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Research Article

SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL SCREENING OF NEW SCHIFF BASES LINKED TO PHTHALIMIDE

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ABSTRACT

In this study a series of new Schiff bases linked to phthalimide through phenyl sulfonate moiety have been synthesized via multistep synthesis. The first step involved reaction of phthalic anhydride with aniline producing N-phenyl phthalamic acid (1) which was subsequently dehydrated to the corresponding N-phenyl phthalimide (2) via treatment with acetic anhydride and anhydrous sodium acetate. The synthesized imide was treated with chlorosulfonic acid in the third step producing compound (3) which was introduced in reaction with 4-hydroxy benzaldehyde in the fourth step producing compound (4) and this in turn was introduced in condensation reaction with various aromatic primary amines affording the desired new Schiff bases (5-10). Also a series of new Schiff bases linked to phthalimide through methylene group have been synthesized via reaction of 4-phenylphenacyl bromide with phthalimide potassium salt producing compound (12) which in turn introduced in reaction with different primary aromatic amines affording the new Schiff bases (13-18).

1. INTRODUCTION

Schiff bases are important intermediates for the synthesis of some bioactive compounds such as β-lactams, and they form a significant class of compounds in medicinal and pharmaceutical chemistry with a variety of interesting biological actions including antibacterial, antifungal, antimouse hepatitis virus (MHV), and adenovirus type 5 (Ad 5), anticancer and herbicidal activities[1-4].

Similarly phthalimides which are bicyclic non-aromatic nitrogen heterocycles are important compounds with a variety of applications and a wide range of properties[5-7]. Generally they are used as starting materials and intermediates for the synthesis of many types of alkaloids and pharmacophores, synthesis of pesticides and lately are being under intense biomedical research due to their important biological effects[8-11]. In light of the interesting variety of biological activities seen in compounds containing phthalimides and azomethine linkages it was thought of interest to examine the effect of having these two functionalities present simultaneously in one structure. Based on this notion we decide to synthesize several new Schiff bases linked to phthalimide moiety and to test their antibacterial activity.

2. EXPERIMENTAL

All chemicals used in this work were purchased from Flucka, Merk, and BDH companies and used without further purification. Melting points were determined on open capillaries Thomas Hoover apparatus and are uncorrected. FTIR spectra were recorded on SHIMADZU FTIR-8400 Infrared spectrophotometer. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker 300 MHz instrument using tetramethylsilane (TMS) as an internal standard and DMSO-d_6 as a solvent.

2.1. Preparation of N-phenylphthalamic Acid [1][12]

To a solution of (0.01 mol, 1.48 g) phthalic anhydride in (25 mL) of acetone, (0.01 mol, 1 mL) of aniline was added dropwise with stirring and cooling. Stirring was continued for two hours at room temperature then the resulted

precipitate was filtered, dried then purified by recrystallization from ethanol.

2.2. Preparation of N-phenyl phthalimide [2][12]

A mixture of compound (1) (0.01 mol, 2.41 g) in (25 mL) of acetic anhydride and and (0.12 g) of anhydrous sodium acetate was refluxed for two hours with stirring. The resulted homogenous solution was cooled to room temperature then poured into crushed ice with stirring and the obtained precipitate was filtered, dried and recrystallized from acetone.

2.3. Preparation of 4-(N-phthalimidyl) phenyl sulfonyl chloride [3][13]

Chlorosulfonic acid (4 mL) was added dropwise to (0.01 mol, 2.23 g) of N-phenyl phthalimide during two hours with stirring and keeping temperature at zero°C. Stirring was continued for ten hours at room temperature then the resulted mixture was poured into crushed ice carefully with stirring. The obtained precipitate was filtered, dried then recrystallized from acetone.

2.4. Preparation of 4-(4\-(N-phthalimidyl) phenyl sulfonate] benzaldehyde [4]

In a three necked flask equipped with a stirrer and a thermometer a mixture of (0.01 mol, 1.22g) of 4-hydroxy benzaldehyde and (3 mL) of pyridine was placed. The flask was surrounded by a bath sufficiently cold to lower the mixture temperature to 10°C then compound (3) (0.01 mol, 3.22g) was added in portions during twenty minutes with continuous stirring. The resulted mixture was refluxed for two hours on a water bath then poured into cold water with stirring until the resulted oily layer solidified. The solid product was filtered, washed with water, dried then recrystallized from ethanol. Physical properties of compounds (1-4) are listed in Table (1).

2.5. Preparation of 4-[4\-(N phthalimidyl) phenyl sulfonate] benzylidene [5-10][14,15]

In a suitable round bottomed flask (0.01 mol, 4.07 g) of compound (4) was dissolved in (20 mL) of absolute ethanol then (0.01 mol) of primary aromatic amine was added followed by addition of (2-3) drops of glacial acetic acid with stirring. The mixture was refluxed for four hours then cooled to room temperature and the obtained precipitate was filtered, dried and purified by recrystallization from a suitable solvent. Physical properties of compounds [5-10] are listed in Table (2).

2.6. Preparation of Phthalimide potassium salt [11]

Phtalimide (0.01 mol, 1.47g) was dissolved in (20 mL) of absolute ethanol then was heated in a water bath. The obtained clear solution was added to alcoholic potassium hydroxide solution (0.01 mol of KOH in 25 mL absolute ethanol) with continuous stirring and cooling, then the obtained precipitate was filtered and dried.

2.7. Preparation of N-(4-phenyl phenacyl) phthalimide [12]

In a suitable round bottomed flask (0.01 mol, 2.75 g) of 4-phenyl phenacyl bromide was dissolved in (25 mL) of absolute ethanol then (0.01 mol, 1.85 g) of potassium salt (11) was added gradually with stirring. The resulted mixture was refluxed for six hours with continuous stirring then was cooled to room temperature and the formed precipitate was filtered, washed with distilled water and dried then recrystallization from ethanol.

2.8. Preparation of Schiff bases [13-18]

A mixture of compound (12) (0.01 mol, 3.41g) and (0.01 mol) of primary aromatic amine in (25 mL) of absolute ethanol and (2-3) drops of glacial acetic acid was refluxed for six hours with stirring. The resulted mixture was cooled to room temperature and the obtained precipitate was filtered, dried then recrystallization from a suitable solvent. Physical properties of Schiff bases (13-18) are listed in Table (3).

2.9. Biological Study

The cup plate method using nutrient agar medium was employed in studying the antibacterial activity of the prepared Schiff bases against four strains of bacteria. DMSO was used as sample solution, sample size of all compounds was fixed at (0.1 mL) and the used concentration for all tested compounds was 100 μg/mL. Using a sterilized cork borer cups were scooped out of agar medium contained in a petridish which was previously inoculated with the microorganisms. The tested compound

solution (0.1 mL) was added in the cups and the petridishes were subsequently incubated at 37°C for 48 hrs. Ampicilline was used as reference drug and DMSO as a control. Zones of inhibition produced by each compound was measured in mm and the results are listed in Table (7).

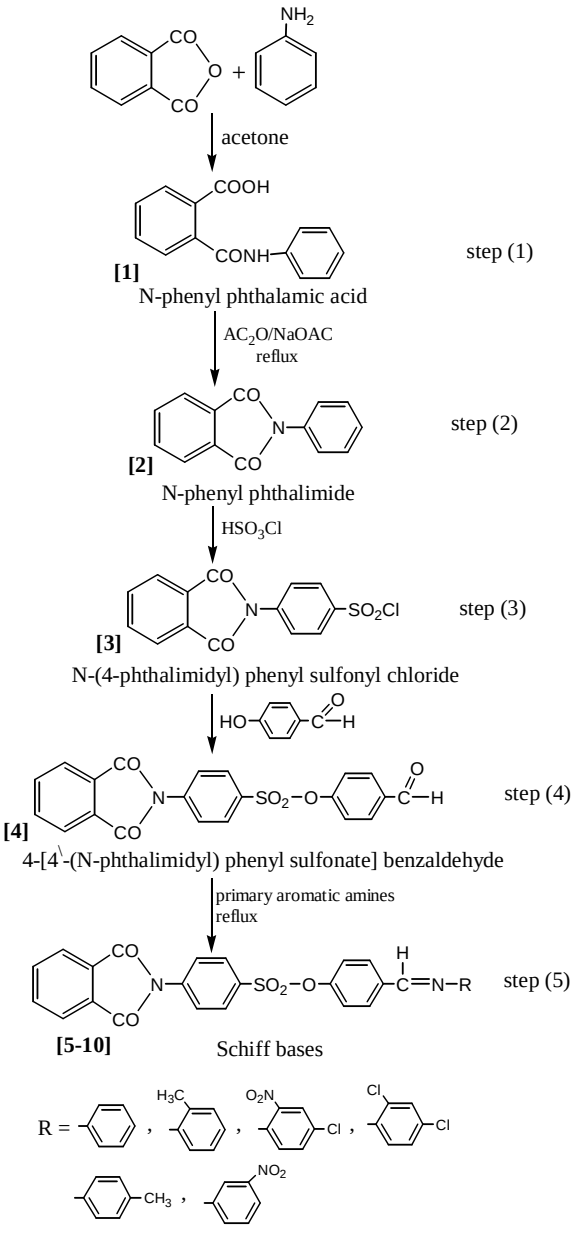
3. RESULTS AND DISCUSSION

3.1. Chemistry

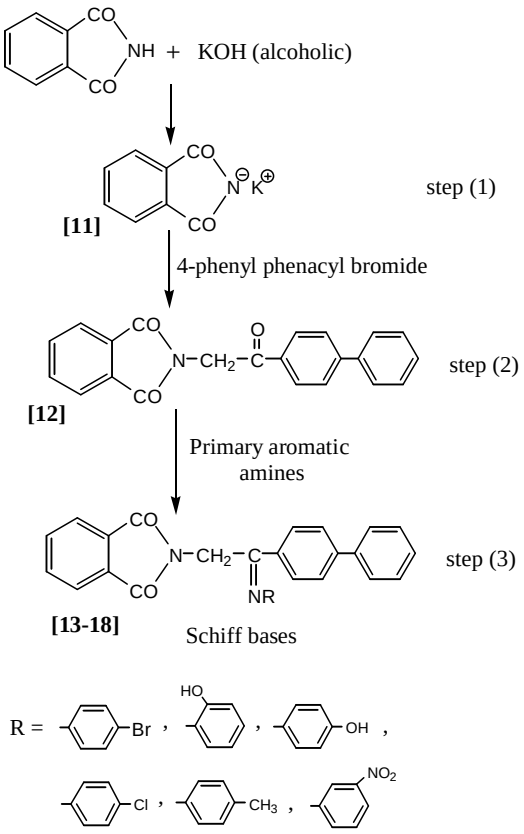
Since both phthalimides and Schiff bases belong to a widely used group intermediates important for production of many types of pharmaceuticals and have wide spectrum of biological applications the target of the present work has been directed towards building of new molecules containing these two active moieties. Performing this target was made by following two different multistep synthetic paths which are described in Scheme (1) and (2).

In the first synthetic path we prepare a series of new Schiff bases (5-10) linked to phthalimide through phenyl sulfonate moiety by applying The strategy which we depend on in preparing compounds (5-10) involved introducing of sulfonyl chloride group in para position of phenyl ring already attached to phthalimide moiety then this compound introduced in esterification reaction in which nucleophilic replacement of chloride with 4-formyl phenoxide moiety was performed and by this step the resulted compound (4) contain carbonyl group which was ready for nucleophilic attack by amines during condensation reaction in the final step affording the desired Schiff bases (5-10). Structures of the prepared compounds were confirmed by FTIR, ^{1}HNMR and ^{13}CNMR spectral data. FTIR spectrum of compound (1) showed strong absorption bands at 3325 and 3136 cm^{-1} due to ν(O-H) carboxylic and ν(N-H) amide[16]. Other absorptions appeared at 1720 cm^{-1}, 1643 cm^{-1} and 1600 cm^{-1} due to ν(C=O) carboxylic, ν(C=O) amide and ν(C=C) aromatic respectively. ^{1}H-NMR spectrum of compound (1) showed signals at δ= (7.04-7.89) ppm belong to aromatic protons and NH proton and a clear signal at δ= 10.33 ppm due to (O-H) carboxylic, while ^{13}C-NMR spectrum showed signals at δ= (119.9-140), 167.8 and 167.92 ppm due to aromatic carbons, (C=O) amide and (C=O) carboxyl respectively.

many steps the first step involved preparation of amic acid (1) via reaction of equimolar amounts of phthalic anhydride and aniline in acetone. Dehydration of compound (1) using acetic anhydride and anhydrous sodium acetate in the second step afforded compound (2). In the third step compound (2) was introduced in chlorosulfonation reaction via treatment with chlorosulfonic acid producing compound (3) which in turn was introduced in the fourth step in esterification reaction with 4-hydroxy benzaldehyde producing compound (4). In the final step compound (4) was introduced in condensation reaction with different primary aromatic amines producing the target Schiff bases (5-10).



Scheme (1): Synthetic path for preparation of Schiff bases [5-10]



Scheme (1): Synthetic path for preparation of Schiff bases [13-18]

FTIR spectrum of compound (2) showed disappearance of ν(O-H) and ν(N-H) absorption bands proving success of dehydration reaction and appearance of two bands at 1735 cm^{-1} and 1708 cm^{-1} due to asym. and sym., of ν(C=O) imide. ^{1}H-NMR spectrum of compound (2) showed disappearance of (OH) carboxyl proton signal and appearance of two multiplet signals at δ= (7.44-7.56) and (7.89-7.97) ppm belong to aromatic rings protons. ^{13}C-NMR spectrum showed signals at δ= (123.8-135.1) ppm and at δ= 167.4 ppm belong to aromatic and (C=O) imide carbons respectively.

FTIR spectrum of compound (3) showed two clear bands at 1365 cm^{-1} and 1188 cm^{-1} due to ν(SO_2)asym. and ν(SO_2)sym. indicating success of introducing sulfonyl chloride moiety in phenyl phthalimide molecule. FTIR spectrum of compound (4) showed absorption bands at 1741 cm^{-1} and 1718 cm^{-1} belong to asym. and sym. ν(C=O) imide. The appearance of new band at 1699 cm^{-1} belong to ν(C=O) aldehyde is a good proof for success of compound (4) formation. Other bands appeared at 1593 cm^{-1}, 1370, 1186 cm^{-1} and 1360 cm^{-1} belong to ν(C=C) aromatic, asym. ν(SO_2), sym. ν(SO_2) and ν(C-N) imide respectively. ^{1}H-NMR spectrum of compound (4) showed signals at δ= (7.37-8.13)ppm for aromatic protons and signal at δ=9.99 ppm due to aldehyde proton. ^{13}C-NMR spectrum showed signals at δ= (123.2-153.5) ppm due to aromatic carbons and signals at δ= 167 and 193 ppm belong to (C=O) imide and (C=O) aldehyde carbons. Finally FTIR spectra of the new Schiff bases (5-10) showed disappearance of absorption band at 1699 cm^{-1} belong to ν(C=O) aldehyde and appearance of clear strong absorption band at (1620-1631) cm^{-1} due to ν(C=N) imine. Other absorption bands appeared at (1740-1741)cm^{-1}, (1720-1722) cm^{-1}, (1585-1596) cm^{-1}, (1365-1375) cm^{-1} and (1168-1199) cm^{-1} and (1300-1350) cm^{-1} which were attributed to asym. ν(C=O) imide, sym. ν(C=O) imide, ν(C=C) aromatic, asym. ν(SO_2), sym. ν(SO_2) and ν(C-N) imide respectively.

^{1}H-NMR spectrum of compound (5) showed multiplet signals at δ= (6.8-7.9) ppm due to aromatic protons and signal at δ=8.9 ppm belong to imine protons while ^{13}C-NMR spectrum showed signals at δ= (124-127.5), 134.8 and 167 ppm belong to aromatic carbons, (C=N) and (C=O) imide carbons respectively.

^{1}H-NMR spectrum of compound (6) showed signal at δ= 1.5 ppm belong to (CH_3) protons, multiplet signals at δ= (7.4-8.4) ppm belong to aromatic protons and signal at δ= 8.95 ppm due to imine proton while ^{13}C-NMR spectrum of compound (6) showed signals at δ= 25, (123-134), 135 and 158.5 ppm belong to (CH_3), aromatic carbons, (C=N) imine and (C=O) carbons respectively.

^{1}H-NMR spectrum of compound (8) showed multiplet signals at δ= (7.29-8.13) ppm for aromatic protons and clear signal at δ= 8.58 ppm for imine proton while ^{13}C-NMR spectrum showed signals at δ= (122-151.7) ppm due to aromatic carbons, signals at (162.4) and (166.8) ppm belong to (C=N) and (C=O) carbons. Finally ^{1}H-NMR spectrum of compound (9) showed clear signal at δ= 2.08 ppm due to (CH_3) protons, multiplet signals at δ= (7.27-8.12) ppm for aromatic protons and signal at δ= 8.61 ppm for imine proton while

^{13}C-NMR spectrum showed signals at δ= 31.1, (121.4-151.5), 159 and 166 ppm belong to CH_3, aromatic carbons, (C=N) and (C=O) carbons respectively. All details of FTIR spectral data of compounds [1-4] and [5-10] are listed in Table (4) and (5).

The present work involved also synthesis of several new Schiff bases (13-18) linked to phthalimide moiety through methylene group.

The synthetic path which was followed in synthesis of these compounds involved three steps, in the first step phthalimide was converted to corresponding potassium salt (11) via treatment with alcoholic KOH solution. The resulted salt (11) represents the strong nucleophile which attack the electron-deficient carbon atom bonded to halogen in phenyl phenacyl bromide in the second step according to Gabrial synthesis producing compound (12). Compound (12) contain a carbonyl group which was ready for introducing in condensation reaction with different primary aromatic amines in the third step producing the desired Schiff bases (13-18).

Compound (12) was purified by recrystallization from ethanol and collected as reddish brown crystals in 65% yield with m.p. (106-108)°C. physical properties of Schiff bases (13-18) are listed in Table (3). FTIR spectrum of compound (12) showed appearance of clear absorption band at 1689 cm^{-1} due to ν(C=O) ketone. Other absorption bands appeared at 1716, 1600 and 1392 cm^{-1} due to ν(C=O) imide, ν(C=C) aromatic and ν(C-N) imide respectively. ^{1}HNMR spectrum of compound (12) showed signal at δ= 4.95 ppm belong to (CH_2) protons and signals at δ= (7.44-8.19) ppm belong to aromatic protons while ^{13}CNMR spectrum showed signals at δ= 34.41, (123.8-139.1), 145.66 and 191.78 ppm belong to (CH_2), aromatic, (C=O) amide and (C=O) ketone carbons respectively.

FTIR spectra of Schiff bases (13-18) showed disappearance of absorption band at 1689 cm^{-1} due to ν(C=O) ketone and appearance of absorption band at (1620-1681) cm^{-1} due to ν(C=N) imine. Also all spectra showed clear absotption bands at (1697-1725) cm^{-1}, (1558-1647) cm^{-1} and (1311-1396) cm^{-1} due to ν(C=O) imide, ν(C=C) aromatic and ν(C-N) imide respectively. All details of FTIR spectral data of compounds (13-18) are listed in Table (6).

^{1}HNMR spectrum of compound (13) showed signal at δ= 5.19 ppm due to (CH_2) protons and signals at δ= (7.25-8.1) ppm due to aromatic protons while ^{13}CNMR spectrum showed signals at δ= 44.9, (112.8-135.2) and 168 ppm belong to (CH_2), aromatic, (C=N) and (C=O) carbons.

^{1}HNMR spectrum of compound (14) showed signals at δ= 5.04 ppm belong to (CH_2) protons and signals at δ= (7.2-8.25) ppm belong to aromatic protons while ^{13}CNMR spectrum showed signals at δ= 45.6, (116-141), 162 and 171 ppm belong to (CH_2), aromatic, (C=N) and (C=O) imide carbons respectively.

^{1}HNMR spectrum of compound (15) showed signals at δ= 5.1 and (7.32-8.19) ppm belong to (CH_2) and aromatic protons while ^{13}CNMR spectrum showed signals at δ= 45.33, (120-144), 159 and 165 ppm belong to (CH_2), aromatic, (C=N) and (C=O) imide carbons respectively.

3.2. Biological Study

To determine the antibacterial activity of the new Schiff bases the cup plate method was used with Ampicillin as the reference antibiotic. The prepared compounds were examined against four strains of bacteria *Staphylococcus aureus Bacillus subtilis, Psuedomonas aeruginosa* and *Escherichia Coli*. Zones of inhibition caused by each compound was measured in mm and the results are listed in Table (7). The results indicated that compounds (9, 13, 14, 15 and 17) are highly active against all types of tested bacteria, while compounds (6, 8, 18) are highly active against *S. aureus* and *E. coli.* Compound (10) is highly active against *S. aureus, P. aeruginosa* and *E. coli,* while compound (7) is highly active against *P. aeruginosa* and *E. coli.* The rest of the compounds were found to be moderately active against the tested organisms.

ACKNOWLEDGEMENT

We are very thankful to Dr. Nadum A. (Baghdad University, Biology. Dep.) for performing antibacterial study for the prepared compounds.

Table 1: Physical properties of prepared compounds [1-4]

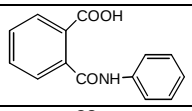
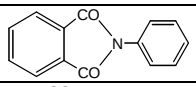
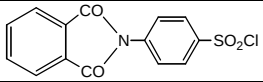
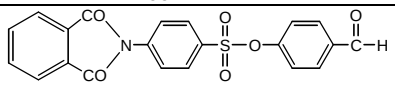
Comp. No.	Compound structure	Color	Melting points °C	Yield %	Recrystallization solvent
1		White	170-172	88	Ethanol
2		Off white	204-205	85	Acetone
3		Brown	200 dec.	72	Acetone
4		Pale brown	176-178	72	Ethanol

Table 2: Physical properties of prepared compounds [5-10]

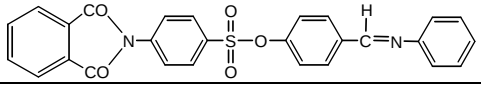
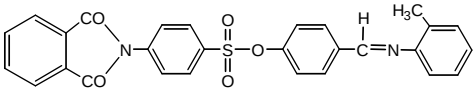
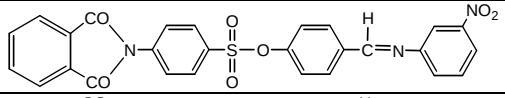
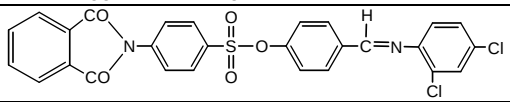
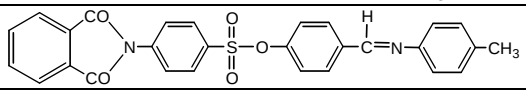
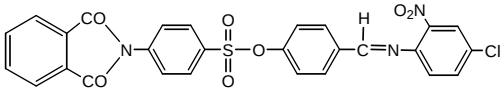
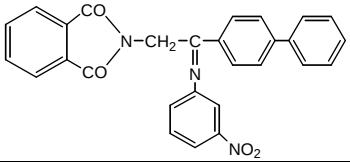
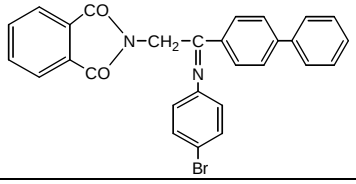
Comp. No.	Compound structure	Color	Melting points °C	Yield %	Recrystallization Solvent
5		Off white	180-182	70	Dioxane
6		yellow	270-272	88	Ethanol
7		Deep yellow	177-178	76	Acetone
8		White	184-186	61	Dioxane
9		White	226-228	93	Ethanol
10		Yellow	190-191	84	Acetone

Table 3: Physical properties of prepared compounds [13-18]

Comp. No.	Compound structure	Color	Melting points °C	Yield %	Recrystallization Solvent
13		Pale green	162-163	92	Acetone
14		Brown	136-138	77	Ethanol

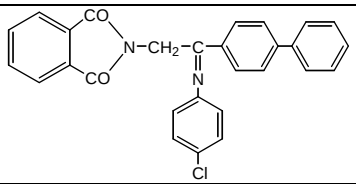
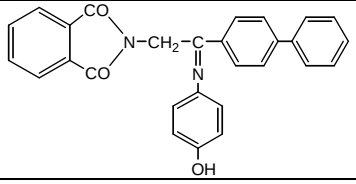
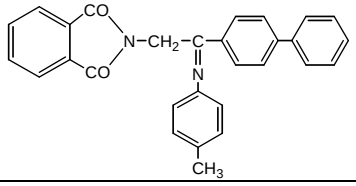
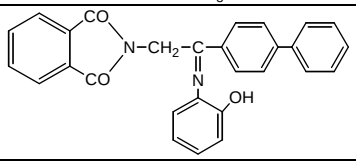
Comp. No.	Compound structure	Color	Melting points °C	Yield %	Recrystallization Solvent
15		Yellow	116-117	81	Dioxane
16		Deep brown	129-130	90	Ethanol
17		Red	112-114	64	Acetone
18		Deep green	165-167	85	Ethanol

Table 4: FTIR spectral data of compounds [1-4]

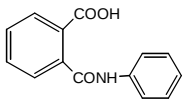
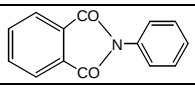
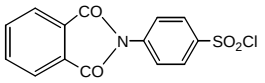
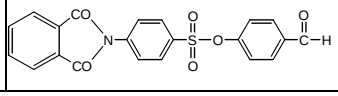
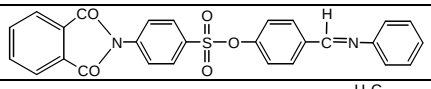
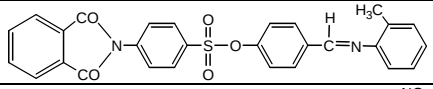
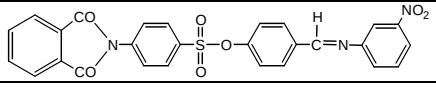
Comp. No.	Compound structure	FTIR spectral data cm^{-1}					
1		ν(O-H) carboxylic	ν(N-H) amide	ν(C-H) aromatic	ν(C=O) carboxlyic	ν(C=O) amide	ν(C=C) aromatic
		3325	3136	3062	1720	1643	1600
2		ν(C-H) aromatic	ν(C=O) imide		ν(C=C) aromatic	ν(C-N) imide	
		3074	1735 1708		1593	1384	
3		ν(C-H) aromatic	ν(C=O) imide	ν(C=C) aromatic	ν(SO_2) asym.	ν(SO_2) sym.	ν(C-N) imide
		3101	1743 1720	1585	1365	1188	1300
4		ν(C=O) imide	ν(C=O) aldehyde	ν(C=C) aromatic	ν(SO_2) asym.	ν(SO_2) sym.	ν(C-N) imide
		1741 1718	1699	1593	1370	1186	1360

Table 5: FTIR spectral data of compounds [5-10]

Comp. No.	Compound structure	FTIR spectral data cm-1							
		ν(C-H) aromatic	ν(C=O) imide	ν(C=N) imine	ν(C=C) aromatic	ν(SO_2) asym.	ν(SO_2) sym.	ν(C-N) imide	Others
5		3080	1720	1620	1585	1375	1190	1345	-
6		3040	1740 1720	1623	1590	1375	1180	1300	-
7		3040	1741 1720	1630	1593	1371	1199	1310	ν(NO_2) 1523 1352

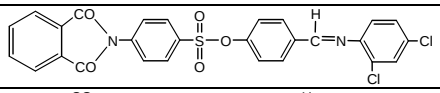
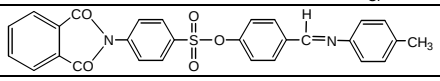
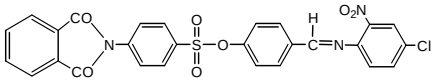
8		3060	1741 1720	1629	1596	1370	1186	1350	**ν(C-Cl)** 1093
9		3080	1740 1722	1630	1593	1373	1186	1346	-
10		3101	1720	1631	1593	1365	1168	1338	**ν(NO_2)** 1504 1404 **ν(C-Cl)** 1068

Table 6: FTIR spectral data of compounds [13-18]

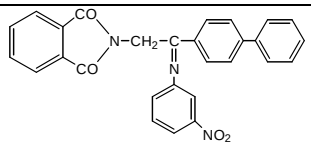
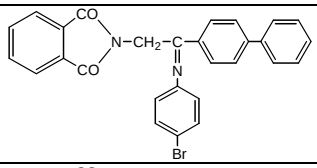
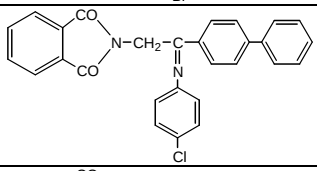
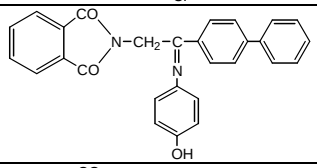
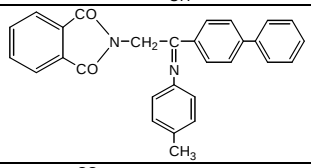
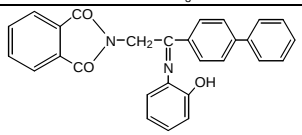
Comp. No.	Compound structure	FTIR spectral data cm^{-1}					
		ν(C-H) aromatic	**ν(C=O) imide**	**ν(C=N) imine**	**ν(C=C) aromatic**	**ν(C-N) imide**	**Others**
13		3062	1697	1624	1597	1350	**ν(NO_2)** 1450 1327
14		3035	1718	1674	1600	1352	**ν(C-Br)** 688
15		3059	1725 1701	1631	1600	**1311**	**ν(C-Cl)** 1083
16		3055	1716	1681	1647	1361	**ν(C-OH) phenolic** 3425
17		3028	1716	1620	1558	1319	-
18		3000	1720 1703	1681	1590	1396	**ν(C-OH) phenolic** 3456

Table (7): Inhibition zone of Antibacterial activity of compounds [5-10] and [13-18] in mm

Comp. No.	Gram positive bacteria		Gram negative bacteria	
	S. aureus	***B. subtilis***	***P. aeruginosa***	***E. coli***
5	11	11.4	10.8	10.5
6	14	11.2	11	15
7	11.7	10.2	14.2	14.4
8	17.5	10.4	11.5	15.8
9	18	12	12.8	20.1
10	12.5	9	12.4	17.2
13	13.2	12.3	15	18.3
14	20.7	11.8	13	16.2
15	20.3	13.5	16.5	18.9
16	11.4	10.6	10.3	11.1
17	19.8	12.1	12.7	18.6
18	18.4	11.1	11.5	14.2
Ampicillin	17	11.5	12	14
DMSO	-	-	-	-

REFERENCES

1. Jarrahpour, A.A., Motamedifar, M., Pakshir, K., Hadi, N. and Zarei, M., synthesis of novel azo Schiff bases and their antibacterial and antifungal activities. Molecules, 2004; 9:815-824.
2. Satyanarayana, V.S., Sreevani, P., Sivakumar, A. and Vijayakumar, V., synthesis and antimicrobial activity of new Schiff bases containing coumarin moiety and their spectral characterization. ARKivoc, 2008; xvii: 221-233.
3. Abdel-Salam, F.H., biological study and complextion behavior of some anionic Schiff base amphiphiles. J. Surfact. Deterg., 2010; 13:423-431.
4. Sathe, B.S., Jayachandran, E. and Jagtap, V.A., Antithelmintic activity of newly synthesized moieties of fluorobenzothiazole Schiff's base. Res. J. Pharm. Bio. and Chem. Sci., 2011; 2:510-515.
5. Sahu S.K., Mishra S.K., Mandal S. and Choudhury P., Synthesis and biological evaluation of 3-(phthalimidoethyl)-4-substituted cinnamoyl substituted benzanilides. J. Indian Chem. Soc., 2006; 83:832-834.
6. Mahapatra S.P., Ghode P., Jain D.K. and Chaturvedi S.C., synthesis and hypoglycemic activity of some phthalimide derivatives. J. Pharm. Sci. and Res., 2010; 2:567-578.
7. Jain L., Synthesis, characterization and antibacterial activity of N-(N-acetic acid-yl-phthalimide-5-yl)maleamic acid dihydrate. J. Chem. Crystallyogr., 2010; 40:428-431.
8. Malgorzata W. and Katarzyna K., synthesis and anticonvulsant evaluation of some N-substituted phthalimides. Acta poloniae pharm., 2009; 66:249-257.
9. Vamecq J., Bac P., Herrenknecht C. and Maurois P., synthesis and anticonvulsant and neurotoxic properties of substituted N-phenyl derivatives of the phthalimide pharmacophore. J. Med. Chem., 2000; 43:1311-1319.
10. Sano H., Noguchi T., Tanatani A., Miyachi H., and Hashimoto Y., N-phenyl phthalimide-type cyclooxygenase inhibitors derived from thalidomide. Chem. Pharm. Bull., 2004; 52:1021-1022.
11. Wanchai P., Sirichai A., Sirintorn Y. and Warinthorn C., synthesis of N-phenyl phthalimide derivatives as α-Glucosidase inhibitors. Arch. Pharm. Res., 2007; 30:1501-1506.
12. Pyriadi T. and Al-Azzawi A., Synthesis, polymerization and curing of N-substituted citraconimidyl acrylate. J. Polym. Sci. Part A: polymer Chem. 1999; 37: 427-433.
13. Sharaf El-Din N., Synthesis of some sulfonamide derivatives with potential antibacterial activity. Chem. Heterocyclic comp. 2000; 36:449-454.
14. Gaurav A., Rupinder K., Gurdeep K., Amrinder S. and Pankaj S., Synthesis and antibacterial activity of some new benzothiazole derivatives. Acta Pharm. Sci., 2010; 52:213-218.
15. Suresh S., Iswar K.B., Mahesh B.P. and Rahul S., Synthesis and antibacterial activity of new 2,5-disubstituted 1,3,4-thiadiazole derivatives. Inter. J. Pharm. Res. Devlop. 2011; 3:144-151.
16. Silverstein, R.M. and Bassler, G.C. and Kiemle D.J., Spectroscopic identification of organic compounds. 2005, 7th Ed., John Wiley and Sons. NJ. USA.