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 $[\mathrm{Pt(en)(Guo)_2}]^{2+}$ 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*-$\mathrm{Pt(amine)_2X_2}$ complexes decreases markedly along the series $NH_3 \sim NH_2R > NHR_2 \gg NR_3$.[2b]

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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

Table I. C–Cl Bond Distances and MINDO/3 Calculated Heats of Formation for *tert*-Butyl Chloride

C–Cl, Å	ΔH, kcal/mol	C–Cl, Å	ΔH, kcal/mol
1.000	+516.4935	1.860[a]	−31.8061
1.400	+44.8638	1.872[a]	−31.7082
1.600	−14.5133	1.882[a]	−31.5830
1.795[a]	−31.2965	1.890[a]	−31.4625
1.808[a]	−31.5516	1.901[a]	−31.2636
1.820[a]	−31.7155	2.030	−26.3900
1.833[a]	−31.8193	2.306	−8.0044
1.845[a]	−31.8504	3.050	+36.1322

[a] These values were used to define the parabola for the force constant evaluation; identical results were obtained using the total energy.

stretched. In the secc d study,[13] where optimization was accomplished, the pote ial surface for ethane was calculated with final errors i the various vibrational stretching, bending, and torsional equencies averaging ca. 100 cm^{-1}. Komornicki and McIver have employed MINDO/2 to evaluate potential surfaces and reaction pathways for several novel organic reactions; force constants evaluated during the course of the studies were derived by a perturbation approach.[14] Attempts at predicting force constants using molecular orbital techniques other than MINDO have met with little success (e.g., see the CNDO/2 values for hydrocarbons[15]).

The C–Cl bond distances and calculated heats of formation are presented in Table I.[16] Gratifyingly, the heat of formation (−31.8 kcal/mol) and dipole moment (2.3 Debye) of the completely optimized ground state of *tert*-butyl chloride calculated in this work are in accord with the values reported by Dewar and co-workers in their recent extensive study of ground state organic molecules.[10] However, the ionization potential obtained here for the optimized ground state is 10.53 eV, in excellent agreement with the experimental value (10.61 eV) of Watanabe and collaborators.[17] The MINDO/3 value of 11.63 eV reported in Table III of ref 10 is a misprint.[18] The calculated heat of formation for the ground state (−31.8 kcal/mol) does not fall within the usual error limits of MINDO/3, the experimental value[19] being −43.1 kcal/mol. Dewar and co-workers have pointed out that MINDO/3 predicts ΔH_f values too positive for compact, globular molecules such as neopentane (calculated,[8] −14.6 kcal/mol; experimental,[20] −40.3 kcal/mol), so the lack of agreement between the two values for *tert*-butyl chloride is not unexpected. The 11 kcal/mol error should not affect the current calculation of the C–Cl stretching force constant because this error would be expected to remain approximately constant at all points near the minimum of the potential curve. The curve plotted from the data of Table I has a dissociation limit which corresponds more nearly to a heterolytic C–Cl bond dissociation to form $(CH_3)_3C^+$ and Cl^-. The equilibrium geometry calculated for *tert*-butyl chloride in this work was essentially the same as that reported previously by Dewar and co-workers.[10] The equilibrium C–Cl bond length was 1.84 Å, which differs appreciably from the experimental value (1.77 Å)[21] and the 1.80 Å model used by Williams and Taylor,[2] but the precise value should have no affect on the determination of the C–Cl stretching force constants.

In calculating the C–Cl stretching force constant, ten points near the minimum of the potential curve were fit to a parabola using double precision data and a quadratic least-squares program. The points represented a total change in C–Cl bond length of ca. 0.11 Å, and the resulting parabolic fit yielded quadratic coefficients of 662.6 kcal/mol, −752.2 kcal/(mol Å), and 203.7 kcal/(mol Å^2). The C–Cl stretching force constant derived from the parabolic fit was 2.83 mdyn/Å. This force constant is in remarkable accord with the value (2.86 mdyn/Å) for the ground state predicted by Williams and Taylor[2] from a detailed normal coordinate analysis and force field calculation. For the normal coordinate analysis,[2] it was necessary to employ a model which assumed a methyl chloride skeleton, with the methyl groups of *tert*-butyl chloride being considered as point masses. The MINDO/3 calculation on the completely optimized *tert*-butyl chloride thus supports the use of such simplified models in normal coordinate analysis/force field calculations. Furthermore, the force field calculation[2] accounted for interactions between the various vibrational modes. The present MINDO/3 calculation does not specifically treat these interactions of the various vibrational modes as did the MINDO/2 calculation of the potential surface for ethane.[13] However, the outstanding agreement of the C–Cl stretching force constant calculated by the two procedures suggests that complete optimization of the remainder of the molecule by MINDO/3 does, in fact, account for interaction of vibrational modes because the cross-constants evaluated by Williams and Taylor[2] were appreciable.[22]

Methyl chloride provides a second example of the use of MINDO/3 for C–Cl force constant evaluation. Using nine points to describe the minimum, the calculated value with the molecule optimized at each point was 3.77 mdyn/Å. Bron[23] lists a value of 3.50 from his normal coordinate analysis.

The results from these two examples suggest that MINDO/3 may provide the desired means of predicting force constants for large organic molecules, or at least that it may provide a decent trial set of force constants to be used in complete force field calculations.

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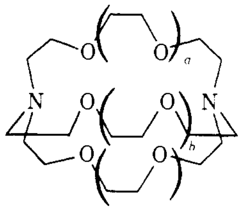
The Kinetics of Complexing of Calcium Ion with Several Cryptands

Sir:

The synthesis of a number of ligands of the type **1–3** has been described by Lehn and his colleagues.[1] These macrobicycles, termed cryptands,[2] have an ability to combine with alkali and alkaline-earth cations to form the metal cryptates. Their stability is dependent on the relative sizes of the cation and the cavity of the ligand, in which the cation is located. Much more is known about the stability and selectivity of metal complexing with these and other macrocycles, than about the dynamic aspects.[1,3] Temperature-dependent NMR spectra for mixtures of **1** and a number of metal ion complexes of **1** in D_2O were observed.[4] Exchange rate constants, associated with these spectra, were equated to rate constants (k_d) for the dissociation of the metal cryptates (M^{n+} = Na^+, K^+, Rb^+, Tl^+, Ca^{2+}, Sr^{2+}, and Ba^{2+}):



1, $a = b = c = 1$
2, $a = b = 1; c = 0$
3, $a = 1; b = c = 0$

$$M^{n+} + \mathbf{1} \rightleftarrows [M^{n+}\cdot\mathbf{1}] \qquad k_f, k_d, K \tag{1}$$

The calculated[1] formation rate constants ($k_f = Kk_d$) for these processes are many orders of magnitude lower than those normally encountered for alkali and alkaline-earth cation reactions, which are near diffusion controlled.[5]

These data suggested to us that the rates of formation and dissociation of these cryptates would be susceptible to measurement by flow methods. Little visible or ultraviolet spectra is associated with the ligand or metal complex, but we have been able to study the complexing of Ca^{2+} with **1–3** using murexide as indicator;[6] the Ca^{2+}-murexide equilibrium is very rapidly established in aqueous[7] and methanol[5] solution. The rate of the reaction of Ca^{2+} ion with the cryptands **1–3** (Merck Laboratories, N.Y.) was measured from 5 to 40° at pH ~11.5 and $I = 0.1$ *M* using a Gibson-Durrum stopped-flow spectrophotometer. Piperidine-piperidine H^+Cl^- was used as a buffer and for adjustment of ionic strength. At these alkalinities, the cryptands are present as unprotonated bases. The approach to equilibrium was strictly first order, when the ligands were used in large excess. The associated rate constant k_{obsd} was related to the cryptand concentration [C] by (2)

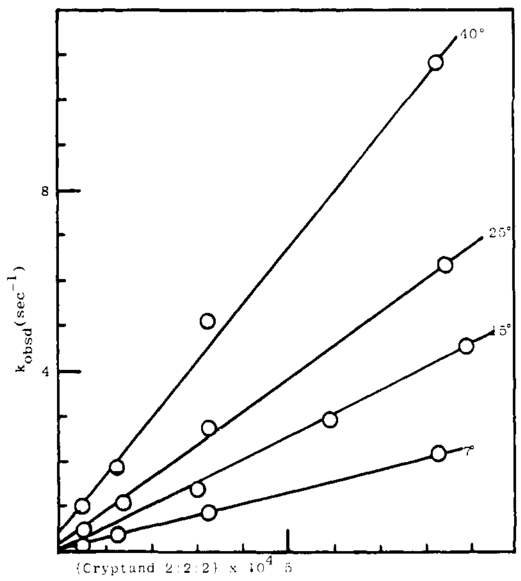


Figure 1. Plot of k_{obsd} vs. concentration of cryptand **1**, at various temperatures. pH 11.3–11.7, $I = 0.1$ *M*.

$$-\frac{1}{[Ca^{2+}]}\cdot\frac{d[Ca^{2+}]}{dt} = k_{obsd} = k_f[C] + k_d \tag{2}$$

Plots of k_{obsd} vs. [C] are shown in Figure 1 for reaction of **1** at various temperatures. Only approximate values for the intercepts can be obtained, and accurate values for k_d were obtained directly by treating the calcium cryptate with an appropriate scavenger ion. For example, dissociation of $[Ca^{2+}\cdot\mathbf{1}]$ could be effected by Ba^{2+} or K^+ ions.[1] The first-order rate constant, using murexide indicator, was independent of the concentration and the nature of the scavenger and could thus be equated with k_d. *Thus no associative path in the metal interchange was important.* Activation parameters determined in these ways are collected in Table I. The independence of rate constants observed from pH ~10 to 11.5 shows that there is no participation of basic form of calcium(II) in the complexing. A small dependence on ionic strength of both the forward and reverse rate constants was noted. The agreement between formation constants from our kinetic data and potentiometric studies is good (Table I). Except for the cryptand **1**, agreement between enthalpies and entropies of reaction from kinetics and calorimetry is very poor. We have no explanation for these discrepancies.

Since the earlier work of Lehn, Sauvage, and Dietrich,[4] there have been several reported NMR studies of exchange reactions of metal cryptates.[2,8–11] It appears that the most stable complex of the triad of cryptands with a common metal ion is a result generally of having the slowest dissociation rate. Our results for the Ca^{2+} complexes show also that the most stable cryptate (with **2**) dissociates by far the slowest. It is attended by a large activation energy, although this is offset by a more positive entropy of activation (compared with cryptates of **1** and **3**). The 10^4 faster dissociation rate for Li^+-**2** than Li^+-**3** in pyridine resides also in a lower $\Delta H^\ddagger$ (by 6 kcal mol^{-1}).[11]

It has been suggested that the mechanism of complexation is intricate because of conformational equilibrium in the ligands.[1,4] A number of cryptate complexes and the solid cryptand **1** have an endo-endo configuration in which the lone pairs of the bridgehead nitrogens are directed inside the cavity.[1] In the exo-exo form the lone pairs are directed away from the cavity and this would not be expected to complex appreciably with metal ions. If therefore this is