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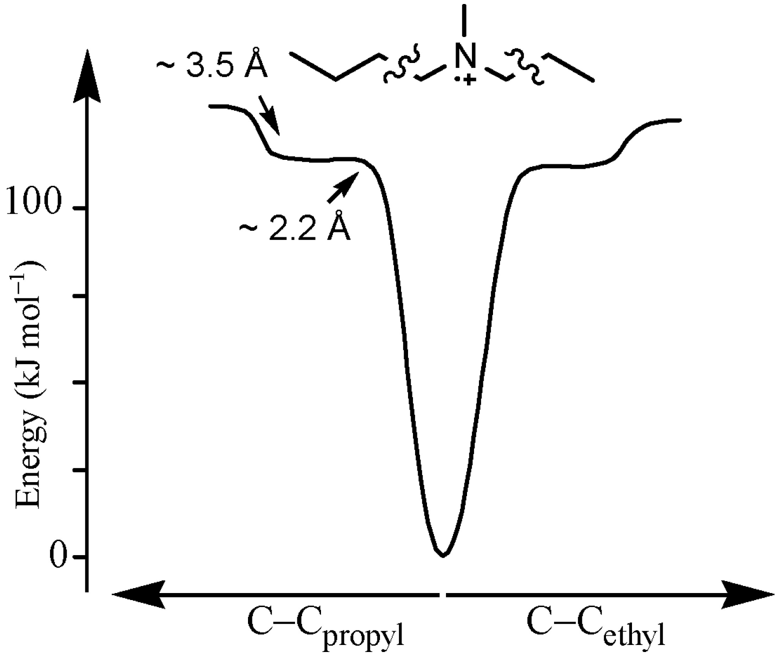

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Competing Simple Cleavage Reactions: The Elimination of Alkyl Radicals from Amine Radical Cations

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Abstract: Two different alkyl radicals can be expelled when unsymmetrical aliphatic amine radical cations undergo C−C bond cleavage. The branching ratio is strongly dependent on the internal energy of the reactant, even when the competition involves loss of closely related alkyl radicals. In mass spectrometers, the rate of loss of the smaller radical (excepting methyl) always exceeds the rate of loss of the larger close to threshold. The preference is reversed for the more highly energized ions that react in the ion source, demonstrating that the rate of loss of the larger radical rises much more rapidly with increasing internal energy than does the rate of loss of the smaller radical. This result is not easily reconciled with a simple RRKM model, given the expected strong resemblance between the transition states involved, whereas it agrees well with a description based on variational transition state theory. The heats of formation of the products determined with the G3 composite ab initio method show that loss of the smaller radical is without exception the more favorable reaction. The relative rates of the competing C−C bond cleavage reactions of the metastable ions vary with the number of degrees of freedom of the reactant, with the critical energy of the reaction, and with the difference between the heats of formation of the products. The presence of intermediate energy barriers when cleavage occurs at a branching point can give rise to variations in relative rates that are not easily interpreted.

Introduction

Simple homolytic cleavage of a carbon−carbon bond is a common reaction of free radicals and molecules with radical-like properties.[1] Among the best known examples are the Norrish type I photofragmentation,[2] the α-cleavage in mass spectrometry,[3−8] and the fragmentation of alkoxy radicals.[9] The factors that govern the selectivity in competing cleavage reactions of tertiary alkoxy radicals have been the subject of many experimental and computational studies,[10] and these reactions have attracted considerable recent attention because of their importance in atmospheric chemistry[11] and synthesis.[12] Experimentally, the simple cleavage can be studied in detail in mass spectrometers, and the factors that determine the detailed course of reaction are possibly best examined by studying the outcome of competing simple cleavages. Many textbooks point out that when a radical cation can undergo two closely related

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(1) Bauld, N. L. *Radicals, Ion Radicals, and Triplets*; Wiley-VCH: New York, 1997. (b) Fossey, J.; Lefort, D.; Sorba, J. *Free Radicals in Organic Chemistry*; Wiley: Chichester, 1995. (c) Huang, R. L.; Goh, S. H.; Ong, S. H. *The Chemistry of Free Radicals*; Edward Arnold: London, 1974.

(2) (a) Jackson, W.; Okabe, H. *Adv. Photochem.* **1986**, *13*, 1−94. (b) Pitts, J. N.; Wan, J. K. S. In *The Chemistry of the Carbonyl Group*; Patai, S., Ed.; Wiley-Interscience: New York, 1966. (c) Noyes, W. A., Jr. In *Photochemistry and Reaction Kinetics*; Ashmore, P. G., Dainton, F. S., Sugden, T. M., Eds.; Cambridge University Press: Cambridge, 1967, pp 1−25. (d) Sølling, T. I.; Diau, E. W. G.; Kötting, C.; De Feyter, S.; Zewail, A. H. *ChemPhysChem* **2002**, *3*, 79−97.

(3) McLafferty, F. W.; Tureček, F. *Interpretation of Mass Spectra*, 4th ed.; University Science Books: Sausalito, CA, 1993.

(4) Hvistendahl, G. *Mass Spectrometry*; University of Oslo: Oslo, Norway, 1996.

(5) Williams D. H.; Fleming, I. *Spectroscopic Methods in Organic Chemistry*, 5th ed.; McGraw-Hill: London, 1995.

(6) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectrometric Identification of Organic Compounds*, 5th ed.; Wiley: New York, 1991.

(7) Howe, I.; Williams, D. H.; Bowen, R. D. *Mass Spectrometry, Principles and Applications*; McGraw-Hill: New York, 1981.

(8) Budzikiewicz, H.; Djerassi, C.; Williams, D. H. *Mass Spectrometry of Organic Compounds*; Holden-Day: San Francisco, 1967.

(9) (a) Newcomb, M.; Daublain, P.; Horner, J. H. *J. Org. Chem.* **2002**, *67*, 8669−8671. (b) Fittschen, C.; Hippler, H.; Viskolcz, B. *Phys. Chem. Chem. Phys.* **2000**, *2*, 1677−1683. (c) Méreau, R.; Rayez, M.-T.; Caralp, F.; Rayez, J.-C. *Phys. Chem. Chem. Phys.* **2000**, *2*, 3765−3772. (d) Caralp, F.; Devolder, P.; Fittschen, C.; Gomez, N.; Hippler, H.; Méreau, R.; Rayez, M.-T.; Streibel, F.; Viskolcz, B. *Phys. Chem. Chem. Phys.* **1999**, *1*, 2935−2944. (e) Hornung, G.; Schalley, C. A.; Dieterle, M.; Schröder, D.; Schwarz, H. *Chem.−Eur. J.* **1997**, *3*, 1866−1883.

(10) (a) Antunes, C. S. A.; Bietti, M.; Lanzalunga, O.; Salamone, M. *J. Org. Chem.* **2004**, *69*, 5281−5289. (b) Nakamura, T.; Watanabe, Y.; Suyama, S.; Tezuka, H. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1364−1369. (c) Nakamura, T.; Busfield, W. K.; Jenkins, I. D.; Rizzardo, E.; Thang, S. H.; Suyama, S. *J. Org. Chem.* **2000**, *65*, 16−23. (d) Wilsey, S.; Dowd, P.; Houk, K. N. *J. Org. Chem.* **1999**, *64*, 8801−8811. (e) Zhang, W.; Dowd, P. *Tetrahedron* **1993**, *49*, 1965−1978. (f) Choo, K. Y.; Benson, S. W. *Int. J. Chem. Kinet.* **1981**, *13*, 833−844. (g) Bacha, J. D.; Kochi, J. K. *J. Org. Chem.* **1965**, *30*, 3272−3278. (h) Greene, F. D.; Savitz, M. L.; Osterholtz, F. D.; Lau, H. H.; Smith, W. N.; Zanet, P. M. *J. Org. Chem.* **1963**, *28*, 55−64. (i) Walling, C.; Wagner, P. J. *J. Am. Chem. Soc.* **1963**, *85*, 2333−2334. (j) Walling, C.; Padwa, A. *J. Am. Chem. Soc.* **1963**, *85*, 1593−1597. (k) Kochi, J. K. *J. Am. Chem. Soc.* **1962**, *84*, 1593−1597.

(11) (a) Orlando, J. J.; Tyndall, L. L.; Wallington, T. *Chem. Rev.* **2003**, *103*, 4657−4697. (b) Jungkamp, T. P. W.; Smith, J. N.; Seinfeld, J. H. *J. Phys. Chem. A* **1997**, *101*, 4392−4401. (c) Kwok, E. S. C.; Arey, J.; Atkinson, R. *J. Phys. Chem.* **1996**, *100*, 214−219. (d) Mörs, V.; Hoffmann, A.; Malms, W.; Zellner, R. *Air Pollut. Res. Rep.* **1996**, *57*, 273−278. (e) Atkinson, R. *Int. J. Chem. Kinet.* **1997**, *29*, 99−111.

(12) (a) Hartung, J.; Gottwald, T.; Spehar, K. *Synthesis* **2002**, 1469−1498. (b) Suarez, E.; Rodriguez, M. S. In *Radicals in Organic Synthesis*; Siba, M. P. Ed.; Wiley-VCH: Weinheim, Germany, 2001; Vol. 2, pp 440−454. (c) Yet, L. *Tetrahedron* **1999**, *55*, 9349−9403.

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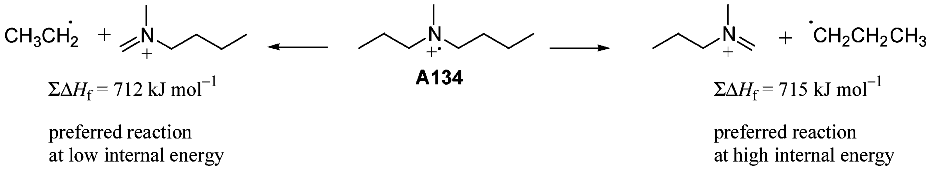

Figure 1. Simple cleavage reactions of the *N*-methyl-*N*-propylbutylamine radical cation (**A134**).

simple cleavage reactions, loss of the larger radical will give rise to the larger peak in the 70 eV mass spectrum.[3−8] The observation that the products of simple cleavage reactions often give rise to prominent peaks in the electron ionization mass spectra of aliphatic compounds such as alcohols or amines is in many of the same textbooks associated with the particular stability of the product onium ions. However, attention is not always drawn to the possible discrepancy between these two statements, a discrepancy that arises because loss of the smaller radical will often yield the thermochemically favored products; one example is shown in Figure 1.

The preference for loss of the larger radical was noted early by mass spectrometrists.[13−15] Systematic studies of electron ionization mass spectra of a variety of compounds by King,[16] Marshall and Williams,[17] and Djerassi and co-workers[18−20] illustrated the general nature of the phenomenon, and their low-voltage ionization mass spectra demonstrated that the observation did not merely reflect differences between the rates of subsequent fragmentation of the product ions. However, the low-voltage experiments also showed that the preference was reversed in some cases (e.g., some ethers, ketones, and oximes) when the internal energy of the reactant ions was reduced. Extensive systematic studies by Záhorsky[21−26] of low-voltage electron ionization mass spectra of a variety of compounds led to the suggestion[26] that the preference observed for loss of the longer alkyl radical was related to the number of degrees of freedom of the product ions.

It is less widely recognized that the behavior of competing simple cleavage reactions of metastable radical cations is the opposite of that observed for the reactions in the mass spectrometer ion source, in that loss of the smaller alkyl radical from the metastable molecular ion is preferred over loss of the larger. This has been reported to be the case for α-cleavage of the radical cations of amines[27−31] and ketones and ketals,[32] as well as for the expulsion of alkyl radicals from ionized carboxylic acid enols[34] and unsaturated ethers.[33] Weiske and Schwarz[34] suggested that hyperconjugative interactions in the transition state were part of the reason ethyl radicals are expelled more rapidly than other alkyl radicals from carboxylic acid enol radical cations, but rationalizations of this nature are difficult to substantiate experimentally. Longevialle et al.[29−31] introduced the ingenious concept of an "ion-neutral reorganization threshold" to account for the behavior observed for metastable amine radical cations and suggested that the relative yield of competing α-cleavage reactions was determined by the ease of formation of the corresponding [alkyl radical + immonium ion] ion molecule complexes rather than by the subsequent dissociation reactions. Unfortunately, Longevialle et al. did not indicate how this threshold would be determined or estimated; they assumed that the thermochemistry of the competing alkyl loss reactions would not differ significantly.

The rates of dissociation are orders of magnitude higher in the ion source than in the field-free regions where the metastable ions react. The internal energy of the reacting species can in turn differ considerably, with the reactions in the ion source involving the higher-energy ions. That the competition between loss of small and large radicals turns out very differently in the ion source and the field-free regions shows that the rate constant for loss of the smaller radical has a more shallow rise with energy than does the rate constant for loss of the larger radical, to such an extent that the k(E) curves for the two reactions cross. This point was made already in 1965 by King,[16] and he as well as Cooks et al.[32] pointed out that it is difficult to account for the energy-dependent change of behavior in terms of simple RRKM theory. To examine the competition between simple cleavage reactions systematically, we have studied the loss of different alkyl radicals (methyl to hexyl) from unsymmetrical tertiary amine radical cations, and we have sought to account for the reversal of the preference within the framework of standard RRKM theory and variational transition state theory. We have further used ab initio methods to examine the thermochemistry of the reactions of the simplest (smallest) ions studied experimentally, as well as the reactions of model systems.

Choice of System. Experimental studies of simple cleavage reactions of ions must take into account that many compounds undergo high-yield simple cleavage in the mass spectrometer ion source but exhibit different reactions in the field-free regions. This is in part because the thermochemistry of simple cleavage in straight-chain systems frequently is not very favorable. However, aliphatic amine radical cations react in good yield by loss of alkyl radicals by homolytic cleavage of the C−C bond next to the nitrogen (α-cleavage), both when highly energized and when close to threshold. Rudat and McEwen[35] showed that the simple cleavage in the ion source is not

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(13) Friedel, R. A.; Schultz, J. L.; Sharkey, A. G. *Anal. Chem.* **1956**, *28*, 926−934.
(14) McLafferty, F. W. *Anal. Chem.* **1957**, *29*, 1782−1789.
(15) Biemann, K. *Mass Spectrometry*; McGraw-Hill: New York, 1962.
(16) King, A. B. *J. Chem. Phys.* **1965**, *42*, 3526−3536.
(17) Marshall, J. T. B.; Williams, D. H. *Tetrahedron* **1967**, *23*, 321−333.
(18) Carpenter, W.; Duffield, A. M.; Djerassi, C. *J. Am. Chem. Soc.* **1967**, *89*, 6167−6170.
(19) Brandt, R.; Djerassi, C. *Helv. Chim. Acta* **1968**, *51*, 1750−1762.
(20) Brown, C. A.; Duffield, A. M.; Djerassi, C. *Org. Mass Spectrom.* **1969**, *2*, 625−630.
(21) Záhorsky, U. I. *Tetrahedron Lett.* **1973**, *38*, 3691−3694.
(22) Záhorsky, U. I. *Org. Mass Spectrom.* **1976**, *11*, 1242−1253.
(23) Záhorsky, U. I. *Org. Mass Spectrom.* **1976**, *11*, 1254−1261.
(24) Záhorsky, U. I. *Tetrahedron Lett.* **1977**, *18*, 2321−2324.
(25) Záhorsky, U. I. *Org. Mass Spectrom.* **1979**, *14*, 66−74.
(26) Záhorsky, U. I. *Org. Mass Spectrom.* **1982**, *17*, 192−196.
(27) Hammerum, S.; Christensen, J. B.; Egsgaard, H.; Larsen, E.; Derrick, P. J.; Donchi, K. F. *Int. J. Mass Spectrom. Ion Phys.* **1983**, *47*, 351−354.
(28) Mandeville, S. J.; Bowen, R. D.; Trikoupis, M. A.; Terlouw, J. K. *Eur. Mass Spectrom.* **1999**, *5*, 339−351.
(29) Longevialle, P. *Rapid Commun. Mass Spectrom.* **1995**, *9*, 1189−1194.
(30) Longevialle, P.; Lefevre, O. *Rapid Commun. Mass Spectrom.* **1996**, *10*, 621−626.
(31) Longevialle, P.; Lefevre, O.; Mollova, N.; Bouchoux, G. *Rapid Commun. Mass Spectrom.* **1998**, *12*, 57−60.
(32) Cooks, R. G.; Yeo, A. N. H.; Williams, D. H. *Org. Mass Spectrom.* **1969**, *2*, 985−995.
(33) Bowen, R. D.; Clifford, P.; Francis, J. T.; Terlouw, J. K. *Int. J. Mass Spectrom.* **1997**, *165*, 155−168.
(34) Weiske, T.; Schwarz, H. *Tetrahedron* **1986**, *42*, 6245−6251.

complicated by concurrent rearrangement of the alkyl radical, and Levsen and McLafferty's collision activation studies[36] suggest that the ionic product, the immonium ion, also retains its structural integrity. However, loss of alkyl radicals from metastable primary and secondary amine radical cations can be preceded by intramolecular hydrogen atom abstraction and skeletal rearrangement,[27,37−41] and the simple cleavage may be accompanied by other reactions, notably loss of neutral alkane molecules when the amino group is situated at a branching point.[29−31,42−44] The possibility of isomerization and the occurrence of competing processes may introduce ambiguity in the interpretation of the experimental observations, but complications of this kind are almost completely absent when tertiary amine radical cations undergo simple cleavage. The expulsions of alkyl radicals from these ions appear to be straightforward simple cleavage reactions in the ion source as well as in the field-free regions, in general free from significant competing reactions.[28,45] We have therefore based the main part of the experimental study on reactions where primary alkyl radicals are lost from tertiary amine radical cations. The competition between alkyl radical expulsion reactions of a number of primary and secondary amines has been included for comparison.

Methods

Mass Spectrometry. A JEOL four-sector double-focusing JMS-HX110/HX110A mass spectrometer (EBEB geometry) was used to record mass spectra (reactions in the ion source) and mass analyzed ion kinetic energy (MIKE) spectra (reactions of metastable amine radical cations). The first three sectors of the instrument were used when recording MIKE spectra.[46] The energy of the ionizing electrons was 70 eV, the accelerating voltage was 10 kV, and the ion source temperature was approximately 200 °C. Amines can occasionally give rise to quite serious memory effects; only one compound was examined on any one day, and isomeric amines never on two successive days. All measurements of relative ion yield were repeated at least 10 times on the same day; the reproducibility of the relative ion yield was better than 2% when measured on different days.

Preliminary studies were performed on a VG ZAB-2F instrument located at the University of Bielefeld and on an unusually large double-focusing instrument (MMM) at Warwick University.

Computational Thermochemistry. Heats of formation were derived from total energies calculated with the G3 and G3(MP2) composite ab initio methods,[47,48] slightly modified for radicals and radical cations in that the geometry optimization was performed at the UMP2(full)/6-31+G(d,p) level. These methods have been shown to yield accurate estimates of the thermochemical properties of ions and radicals.[49,50] The energies were obtained with the *Gaussian 98* suite of programs[51] and converted to 298 K heats of formation as described by Nicolaides et al.;[52] the required auxiliary thermochemical data were taken from the compilation by Chase.[53] The alkyl radical heats of formation used here were calculated on the basis of G3 total energies.[41] Heats of formation of immonium ions obtained with the G2(MP2) and CBS-Q methods were reported recently;[54] the values used in the present study were recalculated with the G3 and G3(MP2) methods for consistency with the alkyl radical results.

To follow the course of the dissociation reactions and to perform preliminary location of transition states, we used stepwise variation of the C−C bond length in question, from 1.5 up to 3.5 Å, with full geometry optimization at the UMP2/6-31G(d) level at each 0.1 Å step.

Zero-point vibrational energy differences for isotope-substituted species were obtained from HF/6-31G(d) vibrational frequencies, scaled by 0.8929.

Synthesis. Most secondary and tertiary amines examined were prepared by $LiAlH_4$ reduction of the appropriate amide in tetrahydrofuran. Secondary amines with an *N*-methyl or *N*-ethyl group were prepared by alkylation of the appropriate benzylidene amine with dimethyl or diethyl sulfate.[55] Identity and purity were ascertained with ^{13}C NMR spectroscopy[56] and GC−MS.

Experimental Results

Mass Spectra. The 70 eV electron ionization mass spectra of the straight-chain tertiary amines with three different alkyl groups on nitrogen examined in the present study are unexceptional (Figure 2). As expected,[57] loss of alkyl radicals by α-cleavage is the predominant reaction in the ion source, typically accounting for >60% of the yield of stable ions. The ratio of the $[M - alkyl]^+$ peak heights in the mass spectra is given in Table 1. The results show a clear preference for loss of the longer alkyl radical, a preference that appears to change systematically, becoming less pronounced with increasing mass of the two alkyl radicals expelled. The ratio of peak heights is not a direct measure of the relative ion yield of the competing simple cleavage reactions in the ion source, inasmuch as the product ions undergo further fragmentation (predominantly by loss of neutral alkene molecules), but the picture does not change materially if the products of the subsequent fragmentation reactions are taken into account. These results agree well with those reported in previous studies.[8,16−26,32,57]

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(35) (a) Rudat, M. A.; McEwen, C. N. *J. Am. Chem. Soc.* **1981**, *103*, 4343−4349. (b) Rudat, M. A.; McEwen, C. N. *J. Am. Chem. Soc.* **1981**, *103*, 4349−4354. (c) Rudat, M. A.; McEwen, C. N. *J. Am. Chem. Soc.* **1981**, *103*, 4354−4359.

(36) Levsen, K.; McLafferty, F. W. *J. Am. Chem. Soc.* **1974**, *96*, 139−144.

(37) Hammerum, S. *Tetrahedron Lett.* **1981**, *22*, 157−160.

(38) Audier, H. E.; Milliet, A.; Denhez, J. P. *Org. Mass Spectrom.* **1983**, *18*, 131−132.

(39) Audier, H. E.; Sozzi, G.; Denhez, J. P. *Tetrahedron* **1986**, *42*, 1179−1190.

(40) Hammerum, S.; Petersen, A. C. *Acta Chem. Scand.* **1998**, *52*, 1045−1050.

(41) Hammerum, S.; Henriksen, T. *Int. J. Mass Spectrom.* **2000**, *199*, 79−89.

(42) Litton, J. F.; Kruger, T. L.; Cooks, R. G. *J. Am. Chem. Soc.* **1976**, *98*, 2011−2013.

(43) Hammerum, S.; Derrick, P. J.; Donchi, K. F. *Int. J. Mass Spectrom. Ion Proc.* **1983**, *47*, 347−350.

(44) Bowen, R. D. In *The Chemistry of Amino, Nitroso, Nitro and Related Groups*; Patai, S., Ed.; Chemistry of Functional Groups, Supplement F2; Wiley: Chichester, 1996; pp 205−248.

(45) Hammerum, S. *Acta Chem. Scand.* **1984**, *38*, 707−708.

(46) Cooks, R. G.; Beynon, J. H.; Caprioli, R. M.; Lester, G. R. *Metastable Ions*; Elsevier: Amsterdam, 1973.

(47) Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Rassolov, V.; Pople, J. A. *J. Chem. Phys.* **1998**, *109*, 7764−7776.

(48) Curtiss, L. A.; Redfern, P. C.; Raghavachari, K.; Rassolov, V.; Pople, J. A. *J. Chem. Phys.* **1999**, *110*, 4703−4709.

(49) (a) Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Pople, J. A. *J. Chem. Phys.* **1997**, *106*, 1063−1079. (b) Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Pople, J. A. *J. Chem. Phys.* **2000**, *112*, 7374−7383. (c) Curtiss, L. A.; Raghavachari, K. *Theor. Chem. Acc.* **2002**, *108*, 61−70.

(50) Hammerum, S. *Chem. Phys. Lett.* **1999**, *300*, 529−532.

(51) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.11.3; Gaussian, Inc.: Pittsburgh, PA, 1998.

(52) Nicolaides, A.; Rauk, A.; Glukhovtsev, M. N.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 17460−17464.

(53) Chase, M. W., Jr. *NIST-JANAF Thermochemical Tables*, 4th ed.; *J. Phys. Chem. Ref. Data* Monograph No. 9; American Chemical Society, Washington, DC, 1998.

(54) Hammerum, S.; Sølling, T. I. *J. Am. Chem. Soc.* **1999**, *121*, 6002−6009.

(55) Lucier, J. J.; Harris, A. D.; Korosec, P. S. *Organic Syntheses*; Wiley & Sons: New York, 1973; Collect. Vol. V, pp 736−739.

(56) Eggert, H.; Djerassi, C. *J. Am. Chem. Soc.* **1973**, *95*, 3710−3718.

(57) Gohlke, R. S.; McLafferty, F. W. *Anal. Chem.* **1962**, *34*, 1281−1287.

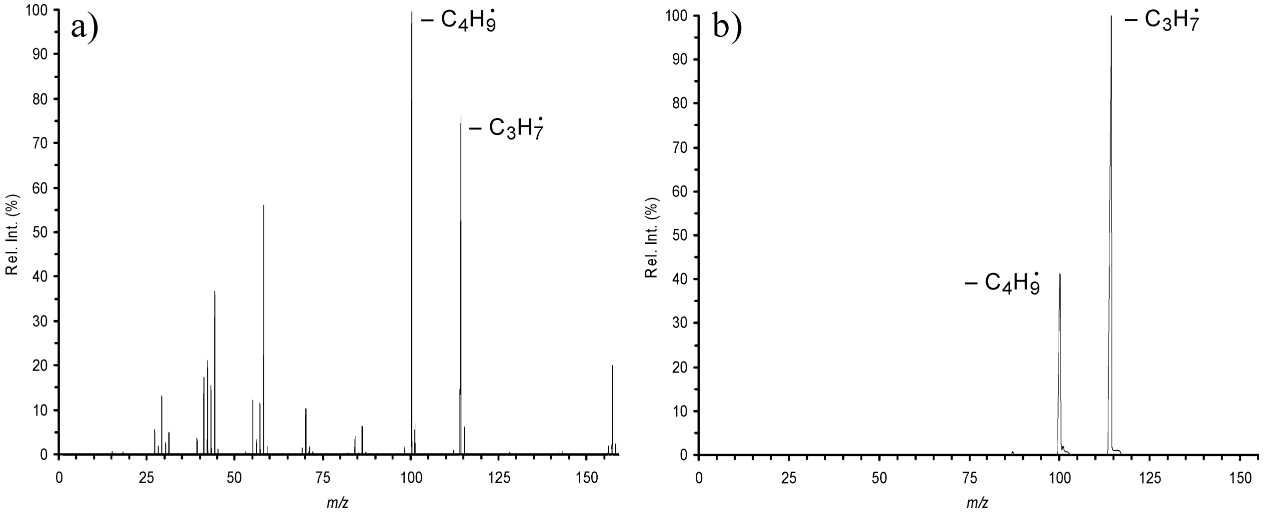

Figure 2. *N*-Butyl-*N*-methylpentylamine (**A145**). (a) EI mass spectrum, (b) MIKE spectrum. Amines with straight-chain alkyl groups are denoted **Axyz**, and amines with the nitrogen atom at a nonterminal position are denoted **Bxyz**; *x*, *y*, and *z* indicate the length of the carbon chains attached to nitrogen.

Table 1. Competing Loss of Alkyl Radicals from Straight-Chain Tertiary Amine Radical Cations

		radicals lost			metastable ions			ion source		
	reactant	R^1	R^2	R^3	M–R^1	M–R^2	M–R^3	M–R^1	M–R^2	M–R^3
A123	*N*-methyl-*N*-ethyl-propylamine$^{\bullet+}$	H	CH_3	C_2H_5	–	6	100	–	11	100
A134	*N*-methyl-*N*-propyl-butylamine$^{\bullet+}$	H	C_2H_5	C_3H_7	–	100	34	–	48	100
A135	*N*-methyl-*N*-propyl-pentylamine$^{\bullet+}$	H	C_2H_5	C_4H_9	–	100	25	–	42	100
A145	*N*-methyl-*N*-butyl-pentylamine$^{\bullet+}$	H	C_3H_7	C_4H_9	–	100	69	–	80	100
A146	*N*-methyl-*N*-butyl-hexylamine$^{\bullet+}$	H	C_3H_7	C_5H_{11}	–	100	45	–	79	100
A156	*N*-methyl-*N*-pentyl-hexylamine$^{\bullet+}$	H	C_4H_9	C_5H_{11}	–	100	70	–	88	100
A167	*N*-methyl-*N*-hexyl-heptylamine$^{\bullet+}$	H	C_5H_{11}	C_6H_{13}	–	100	73	–	96	100
A234	*N*-ethyl-*N*-propyl-butylamine$^{\bullet+}$	CH_3	C_2H_5	C_3H_7	0.3	100	50	6	54	100
A245	*N*-ethyl-*N*-butyl-pentylamine$^{\bullet+}$	CH_3	C_3H_7	C_4H_9	0.8	100	79	6	82	100
A345	*N*-propyl-*N*-butyl-pentylamine$^{\bullet+}$	C_2H_5	C_3H_7	C_4H_9	100	66	55	68	83	100
A456	*N*-butyl-*N*-pentyl-hexylamine$^{\bullet+}$	C_3H_7	C_4H_9	C_5H_{11}	100	90	70	80	95	100

It is interesting that Mandeville's results[28] indicate that the preference for loss of the larger alkyl radical in the ion source reactions is much less pronounced when the C−C bond cleavage takes place at a branching point; these authors even reported that the preference is in certain instances reversed. Our results corroborate these observations.

It is often observed that the loss of methyl radicals by simple cleavage falls outside these generalizations, for reasons that are not clearly understood.[3,7,18,25,44] This applies to reactions in the ion source as well as to reactions of metastable ions; in both cases, methyl radicals are frequently lost much less readily than other alkyl groups.

Metastable Ions. The MIKE spectra show that the metastable molecular ions react virtually exclusively by loss of alkyl radicals; these reactions typically account for >95% of the ion yield (Figure 2). The relative yield (measured as the ratio of peak heights) of the competing simple cleavage reactions of straight-chain tertiary amine radical cations is given in Table 1. It can be seen that loss of the smaller alkyl radical (excepting methyl) predominates in every case; the difference is more pronounced when the two alkyl groups expelled differ by more than one methylene group, whereas the difference becomes less pronounced with increasing mass of the two alkyl groups involved.

When three different alkyl radicals may be lost, the smallest is lost more readily than the medium sized, and the largest least readily. The results in Table 2 illustrate that loss of the smaller radical is also preferred when cleavage takes place at a branching point and that the difference between the yields of the competing reactions can change considerably when alkyl substituents are introduced at the α-carbon atom or removed from the nitrogen atom; both structural modifications reduce the energy required for dissociation.

Table 2. Competing Loss of Alkyl Radicals from Metastable α-Branched Amine Radical Cations

reactant[a]	alkyl radicals lost				reactant[a]	alkyl radicals lost			
B006[b,c]	ethyl	100	propyl	1	**B008**[d]	propyl	100	butyl	10
B106	ethyl	100	propyl	4	**B108**	propyl	100	butyl	21
B206	ethyl	100	propyl	8	**B118**	propyl	100	butyl	86
B116	ethyl	100	propyl	18	**B218**	propyl	100	butyl	91
B117	ethyl	100	propyl	27	**B318**	propyl	100	butyl	92
B145	ethyl	100	propyl	79	**B618**	propyl	100	butyl	95
					B718	propyl	100	butyl	94

[a] See Figure 3. [b] Other species lost: C_2H_6 45, NH_3 20, C_3H_8 30. [c] EI mass spectrum: NIST Webbook. [d] Other species lost: C_3H_8 < 5, C_4H_{10} < 5.

The influence of branching of the carbon skeleton at the site of cleavage is illustrated by the competing expulsion of ethyl and propyl radicals, or propyl and butyl radicals, from the α-branched amines shown in Figure 3; the results are in Table 3. A number of these compounds were also included in the extensive study by Mandeville et al.[28] These authors report that the metastable *N*,*N*-dimethyl-4-octylamine radical cation and two higher homologues expel the larger radical, butyl, more

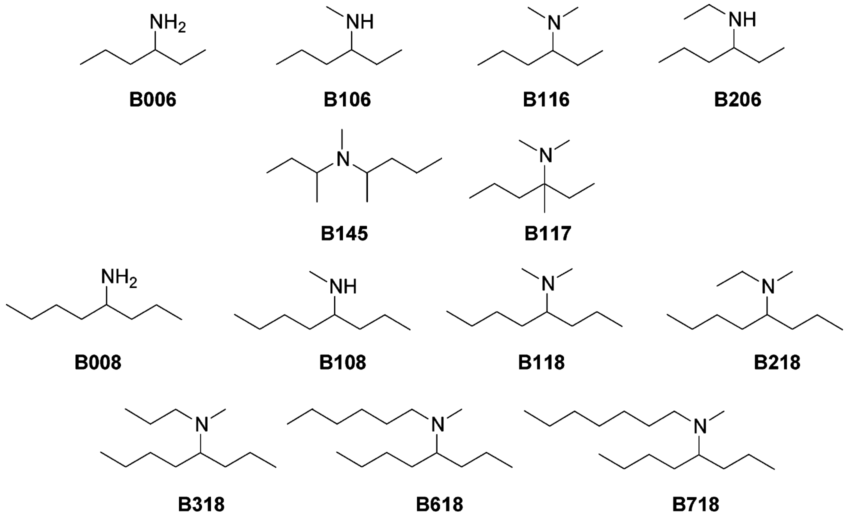

Figure 3. Branched amines examined. Amines with the nitrogen atom in a nonterminal position are denoted **Bxyz**; *x*, *y*, and *z* indicate the length of the carbon chains attached to nitrogen.

Table 3. Pairwise Comparison of the Ratio of Elimination of Alkyl Radicals from Metastable Amine Radical Cations

alkyl radicals lost	amine	Mw	ratio	alkyl radicals lost	amine	Mw	ratio
ethyl/propyl	**A134**	129	2.9	propyl/butyl	**B008**	129	10
	A234	143	2.0		**B108**	143	4.8
	A345[a]	185	1.5		**B118**	157	1.2
	B145	157	1.2		**B218**	171	1.1
	B006[b]	101	100		**B318**	185	1.1
	B106	115	25		**B618**	227	1.1
	B116[c]	129	5.6		**B718**	241	1.1
	B117	143	3.7	butyl/pentyl	**A156**	185	1.4
propyl/butyl	**A145**	157	1.5		**A456**[f]	227	1.3
	A245	171	1.3	pentyl/hexyl	**A167**	213	1.4
	A345	185	1.2				
	A456	227	1.1				

[a] Competing loss of C_3H_7. [b] See footnotes to Table 2. [c] Pressure sensitive. [d] Competing loss of C_2H_5. [e] Competing loss of C_5H_{11}. [f] Competing loss of C_3H_7.

Table 4. Calculated Heats of Formation of Alkyl Radicals

	G3	G3(MP2)		G3	G3(MP2)
$CH_3^\bullet$	142	143	$C_4H_9^{\bullet b}$	80	81
$C_2H_5^\bullet$	120	121	$C_5H_{11}^{\bullet b}$	59	60
$C_3H_7^\bullet$	100	101	$C_6H_{13}^{\bullet b}$	37	39

[a] In kJ mol^{-1}, 298 K; values in excellent agreement with experimental values;[41,59,60] the heats of formation calculated by Marsi et al.[62] are slightly lower. [b] All-trans conformation.

readily than the smaller, propyl. We have not been able to reproduce these results. In our experiments, these compounds exhibit the same behavior as the other amines studied, losing the smaller radical more rapidly than the larger (Tables 2 and 3).

To illustrate the influence of the degree of substitution at the nitrogen atom, Tables 2 and 3 also include results for the loss of alkyl radicals from metastable 3-hexylamine and 4-octylamine radical cations and their *N*-methyl analogues (**B006**, **B106** and **B008**, **B108**); discrimination against loss of the larger radical is more pronounced for the ions with fewer N-substituents, in line with results reported earlier[27] for loss of ethyl and butyl radicals from 3-heptylamine and its *N*-methyl and *N*,*N*-dimethyl analogues.

The MIKE spectra of the metastable branched amine radical cations indicate that the reactions are to some extent sensitive to the pressure in the analyzer regions of the mass spectrometer. The relative abundance of the ions formed by loss of alkyl radicals given in Table 2 is therefore derived from relative peak areas, which were well reproducible. Different background pressure in the instruments used may be part of the reason our results differ somewhat from those reported by Mandeville et al.[28] Collision activation will promote loss of the larger radical (the more favored reaction of highly energized reactant ions), and can possibly cause peak broadening.

Thermochemistry

Tables 4 and 5 summarize the calculated heats of formation of the alkyl radicals and immonium ions formed by simple cleavage of a number of amine radical cations. Our computational resources allow only the smaller of the tertiary amine radical cations studied experimentally to be examined with quantum chemical methods that afford the required accuracy. However, the heats of formation of the products of reactions that involve longer chains or more highly substituted systems can be assessed by considering the products of α-cleavage of the corresponding primary and secondary amines.

The heats of formation of a number of simple immonium ions were recently rederived[54] from the appearance energy measurements of Lossing, Lam, and Maccoll[58] and shown to agree well with the heats of formation calculated with the G2(MP2) and CBS-Q composite ab initio methods. The present G3 and G3(MP2) results complement the earlier computational results;[54] the G3(MP2) heats of formation are systematically some 4 kJ mol^{-1} higher than those obtained with G3, but the differences between homologous immonium ions are the same with the two methods.

Heats of formation calculated with G3-type methods are expected to be within 5−10 kJ mol^{-1} of the experimental values. However, the differences between the energies of closely related species are in all likelihood determined with considerably greater accuracy with these methods.

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(58) Lossing, F.; Lam, Y.-T.; Maccoll, A. *Can. J. Chem.* **1981**, *59*, 2228−2231.

Table 5. G3 and G3(MP2) Heats of Formation of Immonium Ions (298 K, kJ mol^{-1})[a]

	G3	G3(MP2)		G3	G3(MP2)
$CH_2{=}NH_2^+$	753	756	$CH_3CH{=}NH_2^+$	668	671
$C_2H_5CH{=}NH_2^+$	636	639	*n*-$C_3H_7CH{=}NH_2^+$	611	614
n-$C_4H_9CH{=}NH_2^+$	586	590	*n*-$C_5H_{11}CH{=}NH_2^+$	563	567
n-$C_6H_{13}CH{=}NH_2^+$	–	545			
$C_2H_5CH{=}NHCH_3^+$	604	608	*n*-$C_3H_7CH{=}NHCH_3^+$	579	583
n-$C_4H_9CH{=}NHCH_3^+$	555	559	*n*-$C_5H_{11}CH{=}NHCH_3^+$	–	536
$CH_3CH{=}NHCH(CH_3)C_2H_5^+$	527	531	$CH_3CH{=}NHCH(CH_3)C_3H_7^+$	–	508
$CH_3CH{=}N(CH_3)_2^+$	610	614	$C_2H_5CH{=}N(CH_3)_2^+$	584	588
n-$C_3H_7CH{=}N(CH_3)_2^+$	558	562	*n*-$C_4H_9CH{=}N(CH_3)_2^+$	–	538
$C_2H_5CH{=}N(CH_3)C_2H_5^+$	547	551	*n*-$C_3H_7CH{=}N(CH_3)C_2H_5^+$	–	525
$(CH_3)_2C{=}NH_2^+$	592	597	$C_2H_5(CH_3)C{=}NH_2^+$	562	566
n-$C_3H_7(CH_3)C{=}NH_2^+$	537	541	*n*-$C_4H_9(CH_3)C{=}NH_2^+$	513	517
n-$C_5H_{11}(CH_3)C{=}NH_2^+$	–	495			
n-$C_3H_7(C_2H_5)C{=}NH_2^+$	507	512	*n*-$C_4H_9(C_2H_5)C{=}NH_2^+$	–	488
$C_2H_5(CH_3)C{=}NHCH_3^+$	540	545	*n*-$C_3H_7(CH_3)C{=}NHCH_3^+$	516	520
n-$C_4H_9(CH_3)C{=}NHCH_3^+$	–	497			
$(CH_3)_2C{=}N(CH_3)_2^+$	556	561	$C_2H_5(CH_3)C{=}N(CH_3)_2^+$	530	535
n-$C_3H_7(CH_3)C{=}N(CH_3)_2^+$	–	509			
$CH_3NH{=}CH_2^+$	711	715	$C_2H_5NH{=}CH_2^+$	672	676
n-$C_3H_7NH{=}CH_2^+$	646	650	*n*-$C_4H_9NH{=}CH_2^+$	622	626
n-$C_5H_{11}NH{=}CH_2^+$	599	603	*n*-$C_6H_{13}NH{=}CH_2^+$	–	581
$(CH_3)_2N{=}CH_2^+$	672	676	$C_2H_5(CH_3)N{=}CH_2^+$	636	640
n-$C_3H_7(CH_3)N{=}CH_2^+$	611	614	*n*-$C_4H_9(CH_3)N{=}CH_2^+$	587	591
n-$C_5H_{11}(CH_3)N{=}CH_2^+$	–	568			
n-$C_3H_7(C_2H_5)N{=}CH_2^+$	574	578	*n*-$C_4H_9(C_2H_5)N{=}CH_2^+$	–	555

[a] See ref 54 for a discussion and comparison of calculated and experimentally determined heats of formation of immonium ions.

Table 6. Calculated Heats of Formation of the Products Formed by Simple Cleavage Reactions of Aliphatic Amine Radical Cations[a]

reactant	radical lost	$\Sigma\Delta H_f$ (prod.)	radical lost	$\Sigma\Delta H_f$ (prod.)	difference
3-hexylamine$^{\bullet+}$ (**B006**)	ethyl	735	propyl	740	5
N-methyl-3-hexylamine$^{\bullet+}$ (**B106**)	ethyl	604	propyl	609	5
N,*N*-dimethyl-3-hexylamine$^{\bullet+}$ (**B116**)	ethyl	683	propyl	689	6
N-ethyl-*N*-methyl-3-hexylamine$^{\bullet+}$	ethyl	646	propyl	652	6
3-methyl-3-hexylamine$^{\bullet+}$	ethyl	662	propyl	667	5
N,3-dimethyl-3-hexylamine$^{\bullet+}$	ethyl	641	propyl	646	5
N,*N*,3-trimethyl-3-hexylamine$^{\bullet+}$ (**B117**)	ethyl	630	propyl	636	6
N-propyl-butylamine$^{\bullet+}$	ethyl	747	propyl	751	4
N-methyl-*N*-propyl-butylamine$^{\bullet+}$ (**A134**)	ethyl	712	propyl	715	3
N-ethyl-*N*-propyl-butylamine$^{\bullet+}$ (**A234**)	ethyl	676	propyl	679	3
N-(1-methylpropyl)-2-pentylamine$^{\bullet+}$	ethyl	629	propyl	632	3
4-octylamine$^{\bullet+}$ (**B008**)	propyl	691	butyl	695	4
N-methyl-4-octylamine$^{\bullet+}$ (**B108**)	propyl	660	butyl	664	4
N,*N*-dimethyl-4-octylamine$^{\bullet+}$ (**B118**)	propyl	639	butyl	643	4
4-methyl-4-octylamine$^{\bullet+}$	propyl	618	butyl	622	4
4-ethyl-4-octylamine$^{\bullet+}$	propyl	589	butyl	593	4
N,4-dimethyl-4-octylamine$^{\bullet+}$	propyl	598	butyl	601	3
N-butyl-pentylamine$^{\bullet+}$	propyl	704	butyl	707	3
N-methyl-*N*-butyl-pentylamine$^{\bullet+}$ (**A145**)	propyl	669	butyl	672	3
5-decylamine$^{\bullet+}$	butyl	648	pentyl	651	3
N-methyl-5-decylamine$^{\bullet+}$	butyl	617	pentyl	620	3
5-methyl-5-decylamine$^{\bullet+}$	butyl	576	pentyl	577	1
N-pentyl-hexylamine$^{\bullet+}$	butyl	662	pentyl	664	2
6-dodecylamine$^{\bullet+}$	pentyl	606	hexyl	607	1

[a] Based on the G3(MP2) heats of formation (kJ mol^{-1}, 298 K) in Tables 4 and 5.

The differences between the heats of reaction of the competing cleavages considered here are typically 2−5 kJ mol^{-1}, and energy differences this small would perhaps be indicative rather than conclusive if they pertained to the dissociation of a single reactant ion. However, the results in Table 6 summarize the thermochemistry of 24 pairs of reactions and show that it is without exception energetically more favorable to expel the smaller radical in competing simple cleavage reactions of metastable amine radical cations.

An internally consistent set of Benson group additivity values was derived from the ab initio results for immonium ions with up to five carbon atoms,[54] which indicates that any imperfections in the computational model result in systematic rather than random deviations of the calculated heats of formation from the true values. It follows that the differences between the calculated heats of formation of homologous immonium ions should be reasonably accurate. The Benson scheme took into account that the introduction of a methylene group even several bonds removed from the C=N double bond lowers the heat of formation by a few kJ mol^{-1} more than would introduction of a CH_2 group in the corresponding alkane.

The results in Table 6 illustrate this well; the presence of the charge causes the heats of formation of immonium ions that differ by a remote methylene group to be different by slightly more than the 20−21 kJ mol^{-1} predicted by additivity schemes for neutral compounds. The results further show that the

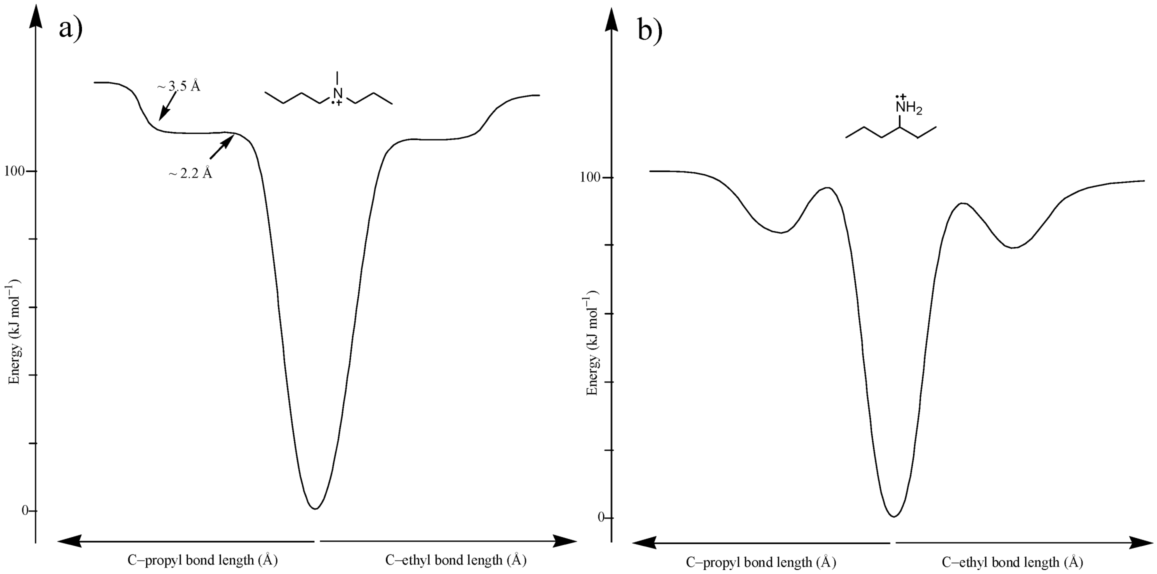

Figure 4. (a) Potential energy profile for dissociation of **A134**. (b) Potential energy profile for dissociation of **B006**.

additional stabilization is slightly larger when the additional methylene group is on the carbon side of an immonium ion than when it is on the nitrogen side.[54]

Similar effects do not appear to influence the heats of formation of alkyl radicals;[59,60] normal additivity rules apply.[61,62] The reaction that leads to the larger immonium ion (i.e., the reaction that involves loss of the smaller alkyl radical) is in consequence the thermochemically more favored process (Table 6).

It appears reasonable to expect (and the results in Table 6 bear this out) that the differences between the heats of reaction will not be very sensitive to the introduction of substituents well removed from the site(s) of cleavage. An additional methyl group in both product ions under consideration does not change the difference between their heats of formation much. The presence of the additional substituent may, however, have noticeable kinetic consequences (see below).

The Reactions of Metastable Ions

Cleavage of Straight-Chain Amines. It is often assumed that endothermic simple cleavage reactions such as those examined in the present study do not have significant energy barriers between reactants and products. This appears to be true for simple cleavage reactions in straight-chain amine radical cations. The corresponding metastable peaks are of simple Gaussian shape, and ab initio modeling of the dissociation processes in two prototype systems, ethyl loss from the *N*,*N*-dimethylpropylamine radical cation and propyl loss from the *N*,*N*-dimethylbutylamine radical cation, indicates that the endothermic C−C bond cleavage proceeds without intermediate barriers and leads directly to the products, an immonium ion and an alkyl radical (Figure 4). Dissociation appears to involve an intermediate plateau, that is, the calculations suggest that the potential energy of the dissociating ion does not change very much when the C−C bond under cleavage is stretched from ~2.5 to ~3.0 Å (Figure 4), but the dissociation of straight-chain amine radical cations apparently does not involve an intermediate barrier, in contrast to the behavior of ions that undergo cleavage at branching points (see below). An intermediate plateau was also observed in a computational study of the dissociation of acetone cation radicals by Heinrich et al.[63]

The transition states in these systems are late, and it is to be expected that the difference between the heats of formation of the products is reflected in the respective transition state energies and therefore in the relative rates of the competing simple cleavage reactions of the metastable ions. The experimental results bear this out; the predominant reaction is always the more favored reaction in thermochemical terms, loss of the smaller radical (excepting methyl). We take the thermochemical differences between the competing reactions to be the major reason this is so. The discrimination between the competing reactions varies with the magnitude of the energy difference, with the number of degrees of freedom of the reactant, and with the critical energy of the C−C cleavage, as described below.

Variation as a Function of Chain Length. The rate of loss of ethyl radicals from metastable **A134** is about three times that of loss of propyl radicals (Table 1). The calculated difference between the energy required for the two reactions is 3 kJ mol^{-1} (Table 6), favoring loss of ethyl; as noted above, this difference reflects the additional stabilization of the cationic product by the extra methylene group. The preference for loss of the smaller radical is less pronounced when larger pairs of radicals are compared, but even the competition between loss of pentyl and hexyl radicals from metastable **A167** shows a 4:3 preference for loss of pentyl. The results in Table 6 show that the difference between the heats of reaction of the two competing reactions diminishes as the size of the alkyl radicals increases, but loss of the smaller alkyl radical remains the thermochemically favored process, even for systems of this size.

That energy differences as small as 1−2 kJ mol^{-1} can cause the branching ratio to be considerably different from unity is

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(59) (a) Seetula, J. A.; Slagle, I. R. *J. Chem. Soc., Faraday Trans.* **1997**, *93*, 1709−1719. (b) Seetula, J. A. *J. Chem. Soc., Faraday Trans.* **1998**, *94*, 891−898.

(60) Tsang, W. In *Energetics of Organic Free Radicals*; Simões, J. A. M., Greenberg, A., Liebman, J. F., Eds.; Blackie Academic: London, 1996; pp 22−58.

(61) Cohen, N. *J. Phys. Chem.* **1992**, *96*, 9052−9058.

(62) Marsi, I.; Viskolcz, B.; Seres, L. *J. Phys. Chem. A* **2000**, *104*, 4497−4504.

(63) Heinrich, N.; Louage, F.; Lifshitz, C.; Schwarz, H. *J. Am. Chem. Soc.* **1988**, *110*, 8183−8192.

Table 7. Calculated Heats of Reaction of Methyl Loss from Simple Amine Radical Cations (G3(MP2), kJ mol^{-1}, 298 K)

reactant	$\Delta H_{formation}$	$\Delta H_{reaction}$
N,*N*-dimethyl-*tert*-butylamine$^{\bullet+}$	630	74
N,*N*-dimethylisopropylamine$^{\bullet+}$	665	92
N,*N*-dimethylethylamine$^{\bullet+}$	704	115
N-methylethylamine$^{\bullet+}$	756	102
ethylamine$^{\bullet+}$	816	83

not unexpected; one example is the substantial secondary isotope effects that influence the α-cleavage reactions of metastable amine radical cations. These isotope effects are caused by the differences between the zero-point vibrational energy of the two transition states.[64−66] Taking the zero-point energy differences of the products as an estimate of the transition state differences (possibly an overestimate), we find Δzpe for the two methyl loss reactions of ionized $CH_3CH_2(CH_3)NCH_2CD_3$ to be 5 kJ mol^{-1}; experiment[67] shows that $CH_3^{\bullet}$ is expelled more than twice as readily as $CD_3^{\bullet}$. Correspondingly, ionized $CD_3CH_2(CH_3CH_2)$-$CHN(CH_3)_2$ loses $CH_3CH_2^{\bullet}$ and $CD_3CH_2^{\bullet}$ in a 3:2 ratio;[66] we calculate the product zero-point energy difference to be 1.2 kJ mol^{-1}.

Spectator Groups on Nitrogen. Increasing the size of the spectator group (the third N-substituent) modifies the branching ratio. The additional methyl group in **A234** (compared to **A134**) causes the ratio of ethyl-to-propyl loss to fall to 2:1 (3:1 in **A134**), even though the extra methyl neither introduces significant additional dissociation reactions nor much modifies the thermochemical differences (see Tables 3 and 6). Correspondingly, the ratio of propyl-to-butyl loss from metastable **A145** and **A245** is 3:2 and 5:4, respectively. We take these variations to reflect that the additional methylene group in **A234** and **A245** increases the number of degrees of freedom of the reactant ion, which attenuates the relative importance of the energy difference that causes loss of the two alkyl radicals to proceed at different rates. This effect also contributes to lower propyl-to-butyl ratios for **A345** and **A456** than for **A245**; however, the situation is less clear-cut for these compounds, owing to the presence of an additional competing reaction (α-cleavage in the third alkyl substituent), which complicates the kinetics.

Comparison with Primary and Secondary Amines. The energy required for the endothermic simple cleavage of amine radical cations changes with the presence of substituents at the nitrogen atom. The introduction of alkyl groups at N lowers the heat of formation of amine radical cations more than it lowers the heat of formation of immonium ions, that is, N-substitution stabilizes the reactant relative to the products. More energy is required for α-cleavage of secondary amine radical cations than of primary, and tertiary amines require again more, as illustrated by the heats of reaction of C−C bond cleavage in ionized ethylamine and *N*-methylethylamine, which are 32 and 13 kJ mol^{-1} lower than the heat of reaction of C−C bond cleavage in *N*,*N*-dimethylethylamine (Table 7).

The lower energy required for simple cleavage of the α-C−C bond in primary and secondary amine radical cations causes the preference for loss of the smaller radical to be more pronounced. This is illustrated by the competing cleavage reactions of metastable 3-hexylamine and 4-octylamine and their *N*-methyl and *N*,*N*-dimethyl analogues (**B006**, **B106**, **B116** and **B008**, **B108**, **B118**; Tables 2 and 3 and Figure 5). The ethyl-to-propyl and propyl-to-butyl ratios are considerably larger for the primary amines than for the secondary amines, and larger for the secondary amines than for the tertiary. The difference between the energy required for the two alkyl loss reactions does not change appreciably with the number of N-substituents (Table 6). Similar results were reported for 3-heptylamine and its *N*-methyl and *N*,*N*-dimethyl analogues[27] and for 3-octylamine.[41]

These differences arise as a consequence of the way the number of states in the two transition states varies with increasing energy and of the way the excess energy in the transition state varies with the critical energy of the reaction. The first relationship is well-known from the theory behind intramolecular isotope effects;[65,68] the ratio of the rate constants for two closely related reactions with slightly different critical energies is expected to approach unity as the internal energy of the reactant increases. The second relationship is known as the kinetic shift;[7,46,68] the excess energy in the transition state increases with increasing critical energy. It follows that the discrimination between two closely related competing reactions will be less pronounced when the energy required for reaction increases, assuming that the thermochemical difference between the two reactions does not change appreciably.

The Influence of α-Branching. Simple C−C bond cleavage of straight-chain amines requires more energy than does cleavage when the amino group is at a nonterminal position, inasmuch as the additional alkyl groups at the α-carbon atom stabilize the product immonium ions more than the reactant radical cations. This is illustrated by the heats of reaction of C−C bond cleavage in ionized *N*,*N*-dimethylethylamine and the isopropyl and *tert*-butyl analogues; the simple cleavage of the latter two requires 23 and 41 kJ mol^{-1} less, respectively (Table 7). The reduced energy requirement brought about by branching should, for the reasons delineated above, cause the preference for loss of the smaller alkyl radical to be more pronounced. An example is the competing loss of ethyl and propyl radicals from metastable *N*,*N*-dimethyl-3-hexylamine molecular ions (**B116**), for which the ethyl/propyl loss ratio is 5.6, compared to the ethyl/propyl ratio observed when the straight-chain ion **A134** reacts (2.9). However, branching appears to modify the detailed course of reaction in a number of ways, and whereas the smaller alkyl radical is always lost more readily, the magnitude of the small/large ratio is not always easily rationalized (see below).

Intermediate Barriers to α-Cleavage. It has been shown experimentally that there are intermediate energy barriers when methyl radicals are expelled from *tert*-butylamine radical cations and related ions.[69,70] These barriers are well-reproduced by calculation,[71] they show up in appearance energy measure-

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(64) Derrick, P. J. *Mass Spectrom. Rev.* **1983**, *2*, 285−298.

(65) Derrick, P. J.; Donchi, K. F. In *Comprehensive Chemical Kinetics*; Bamford, C. H., Tipper, C. F. H., Eds.; Elsevier: Amsterdam, 1981; Vol 24, pp 53−247.

(66) Ingemann, S.; Hammerum, S.; Derrick, P. J. *J. Am. Chem. Soc.* **1988**, *110*, 3869−3873.

(67) Ingemann, S.; Hammerum, S.; Derrick, P. J.; Allison, C. E.; Fokkens, R. H.; Kluft, E.; Nibbering, N. M. M. *Adv. Mass Spectrom.* **1988**, *11*, 772−773.

(68) Levsen, K. *Fundamental Aspects of Mass Spectrometry*; Verlag Chemie: Weinheim, Germany, 1978.

(69) Hammerum, S.; Derrick, P. J. *J. Chem. Soc., Chem. Commun.* **1985**, 996−997.

(70) Aubry, C.; Holmes, J. L. *Int. J. Mass Spectrom.* **2000**, *200*, 277−284.

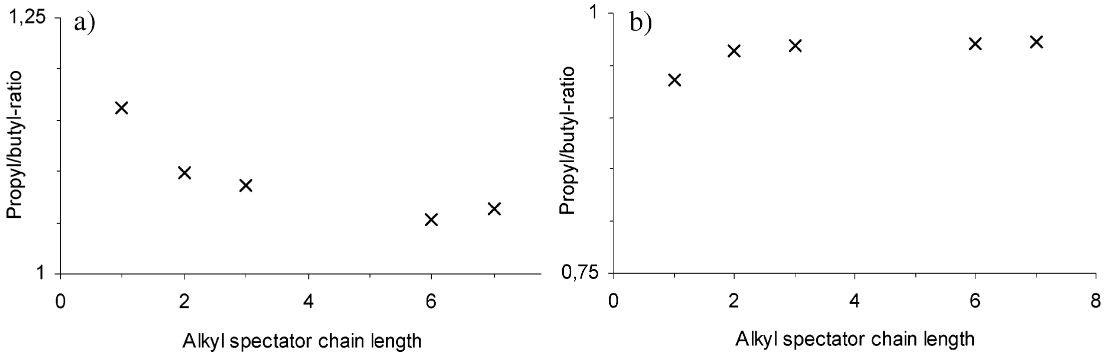

Figure 5. Change in branching ratio with increasing alkyl spectator chain length from different *N*-alkyl-*N*-methyl-4-octylamines. (a) MIKE. (b) EI ion source.

ments,[54,58,70] and their presence can give rise to flat-topped metastable peaks.[69] Our ab initio studies of cleavage reactions at other quaternary carbon atoms in amines (e.g., loss of ethyl and propyl from 3-methyl-3-hexylamine) also indicate the presence of pronounced intermediate energy barriers, and we expect that such barriers will often be present when cleavage occurs at highly branched positions, even when the corresponding metastable peaks are not flat-topped. We note that the energy required to cross the intermediate barriers is in some cases higher than the energy of the final products, in some cases lower. In all cases a well-defined energy minimum separates the barrier from the final products (Figure 4). The geometry of the secondary minima is usually such that the departing alkyl group "turns" with respect to the incipient immonium ion, in that the (N)CCC angle decreases as the CC bond length increases.

The difference between the relative rates of loss of ethyl and propyl radicals from the tertiary carbon in *N*,*N*-dimethyl-3-hexylamine (**B116**) and from the quaternary carbon in *N*,*N*,3-trimethyl-3-hexylamine (**B117**) may be one consequence of the presence of barriers. The ratio of loss of ethyl and propyl radicals from **B117** is relatively high, 3.7, but nonetheless lower than that for **B116**, 5.6, even though C−C bond cleavage in the latter is the more endothermic reaction. The preference for loss of the smaller radical in both cases suggests that the factors that determine the relative barrier heights are the same as those that determine the differences between the heats of formation of the products, but the intermediate barriers apparently influence the relative rates in different ways.

Reactions in the Ion Source

The competition between loss of different alkyl radicals by α-cleavage in an aliphatic amine radical cation in the mass spectrometer ion source in most cases results in preferential loss of the larger radical, contrasting with the behavior of the metastable ions. The rate of loss of the larger radical apparently increases more steeply with increasing internal energy of the reactant; in other words, the *k*(E) curves cross. The textbook examples of crossing *k*(E) curves usually involve transition states with very different properties,[3,4,7,68] such as when a reaction with a tight transition state is in competition with a reaction with a loose transition state. However, the transition states for nearly identical reactions, loss of two only slightly different alkyl radicals from very similar (or identical) positions, should resemble each other very closely. As noted,[16,32] this similarity renders it quite difficult to describe the behavior of these systems within a simple RRKM framework and in particular to account for the reversal of the branching ratio for alkyl loss. The traditional transition state for a monotonically endothermic dissociation reaction resembles the products. An evaluation of the number of states in the transition state will depend critically on how the model adopted accounts for those reactant rovibronic states that are converted to external degrees of freedom in the products. However, we have not been able to determine unambiguous guidelines to choose models for a single transition state for each of the two competing C−C bond cleavage reactions that are sufficiently alike to make chemical sense, yet sufficiently different to allow the *k*(E) curves to cross.

Griffin et al.[72] recently showed that the *k*(E) curves for loss of methyl and ethyl radicals from the 2-butanol and 2-butanone radical cations could indeed be brought to cross, if a number of low-frequency vibrations in the transition state for loss of the ethyl radical were lowered by up to 50%, but they did not indicate why the transition states would be different in this respect.

Mandeville et al.[28] brought forward a suggestion that the preferential loss of the larger alkyl radical could be a consequence of a degrees-of-freedom effect, which would arise from an increased probability of breaking the radical cation into two fragments of similar size, rather than into a large and a small fragment. We have not yet explored this interpretation.

Variational Transition State Theory. One possible way to account for the reversal of the branching ratio of the competing α-cleavages in these systems would be to employ the framework of variational transition state theory (VTST), that is, to assume that the properties of the transition states that determine the behavior of the reactants close to threshold are different from the properties of the transition states that determine the behavior of more highly energized reactants.[73−79] In VTST, the transition state is taken to be at the intersection of the reaction coordinate and that surface perpendicular to the reaction coordinate that

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(71) For the *tert*-butylamine radical cation we find ΔH_f for the reactant, the transition state for methyl loss, and the products to be 717, 751, 734 kJ mol^{-1} (G3 values, 298 K). For the *N*-methyl-*tert*-butylamine radical cation, we find the values to be 666, 728, 713 kJ mol^{-1}.

(72) Griffin, L. L.; Traeger, J. C.; Hudson, C. E.; McAdoo, D. J. *Int. J. Mass Spectrom.* **2002**, *217*, 23−44.
(73) Truhlar, D. G.; Garrett, B. C. *Acc. Chem. Res.* **1980**, *13*, 440−448.
(74) Hase, W. L. *Acc. Chem. Res.* **1983**, *16*, 258−264.
(75) Truhlar, D. G.; Garrett, B. C.; Klippenstein, S. J. *J. Phys. Chem.* **1996**, *100*, 12771−12800.
(76) Lifshitz, C. *Adv. Mass Spectrom.* **1978**, *7A*, 3−18.
(77) Chesnavich, W. J.; Bowers, M. T. In *Gas Phase Ion Chemistry*; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 1, pp 119−151.
(78) Lifshitz, C. *Adv. Mass Spectrom.* **1989**, *11*, 713−729.
(79) Lifshitz, C.; Louage, F.; Aviyente, V.; Song, K. *J. Phys. Chem.* **1991**, *95*, 9298−9302.

separates reactants and products and corresponds to a minimum sum of states; it need not correspond to the top of an actual potential energy barrier.

It has been shown[74] that the transition state for a monotonically endothermic reaction becomes progressively less productlike as the internal energy of the reactant increases. For systems such as those under consideration here that undergo two very similar reactions, this means that the interfragment distance in the transition state will diminish with increasing internal energy, as will the difference between the potential energy of the two transition states, and that the more energy demanding of the two reactions will have the later transition state.

Furthermore, as the dissociating bond stretches, the energy of a number of rovibronic states will gradually diminish, as these states become external degrees of freedom of the final fully dissociated product pair. The corresponding vibrational frequencies will be lower in the transition state for cleavage of the C−C bond in the longer alkyl group (the more productlike transition state) than in the transition state for C−C cleavage of the shorter chain, which implies that the sum of states will increase more rapidly with increasing internal energy in the transition state for cleavage in the longer chain than in the shorter.

The branching ratio will be determined by the ratio of the sum of states of the two transition states. For low internal energy reactants, this ratio will primarily be determined by the difference in critical energy (i.e., by the thermochemistry of the two reactions). The difference between the sum of states for more highly energized reactants will change relative to the near-threshold situation, because the difference between the potential energy of the two transition states will be less than that for the low-energy reactants, and at the same time the sum of states will have increased more in the TS for loss of the larger alkyl radical. It is in turn reasonable that the $k(E)$ curves cross, inasmuch as an increase of the internal energy causes the factor that favors loss of the smaller radical to become less pronounced, whereas the factor that favors loss of the larger radical becomes more pronounced.

Trial VTST calculations describing the loss of ethyl and propyl radicals from 3-hexylamine molecular ions bear this out. We have taken the stretching of the two α-C−C bonds as the reaction coordinates, used projected frequencies[80] [UHF/6-31G(d) as well as UMP2/6-31G(d)], and employed the Beyer−Swinehart direct count algorithm;[81] the calculations did not take anharmonicity and rotational effects into account, nor basis set superposition errors. The results show that loss of ethyl is the faster reaction near threshold, while loss of propyl is faster for higher-energy reactants. Further, they confirm that the transition states occur earlier on the reaction coordinate as the internal energy is increased, that is, that the α-C−C bonds in the transition states are progressively shortened, and, importantly, that the transition state for loss of the larger alkyl radical possesses the longer C−C bond, confirming that loss of the larger alkyl group has the looser transition state. These results are in good agreement with the results reported by Griffin et al.;[72] we propose that the frequency changes adopted by these authors reflect the likelihood that the transition state for loss of the longer alkyl group is also in their case the more productlike.

We note that the calculations are quite sensitive to the absolute values of the low-frequency vibrational modes; the calculated energy at which the $k(E)$ curves cross is significantly changed if the vibrational frequencies are scaled, even if by factors only slightly lower than 1.

Conclusions

The energy-dependent aspects of the simple cleavage illustrate that the process is not quite as straightforward as the terminology implies. The reversal of the preference for loss of small and large radicals observed when the internal energy of the reactant is increased (metastable ions versus ions reacting in the ion source) shows that the rate of loss of the larger alkyl radical increases more steeply with internal energy. Given the difference between the energy requirements of the competing reactions, which favors loss of the smaller radical, and the expectation that the transition state properties for very closely related reactions should not differ greatly, this reversal is not easily reconciled with traditional RRKM theory. However, the reversal of the branching ratio can be accounted for with variational transition state theory, which emphasizes that those properties of the transition state that determine the number of states are different for high- and low-energy reactants. Further, the theory predicts that the location of the transition state on the reaction coordinate changes as a function of the energy of the system. This is not to imply that monotonically endothermic simple cleavage reactions can proceed via different classical transition states, each with an associated local maximum in potential energy. Rather, the change is gradual, and in systems such as those investigated here it could be appropriate not to talk of transition state switching,[82] but of transition state shifting.

The variation of the branching ratios observed for the competing alkyl radical elimination reactions of different straight-chain metastable amine radical cations can be satisfactorily accounted for, taking into account variations of the number of degrees of freedom, variations of the critical energy of the cleavage reactions, and variations of the different energy requirements of the competing reactions. However, the possible presence of intermediate energy barriers when cleavage occurs at a branching point complicates the interpretation of changes of the relative ion yield when structurally different reactants are concerned. It is possible that the ion-neutral reorganization concept proposed by Longevialle et al.[29−31] would be useful when such barriers are present.

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(80) Baboul, A. G.; Schlegel, H. B. *J. Chem. Phys.* **1997**, *107*, 9413−9417.

(81) Beyer, T.; Swinehart, D. F. *Commun. ACM* **1973**, *16*, 379−379.

(82) (a) Chesnavich, W. J.; Bass, L. M.; Su, T.; Bowers, M. T. *J. Chem. Phys.* **1981**, *74*, 2228−2246. (b) Bowers, M. T.; Jarrold, M. F.; Wagner-Redeker, W.; Kemper, P. R.; Bass, L. M. *Faraday Discuss.* **1983**, *75*, 57−76.