Mass Spectra of 1,3-Diarylazetidin-3-ols and Related Compounds

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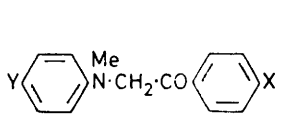
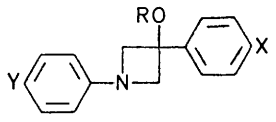
Mass spectra of six 1,3-diarylazetidin-3-ols, two 7-aryl-7-azabicyclo[4.2.0]octan-1-ols, and 1-cyclohexylazetidin-3-ol are reported. Most fragmentation pathways of the diarylazetidinols (2)—(7) are initiated by cleavage of the azetidine ring with or without a specific hydrogen atom transfer from the hydroxy-group. The relative importance of ions containing the nitrogen atom and those containing the oxygen atom is influenced by the abilities of the 1- and 3-aryl groups to stabilise the respective ions. The 1-cyclohexyl derivative (13) differs in that most fragmentation pathways involve initial cleavage of the cyclohexane ring. The azabicyclo-octanols (11) and (12) behave in a similar way to 1-arylazetidinols.

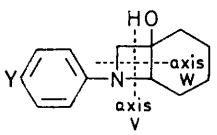
MASS spectra of azetidine,[1,2] alkyl- and aryl-substituted azetidines,[2-5] 3-aroylazetidines,[5,6] diazetidinylmethanes,[2] and many azetidin-2-ones [3,7-11] have been discussed. Spectra of two azetidin-3-ols [3] and a partial spectrum of another [12] have been published, and spectra of some *N*-benzoyl- [13,14] and *N*-*p*-tosyl-azetidin-3-ols [14] have been briefly mentioned. Nothing appears to be known of the mass spectra of *N*-arylazetidin-3-ols and, because of difficulties in making them, little is known of their general chemistry. However, better methods for their



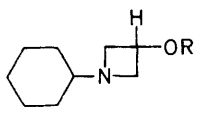
(1)



(2) X=Y=R=H
(3) X=OMe, Y=R=H
(4) X=Ph, Y=R=H
(5) X=R=H, Y=OMe
(6) X=R=H, Y=Cl
(7) X=R=H, Y=Me
(8) X=Y=H, R=D
(9) X=Y=H, R=$SiMe_3$
(10) X=OMe, Y=H, R=D



(11) Y=H
(12) Y=Me



(13) R=H
(14) R=D

synthesis are now available [15-17] and one of these, irradiation of appropriate ω-arylaminoacetophenones, was used to prepare the 1,3-diarylazetidin-3-ols (2)—(7) whose spectra are discussed in this paper.

The spectrum of 1,3-diphenylazetidin-3-ol (2) [Figure 1(a)] is dominated by ions which result from cleavage

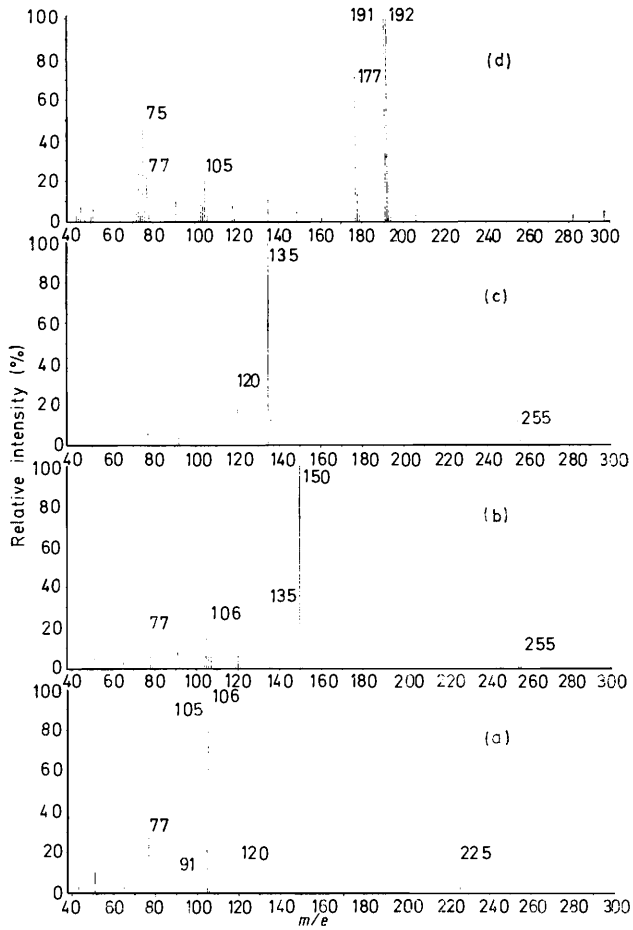


FIGURE 1 Mass spectra of (a) 1,3-diphenylazetidin-3-ol, (b) 3-(4-methoxyphenyl)-1-phenylazetidin-3-ol, (c) 1-(4-methoxyphenyl)-3-phenylazetidin-3-ol, and (d) 1,3-diphenyl-3-trimethylsilyloxyazetidine

of the azetidine ring (Scheme). Scission of the 1,2- and 3,4-bonds with charge retention on either fragment

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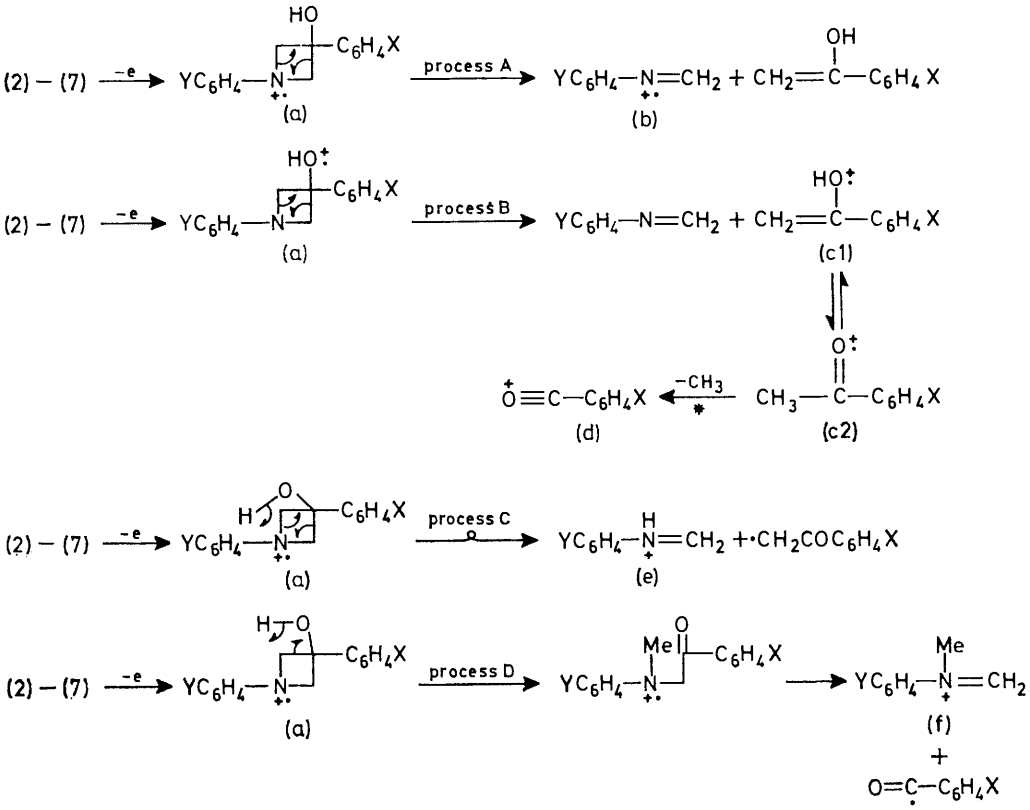
(processes A and B in the Scheme) gives ions of *m/e* 105 (C_7H_7N) (b; Y = H) and 120 (C_8H_8O) (c; X = H). Loss of a methyl radical from the latter gives the acylium ion (d; X = H), *m/e* 105 (C_7H_5O). Ions (b; Y = H) and (d; X = H) contribute about 2/3 and 1/3 respectively to the peak at *m/e* 105. The base peak in the spectrum also results from 1,2- and 3,4-bond scissions but with transfer of a hydrogen atom (process C in the Scheme) to give ion (e; Y = H), *m/e* 106 (C_7H_8N). This was shown to be a specific hydrogen transfer when the *m/e* 106 peak was almost entirely shifted to *m/e* 107 in the spectrum of the 3-deuteroxy-analogue (7). A related hydrogen transfer, probably from a 3-*alkyl* group, occurs with some azetidines.[3] Hydrogen transfer from the 3-hydroxy-group to a neighbouring carbon atom also occurs in the present compound (process D in the Scheme) and the resulting ion (f; Y = H) ($C_8H_{10}N$) contributes about 25% of the intensity of the *m/e* 120 peak. The only other significant ions in the spectrum are the molecular ion (*m/e* 225) and the phenyl ion (*m/e* 77).

The effect on the fragmentation processes in the Scheme of substituents in the 1- and 3-phenyl groups has been explored. In the case of the compound (2) already discussed, most of the ion current was carried by nitrogen-containing ions. However, substituents in the 3-aryl group which stabilise the oxygen-containing ions readily reverse this situation. Thus, in the spectrum of the 3-(4-methoxyphenyl) derivative (3), the two most intense peaks were due to an ion (c; X = OMe), *m/e* 150 ($C_9H_{10}O_2$) (100%), produced by process B, and its decomposition product (d; X = OMe), *m/e* 135 ($C_8H_7O_2$) (36%) [Figure 1(b)]. It seems likely that isomerisation occurs in ion (c) (*m/e* 150) to give ionised *p*-methoxyacetophenone (c2; X = 4-OMe) before fragmentation to give the ion *m/e* 135. However, the corresponding peaks in the spectrum of the 3-deuteroxy-compound (10) are at *m/e* 151 (as expected) and 135/136 (intensity ratio 1 : 2), so if isomerisation of ion (c) occurs, as suggested, then some exchange of the *ortho*-hydrogen atoms with deuterium must occur. ωωω-Trideuterioacetophenone lost $\cdot CD_3$ exclusively.



SCHEME

Process B was again of paramount importance in fragmentation of the 3-(biphenyl-4-yl) derivative (4); it led to the most abundant ion (c; X = Ph), *m/e* 196 (100%) which, in turn, gave the acylium ion (d; X = Ph) *m/e* 181 (27%). However, in this compound process C was also important and it resulted in the nitrogen-containing ion (e; Y = H), *m/e* 106 (C_7H_8N) (63%). The charge was also largely retained by oxygen-containing fragments in the *O*-trimethylsilyl derivative, 1,3-diphenyl-3-trimethylsilyloxyazetidine (9). Most of the ion current was carried by ion (g), *m/e* 192 (100%), produced by process B, and its breakdown products, *m/e* 191 (100%) and 177 (67%) formed by loss of H· and CH_3· respectively (metastables) [Figure 1(d)].

By contrast, nitrogen-containing ions again became dominant in the spectra of 1-(substituted phenyl)-3-phenylazetidin-3-ols. Thus, in the case of the

1-(4-methoxyphenyl) derivative (5) [Figure 1(c)] a large majority of the ion current was carried by the *m/e* 135 ion (b; Y = OMe), produced by process A, and an *m/e*

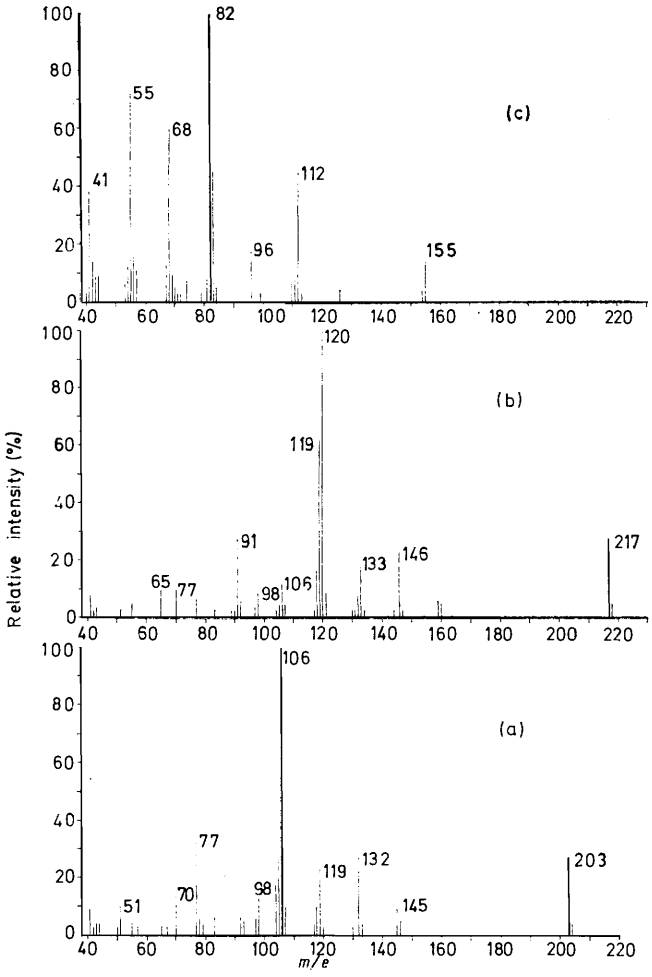


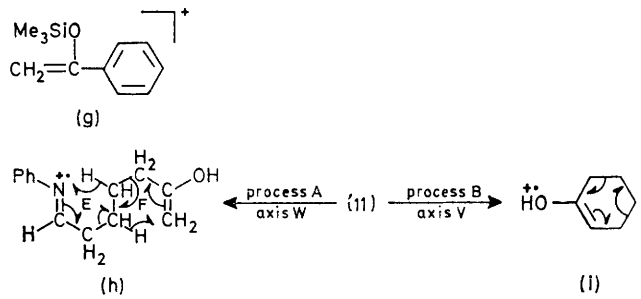
FIGURE 2 Mass spectra of (a) 7-phenyl-6-azabicyclo[4.2.0]octan-1-ol, (b) 7-*p*-tolyl-7-azabicyclo[4.2.0]octan-1-ol, and (c) 1-cyclohexylazetidin-3-ol

120 ion, presumably formed from it by loss of $CH_3^{\bullet}$, from the methoxy-group. Ion (c; X = H) made only a small contribution to the *m/e* 120 peak: there was only a small *m/e* 121 peak in the spectrum of the 3-deuteroxy-analogue.

Spectra of two other 1-(substituted phenyl) derivatives, (6) and (7), were examined; in each case the appropriate ion (b; Y = Cl or Me) produced by process A was responsible for the base peak. However, the rearrangement ions (e; Y = Cl or Me) produced by process C also gave intense peaks in these spectra, particularly in the case of the chloro-compound where the intensities of peaks due to ion (e; Y = Cl), *m/e* 140/142 were (after correction for ^{13}C) about 80% of these due to ion (b; Y = Cl), *m/e* 139/141.

Processes A and C operate simultaneously in all the compounds considered but their relative importance varies markedly. The importance of process A relative to C increases as the ability of the 1-aryl substituent to stabilise ion (b) increases. Thus, the intensity of ion (b) relative to ion (e) varies from about 2 : 3 when the ions are produced from the 1,3-diphenyl derivative (2) (*i.e.* when Y = H) to about 20 : 1 when they are produced from the 1-(4-methoxyphenyl)-3-phenyl compound (5) (*i.e.* when Y = OMe). More generally, the intensity of (b) relative to (e) rises along the series Y = H, Cl, Me, or OMe, so the stabilising influence of the substituent must be more important in the odd-electron ions (b) than the even-electron ions (e).

Fragmentation of some 7-aryl-7-azabicyclo[4.2.0]-octan-1-ols (11) and (12), which are closely related to the compounds already discussed, again proceeded mainly by azetidine ring cleavage [Figure 2(a)]. In these compounds processes A—D are still possible but each can take place along two different axes (V and W) and thus give two different products. In the case of the 1-phenyl compound (11), cleavage by process A along axis V gives the *m/e* 105 ion (b; Y = H) (27%), and cleavage along the same axis by process C gives the *m/e* 106 ion (e; Y = H) (C_7H_8N) (100%) [Figure 2(a)]. The specific nature of the H transfer was again confirmed by showing that the *m/e* 106 peak was shifted to *m/e* 107 in the corresponding deuteroxy-compound. Almost all the other important ions in the spectrum can be accounted for by a process A cleavage along axis W to give the ion (h), followed by appropriate fragmentation. Simple scission at various points along the carbon chain of the ion (h) would lead to the observed ions at *m/e* 104, 118, 132 (27%), and 146, and two different McLafferty rearrangements, E and F, of the ion (h) would lead respectively to ions at *m/e* 119 (C_8H_9N) (23%) and 145 ($C_{10}H_{11}N$) (9%) (metastables). Some incorporation of deuterium into the ions at *m/e* 132 and 146, but not *m/e* 118 and 119, was noted in the spectrum of the deuteroxy-analogue. Comparison of the spectrum of compound (11) with that of the 1-(*p*-tolyl) derivative (12) [Figure 2(b)] confirms that almost all the significant ions contain the phenyl group: the peaks are shifted upwards by 14 mass units in the methyl derivative. Cleavage along axis V by process B gives the ion (i), *m/e* 98,



and this can lose ethylene by a retro-Diels–Alder reaction to give an ion *m/e* 70.

1-Cyclohexylazetidin-3-ol (13) was also examined for comparison with simple *N*-alkylazetidinols.[3] This com-

pound lacks the stabilising influence of an aryl group at position 1 or 3 so it was not surprising that most fragmentation pathways were initiated by breakage of the cyclohexane ring [Figure 2(c)]. This produces the $[M - CH_3]^+$, $[M - C_2H_5]^+$, and $[M - C_3H_7]^+$ ions which retain the hydroxy hydrogen as shown by the spectrum of the deuteroxy-compound (14). The $[M - C_2H_5]^+$ ion subsequently loses C_2H_4O to give the ion at *m/e* 82 (C_5H_8N) (100%) (metastable) and the ions at *m/e* 96 ($C_6H_{10}N$) (18%) and 68 (60%) probably arise by similar losses from the $[M - CH_3]^+$ and $[M - C_3H_7]^+$ ions respectively, although no metastables are observed. The C_2H_4O fragment lost contains the hydroxylic hydrogen since the *m/e* 68, 82, and 96 peaks are not shifted in the mass spectrum of the deuteroxy-compound (14).

Although the spectrum of this cyclohexyl derivative is much more complex than that of the simple *N*-alkylazetidin-3-ols described earlier,[3] the genesis of the major fragments is essentially similar to the α-cleavage and C_2H_4O loss noted previously.[3]

Mass spectra of all the compounds mentioned are listed in the form of *m/e* ratios and relative intensities in Supplementary Publication No. SUP 21792 (7 pp).†

† For details of Supplementary Publications see Notice to Authors No. 7, *J.C.S. Perkin II*, 1975, Index issue.

EXPERIMENTAL

The *N*-arylazetidinols (2)—(7) were obtained by photocyclisation of corresponding α-arylamino-ketones (1).[18] The syntheses will be included in a future publication. The 7-aryl-7-azabicyclo[4.2.0]octan-1-ols (11) and (12) were synthesised as described previously,[17] as was the azetidin-3-ol (13).[19]

Deuteriated specimens were obtained by evaporating the hydroxy-compounds several times with ethan[^{2}H]ol and a little triethylamine. The trimethylsilyl derivative (9) was prepared by treating the hydroxy-compound (2) with Trisil (Pierce Chemical Co.) for several hours.

Spectra were measured with an A.E.I. MS902S spectrometer operating at 70 eV. Samples were introduced on a direct insertion probe into the source maintained at *ca.* 220 °C. Accurate mass measurements were made at a resolving power of 10 000 (10% valley definition). Wherever a formula is quoted for an ion, in the text, it is based on a mass measurement which agrees with the calculated value within 10 p.p.m.

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