones. Both conventional and microwave irradiated synthesis of chalcone has been carried out to compare their yield and reaction time.
Keywords: Benzimidazole, aryl aldehyde, chalcones, microwave, synthesis.

Introduction

Recent advances in technology have now made microwave energy a more efficient means of heating reactions. Chemical transformations that took hours, or even days, to complete their organic reaction, can now be accomplished in minutes. Microwave assisted organic synthesis [1] (MAOS) has emerged as frontier in pharmaceutical research for synthesis of newer drugs. MAOS not only help in implementing GREEN chemistry but also led to the revolution in organic synthesis. Microwave irradiation is well known to promote the synthesis of a variety of organic compounds, where chemical reactions are accelerated because of selective absorption of microwave by polar molecules. Attempt was made to synthesize Benzimidazole [2] and their chalcone derivatives [3]. They play a vital role in pharmaceutical research and exhibit various pharmacological activities like antimicrobial, analgesic, anti-inflammatory, anticancer activity. The presence of reactiveα,β-unsaturated keto group in chalcone is found to be responsible for their biological activity. From the various observations, it has been decided to synthesize benzimidazole [4] by reaction between anthranillic acid and orthophenylene diamine. Further the acetylated product of benzimidazole undergoes Claisen-Schimdt condensation with aryl aldehyde to produce corresponding chalcones [5]. Both conventional and microwave irradiated synthesis of chalcone [6] has been carried out to compare their yield and reaction time. Completion of reaction was monitored by performing TLC and melting point. The structures of the synthesized compounds were confirmed by IR and NMR spectroscopy.

Experimental

Melting points were determined in open capillary tubes, expressed in ^{0}C and are uncorrected. The time required for completion of the reaction was monitored by TLC using precoated Silica gel-G plates and spots were exposed in iodine chamber. The IR spectra of the compounds were recorded on SHIMADZU IR AFFINITY FTIR using KBr discs and the values are expressed in cm^{-1}. The ^{1}H NMR spectra of the selected compounds were recorded on BRUKER AVANCE II 400 NMR Spectrometer using DMSO-d_6 as solvent, TMS as an internal standard and chemical shift values are expressed in δ ppm.

Synthesis of 2-(1H-benzo[d]imidazol-2-yl)benzenamine (1)

Conventional Method

o-Phenylenediamine (1.08g, 0.01mole) was dissolved in ethanol (15 ml) and anthranillic acid (1.37g, 0.01mole) was added to it. The reaction mixture was refluxed for 5 hr. In between the completion of the

reaction was monitored by TLC. After completion of the reaction, ethanol was removed by distillation and the residue was poured into crushed ice. Then it was made alkaline by using 10% NaOH to get the solid product. The product was filtered, dried and recrystallised from ethanol.

Microwave Irradiation Method

o-Phenylenediamine (1.08g, 0.01mole) and anthranillic acid (1.37g, 0.01mole) were dissolved in ethanol (15 ml).To this K_2CO_3 was added and the reaction mixture was placed in microwave oven and refluxed at power level-1(140watt) for 10 min. In between the completion of the reaction was monitored by TLC. After completion of the reaction, ethanol was removed by ditillation and the residue was poured into crushed ice. Then it was made alkaline by using 10% NaOH to get the solid product. The product was filtered, dried and recrystallised from ethanol.

Synthesis of N-(2-(1H-benzo[d]imidazol-2-yl)phenyl)acetamide (2)

Dissolve 2-(1H-benzo[d]imidazol-2-yl)benzenamine **(1)** (2.09 g, 0.01 mole) in chloroform (50 mL) and acetic anhydride (1.02 g, 0.01 mole) was added drop wise with constant stirring at 5-10^{0}C. The reaction mixture was stirred for 4 hr. The excess solvent was distilled off and the solid product was filtered, dried and recrystallised from ethanol to give compound (**2**).

Synthesis of Benzimidazolyl Chalcone derivative (3)

Conventional Method

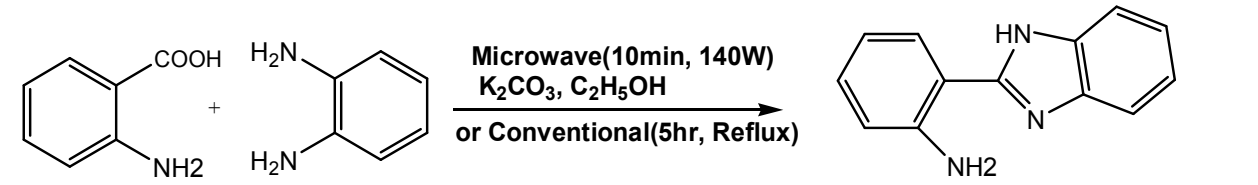
Dissolve N-(2-(1H-benzo[d]imidazol-2-yl)phenyl) acetamide **(2)** (2.51 g, 0.01 mole) in ethanol (30 mL) and various aromatic aldehydes (0.01 mole) were taken and then an aqueous solution of KOH (2%, 5 ml) added to it. The reaction mixture refluxed for 5 hr and then the excess solvent was removed by vacuum distillation and then it was poured into crushed ice and acidified with dil. HCl. The solid separated was filtered and recrystallised from ethanol.

Microwave Irradiation Method

Dissolve N-(2-(1H-benzo[d]imidazol-2-yl)phenyl) acetamide **(2)** (2.51 g, 0.01 mole) in ethanol (30 ml) and various aromatic aldehydes (0.01 mole) were taken and then an aqueous solution of KOH (2%, 5 ml) added to it. The reaction was placed in microwave oven and refluxed at power level-2 (210watt) for 10-20 min. and then the excess solvent was removed by vacuum distillation and then it was poured into crushed ice and acidified with dilute HCl. The solid separated was filtered and recrystallised from ethanol.

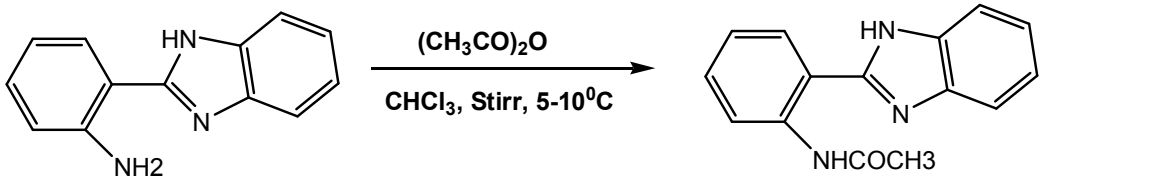
Synthetic Schemes

STEP-I : Synthesis of 2-(1H-benzo[d]imidazol-2-yl)benzenamine (1)



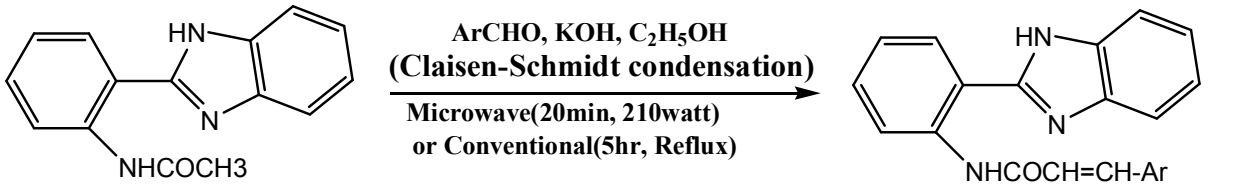
Anthranillic acid **o-Phenylenediamine** **2-(1*H*-benzo[*d*]imidazol-2-yl)benzenamine**

STEP-II: Synthesis of N-(2-(1H-benzo[d]imidazol-2 yl)phenyl)acetamide (2)



2-(1*H*-benzo[*d*]imidazol-2-yl)benzenamine ***N*-(2-(1*H*-benzo[*d*]imidazol-2-yl)phenyl)acetamide**

STEP-III: Synthesis of Benzimidazolyl Chalcone derivative (3)



***N*-(2-(1*H*-benzo[*d*]imidazol-2-yl)phenyl)acetamide** **Benzimidazolyl Chalcone**

Results and Discussion

All the synthesized compounds were characterized by their physical, chemical and spectral data (Tables:- 1–2). IR spectra of synthesized compounds showed the presence of characteristic absorption peaks around 1650 cm^{-1}, 1620 cm^{-1}, 1695cm^{-1}, 3100 cm^{-1}, 3265cm^{-1}. The PMR Spectra of these compound gave signal at δ 5.24(1H, s,-NH-C=O), 6.57(1H, s, -CO-CH), 7.05-7.33 (m, Aromatic-CH), 7.65 (1H, d, =CH-Ar), 12.6(1H, s, -NH hetero aromatic).

Conclusion

Microwave assisted organic synthesis has attracted attention in recent years due to enhanced reaction rates, higher yields, improved purity, ease of work up after the reaction and eco-friendly reaction conditions compared to the conventional methods. Microwave irradiated synthesis of chalcone was carried out to get higher yield with less reaction time period as compared to conventional method. The synthesized benzimidazolyl chalcone produces yield around 60% (conventional) and 80% (microwave).

Tables:-1. Comparisation of conventional and microwave assisted synthesis

COMP.	YIELD (%)		REACTION TIME		ENERGY	
	Conventional	Microwave	Conventional (hr)	Microwave (min)	Conventional (Temp. ^{o}C)	Microwave (Power. Watt)
1	72	86	5	10	120-130	140
2	68	-	4	-	5-10	-
3a	56	71	5	20	120-130	210
3b	62	88	5	20	120-130	210
3c	64	82	5	15	120-130	210
3d	66	80	5	10	120-130	210
3e	58	84	5	10	120-130	210

Tables:-2. Characterisation data of Benzimidazolyl chalcone

COMP.	Ar	M.P. (^{O}C)	R_f value	IR (cm^{-1}) (KBr)
3a	3,4-Cl_2-C_6H_3	145-147	0.62	3265cm^{-1}(-NH), 1620 cm^{-1}(C=N), 1650 cm^{-1}(CH=CH), 1695cm^{-1} (C=O), 3100 cm^{-1}(C-H aromatic), 644cm^{-1}(C-Cl)
3b	4-Cl-C_6H_4	143-145	0.68	3329cm^{-1}(-NH), 1595 cm^{-1}(C=N),1650 cm^{-1}(CH=CH), 1695cm^{-1} (C=O), 3095 cm^{-1} (C-H aromatic), 663 cm^{-1}(C-Cl)
3c	4-Br-C_6H_4	148-150	0.71	3257cm^{-1}(-NH), 1589 cm^{-1}(C=N),1650 cm^{-1} (CH=CH), 1681cm^{-1} (C=O), 3088 cm^{-1}(C-H aromatic), 605 (C-Br)
3d	4-F-C_6H_4	140-142	0.77	3269cm^{-1}(-NH), 1629 cm^{-1}(C=N),1650 cm^{-1}(CH=CH), 1648cm^{-1} (C=O), 3088 cm^{-1} (C-H aromatic), 1134 cm^{-1} (C-F)
3e	3-Cl-C_6H_4	139-143	0.65	3327cm^{-1}(-NH), 1636 cm^{-1}(C=N), 1654cm^{-1}(CH=CH). 1651cm^{-1} (C=O), 3088 cm^{-1} (C-H aromatic), 682 cm^{-1} (C-Cl)

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