SOUTHERN BRAZILIAN JOURNAL OF CHEMISTRY
SOUTH. BRAZ. J. CHEM., Vol 16., N° 16, 2008

SYNTHESIS AND ANTIMICROBIAL STUDIES OF NOVEL IMINES AND OXADIAZOLES

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ABSTRACT
N-benzylidene-2-(4-chloro-3-methylphenoxy)acetohydrazides **(3a-e)**, obtained by arylation of 2-(4-chloro-3-methyl phenoxy)acetohydrazide **(2)**, was cyclized with acetic anhydride to yield 1-(5-((4-chloro-3-methylphenoxy)methyl)-2-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanones **(4a-e)**. All the newly synthesized compounds were analytically and spectrally characterized and evaluated for anti-bacterial and anti-fungal activities.

KEYWORDS
Acetohydrazide, aryloxy acetate, imines, oxadiazoles, antimicrobial activity

RESUMO
N-benzilideno-2-(4-cloro-3-metilfenoxi)acetohidrazidas **(3a-e)**, obtidas pela arilação de 2-(4-cloro-3-metil fenoxi)acetohidrazida **(2)**, foram ciclizadas com anidrido acético para obter 1-(5-((4-cloro-3-metilfenoxi)metil)-2-fenil-1,3,4-oxadiazol-3(2H)-il)etanonas **(4a-e)**. Todos os compostos novos sintetizados foram caracterizados através de espectroscopia e outros métodos analíticos. A atividade antibacterial e antifúngica foram avaliadas.

PALAVRAS-CHAVE
Acetohidrazida, Ariloxi Acetato, Iminas, Oxodiazol, Atividade Antimicrobial

DOI: 10.48141/SBJCHEM.v17.n17.2008.14_2008.pdf

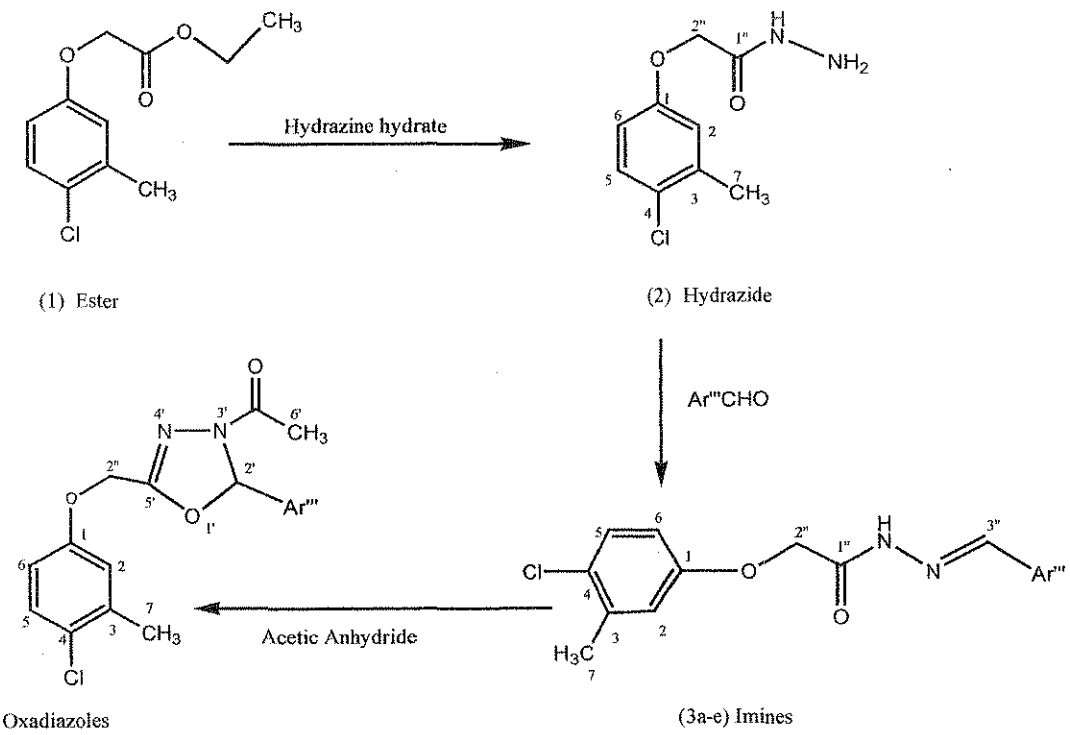
INTRODUCTION

It is an established fact that oxadiazoles, imines and phenolic moieties possess anti-convulsant[1,2], antiproteolytic[2], anantimitotic[3], anticancer[4], antikinetoplastid[5], antitussive[6], hybrid COX-2 inhibitor/nitric oxide donor[7], antimycotic[8], anti-tubercular[9], cosmetic biocide preservative[10], antimicrobial[11], antibacterial[12,13] activities. Phenolic moieties are known as precursor for imines [14], which are precursors for oxadiazoles[15]. As per literature, activities associated with oxadiazoles, imines and phenolic moieties, an attempt was made to synthesize novel potent antibacterial and antifungal by converting a phenolic ester moiety into some novel 1-(5-((4-chloro-3-methylphenoxy)methyl)-2-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanones **(4a-e)**, via synthesis of hydrazide **(2)** and imines **(3a-e)** as intermediates. The novel compounds were characterized and further evaluated for anti-bacterial and anti-fungal activities.

RESULTS AND DISCUSSION

N-(substituted benzylidiene)-2-(4-chloro-3-methylphenoxy)acetamides **(3a-e)**, prepared from compound **1**, when cyclized with acetic anhydride leads to potent antibacterial and antifungal 1-(5-((4-chloro-3-methylphenoxy)methyl)-2-aryl-1,3,4-oxadiazol-3(2H)-yl)ethanones **(4a-e)**. Synthetic procedure for conversion of compound **1** to **2**, **3a-e** and **4a-e** is suggested in **Scheme-1**. Physical data of **1**, **2**, **3a-e** and **4a-e** are given in **Table-1**. The purity of all newly synthesized compounds was checked by TLC (Rf value given in **table-1)** and elemental analysis. The assigned structure, molecular formulae and the anomeric configuration of the newly synthesized compounds **2, 3a-e** and **4a-e** was further confirmed and supported by Mass, ^{1}H NMR and IR spectral data, arise as result of occurrence of molecular ion peak of the assigned structures, downfield shifting of protons and different stretching of bands of the compounds. The fragmentation pattern of compound **3a** and **4a** further supported the structure of newly synthesized compounds **3a-e** and **4a-e** given in **Scheme-II** and **III**. In general the IR spectra of newly synthesized compounds revealed NH, OH, CO (CONH), C-O-C peaks near 3256, 3510, 1645, 1253 cm^{-1} respectively. In the ^{1}H-NMR spectra, signals of respective protons of newly synthesized compounds showed the peaks for –Co-CH_3, -CH_3, -O-CH_2, -OH, aromatic protons, N=CH and NH near 2.06, 2.3, 4.8, 5.2, 6.1-7.4, 8.0 and 9.2 respectively. The general Mass fragmentation pattern for compound **3a** showed the m/z peaks at 345(M^+), 190(base Peak), 330, 198, 155, 147, 141, 120 as a result of loss of -1e^-, -C_8H_8ClO, -CH_3, -$C_9H_{11}N_2$, -$C_9H_{12}N_3O$, -$C_9H_9ClNO_2$, -$C_{11}H_{14}N_3O$, -$C_{10}H_{10}ClN_2O_2$ respectively and compound **4a** showed the m/z peaks at m/z: 387(M^+), 120(base peak), 372, 232, 155, 141 as a result of loss of -1e^-, -$C_{12}H_{12}ClN_2O_3$, -CH_3, -C_8H_8ClO, -$C_{12}H_{14}N_3O_2$, -$C_{13}H_{16}N_3O_2$ respectively. In the same way the fragmentation pattern of all newly synthesized compounds **3b-e** and **4b-e** was identified to further support the structure. The elemental analysis results were within ± 0.4% of the theoretical values. Both analytical and spectral data (IR, ^{1}H-NMR, Mass) of all the synthesized compounds were in full agreement with the proposed structure. The newly

SCHEME-I



(1) Ester

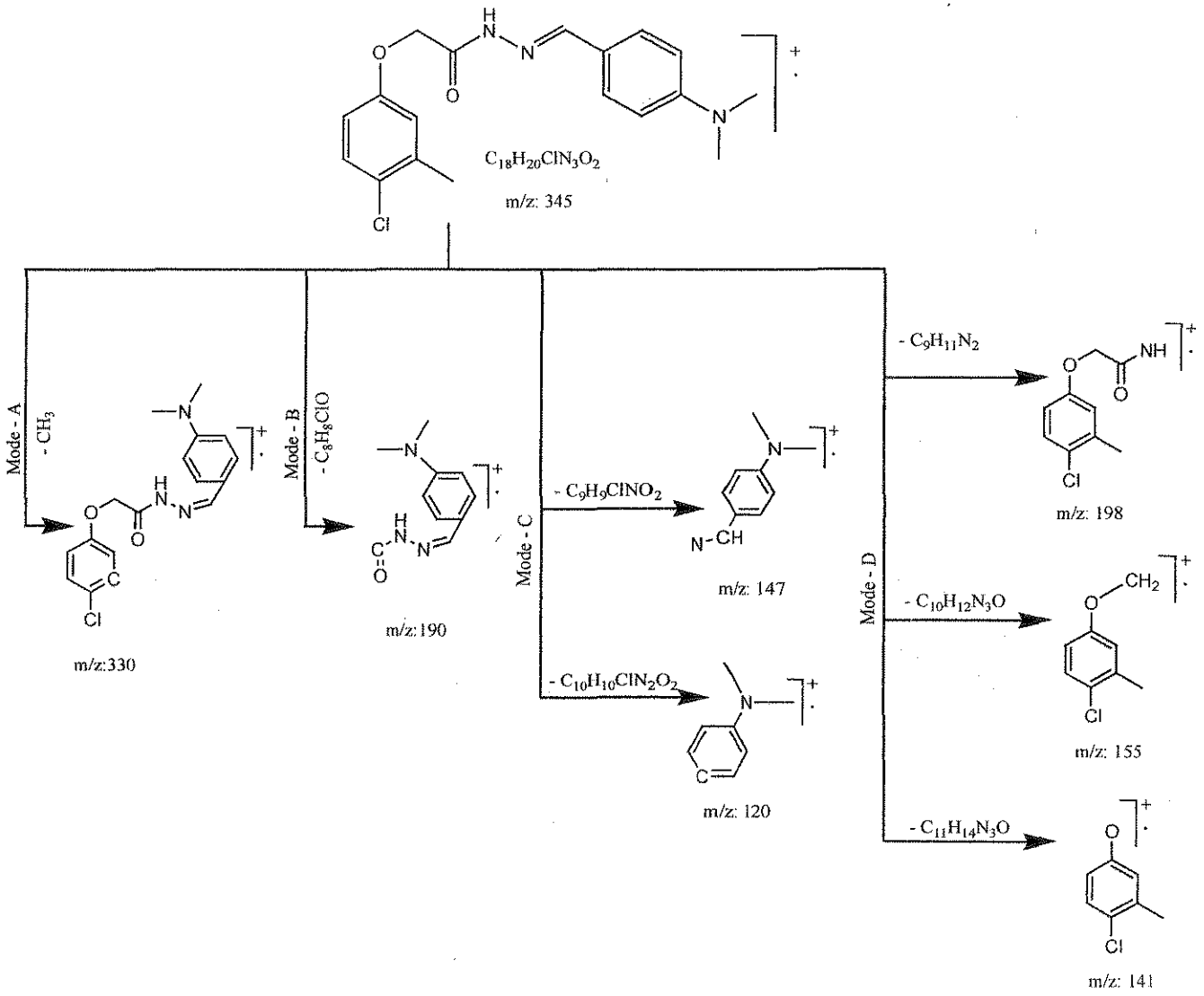
(2) Hydrazide

(3a-e) Imines

(4a-e) Oxadiazoles

Where Ar''' = 4-dimethyl amino phenyl, 4-chloro phenyl, 2,4-dihydroxy phenyl, phenyl and 4-hydroxyphenyl group

SCHEME-II : Fragmentation pattern of Imine (3a)



SCHEME-III : Fragmentation pattern of Oxadiazole (4a)

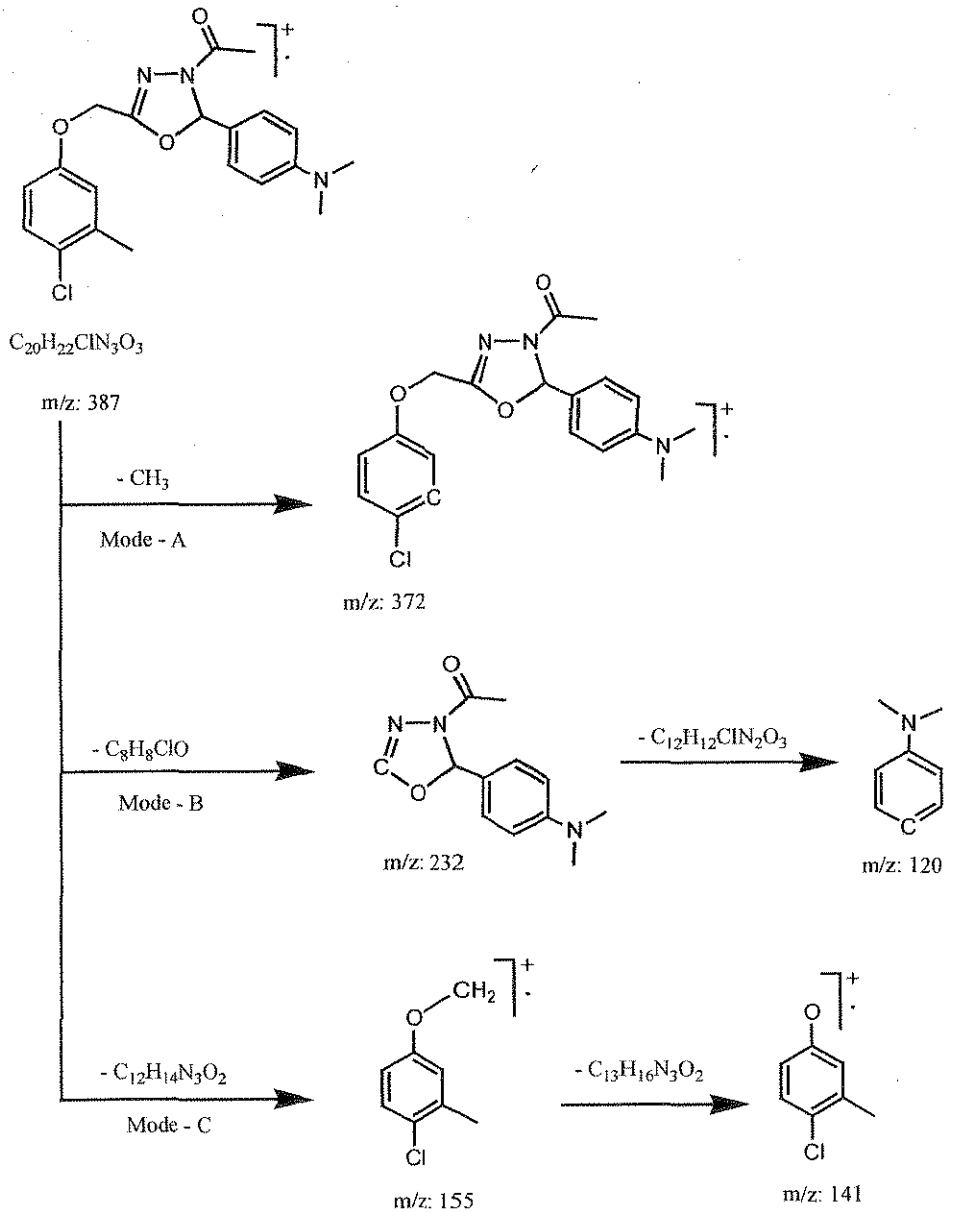
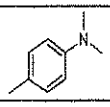
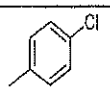
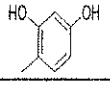
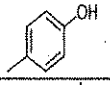
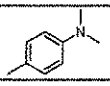
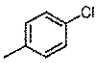
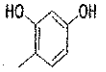
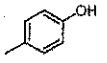


Table: 1 - Physical Data of compound 1, 2, 3(a-e) and 4(a-e)

Compd	Ar''	Physical Characteristics	Yield (%)	Molecular Formulae	Mol. Wt.	m.p. (°C)	Rf Value
1	-	Pale Brown liquid	70	$C_{11}H_{13}O_3Cl$	228.67	145 B.P.	-
2	-	White crystals	85	$C_9H_{11}ClN_2O_2$	214.64	160-161	0.57
3a		White crystals	72	$C_{18}H_{20}N_3O_2Cl$	345.82	194-195	0.59
3b		White crystals	63	$C_{16}H_{14}N_2O_2Cl_2$	337.2	212-213	0.52
3c		White crystals	65	$C_{16}H_{15}N_2O_4Cl$	334.75	220-221	0.55
3d		White cloggy crystals	59	$C_{16}H_{15}ClN_2O_2$	302.76	185-186	0.49
3e		White crystals	57	$C_{16}H_{15}N_2O_3Cl$	318.75	216-217	0.53
4a		Pale yellow crystals	72	$C_{20}H_{22}N_3O_3Cl$	387.86	218-219	0.49
4b		Orange Crystals	69	$C_{18}H_{16}N_2O_3Cl_2$	379.23	203-204	0.65
4c		Pale yellow crystals	70	$C_{18}H_{17}N_2O_5Cl$	376.79	215-216	0.52
4d		Pale yellow crystals	79	$C_{18}H_{17}N_2O_3Cl$	344.79	219-220	0.62
4e		Light brown crystals	75	$C_{18}H_{17}N_2O_4Cl$	360.79	210-211	0.68

synthesized compounds were tested for antibacterial activity against the freshly cultured strains of *S. aureus, E. coli, P. aeruginosa* using sterile Nutrient agar media and antifungal activity against the freshly cultured strains strains of *C. albicans, A. flavus, A. fumigatus* using sterile Sabouraud's agar medium. After comparing the antibacterial and antifungal results of newly synthesized compounds using ampicillin and fluconazole as standards it was found that compounds **3a-e** and **4a-e** possesses antibacterial and antifungal activities to certain extent. Among newly synthesized derivatives, compound **3c** and **4a** was found to be equipotent as ampicillin when tested against the strains of *E. coli,* where as tested compounds **3c, 4a and 4d** have shown good antibacterial and antifungal activity against *S. aureus, P. aeruginosa and C. albicans.,* where as remaining compounds have shown moderate antibacterial and antifungal activity when tested against the strains of *S. aureus, E. coli, P. aeruginosa A. flavus, A. fumigatus* given in **Table-2**. After comparing the antimicrobial results of compounds **3a-e** and **4a-e**, it was concluded that the incorporation of oxadiazole moiety in aryloxy derivatives enhances their antimicrobial activity and also para substitution in Ar'' group of oxadiazoles **4a-e** was found to enhance their potency especially in compound **4a**. Further studies to acquire more information about structure activity relationship are in progress in our laboratory

EXPERIMENTAL

Melting points of newly synthesized compounds were determined in open capillary tubes. IR spectra were recorded (in KBr) on Bruker PCIR, ^{1}H-NMR on bruker, DPX 300 and mass spectra on MASPEC (MSW/9629). Purity of synthesized compounds was checked by TLC aluminium sheets – silica gel 60 F254 (0.2 mm).

2-(4-chloro-3-methylphenoxy)acetohydrazide (2) :

A mixture of ethylaryloxyacetate **1** (0.05mol) and hydrazine hydrate (0.075mol) in ethanol was refluxed for 6 hours. The reaction mixture was distilled off to remove solvent and formed crystals were recrystallised from methanol to yield compound **2** (Physical data and Rf value found using ethyl acetate and petroleum ether in the ratio of 9.5:0.5 are given in **Table 1**). IR (KBr): ν (cm^{-1}) 3276, 3281 (NH and NH_2), 1740 (CO of ester); ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.32 (s, 3H, CH_3), 4.83 (s, 2H, OCH_2), 6.38 (br, 2H, NH_2), 6.51 (d, 1H, J = 2.7 Hz, Ar-H2), 6.53 (dd, 1H, J = 2.7, 6.3 Hz, Ar-H6), 7.04 (d, 1H, J = 6.3 Hz, Ar-H5), 9.35 (s, 1H, NH); ^{13}C-NMR (100MHz, DMSO): δ (ppm) 19.83 (C-7), 66.48 (C-2''), 113.89 (C-6), 117.42 (C-2), 125.22 (C-4), 129.46 (C-5), 136.46 (C-3), 156.58 (C-1) and 166.56 (C-1''); Mass (%): m/z 214 (M^+, 12), 141 (base Peak, 100), 155 (52); Analysis (calculated) found: C (50.36) 50.32, H (5.17) 5.14, N (13.05) 13.02 %.

General procedure for synthesis of 2-{(4-chloro-3-methyl) phenoxy}-N-[substituted benzylidene]acetohydrazides (3a-e) :

A mixture of compound **2** (0.01mol) and aromatic aldehyde (0.01mol) in the presence of few drops of glacial acetic acid was refluxed for 6 hours. Formed products were isolated and recrystallised from methanol to yield compounds **3a-e** (Physical data and Rf values found using chloroform and methanol in the ratio of 9:1 are given in **Table 1**).

N-(4-(dimethylamino)benzylidene)-2-(4-chloro-3-methylphenoxy)acetohydrazide (3a)

IR (KBr): ν (cm^{-1}) 1645 (CO of CONH), 3214(NH of CONH); ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.39 (s, 3H, CH_3), 2.87 (s, 6H, N $(CH_3)_2$), 4.83 (s, 2H, OCH_2), 6.50 (d, 1H, J = 2.7

Table: 2 – Antimicrobial activity-sensitivity testing of 3(a-e) and 4(a-e)

Compd. No.	Zone of inhibition in mm					
	Antibacterial Activity			Antifungal Activity		
	SA	EC	PA	CA	AF	AFU
3a	18	18	13	10	8	9
3b	14	18	14	11	10	8
3c	22	24	22	12	13	10
3d	15	11	13	10	9	8
3e	22	21	21	13	11	12
4a	23	24	21	16	11	10
4b	19	18	14	15	10	8
4c	20	18	21	14	13	9
4d	24	20	23	16	12	8
4e	22	21	19	14	13	11
Ampicillin	25	24	24	-	-	-
Fluconazole	-	-	-	17	16	17

Where SA = *S. aureus*, EC = *E. coli*, PA= *P. aeruginosa*, CA = *C. albicans*, AF = *A. flavus*, AFU = *A. fumigatus*

Hz, Ar-H2), 6.53 (dd, 1H, *J* = 2.7, 6.3 Hz, Ar-H6), 6.62 (d, 2H, *J* = 6.3 Hz, Ar''-H3'' & 5''), 6.95 (d, 2H, *J* = 6.9 Hz, Ar''-H2'' & 6''), 7.04 (d, 1H, *J* = 6.3 Hz, Ar-H5), 8.00 (s, 1H, N=CH), 9.50 (s, 1H, NH); ^{13}C-NMR (100MHz, $CDCl_3$): δ (ppm) 19.56 (C-7), 40.29 ($N(CH_3)_2$), 68.82 (C-2''), 111.03 (C-6), 113.96 (C-3''' and C-5'''), 114.79 (C-2), 121.74 (C-1'''), 127.93 (C-4), 128.86 (C-5), 130.04 (C-2''' and C-6'''), 136.31 (C-3), 144.96 (C-3''), 150.03 (C-4'''), 156.84 (C-1) and 168.48 (C-1''); Mass : m/z 345 (M^+, 10), 190 (base Peak, 100), 330 (12), 198 (22), 155 (38), 147 (20), 141 (40), 120 (24); Analysis (calculated) found: C (62.52) 62.51, H (5.83) 5.82, N (12.15) 12.11 %

N-(4-chlorobenzylidene)-2-(4-chloro-3-methylphenoxy)acetohydrazide (3b)

IR (KBr): ν (cm^{-1}) 1648 (CO of CONH), 3256(NH of CONH); ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.36 (s, 3H, CH_3), 4.80 (s, 2H, OCH_2), 6.50 (d, 1H, *J* = 2.8, Ar-H2), 6.53 (dd, 1H, *J* = 2.7, 6.3 Hz, Ar-H6), 7.04 (d, 1H, *J* = 6.2 Hz, Ar-H5), 7.10 (d, 2H, *J* = 6.3 Hz, Ar''-H2'' & 6''), 7.21 (d, 2H, *J* = 6.8 Hz, Ar''-H3'' & 5''), 8.00 (s, 1H, N=CH), 9.25 (s, 1H, NH); ^{13}C-NMR (100MHz, $CDCl_3$): δ (ppm) 19.92 (C-7), 69.05 (C-2''), 112.96 (C-6), 116.14 (C-2), 126.83 (C-4), 128.06 (C-3''' and C-5'''), 129.18 (C-5), 130.87 (C-2''' and C-6'''), 132.65 (C-1'''), 136.13 (C-4'''), 137.04 (C-3), 143.26 (C-3''), 157.78 (C-1) and 169.46 (C-1''); Mass : m/z 336 (M^+, 10), 198 (base Peak, 100), 321 (16), 181 (24), 155 (30), 141 (18), 138 (16), 111 (26); Analysis (calculated) found: C (56.99) 56.96, H (4.18) 4.16, N (8.33) 8.30 %

N-(2,4-dihydroxybenzylidene)-2-(4-chloro-3-methylphenoxy)acetohydrazide (3c)

IR (KBr): ν (cm^{-1}) 1646 (CO of CONH), 3310(NH of CONH), 3510 (OH); ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.35 (s, 3H, CH_3), 4.80 (s, 2H, OCH_2), 5.16 (s, 1H, OH), 5.18 (s, 1H, OH), 6.20 (d, 1H, *J* = 2.8 Hz, Ar''-H3''), 6.30 (dd, 1H, *J* = 2.7, 6.7 Hz, Ar''-H5''), 6.50 (d, 1H, *J* = 2.7 Hz, Ar-H2), 6.53 (dd, 1H, *J* = 2.6, 6.3 Hz, Ar-H6), 7.03 (d, 1H, *J* = 6.6 Hz, Ar-H5), 7.31 (d, 1H, *J* = 6.6 Hz, Ar''-H6''), 8.01 (s, 1H, N=CH), 9.02 (s, 1H, NH); ^{13}C-NMR (100MHz, $CDCl_3$): δ (ppm) 18.84 (C-7), 68.43 (C-2''), 104.25 (C-3'''), 108.21 (C-5'''), 110.47 (C-1'''), 113.12 (C-6), 114.69 (C-2), 127.26 (C-4), 129.84 (C-5), 132.52 (C-6'''), 137.83 (C-3), 142.48 (C-3''), 158.06 (C-1), 161.91 (C-2'''), 162.02 (C-4''') and 169.42 (C-1''); Mass : m/z 334 (M^+, 6), 198 (base Peak, 100), 179 (34), 155 (50), 141 (30), 136 (24), 109 (28); Analysis (calculated) found: C (57.41) 57.40, H (4.52) 4.51, N (8.37) 8.34 %

N-benzylidene-2-(4-chloro-3-methylphenoxy)acetohydrazide (3d)

IR (KBr): ν (cm^{-1}) 1646 (CO of CONH), 3252(NH of CONH); ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.36 (s, 3H, CH_3), 4.83 (s, 2H, OCH_2), 6.52 (d, 1H, *J* = 2.5 Hz, Ar-H2), 6.55 (dd, 1H, *J* = 2.7, 6.9 Hz, Ar-H6), 7.03 (d, 1H, *J* = 6.7 Hz, Ar-H5), 7.09 (t, 1H, *J* = 7.01, 7.02 Hz, Ar''-H4''), 7.14 (dd, 2H, *J* = 2.7, 6.5 Hz, Ar''-H2''' & 6'''), 7.21 (m, 2H, Ar''-H3''' & 5'''), 8.12 (s, 1H, N=CH), 9.50 (s, 1H, NH); ^{13}C-NMR (100MHz, $CDCl_3$): δ (ppm) 19.26 (C-7), 69.34 (C-2''), 113.08 (C-6), 114.10 (C-2), 126.56 (C-4), 127.28 (C-3''' and C-5'''), 128.75 (C-5), 129.98 (C-2''' and C-6'''), 131.09 (C-4'''), 132.45 (C-1'''), 137.54 (C-3), 143.64 (C-3''), 158.58 (C-1) and 170.23 (C-1''); Mass : m/z 302 (M^+, 6), 104 (base Peak, 100), 287 (18), 252 (30), 198 (28), 155 (24), 147 (22), 141 (26); Analysis (calculated) found: C (63.47) 63.44, H (4.99) 4.96, N (9.25) 9.23 %

N-(4-hydroxybenzylidene)-2-(4-chloro-3-methylphenoxy)acetohydrazide (3e)

IR (KBr): ν (cm^{-1}) 3508 (OH), 1640 (CO of CONH), 3310(NH of CONH); ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.36 (s, 3H, CH_3), 4.84 (s, 2H, OCH_2), 5.00 (s, 1H, OH), 6.50 (d,

1H, J = 2.7 Hz, Ar-H2), 6.53 (dd, 1H, J = 2.7, 6.3 Hz, Ar-H6), 6.79 (d, 2H, J = 6.3 Hz, Ar'''-H3''' & 5'''), 7.04 (d, 1H, J = 6.37 Hz, Ar-H5), 7.40 (d, 2H, J = 6.6 Hz, Ar'''-H2''' & 6'''), 8.12 (s, 1H, N=CH), 9.28 (s, 1H, NH); ^{13}C-NMR (100MHz, $CDCl_3$): δ (ppm) 19.45 (C-7), 69.27 (C-2''), 111.76 (C-6), 113.45 (C-2), 116.73 (C-3''' & C-5'''), 125.11 (C-1'''), 126.62 (C-4), 128.26 (C-5) and 129.47 (C-2''' & C-6'''), 136.88 (C-3), 142.73 (C-3''), 157.36 (C-1), 161.71 (C-4''') and 169.88 (C-1''); Mass : m/z 318 (M^+, 6), 163 (base Peak, 100), 303 (10), 198 (18), 155 (22), 141 (24), 120 (22), 93 (20); Analysis (Calculated) Found: C (60.29) 60.27, H (4.74) 4.72, N (8.79) 8.76 %

1-(5-((4-chloro-3-methylphenoxy)methyl)-2-aryl-1,3,4-oxadiazol-3(2H)-yl) ethanone (4a-e) :

A mixture of compound **3a-e** (0.01mol) and acetic anhydride (0.02 mol) was refluxed for 6 hours. Formed product was isolated and recrystallized from methanol to yield compounds **4a-e**. (Physical data and Rf values found using chloroform and methanol in the ratio of 8:2 are given in **Table 1**).

1-(5-((4-chloro-3-methylphenoxy)methyl)-2-(4-(dimethylamino)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (4a)

IR (KBr): ν (cm^{-1}) 1615 (C=N), 1682 (C=O), 1253 (C-O-C); ^{1}H-NMR (DMSO-D6) : δ (ppm) 2.04 (s, 3H, -CO-CH_3), 2.32 (s, 3H, CH_3), 2.88 (s, 6H, -N(CH_3)$_2$), 4.86 (s, 2H, -O-CH_2), 6.49 (d, 1H, J = 2.6Hz, Ar-H2), 6.54 (m, 3H, Ar-H6, Ar''-H3''' & 5''), 6.60 (s, 1H, -N-CH-Ar''), 7.0 (d, 2H, J = 8.2Hz, Ar'''-H2''' & 6'''), 7.04 (d, 1H, J = 8.3 Hz, Ar-H5); ^{13}C-NMR (100MHz, $CDCl_3$): δ (ppm) 18.56 (C-7), 24.44 (C-7'), 40.87 (C-7''' & C-8'''), 69.23 (C-2''), 74.14 (C-2'), 111.88 (C-6), 114.02 (C-3''' & C-5'''), 115.08 (C-2), 126.12 (C-4), 127.96 (C-2''' & C-6'''), 128.83 (C-5), 129.77 (C-1'''), 136.45 (C-3), 146.45 (C-4'''), 154.63 (C-5'), 157.89 (C-1) and 168.58 (C-6'); Mass : m/z 387(M^+, 4), 120 (base peak, 100), 372 (26), 232 (20), 155 (34), 141 (28), 112 (24); Analysis (Calculated) Found: C (61.93)61.91 , H (5.72)5.71 , N (10.83)10.80 %

1-(5-((4-chloro-3-methylphenoxy)methyl)-2-(4-chlorophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (4b)

IR (KBr): ν (cm^{-1}) 1605 (C=N), 1689 (C=O), 1254 (C-O-C); ^{1}H-NMR (DMSO-D6) : δ (ppm) 2.09 (s, 3H, -CO-CH_3), 2.38 (s, 3H, CH_3), 4.91 (s, 2H, -O-CH_2), 6.54 (d, 1H, J = 2.6Hz, Ar-H2), 6.56 (dd, 1H, J = 2.8, 7.9Hz, Ar-H6), 6.64 (s, 1H, -N-CH-Ar''), 7.04 (d, 1H, J = 8.3 Hz, Ar-H5), 7.13 (d, 2H, J = 8.1Hz, Ar'''-H2''' & 6'''), 7.22 (d, 2H, J = 8.3Hz, Ar'''-H3''' & 5'''); ^{13}C-NMR (100MHz, $CDCl_3$): δ (ppm) 19.25 (C-7), 23.68 (C-7'), 71.27 (C-2''), 73.65 (C-2'), 112.41 (C-6), 115.39 (C-2), 126.18 (C-4), 127.44 (C-2''' & C-6'''), 128.93 (C-3''' & C-5'''), 129.87 (C-5), 133.16 (C-4'''), 137.66 (C-3), 138.92 (C-1'''), 155.36 (C-5'), 158.74 (C-1), 168.45 (C-6'); Mass : m/z 378 (M^+, 6), 223 (base peak, 100), 363 (22), 155 (32), 141 (28), 112 (20), 111 (26); Analysis (Calculated) Found: C (57.01)57.00 , H (4.25) 4.21, N (7.39)7.36 %

1-(5-((4-chloro-3-methylphenoxy)methyl)-2-(2,4-dihydroxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (4c)

IR (KBr): ν (cm^{-1}) 3512 (OH), 1680 (C=O), 1610 (C=N), 1250 (C-O-C), ^{1}H-NMR (DMSO-D6) : δ (ppm) 2.08 (s, 3H, -CO-CH_3), 2.36 (s, 3H, CH_3), 4.89 (s, 2H, -O-CH_2), 5.20 (s, 1H, 4-OH), 5.26 (s, 1H, 2-OH), 6.12 (d, 1H, J = 2.7Hz, Ar'''-H3'''), 6.24 (dd, 1H, J = 2.73, 7.8Hz, Ar'''-H5'''), 6.50 (d, 1H, J = 2.7Hz, Ar-H2), 6.52 (dd, 1H, J = 2.6, 7.6Hz, Ar-H6), 6.62 (s, 1H, -N-CH-Ar''), 6.85 (d, 1H, J = 7.8 Hz, Ar'''-H6'''), 7.04 (d, 1H, J =

8.2 Hz, Ar-H5); ^{13}C-NMR (100MHz, $CDCl_3$): δ (ppm) 18.96 (C-7), 23.59 (C-7'), 65.37 (C-2'), 73.52 (C-2''), 103.66 (C-3'''), 109.51 (C-5'''), 112.33 (C-6), 114.68 (C-2), 122.77 (C-1'''), 125.36 (C-4), 128.43 (C-5), 129.65 (C-6'''), 137.21 (C-3), 155.08 (C-5'), 156.73 (C-2'''), 157.96 (C-1), 158.95 (C-4''') and 168.37 (C-6'); Mass : m/z 376 (M^+, 4), 141 (base peak, 100), 361 (20), 109 (22), 221 (24), 155 (30), 112 (32); Analysis (Calculated) Found: C (57.38)57.34, H (4.55)4.53 , N (7.43)7.42 %

1-(5-((4-chloro-3-methylphenoxy)methyl)-2-phenyl-1,3,4-oxadiazol-3(2H)-yl) ethanone (4d)

IR (KBr): ν (cm^{-1}) 1610 (C=N), 1686 (C=O), 1250 (C-O-C), ^{1}H-NMR (DMSO-D6) : δ (ppm) 2.02 (s, 3H, -CO-CH_3), 2.35 (s, 3H, CH_3), 4.87 (s, 2H, -O-CH_2), 6.51 (d, 1H, *J* = 2.6Hz, Ar-H2), 6.53 (dd, 1H, *J* = 2.5, 7.2Hz, Ar-H6), 6.64 (s, 1H, -N-CH-Ar''), 7.04 (d, 1H, *J* = 8.1 Hz, Ar-H5), 7.19 (m, 5H, Ar''-H2'', 3'', 4'', 5'' & 6''); ^{13}C-NMR (100MHz, $CDCl_3$): δ (ppm) 19.51 (C-7), 23.67 (C-7'), 70.23 (C-2''), 73.81 (C-2'), 112.11 (C-6), 114.63 (C-2), 125.13 (C-4), 126.59 (C-4'''), 127.34 (C-2''' and C-6'''), 128.87 (C-3''' and C-5'''), 129.98 (C-5), 136.41 (C-3), 140.67 (C-1'''), 155.13 (C-5'), 158.23 (C-1) and 169.44 (C-7'); Mass : m/z 344 (M^+, 8), 189 (base peak, 100), 329 (18), 223 (28), 155 (36), 141 (32), 112 (28); Analysis (Calculated) Found: C (62.70)61.98 , H (4.97)4.95 , N (8.12)8.10 %

1-(5-((4-chloro-3-methylphenoxy)methyl)-2-(4-hydroxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (4e)

IR (KBr): ν (cm^{-1}) 3505 (OH), 1685 (C=O), 1618 (C=N), 1256 (C-O-C), ^{1}H-NMR (DMSO-D6) : δ (ppm) 2.06 (s, 3H, -CO-CH_3), 2.38 (s, 3H, CH_3), 4.84 (s, 2H, -O-CH_2), 5.24 (s, 1H, 4-OH), 6.51 (d, 1H, *J* = 2.8Hz, Ar-H2), 6.53 (dd, 1H, *J* = 2.6, 7.8Hz, Ar-H6), 6.61 (s, 1H, -N-CH-Ar''), 6.7 (d, 2H, *J* = 7.6Hz, Ar''-H3'' & 5''), 7.02 (d, 2H, *J* = 7.8Hz, Ar''-H2''& 6''), 7.04 (d, 1H, *J* = 8.1 Hz, Ar-H5); ^{13}C-NMR (100MHz, $CDCl_3$): δ (ppm) 19.86 (C-7), 24.08 (C-7'), 68.72 (C-2''), 74.66 (C-2'), 112.56 (C-6), 114.35 (C-2), 116.83 (C-3''' and C-5'''), 126.04 (C-4), 127.94 (C-2''' and C-6'''), 129.66 (C-5), 133.11 (C-1'''), 137.35 (C-3), 155.34 (C-5'), 157.02 (C-4'''), 158.61 (C-1) and 168.79 (C-6'); Mass : m/z 360 (M^+, 4), 155 (base peak, 100), 345 (20), 205 (22), 141 (34), 112 (30), 93 (24); Analysis (Calculated) Found: C (59.92)59.90, H (4.75) 4.72 , N (7.76)7.72 %

Screening for Biological activity :

The synthesized compounds **3a-e** and **4a-e** were screened for antibacterial (*S. aureus, E. coli, P. aeruginosa*) and antifungal (*C. albicans, A. flavus, A. fumigatus*) activities by disk diffusion method at a concentration of 2mg per ml. using DMF as solvent. The results were recorded in duplicate using ampicillin and fluconazole as standards given in **Table-2**.

ACKNOWLEDGEMENT

The authors are thankful CDRI Lucknow, IIT Delhi and IIT Chennai for carrying out spectral studies. Thanks are also due to Rameesh Institute of Vocational and Technical Education, Greater Noida, for providing necessary facilities.

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The SOUTHERN BRAZILIAN JOURNAL OF CHEMISTRY (ISSN: 2674-6891; 0104-5431) is an open-access journal since 1993. Journal DOI: 10.48141/SBJCHEM.
http://www.sbjchem.com.
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