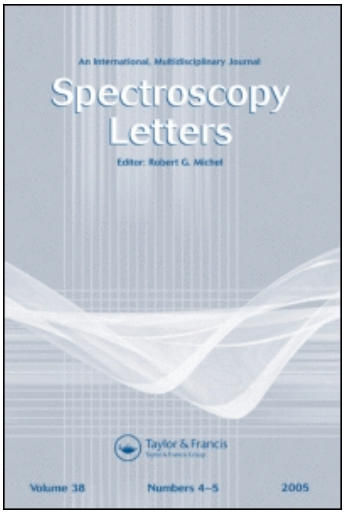

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Mass Spectrometry Study of Coumarins: Correlation Between Charges of Atoms and Fragmentation Processes

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ABSTRACT The mass spectrometry of a number of 6-substituted coumarins was studied in the context of correlating fragmentation pathways and electronic charges of atoms performed by AM_1 semiempirical method. The atomic charges of atoms are found to be good predictors of the fragmentation pathways.

KEYWORDS AM_1, coumarin, electronic charge, fragmentation, mass spectrometry

INTRODUCTION

Coumarins are important, naturally occurring heterocyclic compounds.[1–3] Because of their several properties, they have been synthesized by several methods in laboratories.[4–7] They exhibit important biologic properties and are extensively studied.[8–12] Their physical and chemical properties are also known,[2,12–15] but little attention has been paid to their properties in mass spectrometry. We describe below a study of mass spectral fragmentations in correlation with the electronic charges of atoms performed by AM_1 semiempirical method.[16] AM_1 semiempirical calculation has been used successfully for ^1H and ^{13}C NMR assignments,[17,18] for the study of tautomeric equilibrium,[19,20] reactions mechanism,[21] and so forth. In all these cases, AM_1 calculations are consistent with the experimental results.

As a part of our continuing investigations about coumarins, we report herein some results obtained in the study of correlation between fragmentation processes in electronic impact mass spectrometry (*eims*) and electronic charges of atoms of some coumarins. The electronic charges are performed by AM_1 semiempirical method. To our knowledge, no similar study has been reported about correlation between fragmentation processes in mass spectrometry of coumarin derivatives and electronic charges of their atoms.

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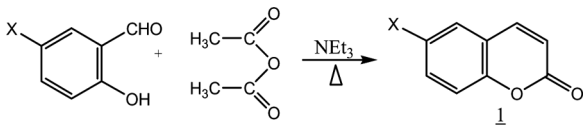
MATERIALS AND METHODS

Synthesis of Coumarins

According to the Perkin reaction procedure,[4] coumarins are obtained with more than 70% yield as colorless crystal after purification. All the



SCHEME 1 1a: X = H; 1b: X = Cl; 1c: X = Br; 1d: X = NO_2.

compounds have been identified by their IR and NMR (^{1}H and ^{13}C) data. Scheme 1 shows the materialization of the reaction.

AM_1 Calculation of Electronic Charges of Atoms

All the electronic charges of atoms are performed by Austin Model 1 (AM_1) semiempirical method[16] from Chem3D Ultra8 software using a Pentium 4 computer.

Mass Spectra

All the mass spectra have been obtained by *eims* on a CPG-JSM AX505 apparatus for 1a, 1c, and 1d and on a Finnigan MAT ITD 880 MS apparatus at 70 eV for 1b.

RESULTS AND DISCUSSION

Tables 1, 2, and 3 summarize mass spectra of prepared coumarins and electronic charges of their atoms.

The ^{13}C NMR data obtained are in good agreement with those of the literature.[22–25]

The m/z ratios of molecular ions of the whole compounds are in good agreement with the expected molecular weight and are an indication of the stability of this ion. According to the charges of different atoms, the most probable point of impact of the electron beam is the oxygen of the carbonyl (O_{11}). That is the reason why most fragmentations are derived from the molecular ion (Scheme 2) obtained by this impact. This molecular ion has been described several times as the molecular ion of coumarins.[24–28]

The carbons 3, 8, and 10 are the bearers of the most negative charge. The significant fragmentations, giving the most important fragments, take place on these carbons or are induced by heteroatoms (oxygen, nitrogen, or halogen). These carbons are the most electron-donating carbons. The carbon 6 gives also some fragmentations: loss of X or transposition of H when X = NO_2. Some common fragmentations have been obtained giving the fragment A, which m/z ratio was M-28, and other fragments with m/z = 117, 89, 63, and 39.

The process with carbonyl loss has been described several times for coumarins[28,29] and for isocoumarins.[30,31] So has the contraction of the cycle of oxygenated fused heterocycles[22,26,32] or phenol derivatives.[30] Presence of the peak with m/z = M-28,

TABLE 1 Relevant Mass Spectra of Coumarins 1

1a (X = H)		1b (X = Cl)		1c(X = Br)		1d (X = NO_2)	
m/e	(%)	m/e	(%)	m/e	(%)	m/e	(%)
146 (M^{*+})	96.8	182 (M^{*+})	56.52	226 (M^{*+})	96	191 (M^{*+})	62.22
131	1.01	180	93.47	224	100	185	2.22
118	100.00	179	1.08	198	58.73	175	2.44
92	2.38	154.6	44.56	196	57.14	173	2.22
90	19.04	152.5	100.00	181	1.10	163	24.44
89	52.38	128.5	0.54	179	0.15	161	26.66
63	18.25	126.5	6.52	172	2.38	154	1.25
39	10.08	124.5	16.30	170	2.38	145	4.44
–		117.5	3.26	143	1.58	143	3.21
–		99.5	2.17	117	11.90	133	33.33
–		89.3	71.73	89	73.01	117	46.66
–		73.3	8.69	63	19.05	105	23.33
–		63.3	34.78	39	3.17	89	95.55
–		62.3	26.08	–		772	8.88
–		61.3	8.69	–		63	100.00
–		–		–		51	46.66

TABLE 2 Electronic Charges of Carbons Atoms Obtained by AM_1

No.	X	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}
1a	H	0.541	−0.124	0.053	−0.029	−0.068	−0.021	−0.095	0.263	−0.012
1b	Cl	0.533	−0.124	0.047	−0.135	0.146	−0.093	−0.087	0.213	−0.009
1c	Br	0.534	−0.124	0.048	−0.114	0.092	−0.078	−0.088	0.223	−0.009
1d	NO_2	0.533	−0.293	0.086	0.085	−0.465	0.201	−0.266	0.301	−0.087

obtained after expulsion of the CO group, described previously,[22,32–34] is another convincing argument. Thus, the fragmentation process of Scheme 3 is proposed.

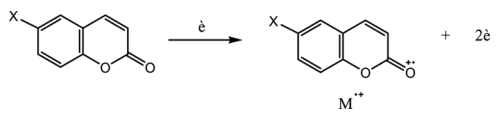
It is observed that the molecular ions of all the compounds and the base peaks come from the process of Scheme 3 and are very stable and present generally an important relative abundance (from 30% to 100%). In this scheme, the fragment m/z = M-17 appears at m/z = M-18 for compound 1a because the substituent X is a hydrogene. The same process (Scheme 4) takes place without losing the X group to give the B and C fragments.

On the other hand, the M-CO fragment A can lose an acetylene molecule to give D. This process is given in Scheme 5.

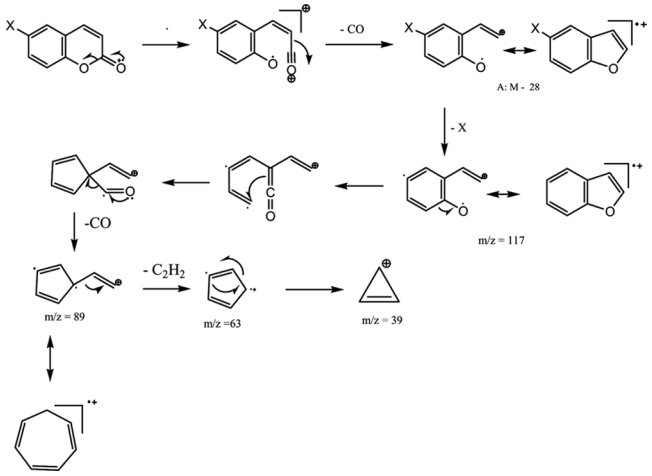
Three surprising fragments have been obtained in the spectrum of 1d (X = NO_2). These are the fragments with m/z = 105, 77, and 51. This compound is the only one that gives these fragments. These pics are characteristics of the formation of a benzoyl fragment.[24,25,32] We assume that this phenomenon can be attributed to the presence of the nitro group, and the process give in Scheme 6 can explain it. The process starts from the fragment A by a hydrogen radical transfer.

The high withdrawing character of the nitro group authorizes this hydrogen transfer. The high positive electronic charges of nitrogen and the very high negative one of C_6 of the compound 1d are in good agreement with this process. A previous study of proton transfer has been made by mass spectrometry and by AM_1 for amidines.[35] It has been found, according to heats of formation (ΔH) of each fragment in gas phase, that the transfer is favored by the electronic effect of substituents, and our results seem to conform to this observation.

Formation of the fragments m/z = 105, 77, and 51 is usually observed for monosubstituted benzoyl derivatives. This behavior has been observed



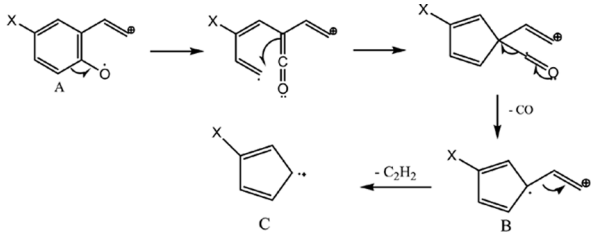
SCHEME 2 Formation of the molecular ions of Coumarins 1.



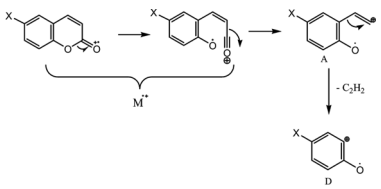
SCHEME 3 Formation of fragment A (M–28) and fragments with m/z = 117, 89, 63, and 39.

TABLE 3 Electronic Charges of Oxygen and Nitrogen Atoms

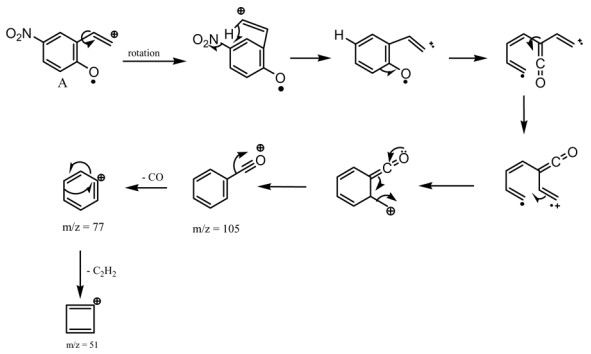
Compound	X	O_1	O_{11}	N
1a	H	0.046	−0.708	–
1b	Cl	0.041	−0.716	–
1c	Br	0.042	−0.714	–
1d	NO_2	0.111	−0.833	0.357



SCHEME 4 B: X = H; m/z = 90; X = Cl, m/z = 126–124; X = Br: m/z = 170–168; X = NO_2: m/z = 135; C: X = H m/z = 63; X = Cl: m/z = 100–98 (as 99.5); X = Br, m/z = 144–142.



SCHEME 5 **A: X = H; m/z = 118; X = Cl: m/z = 154–152. X = Br: m/z = 198–196; X = NO_2: m/z = 163. D: X = H m/z = 92; X = Cl: m/z = 128–126; X = Br: m/z = 172–170; X = NO_2: m/z = 137.**



SCHEME 6 **Formation of fragments m/z = 105, 77, and 51.**

recently for the 4-acyl isochroman-1,3-diones, another type of heterocyclic compound with fused rings.[36]

CONCLUSIONS

In this study, it has been found that the electronic charges of carbons and heteroatoms (oxygen, nitrogen, or halogen) obtained by AM_1 semiempirical method are useful to suggest the site of electronic beam impact and to determine a fragmentation's starting points and its pathways. An unusual fragmentation of one of the coumarins synthesized has been obtained and explained. Those, the 6-nitro coumarin 1d reacts in mass spectrometry like mono-substituted benzoyl derivatives.

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