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MASS SPECTRAL STUDY ON THE FRAGMENTATION OF 3-[2-(3,5-DIMETHYL-1*H*-PYRAZOL-1-YL)THIAZOL-4-YL]-2*H*-CHROMEN-2-ONE BY AM1 METHOD

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ABSTRACT

The mass spectrum of 3-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl]-2*H*-chromen-2-one has been studied in the context of correlating fragmentation pathways with electronic charges of atoms. The atomic charges were found to be good prediction for evaluating the fragmentation mechanism and stability of fragments with the electron bombardment. In this connection, considering an isolated molecular fragments in the gas phase, which was surrounded by vacuum using semi-empirical molecular orbital AM1 method, the heats of formation (ΔH_f^o), dipole moment (μ), ionization potential (IP), full atomic charges and energies of frontier molecular orbitals (E_{HOMO} and E_{LUMO}) have been performed and discussed to evaluate stable fragments.

KEYWORDS: AM1, mass spectrometry, fragments, 3-(2-bromoacetyl)coumarin, thiosemicarbazide, acetylacetone, 3-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl]-2*H*-chromen-2-one, frontier molecular orbital.

INTRODUCTION

Thiazole with two hetero atoms sulphur and nitrogen at 1,3-positions is found in many applications[1] such as anti-cancer[2], anti bacterial[3], anti-malarial[4], anti-tubercular[5], fluorescent dyes.[6] Pyrazole with two nitrogen atoms at 1,2 positions is found a major role as therapeutic agents[7] such as anti oxidants[8], anti-inflammatory[9], anticancer[10], anti-tubercular[11], anti-diabetic[12] etc. Thus, the combination of thiazole, pyrazole and coumarin rings have been extensively examined in the 3-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl]-2*H*-chromen-2-one derivatives for biological activity.[13,14] In continuation of our earlier work[15, 16] we have synthesized the model compound in one step.

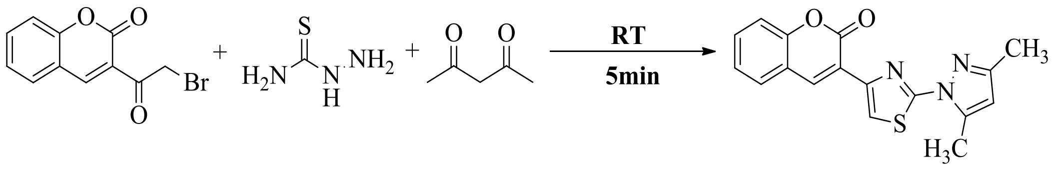
Recently a new approach of analysis of fragmentation processes of organic compounds in electron impact mass spectrometry has been described to give a good correlation with the electronic charges of each atom.[17] The fragmentation process has been taken place mainly at the level of atoms bearing high negative or positive charges.[18, 19] It has been found that the AM1 method presents a good reliability.[20, 21, 22] This is prompted us to investigate the electronic charges of atoms became a valuable data for understanding the fragmentation processes of 3-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl]-2*H*-chromen-2-one in mass spectrum. Austin Model-1 (AM1) is one of the semi-empirical quantum calculation methods, which is based on the MNDO (modified neglect of diatomic overlap) integral approximation, it includes experimental parameters and extensive simplification of the Schrodinger's equation ($H\Psi=E\Psi$) to optimize molecules for calculation of various properties to solve chemical problems.[23-27] In this way quantum chemistry simulates chemical structure and allows studying chemical phenomena by running calculations on computer rather than by examining reactions experimentally. Thus, theoretical investigation is considered and worthwhile to study the fragmentation process of 3-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl]-2*H*-chromen-2-one with a view to calculate their atomic charges, heats of formation (ΔH_f^o), dipole moment (μ), ionization potential (IP), full atomic charges and energies of frontier molecular orbitals (E_{HOMO} and E_{LUMO}), which are an advantage for investigating the stability of fragments during the electron impact mass spectrum.

Electronic properties of 3-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl]-2*H*-chromen-2-one (1) in gas phase usually considering isolated molecules which was surrounded by vacuum and it has been evaluated by AM1 method. From the obtained optimized electronic structure of 3-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl]-2*H*-chromen-2-one (1) and its fragments (2 - 8) which are observed from mass spectrum (Figure-2). The mechanism of fragmentation processes (Scheme-2 to -6) have been studied by comparison of the relative values of net charges at different atoms of the molecule and also observed the predominated fragment.

Experimental

General procedure of 3-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl]-2*H*-chromen-2-one[28]

A mixture of 3-(2-bromoacetyl)coumarin (1.33 g, 0.005 mol) and thiosemicarbazide (0.45 g, 0.005 mol) was taken in 10 ml of acetylacetone and stirred for 5 minutes at room temperature. The solid separated was filtered, washed with ether to remove excess of acetylacetone and crystallised from benzene. Yield (90%), m.p. 220-222°C [Found C, 63.15; H, 4.02; N, 13.00; S, 9.91. $C_{17}H_{13}N_3O_2S$ requires C, 63.16; H, 4.02; N, 13.00; S, 9.91%].



3-(2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl)-2*H*-chromen-2-one

Scheme-1: Synthesis of 3-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl]-2*H*-chromen-2-one.

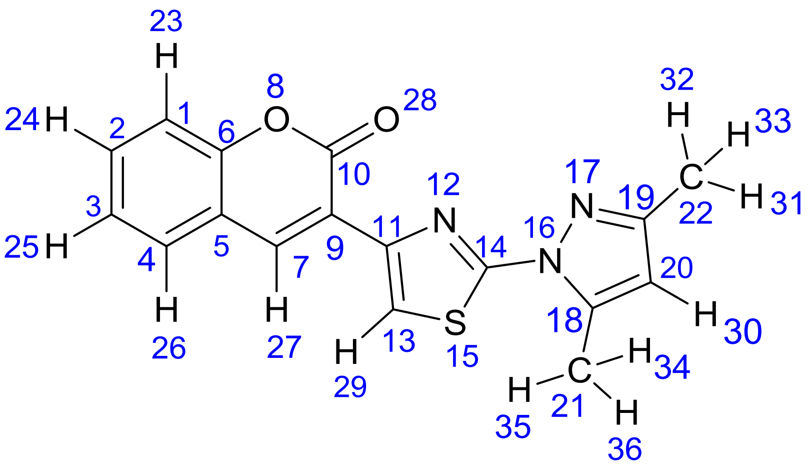


Figure – 1.

Mass spectrum

The mass spectrum was obtained by electron impact mass spectrometry (EIMS) on a CPG-JSM AX505 apparatus at 70 eV as shown in Figure- 2 and the data is presented in Table-I.

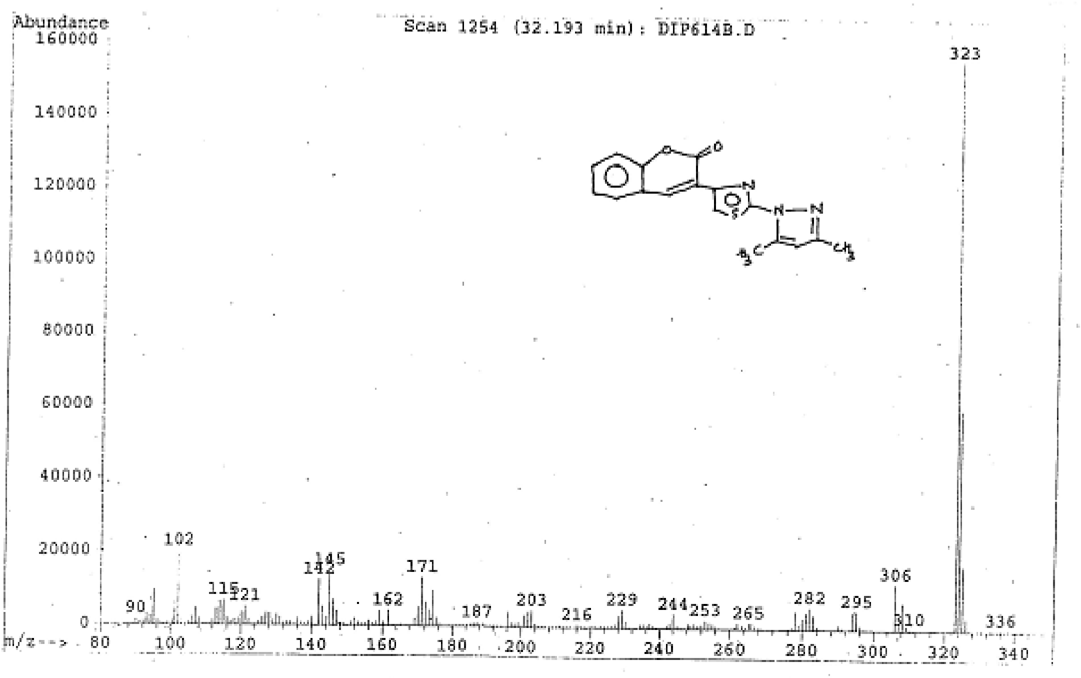


Figure 2: Mass spectrum of 3-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl]-2*H*-chromen-2-one.

Computational methods[23,24]

Semi-empirical molecular orbital calculations were performed on the fragments as shown in Scheme-2, 3, 4, 5 & 6 using the MOPAC93 in WinMOPAC ver 5.13 program by means of Intel Dualcore D102GGC2 DDR2 1GB SDRAM PC. The Austin Model 1 (AM1) method is a modification of MNDO, offering more accurate parameterizations for polar systems and transition states. Geometry calculations in the ground state (keywords: PRECISE, equivalent to GNORM= 1.0, CHARGE, GEO-OK, and MMOK to correct the increase in the barrier to rotation of the amide linkage) were completely optimized until the lowest energy was found. The position of the atom in the molecule is mentioned as subscript shown in Figure- 1.

RESULTS AND DISCUSSION

Electronic structure of 3-(2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl)-2*H*-chromen-2-one (1) and its fragments (2 to 8)

The mass spectrum is a record of the masses and relative abundances of the molecular ion and fragments formed with electron bombardment. The relative intensity of an ion peak depends on its rates of formation and rates of fragmentation. The optimized electronic structure of 3-(2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl)-2*H*-chromen-2-one (1) and its fragments (2 to 8) are shown in Scheme-2 to -6. The calculated net charges on atoms of the fragments (1 to 8) are presented in Table-I. The heats of formation (ΔH_f^o), ionization potential (IP), dipole moment (μ), the energies of frontier molecular orbitals (E_{HOMO} and E_{LUMO}) are presented in Table-II.

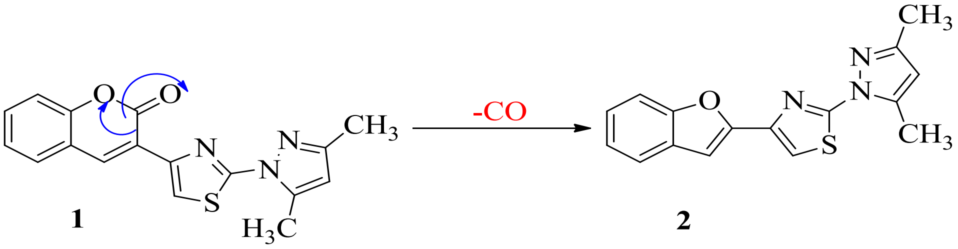
The calculated values of frontier orbital energies (E_{HOMO} and E_{LUMO}) reveal that hardness of molecules 1 to 8 are investigated in the order of $6 < 2 < 3 < 1 < 5 < 4 < 7 < 8$ as per electron excitation energies (Table-II). The promotion of an electron from HOMO to LUMO, in a photochemical reaction, the supra-facial path way may be allowed in the case of molecules 1 to 8, due to the presence of same sign.[29] The dipole moment of molecules depends on the nature of the atoms and bonds comprising the molecules and on their arrangement. The dipole moment is increasing in the order of $1 < 2 < 5 < 8 < 6 < 4 < 7 < 3$. Fragment (3) shows higher dipole moment. The electronegative hetero-atoms cause displacement of electrons that induces an additional dipole moment in the molecule. According to the heat of formation (ΔH_f^o) data, the stability of fragments have decreased in the order of $4 > 3 > 1 > 5 > 6 > 2 > 7 > 8$.

Formation of molecular ion (1), m/z 323

The m/z ratio of molecular ion of the 3-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl]-2*H*-chromen-2-one (1) is in good agreement with the expected molecular weight is an indication of the stability of the parent ion. According to the different charges of atoms, the most probable point of electron may be removed from the oxygen atom (O_{28}). The significant fragmentation processes have been investigated the most important base peak with relative abundance of 100%.

Formation of the fragment (2), m/z 295

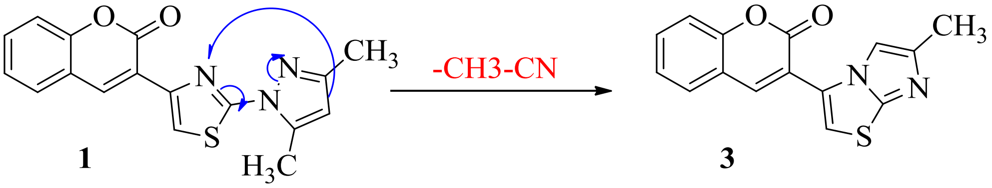
The fragmentation process has been shown with the elimination of CO group bearing C_9 and O_8 atoms in the formation of fragment (**2**) as per Scheme-2. It is found with relative abundance of 3.2%.



Scheme-2

Formation of the fragment (3), m/z 282

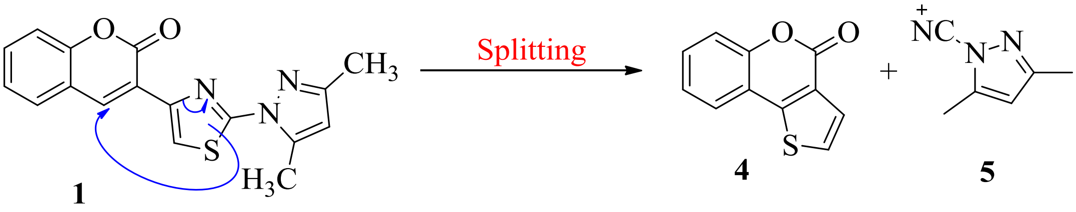
This fragment (3) had been observed with the elimination of CH_3-CN group with rearrangement as shown in Scheme-3 from parent molecule. It is found with the relative abundance of 4.2%.



Scheme-3

Splitting of the parent ion (1)

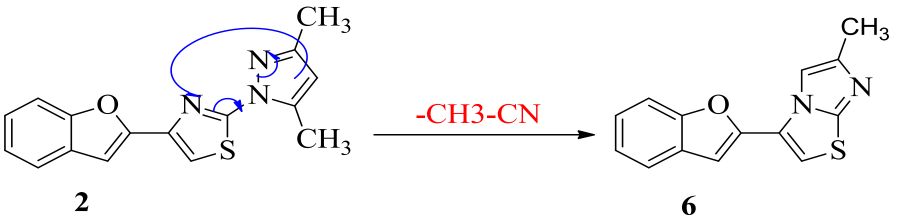
This fragments 4, (m/z 202) and 5 (m/z 121) are formed by direct splitting at C_{14}-S_{15} and C_{11}-N_{12} bonds of parent ion (1) due to the difference of charges. The fragmentation process has been given as per Scheme-4 with simultaneous rearrangement. It is also observed that fragment (4) is more stable than molecular ion as per ΔH_f values. But it is formed with equal 3.2% relative abundance.



Scheme-4

Formation of the fragment (6), m/z 254

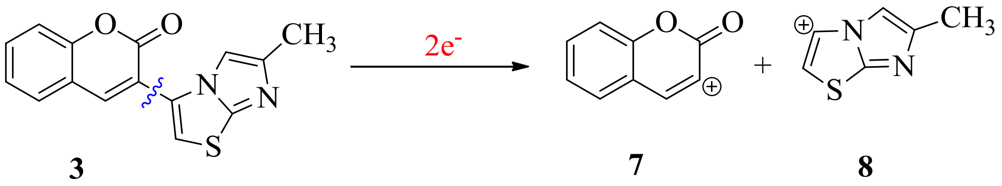
This fragment, **6** (m/z 254) is formed by expulsion of CH_3-CN group with simultaneous rearrangement from the fragment **2**, (m/z 295). The fragmentation process has been agreed as per Scheme-5. It is also observed that fragment is more stable as per ΔH_f values with 2.5% relative abundance.



Scheme – 5.

Splitting of the fragment (3), m/z 282

The splitting of fragment **3** is investigated by breaking of bond between C_9 and C_{11} atoms, due to different charges -0.1220 and +0.0421 respectively on adjacent atoms. The fragmentation process has been given as per Scheme-6. It is also observed that fragments (**7** and **8**) are less stable as per ΔH_f values.



Scheme – 6.

Table I: Atomic charges on Carbon, Sulphur, Nitrogen and Oxygen atoms of 3-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl]-2*H*-chromen-2-one (1) and its fragments (2 to 8) from AM1 calculations.

Atoms*	1	2	3	4	5	6	7	8
C_1	-0.1490	-0.1266	-0.1470	-0.1425	- -	-0.1229	-0.1089	- -
C_2	-0.0814	-0.1087	-0.0774	-0.0914	- -	-0.1057	-0.0215	- -
C_3	-0.1584	-0.1518	-0.1571	-0.1511	- -	-0.1474	-0.1220	- -
C_4	-0.0668	-0.0772	-0.0686	-0.0885	- -	-0.0785	-0.0306	- -
C_5	-0.1451	-0.1004	-0.1462	-0.0791	- -	-0.0961	-0.1557	- -
C_6	+0.1046	+0.0232	+0.1089	+0.1042	- -	+0.0239	+0.0743	- -
C_7	+0.0070	-0.1304	-0.0054	-0.2893	- -	-0.1516	+0.0412	- -
C_9	-0.1124	+0.0451	-0.1220	-0.1921	- -	+0.0426	+0.1760	- -
C_{10}	+0.3483	- -	+0.3447	+0.3754	- -	- -	+0.3610	- -
C_{11}	-0.0255	- -	+0.0421	-0.0774	- -	- -	- -	+0.2616
C_{13}	-0.4530	- -	-0.4428	-0.4622	- -	- -	- -	-0.6134
C_{14}	-0.1245	- -	-0.2887	- -	+0.0058	- -	- -	-0.5358
C_{18}	-0.0566	- -	-0.1254	- -	-0.0136	- -	- -	-0.0965
C_{19}	-0.1064	- -	- -	- -	-0.0866	- -	- -	-
C_{20}	-0.2154	- -	0.1254	- -	-0.2246	- -	- -	+0.0443
C_{21}	-0.1756	-0.1755	-0.1406	- -	-0.1708	-0.1412	- -	-0.1714
C_{22}	-0.1471	-0.1476	- -	- -	-0.1518	- -	- -	-
S_{15}	+0.5094	+0.5060	+0.5819	+0.6390	- -	+0.5883	- -	+1.2920
N_{12}	-0.1016	-0.0813	-0.0863	- -	- -	-0.0867	- -	-0.1785
N_{16}	-0.0707	-0.0724	-0.0983	- -	- -	-0.0978	- -	+0.1195
N_{17}	-0.0284	-0.0238	- -	- -	- -	- -	- -	- -
O_8	-0.1845	-0.1149	-0.1822	-0.1909	- -	-0.1101	-0.1279	- -
O_{28}	-0.3021	- -	-0.2826	-0.2889	- -	- -	-0.1061	- -
* subscript numbers of atom are given as per Figure-1								

Table –II: Heat of formation (ΔH_f^o in kcal/mol), dipole moment (μ in Debye), energies of frontier molecular orbitals (in eV) Electron excitation energy (eV) and Ionization potential (eV) of 3-[2-(3,5-dimethyl-1H-pyrazol-1-yl)thiazol-4-yl]-2H-chromen-2-one (1) and its fragments (2 to 8) from AM1 calculation along with observed molecular weight (m/z) and relative abundance (%) from mass spectrum.

Parameters	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
ΔH_f^o (kcal/mol)	85.0543	138.3421	57.6384	-13.2305	102.4750	108.2446	251.9622	338.6579
μ (Debye)	2.2607	3.2051	7.0182	5.1290	3.6932	3.9199	5.4547	3.8072
E_{HOMO} (eV)	-8.660	-8.440	-8.239	-9.078	-9.975	-8.194	-14.258	-14.024
E_{LUMO} (eV)	-1.142	-0.871	-1.474	-1.139	-0.114	-0.991	-8.274	-7.699
Electron excitation energy (eV)	9.802	9.311	9.713	10.217	10.089	9.185	22.532	21.723
IP (eV)	8.6601	8.4399	8.2392	9.0777	9.9746	8.1941	14.2584	14.0236
Molecular weight	323.369	295.358	282.316	202.227	121.141	254.306	145.137	137.179
*m/z values	323	295	282	202	121	254	145	137
*Relative abundance (%)	100	3.2	4.2	3.2	3.2	2.5	11.2	2.5
*Measured from mass spectrometry as per Figure-2.								

CONCLUSION

We have successfully synthesized a facile 3-[2-(3,5—Dimethyl-1H-pyrazol-1yl)-4-thiazolyl]-2H-1-benzopyran-2-one derivatives via one pot multi component approach under solvent free reaction conditions. The method had the advantages of mild reaction conditions, simple procedure and better yields. Mass spectrometry is an useful tool for the prediction of the fragmentation process in 3-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazol-4-yl]-2*H*-chromen-2-one. It has been considered AM1 semi-empirical method for understanding and explaining of all fragments obtained from the target compound. The correlation between atomic charges and fragmentation process of the molecule had been found to be very appropriate. The utility of theoretical predictions is important for evaluating the fragmentation mechanism and stability of fragments with electron bombardment.

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