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Synthesis of Bisphthaldicarboximide via the reaction of Phthalic anhydridewith diamines and Evaluation of its Biological activity

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Abstract: Six compounds of N, N substituted phthaldicarboximides were synthesized from the reactionof phthalic anhydride with diamines (4,4'-sulfonyldianiline, 6-methyl-1,3,5-triazine-2,4-diamine,6-phenyl-1,3,5-triazine-2,4-diamine, pyridine-2,6-diamine, 4-methylbenzene-1,3-diamine, 2,6-diaminopyrimidin-4-ol,1,2,4-triazole-3,5-diamine).The structural formula of the synthesized compounds were conforemed by physical and spectroscopic methods(^{1}H- NMR, ^{13}C- NMR, I.R,UV-VIS, elemental analysis, and mass spectral data).The synthesized compounds were screened for their antibacterial activity against fourmicroorganisms ***Staphylococcus aureus ,Bacillus. subtilis***, ***Escherichia Coli andKlebsiella pneumonia*** and they were found toexhibit good to moderate antibacterial activity.

Key Words: phthalic anhydride, diamines,N,N substituted phthaldicarboximide, Pharmacologicalactivity, *E. coli*,*K. pneumonia*,*S. aureus*,*B. subtilis.*

Introduction

Phthalimides are of high interest organic compounds used in organic synthesis and other industerial fields such as in drugs synthesis for the acetylenicphthalimides showed pharmacy eutical activity to be anticholinergic agents and anti-Parkinsonian agent [1,2] other substituted phthalimides were found to possess satisfactory analgesic characteor and used as analgesic drug [3], also some of them have been employed as inhibitors against mammalian, plant, bacterial and fungal copper-containing amine oxidases [4]. Whereas other substituted phthalimides demonstrated inhibitory effect on the tested microorganisms [5,6], moreover they also employed as prevulcanization inhibitor used in sulphurcured rubber polymer systems [7].Many amides can be used for the preparation of synthetic polymers, which can be used as insulating coating inelectrical equipment [8] and plastic heat resistant glass fiber [9]. A number of imides also can be used as plant growth regulators and some of them are usefully as herbicides [10,11]. In view of interesting range of the products from the reaction of phthalaldehyde with diamine[12], it wasdecided to prepare these compounds by an alternative rout in order to confirm the various structures. The following synthesis was carried out by using phthalic anhydride instead of phthalaldehyde[13].

Experimental

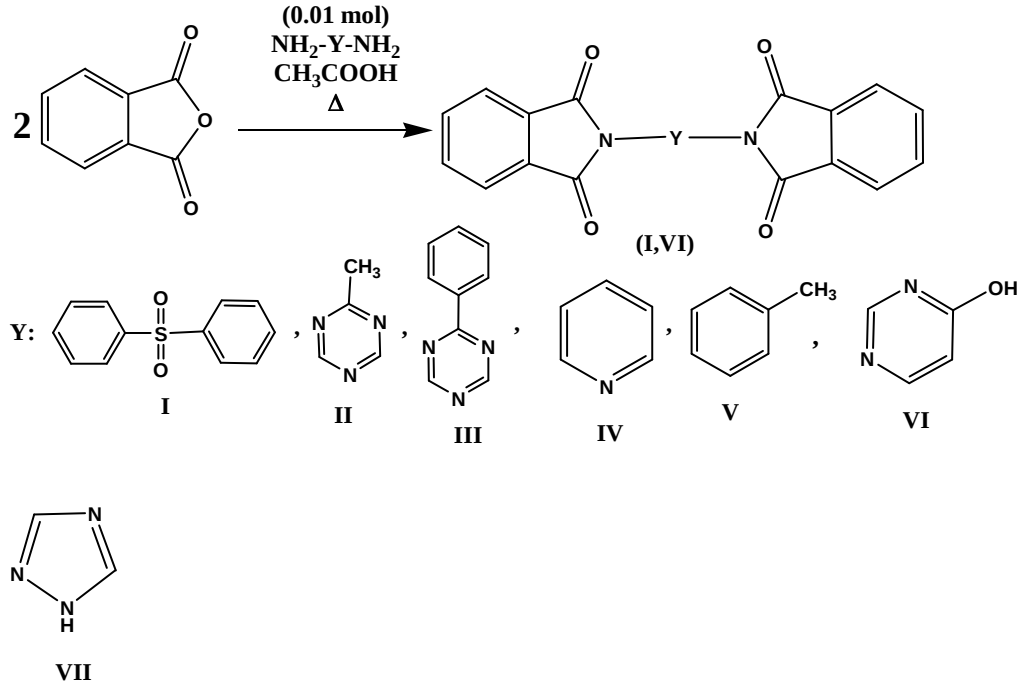
The course of reaction and Purity of the compounds was checked by TLCMelting points were measured by Electrothermal 1A9000 Digital-Series Melting point Apparatus and are uncorrected.FT-IR spectra were recorded on SHIMADZU FTIR –8400 Fourier Transform Infrared spectrophotometer as KBr disc ,

^{1}HNMR and ^{13}C NMR spectra were recorded on Brukerspecrospin ultra shield magnets 300 MHz instrument using tetramethylsilane (TMS) as an internal standared and DMSO-d6 as a solvent,Elemental analysis was performed on a Heraeus CHN-O rapid analyzer,The ESI+VE MS spectra were recorded on a BrukerDaltonics LC-MS spectrometer .U.V. spectrawere obtained from Shimadzu U.V-V isspectrophotometer in $CHCl_3$.

Methods of preparation:

Synthesis of N,N substituted phthaldicarboximide :

Phthalic anhydride (2.962gr, 0.02mole) and (2.48 gr,0.01 mole)4,4'-sulfonyldianiline ,(1.25gr,0.01mole)6-methyl-1,3,5-triazine-2,4-diamine, (1.87gr,0.01mole) 6-phenyl-1,3,5-triazine-2,4-diamine, (1.09gr,0.01mole) pyridine-2,6-diamine,(1.22gr,0.01mole)4-methylbenzene-1,3-diamine,(1.26gr,0.01mole)2,6-diamino pyrimidin-4-ol, (0.99 gr,0.01 mole) 3,5-Diamino-1,2,4-triazolwere refluxed in (50ml) acetic acid for two hourThereaction mixture was filtered off whilehot and the filtrate was allowed to coolThe solvent was evaporated to drynessand the residue was recrystallized fromethyl acetate petroleum ether (40-60ºc)to give the phthaldicarboximide derivatives [14,15,16]. The physical properties, elemental analysis data and spectral datashown in Tables (I,II,III,IV).



Scheme (I)

Table (I) : Physical properties of compounds (I-VII) .

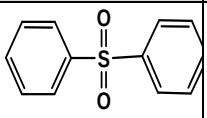
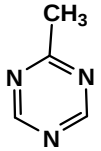
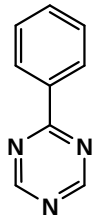
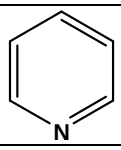
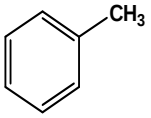
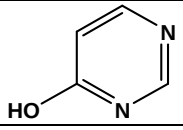
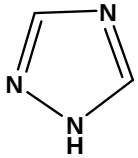
Comp. No.	Y	M.P (^{0}C)	Yield (%)	Molecular Weight	*Molecular formula*	Colour	U.V($CHCl_3$) λ max(nm)
I		**230**	**60**	508.5	$C_{28}H_{16}N_2O_6S$	yellow	295
II		**270**	**30**	385	$C_{20}H_{11}N_5O_4$	White	298
III		**201**	**40**	447	$C_{25}H_{13}N_5O_4$	White	300
IV		**345**	**60**	369	$C_{21}H_{11}N_3O_4$	Brown	310
V		**246**	**65**	382	$C_{23}H_{14}N_2O_4$	White	280
VI		**180**	**70**	386	$C_{20}H_{10}N_4O_5$	White	316
VII		**290**	**75**	359	$C_{18}H_9N_5O_4$	White	317

Table (II) FT-IR Spectral data for compounds (I-IV)

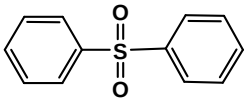
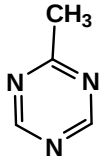
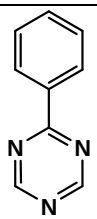
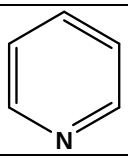
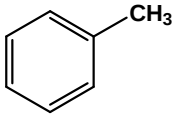
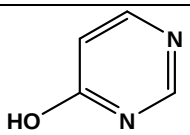
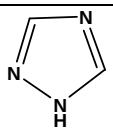
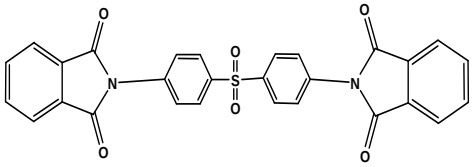
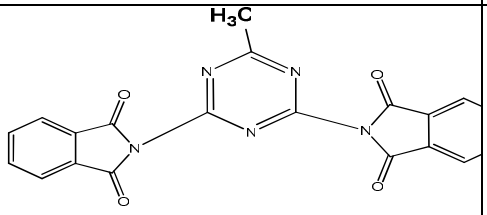
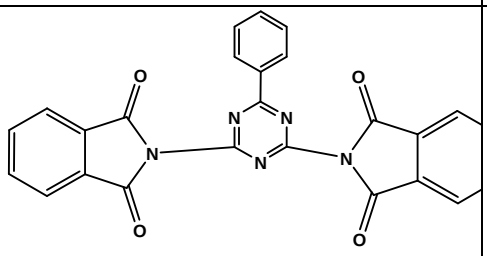
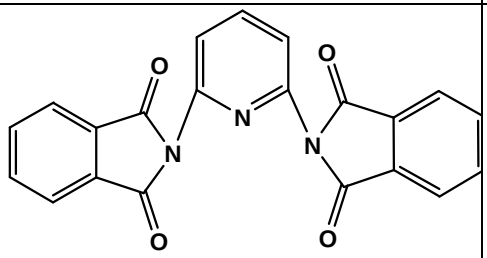
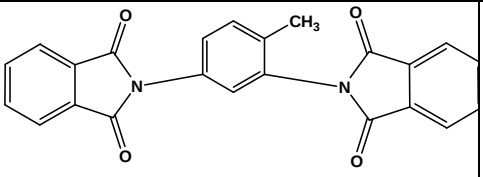
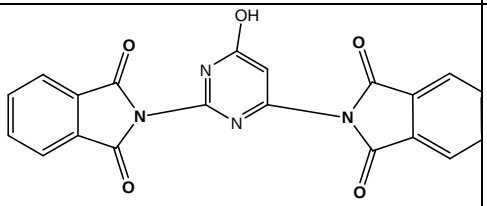
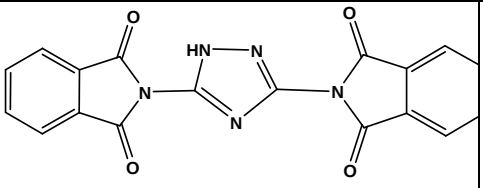
Comp. No.	Y	υ (C–H) *cm^{-1}*	υ(C=C) *cm^{-1}*	· C=O	*Others*
I		3197.4	1575.56	· · · · · · ·	1230.36(asymmetric – SO_2-) 1155.28(symmetric-SO_2-stretch)
II		3186.23	1600	1720.25	
III		3178.91	1610	1715.63	
IV		3169.25	1590.23	1724	
V		3100.01	1509.03	1723.09	
VI		3150.75	1593.23	1709.01	3284.18(OH)
VII		3160.23	159912	1710.16	

Table (III)Depacited Elemental Analysis (C.H.N) of sythesis Compounds

compounds	Calc.			Found		
	H%	N%	C%	H%	N%	C%
I	3.17	5.51	66.14	3.01	5.23	65.12
II	2.88	18.17	62.34	2.08	17.98	61.25
III	2.93	15.65	67.11	2.86	15.23	66.45
IV	3.00	11.38	68.29	2.93	11.03	67.89
V	3.69	7.33	72.25	3.59	6.89	71.56
VI	2.61	14.50	62.18	2.59	14.45	61.45
VII	2.52	19.49	60.17	2.49	19.39	60.01

Table (IV) ^{1}H-NMR and ^{13}C-NMR spectral data for some of the prepared compounds.

Compd. No.	Compd. Structure	^{1}H-NMR spectra data	^{13}C-NMR spectra data
I		7.81-7.86(m,8H,Ar), 7.85(m,8H,Ar phthalic anhydride)	122.6,128.5,137(12C,Ar), 127.6,132,132.3(12C,Ar,phthalic anhydride),170.3(2C,2C=O)
II		2.35(s,H3,$\underline{CH_3}$) ,7.85(s,8H,Ar-phthalic anhydride)	25.2(CH_3),127.6,132,132.3(12C,phthalic anhydride) ,167.1(4C,4C=O),176.8(2C,2$\underline{C}$-N),180.7(1C,CH_3-Ar)
III		7.48,7.50,8.36(m,5H,Ar), 7.85(s,8H,Ar-phthalic anhydride)	127.6,132,132.3(12C,Ar-phthalic anhydride),128.8,129.3,127.5,130.6(6C,Ar),174.9,177.6(3C,Ar),167.1(4C,4C=O)
IV		5.92(d,2H,Ar), 7.13(m,1H,Ar), 7.85(s,4H,Ar)	99.3,140.6,146.7 (5C,Ar),127.6,132.3,132(12C,Ar-phthalic),167.1(2C=O)
V		2.35(s,3H,$\underline{CH_3}$-Ar**),**7,7.02,7.90 (m,3H,Ar),7.85 (s,8H,Ar**)**	19.2(CH_3),117.1,113.2,129.9,135.7,129.9(6c,Ar),127.6,132.3,132(12C,Ar-phthalic anhydride) 167.1(2C=O)
VI		4.96(s,1H,Ar),7.85(s,4H,Ar),11.40(s,1H,O$\underline{H}$)	88,171.7,160.2,165.9(4C,Ar),127.6,132.3,132(6C,Ar-phthalic),170.3(2C,2C=O)
VII		7.85(s,8H,Ar),9.61(s,1H,NH)	127.6,132.3,132(6C,Ar),148(2C,$\underline{C}$-N),167.1(2C,2C=O)

Result and Discussion

The product (I-VII) was formed from the reaction of two molecules of phthalicanhydride for each mole of diamine. The infrared of products exhibited characteristic peak at 1720.25 cm^{-1} due toν (C=O) group and no absorption band due to NH_2 group.The UV spectra showedλmaxat 280-316.^{1}H-NMR for compounds (I-VI)show single signal at (7.85 ppm) due to aromatic proton of phthalic.^{1}H-NMR for compounds (II,V)show single signal at (2.35ppm) due to(CH_3)group,.^{1}H-NMR for compounds (VI)show single signal at (11.40ppm) due to(OH)group and^{1}H-NMR for compound (VII) show single signal at (9.61 ppm) due to(NH)group.^{13}C-NMR of compounds (I-VII)showed signals at (127,132,132.9ppm) due to aromatic carbons ofphthalic anhydrideand signal at (170.3ppm) due toImidic C=O.^{13}C-NMR spectrum of compound (I) showed signal at (122.6,128.5,137.7 ppm) due to aromatic carbons of sulphonyl^{13}C-NMR spectrum of compound (II,V) showed signal at (25.2,19.2 ppm) due to CH_3 group,^{13}C-NMR spectrum of compound (III)showed signal at(128.8,129.3 ,127.5,130.6) ppm due to aromatic carbons of aromatic ring of6-phenyl-1,3,5-triazine-2,4-diamine. ^{13}C-NMR spectrum of compound (VI) showed signals at(99.3,140.6,1467 ppm) due to aromatic carbons of pyridine^{13}C-NMR spectrum of compound (VI)showed signals at (88,171.7,160.2,165.9) due to aromatic carbons of pyrimidin-4-ol,^{13}C-NMR spectrum of compound (VII)showed signal at(148ppm) due to 1,2,4-triazole .

Antimicrobial activity

The antimicrobial activity of both categories of compounds was determined by the disc diffusion method [17]. The *in vitro* antimicrobial activity was carried out in two gram positive bacteria, and two gram negative bacteria The gram positive bacteria used were *Staphylococcus aureus*and *Bacillus subtilis*, gramnegative bacteria used were *Escherichia coli* and *Klebsiella pneumonia.* The compounds were tested at a concentration of 100µg/ml in Dimethylsulfoxide. The zoneof inhibition was compared after 24 h of incubation at 37° against Ciprofloxacin (100µg/ml) as standards forcomparison of antibacterial activity **(table V)**In general, all synthesized compounds exhibited good inhibitory activityagainst tested pathogenic microorganism(***S. aureus,B. subtilis,E. coli,K. pneumonia)***peculiar against (***S. aureus***).

Table(V) Antimicrobial activity of N,N substitutedphthaldicarboximide

Compound	Zone of inhibition (mm)			
	Gram positive bacteria		Gram negative bacteria	
	S. aureus	*B. subtilis*	*E. coli*	*K. pneumonia*
I	**7**	**7.5**	**7**	**7.5**
II	**8**	**8**	**6.5**	**7.5**
III	**7.5**	**7.5**	**7.5**	**7.5**
IV	**8**	**7.5**	**7**	**7**
V	**7.5**	**7.5**	**7.5**	**7.5**
VI	**7**	**7**	**7.5**	**7**
*****	**10**	**10**	**9.5**	**9.5**

*****_Ciprofloxacin (Standard)_

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