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Design, Synthesis and Antimicrobial Evaluation of Indolyl Pyrimidine Derivatives

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ABSTRACT

The reaction of N-cyclopentyl-indole-3-carboxaldehydes with substituted acetophenones in ethanol and KOH as a base gives N-cyclopentylindolylchalcones [3a-3l]. Which on treatment with urea in presence of base resulted in the cyclization of α, β-unsaturated ketone into the substituted pyrimidines [4a-4l] with goodyield after purification. The synthesized compounds were characterised by [1]H-NMR, IR and Mass and screened for their Anti-microbial activity.

Keywords: Chalcones; Anti-microbial activity; Acetophenones; Urea

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INTRODUCTION

Substituted pyrimidine plays very important role in medicinal chemistry for theirtherapeutic action [1]. The activity is due to presence of a pyrimidine base in thymine, cytosine and uracil, which are constituents of nucleic acids [2] DNA and RNA. Pyrimidine and thiopyrimidine derivatives have a unique importance in recent past. Pyrimidine is the parent substance of a large group of heterocyclic compounds. Earlier the compounds belonging to this group were known as breakdown products of uric acid. Pyrimidine derivatives is well documented that various compounds containing pyrimidine ring, are associated with diverse pharmacological activities such as antitumor [3], antiviral [4], anticancer [5], anti-inflammatory [6,7], antifolate activity [8], which also shows antimicrobial [9], antifungal [10] and antiproliferative [11] activities. Over the past decade many pyrimidines with appropriate functional groups have emerged as antihypertensive agents [12-15] and potent calcium channel blockers [16]. In addition, several marine alkaloids with interesting biological activities contain the dihydropyrimidine-5-carboxylate moiety.

One important class of pyrimidine is 2-thiopyrimidine and its derivatives, which are also well known as 2-mercaptopyrimidine compounds [17]. Recently we have extended our scope of research to in vitro screening of pyridines as antimicrobial evaluation for potent bioactive molecules.

EXPERIMENTAL SECTION

Melting points were determined in open capillaries and are uncorrected. The purity of all the synthesized compounds was checked by TLC. IR spectra were obtained in potassium bromide (KBr) on a Bruker IR-spectrometer, and ^{1}H NMR spectra were obtained on chloroform ($CDCl_3$) or DMSO-d_6 solution on a Varian 400 MHz spectrometer. All chemicals used were of commercial grade only [18-21].

Synthesis of N-Cyclopentyl Indole-3-Aldehyde (2)

Amixture of 0.140 mole of 3-formyl indole and 0.150 mole of bromocyclopentane in 100 ml of DMF as a solvent with 0.150 mole of $K_2CO_3$was refluxed for 4 hours.

After cooling, the solid was filtered and washed with DMF. The DMF phase concentrated and the residue was taken up with chloroform, washed twice with water, dried, and 'concentrated to give brown oil which was purified by column chromatography (Si02, 10% methanol / chloroform) to yield 17.8 gm (60%) of the expected N-Cyclopentyl Indole-3-Aldehyde (2) as a Brown oil.

Synthesis of 1-cyclopentyl-1H-indole-3-yl)-3-phenylprop-2-en-1-one (chalcone) *3 (a-l):* Equimolar amounts of N-cyclopentyl-3-formyl Indole (0.0046 mole) and acetophenones (0.0046 mole) were taken in conical flask and dissolved in minimum of ethanol. To this suspension 0.0138 mole KOH in minimum quantity of water was added and the resulting mixture was stirred for overnight. After completion of reaction, 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 recrystallized from ethanol.

The other compounds of this series were prepared according to the general procedure and confirmed by Mass, IR and 1H NMR spectra.

Synthesis of 4-(1-cyclopentyl-1H-indol-3-yl)-6-phenyl-3,4-dihydropyrimidine-2 (1H)-one 4 (a-l): To the stirred suspension of 0.0025 mole of Chalcones in 20 ml of absolute ethanol, added 0.0050 mole of urea and sodiumethoxide (0.0075 mole) at room temp. The reaction mixture was refluxed for 8-10 h. After completion of the reaction, the reaction mass was concentrated on rotavapour. To the residue ice water added and pH of the reaction mass was acidifying using HCl. The solid obtained was filtered, washed with water, and crystallized from ethanol.

Similarly the other derivatives of the series were prepared and have been confirmed by IR, ^{1}H-NMR and Mass spectra.

Spectral Analysis

N-cyclopentyl-1H-indole 3-carbaldehyde (2): Brown Oil.

IR (KBr, cm^{-1}): 3053 (Ar-H), 2873 (-CHO), 1656 (C=O), 1527 (C=C);

^{1}H NMR ($CDC1_3$): δ 1.82-1.92 (m, 7H, CH_2 cyclopentyl H), 2.26 (m, 2H, CH_2 cyclopentyl H), 7.25-7.60 (m, 4H, indoleAr-H), 8.10 (s, lH, indole H), 8.06 (d, 1H, vinylic H), 8.02 (d, 1H, vinylic H), 7.62-7.88 (m, 5H, Ar-H); ESI-MS (m/z): 214 $(M+H)^+$.

3.1) 3-(N-cyclopentyl-1H-indol-3-yl)-1-phenylprop-2-en-1-one (3a): Yellow solid. IR (KBr, cm^{-1})-3070 (Ar-H), 1647 (C=O), 1581 and 1562 (C=C);

^{1}H NMR ($CDC1_3$): δ 1.82-1.90 (m, 7H, CH_2 cyclopentyl H), 2.24 (m, 2H, CH_2 cyclopentyl H), 7.25-7.63 (m, 4H, indoleAr-H), 8.14 (s, lH, indole H), 8.00 (d, 1H, vinylic H), 8.05 (d, 1H, vinylic H), 7.62 (m, 5H, Ar-H); ESI-MS (m/z): 316 $(M+H)^+$.

3.2) 3-(1-cyclopentyl-1H-indol-3-yl)-1-(p-tolyl)prop-2-en-1-one (3b)*:* Yellow solid. IR (KBr, cm^{-1}): 3028 0 (Ar-H),1645 (C=O),1557 (C=C);

^{1}H NMR ($CDC1_3$): δ: 1.71-1.96 (m, 7H, CH_2 cyclopentyl), 2.29 (m, 2H, CH_2 cyclopentyl), 2.44 (s, 3H, methyl),7.37 (m, 4H, indoleAr-H), 8,17 (s, lH, indole H), 7.87 (d, 2H, Ar-H), 7.32 (d, 1H, Ar-H), 7.33 (d, 2H, vinylic H) 7.46 (d, 2H, vinylic H; ESI-MS (m/z): 330 $(M+H)^+$.

3.3) 3-(1-cyclopentyl-1H-indol-3-yl)-1-(4-bromophenyl)prop-2-en-1-one (3c): Pale yellow solid.IR (KBr, cm^{-1}): 3058 (Ar-H), 1685 (C=O),1616 (C=C);

^{1}H NMR ($CDC1_3$): δ: 1.54-1.97 (m, 7H, CH_2 cyclopentyl), 2.25 (m, 2H, CH_2 cyclopentyl), 6.90-7.45 (m, 4H, indoleAr-H), 8.11 (s, lH, indole H), 7.49 (d, 1H, vinylic H),7.63 (d, 1H, vinylic H),7.64 (d, 2H, Ar-H), 7.81 (d, 2H, Ar-H); ESI-MS (m/z): 394 $(M+H)^+$.

3.4) 3-(1-cyclopentyl-1H-indol-3-yl)-1-(4-Flurophenyl)prop-2-en-1-one (3d): Pale yellow solid.IR (KBr, cm^{-1}): 3051 (Ar-H),1667 (C=O),1540 (C=C).

^{1}H NMR ($CDC1_3$): δ: 1.62-2.24 (m, 7H, CH_2 cyclopentyl), 2.39 (m, 2H, CH_2 cyclopentyl), 7.32 (m, 4H, indole), 8.28 (m, lH, indole) 7.34 (d, 1H, vinylic H), 7.58 (d, 1H, vinylic H), 7.48 (d, 2H, Ar-H), 7.66 (d, 2H, Ar-H); ESI-MS (m/z): 334 $(M+H)^+$.

3.5) 3-(1-cyclopentyl-1H-indol-3-yl)-1-(4-Chlorophenyl) prop-2-en-1-one (3e): Pale yellow solid.IR (KBr, cm^{-1}): 3068 (Ar-H), 1654 (C=O), 1544 (C=C).

^{1}H NMR ($CDC1_3$): δ: 1.41-2.27 (m, 7H, CH_2 cyclopentyl), 2.57 (m, 2H, CH_2 cyclopentyl), 7.23 (m, 4H, indole), 8.03 (m, lH, indole) 7.45 (d, 1H, vinylic H),7.53 (d, 1H, vinylic H),7.35 (d, 2H, Ar-H), 7.36 (d, 2H, Ar-H); ESI-MS (m/z): 350 $(M+H)^+$.

3.6) 3-(1-cyclopentyl-1H-indol-3-yl)-1-(4-Iodophenyl)prop-2-en-1-one (3f): Pale yellow solid.IR (KBr, cm^{-1}): 3065 (Ar-H),1658 (C=O),1534 (C=C).

^{1}H NMR ($CDC1_3$): δ: 1.52-2.22 (m, 7H, CH_2 cyclopentyl), 2.42 (m, 2H, CH_2 cyclopentyl), 7.24 (m, 4H, indole), 8.15 (m, lH, indole H) 7.25 (d, 1H, vinylic H),7.35 (d, 1H, vinylic H),7.33 (d, 2H, Ar-H), 7.41 (d, 2H, Ar-H); ESI-MS (m/z): 441 $(M+H)^+$.

3.7) 3-(1-cyclopentyl-1H-indol-3-yl)-1-(2-hydroxyphenyl)prop-2-en-1-one (3g): Yellow liquid.IR (KBr, cm^{-1}): 3022 (Ar-H),1651 (C=O),1599 (C=C), 3359 (OH).

^{1}H NMR ($CDC1_3$): δ: 1.81-2.11 (m, 7H, CH_2 cyclopentyl), 2.22 (m, 2H, CH_2 cyclopentyl), 4.81 (s, 1H, OH), 6.91-7.43 (m, 4H, indole H), 8.41 (s, lH, indole H) 7.41-7.96 (m, 4H, Ar-H),7.46 (d, 1H, vinylic H),7.44 (d, 1H, vinylic H); ESI-MS (m/z): 332 $(M+H)^+$.

3.8) 3-(1-cyclopentyl-1H-indol-3-yl)-1-(4-hydroxyphenyl)prop-2-en-1-one (3h): Pale yellow solid. IR (KBr, cm^{-1}): 3065 (Ar-H), 1676 (C=O), 1544 (C=C), 3323 (OH);

^{1}H NMR ($CDC1_3$): δ: 1.74-2.04 (m, 7H, CH_2cyclopentyl), 2.35 (m, 2H, CH_2cyclopentyl), 4.83 (s, 1H, OH),7.13-7.45 (m, 4H, indole H), 8.23 (s, lH, indole H), 7.55 (d, 2H, Ar-H), 7.63 (d, 2H, Ar-H),7.53 (d, 1H, vinylic H),7.65 (d, 1H, vinylic H); ESI-MS (m/z): 332 $(M+H)^+$.

3.9) 3-(1-cyclopentyl-1H-indol-3-yl)-1-(2-hydroxy-4-methyl phenyl)prop-2-en-1-one (3i): Pale yellow solid.IR (KBr, cm^{-1}): 3039 (Ar-H), 1659 (C=O), 1568 (C=C), 3329 (OH)

^{1}H NMR ($CDC1_3$): δ: 1.83-2.09 (m, 7H, CH_2cyclopentyl), 2.29 (m, 2H, CH_2cyclopentyl), 5.84 (s, 1H, OH), 2.23 (s, 3H, CH_3), 6.92-7.11 (m, 4H, indole H), 8.13 (s, lH, indole H) 7.20 (s, 1H, Ar-H),7.17 (d, 1H, Ar-H), 7.43 (d, 1H, Ar-H), 7.58 (d, 1H, vinylic H),7.53 (d, 1H, vinylic H); ESI-MS (m/z): 346 $(M+H)^+$.

3.10) 3-(1-cyclopentyl-1H-indol-3-yl)-1-(2-hydroxy-4-chlorophenyl)prop-2-en-1-one (3j): Pale yellow solid. IR (KBr, cm^{-1}): 2953 (Ar-H), 1642 (C=O), 1519 (C=C), 3363 (OH).

^{1}H NMR ($CDC1_3$):δ: 1.52-1.91 (m, 7H, CH_2cyclopentyl), 2.23 (m, 2H, CH_2cyclopentyl), 5.23 (s, 1H, OH), 7.42-7.52 (m, 4H, indole H), 8.25 (s, lH, indole H) 7.33 (s, 1H, Ar-H), 7.13 (d, 1H, Ar-H), 7.34 (d, 1H, Ar-H), 7.34 (d, 1H, vinylic H), 7.54 (d, 1H, vinylic H); ESI-MS (m/z): 366 $(M+H)^+$.

3.11) 3-(1-cyclopentyl-1H-indol-3-yl)-1-(2-hydroxy-4-bromophenyl) prop-2-en-1-one (3k): Pale yellow solid.IR (KBr, cm^{-1}): 2998 (Ar-H),1666 (C=O),1564 (C=C), 3380 (OH)

^{1}H NMR ($CDC1_3$):δ: 1.53-2.03 (m, 7H, CH_2 cyclopentyl), 2.35 (m, 2H, CH_2cyclopentyl), 5.24 (s, 1H, OH), 7.17-7.36 (m, 4H, indole H), 8.14 (s, lH, indole H), 7.63 (s, 1H, Ar-H), 7.22 (d, 1H, Ar-H), 7.25 (d, 1H, Ar-H),7.45 (d, 1H, vinylic H),7.56 (d, 1H, vinylic H); ESI-MS (m/z): 410 $(M+H)^+$.

3.12) 3-(1-cyclopentyl-1H-indol-3-yl)-1-(4-methoxyphenyl)prop-2-en-1-one (3l): Pale yellow solid. IR (KBr, cm^{-1}): 3053 (Ar-H), 1656 (C=O), 1612 (C=C); ^{1}H NMR ($CDC1_3$):δ: 1.80-1.96 (m, 6H, CH_2cyclopentyl), 2.25 (m, 2H, CH_2 cyclopentyl), 2.45 (m, 1H, CH cyclopentyl), 3.97 (s, 3H, methoxy H), 6.95-7.55 (m, 4H, indole Ar-H), 8.10 (s, lH, indole H), 7.84 (d, 2H, Ar-H), 8.22 (d, 2H, Ar-H), 7.36 (d, 1H, vinylic H) 7.43 (d, 1H, vinylicH); ESI-MS (m/z): 346 $(M+H)^+$.

4.1) 4-(1-cyclopentyl-1H-indol-3-yl)-6-phenyl-3,4-dihydropyrimidine-2 (1H)-one (4a): Pale yellow solid (65%), M.P.: 110-112°C, IR (KBr, cm^{-1}): 3215 (NH), 3047 and 2934 (Ar-H), 1560 (C=C), 1463 (C=S); ^{1}H NMR ($CDC1_3$): δ: 1.83-2.00 (m, 6H, cyclopentylH), 2.21-2.30 (m, 3H, cyclopentyl H), 4.80 (d, 1H, pyrimidine methine H), 5.29 (d, 1H, pyrimidine methine H), 6.58 (s, 1H, pyrimidine NH), 6.35 (s, 1H, pyrimidine NH), 6.87 (s, 1H, indole H), 6.95-8.23 (m, 9H, Aromatic H); ESI-MS (m/z): 358 $(M+H)^+$.

4.2) 4-(1-cyclopentyl-1H-indol-3-yl)-6-(p-tolyl)-3,4-dihydropyrimidine-2 (1H)-one (4b): Yellow solid (75%), M.P.: 191-193°C, IR (KBr, cm^{-1}): 3113 and 3213 (2NH), 3051 (Ar-H), 1608 and 1550 (C=C), 1400 (C=S); ^{1}H NMR (CDC13): δ: 0.81-0.89 (m, 4H, cyclopentyl H), 1.85-2.01 (m, 4H, cyclopentyl H), 2.30 (m, 1H, cyclopentyl H), 1.24 (s, 3H, methyl H), 4.83 (d, 1H, pyrimidine methine H), 5.30 (d, 1H, pyrimidine methine H),6.37 (s, 1H, pyrimidine NH), 6.71 (s, 1H, pyrimidine NH), 7.25 (s, 1H, indole H), 7.22-7.82 (m, 8H, Aromatic H); ESI-MS (m/z): 372 $(M+H)^+$.

4.3) 6-(4-bromophenyl)-4-(1-cyclopentyl-1H-indol-3-yl)-3,4-dihydropyrimidine-2 (1H)-one (4c): Faint yellow solid (70%), M.P.: 167-169°C, IR (KBr, cm^{-1}): 3307 and 3392 (2NH), 3055 (Ar-H), 1571 (C=C), 1456 (C=S);

^{1}H NMR (CDC13): δ: 1.83-2.00 (m, 6H, cyclopentyl H), 2.21-2.30 (m, 3H, cyclopentyl H), 4.81 (d, 1H, pyrimidine methine H), 5.45 (d, 1H, pyrimidine methine H), 6.60 (s, 1H, pyrimidine NH), 6.16 (s, 1H, pyrimidineNH), 8.21 (s, 1H, indole H), 7.01-7.99 (m, 8H, Aromatic H); ESI-MS (m/z): 437 (M+H)+.

4.4) 4-(1-cyclopentyl-1H-indol-3-yl)-6-(4-fluorophenyl)-3,4-dihydropyrimidine-2 (1H) one (4d): White solid (77%), M.P.: 206-208°C, IR (KBr, cm^{-1}): 3233 and 3276 (2NH), 3025 (Ar-H), 1578 (C=C), 1432 (C=S); ^{1}H NMR (CDC13): δ: 1.65-2.02 (m, 6H, cyclopentyl H), 2.17-2.36 (m, 3H, cyclopentyl H),4.71 (d, pyrimidine methine H),5.54 (d, 1H, pyrimidine methine H), 6.76 (s, 1H, pyrimidine NH), 6.32 (s, 1H, pyrimidine NH), 7.82 (s, 1H, indole H), 7.12-7.83 (m, 8H, Aromatic H); ESI-MS (m/z): 376 $(M+H)^+$.

4.5) 6-(4-chlorophenyl)-4-(1-cyclopentyl-1H-indol-3-yl)-3,4-dihydropyrimidine-2 (1H)-thione (4e): Pale brown solid (68%), M.P.: 160-162°C, IR (KBr, cm^{-1}): 3154 and 3212 (2NH), 3025 (Ar-H), 1565 (C=C), 1412 (C=S); ^{1}H NMR (CDC13): δ: 1.80-2.10 (m, 8H, cyclopentyl H), 2.23 (m, 1H, cyclopentyl H),4.56 (d, 1H, pyrimidine methine H), 5.78 (d, 1H, pyrimidine methine H), 6.89 (s, 1H, pyrimidine NH), 6.44 (s, 1H, pyrimidine NH),8.21 (s, 1H, indole H), 7.23-7.97 (m, 8H, Aromatic H); ESI-MS (m/z): 392 (M+H)+.

4.6) 4-(1-cyclopentyl-1H-indol-3-yl)-6-(4-iodophenyl)-3,4-dihydropyrimidine-2 (1H)-one (4f): Gray colour solid (78%), M.P.: 241-243°C, IR (KBr, cm^{-1}): 3123 and 3276 (2NH), 3046 (Ar-H), 1532 (C=C), 1389 (C=S); ^{1}H NMR (CDC13): δ: 1.82-2.03 (m, 8H, cyclopentyl H), 2.19 (m, 1H, cyclopentyl H), 4.54 (d, 1H, pyrimidine methine H), 5.87 (d, 1H, pyrimidine methine H), 6.66 (s, 1H, pyrimidine NH), 6.21 (s, 1H, pyrimidine NH), 7.91 (s, 1H, indole H), 7.18-7.87 (m, 8H, Aromatic H); ESI-MS (m/z): 484 $(M+H)^+$.

4.7) 4-(1-cyclopentyl-1H-indol-3-yl)-6-(2-hydroxyphenyl)-3,4-dihydropyrimidine-2 (1H)-one (4g): Dark yellow solid (60%), M.P.: 196-198°C, IR (KBr, cm^{-1}): 3112 and 3243 (2NH), 3053 (Ar-H), 1567 (C=C), 1398 (C=S); ^{1}H NMR (CDC13): δ: 1.62-1.87 (m, 8H, cyclopentyl H), 2.04 (m, 1H, cyclopentyl H), 5.21 (s, 1H, hydroxy H), 4.32 (d, 1H, pyrimidine methine H), 5.45 (d, 1H, pyrimidine methine H), 6.82 (s, 1H, pyrimidineNH), 6.35 (s, 1H, pyrimidine NH), 7.98 (s, 1H, indole H), 6.90-7.65 (m, 8H, Aromatic H); ESI-MS (m/z): 390 $(M+H)^+$.

4.8) 4-(1-cyclopentyl-1H-indol-3-yl)-6-(4-hydroxyphenyl)-3,4-dihydropyrimidine-2 (1H)-one (4h): Yellow solid (64%), M.P.: 216-218°C, IR (KBr, cm^{-1}): 3134 and 3212 (2NH), 3029 (Ar-H), 1530 (C=C), 1356 (C=S); ^{1}H NMR (CDC13): δ: 1.80-2.11 (m, 8H, cyclopentyl H), 2.45 (m, 1H, cyclopentyl H), 5.44 (s, 1H, hydroxy H), 4.67 (d, 1H, pyrimidine methine H), 5.80 (d, 1H, pyrimidine methine H), 6.87 (s, 1H, pyrimidine NH),6.04 (s, 1H, pyrimidine NH), 8.01 (s, 1H, indole H), 7.02-7.65 (m, 8H, Aromatic H); ESI-MS (m/z): 374 $(M+H)^+$.

4.9) 4-(1-cyclopentyl-1H-indol-3-yl)-6-(2-hydroxy-4-methylphenyl)-3,4-dihydro pyrimidine-2 (1H)-one (4i): Colourless solid (80%), M.P.: 147-149°C, IR (KBr, cm^{-1}): 3163 and 3222 (2NH), 3050 (Ar-H), 1567 (C=C), 1389 (C=S); ^{1}H NMR (CDC13):δ: 1.86-2.08 (m, 6H, cyclopentyl H), 2.23 (m, 2H, cyclopentyl H),2.33 (m, 1H, cyclopentyl H), 5.34 (s, 1H, hydroxy H), 2.47 (s, 3H, methyl H), 4.23 (d, 1H, pyrimidine methine H), 5.56 (d, 1H, pyrimidine methine H), 6.68 (s, 1H, pyrimidine NH), 6.21 (s, 1H, pyrimidine NH), 8.08 (s, 1H, indole H), 7.23-7.89 (m, 7H, Aromatic H); ESI-MS (m/z): 338 $(M+H)^+$.

4.10) 6-(4-chloro-2-hydroxyphenyl)-4-(1-cyclopentyl-1H-indol-3-yl)-3,4-Dihydro pyrimidine-2 (1H)-one (4j): Yellow solid (72%), M.P.: 151-153°C, IR (KBr, cm^{-1}): 3121 and 3254 (2NH), 3052 (Ar-H), 1534 (C=C), 1358 (C=S); ^{1}H NMR (CDC13): δ: 1.81-2.00 (m, 6H, cyclopentyl H), 2.12 (m, 2H, cyclopentyl H), 2.45 (m, 1H,

cyclopentyl H),5.26 (s, 1H, hydroxy H), 4.50 (d, 1H, pyrimidine methine H), 5.81 (d, 1H, pyrimidine methine H), 1.89 (s, 1H, pyrimidine NH), 13.45 (s, 1H, pyrimidine NH), 8.05 (s, 1H, indole H), 7.03-7.79 (m, 7H, Aromatic H); ESI-MS (m/z): 408 $(M+H)^+$.

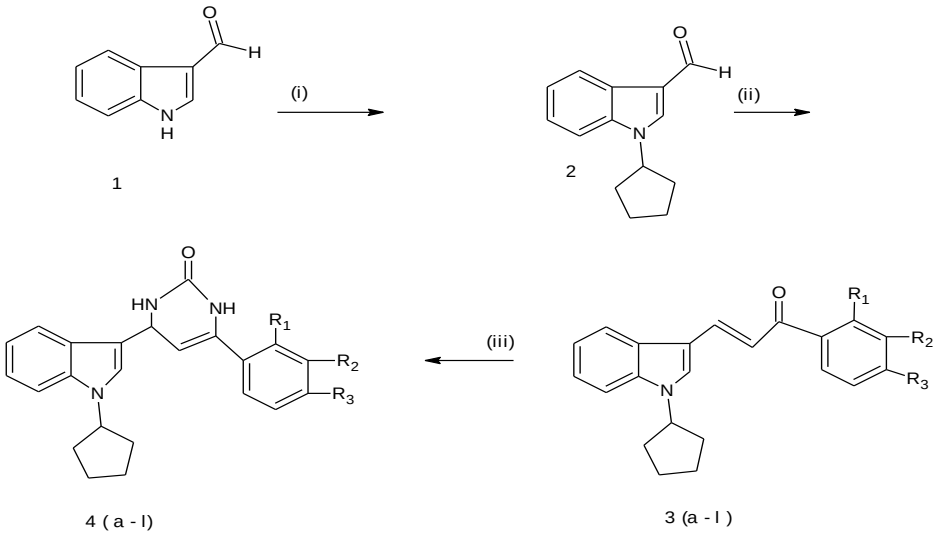
4.11) 6-(4-Bromo-2-hydroxyphenyl)-4-(1-cyclopentyl-1H-indol-3-yl)-3,4-dihydro pyrimidine-2 (1H)-one (4k): brown solid (67%), M.P.: 223-225°C, IR (KBr, cm^{-1}): 3140 and 3288 (2NH), 3028 (Ar-H), 1567 (C=C), 1398 (C=S); ^{1}H NMR (CDC13): δ: 1.91-2.23 (m, 6H, cyclopentyl H), 2.20 (m, 2H, cyclopentyl H), 2.56 (m, 1H, cyclopentyl H), 5.21 (s, 1H, hydroxy H), 4.61 (d, 1H, pyrimidine methine H), 5.76 (d, 1H, pyrimidine methine H), 6.17 (s, 1H, pyrimidine NH), 6.76 (s, 1H, pyrimidine NH), 6.83 (s, 1H, indole H), 7.13-7.92 (m, 7H, Aromatic H); ESI-MS (m/z): 453 $(M+H)^+$.

4.12) 4-(1-cyclopentyl-1H-indol-3-yl)-6-(2-hydroxy-4-methoxyphenyl)-3,4-dihydro pyrimidine-2 (1H)-one (4l): colourless solid (60%), M.P.: 195-197°C, IR (KBr, cm^{-1}): 3132 and 3210 (2NH), 3045 (Ar-H), 1534 (C=C), 1367 (C=S); ^{1}H-NMR (CDC13): δ: 1.76-2.11 (m, 6H, cyclopentyl H), 2.28 (m, 2H, cyclopentyl H), 2.65 (m, 1H, cyclopentyl H),5.34 (s, 1H, hydroxy H), 3.89 (s, 3H, methoxy H), 4.55 (d, 1H, pyrimidine methine H), 5.78 (d, 1H, pyrimidine methine H), 6.08 (s, 1H, pyrimidine NH), 6.46 (s, 1H, pyrimidine NH), 6.91 (s, 1H, indole H), 7.02-7.88 (m, 7H, Aromatic H); ESI-MS (m/z): 404 $(M+H)^+$.

RESULTS AND DISCUSSION

In this reaction Indole-3-Carbaldehyde (1) upon treatment with Cyclopentyl bromide in DMF gave N-cyclopentyl Indole-3-Carbaldehyde (2). It was then further treated with different substituted acetophenones to give substituted Chalcones 3 (a-l) (Scheme 1 and Table 1). Finally, commercially available urea and above prepared Chalcones in C2H5ONa is heated at reflux temperature and precipitation was collected after cooling and filtration to yield the corresponding pyrimidine 4 (a-l) in the good yield (Scheme 1).

The progress and purity of all reactions was monitored by thin layer chromatography. The synthesized derivatives 4 (a-l) were isolated in moderate to good yield.



Scheme 1. Chemical structures

Reagents and Conditions

i) Cyclopentyl Bromide/K_2CO_3/DMF/H_2O,

ii) Substituted Acetophenones/KOH/Ethanol,

iii) Urea/C2H5ONa/ Ethanol/Reflux.

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

Compound	R_1	R_2	R_3	Molecular formula	Yield (%)	M.P/ B.P.^{0}C
3a	H	H	H	$C_{22}H_{21}NO$	82	190-192
3b	H	H	CH_3	$C_{23}H_{23}NO$	80	143-145
3c	H	H	Br	$C_{22}H_{20}NOBr$	64	120-122
3d	H	H	F	$C_{22}H_{20}NOF$	72	88-90
3e	H	H	Cl	$C_{22}H_{20}NOCl$	66	165-167
3f	H	H	I	$C_{22}H_{20}NOI$	81	187-190
3g	OH	H	H	$C_{22}H_{21}NO_2$	70	110-112
3h	H	H	OH	$C_{22}H_{21}NO_2$	78	161-163
3i	OH	H	CH_3	$C_{23}H_{22}NO_2$	65	143-145
3j	H	H	Cl	$C_{22}H_{20}NO_2Cl$	76	198-200
3k	OH	H	Br	$C_{22}H_{20}NO_2Br$	69	98-100
3l	H	H	OCH_3	$C_{23}H_{22}NO_2$	74	113-115

ANTIMICROBIAL ACTIVITY

The antibacterial activity was evaluated against different bacterial strains such as *Staphylococcus aureus* (ATCC 9027), *Bacillus subtilus* (ATCC6633) and *Escherichia coli* (ATCC 8789), *Pseudomonas aeruginosa* (ATCC 9027) and *Salmonella abony* (NCTC-6017). Ciprofloxacin is used as a standard drug for the comparison of antibacterial activity. Applying the agar plate diffusion technique, all of the synthesized compounds (4a-l) were screened in their vitro antibacterial activity against Gram Positive Bacteria and Gram Negative Bacteria.

The antifungal activity was evaluated against different fungal strains such as *Candida albicans* (ATCC 10231) and *Aspergillus niger* (ATCC 16404). MIC values of antifungal activity were determined using standard agar dilution method. Fluconazole is used as standard drugs for the comparison of antifungal activity. Dimethyl sulfoxide issued as solvent control. From the antimicrobial testing compounds 4 (a-l), it is observed that all the newly synthesized compounds shows excellent to moderate level of antibacterial and antifungal activity shown by Table 2.

Table 2. Antimicrobial Activity of Synthesized compounds (4a-l)

Sr. No.	Comp. No.	Inhibition Zone Diameter (mm)						
		I	II	III	IV	V	VI	VII
1	4a	08	09	07	09	08	10	09
2	4b	11	12	10	11	12	11	11
3	4c	12	14	11	12	13	12	11
4	4d	12	15	11	12	14	12	13
5	4e	11	12	10	11	13	11	12
6	4f	10	11	11	12	10	12	10
7	4g	-	-	-	-	-	-	-
8	4h	-	-	-	-	-	-	-
9	4i	10	11	10	11	12	11	10
10	4j	09	10	09	08	10	10	09

11	4k	08	11	09	11	10	09	08
12	4l	12	12	10	11	11	12	10
13	Ciprofloxacin	-	18	-	14	16	15	14
14	Fluconazole	13	-	12	-	-	-	-

Fungus Culture: I-*Aspergillus niger* III-*Candida albicans.*

Gram Positive Bacteria: II-*Bacillus subtilis* VII-*Staphylococcus aureus.*

Gram Negative Bacteria: IV-*E. coli* V-*Pseudomonas aeruginos* VI-*Sallemonella abony.*

The antimicrobial evaluation data indicate that compounds 5b, 5c, 5d, 5e, 5f, 5i, 5l have found to be most active and potent as antimicrobial agents. From this 5c, 5d, 5l have been identified as the most prominent results than the others when compared with standard. The structure activity relationship of the series can be explained that, halogen and electron donating methyl or methoxy groups' present derivatives are more potent antimicrobial activity than the other derivatives. This evaluation shows future scope for optimization.

CONCLUSION

The synthesis of new molecules of pyrimidine was attempted from chalcones, and these novel synthesized derivatives were characterized by means of their mass, IR, H^1 NMR spectral data and their subsequent evaluation as antibacterial and antifungal agent have been explained. In this series of synthesized derivatives, electron donating methyl or methoxy groups' present derivatives displayed decent antibacterial and antifungal profile when compared with standard reference.

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