Synthesis & Antimicrobial Evaluation of Open Chain of Organo–Selenium Compounds

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Abstract :

The organo-selenium compounds are one of important organic compounds in synthesis of different compounds and as anti microbial .The target organo –selenium compounds [3-7] were synthesized from the reaction between diethyl malonate and 4-amino benzoyl chloride to produce compound [1] ,which is react with sodium hydrogen selenide to give corresponding sodium aroylselenide [2] ,which is react with one of aroyl derivatives as shown in scheme (1) to produce compounds [3-7].All the synthesized compounds have been investigated using different chemical techniques ,such as ,(C.H.N)-analysis , (H.NMR–spectra ,FT.IR–spectra) , melting points and biological study.

Keyword :organo selenium, sulphur, selenium.

Introduction :

The structures of organo- selenium compounds are mentioned in the literature as being similar to those of organo-sulphur compounds[1-3] ,but their properties present significant differences ,because of their toxicity and their extremely unpleasant odour organo-selenium compounds have been relatively little explored .

Organo-selenium compounds have been tested as antifungal , antibacterial ,antiparasitic ,ant-inflammatory ,antihistamine ,anticancer agents[4-6] ,industrial ,pharmaceutical applications[7-9] ,antidandruff hair shampoos ,small quantities of selenium compounds are used as human dietary supplements ,dyes applications[3] or as aligands and other uses[10-15] .

Experimental :

-All chemical used were (purity 99.98 %) and supplied from Fluka & BDH-chemical company .

-All measurements were carried out by :

--Melting points :electro thermal 9300 , melting point engineering LTD , U.K .

--FT-IR spectra : fourrier transform infrared shimadzu (8300) (FT-IR) ,KBr-disc was used .

--H-NMR spectra: in DMSO-d_6 as solvent.

-Elemental analysis (C.H.N) : EA-017 Mth.

--Uv–Visible spectra: shimadzu–1700 , double beam with computerized , Japan.

Synthesis Bis (4-amide benzoyl chloride)-methane [1]:

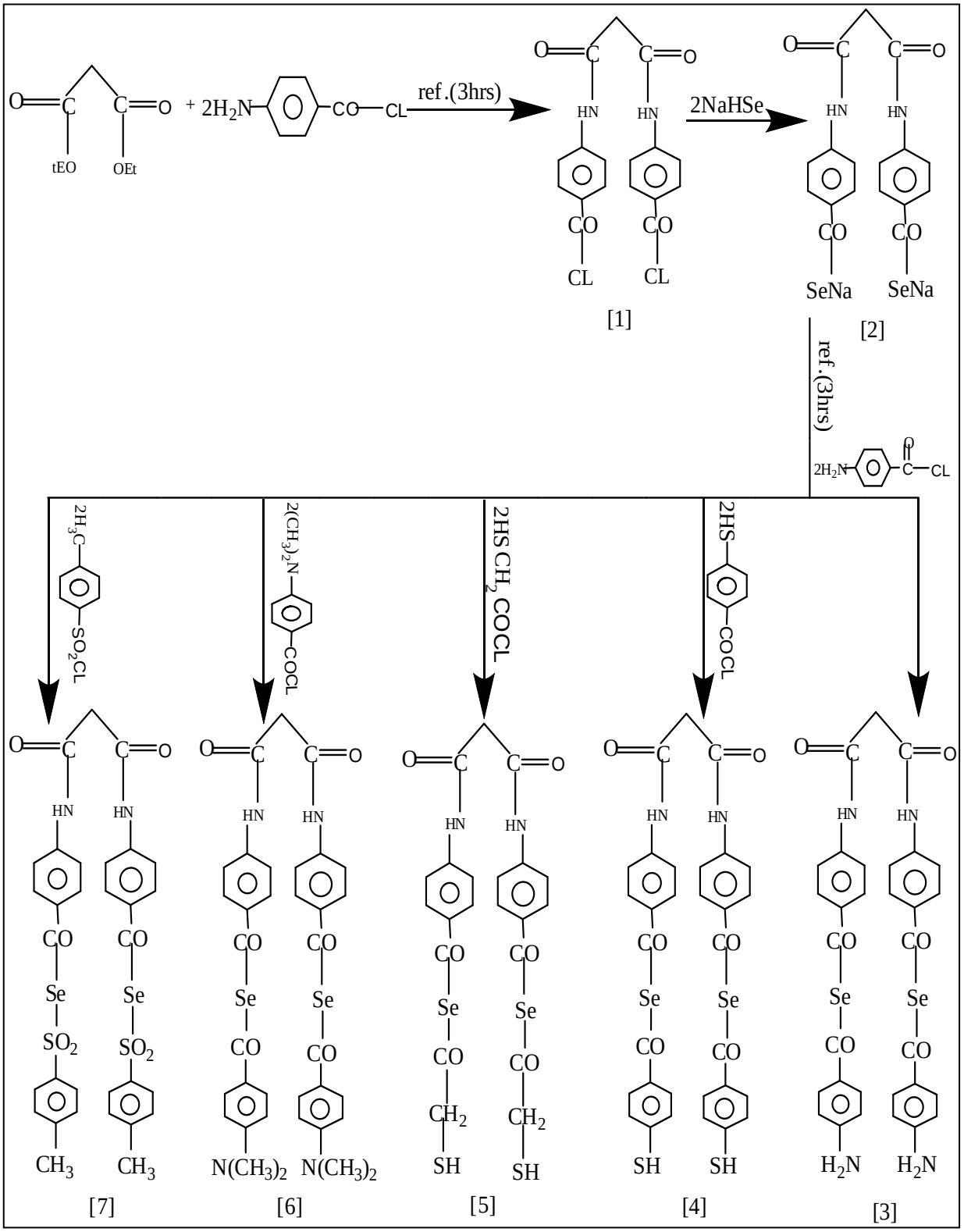
The preparation starts with the reaction between (0.05 mole ,8g) of diethyl malonate and (0.1 mole ,15.5 g) of 4-amino benzoyl chloride with reflux for (3 hrs) in ethanol solvent ,after cooling ,the precipitate was filtered off and recrystallized from ethanol to produce 87% of compound [1] .

Synthesis Bis (4-amide-sodium benzoyl selenide)-methane [2]:

(0.04 mole ,15g) of compound [1] was reacted with (0.08 mole,8.23g) of sodium hydrogen selenide and magnetically stirred for (1 hrs) in ethanol solvent ,the precipitate was filtered off to-produce(%85)of-compound[2].

General-Method:Synthesis[3-7]

A mixture of (0.01 mole,5.11g) of compound [2] with benzoyl chloride (0.02 mole,3.11g of 4-amino benzoyl chloride) were refluxed for (3 hrs) in presence of ethanol as a solvent ,after cooling , the precipitate was filtered off and recrystallized from ethanol to produce (%86) from compound [3]:bis (4-(4-amino benzoyl)-amide-benzoyl selenide)-methane., or (0.02mole ,3.45g) of 4-mercap to benzoyl chloride to produce(%83) from compound[4]: bis(4-(4-mercapto benzoyl)-amide-benzoyl selenide)-methane., or (0.02 mole ,2.2g) of mercapto aceto chloride to produce (%82) of compound [5] :bis(4-(acetothiol)-amide-benzoyl selenide)-methane., or (0.02 mole ,3.6g) of 4-N,N-dimethyl amino benzoyl chloride to yiled (% 85) of compound[6]:bis(4-(4-N,N-dimethyl amino benzoyl)-amide-benzoyl selenide)-methane .,or (0.02 mole ,3.8g) of toluene sulphonyl chloride) to give (% 84) from compound[7]:bis(4-(4-toluine-sulphonyl)-amide-benzoylselenid)-methane.,respectively.



Scheme (1) :Synthesis of compounds[1-7]

Results and Discussion :

Synthesized compounds [1-7] have been characterized by (C.H.N)-analysis, melting points and spectronic techniques(FT.IR ,H.NMR-spectrum) :

FT.IR–Spectra :

FT.IR–spectra showed :appearance band at (740)cm^{-1} due to (C-Cl) in compound [1] ,while this band is disappear in compounds [2-7] and other bands are appear such as:(1685-1700)cm^{-1} due to(CO) of amide ,(3200-3455) cm^{-1} due to (-NH) of amide ,(1655-1685) cm^{-1} due to (CO-Se) carbonyle of selenide ,these bands in compounds[3-7].,band at(3425)cm^{-1} due to ($-NH_2$) in compound [3]., (2611)cm^{-1} due to (-SH) in compound[4]., (2610)cm^{-1} due to (-SH) , (2920)cm^{-1}due to (C-H) aliphatic of ($-CH_2$), (1411)cm^{-1}due to (CH_2-S) in compound [5] .,(1379) cm^{-1} due to ($-N(CH_3)_2$) in compound [6].,(1253,1342)cm^{1}due to($-SO_2$) sulphone group ,(2920) cm^{-1} due to (C-H) aliphatic of ($-CH_3$) group in compound [7].

Appearance of these bands (CO-Se, SH, NH_2, SO_2, CH_2-S) are evidence to synthesised compounds [1-7], other data of functional groups shown in the following table (1) ,figures (1-5).

H.NMR-Spectrum :

H.NMR-Spectrum of compounds [1-7] showed : singlet signal at ∫9.9 for proton)[15] of amide (CO-NH) , singlet signal at ∫ (3.08-3.61) for two protons of methane group (CO-CH_2-CO) malonate after reaction ,doublete of doublet signal at ∫ (7.26-7.82) for protons of venyl group (benzoyl amide) ,all these bands in compounds[1-7]., while other beaks appear in table (2).

(C.H.N)-Analysis :

From table(3) of (C.H.N)-analysis , compared the calculated data for compounds[1-7] are in a good agreement with experimentally , the results were compactable , the data of analysis & melting points are listed in table (3).

Assay of antimicrobial activity [16]:

All material such as (agar for bacteria , DMSO ,betri dish) and bactria supplied from bio-lab in college education of kufa university.

Antimicrobial activity was tested by the filter paper disc diffusion method against gram positive bacteria *(Staphylococcus . aureus)* and gram negative bacteria (*Pseudomonas . aeruginosa*) , 0.1 ml of the bacterial suspensions was seeded on agar

To determine minimum inhibitory concentration(MIC) for each compounds[1-7] were ranged between (5-10)mg/ml by dissolved in (DMSO) and preparation 0.1mg/ml standard antibiotic amoxyline as positive standard and reference .

The positive results or sensitivity were established by the presence of clear zone of inhibition around active compounds which were measured with a meter rule and diameters were recorded based on (mm), the assays were performed with two replicates .

Generally, The results showed that the compounds[1-7] have great inhibitory effect against tested bacteria as compared with Synthetic antibiotic Amoxyline.

Table (4) showed the zone of inhibition of the compounds[1-7] in this study ranged (from 34 to 9) mm. From results, we noted that the compounds[4,5,7] have higher antibacterial activity against *S.aureus and P.aeruginosa* is due to the presence of selenium and sulphone with sulfur atomes(Se, SO_2 ,S) in their structures. Consequently,these compounds become more

effective in precipitating proteins on bacteria cell walls.These atoms form hydrogen bonds with cell wall protein and hence ,destroying the cell membranes,these compounds had abroad antibacterial activity .

Table (1): FT.IR data (cm^{-1}) of compounds [1-7]

Comp. No.	(C=O)of amide	(NH) amide	(—C(=O)—Se—)carbonyl of selenide	Other bands
[1]	1695 S	3320 m	-----	(C-Cl): 740 S
[2]	1690 S	3300 m	1660 S	
[3]	1700 S	3200 m	1685 S	($-NH_2$) :3425 m
[4]	1700 S	3338 m	1665 S	(-SH): 2611 w
[5]	1690 S	3455 m	1665 S	(-SH): 2610 w, (C-H)aliphatic:2920w (CH_2-S): 1411 S
[6]	1685 S	3304 m	1661 S	(4-$N(CH_3)_2$): 1379 S
[7]	1690 S	3450 m	1655 S	($-SO_2$)sulphone:1253S, (C-SO_2) : 1342 S.,(C-H)aliphatic:2920 m

Table(2): H.NMR–data (б PPm) of compounds

Comp.No.	H.NMR (only important peaks)
Compound [3]	Signal at ∫ 8.5 for protons of ($-NH_2$) in
Compound[4].	Signal at ∫ 10.98 for protons of (-SH) aromatic.
Compound [5]	Signal at ∫ 4.27 for protons (-SH) aliphatic.
Compound[6]	Signal at ∫ 3.93 for six protons of (-$N(CH_3)_2$) .
compound[7]	Signal at ∫ 2.97 for three protons of (-CH_3) .

Table(3):Melting points ,M.F & Elemental Analysis of compounds[1-7]

Comp. No.	M.F	M.P C°	Calc. / Found. C%	H %	N %
[1]	$C_{17}H_{12}N_2O_4Cl_2$	139	54.40 54.31	3.20 3.14	7.466 7.348
[2]	$C_{17}H_{12}N_2O_4Se_2Na_2$	147	39.853 39.788	2.344 2.286	5.470 5.410
[3]	$C_{31}H_{24}N_4O_6Se_2$	181	52.697 52.600	3.399 3.265	7.932 7.878
[4]	$C_{31}H_{22}N_2O_6Se_2S_2$	194	50.275 50.189	2.973 2.906	3.784 3.679
[5]	$C_{21}H_{18}N_2O_6Se_2S_2$	162	40.914 40.875	2.922 2.865	4.546 4.469
[6]	$C_{35}H_{32}N_4O_6Se_2$	187	55.123 55.095	4.199 4.107	7.349 7.268
[7]	$C_{31}H_{26}N_2O_8Se_2S_2$	197	47.943 47.855	3.350 3.307	3.608 3.517

Table(4):Antibacterial activity of the compounds[1-7] {diameter of zone (mm)} .

Compounds[1-7] *	diameter of zone(mm)	
	G+: Staphylococcus. aureus	*G-: Pseudomonas. aeruginosa*
compounds[1]	14	9
compounds[2]	19	12
compounds[3]	23	17
compounds[4]	32	26
compounds[5]	31	24
compounds[6]	29	20
compounds[7]	34	
Amoxyline**	36	30

*Minimum Inhibitory concentration (MIC)of compounds[1] (5mg/ml).
xyline (0.1mg/ml) .

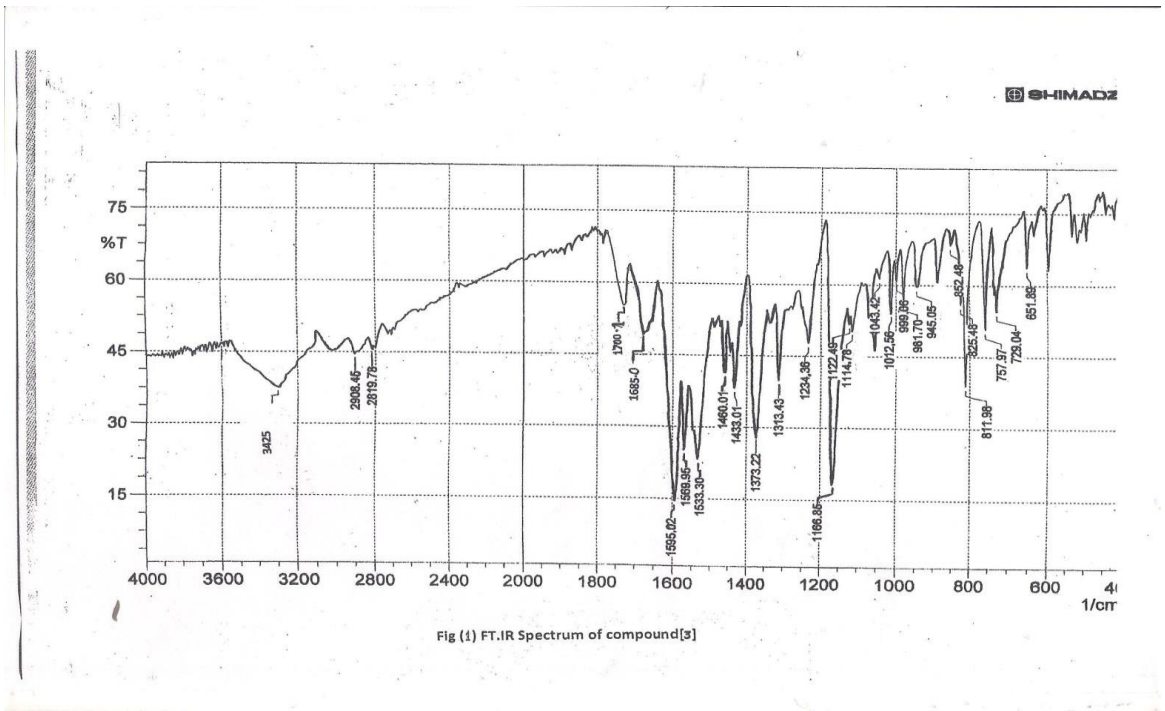


Fig (1) FT.IR Spectrum of compound[3]

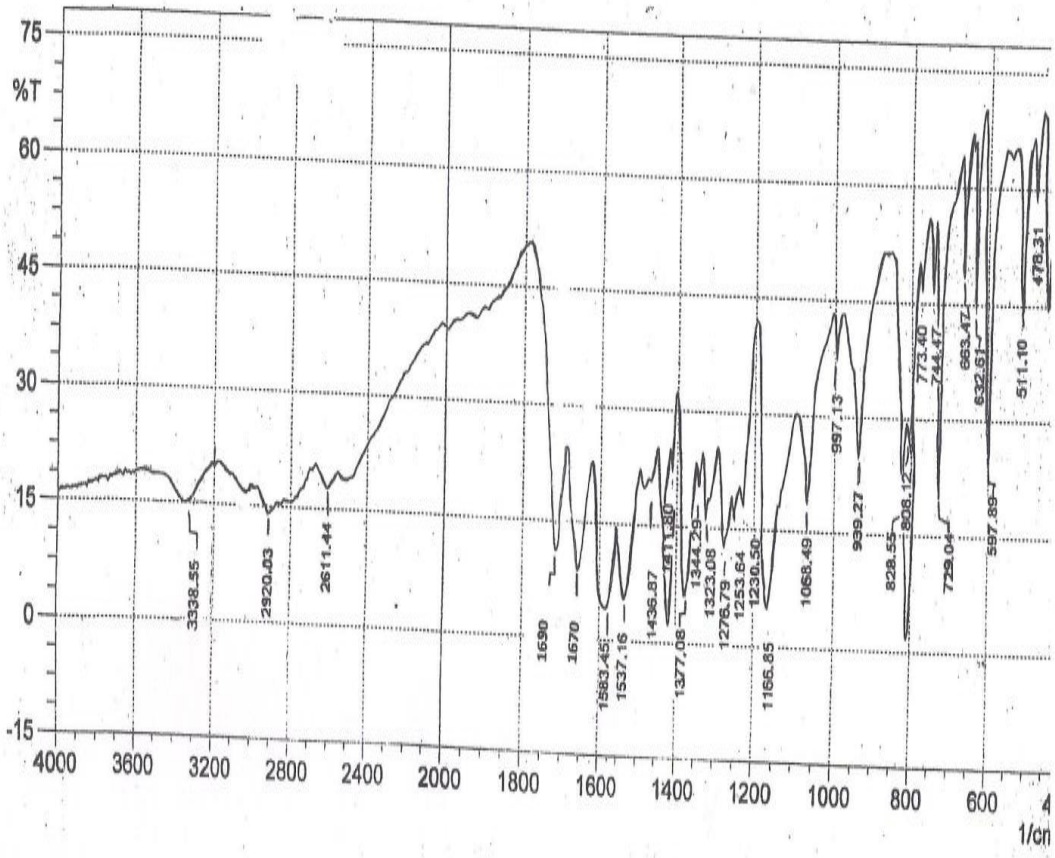


Fig (2) FT.IR Spectrum of compound[4]

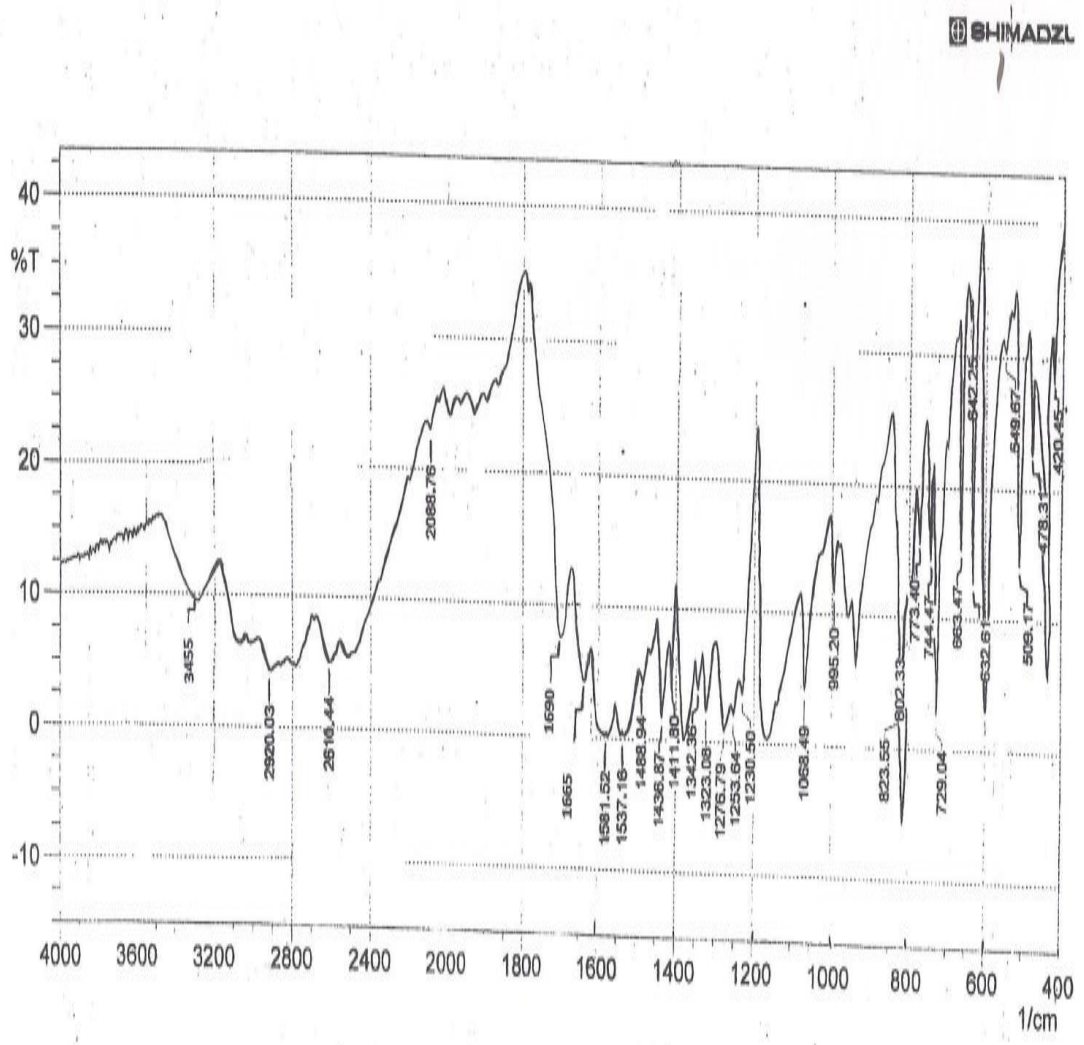


Fig (3) FT.IR Spectrum of compound[5]

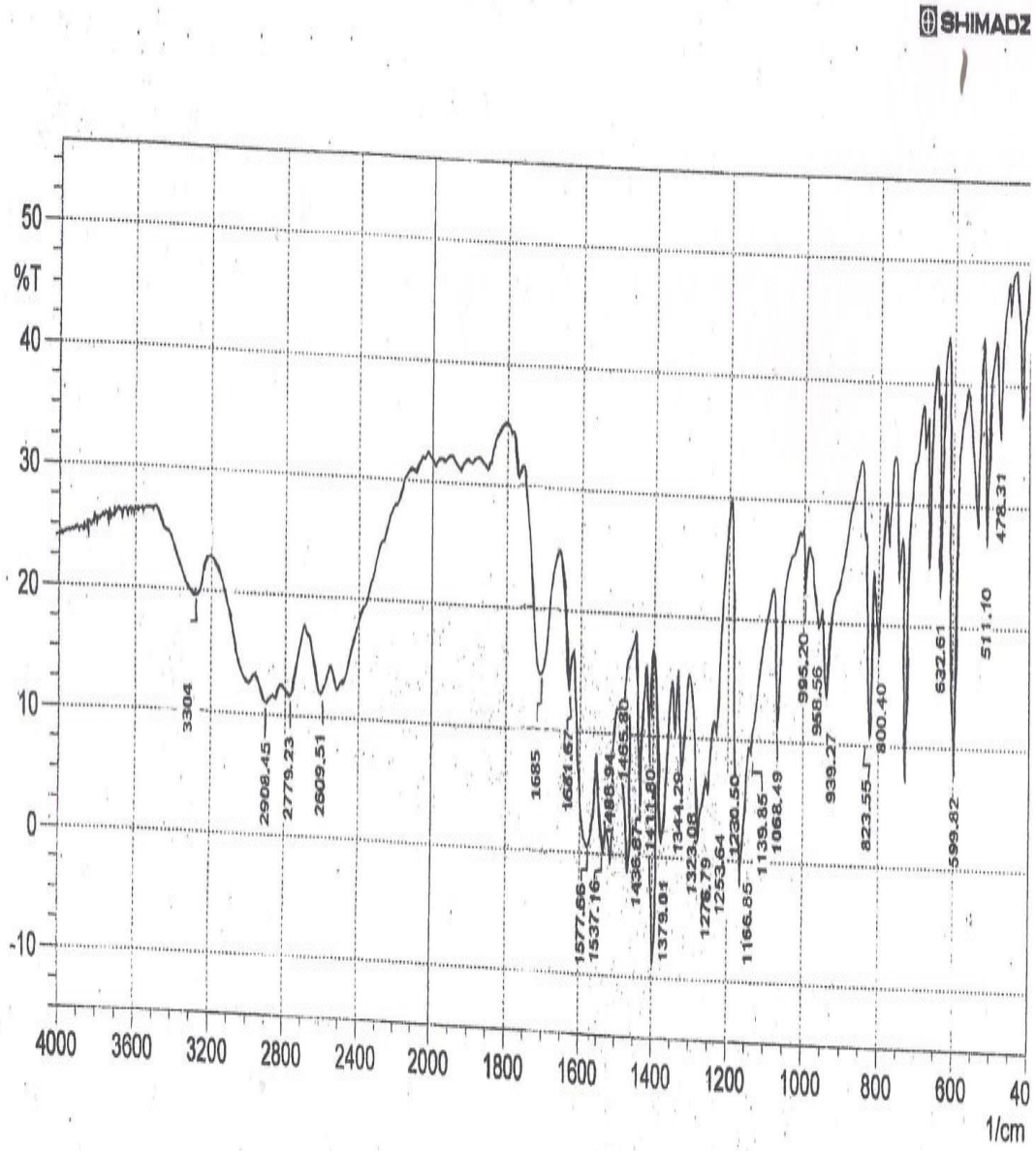


Fig (4) FT.IR Spectrum of compound[6]

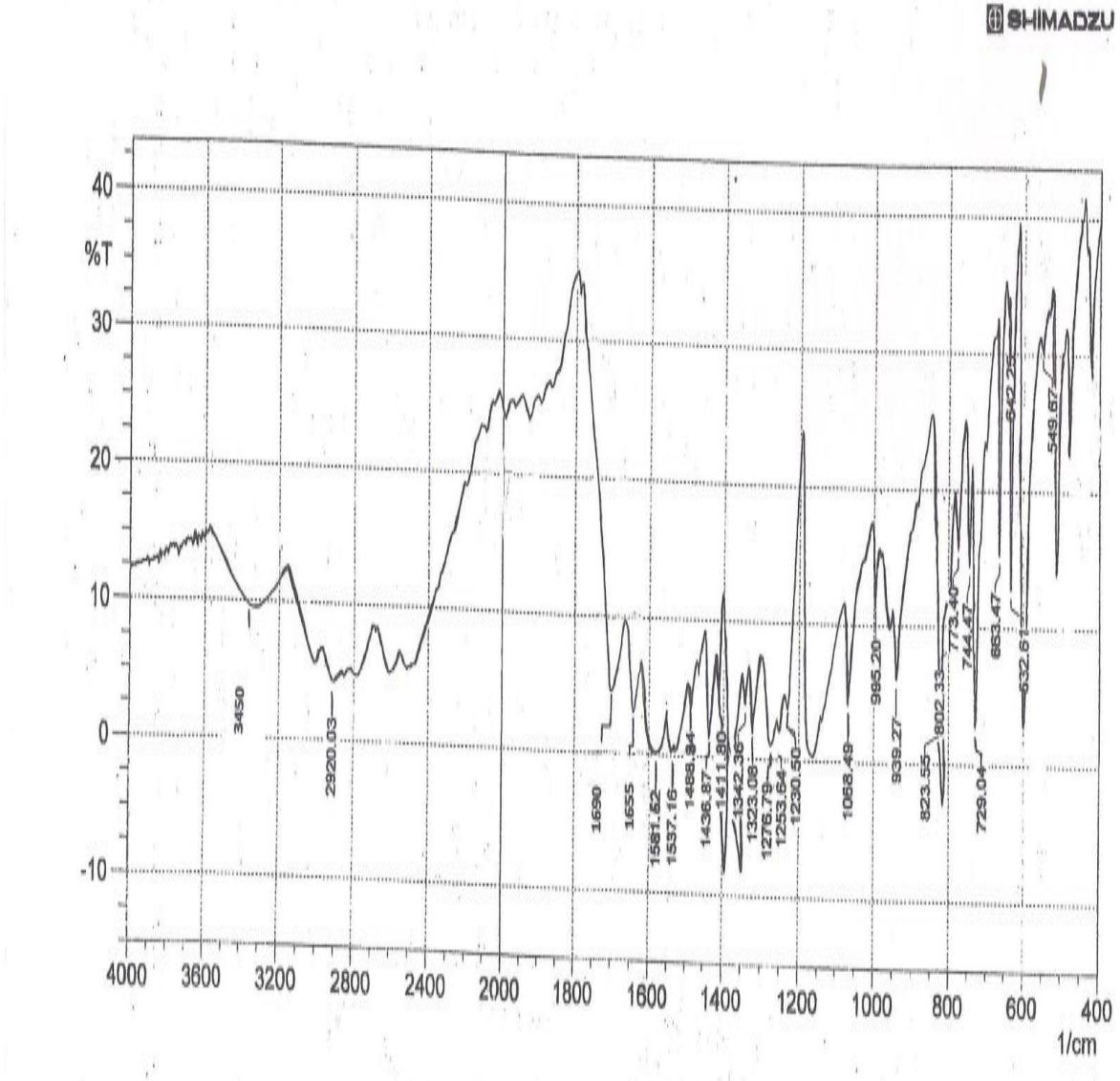


Fig (5) FT.IR Spectrum of compound[7]

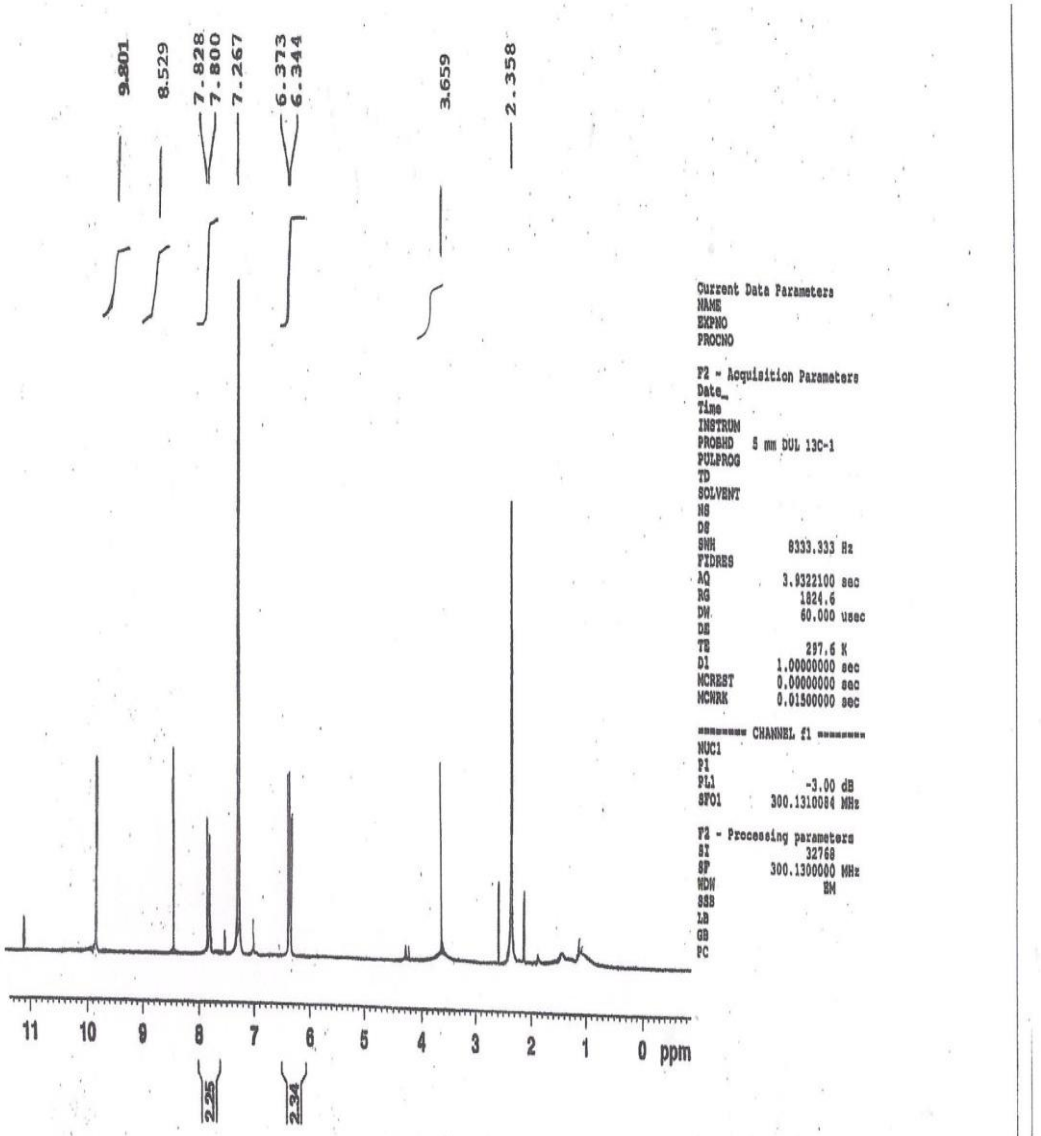
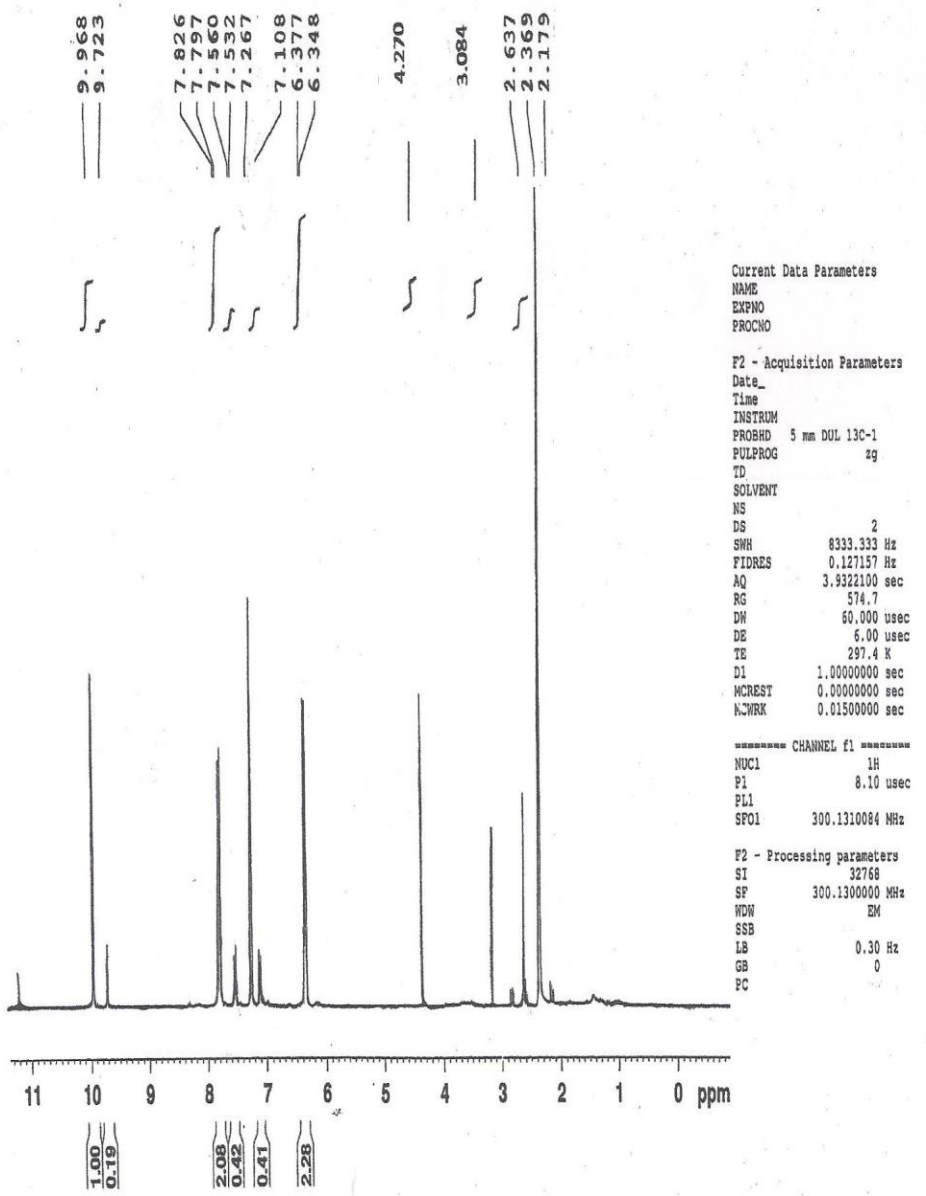
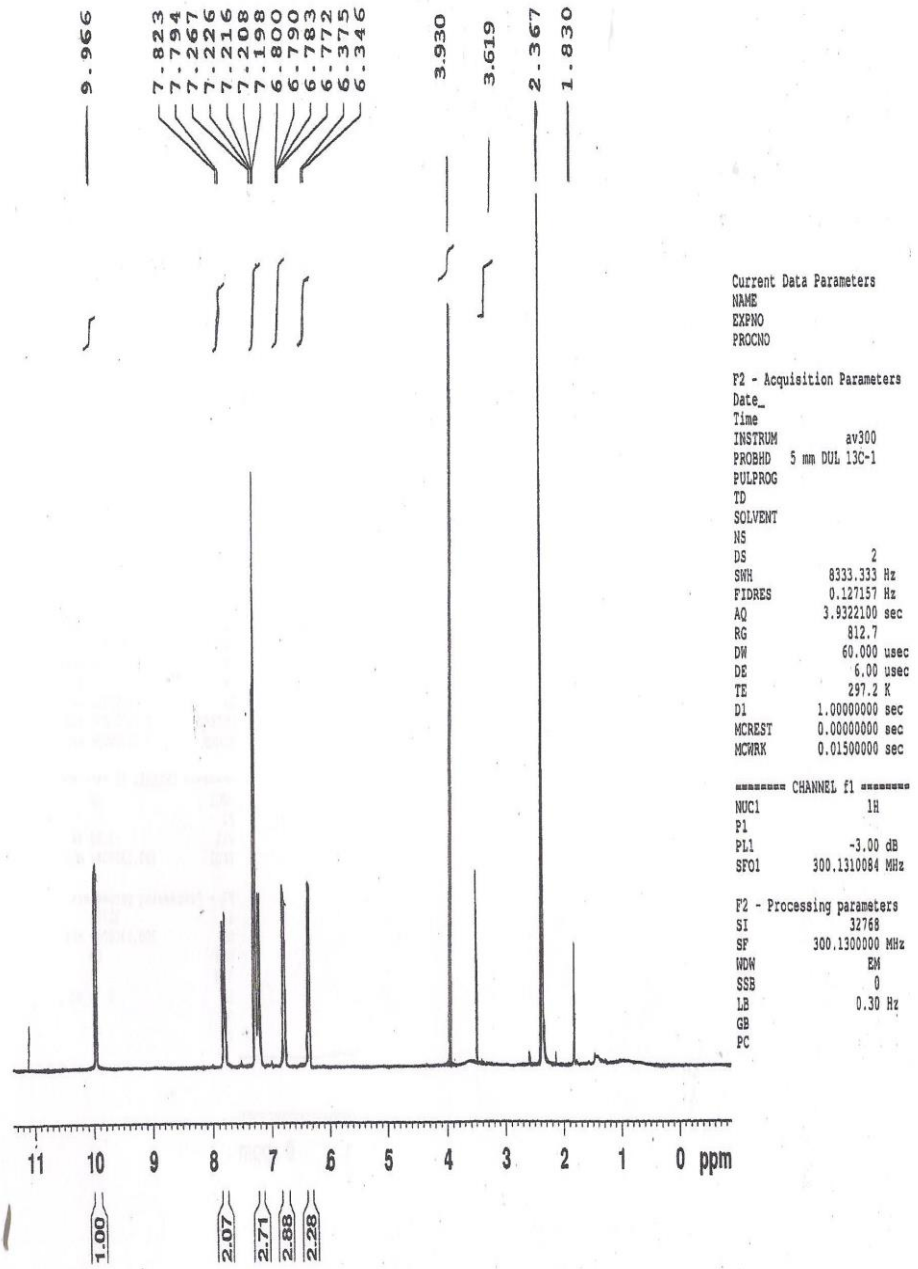


Fig (6) HNMR -Spectrum of compound[3]



Fig(8) H.NMR –Spectra of compound (5)



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EXPNO
PROCNO

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NS
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FIDRES 0.127157 Hz
AQ 3.9322100 sec
RG 812.7
DW 60.000 usec
DE 6.00 usec
TE 297.2 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
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P1
PL1 -3.00 dB
SFO1 300.1310084 MHz

F2 - Processing parameters
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SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB
PC

Fig(9):H.NMR –Spectra of compound (6)

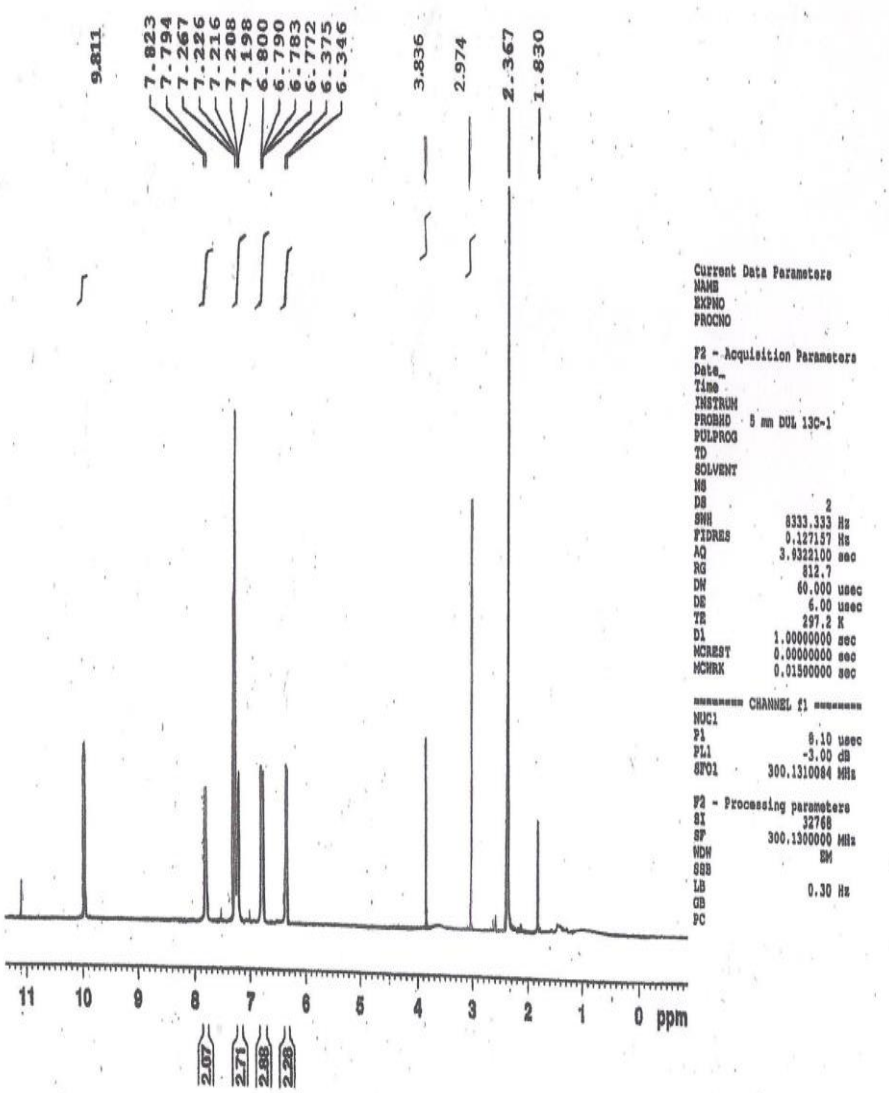

Fig (7d) HNMR -Spectrum of compound[7]

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تحضير ودراسة الفعالية البايولوجية لمركبات السيلينيوم العضوية مفتوحة السلسلة

تاريخ الاستلام : 10\5\2012 تاريخ القبول : 20\11\2012

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الخلاصة :

تُعد مركبات السلينيوم من أصناف المركبات العضوية المهمة والتي ساهمت كثيراً في تحضير العديد من المركبات الحلقية غير المتجانسة ، أذ تنوعت طرق تحضيرها وظروف تفاعلها حسب نوع المركبات المراد تحضيرها وأهميتها البايولوجية التي أشتهرت بها لما تتمتع به مركبات السلينيوم من صفة مضادة بايولوجياً للعديد من الفطريات والبكتريا. حيث حُضرت مركبات السلينيوم العضوية (3-7) في هذا البحث من تفاعل مالونات ثنائي الاثيل مع 4-أمينو كلوريد البنزويل ليعطي المركب (1) ،والذي بدوره يتفاعل مع سيلينيد هيدروجين الصوديوم NaHSe ليعطي سيلينيد بنزويل الصوديوم المقابل (2) ،والذي ايضا بدوره يتفاعل مع احد مشتقات البنزويل الموضحة في مخطط التفاعل رقم (1) لينتج المركبات (3-7) .

شُخصت جميع المركبات المحضرة في هذا البحث بتقنيات كيميائية مختلفة منها التحليل الدقيق للعناصر و (طيف الرنين النووي المغناطيسي ، ،طيف الاشعة تحت الحمراء) ونقاط الانصهار مع دراسة .