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Synthesis and biological evaluation of novel 3-aryl-4-methoxy *N*-alkyl maleimides

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In the present investigation, a series of 3-aryl-4-methoxy *N*-alkyl maleimide **5a-l** have been synthesized and screened for their antimicrobial activity against one Gram positive bacteria (*S. aureus*), one Gram negative bacteria (*E. coli*) and fungal strains (*C. albicans*, *C. tropicalis*, *A. niger* and *A. clavatus*). The structures of the compounds have been substantiated by their IR, NMR, mass and elemental analysis. The minimum inhibitory concentrations (MICs) of synthesized maleimides have been determined by broth microdilution method. Of the newly synthesized maleimides, compounds **5c**, **5f**, **5h**, **5i**, **5k** and **5l** registered significant activity against the tested microorganisms.

Keywords: Maleimide, maleic anhydride, MIC, antifungal, antibacterial

The progression of antimicrobial resistance to the currently marketed drugs represents a great threat to modern society[1]. This situation necessitates continuing research for the development of new and more potent antimicrobial agent. Medicinal chemists are working very hard to design and synthesise the new molecules which possesses more effective and less toxicity, with unusual mode of action than that of existing drug.

The maleimide is a privileged heterocyclic skeleton as they are endowed with several biological and pharmaceutical activities[2]. In recent times, maleimides have received considerable attention due to their remarkable bioactivities such as antifungal[3-5], antibacterial[6], analgesic[7], anti-inflammatory[8], antiprotozoal[9], anticancer[10,11] and nematicidal activities[12]. Some of the derivatives of maleimides are known to be the potent inhibitors of kinase[13], DNMT[14], monoglyceride lipase[15], Bfl-1[16], GSK-3α[17] among others. They are of great interest in area of bioconjugate chemistry and biotechnology due to its reaction specificity with the biothiols *via* Micheal type of addition reaction[18]. Some of its derivatives are reported in the literature as a potent inhibitor of the protein kinase[19] and antiproliferative activities[20].

Encouraged by potential clinical applications of maleimides (Figure 1) and in continuation of our previous research on maleimides[21,22] here in we report a series of novel 3-aryl-4-methoxy *N*-alkyl maleimide **5a-l** and evaluation of their antimicrobial activity.

Result and Discussion

Chemistry

The synthetic route of maleimides is outlined in Scheme 1. Compound **3a**, **3c**, **4a** and **4c** were prepared according to reported method[23]. A Modified procedure than literature[23] was used for synthesise of pyruvate **2a-c**. P-substituted benzyl cyanide **1a-c** were condensed with diethyl oxalate in THF using sodium hydride to get pyruvates **2a-c** which on methylation with dimethyl sulphate (DMS), followed by hydrolysis with con. H_2SO_4 furnished 3-aryl-4-methoxy maleic anhydrides **4a-c**.The target compounds **5a-l** were synthesized by

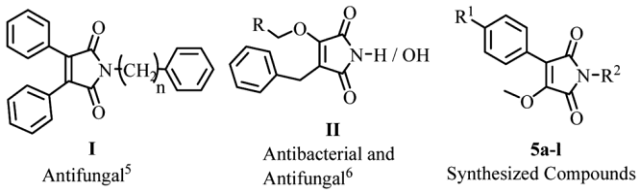
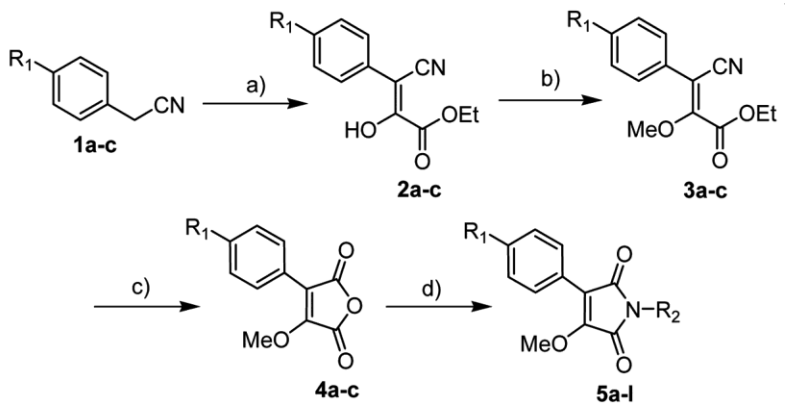


Figure 1 — Structures of some biologically active maleimides and synthesized compounds **5a-l**



Compd	R^1	R^2	Compd	R^1	R^2	Compd	R^1	R^2
1a-4a	H	–	**5c**	OMe	Me	**5h**	Cl	CH_2Ph
1b-4b	Cl	–	**5d**	H	Et	**5i**	OMe	CH_2Ph
1c-4c	OMe	–	**5e**	Cl	Et	**5j**	H	CH_2CH_2OH
5a	H	Me	**5f**	OMe	Et	**5k**	Cl	CH_2CH_2OH
5b	Cl	Me	**5g**	H	CH_2Ph	**5l**	OMe	CH_2CH_2OH

Reagents and Conditions: (a) Diethyl oxalate, NaH, THF, RT, 2 h; (b) DMS, acetone, K_2CO_3, reflux, 2 h; (c) AcOH, H_2O, H_2SO_4, 100°C, 30 min; d) R_2-NH_2, EtOH, Reflux, 30 min.

Scheme 1 — Synthetic pathway of compounds **5a-l**

treating 3-aryl-4-methoxy maleic anhydrides **4a-c** with corresponding amine, in ethanol at reflux temperature with excellent yields.

Spectroscopic analysis

The structures of compound **5a-l** were substantiated by their IR, NMR, mass and elemental analysis. The IR spectrum of compound **5a-l** showed stretching frequencies in the range of 1697 to 1712 cm^{-1} attributed to carbonyl groups. ^{1}H NMR spectra of compound **5a-l** showed signal in the region of δ 1.24 to 4.71 ppm corresponds to the protons of N-alky substituent. In ^{13}C NMR spectra, aromatic carbons appeared around δ 120.80 to 136 ppm. Two signals for imide carbonyl carbons appeared around δ 165.41 and 171.73 ppm. Elemental analysis was found in agreement with molecular formula.

Pharmacology

All maleimides were screened against panel of one Gram positive bacteria (*Staphylococcus aureus* MTCC 96) and one Gram negative bacteria (*Escherichia coli* MTCC 443) and four fungal strains (*Candida albicans* MTCC 227, *Candida tropicalis* MTCC 184, *Aspergillus niger* MTCC 282 *and Aspergillus clavatus* MTCC 1323),. The minimum inhibitory concentrations (MICs) of synthesized maleimides were carried out by broth microdilution method as described by Rattan[24]. Ampicillin and Griseofulvin were used as reference for bacteria and fungi respectively.

In vitro antimicrobial activity

Reviewing of antimicrobial activities of maleimides (Table 1) indicated that, In case of Gram positive bacteria *Staphylococcus aureus*, compound **5i** (R^1 = OMe, R^2 = CH_2Ph) registered remarkable antibacterial activity (MIC = 125 μg/mL) compared to ampicillin (MIC = 250 μg/mL). Compound **5f** (R^1 = OMe, R^2 = Et), **5k** (R^1 = Cl, R^2 = CH_2CH_2OH) and **5l** (R^1 = OMe, R^2 = CH_2CH_2OH) showed equal antifungal activity to the ampicillin (MIC = 250 μg/mL). While in case of Gram negative bacteria *E. coli*, compound **5i** (R^1 = OMe, R^2 = CH_2Ph) showed comparable activity to that of standard ampicillin (MIC = 125 μg/mL).

In case of antifungal activity, compound **5l** (R^1 = OMe, R^2 = CH_2CH_2OH) showed good antifungal activity (MIC = 250 μg/mL) against *Candida albicans* compared to the griseofulvin (MIC = 500 μg/mL). Furthermore, compound **5c** (R^1 = OMe, R^2 = Me) and **5h** (R^1 = Cl, R^2 = CH_2Ph) showed equal antifungal activity (MIC = 500 μg/mL) to the griseofulvin against same species. Tested compounds exhibited marginal or no significant activity against *Candida tropicalis*, *Aspergillus niger*, *and Aspergillus clavatus*.

Experimental Section

Materials and General Synthetic methods

Gallenkamp melting point apparatus was used to check the Melting points and are uncorrected. IR spectra were recorded as KBr discs on a Shimadzu

Table 1 — *In vitro* antimicrobial activity (MIC in µg/mL) of compounds **5a-l**

Compd	Bacteria		Fungus			
	S. a.	*E. c.*	*C. a.*	*C. t.*	*A. n.*	*A. c.*
5a	1000	250	–	–	–	–
5b	–	–	1000	250	1000	–
5c	500	250	500	500	–	500
5d	–	1000	1000	–	–	–
5e	1000	–	–	1000	250	500
5f	250	500	1000	–	500	–
5g	–	1000	–	500	–	–
5h	500	–	500	1000	–	1000
5i	125	125	1000	500	250	250
5j	–	500	–	–	–	–
5k	250	–	–	–	500	250
5l	250	250	250	500	1000	1000
Ampicillin	250	125	NA	NA	NA	NA
Griseofulvin	NA	NA	500	100	100	100

S.a. *Staphylococcus aureus* MTCC 96, E.c. *Escherichia coli* MTCC 443, C.a. *Candida albicans* MTCC 227, C.t. *Candida tropicalis*MTCC 184, A.n. *Aspergillus niger*MTCC 282, A.c. *Aspergillus clavatus*MTCC 1323 (-): Inactive, NA: Not Applicable

FTIR-408 spectrophotometer. The ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were measured with Varian NMR Mercury-300. Chemical shifts were reported as δ values (ppm) relative to internal standard TMS. Mass spectra were performed on a Shimadzu LC-MS mass spectrometer with an ionization potential of 70 eV. Elemental analyses (C, H and N) were carried out on Thermo Finnigan Eager 300 EA 1112 series analyser. Thin layer chromatography (TLC) was used to monitor the progress of reactions.

General procedure for synthesis of compound 2a-c

A solution of *p*-substituted benzyl cyanide **1a-c** (0.039 mol) in THF (25 mL) was slowly added to round bottom flask containing slurry of sodium hydride (60% mineral oil, 0.04 mol) in THF (25 mL) at RT followed by dropwise addition of diethyl oxalate (0.045 mol). The reaction mixture was stirred for 2 h. It was concentrated on rotavapour and poured into cold water (150 mL). On acidification by hydrochloric acid, faint yellow solid obtained was filtered and recrystallized from ethanol.

Ethyl 3-cyano-2-hydroxy-3-phenylacrylate, 2a: Yield 90%. m.p.126-128°C, (130°C)[23].

Ethyl 3-(4-chlorophenyl)-3-cyano-2-hydroxyacrylate, 2b: Yield 88%. m.p.116-118°C. IR: 2216, 1733 cm^{-1}; ^{1}H NMR: (300 MHz, $CDCl_3$): δ 1.34 (t, 3H, CH_3, J = 7.2 Hz), 4.31 (q, 2H, CH_2, J = 7.2 Hz), 7.48 (d, 2H, ArH, J = 8.4 Hz), 7.73 (d, 2H, ArH, J = 8.4 Hz), 7.55 (bs, 1H, OH); MS (70 eV): *m/z* 250 $[M-H]^+$. Anal. Calcd for $C_{12}H_{10}ClNO_3$: C, 57.27; H, 4.01; N, 5.57. Found: C, 57.39; H, 4.19; N, 5.66%.

Ethyl 3-cyano-2-hydroxy-3-(4-methoxyphenyl) acrylate, 2c: Yield 85%. m.p.94-96°C, (94°C)[23].

General procedure for synthesis of compound 3a-c

Dimethyl sulphate (2.76 g, 0.021mol) was slowly added to stirred mixture of **2a-c** (0.021 mol) and anhydrous potassium carbonate (0.024 mol) in dry acetone (55 mL). It was reflux for 2 h, cooled and filtered. On evaporation of acetone, compound **3a-c** was obtained as faint yellow oil is obtained.

Ethyl 3-(4-chlorophenyl)-3-cyano-2-methoxyacrylate, 3b: Yield 80%. IR: 2218, 1735 cm^{-1}; ^{1}H NMR: (300 MHz, $CDCl_3$): δ 1.37 (t, 3H, CH_3), 4.41 (q, 2H, CH_2), 3.90 (s, 3H, OCH_3), 7.55 (d, 2H, ArH, J = 8.4 Hz), 7.77 (d, 2H, ArH, J = 8.4 Hz); MS (70 eV): *m/z* 266 $[M+H]^+$. Anal. Calcd for $C_{13}H_{12}ClNO_3$: C, 58.77; H, 4.55; N, 5.27. Found: C, 58.93; H, 4.68; N, 5.46%.

General procedure for synthesis of compound 4a-c

A solution of **3a-c** (5 g) in acetic acid (60 mL) and water (40 mL) was treated drop wise with H_2SO_4 (50 mL). The temperature of exothermic reaction was maintained at 100°C for 30 min. The reaction mixture was then cooled, diluted with cold water (150 mL) and extracted with ether (3 × 70 mL). The combined ether extracts were washed with 5% KOH, and aqueous extracts were then acidified with dilute H_2SO_4 and extracted with ether. On evaporation of ether, **4a-c** was obtained as solid and purified by column chromatography using hexane: ethyl acetate (8:2).

3-Methoxy-4-phenylfuran-2,5-dione, 4a: Yield 75%. m.p.112-114°C, (116°C)[23]. ^{1}H NMR: (300 MHz, $CDCl_3$): δ 4.39 (s, 3H, OCH_3), 7.26-7.97 (m, 5H, ArH).

3-(4-Chlorophenyl)-4-methoxyfuran-2,5-dione, 4b: Yield 70%. m.p.88-90°C. IR: 1838, 1769 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.43 (s, 3H, OCH_3), 7.43 (d, 2H, ArH, *J* = 8.4 Hz), 7.95 (d, 2H, ArH, *J*= 8.4 Hz); MS (70 eV): *m/z* 239 $[M+H]^+$; HRMS: Found: *m/z* 239.0106 $[M+H]^+$. $C_{11}H_8ClO_4$ requires: 239.0111. Anal. Calcd for $C_{11}H_7ClO_4$: C, 55.37; H, 2.96. Found: C, 55.48; H, 2.78%.

3-Methoxy-4-(4-methoxyphenyl)furan-2,5-dione, 4c: Yield 70%. m.p.96-98°C, (95°C)[23]; ^{1}H NMR: (300 MHz, $CDCl_3$): δ 3.80 (s, 3H), 4.26 (s, 3H, OCH_3), 7.07 (d, 2H, ArH), 7.84 (d, 2H, ArH).

General procedure for synthesis of 3-aryl-4-methoxy N-alkyl maleimides, 5a-l

3-Aryl-4-methoxy maleic anhydrides **4a-c** (4.2 mmol) were refluxed with amines (4.2 mmol), in ethanol (10 mL) for 20-30 minute. After completion of reaction (checked by TLC), reaction mixture was concentrated in vaccuo. On aqueous work up, solid separated was filtered to furnish corresponding maleimide. It was purified by column chromatography using hexane: ethyl acetate (7:3).

3-Methoxy-1-methyl-4-phenyl-1*H*-pyrrole-2,5-dione, 5a: Yield 78%. IR: 1758, 1711, 1612, 1133 cm^{-1}; ^{1}H NMR: (300 MHz, $CDCl_3$): δ 2.91 (s, 3H), 4.16 (s, 3H), 7. 34- 7.76 (m, 5H); ^{13}C NMR: (300 MHz, $CDCl_3$): δ 23.45, 60.18, 113.17, 128.20, 128.65, 129.04, 130.39, 166.18, 170.73, 171.38; MS (70 eV): *m/z* 218 $[M+H]^+$. Anal. Calcd for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.72; H, 4.83; N, 6.81%.

3-(4-Chlorophenyl)-4-methoxy-1-methyl-1*H*-pyrrole-2,5-dione, 5b: Yield 88%. IR: 1756, 1703, 1632, 1113 cm^{-1}; ^{1}H NMR: (300 MHz, $CDCl_3$): δ 3.04 (s, 3H), 4.31 (s, 3H), 7.45 (d, 2H, *J* = 8.4 Hz), 7. 84 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR: (300 MHz, $CDCl_3$): δ 23.39, 60.40, 111.92, 127.00, 128.48, 130.02, 134.38, 151.69, 165.80, 169.78; MS (70 eV): *m/z* 252 $[M+H]^+$. Anal. Calcd for $C_{12}H_{10}ClNO_3$: C, 57.27; H, 4.01; N, 5.57. Found: C, 57.53; H, 4.18; N, 5.62%.

3-Methoxy-4-(4-methoxyphenyl)-1-methyl-1*H*-pyrrole-2,5-dione, 5c: Yield 85%. IR: 1762, 1712, 1609, 1095 cm^{-1}; ^{1}H NMR: (300 MHz, $CDCl_3$): δ 3.03 (s, 3H), 3.83 (s, 3H), 4.24 (s, 3H), 6.94 (d, 2H, *J* = 8.8 Hz), 7. 86 (d, 2H, *J* = 8.8 Hz); ^{13}C NMR: (300 MHz, $CDCl_3$): δ 23.72, 55.27, 60.31, 113.17, 114.10, 121.13, 130.97, 150.78, 160.14, 167.23, 171.03; MS (70 eV): *m/z* 248 $[M+H]^+$. Anal. Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.67. Found: C, 63.39; H, 5.48; N, 5.89%.

1-Ethyl-3-methoxy-4-phenyl-1*H*-pyrrole-2,5-dione, 5d: Yield 85%. IR: 1763, 1712, 1611, 1121 cm^{-1}; ^{1}H NMR: (300 MHz, $CDCl_3$): δ 1.24 (t, 3H, *J* = 7.2 Hz), 3.60 (q, 2H, *J* = 7.2 Hz), 4.23 (s, 3H), 7.35-7.86 (m, 5H); MS (70 eV): *m/z* 232 $[M+H]^+$. Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.78; H, 5.82; N, 5.78%.

3-(4-Chlorophenyl)-1-ethyl-4-methoxy-1*H*-pyrrole-2,5-dione: **5e**: Yield 85%. IR: 1755, 1702, 1621, 1107 cm^{-1}; ^{1}H NMR: (300 MHz, $CDCl_3$): δ 1.27 (t, 3H, *J* = 7.5 Hz), 3.64 (q, 2H, *J* = 7.5 Hz), 4.23 (s, 3H), 7.41 (d, 2H, *J* = 8 Hz), 7.80 (d, 2H, *J* = 8 Hz); MS (70 eV): *m/z* 264 $[M-H]^+$. Anal. Calcd for $C_{13}H_{112}ClNO_3$: C, 58.77; H, 4.55; N, 5.27. Found: C, 58.84; H, 4.64; N, 5.50%.

1-Ethyl-3-methoxy-4-(4-methoxyphenyl)-1*H*-pyrrole-2,5-dione, 5f: Yield 80%. IR: 1748, 1697, 1631, 1135 cm^{-1}; ^{1}H NMR: (300 MHz, $CDCl_3$): δ 1.10 (t, 3H, *J* = 7.2 Hz), 3.44 (q, 2H, *J* = 7.2 Hz), 3.78 (s, 3H), 4.16 (s, 3H), 7.02 (d, 2H, *J* = 8.8 Hz), 7.77 (d, 2H, *J* = 8.8 Hz); MS (70 eV): *m/z* 262 $[M+H]^+$. Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.68; H, 5.67; N, 5.58%.

1-Benzyl-3-methoxy-4-phenyl-1*H*-pyrrole-2,5-dione, 5g: Yield 84%. IR: 1757, 1709, 1611, 1120 cm^{-1}; ^{1}H NMR: (300 MHz, $CDCl_3$): δ 4.25 (s, 3H), 4.71 (s, 2H), 7.30-7.85 (m, 10H); ^{13}C NMR: (300 MHz, $CDCl_3$): δ 41.19, 60.33, 113.12, 127.78, 128.25, 128.39, 128.52, 128.62, 128.65, 129.03, 136.38, 151.56, 165.74, 169.73; MS (70 eV): *m/z* 294 $[M+H]^+$. Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.62; H, 5.31; N, 4.92%.

1-Benzyl-3-(4-chlorophenyl)-4-methoxy-1*H*-pyrrole-2,5-dione: **5h**: Yield 85%. IR: 1758, 1710, 1623, 1118 cm^{-1}; ^{1}H NMR: (300 MHz, $CDCl_3$): δ 4.31 (s, 3H), 4.69 (s, 2H), 7.31-7.87 (m, 9H); ^{13}C NMR: (300 MHz, $CDCl_3$): δ 41.17, 60.44, 111.87, 126.97, 127.82, 128.51, 128.66, 129.10, 130.07, 134.46, 136.23, 151.57, 165.41, 169.41; MS (70 eV): *m/z* 326 $[M-H]^+$. Anal. Calcd for $C_{18}H_{14}ClNO_3$: C, 65.96; H, 4.31; N, 4.27. Found: C, 65.69; H, 4.19; N, 4.38%.

1-Benzyl-3-methoxy-4-(4-methoxyphenyl)-1*H*-pyrrole-2,5-dione: **5i**: Yield 85%. IR: 1757, 1701, 1613, 1104 cm^{-1}; ^1H NMR: (300 MHz, $CDCl_3$): δ 3.83 (s, 3H), 4.25 (s, 3H), 4.69 (s, 2H), 6.93 (d, 2H, *J* = 8.8 Hz), 7.87 (d, 2H, *J* = 8.8 Hz), 7.32-7.94 (m, 5H); ^{13}C NMR: (300 MHz, $CDCl_3$): δ 41.01, 55.18, 60.11, 113.73,121.01, 127.68, 128.41, 128.58, 129.30, 130.38, 136.44, 149.98, 159.70, 165.94, 169.92; MS (70 eV): *m/z* 324 $[M+H]^+$. Anal. Calcd for $C_{19}H_{17}NO_4$: C, 70.58; H, 5.30; N, 4.33. Found: C, 70.92; H, 5.43; N, 4.59%.

1-(2-Hydroxyethyl)-3-methoxy-4-phenyl-1*H*-pyrrole-2,5-dione, 5j: Yield 88%. IR: 1754, 1703, 1623, 1109 cm^{-1}; ^1H NMR: (300 MHz, $CDCl_3$): δ 2.50 (bs, 1H), 3.55 (d, 2H), 3.50 (d, 2H), 4.16 (s, 3H), 7.33-7.76 (m, 5H); ^{13}C NMR: (300 MHz, $CDCl_3$): δ40.37, 60.38, 60.81, 113.04, 128.26, 128.67, 129.06, 129.21, 151.59, 166.38, 170.59; MS (70 eV): *m/z* 248 $[M+H]^+$. Anal. Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.67. Found: C, 63.37; H, 5.47; N, 5.91%.

3-(4-Chlorophenyl)-1-(2-hydroxyethyl)-4-methoxy-1*H*-pyrrole-2,5-dione, 5k: Yield 80%. IR: 1764, 1709, 1612, 1116 cm^{-1}; ^1H NMR: (300 MHz, $CDCl_3$): δ 2.33 (bs, 1H), 3.82 (d, 2H), 3.77 (d, 2H), 4.31 (s, 3H), 7.36 (d, 2H, *J* = 6.3 Hz), 7.86 (d, 2H, *J* = 6.3 Hz); ^{13}C NMR: (300 MHz, $CDCl_3$): δ 40.34, 60.47, 60.85, 111.87, 126.78, 128.52, 130.08, 134.54, 151.57, 166.07, 170.24; MS (70 eV): *m/z* 280 $[M-H]^+$. Anal. Calcd for $C_{13}H_{12}ClNO_4$: C, 55.43; H, 4.29; N, 4.97. Found: C, 55.19; H, 4.17; N, 4.63%.

1-(2-Hydroxyethyl)-3-methoxy-4-(4-methoxyphenyl)-1*H*-pyrrole-2,5-dione, 5l: Yield 80%. IR: 1761, 1701, 1633, 1114 cm^{-1}; ^1H NMR: (300 MHz, $CDCl_3$): δ 2.49 (bs, 1H), 3.74 (d, 2H), 3.79 (d, 2H), 3.82 (s, 3H), 4.23 (s, 3H), 6.94 (d, 2H, *J* = 8.7 Hz), 7.85 (d, 2H, *J* = 6.3 Hz); ^{13}C NMR: (300 MHz, $CDCl_3$): δ 40.30, 55.18, 60.15, 60.97, 113.40, 113.75, 120.80, 130.40, 150.01, 159.75, 166.62, 170.79; MS (70 eV): *m/z* 278 $[M+H]^+$. Anal. Calcd for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05. Found: C, 60.38; H, 5.29; N, 5.28%.

Antimicrobial Assay

The MIC values of all synthesized maleimides were carried out by broth microdilution method as described by Rattan[24]. From Institute of Microbial Technology Chandigarh, all the MTCC cultures were collected and tested against the standard antibacterial (Ampicillin) and antifungal (Griseofulvin) drugs. To grow the bacterial and fungal strains, Mueller Hinton broth was used as a nutrient medium and dilute the drug suspension for the test. The size of inoculum for test the strain was adjusted to 10^8 CFU (Colony Forming Unit) per mL comparing the turbidity. Antimicrobial activity was screened against one gram positive bacteria (*Staphylococcus aureus* MTCC 96) and one gram negative bacteria (*Escherichia coli* MTCC 443) and four fungal strains (*Candida albicans* MTCC 227, *Candida tropicalis* MTCC 184, *Aspergillus niger* MTCC 282 *and Aspergillus clavatus* MTCC 1323).

Conclusion

Twelve novel 3-aryl-4-methoxy *N*-alkyl maleimide **5a-l** were synthesized using simple synthetic protocol with excellent yields. All synthesized maleimides were well characterizes and screened for their antifungal and antibacterial activity. On the basis of results obtained from antimicrobial screening it was concluded that maleimide derivatives possessing electron donating aryl (*para* methoxy and *para* chloro) substituent registered excellent antimicrobial activity. Tested compounds exhibited comparatively good activity against Gram positive (*S. aureus*) than Gram negative bacteria (*E. coli*).

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