Journal of Thermal Analysis and Calorimetry, Vol. 89 (2007) 1, 257–260

STUDY OF THE THERMAL DECOMPOSITION ON Pt(II) COMPLEXES WITH CYCLOALKANESPIRO-5'-HYDANTOINS

A. Bakalova and D. Ivanov*

Department of Chemistry, Faculty of Pharmacy, Medical University, 2 Dunav Str. 1000 Sofia, Bulgaria

The thermal decomposition of the Pt(II) complexes with cyclobutane- and cycloheptanespiro-5'-hydantoins were studied by TG and DTA techniques. The Pt(II) complex with cyclobutanespiro-5'hydantoin (PtCBH) was stable up to 115°C (388 K) and Pt(II) complex with cycloheptanespiro-5'-hydantoin (PtCHTH) was stable up to 150°C (423 K). After the thermal decomposition of PtCBH the solid residue was platinum, while the decomposition of PtCHTH gave a mixture of platinum carbides (PtC_2, Pt_2C_3).

Keywords: *Pt(II) complexes, spirohydantoins, thermal analysis*

Introduction

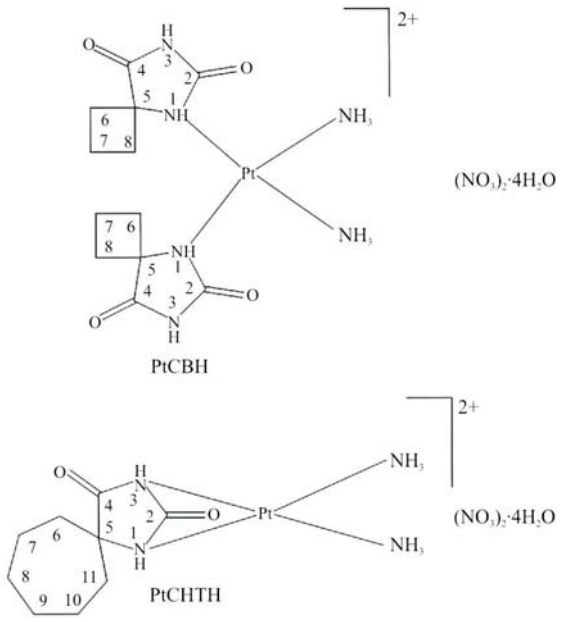
Cisplatin is an important antitumor agent, effective against ovarian, testicular, head and neck cancers [1–3]. Despite the high antitumor activity its clinical application is limited from severe side effects such as nephrotoxicity, cumulative neurotoxicity, ototoxicity and extreme emetogenic potential [2–4]. In recent years, there has been an intense interest in synthesizing new Pt(II) complexes with an aim to reduce the toxicity and/or to achieve a broader antitumor spectrum [5, 6].

In a previous work [7], we reported the synthesis and characterization by physicochemical methods of Pt(II) complexes with cyclobutanespiro-5'-hydantoin (PtCBH) and cycloheptanespiro-5'-hydantoin (PtCHTH). The new Pt(II) complexes were studied pharmacologically and was found that they exert concentration-dependent cytotoxic effect in a panel of human tumor cell lines. Both the new Pt(II) complexes under investigation exhibited cytotoxic effects in micro molar concentrations although far less pronounced than the referent drug cisplatin. The pharmacodynamic investigation of Pt(II) complexes with cyclobutane- and cycloheptanespiro-5'-hydantoins showed that these compounds induce programmed cell death (apoptosis), as evident from the detection of oligonucleosomal DNA fragmentation in HL-60 cells after treatment with these complexes [7].

In this paper we present the thermal behaviour of the Pt(II) complexes in comparison to the free ligands.

Experimental

The syntheses and the physicochemical methods for the characterization of the new Pt(II) complexes with cyclobutane- and cycloheptanespiro-5'-hydantoins were described in our previous work [7]. On the basis of the obtaining results, the following, most probable schematic formulas of the Pt(II) complexes with cyclobutanespiro-5'-hydantoin and cycloheptanespiro-5'-hydantoin were proposed (Scheme 1).



Scheme 1 Schematic structures of the investigated Pt(II) complexes PtCBH and PtCHTH

* Author for correspondence: adrigebk@abv.bg

1388–6150/$20.00

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

TG and DTA studies were carried out in an air atmosphere and the heating rate was fixed at 5°C min^{-1} on a C.MOM thermal analyzer (Budapest, Hungary) with a simultaneous DTA-TG module. The temperature range employed was 22–700°C (295–973 K). The mass of the samples used in this study was 13–20 mg. α- Al_2O_3 was used as a reference material. The X-ray data are obtained on DRON VM-1 powder diffractometer using CuK_α radiation (λ=1.5418 Å).

Results and discussion

Thermogravimetric analysis is a very valuable method with which to study the thermal decompositions of solid substances, such as complex compounds [8, 9]. The curves obtained depict the decrease in sample mass with linear increase in treatment temperature.

In the present investigation, the heating rate was fixed at 5°C min^{-1}. Depending on the total mass loss at around 512°C (785 K), the sample mass was monitored in the range 13–20 mg during the experimental runs.

A stepped thermal decomposition of the coordination compounds occur in the range 50–700°C (323–973 K). The results of the thermal analysis revealed three distinct steps of mass loss. The experimental total mass loss recorded by TG measurements for the complex PtCBH is 75.73% in comparison with the theoretical value of 74.75%.

The ligand cyclobutanespiro-5'-hydantoin is stable up to 95°C (368 K) (Fig. 1). With the increasing of the temperature a slight change in the course of the TG curve can be observed, which corresponds to the beginning of an endothermic effect with a maximum at 219°C (492 K). In the region 219–340°C (492–613 K) the TG curve changes its character at

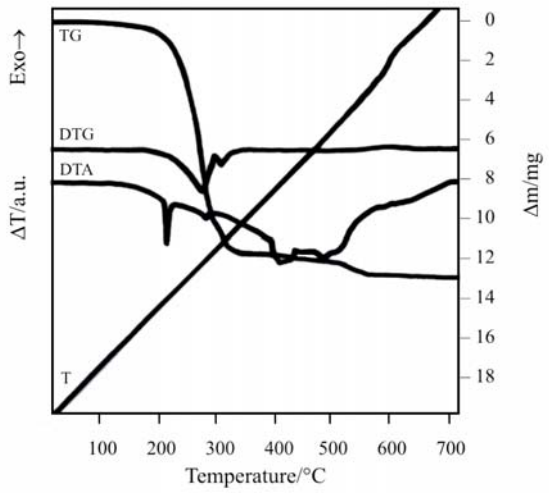


Fig. 1 TG, DTG and DTA curves of CBH

317°C (590 K). The mass loss for this temperature interval is Δm=87.03%. The most probable products of the decomposition are CO_2, H_2O and N_2 or NH_3. From 340°C (613 K) to 440°C (713 K) the TG curve is relatively horizontal. An endothermic effect at T_{max}=411°C (684 K) in the DTA curve can be observed, which is not attended with a change in the mass, probably due to the melting of the solid residue or a polymorphous transformation. The last one is doubtless, as the area of the peak is quite broad.

A more pointed change of the mass occurs in the 490–550°C (763–823 K) temperature range. After this temperature a plateau in the TG curve can be observed until 719°C (992 K). The final residue after the thermal decomposition is 3.13%. The X-ray analyses showed that it is carbon (graphite).

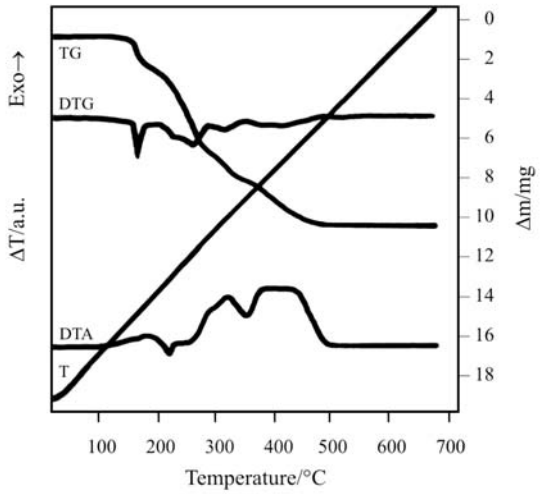


Fig. 2 TG, DTG and DTA curves of PtCBH

The Pt(II) complex with cyclobutanespiro--5'hydantoin is stable up to 115°C (388 K) (Fig. 2).

In the temperature range 115–270°C (388–543 K) an initial exothermic effect can be observed, which overlaps with an endothermic effect followed by a distinct endothermic effect with a maximum at 222°C (495 K). The initial exothermic effect can be assigned to a polymorphous change. This fact is confirmed by a small peak at 159°C (432 K), which is not connected with a mass loss as well as by X-ray powder diffraction.

In the same temperature range 115–270°C (388–543 K) the TG changes its course after 159°C (432 K). At 170°C (443 K) a mass loss Δm=10.90%. (Δm_{calcd}=10.21%) is registered, which corresponds to the disconnection of four molecules of crystal water. This fact is confirmed by the endothermic effect at T_{max}=170°C (443 K) in the DTA curve.

The endothermic effect registered in the DTA curve at 222°C (495 K), to which corresponds a horizontal part in the TG curve, is due to the decomposition of the rest of the compound. It

includes the decomposition and disconnection of two nitrate anions, two amine groups and the initial destruction of the two organic ligands, ending with the obtainment of Pt and most probably two hydantoin fragments.

The theoretical mass loss during the maintenance of these processes should be 43.97%, while the experimental loss is Δm=45.28%. The endothermic effect that follows at 366°C (639 K) is registered as a very broad peak and can be assigned to the destruction of the hydantoin residue. The final residue contains only platinum and carbon –24.27% (calcd–25.25%).

The second ligand cycloheptanespiro-5'-hydantoin starts to melt at 208°C (481 K) (Fig. 3). After this temperature, begins the decomposition of the substance and an endothermic effect in the TG curve is observed with a mass loss Δm=79.48%. Next a multistep destruction with a sufficiently lower speed takes place. In the DTA curve several weak endothermic peaks are outlined in the temperature region 319–585°C (592–858 K). A mixture of several gases are detached (CO, CO_2, N_2, NH_3, water vapour). At the end of the process no solid residue is left.

On Fig. 4 the results from the thermal analyses of PtCHTH are given. This DTA curve is much more complicated than that of the ligand discussed above. This fact is to be expected in connection with coordination ability of Pt(II). The complex is stable up to 150°C (423 K), followed by its decomposition in two steps. The first step, taking place between 150–240°C (423–513 K), is connected with a change of the mass Δm=19.70%. The second step is in the temperature interval from 240°C (513 K) to 350°C (623 K) and with a mass loss Δm=31.25%.

Of certain interest is the DTA curve in which the endothermic effect at T_{max}=160°C (433 K) proceeds

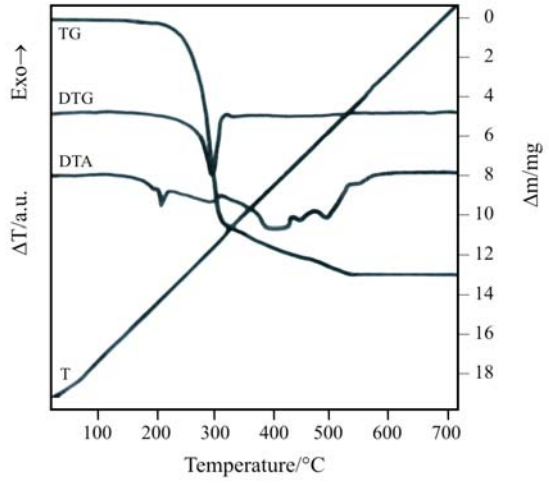


Fig. 3 TG, DTG and DTA curves of CHTP

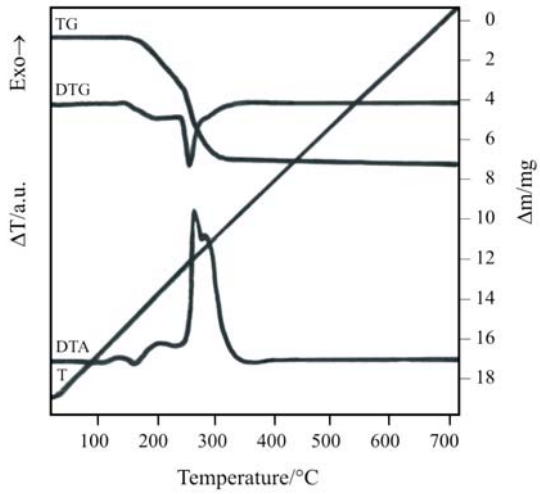


Fig. 4 TG, DTG and DTA curves of PtCHTH

to a small exothermic effect with two maximums at 272°C (545 K) and 293°C (566 K). The existence of these two effects is evidence that except the decompo sition processes of the compound, new compounds are formed. As in a very small temperature interval a lot of successive effects are obtained, it is impossible to separate and identify the different substances at this heating rate (5°C min^{-1}). If the final residue is Pt then theoretically Δm=64.87%. From the TG curve a mass loss of 46.92% is registered. At the final temperature formation of PtO is not possible as it decomposes at much lower temperature T=500°C (773 K) [10]. The registered mass loss Δm=46.92% gives us the reason to suggest that the final residue consists of platinum and platinum carbides. In the literature two kinds of platinum carbides are announced – PtC_2 and Pt_2C_3 [11, 12], but no X-ray data are available for their characterization. There are some data about the existing of PtN [13], but obtained at quite different conditions, then this taking place with the decomposition of the complex.

Conclusions

The TG/DTA curves of the two complexes were different in character. A three-stage mass loss of PtCBH on heating was observed, while PtCHTH decomposed in two stages going through new compounds. The two complexes investigated were more stable than the ligands due to the coordination process. During the decomposition of PtCBH a polymorphous change was detected. After the thermal decomposition of PtCBH the solid residue was platinum, while the decomposition of PtCHTH gave a mixture of platinum carbides (PtC_2, Pt_2C_3).

References

1 P. R. Canal, in: L. G. Grochow and M. M. Ames, A clinician's guide to chemotherapy, pharmacokinetics and pharmacodynamics, Williams and Wilkins, Baltimore, 1998, p. 345.
2 D. Michael, Colvin, Cancer Medicine 4th Ed., Holland, J. F., Frei III, E., Bast, R. C. *et al.*, Williams & Wilkins, Baltimore, 1998, p. 648.
3 B. Desoize and C. Medoulet, Crit. Rev. Oncol., 42 (2002) 317.
4 M. H. Hanigan and P. Devarajan, Canc. Ther., 1 (2003) 47.
5 T. Boulikas and M. Vougiouka, Oncol. Repts, 10 (2003) 1663.
6 C. Xin Zhang and S. J. Lippard, Curr. Opin. Chem. Biol., 7 (2003) 481.
7 A. Bakalova, R. Buyukliev, D. Ivanov, G. Momekov, D. Todorov, S. Konstantinov and M. Karaivanova, Eur. J. Med. Chem., 40 (2005) 590.
8 Lj. Tusek-Bozic and R. Trojko, J. Therm. Anal. Cal., 81 (2005) 153.
9 B.A. Howell, D. Fan and L. Rakesh, J. Therm. Anal. Cal., 85 (2006) 17.
10 Handbuch für Anorganische Synthese, G. Brauer, Berlin, 1980, p. 1818.
11 Tolstykh *et al.*, EXCERPTS and NOTES (Section 5b, from Jedwab 1995 to Zavaridsky), (1996).
12 Gmelins Handbuch der Anorganischen Chemie, Verbindungen bis Platin and Wismut, Verlag Chemie, GMBH., Weinheim/Bergstr. und Berlin, 1939, p. 115.
13 B. R. Sahu, Leonard Kleinman, Phys. Rev. B (Condensed Matter and Materials Physics – 15 (II)), 71, 041101(R) (2005).

Received: December 14, 2005
Accepted: October 10, 2006
OnlineFirst: February 26, 2007

DOI: 10.1007/s10973-005-7474-1