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Enthalpy of Formation of $PtCl_3$(9-Methyladeninium)

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The enthalpy of reaction (1) where 9-MeAd is 9-methyladenine and the symbol H_2O refers to 10^4 mol water, has been determined calorimetrically:

$$[K_2PtCl_4, H_2O](l) + [9\text{-}MeAdHCl, H_2O](l) \rightarrow PtCl_3(9\text{-}MeAdH)(s) + [2KCl, 2H_2O](l)$$

$$[K_2PtCl_4, H_2O](l) + 9\text{-}MeAd(s) + [HCl, H_2O](l) \rightarrow PtCl_3(9\text{-}MeAdH)(s) + [2KCl, 2H_2O](l)$$

as $\Delta H(1) = -77.9 \pm 4.2$ kJ mol^{-1}. The enthalpy of reaction (9) has been calculated to be $\Delta H(9) = -69.3 \pm 4.5$ kJ mol^{-1}. An upper limit of 217 kJ mol^{-1} is derived for the bond dissociation energy D(Pt–N) for the strength of the bond between platinum and the N(7) atom of 9-methyladenine.

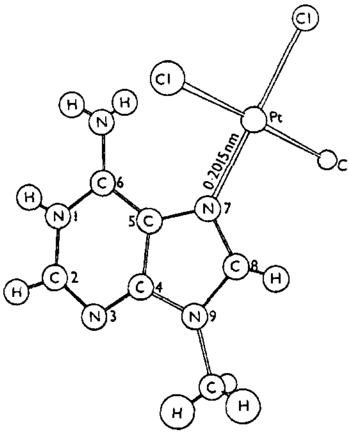

Fig. 1. $PtCl_3$(9-MeAdH).

Introduction

The antitumour activity of platinum compounds, discovered by Rosenberg and coworkers [1], seems to be due to the binding of platinum to the bases of DNA [2] and division of DNA is thus hindered. Following these discoveries, there has been much interest in the chemistry and structure of platinum complexes with nucleotide bases, but no information is available about the thermochemistry of these complexes.

The compound trichloro(9-methyladeninium)platinum(II), $PtCl_3$(9-MeAdH), provides a model compound for a study of the bonding between platinum and a nucleotide base. The structure of this crystalline compound has been determined [3]. The N(9) site, which in the nucleic acids carried a glycosyl residue, is here blocked by a methyl group, the N(1) atom is protonated and coordination to platinum is through N(7). This is the same site as that used by guanine in DNA to coordinate to platinum, although guanine also bonds to platinum through [4] the carbonyl oxygen, O(6), which replaces the NH_2 group of adenine (Fig. 1).

Determination of the enthalpy of reaction between $PtCl_4^{2-}$ and 9-MeAdH$^+$ ions to form $PtCl_3$(9-MeAdH) should provide an indication of the enthalpy of one component of the interaction between $PtCl_4^{2-}$ and the guanine moiety of DNA, namely the formation of the Pt–N(7) bond.

The enthalpy, $\Delta H(1) = -77.9 \pm 4.2$ kJ mol^{-1}, of reaction (1) may be derived from the enthalpies, $\Delta H(2)$ to $\Delta H(8)$ of reactions (2) to (8), where the symbol H_2O refers to 10^4 mol of water, by use of the relationship $\Delta H(1) = -\Delta H(2) + \Delta H(3) - \Delta H(4) + \Delta H(5) - \Delta H(6) + \Delta H(7) - \Delta H(8)$.

$$[K_2PtCl_4, H_2O](l) + [9\text{-}MeAdHCl, H_2O](l) \rightarrow PtCl_3(9\text{-}MeAdH)(s) + [2KCl, 2H_2O](l) \quad (1)$$

$$PtCl_3(9\text{-}MeAdH)(s) + [100KCN, H_2O](l) \rightarrow [K_2Pt(CN)_4, 9\text{-}MeAdHCl, 2KCl, 96KCN, H_2O](l) \quad (2)$$

$$K_2PtCl_4(s) + [100KCN, H_2O](l) \rightarrow [K_2Pt(CN)_4, 4KCl, 96KCN, H_2O](l) \quad (3)$$

$$2KCl(s) + [K_2Pt(CN)_4, 9\text{-}MeAdHCl, 2KCl, 96KCN, H_2O](l) \rightarrow [K_2Pt(CN)_4, 9\text{-}MeAdHCl, 4KCl, 96KCN, H_2O](l) \quad (4)$$

$$2KCl(s) + 2H_2O(l) \rightarrow [2KCl, 2H_2O](l) \quad (5)$$

$$\mathrm{K_2PtCl_4(s) + H_2O(l) \rightarrow [K_2PtCl_4, H_2O](l)} \qquad (6)$$

$$\mathrm{9\text{-}MeAdHCl(s) + [K_2Pt(CN)_4, 4KCl, 96KCN, H_2O](l) \rightarrow [K_2Pt(CN)_4, 9\text{-}MeAdHCl, 4KCl, 96KCN, H_2O](l)} \qquad (7)$$

$$\mathrm{9\text{-}MeAdHCl(s) + H_2O(l) \rightarrow [9\text{-}MeAdHCl, H_2O](l)} \qquad (8)$$

The following values have been obtained: $\Delta H(2) = -409.3 \pm 1.2$ kJ $\mathrm{mol^{-1}}$, $\Delta H(3) = -407.2 \pm 1.9$ kJ $\mathrm{mol^{-1}}$ and $\Delta H(4) = +33.5 \pm 0.2$ kJ for 2 mol KCl. The enthalpies $\Delta H(5) = +34.48 \pm 0.04$ kJ for 2 mol KCl and $\Delta H(6) = +47.7 \pm 0.2$ kJ $\mathrm{mol^{-1}}$ are available from the literature [5]. The enthalpies of reactions (7) and (8) are assumed to be the same as the enthalpies of solution of adenine hydrochloride, under the same conditions, which have been measured as $+10.2 \pm 0.5$ and $+43.5 \pm 0.2$ kJ $\mathrm{mol^{-1}}$, respectively.

The enthalpy, $\Delta H(9)$, of reaction (9), in which solid 9-methyladenine reacts with an aqueous acidic solution of $\mathrm{PtCl_4^{2-}}$ ions to yield the solid complex and an aqueous solution of KCl, is a more appropriate measure of the enthalpy of reaction between an aqueous solution of $\mathrm{PtCl_4^{2-}}$ ions and DNA, than $\Delta H(1)$. The enthalpy, $\Delta H(9)$, can be calculated from the relationship $\Delta H(9) = \Delta H(1) - \Delta H(10) + \Delta H(11)$.

$$\mathrm{[K_2PtCl_4, H_2O](l) + 9\text{-}MeAd(s) + [HCl, H_2O](l) \rightarrow PtCl_3(9\text{-}MeAdH)(s) + [2KCl, 2H_2O](l)} \qquad (9)$$

$$\mathrm{[9\text{-}MeAdHCl, H_2O](l) \rightarrow [9\text{-}MeAd, HCl, H_2O](l)} \qquad (10)$$

$$\mathrm{9\text{-}MeAd(s) + H_2O(l) \rightarrow [9\text{-}MeAd, H_2O](l)} \qquad (11)$$

The enthalpy of deprotonation of the N(1) site of 9-methyladenine, $\Delta H(10)$, has not been measured, but the enthalpy of deprotonation of the N(1) site of adenine has been determined [6] as $\Delta H = +20.13 \pm 0.08$ kJ $\mathrm{mol^{-1}}$. Using this value and the enthalpy $\Delta H(11) = +28.70 \pm 0.18$ kJ $\mathrm{mol^{-1}}$ [7], we calculate the value $\Delta H(9) = -69.3 \pm 4.5$ kJ $\mathrm{mol^{-1}}$.

A further analysis, designed to enable calculation of $\Delta H(12)$, which is a measure of the strength of the Pt–N(7) bond is shown below in the enthalpy cycle.

The enthalpy change associated with the dissociation reaction $\mathrm{PtCl_4^{2-}(aq) \rightarrow PtCl_3^-(aq) + Cl^-(aq)}$ in 0.5 *M* $\mathrm{HClO_4}$ has been determined as $\Delta H(13) = +18.4$ kJ $\mathrm{mol^{-1}}$ from spectroscopic measurement of the temperature variation of the equilibrium constant between 15 and 60 ℃ [8]. The enthalpy of desolvation of the $\mathrm{PtCl_3^-}$ ion is estimated as $\Delta H(14) = +183$ kJ $\mathrm{mol^{-1}}$. De Jonge [9] has calculated a value $\Delta H = -730.1$ kJ $\mathrm{mol^{-1}}$ for the enthalpy of hydration of the $\mathrm{PtCl_4^{2-}}$ ion. Such enthalpies of hydration are proportional to the square of the ionic charge and inversely proportional to the effective radius of the ion. Since the radii of the $\mathrm{PtCl_4^{2-}}$ and $\mathrm{PtCl_3^-}$ ions will be very similar, the enthalpy of hydration of the $\mathrm{PtCl_3^-}$ ion will be roughly one quarter of that of the $\mathrm{PtCl_4^{2-}}$ ion. The enthalpy of sublimation of 9-methyladenine, $\Delta H(15)$ has not been measured, but is assumed to be similar to that of adenine, $\Delta H(\text{sublimation}) = +126.4$ kJ $\mathrm{mol^{-1}}$ [10]. The enthalpy of hydration of the $\mathrm{[PtCl_3(9\text{-}MeAd)]^-}$ is likely to be less than that of the smaller $\mathrm{PtCl_3^-}$ ion, and we assume a value $\Delta H(16) = -160$ kJ $\mathrm{mol^{-1}}$, which is one quarter of that found [9] for the $\mathrm{PtI_4^{2-}}$ ion. The enthalpy of protonation of the N(1) site of 9-methyladenine in the complex $\mathrm{[PtCl_3(9\text{-}MeAd)]^-}$ is not known, but will probably be similar to the enthalpy of protonation of adenine in solution, $\Delta H(17) = -20.1$ kJ $\mathrm{mol^{-1}}$. The justification for this assumption is that coordination at the N(7) site appears to have little effect on the purine molecule [3, 11], in that the bond lengths are only slightly changed. The enthalpy of solution, $\Delta H(18)$ is not available, because of the low solubility of the complex, which leads us to assume that the process will probably be endothermic. Using these additional values and the relationship $\Delta H(12) = \Delta H(9) - \Delta H(13) - \Delta H(14) - \Delta H(15) + \Delta H(18) - \Delta H(17) - \Delta H(16)$, we obtain the value $\Delta H(12) = -317 + \Delta H(18)$. The value $D(\text{Pt–N}) = 217$ kJ $\mathrm{mol^{-1}}$ is likely to be an upper limit.

$$\begin{tikzcd}
\mathrm{PtCl_3^-(g) + Cl^-(aq)} & \mathrm{+\ 9\text{-}MeAd(g)} \arrow[r, "\Delta H(12)"] & \mathrm{[PtCl_3(9\text{-}MeAd)]^-(g) + Cl^-(aq)} \arrow[d, "\Delta H(16)"] \\
\mathrm{PtCl_3^-(aq) + Cl^-(aq)} \arrow[u, "\Delta H(14)"] & & \mathrm{[PtCl_3(9\text{-}MeAd)]^-(aq) + Cl^-(aq)} \arrow[d, "\Delta H(17)"] \\
\mathrm{PtCl_4^{2-}(aq)} \arrow[u, "\Delta H(13)"] & \mathrm{+\ 9\text{-}MeAd(s)} \arrow[uu, "\Delta H(15)"] \arrow[dr, "\Delta H(9)"] & \mathrm{PtCl_3(9\text{-}MeAdH)(aq) + Cl^-(aq)} \\
 & & \mathrm{PtCl_3(9\text{-}MeAdH)(s) + Cl^-(aq)} \arrow[u, "\Delta H(18)"]
\end{tikzcd}$$

Experimental

Potassium tetrachloroplatinite (Johnson Matthey) was used as supplied. Trichloro(9-methyladeninium)-platinum(II) was prepared by reaction of K_2PtCl_4 with 9-methyladenine. Potassium cyanide (BDH) was heated to 100 °C in vacuo for several hours to remove any ammonium acetate formed by hydrolysis. Distilled water used as solvent was degassed and saturated with nitrogen. Enthalpies of reaction were measured by use of the LKB 8700 calorimeter equipped with a 25 ml reaction vessel. Calibration was by the electrical substitution method. Uncertainties quoted are twice the standard deviations of mean values, which refer to 298.15 K.

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