

## SHORT COMMUNICATION

### ANALYSIS OF FRAGMENTATIONS OF COUMARINS IN MASS SPECTROMETRY USING THE ELECTRONIC CHARGES OF ATOMS

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**ABSTRACT.** Recently, we examined a new approach to understand the fragmentations of monosubstituted and disubstituted coumarins with halogens and/or oxygenated moieties, through the electronic charges of their atoms, performed by AM1 method. A good correlation was found between electronic charges of atoms and fragmentation processes. In the present study, another series of coumarins with nitrogenated moieties is used to verify the reliability of this method.

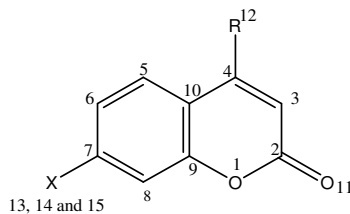
**KEY WORDS:** 4,7-Disubstituted coumarins, Nitrogenated moiety, AM<sub>1</sub>, Electronic charge, Fragmentation, Mass spectrometry

## INTRODUCTION

Because of their interesting properties, coumarins have been extensively studied and synthesised by several methods in laboratories [1-3]. They have many biological properties and their physical and chemical properties have also been studied [4-7]. They have been reported for antifungal and anti-inflammatory [8], antimicrobial and antibacterial [9], and on top, anti-HIV [10] activities. Recently, we found a good correlation between the fragmentation processes in mass spectrometry of two series of coumarins and the electronic charges of their atoms [11-12]. We found that the fragmentation took place at the level of atoms bearing high negative charges. The coumarins used in the previous studies were substituted by halogens or oxygenated moieties. In the present paper, another series of coumarins with nitrogenated moieties is used for comparison with atom of oxygenated one in order to verify the reliability of the method.

## EXPERIMENTAL

Structures of coumarins used for this study are presented in Scheme 1:



**1a:** R = CH<sub>3</sub>, X = NH<sub>2</sub>; **1b:** R = CF<sub>3</sub>, X = NH<sub>2</sub>; **1c:** R = CF<sub>3</sub>, X = N(CH<sub>3</sub>)<sub>2</sub>;  
**1d:** R = CH<sub>3</sub>, X = N(C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>; **1e:** R = CF<sub>3</sub>, X = OH

Scheme 1. Structure of coumarins **1**.

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All the compounds are commercial compounds, except **1e** which was prepared by Peschmann reaction [1]. Thus, 3-hydroxyphenol reacts smoothly with ethyl trifluoromethyl acetyl acetate in nitrobenzene in the presence of sulfuric acid to give 7-hydroxy-4-trifluoromethyl coumarin **1e** in good yields. The mass spectra were been recorded by electronic impact mass spectrometry (EIMS) on a CPG-JSM AX505 apparatus (JEOL, Tokyo, Japan). The electronic charges of atoms were performed by Austin Model 1 (AM1) semi empirical method [13], using "Chem3D Ultra8" software on a "Pentium 4" computer (Germany).

## RESULTS AND DISCUSSION

All the spectra present a good molecular ion ( $M^+$ ) with high stability ( $43.94 \leq \% \leq 100$ ). Near these molecular ions, it may be noticed the presence of  $m/z = (M+1)$  and  $(M-1)$  ions with significant relative abundance. The presence of odd molecular ions in mass spectra is indicative of the identity of the nitrogenated compounds. In previous papers [11-12], fragmentations of coumarins have been found to occur near the atoms bearing high negative charges. When X = OH or halogen,  $O_{11}$  is known to be the site of the electronic beam impact, but when X is nitrogen moiety, the high negative charge of nitrogen suggests that  $N_{13}$  could also be a site of the electronic beam impact, particularly in the case of dialkyl substituted nitrogen. In this case, the more donating are the substituents on nitrogen atom, the more stable is the ammonium cation resulting. All compounds exhibit only three to six important fragments, with relative abundance above 10 %. Table 1 summarizes the mass spectral data for the coumarins studied here, and Tables 2 and 3, the electronic charges of their atoms.

Table 1. Mass spectra of coumarins **1**.

<b>1a</b>		<b>1b</b>		<b>1c</b>		<b>1d</b>		<b>1e</b>	
m/z	%	m/z	%	m/z	%	m/z	%	m/z	%
176	11.36	230	12.12	258	12.21	232	7.57	231	9.02
175 (M)	100	229 (M)	100	257 (M)	100	231 (M)	43.94	230 (M)	79.69
174	2.27	228	2.27	256	40.45	230	3.40	229	1.11
148	8.33	211	3.78	242	2.67	217	15.15	211	3.38
147	78.78	202	11.36	238	3.43	216	100	203	9.77
146	18.94	201	95.07	230	6.87	203	0.1	202	100
132	0.5%	200	1.89	229	40.45	202	2.27	201	2.98
131	1.51	182	2.27	228	49.62	189	3.03	183	4.88
119	30.30	173	14.39	216	3.78	188	25.75	174	7.89
118	18.18	172	29.54	213	9.16	160	3.40	173	8.27
117	5.30	152	4.54	212	5.34	159	6.44	145	12.40
104	3.78	146	4.16	203	3.03	158	5.30	127	3.76
91	5.30	145	3.78	186	4.54	131	4.92	119	1.49
89	1.51	125	3.03	185	4.60	103	5.30	105	4.51
77	4.54	107	1.00	175	3.03	91	2.42	101	5.97
74	6.06	104	11.36	157	2.67	77	6.06	96	6.39
69	3.03	101	6.06	147	2.29	63	1.51	77	3.50
65	4.54	77	5.30	137	2.30	51	2.27	86	2.23
63	3.78	69	2.29	132	4.54			69	9.77
57	4.52	63	4.54	119	2.30			63	5.26
51	4.92	52	6.81	115	6.06			62	4.47
41	6.44			104	3.03			61	1.86
				89	5.34			53	3.73
				69	4.58			52	5.97
				63	3.43			51	6.76

Table 2. Electronic charges of the atoms of carbon of coumarins **1**.

Comp.	X	R	C <sub>2</sub>	C <sub>3</sub>	C <sub>4</sub>	C <sub>5</sub>	C <sub>6</sub>	C <sub>7</sub>	C <sub>8</sub>
<b>1a</b>	NH <sub>2</sub>	CH <sub>3</sub>	0.38843	-0.32092	0.03862	-0.08286	-0.28049	0.13719	-0.28632
<b>1b</b>	NH <sub>2</sub>	CF <sub>3</sub>	0.38658	-0.25705	-0.03582	-0.07300	-0.27924	0.16135	-0.29258
<b>1c</b>	N(CH <sub>3</sub> ) <sub>2</sub>	CF <sub>3</sub>	0.38688	-0.25868	-0.03473	-0.07670	-0.27398	0.18062	-0.28833
<b>1d</b>	N(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	CH <sub>3</sub>	0.38857	-0.32199	0.03917	-0.08865	-0.27456	0.15809	-0.28181
<b>1e</b>	OH	CF <sub>3</sub>	0.38405	-0.24276	-0.04756	-0.07849	-0.29318	0.13214	-0.23285

Table 2 (continued). Electronic charges of the carbons of coumarins **1**.

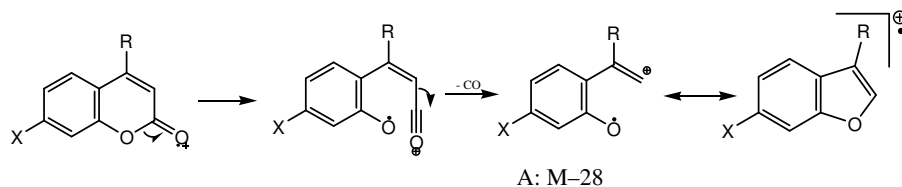
Comp.	X	R	C <sub>9</sub>	C <sub>10</sub>	C <sub>12</sub>	C <sub>14</sub>	C <sub>15</sub>
<b>1a</b>	NH <sub>2</sub>	CH <sub>3</sub>	0.16448	-0.20235	-0.33042	-	-
<b>1b</b>	NH <sub>2</sub>	CF <sub>3</sub>	0.17130	-0.19651	0.50708	-	-
<b>1c</b>	N(CH <sub>3</sub> ) <sub>2</sub>	CF <sub>3</sub>	0.16775	-0.19678	0.50691	-0.19088	-
<b>1d</b>	N(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	CH <sub>3</sub>	0.15913	-0.20164	-0.32988	-0.11488	-0.38329
<b>1e</b>	OH	CF <sub>3</sub>	0.15310	-0.17547	0.51086	-	-

Table 3. Electronic charges of the heteroatoms of coumarins.

Comp.	X	R	O <sub>1</sub>	O <sub>11</sub>	O <sub>13</sub>	N <sub>13</sub>
<b>1a</b>	NH <sub>2</sub>	CH <sub>3</sub>	-0.23950	-0.32699	-	-0.49316 <sup>a)</sup>
<b>1b</b>	NH <sub>2</sub>	CF <sub>3</sub>	-0.23139	-0.30361	-	-0.50957 <sup>b)</sup>
<b>1c</b>	N(CH <sub>3</sub> ) <sub>2</sub>	CF <sub>3</sub>	-0.23220	-0.30613	-	-0.38553 <sup>c)</sup>
<b>1d</b>	N(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	CH <sub>3</sub>	-0.24035	-0.32972	-	-0.35081 <sup>d)</sup>
<b>1e</b>	OH	CF <sub>3</sub>	-0.22559	-0.29420	-0.28984	- <sup>e)</sup>

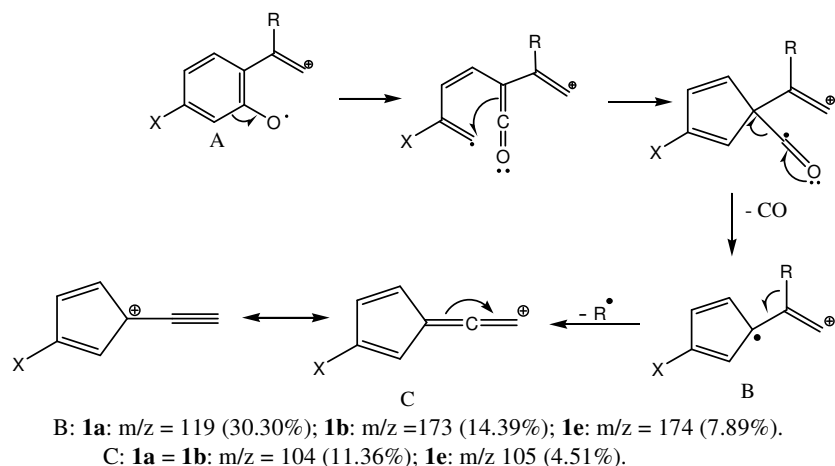
a) X = NH<sub>2</sub> or OH

As described several times for coumarins [14-16], the first fragmentation consisting to the loss of CO group (M-28) to give the fragment A, which can be observed in most of the spectra (compound **1a**, **1b**, **1c** and **1e**). Formation of this fragment A by cleavage of the lactone cycle is controlled by O<sub>1</sub> and C<sub>3</sub>, which present high negative charges. The cleavage of the lactone ring take place at O<sub>1</sub> and then loses the CO after breaking the C<sub>2</sub>-C<sub>3</sub> bond, to give fragment A as indicated in the Schemes 2 and 3. When X = OH or NH<sub>2</sub>, fragment A (M-28) is the most abundant fragment as previously observed [11-12, 14] and can lead to many other fragments as illustrated in the Schemes 2 and 3:



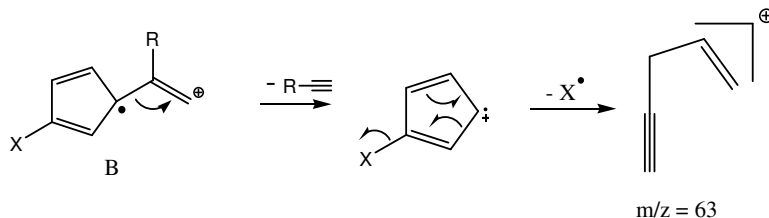
**1a**: m/z = 147 (78.78%); **1b**: m/z = 201 (95.07%); **1c**: m/z = 229 (40.45%); **1d**: m/z = 203 (0.1%); **1e**: m/z = 202 (100%).

Scheme 2. Formation of fragment A.



Scheme 3. Formation of fragments B and C.

The loss of a second CO group leads to fragment B which loses the radical  $R^\bullet$  to give C. These fragmentations take place at  $C_8$  and  $C_{10}$  which bear significant negative charges. At last, B can lose successively all the substituents on the cycle and lead to the common fragment  $m/z = 63$ , as indicated in Scheme 4:

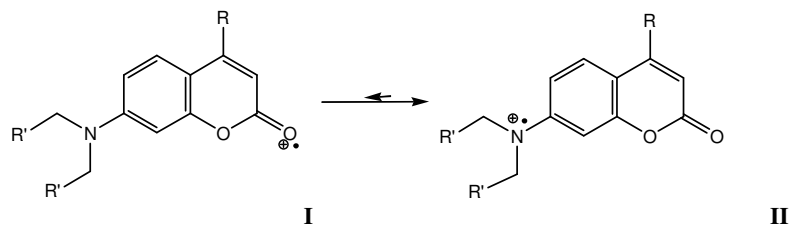
Scheme 4. Formation of fragment with  $m/z = 63$ .

Whether  $X = OH$  or  $NH_2$ , the same fragmentation processes were practically obtained and good correlation with the electronic charges of atoms were observed. In this case, most of important fragmentations took place at the level of atom which exhibited a significant negative charge.

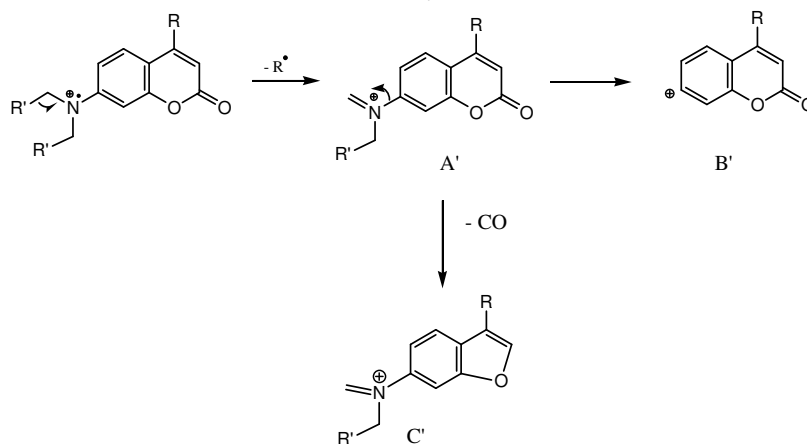
b)  $X = dialkylamino\ moiety$

When  $X$  is dialkylsubstituted nitrogen, as dimethylamino or diethylamino moiety, a competition between two molecular ions would occur, and typical fragmentations of amines could take place, giving different fragments with good relative abundances. In this case, the more donating substituents are on nitrogen atom, the more stable is the ammonium cation [14].

So, the molecular ion is under ammonium form **II** as shown in Scheme 5. This molecular ion undergoes to fragmentations according to Scheme 6. This could also explain why the ammonium cation-radical **II** takes place as molecular ion and why the formation of  $M-28$  peak (loss of CO group) is less important for **1c**  $R' = H$  (40.45%) than for **1a** and **1b** (78.78% and 95.07%) and particularly weak for **1d**  $R' = CH_3$  (0.1%). Most of their fragmentations have been produced from the ammonium molecular ion **II**.

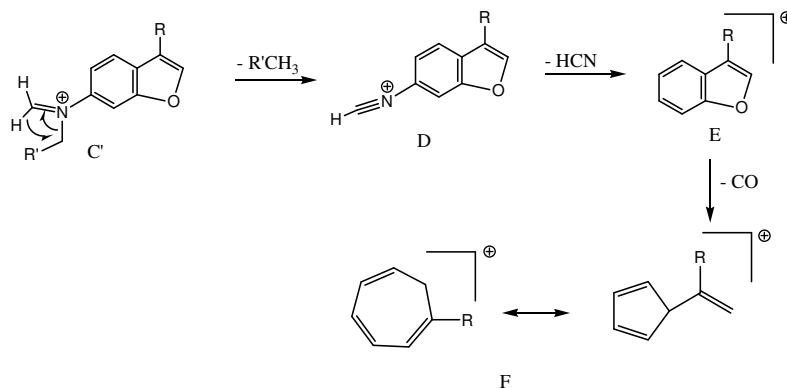


Scheme 5. Structure of molecular ion of 7-dialkylamino coumarins.



A': R' = H: **1c**  $m/z = 256$  (40.45%); R' = CH<sub>3</sub>: **1d**  $m/z = 216$  (100%).  
 B': R = CF<sub>3</sub>: **1c**  $m/z = 213$  (9.16%); R = CH<sub>3</sub>: **1d**  $m/z = 159$  (6.44%).  
 C': R' = H: **1c**  $m/z = 228$  (49.62%); R' = CH<sub>3</sub>: **1d**  $m/z = 188$  (25.75%).

Scheme 6. Fragmentation process of 7-dialkylamino coumarins.



D: R = CH<sub>3</sub>: **1d**  $m/z = 159$  (6.44%); R = CF<sub>3</sub>: **1c**  $m/z = 212$  (5.34%);  
 E: R = CH<sub>3</sub>: **1d**  $m/z = 131$  (5.30%); R = CF<sub>3</sub>: **1c**  $m/z = 185$  (4.60);  
 F: R = CH<sub>3</sub>: **1d**  $m/z = 103$  (5.30%); R = CF<sub>3</sub>: **1c**  $m/z = 157$  (2.67).

Scheme 7. Specific fragmentation of aromatic amines observed on dialkylamino coumarins.

These fragmentations take place at the level of nitrogen or carbons C<sub>14</sub> and C<sub>15</sub>, which display significant negative electronic charges. Other classical fragmentations of aromatic amine [14] like the coumarins **1c** and **1d** were obtained and shown in Scheme 7.

It is notable that the atoms of carbon of dimethyl and diethyl groups are bearers of significant negative charges. They are able to induce the fragmentations observed above to give most of the fragments obtained.

### CONCLUSIONS

This study showed that electronic charges of atoms (carbon, oxygen, and nitrogen) of coumarins disubstituted in 4 and 7 positions, obtained by AM1 semi empirical method can be used to determine the site of the impact of electronic beam, and the fragmentations pathways of the molecular ions. The fragmentations processes are similar to those previously found for coumarins substituted by halogens or oxygenated moieties. In the case of dialkylamino moieties, most of the cleavages are characteristic of aromatic amines. Therefore, these results confirm those of our previous studies: (i) a good correlation between the electronic charges of atoms and the fragmentations processes and (ii) fragmentations take place at the level of atoms bearing significant negative electronic charges. So, the electronic charges of atoms should be regarded as a new instrument for analysis and predicting fragmentation processes in electronic impact mass spectrometry of organic compounds.

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