MASS SPECTRA OF 4-SUBSTITUTED QUINUCLIDINES * **

J. PALEČEK and J. MITERA

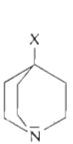
Department of Organic Chemistry and Department of Mass Spectrometry, Institute of Chemical Technology, 166 28 Prague 6

Received July 13th, 1973

Mass spectra of quinuclidines *I* substituted in position 4 are discussed. Characteristic ion species originate both in synchronous homolytic fragmentation and from an open form of the molecular ion (α-splitting). When electronegative substituents are present, the synchronous homolytic mechanism takes place exclusively. Suggested fragmentation mechanisms were verified in some cases with the use of deuterated compounds.

In our previous communication[1] we described mass spectra of quinuclidine, its analogues deuterated in all positions, as well as mass spectra of some methyl and dimethyl homologues. So far there has been no systematic study[1-5] of mass spectra of this series of compounds. The aim of this communication is to elucidate the influence of a substituent on the quinuclidine ring fragmentation in derivatives *I* substituted in the position 4.

Mass spectra of these compounds are summarized in Table I (ionic species of a lower abundance than 5% of relative intensity are reported only if they are of diagnostic

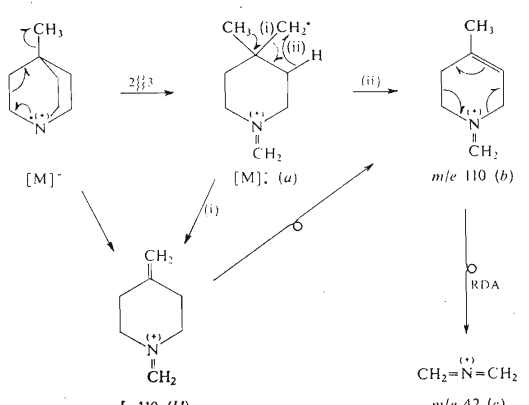


Ia, X = CH_3
Ib, X = CD_3
Ic, X = Br
Id, X = Cl
Ie, X = $COOC_2H_5$
If, X = $CONH_2$
Ig, X = $CON(CH_3)_2$
Ih, X = OH
Ii, X = $OOCCH_3$
Ik, X = CH_2F
Il, X = CH_2Cl
Im, X = CH_2Br
In, X = CD_2Br
Io, X = CH_2I
Ip, X = CH_2OH
Iq, X = CD_2OH
Ir X = CH_2OOCCH_3

* Part XIII in the series Azabicyclo Compounds; Part XII: This Journal *38*, 1985 (1973).

** Contribution at the Fourth Symposium on Chemistry of Heterocyclic Compounds, Ústí nad Labem, Czechoslovakia, 15th–18th May, 1973.

importance). The formation of most ionic species of higher intensity in the mass spectrum of 4-methylquinuclidine (*Ia*) can be explained in a similar way as in the case of the fundamental compound of this series, quinuclidine[1]. A striking feature, however, is an increase of the relative intensity of the ion *m/e* 110 (from 18·9% rel. int. in quinuclidine[1] to 42·3% rel. int. in the 4-methyl-derivative (*Ia*)) formed by the loss of a methyl radical from the molecular ion. Two paths may be considered to explain the formation of this ion: first, breaking of the $C_{(2)}-C_{(3)}$ bond (α-splitting) leading to the formation of an open structure of the molecular ion *a*, followed by a transfer of the α- or β-hydrogen, and a simultaneous loss of a methyl radical gives rise to the ion *b*. The occurrence of this fragmentation path is supported further by the presence of $[M—CH_3]^+$ ion in the spectrum of the 4-trideuteriomethyl derivative *Ib*. This fragmentation process was proved to occur in quinuclidine, too[1]. The ionic species *b* transforms by the Retro-Diels–Alder fragmentation into the most abundant ion *c* of mass 42. The second possibility of a methyl group elimination assumes a homolytic synchronous fragmentation of the molecular ion leading to the 1,4-bismethylenepiperidine cation *b'* of the same mass which can then isomerize to *b*. The mass spectrum of *Ib* contains ionic species $[M—CD_3]^+$ and $[M—CH_3]^+$ in the relative abundance ratio 4 : 1; this indicates that at least 1/5 of methyl radicals is eliminated *via* $[M]^{+\cdot} \rightarrow a \rightarrow b$. However, we suppose that it cannot be unambiguously excluded that the ionic species *b* originates from *a* through mechanism (*i*) as described in Scheme 1. Recently, Grob and coworkers[5] have demonstrated that the dominant species in the mass spectrum of 4-tert.butylquinucli-



SCHEME 1

TABLE I

Mass Spectra of 4-Substituted Quinuclidines I

Ia	*m/e*	125	124	110	97	96	82	70	69	o8	67	57
CH_3	% rel. int.	36·6	7·0	42·3	21·1	43·7	18·3	6·0	19·7	10·7	6·0	11·5
	m/e	56	55	53	42	41	39	29	28	27		
	% rel. int.	6·3	15·5	6·5	100	32·4	13·0	6·6	13·0	14·5		
Ib	*m/e*	128	127	113	110	100	99	98	71	70	68	57
CD_3	% rel. int.	36·0	15·8	6·0	25·3	14·6	32·3	10·8	6·1	7·5	7·7	16·5
	m/e	56	55	54	53	44	42	41	40	39	29	28
	% rel. int.	8·9	15·8	6·8	5·3	7·6	100	28·5	8·9	8·9	9·5	25·3
Ic	*m/e*	181	179	111	110	81	55	53	42	41	39	28
Br	% rel. int.	3·7	3·7	7·7	100	5·8	5·9	8·6	50·5	11·3	8·2	6·8
Id	*m/e*	145	111	110	81	53	42	41	39	28	27	
Cl	% rel. int.	0·8	9·8	100	5·2	8·1	72·2	16·7	11·1	13·3	20·0	
Ie	*m/e*	183	111	110	82	55	53	42	41	29	28	27
$COOC_2H_5$	% rel. int.	16·1	12·9	100	9·7	6·4	6·4	44·4	9·7	9·7	8·9	9·7
If	*m/e*	154	111	110	53	44	42	41	28	27		
$CONH_2$	% rel. int.	13·9	7·9	100	5·3	6·0	31·6	7·7	6·8	6·1		
Ig	*m/e*	182	111	110	96	55	53	42	41			
$CON(CH_3)_2$	% rel. int.	14·7	20·5	100	6·7	6·1	5·4	33·0	7·3			

TABLE I
(*Continued*)

Ih	*m/e*	127	126	112	111	110	99	98	84	70	69	58
OH	% rel. int.	45·6	6·4	6·6	7·6	99·2	9·6	16·0	6·5	16·0	9·9	24·0
	m/e	57	56	55	53	43	42	41	39	29	28	27
	% rel. int.	52·0	30·4	9·0	5·8	19·3	100	20·0	5·7	9·6	20·0	16·8
Ii	*m/e*	169	111	110	56	55	43	42	41	28	27	
$OOCCH_3$	% rel. int.	9·5	7·6	100	7·9	5·0	22·1	37·2	7·4	11·6	5·6	
Ik	*m/e*	143	128	114	110	69	57	55	53	43	42	41
CH_2F	% rel. int.	17·5	5·0	11·0	40·0	14·0	10·0	8·5	5·5	6·0	100	18·5
Il	*m/e*	161	159	125	124	110	96	81	69	67	56	55
CH_2Cl	% rel. int.	4·5	15·6	9·1	92·1	57·1	32·5	5·6	9·1	10·4	14·3	10·4
	m/e	54	53	44	42	41	39	30	29	28	27	
	% rel. int.	6·5	11·7	6·5	100	32·5	18·2	9·1	6·5	19·5	22·1	
Im	*m/e*	205	203	125	124	110	96	81	70	67	56	55
CH_2Br	% rel. int.	8·0	8·0	8·5	100	12·5	10·5	7·6	7·6	8·8	6·6	6·2
	m/e	53	44	42	41	39	28	27				
	% rel. int	6·9	11·5	55·9	23·7	13·6	10·5	13·1				
In	*m/e*	207	205	127	126	125	110	98	88	82	71	70
CD_2Br	% rel. int.	8·0	8·0	9·6	100	6·0	13·8	10·5	5·0	5·1	5·9	5·3
	m/e	69	56	55	45	44	43	42	41	40	28	27
	% rel. int.	6·4	7·8	5·6	6·2	8·2	7·7	55·1	13·0	5·4	26·1	7·4

Io	*m/e*	251	127	125	124	96	81	70	67	56	55	54
CH_2I	% rel. int.	7·9	5·0	9·1	100	5·0	12·5	11·5	15·0	5·7	11·6	6·6
	m/e	53	44	43	42	41	40	39	29	28	27	
	% rel. int.	10·8	21·2	5·5	65·0	32·0	5·7	20·4	10·0	15·0	20·8	
Ip	*m/e*	141	124	113	112	111	110	96	82	70	69	57
CH_2OH	% rel. int.	31·4	10·8	5·4	10·8	10·1	100	16·2	5·3	7·4	14·5	12·2
	m/e	56	55	53	44	43	42	41	39	29	28	27
	% rel. int.	8·8	14·2	8·1	11·5	13·5	72·6	20·9	8·8	9·5	11·8	12·2
Iq	*m/e*	143	142	126	114	111	110	98	69	57	56	55
CD_2OH	% rel. int.	34·2	5·0	8·6	5·7	11·1	100	13·9	14·4	8·1	6·6	8·9
	m/e	53	43	42	41	28	27					
	% rel. int.	5·3	9·7	64·3	12·7	10·6	7·1					
Ir	*m/e*	183	140	124	111	110	108	96	81	69	67	56
CH_2OOCCH_3	% rel. int.	25·3	7·7	74·6	9·3	100	5·8	34·6	6·3	12·8	7·3	8·9
	m/e	55	53	44	43	42	41	39	29	28	27	
	% rel. int.	12·8	9·7	6·2	57·3	94·6	26·6	9·8	7·3	13·3	12·0	

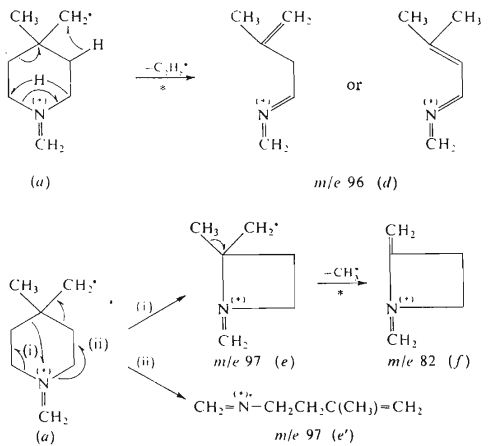
TABLE II
Ionization Potentials of Some 4-Substituted Quinuclidines I

Compound (subst.)	IP, eV[a]	Compound (subst.)	IP, eV[a]
Ic (Br)	8·70 ± 0·05	*Ih* (OH)	8·88 ± 0·03
Ie ($COOC_2H_5$)	8·85 ± 0·03	*Im* (CH_2Br)	8·62 ± 0·10

[a] For quinuclidine the value found was 8·80.

dine was the ion of *m/e* 110 which originated through the loss of the tert-butyl radical; structure *b'* was ascribed to this ion.

The formation of the other ionic species *d*, *e*, *e'* of *m/e* 96 and 97 is quite analogous to the formation of ions $[M—C_2H_5]^+$ or $[M—C_2H_4]^{+\cdot}$ in quinuclidine[1]. The deuterated compound *Ib* shows a shift of mass to *m/e* 99 and *m/e* 100, respectively. The ionic species *e* at *m/e* 97 eliminates a methyl radical and forms *f* (*m/e* 82). In the spectrum of the deuterated analogue *Ib* a metastable ion *m/e* 67·2 (100 → 82 + 18, calculated 67·24) corresponds to the elimination of a CD_3 radical from the ion



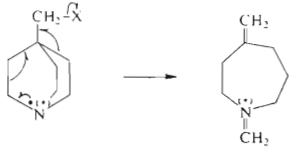
SCHEME 2

species m/e 100. We assume that the cyclic structure *e* of $[M—C_2H_4]^{+\cdot}$ rather than the acyclic one (*e'*) fits better this fragmentation process. Ionic species m/e 70, 69, 57, 56, 55, and 28 are formed from the open structure of the molecular ion *a* by the fragmentation mechanisms described by us earlier[1].

Grob and coworkers[6–8] have shown that with some 4-substituted quinuclidines the action of nucleophilic reagents causes a heterolytic synchronous fragmentation of the quinuclidine core which leads to the formation of 1,4-bismethylenepiperidine salts. The authors' prognosis is that an analogous reaction may be expected with these compounds occurring through the homolytic mechanism

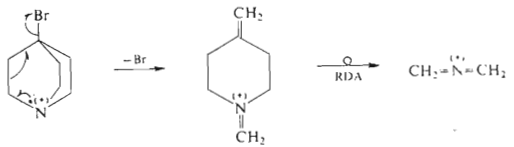
$$\overset{\frown}{a} - b - \overset{\frown}{c} - d - \overset{\frown}{x} \rightarrow a{=}b + c{=}d + x\cdot$$

A suitable method of obtaining the nitrogen-atom radical needed in fragmentation turned out to be electron impact ionization. However, in the case of the studied compounds *I* there are two ionization centers which contain n-electrons, namely the nitrogen atom and the substituent X. We assumed the preferential ionization of the nitrogen atom, having in mind the low ionization potential of the nitrogen atom in amines, with respect to the other atoms containing n-electrons[9]. The plausibility of this assumption follows from the measured ionization potentials of several selected compounds (Table II), and from the fragmentation of the derivative *Ic* and *Id*.



[M]⁺· *m/e* 124 (*g*)

SCHEME 3



[M]⁺· *m/e* 110 (*b'*) *m/e* 42 (*c*)

SCHEME 4

Mass spectra of 4-bromo- (*Ic*) and 4-chloroquinuclidine (*Id*) show, in comparison with the other derivatives studied, a very low relative intensity (3·7% and 0·8%, respectively) of the molecular ion. The main ion species *m/e* 110 of the structure *b'* (carries 40·6% and 36·5% of the total ion current, respectively) is formed from the molecular ion in the synchronous homolytic fragmentation corresponding to $[M]^{+\cdot} \rightarrow$ $\rightarrow b'$. Also, the absence of halogen-containing ionic species is remarkable. An analogous elimination of the position 4 substituent leading to *b'* (*m/e* 110) prevails with 4-ethoxycarbonyl (*Ie*), 4-carbamoyl- (*If*), 4-N,N-dimethylcarbamoyl- (*Ig*), and 4-acetoxyquinuclidine (*Ii*). A very low intensity of ions $[M—CH_3]^+$ in the mass spectra of the compounds (*Ic–Ig*, *Ii*) confirms a practically exclusive occurrence of the synchronous fragmentation mechanism. Other ionic species of low and medium intensity originate in processes described earlier.

As can be seen from Table I, in the case of the 4-hydroxy derivative *Ih*, the synchronous mechanism leading to the ion of *m/e* 110 (*b'*) occurs to about the same extent as the splitting of the $C_{(2)}—C_{(3)}$ bond. The formation of an open form of the molecular ion (*a*) explains the origin of the ion species $[M—CH_3]^+$, $[M—C_2H_4]^{+\cdot}$, $[M—C_2H_5]^+$, *m/e* 70, 69, 58, 57, 56, 42, and 28.

Mass spectra of 4-halogeno derivatives (*Ik–Io*) show a pronounced influence of the halogen atoms. Table III summarizes the influence of the halogen on the breaking of the C—Hlg and C—CH_2Hlg bonds. It is evident that the tendency of increasing resp. decreasing relative intensities of ionic species of this class of compounds is in agreement with the corresponding values reported for alkylhalides[10]. While in the fluoro derivative *Ik* practically no splitting of the C—F bond occurs, with the bromo- (*Im*) and iodo derivative (*Io*) this process is dominant. Even in this case (see an analogous heterolytic fragmentation of 4(*p*-toluenesulphonyloxymethyl)-quinuclidine[11]) 1,4-bismethylene-1-azacycloheptane ion (*g*) of *m/e* 124 is formed in the homolytic synchronous fragmentation process. Contrarily, splitting of the C—CH_2Hlg bond and formation of the ion *b'*(*m/e* = 110) prevails with the fluoro- (*Ik*) and the chloro derivative (*Il*). These ionic species originate through the fragmentation process $[M]^{+\cdot} \rightarrow b'$. A certain support for this conclusion provides the fact that ionic species $[M—CH_3]^+$ are practically absent in the spectra (with the fluoroderivative *Ik* the intensity of this ion species is 5% rel. int., with 4-chloromethyl- (*Il*) it is 1·6%, with bromomethyl- (*Im*) and iodomethyl- (*Io*) it is totally absent). In 4-bromodideuteromethylquinuclidine (*In*) an almost quantitative shift of the mass of the ion species g was observed from *m/e* 124 to *m/e* 126, while *b'* (*m/e* 110) did not contain any deuterium. These results are in agreement with the suggested fragmentation mechanisms. The same mechanism gives rise to the ionic species of *m/e* 110 and 124 in 4-acetoxymethylquinuclidine (*Ir*). The origin of the abundant ion species $[CH_3CO]^+$ of mass 43 (57·3% rel. int.) is explained by a partial ionization and subsequent fragmentation of the acetoxyl group. The presence of the other ionic species can be explained by mechanisms analogous to those described above.

TABLE III

Effect of Halogen on the Cleavage of C—Hlg and C—CH_2Hlg Bond in 4-Halogenmethylquinuclidines I

Compound	Cleavage of the bond C—Hlg		Cleavage of the bond C—CH_2Hlg	
(Hlg)	% rel. int.	% Σ_{33}	% rel. int.	% Σ_{33}
Ik (F)	0·8	—	40·0	13·4
Il (Cl)	92·2	17·8	57·1	11·0
Im (Br)	100	28·4	12·5	3·6
Io (I)	100	24·3	4·0	1·0

In the mass spectra of 4-hydroxymethylquinuclidine (*Ip*) and its deuterio-derivative (*Iq*) (Table I) the mechanisms in which the ion species *b'* is formed plays a significant role. A rather low intensity of g (10·8% and 8·6% rel. int., respectively) at masses 124 and 126 shows clearly a suppression of the fragmentation mehanism $[M]^{+\cdot} \rightarrow g$, *i.e.* breaking of the C—O bond. A relative increase of intensities of the other ion species in comparison with the halogeno derivatives corresponds to an enhanced splitting of the $C_{(2)}-C_{(3)}$ bond and formation of the open from of the molecular ion.

EXPERIMENTAL

The mass spectra were recorded using a LKB 9000 mass spectrometer (a Gas Chromatograph — Mass Spectrometer unit) at the energy of ionizing electrons 70 eV. Samples were introduced either through the gas chromatograph inlet or directly. Ionization potentials were determined with the use of an AEI MS 902 apparatus.

Quinuclidines substituted in the position 4 (*I*) were prepared by the well-known procedures[11–14] and their physicochemical constants and infra-red- spectra agreed with the structure reported here.

4-Fluoromethylquinuclidine (*Ik*)

1.32 mg of 1,1,2-trifluoro-2-chloroethyldiethylamine[15] was added to 493 mg hydroxymethylquinuclidine (*Ir*). The mixture was heated for 6 hours at 95—100°C in nitrogen atmosphere, cooled down, decomposed by 6 ml of diluted hydrochloric acid (1 : 2), extracted by ether (30 ml), alkalized by solid potash, and extracted again by 100 ml of ether. After the etheric layer was dried out by potash, the solvents were distilled off, and by the distillation of the residuum (Hickmann flask, bath temperature 110—115°3/12 Torr) about 200 mg of the product was obtained; a gas chromatograph-mass spectrometer analysis of this products showed that it contained small amounts of the original substance *Ir* and small amounts of the chloroderivative *Il*.

We are indebted to Dr M. Ryska, Institute of Macromolecular Chemistry, Czechoslovak Academy of Sciences, for carrying out the ionization potential measurements. Technical help of Mrs I. Faloutová, Department of Mass Spectrometry, Institute of Chemical Technology, is gratefully acknowledged.

REFERENCES

1. Paleček J., Mitera J.: Org. Mass Spectrom. *6*, 1353 (1972).
2. Kostjanovski R. G., Michlina E. E., Levkojeva E. I., Jachontov L. N.: Org. Mass Spectrom. *3*, 1023 (1970).
3. Michlina E. E., Turčin K. F., Vorobjeva V. J.., Jermakov A. I., Kostjanovski R. G., Jachontov L. N.: Dokl. Akad. Nauk SSSR *195*, 1347 (1970).
4. Jermakov A. I., Šeinker J.. N., Michlina E. E., Mastafanova L. I., Vorobjeva V. J.., Janina A. D., Jachontov L. N., Kostjanovski R. G.: Org. Mass Spectrom. *5*, 1029 (1971).
5. Grob C. A., Simon W., Treffert W. D.: Helv. Chim. Acta *55*, 2439 (1972).
6. Grob C. A., Ostermayer F.: Helv. Chim. Acta *45*, 1119 (1962).
7. Brenneisen P., Grob C. A., Jackson R. A., Ohta M.: Helv. Chim. Acta *48*, 146 (1965).
8. Grob C. A., Kostka K., Kuhnen F.: Helv. Chim. Acta *53*, 608 (1970).
9. Budzikiewicz H., Djerassi C., Williams D. H.: in the book: "*Interpretation of Mass Spectra of Organic Compounds*, p. 63. Holden-Day, San Francisco, 1964.
10. Budzikiewicz H., Djerassi C., Williams D. H. in the book: *Mass Spectrometry of Organic Compounds*, p. 437. Holden-Day, San Francisco, 1967.
11. Grob C. A., Hoegerle R. M., Ohta M.: Helv. Chim. Acta *45*, 1823 (1962).
12. Grob C. A., Renk E.: Helv. Chim. Acta *37*, 1681 (1954).
13. Grob C. A., Kostka K.: Helv. Chim. Acta *53*, 613 (1970).
14. Paleček J., Hlavatý J.: This Journal *38*, 1985 (1973).
15. Jarovenko N. N., Rakša M. A.: Ž. Obšč. Chim. *29*, 2159 (1957).

Translated by Z. Herman.