Four-Component, One-Pot Synthesis of Novel Conjugated Indole-Imidazole Derivatives

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ABSTRACT: *A series of new tetrasubstituted imidazoles 2-phenyl-3-(1, 4, 5-triphenyl-1H-imidazol-2-yl)-1H-indole derivatives substituted with –F, Cl, Br, I,-OCH_3 and -$NHCOCH_3$ were synthesized using a multicomponent reaction. The compounds were obtained in good yields by easy work up and with high purity.*

KEYWORDS: *Indoles; Imidazoles, Multicomponent, NMR.*

INTRODUCTION

It is evident from the literature that conjugated indole-imidazole derivatives known to be associated with a broad spectrum of biological activities like antimicrobial[1], antibacterial[2], anti-inflammatory[3], anticancer[4], anti-viral[5], antifungal[6] and anticonvulsant[7] activities.

Many synthetic strategies have been reported for the synthesis of indole –imidazole compounds. The synthesis of 3-(4,5-dihydro-1*H*-Imidazole-2-yl) -1*H*-indoles has been reported by the reaction of various substituted indoles with 1-acetyl-imidazolidin-2-one in the presence of $POCl_3$[8]. The reaction of indole-3-carboxamidines with 3-bromoacetyl indole has been studied to give diindolylimidazoles [9]. Various 7-(α-azolylbenzyl) -1*H*-indoles and indolines were prepared by acylation of indole derivatives in the presence of benzonitriles and $AlCl_3$ or BCl_3 [10]. The synthesis of 2-(imidazolyl)-tetrahydroindole has been reported by condensation of indole-3-acetamide and imidazole derivatives [11]. An imidazole containing an indole substituent, 1-[(1-Methyl-1*H*-imidazol-5-yl) methyl] -1*H*-indole-5-carbonitrile was prepared by the reaction of 1*H*-indole-5-carbonitrile and hydrochloric salt of 5-(chloromethyl) -1-methyl*1H* imidazol in dimethylformamide in the presence of NaH[12].

1,4,5-trisubstituted imidazoles have been prepared by using aryl substituted Tos MIC from 3-formylindole to give 3-(3-benzyl-5-phenyl-3-*H*-imidazole-4-yl) -1*H*-indole[13]. Synthesis of substituted imidazoles containing indole as a substituent has been reported by one pot reaction of substituted indole-3-carbaldehyde, 1,2-diketones and ammonium acetate under reflux in acetic acid[14]. Tetrasubstituted - 2-(4,5-diphenyl-1(p-tolyl) -1*H*-Imidazole-2-yl) -1*H*-indole has been synthesized in the presence of *N*-methyl-2-pyrrolidonium hydrogen sulfate as Brønsted acidic ionic liquid or (P_2O_5/SiO_2) in one pot reaction of indole aldehyde, toluidine, benzil, and ammonium acetate [15,16].

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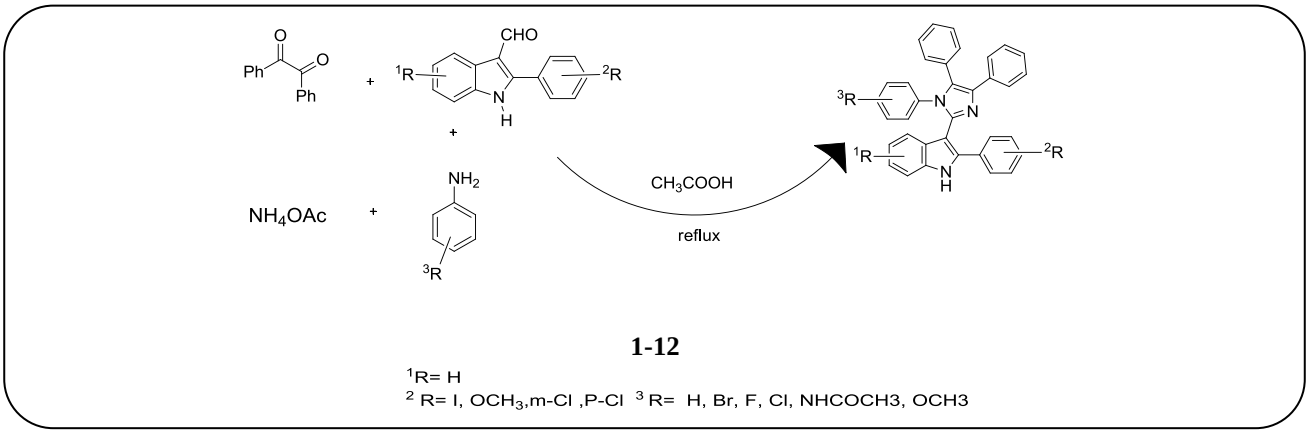
Table 1: Yield and melting points of synthesized compounds.

Sr. No.	Sample code	^{1}R	^{2}R	^{3}R	Yield %	Melting point^{0}C
1	1	H	I	H	50	> 250
2	2	H	I	F	48	> 250
3	3	H	I	OCH_3	52	> 250
4	4	H	I	Br	50	> 250
5	5	H	OCH_3	F	57	> 250
6	6	H	OCH_3	H	52	> 250
7	7	H	OCH_3	Br	61	> 250
8	8	H	m-Cl	H	56	132
9	9	H	m-Cl	OCH_3	56	130
10	10	H	m-Cl	F	72	268-270
11	11	H	P-Cl	OCH_3	53	250
12	12	H	P-Cl	$NHCOCH_3$	53	188-190



1-12

^{1}R= H

^{2} R= I, OCH_3,m-Cl ,P-Cl ^{3} R= H, Br, F, Cl, NHCOCH3, OCH3

Scheme 1: One-pot synthesis of Conjugated indole-imidazole derivatives (1-12).

We have already reported the synthesis of tri and tetraarylimidazoles, using substituted 2-phenylindole -3-carbaldehydes as starting materials, by multicomponent reactions and these compounds exhibited excellently α-glucosidase inhibition [17] and antiurease activities [18]. In continuation of this work, we would now like to report the synthesis of a new series of tetraarylimidazoles in one-pot reaction.

EXPERIMENTAL SECTION

The chemicals and solvents used in this experimental work were of analytical grade and were purchased from Fluka, Merck and Aldrich Chemicals. Melting points were determined in open capillary tubes and are uncorrected. ^{1}H spectra were recorded at 500 MHZ and ^{13}C NMR spectra were recorded at 126 MHZ on a Brucker Avance AV11500B spectrometer. IR spectra were recorded on Perkin Elmer Spectrum BX FT-IR. Analytical TLC was performed on DC-Alufolien Silica Gel 60 F254 Merck. UV lamp of short and long wavelength (model UVGL-25 minor light multiband UV-254/366) was used to visualize TLC plates

General Procedure for the synthesis of conjugated indole-imidazole derivatives (1-12)

A mixture of a substituted 2-phenylindole 3-carbaldehyde (1.0 equiv), benzil (1.0 equiv), ammonium acetate (4.0 equiv) and aromatic amine (1.0 equiv)

in acetic acid was heated at reflux for 5-6 hours[17]. After the completion of the reaction (monitored by TLC) and cooling to room temperature, the reaction mixture was poured into cold water. The solid product was filtered off, washed with an excess of water and recrystallized with EtOH to obtain pure (**1-12**).

The following compounds were prepared from this general method:

2-(p-Iodophenyl)-3-(1,4,5-triphenyl-1H-imidazol-2-yl)-1H-indole (1)

Yield: 50%as a yellow solid.

mp: > 250 ^{0}C;

IR (neat): 3200(indole-NH), 3056, 1597, 1496, 1385, 1328, 1239, 1073 cm^{-1};

HRMS (ES$^+$) calcd. for $C_{35}H_{25}N_3I$ $[M+H]^+$ 614.1093 Found: 614.1076;

^{1}H NMR (500 MHz, DMSO-d_6) δ: 11.61 (s, 1H), 7.73 (d, *J* = 8.5 Hz, 2H), 7.60 – 7.52 (m, 3H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.31 – 7.14 (m, 9H), 7.10 – 6.86 (m, 6H), 6.57 (d, *J* = 7.4 Hz, 2H).

^{13}C NMR (126 MHz, DMSO-d_6) δ: 142.60, 138.00, 137.73, 136.89, 136.43, 135.33, 131.97, 131.68, 131.46, 130.54, 130.49, 129.63, 129.51, 128.86, 128.74, 128.54, 127.97, 127.84, 127.68, 126.96, 123.08, 120.65, 120.10, 112.07, 103.81, 94.58.

3-(1-(p-Fluorophenyl)-4, 5-diphenyl-1H-imidazole-2-yl)-2-(p-iodophenyl)-1H-indole (2)

Yield: 48% as a yellow solid.

mp: > 250 ^{0}C;

IR (neat): 3100(indole-NH), 3077 1600, 1509, 1222, 1153, 1006 cm^{-1};

HRMS (ES$^+$) calcd. for $C_{35}H_{24}N_3FI$ $[M+H]^+$ 632.0999 Found: 632.1006;

^{1}H NMR (500 MHz, DMSO-d_6) δ: 11.67 (s, 1H), 7.74 (d, *J* = 8.5 Hz, 2H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.55 – 7.52 (m, 2H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.34 – 7.14 (m, 12H), 6.78-6.70 (m, 2H), 6.60 (d, *J* = 1.9 Hz, 2H).

^{13}C NMR (75 MHz, DMSO-d_6) δ: 161.75, 159.32, 142.06137.37, 137.15, 137.05, 136.15, 135.82, 134.58, 132.12, 131.21, 131.07, 130.60, 129.93, 129.78, 129.28, 129.91, 128.91, 128.85, 128.53, 128.33, 128.12, 127.01, 126.33, 126.27, 122.45, 120.04, 119.52, 114.89, 114.66, 111.46, 102.84, 94.15.

2-(p-Iodophenyl)-3-(1-(p-methoxyphenyl)-4, 5-diphenyl-1H-imidazol-2-yl)-1H-indole (3)

Yield: 52% as a yellow solid.

mp: > 250 ^{0}C;

IR (neat): 3140(indole-NH), 1513, 1456, 1249, 1034, 1005 cm^{-1};

HRMS (ES$^+$) calcd. for $C_{36}H_{27}N_3OI$ $[M+H]^+$ 644.1199 Found: 644.1195;

^{1}H NMR (500 MHz, DMSO-d_6) δ: 11.65 (s, 1H), 7.74 (d, *J* = 8.5 Hz, 2H), 7.60 – 7.50 (m, 3H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.34 – 7.22 (m, 7H), 7.19 – 7.10 (m, 4H), 7.07 – 7.03 (m, 1H), 6.56 – 6.40 (m, 4H), 3.55 (s, 3H)(OCH_3).

^{13}C NMR (75 MHz, DMSO-d_6) δ: 157.90, 142.16, 137.32, 137.14, 136.85, 136.04, 135.74, 134.76, 131.32, 131.03, 130.88, 130.05, 129.92, 129.04, 128.85, 128.53, 128.50, 128.43, 128.34, 128.20, 128.15, 128.11, 128.06, 127.29, 127.00, 126.23, 126.18, 122.52, 122.34, 119.96, 119.49, 113.06, 111.39, 103.28, 94.03, 54.99(OCH_3).

3-(1-(p-Bromophenyl)-4,5-diphenyl-1H-imidazole-2-yl)-2-(p-iodophenyl)-1H-indole (4)

Yield: 50% as a yellow solid.

mp: > 250 ^{0}C;

IR (neat): 3210(indole-NH), 3063, 1583, 1491, 1389, 1070, 1014 cm^{-1};

HRMS (ES$^+$) calcd. for $C_{35}H_{24}N_3BrI$ $[M+H]^+$ 692.0198 Found: 692.0203;

^{1}H NMR (500 MHz, DMSO-d_6) δ: 11.65 (s, 1H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.54 (d, *J* = 8.2 Hz, 2H), 7.45 – 7.38 (m, 3H), 7.36 – 7.23 (m, 9H), 7.07 (d, *J* = 7.9 Hz, 4H), 6.50 (d, *J* = 7.7 Hz, 2H).

^{13}C NMR (75 MHz, DMSO-d_6) δ :141.90, 137.34, 137.23, 137.15, 136.18, 135.91, 135.84, 135.07, 135.04, 134.49, 131.18, 131.07, 130.87, 130.46, 129.93, 129.51, 129.22, 128.95, 128.81, 128.59, 128.52, 128.42, 128.13, 128.09, 127.31, 127.01, 126.39, 126.30, 126.23, 122.50, 120.51,120.09, 119.53, 111.49, 102.70.

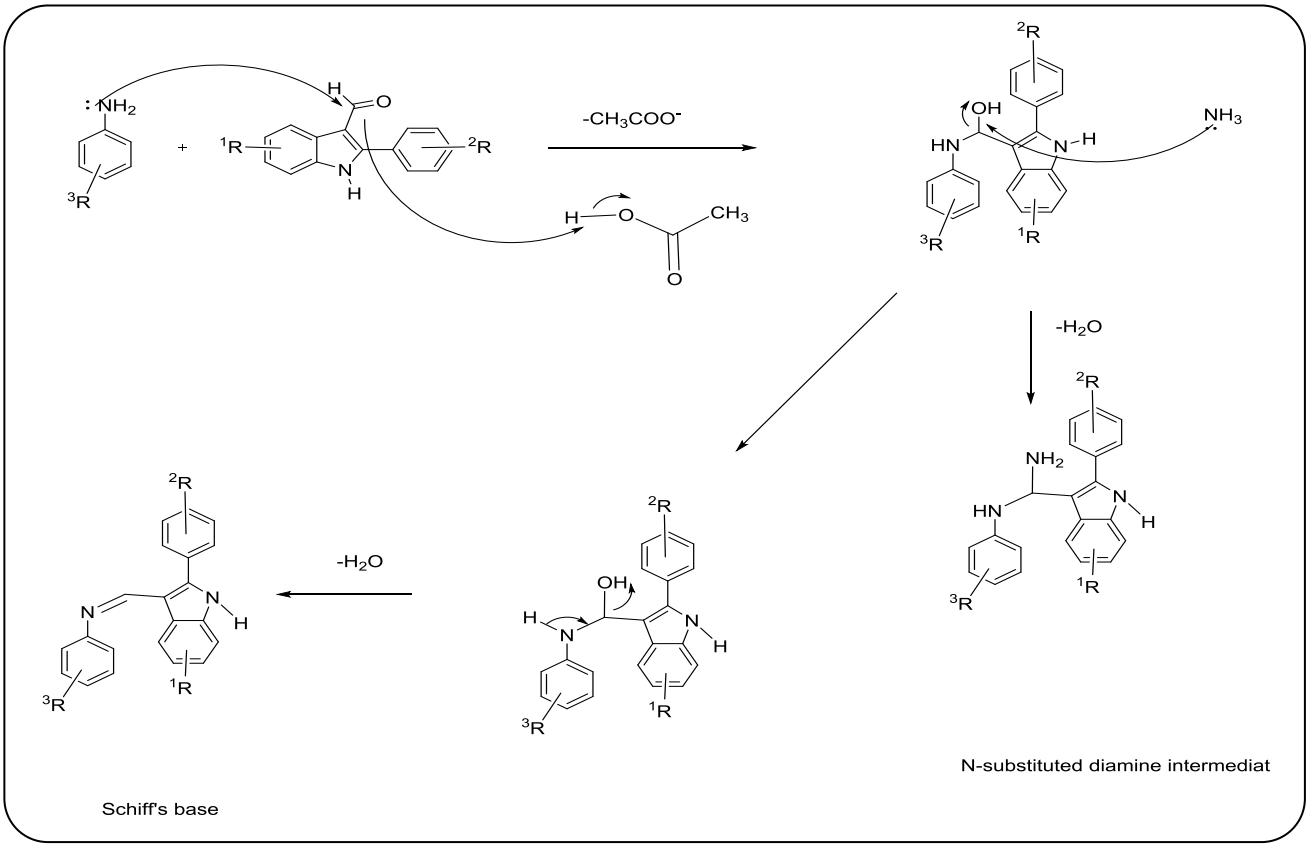
3-(1-(p-Fluorophenyl)-4,5-diphenyl-1H-imidazol-2-yl)-2-(p-methoxyphenyl)-1H-indole (5)

Yield : 57% as a yellow solid.

mp: > 250 ^{0}C;

IR (neat): 3163(indole-NH), 3060, 1613, 1529, 1508, 1248, 1218 cm^{-1};

HRMS (ES$^+$) calcd. for $C_{36}H_{27}N_3OF$ $[M+H]^+$ 536.2183 Found: 536.2128;



Scheme 2: Proposed mechanisim.

^{1}H NMR (500 MHz, DMSO-d_6) δ: 11.46 (s, 1H), 7.55 (d, *J* = 7.3 Hz, 3H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.34 – 7.28 (m, 3H), 7.27 – 7.20 (m, 6H), 7.15 – 6.89 (m, 5H), 6.78 – 6.69 (m, 2H), 6.58-6.54 (m, 2H), 3.77 (s, 3H)(OCH_3).

^{13}C NMR (75 MHz, DMSO-d_6) δ: 162.15, 159.14, 158.90, 142.64, 137.48, 136.91, 135.55, 134.68, 132.27, 132.23, 131.01, 130.70, 129.62, 129.24, 129.13, 129.07, 128.54, 128.30, 128.13, 127.99, 127.03, 126.27, 124.27, 121.75, 119.76, 119.04, 114.90, 114.60, 114.12, 113.89, 111.19, 101.41,55.23(OCH_3).

2-(p-Methoxyphenyl)-3-(1, 4, 5-triphenyl-1H-imidazol-2-yl)-1H-indole (6)

Yield: 52 % as a white solid.

mp: 218 ^{0}C;

HRMS (ES^+) calcd. for $C_{36}H_{28}N_3O$ $[M+H]^+$ 518.2232 Found: 518.2235;

^{1}H NMR (500 MHz, DMSO-d_6) δ: 11.47 (s, 1H), 7.54 – 7.47 (m, 3H), 7.33 (d, *J* = 8.1 Hz, 1H), 7.29 – 7.13 (m, 10H), 7.11 – 7.06 (m, 1H), 7.03 – 6.85 (m, 6H), 6.56 (d, *J* = 6.9 Hz, 2H), 3.75 (s, 3H) (OCH_3).

^{13}C NMR (75 MHz, DMSO-d_6)δ: 159.68, 143.20, 138.13, 137.53, 136.56, 136.09, 135.36, 131.60, 131.45, 130.32, 129.81, 129.11,128.87, 128.82, 128.75, 128.53, 127.95, 127.81, 126.92, 124.92, 122.32, 120.37, 119.57, 114.94, 114.72, 111.80, 102.27, 55.83(OCH_3).

3-(1-(p-Bromophenyl)-4,5-diphenyl-1H-imidazol-2-yl)-2-(p-methoxyphenyl)-1H-indole (7)

Yield: 61% as a white solid.

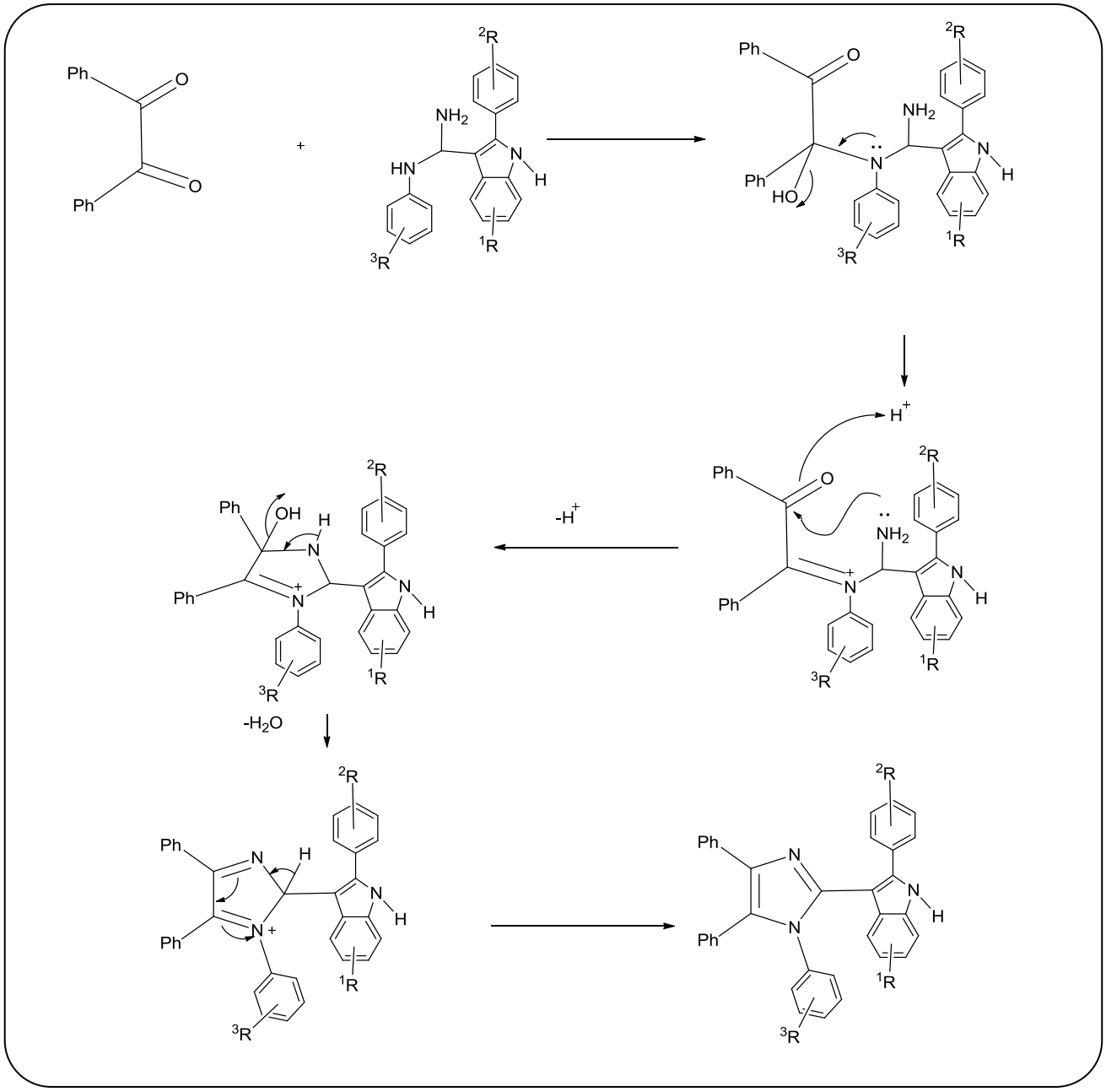
mp: > 250 ^{0}C;

IR (neat):3190(indole-NH), 1491, 1447, 1384, 1250, 1187, 1070, 1046 cm^{-1};

HRMS (ES^+) calcd. for $C_{36}H_{27}N_3OBr$ $[M+H]^+$ 596.1337 Found: 596.1339;

^{1}H NMR (500 MHz, DMSO-d_6)δ: 11.47 (s, 1H), 7.57 – 7.52 (m, 1H), 7.57 – 7.52 (m, 3H), 7.45 (d, *J* = 7.5 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 4H), 7.24 – 7.19 (m, 4H), 7.10 – 7.02 (m, 4H), 6.93 (d, *J* = 8.6 Hz, 2H), 6.46 (d, *J* = 7.7 Hz, 2H), 3.77 (s, 3H) (OCH_3).

^{13}C NMR (75 MHz, DMSO-d_6)δ: 159.16, 142.47, 137.51, 137.10, 135.61, 135.57, 135.20, 134.59, 131.01,



Scheme 3: Proposed mechanisim.

130.82, 130.56, 129.35, 129.27, 129.16, 129.01, 128.59, 128.49, 128.33, 128.11, 127.99, 127.20, 127.02, 126.29, 126.17, 124.23, 121.84, 121.79, 120.40, 119.79,119.68, 119.03, 114.08, 113.88, 111.22, 111.12, 55.23(OCH_3).

2-(m-Chlorophenyl)-3-(1,4, 5-triphenyl-1H-imidazol-2-yl)-1H-indole (8)

Yield: 56% as a yellow solid.

mp: 132 ^{0}C;

IR (neat): 3173(indole-NH), 1598, 1496, 1448, 1377, 1073, 1010 cm^{-1};

HRMS (ES^+) calcd. for $C_{35}H_{25}N_3Cl$ $[M+H]^+$ 522.1737 Found: 522.1722;

^{1}H NMR (500 MHz, DMSO-d_6) δ: 11.71 (s, 1H), 7.63 (d, J = 7.9 Hz, 1H), 7.58 – 7.52 (m, 2H), 7.42 – 7.16 (m, 14H), 7.12 – 6.85 (m, 4H), 6.51 (d, J = 6.5 Hz, 2H).

^{13}C NMR (75 MHz, DMSO-d_6) δ: 141.84, 137.18, 135.83, 135.71, 135.58, 134.62, 133.70, 133.26, 130.97,

130.71, 130.40, 129.81, 128.75, 128.51, 128.27, 128.12, 127.92, 127.42, 127.19, 126.99, 126.58, 126.35, 125.55, 122.59, 120.13, 119.56, 111.52, 103.62.

2-(m-Chlorophenyl)-3-(1-(p-methoxyphenyl)-4,5-diphenyl-1H-imidazol-2-yl)-1H-indole (9)

Yield: 56% as a white solid.

mp: 130 ^{0}C

IR (neat): 3196(indole-NH), 1601, 1513, 1450, 1249, 1167, 1048 cm^{-1};

HRMS (ES$^+$) calcd. for $C_{36}H_{27}N_3OCl$ $[M+H]^+$ 552.1834 Found: 552.1831;

^{1}H NMR (500 MHz, DMSO-d_6) δ: 11.71 (s, 1H), 7.63 (d, *J* = 8.1 Hz, 1H), 7.57 – 7.50 (m, 2H), 7.45 – 7.36 (m, 3H), 7.33 – 7.17 (m, 11H), 7.12 – 7.04 (m, 1H), 6.48-6.39 (m, 4H), 3.55 (s, 3H) (OCH_3).

^{13}C NMR (75 MHz, DMSO-d_6) δ: 157.91, 142.03, 136.99, 135.83, 135.49, 134.73, 133.81, 133.27, 130.98, 130.84, 130.42, 130.19, 130.06, 128.82, 128.52, 128.47, 128.23, 128.12, 127.97, 127.93, 127.60, 127.45, 127.56, 127.00, 126.56, 126.50, 126.31, 125.58, 122.74, 122.57, 120.11, 119.62, 113.10, 111.51, 103.74, 55.01(OCH_3).

2-(m-Chlorophenyl)-3-(1'-(p-fluorophenyl)-4, 5-diphenyl-1H-imidazol-2-yl)-1H-indole(10)

Yield: 72% as a white solid

mp; 268-270 ^{0}C;

3177(indole-NH), 1599, 1562, 1509 cm^{-1}

EI-MS; m/z (%) Calcd.for ($C_{35}H_{23}ClFN_3$) [M$^+$]: 539.15, 541.15; Found: 538.99, 540.99;

^{1}H NMR (300 MHz, DMSO-d_6) δ : 11.73(s, 1H), 7.65(d, *J* =7.8Hz, 1H), 7.55(d, *J* =7.2 Hz , 2H), 7.47.-7.03(m, 15H), 6.80-6.68(m, 2H) , 6.56-6.45(m, 2H).

^{13}C NMR (75 MHz, DMSO-d_6) δ: 162.17, 158.92, 141.94, 137.20, 135.90, 135.57, 134.54, 133.73, 133.32, 132.05, 132.01, 130.99, 130.55, 130.46, 129.75, 129.05, 128.93, 128.63, 128.60, 128.38, 128.14, 127.93, 127.53, 127.01, 126.62, 126.39, 126.35, 125.68, 122.66, 120.17, 119.65, 114.98, 114.6, 111.56, 103.33.

2-(p-Chlorophenyl)-3-(1'-(p-methoxyphenyl)-4, 5-diphenyl-1H-imidazol-2-yl)-1H-indole (11)

Yield: 53% as a white solid.

mp: > 250 ^{0}C;

IR (neat): 3172(indole-NH), 2355, 1511, 1248, 1091, 1029 cm^{-1};

HRMS (ES$^+$) calcd. for $C_{36}H_{27}N_3OCl$ $[M+H]^+$ 552.1843 Found: 552.1831;

^{1}H NMR (500 MHz, DMSO-d_6) δ: 11.66 (s, 1H), 7.58 (d, *J* = 7.4 Hz, 1H), 7.52 (d, *J* = 7.9 Hz, 2H), 7.48 – 7.38 (m, 3H), 7.35 – 7.03 (m, 12H), 6.54 – 6.40 (m, 4H), 3.54 (s, 3H) (OCH_3).

^{13}C NMR (126, DMSO-d_6) δ: 158.55, 142.82, 137.49, 136.52, 136.39, 135.40, 133.13, 131.68, 131.52, 131.34, 130.71, 130.32, 129.65, 129.27, 129.22, 129.18, 129.11, 128.96, 128.84, 128.78, 128.73, 128.39, 127.66, 127.03, 120.48, 120.03, 116.56, 113.86, 111.82, 103.70, 56.73(OCH_3).

N-(4-(2-(2-(4-Chlorophenyl)-1H-indole-3-yl)-4, 5-diaryl-1H-imidazole-1-yl)phenyl)acetamide(12)

Yield: 53% as a yellow solid.

mp: 188-190 ^{0}C;

^{1}H NMR (300 MHz,DMSO-d_6) δ: 11.63 (s,1H), 9.75 (s,1H), 7.50-7.58 (m, 3H), 7.42-7.46 (m, 2H),7.32 (d, *J*=6.0 Hz, 1H), 7.10-7.35 (m,14H), 6.48 (d, *J*=5.7 Hz, 2H), 1.90 (s, 3H)

^{13}C NMR (75 MHz, DMSO-d_6) δ :168.21, 142.11, 138.24, 136.90, 135.98, 135.74, 134.72, 132.48, 131.03, 130.81, 130.68, 130.47, 130.00, 129.67, 128.93, 128.62, 128.58,128.52, 128.45, 128.19, 128.09, 127.50, 127.02, 126.25, 122.35, 119.98, 119.45, 119.32, 117.90,111.43, 103.26, 23.84

EI-MS m/z (%) Calcd.for ($C_{37}H_{27}ClN_4O$) [M$^+$]: 578.18,580.18; Found: 578.04,580.05

RESULTS AND DISCUSSIONS

Imidazoles enjoy an excellent position due to their biological importance. A new series of tetrasubstituted imidazoles containing substituted indoles (**1-12**) (Table 1) was prepared by one pot, four component reaction by cyclization reaction of 2-arylindole-3-carbaldehydes, aromatic amines, benzil and ammonium acetate under reflux in acetic acid **(**Scheme 1). Substituted 2-arylindoles were obtained by Fischer indole synthesis [19]. These were then formylated using Vilsmeir-Haack reaction [20]. The reaction is efficient, rapid, easy and is devoid of formation of hazardous substances.

All these reactions went well with the aniline or anilines substituted with electron donating groups. However, with electron withdrawing groups the reactions failed. For example, the reaction with *p*-nitroaniline, even after

many hours of reflux, only provided a 2,4,5-triarylimidazoleand *p*-nitroacetanilide (which was formed by acetylation during the reaction from acetic acid used as the solvent).In another reaction using *p*-phenylenediamine, a bis tetraarylimiadole or a tetraarylimidazole carrying a p-aminophenyl was expected, however, **12** was isolated from the reaction.Once again the amino group was acylated from the acetic acid solvent.

The structures of these compounds **(1-12)** were characterized on the basis of spectral data. In their HRMS the molecular ion peaks were found to correspond to their expected molecular mass values. The ^{1}HNMR spectra show a down field singlet for –NH of the indole ring in the range of 13–11 and of acetanilide(**12**) at 9.75 ppm The splitting patterns of remaining protons of spectra were as expected according to the substituent. The compounds substituted with –OCH3 (**3, 5, 6, 7** and **9**) showed upfield singlets in the range of 2–4 ppm. The ^{13}CNMR spectra were also as expected. FT-IR and elemental analysis also confirmed the structures.

Mechanism

A probable mechanism of this reaction is given in Scheme 2.

The substituted indole-3-carbaldehyde undergoes a nucleophilic attack by an amino group of the aromatic amine. Removal of a water molecule gives the Schiff's base. Liberated ammonia attacks to give an N-substituted diamine intermediate in a nucleophilic displacement reaction.

This intermediate condenses with diketone to form imino intermediate which rearranges to the tetra substituted imidazole.

CONCLUSIONS

In summary, a series of tetrasubstituted imidazoles derivatives containing 2- phenyl indoles has been synthesized by cyclocondensation of various 2- phenyl indole aldehydes with benzil and ammonium acetate in a one pot reaction.

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REFERENCES

[1] Patel*a* A., Bari*a* S., Talelea G., Patel*a* J., Sarangapani M., Synthesis and Antimicrobial Activity of Some New Isatin Derivatives. *Iran J Pharm Res*, **4**: 249-254 (2006).

[2] Bashir M., Bano A., Ijaz A.S, Chaudhary B.A., Review Recent Developments and Biological Activities of N-Substituted Carbazole Derivatives. *Molecules*, **20**: 13496-13517 (2015).

[3] Guerra A.S.H.S., Diana J.N.M., Laranjeira L.P.M., Maia M.B.S., Colaço .N.C., Lima C.A. Galdino S.L., Pitta I.R., Silva T.G., Anti-Inflammatory and Antinociceptive Activities of Indole–Imidazolidine Derivatives, *Int. J. Immunopharmaco*, **11**: 1816-1822 (2011)

[4] Huesca M., Al-Qawasm R., Young A.H., Lee Y., Aryl Imidazoles and Their use as Anti-Cancer Agents, *US Patent 2008/0262015 A9* (2007).

[5] Tsujii S., Rinehart L.k., Topsentin, Bromotopsentin, and Dihydrodeoxybromotopsentin: Antiviral and Antitumor Bis(indolyl)imidazoles from Caribbean Deep-Sea Sponges of the Family Halichondriidae. Structural and Synthetic Studies, *J. Org. Chem.*, **53**: 5446-5453 (1988).

[6] Na Y.M., Le Borgne M., Pagniez F., Le Baut G., Le Pape P., Synthesis and Antifungal Activity of New 1-halogenobenzyl-3-imidozolylmethylindole Derivatives, *Eur J Med Chem*, **38**: 75-87 (2003).

[7] Kumar N., Sharma P.K., Garg V.K., Singh P., Synthesis and Anticonvulsant Activity of Novel Substituted Phenyl Indoloimidazole Derivatives, *Curr. Res. Chem.*, **3**(2): 114-120 (2011).

[8] Hary U., Roettig U., Michael Paul M., Efficient Synthesis of 3-(4,5-dihydro-1*H*-imidazole-2-yl) -1*H*-indoles, *Tetrahedron Lett.* **42**: 5187–5189 (2001).

[9] Moodya C.J., Jonathan R.A., Roffeya J.A.R., Synthesis of *N*-protected Nortopsentins B., D. *Arkivoc*, (iii), 393-401 (2000).

[10] Marchand P., Borgne M.L., Palzer M., Baut G.L., Hartmann R,W., Preparation and Pharmacological Profile of 7-(α-Azolylbenzyl) -1H-indoles and Indolines as New Aromatase Inhibitors, *Bioorg. Med. Chem .Lett.*, **13**: 1553-1555 (2003).

[11] Berlinck R.G.S., Britton R., Piers E., Lim L., Roberge M., Rocha R.M., Andersen R.J., Granulatimide and Isogranulatimide, Aromatic Alkaloids with G2 Checkpoint Inhibition Activity Isolated from the Brazilian Ascidian *Didemnum granulatum*: Structure Elucidation and Synthesis, *J. Org. Chem.*, **63**: 9850-9856 (1998).

[12] Jagar J.J., Smith V.J., 1-[(1-Methyl-1*H*-imidazol-5-yl)methyl] -1*H*-indole -5-carbonitrile, *Acta Crystatallogr.*, **E68**: 03486(2012).

[13] Sisko J., Kassick A.J., Mellinger M., Filan,J.J., Allen A., Olsen M.A., An Investigation of Imidazole and Oxazole Syntheses Using Aryl-Substituted TosMIC Reagents. *J. Org. Chem.*, **65**(5): 1516–1524(2000).

[14] Biraddar J.S., Somappa S.B., Mugali P.S., One-Pot, Solvent-Free Synthesis of 2,5-Disubstituted Indolylimidazoles by Microwave Irradiation, *Der Pharma Chemica*, **4**(1): 437-441 (2012).

[15] Shaterian H.R., Ranjbar M., An Environmental Friendly Approach for the Synthesis of Highly Substituted Imidazoles Using Brønsted Acidic Ionic Liquid, N-methyl-2-pyrrolidonium Hydrogen Sulfate, as Reusable Catalyst, *J. Mol. Liq.*,**160**: 40-49 (2011).

[16] Shaterian H.R., Ranjbar M., Azizi K., Efficient Multi-Component Synthesis of Highly Substituted Imidazoles Utilizing P_2O_5/SiO_2 as a Reusable Catalyst, *Chinese. J. Chem.*, **29**: 1635-1645 **(**2011).

[17] Naureen S., S. Noreen S., Nazeer A., Ashraf M., Alam U., Munawar M.A., Khan M.A., Triarylimidazoles- Synthesis of 3-(4,5-diaryl-1H-imidazol-2-yl)-2-phenyl-1H-indole Derivatives as Potent a-Glucosidase Inhibitors, *Med. Chem. Res.*, **24**(4): 1584e1595 (2015).

[18] Naureen S., Chaudhry F., Asif N., Munawar M.A., Ashraf M., Nasim F.H., Arshad H., Khan M.A., Discovery of Indole-Based Tetraarylimidazoles as Potent Inhibitors of Urease with Low Antilipoxygenase Activity, *Eur. J. Med. Chem.*, **102**: 464e470 (2015).

[19] Robinson B., The Fischer Indole Synthesis, *Chem. Rev.*, **63**: 373-401 (1963).

[20] Jones G., Stanforth *S*.P., The Vilsmeier Reaction of Non-Aromatic Compounds, *Organic Reactions*, 355-686 (2004).