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MASS SPECTRAL STUDIES ON SOME NITROBENZYLIDENE THIOACETAL DERIVATIVES

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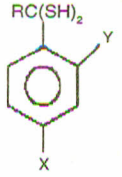
The electron impact mass spectral studies on some nitrobenzylidene thioacetal derivatives showed two different mechanisms of oxygen transfer from the nitro group to the sulfur containing fragments via intra-and inter-oxygen transfer. The two mechanisms are mainly dependent on the position of the nitro group. The relative intensity of the sulfoxonium ion formed via an intra-mechanism is always higher than formed by an inter-oxygen transfer mechanism. The oxygen transfer processes were totally eliminated when a free carboxylic group was introduced in the β-position to the sulfur atom which facilitates hydrogen transfer from the carboxylic group to the sulfur atom, giving rise to the base peak in their mass spectra as the thioglycolic acid fragment ion rather than the sulfoxonium fragment ion. The presence of two nitro groups, substituted at 2-and 4-positions of the benzylidene nucleus neither increased the relative intensity of the sulfoxonium ion nor competed with the hydrogen transfer mechanism. Conversion of the carboxylic acid into the methyl ester, however, decreased the hydrogen transfer process.

Key words: Nitrobenzylidene thioacetal derivatives, Electron impact mass spectra, Oxygen transfer mechanism.

Introduction

Benzylthio compounds and their derivatives have been the subject of several studies [1-3]. There is a considerable interest in the reactions of benzylidene thioacetals and their derivatives. The studies were directed towards oxidation [4] and cleavage by alkali [5] as well as towards their spectral behavior [6]. Several interesting reports were noted as some of these compounds exhibited stabilization effects on polyalkenes and halogen containing resins [7]. Some of them showed antimicrobial, pesticidal [8] and/or antiprotozoal activities, in addition to marked growth inhibition of *Trichomonas vaginalis* [9]. They are either useful as antifungal and antibacterial agents [10] or they seem to be effective as the coprecursor of penicillin [11]. On the other hand, they have been the subject of mass spectral investigation, [12-15] including oxygen transfer mechanism. However, oxygen transfer is a common phenomenon in mass spectra of nitro and oxygen containing compounds [16]. Mass spectral studies of the migration of trimethyl silyl moiety (TMS) from the a-to the ortho position were reported [17-20]. Accordingly, the present investigation was carried out in order to synthesize other derivatives of the basic structure of nitrobenzylidene thioacetal derivatives 1,2 a-g (Table 1) for mass spectral as well as chemical and biological studies.



Basic structure of Nitrobenzylidene thioacetal derivatives 1,2 a-g

Experimental

Melting points are uncorrected and were determined on a Thomas-Hoover capillary apparatus, ^{1}HNMR spectra were obtained in $CDCl_3$ or acetone-d_6, using a BRUKER AM 300L Spectrometer with Me_4Si as the internal standard. The IR spectra (KBr pellets) were measured on a Pye Unicam Combridge Sp^3 200 instrument. The mass spectral studies were performed using Finnigan MAT 4000 mass spectrometer. 70ev was used for EI-MS studies and ammonia gas was used as a reagent gas for CI-MS studies. Analytical thin-layer chromatography (TLC) was carried out on silica gel, using (1:9) ethyl acetate: n-hexane. Sulfur microanalyses were performed by Elemental Analyzer MOD 1104 (Carlo Erba, Strumentazlene).

General procedure for synthesis of nitrobenzylidene thioacetal derivatives 1, 2a-d. The synthetic routes of these compounds are the same as cited in the literature [4,5,21-23]. To 0.03 mol. nitrobenzaldehyde in 25 ml glacial acetic acid, 0.07 mol thiophenol or its derivatives was added with stirring at 60°C for 20 minutes, then 1 ml of ethereal BF_3 solution was added. The reaction was left for 3 h at 60°C. After cooling, it was poured into 200 ml of cold 10% sodium acetate solution and a precipitate was formed. It was washed three times with 10% sodium carbonate solution and finally with water. Good yields were obtained through recrystallization from chloroform or acetone.

General procedure for synthesis of 1g and 2e,g compounds. They were prepared by dropping a freshly prepared ethereal solution of diazomethane in a suspension of the corresponding acids [4,5] in ether at 0°C with stirring for 3 h.

TABLE 1. NITROBENZYLIDENE THIOACETAL DERIVATIVES.

Cpd.	X	Y	R	R'
1a	H	NO_2	H	C_6H_5
b	H	NO_2	H	4'-$CH_3C_6H_4$
c	H	NO_2	H	4'-ClC_6H_4
d	NO_2	NO_2	H	4'-$CH_3C_6H_4$
e	H	NO_2	H	-CH_2COOH
f	NO_2	NO_2	H	-CH_2COOCH
g	NO_2	NO_2	H	CH_2COOCH_3
2a	NO_2	H	H	C_6H_5
b	NO_2	H	H	4'-$CH_3C_6H_4$
c	NO_2	H	H	4'-ClC_6H_4
d	NO_2	H	H	2'-HO_2C-C_6H_4
e	NO_2	H	H	2'-CH_3O_2C-C_6H_4
f	NO_2	H	H	-CH_2COOCH_3
g	NO_2	H	C_2H_5	-CH_2COOCH_3

On distillation of the solvent, substances were obtained and upon washing three times with 10% sodium carbonate solution, solids were produced. The solids were purified by recrystallization from methanol.

Results and Discussion

The series of 1,2a-g compounds (Table 1) were prepared, following procedures cited in the literature [4,5]. The physical properties, S content and ^{1}HNMR data of 1a-d, g and 2a-e, g are listed in Table 2. The electron impact mass spectra (EI-MS) of the thioacetals 1a-f and 2a-c, e-g were conducted in the electron of 70 eV. The major spectral fragment ions, their relative intensities to the base peak and their structural assignments are compiled in Table 3. The EI-MS of the compounds are characterized by low or no molecular ion peak which is attributed to the higher steric effect on the benzylidene CH group leading to a C-S bond cleavage. The relative intensity of

TABLE 2. YIELD, MELTING POINTS, FOUND S% AND ^{1}HNMR SPECTRA OF NITROBENZYLIDENE THIOACETAL DERIVATIVES 1a-d,g AND 2a-e,g.

Cpd.	Yield%	Colour	m.p°C (Lit. m.p°)	Found S% (Calc. S%)	^{1}HNMR (δ ppm) in $CDCl_3$*						
					H_3	H_4	H_5	H_6	$H_2{}^1,{}_6{}^1$	$H_3{}^1,{}_5{}^1$	CH
1a	85	Colour-less	104 (104)[21]	17.89 (18.10)	8.05 (d,1H)	7.82 (t,1H)	17.68 (t,1H)	7.95 (d,1H)	7.39-7.25 (m,10H)		6.40 (S,1H)
b[i]	91	White	65 (65)[12]	16.94 (16.80)	7.95 (d,1H)	7.76 (t,1H)	7.52 (t,1H)	7.84 (d,1H)	7.24 (d,4H)	7.03 (d,4H)	6.32 (S,1H)
c	76	White	76-78 (73)[23]	15.03 (15.17)	7.94 (d,1H)	7.71 (t,1H)	7.56 (t,1H)	7.90 (d,1H)	7.38 (d,4H)	7.30 (d,4H)	6.43 (S,1H)
d[ii]	65	Yellow	79-81	14.79 (15.02)	8.60 (d,1H)	–	8.25 (d,1H)	8.12 (d,1H)	7.18 (d,4H)	7.05 (d,4H)	6.29 (S,1H)
g[iii]	85	Pale yellow	74-76	16.24 (16.41)	8.75 (d,1H)	–	8.46 (d,1H)	8.18 (d,1H)	3.62 (d,HA,2H)	3.28 (d,HB,2H)	6.15 (S,1H)
					$H_{2,6}$	$H_{3,5}$	$H_2{}^1,{}_6{}^1$		$H_3{}^1,{}_5{}^1$	$H_4{}^1$	CH
2a	96	White	99-101 (98-100)[23]	17.97 (18.10)	8.09 (d,2H)	7.69 (d,2H)		7.36-7.18 (m,10H)		–	5.98 (S,1H)
b[iv]	92	White	108-110 (104)[23]	16.70 (16.80)	8.08 (d,2H)	7.40 (d,2H)	7.22 (d,4H)		7.01 (d,4H)	–	5.32 (S,1H)
c	83	White	100-101 (99)[22]	14.86 (15.03)	8.12 (d,2H)	7.42 (d,2H)	7.28 (d,4H)		7.09 (d,4H)	–	5.38 (S,1H)
d	79	White	189-191	14.35 (14.51)	8.22 (d,2H)	7.79 (d,2H)	8.03 (d,H3',2H)	7.82 (d,H6',2H)	7.30 (t,H5',2H)	7.46 (t,2H)	6.45 (S,1H)
e[v]	59	White	94-96	13.41 (13.65)	8.16 (d.2H)	7.79 (d.2H)	7.91 (d,H3',2H)	7.47 (d,H6',2H)	7.22 (t,H5',2H)	7.37 (t,2H)	5.97 (S,1H)
g[vi]	75	White	97	15.00 (15.20)	8.10 (d,2H)	7.65 (d,2H)	7.64-7.22 (m,$H_2{}^1,{}_3{}^1,{}_4{}^1,{}_5{}^1,{}_6{}^1$,5H)			3.19 (S,CH_2,4H)	

*) ^{1}HNMR Spectra of 1a,c and 2a,d compounds were done in acetone-d_6 i) 4'-CH_3-protons appear at δ=2.30 ppm (S,5H); ii) 4'-CH_3-protons appear at δ=2.32 ppm.(S,6H): iii) CH_3-protons appear at δ=3.75 ppm (S,6H); iv) 4'-CH_3protons appear at δ=2.32 ppm (S,6H); v) -CH_3-protons of 2'-$COOCH_3$ groups appear at δ=3.34 ppm (S,6H) and vi) -CH_3-protons of $COOCH_3$ groups appear at δ=3.56 ppm.

TABLE 3. THE MAJOR MASS SPECTRAL FRAGMENT IONS, THEIR RELATIVE INTENSITIES TO THE BASE PEAK AND THEIR STRUCTURAL ASSIGNMENTS OF 1a-f AND 2a-c, e-g COMPOUNDS.

m/z	Compound (RI%)		Structural Assignment
	1a	2a	
353	(3)	(3)	$M^{+\cdot}$
245	(30)	(78)	$M+H-C_6H_5S^{\cdot}+$
244	(100)	(100)	$M-C_6H_5S^{\cdot}+$
199	(22)	(18)	$C_6H_5CHSC_6H_5^+$
125	(75)	(5)	$C_6H_5SO^+$
110	(38)	(33)	$C_6H_5SH^+$
109	(100)	(34)	$C_6H_5S^+$
77	(27)	(31)	$C_6H_5^+$
	1b	2b	
381	(9)	(4)	$M^{+\cdot}$
259	(10)	(4)	$M+H-CH_3C_6H_4S^{\cdot}+$
258	(60)	(9)	$M-CH_3C_6H_4S^{\cdot}+$
244	(49)	(5)	$M+H-CH_3-CH_3-C_6H_4S^{\cdot}+$
139	(30)	(14)	$CH_3C_6H_4SO^+$
124	(21)	(18)	$CH_3C_6H_4SH^+$
123	(100)	(100)	$CH_3C_6H_4S^+$
110	(47)	(15)	$C_6H_5SH^+$
109	(46)	(13)	$C_6H_5S^+$
77	(23)	(32)	$C_6H_5^+$
	1c	2c	
159	(67)	(16)	$ClC_6H_4SO^+$
144	(38)	(18)	$ClC_6H_4SH^+$
143	(100)	(100)	$ClC_6H_4S^+$
111	(38)	(34)	$ClC_6H_4^+$
109	(28)	(10)	$C_6H_5S^+$
77	(21)	(14)	$C_6H_5^+$
	1d		
426	(10)		$M^{+\cdot}$
303	(80)		$M-CH_3C_6H_4S^+$
139	(31)		$CH_3C_6H_4SO^+$
124	(20)		$CH_3C_6H_4SH^+$
123	(100)		$CH_3C_6H_4S^+$
77	(15)		$C_6H_5^+$
	1e		
226	(6)		$M-SCH_2COOH^{\cdot}+$
166	(16)		$O_2NC_6H_4CS^+$
151	(40)		$ONC_6H_4CSH^{+\cdot}$
104	(37)		$HOOCCH_2CSH^{+\cdot}$
92	(100)		$HOOCH_2SH^{+\cdot}$
91	(8)		$HOOCCH_2S^+$
77	(22)		$C_6H_5^+$

(Contd.)

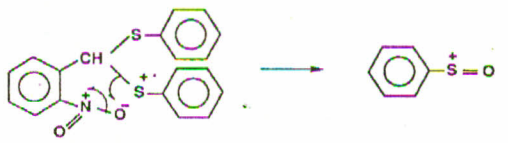
m/z	Compound (RI%)	Structural Assignment
	2e	
302	(35)	$O_2NC_6H_4CHSC_6H_4COOCH_3$
242	(18)	$O_2NC_6H_4CSC_6H_4$
183	(5)	$CH_3OOCC_6H_4SO^+$
167	(100)	$CH_3OOCC_6H_4S^+$
166	(86)	$O_2NC_6H_4CS^+$
136	(38)	$O_2NC_6H_4CS^+$
120	(23)	$ONC_6H_4CH_2^+$
77	(12)	$C_6H_5^+$
	1f	
271	(5)	$M-SCH_2COOH^{\cdot}+$
212	(18)	$NO_2NO_2C_6H_3CSH^+$
211	(10)	$NO_2NO_2C_6H_3CS^+$
196	(40)	$NONO_2C_6H_3CSH^+$
180	(74)	$NONOC_6H_3CSH^+$
166	(30)	$NO_2C_6H_4CS^+$
150	(22)	$NOC_6H_4CS^+$
103	(8)	$HOOCCH_2CS^+$
92	(100)	$HOOCCH_2SH^+$
91	(16)	$HOOCCH_2S^+$
	2f	
345	(8)	$M^{+\cdot}$
272	(24)	$M-CH_2COOCH_3^{\cdot}+$
240	(100)	$MS-CH_2COOCH_3^{\cdot}+$
167	(14)	$O_2NC_6H_4CSH^+$
166	(90)	$O_2NC_6H_4CS^+$
136	(7)	$O_2NC_6H_4CH_2^+$
120	(32)	$ONC_6H_4CH_2^+$
77	(21)	$C_6H_5^+$
	2g	
439	(27)	MNH_4^+ from CI-MS
316	(100)	$M-SCH_2COOCH_3^{\cdot}+$
243	(19)	$O_2NC_6H_4C_6H_5CS^+$
242	(38)	$O_2NC_6H_4C_6H_4CS^+$
197	(12)	$C_6H_5C_6H_4CS^+$
121	(25)	$CH_3OOCCH_2SO^+$
106	(18)	$CH_3OOCCH_2SH^+$
105	(77)	$CH_3OOCCH_2S^+$
77	(40)	$C_6H_5^+$

the formed sulfenium (RS^+) fragment ion based on this type of bond cleavage is in higher percentage because the C-S bond cleavage takes place at the β-position to both nitro and sulfur groups containing benzene rings. The charge carried by either sulfur or carbon atom, is then stabilized by resonance through conjugation with the benzene ring.

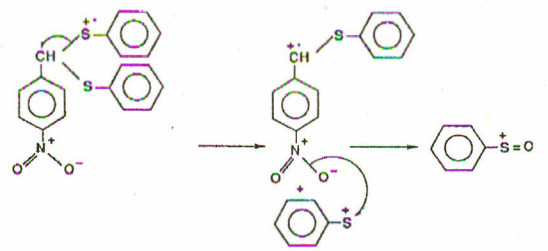
The mass spectra of 1a-c compounds showed interesting peaks at m/z 125, 139 and 159 for 1a, 1b and 1c respectively. These three peaks result from adding 16 amu to m/z 109, 123 and 143 respectively. The structural assignments of these peaks are shown in Table 3 . However, the former three fragment ions are produced through the addition of oxygen atoms to the latter ones. This oxygen transfer takes place through migration of one of the nitro group oxygen atoms to the sulfenium ion in an intra-oxygen transfer mechanism [12]. A comparison between the mass spectral data of 1a-c and 2a-c compounds indicates that the latter one also showed the same process of oxygen transfer, represented by the peaks at m/z 125, 139 and 159 for 2a, 2b and 2c, respectively. This suggests that the sulfenium ion, formed upon fragmentation from the molecular ion, was stable in the mass spectrometer ion source and unsubjected to a direct further fragmentation, but it participated in the oxygen transfer process with the nitro group. Therefore, an inter-atomic oxygen transfer mechanism is suggested to interpret the formation of the sulfoxonium fragment ions in 2a-c. The relative intensity of sulfoxonium ion formed via an inter-oxygen transfer mechanism was obviously lower than that formed via an intra-oxygen transfer mechanism because the former requires two steps, while the latter, only one step, as seen in Scheme 1. In addition to oxygen transfer process a hydrogen uptake was also found in a significant relative intensity in the mass spectra of 1a-c and 2a-c compounds (Scheme 2).

On the other hand, a comparison between the mass spectra of 1a-c and 1e, represented in Figs. 1 and 2, indicates no oxygen transfer process in the mass spectrum of 1e even with the nitro group in the ortho positon of the benzylidene nucleus. This uncommon behavior is attributed to the aliphatic nature of the sulfenium ion moiety and, therefore, its inability to stabilize the charge by resonance as in the case of 1a-c. The instability of the aliphatic sulfenium ion causes a successive fragmentation in mass spectrometer ion source. The base peak in the mass spectrum of 1e is the m/z 92 which corresponds to a thioglycolic fragment ion formed via hydrogen uptake from one of the two carboxylic groups according to Mc-Lafferty rearrangement as shown in Scheme 3. Based on these results, a competition between hydrogen uptake and oxygen transfer was apparent and controlled by the charge stabilization on the sulfenium ion and the presence of acidic hydrogen ion [12].

The same trend was also found in 1f in which only a hydrogen uptake process was dominant in its mass spectrum. Although 1f contains a nitro group in the ortho and another one in the para position of benzylidene nucleus, it did not show any peak corresponding to the sulfoxonium ion, but the base peak is m/z 92. Contrary to 1e was 2f, in which the carboxylic hydrogen ion was substituted by a methyl group which led to complete diminishing of the hydrogen transfer process. The base peak in 2f corresponds to the molecular ion minus the sulfenium fragment ion. The same base peak was also dominant in the mass spectrum of 2g which is a methyl ester derivative. A different fragmentation pathway was followed in both 1g and 1f, as compared to 1a-c compounds. Scheme 3, shows these fragmentation pathways.

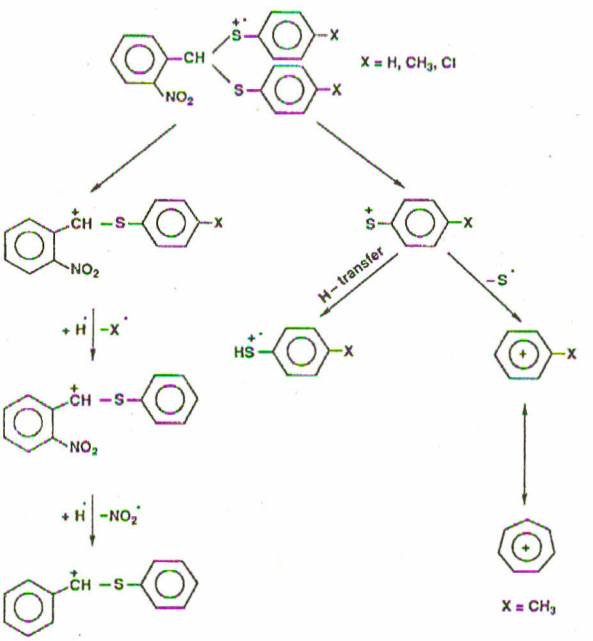


Inter-oxygen transfer mechanism in o-nitrobenzylidene thioacetal derivatives.



Inter-oxygen transfer mechanism in p-nitrobenzylidene thioacetal derivatives.

Scheme 1.



Scheme 2.

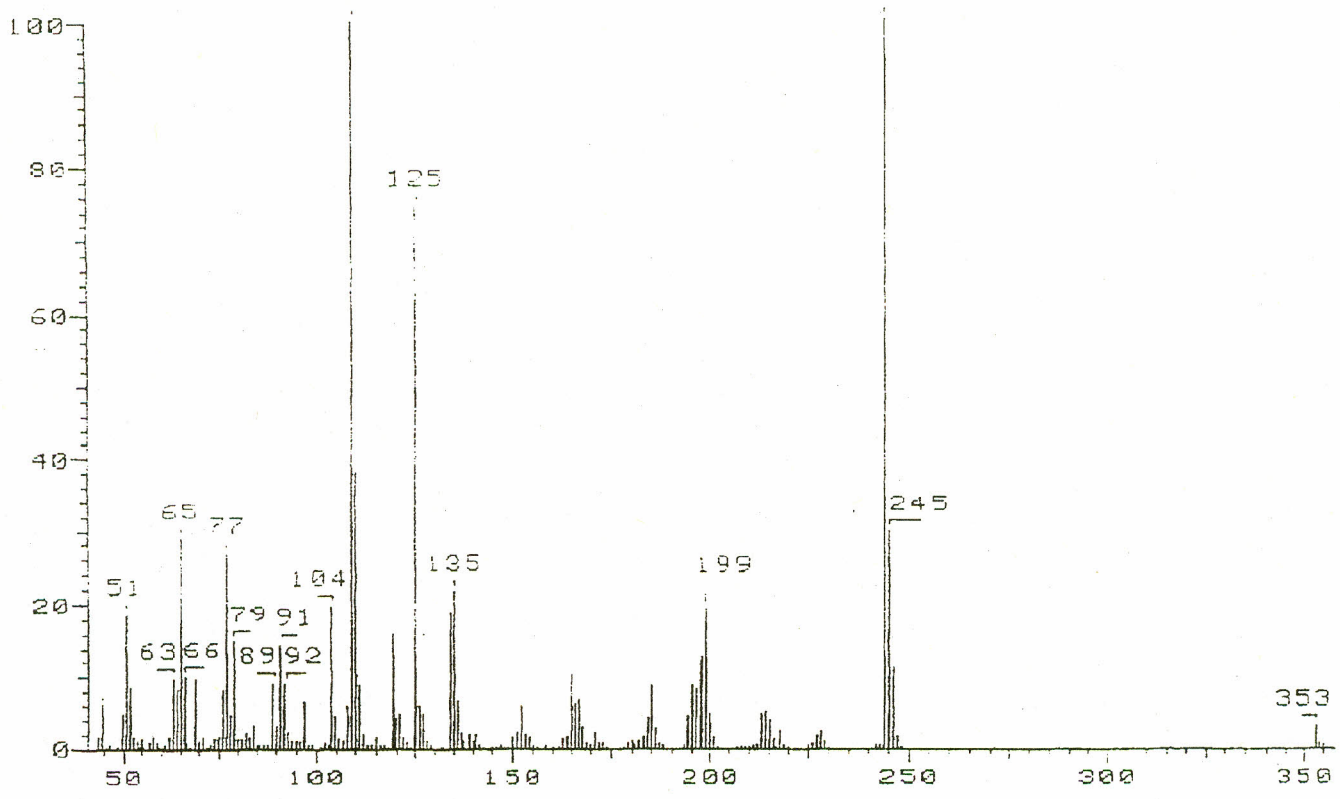


Fig. 1. Mass spectrum of 1a.

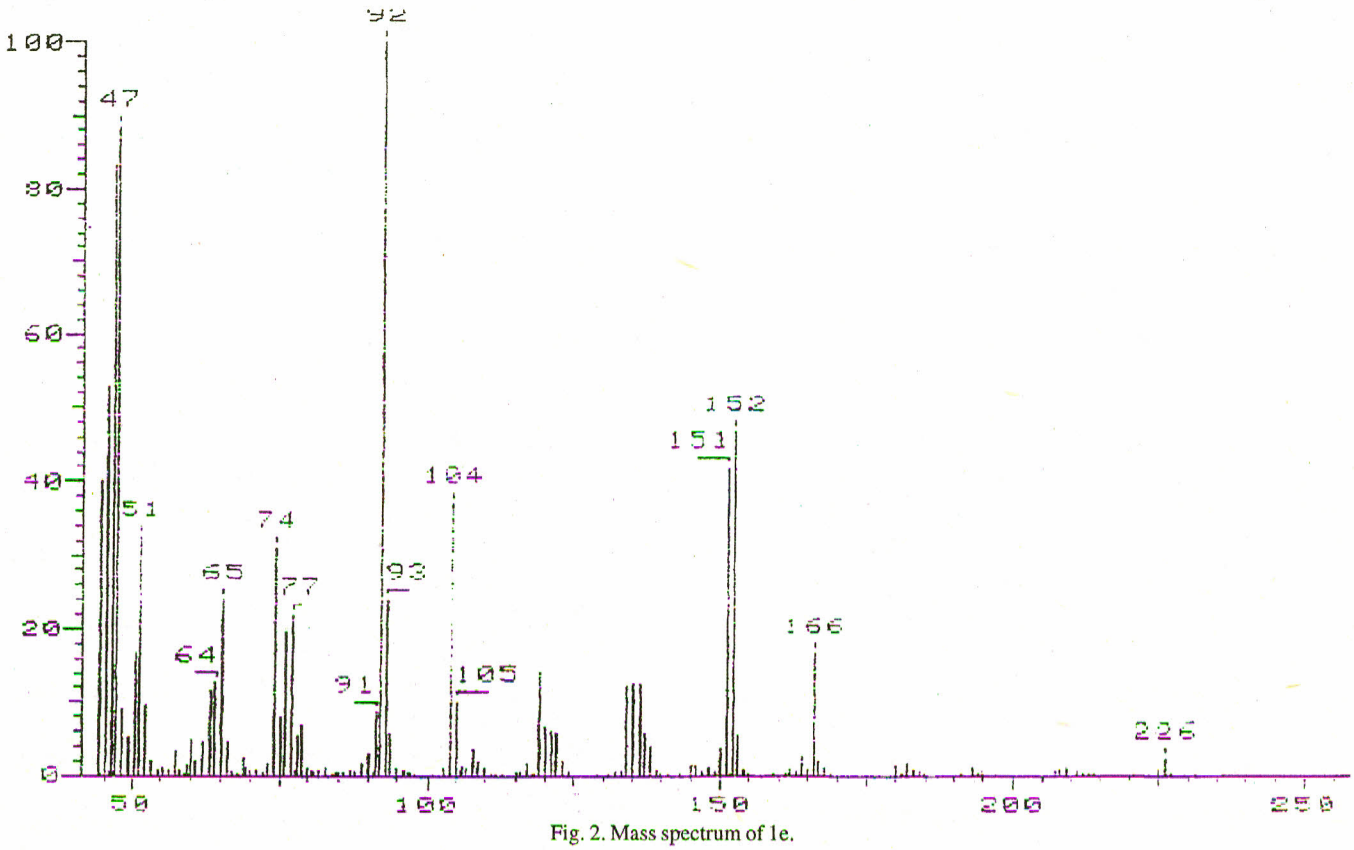
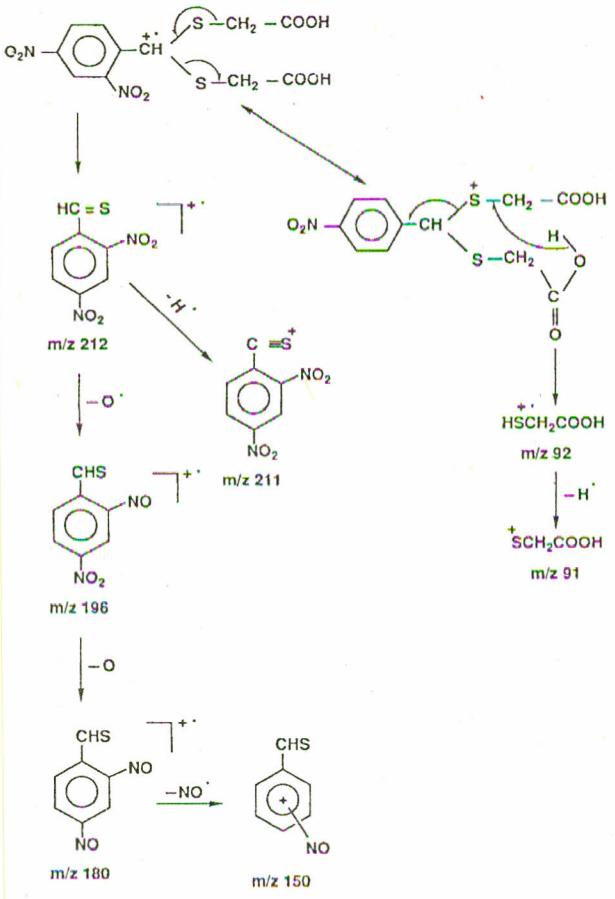
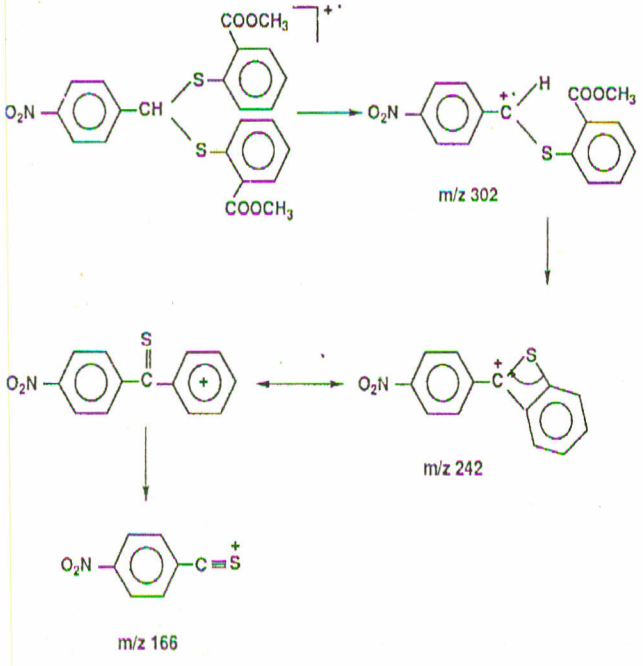


Fig. 2. Mass spectrum of 1e.



Scheme 3. Mass spectral fragmentation pathway of 1f.



Scheme 4. Mass spectral fragmentation pathway of 12e

The mass spectrum of 1d is consistent with that of 1b. The relative intensity of the fragment ion peak at m/z 139 (the sulfoxonium ion) in 1d is 31%, while in 1b is 30% and the relative intensity of the fragment ion at m/z 124 (the ion formed through hydrogen transfer) is 20 and 21% for 1d and 1b, respectively. These comparable numbers indicate that both compounds behave similarly in their fragmentation pathways and oxygen or hydrogen transfer processes regardless of the presence of an extra nitro group in the structure of 1d. The overall hydrogen and oxygen transfer processes are identical in the two compounds.

Finally, the mass spectral data of 2e compound indicates a similar inter-oxygen transfer mechanism, giving rise to low relative intensity peak (5%), the base peak corresponds to the sulfoxonium ion which is stabilized by resonance via the carboxylic group and the second high abundant peak (86%) corresponds to m/z 166 which is formed through successive fragmentation of m/z 302 fragment ion, giving rise to the ion at m/z 242, then m/z 166, as shown in Scheme 4.

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