Electron Impact Studies on 2-Hydroxyimino-Naryl Acetamides

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The mass spectra of 13 2-hydroxyimino-N-aryl acetamides contain abundant arylamine, isocyanate and protonated benzimidazole ions, the mechanisms of formation of which were established by deuterium labelling and formulae by exact mass measurements. Loss of OH' and NO' were postulated to proceed through cyclic and acyclic intermediates respectively. Considerable hydrogen scrambling and rearrangement could be noticed in all the processes.

Derivatives of 2-hydroxyimino-N-phenyl acetamide (also known as glyoxylanilide oxime or isonitroso acetanilide) are intermediates not only in the synthesis of the indigoid dyes¹ but also of many pharmaceuticals.^{2,3} Some of these have pharmacological⁴ and agrochemical⁵ significance by themselves. Since mass spectral investigations on acetanilides reveal many interesting features,⁶⁻¹⁸ it was considered worthwhile as an extension of our earlier investigations on oximes¹⁹⁻²¹ and amides²² to investigate the electron impact induced behaviour of these hitherto unexplored important aromatic amine derivatives (1,4-10). The mass spectra of 1, 2, 3, 4, 5 and 9 are given in Figs. 1-6 and those of 6, 7, 8 and 10-15 in Table 1. The main features of the spectra are discussed below; to help in this the corrected relative abundances for the important peaks for 1, 2 and 3 are summarized in Table 2.

$$R_{2} \xrightarrow{4} V \xrightarrow{1'} NH \xrightarrow{1} C_{2} \xrightarrow{2} CH = NOH \qquad C_{6}D_{5} \xrightarrow{1} NH \xrightarrow{1} C \xrightarrow{1} CH = NOH \qquad U \\ R_{1} \qquad R \qquad U \\ R_{2} \xrightarrow{1} O \qquad O \\ R_{3} \xrightarrow{2} O \qquad O \\ R_{4} \xrightarrow{1} C \xrightarrow{1} O \\ R_{5} \xrightarrow{1} C \xrightarrow{1} O \\ C \xrightarrow$$



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Formation of the aniline radical ion

Loss of CO and HCNO from the molecular ion (Scheme 1) by a concerted process involving the transter of the original oxime hydrogen to the amide nitrogen produces a very abundant peak (except for 11,



12 and 14 which are discussed later), which is the base peak in the spectra of 1, 13 and 15. The process is confirmed by an appropriate metastable peak in each case and must be a low energy process since the spectrum of 1 at 20 eV still displays this ion (a, m/e 93, $[C_6H_7N]^{\dagger}$) as its base peak. Mass measurement in the case of 1 confirmed the elemental formulae of this ion. Examination of the kinetic energy releases suggest that the ions a and the molecular ions of the corresponding anilines have a common decomposition mode (Table 3), with the exception of the o-methyl derivative 4 where (Fig. 7) two structuresone corresponding to the aniline, the second unknown-seem to be present. The slightly larger kinetic energy releases, with the exception of HCN from the ortho chloro compound 5 are not unexpected.23,24

We have observed a similar behaviour for the $[RC_6H_6N]^{\dagger}$ ions from some monosubstituted acet-

0030-493X/78/0013-0224\$04.00



Figure 1. The mass spectrum of compound 1.



Figure 2. The mass spectum of compound 2.



Figure 3. The mass spectrum of compound 3.



Figure 7. Metastable peak shapes for the loss of HCN (a) from the molecular ion of o-toluidine and (b) from the ion(s) of the same formula from compound 4.



Figure 4. The mass spectrum of compound 4.



Figure 5. The mass spectrum of compound 5.



Figure 6. The mass spectrum of compound 9.

anilides,^{10,14} where there is some independent evidence²⁵ to show that the $[RC_6H_6N]^{\dagger}$ ion has the same decomposition pathway as the corresponding aniline ion and reacts by first forming the aniline ion. Thus, structure *a* seems reasonable in this case. The involvement of the original oxime hydrogen in this process is confirmed by the shift of the amine peak to m/e 95 for **3**, and the appearance of the peak at m/e 98 indicates the retention of all aryl hydrogens intact in the resulting amine in the case of **2**. Further fragmentation of the amines is shown in Scheme 2 and proceeds in each case in accordance with earlier observations.²⁶

A competing process leading to the ion a, found to occur to a significant extent with 1 and its labelled derivatives 2 and 3 is the elimination of HCNO from the molecular ion that has undergone McLafferty rearrangement followed by the expulsion of CO. This

	the second s														
6	m/e	200	199	198	183	182	181	180	169	168	167	163	156	155	154
-	%1	8	3	24	9	3	26	2	4	4	9	3	5	10	17
		153	152	129	128	127	126	125	119	118	117	113	112	111	102
		2 9	7	26	19	77	36	20	3	5	5	12	3	37	5
		101	100	99	92	91	90	76	75	74	73	72	69	65	64
		19	12	60	20	39	46	17	56	20	34	37	12	44	51
		63	62	61	57	55	52	51	50	44	43	41	39	38	37
		75	39	20	12	20	27	26	37	100	32	35	58	44	27
7	m/e	200	199	198	183	182	181	167	156	155	154	153	129	128	127
	%1	8	2	23	2	1	6	3	5	12	12	32	24	28	81
		126	125	119	118	117	113	112	111	102	101	100	99	92	91
		58	26	2	5	2	7	2	23	2	23	9	71	12	28
		90	76	75	74	73	72	69	65	64	63	62	61	57	55
		41	14	51	18	41	35	9	24	41	81	32	16	5	12
		52 18	26	35	100	43 23	41 26	39 41	38 32	37 18					
8	m/e	210	209	193	192	179	178	165	164	149	148	147	146	139	138
•	%1	8	60	4	3	3	7	11	31	6	6	4	13	4	49
		134	122	119	118	109	108	107	106	93	92	91	90	81	80
		38	11	17	14	7	60	7	25	11	34	41	62	7	27
		79	78	77	76	75	74	72	65	64	63	62	53	52	51
		11	20	13	28	20	14	53	59	62	70	32	21	45	38
		50	46	44	43	41	39	38							
		42	18	100	14	14	60	41							
10	m/e	209	208	180	179	164	163	137	136	135	127	110	109	108	107
	%1	15	70	16	8	5	28	8	18	42	5	11	46	100	22
		93	92	91	90	81	80	79	78	77	76	75	72	65	64
		3	3		5	31	23	20	9	4	4	3	25	11	11
		14	4	55 4	54 6	53 31	52 31	14	50 7	44 31	43 8	39 11	38 6		
••		300	201	310	220	977	976	975	974	951	950	240	040	047	240
	%I	323 10	20	10	270	13	270	2/5	274	201	250	245	240	24/	240
	/01	227	20	223	198	196	172	171	170	169	168	167	145	144	143
		7	15	8	12	13	5	13	65	25	60	10	8	2	19
		142	141	91	90	89	74	72	64	63	62	61	60	52	51
		2	13	16	24	25	28	48	35	19	100	12	26	14	12
		50	44	43	39	38									
		45	76	18	10	29									
12	m/e	325	323	321	281	280	279	278	277	276	254	253	252	251	250
	%1	9	18	9	8	21	19	42	9	21	5	15	15	30	20
		249	248	229	227	225	200	198	1/4	1/3	1/2	1/1	1/0	169	14/
		15	6	6	12	00	10	10	76	13	CO 66	20	00 64	10	62
		146	145	144	143	92	91	90	70	24	00 //5	20	100	12	30
		54	24 53	52	51	50	13	27 A3	42	24 41	40	39	38	12	
		15	24	42	12	15	66	21	24	24	54	18	39		
13	m/e	214	213	197	170	169	144	143	142	141	128	127	126	117	116
	%1	2	1	1	2	7	13	100	6	6	1	2	4	4	21
		115	114	89	88	87	78	77	76	75	74	71.5	65	64	63
		40	11	10	4	6	3	4	5	6	6	8	7	4	16
		62	61	52	51	50	44	41	39	38					
		10	3	7	11	10	8	4	14	9					
14	m/e	205	187	161	160	135	134	133	132	131	108	107	106	105	104
	%1	12	12	16	36	12	24	36	30	4	12	36	52	24	48
		91	90	81	80	79	78	77	76	72	65	64	63	62	61
		8	16	12	24	30	44 E 1	54 E0	20	12	10	28	28	01 20	12
		0/ 16	55 14	04 AA	53 57	52 100	51	00 24	44 80	43	42 Q	20	+U Q	33	30 20
		27	28	27	26	100	00	24	00	20	U	20	U	JE	20
		24	90	<u>9</u> 1	82										

Table 1. The mass spectra of compounds 6-8, 10 and 11-15

Table 1. (Continued)

15	m/e	237	236	210	185	184	183	182	181	180	179	169	168	167	166
	%1	5	18	19	18	100	18	18	18	10	8	3	6	13	12
		165	164	157	156	155	154	153	152	141	140	139	130	129	128
		6	6	8	26	12	18	15	9	11	15	17	26	12	21
		127	117	115	102	93	92	91	90	89	78	77	76	75	74
		20	21	19	19	18	9	17	18	19	17	30	19	21	18
		69	68	67	66	65	64	63	62	61	57	55	54	53	52
		5	4	11	16	26	30	36	20	8	5	11	20	17	34
		51	50	44	43	41	39	38	37						
		34	21	36	14	26	43	21	18						

Table 2. Corrected relative abundances for the prominent ions in compounds 1, 2 and 3

Compound	[M] ⁺		[M-C), DH],	(M-C	 סס†	[ArN		[Arl	NH2] [†]] [±] [ArNH] ⁺		[ArN] [±]	
	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%
1	164	84	147	45			119	50	93	100	92	35	91	28
							124	35						
2	169	80	152	40	151	10			98	100	97	51	96	35
							123	15						
	166	75					120	20	95	54				
3			149	10	148	40					94	54	91	30
	165	15					119	26	94	44				



Scheme 2

stepwise process is again substantiated by appropriate metastables in each case.



Scheme 3



Table 3. Kinetic energy releases for the decomposition of $[RC_6H_6N]^{\dagger}$ ions for compounds of the type RC_6H_4NHR'

_						
	Loss of	R	R' = H	7 ⁵⁰ (meV) ^b	R' = COCH-NOH	Т ^{БО} (meV)
	HCN	н		82±3		95 ± 3
	HCN	o-Me		110 ± 6		199ª
	CI	o-Cl		118±6		136±8
	HCN	o-Cl		114 ± 4		103±7
	Me	p-MeC)	193±4		215±5

^a In the case of the o-methyl derivative the T^{50} value for the narrow component is c. 116 meV. ^bSee Experimental section.

Hydrogen exchange during amine formation

The appearance of a very intense peak at m/e 94(compared with m/e 92 with 1) in the spectrum of 3 points to a certain amount of exchange between the C-2 hydrogen and the original oxime hydrogen, thus indicating an indirect involvement of the former in the amine formation, as well as lending support to the mechanism shown in Scheme 3. Taking into consideration the contributions of the $[M-H']^+$ fragment from m/e 95 (as 11% based on aniline²⁶), the isotopic peak of m/e 93 and the amine formation from the amidehydrogen undeuterated impurity (approximately on the basis of the molecular ion and amine intensities in 1), the contribution of the $166 \rightarrow 94$ process for this ion works out to about 40%. This figure must represent the extent of exchange referred to above (Scheme 4).

With 10, the amine formation occurs to a major extent from the $[M-C_2H_4]^+$ ion. With 14, the amine peak intensity is only about 10%, perhaps due to the instability of the molecular ion, which is undetected. With 11 and 12 again, no molecular ion could be detected and loss of HCNO and CO takes place only from the $[M-Br']^+$ ion.

That the amine formation is not a thermal process, but only electron impact induced, is confirmed not only by the metastables observed, the low voltage spectra and the low source temperatures employed, but also by the fact that pyrolysis of 1 at 70-80 °C under low pressures did not cause any change in its structure.

Loss of OH'

The spectra of 1, 4 and 6 contained abundant peaks due to the loss of an OH' from their respective molecular ions, while 5, 7, 8 and 9 exhibited intensities of only 3-6% for this ion and the spectrum of 10 did not contain any $[M-OH']^+$ ion. Further, 2 and 3 revealed both OH' and OD' losses, the ratio $[M-OH']^+:[M-OD']^+$ for the former being 5:1 and for the latter 1:4. This again indicates that there is some exchange between the original oxime and the *ortho* phenyl hydrogens, since it is the only method by which 2 can form an $[M-OD']^+$ ion. From the spectrum of 2, it can be deduced that this exchange takes place to the extent of 15%.

Two structures b and c (Scheme 5) are possible to account for this OH loss. Of these, b involves the original oxime hydrogen in the exchange process and the $[M-OH]^+$ ion from it (d) carries a charge on the oxime

nitrogen. On the other hand, c is the enolic form of the amide and if the enolic OH is the entity lost, the amide nitrogen becomes charged in the resulting ion e. In choosing between d and e, the effect of a substituent at the ortho and para positions to the amide nitrogen was informative. An electron-donating group must stabilize the structure d by resonance, via the enolic form d'. On the other hand, there should not be any substituent effect on e. The low abundance of the $[M - OH^{-}]^{+}$ ion for 8 and its high abundance for 4 confirms $d \rightleftharpoons d'$ as the structure for this ion. In the case of 10, loss of ethylene from the molecular ion becomes the primary process because of the labile ethoxy group and an abundant ion is produced by the loss of OH' from the $[M - C_2H_4]^+$ ion, thus lending support to structure d. With 9, owing to a competing process of isocyanate formation (this isocyanate ion is much more intense with 9 than other acetamides) and partly because of the formation of the $[M - CH_2O]^+$ ion (there is 8% loss of OH' from this ion) the abundance of the ion d is considerably reduced. The $[M-OH']^+$ ion abundance exhibited by the chloroacetamides 5, 6 and 7 points to the dominating inductive effect of the halogen.

With the acetamides 11-15, the molecular ions as well as the $[M - OH']^+$ ions were undetected, probably due to the greater stability of the isocyanate ions derived from them by a concerted loss of OH' and CO as discussed below.

Formation of the arylisocyanate and protonated benzimidazole ions

Loss of CO or H_2CN from the $[M-OH]^+$ ion of the oximes 1-10 and 13 afforded respectively the protonated benzimidazole f or the arylisocyanate radical ion g, whose structural formulae were confirmed by exact mass measurements on the appropriate ions derived from 1. Both these processes are substantiated by appropriate metastables in each case and serve to confirm the structure d = d' for the $[M-OH]^+$ ion. The appropriate mass shifts were noticed with the deuterated analogues 2 and 3. The mass measurements also indicated that the isocyanate ion constitutes about 90% of the nominal peak in each case, pointing to the dominance of the enolic form d' over d. If d were to be the major form, loss of carbon monoxide



(Scheme 6) from it must be a predominant process (as observed with pyridones²⁶).



The appearance of a peak at m/e 123 (Scheme 7), coupled with the high intensity of the m/e 97 and 96 ion peaks in the spectrum of 2 (compared with 1), lends support to the occurrence of both these processes. Further, in the formation of m/e 123 the methine or original amide proton transfer can take place to the 2'-carbon of the benzene ring. The appearance of peaks at m/e 119 and 120 with almost equal intensity in the spectrum of 3 points to a 1:1 likelihood for both these processes.

These processes occur only with the $[M-Br']^+$ ion in the case of **11** and **12**, and were found to be concerted, as also with **14** and **15**.

Simple cleavage

All the oximes display marked peaks for the loss of either $C_2H_2NO_2$ or CH_2NO radicals by α -fission of the bond on either side of the amide carbonyl. The occurrence of ions at m/e 72 and 44 (the latter being the base peak in some spectra) confirms this process.



Loss of NO[.]

The amides 1-10 form an $[M-NO']^+$ ion, which is the most intense for 1. The resulting ion then loses a

hydrogen. Compound 4 exhibits a concerted loss of NO' and H'. Any one of the following two mechanisms (Scheme 9) may be operating during this process, since the behaviour of the deuterated analogues 2 and 3 is in accord with either of them.



Scheme 9

Some specific features

The $[M-OH]']^+$ ion from 4 gives rise to a pronounced peak due to the loss of methyl and in analogy with *o*-tolualdoxime,²⁷ it is proposed that the resulting ion has structure k.







A marked distinction could be observed between the chloro derivatives 5, 6 and 7. While the $[M-Cl^{-}]^{+}$ ion is the base peak with 5, it is negligible with 6 and totally absent with 7. This, coupled with the high $[M-OH']^+$ ion intensity in 6, may serve as distinguishing features between isomeric haloanilines.



CONCLUSION

The spectra of 2-hydroxyimino-N-aryl acetamides are far more complex than those of the acetanilides. There are many hydrogen exchanges and rearrangements observed in these spectra. Amine, isocyanate and protonated benzimidazole ion production and loss of OH. and NO· would serve as identifying features for these compounds and hence for aromatic amines.

EXPERIMENTAL

General procedure for making the acetamides

To an aqueous solution of chloral hydrate (1 g, in 15 ml water) were added successively crystalline sodium sulphate (15 g), the amine (0.5 g, in 3 ml water to which 0.5 ml of concentrated hydrochloric acid was added) and hydroxylamine hydrochloride (1.2 g, in)5 ml water). The mixture was heated on a steam bath for 25-30 min and then refluxed for 1-2 min. The solution was cooled under the tap and the resulting solid recrystallized from either water or dilute methanol as the case may be.

 $1,^{28}$ $4,^{2}$ $5,^{3}$ $6,^{29}$ $7,^{30}$ $8,^{31}$ $9,^{32}$ 13^{33} and 14^{31} were reported earlier. The following new compounds were prepared: 4'-ethoxy-2-hydroxyimino-N-phenyl acetamide (10), m.p. 214 °C; N, N'-bis-(4:4'-phenylene)-2-hydroxyimino acetamide (15), m.p. above 300 °C.

Preparation of 2

 d_5 -Nitrobenzene³⁴ was reduced to d_5 -aniline with Fe/HCl following a literature procedure³⁵ for the unlabelled compound. When Sn and HCl were used,³³ it was found that one of the ring deuteriums (most probably the para) was replaced by hydrogen to the extent of 30% (mass spectral data). Compound 2, m.p. 176 °C, was obtained in 90% yield from d_s -aniline by the above general procedure.

Compound 3, m.p. 177 °C, was obtained by recrystallizing 1 from heavy water. Measurements indicated that the product was contaminated to the extent of 10% with the amide unlabelled compound (see Fig. 3). All efforts to make a labelled compound with either the amide or the original oxime hydroxyl alone containing the label were unsuccessful.

Compounds 11 and 12 were prepared by brominating 1 and 2 respectively in water (15 ml) containing potassium bromide and potassium bromate (5:1 molar ratio) by adding a few drops of concentrated hydrochloric acid and stirring for 15 min, m.p. 152 °C.

Measurement of spectra

The low resolution spectra of all the oximes were obtained on an AEI MS-12 mass spectrometer at 70 eV with 100 μ A ionizing current and at an inlet temperature of 80-90 °C (160-170 °C for 13, 14 and 15). Exact mass measurements were performed on an MS-9 mass spectrometer at a resolution of 1 in 10 000 using heptacosafluorotri-n-butylamine to provide reference masses. The metastable peak shapes³⁶ were measured on the MS-9, the T^{50} values were obtained by measuring the width at a position such that the areas above and below this line were equal.

Acknowledgments

One of us (RKMRK) is deeply indebted to the Commonwealth Scholarship Commission of the UK and the Government of India for the award of a post-doctoral fellowship. We thank the Science Research Council for money to buy and upgrade the mass spectrometer. We thank the Central Research Fund (University of London) for money to upgrade the mass spectrometer. We thank Mr Levy for developing the computer programme and Dr M. A. Baldwin and Mr J. T. Hill for help with the computer/mass spectrometer interfacing.

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Received 26 April 1977; accepted (revised) 4 November 1977 © Heyden & Son Ltd, 1978