International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.6, No.1, pp 324-333, Jan-March 2014

Synthetic of Phthalimides via the reaction of phthalic anhydride with amines and evaluating of its biological and anti corrosion activity

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Abstract: A series of phthalimide **(I-VI)** were prepared in satisfactory yields by reaction of phthalic anhydride with amines(amino pyridine,5-methyl amino pyridine,4-methyl amino quinolin ,aminobenzotiazol,4-amino antipyrine, fluoren-9(9aH)-ylidene)hydrazine) The structure of synthesized has been established on the basis of their spectral (FT-IR ,Mass ,^{1}H,^{13}C-NMR,elemental analysis) data. The purity of the compounds was confirmed by TLC. The structures of all the compounds were in good agreement with elemental analysis and spectral data. The synthesized compounds were screened for their antibacterial activity against four microorganisms ***Staphylococcus aureus, Bacillus. subtilis***, ***Escherichia Coli and Klebsiella pneumonia*** and they were found to exhibit good to moderate antibacterial activity, these compounds were tested to determine their ability to inhibit corrosion of mild steel in 1 mol.l^{-1} H_2SO_4.
Keywords: phthalic anhydride ,amines **,**phthalimides, antibacterial activities, anticorrosion, mild steel.

1.Introduction

Phthalimide and *N*-substituted phthalimides are an important class of compounds because they possess important biological activities including anti-inflammatory activity[1], analgesic activity[2] and hypolipidemic activity[3], and also it is used in organic synthesis and other industrial fields such as in drugs synthesis for the acetylenic phthalimides showed pharmaceutical activity to be anticholinergic agents and anti-Parkinsonian agent[4,5]A survey of the literature has revealed that phthalimides derivative and analogues of their potential in a number of areas such as amino piptidase inhabitation[6] anticonvulsants activity[7] and promotion of tumor necrosis factor alpha (TAIF alpha) production[8] Many amides can be used for the preparation of synthetic polymers, which can be used as insulating coating in electrical equipment[9] and plastic heat resistant glass fiber[10] A number of imides also can be used as plant growth regulators and some of them are usefully as herbicides[11,12] also some of them have been employed as inhibitors against mammalian, plant, bacterial and fungal copper-containing amine oxidases[13]. Whereas other substituted phthalimides demonstrated inhibitory effect on the tested microorganisms[14,15], moreover they also employed as prevulcanization inhibitor used in sulphurcured rubber polymer systems[16].

In view of interesting range of the products from the reaction of Phthalic anhydride with heterocylces amines, it was decided 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 phthal aldehyde The chemical structures of the synthesized compounds were confirmed by means of UV, IR, 1H-NMR.,LC-Ms, Elemental analysis, The synthesized compounds were screened for antibacterial activity against *Staphylococcus aureus, Bacillus. subtilis, Escherichia Coli and Klebsiella pneumonia,* And the inhibiting action of compounds on the corrosion steel in 1M H_2SO_4 solution has been investigated. The electro chemical techniques such as polarization measurements were used in this study .Differences in behavior of inhibitors were explained based on structural properties of investigated inhibitors.

2.Experimental

The course of reaction and Purity of the compounds was checked by TLC and iodine as the visualizing agent.,Melting 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 Bruker specrospin ultra shield magnets 300 MHz instrument using tetramethyl silane (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 Bruker Daltonics LC-MS spectrometer . U.V. spectra were obtained from Shimadzu U.V-V is spectrophotometer in $CHCl_3$.

2.1. Methods of preparation:

2.1.1 :Synthesis of N- substituted phthalicarboximide :

Phthalic anhydride (1.48gr, 0.01 mole) and (0.94gr,0.01mole)amiopyridine,(1.08gr,0.01mole)4-methylamino pyridine ,(1.58 gr,0.01mole) 4-Methylamioquinolin,

(1.50gr,0.01mole)2-aminobenzothiazol,(2.03gr,0.01mole)4-aminoantipyrine,(1.96gr,0.01mole) fluoren-9(9aH)-ylidene)hydrazine, were refluxed in (50 ml) acetic acid for 4 hour The reaction mixture was filtered off while hot and the solvent was evaporated The solid separated was filtered and recrystallized from ethanol[17-19]. Scheme. (1).

The physical properties, elemental analysis data and spectral data shown in Tables (**I,II,III,IV**).

3.Result and Discussion:

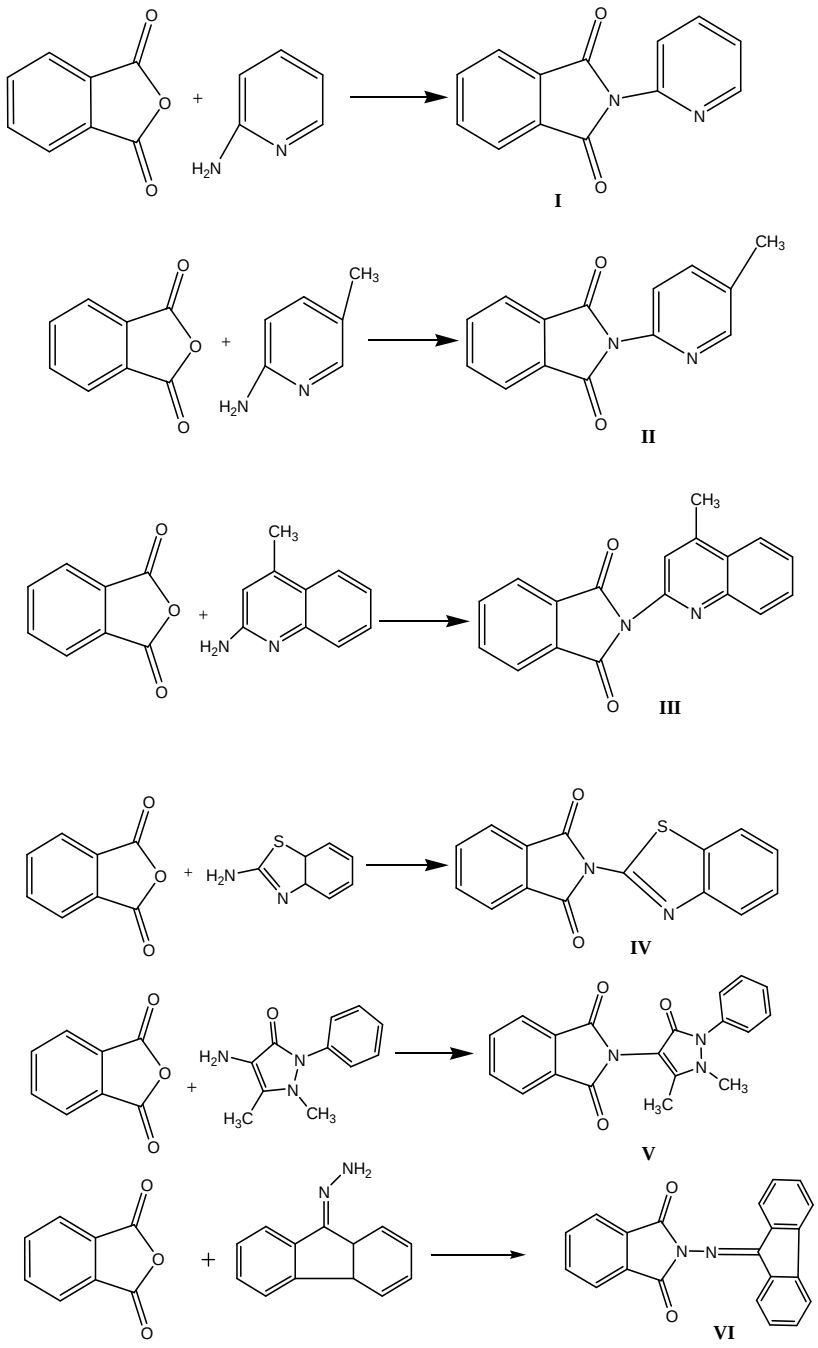
3.1.Chemistry

The product (I-IV) was formed from the reaction of one molecule of phthalic anhydride for mole of amine. The infrared of products exhibited characteristic peak at 1720.25 cm^{-1} due to ν (C=O) group and no absorption band due to NH_2 group. Compound (V) show two absorption at (1720.19) cm^{-1} due to ν (C=O) group of phthalic in addition to absorption at (1720.60) cm^{-1} due to (C=O) of antipyrine group. Compound (VI) show absorption at (1619.98) cm^{-1}due to (C=N). The UV spectra of compounds showed λmax at 298-316.

^{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,III)show single signal at (2.16,2.55ppm) due to(CH_3) group,also ^{1}H-NMR for compounds (V) show single signal at (2.20,3.11ppm) due to(CH_3) group and ^{1}H-NMR for compound (VI) show signals at (7.35-7.82 ppm) due to aromatic proton of a cridine ring

^{13}C-NMR of compounds (I-VI) showed signals at (127.6-132.3ppm) due to aromatic carbons of phthalic anhydride and signal at (170.3ppm) due to Imidic C=O**.** ^{13}C-NMR spectrum of compound (I) showed signal at (109.9,113.3,138.39,147.6ppm) due to aromatic carbons of pyridine, ^{13}C-NMR spectrum of compound (II) showed single signal at (24.3 ppm) due to CH_3 group , and signal at (109.1,137.4,123,148.7,145.3ppm) due to aromatic Carbone of pyridine ^{13}C-NMR spectrum of compound (III) showed single signal at (22.6ppm) due to ($\underline{CH_3}$-Ar) and signal at (111.2,120.3,121.7,122.6,128.3,125.7,144,148.5,167.3) ppm due to aromatic carbons of

aromatic ring of (quinoline) ^{13}C-NMR spectrum of compound (IV) showed signals at(121.8,124.5,125.9,125.2,121.7,149ppm) due to aromatic carbons of benzothiazole.^{13}C-NMR spectrum of compound (VI) showed single signals at(39.3 ,12.5ppm) due to CH_3 group and signal at (103.4ppm) due to (C=O) and signals at (113.2, 119.2 ,129.3,136.2 ppm) due to aromatic carbons ofdimethyl-2-phenyl-pyrazol-3-one, ^{13}C-NMR spectrum of compound (V) showed signal at(127.8,129.7, 130.1, 128,131.6,143,130.1 ppm) due to aromatic carbons of fluorine[20-21].



Scheme 1. :Synthesis of Phthalimide compounds(I-VI)

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

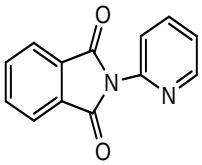
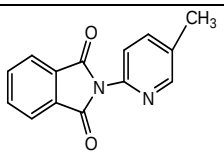
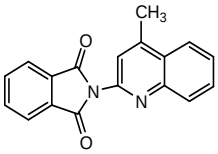
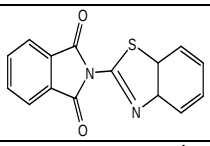
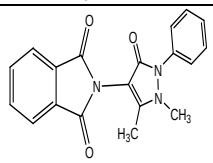
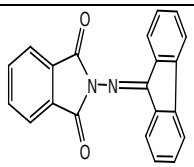
Comp. No.	structure	M.P (^{0}C)	Yield (%)	Molecular Weight	*Molecular formula*	color	U.V($CHCl_3$) λ max (nm)
I		**228**	75	224.21	$C_{13}H_8N_2O_2$	White	298
II		**172**	50	238.24	$C_{14}H_{10}N_2O_4$	White	298
III		**199**	42	238.24	$C_{14}H_{10}N_2O_4$	White	304
IV		**248**	70	282.32	$C_{15}H_{10}N_2O_2S$	White	314
V		**212**	75	333.34	$C_{19}H_{15}N_3O_3$	White	288
VI		**266**	79	326	$C_{21}H_{14}N_2O_2$	Red	316

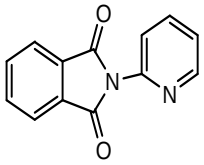
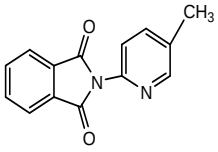
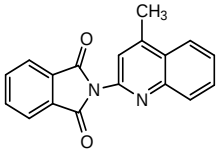
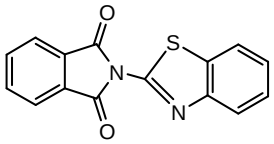
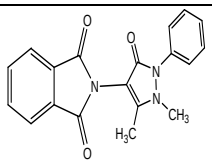
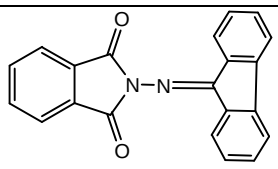
Table (II) FT-IR Spectral data for compounds (I-V)

Comp. No.	υ (C–H) cm^{-1}	υ(C=C) cm^{-1}	υ C=O	*Others*
I	3189.4	1580.38	1713.44	
II	3178.23	1605.45	1720.25	
III	3214.75	1620.88	1715.63	
IV	3168.25	1588.09	1724.05	
V	3120.01	1591.95	1720.19	1720.60cm^{-1}(C=O),
VI	3046.05	1593.88 – 1468.53	1717.3	1617.98 (C=N)

Table (III) Depicted Elemental Analysis (C.H.N) of synthesis Compounds

compounds	Calc.			Found		
	H%	N%	C%	H%	N%	C%
I	3.60	12.49	69.64	3.55	12.50	69.60
II	4.23	11.76	70.58	4.20	11.75	70.50
III	4.23	11.76	70.58	4.22	11.70	70.55
IV	3.57	9.92	63.81	3.5	9.90	63.51
V	4.54	12.61	68.46	4.53	12.59	68.43
VI	4.32	8.58	77.29	4.31	8.56	77.27

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		^{1}H-NMR: 6.70,6.73,7.44,8.11(4H,Ar-pyridine),7.85(4H,Ar-phthalic)	^{13}C-NMR :109.9,113.3,138.3 ,147.6(5C,Ar-pyridin) ,132,132.3,127.6(6C,Ar-phthalic),170.3 (2C,2C=O)
II		^{1}H-NMR:2.16(s,3H,$\underline{CH_3}$-Ar), 7.38(d,1H,Ar-pyridin) ,8.09(s,1H,Ar-pyridin) ,6.61(d,1H,Ar-pyridin) ,7.85(4H,Ar-phthalic)	^{13}C-NMR:24.3 (CH_3-Ar) ,109.1,137.4,123,148.7,145.3 (5C,Ar-pyridin),132.3, 127.6(6C,Ar-phthalic) ,170.3(2C,2C=O)
III		^{1}H-NMR: 2.55(s,3H,CH_3),6.48,7.36,7.62,7.79,8.03(m,4H,Ar),7.85(m,4H,Ar)	^{13}C-NMR: 22.6($\underline{CH_3}$-Ar) 111.2,120.3,121.7,122.6,128.3,125.7,144,148.5,167.3(9C,Ar),127.6,132,132.3(6C,Ar-phthalic) 170.3(2C,2C=O)
IV		^{1}H-NMR: 7.51,7.53,8.12,8.23(4H,Ar),7.85(4H,Ar-phthalic)	^{13}C-NMR: 121.8,124.5,125.9,125.2,121.7,149(6C,Ar),132.3,127.6,132(6C,Ar),167.1(2C,2C=O)
V		^{1}H-NMR: 2.20(s,3H,CH_3),3.11(3H,$\underline{CH_3}$-N),7.07,7.35,7.51(5H,Ar),7.85 (4H,Ar-phthalic)	^{13}C-NMR:39.3(1C,$\underline{CH_3}$-N) ,12.5(1C,CH_3),103.4($\underline{C}$-C=O) ,133.7($\underline{CH_3}$-C-N) ,160.7(C=O), 165.8 (2C,2C=O) ,113.2, 119.2 ,129.3,136.2(6C,Ar),127.6,132,132.3(6C,Ar-phthalic)
VI		^{1}H-NMR:7.35, 7.62,7.82 (8H,Ar-fluorene),7.85(4H,Ar-phthalic)	^{13}C-NMR:127.8,129.7, 130.1, 128,131.6,143,130.1 (12C,Ar) ,155.6(C,$\underline{C}$=N),127.6, 132,132.3(6C,Ar-phthalic) ,168(2C,2C=O)

3.2.Antimicrobial activity

The antimicrobial activity of both categories of compounds was determined by the disc diffusion method[22]. 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*, gram negative bacteria used were *Escherichia coli* and *Klebsiella pneumonia*

The compounds were tested at a concentration of 100µg/ml in Dimethylsulfoxide. The zone of inhibition was compared after 24 h of incubation at 37° against Ciprofloxacin (100µg/ml) as standards for comparison of antibacterial activity (table V) In general, all synthesized compounds exhibited good inhibitory activity against tested pathogenic microorganism (***S. aureus, B. subtilis, E. coli, K. pneumonia)*** peculiar against (***S. aureus, B. subtilis***)

3.3.Anticorroision activity:

Electrochemical measurements: Were carried out in conventional three –electrode system in CHI 604 instrument (USA) at 303 K. The working electrode (mild steel) has ageometric area of 1 cm^2.The saturated calmmel and platinum electrodes were used as reference and auxiliary electrodes. Equation (1) show the calculation of IE from corrosion current[23-26].

$$IE = \left(1 - \frac{icorri}{icorr0}\right) \times 100 \qquad (1)$$

Table **(VI)** shows the corrosion Potential (*Ecorr*), corrosion current (*icorr*) and Tafel slopes (*ba* and *bc*) values of mild steel in 1 $mol.L^{-1}H_2SO_4$ Solution in the absence and presence of inhibitor of all the six compounds at 303K calculated from Scheme(2-7) from Table (**VI**) it is clear that compounds (**IV,V)** offers maximum inhibition efficiency among the six compounds because compound (**IV**) have two heteroatom (S,N) which have unshared pairs of electrons and behave as the reaction centre for the adsorption process and the resulting adsorption film acts as a barrier isolating the metal surface from the corrodent, Compound (**V**) have Aminoantipyrine in his structure and it is evident that 4-AAP is a heterocyclic compound containing nitrogen and oxygen atoms ,which could easily be protonated in acidic solution and some π- electrons exist in this molecule. The studied compounds suppress the anodic reaction to greater extent than the cathodic one. This behavior is typical of mixed type inhibitors with anodic predominance.

The difference in the efficiency is referred to the molecular structure effect,Which have π-delocalized system of phthalimid (C=O) and unshared pairs of electrons of N and O atoms that may cause the increasing or decreasing of the electron density on center of adsorption and leading to an easier electron transfer from the functional group (C=O-group) to the metal ,producing grater coordinate bonding and hence different adsorption and inhibition efficiency.

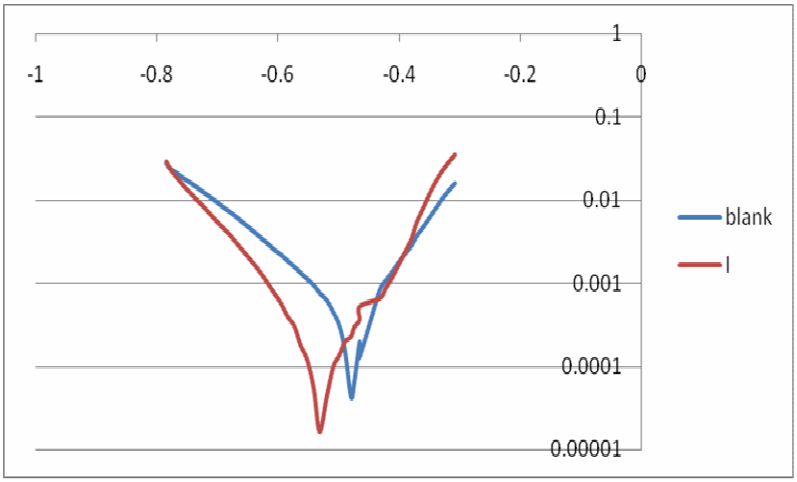
Table(V) Antimicrobial activity of N substituted phthalcarboximide

Compound	Zone of inhibition (mm)			
	Gram positive bacteria		Gram negative bacteria	
	S. aureus	*B. subtilis*	*E. coli*	*K. pneumonia*
I	**9.5**	**7**	**6.5**	**6.5**
II	**10**	**9**	**7**	**6**
III	**12**	**13**	**6**	**6**
IV	**13**	**14**	**5.9**	**8**
V	**11**	**15**	**7**	**6**
VI	**10**	**10**	**8**	**7**
*****	**14**	**9**	**9**	**7.5**

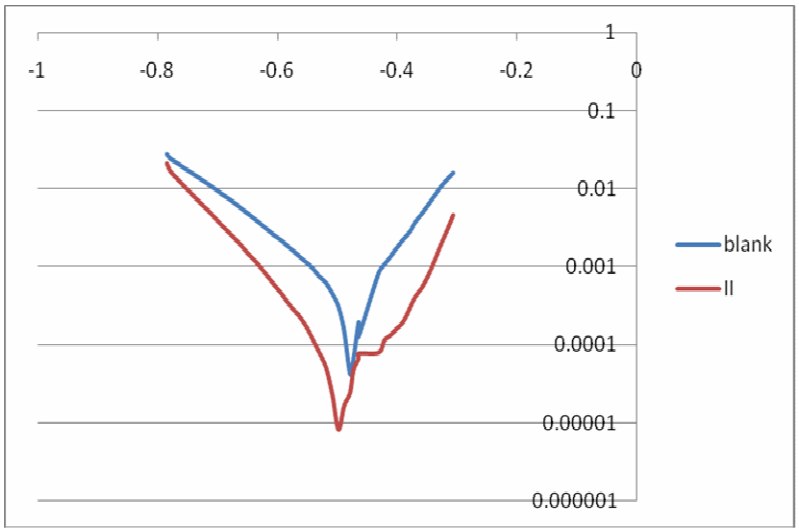
***** *Ciprofloxacin (Standard)*

Table (VI) :Corrosion kinetic parameters of mild steel exposed to 1 mol.L $^{-1}H_2SO_4$solution in absence and presence of inhibitors

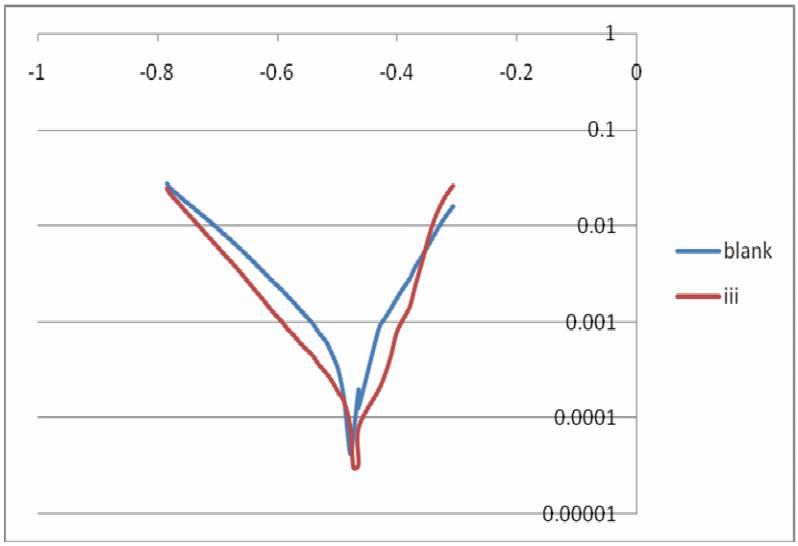
COMPOUND Name	-Ecorr/mv	icorr/ $\mu A.cm^{1-}$	ba /(mv.dec -1)	bc /(mv.dec -1)	Rp	IE(Using icorr) %
blank	480	480	6.38	12.43		BLank
I	510	100	7.86	14.55	221.58	79.16
II	500	70	10.19	11.17	330.54	85.16
III	420	173	4.47	25.78	95.614	63.95
IV	450	199	6.28	19.52	71.13	89.58
V	520	60	8.18	11.82	349.83	87.5
VI	500	70	10.19	11.17	330.54	85.16



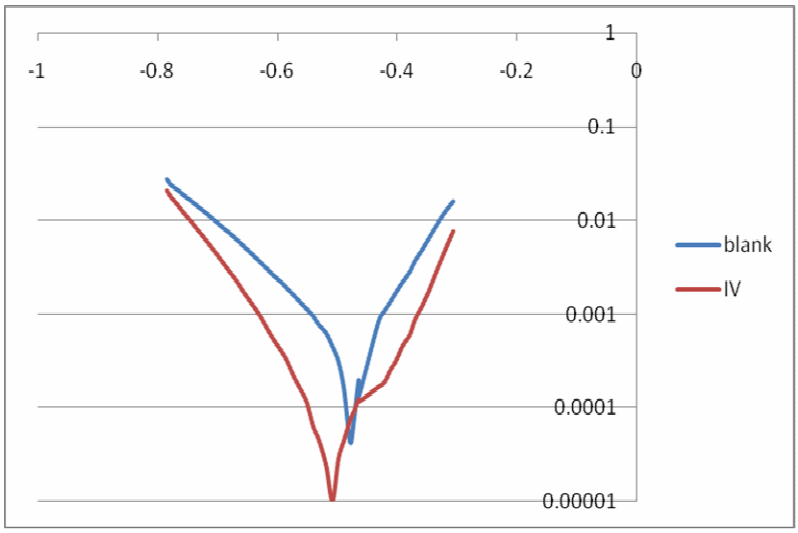
Scheme.2 Tafel plots obtained for mild steel corrosion in absence and presence of compound (I)



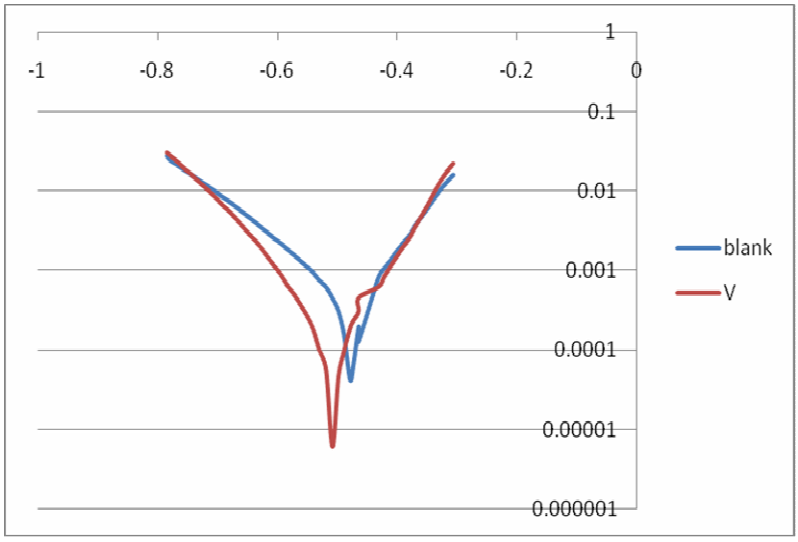
Scheme.3 Tafel plots obtained for mild steel corrosion in absence and presence of compound (II)



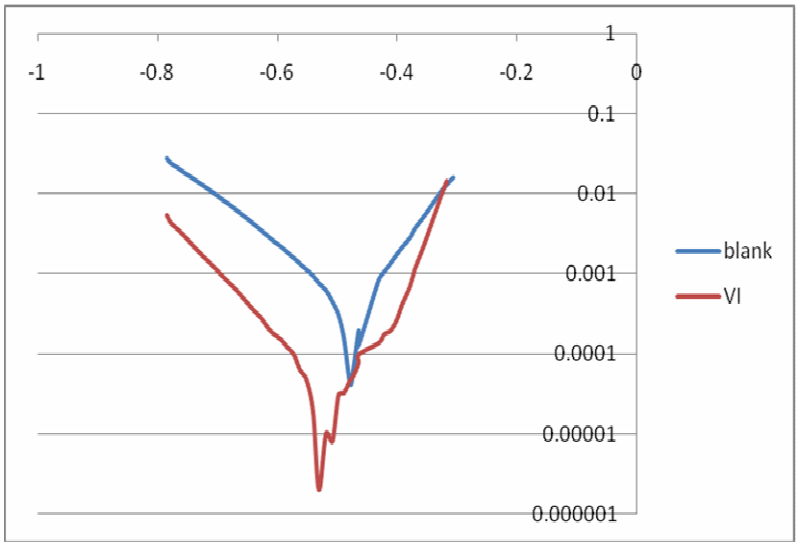
Scheme.4 Tafel plots obtained for mild steel corrosion in absence and presence of compound (III)



Scheme 5. Tafel plots obtained for mild steel corrosion in absence and presence of compound (IV)



Scheme 6. Tafel plots obtained for mild steel corrosion in absence and presence of compound (V)



Scheme .7 Tafel plots obtained for mild steel corrosion in absence and presence of compound (VI)

4.Conclusions

The main aim of the present study is to synthesize and investigate the antimicrobial and anti corrosion activity of new heterocyclic derivatives containing phthalimide ring with the hope of discovering new structures serving as potential broad spectrum antimicrobial agents and anti corrosion agents. Compounds (**I-VI**) which contain functional moiety is most potent against bacterial it's showed good antimicrobial activity.from the results it is obvious that all six studied compounds function as effective corrosion inhibitors in 1 mol.$L^{-1}H_2SO_4$ medium with compounds **II, IV,V,VI** being the best of six compounds.

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