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MASS SPECTRA OF SUBSTITUTED 4-CYANO-1,4-DIHYDROPYRIDINES.

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Abstract: The mass spectra of some 3-substituted (acetyl-; carbamoyl-) N-methyl- and N-benzyl-4-cyano-1,4-dihydropyridines were examined. Unexpected thermolysis occurs prior to ionisation and gives rise to 3-substituted N-methyl- and N-benzyl-1,4-dihydropyridine peaks in the mass spectra of these 4-cyano adducts. High resolution mass measurements were used to substantiate this hypothesis. The corresponding N-methyl- and N-benzyl-1,4-dihydropyridines were synthesised and were used as reference compounds.

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The behaviour of a variety of dihydropyridine compounds (Fig.1) upon electron impact has been outlined in several communications (1-5). The general aspect of the fragmentation pattern is greatly dependent upon the degree of substitution and on the nature of the substituents implanted on the dihydropyridine moiety. Generally, the structure elucidation of this class of compounds by mass spectrometry alone does not offer any insurmountable difficulties. In this communication we present

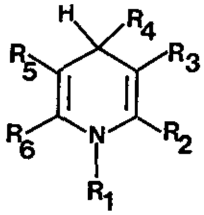
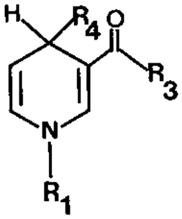


Fig.1

the mass spectral data of some N-methyl- and N-benzyl-4-cyano-1,4-dihydropyridines (I to IV) in which we were particularly interested as a part of a study on model compounds of NAD(H) (6).

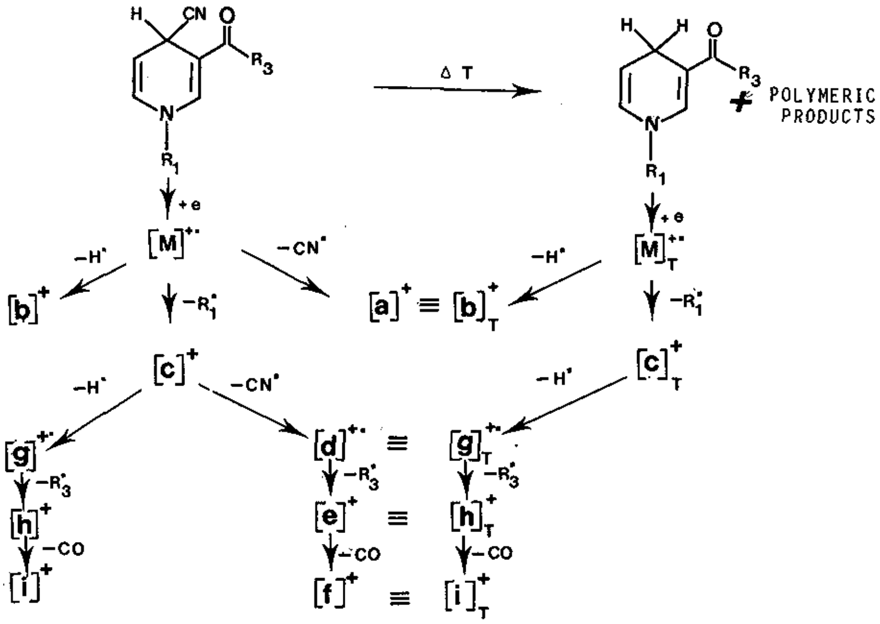


(a)

$I = R_1 = -CH_2-\Phi$ $R_3 = -CH_3$ $R_4 = -CN$ Mp:110-113°C
$II = R_1 = -CH_2-\Phi$ $R_3 = -NH_2$ $R_4 = -CN$ Mp:130-134°C
$III = R_1 = -CH_3$ $R_3 = -CH_3$ $R_4 = -CN$ Mp:110-112°C
$IV = R_1 = -CH_3$ $R_3 = -NH_2$ $R_4 = -CN$ Mp:165-168°C
$V = R_1 = -CH_2-\Phi$ $R_3 = -CH_3$ $R_4 = -H$ Oil
$VI = R_1 = -CH_2-\Phi$ $R_3 = -NH_2$ $R_4 = -H$ Oil
$VII = R_1 = -CH_3$ $R_3 = -CH_3$ $R_4 = -H$ Oil
$VIII = R_1 = -CH_3$ $R_3 = -NH_2$ $R_4 = -H$ Oil

Mass spectrometrically these 4-cyano adducts (I to IV) are characterised by very low abundant molecular ions $[M]^{+\cdot}$. Interpretation of these mass spectra can however be misleading since the mass spectra obtained greatly ressemble the mass spectra of the corresponding 1,4-dihydropyridine compounds (V to VIII). This is obviously a result of thermolysis prior to ionisation. The thermolytic process somehow gives rise to the 1,4-dihydropyridine which then ionises independently of the residual 4-cyano adduct according to Scheme 1.

(a) The 4-cyano adducts (I to IV) were synthesised according to reference 7. The 1,4-dihydropyridines (V to VIII) were synthesised according to reference 8.



Scheme 1.

To illustrate the mutual resemblance of the mass spectra of the 4-cyano adducts (I to IV) and the corresponding 1,4-dihydropyridine compounds (V to VIII) the low resolution data are depicted in Figs. 2 - 11 .

Comparing the mass spectra of compounds I and V, which are shown in Figs.2 and 3 strong peaks are observed at m/z= 213 [R.I.17%] and m/z=122 [R.I.33%]. The genesis of m/z=213 in the mass spectrum of the 4-cyano adduct I, with a molecular ion of m/z=238 [R.I.2%] implies a loss of 25 u. This cannot readily be explained unless the expulsion of an acetylene like fragment is accepted (9). The mass difference

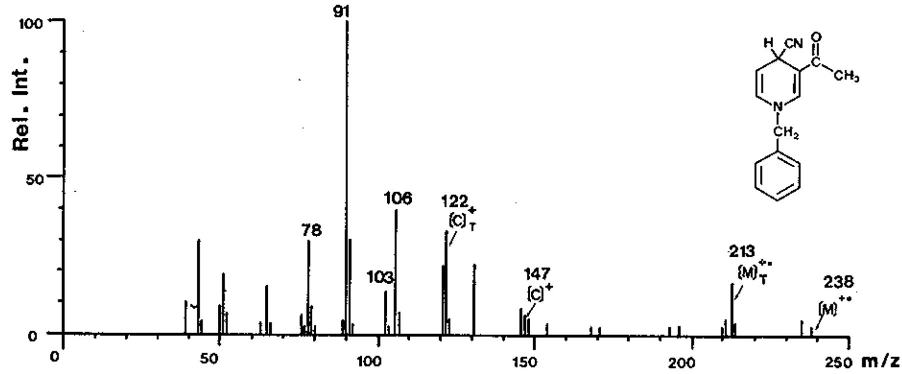


Fig.2.
Low resolution mass spectrum of 3-acetyl-1-benzyl-4-cyano-1,4-dihydropyridine(I). T_{DIP}: 170°C.

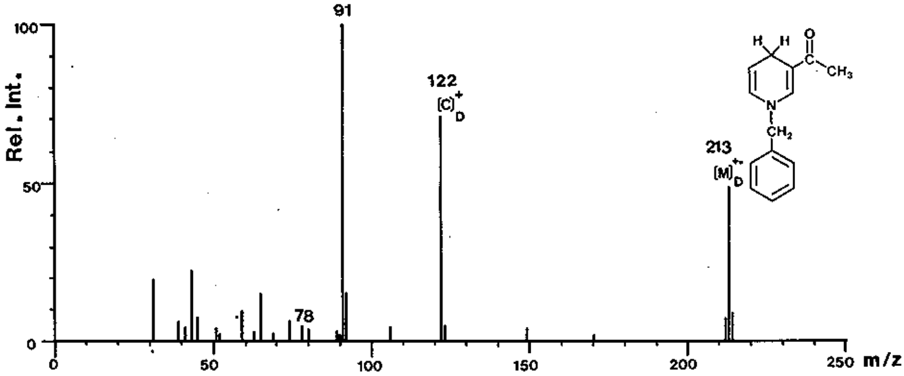


Fig.3.
Low resolution mass spectrum of 3-acetyl-1-benzyl-1,4-dihydropyridine(V). T_{DIP}: 150°C.*(b)* *(c)*

(b) The symbol $[c]^+_D$ drawn on the mass spectra of the 1,4-dihydropyridines (V to VIII) corresponds to the base moiety, its structure is analogous to $[c]^+_T$ in the mass spectra of the 4-cyano-1,4-dihydropyridines.

(c) T_{DIP}: Temperature of the direct insertion probe

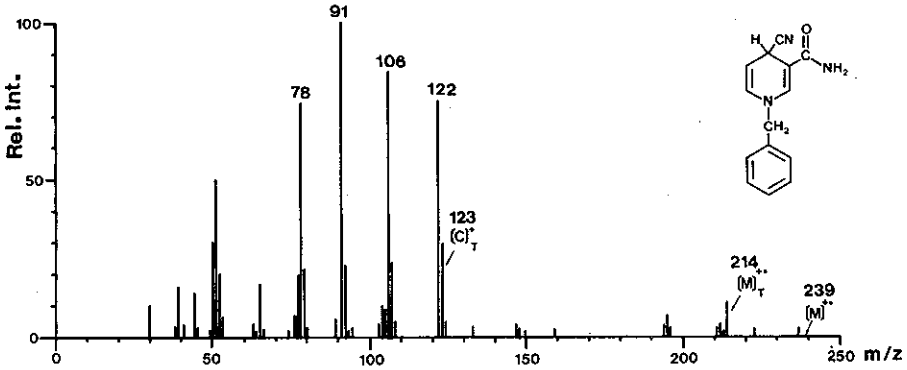


Fig.4

Low resolution mass spectrum of 1-benzyl-3-carbamoyl-4-cyano-1,4-dihydropyridine (II). T_{DIP}: 190°C.

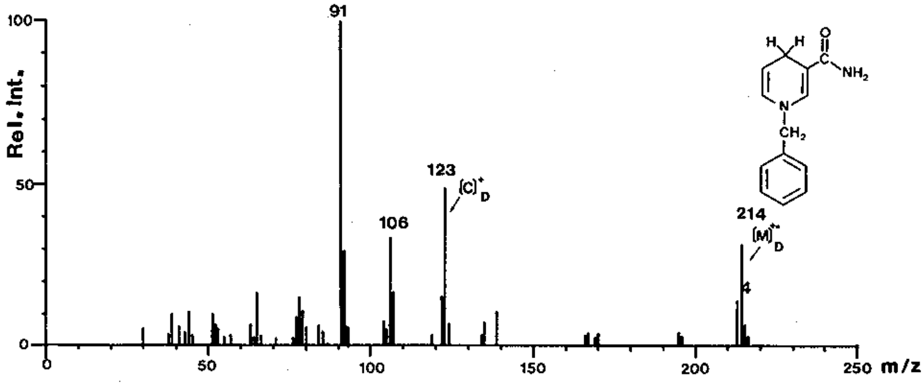


Fig.5

Low resolution mass spectrum of1-benzyl-3-carbamoyl-1,4-dihydropyridine (VI). T_{DIP}:200°C.

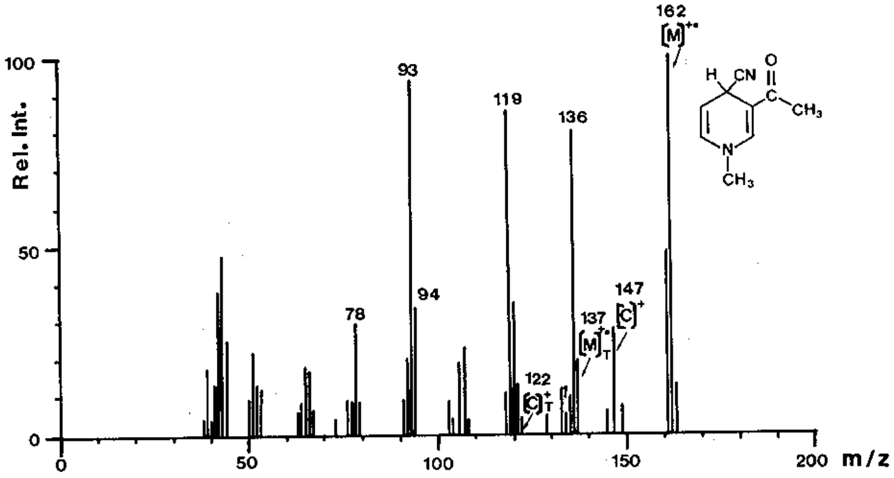


Fig.6
Low resolution mass spectrum of 3-acetyl-4-cyano-1-methyl-1,4-dihydropyridine(III). T_{DIP}:120°C.

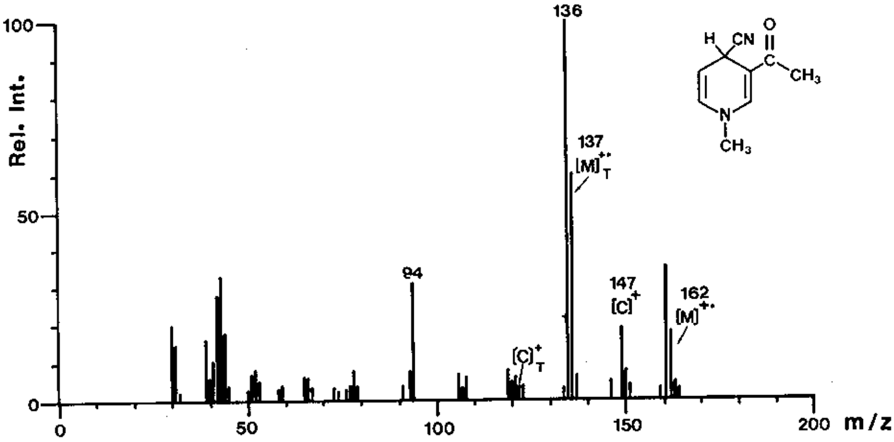


Fig.7
Low resolution mass spectrum of 3-acetyl-4-cyano-1-methyl-1,4-dihydropyridine(III) after external heating at 160°C for 60 seconds. T_{DIP}:200°C

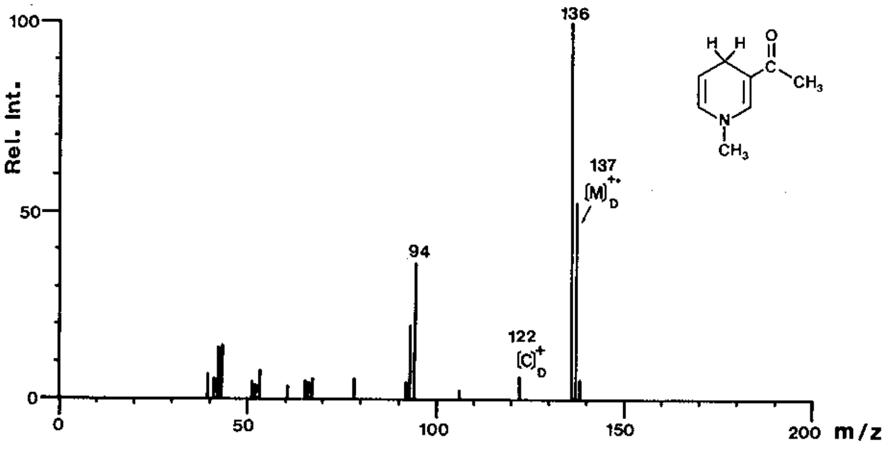


Fig.8
Low resolution mass spectrum of 3-acetyl-1-methyl-1,4-dihydropyridine(VII). T_{DIP}:170°C

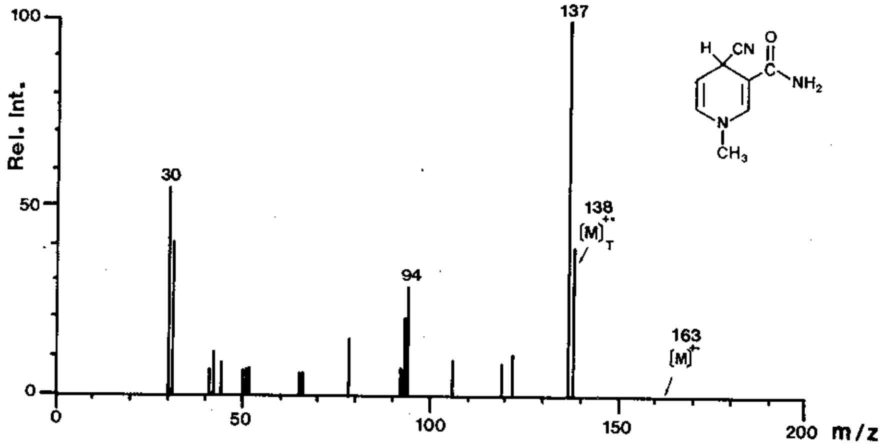


Fig.9
Low resolution mass spectrum of 3-carbamoyl-4-cyano-1-methyl-1,4-dihydropyridine(IV).T_{DIP}:210°C

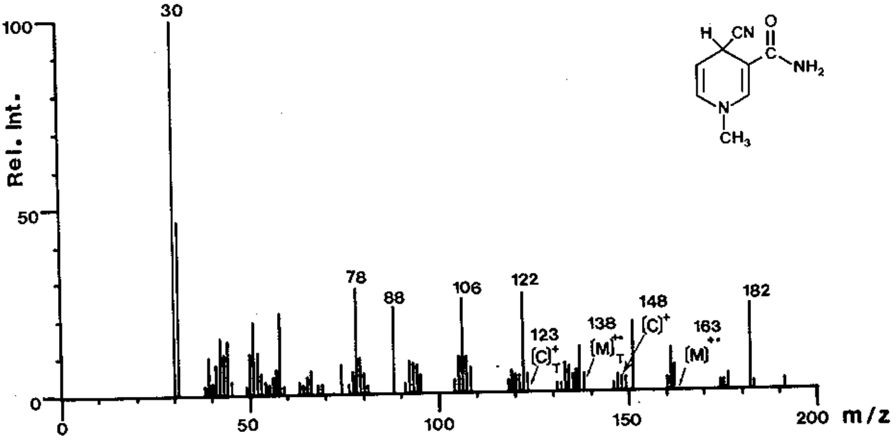


Fig.10
Low resolution mass spectrum of 3-carbamoyl-4-cyano-1-methyl-1,4-dihydropyridine (IV). T_{DIP}:300°C

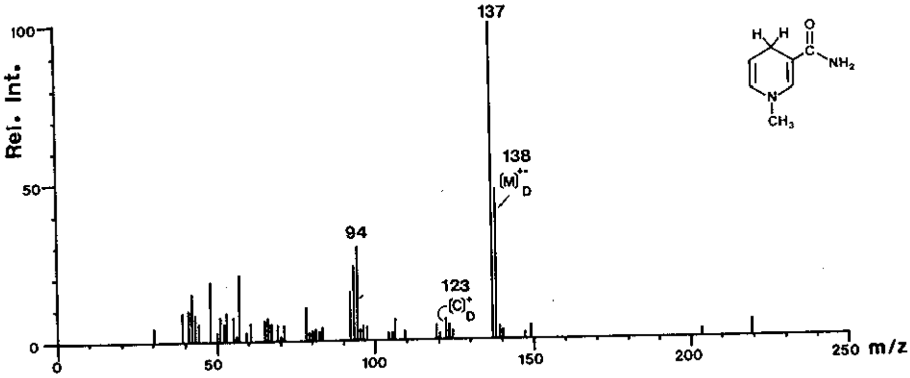


Fig.11
Low resolution mass spectrum of 3-carbamoyl-1-methyl-1,4-dihydropyridine(VIII).T_{DIP}:180°C

Table 1

Low resolution mass spectra of compounds I to IV. (Ions depicted in Scheme 1.) *(d)*

	I T_{DIP}:170°C	II T_{DIP}:190°C	III T_{DIP}:120°C	IV T_{DIP}:210°C
$[M]^{+\cdot}$	238 [2]	239 [<2]	162 [100]	163 [<2]
$[a]^{+}$	212 [5]	213 [3]	136 [80]	137 100]
$[b]^{+}$	237 [-]	238 [-]	161 [48]	162 [-]
$[c]^{+}$	147 [6]	148 [-]	147 [28]	148 [-]
$[d]^{+\cdot}$	121 [21]	122 [75]	121 [13]	122 [9]
$[e]^{+}$	106 [40]	106 [84]	106 [19]	106 [9]
$[f]^{+}$	78 [29]	78 [74]	78 [30]	78 [14]
$[g]^{+\cdot}$	146 [7]	147 [5]	146 [-]	147 [-]
$[h]^{+}$	131 [22]	131 [-]	131 [-]	131 [-]
$[i]^{+}$	103 [13]	103 [4]	103 [8]	103 [-]
$[M]_T^{+}$	213 [17]	214 [9]	137 [17]	138 [40]
$[b]_T^{+}$	212 [5]	213 [3]	136 [80]	137 [100]
$[c]_T^{+}$	122 [33]	123 [28]	122 [4]	123 [<2]
$[g]_T^{+\cdot}$	121 [21]	122 [75]	121 [13]	122 [12]
$[h]_T^{+}$	106 [40]	106 [84]	106 [19]	106 [9]
$[i]_T^{+}$	78 [29]	78 [74]	78 [29]	78 [14]
$[R_1]^{+}$	91 [100]	91 [100]	-	-

(d) Mass spectra were recorded on a JEOL 01SG-2 spectrometer, ionising voltage 70 eV, source temperature ~280°C. Relative intensities are given in parentheses.

Table 2

High resolution mass measurements of the ions $[M]_T^{+\cdot}$ and $[c]_T^{+}$ in the mass spectra of compounds I to IV.

Compound	Ions	Observed	Calculated	Formula
I	$[M]_T^{+\cdot}=213$	213.1166	213.1153	$C_{14}H_{15}NO$
	$[c]_T^{+}=122$	122.0613	122.0605	C_7H_8NO
II	$[M]_T^{+\cdot}=214$	214.1121	214.1106	$C_{13}H_{14}N_2O$
	$[c]_T^{+}=123$	123.0538	123.0558	$C_6H_7N_2O$
III	$[M]_T^{+\cdot}=137$	137.0821	137.0840	$C_8H_{11}NO$
	$[c]_T^{+}=122$	122.0590	122.0605	C_7H_8NO
IV	$[M]_T^{+\cdot}=138$	138.0789	138.0793	$C_7H_{10}N_2O$
	$[c]_T^{+}=123$	123.0544	123.0558	$C_6H_7N_2O$

between m/z=213 and m/z=122 is more evident and points to the loss of a benzyl radical, which is a known fragmentation mechanism (5). High resolution mass measurements of these ions in the mass spectrum of compound I lead to the following results:

m/z=213	213.1166(Obsd.)	213.1153(Calcd.)	$C_{14}H_{15}NO$
m/z=122	122.0613(Obsd.)	122.0605(Calcd.)	C_7H_8NO

If an acetylene like fragment was expelled from the molecular ion m/z=238 ($C_{15}H_{14}N_2O$) an elemental composition of $C_{13}H_{13}N_2O$ would be expected for m/z=213. Since this was not found, this possibility has to be rejected. On the other hand, the experimentally found formula $C_{14}H_{15}NO$, corresponds to the elemental composition of the molecular ion $[M]^{+\cdot}$ of 3-acetyl-1-benzyl-1,4-dihydropyridine (V).

Analogous results are found with the other cyano adducts II to IV. From Scheme 1 it is obvious that only $[M]^{+\cdot}_{T}$ and $[c]^{+}_{T}$ are indicative for the presence of the dihydropyridine compound since other fragmentation mechanisms starting from the 4-cyano adduct lead to coinciding fragment ions. However in compound IV, $[c]^{+}_{T}$ has a very low abundance. Consequently loss of the N-CH_3 substituent is an energetically unfavourable process. The enhanced intensity of $[c]^{+}_{T}$ in 3-acetyl-4-cyano-1-methyl-1,4-dihydropyridine can be explained by contributions due to α-fission of the acetyl function with expulsion of a radical $CH_3^{\cdot}$. Low resolution data are presented in Table 1. High resolution mass measurements of $[M]^{+\cdot}_{T}$ and $[c]^{+}_{T}$ are summarised in Table 2.

Furthermore we like to point out that reproducible spectra are hard to obtain probably due to the thermolytic process dependent upon the temperature of the direct insertion probe (Figs. 9-10). At higher temperature small signals are observed above the molecular ion $[M]^{+\cdot}$ of the cyano adducts.

As can be seen in Fig.6, compound III shows a strong molecular ion in contrast to the other 4-cyano adducts. A possible explanation for this surprising stability can be found in its vapourising at a probe temperature of 120°C in contrast to the other 4-cyano compounds. Indeed, for these analogues an ion current only could be obtained at probe temperatures of at least 170°C. To check this possibility 3-acetyl-4-cyano-1-methyl-1,4-dihydropyridine was heated externally at 160°C for 60 sec. and then inserted in the ion source. The mass spectrum obtained in such a way (Fig.7) gave a much lower abundant molecular ion $[M]^{+\cdot}$ and an increased abundance of the thermolytic dihydro peaks $[M]^{+\cdot}_{T}$ and $[c]^{+}_{T}$. Apparently thermolysis occurs above some threshold temperature.

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