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PREPARATION AND CHARACTERIZATION OF FIVE MEMBERED HETEROCYCLIC DERIVATIVES FROM CHALCONE AND EVALUATION OF THEIR BIOLOGICAL ACTIVITY AS ANTIOXIDANT AND PHYSICAL PROPERTY

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ABSTRACT

Five-membered heterocycles were prepared in two steps. In the first step, 2-acetylnaphthalene was condensed with 4-(2-pyridyl)benzaldehyde or with biphenyl-4-carboxaldehyde in basic ethanol to give chalcones (A) and (B). In the second step, each chalcone reacted with hydroxylamine hydrochloride, phenylhydrazine, 2,4-dinitrophenylhydrazine or hydrazine. This gave two isoxazolines (1, 5) and six pyrazolines (2, 3, 4, 6, 7, 8). The ring closures were run in ethanol at 40 °C for 22–26 h. FT-IR, ^{1}H-NMR and ^{13}C-NMR spectra were used to assign the structures. For all ten compounds, the colour, melting point, R_f value and molecular weight were recorded. Melting points ranged from 213–215 °C for compound (A) to 288–290 °C for compound (7). The biological activity of compounds (3), (4), (5) and (6), which have a strong inhibitory effect, was then studied with the DPPH radical scavenging assay. Five concentrations from 500 to 2500 µg/mL were tested, with ascorbic acid as the reference. Compound (5) gave the highest scavenging value, 93.1 % at 2500 µg/mL. Compound (6) gave the lowest, 38.9 % at 500 µg/mL.

Keywords: *chalcone, Pyrazolines,Isoxazolines, Antioxidant activity, DPPH assay.*

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INTRODUCTION

Chalcones are α,β-unsaturated carbonyl compounds with the core structure 1,3-diaryl-2-propen-1-one. In this skeleton, a three-carbon enone bridge links two aromatic rings. They are classed with the flavonoids and isoflavonoids [1]. Their derivatives show a wide range of pharmacological effects. Reported examples include analgesic [2], anti-arthritic [3], anti-inflammatory [4], antioxidant and anticancer [5] activity. The uses of chalcones reach beyond medicine. They serve as light stabilisers and sweeteners, as reagents for the amperometric determination of copper and the spectrophotometric study of germanium, and as starting materials for heterocycles with biological activity [6]. In the present work, chalcones were used to build pyrazoline and isoxazoline rings. A pyrazoline is a five-membered ring that contains two nitrogen atoms. Three isomeric forms are known: 1-pyrazoline, 2-pyrazoline and 3-pyrazoline (Figure 1) [7].

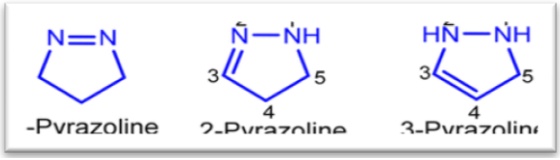


Figure 01: Pyrazoline isomers, with the substitution sites (positions 1, 3 and 5) of 2-pyrazoline.

The pyrazoline unit also occurs in nature, in some vitamins, pigments and alkaloids [8]. Its technical uses are broad. Pyrazolines serve as optical brighteners for synthetic materials, as fluorescent probes in chemosensors that recognise transition-metal ions, as hole-transport materials in organic electronics, and in electrophotography [9]. On the biological side, citroazopyrone, which carries a pyrazoline ring, inhibits the growth of lettuce hypocotyls [10]. Isoxazolines are related five-membered heterocycles whose ring holds both nitrogen and oxygen atoms. They belong to the azole family and hold an important place in medicinal chemistry as anticancer agents [11]. Several isoxazoline drugs are in practical use: fluralaner, afoxolaner, sarolaner, lotilaner, esafoxolaner and tigolaner treat and prevent infestation by fleas, ticks and mites [12].

MATERIALS

2-Acetylnaphthalene, 4-(2-pyridyl)benzaldehyde and biphenyl-4-carboxaldehyde were obtained from Sigma-Aldrich (Germany). All chemicals were of high purity.

INSTRUMENTS

FT-IR spectra were recorded from KBr discs over the range 400–4000 cm^{-1} on a Shimadzu FTIR-8400S Fourier-transform spectrometer.

^{1}H-NMR spectra were recorded on a Varian Agilent spectrometer (USA) at 500 MHz, and all NMR spectra were run in DMSO-d6. The measurements were made at the Department of Chemistry, University of Basrah, Iraq.

Synthesis of chalcones (A) and (B) [13]

2-Acetylnaphthalene (0.170 g, 0.001 mol) and one aldehyde, either 4-(2-pyridyl)benzaldehyde (0.183 g, 0.001 mol) for (A) or biphenyl-4-carboxaldehyde (0.182 g, 0.001 mol) for (B), were dissolved in ethanol (30 mL). A 10 % NaOH solution (6 mL) was added dropwise, and the mixture was stirred vigorously for 35 min. It was then left to stand for 24 h. The chalcone precipitated when the mixture was neutralised with HCl (0.1–0.2 N). The solid was collected by filtration, air-dried and purified by recrystallisation from ethanol.

Synthesis of isoxazolines (1) and (5) [14]

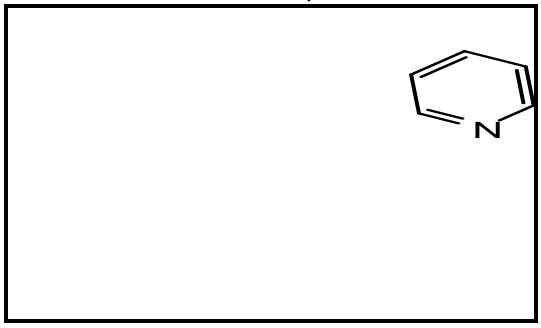
Each chalcone (0.001 mol; 0.335 g of A or 0.334 g of B) was dissolved in absolute ethanol (30 mL). Sodium hydroxide (1 g) and hydroxylamine hydrochloride (0.069 g) were added. The reaction was held at 40 °C for 22 h. The product was isolated by filtration, washed with water and recrystallised from absolute ethanol.

Synthesis of N-aryl pyrazolines (2), (3), (6) and (7) [15]

Chalcone A (0.335 g) or B (0.334 g), 0.001 mol in each case, was taken up in absolute ethanol (30 mL). Phenylhydrazine (0.108 g, 0.001 mol) or 2,4-dinitrophenylhydrazine (0.198 g, 0.001 mol) was then added together with a few drops of glacial acetic acid. The mixture was maintained at 40 °C for 26 h. The resulting precipitate was filtered off, washed and purified by recrystallisation from absolute ethanol.

Synthesis of N-unsubstituted pyrazolines (4) and (8) [16]

A mixture of chalcone A or B (0.001 mol; 0.335 or 0.334 g) and hydrazine (0.001 mol, 0.05 mL) in absolute ethanol (30 mL) was heated under reflux at 40 °C for 26 h. The crystalline product was collected by filtration, dried, and then recrystallised from ethanol.



Scheme 01: Synthetic route from the chalcones (A, B) to the isoxazolines and pyrazolines (1–8).

RESULTS AND DISCUSSION

Chalcone (A): 1-(naphthalen-1-yl)-3-(4-(pyridin-2-yl)phenyl)prop-2-en-1-one. Its IR spectrum (Figure 2a) has the carbonyl (C=O) band at 1681.81 cm^{-1} and a C=N band at 1627.81 cm^{-1}. The aromatic C=C band lies at 1596.95 cm^{-1}, and the olefinic C=C band at 1573.81 cm^{-1}. Aromatic C-H stretching gives bands at 3062.75 and 3008.10 cm^{-1}, while aliphatic C-H appears at 2970.17 and 2923.88 cm^{-1}. The ^{1}H-NMR spectrum (Figure 2b) shows the two olefinic protons as singlets at δ 7.63 (1H, CH-Ph) and 7.68 (1H, CH-C=O). A multiplet at δ 7.9–8.7 accounts for the 15 aromatic protons. In the ^{13}C-NMR spectrum (Figure 2c), the carbonyl carbon (C11) resonates at δ 198, C12 at δ 128 and C13 at δ 127. C20 and C1 give signals at δ 155 and 134, and the other aromatic carbons fall at δ 123–124.

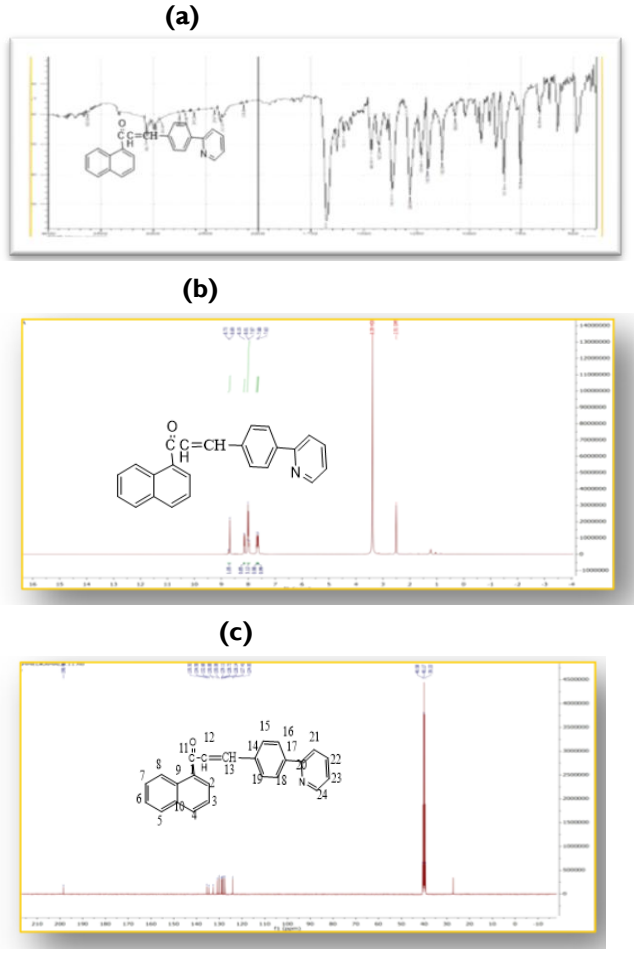
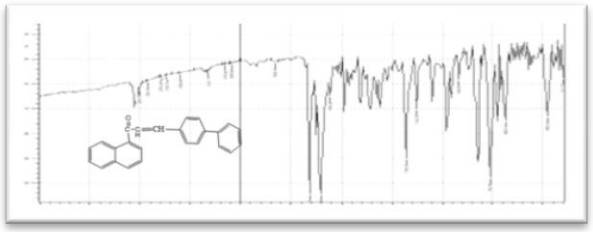


Figure 02. Spectra recorded for chalcone (A): FT-IR (a), ^{1}H-NMR (b) and ^{13}C-NMR (c).

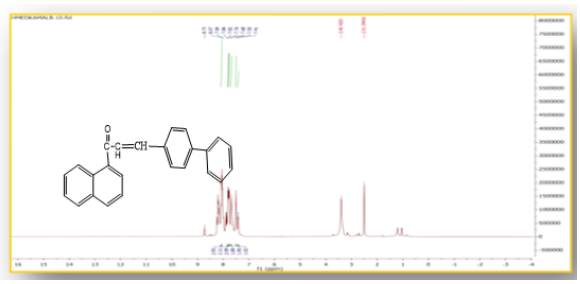
Chalcone (B): 3-([1,1'-biphenyl]-4-yl)-1-(naphthalen-1-yl)prop-2-en-1-one. The C=O band of this chalcone appears at 1658.67 cm^{-1} (Figure 3a). Aromatic C=C absorbs at 1604.66 cm^{-1} and the olefinic C=C at 1558.38 cm^{-1}. The spectrum also shows aromatic C-H at 3008.75 cm^{-1} and aliphatic C-H at 2923.88 cm^{-1}. In the ^{1}H-NMR spectrum (Figure 3b), the olefinic protons give singlets at δ 7.4 (1H, CH-Ph) and 7.5 (1H, CH-C=O). The 16 aromatic protons overlap in a multiplet at δ 7.6–8.7. The ^{13}C-NMR spectrum (Figure 3c)

contains C11 (C=O) at δ 198, C12 at δ 128 and C13 at δ 127. C1 appears at δ 143, and the remaining aromatic carbons between δ 122 and 142.

(a)



(b)



(c)

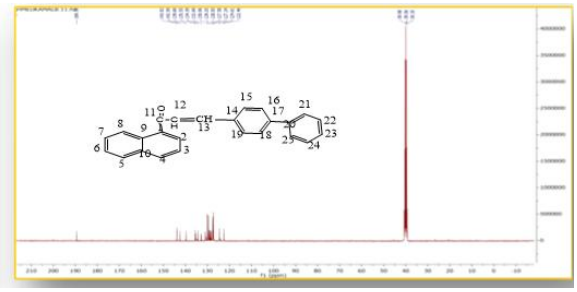
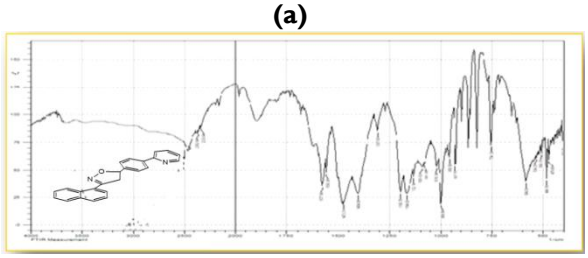


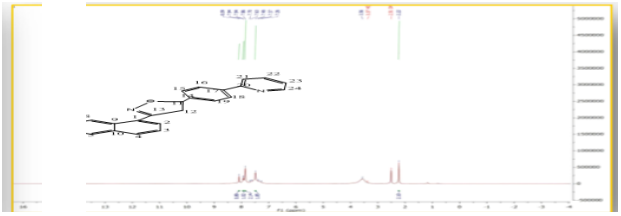
Figure 03: Spectra recorded for chalcone (B): FT-IR (a), ^{1}H-NMR (b) and ^{13}C-NMR (c).

Isoxazoline (1): 3-(naphthalen-1-yl)-5-(4-(pyridin-2-yl)phenyl)-4,5-dihydroisoxazole. In the IR spectrum (Figure 4a), C=N absorbs at 1577.66 and 1558.38 cm^{-1}. The N-O band is at 1307.65 cm^{-1}, and the C-O bands are at 1164.92 and 1195.78 cm^{-1}. Aromatic C=C gives a band at 1473.51 cm^{-1}. The C-H stretches lie at 3037.68 and 3051.18 cm^{-1} (aromatic) and at 2950.89 and 2999.10 cm^{-1} (aliphatic). The ^{1}H-NMR spectrum (Figure 4b) shows the ring CH_2 protons as a doublet at δ 2.2 (2H) and the ring CH proton as a triplet at δ 3.5 (1H). The 15 aromatic protons appear as a multiplet at δ 7.2–8. In the ^{13}C-NMR spectrum (Figure 4c), signals occur at δ 11 (C9), 49 (C11), 122 (C13) and 134 (C20), with the aromatic carbons at δ 123–133.

(a)



(b)



(c)

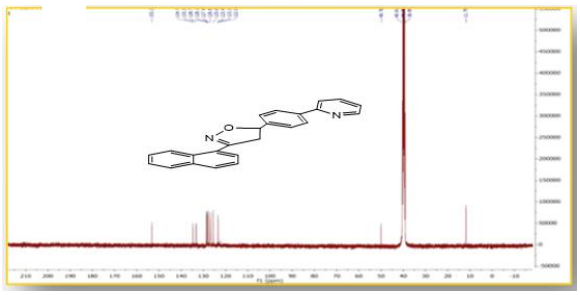
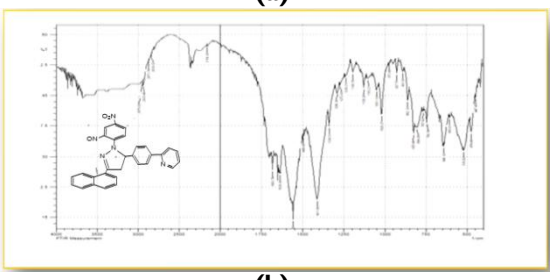


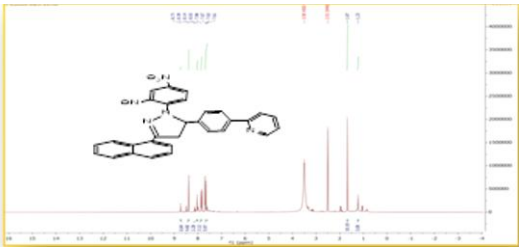
Figure 04: Spectra recorded for isoxazoline (1): FT-IR (a), ^{1}H-NMR (b) and ^{13}C-NMR (c).

Pyrazoline (2): 2-(4-(3-(naphthalen-1-yl)-1-(4-nitro-2-nitrosophenyl)-4,5-dihydro-1H-pyrazol-5-yl)phenyl)pyridine. Its IR spectrum (Figure 5a) contains C=N bands at 1639.38 and 1683.74 cm^{-1}. The N-O band is found at 1383.21 cm^{-1} and the C-O bands at 1128.28 and 1195.78 cm^{-1}. Aromatic C=C absorbs at 1558.38 cm^{-1}. C-H stretching occurs at 3056.96 cm^{-1} for the aromatic rings and at 2935.46 and 2979.82 cm^{-1} for the aliphatic part. On the ^{1}H-NMR spectrum (Figure 5b), the CH_2 group gives a doublet at δ 1.2 (2H) and the CH group a triplet at δ 1.6 (1H). All 18 aromatic protons fall in one multiplet at δ 7.6–8.7. The ^{13}C-NMR spectrum (Figure 5c) has peaks at δ 20 (C12), 25 (C11), 124 (C13) and 168 (C19); the aromatic carbons span δ 127–151.

(a)



(b)



(c)

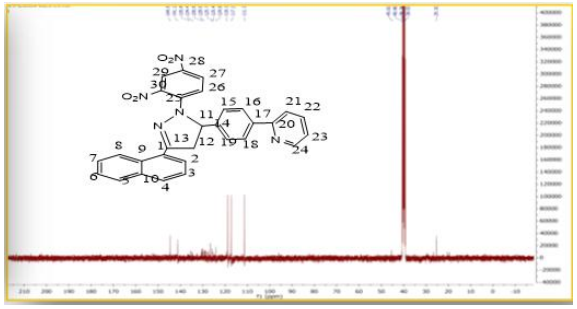
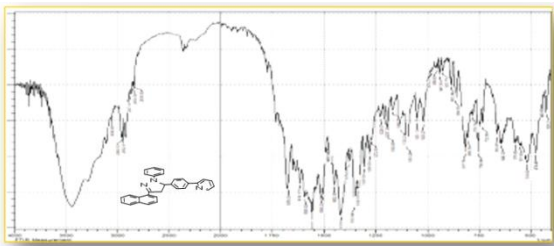


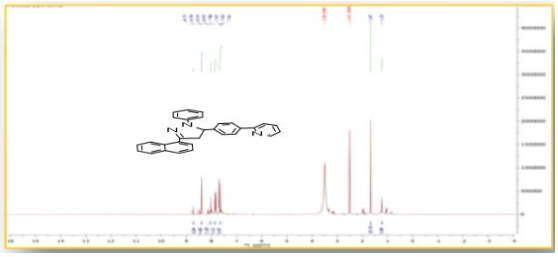
Figure 05: Spectra recorded for pyrazoline (2): FT-IR (a), ^{1}H-NMR (b) and ^{13}C-NMR (c).

Pyrazoline (3): 2-(4-(3-(naphthalen-1-yl)-1-phenyl-4,5-dihydro-1H-pyrazol-5-yl)phenyl)pyridine. Two C=N bands, at 1618.17 and 1676.03 cm^{-1}, are present in the IR spectrum (Figure 6a). The aromatic C=C band is at 1595.02 cm^{-1}. Aromatic C-H stretching is seen at 3058.89 cm^{-1}, and aliphatic C-H at 2952.81 and 2960.53 cm^{-1}. In the ^{1}H-NMR spectrum (Figure 6b), the ring CH_2 protons resonate as a doublet at δ 1.6 (2H) and the CH proton as a triplet at δ 2.7 (1H). A multiplet at δ 7.4–8.7 integrates for 20 aromatic protons. The ^{13}C-NMR spectrum (Figure 6c) shows C12 at δ 12, C11 at δ 25, C13 at δ 147 and C20 at δ 157. The aromatic carbons lie at δ 124–135.

(a)



(b)



(c)

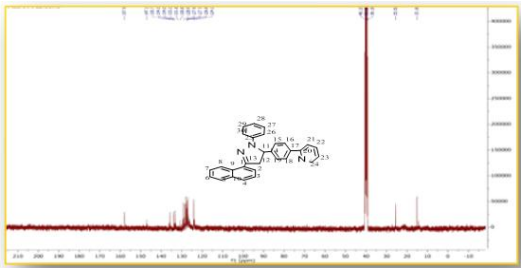
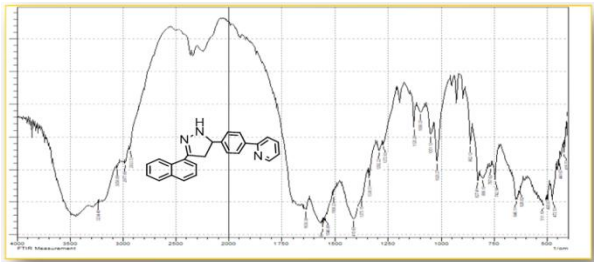


Figure 06: Spectra recorded for pyrazoline (3): FT-IR (a), ^{1}H-NMR (b) and ^{13}C-NMR (c).

Pyrazoline (4): 2-(4-(3-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazol-5-yl)phenyl)pyridine. Made from hydrazine, this pyrazoline has a free N-H group, seen in the IR spectrum (Figure 7a) at 3234.40 cm^{-1}. C=N absorbs at 1558.36 and 1639.38 cm^{-1}, and aromatic C=C at 1546.80 cm^{-1}. The C-H bands are at 3058.89 cm^{-1} (aromatic) and at 2933.53 and 2977.89 cm^{-1} (aliphatic). The ^{1}H-NMR spectrum (Figure 7b) contains the NH singlet at δ 5.7 (1H). The CH_2 doublet (2H) is at δ 1.8, the CH triplet (1H) at δ 2.2, and the aromatic multiplet (15H) at δ 7.4–8.5. The ^{13}C-NMR data are δ 20 (C12), 25 (C11), 124 (C13) and 157 (C19), with the aromatic carbons at δ 127–151.

(a)



(b)

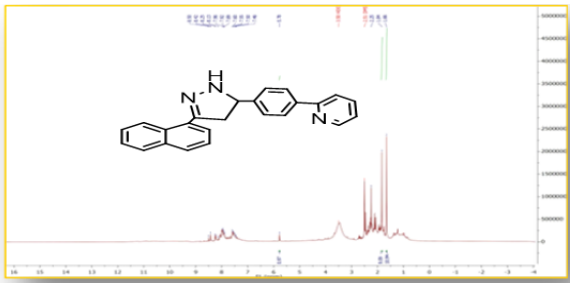
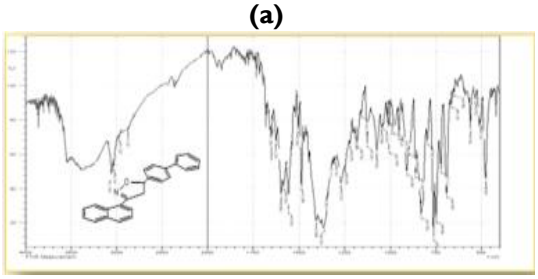


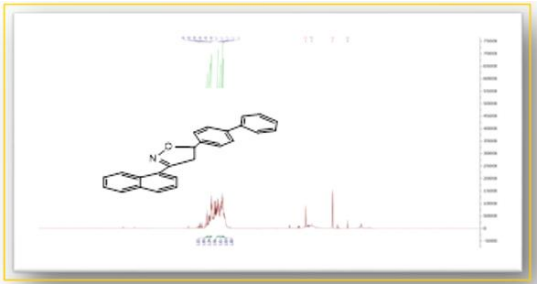
Figure 07: Spectra recorded for pyrazoline (4): FT-IR (a) and ^{1}H-NMR (b).

Isoxazoline (5): 5-([1,1'-biphenyl]-4-yl)-3-(naphthalen-1-yl)-4,5-dihydroisoxazole. The IR spectrum (Figure 8a) shows C=N at 1627.81 and 1647.10 cm^{-1}, N-O at 1487.01 and 1367.44 cm^{-1}, and C-O at 1272.93 cm^{-1}. Aromatic C=C gives a band at 1598.88 cm^{-1}. Aromatic C-H bands are at 3031.89 and 3053.11 cm^{-1}, and aliphatic ones at 2952.60 and 2972.10 cm^{-1}. The ^{1}H-NMR spectrum (Figure 8b) gives the CH_2 doublet at δ 1.8 (2H) and the CH triplet at δ 3.4 (1H). A 16H multiplet at δ 7.4–8.2 belongs to the aromatic protons. In the ^{13}C-NMR spectrum (Figure 8c), C12, C11 and C13 resonate at δ 42, 48 and 124, and C1 at δ 158. The aromatic carbons fall at δ 108–141.

(a)



(b)



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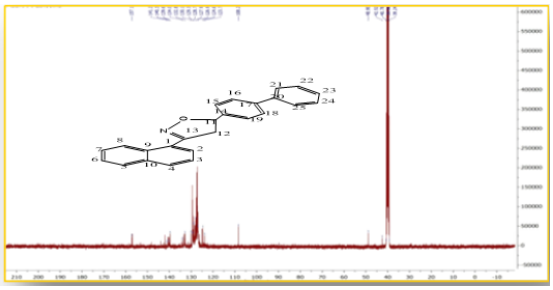
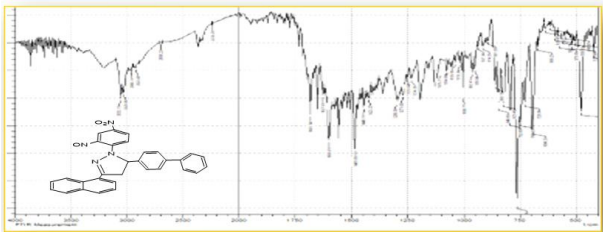


Figure 08: Spectra recorded for isoxazoline (5): FT-IR (a), ^{1}H-NMR (b) and ^{13}C-NMR (c).

Pyrazoline (6): 5-([1,1'-biphenyl]-4-yl)-3-(naphthalen-1-yl)-1-phenyl-4,5-dihydro-1H-pyrazole. The IR spectrum (Figure 9a) shows C=N at 1627.81 and 1683.74 cm^{-1}. The bands at 1485.09 and 1296.08 cm^{-1} are assigned to N-O, and the band at 1271 cm^{-1} to C-O. Aromatic C=C absorbs at 1600.81 cm^{-1}. C-H stretching is observed at 3029.96 and 3053.11 cm^{-1} (aromatic) and at 2923.88 and 2966.31 cm^{-1} (aliphatic). In the ^{1}H-NMR data, the CH_2 doublet (2H) lies at δ 1.1, the CH triplet (1H) at δ 3, and the 19 aromatic protons as a multiplet at δ 7.4–8.9. The ^{13}C-NMR spectrum (Figure 9b) shows signals at δ 47 (C12), 94 (C11), 123 (C13), 168 (C26) and 140 (C29, C30). Its aromatic carbons appear at δ 116–149.

(a)



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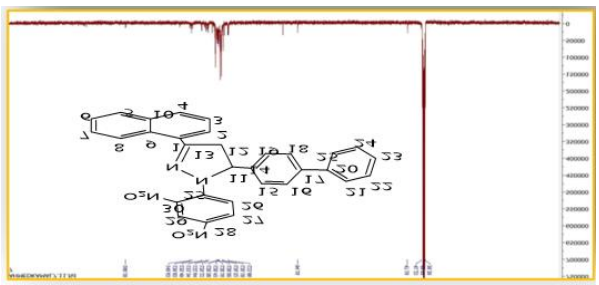
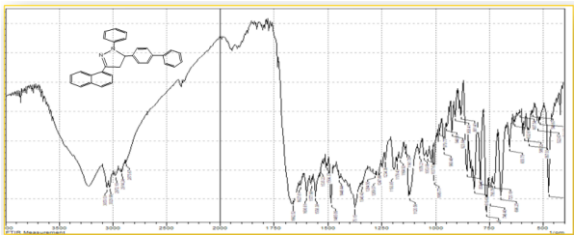


Figure 09: Spectra recorded for pyrazoline (6): FT-IR (a) and ^{13}C-NMR (b).

Pyrazoline (7): 5-([1,1'-biphenyl]-4-yl)-3-(naphthalen-1-yl)-1-phenyl-4,5-dihydro-1H-pyrazole. Here the IR spectrum (Figure 10a) contains a C-N band at 1234.36 cm^{-1} together with C=N bands at 1627.81 and 1662.52 cm^{-1}. Aromatic C=C is at 1600.81 cm^{-1}. The aromatic C-H stretches appear at 3029.96 and 3055.03 cm^{-1}, and the aliphatic ones at 2914.24 and 2972.10 cm^{-1}. The ^{1}H-NMR spectrum (Figure 10b) shows a CH_2 doublet at δ 2.5 (2H), a CH triplet at δ 3 (1H) and a 21H aromatic multiplet at δ 7.4–8.9. The ^{13}C-NMR signals (Figure 10c) are found at δ 49 (C12), 94 (C11), 124 (C13) and 168 (C26), and between δ 100 and 145 for the aromatic carbons.

(a)



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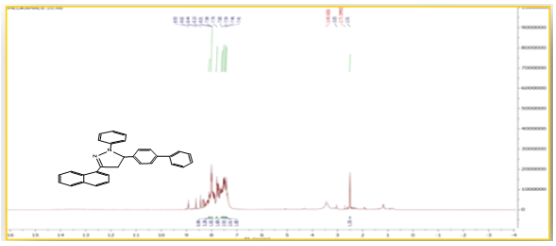

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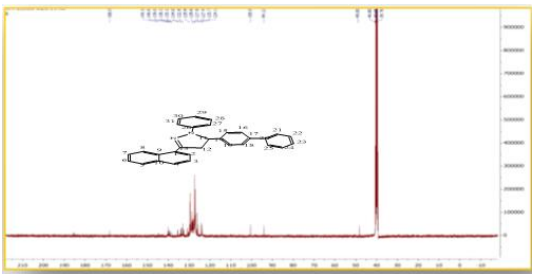
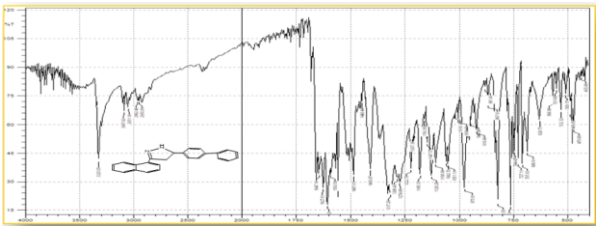


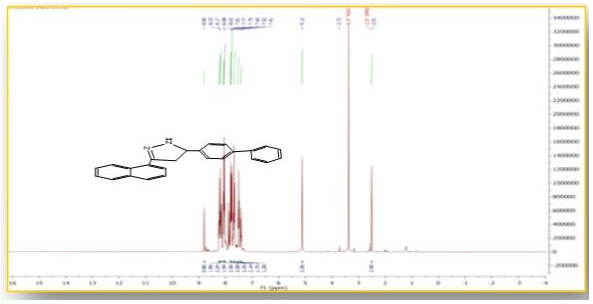
Figure 10: Spectra recorded for pyrazoline (7): FT-IR (a), ^{1}H-NMR (b) and ^{13}C-NMR (c).

Pyrazoline (8): 5-([1,1'-biphenyl]-4-yl)-3-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazole. Like (4), this hydrazine product shows an N-H band, here at 3325.05 cm^{-1} (Figure 11a). The spectrum also has C=N bands at 1627.81 and 1647.10 cm^{-1}, a C-N band at 1222.79 cm^{-1}, and aromatic C=C bands at 1593.09 and 1608.08 cm^{-1}. Aromatic C-H is seen at 3051.18 and 3087.82 cm^{-1}, and aliphatic C-H at 2950.89 and 2962.46 cm^{-1}. In the ^{1}H-NMR spectrum (Figure 11b), the NH proton gives a singlet at δ 5.1 (1H). The CH_2 doublet is at δ 2.5 (2H), the CH triplet at δ 3.7 (1H), and a 16H aromatic multiplet at δ 7.4–8.8. The ^{13}C-NMR spectrum (Figure 11c) gives C12 at δ 28, C11 at δ 81 and C13 at δ 124, with the aromatic carbons at δ 116–149.

(a)



(b)



(c)

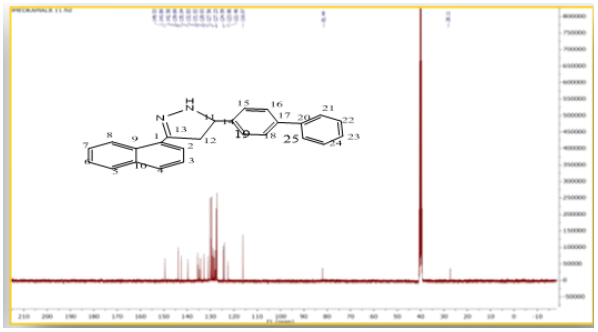


Figure 11: Spectra recorded for pyrazoline (8): FT-IR (a), ^{1}H-NMR (b) and ^{13}C-NMR (c).

Table 01: Physical properties of the derivatives (A,B)and (1-8)

Derivatives	M f	Color	RF	M.P (°C)	M,Wt (g/mol)
A	$C_{24}H_{17}NO$	Reddish brown	0.377	213 - 215	335.41
B	$C_{25}H_{18}O$	yellow	0.44	240 - 242	334.42
1	$C_{24}H_{18}N_2O$	dark orange	0.38	247 - 249	350.42
2	$C_{30}H_{21}N_5O_3$	yellow	O.41	220 - 222	499.53
3	$C_{30}H_{23}N_3$	dark brown	0.36	260 - 262	425.54
4	$C_{24}H_{19}N_3$	Brown	0.28	278 -	349.44
				280	
5	$C_{25}H_{19}NO$	yellow	0.39	270 - 272	349.43
6	$C_{31}H_{22}N_4O_3$	orange	0.31	266 - 268	498.54
7	$C_{31}H_{24}N_2$	dark orange	0.26	288 - 290	424.55
8	$C_{25}H_{20}N_2$	Reddish brown	0.40	276 - 278	348.45

Antioxidant assay with the DPPH radical

Principle of the assay

DPPH (1,1-diphenyl-2-picrylhydrazyl) is a stable free radical. It is often used to measure how well a substance scavenges radicals. In ethanol, the DPPH radical has a purple colour. When an antioxidant donates a hydrogen atom, the radical is reduced to its non-radical form, DPPH-H, and the colour turns yellow. The fading of the purple colour is followed by measuring the absorbance at 517 nm. The drop in absorbance therefore gives the radical-scavenging activity of the sample [17].

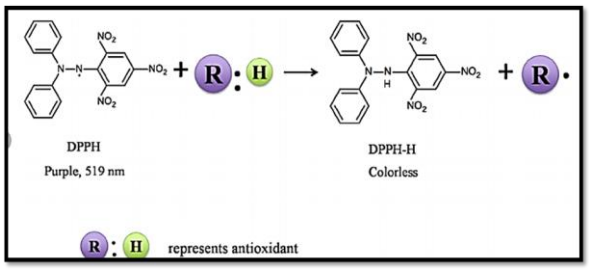


Figure 12: Reaction of the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical with an antioxidant. R:H is the antioxidant that donates the hydrogen atom, and R• is the radical left after the donation [18].

Calculation

$$\text{Inhibition } \% = \frac{\text{Abs. of control} - \text{Abs. of sample}}{\textit{Abs. of control}} \text{X100}$$

The terms are defined as follows:

Abs control = absorbance of the DPPH solution in ethanol without a test compound;

Abs sample = absorbance of the DPPH solution after the test compound is added.

All four tested compounds showed antioxidant properties, and ascorbic acid served as the reference. Compound 3 reached its highest inhibition, 55.7 %, at 2500 ppm, and its lowest, 42.6 %, at 500 ppm (Figure 13).

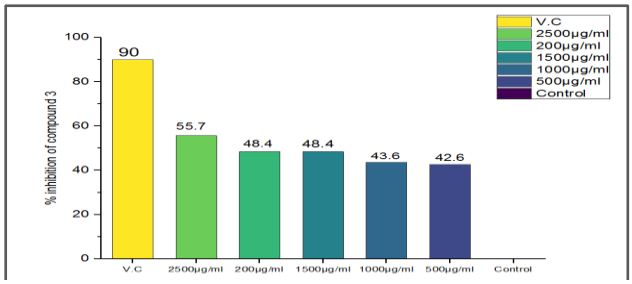


Figure 13: DPPH radical scavenging activity of compound 3 (47.8%)

Table 02: shows the antioxidant activity of compound 3 Compound 4 gave the highest inhibition

Concentration	Absorbance (517 nm)	Inhibition (%)
DPPH control	1.9	0 %
Vitamin C (reference)	0.18	90 %
2500 µg/ml	0.84	55.7 %
2000 µg/ml	0.98	48.4 %
1500 µg/ml	0.98	48.4 %
1000 µg/ml	1.07	43.6 %
500 µg/ml	1.09	42.6 %

Table 02 shows the antioxidant activity of compound 3 Compound 4 gave the highest inhibition percentage of 52.1 at concentration 2500ppm and the lowest inhibition percentage of 45.7 at concentration 500ppm, as shown in Figure 14

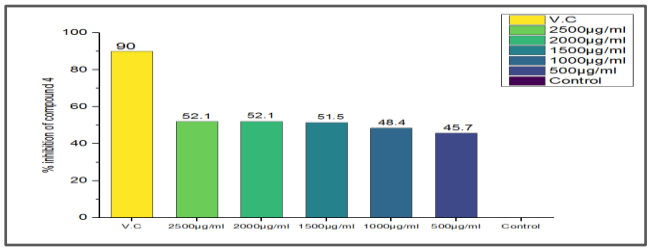


Figure 14: DPPH radical scavenging activity of compound 4 (50%)

Table 03: shows the antioxidant activity of compound 4 Compound 5.

Concentration	Absorbance (517 nm)	Inhibition (%)
DPPH control	1.9	0 %
Vitamin C (reference)	0.18	90 %
2500 µg/ml	0.91	52.1 %
2000 µg/ml	0.91	52.1 %
1500 µg/ml	0.92	51.5 %
1000 µg/ml	0.98	48.4 %
500 µg/ml	1.03	45.7 %

Table 03 shows the antioxidant activity of compound 4 Compound 5 gave the highest inhibition percentage of 93.1 at concentration 2500ppm and the lowest inhibition percentage of 51.1 at concentration 500ppm, as shown in Figure 15

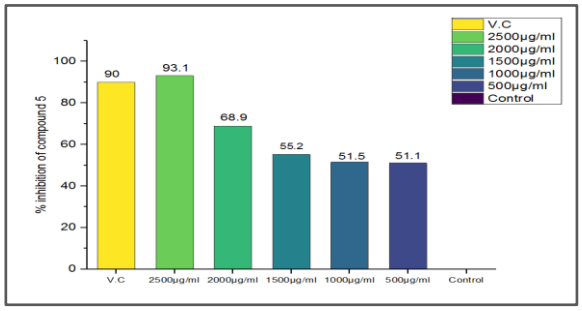


Figure 15: DPPH radical scavenging activity of compound 5 (64.2%)

Concentration	Absorbance (517 nm)	Inhibition (%)
DPPH control	1.9	0 %
Vitamin C (reference)	0.18	90 %
2500 µg/ml	0.13	93.1 %
2000 µg/ml	0.59	68.9 %
1500 µg/ml	0.85	55.2 %
1000 µg/ml	0.92	51.5 %
500 µg/ml	0.93	51.1 %

Table 04: shows the antioxidant activity of compound 5 **Compound 06** gave the highest inhibition percentage of 49.2 at concentration 2500ppm and the lowest inhibition percentage of 38.9 at concentration 500ppm, as shown in Figure 16

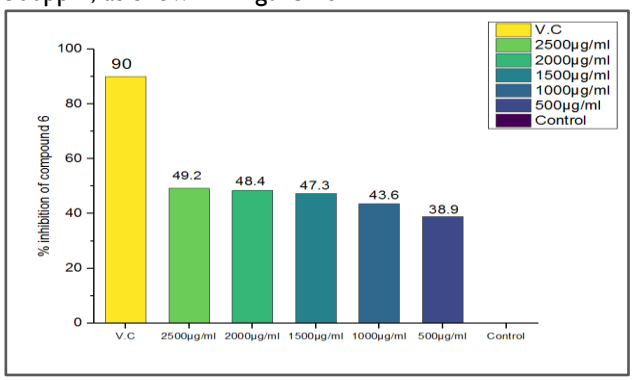


Figure 16: DPPH radical scavenging activity of compound 6 (45.7%)

Table 05: shows the antioxidant activity of compound 06.

Concentration	Absorbance (517 nm)	Inhibition (%)
DPPH control	1.9	0 %
Vitamin C (reference)	0.18	90 %
2500 µg/ml	0.96	49.2 %

Concentration	Absorbance (517 nm)	Inhibition (%)
2000 µg/ml	0.98	48.4 %
1500 µg/ml	1.00	47.3 %
1000 µg/ml	1.07	43.6 %
500 µg/ml	1.16	38.9 %

CONCLUSIONS

Chalcones (A) and (B) were prepared from 2-acetylnaphthalene and either 4-(2-pyridyl)benzaldehyde or biphenyl-4-carboxaldehyde. Cyclisation of these chalcones with hydroxylamine hydrochloride, phenylhydrazine, 2,4-dinitrophenylhydrazine or hydrazine afforded two isoxazolines (1, 5) and six pyrazolines (2, 3, 4, 6, 7, 8). Their structures were confirmed by FT-IR, ^{1}H-NMR and ^{13}C-NMR spectroscopy. The C=O bands of the chalcones at 1681.81 and 1658.67 cm^{-1} were absent in the cyclised products, and new C=N bands between 1558.36 and 1683.74 cm^{-1} appeared, which supports the closure of the five membered ring. The isoxazolines also gave N-O bands, while compounds (4) and (8) gave NH bands at 3234.40 and 3325.05 cm^{-1}. All compounds were coloured solids melting between 213 and 290 °C. The DPPH assay showed that compounds (3), (4), (5) and (6) scavenge free radicals, and that the activity rose with concentration. Compound (5) was the most active and reached 93.1 % inhibition at 2500 µg/mL, close to the 90 % of ascorbic acid.

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Not Declared

INFORM CONSENT AND ETHICAL STATEMENT

Not Applicable

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