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Synthesis of new 2-(((5-Substituted-1H-benzo[d]imidazol-2-yl)methyl)amino)-1-(2-phenyl-1H-Indol-1-yl)ethanones and their antimicrobial activity

DirisinalaPunna Reddy[1], Dr. Rakesh Jat , Dr. Naveen Kumar Podila*

*Department of Chemistry, Shri JagdishprasadJhabarmalTibrewala University is a university in Jhunjhunu, India.**

Email: podilanaveen49@gmail.com

Email:dpunnareddy@gmail.com

Abstract

synthesized fourteen derivatives of new 2-(((5-substituted-1H-benzo[d]imidazole-2-yl)amino)-1-(2-phenyl-1H-indol-1-yl)ethanones (**5a-n**)were prepared from the condensation of 2-chloro-1-(2-phenyl-1H-imidazol-1-yl)ethan-1-one (**3**) with (5-substituted-1H-benzo[d]imidazole-2-yl)methanamines(**4a-n**).2-Chloro-1-(2-phenyl-1H-imidazol-1-yl)ethan-1-one (**3**)is prepared from the reaction of 2-phenyl indole(**1**) with chloroacetyl chloride(**2**) in presence of pyridine. All the synthesized compounds(**5a-n**) were characterized by IR, ^{1}HNMR, ^{13}CNMR and Mass spectral data. All the fifteen derivatives(**5a-n**) were screened for their antimicrobial properties against a broad panel of Gram-positive and Gram-negative bacteria as well as Fungi.

Keywords:N-(1H-indol-5-yl)-2-(((5-substituted-1H-benzo[d]imidazol-2-yl)methyl)amino)acetamides, Substituted benzimidazole methanamine, Chloroacetyl chloride, 2-Phenyl imdole.

INTRODUCTION:

An indole is characterized as a benzene ring fused with nitrogen containing five membered heterocyclic rings. Indoles are of interest in many pharmaceutical areas, since they exhibit a variety of biological properties[1-4].A number of C-3,C-5-substituted indoles were synthesized and studied for their biological affinities[5] . Indole sulfonamide derivatives of (cyclopentyl (3-(2-methoxy-4-((o-tolylsulfonyl)carbamoyl)benzyl)-1-methyl-1H-indol-5-yl)carbamate) act as human Anti-asthamatic[6].

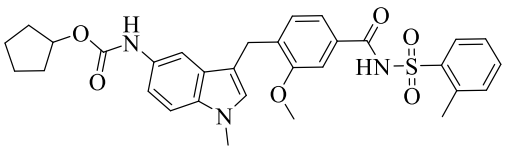


Fig-1

(1-(3-(2-(dimethylamino)ethyl)-1H-indol-5-yl)-N-methylmethanesulfonamide) for the treatment of migraine and cluster headaches.

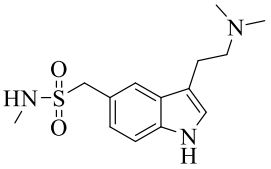


Fig-2

(5-(4-(4-(5-cyano-1H-indol-3-yl)butyl)piperazin-1-yl)benzofuran-2-carboxamide)

actasantidepressant.

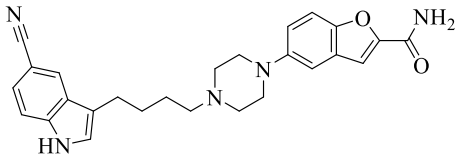


Fig-3

Benzimidazoles are nitrogen containing heteocyclic compounds. These fragments occur in many synthetic and natural products, which are used clinically as drugs, pesticides[7] and Fungicides as well as oral anti-coagulant[8] and rodenticides[9].

4'-((1,7'-dimethyl-2'-propyl-1H,3'H-[2,5'-bibenzo[d]imidazol]-3'-yl)methyl)-[1,1'-biphenyl]-2-carboxylic acid comprises the structural nucleus of benzimidazole derivative for the treatment of anti-hypertensive. Several 2-substituted benzimidazole derivatives, especially those with nitrogen function are endowed with potential therapeutic properties[13].

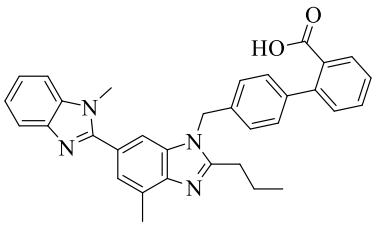


Fig-4

The screening of the protease inhibitory activity of various substituted benzimidazole derivatives 2-((5-methyl-1H-benzo[d]imidazol-2-yl)thio)-1-(4-(p-tolyl)piperazin-1-yl)ethan-1-one(Fig-5),1-(4-benzhydrylpiperazin-1-yl)-2-((5-methyl-1H-benzo[d]imidazol-2-yl)thio)ethan-1-one(Fig-6),1-(4-(4-chlorophenyl)piperazin-1-yl)-2-((5-methyl-1H-benzo[d] imidazole-2-yl)thio)ethan-1-one (Fig-7) and 2-((1H-benzo[d]imidazol-2-yl)thio)-1-(4-(4-chlorophenyl)piperazin-1-yl)ethan-1-one (Fig-8) was performed. The data indicates the importance of substituents at positions 2 and 5 of the benzimidazole ring [14].

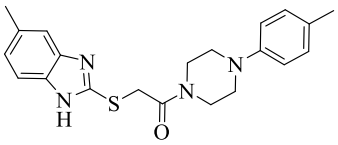


Fig-5

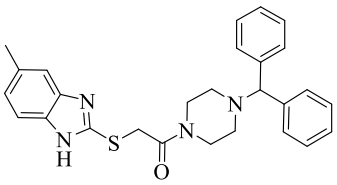


Fig-6

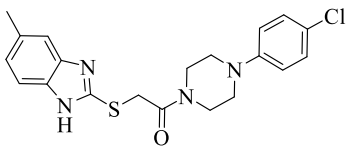


Fig-7

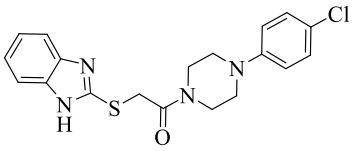
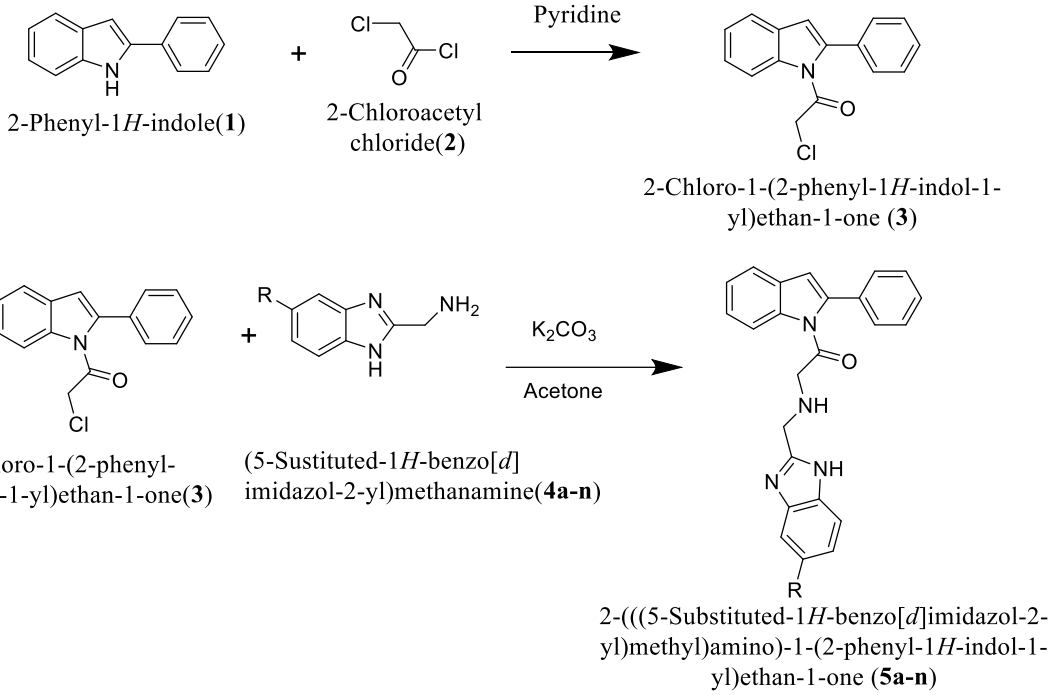


Fig-8

1H-indoleframe work is responsible biological activities such as anti-inflamatory, anti-allergic, anti-migraine and anti-pyretic activities. 1H-benzo[d]imidazole moiety shows activities such as antifungal, anti-coagulant, antibacterial and insecticide. The biological importance and considerable therapeutic potential of above two moieties generate considerable interest to us in designing the synthesis of N-(1H-indol-5-yl)-2-(((5-substituted-1H-benzo[d]imidazol-2-yl)methyl)amino)acetamides.The 2-phenylindole was used as a starting material for making all the title compounds.

As a part of our synthetic program directed towards the synthesis of N-(1H-indol-5-yl)-2-(((5-substituted-1H-benzo[d]imidazol-2-yl)methyl)amino)acetamides(**5a-n**),2-phenyl indole(**1**) was used

as a starting material, which was converted into of 2-chloro-1-(2-phenyl-1H-imidazol-1-yl)ethan-1-one (**3**) by reacting 2-phenyl indole(**1**) with chloroacetyl chloride(**2**) in presence of pyridine.On condensation of 2-chloro-1-(2-phenyl-1H-imidazol-1-yl)ethan-1-one (**3**) with (5-substituted-1H-benzo[d]imidazole-2-yl)methanamines(**4a-n**) in presence of dry potassium carbonate in acetone yields N-(1H-indol-5-yl)-2-(((5-substituted-1H-benzo[d]imidazol-2-yl)methyl)amino)acetamides(**5a-n**) described in the following scheme.



Compound	R
5a	-H
5b	$-CH_3$
5c	-Br
5d	-Cl
5e	-F
5f	$-NO_2$
5g	-CN
5h	$-OCH_3$
5i	$-COOCH_3$
5j	$-C_2H_5$
5k	$-CH_2C_6H_5$
5l	$-CH(CH_3)_2$
5m	$-OCH_2C_6H_5$

5n	$-C(CH_3)_3$

Anti bacterial activity:

The antibacterial activity was carried out by testing all the synthesized compounds against Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus and bacillus subtilis .The compounds were dissolved in acetone at a concentration of 100 µg/ml .The agar medium(nutrient agar for bacteria and Saboured agar for fungi) was inoculated with 1ml of 18hr. old culture of the test organism. Filter paper discs (5mm diameter) saturated with a solution of the test compound(100µg/ml) were placed on the agar. After an incubation period of 36hrs., the zone of inhibition around the discs were measured. Acetone, which exhibited no antibacterial activity against the test organisms, was used as a negative control and ampicillin discs as antibacterial reference standard.

Almost all the compounds showed moderately to highly active, that could be attributed to the presence of imidazole and indole heterocyclic ring systems with their high potency. The compound **5e,5f and 5i** shows high activity with all strains of bacteria.The compounds **5a, 5c, 5d, 5g**, 5k and **5l**are highly active against B.Subtilis and S.Aureus; moderately active against P.aeruginosa and E.Coli. The remaining compounds were showed moderately active against all strains.

Table No. 2

S.No	Compound	R	B.subtilis	S.aureus	P.aeruginosa	E.coli
1	5a	-H	15	17	12	12
2	5b	$-CH_3$	11	10	14	16
3	5c	-Br	15	15	11	11
4	5d	-Cl	17	16	13	13
5	5e	-F	19	20	16	16
6	5f	$-NO_2$	22	21	19	19
7	5g	-CN	17	17	13	13
8	5h	$-OCH_3$	14	14	10	10
9	5i	$-COOCH_3$	18	18	20	19
10	5j	$-C_2H_5$	15	14	14	14
11	5k	$-CH_2C_6H_5$	15	15	11	12
12	5l	$-CH(CH_3)_2$	16	16	13	13
13	5m	$-OCH_2C_6H_5$	15	15	12	12
14	5n	$-C(CH_3)_3$	13	12	10	10
12	Ampicillin		24	26	22	25

Key to symbols: - inactive (inhibition zone < 6 mm); slightly active = + (inhibition zone 7–9 mm); moderately active = + +(inhibition zone 10-14 mm); highly active = + + + (inhibition zone > 14 mm).

Antifungal activity. The antifungal activity of the synthesized compounds **5a-n** against Aspergillousniger and Candida albicans , using fluconazole as standard (Table-3). Compounds **5a, 5f** and **5k** were showed highly active against both the strains. The remaining compounds were slightly to moderately active against both strains.

Table no 3. Antifungal activity of the test compounds 5a-n

S.No	Compound	Aspergillus niger	Candida albicans
1	5a	15(++)	15(++)
2	5b	11(++)	10(++)
3	5c	11(++)	10(++)
4	5d	07(+)	08(+)
5	5e	08(++)	10(++)
6	5f	16(+)	16(+)
7	5g	08(+)	08(+)
8	5h	11(++)	11(++)
9	5i	13(++)	13(++)
10	5j	12(++)	11(++)
11	5k	17(+++)	18(+++)
12	5l	12(+)	13(+)
	5m	09(+)	08(+)
	5n	11(+)	11(+)
13	Fluconazole	22(+++)	19(+++)

Key to symbols: - inactive (inhibition zone < 6 mm); slightly active = + (inhibition zone 7–9 mm); moderately active = + + (inhibition zone 10-13 mm); highly active = + + + (inhibition zone > 14 mm).

EXPERIMENTAL PROCEDURE:

2-Chloro-1-(2-phenyl-1H-indol-1-yl) ethanone:

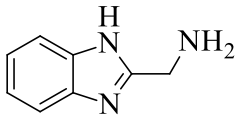
A mixture of 2-phenyl-1H-indole (0.01 mol), chloroacetylchloride (1.0 m.eq) and pyridine (1 ml) in toluene (50 ml) is reflux at 100-105ºC for 10-16hrs. After 2-phenyl completely absent by TLC, distilled off toluene from the reaction mixture till no more solvent distills. Add ethanol (60 ml) to the precipitate and stir at 25-30ºC for 1hr. was Filter the solid and wash it with ethanol (10ml) and dry the compound at 50-55ºC for 5hrs till LOD is less than 1.0%. Yield : 75-80%, m.p.165-168°C. IR

(KBr, cm-1) ν: 3100 (CH aromatic), 2910 (CH aliphatic) and 1692 (C=O), 1H NMR (DMSO-d6) δ ppm: 4.80 (s, 2H, CH2), 6.90 (s, 1H, Ar-H), 7.20-7.26 (m, 2H, Ar-H), 7.23-7.29 (m, 2H, Ar-H), 7.40-7.47 (m, 3H, Ar-H), 7.85-7.91 (m, 2H, Ar-H). MS m/z: 269 (100%)

General procedure for the preparation of (5-substituted-1H-benzo[d]imidazol-2-yl)methanamine(4a-n):

Charge 4N HCl (8 vol) in round bottom flask. Add 5-substituted phenylenediamine (1 mol. Eq) and glycine (1.1 moleq) at RT. Reaction mass heat to 95 – 100°C. Stir the reaction mass for 12 – 18 hours. After completion of reaction cool the reaction mass to room temperature. Reaction mass pH adjust with 20% NaOH solution for pH neutral. Solid formed. Reaction mass cool to 0 – 5°C and stir for 1 hr at 0 – 5°C. Filter the reaction mass and washwd with Water (2 vol). Product is purified by column chromatography (Hexane : Ethyl acetate 7:3). Yield : 45 – 50%.

Compound 4a:(1H-benzo[d]imidazol-2-yl)methanamine:

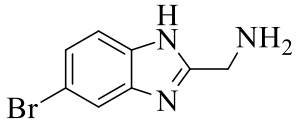


Yield: 89%, M.P.: 139.6-140.4 ºC; 1H NMR (δ): 1.32 (2H, s, NH2), 3.96 (2H, s, CH2), 7.11-7.18 (2H, m, Ar-H), 7.50-7.54 (2H, m, Ar-H), 12.20 (1H, b, NH of imidazole); FAB Mass:m/z 148 ([M + H]+; CHN analysis : Found: C(65.22%); H(6.04%); N(28.74%); Calc : C (65.29%); H (6.16%); N (28.55%).

Compound 4b: (5-methyl-1H-benzo[d]imidazol-2-yl)methanamine:

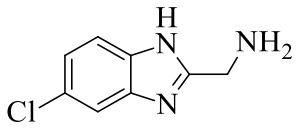
Yield : 60%; M.P. : 230 - 232°C; ^{1}H-NMR(δ) : 12.02(1H, bs, Imidazole N-H), 7.01- 7.44(3H, m, Ar-H),5.65(2H, bs, $-NH_2$), 2.88(2H, s, $-CH_2-$), 2.34(3H, s, $-CH_3$); IR : 3373. 3356 cm^{-1}($-NH_2$),3030(C-H of Aromatic), 2660, 2768(C-H),1640(C=O), 1455, 1590 (C=C); FAB Mass:m/z 162.0 (M+1) CHN analysis : Found: C(67.06%); H(6.88%); N(26.07%); Calc : C(67.12%), H(6.79%), N(26.09%).

Compound 4c:(5-bromo-1H-benzo[d]imidazol-2-yl)methanamine:



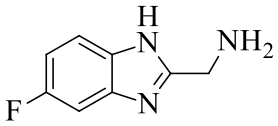
Yield :16%; M.P.: 259- 261°C; ^{1}H-NMR (δ) : 12.43(1H, bs, -NH), 7.40 – 7.86(3H, m, Ar-H), 6.42(2H, bs, -NH_2), 3.56(2H, s, -CH_2); IR :3342 cm^{-1}(-NH_2),
3053 cm^{-1} (Aromatic C-H), 2853cm^{-1}(Aliphatic C-H), 1073cm^{-1}(C-Br); FAB Mass:m/z 226.0 (M+1), 228(M+2); CHN analysis : Found: C (42.48%); H (3.55%); Br (35.36%); N (18.61%); Calc :C (42.50%); H (3.57%); Br (35.34%); N (18.59%).

Compound 4d:(5-chloro-1H-benzo[d]imidazol-2-yl)methanamine:



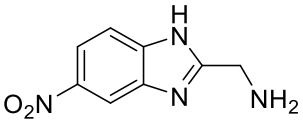
Yield : 66%; M.P. : 252 - 254°C; ^{1}H-NMR (δ): 12,13(1H, bs, -NH), 7.33 – 7.63(3H, m, Ar-H), 4.30(2H, s, -CH_2-), 5.85(1H, s, Imidazole-NH); IR : 3376 cm^{-1}(N-H), 3047 cm^{-1} (Aromatic C-H), 2842cm^{-1}(Aliphatic C-H), 1112 cm^{-1}(C-Cl); FAB Mass:m/z 181.0 (M^+); CHN analysis : Found: C(52.88%); H (4.42%); Cl(19.54%); N (23.16%); Calc : C(52.90%); H (4.44%); Cl(19.52%); N (23.14%).

Compound 4e:(5-fluoro-1H-benzo[d]imidazol-2-yl)methanamine:



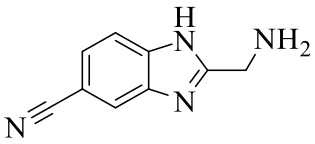
Yield :34%; M.P.: 262-264°C; ^{1}H-NMR (δ): 12.60(2H, s, -NH_2), 6.97 – 7.57(3H, m, Ar-H),6.30(1H, s, Imidazole -NH),3.72(2H, s, -CH_2); IR : 3415 cm^{-1}(N-H),
2998 cm^{-1}, (C-H aromatic), 2858cm^{-1}(C-H aromatic), 1140cm^{-1} (C-F); FAB Mass:m/z 166.0 (M+1); CHN analysis : Found: C (58.19%); H (4.90%); F (11.48%); N (25.42%); Calc :C (58.17%); H (4.88%); F (11.50%); N (25.44%).

Compound 4f:(5-Nitro-1H-benzo[d]imidazol-2-yl)methanamine:



Yield : 40%; M.P.: 248-251°C; ^{1}H-NMR (δ): 11.60(1H, s, Imidazole-NH), 8.34-8.42(2H, dd, -Ar-H), 8.10 (1H, s, Ar-H),6.30(1H, s, -NH_2),4.12(2H, s, -CH_2); IR : 3402 cm^{-1}(N-H), 2979 cm^{-1}, (C-H aromatic), 2856cm^{-1}(C-H aromatic), 1509cm^{-1} and 1350 (-NO_2); FAB Mass:m/z 193.1 (M+1); CHN analysis : Found: C (49.9%); H (3.99%); N (30.2%); Calc :C (50.00%); H (4.20%); N (29.15%).

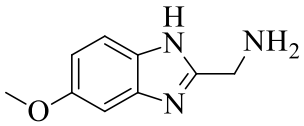
Compound 4g:2-(Aminomethyl)-1H-benzo[d]imidazole-5-carbonitrile



Yield : 42% M.P. : 230.0° - 232.0°C; ^{1}H-NMR (δ) : 10.99(1H, bs, Imidazole),), 6.93- 7.48(3H, m, Ar-H), 5.68(2H, bs, -NH_2), 3.82(2H, s, -CH_2), 3.83; IR : 3388cm^{-1}(N-H), 3053 cm^{-1} (aromatic C-H),2225 cm^{-1} (-CN); FAB Mass:m/z 173.0 (M+1)

CHN analysis : Found: C (62.80%); H (4.72%); N (32.48%); Calc :C (62.78%); H (4.68%); N (32.54%).

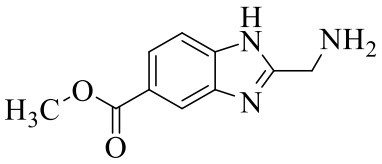
Compound 4h:(5-methoxy-1H-benzo[d]imidazol-2-yl)methanamine:



Yield :42% M.P. : 201 - 203°C; ^{1}H-NMR (δ) : 11.76(1H, bs, Imidazole), 7.05- 7.54(3H, m, Ar-H), 6.31(2H, bs, -NH_2), 3.35(2H, s, -CH_2), 3.98(3H, s, -OCH_3

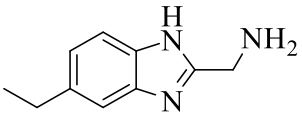
IR :3416 cm^{-1}(N-H), 3022 cm^{-1}, 3049 cm^{-1} (C-H);FABMass:m/z 178.0 (M+1); CHN analysis : Found: C(61.02%); H(6.29%); N(23.68%);O (9.01%); Calc : C (61.00%); H (6.26%); N (23.71%); O(9.03%).

Compound 4i: Methyl 2-(aminomethyl)-1H-benz[d]imidazole-5-carboxylate:



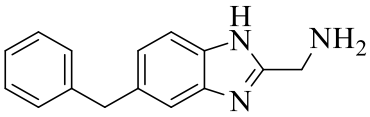
Yield : 33%; M.P. : 226 - 228°C; ^{1}H-NMR (δ) : 12.20(1H, bs, Imidazole-NH), 7.70-7-89(2H, dd, Ar-H), 8.13(1H, s, Ar-H), 6.20(2H, bs, -NH_2), 3.89(3H, s, -OCH_3), 3.53(2H, s, -CH_3). IR :3410 cm^{-1}(N-H), 3066, 3034 cm^{-1} (Aromatic C-H),2933cm^{-1}(C-H Aliphatic), 1730cm^{-1}(C=O), 1602cm^{-1}(C=C);FABMass:m/z 206.1 (M+1); CHN analysis : Found: C(58.10%); H(4.99%); N(20.80%); Calc :C (58.53%); H(5.40%); N (20.48%).

Compound 4j:(5-Ethyl-1H-benzo[d]imidazol-2-yl)methanamine:



Yield : 50%; M.P. :211.0° - 213.0°C; ^{1}H-NMR (δ) :12.17(1H, bs, Imidazole-NH),), 7.19 – 7.60(3H, m, Ar-H), 6.34(2H, bs, -NH_2); 3.78(2H, bs, -NH_2); 2.58(2H, q, -CH2),1.23(3H, t,-CH3); IR : 3395 cm^{-1}(N-H), 3035cm^{-1} (C-H Aromatic); FAB Mass:m/z 176.0 (M+1); CHN analysis : Found: C (68.21%); H (7.50%); N (24.00%); Calc :C (68.54%); H (7.48%); N (23.98%).

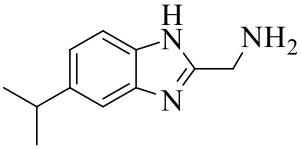
Compound 4k:(5-((4-fluorobenzyl)oxy)-1H-benzo[d]imidazol-2-yl)methanamine:



Yield : 34%; M.P. : 222-224°C ; ^{1}H-NMR (δ) : 12.17(1H, bs, -NH),7.13 – 7.45(8H, m, Ar-H).6.10(2H, bs, -NH_2),4.12(2H, s, -CH_2), 3.33(2H, s, -CH_2);

IR :3426 cm^{-1}(N-H), 3022 cm^{-1} - 3049 cm^{-1} (aromatic C-H) ; FAB Mass:m/z 238.1(M+1) ; CHN analysis : Found: C(75.84%); H (5.20%); N(14.96%); Calc : C(75.92%); H (6.37%); N(17.71%).

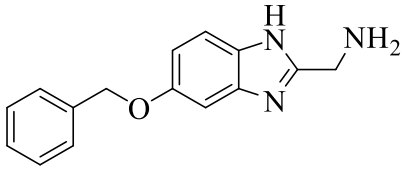
Compound 4l:(5-Isopropyl-1H-benzo[d]imidazol-2-yl)methanamine:



Yield :45%; M.P. : 227.0° - 229.0°C

^{1}H-NMR (δ) : 12.44(1H, bs, Imidazole-NH), 7.23 – 7.82(3H, m, Ar-H), 6.26(2H, bs, -NH_2), 3.23(2H, s, -CH_2), 2.93(1H, m, -CH), 1.19(6H, d, 2x –CH_3); IR : 3395 cm^{-1}(N-H), 3056 cm^{-1} (Aromatic C-H); FAB Mass:m/z 190.3 (M+1); CHN analysis : Found: C (55.90%); H (4.09%); Cl(22.05%); N(13.02%); O (4.95%); Calc :C (69.81%); H (7.99%); N(22.20%).

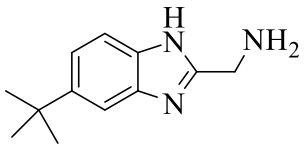
Compound 4m:(5-(difluoromethoxy)-1H-benzo[d]imidazol-2-yl)methanamine:



Yield :36%; M.P. :238.0° - 240.0°C;^{1}H-NMR (δ) : 12.35(1H, bs, Imidazole-NH), 7.10 – 7.64(3H, m, Ar-H), 6.42(2H. bs, -NH_2), 5.20(2H, s, -CH_2 of benzyl). 3.26(2H, s,-CH_2) ; IR : 3406 cm^{-1}(N-H),

3017 cm^{-1} - 3036 cm^{-1} (Aromatic C-H), 1012cm^{-1}(C-O); FABMass:m/z 254.1 (M^+); CHN analysis : Found: C(70.98%); H (5.86%); N (17.00%).
Calc : C(71.13%); H (5.97%); N (16.59%).

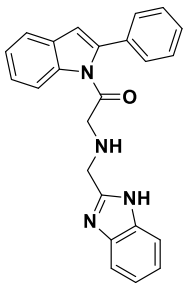
Compound 4n:(5-(tert-butyl)-1H-Benzo[d]imidazol-2-yl)methanamine:



Yield :48%; M.P. : 215.0- 217.0°C; ^{1}H-NMR (δ) : 12.18(1H, bs, Imidazole-NH), 7.08 – 7.62(3H, m, Ar-H); 5.98(2H, bs, -NH_2), 1.28(9H, s, 3x-CH_3), IR : 3376 cm^{-1}(N-H), 3039 cm^{-1} (Aromatic C-H); FAB Mass:m/z 204.14 (M+1); CHN analysis :Found: C (69.98%); H (8.38%); N (21.50%); Calc :C (70.90%); H (8.43%); N (20.67%).

General Procedure for the preparation of N-(1H-indol-5-yl)-2-(((5-substituted-1H-benzo[d]imidazol-2-yl)methyl)amino)acetamides(5a-n): Charge isopropyl alcohol (6 vol) in a RBF. Add (5-substituted benzo[d]oxazol-2-yl)methanamine or (5-substituted benzo[d]thiazol-2-yl)methanamine (or) (5-substituted-1H-benzo[d]imidazol-2-yl)methanamine (1.0 m.eq), 2-chloro-N-(1H-indol-5-yl)acetamide (1.0 m eq) , Cu_2O (1.0 m eq) and KOH (1.5 m eq) at RT. RM heat to 80 – 85°C. Stir the RM for 12 - 18 hours at 80 – 85°C. After completion of reaction filter RM on celite bed and wash with Isopropyl alcohol (2 vol). Take filtrate and distill at 80°C completely. Add 5 vol water at RT. And stir for 1 hour filter RM and wash with Water. Product is purified by column chromatography (Hexane : Ethyl acetate 8:2). Yield: 60 – 65%.

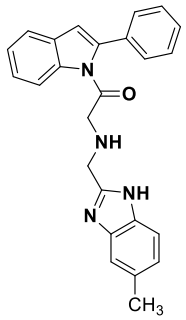
Compound 5a: 2-(((1H-benzo[d]imidazol-2-yl)methyl)amino)-N-(1H-indol-5-yl) acetamide:



Yield : 45%; M.P. : 183-187°C; ^{1}H-NMR (δ) : 12.40(1H, bs, ImidazoleNH), 7.09-7.68 (12H, m, Ar-H), 8.16 (1H, *ddt, Ar-H),*4.83 (1H, bs, -NH)), 4.20 (2H, bs, -CH_2), 3.66(2H, s, -CH_2); ^{13}CNMR(δ): 43.2, 44.7, 101.6, 112.0, 114.3, 118.4, 120.6, 126.8, 127.8,128.2, 128.3, 128.5, 132.8,

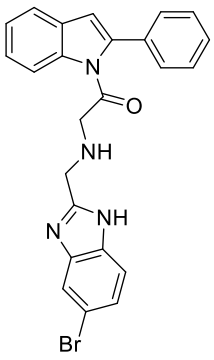
135.7, 137.9, 138.4, 150.9 and 168.2.FAB Mass : m/z 381.2(M+1); CHN analysis : Found: C(75.68%); H (4.95%); N (14.93%) ; Calc :C(75.77%); H (5.30%); N (14.73%).

Compound 5b:2-(((5-methyl-1H-benzo[d]imidazol-2-yl)methyl)amino)-1-(2-phenyl-1H-indol-1-yl)ethan-1-one:



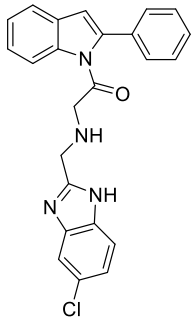
Yield : 52%: M.P. : 212-213ºC; ^{1}H-NMR (δ) : 2.34(3H, s, -CH_3), 3.60(2H, s, -CH2), 4.30(2H, s, -CH_2), 5.15(1H, bs, Sec. Amine), 7.00-7.18(2H, dd, Ar-H), 7.25-7.70(10H, m, Ar-H), 8.15(1H, m, Ar-H);^{13}CNMR(δ): 21.3, 43.2, 44.7, 101.6, 112.0, 114.7, 117.4, 120.6, 126.8, 127.8, 127.9, 128.2, 128.3, 128.5, 132.8, 133.7, 135.7, 136.3, 138.4, 141.4, 150.9, 168.9 IR :1685 cm^{-1}, 3020 cm^{-1}, 3420 cm^{-1}; FAB Mass : m/z 395.3(M+1); CHN analysis : Found: C (75.95%); H (5.26%); N (15.00%); Calc :C (76.12%); H (5.62%); N (14.20%).

Compound 5c: 2-(((5-Bromo-1H-benzo[d]imidazol-2-yl)methyl)amino)-1-(2-phenyl-1H-indol-1-yl)etham-1-one:



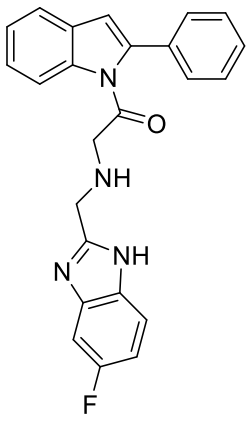
Yield :55%; M.P. : 207-208ºC; ^{1}H-NMR (δ) : 3.63(2H, s, -CH_2), 3.96(2H, s, -CH_2), 4.20(1H, bs, -NH), 7.08(1H, dd, Ar-H), 7.20-7.68(11H, m,Ar-H), 8.19 (1H, m, Ar-H), 12.17(1H, bs, imidazole-NH); ^{13}CNMR(δ) : 42.8, 44.9, 101.8, 112.1, 116.3, 117.5, 120.0, 120.4, 126.8, 127.5, 128.2, 128.3, 128.4, 128.5, 131.7, 132.0, 135.7, 138.4, 141.0, 141.4, 150.9, 168.2.IR :1130 cm-1, 1675 cm^{-1}, 3430 cm^{-1}, 3050cm^{-1}; FAB Mass : m/z 459.1 (M+1), 460.2(M+2); CHN analysis : Found: C (62.76%); H (4.17%); N (12.20%); Calc :C (62.55%); H (3.87%); N (13.02%).

Compound 5d: 2-(((5-Chloro-1H-benzo[d]imidazol-2-yl)methyl)amino)-1-(2=phenyl-1H-indol-1-yl)ethan-1-one:



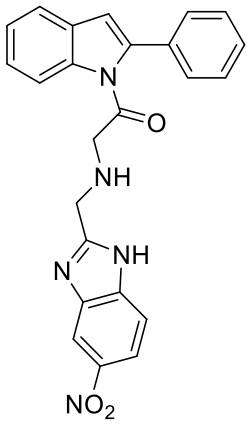
Yield : 39%; M.P. : 237-238°C; ^{1}H-NMR (δ) : 3.73(2H, s, -CH_2), 3.93(2H, s, -CH_2), 4.30(1H, bs, -NH), 7.03-7.11(1H, dd, Ar-H), 7.25-7.69(11H, m, Ar-H), 8.14(1H, m, Ar-H), 12.22(1H, bs, Imidazole-NH);^{13}CNMR:42.9, 45.3, 101.5, 112.0, 117.6, 119.4, 120.6, 126.9, 127.8, 127.9, 128,2, 128.3, 128.4, 128.5, 128.9, 132.3, 136,0, 138.2, 140.9, 150.8, 168.4; IR : 1663 cm^{-1}, 3428 cm^{-1}, 3636 cm^{-1}; FAB Mass : m/z 415.2(M+1), 417.1(M+2); CHN analysis : Found: C (68.95%); H (4.43%); N(13.85%); Calc :C (69.48%); H (4.162%); N(13.50%).

Compound 5e: 2-(((5-Fluoro-1H-benzo[d]imidazol-2-yl)methyl)amino)-1-(2-phenyl-1H-indol-1-yl)ethan-1-one:



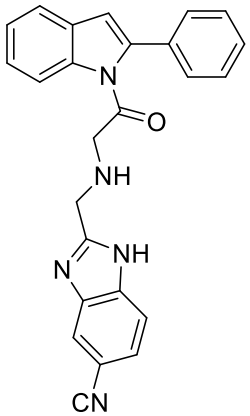
Yield : 24%; M.P. : 176-178°C; ^{1}H-NMR (δ) :3.59(1H, s, -CH_2), 4.18(1H, bs, -NH), 4.30(2H, s, -CH_2), 7.09-7.14(1H, dd, Ar-H), 7.27-7.60(11H, m, Ar-H), 8.15-8.20(1H, m, Ar-H), 12.11(1H, bs, imidazole-NH); 43.0, 45.2, 102.0, 108.2, 112.0, 116.0, 117.6, 120.6, 126.5, 127.8, 127.9, 128.2, 128.3, 128.4, 132.7, 135.5, 138.3, 141.0, 150.9, 160.6, 168.4 IR :1140 cm^{-}1, 1656 cm^{-1}, 3432 cm^{-1}, 3640 cm^{-1}; FAB Mass :m/z 399.2 (M+1), CHN analysis : Found: C (71.95); H (4.21%); N (13.11%).Calc :C (72.35); H (4.81%); N (14.06%).

Compound 5f: 2-(((5-Nitro-1H-benzo[d]imidazol-2-yl)methyl)amino)-1-(2-phenyl-1H-indol-1-yl)ethan-1-one:



Yield :34%; M.P. : 188-190°C; ^{1}H-NMR (δ) : 3.65(2H, s, -CH_2), 4.16(1H, bs, -NH), 4.29(1H, s, -CH_2), 7.28-7.73(10H, m, Ar-H), 8.23-8.30(1H, m, Ar-H), 8.42-8.48(1H, dd, Ar-H), 11.98(1H, bs, Imidazole-NH); ^{13}C-NMR(δ): 43.8, 45.6, 102.0, 111.3, 112.0, 114.3, 121.2, 125.0, 127.0, 128.0, 128.2, 128,3, 128.5, 133.0, 136.0, 138.4, 141.4, 143.0,144.0, 151.0, 168.34. IR :1120 cm^{-}1, 1646 cm^{-1}, 3430 cm^{-1}, 3644 cm^{-1}; FAB Mass : m/z 426.2 (M+1); CHN analysis : Found: C (67.69%); H (3.99%); N (16.98%).Calc :C (67.76%); H (4.50%); N (16.46%).

Compound 5g: 2-(((2-Oxo-2-(2-phenyl-1H-indol-1-yl)ethyl)amino)methyl-1H-benzo[d]-imidazole-5-carbonitrile:

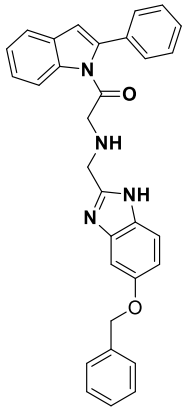


Yield : 44%; M.P. : 212-213°C; ^{1}H-NMR (δ) : 3.86(1H, s, -CH2), 4.16(1H, s, -NH), 4.49(1H, s, -CH_2), 6.86-7.90(11H, m, Ar-H),8.02(1H, s, Ar-H), 8.24-8.32(1H, m, Ar-H) 12.05(1H, bs, imidazole-NH);^{13}C-NMR(δ): 44.2, 45.6, 102.1, 111.5, 112.3, 114.6, 118.3, 119.1, 121.0, 127.1, 127.8, 127.9, 128,3, 128.5, 133.0, 134.1, 135.8, 136.2, 138.3,141.2, 151.2, 169.1 IR : 1128 cm^{-}1, 1660 cm^{-1}, 2220, 3387 cm^{-1}; FAB Mass : m/z 406.3 (M+1); CHN analysis : Found: C (73.89%); H (4.16%); N (17.98%).Calc :C (74.06%); H (4.72%); N (17.27%).

Compound 5h: 2-(((5-methoxy)-1H-benzo[d]imidazol-2-yl)methyl)amino)-1-(2-phenyl-1H-indol-1-yl)ethan-1-one:

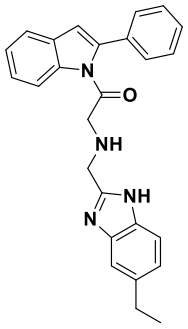
Yield : 40%; M.P. :196-198^{o}C; ^{1}H-NMR (δ) : 3.55(2H, s, -CH_2), 3.65(3H, s, -OCH_3), 4.14(2H, s, -CH2), 4.29(1H, bs, -NH), 4.30(2H, d, -CH2), 6.89-7.16(3H, dd, Ar-H), 7.27-7.60(9H, m, Ar-H), 8.18-8.22(1H, m, Ar-H), 12.05(1H, bs, imidazole-NH); ^{13}CNMR(δ):43.1, 45.3, 56.0, 101.1, 102.0, 112.0, 114.6, 116.8, 120.6, 127.0, 128.0, 128.3, 128.4, 128.5, 133.0, 136.2, 138.2, 141.0, 141.4, 151.2, 168.2. IR :1036 cm^{-}1, 1684 cm^{-1}, 3430 cm^{-1}, 3648 cm^{-1}; FAB Mass : m/z 411.5 (M+1); CHN analysis : Found: C(72.76%), H(5.64%), N(13,94%)xn; Calc : C(73.15%), H(5.40%), N(13.65%).

Compound 5i: 2-(((2-oxo-1(2-pheny-1H-indol-1-yl)ethyl)amino)methyl)-1H-benzo[d] imidazole-5-carboxylate:



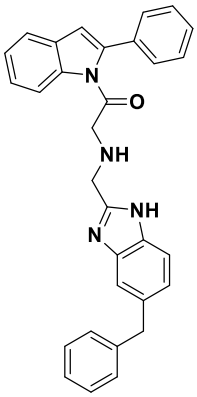
Yield : 24%; M.P. : 182-183^{o}C; ^{1}H-NMR (δ) : 3.58(1H, s, -CH_2), 3.98(3H, s, -CH_3), 4.23(1H, bs, -NH), 4.40(2H, s, -CH_2), 7,19-7.67(10H, m, Ar-H), 7.90-7.95(1H, m, Ar-H), 8.05-8.27(2H, m, Ar-H), 12.11(1H, bs, imidazole-NH);^{13}CNMR(δ):43.0, 44.8, 52.5, 101.8, 112.0, 115.0, 121.1, 127.2, 127.8, 128.0, 136.1, 136.3, 138.4, 142.3, 151.2, 166.1, 169.5 IR : 1012 cm^{-}1, 1686cm^{-1},1748 cm^{-1}, , 3390 cm^{-1}; FAB Mass : m/z 439.2.0(M+1); CHN analysis : Found: C (70.89%); H (4.86%); N (13.38%); Calc :C (71.22%); H (5.06%); N (12.78%).

Compound 5j: 2-(((5-Ethyl-1H-benzo[d]imidazol-2-yl)methyl)amino)-1-(2-phenyl-1H-indol-1-yl)ethan-1-one:



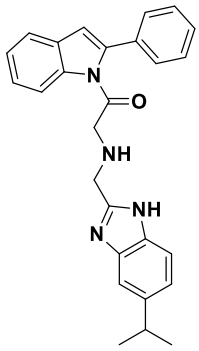
Yield :32%; M.P. : 224-225°C; ^{1}H-NMR(δ) :1.15(3H, t, -CH3),2.73(2H, q, -CH2), 3.54(2H, s, -CH_2), 4.10(1H, bs, -NH), 4.29(2H, s, -CH_2), 6.96-7.12(2H, dd, Ar-H),7.24-7.69(10H, m, Ar-H), 8.05-8,10(1H, m, Ar-H), 11.96(1H, bs, Imidazole-NH);13CNMR(δ) : 15.0, 29.0, 42.8, 45.4, 101.3, 119.0, 120.1, 126.6, 127.7, 127.9, 128.2, 128.4, 128.5, 129.2, 133.0, 136.0, 136.3, 138.4, 141.3, 145.4, 151.0, 168.2; IR : 1650 cm^{-1}, 3428 cm^{-1}, 3646 cm^{-1}; FAB Mass : m/z 409.2.0 (M+1); CHN analysis : Found: C (75.98%); H (5.63%); N (13.94%); Calc :C (76.45%); H (5.93%); N (13.72%)

Compound 5k: 2-(((5-benzyl-1H-benzo[d]imidazol-2-yl)methyl)amino)-1-(2-phenyl-1H-indol-1-yl)ethan-1-one:



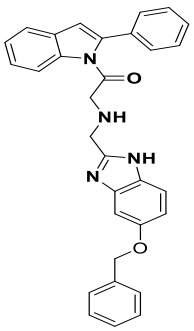
Yield : 35%; M.P. :181-183°C; ^{1}H-NMR (δ) : 3.60(2H, s, -CH_2), 3.78(2H, s, -CH2), 4.06(2H, s, -CH_2), 4.16(1H, bs, -NH), 6.94-6.98(1H, dd, Ar-H),7.08-7.70(16H, m, Ar-H), 8.20-8.25(1H, m, Ar-H), 12.18(1H, bs, imidazole-NH);^{13}CNMR(δ) : 41.0, 42.8, 45.4, 102.0, 112.0, 115.0, 119.2, 121.0, 127.2, 127.8, 127.9, 128.3, 128.4, 128.5, 128.8, 130.1, 132.9, 135.9, 136.3, 136.8, 138.2, 141.4, 142.3, 150.8, 167.8. IR :1677 cm^{-1}, 3468 cm^{-1}; FAB Mass : m/z 471.2 (M+1); CHN analysis : Found: C (78.86%); H(5.12%); N (12.32%); Calc :C (79.12%); H(5.57%); N (11.91%).

Compound 5l: 2-(((5-Isopropyl-1H-benzo[d]imidazol-2-yl)methyl)amino)-1-(2-phenyl-1H-indol-1-yl)ethan-1-one:



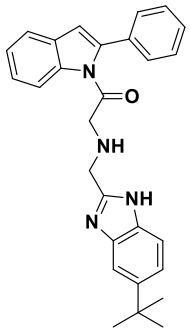
Yield : 34%; M.P. :172-176ºC; ^{1}H-NMR (δ) :1.25(6H, d, 2 X –CH_3)3.04(1H, m, -CH), 3.54(2H, s, -CH2), 4.17(1H, bs, -NH), 4.26(2H, s, -CH_2), 6.89-6.93(1H, dd, Ar-H), 7.03-7.06(1H, dd, Ar-H), 7,15-7.63(10H, m, Ar-H), 8.19-8.23(1H, m, Ar-H), 12.43(1H, bs, imidazole-NH); 13CNMR(δ): 24.0, 34.3, 42.5, 44.9, 102.1, 112.0, 115.0, 119.4, 120.6, 126.8, 127.8, 128.0, 128.2, 128.3, 128.4, 128.5, 133.0, 136.1, 136.3, 136.4, 141.4, 144.4, 151.3, 168.6; IR : 1680 cm^{-1}, 3378 cm^{-1}; FAB Mass :m/z 423.2 (M+1); CHN analysis : Found: C (76.71%); H(6.20%); N (13.26%); Calc : C (76.32%); H(5.76%); N (14.56%).

Compound 5m: 2-(((5-Benzyloxy-1H-benzo[d]imidazol-2-yl)methyl)amino)-1-(-2-phenyl-1H-indol-1-yl)ethan-1-one:



Yield : 64%; M.P. : 287-289ºC; ^{1}H-NMR (δ) : 3.57(2H, s, -CH_2), 4.13(1H, bs, -NH), 4.25(2H, s, -CH_2), 5.18(2H, s, -CH_2), 6.82-6.86(1H, dd, Ar-H),7.10-7.70(16H, m, Ar-H), 8.20-8.24(1H, m, Ar-H) 12.13(1H, bs, imidazole-NH);^{13}CNMR(δ):42.7, 45.0, 70.4, 101.1, 102.0, 112.0, 114.6, 116.7, 120.5, 126.8, 127.7, 127.8, 127.9, 128.2, 128.3, 128.4, 132.8, 136.0, 136.5, 138.3, 141.1, 141.3, 150,9, 152.3, 168.9 IR : 1665 cm^{-1}, 3395 cm^{-1}, ; FAB Mass : m/z 487.2 (M+1); CHN analysis : Found: C (75.97%); H (4.86%); N (12.61%); Calc :C (76.52%); H (5.39%); N (11.51%).

Compound 5n: 2-(((5-tert-butyl)-1H-benzo[d]imidazol-2-yl)methyl)amino)-1-(2-phenyl-1H-indol-1-yl)ethan-1-one:



Yield : 64%; M.P. : 195-197°C; ^{1}H-NMR (δ) : 1.34(9H, s, 3 x -CH_3), 3.53(2H, s, -CH2), 4.17(1H, bs, -NH), 4.27(2H, s, -CH_2), 6.91-6.95(1H, dd, Ar-H), 7.03-7.07(1H, dd, Ar-H), 7.17-7.62(10H, m, Ar-H) 12.24(1H, bs, Imidazole-NH);^{13}CNMR(δ):24.0, 34.3, 42.5, 44.9, 102.9, 112.0, 115.0, 119.4, 120.6, 126.8, 127.8, 128.0, 128.2, 128.3, 128.4, 128.5, 133.0, 136.1, 136.3, 136.4, 141.4, 144.4, 151.3, 168.5; IR : 1678 cm^{-1}, 3340 cm^{-1}; FAB Mass : m/z 423.2(M+1); CHN analysis : Found: C (76.75%), H (6.20%), N (13.26%). Calc :C (76.33%), H (5.98%), N (13.96%)

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