

Synthesis of Some New Maleamic Acid and Maleimide Derivatives of Trimethoprim (TMP), with Evaluating their Biological Activity

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ABSTRACT

Some new Maleamic acid derivatives of trimethoprim and their maleimide derivatives, In first step we obtained Amic which converted to Malimide in second step (cyclization).

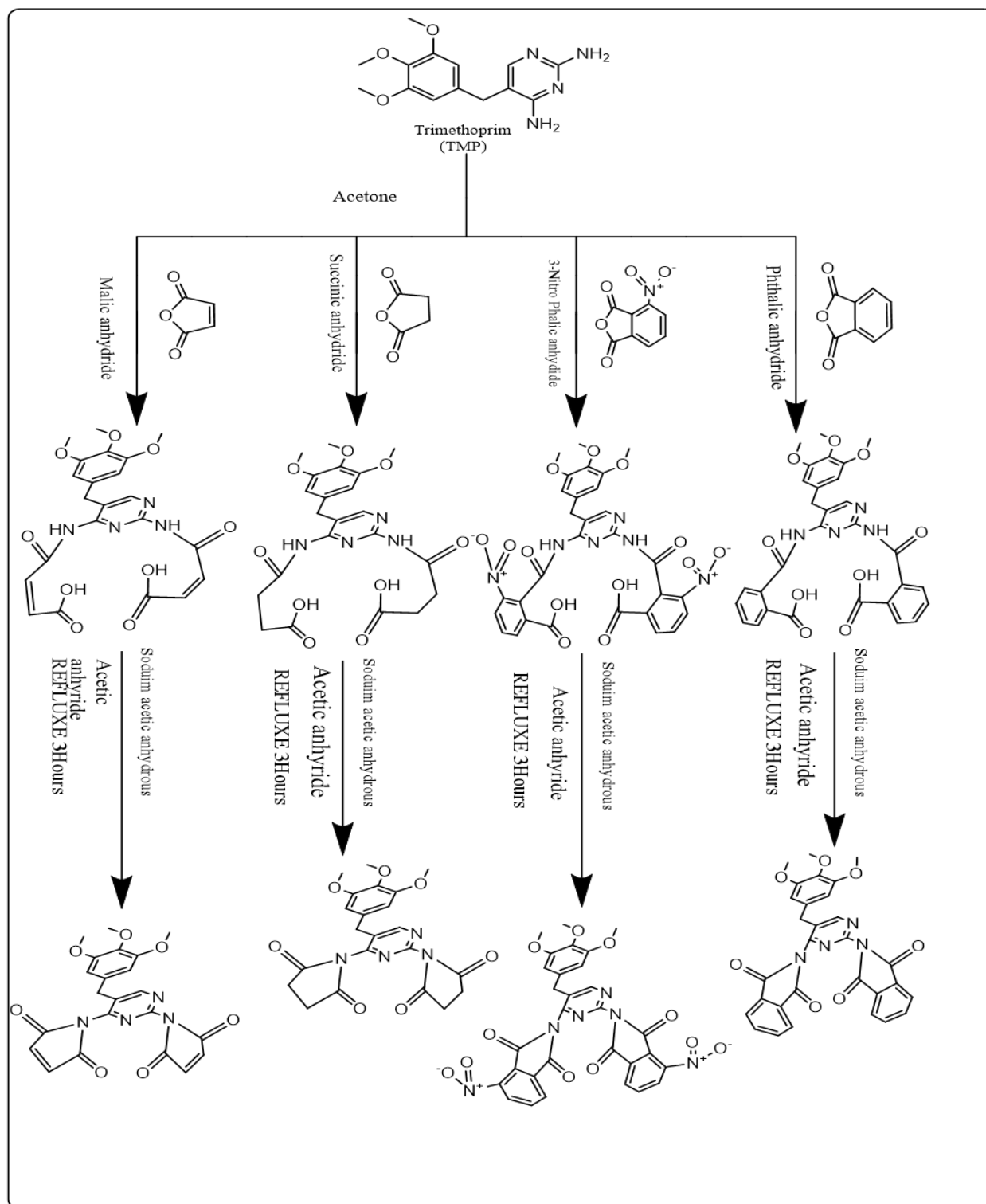
This work includes three different parts as shown below:

The present work involved synthesis of series of new heterocyclic derivatives containing:

First part: This part included the synthesis of trimethoprim derivatives, and produced AMIC compounds.

Second Part: This part including transfer the Amic acid in second step to maleimide via using of sodium acetate and acetic anhydride. See in scheme I.

Third Part: This part includes the evaluating of the antibacterial activities for some of the synthesized compounds. These activities has been specified against E.coli and Staph Areus for Gram strain, the results that has been obtained exhibited measurable activities, which is seen in Table 3-6.



Scheme (I)

INTRODUCTION:

Trimethoprim (TMP) is a heterocyclic amine with a wide spectrum of pharmaceutical applications. Trimethoprim is 2,4-diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine; the molecular formula is $C_{14}H_{18}N_4O_3$. It is a white to light yellow, odorless, bitter compound with a molecular weight of 290.3 and the following structural formula:

EXPERIMENTAL SECTION

Melting points were determined in open capillaries and are uncorrected. The IR spectra were recorded on Shimadzu FT IR – 8400S spectrophotometer using KBr pellets. ^1H NMR were recorded on Bruker 400 MHz.

Trimethoprim:

In this study, take (1 g) from trimethoprim, molecular weight (290.32g/mole) in addition solute with acetone in addition take (1.13 g) from malic anhydride, molecular weight (98.6 g/mole) and solute with acetone, in addition mixed together with motivation only will produced Amic 1 .

Note: take two mole from anhydrides for this reason, Adipic acid dihydrazide contain two side from carbonyl groups.

Anhydrides = malic, succinic, 3-nitro phthalic, phthalic and acetic.

Melting points

Nu	Materails	Points
1	D / Methibrine + 3-Nitro phthalic anhydride + Acetone	152 °C
2	E / Methibrine + Phthalic anhydride + Acetone	193 °C
3	G / Methibrine + Maleic anhydride + Acetone	171 °C
4	K / Methibrine + Succinic anhydride + Acetone	120 °C
5	M / Methibrine + 3-Nitro phthalic anhydride	More than 256 °C
6	L / Methibrine + Maleic anhydride (Direct)	More than 256 °C
7	Methibrine + Phthalic anhydride (Direct)	211 °C

8	Methibrine + Succinic anhydride (Direct)	174 °C
9	Methibrine	202 °C

Results and Discussion

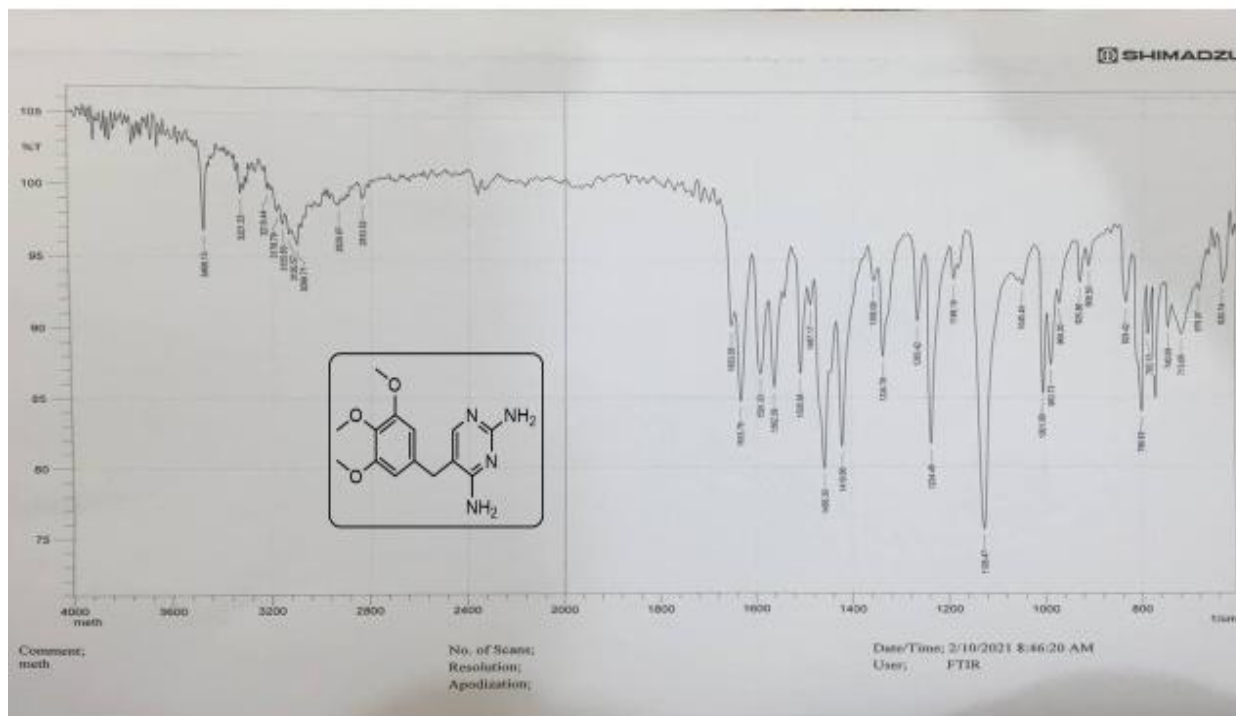


Figure (1) FT-IR for trimethoprim .

Comp. No.	ν (O-H)	ν (N-H)	ν (C-H) aromatic	ν (C-H) aliph.	ν (C=O) carbonyl	ν (C=O) amide	ν (C=C) aromatic
Trimeth	-	3400	3100	3000	-	-	1600
D	3640	3300	3075	2900	1700	1675	1475
E	3635	3255	3125	2950	1705	1688	1490
G	3640	3350	3050	2975	1710	1990	1525
K	3650	3300	3075	2900	1700	1675	1475
L	3640	3255	3125	2950	1705	1688	1490
M	3650	3350	3050	2975	1710	1990	1525

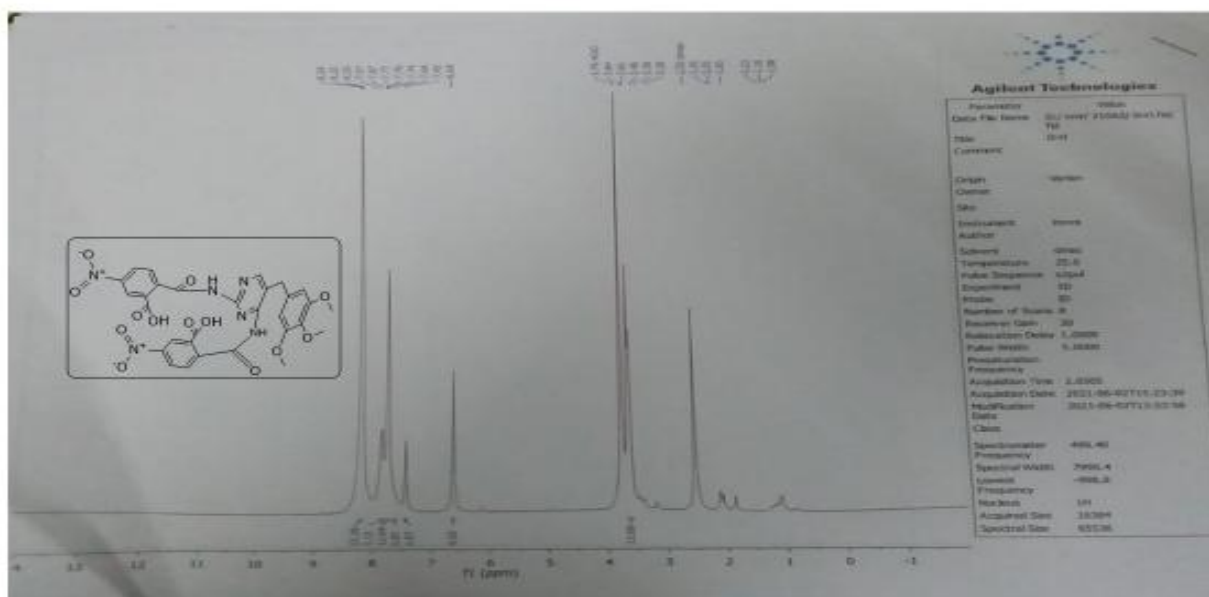


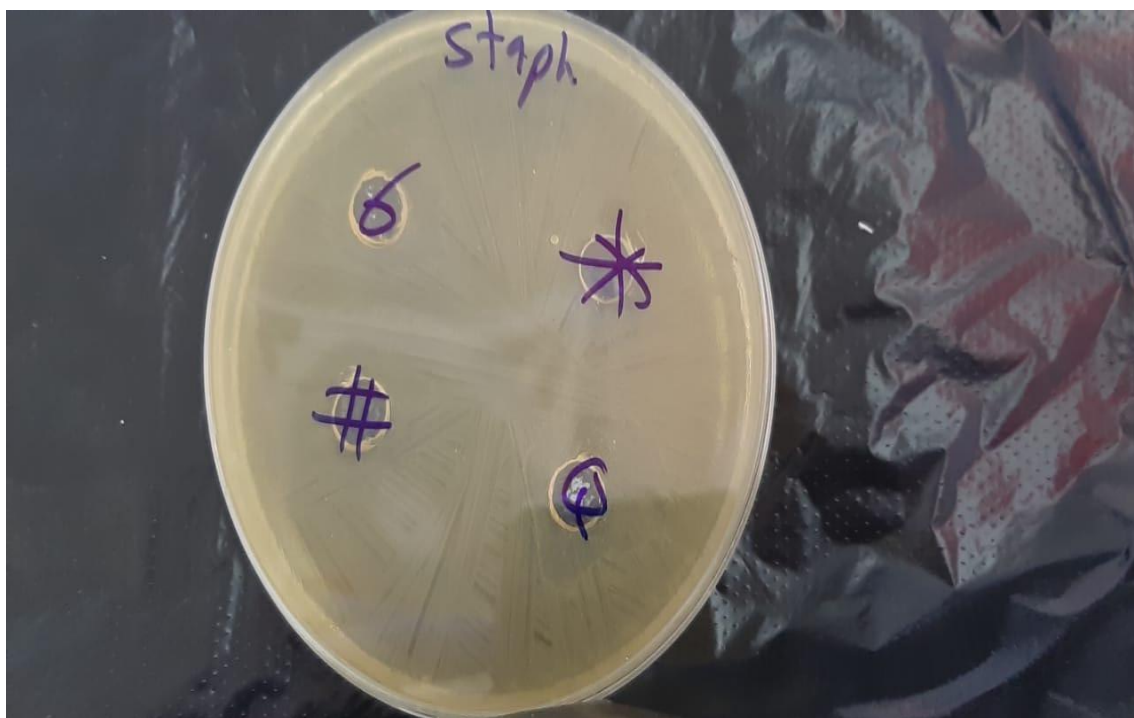
Figure (2) ^1H -NMR for compound (D)

Biological activity:

The biological activity of the following samples was carry out, and the results were as follows:

samples	E.coli	Staphylococcus
1	17	18
2	20	17
3	26	32
5	15	18
6	14	15
*	14	14
#	15	15
Q	13	13

Table 3-6



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