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MASS SPECTRAL STUDIES OF NEWER INDOLES

ASHOK KUMAR, R.S. VERMA AND S.K. BHATIA

Department of Pharmacology and Pharmacy,L.L.R.M. Medical College, Meerut - 250 004 (U.P.) India

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The fragmentation pattern of 2- substituted -3`- (substituted indol-3-yl- methylene)imino]chalcones(Ia-Ie). 1-Acetyl-(5-substituted phenyl)-3-[*m*-(2-substituted indol-3-yl-methylene)imino]- phenyl-3-pyrazolines (IIa-IIe) and 1-Acetyl-3-[*m*-(5-methyl-2-phenylindol-3-yl-4-oxo-1-thiazolidinyl)]-5-(substituted-phenyl)-3- pyrazolines (IIIa-IIIe) have been studied. The structure of the major fragment ions and pathway resulting to their formation have been postulated by the recognition of the appropriate meta-stable peaks.

Keywords: Mass spectra, Fragmentation, Indoles.

Introduction

Several workers have utilized the LR-EIMS technique [1-6] to delineate the fragmentation pattern of different heterocyclic derivatives [7-12]. In addition, many researchers have also choosen the metastable ions, as proof of fragmentation mechanism [3,6,13,14]. Recently we have also reported the fragmentation pathway of some indole derivatives [13], which were found to possess potent hypotensive and anti-inflammatory activities [5,6]. However, the literature on 2-substituted indoles and its derivatives like chalcones, thiazolidinones and pyrazolines is yet not available. Furthermore, application of indole and its derivatives in the field of medicinal and biochemistry needs the exploration of their mass specterometric details. It was, therefore, worthwhile to synthesize a series of 1-Acetyl-3-[*m*-(5-methyl-2-phenylindol-3-yl-4-oxo-1-thiazolidinyl)]-5-(substituted- phenyl)-3-pyrazolines with a view to investigate the fragmentation mechanism of the title compounds.

Experimental

The mass spectra were recorded on a JMSD300 double focussing spectrometer with JMA-2000 data operating at an ionisation potential 70eV. The source temperature was ranged between 200- 300°, subject to the volatility of the compounds.

2-Substituted-3'-[(substituted indol-3-yl-methylene) imino]- chalcones (Ia-Ie)and1-Acetyl-(5-substituted phenyl)-3-[*m*-(2-phenylindol-3-yl-methylene)imino]-phenyl-3-pyrazolines (IIa-IIe) were synthesized according to already reported method [15].

1-Acetyl-3-[m-(5-methyl-2-phenylindol-3-yl-4-oxo-1-thiazolidinyl)phenyl]-5-(2-methoxyphenyl)-3-pyrazoline (IIIa): To a solution of IIa (0.01 mol) and trimethylamine (0.02 mol) in dry benzene was added thiolactic acid (0.02 mol) drop wise at ambient temperature and the reaction mixture was refluxed for 4 hrs, filtered, concentrated and poured into crushed ice. The solid thus obtained was recrystalized from the appropriate solvent. Other members (IIIb - IIIe) were prepared in similar ways. The analytical data are given in Table 1.

Results and Discussion

The mass spectral fragmentation pattern of 2-substituted-3- [(substituted indol-3-yl-methylene)imino]-chalcones (Ia-Ie, Table- 1) show analogies with those of benzalacetophenones, which were supported by earlier workers [16-18]. The molecular ion forms the base peak for compounds Ia-Ib, while the base peak in compounds Ic, Id and Ie are $(M\text{-}C1)^+$ and $(M\text{-}F)^+$, may be due to the ortho effect, which is responsible for the rapid elimination of chlorine and fluorine from the original molecules. These observations are in hormony with results of previous researchers, who have reported a similar ortho effect

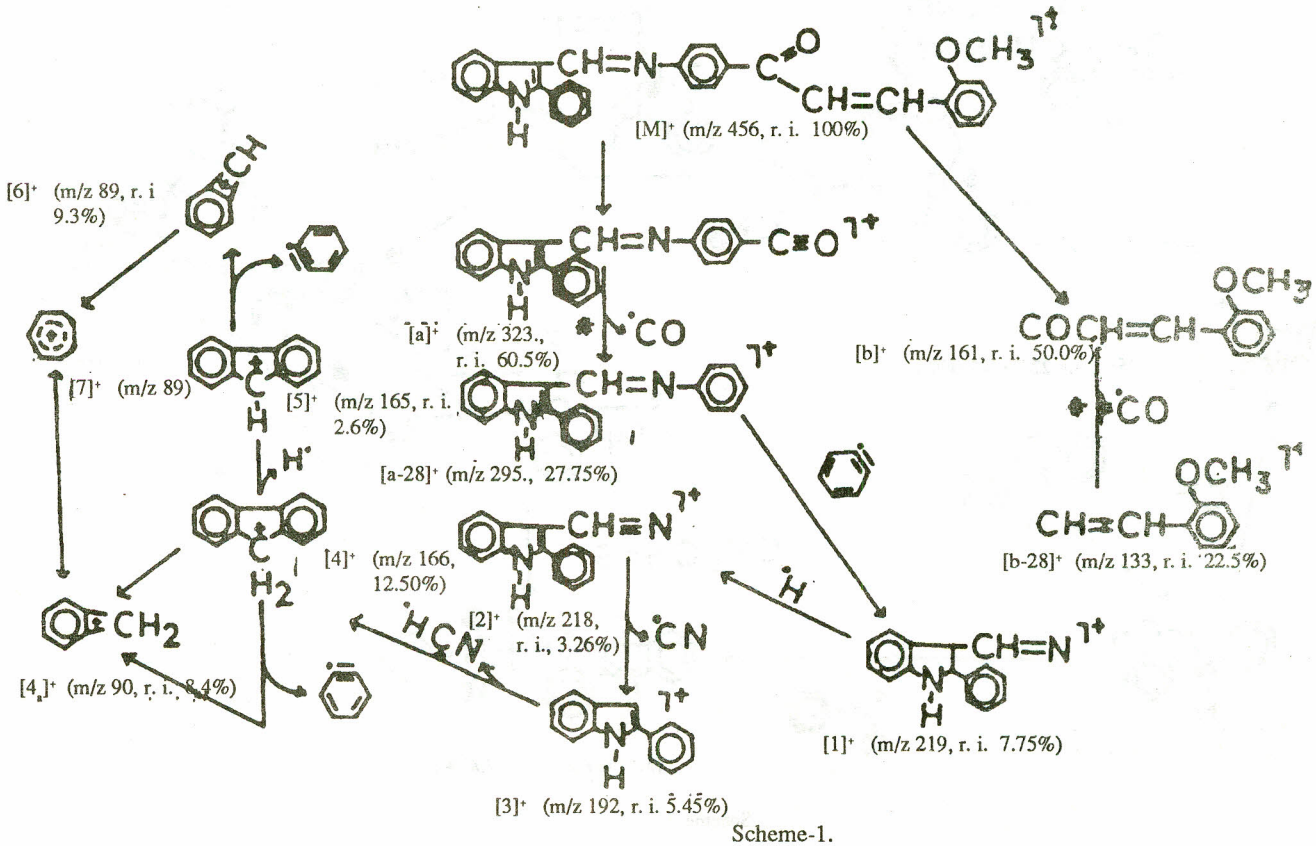
TABLE 1. ANALYTICAL AND PHYSICAL DATA OF COMPOUNDS TYPE I, II AND III.

S.No.	R	M.P. °C	Yield %	Mol. formula
Ia	*o*-OCH_3	236	70	$C_{31}H_{24}N_2O_2$
Ib	*o*-CH_3	201	75	$C_{31}H_{24}N_2O$
Ic	*o*-Cl	196	65	$C_{30}H_{21}N_2OCl$
Id	*o*-F	183	60	$C_{30}H_{21}N_2OF$
Ie	*p*-F	175	55	$C_{30}H_{21}N_2OF$
IIa	*o*-OCH_3	276	60	$C_{33}H_{28}N_4O_2$
IIb	*o*-CH_3	216	65	$C_{33}H_{28}N_4O$
IIc	*o*-Cl	203	50	$C_{32}H_{25}N_4OCl$
IId	*o*-F	198	45	$C_{32}H_{25}N_4OF$
IIe	*p*-F	191	50	$C_{32}H_{25}N_4OF$
IIIa	*o*-OCH_3	217	40	$C_{36}H_{32}N_4O_3S$
IIIb	*o*-CH_3	256	45	$C_{36}H_{32}N_4O_2S$
IIIc	*o*-Cl	176	35	$C_{35}H_{29}N_4O_2SCl$
IIId	*o*-F	213	40	$C_{35}H_{29}N_4O_2SF$
IIIe	*p*-F	199	35	$C_{35}H_{29}N_4O_2SF$

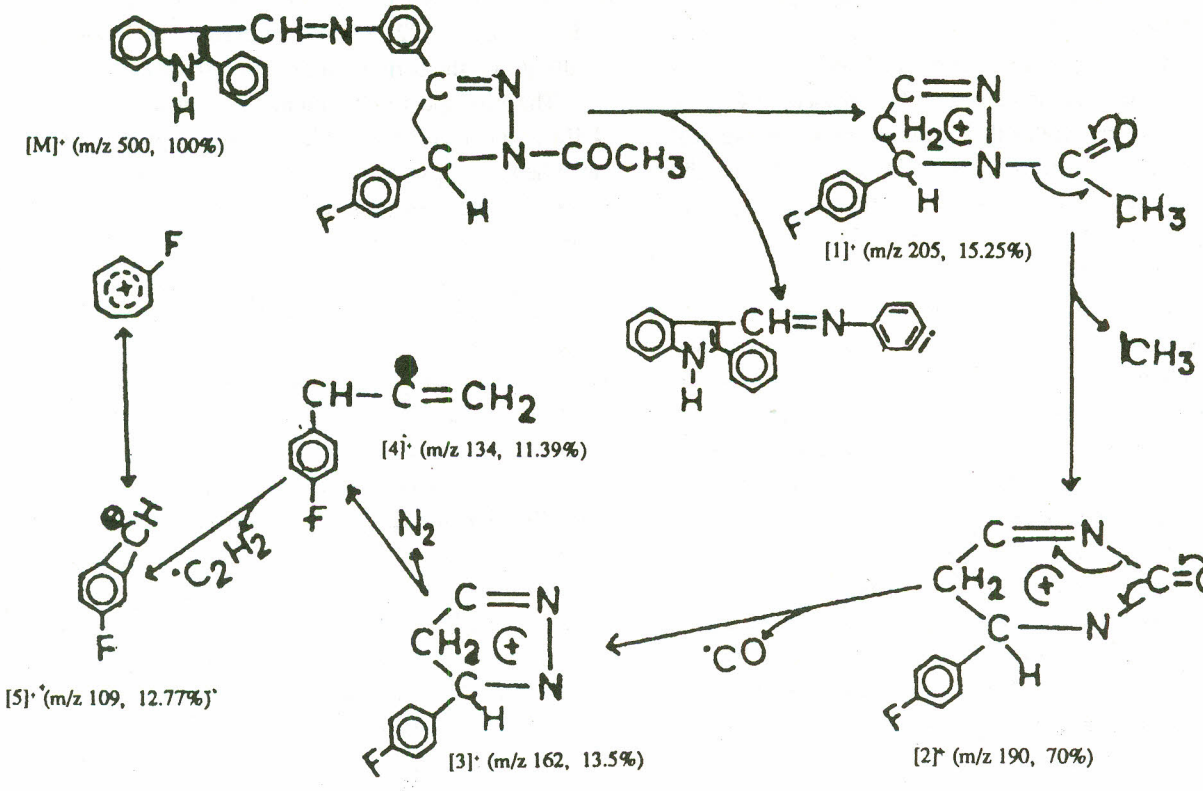
in the substituted benzalacetones [19]. The mass spectral fragmentation pattern of 2-methoxy-3-[(2- phenylindol-3-yl-methylene) imino] chalcone (compound Ia) is shown in Scheme1 and its molecular ion peak is base peak (*m/z* 456, r.i. 100%). This chalcone yields the common fragment ions $(a)^+$ (*m/z* 323, r.i. 60.5%) and $(b)^+$ (*m/z* 151, r.i. 50.0%) by the cleavage of the molecule at α position to the carbonyl group. Such type of fragmentation is reported in other chalcones and some benzalacetophenones [20]. Moreover, ions $(a)^+$ and $(b)^+$ readily eliminate the CO radical to yield ions $(a\text{-}28)^+$ (*m/z* 295, r.i. 27.75%) and $(b\text{-}28)^+$ (*m/z* 133, r.i. 22.50%). The existence of these two later ions have been confirmed on the basis of observed metastable peaks at 254.42 (323-295) and *m/z* 109.86 (161-133) respectively. This observation is also in accordance with the results of our previous report [13]. The ions $(a\text{-}28)^+$ eliminates the phenyl radical to produce cation $(1)^+$ (*m/z* 219, r.i. 7.75). Ion $(1)^+$ subsequently eliminates neutral radicals H and CH, resulting in the formation of cation $(3)^+$ (*m/z* 192, r.i. 5.45). Cation $(3)^+$ after elimination of neutral HCN molecule [3] with rearrangement yields a stable cation $(4)^+$ (*m/z* 166, r.i. 12.75). This path was further confirmed on the basis of observed metastable peak at *m/z* 143.52 (192-166). Cation $(4)^+$ can also produce a radical ion $(4a)^+$ (*m/z* 90, r.i. 12.50%). Further, the decomposition of ion $(4)^+$ yields ions $(5)^+$ and $(6)^+$. Ion $(5)^+$ and $(6)^+$ rearrange into tropylium ions, which are more stable due to high degree of aromaticity. Lower fragmentations are in accordance with characteristic fragmentations of hydrocarbons [21,22]. Likewise ion $[b]^+$ readily loses the CO, resulting into the formation of cation $[b\text{-}28]^+$.

The mass spectral fragmentation pathways of 1-acetyl-5-(4-fluorophenyl)-3-[*m*-(2-phenylindol-3-yl-methylene)-imino]-phenyl-3- pyrazoline (compound IIe) are shown in Scheme2. The proposed molecular ion gives base peak at *mz*500. The mass spectra of other members of pyrazolines (IIa-IId, Table 1) show analogies with those of IIe. The molecule (IIe) readily eliminates 2-phenyl-3- benzylidene indole radical giving cation $[1]^+$ (*m/z* 205, r.i. 55.25%). The later ion eliminates the methyl group and rearranges to a highly conjugated six membered heterocyclic cation $[2]^+$ at *m/z* 190, which is more stable due to increased degree of resonance. This path was confirmed on the observed metastable peak at *m/z* 176.09 (205-190). The ion $[2]^+$, further loses one unit of CO and N_2, yielding a cation $[4]^+$ (*m/z* 134, r.i. 13.35%). This ion after rearrangement produce an ion $[5]^+$ (*m/z* 109, r.i. 8.75%). Later ion may be stabilized due to their further rearrangement into fluorotropylium ion. Other fragmentation patterns are similar as in case of 2-substituted-3- [(substituted indol-3-yl-methylene)- imino]-chalcones (Scheme 1).

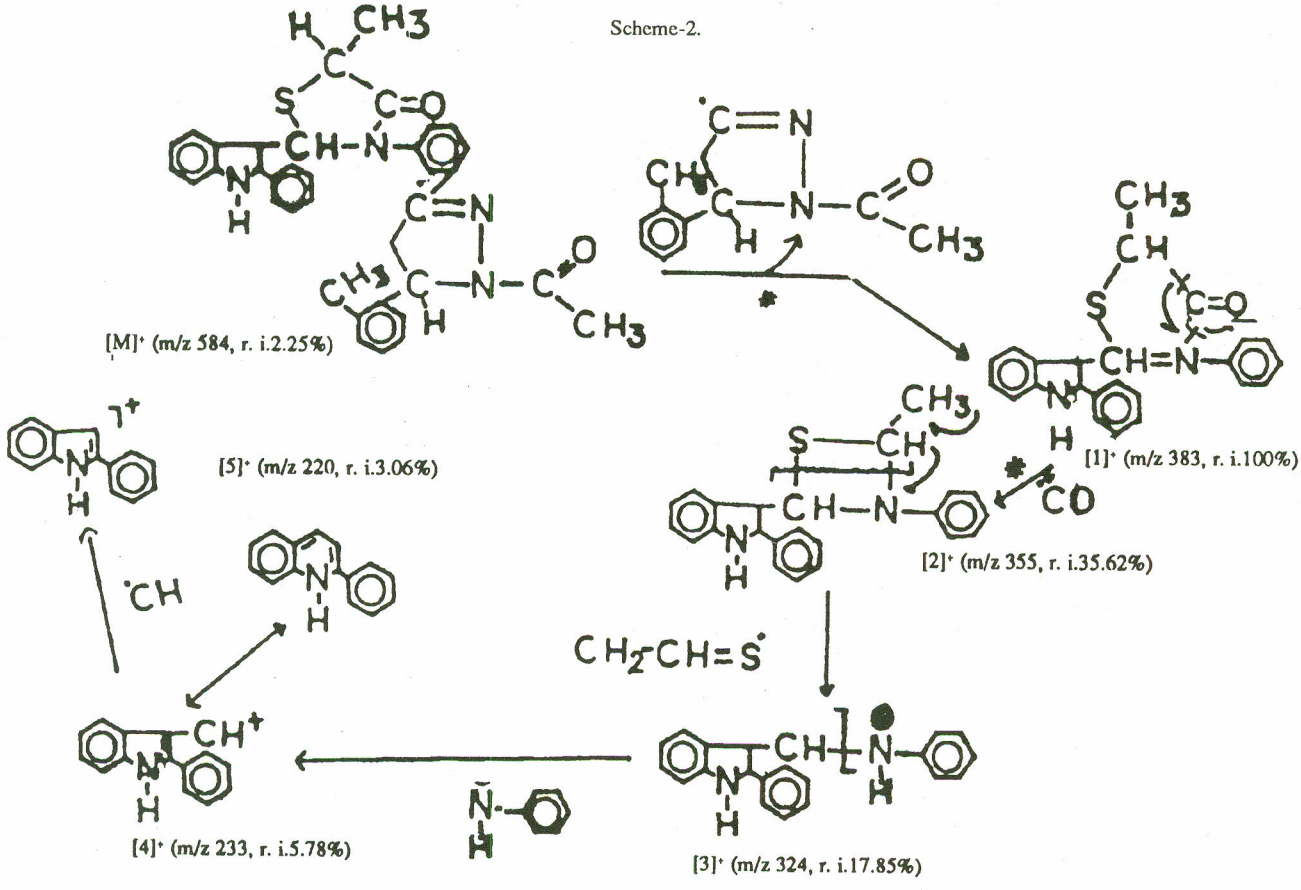
The various fragments of 1-acetyl-3-[*m*-(5-methyl-2-phenylindol-4-oxo-1-thiazolidinyl)]-5-(0-tolyl)-3-pyrazoline (compound IIIb) are represented in Scheme 3. The molecular ion at *m/z* 584 is of very low abundance. Other members of



Scheme-1.



Scheme-2.



Scheme-3.

TABLE 2. IMPORTANT PEAKS AND METASTABLE NON PEAKS FOR COMPOUNDS IA-IE, IIA-IIE AND IIIA-IIIE.

Compound No.	Ions	m/z (Rel. int. %)	Metastable ions m/z (m*)
Ia	$[m]^+$	456(100)	-
	$[a]^+$	323(60.5)	-
	$[a-28]^+$	295(27.75)	264.42
	$[b]^+$	161(50.00	-
	$[b-28]^+$	133(22.50)	109.86
	$[1]^+$	219(7.75)	-
	$[2]^+$	218(3.26)	-
	$[3]^+$	192(5.45)	-
	$[4]^+$	166(12.50)	142.52
	$[5]^+$	165(02.60)	-
	$[6]^+$	89(09.30)	-
	$[4a]^+$	90(08.40)	-
Ib	$[M]^+$	440(100)	-
	[a]+	323(65.0)	-
	$[a-28]^+$	295(25.35)	264.42
	$[b]^+$	145(45.00)	-
	$[b-28]^+$	117(20.15)	94.40
	$[1]^+$	219(8.25)	-
	$[2]^+$	218(4.10)	-
	$[3]^+$	192(5.70)	-
	$[4]^+$	166(12.70)	142.52
	$[5]^+$	165(3.10)	-
	$[6]^+$	89(8.75)	-
	$[4a]^+$	90(8.40)	-
Ic	$[M]^+$	460.5(3.25)	-
	$[M-Cl]^+$	425.0(100)	-
	$[a]^+$	323.0(60.0)	-
	$[a-28]^+$	295.0(25.25)	264.42
	$[b]^+$	165.5(55.00)	-
	$[b-28]^+$	137.5(18.25)	144.23
	$[1]^+$	219.0(9.10)	-
	$[2]^+$	218.0(3.24)	-
	$[3]^+$	192.0(5.60)	-
	$[4]^+$	166.0(12.95)	142.52
	$[5]^+$	165.0(3.75)	-
	$[6]^+$	89.0(8.70)	-
	$[4a]^+$	90.0(7.85)	-
Id	$[M]^+$	444(4.25)	-
	$[M-F]^+$	425(100)	-
	$[a]^+$	323(65.5)	-
	$[a-28]^+$	295(30.25)	264.42
	$[b]^+$	149(40.35)	-
	$[b-28]^+$	121(98.26)	98.26
	$[1]^+$	219(8.25)	-
	$[2]^+$	218(3.35)	-

(Table 2 Contd.....)

(Table 2 Continue.....)

	$[3]^+$	192(5.65)	-
	$[4]^+$	166(12.75)	142.52
	$[5]^+$	165(3.80)	-
	$[6]^+$	89(8.60)	-
	$[4a]^+$	90(8.55)	-
Ie	$[M]^+$	444(100)	-
	$[M-F]^+$	425(3.35)	-
	$[a]^+$	323(63.65)	-
	$[a-28]^+$	295(27.25)	264.42
	$[b]^+$	149(38.30)	-
	$[b-28]^+$	121(19.15)	98.26
IIa	$[M]^+$	512(100)	-
	$[1]^+$	217(11.25)	-
	$[2]^+$	202(50.95)	188.03
	$[3]^+$	174(7.74)	-
	$[4]^+$	146(2.25)	-
IIb	$[M]^+$	496(100)	-
	$[1]^+$	201(10.35)	-
	$[2]^+$	186(55.65)	172.11
	$[3]^+$	158(5.23)	-
	$[4]^+$	130(3.78)	-
IIc	$[M]^+$	516.5(100)	-
	$[M-Cl]^+$	481(3.45)	-
	$[1]^+$	221.5(12.33)	-
	$[2]^+$	206 (62.25)	192.51
	$[3]^+$	178 (9.24)	-
	$[4]^+$	150.5(7.75)	-
IId	$[M]^+$	500(100)	-
	$[M-F]^+$	481(4.45)	-
	$[1]^+$	205(15.00)	-
	$[2]^+$	190(65.00)	176.09
	$[3]^+$	162(7.5)	-
	$[4]^+$	134(13.00)	-
IIe	$[M]^+$	500(100)	-
	$[M-F]^+$	481(3.47)	-
	$[1]^+$	205(15.25)	-
	$[2]^+$	190(70.00)	176.09
	$[3]^+$	162(13.5)	-
	$[4]^+$	134(11.39)	-
	$[5]^+$	109(12.77)	-
IIIa	$[M]^+$	600(2.76)	-
	$[1]^+$	383(100)	251.17
	$[2]^+$	355(40.6)	329.04
	$[3]^+$	324(15.39)	-
	$[4]^+$	233(4.80)	-
	$[5]^+$	220(2.23)	-
IIIb	$[M]^+$	584(2.25)	-
	$[1]^+$	383(100)	251.17
	$[2]^+$	355(35.62)	329.04
	$[3]^+$	324(17.85)	-

(Table 2 Contd.....)

(Table 2 Continue.....)

	$[4]^+$	233(5.78)	-
	$[5]^+$	220(3.85)	-
IIIc	$[M]^+$	604.5(3.61)	-
	$[1]^+$	383(100)	251.17
	$[2]^+$	355(39.47)	329.04
	$[3]^+$	324(15.33)	-
	$[4]^+$	233(5.62)	-
	$[5]^+$	220(3.06)	-
IIId	$[M]^+$	588(2.35)	-
	$[1]^+$	383(100)	-
	$[2]^+$	355(41.23)	251.17
	$[3]^+$	324(12.37)	329.04
	$[4]^+$	233(5.50)	-
	$[5]^+$	220(3.67)	-
IIIe	$[M]^+$	588(2.69)	-
	$[1]^+$	383(100)	251.17
	$[2]^+$	355(38.44)	329.04
	$[3]^+$	324(10.75)	-
	$[4]^+$	233(9.29)	-
	$[5]^+$	220(2.95)	-

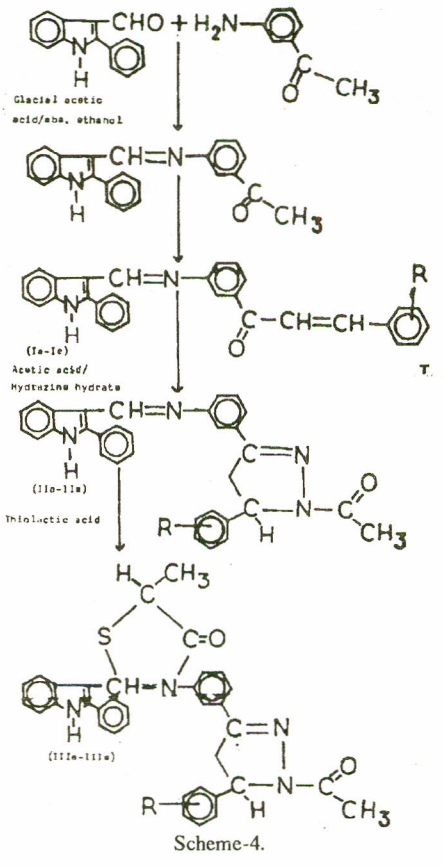
stage third compounds (IIIa, IIIc, IIId and IIIe, Table 2) show analogies with those of IIIb. The base peak $[1]^+$ (*m/z* 383, r.i. 100%) is produced after elimination of 1-Acetyl-2-pyrazoline radical. Cation $[1]^+$ readily eliminates the CO radical and rearranges into cation $[2]^+$ (*m/z* 355, r.i. 35.62%). This ion is supported by the presence of metastable peak at *m/z* 329.04 (383-355). The later ion further gives cation $[3]^+$ (*m/z* 324, r.i. 17.86%) after removal of one neutral CH_2 = CH-S radical with concomitant rearrangement of ion $[2]^+$. The ion $[4]^+$ is formed after elimination of a neutral radical (secondary aromatic amine). The stability of this ion radical (cation) may be due to its rearrangement into quinolium cation $[5]^+$ in another fragment pathways may lose a methine radical, resulting in the formation of an ion $[4a]^+$. This ion further yields ion $[6]^+$ and $[7]^+$ as depicted in Scheme 1.

Conclusion

In case of chalcones, it can be concluded that cleavage of molecules at a position to the carbonyl group plays a vital role in postulating the fragmentation pattern of substituted indolyl chalcones.

The presence of a phenyl group in a number of ion and formation of benzopyrolene type of compounds (Scheme 4) under the electron impact shows that the bond at 2-position of the indole nucleus is considerably strong. This may be due to high degree of conjugation between indole and 2-phenyl ring. The presence of quinolium ion [3] is another characteristic feature of indole derivatives (Scheme 2).

In case of pyrazoline derivatives (cyclized products) of indolyl chalcones, it has been observed that pyrazoline ring



Scheme-4.

after elimintion of CO radical forms a stable six membered heterocyclic benzoid type of cation. The stability of this ion $[2]^+$ may be due to high degree of conjugation with 4-fluorophenyl ring.

However, in case of thiazolidinyl pyrazolines (IIIa-IIIe) most characteristic feature is the formation of cation $[2]^+$ (β-thialactam ring) which is supported by metastable peak. Other feature in the pathways of such type of compounds (IIIa-IIIe) are formation of similar ions as in case of 2-phenylindole derivatives.

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