Mass spectrometry of aromatic cyclic imides and amides. Part II: electron ionization induced decomposition of *N*-substituted 3,4-pyridinedicarboximides

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Abstract

The behaviour of a series of *N*-substituted 3,4-pyridinedicarboximides under electron impact at 70 eV is analyzed. Compounds under study were divided into three groups: 3,4-pyridinedicarboximidoacetic, β-3,4-pyridinedicarboximidopropionic and γ-3,4-pyridinedicarboximidobutyric acid derivatives (compounds **1**, **2** and **3** respectively), which in turn determine the dominant fragmentations. The proposed fragmentation patterns are supported by HRMS and tandem mass spectrometry. Results are in some cases compared to data from the related 2,3-pyridinedicarboximides **4**.

Keywords: Electron ionization mass spectrometry, imides, 3,4- and 2,3-pyridinedicarboximides, fragmentation pathways

Introduction

Mass spectrometry (MS) is a widely employed method for characterization and structural determination of organic compounds. Its advantage over other spectroscopic methods is that it requires a minimal amount of substance. On the other hand, contaminated samples or mixtures of compounds can be analyzed in equipments where mass spectrometry is combined with chromatographic methods without previous purification. From its early days, this method has been effectively employed for the structural characterization of aromatic cyclic imides. In particular, fragmentation of phthalimides under electron impact (EI)[1] was extensively studied among them. Recently we have focused our attention in analogous imides with pyridine nucleus. Thus, the behavior of a series of *N*-substituted 2,3-pyridinedicarboximides under EI at 70 eV was analyzed.[2] Ongoing with our research line, we were interested in evaluating the behavior of the isomeric 3,4-pyridinedicarboximides. Although they proved to be interesting as synthetic intermediates[3] and by the biological activity observed for some terms,[4] MS of such compounds, has almost not been studied. Bentley and Johnstone described spectra of *N*-methyl and *N*-phenyl-3,4-

pyridinedicarboximides and concluded that such compounds undergo fragmentation mainly by expulsion of molecules from molecular ion: formimine in *N*-methyl derivative and phenyl isocyanate in *N*-phenyl derivative.[1a]

We present in this work special features of mass spectra under EI of a series of *N*-functionalized alkyl 3,4-pyridinedicarboximides. We had special interest in the behavior of the corresponding ω-imidoalkanoic acids and their derivatives (esters, amides and related ketone). For a better analysis of their fragmentation, compounds under study were divided into three groups: 3,4-pyridinedicarboximidoacetic acid, β-(3,4-pyridinedicarboximido)propionic acid and γ-(3,4-pyridinedicarboximido)butyric acid derivatives (compounds **1, 2** and **3** respectively) (Figure 1). In order to observe the influence of pyridine nitrogen position, results were compared in some cases with the corresponding 2,3-pyridinedicarboximide derivatives **4**.

Proposed fragmentation pathways are supported on high resolution mass spectrometry (HRMS) data and MS/MS experiments of selected compounds.

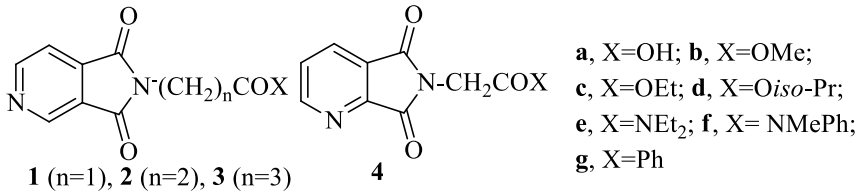


Figure 1. 3,4-Pyridinedicarboximides **1-3** and 2,3-pyridinedicarboximides **4** studied.

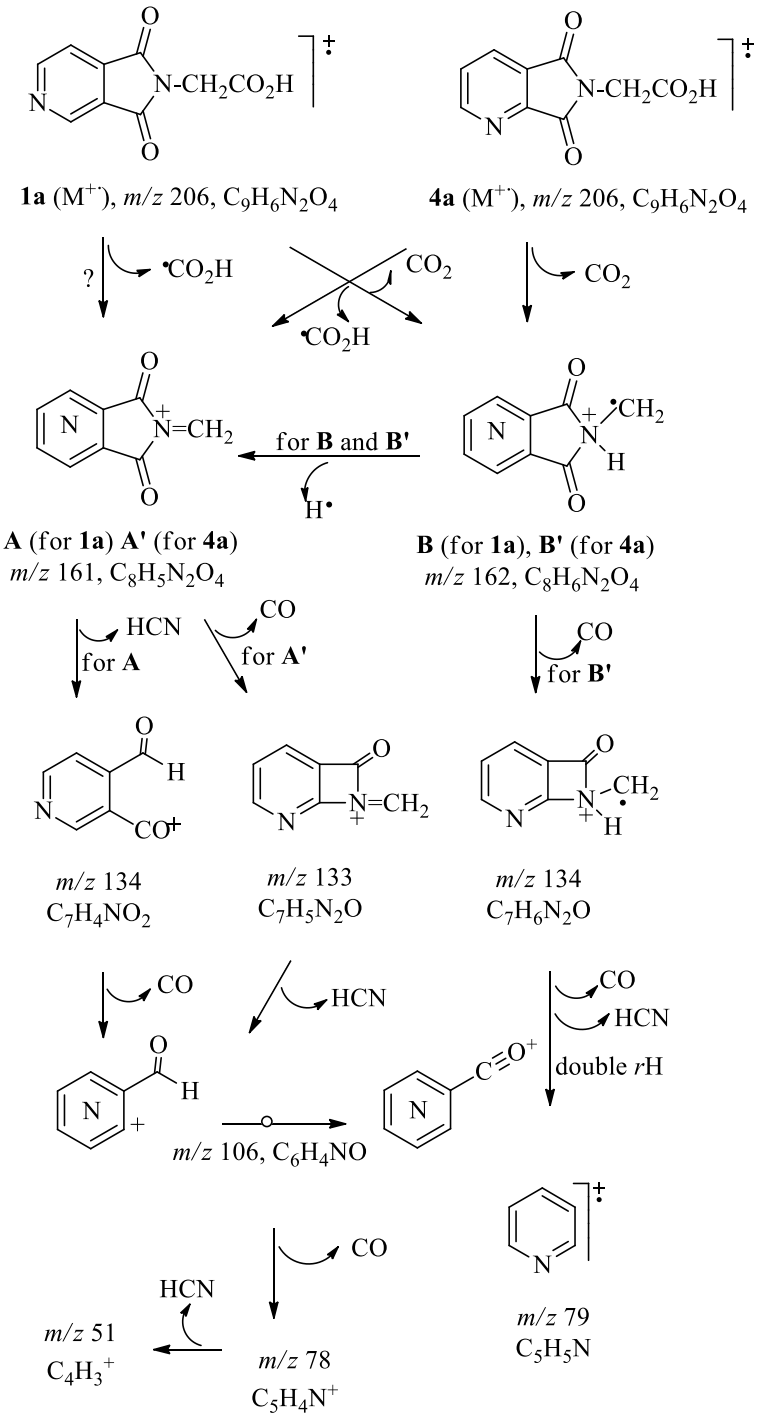
Results and Discussion

3,4-Pyridinedicarboximidoacetic acid (1a)

Mass spectrum of acid **1a** displays $M^{+\cdot}$ of low abundance (3%) (Table 1) and presents two characteristic peaks at *m/z* 161 and 162 which relative intensities vary according to the electron energy employed. HRMS shows that ion at *m/z* 161 (base ion) corresponds to formula $C_8H_5N_2O_2$, so stabilized iminium ion **A** structure is assigned. Further degradation explains the presence of ions at *m/z* 134, 106, 78 and 51 as the result of successive expulsion of HCN, 2 CO and HCN again (Scheme 1).

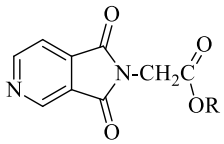
HRMS of the *m/z* 162 ion shows that it corresponds in composition to $C_8H_6N_2O_2$ originated from molecular ion decarboxylation. Structure **B** arising from a rearrangement which involves carboxyl hydrogen transfer to imide nitrogen with simultaneous cleavage of side chain Cα-Cβ bond is proposed. Similar rearrangements were observed for 2,3-pyridinedicarboximidoacetic acid **4a**[2] and other *N*-substituted imides[1c,5] and require the presence of a γ-hydrogen to imide nitrogen. Other probable structure would be that corresponding to *N*-methyl-3,4-pyridinedicarboximide molecular ion. However, absence of ions at *m/z* 133, 118 and 105, characteristic of such compound[6] allows us to discard it. MS/MS experiments show that degradation of *m/z* 162 ion involves loss of hydrogen radical leading to iminium ion **A** (*m/z* 161). This pathway (**B** → **A**) accounts for differences

between relative abundances of *m/z* 162 ion in spectra taken at 20 eV (97%) and 70 eV (47%).[7] However, direct transformation of $M^{+\cdot}$ by loss of CO_2H can not be discarded as another source of iminium ions **A** (Scheme 1).



Scheme 1. Fragmentation pathways of 3,4- and 2,3-pyridinedicarboximidoacetic acids **1a** and **4a** under EI conditions.

Table 1. Select fragments in the EI mass spectra of 3,4-pyridinedicarboximidoacetic acid **1a** and the corresponding esters **1b,c**



Ion	**1a** (R=H) *m/z* (*RA*%)[a]	**1b** (R=Me) *m/z* (*RA*%)[a]	**1c** (R=Et) *m/z* (*RA*%)[a]
$[M]^{+\cdot}$	206 (3). HRMS: 206.0364. Calcd for $C_9H_6N_2O_4$: 206.0328	220 (36). HRMS: 220.0487. Calcd for $C_{10}H_8N_2O_4$: 220.0484	234 (8). HRMS: 234.0641. Calcd for $C_{11}H_{10}N_2O_4$: 234.0641
$[M\text{-}RO]^+$	-	189 (4). HRMS: 189.0315. Calcd for $C_9H_5N_2O_3$: 189.0300	189 (3). HRMS: 189.0342. Calcd for $C_9H_5N_2O_3$: 189.0300
m/z 162 $[\mathbf{B}]^{+\cdot}$	(48).[b] HRMS: 162.0428. Calcd for $C_8H_6N_2O_2$: 162.0429	-	(39).[b] HRMS: 162.0419. Calcd for $C_8H_6N_2O_2$: 162.0429
m/z 161 $[\mathbf{A}]^+$	(100). HRMS: 161.0352. Calcd for $C_8H_5N_2O_2$: 161.0351	(100). HRMS: 161.0356. Calcd for $C_8H_5N_2O_2$: 161.0351	(100). HRMS: 161.0349. Calcd for $C_8H_5N_2O_2$: 161.0351
m/z 134 $[\mathbf{A}\text{-}HCN]^+$	(15). HRMS: 134.0262. Calcd for $C_7H_4NO_2$: 134.0242	(10). HRMS: 134.0260. Calcd for $C_7H_4NO_2$: 134.0242	(7). HRMS: 134.0261. Calcd for $C_7H_4NO_2$: 134.0242
m/z 106	(16). HRMS: 106.0299. Calcd for C_6H_4NO: 106.0293	(10). HRMS: 106.0311. Calcd for C_6H_4NO: 106.0293	(8). HRMS: 106.0297. Calcd for C_6H_4NO: 106.0293
m/z 105		(18). HRMS: 105.0248. Calcd for C_6H_3NO: 105.0215	(16). HRMS: 105.0228. Calcd for C_6H_3NO: 105.0215
m/z 78	(57). HRMS: 78.0334. Calcd for C_5H_4N: 78.0344	(30). HRMS: 78.0353. Calcd for C_5H_4N: 78.0344	(26). HRMS: 78.0328. Calcd for C_5H_4N: 78.0344
m/z 77		(16). HRMS: 77.0278. Calcd for C_5H_3NO: 77.0266	(15). HRMS: 77.0277. Calcd for C_5H_3NO: 77.0266
m/z 51	(77). HRMS: 51.0243. Calcd for C_4H_3: 51.0235	(17)	(17). HRMS: 51.0246. Calcd for C_4H_3: 51.0235
m/z 50		(39)	(43)

[a]Relative abundances (*RA*) indicated between parenthesis correspond to low resolution spectra at 70 eV.

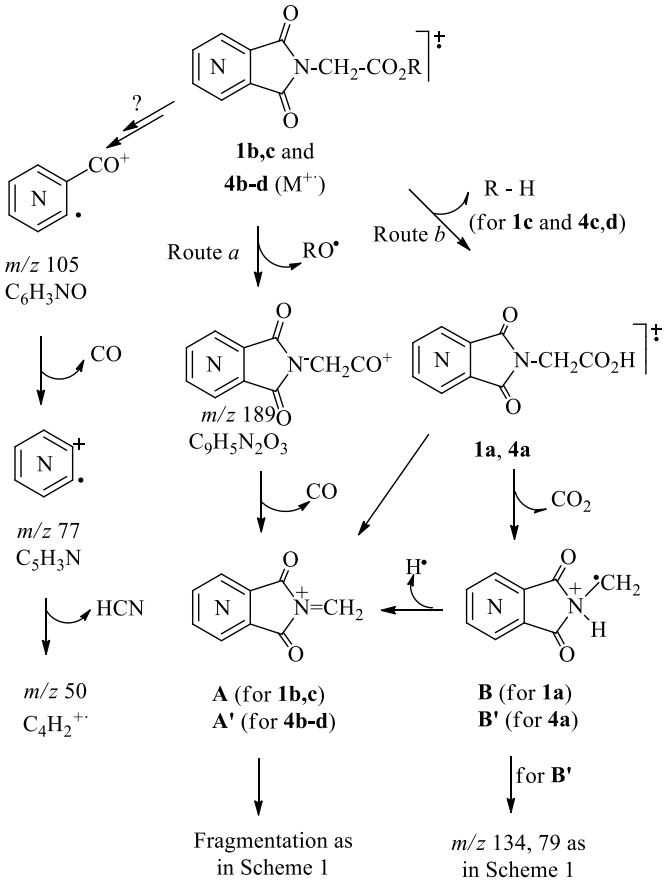
[b]*RA* of $\mathbf{B}^{+\cdot}$ corrected from the isotopic contribution of $\mathbf{A}^+$.

In order to observe the influence of pyridine nitrogen position, it is convenient to compare above results with those from isomeric acid **4a** described in our previous paper.[2] It was observed in this compound that both primary fragmentations leading to the corresponding ions at *m/z* 161 (**A'**) and 162 (**B'**), and **B' → A'** conversion are similar to that of compound **1a** (Scheme 1).

However, the presence of pyridine nitrogen adjacent to imide carbonyl favors decarbonylation of such ions. Thus, expulsion of CO from ions at *m/z* 161 (**A'**) and 162 (**B'**), coming from compound **4a**, leads initially to ions at *m/z* 133 and 134 respectively. Subsequent degradation of *m/z* 134 ion leads to pyridine odd electron (*m/z* 79) as the result of CO and HCN expulsion with a double hydrogen transfer to pyridine nucleus.[8] On the other hand, decarbonylation is not observed in the fragments **A** and **B** generated from acid **1a**.

Alkyl 3,4- and 2,3-pyridinedicarboximidoacetates (1b,c and 4b-d)

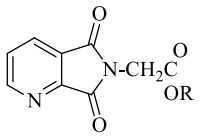
The most important ions of esters **1b,c** and **4b-d** are depicted in Tables 1 and 2 respectively. Abundances of $M^{+\cdot}$ are in general low, and decreasing as the size of alkyl groups increase. Primary fragmentations of both series of compounds are similar and are shown in Scheme 2.



Scheme 2. Fragmentation pathways of 3,4- and 2,3-pyridinedicarboximideacetic acid alkyl esters **1b,c** and **4b-d** under EI conditions.

The main fragmentation pathway involves loss of RO$^{\cdot}$ by homolytic cleavage originating acylium ion at *m/z* 189, always present although with low intensity, which allows to determine the nature of alkyl group (Route ***a***). Subsequent expulsion of CO generates the corresponding iminium ions (**A** and **A'**, base ions) and ions derived from them.

Table 2. Select fragments in the EI mass spectra of 2,3-pyridinedicarboximidoacetic acid alkyl esters **4b-d**



Ion	**4b** (R=Me) *m/z* (*RA*%)[a]	**4c** (R=Et) *m/z* (*RA*%)[a]	**4d** (R=*iso*-Pr) *m/z* (*RA*%)[a]
$[M]^{+\cdot}$	220 (23)	234 (3)	248 (<1)[c]
$[M\text{-}RO]^{+}$	189 (2)	189 (1)	189 (8). HRMS: 189.0306. Calcd for $C_9H_5N_2O_3$: 189.0300
$[M\text{-}CO_2]^{+\cdot}$	176 (2)	190 (2)	204 (1). HRMS: 204.0879. Calcd for $C_{11}H_{12}N_2O_2$: 204.0899
m/z 162 [**B'**]$^{+\cdot}$	-	(25)[b]	(52).[b] HRMS: 162.0430. Calcd for $C_8H_6N_2O_2$: 162.0429
m/z 161 [**A'**]$^{+}$	(100)	(100)	(100). HRMS: 161.0363. Calcd for $C_8H_5N_2O_2$: 161.0351
m/z 134 [**B'**-CO]$^{+\cdot}$	-	(4)	(13). HRMS 134.0501. Calcd for $C_7H_6N_2O$: 134.0480
m/z 133 [**A**'-CO]$^{+}$	(7)	(5)	(8). HRMS: 133.0389. Calcd for $C_7H_5N_2O$: 133.0402
m/z 106	(37)	(28)	(34). HRMS: 106.0307. Calcd for C_6H_4NO: 106.0293
m/z 105	(9)	(15)	(13). HRMS: 105.0243. Calcd for C_6H_3NO: 105.0215
m/z 79	(1)	(9)	(21). HRMS: 79.0430. Calcd for C_5H_5N: 79.0422
m/z 78	(13)	(23)	(31). HRMS: 78.0338. Calcd for C_5H_4N: 78.0344
m/z 77	(3)	(19)	(23). HRMS: 77.0276. Calcd for C_5H_3N: 77.0266
m/z 51	(2)	(7)	(24)
m/z 50	(15)	(7)	(23)

[a] Relative abundances (*RA*) indicated between parenthesis correspond to low resolution spectra at 70 eV. [b] *RA* of $\mathbf{B}^{+\cdot}$ corrected from the isotopic contribution of $\mathbf{A}^{+}$. [c] This ion is not detected in the HRMS.

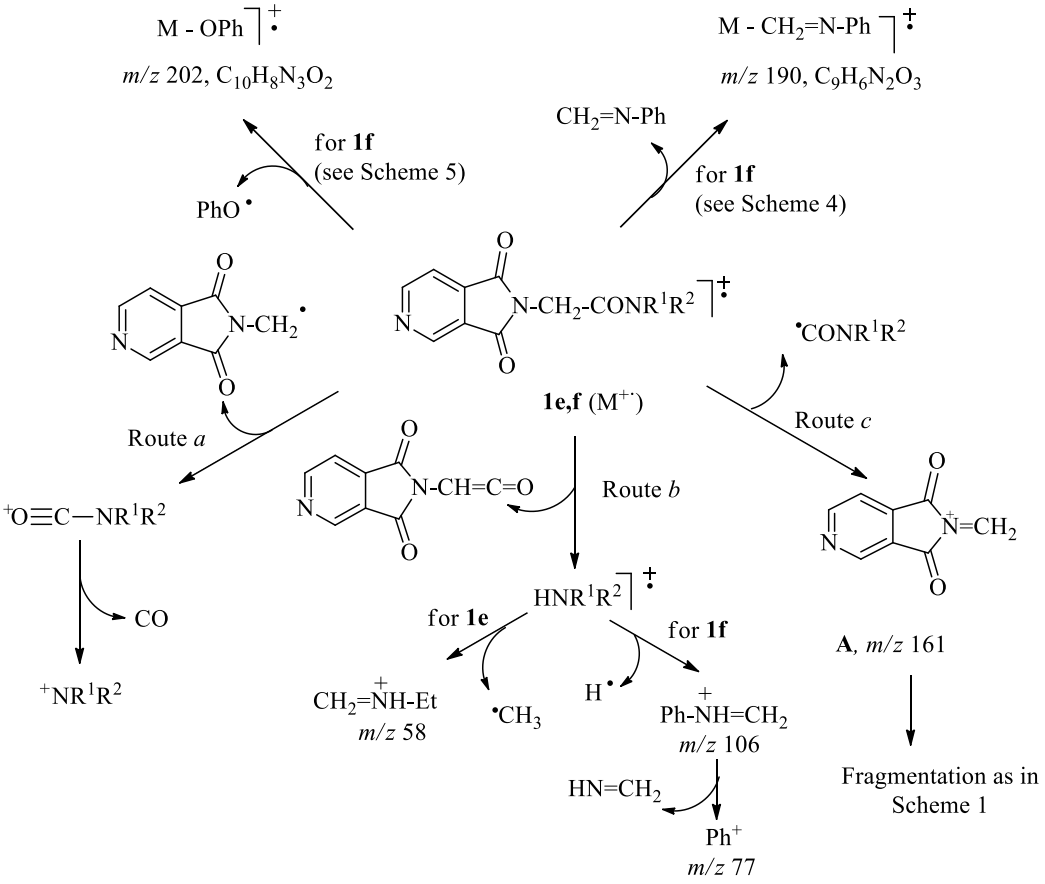
Ethyl **1c** and **4c** and isopropyl **4d** ester spectra show *m/z* 162 ions (25-52%) assigned to structures **B** and **B'**. The presence of such ions is probably the result of a McLafferty rearrangement of esters having γ–hydrogen to carbonyl leading to the **1a** and **4a** molecular ions (*m/z* 206) (Route ***b***). Although spectra of those compounds at 70 eV do not show these ions, spectrum of **1c** recorded at 20 eV shows a low intensity peak at *m/z* 206 (5%), endorsing route ***b***.[9]

On the other hand, experimental results performed with isopropyl ester **4d**, having two methyls capable to transfer their hydrogens in a McLafferty rearrangement generating **4a** molecular ion, also support the route ***b***. Thus, when **4d** spectra were recorded using different electron been energy, abundances of ions at *m/z* 162, 134 and 79 (in relation to that of *m/z* 161 ion) increase as electron energy decrease following the behaviour observed for acid **4a**.[10]

All esters also present ions at *m/z* 105 (C_6H_3NO), 77 (C_5H_3N) and 50 (C_4H_2), common in this type of pyridine derivatives, which probably result from other fragmentation pathways of $M^{+\cdot}$ (Scheme 2).

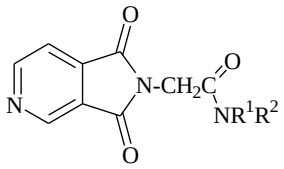
3,4-Pyridinedicarboximidoacetamides (1e,f)

Decomposition of amides **1e,f** reflects the strong tendency of carboxamide nitrogen to undergo reactions originating ions with charge retention (Table 3). Three primary fragmentation pathways are observed in the spectra, depicted in Scheme 3.



Scheme 3. Fragmentation pathways of 3,4-pyridinedicarboximidoacetamides **1e,f** under EI conditions.

Table 3. Select fragments in the EI mass spectra of 3,4-pyridinedicarboximidoacetamides **1e,f**



Ion	**1e** (R^1=R^2=Et) *m/z* (*RA*%)[b]	**1f** (R^1=Me, R^2=Ph) *m/z* (*RA*%)[b]
$[M]^{+\cdot}$	261 (16)	295 (63). HRMS: 295.0956. Calcd for $C_{16}H_{13}N_3O_3$: 295.0957
$[CONR^1R^2]^+$	100 (86)	134 (100). HRMS: 134.0610. Calcd for C_8H_8NO: 134.0606
$[NR^1R^2]^+$	72 (100)	106 (55). HRMS 106.0655[c]. Calcd for C_7H_8N 106.0657
$[HNR^1R^2]^{+\cdot}$	-	107 (57)[d]. HRMS: 107.0729. Calcd for C_7H_9N: 107.0735
m/z 189 $[M\text{-}NR^1R^2]^+$	(1)	(1)[e]
m/z 161 $[\mathbf{A}]^+$	(29)	(60). HRMS: 161.0360. Calcd for $C_8H_5N_2O_2$: 161.0351
m/z 134 $[\mathbf{A}\text{-}HCN]^+$	(2)	[f]
m/z 106	(3)	[c]
m/z 78	(15)	(33). HRMS: 78.0365. Calcd for C_5H_4N: 78.0344
m/z 51	(12)	(28). HRMS: 51.0242. Calcd for C_4H_3: 51.0235
m/z 50	(26)	(29)
Others[a]	58 (19) $[HNEt_2\text{-}Me]^+$	202 (3). HRMS: 202.0602. Calcd for $C_{10}H_8N_3O_2$: 202.0617, $[M\text{-}PhO]^+$ 190 (2). HRMS: 190.0361. Calcd for $C_9H_6N_2O_3$ 190.0378, $[M\text{-}CH_2{=}NPh]^{+\cdot}$ 77 (64). HRMS: 77.0391. Calcd for C_6H_5: 77.0391

[a]Characteristic peaks and/or with relative abundance higher than 15% are depicted.
[b]Relative abundances (*RA*) indicated between parenthesis correspond to low resolution spectra at 70 eV.
[c]The most abundant ion at *m/z* 106 corresponds to formula C_7H_8N and results from the contributions of two isomeric ions (see text).
[d]*RA* of $[HNR^1R^2]^{+\cdot}$ corrected from the isotopic contribution of $[NR^1R^2]^+$.
[e]This ion is not detected in the HRMS.
[f]The most abundant ion at *m/z* 134 corresponds to $[CONMePh]^+$.

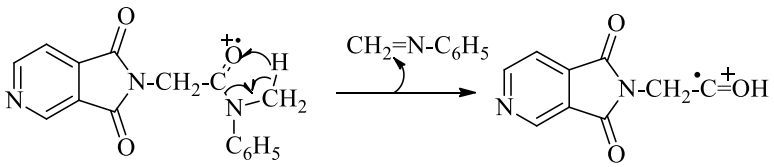
The most important pathway involves an α–cleavage leading to carboxamide ion $[CONR^1R^2]^+$, base ion for **1f** (*m/z* 134) (Route ***a***). Fragmentation continues with the loss of CO originating $[NR^1R^2]^+$), base ion for **1e** (*m/z* 72).

Route ***b*** involves CO-N cleavage with hydrogen transfer to nitrogen. Such cleavage is typical of acetamides[11] leading to odd electron ions $[HNR^1R^2]^{+\cdot}$ (*m/z* 107, 62% for compound **1f**). It is interpreted as the result of a methylene hydrogen transfer to carboxamide nitrogen, subsequent homolytic cleavage with charge retention on nitrogen and expulsion of a substituted ketene. On the other hand, MS/MS experiments demonstrate that the strong peak at *m/z* 106 (64%) results from the contribution of two isomeric ions of formula C_7H_8N: the expected $[NMePh]^+$ arising from carboxamide cation $[CONMePh]^+$ (*m/z* 134) decarbonylation and the phenylmethaniminium ion $[CH_2{=}NHPh]^+$ resulting from $[HNMePh]^{+\cdot}$ (*m/z* 107) α-cleavage.[12]

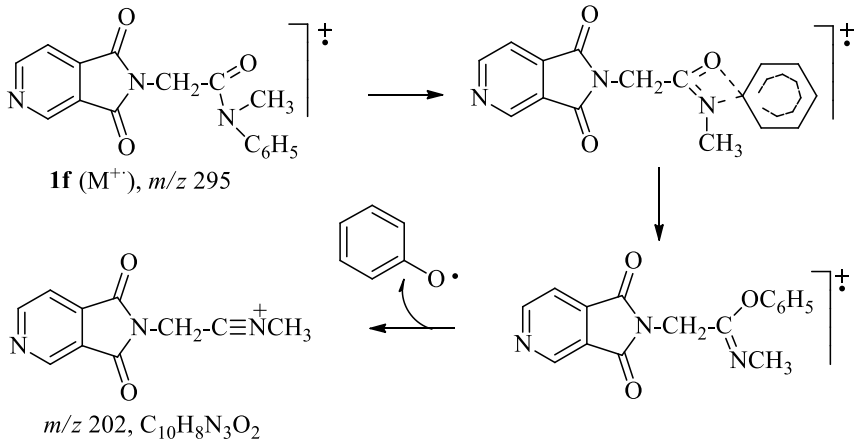
Although compound **1e** spectrum lacks of $[NHEt_2]^{+\cdot}$ radical ion (*m/z* 73), *m/z* 58 ion $[HNEt_2\text{-}Me]^+$ arising from α-cleavage, is observed; therefore Route ***b*** cannot be discarded for this compound.

Route ***c*** leads to the stabilized iminium ion **A** (*m/z* 161), either through an intermediary acyl ion $[M\text{-}NR^1R^2]^+$ (*m/z* 189) which is detected with very low abundance, or by direct α-cleavage of the molecular ion.

1f Spectrum also exhibits ions which are characteristic of *N*-methylanilides at *m/z* 190 and 202, of low intensity but easily recognized in the high mass zone. *M/z* 190 ion results from expulsion of *N*-phenylmethanimine as a consequence of a carboxamide five center rearrangement[13] which requires the presence of a β-hydrogen to carbonyl (Scheme 4). Ion at *m/z* 202 has its origin in the loss of $PhO^{\cdot}$ from the molecular ion. It is an example of amide rearrangement rationalized by Bentley and Johnstone[14] occurring through a tetra-membered transition state in which pπ–centres participation plays a fundamental role (Scheme 5).



Scheme 4. Fragmentation of compound **1f** with loss of *N*-phenylmethanimine.



Scheme 5. Fragmentation of compound **1f** with loss of phenoxide radical.

β-(3,4-Pyridinedicarboximido)propionic acid and esters (2a-c)

Spectra of β-(3,4-pyridinedicarboximido)propionic acid **2a** and its esters **2b** and **2c** show similar features, with low $M^{+\cdot}$ abundances (Table 4). The main fragmentation pathway leads to the base ion at *m/z* 174, of formula $C_9H_6N_2O_2$ compatible with that of the *N*-vinyl-3,4-pyridinedicarboximide (Scheme 6, Route ***a***). It results from the loss of ROH as a consequence of hydrogen rearrangement from the alkyl side chain to a saturated oxigen with adjacent cleavage, followed by the expulsion of CO. MS/MS experiments show that *m/z* 174 ion degrades through two main routes: subsequent loss of two molecules of CO accounting for ions at *m/z* 146 and 118, and expulsion of vinyl isocyanate originating ion at *m/z* 105 and those derived from it (*m/z* 77 y 50).

Route ***b*** begins by the loss of $RO^{\cdot}$ (α-cleavage) leading to acylium ion at *m/z* 203, for which two fragmentation pathways are proposed (Scheme 6). In the first one, ketene is eliminated leading to a prominent iminiun ion **A** (*m/z* 161) (79-83%) and ions derived from them (Scheme 1). In the second one, two molecules of CO are subsequently lost, thus justifying the presence of ions at *m/z* 175 and 147.

Formation of *m/z* 148 ion, for which structure **C** is proposed**,** is probably due to a McLafferty rearrangement (Route ***c***) as the result of a hydrogen transfer from the alkyl side chain to the imide carbonyl group with charge retention on the imide moiety. Thus, the required presence of hydrogen on a β-carbon to imide nitrogen is responsible for the appearance of such ions in this series and not in compounds **1**. Fragmentation follows with loss of $HO^{\cdot}$ affording *m/z* 131 ions.[15] Further loss of $CN^{\cdot}$, CO and HCN leads to ions at *m/z* 105, 103, 77 and 50.

γ-(3,4-Pyridinedicarboximido)butyric acid ethyl ester (3c)

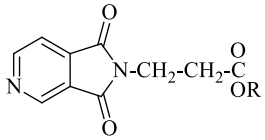
As in the preceding series, the main fragmentation pathways begins with the loss of ROH (Route ***a***) and $RO^{\cdot}$ (Route ***b***), thus originating abundant ions at *m/z* 216 and 217 respectively. Further side chain degradation leads to characteristic ions at *m/z* 189, 188, 175, 174 and 161 (**A**, base ion) as it is shown in Scheme 7.

Although less abundant, spectrum also displays characteristic peaks resulting from hydrogen transfer from trimethylene side chain to imide nucleus: ion **C** at *m/z* 148 resulting from a McLafferty rearrangement (Route ***c***) as in the previous series, and the protonated imide **D** at *m/z* 149 (Route ***d***). Such ion can be proposed to originate through a double hydrogen transfer, from β- and γ-carbon atoms of the alkyl chain and C-N bond cleavage.

N-Benzoylmethyl-3,4- and 2,3-pyridinedicarboximides (1g and 4g)

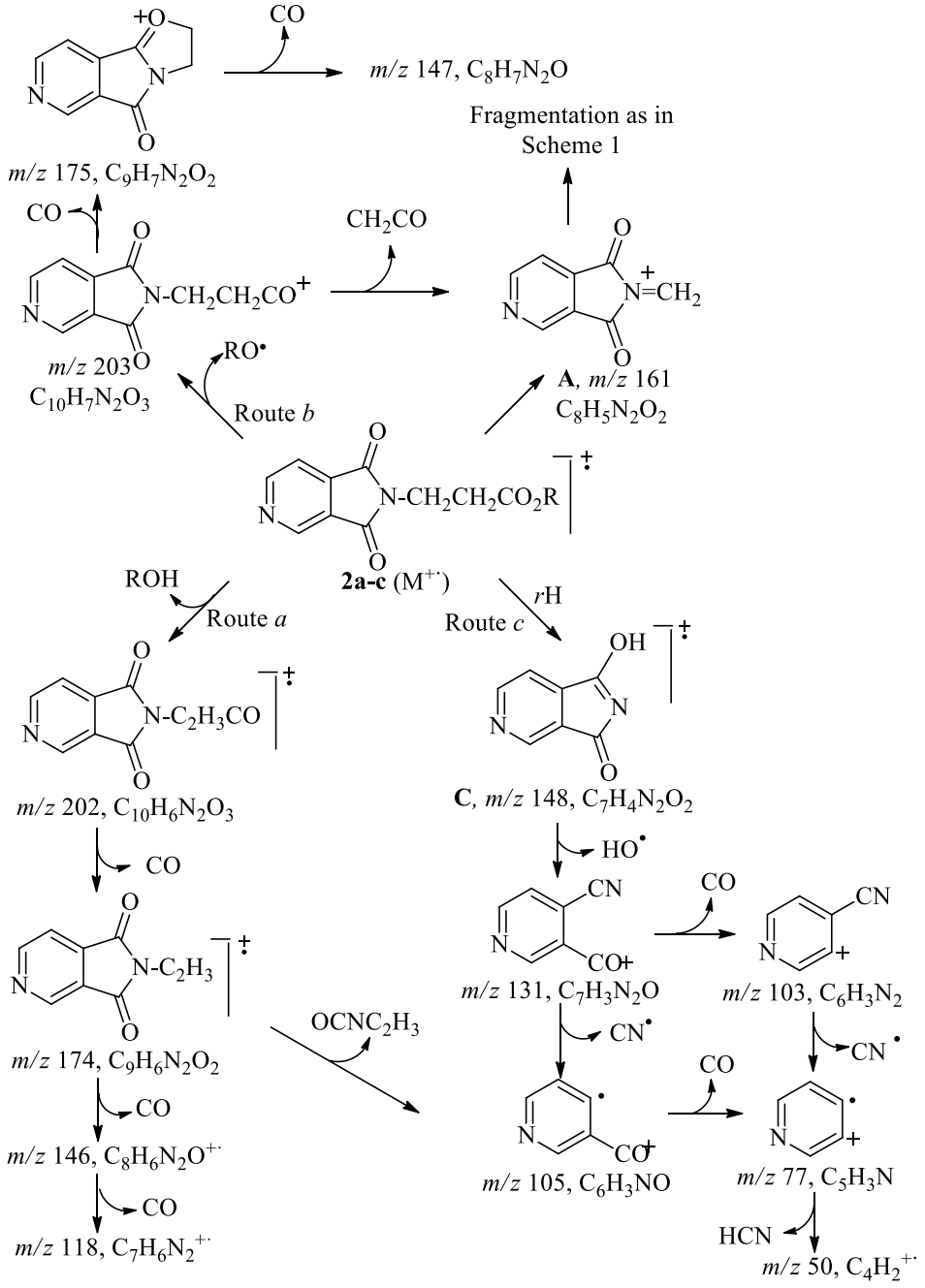
Ketone **1g** and **4g** fragmentations (See Experimental Section) are as expected according to their phenyl ketone character, leading to base ions at *m/z* 105 corresponding to $C_6H_5CO^+$. Instead, the α-cleavage leading to iminium ions **A**,**A'**, is in both cases of low importance. The only observable difference between both compounds is the presence in **4a** spectrum of an ion at *m/z* 238, of low abundance but easily recognized, corresponding to $M^{+\cdot}$ decarbonylation. This fact is again related to the presence of pyridine nitrogen adjacent to imide carbonyl. The effect is in agreement with other substituted pyridine compounds in which differences are observed with substituents in the α- and β-positions.

Table 4. Select fragments in the EI mass spectra of β-(3,4-pyridinedicarboximido)propionic acid **2a** and the corresponding esters **2b,c**

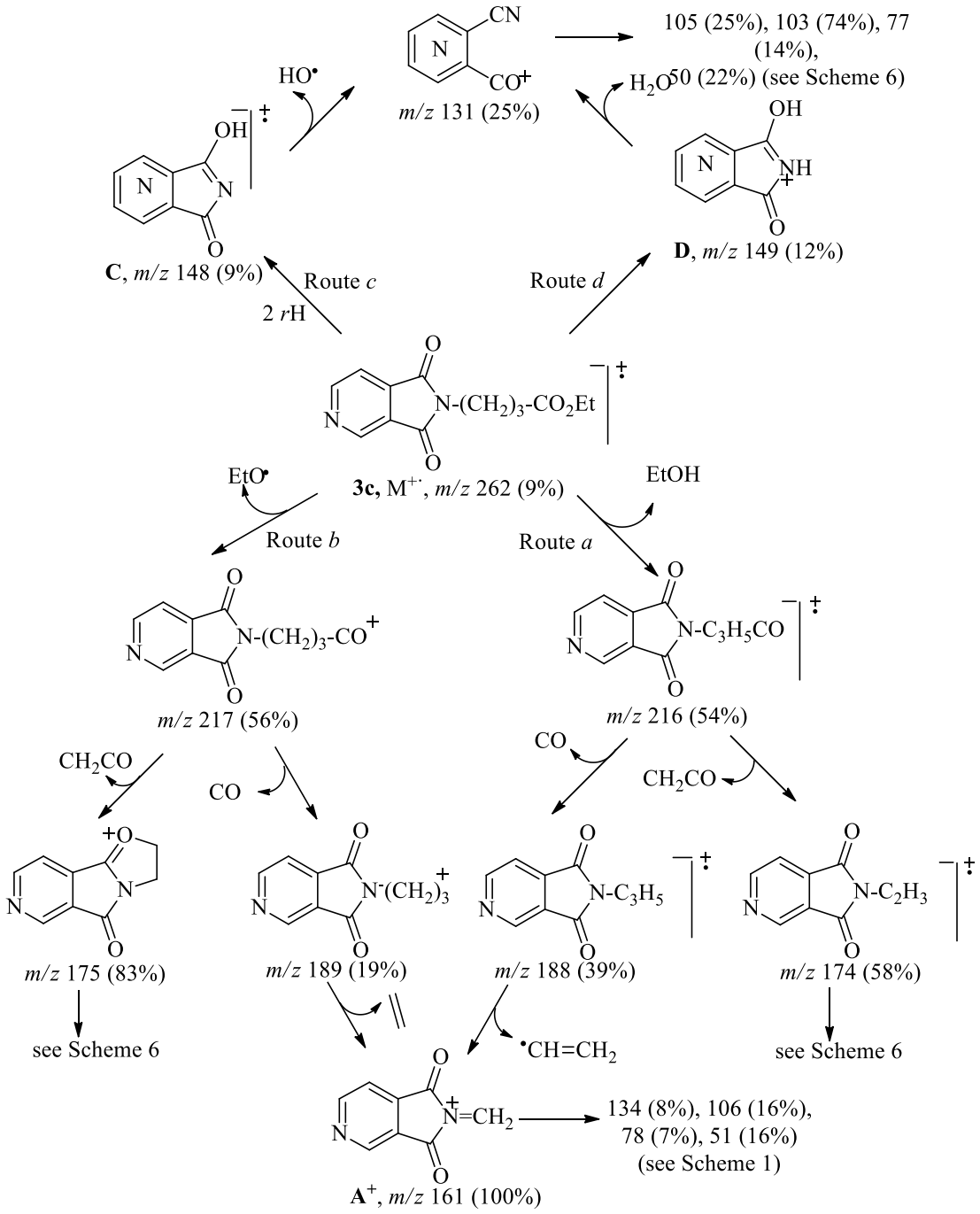


Ion	**2a** (R=H) *m/z* (*RA*%)[a]	**2b** (R=Me) *m/z* (*RA*%)[a]	**2c** (R=Et) *m/z* (*RA*%)[a]
$[M]^{+\cdot}$	220 (4). HRMS: 220.0536. Calcd for $C_{10}H_8N_2O_4$: 220.0484	234 (19)	248 (5)
m/z 203 $[M\text{-}RO]^+$	(5). HRMS: 203.0456. Calcd for $C_{10}H_7N_2O_3$: 203.0457	(32)	(20)
m/z 202 $[M\text{-}ROH]^{+\cdot}$	(12). HRMS: 202.0391. Calcd for $C_{10}H_6N_2O_3$: 202.0378	(50)	(18)
m/z 175	(29). HRMS: 175.0489. Calcd for $C_9H_7N_2O_2$: 175.0508	(36)	(16)
m/z 174	(100). HRMS: 174.0438. Calcd for $C_9H_6N_2O_2$:174.0429	(100)	(100)
m/z 161 $[\mathbf{A}]^+$	(79). HRMS: 161.0359. Calcd for $C_8H_5N_2O_2$: 161.0351	(83)	(79)
m/z 148 $[\mathbf{C}]^{+\cdot}$	(15). HRMS 148.0290. Calcd for $C_7H_4N_2O_2$: 148.0273	(16)	(8)
m/z 147	(31). HRMS: 147.0534. Calcd for $C_8H_7N_2O$: 147.0558	(28)	(9)
m/z 146	(36). HRMS: 146.0493. Calcd for $C_8H_6N_2O$: 146.0480	(36)	(10)
m/z 134 $[\mathbf{A}\text{-}HCN]^+$	(21). HRMS: 134.0262. Calcd for $C_7H_4NO_2$: 134.0242	(18)	(5)
m/z 131	(26). HRMS: 131.0270. Calcd for $C_7H_3N_2O$: 131.0246	(28)	(12)
m/z 118	(8). HRMS: 118.0549. Calcd for $C_7H_6N_2$: 118.0531	(7)	(2)
m/z 106	(25). HRMS: 106.0299. Calcd for C_6H_4NO:106.0293	(20)	(10)
m/z 105	(38). HRMS: 105.0226. Calcd for C_6H_3NO: 105.0215	(32)	(17)
m/z 103	(13). HRMS: 103.0317. Calcd for $C_6H_3N_2$:103.0297	(10)	(4)
m/z 78	(67). HRMS: 78.0291. Calcd for C_5H_4N: 78.0344	(53)	(19)
m/z 77	(60). HRMS: 77.0261. Calcd for C_5H_3N: 77.0265	(44)	(15)

[a]Relative abundances (*RA*) indicated between parenthesis correspond to low resolution spectra at 70 eV.



Scheme 6. Fragmentation pathways of β-3,4-pyridinedicarboximidopropionic acid **2a** and esters **2b,c** under EI conditions.



Scheme 7. Fragmentation pathways of γ-3,4-pyridinedicarboximidobutyric acid ethyl ester **3c** under EI conditions.

Conclusions

The fragmentation of a series of ω-(3,4-pyridinedicarboximido)alkanoic acids and their derivatives **1-3** under EI show differences depending on the length and the function of the imide *N*-substituent.

Generally, main fragmentations lead to total or partial loss the side chain with charge retention on the imide moiety. Instead, decomposition of the 3,4-pyridinedicarboximidoacetamides reflects the strong tendency of carboxamide nitrogen to undergo reactions originating ions with charge retention: $[CONR^1R^2]^+$, $[NR^1R^2]^+$ and $[HNR^1R^2]^+$.

The difference amongst 3,4-pyridinedicarboximides **1-3** to the corresponding 2,3-pyridinedicarboximides **4** is observed in the fragmentations which produce the cleavage of the imide nucleus.

Experimental Section

General. Mass spectra were obtained operating under electron impact at 70 eV unless otherwise indicated. Low resolution mass spectra at were recorded with a GC-MS Shimadzu QP-1000 spectrometer. High resolution mass spectra, were acquired with *a model* GCT *(Waters, Milford, MA, USA)*, operating at a 8000 resolving power (50% valley definition) using heptacose (*m/z* 219) as the reference compound. Samples were dissolved in chloroform or methanol and introduced into the spectrometer through a gas chromatograph Agilent, model 6890N (injector temperature: 300 ºC, initial temperature: 100 ºC, temperature "ramp": 20 ºC /min, final temperature: 300 ºC). Spectra at 20 and 35 eV were recorded in the GCT spectrometer (Waters) or in a Thermo DSQ II spectrometer. MS/MS analysis were obtained with a triple quadrupole 1200L (Varian, Walnut Creek, CA, USA) associated to a chromatograph Varian 3800. The conditions are: ionizing energy, 70 eV; collision gas: argon at a pressure of 2.04 mTorr; collision energy: 16v.
Compounds **1a,4a,**[16] **1c,1e-g**[3d] and **4b-d,g**[17] were synthesized according literature procedures. Preparation and analytical characterization of new compounds are described below. Melting points were taken on a Büchi capillary apparatus and are uncorrected. The ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker MSL 300 MHz spectrometer employing TMS as internal reference. Deuteriochloroform or DMSO-d_6 were used as the solvent, and the standard concentration of the samples for ^{1}H-NMR was 10 mg/mL and 25 mg/mL for ^{13}C-NMR. Chemical shifts are reported in ppm (δ) relative to TMS as an internal standard. Splitting multiplicities are reported as singlet (s), broad signal (br s), doublet (d), triplet (t), quartet (q), and multiplet (m).

Methyl 3,4-pyridinedicarboximidoacetate (1b). A mixture of 3,4-pyridinedicarboximide (148 mg, 1 mmol), triethylamine (0.56 mL, 4 mmol), methyl chloroacetate (0.11 mL, 1.2 mmol) and DMF (2 mL) was heated for 3 h in an oil bath (65 °C). The reaction mixture was poured into ice-water and the resulting solid filtered, washed with water and recrystallized. Yield 62%; mp 61-63 ºC (from 2-propanol); ^{1}H NMR δ ($DCCl_3$) 9.19 (s, 1H, H-2), 9.11 (d, $^3J_{5,6}$= 4.6 Hz, 1H, H-6), 7.82 (d, $^3J_{5,6}$= 4.6 Hz, 1H, H-5), 4.45 (s, 2H, NCH_2), 3.78 (s, 3H, OCH_3); ^{13}C NMR δ ($DCCl_3$) 167.1, 166.2 and 165.9 (3 CO), 155.8 (C-6), 145.0 (C-2), 139.3 (C-4), 125.7 (C-3), 117.1 (C-5), 52.8 (OCH_3), 38.9 (NCH_2). Anal. Calcd for $C_{10}H_8N_2O_4$: C, 54.55; H, 3.66; N, 12.72. Found: C, 54.61; H, 3.70; N, 12.79.
β-(3,4-Pyridinedicarboximido)propionic acid (2a). A mixture of 3,4-pyridinedicarboxylic anhydride (149 mg, 1 mmol), β-aminopropionic acid (82 mg, 1.1 mmol) and DMF (2 mL) was

mantained with stirring for 50 min at 110 ºC. The mixture was cooled, triturated with cold water and then filtered. Yield 80%; mp 202-204ºC (methanol). ^{1}H NMR δ (DMSO) 13.02 (bs, 1H, OH), 9.11 (s, 1H, H-2), 9.08 (d, $^3J_{5,6}$= 4.7 Hz, 1H, H-6), 7.89 (d, $^3J_{5,6}$= 4.7 Hz, 1H, H-5), 3.79 (t, $^3J_{CH2-CH2}$= 7.3 Hz, 2H, NCH_2), 2.60 (t, $^3J_{CH2-CH2}$= 7.3 Hz, 2H, CH_2CO); ^{13}C NMR δ (DMSO) 167.5, 166.9 and 163.0 (3 CO), 155.5 (C-6), 147.0 (C-2), 139.5 (C-4), 125.8 (C-3), 119.4 (C-5), 38.2 (NCH_2), 33.3 (*C*H_2CO). Anal. Calcd for $C_{10}H_8N_2O_4$: C, 54.55; H, 3.66; N, 12.72. Found: C, 54.48; H, 3.72; N, 12.68.

Methyl β-(3,4-pyridinedicarboximido)propionate (2b). To a solution of acid **2a** (110 mg, 0.5 mmol) in anhydrous methanol (5 mL) an ethereal solution of diazomethane was added in small portions until the solution acquired a pale yellow colour. After 2 h at room temperature, the reaction mixture was concentrated *in vacuo* and the crude product was purified by column chromatography (silica gel 60, 0.063-0.200 mesh) eluting with DCM. Yield 32%; oil; ^{1}H NMR ($DCCl_3$) δ 9.10 (s, 1H, H-2), 9.04 (d, $^3J_{5,6}$= 4.9 Hz, 1H, H-6), 7.77 (d, $^3J_{5,6}$= 4.9 Hz, 1H, H-5), 3.99 (t, $^3J_{CH2-CH2}$= 7.1 Hz, 2H, NCH_2), 3.75 (s, 3H, OCH_3), 2.70 (t, $^3J_{CH2-CH2}$= 7.1 Hz, 2H, CH_2CO); ^{13}C NMR δ ($DCCl_3$) 167.2, 166.8 and 166.1 (3 CO), 155.8 (C-6), 145.4 (C-2), 138.9 (C-4), 125.4 (C-3), 117.6 (C-5), 51.7 (OCH_3), 34.1 (NCH_2), 33.2 (*C*H_2CO). Anal. Calcd for $C_{11}H_{10}N_2O_4$: C, 56.41; H, 4.30; N, 11.96. Found: C, 56.34; H, 4.35; N, 11.90.

Ethyl β-(3,4-pyridinedicarboximido)propionate (2c). A mixture of 3,4-pyridinedicarboximide (146 mg, 1 mmol), ethyl β-bromopropionate (0.11 mL, 1.1 mmol), triethylamine (0.56 mL, 4 mmol), and DMF (2 mL) was heated for 9 h in an oil bath at 50 °C. The reaction mixture was poured into ice-water and the aqueous layer was extracted with DCM (2 x 4 mL). The combined organic layers were dried over anhydrous sodium sulfate. After filtration the solvent was evaporated and the crude product was purified by column chromatography (silica gel 60, 0.063-0.200 mesh) eluting with DCM. Yield 12%; oil; ^{1}H NMR δ ($DCCl_3$) 9.15 (s, 1H, H-2), 9.06 (d, $^3J_{5,6}$= 4.9 Hz, 1H, H-6), 7.75 (d, $^3J_{5,6}$= 4.9 Hz, 1H, H-5), 4.12 (q, $^3J_{CH2-CH3}$= 7.1 Hz, 2H, OCH_2), 4.03 (t, $^3J_{CH2-CH2}$= 7.2 Hz, 2H, NCH_2), 2.72 (t, $^3J_{CH2-CH2}$= 7.2 Hz, 2H, *C*H_2CO), 1.20 (t, $^3J_{CH2-CH3}$= 7.1 Hz, 3H, CH_3); ^{13}C NMR δ ($DCCl_3$) 166.6, 166.3 and 166.1 (3 CO), 156.0 (C-6), 145.1 (C-2), 139.0 (C-4), 125.4 (C-3), 118.2 (C-5), 62.1 (OCH_2), 33.8 (NCH_2), 33.0 (*C*H_2CO), 14.1 (CH_3). Anal. Calcd for $C_{12}H_{12}N_2O_4$: C, 58.06; H, 4.87; N, 11.28. Found: C, 57.98, H, 4.92; N, 11.21.

Ethyl γ-(3,4-pyridinedicarboximido)butyrate (3c). This compound was obtained employing similar method to described above for compound **2c** using ethyl γ-bromobutyrate (0.15 mL, 1.1 mmol) and heating at 60 ºC for 3 h. Yield 38%; oil; ^{1}H NMR δ ($DCCl_3$) 9.16 (s, 1H, H-2), 9.10 (d, $^3J_{5,6}$= 4.9 Hz, 1H, H-6), 7.79 (d, $^3J_{5,6}$= 4.9 Hz, 1H, H-5), 4.24 (t, $^3J_{CH2-CH2}$= 7.7 Hz, 2H, NCH_2), 4.08 (q, $^3J_{CH2-CH3}$= 7.1 Hz, 2H, OCH_2), 2.43 (t, $^3J_{CH2-CH2}$= 7.7 Hz, 2H, CH_2CO), 2.10 (m, $^3J_{CH2-CH2}$= 7.7 Hz, 2H, CH_2-C*H*$_2$-CH_2), 1.21 (t, $^3J_{CH2-CH3}$= 7.1 Hz, 3H, CH_3); ^{13}C NMR δ ($DCCl_3$) 167.2, 166.8 and 166.0 (3 CO), 155.5 (C-6), 144.6 (C-2), 139.5 (C-4), 125.9 (C-3), 116.7 (C-5), 62.0 (OCH_2), 37.6 (NCH_2), 34.3 (*C*H_2CO), 30.6 (CH_2-*C*H_2-CH_2), 13.7 (CH_3). Anal. Calcd for $C_{13}H_{14}N_2O_4$: C, 59.54; H, 5.38; N, 10.68. Found: C, 59.47, H, 5.42; N, 10.61.

Mass and relative abundance of characteristic ions of compounds **1a-f**, **2a-c** and **4b-d** are presented in Tables 1-4. Data for compound **3c** are depicted in Scheme 7.

MS of compound (1g). (70 eV): *m/z* (*RA* %) 266 ($M^{+\cdot}$, 3), 161 (**A**$^+$, 6), 105 ($PhCO^+$, 100), 77 (Ph^+, 56), 51 ($C_4H_3^+$, 26).
MS of compound (4g). (70 eV): *m/z* (*RA* %) 266 ($M^{+\cdot}$, 6), 238 ($M^{+\cdot}$-CO, 2),161 (**A**$^+$, 6), 105 ($PhCO^+$, 100), 77 (Ph^+, 76), 51 ($C_4H_3^+$, 30).
HRMS of 3,4-pyridinedicarboximide. *m/z* (*RA*%) 148.0271 (100%), $[M]^{+\cdot}$, calcd for $C_7H_4N_2O_2$: 148.0273; 105.0222 (59), $[M\text{-}HNCO]^{+\cdot}$, calcd for C_6H_3NO: 105.0215; 77.0267 (39), $[M\text{-}HNCO\text{-}CO]^{+\cdot}$, calcd for C_5H_3N: 77.0265; 50.0170 (34), $[M\text{-}HNCO\text{-}CO\text{-}HCN]^{+\cdot}$, calcd for C_4H_2: 50.0157.
HRMS of *N*-methyl-3,4-pyridinedicarboximide. *m/z* (*RA*%) 162.0434 (100), $[M]^{+\cdot}$, calcd for $C_8H_6N_2O_2$: 162.0429; 161.0371 (2), $[M\text{-}H]^+$, calcd for $C_8H_5N_2O_2$: 161.0351; 133.0390 (3), $[M\text{-}H\text{-}CO]^+$, calcd for $C_7H_5N_2O$: 133.0402; 118.0534 (8), $[M\text{-}CO_2]^{+\cdot}$, calcd for $C_7H_6N_2$: 118.0531; 106.0290 (5), $[M\text{-}HCN\text{-}CO]^{+\cdot}$, calcd for C_6H_5NO: 106.0293; 105.0230 (23), $[M\text{-}MeNCO]^{+\cdot}$, calcd for C_6H_3NO: 105.0215; 77.0270 (17), $[M\text{-}MeNCO\text{-}CO]^{+\cdot}$, calcd for C_5H_3N: 77.0265.

Acknowledgements

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6. We confirmed the data reported by Johnstone[1a] and determined the composition of the main peaks by HRMS (see Experimental Section).

7. Relative abundances of *m/z* 162 ion at 70 and 20 eV using a CGT Waters spectrometer: 47% and 97% respectively).
8. In our previous work[2] based on HRMS data, it was considered that the main degradation pathway of ion at 134 (**B'**-CO) involved the loss of $CH_{2=}NH$ leading to an ion at *m/z* 105 (C_6H_3NO). This must now be rectified in the light of MS/MS experiments performed lately and presented in the present work, which demonstrate that the main transformation of *m/z* 134 ions leads to ion *m/z* 79 (C_5H_5N) (corresponding to pyridine odd electron ion). Ion at *m/z* 105 (C_6H_3NO) and those derived from it (*m/z* 77 and 50) are common in this type or pyridine derivatives. They may have multiple origins and probably arise from another fragmentation pathway of $M^{+\cdot}$.
9. MS of compound **1c** at 20 eV using a Thermo DSQ II spectrometer: *m/z* (*RA* %) 234 (77), 206 (5), 189 (27), 162 (100), 161 (63), 134 (30), 106 (13), 105 (15), 78 (12).
10. Relative abundances (*RA* %) of select ions at 70, 35 and 20 eV using a CGT Waters spectrometer: *m/z* 162 (20, 36 and 77% respectively), *m/z* 134 (5, 7 and 20% respectively) and *m/z* 79 (8, 12 and 16% respectively).
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