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Synthesis of Phthalyl Substituted Imidazolones and Schiff Bases as Antimicrobial Agents

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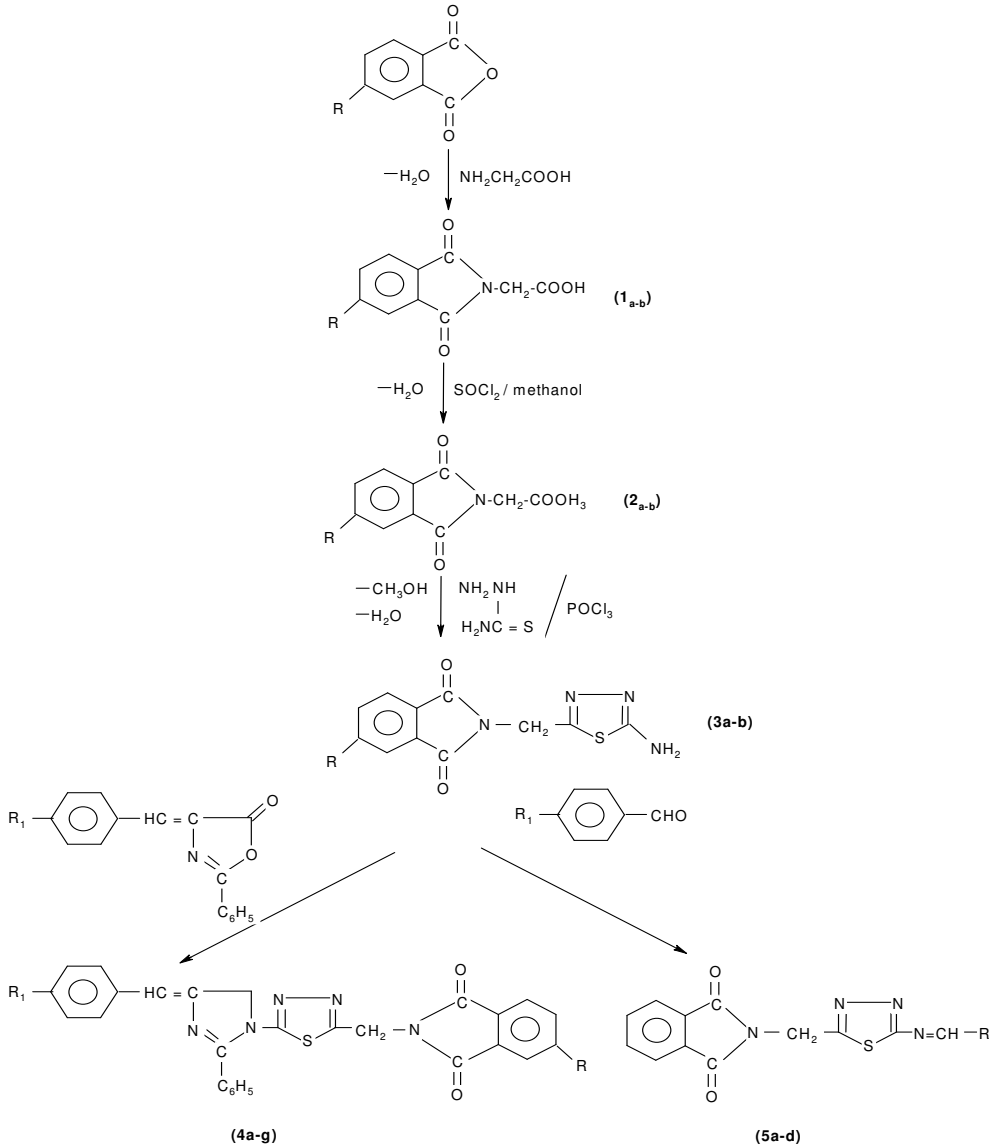
Abstract: A new series of phthalyl substituted imidazolones (**4**$_{a–g}$) and Schiff bases (**5**$_{a–d}$) were synthesized from 2-methyl-(*m*-nitro-1,3-dioxo-1,3-dihydro-(2*H*)-isoindole-2-yl)-5-amino-1,3,4-thiadiazole (**3**$_{a–b}$). Compounds (**3**$_{a–b}$) were prepared by cyclisation of 2-(*m*-nitro-1,3-dioxo-1,3-dihydro-(2*H*)-isoindole-2-yl)methyl ethanoate (**2**) with thiosemicarbazide. 2-(*m*-nitro-1,3-dioxo-1,3-dihydro-(2*H*)-isoindole-2-yl)ethanoic acid (**1**) in presence of thionyl chloride and methanol gave the ester (**2**) while compound (**1**) was synthesized by aminolysis of phthalic anhydride with glycine. The compounds were characterized by spectral techniques of IR, ^{1}H NMR, Mass and elemental analysis. All the synthesized compounds (**4**$_{a–g}$) and (**5**$_{a–d}$) were screened for their antibacterial activity against the pathogenic strains *E. coli, P. aureus, C. freundii* while antifungal activity was evaluated against *A. niger, A. flavus, Penicillium* sp. and *C. albicans*.

Keywords: Isoindole, 1,3,4–Thiadiazole, Imidazolones, Schiff bases, Antibacterial and antifungal activities.

Introduction

1,3,4–Thiadiazole has a broad spectrum of biological activities *i.e.* antimicrobial[1], antidepressant[2–3], antitubercular[3], antidiabetic[4], anti HIV[5] *etc*. The imidazolone ring often appears as the core structure in many drug formulations covering a wide range of pharmaceutical activities *viz.* antileshmanial[6], antiprotozoal[7], antioxidant[8], antiinflammatory[9] *etc.* Oxazolones have also received much attention being antimicrobial[10], antitubercular[11], antiangiogenic[12] *etc*. It has been reported that Schiff bases act as antibacterial agents due to their chelating property. These observation prompted us to indirectly cyclise oxazolones and new Schiff bases with phthalyl substituted 1,3,4–thiadiazoles and evaluate their antimicrobial action.



R = H, R_1 = H = 4_a, R = $-C_6H_5$ = 5_a, R = H, R_1 = 4'''–OH = 4_b, R =4''-OH- C_6H_4– = 5_b, R = H, R_1 =2'''– Cl = 4c, R =2''–Cl–C_6H_4 – = 5_c, R = H, R_1 = (3'''–OCH_3–4'''–OH) = 4_d, R_1 = (3''–OCH_3–4''–OH) –C_6H_3– = 5_d, R = NO_2, R_1 = H= 4e, R = NO_2, R_1 =2'''– Cl = 4_f, R = NO_2, R_1 = (3'''–OCH_3–4'''–OH) = 4_g

Scheme 1. Synthesis of imidazolones and Schiff bases

The synthetic route is given in Scheme 1. 2-(*m*-Nitro-1,3-dioxo-1,3-dihydro-(2*H*)-isoindole-2-yl)-ethanoic acids (**1$_{a–b}$**) were prepared by aminolysis of phthalic anhydride with glycine and further esterification with thionyl chloride and methanol yielded 2-(*m*-nitro-1,3-dioxo-1,3-dihydro-(2*H*)-isoindole-2-yl)-methyl ethanoate (**2$_{a–b}$**). Cyclisation of (**2$_{a–b}$**) with thiosemicarbazide in $POCl_3$ gave the phthalyl substituted 1,3,4-thiadiazoles (**3$_{a–b}$**). Compounds (**3$_{a–b}$**) were fused with substituted oxazolones initially prepared by the

Erlenmeyer azlactone synthesis to give the subsequent imidazolones ($\mathbf{4_{a–g}}$). Derivatives ($\mathbf{3_{a–b}}$) were also reacted with different aromatic aldehydes forming the Schiff bases ($\mathbf{5_{a–d}}$). All the synthesized compounds were characterized by elemental analysis, IR, ^{1}H NMR and mass spectrometer techniques (Table 1). The antimicrobial activities of the title compounds ($\mathbf{4_{a–g}}$) and ($\mathbf{5_{a–d}}$) were evaluated against three bacterial and four fungal strains

Table 1. Analytical data of ($\mathbf{4_{a–g}}$) and ($\mathbf{5_{a–d}}$)

Compd. No.	Yield %	M.P. °C	Molecular Formula	Elemental analysis, %					
				Carbon		Hydrogen		Nitrogen	
				Calc.	Found	Calc.	Found	Calc.	Found
$\mathbf{1_a}$	70	140	$C_{10}H_7O_4N$	58.54	58.50	3.41	3.45	6.83	6.78
$\mathbf{1_b}$	65	155	$C_{10}H_6O_6N_2$	48.00	47.85	2.40	2.35	11.20	11.25
$\mathbf{2_a}$	60	60	$C_{11}H_9O_4N$	60.27	60.32	4.10	4.12	6.39	6.45
$\mathbf{2_b}$	62	80	$C_{11}H_8O_6N_2$	50.00	50.05	3.03	3.08	10.60	10.53
$\mathbf{3_a}$	65	120	$C_{11}H_8O_2N_4S$	50.76	50.66	3.07	3.09	21.53	21.47
$\mathbf{3_b}$	64	150	$C_{11}H_7O_4N_5S$	43.27	43.23	2.29	2.31	22.95	23.07
$\mathbf{4_a}$	60	>320	$C_{27}H_{17}O_3N_5S$	65.98	66.09	3.46	3.56	14.25	14.35
$\mathbf{4_b}$	70	>320	$C_{27}H_{17}O_4N_5S$	63.90	63.99	3.35	3.29	13.81	13.89
$\mathbf{4_c}$	65	>320	$C_{27}H_{16}O_4N_5SCl$	61.65	61.72	3.04	3.14	13.32	13.28
$\mathbf{4_d}$	55	>320	$C_{28}H_{19}O_5N_5S$	62.56	62.50	3.53	3.60	13.04	13.14
$\mathbf{4_e}$	62	>320	$C_{27}H_{16}O_5N_6S$	60.44	60.34	2.98	3.01	15.97	15.90
$\mathbf{4_f}$	64	>320	$C_{27}H_{15}O_5N_6SCl$	56.79	56.70	2.62	2.70	14.72	14.62
$\mathbf{4_g}$	72	>320	$C_{28}H_{18}O_6N_6S$	59.36	59.30	3.18	3.20	14.84	14.80
$\mathbf{5_a}$	70	90	$C_{18}H_{12}O_2N_4S$	62.06	62.26	3.44	3.34	16.09	16.19
$\mathbf{5_b}$	72	140	$C_{18}H_{12}O_3N_4S$	59.34	59.30	3.29	3.22	15.38	15.30
$\mathbf{5_c}$	71	100	$C_{18}H_{11}O_2N_4SCl$	56.47	56.40	2.87	2.92	14.64	14.60
$\mathbf{5_d}$	74	120	$C_{19}H_{14}O_4N_4S$	57.86	57.80	3.55	3.62	14.21	14.24

Antimicrobial studies

The antimicrobial activity was assayed by agar plate diffusion technique[14] at a concentration of 250 and 500 µg/disc. All the synthesized compounds were tested *in vitro* for their antibacterial activity against *E. coli, Pseudomonas aureus* and *Cytobacteria freundii*. The four species of fungi namely *Aspergillus niger, Aspergillus flavus, Penicillium* sp and *Candida albicans* were taken for antifungal activity. The plates were incubated for 24 h (antibacterial) and 48 hrs for antifungal activity respectively at 37 °C. The zone of inhibition was measured in mm (Table 2 and 3). Streptomycin and griseofulvin were used as the standard drugs for bacterial and fungal activity respectively.

Table 2. Antibacterial activity of compounds ($\mathbf{4_{a–g}}$) and ($\mathbf{5_{a–d}}$) (Zone inhibition in mm)

Compound	*E. coli*		*P. aureus*		*C. freundii*	
	250 µg	500 µg	250 µg	500 µg	250 µg	500 µg
$\mathbf{4_a}$	17	19	12	13	16	17
$\mathbf{4_b}$	21	22	15	16	18	19
$\mathbf{4_c}$	22	23	16	17	20	21
$\mathbf{4_d}$	22	23	16	18	21	22
$\mathbf{4_e}$	22	24	17	19	21	22
$\mathbf{4_f}$	24	24	18	19	22	23
$\mathbf{4_g}$	25	25	19	20	22	23
$\mathbf{5_a}$	16	17	12	13	16	18
$\mathbf{5_b}$	19	20	15	16	17	19
$\mathbf{5_c}$	20	20	17	18	18	20
$\mathbf{5_d}$	20	20	17	18	18	20
Ref. Std.	28		24		24	

Control: DMSO (negative); reference standard: streptomycin

Table 3. Antifungal activity of compounds (**4**$_{a–g}$) and (**5**$_{a–d}$) (Zone inhibition in mm)

Compound	*A. niger*	*A. flavus*	*Penicillium* sp.	*C. albicans*
4$_a$	24	21	22	23
4$_b$	25	24	24	24
4$_c$	26	25	25	25
4$_d$	26	25	25	25
4$_e$	27	24	24	24
4$_f$	27	25	25	25
4$_g$	28	25	26	26
5$_a$	19	16	18	18
5$_b$	20	18	19	19
5$_c$	22	19	20	20
5$_d$	22	19	20	21
Ref. Std.	30	28	28	20

Control: DMSO (negative); reference standard: griseofulvin

Experimental

All the melting points were taken in open capillary tubes and were uncorrected. IR (KBr) spectra were recorded on FTIR RX 1 Perkin-Elmer spectrophotometer. ^{1}H NMR were determined on Bruker DRX 400 MHz Spectrophotometer with DMSO as the solvent. Mass was recorded on a JEOL–Accu TOF JMS–T100LC mass spectrometer having a DART source. The substituted azlactones were synthesized following the Erlenmeyer azlactone synthesis.

*Synthesis of 2-(m-nitro-1,3-dioxo-1,3-dihydro-(2H)-isoindole-2-yl)-ethanoic acid (**1**$_{a–b}$)*

0.5 g Glycine and 1 g phthalic anhydride/m–nitrophthalic anhydride were taken in a test tube and immersed in an oil bath at 180-185 °C temperature. The contents were thoroughly stirred during the first 10 min. which finally solidified after 5 min. The solid mass was filtered, dried and recrystallized with 10% ethanol.

*2-(1,3-Dioxo-1,3-dihydro-(2H)-isoindole-2-yl)-ethanoic acid (**1**$_a$)*

IR (KBr) : 1710, 1680 cm^{-1}; ^{1}H NMR δ : 2.33 (s, 2H, CH_2), 7.12 - 7.66 (m, 4H, ArH).

*2-(m-Nitro-1,3-dioxo-1,3-dihydro-(2H)-isoindole-2-yl)-ethanoicacid (**1**$_b$)*

IR (KBr) : 1720, 1685, 1532 cm^{-1}; MS (EI) : *m/z* 251.

*Synthesis of 2-(m-nitro-1,3-dioxo-1,3-dihydro-(2H)-isoindole-2-yl)-methyl ethanoate (**2**$_{a–b}$)*

0.01 mole of compounds (**1**$_{a–b}$), 0.01 mol of thionyl chloride and 10-12 mL of methanol were taken in a round bottomed flask and refluxed for 15 h. The solution was cooled and neutralized with 10% sodium carbonate. A solid separated out which was filtered, dried and recrystallized with ethanol.

*2-(1,3-Dioxo-1,3-dihydro-(2H)-isoindole-2-yl)-methyl ethanoate (**2**$_a$)*

IR (KBr) : 1710, 1726 cm^{-1}; ^{1}H NMR δ : 2.33 (s, 2H, CH_2), 3.52 (s, 3H, CH_3), 7.01 – 7.52 (m, 4H, ArH), MS (EI) : *m/z* 219.

*2-(m-Nitro-1,3-dioxo-1,3-dihydro-(2H)-isoindole-2-yl)-methyl ethanoate (**2**$_b$)*

IR (KBr) : 1532, 1715, 1730 cm^{-1}; ^{1}H NMR δ : 2.33 (s, 2H, CH_2), 3.52 (s, 3H, CH_3), 7.01-7.52 (m, 4H, ArH), MS (EI) : *m/z* 265.

*Synthesis of 2–methyl(m–nitro-1,3–dioxo–1,3–dihydro–(2H)–isoindole–2–yl)5–amino–1,3,4–thiadiazole (**3**$_{a–b}$)*

Compound **2** (0.01 mol) and thiosemicarbazide (0.012 mol) were refluxed in presence of phosphorous oxychloride (0.012 mol) for 3 h. The contents were then poured on to crushed ice. A solid separated out which was filtered, dried and recrystallized from dioxane.

*2–Methyl–(1,3–dioxo–1,3–dihydro–(2H)–isoindole–2–yl)–5–amino–1,3,4–thiadiazole (**3**$_a$)*

IR (KBr) : 1049, 1288, 1373, 1500, 3201 cm^{-1}; ^{1}H NMR δ : 2.33 (s, 2H, CH_2), 5.22 (s, 2H, NH_2), 7.11 – 7.54 (m, 4H, ArH), MS (EI) : *m/z* 260.

2–Methyl–(m–nitro–1,3–dioxo–1,3–dihydro–(2H)–isoindole–2–yl)–5–amino–1,3,4–thiadiazole (3$_b$)

IR (KBr) : 1052, 1290, 1370, 1510, 1535 cm^{-1}; ^{1}H NMR δ : 2.38 (s, 2H, CH_2), 5.19 (s, 2H, NH_2), 7.05 – 7.69 (m, 3H, ArH), MS (EI) : *m/z* 306.

*Synthesis of 2”–methyl–[m–nitro–1’,3’–dioxo–1’,3’–dihydro–(2’H)–isoindole–2’–yl)–1”,3”,4”–thiadiazol–5”–yl]–4–{benzylidene/substituted benzylidene}–4,5–dihydro–2–phenyl–imidazol–5–ones (**4**$_{a–g}$)*

A mixture of 0.01 mol of compounds (**3**$_{a–b}$) and appropriate oxazolones were taken in a round bottom flask and refluxed for 5-6 h in 10-12 mL DMF as the solvent. The resultant solution was cooled and poured into crushed ice containing small amount of dil HCl (2N). The product obtained was filtered, dried and recrystallized with petroleum ether.

*2”–Methyl–[1’,3’–dioxo–1’,3’–dihydro–(2’H)–isoindole–2’–yl)–1”,3”,4”–thiadiazol–5”–yl]–4–benzylidene–4,5–dihydro–2–phenyl–imidazol–5–one (**4**$_a$)*

IR (KBr) : 1049, 1288, 1373, 1500, 1710, 1791, 2954, 3000–3010 cm^{-1}; ^{1}HNMR δ : 2.37 (s, 2H, CH_2), 6.17 (s, 1H, CH=C), 7.35 - 7.98 (m, 14H, ArH), MS (EI) : *m/z* 491.

*2”–Methyl–[1’,3’–dioxo–1’,3’–dihydro–(2’H)–isoindole–2’–yl)–1”,3”,4”–thiadiazol–5”–yl]–{4”’–hydroxybenzylidene}–4,5–dihydro–2–phenyl–imidazol–5–one (**4**$_b$)*

IR (KBr) : 1049, 1288, 1373, 1500, 1710, 1791, 2954, 3500, 3240 cm^{-1}; ^{1}H NMR δ : 2.30 (s, 2H, CH_2), 6.22 (s, 1H, CH=C), 7.35 – 7.82 (m, 13H, ArH), 10.01 (s, 1H, OH), MS (EI) : *m/z* 507.

*2”–Methyl–[1’,3’–dioxo–1’,3’–dihydro–(2’H)–isoindole–2’–yl)–1”,3”,4”–thiadiazol–5”–yl]–4–{2”’–chlorobenzylidene}–4,5–dihydro–2–phenyl–imidazol–5–one (**4**$_c$)*

IR (KBr) : 1052, 1291, 1365, 1520, 1715, 1795, 2958, 3000–3020 cm^{-1}; ^{1}H NMR δ : 2.29 (s, 2H, CH_2), 6.12 (s, 1H, CH=C), 7.22 – 7.98 (m, 13H, ArH), MS (EI) : *m/z* 525.5, M+2, 528.

*2”–Methyl–[(1’,3’–dioxo–1’,3’–dihydro–(2’H)–isoindole–2’–yl)–1”,3”,4”–thiadiazol–5”–yl]–4–{3”’–methoxy–4”’–hydroxy benzylidene}–4,5–dihydro–2–phenyl–imidazol–5–one (**4**$_d$)*

IR (KBr) : 1055, 1291, 1370, 1520, 1715, 1788, 2376, 2954, 3000–3010, 3240 cm^{-1}; ^{1}H NMR δ : 2.36 (s, 2H, CH_2), 3.82 (s, 3H, OCH_3), 6.15 (s, 1H, CH=C), 7.17 – 7.79 (m, 12H, ArH), 10.21 (s, 1H, OH), MS (EI) : *m/z* 537.

*2"–Methyl–[(m–nitro–1',3'–dioxo–1',3'–dihydro–(2'H)–isoindole–2'–yl)–1",3",4"–thiadiazol–5"–yl]–4–benzylidene–4,5–dihydro–2–phenyl–imidazol–5–one (**4**$_e$)*

IR (KBr) : 1050, 1280, 1365, 1515, 1535, 1720, 1788, 2954, 3015–3025 cm^{-1}; ^{1}H NMR δ : 2.31 (s, 2H, CH_2), 6.17 (s, 1H, CH=C), 7.35 – 7.82 (m, 13H, ArH), MS (EI) : *m/z* 536.

*2"–Methyl–[(m–nitro–1',3'–dioxo–1',3'–dihydro–(2'H)–isoindole–2'–yl)–1",3",4"–thiadiazol–5"–yl]–4–{2"'–chlorobenzylidene}–4,5–dihydro–2–phenyl–imidazol–5–one (**4**$_f$)*

IR (KBr) : 680, 1000, 1281, 1370, 1512, 1535, 1715, 1780, 1791, 2954, 3000–3010 cm^{-1}; ^{1}H NMR δ : 2.33 (s, 2H, CH_2), 6.17 (s, 1H, CH=C), 7.35 – 7.82 (m, 7H, ArH), MS (EI) : *m/z* 570.5, 572.5.

*2"–Methyl–[(m–nitro–1',3'–dioxo–1',3'–dihydro–(2'H)–isoindole–2'–yl)–1",3",4"–thiadiazole–5"–yl]–4–{3"'–methoxy–4"'–hydroxybenzylidene}–4,5–dihydro–2–phenyl– imidazol–5–one (**4**$_g$)*

IR (KBr) : 1044, 1290, 1373, 1378, 1525, 1535, 1700, 1780, 2376, 2954, 3240 cm^{-1}; ^{1}H NMR δ : 2.29 (s, 2H, CH_2), 6.17 (s, 1H, CH=C), 7.35 – 7.82 (m, 11H, ArH), MS (EI) : *m/z* 566.

*Synthesis of 2–methyl–[(1',3'–dioxo–1',3'–dihydro–(2'H)–isoindole–2'–yl)–1,3,4–thiadiazol–5–yl]–{benzylidene/substituted benzylidene}–imines (**5**$_{a–d}$)*

0.01 mol of compound (**3**$_a$) and equimolar ratio of different aromatic aldehydes were refluxed in 15 mL of acetic acid under anhydrous conditions using sodium acetate (0.82 g) for 6 h. The reaction mixture was diluted with water, with the subsequent formation of a solid. It was filtered, dried and recrystallized from ethanol.

*2–Methyl–[(1',3'–dioxo–1',3'–dihydro–(2'H)–isoindole–2'–yl)–1,3,4–thiadiazol–5–yl]–benzylidene imine (**5**$_a$)*

IR (KBr) : 1033, 1280, 1288, 1373, 1500, 1710 cm^{-1}; ^{1}H NMR δ : 2.33 (s, 2H, CH_2), 8.97 (s, 1H, N=CH), 7.35 – 7.82 (m, 9H, ArH), MS (EI) : *m/z* 348.

*2–Methyl–[(1',3'–dioxo–1',3'–dihydro–(2'H)–isoindole–2'–yl)–1,3,4–thiadiazol–5–yl]–{4"–hydroxy benzylidene} imine (**5**$_b$)*

IR (KBr) : 1025, 1282, 1288, 1370, 1510, 1710, 3240 cm^{-1}; ^{1}H NMR δ : 2.25 (s, 2H, CH_2), 8.91 (s, 1H, N=CH), 7.21 – 7.78 (m, 8H, ArH), 10.11 (s, 1H, OH), MS (EI) : *m/z* 364.

2–Methyl–[(1',3'–dioxo–1',3'–dihydro–(2'H)–isoindole–2'–yl)–1,3,4–thiadiazol–5–yl]–{2"–chloro benzylidene} imine (5$_c$)

IR (KBr) : 690, 1033, 1280, 1288, 1373, 1500, 1710 cm^{-1}; ^{1}H NMR δ : 2.33 (s, 2H, CH_2), 8.88 (s, 1H, N=CH), 7.27 – 7.93 (m, 8H, ArH), MS (EI) : *m/z* 382.5, M+2, 384.5.

2–Methyl–[(1',3'–dioxo–1',3'–dihydro–(2'H)–isoindole–2'–yl)–1,3,4–thiadiazol–5–yl]–{3"–methoxy–4"–hydroxy benzylidene}–imine (5$_d$)

IR (KBr) : 1033, 1280, 1288, 1373, 1500, 1710, 2376, 3300 cm^{-1}; ^{1}H NMR δ : 2.32 (s, 2H, CH_2), 8.88 (s, 1H, N=CH), 7.39 – 7.84 (m, 7H, ArH), 9.98 (s, 1H, OH), MS (EI) : *m/z* 394.

Results and Discussion

The FTIR spectrum of Compound (**1**$_a$) gave two characteristic vibrations at 1680 and 1710 cm^{-1} which were identified as the (C=O, carboxylic) and (C=O, phthalimido) groups respectively. The structure was further supported by the ^{1}H NMR spectrum which showed two signals

at δ 2.33 as a singlet integrating for two protons and a multiplet between 7.12 - 7.66 integrated for four aromatic hydrogens. Conversion to ester (**2$_a$**) showed the appearance of a new vibration mode at 1726 cm^{-1} which was characterized as the carbonyl peak now part of an ester linkage. Cyclisation of (**2$_a$**) with thiosemicarbazide in $POCl_3$ gave compound (**3$_a$**). The FTIR showed five new stretching vibrations at 1049, 1288, 1373, 1500 and 3201 cm^{-1}. These were characterized as the C–N, N–N–C, N=C=S, C–S–C, NH_2 groups, hence confirming the cyclisation. The NMR spectrum in DMSO also gave new signals at δ 5.22 which integrated for two protons of amino group. The active amino group of thiadiazole was then blocked by appropriate oxazolones/ azalactones. The NMR spectrum of compound (**4$_a$**) showed a new downfield signal at δ 6.17 which integrated for a single proton identified as a methene proton. FTIR also showed new stretching vibrations at 1791 and 3000-3010 cm^{-1}, identified as (C=O, cyclic) and (C=CH) groups. In another set of reactions, the thiadiazole (**3$_a$**) was reacted with benzaldehyde to form (**5$_a$**). Characteristic vibrations at 1280 cm^{-1} was visible which confirmed the presence of (N=CH) linkage. ^{1}HNMR also supported the chemical structure by showing a singlet at δ 8.91 which integrated for one proton and was identified as the proton of an N=CH group. The mass spectrum gave the molecular ion peak at 205 (**1$_a$**), 219 (**2$_a$**), 260 (**3$_a$**), 491 (**4$_a$**) and 348 (**5$_a$**) respectively supporting the molecular weight and the molecular formula of these derivatives. The isotopic peaks in **4c**, **4f** and **5c** confirmed the presence of halogen as a substituent.

Antimicrobial activity

Antibacterial

Two derivatives **4$_f$** and **4$_g$** while **4$_e$** at the higher concentration (500 µg/disc) gave a zone size between 24-25 mm comparable to the standard drug against *E. coli*. The other derivatives **4$_a$**, **4$_b$–4$_d$** were less active (17-20 mm). Against *P. aureus*, lesser inhibition of the bacterial strain was observed (12–19 mm) except **4$_g$** which gave the maximum zone size of 20 mm.

However, against *C. freundii*, all the imidazolone derivatives were active (21-23 mm) comparable to the reference drug streptomycin except **4$_a$** and **4$_b$** respectively (16-19 mm). The substituted benzylidene imines (**5$_a$–5$_d$**) were less active against all the bacterial strains (16-20 mm).

Antifungal

Three derivatives **4$_e$**, **4$_f$** and **4$_g$** showed the maximum inhibition comparable to griseofulvin (27-28 mm) followed by **4$_a$–4$_d$** (24-26 mm) against the fungus *Aspergillus niger*. Against *A. flavus*, derivatives **4$_c$**, **4$_d$**, **4$_f$** and **4$_g$** gave the zone size of 25 mm followed by **4$_b$** and **4$_e$** (24 mm). The derivative **4$_a$** was the least active (21 mm).

Maximum inhibition was observed against the penicillin species by **4$_g$** (26 mm) while three derivatives **4$_c$**, **4$_d$** and **4$_f$** were also highly active (25 mm). Least inhibition was observed when the testing compound was **4$_a$** (22 mm). Against *C. albicans* as the fungal strain, **4$_g$** displayed the maximum inhibition (26 mm) followed by **4$_c$**, **4$_d$** and **4$_f$** (25 mm); **4$_b$** and **4$_e$** (24 mm), the least being **4$_a$** (23 mm).

The other series *i.e.* **5$_a$–5$_d$** showed a similar behaviour when compared to the antibacterial activity. All the derivatives showed lesser inhibition against all the fungal strains. The zone of inhibition ranged between 16-22 mm.

A comparative study has shown that the bacterial strain *E. coli* was the most inhibited followed by *C. freuindii* by the substituted imidazolones, while the growth of all the fungal strains was inhibited. The structure activity relationship shows that a chloro, nitro, methoxy and a hydroxy substituent on the phenyl ring of the heterocyclic nucleus enhanced the activity.

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