

Fragmentations processes of 3-coumarinyl carboxylates in ESI / MS and their Correlation with the Electronic charges of their atoms

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Abstract

3-coumarinyl carboxylates are 3-hydroxyl-coumarin derivatives obtained by O-acylated. In this work, we have studied the correlation between electronic charges of atoms and the fragmentation processes of these compounds. The method has been successfully applied many times for EIMS, but only one time for ESI/MS. In this paper, we would like to apply the method to the ESI/MS spectra of another sery of 3-coumarinyl carboxylates. Good correlations was obtained.

Keywords: 3-coumarinyl carboxylate, ESI/MS, fragmentations, Electronic charge.

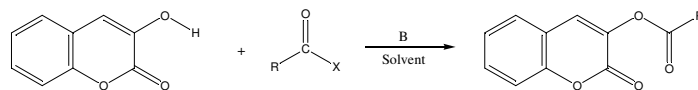
Introduction

Natural or synthetic coumarin derivatives are of great interest, since many of them show several important properties¹⁻⁹. Furthermore, coumarins derivatives are well-known fluorescent dyes⁷⁻¹¹ and high photoluminescent compounds¹². They have been intensively investigated because of their biologic properties. So they have been identified as anticoagulant¹, antibiotic⁹, antiviral, cytotoxic^{9,11} and herbicides compounds. Additionally, coumarin derivatives are widely used as food, perfumes and cosmetic. complements^{10,13}. Most of their spectra (UV-Visible, IR, MNR and Mass) have also been reported^{14,15}. Literature shows that the mass spectra study in correlation with electronic charges of atoms has already been described. So, the correlation between the fragmentation processes in EIMS and the electronic charges of atoms of some monosubstituted and disubstituted coumarins have been reported¹⁶⁻¹⁸. The method has been applied only one time to ESI/MS. It has been successfully applied both on EIMS¹⁹ and ESI/MS of 4-acyl isochroman-1, 3-diones²⁰. The electronic charges of the atoms were performed by AM1 semi empirical method²⁰. It has been found that fragmentations processes in eims take place generally at the level of atoms bearing high negative charge. Nevertheless, in positive mode ESI/MS, fragmentations are guided by the atoms bearing high positive charge.

So, in Mass Spectrometry, the fragmentations are most often obtained at the level of atoms exhibiting the same type of charge than the ionization projectile. In EIMS the atom must bear a high positive charge, but a high negative charge in ESI/MS. So, it would be possible to predict and explain most of the behavior of organic compounds in mass spectrometry by using electronic charges of atoms. In this paper, we should like to apply the method using the electronic charges of atoms in the study of the fragmentations of title compounds in ESI/MS. Interesting results have been obtained.

Material and Methods

Preparation of 3-coumarinyl carboxylates 1: The method used for the synthesis of compounds **1** have been early described for 4-acyl isochroman-1,3-diones²¹. Thus, action of acid chlorides or acid anhydrides on 3-hydroxycoumarin in the presence of an appropriated base, lead to give compounds **1**, with more than 60% yield (scheme-1). They have been identified by IR, ¹H and ¹³C NMR spectra.



Scheme-1

Synthesis of 3-coumarinyl carboxylates 1

X = Cl or OCOR, B = Pyridine (py) or Triethylamine (Et₃N). **1a** : R = CH₃ ; **1b** : R = C₂H₅ ; **1c** : R = C₆H₅ ; **1d** : R = *p*-ClC₆H₄ ; **1e** : R = *p*-NO₂C₆H₄ ; **1f** : R = *p*-CNC₆H₄ ; **1g** : R = *p*-MeOC₆H₄ ; **1h** : R = 3,5-(NO₂)₂C₆H₃.

Recording spectra: ESI/MS spectra, described in the below table 1 have been recorded on a 3200 QTRAP (Applied Biosystems SCIEX) mass spectrometer apparatus equipped with an atmospheric pressure ionization source (API). The sample is dissolved in 450mL of dichloromethane and diluted at 1/100 in a 3mM methanolic solution of ammonium acetate. It is then ionized in positive electrospray mode in the following conditions: electrospray tension (ISV): 5500V; Orifice tension (OR): 20V; pression of nebulisation gas (air): 20psi; debit: 10μL/min. The fragmentation spectra are obtained after dissociation induced by collision; collision gas is N₂ ; energy of collision 20eV; two quadripôles tandem mass analysers. Results are reported in the tables 1.

AM1 Calculation of electronic charges: Electronic charges of atoms have been obtained by Austin Model 1 semi empirical method²² with a "Chem3D Ultra 8" software, A "Pentium 4" computer has been used. Results are reported in tables 2, 3, 4 and 5.

Table-1
ESI/Mass Spectra of compounds 1

1a R = CH ₃	1b R = C ₂ H ₅	1c R = C ₆ H ₅	1d R = <i>p</i> -ClC ₆ H ₄
m/z %	m/z %	m/z %	m/z %
205[MH] ⁺ 100	219[MH] ⁺ 89.33	267[MH] ⁺ 29.33	301/303[MH] ⁺ 40
163 53,33	163 100	105 100	139/ 141 100
-	57 53.33	-	-

Table-2
Electronics charges (carbon)

1e R = <i>p</i> -NO ₂ C ₆ H ₄	1f R = <i>p</i> -CNC ₆ H ₄	1g R = <i>p</i> -MeOC ₆ H ₄	1h R = (NO ₂) ₂ C ₆ H ₃
m/z %	m/z %	m/z %	m/z %
312[MH] ⁺ 58.66	292[MH] ⁺ 31,81	297[MH] ⁺ 13,33	357[MH] ⁺ 100
285 100	130 100	135 100	295 58,66
-	-	-	-

Table-3
Electronics charges (carbon)

R	C ₂	C ₃	C ₄	C ₅	C ₆	C ₇	C ₈
CH ₃	0.3937	-0.0332	-0.1480	-0.1249	-0.2183	0.1455	-0.2012
CH ₃ CH ₂	0.3993	-0.0392	-0.0920	-0.12554	-0.2179	-0.1477	-0.2003
C ₆ H ₅	0.3916	-0.0258	-0.8525	-0.1262	-0.2185	-0.1461	-0.2010
<i>p</i> -ClC ₆ H ₄	0.3982	-0.0347	-0.0908	-0.1268	-0.2154	-0.1473	0.1997
<i>p</i> -NO ₂ C ₆ H ₄	0.3395	0.1613	-0.1275	-0.1282	-0.1931	-0.0404	-0.2281
<i>p</i> -CNC ₆ H ₄	0.3829	-0.0254	-0.1193	-0.1306	-0.2117	-0.1472	-0.1964
<i>p</i> -MeOC ₆ H ₄	0.3746	-0.1721	-0.1286	-0.1320	-0.2101	-0.1513	-0.1958
3,5-(NO ₂) ₂ C ₆ H ₃	0.3029	0.3001	-0.1512	-0.1234	-0.1625	0.0991	-0.2487

Table-4
Electronics charges (carbon)

R	C ₉	C ₁₀	C ₁₁	C ₁₂	C ₁₃	C ₁₄	C ₁₅
CH ₃	0.1088	-0.0798	0.3516	-0.3930	-	-	-
CH ₃ CH ₂	-0.1031	-0.1426	0.3527	-0,2647	-0.3522	-	-
C ₆ H ₅	0.1094	-0.1480	0.4092	-0.1323	-0.1236	-0.2110	-0.1565
<i>p</i> -ClC ₆ H ₄	0.1082	0.1399	0.4053	-0.1223	-0.1169	-0.1242	-0.0526
<i>p</i> -NO ₂ C ₆ H ₄	0.1676	-0.0744	0.4281	-0.1245	-0.1382	-0.1193	-0.0721
<i>p</i> -CNC ₆ H ₄	-0.0956	-0.1278	0.4071	-0.0974	-0.1244	-0.1686	0.0132
<i>p</i> -MeOC ₆ H ₄	0.0876	-0.1178	0.4261	-0.1627	-0.0854	-0.2867	-0.1274
3,5-(NO ₂) ₂ C ₆ H ₃	0.18548	0.0460	0.3912	-0.1810	-0.0186	-0.0667	-0.0019

Table-5
Electronics charges (carbon)

R	C ₁₆	C ₁₇	O ₁	O ₂	O ₃	O ₄
CH ₃	-	-	-0.2281	-0.3029	-0.2635	-0.3542
CH ₃ CH ₂	-	-	-0.2292	-0.2997	-0.2552	-0.3625
C ₆ H ₅	-0.2090	-0.1272	-0.2274	-0.2988	-0.2628	-0.3515
<i>p</i> -ClC ₆ H ₄	-0.1968	-0.1965	-0.2214	-0.2971	-0.3595	-0.2485
<i>p</i> -NO ₂ C ₆ H ₄	-0.1419	-0.1267	-0.1816	-0.1681	-0.2441	-0.2636
<i>p</i> -CNC ₆ H ₄	-0.1699	-0.1443	-0.1837	-0.3202	-0.2274	-0.3488
<i>p</i> -MeOC ₆ H ₄	-0.2314	0.0896	-0.2015	-0.1897	-0.3169	-0.34280
3,5-(NO ₂) ₂ C ₆ H ₃	-0.0648	-0.0571	-0.0968	-0.0721	-0.1369	-0.2109

Table-6
Charge of atoms of substituent X

X	Cl	N	C	O	O	N	O	O
Cl	-0,00890	-	-	-	-	-	-	-
NO ₂	-	0.5190	-	-0.3177	-0.3117	-	-	-
CN	-	-	-0.0731	-	-0.0644	-	-	-
OCH ₃	-	-	-0.2015	-0.2477	-	-	-	-
(NO ₂) ₂	-	0.3927	-	-0.3168	-0.2293	0.3958	-0.2539	-0.2688

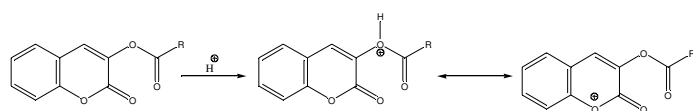
Results and Discussion

Modes of fragmentations: In the hydrocarbon skeleton of compounds **1**, it is notable that only the two atoms of carbon, C₂ and C₁₁, present a high positive charge. This could explain the small number of fragmentations. So, only two kinds of fragmentations have been obtained for each compound. In the early studies, the same results have been obtained and it has been found that the fragmentations processes are directed by the atoms exhibiting the same type of charge than the one of ionization projectile. So, in positive mode ESI/MS of the compounds **1**, only these two carbons would guide the fragmentations¹⁹.

Fragmentations of compounds 1 in ESI-MS: Formation of the pseudo molecular ion [MH]⁺.

The pseudo molecular ion [MH]⁺ has been described to be obtained by the reaction shown in the below scheme 2.

It is remarkable that the formation of this ion is obtained at the level of heteroatom under SP³ hybridization (O₂ and O₃). This can be explain by the easiest mobility of p electrons doublets and their best ability to react with acids (scheme 2)¹⁹.

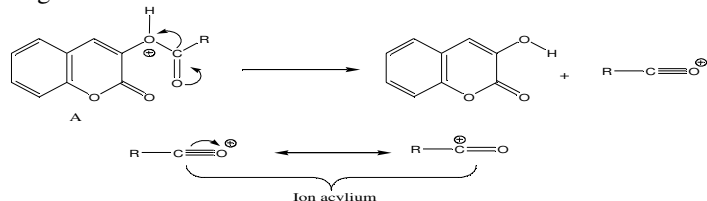


1a : R = CH₃, MH⁺ = 205 ; **1b** : R = C₂H₅, MH⁺ = 219 ; **1c** : R = C₆H₅, MH⁺ = 267 ; **1d** : R = *p*-ClC₆H₄, MH⁺ = 301/303 ; **1e** : R = *p*-NO₂C₆H₄, MH⁺ = 312 ; **1f** : R = *p*-NC₆H₄, MH⁺ = 292 ; **1g** : R = *p*-CH₃OC₆H₄, MH⁺ = 297 ; **1h** : R = 3,5-(NO₂)₂C₆H₃, MH⁺ = 358

Scheme-2

Formation of pseudo molecular ions A and B

Formation of acylium ion: The pseudo molecular ion A described in scheme 2, leads to the formation of acylium fragment as shown in the below scheme 3.



Scheme-3

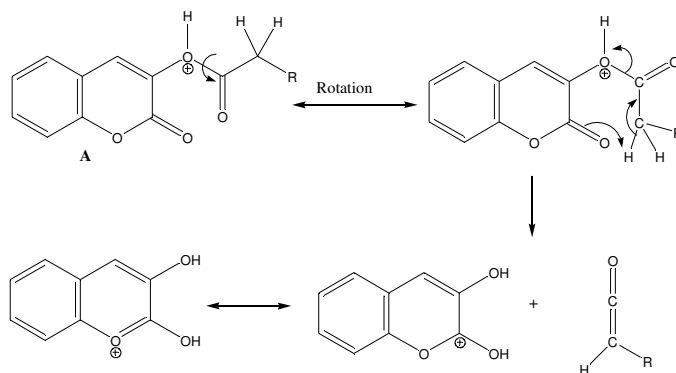
Formation of ion acylium

1b : R = C₂H₅, m/z = 57 ; **1c** : R = C₆H₅, m/z = 105 ; **1d** : R = *p*-ClC₆H₄, m/z = 139/141 ; **1e** : R = *p*-NO₂C₆H₄, m/z = 150 ; **1f** : R = *p*-CNC₆H₄, m/z = 130 ; **1g** : R = *p*-CH₃OC₆H₄, m/z = 135 ; **1h** : R = 3,5-(NO₂)₂C₆H₃, m/z = 196.

This fragmentation has been guided by the carbon C₁₁, which is highly positively charged. This result is in accordance with the early results¹⁷⁻²⁰, which stipulated that “the fragmentations

processes take place at the level of atoms bearing the same type of charge as the projectile particle used for ionization”. For ESI/MS of compounds **1**, these atoms are C₂ and C₁₁. Surprisingly, it is notable to observe that the compound **1a** (R = CH₃) does not present this fragment. Due to the very high negative charge of its carbon C₁₂ (-0.3930), the most high negative charge of this compound, this carbon C₁₂ could equilibrate the charge of C₁₁ (+0.3516) and obstruct this fragmentation. For the other compounds, this situation does not exist.

An atypical fragmentation: It has been observed that when R is a methyl moiety (R = CH₃), the acylium cation is not formed. It has been obtained on behalf of this acylium cation, an atypical fragmentation, not only for this compound **1a**, but for **1b** (R = C₂H₅) too. In both the cases when R is an aliphatic moiety, it is produced a fragment with m/z = 163Da. This fragmentation could take place by the lost of a neutral ketene molecule (R-CH=C=O). It is possible to explain this fragmentation by the follow scheme 4, from the pseudo molecular ion A. Considering the high positive charge of atoms C₂ and C₁₁, which can guide the process, it is reasonable to admit the follow mechanism, shown in the scheme 4 for the formation of this fragment.



R = H or CH₃

Scheme-4

Process of formation of the fragment m/z = 163

This fragmentation, initiated by C₂, leads to give a particularly stable cation as the 2,3-dihydroxy-1-benzopyrylium cation. The compounds with an aromatic moiety are not able to give this cation, due to the absence of a removable hydrogen on their carbon C₁₂. When R is an aliphatic moiety, this hydrogen has an acidic character due to its α position from a carbonyl group (C₁₁). Moreover, due to its initiation by C₂, this fragmentation could take place when R is all type of aliphatic moiety bearing at least, one atom of hydrogen on its C₁₂.

Conclusion

In positive mode ESI/MS, the fragmentation of molecular ions [MH]⁺ of organic compounds takes place more often, at the level of the elements with a significant positive charge, as C₂ and C₁₁ for the title compounds **1**. As observed in the table of

electronic charges of atoms, the compounds **1** contain only two high positively charged atoms that strongly influence their fragmentations. The small numbers of fragmentations in positive mode ESI-MS could thus be explained through the reduced number of high positively charged atoms. In this study, we found, one more time, that there is a relationship between the nature of the charge of the projectile used to obtain the ionization and the nature of the charge of atoms which orientate the fragmentation processes. These charges must have the same nature. This relationship could orientate the research of fragmentations processes. So, the way for explaining and predicting fragmentations processes in mass spectrometry by using the electronic charges of atoms of the hydrocarbon skeleton of organic compounds seemed to be really open.

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