

New Palladium (II) Complexes Bearing Benzopyran Derivative Ligands: Synthesis and Characterization

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PALLADIUM complexes of (4-methoxyphenyl benzopyran, 4-fluorophenyl benzopyran and 4-(2-chloro-5-nitro)phenyl benzopyran ligands) have been synthesized and characterized using different tools such as IR, UV/Vis, ¹H-NMR, elemental analysis, thermal analysis, and mass spectroscopy. The mode of binding Pd (II) ion with the ligands shows that the Pd (II) ion binds with the ligands through the amino group nitrogen atom and cyanide group nitrogen atom of the ligands which revealed a square-planar coordination geometry at the metal center [Pd L₁.2Cl] 0.5H₂O, [Pd L₂.2Cl] 1.5H₂O and [Pd L₃.2Cl].

Keywords: Palladium, Benzopyran and Microwave .

Bidentate chelating ligands are often used to fix the active coordination sites of Pd (II) complexes in a *cis*-arrangement⁽¹⁾. The significant similarity between the coordination chemistry of palladium (II) and platinum (II) compounds has advocated studies of Pd (II) complexes as antitumor drugs. A key factor that might explain why platinum is most useful comes from the ligand-exchange kinetics. The hydrolysis in palladium complexes is too rapid: 105 times faster than for those of corresponding platinum analogues⁽²⁾. They dissociate readily in solution leading to very reactive species that are unable to reach their pharmacological targets. Compared to cisplatin, the corresponding cis-palladium, *cis*- [PdCl₂(NH₃)₂] does not show antitumoral activity. It is well known that it undergoes an inactive *trans*-conformation and that the two compounds hydrolyze very fast assuming that they interact *in vivo* with a lot of molecules particularly proteins preventing them to reach the DNA, their pharmacological target⁽³⁾. The considerably higher activity of palladium complexes implies that if an antitumor palladium drug is to be developed, it must somehow be stabilized by a chelate or a strongly coordinated, bulky monodentate nitrogen ligand and a suitable leaving group^(4,5).

Due to the steric effect that results from the bulk on the donor atoms, these ligands could minimize any possible *cis*-*trans* isomerism and insure the direct separation of the desired *trans*-Pd isomers⁽⁶⁾. In general, research results indicated that most of the *trans*-palladium complexes showed a better activity than the cisplatin isomers and superior activity than that of the *cis*-palladium isomers. More importantly, they showed activities equal to (or superior than) those of cisplatin,

carboplatin, and oxaliplatin (the anticancer drugs in clinical use) *in vitro*⁽⁴⁾. Studies of platinum and palladium compounds with biologically active carriers have yielded promising results in the field of anticancer chemistry and there is potential for varying the biological activity of these complexes by changing the structure of the carrier⁽⁷⁾. Significant advances have emerged from this methodology of design^(2, 4).

The use of microwave radiation to enhance organic reactions in environmentally benign solvents such as water, which is inexpensive and not dangerous, represents very powerful green chemical technology both from economic and synthetic points of view. This not only reduces the burden of organic solvent disposal but also enhances the rate of the reaction. In recent years, the synthesis of compounds having benzopyran rings has attracted great interest, because they have diverse pharmacological activities⁽⁸⁾. In addition, a large number of benzopyran derivatives possess potent relaxant activity on blood vessels, cardiac muscle, and other smooth muscles^(9,10). We have prepared a new palladium (II) complexes containing benzopyran moiety.

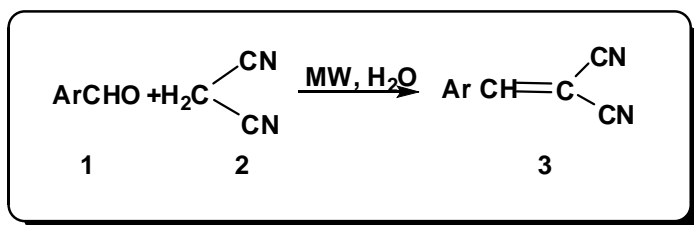
Experimental

Materials and methods

benzaldehyde and its substituted derivatives, were purchased from Aldrich Chemical Co. Dimedone was purchased from Across Organics Co. (Belgium), malononitrile was obtained from Merck Co., Germany. Hydrochloric acid, potassium hydroxide, potassium fluoride, sodium acetate trihydrate, basic alumina, anhydrous sodium sulphate and sodium nitrite were purchased from El-Nasr Pharmaceutical Co. Kojic acid and palladium chloride were purchased from Merck company.

Synthesis of-(4-methoxyphenyl benzopyran(L₁),4-fluorophenyl benzopyran (L₂) and 4-(2-chloro-5-nitro) phenyl benzopyran(L₃)) ligands

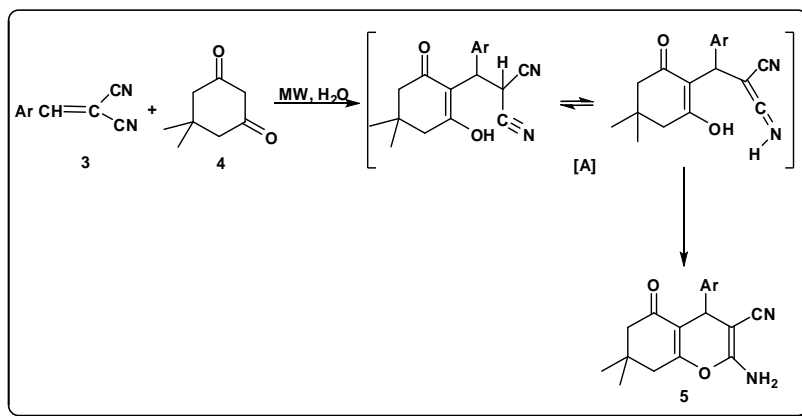
A mixture of aromatic aldehyde 1 (5mmol) and malononitrile 2 (0.33 g, 5mmol) were mixed together in water (2 ml) in a tightly closed tube, and subjected to microwave irradiation for the appropriate time until completion of the reaction for (L₁,4 min, L₂,2 min and L₃,1min) (monitored by TLC). The precipitate formed was filtered, washed with water to give the pure product 3 with sharp melting point (Scheme 1).



Scheme 1.

An equimolar amount of arylidene malononitrile 3 (5mmol) and dimedone 4 (0.7 g, 5mmol) were mixed together in water (2 ml) in a tightly closed tube, and
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subjected to microwave irradiation for the appropriate time until completion of the reaction (L_1 , 4 min, L_2 , 2 min and L_3 , 3 min) (monitored by TLC). The precipitate formed filtered and washed with water gave pure product 5 (Scheme 2).



Scheme 2.

Synthesis of Pd (II) complex

Palladium (II) chloride 2-3 gm (0.1 moles) was dissolved in ~ 40 ml absolute ethanol, and then added to 0.1 mole of the prepared ligands (L_1 , L_2 and L_3) dissolved in ~ 40 ml absolute ethanol. The mixture was heated under reflux for two hr; the bluish precipitate formed were filtered off and finally washed by hot ethanol several times.

Physical methods

Carbon, hydrogen and nitrogen contents were determined at the Microanalytical Unit, Cairo University, Egypt. IR spectra of the ligand and its solid complexes were measured in KBr on a Mattson 5000 FTIR spectrometer at National Research Centre, Dokki, Cairo, Egypt.

All electronic spectra and kinetic measurement were performed using Varian Cary 4 Bio UV/vis spectrophotometer at National Research Centre, Dokki, Cairo, Egypt. Thermal analysis measurements (TGA, DTA) were recorded on a Shimadzu thermo-gravimetric analyzer model TGA-50H, using 20 mg samples. The flow rate of nitrogen gas and heating rate were $20 \text{ cm}^3 \text{ min}^{-1}$ at $10^\circ\text{C min}^{-1}$, respectively. Mass spectra were recorded at Al-Azhar University, Egypt.

Results and Discussion

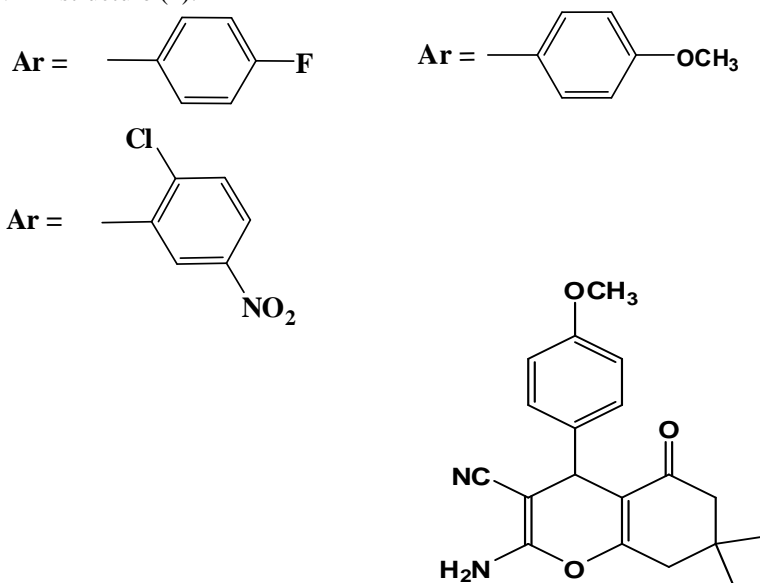
Characterization of the ligands (L_1 , L_2 , and L_3)

Characterization of L_1 ⁽¹¹⁾

The infrared spectrum of the 4-methoxyphenyl benzopyran L_1 shows weak bands at 3000 and 2839 cm^{-1} , which were assigned to the aromatic and aliphatic C-H stretches, respectively. A strong band observed at 2192 cm^{-1} is likely to be due to $\nu \text{C}\equiv\text{N}$ stretches^(12,13). Band at 3372 cm^{-1} was assigned to νNH_2 . The ligand showed band at 1653 was assigned to $\nu \text{C}=\text{O}$ ⁽¹⁴⁾.

The $^1\text{H-NMR}$ spectrum revealed peaks which were attributed to $\delta = 1.03$ (s, 3H, CH_3), 1.19 (s, 3H, CH_3), 2.23 (d, 1H, $J_{\text{AB}} = 16$ Hz, H-8a), 2.31 (d, 1H, $J_{\text{AB}} = 16$ Hz, H-8b), 2.45 (s, 2H, $\text{C}_6\text{-H}$), 3.79 (s, 3H, OCH_3), 4.02 (s, 1H, $\text{C}_4\text{-H}$), 4.95 (s, 2H, NH_2 , D_2O exchangeable), 7.11-7.29 (m, 4H, Ar-H).

All these data together with the molecular weight from the mass spectrum ($m/z = 324$) and elemental analysis proposed the structure of the ligand as shown in structure (1).



2-Amino-4-(4-methoxyphenyl)-5, 6, 7, 8-tetrahydro-7, 7-dimethyl-5-oxo-4H-chromene-3-carbonitrile

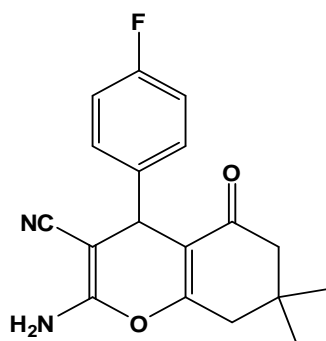
Structure (1) (L_1)

Characterization of L_2 ⁽¹⁵⁾

The IR spectrum of the (4-fluorophenyl) benzopyran (L_2) shows band at 3356 cm^{-1} was assigned to νNH_2 . The ligand showed bands at 1650 and 2190 cm^{-1} were assigned to $\nu \text{C}=\text{O}$, $\nu \text{C}\equiv\text{N}$.

^1H NMR (CDCl_3): $\delta = 1.05$ (s, 3H, CH_3), 1.083 (s, 3H, CH_3), 1.67 (d, 1H, $J_{\text{AB}} = 16$ Hz, H-8a), 2.23 (d, 1H, $J_{\text{AB}} = 16$ Hz, H-8b), 2.44 (s, 2H, $\text{C}_6\text{-H}$), 4.33 (s, 1H, $\text{C}_4\text{-H}$), 5.91 (s, 2H, NH_2 , D_2O exchangeable), 6.79-7.23 (m, 4H, Ar-H).

All these data together with the molecular weight determined from the mass spectrum ($m/z = 312$) and elemental analysis proposed the structure of the ligand as shown in structure (2).

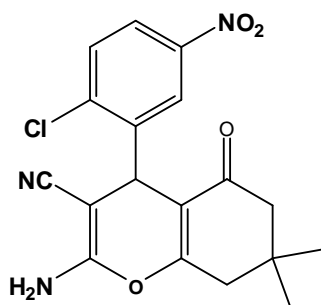


2-Amino-4-(4-fluorophenyl)-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4H-chromene-3-carbonitrile
Structure (2) (L_2)

Characterization of L_3

The IR spectrum of the (2-chloro-5-nitrophenyl) benzopyran (L_3) shows bands at 3447, 3332 cm^{-1} assigned to νNH_2 . The ligand also showed bands at 1664, 2186 cm^{-1} assigned to $\nu\text{C}=\text{O}$, $\nu\text{C}\equiv\text{N}$.

The ^1H -NMR spectrum revealed peaks which were attributed to $\delta = 1.09$ (s, 3H, CH_3), 1.13 (s, 3H, CH_3), 2.17-2.29 (m, 2H, $\text{C}_8\text{-H}$), 2.48-2.55 (m, 2H, $\text{C}_6\text{-H}$), 4.01 (s, 1H, $\text{C}_4\text{-H}$), 5.55 (s, 2H, NH_2 , D_2O exchangeable), 7.23-7.39 (m, 3H, Ar-H).



2-Amino-4-(2-chloro-5-nitrophenyl)-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4H-chromene-3-carbonitrile
Structure (3) (L_3)

All these data together with the molecular weight determined from the mass spectroscopy ($m/z = 373$) and elemental analysis proposed the structure of the ligand as shown in structure (3).

Characterization of palladium complexes (Characterization of [Pd L₁. 2Cl] 0.5H₂O, [Pd L₂.2Cl] 1.5H₂O and [PdL₃.2Cl] complexes)

IR spectra of Pd (II) complexes

The IR spectra of these complexes in KBr discs show that all the ligands behave as a bidentate coordinating to metal ions through the nitrogen atoms of NH₂ and C≡N forming stable five membered ring around the metal ion. By comparing the IR spectrum of the ligands with their complexes shown in Fig. 1-3, one can suggest the following: by disappearance of the band of cyano group there is a weak band in the curve which may be due to the cyano group in the complexes spectra; at the same time appearance of broad band completes the sentence. The coordination of NH₂ nitrogen atom is also consistent with the presence of band at (450-475) cm⁻¹ due to νM-N. Indeed, the appearance of new bands in the IR spectra of metal complexes as shown in Table 1 assigned M-N in addition to M-Cl indicates the formation of the chelates, where chlorides compensate the positive charge on the metal ions in PdL₁, PdL₂ and PdL₃^(16, 17) in the proposed structures.

Electronic spectral data of palladium complexes

The electronic spectra of all palladium complexes (Fig.4-6) show three *d-d* spin allowed transitions. These are corresponding to the transitions from the three lower lying "d" levels to the empty $d_{x^2-y^2}$ orbital. The ground state is ¹A_{1g} and excited states corresponding to the above transitions are ¹A_{2g}, ¹B_{1g} and ¹E_g in order of increasing energy. Three d-d bands are observed in the region 205-265 nm, 295-351 nm and 351-405 nm. These bands are due to

¹A_{1g} → ¹A_{2g}, ¹A_{1g} → ¹B_{1g} and ¹A_{1g} → ¹E_g transitions⁽¹⁸⁾, respectively.

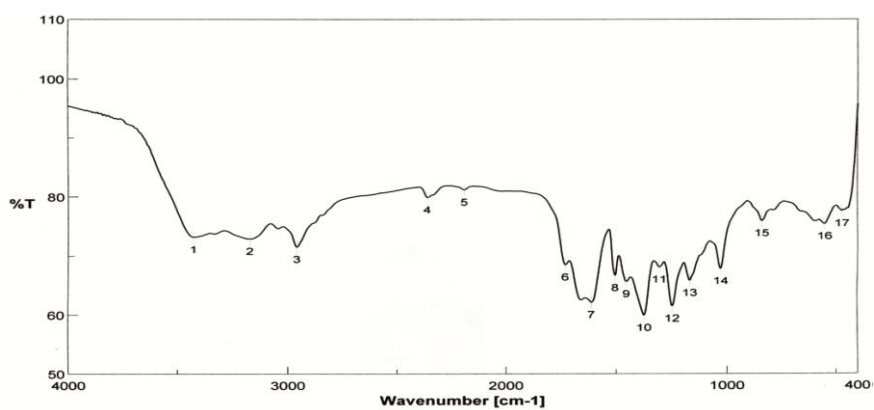
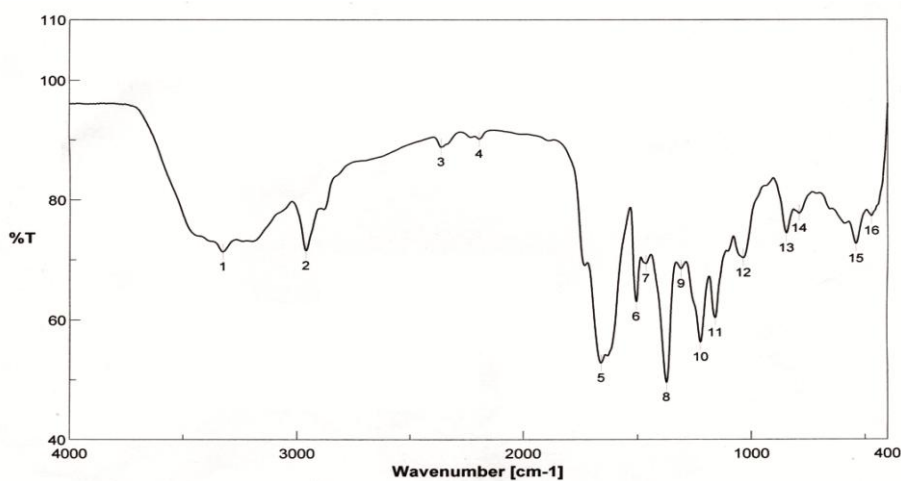
The electronic spectra of these complexes as well as their diamagnetic behavior indicate the square planar geometrical structure of the palladium complexes.

Mass spectra of palladium complexes

The mass spectrum of the palladium complexes (Fig.7) shows a molecular ion peak at $m/z = 513$ (3.43%) which is corresponding to the cyclopalladate moiety (C₁₉H₂₁Cl₂N₂O_{3.5}Pd) of [Pd. L₁.2Cl] 0.5H₂O complex and the base peak was found in the spectrum at $m/z = 287$ corresponding to (C₁₇H₁₇FNO₂).

TABLE 1. IR spectral data of ligands (L₁, L₂, L₃) and their complexes with Pd (II).

Compd	$\nu_{\text{CH}^{\text{arom}}}$	$\nu_{\text{CH}^{\text{aliph}}}$	$\nu_{\text{C}\equiv\text{N}}$	ν_{CO}	ν_{NH_2}	$\nu_{\text{M-N}}$
L ₁	3008	2833	2192	1653	3373,3314	
PdL ₁	3064	2846		1654	3423,3245	470
L ₂	3091	2875	2190	1650	3356,3258	
PdL ₂	3075	2835		1658	3440,332	2472
L ₃	3091	2873	2190	1658	3447,3332	
PdL ₃	3082	2810		1657	3439,3212	458

Fig 1. IR spectrum of [PdL₁.2Cl] 0.5H₂O complex .Fig. 2. IR spectrum of [PdL₂.2Cl]1.5H₂O complex .

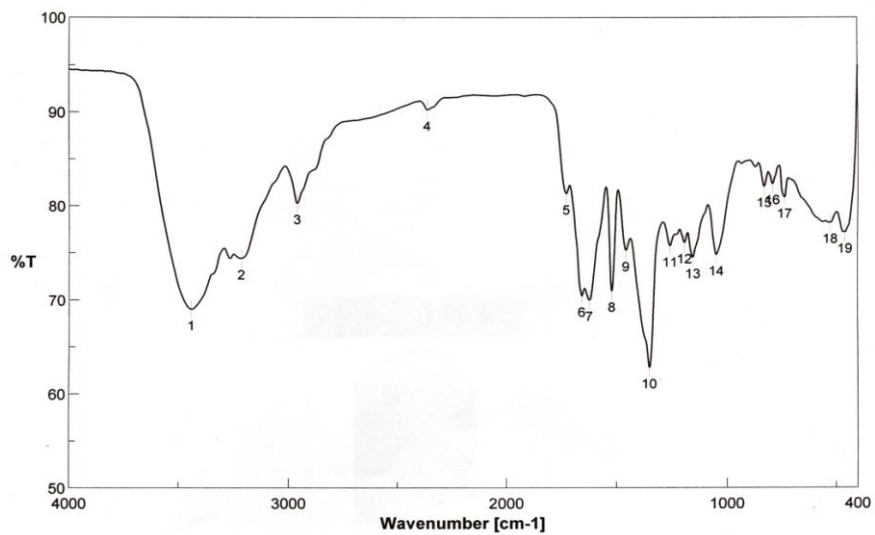


Fig. 3. IR spectrum of [PdL₃.2Cl] complex.

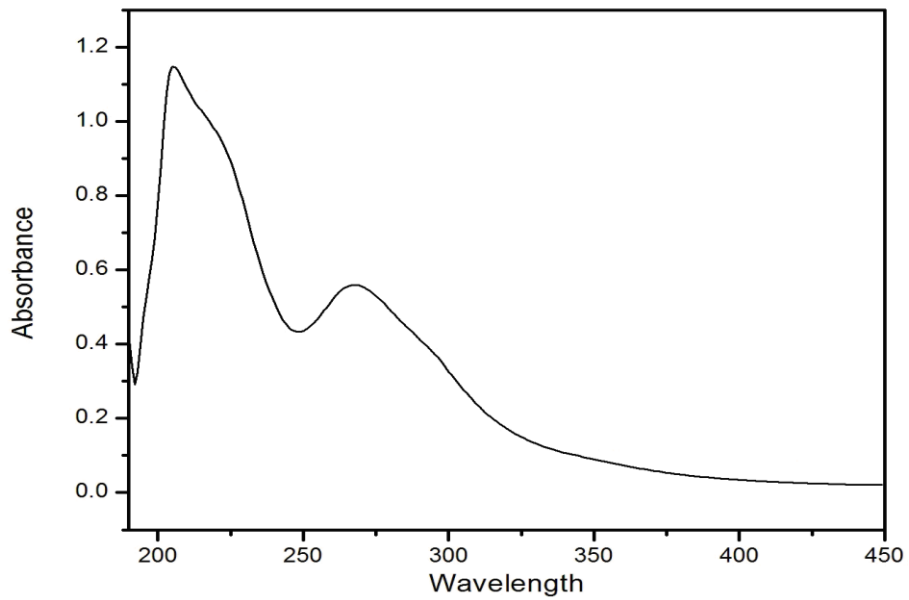


Fig. 4. Electronic spectra of [PdL₁.2Cl]0.5H₂O complex.

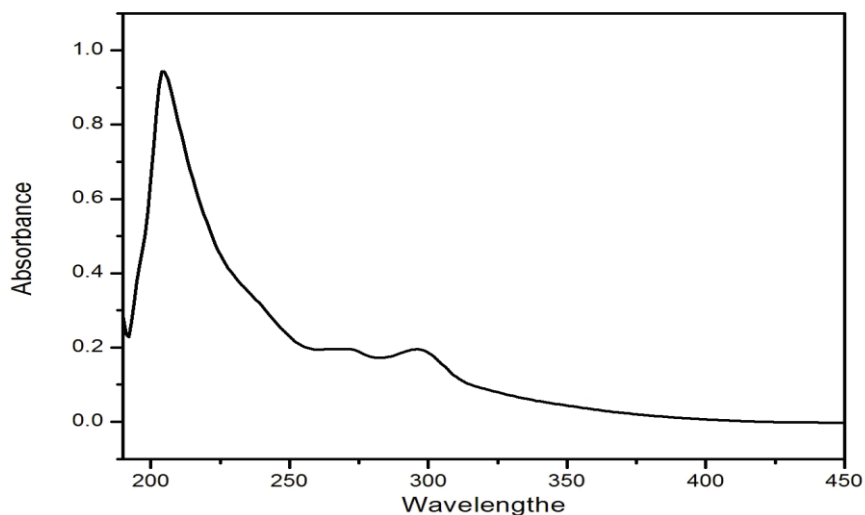


Fig. 5. Electronic spectra of [PdL₂.2Cl]·1.5H₂O complex.

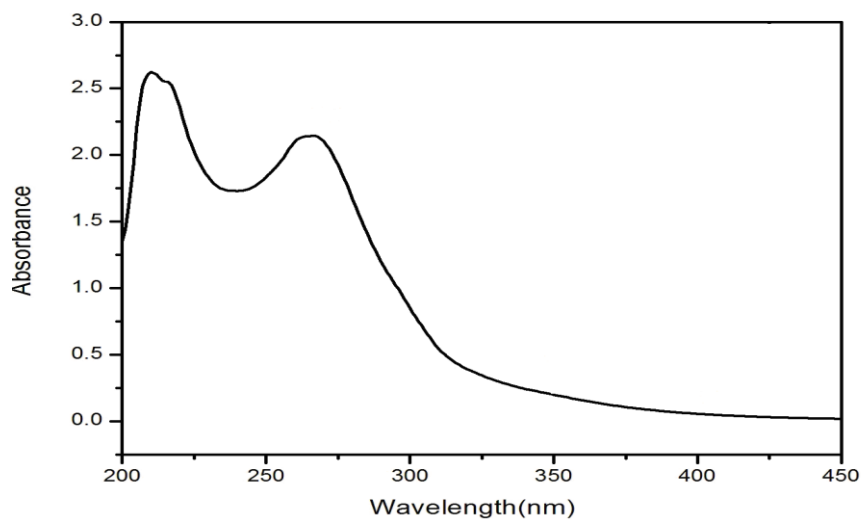


Fig. 6. Electronic spectra of [PdL₃.2Cl] complex .

The mass spectrum of palladium complex [Pd .L₂.2Cl] 1.5H₂O (Fig.8), shows a molecular ion peak at $m/z = 517$ (2.21%) corresponding to the cyclopalladate moiety (C₁₈H₂₀FCl₂N₂O_{3.5}Pd). The base peak was found in the spectrum at $m/z = 210$ corresponding to the (C₁₄H₁₂NO).

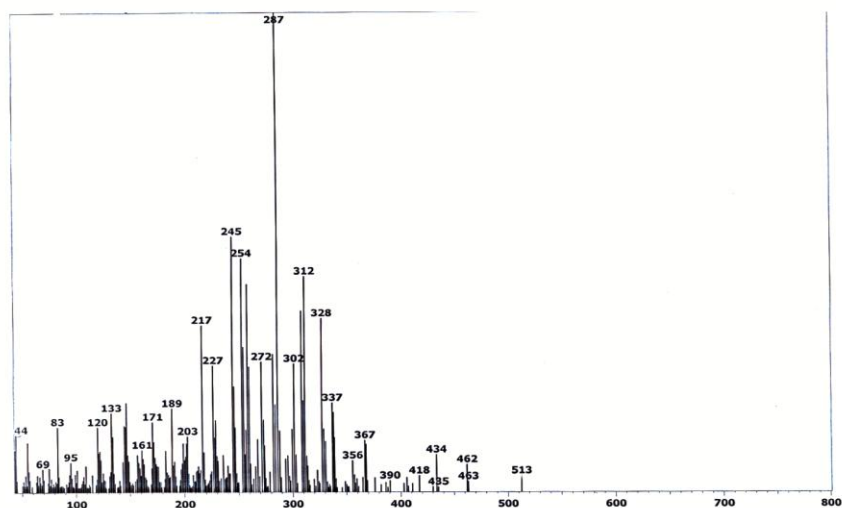


Fig. 7. Mass spectrum of $[\text{PdL}_{1.2}\text{Cl}] \cdot 0.5\text{H}_2\text{O}$ complex.

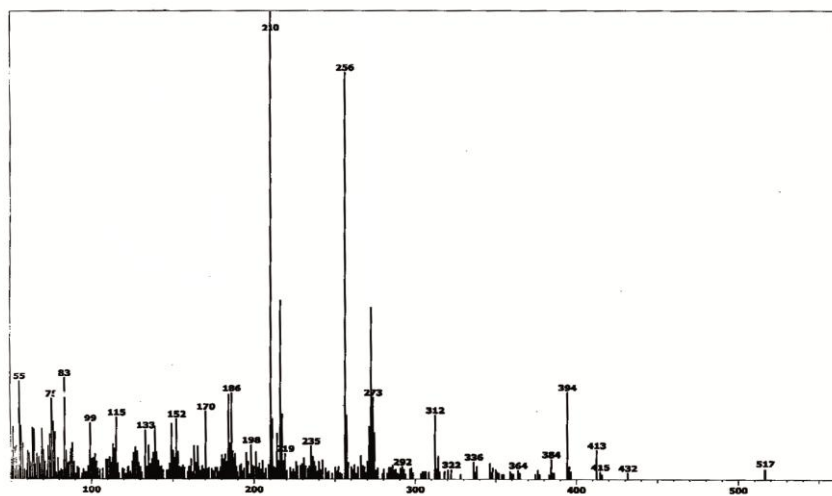


Fig. 8. Mass spectrum of $[\text{Pd L}_{2.2}\text{Cl}] \cdot 1.5\text{H}_2\text{O}$ complex.

The mass spectrum of palladium complex $[\text{Pd} \cdot \text{L}_3 \cdot 2\text{Cl}]$ (Fig.9), showed a molecular ion peak at $m/z = 547$ (2.31%) corresponding to the cyclopalladate moiety ($\text{C}_{18}\text{H}_{16}\text{Cl}_3\text{N}_4\text{O}_3\text{Pd}$). The base peak was found in the spectrum at $m/z = 272$ (100%) corresponding to the ($\text{C}_{15}\text{H}_{13}\text{ClN}_2\text{O}$).

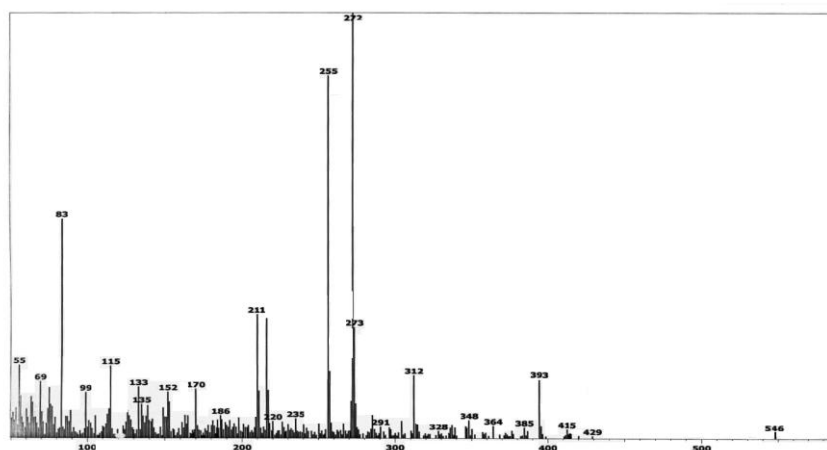


Fig. 9. Mass spectrum of $[\text{PdL}_2.2\text{Cl}]$ complex.

Thermal analysis of palladium complexes

The majority of compounds including complexes suffer physical and chemical changes when subjected to heat energy. Under defined experimental conditions, these changes are characteristic of such substances and can be used for their qualitative and quantitative analysis. When the sample to be analyzed is heated, various chemical changes (*e.g.* thermal decomposition, oxidation..., etc) and several physical processes (solvent and water elimination, evaporation, sublimation...etc) may take place with a consequent change in the weight of the sample. The examination of these processes is the task of thermo gravimetric analysis (TGA) method.

Palladium complexes showed four stages of decomposition. The first weight loss stage in complexes corresponds to the elimination of crystalline water molecules as shown in Fig. 10-12.

The thermal decomposition is finally yielding the corresponding metal oxides, carbides, metallic residue or mixtures.

$^1\text{H NMR}$

The $^1\text{H NMR}$ spectrum (Fig.13) of $[\text{Pd.L1.2CL}]0.5\text{H}_2\text{O}$ in (CDCl_3) solvent indicated a signals at $\delta:0.915-1.22$ (*m*, 8H, $[6\text{H},2\text{CH}_3]+ 2\text{H},(\text{CH}_2)]$), δ 3.84 (*s*, 3H, OCH_3), δ 7.24-8.03 (*m*, 6H, Ar-H and NH_2).

Elemental analysis

The elemental analysis shown in Table 2, together with the IR, electronic spectra ,mass spectra, thermal analysis and NMR spectra as well as the palladium content Pd(L₁) calc.(21.2),found (20.93),Pd(L₂) calc.(20.43), found (20.01)] and Pd (L₃) calc. (19.84), found (19.32) suggest that the structures of the palladium complexes are as shown in structures 4-6.

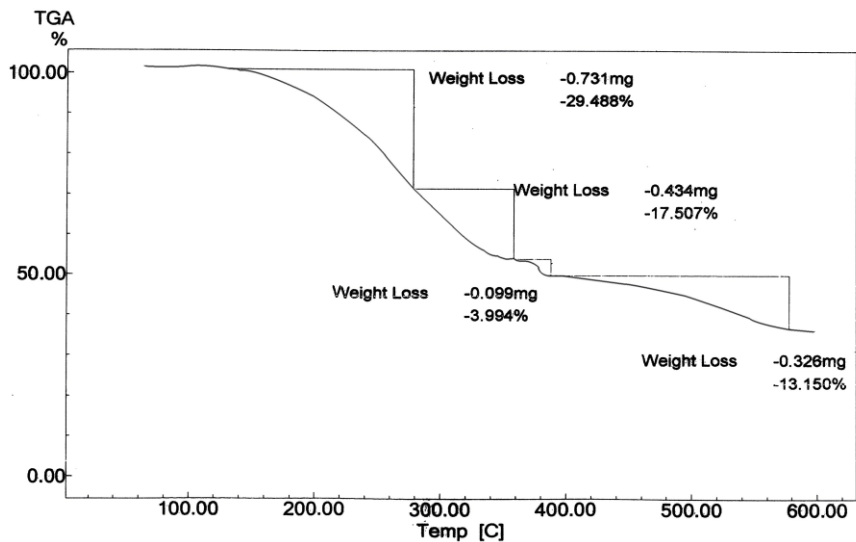


Fig. 10. TGA of the copper complex of $[Pd L_{1.2}Cl] 0.5H_2O$.

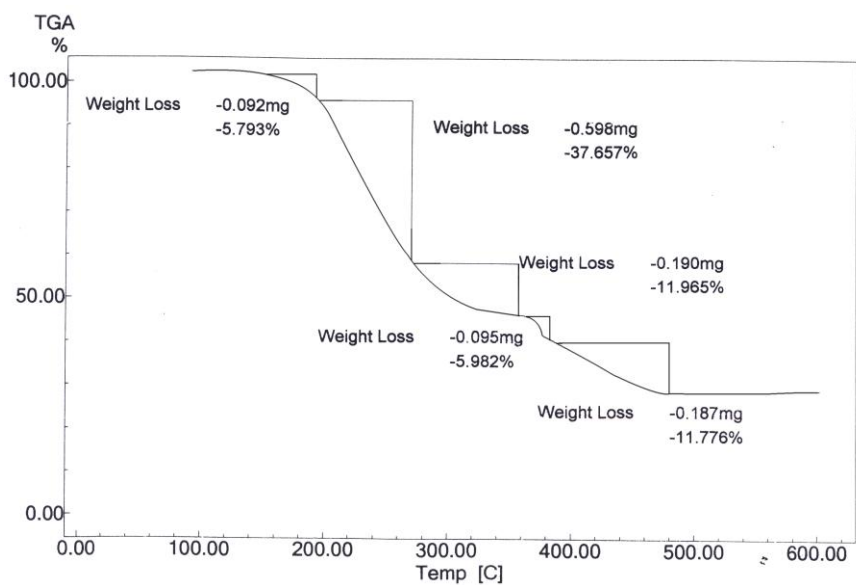


Fig. 11. TGA of the complex of $[Pd L_{2.2}Cl] 1.5H_2O$.

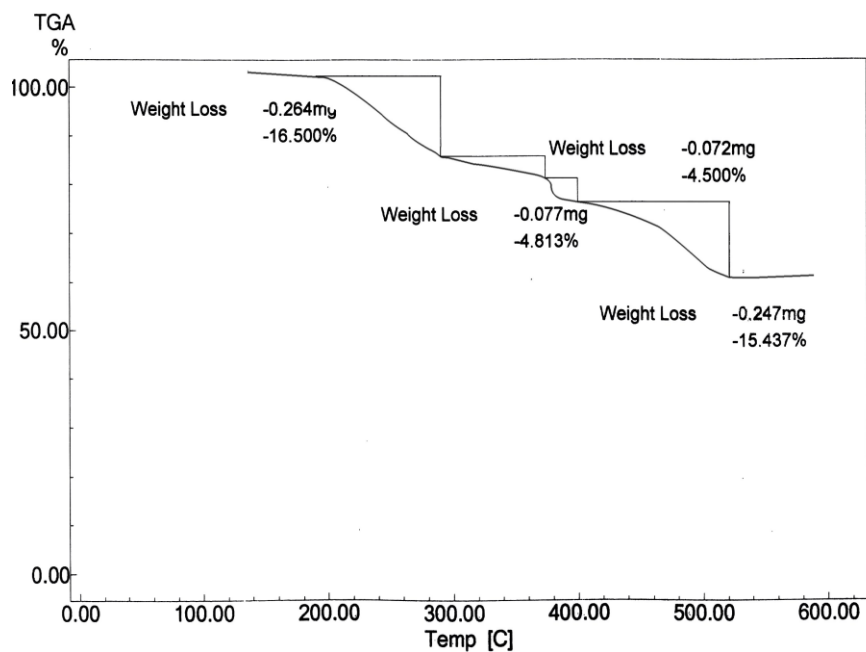


Fig. 12. TGA of the complex of [Pd L₃, 2Cl].

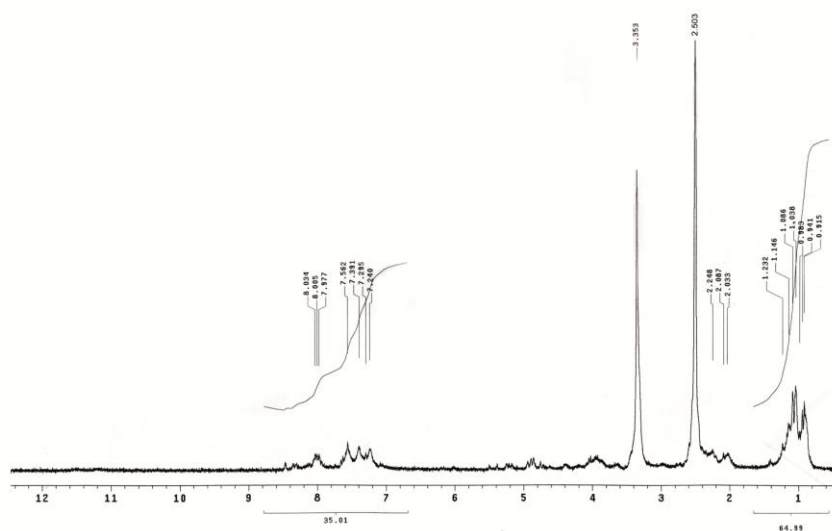
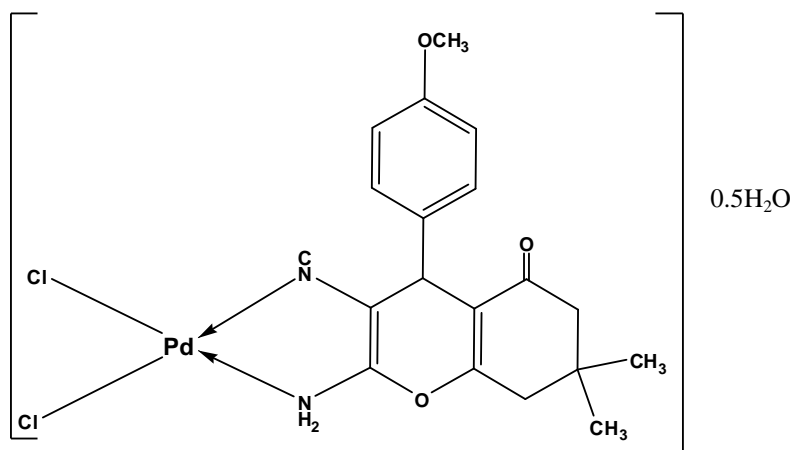
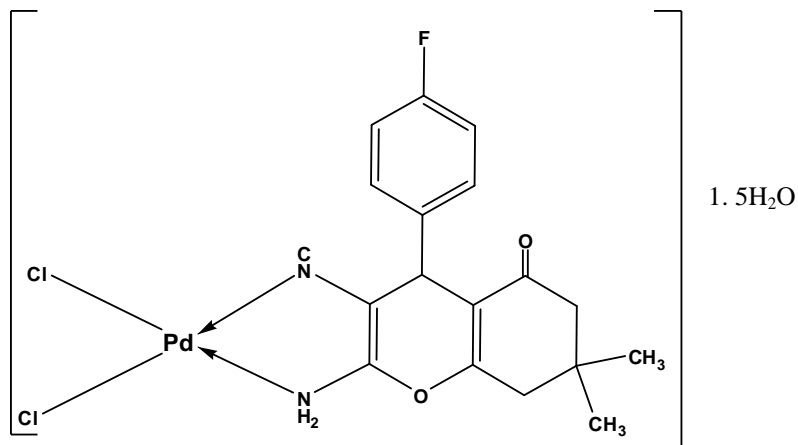
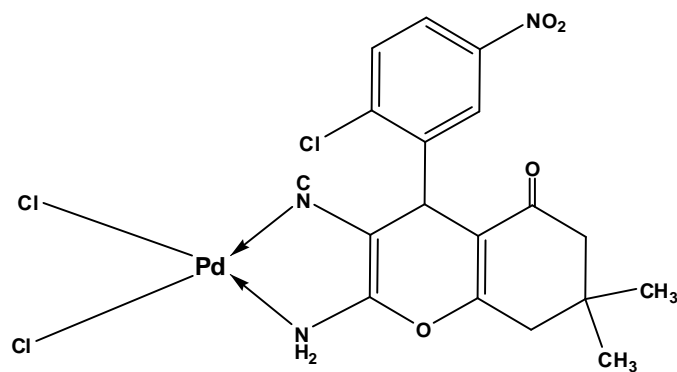


Fig. 13. ¹H NMR of [Pd L₁, 2Cl] 0.5H₂O complex.

TABLE 2. Suggestion of the elemental analysis of the Pd complexes .

Complex M.wt	% C		% H		% N		% Pd		MP
	Calc	Foud	Calc	Foud	Calc	Foud	Calc	Foud	
[Pd L ₁]									
512.5	45.31	44.49	4.86	4.32	5.46	5.13	21.2	20.93	280
[Pd L ₂]									
516	41.36	40.86	4.28	4.01	5.43	5.03	20.43	20.01	270
[Pd L ₃]									
550	39.23	39.03	2.93	2.91	7.62	9.89	19.31	19.13	290

Structure (4) of [Pd L₁] complex.Structure (5) of [Pd L₂] complex.

Structure (6) of $[Pd L_3]$ complex.

Conclusion

The well known of benzopyran derivatives have been synthesis by microwave radiation as green chemistry (L_1 , L_2 , L_3) these ligands have been used to synthesize their palladium (II) complexes This complexes were fully characterized by different tools. The geometry around the palladium ion is found to be square-planar $[Pd L_1.2Cl] 0.5H_2O$, $[Pd L_2 .2Cl] 1.5H_2O$ and $[Pd L_3 .2Cl]$.

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تخليق ودراسة التركيب الكيميائي لمتراكبات البلاديوم الثنائي مع مشتقات البنزوبيران

على مصطفى على حسن ، أحمد امام حنفي سيد ، نجلاء محمد عبدالرحمن*
ومحمد محمد محمود السيد
قسم الكيمياء – كلية العلوم – جامعة الأزهر و*قسم الكيمياء الخضراء – المركز
القومي للبحوث – القاهرة – مصر.

في هذه الدراسة تم تحضير وتوصيف المترابط الثنائي وهو مشتقات البنزوبيران وذلك باستخدام الميكرويف . تم أيضا تحضير متراكبات هذا المترابط مع عنصر البلاديوم الثنائي .

وبعد ذلك تم دراسة خصائص هذه المتراكبات بواسطة التحليل العنصري والأشعة تحت الحمراء و الأشعة فوق البنفسجية والرنين النووي المغناطيسي ومطياف الكتلة وكذلك قياس القابلية المغناطيسية للمتراكبات وقياس الرنين البرمي الإلكتروني وقد تم إثبات التركيب الكيميائي والتعرف على طرق إرتباط المرتبطات بأيونات العناصر الفلزية.

وبناء على هذه النتائج وجد أن البنزوبيران يتصرف كمترباط ثنائي عند تفاعله مع البلاديوم الثنائي وذلك من خلال مجموعتي (NH₂,CN) .

وفي هذه الدراسة أثبتت القياسات الحرارية وجود جزيئات الماء داخل وخارج اقواس التناسق.