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International Journal of Mass Spectrometry 217 (2002) 153–168

International Journal of Mass Spectrometry

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Functional group migration in benzaldoxime-*O*-*n*-propyl ether radical cation

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Received 23 August 2001; accepted 27 November 2001

Dedicated to the memory of Professor Pierre Longevialle.

Abstract

The mechanism of the elimination of CH_2O and C_2H_4O from the molecular ions of benzaldoxime-*O*-*n*-propyl ether (**1**) was studied using specifically deuterated derivatives, methods of tandem mass spectrometry, and ab initio calculation of the minimum energy reaction path (MERP) at the B3LYP/6-311G*//UHF/3-21G* level of theory. The results show that the eliminated CH_2O (major) and C_2H_4O (minor) contain specifically the α- and β-CH_2 groups, respectively, of the propoxy chain of **1**, requiring a rearrangement of the molecular ion of **1** by a 1,5-shift of the benzaldimine moiety along the propoxy chain. This rearrangement reaction follows the general Longevialle mechanism of functional group transposition along an aliphatic chain by rearrangement of distonic ions. In the case of $\mathbf{1}^{\bullet+}$ the initial δ-distonic ion **1dist** is generated by a 1,5-H shift from the terminal CH_3 group to the N-atom of the oxime group. The compound **1dist** is converted to the α-distonic isomer **5dist** by cyclization of the molecular ion of *N*-benzyl-1,2-oxazolidine (**5**) and by subsequent ring opening into the δ-distonic isomer **2dist** of *N*-(3-hydroxypropyl)benzaldimine (**2**) (see Scheme 4). Eventually the distonic ion **2dist** fragments by loss of CH_2O and C_2H_4O. The possibility that the distonic isomers of $\mathbf{1}^{\bullet+}$ and $\mathbf{2}^{\bullet+}$ interconvert with their cyclic isomers *2H*-3,4,5,6-tetrahydro-3-phenyl-1,2-oxazine radical cation ($\mathbf{3}^{\bullet+}$) and *2H*-3,4,5,6-tetrahydro-3-phenyl-1,3-oxazine radical cation ($\mathbf{4}^{\bullet+}$) was also examined by comparing the EI- and MIKE-spectra and the CID of the molecular ions of the isomers and by ab initio calculation. (Int J Mass Spectrom 217 (2002) 153–168) © 2002 Elsevier Science B.V. All rights reserved.

Keywords: *O*-alkyl benzaldoximes; Fragmentation mechanism; Rearrangement; Distonic ion; Metastable ion; Deuterated derivatives; Ab initio

1. Introduction

Rearrangement reactions in organic and elementorganic molecular ions are important for analytical mass spectrometry as well as for gas-phase ion chemistry. It is obvious that a rearrangement of the molecular ion before fragmentation may interfere with a determination of the connectivity of atoms in the original compound, i.e., with a mass spectral structure analysis. This is one reason why rearrangement reactions have been studied much in detail from the beginning of organic mass spectrometry [1]. Further, electron deficient species like carbenium ions and radical cations are disposed for rearrangements, so a study of their reactions in the gas phase is an important aid in the

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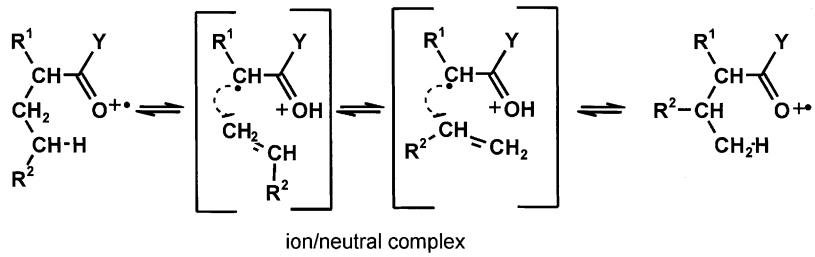
1387-3806/02/$ – see front matter
PII S1387-3806(02)00571-7



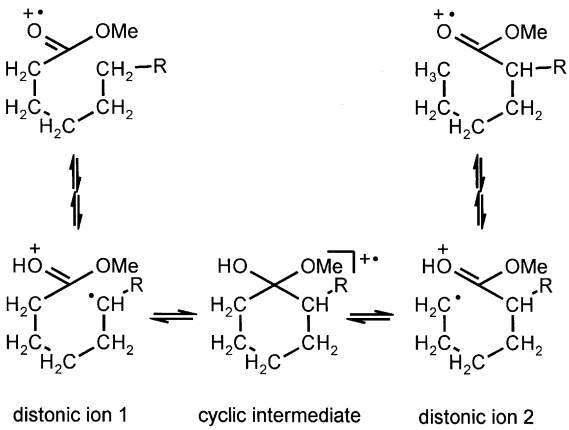
Scheme 1. Functional group transposition by reaction in ion/neutral complex.

interpretation of the chemistry of these reactive species. Rearrangements by migration of hydrogen atoms are ubiquitous in organic mass spectrometry, and in most cases these rearrangements of radical cations can be viewed as an internal H abstraction by the radical site, which initiates follow-up reactions, mostly fragmentation of intermediate distonic ions by elimination reactions. The mechanisms of these fragmentations are well explored, and they do not pose severe problems to a mass spectral structure analysis [2]. More distressing difficulties may arise from skeletal rearrangements. The best known one of these rearrangements is the toluene radical cation/cycloheptatriene radical cation interconversion and that of related aromatic radical cations (for a review see [3]), but alkyl shifts in aromatic and aliphatic radical cations are also known (see for example [4]). However, the most intriguing problems—both for structure analysis by mass spectrometry and for a mechanistic description of reactions of organic radical cations—arise in case of rearrangements by migration of functional groups around a carbon ring or along a carbon chain.

Basically, the transposition of functional groups within an organic radical cation may proceed by one of two fundamentally different mechanisms. The first one involves an intermediary ion/neutral complex as first introduced into mechanistic mass spectrometry by Longevialle and Botter [5]. If the functional group is eliminated in the first step of a fragmentation reaction but stays around with the other fragment in an ion/neutral complex, re-addition may occur at a different position of the fragment to create a rearranged molecular ion. An example of this type of functional group migration is the rearrangement of ionized carbonyl compounds during the McLafferty fragmentation into an enol radical cation and an alkene [6]. As shown in Scheme 1, the enol radical cation may add at the two different C atoms of the alkene double bond giving rise to a radical cation with a rearranged carbon skeleton besides the original one. Since intermediary ion/neutral complexes dissociate quickly at high internal energy, this type of rearrangement mechanism is primarily observed during the fragmentation of low-energy metastable ions.

The other type of mechanism of transposition of a functional group requires an intermediate distonic ion generated by a rearrangement of the molecular ion. Here, an example well studied by Schwarz and coworkers is the 1,2-shift of an ester group in the distonic ion generated from ionized methyl isobutyrate [7]. However, migration of the ester group even over large distances along an alkyl chain in the molecular ions of fatty acid esters as evidenced by "internal losses" of alkyl fragments from the inner part of the alkyl chain has already been suggested in the 1960s [8]. The mechanism of this intriguing rearrangement has eventually been settled in a famous (and complicated!) paper by Longevialle and coworkers [9]. In this mechanism the transposition of the ester group occurs via a six-membered cyclic intermediate which is formed by attack of the radical site on the carbonyl-C of the protonated ester group in a ε-distonic ion (Scheme 2).

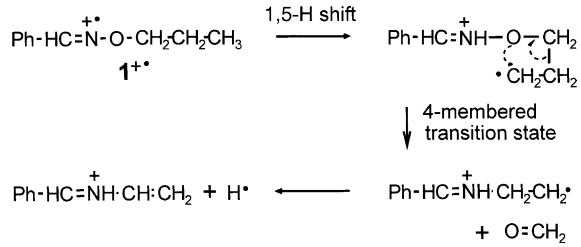
Cleavage of the C–C bond at either side of the quaternary C atom gives rise to the original distonic ion and to a rearranged distonic ion, respectively, in which



Scheme 2. Functional group transposition by ring formation/ring opening of distonic ions (Longevialle mechanism).

the protonated ester group has been 1,5-shifted along the CH_2-chain. It is not clear, however, if the cyclic intermediate is a true intermediate or the transition state of this reaction. Long distance shifts of protonated carbonyl functionalities are probably rather frequent, and an example showing the involvement of larger cyclic intermediates (or transition states) are the transposition of the carboxamide group in the radical cations of aliphatic carboxamides [10]. A special feature of this type of rearrangements by migration of functional groups is the appearance of the resulting product ions also in the normal 70 eV mass spectra because distonic ions are involved. However, the intensity of the relevant fragment ions may be quite small because of the low frequency factors of rearrangement reactions.

An interesting rearrangement involving functional group migration has been reported by Cooks and Varvoglis [11] in the mass spectrum of the *O*-*n*-propyl ether of benzaldoxime (**1**, *m*/*z* 163), which was quoted to uniquely exhibit signals at *m*/*z* 133 and 132 owing to the loss of CH_2O followed by loss of H. The mechanism suggested for this fragmentations starts by a 1,5-H shift from the terminal CH_3 group of the *n*-propyl chain to the oxime-N atom and elimination of CH_2O in a four-membered transition state. H-elimination from the resulting β-distonic *N*-ethylene benzaldiminium ion yields eventually a *N*-vinyl benzaldiminium ion *m*/*z* 132 (Scheme 3).



Scheme 3.

Recently, the Regensburg group has studied the mass spectrometric behavior of the *O*-alkyl ethers of a series of oximes by deuterium labeling, high mass resolution and metastable ion techniques [12]. The results show, that elimination of CH_2O is not a specific feature of the mass spectrum of the *O*-*n*-propyl ether of benzaldoxime as originally proposed [11] but is a common feature of the mass spectra of oxime ethers with alkyl chains longer than CH_2CH_3 and can be detected also in the mass spectra of *O*-alkyl ethers of certain aliphatic oximes. Further, D-labeling reveals that it is indeed in all cases the α-CH_2 group of the *O*-alkyl chain which is specifically lost with the CH_2O without any preceding H/D exchange. However, the H atom lost in the next fragmentation step of aromatic oxime ethers stems almost exclusively from the aromatic ring. This concurs with a mechanism by which the loss of CH_2O gives rise to the β-distonic *N*-ethylene benzaldiminium ion as suggested by Cooks and Varvoglis [11] but by further reaction of the β-distonic ion by intramolecular aromatic substitution to yield eventually a stable dihydroisoquinolinium ion. This intramolecular substitution process was corroborated by substituent loss from $[M - CH_2O]^{\bullet +}$ in the mass spectra of substituted **1** [13]. Additionally, D-labeling and metastable ion spectra of **1** revealed also the elimination of fragments C_2H_4O and C_2H_5O which specifically contain the α- and β-CH_2 groups of the propyl chain. This is a strong indication that the elimination of CH_2O does not occur by a four-center transition state from the distonic ion generated by a 1,5-H shift from the molecular ion $\mathbf{1}^{\bullet +}$ but that loss of CH_2O as well as loss of C_2H_4O occurs from a distonic intermediate in

which the benzaldiminium group has migrated from the O-atom to the γ-C atom of the original propoxy chain. This would be a new example of a functional group transposition along an aliphatic chain, transforming the radical cation of **1** into the radical cation of *N*-(3-hydroxypropyl)benzaldimine (**2**).

The full mass spectral data of the study of the *O*-alkyl ethers of oximes and of their deuterated analogues and the synthesis of these compounds will be published elsewhere [14]. In this paper we concentrate on the mechanistic details of the functional group transposition preceding the elimination of CH_2O from $\mathbf{1}^{\bullet+}$ and the fate of the intermediate distonic ions derived from $\mathbf{1}^{\bullet+}$ and $\mathbf{2}^{\bullet+}$, making use of the D-labeling data and of ab initio calculation of the MERP of the rearrangement reaction. It will be shown that the migration of the (protonated) benzaldimine group occurs indeed via a C-distonic isomer of $\mathbf{1}^{\bullet+}$ and an O-distonic isomer of $\mathbf{2}^{\bullet+}$, and that these distonic isomers likely communicate also with the radical cations of *2H*-3,4,5,6-tetrahydro-3-phenyl-1,2-oxazine radical cation ($\mathbf{3}^{\bullet+}$) and *2H*-3,4,5,6-tetrahydro-3-phenyl-1,3-oxazine radical cation ($\mathbf{4}^{\bullet+}$), which are cyclic isomers of **1** and **2**, respectively.

2. Experimental

The synthesis of the compounds used in this study followed standard techniques of organic chemistry and will be published elsewhere [14].

2.1. Mass spectrometry

The 70 eV EI mass spectra were obtained with a double focusing mass spectrometer MAT 95 [15] at the Regensburg laboratory and a double focusing mass spectrometer VG AutoSpec [16] at the Bielefeld laboratory under the following conditions. MAT 95: electron energy 70 eV, accelerating voltage 5 kV, ion source temperature 200 °C, direct inlet system. VG AutoSpec: electron energy 70 eV, accelerating voltage 8 kV, ion source temperature 200 °C; heated septum inlet system or direct inlet system for the hydrochloride of **3**. The EI mass spectra obtained with both instruments agreed very well with exception of a slight intensity variation of the molecular ion peak. Metastable ion fragmentation and collision-induced decomposition (CID) were analyzed with the MAT 95 using a B/E linked scan (first field free region (FFR) between ion source slit and magnetic sector) using the set-up of the ion source and the inlet system as given before, and product ion scans by a combined variation of the field strength of the magnetic field and the deflecting field of the electrostatic analyzer (ESA). The 10 single spectra were combined to increase the signal-to-noise ratio. CID was investigated by the same linked scan method and introduction of argon into the collision cell of the first FFR until the intensity of the main beam was reduced to 30%. With the VG AutoSpec metastable ion fragmentation and CID were analyzed by the MIKE technique using the following conditions. Set-up of the ion source is described and focusing of the selected precursor ions by the appropriate magnetic field into the third FFR between the magnetic analyzer and the second ESA. The MIKE spectrum was obtained by scanning the deflecting voltage of the second ESA. For optimizing the signal/noise ratio 20–50 single spectra were accumulated. CID of the selected precursor ions was studied by the same technique and set-up of the instrument but introducing Ar into the collision chamber of the third FFR until the intensity of the ion main beam was reduced to 30–50% of its original value.

2.2. Computations

The ab initio calculations were performed using the GAUSSIAN 98 package of programs [17]. The search for possible minima on the hypersurface and the geometry optimization of the species of interest was achieved first by the semi-empirical method PM3. This method detects reliably the most stable conformation of the neutrals and of the molecular ions, but in the case of open-chain distonic ions several minima on the potential energy were found with differently coiled conformations of the propoxy chain. The energy of these conformations differs only by a few kilojoules per moles, and it is not always guaranteed

that the most stable one was found. The geometry of the structures found were re-optimized by ab initio methods using UHF/3-21G*. For the location and geometry optimization of transition states the routine Opt = QST2 or Opt = QST3 of the GAUSSIAN 98 package and UHF/3-21G* were used. All species at the stationary points of the MERPs were characterized by calculation of harmonic vibrations with only transition state giving one imaginary vibration. The zero point energy correction (ZPE) was derived from the frequencies calculated at the UHF/3-21G* level of theory. Finally, the electronic energy E_{el} of all species was obtained using single point calculation at the B3LYP/6-311G* level of theory, and the zero point energy E_0 was derived by adding the ZPE from the UHF/3-21G* calculation. Since it has been stated that energy calculation by the DFT B3LYP method is not very sensitive to slight changes in the geometry of species at potential energy minima [18], this procedure B3LYP/6-311G*//UHF/3-21G* is a reasonable compromise between computational economy and reliability of the calculations of the rather large systems of this paper. However, it is uncertain, whether this holds also for transition states. It should be noted that for an estimation of a MERP only relative energies are required, hence some systematic errors of the methods used cancel. Further, for the construction of a MERP the aim of ab initio calculations is the selection of the appropriate intermediates rather than to obtain accurate numbers for their energy. This justifies the use of B3LYP/6-311G*//UHF/3-21G*.

3. Results and discussion

*3.1. The mechanism of elimination of CH_2O from molecular ions of benzaldoxime-O-n-propyl ether (**1**)*

The 70 eV mass spectrum of **1**, the mass-analyzed ion kinetic energy (MIKE) spectrum of the molecular ion $\mathbf{1}^{\bullet+}$ $C_{10}H_{12}NO^{\bullet+}$ ($M^{\bullet+}$, *m/z* 163), and the spectrum obtained by CID of $M^{\bullet+}$ are shown in Fig. 1a–c. The EI mass spectrum (Fig. 1a) agrees well with published data [11], and the relative intensity of the ion $[M - CH_2O]^{\bullet+}$ of interest here is about 9% (after ^{13}C-correction from the ion $[M - CH_3O]^+$, *m/z* 132). Interestingly, high mass resolution of the peak *m/z* 133 reveals a small contribution of $[M - NO]^{\bullet+}$ which may indicate some additional rearrangement of $\mathbf{1}^{\bullet+}$ (see Section 3.2). Loss of CH_2O from $M^{\bullet+}$ gives rise to the most abundant fragment ion *m/z* 133 in the MIKE spectrum (Fig. 1b), and the peak of the ion $[M - CH_3O]^+$, *m/z* 132, gives rise only to a shoulder of the signal at *m/z* 133, accounting for less than 10% of the total signal. Other significant peaks in the MIKE spectrum appear at *m/z* 162 ($[M - H]^+$), *m/z* 121 ($[M - C_3H_6]^{\bullet+}$), *m/z* 119 ($[M - C_2H_4O]^{\bullet+}$), *m/z* 104, and *m/z* 86.This last signal arises from the loss of a phenyl radical from $\mathbf{1}^{\bullet+}$, a fragmentation not expected to occur at low energy for ions of the structure of $\mathbf{1}^{\bullet+}$. As expected the spectrum obtained by CID of $M^{\bullet+}$ exhibits signals of additional fragment ions similar to those of the 70 eV EI spectrum. However, the ion $[M - CH_2O]^{\bullet+}$ remains one of the most abundant ions in this spectrum, contrasting the rather small intensity of this ion in the EI mass spectrum. Therefore, it is clear from the spectra shown in Fig. 1 that elimination of CH_2O from $M^{\bullet+}$ of **1** is a process of low critical energy, but also a slow process as expected for a rearrangement reaction.

For elucidation of the mechanism of this fragmentation of $M^{\bullet+}$ by a rearrangement reaction the stationary points of the MERP were examined by ab initio calculation at the B3LYP/6-31G*//UHF/3-21G* level of theory using the GAUSSIAN 98 program package [17].The results of these calculations are collected in Table 1. As already suggested by Cooks and Varvoglis [11] it was assumed that the rearrangement of $M^{\bullet+}$ starts with the formation of a distonic ion by migration of a H-atom from the γ-CH_3 group of the *O*-propyl chain. Terminus of this H migration can be either the N- or the O-atom of the oxime group, resulting in the distonic iminium ion C_6H_5–CH=NH^+–O–$CH_2CH_2CH_2^\bullet$ (**1Ndist**) and the distonic oxonium ion C_6H_5–CH=N–OH^+–$CH_2CH_2CH_2^\bullet$ (**1Odist**), respectively. An essential requirement of the rearrangement reaction is that it has to

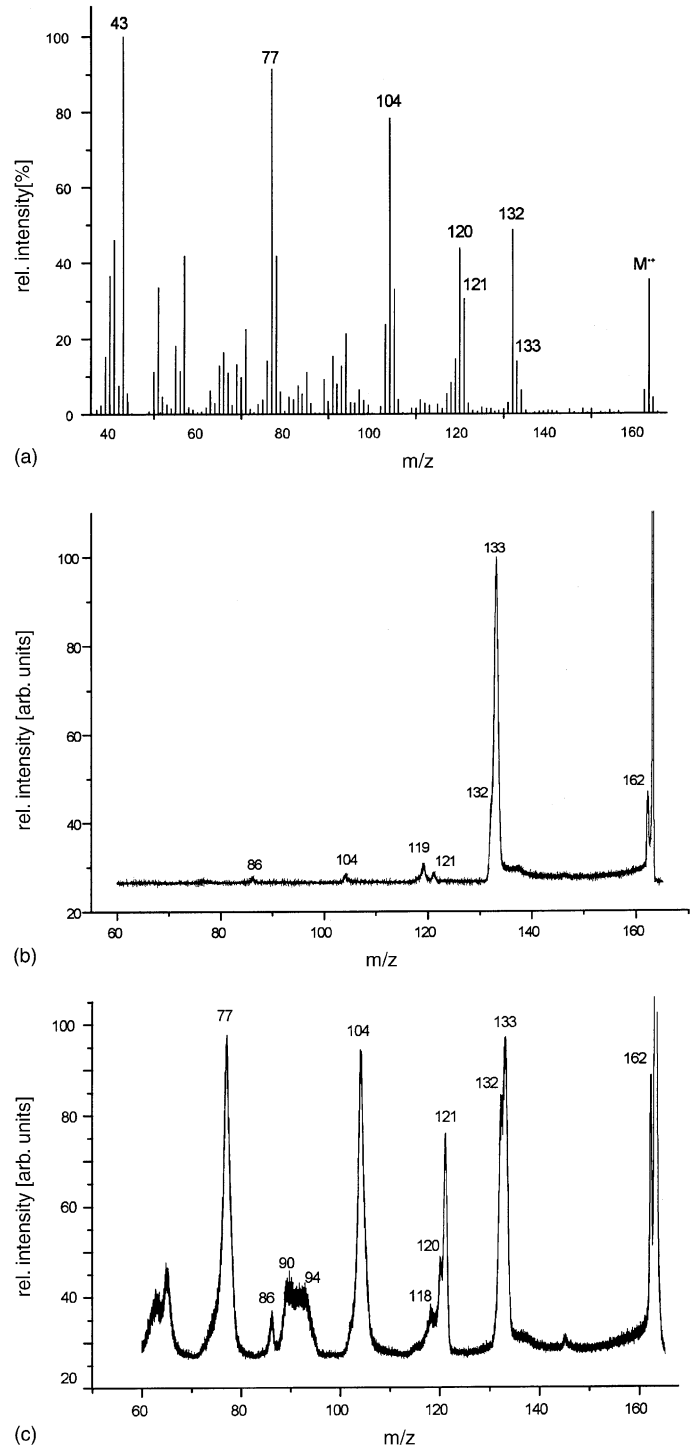


Fig. 1. (a) EI mass spectrum; (b) MIKE spectrum of $M^{\bullet+}$; (c) CA mass spectrum of $M^{\bullet+}$ of **1**.

Table 1
Electronic energy, E_{el}, zero point energy correction and relative zero point energy E_0^r of relevant species calculated by ab initio methods

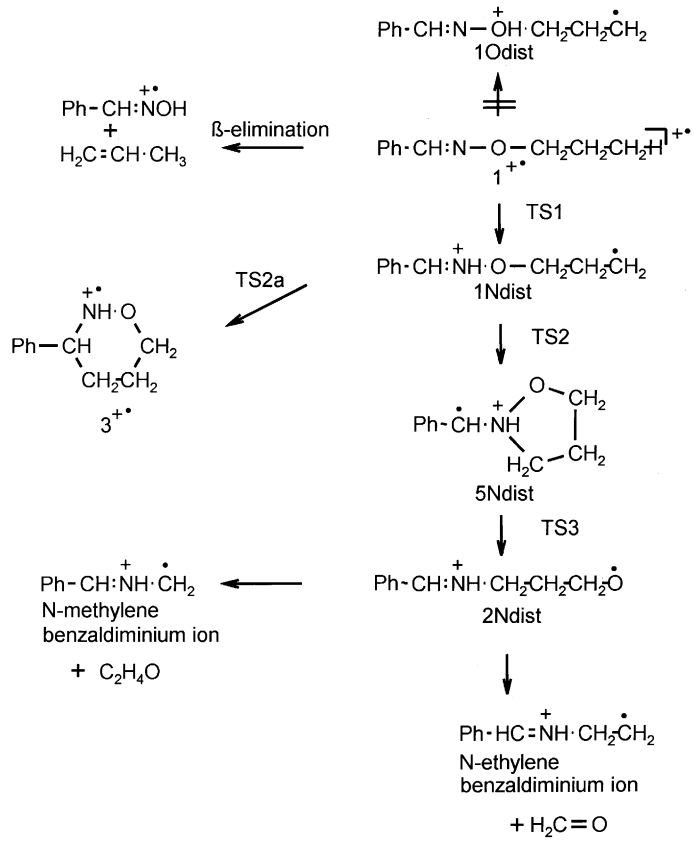
Species	E_{el} (B3LYP/6-311G*) (Hartree)	ZPE (UHF/3-21G*) (Hartree)	E_0^r (kJ/mol)
1$^{\bullet+}$	−518.645824	0.225356	0
1Odist	−518.580808	0.223435	166[a]
TS1	−518.604573	0.218836	91[a]
1Ndist	−518.615603	0.226057	81[a]
TS2	−518.608108	0.223163	93[a]
5Ndist	−518.636180	0.227866	32[a]
TS2a	−518.646044	0.223565	6[a]
3$^{\bullet+}$	−518.646928	0.230329	10[a]
2Ndist	−518.683356	0.230595	−85[a]
2$^{\bullet+}$	−518.670232	0.225142	−65[a]
TS4a	−518.659276	0.229279	−25[a]
4$^{\bullet+}$	−518.674025	0.230113	−62[a]
[**4** − H]$^+$	−518.161805	0.222220	−56[a,b]
Benzaldoxime$^{\bullet+}$	−400.668398	0.133862	102[a]
Propene	−117.932317	0.085399	102[a]
N-Ethylene benzaldimine$^{\bullet+}$	−404.119000	0.192128	−41[a]
Formaldehyde	−114.538129	0.028975	−41[a]
N-Methylene benzaldimine$^{\bullet+}$	−364.811345	0.158966	4[a]
Oxirane	−153.827963	0.061407	4[a]
N-Vinyl benzaldimine$^{\bullet+}$	−403.556585	0.182640	133[b,c]
Tetrahydroisoquinoline molecular ion	−404.126149	0.194596	−12[b]
Tetrahydroisoquinoline distonic ion	−404.150509	0.194506	−76[b]
TS(subst)	−404.104080	0.190471	35[b]
Dihydroisoquinolinium ion	−403.590844	0.186169	53[b,c]
2-Phenyl-azetidine$^{\bullet+}$	−404.086269	0.192549	87[b]
TS(cycl)	−404.078390	0.187980	96[b]
Styrene$^{\bullet+}$	−309.416371	0.142146	107[b]
Formimine	−94.654709	0.042813	107[b]
Benzaldimine$^{\bullet+}$	−325.435246	0.127151	173[b]
Ethene	−78.607743	0.055080	173[b]
H$^{\bullet}$	−0.502156	–	–

[a] E_0 relative to E_0(**1**$^{\bullet+}$).
[b] H$^{\bullet}$.
[c] E_0 relative to E_0(*N*-ethylene benzaldimine$^{\bullet+}$).

compete favorably with other fragmentation reactions of the radical cations of oxime-*O*-alkyl ethers to be observed in the MIKE spectrum of M$^{\bullet+}$. Typically, the fragmentation of ionized oxime-*O*-alkyl ethers occurs by elimination of the *O*-alkyl group as a neutral alkene [11,12]. This fragmentation is already abundant in the mass spectrum of benzaldoxime-*O*-ethyl ether and continues to give a significant peak in the mass spectra of higher *O*-alkyl ethers. In the case of **1** this fragmentation corresponds to the loss of propene C_3H_6, and the corresponding peak at *m*/*z* 121 is clearly seen in all three types of mass spectra of **1** presented in Fig. 1. It is assumed that this fragmentation is a β-elimination resulting in the oxime radical cation and an 1-alkene [11], but the details of the fragmentation mechanism are not known. However, for the present purpose of setting a limiting energy level for the rearrangement reactions of **1**$^{\bullet+}$ it is sufficient to assume that the elimination generates benzaldoxime radical cation and propene, because these are the most stable products which can be formed by elimination of C_3H_6 from M$^{\bullet+}$. Hence, a reaction of M$^{\bullet+}$ with an critical energy below the threshold of the β-elimination will also be lower in energy for

any other products of the C_3H_6 elimination. The data given in Table 1 for the calculated potential energy E_0 of $M^{\bullet+}$, of the benzaldoxime radical cations, and of propene define this energy level at 102 kJ/mol above $E_0(M^{\bullet+})$. The ΔE_0^r(**1Odist**), defined as the potential energy relative to $E_0(M^{\bullet+})$ as the starting point of all fragmentations, corresponds to 166 kJ/mol, while ΔE_0^r(**1Ndist**) is only 81 kJ/mol, reflecting the higher energy gain by protonation of the more basic oxime-N atom. These data definitely exclude **1Odist** as an intermediate of the CH_2O elimination reaction. ΔE_0^r(**1Ndist**) is well below the limiting energy level, but for this ion to be a competitive intermediate it is crucial that the potential energy of the transition state of the 1,5-hydrogen shift generating **1Ndist**, ΔE_0^r(**TS1**), stays also below the limiting energy level. This is indeed the case with ΔE_0^r(**TS1**) = 87 kJ/mol.

The elimination of CH_2O requires a further rearrangement of **1Ndist** by a transposition of the benzaldiminium moiety $(C_6H_5–CH=NH)^+$ from the O-atom to the terminal $^{\bullet}CH_2$ radical site, which generates the distonic isomer $C_6H_5–CH=NH^+–CH_2CH_2CH_2O^{\bullet}$ (**2Ndist**) of *N*-(3-hydroxypropyl)benzaldimine radical cation ($\mathbf{2}^{\bullet+}$). The ab initio calculation shows that this δ-distonic iminium ion is very stable with ΔE_0^r(**2Ndist**) = −85 kJ/mol. The large energy gain of 166 kJ/mol by the transformation of **1Ndist** into **2Ndist**, which makes the rearrangement **1Ndist** → **2Ndist** very exothermic, is explained reasonably by the increased stability of an O-radical compared to a primary C-radical. The transformation **1Ndist** → **2Ndist** may start by the attack of the terminal $^{\bullet}CH_2$ group on the (protonated) C=N double bond of the oxime group either in a five- or in a six-membered transition state (exo- or endo-trig radical cyclization). In the latter case the molecular ion of $\mathbf{3}^{\bullet+}$ is formed as an intermediate. The role of $\mathbf{3}^{\bullet+}$ in the gas phase ion chemistry of $\mathbf{1}^{\bullet+}$ and **1Ndist** will be discussed in the next section, but it is difficult to envisage the formation of **2Ndist** or the β-distonic *N*-ethylene benzaldiminium ion by loss of CH_2O from $\mathbf{3}^{\bullet+}$. Exo-trig ring closure of **1Ndist** by attack on the N-atom gives rise to an α-distonic isomer (**5Ndist**) of the molecular ion of *N*-benzyl-1,2-oxazolidine (**5**), in which one of the benzylic hydrogens of **5** has been shifted to the N-atom. According to ab initio calculation this interesting distonic ion **5Ndist** is quite stable with ΔE_0^r = 32 kJ/mol. However, contrary to the formation of $\mathbf{3}^{\bullet+}$ the cyclization of **1Ndist** to **5Ndist** requires a considerable critical energy. Nonetheless, the calculated potential energy ΔE_0^r(**TS2**) = 93 kJ/mol of the transition state **TS2** is still below the limiting energy level of the β-elimination from $\mathbf{1}^{\bullet+}$. The distonic ion **5Ndist** is an attractive intermediate for the interconversion of **1Ndist** and **2Ndist**, since this requires only the cleavage of the N–O– and the N–C– bond, respectively, at the central tetrahedral nitrogen. In addition, formation of **5Ndist** as an essential intermediate provides a satisfying explanation why the loss of CH_2O is abundant only in the mass spectra of *O*-oxime ethers of aromatic aldehydes and ketones, since stabilization of the radical site of distonic ions analogous to **5Ndist** by at least one aromatic substituent is prerequisite for the stability of this intermediate. While the transition state **TS2** for the ring closure **1Ndist** → **5Ndist** was correctly found by ab initio calculation, we were not able to locate transition state **TS3** for the ring opening **5Ndist** → **2Ndist**. All transition states located by the routines of the GAUSSIAN 98 program for this reaction had a potential energy well below that of **5Ndist** and turned out to be instead transition states for the conversion between different conformations of **2Ndist**. Nonetheless, **5Ndist** was correctly characterized as a stable species by the calculations of the frequencies and not as a transition state. Very likely the critical energy for the very exothermic ring cleavage **5Ndist** → **2Ndist** is small and may have escaped detection. Eventually, **2Ndist** fragments to eliminate CH_2O and C_2H_4O (probably oxirane) by simple bond cleavages to generate the β-distonic *N*-ethylene benzaldiminium ion and α-distonic *N*-methylene benzaldiminium ion, respectively. Of these two reactions, the elimination of CH_2O is energetically more favorable, but the potential energy level defined by the products of the loss of C_2H_4O is still below the limiting energy level of the β-elimination. D-labeling has shown that the elimination of C_2H_4O from the molecular ions of **1** leaves the atoms of the γ-CH_3 group of



Scheme 4.

the propyl chain in the resulting product ion. This was originally interpreted as a corresponding methyl shift in $\mathbf{1}^{\bullet+}$ [12]. The present results disprove a methyl shift and show that instead the atoms of the γ-CH_3 group are transferred in two separate reaction steps. First one H-atom of the γ-CH_3 is transferred to the N-atom of the oxime moiety in the initial rearrangement step to yield **1Ndist**, and the remaining CH_2 becomes attached to this N-atom during the transposition of the benzaldiminium group according to the **1Ndist** → **5Ndist** → **2Ndist** reaction sequence. The complete mechanism of the elimination of CH_2O (and C_2H_4O) from $\mathbf{1}^{\bullet+}$ is formulated in Scheme 4 and the MERP constructed by the data of Table 1 is presented in Fig. 2.

To complete the MERP of the elimination of CH_2O we shortly examined the fate of the resulting *N*-ethylene benzaldiminium ion in the mass spectrum of **1**. The MERP for the reaction of the *N*-ethylene benzaldiminium ion is shown in Fig. 3 and the reactions are depicted by formula in Scheme 5. Cooks and Varvoglis [11] have suggested that loss of H, which is the most abundant reaction of the *N*-ethylene benzaldiminium ion in its MIKE spectrum and on CID, occurs from the ethylene group to produce a *N*-vinyl benzaldiminium ion. While this appears to be a reasonable and stable product ion, its formation is not consistent with the D-labeling data. These demonstrate that at least 90% of the H-atoms lost stem from the aromatic ring, as expected for the proposed intramolecular aromatic substitution [13]. The ab initio calculation now shows that this route resulting in a 3,4-dihydrosiocquinolinium ion is energetically much more favorable than formation of

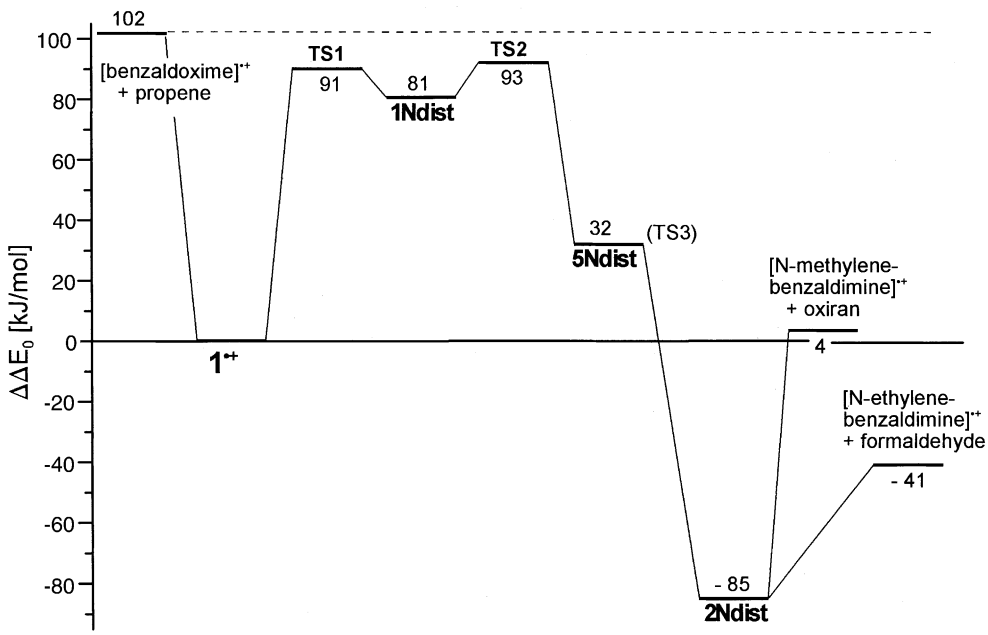


Fig. 2. MERP for the fragmentation of the radical cation of **1**.

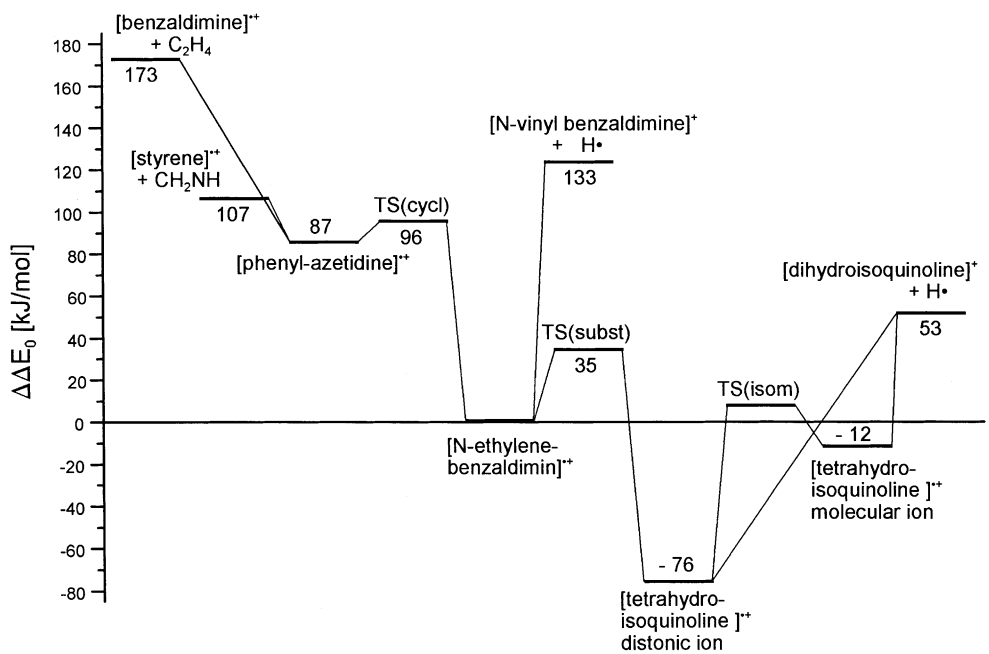
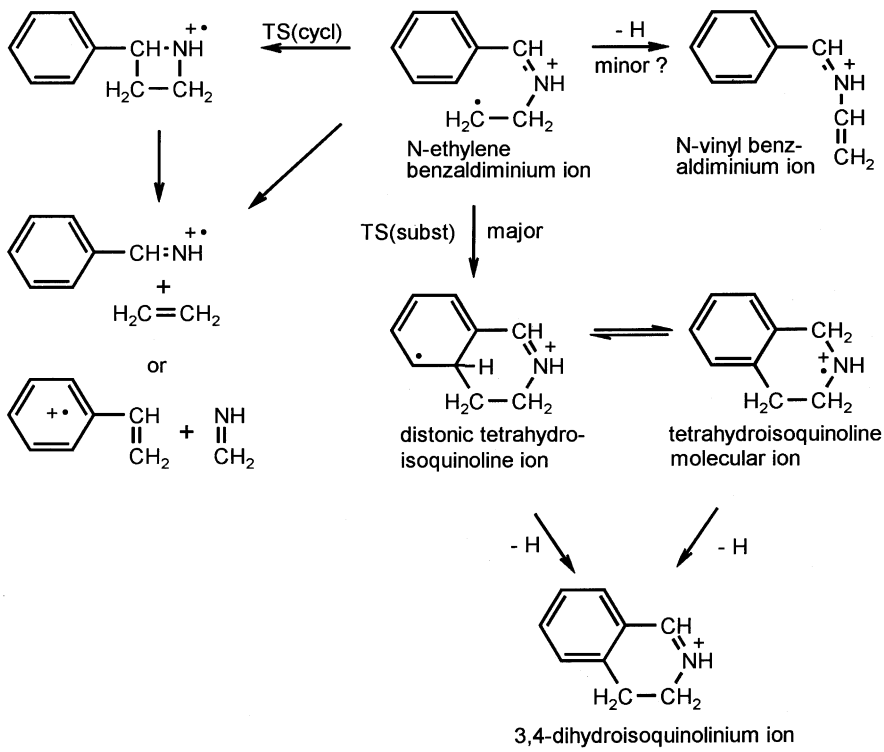


Fig. 3. MERP for the fragmentation of the *N*-ethylene benzaldimine distonic ion.

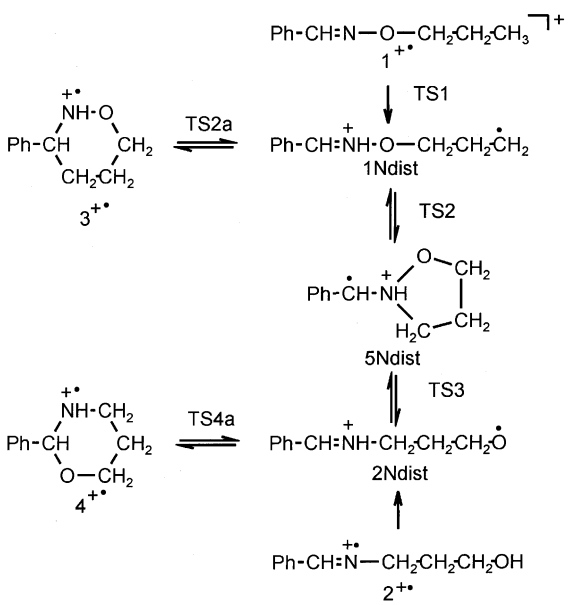


Scheme 5.

a *N*-vinyl benzaldiminium ion. The calculation also demonstrates that H-migration by 1,2-shifts within the distonic tetrahydroisoquinoline radical cation, produced by the radical attack in the *N*-ethylene benzaldiminium ion on the phenyl ring, appears feasible. This agrees with the reported loss of substituents from the aromatic ring in related ions [13]. A second possible reaction route of the *N*-ethylene benzaldiminium ion is a cyclization affording a *N*-phenyl azetidine which may fragment either by loss of ethylene and formation of the molecular ion of benzaldimine or by loss of formimine and formation of the styrene radical cation. Indeed, high mass resolution experiments showed that some $C_8H_8^{\bullet+}$ ions besides $C_7H_6N^{\bullet+}$ ions contribute to the signal *m*/*z* 104 in the EI mass spectrum of **1**, but in agreement with the ab initio calculations this fragmentation route is open only for *N*-ethylene benzaldiminium ions of high internal energy.

3.2. Possible interconversions of isomeric $[C_{10}H_{13}NO]^{\bullet+}$ ions $\mathbf{1}^{\bullet+}$, $\mathbf{2}^{\bullet+}$, $\mathbf{3}^{\bullet+}$, $\mathbf{4}^{\bullet+}$

As mentioned in Section 3.1, the distonic ion **1Ndist** derived from $\mathbf{1}^{\bullet+}$ by a 1,5-H shift from the terminal CH_3 group to the oxime N-atom may be easily converted by an endo-trig cyclization involving a six-membered transition state into the molecular ion $\mathbf{3}^{\bullet+}$ of *2H*-3,4,5,6-tetrahydro-3-phenyl-1,2-oxazine. Such an isomerization would explain the observation of some ions $[M - NO]^{\bullet+}$ in the EI mass spectrum of **1**. Similarly, the distonic ion **2Ndist** may undergo endo-trig cyclization to provide the molecular ion $\mathbf{4}^{\bullet+}$ of *2H*-3,4,5,6-tetrahydro-3-phenyl-1,3-oxazine. This isomerization would account for the detection of ions $[M - C_6H_5]^+$, *m*/*z* 86 in the MIKE spectrum of $\mathbf{1}^{\bullet+}$. Further, since the distonic ions **1Ndist** and **2Ndist** may interconvert by the five-membered cyclic distonic ion **5Ndist**, it is conceivable that the



Scheme 6.

structures of all these isomeric ions $[C_{10}H_{13}NO]^{\bullet+}$ play a role in the mass spectrometric decomposition of the corresponding isomeric compounds **1**–**4** (Scheme 6). To test this possibility, the 70 eV mass spectra of **1**, **3**, and **4**, the MIKE spectra of the respective molecular ions and the spectra of the CID of the molecular ions were examined (see Figs. 1 and 4). In the case of **4** the compound studied is a mixture of the cyclic tautomer *2H*-3,4,5,6-tetrahydro-3-phenyl-1,3-oxazine (**4**) and the open-chained tautomer (**2**). This tautomeric system has been studied before by mass spectrometry [19], but it is not clear which of the tautomers prevails in the gas phase of a mass spectrometer. Additionally, the MERP of the isomerization of the relevant radical cations $[C_{10}H_{13}NO]^{\bullet+}$ was determined by ab initio calculation. This result is shown in Fig. 6.

The EI mass spectra of **1**, **3**, and **4** exhibit indeed all a significant peak of ion $[M - CH_2O]^{\bullet+}$. As already mentioned, the peak at *m*/*z* 133 in the EI mass spectrum of **1** contains a small contribution of ions $[M - NO]^{\bullet+}$, and this is also observed in the mass spectrum of **3**, but not of **4**. Most importantly, the MIKE- and CA-spectra of the ions $[M - CH_2O]^{\bullet+}$ derived from **1**, **3**, and **4** are identical (Fig. 5), so the structure of a β-distonic *N*-ethylene benzaldiminium ion is assigned to this ion in all three cases.[1] Obviously, the fragmentation of all three isomeric molecular ions to the same ion $[M - CH_2O]^{\bullet+}$ should entail also identical intermediates. However, the EI mass spectra of these isomers are different, excluding a rapid and complete equilibration of the molecular ions before fragmentation. Further, characteristic fragment ions of each of these mass spectra can be easily linked to the original structure of the molecular ion. Thus, the mass spectrum of *2H*-3,4,5,6-tetrahydro-3-phenyl-1,2-oxazine (**3**) is distinguished by a very intense peak at *m*/*z* 104, and the mass spectrum of **4** exhibits only a rather small peak of the molecular ions at *m*/*z* 163 and a much more intense peak of ions $[M - H]^+$, *m*/*z* 162, which is explained by a facile loss of the H-atom from C_2 resulting in an ion $[M - H]^+$ stabilized by resonance. This is also indicated by the very large peak of ion $[M - H]^+$ in the MIKE spectrum of $\mathbf{4}^{\bullet+}$. Further, the mass spectrum of **4** shows intense peaks at *m*/*z* 119 and *m*/*z* 118 of ions $[M - C_2H_4O]^{\bullet+}$ and $[M - C_2H_5O]^+$, which may indicate the presence of the open chain tautomer **2** [19], and a large peak at *m*/*z* 105 of benzoyl ions, which incorporate the C_7H_5O moiety of **4**. In addition, a characteristic peak at *m*/*z* 86 of ions $C_4H_7NO^+$ is observed, which arise from the loss of the phenyl substituent at C_2 to produce an ion stabilized by resonance.

According to the ab initio calculations the potential energy $E_0(\mathbf{4}^{\bullet+})$ is larger than that of the open-chained distonic isomer **2dist**, so loss of CH_2O from $\mathbf{4}^{\bullet+}$ by ring opening and bond cleavage in the resulting **2dist** is uncomplicated. The MIKE spectrum of $\mathbf{4}^{\bullet+}$ shows, however, that fragmentation by loss of CH_2O can hardly compete with the much more favored loss of H, which gives the by far the most abundant peak in the spectrum. It should be noted that although **2dist**

[1] A small additional peak at *m*/*z* 106 appears in the MIKE spectra of the ion $[M - CH_2O]^{\bullet+}$ derived from **4**, indicating the presence of a small amount of an unknown second species at *m*/*z* 133. The intensity of this peak does not increase by CID.

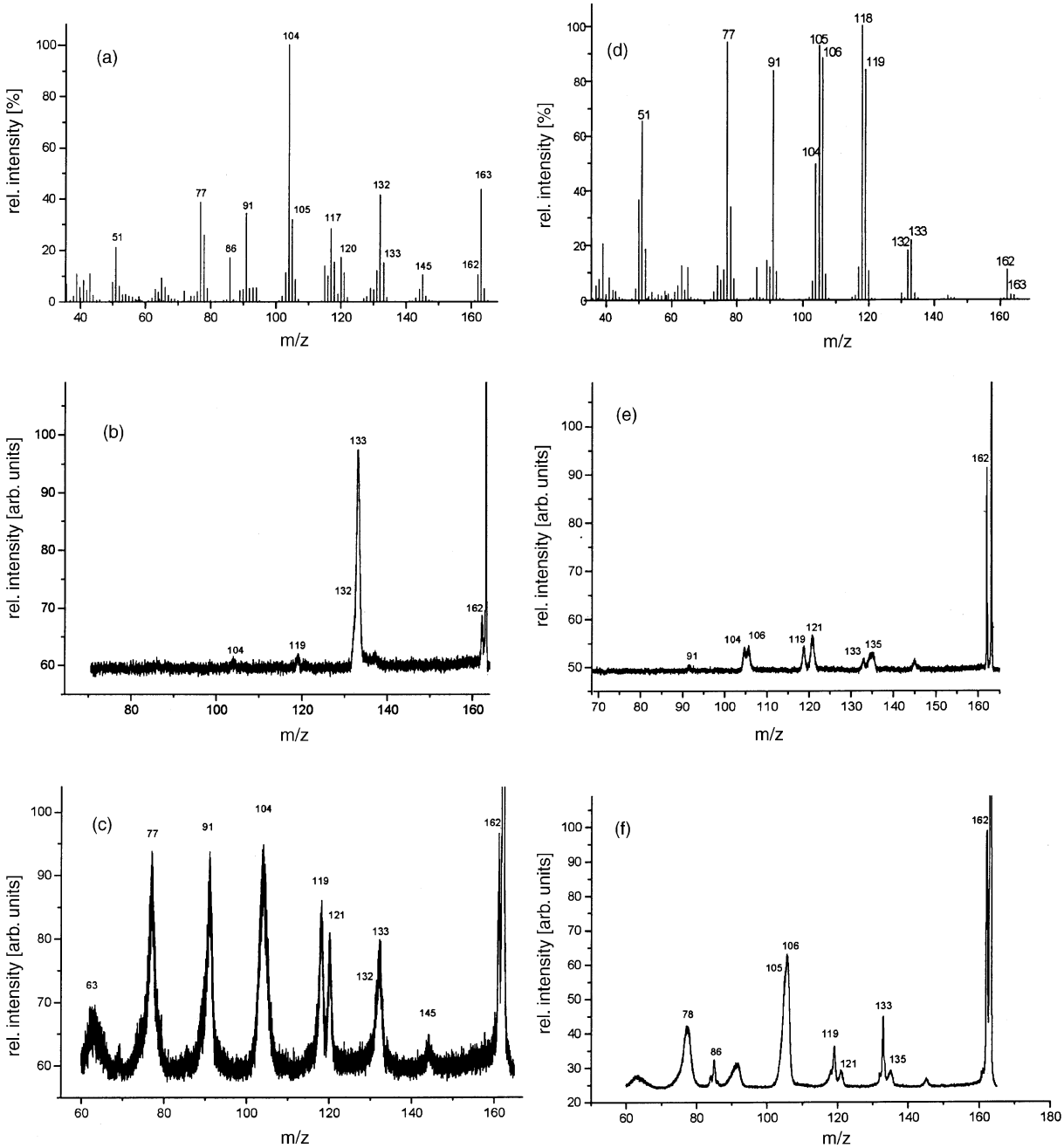


Fig. 4. (a) EI mass spectrum; (b) MIKE spectrum of $M^{\bullet+}$; (c) CA mass spectrum of $M^{\bullet+}$ of 3-phenyl-tetrahydro-1,2-oxazine (**3**) (d) EI mass spectrum; (e) MIKE spectrum of $M^{\bullet+}$; (f) CA mass spectrum $M^{\bullet+}$ of 2-phenyl-tetrahydro-1,3-oxazine (**4**).

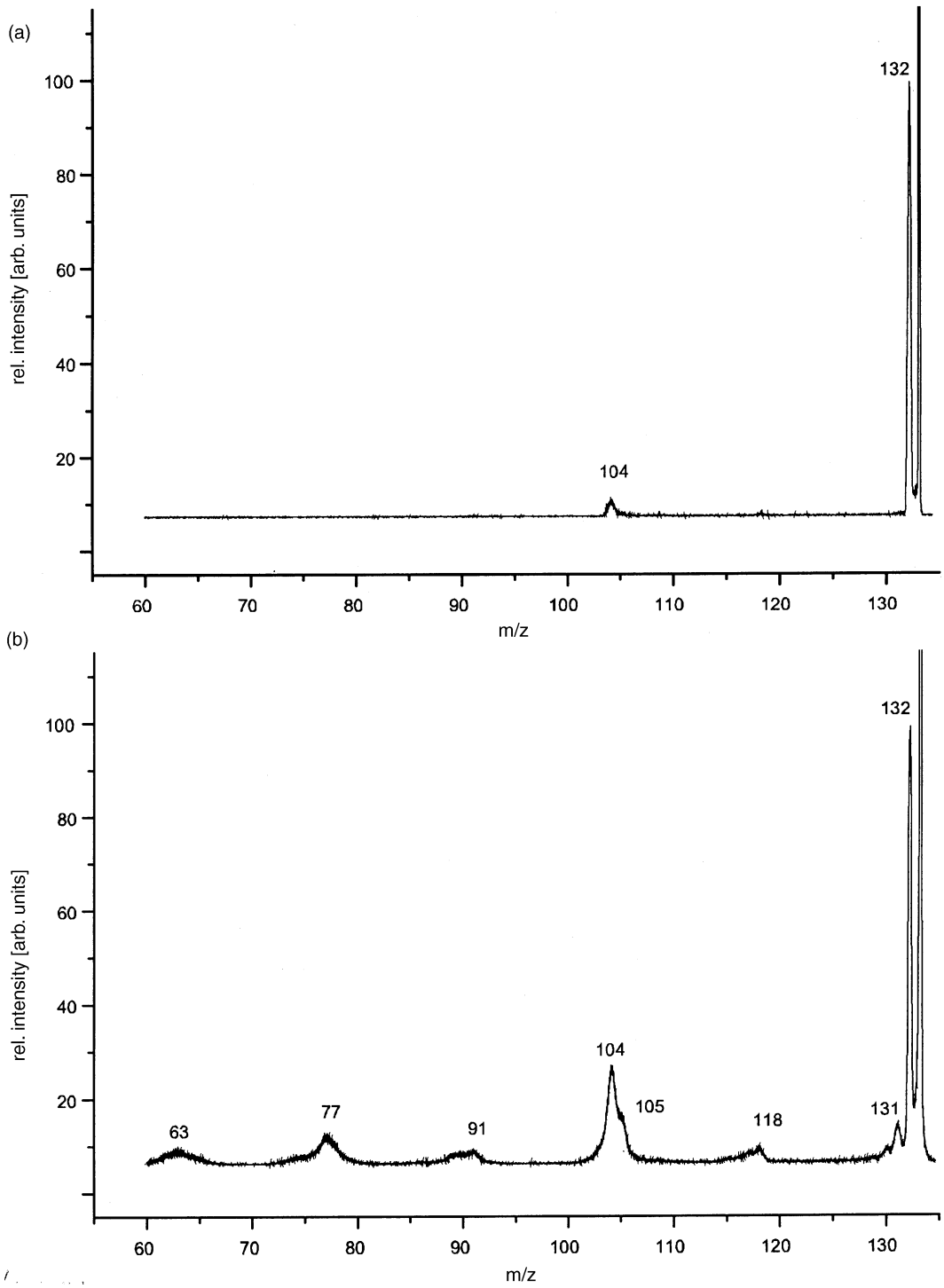


Fig. 5. (a) MIKE spectrum of $[M - CH_2O]^{\bullet+}$, and (b) CA mass spectrum of $[M - CH_2O]^{\bullet+}$ from **1**, **3**, or **4**.

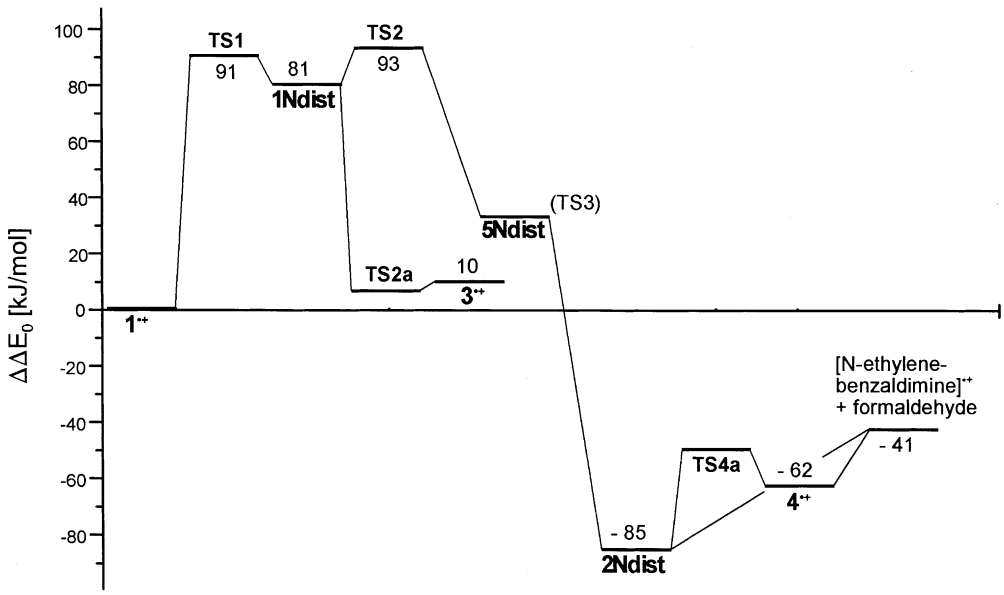


Fig. 6. MERP for the isomerization and fragmentation of $C_9H_{14}NO$ radical cations of **1**, **2**, **3**, and **4**.

is a common intermediate in the decomposition of the molecular ion of **1** and **4**, it arises from $\mathbf{1}^{\bullet+}$ by a sequence of rearrangements with much more internal energy than from $\mathbf{4}^{\bullet+}$ (see MERP in Fig. 6). If the molecular ions $\mathbf{4}^{\bullet+}$ surviving in the ion source are energetically activated by collision in the third FFR of the VG AutoSpec mass spectrometer, the relative intensity of the ions $[M - CH_2O]^{\bullet+}$ increases considerably. Thus, the differences with respect to the ion intensity of ions $[M - CH_2O]^{\bullet+}$ in the MIKE spectra and CID spectra of $\mathbf{1}^{\bullet+}$ and $\mathbf{4}^{\bullet+}$ are safely explained by a different excess energy of the common intermediate **2dist** from the two different sources. The loss of CH_2O directly from a radical cation of structure **3** is not likely because of the formation of a distonic ion containing an unstable nitrene cation and an unfavorable primary C-radical. Hence, the elimination of CH_2O from $\mathbf{3}^{\bullet+}$ occurs more easily by C–C ring cleavage at the benzylic position to produce the distonic intermediate **1dist** which subsequently follows the same rearrangement and fragmentation route as if derived from $\mathbf{1}^{\bullet+}$. In line with the argument, that $\mathbf{1}^{\bullet+}$ and $\mathbf{3}^{\bullet+}$ produce the essential intermediate **2dist** with similar internal energy by the same rearrangement processes is the observation that the MIKE spectra of the molecular ions of **1** and **3** are almost identical. Both are characterized by the most intense peak at *m*/*z* 133 due to the loss of CH_2O and a shoulder for ions at *m*/*z* 132 formed by the additional loss of H. Thus, the conclusion of this section is that the molecular ions of the $C_{10}H_{13}NO$ isomers **1**, **3**, and **4** do not equilibrate prior to fragmentation. Nonetheless, some of the fragmentation routes, in particular the loss of CH_2O, incorporate the same intermediates, but the excess energy in these intermediates is different because of different energy levels at the starting point of their generation. This is reflected in intensity variations of competing reaction channels in particular of isomer **4**.

4. Conclusion

The molecular ions of oxime-*O*-alkyl ether, especially those of aromatic aldehydes and ketones, with a linear alkyl chain contains at least three C-atoms eliminate CH_2O and C_2H_4O fragments. It has been

proven by a mass spectrometric investigation of **1** and its deuterated derivatives that these fragments contain specifically the α- and β-CH_2 groups of the propyl chain, respectively. Obviously, these fragmentations occur by a rearrangement reaction in which the imine functionality of the oxime migrates from the O-atom to the γ-C atom of the ether alkyl chain. The study of this reaction by ab initio calculation, combined with the results of a D-labeling study, show that this fragmentation is a new example of a functional group migration along an aliphatic chain by the Longevialle mechanism. In the case of $\mathbf{1}^{\bullet+}$ the initial δ-distonic ion **1dist** is generated by a 1,5-H shift from the γ-CH_3 group of the propoxy chain to the N-atom of the oxime function. Subsequent ring closure by addition of the radical site to the protonated N-atom forms the new distonic ion **5dist**. These rearrangements turn out to be the most energy demanding steps of the total reaction, but the energy required is still less than the energy needed for a competing β-elimination of the *O*-alkyl group. Ring opening of **5dist** to the distonic ion **2dist**, a distonic isomer of the molecular ion of **2**, is highly exothermic, and the further fragmentation of **2dist** by losses of CH_2O and C_2H_4O is straightforward. Thus, these eliminations are the result of the formation of three distonic ions in sequence, and the functional group migration in the mass spectra of suitable oxime-*O*-alkyl ethers described in this paper is a striking example of the importance of distonic ions for the Longevialle mechanism of functional group transposition along aliphatic chains.

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