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Synthesis and Biological Activity of Sulfonamide and Carbamate Derivatives of

Chemistry

KEYWORDS : 5-Chloro-2-phenoxy-aniline, sulfonylchlorides, chloroformates, Antimicrobial activity.

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ABSTRACT

Synthesis of a series of novel sulfonamide and carbamate derivatives of 5-chloro-2-phenoxy-aniline (1), were prepared by reacting(1) with various substituted sulfonylchlorides and chloroformates in the presence of triethylamine in THF at 500C.Their structures were established by IR, 1H, 13C-NMR, Mass spectral data and elemental analysis. Theirinvitro antimicrobial activity was evaluated and the title compounds 2a, 2e, 3a and 3d exhibited excellent activity against all the bacterial strains, 2a and 3a showed good activity against E.coliandP. Vulgaris.

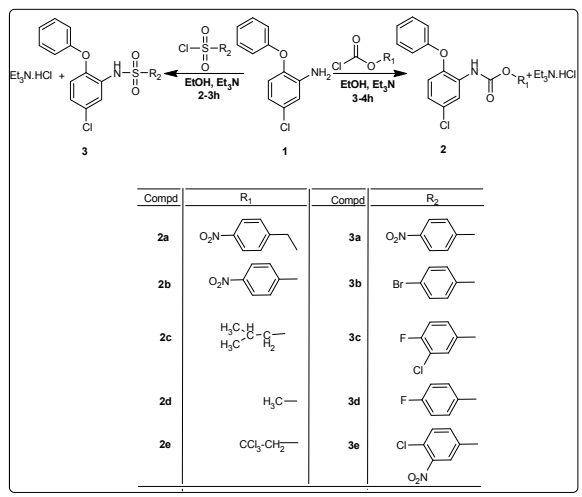
INTRODUCTION

Sulfonamides are important pharmacophoric groups in medicinal chemistry as they have many desirable properties such as their ability to act as H-bond donors and acceptors. They are used in the prevention and treatment of bacterial infections, diabetes mellitus, oedema, hypertension and gout. Some of them have proved to be useful as herbicides [1] and plaguicides [2], antibiotics such as the sulfathiazole. The applications of sulfonamides are greatly extended from their primary function as antitumor [3], hypoglycaemic [4], anti-thyroid [5] anti-carbonic anhydrase [6], anti-inflammatory [7], diuretic [8], COX-inhibitors, the enzyme dihydropteroatesynthetase (DHPS)-the key enzyme involved in folate synthesis, anti-impotence drugs [9] and also have been used as azo dyes for achieving improved light stability, water solubility and fixation to fiber. Carbamates are very useful scaffolds in the synthesis of insecticides such as carbofuran, carbaryl, ethienocarb, fenobucarb, oxamyl and methomyl. Carbamates are very important organic intermediate [10], which are found in both biologically active compounds [11] and polymers [12]. Further carbamates play an important role in drug design and as hydrolytically resistant ester [13] or phosphonates [14].

It is well known fact that sulfonamides and carbamates act as an antibiotic and insecticide activities respectively. 5-Chloro-2-phenoxy-aniline is a structural isomer of Nimesulide which possess non-steroidal anti-inflammatory and analgesic properties. As a part of our research programme on enhancement of biological activity of the drug moieties, we synthesized 5-chloro-2-phenoxy-aniline carbamates and sulfonamides derivatives and studied their antibacterial and antifungal activities.

CHEMISTRY:

Synthesis of a series of 5-chloro-2-phenoxy-phenyl carbamates **2a-e** and 5-chloro-2-phenoxyphenylsulfonamides **3a-e** derivatives has been synthesized from 5-chloro-2-phenoxy-aniline (**1**) in ethanol as a green solvent in the presences of triethylamine at 40-60 ºC for 2-4 h and depicted in **Scheme 1**.



Compd	R_1	Compd	R_2
2a	O_2N	3a	O_2N
2b	O_2N	3b	Br
2c	H_3C, H_3C, H, C, H_2	3c	F, Cl
2d	H_3C	3d	F
2e	CCl_3-CH_2	3e	Cl, O_2N

Scheme 1

Initially to optimize the reaction conditions, 5-chloro-2-phenoxy-aniline (**1**) and 4-nitrobenzenesulfonyl chloride was chosen as substrates to perform the model reaction. At first the reaction of 5-chloro-2-phenoxy-aniline (**1**) and 4-nitrobenzenesulfonyl chloride was carried out using 1.2 mmol of triethylamine as a base in different solvents such as tetrahydrofuran (THF), dichloromethane (DCM), toluene, acetonitrile and ethanol. It was observed that the reaction in ethanol gives better yield of 84 % than the remaining solvents (THF-74 %, DCM-70 %, toluene-77 % and acetonitrile-73 %). Hence ethanol selected as solvent. The same procedure was adopted for the synthesis of remaining sulfonamide**3b-e** and carbamate **2a-e** derivatives

It was also observed that electron withdrawing groups (electronegative atoms) like nitro, fluoro and chloro substituted sulfonyl chlorides and chloroformates afforded more yield than the electron donating group substituted sulfonyl chlorides and chloroformates. In comparision of yield of carbamates and sulfonamides, sulfonamides were obtained in slightly higher yield than the carbamates.

RESULTS AND DISCUSSION

General Procedure for the synthesis of carbamate and sulfonamide derivatives of 5-chloro-2-phenoxy aniline:

To a solution of 5-chloro-2-phenoxy-aniline (220 mg, 1 mmol) (1) in dry ethanol, 4-nitrophenyl chloroformate(180 mg, 1 mmol) was added in the presence of triethylamine (1.7 mL, 1.2 mmol) as a base at 10 ºC. The reaction mixture was heated to 40 ºC and stirred for 2 h and the progress of the reaction was monitored by thin layer chromatography in n-hexane:ethyl acetate (3:2). After completion of the reaction, Et3N.HCl salt was removed by filtration and the mixture was concentrated under reduced pressure.

To the reaction mixture water was added and then contents were extracted with ethyl acetate. The ethyl acetate layer was separated and dried over anhydrous sodium sulphate, filtered and solvent was removed in a rota-evaporator. To afford pure 4-Nitrophenyl-5-chloro-2-phenoxyphenylcarbamate (2a): column chromatography was performed n-hexane:ethyl acetate (4:1)as an eluent. The same procedure was adopted for the remaining carbamates 2b-e.

To a solution of 5-chloro-2-phenoxy-aniline (220 mg, 1 mmol) (**1**) in dry ethanol, 4-nitrobenzenesulfonyl chloride (180 mg, 1 mmol) was added in the presence of triethylamine (1.7 mL, 1.2 mmol) as base at 10 °C. The reaction mixture was heated at 40 °C for 2 h and the progress of the reaction was monitored by thin layer chromatography in n-hexane:ethyl acetate (3:2). After completion of the reaction, Et3N.HCl salt was removed by filtration and the mixture was concentrated under reduced pressure. To the reaction mixture water was added and then contents were extracted with ethyl acetate. The ethyl acetate layer was separated and dried over anhydrous sodium sulphate, filtered and solvent was removed in a rota-evaporator. To afford pure N-(5-chloro-2-phenoxyphenyl)-4-nitrobenzenesulfonamide (**3a**) column chromatography was performed in n-hexane:ethyl acetate (4:1) as an eluent. The same procedure was adopted for the remaining sulfonamides**3b-e**.

All the newly synthesized compounds were characterized by IR 1H and ^{13}C NMR and mass spectral data.; IR spectra of compounds 2(a-e) exhibited absorption bands in the region of 3246-3279 cm^{-1} indicating the presence of amine –N-H, the bands at 1702-1720, 1550-1557 cm^{-1} and 823-828cm-1 confirmed the functional groups C=O, NO2 and C-Cl respectively. The IR spectra of sulfonamides revealed the presence of characteristic bands for SO_2 at 1459-1486 cm-1. In ^{1}H NMR spectra, the peaks at δ 7.80-8.34 ppm is confirmed the–C-NH- protons in carbamates and sulphonamides. In ^{13}C NMR spectra the aromatic carbons resonated in the region 116.7-170.4 ppm based on the functionalities attached to phenyl ring. The mass spectral data of all the title compounds 2(a-e) and 3(a-e) are given in the experimental part. The molecular ions and fragmented peaks of the daughter ions of obtained mass spectra are in agreement with the proposed structures. The C, H, N analyses data were obtained for representative compounds. This new approach can prompt synthetic chemists to develop a cost effective method for the synthesis of this important class of drugs. The newly synthesized compounds were screened against both the Gram positive and Gram negative bacteria and the results are presented in tables (1&2).

EXPERIMENTAL

All the chemicals and solvents were purchased from Sigma-Aldrich and Merck and used without further purification. Melting points were determined in open capillary on Guna melting point apparatus which were uncorrected. IR spectra were recorded on Bruker K Alpha instrument. NMR spectra were recorded on Bruker instrument 400 MHz (Proton NMR at 400.13 MHz and carbon-13 at 100.62 MHz) and tetramethylsilane was used as internal standard in DMSO solvent. Chemical shift (δ) and coupling constant (J) were expressed in ppm and Hertzs respectively. Mass spectra were recoreded on Shimadzu LCMS mass instrument and Elemental analysis was performed on FLASH EA Thermo Finnigan 1112 instrument.

SPECTRAL CHARACTERIZATION

4-Nitrophenyl 5-chloro-2-phenoxyphenylcarbamate (2a):

M. F: $C_{19}H_{13}ClN2O5$;Solid; Yield 80 %;m.p. 158-160 oC. IR (KBr, cm-1) νmax: 3276 (-N-H, str), 2934 (Ar-H, str), 2847 (C-H, str), 1702 (C=O, str), 1550 (-NO2, str), 1503 (C-N, str),1307 (C-C,str), 1101 (C-OEster, str), 1060 (C-OEster, str) and 828 (C-Cl, str). 1H-NMR (400 MHz, DMSO-d6): δ 8.34 (s, 1H, NH), 8.17 (d, 2H, J = 8.0 Hz, Ar-H), 7.88 (d, 2H, J = 8.0 Hz, Ar-H), 7.78 (d, 2H, J = 8.0 Hz, Ar-H), 7.69-7.65 (m, 1H, Ar-H), 7.55-7.52 (m, 3H, Ar-H), 7.34 (d, 2H, J = 6.4 Hz, Ar-H). 13C-NMR (100.16 MHz, DMSO-d6): δ 159.4, 156.9, 151.0, 144.4, 143.8, 140.2, 128.2, 127.4, 126.3, 126.2, 123.1, 122.4, 119.8, 118.6, 117.2. LC-MS (+ mode) m/z: 385 (M+H)$^+$.

4-Nitrobenzyl 5-chloro-2-phenoxyphenylcarbamate (2b):

MF $C_{20}H_{15}ClN_2O_5$; Solid; Yield 78 %;m.p. 137-139 oC. IR (KBr, cm^{-1}) ν_{max}: 3274 (-N-H, str), 2936(Ar-H str), 2842 (C-H str), 1709 (C=O, str), 1557 (-NO_2, str),1519 (C-N str), 1331(C-C,str), 1121 (C-O_{Ester}, str), 1067 (C-OEster, str) and 823 (C-Clstr). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.14 (s, 1H, NH), 8.02 (d, 2H, J = 8.0 Hz, Ar-H), 7.67 (d, 2H, J = 8.0 Hz, Ar-H), 7.47 (d, 2H, J = 8.0 Hz, Ar-H), 7.69-7.25 (m, 6H, Ar-H), 4.20 (s, 2H, CH2). 13C-NMR (100.16 MHz, DMSO-d6): δ 156.8, 152.9, 145.5, 143.6, 141.3, 128.5, 127.9, 127.3, 126.2, 125.7, 124.9, 123.2, 119.8, 118.7,117.2, 64.5. LC-MS (+ mode) m/z: 399 (M+H)+.

Iso-butyl5-chloro-2-phenoxyphenylcarbamate (2c):

MF $C_{17}H_{18}ClNO_3$; Yellow liquid; Yield 78 %.m.p. 147-149 °C. IR (KBr, cm^{-1}) ν_{max}: 3279 (-N-H, str), 2934(Ar-H str), 2847(C-H str), 1706 (C=O, str), 1524 (C-N str), 1315(C-Cstr), 1104 (C-OEster, str), 1066 (C-O_{Ester}, str) and 827 (C-Clstr). 1H-NMR (400 MHz, DMSO-d6): δ 8.09 (s, 1H, NH), 7.70 (d, 2H, J = 6.4 Hz, Ar-H), 7.65 (d, 2H, J = 6.4 Hz, Ar-H), 7.50-7.35 (m, 4H, Ar-H), 3.42 (t, 2H, -O-CH2), 1.52-1.16 (m, 7H). 13C-NMR (100.16 MHz, DMSO-d6): δ 156.8, 153.0, 143.7, 128.0, 127.3, 127.3, 126.3, 125.8,123.0, 119.6, 118.5, 117.3, 66.4, 29.6,17.4, 13.5. LC-MS (+ mode) m/z: 320 (M+H)+.

Methyl5-chloro-2-phenoxyphenylcarbamate (2d):

MF $C_{14}H_{12}ClNO_3$; Yellow liquid; Yield 70 %.m.p. 153-155 °C. IR (KBr, cm^{-1}) ν_{max}: 3246 (-N-H, str), 2943 (Ar-H, str), 2874 (C-H str), 1720 (C=O, str), 1504 (C-N str),1301(C-Cstr), 1114 (C-O_{Ester}, str), 1080 (C-O_{Ester}, str) and 848 (C-Clstr). 1H-NMR (400 MHz, DMSO-d_6): δ 8.12 (s, 1H, NH), 7.67 (d, 2H, J = 6.8 Hz, Ar-H), 7.59 (d, 2H, J = 6.8 Hz, Ar-H), 7.37 (s, 1H, Ar-H), 7.25-7.19 (m, 3H, Ar-H), 3.70 (s, 3H, -CH_3). ^{13}C-NMR (100.16 MHz, DMSO-d6): δ 157.0, 152.9, 143.8, 128.0, 127.2, 126.1, 125.7, 123.1, 119.7, 118.6, 117.2, 55.1. LC-MS (+ mode) m/z: 278 (M+H)$^+$, (M+2), (M+4).

2,2,2-Trichloroethyl 5-chloro-2-phenoxyphenylcarbamate (2e):

MF $C_{15}H_{11}C_{l4}NO_3$; Yellow liquid; Yield 75 %.m.p. 164-166 oC.IR (KBr, cm^{-1}) ν_{max}: 3272 (-N-H, str), 2945(Ar-H str), 2841(C-H str), 1712 (C=O, str), 1514(C-N str),1321(C-Cstr), 1110 (C-O_{Ester}, str), 1063 (C-O_{Ester}, str), 842 (C-Clstr), and 782 (C-Clstr). 1H-NMR (400 MHz, DMSO-d_6): δ 8.17 (s, 1H, NH), 7.66 (d, 2H, J = 6.4 Hz, Ar-H), 7.58 (d, 2H, J = 6.4 Hz, Ar-H), 7.39 (s, 1H, Ar-H), 3.82 (s, 2H, -CH_2CCI_3). ^{13}C-NMR (100.16 MHz, DMSO-d6): δ 156.7, 152.8, 143.5, 128.1, 127.2, 126.0, 125.6, 123.0, 119.6, 118.7, 117.3, 101.2, 67.4. LC-MS (+ mode) m/z: 393 (M+H)+.

N-(5-chloro-2-phenoxyphenyl)-4-nitrobenzenesulfonamide (3a):

MF $C_{18}H_{13}ClN_2O_5S$; Solid; Yield 84 %; m.p. 147-149 °C. IR (KBr, cm^{-1}) ν_{max}: 3248 (-N-H, str), 1595(C-Cstr),1551 (-N=Ostr), 1484 (S=O str), 1343 (S=O str), 1228(C-N str),1057(C-O-C str), and 876 (C-Clstr); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.80 (d, 2H, J = 8.0 Hz, Ar-H), 7.57 (d, 2H, J = 8.0 Hz, Ar-H), 7.33-7.07 (m, 3H, Ar-H), 6.96 (s, 1H, NH), 6.80 (d, 2H, J = 8.8 Hz, Ar-H), 6.78-6.64 (m, 2H, Ar-H), 6.59 (d, 2H, J = 8.8 Hz, Ar-H).13C-NMR (100.16 MHz, DMSO-d_6): δ 152.8, 149.4, 141.0, 135.0, 133.0, 127.4, 125.9, 124.8, 122.6, 120.3, 119.2, 118.3, 117.4, 115.0. LC-MS (+ mode) m/z: 405 (M+H)$^+$.

N-(5-chloro-2-phenoxyphenyl)-4-Bromo-benzenesulfonamide (3b):

MF $C_{18}H_{13}BrClNO_3S$; Solid; Yield 78 %;m.p. 133-135 oC. IR (KBr, cm_{-1}) ν_{max}: 3258 (-N-H, str), 1591(C-Cstr), 1486 (S=O str), 1353 (S=O str), 1224 (C-N str),1077 (C-O-C str), 828 (C-Clstr) and 622 (C-Br str) ;^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.80 (d, 2H, J = 8.0 Hz, Ar-H), 7.57 (d, 2H, J = 8.0 Hz, Ar-H), 7.33-7.07 (m, 3H, Ar-H), 6.96

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(s, 1H, NH), 6.80 (d, 2H, J = 8.8 Hz, Ar-H), 6.78-6.64 (m, 2H, Ar-H), 6.59 (d, 1H, J = 8.8 Hz, Ar-H). 13C-NMR (100.16 MHz, DMSO-d_6): δ 153.6, 135.7, 135.3, 133.2, 129.7, 127.1, 125.5, 125.2, 124.3, 119.7, 118.9, 118.5, 117.2, 114.8. LC-MS (+ mode) m/z: 439 $(M+H)^+$.

N-(5-chloro-2-phenoxyphenyl)-3-Chloro-4-fluorobenzenesulfonamide (3c):

MF $C_{18}H_{12}Cl_2FNO_3S$; Solid; Yield 80 %;m.p140-142 ºC. IR (KBr, cm^{-1}) ν_{max}: 3256 (-N-H, str), 1597 (C-Cstr), 1481 (S=O str), 1415(C-F str), 1359 (S=O str), 1234(C-N str),1047(C-O-C str), 856 (C-Clstr) and 746 (C-Clstr); 1H-NMR (400 MHz, DMSO-d_6): δ 7.80 (d, 2H, J = 8.0 Hz, Ar-H), 7.57 (d, 2H, J = 8.0 Hz, Ar-H), 7.33-7.07 (m, 3H, Ar-H), 6.96 (s, 1H, NH), 6.80 (d, 2H, J = 8.8 Hz, Ar-H), 6.78-6.64 (m, 2H, Ar-H), 6.59 (d, 2H, J = 8.8 Hz, Ar-H). 13C-NMR (100.16 MHz, DMSO-d_6): δ 157.5, 153.0, 134.8, 133.4, 133.0, 126.2, 125.8, 125.7, 124.6, 120.9, 120.3, 119.0, 118.2, 117.2, 116.8, 115.2. LC-MS (+ mode) m/z: 413 $(M+H)^+$.

N-(5-chloro-2-phenoxyphenyl)-4-fluorobenzenesulfonamide (3d):

MF $C_{18}H1_3ClFNO_3S$;Solid; Yield 79 %;m.p. 126-128 oC. IR (KBr, cm^{-1}) vmax: 3285 (-N-H, str), 1594 (C-Cstr), 1476 (S=O str), 1428 (C-F str), 1349 (S=O str), 1242 (C-N str),1076 (C-O-C str) and 859 (C-Clstr). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.88 (d, 2H, J = 8.4 Hz, Ar-H), 7.66 (d, 2H, J = 8.4 Hz, Ar-H), 7.33-7.07 (m, 3H, Ar-H), 7.02 (s, 1H, NH), 6.80 (d, 2H, J = 8.8 Hz, Ar-H), 6.78-6.64 (m, 2H, Ar-H), 6.59 (d, 2H, J = 8.8 Hz, Ar-H). 13C-NMR (100.16 MHz, DMSO-d^6): δ 158.6, 153.4, 134.9, 134.1, 133.3, 128.4, 125.6, 125.0, 120.0, 118.9, 118.0, 117.1, 116.9, 114.7. LC-MS (+ mode) m/z: 378 $(M+H)^+$.

N-(5-chloro-2-phenoxyphenyl)-4-Chloro-3-nitrobenzenesulfonamide (3e):

MF $C_{18}H_{12}Cl_2N_2O_5S$; Solid; Yield 81 %;m.p. 171-173 oC. IR (KBr, cm^{-1}) ν_{max}: 3288 (-N-H, str), 1567 (-N=Ostr), 1592 (C-Cstr) 1459 (S=O str), 1229(C-N str),1075(C-O-C str), 874 (C-Clstr) and 756 (C-Clstr) 1H-NMR (400 MHz, DMSO-d_6): δ 8.20-8.12 (m, 3H, Ar-H), 7.66 (d, 2H, J = 8.0 Hz, Ar-H), 7.40-7.22 (m, 3H, Ar-H), 7.14 (s, 1H, NH), 6.88-6.64 (m, 3H, Ar-H). 13C-NMR (100.16 MHz, DMSO-d_6): δ 153.5, 145.4, 135.2, 134.0, 133.1, 130.9, 129.5, 128.3, 125.7, 125.1, 121.9, 119.9, 118.8, 118.1, 117.0, 114.8.LC-MS (+ mode) m/z: 440 $(M+H)^+$, (M+2).

Biological assays:

Antimicrobial activity:

Antibacterial screening test: The antibacterial activity of the synthesized compounds **(2a-e&3a-e)** were studied against different Gram-positive [Bacillus subtilis (MTCC2274) and Staphylococcus aureus (ATCC 9144)] and Gram-negative [Escherichia coli (ATCC 9637) and Proteus vulgaris(MTCC0426)]. For detection of antibacterial activity the filter papaer disc diffusion method [15] was employed. Nutrient agar (NA) was used as the basal medium for test bacteria. These agar media were inoculated with 0.5 mL of the 24 hr liquid cultures containing 1x107 cells/mL. The diffusion time was 24 hr at 50C and the incubation time was 12 hr at 370C for bacteria. Discs with only DMSO were used as control. The diameter (in mm) of the observed inhibition zones were taken as a measure of inhibitory activity.

Table 1: Antibacterial zone of inhibition (mm) of the synthesized compounds(2a-e&3a-e):

Compound	Zone of inhibition (in mm) at conc. 200µg/mL after 24 hours			
	B. subtilis (MTCC2274)	***S.aureus (ATCC 9144)***	***E.coli (ATCC 9637)***	***P.vulgaris (MTCC0426)***
2a	25	23.2	24	25.6
2b	15	17	15	17
2c	16	18	17.9	16.4
2d	14.5	16.3	15.2	13.7
2e	23.3	22.8	20.9	24.3
3a	26.5	22.9	24.2	25
3b	17	18.5	14.2	15.3
3c	20	19.8	18	19.5
3d	23.6	22.4	23.6	24.5
3e	18	19	17	19.5
Ciprofloxacin	28	25	26	27

Antifungal screening test:

The antifungal activity of compounds (46a-e&47a-e) were evaluated against two plant pathogenic andmold fungi, viz., ***Aspergillus niger(MTCC1881)*** and ***Aspergillus fumigates (ATTC 9197).*** The antifungal activity was assessed by poisoned food technique [16] with some modifications. Potato dextrose agar (PDA) was used as basal medium for test fungi. Glass petri dishes were sterilized and 15 mL of sterilized melted PDA medium (~ 450C) was poured into each petri dish (90mm). After solidification of the medium small portions of mycelium of each fungus were spread carefully over the center of each PDA plate with the help of sterilized needlels. Thus each fungus was transferred to a number of PDA plates. The PDA plateds were then incubated at (25±20C) and after five days of incubation they were ready for use. The prepared discs of test samples were placed gently on the solidified agar plates freshly seeded with the test organisms with sterile forceps. Control discs were also placed on the test plates to compare the effect of solvents. The plates were then kept in a refrigerator at 40C for 24 hr in order that the materials had sufficient time to diffuse to a considerable area of the plates. Afterwards the plates were incubated at 370C for 72 hr.

Table:2. Antifungal Zone of inhibition of title compounds 2a-e and 3a-e

Compound	Zone of inhibition (in mm) at 200µg/mL	
	***A.Niger* (MTCC1881)**	**A.fumigates (ATTC 9197)**
2a	24	25.3
2b	17.5	19.6
2c	16.2	19.3
2d	12.3	15
2e	23	24
3a	24.2	25
3b	14.8	17.8
3c	15.6	18
3d	22	23
3e	21	22.3
Ketoconazole	26	27

The bioassay results revealed that all the title compounds 2a-e and 3a-e showed potent to moderate zone of inhibition by killing the bacterial and fungal strains. A few of the compounds 2a, 2e, 3a and 3d were exhibited excellent activity against all the bacterial strains, 2a and 3a showed good activity against ***E.coli***and***P. vulgaris***. The compounds 3aand showed high activity against the two fungal strains, the compounds 2a, 2e, 3a and 3d exhibited good activity against ***A. niger*** and ***A.fumigates*** and especially, 2e showed good activity against ***A.fumigates***. When compared to carbamates, sulfonamides showed better activity. The comparision of aliphatic and aromatic carbamate derivatives of 5-chloro-2-(phenoxy)aniline, the compounds having aromatic substituents exhibited good activity. Nitro substited compounds exhibited better antibacterial activity. The zones of inhibitions of the mentioned compounds are almost close to the standard. A few of the compounds which are bearing fluorine and chloro groups exhibited potent activity.

Conclusion:

The5-chloro-2-phenoxy-aniline derivatives of sulphonamide and carbamates were synthesized by simple method and the products are obtained in high yield (%). The synthesized compounds were screened for antimicrobial activity. A few compounds **2a, 2e, 3a** and **3d** were exhibited excellent activity against all the bacterial strains, **2a** and **3a** showed good activity against ***E.coli***and***P. vulgaris.***The compounds **2a, 2e, 3a** and **3d** exhibited good activity against ***A. niger*** and ***A.fumigates*** and especially, **2e** showed good activity against ***A.fumigates***. Finally, we concluded that sulphonamide and carbamate derivatives of 5-chloro-2-(phenoxy)aniline **2a** and **3a** showed high antimicrobial activity.

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