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SYNTHESIS OF AND CHARACTERIZATION SOME PLATINUM(IV) COMPLEXES DERIVED FROM SUBSTITUTED IMIDES AND EVALUATION OF THEIR BIOLOGICAL ACTIVITY

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ABSTRACT. This research paper explores preparation of furanoanthracene-12,14-dione (**1**) via the addition of malic anhydride to anthracene. The resultant compound was treated with urea to form the imide derivative (**2**). Subsequently (**2**) was reacted with formaldehyde, leading to the substitution of the nitrogen-bound proton with a hydroxymethyl group, yielding hydroxymethyl pyrroloanthracene (**3**). In the following step, various substituted anilines were reacted with (**3**) in the presence of triethylamine through an SN2 reaction to replace the hydroxyl group and producing substituted amino methyl-epipyrroloanthracene derivatives (**4-10**). Three of these derivatives (**4-6**) were employed as a ligands to synthesize three complexes square planer platinum(IV). The result of conductivity measurement, magnetic and C.H.N. prove the synthesis of the platinum(IV) complexes. The biological activities of the synthesized compounds were evaluated against four bacterial strains. Additionally, (**4-10**) were subjected to molecular docking studies against the target protein Penicillin Binding Protein (PDB ID: 3vsl), with Penicillin G serving as the control.

KEYWORDS: Platinum complexes, Imides, Molecular docking, Biological activity

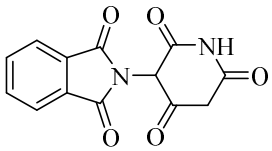
INTRODUCTION

In organic chemistry, heterocyclic nitrogenous chemicals make a large class of chemical compounds. Nitrogen often endows the compounds with strong characteristics [1]

In general, imides can easily be prepared from anhydride by replace the oxygen between two carbonyls with nitrogen atom. This can be achieved by the reaction of the anhydride with ammonia, ammonium carbonate, amines or urea [2].

Important components of several medication prospects are substituted succinimides. The creation and synthesis of compounds with potential use as human therapeutic agents is one of the core goals of organic and medicinal chemistry. In vivo, cyclic imides and their derivatives permeate biological membranes because they have an imide ring with the general structure CO–N(R)–CO– [3].

Numerous medications are made using substituted succinimides, such as N-arylphathalamide (Figure 1), which are significant drug substances which is used against number of cancers [4].



Thalidomide

Figure 1. General structure of N-arylsuccinimide.

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They have been linked to a wide range of biological activities and medicinal applications. For example, succinimide is a component of several active molecules that have been linked to a variety of biological activities, including CNS depressant [5], analgesic [6], antitumor [7], cytostatic [8], anorectic [9], nerve conduction blocking [10], antispasmodic [11], bacteriostatic [12], muscle relaxant [13], hypotensive [14], antibacterial [l5], antifungal [16], anti-convulsant [17], and anti-tubercula [18].

EXPERIMENTAL

Materials and methods

All chemicals and solvents were utilized without further purification and come from well-known, readily available commercial sources. Using KBr discs, infrared spectra (V_{max} in cm^{-1}) were examined on a Bruker FT-IR 8400 spectrometer. Furthermore, ^{1}H-NMR spectroscopy was carried out with DMSO-d_6 as the solvent and TMS as the chemical reference standard on a Bruker apparatus running at 400 MHz.

Synthesis of 9,10-dihydro-9,10-[3,4] furanoanthracene-12,14-dione(1) [19]

A 100 mL round-bottom flask was filled with 25 mL of dry xylene, (0.012 mol, 2.13 g) of anthracene was dissolved in 25 mL of dry xylene, followed by the addition of (0.012 mol, 1.17 g) of maleic anhydride. The mixture was then agitated for 30 min, allowed to cool, and the precipitate was filtered through Buchner funnel to produce a white precipitate (crystal) in 83%, m.p. (258-260 °C). FT-IR (KBr, ν, cm^{-1}) 3067, 3037 (=C-H), 2968 (-C-H), (1862, 1780) the symmetric and asymmetric ν(C=O) of the imide, 1068 (C-O). ^{1}H-NMR (ppm): δ 7.46–7.16 (m, 8H) aromatic, 3.39 (t, 2H) 2CH, 4.88 (t, 2H) 2CH. ^{13}C NMR (ppm): (DMSO d_6, 400 MHz) δ 39.35, 41.03, 123.37, 124.87, 139.75, and 171.24.

Synthesis of 9,10-dihydro-9,10-[3,4]epipyrroloanthracene-12,14-dione(2) [20]

In a 50 mL round bottom flask mixed (8.13 mmol, 2.25 g) of (**1**) and (16.3 mmol, 0.95 g) of urea. The mixture was then allowed to come to room temperature and stirred for 15 min. After that, (10 mL) of cold distilled water was added and the mixture was stirred for 15 min. The mixture was then filtered and recrystallized with ethanol. Then, dried at (40 °C) to produce a white powder precipitate in 89%, m.p. (195-198 °C), FT-IR (KBr, ν, cm^{-1}) 3288 (N-H), 3038 (=C-H), 2970 (C-H), (1754, 1698) the symmetric and asymmetric ν(C=O) of the imide, 1598 (N-H) bending, 1226 (C-N). ^{1}H-NMR (ppm): (DMSO d_6, 400 MHz) δ: 8.11 (s, 1H) N-H, 7.28-7.11 (m, 8H) aromatic, 3.39 (t, 2H) 2CH, 4.79 (t, 2H) 2CH. ^{13}C NMR (ppm): (DMSO d_6, 400 MHz) δ 39.51, 44.69, (123.37, 124.87, 139.75), and 178.97.

*Synthesis of 13-(hydroxymethyl)-9,10-dihydro-9,10-[3,4]epipyrroloanthracene-12,14-dione (**3**) [21]*

(4 mmol, 1.1 g) of (**2**) and (2.5 mL of 40%) formaldehyde were mixed in (50 mL) round-bottom flask. Then, (2 mL) of dimethylformamide (DMF) and (6 mL) of distilled water were added to the mixture. After 35 hours of stirring of the mixture a white precipitate was filtered and recrystallization from ethanol. A white powder resulted in 93%, m.p. (228-232 °C), IR cm^{-1} 3382 (O-H), 3048 (=C-H), 2969 (C-H), (1717, 1695) the symmetric and asymmetric ν(C=O) of the imide, 1461 (C-H) bending, and 1390 (O-H) bending. ^{1}H-NMR δ: 7.38–7.12 (m, 8H) aromatic, 5.67 (s, 2H) CH2, 4.09 (s, 1H) O-H, 4.76 (t, 2H) 2CH, 3.36 (t, 2H) 2CH. ^{13}C NMR (ppm): (DMSO d_6, 400 MHz) δ: 39.04, 41.72, 63.68 (123.37, 124.87, 139.75)), and 173.74.

*Synthesis of 13-((substilamino)methyl)-9,10-dihydro-9,10-[3,4] epipyrrolo anthracene-12,14-dione (**4-10**) [22-24]*

One drop of triethylamine (TEA) and one drop of dimethylformamide (DMF) were added to (1 mmol, 0.305 g) of (**3**) and (1 mmol) of aniline substitutes. After 20 min of heating the mixture in an oil bath between (110 and 120 °C), it was cooled by adding 5 mL of cold water. The resulted precipitate filtered, recrystallized from acetone and dried (Table 1).

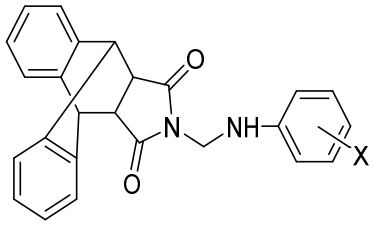


Figure 2. Gineral structure for (**22-24**).

Table 1. Physical properties of (**4-10**).

Comp no.	X	Molecular formula	M.Wt g/mol	Color	m.p. (°C)	Yield %
4	4-H	$C_{25}H_{20}N_2O_2$	380.45	Pale yellow	175-177	91%
5	4-Cl	$C_{25}H_{19}ClN_2O_2$	414.88	White	235-238	79%
6	4-Br	$C_{25}H_{19}BrN_2O_2$	459.33	Pale yellow	243-245	85%
7	4-CH3	$C_{26}H_{22}N_2O_2$	394.47	White	178-183	80%
8	4-NH_2	$C_{25}H_{21}N_3O_2$	395.46	Gray	201-204	93%
9	3-NO2	$C_{25}H_{19}N_3O_4$	425.43	Yellow	190-192	89%
10	4-NO2	$C_{25}H_{19}N_3O_4$	425.43	Dark yellow	195-198	83.5%

*13-((Phenylamino)methyl)-9,10-dihydro-9,10-[3,4]epipyrroloanthracene-12,14-dione (**4**)*

FT-IR (KBr, ν, cm^{-1}) 3325 (N-H), 3048 (=C-H), 2973 (C-H), (1773, 1701) the symmetric and asymmetric ν(C=O) of the imide, 1523 (N-H) bending, 1248 (C-N). ^{1}H-NMR (ppm): (DMSO d_6, 400 MHz) δ: 7.39–7.09 (m, 8H), 7.07-6.76 (m, 5H), 6.41 (s, 1H) N-H, 4.85-4.79 (s, 2H), 4.24-4.22 (t, 2H) 2CH, 3.40-3.36 (t, 2H) 2CH. ^{13}C NMR (ppm): (DMSO d_6, 400 MHz) δ: 39.04, 41.72, 48.93 (116.12, 119.61, 123.37, 124.87, 128.87, 139.75,146.00), and 179.78 belong to 2CH,CH_2 groups, aromatic rings carbons, and (C=O) imide.

*13-(((4-Chlorophenyl)amino)methyl)-9,10-dihydro-9,10-[3,4]epipyrroloanthracene-12,14-dione (**5**)*

FT-IR (KBr, ν, cm^{-1}) 3339 (N-H), 3036 (=C-H), 2957 (C-H), (1754, 1695) the symmetric and asymmetric ν(C=O) of the imide, 1523 (N-H) bending, 1300 (C-N) and 755 (C-Cl). ^{1}H-NMR (ppm): (CD_3CN, 400 MHz)) δ: 7.47–7.10 (m, 8H), 7.09-6.58 (m, 4H), 5.73 (s, 1H) N-H, 4.87-4.85 (s, 2H) CH_2 , 4.24-4.22 (t, 2H) 2CH, 3.17-3.16 (t, 2H) 2CH. ^{13}C NMR (ppm): (DMSO d_6, 400 MHz) δ: 39.04, 41.72, 48.93 (116.92, 123.37, 124.89, 128.67, 139.75,144.80), and 179.78 ppm belong to 2CH,CH_2 groups, aromatic rings carbons, and (C=O) imide.

13-(((4-Bromophenyl)amino)methyl)-9,10-dihydro-9,10-[3,4]epipyrroloanthracene-12,14-dione ***(6)***

FT-IR (KBr, ν, cm^{-1}) 3420 (N-H), 3072, 3049 (=C-H), 2972 (C-H), (1771, 1700) the symmetric and asymmetric ν(C=O) of the imide, 1533 (N-H) bending, 1248 (C-N) and 769 (C-Br). ^{1}H-NMR (ppm): (DMSO d_6, 400 MHz)) δ: 7.49–7.14 (m, 8H), 7.10-6.60 (m, 4H), 5.70 (s, 1H) N-H, 4.85-4.83 (s, 2H) CH_2, 4.22-4.20 (t, 2H) 2CH, 3.16-3.13 (t, 2H) 2CH. ^{13}C NMR (ppm): (DMSO d_6, 400 MHz) δ: 39.04, 41.72, 48.93 (110.11, 118.34, 123.37, 124.87, 131.87, 139.75,145.05), and 179.78 ppm belong to 2CH,CH_2 groups, aromatic rings carbons, and (C=O) imide.

*13-((p-Tolylamino)methyl)-9,10-dihydro-9,10-[3,4]epipyrroloanthracene-12,14-dione (****7****)*

FT-IR (KBr, ν, cm^{-1}) 3349 (N-H), 3047(=C-H), 2948 (C-H), (1771, 1705) the symmetric and asymmetric ν(C=O) of the imide, 1619 (N-H) bending, 1511 (C-C), and 1254 (C-N). ^{1}H-NMR (ppm): (DMSO d_6, 400 MHz) δ: 7.40–7.15 (m, 8H), 7.02-6.74 (m, 4H), 5.87 (s, 1H) N-H, 5.02-4.96 (s, 2H) CH_2, 4.28-4.26 (t, 2H) 2CH, 3.15-3.13 (t, 2H) 2CH, 2.05 (s, 3H) CH3. ^{13}C NMR (ppm): (DMSO d_6, 400 MHz) δ: 21.13, 39.04, 41.72, 48.93 (115.69, 123.37, 124.87, 128.46, 129.36, 139.75, 143.31), and 179.78 ppm belong to CH3, 2CH, CH2 groups, aromatic rings carbons, and (C=O) imide.

13-(((4-aminophenyl)amino)methyl)-9,10-dihydro-9,10-[3,4]epipyrroloanthracene-12,14-dione ***(8)***

FT-IR (KBr, ν, cm^{-1}) 3462 (N-H), 3381, 3351 (NH_2), 3047 (=C-H), 2959 (C-H), (1778, 1708) the symmetric and asymmetric ν(C=O) of the imide, 1619 (N-H) bending, 1511 (C-C), and 1254 (C-N). ^{1}H-NMR (ppm): (DMSO d_6, 400 MHz)) δ: 7.30–7.15 (m, 8H), 6.80-6.60 (m, 4H), 5.32 (s, 1H) N-H, 4.80-4.75 (s, 2H), 4.26-4.24 (t, 2H) 2CH, 3.99 (m, 2H) NH_2, 3.40-3.36 (t, 2H) 2CH. ^{13}C NMR (ppm): (DMSO d6, 400 MHz) δ: 39.04, 41.72, 48.93 (116.25, 117.84, 123.37, 124.87, 137.26, 139.75, -142.44), and 179.78 ppm belong to 2CH,CH_2 groups, aromatic rings carbons, and (C=O) imide.

13-(((3-nitrophenyl)amino)methyl)-9,10-dihydro-9,10-[3,4]epipyrroloanthracene-12,14-dione ***(9)***

FT-IR (KBr, ν, cm^{-1}) 3435 (N-H), 3047(=C-H), 2956 (C-H), (1774, 1710) the symmetric and asymmetric ν(C=O) of the imide, 1620 (N-H) bending, 1529 asymmetric (N-O), 1340 symmetric (N-O), and 1286 (C-N). ^{1}H-NMR (ppm): (DMSO d6, 400 MHz))δ: 8.11-8.09 (m,2H), 7.32–7.05 (m, 8H), 6.98-6.96 (m, 2H), 6.11 (s, 1H) N-H, 5.31 (s, 2H) CH2 , 4.36-4.37 (t, 2H) 2CH, 3.11-3.09 (t, 2H) 2CH. ^{13}CNMR (ppm): (DMSO d_6, 400 MHz) δ : 39.04, 41.72, 48.93 (111.54, 111.97, 118.77, 123.37, 124.87, 129.87, 139.7, 149.54, 149.82), and 179.78 ppm belong to 2CH,CH_2 groups, aromatic rings carbons, and (C=O) imide.

13-(((4-Nitrophenyl)amino)methyl)-9,10-dihydro-9,10-[3,4]epipyrroloanthracene-12,14-dione ***(10)***

FT-IR (KBr, ν, cm^{-1}) 3425 (N-H), 3036(=C-H), 2945 (C-H), (1777, 1707) the symmetric and asymmetric ν(C=O) of the imide, 1618 (N-H) bending, 1525 asymmetric (N-O), 1338 symmetric (N-O), and 1280 (C-N). ^{1}H-NMR (ppm): (DMSO d_6, 400 MHz) δ: 8.10-8.08 (m, 2H), 7.30–7.10 (m, 8H), 6.98-6.96 (m, 2H), 6.09 (s, 1H) N-H, 5.29 (s, 2H) CH_2 , 4.36-4.37 (t, 2H) 2CH, 3.11-3.09 (t, 2H) 2CH. ^{13}C NMR (ppm): (DMSO d_6, 400 MHz) δ: 39.04, 41.72, 48.93 (116.07, 123.37, 124.87, 126.39, 139.75, 140.42, 154.22), and 179.78 belong to 2CH,CH_2 groups, aromatic rings carbons, and (C=O) imide.

General procedure of preparation of complexes in a ratio of (1:2) [25]

Complexes were prepared at room temperature by self-assembly between an aqueous solution of chloroplatinic acid hydrate $H_2PtCl_6.6H_2O$ (0.25 mmol, 0.102 g) and a mixture solution of prepared ligands (0.5 mmol) in 25 mL acetonitrile and 10 mL H_2O. The yellow solution mixture was stirred at room temperature for 30 min, and then the solution was kept enclosed at room temperature. After that, the resulting precipitate was filtered, recrystallized and washed with mixed solvents of CH_3CN and H_2O and were air-dried.

Complex (**11**) was prepared from ligand (**4**) with ($H_2PtCl_6.6H_2O$) and result in 53% as a pale yellow powder (m.p. 275-278 ºC) , FT-IR (KBr, ν, cm^{-1}) 3387 (N-H), 3043-3022 (=C-H), 2978-2946 (C-H) alphate, (1736, 1681) the symmetric and asymmetric ν(C=O) of the imide, 1511 (N-H) bending, 1260 (C-N), 462 (Pt-N) and 423 (Pt-O). CHNS elemental analysis calculated for $C_{50}H_{40}Cl_4N_4O_4Pt$: C, 54.71%; H, 3.67%; N, 5.10%; Pt, 17.77%. Found: C, 54.29%; H, 3.44%; N, 4.87%; Pt, 17.31%.

Complex (**12**) was prepared from ligand (**5**) with ($H_2PtCl_6.6H_2O$) and result in 66% as a orange powder (m.p. 209-210d ºC) , FT-IR (KBr, ν, cm^{-1}) 3401 (N-H), 3054-3027 (=C-H), 2989-2955 (C-H) aliphatic, (1728, 1669) the symmetric and asymmetric ν(C=O) of the imide, 1501 (N-H) bending, 1245 (C-N), 760 (C-Cl), 438 (Pt-N) and 410 (Pt-O). CHNS elemental analysis calculated for $C_{50}H_{38}Cl_6N_4O_4Pt$: C, 51.48%; H, 3.28%; N, 4.80%; Pt, 16.72%. Found: C, 51.08%; H, 3.01%; N, 4.43%; Pt, 16.59%.

Complex (**13**) was prepared from ligand (**6**) with ($H_2PtCl_6.6H_2O$) and result in 45% as a yellow powder (m.p. 235-238 ºC) , FT-IR (KBr, ν, cm^{-1}) 3355 (N-H), 3055-3025 (=C-H), 2961-2954 (C-H) aliphatic, (1720, 1670) the symmetric and asymmetric ν(C=O) of the imide, 1500 (N-H) bending, 1243 (C-N), 432 (Pt-N) and 415 (Pt-O). CHN elemental analysis calculated for $C_{50}H_{38}Br_2Cl_4N_4O_4Pt$: C, 47.83%; H, 3.05%; N, 4.46%; Pt, 15.86%. Found: C, 47.23%; H, 2.88%; N, 4.18%; Pt, 15.55%.

Biological activity of the compounds

Both Gram-positive and Gram-negative bacteria were used in this investigation of the effects of several manufactured chemicals on four different genera of bacteria. *Salmonella typhi*, *Staphylococcus aureus*, Escherichia coli, and *Pseudomonas aeruginosa* were used kindly provided by Biology Department of the College.

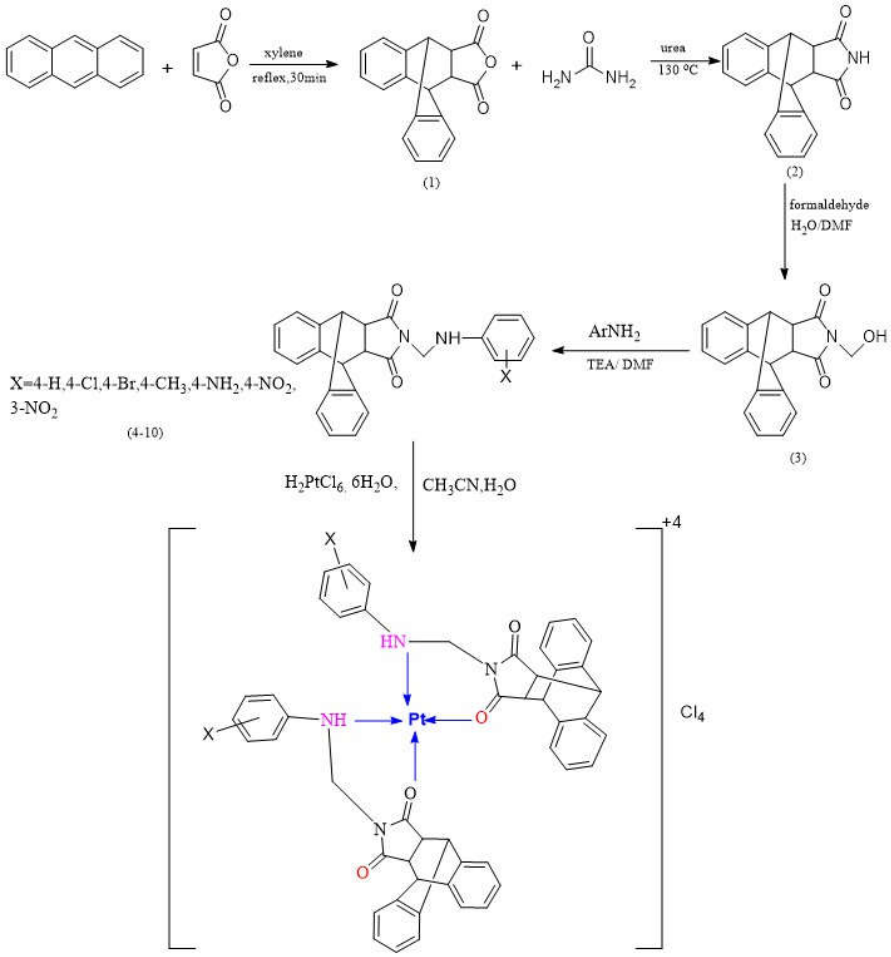
Inhibitory efficacy test

Test for inhibitory efficacy: The Levne technique [26], which was taken from the Vandepitte technique [27], was kept. This entails adding individual colonies of the previously mentioned bacteria to the Nutrient Saline medium by injection, followed by incubation. For eighteen to twenty-four hours, the bacteria were cultivated at 37 ºC. After then, a concentration of 108 cells/mL was obtained by a series of dilutions using regular saline solution, and this concentration was subsequently compared to the concentration in tube No. 1 (Macfarland standard tubes 1) Using a sterilized glass diffuser, the bacterial suspension was spread over the conventional nutritional agar surface. After that, the plates were incubated for 30 min to allow imbibition to occur.

Paper discs were created. The carefully selected chemicals were then absorbed into these discs in predetermined amounts after being dissolved in dimethyl sulfoxide. Following that, the discs were applied to the agar plate surface using sterile forceps and incubated for eighteen to twenty-four hours at 37 ºC. The diameter of inhibition was evaluated after incubation, and some plates were compared with control samples that included conventional antibiotics ampicillin.

RESULTS AND DISCUSSION

The capacity to create substituted-9,10-dihydro-9,10-[3,4]epipyrroloanthracene derivatives, which may prove to be helpful building blocks for the synthesis of different chemicals, which may be used in different applications, Scheme 1.



Scheme 1. Total synthesis.

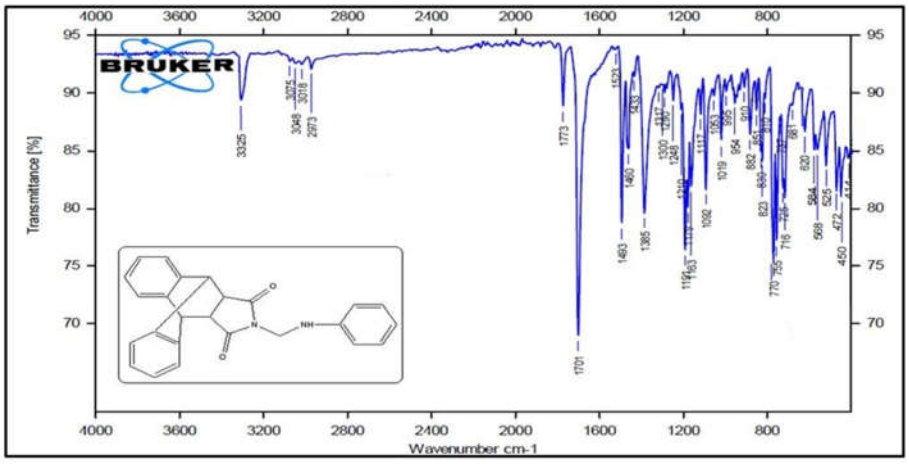
The synthesis of 9,10-dihydro-9,10-[3,4]furanoanthracene-12,14-dione (**1**) was well known through [1, 4] addition of malic anhydride to anthracene via Dials Alder cycloaddition reaction. The resulted compound confirmed by their physical properties. In addition, IR spectra show bands belong to two anhydride carbonyls at 1780 cm^{-1}, ^{1}H NMR spectrum gives a doublet signal at δ 4.88 and triplet at δ 3.39 belongs to 4 CH. Also, ^{13}C NMR conform the structure.

In the next step imide (**2**) was prepared by using two equivalents of urea as a source of amine, to react with anhydride (**1**) without solvent. The reaction depends on simple hand mixed to let the reaction start and be easier to mix by stirrer. The physical properties of the resulting compound, such as differences in color and melting point comparing with starting material, as well as the characteristic infrared absorption spectra, were identified it by medium band in 3381 corresponding to the secondary amine. In addition, 1770, 1716 cm^{-1} for symmetric and asymmetric of (C=O) imide. In ^{1}H NMR the new singlet band at δ 8.11 corresponding the proton of imide. The ^{13}C NMR band number confirms the carbon number of the compound.

In the next step, the product (**2**) was reacted with 40% formaldehyde in water in the presence DMF as a solvent to give (**3**), This compound was identified by its physical properties (colour, melting point and infrared absorption bands), with peaks at 3382 cm^{-1} corresponding to OH and at 1781, 1651 cm^{-1} for symmetric and asymmetric of (C=O) imide for carbonyl of amide. In addition, the ^{1}H NMR spectrum shows the absent of N-H proton and the appearance of new singlet band at δ 5.67 belong to CH_2 with another band belong to O-H proton at δ 4.09. The ^{13}C NMR bands number confirms the carbons number of the compound.

In the last stage of the reaction, compounds (**4-10**) were formed in a moderate to excellent proportion when (**3**) was reacted with different aniline substituted using a straightforward SN2 one-step reaction. The IR absorption at 3325, 3339, 3420, 3349, 3462, 3435 and 3425 cm^{-1}, which correspond to the new N-H groups. Moreover, the nitro group of compounds (**9**, **10**) has a unique value that falls between the stretches of symmetry (two oxygen atoms are bonded to nitrogen by a single bond) at 1340, 1345 cm^{-1} and asymmetry (one oxygen atom bonds to nitrogen by a single bond) at 1529, 1521 cm^{-1}. The ^{1}H NMR charts show new bands at δ 6.41-5.31ppm belongs to N-H proton depending on the substituent on the aryl ring. The ^{13}C NMR bands number confirm the carbons number of the compound, Figures 3 and 4.

Finally, the platinum(IV) complexes were prepared by using compounds (**4-6**) as a ligands form complex (**11-13**), respectively. These complexes were characterized by their physical properties and by IR spectra and CHN. A comparison between infrared spectra of the ligand and their complex show that the absorption of N-H was in complexes more than the ligand in 62 cm^{-1} for ligand (**4**, **5**) and complexes (**11**, 12), while complex (**13**) have less absorption than (**6**) in 65 cm^{-1}. In addition, the absorption of C=O in the ligand were more than their complexes for about 16 to 30 cm^{-1}, Figure 5 [32]. This result led to confirm that the coordination with the metal ion happened.



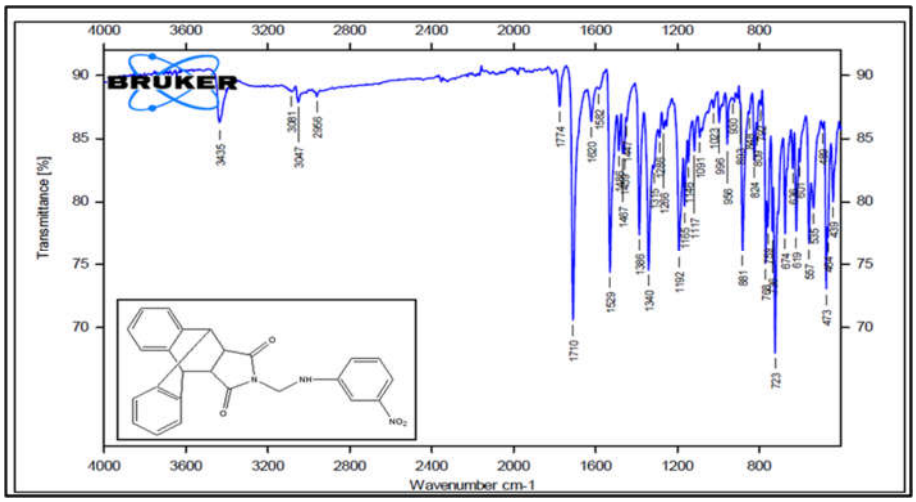
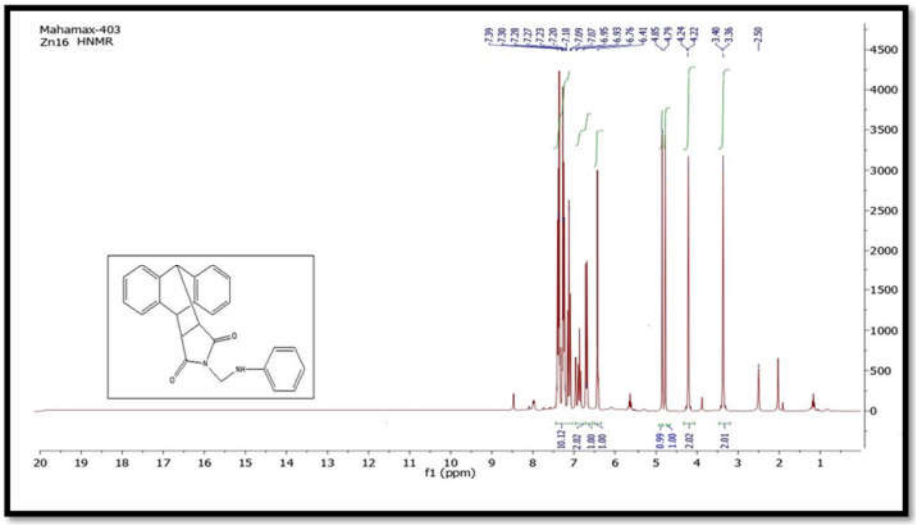


Figure 3. IR spectra of (**4**, **9**)

Magnetic measurement and electronic spectra

The prepared platinum complexes of type (1:2) fall into the category of complexes with electrically conductive behaviors, and the molar electrical conductivity values of these complexes in the solvent (DMSO) ranged between (142.6-148.3) ($cm^2.ohm^{-1}.mol^{-1}$)[28]. This confirms of four chlorine atoms side the coordination sphere [29]. The IR spectrum and molar conductivity values confirm the asymmetry of the compound.



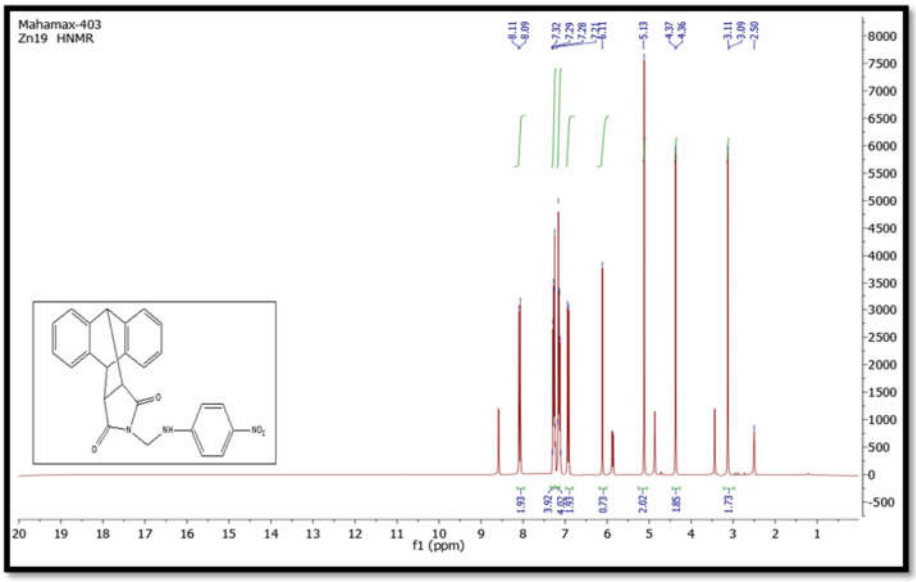


Figure 4. ^{1}H-NMR spectra of (**4**, **10**).

Table 2 shows the electronic spectra of platinum complexes(IV). Complexes (**11-13**) have three bands, the first band is located ν1 (12048-12626) cm^{-1} and the second band is ν2 (15923-17241) cm^{-1} and the third is ν3 (22321-23923) cm^{-1} in addition to the charge transfer band, which appears above (30000) cm^{-1} [30-32]. The appearance of these four transitions indicates the symmetry of the platinum(IV) complexes as square planar. The square planar geometry of the complexes was confirmed by magnetic measurements and electronic spectra.

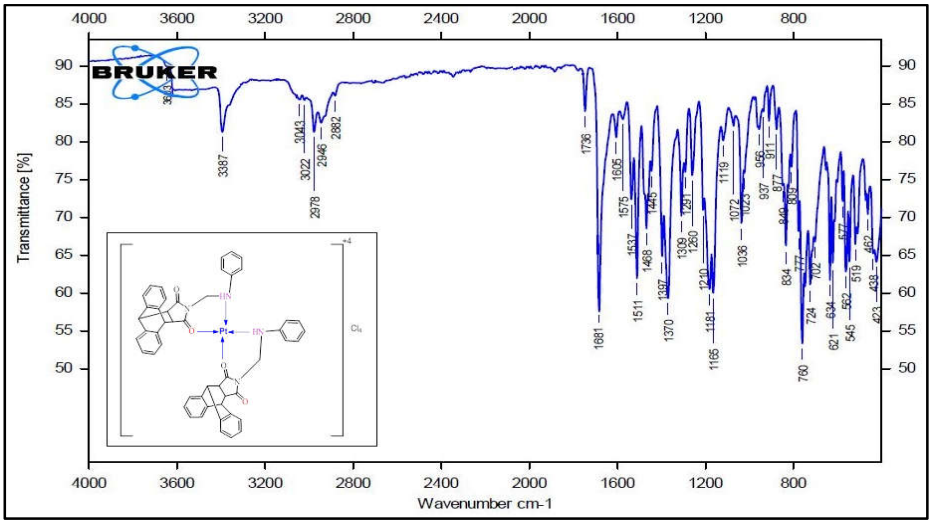


Figure 5. IR spectrum of complex (**11**).

Table 2. Molar conductivity, electronic and magnetic properties of platinum complexes.

Comp. No.	Ligand No.	Molar conductivity ($cm^2.ohm^{-1}.mol^{-1}$) Λm (DMSO)	$^1A_1g \rightarrow {}^3T_1g$ cm^{-1} ν_1	$^1A_1g \rightarrow {}^3T_2g$ cm^{-1} ν_2	$^1A_1g \rightarrow {}^1T_1g$ cm^{-1} ν_3	C.T. (cm^{-1})	μeff B.M.	Suggested structure
11	4	142.6	12048	15923	23923	34482	Dia.	Square planar
12	5	148.3	12626	16611	22727	33444	Dia.	Square planar
13	6	146.1	12077	17241	22321	34013	Dia.	Square planar

Docking study

The synthesized compounds were subjected to molecular docking against the target protein penicillin binding protein (PDB ID: 3vsl) and Penicillin G (PNM) as the control. Docking was performed via the online server CB-dock2 [33], Table 3.

Table 3. Binding affinity score, the hydrogen bonds and hydrophobic interactions compound.

Compound	Docking score	Hydrogen bonding	Hydrophobic interactions
PNM	-7.6	Arg484, Arg504	Lys273, Ser274, Asn501, Val493, Lys494, Leu256, Glu255
4	-9.6	Tyr275, Asn501, Arg504	Glu255, Ser274, Lys273, Leu256, Arg484, Asn487
5	-10.6	Tyr275,Arg504	Pro500,Lys273,Arg484,Glu255,Ser274 Asn501,Asn487,Ile507,Ile381
6	-10.6	Tyr275,Asn501, Arg504	Ser274,Leu256,Glu255,Arg484, Lys273,Asn487,Ile381,Ile507
7	-10.6	Tyr275,Asn501, Arg504	Ser274,Lys273,Glu255,Arg484, Asn487,Ile381,Ile507,Pro509
8	-10.4	Tyr275,Arg504	Ser274,Glu255,Lys273,Arg484, Asn487,Ile507,Asn501,Ile381
9	-3.0	Tyr379,Ser386, Thr385,Arg504	Glu505,Ile507, Ile381
10	-3.1	Ser66	Arg270,Asp227,Trp228,His50

Table 3 shows that highest binding affinity score was (-10.6) belong to (**5**, **6**, **7**). While the lowest score was (-3.0) belong to (**9**). Due to the emerging of antimicrobial resistance, it is crucial to find new potential targets and new antibiotics [34]. Penicillin binding proteins is the target of β-lactam antibiotics where they are involved in biosynthesis of bacterial cell wall since it is responsible in cross-linking of the stem peptides [35]. In the study of Akves *et al.* [36] natural products from mushroom were used in docking several bacterial targets including pencilling binding proteins as virtual screening for new antimicrobials.

Docking analysis found the compounds have higher binding affinity for the target than Penicillin G so these ligands may serve as lead compounds for developing new antibiotics. Figure 6 shows the results, and the hydrogen bonds and hydrophobic interactions involved [37].

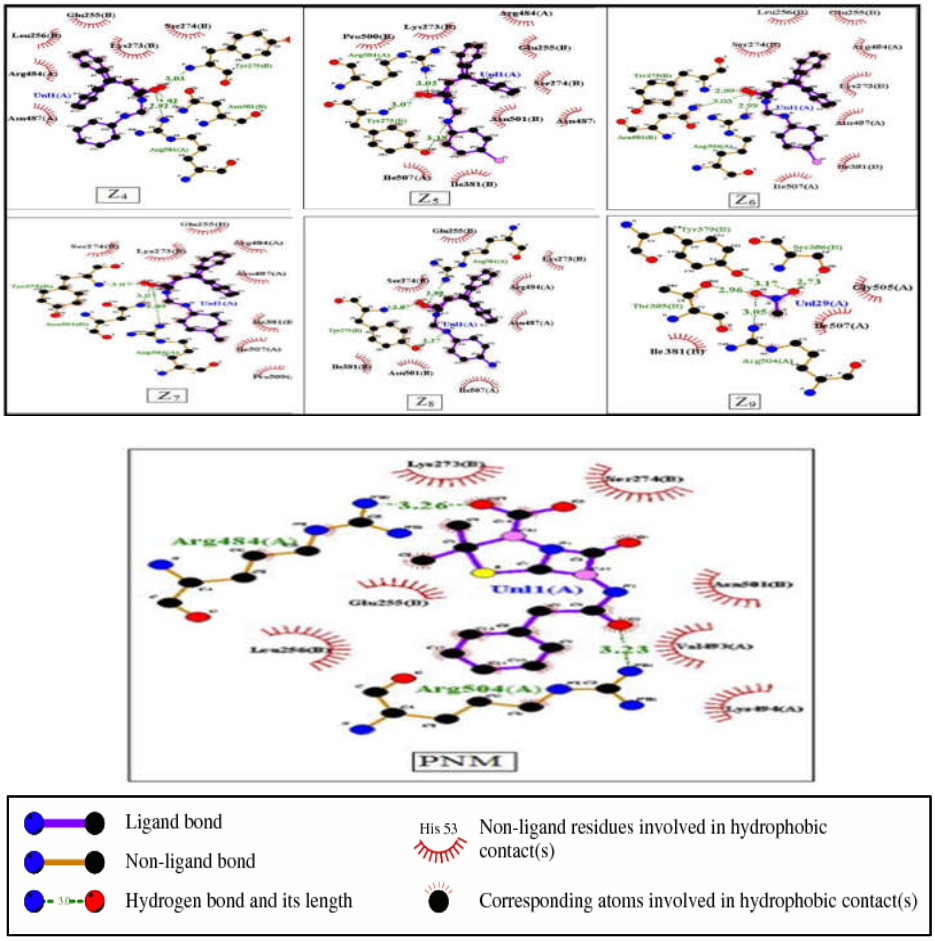


Figure 6. Interaction of target protein with compounds (**4-9**). Visualized by Lig plot.

Biological effectiveness

Salmonella typhi, *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa* are the four types of Gram-positive and Gram-negative bacteria that have been used to evaluate the biological effects of a number of prepared compounds (**4**, **5**, **6**, **10**, **11**, **12**, **13**).

Due to the importance of these bacteria in the medical field, the range of diseases they may cause, and their varying resistance to antibiotics and other drugs, the disc diffusion method was used for their selection. The inhibitory results in Table 4 show that a number of the compounds prepared have antibacterial properties.

According to the inhibition domain, compounds (**4**, **5**) had significant activity against *Escherichia coli*. Compounds (**4**, **5**) had weak activity against *Pseudomonas aeruginosa* and *Staphylococcus aureus*, while the rest of the compounds showed good to moderate results.

Table 4. Biological activity of some prepared compounds (**4-10**).

Comp. No.	*Staphylococcus aureus* 10 (mg/mL) *ZI mm	*Eschershia coli* 10 (mg/mL) ZI mm	*Pseudomonas aeruginosa* 10 (mg/mL) ZI mm	*Salmonella typhi* 10 (mg/mL) ZI mm
4	0	18	0	8
5	16	18	0	15
6	14	16	15	12
10	15	17	16	13
11	11	15	25	15
12	19	18	20	17
13	19	16	17	15
Ampicillin 10 mg/disk	25	20	20	15

*ZI = zone inhibiter in millimeter: 1 to 6 mm levels are considered as low activity, ranging from 6 to 12 mm considered moderate activity, and levels more than 12 mm are considered high active.

CONCLUSION

In this research paper we successfully prepared three platinum complexes derived from imides ligand which prepared from anthracene as starting material. The prepared compounds (**4-6**) were subject to docking analysis against penicillin binding protein and Penicillin G as the control. The result show that (**5**, **6**, **7**) have highest binding affinity score (-10.6) compare with the control. In addition, the biological activity of ligands (**4**, **5**, **6**) and their complexes (**11**, **12**, **13**) was tested against four types of bacteria strain, the result fluctuated from high inhibition to moderate and weak.

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REFERENCES

1. Tran, T.N.; Henary, M. Synthesis and applications of nitrogen-containing heterocycles as antiviral agents. *Molecules* **2022**, 27, 2700.
2. Quaranta, E.; Aresta, M. *Carbon Dioxide as Chemical Feedstock*. 2nd ed., Wiley-VCH: New York; **2010**; p. 121.
3. Hargreaves, M.; Pritchard, J.; Dave, H. Cyclic carboxylic monoimides. *Chem. Rev.* **1970**, 70, 439-69.
4. Elham, J.; Najmeh, T.N.; Ali, J.N; Safoora, P.; Farshid, H.; Sedighe, S. Synthesis and evaluation of antimicrobial activity of cyclic imides derived from phthalic and succinic anhydrides. *Res. Pharm. Sci.* **2017**, 12, 526-534.
5. Aeberli, P.; Gogerty, J.; Houlihan, W.; Iorio, L.C. Synthesis and central nervous system depressant activity of some bicyclic amides. *J. Med. Chem.* **1976**, 19, 436-438.
6. Correa, R.; Filho, V.C.; Rosa, P.W.; Pereira, C.; Schlemper, V.; Nunes R.J. Synthesis of new succinimides and sulphonated derivatives with analgesic action in mice. *JPP* **1997**, 3, 67-71.
7. Hall, I.; Wong, O.; Scovill, J. The cytotoxicity of N-pyridinyl and N-quinolinyl substituted derivatives of phthalimide and succinimide. *Bio. Pharm.* **1995**, 49, 251-258.
8. Crider, A.; Kolczynski, T.; Yates, K. Synthesis and anticancer activity of nitrosourea derivatives of phensuximide. *J. Med. Chem.* **1980**, 23, 324-326.

9. Rich, D.; Gardner, J. Synthesis of the cytostatic cyclic tetrapeptide, chlamydocin. *Tetrah. Lett* **1983**, 24, 5305-5308.
10. Kaczorowski, G.; McManus, O.; Priest, B.; Garcia, M. Ion channels as drug targets: The next GPCRs. *J. Gen. Phys.* **2008**, 131, 399-405.
11. Filho, V.; Nunes, R.; Calixto, J.; Yunes R. Inhibition of *Guinea-pigileum* contraction by phyllanthimide analogues: Structure-activity relationships. *Pharm. Pharmacol. Commun.* **1995**, 1, 399-401.
12. Johnston, T.; Piper, J.; Stringfellow, C. Terminal dicarboximido analogs of S-2-; omega-aminoalkylamino) ethyl dihydrogen phosphorothioates and related compounds as potential antiradiation agents. 2. Succinimides, glutarimides, and cis-1,2-cyclohexanedicarboximides. *J. Med. Chem.* **1971**, 14, 350-354.
13. Musso, D.; Cochran, F.; Kelley, J.; McLean, E.; Selph, J.; Rigdon, G. Design and synthesis of (E)-2-(4,6-difluoro-1-indanylidene) acetamide, a potent, centrally acting muscle relaxant with antiinflammatory and analgesic activity. *J. Med. Chem.* **2003**, 46, 399-408.
14. Pennington, F.; Guercio, P.; Solomons, I.; Coram, W.M.; Brezenoff, H.E. The antihypertensive effect of a selective central muscarinic cholinergic antagonist: N-(4-diethylamino-2-butynyl)-succinimide. *J. Am. Chem. Soc.* **1983**, 3, 503-516.
15. Zentz, F.; Valla, A.; Guillou, R.; Labia, R.; Mathot, A.; Sirot, D. Synthesis and antimicrobial activities of N-substituted imides. *Farmaco* **2002**, 57, 421-6.
16. Hazra, B.; Pore, V.; Day, S.; Datta, S.; Darokar, M.; Saikia, D. Bile acid amides derived from chiral amino alcohols: novel antimicrobials and antifungals. *Bioorg. Med. Chem. Lett.* **2004**, 14, 773-7.
17. Kornet, M.; Crider, A.; Magarian E. Potential long-acting anticonvulsants. *J. Med. Chem.* **1977**, 20, 405-9.
18. Isaka, M.; Prathumpai, W.; Wongsa, P.; Tanticharoen, M.; Hirsutellone, F. A dimer of antitubercular alkaloids from the seed fungus Trichoderma species BCC 7579. *Org. Lett.* **2006**, 8, 2815-7.
19. Madhurambal, G.; Ramasamy, P.; Srinivasan, P.; Mojumdar, S. Synthesis and characterization of a novel non-linear optical (NLO) material: Endo anthracene maleic anhydride–Diel's–Alder adduct of anthracene. *J. therm. Analy. Calo.* **2006**, 86, 601-604.
20. Salazar, I.; Albino, E.; Enríquez, F.; Tapia, D.; Tito, N.; Herrera, L. Synthesis of pyrrolo[3,4-b]pyridin-5-ones via Ugi–Zhu reaction and in vitro–in silico studies against breast carcinoma. *Pharm.* **2023**, 16, 1562.
21. Kamps, A.; Hopkinson, R.; Schofield, C.; Claridge, D. How formaldehyde reacts with amino acids. *Commun Chem.* **2019**, 2, 1-14.
22. Hofmann, N.; Hultzsch, K. Switching the N-alkylation of arylamines with benzyl alcohols to imine formation enables the one-pot synthesis of enantioenriched α-N-alkylaminophosphonates. *Eur. J. Org. Chem.* **2019**, 20, 3105–3111.
23. Fathi, A.; Al Jawaheri, Y.; Ismaeel, Sh. Synthesis of some new substituted imines from aldehydes and ketones derived from quinolinic acid. *Eclet. Quim.* **2023**, 48, 49-65.
24. Fathi, A.A.; Al Jawaheri, Y.A. Synthesis and characterization of new N-Aryl sulfonyl hydrazone compounds. *Egypt. J. Chem.* **2022**, 65, 179-183.
25. El-Bendary, M.M.; Saleh, T.S.; Alomari, M.M.; Ali, E.M.; Davaasuren B.; Jaremko M.; Babgi, B.A. Potential anticancer activities and catalytic oxidation efficiency of platinum(IV) complex. *Molecules* **2022**, 27, 4406.
26. Leven, M.; Berghe, V.; Mertens, F.; Vlietinck, A.; Lammens, E. Screening of higher plants for biological activities I. Antimicrobial activity. *Planta Med.* **1979**, 36, 311-321.
27. Vandepitte, J.; Engback, K.; Piot, P.; Heuck, C.C. *Basic Laboratory Procedures in Clinical Bacteriology*, *WHO* **1991**, 1, 121.

28. Al-Saif, F. A. Spectroscopic, molar conductance and biocidal studies of Pt(IV), Au(III) and Pd(II) chelates of nitrogen and oxygen containing Schiff base derived from 4-amino antipyrine and 2-furaldehyde. *Int. J. Electrochem. Sci.* **2013**, 8, 10424-10445.
29. Abdulameer, J.H.; Abbas, S.K.; Mosa, M.J. Synthesis and characterization of nickel, palladium, platinum and cupper with new oxazipine ring. *IOP Conf. Ser. Mater. Sci. Eng.* **2019**, 571, 12099.
30. Al-Daffy, R.K.; Al-Hamadani, A.A.S. Synthesis and characterization of some metals complexes with new acid azo ligand (4-(amino-4-phenyl azo)-methyl)-cyclohexane carboxylic acid. *Iraqi J. Sci.* **2022**, 63, 3264-3275.
31. Husain, A.Z.; Al- Jawaheri, Y.S.; Al-Assafe, A.Y. Synthesis of substituted 2-amino oxazoles with their cobalt(II) and platinum(IV) complexes and evaluation of their biological activity. *Bull. Chem. Soc. Ethiop.* **2024**, 38, 1667-1679.
32. Husain, A.Z.; Al- Jawaheri, Y.S.; Al-Assafe, A.Y. Synthesis of substituted heterocyclic with their cobalt(II) complexes from 2-aminothiazoles and evaluation of their biological activity. *Bull. Chem. Soc. Ethiop.* **2024**, 38, 909-922.
33. Yang, L.; Xiaocong, Y.; Jianhong, G.; Shuang, C.; Zhi-Xiong X.; Yang, C. CB-Dock2: Improved protein–ligand blind docking by integrating cavity detection, docking and homologous template fitting. *Nucl. Acid Res.* **2022**, 50, 159.
34. Van, E.E.; Wittekoek, B.; Kuijper, E.; Smits, W. DNA replication proteins as potential targets for antimicrobials in drug-resistant bacterial pathogens. *J. Antim. Chemo.* **2017**, 72, 1275-1284.
35. Bertonha, A.; Silva, C.; Shirakawa, K.; Trindade, D.; Dessen A. Penicillin-binding protein (PBP) inhibitor development: A 10-year chemical perspective. *Exp. Biol. Med.* **2023**, 248, 1657-1670.
36. Alves, M.; Froufe, H.; Costa, A.; Santos, A.; Oliveira, L.; Osório, S.; Abreu, R.; Pintado, M.; Ferreira, I. Docking studies in target proteins involved in antibacterial action mechanisms: Extending the knowledge on standard antibiotics to antimicrobial mushroom compounds. *Molecules* **2014**, 19, 1672-84.
37. Laskowski, R.A.; Swindells, M.B. Multiple ligand-protein interaction diagrams for drug discovery. *J. Chem. Inf. Model.* **2011**, 51, 2778-2786.