Mass Spectra of Stereoisomers of 3-Piperidinocyclohexanol Derivatives

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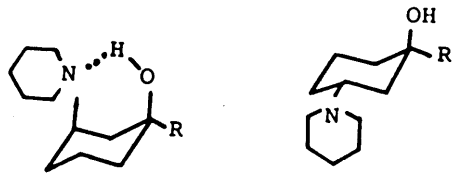
The mass spectra of 3-piperidinocyclohexanol derivatives (1—6) were measured by electron impact ionization. Characteristic fragment ions were observed at $[M-43]^+$, *m/z* 182, *m/z* 164, *m/z* 140, *m/z* 138, *m/z* 124, *m/z* 111, *m/z* 98, *m/z* 85 and *m/z* 84.

The *cis*- and *trans*-configurations of 3-piperidinocyclohexanol derivatives could be distinguished by the peak intensities at *m/z* 140 and *m/z* 85. The difference between alkyl and phenyl substituents could be recognized from the peak intensities at *m/z* 182 and *m/z* 164.

Keywords amino alcohol; 3-piperidinocyclohexanol; *cis–trans* isomer; mass spectrum; stereospecific effect; electron impact ionization mass spectrum

In connection with the synthetic study of amino alcohols having analgesic activity, 3-piperidinocyclohexanol derivatives (**1**—**6**), involving *cis*- and *trans*-isomers, were synthesized (Fig. 1). The distinction between these isomers was examined by mass spectrometric methods. The information should be helpful in configurational assignment in analogous systems. In certain cases, mass spectrometry was found to be the best method for configurational determination.

In the study of stereoisomers by mass spectrometric methods, stereospecific cleavage of 1,3-disubstituted cyclohexane derivatives has already been reported.[1-4] This is based on stereospecific elimination between the substituent at the 1-position (hydroxyl,[2] methoxy[3] and acetyl groups[4]) and the hydrogen atom at the 3-position. 3-Piperidinocyclohexanol derivatives have two characteristic properties: (1) these compounds contain two heteroatoms (an oxygen atom and a nitrogen atom); (2) *cis*-isomers have an intramolecular hydrogen bond between the hydroxyl group at the 1-position and the piperidino group at the 3-position.[5]



cis-isomer *trans*-isomer

1: R = CH_3 **4**: R = *n*-C_4H_9
2: R = C_2H_5 **5**: R = *n*-C_5H_{11}
3: R = *n*-C_3H_7 **6**: R = C_6H_5

Fig. 1. 3-Piperidinocyclohexanol Derivatives (**1**—**6**)

In this paper, we described the results of our comparative investigation of the stereoisomers in a series of 3-piperidinocyclohexanol derivatives.

Results and Discussion

The mass spectral data for compounds **1**—**6** are shown in Table I, and for **4** the mass spectra (MS) are shown in Fig. 2. The fragmentations are shown in Chart 1, in which an asterisk, (*) indicates that a metastable peak is observed for the indicated fragmentation path. Empirical formulas of the major ions were also obtained by exact mass measurement (Table II). The important metastable peaks are shown in Table III.

Molecular Ion Stability Stereoisomers of the series studied here show significant differences in the stability of their molecular ions. For instance, the molecular ions of the *trans*-isomers are more stable than those of the *cis*-counterparts. The stability of the molecular ion reflects the internal energy in the ground state. In this case, it seems that the internal energies of *trans*-isomers are lower than those of the *cis*-counterparts. The molecular ion intensities of *trans*-isomers are greater than those of the *cis*-counterparts.

***m/z* 140 and *m/z* 85 Ions** The characteristic fragment ions at *m/z* 140 and *m/z* 85 were observed in the MS of all compounds listed in Table I. However, the ion intensities in

TABLE I. Characteristic Peaks and Their Relative Intensities in the MS of 3-Piperidinocyclohexanol Derivatives

Compound		*m/z* (Relative intensity, %)												
		$M^{+\cdot}$	182	$[M-43]^+$	164	140	138	124	112	111	98	96	85	84
1: R = CH_3	*cis*	12.5	8.1	100	1.0	13.7	7.7	97.2	15.5	15.3	5.1	13.5	16.1	34.3
	trans	15.2	10.4	93.5	2.8	1.1	8.2	100	13.0	18.2	4.3	15.9	4.1	16.4
2: R = C_2H_5	*cis*	11.9	39.3	61.0	3.4	14.0	8.1	100	15.3	17.0	5.3	11.2	19.2	30.5
	trans	13.3	41.3	55.7	4.3	5.9	8.1	100	13.0	17.9	7.2	15.7	5.4	16.5
3: R = *n*-C_3H_7	*cis*	11.9	100	100	3.4	19.2	12.3	99.8	15.1	20.6	13.1	23.9	27.8	38.5
	trans	13.5	100	100	3.8	4.7	13.7	97.6	11.1	22.8	15.4	12.7	5.1	14.0
4: R = *n*-C_4H_9	*cis*	11.3	61.1	53.8	3.3	20.8	12.6	100	17.8	26.5	13.4	12.9	32.3	42.0
	trans	12.9	60.7	47.3	3.6	3.0	14.5	100	11.0	26.8	15.1	14.2	9.0	16.6
5: R = *n*-C_5H_{11}	*cis*	11.4	66.0	58.8	3.5	22.7	15.1	100	16.9	27.0	18.9	12.1	27.9	42.3
	trans	12.6	63.9	49.9	4.0	2.7	12.2	100	11.6	28.6	15.4	20.1	6.3	15.7
6: R = C_6H_5	*cis*	16.1	2.1	100	—	18.8	9.5	69.2	17.4	19.6	51.3	12.0	22.3	44.1
	trans	17.2	3.2	100	—	3.2	10.1	74.1	19.6	20.7	58.6	17.2	4.8	19.3

TABLE II. High-Resolution MS Data for the Characteristic Fragment Ions of 3-Piperidinocyclohexanol Derivatives

Compd.	Ion m/z	Elemental composition	Calculated	*cis*-Isomer		*trans*-Isomer	
				Observed	Error (mu)	Observed	Error (mu)
1: R=CH_3	197	$C_{12}H_{23}NO$	197.1778	197.1809	3.0	197.1697	−0.2
	182	$C_{11}H_{20}NO$	182.1543	182.1576	3.3	182.1550	0.7
	164	$C_{11}H_{18}N$	164.1438	164.1414	−2.4	164.1441	0.3
	154	$C_9H_{16}NO$	154.1231	154.1241	1.0	154.1261	3.0
	140	$C_9H_{18}N$	140.1438	140.1456	1.8	140.1417	−2.0
	138	$C_9H_{16}N$	138.1281	138.1270	−1.1	138.1304	2.2
	124	$C_8H_{14}N$	124.1126	124.1138	1.2	124.1134	0.8
	112	$C_7H_{14}N$	112.1125	112.1148	2.3	112.1130	0.5
	111	$C_7H_{13}N$	111.1047	111.1069	2.1	111.1046	−0.1
	98	$C_6H_{12}N$	98.0968	98.0961	−0.7	98.0965	−0.3
	96	$C_6H_{10}N$	96.0812	96.0827	1.5	96.0810	−0.2
	85	$C_5H_{11}N$	85.0891	85.0921	3.0	85.0891	0.0
	84	$C_5H_{10}N$	84.0812	84.0857	4.5	84.0807	−0.5
2: R=C_2H_5	211	$C_{13}H_{25}NO$	211.1934	211.1922	−1.2	211.1970	3.6
	182	$C_{11}H_{20}NO$	182.1543	182.1497	−4.6	182.1556	1.2
	168	$C_{10}H_{18}NO$	168.1387	168.1385	−0.1	168.1388	0.0
	164	$C_{11}H_{18}N$	164.1438	164.1418	−2.0	164.1438	0.0
	140	$C_9H_{18}N$	140.1438	140.1447	0.9	140.1409	−2.9
	138	$C_9H_{16}N$	136.1281	138.1231	−5.0	138.1276	−0.5
	124	$C_8H_{14}N$	124.1125	124.1134	0.9	124.1122	−0.3
	112	$C_7H_{14}N$	112.1125	112.1092	−3.3	112.1135	1.0
	111	$C_7H_{13}N$	111.1047	111.1065	1.8	111.1075	2.8
	98	$C_6H_{12}N$	98.0969	98.0935	−3.3	98.0990	2.0
	96	$C_6H_{10}N$	96.0812	96.0811	−0.1	96.0825	1.2
	85	$C_5H_{11}N$	85.0891	85.0881	−1.0	85.0914	2.3
	84	$C_5H_{10}N$	84.0812	84.0821	0.9	84.0832	1.9
3: R=*n*-C_3H_7	225	$C_{14}H_{27}NO$	225.2092	225.2105	1.3	225.2042	−5.0
	182	$C_{11}H_{20}NO$	182.1544	182.1551	0.7	182.1530	−1.4
	164	$C_{11}H_{18}N$	164.1438	164.1417	−2.0	164.1448	1.0
	140	$C_9H_{18}N$	140.1438	140.1446	0.8	140.1409	−2.8
	138	$C_9H_{16}N$	138.1281	138.1276	−0.5	138.1265	−1.6
	124	$C_8H_{14}N$	124.1124	124.1092	−3.2	124.1112	−1.2
	112	$C_7H_{14}N$	112.1126	112.1155	2.9	112.1151	2.5
	111	$C_7H_{13}N$	111.1048	111.1082	3.4	111.1059	1.2
	98	$C_6H_{12}N$	98.0968	98.0946	−2.2	98.0931	−3.7
	96	$C_6H_{11}N$	96.0812	96.0801	−1.1	96.0830	1.8
	85	$C_5H_{11}N$	85.0891	85.0905	1.4	85.0846	−4.5
	84	$C_5H_{10}N$	84.0812	84.0829	1.7	84.0773	−3.9
4: R=*n*-C_4H_9	239	$C_{15}H_{29}NO$	239.2247	239.2263	1.6	239.2233	−1.4
	196	$C_{12}H_{22}NO$	196.1700	196.1704	0.4	196.1725	2.5
	182	$C_{11}H_{20}NO$	182.1543	182.1543	0.0	182.1532	−1.1
	164	$C_{11}H_{18}N$	164.1438	164.1428	−1.0	164.1440	0.2
	140	$C_9H_{18}N$	140.1438	140.1471	3.3	140.1425	−1.3
	138	$C_9H_{16}N$	138.1281	138.1265	−1.6	138.1302	2.1
	124	$C_8H_{14}N$	124.1124	124.1107	−1.7	124.1103	−2.1
	112	$C_7H_{14}N$	112.1125	112.1122	−0.3	112.1127	0.2
	111	$C_7H_{13}N$	111.1047	111.1036	−1.1	111.1080	3.3
	98	$C_6H_{12}N$	98.0969	98.0996	2.7	98.0985	1.6
	96	$C_6H_{10}N$	96.0812	96.0781	−3.1	96.0781	−3.1
	85	$C_5H_{11}N$	85.0890	85.0933	4.3	85.0927	3.7
	84	$C_5H_{10}N$	84.0812	84.0852	4.0	84.0811	0.0
5: R=*n*-C_5H_{11}	253	$C_{16}H_{31}NO$	253.2403	253.2435	3.2	253.2438	3.4
	210	$C_{13}H_{24}NO$	210.1857	210.1871	1.4	210.1874	1.7
	182	$C_{11}H_{20}NO$	182.1543	182.1498	−4.5	182.1545	0.2
	164	$C_{11}H_{18}N$	164.1438	164.1425	−1.3	164.1418	−2.0
	140	$C_9H_{18}N$	140.1438	140.1395	−4.3	140.1440	0.2
	138	$C_9H_{14}N$	138.1281	138.1234	−4.7	138.1278	−0.3
	124	$C_8H_{14}N$	124.1125	124.1106	−1.9	124.1130	0.5
	112	$C_7H_{14}N$	112.1125	112.1105	−2.0	112.1093	−3.2
	111	$C_7H_{13}N$	111.1048	111.1073	2.5	111.1041	−0.7
	98	$C_6H_{12}N$	98.0969	98.0978	0.8	98.0969	0.0
	96	$C_6H_{10}N$	96.0813	96.0846	3.3	96.0788	−2.4
	85	$C_5H_{11}N$	85.0891	85.0903	1.2	85.0893	0.2
	84	$C_5H_{10}N$	84.0813	84.0824	1.1	84.0830	1.7
6: R=C_6H_5	259	$C_{17}H_{25}NO$	259.1934	259.1958	2.4	259.1964	3.0
	242	$C_{17}H_{24}N$	242.1907	242.1885	−2.2	242.1940	3.2

TABLE II. (continued)

Compd.	Ion m/z	Elemental composition	Calculated	cis-Isomer		trans-Isomer	
				Observed	Error (mu)	Observed	Error (mu)
6: R=C_6H_5	216	$C_{14}H_{18}NO$	216.1387	216.1390	0.3	216.1419	3.2
	182	$C_{11}H_{20}NO$	182.1544	182.1512	−3.2	182.1499	−4.5
	140	$C_9H_{18}N$	140.1438	140.1444	0.6	140.1450	1.2
	138	$C_9H_{16}N$	138.1281	138.1279	−0.2	138.1325	4.4
	124	$C_8H_{14}N$	124.1124	124.1102	−2.2	124.1110	−1.4
	112	$C_7H_{14}N$	112.1125	112.1155	3.0	112.1092	−3.3
	111	$C_7H_{13}N$	111.1047	111.1081	3.4	111.1040	−0.7
	105	C_7H_5O	105.0340	105.0373	3.3	105.0351	1.1
	98	$C_6H_{12}N$	98.0968	98.0955	−1.3	98.0971	0.3
	96	$C_6H_{10}N$	96.0812	96.0797	−1.5	96.0822	1.0
	85	$C_5H_{11}N$	85.0891	85.0914	2.3	85.0898	0.7
	84	$C_5H_{10}N$	84.0813	84.0825	1.2	84.0825	1.2
	77	C_6H_5	77.0391	77.0403	1.2	77.0401	1.0

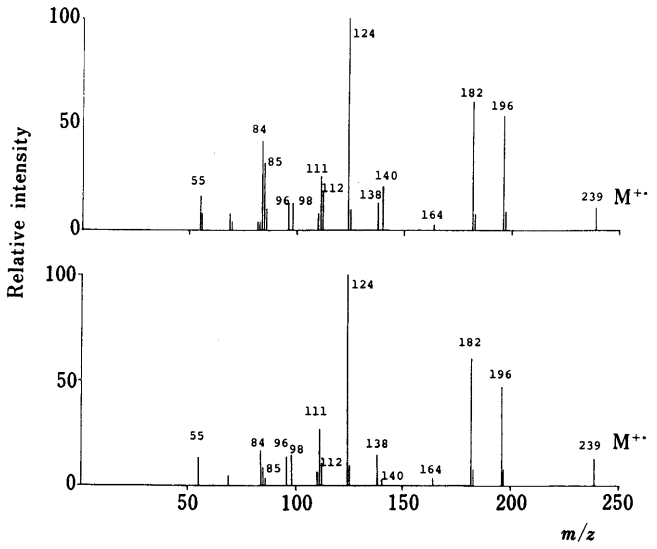


Fig. 2. MS of 1-Butyl-3-piperidinocyclohexanol (4)

the MS of the *cis*-isomers are stronger than those of the *trans*-counterparts. The elemental compositions were found to be $C_9H_{18}N$ and $C_5H_{11}N$ from the high-resolution observation.

It was clear from the infrared (IR) spectra that the *cis*-isomers form an intramolecular hydrogen bond between the hydroxyl group and the amino group.[5] It seems that the intramolecular hydrogen bond is involved in the formation of the ions at *m/z* 140 and *m/z* 85. In the analogue deuterated at the hydroxyl group the peak at *m/z* 140 of *cis*-isomers is shifted one mass unit higher. Therefore, this fragmentation which is accompanied with a hydrogen migration from the hydroxyl group to the amino group give arise to the ions at *m/z* 140 and *m/z* 85 through a six-membered ring transition state containing the intramolecular hydrogen bond (Chart 2). This fragmentation mechanism of *cis*-isomers is similar to the McLafferty rearrangement (Chart 3). This transition state can not be formed by *trans*-isomers. The metastable peaks for $M^{+\cdot} \rightarrow$ *m/z* 140 and $M^{+\cdot} \rightarrow$ *m/z* 85 were observed for all compounds (Table III).

From the results, the differences in peak intensities between *cis*- and *trans*-isomers may be applicable to distinguish the *cis*- from the *trans*-configuration.

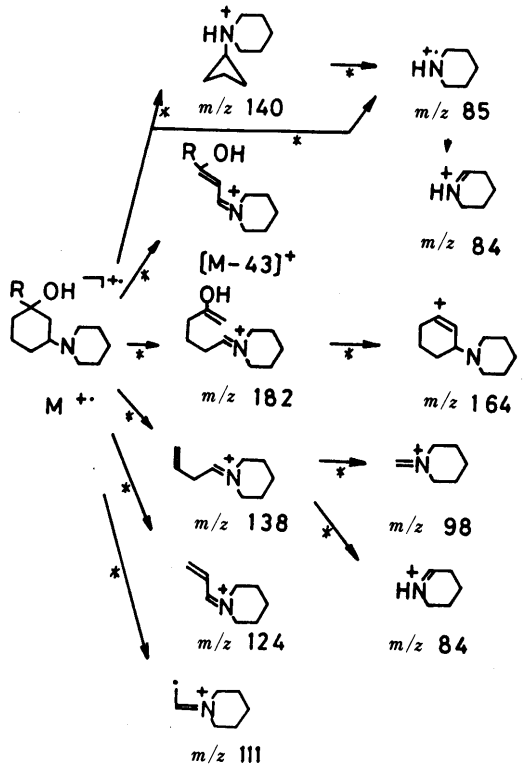


Chart 1. Fragmentation Pathways of 3-Piperidinocyclohexanol Derivatives **1**—**6**

Mandelbaum[1] found that the accessibility of cyclic transition states based on the configuration of the stereoisomers in the ground state is of great value in predicting the stereospecificity of fragmentation processes involving a transfer of specific atoms or groups.

Moreover, the ion at *m/z* 140 loses a cyclobutane radical to give the ion at *m/z* 85. This fragmentation is shown in Chart 1 and is supported by the observation of a metastable peak for *m/z* 140→*m/z* 85.

***m/z* 182 and *m/z* 164 Ions** As seen in Table I, the ion at *m/z* 182 was observed in all compounds. The elemental composition of this ion was estimated as $C_{11}H_{20}NO$ from the high resolution MS. The ions are formed from the molecular ions by loss of an alkyl radical.

Although in the alkyl derivatives **1**—**5** the relative inten-

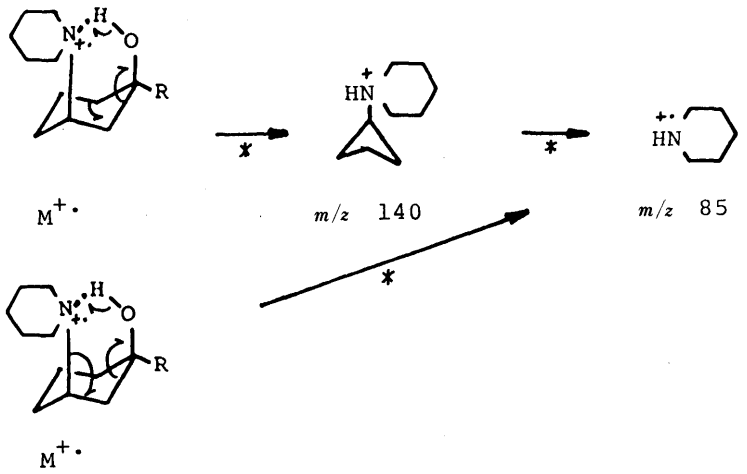


Chart 2. Formation Mechanisms of the Ions at m/z 140 and m/z 85

TABLE III. Metastable Peaks (m^*) and Associated Transitions ($m_1 - m_2$)

	Calcd	cis Found	trans Found		Calcd	cis Found	trans Found
$m_1 - m_2$	m^*	m^*	m^*	$m_1 - m_2$	m^*	m^*	m^*
Compd. **3**							
225 – 182	147.2	147.2	147.2	225 – 140	87.1	87.1	—
225 – 138	84.6	84.4	84.6	225 – 124	68.3	68.3	68.3
225 – 85	32.1	32.0	—	182 – 164	147.8	147.8	147.7
182 – 112	68.9	68.8	68.8	182 – 111	67.7	67.6	67.7
140 – 85	51.6	51.5	—	138 – 98	69.6	69.6	69.6
138 – 84	51.1	51.0	51.2	98 – 96	94.0	93.8	94.0
Compd. **4**							
239 – 196	160.7	160.7	160.6	239 – 182	138.6	138.5	138.6
239 – 140	82.0	81.8	—	239 – 138	79.7	79.7	79.6
239 – 124	64.3	64.2	64.2	239 – 85	30.2	30.2	—
196 – 112	64.0	64.1	64.2	196 – 111	62.9	62.9	63.0
182 – 164	147.8	147.7	147.7	140 – 85	51.6	51.6	—
138 – 98	69.6	69.6	69.6	138 – 84	51.1	51.1	51.1
98 – 96	94.0	93.9	93.8				
Compd. **5**							
253 – 210	174.3	174.2	174.3	253 – 182	130.9	130.8	130.9
253 – 140	77.5	77.5	—	253 – 138	75.3	75.1	75.1
253 – 124	60.8	60.7	60.7	253 – 85	28.6	28.6	—
210 – 112	59.7	59.7	59.7	210 – 111	58.7	58.8	58.7
182 – 164	147.8	147.8	147.8	140 – 85	51.6	51.6	—
138 – 98	69.6	69.6	69.7	138 – 84	51.1	51.1	51.1
98 – 96	94.0	93.9	93.8				
Compd. **6**							
259 – 216	180.1	180.1	180.1	259 – 182	127.9	127.6	127.8
259 – 140	75.7	75.7	—	259 – 138	73.5	73.4	73.5
259 – 124	59.4	59.4	59.4	259 – 85	27.9	27.9	—
216 – 112	58.1	57.9	57.9	216 – 111	57.0	57.1	57.1
216 – 105	42.6	42.4	42.5	182 – 164	147.8	147.7	147.6
140 – 85	51.6	51.4	—	138 – 98	69.6	69.6	69.4
138 – 84	51.1	51.0	51.0	105 – 77	56.5	56.4	56.5
98 – 96	94.0	93.8	93.8				

sities of these ions were very strong, in the phenyl derivative **6** the intensity was remarkably weak. The common abundant ion at m/z 182 in the alkyl derivatives **1**—**5** clearly indicates an easy loss of the alkyl radical from the molecular ion. However, the low intensity of the ion at m/z 182 of the phenyl compound **6** is presumably due to the difficulty of loss of the phenyl radical.

It is considered that the ion at m/z 164 is connected with the ion at m/z 182 from the elemental composition

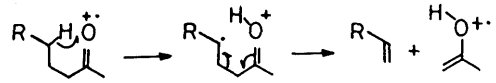


Chart 3. General McLafferty Rearrangement

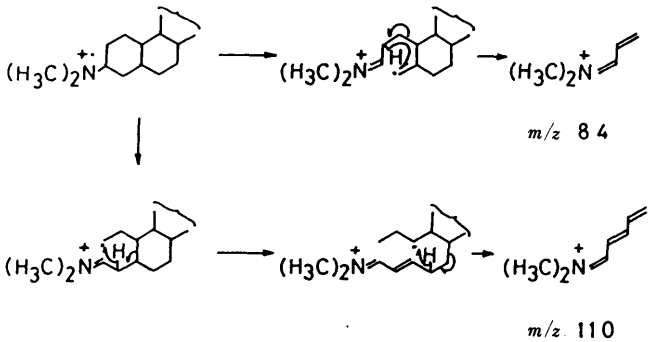


Chart 4. Formation Mechanism of the Ion at m/z 84 in Steroidal Dimethylamine

($C_{11}H_{18}N$), corresponding to loss of H_2O. Although the peak at m/z 182 is shifted one mass unit higher by the deuteration of the hydroxyl group, the peak at m/z 164 remained unshifted. The metastable peaks for the processes, $M^{+\cdot} \rightarrow m/z\ 182 \rightarrow m/z\ 164$, were observed for all alkyl derivatives **1**—**5**. From these facts, the ion at m/z 164 is concluded to be formed from the ion at m/z 182 by loss of H_2O.

$[M-43]^+$ Ion The ions at $[M-43]^+$ in all compounds are observed with very strong intensities in the range of about 47.3 to 100% and are formed from the molecular ions by loss of a propyl radical judging from their high resolution MS.

The ion at $[M-43]^+$ is considered to form a stable conjugated immonium structure. The formation of the ion at $[M-43]^+$ is similar to the formation of the ion at m/z 84 in steroidal dimethylamines[6] (Chart 4). In particular, the ion at $[M-43]^+$ of the phenyl derivative **6** is the base peak. This is presumably because of the stabilization by conjugation between the conjugated immonium ion formed and the phenyl group.

In the phenyl derivative **6**, the $[M-43]^+$ ion gives the ion at m/z 105 followed by loss of CO to yield the ion at m/z 77. Those pathways are supported by the observed metastable peaks.

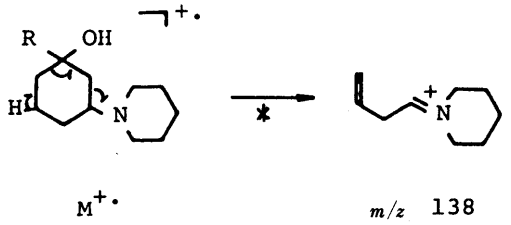


Chart 5. Formation Mechanism of the Ion at *m/z* 138

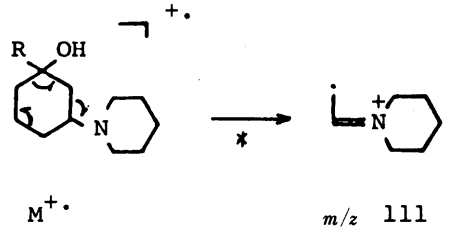


Chart 6. Formation Mechanism of the Ion at *m/z* 111

***m/z* 138, *m/z* 124 and *m/z* 111 Ions** The elemental compositions of the ions at *m/z* 138 and *m/z* 124 were proved to be $C_9H_{16}N$ and $C_8H_{14}N$, respectively, by the high resolution analysis. The abundant ions at *m/z* 138 and *m/z* 124 correspond to the ions formed from the molecular ion by the elimination of $[R+C_2H_3+OH]^{\cdot}$ and $[R+C_3H_5+OH]^{\cdot}$, respectively.

The ion at *m/z* 124 in the alkyl derivatives **1**—**5** is the base peak or is similar in intensity to the base peak. This is a result of the stabilization of the conjugated immonium ion structure. The formation mechanism is similar to that of the ion at *m/z* 84 in steroidal dimethylamines.

The ion at *m/z* 138 is formed from the molecular ion by *β*-cleavage of the nitrogen atom and loss of a hydrogen radical (Chart 5). The further decomposition of the ion at *m/z* 138 yields the ions at *m/z* 98 and *m/z* 84.

The ion at *m/z* 111 is formed from the molecular ion by *β*-cleavage of the nitrogen atom (Chart 6).

These all processes are supported by observation of the corresponding metastable peaks.

Conclusion

Electron impact ionization MS of 1-substituted-3-piperidinocyclohexanols were determined.

The *cis*- and *trans*-configurations of 1-substituted-3-piperidinocyclohexanols are distinguishable by comparison of the peak intensities at *m/z* 140 and *m/z* 85. These compounds show the common ion at $[M-43]^+$, formed by the loss of a propyl radical. Finally, the distinction of alkyl derivatives from phenyl derivatives is possible by observing the peak intensities at *m/z* 182 and *m/z* 164.

Experimental

Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected.

MS were obtained at low and high resolutions by using a Hitachi RMU-7MG double-focusing mass spectrometer. All compounds were introduced *via* a direct inlet system at appropriate temperatures. The ion accelerating voltage was maintained at 3.2 kV, the ionizing voltage at 70 eV, the total ion current at 80 μA and the ion source temperature at 180 °C. Proton and carbon-13 nuclear magnetic resonance (^{1}H- and ^{13}C-NMR) spectra were recorded on JEOL FX-200 spectrometers, with tetramethylsilane as an internal standard.

All compounds used in this work were prepared according to the procedures described in the previous papers.[5,7] The purities of the compounds were checked by using a gas chromatograph-mass spectrometer.

General Procedure for the Synthesis of 1-Substituted-3-piperidinocyclohexanols (1—6) A solution of crude 3-piperidinocyclohexanone (0.05 mol) in 20 ml of dry ether was added dropwise with stirring to a solution of freshly prepared alkyllithium (0.10 mol) in ether in an ice bath. After the addition, the mixture was stirred overnight at 20 °C. The reaction mixture was poured into ice-water. The ethereal layer was separated from the aqueous layer. The aqueous layer was extracted with $CHCl_3$. The combined organic portions were washed with 5% HCl. The HCl layer was made alkaline with 10% NaOH and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with H_2O, dried over Na_2SO_4, and evaporated to afford the crude amino alcohol, which was purified by distillation. The *cis*- and *trans*-isomers were separated by thin-layer chromatography on alumina (Merck, Aluminiumoxid 60 PF_{254}) and column chromatography (Merck, Aluminiumoxid 90).

Compound 1 *cis*-Isomer: Colorless oil. Yield 7%. IR (CCl_4): 3200 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 1.16 (3H, s, CH_3), 1.20—2.20 (18H, m), 2.44 (1H, t, *J*=4 Hz, C_3-H), 2.54 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) *δ*: 70.0 (C_1). *trans*-Isomer: Colorless oil. Yield 11%. IR (CCl_4): 3600 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 1.24 (3H, s, CH_3), 1.30—2.60 (18H, m), 2.72 (1H, t, *J*=12 Hz, C_3-H), 2.90 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) *δ*: 71.0 (C_1).

Compound 2 *cis*-Isomer: Colorless oil. Yield 28%. IR (CCl_4): 3200 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 0.88 (3H, t, *J*=8 Hz, CH_3), 1.20—2.20 (20H, m), 2.44 (1H, t, *J*=4 Hz, C_3-H), 2.54 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) *δ*: 71.7 (C_1). *trans*-Isomer: Colorless oil. Yield 35%. IR (CCl_4): 3600 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 0.90 (3H, t, *J*=8 Hz, CH_3), 1.00—2.60 (20H, m), 2.72 (1H, t, *J*=12 Hz, C_3-H), 3.00 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) *δ*: 72.9 (C_1).

Compound 3 *cis*-Isomer: Colorless oil. Yield 7%. IR (CCl_4): 3200 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 0.90 (3H, t, *J*=8 Hz, CH_3), 1.10—2.20 (22H, m), 2.44 (1H, t, *J*=4 Hz, C_3-H), 2.60 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) *δ*: 71.7 (C_1). *trans*-Isomer: Colorless oil. Yield 10%. IR (CCl_4): 3600 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 0.90 (3H, t, *J*=8 Hz, CH_3), 1.00—2.60 (22H, m), 2.72 (1H, t, *J*=12 Hz, C_3-H), 3.68 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) *δ*: 72.8 (C_1).

Compound 4 *cis*-Isomer: Colorless oil. Yield 14%. IR (CCl_4): 3200 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 0.90 (3H, t, *J*=8 Hz, CH_3), 1.10—2.10 (24H, m), 2.42 (1H, t, *J*=4 Hz, C_3-H), 2.54 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) *δ*: 71.7 (C_1). *trans*-Isomer: Colorless oil. Yield 25%. IR (CCl_4): 3600 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 0.90 (3H, t, *J*=8 Hz, CH_3), 1.00—2.60 (24H, m), 2.72 (1H, t, *J*=4 Hz, C_3-H), 3.30 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) *δ*: 72.8 (C_1).

Compound 5 *cis*-Isomer: Colorless oil. Yield 16%. IR (CCl_4): 3200 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 0.90 (3H, t, *J*=8 Hz, CH_3), 1.10—2.10 (26H, m), 2.42 (1H, t, *J*=4 Hz, C_3-H), 2.50 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) *δ*: 71.7 (C_1). *trans*-Isomer: Colorless oil. Yield 24%. IR (CCl_4): 3600 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 0.90 (3H, t, *J*=8 Hz, CH_3), 1.00—2.60 (26H, m), 2.70 (1H, t, *J*=12 Hz, C_3-H), 3.90 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) *δ*: 72.7 (C_1).

Compound 6 *cis*-Isomer: Colorless needles, mp 81—82 °C. Yield 10%. IR (CCl_4): 3150 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 1.20—2.40 (18H, m), 2.36 (1H, t, *J*=4 Hz, C_3-H), 7.10—7.60 (5H, m, aromatic H), 7.92 (1H, br s, OH). ^{13}C-NMR ($CDCl_3$) *δ*: 73.5 (C_1). *trans*-Isomer: Colorless prisms, mp 112—113 °C. Yield 25%. IR (CCl_4): 3600 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) *δ*: 1.20—2.60 (18H, m), 2.72 (1H, t, *J*=12 Hz, C_3-H), 2.80 (1H, br s, OH), 7.10—7.60 (5H, m, aromatic H). ^{13}C-NMR ($CDCl_3$) *δ*: 74.6 (C_1)

References

1) A. Mandelbaum, *Mass Spectrometry Review*, **2**, 223 (1983).
2) *a*) M. M. Green, R. J. Cook, J. M. Schwab and R. B. Roy, *J. Am. Chem. Soc.*, **92**, 3076 (1970); *b*) F. J. Winkler and F. W. McLafferty, *Tetrahedron*, **30**, 2971 (1974).
3) *a*) L. Dhaenens, C. C. Van de Sande and F. Vangaever, *Org. Mass Spectrom.*, **14**, 145 (1979); *b*) R. Bar-Shai, A. Bortinger, J. Sharvit and A. Mandelbaum, *Israel J. Chem.*, **20**, 137 (1980).
4) J. Respondek, C. C. Van de Sande and F. Vangaever, *Org. Mass Spectrom.*, **13**, 618 (1978).
5) J. V. Greenhill, *J. Med. Chem.*, **14**, 971 (1971).
6) Z. Pelah, D. H. Williams, H. Budzikiewicz and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 574 (1965).
7) G. Stork and W. N. White, *J. Am. Chem. Soc.*, **78**, 4604 (1956).