ISSN: 0067-2904

Synthesis, Characterization and Anticancer Activity of polyester Derived from Polyvinyl Alcohol with New Oxazolidine-5-one Derivatives

Elaf Noori Talib*[1], Maha A.Younus[2]
[1]*Department of Chemistry, College of Science, University of Baghdad, Iraq*
[2]*Department of Chemistry, College of Education for Pure Sciences (Ibn al-Haytham), University of Baghdad*

Received: 5/2/2024 Accepted: 29/9/2024 Published: 30/10/2025

Abstract

In this study, compound [A], an oxime derivative, was synthesized through the reaction of 4-aminoacetophenone with hydroxylamine hydrochloride, using sodium acetate as a catalyst. Subsequently, Schiff bases [A1-A3] were prepared by reacting compound [A] with various aromatic aldehydes in the presence of glacial acetic acid. Acid derivatives containing oxazolidinone ring [A4- A6] were synthesized from the reaction of Schiff bases [A1- A3] with chloroacetic acid. The resulting compounds [A4-A6] reacted with thionyl chloride to produce the corresponding acid chloride [A7-A9]. Polyesters [A10-A12] were produced by reacting polyvinyl alcohol with compounds [A7-A9]. All prepared compounds were characterized using infrared spectroscopy FTIR and nuclear magnetic resonance NMR spectroscopy. Additionally, the anticancer activity of some of the prepared compounds (A10, A12) against liver cancer cell line hepG2 was evaluated in vitro.

Keywords: Liver anticancer, Oxazolidinone, Polyester, Polyvinyl alcohol.

تحضير و تشخيص والفعالية المضادة للسرطان للبولي استر المشتق من البولي فينيل الكحول مع مشتقات الأوكسازوليدينون الجديدة

إيلاف نوري طالب*[1], مها عبد الوهاب يونس[2]
[1]قسم الكيمياء, كلية العلوم, جامعة بغداد
[2]قسم الكيمياء، كلية التربيه للعلوم الصرفة (ابن الهيثم)، جامعة بغداد

الخلاصة

في هذا الدراسة، تم تحضير مركب مشتق الأوكزيم [A] من تفاعل 4-أمينو أسيتوفينون مع هيدروكسيل امين هيدروكلورايد بوجود أسيتات الصوديوم كمحفز. بعد ذلك, تم تحضير قواعد شيف [A1-A3] من تفاعل المركب [A] مع الألديهيدات العطرية المختلفة في وجود حامض الخليك الثلجي.

تم تحضيرمشتقات الحامض التي تحتوي على حلقة أوكسازوليدينون [A4-A6] من تفاعل قواعد شيف مع كلوروحامض الخليك. تم مفاعلة المركبات المحضرة [A4-A6]مع كلوريد الثايونيل لانتاج كلوريد الحامض المقابل [A7-A9] . تم تحضير البولي استرات [A10-A12] من تفاعل البولي فاينيل الكحولي مع المركبات [A7-A9].

*Email: elafnori80@gmail.com

شخصت المركبات المحضرة باستخدام مطيافية الاشعة تحت الحمراء ومطيافية الرنين المغناطيسي النووي. تم قياس الفعالية المضادة للسرطان لبعض المركبات المحضرة [A10, A12] ضد خلايا الخط السرطاني للكبد مختبريا.

1. Introduction

The oxime functional group is typically formed through condensation of an aldehyde or a ketone, including of steroidal origin, with hydroxylamine to produce aldoximes and ketoximes. These oximes, along with their substituted derivative, display antifungal, antibacterial, antimicrobial, and anticancer activities [1]. Additionally, some compounds that contain both ether and oxime groups have demonstrated anti-HIV and anti-inflammatory effects [2, 3].

Oxazolidinones are heterocyclic compounds containing both oxygen and nitrogen. These compounds play a crucial role in medicinal chemistry, industry, and biological materials and aid in the comprehension of life processes [4,5]. Natural and synthetic oxazolidinone derivatives possess important biological activities; such as anticancer, antibacterial, antifungal, anticonvulsant, anti-inflammatory, antituberculosis, cardiotonic, anti-HIV, antidiabetic, and antihypertensive activity [6,7].

Polyvinyl alcohol (PVA) is a synthetic polymer widely used in various fields, including medicine. It is a highly desirable polymer due to its characteristic properties such as biodegradability, biocompatibility, and water solubility. As a hydrogel polymer, PVA exhibits excellent biocompatibility and serves as a non-toxic biological glue for scaffold bonding, cartilage tissue engineering, a cell carrier, and drug delivery systems [8,9]. One of the most important properties of PVA is its hydrophilicity which makes it suitable in medical fields such as contact lenses, drug systems, and prosthetic organs. PVA can undergo various reactions via its hydroxyl group such as acetylation, etherization, and esterification. The reactions of PVA by adding different functional groups may improve its properties chemically, physically, and biologically [10]. Esterification is a well-known chemical reaction. That can eliminate OH groups and create covalent bonds between polymer chains. This process is useful for enhancing the waterproof behavior of hydrophilic polymers such as PVA, starch, and cellulose [11]. This study aims to synthesise, and characterize the polyester derived from PVA and investigate its effects on the HepG2 liver cancer cell line.

2. Experimental

2.1 Material and Instrumentation

All chemicals and solvents were sourced from CDH, Sigma-Aldrich, and Merck companies. TLC plates were supplied by Merck and iodine fumes were utilized for spot identification. The melting point was measured using a thermal melting point apparatus. FTIR data were recorded using a Shimadzu FTIR Spectrophotometer (FTIR-8400S) was used to record data at the University of Baghdad, College of Sciences. Nuclear magnetic resonance spectroscopy (400 MHz) was employed to obtain the ^{1}H-NMR and ^{13}C-NMR data in DMSO-d6, with chemical shifts measured in parts per million (ppm) relative to tetramethylsilane (TMS) as an internal reference in Iran.

2.1.1 Synthesis of 1-(4-aminophenyl)ethan-1-oneoxime A. [12]

In a round bottom flask, 4-aminoacetophenone (5.5 g, 0.04 mol) was dissolved in 30 mL of ethanol. Hydroxylamine hydrochloride (2.77 g, 0.04 mol) and sodium acetate as catalyst (3.28 g, 0.04 mol) were dissolved in a mixture of 20 mL ethanol and 5ml of water, which was then gradually added to the round bottom flask. The mixture was refluxed for 6 hrs. Upon

completion of the reflux, the solution was left at room temperature and then added to ice water. The resulting crystals were filtered, dried, and recrystallized using ethanol.

2.1.2 Synthesis of compounds A1-A3. [13-15]

Schiff base derivatives A1-A3 were synthesized using the following procedure. First, 0.01 mol of different aromatic aldehydes, namely 4-dimethylaminobenzaldehyde, 4-bromobenzaldehyde, and 4-nitrobenzaldehyde were dissolved in 15 ml of ethanol. A few drops of glacial acetic acid were added to the solution, which was then stirred for several minutes. Next, 0.01 mol of compound A was introduced to the mixture, and the reaction was refluxed for 8-12 hrs. After cooling, the solvent was evaporated, and the resulting product underwent recrystallization using a suitable solvent.

2.1.3 Synthesis of compounds A4-A6. [16-19]

To synthesize A4-A6 compounds, the products (A1-A3) (0.01 mol) were first dissolved in DMF (20 mL) with triethylamine. The resulting mixture was stirred in a round flask. Then, chloroacetic acid (0.02 mol) was then gradually added to the mixture and refluxed for 20-24 hrs. The reaction was monitored by TLC using hexane: ethyl acetate (1:2) as the solvent. Finally, the solvent was evaporated and the products were washed with dry ether.

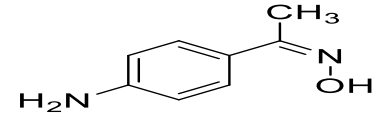
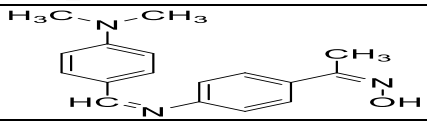
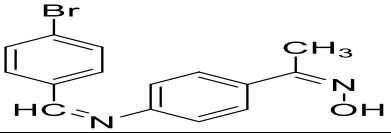
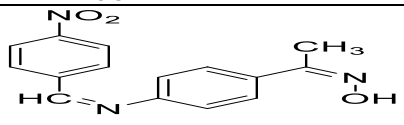
2.1.4 Synthesis of compounds (A7-A9). [21-23]

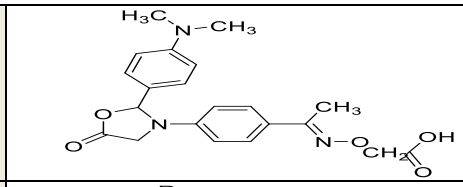
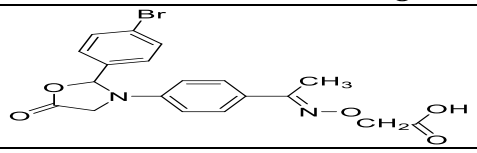
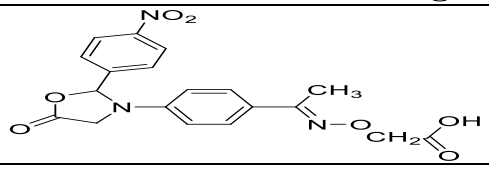
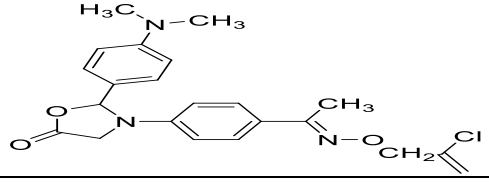
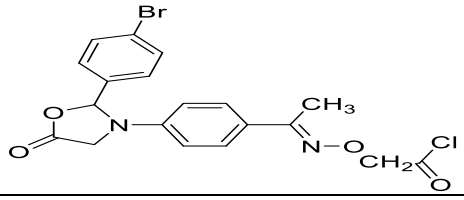
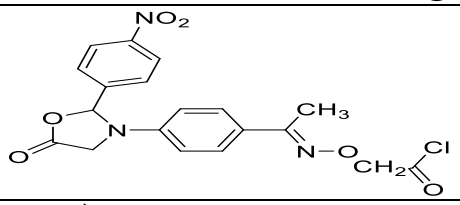
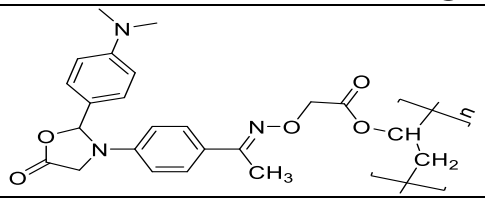
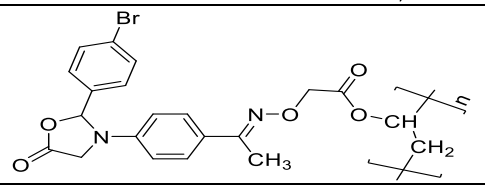
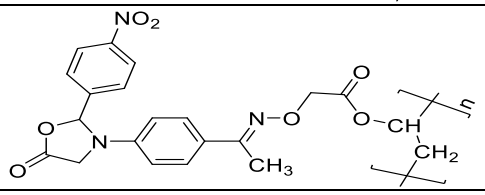
Compounds A4-A6 (0.002 mol) were dissolved in 25 ml of DMF while kept in an ice bath. An excess amount of thionyl chloride was added drop by drop, and the mixture was stirred for 4 hrs. with reflux. After that, the solvent was evaporated and the resulting product was washed with dry ether. The physical properties of the resulting product can be found in Table 1.

2.1.5 Synthesis of compounds (A10-A12). [10]

PVA derivatives A10-A12 were synthesized by dissolving PVA (0.01 mmol) in (25 mL) DMSO. A few drops of triethyl amine were added to the solution, which was stirred for 10 minutes before adding the compounds (A7-A9) (0.01 mmol) and reflux for 24 hrs. The solvent was then evaporated and washed with acetone.

Table 1:Some of the physical properties of the prepared compounds **A- A12**

No.	Compound structure	Molecular formula and M.W(g\mol)	m.p.(°C)	Colour	Yield (%)
A		$C_8H_{10}N_2O$, 150.18	128-130	off white	70
A1		$C_{17}H_{19}N_3O$ 281.36	246-248	light yellow	84
A2		$C_{15}H_{13}BrN_2O$ 317.19	196-198	off white	70
A3		$C_{15}H_{13}N_3O_3$ 283.29	220-222	yellow	76

A4		$C_{21}H_{23}N_3O_5$ 397.43	gummy	brown	57
A5		$C_{19}H_{17}BrN_2O_5$ 433.26	157-159	brown	63
A6		$C_{19}H_{17}N_3O_7$ 399.36	oily	brown	66
A7		$C_{21}H_{22}ClN_3O_4$ 415.87	gummy	brown	64
A8		$C_{19}H_{16}BrClN_2O_4$ 451.70	189-191	brown	57
A9		$C_{19}H_{16}ClN_3O_6$ 417.80	oily	brown	66
A10		$C_{25}H_{31}N_3O_5$ 453.23	Rubbery	brown	93
A11		$C_{23}H_{25}BrN_2O_5$ 489.37	Rubbery	brown	90
A12		$C_{23}H_{25}N_3O_7$ 455.47	Rubbery	brown	87

2.2 Cytotoxic Effect of compounds A10 and A12

An in vitro study was conducted to evaluate the impact of compounds A10 and A12 on the HepG2 cell line.

2.2. 1 Cell Line Maintenance. [24]
A layer of cells is formed in a vessel by following these steps:
1. Remove the growth medium and wash the cell sheet with PBS.
2. Add 2-3 ml of Trypsin/versine solution to the cells and gently rock the vessel to ensure that the entire cell layer is covered.
3. Incubate the vessel at 37°C for 1 to 2 minutes to help detach the cells from the surface.
4. Next, add fresh complete RPMI medium (15-20ml) to disperse the cells into the growth medium using pipetting.
5. Culture cells based on required concentration and incubate them in a 5% CO_2 incubator at 37°C.
6. Determine the cell concentration by counting the cells using a hemocytometer. The formula used for the total cell count per ml is cell count × dilution factor × $10^{\wedge 4}$.

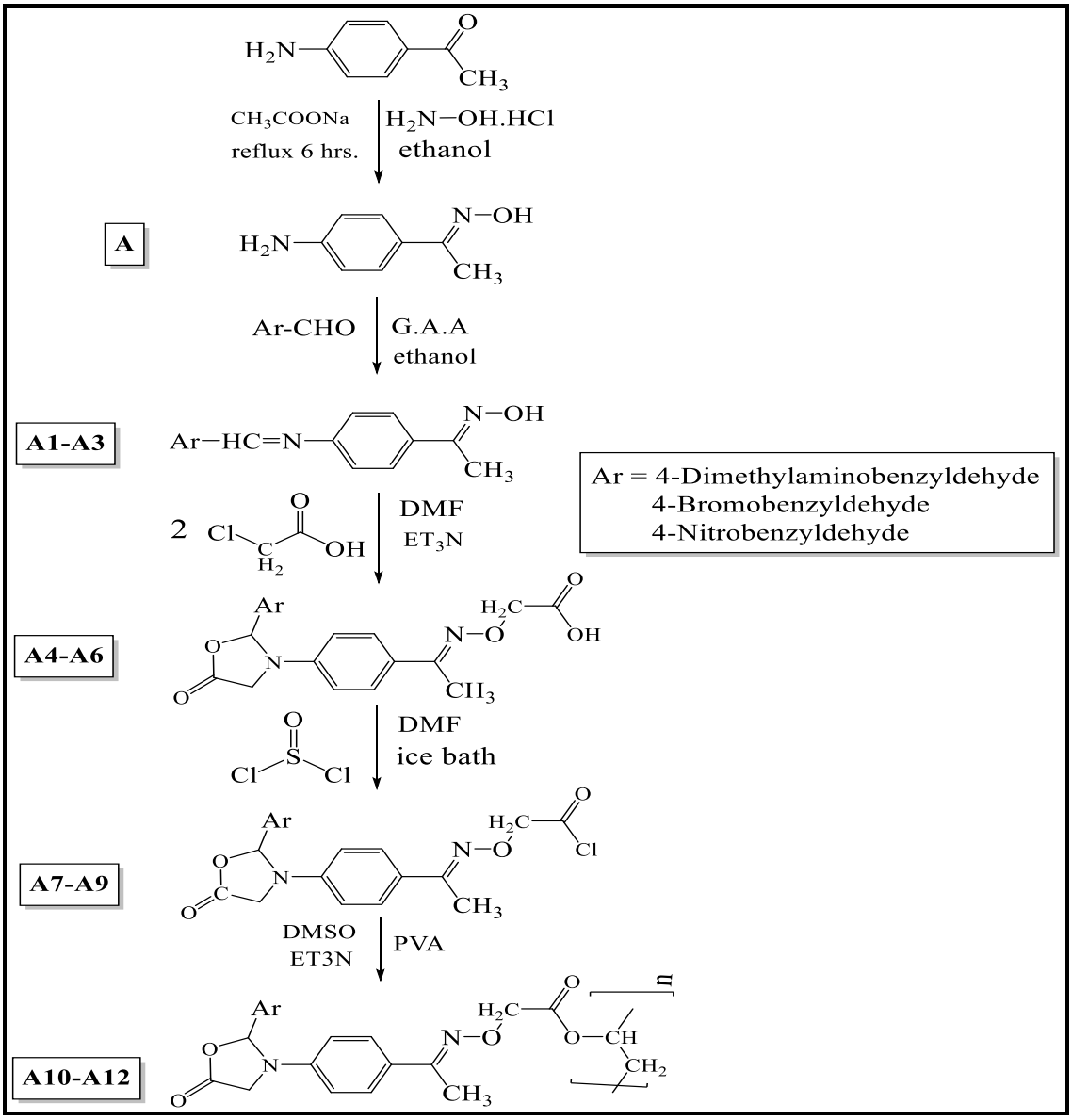
2.2.2 MTT Assay

This study aimed to evaluate the cytotoxic effects of various concentrations (25, 50, 100, 200, and 400 µg/mL) of green synthetic nanoparticles loaded on S. officinalis. To achieve this, MTT kit includes 10 vials of 1ml and 2 bottles of 50ml of solubilization solution.

2.2.2.1 Assay [24]
Cancer cells with 200µL of complete culture medium per well and a concentration range of 1x104–1x106 cells/ml were cultured in 96 flat well micro-titer plates. Sterilized parafilm was used to cover the microplate with gently shaken. Following a 24-hour incubation period at 37°C and 5% CO2, the plates were treated with serially diluted concentrations of compounds A10 and A12, ranging from 25 to 400 µg/mL, which were added to the respective wells. Each concentration, including cells treated with serum-free medium (controls), was Triplicated. Then cells were incubated for 24 hours at 37°C and 5% CO_2. Further incubation for 4 hours at 37°C and 5% CO_2 after adding solution to each well of 10µL of MTT.
After the incubation, the media was removed, and 100 µL of dissolution solution was added to each well. The plates were then left for 5 min. Subsequently, an ELISA reader was used to measure the optical density at a wavelength of 575nm. The concentration of compounds needed for a 50% reduction in cell viability for each cell line was determined by statistically analyzing the data.

3. Results and discussion

3.1 Synthesis of compounds A- A12



Scheme 1: Synthesis of compounds **A- A12**

Compound [A], an oxime derivative, was synthesised by reacting 4-aminoacetophenone with hydroxylamine hydrochloride, using sodium acetate as catalysts. In the next step, compound [A] was reacted with various aromatic aldehydes in the presence of glacial acetic acid to produce Schiff bases [A1-A3]. The data obtained from FTIR spectroscopy demonstrated that the stretching peaks of the hydroxyl group of oxime (OH-) were located in the range of 3228-3222 cm^{-1}, After the disappearance of the NH_2 band, new peaks attributed to C=N appeared in the 1623-1583cm^{-1} region. The ^{1}H NMR spectrum analysis of [A2, A3] showed individual signals at (7.34, 8.61) ppm for the imine bond (-CH=N) of Schiff bases. Several signals were detected in the range of 8.61 to 6.52ppm, attributed to the HC=CH aromatic protons. The compounds A2 and A3 showed signals at 153.31 and 160.09 ppm for the imine bond (C=N) of Schiff bases. Signals at 113 and 152 ppm were observed for C=C aromaticity in The ^{13}C NMR spectrum. Overall, these results demonstrate the successful synthesis of Schiff bases [A1-A3] from compound [A].

Table 2: Shows the FTIR spectral data (ν, cm^{-1}) for **(A-A3).**

Comp. No.	O-H Oxime	C-H Aromatic	C-H Aliphatic	C=N Oxime	C=N Imine	C=C Aromatic	Other bands
A	3217	3066	2908, 2854	1606		1514, 1479	3353 3296 NH_2
A1	3224	3132 3089	2900, 2858	1585	1610	1548, 1529	
A2	3222	3132 3085	2923, 2883	1583	1623	1560, 1502	
A3	3228	3037	2933, 2891	1598	1620	1583	1517Asymmetric 1340 Symmetric NO_2

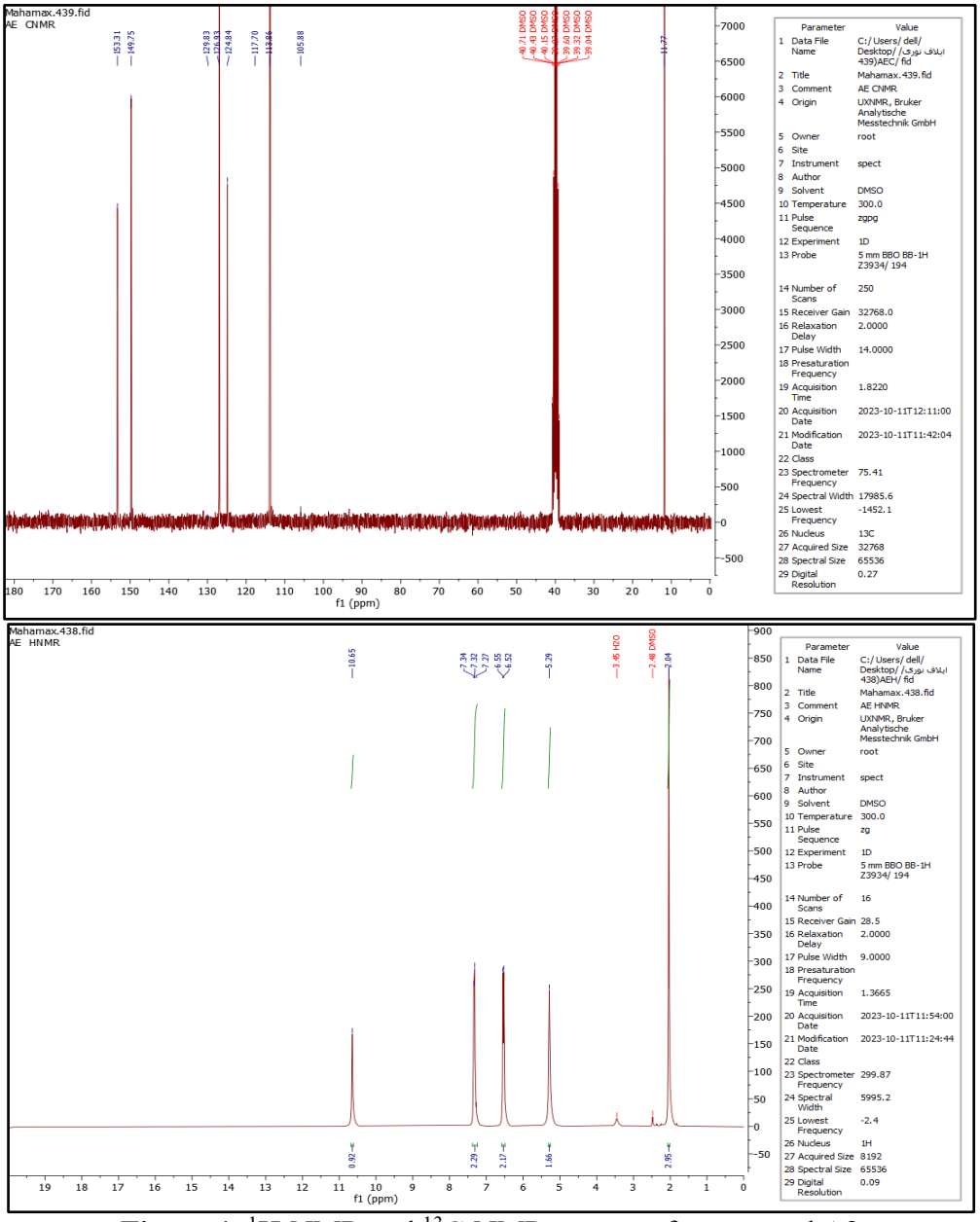


Figure 1: ^{1}H-NMR and ^{13}C-NMR spectra of compound A2

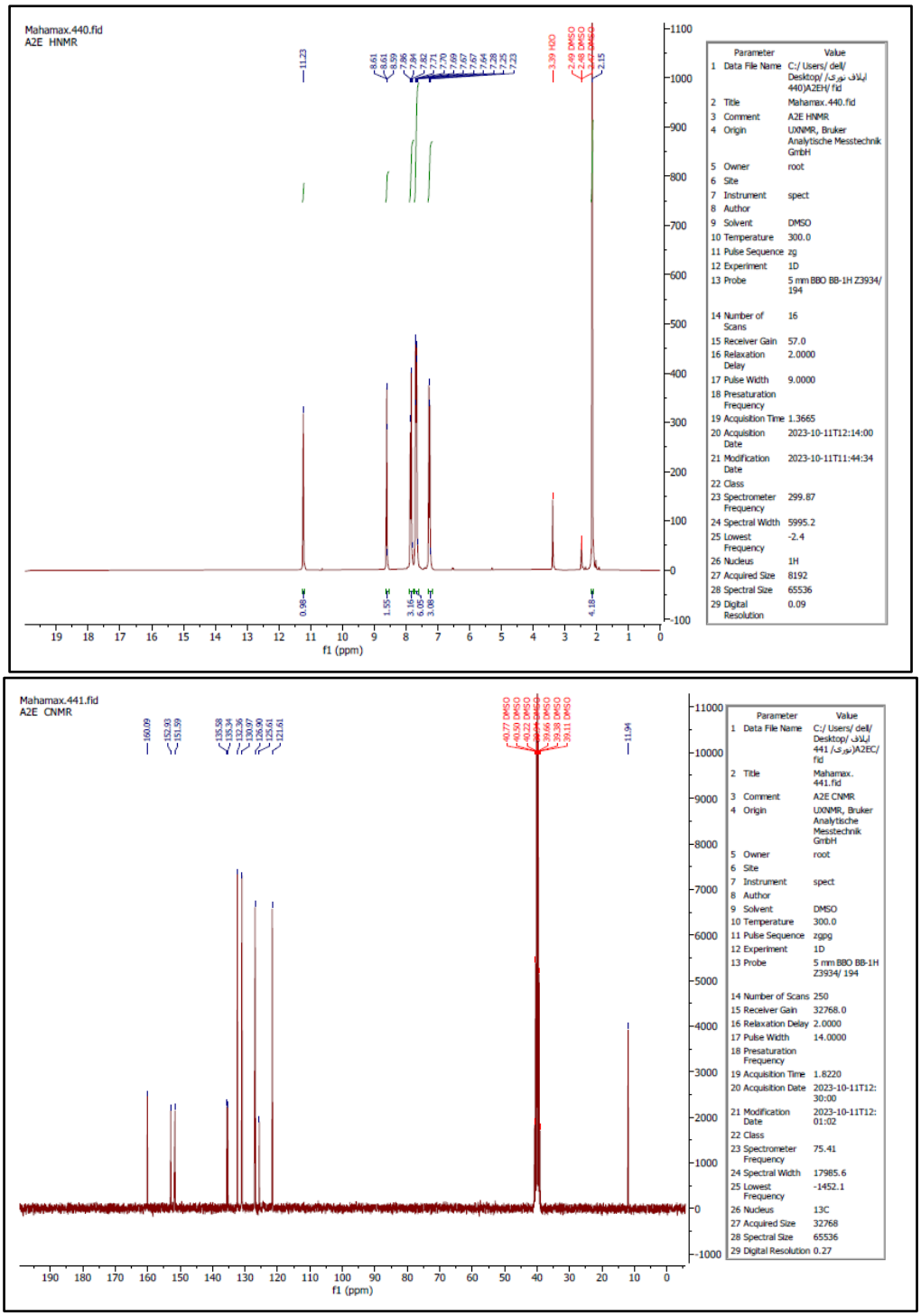
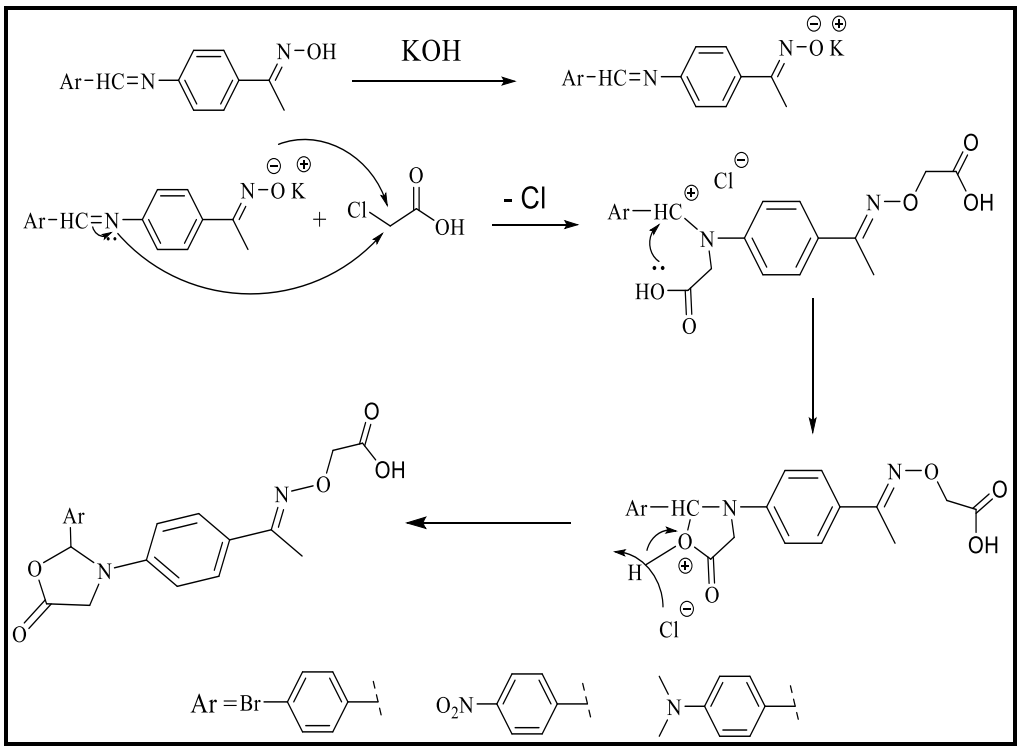


Figure 2: ^{1}H-NMR and ^{13}C-NMR spectra of compound A3

Acid derivatives are produced by reacting prepared Schiff bases [A1-A3] with two equivalents of chloroacetic acid to produce [A4-A6]. The general mechanism of this reaction is shown in Scheme -2- [19, 20].



Scheme 2: The general mechanism of synthesizers [A4-A6]

The FT-IR results confirm the successful formation of the desired compounds, indicated by the presence of the hydroxyl group of the carboxylic acid in the range of (3429-2771) cm^{-1}. The appearance of new C=O peaks of cyclic ester and acid in the regions 1739 and 1710 cm^{-1} and the disappearance of the imine bond (C=N) peaks for Schiff bases. The ^{1}HNMR spectra of compound A6 also showed individual signals at 3.14 and 4.13 ppm belonging to the CH_2CO for acid, CH_2 of the cyclic ester, respectively, and a signal appearing at 11.27 ppm belonging to the OH of the carboxylic acid derivative. The ^{13}C NMR spectrum exhibited a signal at 177.33 ppm, which was attributed to the carbon atom of the carboxylic acid group (C-OH).

Table 3: shows FTIR spectral data (ν, cm^{-1}) for (**A4-A6).**

Comp. No.	O-H Carboxylic acid	C-H Aromatic	C-H Aliphatic	C=O Ester	C=O Acid	C=N Oxime	C=C Aromatic	Other bands
A4	3400-2779	3024	2972 2854	1731	1710	1596	1546	
A5	3429-2773	3026	2966 2860	1739	1713	1600	1517 1465	
A6	3400-2771	3107 3051	2943 2866	1735	1719	1596	Overlap	1519Asymmetric, 1344 Symmetric NO_2

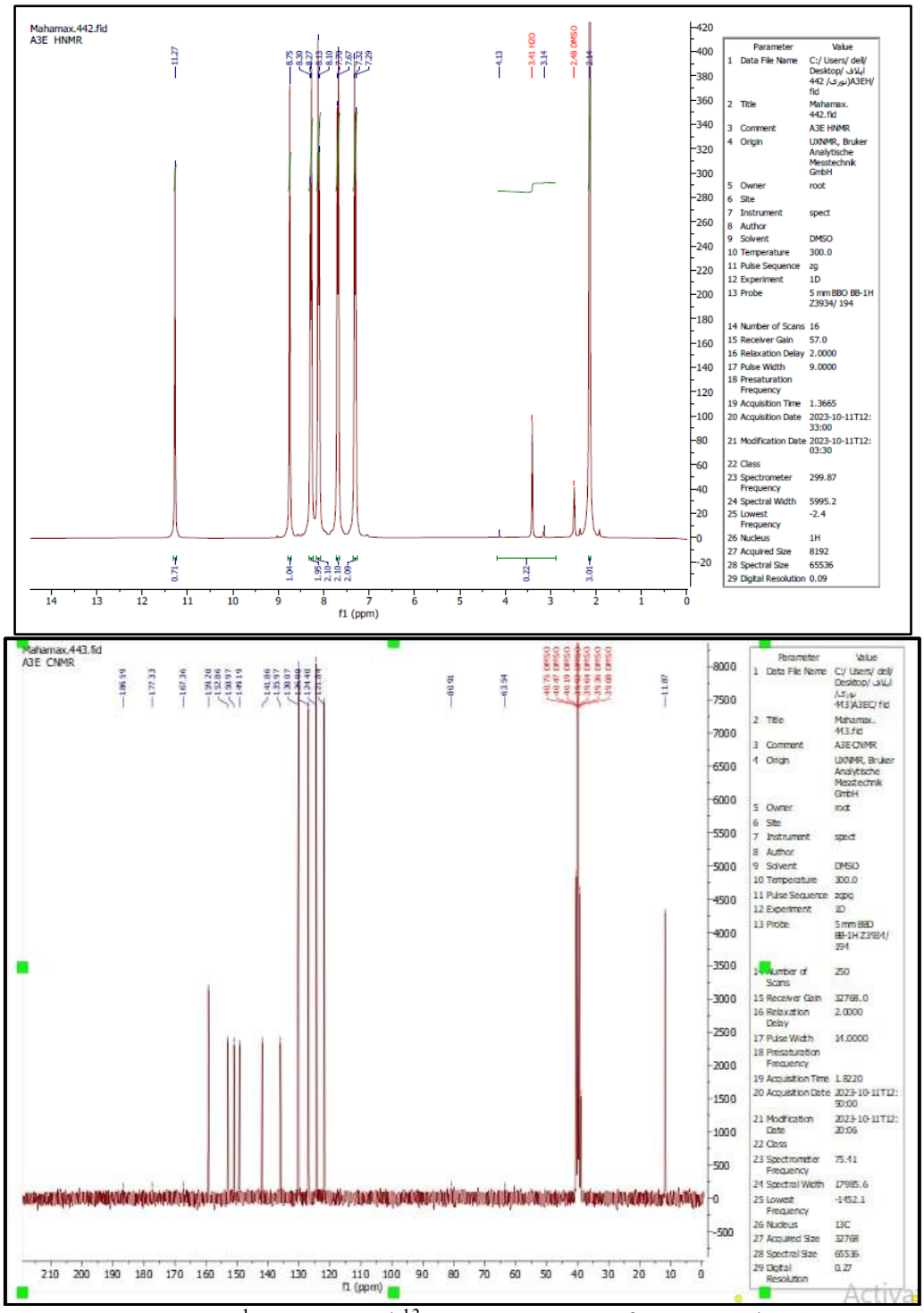


Figure 3: ^{1}H-NMR and ^{13}C-NMR spectra of compound A6

The compounds [A4-A6] were reacted with thionyl chloride to produce the corresponding acid chloride[A7- A9]. The FTIR results showed the presence of an acetyl chloride group band at 1784 cm^{-1} with the disappearance of the acid hydroxyl band. Acid chloride derivatives [A7-A9] were introduced by reacting with polyvinyl alcohol to produce modified polyvinyl alcohol [A10-A12]. The FTIR spectroscopic analysis revealed the formation of a new ester group in the compounds, as evidenced by the appearance of new absorption bands at 1733 cm^{-1} and 1722 cm^{-1}, accompanied by the disappearance of the acid chloride band at 1784 cm^{-1}. The ^{1}HNMR spectra of compound A10 displayed a signal at 3.24 ppm, attributable to the CH_2 group in the ester, and a signal at 9.98 ppm, corresponding to the OH group in PVA. The ^{13}CNMR

spectrum of A10 displayed signals at 34.45 ppm and 60.00 ppm, which are associated with -CH_2 and -CH in PVA, providing strong evidence for the formation of [A10-A12] compounds. All Synthesized compounds A- A12 are shown in Scheme 1.

Table 4: shows FT-IR spectral data (ν, cm^{-1}) for **(A7-A9).**

Comp. No.	C-H Aromatic	C-H Aliphatic	C=O Acetyl chloride	C=O Ester	C=N Oxime	C=C Aromatic
A7	3022	2977, 2891	1784	1735	1589	1527, 1469 $CH_{2bending}$
A8	3024	2977, 2889	1784	1724	1589	1533, 1469 $CH_{2bending}$
A9	3024	2977, 2889	1784	1735	1589	1537 1471 $CH_{2bending}$

Table 5: shows FT-IR spectral data (ν, cm^{-1}) for **(A10-A12).**

Comp. No.	C-H Aromatic	C-H Aliphatic	C=O Ester(Oxa, poly)	C=N Oxime	C=C Aromatic	(C-O-C)
A10	3234 3016	2964 2931	Overlap 1722	Overlap 1629	1508, 1463 $CH_{2bending}$	1124
A11	3238 3213	2983	Overlap 1733	1612	1510, 1467 $CH_{2bending}$	1191
A12	3176 3022	2977	Overlap 1731	1591	1529 1469 $CH_{2bending}$	1124

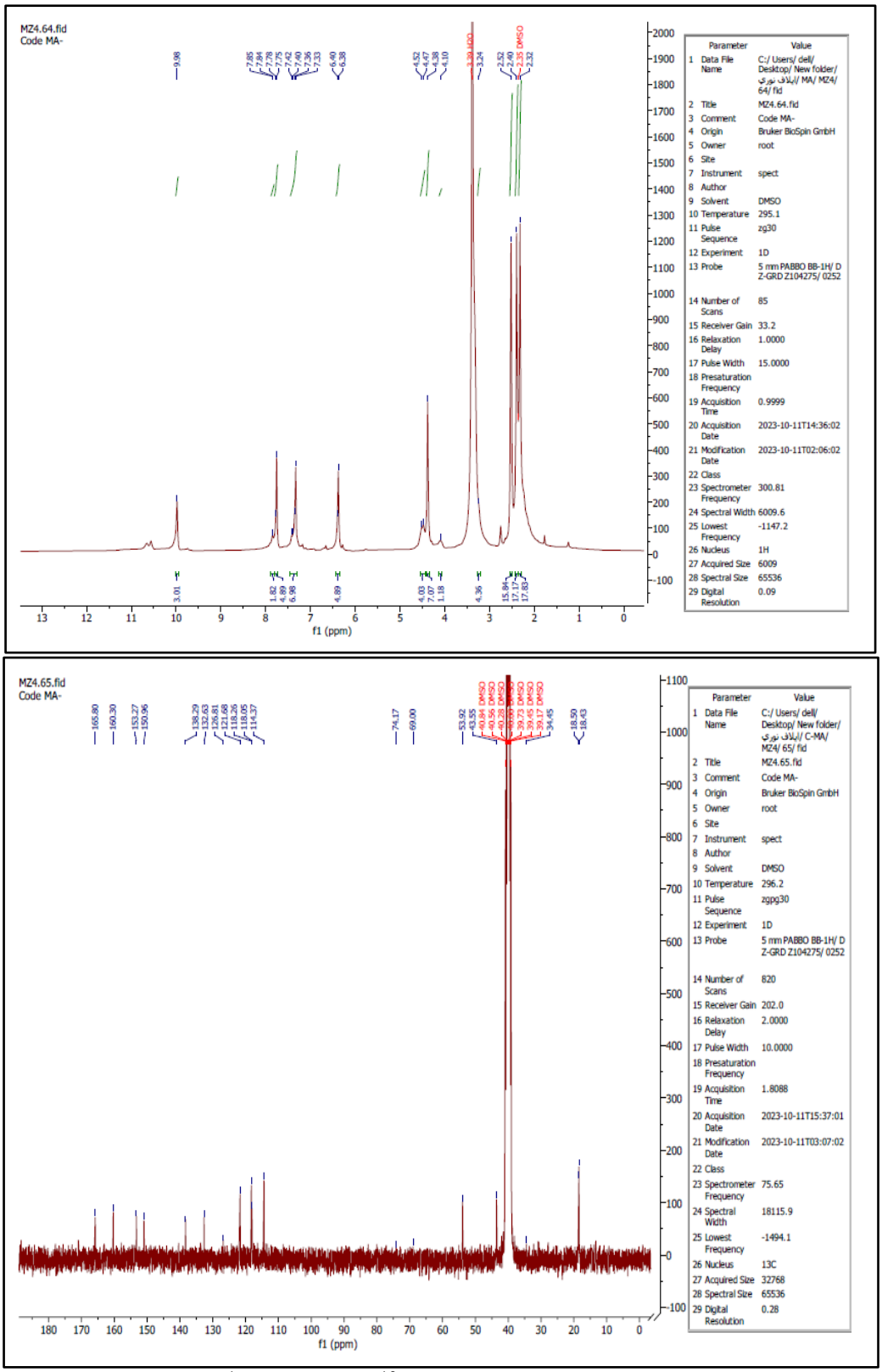
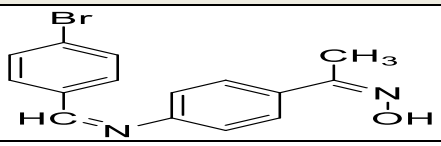
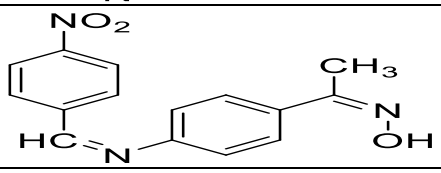
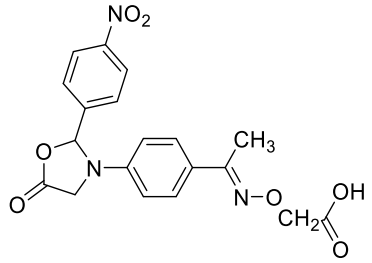
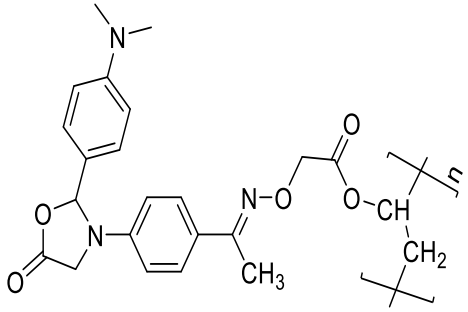


Figure 4: ^{1}H-NMR and ^{13}C-NMR spectra of compound A10

Table 6: shows NMR spectral data (δ, ppm)

Comp. No.	Structure	^{1}H NMR spectral data (δ ppm)	^{13}C NMR spectral data (δ ppm)
A2		2.04 (3H, s, CH_3-C=N), 6.52-7.32 (8H, s, Ar-H), 7.34 (1H, s, -CH=N), 10.65 (1H, s, -OH).	11.77 ($\underline{C}H_3$-C=N) , 113.86-149.75 (12C, Ar-C), 153.31 (-$\underline{C}$H=N).
A3		2.15 (3H, s, CH_3-C=N), 7.23-8.61 (8H, Ar-H), 8.61 (1H, s, -CH=N), 11.23 (1H, s, -OH).	11.94 ($\underline{C}H_3$-C=N) , 121.61-152.93 (12C , Ar-C) , 160.09 (-CH=N).
A6		2.14 (3H, s, CH_3-C=N), 3.14 (2H, s, -O-CH_2-COOH), 4.13 (2H,s ,(-CO-CH_2-$N_{oxazolidinone}$), 7.29-8.75 (8H, Ar-H), 7.32 (1H, s, CH in ring oxazolidinone), 11.27 (1H, s, -COOH).	11.47 ($\underline{C}H_3$-C=N), 63.54 (-OCH_2-COOH), 80.91 (-CO-CH_2-N) 93.90 (CH $_{oxazolidinone}$), 121.04 – 159.20 (12C, Ar-C), 167.36 (CH3-$\underline{C}$=N), 177.33 ($\underline{C}$OOH), 186.59 (C=O ring).
A10		2.32 (3H, s, CH_3-C=N), 2.52 (6H, s, $(CH_3)_2$-N), 3.24 (2H, s, -O-CH_2-COO-R), 4.10 (2H, s,-CO-CH_2-N in oxazolidinone ring), 4.47-4.52 (1H, t, -CH in polymer), 6.52 (1H, s, -CH in oxazolidinone ring),7.33-7.85 (8H, Ar-H), 9.98 (1H, s, OH -PVA).	18.43 ($\underline{C}H_3$-C=N) , 34.45(-CH_2 in polymer) , 43.55 $(CH_3)_2$-N , 53.92 (-O-$\underline{C}H_2$-COO-R) , 60.00 (-CH in polymer) , 74.17 (-CO-$\underline{C}H_2$-N in oxazolidinone ring) , 114.37 (-CH in oxazolidinone ring) , 118.26-153.27 (12C , Ar-C) , 165.80 (CH_3-$\underline{C}$=N), 170.94 (-COOR).

3.2. Anticancer cell line [25, 26]

The objective of this research is to develop a new compound that can effectively treat liver cancer. The study analyzed the effects of two compounds, A10 and A12, on human hepatocellular carcinoma (hepG2) cells through experiments analysis. After 24 hours of incubation, the cytotoxic effects of samples A10 and A12 were assessed on both hepG2 and normal cells, with the results presented in Tables 7 and 8. The findings indicated that between the two compounds, A10 is more effective against hepG2 liver cancer cells. The evaluated cytotoxic effect of A10 and A12 on hepG2 hepatocellular carcinoma cell lines using the MTT assay. An assay was conducted to determine cell viability and cancer cell line inhibition rate using varying compound concentrations (25-400 µg/mL), as shown in Tables 7 and 8. The results indicated that as the concentration of compounds A10 and A12 increased, cell viability decreased. The most significant decrease in HepG2 cell viability (39.96% ± 2.75%) was observed when treated with compound A10 at a concentration of 400 µg/mL, while the highest hepG2 cell viability was measured at 25 µg/mL (94.36 ± 0.67). The synthetic compounds exhibited significantly potent cytotoxic activity, with an IC_{50} value of 113.3 µg/mL. In contrast, the IC_{50} of A10 on the normal cell line WRL68 was 237 µg/mL (Figure 1). The highest viability of hepG2 cells was observed at 25 µg/mL (94.67 ± 0.60), while the maximum decrease in compound A12 in hepG2 cell viability (%) was seen at 400 µg/mL (72.87 ± 4.78). The synthetic

compounds exhibited the highest cytotoxic activity, with an IC_{50} value of 125.5 µg/mL, which showed an IC_{50} of 145.4 µg/mL on the normal WRL68 cell line (Figure 2).

Table 7: displays the cytotoxicity effects of compound A10 on HepG2 and WRL68 cells after (24 hrs.) of incubation at 37°C.

Conc. (µg/mL)	WRL68 mean ± S.D	hepG2 mean ± S.D
400	73.14 ± 1.13	39.96 ± 2.75
200	84.02 ± 1.25	49.76 ± 6.65
100	92.28 ± 0.99	70.79 ± 5.26
50	96.33 ± 0.40	89.73 ± 4.82
25	96.29 ± 0.87	94.36 ± 0.67

Table 8: displays the cytotoxicity effects of compound A12 on HepG2 and WRL68 cells after (24 hrs.) of incubation at 37°C.

Conc. (µg/mL)	WRL68 mean ± S.D	hepG2 mean ± S.D
400	74.88 ± 5.00	72.87 ± 4.78
200	86.07 ± 3.07	74.69 ± 2.55
100	90.08 ± 1.04	89.19 ± 2.41
50	93.86 ± 1.10	93.98 ± 0.53
25	94.63 ± 0.48	94.67 ± 0.60

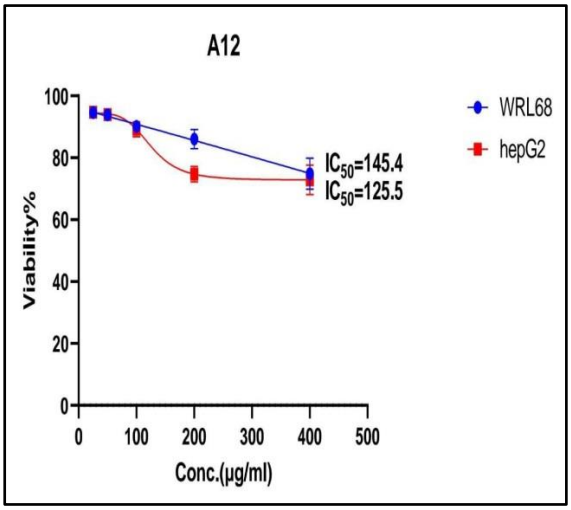


Figure 2: The cytotoxicity effect of compound A12 on HepG2 and WRL68 cells measured after a 24-hour incubation at 37°C.

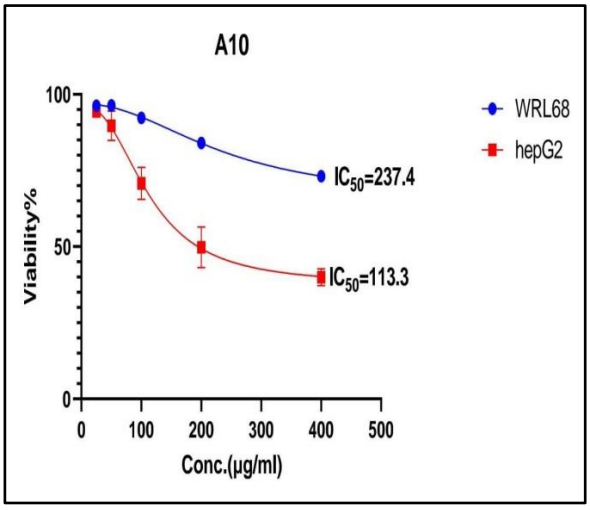


Figure 1: The cytotoxicity effect of compound A10 onHepG2 and WRL68 cells measured after a 24-hrs. incubation at 37°C.

Conclusion

In this work, the anticancer activities of the synthesised modified polyvinyl alcohol were examined. The obtained compounds were characterized using FT-IR and NMR spectroscopy. The anticancer activity against the hepG2 Liver cancer Cell line was evaluated. The results indicated that compound A10 exhibited greater anticancer activity than compound A12.

Acknowledgement

We extend our thanks to the Department of Chemistry, College of Science, University of Baghdad, for their assistance in completing the research.

References

[1] C. Canário, M. Matias, V. Brito, A. O. Santos , A. Falcão , S. Silvestre and G. Alves "New estrone oxime derivatives: Synthesis, cytotoxic evaluation and docking studies," *Molecules*, vol. 26, no. 9, p. 2687, 2021.

[2] N. Naik and G. K. Rao, "Synthesis and characterization of novel oxime analogues," *Indian Journal of Chemistry*, vol. 61, pp. 1169–1172, 2022.

[3] T. Kosmalski, D. Kupczyk, S. Baumgart, R. Paprocka, and R. Studzińska, "A Review of Biologically Active Oxime Ethers," *Molecules*, vol. 28, no. 13, p. 5041, 2023.

[4] R. M. Kubba and N. M. Al-Joborry, "Theoretical study of a new oxazolidine-5-one derivative as a corrosion inhibitor for carbon steel surface," *Iraqi Journal of Science*, vol. 62, pp. 1396–1403, 2021.

[5] R. M. Kubba, N. M. Al-Joborry, and N. J. Al-Lami, "Theoretical and experimental studies for inhibition potentials of imidazolidine 4-one and oxazolidine 5-one derivatives for the corrosion of carbon steel in Sea Water," *Iraqi Journal of Science*, vol. 61, no. 11, pp. 2776–2796, 2020.

[6] V. Patil Chetan, V. Patil Bhushan, K. Patil Akshay, T. P. Sunila, and P. P. Sunil, "A BRIEF REVIEW ON OXAZOLIDINONE," *Indian Journal of Drugs*, vol. 7, no. 3, pp. 96–107, 2019.

[7] O. H.Abid, A. K. Mohamed, "Synthesis and Characterization of Novel Oxazolidinones Via Schiff Base Reactions" *Journal of University of Anbar for Pure Science*, vol. 7, pp.74-80, 2013.

[8] R. E-Keihan, F. Khalili, H. A. M. Aliabadi, A. Maleki, H. Madanchi, E. Z. Ziabari, M. S. Bani, "Alginate hydrogel-polyvinyl alcohol/silk fibroin/magnesium hydroxide nanorods: A novel scaffold with biological and antibacterial activity and improved mechanical properties," *International Journal of Biological Macromolecules*, vol. 162, pp. 1959–1971, 2020.

[9] A. Amalraj, J. T. Haponiuk, S. Thomas, and S. Gopi, "Preparation, characterization and antimicrobial activity of polyvinyl alcohol/gum arabic/chitosan composite films incorporated with black pepper essential oil and ginger essential oil," *International Journal of Biological Macromolecules*, vol. 151, pp. 366–375, 2020.

[10] B. J. Ahmed, M. H. Saleem, and F. S. Matty, "Synthesis and Study of the Antimicrobial Activity of Modified Polyvinyl Alcohol Films Incorporated with Silver Nanoparticles," *baghdad science journal*, vol. 20, no. 5, pp. 1643–1653, 2023.

[11] H. U. Ko, J. W. Kim, H. C. Kim, L. Zhai, and J. Kim, "Esterified PVA-lignin resin by maleic acid applicable for natural fiber reinforced composites" *Journal of Applied Polymer Science*, vol. 137, no. 26, 2020.

[12] A. G. A. Maged and A. A. Fayad, "Synthesis and spectroscopic characterization of new heterocyclic compounds derivatied from 1-(4-aminophenyl) ethan-1-oneoxime as a starting material with evaluate their biological activity," *Biochemical and Cellular Archives*, vol. 20, no. 2, pp. 5211–5222, 2020.

[13] T. M. Yassen and A. M. AL-Azzawi, "Synthesis and Characterization of New Bis-Schiff Bases Linked to Various Imide Cycles," *Iraqi Journal of Science*, pp. 1062–1070, 2023.

[14] M. A. Younus and B. F. Abdallaha, "Synthesis, Characterization and Anticancer Activity of Chitosan Schiff Base/PVP Gold Nano Composite in Treating Esophageal Cancer Cell Line," *baghdad science journal,* vol. 21, no. 1, p. 95, 2024.

[15] M. M. Rabeaa, M. I. Khalaf, and F. A. Kandil, "Modification, Characterization of New Thiazolidinone and Oxazolidinone Derived from Levofloxacin and Evaluation of Anti-Oxidant," *Ibn AL-Haitham Journal For Pure and Applied Sciences,* vol. 37, no. 1, pp. 283–297, 2024.

[16] H. Al-Adhami and S. M. H. Al-Majidi, "Synthesis, Characterization of Thiazolidin-4-one, Oxazolidin-4-one and Imidazolidin-4-one Derivatives from 6-Amino-1, 3-dimethyluracil and evaluation of their Antioxidant and Antimicrobial Agent," *Al-Qadisiyah Journal of Pure Science*, vol. 26, no. 4, pp. 59–72, 2021.

[17] B. S. Salman and M. R. Ahmed, "Synthesis and Characterization of New Thiazolidinone and

Oxazolidinone Heterocyclic Derivatives from 2-Marcapto-1, 3, 4- Thiadiazole Compounds," *Chemical Method,* vol. 6, pp. 997–1006, 2022.

[18] X. Xu, X. Cai, B. Wang, W. Min, Q. Wang, C. Lai, H. Hu, and D. Xu, "Synthesis and Herbicidal Activities of Novel Substituted Acetophenone Oxime Esters of Pyrithiobac" *ChemistrySelect,* vol. 5, pp. 69-74, 2020.

[19] R. Zheng, F. Feng, Z. Zhang, J. Fu, Q. Su, Y. Zhang, and Q. Gu, "Microwave-assisted efficient synthesis of 3-substituted bis-isoxazole ether bearing 2-chloro-3-pyridyl via 1,3-dipolar cycloaddition" *Molecular Diversity*, vol. 24, pp. 423–435, 2020.

[20] T. Kosmalski, R. Studzinska, N. Daniszewska, M. Ullrich, A. Sikora, M. Marszall, and B. Modzelewska-Banachiewicz, "Study of the Room-Temperature Synthesis of Oxime Ethers by using a Super Base" *ChemistryOpen*, vol. 7, pp. 551 –557, 2018.

[21] G. A. Jaber and I. K. Jassim, "Preparation of polymers containing oxadiazole and study the anti-bacterial activity for some of them," *Journal of Pharmaceutical Sciences and Research*, vol. 11, no. 3, pp. 688–691, 2019.

[22] A. S. Hamed and R. S. Dawood, "Synthesis and Identification of Some New Derivatives of Benzoxazole Bearing Pyrazole and 1, 2, 4-Triazine Rings," *Journal of Global Pharma Technology*, vol. 12, no. 2, pp. 737–744, 2020.

[23] M. M. Rabeaa and M. I. Khalaf, "Modification and Characterization of Some New Levofloxacin Heterocyclic Derivatives as COX-2 Enzyme Inhibitors and Evaluate Their Efficacy Pharmacokinetics by Molecular Docking and the Swiss ADME Studies," *Baghdad Sci. J.*, 2023.

[24] P. J. F. da Silva, "Development of a Localized Drug Delivery System With Chitosan and Ferromagnetic Nanoparticles Produced by Wetspinning for Cancer Treatment." Universidade do Minho (Portugal), 2022.

[25] A. G. A. Maged and A.-L. Naeemah, "Synthesis of New Oxopyrimidine and Cyanopyridine Derivatives Containing the Pyrimidine Benzothiazole Moiety with the Evaluating their Colon Anticancer Bioactivity," *Iraqi Journal of Science*, vol. 64, no. 8, pp. 3725–3734, 2023.

[26] V. A. Arzumanian, O. I. Kiseleva, and E. V Poverennaya, "The curious case of the HepG2 cell line: 40 years of expertise," *International Journal of Molecular Sciences,* vol. 22, no. 23, p. 13135, 2021.