lis, S. G. Mylonakis, M. T. Nieh, and S. Seltzer, *J. Am. Chem. Soc.*, **94**, 829 (1972).
(6) (a) N. A. Porter, M. E. Landis, and L. J. Marnett, *J. Am. Chem. Soc.*, **93**, 795 (1971); (b) N. A. Porter and P. M. Illoff, *Chem. Commun.*, 1575 (1971).
(7) (a) S. Seltzer, *J. Am. Chem. Soc.*, **83**, 2625 (1961); (b) S. Seltzer, *ibid.*, **85**, 14 (1963); (c) S. Seltzer and F. T. Dunne, *ibid.*, **87**, 2628 (1965).
(8) S. W. Benson and H. E. O'Neal, "Kinetic Data on Gas Phase Unimolecular Reactions", NSRDS, NBS-21, U.S. Government Printing Office, Washington, D.C., 1970, p 32.
(9) A. Oberlinner and C. Rüchardt, *Tetrahedron Lett.*, 4685 (1969).
(10) P. S. Engel and D. J. Bishop, *J. Am. Chem. Soc.*, **97**, 6754 (1975).
(11) Observations of pronounced steric effects in alkyldiazene decompositions are well known. C. G. Overberger, W. F. Hale, M. B. Berenbaum, and A. B. Finestone, *J. Am. Chem. Soc.*, **76**, 6185 (1954); W. Duismann and C. Rüchardt, *Tetrahedron Lett.*, 4517 (1974).
(12) B. K. Bandlish, A. W. Garner, M. L. Hodges, and J. W. Timberlake, *J. Am. Chem. Soc.*, **97**, 5856 (1975).
(13) P. S. Engel, R. A. Melaugh, M. Månsson, J. W. Timberlake, A. W. Garner, and F. D. Rossini, *J. Chem. Thermodyn.*, in press.
(14) Strain energies are gas phase values while $\Delta H^{\ddagger}$ was determined in solution. However, it would be surprising if the strain energy of TBTO and TOTO depended much on phase. Moreover, at least one compound (TBTB) has the same activation parameters in both phases. J. C. Martin and J. W. Timberlake, *J. Am. Chem. Soc.*, **92**, 978 (1970).
(15) Diazenes are thought to be good precursors of radicals because the transition state is achieved relatively late on the energy profile. Furthermore, the tertiary alkyl radicals derived from TBTB, TBTO, and TOTO should be of comparable stability, having nearly achieved sp^2 geometry at the transition state. For discussions of these points and for comparison of diazenes with other radical precursors see ref 12 and C. Rüchardt, *Agnew. Chem., Int. Ed. Engl.*, **9**, 830 (1970); G. J. Abruscato and T. T. Tidwell, *J. Am. Chem. Soc.*, **94**, 672 (1972); J. A. Ernst, C. Thankachan, and T. T. Tidwell, *J. Org. Chem.* **39**, 3614 (1974).
(16) Since 2,2,4-trimethylphentane (*tert*-octyl-H) possess 3.7 kcal mol^{-1} of strain, it is reasonable that the *tert*-octyldiazenyl radical would be strained by at least this amount.

A. W. Garner, J. W. Timberlake*
Department of Chemistry, University of New Orleans
New Orleans, Louisiana 70122

Paul S. Engel,* Robert A. Melaugh
Department of Chemistry, Rice University
Houston, Texas 77001

Received June 13, 1975

The Structure of the [Platinum(ethylenediamine)(guanosine)$_2$]$^{2+}$ Cation

Sir:

The surprisingly potent antitumor properties of *cis*-Pt(NH$_3$)$_2$Cl$_2$, Pt(en)Cl$_2$, and related compounds have been the subject of intensive investigation for the past few years.[1-3] Clinical trials using *cis*-Pt(NH$_3$)$_2$Cl$_2$ as a chemotherapeutic agent have been in progress in several hospitals since 1971.[3,4] It is suspected that the activity of these compounds is related to their ability to interact with DNA,[5-7] and several models involving the formation of platinum-bridged covalent cross-links have been proposed.[6-10] These models generally involve a *cis*-Pt(amine)$_2$ fragment chelated by certain atoms from DNA, usually nitrogen or oxygen atoms from the purine or pyrimidine bases.[7-10] Guanine in particular is thought to be especially vulnerable to attack,[9-12] since guanine derivatives are known to react more rapidly with platinum complexes than derivatives of the other nucleotide bases.[12] In this communication we wish to report the crystal structure of the [platinum(ethylenediamine)(guanosine)$_2$]$^{2+}$ cation and suggest a possible model for Pt-DNA interaction.

[Pt(en)(Guo)$_2$]$^{2+}$, prepared by treating Pt(en)Cl$_2$ with guanosine,[13] was isolated as crystals of a mixed chloride-iodide salt[14] by vapor diffusing[16] the reaction mixture against 1-propanol. Crystals of [Pt(en)(Guo)$_2$]Cl$_{1.5}$I$_{0.5}$·2H$_2$O are tetragonal (space group $I4_122$), with $a = 17.557$ (4) Å, $c = 23.883$ (6) Å, and $Z = 8$. Two asymmetric sets of data were collected on a Nonius CAD-3 automated diffractometer using a $\theta/2\theta$ scan mode with Mo Kα radiation up to a 2θ limit of 50°. The data were corrected for absorption effects and merged to give 1146 nonzero reflections. The structure was solved by heavy atom methods and refined anisotropically to a final R factor of 5.9%.[17]

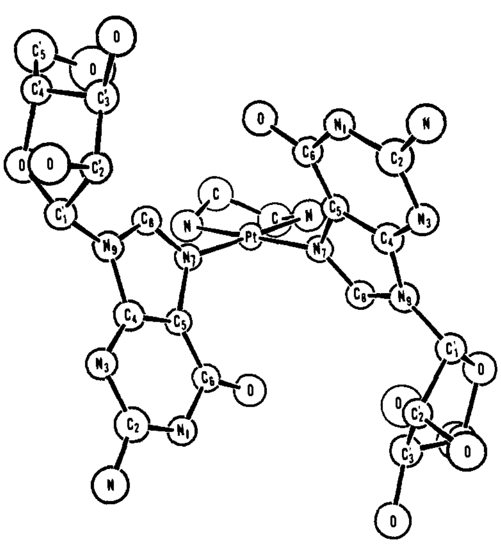

Figure 1. The geometry of the [Pt(en)(Guo)$_2$]$^{2+}$ cation. A crystallographic twofold rotation axis bisects the N$_7$-Pt-N$_7$ angle.

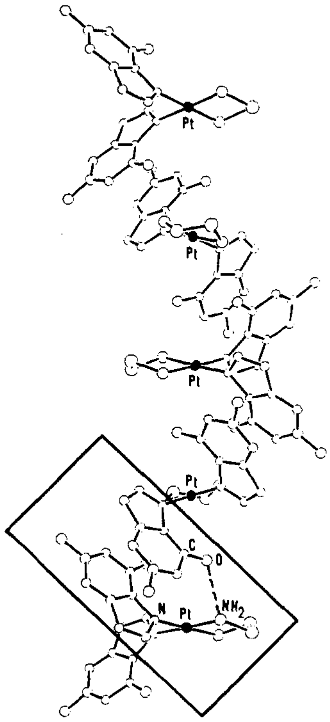

Figure 2. Part of the infinite spiral consisting of stacked [Pt(en)(Guo)$_2$]$^{2+}$ units, showing the pairing of the guanine bases. The ribose groups have been omitted for clarity. A crystallographic 4_1 screw axis is approximately defined by the row of platinum atoms. The boxed area shows a Pt(en) fragment forming a bridge between two parallel guanine rings. Hydrogen bonds connect the NH$_2$ groups of the ethylenediamine ligands to the carbonyl groups of the guanines. One of these is indicated (dotted line).

The square-planar geometry of the [Pt(en)(Guo)$_2$]$^{2+}$ cation is shown in Figure 1. A crystallographic twofold rotation axis passes through the platinum atom and the mid-point of the C-C bond of the ethylenediamine ligand. Each guanosine molecule coordinates in a monodentate fashion through the N$_7$ position of the guanine base, making a Pt-N$_7$ bond of 1.967 (15) Å and a N$_7$-Pt-N$_7$ angle of 87.0 (7)°. The planes of the guanine rings are tilted in such a way that the normals to the planes intersect at an angle of 71°. Other distances and angles in the molecule are: Pt–N(en) = 2.036 (17) Å, N(en)–Pt–N(en) = 83.9 (9)°, N_7–Pt–N(en) = 94.6 (8)°, 177.0 (8)°, and $N_7 \cdots N_7$ = 2.71 (2) Å. The ribose ring is in the C(3′)-endo conformation and the torsion angles within the nucleoside are: $\chi = 224.0°$, $\psi = 44.2°$, $\psi' = 85.9°$, $\tau_0 = 358.7°$, $\tau_1 = 339.8°$, $\tau_2 = 35.9°$, $\tau_3 = 323.7°$, $\tau_4 = 22.9°$.[18] The carbonyl oxygen at C_6 is hydrogen-bonded to an ethylenediamine nitrogen of a neighboring molecule at a distance of 2.84 Å. Additionally, each guanine ring is in perfectly parallel contact with a guanine ring on a neighboring cation at a distance of 3.31 Å. This effect, coupled with a crystallographic 4_1 screw axis which is approximately coincident with the row of platinum atoms, creates an infinite spiral of stacked $[Pt(en)(Guo)_2]^{2+}$ units along the 4_1 axis (Figure 2).

Our result reinforces the belief that the preferred site for Pt complexation to guanosine is N_7.[21] This is significant since N_7, an atom not involved in Watson–Crick base pairing, is exposed on the surface of the DNA molecule and would be a logical site for initial attack by an electrophilic species.

The orientation of the Pt(en) moiety with respect to a pair of parallel guanine rings from different cations suggests a possible model for initial attachment of a platinum-containing fragment to DNA. A closer examination of this region (boxed area in Figure 2) shows the Pt(en) group forming a bridge $[C_6{=}O \cdots H{-}N(en){-}Pt{-}N_7]$ across the pair of parallel guanine rings. The hydrogen bonding observed between the NH_2 group of the ethylenediamine ligand and the carbonyl group of the guanine is especially interesting in view of the fact that antitumor activity of *cis*-$Pt(amine)_2X_2$ complexes decreases markedly along the series $NH_3 \sim NH_2R > NHR_2 \gg NR_3$.[2b]

Acknowledgments. This research was supported by NIH Grants CA-17367 and AM-15846. Computer time was supplied by the University of Southern California Computing Center. R.B. is a recipient of a NIH Research Career Development Award (#CA-00015).

References and Notes

(1) B. Rosenberg, L. Van Camp, J. E. Trosko, and V. H. Mansour, *Nature (London)*, **222**, 385 (1969).

(2) (a) B. Rosenberg, *Naturwissenschaften*, **60**, 399 (1973); (b) M. J. Cleare and J. D. Hoeschele, *Bioinorg. Chem.*, **2**, 187 (1973); (c) M. J. Cleare, *Coord. Chem. Rev.*, **12**, 349 (1974); (d) A. J. Thomson, R. J. P. Williams, and S. Reslova, *Struct. Bonding (Berlin)*, 11, 1 (1972).

(3) (a) Advances in Antimicrobial and Antineoplastic Chemotherapy. (Proceedings of the 7th International Congress of Chemotherapy, Prague, 1971), University Park Press, Baltimore, 1972; (b) T. A. Connors and J. J. Roberts, Ed., "Platinum Coordination Complexes in Cancer Chemotherapy", Springer-Verlag, Heidelberg, 1974.

(4) (a) J. M. Hill, E. Loeb, A. MacLellan, N. O. Hill, A. Kahn, and J. J. King, *Cancer Chemother. Rep.*, **59**, 647 (1975); (b) J. A. Gottlieb and B. Drewinko, *ibid.*, **59**, 621 (1975), and references therein.

(5) (a) P. Horacek and J. Drobnik, *Biochim. Biophys. Acta*, **254**, 341 (1971); (b) J. A. Howle, G. R. Gale, and A. B. Smith, *Biochem. Pharmacol.*, **21**, 1465 (1972); (c) J. Drobnik and P. Horacek, *Chem.-Biol. Interact.*, **7**, 223 (1973).

(6) K. V. Shooter, R. Howse, R. K. Merrifield, and A. B. Robins, *Chem.-Biol. Interact.*, **5**, 289 (1972),

(7) J. J. Roberts and J. M. Pascoe, *Nature (London)*, **235**, 282 (1972).

(8) I. A. G. Roos, A. J. Thomson, and S. Mansy, *J. Am. Chem. Soc.*, **96**, 6484 (1974).

(9) C. R. Morris and G. R. Gale, *Chem.-Biol. Interact.*, **7**, 305 (1973).

(10) S. Mansy and B. Rosenberg, submitted for publication.

(11) L. L. Munchausen and R. O. Rahn, *Cancer Chemother. Rep.*, **59**, 643 (1975).

(12) (a) A. B. Robins, *Chem.-Biol. Interact.*, **6**, 35 (1973); (b) *ibid.*, **7**, 11 (1973).

(13) P. C. Kong and T. Theophanides, *Inorg. Chem.*, **13**, 1167 (1974).

(14) The presence of iodine can be attributed to contamination by $Pt(en)I_2$, a precursor[15] of $Pt(en)Cl_2$, in the reaction mixture. The 3:1 ratio of Cl and I in these crystals was subsequently confirmed by refining their occupancy factors during least-squares refinement.

(15) S. C. Dhara, *Indian J. Chem.*, **8**, 193 (1970).

(16) G. H. Stout and L. H. Jensen, "X-ray Structure Determination: A Practical Guide", MacMillan, New York, N.Y., 1968, p 65.

(17) The major computations in this work were performed using CRYM, an amalgamated set of crystallographic programs developed by Dr. R. E. Marsh's group at the California Institute of Technology.

(18) The terminology used to describe the puckering of the sugar ring and the definitions of the various torsion angles are given in ref 19 and 20. In this paper χ is defined as the torsion angle O(1′)–C(1′)–N(9)–C(4),[20] and its value characterizes the configuration about the glycosidic C(1′)–N(9) bond as anti. The C(5′)–O(5′) bond is in a gauche, gauche conformation relative to the ribose ring, with $\phi_{OO} = 291.5°$ and $\phi_{OC} = \psi = 44.2°$. The torsion angles found in this molecule are consistent with values found in other purine nucleosides with C(3′)-endo puckering.

(19) M. Sundaralingam, *Biopolymers*, **7**, 821 (1969).

(20) W. Saenger, *Angew. Chem.*, **83**, 680 (1973); *Angew Chem., Int. Ed. Engl.*, **12**, 591 (1973).

(21) N_7 is the site favored by most investigators who have studied the interaction of guanine with Pt complexes[9-12] and was in fact predicted for $[Pt(en)(Guo)_2]^{2+}$ by Kong and Theophanides.[13] Recent crystallographic investigations on $[Pt(NH_3)_2(5'\text{-}IMP)_2]^{2-}$,[22] $[Pt(9\text{-}methyladenine)Cl_3H]^+$,[23] and complexes of 5′-GMP with other metals[24] also indicate that the N_7 position of purines is the site usually involved in metal complexation. With unsubstituted guanine, however, coordination through N(9) is sometimes found.[25]

(22) D. M. L Goodgame, I. Jeeves, F. L. Phillips, and A. C. Skapski, *Biochim. Biophys. Acta*, **378**, 153 (1975).

(23) A. Terzis, N. Hadjiliadis, R. Rivest, and T. Theophanides, *Inorg. Chim. Acta*, **12**, L5 (1975).

(24) (a) P. DeMeester, D. M. L. Goodgame, A. C. Skapski, and B. T. Smith, *Biochim. Biophys. Acta*, **340**, 113 (1974); (b) P. DeMeester, D. M. L. Goodgame, T. J. Jones, and A. C. Skapski, *Biochem. J.*, **139**, 791 (1974).

(25) (a) J. A. Carrabine and M. Sundaralingam, *J. Am. Chem. Soc.*, **92**, 369 (1970); (b) L. Srinivasan and M. R. Taylor, *Chem. Commun.*, 1668 (1970).

(26) Alfred P. Sloan Fellow, 1974–1976.

Robert W. Gellert, Robert Bau*[26]
Department of Chemistry, University of Southern California
University Park, Los Angeles, California 90007

Received August 6, 1975

Evaluation of the Force Constant for the Carbon–Chlorine Stretching Vibration for *tert*-Butyl Chloride Using MINDO/3

Sir:

Recent work in these laboratories has illustrated the promise of kinetic isotope effects (KIE) as a chemical tool for studying reaction mechanisms and transition states.[1-5] In the course of such studies, vibrational frequencies, isotopic shifts, and vibrational force constants are necessary items for KIE calculations. The procedure involves the use of the Wilson FG method[6] and the process is an iterative one, requiring experimental frequencies and an initial trial set of force constants. It would be desirable to have a theoretical means of obtaining these initial values. The purpose of this communication is to demonstrate that the MINDO/3 SCF MO method shows promise for producing such force constants for molecular vibrational modes of organic molecules.

The MINDO/3 SCF MO method developed by Dewar and co-workers has been described in detail recently in this journal.[7-11] It is a semiempirical SCF molecular orbital treatment which is quite successful in predicting such molecular properties as heats of formation, ionization energies, and dipole moments. The primary attribute of MINDO/3 of interest here is in optimizing molecular geometries of reactants, products, and transition states. The importance of this capability is evidenced by two studies employing an earlier version of MINDO (MINDO/2). In one study[12] where the molecular geometry was not optimized, the calculated stretching force constants agreed with experimental data to within a few tenths of a millidyne per angstrom for typical hydrocarbons but differed by more than 10% for all studied molecules containing heteroatoms. Much of the error could be attributed to the importance of the interactions of vibrational modes as the bond in question was