The Mass Spectra of Alkyl- and Phenyl-4-imidazolin-2-ones

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The mass spectra of a variety of alkyl- and aryl-4-imidazolin-2-ones have been determined and the fragmentation mechanisms have been analyzed by deuterium labelling, high resolution and metastable transitions allowing certain differentiations of positional isomers. In contrast to the benzoid systems the mass spectra of isomeric alkyl-4-imidazolin-2-ones are distinctive. The influence of the position of substituents is demonstrated by phenyl-4-imidazolin-2-ones establishing an exact prediction of fragmentation pathways. Fragment ions (*e.g.* $[M-HNCO]^{+\cdot}$) which are the result of rearrangement processes were excluded for structure determinations. The ion structures involved were elucidated by collisional activation comparing model ions. Alkyl-phenyl-4-imidazolin-2-ones give almost identical mass spectra, but the positional isomers can easily be distinguished by different fragmentation patterns in both metastable and collisional activation spectra of the molecular ions.

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Introduction

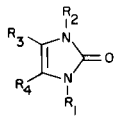
The application of mass spectra to characterize geometric or positional isomers of heterocyclic compounds is based on fundamental differences in the fragmentation patterns (2). Otherwise, under the energetic conditions of the commonly used electron impact, isomerization or rearrangement processes of the molecular ion or daughter ions may occur in the ion source or in the analyser part restricting the exact determination of the structure. Change in ionization conditions (3-6) or the analysis of metastable transitions (7,8) together with labelling experiments and high resolution, or the determination of the ion structures (9-11) are favoured to elucidate the mechanistic aspects of isomerization processes with the aim of demonstrating the original structure of heterocyclic molecules. Differences in fragmentation pathways or in the genesis of characteristic fragment ions in metastable spectra (7,8) can be used for an exact analysis of positional isomers (12). In a mass spectra study of 4-imidazolin-2-ones we have observed general fragmentation patterns by analysis of metastable transitions and main fragmentation products which enable us to distinguish between positional isomers normally difficult to establish by other spectroscopic methods.

Results and Discussion.

Representative alkyl, aryl and alkyl/aryl derivatives of 4-imidazolin-2-ones were prepared for this study (see Experimental). The details of the mass spectra are summarized in Table 1 and Figures 1-2 (only ions which had been determined by high resolution and metastable characteristics were taken into consideration). Initially we shall describe the general fragmentation behaviour of the 4-imidazolin-2-one **1** and then discuss the differences observed in positional isomers.

Table 1

EI Spectra of Imidazolin-2-ones



1 $R_1, R_2, R_3, R_4 = H$

m/e (relative %): 26 (0.8), 27 (10.7), 28 (90.1), 29 (44.7), 30 (0.9), 32 (1.9), 39 (1.9), 40 (3.5), 41 (10.8), 42 (3.7), 43 (3.6), 44 (2.3), 44.5 (1.0), 53 (2.3), 54 (2.8), 55 (2.8), 56 (48.5), 57 (1.5), 77 (0.7), 83 (2.0), 84 (100), 85 (5)

6e $R_1 = CD_3$, $R_2 = H$, $R_3, R_4 = Ph$

m/e (relative %): 46 (2.3), 76 (1.6), 77 (2.3), 89 (10.2), 103 (2.9), 104 (12.6), 105 (5.3), 119 (1.0), 121 (13.7), 125 (1.0), 126 (4.3), 165 (5.8), 166 (1.3), 180 (1.0), 192 (1.6), 193 (8.1), 194 (1.6), 205 (1.1), 206 (2.4), 207 (2.5), 208 (2.0), 209 (1.1), 210 (1.7), 223 (3.0), 224 (1.6), 235 (4.4), 236 (10.7), 251 (1.7), 252 (9.7), 253 (100)

7a $R_1 = C_2H_5$, $R_2 = H$, $R_3, R_4 = Ph$

m/e (relative %): 43 (4), 51 (8.3), 76 (4.2), 77 (26.1), 88 (1.2), 89 (3.1), 90 (2.1), 91 (1.5), 102 (1.8), 103 (10), 104 (32.4), 105 (21.1), 117 (2.3), 118 (1.5), 119 (1.4), 131 (1), 132 (2.6), 151 (1.5), 152 (1.9), 164 (1.4), 165 (10.9), 166 (2.3), 178 (3.6), 179 (3.6), 180 (2.4), 191 (1.3), 192 (3.7), 193 (16.2), 205 (3.5), 206 (10.8), 207 (6.2), 208 (2.4), 221 (8.2), 235 (22.7), 236 (33.3), 249 (58.4), 250 (1.7), 263 (10.9), 264 (100)

7b R_1 = *t*-Butyl-, $R_2 = H$, $R_3, R_4 = Ph$

m/e (relative %): 54 (2.9), 55 (1.1), 76 (1.8), 77 (9.0), 78 (1.4), 89 (0.9), 103 (2.9), 104 (25.2), 105 (23.9), 151 (0.9), 164 (10), 165 (1.4), 178 (0.8), 180 (2.1), 190 (1.2), 192 (2.6), 193 (2.7), 194 (2.7) 205 (3.3), 206 (2.5), 207 (2.6), 208 (1.7), 221 (2.7), 234 (3.2), 235 (10.2), 236 (100), 237 (27.2). 291 (2.1), 292 (18.9)

7c R_1 = Benzyl-, $R_2 = H$, $R_3, R_4 = Ph$

m/e (relative %): 39 (1.1), 44 (1.5), 51 (2.5), 65 (8.6), 76 (2.2), 77 (12.8), 89

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Table 1, continued

(4), 90 (3), 91 (47.5), 103 (5.7), 104 (8.6), 105 (3.1), 157 (6.7), 165 (6.7), 178 (1.8), 180 (2.3), 190 (2.5), 191 (1.5), 192 (4.2), 193 (40.4), 205 (2.2), 206 (7.3), 207 (9.4), 208 (5.6), 217 (12.9), 218 (2.7), 234 (2.8), 235 (100), 236 (19.7), 325 (1.3), 326 (79.5)

8a $R_1 = C_2H_5$, $R_2 = H$, $R_3 = Ph$, R_4 CH_3

m/e (relative %): 51 (3.3), 64 (1.4), 65 (2.4), 76 (4.3), 77 (28.4), 78 (4.6), 89 (2.1), 91 (3.7), 102 (1.3), 103 (11.7), 104 (16.2), 105 (11.4), 115 (4.6), 116 (2.0), 117 (2.8), 118 (1.2), 130 (16.3), 131 (3.8), 144 (2.4), 158 (1.8), 159 (10.7), 172 (4.1), 173 (26.6), 187 (12.5), 188 (1.8), 201 (7.9), 202 (100)

8b $R_1 = C_2H_5$, $R_2 = H$, $R_3 = CH_3$, $R_4 = Ph$

m/e (relative %): 42 (4.6), 43 (5.9), 51 (2.6), 77 (1.8), 78 (9.0), 89 (1.3), 91 (1.3), 103 (6.9). 104 (12.7), 105 (3.7), 115 (2.5), 116 (1.1), 117 (1.9), 118 (0.9), 130 (10.5), 131 (7.3), 144 (3.3), 158 (5.8), 159 (6.3), 172 (0.7), 173 (19.9), 174 (30.7), 187 (13.4), 200 (0.8), 201 (17.4), 202 (100)

9a $R_1, R_2 = H$, $R_3, R_4 = CH_3$

m/e (relative %): 41 (9.8), 42 (26.1), 43 (94), 52 (6.7), 54 (3.9), 56 (5.6), 68 (13.8), 69 (5.6), 70 (2.1), 84 (3), 97 (15.4), 110 (2.8), 111 (40.9), 112 (100)

9b $R_1 = CH_3$, $R_2 = H$, $R_3, R_4 = CH_3$

m/e (relative %): 40 (42.6), 48 (4.3), 49 (10.5), 50 (7.4), 52 (9.7), 53 (26.9), 54 (20.6), 55 (99.5), 56 (9.7), 63 (4.6), 65 (2.9), 66 (2.6), 67 (31.4), 68 (15.7), 69 (17), 70 (4.7), 81 (3.3), 82 (12.4), 83 (3.8), 84 (5.8), 95 (3.3), 97 (24.3), 111 (35.2), 119 (2.8), 125 (53), 126 (100)

9c $R_1 = Ph$, $R_2 = H$, $R_3, R_4 = CH_3$

m/e (relative %): 48 (12.4), 55 (1), 70 (2.9), 76 (1.9), 77 (30.9), 78 (6.1), 93 (1.4), 94 (3.7), 103 (1.7), 104 (8.8), 105 (1.2), 110 (2.8), 111 (2.0), 116 (1.1), 117 (2.2), 118 (37), 119 (9.7), 130 (2.9), 132 (1.7), 143 (1.4), 144 (8.4), 145 (1.9), 146 (1.1) 159 (6.3), 171 (0.9), 173 (7.6), 186 (0.7), 187 (28.3), 188 (100)

9d $R_1 = C_2H_5$, $R_2 = H$, $R_3, R_4 = CH_3$

m/e (relative %): 43 (7.0), 51 (3.5), 55 (2.8), 65 (1.3), 67 (1.2), 68 (17.6), 69 (8.5), 70 (9.3), 84 (3.8), 96 (1.3), 97 (34.0), 106 (1.2), 107 (1.6), 110 (1.1), 111 (65.6), 112 (42.1), 113 (2.8), 125 (18.1), 138 (1.7), 139 (7.8), 140 (100)

9e $R_1 = CH_3$, $R_2 = H$, $R_4 = CH_3$, $R_5 = Ph$

m/e (relative %): 65 (2.4), 76 (4.0), 77 (28.5), 78 (3.8), 89 (3.2), 90 (1.7), 91 (5.4), 94 (5.7), 102 (1.8), 103 (10.6), 104 (8.3), 105 (12.9), 111 (14.6), 116 (3.2), 117 (4.3), 118 (35.7), 119 (4.0), 130 (15.0), 131 (8.6), 132 (2.4), 143 (1.0), 144 (8.1), 145 (2.3), 146 (2.9), 147 (1.3), 158 (6.0), 159 (6.2), 163 (1.4), 172 (0.9), 173 (9.1), 186 (2.2), 187 (63.8), 188 (100)

9f $R_1, R_2, R_3 = CH_3$, $R_4 = Ph$

m/e (relative %): 55 (6.2), 56 (1.8), 76 (3.6), 77 (27.4), 85 (5.8), 89 (6.2), 90 (3.3), 91 (7.4), 102 (2.3), 103 (5.2), 104 (4.2), 105 (30.1), 117 (3.3), 118 (66.2), 119 (15.5), 127 (2.1), 130 (4.8), 131 (6.0), 132 (17.5), 158 (5.1), 159 (11.6), 173 (19.6), 174 (2.4), 187 (16.7), 188 (100), 189 (13.8), 191 (3.6), 192 (6.0), 204 (33.7)

10 $R_1 = C_2H_5$, $R_2, R_3 = H$, $R_4 = Ph$

m/e (relative %): 48 (13.7), 51 (0.7), 63 (6.2), 64 (2.0), 65 (2.2), 76 (1.2), 77 (2.7), 78 (8.6), 79 (34.9), 89 (13.3), 90 (6.8), 91 (6.1), 102 (3.2), 103 (11.4), 104 (83.3), 105 (12.6), 116 (13.0), 117 (21.9), 118 (6.4), 130 (5.2), 131 (5.0), 132 (12.5), 144 (2.2), 145 (19.3), 158 (2.1), 159 (12.0), 160 (70.9), 173 (12.8), 174 (1.3), 186 (0.6), 187 (20.8), 188 (100)

11a $R_1, R_2 = H$, $R_3, R_4 = C_2H_5$

m/e (relative %): 51 (7.5), 52 (6.3), 54 (15.9), 55 (12.8), 56 (27.1), 65 (2.5), 66 (1.6), 67 (4.6), 68 (5.3), 77 (0.9), 79 (1.4), 80 (7.2), 81 (3.2), 82 (19.8), 94 (2.2), 95 (1.7), 96 (1.7), 97 (4.4), 98 (3.0), 110 (1.6), 111 (3.5), 112 (0.9), 123 (3.8), 124 (2.8), 125 (100), 126 (7.1), 139 (4.8), 140 (33.2)

11b $R_1 = Ph$, $R_2 = H$, $R_3, R_4 = C_2H_5$

m/e (relative %): 48 (4.8), 54 (2.3), 77 (13.4), 84 (3.8), 104 (3.2), 108 (2.4), 117 (3.3), 118 (7.5), 130 (3.3), 132 (4.4), 143 (3.6), 144 (3.2), 158 (5.9), 171 (2.6), 201 (100), 202 (13.7), 215 (4.6), 216 (63.3)

11c $R_1, R_3, R_4 = C_2H_5$, $R_2 = H$

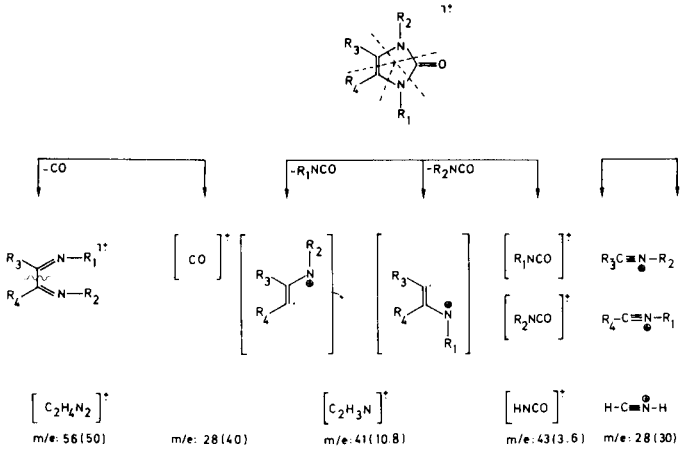
m/e (relative %): 67 (2.4), 68 (3.3), 69 (2.4), 76 (0.8), 77 (1.3), 81 (3.3), 82 (2.3), 83 (7.9), 96 (1.4), 97 (1.1), 123 (3.1), 124 (1.1), 125 (50.4), 139 (11.6), 151 (3.5), 152 (0.7), 153 (100), 154 (10.2), 166 (2.7), 167 (7.8), 168 (63.6)

11d $R_1 = CH_3$, $R_2 = H$, $R_3, R_4 = C_2H_5$

m/e (relative %): 51 (2.5), 57 (8.5), 66 (1.8), 67 (2.3), 68 (3.4), 69 (2.7), 77 (1.8), 80 (1.5), 94 (1.9), 96 (1.5), 111 (2.5), 124 (3.2), 125 (2.8), 137 (4.9), 138 (2.4), 139 (100), 140 (9.5), 152 (1.9), 153 (7.6), 154 (40.5)

The mass spectra of the 4-imidazolin-2-one **1** can be compared with unsubstituted aromatic compounds; the stability of the molecular ion constitutes the base peak. The fragmentation is characterized by concurring formation and/or elimination of structural parts of the molecular ion reflecting constitutional details of the original compound (Scheme 1). This fragmentation pattern can be used for the analysis of the structure.

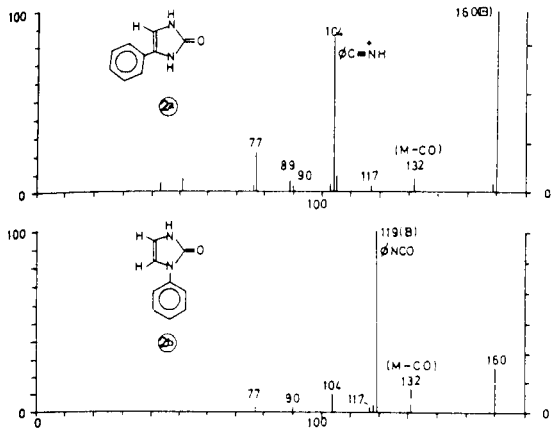
Scheme 1: Fragmentation of the molecular ions of substituted 4-imidazolin-2-ones (R_1, R_2, R_3 and R_4: H, CH_3, C_2H_5, t-butyl, benzyl-, phenyl) (rel. intens. %).



In contrast with these results alkyl or phenyl substituents have a large influence on the formation or elimination of fragments. These differences based on the stabilization effects of $[RCHN]^+$ or $[RCN]^{+\cdot}$ and $[M\text{-}CO]^{+\cdot}$ or $[M\text{-}HCNO]^{+\cdot}$ species by alkyl or aryl substituents (Tables 1, 2 and 4, Figures 1-3, Schemes 1 and 2) are useful for an exact determination of isomeric derivatives. In the case of 4-phenyl-4-imidazolin-2-one (**2a**) (Figure 1) the formation of m/e 104 ($[C_7H_6N]^+$) is favoured by the stability of the protonated benzenenitrile while the *N*-phenyl derivative **2b** gives rise to m/e 119 ($[C_6H_5NCO]^{+\cdot}$). Both isomers show fragmentation given

in Scheme 2 including sequentially elimination of CO and HNCO. The $[M\text{-}HNCO]^{+\cdot}$ ion (m/e 117, $[C_8H_7N]^{+\cdot}$) ejects HCN to yield $[C_7H_6]^{+\cdot}$ (m/e 90) affirming rearrangement processes.

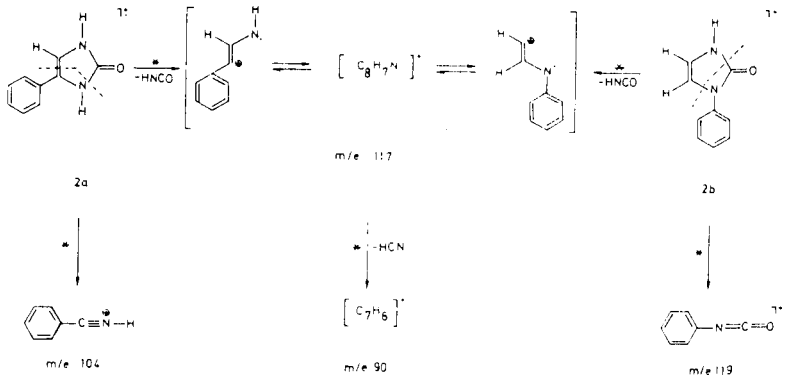
Figure 1



The rearrangements of the "stable" $[C_8H_7N]^{+\cdot}$ ions (stable ions are characterized by a lifetime of 10^{-5} seconds) may be described by several ion structures, *e.g.* benzylcyanid (13) or phenylazirine (14) which under electron impact conditions are known to yield common intermediates (13). Consequently, these ions have to be excluded for a differentiation of positional isomers. Analogously, care must be taken in the interpretation of the mass spectra of diphenyl-4-imidazolin-2-ones **3a-c** because of this same tendency to produce rearrangement ions (Scheme 3, Table 2) as evidenced by the formation of $[C_{14}H_{11}N]^{+\cdot}$ (m/e 193) and $[C_{13}H_9]^+$ (m/e 165).

The ion structures of the significant $[C_{14}H_{11}N]^{+\cdot}$ and $[C_{13}H_9]^+$ ions have been the subject of intense investigations (15-18). Our results (17) concerning this problem show that the loss of H/HCN from $[C_{14}H_{11}N]^{+\cdot}$ ions, which gives rise to $[C_{13}H_9]^+$, is accompanied with complex rearrangement processes including both bond forming and hydrogen shifts to open-chain and cyclic species of common interconverting ion structures. Thus, the supposed

Scheme 2: Fragmentation of phenyl-4-imidazolin-2-ones **2a** and **2b**



Scheme 3: MI-spectra (DADI[7] - and Defocussing [8,9]-technique) of the molecular ions of isomeric diphenyl-4-imidazolin-2-ones **3a-c**

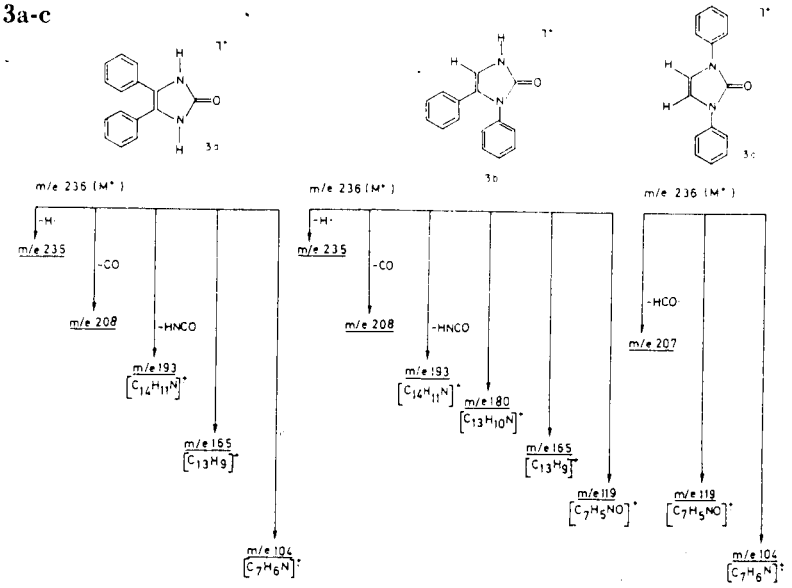
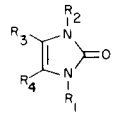


Table 2

Main Fragment Ions of Isomeric Diphenyl- and Triphenyl-4-imidazolin-2-ones (**3a-c**; **4a-c**) (Relative %)



	3a	**3b**	**3c**		**4a**	**4b**	**4c**
R_1	H	Ph	Ph	R_1	Ph	Ph	Ph
R_2	H	H	Ph	R_2	H	Ph	Ph
R_3	Ph	H	H	R_3	Ph	H	Ph
R_4	Ph	Ph	H	R_4	Ph	Ph	Ph-CH_2
m/e				m/e			
				312 $[M]^+$	100	100	24.2 (a)
				311 $[M-H]^+$	10.7	24.2	100 (a)
				284 $[M-CO]^+$			
				283 $[M-HCO]^+$	1.4	4.7	3.8 (a)
				269 $[M-HNCO]^+$	10.3	0.7	21.9 (a)
				268 $[M-H/HNCO]^+$	2.0	2.3	5.3 (a)
236 $[M]^+$	100	100	100				
235 $[M-H]^+$	7.0	49.9		235 $[M-Ph]^+$		1.5	
208 $[M-CO]^+$	1.7	2.0	4.7				
207 $[M-HCO]^+$	2.9	8.8	25.4				
193 $[M-HNCO]^+$	4.7	4.8		193 $[M-PhNCO]^+$	3.0	2.6	1.0 (a)
192 $[M-H/HNCO]^+$	2.8	22.1		192 $[M-H/PhNCO]^+$	0.1	7.1	1.0
180 $[Ph-\dot{N}\equiv C-Ph]$		30.1		180 $[Ph-C\equiv\dot{N}-Ph]$	24.7	91.2	6.3
165 $[C_{13}H_9]^+$	9.4	3.8		165 $[C_{13}H_9]^+$	11.8	4.8	6.2
119 $[PhNCO]^+$		4.5	11.7	119 $[PhNCO]^+$	2.8	1.8	
105 $[C_7H_5O]^+$	31.8	2.6	16.3	105 $[C_7H_5O]^+$	2.3	4.6	2.5
104 $[PhCNH]^+$	35.7	10.5	29.4	104 $[PhCHN]^+$	11.2	8.3	1.1
103 $[PhCN]^+$	6.9	10.7		103 $[PhCN]^+$	2.9	8.3	1.4
				91 $[C_7H_7]^+$			9.8
89 $[C_7H_5]^+$	1.2	6.9	3.2	89 $[C_7H_5]^+$	0.4	6.3	0.9
				77 $[C_6H_5]^+$	32.1	88.8	18.9
43 $[HNCO]^+$	0.3	4.5	0.3	43 $[HNCO]^+$	2.8	2.3	5.3

(a) $[M-91]^+$ ion.

significance of $[C_{13}H_9]^+$ ions indicating the "stilbene moiety" of heterocyclic systems (15) is restricted. Likewise, the fragmentation pathway of this ion to m/e 165, 152, 139, 115, 90, 89 (Table 2) cannot be used for an exact analysis of isomeric diphenyl-4-imidazolin-2-ones. However, the direct formation of m/e 180, ($[C_{13}H_{10}N]^+$) in **3b** (Scheme 3) reflects the Ph-C=N-Ph moiety of this isomer, whereas m/e 104 characterizes the phenyl position in **3a** and **3c**.

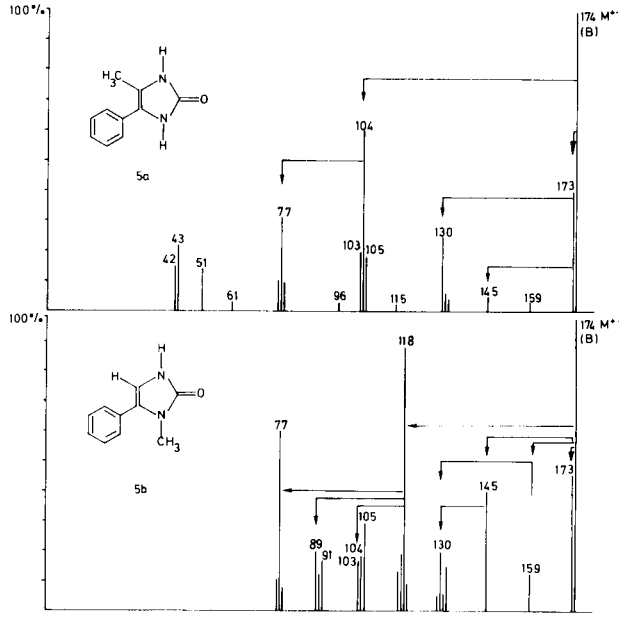
The differences in fragmentation patterns and the variability of intensities of main fragment ions were checked by metastable transitions (7,8). The application of these methods easily distinguishes between the isomers **3a-c** (Scheme 3) because of the complete differences in fragmentation pathways, *e.g.* **3c** is characterized by the intense formation of $[M-HCO]^+$ ions (m/e 207) and the increased formation of $[C_6H_5NCO]^+$ (m/e 119) and $[C_7H_6N]^+$ (m/e 104) compared with **3a** and **3b**.

In the series of triphenylimidazolin-2-ones **4a-c**, the differences in intensity of m/e 180 (Ph-C$\equiv\dot{N}$-Ph) depend on the positions of the phenyl substituents (Table 2). The usefulness of structural dependence of the fragmentation pathways is well represented by the variability of the abundances of $[M-HNCO]^+$ or $[M-PhNCO]^+$, *e.g.* **4a** (m/e 269, $[C_{20}H_{15}N]^+$) shows higher yields of $[M-HNCO]^+$ compared with **4b**, while $[M-PhNCO]^+$ (m/e 193) is markedly reduced. Because of the rearrangements of the latter ion to m/e 165 $[C_{13}H_9]^+$, these fragmentations were excluded for structural differentiations.

The electron impact-induced fragmentations of isomeric *C*- or *N*-alkyl substituted phenyl-4-imidazolin-2-ones (Table 1, Figure 2) show characteristic differences. This behaviour is in sharp contrast to benzoid systems, which give virtually identical spectra (3,19), but may be compared with alkyl-pyridines (2b,12), giving distinctive fragmentation patterns (Figure 2).

For example, 4-methyl-5-phenyl-4-imidazolin-2-one (**5a**) and 1-methyl-5-phenyl-4-imidazolin-2-one (**5b**) show no indication of isomerizations of the $[M-H]^+$ fragment ion, which would be assigned by identical fragmentations in the lower mass region. Obviously the presence of heteroatoms in the ring system prevents or retards rearrangement processes by which alkyl-benzenes (19) become equivalent. The $[M-H]^+$ fragmentation is followed by loss

Figure 2



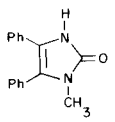
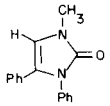
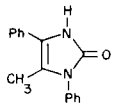
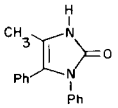
of CO to m/e 145 which is considerably more abundant in **5b** than in **5a**. The consecutive loss of H/CO may be compared with the typical ring extension in heterocyclic compounds (10,12) (m/e 145). The resulting ion can be described as phenylimidazole. The hydrogen involved in this process was determined as a methyl residue by deuterium labelling of the *N*-methyl substituent in **5b**. The absence of the *N*-methyl moiety in **5a** is assigned by the lower intensity of m/e 145.

On the other hand, the concurring formation of m/e 104 ($[PhCHN]^+$) in **5a** and of m/e 118 ($Ph\text{-}C\equiv\overset{+}{N}\text{-}CH_3$) in **5b** can be used for an exact analysis of these isomers. On the basis of these results certain predictions can be made concerning the fragmentation mechanisms of isomeric phenyl-4-imidazolin-2-one derivatives.

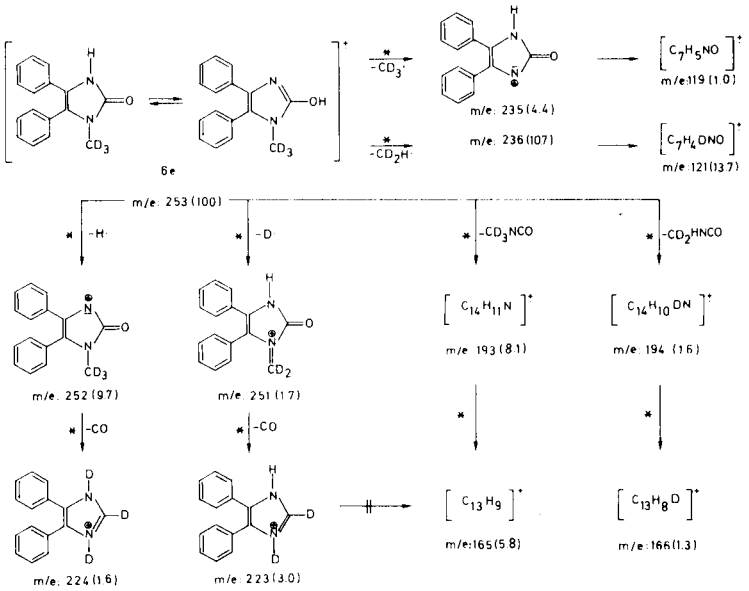
For example, diphenylmethyl-4-imidazolin-2-one systems **6a-d** (Table 3) differ markedly in their fragmentation pattern; $[M\text{-}H]^+$ elimination in **6a** is favoured whereas the *N*-methyl moiety is characterized by an increasing methyl loss (**6a,6b**) or by the specific formation of m/e 118 ($Ph\text{-}C\equiv\overset{+}{N}\text{-}CH_3$) (**6a,6c**). For further differentia-

Table 3

Intensities of Main Fragment Ions of Methyl-diphenyl-4-imidazolin-2-one Derivatives **6a-d** (Relative %)

					
	m/e	**6a**	**6b**	**6c**	**6d**
$[M]^+$	250	100	100	100	100
$[M\text{-}H]^+$	249	58.4	18.8	17.0	1.5
$[M\text{-}CH_3]^+$	235	22.7	5.3		
$[M\text{-}CO]^+$	222	2.1	1.8	0.6	0.3
$[M\text{-}CHO]^+$	221	7.9	10.1	3.3	1.3
$[M\text{-}HNCO]^+$ / $[M\text{-}CH_3/CO]^+$	207	27.2	2.1	5.2	0.9
$[M\text{-}H/NHCO]^+$	206	21.2	1.2	15.2	3.5
$[M\text{-}CH_3NCO]^+$	193	49.0	3.8		
$[M\text{-}H/CH_3NCO]^+$	192	10.1	9.4		
$[PH\text{-}C\equiv\overset{+}{N}\text{-}Ph]$	180	6.4	53.8		19.3
$[M\text{-}Ph]^+$	173			3.0	0.4
$[C_{13}H_9]^+$	165	35.3	3.8	2.6	1.4
$[M\text{-}118]^+$	132		6.2	4.0	2.9
$[M\text{-}PhNCO]^+$	131		1.7		5.1
$[M\text{-}H/PhNCO]^+$	130			6.3	17.4
$[PhNCO]^+$	119		1.0	15.2	4.4
$[Ph\text{-}C\equiv\overset{+}{N}\text{-}CH_3]$	118	97.7	1.3	44.6	3.8
$[PhCNH]^+$	104	86.1	4.4	28.2	2.7
$[PhCN]^+$	103	41.4	4.0	22.5	1.3
$[C_7H_5]^+$	89	22.5	4.9		5.7
$[C_6H_5]^+$	77	97.8	49.0	4.1	96.7
$[CH_3NCO]^+$	57				
$[HNCO]^+$	43	5.1	2.1		13.6

Scheme 4: Fragmentation of 1-trideuteromethyl-4,5- diphenyl-4-imidazolin-2-one **6e** (rel intens. %)



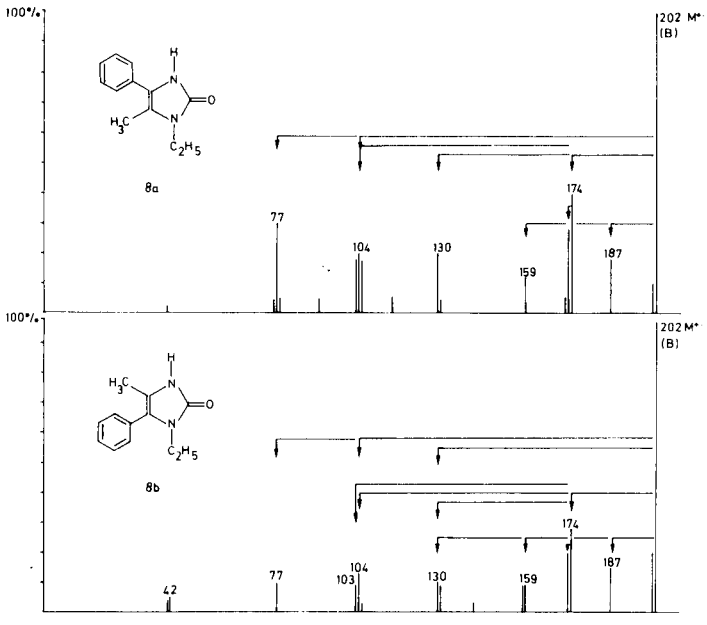
tion the $[M\text{-}CH_3NCO]^+$ or the $[M\text{-}H/CH_3NCO]^+$ fragmentation may be used (**6a,6b**). The Ph-N=C-Ph structural part in **6b** and **6d** is marked by the direct formation of this species (m/e 180) from the molecular ions. As expected, the $[C_7H_6N]^+$ ions (m/e 104) in **6a** and **6c** compete more effectively with the formation of $[CH_3CHN]^+$ (m/e 42).

The increasing intensities of the significant fragment ion $[M\text{-}H/CO]^+$ (m/e 221) of the *N*-methyl derivatives **6a** and **6b** should be explained by stabilization effects depending on the assumption of cyclization processes (Scheme 4) involving diphenylimidazole systems.

The hydrogen involved arises from both the NH and N-CH_3 residues, demonstrated by labelling of the *N*-methyl substituent (Table 1; **6e**). Rearrangement of the $[M\text{-}HCO]^+$ fragments to 4,5-diphenylimidazoles were excluded by comparison of the metastable spectra of m/e 221 (**6a**) and m/e 224 (**6e**) and the model ion (Scheme 4) showing no direct formation of $[C_{13}H_9]^+$ (m/e 165) which is a specific fragment ion of 4,5-diphenyl-imidazole (15). In our case this ion is exclusively produced by the unspecific $[C_{14}H_{11}N]^+$ ion (m/e 193) (16-18) as discussed previously. The labelling experiment further demonstrates that partial scrambling occurs as evidenced by the formation of $[M\text{-}CD_2H]^+$ to m/e 236 (10.7%), m/e 166 ($[C_{13}H_8D]^+$) and m/e 121 ($[C_7H_4DNO]^+$) (13.7%).

The dominating loss of *N*-alkyl or *N*-benzyl substituents in **7a-c** (Table 1) yields the $[M\text{-}H]^+$ ion of 4,5-diphenyl-4-imidazolin-2-one (**3a**), followed by an intense elimination of CO (**7a**) or H/CO (**7b,c**). As previously described further information of structural details was gained by the loss and/or formation of significant mass units.

Figure 3



In contrast to these results, *C*-alkylation together with various substitution of the 4-imidazolin-2-one system by alkyl or phenyl groups gives almost identical spectra, which may be described by the fragmentational behaviour of **8a** and **8b** (Figure 3). In this case the primary loss of

Table 4

MI and CA Spectra of Molecular Ions (m/e 202) and $[M-C_2H_4]^+$ Ions (m/e 174) of 1-Ethyl-5-methyl-4-phenyl-4-imidazolin-2-one (**8a**) and 1-Ethyl-4-methyl-5-phenyl-4-imidazolin-2-one (**8b**)

	m/e 202 $[M]^+$			m/e 174 $[M-C_2H_4]^+$		
m/e	**8a**	**8b**	m/e	**8a**	**8b**	**5a**
187 (a)	135 (77.6)	104 (100)	158 (a)	8.6	23	23
174 (a)	200 (100)	220 (70.2)	146 (a)	16	20	19
158 (a)	50 (1.2)	29 (1.40)	130 (a)	40	57	51
143	14.7	13.5	120	2.6	1.9	5
130 (a)	47 (0.6)	43 (1.4)	115	16.9	15.0	14
115	23	19.8	104 (a)	71	92	87
103 (a)	49 (0.9)	52 (0.7)	96 (a)	14	27	30
88	11.4	7.5	88	11.3	12.0	11.5
76	18.8	23.5	85	3.0	3.8	3.5
63	5.3	4.4	76	31.5	33.1	31.0
50	8.6	9.3	67	2.3	1.9	3.5
42	14.7	16.5	62	7.4	6.9	7.5
28	4.5	6.0	50	16.5	16.6	16.5
			43 (a)	32	45	50
			38	5.8	5.6	5.5
			27	2.7	3.2	2.7

(a) The intensities are relative to the sum of collisional induced fragments exclusing ions (a) as results of decomposing precursors. The relative abundances of MI spectra are given in paranthesis.

C_4H_4 leads to a common ion m/e 174, determined by collisional activation spectra (10) as 4-methyl-5-phenyl-4-imidazolin-2-one (**5a**) (Table 4), which further framentation rules the lower mass range of the spectra. Therefore the determination of positional isomers based only on the formation or non-formation of significant fragment ions is restricted. More differentiations were expected by use of metastable spectra (7,8) (Table 4), assuming structural dependence of the decomposing molecular ions. However, slight differences in the abundances of $[M-CH_3]^+$ and $[M-C_2H_4]^+$ were obtained. The assumption that the decomposing molecular ions may undergo rearrangement processes to a common ion or a mixture of interconverting species are evidenced by the formation of m/e 103 ($[PhCN]^+$) in both **8a** and **8b**. To exclude isomerizations prior fragmentations and to eliminate influences of internal energy distributions of the precursors which should lead to corresponding fragmentation patterns the collision activation spectra of the molecular ions were determined. This method allows the differentiation of structures of "stable" gaseous ions with a lifetime of 10^{-5} seconds, since the relative abundances of the collision-induced fragments are independent of the internal energy variations (10). Identical collision activation spectra are used as criterion for identical structures and *vice versa*.

As demonstrated in Table 4, the differences in abundances of m/e 115, 88, 76 confirm the structural stability of the molecular ions of **8a** and **8b**. The decomposing species rearrange to common intermediates which give rise to identical fragmentation patterns.

To summarize, this study establishes the mass spectrometric differentiation of isomeric heterocyclic compounds by their distinctive fragmentations, reflecting structural moieties of the molecular ions. The differences in abundance of the loss and formation of significant mass units were confirmed by metastable spectra. Phenyl substitution gives rise to rearragements of fragment ions which were excluded for further differentiations. The ion structures involved in these processes were determined by collisional activation comparing model ions. Differentiations of isomeric compounds are limited if rearrangement processes occur within the decomposing molecular ions yielding almost identical mass spectra. However, in these cases differentiations of the stable molecular ions are possible by the use of metastable and collisional activation spectra.

On the basis of the general fragmentation mechanisms the determination of a great number of isomeric 4-imidazolin-2-one derivatives is possible even in those regions (10^{-9} g.) which normally are difficult to elucidate by other spectrospcopic methods. Thus, in order to obtain substance-specific information, the analytical application of mass spectroscopic methods may be used to answer pharmacological questions.

EXPERIMENTAL

Chemicals.

Methods previously described in the literature were used to prepare most of the compounds needed. All compounds were purified by liquid chromatography and the constitution was verified by spectroscopic

methods. Proton nuclear magnetic resonance spectra were recorded on a Varian XL-100 instrument with TMS as internal reference. Melting points are uncorrected.

The following compounds were prepared according to literature reported procedures: 4-imidazolin-2-one (**1**) (20); 4-phenyl- (**2a**) (21); 1-phenyl- (**2b**) (22); 4,5-diphenyl- (**3a**) (23); 1,5-diphenyl- (**3b**) (24); 1,3-diphenyl- (**3c**) (25); 1,4,5-triphenyl- (**4a**) (26); 1,3,5-triphenyl- (**4b**) (27); 3-benzyl-1,4,5-triphenyl- (**4c**) (28); 4-methyl-5-phenyl- (**5a**) (29); 1-methyl-5-phenyl- (**5b**) (30); 1-methyl-4,5-diphenyl- (**6a**) (31); 3-methyl-1,5-diphenyl-(**6b**) (32); and 5-methyl-1,3-diphenyl-4-imidazolin-2-one (**6c**) (33).

4-Methyl-1,5-diphenyl-4-imidazolin-2-one (**6d**).

a) *N*-(α-Methylphenacyl)-*N'*-phenylurea (**6da**).

α-Aminopropiophenone hydrochloride salt (1.86 g., 10 mmoles) was suspended in 50 ml. of absolute acetone; the mixture was cooled to 0° and 1.4 g. (11.6 mmoles) of phenylisocyanate were added. Then, 2.00 g. (20 mmoles) of triethylamine, dissolved in 50 ml. of absolute acetone, were added dropwise to the mixture with stirring. After stirring for two hours, the mixture was filtered and the acetone evaporated to half volume. Water was then added at 0°, at which time the urea separated, m.p. 151-153° (ethanol/water), yield 0.67 g. (25%).

Anal. Calcd. for $C_{16}H_{16}N_2O_2$ (268.3): C, 71.62; H, 6.01; N, 10.44. Found: C, 71.51; H, 6.05; N, 10.43.

b) Compound **6d** from **6da**.

Compound **6da** (0.90 g., 3.36 mmoles) was heated for 30 minutes at 250° giving **6d**, m.p. 310-313° (ethanol), yield 0.30 g. (38%); ^{1}H-nmr (acetic acid-d_4): δ 2.15 (s, 3H, CH_3), 7.05-7.35 (m, 10H, phenyl).

Anal. Calcd. for $C_{16}H_{14}N_2O$ (250.3): C, 76.78; H, 5.65; N, 11.19. Found: C, 76.48; H, 5.74; N, 11.07.

1-Trideuteromethyl-4,5-diphenyl-4-imidazolin-2-one (**6e**).

Trideuteromethylamine hydrochloride salt (3.53 g., 50 mmoles) was dissolved in a mixture of 20 ml. of acetic acid and 50 ml. of water at 40°. Potassium cyanate (8.1 g.) dissolved in 15 ml. of water was then added at 40°. After standing for 3.5 hours at room temperature, the solvents were evaporated at 80° and the residue extracted with ethanol; after filtering and evaporating the ethanol, the resulting residue was refluxed for 3 hours with a mixture of 10.37 g. of benzoin in 50 ml. of acetic acid. The work-up according to the literature (31) yielded 3.1 g. of **6e**; m.p. 264-265°.

Anal. Calcd. for $C_{16}D_3H_{11}N_2O$ (253.3): N, 11.06. Found: N, 11.10.

The following compounds were prepared according to literature reported procedures: 1-ethyl-4,5-diphenyl- (**7a**) (34); 1-*t*-butyl-4,5-diphenyl- (**7b**) (35); and 1-benzyl-4,5-diphenyl-4-imidazolin-2-one (**7c**) (28).

1-Ethyl-5-methyl-4-phenyl-4-imidazolin-2-one (**8a**).

Triethylamine (3.00 g., 30 mmoles) was added dropwise within 30 minutes to a solution of 1.86 g. (10 mmoles) of α-amino-α-phenyl-acetone hydrochloride salt (36) and 1.00 g. (14.1 mmoles) of ethylisocyanate in 100 ml. of absolute acetone at 0° with stirring. After 1 hour the solution was filtered and the acetone evaporated. The residue crystallized after standing over night, m.p. 215-217° (ethanol/water), yield 1.00 g. (50%); ^{1}H-nmr (DMSO-d_6): δ 1.22 (t, 3H, C-CH_3), 2.30 (s, 3H, CH_3-C=C), 3.75 (q, 2H, C-CH_2-N), 7.20-7.73 (m, 5H, phenyl).

Anal. Calcd. for $C_{12}H_{14}N_2O$ (202.3): C, 71.26; H, 6.98; N, 13.85. Found: C, 71.13; H, 6.99; N, 13.60.

1-Ethyl-4-methyl-5-phenyl-4-imidazolin-2-one (**8b**).

a) 1-Ethyl-5-hydroxy-4-methyl-5-phenylimidazolidone (2) (**8ba**).

Analogously to the preparation of **6da**, 1.86 g. (10 mmoles) of α-amino-propiophenone hydrochloride salt, 1.00 g. (14.1 mmoles) of ethylisocyanate and 2.00 g. (20 mmoles) of triethylamine in 100 ml. of absolute acetone gave **8ba**, m.p. 180-182° (ethanol), yield 0.60 g. (27%); ^{1}H-nmr (DMSO-d_6): δ 0.98 (t, 3H, C-CH_3); 2.93 (q, 2H, CH_2-C), 3.56 (m, CH-C), 6.08 (s, OH), 6.67 (s, NH), 7.20-7.65 (m, 5H, phenyl).

Anal. Calcd. for $C_{12}H_{16}N_2O_2$ (220.3): C, 65.43; H, 7.32; N, 12.72. Found: C, 65.19; H, 7.31; N, 12.44.

b)Compound **8b** from **8ba**.

Analogously to the preparation of **6d**, 1.10 g. (5 mmoles) of **8ba** heated at 240° gave **8b**, m.p. 144-146° (ethanol/water), yield 0.50 g. (50%); ^{1}H-nmr (deuteriochloroform): δ 1.07 (t, 3H, C-CH_3), 2.07 (s, 3H, C=C-CH_3), 3.73 (q, 2H, N-CH_2-C), 7.20-7.75 (m, 5H, phenyl).

Anal. Calcd. for $C_{12}H_{14}N_2O$ (202.3): C, 71.26; H, 6.98; N, 13.85. Found: C, 71.21; H, 6.99; N, 13.68.

The following compounds were prepared according to literature reported procedures: 4,5-dimethyl- (**9a**) (31); 1,4,5-trimethyl- (**9b**) (30); 4,5-dimethyl-1-phenyl- (**9c**) (30); and 1-ethyl-4,5-dimethyl-4-imidazolin-2-one (**9d**) (30).

1,4-Dimethyl-5-phenyl-4-imidazolin-2-one (**9e**).

a) 5-Hydroxy-1,4-dimethyl-5-phenylimidazolidone (2) (**9ea**).

Analogously to the preparation of **6da**, 3.72 g. (20 mmoles) of α-amino-propiophenone hydrochloride salt, 2.00 g. (35.1 mmoles) of methylisocyanate and 6.00 g. (60 mmoles) of triethylamine in 200 ml. of absolute acetone gave **9ea**, m.p. 208-212° (ethanol), yield 3.00 g. (73%); ^{1}H-nmr (DMSO-d_6): δ 0.99 (d, 3H, C-CH_3); 3.40 (s, 3H, N-CH_3); 3.43 (m, CH-C); 6.04 (s, OH); 6.64 (s, NH); 7.20-7.50 (m, 5H, phenyl).

Anal. Calcd. for $C_{11}H_{14}N_2O_2$ (206.2): C, 64.06; H, 6.84; N, 13.58. Found: C, 63.81; H, 7.10; N, 13.74.

b) Compound **9e** from **9ea**.

Analogoulsy to the preparation of **6d**, 2.70 g. (15.5 mmoles) of **9ea** heated at 230° gave **9e**, m.p. 164-166° (ethanol/water), yield 1.50 g. (61%); ^{1}H-nmr (acetic acid-d_6): δ 2.08 (s, 3H, C=C-CH_3), 3.18 (s, 3H, N-CH_3), 7.15-7.70 (m, 5H, phenyl), 11.40 (s, NH).

Anal. Calcd. for $C_{11}H_{12}N_2O$ (188.2): C, 70.18; H, 6.43; N, 14.88. Found: C, 70.44; H, 6.47; N, 14.97.

1,3,4-Trimethyl-5-phenyl-4-imidazolin-2-one (**9f**).

Methyl iodide (2.70 g., 19 mmoles) in 50 ml. of absolute acetone was added dropwise within 30 minutes to a refluxing solution of 3.40 g. (18.1 mmoles) of **9e** and 10.0 g. of powdered potassium hyroxide in 100 ml. of absolute acetone. After refluxing for 1 hour, the mixture was filtered, the acetone evaporated, the residue extracted with chloroform and the organic layer washed with water. The chloroform layer was then dried and the organic solvent evaporated under vacuum giving a colourless oil yield 1.20 g. (33%); ^{1}H-nmr (deuteriochloroform): δ 2.06 (s, 3H, C=C-CH_3), 3.15 (2, 3H, N-CH_3), 3.30 (s, 3H, N-CH_3), 7.20-7.80 (m, 5H, phenyl).

Anal. Calcd. for $C_{12}H_{14}N_2O$ (202.3): C, 71.26; H, 6.98; N, 13.85. Found: C, 71.13; H, 708; N, 13.90.

The following compounds were prepared according to literature reported procedures: 1-ethyl-5-phenyl- (**10**) (30); 4,5-diethyl- (**11a**) (37); 4,5-diethyl-1-phenyl- (**11b**) (30); 1,4,5-triethyl- (**11c**) (30); and 4,5-diethyl-1-methyl-4-imidazolin-2-one (**11d**) (30).

Intstrumental Details.

Metastable spectra were obtained with a CH 5 DF (VARIAN MAT, Bremen) instrument. The electron ionization spectra were determined with the following general conditions: temperature of the ion source: 120°, direct inlet system; electron energy: 70 eV; emission: 0.8 A; acceleration voltage: 3 kV. The high resolution experiments were obtained with a MAT 711 instrument; acceleration voltage: 8 kV; resolution: 15,000 (10% rel. val. def.). The collisional activation spectra were obtained with a CH 5 DF instrument using air as the target gas at a leak rate increased until the precursor ion intensity decreased to ⅓ of its original value due to scattering and decomposition (5×10^{-5} torr).

REFERENCES AND NOTES

(1) To whom correspondence should be addressed.

(2a) M. Marx and C. Djerassi, *J. Am. Chem. Soc.*, **90**, 678 (1968); (b) J.

Collin, *Bull. Soc. Chim. Belg.*, **69**, 575 (1960); (c) H, Budzikiewicz, C. Djerassi, A. H. Jackson, G. W. Kenner, V. D. J. Newman and J. M. Wilson, *J. Chem. Soc.*, 1949 (1964).

(3a) H. Budzikiewicz, C. Djerassi and D. H. Williams, "Mass Spectrometry of Organic Compounds", Holden-Day, Inc., San Francisco, Calif., 1967, chapters 20, 22-24; (b) G. Spiteller, *Adv. Heterocycl. Chem.*, **6**, 301 (1966).

(4a) P. Brown, G. R. Pettit and R. K. Robins, *Org. Mass Spectrom.*, **2**, 521 (1969); (b) H. D. Beckey, *Angew. Chem.*, **81**, 662 (1969).

(5) H. W. Winkler and H. D. Beckey, *Org. Mass Spectrom.*, **6**, 885 (1972).

(6) H. M. Fales, in "Mass Spectrometry - Techniques and Applications", G. W. A. Milne, Ed., Wiley - Interscience, p. 602.

(7) U. P. Schlunegger, *Angew. Chem.*, **87**, 731 (1975).

(8a) J. H. Beynon, *Anal.* Chem., **42**, 971 (1970); (b) K. Aizawa, S. Yoshida and N. Takahashi, *Org. Mass Spectrom.*, **9**, 470 (1974).

(9a) J. P. Elder, jr., R. G. Cooks and J. H. Beynon, *ibid.*, **11**, 423 (1976); (b) E. G. Jones, L. E. Bauman, J. H. Beynon and R. G. Cooks, *ibid.*, **7**, 185 (1973).

(10) K. Levsen and H. Schwarz, *Angew. Chem.*, **88**, 589 (1976).

(11) F. Borchers, K. Levsen, H. Schwarz, C. Wesdemiotis and R. Wolfschütz, *J. Am. Chem. Soc.*, **99**, 1716 (1977).

(12) S. Safe, W. D. Jamieson and O. Hutzinger, *Org. Mass Spectrom.*, **6**, 33 (1972).

(13a) P. Brown, *ibid.*, **2**, 1085 (1969); (b) A. Venema and N. M. M. Nibbering, *ibid.*, **9**, 1234 (1974).

(14a) T. A. Molenaar-Langeveld, N. M. M. Nibbering and Th. J. DeBoer, *ibid.*, **5**, 725 (1971); (b) A. Venema, N. M. M. Nibbering and Th. J. DeBoer, *ibid.*, **6**, 675 (1972).

(15a) J. H. Bowie, P. F. Donaghue, H. J. Rodda and B. K. Simons, *Tetrahedron*, **24**, 3965 (1968); (b) J. H. Bowie, R. G. Cooks, S. -O. Lawesson and G. Schroll, *Aust. J. Chem.*, **20**, 1613 (1967); (c) W. D. Crow, J. H. Hodgkin and J. S. Shannon, *ibid.*, **18**, 1433 (1965); (d) J. L. Cotter, *J. Chem. Soc.*, 5491 (1964); (e) M. M. Bursey, L. R. Dusold and A. Padwa, *Tetrahedron Letters*, 2649 (1967).

(16a) B. K. Simons, R. K. M. R. Kallury and J. H. Bowie, *Org. Mass Spectrom.*, **2**, 739 (1969); (b) G. L. Aldous and J. H. Bowie *ibid.*, **10**, 64 (1975).

(17) G. Holzmann, B. Krieg, H. Lautenschläger, K. Levsen, H. Heimbach and B. Steiner, *ibid.*, in press.

(18a) J. H. Bowie, B. K. Simons, D. F. Donaghue and R. K. M. R. Kallury, *Tetrahedron*, **25**, 3969 (1969); (b) B. K. Simons, B. Nussey and J. H. Bowie, *Org. Mass Spectrom.*, **3**, 925 (1970).

(19a) F. W. McLafferty and J. Winkler, *J. Am. Chem. Soc.*, **96**, 5182 (1974); (b) H. Schwarz, C. Wesdemiotis, H. Heimbach and K. Levsen, *Org. Mass Spectrom.*, **12**, 213 (1977); (c) C. Köppel, H. Schwarz, F. Borchers and K. Levsen, *Int. J. Mass Spectrom. Ion Phys.*, **21**, 15 (1976); (d) P. N. Rylander, S. Meyerson, and H. M. Grubb, *J. Am. Chem. Soc.*, **79**, 842 (1957); (e) J. T. Bursey, M. M. Bursey, and D. G. I. Kingston, *Chem. Rev.*, **73**, 191 (1973).

(20) G. E. Hilbert, *J. Am. Chem. Soc.*, **54**, 3413 (1932).

(21) H. Rupe, *Ber.*, **28**, 251 (1895).

(22) D. Fritsch, *ibid.*, **26**, 427 (1893).

(23) H. Biltz and C. Stellbaum, *Ann. Chem.*, **339**, 264 (1905).

(24) A. Marsili, M. F. Saettone and E. Bucci, *J. Org. Chem.*, **33**, 2884 (1968).

(25) H. J. Schönherr and H. W. Wanzlick, *Chem. Ber.*, **103**, 1037 (1970).

(26) H. G. Aurich, *Ann. Chem.*, **732**, 195 (1970).

(27) H. McCombie and H. A. Scarborough, *J. Chem. Soc.*, **103**, 56 (1913).

(28) B. Krieg and H. Lautenschläger, *Ann. Chem.*, 1471 (1976).

(29) L. Behl-Bregowsky, *Ber.*, **30**, 1515 (1897).

(30) B. Krieg and H. Lautenschläger, *Ann. Chem.*, 208 (1976).

(31) H. Biltz, *Ber.*, **40**, 4799 (1907).

(32) M. F. Saettone, *J. Org. Chem.*, **31**, 3914 (1966).

(33) H. Lettau, *Z. Chem.*, **12**, 462 (1970).

(34) H. Biltz and Th. Kosegarten, *Ann. Chem.*, **368**, 228 (1909).

(35) B. Krieg and H. Lautenschläger, *ibid.*, 788 (1976).

(36) P. W. Neber and A. V. Friedolsheim, *ibid.*, **449**, 121 (1926).

(37) C. F. Winans and H. Adkins, *J. Am. Chem. Soc.*, **55**, 4167 (1933).