Available online at www.derpharmachemica.com

Scholars Research Library

Der Pharma Chemica, 2015, 7(11):240-242
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

Synthesis, characterization and antimicrobial activity of some new phthalimide derivatives

Omran Fhid*[1], A. M. Doma[2], Talal H. Zeglam[1], Jamal Baki[1], Majda Zitouni[1] and Wafa Sdera[1]

[1]*Department of Pharmaceutical Chemistry[1], Department of Pharmacology 2, Faculty of Pharmacy, University of Tripoli- Libya*
[2]*Department of Pharmacology, Faculty of Pharmacy, University of Al-mergab– Libya*

ABSTRACT

*The synthesis, characterization and spectroscopic studies of new N-substituted pthalimide analogues **2–5**with antibacterial activity were described. The compounds were synthesized using phthalic anhydride with various amines (aminoethanol , aminopropanol,amino ethyl morphline, amino ethyl morphline iodide)in reflux synthesizer. The purity of the synthesized products were monitored by using TLC in an appropriate developing system. The structures of the new synthesized compounds were confirmed byusing physical and spectral analysis. Antibacterial activity of the synthesized derivatives **2-5** were done in comparison with Phenol as standard compound. All the selected compounds **2-5** showed very good activity against staphylococcus aureus(S.aureus), Escherichia coli (E. Coli) when compared with Phenol.*

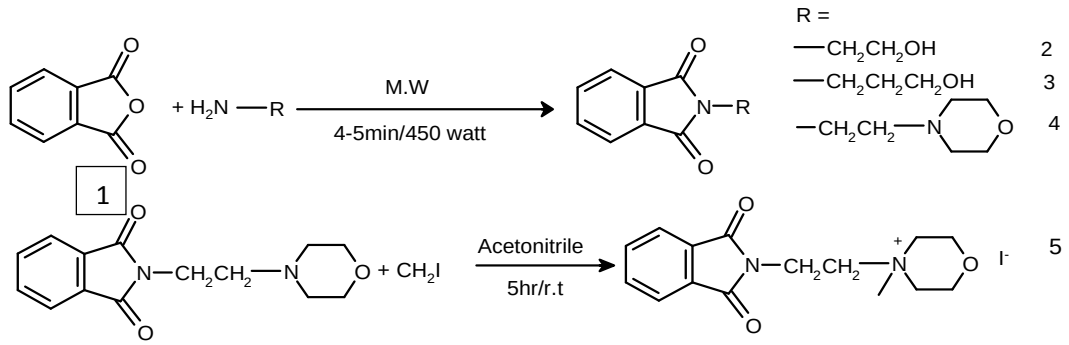
Key words: Phthalimide, Phenol, Antimicrobial activity, Reflux synthesizer.

INTRODUCTION

Recently, phthalimide and some of its derivatives have proved to have important biological effects similar or even higher than known pharmacological molecules and so their biological activity is being a subject of biomedical research [1-4].

“Antimicrobial agent” is a general term used to refer to any compound which include antibiotics, antiseptic and disinfectants, and other substances that acts against microorganisms. Antibiotics are antimicrobial agents produced by bacteria, fungi or of synthetic in nature [5] that kill (bactericidal) or inhibit (bacteriostatic) other microorganisms [6].

In general, they are an essential part of infection control practices to decrease the rate of hospital acquired infections [7].Many studies shown that phalimide derivatives have a significant antimicrobial activity [8]. As a result, we have synthesized and evaluated the antibacterial activity of some new N-substituted-phthalimides (**Schemes 1**) and interestingly, All of them have shown significant antibacterial activity.



Scheme.1. synthesis of phthalimide derivatives 2-5

MATERIALS AND METHODS

All chemicals and solvents, reagents used in the present study were of analytical grade purchased from Sigma**,**Fischer. All the solvents were used after distillation. The melting points were determined by open capillary methodand were uncorrected. The purity of compounds was confirmed by thin layer chromatography using Silica coatedaluminium sheets(silica gel 60 F254). IR spectra were recorded using KBr on FTIR Shimadzu.

Table .1. physicochemical properties of the new synthesized compounds 2-5

Compounds	Rec.Solvent	M.P C°	Yield	IR(KBr) cm^{-1}
2-(hydroxyethyl)isoindoline-1,3-dione $C_{10}H_{11}O_3N$ (194.1)**2**	Petr.ether Chloroform (1:1)	138-140	64	3400 O-H 2900 C-H 1700 C=O 1050 C-N
2-(3-hydroxypropyl)isoindoline-1,3-dione $C_{11}H_{13}O_3N$ (213.8)**3**	Petr.ether Ethyl acetate (2:1)	77-79	88	3400 O-H 2900 C-H 1700 C=O 1050 C-N
2-(2-morpholinoethyl)isoindoline-1,3-dione $C_{14}H_{18}O_3N_2$ (263.8)**4**	Petr.ether	139-140	62	2800 C-H 1700 C=O 1050 C-N 1150 C-O 1030 C-N 1400 C-N
4-[2-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)ethyl]-4-methylmorpholin-4-ium iodide $C_{15}H_{21}O_3N_2$ I (390.8)**5**	Acetonitrile	294-296	54	=

General procedure for synthesis of compounds 2-4

Phthalic anhydride **1** (0.005 mole) was reacted with an equimolar amount of amine in microwave synthesizer. Themixture was heated at 450 watt, for 4-5 minutes. After cooling the precipitate was filtered off, washed with water and then recrystallized fromappropriate solvent (**Scheme.1. Table 1**).

Synthesis of morphline-ethyl-phthalimide iodide 5

To a solution of 2-(2-morpholinoethyl) isoindoline-1,3-dione **4** (1.0 mmol) in 5 ml of dry acetonitrile was added anequivalent amount of methyl iodide (1.0 mmol), and stirred at room temperature for 5h. The resulting precipitatewas filtered off, and recrystallized from acetonitrile (**Scheme. 1. Table. 1)**

RESULTS AND DISCUSSION

CHEMISTRY:

N-substituted-phthalimide derivatives were synthesized according to the preferred synthetic route. These derivatives were prepared from phthalic anhydride and appropriate aliphatic amines via direct fusion, with a yield varying from 62-88%. The purity of these compounds was determined by TLC and their structures were confirmed by IR. The physicochemical properties of the synthesized compounds are reported in **Table 1**.

BIOLOGICAL ACTIVITY:

All described, new phthilimido derivatives **2-5,** were evaluated *in vitro*for their antibacterial activity against *staphylococcus aureus*, *Escherichia coli*at conc. 100µg using phenol as standard . DMSO was used as a solvent control, nutrient agar was used as culture medium and the method employed was cup plate method [9,10]. All thecompound showed high brood-spectrum inhibitory activity against the tested Gram positive organisms. The results are listed in **Table. 2**.

Table .2. Antibacterial activity of the compounds 2-5

Comp. No.	Conc (100µg/100ml)	Antibacterial activity Zone inhibition (mm)	
		Gram-positive bacteria	Gram-negative bacteria
		S. aureus	*E. coli*
2	(100µg/100ml)	**2.2**	-
3	(100µg/100ml)	**3**	**1.3**
4	(100µg/100ml)	**3.2**	-
5	(100µg/100ml)	**2.9**	-
Phenol	5%	1	2
DMSO	-	-	-

CONCLUSION

Thus, we concluded that novel N-substituted Phthilimide produce significant antibacterial activity against *staphylococcus aureus (S.aureus*), *Escherichia coli (E. Coli*) when compared with standard compound.

Acknowledgment

The authors are thankful to the industrial research center for providing spectral data.

REFERENCES

[1] L.M. Lima, F.C.F. Brito, S.D. Souza, A.L.P. Miranda, C.R. Rodrigues, A.M. Fraga and .J.Barreiro, *Bioorg.Med. Chem. Lett.*, **2002**., 12, 1533.
[2] V.L.M. Sena, M. Srivastava, R.O. Silva and V.L.M. Luis, *IL Farmaco*., **2003**., 58, 1283.
[3] S. Barman, E.I. Newhouse and W.C. Neely, *Polym. Eng. Sci*., **2004**., 34, 279.
[4] T. Wang, Y.H. Zhang, H. Ji, Y.P. Chen and S.X. Peng, *Chinese Chem. Lett*., **2008**., 19, 26.
[5] L.M. Lima, F.C.F. Brito, S.D. Souza, A.L.P. Miranda, C.R. Rodrigues, A.M. Fraga and E.J. Barreiro, *Bioorg. Med. Chem.Lett.*, **2002**., 12, 1533.
[6] AhlamMarouf Al-Azzawi, *J. of university of anbar for pure science*, **2011** *Vol.5:NO.2* .
[7] Liasi, S. A.,1 Azmi, T. I., *Malaysian Journal of Microbiology*,**2009** , 5(1), pp. 33-37
[8] Gerald mcdonnell, *clinical microbiology reviews*,**1999**, 893-8512.
[9] Seeley H W& Van Denmar; P J, microbes in action: A laboratory manual of microbiology, (*DBTaraporevala Sons &Co Pvt Ltd*) **1975**, 55.
[10] Kavanagh F, *Analytical microbiology, (Academic Press, New york)*, **1963**, 12.