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Isomeric dependence of the formation of ion/neutral complexes in dissociation reactions of ionized propoxypyridines

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Abstract

The mechanistic aspects of the dissociation reactions of the molecular ions of isomeric propoxypyridines have been examined with the use of deuterium labelling and tandem mass spectrometry. The ionized 2- and 3-propoxypyridines dissociate predominantly by the loss of propene, whereas the molecular ions of 4-propoxy- and 4-isopropoxypyridine react by the competing losses of a propene molecule and an allyl radical. The loss of propene from the metastable molecular ions of the 2-isomer involves a 1,5-H shift from the 2-position of the propyl group to the ring as evidenced by the labelling experiments. For the metastable molecular ions of 3-propoxypyridine, the results are in agreement with propene loss by a pathway involving formation of a $[C_5H_4NO^{\cdot}/(CH_3)_2CH^+]$ complex which reacts further by proton transfer prior to dissociation. In contrast to these findings, interchange between the hydrogen atoms at the 2-position of the propyl group, and the 3- or 5-position of the pyridine ring, occurs in ionized 4-propoxypyridine. This interchange can precede the formation of a $[C_5H_4NO^{\cdot}/(CH_3)_2CH^+]$ complex and the occurrence of proton transfer within this species. The $[C_5H_5NO^{+\cdot}/C_3H_6]$ complex formed in the proton transfer step may either expel propene or react by hydrogen atom transfer prior to the loss of an allyl radical. For the metastable ions of 4-isopropoxypyridine, interchange between a hydrogen atom from one of the methyl groups of the alkyl chain and the aromatic ring appears to be of minor importance. (Int J Mass Spectrom 199 (2000) 1–16) © 2000 Elsevier Science B.V.

Keywords: Propoxypyridines; Ion/neutral complexes; Reaction mechanism; Metastable ions; Deuterium labelling

1. Introduction

The dissociation reactions of (radical) cations of various organic molecules are commonly viewed as involving intermediate formation of noncovalently bonded complexes as discussed in a number of reviews [1–6]. These ion/neutral complexes are considered to be short-lived species whose existence is manifested in the results of labelling experiments and the energetics of the unimolecular reactions. Notwithstanding that the ion/neutral complexes are not observed directly, a large number of apparently simple dissociation reactions has been suggested to proceed with the intermediacy of such species. The reported examples include the loss of CO from aliphatic acylium ions [7,8], the elimination of an alkene from oxonium [5] or immonium ions [9], and the loss of alkenes or the formation of an alkyl carbenium ion in the dissociations of protonated alkyl arenes [10–12].

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Dedicated to Professor Henri-Edouard Audier on the occasion of his 60th birthday and for his friendship and important contributions to gas-phase ion chemistry.

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In the discussions of ion/neutral complexes as intermediates in dissociation reactions, the loss of an alkene from the molecular ions of alkyl phenyl ethers [13–21] and from the protonated ethers [22–26] has received particular attention. In this respect, the loss of propene from the molecular ion of phenyl propyl ether has been put forward repeatedly as a typical reaction, which can be described adequately only in terms of a pathway involving the formation of an ion/neutral complex composed of a phenoxy radical and a secondary propyl carbenium ion. Subsequently, this complex reacts by proton transfer prior to dissociation with formation of $C_6H_6O^{+\cdot}$ ions, which are known to have the structure of ionized phenol exclusively [13,16,18]. Recently, a more complex mechanistic picture has been advanced for this process on the basis of photoionization experiments with an extended series of deuterium labelled phenyl propyl ethers [21]. This mechanistic picture includes the additional involvement of complexes containing corner-protonated cyclopropane and the loss of propene by a conventional 1,5-H shift from the 2-position of the propyl group to the remaining part of the reactant ion. The occurrence of a 1,5-H shift in ionized alkyl phenyl ethers has been indicated previously for the loss of a pentene molecule from the molecular ion of 2-methyl-2-butyl phenyl ether [14]. For this ionized species, the loss of C_5H_{10} is reported to involve a preference for transfer of a hydrogen atom from the methylene group at the 3 position of the 2-methyl-2-butyl group to the 2 or 6 position of the phenyl ring. Subsequently, a 1,3-H shift to the oxygen atom was suggested to take place prior to the expulsion of C_5H_{10} with formation of ionized phenol. This mechanism was formulated in analogy with the pathway described previously for the process leading to the formation of $C_6H_6O^{+\cdot}$ ions with the phenolic structure by the loss of a halogen substituted ethene from the molecular ions of phenoxy ethyl halides with a relatively high internal energy [27–31]. For these latter species, however, the initial 1,5-H shift to the aromatic ring is reported to be associated in part with the loss of a halogen substituted ethene to afford 2,4-cyclohexadienone radical cations.

The influence of substituents on the aromatic ring on the mechanism of the loss of an alkene was studied recently by our group for an extensive series of substituted aryl propyl ethers [20]. Notably, propene loss from the metastable molecular ions of 3-methoxy and 3-thiomethoxy substituted phenyl propyl ethers was concluded to proceed preferentially by a 1,5-H shift, whereas no evidence for the occurrence of this pathway was obtained for ionized ethers with an electron-withdrawing group such as NO_2 and CF_3. Instead, the results for the molecular ions of the aryl propyl ethers containing a NO_2 or CF_3 group at the 3-position of the ring as well as for the molecular ions of various 4-substituted ethers were concluded to be consistent with propene loss with intermediate formation of ion/neutral complexes. The marked effect of the presence of substituents on the mechanism(s) for propene loss from ionized aryl propyl ethers motivated further studies on the interplay between ion/neutral complex formation and the occurrence of alkene loss by a 1,5-H shift. In the present study, the molecular ions of 2-, 3- and 4-propoxypyridines as well as 4-isopropoxypyridine were selected for a closer study. These species were chosen because they offer an examination of the dependence of the position of the ether function with respect to the nitrogen atom of the ring on the mechanism of propene loss. In particular, the presence of a nitrogen atom in the ring may be thought to influence the formation of ion/neutral complexes composed of a secondary propyl carbenium ion and a $C_5H_4NO^{\cdot}$ radical, as well as the ensuing proton transfer in such a complex prior to propene elimination. Moreover, a previous study has been concerned with the involvement of ion/neutral complexes in the dissociation reactions of the molecular ion of 4-[cyclo-octyloxy]-pyridine [32]. Briefly, the molecular ion of this latter species was observed to expel a cyclo-octenyl radical with formation of protonated 4-hydroxypyridine by a pathway involving the formation of a complex composed of a cyclo-octyl carbenium ion and a $C_5H_4NO^{\cdot}$ radical. Subsequently proton transfer to the nitrogen atom of the $C_5H_4NO^{\cdot}$ radical was suggested to occur prior to hydrogen atom abstraction and the expulsion of the cyclo-octenyl

radical. With the exception of this study and a few reports concerned with dissociation reactions of pyridinium ions [33,34], little is known about the intermediacy of ion/neutral complexes in the reactions of species containing a pyridine ring. This absence of insight reinforced our motivation for a closer examination of the mechanistic details of the unimolecular reactions of isomeric propoxypyridines with the use of deuterium labelling and tandem mass spectrometry.

2. Experimental

2.1. Instrument

The electron ionization (EI), chemical ionization (CI), mass analyzed ion kinetic energy (MIKE) [35], and collision-induced dissociation (CID) [36] spectra were recorded with the use of a Micromass ZAB-2HFqQ reverse-geometry double-focussing quadrupole hybrid mass spectrometer [37,38]. The liquid compounds were introduced into a combined EI/CI ion source through a septum inlet system heated to 150 °C. Solid compounds were introduced with a direct insertion probe. The ion-source conditions were: electron energy 70 eV, acceleration voltage 8 kV, repeller voltage 0 V, and temperature 150 °C. The CID spectra were recorded with a 50% reduction of the main beam intensity and with the use of He as the collision gas. The protonated 4-hydroxypyridine was formed by CI with methanol as the reagent gas according to the procedure described in our CI studies of aryl propyl ethers [24,26].

2.2. Materials and synthesis

The unlabelled 2-, 3-, and 4-hydroxypyridines, 4-chloropyridine, 1,1-d_2-1-propanol, d_8-1-propanol, 2-d_1-2-propanol and d_8-2-propanol were commercially available and used without further purification. The labelled propanols were reacted (if required) with 48% HBr in water in order to obtain the related bromopropanes.

2.2.1. 2,2-d_2-1-propanol and 2,2-d_2-1-bromopropane [39]

The 1-propanol and 1-bromopropane labelled at the 2-position were prepared by repeated hydrogen–deuterium exchange of methylmalonic acid with D_2O to afford $DOOCCD(CH_3)COOD$. Subsequently, decarboxylation of one of the carboxylic groups followed by reduction of the other carboxylic group gave 2,2-d_2-1-propanol. This compound was reacted with 48% HBr in water in order to form 2,2-d_2-1-bromopropane.

2.2.2. 2-propoxypyridine, 3-propoxypyridine and deuterated analogues [40]

The unlabelled 2- or 3-propoxypyridines and their deuterated analogues (2-$CH_3CH_2CD_2$–O–C_5H_4N, 2-$CH_3CD_2CH_2$–O–C_5H_4N, and 3-$CH_3CD_2CH_2$–O–C_5H_4N) were prepared by reacting the 2- or 3-hydroxypyridine with sodium ethanolate followed by reaction with the appropriately labelled 1-bromopropane.

2.2.3. 4-propoxypyridine, 4-isopropoxypyridine and deuterated analogues [41]

The 4-propoxypyridine and the deuterated analogues (4-$CH_3CH_2CD_2$–O–C_5H_4N, 4-$CH_3CD_2CH_2$–O–C_5H_4N, and 4-$CD_3CD_2CD_2$–O–C_5H_4N) were prepared by reaction of 4-chloropyridine with the sodium salt of the appropriate 1-propanol. Likewise, the 4-isopropoxypyridine and the deuterium labelled analogues ($(CH_3)_2CD$–O–C_5H_4N and $(CD_3)_2CD$–O–C_5H_4N) were prepared by reacting 4-chloropyridine with the sodium salt of 2-propanol or the appropriately labelled alcohol.

All propoxypyridines were purified by GC with the use of a Reoplex 400 column (temperature 125 °C). The label contents of the propoxypyridines are given in Table 1.

3. Results

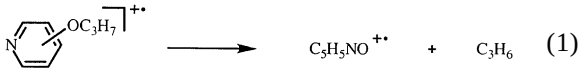
The 70 eV EI mass spectra of the 2-, 3- and 4-propoxypyridines as well as of the 4-isopropoxypyridine are given in Table 2. The base peak in the

Table 1
Label content (in %) of the deuterium-containing (iso)propoxypyridines

Compound	Unlabelled	d_1	d_2	d_5	d_6	d_7
2-$CH_3CH_2CD_2$–O–C_5H_4N[a]		2	98			
2-$CH_3CD_2CH_2$–O–C_5H_4N[b]		11	89			
3-$CH_3CD_2CH_2$–O–C_5H_4N[b]		11	89			
4-$CH_3CH_2CD_2$–O–C_5H_4N[a]		2	98			
4-$CH_3CD_2CH_2$–O–C_5H_4N[b,c]	5	10	85			
4-$CD_3CD_2CD_2$–O–C_5H_4N[a]				2	6	92
4-$(CH_3)_2CD$–O–C_5H_4N[a]	1	99				
4-$(CD_3)_2CD$–O–C_5H_4N[a]				1	2	97

[a] Deuterium content of the commercially available samples of the labelled 1- or 2-propanols (see Experimental).
[b] Label content as determined by 15 eV EI mass spectrometry.
[c] The label content of this compound is lower than of the 2- and 3-$CH_3CD_2CH_2O$–C_5H_4N ethers since a different sample of the 2,2,-dideutero-1-propanol was used in the preparation of this particular species (see also text).

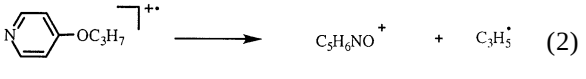
mass spectra for all four isomers corresponds to the loss of propene from the molecular ion [Eq. (1)].



(1)

m/z 137 m/z 95

The molecular ion of the 2-isomer reacts in the ion source also by the competing losses of a methyl and ethyl radical with formation of ions with *m/z* values of 122 and 108, respectively (Table 2). These two latter processes are not observed for the ionized 3-propoxypyridine and are of minor importance for the molecular ions of the 4-propoxypyridine. The ionized 4-propoxypyridine is observed, however, to expel an allyl radical with the formation of ions with a *m/z* value of 96 [Eq. (2)].



(2)

m/z 137 m/z 96

For the molecular ions of 4-isopropoxypyridine, the loss of a methyl radical is a relatively insignificant process, whereas the loss of an allyl radical is somewhat more pronounced than observed for the ionized 4-propoxypyridine. In conclusion, the differences between the isomeric propoxypyridines allow a relatively straightforward distinction between these species on the basis of their mass spectra even though the spectra of the 4-propoxy- and 4-isopropoxypyridines are less dissimilar than the spectra of the 2- and 3-propoxypyridines.

3.1. 2-propoxypyridine

The elimination of propene from the molecular ions of the 2-[1,1-d_2-propoxy]-pyridine in the ion source involves only the loss of $C_3H_4D_2$ as indicated by the negligible abundance of the *m/z* 96 ions ($C_5H_4DNO^{+\cdot}$) (see Tables 2 and 3). On the μs time scale, the molecular ions of 2-propoxypyridine dissociate by the competing losses of an ethyl radical, a formaldehyde molecule, and a propene molecule (Fig. 1). The loss of propene is the most important reaction of the metastable ions and gives rise to a Gaussian shaped metastable peak and a small kinetic energy release, $T_{0.5}$ = 10 meV (as measured from the width at half height of the peak) [35]. For the ionized 2-[1,1-d_2-propoxy]-pyridine, the elimination of propene on the μs time scale involves exclusively the loss of $C_3H_4D_2$. In addition, the metastable molecular ions of the 2-[2,2-d_2-propoxy]-pyridine dissociate by the loss of C_3H_5D; that is, no losses of $C_3H_4D_2$ or C_3H_6 are observed for these ions on the μs time scale (Table 4).

3.2. 3-propoxypyridine

The molecular ions of the 3-[2,2-d_2-propoxy]-pyridine eliminate in the ion source C_3H_5D and

Table 2
Electron ionization (70 eV) mass spectra of the unlabelled 2-, 3- and 4-propoxypyridines and 4-isopropoxypyridine[a]

m/z	2-propoxy-pyridine	3-propoxy-pyridine	4-propoxy-pyridine	4-isopropoxy-pyridine
138		3.6	6.4	6.3
137	6.3 ($M^{+\cdot}$)	51.9 ($M^{+\cdot}$)	73.9 ($M^{+\cdot}$)	65.6 ($M^{+\cdot}$)
136	3.0		2.1	4.4
122	11.8	—	2.3	6.3
109	1.8	—	2.1	2.1
108	42.9	—	3.8	—
107	3.4	—	—	—
97			1.5	1.6
96	11.8	8.4	28.3	31.7
95	100.0	100.0	100.0	100.0
94	1.3	1.0	1.8	1.3
80	3.9	—	—	—
79	16.6		1.6	
78	32.6	4.6	17.8	8.0
69		—		1.1
68	4.5	3.2	8.7	6.6
67	37.8	3.5	13.2	6.6
66	4.3		2.5	
61				1.2
58				1.4
55			2.1	1.1
54			1.4	—
53		—	2.8	
52	7.6	0.7	3.1	1.0
51	11.6	2.7	20.7	7.5
50	3.1	1.0	6.9	1.6
44	—	3.0		—
43	4.7	5.9	25.7	11.4
42			2.3	1.4
41	13.5	7.2	22.5	8.4
40	4.6	1.8	6.8	2.8
39	18.8	6.7	17.5	6.8
38	2.1	1.0	4.0	1.0
37	1.5	—	1.6	—

[a] Peaks with a relative intensity below 1% of the base peak have been omitted.

Table 3
Normalized intensities (in %) of the peaks in the *m/z* 94–99 region in the 70 eV mass spectra of the (un)labelled 2-, 3- and 4-propoxypyridines and 4-isopropoxypyridine (see also text)[a]

	m/z					
Compound	94	95	96	97	98	99
2-$CH_3CH_2CH_2$–O–C_5H_4N	1	94	5			
2-$CH_3CH_2CD_2$–O–C_5H_4N		98	2			
3-$CH_3CH_2CH_2$–O–C_5H_4N	1	97	2			
3-$CH_3CD_2CH_2$–O–C_5H_4N	1	81	16	2		
4-$CH_3CH_2CH_2$–O–C_5H_4N	1	83	16			
4-$CH_3CH_2CD_2$–O–C_5H_4N		61	32	6	1	
4-$CH_3CD_2CH_2$–O–C_5H_4N		70	24	6		
4-$CD_3CD_2CD_2$–O–C_5H_4N		3	66	6	24	1
4-$(CH_3)_2CH$–O–C_5H_4N	1	79	20			
4-$(CH_3)_2CD$–O–C_5H_4N	1	78	17	3	1	
4-$(CD_3)_2CD$–O–C_5H_4N		1	78	3	17	1

[a] The values given in the table have been corrected for ^{13}C isotope contributions.

$C_3H_4D_2$ with the formation of ions with *m/z* values of 96 and 95, respectively (Table 3). The prepared sample of this ether contained, however, 89% d_2- and 11% d_1-labelled 3-propoxypyridine as shown in Table 1. The molecular ions of the d_1 species can be expected to eliminate C_3H_5D as well as C_3H_6, thus forming ions with the same *m/z* values as formed in the loss of propene from the ionized 3-[2,2-d_2-propoxy]-pyridine. In other words, the relative abundances of the losses of C_3H_5D and $C_3H_4D_2$ in the ion–source reactions of the molecular ion of the labelled species cannot be determined directly (see also Discussion).

The MIKE spectrum of 3-propoxypyridine is shown in Fig. 1 and reveals that loss of propene is also the most important process in the second field free region (FFR) of the instrument. The competing losses of a methyl radical and an ethene molecule from the metastable molecular ions can be observed but give rise to peaks with a very low intensity. For this isomer propene loss is also associated with a Gaussian shaped metastable peak, notwithstanding that the kinetic energy release ($T_{0.5}$ = 35 meV) is larger than for the related process of the metastable ions of the 2-propoxypyridine (vide supra). For the metastable molecular ions of the 3-[2,2-d_2-propoxy]-pyridine, the ratio between the losses of $C_3H_4D_2$ and C_3H_5D is observed to be 86:14 (Table 4).

3.3. 4-propoxypyridine

The molecular ions of 4-propoxypyridine expel a propene molecule and an allyl radical in a ratio of 83:16 in the ion source as manifested in the relative abundances of the *m/z* 95 and 96 ions [see Eqs. (1) and (2) as well as Tables 2 and 3]. The occurrence of

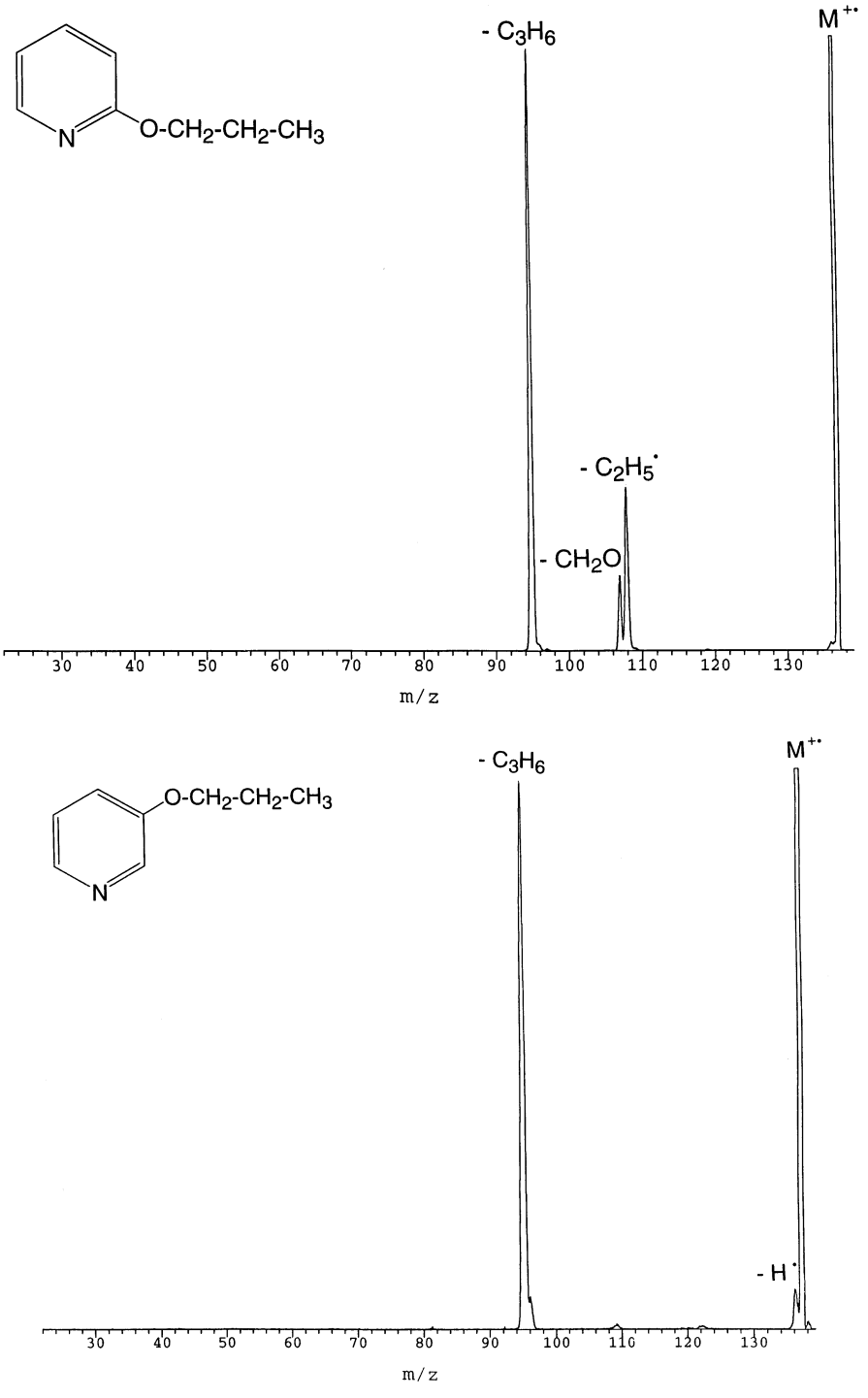


Fig. 1. (a–d) MIKE spectra of the metastable molecular ions of 2-, 3- and 4-propoxypyridines and 4-isopropoxypyridine (see also text).

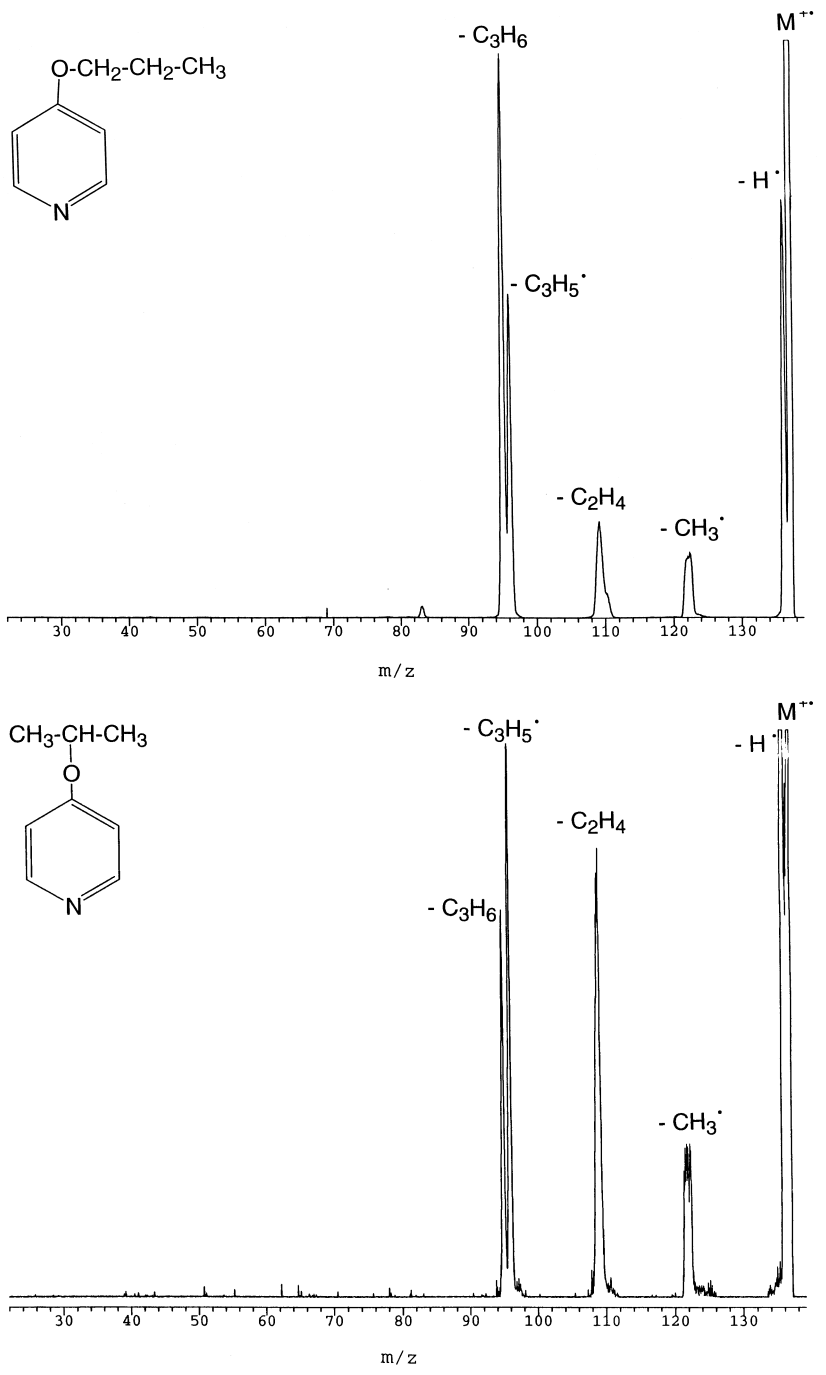


Fig. 1 *(continued)*

both of these processes prevents a straightforward estimation of the extent of the retention of the label in the propene molecules and the allyl radicals, which are eliminated in the ion source from the ionized 4-[1,1-d_2-propoxy]- and 4-[2,2-d_2-propoxy]-pyridines. In particular, the losses of C_3H_5D and $C_3H_3D_2^{\cdot}$

Table 4
Normalized abundances (in %) of the losses of propene molecules and/or allyl radicals from the metastable molecular ions of the 2-, 3- and 4-propoxypyridines and 4-isopropoxypyridine

	Loss of			
Compound	$C_3H_5^{\cdot}$	C_3H_6 and/or $C_3H_4D^{\cdot}$	C_3H_5D and/or $C_3H_3D_2^{\cdot}$	$C_3H_4D_2$
2-$CH_3CH_2CH_2$–O–C_5H_4N		100[a]		
2-$CH_3CH_2CD_2$–O–C_5H_4N				100
2-$CH_3CD_2CH_2$–O–C_5H_4N			100[b]	
3-$CH_3CH_2CH_2$–O–C_5H_4N	3	97[a]		
3-$CH_3CD_2CH_2$–O–C_5H_4N		1	14[b]	85
4-$CH_3CH_2CH_2$–O–C_5H_4N	36	64[a]		
4-$CH_3CH_2CD_2$–O–C_5H_4N	1	14	35	50
4-$CH_3CD_2CH_2$–O–C_5H_4N	7	28	43	22
4-$(CH_3)_2CH$–O–C_5H_4N	60	40[a]		
4-$(CH_3)_2CD$–O–C_5H_4N	3	55[c]	42	

	Loss of				
	$C_3H_2D_3^{\cdot}$	$C_3HD_4^{\cdot}$	$C_3D_5^{\cdot}$	C_3HD_5	C_3D_6
4-$CD_3CD_2CD_2$–O–C_5H_4N	2	12	21	33	32
4-$(CD_3)_2CD$–O–C_5H_4N	2	5	48	3	42

[a] Loss of C_3H_6.
[b] Loss of C_3H_5D.
[c] Loss of $C_3H_4D^{\cdot}$.

lead to isobaric product ions with a nominal *m/z* value of 96 and a similar situation applies to the product ions of the possible losses of C_3H_6 and $C_3H_4D^{\cdot}$ (see also Sec. 4).

The metastable ions of the 4-propoxypyridine display a more complex chemistry than the related ions of 2- and 3-propoxypyridine (see Fig. 1); that is, on the μs time scale the molecular ions of 4-propoxypyridine expel a hydrogen atom, a methyl radical, ethene, an allyl radical, propene, and HCN (or HNC, for simplicity the notation HCN is used throughout this article; it can be noted here that the molecular ions of aryl amines expel HNC, whereas ionized pyridines normally eliminate HCN [42]). The main processes are the competing losses of a propene molecule and an allyl radical, which occur in a ratio of 64:36. Both of these processes give rise to a narrow Gaussian shaped peak and a relatively low kinetic energy release; that is, for propene loss the value of $T_{0.5}$ is determined to be 28 meV and for loss of an allyl radical $T_{0.5}$ is 22 meV.

For the metastable molecular ions of the 4-[1,1-d_2-propoxy]- and 4-[2,2-d_2-propoxy]-pyridines, a direct estimation of the relative abundances of the competing losses of propene and an allyl radical is hampered because of formation of isobaric ions, as mentioned for the ion–source reactions. For the ionized 4-[d_7-propoxy]-pyridine, the loss of a completely labelled allyl radical ($C_3D_5^{\cdot}$) leads to ions with a *m/z* value of 98, whereas the expulsion of partly labelled allyl radicals leads to ions with higher *m/z* values. This implies that the ions with *m/z* values of 96 and 97 can be ascribed to the loss of propene (Table 4); that is, the metastable ions of 4-[d_7-propoxy]-pyridine are indicated to expel 32% C_3D_6 (*m/z* 96) and 33% C_3HD_5 (*m/z* 97). In other words, the ionized 4-[d_7-propoxy]-pyridine is likely to expel propene and an allyl radical in a ratio of 65:35 on the μs time scale in line with the findings for the unlabelled species. Within this interpretation, the normalized ratio between the losses of C_3D_6 and C_3HD_5 becomes 49:51, whereas the ratio between the losses of labelled allyl radicals, $C_3D_5^{\cdot}$:$C_3HD_4^{\cdot}$:$C_3H_2D_3^{\cdot}$, becomes 60:34:6 (see also Table 4).

Table 5
Summary of the dissociation reactions of the metastable ions generated by propene loss from the molecular ions of the 2-, 3-, and 4-(iso)propoxypyridine and by ionization of 4-hydroxypyridine (see also text)

Compound	$[M–propene]^{+\cdot}$	Loss of		
		HCN[a]	DCN[a]	CO[a]
2-$CH_3CH_2CH_2$–O–C_5H_4N	$C_5H_5NO^{+\cdot}$	no	no	yes
3-$CH_3CH_2CH_2$–O–C_5H_4N	$C_5H_5NO^{+\cdot}$	yes	no	yes
4-$CH_3CH_2CH_2$–O–C_5H_4N	$C_5H_5NO^{+\cdot}$	yes	no	yes
4-$CD_3CD_2CD_2$–O–C_5H_4N	$C_5H_4DNO^{+\cdot}$	no	yes	yes
4-$(CH_3)_2CH$–O–C_5H_4N	$C_5H_5NO^{+\cdot}$	yes	no	yes
4-$(CD_3)_2CD$–O–C_5H_4N	$C_5H_4DNO^{+\cdot}$	no	yes	yes
4-HO–pyridine: $C_5H_5NO^{+\cdot}$		yes	no	yes
4-DO–pyridine: $C_5H_4DNO^{+\cdot}$		no	yes	yes

[a] The loss of HCN or HNC (and labelled analogues) gives rise to a narrow Gaussian type metastable peak. The loss of CO is associated with a broad dish-topped metastable peak. The different shapes of the metastable peaks associated with DCN and CO loss from the $C_5H_4DNO^{+\cdot}$ ions allow the two processes to be distinguished even though the nominal mass of the two neutral species is the same.

3.4. 4-isopropoxypyridine

In the ion source, the molecular ions of 4-isopropoxypyridine expel propene and an allyl radical in a ratio of 80:20 (Tables 2 and 3). For the ionized 4-[1-d_1-isopropoxy]-pyridine, the relative abundance of the *m/z* 95 ions indicates that propene elimination involves exclusively C_3H_5D loss in the ion source. With respect to the loss of allyl radicals, the low abundance of the *m/z* 97 ions as compared to the *m/z* 96 ions indicates that loss of unlabelled allyl radicals is of minor importance as compared to the loss of $C_3H_4D^{\cdot}$ (see Table 3). For the ionized 4-[d_7-isopropoxy]-pyridine, the abundance of the *m/z* 96 ions is essentially the same as the abundance of the *m/z* 95 ions formed in the ion–source reactions of the unlabelled species. Thus, the molecular ions of the 4-[d_7-isopropoxy]-pyridine are indicated to eliminate nearly exclusively C_3D_6 in the ion source. In addition, the relative abundances of the *m/z* 97 and 98 ions given in Table 3 suggest that only minor amounts of $C_3HD_4^{\cdot}$ radicals are expelled in addition to completely labelled allyl radicals.

With respect to the metastable ions, the MIKE spectrum of the molecular ion of 4-isopropoxypyridine (Fig. 1) reveals the occurrence of the competing losses of a methyl radical, an ethene molecule, an allyl radical, and a propene molecule. The results of the labelling experiments indicate that the metastable ions of the 4-[1-d_1-isopropoxy]-pyridine expel a propene molecule and an allyl radical with predominant retention of the label (Table 4). The metastable molecular ions of 4-[d_7-isopropoxy]-pyridine expel mainly perdeuteropropene and a fully labelled allyl radical as indicated by the occurrence of not more than 3% C_3HD_5 loss in addition to C_3D_6 loss. With respect to the elimination of allyl radicals, the losses of $C_3H_2D_3^{\cdot}$ and $C_3HD_4^{\cdot}$ are of negligible importance as compared to the expulsion of $C_3D_5^{\cdot}$ radicals.

3.5. Reactions of the product ions

The reactions of the metastable product ions generated by the losses of propene or an allyl radical are summarized in Table 5. The ions formed by loss of propene from the molecular ions of 2-propoxypyridine expel only a CO molecule, whereas the related ions generated from the 3- and 4-isomers undergo the additional loss of HCN. Interestingly, with regard to the latter reaction the metastable $C_5H_4DNO^{+\cdot}$ ions formed by loss of C_3D_6 from the molecular ions of the 4-d_7-propoxy- and isopropoxypyridines expel only DCN [Eq. (3)]. Moreover, the metastable $C_5H_4DNO^{+\cdot}$ ions formed by hydrogen–deuterium exchange between a sample of 4-hydroxypyridine and D_2O in the inlet system of the instrument followed by ionization are also observed to undergo only the

competing losses of CO and DCN (Table 5) in agreement with a previous study [43].

$$\underset{m/z\ 96}{C_5H_4DNO^{+\cdot}} \rightarrow \underset{m/z\ 68}{C_4H_4O^{+\cdot}} + DCN \quad (3)$$

With respect to the metastable ions formed by allyl radical loss from the ionized 4-propoxypyridine, these species expel a water molecule in addition to dissociation by the competing losses of HCN and CO. The $C_5H_4D_2NO^+$ ions generated by the loss of $C_3D_5^{\cdot}$ from the ionized 4-[d_7-propoxy]-pyridine are observed to eliminate H_2O, HDO and D_2O together with CO, DCN, and HCN.

In order to further probe the structures of the product ions of propene or allyl radical loss, the CID spectra of these ions were recorded and compared to the spectra of the corresponding species formed by ionization or protonation of the appropriate hydroxypyridines. No significant differences could be observed between the spectra of the product ions of propene loss from one of the propoxypyridines and the molecular ions of the related hydroxypyridines (see Fig. 2 for an example). Likewise, the CID spectrum of the ions formed by loss of an allyl radical from the molecular ion of 4-propoxypyridine and of the protonated 4-hydroxypyridine appeared to be practically indistinguishable (see Fig. 3).

4. Discussion

The present results indicate clearly that propene can be expelled by different pathways from the molecular ions of the isomeric propoxypyridines. Unfortunately, appropriate thermodynamic data are not available for these species thus preventing estimations of, for example, the enthalpy change for propene loss for the different isomeric species. The results of the deuterium labelling experiments allow, however, the possible mechanisms for the loss of propene to be discussed in a qualitative manner. In summary, the pathways for loss of propene may be formulated as (**i**) a 1,5-H shift from the 2-position of the propyl group to the aromatic ring either prior to or concomitant with propene loss, and (**ii**) cleavage of the bond between the oxygen atom and the carbon atom of the propyl group with formation of a $[C_5H_4NO^{\cdot}/C_3H_7^+]$ ion/neutral complex, which reacts further by proton transfer prior to dissociation.

For the 2-isomer, the selective loss of C_3H_5D from the metastable ions of the 2-[2,2-d_2-propoxy]-pyridine reveals that propene elimination involves a 1,5-H shift as shown in Scheme 1. In addition, the absence of any C_3H_5D loss from the ionized 2-[1,1-d_2-propopxy]-pyridine in the ion source indicates that a similar situation may also apply to propene loss from molecular ions with a relatively high internal energy. In Scheme 1, the loss of propene is shown to involve transfer of the hydrogen atom to the nitrogen atom of the ring with formation of the keto-form (2-pyridone) of ionized 2-hydroxypyridine. An unequivocal assignment of the structure(s) of the product ions of propene loss appeared, however, not to be straightforward. This is reflected in the fact that the metastable product ions of propene loss expel only CO and a similar finding has been reported for the metastable ions of 2-hydroxypyridine [43]. In addition, the present series of experiments reveal that the CID spectrum of the product ions of propene loss is indistinguishable from the CID spectrum of ionized 2-hydroxypyridine (vide supra).

With respect to the loss of propene from the ionized 3-[2,2-d_2-propoxy]-pyridine, the results for the metastable ions are in line with formation of ion/neutral complexes. In particular, the ratio between the losses of C_3H_5D and $C_3H_4D_2$ is observed to be 14:86 and thus close to the ratio (16.6:83.4) predicted in the absence of isotope effects for a pathway involving cleavage of the O–C bond accompanied by an irreversible 1,2-D shift in the incipient carbenium ion followed by transfer of a proton or deuteron from the secondary carbenium ion to the $C_5H_4NO^{\cdot}$ radical (Scheme 2).

For the ion–source reactions of the ionized 3-[2,2-d_2-propoxy]-pyridine, the ratio between the losses of C_3H_5D and $C_3H_4D_2$ is not directly obtainable, owing to the fact that the sample was insufficiently labelled (see Results and Table 1). Nonetheless, if the pathway indicated in Scheme 2 is assumed for both the d_1- and d_2-labelled species, a ratio between the abundances of

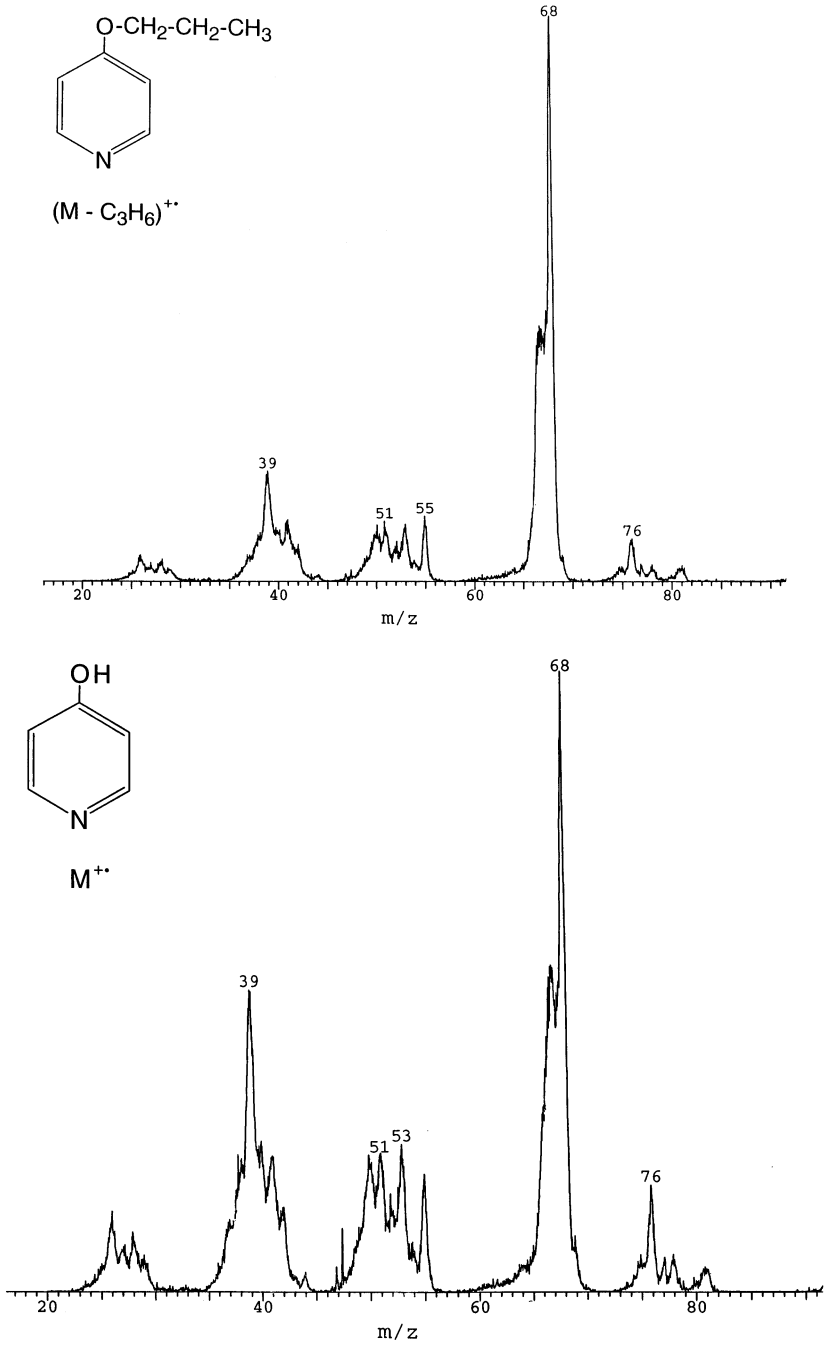


Fig. 2. (a,b) Collision-induced dissociation (CID) spectra of the product ion of propene loss from the molecular ion of 4-propoxypyridine and of ionized 4-hydroxypyridine (see also text).

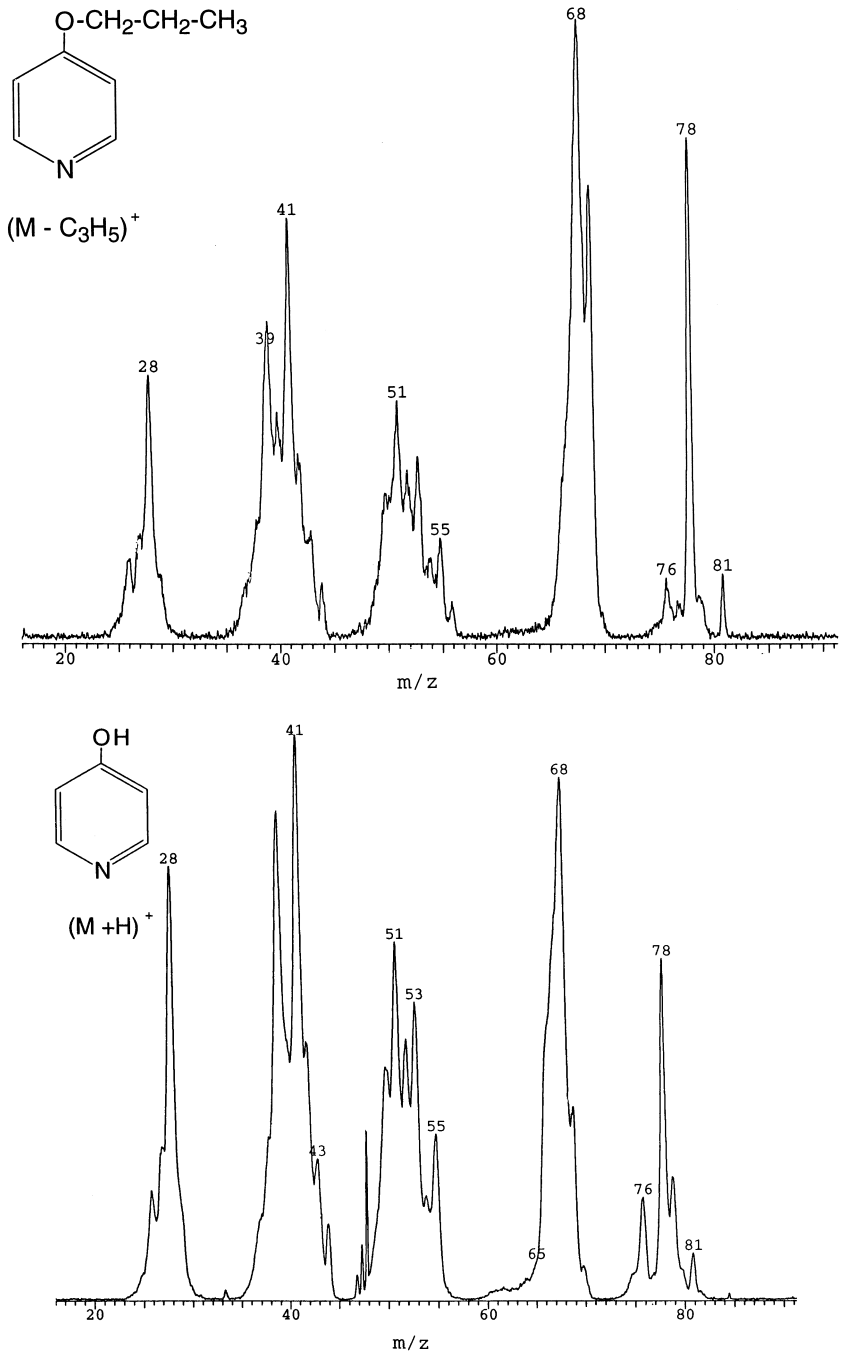
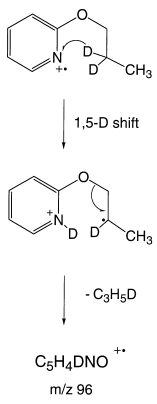
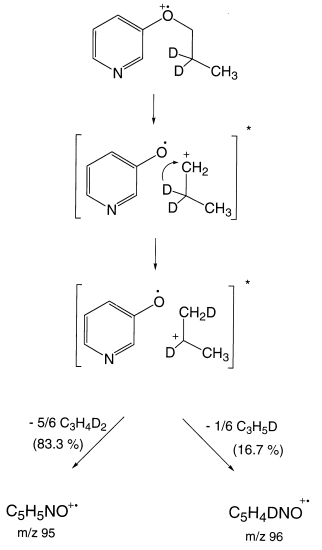


Fig. 3. (a,b) Collision-induced dissociation (CID) spectra of the product ion of allyl radical loss from the molecular ion of 4-propoxypyridine and protonated 4-hydroxypyridine (see also text).



Scheme 1. Proposed mechanism for the loss of propene from the molecular ion of 2-propoxypyridine.

the *m/z* 96 and 95 ions (as formed by the losses of C_3H_6 and C_3H_5D for the d_1 species and by the losses of C_3H_5D and $C_3H_4D_2$ for the d_2 species) of 15.5 to 85.5 can be estimated; that is, the experimentally obtained values for the ratio between the abundances of the *m/z* 95 and 96 ions as formed in the ion source (Table 3) can be reproduced by the mechanistic model shown in Scheme 2 if the label content of the present sample is taken into account.



Scheme 2. Proposed mechanism for the loss of propene from the molecular ion of 3- propoxypyridine. The ratio between the losses of $C_3H_4D_2$ and C_3H_5D is estimated upon the assumption that isotope effects are not operating in these reactions.

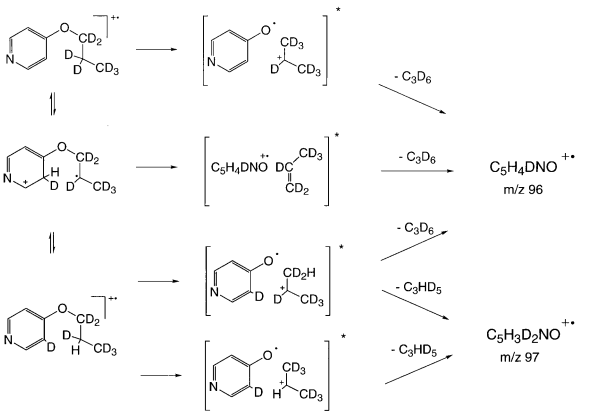
In conclusion, the results for the loss of propene from the ionized 3-propoxypyridine resemble the experimental findings for the molecular ions of phenyl propyl ether [17,20,21]. Notably, the metastable ions of the phenyl-[2,2-d_2-propyl] ether expel C_3H_5D and $C_3H_4D_2$ in a ratio of 16 to 84 with only a slight increase in the relative abundance of C_3H_5D loss in the ion–source reactions (the experimental ratio is 20:80; see for example [20]). In view of the recent study concerned with competing pathways for propene loss from ionized phenyl propyl ether [21], it could be anticipated that a similarly complex mechanistic scheme should be advanced for the ionized 3-propoxypyridine. However, this would require a study of an extended series of labelled 3-propoxypyridines in combination with more insight into the dynamic aspects of propene loss. Based on the presently limited results, it may be stated that loss of propene from the ionized 3-propoxypyridine can be understood on the basis of Scheme 2 even though the precise structure of the product ions of propene loss is uncertain (see also Sec. 3).

The results for the 4-propoxypyridine reveal a relatively complex chemistry as manifested in the occurrence of propene as well as allyl radical loss. The ratio between these processes changes from 83:16 in the ion source to 64:36 in the second FFR of the instrument, indicating that the overall loss of propene is associated with a higher critical energy than allyl radical loss. In the ion source, the molecular ions of the 4-[1,1-d_2-propoxy]-pyridine (98% d_2, see Table 1) dissociate to afford ions with *m/z* values of 97, 96, and 95 in a normalized ratio of 6:32:62. Upon the assumption that the ratio between propene and allyl radical loss is the same for the labelled and the unlabelled species, it could be expected that $C_3H_4D^{\cdot}$ loss from the ionized 4-[1,1-d_2-propoxy]-pyridine is responsible for the 6% *m/z* 97 ions and that the loss of $C_3H_3D_2^{\cdot}$ leads to 10% *m/z* 96 ions. As a result, propene loss may be thought to give rise to 22% *m/z* 96 ions and the 62% *m/z* 95 ions; that is, a normalized ratio of 26:74 between the losses of C_3H_5D and $C_3H_4D_2$ is obtained for the ion–source reactions of the ionized 4-[1,1-d_2-propoxy]-pyridine. This latter ratio is close to the ratio (28.6:71.4) predicted in the absence of

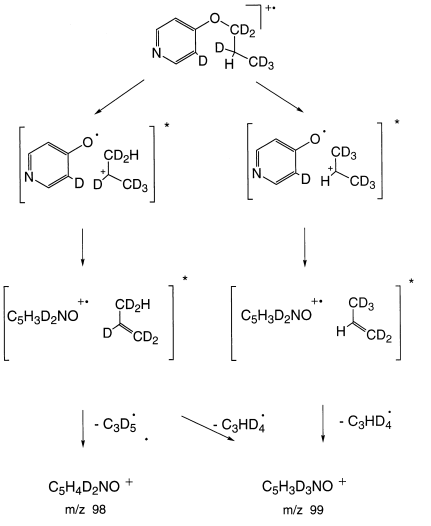
isotope effects for a pathway involving formation of an ion/neutral complex containing a $C_3H_5D_2^+$ carbenium ion, which undergoes hydrogen–deuterium randomization prior to proton or deuteron transfer to the $C_5H_4NO^{\cdot}$ radical and the subsequent losses of C_3H_5D and $C_3H_4D_2$.

The mechanism of propene loss from the metastable ions is likely to be more complex than suggested for the ion–source reactions. For example, the loss of propene and an allyl radical could be thought to proceed on the μs time scale with formation of ion/neutral complexes containing secondary propyl carbenium ions with sufficient internal energy to undergo hydrogen atom randomization. Such a mechanistic scheme would lead to the prediction that the results for the 4-[1,1-d_2-propoxy]-pyridine and the related 2,2-d_2-labelled species should be the same, in contrast to the experimental findings summarized in Table 4. Notably, the 1,1-d_2-labelled ions expel much more $C_3H_4D_2$ than the 2,2-d_2-labelled species and—in addition—loss of $C_3H_5^{\cdot}$ is significant for the latter ions but hardly observable for the former species. A complex nature of the dissociation reactions of the metastable ions of 4-propoxypyridine is further revealed by the pronounced loss of C_3HD_5 from the species with a fully labelled propyl group (Table 4). This result provides evidence for the occurrence of interchange between a deuterium atom of the propyl group and a hydrogen atom of the pyridine ring. In Scheme 3 this interchange is visualized as a 1,5-D shift leading to a distonic ion, which may either react further to expel propene or revert to the structure of the parent species. Subsequently, an ion/neutral complex composed of a $C_5H_3DNO^{\cdot}$ radical and a $C_3HD_6^+$ ion may be formed prior to the occurrence of proton or deuteron transfer and the losses of C_3D_6 or C_3HD_5.

Within this mechanistic proposal, the loss of an allyl radical may be ascribed to deuterium or hydrogen atom abstraction in the appropriate complexes containing a propene molecule (see also [32]). As indicated in Scheme 4, the loss of a $C_3HD_4^{\cdot}$ radical to afford a $C_5H_3D_3NO^+$ ion is suggested to be a result of the reactions of the ion/neutral complexes formed after interchange between a deuterium atom of the propyl group and a hydrogen atom of the ring. It should be reemphasized that the precise structure of the ions generated by loss of an allyl radical is unknown notwithstanding that the CID spectrum of the $C_5H_6NO^+$ ions formed by dissociation of ionized 4-propoxypyridine is essentially identical to the spectrum of the protonated 4-hydroxypyridine (see Fig. 3).



Scheme 3. Proposed mechanism for the interchange of a deuterium atom at the 2-position of the propyl group and a hydrogen atom at the ring of ionized 4-[d_7-propoxy]-pyridine. This interchange may compete with or be followed by the formation of ion/neutral complexes (see also Discussion).



Scheme 4. Possible pathways leading to the losses of $C_3HD_4^{\cdot}$ and $C_3D_5^{\cdot}$ radicals from ionized 4-[d_7-propoxy]-pyridine. The starting ion is formed as suggested in Scheme 3 (see also Discussion).

An important aspect of the mechanistic proposals for propene loss from the molecular ions of 4-propoxypyridine is the site in the $C_5H_4NO^{\cdot}$ radical to which a proton is transferred. In the study of the loss of a cyclo-octenyl radical from the ionized 4-[cyclo-octyloxy]-pyridine, the first step in the reaction sequence was suggested to be formation of an ion/neutral complex containing the $C_5H_4NO^{\cdot}$ radical and a cyclo-octyl carbenium ion followed by proton transfer to the nitrogen atom in the radical [4,32]. A similar suggestion could be advanced for the present systems in view of the finding that the metastable $C_5H_4DNO^{+\cdot}$ ions generated from the 4-[d_7-propoxy]-pyridine expel only DCN (Table 5). However, the metastable ions generated by exchange between the neutral 4-hydroxypyridine and D_2O in the inlet system followed by electron ionization are observed also to eliminate only DCN. In view of the literature reports which indicate that the enol form of 4-hydroxypyridine is preferred over the keto form in the gas phase [44–46], it is likely that the exchange with D_2O leads to 4-DO–C_5H_4N as suggested previously [43]. Irrespective of the fact that the selective loss of DCN from the metastable molecular ions of the 4-DO–C_5H_4N species still has to be solved mechanistically, the occurrence of this process prevents a clear-cut assignment of the protonation site in the $C_5H_4NO^{\cdot}$ radical present in the ion/neutral complexes.

Interestingly, the metastable ions of the 4-[d_7-isopropoxy]-pyridine eliminate C_3HD_5 only to a minor extent, indicating that interchange between the hydrogen atoms of the isopropyl group and the aromatic ring is of negligible importance (Table 4). This might be due to a lower critical energy for cleavage of the O–C bond for the ionized isopropoxypyridine than for the related propoxypyridine. As a result, the formation of an ion/neutral complex composed of a $C_5H_4NO^{\cdot}$ radical and a secondary propyl carbenium ion may be a relatively facile process for the molecular ions of 4-isopropoxypyridine. The present results do not rule out, however, that propene may be expelled from the ionized 4-isopropoxypyridine by a conventional and irreversible 1,5-H shift even though the pronounced loss of allyl radicals appears to be in favour of the intermediacy of ion/neutral complexes. It is obvious, however, that more elaborate considerations of the dissociation reactions of the molecular ions of the isopropoxypyridine and the isomeric propoxypyridines require insight into the (thermo)dynamic aspects of these reactions. Stated otherwise, more experimental as well as theoretical studies are needed in order to further explore the gas phase chemistry of these apparently simple ionic systems.

Acknowledgements

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