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# Triphenylmethylphosphonium Trichloro(caffeine)platinum(II), $[P(C_6H_5)_3(CH_3)][PtCl_3(caffeine)]$, Structure and Anticancer Activity

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The salt $[PPh_3Me][PtCl_3(caffeine)]$ has been synthesized and its structure determined. It crystallizes in the triclinic space group $C_i^1$-$P\bar{1}$ with cell dimensions at −162 °C of $a$ = 12.332 (5) Å, $b$ = 13.230 (6) Å, $c$ = 8.712 (4) Å, $\alpha$ = 97.07 (2)°, $\beta$ = 99.78 (4)°, $\gamma$ = 93.63 (1)°, $V$ = 1385 Å$^3$, and $Z$ = 2. The structure was solved by heavy-atom methods, and the 217 variables were refined by least-squares techniques to a final $R$ index on $F$ of 0.038 for the 5670 data. The structure consists of discrete $[PPh_3Me]^+$ cations and $[PtCl_3(caffeine)]^-$ anions. The square-planar Pt(II) ion is bound to atom N(9) of the caffeine ligand at a distance of 2.021 (5) Å. The related salt $K[PtCl_3(caffeine)]$ has significant anticancer activity.

## Introduction

Caffeine is an inhibitor of DNA repair, and it has been shown in cell culture studies that caffeine greatly increases cell kill caused by *cis*-$PtCl_2(NH_3)_2$.[2] Further, a single in vivo study indicates that caffeine potentiates the activity of cyclophosphamide.[3] With the thought of producing a complex which would potentiate *cis*-$PtCl_2(NH_3)_2$ or which might have anticancer activity of its own, we synthesized the $[PtCl_3(caffeine)]^-$ anion. Here we report its structure and the fact that it has anticancer activity against the P388 tumor test system.

## Experimental Section

The complex $[PPh_3Me][PtCl_3(caffeine)]$ was prepared by reacting 0.249 g of $K_2PtCl_4$ with 0.116 g of caffeine in 10 mL of $H_2O$ for a period of 4 days. Dilution of 1.5 mL of this solution with 15 mL of $H_2O$ was followed by the addition of 1.5 mL of 0.2 M $[P(C_6H_5)_3(CH_3)]Cl$. Evaporation of this solution to near dryness produced a mushy, pale yellow, solid mass. Extraction of this solid mass with 5 mL of $CH_3OH$ produced a yellow solution which was allowed to evaporate over a period of 5 days to produce a white solid and two types of yellow crystals. The white solid was dissolved in $H_2O$ in which the yellow crystals are insoluble. The structure reported here is for the yellow, triclinic crystals. The other yellow crystals may be of higher symmetry, but no structural work has yet been attempted.

Both Weisenberg and precession film data indicated a lack of symmetry. Successful refinement of the structure in space group $C_i^1$-$P\bar{1}$ suggests it to be the correct choice. Cell dimensions at −162 (2) °C, obtained by manual centering[4] of 21 reflections in the range 30° ≤ $2\theta$ (Mo $K\alpha_1$) ≤ 35° on a Picker FACS-I diffractometer, are $a$ = 12.332 (5) Å, $b$ = 13.230 (6) Å, $c$ = 8.712 (4) Å, $\alpha$ = 97.07 (2)°, $\beta$ = 99.78 (4)°, $\gamma$ = 93.63 (1)° for the Delaunay reduced cell. For a cell volume of 1385 Å$^3$ and a formula weight of 772.97 amu the density of 1.853 g/cm$^3$ calculated for two formula units in the cell at −162 °C is in reasonable agreement with 1.88 (2) g/cm$^3$ measured by flotation methods at room temperature.

Parameters for data collection are listed in Table I. The intensities of seven check reflections, measured periodically throughout data collection, were stable. The data, corrected for Lorentz and polarization effects, were processed as previously described[5] using a value of $p$ of 0.04.

The structure was solved by standard methods.[5] The positions of the $Pt^{2+}$ ion, all three chloro ligands, and atom N(9), i.e., the coordination sphere, were determined from a sharpened, origin-removed, Patterson function. The remaining nonhydrogen atoms were located in the ensuing Fourier map. The atomic parameters were refined by least-squares methods by minimization of the function $\sum w(|F_o| - |F_c|)^2$ in which $w = 4F_o^2/\sigma^2(F_o^2)$ and $|F_o|$ and $|F_c|$ are the observed and calculated structure amplitudes.

Each phenyl group was treated throughout the refinement as a planar rigid body with uniform C–C distances of 1.392 Å and with each carbon atom being assigned an individual isotropic thermal parameter. All aromatic hydrogen atom positions were idealized; the C–H distance was assumed to be 0.95 Å with normal C–C–H bond

**Table I.** Summary of Crystal Data and Intensity Collection

| | |
|---|---|
| compd | $[PPh_3Me][PtCl_3(caffeine)]$ |
| formula | $C_{27}H_{28}Cl_3N_4O_2PPt$ |
| fw | 772.97 |
| $a$ | 12.332 (5) Å |
| $b$ | 13.230 (6) Å |
| $c$ | 8.712 (4) Å |
| $\alpha$ | 97.07 (2)° |
| $\beta$ | 99.78 (4)° |
| $\gamma$ | 93.63 (1)° |
| $V$ | 1385 Å$^3$ |
| $Z$ | 2 |
| density | 1.853 g/cm$^3$ (calcd, −162 °C),[a] 1.88 g/cm$^3$ (exptl, 20 °C) |
| space group | $C_i^1$-$P\bar{1}$ |
| cryst dimens | 0.05 × 0.06 × 0.17 mm |
| cryst vol | 0.0011 mm$^3$ |
| cryst shape | parallelepiped with {11$\bar{1}$}, {010}, and {001} |
| radiation | Mo Kα (λ(Mo $K\alpha_1$) = 0.7093 Å) from graphite monochromator |
| temp | −162 (2) °C[a] |
| $\mu$ | 55.0 cm$^{-1}$ |
| transmission factors | 0.693–0.775 |
| receiving aperature | 3.3 mm wide × 5.9 mm high, 32 cm from crystal |
| takeoff angle | 3.2° |
| scan speed | 2.0° in $2\theta$/min |
| scan range | 1.0° below $K\alpha_1$ to 0.90° above $K\alpha_2$ |
| bkgd counting | 10 s with rescan option[b] |
| $2\theta$ limit | 56.5° |
| $p$ | 0.04 |
| final no. of variables | 217 |
| unique data measd | 6535 |
| unique data used ($F_o^2 > 3\sigma(F_o^2)$) | 5670 |
| $R$ | 0.038 |
| $R_w$ | 0.045 |
| error in obsn of unit wt | 1.32 electrons |

[a] The low-temperature system is based on a design by: Huffman, J. C. Ph.D. Thesis, Indiana University, 1974. [b] The diffractometer was run under the Vanderbilt disk-oriented system (Lenhert, P. G. *J. Appl. Crystallogr.* **1975**, *8*, 568–571).

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(2) van den Berg, H. W.; Fravol, H. N. A.; Roberts, J. J. *J. Clin. Hematol. Oncol.* **1977**, *7*, 349–373.
(3) Gaudin, D.; Yielding, K. L. *Proc. Soc. Expt. Biol. Med.* **1969**, *131*, 1413–1416.
(4) Corfield, P. W. R.; Doedens, R. J.; Ibers, J. A. *Inorg. Chem.* **1967**, *6*, 197–204.
(5) Doedens, R. J.; Ibers, J. A. *Inorg. Chem.* **1967**, *6*, 204–210.

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**Table II.** Positional and Thermal Parameters for the Nongroup Atoms of $[P(C_6H_5)_3(CH_3)][PtCl_3(caffeine)]$

| atom | $x$[a] | $y$ | $z$ | $B_{11}$[b] | $B_{22}$ | $B_{33}$ | $B_{12}$ | $B_{13}$ | $B_{23}$ |
|---|---|---|---|---|---|---|---|---|---|
| Pt | 0.12865 (2) | 0.18832 (2) | 0.06429 (2) | 1.44 (1) | 1.29 (1) | 4.31 (3) | 0.28 (1) | 0.45 (1) | 0.03 (1) |
| Cl(1) | 0.0414 (1) | 0.1687 (1) | −0.1951 (2) | 2.70 (8) | 2.16 (7) | 4.6 (2) | 0.51 (6) | 0.71 (9) | 0.22 (9) |
| Cl(2) | 0.0345 (1) | 0.3281 (1) | 0.1219 (2) | 2.60 (8) | 1.71 (7) | 5.7 (2) | 0.64 (6) | 0.41 (10) | −0.30 (9) |
| Cl(3) | 0.2102 (1) | 0.1975 (1) | 0.3242 (2) | 2.97 (9) | 3.02 (9) | 5.3 (2) | 0.82 (7) | −0.4 (1) | −0.35 (10) |
| P | 0.2102 (1) | −0.3713 (1) | 0.4251 (2) | 1.48 (8) | 1.62 (7) | 3.8 (2) | 0.21 (6) | 0.30 (9) | 0.15 (9) |
| N(1) | 0.4538 (4) | −0.0364 (3) | −0.2086 (5) | 1.7 (3) | 2.1 (2) | 4.5 (7) | 0.3 (2) | 0.3 (3) | 0.2 (3) |
| C(1) | 0.5394 (4) | −0.0751 (5) | −0.2926 (7) | 2.2 (3) | 3.4 (3) | 4.8 (7) | 0.6 (3) | 1.0 (4) | 0.1 (4) |
| C(2) | 0.4398 (4) | 0.0674 (4) | −0.2075 (7) | 2.1 (3) | 2.3 (3) | 4.4 (8) | 0.2 (3) | 0.0 (4) | 0.3 (4) |
| O(2) | 0.4965 (3) | 0.1212 (3) | −0.2707 (5) | 2.8 (3) | 3.1 (2) | 7.5 (6) | 0.5 (2) | 1.9 (3) | 1.4 (3) |
| N(3) | 0.3581 (4) | 0.1069 (4) | −0.1311 (6) | 2.5 (3) | 1.7 (3) | 6.3 (7) | 0.4 (2) | 1.1 (4) | 1.2 (3) |
| C(3) | 0.3479 (5) | 0.2158 (5) | −0.1259 (9) | 3.7 (4) | 2.3 (4) | 13 (1) | 0.5 (3) | 3.7 (6) | 1.4 (5) |
| C(4) | 0.2959 (4) | 0.0419 (4) | −0.0627 (6) | 1.5 (3) | 1.7 (3) | 4.8 (7) | 0.2 (2) | 0.6 (4) | 0.8 (3) |
| C(5) | 0.3134 (4) | −0.0589 (4) | −0.0644 (6) | 1.3 (3) | 2.0 (3) | 4.4 (7) | 0.3 (3) | 0.2 (4) | 0.3 (4) |
| C(6) | 0.3927 (4) | −0.1072 (4) | −0.1423 (6) | 1.2 (3) | 2.0 (3) | 3.7 (6) | −0.2 (2) | −0.5 (3) | −0.1 (4) |
| O(6) | 0.4085 (3) | −0.1982 (3) | −0.1538 (5) | 2.4 (3) | 1.8 (2) | 6.7 (6) | 0.5 (2) | 1.0 (3) | −0.4 (3) |
| N(7) | 0.2380 (3) | −0.1006 (3) | 0.0157 (5) | 1.5 (3) | 1.6 (2) | 4.6 (6) | 0.0 (2) | 0.7 (3) | 0.0 (3) |
| C(7) | 0.2240 (5) | −0.2055 (4) | 0.0472 (7) | 3.0 (4) | 1.6 (3) | 6.7 (8) | 0.5 (3) | 1.2 (4) | 0.6 (4) |
| C(8) | 0.1784 (4) | −0.0254 (4) | 0.0614 (6) | 1.5 (3) | 1.6 (3) | 4.7 (7) | 0.1 (2) | 0.3 (4) | 0.0 (3) |
| N(9) | 0.2094 (4) | 0.0636 (4) | 0.0142 (6) | 2.0 (3) | 1.8 (3) | 5.2 (7) | 0.5 (2) | 0.9 (4) | 0.6 (3) |
| C(40) | 0.1083 (4) | −0.4109 (4) | 0.2527 (7) | 2.0 (3) | 2.1 (3) | 5.8 (8) | 0.2 (3) | −0.3 (4) | 0.0 (4) |

[a] Estimated standard deviations in the least significant figure(s) are given in parentheses in this and all subsequent tables. [b] The form of the anisotropic thermal ellipsoid is $\exp[-(B_{11}h^2 + B_{22}k^2 + B_{33}l^2 + 2B_{12}hk + 2B_{13}hl + 2B_{23}kl)]$. The quantities given in the table are the thermal coefficients $\times 10^3$.

**Table III.** Derived Parameters for the Rigid-Group Atoms of $[P(C_6H_5)_3(CH_3)][PtCl_3(caffeine)]$

Positional and Thermal Parameters

| atom | $x$ | $y$ | $z$ | $B$, Å$^2$ | atom | $x$ | $y$ | $z$ | $B$, Å$^2$ |
|---|---|---|---|---|---|---|---|---|---|
| C(10) | 0.1922 (3) | −0.4494 (2) | 0.5729 (3) | 1.13 (8) | C(23) | 0.5531 (2) | −0.4321 (3) | 0.3264 (5) | 2.3 (1) |
| C(11) | 0.2252 (3) | −0.4081 (2) | 0.7305 (4) | 1.50 (9) | C(24) | 0.4595 (3) | −0.4851 (3) | 0.2308 (4) | 2.7 (1) |
| C(12) | 0.2210 (3) | −0.4700 (3) | 0.8482 (3) | 1.74 (10) | C(25) | 0.3546 (3) | −0.4642 (3) | 0.2589 (4) | 2.0 (1) |
| C(13) | 0.1837 (3) | −0.5733 (2) | 0.8084 (3) | 1.58 (9) | C(30) | 0.1961 (3) | −0.2405 (2) | 0.4940 (4) | 1.22 (8) |
| C(14) | 0.1506 (3) | −0.6145 (2) | 0.6508 (4) | 1.70 (9) | C(31) | 0.1097 (3) | −0.2197 (2) | 0.5745 (4) | 1.46 (9) |
| C(15) | 0.1549 (3) | −0.5526 (2) | 0.5331 (3) | 1.41 (8) | C(32) | 0.0862 (2) | −0.1189 (3) | 0.6128 (4) | 1.58 (9) |
| C(20) | 0.3433 (2) | −0.3904 (3) | 0.3828 (4) | 1.18 (8) | C(33) | 0.1492 (3) | −0.0389 (2) | 0.5706 (5) | 1.69 (9) |
| C(21) | 0.4370 (3) | −0.3374 (3) | 0.4784 (4) | 1.7 (1) | C(34) | 0.2355 (3) | −0.0597 (2) | 0.4901 (4) | 1.63 (9) |
| C(22) | 0.5419 (2) | −0.3583 (3) | 0.4503 (5) | 2.2 (1) | C(35) | 0.2590 (2) | −0.1605 (3) | 0.4518 (4) | 1.40 (8) |

Rigid-Group Parameters

| group | $x_c$[a] | $y_c$ | $z_c$ | $\delta$[b] | $\epsilon$ | $\eta$ |
|---|---|---|---|---|---|---|
| phen1 | 0.1879 (2) | −0.5113 (2) | 0.6907 (3) | 2.664 (3) | 2.444 (2) | −1.289 (3) |
| phen2 | 0.4482 (2) | −0.4113 (2) | 0.3546 (3) | 2.515 (3) | 2.352 (3) | 0.505 (3) |
| phen3 | 0.1728 (2) | −0.1397 (2) | 0.5323 (3) | −1.155 (2) | 2.528 (2) | −0.343 (3) |

[a] $x_c$, $y_c$, and $z_c$ are the fractional coordinates of the origin of the rigid group. [b] The rigid-group orientation angles $\delta$, $\epsilon$, and $\eta$ (radians) have been defined previously: LaPlaca, S. J.; Ibers, J. A. *Acta Crystallogr.* **1965**, *18*, 5.

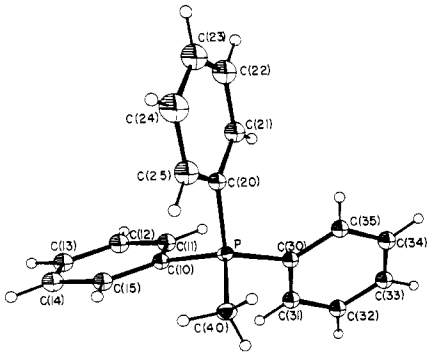


**Figure 1.** Perspective view of the $[P(Ph)_3Me]^+$ cation. The 50% probability thermal ellipsoids are shown except for hydrogen atoms which are artificially set at $B = 0.6$ Å$^2$.

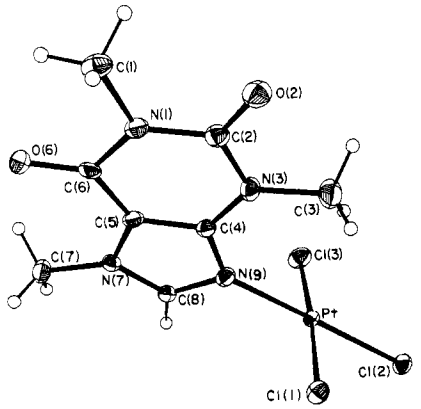


**Figure 2.** Perspective view of the $[PtCl_3(caffeine)]^-$ anion. Thermal ellipsoids are as described for Figure 1.

angles. The positions of the hydrogen atoms of the four methyl groups were found in a difference Fourier map and were idealized. All hydrogen atoms were included as fixed contributions in the final anisotropic refinements.[6]

The final agreement indices, based on refinement on $F_o$ for 5670 unique, absorption-corrected data for which $F_o^2 \geq 3\sigma(F_o^2)$ and on 217 variables, are $R = 0.038$ and $R_w = 0.045$. The final positional and thermal parameters of individual atoms appear in Table II, while those for the rigid groups are in Table III. The idealized positions

(6) Computer programs used are as listed in: Kaduk, J. A.; Ibers, J. A. *Inorg. Chem.* **1977**, *16*, 3278–3282.

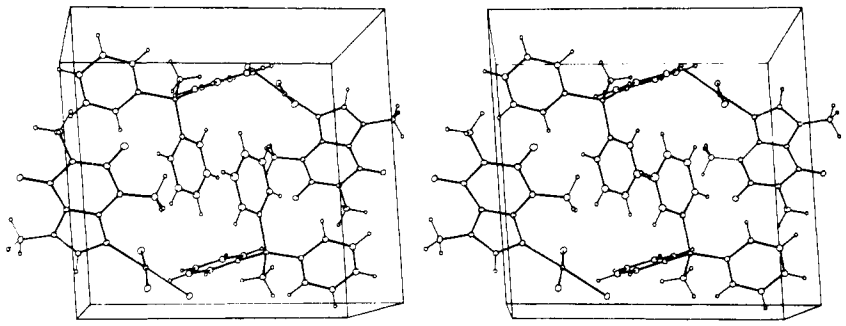

**Figure 3.** Stereoview of the contents of a single unit cell of $[Pt(Ph)_3Me][PtCl_3(caffeine)]$ down $c$. The 20% thermal ellipsoids are shown, except for hydrogen atoms which have been artificially set at $B = 0.6$ Å.

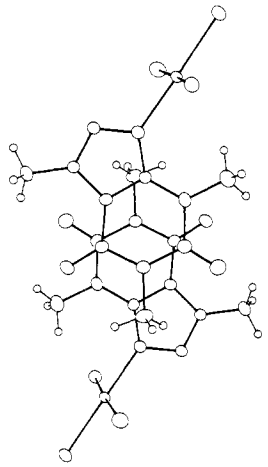

**Figure 4.** Drawing illustrating the base stacking arrangement between molecules. The purine plane lies in the page. Thermal ellipsoids are as described for Figure 1.

**Table V.** Bond Lengths (Å) and Bond Angles (Deg) for $[PPh_3Me][PtCl_3(caffeine)]$

| atoms | dist | atoms | dist |
|---|---|---|---|
| | Coordination Sphere | | |
| Pt-N(9) | 2.021 (5) | Pt-Cl(1) | 2.308 (2) |
| Pt-Cl(2) | 2.294 (2) | Pt-Cl(3) | 2.301 (2) |
| | Caffeine | | |
| N(1)-C(1) | 1.467 (7) | C(4)-N(9) | 1.379 (7) |
| N(1)-C(2) | 1.395 (7) | C(5)-N(7) | 1.381 (6) |
| N(1)-C(6) | 1.403 (7) | C(5)-C(6) | 1.422 (7) |
| C(2)-O(2) | 1.210 (7) | C(6)-O(6) | 1.227 (7) |
| C(2)-N(3) | 1.392 (7) | N(7)-C(8) | 1.335 (7) |
| N(3)-C(4) | 1.371 (6) | N(7)-C(7) | 1.453 (7) |
| N(3)-C(3) | 1.451 (8) | C(8)-N(9) | 1.349 (7) |
| C(4)-C(5) | 1.364 (7) | | |
| | Cation | | |
| P-C(40) | 1.786 (6) | P-C(20) | 1.770 (3) |
| P-C(10) | 1.781 (4) | P-C(30) | 1.789 (3) |
| **atoms** | **angle** | **atoms** | **angle** |
| | Coordination Sphere | | |
| N(9)-Pt-Cl(2) | 179.1 (1) | N(9)-Pt-Cl(1) | 89.1 (1) |
| Cl(3)-Pt-Cl(1) | 176.24 (5) | Cl(2)-Pt-Cl(3) | 90.85 (6) |
| N(9)-Pt-Cl(3) | 89.1 (1) | Cl(2)-Pt-Cl(1) | 90.88 (5) |
| | Cation | | |
| C(10)-P-C(20) | 105.7 (2) | C(11)-C(10)-P | 118.8 (2) |
| C(10)-P-C(30) | 110.2 (2) | C(15)-C(10)-P | 120.9 (2) |
| C(10)-P-C(40) | 110.1 (2) | C(21)-C(20)-P | 120.5 (3) |
| C(20)-P-C(30) | 112.5 (2) | C(25)-C(20)-P | 119.3 (2) |
| C(20)-P-C(40) | 109.9 (2) | C(31)-C(30)-P | 117.8 (2) |
| C(30)-P-C(40) | 108.5 (2) | C(35)-C(30)-P | 121.7 (3) |

of the hydrogen atoms are listed in Table IV.[7] A listing of the observed and calculated structure amplitudes is available.[7]

**Table VI.** Best Weighted Least-Squares Planes

| plane 1 | | plane 2 | | plane 3 | |
|---|---|---|---|---|---|
| atom | dev, Å | atom | dev, Å | atom | dev, Å |
| N(9) | −0.008 (5) | N(1) | 0.006 (5) | Pt | 0.0028 (2) |
| C(8) | 0.006 (5) | C(2) | 0.001 (6) | Cl(1) | −0.054 (1) |
| N(7) | −0.001 (4) | N(3) | −0.001 (5) | Cl(2) | −0.002 (1) |
| C(4) | 0.008 (5) | C(4) | −0.008 (5) | Cl(3) | −0.074 (2) |
| C(5) | −0.005 (5) | C(5) | 0.017 (5) | N(9) | −0.026 (5) |
| Pt | −0.049[a] | C(6) | −0.013 (5) | | |
| C(7) | 0.001 | O(6) | −0.054 | | |
| | | C(1) | −0.016 | | |
| | | O(2) | −0.001 | | |
| | | C(3) | 0.049 | | |

Angles (Deg) between Planes

plane 1-plane 2 1.7 plane 1-plane 3 73.5

Parameters Defining Planes[b]

| | plane 1 | plane 2 | plane 3 |
|---|---|---|---|
| $\sigma$ | 0.006 | 0.008 | 0.03 |
| $A$ | 6.172 | 6.356 | 9.299 |
| $B$ | 1.088 | 0.750 | 7.659 |
| $C$ | 6.425 | 6.382 | −3.487 |
| $D$ | 1.461 | 1.520 | 2.412 |

| plane 4 | | plane 5 | | plane 6 | |
|---|---|---|---|---|---|
| atom | dev, Å | atom | dev, Å | atom | dev, Å |
| C(10)-C(15) | 0.0 (0) | C(20)-C(25) | 0.0 (0) | C(30)-C(35) | 0.0 (0) |
| P | −0.151 | P | 0.117 | P | −0.228 |

Angles (Deg) between Planes

plane 4-plane 5 96.7 plane 4-plane 6 116.8

plane 5-plane 6 55.8

Parameters Defining Planes[b]

| | plane 4 | plane 5 | plane 6 |
|---|---|---|---|
| $\sigma$ | 0.0 | 0.0 | 0.0 |
| $A$ | −12.013 | −0.415 | 6.016 |
| $B$ | 3.747 | −10.413 | −1.169 |
| $C$ | 1.539 | 6.172 | 6.754 |
| $D$ | −3.111 | 6.286 | 4.797 |

[a] If no error is given, the atom was not used in the calculation of the plane. [b] The equation of the plane is $Ax + By + Cz - D = 0$ in triclinic coordinates.

## Description of the Structure

The structure consists of discrete $[P(Ph)_3Me]^+$ cations (Figure 1) and $[PtCl_3(caffeine)]^-$ anions (Figure 2). A drawing of the contents of a unit cell is shown in Figure 3. Bond distances and angles are listed in Table V.

The most interesting feature of the packing is a base-stacking arrangement of two caffeine molecules, one at $x$, $y$, $z$ and the other at $1 - x$, $-y$, $-z$, which are separated by 3.31 (4) Å (Figure 4). There are only four other short contacts:

(7) Supplementary material.

**Table VII.** Comparison of Caffeine Bond Angles in Various Caffeine Structures

| | angles,[g] deg | | | | | |
|---|---|---|---|---|---|---|
| atoms | caffeine[a] | $[H(caffeine)]^+$ [c] | $[PtCl_3(caffeine)]^-$ | $CuCl_2(caffeine)(H_2O)$ [d] | $[Cu(NO_3)(caffeine)(H_2O)_3]^+$ [e] | $[RuCl_2(caffeine)(NH_3)_3]^+$ [f] |
| C(2)-N(1)-C(6) | 127.4 (6)[b] | 127.0 (3) | 126.9 (4) | 126.1 (8) | 126.3 (3) | 127 (1) |
| C(2)-N(1)-C(1) | 115.8 (4) | 115.3 (3) | 115.8 (4) | 116.6 (10) | 115.3 (4) | 114 (1) |
| C(6)-N(1)-C(1) | 116.8 (5) | 117.6 (3) | 117.4 (4) | 117.3 (9) | 118.4 (3) | 119 (1) |
| O(2)-C(2)-N(3) | 121.4 (4) | 122.0 (3) | 121.2 (5) | 121.3 (9) | 121.7 (3) | 119 (1) |
| O(2)-C(2)-N(1) | 121.9 (5) | 120.7 (3) | 121.2 (5) | 121.2 (9) | 121.3 (4) | 123 (1) |
| N(3)-C(2)-N(1) | 116.6 (7) | 117.2 (3) | 117.6 (5) | 117.5 (8) | 117.1 (3) | 118 (1) |
| C(4)-N(3)-C(2) | 119.7 (4) | 118.6 (3) | 118.6 (5) | 118.9 (8) | 118.9 (3) | 117 (1) |
| C(4)-N(3)-C(3) | 121.4 (4)* | 121.9 (3)* | 124.7 (5) | 122.2 (8) | 122.1 (3)* | 123 (1) |
| C(2)-N(3)-C(3) | 118.5 (4) | 119.2 (3)* | 116.7 (5) | 118.4 (8) | 118.5 (3)* | 119 (1) |
| C(5)-C(4)-N(3) | 121.8 (4) | 123.8 (3) | 122.0 (5) | 122.6 (8) | 122.1 (3) | 123 (1) |
| C(5)-C(4)-N(9) | 111.6 (4)* | 107.9 (3)* | 109.7 (4) | 110.8 (8) | 110.0 (3) | 109 (1) |
| N(3)-C(4)-N(9) | 126.6 (4) | 128.4 (3) | 128.3 (5) | 126.6 (8) | 127.9 (3) | 127 (1) |
| C(4)-C(5)-N(7) | 105.7 (5) | 106.8 (3) | 106.6 (4) | 106.1 (8) | 106.0 (3) | 107 (1) |
| C(4)-C(5)-C(6) | 123.4 (4) | 122.3 (3) | 123.8 (5) | 122.1 (9) | 122.0 (3)* | 123 (1) |
| N(7)-C(5)-C(6) | 130.8 (5) | 131.0 (3) | 129.5 (5) | 131.8 (9) | 132.0 (3)* | 129 (1) |
| O(6)-C(6)-N(1) | 121.9 (4) | 122.4 (3) | 122.3 (5) | 121.6 (8) | 121.7 (3) | 121 (1) |
| O(6)-C(6)-C(5) | 127.1 (4) | 126.7 (3) | 126.6 (5) | 126.4 (10) | 125.8 (3) | 128 (1) |
| N(1)-C(6)-C(5) | 110.9 (4) | 111.0 (3) | 111.1 (5) | 112.0 (8) | 112.5 (2) | 119 (1)* |
| C(8)-N(7)-C(5) | 105.9 (7) | 107.9 (3) | 107.0 (4) | 107.4 (8) | 107.2 (2) | 108.4 (9) |
| C(8)-N(7)-C(7) | 127.0 (5) | 126.3 (3) | 125.3 (4) | 124.5 (9) | 125.4 (3) | 127 (1) |
| C(5)-N(7)-C(7) | 127.7 (1) | 125.8 (3)* | 127.8 (4) | 127.8 (8) | 127.1 (3) | 124 (1)* |
| N(7)-C(8)-N(9) | 113.3 (4) | 109.6 (3)* | 112.0 (5) | 112.6 (9) | 112.2 (3) | 107.8 (9)* |
| C(8)-N(9)-C(4) | 103.5 (4) | 107.8 (3)* | 104.7 (4) | 103.1 (8) | 104.6 (2) | 108.0 (9)* |
| C(8)-N(9)-M | | 128 (2)* | 119.4 (4) | 123.6 (7)* | 122.8 (2)* | |
| C(4)-N(9)-M | | 124 (2)* | 135.8 (4) | 132.1 (7)* | 130.8 (2)* | |

[a] Average of the values found for caffeine-5-chlorosalicyclic acid[11] and caffeine-bis(5,5-diethylbarbuteric acid).[12] [b] The number in parentheses is the larger of the standard deviations estimated for an individual value from the inverse matrix or calculated on the assumption that the two reported values are from the same population. [c] Reference 10. [d] Reference 9. [e] Reference 8. [f] Reference 13. [g] Angles judged to be significantly different from those found in $[PtCl_3(caffeine)]^-$ are designated with an asterisk.

N(1)···C(34) = 3.395, O(6)···C(11) = 3.402, C(40)···C(14) = 3.463, and C(4)···C(33) = 3.402 Å. There may be a very weak CH···Cl hydrogen bond as atom Cl(2) is 3.511 Å from atom C(40) and the calculated C(40)—HC(40)—Cl(2) angle is 164°.

The geometry of the Pt(II) coordination sphere is essentially square planar as can be seen from the bond angles in Table V and the parameters of the least-squares plane in Table VI. Deviations from the coordination plane are as large as 0.074 (2) Å, and all four ligand atoms are displaced in the same direction.

While the imidazole ring is planar (plane 1, Table VI), the Pt(II) ion is displaced from this plane by 0.049 Å. Somewhat larger displacements have been observed in other metal complexes of caffeine.[8,9] The pyrimidine ring is also planar (plane 2, Table VI). As is usually observed for purines,[10] the pyrimidine and imidazole planes define a nonzero dihedral angle, 1.7° in this case. Finally, as is always observed for Pt(II) complexes of purines, the imidazole plane is rotated away from the coordination plane, 73.5° in the present structure.

Comparison of bond lengths of the caffeine ligand in this complex with those reported for caffeine,[11,12] $(H(caffeine))^+$,[10] $CuCl_2(caffeine)(H_2O)$[9], $[Cu(NO_3)(caffeine)(H_2O)_3]^+$,[8] and $[RuCl_2(caffeine)(NH_3)_3]^+$[13] reveals no significant differences except in the latter complex where the metal ion is bound at atom C(8). Bond angles in these various caffeine derivatives are listed in Table VII. A few of the bond angles, those marked with an asterisk, appear to be altered significantly by coordination. Comparison of caffeine and $(H(caffeine))^+$ shows that upon protonation of atom N(9), the angles C(5)–C(4)–N(3) and C(8)–N(9)–C(4) increase while C(5)–C(4)–N(9), C(5)–N(7)–C(7), and N(7)–C(8)–N(9) decrease significantly. The values observed for these angles in the present complex are in close agreement with those found for the Cu(II) complexes and are intermediate to those for the free and protonated base, although they are much closer to those of the free base. Therefore the effect on the caffeine ligand of metal coordination at atom N(9) is similar to but smaller than that of protonation.

Trends observed in Table VII for four angles suggest there is a steric interaction between the C(3) methyl group and the metal ion (M) coordination sphere. Such a repulsive interaction would cause the C(4)–N(3)–C(3) and C(4)–N(9)–M angles to increase and the C(2)–N(3)–C(3) and C(8)–N(9)–M angles to decrease. The observed trend indicates that this repulsive interaction increases in the caffeine derivatives in the order $(H(caffeine))^+ < [Cu(NO_3)(caffeine)(H_2O)_3]^+ \approx CuCl_2(caffeine)(H_2O) < [PtCl_3(caffeine)]^-$, which is also the order of increasing steric bulk of the other ligands coordinated to the metal ion.

Bushnell et al. have pointed out that complexes of the type $[PtCl_3L]^-$ are very suitable for the determination of the structural trans influence of the ligand L.[14] The Pt–Cl bond trans to L decreases in length (given in angstroms) in the following order: $[PtCl_3(PEt_3)]^-$, 2.382 (4);[14] $[Pt(Cl_3)(C_2H_4)]^-$, 2.327 (5);[15] $[PtCl_3(Me_2SO)]^-$, 2.318 (5);[16] $[PtCl_4]^{-2}$, 2.317 (2);[17] $[PtCl_3(9\text{-methyladeninium})]$, 2.302 (2);[18] $[PtCl_3(2,6-$

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$Me_2Py)]^-$, 2.299 (2);[19] $[PtCl_3(caffeine)]^-$, 2.294 (2); $[PtCl_3CO]^-$, 2.289 (3).[20] Thus the structural trans influence of caffeine is slightly less than that of $Me_2SO$ or a chloro ligand, similar to that of other heterocyclic nitrogen donors and slightly greater than that of CO.

The triphenylmethylphosphonium cation is tetrahedral with the phenyl rings arranged as the blades of a propeller, as is usually found for this cation.[21-27] The phosphorus atom does not lie in any of the phenyl planes (Table VII). Smaller deviations of 0.013–0.136 Å have been reported before.[23-25]

Several workers have stated that the P–$CH_3$ bond is expected to be longer than the P–$C_6H_5$ bond because of the differing hybridization of the carbon atoms.[22,23,27,28] The P–$CH_3$ bond has been observed to be longer in several structures,[22,23,25] including the compound reported here, where the P–$CH_3$ bond (1.786 (6) Å) is insignificantly longer than the average of the P–$C_6H_5$ bonds (1.780 (10) Å). However, in all cases the differences in the P–$CH_3$ and P–$C_6H_5$ bond lengths are small enough to be accounted for by experimental error. We have averaged the P–$CH_3$ and P–$C_6H_5$ lengths found in all reported structures of the $[P(C_6H_5)_3CH_3]^+$ cation for which the standard deviations are less than 0.01 Å.[22-24,28] The results averaged over six cations are as follows: P–$CH_3$, 1.785 (8) Å; P–$C_6H_5$, 1.784 (12) Å. There is, therefore, no detectable difference in the P–$CH_3$ and P–$C_6H_5$ distances in the $[P(C_6H_5)_3CH_3]^+$ cation. There is a difference in the P–$C_6H_5$ distance in structures where the $C_6H_5$ portion is refined as a rigid group (1.774 (8) Å, ref 22 and this work) and where the carbon atoms are refined independently (1.795 (4) Å[23,24,28]), but the difference is not significant.

### Anticancer Activity

The salt $K[PtCl_3(caffeine)]$ was examined for anticancer activity against the P388 lymphocytic leukemia by using a protocol previously described.[29] At a dose of 36 mg/kg in saline solution the compound produced a $T/C$ of 150%, indicating substantial anticancer activity. However tests at the National Cancer Institute against L1210 lymphoid leukemia gave a best $T/C$ of only 118%. These results establish that $K[PtCl_3(caffeine)]$ has substantial anticancer activity against at least one type of cancer in mice. While more work is necessary to establish the most effective dose and to determine the scope of its activity, it seems that $K[PtCl_3(caffeine)]$ represents a new class of antitumor compounds.

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**Supplementary Material Available:** Listings of hydrogen atom parameters (Table IV) and observed and calculated structure amplitudes (21 pages). Ordering information is given on any current masthead page.

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# Investigation of Unique Metal Complexes Produced with Polystyrene–2,2′-Bipyridine and Several Hydrogenation Catalysts Derived from This Copolymer

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The cleavage reactions between polystyrene-bound pyridine and 2,2′-bipyridine ligands, [P]-py and [P]-bpy, and the dimers $[Rh(X)(CO)Cl]_2$ (X = CO, $(C_6H_5)_3P$, or $(tol)_3P$) were studied. While the [P]-py cleavages produced products analogous to those found homogeneously, the reactions using [P]-bpy resulted in the formation of several metal complexes not found in solution. This is at least in part the result of the accessibility of the initially formed [P]-bpyRh complexes to subsequent reactions which cannot occur in the homogeneous case due to precipitation of the rhodium complex initially formed. These supported rhodium systems, as well as [P]-bpy$PdCl_2$ and [P]-bpy$PtCl_2$, were investigated as hydrogenation catalysts. In the case of the former two systems it was found that metal aggregates were formed. This was surprising in light of the general stability of bipyridine complexes. The [P]-bpy$PtCl_2$ system is an active catalyst for the hydrogenation of a number of substrates. Metal formation did not occur in this case.

## Introduction

Much emphasis has been placed on demonstrating the usefulness of supporting metal complexes on functionalized polymers with regard to producing systems with unique chemical behavior. While this "heterogenization" is in itself advantageous in the case of catalytic systems, it has long been recognized that the support may be made to more directly influence chemical reactivity. This influence may be divided into active and passive categories. The substrate size selectivity exhibited by many polymer-supported catalysts[1] is an example of an active polymer role. Site isolation of a complex, to inhibit metal dimer or cluster formation, is an example of a passive role by a support. Passive polymer influence is not limited to cases of effective site isolation. The precipitation of a solid product from a homogeneous solution provides a barrier to a more complete reaction (whether it be a thermodynamic or kinetic barrier). The dispersal of the product over a func-

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