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Synthesis of New Heterocyclic Compounds from Reaction of *N*-Aryl Maleimide with Cinnamal aryl hydrazones and Their Antimicrobial Activity

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Abstract
The methods of cycloaddition reaction between cinnamal aryl hydrazones 1 or 2 with *N*-Aryl Maleimide 3a-e to give 8-phenyl-4,11-bis(aryl)-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,5,10,12-tetraone 4a-e and 5a-e in good yields. Some of the synthesized compounds were directed toward hydrogenation, hydrolysis and dehydrogenation reactions to afford the expected compounds 6a-c,e, 7a-e, 8b, 9a,b, 10a-e and 11a,b,d,e. The structural formulas for new synthesis compounds were assigned using chemical and physical methods as elemental analysis, mass spectroscopy, infrared and proton nuclear magnetic resonance spectroscopy. However, some of the synthesized compounds were studied against toward antimicrobial activity against some types of bacteria and fungi.

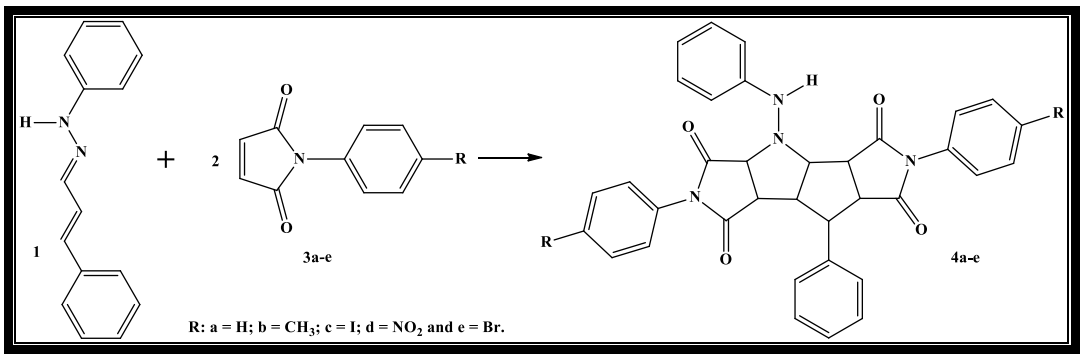
Keywords: criss-cross cycloaddition, 1,3-dipolar reaction, N-Aryl Maleimide, Aldazines, Hydrazones

1. Introduction

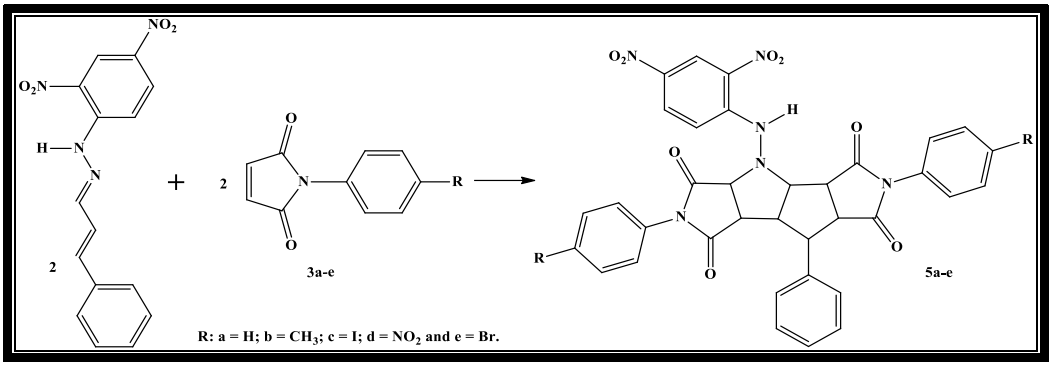
Criss-cross cycloaddition reaction was described in 1917 as intermolecular reaction of benzaldehyde with two equivalents of isothiocyanate affording a heterocyclic compound having two fused five-membered rings [1]. The reaction was named in the subsequent paper [2]. Criss-cross cycloadditions may be classified as a special type of [3+2] cycloaddition or 1,3-dipolar cycloaddition, respectively [3, 4]. The formation of their products was explained in 1963 by Huisgen [5, 6] as a success of two successive 1,3-dipolar cycloadditions. This assumption was proved in 1974 when a stable 1,3-dipole was identified by X-ray crystallographic analysis [7].

Bruntons and jones [8] reported that the reduction of *N*-Aryl Maleimide by sodium borohydride lead to the formation of one of the hydroxyl compound in 74% yields along with 26% of a ring-opened product with one of hydroxyl. Bessho *et al.* [9] showed that the treatment of maleimide derivatives with $NaBH_4$ gave 5-hydroxyl-1,5-dihydropyrrol-2-one derivatives. In the light of electrochemical data, Barradas *et al.* [10] deduced that the following the reaction a cleavage of the C-N bond as the rate determining step is explaining the hydrolysis mechanism of maleimide, in alkaline solution.

Recently, we have been reported the reaction between the hydrazines with *N*-aryl maleimides [11]. Continuing our previous studies and investigation of criss-cross cycloaddition as a type of [3+2] cycloaddition, we are synthesized the reaction between the cinnamal aryl hydrazones 1 and 2 with *N*-aryl maleimides 3a-e, Schemes 1 and 2.



Scheme 1: The reaction of produce 1-anilino-4,11-bis(4-aryl)-8-phenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,5,10,12-tetraone **4a-e**.



Scheme 2: The reaction of produce 1-(2,4-dinitroanilino)-8-phenyl-4,11-bis(4-aryl)-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,5,10,12-tetraone **5a-e**.

2. Materials and methods

2.1 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 [12]. 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.

2.2 Synthesis

2.2.1 General procedure for the synthesis of 8-aryl-1,4,11–triazatetracyclo[6,6,0,^{2,6}0,^{9,13}0] tetratetracyclodane-3,5,10,12-tetraone 4a-e and 5a-e

The synthetic method of **3a-e** was described previously [11]. A mixture of cinnamalphenylhydrazone **1** 556 mg, 2.5 mmol or cinnamal-2,4-dinitrophenylhydrazone **2** 866 mg, 2.5 mmol with *N*-Aryl Maleimide **3a-e** 5.0 mmol were fused in an oil different bath degree at 200-220ºC or 240-260ºC, respectively. TLC showed that the reaction was completed after 90 min. The solid obtained after cooling recrystallized from Ethanol 50% to give **4a-e** or from benzene to give **5a-c**. The structural determination for these compounds confirmed by elemental analyses and spectral data.

4a:1-Anilino-4,8,11-triphenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradcane-3,5,10,12-tetraone:

Orange powder, m.p.: 200ºC. Yield: 74.05 %. IR: K Br, ν_{max} (cm^{-1}) 3336 for NH; 3010 for C-H arom.; 2952, 2918, 2860 for C-H aliph.; 1716 for C=O; 1598, 1496 for C=C arom.; 1186 for C-N amide; 1448, 1382 for def., bend. C-H aliph.; and 750, 694 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{28}N_4O_4$ (568): C: 73.94; H: 4.92; N: 9.85. Founds: C: 73.90; H: 4.44; N: 9.50.

4b:1-Anilino-4,11-bis(4-methylphenyl)-8-phenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,5,10,12-tetraone:

Orange powder. m.p.: 230ºC. Yield: 73.79%. IR: KBr, ν_{max} (cm^{-1}) 3344 for -NH; 3030 for C-H arom.; 2920, 2722 for C-H aliph.; 1714 for C=O; 1598, 1514 for C=C arom.; 1186 for C-N amide; 1452, 1380 for def., bend C-H aliph.; 812 for C-H (2 adj. H, wag.), oop, def. arom. and 750, 694 for C-H (5 adj. H, wag.), oop, def. arom. ^{1}H NMR (DMSO-d_6, 300 MHz) δ ppm = 2.23 (*m*, 1H: *H*-7); 2.27-2.49 (*m*, 6H: 2 C*H*$_3$); 2.60-3.50 (*m*, 5H: *H*-6,8,9,13,14); 5.00 (*d*, 1H: *H*-2); 7.03-7.90 (*m*, 19H, *arom.* and N*H*). Anal. Calcd. % for $C_{37}H_{32}N_4O_4$ (596): C: 74.49; H: 5.36; N: 9.39. Founds: C: 73.99; H: 5.34; N: 9.67.

4c:1-Anilino-4,11-bis(4-iodophenyl)-8-phenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,5,10,12-tetraone:

Colorless powder. m.p.: 232ºC. Yield: 83.52%. IR: KBr, ν_{max} (cm^{-1}) 3394 for -NH; 3064 for C-H arom.; 2935 for C-H aliph.; 1716 for C=O; 1597 for C=C arom.; 1180,1110 for C-N amide; 1452, 1380, 1311 for def., bend C-H aliph.; 852 for C-H (2 adj. H, wag.), oop, def. arom. and 746, 692 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{26}N_4O_4I_2$ (820): C: 51.21; H: 3.17; N: 6.82. Founds: C: 51.27; H: 3.62; N: 6.36.

4d:1-Anilino-4,11-bis(4-nitrophenyl)-8-phenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,5,10,12-tetraone:

Colorless powder. m.p.: 240ºC. Yield: 78.99%. IR: KBr, ν_{max} (cm^{-1}) 3326 for -NH; 3084 for C-H arom.; 2920 for C-H aliph.; 1720 for C=O; 1598, 1524 for C=C arom.; 1526 for -NO_2; 1178, 1112 for C-N amide; 1344 for def., bend C-H aliph.; 852 for C-H (2 adj. H, wag.), oop, def. arom. and 748, 692 for C-H (5 adj. H, wag.), oop, def. arom. ^{1}H NMR (DMSO-d_6, 200 MHz) δ ppm = 2.13 (*q*, 1H, *H*-7); 3.00 (*m*, 5H, for *H*-6,8,9,13,14); 5.00 (*d*, 1H, *H*-2); 7.50-8.50 (*m*,19H, *arom.* and -N*H*). Anal. Calcd. % for $C_{35}H_{26}N_6O_8$ (658): C: 63.82; H: 3.95; N: 12.76. Founds: C: 63.20, H: 4.43; N: 12.39.

4e:1-Anilino-4,11-bis(4-bromophenyl)-8-phenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,5,10,12-tetraone:

Colorless powder. m.p.: 217ºC. Yield: 74.95%. IR: KBr, ν_{max} (cm^{-1}) 3324 for -NH; 3084 for C-H arom.; 2928 for C-H aliph.; 1718 for C=O; 1598,1526 for C=C arom.; 1178,1110 for C-N amide; 1380, 1344 for def., bend C-H aliph.; 852 for C-H (2 adj. H, wag.), oop, def. arom. and 747, 694 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{26}N_4O_4Br_2$ (726): C: 57.85; H: 3.58; N: 7.71. Founds: C: 57.80; H: 3.21; N: 7.63.

5a:1-(2,4-Dinitroanilino)-4,8,11-triphenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,5,10,12-tetraone:

Black powder. m.p.: 313ºC. Yield: 75.83%. IR: KBr, ν_{max} (cm^{-1}) 3298 for -NH; 3095 for C-H arom.; 2898, 2760 for C-

H aliph.; 1714 for C=O; 1616, 1524 for C=C arom.; 1500 for -NO_2; 1188, 1070 for C-N amide; 1384, 1338 for def., bend C-H aliph.; 832 for C-H (2 adj. H, wag.), oop, def. arom. and 750, 694 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{26}N_6O_8$ (658): C: 63.83; H: 3.95; N: 12.76. Founds: C: 63.29; H: 4.12; N: 12.14.

5b:1-(2,4-Dinitroanilino)-8-phenyl-4,11-bis(4-methylphenyl)-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetra decane-3,5,10,12-tetraone:

Black powder. m.p.: >350ºC. Yield: 79.44%. IR: KBr, ν_{max} (cm^{-1}) 3302 for -NH; 3020 for C-H arom.; 2850, 2726 for C-H aliph.; 1714 for C=O; 1614 for C=C arom.; 1514 for -NO_2; 1186, 1112 for C-N amide; 1388, 1336 for def., bend C-H aliph.; 820 for C-H (2 adj. H, wag.), oop, def. arom. and 746, 702 for C-H (5 adj. H, wag.), oop, def. arom. ^{1}H NMR (C*D*Cl_3, 200 MHz) δ ppm = 2.13 (*q*, 1H, *H*-7); 2.34 (*s*, 6H, 2 C*H*$_3$); 3.25-3.75 (*m*, 5H, *H*-6,8,9,13,14); 5.00 (*d*, 1H, *H*-2); 7.80-8.20 (*m*, 17H, *arom.* and -N*H*). Anal. Calcd. % for $C_{37}H_{30}N_6O_8$ (686): C: 64.72; H: 4.37; N: 12.24. Founds: C: 64.57; H: 4.81; N: 12.29.

5c:1-(2,4-Dinitroanilino)-8-phenyl-4,11-bis(4-iodophenyl)-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetra decane-3,5,10,12-tetraone:

Gray powder. m.p.: 310ºC. Yield: 75.79%. IR: KBr, ν_{max} (cm^{-1}) 3202 for -NH; 3020 for C-H arom.; 2920, 2770 for C-H aliph.; 1720 for C=O; 1660 for C=C arom.; 1488 for -NO_2; 1190, 1120 for C-N amide; 1376 for def., bend C-H aliph.; 818 for C-H (2 adj. H, wag.), oop, def. arom. and 750, 700 for C-H (5 adj. H, wag.), oop, def. arom. ^{1}H NMR (DMSO-d_6, 200 MHz) δ ppm = 2.13 (*q*, 1H, *H*-7); 3.10-3.70 (*m*, 5H, *H*-6,8,9,13,14); 5.00 (*d*, 1H, *H*-2); 6.80-8.40 (*m*, 17H, *arom.* and -N*H*). Anal. Calcd. % for $C_{35}H_{24}N_6O_8I_2$ (910): C: 46.15; H: 2.63; N: 9.23. Founds: C: 45.82; H: 2.22; N: 9.03.

5d:1-(2,4-Dinitroanilino)-4,11-bis(4-nitro-phenyl)-8-phenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetra decane-3,5,10,12-tetraone:

Brown powder. m.p.: 298ºC. Yield: 71.37%. IR: KBr, ν_{max} (cm^{-1}) 3425 for -NH; 3059, 3020 for C-H arom.; 2923 for C-H aliph.; 1720 for C=O; 1636 for C=C arom.; 1490 for -NO_2; 1176, 1070 for C-N amide; 1419, 1390 for def., bend C-H aliph.; 819 for C-H (2 adj. H, wag.), oop, def. arom. and 743, 700 for C-H (5 adj. H, wag.), oop, def. arom. ^{1}H NMR (DMSO-d_6, 200 MHz) δ ppm = 2.13 (*q*, 1H, *H*-7); 2.90-3.30 (*m*, 5H, *H*-6,8,9,13,14); 5.00 (*d*, 1H, *H*-2); 6.80-8.40 (*m*, 17H, *arom*. and -N*H*). Anal. Calcd. % for $C_{35}H_{24}N_8O_{12}$ (748): C: 56.14; H: 3.20; N: 14.97. Founds: C: 56.33; H: 3.20; N: 13.73.

5e:1-(2,4-Dinitroanilino)-8-phenyl-4,11-bis(4-bromophenyl)-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetra decane-3,5,10,12-tetraone:

Gray powder. m.p.: 280ºC. Yield: 70.46%. IR: KBr, ν_{max} (cm^{-1}) 3396 for -NH; 3061, 3028 for C-H arom.; 2928 for C-H aliph.; 1720 for C=O; 1523 for C=C arom.; 1487 for -NO_2; 1180, 1058 for C-N amide; 1382 for def., bend C-H aliph.; 816 for C-H (2 adj. H, wag.), oop, def. arom. and 746, 702 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{24}N_6O_8Br_2$ (816): C: 51.47; H: 2.94; N: 10.29. Founds: C: 51.27; H: 2.55; N: 10.86.

2.2.2 General procedure for the synthesis of 5-phenyl-2,6-dicarboxy-3,7-bis(*N*-arylcarbonamide)-1-azadicyclo [3,3,0] octane 6a-c, e and 7a-e:

Dissolve of **4a-c**, **e** or **5a-e** 5.0 mmol in 20 mL of 20% NaOH was stirred under reflux for 2 hrs. After cooling the resulting mixture neutralized with 0.01 M HCl and extracted by $CHCl_3$. The solvent evaporated under reduced pressure and the residue recrystallized from ethanol to give each of compounds **6a-c**, **e** or **7a-e**, respectively. The structural determination for these compounds confirmed by elemental analyses and spectral data.

6a:1-Anilino-5-phenyl-2,6-dicarboxy-3,7-bis(*N*-phenylcarbonamide)-1-azadicyclo [3,3,0] octane:

Orange powder. m.p.: 191ºC. Yield: 76.41%. IR: KBr, ν_{max} (cm^{-1}) 3400-2400 for -OH carboxyl, 3278 for -NH; 3065, 3024 for C-H arom.; 2920, 2748 for C-H aliph.; 1712 for C=O; 1600, 1540, 1496 for C=C arom.; 1246, 1198 for C-N amide; 1444, 1314 for def., bend C-H aliph.; 1076, 1028 for C-O; and 752, 694 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{32}N_4O_6$ (604): C: 69.53; H: 5.29; N: 9.27. Founds: C: 68.96; H: 5.23; N: 9.85.

6b:1-Anilino-5-phenyl-2,6-dicarboxy-3,7-bis(*N*-4-methylphenylcarbonamide)-1-azadicyclo [3,3,0] octane:

Brown powder. m.p.: 210ºC. Yield: 70.13%. IR: KBr, ν_{max} (cm^{-1}) 3500-2800 for -OH carboxyl, 3278 for -NH; 3131 for C-H arom.; 2952, 2748 for C-H aliph.; 1685 for C=O; 1602, 1516 for C=C arom.; 1248, 1168, 1114 for C-N amide; 1406, 1316 for def., bend C-H aliph.; 1060 for C-O; 816 for C-H (2 adj. H, wag.), oop, def. arom. and 750, 698 for C-H (5 adj. H, wag.), oop, def. arom. ^{1}H NMR (DMSO-d_6, 300 MHz) δ ppm = 2.27 (*m*, *H*-4); 2.34-2.50 (*s*, 7H, 2 C*H*$_3$ and *H*-4); 2.88 (*s*, *d*, 2H, N*H* amine, and *H*-3); 2.90-3.34 (*m*, 4H, *H*-5,6,7,8); 4.20 (*d*, *H*-2); 6.70-7.60 (*m*, 20H, *arom* and *amide*). EIMS: *m*/*z* = 632 for molecular ion peak and a base peak at *m*/*z* = 58. Anal. Calcd. % for $C_{37}H_{36}N_4O_6$ (632): C: 70.25; H: 5.69; N: 8.86. Founds: C: 69.88; H: 6.18; N: 7.93.

6c:1-Anilino-5-phenyl-2,6-dicarboxy-3,7-bis(*N*-4-iodophenylcarbonamide)-1-azadicyclo [3,3,0] octane:

Brown powder. m.p.: 272ºC. Yield: 76.09%. IR: KBr, ν_{max} (cm^{-1}) 3500-2400 for -OH carboxyl, 3326 for -NH; 3031 for C-H arom.; 2918 for C-H aliph.; 1704 for C=O; 1594, 1492 for C=C arom.; 1242, 1186 for C-N amide; 1388, 1308 for def., bend C-H aliph.; 1006 for C-O; 818 for C-H (2 adj. H, wag.), oop, def. arom. and 752, 698 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{30}N_4O_6I_2$ (856): C: 49.06; H: 3.50; N: 6.54. Founds: C: 48.74; H: 4.00; N: 6.15.

6e:1-Anilino-5-phenyl-2,6-dicarboxy-3,7-bis(*N*-4-bromophenylcarbonamide)-1-azadicyclo[3,3,0]octane:

Brown powder. m.p.: 178ºC. 77.96%. IR: KBr, ν_{max} (cm^{-1}) 3600-2400 for -OH carboxyl, 3316 for -NH; 3042 for C-H arom.; 2926, 2868, 2776 for C-H aliph.; 1714 for C=O; 1598, 1530 for C=C arom.; 1242 for C-N amide; 1394, 1306 for def., bend C-H aliph.; 1072, 1010 for C-O; 820 for C-H (2 adj. H, wag.), oop, def. arom. and 750, 696 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{30}N_4O_6Br_2$ (762): C: 55.11; H: 3.93; N: 7.34. Founds: C: 55.69; H: 3.70; N: 7.64.

7a:1-(2,4-Dinitroanilino)-5-phenyl-2,6-dicarboxy-3,7-bis(*N*-phenylcarbonamide)-1-azadicyclo[3,3,0] octane:
Brown powder. m.p.: >350ºC. Yield: 78.12%. IR: KBr, ν_{max} (cm^{-1}) 3600-2400 for -OH carboxyl, 3354 for -NH; 3042 for C-H arom.; 2834 for C-H aliph.; 1716 for C=O; 1598, 1530 for C=C arom.; 1480 for -NO_2; 1242 for C-N amide; 1398 for def., bend C-H aliph.; 1030 for C-O; 820 for C-H (2 adj. H, wag.), oop, def. arom. and 750, 696 for C-H (5 adj. H, wag.), oop, def. arom. ^{1}H NMR (DMSO-d_6, 300 MHz) δ ppm = 2.27 (*m*, *H*-4); 2.50 (*s*, 1H, *H*-4); 2.88 (*s*, *d*, 2H, N*H* amine, and *H*-3); 2.90-3.34 (*m*, 4H, *H*-5,6,7,8); 4.20 (*d*, *H*-2); 7.00-7.70 (*m*, 22H, *arom.* and *amide*). EIMS: *m*/*z* = 694 for molecular ion peak and a base peak at *m*/*z* = 123. Anal. Calcd. % for $C_{35}H_{30}N_6O_{10}$ (694): C: 60.51; H: 4.32; N: 12.10. Founds: C: 60.51; H: 4.73; N: 11.39.

7b:1-(2,4-Dinitroanilino)-5-phenyl-2,6-dicarboxy-3,7-bis (*N*-4-methylphenyl carbonamide)-1-azadicyclo [3,3,0] octane:
Black powder. m.p*:.* >350ºC. Yield: 69.39%. IR: KBr, ν_{max} (cm^{-1}) 3600-2400 for -OH carboxyl, 3442 for -NH; 3010 for C-H arom.; 2912, 2726 for C-H aliph.; 1712 for C=O; 1626, 1530 for C=C arom.; 1518 for -NO_2; 1214 for C-N amide; 1390 for def., bend C-H aliph.; 1010 for C-O; 816 for C-H (2 adj. H, wag.), oop, def. arom. and 750, 696 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{37}H_{34}N_6O_{10}$ (722): C: 61.49; H: 4.70; N: 11.63. Founds: C: 59.19; H: 4.52; N: 10.11.

7c:1-(2,4-Dinitroanilino)-5-phenyl-2,6-dicarboxy-3,7-bis (*N*-4-iodophenyl carbonamide)-1-azadicyclo [3,3,0] octane:
Black powder. m.p.: >350ºC. Yield: 72.31%. IR: KBr, ν_{max} (cm^{-1}) 3600-2400 for -OH carboxyl, 3348 for -NH; 3070 for C-H arom.; 2900 for C-H aliph.; 1718 for C=O; 1604, 1488 for C=C arom.; 1528 for -NO_2; 1214 for C-N amide; 1388 for def., bend C-H aliph.; 1008 for C-O; 820 for C-H (2 adj. H, wag.), oop, def. arom. and 756, 698 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{28}N_6O_{10}I_2$ (946): C: 44.39; H: 2.95; N: 8.87. Founds: C: 44.60; H: 3.61; N: 8.51.

7d: 1-(2,4-Dinitroanilino)-5-phenyl-2,6-tetracarboxy-3,7-bis (*N*-4-nitrophenyl carbonamide)-1-azadicyclo [3,3,0] octane:
Black powder. m.p.: >350ºC. Yield: 77.27%. IR: KBr, ν_{max} (cm^{-1}) 3600-2400 for -OH carboxyl, 3400 for -NH; 3010 for C-H arom.; 2930 for C-H aliph.; 1716 for C=O; 1620,1512 for C=C arom.; 1480 for -NO_2; 1124 for C-N amide; 1388 for def., bend C-H aliph.; 1020 for C-O; 822 for C-H (2 adj. H, wag.), oop, def. arom. and 756, 698 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{28}N_8O_{14}$ (784): C: 53.57; H: 3.57; N: 14.28. Founds: C: 53.75; H: 3.45; N: 14.76.

7e:1-(2,4-Dinitroanilino)-5-phenyl-2,6-dicarboxy-3,7-bis (*N*-4-bromophenyl carbonamide)-1-azadicyclo [3,3,0] octane.
Black powder. m.p.: >350ºC. Yield: 79.17%. IR: KBr, ν_{max} (cm^{-1}) 3600-2400 for -OH carboxyl, 3352 for -NH; 3020 for C-H arom.; 2922, 2718 for C-H aliph.; 1710 for C=O; 1606, 1500 for C=C arom.; 1490 for -NO_2; 1144 for C-N amide; 1390 for def., bend C-H aliph.; 1008 for C-O; 822 for C-H (2 adj. H, wag.), oop, def. arom. and 756, 698 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{28}N_6O_{10}Br_2$ (852): C: 49.29; H: 3.28; N: 9.85. Founds: C: 49.16; H: 3.08; N: 9.95.

2.2.3 General procedure for the synthesis of 8-phenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradeca-2,7,9-triene-3,5,10,12-tetraone:
Dissolve each of **4b** or **5a**,**b** 5.0 mmol in 20 mL of nitrobenzene was stirring under reflux for 5 hrs. After cooling the solid obtained was filtrated and recrystallized from acetone to give each of compounds **8b** or **9a**,**b**, respectively. The structural determination for these compounds confirmed by elemental analyses and spectral data.

8b: 1–Anilino-4,11-bis(4-methylphenyl)-8-phenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradeca-2,7,9-triene-3,5,10,12-tetraone:
Brown powder. m.p.: 247ºC. Yield: 72.76%. IR: KBr, ν_{max} (cm^{-1}) 3600-2400 for -OH carboxyl, 3411 for -NH; 3020 for C-H arom.; 2920 for C-H aliph.; 1714 for C=O; 1593 for C=C arom.; 1214 for C-N amide; 1370 for def., bend C-H aliph.; 1010 for C-O; 850 for C-H (2 adj. H, wag.), oop, def. arom. and 750, 696 for C-H (5 adj H, wag.), oop, def. arom. ^{1}H NMR (DMSO-d_6, 300 MHz) δ ppm = 2.34 (*s*, 6H, 2C*H*$_3$); 3.50 (*s*, N*H*); 4.70 (*s*, *H*-8); 6.80-7.70 (*m*, 18H, *arom*.). EIMS: *m*/*z* = 590 for molecular ion peak and a base peak at *m*/*z* = 57. Anal. Calcd. % for $C_{37}H_{26}N_4O_4$ (590): C: 75.25; H: 4.40; N: 9.49. Founds: C: 75.69; H: 4.40; N: 9.78.

9a: 1–(2,4-Dinitroanilino)-4,8,11-triphenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradeca-2,7,9-triene-3,5,10,12-tetraone:
Brown powder. m.p.: 330ºC. Yield: 81.46%. IR: KBr, ν_{max} (cm^{-1}) 3600-2400 for -OH carboxyl, 3411 for -NH; 3062 for C-H arom.; 2924 for C-H aliph.; 1716 for C=O; 1593, 1527 for C=C arom.; 1496 for -NO_2; 1214 for C-N amide; 1378 for def., bend C-H aliph.; 1010 for C-O; 850 for C-H (2 adj. H, wag.), oop, def. arom. and 750, 696 for C-H (5 adj. H, wag.), oop, def. arom. ^{1}H NMR (DMSO-d_6, 300 MHz) δ ppm = 4.80 (*s*, *H*-8) and 7.00-7.90 (*m*, 20H, *arom*. and N*H*). EIMS: *m*/*z* = 652 for molecular ion peak and a base peak at *m*/*z* = 95.

9b: 1–(2,4-Dinitroanilino)-4,11-bis(4-methylphenyl)-8-phenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetra deca-2,7,9-triene-3,5,10,12-tetraone:
Brown powder. m.p.: 283ºC. Yield: 79.16%. IR: KBr, ν_{max} (cm^{-1}) 3600-2400 for -OH carboxyl, 3415 for -NH; 3023 for C-H arom.; 2928 for C-H aliph.; 1711 for C=O; 1590 for C=C arom.; 1549 for -NO_2; 1212 for C-N amide; 1375 for def., bend C-H aliph.; 1014 for C-O; 854 for C-H (2 adj. H, wag.), oop, def. arom. and 748, 693 for C-H (5 adj. H, wag.), oop, def. arom. ^{1}H NMR (DMSO-d_6, 300 MHz) δ ppm = 2.37 (*s*, 6H, 2 C*H*$_3$); 4.74 (*s*, *H*-8), 6.60-9.00 (*m*, 17H, *arom*. and N*H*). Anal. Calcd. % for $C_{37}H_{24}N_6O_8$ (680): C: 65.29; H: 3.52; N: 12.35. Founds: C: 65.70; H: 3.72; N: 12.78.

2.2.4 General procedure for the synthesis of 8-phenyl-1,4,11-triazatetracyclo-[6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,10-dihydroxy-5,12-dione.
Dissolve each of **4a-e** or **5a**,**b**,**d**,**e** 5.0 mmol in absolute ethanol and $NaBH_4$ 2.0 g, 5.4 mmol was added and stirred

under reflux for 5 hrs. The resulting mixture was neutralized with diluted HCl and extracted by diethyl ether. The solvent was evaporated under reduced pressure and the residue recrystallized from ethanol to give each of compounds **10a-e** or **11a**,**b**,**d**,**e**, respectively. The structural determination for these compounds confirmed by elemental analyses and spectral data.

10a: 1-Anilino-4,8,11-triphenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,10-dihydroxy-5,12-dione:
Orange powder. m.p.: 232^{o}C. Yield: 72.52%. IR: KBr, ν_{max} (cm^{-1}) 3550 for -OH hydroxyl, 3342 for -NH; 3010 for C-H arom.; 2922, 2724 for C-H aliph.; 1710 for C=O; 1598, 1528, 1496 for C=C arom.; 1126 for C-N amide; 1444, 1386, 1310 for def., bend C-H aliph.; 1072 for C-O; and 754, 694 for C-H (5 adj. H, wag.), oop, def. arom. ^{1}H NMR (C*D*Cl$_3$, 300 MHz) δ ppm =2.20 (*m*, 3H, *H*-7, 2 O*H*); 2.70 (*m*, 2H, *H*-14 and N*H*); 3.00-4.30 (*m*, 7H, *H*-2,3,6,8,9,10,13) and 7.00-8.30 (*m*, 20H, *arom*.). EIMS: *m*/*z* = 572 for molecular ion peak and a base peak at *m*/*z* = 88. Anal. Calcd. % for $C_{35}H_{32}N_4O_4$ (572): C: 73.42; H: 5.59; N: 9.79. Founds: C: 73.80; H: 5.14; N: 9.50.

10b: **1-Anilino-4,11-bis(4-methylphenyl)-8-phenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,10-dihydroxy-5,12-dione:**
Brown powder. m.p.: 200^{o}C. Yield: 66.78%. IR: KBr, ν_{max} (cm^{-1}) 3500 for -OH hydroxyl, 3318 for -NH; 3011 for C-H arom.; 2892 for C-H aliph.; 1704 for C=O; 1602, 1516 for C=C arom.; 1122 for C-N amide; 1450, 1402, 1312 for def., bend C-H aliph.; 1074, 1040 for C-O; 854 for C-H (2 adj. H, wag.), oop, def. arom. and 750, 698 for C-H (5 adj. H, wag.), oop, def. arom. ^{1}H NMR (C*D*Cl$_3$, 300 MHz) δ ppm = 1.27 (*s*, 2H, 2 O*H*), 1.80-2.40 (*m*, 8H, 2C*H*$_3$, and *H*-7,9), 2.80-3.80 (*m*, 6H, *H*-2,6,8,13,14 and N*H*); 5.63 (*d*, 2H, *H*-3,16) and 6.60-7.80 (*m*, 18H, *arom*). EIMS: *m*/*z* = 600 for molecular ion peak and a base peak at *m*/*z* = 64. Anal. Calcd. % for $C_{37}H_{36}N_4O_4$ (600): C: 74.00; H: 6.00; N: 9.33. Founds: C: 73.89; H: 5.84; N: 9.67.

10c: 1-Anilino-4,11-bis(4-iodophenyl)-8-phenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,10-dihydroxy-5,12-dione:
Brown powder. m.p.: 205^{o}C. Yield: 77.80%. IR: KBr, ν_{max} (cm^{-1}) 3520 for -OH hydroxyl, 3298 for -NH; 3000 for C-H arom.; 2918, 2780 for C-H aliph.; 1688 for C=O; 1594, 1526, 1488 for C=C arom.; 1150 for C-N amide; 1392, 1306 for def., bend C-H aliph.; 1064, 1006 for C-O; 820 for C-H (2 adj. H, wag.), oop, def. arom. and 750, 696 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{30}N_4O_4I_2$ (824): C: 50.97; H: 3.64; N: 6.79. Founds: C: 51.27; H: 3.52; N: 6.63.

10d: 1-Anilino-4,11-bis(4-nitrophenyl)-8-phenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,10-dihydroxy-5,12-dione:
Brown powder. m.p. 245^{o}C. Yield: 66.57%. IR: KBr, ν_{max} (cm^{-1}) 3530 for -OH hydroxyl, 3392 for -NH; 3132, 3028 for C-H arom.; 2918 for C-H aliph.; 1710 for C=O; 1598 for C=C arom.; 1508 for -NO_2; 1180 for C-N amide; 1401, 1338 for def., bend C-H aliph.; 1112 for C-O; 852 for C-H (2 adj. H, wag.), oop, def. arom. and 752, 696 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{30}N_6O_8$ (662): C: 63.44; H: 4.53; N: 12.68. Founds: C: 63.34; H: 4.49; N: 12.28.

10e: 1-Anilino-4,11-bis(4-bromophenyl)-8-phenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,10-dihydroxy-5,12-dione:
Brown powder. m.p.: 185^{o}C. Yield: 67.77 %. IR: KBr, ν_{max} (cm^{-1}) 3500 for -OH hydroxyl, 3318 for -NH; 3102, 3056 for C-H arom.; 2902, 2780 for C-H aliph.; 1686 for C=O; 1592, 1488 for C=C arom.; 1155 for C-N amide; 1390, 1304 for def., bend C-H aliph.; 1066, 1006 for C-O; 818 for C-H (2 adj. H, wag.), oop, def. arom. and 750, 696 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{30}N_4O_4Br_2$ (730): C: 57.53; H: 4.10; N: 7.67. Founds: C: 57.67; H: 3.87; N: 7.51.

11a: 1-(2,4-Dinitroanilino)-4,8,11-triphenyl-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,10-dihydroxy-5,12-dione:
Brown powder. m.p.: 272^{o}C. Yield: 82.37%. IR: KBr, ν_{max} (cm^{-1}) 3510 for -OH hydroxyl, 3318 for -NH; 3100, 3030 for C-H arom.; 2906 for C-H aliph.; 1686 for C=O; 1600, 1528 for C=C arom.; 1498 for -NO_2; 1160 for C-N amide; 1444, 1388, 1322 for def., bend C-H aliph.; 1050 for C-O; 828 for C-H (2 adj. H, wag.), oop, def. arom. and 754, 696 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{30}N_6O_8$ (662): C: 63.44; H: 4.53; N: 12.68. Founds: C: 63.17; H: 4.13; N: 12.23.

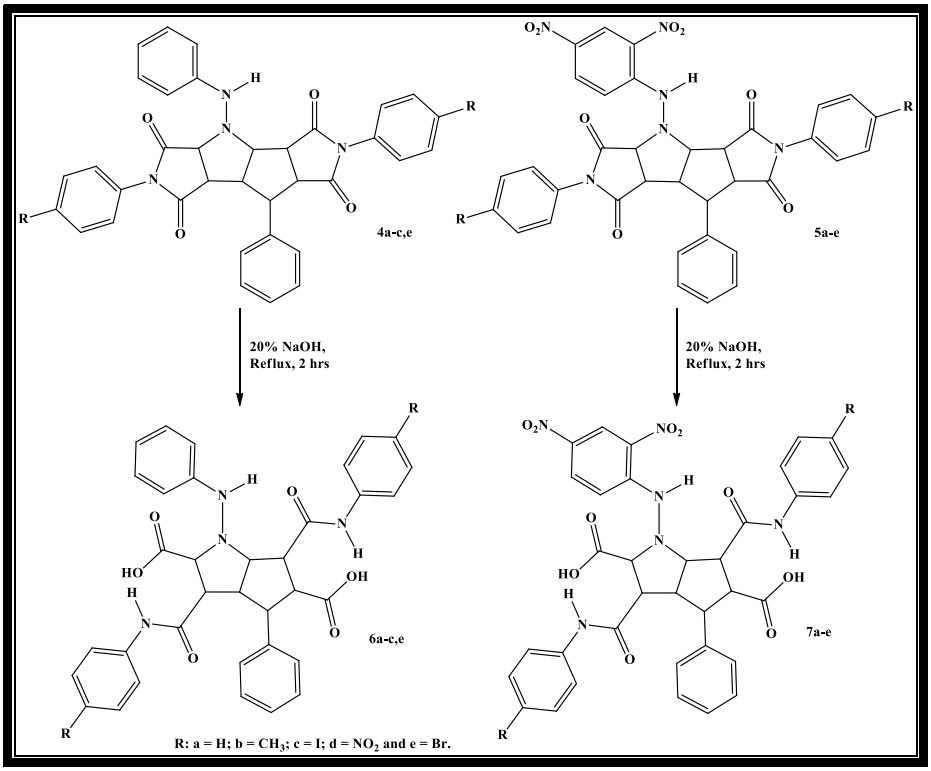
11b: 1-(2,4-Dinitroanilino)-8-phenyl-4,11-bis (4-methylphenyl)-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,10-dihydroxy-5,12-dione:
Brown powder. m.p.: 280^{o}C. Yield: 73.18%. IR: KBr, ν_{max} (cm^{-1}) 3530 for -OH hydroxyl, 3260, 3220 for -NH; 3028 for C-H arom.; 2920 for C-H aliph.; 1708 for C=O; 1590 for C=C arom.; 1514 for -NO_2; 1140 for C-N amide; 1390, 1342 for def., bend C-H aliph.; 1050 for C-O; 816 for C-H (2 adj. H, wag.), oop, def. arom. and 754, 700 for C-H (5 adj. H, wag.), oop, def. arom. ^{1}H NMR (C*D*Cl$_3$, 300 MHz) δ ppm = 1.12 (*s*, O*H*); 1.50 (*s*, N*H*); 2.20 (*m*, 2H, *H*-10 and O*H*); 2.34 (*m*, 8H, 2 C*H*$_3$, *H*-9,14); 2.80-4.00 (*m*, 6H, *H*-2,3,6,7,8,13); 7.30-8.20 (*m*, 16H, *arom*.). EIMS: *m*/*z* = 690 for molecular ion peak and a base peak at *m*/*z* = 80. Anal. Calcd. % for $C_{37}H_{34}N_6O_8$ (690): C: 64.34; H: 4.92; N: 12.17. Founds: C: 64.43; H: 5.17; N: 12.25.

11d: 1-(2,4-Dinitroanilino)-8-phenyl-4,11-bis(4-nitrophenyl)-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,10-dihydroxy-5,12-dione:
Brown powder. m.p.: 280^{o}C. Yield: 70.32%. IR: KBr, ν_{max} (cm^{-1}) 3450 for -OH hydroxyl, 3300 for -NH; 3032 for C-H arom.; 2900, 2850 for C-H aliph.; 1708 for C=O; 1596 for C=C arom.; 1506 for -NO_2; 1180 for C-N amide; 1401, 1388 for def., bend C-H aliph.; 1010 for C-O; 850 for C-H (2 adj. H, wag.), oop, def. arom. and 750, 698 for C-H (5 adj. H, wag.), oop, def. arom. ^{1}H NMR (C*D*Cl$_3$, 300 MHz) δ ppm = 2.00 (*m*, 3H, *H*-7, 2 O*H*); 2.70 (*m*, 2H, *H*-14 and N*H*); 3.00-4.30 (*m*, 7H, *H*-2,3,6,8,9,10,13) and 6.40-8.50 (*m*, 16H, *arom*.). Anal. Calcd. % for $C_{35}H_{28}N_8O_{12}$ (752): C: 55.85; H: 3.72; N: 14.89. Founds: C: 56.33; H: 3.20; N: 13.73.

11e: 1-(2,4-Dinitroanilino)-8-(phenyl)-4,11-bis(4-bromophenyl)-1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,10-dihydroxy-5,12-dione:
Brown powder. m.p.: 270ºC. Yield: 79.66 %. IR: KBr, ν_{max} (cm^{-1}) 3500 for -OH hydroxyl, 3346 for -NH; 3020 for C-H arom.; 2850, 2804 for C-H aliph.; 1686 for C=O; 1580, 1528 for C=C arom.; 1490 for -NO_2; 1194 for C-N amide; 1396, 1344 for def., bend C-H aliph.; 1070, 1010 for C-O; 826 for C-H (2 adj. H, wag.), oop, def. arom. and 756, 702 for C-H (5 adj. H, wag.), oop, def. arom. Anal. Calcd. % for $C_{35}H_{28}N_6O_8Br_2$ (820): C: 51.21; H: 3.41; N: 10.24. Founds: C: 51.43; H: 2.95; N: 10.58.

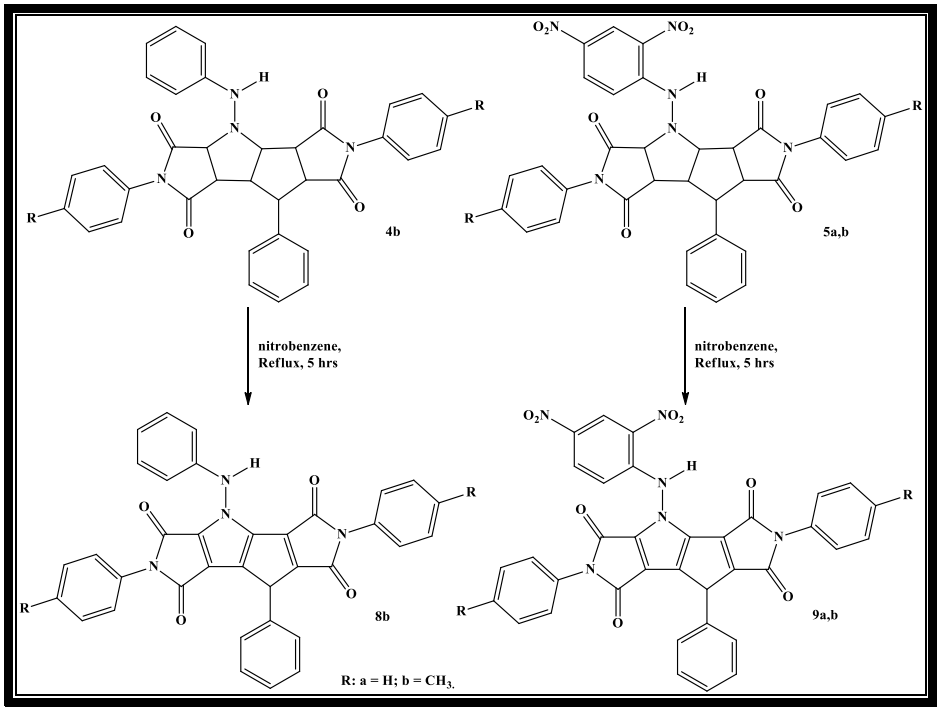
2.3 Antimicrobial activity
The filter paper disc method was performed in Nutrient agar for bacteria and Dox agar for fungi [13]. These agar media were incubated with bacteria or fungi respectively. The filter paper disc 6 mm diameter saturated with a solution of each compound 10 mg/mL of DMSO-d_6 were incubated in agar media. The incubation time was 48 hrs at 37ºC for bacteria and 28ºC for fungi. Discs saturated with compounds free DMSO-d_6 were used as a control, while Ciprofloxacin and Griseofulvin were used as a reference for evaluation of antibacterial [14] and antifungal activities [15]. 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 gram –ve and *Staphylococcus aureus* gram +ve and two species of fungi *Aspergillus niger* and *Aspergillus terreus*.

3. Results & Discussion
3.1 Chemistry analysis
The initial starting from cinnamalphenylhydrazone 1 and cinnamal-2,4-dinitrophenyl-hydrazone 2 for the cycloaddition reactions were prepared according to the literature procedure [16]. The *N*-Aryl Maleimide 3a-e were chosen as the dipolarophiles for the same purpose and were prepared according to the literature procedure [17]. The reaction mixture of hydrazone 1 or 2 with each of *N*-Aryl Maleimide 3a-e were fused in an oil bath at different times and temperatures give good solid yields of cycloadduct 8-phenyl-4,11-bis(aryl)-1,4,11-triazatetracyclo[6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,5,10,12-tetraone 4a-e or 5a-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.
This reaction is envisaged as a tandem [3+2] cycloaddition (1,3-dipolar) reaction. In the first step, one of the two hydrazone moieties forms a monocyclic intermediate with an azomethine imine (azomethine imide) function, which, in turn, trapped *in situ* with the second mole of *N*-Aryl Maleimide by a subsequent [3+2]-cycloaddition reaction to afford the bicycloadducts. This reaction subsequent is known as a criss-cross cycloaddition [3, 4]. In last our investigation, we tried to interest in the effect of substituents on the *N*-aryl group of the maleimides 3a-e on the *exo-endo* selectivity of the cycloaddition reaction with hydrazones 1 or 2, respectively [18].
In the 1,3-dipolar reaction of nitrones with *N*-Aryl Maleimide, Coskun *et al.* [19] showed that, the *exo-endo* ratio increases when the electron-donating group are present on the *N*-aryl as nitrones and decreases when the groups are electron withdrawing. So, to elucidate the effect of substituents on the 3a-e. Besides, the steric effects of contributing to the *exo-endo* ratio, secondary orbital interactions between the rings at 1 and 4 positions of hydrazone, and the carbonyls at the pyrrolidine ring maleimide moiety are probably. Also, responsible for the stabilization of the transition state leading to endo adduct. The *endo* stereochemistry is good accordance with the results observed by Coskun *et al.* [19]. The first possible pathway is mentioned below as criss-cross cycloaddition as Ibrahim *et al.* [20]. Thus, the criss-cross cycloaddition reaction of hydrazones 1 and 2 with 3a-e corresponding 1:2 ratio gave adducts 4a-e and 5a-e, respectively, Schemes 1 and 2.
In this work, both structures of criss-cross cycloaddition products 4a-e and 5a-e were confirmed using IR spectra, ^{1}H NMR spectra, Mass spectra and their elemental analyses are listed in the experimental part. The IR spectra for compounds 4a-e and 5a-e exhibited stretch absorption bands corresponding to N-H at 3400-3200 cm^{-1}; aromatic C-H at 3085-3030 cm^{-1}; aliph. C-H at 2950-2900 cm^{-1}; C=O at 1725-1700 cm^{-1}; arom. C=C at 1620-1520 cm^{-1} and N-C in *N*-Aryl Maleimide moiety at 1190-1170 cm^{-1}. Another good evidence can be seen also in the fingerprints region of same IR spectra. A signal bands for N-H group (s, oop bend, wag.) at 910 to 660 cm^{-1}. The C-H in *p*-aromatic substituted, oop bend (2 adj. H, wag.) at 850, 800 cm^{-1} and two bands for C-H in *mono* aromatic substituted, oop bend at 750, 690 cm^{-1}. The lack of any bands, due to aliphatic C=C and C=N, in their typical ranges 1620 and 1580 cm^{-1} indicates the formation of adducts and the absence of any initial compounds, *N*-Aryl Maleimide and hydrazones. These data are in good agreement with the literatures [21, 22, 23].
The ^{1}H NMR for 4b and 5b typical example for this series where showed a singlet for 4b at δ = 2.23 (*m*, 1H, *H*-7); 2.27-2.49 (*m*, 6H, 2CH_3); 2.60-3.50 (*m*, 5H, *H*-6,8,9,13,14); 5.00 (*d*, 1H, *H*-2); 7.03-7.90 (*m*, 19H, *arom.* and N*H* protons) ppm, while 5b showed a singlet at δ = 2.13 (*q*, 1H, *H*-7); 2,34 (*s*, 6H, 2CH_3); 3.25-3.75 (*m*, 5H, *H*-6,8,9,13,14); 5.00 (*d*, 1H, *H*-2); 7.80-8.20 (*m*, 17H, *arom*. and -N*H* protons) ppm. The some synthetic of 4a-e and 5a-e were directed towered the synthesis of other compounds 6a-c,e, 7a-e, 8b, 9a,b; 10a-e and 11a,b,d,e, Schemes 3, 4 and 5 [11, 24].
Hydrolysis of 4a-c,e or 5a-e in basic media and neutralized with aqueous acid to give 6a-c,e or 7a-e, respectively, Scheme 3. The structural of these compounds were confirmed by elemental analysis and spectral data. The IR spectra showed a strong absorption broad band at 3400-2500 cm^{-1} for carboxyl groups is well evidence for proceeding. The ^{1}H NMR spectra for compounds 6b and 7a as a typical example for this series showed the appearance of signals for aliphatic, aromatic amide and carboxylic acids protons. While the mass spectrum of 6b as a typical example of this series showed a molecular ion pack at *m*/*z* = 632 and a base peak at *m*/*z* = 58. Also, compound 7a showed the molecular ion peak at *m*/*z* = 698 and a base peak at *m*/*z* = 123.

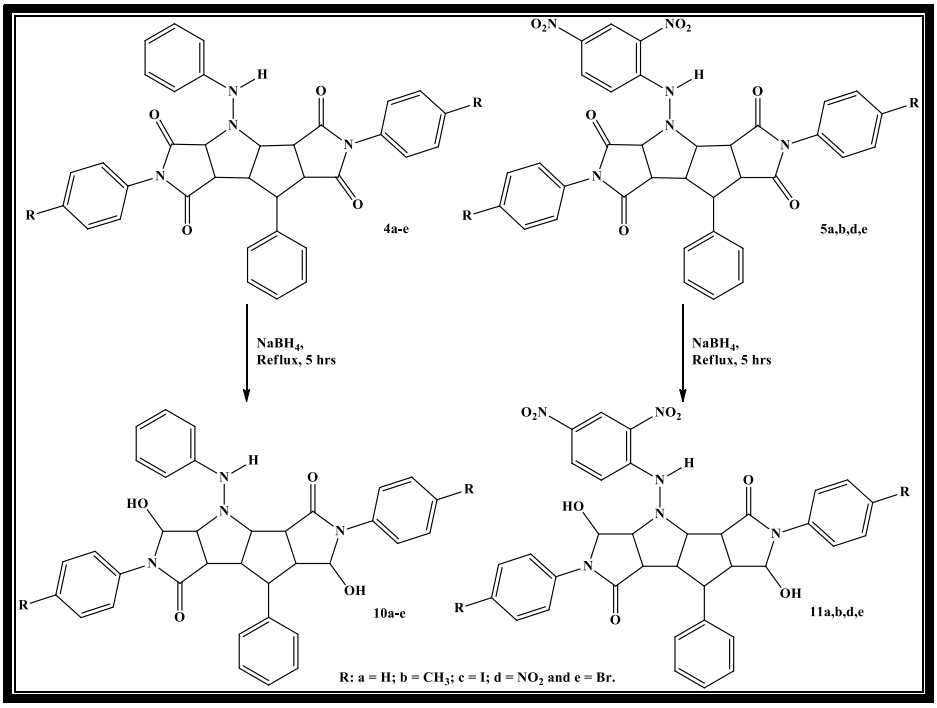


Scheme 3: The hydrolysis of 4a-c,e and 5a-e by 20% NaOH to produce 5-phenyl-2,6-dicarboxy-3,7-bis(*N*-arylcarbonamide)-1-azadicyclo[3,3,0] octane 6a-c,e and 7a-e.

Dehydrogenation of 4b or 5a,b were obtained through reactions of these compounds with nitrobenzene under reflexes conditions to give compounds 8b and 9a,b, respectively, Scheme 4. The characteristic frequencies of the C=C double bond were observed at the typical range 1680 to1620 cm^{-1}. While the reductions of each of 4a-e or 5a,b,d,e by $NaBH_4$ afforded the corresponding hydroxyl compounds 10a-e or 11a,b,d,e, respectively, Scheme 5. The IR spectra of these compounds showed absorption bands at 3450 or 3400 cm^{-1} for hydroxyl groups and strong absorption band at the typical range 1725 to 1700 cm^{-1} for carbonyl groups. The ^1H NMR for 11b typical example for this series where showed a singlet at δ = 1.12 (*s*, O*H*); 1.50 (*s*, N*H*); 2.20 (*m*, 2H, *H*-10 and O*H*); 2.34 (*m*, 8H, 2 CH_3, *H*-9,14); 2.80-4.00 (*m*, 6H, *H*-2,3,6,7,8,13); 7.30-8.20 (*m*, 16H, *arom*) ppm. Also, the mass spectrum for 11b showed a molecular ion peak appeared at *m*/*z* = 690 and abase peak at 80.



Scheme 4: The dehydrogenation reaction of 4b and 5a,b by nitrobenzene to produce 8-phenyl-1,4,11-triazatetracyclo[6,6,0,^{2,6}0,^{9,13}0] tetradeca-2,7,9-triene-3,5,10,12-tetraone 8b and 9a,b.



Scheme 5: The reduction reaction of 4a-e and 5a,b,d,e by $NaBH_4$ to produce 8-phenyl-1,4,11-triazatetracyclo[6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,10-dihydroxy-5,12-dione 10a-e and 11a,b,d,e.

3.2 Estimation of antimicrobial activity

Some of the synthesized compounds were using screened *in vitro* for their antimicrobial activities. As our previous studies, most of the bacterial pathogens tested were resistant to synthesized compounds [11]. However, compound 4b is exhibit slightly effect against *Aspergillus niger*, while compound 5d show slightly effects against *Pseudomonas aeruginosa* and *Staphylococcus aureus*.

The main core structure of both compounds 4b and 5d are shown the same, except dinitro main functional groups in 2,4-dinitrophenylhydrazone with pink eclipsed and dinitro functional groups in *para* position of phenyl rings with blue circle of 5d, while 4b has dimethyl functional groups in *para* position of phenyl rings with blue circle too, Fig. 1. On the other hand, Al–Douh *et al.* [25] have been studied some diazo dyes contain nitro functional groups in deferent positions, which they possess moderately active especially one of diazo dye have two nitro functional groups in *ortho* positions against *Proteus mirabilis*. The reasons for that resistant may to: depolarize cell membrane, inhibit cell wall synthesis, inhibit nucleic acid synthesis, inhibit protein synthesis or inhibit metabolic pathways. [26].

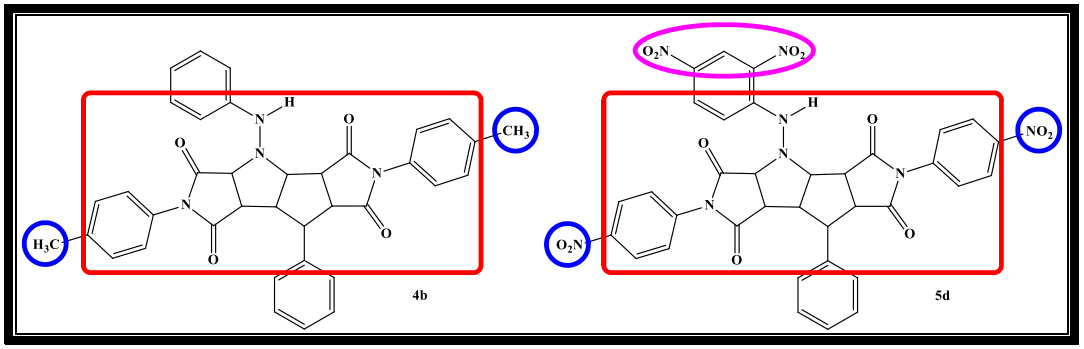


Fig 1: The structures of **4b** and **5d** which have moderate activity against *Aspergillus niger*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*, respectively.

We believe that methyl functional groups in *para* positions of 4b increase an effecting against *Aspergillus niger* comparing with *Aspergillus terreus*, while an effecting of that compounds against *Pseudomonas aeruginosa* and *Staphylococcus aureus* is inactive and slightly active, especially in compound 5d, which has four nitro functional groups in its structure, Fig. 1 and Table 1.

Table 1: The antimicrobial activity of some representative compounds (diameter of inhibition zone).

Microbes	Test Compounds (mm)														
	4b	**4c**	**4d**	**4e**	**5a**	**5b**	**5c**	**5d**	**7a**	**7e**	**9a**	**10a**	**11b**	**Cf**	**Gf**
Bacteria															
Pseudomonas aeruginosa	–	–	–	–	–	–	–	+	–	–	–	–	–	+++	
Staphylococcus aureus	–	–	–	–	–	–	–	+	–	–	–	–	–	+++	
Fungi															
Aspergillus niger	+	–	–	–	–	–	–	–	–	–	–	–	–		+++
Aspergillus terreus	–	–	–	–	–	–	–	–	–	–	–	–	–		+++

Key to symbols: Disc diameter = 6 mm, Highly active = +++ (inhibition zone > 19 mm), Moderately active = ++ (inhibition zone 13-19 mm), Slightly active = + (inhibition zone 7-13 mm), Inactive = – (inhibition zone <7 mm).

4. Conclusion

The methods of thermal intermolecular criss-cross cycloaddition reactions of cinnamal aryl hydrazones 1 and 2 with *N*-Aryl Maleimide 3a-e were successfully applied. This, new fused substituted cycloadducts 1,4,11-triazatetracyclo [6,6,0,^{2,6}0,^{9,13}0] tetradecane-3,5,10,12-tetraone were prepared in good yield. In these reactions, no catalyst was required for the generation of the azomethine imines, and this takes place only by fusing the reaction mixture in solvent-free phase. Criss-cross cycloadducts and their trans-formed products were characterized by IR, ^{1}H NMR spectroscopy, Mass spectra and by elemental analysis. Some of the obtained products were shown to display antibacterial and/or antifungal activities against some of the bacterial and fungal strains.

5. Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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