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SYNTHESIS AND CHARACTERIZATION OF A NEW SERIES OF CHALCONES CONTAINING INDOLE MOIETY.

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ABSTRACT

Indole derivatives are prime important in medicinal & Drug chemistry as a pharmacological agent. In the present work a new series of chalcones were prepared by claisen- schmidt condensation of N-protected 3-formyl Indole moiety with substituted acetophenone in presence of aq. solution of potassium hydroxide & ethanol at room temperature. The synthesized chalcones were characterised by means of their IR, H^1-NMR &Mass spectral data.

KEYWORDS

Chalcones, Indolemoiety ,claisen- schmidt condensation , pharmacological agent .

INTRODUCTION

Chalcones are 1, 3-diphenyl-2-propene-1-one, in which two aromatic rings are linked by a three carbon α, β-unsaturated carbonyl system. Chalcones are found to possess a wide range of biological activities. Due to the presence of enone functional group in chalcones, they possess various pharmacological activities. It has been reported that many homocyclic and heterocyclic Chalcones possess antimicrobial,[1-2] anti-inflammatory [3] and carcinogenic activities.[4]Chalcones have been found to show interesting biological activities such as analgesic,[5] hypoglycemic,[6] antihepatotoxic,[7] antimalerial,[8-10] antileishmanial,[11] Tyrosinase inhibitors,[12] antineoplastic,[13] spasmolytic,[14] antifungal, diuretic,[15] antitumor,[16] inhibition of tyrosinase,[17] inhibition of aldose reductase,[18] antirhinovirus,[19] antiinvasive,[20] herbicidaland gastric protectant. The indole

derivatives have been widely studied,α, β-unsaturated ketones of chalcone types containing this heterocycle in which products of crotonic condensation of 3-formyl indole derivatives with different acetophenones were described previously in basic media using mostly as a catalyst.

MATERIALS & METHODS

Melting points were taken on a precision melting point apparatus (DBK) instrument and are uncorrected. IR spectra were obtained in potassium bromide (KBr) disks on a Bruker IR spectrometer, and 1H NMR spectra were obtained on deuterated chloroform (CDCl3) or DMSO-d6 solution on a Varian 400 MHz spectrometer. Mass spectra were recorded on a MicroMass spectrometer by Waters. The yields unless otherwise mentioned are for pure product. All the raw materials, reagents and solvents used were of commercial grade only.

EXPERIMENTAL

General procedure for the synthesis of 1H-indole-3-carbaldehyde (I) : (Vilsmeyer - HaackFormylation Reaction)

A solution of indole (0.21 mol) in 100 mL dimethylformamide was prepared and kept aside. A formylation complex was also prepared by cooling 80 mL dimethylformamide in an external ice bath (internal temperature about 12^0C), followed by the addition of 20 mL phosphorus oxychloridedropwise over the course of 30 min. This formylation mixture was then warmed to 25 ^{0}C and added the solution of indole in dimethylformamidedropwise (with continued stirring) over a period of 30 min. Stirring was continued for yet another 45 min, during which time the temperature was raised to40 ^{0}C. The reaction mixture was then poured onto chipped ice which produced a clear red solution. This was made basic with the addition of 200 mL of 5 N sodium hydroxide which allowed the separation of a yellow solid. This was diluted by the addition of 200 mL hot water and, after cooling the product was removed by filtration and washed with cold water. The product was recrystallized from aqueous dimethylformamide to yield 1H-indole-3- carbaldehyde(98%) as faint orange needles.

M.P.:196-198^{0}C

'H NMR (DMSO-d6):δ : 8.29(1H,S) 7.53(1H,S),9.94(1H,S,D_2O-exchangeble),8.11(1H ,d),7.2(t,2H), 8.09(d,1H).

IR(cm^{-1}) - 3163,3039,1627,1435,1573,1240.

MS(m/z) : 146 (M+1).

***GeneralProcedure for the synthesis of 1-Cyclopentyl-3-formyl Indole(II)* :**

A mixture of 20 g (140 mmol) of 3-formylindole, 15.6 mL (150 mmol) of Bromocyclopentane, 100mL of DMF, and 20.7 g **(150** mmol) of K_2C0_3 was refluxed for 4 h. Upon cooling, the solid was filtered off and washed with DMF and the DMF phase concentrated. The residue was taken up with chloroform, washed twice with water, dried, and concentrated to give a brown oil which was purified by column chromatography (Si02,10% methanol / chloroform) to yield 17.8 g (60%) of the expected 1-cyclopentyl-3-formylindole as an oil(Brown).

'H NMR ($CDC1_3$):δ :1.56 (m, 6H, CH_2cyclopentyl), 2.08 (m, 2H, CH_2cyclopentyl), 3.71 (m, lH, CH cyclopentyl), 7.4 (m, 2H, indole), 7.81 (s, lH, indole), 8.5 (m, lH, indole),7.1(m, 1H, indole), 9.99 **(s,** lH,-CHO, D_2O-exchangeble).

IR(cm^{-1}) – 3053,2962,2873,1656,1527,1265,731.

MS(m/z) : 214 (M+1).

***General Synthesis of 1-cyclopentyl-1H-indole-3-yl)-3-phenylprop-2-en-1-one(chalcone)*:**

Equimolar quantities of 1-cyclopentyl-3-formylIndole (0.0046mol) and acetophenones (0.0046 mol) were taken in conical flask and dissolved in minimum of ethanol (15 mL). To this suspension KOH (0.0138 mol) in minimum quantity of water was added and the resulting mixture was stirred for overnight. After completion of reaction (monitored by TLC), the reaction mixture was cooled to room temperature and the crude product was collected by filtration and washed with cold ethanol. The final compound was recrystallised from ethanol.

The other compounds of this series were prepared according to the general procedure. Their percentage yield and melting points are recorded in Table 1. Their structures have been confirmed by Mass, IR and 1H NMR spectra.

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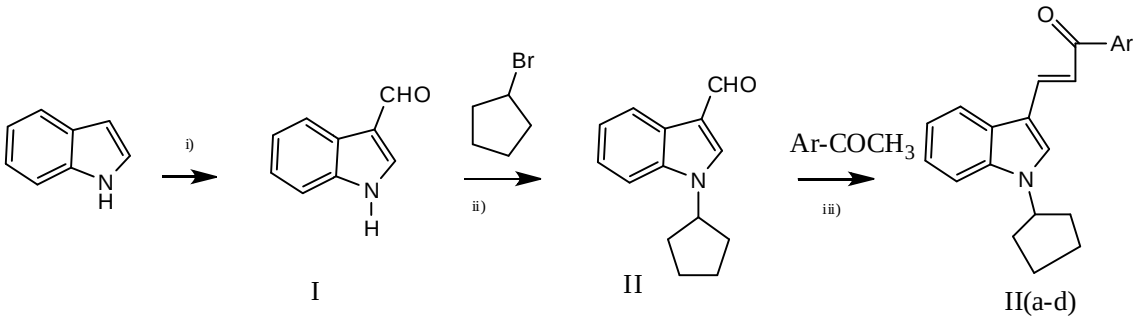
SCHEME-I



Reagents and conditions: i) DMF/$POCl_3$, 0-35^{0}C ii) K_2CO_3/DMF/H_2O,Reflux. iii) KOH / Ethanol.

Results and Discussion

All the new compounds were synthesized in good yields and the physical data of all new synthesized compounds are recorded in the table.

Table 1. Physical data of new series of 3-(1-cyclopentyl-1H-indol-3-yl)-1-phenylprop-2-en-1-one(chalcone) (IIa-d)

Compound	Ar	Molecular formula	Yield	M.P/B.P. ^{0}C
IIa	Phenyl	$C_{22}H_{21}N$	82%	190-192
IIb	2-OH Phenyl	$C_{22}H_{21}NO_2$	70%	110-112
IIc	4-OH Phenyl	$C_{22}H_{21}N\ NO_2$	78%	161-163
IId	4- Methyl Phenyl	$C_{23}H_{23}NO$	80%	143-145

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SPECTRAL ANALYSIS

IIa) 3-(*1-cyclopentyl-1H-indol-3-yl)-1-phenylprop-2-en-1-one(chalcone)*:Yellow solid.

'H NMR (CDC1$_3$):δ : 1.8-1.9 (m, 6H, CH_2cyclopentyl), 2.2 (m, 2H, CH_2cyclopentyl), 4.8 (m, lH, CH cyclopentyl), 7.4 (m, 2H, indole), 7.6 (s, lH, indole), 7.1(m, 1H, indole), 8.0(m, lH, indole), 8.01(1H,d), 7.6(1H,d), 7.5(5H,m)

IR(cm^{-1}) – 3070,2949,1647,1562,1462,1562,1276.

MS(m/z) : 316 (M+1).

IIb) 3-(*1-cyclopentyl-1H-indol-3-yl)-1-(2-hydroxyphenyl)prop-2-en-1-one:*Yellow liquid.

'H NMR (CDC1$_3$): δ : 1.56 (m, 6H, CH_2cyclopentyl), 2.08 (m, 2H, CH_2cyclopentyl), 3.71 (m, lH, CH cyclopentyl), 7.4 (m, 2H, indole), 7.1(m, 1H, indole), 7.81 (s, lH, Hz indole), 8.5 (m, lH, indole)), 8.01(1H,d), 7.6(1H,d), 5.2(1H ,s ,Hydroxy) ,6.9(1H,d) ,7.2(1H,d) ,7.2(1H,t) 7.4(1H,d) 8.2(1H,d) .

IR(cm^{-1}) – 3577,2956,2870,1625,1519,1462,1552,1294

MS(m/z) : 332 (M+1).

IIc) 3-(*1-cyclopentyl-1H-indol-3-yl)-1-(4-hydroxyphenyl)prop-2-en-1-one:* Yellow solid.

'H NMR (CDC1$_3$): δ : 1.56 (m, 6H, CH_2cyclopentyl), 2.08 (m, 2H, CH_2cyclopentyl), 3.71 (m, lH, CH cyclopentyl), 7.4 (m, 2H, indole), 7.81 (s, lH, indole), 8.5 (m, lH, indole),7.3(1H,m) 7.8(1H,d), 7.4(1H,d), 5.3(1H ,s ,Hydroxy)7.4(2H, d)7.3(2H,d).

IR(cm^{-1}) – 3594,2922,1649,1523,1408,997.

MS(m/z) : 332 (M+1).

IId) 3-(*1-cyclopentyl-1H-indol-3-yl)-1-(p-tolyl)prop-2-en-1-one:* Yellow solid.

'H NMR (CDC1$_3$): δ : 1.56 (m, 6H, CH_2cyclopentyl), 2.08 (m, 2H, CH_2cyclopentyl), 3.71 (m, lH, CH cyclopentyl), 7.4 (m, 2H, indole), 7.81 (s, lH, indole), 8.0 (m, lH, indole) 7.9(1H,m) 7.6(1H,d), 7.5(1H,d), 2.4(3H ,s ,methyl), 7.4(2H, d) 7.6(2H,d).

IR(cm^{-1}) – 3028,2951,1647,1556,1462,1278,977

MS(m/z) : 330 (M+1).

CONCLUSION

We have efficiently synthesized a biologically interesting new series of chalcones containing Indolemoiety(**IIa-d**) according to a Conventional method. These novel chalcones may trigger a new area of research to unravel their biological properties and lead to the discovery of better antimicrobial agents.

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