Synthesis and Characterization of Compounds Containing 1,3 Oxazepine ring

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Abstract.

This study includes the synthesis of some new compounds of 1,3 oxazepine derivatives by the reaction of D- glucose with acetone and conc. Sulfuric acid to give (1) which treatment with 80% acetic acid selectively removed the isopropylidene at the positions 5 and 6 of the sugar to give compound (2),this compound treated with sodium periodate gave (3) .The reaction between compound (3) with different amines gave schiff-base compounds (4-6) .Then the reaction between these shiff-basese with phtalic anhydride gave target compounds (7-9). The prepared compounds identified by physical properties and spectral methods (FT-IR, ^{1}H-NMR, ^{13}C-NMR) .

Keyword :. 1,3 Oxazepine, phthalic anhydride, glucose, Schiff base

تحضير وتشخيص مركبات تحتوي على الحلقة 1,3 اوكسازيبين

الخلاصة.

تضمنت هذه الدراسة تحضير مركبات جديدة ل 1,3 اوكسازيبين وذلك بتفاعل الكلوكوز مع الاسيتون بوجود حامض الكبريتيك المركز للحصول على المركب (1) والذي تم معاملته مع 80 % حامض الخليك الذي ازال وبانتقائية مجموعتي الايزوبروبليدين من الموقعين 5 و 6 ليعطي المركب (2) ، عومل هذا المركب مع بيريودات الصوديوم واعطى المركب (3) والذي تفاعل مع امينات مختلفة اعطى قواعد شف (4-6) . بعد ذلك تم مفاعلة هذه القواعد مع انهدريد الفثاليك تم الحصول على المركبات الهدف (7-9

(FT-IR, ^{1}H-NMR, ^{13}C-NMR) . تم التعرف على المركبات المحضرة من خلال القياسات الفيزياوية والطيفية

Introduction

Schiff bases are well known in the pharmaceutical industry and medicinal field they have been shown to possess a broad spectrum of biological activities [1] including antibacterial [2,3] , antifungal [4] anticancer [5] and herbicidal [6] activities . The oxazepine are unsaturated compounds of 7-membered heterocyclic ring which contains five carbon atoms and 2-non hetero atoms (oxygen and nitrogen). For 7-members [7,8] which interest the researcher to discover different ways for7-members heterocyclic double-bound synthesis [9] .The reaction between (-C=N-) for Schiff bases with phthalic anhydride produce different new compounds [10] , which are used in drugs and other medicinal pharmaceutical uses [11] ,for example in treatment of cancer diseases [12] and schezofrenia [13] , for example (dibenzoxazepine, amoxapine) and they have inhibitor action to presynaptic reuptake of Norepinephrine and serotonin also blocked the response of dopamine receptors to dopamine [14] . The interesting biological activities attracted our attention to the chemistry of nitrogen and oxygen heterocycles compounds.

Experimental

A –Instrumental

1. Melting points were determined on melting points apparatus SMP 30, in Missan University, College of Science.

2. FTIR spectra were recorded using KBr disc on SHIMADZU FTIR-8400 S Fourier Transform Infrared spectrophotometer, in college of science, Missan University.

3- ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Fourier transform varian spectrometry , company, Bruker, model, Ultra shield 300MHz origin: Switzerland , with tetramethyl silane as internal standard in DMSO-d^{6} as solvent . In Iran , Tarbit Modares University .

B-Materials

All materials from BDH and Fluka companies .

Synthesis of 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose(1)[15]

Pure α-D-glucose (10 g; 55.5 mmol.) was added into 500 ml Erlenmeyer flask. Dry acetone (200 ml) was added, the suspension was stirred in an ice-bath then concentrated sulfuric acid (8 ml) was added dropwise using a pipette, then the flask was stoppered , and the suspension was stirred magnetically for (5hrs.). To a stirred mixture, a suspension of (12.25g) of sodium hydroxide in 15ml of water was added gradually. The suspension was filtered under suction, and the preci- pitate was washed several times with acetone. The solution was evaporated until the acetone has been removed ,the desired acetal was separated as an oily upper layer , which was dissolved in chloroform on a water bath the chloroform extract was dried over anhydrous $MgSO_4$ then evaporated to give white crystals which was recrystlized from cyclohexane.

Synthesis of 1,2-O-isopropylidene-3-hydroxy α-D-glucofuranose(2)[15]

A solution of compound (1) (3.64 g,10 mmol) in 80% acetic acid (50 mL) was kept at room temp. for (48 hrs.), after this time the solution was concentrated and co- evaporated with n-butanol (3x15 mL), the residue was extracted with ethyl acetate then dried. A white Precipitate (2.90 g, 81% yield), m.p. (72-75 ^{0}C).

Synthesis of Aldehyde(3) [16]

A solution of diol (2) (5mmol) in 20ml of ethanol was added over (30min.) to the solution sodium periodate (5 mmol) in water (10 mL), the oxidation was allowed to proceed for (2 hrs.) at (^{0}0C), the solvents were removed, the residue was taken up in ethyl acetate (20 mL) and washed with water and dried with $MgSO_4$, evaporation of solvent under reduced pressure followed by column resin of the residue using (EtOAc: petroleum ether 2:1) as eluent afforded the pure aldehyde (3) as a colorless syrup (76%).

Synthesis of Schiff bases (4-6)

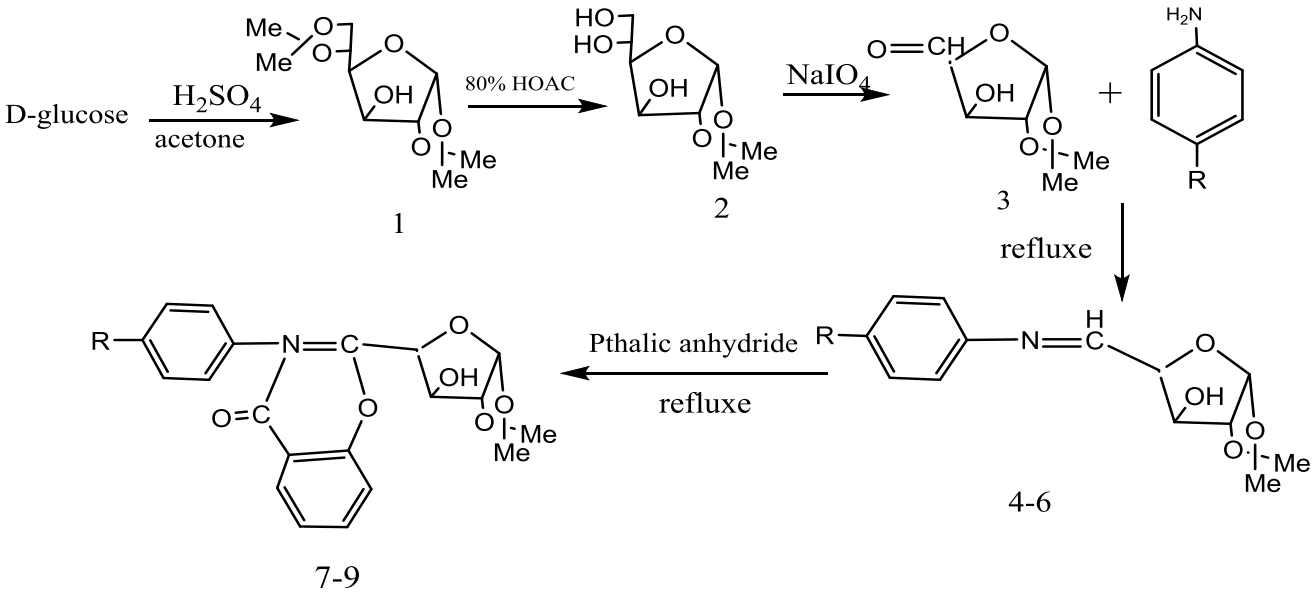
A solution of amine (5mmol) in a small amount of ethanol was added to the solution of aldehyde (3) (5 mmol) in (25 mL) absolute ethanol with 4-5 drops of glacial acetic acid, the solution was refluxed for (1 hrs.), the solvent was evaporated under reduced pressure to give the compounds: (4-6) as a light yellow solid .

Synthesis of 1,3 Oxazepine (7-9)[17]

A mixture of equimolar amounts (5 m mole) of schiff's bases [4-6] and phthalic anhydride in dry toluene was refluxed for (5 hrs.), the solvent was removed to give pale yellow soild which recrystallized from hexane afforded the target products (7-9).

Results and Discussion

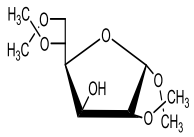
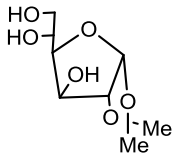
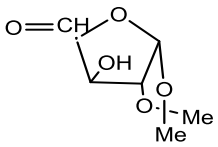
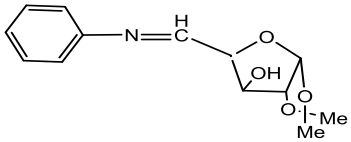
The overall synthetic steps of this work is shown in the following scheme:



R= H, OH , OCH_3

The reaction of D-glucose with acetone in the presence of conc. Sulfuric acid afforded compound (1). FT-IR spectrum of compound (1) showed characteristic absorption at (3360) cm^{-1} ,(2880-2930) $cm^{-1}$and (1050-1240) cm^{-1} due toν(OH) hydroxyl group , ν(C-H) aliphatic and ν(C-O-C) cyclic acetal respectively as shown in table (1) , and (Figure 1) [18]. Treatment of compound (1) with 80% acetic acid selectively removed the isopropylidene at the positions 5 and 6 of the sugar to give compound (2). FT-IR spectrum of (2) showed the following bands; 3400 cm^{-1} for hydroxyl stretching groups. The reaction of

compound (2) with sodium periodate in mixture of alcohol-water gave the aldehyde (3). FT-IR spectrum of (3) showed the bands at: 2987 cm^{-1} and 2888 cm^{-1} aliphatic (C-H) stretching , 2800 cm^{-1} and 2700 cm^{-1} aldhehydic (C-H) stretching, 1690 cm^{-1} aldehydic (C=O) stretching . The reaction between compound (3) with different amines gave compounds (4-6) . FT-IR spectra of (4-6) showed in Table (1). The reaction between schiff-base compounds (4-6) with phtalic anhydride gave target compounds (7-9). FT-IR spectrum of (7-9) showed in Table (1), and Figures (1-3) .

comp. no	Structure	V(C-H) alephatic	V(CH) aromatic	(OH) V	(C=N) V	Other bands
1		2880-2930	-	3360	-	1050-1240 (C-O-C)
2		2850-2920	-	3400	-	1050-1210 (C-O-C
3		2888-2987	-	3380	-	1050-1230 (C-O-C 1690 (C=O)
4		2850-2940	3040	3410	1660	1050-1230 (C-O-C

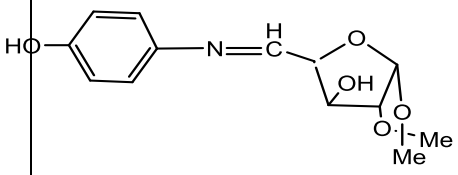
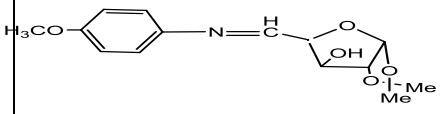
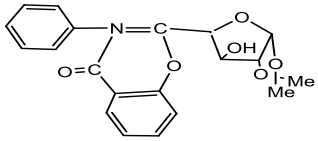
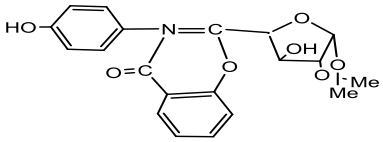
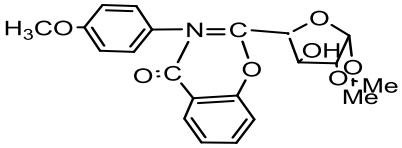
5		2870-2930	3070	3400	1665	1150-1210 (C-O-C
6		2880-2920	3050	3410	1650	1150-1240 (C-O-C)
7		2850-2940	3100	3400	1638	1675 (C=O) 1050-1240 (C-O-C
8		2830-2940	3110	3415 - 3467	1640	1680 (C=O) 1120-1240 (C-O-C
9		2850-2930	3080	3420	1635	1150-1230 (C-O-C) 1665 (C=O)

Table-1- FT-IR Spectra of compounds (1-9)

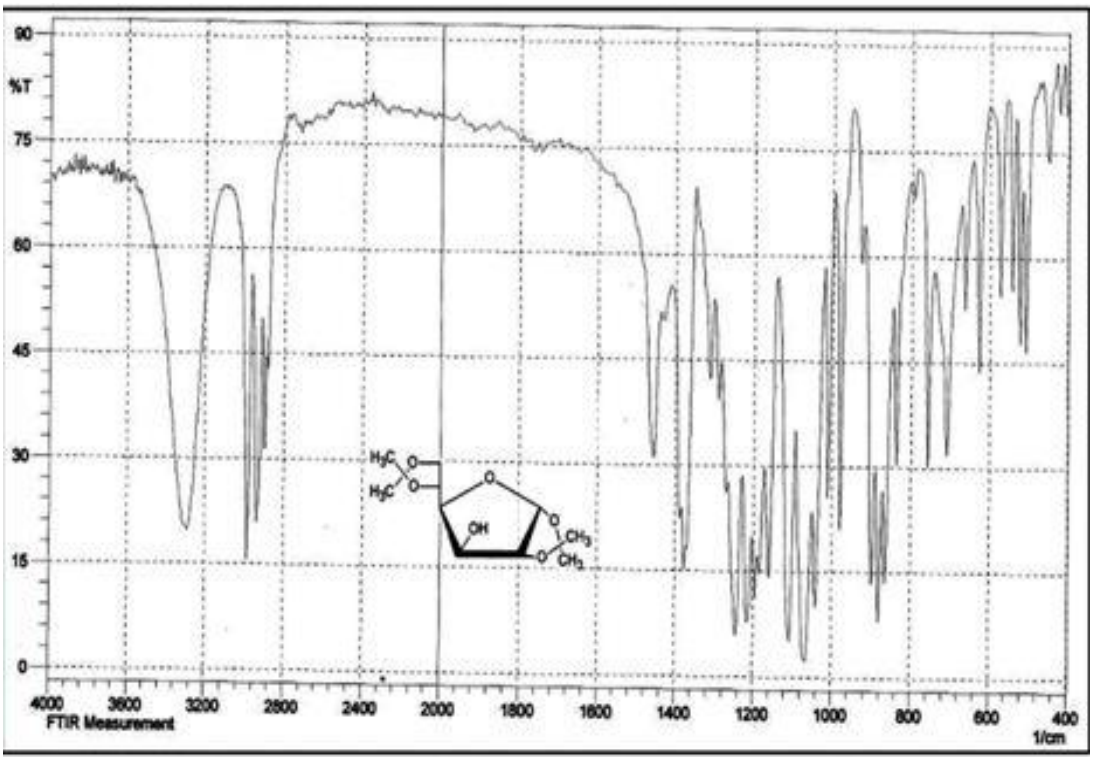


Fig (1) : FT-IR Spectrum of compound (1)

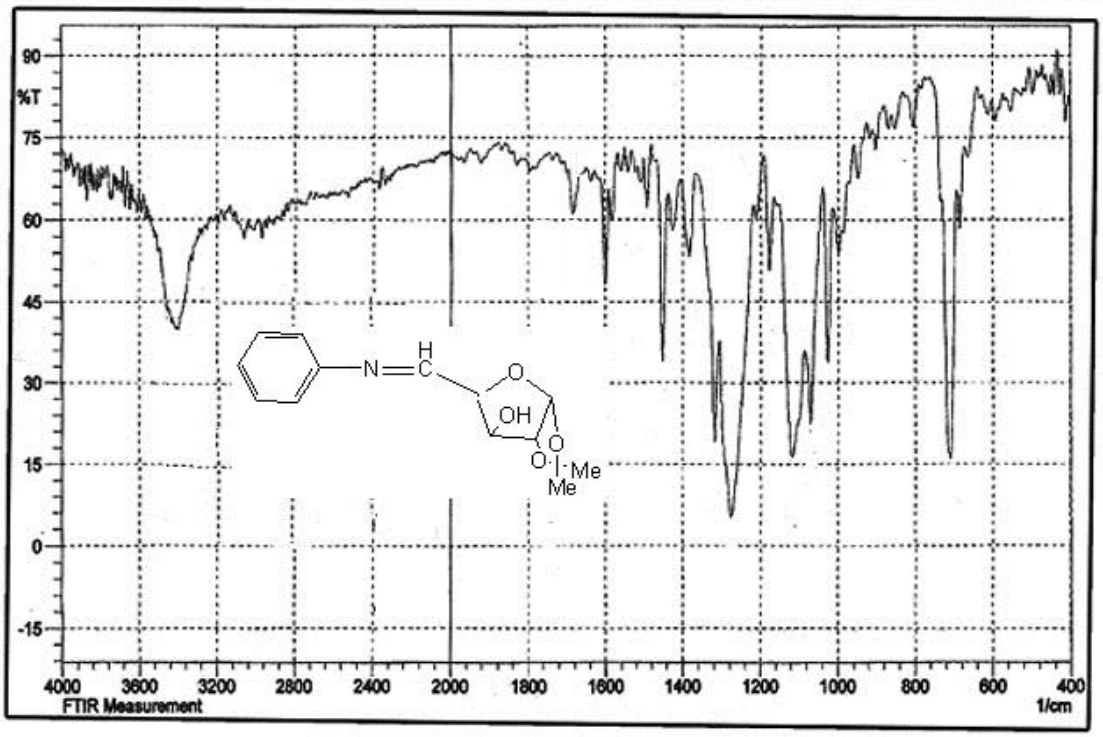


Fig (2) : FT-IR Spectrum of compound (4)

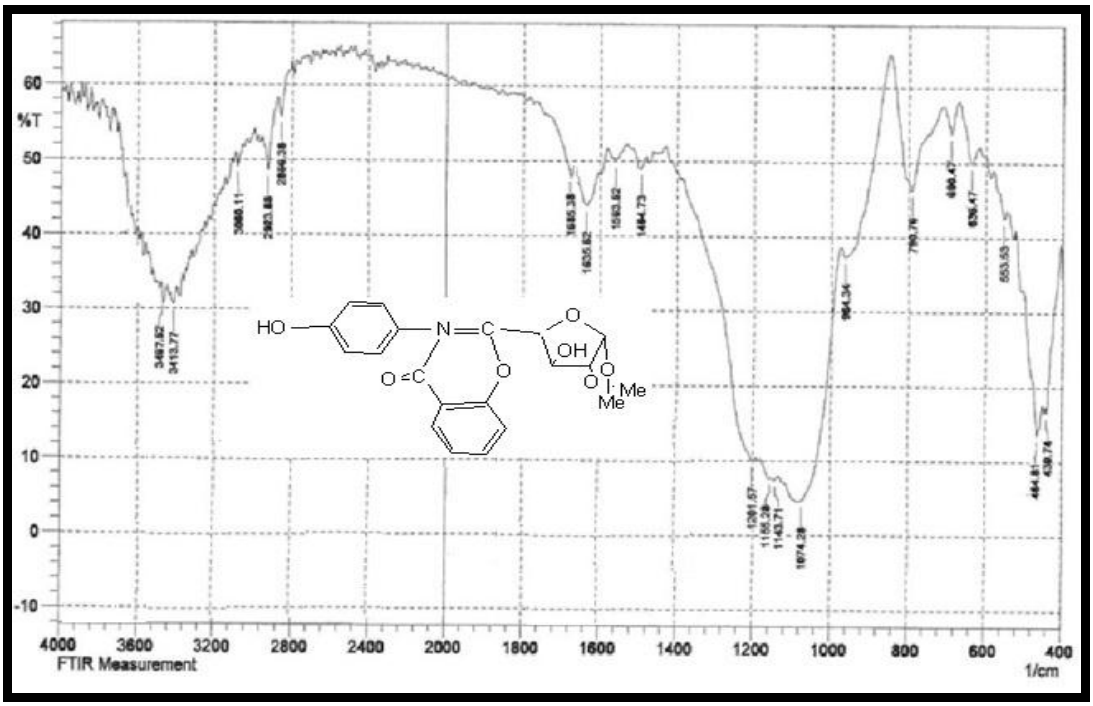


Fig (3) : FT-IR Spectrum of compound (8)

The ^{1}H-NMR spectrum of compound (4) in (δ ppm) showed two singlet signals at 3.10 -3.59 due to the protons of (CH_3) , two signals at 5.45 - 5.73 due to protons for furan ring , the signals at 7.29 to 7.977 due to the protons for phenyl ring, signal at 8.231 due to proton CH=N

^{13}C-NMR spectrum of compound (4) in (δ ppm) showed two signals at 58.36 and 59.11 due to 2 (CH_3) , mulity signals from 69.00 to 101.11 due to C of furan ring , the signals at 114.13 - 126.38 due to C of phenyl ring . The singlet signal at 162.18 due to C=N.

The ^{1}H-NMR spectrum of compound (8) in (δ ppm) showed two singlet signals at 3.23 - 3.58 due to protons of 2 (CH_3) , signals at 4.22 - 5.63 due to protons for furan ring . The protons of phenyl ring showed signals at 7.24 - 8.22 , the singlet signal at 9.53 due to proton of phenolic .

^{13}C-NMR spectrum of compound (8) in (δ ppm) showed signal at 63.32 due to (CH_3) , signals at 63.32 - 84.53 due to C for furan ring , signals from 128.53 to 129.14 due to phenyl ring , signals between 132.20 to 134.56 due to ring of pthalic , the singlet. signal at 160.14 due to C=N and finally carbonyl group showed signal at 165.82 .

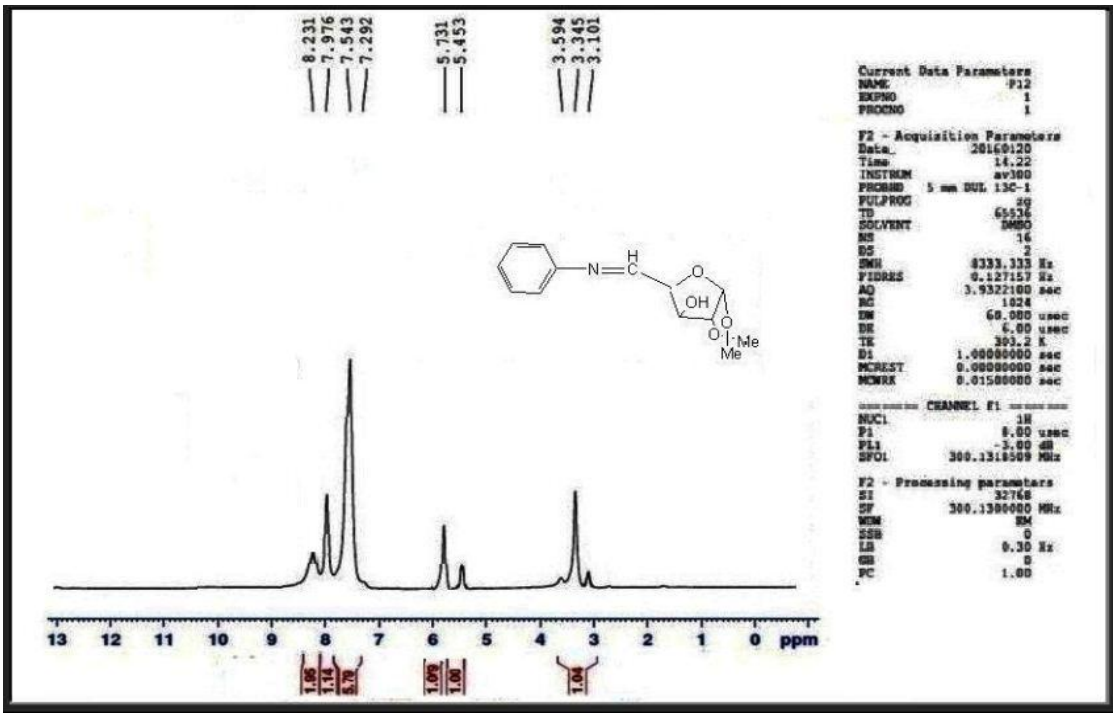


Fig (4) :[1] H-NMR Spectrum of compound (4)

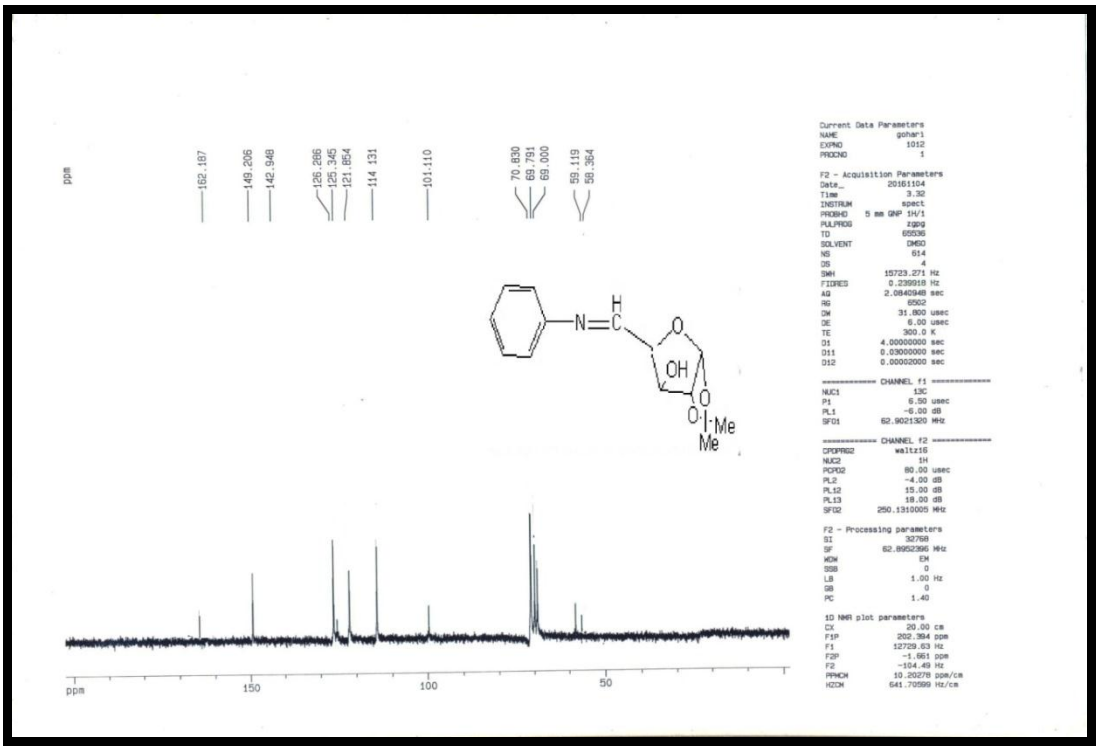


Fig (5) :[13] C-NMR Spectrum of compound (4)

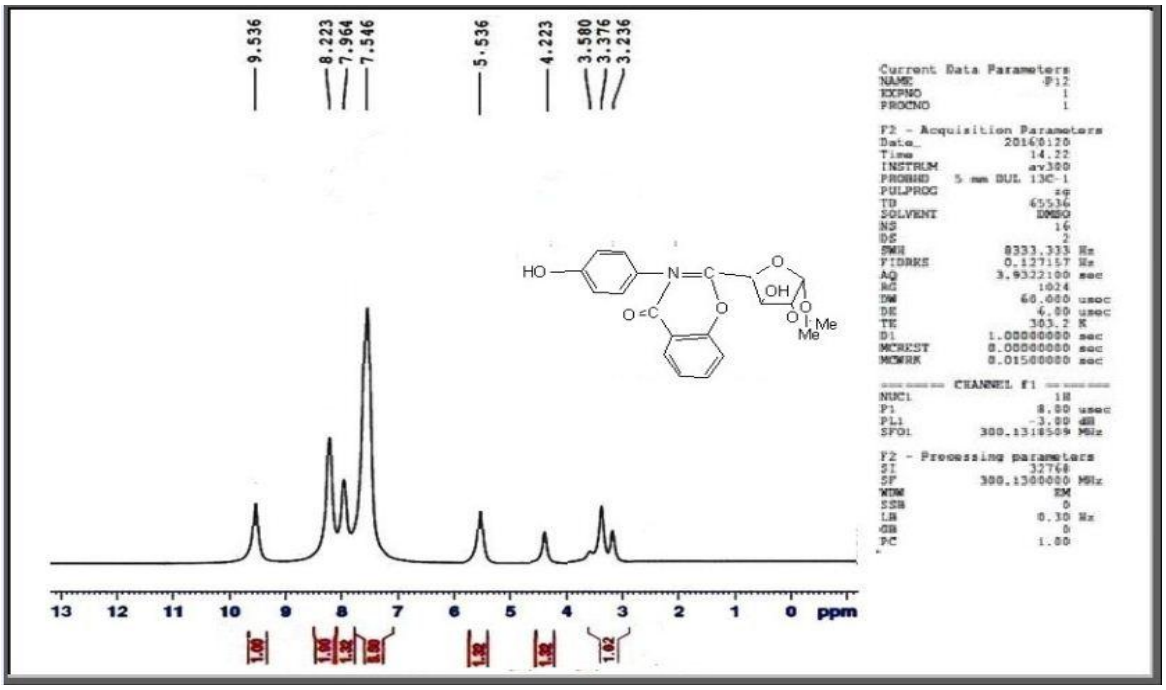


Fig (6) :[1] H-NMR Spectrum of compound (8)

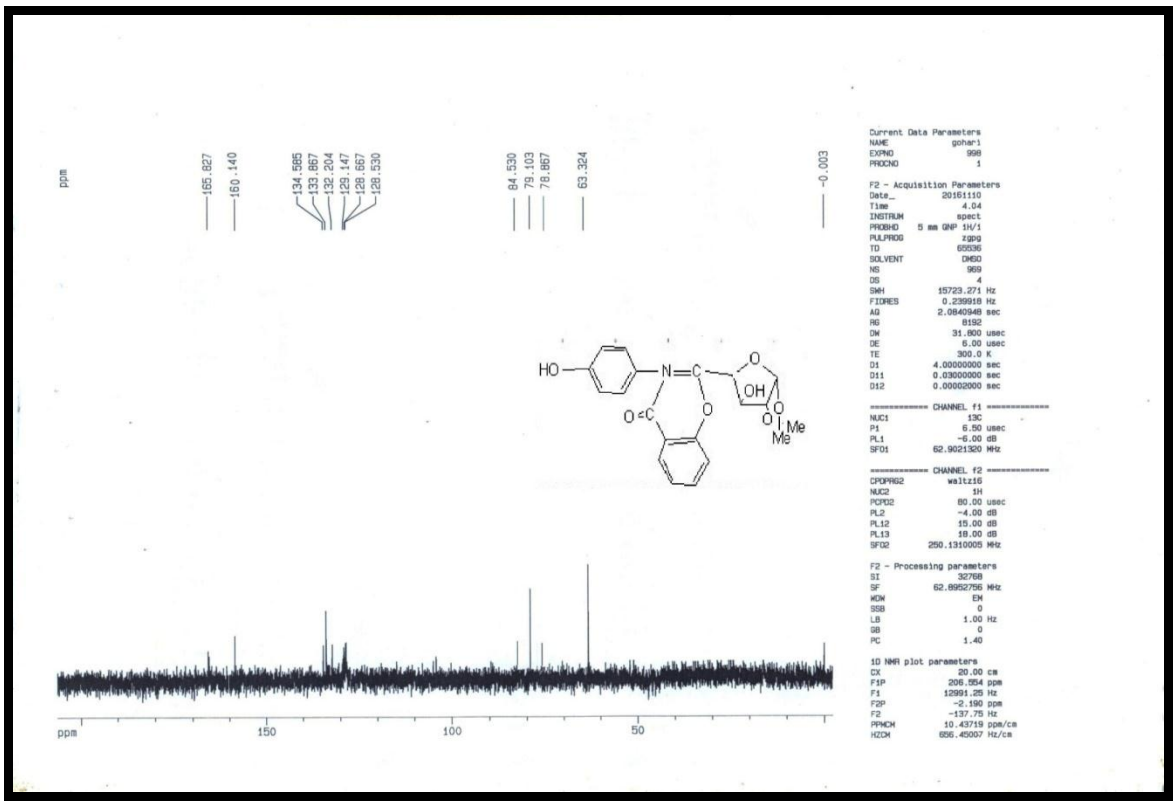


Fig (7) :[13] C-NMR Spectrum of compound (8)

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