# SYNTHESIS AND ANTIMICROBIAL STUDY OF SOME POLYCYCLIC COMPOUNDS BY [3+2] CYCLOADDITION REACTIONS OF ALDAZINES WITH *N*-ARYL MALEIMIDES

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**Abstract:** In good yields, the cycloaddition reactions between 1,4-bis[(aryl) benzylidene] hydrazine **1** and **2** with *N*-aryl maleimides **3(a-e)** were produced 2,9-bis(aryl)-5,12-bis(aryl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,6,11,13-tetraone **4,5(a-e)**. These compounds were directed toward hydrogenation, hydrolysis and dehydrogenation reactions to afford the expected derivatives **6,7(a-e)**, **8(b,d,e)**, **9d**, **10(c,d)** and **11(a,b)**, respectively. The new synthesized compounds were assigned using elemental analysis, mass spectroscopy, infrared and proton nuclear magnetic resonance spectroscopy. However, the microbial activity of these compounds were studied.

**Keywords:** Criss-Cross cycloaddition; 1,3-dipolar reaction; Aldazines; Hydrazones; Antimicrobial.

## Introduction

There are large group of reactions [3+2] cycloadditions in which five membered heterocyclic compounds are prepared by addition of 1,3-dipolar compounds to double bonds. This reaction is quite useful in the synthesis of alkaloids (Broggini and Zecchi, 1999; Choi *et al*., 2005; Morita *et al*., 2005). Examples of dipolarophiles are alkenes, alkynes and molecules that possess related heteroatom functional groups (such as carbonyls and nitriles). Not all alkenes undergo 1,3-dipolar cycloaddition equally. Well the reaction is most successful for those that are good dienophiles in the Diels-Alder reaction (Smith, 2013). Electron withdrawing groups on the dipolarophile normally favor an interaction of the LUMO of the dipolarophile with the HOMO of the dipolar compounds that leads to the formation of the new bonds, whereas electron-donating groups on the dipolarophile normally favor the inverse of this interaction (Huisgen *et al*., 1964; Sustmann, 1971; Sustmann and Trill, 1972).

Additionally, the 1,3-dipolar cycloaddition known as the Huisgen cycloaddition or Huisgen reaction, if the reaction of a 4π e-zwitterionic system as the 1,3-dipolar with a 2π e-neutral system dipolarophile to form a five membered heterocycles. The number of $\sigma$ bonds increase at the expense of $\pi$ bonds (Huisgen, 1963*a*,*b*, 1984). In the presence work, we used the 1,4-bis[(aryl) benzylidene] hydrazine **1** and **2** as the 1,3-dipolar to react with *N*-aryl maleimides **3a-e** as dipolarophile to synthesis new derivatives of 2,9-bis(aryl)-5,12-*N,N′*-bis(aryl)-1,5,8,12-tetraazatetracyclo [6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,6,11,13-tetraone at the respective **4**, **5(a-e)**, (Schemes 1 and 2). The antimicrobial activity of these derivatives were studied.

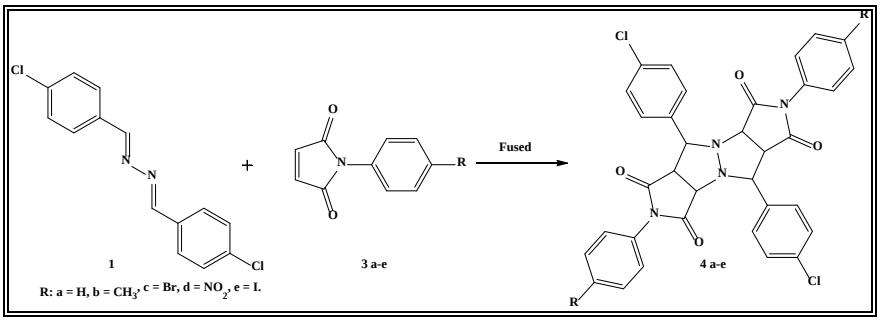


**Figure 1**: The reaction of produce 2,9-bis(aryl)-5,12-*N,N′*-bis (aryl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,6,11,13-tetraone **4a-e**.

  

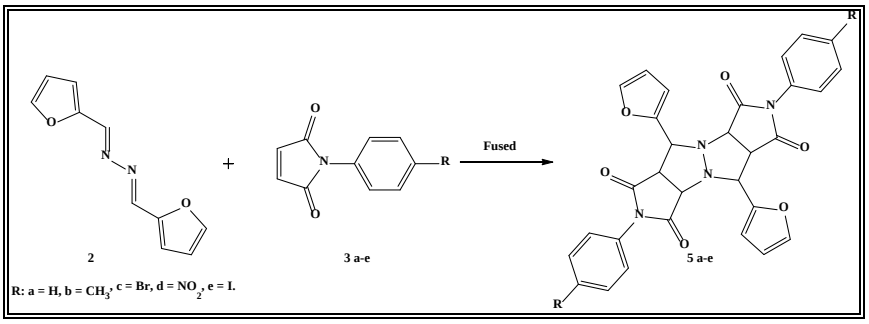


**Figure 2**: The reaction of produce 2,9-bisfuryl-5,12-*N,N′*-bis(aryl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,6,11,13-tetraone **5a-e**.

## Experimental Work

### *General*

Melting points were determined by an Electro thermal 9200 apparatus under uncorrected. The IR spectra were recorded by Shimadzu 470 IR spectrophotometer, using KBr disk. $^1$H NMR spectra were measured by a Varian 200 and 300 MHz $^1$H NMR spectrometer and the chemical shifts (δ) are expressed in ppm, and tetramethylsilane (TMS) used as internal standard (Berger and Braun, 2004). The mass spectra were recorded by Jeol-JMS-600 apparatus. Microanalyses were performed using a Perkin-Elmer 2400. CHN elemental analyzer. Elemental analyses were performed on Perkin-Elmer 240 C microanalyses.

### *Synthesis*

**General synthesis of 2,9-bis(aryl)-5,12-*N,N′*-bis(aryl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,6,11,13-tetraone 4,5(a-e):**

A mixture of *N*, *N*-bis[(aryl) benzylidene] hydrazine **1** and **2** (693 and 470 mg, 2.5 mmol) and *N*-aryl maleimides **3a-e** (5.0 mmol) were fused in an oil different bath degree at 200-220ºC and 140-160ºC, respectively. TLC showed that the reaction was completed after 30 min. The solid obtained after cooling recrystallized from benzene to give each of adducts **4,5(a-e)**, respectively. The structural determination for these compounds confirmed by elemental analyses and spectral data.

**4a: 2,9-bis(4-chlorophenyl)-5,12-*N,N′*-bis(phenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,6,11,13-tetraone:**

White powder, m.p.: 350ºC. Yield: 76.52%. IR: KBr, $\nu_{max}$ (cm$^{-1}$), 3070 for C-H arom.; 2972 for C-H aliph.; 1725 for C=O; 1595, 1494 for C=C arom.; 1085, 1010 for C-N; 814 for C-H (2adj H, wag), oop, def arom. and 742, 692 for C-H (5adj H, wag), oop, def arom. $^1$H NMR (DMSO-$d_6$, 200 MHz) δ ppm = 3.57 (*q*, 2*H*, *H*-3,10, $^3J_{3.2}$ = 7.4 Hz, $^3J_{3.7}$ = 9.4 Hz); 3.85 (*d*, 2*H*,*H*-7,14, $^3J_{7,3}$= 9.4 Hz,); 4.35 (*d*, 2*H*,*H*-2,9, $^3J_{2,3}$= 7.4 Hz); 7.44-8.75 (*m*, 18*H* arom. protons). Anal. Calcd (%) for $C_{34}H_{24}N_4O_4Cl_2$ (623): C: 65.48; H: 3.85; N: 8.98. Found: C: 64.71; H: 3.99; N: 8.73.

**4b: 2,9-bis(4-chlorophenyl)-5,12-*N,N′*-bis(4-methylphenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,6,11,13-tetraone:**

White powder, m.p.: 290ºC. Yield: 75.08%. IR: KBr, $\nu_{max}$ (cm$^{-1}$) 3034 for C-H arom.; 2924 for C-H aliph., 1719 for C=O; 1514 for C=C; 1383 for C-H aliph. bend; 1191, 1016 for C-N and 816 for C-H (2adj H, wag), oop, def arom.$^1$H NMR ($CDCl_3$, 200 MHz) δ ppm = 2.37(*s*, 6*H*, 2C*H*$_3$); 3.57 (*q*, 2*H*, *H*-3,10, $^3J_{3.2}$ = 7.4 Hz, $^3J_{3.7}$ = 9.4 Hz); 3.85 (*d*, 2*H*,*H*-7,14, $^3J_{7,3}$= 9.4 Hz,); 4.35 (*d*,2*H*, *H*-2.9, $^3J_{2,3}$= 7.4 Hz); 7.00-7.85 (*m*, 16*H*, arom. protons). EIMS: *m*/*z* = 651 for molecular ion peak and a base peak at *m*/*z* = 252. Anal. Calcd (%) for $C_{36}H_{28}N_4O_4Cl_2$ (651): C: 66.35; H: 4.30; N: 8.60. Found: C: 67.21; H: 4.66; N: 7.68.

**4c: 2,9-bis(4-chlorophenyl)-5,12-*N,N′*-bis(4-bromophenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,6,11,13-tetraone:**

White powder, m.p.: 303ºC. Yield: 70.25%. IR: K Br, $\nu_{max}$ (cm$^{-1}$), 1724 for C=O; 1597, 1545 for C=C arom.; 1379 for C-H aliph. bend; 1185 for C-N and 816 for C-H (2adj H, wag), oop, def arom. $^1$H NMR (DMSO-$d_6$, 200 MHz) δ ppm = 3.57 (*q*, 2*H*,*H*-3,10, $^3J_{3.2}$ = 7.4 Hz, $^3J_{3.7}$ = 9.4 Hz); 3.85 (*d*, 2*H*,*H* 7,14, $^3J_{7,3}$= 9.4 Hz,); 4.35(*d*, 2*H*,*H*-2,9, $^3J_{2,3}$= 7.4 Hz); 7.44-8.75 (*m*,16*H*, arom. protons). Anal. Calcd (%) for $C_{34}H_{22}N_4O_4Cl_2Br_2$ (781): C: 52.24; H: 2.81; N: 7.17. Found: C: 52.74; H: 3.74; N: 6.79.

**4d: 2,9-bis(4-chlorophenyl)-5,12-*N,N′*-bis-(4-nitrophenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,6,11,13-tetraone:**

White powder, m.p.: 315ºC. Yield: 74.22%. IR: KBr, $\nu_{max}$ (cm$^{-1}$) 3070 for =C-H arom.; 2926 for C-H aliph.; 1728

  

for C=O; 1598, 1529 for C=C arom.; 1529 for N=O in ($NO_2$); 1368, 1343 for C-H aliph. (bend); 1162 for C-N and 848, 813 for C-H (2adj H, wag), oop, def arom. $^1$H NMR (DMSO-$d_6$, 200 MHz) δ ppm = 3.57 (*q*, 2*H*,*H*-3,10, $^3J_{3.2}$ = 7.4 Hz, $^3J_{3.7}$ = 9.4 Hz); 3.85 (*d*, 2*H*,*H*-7,14, $^3J_{7,3}$= 9.4 Hz,); 4.35 ( *d*, 2*H*,*H*-2,9, $^3J_{2,3}$= 7.4 Hz); 7.44-8.75 (*m*, 16*H* arom. protons). Anal. Calcd (%) for $C_{34}H_{22}N_6O_8Cl_2$ (713): C: 57.22; H: 3.08; N: 11.78. Found: C: 56.64; H: 3.36; N: 10.91.

**4e: 2,9-bis(4-chlorophenyl)-5,12-*N*,*N'*-bis(4-iodophenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,6,11,13-tetraone:**
White powder, m.p.: 312ºC, Yield: 81.08%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) 3066 for C-H arom.; 2952, for C-H aliph.; 1721 for C=O; 1596 for C=C arom.; 1486, 1375 for C-H aliph. (bend); 1131 for C-N and 814 for C-H (2adj H, wag), oop, def arom. $^1$H NMR (DMSO-$d_6$, 200 MHz) δ ppm = 3.57 (*q*, 2*H*, *H*-3,10, $^3J_{3.2}$ = 7.4 Hz, $^3J_{3.7}$ = 9.4 Hz); 3.85 (*d*, 2*H*,*H*-7,14, $^3J_{7,3}$= 9.4 Hz,); 4.35 (*d*, 2*H*,*H*-2,9, $^3J_{2,3}$= 7.4 Hz); 7.44-8.75 (*m*, 16*H* arom. protons). Anal. Calcd (%) for $C_{34}H_{22}N_4O_4Cl_2I_2$ (873): C: 46.73; H: 2.52; N: 6.41. Found: C: 46.17; H: 2.94; N: 5.85.

**5a: 2,9-bisfuryl-5,12-diphenyl-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,6,11,13-tetraone:**
Was crystallized from benzene as white powder, m.p.: 310ºC. Yield: 73.65%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) 3147, 3117 for C-H in furyl; 3067 for C-H arom.; 2920 for C-H aliph.; 1782, 1720 for C=O groups; 1595, 1494, 1458 for C=C arom.; 1381 for C-H *sym*, def; 1181 for N-C in maleimide; 754, 692 for C-H oop, def arom. $^1$H NMR (DMSO-$d_6$, 300 MHz) δ ppm = 3.57 (*q*, 2*H*, *H*-3,10, $^3J_{3.2}$ = 10.8 Hz, $^3J_{3.7}$ = 13.8 Hz); 3.85 (*d*, 2*H*,*H*-7,14, $^3J_{7,3}$= 13.8 Hz); 4.35 (*d*, 2*H*,*H*-2,9, $^3J_{2,3}$= 10.8 Hz) and 6.50-7.43 (*m*, 16*H*, arom. protons). Anal. Calcd (%) for $C_{30}H_{22}N_4O_6$ (534): C: 67.41; H: 4.15; N: 10.48. Found: C: 66.98; H: 4.30; N: 9.66.

**5b: 2,9-bisfuryl-5,12-bis(4-methylphenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,6,11,13-tetraone:**
Was crystallized from benzene as white powder, m.p.: 297ºC. Yield: 70.77%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) 3112 for C-H in furyl; 3036 for C-H arom.; 2922, 2877 for C-H aliph.; 1719 for C=O groups; 1562, 1512 for (C=C) arom.; 1382 for aliph., C-H, *sym*, def; 1182 for C-N; 810 for C-H, (2adj H, wag), oop, def arom. EIMS: *m/z* = 562 for molecular ion peak and a base peak at *m/z* = 186. Anal. Calcd (%) for $C_{32}H_{26}N_4O_6$ (562): C: 68.32; H: 4.62; N: 9.96. Found: C: 67.84; H: 4.83; N: 9.31.

**5c: 2,9-bisfuryl-5,12-bis(4-bromophenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,6,11,13-tetraone:**
Was crystallized from benzene as white powder, m.p.: 308ºC. Yield: 71.74%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) IR: KBr, $\nu_{max}$ ($cm^{-1}$) 3113 for C-H in furyl; 3070 for C-H arom.; 1723 for C=O groups; 1544, 1489 for C=C arom.; 1187, 1069 for C-N; 812 for C-H, (2adj H, wag), oop, def arom. $^1$H NMR (DMSO-$d_6$, 300 MHz) δ ppm = 3.57 (*q*, 2*H*, *H*-3,10, $^3J_{3.2}$ = 10.8 Hz, $^3J_{3.7}$ = 13.8 Hz); 3.85 (*d*, 2*H*, *H*-7,14, $^3J_{7.3}$= 13.8 Hz); 4.35 (*d*, 2*H*, *H*-2,9, $^3J_{2,3}$= 10.8 Hz) and 6.50-7.43 (*m*, 14*H*, arom. protons). Anal. Calcd (%) for $C_{30}H_{20}N_4O_6Br_2$ (692): C: 52.02; H: 2.89; N: 8.09. Found: C: 51.93; H: 2.94; N: 7.85.

**5d: 2,9-bisfuryl-5,12-bis(4-nitrodiphenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,6,11,13-tetraone:**
Was crystallized from benzene as yellow-pale powder, m.p.: 280ºC. Yield: 78.04%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) IR: KBr, $\nu_{max}$ ($cm^{-1}$) 3119 for C-H in furyl; 3088 for C-H arom.; 2972 for C-H aliph.; 1727 for C=O groups; 1598, 1479 for C=C arom.; 1527 for $NO_2$; 1188, 1096 for C-N; 853 for C-H, (2adj H, wag), oop, def arom. Anal. Calcd (%) for $C_{30}H_{20}N_6O_{10}$ (624): C: 57.69; H: 3.20; N: 13.46. Found: C: 57.32; H: 3.50; N: 12.84.

**5e: 2,9-bisfuryl-5,12-bis(4-iodophenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,6,11,13-tetraone:**
Was crystallized from benzene as white powder, m.p.: 310ºC. Yield: 69.94%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) 3115 for C-H in furyl; 3036 for C-H arom.; 2970 for C-H aliph.; 1721 for C=O groups; 1586 for C=C arom.; 1185 for C-N; 819 for C-H, (2adj H, wag), oop, def arom. $^1$H NMR (DMSO-$d_6$, 300 MHz) δ ppm = 3.57 (*q*, 2*H*,*H*-3,10, $^3J_{3.2}$ = 10.8 Hz, $^3J_{3.7}$ = 13.8 Hz); 3.85 (*d*, 2*H*,*H*-7,14, $^3J_{7,3}$= 13.8 Hz); 4.35 (*d*, 2*H*,*H*-2,9, $^3J_{2,3}$= 10.8 Hz) and 6.50-7.43 (*m*, 14*H*, arom. protons). Anal. Calcd (%) for $C_{30}H_{20}N_4O_6I_2$ (786): C: 45.80; H: 2.54; N: 7.12. Found: C: 45.96; H: 3.08; N: 7.02.

**General synthesis of 2,9-bis(aryl)-5,12-*N*,*N'*-bis(aryl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,11-dihydroxy-6,13-dione 6,7(a-e):**
Dissolve of each of **4, 5(a-e)** (5.0 mmol) in ethanol abs. and $NaBH_4$ (2,000 mg, 54.0 mmol) was added and stirred under reflex for 5 hours. The resulting mixture was neutralized with dilute HCl and extracted by diethyl ether. The solvent was evaporated under reduced pressure and the residue recrystallized from ethanol to give each of

  

compounds **6, 7(a-e)**, respectively. The structural determination for these compounds confirmed by elemental analyses and spectral data.

**6a: 2,9-bis(4-chlorophenyl)-5,12-*N*,*N*′-diphenyl-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,11-dihydroxy-6,13-dione**:
Orange powder, m.p.: 185ºC. Yield: 74.36%. IR: KBr, $\nu_{max}$ (cm$^{-1}$) 3500, 3316 for -OH; 3062 for =C-H arom.; 2960, 2926 for C-H aliph.; 1676 for C=O; 1600, 1542 for C=C arom.; 1446, 1388 for C-H aliph. bend; 1194 for C-N; 1094, 1014 for C-O; 830 for C-H (2adj H, wag), oop, def. arom. and 754, 692 for C-H (5adj H, wag), oop, def arom. $^1$H NMR (DMSO-$d_6$, 200 MHz) δ ppm = 3.05 (*q*, 2*H*, *H*-3.10); 3.5-5.00 (*br*, 8*H*, for *H*-2,4,7,9,11,14 and 2O*H*), 7.00-7.80 (*m*, 18*H*, arom. protons). EIMS: *m/z* = 627 for molecular ion peak and a base peak at *m/z* = 124. Anal. Calcd (%) for $C_{34}H_{28}N_4O_4Cl_2$ (627): C: 65.07; H: 4.46; N: 8.93. Found: C: 65.31; H: 3.99; N: 8.84.

**6b: 2,9-bis(4-chlorophenyl)-5,12-*N*,*N*′-bis(4-methylphenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,11-dihydroxy-6,13-dione:**
Orange powder, m.p.: 200ºC, Yield: 73.93%. IR: KBr, $\nu_{max}$ (cm$^{-1}$) 3500, 3316 for -OH groups; 3070 for =C-H arom.; 2922 for C-H aliph.; 1672 for C=O groups; 1606, 1520 for C=C arom.; 1408, 1308 for C-H aliph. bend; 1178, 1206 for C-N; 1092 for C-O and 818 for C-H (2adj H, wag), oop, def arom. $^1$H NMR ($CDCl_3$, 300 MHz) δ ppm = 1.27 (*s*,2*H*,2O*H*); 2.34 (*s*,6*H*,2C$H_3$); 3.5-4.5 (*m*,6*H*,*H*-2,3,7,9,10,14); 5.50 (*d*,2*H*,*H*-4,11); 3.4-4.2 (*m*,5*H*,*H*-2,4,7,9,11); 7.20-7.70 (*m*, 16*H*, arom. protons). EIMS: *m/z* = 655 for molecular ion peak and a base peak at *m/z* =186. Anal. Calcd (%) for $C_{36}H_{32}N_4O_4Cl_2$ (655): C: 65.95; H: 4.88; N: 8.54. Found: C: 66.29; H: 4.56; N: 8.18.

**6c: 2,9-bis(4-chlorophenyl)-5,12-*N*,*N*′-bis(4-bromophenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,11-dihydroxy-6,13-dione:**
Orange powder, m.p.: 187ºC. Yield: 71.36%. IR: KBr, $\nu_{max}$ (cm$^{-1}$) 3552, 3426 for -OH groups; 3052 for =C-H arom.; 2968 for C-H aliph; 1672 for C=O groups; 1596, 1490 for C=C arom; 1302 for C-H aliph (bend); 1206 for C-N; 1012 for C-O and 824 for C-H (2adj H, wag), oop, def arom. $^1$H NMR (DMSO-$d_6$, 200 MHz) δ ppm = 3.05 (*q*,2*H*,*H*-3,10); 3.5-5.00 (*br*, 8*H*, for *H*-2,4,7,9,11,14 and 2O*H*), 7.00-7.80 (*m*,16*H*, arom. protons) Anal. Calcd (%) for $C_{34}H_{26}N_4O_4Cl_2Br_2$ (785): C: 51.97; H: 3.31; N: 7.13. Found: C: 52.34; H: 3.74; N: 6.83.

**6d: 2,9-bis(4-chlorophenyl)-5,12-*N*,*N*′-bis-(4-nitrophenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,11-dihydroxy-6,13-dione:**
Orange powder, m.p.: 160ºC. Yield: 69.19%. IR: KBr, $\nu_{max}$ (cm$^{-1}$) 3534 for -OH groups; 3030 for =C-H arom.; 2920 for C-H aliph.; 1718 for C=O groups; 1600, 1506 for C=C arom; 1336 for C-H aliph. bend; 1182 for C-N, 1108, 1070 for C-O and 836 for C-H (2adj H, wag), oop, def arom. EIMS: *m/z* = 717 for molecular ion peak and a base peak at *m/z* = 125. Anal. Calcd (%) for $C_{34}H_{26}N_6O_8Cl_2$ (717): C: 56.90; H: 3.62; N: 11.71. Found: C: 56.61; H: 3.33; N: 11.31.

**6e: 2,9-bis(4-chlorophenyl)-5,12-*N*,*N*′-bis(4-iodophenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,11-dihydroxy-6,13-dione:**
Colorless powder, m.p.: 204ºC. Yield: 67.96%. IR: KBr, $\nu_{max}$ (cm$^{-1}$) 3564 for –OH groups; 3070 for C-H arom.; 2924, 2890 for C-H aliph.; 1668 for C=O groups; 1596, 1530 for C=C arom; 1400 for C-H aliph. bend; 1240, for C-N 1092, 1010 for C-O; and 820 for C-H (2adj H, wag), oop, def arom. $^1$H NMR (DMSO-$d_6$, 200 MHz) δ ppm = 3.05 (*q*,2*H*,*H*-3,10); 3.5-5.00 (*br*,8*H*,*H*-2,4,7,9,11,14 and 2O*H*), 7.00-7.80 (*m*,16*H*, arom. protons) Anal. Calcd (%) for $C_{34}H_{26}N_4O_4Cl_2I_2$ (877): C: 46.52; H: 2.96; N: 6.38. Found: C: 46.27; H: 3.14; N: 5.98.

**7a: 2,9-bisfuryl-5,12-bis(phenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,11-dihydroxy-6,13-dione:**
Orange powder, m.p.: 289ºC. Yield: 67.79%. IR: KBr, $\nu_{max}$ (cm$^{-1}$) 3550 for -OH groups; 3113 for C-H in furyl; 3065 for C-H arom.; 2921 for C-H aliph.; 1686 for C=O groups; 1598, 1490 for C=C arom.; 1383 for aliph.; C-H, *asym*, def; 1183 for C-N and 749, 690 for C-H, (5adj H, wag), oop, def arom. EIMS: *m/z* = 538 for molecular ion peak and a base peak at *m/z* = 95. Anal. Calcd (%) for $C_{30}H_{26}N_4O_6$ (538): C: 66.91; H: 4.83; N: 10.41. Found: C: 66.74; H: 4.67; N: 9.98.

**7b: 2,9-bisfuryl-5,12-bis(4-methylphenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,11-dihydroxy-6,13-dione:**
Colorless powder, m.p.: 185ºC. Yield: 68.68%. IR: KBr, $\nu_{max}$ (cm$^{-1}$) 3580 for -OH groups; 3119 for C-H in furyl; 3088 for C-H arom.; 2920, 2854 for C-H aliph.; 1696 for C=O groups; 1604, 1524 for C=C arom.; 1450, 1406 for aliph., C-H, *asym*, def); 1188 for C-N, 1136 for C-O and 816 for C-H, (2adj H, wag), oop, def arom. Anal. Calcd (%) for $C_{32}H_{30}N_4O_6$ (566): C: 67.84; H: 5.30; N: 7.89. Found: C: 68.15; H: 4.97; N: 9.72.

  

**7c: 2,9-bisfuryl-5,12-bis(4-bromophenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,11-dihydroxy-6,13-dione:**
Orange powder. m.p.: 170ºC. Yield: 65.03%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) 3580 for -OH groups; 3112 for C-H in furyl; 3070 for C-H arom.; 1682 for C=O groups; 1596, 1528 for C=C arom.; 1146 for C-N, 1074 for C-O and 824 for C-H, (2adj H, wag), oop, def arom. $^1$H NMR (DMSO-$d_6$, 200 MHz) δ ppm = 3.05 (*q*,2*H*,*H*-3,10); 3.5-5.00 (*br*,8*H*,*H*-2,4,7,9,11,14 and 2O*H*), 7.00-7.80(*m*, 14*H*, arom. protons). Anal. Calcd (%) for $C_{30}H_{24}N_4O_6Br_2$ (696): C: 51.72; H: 3.44; N: 8.04. Found: C: 52.13; H: 3.69; N: 8.18.

**7d: 2,9-bisfuryl-5,12-bis(4-nitrophenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,11-dihydroxy-6,13-dione:**
Brown powder. m.p.: 115ºC. Yield: 74.04%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) 3570 for -OH groups; 3112 for C-H in furyl; 3080, 3030 for C-H arom.; 2922 for C-H aliph.; 1700 for C=O groups; 1598, 1504 for C=C arom.; 1196 for C-N, 1110 for C-O and 842 for C-H, (2adj H, wag), oop, def arom. $^1$H NMR (DMSO-$d_6$, 200 MHz) δ ppm = 3.05(*q*,2*H*,*H*-3,10); 3.5-5.00 (*br*,8*H*,*H*-2,4,7,9,11,14 and 2O*H*), 7.00-7.80 (*m*,14*H*, arom. protons). Anal. Calcd (%) for $C_{30}H_{24}N_6O_{10}$ (628): C: 57.32; H: 3.82; N: 13.37. Found: C: 57.69; H: 4.05; N: 12.84.

**7e: 2,9-bisfuryl-5,12-bis(4-iodophenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,11-dihydroxy-6,13-dione:**
Brown powder. m.p.: 184ºC. Yield: 72.01%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) 3570 for -OH groups; 3112 for C-H in furyl; 3070 for C-H arom.; 2924 for C-H aliph.; 1682 for C=O groups; 1588, 1524 for C=C arom.; 1146 for C-N, 1062, 1008 for C-O and 818 for C-H, (2adj H, wag), oop, def arom. EIMS: *m/z* = 790 for molecular ion and a base peak at *m/z* = 218. Anal. Calcd (%) for $C_{30}H_{24}N_4O_6I_2$ (790): C: 45.56; H: 3.03; N: 7.08. Found: C: 45.43; H: 3.38; N: 7.23.

**General synthesis of 2,6-bis(aryl)-3,7-dicarboxy-4,8-*N,N′*-bis(aryl carbonylamide)-1,5-diazadicyclooctane 8(b,d,e) and 9d:**
Dissolve of each of **4b-e** and **5d** (5.0 mmol) in 20 ml of 20% aqueous NaOH was stirred under reflux for 2 hours. After cooling the resulting mixture neutralized with (0.01 M) HCl and extracted by chloroform. The solvent evaporated under reduced pressure and the residue recrystallized from ethanol to give each of compounds **8b-e** and **9d**, respectively. The structural determination for these compounds confirmed by elemental analyses and spectral data.

**8b: 2,6-bis(4-chlorophenyl)-3,7-dicarboxy-4,8-*N,N′*-bis(4-methylphenyl carbonylamide)-1,5-diazadicyclooctane:**
Orange powder, m.p.: 260ºC. Yield: 73.23%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) 3500-2400 for -OH in carboxylic groups; 2896, 2876 for C-H aliph.; 1700 for C=O groups; 1600 for C=C arom.; 1522 for N=O; 1424, 1394 for C-H aliph. bend; 1174 for C-N; 1092 for C-O and 812 (s) for C-H (2adj H, wag), oop, def arom. $^1$H NMR (DMSO-*d6*, 300 MHz) δ ppm = 2,40 (*s*,6*H*,2C$H_3$), 3.62 (*q*,2*H*,*H*-3,7 $^3J_{3.2}$ = 10.8 Hz, $^3J_{3.7}$ = 13.8 Hz), 4.04 (*d*,2*H*,*H*-4,8 $^3J_{7,3}$= 13.8 Hz), 4.30 (*d*,2*H*,*H*-2,6 $^3J_{2,3}$= 10.8 Hz), 6.95 -7.60 (*m*, 18*H*, arom. and amide protons), 10.87 (s,2*H*,2O*H* protons). EIMS: *m/z* = 687 for molecular ion peak and a base peak at *m/z* = 64. Anal. Calcd (%) for $C_{36}H_{32}N_4O_6Cl_2$ (687): C: 62.88; H: 4.65; N: 8.15. Founds: C: 61.71; H: 4.36; N: 7.88.

**8d: 2,6-bis(4-chlorophenyl)-3,7-dicarboxy-4,8-*N,N′*-bis(4-nitrophenyl carbonylamide)-1,5-diazadicyclooctane:**
Orange powder, m.p.: 228ºC, Yield: 79.27%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) 3500-2550 for -OH in carboxylic groups; 2922, 2888 for C-H aliph.; 1716 for C=O groups; 1598 for C=C arom.; 1492 for N=O; 1424,1340 for C-H aliph. bend; 1152 for N-C; 1092 for C-O and 830 for C-H (2adj H, wag), oop, def. arom. $^1$H-NMR (DMSO-$d_6$, 200 MHz) δ ppm = 3.0-4.5 (*m*,6*H*,*H*-2,3,4,6,7,8), 7.00-7.80 (*m*,18*H*, arom. and amide protons); 11.00 (*s*,2*H*,2O*H*). EIMS: *m/z* = 749 for molecular ion peak and a base peak at *m/z* = 221. Anal. Calcd (%) for $C_{34}H_{26}N_6O_{10}Cl_2$ (749): C: 54.47; H: 3.47; N: 11.21. Founds: C: 54.69; H: 3.97; N: 10.95.

**8e: 2,6-bis(4-chlorophenyl)-3,7-dicarboxy-4,8-*N,N′*-bis(4-iodophenyl carbonylamide)-1,5-diazadicyclooctane:**
Orange powder, m.p.: 197ºC, Yield: 71.92%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) 3500-2400 for -OH in carboxylic groups; 2896 for C-H aliph.; 1678 for C=O groups; 1598 ,1528 for C=C arom.; 1488, 1390 for C-H aliph. bend; 1186 for C-N; 1094 for C-O and 822 (s) for C-H (2adj H, wag), oop, def arom. $^1$H-NMR (DMSO-$d_6$, 200 MHz) δ ppm = 3.0-4.5 (*m*,6*H*,*H*-2,3,4,6,7,8), 7.00-7.80 (*m*, 18*H*, arom. and amide protons); 11.00 (*s*,2*H*,2O*H*). Anal. Calcd (%) for $C_{34}H_{26}N_4O_6Cl_2I_2$ (911): C: 44.78; H: 2.85; N: 6.14. Founds: C: 44.30; H: 3.32; N: 6.21.

  

**9d: 2,6-bisfuryl-3,7-dicarboxy-4,8-bis(*N*-*p*-nitrophenyl carbonylamide)-1,5-diazadicyclooctane:**
Orange powder. m.p.: 350ºC. Yield: 66.67%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) 3330-2500 for -NH, -OH groups; 1686 for C=O groups; 1588 C=C arom., 1492 for $NO_2$; 1146 for C-N, 1116, 992 for C-O and 854 for C-H, (2adj H, wag), oop, def arom. $^1$H NMR (DMSO-$d_6$, 200 MHz) δ ppm = 3.00-4.00 (*m*,6*H*,*H*-2,3,4,6,7,8); 6.50-7.80 (*m*,16*H*, arom. and amide protons) and 11.00 (*s*,2*H*, for carboxyl protons). Anal. Calcd (%) for $C_{30}H_{24}N_6O_{12}$ (660): C: 54.54; H: 3.63; N: 12.72. Founds: C: 55.00; H: 4.11; N: 13.16.

**General synthesis of 2,9-bis(aryl)-5,12-*N*,*N′*-bis(aryl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradeca-3,10-diene-4,6,11,13-tetraone 10(c,d) and 11(a,b):**
Dissolve of each of **4c-d** and **5a-b** (5.0 mmol) in 20 ml of nitrobenzene was stirring under reflux for 5 hours. After cooling the solid obtained was filtrated and recrystallized from acetone to give each of compounds **10c-d** and **11a-b**, respectively. The structural determination for these compounds confirmed by elemental analyses and spectral data.

**10c: 2,9-bis(4-chlorophenyl)-5,12-*N*,*N′*-bis(4-bromophenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradeca-3,10-diene-4,6-,11,13-tetraone:**
White powder, m.p.: 269ºC.Yield: 79.79%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) 2914 for C-H aliph.; 1720 for C=O groups; 1630, 1512 for C=C aliph. and arom.; 1490, 1377 for C-H aliph. bind; 1177 for C-N; 1090 for C-O and 824 for C-H (2adj H), oop, def arom. $^1$H NMR (DMSO-*d*6, 300 MHz) δ ppm = 4.9 (*m*,2*H*,*H*-2,9), 7.27-8.37 (*m*,16*H*, arom. protons). Anal. Calcd (%) for $C_{34}H_{18}N_4O_4Cl_2Br_2$ (777): C: 52.50; H: 2.31; N: 7.20. Founds: C: 52.14; H: 2.34; N: 7.26.

**10d: 2,9-bis(4-chlorophenyl)-5,12-*N*,*N′*-bis(4-nitrolphenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradeca-3,10-diene-4,6,-11,13-tetraone.**
Colorless powder, m.p.: 290ºC. Yield: 84.87%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) 2919 for C-H aliph.; 1726 for C=O groups; 1598, 1526 for C=C aliph. and arom.; 1492 for N=O; 1342 for C-H aliph. bend; 1163 for N-C; 1015 for C-O and 830 for =C-H (2adj H, wag), oop, def. arom. $^1$H NMR (DMSO-*d*6, 300 MHz) δ ppm = 4.9 (*m*,2*H*,*H*-2,9), 7.27-8.37 (*m*,16*H*, arom. protons). EIMS: *m/z* = 709 for molecular ion peak and a base peak at *m/z* = 217. Anal. Calcd (%) for $C_{34}H_{18}N_6O_8Cl_2$ (709): C: 57.54; H: 2.53; N: 11.84. Founds: C: 56.56; H: 2.60; N: 11.46.

**11a: 2,9-bisfuryl-5,12-diphenyl-1,5,8,12-tetraazatetracyclo[6,6,0,$^{37}$0,$^{10,14}$0] tetradeca-3,10-diene-4,6,11,13-tetraone:**
White powder. m.p.: 297ºC. Yield: 83.52%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) 3119 for C-H in furyl; 3030 for C-H arom.; 2922 for C-H aliph.; 1716 for C=O groups; 1630, 1496 for C=C arom.; 1196 for C-N, 1110 for C-O and 743, 692 (s) for C-H (5adj H, wag), oop, def arom. $^1$H NMR (DMSO-*d*6, 300 MHz) δ ppm = 4.9 (*m*,2*H*,*H*-2,9), 7.27-8.37 (*m*,14*H*, arom. protons). Anal. Calcd (%) for $C_{30}H_{18}N_4O_6$ (530): C: 67.92; H: 3.39; N: 10.56. Founds: C: 67.55; H: 4.08; N: 10.43.

**11b: 2,9-bisfuryl-5,12-bis(4-methylphenyl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{37}$0,$^{10,14}$0] tetradeca-3,10-diene-4,6,11,13-tetraone:**
White powder. m.p.: 298ºC. Yield: 77.58%. IR: KBr, $\nu_{max}$ ($cm^{-1}$) 3119 for C-H in furyl; 3075, 3036 for C-H arom.; 2980 for C-H aliph.; 1721 for C=O groups; 1629, 1511 for C=C arom.; 1378 for aliph., C-H, *sym*, def, 1110 for C-O and 810 (s) for C-H (2adj H, wag), oop, def arom. Anal. Calcd (%) for $C_{32}H_{22}N_4O_6$ (558): C: 68.81; H: 3.94; N: 10.03. Founds: C: 68.31; H: 4.43; N: 9.99.

## Methodology of antimicrobial activity

The filter paper disc method was performed in Nutrient agar for bacteria and Dox agar for fungi (Abdel-Rahman *et al*., 2002). These agar media were incubated with bacteria or fungi, respectively. The filter paper disc (6 mm diameter) saturated with a solution of each compound (10 mg/mL of DMSO) were incubated in agar media. The incubation time was 48 hours at 37ºC for bacteria and 28ºC for fungi. Discs saturated with compounds and free DMSO were used as control. Ciprofloxacin and Griseofulvin were used as a reference for evaluation of antibacterial (Lundstrom, 1983) and antifungal activities (Scrowston, 1981). By this manner some of the newly synthesized compounds were screened in vitro for their antibacterial activity against two strain of bacteria (*Pseudomonas aeruginosa* as –ve Gram and *Staphylococcus aureus* as +ve Gram) and two species of fungi (*Aspergillus niger* and *Aspergillus terreus*).

  

## Results and discussion

The initial starting 1,4-bis[(4-chlorophenyl) benzylidene] hydrazine **1** and 1,4-bis[(furyl) benzylidene] hydrazine **2** for the cycloaddition reactions were early reported (Abdou *et al*., 1982). The *N*-aryl maleimides **3a-e** were chosen as the dipolarophiles for the same purpose (Cava *et al*., 1961). The reaction mixture of aldazine **1** or **2** with each of *N*-aryl maleimides **3a-e** were fused in an oil bath at different times and temperatures give good solid yields of cycloadduct compounds **4**, **5(a-e)**, respectively, (Schemes 1 and 2).

All these described adducts are crystallized by very low solubility in common solvents. The data of chemical and physical methods confirmed the formation of cycloadduct (Houk and Yamaguchi, 1984; Huisgen, 1984). This reaction is envisaged as a tandem [3+2] cycloaddition (1,3-dipolar) reaction. This reaction subsequent is known as a criss-cross cycloaddition (Pezdirc *et al*., 2005). In our investigation, we tried to interest in the effect of substituents in the *N*-aryl maleimides **3a-e** on the *exo-endo* selectivity of the cycloaddition reaction with aldazine **1** and **2** to give compounds (Al-Sharae'y and Gahnem, 2014) **4, 5(a-e)**, respectively.

The IR spectra for compounds **4, 5(a-e)** exhibited stretch absorption bands corresponding to C-H aliphatic at 2950-2900 $cm^{-1}$; aromatic C-H at 3075-3030 $cm^{-1}$; C=O at 1725-1700 $cm^{-1}$; arom. C=C at 1620-1520 $cm^{-1}$ and N-C in maleimide moiety at 1190-1170 $cm^{-1}$. Another good evidence can be seen also in the finger prints region of same IR spectra. Including, a signal bands for C-H in *p*-aromatic substituted, oop bend (2 adj H, wag) at 850, 800 $cm^{-1}$, two bands for C-H in mono aromatic substituted, and oop bend at 750, 690 $cm^{-1}$ are appeared. The lack of any bands, due to aliphatic C=C and C=N, in their typical ranges 1620 to 1580 $cm^{-1}$ indicates the formation of adducts and the absence of any initial compounds, *N*-aryl maleimides and aldazines as previously reported (Silverstein *et al*., 2005; Stewart, 2006; Al-Sharae'y *et al*., 2010).

The $^1$H NMR for **4b** and **5b** as typical example for this series, showed a singlet at δ = 2.37 (*s*, 6H, 2C$H_3$); 3.57 (*q*, 2H, *H*-3,10, $^3J_{3.2}$ = 7.4 Hz, $^3J_{3.7}$ = 9.4 Hz); 3.85 (*d*, 2H, *H*-7,14, $^3J_{7,3}$= 9.4 Hz,); 4.35( *d*, 2H, *H*-2.9, $^3J_{2,3}$= 7.4Hz); 7.00-7.85 (*m*, 16*H*, aromatic protons) ppm. While the mass spectrum of **4b** showed a molecular ion peak appeared at *m/z* = 651 and a base peak at 252, while **5b** showed a molecular ion peak appeared at *m/z* = 562 and a base peak at 186.

Some of **4, 5(a-e)** were directed toward to synthesize each **6, 7(a-e)**, **8(b-e)**, **9d**, **10(c-d)** and **11(a-b)**, (Schemes 3, 4 and 5). Thus it has been found the reduction of each **4, 5(a-e)** by $NaBH_4$ afforded the corresponding hydroxyl derivatives **6, 7(a-e)**, respectively (Brunton and Jones, 2000; Takabe *et al*., 2004; Scheme 3). The IR spectra of these compounds showed absorption bands at 3450 or 3400 $cm^{-1}$ for hydroxyl groups and strong absorption band at. 1720 or 1700 $cm^{-1}$ for carbonyl groups (Barradas *et al*., 1976). The $^1$H NMR spectra revealed the signals for aliphatic, hydroxyl and aromatic protons in the proper positions. However, the mass spectrum for **6a** showed a molecular ion peak appeared at *m/z* = 627 with a base peak at 124, while **7a** showed a molecular ion peak appeared at *m/z* = 538 with a base peak at 95.

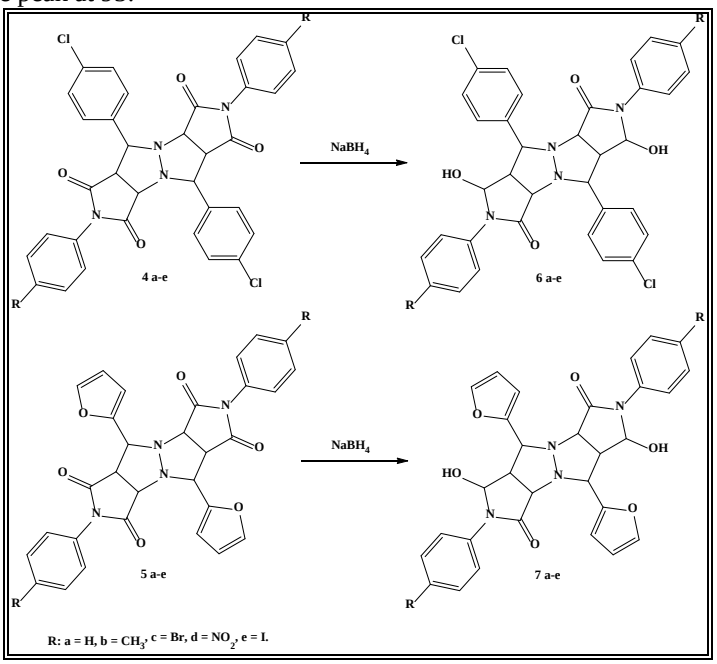


**Figure 3**: The reduction reaction of **4, 5(a-e)** by $NaBH_4$ to produce 2,9-bis(aryl)-5,12-*N,N'*-bis(aryl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradecane-4,11-dihydroxy-6,13-dione **6, 7(a-e)**.

  

Hydrolysis of **4b-e** and **5d** in basic media and neutralized with aqueous acid to give **8b-e** and **9d**, respectively, (Scheme 4). The structural of these compounds were confirmed by elemental analysis and spectral data, which the IR spectra showed a strong absorption broad band at 3400-2500 $cm^{-1}$ for carboxyl groups is a well evidence for proceeding (Al-Sharae'y *et al*., 2010; Brunton and Jones, 2000; Takabe *et al*., 2004). While the $^1H$ NMR spectra for **8b** and **9d** showed appearance of signals for aliphatic, aromatic, amide and carboxylic acids protons. The mass spectrum of **8b** showed a molecular ion pack at *m/z* = 687 and a base peak at 15.

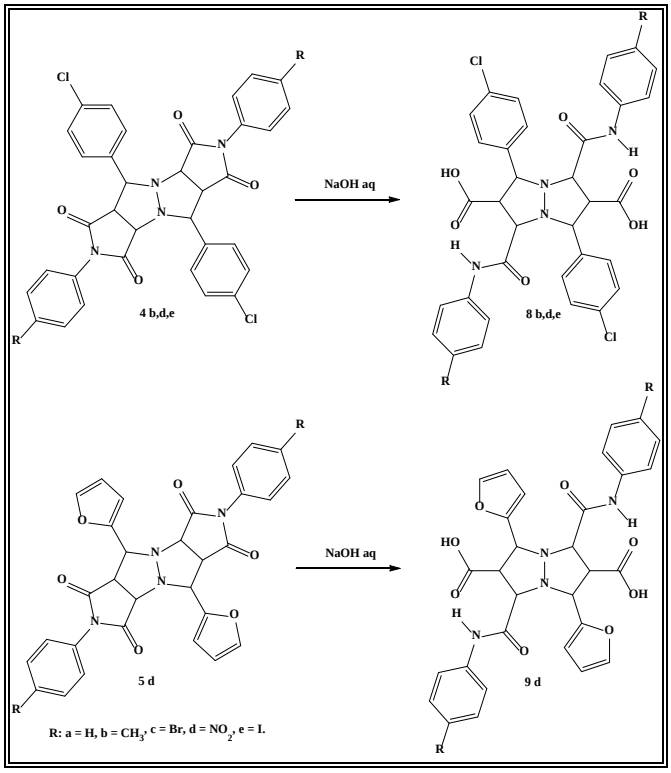


**Figure 4**: The hydrolysis of **4b-e** and **5d** by NaOH to produce 2,6-bis(aryl)-3,7-dicarboxy-4,8-*N*,*N*′-bis(aryl carbonylamide)-1,5-diazadicyclooctane **8b-e** and **9d**.

Dehydrogenation of **4c-d** and **5a-b** were obtained through reactions of these compounds with nitrobenzene under reflex conditions to give at the respective **10c-d** and **11a-b**, which were formed double bond at both carbons 3 and 10, (Scheme 5). The IR spectra of **10c-d** and **11a-b** showed absorption band for carbonyl groups and aliphatic, aromatic, C=C at 1620-1580 $cm^{-1}$. The $^1H$ NMR spectra showed appearance of signals for aliphatic and aromatic protons, while mass spectrum of **10c** showed a molecular ion pack at *m/z* = 619 with a base peak 294, and **10d** showed a molecular ion pack at *m/z* = 709 with a base peak at 217.

  

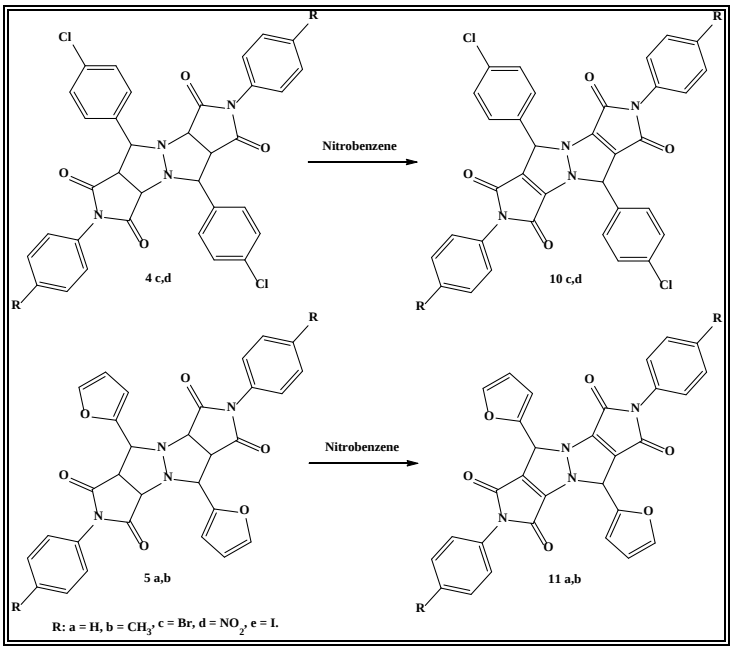


**Figure 5**: The dehydrogenation reaction of **4c-d** and **5a-b** by nitrobenzene to produce 2,9-bis(aryl)-5,12-*N,N'*-bis(aryl)-1,5,8,12-tetraazatetracyclo[6,6,0,$^{3,7}$0,$^{10,14}$0] tetradeca-3,10-diene-4,6,11,13-tetraone **10c-d** and **11a-b**.

***Estimation of antimicrobial activity***

Some of the synthesized compounds were using screened *in vitro* for their antimicrobial activities. Most of the bacterial pathogens tested were resistant to synthesized compounds. Each of **4d**, **5b-d** and **9d** show moderate activity against *Aspergillus niger*, while slightly effect for other compounds against some bacterial and fungi species as shown on **Table 1**. Interestingly, compounds **4d**, **5d**, **8d** and **9d** have the same core structures in bis-aryl pyrazolo[1,2-a]pyrazole and two 4-nitrophenyl functional groups. Shared functional groups in **4d** and **5d** have two diamides, while in both **8d** and **9d** have twice of each carboxylic acids and amides comparing to other tested compounds, **Figure 6**. We believe that functional groups increase an effecting against *Aspergillus niger* comparing with *Aspergillus terreus*.

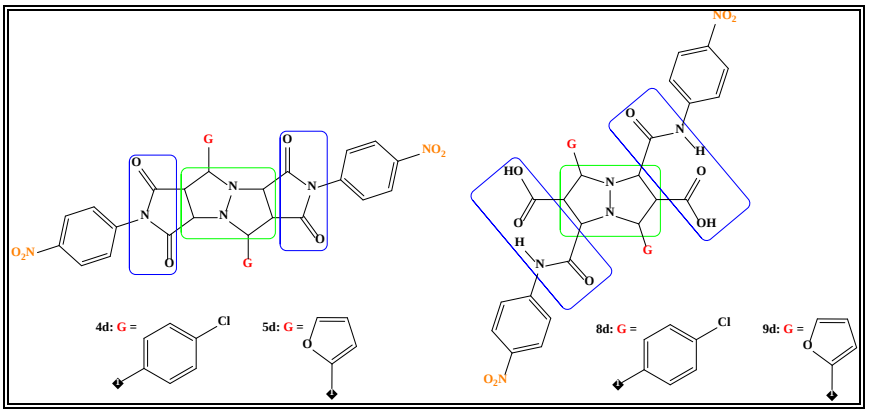


**Figure 6**: The structures of **4d**, **5d** and **9d** which have moderate activity against *Aspergillus niger*.

  

**Table 1**: Antimicrobial activity of some representative compounds (diameter of inhibition zone = IZ)

| Microbes | Test Compounds (mm) | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 4b | 4c | 4d | 4e | 5b | 5c | 5d | 6c | 6e | 8c | 8d | 9d | 10c | 11c | 11d | Cf | Gf |
| **Bacteria** | | | | | | | | | | | | | | | | | |
| ***Pseudomonas aeruginosa*** | – | – | – | – | – | – | – | + | – | – | + | + | – | – | + | +++ | |
| ***Staphylococcus aureus*** | – | + | – | – | – | – | – | – | – | + | + | – | + | – | – | +++ | |
| **Fungi** | | | | | | | | | | | | | | | | | |
| ***Aspergillus niger*** | + | + | ++ | + | ++ | ++ | ++ | – | – | – | – | ++ | – | – | – | | +++ |
| ***Aspergillus terreus*** | – | – | – | – | – | – | – | + | + | + | – | – | – | + | + | | +++ |

Key to symbols: **Cf**: Ciprofloxacin as antibacterial, **Gf**: Griseofulvin as antifungal, Disc diameter = 6 mm, Highly active: +++ (IZ > 19 mm), Moderately active: ++ (IZ 13-19 mm), Slightly active: + (IZ 7-13 mm), Inactive: – (IZ < 7 mm).

## Conclusions

These synthesis are in a good yields. In these reactions, no catalyst required for the generation of the azomethine imines, and this takes place only by fusing the reaction of mixture in solvent-free phase, it is an economically feasibility in terms, also, microbial effectiveness of their against bacteria and fungi.

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