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The thermal study of palladium(II) complexes of monoethyl 2-quinolylmethylphosphonate

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Abstract

Thermal study (TG, DTA) of the palladium(II) complexes of monoethyl 2-quinolymethylphosphonate (2-mqmp): neutral dihalide adducts $Pd(2\text{-mqmp})_2X_2$, ion-pair salt complexes $[2\text{-Hmqmp}]^+[Pd(2\text{-mqmp})X_3]^-$(X = Cl, Br) and chelate dihydrate $Pd(2\text{-mqmp-H})_2{\cdot}2H_2O$, has been carried out in order to determine decomposition properties of these biologically interesting complex compounds. Thermal decomposition of the complexes occured in two steps: dehalogenation along with ligand deesterification is followed by complex pyrolysis that leads to the residue identified as a mixture of the element, Pd and P_2O_5. This was confirmed by infrared spectroscopic study. No stable intermediate products, except the corresponding anhydrous complex in the case of chelate compound, were found during thermal decomposition due to the complex nature and the overlap of the degradation processes. The results were compared with those obtained for the complexes of diethyl 2-quinolylmethylphosphonate and discussed with respect to their cytostatic activity.

Keywords: Palladium(II) complex; Phosphonate complex; Thermal decomposition; Quinoline complex; DTA

1. Introduction

There is a great interest in the coordination chemistry of phosphonate ligands containing mononitrogen aromatic bases such as pyridine and quinoline largely because of their potential biological and pharmaceutical properties [1,2]. While a number of free organophosphorus derivatives posses bactericidal and herbicidal activity, some of their palladium and platinum halide complexes have been found to be cytostatic to various animal and human tumor cells [3–5]. There is general agreement that DNA is an important pharmacological target for these complexes [6] and that the breaking ability of the Pt,Pd–halogen bond is the rate determining step in their reactions with DNA strands [7]. An understanding of the dependence of the cytostatic activity on these mechanistic aspects is a requirement for the development of complex compounds with higher efficiency.

As a part of our continuous study on palladium(II) halide complexes with various alkyl phosphonates derived from quinoline [3,4,8,9] and aniline [10–12], which might be of interest as anticancer agents, we recently reported the synthesis as well as spectroscopic analyses and biological properties of palladium(II) complexes with monoethyl 2-quinolylmethylphosphonate (2-mqmp) [13,14]. The preliminary screening tests showed that these compounds exhibited a certain cell

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growth inhibitory effects against cell derived from human epidermoid carcinoma and murine leukemia. In this report we describe the decomposition behavior of these metal complexes investigated by thermogravimetry (TG) and differential thermal analysis (DTA) accompanied by the IR spectroscopic studies. The results obtained were compared with those obtained for the palladium(II) halide complexes of diethyl 2-quinolylmethylphosphonate (2-dqmp) [8]. The thermal and spectral properties of the complexes in terms of their biological activity are also discussed.

2. Experimental

The palladium(II) dihalide complexes, Pd(2-mqmp)$_2$X$_2$ (X = Cl, Br), ion-pair salt complexes [2-Hmqmp][Pd(2-mqmp)X$_3$] (X = Cl, Br) as well as chelate complex Pd(2-mqmp–H)$_2$ 2H$_2$O, were prepared according to published methods [13].

TG analyses were performed with a Cahn RG electromicrobalance in an air atmosphere at a heating rate of 4°C min^{-1} up to 800°C. DTA were carried out on a Netzsch differential thermal analyzer applying a heating rate of 5°C min^{-1} in static air atmosphere. The reference substance was pure alumina.

Infrared spectra were recorded on a Perkin Elmer 580 B spectrophotometer using KBr pellets (4000–250 cm^{-1}) and Nujol mulls in polyethylene (400–200 cm^{-1}).

The X-ray powder diffraction patterns were measured with a Philips counter diffractometer (monochromatised Cu Kα radiation).

3. Results and discussion

Monoethyl 2-quinolylmethylphosphonate forms three types of palladium(II) complexes depending on acidity of the the reacted solution. As can be seen in Fig. 1, over a wide pH range it exhibits either (a) molecular, (b) zwitterion or (c) anionic form forming consequently the molecular dihalide complexes Pd(2-mqmp)$_2$X$_2$ (X = Cl, Br) with mutually *trans*-bonded ligand through the quinoline nitrogen, the ion-pair salt complexes [2-Hmqmp]$^+$[Pd(2-mqmp)X$_3$]$^-$ (X = Cl, Br) with the protonated quinolylmethylphosphonate ligand as cation and the quinolylmethylphosphonate-trihalopalladium(II) complex as anion, or the chelate dihydrate complex Pd(2-mqmp–H)$_2$·2H$_2$O containing the phosphonate ligand co-ordinated to the metal through the quinoline nitrogen and the phosphonic acid oxygen. The decomposition behavior of these complexes was investigated by thermal analysis accompanied by infrared spectroscopic study. IR spectra were recorded every 50°C and were compared with the corresponding spectra at room temperature. The results obtained from the TG and DTA curves presented in Figs. 2 and 3, as well as the IR frequencies associated with the Pd–X (X = Cl, Br) stretching vibration, are summarized in Table 1. Although thermal decomposition of the complexes occurs in a few steps without formation of a stable intermediate, some interesting points related to the mode of their decomposition could be determined. In the case of the dihalide adducts the first rather sharp decomposition step is attributed to dehalogenation overlapped with deesterification of the ligand. The weight loss of about

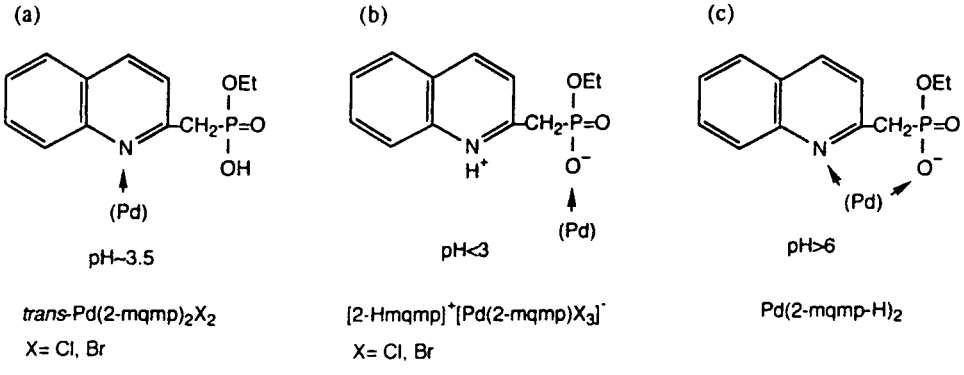

Fig. 1. Palladium(II) complexes formed with the (a) molecular, (b) zwitterion and (c) anionic form of (2-mqmp).

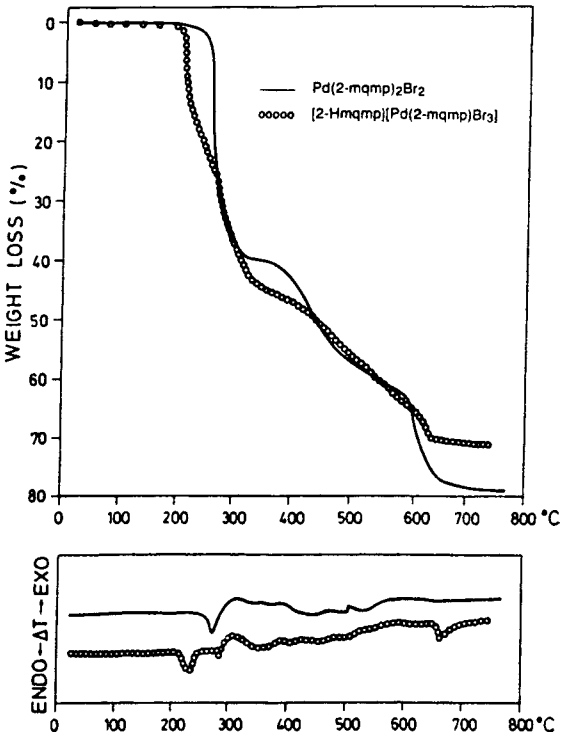

Fig. 2. TG–DTA curves for Pd(II) complexes: $Pd(2\text{-mqmp})_2Br_2$ (−) and [2-Hmqmp][$Pd(2\text{-mqmp})Br_3$] (○○○○).

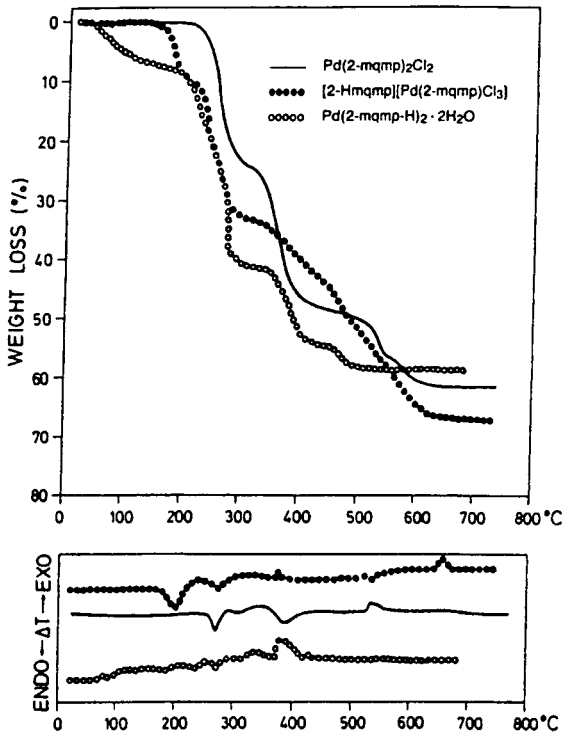

Fig. 3. TG–DTA curves for Pd(II) complexes: $Pd(2\text{-mqmp})_2Cl_2$ (−), [2-Hmqmp][$Pd(2\text{-mqmp})Cl_3$] (●●●●) and Pd(2-mqmp–$H)_2{\cdot}2H_2O$ (○○○○).

Table 1
TG, DTA and selected IR data for palladium(II) complexes of 2-mqmp and 2-dqmp

Complex	Dehydration		Dehalogenation and pyrolysis (Tempearature range[b])		IR (cm^{-1}) ν (Pd–Cl/Br)
	H_2O[a] (%)	Temperature range TG (°C)	TG (°C)	DTA (°C)	
$Pd(2\text{-mqmp})_2Cl_2$	–	–	225–737	270 (endo), 310 (endo), 385 (endo), 530 (exo)	358
$Pd(2\text{-dqmp})_2Cl_2$[c]	–	–	190–751	225 (endo), 300 (endo), 600 (exo)	352
$Pd(2\text{-mqmp})_2Br_2$	–	–	230–768	270 (endo), 330 (endo), 380 (endo), 440 (endo), 505 (exo)	326
$Pd(2\text{-dqmp})_2Br_2$[c]	–	–	172–727	215 (endo), 255 (exo)	321
[2-Hmqmp][$Pd(2\text{-mqmp})Cl_3$]	–	–	165–704	210 (endo), 285 (endo), 375 (exo), 540 (endo), 655 (exo)	338, 220
[2-Hdqmp]$_2$[$PdCl_4$]$\cdot 2H_2O$[c]	4.40 (4.26)	73–100	110–755	115 (endo), 130 (endo), 235 (exo)	325
[2-Hmqmp][$Pd(2\text{-mqmp})Br_3$]	–	–	190–741	225 (endo), 290 (endo), 310 (exo), 350 (endo), 660 (endo)	320, 259
[2-Hdqmp]$_2$[$PdBr_4$]$\cdot 2H_2O$[c]	4.09 (3.52)	34–65	100–635	100 (endo), 150 (endo), 570 (exo)	252
$Pd(2\text{-mqmp-H})_2{\cdot}2H_2O$	7.01 (6.91)	50–160	170–685	90 (endo), 230 (endo), 280 (endo), 380 (exo)	–

[a] Calculated values are given in paranthesis.
[b] Most of the DTA peaks over 300°C are small and diffuse.
[c] Data taken from [8].

17% for the chloride and 27% for the bromide complex corresponds well with this assumption. It was shown that decomposition of these complexes started with their dehalogenation at 225–230°C, and is indicated by an intensity decrease of the Pd–X stretching vibration which appeared at 358 and 326 cm^{-1}, respectively [13]. On the other hand the loss of the ethyl ester group is accompanied by a decrease of the absorption bands arising from various modes of the P–O–Et vibrations in the region of 1160–1040 cm^{-1} and C–C ethyl vibrations between 980 and 930 cm^{-1} as well as by an increase of the ν(P=O) band around 1230 cm^{-1} [8,15]. It was shown that dehalogenation and deesterification processes were completed at ca. 300°C and were accompanied by an endothermic effect in DTA curves at 270°C in both complexes. In the ionic quinolinium trihalopalladium complexes dehalogenation starts at lower temperatures and occurs in two steps separated by an inflection in the TG curve but without a distinct plateau. The first step between 165°C and 185°C for the chloride and between 190°C and 210°C for the bromide complex corresponds approximately to the loss of one halide ion forming dihalide complexes, similarly as was obtained by heating these complexes in methanol and some other solvents. Palladium as a soft metal has a strong preference for N-donor ligands and therefore complexes with O-phosphonate-bonding were easily transformed into those with N-quinoline-bonding. In addition, it has been shown that some ion-pair palladium salt complexes of various amine, pyridine and quinoline also give neutral palladium(II) dihalide complexes by solid-phase thermal transformation [8,16,17]. In the second step the complete dehalogenation along with deesterification ends at ca. 300°C, similarly as was observed in dihalide adducts. In the DTA curves these processes are visible as two endothermic peaks at 210°C and 285°C for the chloride and at 225°C and 290°C for the bromide complex. These decomposition steps are followed by a continuous weight loss with several unclear peaks in the DTA curves. On the bases of the initial decomposition temperatures, which correspond to the beginning of the dehalogenation process, it could be concluded that the thermal stability of the complexes depends on both the type of the complex and the halide ligand bonded to palladium. In general, dihalide adducts are more stable than ionic trihalopalladium complexes as well as are bromo complexes compared to their chloro analogues, most probably due to the higher capacity of bromide ligands to establish a π-bond with the metal by retrodonation. Chelate complex is dehydrated and exhibits a broad dehydration step over the range of 34–160°C, indicating that two water molecules are lattice-held [18]. Decomposition of the complex includes deesterification and other ligand degradation processes. The final decomposition product of all the complexes is a mixture of metallic Pd and P_2O_5, similarly as was obtained for palladium(II) halide complexes of various aminophosphonic acid derivatives [8,11]. This was confirmed by infrared spectroscopic and X-ray diffraction analysis. Differences obtained between the calculated and found pyrolytic residue could be ascribed to partial sublimation of P_2O_5 which takes place above 300°C [19].

The thermal data of palladium(II) halide complexes of 2-mqmp were compared with those obtained for the complexes of 2-dqmp [8], which are included in Table 1 for comparison. The diester ligand, similarly as its monoester analogue, forms N-bonded palladium dihalide complexes $Pd(2\text{-dqmp})_2X_2$ (X = Cl, Br), while in the acidic media the quinolinium salts of tetrahalopalladate anions $[2\text{-Hdqmp}]_2^+[PdX_4]^{2-}\cdot 2H_2O$ (X = Cl, Br) as dihydrate compounds are formed. From the results obtained it could be concluded that complexes of the monoester are more stable. Thus in the case of dihalide complexes, dehalogenation in complexes of 2-mqmp begins at higher temperatures (30–60°C) than for the corresponding 2-dqmp complexes. This observation is interesting in view of the importance of the Pd–halogen bond strength for the binding of the complexes to DNA strands, which in turn is related to their antitumor activity. It has been suggested that the requirements for a potential antitumor complex compound are a pair of strongly covalently bonded ligands and a pair of moderately labile ligands such as halides [20]. A smaller antitumor effect might be expected when the leaving ability of the labile ligands is lower. Our results are in agreement with this assumption. It was found that complexes of the diester are in general more effective than the corresponding complexes of the monoester [3,14]. It should be pointed out, that although the Pd–X stretching frequency was found to increase in monoester complexes with respect to the corresponding diester complexes, these differences are rather small suggesting the simi-

lar palladium–halide strength in complexes of both phosphorus ligands and indicating that other factors also contribute to the increased stability of the monoester complexes. It may be presumed that the complex stability decreases with the number of the ethyl ester groups, most probably due to the increase of the steric hindrance effects. It should be noted that in the case of the ionic complexes it is difficult to investigate and correlate the stability and the possible structure/activity relationship with respect to the leaving ability of the halogen ligands. Besides the fact that 2-dqmp and 2-mqmp form different types of the ion-pair salt complexes with different properties in hydrolysis, most probably these complexes possess also different DNA binding and nicking ability, specially to that proposed for the dihalide adducts.

Acknowledgements

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