the low end of the S-bonded range reported by Burmeister.[16]

The concentration of the $Tl(SCN)^{2+}$ complex is large at the beginning of the redox reaction and decreases gradually with concomitant formation of thallium(III) cyanide complexes[17] and thallium(I). We have not been able to find any other Tl(III)–SCN^--containing species in the investigated solutions.[18] The redox reaction between thallium(III) and thiocyanate was suggested[5] to proceed through a short-lived binuclear intermediate, $Tl(SCN)Tl^{5+}$. Even if we cannot rule out that this species is so short-lived that it escapes discovery by means of NMR spectroscopy, it seems probable that $Tl(SCN)^{2+}$ is the predominant reaction intermediate. This is in agreement with the suggestion of Gupta et al.[6] that the rate of the reaction (2) is proportional to $[Tl(SCN)^{2+}]^2$. However, their conclusions concerning the composition of other Tl(III)–SCN^- species as well as their mechanistic suggestions should probably be modified, since they have not considered the existence of complexes between Tl(III) and cyanide/sulfate.[7,17]

Acknowledgment. We thank Prof. Ingmar Grenthe for suggesting the study of the redox reaction and for the comments on the manuscript. We are grateful to The Swedish Natural Sciences Research Council (NFR) for financial support and, together with the Knut and Alice Wallenberg Foundation, for providing funds for purchasing the NMR spectrometer. Financial support from The Swedish Institute toward R.K.D.'s stay in Stockholm is kindly acknowledged.

(16) Cargol, J. A.; Crecely, R. W.; Burmeister, J. L. *Inorg. Chem.* **1979**, *18*, 2532.

(17) At 25 °C, ^{15}N NMR parameters for these cyanide complexes are as follows. $TlCN^{2+}$: $\delta = 75.9_4$ ppm (from an external 0.032 M aqueous solution of NaSCN at 0 °C); $^2J(^{205}Tl-^{15}N) = 54$ Hz; line width = ~5 Hz. $Tl(CN)_2^+$: $\delta = 75.8_9$ ppm; $^2J(^{205}Tl-^{15}N) = 108$ Hz; line width = ~6 Hz.

(18) However, at least one more species containing thallium(III) and SCN was observed by means of ^{205}Tl NMR spectroscopy in solutions prepared by mixing a solution containing Tl(III) in the form of $Tl(CN)_2^+$ and $Tl(CN)_3$ and a solution of sodium thiocyanate. This species was assigned to $Tl(CN)_2(SCN)$ and was found to be in fast exchange with $Tl(CN)_2^+$. The redox reaction in such solutions was much slower (several days at room temperature) because Tl(III) is protected by the strong complex formation with cyanide.[7]

Contribution from the Department of Chemistry, University of Turku, SF-20500 Turku, Finland

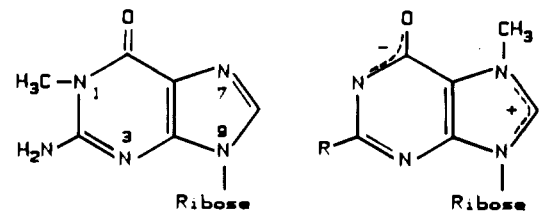
Platinum(II) Binding to the N1 and N7 Ring Nitrogens of Guanosine. Kinetics of Complexation of Aquated Pt^{II}(dien) with 1- and 7-Methylguanosines

Mikko Ritala and Jorma Arpalahti*

Received December 17, 1990

Pt(II) exhibits a marked tendency to bind 6-oxopurine nucleosides through the N7 ring nitrogen, particularly in acidic medium.[1] With increasing pH, however, coordination also to the more basic N1 position becomes possible upon deprotonation of N1H. Despite the intensive study in recent years, no quantitative data appear to exist about the relative binding ability of these sites in the guanine moiety, although this nucleobase represents the main target of anticancer Pt drugs in cellular DNA.[1,2] Recently we have used kinetic approach to study the pH-dependent distribution of mono- and bifunctional Pt(II) between the N1 and N7 ring nitrogens in the hypoxanthine moiety.[3,4] In the case of bifunctional Pt(II), in particular, quantitative estimation of various binding modes becomes rather complicated at higher pH due to the multisite binding behavior of the ligand.[4] On the other hand, blocking of the N1 site with a methyl group considerably simplifies the complexation pattern.[3,4] This observation prompted us to study the kinetically controlled distribution of monofunctional Pt^{II}(dien) in the guanine moiety by employing N1- and N7-methylated guanosines as model compounds (Chart I).[5] The binding of Pt(II) to these ligands can be related to the formation of a 2:1 Pt–guanosine complex from N1- and N7-bound 1:1 complexes. The validity of this assumption is tested by comparing the complexing ability of the corresponding inosine derivatives to the formation of N1,N7-bound Pt–inosine 2:1 complexes from the various 1:1 complexes.[3]

Chart I



1-MeGuo 7-MeGuo (R=NH_2) 7-MeIno (R=H)

Experimental Section

Materials. *N*-Methyl derivatives of guanosine and inosine were purchased from Sigma and were used as received.[6] Aquated Pt^{II}(dien) was prepared as described previously.[3]

Kinetic Measurements. The complexation of aquated Pt^{II}(dien) with *N*-methyl nucleosides in buffered aqueous solution (pH 4.3–8.3) at 298.2 K was followed by HPLC as described earlier.[3,7] During the kinetic runs, signal height was used as the measure of the concentration. With 1-methylguanosine and 7-methylinosine, the complex formation was studied in excess Pt(II) ($[Pt]_T:[L]_T \geq 20:1$), and the time-dependent concentration of the free ligand gave the pseudo-first-order rate constants, $k'_{1,obs}$, for the formation of 1:1 complexes by eq 1. Here $[L]_0$ is the initial

$$\ln [L]_t = -k'_{1,obs}t + \ln [L]_0 \quad (1)$$

ligand concentration and $[L]_t$ is the concentration at time t. In the case of 7-methylguanosine, excess of the ligand provided pseudo-first-order conditions for the formation of the 1:1 complex ($[L]_T:[Pt]_T \geq 20:1$), and the rate constants were obtained by employing least-squares fitting to eq 2. Here $[ML]_t$ is the concentration of the complex at time t, and $[ML]_T$

$$[ML]_t = [ML]_T(1 - e^{-k'_{1,obs}t}) \quad (2)$$

is the final concentration. A calibration sample prepared from a known amount of ligand in Pt(II) excess was employed to transform the peak heights of ML into concentrations.

Results and Discussion

Chromatographic analysis revealed the formation of a single reaction product in all Pt(II)–nucleoside mixtures, as seen from Figure 1. In the case of 1-methylguanosine, the product is assumed to be the N7-bound 1:1 complex, analogous to that observed earlier with 1-methylinosine.[3] With 7-methylguanosine and -inosine, the reaction products are assumed to be the N1-bound 1:1 complexes. It is known that soft metal species, such as Pt(II), exclusively bind to the N1 ring nitrogen in N7-alkylated, N9-blocked 6-oxopurines.[8] In all cases, Pt(II) coordination to

(1) For a recent review, see: Lippert, B. In *Progress in Inorganic Chemistry*; Lippard, S. J., Ed.; Wiley: New York, 1989; Vol. 37, pp 1–97.

(2) (a) Reedijk, J. *Pure Appl. Chem.* **1987**, *59*, 181–192. (b) Lippard, S. J. *Pure Appl. Chem.* **1987**, *59*, 731–742.

(3) Arpalahti, J.; Lehikoinen, P. *Inorg. Chem.* **1990**, *29*, 2564–2567.

(4) Arpalahti, J. *Inorg. Chem.* **1990**, *29*, 4598–4602.

(5) Abbreviations used: MeGuo = methylguanosine; MeIno = methylinosine; Ino = inosine.

(6) The 90% purity of commercial 7-methyguanosine confirmed by UV spectroscopy[17] was taken into account in the concentration of this compound.

(7) The ionic strength was adjusted to 0.1 M with $NaClO_4$.

0020-1669/91/1330-2826$02.50/0

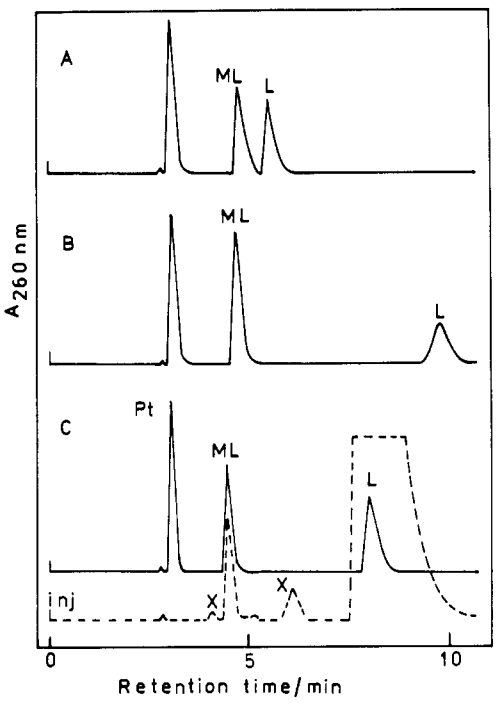


Figure 1. HPLC analysis of the mixtures of aquated Pt^{II}(dien) with (A) 7-methylinosine, (B) 1-methylguanosine, and (C) 7-methylguanosine: solid line, Pt excess; dotted line, ligand excess. Eluent: 0.05 M $NaClO_4$ and 5×10^{-4} M HNO_3 in water–methanol mixtures (A, 94:6; B, 91:9; C, 97:3); flow rate 0.8 mL/min. Notation: L, free ligand; ML, 1:1 complex; Pt, aquated Pt^{II}(dien); X, unknown impurity of 7-methylguanosine.

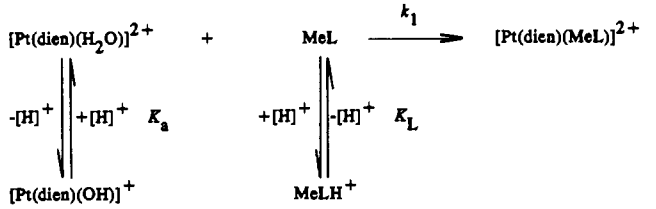
Table I. Observed Rate Constants, $k_{1,obs}/10^{-3}$ M^{-1} s^{-1}, for the Complexation of N-Methylated Nucleosides with Aquated Pt^{II}(dien) in Buffered Aqueous Solution (pH 4.3–8.3) at 298.2 K[a]

1-MeGuo		7-MeGuo		7-MeIno	
pH	$k_{1,obs}$	pH	$k_{1,obs}$	pH	$k_{1,obs}$
4.28	810	6.31	6.88	5.35	54.2
4.38	706	6.35	6.97	5.40	57.8
5.28	667	6.50	7.49	6.27	152
5.83	562	6.84	6.70	6.28	157
5.83	515	6.84	6.85	7.25	47.2
6.25	416	7.20	4.15	7.26	48.0
6.42	331	7.22	4.27	7.36	48.0
7.00	132			8.28	5.6[b]
7.47	50.4			8.30	5.6[b]
7.86	16.1				

[a] In 0.1 M $NaClO_4$. [b] Obtained by subtracting the hydrolysis rate of the ligand (3.4×10^{-3} s^{-1}) from the overall rate of disappearance of the ligand under pseudo-first-order conditions (7.9×10^{-5} s^{-1}, $[Pt]_T$ = 0.008 M).

N3 is assumed negligible due to the steric hindrance of the ribose group.[9] The observed second-order rate constants, $k_{1,obs}$, for the formation of 1:1 complexes are recorded in Table I. The data for 1-methylguanosine and 7-methylinosine were calculated by dividing the pseudo-first-order rate constants $k'_{1,obs}$, obtained by eq 1, with the total Pt(II) concentration employed. Besides complex formation, hydrolytic decomposition may also affect the concentration of the free ligand, particularly in the case of 7-methylinosine.[10,11] Below pH 8, the rate of hydrolysis was less

Scheme I



than 5% from the complexation rate under pseudo-first-order conditions. Above this pH, the hydrolysis rate of the ligand was measured independently, and this value was subtracted from the overall rate of disappearance of the ligand observed in Pt(II) excess, which gave the pseudo-first-order complexation rate. With both ligands, the plots of ln [L] vs t were strictly linear in all kinetic runs. By contrast, the disappearance of 7-methylguanosine did not obey the pseudo-first-order rate law in Pt(II) excess. The plots of ln [L] vs t showed upfield curvature in the progress of the reaction, suggesting a decrease in the effective Pt(II) concentration during the complex formation, most probably due to the formation of an OH-bridged Pt dimer.[12] Hence, the formation of the 1:1 complex between aquated Pt^{II}(dien) and 7-methylguanosine was studied in ligand excess. The pseudo-first-order rate constants $k'_{1,obs}$, obtained from eq 2, were divided by the total ligand concentration employed to give the rate data listed in Table I. Although the ligand undergoes hydrolytic decomposition under neutral conditions,[11] this side reaction appears not to affect seriously the complex formation.[13] The complexation of 7-methylguanosine was studied also in Pt(II) excess in order to verify the retention time of reaction product observed in ligand excess (Figure 1), as well as to calibrate the signal height of ML into its concentration from the diminution of the free-ligand concentration. In each run, the value computed by eq 2 for the final concentration of the complex, $[ML]_T$, correlated well with that found experimentally for the formation of ML from a known amount of Pt(II).

The assumed pathway for the complexation of N-methylated 6-oxopurine nucleosides (MeL) with aquated Pt^{II}(dien) is depicted in Scheme I. In the case of 1-methylguanosine, however, protonation equilibrium of the ligand ($pK_a = 2.2$[14]) can be neglected under the experimental conditions employed and, hence, the diminution of the observed second-order rate constant with increasing pH (Table I) refers to the deprotonation of the aqua ligand coordinated to Pt(II).[3] The pH-dependent rate constant, $k_{1,obs}$, can thus be expressed by eq 3, where k_1 represents the

$$k_{1,obs} = k_1 \frac{[H^+]}{[H^+] + K_a} \qquad (3)$$

second-order rate constant for the formation of the [Pt(dien)(1-MeGuo-*N7*)]$^{2+}$ ion and K_a is the known acidity constant of the [Pt(dien)$(H_2O)]^{2+}$ ion, viz. $10^{-6.24}$ M.[3] Least-squares fitting to the kinetic data gave the value 0.79 M^{-1} s^{-1} for k_1.[15] Comparison with 1-methylinosine reveals that the guanosine derivative reacts with the [Pt(dien)$(H_2O)]^{2+}$ ion about 1.5 times more readily than the inosine compound (k_1 = 0.54 M^{-1} s^{-1}).[3] Almost the same reactivity difference between these ligands has been observed previously in the case of the *cis*-[Pt$(NH_3)_2(H_2O)_2]^{2+}$ ion at pH 4.[16]

The observed second-order rate constant for the N7-methylated nucleosides has a maximum value at about pH 6.5 (Table I), suggesting a competition of proton and Pt(II) for the same site

(8) Shinozuka, K.; Wilkowski, K.; Heyl, B. L.; Marzilli, L. G. *Inorg. Chim. Acta* **1985**, *100*, 141–150 and references cited therein.
(9) Marzilli, L. G. In *Advances in Inorganic Biochemistry*; Eichhorn, G. L.; Marzilli, L. G., Eds.; Elsevier/North-Holland: New York, 1981; Chapter 2.
(10) Darzynkiewicz, E.; Stepinski, J.; Tahara, S. M.; Stolarski. R.; Ekiel, I.; Haber, D.; Neuvonen, K.; Lehikoinen, P.; Labadi, I.; Lönnberg, H. *Nucleosides, Nucleotides* **1990**, *9*, 599–618.
(11) Lahti, M.; Santa, H.; Darzynkiewicz, E.; Lönnberg, H. *Acta Chem. Scand.* **1990**, *44*, 636–638.
(12) Erickson, L. E.; Erickson, H. L.; Meyer, T. Y. *Inorg. Chem.* **1987**, *26*, 997–999.
(13) The minimum value for the observed pseudo-first-order rate constants was 1.67×10^{-4} s^{-1} at pH 7.20 ($[L]_T$ = 0.04 M), which is about 100 times greater than the hydrolysis rate at 298.2 K.[10]
(14) Jones, J. R.; Taylor, S. E. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1587–1589.
(15) The employment of the term K_a as an unknown parameter in eq 3 gave the values k_1 = 0.76 M^{-1} s^{-1} and $K_a = 10^{-6.27}$ M by least-squares fit.
(16) Arpalahti, J.; Lippert, B. *Inorg. Chem.* **1990**, *29*, 104–110.

in both ligand moieties. The pH-dependent rate constant, $k_{1,obs}$, can be expressed by eq 4, where K_L denotes the acidity constant

$$k_{1,obs} = k_1 \frac{[H^+]K_L}{([H^+] + K_a)([H^+] + K_L)} \quad (4)$$

of the ligand. The employment of least-squares fitting to the pH-dependent rate data gave the values $k_1 = 0.65\ M^{-1}\ s^{-1}$ and $K_L = 10^{-6.33}$ M for 7-methylinosine. The latter is comparable to the pK_a value of 6.28 reported for the base moiety in 7-methylinosine 5'-monophosphate at 298.2 K,[10] which lends support to the validity of the kinetic data. The calculated value for the rate constant is compatible with that found earlier for the binding of the $[Pt(dien)(H_2O)]^{2+}$ ion to the N1 position of the [Pt(dien)(Ino-*N7*)]$^+$ complex, viz. 0.74 $M^{-1}\ s^{-1}$.[3] In other words, a methyl group at N7 affects the coordination ability of the N1 site in the same manner as Pt(II) bound to the N7 position. Similarly, when bound to the N1 ring nitrogen, a methyl group and a Pt(II) ion have comparable influences on the coordination properties of the N7 site, as can be seen from the rate constants of 1-methylinosine and the [Pt(dien)(Ino-*N1*)]$^+$ ion, viz. 0.54 and 0.75 $M^{-1}\ s^{-1}$.[3] Accordingly, N1- and N7-methylated 6-oxopurine nucleosides can be employed as model compounds to study the relative binding ability of the N1 and N7 sites of the parent nucleoside.

An analogous treatment of the rate data for 7-methylguanosine gave the values 0.07 $M^{-1}\ s^{-1}$ for k_1 and $10^{-6.8}$ M for K_L. The latter is in agreement with the pK_a value 6.7 reported for 7-methylguanosine in the literature.[17] Comparison of the rate constants for 1- and 7-methylguanosines reveals that the former reacts with the $[Pt(dien)(H_2O)]^{2+}$ ion 10 times more readily than the latter. By contrast, in the case of inosine derivatives, the reactivity of the 7-methylated compound is slightly higher than that of the N1 isomer. Accordingly, the diminution in the coordination ability of the guanine N1 position must be attributed to sterical retardation of the $C2NH_2$ group, although this substituent inductively favors complexation (vide supra). The influence of the $C2NH_2$ group thus parallels the effect of the $C6NH_2$ group of adenosine, though the latter sterically prevents platination of both N1 and N7.[16]

Registry No. Aquated Pt^{II}(dien), 48102-16-5; 1-MeGuo, 2140-65-0; 7-MeGuo (R = NH_2), 20244-86-4.

(17) Hendler, S.; Fürer, E.; Srinivasan, P. R. *Biochemistry* **1970**, *9*, 4141-4153.

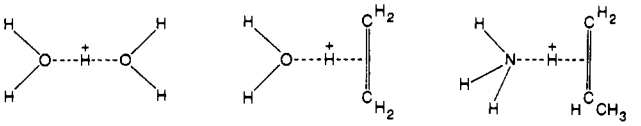
Contribution from the Department of Chemistry and Guelph-Waterloo Centre for Graduate Work in Chemistry, University of Waterloo, Waterloo, Ontario, Canada N2L 3G1

High-Pressure Mass Spectrometric Observation of Metal Carbonyl/Alkyl Adduct Ions of Novel Structure

C. E. C. A. Hop and T. B. McMahon*

Received September 28, 1990

Bonding in gas-phase transition-metal species has been studied extensively,[1] because of its importance for catalysis, and novel structures are frequently invoked to explain the chemistry involved. In recent years the concept of noncovalent bonding has been extensively used to describe ionic species observed in mass spectrometric experiments.[2-4] For example, we have obtained unambiguous evidence for the existence of a weakly bound noncovalent $(CO)_5Mn^+/CH_4$ complex.[5] Odd-[2] and even-electron[2a,3] hydrogen-bridged cations, $[A\cdot\cdot H\cdot\cdot B]^+$, and odd- and even-electron ion-molecule complexes,[4] $[A\cdot\cdot B]^+$, have been proposed both as stable species and as transient intermediates to explain the metastable and collision-induced fragmentation characteristics of (organic) ions. While isotopic labeling experiments and high-level ab initio molecular orbital theory calculations have been performed to support the proposed structures, the evidence for these novel complexes is sometimes inconclusive. In addition, fragmentation mechanisms can sometimes better be explained by "conventional" mechanisms.[6] However, even-electron proton-bound cations have been unequivocally identified as the products of many ion-molecule reactions[3] and some dissociative ionization processes.[7] A great deal of attention has been directed toward those species in which a proton interacts with the lone pairs of the oxygen atoms of two (stable) neutral molecules, e.g. **1**. The



1 **2** **3**

latter type of interaction renders the ion unconventional in the sense of a valence bond description, but the bonding can approach covalent bond energies with the stabilization energy relative to the dissociation products, $AH^+ + B$ or $A + BH^+$, often in the range 120-140 kJ·mol^{-1}.[3c]

Alternatively, a proton can interact with the π system of one (stable) molecule and the lone pairs of an oxygen or nitrogen atom in another (stable) molecule to give novel structures, e.g. **2**[8] and **3**.[9] To date, the latter species have not been unambiguously identified, but both theory[8b,9] and experiment[8-10] lend support to their existence. They have been proposed as intermediates to explain metastable and collision-induced fragmentation pathways of certain ions, and ab initio molecular orbital theory calculations have identified them as stable species on the potential energy surface. In general, the stabilization energy of these species is considerably lower than that of the above mentioned -O··H··O-

(1) See e.g.: (a) Russell, D. H., Ed. *Gas Phase Inorganic Chemistry*: Plenum Press: New York, 1989. (b) Marks, T. J., Ed. *Bonding Energetics in Organometallic Compounds*; American Chemical Society: Washington, DC, 1990.

(2) See e.g.: (a) Morton, T. H. *Tetrahedron* **1982**, *38*, 3195. (b) Heinrich, N.; Schmidt, J.; Schwarz, H.; Apeloig, Y. *J. Am. Chem. Soc.* **1987**, *109*, 1317. (c) Burgers, P. C.; Holmes, J. L.; Hop, C. E. C. A.; Postma, R.; Ruttink, P. J. A.; Terlouw, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 7315.

(3) See e.g.: (a) Beauchamp, J. L. In *Interactions between Ions and Molecules*; Ausloos, P., Ed.; Plenum Press: New York, 1975; pp 413-444. (b) Larson, J. W.; Clair, R. L.; McMahon, T. B. *Can. J. Chem.* **1982**, *60*, 542. (c) Larson, J. W.; McMahon, T. B. *J. Am. Chem. Soc.* **1982**, *104*, 6255.

(4) See e.g.: (a) Postma, R. Ph.D. Thesis, University of Utrecht, Utrecht, The Netherlands, 1987. (b) McAdoo, D. J. *Mass Spectrom. Rev.* **1988**, *7*, 363. (c) Hammerum, S. *J. Chem. Soc., Chem. Commun.* **1988**, 858. (d) Hammerum, S.; Audier, H. E. *J. Chem. Soc., Chem. Commun.* **1988**, 860.

(5) Hop, C. E. C. A.; McMahon, T. B. *J. Am. Chem. Soc.* **1991**, *113*, 355.

(6) See e.g.: Bissonnette, M. C.; George, M.; Holmes, J. L. *Int. J. Mass Spectrom. Ion Processes*, in press.

(7) (a) Van Driel, J. H.; Heerma, W.; Terlouw, J. K.; Halim, H.; Schwarz, H. *Org. Mass Spectrom.* **1985**, *20*, 665. (b) Van Baar, B.; Halim, H.; Terlouw, J. K.; Schwarz, H. *J. Chem. Soc., Chem. Commun.* **1986**, 728. (c) Van Baar, B. L. M.; Terlouw, J. K.; Akkök, S.; Zummack, W.; Weiske, T.; Schwarz, H. *Chimia* **1988**, *42*, 226.

(8) (a) Harrison, A. G. *Org. Mass Spectrom.* **1987**, *22*, 637. (b) Bouchoux, G.; Hoppilliard, Y. Y. *J. Am. Chem. Soc.* **1990**, *112*, 9110.

(9) Reiner, E. J.; Poirier, R. A.; Peterson, M. R.; Csizmadi, I. G.; Harrison, A. G. *Can. J. Chem.* **1986**, *64*, 1652.

(10) (a) Hiraoka, K.; Kebarle, P. *J. Am. Chem. Soc.* **1977**, *99*, 360. (b) Bowen, R. D.; Williams, D. H. *J. Am. Chem. Soc.* **1978**, *100*, 7454. (c) Bowen, R. D.; Williams, D. H. *Int. J. Mass Spectrom. Ion Phys.* **1979**, *29*, 47. (d) Bowen, R. D.; Williams, D. H. *J. Am. Chem. Soc.* **1980**, *102*, 2752. (e) Meot-Ner, M.; Deakyne, C. A. *J. Am. Chem. Soc.* **1985**, *107*, 469. (f) Meot-Ner, M.; Ross, M. M.; Campana, J. E. *J. Am. Chem. Soc.* **1985**, *107*, 4838. (g) Stamp, J. J.; Siegmund, E. G.; Cairns, T.; Chan, K. K. *Anal. Chem.* **1986**, *58*, 873. (h) Terlouw, J. K.; Weiske, T.; Schwarz, H.; Holmes, J. L. *Org. Mass Spectrom.* **1986**, *21*, 665. (i) Weiss, M.; Crombie, R. A.; Harrison, A. G. *Org. Mass Spectrom.* **1987**, *22*, 216. (j) Wright, A. D.; Bowen, R. D.; Jennings, K. R. *J. Chem. Soc., Perkin Trans. II* **1989**, 1521.

0020-1669/91/1330-2828$02.50/0