Communication: Site-selective bond excision of adenine upon electron transfer

T. Cunha, M. Mendes, F. Ferreira da Silva, S. Eden, G. García, and P. Limão-Vieira

Citation: The Journal of Chemical Physics **148**, 021101 (2018); doi: 10.1063/1.5018401
View online: https://doi.org/10.1063/1.5018401
View Table of Contents: http://aip.scitation.org/toc/jcp/148/2
Published by the American Institute of Physics

Communication: Site-selective bond excision of adenine upon electron transfer

T. Cunha,[1] M. Mendes,[1,2] F. Ferreira da Silva,[1] S. Eden,[3] G. García,[2] and P. Limão-Vieira[1,a)]
[1]*Atomic and Molecular Collisions Laboratory, CEFITEC, Department of Physics, Universidade NOVA de Lisboa, Campus de Caparica, 2829-516 Caparica, Portugal*
[2]*Instituto de Física Fundamental, Consejo Superior de Investigaciones Científicas, Serrano 113-bis, 28006 Madrid, Spain*
[3]*School of Physical Sciences, The Open University, Walton Hall, MK7 6AA Milton Keynes, United Kingdom*

(Received 6 December 2017; accepted 2 January 2018; published online 11 January 2018)

This work demonstrates that selective excision of hydrogen atoms at a particular site of the DNA base adenine can be achieved in collisions with electronegative atoms by controlling the impact energy. The result is based on analysing the time-of-flight mass spectra yields of potassium collisions with a series of labeled adenine derivatives. The production of dehydrogenated parent anions is consistent with neutral H loss either from selective breaking of C–H or N–H bonds. These unprecedented results open up a new methodology in charge transfer collisions that can initiate selective reactivity as a key process in chemical reactions that are dominant in different areas of science and technology. *Published by AIP Publishing.* https://doi.org/10.1063/1.5018401

I. INTRODUCTION

Radiation-driven control of reactivity is a major goal in chemical physics/physical chemistry. This has been reported previously using ultrafast laser pulses,[1] quantum molecular dynamics of photo-excited molecules,[2] and coherent quantum manipulation.[3] However these methods are not readily scalable for many potential technological or medical applications. Therefore, the achievement of electron-induced site- and bond-specific dissociation (on surfaces using STM tips[4] and in the gas phase using low-energy electron beams[5–9]) in the mid 2000s was highly significant. The only previous control over dissociation pathways in atom-molecule collisions was demonstrated for potassium impact on gas-phase thymine and uracil.[10] By achieving controlled dissociation of purines, the present experiments show that selective reactivity in charge transfer collisions is not restricted to the particular case of pyrimidine nucleobases. Indeed, we anticipate that this new route for controlled chemistry can be adapted for numerous collision systems.

As the most abundant secondary species produced by ionising radiation, low-energy electrons (defined here as <15 eV) are recognized as critically important reactive species in irradiated materials.[11] In particular, dissociative electron attachment (DEA)[12] and intermolecular charge transfer[13] play key roles in radiation damage to DNA. These results have stimulated extensive experimental and theoretical research into low-energy electron interactions with gas-phase DNA/RNA constituents, revealing detailed understanding of their transient negative ion states.[14] In aqueous conditions that evidently provide a closer approximation of biological environments,[15] Wang *et al.*[16] have shown that deoxyribonucleotides comprising adenine and guanine are more efficient at capturing pre-hydrated electrons than those comprising thymine and cytosine. Therefore, we expect electron-capture-induced reactive processes in the purine nucleobases to play a particularly important role in radiation-induced DNA damage.

In the present experiments, an alkali atom, potassium, is used as an electron donor to the nucleobase molecules, adenine and its derivatives. The donor-acceptor interaction changes from covalent (neutral) to ionic at a particular distance, R_c,[17] i.e., the crossing of the covalent and ionic diabatic states. For large potassium-molecule distances, the van der Waals and induction forces can be neglected and consequently the covalent potential is zero and the ionic potential is purely Coulombic ($\propto -1/R$). At infinite separation, the energy difference ΔE between the ionic and covalent configurations (the endoergicity of the electron transfer process), is given by IE(K)–EA(M), where IE(K) is the ionisation energy of the potassium atom and EA(M) is the electron affinity of the molecule. R_c is given by $14.41/\Delta E$ (Å),[18] where ΔE is expressed in eV. Taking the experimental vertical electron affinity of adenine as –0.54 eV[19] (adiabatic value of 11 meV[20]), the value found for R_c is ~3.0 Å, meaning that the corresponding total cross sections for ion-pair formation (of the order of πR_c^2) is much larger (even one order of magnitude) than the corresponding gas kinetic cross sections.

Another relevant aspect pertaining significant differences between electron transfer and DEA experiments needs to be properly accounted for within the context of negative ion formation. Although the information gained in DEA experiments is relevant to assess which resonances may be involved in the attachment process, the role of a third body (K^+) in the vicinity of the temporary negative ion (TNI) is solely responsible to either shift or give access to other (diabatic) resonant states (i.e., in the K-M coordinate) probed in the collision

a)Author to whom correspondence should be addressed: plimaovieira@fct.unl.pt. Tel.: (+351) 21 294 78 59. Fax: (+351) 294 85 49.

dynamics.[18] Comparisons with electron scattering and DEA experiments are valuable when considering which temporary negative ion (TNI) states may be involved in collisional electron transfer. However, the presence of the electron donor (pre-transfer and post-transfer) can lead to major differences compared with DEA. These differences can be traced to shifting the energies of key orbitals in the neutral molecule and/or the TNI, as well as modifying TNI lifetimes with respect to electron autodetachment.[21]

II. EXPERIMENTAL SECTION

Negative ion mass spectra were obtained in a crossed beam setup consisting of a potassium source, an oven, and a time-of-flight (TOF) mass analyser.[22] The components were housed in two high-vacuum chambers at a base pressure of 10^{-5} Pa. A neutral potassium beam generated from a charge exchange chamber intersected at right angles an effusive molecular beam consisting of the target molecules. Atomic K^+ ions, obtained from a potassium ionic source, were accelerated through a chamber containing potassium vapour where they resonantly charge exchanged to form a beam of fast neutral K fast atoms. The energy of the resultant K neutral beam was established by the initial acceleration of the K^+ ions and the geometry of the collimating slits in the charge exchange source. The lab-frame collision energy ranged from 15 to 100 eV, and the beam energy resolution at full width half maximum was 0.5 eV as measured with an energy loss analyser. The resulting neutral K beam entered a high vacuum chamber where it was monitored by an iridium surface ionisation detector operating in a temperature regime that only allows the detection of the fast beam. This sampled the beam intensity but did not interfere with the beam passing to the collision region. The biomolecular target beams were produced in a hot gas cell (oven) and admitted to vacuum by an effusive source through a 1-mm-diameter orifice where they were crossed with the

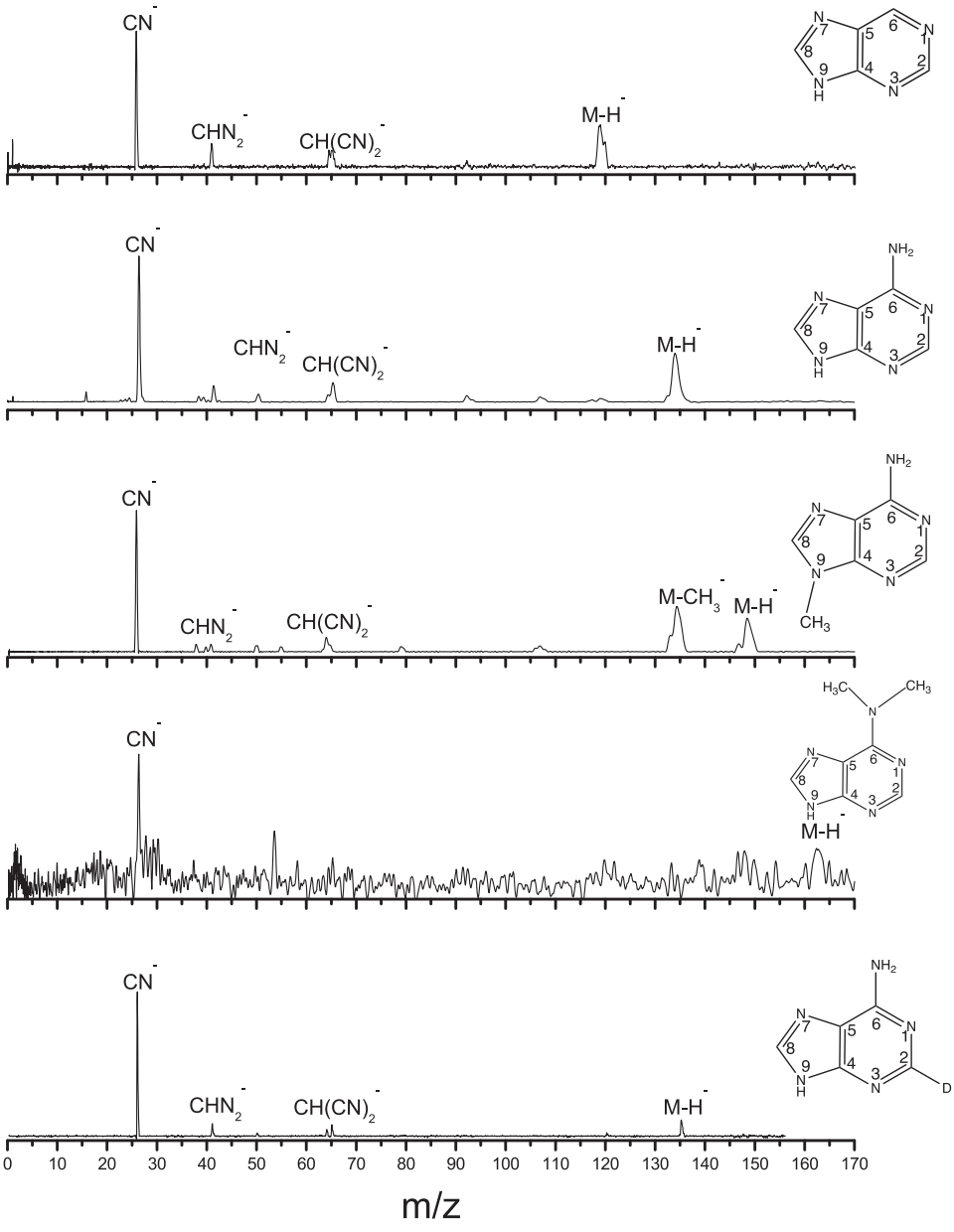

FIG. 1. Time-of-flight mass spectra showing the anions produced following electron transfer from potassium to purine, adenine, methylated adenine at the N9 position (9-methyladenine), methylated adenine at the N–C6 position (6-dimethyladenine), and adenine-2-d in collisions at a 100 eV lab frame energy (63.6, 65.5, 67.0, 68.3, and 65.6 eV available energy in the centre-of-mass, respectively). $(M–H)^-$ signifies the dehydrogenated parent ion.

neutral hyperthermal potassium beam. The molecular oven was operated at a lower temperature (400 K measured by a platinum resistance probe) than previous experimental studies which reported no evidence for thermal decomposition of neutral adenine.[19,23] The negative ions produced in the collision region were extracted by a 250 V/cm pulsed electrostatic field towards the entrance of the TOF where they were analysed and detected in single-pulse counting mode. In the present electron transfer experiments, the total energy available for anion excitation (the collision energy in the centre-of-mass frame minus the ionisation energy of potassium) varied from ~6 up to ~68 eV. Purine, adenine, 9-methyladenine, and 6-dimethyladenine were supplied by Sigma Aldrich with stated purities of 98%, ≥99%, 97%, and ≥98%, respectively, and adenine-2-d (adenine deuterated at the C2 position) was supplied by CDN Isotope Inc. with isotope enrichment of 97%. Experimental[24,25] and theoretical[26–28] studies of adenine's tautomers have shown that the canonical form N(9)H dominates in the gas phase, while the N(7)H form is ~33 kJ/mol (0.342 eV) higher in energy.[25,27,28]

III. RESULTS AND DISCUSSION

Figure 1 shows the time-of-flight (TOF) mass spectra recorded at 100 eV lab frame collision energy of neutral potassium atoms with purine, adenine, 9-methyladenine, 6-dimethyladenine, and adenine-2-d (63.6, 65.5, 67.0, 68.3, and 65.6 eV available energy in the centre-of-mass, respectively). The TOF mass spectra show no evidence of parent anion formation (M^-), and this communication focuses on the dehydrogenated parent anion yield $(M–H)^-$ only. $(M–H)^-$ is produced from all five molecules where in 6-dimethyladenine, such yield is barely visible above background noise in the present measurements.

Adenine branching ratios (not shown here) reveal that loss of a neutral H atom is a precursor in the formation of other fragment anions. Such is discernible in Fig. 2 (15 eV lab frame collision energy) where $(M–H)^-$ dominates for the case of adenine and 6-dimethyladenine. The threshold for electron transfer (IE(K)–EA(M) ≈ 4 eV) is smaller than the collision energy, so the molecular anion can be formed with an excess of internal energy. For the molecular compounds

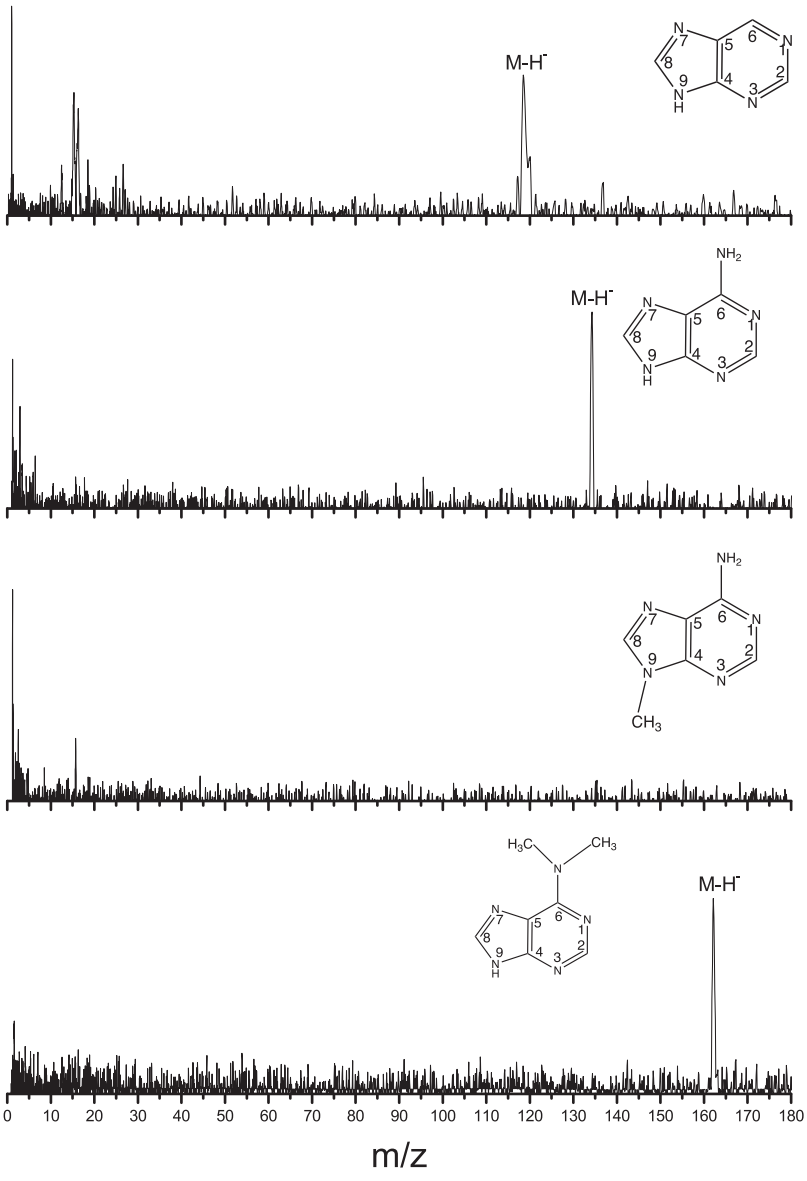

FIG. 2. Time-of-flight mass spectra showing anions produced from purine, adenine, methylated adenine at the N9 position (9-methyladenine), and methylated adenine at the N–C6 position (6-dimethyladenine) in collisions with potassium atoms at 15 eV lab frame (5.8, 6.1, 6.4, and 6.6 eV available in the centre-of-mass, respectively). The dehydrogenated parent ion $(M–H)^-$ is visible in all cases except for the 9-methyladenine measurement. From purine NH^-, NH_2^-, and CN^- ions are also formed.

investigated here, 6-dimethyladenine exhibits the highest number of degrees of freedom (57 modes), among which the excess energy can be redistributed resulting in fragmentation (100 eV lab frame). However, if the lifetime of the metastable anion is long enough, intramolecular energy redistribution may occur competing with direct dissociation. Such is the dominant case of longer collision times as revealed in the TOF mass spectra in Fig. 2.

Clearly, all of the conceivable H loss reaction pathways [from the N9, C8, C6, and C2 sites of purine and from the N9, C8, (NH_2)C6, and C2 sites of adenine] are energetically accessible at the relatively high lab frame collision energy of 100 eV. However, the absence of an $(M–D)^-$ signal in the measurement on partially deuterated adenine indicates that hydrogen loss from the C2 position on adenine can be ruled out. This may be rationalised in terms of strong autodetachment competing with dissociation for this specific channel. It is also interesting to consider the present results in the context of previously calculated electrostatic potential maps and isodensity maps of the lowest virtual σ^* molecular orbitals at the B3LYP/aug-cc-pVTZ level for purine, adenine, and 6-dimethyladenine.[29] These show that for purine, the regions accessible for H loss are around the N9–H and C8–H sites, whereas in adenine and 6-dimethyladenine, an extra region around the NH_2 and $N(CH_3)_2$ groups is also available. Furthermore, these results show that there is no wave-function density in the C6–H region for purine.

Figure 2 shows the negative ion yields of $(M–H)^-$ from purine, adenine, 9-methyladenine, and 6-dimethyladenine with a lab frame collision energy of 15 eV (5.8, 6.1, 6.4, and 6.6 eV available energy in the centre-of-mass frame, respectively). Blocking the H positions at the amino group with CH_3, where NH_2 is replaced with a $N(CH_3)_2$ group in 6-dimethyladenine, means that H loss can only occur from the N9 or C8 positions. For a conclusive check of these two positions, we have performed an additional experiment on 9-methyladenine, thus blocking the N9 site. Significantly, the ion yield of $(M–H)^-$ is completely suppressed. This means that H loss proceeds from the N9 site only.

Denifl *et al.*[29] showed that selective H cleavage from the N9 site of adenine can also be achieved in DEA, notably via resonances observed experimentally below around 1.07 eV. However, the present results cannot be understood purely on the basis of a direct analogy with DEA. In DEA to adenine, the calculated minimum electron energy required to cleave a hydrogen atom from N9–H, (NH_2)C6, C8–H, and C2–H and hence produce a dehydrogenated parent anion varies between 0.94 and 3.63 eV,[29] respectively. This is distinctly lower than the available energies in the centre-of-mass frame in the collisions probed in Fig. 2. Therefore, the remarkable bond- and site-selectivity observed here for $(M–H)^-$ formation in potassium collisions with adenine does not result purely from energetic constraints. We expect that the electronic structures of the metastable anions accessed by electron transfer at different collision energies are most likely to be responsible for the present result. This seems reasonable since the presence of the electron donor may affect the electronic structure of the target molecule (the lowest unoccupied molecular orbitals – LUMOs). Indeed, the stabilization of specific orbitals of thymine and uracil due to the presence of the potassium atom in the collision system has recently been reported in state-averaged complete active space self-consistent field (CASSCF) calculations.[30] Analogous theoretical studies of the effects of the incident potassium atom (pre- and post-electron transfers) on neutral and anionic adenines are required to better understand the mechanisms responsible for the presently observed selective H loss.

IV. CONCLUSION

We show here that selective hydrogen removal from the adenine molecule can be achieved in collisional charge transfer experiments by tuning the collision energy. It is striking that such fine control over reactivity can be achieved in an energetic collision between an atom and a relatively complex molecule with numerous competing relaxation pathways. Indeed, the observed selectivity cannot be explained solely in terms of the threshold energies required to break specific bonds in the temporary negative ion. On the contrary, it reflects the specific dynamics of the three-body interaction involving the molecule, the transferred electron, and the donor atom. Considerable progress has been made in recent years towards understanding these complex dynamics both experimentally and via *ab initio* calculations.[24] Therefore there is great potential in the future to identify many more charge transfer collisions that can initiate selective reactivity of the kind demonstrated here, extending to tailored chemical control for industrial and even medical applications.

ACKNOWLEDGMENTS

T.C., M.M., and F.F.S. acknowledge the Portuguese National Funding Agency FCT-MCTES through No. SFRH/BD/52538/2014, PD/BD/106038/2015, and researcher position No. IF-FCT IF/00380/2014, respectively, and together with PLV the research Grant No. UID/FIS/00068/2013. This work was also supported by Radiation Biology and Biophysics Doctoral Training Programme (RaBBiT, No. PD/00193/2010); No. UID/Multi/04378/2013 (UCIBIO). GG acknowledges partial financial support from the Spanish Ministerio de Economia, Industria y Competitividad (Project No. FIS2016-80440). S.E. acknowledges support from the British EPSRC through a Career Acceleration Fellowship (No. EP/J002577/1).

[1] E. D. Potter, J. L. Herek, S. Pedersen, Q. Liu, and A. H. Zewail, Nature **355**, 66 (1992).
[2] H. Rabitz, R. de Vivie-Riedle, M. Motzkus, and K. Kompa, Science **288**, 824 (2000).
[3] L. Ratschbacher, C. Zipkes, C. Sias, and M. Köhl, Nat. Phys. **8**, 649 (2012).
[4] P. A. Sloan and R. E. Palmer, Nature **434**, 367 (2005).
[5] S. Ptasińska, S. Denifl, V. Grill, T. D. Märk, E. Illenberger, P. Scheier, Phys. Rev. Lett. **95**, 093201 (2005).
[6] S. Ptasinska, S. Denifl, V. Grill, T. D. Märk, P. Scheier, S. Gohlke, M. A. Huels, E. Illenberger, Angew. Chem., Int. Ed. **44**, 1647 (2005).
[7] H. Abdoul-Carime, S. Gohlke, and E. Illenberger, Phys. Rev. Lett. **92**, 168103 (2004).
[8] V. S. Prabhudesai, A. H. Kelkar, D. Nandi, and E. Krishnakumar, Phys. Rev. Lett. **95**, 143202 (2005).
[9] I. Bald, J. Kopyra, and E. Illenberger, Angew. Chem., Int. Ed. **45**, 4851 (2006).
[10] D. Almeida, F. Ferreira da Silva, G. García, and P. Limão-Vieira, Phys. Rev. Lett. **110**, 023201 (2013).

[11]L. Sanche in *Radiation Induced Molecular Phenomena in Nucleic Acids: Low Energy Electron Damage to DNA*, edited by M. Shukla and J. Leszczynski (Springer Netherlands, Dordrecht, 2008), Chap. 19.
[12]B. Boudaïffa, P. Cloutier, D. Hunting, M. A. Huels, and L. Sanche, Science **287**, 1658 (2000).
[13]A. Kumar and M. D. Sevilla, Chem. Rev. **110**, 7002 (2010).
[14]I. Baccarelli, I. Bald, F. A. Gianturco, and E. Illenberger, Phys. Rep. **508**, 1 (2011).
[15]L. Sanche, Nature **461**, 358 (2009).
[16]C.-R. Wang, J. Nguyen, and Q.-B. Lu, J. Am. Chem. Soc. **131**, 11320 (2009).
[17]A. W. Kleyn, J. Los, and E. A. Gislason, Phys. Rep. **90**, 1 (1982).
[18]A. W. Kleyn and A. M. C. Moutinho, J. Phys. B: At., Mol. Opt. Phys. **34**, R1 (2001).
[19]K. Aflatooni, G. A. Gallup, and P. D. Burrow, J. Phys. Chem. **102**, 6205 (1998).
[20]S. Carles, F. Lecomte, J. P. Schermann, and C. Desfrançois, J. Phys. Chem. A **104**, 10662 (2000).
[21]F. Ferreira da Silva, G. Meneses, O. Ingólfsson, and P. Limão-Vieira, Chem. Phys. Lett. **662**, 19 (2016).
[22]R. Antunes, D. Almeida, G. Martins, N. J. Mason, G. García, M. J. P. Maneira, Y. Nunes, and P. Limão-Vieira, Phys. Chem. Chem. Phys. **12**, 12513 (2010).
[23]J. Tabet, S. Eden, S. Feil, H. Abdoul-Carime, B. Farizon, M. Farizon, S. Ouaskit, and T. D. Märk, Int. J. Mass Spectrom. **292**, 53 (2010).
[24]C. Pluetzer, E. Nir, M. S. de Vries, and K. Kleinermanns, Phys. Chem. Chem. Phys. **3**, 5466 (2001).
[25]C. Pluetzer and K. Kleinermanns, Phys. Chem. Chem. Phys. **4**, 4877 (2002).
[26]A. C. Borin, L. Serrano-Andres, M. P. Fulscher, and B. O. Roos, J. Phys. Chem. A **103**, 1838 (1999).
[27]M. Hanus, M. Kabelac, J. Rejnek, F. Ryjacek, and P. Hobza, J. Phys. B **108**, 2087 (2004).
[28]Y.-F. Wang and S. X. Tian, Phys. Chem. Chem. Phys. **13**, 6169 (2011).
[29]S. Denifl, P. Sulzer, D. Huber, F. Zappa, M. Probst, T. D. Märk, P. Scheier, N. Injan, J. Limtrakul, R. Abouaf, and H. Dunet. Angew. Chem., Int. Ed. **46**, 5238 (2007).
[30]D. Almeida, M. C. Bacchus-Montabonel, F. Ferreira da Silva, G. García, and P. Limão-Vieira, J. Phys. Chem. A **118**, 6547 (2014).