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Research Article

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On water: Alum catalyzed synthesis of 3-(1*H*-indol-3-yl)-1,3-diphenylpropan-1-ones under microwave irradiation method

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ABSTRACT

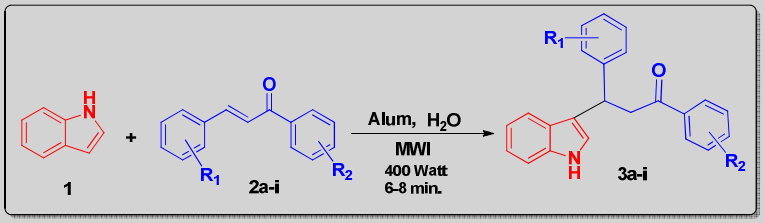
*The nucleophilic addition of Indole**1** withα, βcarbonyl compound (Chalcone)**2**'Michael addition' in presence of catalytic amount of Alum (KAl $(SO_4)_2.12H_2O$) in presence of water as solvent. Various 3-substituted indoles were synthesized in less time of reactions with good to excellent yields under the microwave irradiation method.*

Keywords: Michael addition, 3-substituted indoles, Alum, Water.

INTRODUCTION

Five member fused heterocyclic compound such as Indole and its derivatives are found to possess potential biological activities [1] physiological properties [2]. They are also used in the synthesis of natural products and its important building blocks substructures [3].

Alum $[KAl(SO_4)_2{\cdot}12H_2O]$, which is used in organic transformations, for example the Beginelli, coumarins, benzylpyrazolyl coumarin and quinolinone, trisubstituted dimidazole,1*H*-spiro[isoindoline-1,2'-quinazoline]-3,4'(3*H*)-diones, 1,3,4-oxadiazoles, 1,5-benzodiazepines[4]. Use of water as a reaction medium results in increase the rate and selectivity of many organic reactions [5]. In addition to using of green solvent, microwave irradiation reactions were performed and reduced the time compared to thermal reactions [6-14]. Herein, we report a facile, mild and effective methodology by using environmentally benign catalyst and solvent under microwave irradiation method for the synthesis of 3-(1*H*-indol-3-yl)-1,3-diphenylpropan-1-ones.In continuation of our earlier research work to search an environmentally benign protocol [15-19] Herein, we wish to report a new access for the synthesis of a series 3-(1*H*-indol-3-yl)-1,3-diphenylpropan-1-one**3a-i** by using alum an efficient catalyst on water under microwave irradiation method (Scheme **1**).



Scheme 1. Synthesis of 3-(1H-indol-3-yl)-1,3-diphenylpropan-1-ones

Previously, few methods have been reported for the synthesis of 3-substituted indoles by using different catalysts such as molecular iodine [20], $CuBr_2$[21], $InBr_3$[22], GaI_3 and $GaCl_3$[23], $CeCl_3$•7 H_2O– NaI [24], SmI3 [25], $ZrCl_4$[26], CAN [27], ionic liquids [28], and sodium dodecyl sulphate(SDS) [29], Lanthanide triflates [30]andAmberlite IR 120[31].However, these suffer from disadvantages use of hazardous, toxic, and expensive reagent and catalyst.Aim to carry out the same reaction using alum-water as more environmentally benign catalyst and solvent.

EXPERIMENTAL SECTION

All chemicals were purchased from SD Fine chemicals. All the reported products were characterized and confirmed by comparison with those reported literature. NMR spectra and Mass spectrometer were recorded on a Bruker advance spectrometer 300 MHz, DMSO- d_6 as a solvent. Chemical shifts are reported as δ_{ppm} units. All the compounds were checked by thin layer chromatography.

General procedure for the synthesis of 3-(1H-indol-3-yl)-1,3-diphenylpropan-1-ones:
Indole**1** (1mmol) and chalcone**2** (1mmol) are mixed with Alum (0.15g) in water(8ml) and subjected to microwave irradiation programmed at 400 watt and 90ºC for appropriate time (Table **2**)Progress reaction was monitored by TLC. After completion of the reaction cold water was added, filtered gives crude product which is purified by recrystallization from ethanol. Yield (92-98%).

Spectral data for representative compounds:
3-(1*H*-indol-3-yl)-1,3 -diphenylpropan-1-one (3a):
M.P 129-130^{o}C; ^{1}H NMR (400 MHz,$CDCl_3$): d = 3.71 (dd, J = 7.6, 7.6 Hz,1 H); 3.82 (dd, J = 6.8, 6.8 Hz, 1 H), 5.08 (t, J = 7.2 Hz, 1 H,.97 (s, 1 H), 7.01 (t, J = 7.4 Hz, 1 H), 7.15 (q, J = 7.2, 7.3 Hz,2 H), 7.23–7.31 (m, 3 H), 7.36 (d, J = 7.2 Hz, 2 H), 7.40–7.45 (m, 3 H), 7.54 (t, J = 7.4 Hz, 1 H), 7.94 (d, J = 7.2 Hz, 2H), 7.98 (bs, 1 H);
MS: m/z = 325.12.; M. F.: $C_{23}H_{19}NO$

3-(4-chlorophenyl)-3-(1*H*-indol-3-yl)-1-phenylpropan-1-on (3f);
M.P 115-116^{o}C; ^{1}HNMR (400 MHz, $CDCl_3$) δ 8.03 (br, s, 1H), 7.96 – 7.91 (m, 2H), 7.61 – 7.56 (m, 1H), 7.47– 7.35 (m, 4H), 7.32 – 7.24 (m, 4H), 7.21 – 7.18 (m, 1H), 7.08 – 6.2 (m, 2H), 5.08 (t, J = 7.2 Hz , 1H) 3.85 (dd, J = 16.8, 6.4 Hz, 1H), 3.74 (dd, J = 16.9, 8.2 Hz, 1H);
MS: m/z = 359.1.; M. F.: $C_{23}H_{18}ClNO$

RESULTS AND DISCUSSION

In our literature survey there is no any report synthesis of 3-(1*H*-indol-3-yl)-1,3-diphenylpropan-1-ones using selected alum as catalyst under the microwave irradiation method.

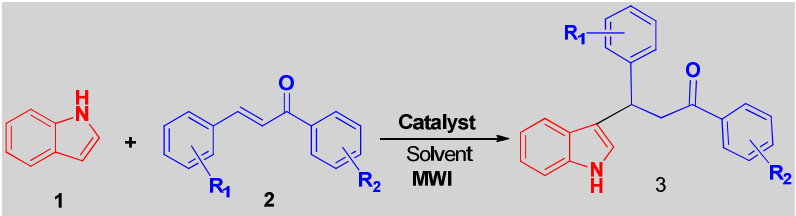
Initially, we screened various solvents for the synthesis of compound **3** with different time interval, series of solvents DCM, DMSO, Toluene, THF, EtOH, MeOH, CH_3CN,and water were screened with selected alum catalyst (catalytic amount) and we found that the used of polar protic solvents such as EtOH and MeOH forcefully reduces the reaction time with improved yield of product at reflux and microwave irradiation method, especially with water (Table **1,** entry **8**). The required amount of the catalyst evaluated for this transformation of same compound. Without solvent, the reaction gave corresponding to good yield (Table **1,** entry **9**). If we compared both methods an excellent yield was obtained in very short time of reaction (6 min) by microwave irradiation method. In our observation for model reaction an excellent yield was obtained in presence of alum in water, thus all examples were tested in catalytic amount of alum in 8mL of water, reasonably good to excellent yield (Table **2**). The product **3a-3i** were purified by simple filtration and recrystallization from hot EtOH. Finally, the structure of the compounds **3** were confirmed by NMR spectroscopy and mass spectrophotometer compared with those reported methods (Table **3**.) According to our observation, the presence of alum catalyst on water as solvent for the synthesis of compound **3** under microwave method can be considered as an efficient, green protocol for the preparation of desired product in high yield, short reaction time comparison with previously reported method.

Table 1. Optimization of reaction for the synthesis of 3 substituted indole under the conventional and microwave irradiation method

Entry	Solvent	Reaction Condition (R.C.)	
		Conventional Method[a] Time (hr)/ Yield(%)	Microwave Method[b] Time (hr)/Yield(%)
1	DCM	20/38	12/49
2	DMSO	20/30	12/42
3	Toluene	18/40	10/60
4	THF	20/Trace	10/45
5	EtOH	18/86	10/90
6	MeOH	20/69	12/84
7	CH_3CN	12/92	10/96
8	**H_2O**	**12/83**	**6/98**
9	Solvent free	15/65	10/76

Reaction Condition: [a]Reflux; [b]Microwave; 400Watt. 90°C
Catalytic amount of alum selected for each entry of solvent.

Table 2. Synthesis of 3 substituted indoles under microwave irradiation method



Entry	R_1	R_2	Time (min)	Yield[a] (%)	M.P. Found	M.P. Reported
3a	H	H	8	96	129-130	127-128[28(a)]
3b	4-OCH_3	H	6	98	127-128	128-130[31]
3c	H	4-OCH_3	8	98	171-172	174-177[28(b)]
3d	4-Cl	4-OCH_3	8	95	200-201	202-205[28(b)]
3e	H	4-OH	8	94	121-122	122-126[31]
3f	4-Cl	H	8	92	115-116	118-121[28(b)]
3g	4-OCH_3	H	8	93	120-121	120-122[31]
3h	4-CH_3	4-OCH_3	6	96	178-180	183-186[28(b)]
3i	H	4-OCH_3	8	96	129-130	------

[a]Isolated yield.; Indole 1 (1mmol) and chalcone 2 (1mmol) are mixed with Alum (0.15g) in water (8ml), 400 watt and 90°C 6-8 min.

CONCLUSION

In conclusion, we have successful developed an eco-friendly strategy for the synthesis of 3-(1*H*-indol-3-yl)-1, 3-diphenylpropan-1-ones using alum catalyzed in water under microwave irradiation method. The reaction was performed in very less time of reaction with excellent yield.

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