Their Corresponding Organometallic Chelates of Chromium Group

1. Introduction

Numerous compounds containing metal and carbon monoxide have been prepared for a long time. Compounds having at least one bond between carbon and metal are known as organometallic compounds. Metal carbonyls are the transition metal complexes of carbon monoxide containing metal-carbon bonds. Lone pairs of electrons are available on both carbon and oxygen atoms of carbon monoxide ligand. However, as the carbon atoms donate electrons to the metal, these complexes are named as carboxyls [1]. Metal carbonyls are most of the time nonpolar and electrically neutral compounds and demonstrate physical properties of organic compounds. The general formula of metal carbonyls is \( \text{M}_x(\text{CO})_y \). These complexes may be homoleptic, that is containing only CO ligands, such as nickel carbonyl (Ni(CO)\(_4\)), but more commonly metal carbonyls contain a mix of ligands such as Re(CO)\(_3\)(2,2'-bipyridine)Cl. Metal carbonyls are highly toxic compounds because of their tendency to carboxylate hemoglobin to give carboxyhemoglobin, which will not bind \( \text{O}_2 \). They react vigorously with oxygen and oxidizing substances, and some ignite spontaneously. Metal carbonyls include solubility in only organic solvents but have poor solubility with water and volatile solid or liquid appearance at room temperature. Nevertheless, metal carbonyls serve as precursors for the preparation of other organometallic complexes [2].

On the other side, the chemistry of the amide group (−CONH\(_2\)) containing ligands is of great importance because it offers two potential binding atoms (the carboxylate oxygen and the amide nitrogen atom) as two coordination sites. This is in addition to their analytical, industrial, and pharmacological properties [3,4,5]. Maleanilic acid and its derivatives are one of the most important amide groups containing ligands; they are endowed with various types of biological activities. They are antitubercular agents; in addition to other pharmacological uses [6,7,8]. Furthermore, these compounds act as fungicides, herbicides, and plant growth regulators [9,10,11,12]. In organometallic chemistry, a number of complexes were reported with amide group ligands, which exhibit diverse coordinating behavior with different metal ions [13,14,15,16]. This feature returns to the fact that the maleanilic acid ligands coordinate to metals through the nitrogen of secondary amide and the oxygen of the carboxylate groups [5].

The above facts motivated us to prepare two derivatives of maleanilic acid ligands, \( p \)-methoxyphenyl (ML) and \( p \)-fluorophenyl (FL) maleanilic acid free ligands. Hence, we synthesized novel mixed ligand complexes with general formula \([\text{M(CO)}_4\text{L}]\) (where \( \text{M} = \text{Cr}, \text{Mo} \) or \( \text{W} \); and \( \text{L} = \text{ML} \) or \( \text{FL} \)) by the reaction of ML or FL free ligands with the metal atom in the form of hexacarbonyl metals \( \text{M(CO)}_6 \) (where \( \text{M} = \text{Cr}, \text{Mo} \) or \( \text{W} \)). The molecular structures of the synthesized mixed ligand complexes were characterized and studied by elemental analyses, Fourier-transform infrared spectroscopy (FT-IR), electron ionization mass...
2. Experimental

2.1. Materials and reagents

All chemicals used in the present study are of analytical reagent grade and of the highest purity available. They include maleic anhydride, 4-fluoroaniline, 4-methoxyaniline, Cr(CO)₆, Mo(CO)₆, and W(CO)₆. They are purchased from Sigma Aldrich (MO, USA). This is in addition to absolute ethanol, dimethylformamide (DMF), and dimethylsulfoxide (DMSO) which are purchased from Alpha Aesar and used without further purification.

2.2. Instrumentation

Weights measurement was performed using sensitive analytical balance (0.0001 g, SCALTEC; Germany). Stirring and heating were performed using a thermostat hotplate magnetic stirrer (VELP; Europe). A melting-point apparatus (GallenKamp; Germany) was used to investigate the melting points. Elemental microanalysis of the separated solid compounds for C, H, and N was performed in the Microanalytical Centre, Cairo University. The infrared spectra were measured using a Perkin Elmer FT-IR type 1650 spectrophotometer in the wavenumber region 4000–400 cm⁻¹ as KBr disks. ¹H-NMR spectroscopy was recorded on a Bruker DPX 400 spectrometer (300.068787 MHz); DMSO was used as the internal reference solvent. The EI-MS measurements were obtained using Shimadzu GC-MS-Qp 1000 PX quadruple mass spectrometer. The thermal analyses of the novel compounds were made using a conventional thermal analyzer (Shimadzu system of 30 series TG-50). These instruments were calibrated using indium metal as a thermally stable material. The reproducibility of the instrument reading was determined by repeating each experiment more than twice.

2.3. Synthesis of free ligands and complexes

2.3.1. Synthesis of free ligands

ML was prepared by mixing both of p-methoxyaniline (0.1 mol, 12.32 g) and maleic anhydride (0.1 mol, 9.8 g) in a 1:1 molar ratio and grinding them at room temperature for 40 min using an agate mortar [17]. During crushing, a nice greenish-yellow product appeared. The product was recrystallized from absolute ethanol and dried under vacuum over P₂O₅ to calculate the yield (92%). All the above steps were repeated for FL maleanilic acid with a yield of about 88%. The synthesis of maleanilic acid derivatives ML and FL as ligands are schematically represented in Scheme 1.

2.3.2. General procedures for the synthesis of the novel complexes of maleanilic acid derivatives

Chromium complex of ML ligand was prepared by Cooper et al. modified method [18] in which the prepared ML maleanilic acid ligand (0.11 g, 0.5 mmol) was dissolved in the least amount of DMF, then added to Cr(CO)₆ (0.11 g, 0.5 mmol). The volume of the reaction mixture solution was completed to 20 mL using DMF solvent. It was stirred for 40 min under reflux at 90–100 °C. After refluxing, a dark yellow solution appeared. The collected product was filtered off, washed thoroughly with absolute ethanol, recrystallized from DMF/ethanol mixture and dried under vacuum. All the above steps were repeated for all the selected transition metal complexes 1–6. The synthesis of the novel complexes of maleanilic acid derivatives is schematically represented in Scheme 1.

2.4. Pharmaceutical materials and methods

The cell lines of HCT-116, HepG-2, and MCF-7 cells were obtained from VACSERA Tissue Culture Unit (Giza, Egypt); crystal violet and trypan blue dyes were purchased from Sigma Aldrich. DMSO, fetal bovine serum, DMEM, RPMI-1640, HEPES buffer solution, L-glutamine, gentamycin, and 0.25% trypsin-EDTA were purchased from Lonza (Basel, Switzerland); crystal violet stains were 1%. The cells were propagated in Dulbecco’s Modified Eagle’s Medium (DMEM) supplemented with 10% heat-inactivated fetal bovine serum, 1% L-glutamine, HEPES buffer, and 50 μg mL⁻¹ gentamycin. All cells were maintained at 37 °C in a humidified atmosphere with 5% CO₂ and were subcultured two times a week. The cells were seeded in 96-well plate at a cell concentration of 1 × 10⁴ cells per well in 100 μL of growth medium. Fresh medium containing different concentrations of the tested chemical compound were added to confluent cell monolayers dispersed into 96-well, flat-bottomed microtiter plates (Falcon; NJ, USA) using a multichannel pipette. The microtiter plates were incubated at 37 °C in a humidified incubator with 5% CO₂ for a period of 48 h.
Three wells were used for each concentration of the test sample. Control cells were incubated without test sample and with or without DMSO. The little percentage of DMSO present in the wells (maximal 0.1%) was found not to affect the experiment. After incubation of the cells for at 37 °C, various concentrations of the sample were added, the incubation was continued for 24 h, and viable cells yield was determined using MTT assay [19,20].

3. Results and discussion

3.1. Characterization of ML and FL ligands and their novel metal complexes

ML and FL ligands were prepared by the method described above (Scheme 1). The structures of the synthesized ligands were established by elemental analyses, FT-IR, EI-MS, 1H-NMR spectrometry, and thermal analyses. Cr, Mo or W novel complexes of the ML and FL ligands were synthesized in a 1:1 molar ratio (metal:ligand), using the described metal atoms in the form of hexacarbonyl metals M(CO)6 (Scheme 1). The synthesized metal complexes of the chemical formula of [M(CO)4L], where M = Cr, Mo or W and L = ML or FL, are microcrystalline in nature and stable at room temperature. They are insoluble in common organic solvents such as chloroform and acetone but they are completely soluble in DMSO and DMF. Unfortunately, we failed to grow the single crystal of metal complexes. Therefore, in order to have a better understanding of the molecular structure, we have performed the elemental analysis, FT-IR, EI-MS, 1H-NMR spectroscopy, and thermal analyses. Physical measurements and elemental analyses data of the novel complexes 1–6 are given in Table 1. The elemental analyses of the ligands and their complexes reveal good agreement with the proposed structures.

3.2. 1H-NMR spectra

The 1H-NMR spectra for ML, FL ligands and their complexes have been recorded in DMSO solvent. The 1H-NMR spectrum of ML showed that a singlet at δ 3.71 ppm of relative intensity 3H may be attributed to OCH3 protons. Another singlet at δ 12.88 ppm of relative intensity 1H is observed and may be assigned to OH proton of the carboxylic acid. The amide proton HNCO is observed as a singlet at δ 10.38 ppm. The aromatic protons ortho to the methoxy group (H e,H d) are observed as a doublet of doublets at δ 7.51–7.58 ppm and another doublet of doublets at δ 7.88–6.92 ppm for the protons which are ortho to the amide group (Hc,H f). The two doublets signals (Hc,H f) and (He,H d) have the same coupling constant J and the same integrated area, indicating the presence of four protons with two couples that are chemically equivalent but not magnetically equivalent [21]. The vinylic protons (H a,H b) are observed as a doublet of doublets at δ 6.45–6.44 ppm and δ 6.27–6.30 ppm of relative intensity 1H. The proposed structure of the free ligands is given in Figure 1.
On the other hand, the spectra of ML ligand complexes 2–3 of the type [M(CO)₄ML] (Figures 2(a) and 2(b)) show a shift in the free ligand carboxylic OH proton signal, confirming the possibility of chelation through OH group of the free ligand carboxylic group. The signal of H-NCO free ligand proton is slightly shifted in the spectra of the metal complexes indicating the possibility of sharing the ML amide group in the coordination process. The doublet of doublets signals of the ML ligand aromatic protons are slightly shifted in the spectra of its complexes. The free ligand vinylic proton Hα is slightly shifted to δ 6.37–6.25 ppm and δ 6.34–6.24 ppm for Mo and W complexes, respectively. The other vinylic proton Hβ is slightly shifted to δ 6.41–6.29 ppm and δ 6.38–6.28 ppm for [Mo(CO)₄ML] and [W(CO)₄ML], respectively. All ¹H-NMR data are listed in Table 2. The above discussion of the ¹H-NMR spectrum of ML maleamic acid confirms the proposed structure presented in Figure 3.

3.3. FT-IR spectra
The FT-IR spectrum of ML ligand shows a broadband at 3,262 cm⁻¹, which may be attributed to ν (O–H) of carboxylic acid group vibration frequency [22]. The strong stretching band at 1,699 cm⁻¹ may be assigned to ν (C=O) of the carboxylic group. The strong bands observed at 3,000 cm⁻¹ and 3,068 cm⁻¹ may be attributed to the aromatic ν (C–H) [23]. The medium bands observed at 2,841 cm⁻¹, 2,834 cm⁻¹, 2,837 cm⁻¹, and 2,833 cm⁻¹ may be assigned to ν (O–CH₃) of the methoxy group [24]. The ν (N–H) amide stretching band is observed at 3,198 cm⁻¹ and the stretching frequency band of the amide carbonyl group ν (C=O) is observed at 1,620 cm⁻¹ [25,26]; see Figure 4.

FT-IR frequencies of ML ligand metal complexes are presented in Figures 5–7 and its corresponding data are tabulated in Table 3. The broad ν (O–H) band of the carboxylic acid group of ML ligand is shifted to a higher value in the spectrum of its metal complexes; which means that it is affected by chelation. The strong ν (C=O) stretching band at 1,699 cm⁻¹ of the free ligand carboxylic group is shifted to 1,710 cm⁻¹, 1,705 cm⁻¹, and 1,707 cm⁻¹ for [Cr(CO)₄ML], [Mo(CO)₄ML], and [W(CO)₄ML], respectively [22,23,24,27]. The ν (C=O) band of the free ligand carboxylic group
Table 2: $^1$H-NMR data of ML, FL ligands and their Mo and W complexes.

| Compound | $\delta$-O−H | $\delta$N−H | $\delta$O−CH$_3$ | $\delta$H$^a$ | $\delta$H$^b$ | $\delta$H$^c$ | $\delta$H$^d$ | $\delta$H$^f$ | $^3$J (H$^a$−H$^b$) | $^3$J (H$^c$−H$^d$) | $^3$J (H$^e$−H$^f$) |
|----------|--------------|-------------|----------------|------------|------------|------------|------------|------------|----------------|----------------|----------------|
| ML       | 12.88        | 10.38       | 3.73           | 6.42       | 6.40       | 7.57       | 6.93       | 6.93       | 7.56           | 6             | 3             | 2.4          |
| FL       | 11.99        | 10.35       | —              | 7.23       | 7.21       | 7.78       | 7.48       | 7.48       | 7.78           | 6.3           | 6.6           | 1.8          |
| 2        | 10.96        | 10.25       | 3.73           | 6.37       | 6.41       | 6.91       | 6.88       | 6.88       | 6.91           | 12            | 9             | 9            |
| 3        | 11.3         | 10.36       | 3.73           | 6.34       | 6.38       | 6.90       | 6.93       | 6.93       | 6.90           | 12            | 9             | 9            |
| 5        | 10.82        | 10.59       | —              | 6.40       | 6.44       | 7.63       | 7.66       | 7.66       | 7.63           | 12            | 9             | 9            |
| 6        | 10.66        | 10.50       | —              | 6.41       | 6.45       | 7.62       | 7.65       | 7.65       | 7.62           | 12            | 9             | 9            |

Table 3: FT-IR spectra of ML, FL free ligands and their complexes 1–6.

| Compound | $\nu$ (C=O) (COOH) | $\nu$ (C=O) amide(I) | $\nu$ (OH) | $\nu$ (C−H) aromatic | $\nu$ (C=O) (OCOH) | $\nu$ (NH) amide | $\nu$ (M−O) | $\nu$ (C=O) carbonyl | $\nu$ (M−C) |
|----------|-------------------|----------------------|-----------|----------------------|-------------------|----------------|------------|---------------------|------------|
| ML       | 1,699 s 1,620 m   | 3,262 s              | 3,068 w | 1,304 m              | 3,198 w           | —              | —          | —                   | —          |
| FL       | 1,702 s 1,595 m   | 3,270 s              | 3,093 w | 1,320 m              | 3,209 w           | —              | —          | —                   | —          |
| Cr(CO)$_6$ | —        | —                   | —        | —                    | —                 | —              | —          | —                   | 2,043 s   | 600 |
| Mo(CO)$_6$ | —        | —                   | —        | —                    | —                 | —              | —          | 2,000 s              | 550       |
| W(CO)$_6$ | —        | —                   | —        | —                    | —                 | —              | —          | —                   | 2,073 s   | 540 |
| 1        | 1,710 s 1,611 m   | 3,049 s              | 3,073 w | 1,243 m              | 3,409 w           | 550            | 2,047-1,935-1,869 | 527 s     |                   |
| 2        | 1,705 s 1,625 m   | 3,436 s              | 3,067 w | 1,243 m              | 3,436 w           | 558            | 2,049-1,914-1,872 | 521 m     |                   |
| 3        | 1,707 s 1,632 m   | 3,425 s              | 3,063 w | 1,241 m              | 3,429 w           | 594            | 2,049-1,918-1,873 | 520 m     |                   |
| 4        | 1,704 s 1,657 m   | 3,342 s              | 3,072 w | 1,217 m              | 3,294 w           | 516            | 2,208-1,953-1,878 | 542 m     |                   |
| 5        | 1,701 s 1,633 m   | 3,420 s              | 3,067 w | 1,221 m              | 3,355 w           | 601            | 2,076-1,903-1,879 | 487 m     |                   |
| 6        | 1,702 s 1,633 m   | 3,416 s              | 3,066 w | 1,219 m              | 3,250 w           | 595            | 2,056-1,901-1,876 | 485 m     |                   |

Figure 5: FT-IR of ML chromium complex 1 [Cr(CO)$_4$ML].

is shifted to 1,243 cm$^{-1}$, 1,243 cm$^{-1}$, and 1,241 cm$^{-1}$ in the spectra of Cr, Mo, and W complexes, respectively. This may indicate to the sharing of the free ligand hydroxyl oxygen atom in the coordination process. The aromatic

Figure 6: FT-IR of ML molybdenum complex 2 [Mo(CO)$_4$ML].
\( \nu \) (C–H) strong bands of the ML ligand are slightly shifted to (3,073 cm\(^{-1}\), 3,020 cm\(^{-1}\), 3,067 cm\(^{-1}\), 3,010 cm\(^{-1}\)), and (3,063 cm\(^{-1}\), 3,017 cm\(^{-1}\)) in the spectra of Cr, Mo, and W complexes, respectively. The medium bands of the methoxy group \( \nu \) (O–CH\(_3\)) are observed at 2,834 cm\(^{-1}\), 2,837 cm\(^{-1}\), and 2,833 cm\(^{-1}\) in the spectra of [Cr(CO)\(_4\)ML], [Mo(CO)\(_4\)ML], and [W(CO)\(_4\)ML], respectively [23].

The \( \nu \) (N–H) amide stretching band of the ML ligand is shifted by 200–240 cm\(^{-1}\) compared to (1,869, 1,872, and 1,873) cm\(^{-1}\) in the spectra of [Cr(CO)\(_4\)ML], [Mo(CO)\(_4\)ML], and [W(CO)\(_4\)ML], respectively. This result may indicate the coordination of the free ligand upon the nitrogen of the amide group [28]. The \( \nu \) (N–H) deformation band of ML free ligand observed at 761 cm\(^{-1}\) is slightly shifted in the spectrum of its metal complexes. This confirms the coordination of ML ligand with the metal atoms [29]. The \( \nu \) (C–O) bond of hexacarbonyl metals Cr(CO)\(_6\), Mo(CO)\(_6\), and W(CO)\(_6\) is shifted from 441 cm\(^{-1}\), 368 cm\(^{-1}\), and 374 cm\(^{-1}\) [33] to 527 cm\(^{-1}\), 521 cm\(^{-1}\), and 510 cm\(^{-1}\) in the spectra of [Cr(CO)\(_4\)ML], [Mo(CO)\(_4\)ML], and [W(CO)\(_4\)ML] metal complexes, respectively [34].

### 3.4. EI-MS Measurements

The mass spectra of all metal complexes are generally similar. The mass spectrum of chromium complex 1 (Figure 8) is characterized by many competitive and consecutive pathways, forming the main molecular ion and many fragment ions. The fragments are shown in Scheme 2. The signal of moderate intensity (RI = 15%) at m/z = 383.3 (M\(^+\)) may be attributed to the molecular ion of [CrC\(_{15}\)H\(_8\)O\(_8\)N\(^\cdot\)]\(^+\) (mole mass = 384). The fragment ion is fragmented through four parallel pathways. Pathway I shows a fragment ion at m/z = 163 (mole mass = 164, RI = 10\%); this signal may refer to the rupture of ML maleanilic acid. Pathway II shows fragment ions CrC\(_{13}\)H\(_{11}\)O\(_8\)N\(^\cdot\), CrC\(_6\)H\(_5\)O\(_2\)N\(^\cdot\), and CrC\(_2\)O\(_2\)\(^\cdot\). These fragment ions are observed at m/z = 329, 119, and 111; they may be assigned to the loss of two molecules of CO group from the molecular ion followed by separating \( p \)-methoxybenzene, then the loss of 4-amino-4-oxobut-2-enoic acid. In pathway III, the signal at m/z = 221 (mole mass = 221, RI = 40\%) may be assigned to the rupture of Cr(CO)\(_4\) from the molecular ion. The peak at m/z = 113 (mole mass = 113, RI = 17\%) may be assigned to the loss of 4-methoxybenzene. The final pathway shows signals at m/z = 276, 219, and 113 (mole masses = 276, 220, and 115 with RI = 15\%, 20\%, and 20\%), respectively.

### 3.5. Thermal Analyses of the Novel Metal Complexes

The thermal behavior of all ML metal complexes and all FL metal complexes is generally similar. The TGA curve (Figure 9) illustrates the thermal decomposition of complex 1 through two main steps of mass losses. The first step occurs within the temperature range of 250–330°C and at exactly DTG temperature of 330°C. This step requires an energy 141.557 kJ.mol\(^{-1}\) of estimated mass loss of 41.7% (calcd. 42.7%), which may be attributed to the removal of both \( p \)-methoxybenzene group of chemical formula C\(_7\)H\(_8\)O (mole mass = 108 g) and two molecules of CO gas (mole mass = 56 g). The second step occurs within the temperature range 330–450°C and with a
Table 4: Thermoanalytical results (TG and DTG) of ML, FL complexes 1–6.

| Compound     | Temp. range (°C) | % Mass loss found (calcd.) | Assignment                                                                 |
|--------------|------------------|----------------------------|-----------------------------------------------------------------------------|
| [Cr(CO)₄ML]  | 1 250–330        | 41.7 (42.7)                | – The loss of 4-methoxybenzene + 2CO                                        |
| [Cr(CO)₄ML]  | 2 330–450        | 27.92 (29)                 | – The loss of 4-amino-4-oxobut-2-enoic acid                                 |
| [Mo(CO)₄ML]  | 3 130–180        | 22.44 (21.57)              | – The loss of OH C–C₆H₅                                                     |
| [Mo(CO)₄ML]  | 4 180–385        | 13.05 (12.18)              | – The loss of HO–CH₂–CH₂–NH₂                                               |
| [W(CO)₄ML]   | 5 131–280        | 34.6 (37.32)               | – The loss of ML maleamic acid ligand                                       |
| [W(CO)₄ML]   | 6 280–350        | 4.33 (4.74)                | – The loss of HO–CH₂–CH₂–NH₂                                               |
| [W(CO)₄ML]   | 7 350–589        | 4.64 (4.74)                | – The loss of ML maleamic acid ligand                                       |
| [Cr(CO)₄FL]  | 8 131.9–395.8    | 32.69 (30)                 | – The loss of p-fluoroaniline                                               |
| [Mo(CO)₄FL]  | 9 399–509        | 28.65 (26.8)               | – The loss of (Z)-4-oxobut-2-enoic acid                                    |
| [Mo(CO)₄FL]  | 10 140.7–233.3   | 2.9 (3.8)                  | – The loss of fluorene                                                      |
| [W(CO)₄FL]   | 11 233.3–431.3   | 37.76 (38.78)              | – The loss of maleamic acid ligand                                         |
| [W(CO)₄FL]   | 12 141–336       | 16.83 (17.81)              | – The loss of p-fluoroaniline                                               |

Table 5: Kinetic and thermodynamic parameters data of the metal complexes 1–6.

| Compound     | Step | Temp. range (°C) | E* (kJ.mol⁻¹) | A (S⁻¹) | ΔS* (JK⁻¹.mol⁻¹) | ΔH* (kJ.mol⁻¹) | ΔG* (kJ.mol⁻¹) |
|--------------|------|------------------|--------------|---------|-----------------|---------------|---------------|
| [Cr(CO)₄ML]  | 1    | 250–330          | 141.557      | 1.23442E+12 | −234.19         | 136.534       | 277.887       |
| [Cr(CO)₄ML]  | 2    | 330–450          | 116.846      | 1.2383241.1 | −236.66         | 111.116       | 269.50        |
| [Mo(CO)₄ML]  | 3    | 131–180          | 197.467      | 1.40428E+23 | −228.69         | 193.851       | 293.261       |
| [Mo(CO)₄ML]  | 4    | 399–509          | 28.65 (26.8) | 759103782.8 | −251.44         | 14.976        | 193.222       |
| [Cr(CO)₄FL]  | 5    | 131–280          | 46.73        | 5.4131E+07  | −103.04         | 41.53         | 105.93        |
| [Cr(CO)₄FL]  | 6    | 131–395          | 31.00        | 5.670E+07   | −99.41          | 27.48         | 69.54         |
| [Mo(CO)₄FL]  | 7    | 390–509          | 158.93       | 3.689E+10   | −49.59          | 153.20        | 187.36        |
| [W(CO)₄FL]   | 8    | 140–233          | 132.64       | 1.429E+14   | −22.42          | 128.78        | 118.41        |
| [W(CO)₄FL]   | 9    | 233–431          | 43.89        | 4.671E+07   | −104.55         | 38.50         | 110.6         |

DTG peak at 396 °C. This step requires an energy of 116.68 kJ.mol⁻¹ and it may refer to the estimated mass loss of 27.92% (calcd. 29%), which may be attributed to the loss of 4-amino-4-oxobut-2-enoic acid (mole mass = 115 g). The total mass loss may be 69.26% (calcd. 71.7%) and the remainder may be Cr(CO)₂ of estimated mass loss of 30.38% (calcd. 28.3%). These data are tabulated in Table 4. The values of the obtained thermodynamic parameters are E* (141.557 and 116.684 kJ.mol⁻¹), ΔS* (−234.19 and −236.66 JK⁻¹.mol⁻¹), ΔH* (136.534 and 111.116 kJ.mol⁻¹), and ΔG* (277.887 and 269.50 kJ.mol⁻¹); see Table 5. The thermal behavior of the other metal complexes is presented in Tables 4 and 5.

3.6. The correlation between the mass spectrum and the thermal analyses of the metal chelates

The mass spectrum of [Cr(CO)₄ML] (Scheme 2, pathway II) shows that the molecular ion of the metal chelate is observed at m/z = 383.3 (mole mass = 384). This parent ion is exposed to consecutive fragmentations CrC₃H₁₁O₆N⁺, CrC₆H₂O₂N⁺, and CrC₂O₂⁺, respectively. These fragment ions are observed at m/z = 329, 119, and 108, respectively. They may be assigned to the loss of two molecules of CO groups from the molecular ion followed by separating p-methoxybenzene, then the loss of 4-amino-4-oxobut-2-enoic acid. This possibility of fragmentation is confirmed by the thermal decomposition of the metal chelate. The
TGA and DTGA thermogram (Figure 9) shows that [Cr(CO)₄ML] is decomposed through two steps. The first step occurs within the temperature range 250–330 °C of mass loss = 41.7% (calcd. 42.7%), which may be attributed to the removal of both p-methoxybenzene compound and two molecules of CO gas. The second step occurs in the temperature range of 330–396 °C; it may refer to the loss of 4-amino-4-oxobut-2-enolic acid. The total mass loss may be 69.26% (calcd. 71.7%) and the remainder may be Cr(CO)₂ of an estimated mass loss of 30.38% (calcd. 28.3%).

3.7. Biological activity of FL and its chromium complex

Evaluation of the efficacy of FL free ligand as an inhibitor revealed a higher potency against HepG-2, MCF-7, and HCT-116 human cancer cell lines; as shown in Figure 10. The calculated IC₅₀ values are 60.4 μg mL⁻¹, 60.4 μg mL⁻¹, and 53.7 μg mL⁻¹ for HepG-2, MCF-7, and HCT-116 cell lines, respectively; as shown in Table 6. The cytotoxic activity of [Cr(CO)₄FL] was assayed using HepG-2, MCF-7, and HCT-116 cell lines; the cell viability (%) obtained with continuous exposure for 24 h is depicted in Figure 11.

4. Conclusion

ML and FL maleanilic acid derivatives were successfully prepared by crushing the mixture powders of maleic anhydride and different aniline derivatives using an agate mortar at room temperature in a good yield. Elemental analyses, FT-IR, and ¹H-NMR results confirm the proposed structures of these compounds. Also, they prove the success of the synthetic method of these compounds. The synthesized ML and FL ligands coordinate in a molar ratio 1:1 with some transition metals in the form of hexacarbonyl metals M(CO)₆ (where M = Cr, Mo or W). The structure of the novel complexes was confirmed by elemental analyses,
FT-IR, ¹H-NMR, EI-MS, and thermal analyses. These analytical tools confirm that the maleanilic acid derivatives ligands have succeeded in replacing two carbonyl groups from the hexacarbonyl metals. Furthermore, they prove that the metal carbonyl complexes are in a good agreement with their proposed structures of [M(CO)₅L] in which M = Cr, Mo or W and L = ML or FL maleanilic acid derivatives. The antitumor activities (in vitro) of FL maleanilic acid derivative and its chromium complex against three types of cancer cells [HepG-2, MCF-7, and HCT-116] are studied. It is found that FL free ligand has more antitumor activity than that of its chromium complex.

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Conflict of interest The authors declare that they have no conflict of interest.

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