Journal of Thermal Analysis and Calorimetry, Vol. 81 (2005) 153–157

THERMAL BEHAVIOUR OF PLATINUM(II) COMPLEXES OF DIETHYL AND MONOETHYL 2-QUINOLYLMETHYLPHOSPHONATES

Lj. Tušek-Božić[*] *and R. Trojko*

Ruđer Bošković Institute, Bijenička 54, 10002 Zagreb, Croatia

Thermal study of the molecular and ionic platinum(II) complexes of diethyl (2-dqmp) and monoethyl (2-Hmqmp) ester of 2-quinolylmethylphosphonic acid: dihalide adducts *trans*-PtL_2X_2 (*L*=2-dqmp, *X*=Cl, Br; *L*=2-Hmqmp, *X*=Cl), methylquinolinium tetrahaloplatinates $[LH^+]_2[PtX_4^{2-}]$ (*L*=2-dqmp, *X*=Cl, Br; *L*=2-Hmqmp, *X*=Cl, Br), methylquinolinium hexahalodiplatinates $[LH^+]_2[Pt_2X_6^{2-}]$(*L*=2-Hmqmp, *X*=Cl, Br) and chelate complex $Pt(2\text{-mqmp})_2 \cdot 2H_2O$, has been carried out using TG-DTA techniques and the infrared spectroscopic study. There are great differences in the thermal behaviour between various types of complexes, especially between the molecular and the ion-pair salt complexes.

Keywords: *DTA, phosphonate complex, platinum antitumor agent, platinum(II) complex, quinoline complex, thermal decomposition*

Introduction

Studies of platinum(II) and palladium(II) complexes with nitrogen donor ligands are of current interest not only because of their wide-range application in organic synthesis and catalysis [1, 2], but also owing to their biological and pharmacological importance [3, 4]. Following the discovery of the antitumor activity of cisplatin and its analogues, a great deal of effort was expanded in developing of new platinum-based complexes with intention of improving the cytotoxicity and therapeutic properties of this class of compounds. Our studies in this field are directed to palladium(II) and platinum(II) complexes of quinoline and aniline-based alkyl phosphonates, which might be of interest due to their biological activity [5–8]. A different type of molecular and ionic metal complexes, such as molecular dihalide adducts with *trans* and *cis* configuration, mononuclear and binuclear metallocyclic and ion-pair salt complexes with antitumor activity, have been prepared and investigated.

We recently reported the synthesis of platinum(II) complexes with diethyl (2-dqmp) and monoethyl (2-Hmqmp) 2-quinolylmethylphosphonates as well as their spectroscopic analysis and antitumor activity [7]. Most of these compounds have been found cytostatic in vitro against human and animal tumor cell lines. As an extension of these investigations, in the present paper we describe the decomposition behaviour of these biologically interesting metal complexes investigated by thermogravimetry (TG) and differential thermal analysis (DTA) accompanied by the IR spectroscopic studies. The results obtained were compared with those previously reported for the palladium(II) complexes of the same phosphonate ligands [9, 10] and discussed with respect to their structure-stability relationship.

Experimental

The platinum(II) complexes of 2-dqmp and 2-Hmqmp were prepared and characterized according to the published methods [7].

The thermogravimetric analyses (TG) were carried out on a Cahn RG electromicrobalance in air atmosphere at a heating rate of 4 K min^{-1} up to 850°C. Differential thermal analyses (DTA) were performed with a Netzsch 406 differential thermal analyzer applying a heating rate of 5 K min^{-1} in static air atmosphere. The reference substance was pure alumina. The samples were diluted with the reference substance in the ratio 1:1 by mass.

FTIR spectra were recorded on an ABB Bomem MB102 spectrophotometer using KBr (4000–250 cm^{-1}) and polyethylene (400–200 cm^{-1}) pellets.

The X-ray powder diffraction patterns were taken with a Philips counter diffractometer (monochromatised CuK_α radiation).

Results and discussion

Investigations of the interaction of diethyl ester and monoethyl ester of 2-quinolylmethylphosphonic acid with PtX_4^{2-} (*X*=Cl, Br) have shown that either the molecular or the ionic complexes could be formed de-

* Author for correspondence: tusek@rudjer.irb.hr

1388–6150/$20.00

Akadémiai Kiadó, Budapest, Hungary
Springer, Dordrecht, The Netherlands

pending on the acidity of the alcoholic/aqueous reaction solution (Fig. 1) [7]. While in the neutral medium dihaloplatinum complexes, PtL_2X_2, containing N-bonded ligand in a trans square planar fashion were obtained, from the HX acidic medium at pH<3 the salt complexes, $[LH^+]_2[PtX_4^{2-}]$, were isolated. The ligand is protonated forming methylquinolinium ion, while platinum remains in the form of square planar monomeric tetrahaloplatinum complexes. In addition, the monoethyl ester at pH~3 forms dimeric hexahalodiplatinum complexes $[LH^+]_2[Pt_2X_6^{2-}]$, while the chelate complex $PtL_2{\cdot}2H_2O$ with N,O bonded ligand through the quinoline nitrogen and the phosphonic acid oxygen was obtained at pH>6. Decomposition behaviour of the complexes was investigated by thermogravimetry and differential thermal analysis, and examples of the appropriate TG-DTA plots are presented in Figs 2–4. Thermal decomposition of the complexes is not simple; it takes place through a multistep process. Although no stable intermediate products, except the corresponding anhydrous compounds in the case of the hydrated complexes, were found owing to the complexity and the overlap of the degradation processes, thermal analysis subsequently followed by the infrared spectroscopic study provides valuable information about decomposition properties of the complexes. IR spectra were recorded every 50°C and are compared with the corresponding spectra at room temperature [7]. The hydrated complexes exhibit a single, somewhat broad, dehydration step between 42–112°C with the mass loss close to the calculated value for evolution of two molecules of water. In the IR spectra the water loss is indicated by a disappearance of the rather intense absorptions in the ν(OH) region between 3460–3210 cm^{-1}. Degradation of the halide complexes begins by a dehalogenation process overlapped with deesterification of the organophosphorus ligand, and is strongly influenced by the type of complex. In dihalide adducts of 2-dqmp this step is rather sharp and covers approximately the range of 150°C (Fig. 2). The mass loss of about 22% for the chloro and 40% for the bromo complex corresponds approximatively to evolution of two halide ions and four ethyl ester groups (calc. values 19.5 and 37.2%, respectively). The decomposition of the complexes started with their dehalogenation, which is indicated by an intensity decrease of the Pt–Cl/Br stretching vibrations in the far infrared region between 400–200 cm^{-1}. On the other hand, the loss of the ethyl ester groups is accompanied by a decrease of the absorption bands arisen from various modes of the P–O–Et vibrations between 1150–1020 cm^{-1} and C–C ethyl vibrations in the region of 990–960 cm^{-1}. The dehalogenation and deesterification processes are completed at ca. 300°C and are accompanied by broad and poorly resolved endothermic peaks in DTA curves. The decomposition of the complexes continues with a progressive mass loss to a mixture of Pt and P_2O_5. The platinum metal was

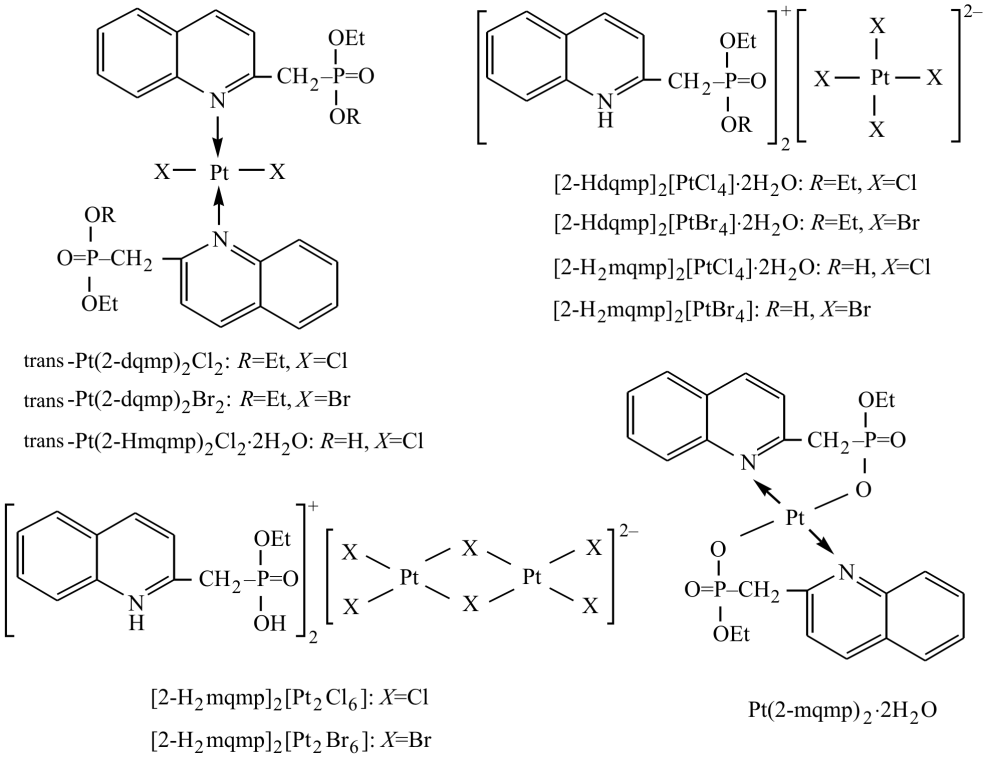

Fig. 1 Platinum(II) complexes of 2-dqmp and 2-Hmqmp

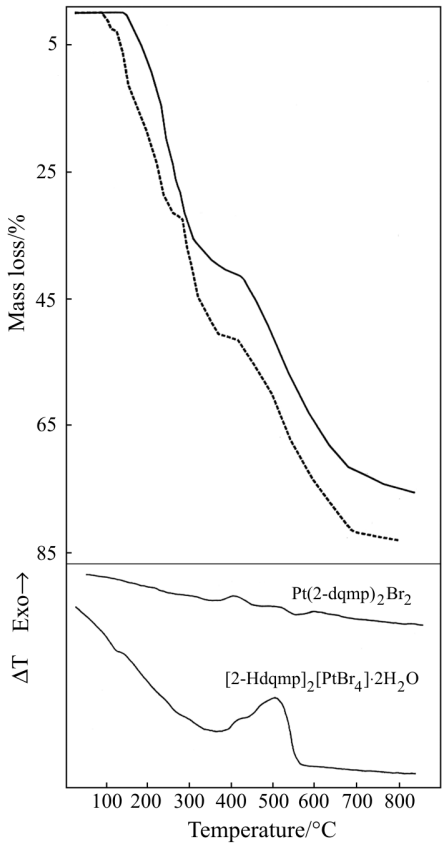

Fig. 2 TG-DTA curves for complexes: — – $Pt(2\text{-dqmp})_2Br_2$ and --- – $[2\text{-Hdqmp}]_2[PtBr_4]\cdot 2H_2O$

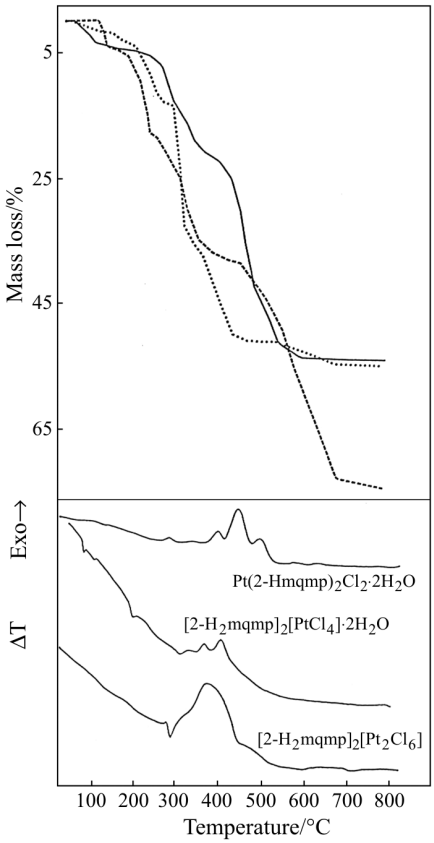

Fig. 3 TG-DTA curves for complexes:
— – $Pt(2\text{-Hmqmp})_2Cl_2\cdot 2H_2O$,
--- – $[2\text{-}H_2\text{mqmp}]_2[PtCl_4]\cdot 2H_2O$ and
··· – $[2\text{-}H_2\text{mqmp}]_2[Pt_2Cl_6]$

identified as the pyrolytic residue in a number of platinum complexes [11, 12]. Formation of P_2O_5 in the IR spectra is followed by the intensity decrease of the phosphonate ester bands and by the intensity increase of the P=O stretching vibrations around 1260 cm^{-1} [13–15]. Dichloro adduct of monoester 2-Hmqmp is more stable than the corresponding dichloro adduct of diester 2-dqmp. Its dehalogenation and deesterification process occurs at higher temperatures between 190–390°C (Fig. 3). This decomposition step is continued by the pyrolytic decomposition of ligand visible in the DTA curve as a few exothermic peaks.

In the ionic tetrahaloplatinate complexes after the dehydration step begins dehalogenation process between 120–130°C, at lower temperatures than in the corresponding dihaloplatinate adducts. It occurs in two steps, as revealed by the very distinct inflections in the TG curves, although well-defined TG plateaus are not reached (Figs 2 and 3). In the DTA curves these processes are visible as slight endothermic effects. First step, ranged up to 260–270°C for the 2-dqmp complexes and up to 220–240°C for the 2-Hmqmp complexes, corresponds to the loss of two halogens accompanied by the ligand deesterification (found mass loss: 27.6, 28.7, 17.9 and 22.8%; calc. 26.9, 30.5, 18.4 and 24.5% for $[2\text{-Hdqmp}]_2[PtCl_4]\cdot 2H_2O$, $[2\text{-Hdqmp}]_2[PtBr_4]\cdot 2H_2O$, $[2\text{-}H_2\text{mqmp}]_2[PtCl_4]\cdot 2H_2O$ and $[2\text{-}H_2\text{mqmp}]_2[PtBr_4]$ complex, respectively). The mass loss in the second step corresponds approximately to the release of two remaining halogens (found mass loss: 8.4, 15.8, 9.1 and 17.1%; calc. 7.6, 14.4, 8.1 and 15.7%).

Dehalogenation in hexahalodiplatinum complexes of 2-Hmqmp also occurs in two steps. The first relatively broad step starts at about 70°C covering approximately the range up to 220°C. The mass loss of ca. 13% (calc. 14.5%) for the chloro and of ca. 17% (calc. 18.2%) for the bromo complex corresponds approximately to two halide ions and two ethyl ester groups. The second rather sharp step ranged up to ca. 320–330°C could be attributed to complete dehalogenation of the complexes what is confirmed by the absence of the ν(Pt–Cl/Br) absorptions in the IR spectra. It is overlapped by the pyrolytic decomposition of the ligand, which continues with a progressive mass loss and a strong exothermic peak around 360°C.

Chelate complex exhibits a broad dehydration step between 50–120°C (Fig. 4), indicating that two water

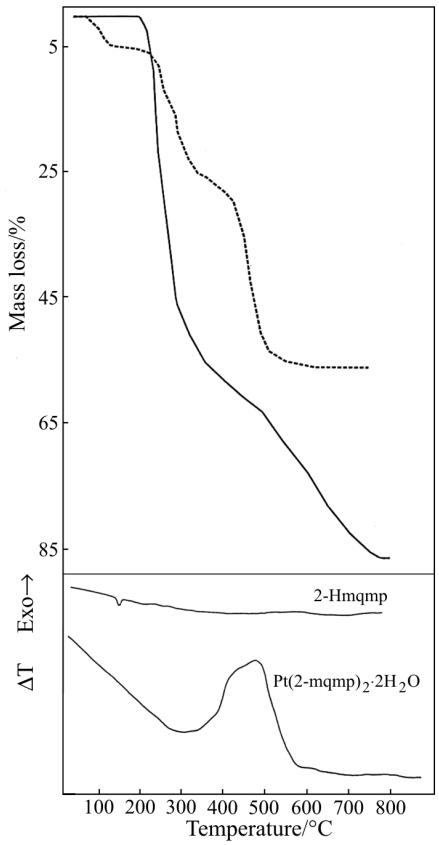

Fig. 4 TG-DTA curves for — – 2-Hmqmp and --- – its complex $Pt(2\text{-mqmp})_2 \cdot 2H_2O$

molecules are lattice-held [16]. Decomposition of the complex includes deesterification and other ligand degradation processes in the 200–500°C region visible in the DTA curve as a broad exothermic peak centered around 450°C. A continuous thermal degradation could be seen also in the free monoester (Fig. 4). Its TG curve shows a rather strong mass loss of ca. 45% between 170 and 290°C arisen from its partial pyrolytic decomposition, which is continued in the second broad step over 290°C giving the pyrolytic residue P_2O_5. This is confirmed by the IR and X-ray data. Difference obtained between the calculated and found residue value could be ascribed to partial sublimation of P_2O_5, which takes place at higher temperatures [14, 17]. Decomposition of 2-mqmp is not followed by clear peaks in the DTA curve. Only is visible one endothermic effect at 150°C, which is not accompanied by the mass loss in the TG curve, and corresponds approximately to the melting point of this monoester [18].

It could be concluded that stability of complexes greatly varies depending on the type of complex as well as on the halide and organophosphorus ligand bonded to platinum. In general, molecular complexes are more stable than the ionic complexes. From the initial decomposition temperatures, which correspond to the beginning of the dehalogenation process in the halide complexes, it was shown that dihalide adducts of the monoethyl ester are more stable compounds with respect to those of the diethyl ester, as well as are chloro complexes compared to their bromo analogues. It may be presumed that this arises from the steric effects that increase from monoester to diester and from chloro to bromo derivatives. In the ion-pair salt complexes with the protonated phosphonate ligand as cation and the tetrahaloplatinate or hexahalodiplatinate complex as anion, these differences are less pronounced. Comparing thermal properties of the platinum and palladium quinolylmethylphosphonate complexes, it could be shown that there are small differences in thermal stability between their ionic complexes and N,O-chelates [9, 10]. On the other hand, palladium dihalide adducts are more stable than their platinum analogues. Their dehalogenation process begins at 20–40°C higher temperatures. It is interesting to note that most of platinum complexes of 2-Hmqmp show smaller antitumor activity than their palladium analogues [6, 7] while activity of 2-dqmp complexes of both metals are more or less comparable [5, 7]. In addition, complexes of diester are more active than those of monoester. These findings indicate that besides the breaking ability of the Pt/Pd-halogen bonds which promotes binding of the metal complexes to DNA strands, there are a lot of other factors that influence biological activity of the complexes such as their solubility, lipophilicity as well as their reactions prior to DNA binding [19].

It was shown that dehalogenation of the complexes and ligand deesterification are the main processes in the course of decomposition of the platinum(II) and palladium(II) halide complexes of both phosphonate ligands. These results are in agreement with those obtained by studying decomposition behaviour of a number of halide complexes with various alkyl aminophosphonates by FAB-mass spectroscopy, in which the main fragment ions are those obtained by the sequentially losses of halide ions and those corresponding to loss of the phosphonate ester group or its fragments [20].

Acknowledgements

The financial support of the Croatian Ministry of Science, Education and Sports (grants 0098035 and 0098065) is gratefully acknowledged.

References

1 J. Tsuji, Palladium Reagents and Catalysts, Innovation in Organic Synthesis, Wiley, New York 1995.

2 P. B. Kettler, Org. Process Res. Dev., 7 (2003) 342.
3 P. J. O'Dwyer, P. Stevenson and S. W. Johnson, Clinical Status of Cisplatin, Carboplatin, and other Platinum-based Antitumor Drugs, in: B. Lippert (Ed.), Cisplatin: Chemistry and Biochemistry of a Leading Anticancer Drug, VHCA and Wiley-VCH, Zürich and Weinheim 1999, p. 31.
4 M. J. Bloemik, J. H. Diederen, J. P. Dorenbos, R. J. Heeterbij, B. K. Keppler and J. Reedijk, Eur. J. Inorg. Chem., 10 (1999) 1655.
5 Lj. Tušek-Božić, I. Matijašić, G. Bocelli, G. Calestani, A. Furlani, V. Scarcia and A. Papaioannou, J. Chem. Soc., Dalton Trans., (1991) 195.
6 Lj. Tušek-Božić, A. Furlani, V. Scarcia, E. De Clercq and J. Balzarini, J. Inorg. Biochem., 72 (1998) 201.
7 Lj. Tušek-Božić, F. Frausin, V. Scarcia and A. Furlani, J. Inorg. Biochem., 95 (2003) 259.
8 Lj. Tušek-Božić, M. Komac, M. Ćurić, A. Lyčka, M. D'Alpaos, V. Scarcia and A. Furlani, Polyhedron, 19 (2000) 937, and references therein.
9 Lj. Tušek-Božić and R. Trojko, Thermochim. Acta, 189 (1991) 175.
10 Lj. Tušek-Božić and R. Trojko, Thermochim. Acta, 339 (1999) 41.
11 B. A. Howell, L. G. Beholz and B. B. S. Sastry, J. Thermal Anal., 40 (1993) 395.
12 G. Matuschek, A. A. Kettrup and A. Prior, J. Therm. Anal. Cal., 56 (1999) 471.
13 L. C. Thomas, Interpretation of the Infrared Spectra of Organophosphorus Compounds, Plenum Press, New York 1974.
14 E. Princz, I. Szilágyi, K. Mogyorósi and I. Labádi, J. Therm. Anal. Cal., 69 (2002) 427.
15 E. Princz, K. Mogyorósi and I. Labádi, J. Therm. Anal. Cal., 77 (2004) 767.
16 S. P. Perleps, P. Jacops, H. O. Desseyn and J. M. Tsangaris, Spectrochim. Acta, 43A (1987) 771.
17 D. R. Lide (Ed.), Handbook of Chemistry and Physics, The Chemical Rubber Co., Boca Raton, Florida 1998–1999, p. 76.
18 V. Jagodić, B. Božić, Lj. Tušek-Božić and M. J. Herak, J. Heterocycl. Chem., 17 (1980) 685.
19 E. R. Jamieson and S. Lippard, Chem. Rev., 99 (1999) 2467.
20 Lj. Tušek-Božić and M. D'Alpaos, Polyhedron, 17 (1998) 1481, and references therein.

Received: November 22, 2004
In revised form: January 27, 2005

DOI: 10.1007/s10973-005-6849-7