Synthesis of N-Trimethoprim derivatives imides on polymeric chain

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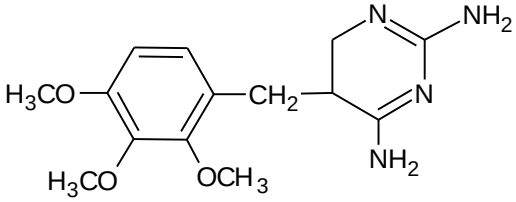
Abstract:-

The present work involved synthesis of several new N-Trimethoprim derivatives imides on polymeric chain by two steps. The first step involved preparation of N- sub or unsub benzoyl and sub unsub acetyl amidyl sub trimethoprim (1-5) by condensation of trimethoprim drug with many substituted acid chloride. Then the second step include. Preparation new five N- (acrly–N–sub or unsub benzoyl) imidyl substituted trimethoprim (6-10) by reaction of poly acryloyl chloride with the prepared compound (1-5) in first step in a suitable solvent in the presence amount triethylamine (Et_3N) with heating. The structure confirmations of all polymers were confirmed using FT-IR, ^{1}H-NMR,^{13}C-NMR and UV.Spectroscopy. Other physical properties including softening points', melting point, and solubility of the polymers were also measured.

Key Word: trimethoprim drug poly acryloyl chloride. Polyimides derivatives.

Introduction:

Trimethoprim and trimethoprim derivative type of medicine called an antibiotic [1], It is used to treat infections with bacteria. [2] It is a sign if: cant antimicrobial activities[3,4]and its analognes[5], the chemical designation of trimethoprim is 2,4-diamine-(3,4,5-trimethoxypenzyl) pyrimidine ($C_{14}H_{18}N_4O_3$).It was first described by Roth and co workers[3], it is a white to yellowish compound with better taste the trade names of the combined product are bacterium and spectra[2].



It was reacted with sub or unsub. Benzoyl and sub or unsub. Acetyl in the presence amount triethyl amine (Et_3N) to give N-(sub. or unsub. Benzoyl and sub. or unsub, acetyl amidyl sub. Trimethoprim, which react with poly acryloyl chloride with triethyl amin to give new five poly imides

derivatives for trimethoprim. Polyimides have been widely used as high temperature insulators and dielectrics, coating, adhesives and materials in arariety of advanced technologies related to micro electronics, where miniaturization and large scale integration are important technical issues. [5-6] Then high thermal stability and balance mechanical and electrical properties. Poly imides are mainly used in the aerospace and electronics industries in the form of film and moldings, but high melting point and instability inorganic solvent limited there. [7] Applications further more success full attempts have been model convert or modify some specific N-Substituted imides to serve as ion exchange resins, such as cross linked poly [N-Phenyl maleimide] which was prepared by free radical polymerization of the corresponding imides in benzene. Also Polyimides electronic memories, Evaporation, biofiels separation [8-9] and many other fields of microelectronics, optics aerospace industries and biomedical engineering [10], However polyimide material are usually difficult to be processed because of their infusibility at high temperature and insolubility in most organic solvents [11-13].

Material and Methods:

General:

All chemicals used in this work from BDH, Merk, Fluka and were used without further determined, melting point were determined in galler Kamp melting point apparatus and were uncorrected. UV-Visible spectra were recorded on shimadzu T6O4 spectrophotometer using DMFas a solvent FT-IR-8400 Fourier trans form infrared c. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker specrospin Ultra shield magnets 300MHz in strument using tetra methyl silane (TMS)as an internal standard and DMSo d6 as a solvent in AL-Albate University in Jordan.

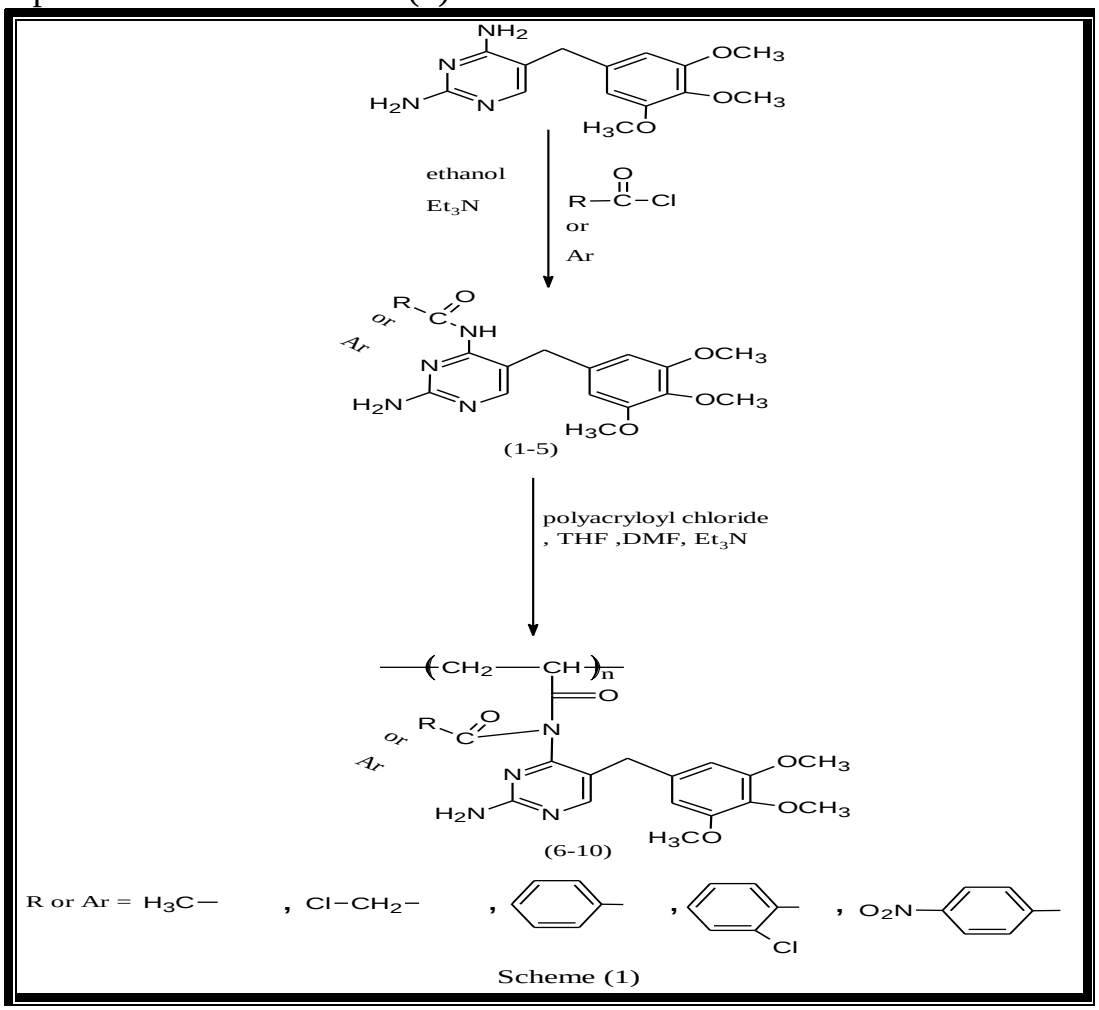
General procedure preparation of [(subs. Aryl or alkyl) subs. Trimethoprim] amide [7]:

In around bottom flask equipped with a magnetic bar stirrer and reflux condenser was placed. The mixture consists of sub. Benzoyl chloride (0.06 mol) and (0.06 mol) trimethoprim with (4) drops of triethyl amine (Et_3N) in 25 ml of suitable solvent (benzene) and refluxed (3-4) hrs. After that the solvent was removed and recrystallized from ethanol. All physical properties are listed in table (1).

General procedure preparation of poly [(N -acryl –N -sub or unsub. Acetyl of benzoyl)] imidyl substituted Trimethoprim.

In around bottom flask equipped with a magnetic bar stirrer was placed. The mixture consists of poly (acryloyl chloride) (0.06 mol) and (0.0.6mol)

of N-Sub amidyl sub. Trimethoprim or [(subs. Aryl or acetyl) subs. Trimethoprim] amide (in first step) with (1ml) of tri ethyl amine (Et_3N) in 25ml of suitable solvent (THF) and refluxed for (6-7) hrs. After cooling the solvent was removed. The separated sold was filtered and purified by dissolving at DMF and repreciptating from water or acetone. This procedure was applied on compound as is shown in table (2) –All physical properties are listed in table (2).



Scheme (1)

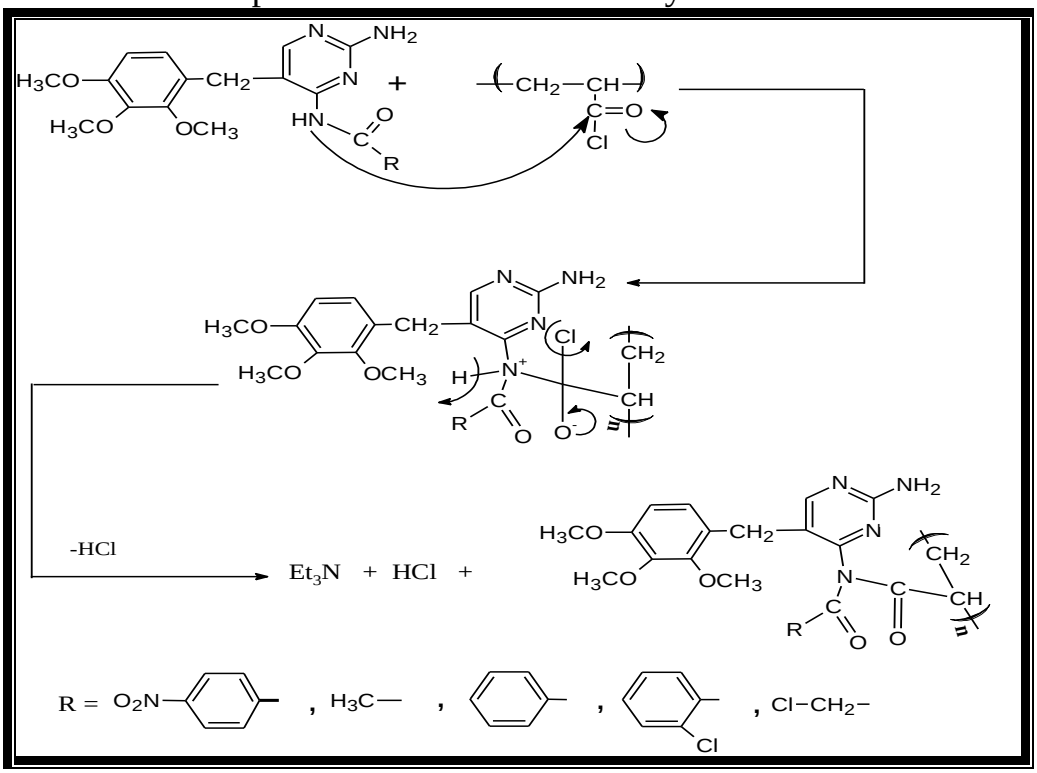
Results and Discussion:

New polyimides containing hetro cyclic moiety was synthesized following reaction sequence out lined in scheme (1).The starting material for the synthetic poly acryloyl imides is trimethoprim which condensed with different substituted acid chloride through nucleophilic substitution of chloride with amino group lead to amides (1-5). The FT-IR spectrum of compound [2] showed the absence of ($-NH_2$) stretching to gather with appearance of band at 3336cm^{-1}, 1654cm^{-1} attributed to (N-H) stretching of amide, amide and amid respectively [14], which indicated the substitution and formation of amides as shown in table (3). Figer (5), attributed

UV.Spectrom of compound [4] and [5] showed an absorption λ_{max} at (280) nm and (270) nm which to (π-π□). The absorption is listed in Figer (1) and(3).

The ^{1}H-NMR of compound [2] showed the signals at (3.118-4.075) ppm was at tribute to (-CH_3) Proton and multiple signals at (6.165-6.254) ppm due to aromatic protons and singlet signal at (9.387) ppm due to (N-H) protons for amide [12-14] as shown in Figer (7). In the ^{13}C-NMR spectrum of compound (2) showed the signal at (116.1-140.1) ppm for carbonyl group while the aromatic carbon appeared at (161.3-167.5) ppm, as showing Figer (8) and.

In order to obtain polyimides (6-10), the amides (1-5) were subjected to another nucleophilic substitution by treating with polyacryloyl chloride using triethyl amine (Et_3N) as a catalyst. The mechanism of reaction in valves nucleophilic attach and the carbonyl as shown below [7].



The FT-IR spectrum compound [7] showed the disappearance of amide bands γ (N-H), γ(C=O) amide as shown in table (3) Figer (6). Compounds (9) and (10) showed an absorption λ_{max} of (266) nm, (240) nm which attributed to (π-π□) as shown in Figer (2) and (4).

Another evidence for compounds (7) and (9) its ^{1}H-NMR spectrum showed different signals. Two multiplet at (1.071) ppm and (2.992) ppm as signals for ethylene (acryl) protons as shown in Figer (9) and (11).

The ^{13}C-NMR spectrum of compounds (7) and (9) the ethylene carbon appeared at (39.99) ppm and (40.26) ppm and aromatic carbon at

(127.4-143.8) ppm while the imides carbonyl appeared at (164.03-167.82) ppm as shown in Figer (10) and (12).

Table (1) the physical properties for [(sub. Aryl or acetyl) sub. (Trimethoprim)]Amide

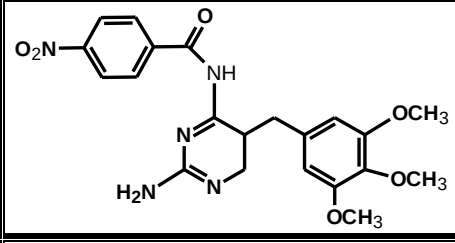
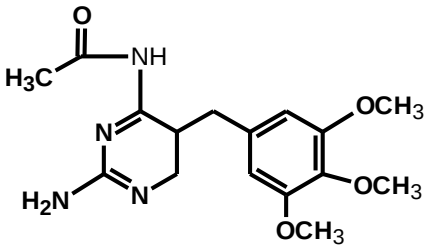
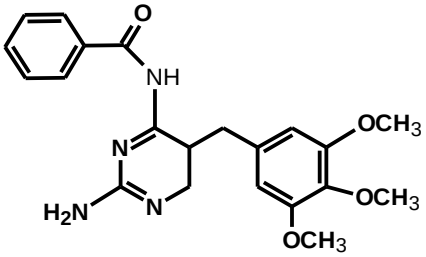
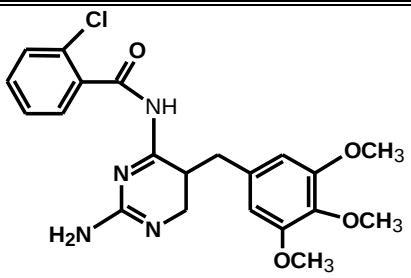
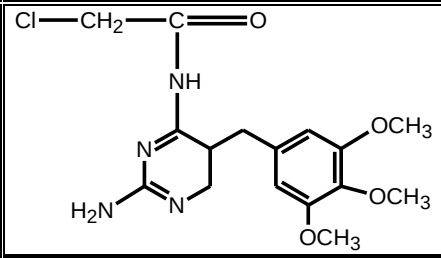
Comp. No	Compound structure	Color	Melting point	%conversion	Solvent used in reaction
1		Whit	238-240	80	Ethanol
2		Yellow	196-198	65	Ethanol
3		Off White	264-266	75	Ethanol
4		Light yellow	290-293	70	Ethanol
5		Light brown	Oily	60	Ethanol

Table (2) the physical properties of product polymers

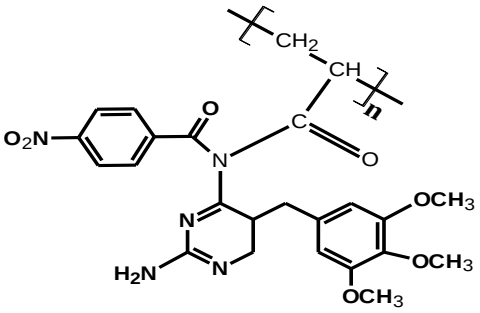
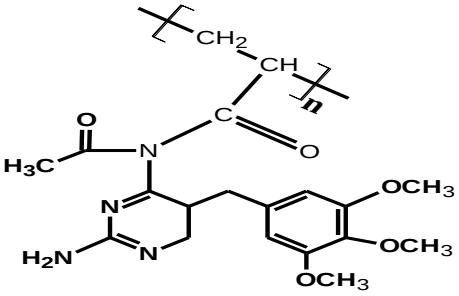
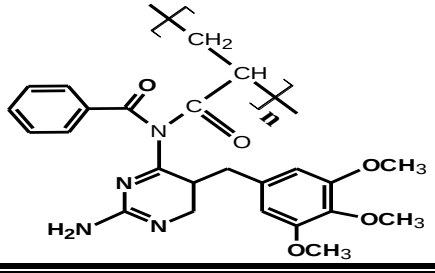
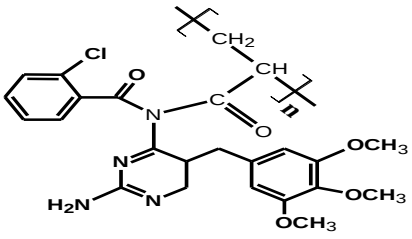
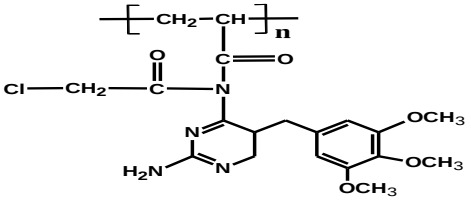
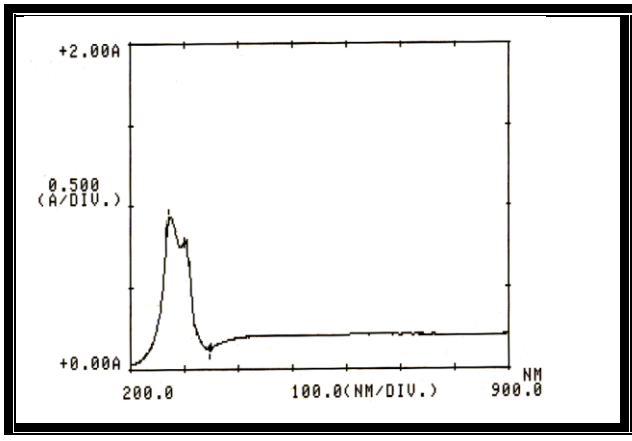
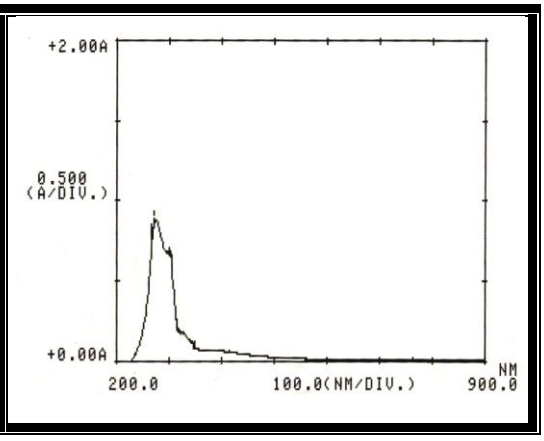
Comp. No	Compound structure	Color	Melting point	%conversion	Solvent used in reaction
6		redish brown	200-208	70	DMF
7		Brown	268-273	55	DMF
8		Deep brown	165-170	65	DMF
9		Yellow	Oily	60	DMF
10		Brown	Oily	50	DMF

Table (3): FT-IR Spectral data for all product compounds

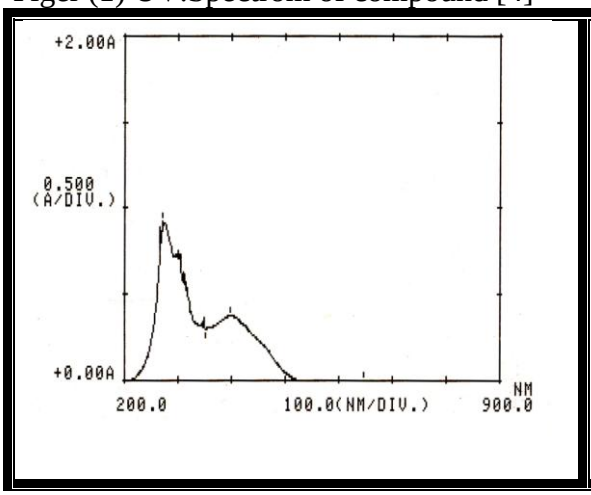
Com. No	γ(NH_2) cm^{-1}	γ(C-H) cm^{-1} aliph.	γ(C-H) cm^{-1} arom.	γ (C-N) cm^{-1}	γ (C=O) cm^{-1}	γ (C=C) cm^{-1}	Others
1	3404 3336	2731-2950	3163	1458	1654	1508	γ (C-NO_2) cm^{-1} 1591,1342
2	3469 3317	2835	3132	1400	1654	1508	____
3	3406, 3323	2729-2850	3163	1498	1681	1589	____
4	3406, 3323	2837	3163	1419	1643	1589	γ (C-Cl) cm^{-1} 1130
5	3420, 3315	2920	3070	1482	1678	1575	γ (C-Cl) cm^{-1} 1167
6	3469 3270	2860	3060	1450	1670	1510	γ (C-NO_2) cm^{-1} 1580,1360
7	3406, 3325	2731-2837	3167	1500	1681 1641	1589	____
8	3408, 3340	2856	3055	1500	1641	1526	____
9	3410, 3336	2738-2939	3077	1473	1678	1560	γ (C-Cl) cm^{-1} 1145
10	3406, 3310	2731-2943	3190	1465	1662	1593	γ (C-Cl) cm^{-1} 1126



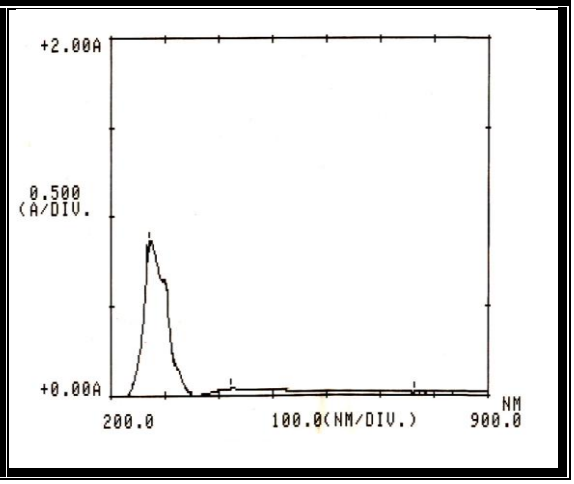
Figer (1) UV.Spectrom of compound [4]



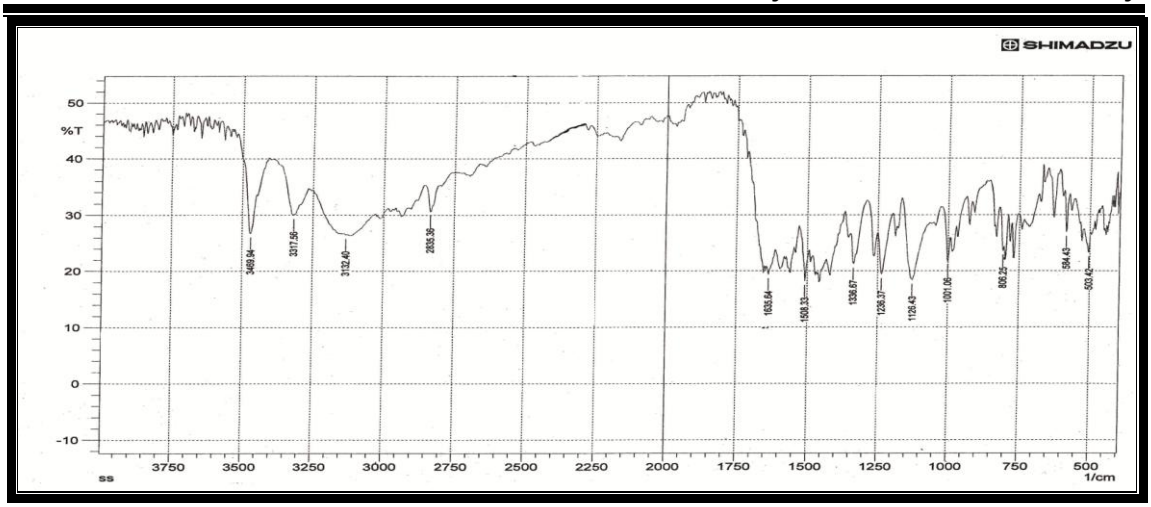
Figer (3) UV.Spectrom of compound [5]



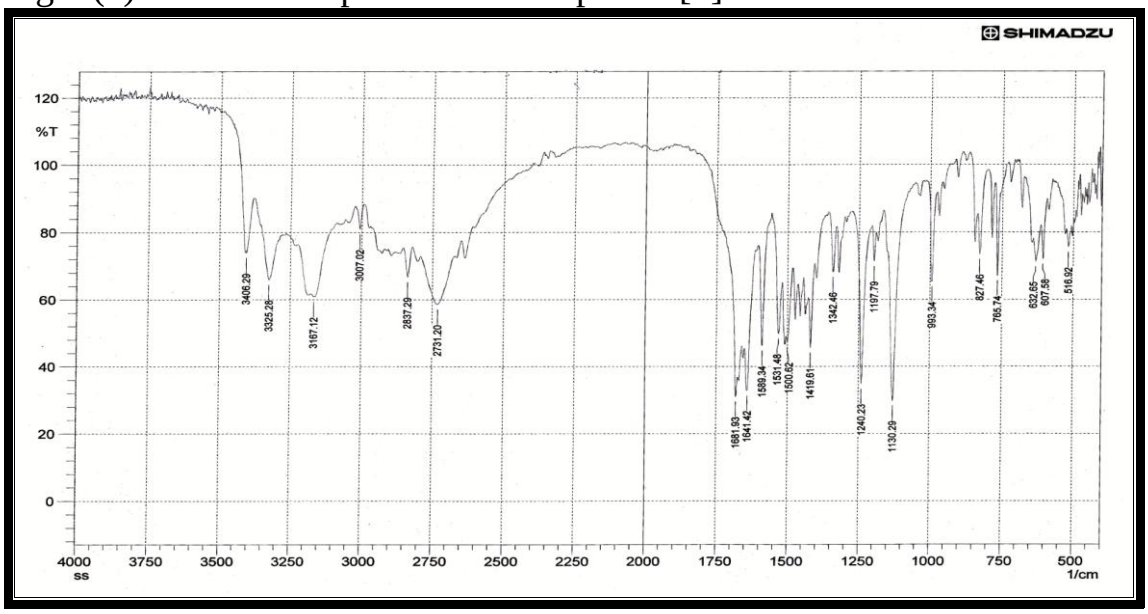
Figer (2) UV.Spectrom of compound [9]



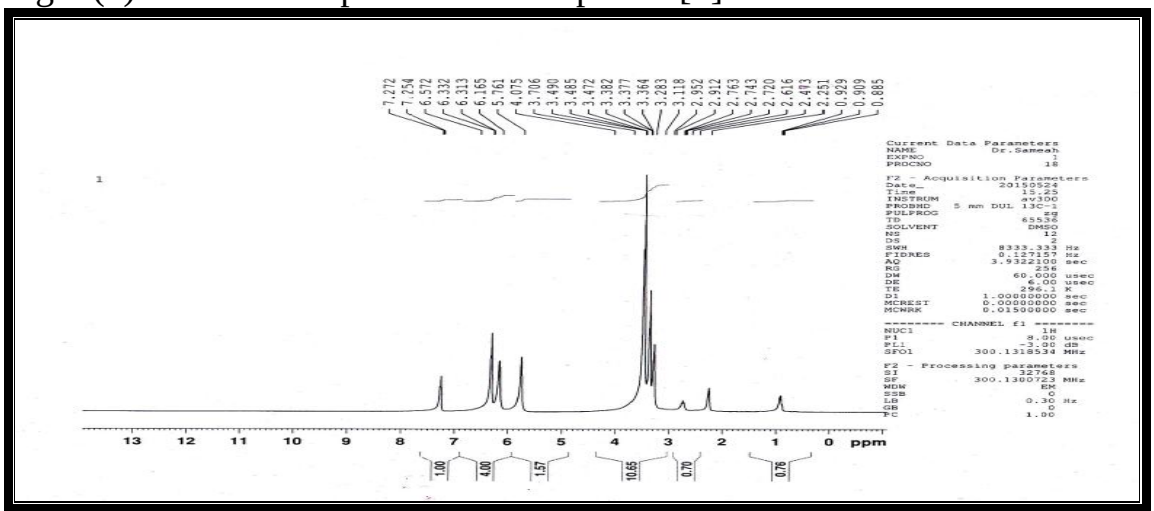
Figer (4) UV.Spectrom of compound [10]



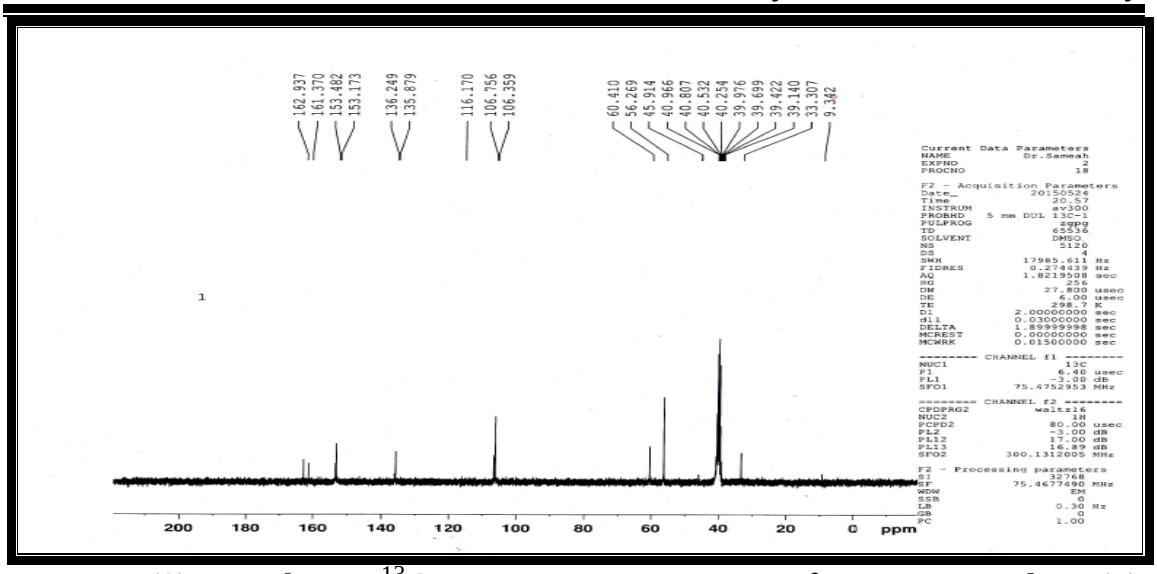
Figer (5): The FT-IR spectrum of compound [2]



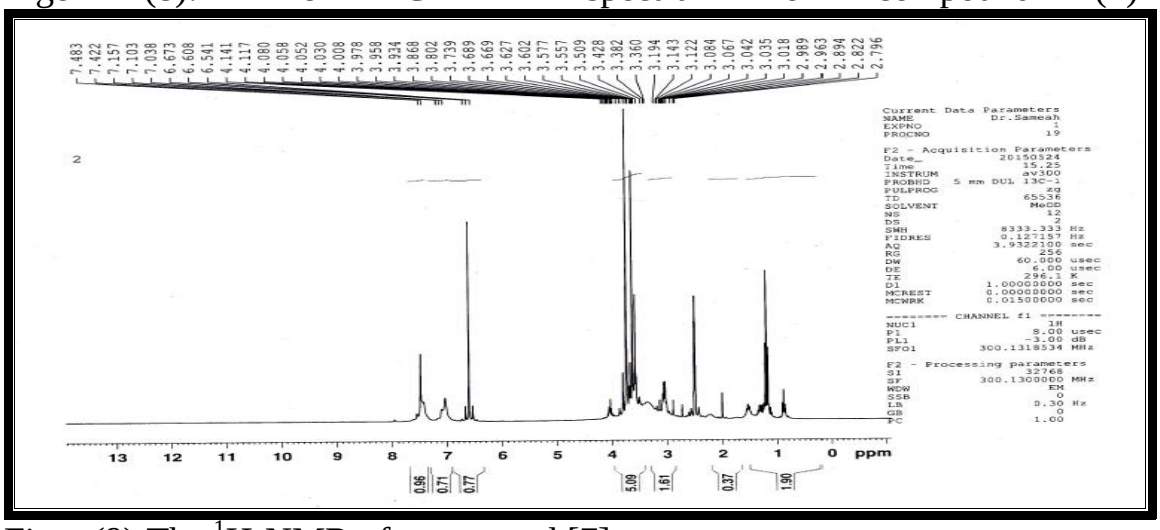
Figer (6): The FT-IR spectrum of compound [7]



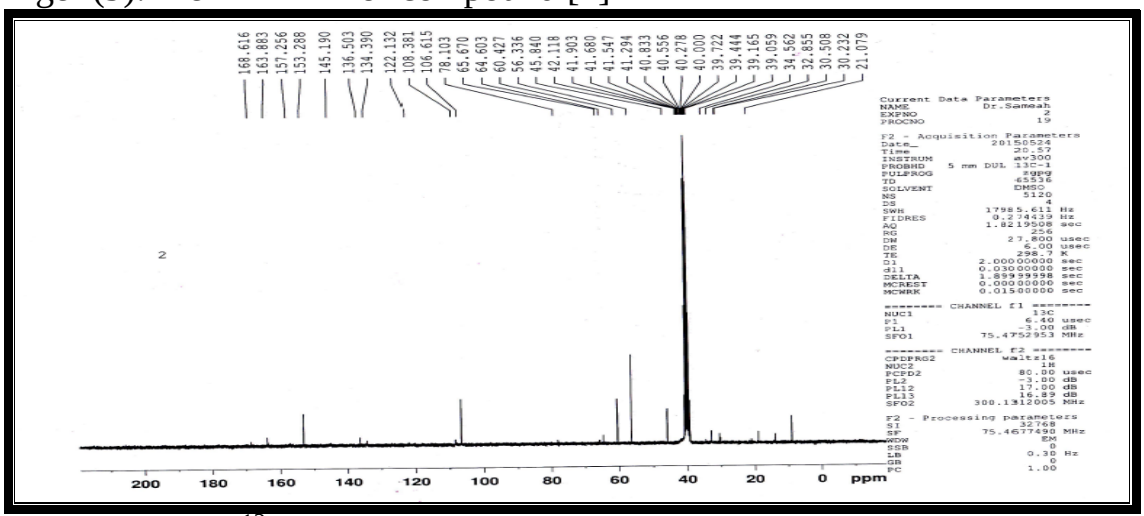
Figer (7): The ^{1}H-NMR of compound [2]



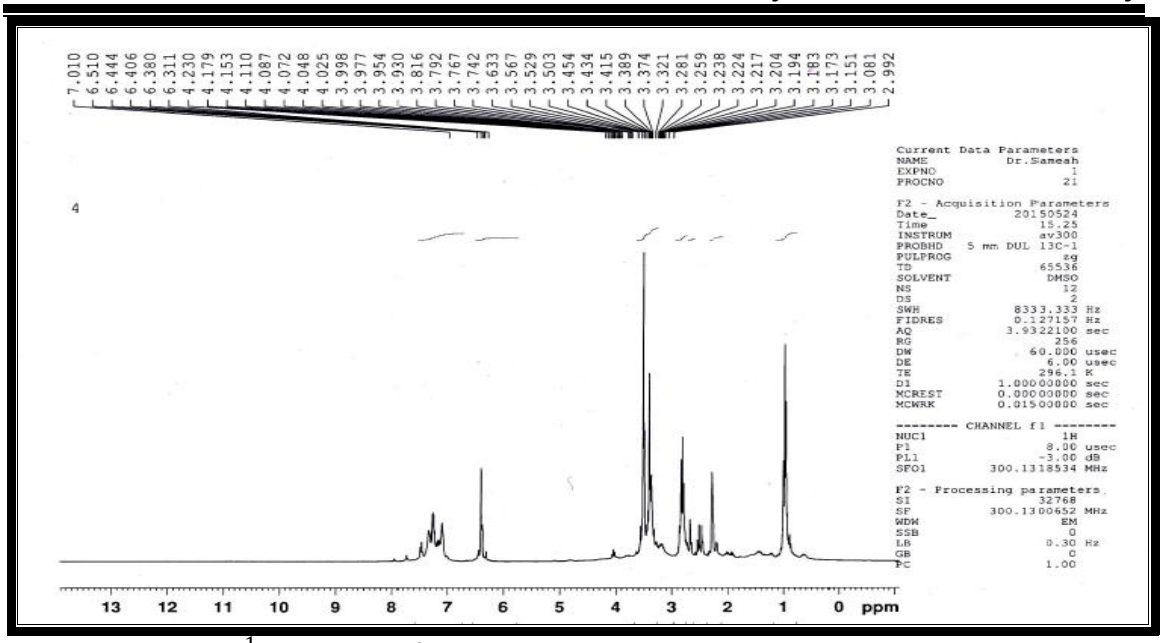
Figer (8): The ^{13}C-NMR spectrum of compound (2)



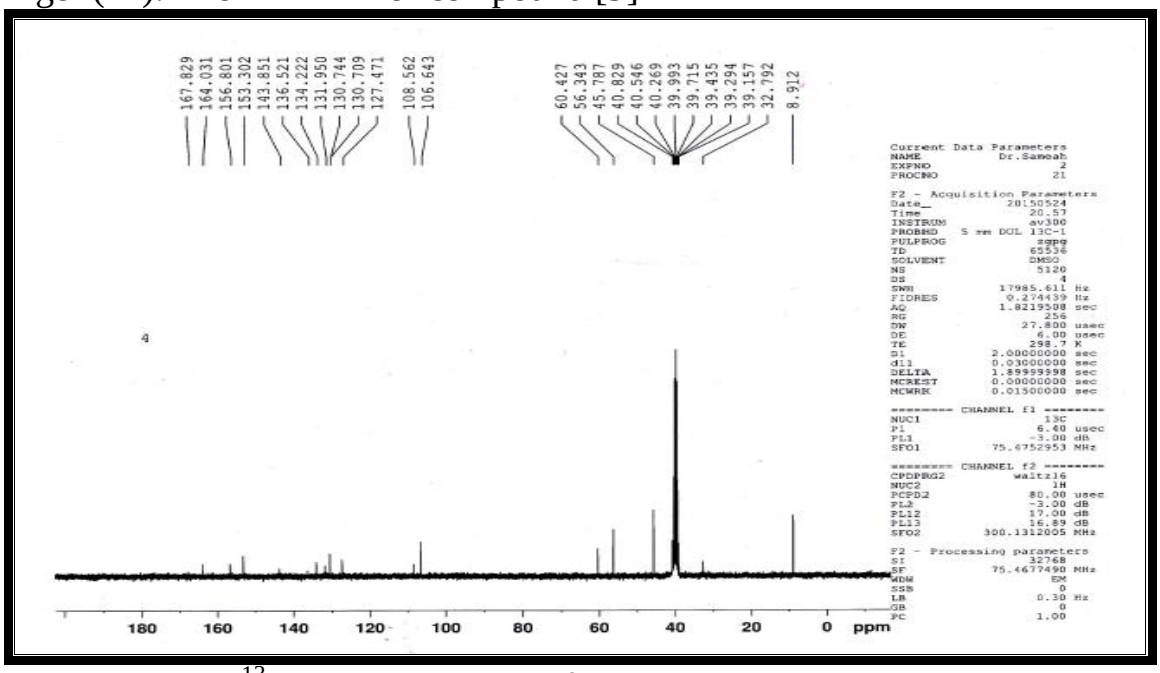
Figer (9):The ^{1}H-NMR of compound [7]



Figer (10): The ^{13}C-NMR spectrum of compound (7)



Figer (11): The ^{1}H-NMR of compound [9]



Figer (12): The ^{13}C-NMR spectrum of compound (9)

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الخلاصة :

تم في هذا البحث تحضير بعض المشتقات ن–تراي مثبريم ايمايد على السلسلة البوليمرية وذلك من خلال اجراء خطوتين حيث تضمنت الخطوة الاولى تحضير(5–1) N-(Sub or un sub acetyl) amidyl sub trimethoprim

وذلك بتكاثف دواءالتراي مثبريم مع كلوريدات الحوامض المعوضة وغير المعوضة (اليفاتية ، اروماتية) اما الخطوة الثانية فقد تم تحضير بولي ايمايدات جديدة معوضة وغير معوضة (10–6) من تفاعل بولي اكريلويل كلورايد مع بعض الامايدات المختلفة (الاليفاتية،اروماتية) المحضرة في الخطوة الاولى (5–1) في مذيب مناسب وكمية مناسبة في ثلاثي اثيل امين (Et_3N) مع التسخين وتم اثبات التراكيب الكيميائية للبوليمرات المحضرة باستخدام الطرق الطيفية ، اطياف الاشعة فوق البنفسجية UV واطياف الرنين النووي المغناطيسي ^{1}H-NMR و اطياف ^{13}C-NMR بالاضافة الى القياسات الفيزيائية المختلفة من درجات التلين ودرجات الانصهار .