Locating the Charge Site in Heteroaromatic Cations

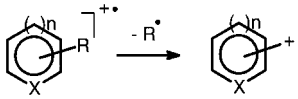
Márcia Carvalho, Fábio C. Gozzo, Maria Anita Mendes, Regina Sparrapan, Concetta Kascheres, and Marcos N. Eberlin*

Abstract: Low-energy collision-induced dissociation (CID) and ion–molecule reactions with 2-methyl-1,3-dioxolane (MD) performed by pentaquadrupole (QqQqQ) mass spectrometry were applied to locate the charge site in isomeric heteroaromatic cations. The 2-, 3-, and 4-pyridyl cations are indistinguishable by CID. However, as suggested by MS^3 experiments and ab initio calculations, the 2-pyridyl cation reacts extensively with MD by a transacetalization-like mechanism to afford a bicyclic dihydrooxazolopyridyl cation. The 3- and 4-pyridyl cations, on the contrary, react predominantly with MD by proton transfer, as does the analogous phenyl cation. The 2-, 4-, and 5-pyrimidyl cations display characteristic CID behavior. In addition, the 2-pyrimidyl cation reacts extensively with MD by the transacetalization-like mechanism, whereas proton transfer occurs predominantly for the 4- and 5-pyrimidyl cations. The ions thought to be the 2- and 3-furanyl and 2- and 3-thiophenyl cations show indistinguishable CID and ion–molecule behavior. This is most likely the result of their inherent instability in the gas phase and their spontaneous isomerization to the corresponding butynoyl and butynethioyl cations $HC{\equiv}CHCH_2C{\equiv}O^+$ and $HC{\equiv}CHCH_2C{\equiv}S^+$. These isomerizations, which are considerably exothermic according to G2(MP2) ab initio calculations, are indicated by a series of experimental results. The ions dissociate upon CID by loss of CO or CS and undergo transacetalization with MD. Most informative is the participation of $HC{\equiv}CHCH_2C{\equiv}S^+$ in a transacetalization/dissociation sequence with replacement of sulfur by oxygen, which is structurally diagnostic for thioacylium ions. It is therefore possible to locate the charge site of the 2-pyridyl and the three 2-, 4-, and 5-pyrimidyl cations and to identify the isomeric precursors from which they are derived. However, rapid isomerization to the common $HC{\equiv}CH\text{-}CH_2\text{-}C{\equiv}O(S)^+$ ion eliminates characteristic chemical behavior that could result from different charge locations in the heteroaromatic 2- and 3-furanyl and 2- and 3-thiophenyl cations.

Keywords: ab initio calculations · cations · collision-induced dissociation · ion–molecule reactions · mass spectrometry

Introduction

Distinction of positional isomers has been a central issue in mass spectrometry. It is desirable that the mass spectra of the isomers contain unique structurally diagnostic fragment ions. If not, then the collision-induced dissociation (CID)[1] behavior or ion–molecule chemistry[2] of the molecular ion, the protonated molecule, or adduct ions of the isomers may be sufficiently distinct to allow structural elucidation. An alternative to these approaches is the analysis by CID[1] or ion–molecule reaction[2] of the structures of fragment ions that could retain the positional information of the isomeric ions from which they are derived. This possibility exists for isomeric heteroaromatic compounds. Location of substituents in different ring positions leads to the generation of isomeric heteroaromatic cations (Scheme 1) in which information on substituent position may be retained because of charge localization in sp^2 σ orbitals. Hence, unique dissociation behavior or ion–molecule reactivity might be displayed by isomeric heteroaromatic cations due to different locations of the charge site in the aromatic ring. If the specific position of a substituent in the precursor ion is revealed by a common fragment ion, then such a strategy could be applied generally for the whole class of substituted aromatic compounds.

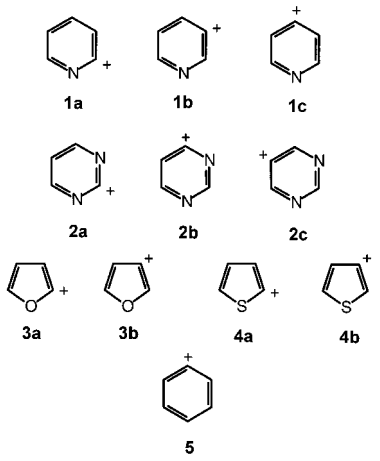


Scheme 1.

Here we report a pentaquadrupole (QqQqQ) mass spectrometric[3] study aimed at exploring the gas-phase chemistry of the isomeric heteroaromatic pyridyl (**1a–c**), pyrimidyl (**2a–c**), furanyl (**3a**,**b**), and thiophenyl (**4a**,**b**) cations. Comparisons are made with the chemistry of the phenyl cation (**5**).

[*] M. N. Eberlin, M. Carvalho, F. C. Gozzo, M. A. Mendes, R. Sparrapan, C. Kascheres
Institute of Chemistry
State University of Campinas
UNICAMP, CP 6154
13083-970 Campinas, SP (Brazil)
Fax: (+55) 19-788-3023
E-mail: eberlin@iqm.unicamp.br

  0947-6539/98/0407-1161 $ 17.50+.25/0



The low-energy CID and ion–molecule behavior of the ions were investigated with the aim of finding unique structural characteristics of the ions that would reveal the identity of their isomeric precursors. In addition, ab initio calculations were performed to address relative ion stabilities and to gain insights into the most likely reaction mechanisms.

Abstract in Portuguese: *Dissociações induzidas por colisão (CID) de baixa energia e reações íon/molécula com 2-metil--1,3-dioxolano (MD) realizadas através de espectrometria de massas pentaquadrupolar (QqQqQ) foram empregadas com o objetivo de localizar o sítio de carga de cátions isômeros heteroaromáticos. Os cátions 2-, 3-, e 4-piridila se mostram indistinguíveis por CID. Porém, experimentos MS³ e cálculos ab initio sugerem que o cátion 2-piridila reage com MD via um mecanismo tipo transacetalização formando um cátion bicíclico di-hidrooxazolopiridila. Porém, os cátions 3- and 4-piridila, semelhantemente ao cátion fenila, reagem com MD principalmente por transferência de próton. Os cátions 2-, 4-, e 5-pirimidila apresentam comportamentos dissociativos por CID bastante distintos. Além disto, o cátion 2-pirimidila reage prontamente com MD via o mecanismo tipo transacetalização, enquanto que transferência de próton predomina para os cátions 4- e 5-pirimidila. Os íons postulados como os cátions 2- e 3- furanila e tiofenila, provavelmente devido as suas inerentes instabilidades na fase gasosa e isomerização espontânea para os cátions butinoila e butinotioila, ou seja, $HC{\equiv}CHCH_2C{\equiv}O(S)^+$, apresentam comportamento dissociativo por CID e reatividade química indistinguíveis. Uma série de resultados experimentais sugerem a ocorrência destas isomerizações, as quais são substancialmente exotérmicas de acordo com cálculos ab initio G2(MP2). Os íons $HC{\equiv}CHCH_2C{\equiv}O(S)^+$ perdem CO e CS por CID, respectivamente, e reagem com MD via transacetalização. Ainda mais informativa é a participação de $HC{\equiv}CHCH_2C{\equiv}S^+$ em uma sequência de transacetalização/dissociação, diagnóstica para estruturas iônicas tioacílicas, pela qual se procede a troca de um átomo de enxofre por um de oxigênio. É possível, portanto, localizar o sítio de carga do cátion 2-piridila e dos três cátions 2-, 4- e 5-pirimidila, e identificar assim os precursores isômeros dos quais estes íons são formados. A rápida isomerização para $HC{\equiv}CH\text{-}CH_2\text{-}CO(S)^+$ elimina, porém, comportamentos químicos distintos que poderiam resultar da localização da carga em posições diferentes nos íons heteroaromáticos 2- e 3-furanila e 2- e 3-tiofenila.*

Experimental Section

The MS^2 and MS^3 experiments were performed with an Extrel pentaquadrupole (QqQqQ) mass spectrometer.[4] The QqQqQ consists of three mass-analyzing quadrupoles (Q1, Q3, Q5), in which ion-mass selection and analysis are performed, and two reaction quadrupoles (q2, q4), which are used to perform either low-energy ion–molecule reactions or CID. For the two-stage MS^2 experiments, the ion of interest was generated by dissociative 70 eV electron ionization (EI) of the following precursors: **1a** (2-chloropyridine), **1b** (3-chloropyridine), **1c** (4-chloropyridine), **2a** (2-chloropyrimidine), **2b** (4-methylpyrimidine), **2c** (5-bromopyrimidine, **3a** (2-bromofuran), **3b** (3-bromofuran), **4a** (2-bromothiophene), **4b** (3-bromothiophene), and **5** (chlorobenzene). After ion–molecule reactions with 2-methyl-1,3-dioxolane or CID with argon in q2, Q3 was scanned to record the product-ion spectrum, while Q5 was operated in the non-mass-analyzing rf-only mode. The target gas pressures in q2 and q4 corresponded to a typical beam attenuation of 40–60%, that is, multiple-collision conditions. However, lower reaction yields but similar product distributions were always observed at lower pressures in q2, that is, under single-collision conditions.

For the triple-stage MS^3 experiments, the reaction product of interest was selected in Q3 and dissociated by collision with argon in q4, while Q5 was scanned to record the sequential product spectrum. The collision energies, calculated as the voltage difference between the ion source and the collision quadrupole, were typically near 0 eV for ion–molecule reactions and 15 eV for CID in both MS^2 and MS^3 experiments.

Molecular orbital calculations were performed with GAUSSIAN 94.[5] Structure optimization and the total energy of the ions were obtained with the high-accuracy G2(MP2) model[6] or at the MP2/6-311G(d,p)//6-311G(d,p) + ZPE level of theory.[7] The G2(MP2) model achieves high accuracy[8] by adopting a composite procedure based effectively on QCISD-(T)/6-311G + (3df,2p)//MP2(full)/6-31G(d) energies (evaluated by making certain additivity assumptions) together with ZPE and isogyric corrections.

Results and Discussion

CID behavior: The three isomeric pyridyl cations **1a–c** display indistinguishable collisional dissociation behavior, as shown by their practically identical CID product-ion spectra. Upon 15 eV collisional activation with argon, **1a–c** dissociate by consecutive loss of HCN and H to give fragment ions of *m*/*z* 51 and 50, respectively, as shown for **1a** in Figure 1a. Note that the same fragments are formed from the analogous phenyl cation (**5**) by a similar dissociation route, namely, consecutive loss of acetylene and H (Figure 1b). That the fragment ion of *m*/*z* 50 ($C_4H_2^+$) is formed (at least in part) by H from the ion of *m*/*z* 51 ($C_4H_3^+$) loss is confirmed by the triple-stage mass spectrum of the *m*/*z* 51 ion (Figure 2).

Characteristic CID behavior is displayed by the three isomeric pyrimidyl cations **2a–c**. Loss of acetylene from **2a** (Figure 3a) yields a unique and abundant fragment of *m*/*z* 53. Ion **2b** (Figure 3b) fragments exclusively by HCN loss to afford the *m*/*z* 52 ion, whereas **2c** (Figure 3c) forms two fragments of *m*/*z* 52 and 51 by consecutive loss of HCN and H. These characteristic dissociations can be easily rationalized in terms of the influence of the charge site and its location on the heteroaromatic pyrimidine ring of **2a–c** (Scheme 2). Isomeric $C_3H_2N^+$ ions of *m*/*z* 52 are probably formed from **2b** and **2c**, as expected from the structures of their precursor ions and the dissociation mechanisms depicted in Scheme 2. The ion of *m*/*z* 52 from **2c** (Figure 3c) readily loses a hydrogen atom, whereas that from **2b** (Figure 3b) is

0947-6539/98/0407-1162 $ 17.50+.50/0 *Chem. Eur. J.* **1998**, *4*, No. 7

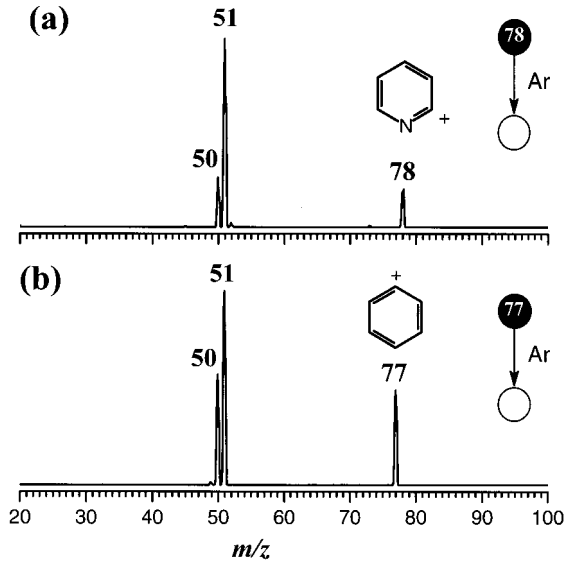


Figure 1. Double-stage (MS^2) 15 eV CID product spectra of a) the 2-pyridyl cation (**1a**) and b) of the phenyl cation (**5**). The spectra of the isomeric ions **1b** and **1c** are practically identical to that of **1a** and are not shown. In the terminology used to describe the type of MS^n experiment and scan mode employed, a filled circle represents a fixed (or selected) mass, and an open circle, a variable (or scanned) mass. The neutral reagent or collision gas that causes the mass transitions are shown between the circles. For more details on this terminology, see J. C. Schwartz, A. P. Wade, C. G. Enke, R. G. Cooks, *Anal. Chem.* **1990**, *62*, 1809.

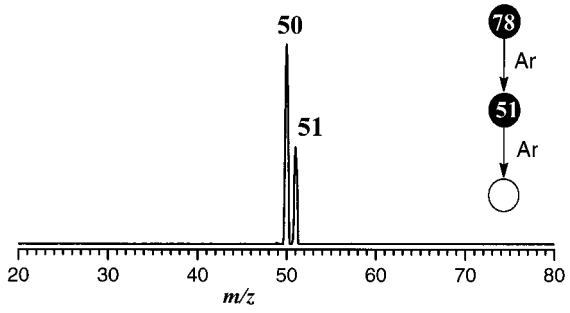


Figure 2. Triple-stage (MS^3) sequential product spectra for the fragment ion of *m*/*z* 78 formed by 70 eV EI of the 2-pyridyl cation (**1a**).

stable towards further dissociation under the applied collision conditions. Our suggestions of possible structures for these fragment ions, which help to rationalize different dissociation behaviors, are presented in Scheme 2.

The ions thought to be the isomeric 2- (**3a**, Figure 4a) and 3-furanyl (**3b**) cations and the isomeric 2- (**4a**, Figure 4b) and 3-thiophenyl (**4b**) cations display pratically identical CID behavior and are therefore indistinguishable by low-energy collisional dissociation. The putative ions **3a**, **b** (*m*/*z* 67) dissociate mainly by loss of C_2H_2 (*m*/*z* 41) and CO (*m*/*z* 39), whereas loss of CS (*m*/*z* 39) dominates for the ions **4a**,**b**.

It has been shown by experiment[9] and theory[10, 11] that the aromatic cyclopropenyl cation and the aliphatic propagyl cation are the most stable $C_3H_3^+$ isomers. Therefore, the dissociation pathways depicted in Scheme 3 are proposed for the loss of CO and CS from **3a**,**b** and **4a**,**b**, respectively, by which the corresponding $C_3H_3C{\equiv}O^+$ and $C_3H_3C{\equiv}S^+$ ions (**3c**,**d** and **4c**,**d**, respectively) are formed. Note, however,

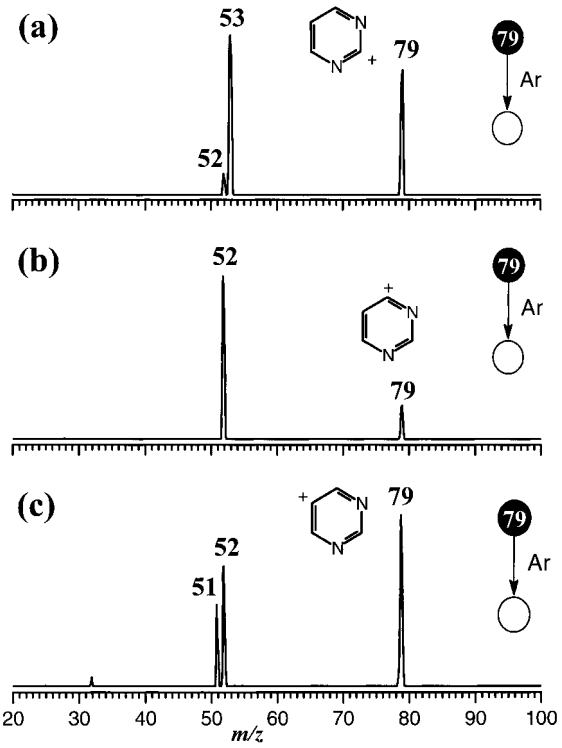
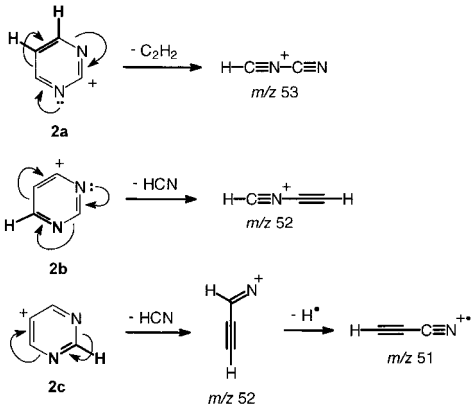


Figure 3. Double-stage (MS^2) 15 eV CID product spectra of the isomeric a) 2-pyrimidyl (**2a**), b) 3-pyrimidyl (**2b**), and c) 4-pyrimidyl (**2c**) cations.



Scheme 2.

that isomerization of the primary 2- and 3-furanyl and 2- and 3-thiophenyl cations may either be induced by the collisions or occur spontaneously prior to collisional dissociation. Isomerization prior to collisional activation is suggested by ab initio calculations and the ion–molecule chemistry of the ions (see below).

Ion–molecule behavior: The position of the charge site in the heteroaromatic ring may influence considerably the electronic structure and consequently the ion–molecule behavior of the isomeric heteroaromatic cations. A recent study[12] has shown for **1a**, **2a**, and **2b** that very effective overlap occurs between the fully occupied sp^2 nitrogen orbital and the adjacent and coplanar empty sp^2 orbital of C^+. Such effective orbital overlap leads to the prevalence of heteroaryne[13] structures for **1a**, **2a**, and **2b** that are characterized by

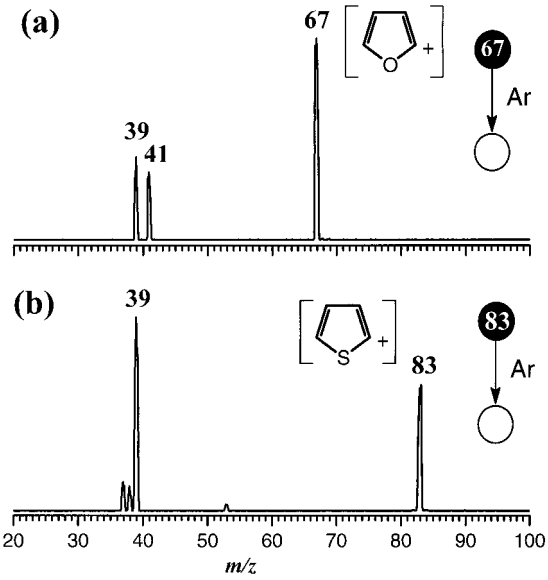
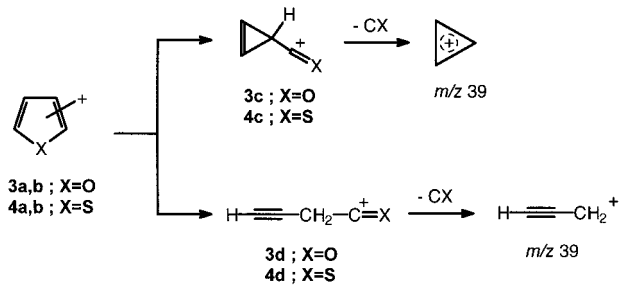
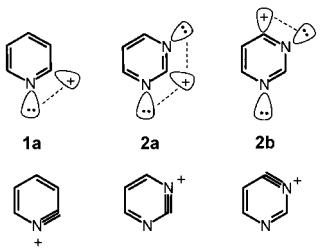


Figure 4. Double-stage (MS^2) 15 eV CID product spectra of the putative a) 2-furanyl (**3a**) and b) 2-thiophenyl (**4a**) cations. The spectra of the corresponding 3-isomers **3b** and **4b** are practically identical and are not shown. The ions **3a**,**b** and **4a**,**b** are probably unstable in the gas phase, and isomerize to the same acylium (**3d**) and thioacylium (**4d**) ions (see text).

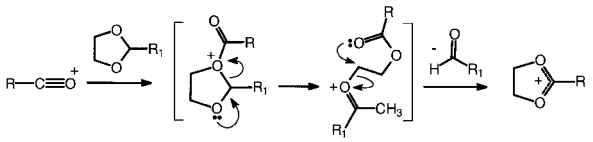


Scheme 3.

substantially shorter $N-C^+$ bond lengths (1.19–1.23 Å) and extensive resonance stabilization on the order of 18–28 kcal mol^{-1}. Hence, as predicted by Kauffmann et al.,[14] **1a**, **2a**, and **2b** are most appropriately regarded as *ortho*-azabenzynium ions. No substantial orbital overlap occurs for the 2-furanyl (**3a**) and 2-thiophenyl (**4a**) cations.[12]

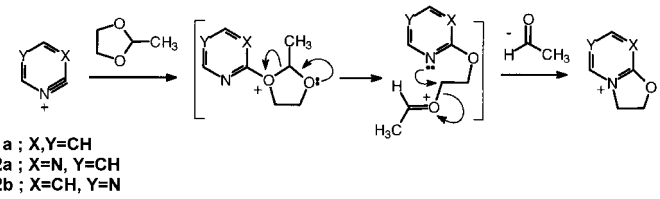


In addition, a series of studies has shown that acylium ions ($RC^+{=}O \leftrightarrow RC{\equiv}O^+$) and their sulfur analogues, the thioacylium ions ($RC^+{=}S \leftrightarrow RC{\equiv}S^+$), react extensively in the gas phase with cyclic acetals and ketals by transacetalization[15] (Scheme 4) and ketalization.[16] The electronic structure of **1a**, as well as those of **2a** and **2b**, are similar to those of acylium ions in that a positively charged carbon atom is adjacent to a heteroatom, so that extensive orbital overlap and therefore resonance stabilization can occur. Considering this similarity, the *ortho*-azabenzynium ions **1a**, **2a**, and **2b** can be expected to react with cyclic acetals to afford bicyclic dihydrooxazolopyridyl



Scheme 4.

cations by a transacetalization-like mechanism (Scheme 5). This reaction is not expected, however, for isomers **1b**,**c** and **2c** due to the separation between the charge site and the nucleophilic heteroatom.



Scheme 5.

The product spectra for the reaction of the isomeric pyridyl cations **1a**–**c** with 2-methyl-1,3-dioxolane are shown in Figure 5. Reactions of **1a** (*m*/*z* 78, Figure 5a) yield an abun-

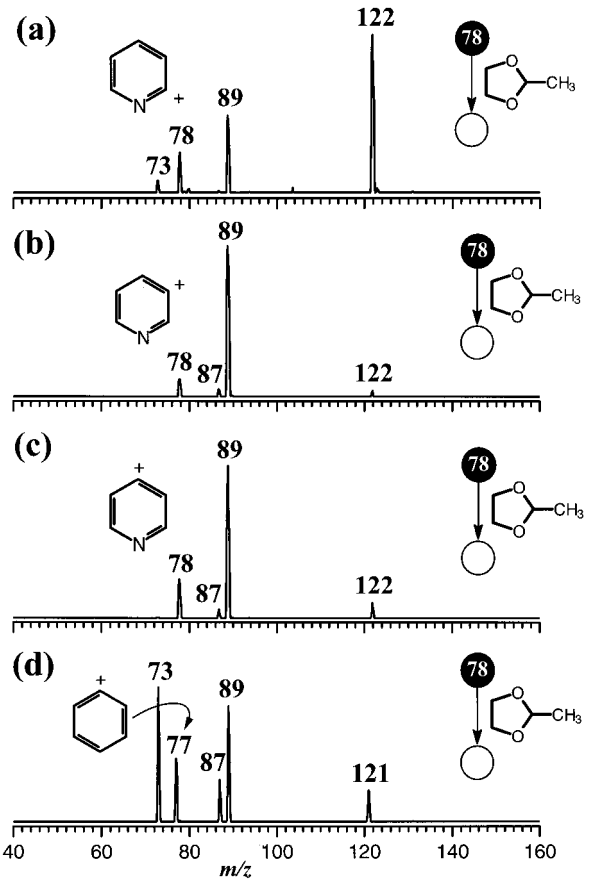
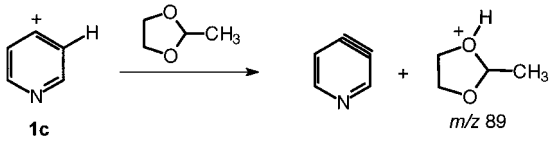


Figure 5. Double-stage (MS^2) product spectra for reaction with 2-methyl-1,3-dioxolane of the isomeric a) 2-pyridyl (**1a**), b) 3-pyridyl (**1b**), c) 4-pyridyl (**1c**) cations, and d) of the phenyl cation (**5**).

0947-6539/98/0407-1164 $ 17.50+.50/0 *Chem. Eur. J.* **1998**, *4*, No. 7

dant product of *m*/*z* 122, which corresponds to net addition of 44 u (C_2H_4O) to the reactant ion. Therefore, transacetalization-like reactions[15] probably took place. The isomeric **1b** (Figure 5b) and **1c** (Figure 5c), on the other hand, react mainly by proton transfer (*m*/*z* 89) and to a modest extent by hydride abstraction (*m*/*z* 87). The participation of the phenyl cation (**5**) in the transacetalization-like reaction is limited; it affords a minor product of *m*/*z* 121 (Figure 5d). The ions **1b** and **1c**, as opposed to the *ortho*-azabenzynium ion **1a**, can both be regarded as protonated forms of *ortho*-azabenzynes,[14] just as the phenyl cation can be regarded as the protonated form of *ortho*-benzyne. Hence, **1b** and **1c** are expected to be much more acidic than **1a**. It is therefore not surprising that **1b** and **1c** react predominantly by proton transfer (*m*/*z* 89) to give the corresponding neutral *ortho*-azabenzyne (Scheme 6).



Scheme 6.

With regard to the isomeric pyrimidyl cations, the *ortho*-1,3-diazabenzynium ion **2a** (Figure 6a) reacts, as expected, extensively by the transacetalization-like mechanism to afford

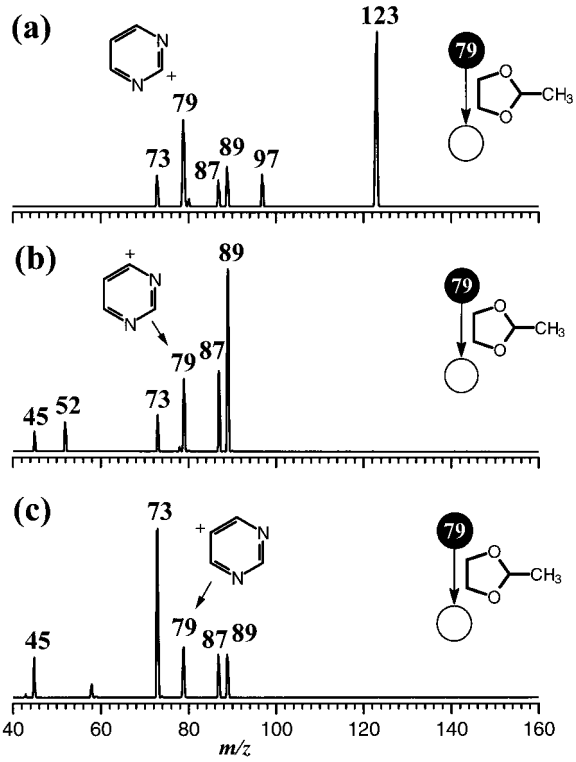


Figure 6. Double-stage (MS^2) product spectra for reaction with 2-methyl-1,3-dioxolane of the isomeric a) 2-pyrimidyl (**2a**), b) 4-pyrimidyl (**2b**), and c) 5-pyrimidyl (**2c**) cations.

the dihydrooxazolopyrimidyl cation of *m*/*z* 123. Ions **2b** (Figure 6b) and **2c** (Figure 6c) react mainly by proton transfer (*m*/*z* 89) and hydride abstraction (*m*/*z* 87). Given the extensive reactivity of the analogous *ortho*-azabenzynium ions **1a** and **2a**, it is surprising that the analogous *ortho*-1,3-diazabenzynium ion **2b** does not react by the transacetalization-like mechanism. A likely explanation for the unexpected behavior of **2b** is the ease with which it is fragmented by collision to give the $C_3H_2N^+$ fragment ion of *m*/*z* 52 (Figure 3b). The $C_3H_2N^+$ fragment, formed preferentially from **2b** even under the mild collision conditions used for ion–molecule reactions (note its presence in Figure 6b), may react further with 2-methyl-1,3-dioxolane to afford the proton-transfer (*m*/*z* 89), and hydride- (*m*/*z* 87) and methyl-abstraction (*m*/*z* 73) products.

Both positional isomers, that is, the ions thought to be the 2- and 3-furanyl and 2- and 3-thiophenyl cations, react similarly with 2-methyl-1,3-dioxolane. The putative furanyl cations **3a** (Figure 7a) and **3b** undergo, to a moderate extent, addition of 44 u to afford the product ion of

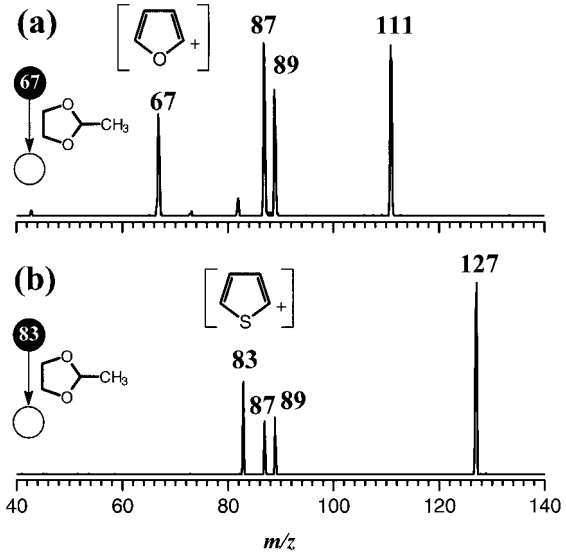
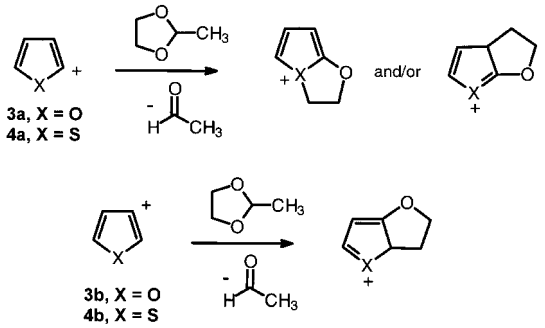


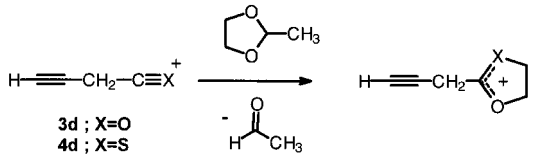
Figure 7. Double-stage (MS^2) product spectra for reaction of the putative a) 2-furanyl (**3a**) and b) 2-thiophenyl (**4a**) cations with 2-methyl-1,3-dioxolane. The spectra of the corresponding 3-isomers **3b** and **4b** are practically identical and are not shown. The ions **3a**,**b** and **4a**,**b** are probably unstable in the gas phase and isomerize to common acylium (**3d**) and thioacylium (**4d**) ions (see text).

m/*z* 111; the product of such reaction (*m*/*z* 127) dominates for the thiophenyl cations **4a** (Figure 7b) and **4b**. Transacetalization-like mechanisms for these reactions are briefly depicted in Scheme 7.

An alternative exists for the furanyl and thiophenyl cations. Their reactions may involve not the primary ions **3a**,**b** and **4a**,**b** but the isomeric (thio)acylium ions **3c**,**d** and **4c**,**d** (Scheme 3). These secondary (thio)acylium ions could then react by the original transacetalization mechanism[15] to afford the cyclic ionic (thio)ketals shown for **3d** and **4d** in Scheme 8. Isomerizations to **3d** and **4d** are supported by ab initio calculations and triple-stage mass spectrometric experiments (see below).



Scheme 7.



Scheme 8.

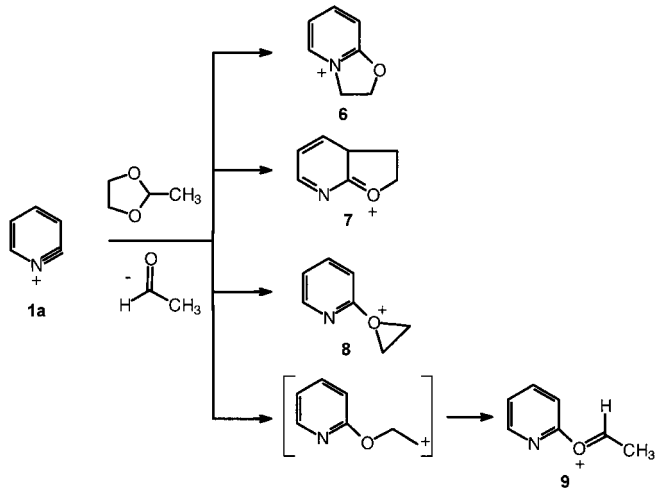
Ab initio calculations: *Gas-phase stability of the 2- and 3-furanyl and 2- and 3-thiophenyl cations:* As discussed above, CID and product-ion spectra suggest that isomerization of **3a**,**b** and **4a**,**b** to the corresponding (thio)acylium ions **3c**,**d** and **4c**,**d** may occur prior to or in the course of dissociation and reaction. To evaluate the likelihood of such processes, ab initio calculations were performed with the high-accuracy G2(MP2) model[6]. The two additional isomeric structures **3e**,**f** and **4e**,**f** were also considered for both $C_4H_3O^+$ and $C_4H_3S^+$ systems.

The G2(MP2) energies (Table 1) show that the butynoyl (**3d**) and butynethioyl (**4d**) cations are the most stable isomers in each case; they are far more stable than the corresponding heteroaromatic furanyl (**3a**,**b**) and thiophenyl (**4a**,**b**) cations. The energy differences in favor of **3d** (53.1 – 54.7 kcal mol^{-1}) and **4d** (26.9 – 18.5 kcal mol^{-1}) are even more pronounced in the case of **3d**, most likely due to the greater stability of acylium ions compared to thioacylium ions.[17] Therefore, although formation of isomeric ionic mixtures is not excluded, the G2(MP2) prediction of thermodynamically favorable ring opening to give **3d** and **4d** suggests that these isomerizations are the cause of the identical CID and ion – molecule behavior of the (unstable) 2- and 3-furanyl (**3a**,**b**) and 2- and 3-thiophenyl (**4a**,**b**) cations. One must, however, also consider the activation energies of the isomerization steps. These barriers were not estimated, but apparently they are readily overcome by the internal energies of the nascent **3a**,**b** and **4a**,**b.**

Table 1. Total and relative energies from G2(MP2) ab initio calculations.

Ion	G2(MP2) Energy [hartree]	Relative energy [kcal mol^{-1}]
3a	– 228.59123	53.1
3b	– 228.58864	54.7
3c	– 228.66919	4.2
3d	– 228.67589	0
3e	– 228.65395	13.8
3f	– 228.65856	10.9
4a	– 551.22860	26.9
4b	– 551.24198	18.5
4c	– 551.26165	6.2
4d	– 551.27152	0
4e	– 551.25964	7.5
4f	– 551.26050	6.9

*The transacetalization-like products of **1a** and **2a***: By analogy with the cyclic ionic ketals formed in reactions with acylium ions (Scheme 4), the bicyclic dihydrooxazolopyridyl and -oxazolopyrimidyl cations depicted in Scheme 5 are expected to be formed in reactions of **1a** and **2a** with 2-methyl-1,3-dioxolane. However, other alternative products could be considered, as exemplified for **1a** in Scheme 9. To evaluate the likelihood of these processes, an MP2/6-311G(d,p)//6-311G(d,p) + ZPE ab initio potential energy reaction surface diagram for **1a** was calculated (Table 2 and Figure 8). The proposed bicyclic ion **6** is indeed by far the most likely and thermodynamically favorable product. Its formation is overall – 87.6 kcal mol^{-1} exothermic (– 22.2 kcal mol^{-1} exothermic relative to the adduct). Such an exothermic reaction to form **6** is in agreement with the rapid dissociation of the adduct. The processes



Scheme 9.

Table 2. Total energies from MP2/6-311G(d,p)//6-311G(d,p) + ZPE ab initio calculations.

Species	MP2/6-311G(d,p)// 6-311G(d,p) [hartree]	ZPE [hartree]	Total energy[a] [hartrees]
1a	– 246.64905	0.08031	– 246.57758
2-methyl-1,3-dioxolane	– 306.88788	0.12917	– 306.77292
adduct	– 553.64634	0.21536	– 553.45467
acetaldehyde	– 153.44077	0.05916	– 153.38812
6	– 400.23706	0.15181	– 400.10195
7	– 400.17834	0.15050	– 400.04440
8	– 400.14558	0.14857	– 400.01336
9	– 400.18647	0.14634	– 400.05623

[a] ZPE energies were scaled by 0.89.

0947-6539/98/0407-1166 $ 17.50+.50/0 *Chem. Eur. J.* **1998**, *4*, No. 7

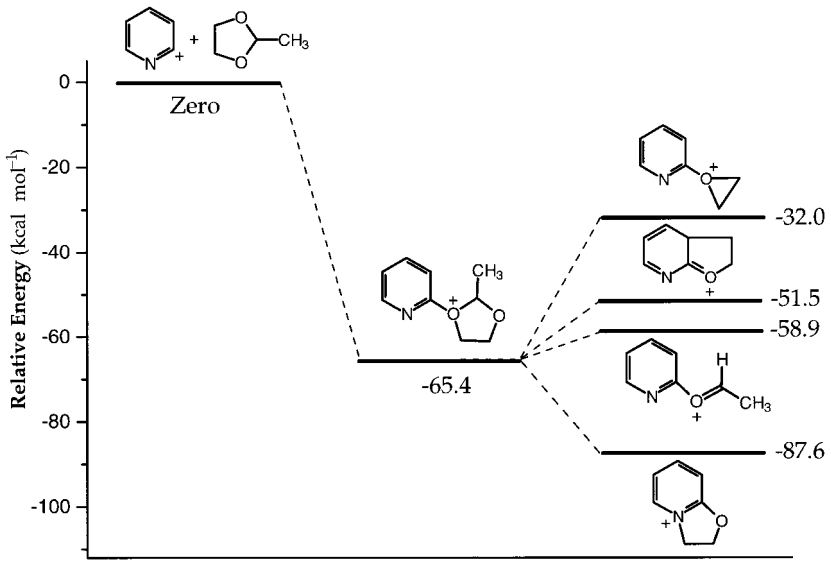


Figure 8. Ab initio MP2/6-311G(d,p)//6-311G(d,p) + ZPE potential energy reaction surface diagram for reaction of the 2-pyridyl cation (**1a**) with 2-methyl-1,3-dioxolane. Acetaldehyde, which is not indicated in the figure, is the neutral product in all cases.

leading to the other alternative products **7**–**9** are, on the contrary, all endothermic relative to the adduct.

MS³ experiments: The products of net addition of 44 u to **1a** and **2a** in reactions with 2-methyl-1,3-dioxolane are shown by their triple-stage sequential-product spectra to dissociate exclusively upon collisional activation to reform the corresponding reactant ion of *m*/*z* 78 (Figure 9a) and *m*/*z* 79 (Figure 9b). Similar dissociation to re-form the reactant ion is observed for the net 44 u addition products of **3a**,**b** (spectra not shown). This dissociation, which is similar to the hydrolysis of acetals and ketals to re-form the carbonyl compounds, is a characteristic of the transacetalization[15] and ketalization[16] products of acylium ions; it is also easily rationalized for the transacetalization-like products of **1a** and **2a** (Scheme 10).

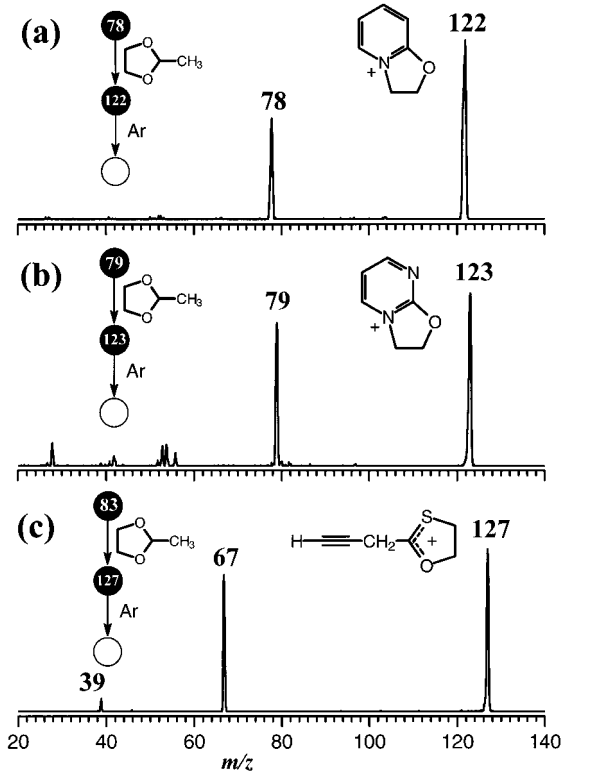
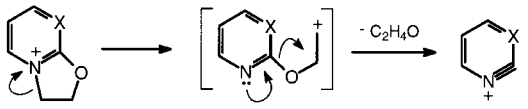


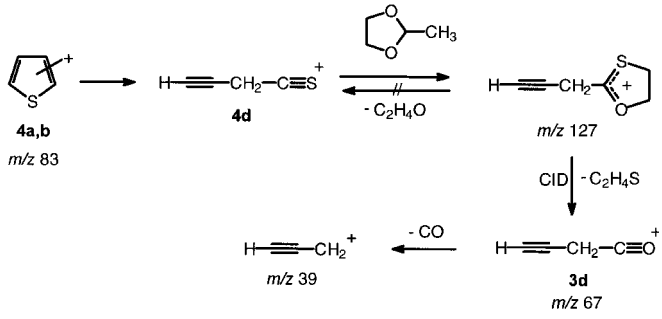
Figure 9. Triple-stage (MS³) sequential product spectra for the ionic products of transacetalization-like reactions of the a) 2-pyridyl (**1a**), b) 2-pyrimidyl (**2a**), and c) the unstable 2-thiophenyl (**4a**) cation (most likely **4d**).

Contrasting CID behavior is displayed by the net 44 u addition products of the (unstable) thiophenyl cations **4a** (Figure 9c) and **4b** (spectrum not shown). Both spectra are very similar, and show that the product ions dissociate to form a fragment of *m*/*z* 67 (Figure 9c). Generation of an ion of *m*/*z* 67 ($C_4H_3O^+$), rather than the $C_4H_3S^+$ reactant ion of *m*/*z* 83, indicates formal



Scheme 10.

replacement of sulfur by oxygen. Such a distinct transacetalization/dissociation sequence recently has been shown to be a unique characteristic of—and a structurally diagnostic test for—thioacylium ions, allowing their gas-phase conversion into acylium ions.[15d] By this sequence, the thioacylium ions react with cyclic acetals to form cyclic ionic thioacetals, which dissociate on collisional activation to exclusively afford the analogous and more stable acylium ions.[17] Therefore the replacement of sulfur by oxygen observed for the $C_4H_3S^+$ ions is best rationalized if one assumes that indeed the ions thought to be the 2- and 3-thiophenyl cations (**4a**,**b**) isomerize to **4d** ($HC{\equiv}CHCH_2C{\equiv}S^+$) prior to reaction (Scheme 11). If the primary thiophenyl cations **4a**,**b** participated in the reaction, their possible transacetalization-like products (Scheme 7) would not be expected to lose C_2H_4S.



Scheme 11.

In the case of the putative furanyl cations, the fact that their transacetalization (or transacetalization-like) products dissociate to re-form the reactant ion cannot be used to support either the heteroaromatic structure **3a**,**b** or the acyclic structure **3d**. However, their CID behavior and ab initio thermochemistry point to a $C_4H_3O^+$ composition in which the acylium ion **3d** dominates.

Conclusions

The isomeric 2-, 3-, and 4-pyridyl cations are indistinguishable by low-energy CID. The 2-pyridyl cation is characterized, however, by its transacetalization-like reactivity with 2-methyl-1,3-dioxolane, which likely results from activation of the charge site by the adjacent heteroatom. The three isomeric 2-, 4-, and 5-pyrimidyl cations display quite characteristic dissociation behavior, and are therefore easily distinguished by CID. In addition, only the 2-pyrimidyl cation participates in transacetalization-like reactions with 2-methyl-1,3-dioxolane. It is therefore possible to locate the charge site in the 2-pyridyl and all three pyrimidyl heteroaromatic cations; hence, the unique CID behavior or transacetalization-like reactivity of these common fragment ions can be applied generally to reveal the position of the substituent in the whole class of substituted pyridines and pyrimidines. Charge location is not possible, however, in the 2- and 3-furanyl and 2- and 3-thiophenyl cations because of their instability in the gas phase. Rapid isomerization of the nascent furanyl and thiophenyl cations, most likely to the same (thio)acylium ion $HC{\equiv}CHCH_2C{\equiv}O(S)^+$, results in identical CID and ion-molecule behavior.

Acknowledgements: This work was supported by the Research Support Foundation of the State of São Paulo (FAPESP) and the Brazilian National Research Council (CNPq).

Received: October 20, 1997
Revised version: January 27, 1998 [F860]

[1] a) F. W. McLafferty, *Tandem Mass Spectrometry*, Wiley, New York, **1983;** b) K. Levsen, H. Schwarz, *Mass Spectrom. Rev.* **1983**, *2*, 77; b) J. L. Holmes, *Org. Mass Spectrom.* **1985**, *20*, 169; c) K. L. Busch, G. L. Glish, S. A. McLuckey, *Mass Spectrometry/Mass Spectrometry: Techniques and Applications of Tandem Mass Spectrometry*, VCH, New York, **1988**.

[2] a) *Ion-Molecule Reactions* (Ed.: J. L. Franklin), Plenum Press, New York, **1972;** b) *Gas Phase Ion/Molecule Reactions Vols. 1–3*,(Ed.: M. T. Bowers), Academic Press, New York, **1979;** c) *Chemical Ionization Mass Spectrometry* (Ed.: A. G. Harrison), CRC Press, Boca Raton, **1983.**

[3] a) F. C. Gozzo, M. N. Eberlin *J. Am. Soc. Mass Spectrom.* **1995**, *6*, 554; b) A. E. P. M. Sorrilha, F. C. Gozzo, R. S. Pimpim, M. N. Eberlin *ibid.* **1996**, *7*, 1126; c) M. N. Eberlin, A. E. P. Sorrilha, F. C. Gozzo, R. Sparrapan *J. Am. Chem. Soc.*, **1997**, *119*, 3550; d) M. N. Eberlin, *Mass Spectrom. Rev.*, **1997**, *16*, 113.

[4] V. F. Juliano, F. C. Gozzo, M. N. Eberlin, C. Kascheres, C. L. Lago, *Anal. Chem.* **1996**, *68*, 1328.

[5] GAUSSIAN 94, Revision B.3, M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Ortiz, J. B. Foresman, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez, J. A. Pople, Gaussian, Inc., Pittsburgh, PA, **1995**.

[6] L. A. Curtis, K. Raghavachari, J. A. Pople, *J. Chem. Phys.* **1993**, *98*, 1293.

[7] a) W. J. Hehre, R. Ditchfield, J. A. Pople, *J. Chem. Phys.* **1972**, *56*, 2257; b) C. Møller, M. S. Plesset, *Phys. Rev.* **1934**, *46*, 618.

[8] J. B. Foresman, A. E Frisch, *Exploring Chemistry with Electronic Structure Methods*, Gaussian, Inc. Pittsburgh **1993**.

[9] F. P. Lossing, *Can. J. Chem.* **1972**, *50*, 139.

[10] a) L. Radom, P. C. Hariharan, J. A. Pople, P. von R. Schleyer, *J. Am. Chem. Soc.* **1976**, *98*, 10; b) J. Leszczynski, B. Weiner, M. C. Zerner, *J. Phys. Chem.* **1989**, *93*, 139.

[11] a) A. S. Tsai, A. S. Werner, T. Baer, *J. Chem. Phys.* **1975**, *63*, 4384; b) J. C. Holmes, F. P. Lossing, *Can. J. Chem.* **1979**, *57*, 249; c) K. C. Smyth, S. G. Lias, P. Ausloos *Combust. Sci. Tech.* **1982**, *28*, 147; d) P. J. Auloos, S. G. Lias, *J. Am. Chem. Soc.* **1981**, *103*, 6505; e) G. Baykut, F. W. Brill, J. R. Eyler, *Combust. Sci. Tech.* **1986**, *45*, 233.

[12] F. C. Gozzo, M. A. Mendes, R. Sparrapan, M. N. Eberlin *J. Org. Chem.* submitted.

[13] a) T. Kauffmann, *Angew. Chem.* **1965**, *77*, 557; *Angew. Chem. Int. Ed. Engl.* **1965**, *4*, 543; b) H. J. Den Hertog, H. C. van Der Plas, *Heterocycl. Chem.* **1965**, *4*, 121; c) T. Kauffmann, R. Wirthwein, *Angew. Chem.* **1971**, 83, 21; *Angew. Chem. Int. Ed. Engl.* **1971**, *10*, 20.

[14] a) T. Kauffmann, F.-P. Boettcher, *Chem. Ber.* **1962**, *95*, 949; b) T. Kauffmann, H. Marhan, *ibid.* **1963**, *96*, 2519.

[15] a) M. N. Eberlin, R. G. Cooks, *Org. Mass Spectrom.* **1993**, 28, 679; b) L. A. B. Moraes, F. C. Gozzo, M. N. Eberlin, P. Vainiotalo, *J. Org. Chem.*, **1997**, *62*, 5096; c) L. A. B. Moraes, M. N. Eberlin, *J. Chem. Soc. Perkin Trans. 2* **1997**, *10*, 2105; d) M. C. Carvalho, V. F. Juliano, C. Kascheres, M. N. Eberlin, *ibid.* **1997**, 2347.

[16] L. A. B. Moraes, M. N. Eberlin, *J. Org. Chem.* **1996**, *61*, 8726.

[17] M. C. Caserio, J. K. Kim, *J. Am. Chem. Soc.* **1983**, *105*, 6896.

  0947-6539/98/0407-1168 $ 17.50+.50/0