FACILE SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF NOVEL N,N-DIALKYL-(1H-INDOL-3-YL)METHYLARYLAMIDES

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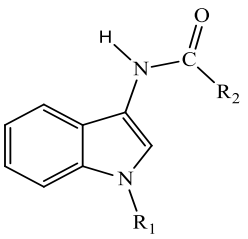
***Abstract*:** A series of new1-(1-(3-phenylpropyl)-1H-indol-3-yl)-methanamines were synthesised by reductive amination of 1-(3-phenylpropyl)-1H-indole-3-carbaldehyde and primary amines using $NaBH_4$ as reducing agent. The higher amines were then subjected to Schotten Baumann reaction to obtain tertiary amides. The chemical structures of synthesized compounds were confirmed by IR, ^1H NMR and Mass spectroscopic and elemental data. These compounds were also screened for their in vitro antimicrobial activity by cup plate method using Ciprofloxacin and Amphotericin B as standards against gram positive and gram negative bacteria and fungi respectively and antioxidant activity by DPPH method.

Keywords: Indole-3-carboxaldehyde, Thiophene, Pyridine, antimicrobial and antioxidant activity.

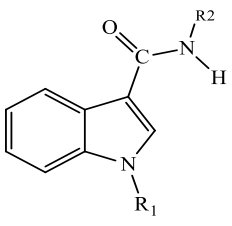
Introduction

The increasing resistance of clinically important pathogens to antibiotic treatment is of worldwide concern. [1] New antibacterial agents that operate with distinctly different mechanism of action from current drug therapies offer hope towards combating these multidrug resistant organisms [2]. In an effort to develop a novel class of antibacterial compounds, we targeted the synthesis of N- alkyl Indole tertiary amides.
It is known from the literature that indole derivatives exhibit varied biological and pharmacological properties [3-9]. In particular, *C*-3-substituted indoles are important building blocks for the synthesis of many biologically active compounds which possess antimalarial [10], inhibitors of HIV-1 [11], antimicrobial, anticancer, antioxidant [12], cytotoxic [13], inhibitors of hepatitis C virus [14], anti-diabetic [15] and neuro protective [16], activities. On the other hand, *N*-1 and *C*-3-substituted indole derivatives have been found to play an important role in many biologically active compounds especially with anti-inflammatory [17], anticancer [18], anti-nociceptive [19] and antipsychotic [20] activities. So we tried to synthesis Novel N, N-dialkyl-(1H-indol-3-yl) methyl aryl amides.

N-alkyl (Indole-3-yl) aryl amides look like a simple molecular structure. But there are two different motifs.



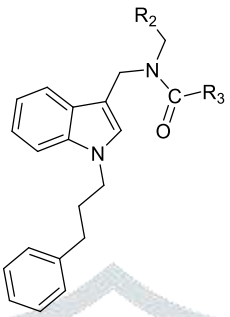
I



II

Only 899 molecules bearing N-alkyl (Indole-3-yl) aryl amides (structure I) have been reported across a total of 84 articles. In contrast 68,422 reported structures are present in the literature for the reversed indole-3-carboxamides (structure II).[21]

Indole scaffold already being an important structure in drug discovery, the rarity in the literature of structure I made us to design N, N-dialkyl-(1H-indol-3-yl) methyl aryl amides.



As an alternative to known methods, we have developed a feasible path for synthesis. The reaction of N-alkyl Indole carboxaldehyde with aromatic amines proceeds through the formation of immine followed by in situ reduction to an amine of higher order by $NaBH_4$ in the presence of p-toluene sulphonic acid. $NaBH_4$ is an inexpensive, safe to handle and environmental friendly reducing agent for the reductive amination of carbonyl compounds. The neat part of this reaction is we don't actually need to isolate the immines in order to reduce it. The whole process is done in one reaction flask. Therefore, reductive amination is an important method in organic chemistry because of their versatile utility as intermediates for synthesis of pharmaceuticals and agrochemicals [22]. The reductive amination of carbonyl compounds is one of the most useful methods of synthetic organic chemistry, which provides an access to structurally diverse amine [23].
The secondary amines then act as a precussor for the synthesis of tertiary amides by Schotten Baumann reaction.

In amides all the three atoms in the O-C-N chain are reactive which makes them useful moiety in organic compounds and hence become a key part for medicinal chemist. On the other hand amide derivatives possess different kinds of pharmacological activities like antimicrobial, analgesic, anti-inflammatory, anticancer, cardiovascular, and other biological activities. Due to these biologically significances, chemists have interest in developing various new benzamide derivatives. [24]
Due to vast biological significance of indole and amides, the present study was designed to synthesis the benzamide analogues of indole in order to find new biologically active compounds.

Materials and Methods

All the chemicals and solvents were of laboratory reagent grade and used as received from Sigma Aldrich and SD fine. Melting points were determined in open capillaries and are uncorrected. The purity of the compounds was checked by TLC using silica gel-G coated aluminium plates (Merck) and spots were visualized by exposing the dry plates to iodine vapours. The IR (KBr) spectra were recorded on a Perkin-Elmer spectrometer on FT-IR spectrometer. The ^{1}H NMR (DMSO-d6) spectra recorded on a Bruker (400 MHz) and the chemical shifts were expressed in ppm (δ scale) downfield from TMS. Mass spectral data were recorded by electron impact method on JEOL GCMATE II GC-MS mass spectrometer. Elemental

analysis was carried out using Flash EA 1112 series elemental analyser. All the compounds gave C, H and N analysis within ± 0.5% of the theoretical values.

Synthesis of 1-(3-phenylpropyl)-1H-indole-3-carbaldehyde

To a stirred solution 1H-indole-3-carbaldehyde (2.0 g, 13.0 mmol) in DMF (40 ml) was added K_2CO_3 (4.75 g, 34.0 mmol). Reaction mixture was stirred for 10 minutes and was added (3-chloropropyl) benzene (1.5 ml, 7.0 mmol) and the reaction mixture was heated at 80 ^oC for 16 h. The reaction mixture was cooled, pour into ice cold water, precipitated brown solid was filtered, and washed with cold H_2O to yield desired product as brown solid.

1-(3-phenylpropyl)-1H-indole-3-carbaldehyde (2)

IR (KBr) (ƛmax in cm^{-1}):1729 (C=O), 2858 (C-H),1082(C-N); ^1H NMR (400 MHz, CDCl3) δ (ppm): 4.2 (t, 2H,N- CH_2), 2.10 (m, 2H, CH_2), 2.62 (t, 2H, - CH_2), 7.29-8.57 (m, 10H, Ar-H), 9.73 (s,1H,CHO) LCMS: m/z = 263 [M]. Analysis: Calcd for C_{18} $H_{17}NO$ (263), C,82.10 H, 6.51; N,5.32. Found C,82.09; H,6.49; N,5.30.

General procedure for the synthesis of N-alkyl-indole-3-methanamines

To a stirred solution of 1-(3-phenylpropyl)-1H-indole-3-carbaldehyde (2.4 g, 9.5mmol) in EtOH (30 ml) were added thiophen-2-ylmethanamine (1.19 g, 10.0mmol), and different primary amines like pyridin-3-ylmethanamine (1.1 g, 10.1mmol), 4-fluorobenzyl amine (0.52 g, 4.1mmol), *p*-toluene sulfonic acid (20 mg) and the reaction mixture was stirred at 80 ^oC for 3 h. After consumption of the starting material (checked by TLC), to the reaction mixture was added $NaBH_4$ (1.1 g, 28.7mmol) at 0 ^oC. Reaction mixture was warmed to room temperature and stirring continued for 45 minutes. Reaction mixture was cooled, quenched with cold water, filtered, and the filtrate was extracted with ether. Combined organic phase was dried over Na_2SO_4 and concentrated. The crude product was purified by flash column chromatography on neutral alumina using gradient hexane/EtOAc mixture to yield desired product.

1-(1-(3-phenylpropyl)-1H-indol-3-yl)-N-(thiophen-2-ylmethyl methanamine (3)

IR (KBr) (ƛmax in cm^{-1}):3325 (N-H str),3013(Ar C-H); ^1H NMR (400 MHz, CDCl3) δ (ppm): 2.62 (t, 2H, CH_2), 2 (m, 2H, CH_2), 4.15(t, 2H, N-CH_2,), 7-7.5(m, 12H, Ar-H), 3.64 (s, 2H, CH_2), 3.81 (s, 2H, CH_2),2.3(s,1H,-NH),6.35(s,1H,-CH). LCMS: m/z = 360[M]. Analysis: Calcd for C_{23} $H_{24}N_2S$ (360),C, 76.69; H, 6.7; N,7.77.Found C,76.51;H,6.69; N,7.7.

1-(1-(3-phenylpropyl)-1H-indol-3-yl)-N-(pyridin-3-ylmethyl) methanamine (4)

IR (KBr) (ƛmax in cm^{-1}):3325 (N-H str.), 3013(Ar C-H); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.62 (t, 2H, CH_2), 2 (m, 2H, CH_2), 4.15(t, 2H, N-CH_2,), 7-8.5(m, 13H ,Ar-H), 3.64 (s, 2H, CH_2), 3.76 (s, 2H,CH_2), 2.25 (s,1H,-NH),6.35 (s,1H,-CH). LCMS: m/z = 355[M]. Analysis: Calcd for $C_{24}H_{25}N_3$ (355),C, 81.09; H, 7.09; N,11.82. Found C,81.02.51; H,7.09; N,11.8.

N-(4-fluorobenzyl)-1-(1-(3-phenylpropyl)-1H-indol-3-yl) methanamine (5)

IR (KBr) (ƛmax in cm^{-1}):3325(N-H str),3013(Ar C-H); .. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 2.62 (t, 2H, CH_2), 2.10 (m, 2H, CH_2), 4.15(t, 2H, N-CH_2,), 7.1-7.52(m, 13H,Ar-H), 3.64 (s, 2H, CH_2), 3.76 (s, 2H,CH_2), 2.34(s,1H,-NH),6.35(s,1H,-CH). LCMS: m/z = 372[M]. Analysis: Calcd for $C_{25}H_{25}FN_2$ (372),C, 80.58; H, 6.74; N,7.5. Found C,80.6;H,6.77; N,7.52.

General procedure for the Synthesis of N-alkyl indolyl-3-methylamides.

To a stirred solution of1-(1-(3-phenylpropyl)-1H-indol-3-yl)-N-(thiophen-2-ylmethyl) methanamine(3) (0.5 g, 1.4mmol) in tetrahydrofuran (20 ml) were added trimethylamine (0.423 g, 4.19 mmol), and various benzoyl chloride analogues like 4-nitrobenzoyl chloride (0.285 g, 1.536 mmol), 4-methoxybenzoyl chloride (0.21 g, 1.23 mmol),and 4-fluorobenzoyl chloride (0.147 g, 0.92 mmol) at 0^{o}Cand the reaction mixture was warmed to room temperature and stirred for 3 h. Reaction mixture was diluted with water and extracted with ether. The combined organic layer was dried over Na_2SO_4 and concentrated. The crude product was purified by flash column chromatography on silica gel using gradient hexane/ EtOAc mixture to yield desired product. Similar procedure was carried out for 4 and 5.

4-nitro-N-((1-(3-phenylpropyl)-1H-indol-3-yl) methyl)-N-(thiophen2ylmethyl) benzamide 3a

IR (KBr) (ƛmax in cm^{-1}): 1639 (C=O),1525 (N =O str), 678(C-S),2858(C-H),3059(Ar-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.62 (t, 2H, CH_2), 2.16 (m, 2H, CH_2), 4.15(t, 2H, N-CH_2,), 7.02-7.73(m, 17H,Ar-H), 4.45 (s, 2H, CH_2), 4.9 (s, 2H,CH_2), LCMS: m/z = 509 [M]. Analysis: Calcd for $C_{30}H_{27}N_3O_3S$ (509),C,70.68; H,5.31; N,8.22. Found C,70.70;H,5.34; N,8.25.

4-methoxy-N-((1-(3-phenylpropyl)-1Hindol3yl) methyl) N(thiophen2ylmethyl) benzamide 3b

IR (KBr) (ƛmax in cm^{-1}): 1638(C=O),1030(C-O-C)),684(C-S),2848(C-H),3013(Ar-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) :2.62 (t, 2H, CH_2), 2.19 (m, 2H, CH_2), 4.15(t, 2H, N-CH_2,), 7.02-7.9(m, 16H,Ar-H), 4.4 (s, 2H, CH_2), 4.75 (s, 2H,CH_2),3.81(s,3H, OCH_3),6.8(s, 1H,=CH)LCMS: m/z = 494 [M]. Analysis: Calcd for $C_{31}H_{30}N_2O_2S$ (494),C75.27; H,6.11; N,5.66. Found C,75.25;H,6.1; N,5.64

4-fluoro-N-((1-(3-phenylpropyl)-1H-indol-3-yl) methyl) N(thiophen2ylmethyl) benzamide3c

IR (KBr) (ƛmax in cm^{-1}): 1629(C=O),1355 (C-F),684(C-S),2853(C-H),3023(Ar-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 2.67 (t, 2H, CH_2), 2.19 (m, 2H, CH_2), 4.15(t, 2H, N-CH_2,), 7.04-7.28(m, 16H,Ar-H), 4.5 (s, 2H, CH_2), 4.9 (s, 2H,CH_2), 6.8(s, 1H,=CH) LCMS: m/z = 483 [M+1]. Analysis: Calcd for $C_{30}H_{27}FN_2OS$ (482),C.74.66; H,5.64; N,5.80. Found C,74.65; H,5.62; N,5.78**.**

4-nitro-N-((1-(3-phenylpropyl)-1H-indol-3-yl) methyl)-N-(pyridin-3-ylmethyl) benzamide 4a

IR (KBr) (ƛmax in cm^{-1}): 1638(C=O),1525(N=O),2848(C-H),3059(Ar-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.6 (t, 2H, CH_2), 2.1 (m, 2H, CH_2), 4.12(t, 2H, N-CH_2,), 6.9-8.5(m, 17H,Ar-H), 4.3 (s, 2H, CH_2), 4.9

(s, 2H,CH_2), 6.8(s, 1H,=CH) LCMS: m/z = 506 [M+2]. Analysis: Calcd for $C_{31}H_{28}N_4O_3$ (504),C,73.79; H,5.59; N,11.10. Found C,73.75;H,5.56; N,11.08.

4-methoxy-N-((1-(3-phenylpropyl)-1H-indol-3yl) methyl) N(pyridin3ylmethyl) benzamide

4b

IR (KBr) (λmax in cm^{-1}): 1629(C=O),1030(C-O-C),2848(C-H),3052(Ar-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) :2.65 (t, 2H, CH_2), 2.16 (m, 2H, CH_2), 4.12(t, 2H, N-CH_2,), 7.02-8.5(m, 18H,Ar-H), 4.785 (s, 2H, CH_2), 4.3(s, 2H,CH_2),3.82(s,3H, OCH_3). LCMS: m/z = 490 [M+1]. Analysis: Calcd for $C_{32}H_{31}N_3O_2$ (489),C,78.50; H,6.38; N,8.58. Found C,78.48; H,6.36; N,8.55.

4-fluoro-N-((1-(3-phenylpropyl)-1H-indol-3-yl) methyl)-N-(pyridin3ylmethyl) benzamide

4c

IR (KBr) (λmax in cm^{-1}): 1631(C=O),1448(C-F), 2853(C-H),3059(Ar-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) :2.64 (t, 2H, CH_2), 2.1 (m, 2H, CH_2), 4.12(t, 2H, N-CH_2,), 7.0-8.5(m, 17H,Ar-H), 4.37 (s, 2H, CH_2), 4.7 (s, 2H,CH_2), 6.8(s, 1H,=CH) LCMS: m/z = 478 [M+1]. Analysis: Calcd for $C_{31}H_{28}FN_3O$ (477),C.77.96; H,5.91; N,8.80. Found C,77.94;H,5.90; N,8.78.

N-(4-fluorobenzyl)-4-nitro-N-((1-(3-phenylpropyl)-1H-indol-3-yl) methyl) benzamide

5a

IR (KBr) (λmax in cm^{-1}): 1638(C=O),1524(N=O),2848(C-H),1355(C-F),3059(Ar-H); ^{1}H NMR (400 MHz, $CDCl_3$) $^{\delta}$(ppm): 2.64 (t, 2H, CH_2), 2.1 (m, 2H, CH_2), 4.12(t, 2H, N-CH_2,), 7.0-8.5(m, 17H,Ar-H), 4.37 (s, 2H, CH_2), 4.7 (s, 2H,CH_2), 6.8(s, 1H,=CH) LCMS: m/z = 521 [M]. Analysis: Calcd for $C_{32}H_{28}FN_3O_3$ (521), C.73.69; H,5.41; N,8.06. Found C,73.64; H,5.40; N,8.03.

N-(4-fluorobenzyl)-4-methoxy-N-((1-(3-phenylpropyl)-1H-indol-3-yl) methyl) benzamide

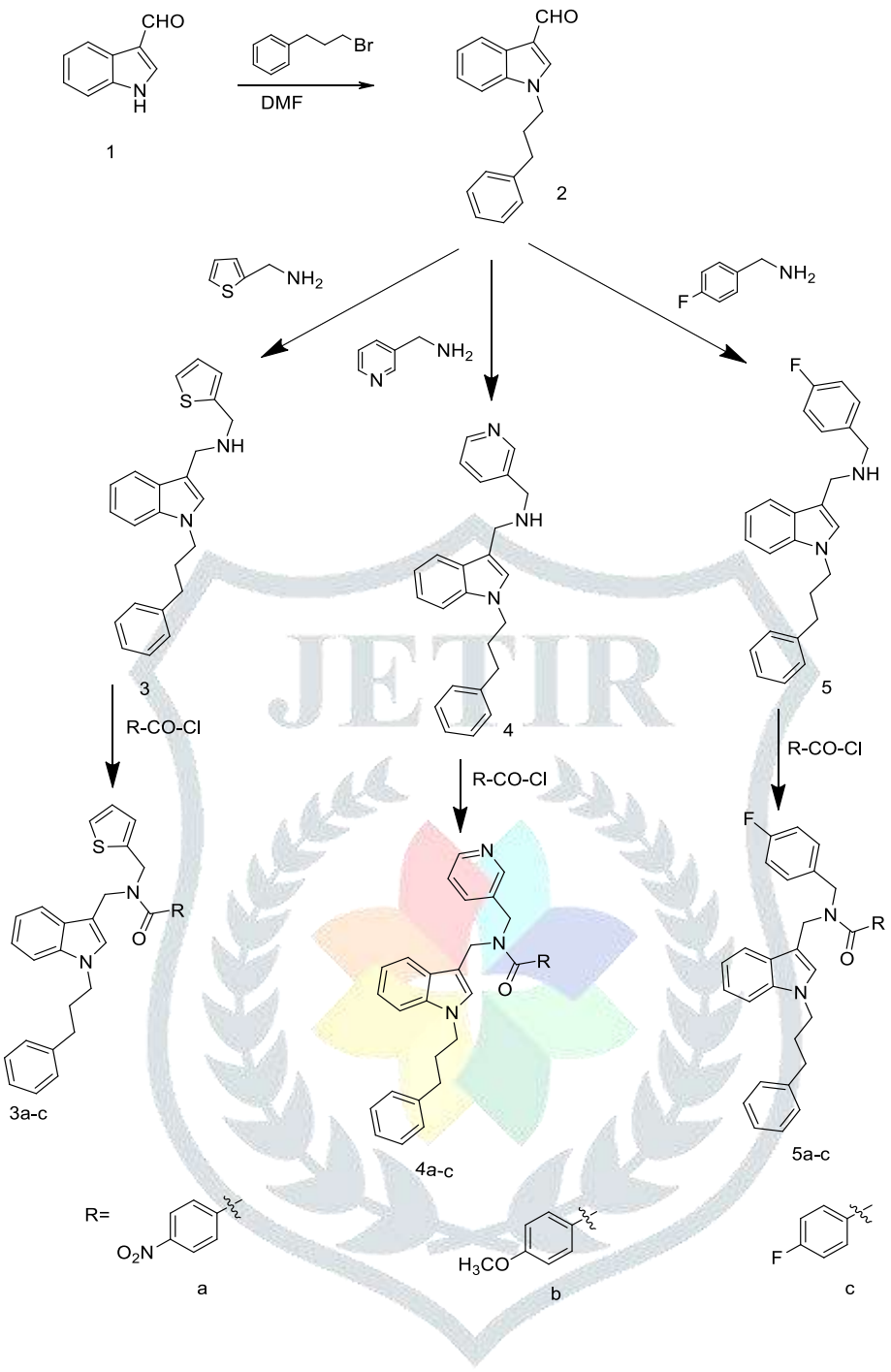
5b

IR (KBr) (λmax in cm^{-1}): 1624(C=O),1030 (C-O-C), 2848 (C-H) ,3059(Ar-H) ;^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.6 (t, 2H, CH_2), 2.19 (m, 2H, CH_2), 4.1(t, 2H, N-CH_2,), 7.05-7.8(m, 18H,Ar-H), 4.60 (s, 2H, CH_2), 4.9(s, 2H,CH_2),3.817(s,3H, OCH_3). LCMS: m/z = 506 [M]. Analysis: Calcd for $C_{33}H_{31}FN_2O_2$ (506),C,78.24; H,6.17; N,5.53. Found C,78.25; H,6.14; N,5.51.

4-fluoro-N-(4-fluorobenzyl)-N-((1-(3-phenylpropyl)-1H-indol-3-yl)methyl)benzamide

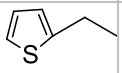
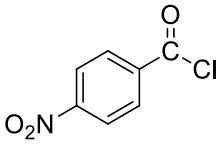
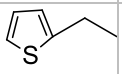
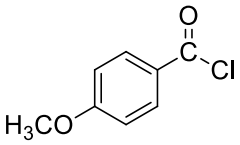
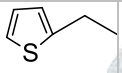
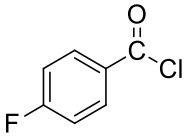
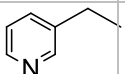
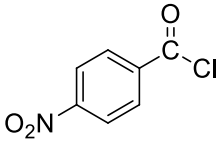
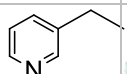
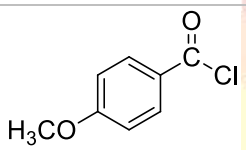
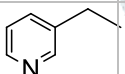
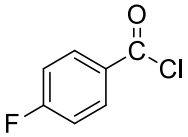
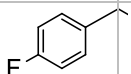
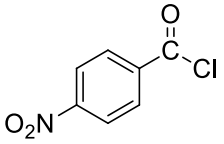
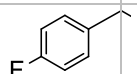
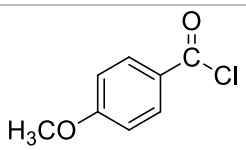
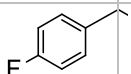
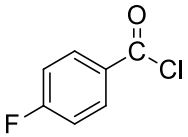
5c

IR (KBr) (λmax in cm^{-1}): 1631(C=O),1355 (C-F), 2853(C-H),3054(Ar-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) :2.62 (t, 2H, CH_2), 2.1 (m, 2H, CH_2), 4.16(t, 2H, N-CH_2,), 7.0-8.12(m, 17H,Ar-H), 4.78 (s, 2H, CH_2), 4.91 (s, 2H,CH_2), 6.35(s, 1H,=CH) LCMS: m/z = 494 [M]. Analysis: Calcd for $C_{32}H_{28}F_2N_2O$ (494), C.77.71; H,5.71; N,5.66. Found C,77.69; H,5.70; N,5.64.



Experimental scheme (i) for the synthesis ofN,N-dialkyl-(1H-indol-3-yl) methylaryl amide derivatives

Table 1: physical properties of N,N-dialkyl-(1H-indol-3-yl) methyl aryl amide derivatives

Comp. No		R_1	M.F.	M. W.	%Yield	M.P, ° C
3a			$C_{30}H_{27}N_3O_3S$	509	84	72-73
3b			$C_{31}H_{30}N_2O_2S$	494	80	83-84
3c			$C_{30}H_{27}FN_2OS$	482	76	102-103
4a			$C_{31}H_{28}N_4O_3$	504	86	80-81
4b			$C_{32}H_{31}N_3O_2$	489	62.5	70-72
4c			$C_{31}H_{28}FN_3O$	477	87	97-98
5a			$C_{32}H_{28}FN_3O_3$	521	72	87-88
5b			$C_{33}H_{31}FN_2O_2$	506	68	77-78
5c			$C_{32}H_{28}F_2N_2O$	494	70	99-100

Comp. no.–compound number. M.F. molecular formula, M. W.-molecular weight, M. P-melting point

Biological Activities

Antimicrobial Activity

The antibacterial activities of compounds 4(a-i), were carried out using the Cup plate diffusion method . This method depends on the diffusion of the antibiotic from a cavity through the solidified agar layer in a Petri dish to an extent such that the growth of the added microorganism is prevented in a circular zone around the cavity containing a solution of the antibiotic. For antibacterial activity, antibacterial species used are two Gram negative species, Escherichia coli (ATCC 9637), Salmonella typhi (ATCC 6539) and two Gram-positive species, Bacillus subtilis (ATCC 6633), Staphylococcus aureus (ATCC 29737). Two fungal strains Aspergillus Niger (ATCC 16509), Aspergillus fumigates (ATCC16406) were used for antifungal activity. Solution of each compound at a concentration of 1000µg/ml in DMSO was prepared and the inhibition zone diameter in millimetre was used as the criterion for measuring the microbial activity after 24h for bacteria and 72h for fungi. Ciprofloxacin is used as bacterial standards and Amphotericin B is used as fungal standards for references to evaluate the efficacy of the tested compounds under the same conditions. DMSO used as control and solvent to prepare compound solutions. Measurements of results are shown in table 2

Antioxidant Activity Assay

1, 1-diphenyl-2-picryl hydrazyl (DPPH) radical scavenging activity (RSA)

The free radical scavenging activity (RSA) of all the compounds at concentrations of 25, 50, 75 and 100 µg/ml was carried out in the presence of a freshly prepared solution of stable free radical DPPH (0.04% w/v) following a Hatano's method . Ascorbic acid (AA) is used as standards. All the test analyses were performed on three replicates and the results are averaged. The results in percentage are expressed as the ratio of absorption decrease of DPPH in the presence of test compounds and absorption of DPPH in the absence of test compounds at λ 517 nm on ELICO SL 171 Mini Spec, spectrophotometer. The percentage scavenging activity of the DPPH free radical was measured using the following equation:

$$\%\ of DPPH RSA = \frac{Absorbance of Control - Absorbance of Sample}{Absorbance of Control} \times 100$$

Table-2: antibacterial activity, size of inhibition zone (mm) formed at concentration 1000 µg/ml of synthesized compounds

Zone of inhibition in mm.						
Compound	Antibacterial activity				Antifungal activity	
	Gram positive		Gram negative			
	Bacillus Subtilis	*Staphylococcus aureus*	*Escherichia coli*	*Salmonella typhi*	*Aspergillus fumigatus*	*Aspergillus Niger*
3a	18±.47	34±.27	36.33±.27	14.66±.27	38±.471	35±.47
3b	21.3±.272	33±.47	34±0	16.55±.23	34.66±.007	33±,41
3c	17.3±.272	23.33±.27	19.66±.26	15.66±.33	28.2±.22	=======
4a	14±.471	28.33±.27	23.33±.25	10.66±.25	23.66±.007	21.6±.72
4b	16±1.187	32.2t±.47	26.3±.27	=====	35±.471	28±.43
4c	19±.472	31.3±.27	35.33±.54	13.55±.22	36.33±.54	32.3±.97
5a	11.33±.72	26.66±.54	20.33±.25	11.66±.19	21±.45	21±.35
5b	12.33±.72	28.33±.27	22,66±.22	12.66±.24	24.33±.27	17.33±.74
5c	14.66±.272	27.33±,27	19.33±.23	10.35±.28	18±.47	14.66±.61
Ciprofloxacin	38	34	37	39		
Amphotericin B					40	38

No Activity=----------
Mean values are expressed as mean ± SD(n=3)

Results and Discussion

The synthesis of the title compounds was an account of biological activity of indole which is the key building block of variety of compounds .A simple practical procedure was developed for the synthesis of final products with the use of affordable reagents, and this easy method is expected to find use in giving other heterocyclic amides.

The precursors for the preparation of N-alkyl indolyl-3-methylamides, were obtained by the reductive amination of 1-(3-phenylpropyl)-1H-indole-3-carbaldehyde with heterocyclic amines*viz*thiophen-2-yl-methanamine, pyridin-3-ylmethanamineand4-fluorobenzyl amine. The reaction of 1-(3-phenylpropyl)-1H-indole-3-carbaldehyde with benzyl amines proceeds through the formation of imine followed by in situ reduction to an amine of higher order in the presence of mixture of p-TSA and $NaBH_4$(3,4&5). These were then benzoylated to protect the secondary amines to obtain the final products 3(a-c),4(a-c) and 5(a-c).

The structure elucidation of the final products was carried out by IR, 1H-NMR and Mass spectral data. IR peaks of the compound were recognized from 1600-1640 $cm^{-1}$for C=O stretching of amide, 3050- 3075cm^{-}

[1]for aromatic stretching, 2848-2853 cm^{-1} for C-H aliphatic stretching and some stretching bands were also found for C=C at1575-1490 cm^{-1}. In 1H-NMR spectra typical proton signals for C-H aliphatic were observed between 2.6 -4.8 for -CH_2protons and6.9-8.5 for aromatic protons.1H-NMR spectra also indicated that compounds obtained were amide rotomers.

Antimicrobial Activity

Antibacterial screening data (table- 2) revealed that the synthesised compounds exhibited good activity against gram positive bacteria *S. aureus*(ATCC 29737) and gram negative bacteria *E.coli*(ATCC 9637).The synthesised compounds 3(a-c) were found more active than compounds 4(a-c) and 5(a-c)..compounds **3a, 3b,4b,and4c** exhibited good antibacterial activity. All the synthesised compounds exhibited good antifungal activity than antibacterial activity. Amongst them **3a, 3b,4b and 4c** exhibited excellent antifungal activity against *A. fumigatus.* However, none of the compounds exhibited zone of inhibition more than that of standard.

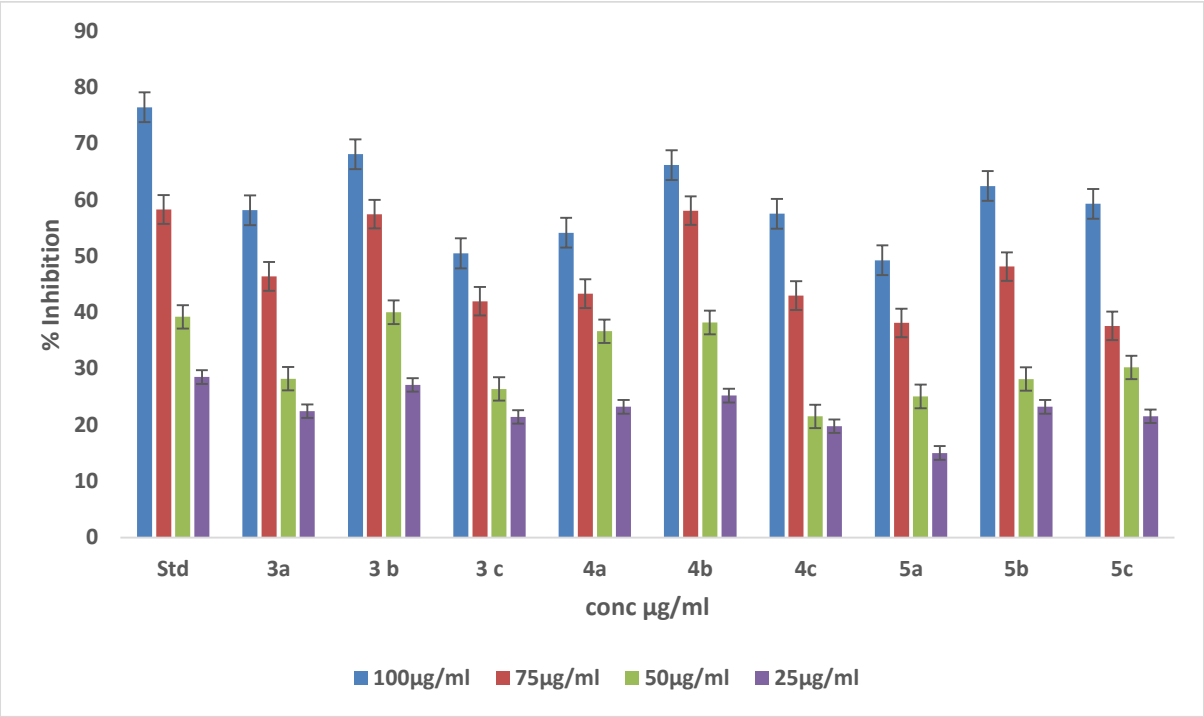
Antioxidant Activity

1, 1-Diphenyl-2-picryl hydrazyl (DPPH) radical scavenging activity (RSA)

In vitro method of scavenging of the stable DPPH radical is extensively used to evaluate the antioxidant activity in less time than other methods. DPPH is a stable free radical that can accept hydrogen radical or an electron and must thus be converted to a stable diamagnetic molecule. DPPH has an odd electron and so has a strong absorption band at 517 nm. When this electron becomes paired off, the absorption decreases stoichiometrically with respect to the number of electrons or hydrogen atoms taken up. The DPPH antioxidant assay measures the hydrogen donating capacity of the molecules under study. When the free-radical DPPH is reduced by the sample, its colour changes from violet to yellow.

The RSA results suggests that compound **3b,4b and 5b** exhibited good radical scavenging activity at concentration 100µg/ml.compounds**3a,4a,4c and 5c** are found to be moderately active and rest of the compounds were found to be less active. The highest activity of the compounds **3b,4b and 5b** may be due to electron releasing group of –OCH_3 attached to para position of aromatic ring so that DPPH radical becomes stable diamagnetic molecule. This fact confirms that electron donating ability can act as good radical scavenger.

Graphical representation of Antioxidant activity of N,N-dialkyl-(1H-indol-3-yl) methylaryl amide derivatives



Conclusion

A series of nine compounds novel N,N-dialkyl-(1H-indol-3-yl) methyl aryl amide derivatives 3(a-c),4(a-c) and5(a-c) were prepared and characterized by TLC, M. P, spectral and analytical data. All the synthesized compounds were evaluated for in vitro antimicrobial activity and antioxidant activity against different bacterial and fungal strains. Compounds **3a, 3b, 4b and 4c** were highly active against gram positive and gram negative bacteria,. Compounds **3a,3b 4b, and 4c**exhibited potent antifungal activity and **3b,4b and 5b**exhibited good antioxidant activity. All the experiments were found in triplicate and the mean were calculated.

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