Analogs of Sparteine. IV. Mass Spectral Features of a Series of *N,N'*-Disubstituted Bispidines

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The mass spectra of a series of *N,N'*-disubstituted bispidine derivatives have been investigated, and salient features analogous to those seen in the spectra of related azabicyclic compounds observed. The most important feature observed in the spectra is the common base peak (m/e 58), which results from the generation of *N,N*-dimethylformimmonium ion **24**. The pathway by which this ion originates is discussed.

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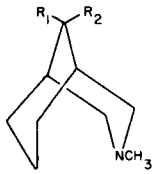
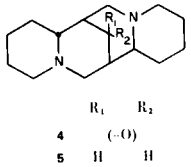
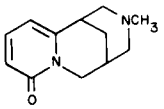
During the course of a study of the chemistry of 3,7-diazabicyclo[3.3.1]nonanes (bispidines), a number of consistent mass spectral features became apparent. Also, comparison of the spectra of these compounds to those of their monoazabicyclic counterparts (**1-3**) (4), and to those of structurally related quinolizidine alkaloids and derivatives, especially **4-6** (5,6), indicated considerable similarity. In this paper, we report the principal spectral features observed, and compare the origin of some of these with the origin of analogous features in the spectra of **1-6**.



	R_1	R_2
1	(=O)	
2	OH	C_6H_5
3	OH	D



	R_1	R_2
4	(=O)	
5	H	H



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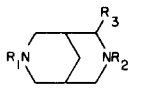
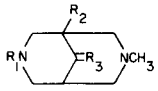
The syntheses of the *N,N'*-dialkylbispidines **7-17, 19** and **22-23** have been described previously (7). Amino alcohols **20** and **21** were prepared by reduction of amino ketone **17** with sodium borohydride and sodium borodeuteride respectively. Reduction of the tosylhydrazone of **17** with the latter reagent furnished **18** (12). Major



	R_1	R_2	R_3
7	CH_3	$PhCH_2$	H
8	CH_3	$PhCH_2$	*ex*-CH_3
9	*n*-C_4H_9	$PhCH_2$	H
10	C_2H_5	CH_3	H
11	CH_3	CH_3	*ex*-CH_3
12	CH_3	CH_3	*en*-CH_3
13	CH_3	CH_3	*ex-iso*-C_3H_7
14	CH_3	CH_3	H
15	CH_3	CH_3	(=O)



	R_1	R_2	R_3
16	$PhCH_2$	H	O
17	CH_3	H	O
18	CH_3	H	D_2
19	CH_3	CH_3NHCH_2	H_2

fragments in the spectra of these compounds are listed, in comparison with those seen in the spectra of **1-6**, in Tables I-III.

Two features in the spectra of the bispidines which proved most useful in structural confirmation were the ever present parent peaks, and the base peak of m/e 58 exhibited by *all* of the compounds. This latter feature is of lesser importance in the spectra of piperidines (8), and

Table I

Major Fragment Ions in the Mass Spectra of Sparteine and *N,N'*-Dialkylbispidines

Compound	M^+	Most Abundant Ions (% Relative Abundance)				
5	234 (81)	137 (100)	234 (91)	98 (78)	193 (40)	136 (31)
7	230 (4)	58 (100)	91 (96)	44 (78)	96 (43)	65 (24)
8	244 (5)	58 (100)	91 (46)	44 (20)	42 (19)	153 (11)
9	272 (23)	58 (100)	91 (51)	100 (38)	272 (23)	134 (22)
10	168 (26)	58 (100)	44 (56)	72 (35)	96 (32)	82 (26)
11	168 (9)	58 (100)	42 (26)	96 (25)	44 (22)	72 (21)
12	168 (65)	58 (100)	168 (65)	72 (51)	96 (42)	138 (38)
13	196 (1)	58 (100)	153 (31)	94 (7)	43 (7)	44 (1)
14	154 (71)	58 (100)	97 (77)	96 (77)	44 (76)	84 (74)
18 (a)	156 (100)	156 (100)	58 (100)	59 (82)	99 (73)	98 (64)
19	197 (48)	58 (100)	108 (68)	44 (67)	197 (48)	122 (43)

(a) Recorded at 30 eV.

Table II

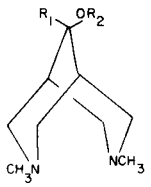
Major Fragment Ions in the Mass Spectra of Bicyclic Amino Ketones

Compound	M^+	Most Abundant Ions (% Relative Abundance)				
1	153 (38)	44 (100)	42 (53)	57 (40)	153 (38)	55 (35)
4	248 (26)	98 (100)	150 (76)	97 (64)	96 (41)	151 (33)
6	204 (26)	58 (100)	204 (26)	146 (7)	160 (5)	205 (4)
15	168 (71)	58 (100)	168 (71)	44 (47)	96 (40)	70 (25)
16	244 (2)	91 (100)	58 (100)	42 (70)	44 (38)	110 (35)
17	168 (23)	58 (100)	110 (72)	44 (32)	84 (26)	70 (26)

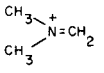
Table III

Major Fragment Ions in the Mass Spectra of *N,N'*-Dimethylbispidinols and Related Compounds

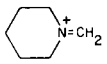
Compound	M^+	Most Abundant Ions (% Relative Abundance)				
2	231 (57)	42 (100)	44 (79)	170 (70)	231 (56)	58 (56)
3	156 (20)	59 (100)	44 (70)	58 (35)	42 (32)	156 (20)
20	170 (36)	58 (100)	57 (70)	44 (59)	70 (45)	84 (43)
21	171 (52)	58 (100)	44 (80)	42 (80)	95 (60)	59 (48)
22	246 (80)	58 (100)	170 (93)	84 (93)	246 (80)	44 (80)
23	302 (27)	58 (100)	170 (98)	44 (54)	198 (32)	184 (30)



	R_1	R_2
20	H	H
21	D	H
22	C_6H_5	H
23	C_6H_5	COC_2H_5



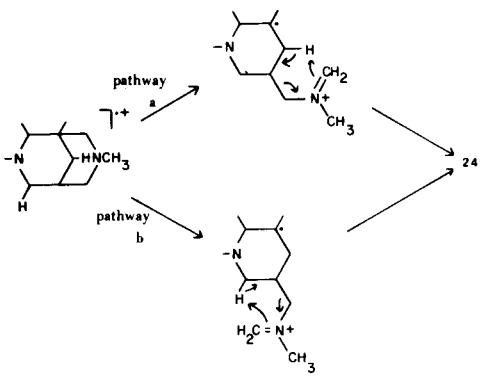
24, m/e 58



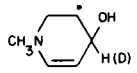
25, m/e 98

monoazabicyclic compounds **1** and **2** (4), but constitutes the base peak in **6** (6). It results from the formation of cation **24**. By analogy with the postulated origin of homologous cation **25** in the spectra of **4**, **5**, and related compounds (5,6), it is produced primarily *via* McLafferty-type rearrangement of ring-opened immonium ion intermediates (Scheme I). Bridge deuteration of **14** caused an increase in the intensity of the m/e 59 peak in the spectrum of **18**, indicating participation of a methylene bridge hydrogen (path a). The base peak in **18** remains at m/e 58 however, indicating also the involvement of an *N*-methylene hydrogen as in path b. Cation **25** had been found to originate primarily by a path analogous to b in the spectrum of **5**, based on the appearance of spectra of derivatives suitably labeled with deuterium (6). Comparison of the spectra of

Scheme I



3, **20**, and **21** (Table III) indicates that while **3** rearranges by path a (Scheme I), the latter compounds favor path b, since the base peak is at m/e 59 in **3** (shifted from m/e 58 in the unlabeled amino alcohol) but is seen at m/e 58 in



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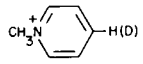
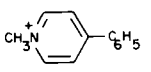


27, m/e 94 (95)

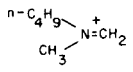
both the labeled and unlabeled diamino alcohols. This preference for *N*-methylene hydrogen participation in the rearrangement of **20** and **21** after electron impact could be due to the ease of aromatization of the resulting piperidinol radicals **26** to give cations **27**: m/e 94 (R.A. 38) and m/e 95 (R.A. 60) in the spectra of **20** and **21** respectively. However, the possibility that **27** originates at least in part by other paths cannot be ruled out. In the spectra of the other bispidinols and bispidinones (Tables II and III), path b predominates due to the absence of bridge hydrogens.

The bispidinols with bridge phenyl groups (**22-23**) have strong peaks of m/e 170 in their spectra, as does related monoazabicyclic alcohol **2** (Table III). This is due to the presence of the *N*-methyl-4-phenyl pyridinium cation (**28**).

The spectra of compounds **7-9**, and **16** exhibit intense peaks at m/e 91, characteristic of compounds containing *N*-benzyl substituents (9). In addition, **9** has a base peak at m/e 58 though it has no *N*-methyl substituent. The expected base peak of m/e 100, resulting from formation of **29** (*cf.*, Scheme I), is less intense. This suggests that **29** or a precursor decomposes to yield **24**, as do related *N*-*n*-butyl substituted ions (10).



28, m/e 170



29, m/e 100

EXPERIMENTAL

High and low resolution mass spectra were recorded at 70 eV using Varian CH 5 and Finnegan 1015 spectrometers respectively. Compounds were analyzed as the free bases, except **9** and **12**, which were analyzed as dihydrochloride and dihydrobromide salts respectively. Nmr spectra were obtained on a Varian T-60 spectrometer, ir spectra on a Beckman IR 33 spectrophotometer.

N,N'-Dimethylbispidinol (**20**).

Amino ketone **17** (0.2 g., 1.2 mmoles) was dissolved in 4 ml. of water, cooled to 5°, and sodium borohydride (0.1 g., 2.6 mmoles) was added in one portion. After the solution had been stirred at 25° for 1 hour, the *p*H of the solution was adjusted to *ca.* 1 by slow addition of cold 10% aqueous hydrochloric acid. After stirring for 1 hour at 25°, the solution was made strongly basic with cold 10% aqueous sodium hydroxide and extracted with five 10 ml. portions of chloroform. The combined, dried (anhydrous sodium sulfate) extracts were filtered and concentrated *in vacuo* to afford 0.19 g. (94%) of a white solid, m.p. 123-128° (subl.); ir (potassium bromide): 3.38 (OH), 3.57 μ (CH); nmr (perdeuteriobenzene, 1% TMS): δ 1.95 and 2.00 (s, 6, NCH_3), 3.50 (t, J = 3 Hz, 1, C*H*OH), 4.85 (s, W½ = 8 Hz, 1, deuterium oxide exchangeable, OH). Treatment of a cold aqueous solution of the base with two molar equivalents of cold 10% aqueous hydrochloric acid followed by lyophilization gave the dihydrochloride, m.p. 174-190° dec.

Anal. Calcd. for $C_9H_{20}Cl_2N_2O$: C, 44.45; H, 8.29; N, 11.52. Found: C, 44.48; H, 8.59; N, 11.49.

Treatment of **17** as above with sodium borodeuteride furnished *N,N'*-dimethylbispidinol-d_1 (**21**). Its nmr spectrum was nearly identical to that of **20** except that the triplet at 3.50 ppm was absent. Its mass spectrum exhibited a ratio of M/M-1 identical to that of **20**.

N,N'-Dimethylbispidine-d_2 (**18**).

The tosylhydrazone of **17** was prepared (11) from tosylhydrazide (1.07 g., 5.7 mmoles) and **17** (0.92 g., 5.5 mmoles). The product crystallized from methanol-benzene to yield 1.02 g. (55%) of white crystals, m.p. 148-152° (dec. with foaming); ir (potassium bromide): 6.25 μ (C=N).

Anal. Calcd. for $C_{16}H_{24}N_4O_2S$: C, 57.12; H, 7.19. Found: C, 57.61; H, 7.32.

To the tosylhydrazone (0.085 g., 0.25 mmole) in 5 ml. of methanol-d, was added sodium borodeuteride (12) (0.247 g., 5.9 mmoles). The solution was heated at reflux for 8.25 hours, then cooled and added to 20 ml. of ether and 6 ml. of water. The aqueous phase was extracted with an additional 20 ml. of ether. The organic extracts were combined, dried (sodium sulfate) and treated with excess ethereal hydrogen chloride. The filtered precipitate was recrystallized from ethanol-acetone affording 0.02 g. (35%) of white needles, m.p. 252-254° dec.; mixed m.p. with the unlabeled compound (**14** dihydrochloride) was not changed; gas liquid chromatography of a mixture of **14** and **18** (free bases), under conditions previously described (7), gave chromatograms displaying a single peak; deuterium content: *ca.* 90% d_2, 10% d, 0% d_0.

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