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MICROWAVE SYNTHESIS AND ANTIMICROBIAL INFLUENCE OF SOME NOVEL 2,2'-(N-PHENYLPIPERIDINE-2,6-DIYLIDENE)DIMALONONITRILE COMPOUNDS DERIVED FROM N-PHENYL GLUTARIMIDES

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Abstract:
The six membered cyclic imide derivatives were synthesized by reacting glutaric anhydride with different substitutedaromatic amines underwent with acetyl chloride developed the substituted phenylpiperidine-2, 6-diones or phenyl glutarimides. Thereafter the novel malononitrilederivatives were synthesized by the treatment of the different substituted N-phenylpiperidine-2, 6-dione with dicyanomethane to get 2, 2'-(N-phenylpiperidine-2,6-diylidene)dimalononitrile using microwave solvent-free method. All the afforded synthones were characterized screened and examined their antimicrobial activities.

Keywords: Cyclic Imides, Dimalononitrile Derivatives, Antimicrobial Activities

Introduction:

Malononitrile plays a very important role in the development of heterocyclic synthesis. The malononitrile[i]derivatives were synthesized by Knoevenagel condensation reaction by using active methylene groups with the substituted ketone, aldehydes[ii], hetero-aromatic aldehydes or ketones and indole derivatives. These are prepared by several methods in orderto aqueous media[iii]. Chemo-selective heterogeneous catalyst by solvent free method[iv], eco-friendly one pot aqueous synthesis[v], catalytic agent of NaOH or KOH[vi], ZnOpromoter[vii] and silica supported ammonium acetate[viii], ionic liquefiedmedia[ix] and tamarind extractcatalyst[x]. The L-proline catalyzed malononitrile derivatives revealed the significant biological activities[xi], riot-control moiety of chloro-benzylidenemalononitrile[xii], antimicrobial moiety of chromene[xiii], arylalkenemalononitrile[xiv], anti-tubercular inhibitory activity ofmethoxynicotinonitrileanalogs[xv]and urease inhibitory activities of pyrano-pyrimidine dionederivatives[xvi]. As well as these malononitrile derivatives correspondingly possesses a beneficial antiproliferative[xvii], anti-inflammatory [xviii], anticancer [xix], anti-oxidant and antitumor [xx] activities so on.Knoevenagel condensation is the standard reaction between carbon-carbon bonds formation occur in cyclic ketones, aldehydes by using active methylene

malononitrile group in the solvent free or catalytic or organic solvent synthesis. Due to higher acidity of active methylene groups will converts to nitrile derivatives. Severalmalononitrile derivatives for example cyano-methyl group [xxi], cyano-acetanilides[xxii], benzo-pyranones[xxiii], cyanohexylidenemalononitrile[xxiv], benzopyranes[xxv], carbo-nitriles [xxvi] from glycine [xxvii] are definitely synthesized with active methylene group by Knoevenagel condensation [xxviii] in conventional, grindstone [xxix] method, solvent less single or multicomponent systems and microwave assisted [xxx] neat or solvent free eco-friendly methods.

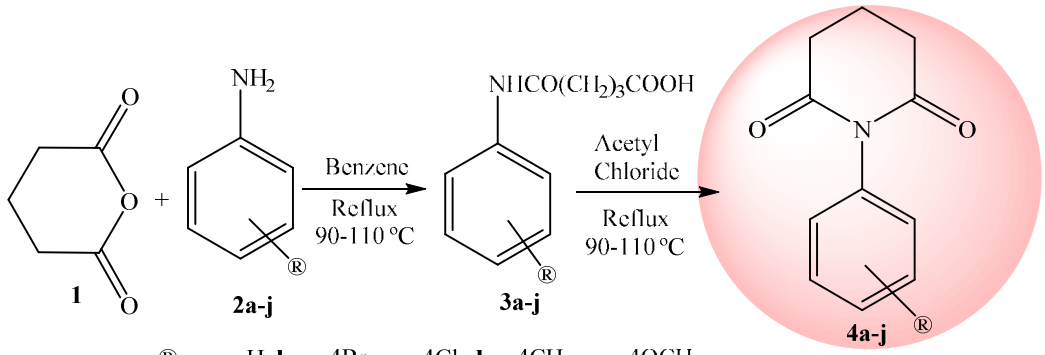
Experimental:

Materials and Reagents:

Melting points of all the synthesized compounds were recorded in an open glass capillaries and were uncorrected. IR spectra in (KBr pallets) were notedby Shimadzu FTIR-8400S and ATR Brucker alpha FT-IR spectrophotometer. ^{1}HNMR spectra were recorded on 400 MHz and 500.13 MHz by Brucker spectrophotometer. The reaction was monitored by TLC which was accomplished by using pre-coated silica gel aluminium plates with the mixture of diethyl ether and ethyl acetate 7:3 proportion or benzene. Commercially purchased glutaric anhydride, substituted anilines, acetyl chloride, benzene, dicyanomethane, neutral alumina (Al_2O_3) and ethanol were used for the preparation.

General Procedure for the Synthesis of N-phenylpiperidine-2, 6-dione or N-Phenyl Glutarimides (4a-j):

To accomplish the work glutaric anhydride (0.1 moles) benzene was added and heated under reflux with constant stirring for 15 to 20 min till the solution becomes clear. Into this solution the primary aromatic amines (0.2 moles) in 5 ml benzene was slowly poured with constant stirring for 15- 20 min till the solution becomes homogenized. On the vaporization of benzene amorphous powder of 4-(N-phenyl-carbamoyl) butanoic acid was obtained and their physical data shown in the table-1. Further the mixture of 4-(N-phenyl-carbamoyl) butanoic acid and acetyl chloride (0.9 moles) was refluxed for 15-20 min by thoroughly evolution of HCl fumes. The reaction mixture was cooled at room temperature the solid product was obtained and recrystallized by ethanol as shown in the **Scheme-I**.



® , **a** = -H, **b** = -4Br, **c** = -4Cl, **d** = -4CH_3, **e** = -4OCH_3,
f = -4F, **g** = -4NO_2, **h** = -phenyl, **i** = -3Cl,-4F, **j** = -2,4,5Cl

Scheme -I: Synthesis of N-phenylpiperidine-2, 6-dione

Table-I: Physical Characteristics of 4-(N-phenyl-carbamoyl) butanoic acid (3a-j):

Compd Code	Molecular Formula	M. Wt.	Melting Point (ºC)	Colour
3a	$C_{11}H_{13}NO_3$	207.23	110-112 ºC	White Powder
3b	$C_{11}H_{12}BrNO_3$	286.12	138-140 ºC	Whitish Brown Powder
3c	$C_{11}H_{12}ClNO_3$	241.67	108-110 ºC	Brown Powder
3d	$C_{12}H_{15}NO_3$	221.25	147-149 ºC	Cream Coloured Powder
3e	$C_{12}H_{15}NO_4$	237.25	131-133 ºC	Brownish White Powder
3f	$C_{11}H_{12}FNO_3$	225.22	111-113ºC	Brownish Gray Powder
3g	$C_{11}H_{12}N_2O_5$	252.22	121-123 ºC	Greenish Gray Powder
3h	$C_{15}H_{15}NO_3$	257.28	142-144 ºC	Brown Powder
3i	$C_{11}H_{11}ClFNO_3$	259.66	110-112 ºC	Wheat Coloured Powder
3j	$C_{11}H_{10}Cl_3NO_3$	310.56	127-129 ºC	White Powder

1-phenylpiperidine-2, 6-dione (4a):M. F.: $C_{11}H_{11}NO_2$, White Crystals, M. W.: 189.21, Yield: 77.92%, M. P. (ºC): 120-122 ºC, C, H, N Anal:C, 69.89; H, 5.46; N, 7.49, FTIR (ATR):>C=O (2-Peaks): 1694 cm^{-1} and 1770 cm^{-1}, cyclic CH_2-CH_2: 2971 cm^{-1}, cyclic imines 1314 cm^{-1}, aromatic ring (3-Peaks): 1499 cm^{-1}, 1535 cm^{-1} and 1598 cm^{-1}

1-(4-bromophenyl) piperidine-2, 6-dione (4b):M. F.: $C_{11}H_{10}BrNO_2$, Whitish Brown Crystals, M. W.: 268.11 Yield: 82.94%, M. P. (ºC): 144-146 ºC, C, H, N Anal:C, 49.55; H, 3.96; N, 5.36, FTIR (ATR): >C=O (2-Peaks): 1695 cm^{-1} and 1719 cm^{-1}, cyclic CH_2-CH_2: 2992 cm^{-1}, cyclic imines 1301 cm^{-1}, aromatic ring (3-Peaks): 1490 cm^{-1}, 1526 cm^{-1} and 1589 cm^{-1}, Ar-Br: 1070 cm^{-1}

1-(4-chlorophenyl) piperidine-2, 6-dione (4c):M. F.: $C_{11}H_{10}ClNO_2$, Faded Lavender Solid, M. W.: 223.66 Yield: 86.70%, M. P. (ºC): 120-122 ºC, C, H, N Anal:C, 59.25; H, 4.47; N, 6.37, FTIR (ATR): >C=O (2-Peaks): 1726 cm^{-1}, 1782 cm^{-1}, cyclic CH_2-CH_2: 2979 cm^{-1}, cyclic imines 1300 cm^{-1}, aromatic ring (3-Peaks): 1495 cm^{-1}, 1527 cm^{-1} and 1591 cm^{-1}, Ar-Cl: 1090 cm^{-1}

1-p-tolylpiperidine-2, 6-dione (4d):M. F.: $C_{12}H_{13}NO_2$, White Solid, M. W.: 203.24 Yield: 77.07%, M. P. (ºC): 179-181 ºC, C, H, N Anal:C, 71.20; H, 6.35; N, 6.86, FTIR (ATR): >C=O (2-Peaks): 1698 cm^{-1} and 1746 cm^{-1}, cyclic CH_2-CH_2: 2962 cm^{-1}, cyclic imines 1310 cm^{-1}, aromatic ring (3-Peaks): 1536 cm^{-1}, 1599 cm^{-1} and 1661 cm^{-1}

1-(4-methoxyphenyl) piperidine-2, 6-dione (4e):M. F.: $C_{12}H_{13}NO_3$, Brownish Lavender Solid, M. W.: 219.24 Yield: 76.66%, M. P. (ºC): 138-140 ºC, C, H, N Anal:C, 64.79; H, 5.84; N, 6.28, FTIR (ATR): >C=O (2-Peaks): 1697 cm^{-1}, 1718 cm^{-1}, cyclic CH_2-CH_2: 2954 cm^{-1}, cyclic imines 1302 cm^{-1}, aromatic ring (3-Peaks): 1515 cm^{-1}, 1536 cm^{-1} and 1600 cm^{-1}, Ar-OCH_3: 1272 cm^{-1}

1-(4-fluorophenyl) piperidine-2, 6-dione (4f):M. F.: $C_{11}H_{10}FNO_2$, Yellowish Crystals, M. W.: 207.2 Yield: 76.35%, M. P. (ºC):119-121 ºC, C, H, N Anal.:C, 63.56; H, 4.74; N, 6.53, FTIR (ATR): >C=O (2-Peaks): 1696 cm^{-1} and 1722 cm^{-1}, cyclic CH_2-CH_2: 2961 cm^{-1}, cyclic imines 1305 cm^{-1}, aromatic ring (3-Peaks): 1519 cm^{-1}, 1613 cm^{-1} and 1658 cm^{-1}, Ar-F: 1186 cm^{-1}, ^{1}H NMR-(300 MHz; $CDCl_3$; δ ppm): 7.55-7.06 (d, 4H, Ar-H), 1.68 (m, 2H, –CH_2-CH_2-CH_2–), 2.15 (t, 4H, imide)

1-(4-nitrophenyl) piperidine-2, 6-dione (4g):M. F.: $C_{11}H_{10}N_2O_4$, Yellow Solid, M. W.: 234.21, Yield: 84.01%, M. P. (ºC):168-170 ºC, C, H, N Anal:C, 56.35; H, 4.10; N, 11.79, FTIR (ATR): >C=O (2-Peaks): 1710 cm^{-1} and 1750 cm^{-1}, cyclic CH_2-CH_2: 2960 cm^{-1}, cyclic imines 1300 cm^{-1}, aromatic ring (3-Peaks): 1520 cm^{-1}, 1590 cm^{-1} and 1600 cm^{-1}, Ar-NO_2: 1500 cm^{-1}

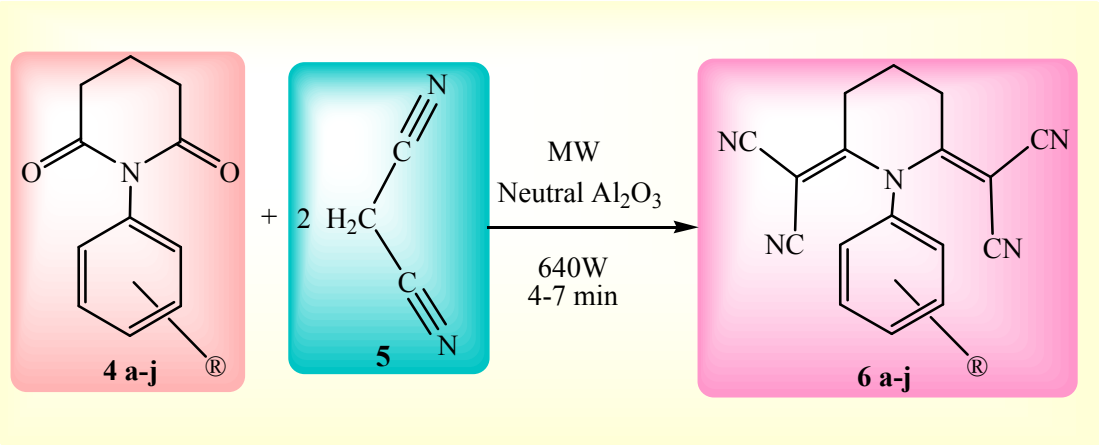
1-(naphthalen-4-yl) piperidine-2, 6-dione (4h):M. F.: $C_{15}H_{13}NO_2$, Dark Lavender Solid, M. W.: 239.27, Yield: 83.61%, M. P. (ºC):153-155 ºC, C, H, N Anal:C, 74.80; H, 5.12; N, 5.78, FTIR (ATR): >C=O (2-Peaks): 1651 cm^{-1} and 1703 cm^{-1}, cyclic CH_2-CH_2: 2958 cm^{-1}, cyclic imines 1316 cm^{-1}, aromatic ring (5-Peaks): 1405 cm^{-1}, 1443 cm^{-1}, 1500 cm^{-1} , 1529 cm^{-1} and 1596 cm^{-1}, ^{1}H NMR-(300 MHz; C$\underline{D}$$Cl_3$; δ ppm): 7.57-7.30 (m, 6H, Ar-H), 1.62 (m, 2H, –CH_2-CH_2-CH_2–), 2.22 (t, 4H, imide)

1-(3-chloro-4-fluorophenyl) piperidine-2, 6-dione (4i):M. F.: $C_{11}H_9ClFNO_2$, Whitish Solid, M. W.:241.65, Yield: 91.30%, M. P. (ºC):104-106 ºC, C, H, N Anal:C, 54.34; H, 3.64; N, 5.86, FTIR (ATR): >C=O (2-Peaks): 1638 cm^{-1} and 1700 cm^{-1}, cyclic CH_2-CH_2: 2951 cm^{-1}, cyclic imines 1312 cm^{-1}, aromatic ring (3-Peaks): 1497 cm^{-1}, 1546 cm^{-1} and 1600 cm^{-1}, Ar-4F: 1191 cm^{-1}, Ar-3Cl: 1055 cm^{-1}, ^{1}H NMR-(500.13 MHz; D$\underline{M}$SO-d^6; δ ppm): 7.92-7.34 (m, 3H, Ar-H), 1.80 (m, 2H, –CH_2-CH_2-CH_2–), 2.28 (t, 4H, imide), ^{13}C NMR-(125.77 MHz; D$\underline{M}$SO-d^6; δ ppm): 20.72, 33.35, 35.75, 39.95, 117.19, 119.70, 120.82, 136.93, 152.35, 154.29, 171.42 and 174.56

1-(2,4,5-trichlorophenyl) piperidine-2,6-dione (4j):M. F.: $C_{11}H_8Cl_3NO_2$, White Solid, M. W.: 292.55, Yield: 85.73%, M. P. (ºC):138-140 ºC, C, H, N Anal:C, 45.33; H, 2.62; N, 4.67, FTIR (ATR): >C=O (2-Peaks): 1665 cm^{-1} and 1697 cm^{-1}, cyclic CH_2-CH_2: 2968 cm^{-1}, cyclic imines 1306 cm^{-1}, aromatic ring (3-Peaks): 1457 cm^{-1}, 1513 cm^{-1} and 1570 cm^{-1}, Ar-2,4,5Cl: 1076 cm^{-1}, ^{1}H NMR (500.13 MHz, C$\underline{D}$$Cl_3$, δ ppm): 7.49-7.28 (d, 2H, Ar-H), 2.10 (m, 2H, –CH_2-CH_2-CH_2–), 2.27 (t, 4H, imide)

General Procedure for the Synthesis of Malononitrile Derivatives from N-Phenyl Glutarimides:

To achieve the target molecule 2,2'-(N-phenylpiperidine-2,6-diylidene)dimalononitrile**(6a-j)** derivatives were synthesized by the mixture of 4mmole of afforded N-phenyl glutarimides**(4a-j)** and 8mmole of dicyanomethane in 2 gm of neutral Al_2O_3 under the microwave assisted solvent free conditions on 640W power for 4-7 minutes. The afforded brownish and coffee coloured compounds were recovered and recrystallized by ethanol **Scheme – II**.



® , **a** = -H, **b** = -4Br, **c** = -4Cl, **d** = -4CH_3, **e** = -4OCH_3,
f = -4F, **g** = -4NO_2, **h** = -phenyl, **i** = -3Cl,-4F, **j** = -2,4,5Cl

Scheme -II: 2,2'-(N-phenylpiperidine-2,6-diylidene)dimalononitrile (6a-j)

2,2'-(1-phenylpiperidine-2,6-diylidene)dimalononitrile(6a):M.F.: $C_{17}H_{11}N_5$, Needle Shaped Coffee Coloured Crystals, M. W.: 285.3, Yield: 61.40%, M. P. (ºC): 97-99 ºC, C, H,NAnal:C, 71.84; H, 4.42; N, 24.78, FTIR (KBr): -C≡N (1-Peak): 2338 cm^{-1}, cyclic CH_2-CH_2: 2962 cm^{-1}, cyclic imines 1317 cm^{-1}, aromatic ring (3-Peaks): 1501 cm^{-1}, 1541 cm^{-1} and 1602 cm^{-1}, ^{1}H NMR-(500.13 MHz; DMSO-d^6; δ ppm): 1.81 (m, 2H, imide), 2.28 (m, 4H, imide), 7.58-7.02 (m, 5H, Ar-H)

2,2'-(1-(4-bromophenyl)piperidine-2,6-diylidene)dimalononitrile(6b):M.F.: $C_{17}H_{10}BrN_5$, Whitish Brown Flakes, M. W.: 364.2, Yield: 35.71%, M. P. (ºC): 133-135 ºC, C, H, NAnal:C, 56.46; H, 2.85; N, 19.48, FTIR (KBr): -C≡N (1-Peak): 2338 cm^{-1}, cyclic CH_2-CH_2: 2886 cm^{-1}, cyclic imines 1299 cm^{-1}, aromatic ring (3-Peaks): 1489 cm^{-1}, 525 cm^{-1} and 1589 cm^{-1}, Ar-Br: 1070 cm^{-1}

2,2'-(1-(4-chlorophenyl)piperidine-2,6-diylidene)dimalononitrile(6c):M.F.: $C_{17}H_{10}ClN_5$, Whitish GranularSolid, M. W.: 319.75, Yield: 74.60%, M. P. (ºC): 80-82 ºC, C, H, N Anal: C, 64.36; H, 3.68; N, 22.27, FTIR (KBr): -C≡N (1-Peak): 2291 cm^{-1}, cyclic CH_2-CH_2: 2883 cm^{-1}, cyclic imines 1300 cm^{-1}, aromatic ring (3-Peaks): 1491 cm^{-1}, 1527 cm^{-1} and 1590 cm^{-1}, Ar-Cl: 1093 cm^{-1}

2,2'-(1-(p-tolyl)piperidine-2,6-diylidene)dimalononitrile(6d):M.F.: $C_{18}H_{13}N_5$, Brownish Pink Solid, M. W.: 299.33, Yield: 48.49%, M. P. (ºC): 164-166 ºC, C, H, NAnal:C, 72.43; H, 4.61; N, 23.73, FTIR (KBr): -C≡N (1-Peak): 2338 cm^{-1}, cyclic CH_2-CH_2: 2969 cm^{-1}, cyclic imines 1321 cm^{-1}, aromatic ring (3-Peaks): 1514 cm^{-1}, 1536 cm^{-1} and 1604 cm^{-1}

2,2'-(1-(4-methoxyphenyl)piperidine-2,6-diylidene)dimalononitrile (6e):M. F.: $C_{18}H_{13}N_5O$, Brown FluffySolid, M. W.: 315.33, Yield: 40.95%, M. P. (ºC): 107-109 ºC, C, H, NAnal:C, 68.82; H, 4.48; N, 22.75, FTIR (KBr): -C≡N (1-Peak): 2338 cm^{-1}, cyclic CH_2-CH_2: 2962 cm^{-1}, cyclic imines 1298 cm^{-1}, aromatic ring (3-Peaks): 1514 cm^{-1}, 1541 cm^{-1} and 1604 cm^{-1}, Ar-OCH_3: 1242 cm^{-1}

2,2'-(1-(4-fluorophenyl)piperidine-2,6-diylidene)dimalononitrile(6f):M.F.: $C_{17}H_{10}FN_5$, BrownishGranular Crystals, M. W.: 303.29, Yield: 67.65%, M. P. (ºC): 119-121 ºC, C, H, N Anal: C, 67.84; H, 3.72; N, 23.27, FTIR (KBr): -C≡N (1-Peak): 2337 cm^{-1}, cyclic CH_2-CH_2: 2962 cm^{-1}, cyclic imines 1310 cm^{-1}, aromatic ring (3-Peaks): 1458 cm^{-1}, 1515 cm^{-1} and 1613 cm^{-1}, Ar-F: 1181 cm^{-1}, ^{1}H NMR-(500.13 MHz; DMSO-d^6; δ ppm): 1.81 (m, 2H, imide), 2.28 (m, 4H, imide), 7.25-7.12 (dd, 2H, Ar-H), 7.59 (dd, 2H, Ar-H)

2,2'-(1-(4-nitrophenyl)piperidine-2,6-diylidene)dimalononitrile(6g):M.F.: $C_{17}H_{10}N_6O_2$, Coffee ColouredGranular Crystals, M. W.: 330.3, Yield: 28.78%, M. P. (ºC): 115-117 ºC, C, H, NAnal:C, 61.95; H, 3.16; N, 25.58, FTIR (KBr): -C≡N (1-Peak): 2221 cm^{-1}, cyclic CH_2-CH_2: 2976 cm^{-1}, cyclic imines 1345 cm^{-1}, aromatic ring (3-Peaks): 1553 cm^{-1}, 1611 cm^{-1} and 1682 cm^{-1}, Ar-NO_2: 1507 cm^{-1}, ^{1}H NMR-(500.13 MHz; DMSO-d_6; δ ppm): 1.83 (m, 2H, imide), 2.12 (m, 4H, imide), 7.49-7.47 (dd, 2H, Ar-H), 8.31-8.19 (dd, 2H, Ar-H), ^{13}C NMR-(125.77 MHz; DMSO-d^6; δ ppm): 16.90, 20.57, 24.66, 32.77, 39.80, 39.97, 40.15, 112.50, 118.99, 124.36, 125.39, 131.01 and 173.10

2,2'-(1-(naphthalen-1-yl)piperidine-2,6-diylidene)dimalononitrile(6h):M.F.: $C_{21}H_{13}N_5$, Whitish Ash, M. W.: 335.36, Yield: 28.05%, M. P. (ºC): 95-97 ºC, C, H, NAnal:C, 75.48; H, 4.21; N, 21.18, FTIR (KBr): -C≡N (1-Peak): 2213 cm^{-1}, cyclic CH_2-CH_2: 2960 cm^{-1}, cyclic imines 1359 cm^{-1}, aromatic ring (3-Peaks): 1460 cm^{-1}, 1507 cm^{-1}, 1536 cm^{-1}, 1597 cm^{-1} and 1681 cm^{-1}

2,2'-(1-(3-chloro-4-fluorophenyl)piperidine-2,6-diylidene)dimalononitrile(6i):M.F.: $C_{17}H_9ClFN_5$, Whitish Brown Solid, M. W.: 337.74, Yield: 54.89%, M. P. (ºC): 91-93 ºC, C, H, N Anal: C, 60.59; H, 2.87; N, 20.89, FTIR (KBr): -C≡N (1-Peak): 2213 cm^{-1}, cyclic CH_2-CH_2: 2954 cm^{-1}, cyclic imines 1317 cm^{-1}, aromatic ring (3-Peaks): 1548 cm^{-1}, 1608 cm^{-1} and 1644 cm^{-1}, Ar-F: 1250 cm^{-1}, Ar-Cl: 1062 cm^{-1}

***2,2'-(1-(2,4,5-trichlorophenyl)piperidine-2,6-diylidene)dimalononitrile(6j)*:**M.F.: $C_{17}H_8Cl_3N_5$, Whitish Granular Crystals, M. W.: 388.64, Yield: 38.65%, M. P. (ºC): 109-111 ºC, C, H, NAnal:C, 52.88; H, 2.24; N, 18.18, FTIR (KBr): -C≡N (1-Peak): 2216 cm^{-1}, cyclic CH_2-CH_2: 2883 cm^{-1}, cyclic imines 1306 cm^{-1}, aromatic ring (3-Peaks): 1517 cm^{-1}, 1571 cm^{-1} and 1672 cm^{-1}, Ar-2, 4,5Cl: 1077 cm^{-1}

Results and Discussion:

Chemistry:

The starting compounds N-phenyl-piperidine-2, 6-dione **4a-j** were prepared by the reaction of substituted anilines and glutaric anhydride using benzene and acetyl chloride. The series of 2,2'-(N-phenylpiperidine-2,6-diylidene)dimalononitrile**6a-j** were synthesized in affordable yields by the microwave irradiation of cyclic imides **4a-j** with dicyanomethane in presence of neutral alumina in solvent free condition. The structure of phenyl glutarimides and malononitriles was confirmed by IR, ^{1}HNMR, ^{13}CNMR and elemental analysis.

Antimicrobial activities (4a-j and 6a-j):

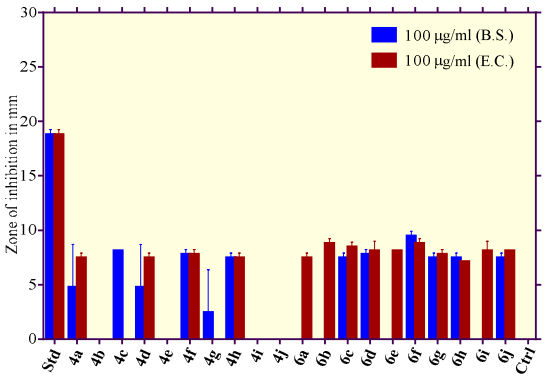
All the synthesized compounds **4a-j**and **6a-j**were evaluated *in-vitro* for antibacterial activity against bacterial strains gram positive *Bacillus subtilis*(MCMB-310)and gram negative *Escherichia coli*(MCMB-301)at the concentrations of 100µg/ml by bore plate method using DMF as solvent and nutrient agar was employed as culture media. After 48 hrs of incubation at 37ºC, the results were obtained in the form of clearing zone and were noted after the endof incubation period. Similarly the same compounds **4a-j**and **6a-j** were evaluated *in-vitro* for antifungal activity against fungal strains *Candida albicans*(NCIM-3471) and*Aspergillusniger*(NCIM- 545) at the concentration 100µg/ml per disc by paper disc diffusion method using DMSO as solvent. The yeast *Candida albicans*cultured using a malt extract, glucose yeast extract peptone agar medium (MGYP medium) and for fungi *Aspergillusniger*potato dextrose agar medium was used. After 3-7 days of incubation at 30ºC. The diameters of inhibition zones were measured and tabulated in the table–II. Ampicillin was used as a standard drug for antibacterial activities and Amphotericin-B used for antifungal activities.

Table-II: Antimicrobial activities of N-phenyl Glutarimides and Dimalononitriles

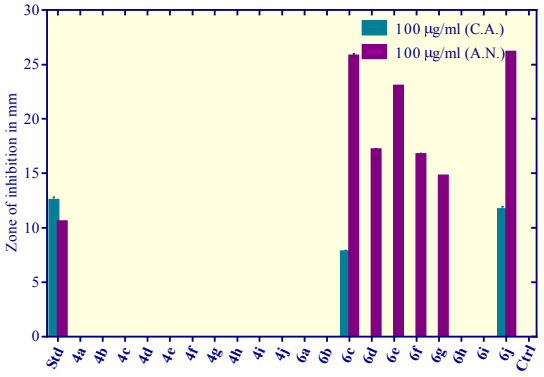
Compd Code	Zone diameter calculated in mm and tabulated by (Mean±S.D.)			
	Bacillus subtilis	***Escherichia coli***	***Candida albicans***	***Aspergillusniger***
	100 µg/ml	100 µg/ml	100 µg/ml	100 µg/ml
4a	4.66±4.04**	7.33±0.57**	--	--
4b	--	--	--	--
4c	8±0**	--	--	--
4d	4.66±4.04**	7.33±0.57**	--	-
4e	--	--	--	--
4f	7.66±0.57**	7.66±0.57**	--	--
4g	2.33±4.04**	-	--	--
4h	7.33±0.57**	7.33±0.57**	-	--
4i	--	--	--	--
4j	--	--	--	--
6a	--	7.33±0.57**	--	--
6b	--	8.66±0.57**	--	--
6c	7.33±0.57**	8.33±0.57**	7.68 ± 0.26**	25.68 ± 0.31**
6d	7.66±0.57**	8±1**	--	17.05 ± 0.19**
6e	--	8±0**	--	22.92 ± 0.11**
6f	9.33±0.57**	8.66±0.57**	--	16.61 ± 0.24**
6g	7..33±0.57**	7.66±0.57**	--	14.64 ± 0.12**
6h	7..33±0.57**	7±0**	--	--
6i	--	8±1**	--	--
6j	7.33±0.57**	8±0**	11.56 ± 0.37**	26.00 ± 0.12**
Ctrl	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0
Std	18.33±0.57	18.33±0.57	12.40 ± 0.43	10.45 ± 0.11
Keynote: *Zone of inhibition measured in mm (Mean±S.D.) (N=3) ('--' means no zone)*				

Statistical Analysis:

The completeresults of the synthesized compound **4a-j**and **6a-j** series were calculated by N=3 with mean plus standard deviationindicatedin the graph-1 and graph-2.The statistical tests were executed by using GraphPad prism-6 software. The statistical significance was measured by one way ANOVA followed byDunnett multiple comparisontest performed by standard drug against synthesized compounds. P value < 0.05 was considered as statistically significant assumedby *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 compared to standard groups.



Graph 1: Antibacterial activities of 4a-j and 6a-j (B. S. and E.C.) Mean±SD



Graph 2: Antifungal activities of 4a-j and 6a-j (C.A. and A.N.) Mean±SD

Conclusion:

Thecomprehensiveecofriendly microwave centered green methodof synthesis of themalononitrile derivatives **6a-j** has been accumulated in the form of good yields.Thesesynthones were found significantlyactive against gram positive *Bacillus subtilis* and gram negative *Escherichia coli*bacterial strains. In the same way theyshowedthe prominent antifungal activity against*Candida albicans*and*Aspergillusniger* fungal strains. These synthesized compoundsmightbeutilized for the fabrication of various heterocyclic systems.

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