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CENTRAL ASIAN STUDIES

Preparation and Evaluation of Bacterial Activity and Study of the Crystalline Properties of Some 1,3-Oxazepine-4,7-Dione Derivatives

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Abstract: This study prepared N-(4-sulfamoyl phenyl)hydrazinecarbothioamide by reacting para-amino sulfamide, carbon sulfide, and aqueous hydrazine. Next, hydrazones were prepared using benzaldehyde substitutes in the hydrazide reactor, and lastly, the hydrazone reaction was used to create derivatives of 1,3-oxazepine-4,7-dione. utilizing anhydride maleic acid. Using spectroscopic and physical methods (mp, colour, proton nuclear magnetic resonance spectroscopy (1H-NMR, 13C-NMR, and FT-IR) to measure biological activity on different bacteria (e.g., Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, and streptococci) and confirm the structure of compounds. Determine the changes that take place inside the liquid crystals by examining their phases with a polarized optical microscope that is heated.

Keywords: hydrazone, oxazepine, biological activity, liquid crystal

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1. Introduction

1.1. Oxazepine

These substances, commonly called oxazepines, have unsaturated, heterogeneous seven-membered rings [1]. They have three isomers, which are numbered based on the locations of the oxygen and nitrogen atoms in the heptagonal ring [2]. They can also be saturated, which is referred to as oxazepines. They include an oxygen atom, a nitrogen atom, two heterocycles, and five carbon atoms [3]. Compared to the hexagonal aromatic benzene ring, the seven-membered oxynitrogen heterocycle's ring is more extensive and less homogeneous. In addition, the heterocycle's seven-membered ring's boat-shaped spatial distribution of atoms contributes to its stability and lowers Ring strain, rendering it non-aromatic [4]. Owing to its significant biological effect against depression [5], as well as against cancer [6], inflammation [7], anxiolytic [8], antioxidant [9], antiviral [10], antifungal [11], bacteria [12], and malaria [13], pharmacology has experienced a spike in attention owing to seven rings.

1.2. Hydrazones

These are among the significant organic compounds with the following structure (R1R2C=N-NH2) derived from aldehydes and ketones, where the functional or active group (N-NH2) has replaced oxygen. Hydrazine is typically used to prepare these compounds, and the C-N linkage is necessary for biological activity. Due to its physical solid action against germs, yeast, cancer, inflammatory diseases, antioxidants, diabetes, anxiolytics, and malaria, it attracted much attention in the pharmacy sector

[14,15,16,17,18,19,20,21].

1.3. Hydrazide

Hydrazides are adaptable substances that can be used to create heterocyclic systems. Furthermore, because of their broad range of biological activities as antidiabetic [22], antimalarial [23], anticancer [24], antimicrobial [25], antioxidant [26], anti-inflammatory [27], and anxiolytic [28], hydrazide-hydrazones are still of great interest in the field of medicinal chemistry.

1.4. Liquid crystals

These compounds appear to be liquids. On the other hand, their particles are arranged into discrete layers, just like in crystals [29]. It is between a stable crystalline solid state and a stable liquid state. According to some, liquid crystals may represent the fourth state of matter [30]. Liquid crystals exhibit a transitional condition between the isotropic phase, also known as the liquid phase, where particle mobility is accessible, and the solid phase, which has integrated molecular structure in both position and direction and limits particle mobility [31].

2. Materials and Method

2.1. Material

Without any additional purification, all of the compounds utilized in this investigation were acquired from BDH, Fluka, and Aldrich.

2.2. Devices used

A thermoelectric melter 9300 was used to determine melting points. Using KBr disk at a scale of (400–4000) cm-1, Shimadzu FT-IR 8400S spectrophotometer; 1H-NMR and 13C-NMR spectra using Bruker apparatus operating at 400 MHz. Thicknessed at 0.2 mm, Fluka silica gel plates were employed in thin-layer chromatography (TLC). The plates were activated with fluorescent silica gel G, and visibility was achieved by UV light.

2.3. Preparation Of N-(4-sulfamoylphenyl) hydrazinecarbothioamide (AB1) [32]

0.01moles of para-amino sulfamide are dissolved in 50 millilitres of 95% ethanol and 20 millilitres of ammonium hydroxide (NH4OH). After 15 minutes of stirring and an hour of standing, 20 ml of carbon disulfide (CS2) is gradually added to the mixture. To create a white residue, 40 millilitres of 80% concentration aqueous hydrazine (N2H4.H2O) was added, and the combination was cooled in an ice bath. After filtering and recrystallizing the ethanol and water mixture in a 1:3 ratio, the product had an 80% melting point. A 278 C0 output is present.

2.4. Preparation of Hydrazones (AB2-AB6) [33]

In a suitable, heat-resistant glass baker, without using a solvent, equivalent moles of the thiosemicarbazone derivative were mixed with the benzaldehyde derivative. The mixture was heated gently and slowly until melting, with stirring and mixing well for 5-10 minutes until the nature of the reactants changed in terms of color and texture. The result was collected and returned. Crystallized from ethanol. The physical characteristics of the produced compounds [AB2-AB6] are displayed in Table 1.

Table 1. The produced chemicals' physical attributes (AB2-AB11)

Comp. No.	R	Molecular formula	m.p. °C	Yield%	Color
AB2	OH	$C_{14}H_{14}N_4O_3S_2$	206-208	83	Orange
AB3	H	$C_{14}H_{14}N_4O_2S_2$	186-188	88	Yellow
AB4	4-Cl	$C_{14}H_{13}N_5O_4S_2$	164-166	81	Orange
AB5	4- $N(CH_3)_2$	$C_{16}H_{19}N_5O_2S_2$	174-176	89	Orange
AB6	4-NO_2	$C_{15}H_{16}N_4O_3S_2$	204-206	87	Orange
AB7	OH	$C_{18}H_{16}N_4O_6S_2$	186-188	80	Yellow
AB8	H	$C_{18}H_{16}N_4O_5S_2$	186-188	83	Orange
AB9	4-Cl	$C_{18}H_{15}N_5O_7S_2$	194-196	78	Magenta
AB10	4- $N(CH_3)_2$	$C_{20}H_{21}N_5O_5S_2$	192-193	78	Magenta
AB11	4-NO_2	$C_{19}H_{18}N_4O_6S_2$	189-191	74	Brown

2.5. Preparation of 1,3-Oxazepine-4,7-dione derivatives (AB7-AB11) [34]

Mix 0.01 mole of hydrazone derivatives and 0.01 mole of maleic anhydride without using a solvent in an appropriate heat-resistant glass container. Gently heat the mixture until it melts, stirring and mixing well for ten to fifteen minutes or until the colour and texture of the reactants change. The product was extracted from the ethanol and then recrystallized. Table 1 displays the oxazepine derivatives' physical characteristics, percentages, and reverse sublimation times (AB7-AB11).

2.6. Examination of several produced compounds' liquid crystal characteristics (AB7, AB8, AB11) [35]

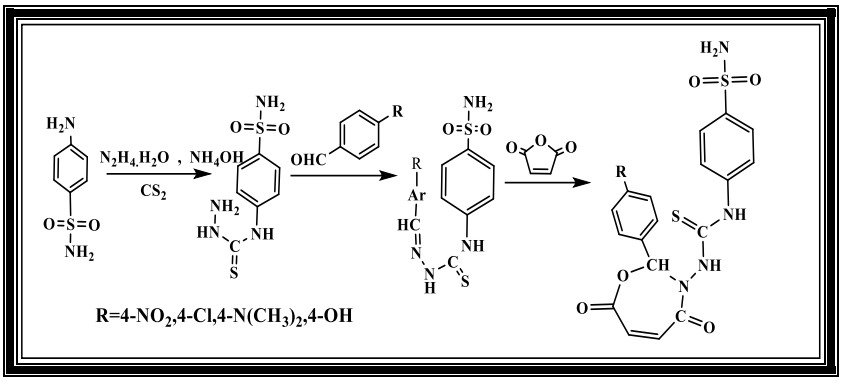
A hot-stage heater-equipped polarizing microscope was utilized to investigate the texture of a few synthesized compounds (AB7, AB8, AB11). MEIJI, an American company, has a 38MP FHD Camera V6 with 20X magnification, an electronic thermometer to track temperature variations, and an E-PLAN 10X/0.25 160/0.17 lens. The model was thoroughly inspected with a magnifying lens and an automated thermal camera to take pictures of the textures of the compounds under research, all of which were thin-film generated.

2.7. Evaluation of biological activity of (AB4, AB8, AB9, AB10)

The propagation approach of the Kirby Bauer movement, which involves spreading 0.1 ml of bacterial solution on ager Muller Hinton plates and letting them absorb the fluid for five minutes, has been used to measure biological activity [36,37]. A cork plunger and a five mm diameter cork were used to create holes in each dish. Then, 0.1 ml of the produced solutions for the fourth hole, which employed Ciprofloxacin as a reference sample, were incubated at 37 °C for twenty-four hours. Using Prescott's approach [38], the inhibitory zone widths surrounding each hole have been determined in millimetres.

3. Results and Discussion

This study involved the preparation of several compounds, including hydrazide (AB1), which was made using an amine reactor with hydrazine in the presence of CS2 and NH4OH, and five other compounds, which included hydrazone derivatives (AB2-AB6), which were made by reacting hydrazide (AB1) with substitutes for benzaldehyde and five other compounds, which included oxyazepine derivatives (AB7-AB11). Through the melting process, as shown in Scheme 1, of hydrazone derivatives with maleic anhydride. FT-IR, 1H-NMR, and 13C-NMR spectra were used to describe these compounds.



Scheme 1. Path of the Ready Compounds (AB1-AB11)

3.1. Characterization of Of N-(4-sulfamoylphenyl)hydrazinecarbothioamide (AB1)

The product was identified through some physical properties and using the infrared spectrum. The spectrum showed a stretch band at frequency (1156) cm-1 attributed to the thiocarbonyl group. As for (-NH2), the stretch band showed (3215) cm-1, and two bands also appeared at (1509 and 1594) cm-1 are due to the constrictor stretching (-C=C-) of the aromatic ring. As for the constrictor stretching band (=C-H) it appeared at (3068) cm-1, in addition to the appearance of another band at (846) cm-1 that is due the group (C=S) [39] as shown in the Figure 1.

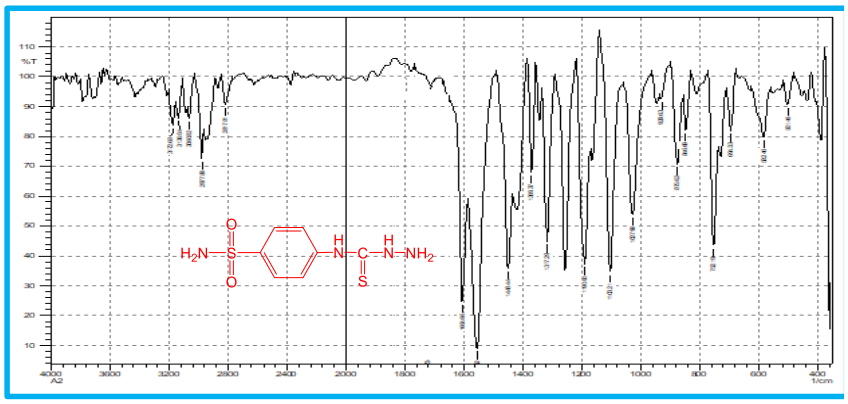


Figure 1. The compound's infrared spectrum (AB1)

Examining the 1H-NMR spectra of the chemical [AB1], a signal was seen at the site (3.44) ppm attributable to the proton of the (-NH2) hydrazide group and at the site ppm (4.31) attributed to the proton of the attached (-NH2) group. (O=S=O) group and the signal at the site (9.47) ppm is caused by the proton of the hydrazide (NH) group. As shown in Figure 2, the signal at the site (2.52 ppm) returns to the protons of the solvent (DMSO-d6), while two duplicate signals in the 7.68–7.35 ppm region are attributed to the protons of the aromatic rings.

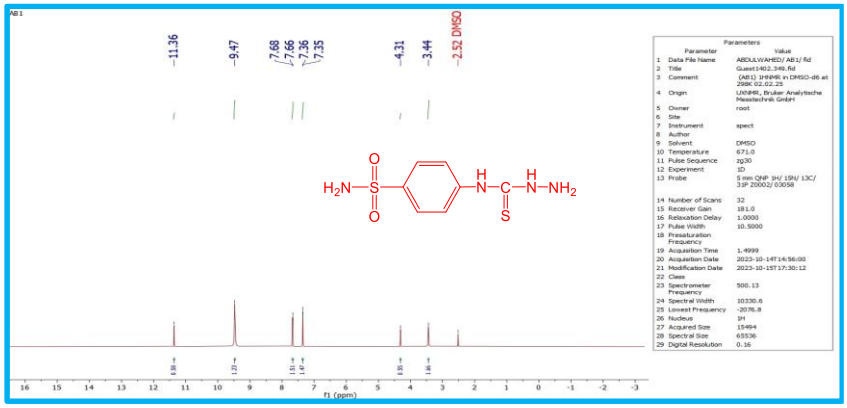


Figure 2. The chemical's ^{1}H-NMR spectra (AB2)

The ^{13}C-NMR spectra of the compound (AB1), as shown in Figure 3, showed the presence of several signals in the aromatic system's range (121.66-137.75) ppm, a signal attributed to the solvent's carbon (DMSO-d6) in the range (40.47-39.47) ppm, and a signal at frequency (178.97) ppm associated with the carbon group (C=S).

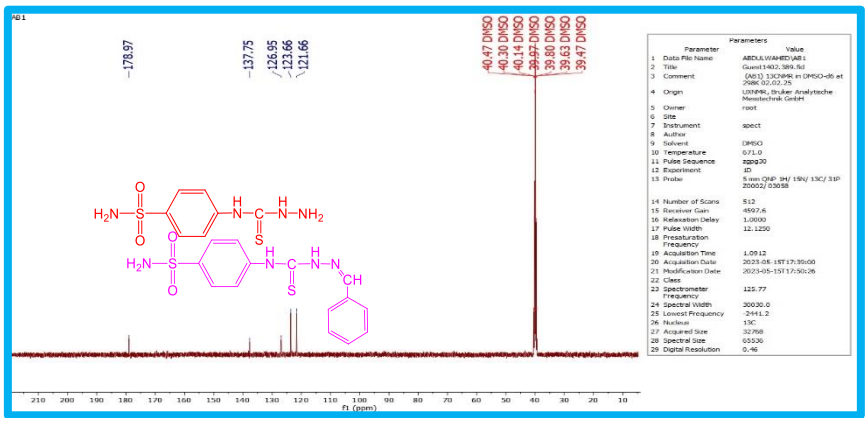


Figure 3. ^{13}C-NMR spectra of the substance (AB1)

3.2. Characterization of Hydrazone derivatives

The infrared (IR) spectrum was examined, and it revealed absorption bands in the range of (1621-1628) cm-1, which are associated with the stretching of the atom (C=N), as well as absorption bands in the range of (1507-1592) cm-1. Aromatics with a C=C bond and absorption bands resulting from (C-H) bond stretching in the range (3008-3082) cm-1. Aromatics also exhibit absorption bands owing to (N-H) bond stretching in the region of (3164-3198) cm-1 [42]. IR data is in Table 2 and in Figure 4.

Table (2): The synthesized compounds' FT-IR data (AB2-AB6) cm-1

Comp. No.	R	IR (KBr) cm^{-1}					
		ν(C-H) Arom.	ν(C=N)	ν C=S	ν(N-H)	ν(C=C) Arom.	Others
AB2	OH	3060	1604	1128	3172	1534	ν (C-OH) 3315
AB3	H	3048	1623	1182	3164	1557	----
AB4	4-Cl	3010	1608	1102	3146	1509	ν (C-Cl) 748
AB5	4- $N(CH_3)_2$	3048	1618	1143	3195	1568	ν (C-H)2931
AB6	4-NO_2	3028	1628	1096	3198	1592	ν (N-O)1375

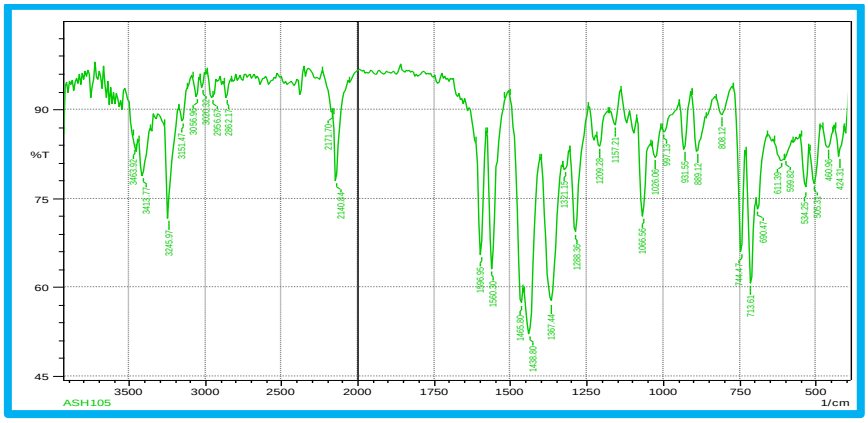


Figure 4. The compound's infrared spectrum (AB2)

A signal was seen at the site (8.06) ppm ascribed to the proton of the (CH) isomethene group and at the site (5.47) ppm attributed to the proton of the (-NH2) group linked to the isomethene group when the 1H-NMR spectra of the chemical [AB4] were examined. (O=S=O), and as Figure 5 illustrates, many signals that are attributed to the protons of the aromatic rings emerge at different points in the spectrum (7.81-7.31) ppm, along with a signal that reverts to the solvent protons at a site (2.52 ppm) (DMSO-d6). The signal at the ppm position (10.36) is caused by the proton of the (NH) group attached to the isomethene group.

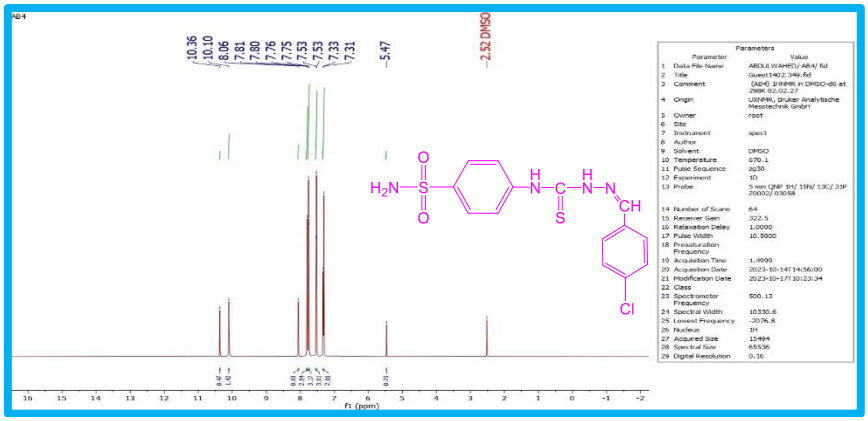


Figure 5. The [1]H-NMR spectrum of the combination (AB4)

The 13C-NMR spectra of the chemical (AB4) showed the presence of a signal at the ppm frequency (146.59) attached to the carbon of the isomine group (CH=N). It was also reported that a signal corresponding to the carbon frequency of the group (185.22) ppm belonging to carbon (c = s) was found. As is evident in Figure 6, several signals in the range (121.59-143.52) ppm indicate the aromatic system, while the signal in the range (40.46-39.45) ppm indicates the carbon of the solvent (DMSO-d6).

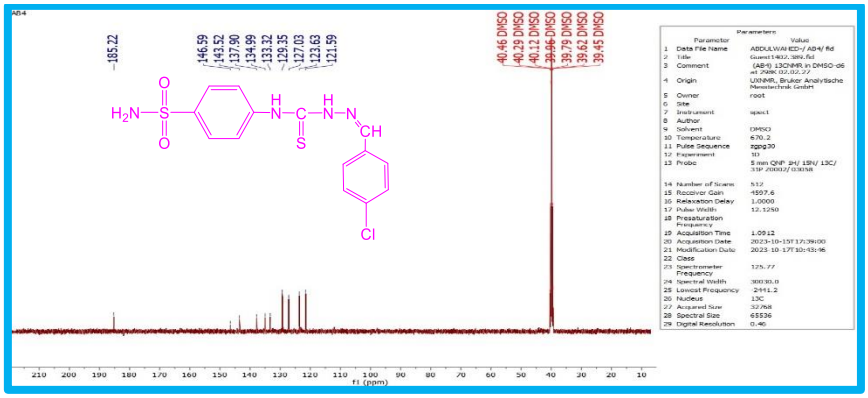


Figure 6. The ^{13}C-NMR spectrum of the combination (AB4)

3.3. Characterization of of 1,3-Oxazepine-4,7-dione derivatives

When researching the far-infrared range. The lactam carbonyl group (-N-CO-) displayed an absorption band at (1635-1690) cm-1, and it was noticed that the lactone carbonyl group (–O–CO) showed an absorption band in the range (1709-1745) cm-1. The aromatic ring's (C=C) stretch band was seen at (1508-1565) cm-1 as a sharp, vital to moderate intensity band, whereas the aromatic group (C-H) stretch band was observed at (3020-3090) as weak to medium intensity band, as indicated by Tables 3 and Figure 7 for all compounds and bands associated with the stretching of the (N-H) group that emerged at (3140-3360) cm–1 [40].

Table 3. The synthesized compounds' FT-IR data (AB7-AB11) cm^{-1}

Comp. No.	R	IR (KBr) cm^{-1}							
		νC-H Ar	**νC=C Ar**	**νC=O L.N**	**νC=O L.M**	**νC-O E.R**	**νC=S**	**νN-H**	Others
AB7	OH	3060	1560	1666	1635	1205	1126	3317	ν (C-OH) 3312
AB8	4-OCH_3	3090	1521	1720	1660	1225	1040	3210	ν (C-H)2819
AB9	4-Cl	3030	1530	1709	1665	1191	1050	3197	ν (C-Cl) 723
AB10	4-$N(CH_3)_2$	3050	1520	1745	1690	1190	1030	3167	ν (C-H)2922
AB11	4-NO_2	3060	1508	1735	1650	1250	1120	3160	ν (N-O)1379

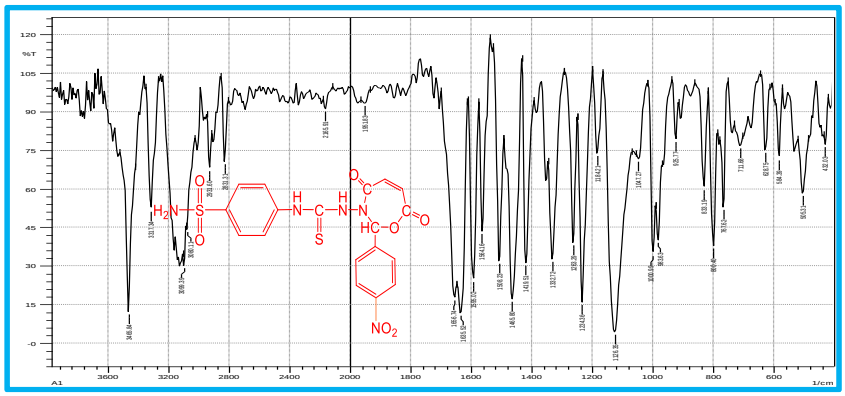


Figure 7. The infrared spectrum of the combination (AB7)

The protons of the oxazepine ring's (CH=CH) group were identified as the source of two duplicate signals observed at the 6.08–6.50 ppm location in the compound's 1H-NMR

spectra [AB11]. Additionally, a signal was detected at the 8.11 ppm location, which was identified as the oxazepine ring group's proton. (O-CH-N) the oxazepine ring, as well as the signal that appeared at the site (11.91) ppm and was ascribed to the (NH) group's proton linked to the oxazepine ring and the aromatic ring at the site (12.18) ppm; the protons of the aromatic rings are responsible for the multiple signal that appears in the region of 6.77-7.92 ppm. At the location (2.52) ppm, a signal is produced by the solvent's protons (DMSO-d6).

The 13C-NMR spectra of compound (AB11) showed the appearance of two signals at a frequency (127.95–132.19 ppm) corresponding to the oxazepine ring's carbons (CH = CH) and one signal at ppm (112.05) corresponding to the oxazepine ring's (CH) group carbon (Figure 8). Furthermore, two signals with a frequency of (167.66-169.77) ppm were found to be connected to the carbons in the (C=O) group of the oxazepine ring. As seen in Figure 9, other signals that were found were linked to the aromatic system in the range of (123.23-144.04) ppm and the solvent's (DMSO-d6) carbon in the range of (40.45 - 39.45) ppm.

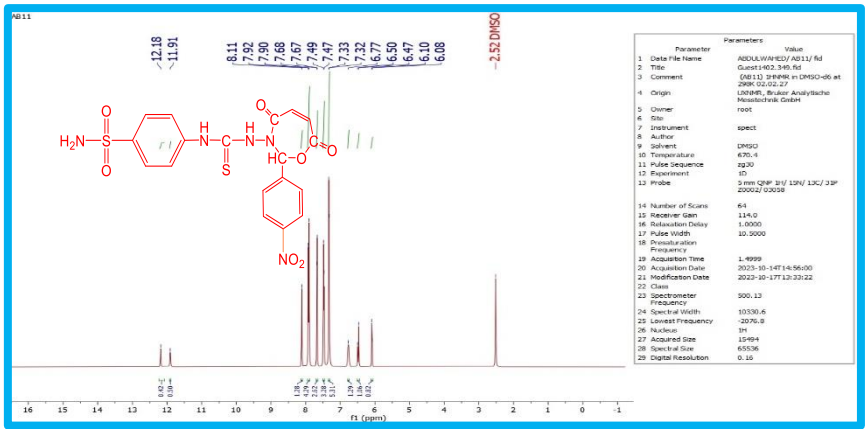


Figure 8. The chemical's 1H-NMR spectra (AB11)

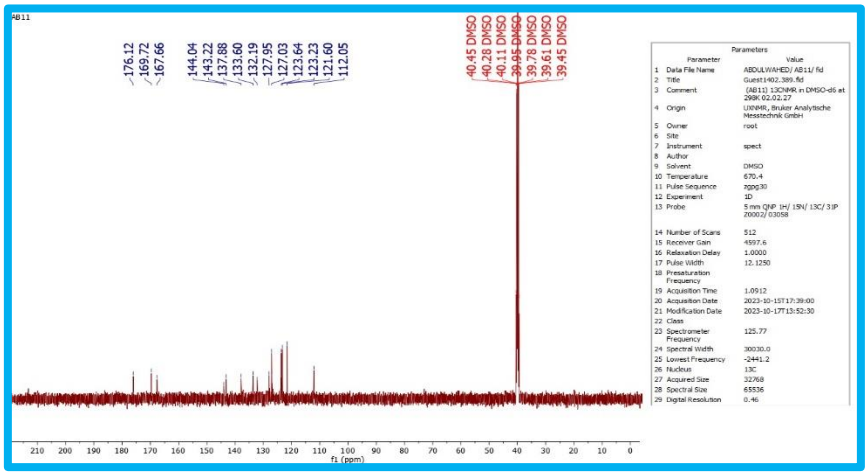


Figure 9. 13C-NMR spectra of the substance (AB11)

3.4. Evaluation of biological activity of AB7, AB8, AB9, AB10, AB11

A number of the generated compounds (AB4, AB8, AB9, and AB10) were tested using the cup plate agar diffusion technique against various bacterial strains, including gram-positive bacteria Streptococci and Escherichia coli as well as gram-negative bacteria Escherichia coli and Pseudomonas aeruginosa [41]. 0.8% sterile saline was added to the

microbial cultures after they were incubated for eight hours at 37 °C [42]. The concentration of the drug solution in DMSO was maintained at 100µg/mL. Ciprofloxacin was employed as a negative control. By measuring the inhibition diameter of bacterial growth surrounding the in-use disk, the biological activity was determined [43,44], as seen in Table 3 and Figure 10.

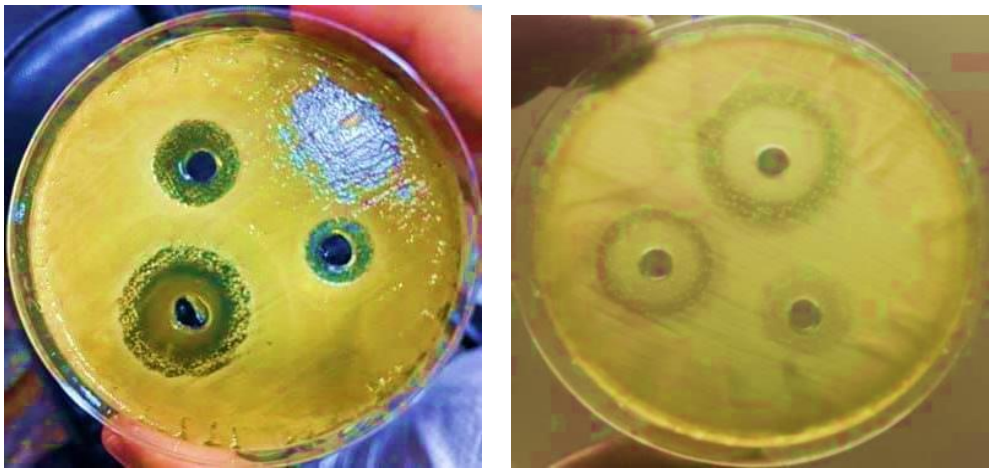


Figure 10. Compounds' biological effects and sensitivity tests on microorganisms

3.5. Identification and discussion of liquid crystal phases of AB7, AB8, AB11

The liquid crystalline phases were analyzed, diagnosed, and the types of changes in various stages were identified with the use of a heater-equipped polarized light microscope, as shown in Table 4. Compound [AB7] showed a nematic phase (N only) due to terminal hydroxy groups. A strong electronic sequence in the middle of the molecule and polarized peripheral hydroxy groups that raise peripheral attractive forces and, eventually, the nematic crystalline phase ((N) [45] are two features of the compound that indicate the appearance of the nematic phase. According to Figure 11, due to the presence of the terminal nitro group, a polarized and flexible terminal group, and a high electronic sequence in the middle of the molecule, which also suggests the appearance of the nematic (N) phase, the compound [AB11] displayed the smectic (S) and nematic (N) phases with a high-temperature range. Figures 12 and 13 illustrates how higher lateral bonding pressures [46] cause the smectic phases.

Table 4. Antibiotics and other generated chemicals (AB7, AB8, AB9, AB10, AB11) have the ability to prevent the growth

Comp. No.	**Conc. mg/ml**	**E. coli**	**p.s. aenginosa**	**St. aurew**	**Strept ococcut**
AB7	50	10	12	15	--
	100	5	8	10	13
	150	11	--	5	8
AB8	50	--	5	7	12
	100	12	8	--	12

	150	12	10	8	14
AB9	50	--	8	12	11
	100	12	12	--	12
	150	5	8	12	14
AB10	50	13	--	12	12
	100	5	10	10	12
	150	5	5	5	14
AB11	50	12	12	10	8
	100	15	--	10	16
	150	17	10	12	18

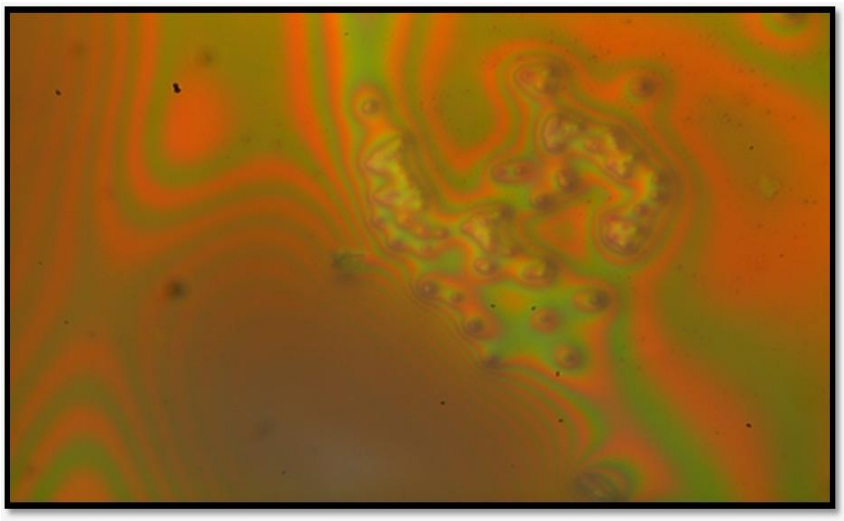


Figure 11. Phase S of the smectic compound [AB7]

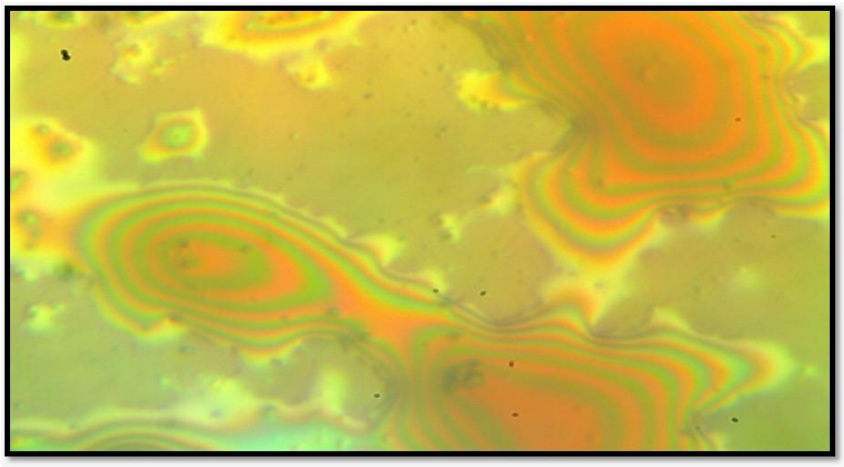


Figure 12. Phase N of the compound's nematode [AB11]

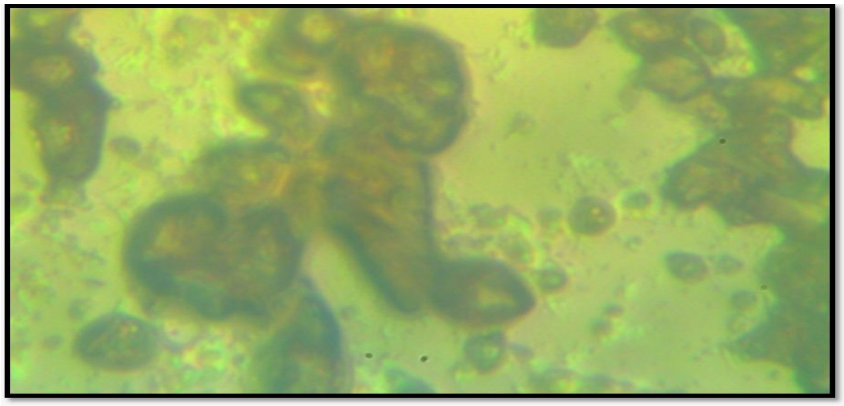


Figure 13. Phase S of the smectic compound [AB11]

Table 5. The characteristics of certain prepared compounds' liquid crystalline phase transitions

NO.	Crystal	S	N	ΔT_S	ΔT_N
AB7	**Gum**	**------**	**300**	-----	**------**
AB8	**Gum**	**280**	**300**	-----	**20**
AB10	**132**	**120**	**140**	**12**	**20**

4. Conclusion

Through spectroscopic and physical tests, the validity and correctness of the synthesized compounds were verified. The validity of the obtained compositions was demonstrated by nuclear magnetic resonance spectroscopy of the carbon and proton spectra and infrared spectroscopy. These substances do not break down or change colour at laboratory temperature, and they are stable. While some of the produced compounds had inhibitory effects against Gram-positive and Gram-negative bacteria, others exhibited no activity. The outcomes were contrasted with antibiotic control samples. The existence of successively polarized end groups over the length of the system was shown by the analysis of liquid crystals containing chemicals belonging to the nematic (N) and smectic (S) phases.

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