Behaviour of 1,4,5-Substituted Tetrazolines under Electron Impact: Unambiguous Identification of Tetrazolium Ions by CAD/MIKE Spectrometry

Bertrand Carboni and Robert Carrié *
Groupe de Physicochimie Structurale, E.R.A. no. 389 Université de Rennes I, 35042 Rennes Cedex, France
Pierre Hervé Lambert and Pierre Guenot
Centre Régional de Mesures Physiques, Université de Rennes I, 35042 Rennes Cedex, France

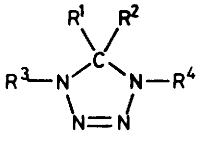
The mass spectra of some 1,4,5-substituted tetrazolines were studied in order to establish the structure of the compounds. An unusual cleavage of the molecular ion of the 5-phenyl-substituted tetrazolines was observed, *i.e.* the loss of a phenyl radical leading to a tetrazolium ion. The tetrazolium ions undergo one or two cycloreversions, depending on whether the tetrazoline bears two similar or two different substituents on the cyclic nitrogen atoms, thus leading to the formation of one or two nitrilium ions.

The behaviour of 1,4,5-tetrazolines (**1**) under electron impact has not previously been reported. Some investigations of methylenetetrazolines,[1] tetrazolinones,[2,3] and tetrazolium salts[4] have been performed.

Under electron impact, the main observed fragmentations may be classifed into three classes (Scheme 1). (1) The first is the cleavage of the C(5)–R^1 or C(5)–R^2 bond leading to the formation of tetrazolium ions (**3**) and (**3′**) when $R^1 \neq R^2$. (2) The molecular ions (**2**) resulting from the tetrazolines give the two possible cycloreversions *a* and *b* when the substituents R^3 and R^4 are different leading to the imine molecular ions (**4**) and (**4′**). The same phenomenon occurs with tetrazolium ion (**3**) and (**3′**) leading in this case to nitrilium ions (**6**), (**6′**), (**7**), and (**7′**). (3) The tetrazoline molecular ion may lose nitrogen; this was observed only in a few cases (mainly when R^1 = H, R^2 = Me).

The fragmentation paths that take place are clearly established by analysis of the MIKE spectra of the various ions.[5] The exact masses of these ions have been measured using the peak-matching technique and correspond to the proposed structures.

The tetrazolines we have studied are obtained by reduction or alkylation of tetrazolium salts resulting from the cycloaddition of azides to nitrilium salts.[6] The formation, under electron impact, of the nitrilium ions (**6**), (**6′**), (**7**), and (**7′**) clearly shows that the tetrazolines are 1,4,5- and not 1,2,5-substituted. This establishes unambigously the orientation of the cycloaddition.



(**1**)

In order to facilitate our understanding of the competition during the fragmentation process, we have brought together in Tables 1 and 2 the relative intensities of the various ions appearing in the conventional mass spectrum.

Formation of the Tetrazolium Ions.—The loss of the radical R^1 = Ph, an unusual fragmentation, can be seen for all the molecular ions (**2**). It competes with the loss of a methyl radical (an expected preferential fragmentation) when R^1 = Ph and R^2 = Me. When $R^1 = R^2$ = Me or Ph, we observe the formation of only one tetrazolium ion, which makes the study of their fragmentations much easier. The loss of hydrogen from (**2**) is hardly observed [the resulting $(M - H)^+$ ion shows a relative intensity of < 1%], except for (**2a**) [(**3a**) 12%].

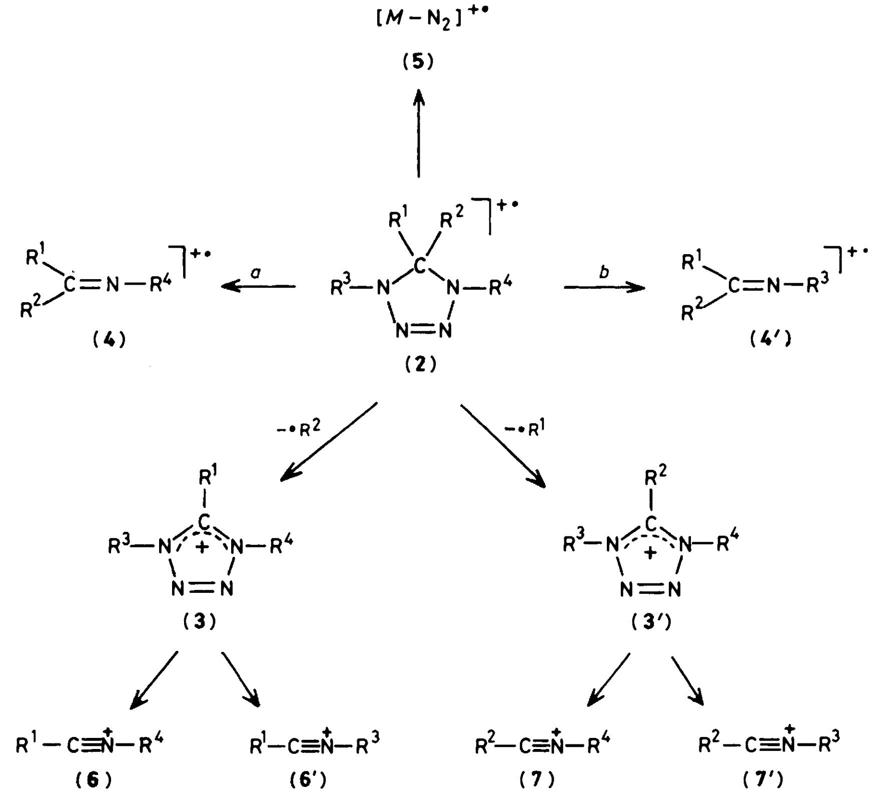
The loss of a phenyl radical occurs whenever R^1 = Ph (whatever R^2—R^4 may be). This does not appear when R^1 (or R^2) ≠ Ph even if R^3 or R^4 = Ph [tetrazolines (**1l** and **m**)]. In order to check the validity of this specific fragmentation we have studied the mass spectrum of the aminal (**8**) and looked for the

Table 1. Tetrazolines (**1**; $R^3 = R^4$)

	$R^3 = R^4$ = Me								$R^3 = R^4$ = Et						$R^3 = R^4$ = Ph			
R^1	Ph		Ph				Ph		Me		Ph		Ph		Ph		Ph	
R^2	H		Me		Ph		C≡C–Ph		Me		Me		Ph		H		Me	
Tetrazoline	(**1a**)		(**1b**)		(**1c**)		(**1d**)		(**1e**)		(**1f**)		(**1g**)		(**1h**)		(**1i**)	
	m/z	%	*m/z*	%	*m/z*	%	*m/z*	%	*m/z*	%	*m/z*	%	*m/z*	%	*m/z*	%	*m/z*	%
(**2**)	176	14.5	190	7	252	7.5	276	3.6	156	16	218	5.0	280	6.7	300	3.5	314	4.4
(**3**) ($-\cdot R^2$)	175	12	175	39	175	76	175	3.5	141	65	203	25	203	83	299		299	5.2
(**3′**) ($-\cdot R^1$)	99	95	113	26			199	100			141	17			223	0.7	237	2.5
(**4**) ≡ (**4′**)	119	42	133	12	195	18.5	219	66	85	8	147	21	209	35	181	100	195	59
(**5**) ($-N_2$)	148	2.7	162	0.1	224	0.1	248	0.5	128	0.1	190	0.1	252	0.1	272	2	286	0.2
(**6**) ≡ (**6′**)	118	100	118	100	118	100	118	14	70	100	132	63	132	67	180	91	180	100
(**7**) ≡ (**7′**)	42	68	56	60			142	98			70	25			104	18	118	15
Other base peak											104	100	104	100				

Table 2. Tetrazolines (1; $R^3 \neq R^4$)

	R^3 = Me, R^4 = CH_2Ph				R^3 = Me, R^4 = Ph						R^3 = Ph, R^4 = CH_2Ph			
R^1	Ph		Ph		H		Me		Ph		Ph		Ph	
R^2	Me		Ph		H		H		Ph		H		Ph	
Tetrazoline	**(1j)**		**(1k)**		**(1l)**		**(1m)**		**(1n)**		**(1p)**		**(1g)**	
	m/z	%	*m/z*	%	*m/z*	%	*m/z*	%	*m/z*	%	*m/z*	%	*m/z*	%
(2)	266	3	328	2.2	162	22.5	176	22	314	4	314	4.4	390	0.6
(3) ($-\cdot R^2$)	251	26	251	36	161	0.7	175	1.2	237	13.3	313	0.3	313	0.8
(3′) ($-\cdot R^1$)	189	11					161	48			237	2.7		
(4) ($-R^3N_3$)	209	5	271	16	105	100	119	77	257	12	195	18	271	66
(4′) ($-R^4N_3$)	133	10	195	23	43	6	57	11	195	44	181	81	257	4
(5) ($-N_2$)	238	0.4	300	0.5	134	47.5	148	17	286	0.3	286	1.4	362	
(6) ($-R^3N_3$)	194	1.3	194	41	104	63	118	36	180	27.5	194	13	194	6.7
(7) ($-R^3N_3$)	132	7					104	90			118	2.9		
(6′) ($-R^4N_3$)	118	36	118	74	42	20	56	27	118	100	180	56	180	14.3
(7′) ($-R^4N_3$)	56	14					42	42			104	25		
Other base peak	91	100	91	100			77	100			91	100	91	100

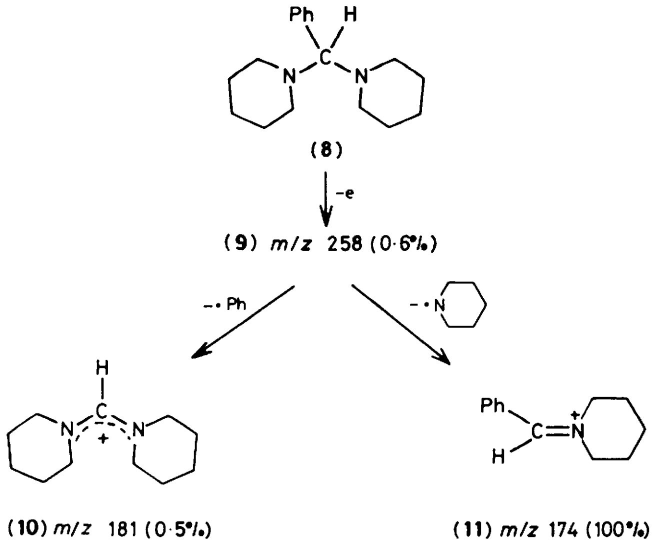


Scheme 1.

possible loss of a phenyl radical (Scheme 2). The fragmentation of the molecular ion (**9**) under electron impact gives almost exclusively ion (**11**) (100%) whereas ion (**10**) has a relative intensity of 0.5%. The MIKE spectrum of (**9**) shows only ion (**11**). As expected it is easier to obtain (**11**) from (**9**) (cleavage at the β-position from a nitrogen atom) and hence we may conclude that the loss of phenyl radical seems to be characteristic of the molecular ion structure of 1,4,5-substituted tetrazolines.

Evidence for the tetrazolium structure by CAD/MIKE spectrometry. In order to establish the structure of the tetrazolium ions (**3**) and (**3′**), we have scanned their CAD/MIKE spectra[7] and also those of the tetrazolium ions obtained from the corresponding synthesized salts.[6] Provided the counter-ion of the salt is correctly chosen, the spectra are superposable, thus stressing the strong probability of the identity of the two ions. The Figure shows the similarity of the CAD/MIKE spectra of the tetrazolium ions formed by fragmentation of the tetrazolines and those obtained from the tetrazolium perchlorates.

Influence of the counter-ion of the tetrazolium salts. 1,4,5-Tetrazolines are usually obtained from tetrazolium fluorosulphonates or hexachloroantimonates. The anions of these salts are inconvenient for mass spectrometry. In order to choose



Scheme 2.

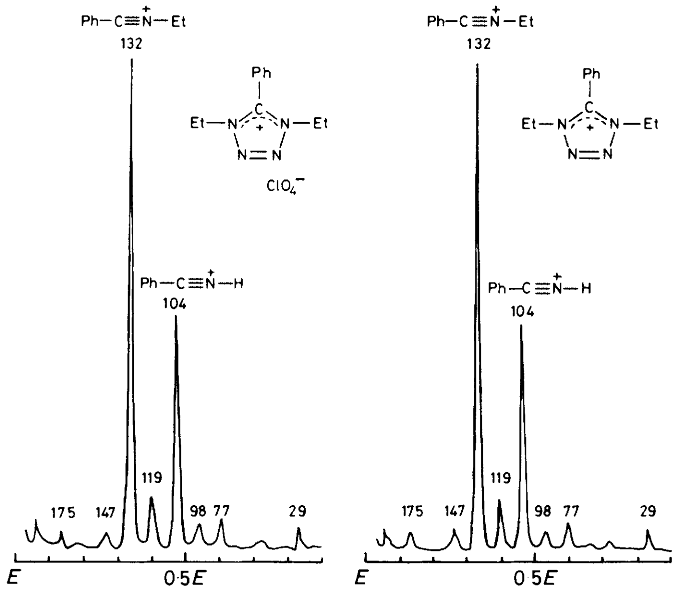
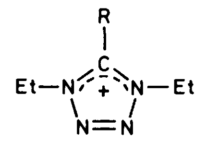
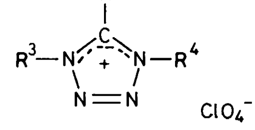


Figure. CAD/MIKE Spectra of m/z 203 ions

the most appropriate anion, we have examined the behaviour of the following tetrazolium salts under electron impact. The $SbCl_6^-$ anion is inadequate as a number of the fragment ions can be spotted in the same area as those of the cation. Moreover, they show an important 'memory effect'. The PF_6^- anion was not chosen for two reasons. On the one hand, the probe temperature required is too high (>150 °C) inducing thermal decomposition. On the other hand, the anion is basic enough to attract a proton when R = Me, leading to a methylenetetrazoline ion. The FSO_3^- anion behaves like PF_6^- but the temperature requirement is less drastic so that it can be used if R is an aryl substituent or when the formation of the tetrazolium salts with other anions is difficult. The tetrazolium tetrafluoroborates are fairly interesting: BF_4^- anion is less basic than the others. However, when R = Me, we notice that the relative abundance of the m/z 140 $(M - 1)^{+\bullet}$ ion is greater than that of m/z 141 (M^+). Tetrazolium perchlorates turned out to be best for our purpose although the required probe temperature is slightly higher than for the fluoroborates. The ClO_4^- anion is less basic than BF_4^- towards the tetrazolium ions. For example, with a direct-inlet temperature of 100 °C, when R = Me, m/z 141 (M^+) is more abundant than m/z 140 $(M - 1)^{+\bullet}$. Consequently, ClO_4^- was selected for the CAD/MIKE study of cations (**3**) and (**3'**) for tetrazolium salts (**I**)—(**V**).



R = Me with FSO_3^-, BF_4^-, PF_6^-, ClO_4^-
R = Ph with $SbCl_6^-$, FSO_3^-, PF_6^-, ClO_4^-, BF_4^-



(**I**)	$R^3 = R^4 =$ Me	R = Me	m/z 113
(**II**)	$R^3 = R^4 =$ Me	R = Ph	m/z 175
(**III**)	$R^3 = R^4 =$ Et	R = Me	m/z 141
(**IV**)	$R^3 = R^4 =$ Et	R = Ph	m/z 203
(**V**)	$R^3 =$ Me, $R^4 =$ Ph	R = Me	m/z 175

Cycloreversions from molecular ions (**2**) *of the tetrazolines.* Some of the ions (**4**) and (**4'**) are the result of a cycloreversion from molecular ions, as shown by the MIKE spectra of (**2**). However, the origin is not unequivocal. They also originate from the imines formed by the thermal cycloreversion of the tetrazolines.[8] When $R^3 = R^4 =$ Me, Et, or Ph, only one ion is observed (**4**) ≡ (**4'**). In the case of (**1h** and **i**), the relative intensity of the ion (**4**) is very high. If $R^3 \neq R^4$, competition between the two possibilities *a* or *b* is observed. It is very slight when $R^3 =$ Me and $R^4 = CH_2Ph$ and more appreciable in the other cases (for example, $R^3 =$ Me, $R^4 =$ Ph).

Cycloreversions from tetrazolium ions (**3**) *and* (**3'**). The cycloreversion of azides leads to the formation of nitrilium ions (**6**), (**6'**), (**7**), and (**7'**) starting from (**3**) and (**3'**) (MIKE spectra). When $R^3 = R^4 =$ Me, Et, or Ph, only one cycloreversion is observed and the relative abundance of the ions (**6**) ≡ (**6'**) and (**7**) ≡ (**7'**) is very high. When $R^3 \neq R^4$, the two expected cycloreversions take place with relatively slight competition.

Loss of Nitrogen from Molecular Ions (**2**).—The relative abundance of ions (**5**) $(M - N_2)^{+\bullet}$ is usually small (<0.5%) except for when R^1 = H or Me and R^2 = H (47.5 and 17%, respectively). MIKE spectrometry shows that at least part of these ions results from molecular ion (**2**) by the loss of nitrogen. Ions (**5**) may also result from the ionization of the diaziridines produced in the thermal decomposition of the tetrazolines as shown previously when R^1 and R^2 = H or Me.[8] CAD/MIKE spectra of ions (**5**), and of the molecular ion of the corresponding diaziridines,[8] are different. This shows that a great part of the ions (**5**) does not have the diaziridine molecular ion structure. Because of their small relative abundance, this study was not continued.

Experimental

The mass spectra were recorded on a Varian MAT 311 double-focusing mass spectrometer with a reversed Nier-Johnson geometry. Samples were introduced for electron-impact studies *via* a direct-insertion probe. The emission current for 70 eV mass spectra was 300 μA. The accelerating voltage was 3 kV. All mass spectra were obtained at 1 500 resolution (10% valley definition). The source temperature was set at 120—130 °C for tetrazolines and 170 °C for tetrazolium salts. The direct-inlet temperature is indicated for each compound. High-resolution measurements were made at a resolution of 10 000 (10% valley definition). The MIKE and CAD/MIKE spectra were recorded on the same spectrometer with a helium pressure of *ca.* 10^{-4} Torr in the collision chamber.

The synthesis of tetrazolines and tetrazolium salts was described in a previous paper.[6] Some new compounds have been prepared and are listed in Table 3. The imines Ph(Me)C=N–Me and Ph(Me)C=N–CH_2Ph were obtained from acetophenone and methylamime or benzylamine.[9] Compound (**9**) was prepared according to ref. 10: *m/z* (inlet temperature 35 °C) 258 ($M^{+\cdot}$ 0.6%), 181 (0.5), 174 (100), 173 (12), 172 (6.8), 118 (2.4), 117 (2.1), 106 (2.4), 104 (3.7), 98 (2.7), 96 (4), 92 (4.2), 91 (3.5), 85 (4.3), 84 (11.2), 69 (2.1), 65 (4.9), 52 (3.5), 51 (4.4), 50 (6.1), 44 (3.5), 43 (2.4), 42 (6.1), 41 (11.1), 39 (4), and 30 (3.4). Mass spectral data of tetrazolines (**1a**—**q**) and tetrazolium salts (**I**)—(**V**) are available as Supplementary Publication No SUP 56291 (7 pp.).*

Table 3. Data for new compounds

(a) Tetrazolium salts[a]

Salts	R	R^3	R^4	Anion	M.p. (°C)
(**I**)	Me	Me	Me	ClO_4	205
(**II**)	Ph	Me	Me	ClO_4	158
(**III**)	Me	Et	Et	ClO_4	153
(**III′**)	Me	Et	Et	PF_6	153
(**IV**)	Ph	Et	Et	ClO_4	185
(**V**)	Me	Me	Ph	ClO_4	160

(b) Tetrazolines

Compounds	R^1	R^2	R^3	R^4	M.p. (°C)	Yield (%)
(**1f**)	Ph	Me	Et	Et	34	75
(**1g**)	Ph	Ph	Et	Et	87	73
(**1k**)	Ph	Ph	Me	CH_2Ph	94	50
(**1p**)	H	H	Me	Ph	76	41
(**1q**)	Ph	Ph	Ph	CH_2Ph	107	52

[a] These salts were obtained by anion exchange: perchlorate–fluorosulphonate (50—60% yield), except for the hexafluorophosphate (**III′**) which was prepared by treating the corresponding nitrilium salt (obtained from triethyloxonium hexafluorophosphate with acetonitrile) and ethyl azide in 55% yield.

Acknowledgements

We are indebted to Mr. R. Trépart and Dr. Vaultier for help with the English translation.

References

1 N. W. Rokke, J. J. Worman, and W. S. Wodsworth, *J. Heterocycl. Chem.*, 1975, **12**, 1031.
2 G. Denecker, G. Smets, and G. L'Abbé, *Tetrahedron*, 1975, **31**, 765.
3 H. Quast and L. Bieber, *Chem. Ber.*, 1981, **114**, 216.
4 L. A. Lee and J. W. Wheeler, *J. Org. Chem.*, 1972, **37**, 348.
5 R. G. Cooks, J. H. Beynon, R. M. Caprioli, and G. R. Lester, 'Metastables Ions,' Elsevier, 1973.
6 B. Carboni and R. Carrié, *Tetrahedron*, 1984, **40**, 4115.
7 R. G. Cooks, 'Collision Spectroscopy,' Plenum Press, 1978.
8 B. Carboni, Thèse de Docteur Ingénieur, University of Rennes, 1980.
9 K. Taguchi and F. H. Westheimer, *J. Org. Chem.*, 1971, **36**, 1570.
10 A. P. Terent'ev, E. G. Rukhadze, I. G. Il'ina, and N. N. Pavlova, *Zh. Obsch. Khim.*, 1968, **38**, 1683.

Received 29*th August* 1984; *Paper* 4/1502

---

* For details of Supplementary Publications see Instructions for Authors in *J. Chem. Soc., Perkin Trans. 2*, 1985, Issue 1.