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Preparation and identification of some a new derivative for Trimethoprim drug

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Abstract: In this reaction new derivatives for Ttrimetheprim compound, which have high medicinal effectiveness, was prepared by the interaction of its coupling diazonium salt with some substituted phenol compounds (2-naphthol , 4-bromo phenol, 2,5-dimethoxy phenol ,2,4-dinitro phenol , 3-chloro phenol.Chemical structures of all products were confirmed by photometric methods such as U.V. visible and FTIR.The biological activities was also examined for these compounds.Gram + ve bacteria (bacillus) , Gram –ve bacteria (E-Coli) and fungi (Aspiringussb).

Key words: Preparation , identification , derivative , Trimethoprim .

Introduction

Trimethoprim and Trimethoprim derivative are type of medicine called an antibiotic[1], and its analogues[2]. It is formula structure C14H18N4O, and its molecular weight 290.32 g/mole its white to yellowish compound with bitter taste[3,4].The trade names of the combined product are Bactrim and Septra[3].

Therapeutic azo-compounds for drug delivery demostrete by Uhrich and Kathryn[5],and evaluation a novel vital dyes for intraocular surgery[6]

Azo compounds are chemical compounds with the general formula R-N=N-R', where R and R' can be either aryl (aromatic) or alkyl (aliphatic) functional groups. The N=N group is called an azo group, although the parent compound, HNNH, is called diimide. The more stable azo compounds contain two aryl groups. Azo compounds with alkyl functional groups are particularly unstable and should be handled with care, to prevent them from exploding.

Aryl azo compounds have vivid colors, especially reds, oranges, and yellows. They are therefore used as dyes and are classified as azo dyes. Examples include methyl red and Disperse Orange 1. The ability to manufacture azo dyes was an important step in the development of the chemical industry.Daizonium salt that product from use primary aromatic amine be constant in low temperatures between (0-5)C0,but it dissociation rapidly in the high temperatures[7] Diazonium salt is very active and it important and common compounds for prepare azo compounds[8]..

Phenols common compounds that associated in coupling reaction, this reaction happened in alkali medium [9,10].

Experimental methods

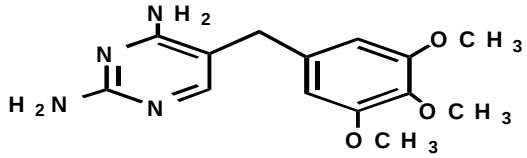
Preparation of azo compounds (1-azo-[substitute benzene]5- Trimethoprim)

Added (0.021 mole, 5.2g) Trimethoprim in beaker that capacity (100ml) contain (12.8 ml) from (50%)hydrochloric acid using water path in temperatures (0-5)C0, and then added (8ml)from (20%) sodium nitrate solution ,drop by drop with continuous stirring and cooling for production Diazonium salt.

Dilute (0.022 mole) variation substituted phenol compounds in 18 ml from(10%) sodium hydroxide in ice path at 0C°,then added Diazonium salt slowly with continuous stirring and cooling. Set aside the mixture for two hours at same temperature ,then added(30%) of hydrochloric acid . crystal precipitation apparent , live it to stabile for one hour then filter and wash with cooling water ,dry the crystal and recrystalation with ethanol .

Compounds Prepared

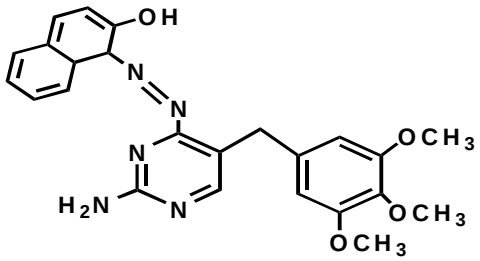
From Trimethoprim compound, we prepare five derivatives physical probatives of the prepare compound are listing in table (1).



5-(3,4,5-Trimethoxy-benzyl)-pyrimidine-2,4-diamine

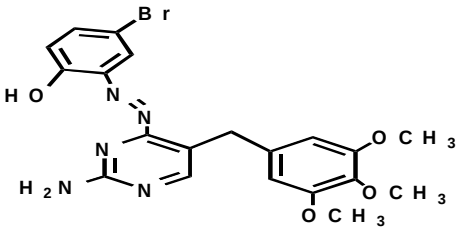
(Trimethoprim)

1



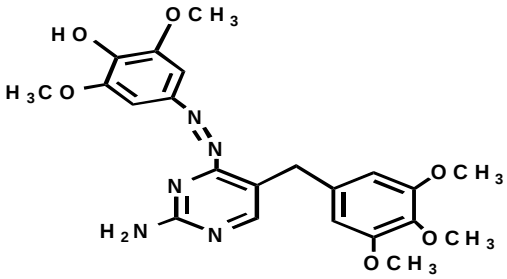
1-[2-Amino-5-(3,4,5-trimethoxy-benzyl)-pyrimidinyl-4-azo]-1,8a-dihydro-naphthaline-2-ol

2



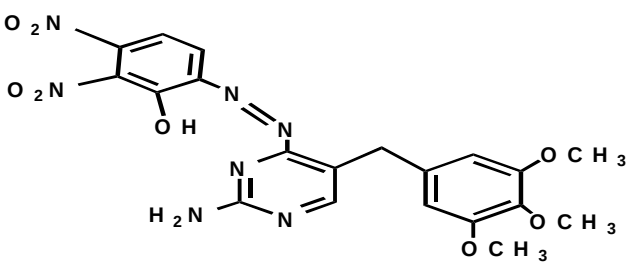
2-[2-Amino-5-(3,4,5-trimethoxy-benzyl)-pyrimidinyl-4-azo]-4-bromo-phenol

3



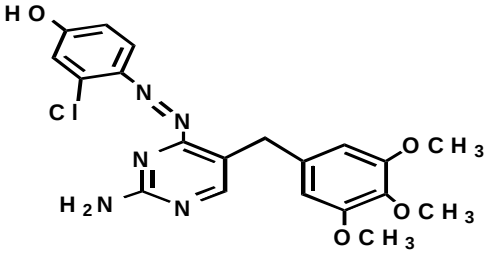
4-[2-Amino-5-(3,4,5-trimethoxy-benzyl)-pyrimidinyl-4-azo]-2,6-dimethoxy-phenol

4



6-[2-Amino-5-(3,4,5-trimethoxy-benzyl)-pyrimidinyl-4-azo]-2,3-dinitro-phenol

5



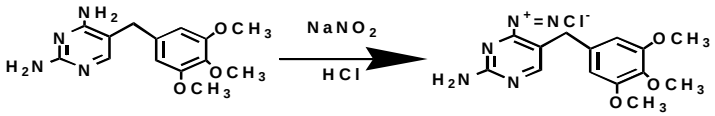
4-[2-Amino-5-(3,4,5-trimethoxy-benzyl)-pyrimidinyl-4-azo]-3-chloro-phenol

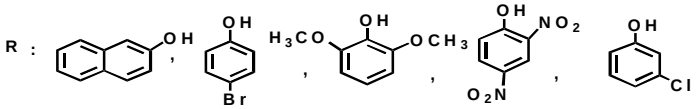
Table (1):physical properties of azo compounds				
No.	**Molecular formula**	**Color**	**Molecular weight**	**Melting point C^0**
1	$C_{24}H_{25}N_5O$	**Dark Green**	**447.49**	**252-254**
2	$C_{20}H_{20}BrN_5O_4$	**Light Brown**	**474.31**	**250**
3	$C_{22}H_{25}N_5O_6$	**Purple**	**455.46**	**256-258**
4	$C_{20}H_{19}N_7O$	**Yellow**	**485.41**	**102-104**
5	$C_{20}H_{20}ClN_5O_4$	**Dark-Brown**	**429.86**	**234-236**

Discussion

in this paper, we would present the syntheses of some new Trimethoprim derivatives.

The new derivative for Trimethoprim were prepared by reaction Diazonium salt of Trimethoprim with different phenol compounds. The following mechanism explain the reaction.





1 2 3 4 5

The formula structure of Trimethoprim derivatives were identificated using melting point that explain in table(1) and IR spectroscopy that explain in table(2) As well as UV-Visible spectroscopy biological activity In Trimethoprim derivatives.

The stretching of O-H phenolic and al-choholic demonstrate wide absorption band in the region (3400-3100)cm-1

Table (2):The value of IR spectroscopy for some functional group						
No.	**N=N str. cm^{-1}**	**N=N bend. cm^{-1}**	**H-N bend.asym. cm^{-}**	**OH Phenolic cm^{-1} str.**	**CH Aliphatic cm^{-1}**	**Other cm^{-1}**
1	**1504**	**1408**	**1620**	**3475**	**2997**	**Aromatic CH str.3114**
2	**1419asym. 1531sym.**	**1400**	**1643**	**3420**	**2938**	**NH str.3329,3388**
3	**1531**	**1400**	**1625**	**3398**	**2823**	**Aromatic CH str.3047**
4	**1528**	**1405**	**1640**	**3377**	**2953**	**Aromatic CH str. 3020 Out of plan CH bend.742**
5	**1530**	**1402**	**1640**	**3392**	**2927**	**Aromatic CH str.3030 Out of plan C=C bend.502**

with disappearance of absorption for NH2 group that it be secondary demonstrate in the region (3000-3400) cm-1 (11).

The appearance of beam that intensity medium in the region (1595-1490)cm-1 belong to the frequency matched stretching for N=N group, so The appearance of medium beam at (1400-1410)cm-1 and bending for N=N group, as well as the appearance of different beam that explain in table (2).

The UV-Visible spectroscopy was demonstrated absorption beams at (288,360)nm belongs (n-Π*) transition for (N=N) azo group and demonstrate as well as absorption beam at 230 nm belong to cycle benzene that result for (Π-Π*) transitions other absorption beams that weak absorbance demonstrate in the visible region up 420 nm this weak peak give reason of produce color.

Table 3 : biological activity of product

Camp 30 mg/L	Activity against G^- bacteria E-Coli	Activity against G^+ bacteria Bacillus	Activity against Fungi Aspiriginussb
Salbutamol+1	-	-	-
Salbutamol+2	-		-
Salbutamol+3	++	+++	-
Salbutamol+4	+	+	+++
Salbutamol+5 Salbutamol+6	-	+	-

(-) No inhibition (+) Inhibition diameter of 20-25 mm (++) Inhibition of 25-30 mm in diameter
(+++) Inhibition of 30-40 mm in diameter

From the above table No. (3) Noted the following:
Most of the vehicles prepared to the effectiveness of a biological positive bacteria (bacillus) at The most inhibitory compounds is the compound No. 4 due to its totals Effective relative to the rest of the compounds prepared

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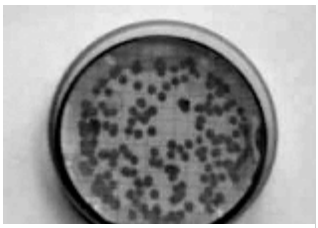
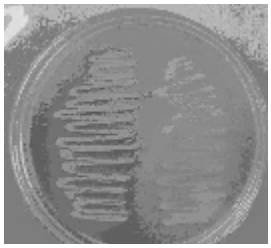


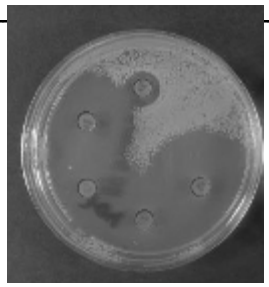
Trimethoprim + 1
with bacteria G+



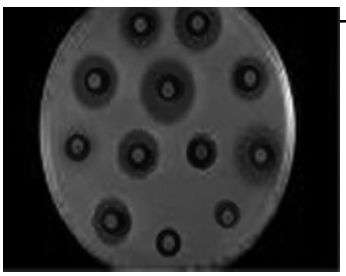
Trimethoprim + 1
with bacteria G+

Trimethoprim + 2
with bacteria G+

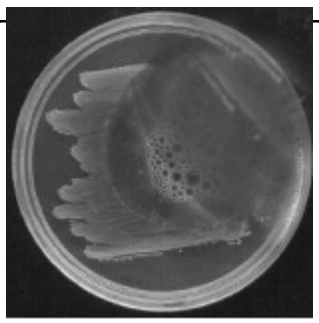
Trimethoprim + 3
with bacteria G^-



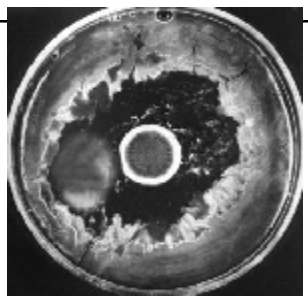
Trimethoprim + 3
with bacteria G+



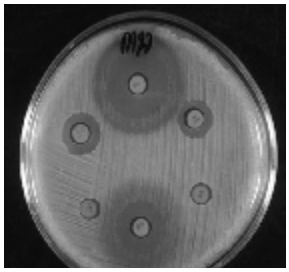
Trimethoprim + 4
with bacteria G^-



Trimethoprim + 4
with bacteria G+



Trimethoprim + 4 with
Fung bacteria



Trimethoprim + 5
with bacteria G+

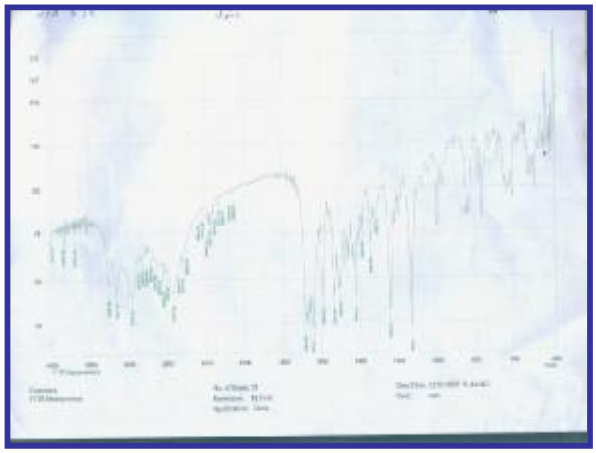


Figure (1) FT-IR spectrum of1-[2-Amino-5-(3,4,5-trimethoxy-benzyl)-pyrimidinyl-4-azo]-1,8a-dihydro-naphthaline-2-ol

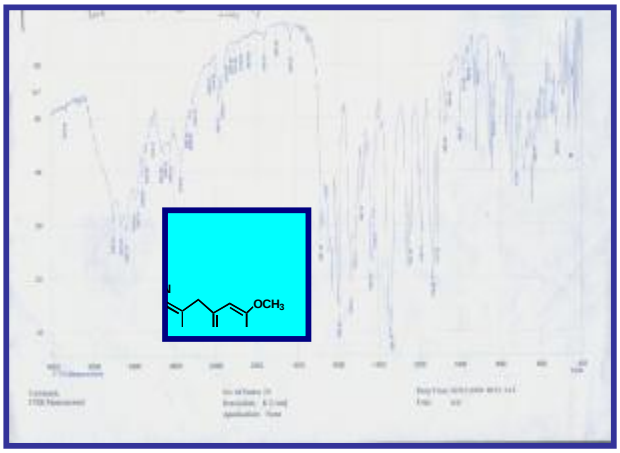


Figure (2) FT-IR spectrum of 6-[2-Amino-5-(3,4,5-trimethoxy-benzyl)-pyrimidinyl-4-azo]-2,3-dinitro-phenol.

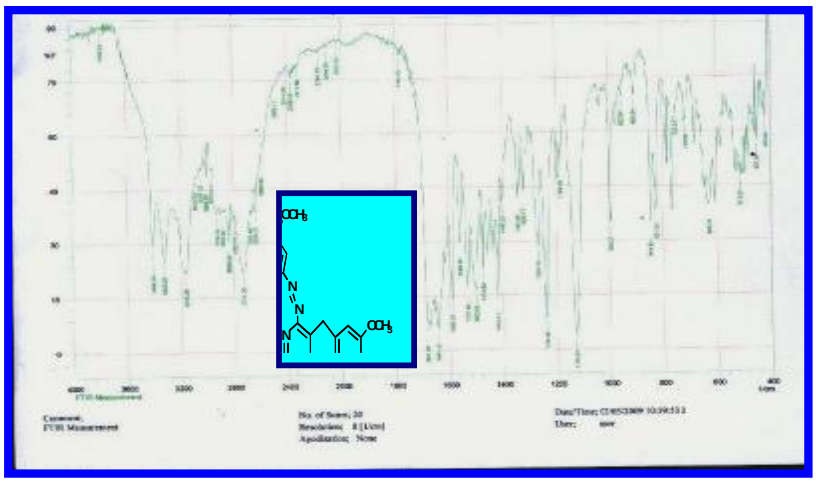


Figure (3) IR spectrum of 4-[2-Amino-5-(3,4,5-trimethoxy-benzyl)-pyrimidinyl-4-azo]-2,6-dimethoxy-phenol.

تحضير وتشخيص بعض المشتقات الجديدة لدواء التراي مثبرين

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الخلاصة

تم في هذا البحث تحضير مركبات جديدة للمركب التراي مثبرين المعروف بفعاليته الدوائية العالية من خلال تفاعل ازدواج ملح الديازونيوم لها مع بعض معوضات الفينول(2- نفثول ،4- برومو فينول5,2-داي ميثوكسي فينول،4,2-داي نايترو فينول ،3- كلورو فينول). تم تشخيص المركبات المحضرة باستخدام بعض الطرق الطيفية UV-Visible, FTIR الأنشطة البايولوجية قد تم بحثها أيضا لهذه مركبات مع البكتريا الموجبة والبكتريا السالبة والفطريات .