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Synthesis , Characterization and Biological Activity of Some New Heterocyclic Compounds Containing Azo group

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الخلاصة :

تضمنت هذه الدراسة تحضير مركب آزو جديد (D_H) بإذابة 1,4- phenylenediamine في مزيج من نتريت الصوديوم ، حامض الهيدروكلوريك المركز و 4-hydroxyacetophenone ثم تحضير قاعدة شف (D) بواسطة تفاعل الآزو المحضرة مع 2-aminoanthraquinone بوجود قطرات من حامض الخليك الثلجي عن طريق اشعة المايكروويف ، حضرت مشتقات الأميدازوليدين (D_1 , D_2) بواسطة تفاعل (D) مع الأحماض الأمينية Lucien و Tyrosine على التوالي ، ثم مفاعلة (D) مع الإنهدريدات المالك و الفثالك لتحضير الحلقات السباعية Oxazepane (D_3) و Benzoxazepene (D_4) على التوالي ، استخدمت تقنية الـ TLC لمراقبة التفاعل واستخدام اليود كمظهر ، وبعد تنقية المشتقات المحضرة قيست درجات الإنصهار لها ، تم تسجيل اطياف الأشعة تحت الحمراء (FT-IR) وتم تسجيل اطياف (^{1}H NMR) .

الكلمات المفتاحية : اصباغ الآزو ، قواعد شف ، اميدازوليدين و اوكسازبين .

Abstract : This study includes preparing the new Azo compound (D_H) Dissolved of 1,4- phenylenediamine in a mixture of Sodium nitrite ,concentrated hydrochloric acid and 4-hydroxyacetophenone then preparing the Schiff base (D) By reacting the prepared Azo with 2-aminoanthraquinone in the presence of drops from Glacial acetic acid ,via microwave method , the Synthesis of Imidazolidine derivatives (D_1-D_2) by reacting (D) with the amino acids Lucien and Tyrosine respectively, then react (D) with Maleic Anhydride and Phthalic Anhydride to Prepare the seven membered rings of Oxazepane (D_3) and Benzoxazepene (D_4) , respectively . The (TLC) technique was used to follow the reaction , iodine was used as a moderator, and after purification of the prepared derivatives the melting Points were measured. The infrared (FT-IR) spectra and The spectra of Proton NMR (^{1}H NMR) .

Key Word: Azo dyes, Schiff base , Imidazolodine and oxazepine .

INTRODUCTION

One of the most widespread organic compounds is azo pigments because of their many uses, which are introduced as pigments in foods and cosmetics in addition to their applications in modern technology as well as

enter in the field of agriculture, industry and the medical field because of the high vital effectiveness found against fungi and bacteria Due to their the azo group[1-3]. Azo dyes aliphatic disintegrate into nitrogen and hydrocarbons ([4]), Characteristics of the azo compounds are highly selective and sensitive[5].

Imine compounds, which included the Azomethine group[6,7], By the scientist h. Schiff their discovery in 1864 through the condensation of ketones or aldehydes aliphatic or aromatic [8] with primary aromatic or aliphatic amines ,they are widely used In industrial purposes and biological activities as they have shown effectiveness against fungi [9,10], malaria [11], viruses [12,13] , bacteria [14,15].

Imidazolodine is a heterogeneous pentagram has a molecular formula ($C_3H_8N_2$) produced by amedazolidine after the addition of four atoms (H) of amedazol [16] figure 1.

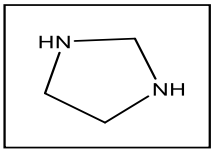


Figure 1. Imidazolidine

The Imidazoldine ring is important as its building units for the formation of bioactive compounds[17]. Some of its derivatives are considered antiviral, fungal, inflammatory, cancer, antihypertensive or digestive antibiotic [18].

Oxazepine compounds are of great importance because they have a wide biological and pharmacological activity [19] such as anti-epileptic activity [20], analgesic [21], anti-allergic [22] , anti-depressant [23], and hepatitis [24,25], muscle relaxant [26] , anti-fungal [27] , Efficacy against types of cancer [28] . The importance of heterocyclic compounds in the industrial, pharmaceutical and medical fields [29,31]. Therefore, the current research aims to use these derivatives in the pharmaceutical , medical and industrial fields .

Experimental Synthesis of new Azo dyes

1,1'-((1,4-phenylenebis(diazene-2,1-diyl))bis(4-hydroxy-3,1-phenylene))bis(ethan-1-one)

Dissolving 0.01mole of 1.4- phenylenediamine in a mixture of 5ml concentrated hydrochloric acid and 15ml of distilled water in an ice bath , then added to the resulting mixture of sodium nitrite solution 0.02mole of dissolved in 10 ml distilled water gradually with constant stirring and note that the temperature does not rise above (5)°C leaving the solution to settle for a period of 15min. to complete the nitrogenation process , Diazonium salt is added in drops with continuous stirring to a solution of 0.02mole of 4-hydroxyacetophenone dissolved in a mixture of 30ml ethanol and 10ml sodium hydroxide solution (10%NaOH) observed to be brown, then the solution is left until the next day and for the purpose of obtaining the Azo dyes in its solid form was added hydrochloric acid (0.1M) in

droplets for the purpose of modifying the acidic function to reach (pH=7) sprayed the precipitate and washed with distilled water, then recrystallized twice from the ethanol mixture: water (1:1) and dried .

Identification of compound (D_H) ,The FTIR spectrum(cm^{-1}) Figure 2. Shows ($OH_{Phenolic}$ = 3387) , ($CH_{Arom.}$ = 3062) , (CH_{Alph} = 2922), (C = O $_{keton}$ = 1672) , (N=N = 1498) and (C-N = 1240) .

The proton magnetic resonance spectrum of the compound (D_H) Fig. 3. Showed the following signals: ($OH_{Tot.}$ = singlet at 10.33 ppm), (OH_{Phenol}= singlet at 8.14 ppm), (H aromatic = multiplet at 6.5 - 8.50 ppm) and (H $_{Aliph.}$ = singlet at 3.34ppm), (DMSO = 2.5ppm) .

1- ***2,2,-((1E,1E,)-((1,4-phenylenebis(diazene-2,1-diyl))bis(4-hydroxy-3,1-phenylne))bis(ethan-1-yl-1-ylidene))bis(azaneylyidene))bis(anthracene-9,10-dione) (D)***

Using microwave irradiation crushed 0.001mole from azo previously prepared and then dissolved in 5ml of absolute ethanol and then added 3 drops of Glacial acetic acid and then added 0.00 2mole of (2-aminoanthraquinone crush the mixture well to complete the homogeneity and then put in the microwave at (326w) for (30min.), the reaction was followed by using TLC (3ml Benzene: 2ml EtOH abs) and then perform recrystallization. Physical properties are listed in table 1.

Identification of compound (D) ,The FTIR spectrum(cm^{-1}) Figure 4. Shows (OH = 3334) , ($CH_{Aromatic}$ = 3051), ($CH_{Aliph.}$ = 2918), ($C=O_{(endocyclic)}$ = 1672), (C=N = 1579) , (N=N = 1583) and (C=C =1477).

2- ***imidazolidine-4-one derivatives :***

2,2'-(((1,4-phenylenebis(diazene-2,1-diyl))bis(4-hydroxy-3,1-phenylene))bis(4-isobutyl-2-methyl-5-oxoimidazolidine-2,1-diyl))bis(anthracene-9,10-dione) . (D_1)

2,2'-(((1,4-phenylenebis(diazene-2,1-diyl))bis(4-hydroxy-3,1-phenylene))bis(4-(4-hydroxybenzyl)-2-methyl-5-oxoimidazolidine-2,1-diyl))bis(anthracene-9,10-dione) . (D_2)

By using microwave irradiation crushed 0.001mole from the Schiff base of the prepared (D) with 0.002mole from Lucien for preparation (D1) and 0.002mole of The Tyrosine for preparation (D2) crush the mixture well to complete homogenization and then dissolved in 10ml Benzene and then put in the microwave at (326w) for (31-34min.), the reaction was followed using TLC (Benzene:EtOH abs.) Physical properties are included in the table 1.

Identification of compound (D_1) ,The FTIR spectrum (cm^{-1}) Figure 5. Shows (OH = 3356) , (NH = 3457), ($CH_{Aromatic}$ = 3028), ($CH_{Aliph.}$ = 2971), (C = O = 1666) , (C=C = 1516) and (N=N = 1583).

The proton magnetic resonance spectrum of the compound (D_1) Fig. 6. Showed the following signals: (OH_{Phenol}= singlet at 9.16 ppm), (N-H. = singlet at 7.89ppm), (N-CH-C = multiplet at 3.63 ppm) , ($CH_{3\ incyclic}$ = singlet at 2.13 ppm) , (H aromatic = multiplet at 6.52 - 8.50 ppm) and ($H_{Aliph.}$ = singlet at 0.92 , 1.49ppm), (DMSO = 2.5ppm) .

Identification of compound (D_2) ,The FTIR spectrum (cm^{-1}) Figure 7. Shows (OH = 3319) , (NH = 3371), ($CH_{Aromatic}$ = 3090), ($CH_{Aliph.}$ = 2958), (C = O = 1666) , (C=C = 1512) and (N=N = 1581).

3- ***Preparation of oxazepine derivatives :***

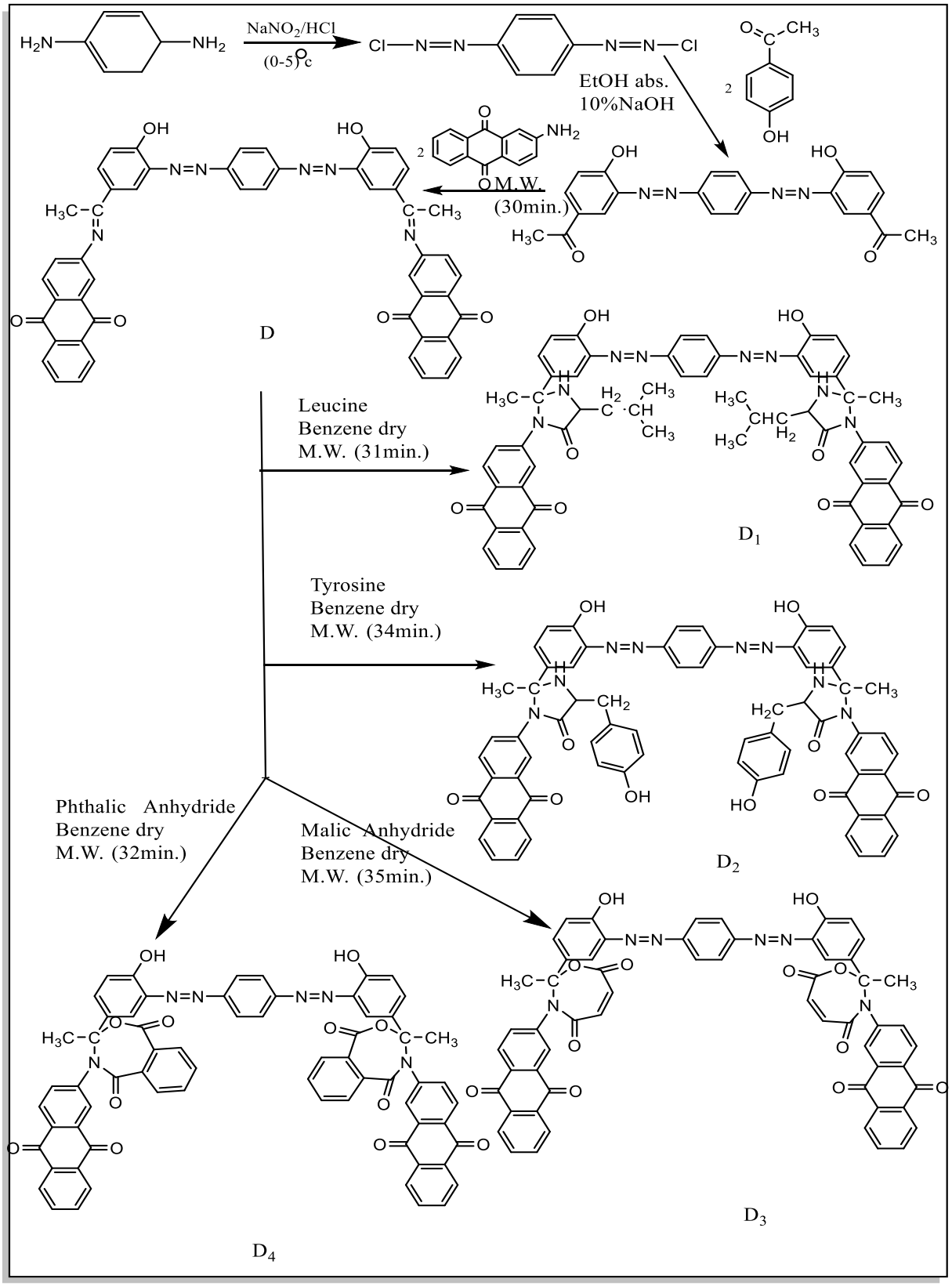
2,2'-((1,4-phenylenebis(diazene-2,1-diyl))bis(4-hydroxy-3,1-phenylene))bis(3-(9,10-dioxo-9,10-dihydroanthracen-2-yl)-2-methyl-2,3-dihydro-1,3-oxazepine-4,7-dione) . (D_3)

3,3'-((1,4-phenylenebis(diazene-2,1-diyl))bis(4-hydroxy-3,1-phenylene))bis(4-(9,10-dioxo-9,10-dihydroanthracen-2-yl)-3-methyl-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione) . (D_4)

By using microwave irradiation crushed 0.001mole from the schiff base of the prepared (D) with 0.002mole of Maleic anhydride for preparation (D_3) and 0.002mole of Phthalic anhydride for preparation (D_4) crushed well to complete homogenization then dissolved in 10ml of benzene and then put in the microwave at (326w) for (32-35min.), the reaction was followed using TLC (Benzene:EtOH abs.) Physical properties are listed in the table 1.

Identification of compound (D_3) ,The FTIR spectrum(cm^{-1}), Fig. 8. Shows (OH = 3358) , ($CH_{Arom.}$ = 3062) , ($CH_{Alph.}$ = 2857) , (lactone=1710) , (lactam=1672) , (N=N = 1585), (C=C = 1517).

Identification of compound (D_4) ,The FTIR spectrum(cm^{-1}), Fig. 9. Shows (OH = 3371) , ($CH_{Arom.}$ = 3074) , ($CH_{Alph.}$ = 2899) , (lactone=1693) , (lactam=1685) , (N=N = 1587), (C=C = 1533).



Scheme 1. synthesis of Comp. (D_H-D_4)

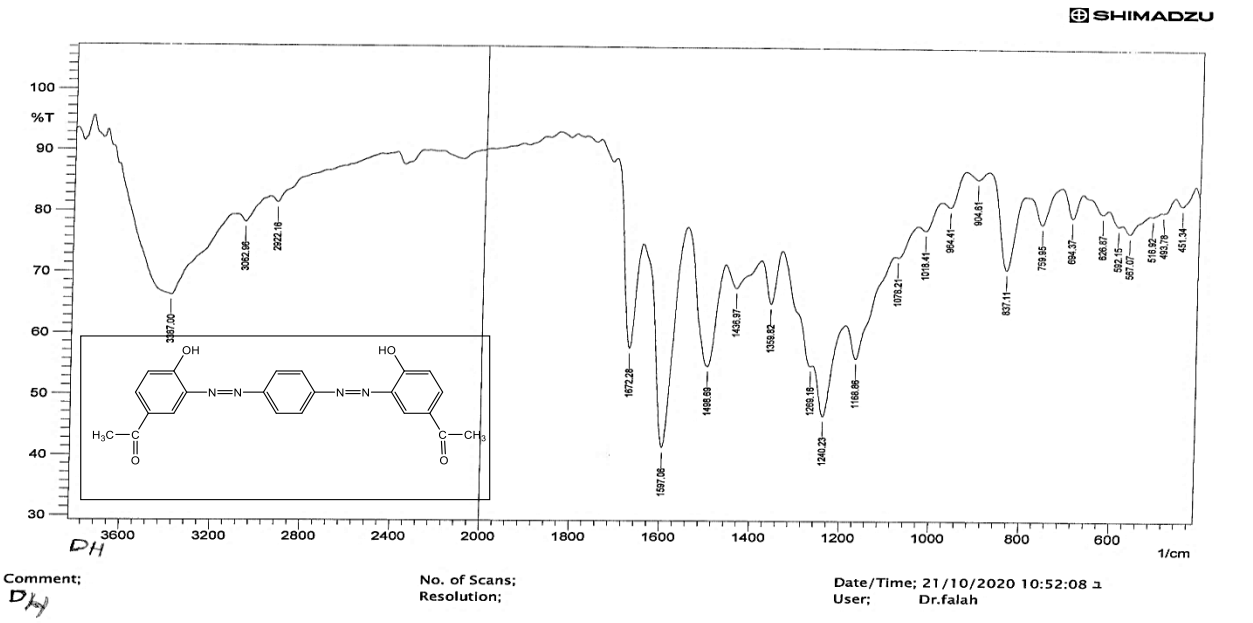


Figure 2. (FT-IR) spectrum of the Azo dyes (D_H)

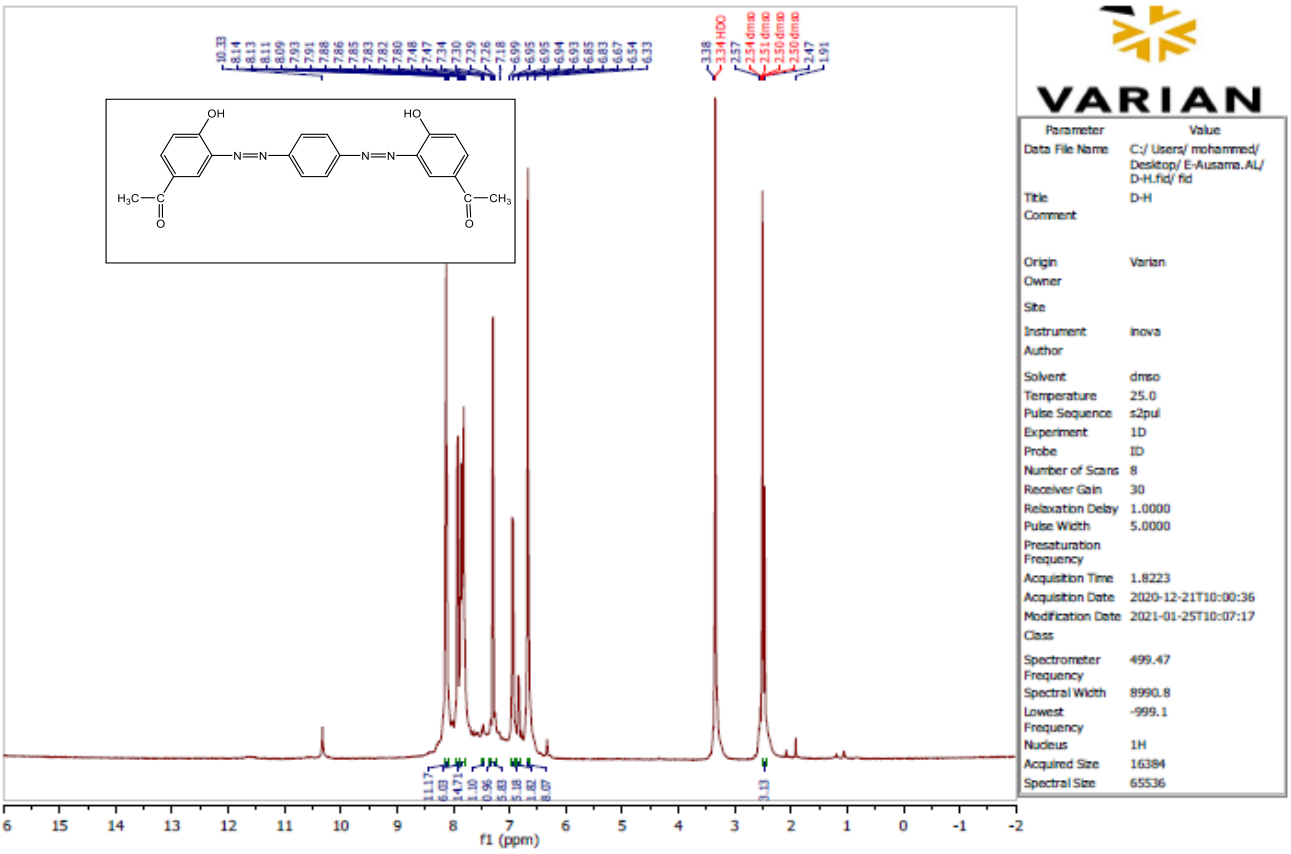


Figure 3. ^{1}H-NMR spectrum of Comp. (D_H)

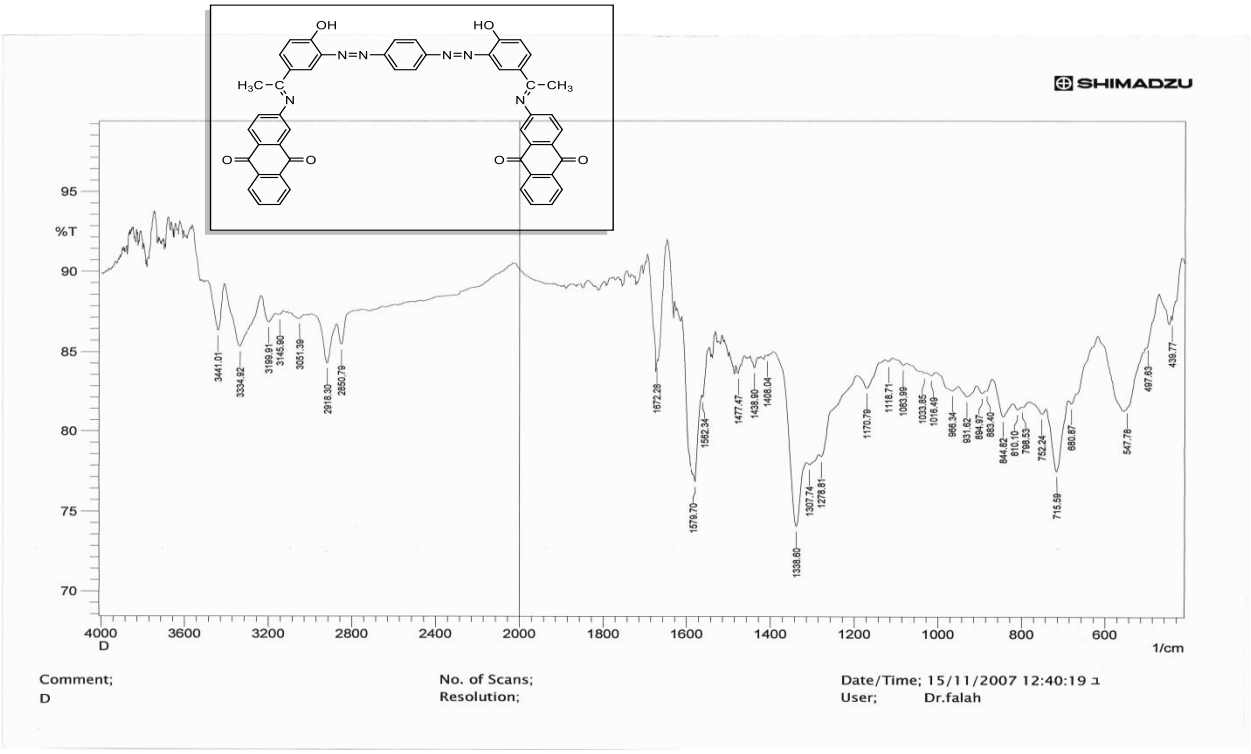


Figure 4. (FT-IR)spectrum of Comp. (D)

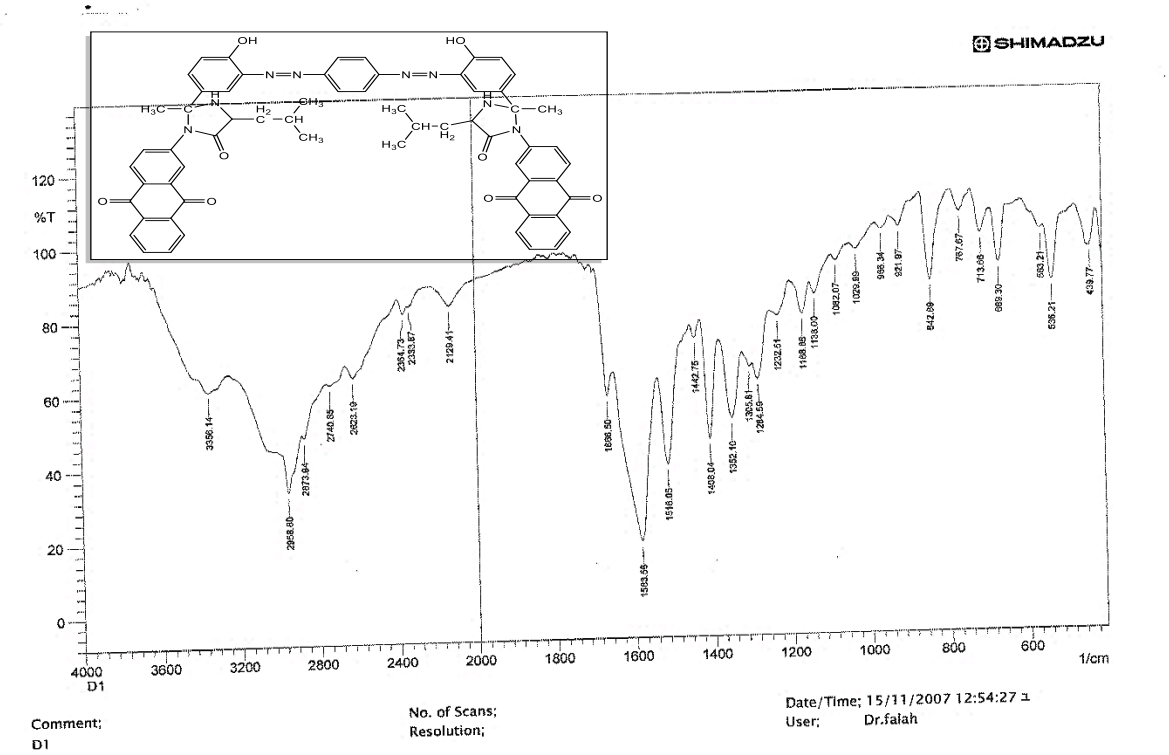


Figure 5. (FT-IR) spectrum of Comp. (D_1)

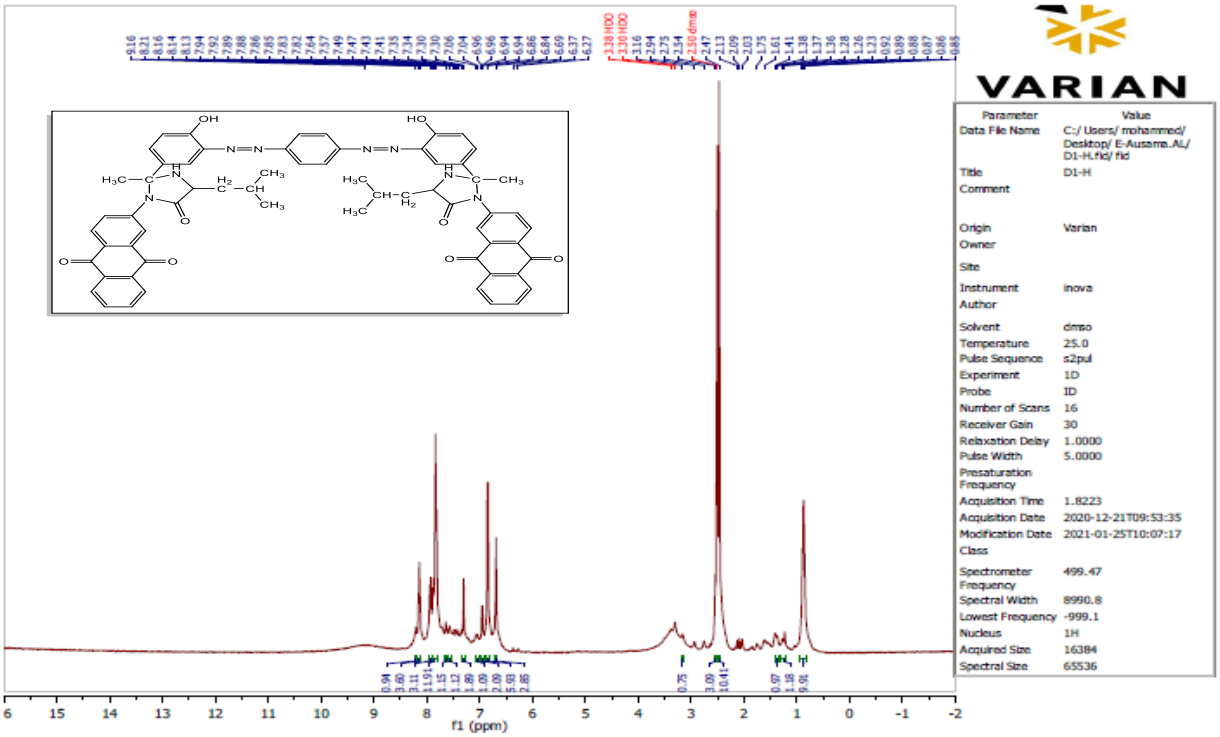


Figure 6. ^{1}H-NMR spectrum of Comp. (D_1)

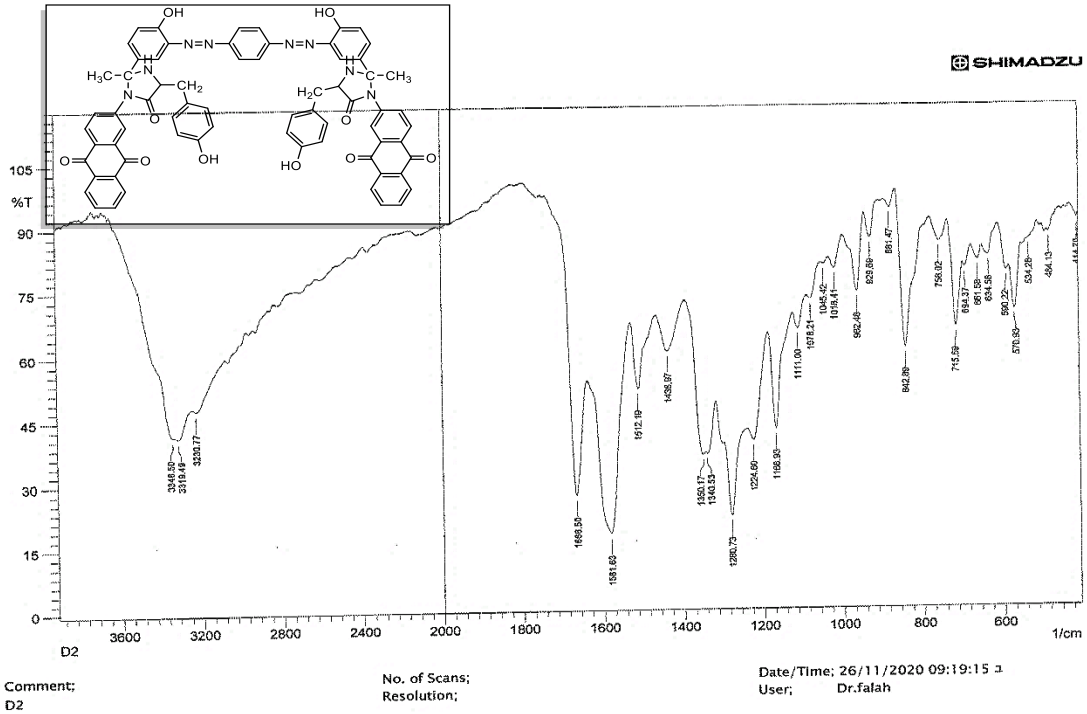


Figure 7. (FT-IR) spectrum of Comp. (D_2)

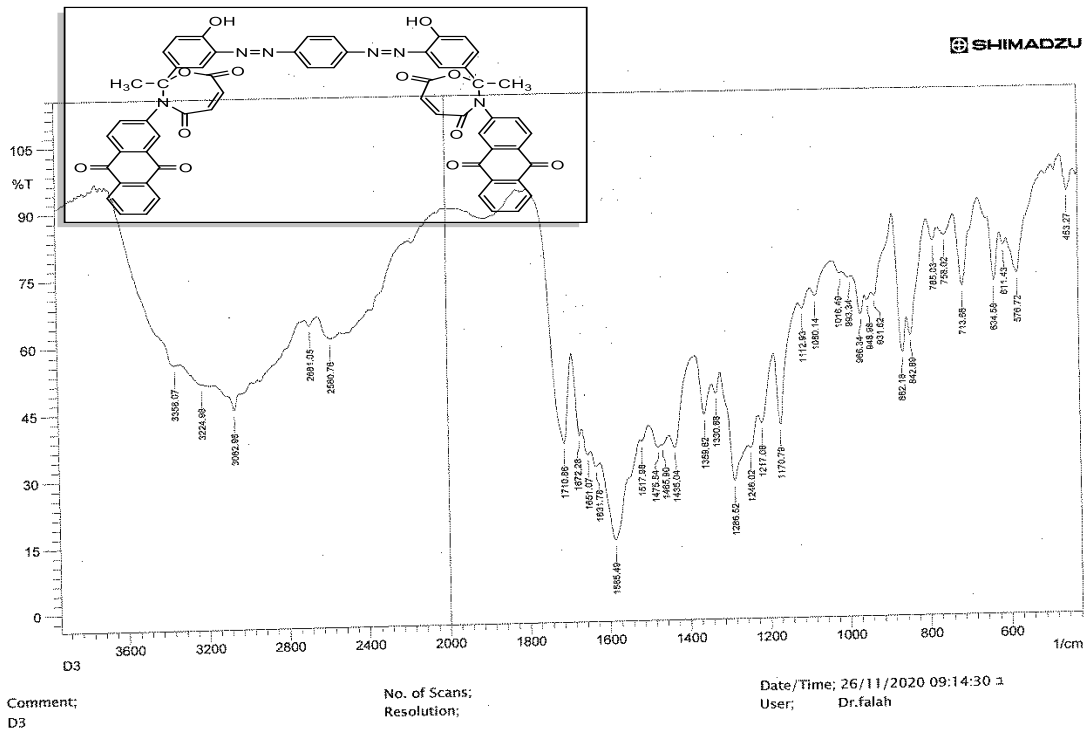


Figure 8. (FT-IR) spectrum of Comp. (D_3)

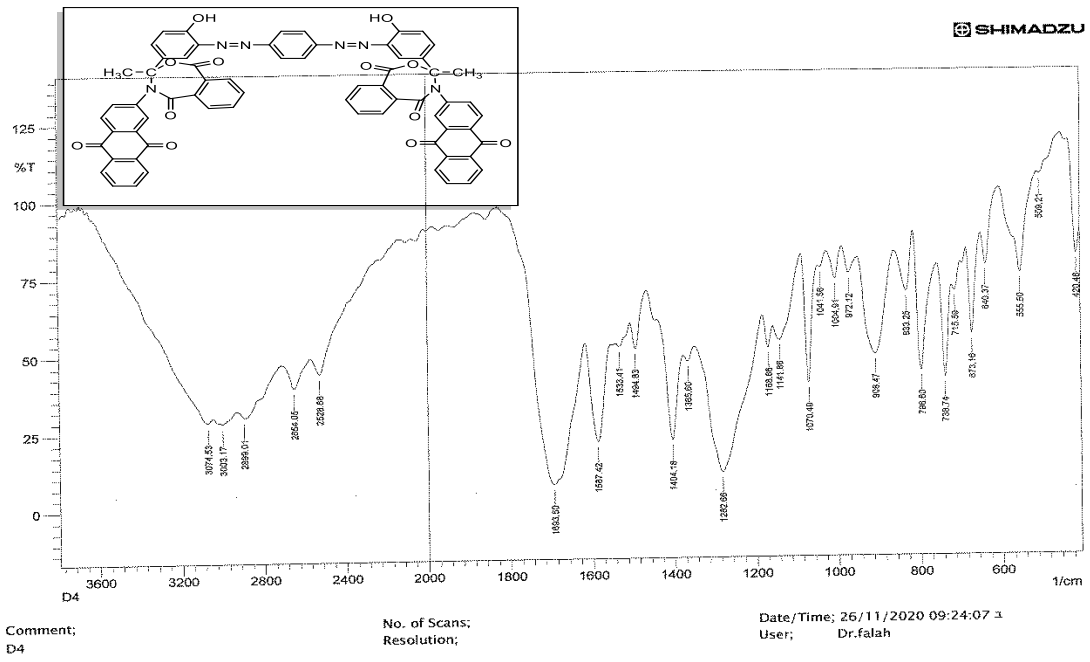


Figure 9. (FT-IR) spectrum of Comp. (D_4)

Table 1. Physical properties of compounds (D – D_4)

N	M.f.	Name of compound	M.wt	m.p (^{0}C)	R_f	Color	Yield %	Time	Solvent
D	$C_{50}H_{32}N_6O_6$	2,2'-((1E,1E')-((1,4-phenylenebis(diazene-2,1-diyl))bis(4-hydroxy-3,1-phenylne))bis(ethan-1-yl-1-ylidene))bis(azaneylyidene))bis(anthracene-9,10-dione)	812.84	270 Decomp.	0.80	Yellow	72	M.W 30min	EtOH
D_1	$C_{62}H_{54}N_8O_8$	2,2'-(((1,4-phenylenebis(diazene-2,1-diyl))bis(4-hydroxy-3,1-phenylene))bis(4-isobutyl-2-methyl-5-oxoimidazolidine-2,1-diyl))bis(anthracene-9,10-dione)	1039.16	212-215	0.81	Brown	76	M.W 31min.	dry Benzene
D_2	$C_{68}H_{50}N_8O_{10}$	2,2'-(((1,4-phenylenebis(diazene-2,1-diyl))bis(4-hydroxy-3,1-phenylene))bis(4-(4-hydroxybenzyl)-2-methyl-5-oxoimidazolidine-2,1-diyl))bis(anthracene-9,10-dione)	1139.19	278-280	0.69	Light Brown	67	M.W 34min	dry Benzene
D_3	$C_{58}H_{36}N_6O_{12}$	2,2'-((1,4-phenylenebis(diazene-2,1-diyl))bis(4-hydroxy-3,1-phenylene))bis(3-(9,10-dioxo-9,10-dihydroanthracen-2-yl)-2-methyl-2,3-dihydro-1,3-oxazepine-4,7-dione)	1008.96	108-110	0.76	Dark Brown	78	M.W 35min	dry Benzene
D_4	$C_{66}H_{40}N_6O_{12}$	3,3'-((1,4-phenylenebis(diazene-2,1-diyl))bis(4-hydroxy-3,1-phenylene))bis(4-(9,10-dioxo-9,10-dihydroanthracen-2-yl)-3-methyl-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione)	1109.08	172-175	0.70	Light Brown	67	M.W 32min	dry Benzene

Anti- bacterial Activity Assay

The biological activity for the compounds (D –D_4) Was studied using (EtOH) solvent and studying its effect on two types of bacteria which are G+ (*Staphylococcus Aurous*) for and G-(*Escherichia Coli*)with solutions of (1×10^{-3} M) , (2.5×10^{-3} M) and (5×10^{-3} M) , The effect of the solvent was measured and subtracted from the product . The zone of inhibition of the prepared compound measured using the ruler and the table 2. show that the vital amount of inhibition.

Table 2. The biological effectiveness of the heterocyclic compound Were the zone inhibiters ; (-) no inhibition , (+) 5-14 mm, (++) 15-20 mm

Comp.	*Staph.Auous* $1x10^{-3}M$	*E.Coli* $1x10^{-3}M$	*Staph.Auous* $2x10^{-3}M$	*E.Coli* $2x10^{-3}M$	*Staph.Auous* $5x10^{-3}M$	*E.Coli* $5x10^{-3}M$
D	++	-	+	-	-	_
D_1	+	-	+	+ +	+ +	+
D_2	++	-	+	-	+	+
D_3	++	-	++	+	+	+
D_4	+	+	++	-	+	-

CONCLUSION

Microwaving is an easy-to-use, fast and high-product method, Shaf's bases were characterized by stability and were not affected by light and moisture and had high melting points. The effect of pulling groups and their motive on the interaction, Most of the prepared compounds have a high bioactivity and a high bacteriostatic effect.

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