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Syntvhesis of Indolyl Chalcones under Microwave Irradiation

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Abstract: Chalcones having diverse array of bioactivities can be synthesized by Claisen-Schmidt condensation under conventional (heating) method possess some draw backs as like low yield, required reaction time is more and use of large amount of solvents etc. To overcome these draw backs, a new method can be used i.e. Microwave irradiation method which have very important features i.e., short reaction time, high yields with single product, being environmentally friendly, high functional group tolerance etc. In this work, we in search of new bioactive compounds Indole and different ketones are used to prepare a series of Indolyl-chalcones (**3a-e**) by microwave irradiation method and characterized by different spectroscopic techniques as like IR, ^{1}H NMR and ^{13}C NMR.

Key Words: Microwave, Chalcones, Indole

Introduction

Chalcones have attracted many chemists around the world to develop new synthetic strategies for synthesizing various new chalcones due to their great pharmacological and biological properties and synthetic utility. Chalcone derivatives possess various potential biological activity as like anti-analgesic[1], anti-malarial[2], anticulcerative[3], anti-inflammatory[4] , immunomodulatory[5], anti-tuberculosis[6], inhibition of tyrosinase[7], anti-hyperglycemic[8], antiplatelet[9] , anti-cancer[10], antiviral[11], antimitotic[12], antioxidant[13], inhibition of chemical mediator release[14] , inhibition of aldose reductase[15], antimicrobial[16], inhibition of leukotriene B4[17] and antibacterial[18]. Search and development of new green synthetic methodologies in organic synthesis is always essential and worthwhile to minimize the environmental pollution directly and/or indirectly. Due to many stringent and growing environmental factors and consciousness, the development of new technologies is directed for environmental free and ecofriendly synthetic methodologies for synthesis and detailed reexamination of various important synthetic processes[19].

Microwave chemistry is the study of chemical reactions under the influence of microwave radiation. Microwave heating has been shown to dramatically reduce reaction times, increase product yields and enhance product purities by reducing unwanted side reactions compared to conventional heating methods.

In the present investigation it has been considered worthwhile to synthesize some new Indolyl-chalcones by microwave irradiation method. Important features of this technique are easy access to very high temperature, good control over energy input in a reaction, higher yields and rapid synthesis of organic compounds. The synthesized compounds were purified by recrystallization and chromatography.

Materials and Methods

All reactions were run in dried glassware. Reagents were purchased (Spectrochem, Avra, SRL or Sigma-Aldrich) and used without further purification. Reactions were carried out in a domestic microwave oven. ^{1}H NMR spectrum was obtained in DMSO d6 on Bruker AV-400 (400 MHz) spectrometers using TMS as an internal standard.

General procedure for synthesis of Indolyl chalcones under microwave irradiation

Indole 3-carboxaldehyde (1 mole) and acetophenones (1mole) was dissolved in aqueous ethanol (50 mL) taken in a borosil conical flask (100 mL) and potassium hydroxide (2 mole) was added in the reaction mixture. This conical flask was then placed inside a domestic microwave oven for 2 to 3 minutes at 50% power input. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled at room temperature and was poured into crushed ice (100 mL). Extraction was carried out with diethyl ether (25 x 3 mL) and dried over anhydrous sodium sulphate. Solvent was removed by simple heating on hot water bath (40 ^{0}C) and further purification was done by column chromatography.

Spectral data:

1. (E)-1-(4-hydroxyphenyl)-3-(1H-indol-3-yl)prop-2-en-1-one (3a)

Orange solid, Yield: 60%, **^{1}H NMR** (DMSO-d6, 400 MHz): δ 7.43 – 6.87 (m, 4H), 7.58 (d, *J* = 7.8 Hz, 2H), 7.98 – 7.68 (m, 2H), 8.16 (d, *J* = 7.8 Hz, 2H), 8.34 (s, 1H), 10.00 (s, 1H), 12.15 (s, 1H). **^{13}C NMR** (101 MHz, DMSO-d6): δ 185.47 (s), 138.94 (s),

137.52 (s), 124.57 (s), 123.92 (s), 122.59 (s), 121.28 (s), 118.62 (s), 112.90 (s). **IR** (KBr, cm^{-1}): 3401.0, 3178.1, 1711.2, 1607.1, 1261.6, 1456.2.

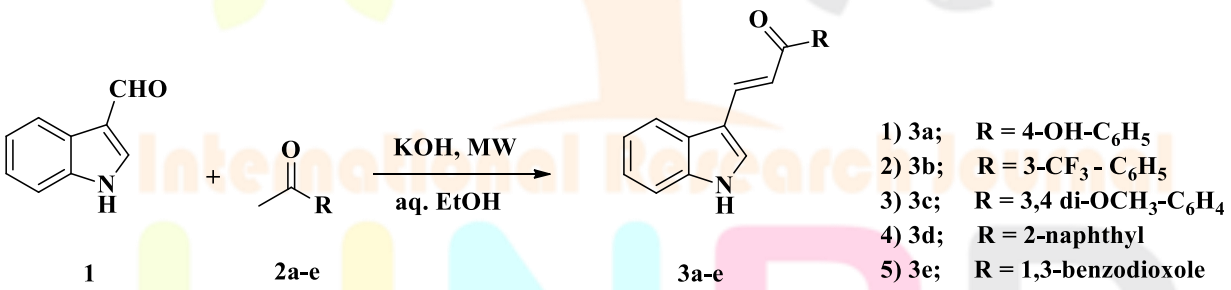
2. (E)-3-(1H-indol-3-yl)-1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (3b)
Reddish brown solid, Yield:90%, **^{1}H NMR** ($CDCl_3$, 400 MHz):δ 7.25 – 7.01 (m, 2H), 7.52 – 7.38 (m, 2H), 7.60 (d, *J* = 20.4 Hz, 2H), 7.71 (dd, *J* = 13.1, 8.1 Hz, 2H), 8.02 – 7.94 (2H, m), 8.10 – 8.05 (2H, m), 10.27 (1H, s). **^{13}C NMR** ($CDCl_3$,101 MHz): δ 189.71 (s), 140.46 (s), 139.61 (s), 137.40 (s), 131.47 (s), 131.26 (s), 130.96 (s), 129.21 (s), 128.72 (s), 125.25 (d, J = 14.8 Hz), 124.43 (s), 123.72 (s), 122.54 (s), 122.02 (s), 120.61 (s), 116.72 (s), 114.29 (s), 112.23 (s). **IR** (KBr, cm^{-1}): 3414.1, 3064, 1677.5, 1608.6, 1412.9, 1323.0.

3. (E)-1-(3,4-dimethoxyphenyl)-3-(1H-indol-3-yl)prop-2-en-1-one (3c)
Brown solid, Yield: 89%, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.96 (d, J = 73.0 Hz, 1H), 8.37 – 8.26 (m, 97H), 8.15 (s, 4H), 8.15 – 7.98 (m, 346H), 7.87 – 7.56 (m, 809H), 7.54 – 7.26 (m, 859H), 6.96 (d, J = 8.3 Hz, 206H), 3.95 (dd, J = 12.3, 5.5 Hz, 1195H), 2.58 (s, 57H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 188.99(s), 152.65 (s), 149.00 (s), 138.72 (s), 132.09 (s), 125.41 (s), 122.96 (s), 122.54 (s), 121.27 (s), 120.40 (s), 110.74 (s), 110.04 (s), 56.01 (d, J = 5.9 Hz). **IR** (KBr, cm^{-1}): 3186.1, 1264.9, 1711.5, 1638.4.

4. (E)-3-(1H-indol-3-yl)-1-(naphthalen-2-yl)prop-2-en-1-one (3d)
Yellow solid, Yield: 66%, **^{1}H NMR** (400 MHz, DMSO): δ 11.79 (s, 1H), 8.39 (d, J = 7.9 Hz, 1H), 8.12 – 7.79 (m, 5H), 7.69 – 7.47 (m, 7H), 7.35 – 7.26 (m, 1H). **^{13}C NMR** (101 MHz, DMSO): δ 163.67 (s), 162.81 (s), 152.68 (s), 151.04 (s), 137.55 (s), 137.15 (s), 133.81 (s), 130.64 (s), 130.11 (s), 128.86 (s), 128.16 (s), 127.31 (s), 126.68 (s), 125.78 (d, J = 6.2 Hz), 120.50 (s), 109.00 (s). **IR** (KBr, cm^{-1}): 3214.6, 3081.4, 1747.4, 1691.2, 1464.8, 1605.3.

5. (E)-1-(benzo[d][1,3]dioxol-5-yl)-3-(1H-indol-3-yl)prop-2-en-1-one (3e)
Yellow solid, Yield: 87%, **^{1}H NMR** (DMSO-d6, 400 MHz) δ 11.92 (s, 1H), 8.29 (s, 1H), 8.08 (dd, J = 12.4, 10.7 Hz, 2H), 7.82 (dd, J = 8.2, 1.7 Hz, 1H), 7.64 – 7.56 (m, 1H), 7.54 – 7.47 (m, 2H), 7.41 (d, J = 1.7 Hz, 1H), 7.28 – 7.19 (m, 1H), 7.05 (dd, J = 19.2, 8.2 Hz, 2H), 6.13 (s, 2H).**^{13}C NMR** (DMSO-d6, 101 MHz): δ 196.41 (s), 151.87 (s), 148.25 (s), 132.04 (s), 125.22 (s), 108.44 (s), 107.86 (s), 102.47 (s). **IR** (KBr, cm^{-1}): 3177.5, 2903.0, 1672.0, 1632.4, 1440.

Results and Discussion
Indolyl-Chalcone derivatives **3a-e** was prepared by treating indole-3-carboxaldehyde **1** with different substituted acetophenones **2a-e** through Claisene-Schmidt condensation under microwave irradiation using potassium hydroxide as base (**Scheme 1**) and ethanol is used as solvent. The reactions are carried in open borosil glass conical flasks. The products obtained are in good yield (60-90%) in very shorter reaction time (2-3min.).



Scheme 1: Synthesis of Indolyl Chalcones

Conclusion:
In conclusion, we have developed a practically convenient methodology for the synthesis of Indole chalcones under microwave irradiation. The notable merits offered by this protocol are mild reaction condition, simple procedure, very short reaction time and excellent yield of the product. The identification of compounds was established by single spot TLC and spectral analysis involving IR, ^{1}H NMR and ^{13}C NMR spectroscopy.

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