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Synthetic method and characterization of novel phthalamide derivatives

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ABSTRACT

The aim of present scheme is to synthesize of new phthalamide heterocycles and elucidates their biological activity. For the synthesis, phthalamide molecule was treated with various reagents as per the requirement of reaction and every time it result in to the formation of novel derivative of phthalamide. Derivatives obtained were bromo, benzimidazol, isothiocyanate, acetyl, benzothiazol, isothiocyanate and diazepin. Obtained derivatives further studied for their characterization using spectral techniques like IR, NMR and elemental analysis which established the structure of derivative. Derivatives tested for their antibacterial activity against gram positive and gram negative bacterial strains like E. coli and S. aureus.

Keywords: 1*H*-isoindole-1,3(2*H*)dione, benzimidazol, benzothiazol, isothiocyanate, diazepin

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INTRODUCTION

Heterocyclic molecules are fundamental building blocks of biological systems.Heterocycles have enormous potential as the most promising molecules as lead structures for the design of new drugs. In short, heterocyclic chemistry is the branch of chemistry dealing with synthesis, properties and applications of heterocycles. About one half of over six million compounds recorded in Chemical Abstracts are heterocyclic.Phthalimides are one such group of compounds that can be described as the imides of phthalic acids. Certain phthalimides are used in the agrochemical industry. As they display a wide range of properties they can be used as herbicides, insecticides and fungicides *e.g.* Diamate, Imidan and Folpet. Phthalimide derivatives are also used as anesthetics,[1] DNA cleaving agents,[2]tumericidals,[3]opticalbrighteners[4]and as dyes[5].Looking after this biological range of phthalamide,we planned the synthetic route where we can incorporate various heterocycles like benzimidazol, benzothiazol, isothiocyanate and diazepin over phthalamide and screening of these molecules for antimicrobial activity.

MATERIALS AND METHODS

All commercial reagents and solvents were procured from S.D. Fine. The reactions were monitored by TLC using 0.25 mm E-Merck silica gel plates, which were visualized in Iodine Chamber and if needed in UV light. Melting points were taken in open capillaries and are uncorrected. ^{1}H spectra in DMSO-d_6 were recorded on VXR-300 MHz using TMS as internal standard.

Synthesis of Compounds

2$^{/}$-(4-oxocyclohexyl)-1*H*-isoindole-1$^{/}$,3$^{/}$(2*H*)dione1(a-b)

Benzene-1,2-dicarboxylic acid (0.01 mol) was refluxed with 4-aminocyclohexanone (0.01 mol) in dry ethanol (25 cm^3) for 6 hrs. The reaction progress and completion was monitored by TLC. After completion of reaction, reaction mass was poured on to the ice. The solid product 1(a-b) obtained was then washed with water, filtered, dried and recrystalized from ethanol.

2′-(3-bromo-4-oxocyclohexyl)-1*H*-isoindole-1′,3′(2*H*)-dione 2(a-b)

Compound 1(a-b) 2′-(4-oxocyclohexyl)-1*H*-isoindole-1′,3 dione (0.01 mol) and*N*-bromosuccinamide (0.01 mol) was stirred in dichloromathane at room temperature for 3 hrs. The reaction progress and completion was monitored by TLC. After completion of reaction, reaction mass was poured on to the ice. The solid product 2′-(3-bromo-4-oxocyclohexyl)-1*H*-isoindole-1′,3′(2*H*)-dione**2(a-b)** obtained was then washed with water, filtered, dried and recrystalized from ethanol.

2′-(2-amino-benzimidazol-5-yl)-1*H*-isoindole-1′,3′(2*H*)dione 3(a-b)

With an interest to prepare the above mentioned benzimidazole derivative, compound 2′-(3-bromo-4-oxocyclohexyl)-isoindole-1′,3′(2*H*)-dione 2(a-b) was refluxed with guanidine (0.01 mol) in presence of catalyst pottasium tert-butoxide in a solvent tert-butanol. The reaction progress and completion was monitored by TLC. After completion of reaction, reaction mass was poured on to the ice. The solid product 2′-(2-amino-benzimidazol-5-yl)-1*H*-isoindole-1′,3′(2*H*)dione 3(a-b)obtained was then washed with water, filtered, dried and recrystalized from ethanol.

2′-(2-isothiocyanate-benzimidazol-5-yl)-1*H*-isoindole-1′,3′(2*H*)dione 4 (a-b)

A solution of iodineand carbon disulphide was added drop wise to a suspension of 2′-(2-amino-benzimidazol-5-yl)-1*H*-isoindole-1′,3′(2*H*)dione 3(a-b) and pyridine at 0°C. The contents were stirred for 3 hrs, to obtain 2′-(2-isothiocyanate-benzimidazol-5-yl)-1*H*-isoindole-1′,3′(2*H*)dione 4(a-b) as a product.

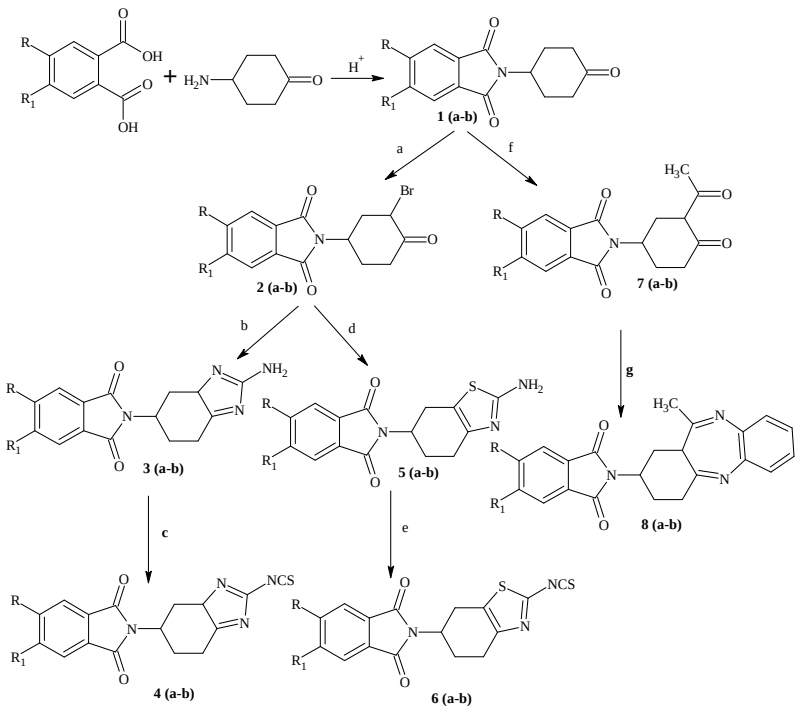
2′-(2-amino-1,3-benzothiazol-6-yl)-1*H*-isoindole-1′,3′(2*H*)-dione5(a-b)

2′-(3-bromo-4-oxocyclohexyl)-1*H*-isoindole-1′,3′(2*H*)-dione 2(a-b) (0.01 mol) and thiourea (0.01 mol) were refluxed in ethanol. The reaction progress and completion was monitored by TLC. After completion of reaction, reaction mass was poured on to the ice. The solid product 2′-(2-amino-1,3-benzothiazol-6-yl)-1*H*-isoindole-1′,3′(2*H*)-dione 5(a-b) obtained was then washed with water, filtered, dried and recrystalized from ethanol.

2′-(2-isothiocyanato-1,3-benzothiazol-6-yl)-1*H*-isoindole-1′,3′(2*H*)-dione 6 (a-b)

A solution of iodineand carbon disulphide was added drop wise to a suspension of 2-(2-amino-1,3-benzothiazol-6-yl)-1*H*-isoindole-1′,3′(2*H*)-dione 5(a-b) and pyridine at 0°C. The contents were stirred for 3 hrs, to obtain the product 2′-(2-isothiocyanato-1,3-benzothiazol-6-yl)-1*H*-isoindole-1′,3′(2*H*)-dione 6(a-b) as a product.

Scheme



1a-8a : R = H, R_1 = H
1b-8b : R = OCH_3, R_1= OCH_3

***a* : *N*-Bromo succinamide**
b : Guanidine
c : CS_2/ I_2
d : Thiourea
e : CS_2/ I_2
f : $POCl_3$, Acetic Acid
g : *O*-phenyldiamine

2′-(3-acetyl-4-oxocyclohexyl)-1*H*-isoindole-1′,3′(2*H*)dione 7(a-b)
To the solution of 2′-(4-oxocyclohexyl)-1*H*-isoindole-1′,3′(2*H*)dione (0.01 mol) 1(a-b) (0.01 mol) in glacial acetic acid (15 cm^3), phosphorous oxychloride (5-6 ml) was added slowly. The reaction was refluxed at 120-130^{0}C for 5hrs. The reaction progress and completion was noted by using TLC. After completion of reaction, the reaction mass poured on to ice. The product obtained 2-(3′-acetyl-4′-oxocyclohexyl)-1*H*-isoindole-1,3(2*H*)dione 7 (a-b) was filtered and recrystallized from ethanol.

2′-(11-methyl-2,3,4,11a-tetrahydro-1*H*-dibenzo-[1,4]-diazepin-2-yl)-1*H*-isoindole-1′,3′(2*H*)-dione 8(a-b)
A mixture of *o*-phenylenediamine (0.01 mol) and 2-(3′-acetyl-4′-oxocyclohexyl)-1*H*-isoindole-1,3(2*H*)dione 7(a-b) (0.01 mol) was stirred in alcohol at room temperature in presence of catalytic amount of sulfuric acid for 2.5 hrs. After completion of the reaction organic layer was concentrated and the product obtain 2-(11-methyl-2,3,4,11a-tetrahydro-1*H*-dibenzo-[1,4]-diazepin-2-yl)-1*H*-isoindole-1,3(2*H*)-dione 8 (a-b) was purified with alcohol.

RESULTS AND DISCUSSION

Characterization of Synthesized Compounds
2′-(4-oxocyclohexyl)-1*H*-isoindole-1′,3′(2*H*)dione 1a
Molecular Formula: $C_{14}H_{13}NO_3$, Melting Point: 248-249, Yield: 63%; Elemental Analysis% (Calculated) Found: C (69.12)69.13, H (5.39)5.40, N (5.76)5.70; IR (KBr): 2940, 1720, 1599, 1325 and 1150 cm^{-1}, ^{1}H NMR (DMSO-d_6): δ 1.9-2.27 (m, 8H, at C_2, C_3 ,C_5, C_6), 3.95 (m, 1H, at C_1), 7.9-8.07 (m, 4H, Ar-H, C_4' to C_7'), ^{13}C NMR (δ ppm): δ 26.1 (C_2 and C_6), 40.3 ($C_3$and C_5), 49.8 (C_1), 124.6, 129.3, 137.32 and 169.8 for phthalimide ring, 206.5 (C_4).

2′-(4-oxocyclohexyl)-5,6-dimethoxy-1*H*-isoindole-1′,3′(2*H*)dione 1b
Molecular Formula: $C_{16}H_{17}NO_5$, Melting Point: 256-257, Yield: 58%; IR (KBr): 2930, 1715, 1605, 1330 and 1143 cm^{-1}.; Elemental Analysis% (Calculated) Found: C (63.36)63.34, H (5.65)5.59, N (4.62)4.63

2′-(3-bromo-4-oxocyclohexyl)-1*H*-isoindole-1′,3′(2*H*)-dione 2a
Molecular Formula: $C_{14}H_{12}BrNO_3$, Melting Point: 252-254, Yield: 52%; Elemental Analysis% (Calculated) Found: C (52.20)52.18, H (3.75)3.76, N (4.35)4.33; IR (KBr): 2995, 1710, 1690, 1560, 1310 and 865 cm^{-1}, ^{1}H NMR (DMSO-d_6): δ 1.91-2.27 (m, 6H, C_2 ,C_5, C_6), 3.87 (m,1H, C_1), 4.2 (t, 1H, C_3),7.8-8.15 (m, 4H, C_4' to C_7'), ^{13}C NMR (δ ppm): δ 21.0 for C_6 , 31.5 (C_5), 35.7 (C_2), 43.6 (>C-N), 55.3 (C_3),125.6, 130.1, 138.3 and 169.5 for phthalimide ring. Signal at 205.0 for C_4.

2′-(3-bromo-4-oxocyclohexyl)-5,6-dimethoxy-1*H*-isoindole-1′,3′(2*H*)-dione 2b
Molecular Formula: $C_{16}H_{16}BrNO_5$, Melting Point: **261-263**, Yield: 54%; IR (KBr): 2925, 1714, 1678, 1313, 1566, 1525, 1120 and 865 cm^{-1}.; Elemental Analysis% (Calculated) Found: C (50.28)50.30, H (4.22)4.24, N (3.66)3.67

2′-(2-amino-benzimidazol-5-yl)-1*H*-isoindole-1′,3′(2*H*)dione 3a
Molecular Formula: $C_{15}H_{14}N_4O_2$, Melting Point: 270-273, Yield: 69%; Elemental Analysis% (Calculated) Found: C (63.82)63.80, H (5.0)4.98, N (19.85)19.81; IR (KBr): 3395, 2995, 1694, 1650, 1390, 1150 cm^{-1}.; ^{1}H NMR (DMSO-d_6): δ 1.40-1.62 (m, 7H, C_{3a}, C_4 ,C_6 ,C_7), 2.0 (s, 2H, -NH_2 ,), 3.90 (m, 1H,C_5), 7.65-7.95 (m,4H, C_4' to C_7'), ^{13}C NMR (δ ppm): . δ 21.4 (C_6), 29.1 (C_7), 36.3 (C_4), 46.2 (C_5), 52.0 (C_{3a}),125.6, 129.7, 136.3 and 169.6 of phthalimide ring,162 (C_2), 164.1 (C_{7a}).

2′-(2-amino-benzimidazol-5-yl)-5,6-dimethoxy-1*H*-isoindole-1′,3′(2*H*)dione 3b
Molecular Formula: $C_{17}H_{18}N_4O_4$, Melting Point: 278-279, Yield: 58%; IR (KBr): 3390, 3005, 1690, 1645, 1595, 1394, 1154 cm^{-1}.; Elemental Analysis% (Calculated) Found: C (59.64)59.62, H (5.30)5.33, N (16.37)16.38

2′-(2-isothiocyanate-benzimidazol-5-yl)-1*H*-isoindole-1′,3′(2*H*)dione 4a
Molecular Formula: $C_{16}H_{12}N_4O_2S$, Melting Point: 275-278, Yield: 59%; Elemental Analysis% (Calculated) Found: C (59.25)59.20, H (3.73)3.78, N (17.27)17.18; IR (KBr): 2980, 1690, 1625, 1599, 1405 and 950 cm^{-1}, ^{1}H NMR (DMSO-d_6): δ 1.47-1.6 (m, 7H, C_4 ,C_6 , C_{3a} and C_7), 3.86 (m, 1H, C_5), 8.0-8.18 (m, 4H, Ar-H, C_4' to C_7'), ^{13}C NMR (δ ppm): Signals at δ 21.5 (C_6), 29.3 (C_7), 37.5 (C_4), 46.8 (C_5), 52.1 (C_{3a}),124.6, 129.9, 136.1 and 169.1 for phthalimide ring,142.6 (-NCS) 162.1 (C_2), 164.6 (C_{7a}).

2′-(2-isothiocyanate-benzimidazol-5-yl)-5,6-dimethoxy-1*H*-isoindole-1′,3′(2*H*)dione 4b
Molecular Formula: $C_{18}H_{16}N_4O_4S$, Melting Point: **280-282**, Yield: 55%; IR (KBr): 2986, 1690, 1625, 1605, 1405, 1105 and 950 cm^{-1}.; Elemental Analysis% (Calculated) Found: C (56.24)56.12, H (4.20)4.09, N (14.57)14.49

2′-(2-amino-1,3-benzothiazol-6-yl)-1*H*-isoindole-1′,3′(2*H*)-dione 5a
Molecular Formula: $C_{15}H_{13}O_2N_3S$, Melting Point: 260-262, Yield: 58%; Elemental Analysis% (Calculated) Found: C (60.18)60.11, H (4.38)4.41, N (14.04)13.96; IR (KBr): 3395 (NH_2), 2995, 1694, 1650, 1600, 1390, 1150 cm^{-1}, ^1H NMR (DMSO-d_6): δ 2.54-2.84 (m, 6H, Ar-H), 4.63 (m, 1H, C_6), 5.2 (s, 2H, NH_2, D_2O exchangeable), 7.87-8.08 (m, 4H, C_4' to C_7'); ^{13}C NMR (δ ppm): 20.2 (C_4), 25.8 (C_5), 30.2 (C_7), 49.6 (C_6), 119.1 (C_{7a}), 127.3, 130.5, 132.3 and 167.8 for phthalimide ring. 148.2 (C_{3a}), 169.8 (C_2)

2′-(2-amino-1,3-benzothiazol-6-yl)-5,6-dimethoxy-1*H*-isoindole-1′,3′(2*H*)-dione 5b
Molecular Formula: $C_{17}H_{17}O_4N_3S$, Melting Point: 271-272, Yield: 55%; IR (KBr): 3390 (NH_2), 3005, 1690, 1645, 1605, 1394, 1154 cm^{-1}.; Elemental Analysis% (Calculated) Found: C (56.81)56.76, H (4.77)4.69, N (11.69)11.63

2′-(2-isothiocyanato-1,3-benzothiazol-6-yl)-1*H*-isoindole-1′,3′(2*H*)-dione 6a
Molecular Formula: $C_{16}H_{11}O_2N_3S_2$, Melting Point: 268-271,Yield: 62%; Elemental Analysis% (Calculated) Found: C (56.29)56.23, H (3.25)3.27, N (12.31)12.29; IR (KBr): 2980, 1690, 1625, 1601, 1405 and 950 cm^{-1}, ^1H NMR (DMSO-d_6): δ 2.43-2.72 (m, 6H, C_4, C_6, C_7), 4.92 (m, 1H, C_6), 7.91-8.03 (m, 4H, Ar-H, C_4', C_5', C_6 , C_7'), ^{13}C NMR (δ ppm): 23.1 (C_4), 28.5 (C_5), 31.1(C_7), 48.5 (C_6), 129.8 (C_{7a}),136.9 (>NCS), 126.0,132.2, 134.1 and 165.4 for of phthalimide ring and 152.1 (C_{3a}), 172.1 (C_2).

2′-(2-isothiocyanato-1,3-benzothiazol-6-yl)-5,6-dimethoxy-1*H*-isoindole-1′,3′(2*H*)-dione 6b
Molecular Formula: $C_{18}H_{15}O_4N_3S_2$, Melting Point: 281-282, Yield: 57%; IR (KBr): 2986, 1690, 1625, 1405, 1105 and 950 cm^{-1}.; Elemental Analysis% (Calculated) Found: C (53.85)53.76, H (3.77)3.79, N (10.47)10.42

2′-(3-acetyl-4-oxocyclohexyl)-1*H*-isoindole-1′,3′(2*H*)dione 7a
Molecular Formula: $C_{16}H_{15}NO_4$, Melting Point: 258-261, Yield: 63%; Elemental Analysis% (Calculated) Found: C (67.36)67.31, H (5.30)5.27, N (4.91)4.87; IR (KBr): 2975, 1721, 1682, 1610, 1325, 1100 cm^{-1}, ^1H NMR (DMSO-d_6): δ 1.9-2.2 (m, 9H, C_2,C_5, C_6 and –CH_3), 3.25 (t, 1H, C_3), 3.93 (m, 1H, C_1), 7.8-8.16 (m, 4H, Ar-H, C_4' to C_7'), ^{13}C NMR (δ ppm): δ 20.0 (C_2), 24.5 (C_6), 28.2 for CH_3, 38.3 (C_5), 46.5 (C_1), 67.4 (C_3),124.8, 129.1, 136.3 and 171.8 for phthalimide ring, 201.4 (C_4), 209.2 (>C=O).

2′-(3-acetyl-4-oxocyclohexyl)-5,6-dimethoxy-1*H*-isoindole-1′,3′(2*H*)dione 7b
Molecular Formula: $C_{18}H_{19}NO_6$, Melting Point: 270-271, Yield: 58%; IR (KBr): 2960, 1725, 1687, 1611, 1316, 1735, 1120 cm^{-1}.; Elemental Analysis% (Calculated) Found: C (62.60)62.58, H (5.55)5.51, N (4.06)4.09

2′-(11-methyl-2,3,4,11a-tetrahydro-1*H*-dibenzo-[1,4]-diazepin-2-yl)-1*H*-isoindole-1′,3′(2*H*)-dione 8a
Molecular Formula: $C_{22}H_{19}N_3O_2$, Melting Point: 288-291, Yield: 59%; Elemental Analysis% (Calculated) Found: C (73.93)73.86, H (5.36)5.32, N (11.76)11.68; IR (KBr): 2990, 1675, 1594, 1332, 1115 and 745 cm^{-1}, ^1H NMR (DMSO-d_6): δ 0.95 (s, 1H, CH_3), 1.5-1.61(m, 6H, C_1, C_3 and C_4), 3.58 (m, 1H, C_2), 7.52-7.63 (m, 8-H, Ar-H, C_6 to C_9 and C_4' to C_7').; ^{13}C NMR (δ ppm): 18.2 for CH_3, 21.2 (C_1), 25.8 (C_3), 26.6 (C_{11a}), 30.1 (C_4), 46.4 (C_2), 124.5, 128.0, 138.0 and 168.1 for phthalimide ring 122.1 (C_6) and(C_9), 127.0 (C_8) and (C_7), 141.2 (C_{5a}) and (C_{9a}), 161.8 (C_{4a}) and 164.3 (C_{11}).

2′-(11-methyl-2,3,4,11a-tetrahydro-1*H*-dibenzo-[1,4]-diazepin-2-yl)-5,6-dimethoxy-1*H*-isoindole-1′,3′(2*H*)-dione 8b
Molecular Formula: $C_{24}H_{23}N_3O_4$, Melting Point: 296-297, Yield: 61%; IR (KBr): 2982, 1681, 1590, 1321, 1098 and 760 $cm^{-1;}$ Elemental Analysis% (Calculated) Found: C (69.05)69.01, H (5.55)5.52, N (10.07)10.09

RESULTS AND DISCUSSION

In order to prepare bio-active heterocyclic molecule previously synthesized 2-(4-oxocyclohexyl)-1*H*-isoindole-1, 3(2*H*)dione**1(a-b)** was used as a building block for synthesis of various derivatives. 2-(4-oxocyclohexyl)-1*H*-isoindole-1,3(2*H*)dione**1(a-b)** on treatment with bromine gave 2-(3′-bromo-4′-oxocyclohexyl)-1*H*-isoindole-1,3(2*H*)dione**2(a-b)**. ^1H NMR spectrum of compound showed a triplet at δ 4.2 for one proton of C_3. 2-(3′-bromo-4′-oxocyclohexyl)-1*H*-isoindole-1,3(2*H*)dione**2(a-b)** which was further treated with guanidine hydrochloride to gave 2-(2′-amino-benzimidazol-5′-yl)-1*H*-isoindole-1,3(2*H*)dione**3(a-b)**. IR and ^1H NMR spectrum of compound showed that aband at 3395for NH_2 andsinglet at δ 2.0 for two protonof -NH_2 respectively. Compound **3(a-b)** treated with carbon disulfide to obtain 2-(2′-isothiocyanate-benzimidazol-5′-yl)-1*H*-isoindole-1,3(2*H*)dione **4(a-b)**. Non presence of strong NH_2 band in IR spectra and singlet of 2H confirmed that conversion of NH_2 to NCS is achieved. 2-(3′-bromo-4′-oxocyclohexyl)-1*H*-isoindole-1,3(2*H*)dione**2(a-b**) on further coupled withthiourea to gave 2-(2′-amino-1′,3′-benzothiazol-6′-yl)-1*H*-isoindole-1,3(2*H*)dione**5(a-b)**. IR and ^1H NMR spectrum of compound showed that a

band at 3395andsinglet at δ 5.2 for two proton for -NH_2 respectively. Carbon disulfide reacted with **5(a-b)** to obtain 2-(2′-isothiocyanate-1′,3′-benzothiazol-6′-yl)-1*H*-isoindole-1,3(2*H*)dione **6(a-b)**. Non presence of strong NH_2 band in IR spectra and singlet of 2H confirmed that conversion of NH_2 to NCS achieved. Acylation of Compound 2-(4-oxocyclohexyl)-1*H*-isoindole-1,3(2*H*)dione**1(a-b)**gave 2-(3′-acetyl-4′-oxocyclohexyl)-1*H*-isoindole-1,3(2*H*) dione**7 (a-b)**. ^{1}H NMR spectrum of compound showed that a triplate at δ 3.25 for one proton of C_3. Orthophenyldiamine (OPD) on treatment with compound **7(a-b)** gives molecule 2-(11′-methyl-1*H*-dibenzo-[1,4]diazepin-2′-yl)-1*H*-isoindole-1,3(2*H*)dione. **8(a-b)**.^{1}H NMR spectrum of compound showed that a singlet at δ 0.95 for proton of CH_3.

Antimicrobial Study

All the synthesized compounds **1(a-b)**, **2(a-b)**, **3(a-b)**, **4(a-b)**, **5(a-b,6(a-b), 7(a-b)** and **8(a-b)** were screened for their antibacterial activity against Gram negative strain *E. coli* and Gram positive strain *S. aureus*. Study carried out at four different concentrations 50 and 100µg/ml. The standard drug used for comparison was streptomycin.

Table 1: Antibacterial activity of compounds 1(a-b) to 7(a-b)

Compound No	Zone of inhibition in mm*			
	E. coli		S.aureus	
	50µg	100µg	50µg	100µg
1a	11	13	12	14
1b	11	12	12	13
2a	15	17	12	14
2b	16	17	14	17
3a	14	16	13	13
3b	13	15	12	14
4a	16	17	13	14
4b	15	18	14	16
5a	13	15	12	13
5b	14	15	11	13
6b	16	17	15	16
6b	15	17	16	18
7a	13	13	14	16
7b	12	14	15	17
8a	15	17	16	18
8b	14	17	17	18
Erythromycin	17	20	18	22

**Diameter of the well (bore size)- 6mm*

Disc size: 6.35mm Standard: Streptomycin Control: DMSO

Duration: 24 hrs Resistant (11mm/less) Intermediate (12-14mm)

Sensitive (15mm/more)

Regarding the activity of Phthalamide derivatives, compound containing isothiocyanate functional group showed higher activity against tested organism whereas other compound showed moderately activity in comparison with standard (Erythromycin).

CONCLUSION

Spectral techniques used in the scheme confirm the formation and synthetic route of newly synthesized derivatives. From the result of antibacterial activity it is seen that synthesized derivatives exhibited significant to moderate activity. This confers all the newly synthesized heterocyclic derivatives of Phthalamide are biologically active towards the tested bacterial strains.

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