Synthesis of N –sulfamethoxazolederivative imide on polymeric chain

Sameaa J. Khammas Al-Bayati *** ***Amal S. Sadiq*
Tamador A. Mahmood*

Received 12, June, 2014
Accepted 6, August, 2014

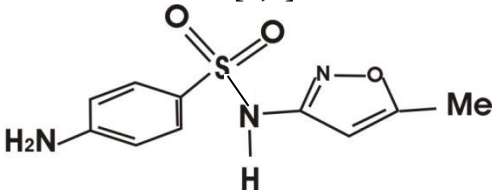
Abstract:

The present work involved synthesis of several new N-Sulfamethoxazol derivatives imide on Polymeric chain by two steps. The first stip involved preparation of N-(sub.orunsub benzoyl and sub unsub acetyl) amidyl sub sulfamethoxazole (1-5) by condensation of sulfamethoxazole drug with many substituted acid chloride, then the second step include, preparation new five N-(acrly-N–sub or unsub benzoyl) imidyl substituted sulfamethoxazol(6-10) by reaction of poly acryloyl chloride with the prepared compound (1-5) in first stepin asuitable solvent in the presenceamount triethylamine (Et_3N) with heating. The structure confirmations of all polymers wereconfirmed using FT-IR,^{1}H-NMR,^{13}C-NMR and UV spectroscopy. Other physical properties including softeningpoint's, melting point, and solubility of the polymers were also measured.

Key words: Sulfamethoxzole drug, poly acryloyl chloride, polyamides derivatives.

Introduction:

Sulphadrug are also referred to as antibacterials, sulfa drugs represent group of compounds discovered in a consciousserach of antibiotics. The search on sulfa drug with azo dye and testing with many germs lead to synthesing and testing anumber of substituted sulfanilamide for antibacterial activity[1,2]. Sulfamethoxazole is commonly used in combination withtrimethoprim for antibacterial action [1, 2]. Sulfamethoxazoleis4-Amino–N–(5-methyl-3-isoxazolyl) benzene sulfonamide with the following structural formula[3,4].



It is sulfonamide bacteriostatic antibiotic. Sulfonamides are structural analogs and competitive antagonists of para – amino benzoic acid (PABA) [5], sulfamethoxazoleprevents. The formation of dihydrofolic acid acompounds that becteria must be able to make in order tosurvive[6,7].It was reacted with sub or unsub. benzoyl and sub. orunsub acetyl in the presence amount triethyl amine (Et_3N) to give N- (sub. or unsub. benzoyl and sub. or unsub. acetyl amidyl sub. Sulfamethoxazole, which reacted with poly acryloyl chloride with triethyl amine to give new five poly imides derivatives for sulfamethoxazole[8]. Polyimides have been widely used as high temperature insulators and dielectrics, coatings, adhesives and materials in avariety of advanced technologies related to micro electronies, where miniaturization and large-scale integration are important technicalissues [9, 10].Then high

*Department of Chemistry, College of Science for Woman, University of Baghdad, Iraq

thermal stability and balanced mechanical and electrical properties [11-13].

Polyimides are mainly used in the aerospace and electronics industries in the form of film and moldings, but high melting point and instability in organic solvent limitedtheir [14-16]. Application further more few successful attempts have been mode convert or modify some specific N-substituted imide to serve as ion exchange resins, such as cross linked poly [N- phenyl maleimide] which was prepared by free radical polymerization of the corresponding imide in benzene [17].

Material and Methods:

General:

Chemicals employed were of analytical used without further purification, melting point were determined ingallerkampmelting point apparatus and were uncorrected. UV – visible spectra were recorded on shimadzuT_{60}u spectrophotometer using DMF as a solvent FT-IR spectra were recorded on shimadzu- 8400 Fourier transforminfrared spectrophotometer as KBr disc. ^{1}H-NMR and ^{13}C- NMR spectra were recorded on Brukerspecrospin Ultra shield magnets 300MHz in strument using tetra methylsilane (TMS) as an internal standard and DMSO. d6 as a solvent in Al-Albate University in Jordan.

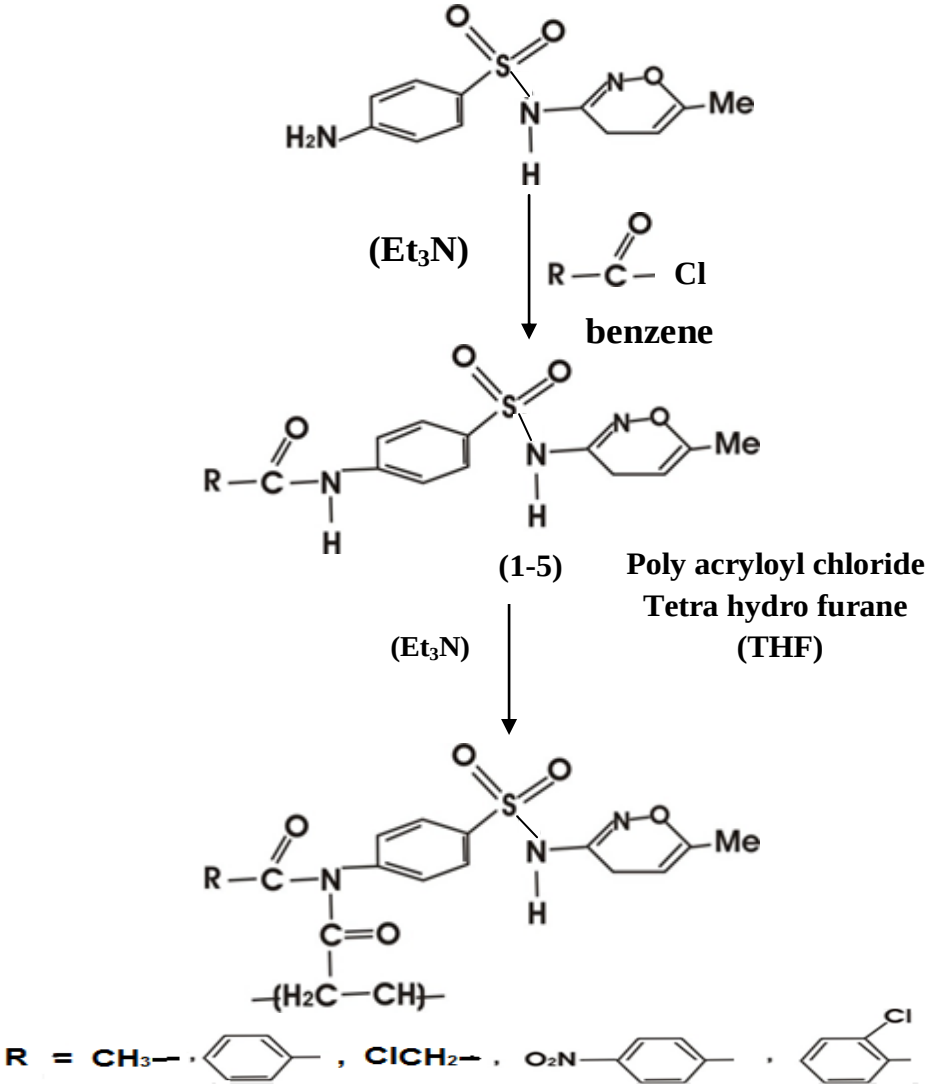
- **General procedure preparation of [(subs. Aryl or acetyl)subs. Sulfamethoxazole] Amide**

In around bottom flask equipped with amagneticbar stirrer and reflux condenser was placed. The mixture consists of sub-benzoyl chloride (0.06 mol) and (0.06 mol) sulfamethoxazole with (3) drops of triethyl amine (Et_3N) in 25 ml of suitable solvent (benzene) and refluxed (2-3) 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 un sub. acetyl of benzoyl) Imidyl substituted sulfamethoxazole[8]**

In around bottom flask equipped with amagnetic bar stirrer was placed.The mixture consists of poly (acryloyl chloride) (0.06 mol) and (0.06 mol) of N-subamidyl – sub. sulfamethoxazole with (1ml) of triethylamin (Et_3N) in (25 ml) of suitable solvent (THF) and refluxed for (5-7)hrs. After cooling the solvent wasremoved. The separated sold was filtered and purified by dissolving at DMF and repreciptating from water or acetone. This procedure was applied on compounds as is shown in table (2). All physical properties are listed in Table (2).



Scheme(1)

Table (1)The physical properties for [(sub. Aryl or actyl) sub. Sulfamethoxazole)] Amide

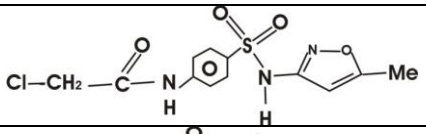
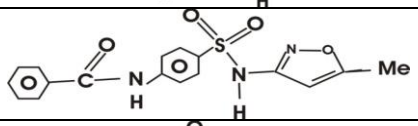
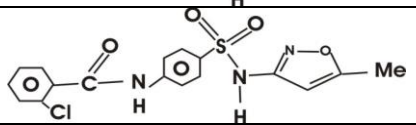
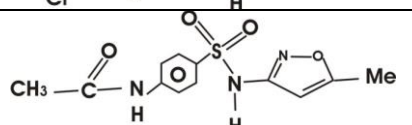
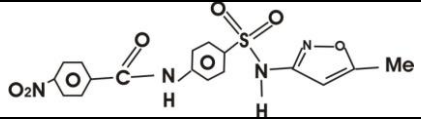
Comp No.	Compound structure	Colour	Melting point c°	%conversion	Solvent used inreaction
1.		white	198-200	84	Benzene
2.		white	225-227	90	Benzene
3.		Faint Yellow	180-182	72	Benzene
4.		Brown	210-212	85	Benzene
5.		Yellow	182-184	95	Benzene

Table (2)The physical properties of all product polymers

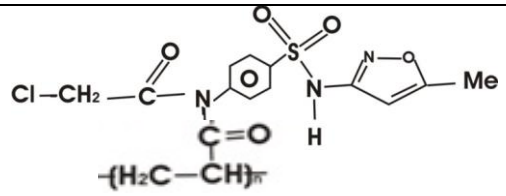
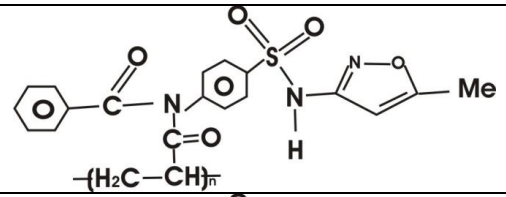
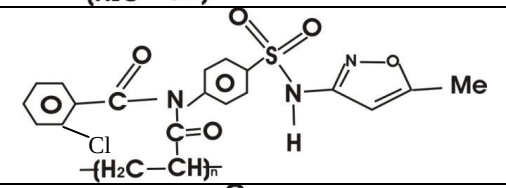
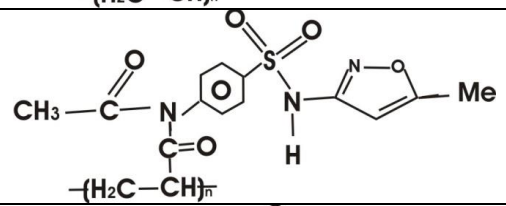
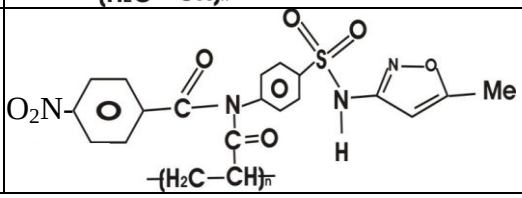
Comp No.	Compound structure	Colour	softing point c°	%conversion	Solvent used in reaction
6.		Whit	120-128	70	THF
7.		Faint brown	222-232	90	THF
8.		Faint brown	160-168	82	THF
9.		Faint brown	170-176	80	THF
10.		Brown	184-190	94	THF

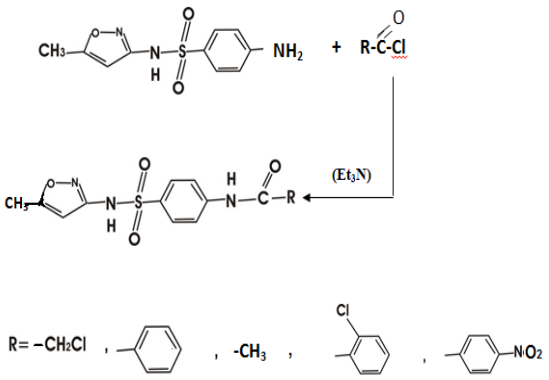
Table (3) FT-IR spectral data for all product compounds

Comp No.	υ (C-H) aromatic cm^{-1}	υ (C-H) aliphatic cm^{-1}	υ (C=O) cm^{-1}	υ (C-N) cm^{-1}	υ (N-H) cm^{-1}	υ (SO_2) cm^{-1}	Others cm^{-1}
1.	3051	2993	1678	1404	3236	1334 1164	(C-Cl) 752
2.	3070	2993	1662	1400	3363	1334 1161	-
3.	3043	2924	1670	1392	3352	1392 1157	(C-Cl) 794
4.	3066	2993	1681	1400	3302	1334 1134	-
5.	3080	2981	1693	1396	3113	1346 1168	(C-NO_2) 1396 1531
6.	3053	2993	1680	1404	3234	1373 1186	(C-Cl) 742
7.	3066	2991	1660	1400	3365	1373 1186	-
8.	3082	2891	1668	1394	3329	1385 1175	(C-Cl) 794
9.	3095	2995	1683	1400	3302	1379 1184	-
10.	3007	2899	1695	1465	3277	1375 1184	(C-NO_2) 1593 1398

Results and Discussion:

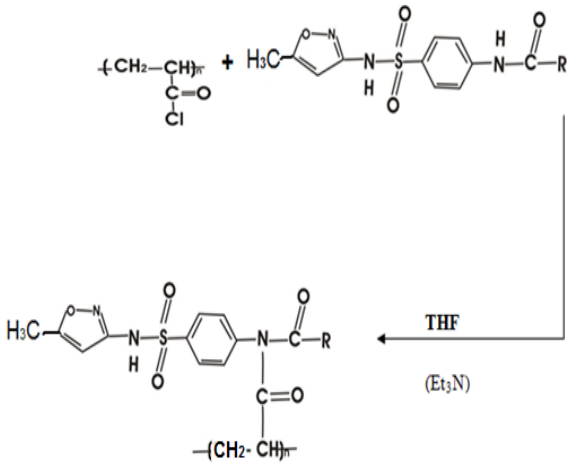
The present work involved two steps:

First step: including preparation of new five derivatives of N-(sub or unsub benzoyl and sub or unsub acetyl) amidyl sub sulfamethoxazole (1-5) were prepared by reaction sulfamethazole with different substituted acid chloride.

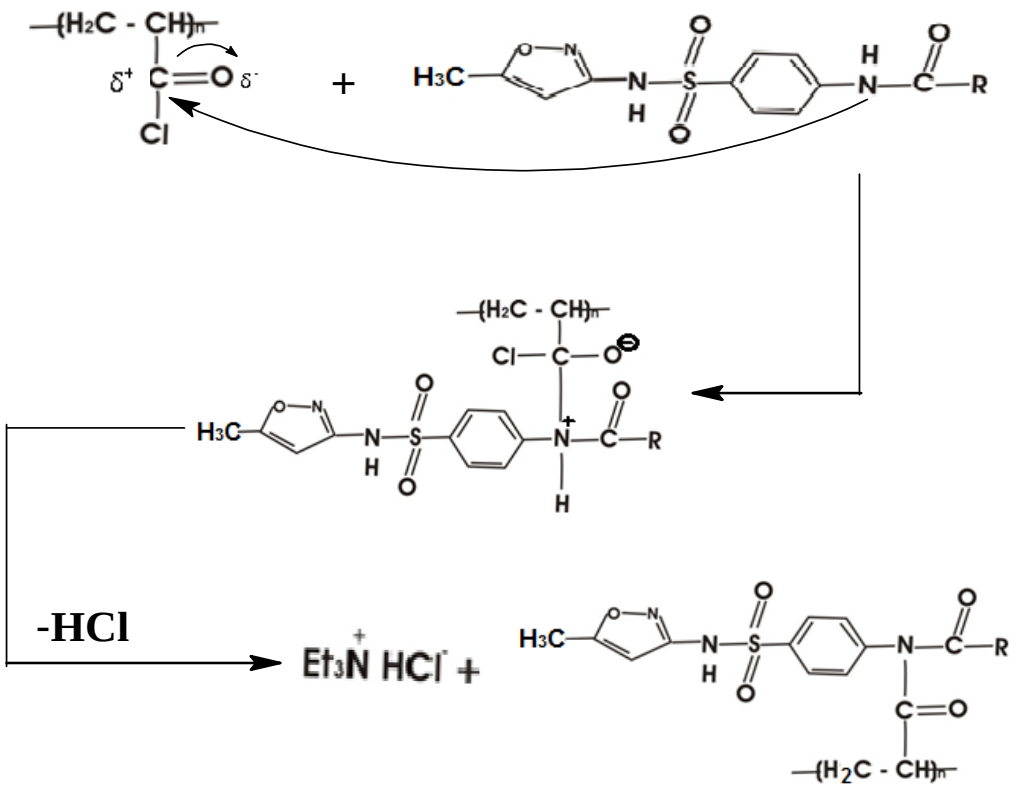


The synthesis of these compounds was carried out lined in scheme [1] and the physical properties for N- sub. orunsub. benzoyl and sub. Or unsub. Actyl) amidylsub.Sulfamethexazole (1-5) including melting point range of (180 – 227)c^{o}and % yield were range of (72-95) and these compounds were identified by FT-IR spectroscopy , |FT-IR spectrum of compound [5] showed characteristic absorption bands (1693)cm^{-1},(3443) cm^{-1} , (1346,1168) cm^{-1} and (3080) cm^{-1}due to υ(C=N) , υ(N-H),υ(SO),υ(C-H) aromatic ,υ(C-H)alphatic and υ(SO_2).Respectively as it is shown in table [3], fig [6] , attributed uv. Spectrum of compounds [3], and [4] showed an absorption λ max at (277mm) and (274mm) which to (π –π*) the absorption is listed in fig [1].

Second Step: including new substituted and un substituted poly imides compounds (6-10) were synthesized by reaction of poly acryloyl chloride with different amides (aliphatic and aromatic) (1-5) in first step in theasuitable solvent in the presence amount triethylamin (Et_3N)



The mechanism of reaction involves anucleophilic attack on the carbonyl as shown below [18-19].



This compound was carried out lined inscheme(1) and the physical properties for compound (6-10) including softening point rang of (120 – 232)c^{o} and % yield were rang of (70-94) and those compounds were identified by FT-IR , UV. , H-NMR and ^{13}C –NMR spectroscopy [20-21]. FT-IR spectrum of compound [10] showed characteristic absorption band at(1695)cm^{-1},(3277)cm^{-1},(1375,1184) cm^{-1},(3007)cm^{-1},and(2899)cm^{-1} due to υ (C=O), υ (N-H) , υ (SO_2) , υ (C-H) aromatic and υ(C-H) aliphatic – 135.03) ppm for aromatic carbonyl, while the signal at (39.73) ppm for carbon methyl group (CH_3), as shown as in fig (8) and (10). UV. Spectrum of respectively as shown in table(3), fig (5).

In the ^{1}H-NMRspectrum of compounds (2) and (5) showed the signals at (2.45)ppm was attributed to (CH_3) proton and multiple signals at (7.506 – 7.828)ppm due to aromatic protons and signlet signal at (7.972)ppm due to (N-H) proton for sulfamethoxazole drug as shown in fig (7) and (9).

In the ^{13}C-NMR spectrum of compounds (2) and (5) showed the signal at (170.21) for carbonyl group (C=O), while the signal at (120.4 compounds (8) and (9) showed an absorption λmax of (276) nm, (280) nm which attributed to ($\pi - \pi^{*}$) as shown in fig (3) and (4).

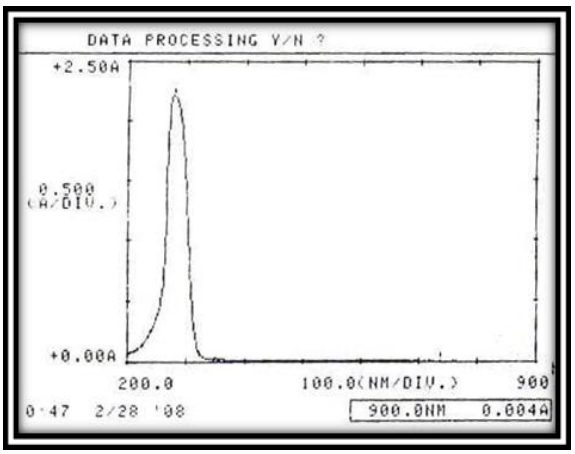


Fig (1): UV. Spectrum of compound (3)

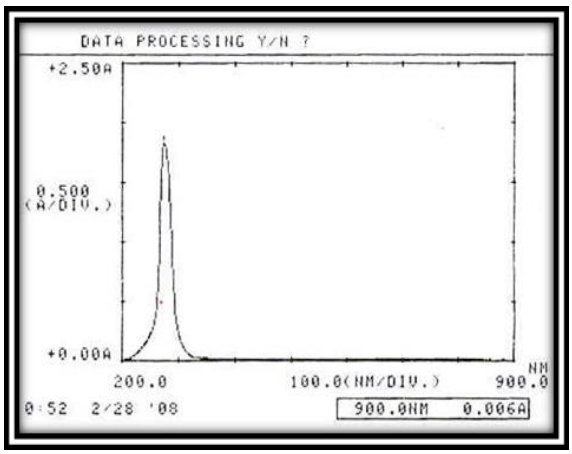


Fig (2): UV. Spectrum of compound (4)

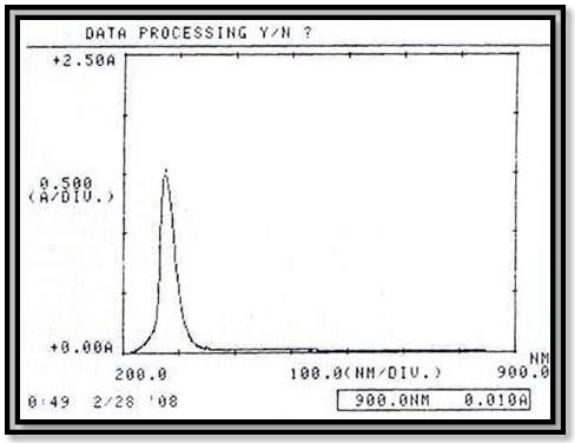


Fig (3): UV. Spectrum of compound (8)

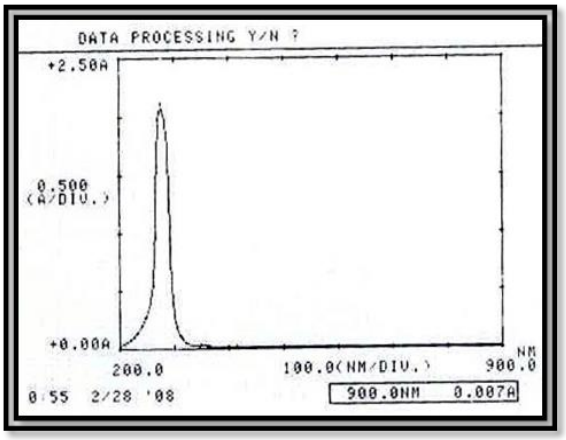


Fig (4): UV. Spectrum of compound (9)

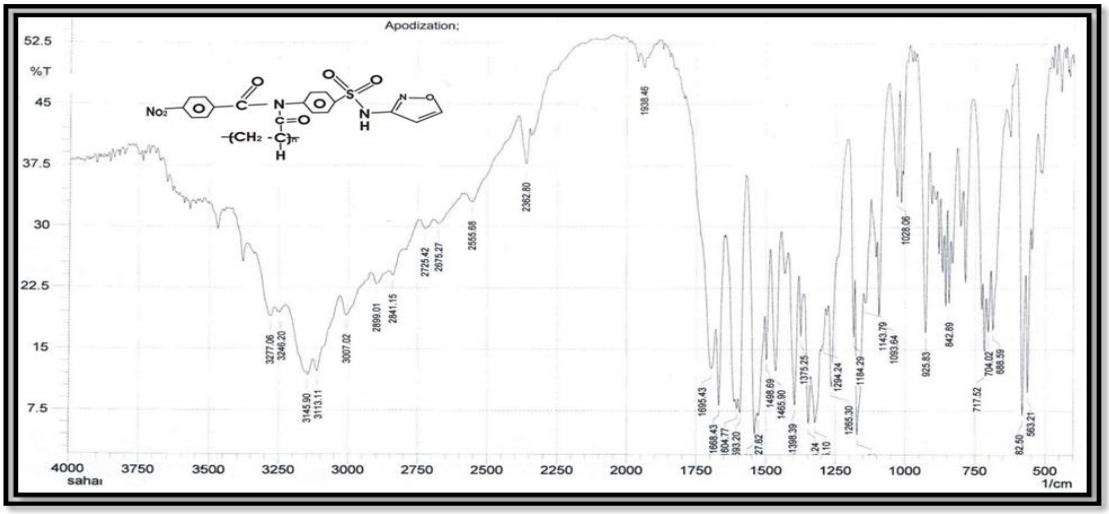


Fig (5) FT-IR for compound (10)

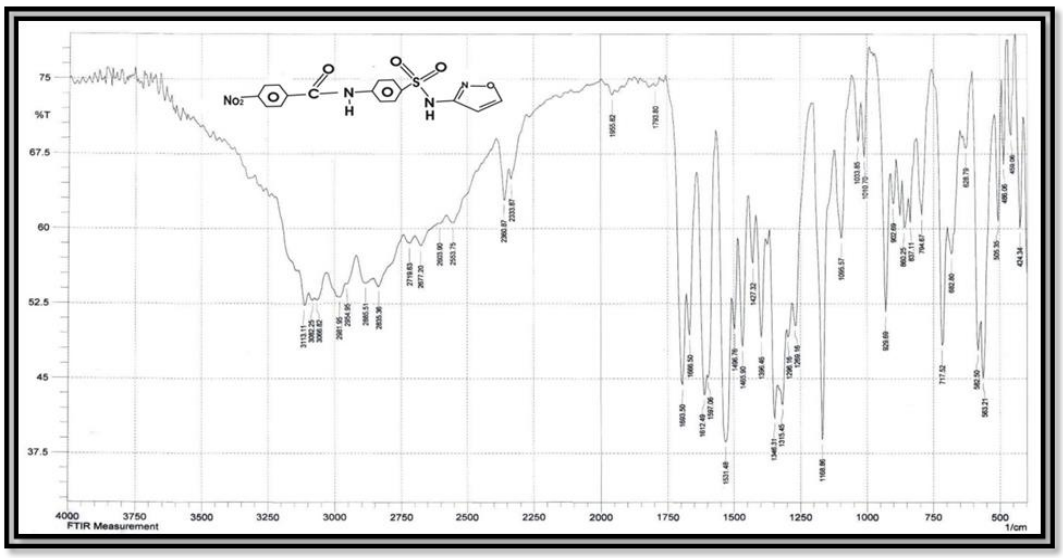


Fig (6) FT-IR for compound (5)

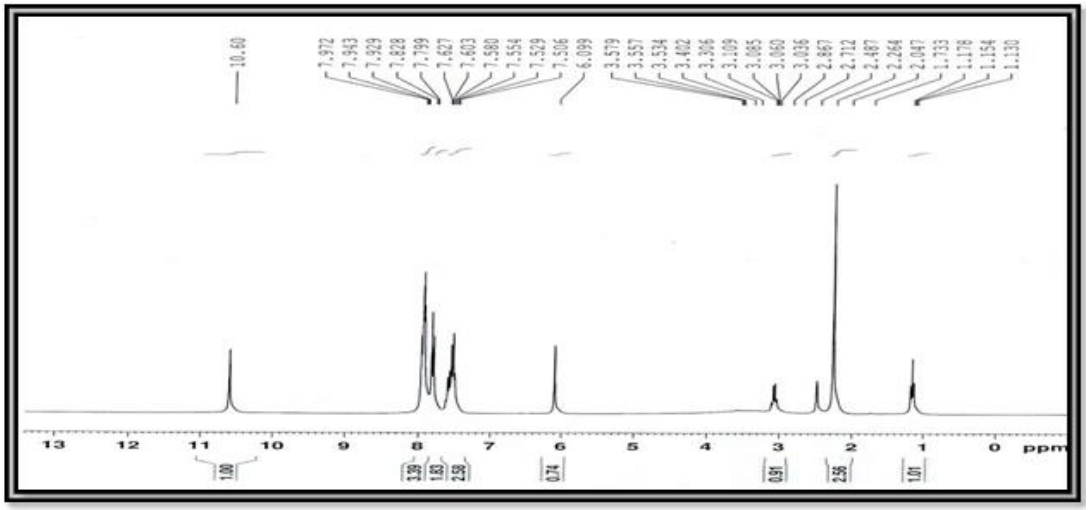


Fig (7) ^{1}H-NMR spectrum of compound (2)

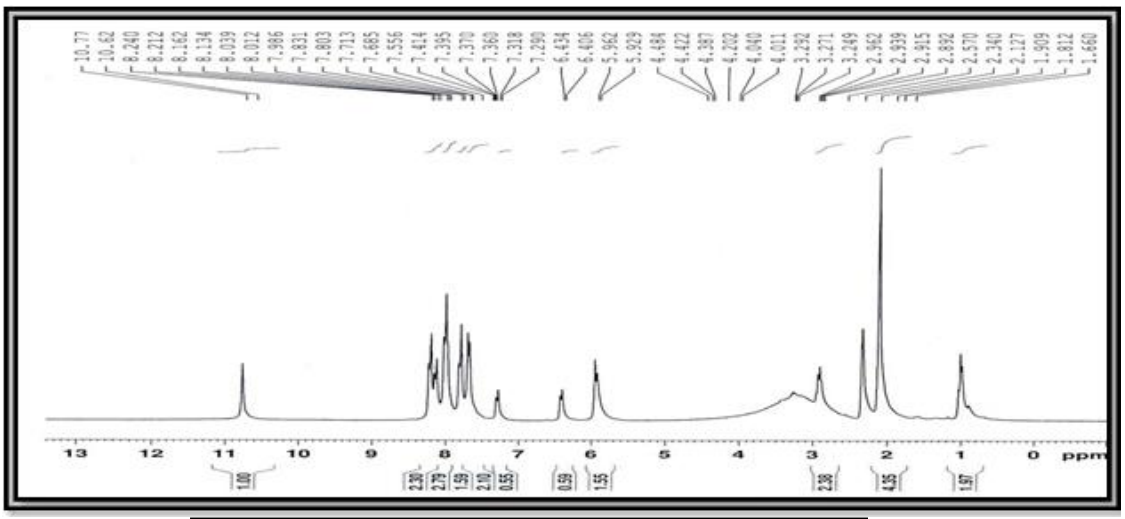


Fig (8) ^{13}C-NMR spectrum of compound (2)

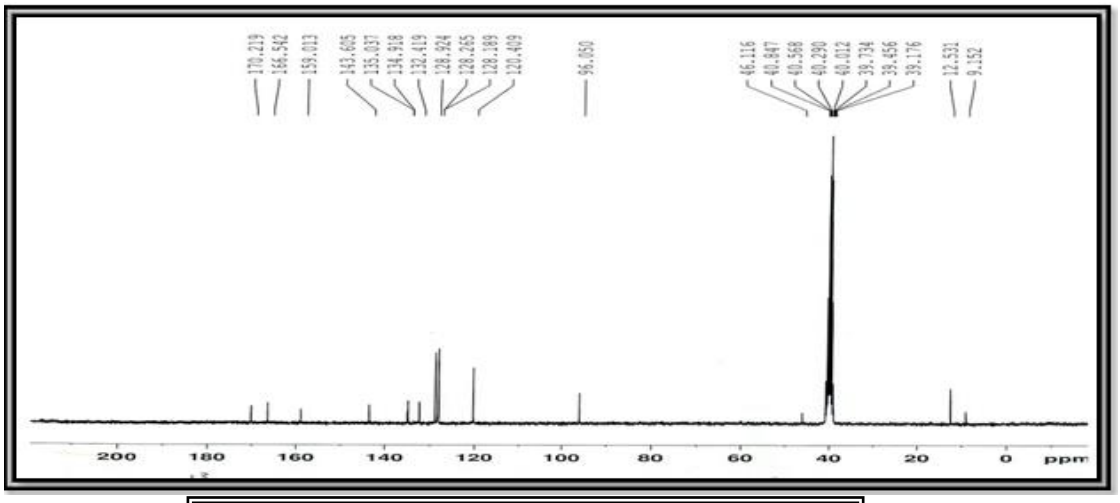


Fig (9) ^{1}H-NMR spectrum of compound (5)

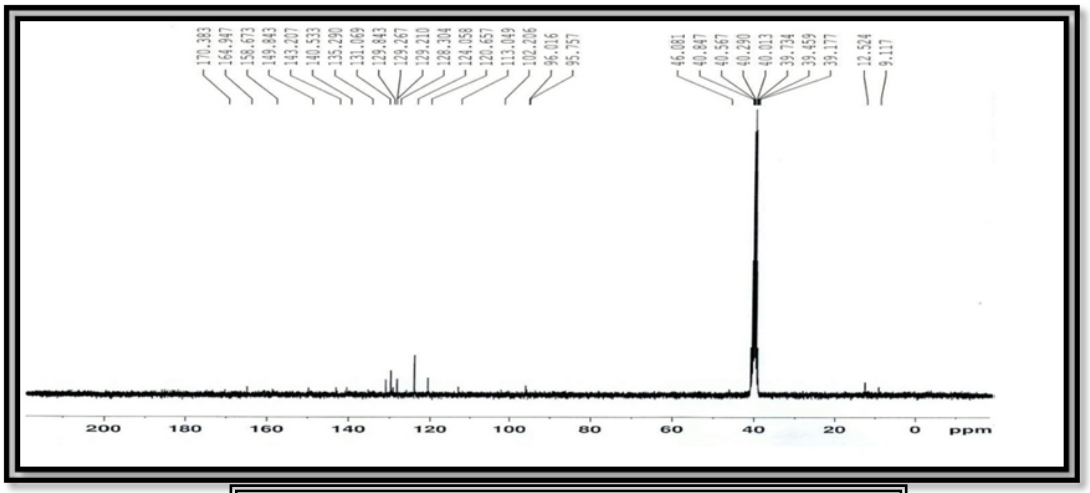


Fig (10) ^{13}C-NMR spectrum of compound (5)

References:

1- Khan, A.H. andLoother, B.A. 2010.pharmaceutical Development and Technology, 15(6): 613-618.

2- Mitscher, A.L.2002. Antibiotics and Antimicrobial Agents, Foyes principles of Medicinal chemistry, 15th:819-862.

3- Tamami, B. and Yeganeh, H.2001. synthesis and characterization of novelaromatic polyimides derived from 4-arly-2,6-bis (4-amino phenyl) pyridine. Polymer.42:415-420.

4- Feger,C.; Khojastehand,M.M. and Garth, E.J.1989. polyimides materials chemistry and characterization amesterdam, Elsevier. 453-478.

5- Wilson, D. :stenzeberger,H.D. and Hegenrother,P.M.1990.polyimide, Glasgow, black.360-395.

6- Al-Tamimi, E.O.;Al-Issa,M.A. andAl-Gburi,H.F.2013. Synthesis of N-benzothiazole derivative imide on polymeric chain, have possible biological activity, J. Bag, hdad for sci. 10(3): 673-685.

7- Al-Farajy, G.H.A.2003.Colleg of Science , University of Baghdad.

8- Yass,I. A.2010. Synthesis of substitutead 1,3- Oxazepine and 1,3 –Diazepine via Schiff Bases for selfamethoxazole drug, Kerbala J. of pharmaceutical scinces .1: 49-58.

9- RozhanskiiI.; Okuyama,K. and Goto, K.2002.Synthesis and properties of polyimides derived from isomeric biphenyl – tetra carboxylic dianhydridesi polymer. 41:7057-7065.
10- Lindon,J.C.;Tranter,G.E.andHolmes,J.L. 2000. Encyclopedia of spectros copy and spectrometry. part 1.
11- Der- Jang, L.; Been – Yang,L. and chia-wei,Y.2001. Synthesis and characterization of new organosaluble, polyimides based on flexible diamine. polymer,42: 839-849.
12- Barikani,M.2002. polyimides drived from disocyanate. Iran. Polym. J.11: 215-236.
13- Tambe,M.andSiddappaetal,K.2011 .J. of pharmacy Research,4(2). 308-311.
14- Bureau,M.J.andMittal,P.J. 1996. Application of polyimides as photosensitive materials. M.K Ghoh, K.L. Mittal. Marcel Dekker, New York, 743.
15- Tygi, O.D. and Sdav, M.Y. 2004.AText book of synthetic Drug. Anmol publication PVT ITD, New Delhi . 34:328-329.
16- Crews ,P. Rodrigues J. and |Jaspars, M. 1998.Organic structure analysis. Oxford university press, New York.
17- Siverstein,R.M and Bassler, G.C. 1967.Spectrometric identification of organic compounds, 2nd Ed. John wiley and Sons Ltd.
18- Dhahir,S. A.;Hamed,A.H. ; Salman,M.K.andAhmed,R.K.2010. Baghdad Science J. 7(1):607-613.
19- Hussain,S.M.2003. Ph.D. Thesis, College of Science, University of Baghdad.
20- Khamvnas,S.T.2012.Synthesis and characterization of (Oxazepine, Diazepine, Tetrazole) for Derivatives of sulfamethoxazole drug. Tikrit J. of pure science. 17(4):84-96.
21- Omote, T. 1996. polyimide-fundamentals and application M.K. Ghosh and K.L. Mittal, Ed. MarcellDekkor. Inc, New York. 121-128.

تحضير مشتقات ن_ سلفاميثاكسازول ايمايد على السلسلة البوليمرية

سميعة جمعة خماس البياتي ***أمال سمير صادق*** ***تماضر علي محمود****

*قسم الكيمياء ، كلية العلوم للبنات ، جامعة بغداد ، بغداد ، العراق

الخلاصة :

تم في هذا البحث تحضير بعض المشتقات ن- سلفاميثاكسازول ايمايد على السلسلة البوليمرية وذلك من خلال اجراء خطوتين ، حيث تضمنت الخطوة الاولى تحضير (1-5) N-(sub or unsubbenzoyle and sub or un sub acetyl) amidyl sub sulfamethoxazole وذلك بتكاثف دواء السلفاميثوكسازول مع بعض كلوريدات الحوامض المعوضة وغير المعوضة (الاليفاتية ، اروماتية) .

اما في الخطوة الثانية فقد تم تحضير بولي ايمايدات جديدة معوضة وغير معوضة (6-10) من تفاعل بولي اكريلويل كلورايد مع بعض الامايدات المختلفة (اليفاتية ، ارومانية) المحضرة في الخطوة الاولى (1-5) في مذيب مناسب وكمية مناسبة في ثلاثي اثيل امين (Et^3N) مع التسخين وتم اثبات التراكيب الكيميائية للبوليمرات المحضرة باستخدام الطرق الطيفية ، اطياف الاشعة تحت الحمراء FT–IR، اطياف الاشعة فوق البنفسجية UV. واطياف الرنين النووي المغناطيسي H-NMR ، اطياف ^{13}C- NMR بالاضافة الى القياسات الفيزيائية المختلفة من درجات التلين ودرجات الانصهار.