Gas-phase Rearrangements of Deprotonated Ketoximes, Ketoxime Ethers, and Aldoximes. A Negative-ion Beckmann Rearrangement

Gregory W. Adams and John H. Bowie *
Department of Organic Chemistry, The University of Adelaide, South Australia, 5001
Roger N. Hayes
Department of Chemistry, University of Nebraska, Lincoln, Nebraska, 68588-0362, USA

Evidence is presented which indicates that the pronounced loss of water from deprotonated ketoximes involves specific proton transfer followed by a negative-ion Beckmann rearrangement. For example, $Me_2C{=}NO^- \longrightarrow {}^-CH_2(Me)C{=}NOH \xrightarrow{O} [(CH_2{=}C{=}NMe)\,{}^-OH] \longrightarrow CH_2{=}C{=}NCH_2^- + H_2O$. Deprotonated aldoximes, *e.g.* $MeCH{=}NO^-$, fragment in this way, but also undergo the competing process $MeCH{=}NO^- \longrightarrow MeC{=}NOH \longrightarrow [(MeCN)\,{}^-OH] \longrightarrow {}^-CH_2CN + H_2O$. Other rearrangements occur when proton transfer to oxygen does not occur; *e.g.* $Ph_2C{=}NO^- \xrightarrow{O} PhC{=}NOPh \longrightarrow PhO^- + PhCN$.

We have recently reported a number of simple 'rules' for fragmentations of even-electron negative ions including enolates, C^-, N^-, and O^- species.[1,2] Most fragmentations involve loss of a neutral molecule, and many such reactions are initiated from the charged centre through ion complexes [*e.g.* equation (1), R^1 = H, alkyl or aryl]. When such reactions are either unfavourable or not possible, one of two events generally occurs, *viz.* (*i*) proton transfer to the original charged centre produces a new anion which may fragment [*e.g.* carboxylate species, equations (2) and (3)[3]† or (*ii*) some type of internal (skeletal) rearrangement occurs {*e.g.* sigmatropic[5,6] and Smiles[7] [equation (4)] rearrangements}.

Deprotonated oximes $(R^1)(R^2CH_2)C{=}NO^-$ (R^1 and R^2 = H, alkyl or aryl), are somewhat akin to carboxylate species [see equations (2) and (3)], since it is unlikely that fragmentation can be directly effected through O^-. Either proton transfer to oxygen, or some internal rearrangement would be expected to precede fragmentation. Proton transfer [see equation (5)] could be facile since the acidities at the two centres should differ only by some 30 kJ mol^{-1}. For example, the gas phase ΔH^0_{acid} values for $Me_2C{=}NOH$[8] and $(CH_3)_2C{=}NOMe$[9] are 1 532 and 1 561 kJ mol^{-1} respectively.

This paper reports the basic fragmentations of deprotonated ketoximes, ketoxime ethers and aldoximes, and provides evidence in favour of a number of rearrangement reactions including the negative-ion Beckmann rearrangement.

Results and Discussion

Collision-induced Dissociations of Deprotonated Alkyl Ketoximes.—Alkyl ketoxime spectra are listed in Table 1 or recorded in Figures 1–3. Deprotonation was effected by NH_2^-: under these conditions, $R_2C{=}NOD$ systems yield $M - D^+$ and $M - H^+$ ions in the approximate ratio 4–5:1. This is the expected result since although the O*H* position is the more acidic, O*H* and –C*H*C=N– differ in acidity by only some 30 kJ mol^{-1}. Labelling experiments are crucial for this study, and exchange reactions must be carried out with care because of the similarities in acidity at the two described positions. Full details are provided in the Experimental section.

The oxime of acetone is prototypical in this series; its decompositions are shown in Figures 1 and 2. Major fragmentations shown in Figure 1 are the loss of H•, the losses of H_2O and CH_4 and the formation of HO^-. Less abundant peaks are observed for the loss of HON• and the formation of CNO^-, $^-CH_2CN$, NO^-, and CN^-. The characteristic decomposition of virtually all oximes is loss of water; for the majority of alkyl ketoximes this process gives the base peak of the spectrum (Table 1). Loss of water is not a usual feature in negative ion spectra of systems containing O^- functionality, but is sometimes pronounced when such a loss gives a stabilized anion (*e.g.* formation of conjugated benzyl anions[10]). The spectrum of the $M - H^+$ ion from $Me_2C{=}NOD$ is shown in Figure 2; this species loses H_2O and HOD in the ratio 6.5:1. Thus, the loss of water follows rapid interconversion of (**1**) and (**2**) (Scheme 1); in this case the data may be interpreted in terms of random loss of water together with a small isotope effect (H/D = 1.3) in favour of H_2O rather than HOD loss.‡

We suggest that the loss of water occurs from (**2**) (Scheme 1) by a negative-ion Beckmann rearrangement, with methyl-anion migration proceeding to N to form ion complex (**3**). This species is the precursor of three of the fragmentations observed in Figure 1 (also Figure 2); *viz.* the formation of HO^- by direct displacement [equation (8)], the elimination of water [equation (9)] together with the production of deprotonated acetonitrile by the S_Ni reaction shown in equation (10). The competitive loss of methane can be rationalised by a similar process: here, methyl anion migration from (**2**) forms a transient species (**4**) in which the methyl anion may deprotonate the acidic hydrogen attached to O as shown in equation (11). The final major fragmentation is loss of H•. Loss of a radical to form a stabilized ion radical is a common fragmentation of even-electron anions,[1,2] in this case loss of a hydrogen atom from either (**1**) or (**2**) will form the products shown in equation (6) and (7). Of the minor fragmentations, loss of •NOH may occur through (**2**) to form

† When the electron affinity of $RCH_2^\bullet$ is positive, the simple reaction $RCH_2CO_2^- \longrightarrow RCH_2^- + CO_2$ is observed.[3,4]

‡ The data in Table 1 show that the loss of H_2O is always more pronounced than loss of HOD from $(M - H^+)^-$ ions of appropriately labelled (D_1) systems. In the cases of unsymmetrically substituted ketoximes, equilibration of O*H* with both carbanion centres occurs. The extent of exchange is not the same in all cases, and no clear trend is apparent. In this context it must be noted that however carefully the exchange experiment is carried out (see Experimental section), a small amount of a D_2 component could affect the H_2O/HOD ratio. For example $R^1(R^2CHD)C{=}NOD$ will yield mainly $R^1(R^2CHD){=}NO^-$ and this ion may give different H_2O/HOD ratios than will $R^1(R^2CH)^-{=}NOD$, unless complete equilibration has occurred.

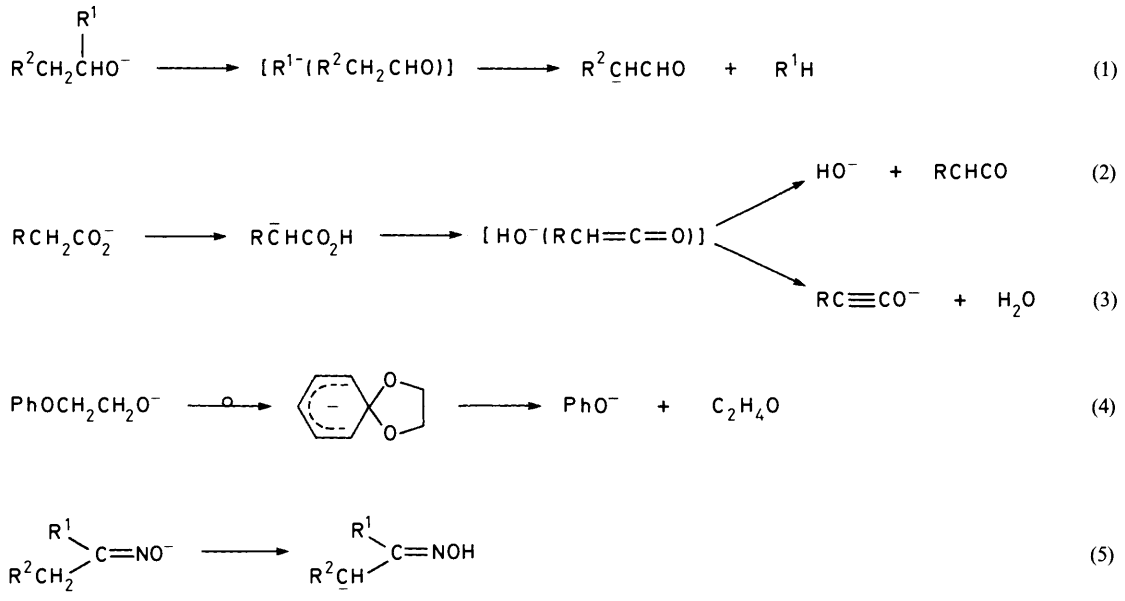


Table 1. Collisional activation mass spectra of deprotonated alkyl ketoximes.*

	Loss													
Parent ion	H$^{\bullet}$	D$^{\bullet}$	Me$^{\bullet}$	CH_4	CD_4	H_2O	HOD	D_2O	Et$^{\bullet}$	NOH$^{\bullet}$	NOD$^{\bullet}$	MeOH	C_3H_8	Pr$^{\bullet}$
$Me_2CNOH - H^+$	100			15		85				6		2[a]		
$(CD_3)_2CNOD - D^+$		100			10			70			4			
$Me(Et)CNOD - D^+$	55		5			100						0.5		
$Me(Et)CNOD - H^+$	100	8				79	42							
$Me(CD_3CH_2)CNOH - H^+$	95	5				100								
$Me(Pr)CNOH - H^+$	25					100			30			0.2	4	
$CD_3(EtCD_2)CNOD - D^+$		15					4	100	31				*b*	
$Me(Pr^i)CNOH - H^+$	24			8		100							1	
$CD_3(Me_2CD)CNOD - D^+$		20		6			7	100					*d*	
$Me(Bu)CNOH - H^+$	34					100								18
$Me(Bu^s)CNOH - H^+$	28					100			14					
$Me(Bu^t)CNOH - H^+$	31			32		100								
$Et_2CNOH - H^+$	22					100								
$Et(Pr)CNOH - H^+$	21					100			30					
$Pr_2CNOD - D^+$ (*d*)	18					100			67					
$Pr^i_2CNOH - H^+$	19			15		100								

	Formation							
Parent ion	CNO^-	$^-CH_2CN$	^-CHDCN	$^-CD_2CN$	NO^-	CN^-	HO^-	DO^-
$Me_2CNOH - H^+$	2	2[a]			1	1	8	
$(CD_3)_2CNOD - D^+$	2			1	1	1		6
$Me(Et)CNOD - D^+$	2	2			1	1	25	
$Me(Et)CNOD - H^+$	1	1[b]	1[b]		0.5	0.5	15	8
$Me(CD_3CH_2)CNOH - H^+$	1	1			0.5	0.3	18	
$Me(Pr)CNOH - H^+$	1	2			1	0.5	6	
$CD_3(EtCD_2)CNOD - D^+$	3[c]			3[c]	0.5	0.5		6
$Me(Pr^i)CNOH - H^+$	2	2			1	0.5	17	
$CD_3(Me_2CD)CNOD - D^+$	4[c]			4[c]	1	1		9
$Me(Bu)CNOH - H^+$	1	1			0.5	0.2	9	
$Me(Bu^s)CNOH - H^+$	1	1			0.4	0.2	6	
$Me(Bu^t)CNOH - H^+$	1	2			0.1		51	
$Et_2CNOH - H^+$							3	
$Et(Pr)CNOH - H^+$							9	
$Pr_2CNOD - D^+$ (*d*)							7	
$Pr^i_2CNOH - H^+$							3	

* Numbers listed in the table refer to relative abundances of peaks with reference to base peak (100%) of that spectrum.
[a] Loss of MeOH yields $^-CH_2CN$. [b] Not resolved. [c] CNO^- and $^-CD_2CN$ = 42 amu. [d] The ion $Pr_2CNOD - H^+$ loses H_2O and HOD in the approximate ratio 2:1 (weak spectrum).

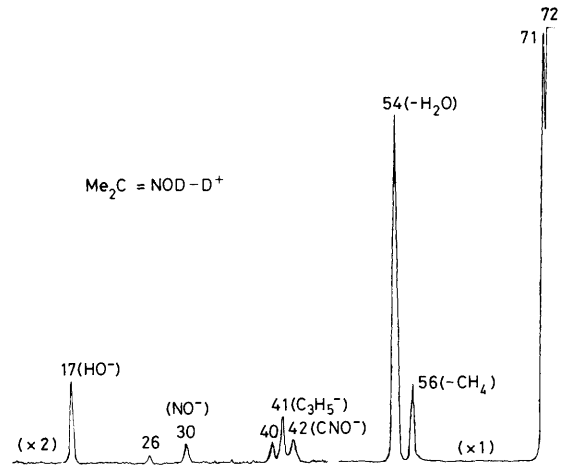


Figure 1. Collisional activation mass spectrum of $[Me_2C{=}NOD - D^+]^-$. See the Experimental section for details.

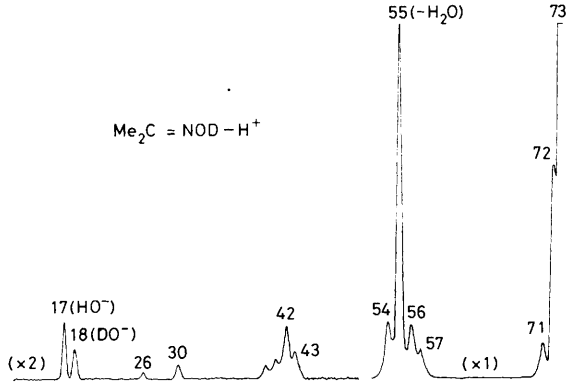


Figure 2. Collisional activation mass spectrum of $[Me_2C{=}NOD = H^+]^-$.

$Me\text{–}\bar{C}{=}CH_2$, and NO^- could be formed from (**1**). The mechanisms of the processes forming CN^- and CNO^- are not known.

The classical Beckmann rearrangement[11] in the condensed phase is an acid-catalysed reaction: protonation at oxygen aids the reaction by elimination of H_2O, a good leaving group.[12] The group which migrates to N is often that *trans* to hydroxyl, but isomerisation occurring prior to migration is also known.[13] Beckmann rearrangements of molecular radical cations have not been reported, but such reactions do occur for protonated oximes in the gas phase.[14]

In the case of the negative-ion Beckmann rearrangement, elimination of H_2O from intermediate (**2**) (Scheme 1) should yield $CH_2{=}C{=}N\bar{C}H_2$ [*m/z* 54 in Figure 1; see also equation (9)]. The collisional activation and charge reversal (positive ion)[15] mass spectra (MS/MS/MS) of *m/z* 54 are recorded in Table 2. The spectra are consistent with structure $CH_2{=}C{=}N\bar{C}H_2$, *i.e.* both CA and CR spectra show pronounced loss of CH_2 (Table 2). In the case of an unsymmetrical oxime, specific *trans* migration would not be expected since isomerisation of the double bond should occur [see (**1**), Scheme 1]. Thus the simplest example, deprotonated butan-2-one ketoxime, should give two Beckmann rearrangements: ethyl and methyl anion migration should yield (**5**) and (**6**) respectively, and internal deprotonation in these intermediates should occur as shown in equations (12), (14), and (15). Since $Me(CD_3CH_2)CNO^-$ loses H_2O exclusively (Table 1), process (14) does not occur. This is in accord with the greater acidity of the protons

Table 2. The collisional activation (CA) and charge reversal (CR) mass spectra (MS/MS/MS) of Beckmann product ions from Me_2CNO^- and $^-CH_2(Me)CNOMe$.

Precursor ion	Product ion	Spectrum [*m/z* (abundance)]
$(Me_2CNOH - H^+)^-$	$CH_2{=}C{=}N\bar{C}H_2$ ($-H_2O$, *m/z* 54)	CA: 40(100). CR: 54(4), 53(26), 52(100), 51(32), 40(24), 39(33), 38(14), 37(5), 28(31), 27(32), 26(38), 25(5), 14(4).
$(Me_2CNOMe - H^+)^-$	$CH_2{=}C{=}N\bar{C}H_2$ ($-$MeOH, *m/z* 54)	CA: 40(100). CR: 54(3), 53(24), 52(100), 51(31), 40(26), 39(35), 38(15), 37(5), 28(35), 27(30), 26(38), 25(5), 14(4).

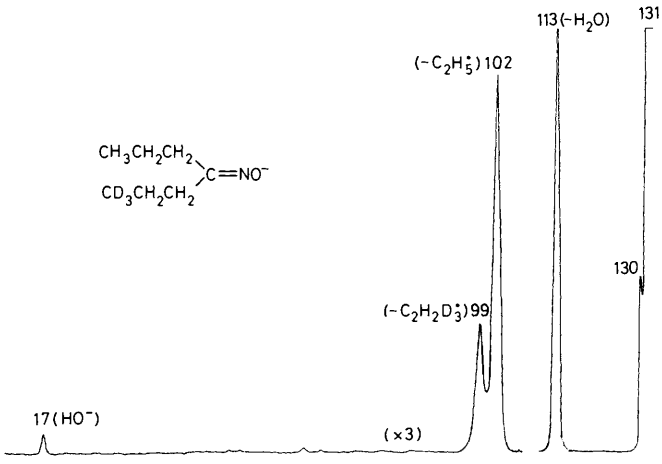
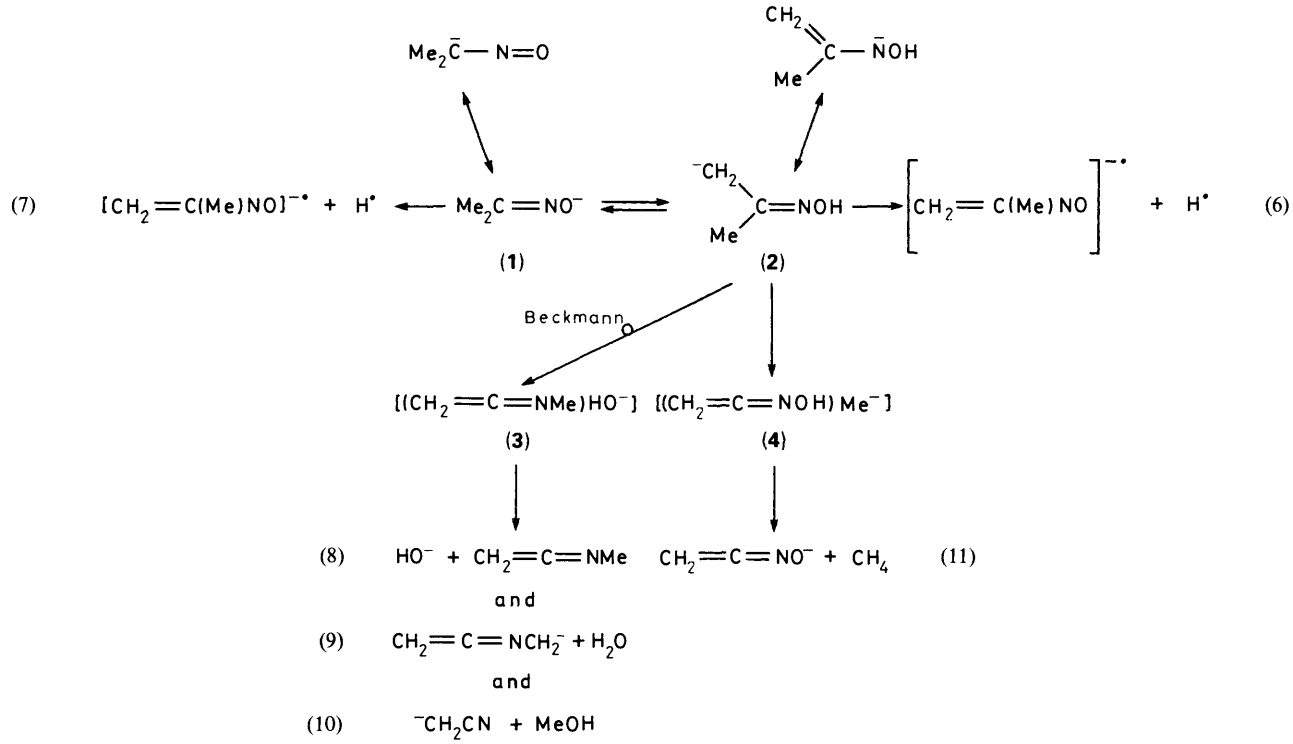


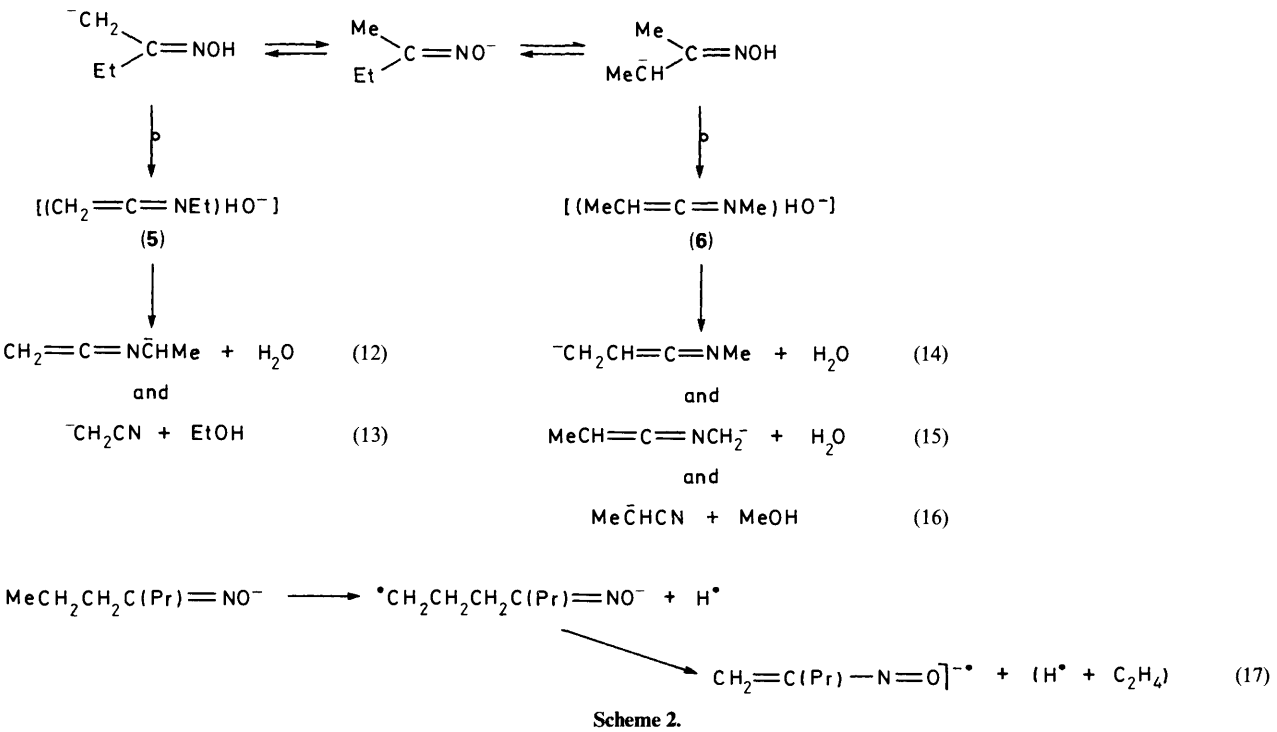
Figure 3. Collisional activation mass spectrum of $[Pr[CD_3(CH_2)_2]C{=}NOH - H^+]^-$.

on the NMe group [equation (15)]. That both methyl and ethyl substituents migrate is substantiated by the detection of the two S_Ni reactions [equations (13) and (16)]. Ethyl migration gives loss of ethanol [equation (13)], methyl migration loss of methanol [equation (16)]. The larger alcohol is lost preferentially, *e.g.* $Me(Et)CNO^-$ (EtOH:MeOH = 4:1), $Me(Pr)CNO^-$ (PrOH:MeOH = 5:1), whereas $Me(Bu)CNO^-$ loses only butanol to yield $^-CH_2CN$ (Table 1). This trend is likely to reflect the thermochemistry of the competing processes; not the migratory aptitude of the various substituents.

The final cleavage of ketoximes is that which apparently involves loss of the elements of an alkyl radical β to the trigonal carbon. Examination of Table 1 shows that $Me(Et)CNO^-$ has a small loss of Me$^\bullet$, a reaction analogous to that shown in equation (7) (Scheme 1). In contrast, $Me(Pr)CNO^-$ and $Me(Bu)CNO^-$ show substantial losses of C_2H_5 and C_3H_7 respectively. Labelling studies in cognate systems have shown that for R ⩾ Et, such processes do not involve simple cleavage resulting in loss of R$^\bullet$. For example, the losses of C_2H_5 from $(Et_2C\bar{C}O_2^-)$[3] and $(Ph\bar{C}Et_2)$[16] involve initial loss of H$^\bullet$ followed by loss of ethene. An analogous situation is shown in Figure 3 for $Pr(CD_3CH_2CH_2)CNO^-$—here the losses of C_2H_5 and $C_2H_2D_3$ occur in the ratio 100:33. This isotope effect, H/D =



Scheme 1.



Scheme 2.

3.0, indicates that the rate determining step involves either loss or transfer of a terminal hydrogen. We suggest the mechanism shown in equation (17); a mechanism consistent with the previously cited examples.[3,16]

Ketoxime Alkyl Ethers.—If our proposal for a negative-ion Beckmann rearrangement of oximes is correct (see Scheme 1), then deprotonated ketoxime methyl ethers $^{-}CH_2(R)C{=}NOMe$ should form MeO^- and eliminate MeOH by a Beckmann mechanism. The collisional activation spectra of related ketoxime alkyl ethers are listed in Table 3. The spectra are simple, and are dominated by the expected losses; these are rationalised for the methyl ether of acetone ketoxime by the Beckmann process shown in equations (18) and (19).

The product ion of equation (19), $CH_2{=}C{=}NCH_2^-$ (*m/z* 54), should be the same as that formed by the analogous reaction of deprotonated acetone ketoxime [equation (9), Scheme 1]. The collisional activation and charge reversal spectra (MS/MS/MS)

Table 3. Collisional activation mass spectra of deprotonated ketoxime ethers.*

	Loss						Formation				
Parent ion	H•	Me•	Et•	MeOH	EtOH	C_6H_6	$C_6H_5^-$	EtO^-	MeO^-	$^-CH_2CN$	CN^-
$^-CH_2(Me)C{=}NOMe$	84	5		100					24		
$^-CH_2(Me)C{=}NOEt$	88		15		100			91			
$^-CH_2(Ph)C{=}NOMe$	100	16		99		9			18	1	1

* Numbers listed in Table 3 refer to relative abundances of peaks with reference to the base peak (100%) of that spectrum.

Table 4. Collisional activation mass spectra of deprotonated aryl ketoximes.*

	Loss											
Parent ion	H•	D•	H_2	CH_4	CD_3H	H_2O	HOD	Et•	NOH•	C_6H_6	PhMe	PhOH	$PhCH{=}CH_2$
$Ph(Me)CNOH - H^+$	100			6		33			19				
$Ph(CD_3)CNOD - D^+$	100	25			7		40		6[a]				
$Ph(Pr)CNOH - H^+$	100					40		29					
$Ph_2CNOH - H^+$	100		35							25		1	
$Ph(PhCH_2)CNOH - H^+$	100					20					3		
$Me[Ph(CH_2)_3]CNOD - D^+$	47										31		100
$Me[Ph(CH_2)_3]CNOD - H^+$	61										27		100
$Me[PhCD_2(CH_2)_2]CNOH - D^+$	35	17									38[b]		c

	Formation							
Parent ion	PhO^-	$PhCH_2^-$	Ph^-	$^-CH_2CN$	$^-CD_2CN$	NO^-	CN^-	HO^-
$Ph(Me)CNOH - H^+$	2		0.1	0.6		0.1	0.4	0.3
$Ph(CD_3)CNOD - D^+$	1		0.1		1			0.2
$Ph(Pr)CNOH - H^+$								0.1
$Ph_2CNOH - H^+$	19		1				0.1	
$Ph(PhCH_2)CNOH - H^+$		2	1					
$Me[Ph(CH_2)_3]CNOD - D^+$		48						
$Me[Ph(CH_2)_3]CNOD - H^+$		65						
$Me[PhCD_2(CH_2)_2]CNOH - D^+$		75[d]						

* Numbers listed in Table 4 refer to relative abundances of peaks with reference to the base peak (100%) of that spectrum.
[a] There is also a loss of NOD• (13%). [b] In this case loss of $PhCH_2D$. [c] $-PhCH{=}CH_2$ (100%), $-PhCD{=}CH_2$ (91%). [d] In this case $PhCD_2^-$.

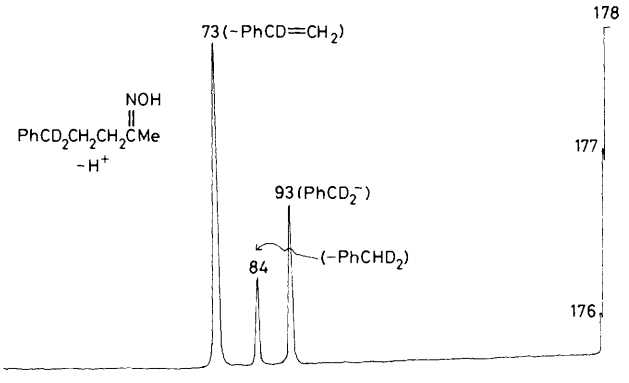


Figure 4. Collisional activation mass spectrum of $[PhCD_2CH_2CH_2C(Me){=}NOH - H^+]^-$.

of these two ions are compared in Table 2. The spectra are identical.

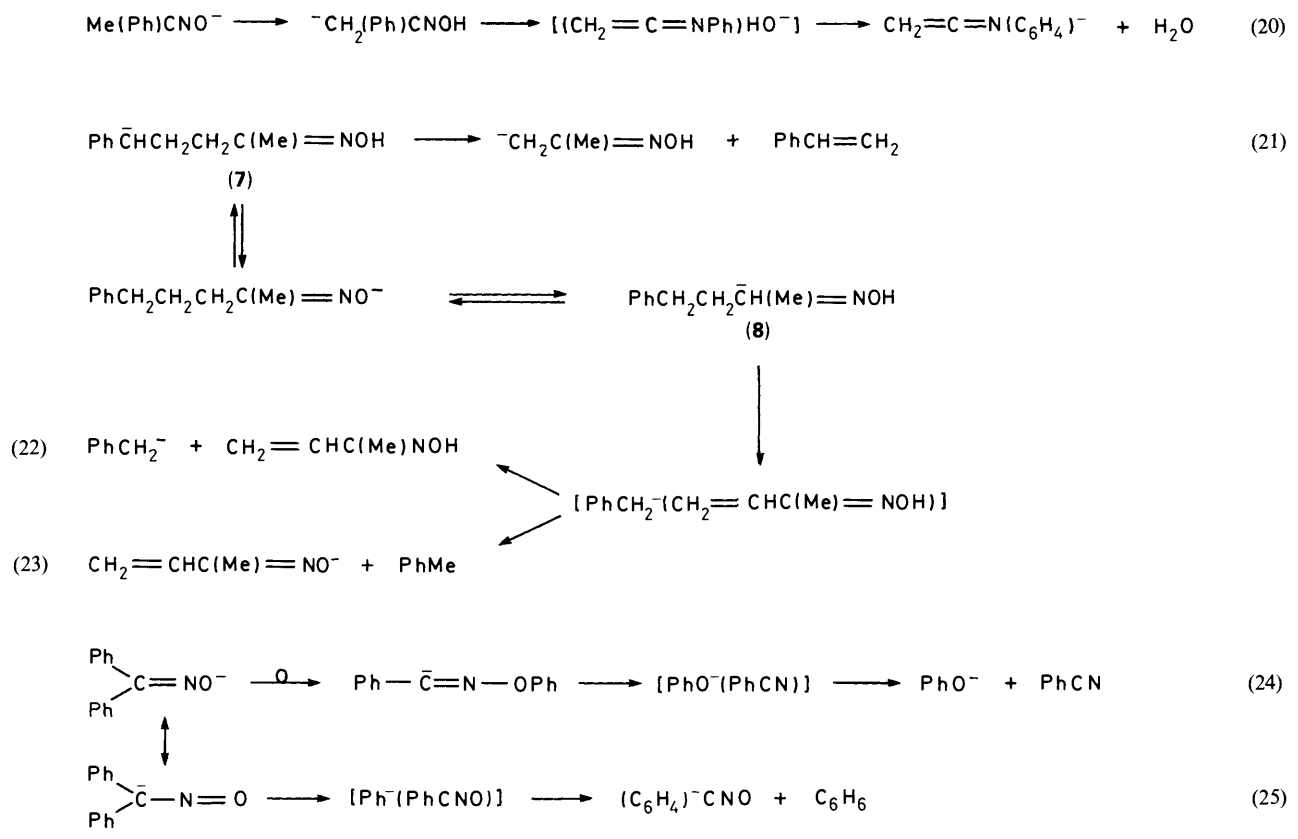
$$^-CH_2(Me)C{=}NOMe \longrightarrow [(CH_2{=}C{=}NMe)MeO^-]$$

$$MeO^- + CH_2{=}C{=}NMe \quad (18) \qquad CH_2{=}C{=}NCH_2^- + MeOH \quad (19)$$

Aryl Ketoximes.—Spectra are listed in Table 4, and a particular example is illustrated in Figure 4. Alkyl aryl ketoximes behave normally; for example, deprotonated acetophenone ketoxime eliminates water as shown in equation (20) (Scheme 3). The spectrum of deprotonated $Me(PhCH_2CH_2CH_2)C{=}NOH$ is particularly interesting since it emphasises the ready methylene proton transfer reactions which may occur in such systems. The fragmentations are best illustrated by the spectra of the labelled ions shown in Figure 4 and Table 4. In these cases the Beckmann rearrangement is completely suppressed by more energetically favourable fragmentations. For example, proton transfer from the benzylic position to O^- yields (**7**) which decomposes as shown in equation (21). Alternatively, proton transfer to O^- gives (**8**) which fragments to produce $PhCH_2^-$ [equation (22)] and to eliminate toluene [equation (23)].

Finally, deprotonated benzophenone cannot undergo the negative-ion Beckmann rearrangement. Instead, a phenyl group migrates to oxygen with the ultimate formation of PhO^- [equation (24)].* The alternative elimination of phenol is minor in comparison because PhO^- is not a strong enough base to effectively deprotonate benzonitrile (see Table 4; also ΔH^0_{acid} PhOH = 1 461 kJ mol^{-1}).[17] In addition, benzene is eliminated by the process shown in equation (25) (in this case $C_6H_5^-$ is a strong enough base to deprotonate PhCNO – ΔH^0_{acid} C_6H_6 = 1 677 kJ mol^{-1}).[18]

* An alternative mechanism could involve a Smiles intermediate.[7] Even if this were so, the reaction would then proceed through the ion complex $[PhO^-(PhCN)]$.



Scheme 3.

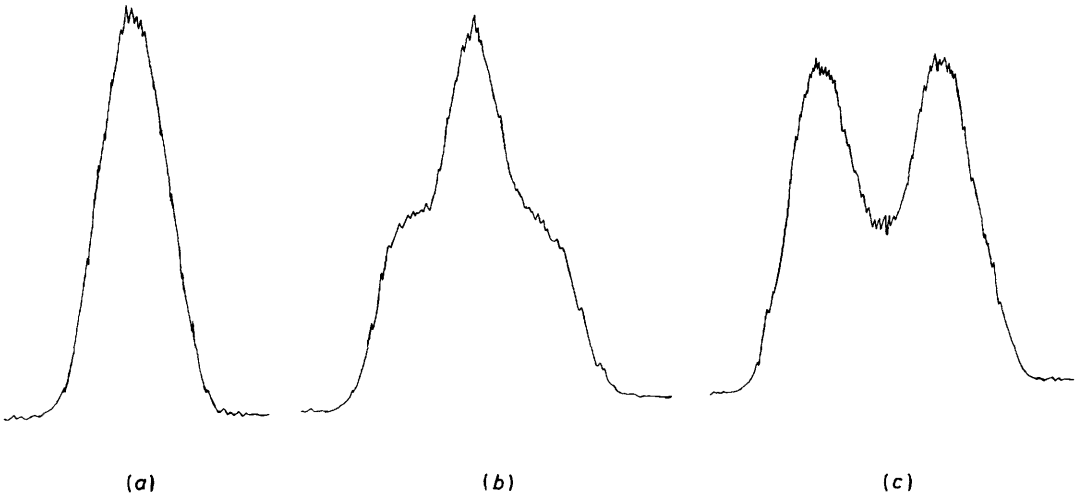


Figure 5. Peak profiles of HO^- ions in the spectra of $[Me_2C{=}NOD - D^+]^-$ (*a*), $[MeCH{=}NOD - D^+]^-$ (*b*) and $[PhCH{=}NOD - D^+]^-$ (*c*). Width of peaks at half height [(volts ±2), an average of 10 scans, are 59 (*a*), 97 (*b*), and 113 (*c*).

Aldoximes.—We have left the discussion of aldoximes until last, since they have the most complex fragmentations of all oximes studied. This result was not unexpected since the conventional Beckmann rearrangement is known to be sluggish with aldoximes; hydrogen only migrates under special catalytic conditions.[19] The clue to the complexity of the spectra is demonstrated by the HO^- peak profiles shown in Figure 5. The HO^- peak from deprotonated acetone ketoxime is Gaussian with no fine structure, suggestive of formation by a single mechanism (see also Figure 1 and Scheme 1). The corresponding peak from acetaldehyde aldoxime is composite, with a sharp peak superimposed on a dish-shaped peak. This is indicative of two modes of formation of HO^- in this case. Most significant is the dish-shaped peak from $PhCH{=}NO^-$, an ion which cannot undergo a negative-ion Beckmann rearrangement of the type shown in Scheme 1.

The spectra of selected aldoximes are listed in Table 5, and it is most convenient to start with $PhCH{=}NO^-$. The first observation is that *Z* and *E* isomers have identical spectra; the second that the major fragmentation involves statistical (random) loss of H• from the phenyl ring. But the characteristic fragmentations are the formation of HO^- and the loss of H_2O. Labelling studies (Table 5) show that the formation of HO^- specifically involves the methine hydrogen, and that the loss of this hydrogen together with statistical loss of a ring hydrogen constitutes the H_2O loss. These processes are summarised in

Table 5. Collisional activation mass spectra of deprotonated aldoximes.*

Parent ion	Loss									
	$H^{\cdot}$	$D^{\cdot}$	CH_4	CH_3D	CD_3H	H_2O	HOD	D_2O	$Et^{\cdot}$	$(H_2O + CH_4)$
$MeCH{=}NOD - D^+$	100		23[a]			42				
$MeCH{=}NOD - H^+$	100	21			32[b]	60	27			
$MeCD{=}NOH - H^+$	100			28[b]			61			
$CD_3CH{=}NOD - D^+$		35			100[b,c]		100[c]			
$EtCH{=}NOH - H^+$	100					88				
$PrCH{=}NOD - D^+$	33					54[d]			100	58
$PrCH{=}NOD - H^+$	100	33				35[e]	20[e]		67	58[f]
$EtCD_2CH{=}NOD - D^+$							20[g]		100	*h*
syn $PhCH{=}NOD - D^+$	100					4				
anti $PhCH{=}NOD - D^+$	100					4				
syn $PhCD{=}NOH - H^+$	100						5			
syn  $CD{=}NOH - H^+$	100	53				12	18			

Parent ion	Formation							
	CNO^-	NO^-	$C_2H_3^-$	$C_2H_2D^-$	$C_2HD_2^-$	CH^-	HO^-	DO^-
$MeCH{=}NOD - D^+$	23[a]	5	8			7	7	
$MeCH{=}NOD - H^+$	32[b]	5	7	9		12	12	5
$MeCD{=}NOH - H^+$	28[b]	5		14		14	8	
$CD_3CH{=}NOD - D^+$	100[b]	5			15	22	8	16
$EtCH{=}NOH - H^+$	18					6	6	
$PrCH{=}NOD - D^+$	5					8	6	
$PrCH{=}NOD - H^+$	8					10	6	6
$EtCD_2CH{=}NOD - D^+$	6					12	4	6
syn $PhCH{=}NOD - D^+$	0.5					0.2	0.3	
anti $PhCH{=}NOD - D^+$	0.5					0.2	0.3	
syn $PhCD{=}NOH - H^+$	0.4					0.2		0.6
syn  $CD{=}NOH - H^+$	2					0.5		0.5

* Numbers listed in Table 5 refer to relative abundances of peaks with reference to the base peak (100%) of that spectrum.
[a] Loss of CH_4 gives CNO^-. [b] Loss of CH_3D or CD_3H (as appropriate) gives CNO^-. [c] D_2O and CD_3H = 20 amu. [d] This spectrum also shows a peak at *m/z* 66 (35%) corresponding to $-(H_2O + H_2)$. [e] This spectrum shows the following peaks in this region—*m/z* 69 (35%, $-H_2O$), 68 (20%, $-HOD$), 67 [17%, $-(H_2O + H_2)$], and 66 [19%, $-(HOD + H_2)$ and/or $-(H_2O + HD)$]. [f] In this case the peak at *m/z* 52 corresponds to $-(H_2O + CH_3D)$ and/or $-(HOD + CH_4)$. [g] Also peaks at *m/z* 67 [25%, $-(HOD + H_2)$] and 66 [12%, $-(HOD + HD)$]. [h] Peaks in this region are *m/z* 53 [27%, $-(HOD + CH_4)$] and 52 [41%, $-(HOD + CH_3D)$].

equations (26) and (27) (Scheme 4), and it is process (26) which gives rise to the dish-shaped peak shown in Figure 5(*c*). There is no formation of PhO^- noted in this spectrum [*cf.* equation (24), Scheme 3], hence in this reaction the migratory aptitude of H is greater than phenyl.

The two alkyl aldoximes and their labelled derivatives show many features in common with the ketoximes discussed earlier. But they are different in several respects, and these differences are discussed for acetaldehyde aldoxime, since its characteristic fragmentations are similar to those (Table 5) of the butyraldehyde derivative. There are two mechanisms for both the formation of HO^- and the loss of H_2O. The first is the Beckmann rearrangement involving hydrogen transfer to nitrogen [equations (28) and (29)]. Formation of HO^- by the Beckmann process produces the sharp central component of Figure 5(*b*) [*cf.* Figure 5(*a*)]. The second process is analogous to that shown in equations (26) and (27), *viz.*, methine H transfer to oxygen [equations (30) and (31)], with the formation of HO^- by this route producing the dish-shaped component of Figure 5(*b*) [*cf.* Figure 5(*c*)]. Finally, the ions CNO^- and $C_2H_3^-$ are pronounced in this spectrum; we suggest formation as shown in equations (32) and (33).

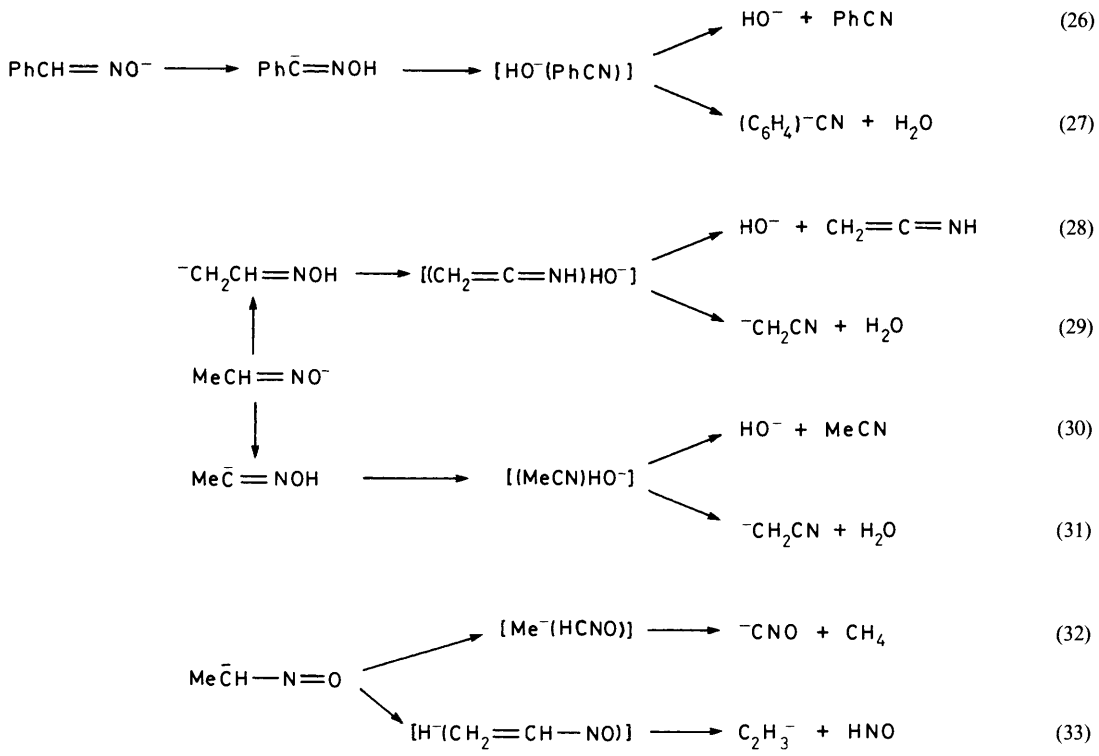
* 1 Torr = 133.332 Pa.

Conclusions

The compounds used in this study were chosen because deprotonation should yield a charged species which should not be able to fragment directly. This expectation is realised: elimination of neutral molecules from deprotonated oximes follow either proton transfer and/or skeletal rearrangement. The characteristic fragmentation involves a Beckmann type rearrangement, however other rearrangements involving migration of substituents to the O^- centre are also noted.

Experimental

Collisional activation mass spectra (MS/MS) were recorded using a Vacuum Generators ZAB 2HF mass spectrometer operating in the negative chemical-ionization mode.[20] All slits were fully open to obtain maximum sensitivity and to minimize energy resolution effects.[21] The chemical ionization slit was used in the ion source, ionizing energy 70 eV (tungsten filament); ion source temperature 180 °C, accelerating voltage 7 kV. Deprotonation of all neutrals was effected by H_2N^- (from NH_3). The indicated source pressure of NH_3 was 1×10^{-5} Torr.* The substrate pressure (liquids introduced through the septum inlet at 150 °C; solids through the direct probe with no heating) was typically 5×10^{-7} Torr. The estimated total pressure in the ion source is 10^{-1} Torr. The pressure of helium in



Scheme 4.

the second collision cell was 2×10^{-7} Torr measured by an ion gauge situated between the electric sector and the second collision cell. This produced a decrease in the main beam signal of *ca.* 10%, and corresponds to essentially single collision conditions.

Consecutive collision induced dissociation spectra (MS/MS/MS) and charge reversal[15] MS/MS/MS spectra were measured with a Kratos MS 50 TA instrument previously described.[22] Neutral substrates were deprotonated by MeO^- (from MeONO[23]) in a Kratos Mark IV chemical ionization source: ion source temperature 100 °C, electron energy 280 eV, emission current 500 μA and accelerating voltage 8 kV. Samples were introduced through an all glass heated inlet system at 100 °C. The indicated source pressure of substrate was 2×10^{-5} and of methyl nitrite 1×10^{-6} giving an estimated source pressure of *ca.* 10^{-1} Torr. The indicated pressure of helium in the collision cells was 2×10^{-6} Torr giving a decrease in the main beam signal of 30%.

Oximes derived from acetaldehyde,[24] propanal,[24] butanal,[24] acetone,[24] butan-2-one,[24] pentan-2-one,[24] 2-methylbutan-3-one,[25] hexan-2-one,[24] 3-methylpentan-2-one,[26] 2,2-dimethylbutan-3-one,[27] pentan-3-one,[24] hexan-3-one,[24] heptan-4-one,[24] 2,4-dimethylpentan-3-one,[27] acetophenone,[28] butyrophenone,[29] and benzyl phenyl ketone[30] are known compounds, and were prepared by standard method.[24] *Z*- and *E*-Benzaldoximes were prepared by the method of Vogel.[31]

5-Phenylpentan-2-ketoxime was prepared from 5-phenylpentan-2-one by the standard method.[24] Yield, 78%, b.p. 91–94 °C/0.15 mmHg. (Found: C, 74.65; H, 8.35%. $C_{11}H_{15}NO$ requires C, 74.55; H, 8.5%).

The Labelled Compounds.—α,O Deuterium exchange. The following compounds were prepared by the general procedure outlined below: 2,2,2-[$^2H_3$]ethanaldoxime-*O*-[$^2H_1$], 2,2,2,2′,2′,2′-propan-2-ketoxime-*O*-[$^2H_1$], 1,1,1,3,3-[$^2H_5$]-butan-2-ketoxime-*O*-[$^2H_1$], 2,4,4,4-[$^2H_4$]-2-methylbutan-3-ketoxime-*O*-[$^2H_1$], ([$^2H_3$]methyl) phenyl ketoxime-*O*-[$^2H_1$], and *syn*- and *anti*-benzaldoximes-*O*-[$^2H_1$].

A mixture of the appropriate aldehyde/ketone (1.0 g), deuterium oxide (7.5 cm^3) and sodium (10 mg), was heated under reflux for 24 h under an atmosphere of nitrogen. Hydroxylamine hydrochloride (1.2 mol equiv.) and sodium hydroxide (1.2 mol equiv.) were added and the mixture heated under reflux for 1 h. On cooling, sodium chloride (2 g) was added, the mixture extracted with diethyl ether (2×10 cm^3) the ethereal solution dried (Na_2SO_4) and the solvent removed to yield the labelled oxime. This procedure gave better than 90% incorporation of the appropriate number of deuterium atoms.

O-Deuteriated oximes. The *O*-deuteriated oximes of ethanaldoxime, butanaldoxime, butan-2-ketoxime, heptan-4-ketoxime and 5-phenylpentan-2-one were made in the following way.

The oxime (0.3 cm^3) and deuterium oxide (1 cm^3) were shaken together at 60 °C. Samples of the oxime (the upper layer) were pipetted off every 30 s, inserted into the septum inlet of the mass spectrometer, and the deuterium incorporation determined by positive-ion mass spectrometry. Generally, incorporation was *ca.* 10% $^2H_0$, 90% $^2H_1$ at 3 min, and 90% $^2H_1$, 10% $^2H_2$ at 4 min (100% $^2H_1$ could not be achieved). The time required to achieve an incorporation 10% $^2H_0$, 90% $^2H_1$ was determined, the mass spectrometer switched to the negative-ion mode, the labelling experiment repeated under identical conditions, the (10% $^2H_0$, 90% $^2H_1$) sample inserted into the septum inlet of the mass spectrometer, and the DO^-/CA/NICI spectrum recorded (by fast scan) within 30 s of insertion of the sample.

1-[$^2H_1$]Ethanaldoxime was prepared from 1,1-[$^2H_2$]nitroethane[32] by the method of Leitch.[32] Yield, 42%; $^2H_1$ = 98%.

syn-Phenyl([$^2H_1$]methan)aldoxime. Phenyl([$^2H_2$]methan)ol[33] was oxidised[34] to phenyl([$^2H_1$]methan)al, which was converted into the oxime by the standard method[24] (overall yield from $PhCD_2OH$, 22%; $^2H_1$ = 98%).

syn(2,4,6-[$^2H_3$]Phenyl)([$^2H_1$]methan)aldoxime. 2,4,6-[$^2H_3$]-Aniline ($^2H_3$ = 96%)[35] was converted[36] into 2,4,6-[$^2H_3$]-bromobenzene in 58% yield, which in turn was converted into 2,4,6-[$^2H_3$]benzoic acid (62% yield),[37] methyl 2,4,6-[$^2H_3$]benzoate (68% yield),[38] 2,4,6-phenyl([$^2H_2$]methan)ol (81% yield),[39]

2,4,6-[$^2H_3$]phenyl([$^2H_1$]methan)al (73% yield),[34] and finally *syn*-(2,4,6-[$^2H_3$]phenyl)([$^2H_1$]methan)aldoxime (62% yield, $^2H_4$ = 96%.[24]

4,4,4-[$^2H_3$]*Butan-2-ketoxime*. The reaction[40] of ethyl 3-oxobutanoate with [$^2H_3$]methyl iodide gave ethyl 2([$^2H_3$]methyl)-3-oxobutanoate (74% yield), which on hydrolysis/decarboxylation[40] gave 4,4,4-[$^2H_3$]butan-2-one (68% yield) which was converted into the oxime by the standard method (75% yield; $^2H_3$ = 99%).[24]

1,1,1-[$^2H_3$]*Heptan-4-ketoxime*. This was prepared as for 4,4,4-[$^2H_3$]butan-2-ketoxime (above), except that the starting materials are ethyl 3-oxohexanoate and 2,2,2-[$^2H_3$]ethyl iodide. Overall yield 40%; $^2H_3$ = 98%.

5,5-[$^2H_2$]5-*Phenylpentan-2-ketoxime*. Methyl phenylacetate when treated[41] with methanol *O*-[$^2H_1$]/sodium gives methyl 2,2-[$^2H_2$]phenylacetate ($^2H_2$ = 98%), which upon reduction[33] with lithium aluminium hydride yields 2-phenyl-2,2-[$^2H_2$]-ethanol (66% yield), which in turn may be converted into 2-phenyl-2,2-[$^2H_2$]ethyl bromide (72% yield),[42] ethyl 2(2-phenyl-2,2-[$^2H_2$]ethyl)-3-oxobutanoate (65% yield),[43] 5,5-[$^2H_2$]5-phenylpentan-2-one (68% yield),[43] and finally 5,5-[$^2H_2$]5-phenylpentan-2-ketoxime (82% yield; $^2H_2$ = 98%).[24]

Acknowledgements

We thank the Australian Research Council for the financial support of this project.

References

1 M. J. Raftery, J. H. Bowie, and J. C. Sheldon, *J. Chem. Soc., Perkin Trans. 2*, 1988, 563.
2 M. J. Raftery and J. H. Bowie, *Int. J. Mass. Spectrom. Ion Processes*, 1988, **85**, 167.
3 M. B. Stringer, J. H. Bowie, P. C. H. Eichinger, and G. J. Currie, *J. Chem. Soc., Perkin Trans. 2*, 1987, 385.
4 S. T. Graul and R. R. Squires, *J. Am. Chem. Soc.*, 1988, **110**, 607; J. C. Sheldon, J. H. Bowie, and R. N. Hayes, *J. Am. Chem. Soc.*, in the press.
5 P. C. H. Eichinger, J. H. Bowie, and R. N. Hayes, *J. Org. Chem.*, 1987, **52**, 5224.
6 P. C. H. Eichinger and J. H. Bowie, *J. Chem. Soc., Perkin Trans. 2*, 1987, 1499.
7 P. C. H. Eichinger, J. H. Bowie, and R. N. Hayes, *J. Am. Chem. Soc.*, 1989, **111**, 4226.
8 J. E. Bartmess, J. A. Scott, and R. T. McIver, *J. Am. Chem. Soc.*, 1979, **101**, 6047.
9 R. A. J. O'Hair, S. Gronert, K. E. Karrigan, V. M. Bierbaum, C. H. DePuy, and J. H. Bowie, *Int. J. Mass Spectrom. Ion Processes*, 1989, **90**, 295.
10 P. C. H. Eichinger and J. H. Bowie, *J. Chem. Soc., Perkin Trans. 2*, 1988, 497.
11 E. Beckmann, *Chem. Ber.*, 1887, **20**, 1507.
12 G. Donamura and W. Z. Heldt, *Org. React.*, 1960, **11**, 1.
13 P. T. Lansbury and N. R. Mancuso, *Tetrahedron Letters*, 1965, 2445.
14 A. Maquestiau, Y. van Haverbeke, C. de Meyer, C. Duthoit, P. Meyrant, and R. Flammang, *Nouv. J. Chim.*, 1979, **3**, 517; A. Maquestiau, Y. Van Haverbeke, R. Flammang, and P. Meyrant, *Org. Mass Spectrom.*, 1980, **15**, 80.
15 J. H. Bowie and T. Blumenthal, *J. Am. Chem. Soc.*, 1975, **97**, 2959; J. E. Szulejko, J. H. Bowie, I. Howe, and J. H. Beynon, *Int. J. Mass Spectrom. Ion Phys.*, 1980, **13**, 76.
16 G. J. Currie, J. H. Bowie, R. A. Massy-Westropp, and G. W. Adams, *J. Chem. Soc., Perkin Trans. 2*, 1988, 403.
17 J. B. Cumming and P. Kebarle, *Can. J. Chem.*, 1978, **56**, 1.
18 M. Meot-Ner and L. W. Sieck, *J. Phys. Chem.*, 1986, **90**, 6687.
19 L. Field, P. B. Hughmark, S. H. Shumaker, and W. S. Marshall, *J. Am. Chem. Soc.*, 1961, **83**, 1982.
20 J. K. Terlouw, P. C. Burgers, and H. Hommes, *Org. Mass Spectrom.*, 1979, **14**, 307.
21 P. C. Burgers, J. L. Holmes, A. A. Mommers, and J. Szulejko, *J. Am. Chem. Soc.*, 1984, **106**, 521.
22 D. J. Burinsky, R. G. Cooks, E. K. Chess, and M. L. Gross, *Anal. Chem.*, 1982, **54**, 295; M. L. Gross, E. K. Chess, P. A. Lyon, F. W. Crow, S. Evans, and H. Tudge, *Int. J. Mass Spectrom. Ion Phys.*, 1982, **42**, 243.
23 D. P. Ridge and J. L. Beauchamp, *J. Am. Chem. Soc.*, 1974, **96**, 3595.
24 A. I. Vogel, W. T. Creswell, G. H. Jeffery, and J. Leicester, *J. Chem. Soc.*, 1952, 514.
25 P. Karrer, *Helv. Chim. Acta*, 1922, **5**, 478.
26 A. Dornow and H. D. Jordan, *Chem. Ber.*, 1961, **94**, 76.
27 F. Asinger, M. Thiel, G. Peschel, and K. Meinickie, *Justus Liebigs Ann. Chem.*, 1958, **619**, 145.
28 C. M. French and D. Harrison, *J. Chem. Soc.*, 1955, 3514.
29 M. S. Malinovskii, *Zh. Obshch. Khim.*, 1949, **19**, 130.
30 W. J. P. Neish, *Recl. Trav. Chim.*, 1949, **68**, 337.
31 A. I. Vogel, 'Textbook of Practical Organic Chemistry,' Longmans and Green, 1957, 3rd edn., p. 719.
32 L. C. Leitch, *Can. J. Chem.*, 1955, **33**, 400.
33 W. H. Saunders, S. Asperger, and D. H. Edison, *J. Am. Chem. Soc.*, 1958, **80**, 2421.
34 R. Ratcliffe and R. Rodehurst, *J. Org. Chem.*, 1970, **35**, 4000.
35 A. P. Best and C. L. Wilson, *J. Chem. Soc.*, 1946, 239.
36 Ref. 31, p. 602.
37 Ref. 31, p. 756.
38 Ref. 31, p. 781.
39 R. F. Nystrom and W. G. Brown, *J. Am. Chem. Soc.*, 1947, **69**, 1197.
40 W. B. Renfrow, *J. Am. Chem. Soc.*, 1944, **66**, 144.
41 W. G. Brown and K. Eberly, *J. Am. Chem. Soc.*, 1940, **62**, 113.
42 W. B. Smith and J. D. Anderson, *J. Am. Chem. Soc.*, 1960, **82**, 656.
43 I. M. Hebron, R. N. Heslop, F. Irving, and J. S. Wilson, *J. Chem. Soc.*, 1931, 1336.

Received 17*th April* 1989; *Paper* 9/01564G