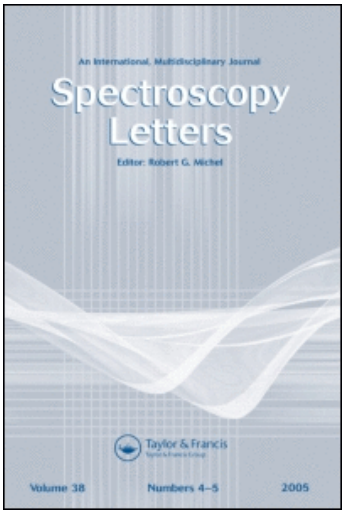


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# Spectroscopic Elucidation of the Coordination Ability of 2-Oxo-2*H*-Chromene-3-Phosphonic Acid with Pt(II)

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**ABSTRACT** The coordination ability of 2-oxo-2*H*-chromene-3-phosphonic acid with Pt(II) both in solution and in solid state is elucidated by means of conventional and linear-polarized IR spectroscopy of oriented colloid suspensions in nematic liquid crystal, $^{1}$H-, $^{13}$C-, and $^{31}$P-NMR, UV-Vis spectroscopy, positive and negative mass spectrometry (ESI and FAB), and TGV and DSC methods. A comparison with the spectroscopic data of ammonium salt of 2-oxo-2*H*-chromene-3-phosphonic acid is carried out as well.

**KEYWORDS** 2-Oxo-2*H*-chromene-3-phosphonic acid, Pt(II) complex, spectroscopic and structural elucidation

## INTRODUCTION

As a part of our systematic study on the synthesis and spectroscopic and structural characterization of phosphorus-containing coumarins with potential biological activity,[1–5] we report the new Pt(II) complexes of 2-oxo-2*H*-chromene-3-phosphonic acid (Scheme 1). The coordination ability of the ligand is elucidated both in solution and in solid state using the possibilities of conventional and linear-polarized IR spectroscopy of oriented colloid suspensions in nematic liquid crystal, $^{1}$H-, $^{13}$C-, and $^{31}$P-NMR, UV-Vis spectroscopy, positive and negative mass spectrometry (electro shprei ionisation (ESI) and fast atom bombardment (FAB)), and thermogravimetry (TGV) and differential scanning calorimetry (DSC) methods. In parallel, the detailed elucidation of the manner of coordination of the ligand through the metal ion and a comparison between the neutral 2-oxo-2*H*-chromene-3-phosphonic acid and its ammonium salt (Scheme 1) is carried out.

Coumarins, an old class of compounds, are naturally occurring benzopyrene derivatives. A lot of coumarins have been identified from natural sources, especially green plants. The pharmacologic and biochemical properties and therapeutic applications of simple coumarins depend upon the pattern of substitution. Coumarins have attracted intense interest in recent years because of their diverse pharmacologic properties. Among these properties, their cytotoxic effects were most extensively examined. Their broad range of effects on tumors as shown by various *in vitro* and *in vivo* experiments and clinical

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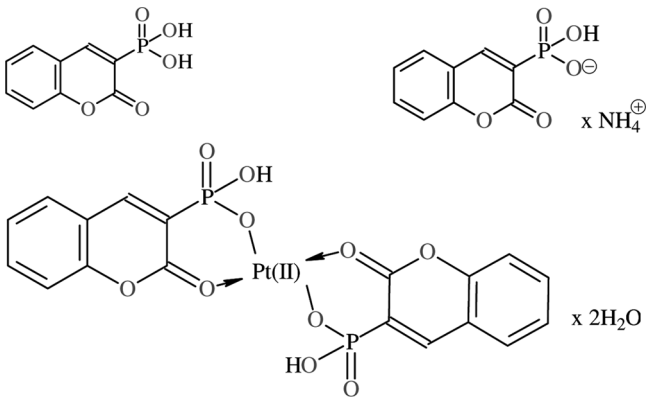


**SCHEME 1** **Chemical diagram of 2-oxo-2*H*-chromene-3-phosphonic acid, ammonium salt, and Pt(II) complex.**

studies have been discussed.[6–9] These cytotoxic coumarins represent an exploitable source of new anticancer agents, which might also help address side-toxicity and resistance phenomena. These natural compounds have served as valuable leads for further design and synthesis of more active analogues.[6–9] Owing to their diverse effects and inconclusive results from different *in vitro* studies, the mechanism of their action is not yet fully understood, and correlation of effects with chemical structures is not conclusive at the moment. It has been concluded that there is still a long way to go until we know which cytotoxic agent will clinically be suitable for what tumor entity for treatment. Their ability to bind metal ions represents an additional means of modulating their pharmacologic responses. On the other side, platinum complexes are widely used as anticancer medications,[10,11] and for these reasons the synthesis and spectroscopic and structural elucidation of Pt(II) complexes with coumarins can open a new path in the design of the anticancer medications. The cytotoxic activity of new zirconium (II) complex with coumarins has been proved.[12] New samarium (III), gadolinium (III), and dysprosium (III) complexes of coumarin-3-carboxylic acid as antiproliferative agents have been presented. Cytotoxic effect of new Pd(II) and Pt(II) complexes with 2-ethanimidolyl-2-methoxy-2*H*-1,2-benzoxaphosphinin-4-ol-2-oxide are also studied.[12,13]

# MATERIALS AND METHODS

## Methods

*Conventional and polarized IR spectra* were measured on a Thermo Nicolet OMNIC FTIR spectrometer (4000–400 $cm^{-1}$, 2 $cm^{-1}$ resolution, 200 scans) equipped with a Specac wire-grid polarizer. Non-polarized solid-state IR spectra were recorded using the KBr disk technique. The oriented samples were obtained as a colloid suspension in a nematic liquid crystal ZLI 1695. The theoretical approach, experimental technique for preparing the samples, procedures for polarized IR spectra interpretation, and the validation of this new linear-dichroic infrared (IR-LD) orientation solid-state method for accuracy and precision has been presented. The influence of the liquid crystal medium on peak positions and integral absorbances of the guest molecule bands, the rheological model, the nature and balance of the forces in the nematic liquid crystal suspension system, and morphology of the suspended particles has also been discussed.[14–17]

The *positive and negative ESI mass* as well as *FAB* spectra were recorded on a Fisons VG autospect instrument employing 3-nitrobenzylalcohol (Sigma-Aldrich, Germany) as the matrix.

*Ultraviolet (UV) spectra* were recorded on a Specord UV-VIS (Carl Zeiss-Jena, Germany) using water as solvent and 0.0921-cm quartz cells.

The *thermal analyses* were performed in the 300–500 K region on a differential scanning calorimeter (Perkin-Elmer DSC-7) and a differential thermal analyzer (DTA/TG, Seiko Instrument, model TG/DTA 300). The experiments were carried out with scanning rate of 10 K/min under an argon atmosphere.

The *elemental analysis* was carried out according to the standard procedures for C and H (as $CO_2$ and $H_2O$) and N (by the Dumas method).

The *$^1$H-, $^{13}$C-, and $^{31}$P-NMR measurements* were performed at 298 K with a Bruker (Germany) DRX-600 spectrometer using 5-mm tubes and $D_2O$ as solvent. The chemical shift reference was sodium 3-(trimethylsilyl)tetradeuteriopropionate.

## Synthesis

The ammonium salt of 2-oxo-2*H*-chromene-3-phosphonic acid was obtained in the following way: 10 mL water solution containing 0.4901 g of the 2-oxo-2*H*-chromene-3-phosphonic acid (synthesized according to procedure described in Ref. 5) were mixed with 45 mL k-concentrated. $NH_4OH$ under continuous stirring at room temperature for 2-h. After a week, the obtained white precipitate was filtered off and dried under air (found: C,

44.50%; H, 4.15%, N, 5.78%; [$C_9H_{10}NO_5P$] calcd.: C, 44.46%; H, 4.15%; N, 5.76%). The most intensive signal in the negative ESI mass spectrum is that of the peak at $m/z$ 225.23, corresponding with the charged anion $[C_9H_6O_5P]^-$ with a molecular weight of 225.11.

The Pt(II) complex with 2-oxo-2*H*-chromene-3-phosphonic acid was obtain as follows: 0.6521 g of the ligand are dissolved in 15 mL water and to the obtained solution is added 1 mL 1 M HCl. Then, 10 mL $K_2PtCl_4$ (0.1212 g) is added to first solution under continuously stirring and heating at 70°C for 2 h. After 48 h, the obtained yellow precipitate was filtered off and dried under air. The red color of the starting Pt(II) salt (Fig. 1) is changed to yellow after the coordination (found: C, 31.88%; H, 2.70%; [$C_{18}H_{16}O_{12}P$] calcd.: C, 31.73%; H, 2.73%). The formed complex is stable during the period of 1 month. The most intensive signal in the FAB mass spectrum is that of the peak at $m/z$ 646.80, corresponding with the charged ion $[C_{18}H_{16}O_{12}P_2Pt]^+$with with a molecular weight of 646.32.

## RESULTS AND DISCUSSION

### UV-Vis Spectroscopic Data

The electronic spectra of the 2-oxo-2*H*-chromene-3-phosphonic acid, its ammonium salt, and Pt(II) complex in methanol are depicted in Fig. 1. The UV spectrum of the ligand is characterized with two maxima with $\lambda_{max}$ at 286 nm ($\varepsilon = 13\,243\,L\,mol^{-1}\,cm^{-1}$) and 322 nm ($\varepsilon = 1034\,L\,mol^{-1}\,cm^{-1}$) belonging to *B*-band of the aromatic ring and conjugated $n \rightarrow \pi^*$ transition of carbonyl group. The deprotonation of both the OH groups in phosphonic acid result in a hypsochromic shift of the last band with 15 nm and weak decreasing of the intensity ($\varepsilon = 985\,L\,mol^{-1}\,cm^{-1}$), respectively. Similar tendency is observed looking on the UV spectrum of corresponding Pt(II) complex. However, the last spectrum shows a broad absorption band within the whole 350–500 nm, usually observed in the Pt(II) complexes with significant charge transfer effect, when the metal ion is coordinated with O-heteroatoms.[11] These results proposed that in solution, Pt(II) is coordinated through the O-atom of phosphonic acid by preliminary deprotonation of the OH groups.

### Conventional and Linear-Polarized IR Spectroscopic Data

The adequate characterization of coordination ability of 2-oxo-2*H*-chromene-3-phosphonic acid requires a preliminary detailed IR-characteristic IR-band assignment of the free ligand. The compound in solid

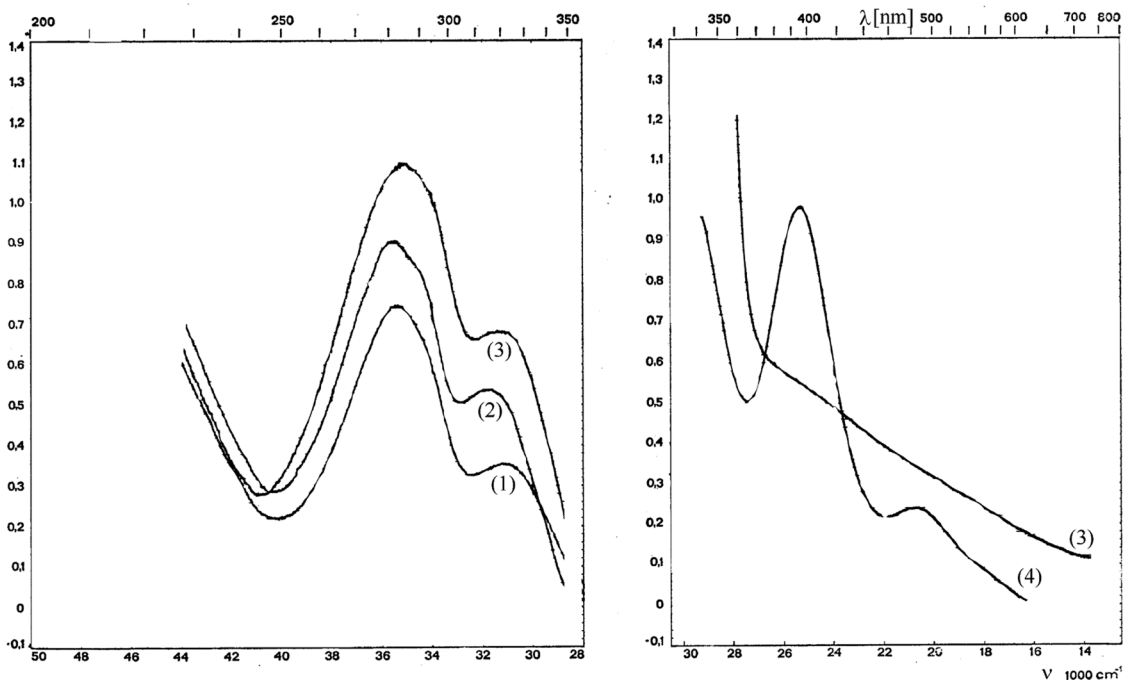


**FIGURE 1** **UV-Vis spectra of 2-oxo-2*H*-chromene-3-phosphonic acid (1), its ammonium salt (2), and Pt(II) complex (3); Vis spectrum of $K_2PtCl_4$ (4).**

state is characterized with significant degree of orientation in nematic host (see the difference IR-LD spectrum in Fig. 2 and Ref. 14–17), thus assuming a precise interpretation of the data by the reducing-difference procedure.

The IR spectrum in Fig. 2 is characterized with broad absorption band within 3400–2000 $cm^{-1}$ belonging to OH stretching vibrations ($\nu_{OH}$) of phosphonic acid, when strong intermolecular interactions are observed in condensed phase.[14–17] The intensive pairs of bands at 1720 $cm^{-1}$ correspond with C=O stretching vibration ($\nu_{C=O}$). The in-plane (i.p.) stretching modes of aromatic fragment are observed at 1612 $cm^{-1}$, 1565 $cm^{-1}$, and 1486 $cm^{-1}$. These bands are eliminated at equal dichroic ratio thus confirming their origin. Out-of-plane (o.p.) modes of the discussed fragment are observed at 761, 640, and 617 $cm^{-1}$, which are negative oriented in corresponding difference IR-LD spectrum (Fig. 2). The phosphonic acid is characterized with a series of bands within 1200–900 $cm^{-1}$ (Fig. 3). The band at 1180 $cm^{-1}$ belongs to stretching P = O ($\nu_{P=O}$) mode and the bands at 1145 $cm^{-1}$ and 941 $cm^{-1}$ belong to $\nu_{PO2}{}^{as}$ and $\nu_{PO2}{}^{s}$ stretching vibrations. These data correlated well with previously reported data of phosphonic acid.[2–4] The broad absorption band at 1022 $cm^{-1}$ can be associated with bending $\delta_{P\text{-}O(H)}$ vibration.

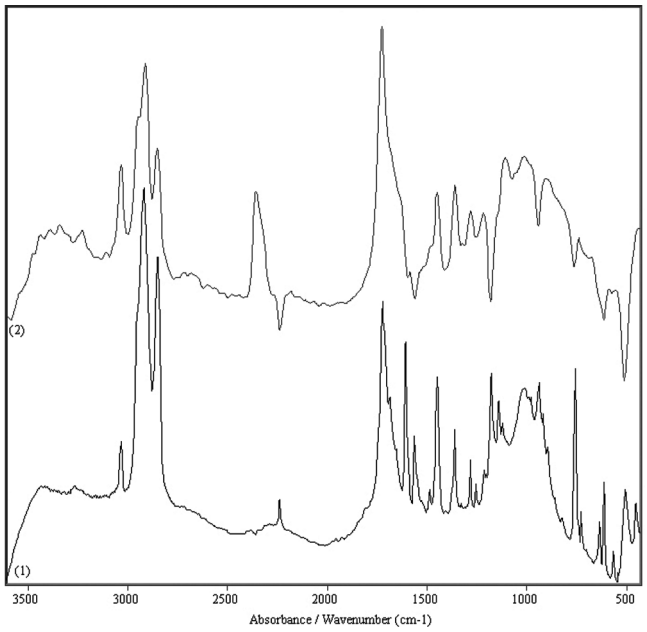


**FIGURE 2** **Nonpolarized IR (1) and difference IR-LD (2) spectra of 2-oxo-2*H*-chromene-3-phosphonic acid in nematic host.**

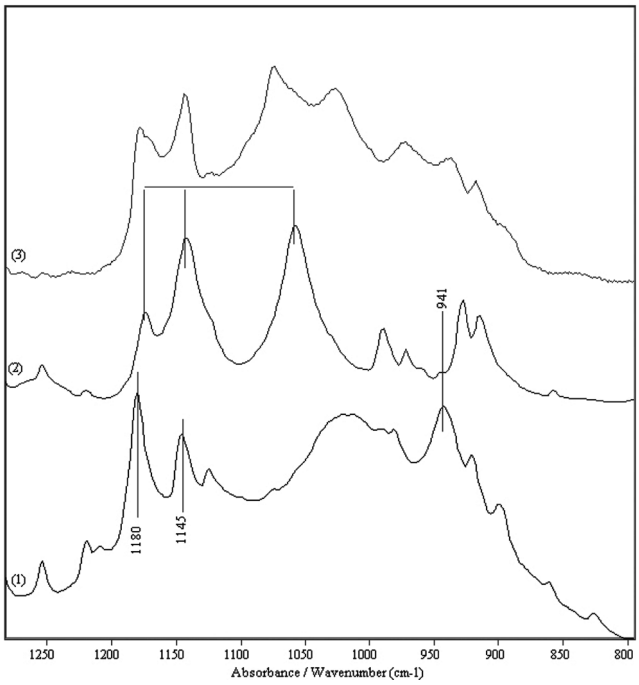


**FIGURE 3** **IR-spectra of 2-oxo-2*H*-chromene-3-phosphonic acid (1), its ammonium salt (2), and Pt(II) complex (3) within 1250–800 $cm^{-1}$ range.**

The formation of the ammonium salt of 2-oxo-2*H*-chromene-3-phosphonic acid leads to following changes in the IR spectrum of the ligand. The band at 3517 $cm^{-1}$ belongs to $\nu_{OH}$ of the included $H_2O$ molecule. The broad band within 3300–2000 $cm^{-1}$ corresponds with $\nu_{NH4+}{}^{as}$ and $\nu_{NH4+}{}^{s}$ stretching modes. The $\nu_{C=O}$ band is low frequency shifted with 10 $cm^{-1}$, whereas the i.p. and o.p. modes of aromatic system are unaffected (Fig. 3). Interesting changes are observed within the 1200–900 $cm^{-1}$ region. Relatively intensive bands at 1174 $cm^{-1}$, 1141 $cm^{-1}$, and 1056 $cm^{-1}$are observed. According to the theory, the deprotonation of the phosphonic acid in the molecule leads to high symmetry. Three bands characterized this local system meaning that the discussed maxima belong to $\nu_{P\text{-}O}$ stretching vibrations.

If we compare the IR spectroscopic patterns of the free ligand, its ammonium salt, and corresponding Pt(II), the following assignment can be drawn. The 3500–3000 $cm^{-1}$ IR spectroscopic region is characterized with an intensive band at 3420 $cm^{-1}$ corresponding with $\nu_{OH}$ of the included $H_2O$ molecules in the complex and of the associated $\nu_{OH}$ band of phosphonic acid. The carbonyl C = O stretching region is affected and the $\nu_{C=O}$ band is observed at 1712 $cm^{-1}$. The characteristic stretching and banding

modes of aromatic coumarin fragment are weak affected only. The 1200–900 $cm^{-1}$ spectroscopic region is like that of neutral ligand, but the $\nu_{P=O}$ and $\nu_{PO2}{}^{as}$ are low frequency shifted within 10–7 $cm^{-1}$. However, a significant high frequency shifting of $\nu_{PO2}$ with 106 $cm^{-1}$ is observed (Fig. 3).

The IR spectroscopic data indicates that 2-oxo-2*H*-chromene-3-phosphonic acid acted as bidentate ligand with Pt(II), through O-atoms from the deprotonated OH group and in phosphonic acid C=O fragment. Two solvent molecules are included in the complex (Scheme 1).

## $^{1}$H-, $^{13}$C-, and $^{31}$P-NMR Data

The effect of deprotonation and coordination of 2-oxo-2*H*-chromene-3-phosphonic acid weak affected on the chemical shift signals in $^{1}$H- and $^{13}$C-NMR spectra of the ligand and the typical signals about 8.50 ppm, 7.70 ppm, and 7.20 ppm are observed. The signals in $^{13}$C-NMR spectra at 155.00, 150.00, 135.00, 130.00, 125.00, 120.00, and 115.00 ppm are similar to previously reported signals of the free ligand.[5] The carbon C=O signal is only downfield shifted and is observed at 159.00 ppm. The $^{31}$P-NMR spectroscopic data is informative, showing that the signal observed at 17.2 ppm (J = 9.21 Hz) of free ligand is downfield shifted with 4.1 ppm (J = 8.13 Hz) in the corresponding Pt(II) complex. In the ammonium salt, the value is 9.17 ppm (J = 8.95 Hz), respectively. The obtained values correlated well with other $^{31}$P-NMR of derivatives of phosphonic acid.[18–20] This result additionally confirms that the coordination of the Pt(II) is through both the O-atom from the deprotonated OH group in phosphonic acid and C = O fragment forming a stable six-member chelate ring (Scheme 1).

## TGV and DSC Data

The performed thermal analysis within 300–500 K of the ammonium salt and Pt(II) complex of 2-oxo-2*H*-chromene-3-phosphonic acid shows that in the first case, a weight loss of 6.4% and delta(H) effect of 6.88 kcal/mol is observed about 393 K, corresponding with one $H_2O$ molecule included in the quantitative amount of the salt. The thermal analysis of the Pt(II) complex shows a weight decreasing with 7.8% within the temperature interval of 405–415 K and two enthalpy effects of 3.6 and 3.9 kcal/mol

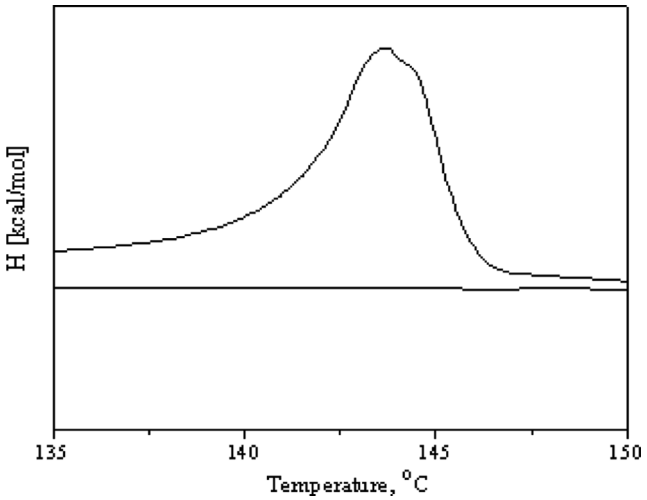


**FIGURE 4** DSC data ($\Delta H$ [kcal/mol] vs. $T$ [°C]) of the Pt(II) complex.

(Fig. 4), indicating the presence of two water molecules in the complex. The obtained weight loss at relatively higher temperatures indicates that the solvent molecules may be participating in the interactions with metal ion.

## CONCLUSIONS

The coordination processes between Pt(II) and 2-oxo-2*H*-chromene-3-phosphonic acid are elucidated both in solution and in solid state by means of conventional and linear-polarized IR spectroscopy of oriented colloid suspensions in nematic liquid crystal, $^{1}$H-, $^{13}$C-, and $^{31}$P-NMR, UV-Vis spectroscopy, positive and negative mass spectrometry (ESI and FAB), and TGV and DSC methods. In addition, the spectroscopic data of ammonium salt of 2-oxo-2*H*-chromene-3-phosphonic acid are compared with those of the free ligand and the corresponding Pt(II) complex. 2-Oxo-2*H*-chromene-3-phosphonic acid acts as bidentate ligand, coordinating through its O-atom of the deprotonated phosphonic acid fragment and C = O group, thus forming a mononuclear Pt(II) complex with stable six-member chelate ring. The molar ratio of metal to ligand is 1:2. The geometry of the chromophore $PtO_4$ is square planar. Two $H_2O$ molecules are included in the complex, and specific interactions with Pt(II) are proposed.

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