Charge-Remote Fragmentation and the Two-Step Elimination of Alkanols from Fast Atom Bombardment-Desorbed $(M + H)^+$, $(M + Cat)^+$, and $(M - H)^-$ Ions of Aromatic β -Hydroxyoximes

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Aromatic β -hydroxyoximes undergo unusual fragmentation reactions as protonated or cationized species, as radical cations, or as $(M - H)^-$ ions. As protonated species, they expel $OH^\bullet$ from the oxime functionality in violation of the even electron rule. Parallel eliminations of alkyl radicals follow $OH^\bullet$ loss when the aromatic ring is substituted with an alkyl chain. Alkyl radical losses appear to be characteristic of radical cations that can isomerize to ions in which the alkyl chain bears a radical site and the charged site is the conjugate acid of a basic functionality (e.g., oxime or imine). Evidence for the mechanisms was found in the ion chemistry of oxime and imine radical cations. The imine reference compounds were conveniently generated by fast atom bombardment-induced reduction of oximes, removing the requirement for using conventional chemical synthesis. Protonated imines and the $(M - H)^-$ ions of oximes fragment extensively via charge-remote processes to eliminate the elements of alkanes. This chemistry is not shared by the protonated oximes. (*J Am Soc Mass Spectrom* 1993, 4, 819–827)

Compounds containing the oxime functional group have wide application in the industrial [1], analytical [2], and pharmaceutical [3] fields. Until now, mass spectrometric studies of oximes made use of electron ionization (EI) [4–6] and chemical ionization (CI) [7, 8]. Secondary ion mass spectrometry (SIMS) (without the use of a matrix) was also used to investigate quaternary pyridine oximes [9]. To our knowledge, however, fast atom bombardment (FAB) has not been used to study oximes, except as reported in our previous study of FAB-induced reduction of oximes to imines [10] and in a study of a few *N*-hydroxyl nitrogen compounds (benzohydroxamic acid, 1-hydroxybenzotriazole and *N*-hydroxysuccinimide) [11].

Oximes are reduced to imines upon FAB [10]. As oximes often occur in complex mixtures, this reduction can be used to detect individual components by obtaining mass spectra as a function of time. For each oxime, the mass peak corresponding to the protonated oxime, $(M + H)^+$, decreases with time, where-

as that corresponding to the protonated imine, $[(M + H) - O]^+$, increases with time. The $(M + H)^+$ and $[(M + H) - O]^+$ ions, in principle, can be mass analyzed and identified by their product ion spectra. FAB with tandem mass spectrometry, therefore, is well suited for the study of such mixtures.

The present work was undertaken to study the fragmentation of the ions produced by FAB of compounds containing one oxime group. The oximes studied are aromatic β -hydroxyoximes of the type used in hydrometallurgy as metal extractants [12]. The decomposition ion chemistry of these compounds is reported here because the decomposition reactions are unusual and because different classes of fragmentation can be accessed by obtaining separately the product ion spectra of different FAB-desorbed ions. A comparison with data from electron ionization is also made to substantiate fragmentation mechanisms.

Results and Discussion

Positive Ion FAB Mass Spectral Data

Mass spectra. Upon FAB [or liquid SIMS (LSIMS)] the β -hydroxyoximes with the general formula

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$\text{RC}_6\text{H}_3\text{OHC(R')} = \text{NOH}$ give prominent molecular $(\text{M} + \text{H})^+$ and $[(\text{M} + \text{H}) - \text{O}]^+$ ions; their relative abundances vary, decreasing and increasing, respectively, with time [10]. Formation of the molecular radical cation and the radical cation arising by hydroxyl loss from $(\text{M} + \text{H})^+$ is significant for some of the β -hydroxybenzaldoximes ($\text{R}' = \text{H}$). For the β -hydroxyoximes with larger, branched R substituent groups, losses of the elements of the alkanols occur from the $(\text{M} + \text{H})^+$ ions. The abundances and the mass-to-charge ratio values of the most important fragments of the β -hydroxyoximes of Table 1 are shown in Table 2.

$(\text{M} + \text{H})^+$ and $[(\text{M} + \text{H}) - \text{O}]^+$ ions. The metastable ion spectra of the $(\text{M} + \text{H})^+$ ions of the β -hydroxyoximes 1-6 show exclusively ions formed by $\text{OH}^\cdot$ and H_2O losses. Although the loss of a hydroxyl radical from closed-shell $(\text{M} + \text{H})^+$ ions is unusual and violates the even electron rule, it is not unprecedented. (The even electron rule states that even electron ions prefer to fragment to give even electron products.) It was reported before for aromatic nitro compounds under CI [13, 14] and FAB [15] conditions and was shown to be consistent with the formation of ions protonated at the nitro group $[-\text{N}(\text{OH})\text{O}]^+$ [13, 14].

Interesting reactions pertain to the metastable ion and collision-activated decompositions (CAD) of β -hydroxyoximes with sizeable alkyl (R) substituents. For β -hydroxyoxime 7, which contains a straight-chain alkyl substituent, the nearly exclusively metastable ion decomposition is loss of $\text{OH}^\cdot$ (see Figure 1a). Small losses of H_2O , C_7H_{16} , C_8H_{16} , and the elements of $\text{C}_7\text{H}_{15}\text{OH}$ also occur. Upon collisional activation (CA), the loss of $\text{C}_7\text{H}_{15}\text{OH}$ dominates, possibly depleting the product ion formed by loss of $\text{OH}^\cdot$, which is approximately of equal abundance as those ions formed by losses of H_2O and C_7H_{16} (Figure 1b). The latter ion is likely to be a result of charge-remote fragmentation [16, 17].

To assess the importance of the $\text{OH}^\cdot$ group of the oxime functionality on the fragmentation chemistry, advantage is taken of the FAB-induced chemical reduction of the oxime to give an imine [10] (see Scheme I).

The CAD spectrum of the $[(\text{M} + \text{H}) - \text{O}]^+$ ion of oxime 7 shows that the fragmentation is almost entirely dominated by charge-remote processes (i.e., losses of $\text{C}_n\text{H}_{2n+2}$), exceptions being weak losses of H_2O and HCN (see Figure 1c). The largest alkane lost abundantly (C_7H_{16}) contains one less than the total carbons in the side chain. The product ion of m/z 135 formed by loss of the C_7H_{15} alkyl group may be regarded as formed from a homolytic charge-remote cleavage of the benzylic bond to give the radical cation, A. Radical loss appears to be facile only when a product ion such as A is stable.

The contrast between the decomposition reactions of the $(\text{M} + \text{H})^+$ and $[(\text{M} + \text{H}) - \text{O}]^+$ ions is remark-

Table 1. β -Hydroxyoximes of the general formula

	R	R'	β -hydroxyoxime	M. W.
1	H	H	2-hydroxybenzaldoxime (salicylaldoxime)	137
2	H	CH_3	2-hydroxyacetophenone oxime	151
3	H	C_6H_5	2-hydroxybenzophenone oxime	213
4	CH_3	H	2-hydroxy-5-methylbenzaldoxime	151
5	CH_3	CH_3	2-hydroxy-5-methylacetophenone oxime	165
6	CH_3	C_6H_5	2-hydroxy-5-methylbenzophenone oxime	227
7	C_8H_{17}	H	2-hydroxy-5-octylbenzaldoxime	249
8	$\text{C}_6\text{H}_{13}(\text{CH}_3)_2\text{C}$	H	2-hydroxy-5-(1',1'dimethylheptyl)benzaldoxime	263
9	$\text{C}_6\text{H}_{13}(\text{CH}_3)_2\text{C}$	CH_3	2-hydroxy-5-(1',1'dimethylheptyl)acetophenone oxime	277
10	$\text{C}_6\text{H}_{13}(\text{CH}_3)_2\text{C}$	C_6H_5	2-hydroxy-5-(1',1'dimethylheptyl)benzophenone oxime	339

able. The former undergoes loss of $\text{OH}^\cdot$, which is apparently followed by radical loss, whereas the latter undergoes charge-remote fragmentation to expel the elements of the alkanes. Clearly the $\text{OH}^\cdot$ loss from the oxime $(\text{M} + \text{H})^+$ must involve the oximic $\text{OH}^\cdot$ and not the phenolic $\text{OH}^\cdot$. For compounds of this nature, the analyst has the opportunity to choose the fragmentation chemistry by taking advantage of the FAB-induced reduction to form a differently fragmenting imine.

Scheme I

Table 2. Fast atom bombardment positive ion mass spectra of hydroxyoximes m/z and abundance (% of base peak)

1	2	3	4	5	6	7	8	9	10
138 (100%) [M+H] ⁺	152 (75%) [M+H] ⁺	214 (85%) [M+H] ⁺	152 (100%) [M+H] ⁺	166 (100%) [M+H] ⁺	228 (80%) [M+H] ⁺	250 (100%) [M+H] ⁺	264 (83%) [M+H] ⁺	278 (84%) [M+H] ⁺	340 (86%) [M+H] ⁺
137 (58%) M ⁺	150 (5%) [M+H] ⁺	198 (90%) [(M+H)-O] ⁺	151 (40%) M ⁺	164 (8%) [M+H] ⁺	212 (100%) [(M+H)-O] ⁺	249 (80%) M ⁺	248 (100%) [(M+H)-O] ⁺	262 (100%) [(M+H)-O] ⁺	324 (100%) [(M+H)-O] ⁺
122 (54%) [(M+H)-O] ⁺	136 (100%) [(M+H)-O] ⁺	196 (28%) [(M+H)-H ₂ O] ⁺	136 (80%) [(M+H)-O] ⁺	150 (96%) [(M+H)-O] ⁺	210 (25%) [(M+H)-H ₂ O] ⁺	248 (23%) [M+H] ⁺	246 (15%) [(M+H)-H ₂ O] ⁺	260 (26%) [(M+H)-H ₂ O] ⁺	322 (23%) [(M+H)-H ₂ O] ⁺
121 (28%) [(M+H)-OH] ⁺	134 (8%) [(M+H)-H ₂ O] ⁺	170 (10%) ---	135 (20%) [(M+H)-OH] ⁺	148 (8%) [(M+H)-H ₂ O] ⁺	195 (15%) [(M+H)-NHOH] ⁺	234 (88%) [(M+H)-O] ⁺	206 (10%) [(M+H)-C ₄ H ₉] ⁺	248 (10%) [(M+H)-C ₂ H ₅] ⁺	310 (15%) [(M+H)-C ₂ H ₅] ⁺
120 (16%) [(M+H)-H ₂ O] ⁺	121 (15%) [(M+H)-NHOH] ⁺	181 (18%) ---	134 (14%) [(M+H)-H ₂ O] ⁺	135 (7%) [(M+H)-NHOH] ⁺	195 (13%) ---	233 (33%) [(M+H)-OH] ⁺	204 (10%) [(M+H)-O-C ₃ H ₇] ⁺	232 (8%) [(M+H)-O-C ₂ H ₅] ⁺	266 (11%) [(M+H)-O-C ₂ H ₅] ⁺
119 (10%) C ₆ H ₄ (OH)CN ⁺	120 (10%) [(M+H)-NHOH] ⁺	148 (20%) ---	119 (6%) C ₆ H ₄ (OH)CN ⁺	134 (10%) [(M+H)-NHOH] ⁺	151 (45%) [(M+H)-C ₆ H ₅] ⁺	232 (24%) [(M+H)-H ₂ O] ⁺	192 (15%) [(M+H)-C ₅ H ₁₁] ⁺	206 (15%) [(M+H)-C ₅ H ₁₁] ⁺	266 (13%) [(M+H)-C ₄ H ₉] ⁺
107 (8%) C ₇ H ₉ OH ⁺	107 (10%) C ₇ H ₉ OH ⁺	137 (20%) [(M+H)-C ₆ H ₅] ⁺	107 (7%) C ₇ H ₉ OH ⁺	119 (8%) C ₆ H ₄ (OH)CN ⁺	149 (20%) ---	150 (85%) [(M+H)-C ₇ H ₁₃] ⁺	178 (28%) [(M+H)-C ₆ H ₅] ⁺	204 (8%) [(M+H)-O-C ₄ H ₉] ⁺	254 (15%) [(M+H)-C ₆ H ₅] ⁺
---	106 (15%) C ₆ H ₅ CH ₂ OH ⁺	135 (25%) ---	---	107 (8%) C ₇ H ₉ OH ⁺	133 (30%) ---	134 (15%) [(M+H)-O-C ₇ H ₁₃] ⁺	176 (20%) [(M+H)-O-C ₆ H ₁₁] ⁺	192 (28%) [(M+H)-C ₆ H ₅] ⁺	252 (18%) [(M+H)-O-C ₅ H ₁₁] ⁺
---	---	121 (18%) ---	---	105 (7%) C ₆ H ₅ CH ₂ OH ⁺	119 (50%) C ₆ H ₅ (OH)CN ⁺	132 (15%) [(M+H)-H ₂ O-C ₇ H ₁₃] ⁺	162 (49%) [(M+H)-O-C ₆ H ₁₁] ⁺	190 (18%) [(M+H)-O-C ₅ H ₁₁] ⁺	238 (50%) [(M+H)-O-C ₆ H ₅] ⁺
---	---	119 (100%) C ₆ H ₄ (OH)CN ⁺	---	---	104 (30%) C ₆ H ₅ CH ₂ OH ⁺	121 (15%) [(M+H)-OH-C ₆ H ₁₁] ⁺	107 (29%) C ₇ H ₉ OH ⁺	175 (40%) [(M+H)-O-C ₆ H ₅] ⁺	198 (20%) [(M+H)-O-C ₆ H ₅] ⁺
---	---	103 (80%) C ₆ H ₅ CH ₂ OH ⁺	---	---	103 (40%) C ₆ H ₅ CH ₂ OH ⁺	107 (6%) C ₇ H ₉ OH ⁺	103 (28%) C ₆ H ₅ CH ₂ OH ⁺	107 (18%) C ₇ H ₉ OH ⁺	119 (50%) C ₆ H ₄ (OH)CN ⁺

Figure 1. Product ion spectra of: (a) $(M+H)^+$ of oxime 7 (metastable ion decompositions), (b) $(M+H)^+$ of oxime 7 (CAD, 30% beam reduction), (c) $[(M+H)-O]^+$ of oxime 7 (CAD, 30% beam reduction). The mass scale is the same width for all of the spectra so the precursor ion in spectrum c does not appear at the far right. Δ indicates alkane loss; $\blacksquare$ indicates alkene loss; $*$ indicates alkanol loss; ∇ indicates alkyl loss.

Turning to the analogs that have a branched alkyl chain substituted on the aromatic ring, we see that loss of OH^- again occurs (see Figure 2a), but unlike the oxime having the straight-chain alkyl group, these branched compounds show formation of a series of product ions from losses of the elements of the alkanols. Competitive processes are losses of C_2H_5 and C_9H_{18} , to give products of m/z 235 and 138, respectively, and formation of a set of carbocations of m/z 57, 71, and 85. Comparing the spectra in Figures 1a and 2a, we are led to the hypothesis that alkanol loss is really a two-step process: loss of OH^- followed by the competitive losses of various alkyl groups.

Collisional activation of the branched $(M+H)^+$ ion of oxime 8 causes only small changes in the chemistry (see Figure 2b). The loss of OH^- now appears to be minor, although as in Figure 1b, CA may serve to deplete the initially formed $[(M+H)-OH]^{++}$ ion. Losses of the elements of hexanol point to C—C bond cleavage at the branch point, whereas those of heptanol and octanol (to give ions of m/z 134 and 148) suggest some rearrangements of the alkyl side chain are occurring. Some indication of competitive charge-remote chemistry can also be found (i.e., losses of C_5H_{12} and C_6H_{14} are seen).

In the case of the branched oxime $[(M+H)-O]^+$ ion, the major metastable ion decomposition is loss of the complete set of alkyl side chain radicals (Figure 2c). The fragment ions attributed to loss of C_7H_{15} and C_8H_{17} require rearrangement and are of low abundance. Losses of an interrupted series of alkenes, including one involving the entire side chain, occur competitively. Collisional activation of the $[(M+H)-O]^+$ ion, however, pushes the fragmentation chemistry into the charge-remote regime. This strategy of collisionally activating the bombardment-produced imine

Figure 2. Product ion spectra of: (a) $(M+H)^+$ of oxime 8 (metastable ion decompositions), (b) $(M+H)^+$ of oxime 8 (CAD, 30% beam reduction), (c) $[(M+H)-O]^+$ of oxime 8 (metastable ion decompositions), (d) $[(M+H)-O]^+$ of oxime 8 (CAD, 30% beam reduction). The mass scale is the same width for all of the spectra so the precursor ions in spectra c and d do not appear at the far right. $\blacktriangle$ indicates alkane loss; $\blacktriangle$ indicates alkene loss; $*$ indicates alkanol loss; ∇ indicates alkyl loss.

$[(M+H)-O]^+$ ion appears to be a general means of obtaining charge-remote fragmentations from the parent oxime and is superior to one in which CA of the oxime $(M+H)^+$ ion is used. As expected for the dimethyl branched oxime, there is an uninterrupted series of alkane losses up to the branch point, after which the pattern of the losses is interrupted; the largest alkane lost abundantly (C_6H_{14}) contains three less than the total carbons in the side chain. Of course, the metastable losses of the alkyl radicals are still observed and may be increased upon CA.

In summary, the oximes, both straight-chain and branched, lose $OH^\cdot$ and expel alkyl groups (to give overall the loss the alkanols), whereas the imines show charge-remote fragmentation to eliminate the elements of alkanes. The striking similarity in the CA spectra of the straight-chain (Figure 1c) and branched-chain imine $[(M+H)-O]^+$ ions, except for the differences produced by the branching, demonstrates that the oxime-O removed upon reduction to the imine has, as expected, little effect on the charge-remote fragmentation,

whereas it has a strong influence on the fragmentations of the $(M+H)^+$ ions, a fact that will be now addressed in a proposed mechanism.

The loss of an entire series of alkanols, which is a signature not only of $(M+H)^+$ ions of the oxime 8 but also the oximes 9 and 10, occurs at least in part by a two-step process. First, loss of $OH^\cdot$, a characteristic reaction of most oximes, takes place to give an ion that corresponds to the imine radical cation. The loss of $OH^\cdot$ dominates the metastable ion decompositions of oxime 7 (see Figure 1a) and is apparently followed by subsequent and facile losses of alkyl groups for oximes 8, 9, and 10 (see Figure 2a). Collision-activated decomposition spectra are misleading because the $[(M+H)-OH]^{+\cdot}$ ion is not abundant and is easily overlooked. The low abundance is due to rapid subsequent fragmentations, not slow rates of production. The metastable ion spectra, however, offer better perspective on $OH^\cdot$ loss.

Support for this overall picture comes from the metastable ion and CAD spectra of the $[(M+H)-OH]^{+\cdot}$ radical cations (see Figure 3a and b). Both spectra are surprisingly similar and show that the $[(M+H)-OH]^{+\cdot}$ ions fragment to expel a series of alkyl radicals. Thus, the $[(M+H)-OH]^{+\cdot}$ ion is established as an important precursor for the alkyl radical loss products. Although the release of C_6H_{13} is expected, being triggered by the aromatic ring and the two methyl branches, the other alkyl losses that also occur for the $[(M+H)-OH]^{+\cdot}$ ion of oximes 9 and 10 are unexpected.

We propose that the loss of $OH^\cdot$ gives rise to the radical cation of the imine. This radical cation readily isomerizes by abstracting $H^\cdot$ from various positions along the alkyl chain (in Scheme II is shown abstraction from the fourth alkyl carbon from the aromatic ring) analogous to the scorpion mechanism reported by others [18, 19]. Abstraction is rapidly followed by a phenyl shift (shown to be 1,4 in Scheme II) to give the tertiary radical product, an ion that cannot form readily for straight-chain analogs because the product would have a more unstable primary radical site. A 1,4-hydrogen atom shift followed by free radical-triggered C—C bond cleavage leads to competitive elimination of butyl and ethyl groups from the chain.

Similar abstraction/rearrangement reactions produce species with radical sites at different positions on the chain from which C_3H_7 and C_5H_{11} losses can occur. In that way, a series of alkyl losses follows rapidly the expulsion of the $OH^\cdot$ group. The final products are the stable closed-shell conjugate acids of the imines.

If the mechanism is correct, then aromatic systems of this general nature will exhibit losses of the elements of the alkanols. A test is readily designed by examining the metastable ion and CAD spectra of the radical cations of the starting oximes. These radical cation or $M^{+\cdot}$ species can also be produced by FAB by using matrices such as 3-nitrobenzyl alcohol. The radi-

Figure 3. Product ion spectra of: (a) $(M + H - OH)^+$ of oxime 8 (metastable ion decompositions), (b) $(M + H - OH)^+$ of oxime 8 (CAD, 30% beam reduction), (c) the radical cation, $M^{\bullet+}$, of oxime 8 (metastable ion decompositions), (d) the radical cation, $M^{\bullet+}$, of oxime 8 (CAD, 30% beam reduction). The mass scale is the same width for all of the spectra so the precursor ions in spectra a and b do not appear at the far right. ∇ indicates alkyl loss.

Scheme II

radical site, however, occurs when the precursor ion itself is a radical cation such as that formed by OH loss from a protonated oxime. For closed-shell ions such as the protonated imines discussed here, charge-remote losses of the elements of alkanes do occur, whereas radical loss is not apparent. Thus, it is unlikely that radical production is the first step of a charge-remote fragmentation.

$(M + Li)^+$ and $(M + Na)^+$ ions. The unusual loss of OH from closed-shell ions is found also among the CAD of $(M + Li)^+$ and $(M + Na)^+$ ions of these β -hydroxyoximes. Although the alkali-metal-cationized oximes also react to eliminate alkyl groups after OH is expelled, they are more likely than the $(M + H)^+$ ions to undergo charge-remote fragmentations to eliminate the elements of the alkanes. The increased propensity for charge-remote fragmentation is likely a sign of the more stable, more tightly localized charge site of the metal-cationized species.

These cationized species also provide evidence in their CAD spectra that the loss of H_2O from $(M + H)^+$ ions also involves the oxime functionality. When H^+ is replaced by Li^+ , for example, loss of water is no longer facile because the expelled species would now become $LiOH$. A most abundant fragmentation of the $(M + Li)^+$ ion is the loss of OH.

The $(M + Na)^+$ ions also lose OH, but the product is of lower abundance. This may be due to the larger size of Na^+ (with respect to Li^+), which in the $(M + Na)^+$ ion case probably allows for binding of the metal ion at two different sites (oximic nitrogen and phenolic oxygen, for example), with formation of an ionic com-

cal cation of the oxime should abstract H^+ as readily as that of the imine, to initiate the sequence of rearrangements pictured in Scheme II. In fact, the metastable ion and CAD spectra (see Figure 3c and d) are remarkably the same and similar to the corresponding spectra of the imine radical cations. The losses of nearly all alkyl radicals are once again observed.

Decompositions of this type are likely to be found for aromatic or aliphatic radical cations that possess a basic site (such as oxime, imine, or amine) and a long alkyl chain. Likely precedents for this chemistry are the interesting and structurally diagnostic alkyl radical losses from picolinyl esters [20, 21] and pyrrolidide derivatives of fatty acids [22]. If the mechanism is correct, we see an important analytical or structural application of this radical ion chemistry.

Radical-induced cleavages have been proposed as an alternative to the six-centered mechanism for charge-remote reactions along an alkyl chain [23]. The results of this work make clear that the existence of a free-radical site on an alkyl chain indeed can initiate cleavage to expel an alkyl radical. The production of a

plex [24], thus opening the possibility of competitive fragmentation processes, such as the losses of the elements of the alkanes. The increase of the latter upon CA of the $(M + Na)^+$ ions (and to a lesser extent in the case of the $(M + Li)^+$ ions), is consistent with the occurrence of charge-remote losses.

The spectrum of $(M + Na)^+$ ion, in contrast with that of the corresponding $(M + H)^+$ ion (see Figure 4), offers convincing proof of the ideas discussed above. Whereas the spectrum of the $(M + H)^+$ ion is dominated by peaks corresponding to losses of the elements of alkanols, and those arising from losses of the elements of alkanes are of lesser importance, the situation is reversed in the spectrum of the $(M + Na)^+$ species.

Negative Ion FAB Mass Spectral Data

The importance of the additional proton and the hydroxyl group in the alkanol losses from $(M + H)^+$ ions is confirmed by the behavior of the FAB-produced negative ions of the β -hydroxyoximes. The most abundant ions in the FAB mass spectra of negative ions are formed by losses of R'OH from the $(M - H)^-$ ion. The $(M - H)^-$ and $[(M - H) - O]^-$ ions are also formed with high relative abundances. For the β -hydroxyoximes with larger R alkyl substituent groups, ions from the losses of the elements of the alkanes from the $(M - H)^-$ and $[(M - H) - O]^-$ ions are also produced, as are fragment ions from losses of R'OH plus alkanes from the $(M - H)^-$ ions. The abundances and the mass-to-charge ratio values of the most important peaks of FAB negative mass spectra of the β -hydroxyoximes 7-10 are presented in Table 3.

The metastable and CAD mass-analyzed ion kinetic energy (MIKE) spectra of $(M - H)^-$ ions show that parallel alkanol losses do not occur for negative ions of this type. Instead, upon CA, losses of R'OH take place. As seen in the metastable ion spectra of the β -hydroxybenzaldoximes ($R = H$), the only product ion is from the loss of H_2O . Losses of NO and $R'CHNOH$ give rise to the other ions observed in the metastable ion spectra of the other β -hydroxyoximes ($R' = CH_3$ or C_6H_5).

The ions carrying the highest percentage of the total fragment ion current are produced by NO losses under CA conditions. For the β -hydroxyoximes with the larger R groups, the losses of H_2O and NO compete with those of the elements of the alkanes and R'OH. The alkane losses are rationalized as charge-remote decompositions [16, 17]. The CAD spectra of the $(M - H)^-$ ions of the β -hydroxyoximes 7-10 are given in Table 4.

The R'OH losses from the $(M - H)^-$ ions lead probably to the formation of the corresponding β -cyanophenoxide ions. Phenols are stronger acids than oximes, and reduction to $[(M - H) - O]^-$ would remove the possibility of ionization of the $>CNOH$ group. If the hydrogen atom lost were oximic and not phenolic, reduction with $[(M - H) - O]^-$ formation

Figure 4. Product ion spectra of: (a) $(M + H)^+$ of oxime 9 (CAD, 30% beam reduction), (b) $(M + Na)^+$ of oxime 9 (CAD, 30% beam reduction). Δ indicates alkane loss; $\blacksquare$ indicates alkene loss; * indicates alkanol loss.

would not occur, as we have observed for aromatic oximes (without the hydroxyl group) for which the $>CNO^-$ anion is formed. This is in agreement with solution data in basic media. Although some oximes are reduced to their corresponding imines in weakly alkaline solutions, this does not occur in strong alkaline solutions because formation of the corresponding $>CNO^-$ oxime anions occurs more readily [25, 26].

To verify the β -cyanophenoxide structure of the ions formed by R'OH loss from the $(M - H)^-$ ions upon CA of β -hydroxyoximes, the CAD spectrum of the α -cyanophenoxide ion of m/z 118, formed in the negative FAB mass spectra of the 2-hydroxybenzonitrile, was compared with the spectra for the m/z 118 ions formed in the spectra of hydroxyoximes 1, 2, and 3. These CAD spectra are nearly identical. Further evidence for the β -cyanophenoxide structure comes from the CAD spectra of the negative ions of the β -hydroxyoximes with the same large R substituent groups and with different R', as illustrated in Figure 5 in which the spectra of the putative β -cyanophenoxide ion of m/z 244 from oximes 8 and 9 are shown. Although the ion of m/z 244 can also be formed by a loss of H_2 from the $[(M - H) - O]^-$ on produced from oxime 8, the dominant fragmentation processes are losses from the side chain, and the differences between the two spectra are few.

EI Mass Spectra and Metastable MIKE Spectra

The chemistry of oxime radical cations was also investigated because a radical cation is proposed to be an important intermediate in the decomposition of $(M + H)^+$ ions of oximes. In the EI mass spectra of the β -hydroxyoximes with larger R groups (compounds 7-10), the molecular radical cation is not very abundant, contrasting with the abundant molecular $(M + H)^+$ ions obtained under FAB. Ions arising by losses of alkyl radicals 14 u apart (from methyl to increasing higher homologues, up to the branching point, or the

Table 3. Fast atom bombardment negative ion mass spectra of hydroxyoximes 7-10 (abundances as % of the base peak)

7	8	9	10
$m/z = 248$ (100%) [M - H] ⁻	$m/z = 262$ (100%) [M - H] ⁻	$m/z = 276$ (100%) [M - H] ⁻	$m/z = 338$ (100%) [M - H] ⁻
$m/z = 232$ (65%) [(M - H) - O] ⁻	$m/z = 246$ (54%) [(M - H) - O] ⁻	$m/z = 260$ (35%) [(M - H) - O] ⁻	$m/z = 322$ (65%) [(M - H) - O] ⁻
$m/z = 230$ (90%) [(M - H) - R'OH] ⁻	$m/z = 244$ (56%) [(M - H) - R'OH] ⁻	$m/z = 244$ (20%) [(M - H) - R'OH] ⁻	$m/z = 308$ (60%) [(M - H) - NO] ⁻
$m/z = 162$ (10%) [(M - H) - C ₆ H ₄] ⁻	$m/z = 219$ (11%) [(M - H) - O - NO] ⁻	$m/z = 261$ (15%) [(M - H) - CH ₃] ⁻	$m/z = 266$ (2%) [(M - H) - R'OH] ⁻
$m/z = 146$ (4%) [(M - H) - O - C ₆ H ₄] ⁻	$m/z = 172$ (9%) [(M - H) - O - C ₅ H ₁₂] ⁻	$m/z = 158$ (12%) [(M - H) - R'OH - C ₆ H ₄] ⁻	$m/z = 158$ (26%) [(M - H) - R'OH - C ₆ H ₄] ⁻
$m/z = 144$ (18%) [(M - H) - R'OH - C ₆ H ₄] ⁻	$m/z = 158$ (28%) [(M - H) - R'OH - C ₆ H ₄] ⁻	$m/z = 219$ (10%) [(M - H) - R'CN] ⁻	$m/z = 236$ (8%) [(M - H) - O - C ₆ H ₄] ⁻
$m/z = 130$ (29%) [(M - H) - R'OH - C ₇ H ₆] ⁻	$m/z = 160$ (15%) [(M - H) - O - C ₆ H ₄] ⁻	$m/z = 174$ (6%) [(M - H) - O - C ₆ H ₄] ⁻	----

$n-1$ carbon atom in a linear alkyl chain with n carbons) are seen just as they are in the CAD spectra.

For the β -hydroxyoximes with smaller R groups (compounds 1-6) the molecular radical cation and the (M - OH)⁺ are abundant, and for the 2-hydroxy-5-methylacetophenone oxime, an ion of m/z 146 (loss of 19 u from M⁺) is found, as was previously reported in the EI mass spectrum of this compound [27].

The metastable ion decomposition of the molecular radical cations follows closely the mass spectral pattern; that is, alkyl losses are prominent. Alkyl losses upon EI for other compounds containing large chains were reported previously [19] and were rationalized as specific radical-induced cleavages following random hydrogen abstraction from the alkyl chain, a mechanism that is entirely consistent with the results reported here.

Experimental

Some of the β -hydroxyoximes were synthesized from their corresponding aldehydes and ketones by using standard procedures [28]. Some of the aldehydes were

synthesized from the corresponding p -alkylphenols by the Reimer-Tiemann synthesis [29]. β -Hydroxyoximes 8-10 were purified first by complexation with Cu [30] and further by high pressure liquid chromatography [31]. 2-Hydroxybenzaloxime and 2-hydroxybenzonitrile were purchased from Aldrich (Milwaukee, WI).

FAB mass spectra were obtained with a Kratos MS-50 triple analyzer mass spectrometer, which was described elsewhere [32]. A standard Kratos FAB source equipped with an Ion Tech Gun was used. The samples were dissolved in glycerol and DT (dithiothreitol/dithioerythritol) when in the positive mode, and in triethanolamine and glycerol when in the negative mode. Cationization was accomplished by using lithium and sodium chlorides. The cationized species, however, are more difficult to desorb than the protonated ones. Normal spectra were acquired at low resolution (~ 3000). Metastable and CAD MIKE spectra were obtained by scanning the second electrostatic sector. Collision-activated decomposition spectra were obtained by using helium as collision gas (in the collision cell located between the magnetic sector and the second electrostatic sector) and sufficient helium was

Table 4. CA MIKE spectra of $[(M - H)^-]$ ions of hydroxyoximes 7-10 (abundances as % of the base peak)

7	8	9	10
$m/z = 231$ (21%) $[(M - H) - OH]^-$	$m/z = 244$ (100%) $[(M - H) - R'OH]^-$	$m/z = 274$ (60%) $[(M - H) - 2H]^-$	$m/z = 320$ (9%) $[(M - H) - H_2O]^-$
$m/z = 230$ (100%) $[(M - H) - R'OH]^-$	$m/z = 232$ (37%) $[(M - H) - NO]^-$	$m/z = 258$ (50%) $[(M - H) - H_2O]^-$	$m/z = 308$ (100%) $[(M - H) - NO]^-$
$m/z = 218$ (28%) $[(M - H) - NO]^-$	$m/z = 218$ (5%) $[(M - H) - C_3H_8]^-$	$m/z = 246$ (10%) $[(M - H) - NO]^-$	$m/z = 266$ (3%) $[(M - H) - C_5H_{12}]^-$
$m/z = 203$ (4%) $[(M - H) - R'CHNOH]^-$	$m/z = 204$ (3%) $[(M - H) - C_4H_{10}]^-$	$m/z = 244$ (100%) $[(M - H) - R'OH]^-$	$m/z = 252$ (3%) $[(M - H) - C_7H_{16}]^-$
$m/z = 162$ (13%) $[(M - H) - C_6H_{14}]^-$	$m/z = 190$ (5%) $[(M - H) - C_5H_{12}]^-$	$m/z = 218$ (35%) $[(M - H) - C_4H_{10}]^-$	$m/z = 244$ (3%) $[(M - H) - R'OH]^-$
$m/z = 148$ (8%) $[(M - H) - C_7H_{16}]^-$	$m/z = 176$ (8%) $[(M - H) - C_6H_{14}]^-$	$m/z = 217$ (50%) $[(M - H) - R'CHNOH]^-$	$m/z = 236$ (3%) $[(M - H) - NO - C_5H_{12}]$
$m/z = 132$ (8%) $[(M - H) - OH - C_7H_{16}]^-$	$m/z = 158$ (7%) $[(M - H) - R'OH - C_6H_{14}]^-$	$m/z = 190$ (45%) $[(M - H) - C_6H_{14}]^-$	$m/z = 222$ (3%) $[(M - H) - NO - C_6H_{14}]^-$

Figure 5. Product ion spectra of: (a) $(M - H - R'OH)^-$ of oxime 8 (CAD, 50% beam reduction), (b) $(M - H - R'OH)^-$ of oxime 9 (CAD, 50% beam reduction).

added to cause a 50% suppression of the intensity of the signal. The data were processed with a standard DS-55 data system using software written at the Midwest Center for Mass Spectrometry.

In the course of publishing this work, a four-sector tandem mass spectrometer (Fisons VG ZAB-T) was installed at the University of Nebraska. Tandem mass spectra for many of the figures of this article were reacquired on that instrument. For a preliminary description, see ref 33. Ions were desorbed by using Cs^+ LSIMS (Cs^+ ion energy was 25 keV) and a standard VG LSIMS source operated at 8 kV. The resolving power of MS-I was 1500, whereas that of MS-II was that which applied when the object slit of MS-II was closed until the peak shape for the parent ion became "rounded off" (slit fully illuminated). The collision cell was unflashed. Spectra were acquired by scanning MS-II and using the single point detector.

Full-scan, high-resolution ($R = 10000$, 10% valley definition) EI mass spectra were obtained with a Kratos MS-50 double focusing mass spectrometer, interfaced

to a Nova -4X computer and operating with DS-55 software.

Low resolution EI mass spectra and metastable MIKE spectra were obtained with a Varian MAT 112S medium resolution reverse geometry instrument, with a custom-built system for scanning either the electric field of the electrostatic analyzer or the accelerating potential. The system is based on a Motorola 6802 microprocessor, which can generate analog displays of the data, and a microcomputer-based data acquisition system developed at the University of Aveiro [34].

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References

- Ashbrook, A. W. *Coord. Chem. Rev.* **1975**, *16*, 285.
- Singh, R. B.; Garg, B. G.; Singh, R. D. *Talanta* **1979**, *26*, 425.
- Kewitz, H.; Wilson, I. B.; Nachmansohn, D. *Arch. Biochem. Biophys.* **1956**, *64*, 456.
- Cooks, R. G.; Varvoglis, A. G. *Org. Mass Spectrom.* **1971**, *5*, 687.
- Leyshon, W. M.; Wilson, D. A. *Org. Mass Spectrom.* **1973**, *7*, 251.
- Vijfhuizen, P. C.; Terlow, J. K. *Org. Mass Spectrom.* **1977**, *12*, 245.
- Maquestiau, A.; van Haverbeke, Y.; de Meyer, C.; Duthoit, C.; Meyrant, P.; Flammang, R. *Nouveau J. Chimie* **1979**, *3*, 517.
- Maquestiau, A.; van Haverbeke, Y.; Flammang, R.; Meyrant, P. *Org. Mass Spectrom.* **1980**, *15*, 80.
- Vincze, A.; Bush, K. L.; Cooks, R. G. *Anal. Chim. Acta* **1982**, *136*, 143.
- Santana-Marques, M. G.; Ferrer-Correia, A. J.; Gross, M. L. *Anal. Chem.* **1989**, *61*, 1442.
- Nakamura, T.; Nagaki, H.; Kinoshita, T. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2798.
- Burkin, A. R. *Chem. Ind.* **1983**, *18*, 690.
- Kruger, T. L.; Litton, J. F.; Kondrat, R. W.; Cooks, R. G. *Anal. Chem.* **1976**, *48*, 2113.
- Harrison, A. G.; Kallury, R. K. M. R. *Org. Mass Spectrom.* **1980**, *15*, 284.
- Balasanmugan, K.; Miller, J. M. *Org. Mass Spectrom.* **1988**, *23*, 267.
- Jensen, N. J.; Tomer, K. B.; Gross, M. L. *Anal. Chem.* **1985**, *57*, 2018.
- Jensen, N. J.; Tomer, K. B.; Gross, M. L. *J. Am. Chem. Soc.* **1985**, *107*, 1863.
- Harvey, D. J. *Biomed. Mass Spectrom.* **1984**, *11*, 187.
- Vetter, W.; Meister, W.; Oesterheld, G. *Helv. Chim. Acta* **1977**, *60*, 1203.
- Harvey, D. J. *Biomed. Mass Spectrom.* **1982**, *9*, 33.
- Harvey, D. J. *Biomed. Mass Spectrom.* **1984**, *11*, 340.
- Anderson, B. A.; Holman, R. T. *Lipids* **1974**, *9*, 185.
- Wysocki, V. H.; Ross, M. M. *Int. J. Mass Spectrom. Ion Processes* **1991**, *104*, 179.
- Mallis, L. M.; Russell, D. H. *Anal. Chem.* **1986**, *58*, 1076.
- Lund, H. *Acta Chim. Scan.* **1959**, *13*, 249.
- Gardner, H. J.; Georgans, W. P. *J. Chem. Soc.* **1956**, 4180.
- Lozynski, M.; Krzyzanowska, E. *Org. Mass Spectrom.* **1986**, *21*, 33.
- Vogel, A. I. *Practical Organic Chemistry*; Longman: London, 1974; pp 345, 721.
- Stepniak-Biniakiewicz, D. *Polish J. Chem.* **1980**, *54*, 1567.
- Preston, J. S.; Whewell, R. J. *J. Inorg. Nucl. Chem.* **1977**, *39*, 1675.
- Sowa, W.; Licht, B. H.; Itzkovitch, I. J. *J. Chromatog.* **1976**, *116*, 197.
- Gross, M. L.; Chess, E. K.; Lyon, P. A.; Crow, F. W.; Evans, S.; Tudge, H. *Int. J. Mass Spectrom. Ion Phys.* **1982**, *42*, 243.
- Gross, M. L. In: *Methods in Enzymology*, vol. 193: *Mass Spectrometry*; McCloskey, J. A., ed. Academic: San Diego, 1990, pp 150-151.
- Cardoso, A. M. M.; Santana-Marques, M. G.; Ferrer-Correia, A. J. *Rev. Port. Quim.* **1986**, *28*, 101.