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## Mass Spectral Fragmentation Pattern and Semi Empirical Studies of N, N'-Linked Bis Azaheterocycles and Quinazolinone Based Benzamides.

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### ABSTRACT

Electron Impact induced mass spectral fragmentation pattern of 2,2-tetrasubstituted-tetrahydro-3,3'-bisquinazolin-4,4'-diones (**2a-c**), 2-amino-N-[1,2-disubstituted-1,2-dihydro-4-oxo-3-(4H)-quinazoliny]benzamides (**3a-c**) and 2-methylamino-N-[1,2-dimethyl2'-ethyl-1,2-dihydro-4-oxo-3-(4H)-quinazoliny]-benzamide (**4**) is studied and the results are presented. The mass spectral studies on these compounds indicate the N,N-bond susceptibility in their molecules by showing the  $M^+ / 2$  ion peak in their mass spectra. The retro Diels-Alder path is also noticed in the mass spectral fragmentation pattern. The observations are strengthened by their agreement with the computationally calculated heats of formation values using parametric method PM3.

**Keywords:** N,N- Linked bisazaheterocycles, 2-amino-N-quinazolinonylbenzamides, 2-methylamino-N-quinazolinonylbenzamides, mass spectral fragmentation pattern, PM3.

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## INTRODUCTION

Quinazolin-4(3H)-ones play an important role in the fields of both synthetic and medicinal chemistry. Bisazaheterocycles containing the quinazolinone skeleton, are associated with a wide variety of biological activities such as antimicrobial [1], anti tubercular [2], antifungal[3], antipsychotic [4], anti-inflammatory [5], antihypertensive [6], CNS depressant [7], anti convulsant [8], anti HIV [9], ulcerogenic [10] and anticancer activities [11]. 3-(4-Quinazoliny)-3,4-dihydro-4-quinazolinones show anti-inflammatory activity [12], 2-[(4-hydroxy-2-quinazoliny)amino]-3,4-dihydro-4-quinazolinones [13] are useful as bacteriostatic and bacteriocidal agents. Silicone derivatives containing two units of quinazolin-4-one, are potential therapeutic agents against HIV and 3-acetamido-6'-chloro-3-methyl-2,2'-bisquinazolin-4(3H)-one has antifungal activity. Particularly, 6,6'-bis-4(3H)-quinazolinones have industrial importance and their polymers have excellent thermal, mechanical and dielectric properties [14].

Quinazolin-4(3H)-one based N,N-linked bisazaheterocycles also represent an important class ofazaheterocycles in view of their biological properties and chemical reactivity. Some of them exhibit antimicrobial [15], anti-parkinsonian [16], anti-convulsant [17] and anti-inflammatory activities [18].

Furthermore, N,N-linked bisazaheterocycles act as excellent precursors for nitrogen centered free radicals, which have a significant role in biological processes[19] and in industrial applications. For example, the metal complexes of verdazylradicals act as molecular magnetic superconductors [20].The activity of antimicrobial drugsMetronidazole and Isoniazidis through the nitrogen centered free radicals [21]. Many N-centered free radicals are the source for synthesis of novel heterocyclic compounds [22]. Generally, thermolysis or photolysis of N,N'-linked bisazaheterocycles generate the nitrogen centered free radicals which undergo various types of reactions such as dimerisation, rearrangements, addition reactions to form novel azaheterocycles [23].

These observations, have thrown special interest in N.N'-linked bisazaheterocycles, particularly 3,3'-bisquinazolin-4,4'-dione derivatives. In continuation, the synthesis and characterization of 2,2-tetrasubstituted-tetrahydro-3,3'-bisquinazolin-4,4'-diones (**2a-c**), 2-amino-N-[1,2-disubstituted-1,2-dihydro-4-oxo-3-(4H)-quinazoliny]benzamides (**3a-c**) and 2-methylamino-N-[1,2-dimethyl2'-ethyl-1,2-dihydro-4-oxo-3-(4H)-quinazoliny]-benzamide (**4**)are reported from our group[24].Here, we discuss the Electron impact (EI) Induced partial mass spectral fragmentation pattern studies of the **2a-c**, **3a-c** and**4**. The EI mass spectral fragmentation studies on the monomer, 2,3-dihydro-4(3H)-quinazolinones reported earlier indicate the loss of CO and C-2 and N-3 substituent as main fragmentation path, besides the skeletal fission [25]. However, the mass spectral fragmentation pattern oftetrahydro-N,N'-linked-bisquinazolinones and 2-amino-N-(4-oxo-3-(4H)-quinazoliny)-benzamidesare not reported in literature. Here, wediscuss some aspects of electron impact mass spectral fragmentation pattern characteristics of **2a-c**, **3a-c** and **4**, which are the potential source for cyclic nitrogen centered free radicals.

Molecular orbital calculations of **2a-c**, **3a-c** and **4** are performed using the reasonably accurate semi empirical PM3 method belonging to NDDO (neglect of double differential overlap) [26]. Minimum energy values, binding energies, dipole moment, logp values and heat of formation of optimized geometries of **2a-c**, **3a-c** and **4** are calculated.

## MATERIALS AND METHODS

Melting points were recorded in capillary tubes using conc.H<sub>2</sub>SO<sub>4</sub> bath, and are uncorrected. IR spectra were recorded in potassium bromide disks on a Shimadzu-435 spectrophotometer. <sup>1</sup>H NMR spectra were recorded in CDCl<sub>3</sub> and DMSO-*d*<sub>6</sub> on a 270 MHz JOEL, 300 MHz Bruker FT-NMR spectrometer with TMS as an internal standard and chemical shifts are expressed in δ ppm. Mass spectra were recorded on Perkin-Elmer Hitachi RMU-62 and VG-Micromass 7070H instrument of direct inlet probe.

The compounds **2a-c**, **3a-c** and **4** were prepared according to the procedure reported in literature from our group [24].

### Typical procedure for the synthesis of **2a-c**, **3a-c** and **4**

To a solution of 1,2-bis(2-amino/methylamino-benzoyl)hydrazine (**1a/1b**, 2mmol) in methanol(10 ml) containing p-toluenesulfonic acid (2mg), appropriate ketone ( 5mmol) was added and the reaction mixture was refluxed for 6 – 8h. The excess methanol was distilled off, on cooling the concentrated solution, the corresponding products **2a-c**, **3a-c** and **4** were separated out and compounds were characterized by spectral data and by analogy.

### **2,2,2',2'-Tetramethyl-tetrahydro-3,3'-bisquinazolin-4,4'-dione (2a)**

Acetone is used as a ketone; M.P. 272-275 °C; yield 75%; IR (KBr, ν cm<sup>-1</sup>): 3300, 1660, 1640; <sup>1</sup>H NMR (TFA, δ ppm): 2.53 (s, 12H, CH<sub>3</sub>), 7.3-8.04(m, 8H, Ar-H) EI-MS: m/z (rel. int., %) 350 (M<sup>+</sup>, 12), 336 (25 (24), 175 (3), 161 (21), 160 (base peak), 120 (13), 119 (14), 77 (6), 56 (2), 42 (10), 32 (67).

### **2,2'-Dispirocyclopentane-tetrahydro-3,3'-bisquinazolin-4,4'-dione (2b)**

Cyclopentanone was used as a ketone; M.P. 255-258°C; yield 65%; IR (KBr, ν cm<sup>-1</sup>): 3320, 1670, 1650; <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ ppm): 1.66 - 2.48 (m, 16H, CH<sub>2</sub>), 4.54 (b, 2H), 6.66 -8.04(m, 8H, Ar-H) EI-MS: m/z (rel. int., %) 402 (M<sup>+</sup>, 16), 373 (6), 203 (27), 201(60), 200(20), 199 (10), 186 (base peak) 185 (24), 173 (40), 160 (20), 120 (39), 119 (18), 77 (24), 65(15), 41 (23), 40 (52).

### **2,2'-Dispirocyclohexane-tetrahydro-3,3'-bisquinazolin-4,4'-dione (2c)**

Cyclohexanone was used as a ketone; M.P. 260-262°C; yield 60%; IR (KBr, ν cm<sup>-1</sup>): 3320, 1680, 1645; <sup>1</sup>H NMR (DMSO-*D*<sub>6</sub>, δ ppm): 1.32 - 2.06 (m, 20H, CH<sub>2</sub>), 6.69 - 7.71 (m, 10H, Ar-H)

and NH) EI-MS: m/z (rel. int., %) 430 ( $M^+$ , 18), 387 (10), 290 (7), 217b(35), 216 (36), 215(80), 201(25), 200(80), 199 (30), 186 (22) 185 (21), 173 (70), 172 (49), 161 (20), 160 (38), 120 (51), 119 (39), 77 (85), 69(base peak), 55 (69), 41 (23), 40 (39).

### **2-Amino-N-[2-ethyl-2-methyl-1,2-dihydro-4-oxo-3-(4H)-quinazolinyl]benzamide (3a)**

2-Butanone was used as a ketone; M.P. 190-192°C; yield 60%; IR (KBr,  $\nu$   $\text{cm}^{-1}$ ): 3450, 3320, 3250, 1660, 1640;  $^1\text{H}$  NMR (DMSO- $\text{D}_6$ ,  $\delta$  ppm): 0.88 (t, 3H,  $\text{CH}_3$ ), 1.46 (s, 3H,  $\text{CH}_3$ ), 1.8(m, 2H,  $\text{CH}_2$ ), 5.5 (b, 2H, NH), 6.31 - 7.62 (m, 10H, Ar-H and NH), 9.9 (s, 1H); EI-MS: m/z (rel. int., %) 324 ( $M^+$ , 7), 295 (21), 270(13), 239 (10), 174 (23), 161 (98), 160 (5), 120 (base peak), 119 (4), 92 (22), 77 (3), 65 (14), 32(26).

### **2-Amino-N-[2-phenyl-2-methyl-1,2-dihydro-4-oxo-3-(4H)-quinazolinyl]benzamide (3b)**

Acetophenone was used as a ketone; M.P. 185-187°C; yield 60%; IR (KBr,  $\nu$   $\text{cm}^{-1}$ ): 3410, 3320, 3250, 1665, 1635;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$  ppm): 2.1 (s, 3H,  $\text{CH}_3$ ), 4.8(s, 1H), 5.45 (b, 2H, NH), 6.61 - 8.04 (m, 9H, Ar-H and NH); EI-MS: m/z (rel. int., %) 372 ( $M^+$ , 2), 222 (12), 120 (16), 119 (4), 92 (5), 78 (base peak), 77 (26), 52 (36), 39(18), 32(18).

### **2-Amino-N-[2,2'-benzyl-1,2-dihydro-4-oxo-3-(4H)-quinazolinyl]benzamide (3c)**

Dibenzyl ketone was used as a ketone; M.P. 195-197°C; yield 60%; IR (KBr,  $\nu$   $\text{cm}^{-1}$ ): 3450, 3340, 3240, 1680, 1645;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$  ppm): 3.3 (AB quartet, 4H,  $\text{CH}_2$ ), 4.3(s, 1H), 5.5 (b, 2H, NH), 6.51 - 7.9 (m, 19H, Ar-H and NH); EI-MS: m/z (rel. int., %) 462 ( $M^+$ , not recorded), 371(2), 237(5), 235(4), 120 (9), 119 (4), 92 (5), 78 (base peak), 77 (40), 52 (36), 39(26), 32(100).

### **2-Methylamino-N-[2-ethyl-1,2-dimethyl-1,2-dihydro-4-oxo-3-(4H)-quinazolinyl]benzamide (4)**

2-Butanone was used as a ketone; M.P. 185-187°C; yield 67%; IR (KBr,  $\nu$   $\text{cm}^{-1}$ ): 3380, 3200, 1670, 1630;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$  ppm): 0.8 (t, 3H,  $\text{CH}_3$ ), 1.62 (s, 3H,  $\text{CH}_3$ ), 1.94 (m, 2H,  $\text{CH}_2$ ), 2.81 (s, 3H,  $\text{CH}_3$ ), 2.93 (s, 3H,  $\text{CH}_3$ ), 6.42 - 7.67 (m, 9H, Ar-H), 8.37 (b, 1H, NH); EI-MS: m/z (rel. int., %) 352 ( $M^+$ , 6), 324(5), 323(12), 298 (18), 280 (4), 203(2), 175(13), 165(5), 149(10), 134(base peak), 70 (10), 57 (12), 32(100).

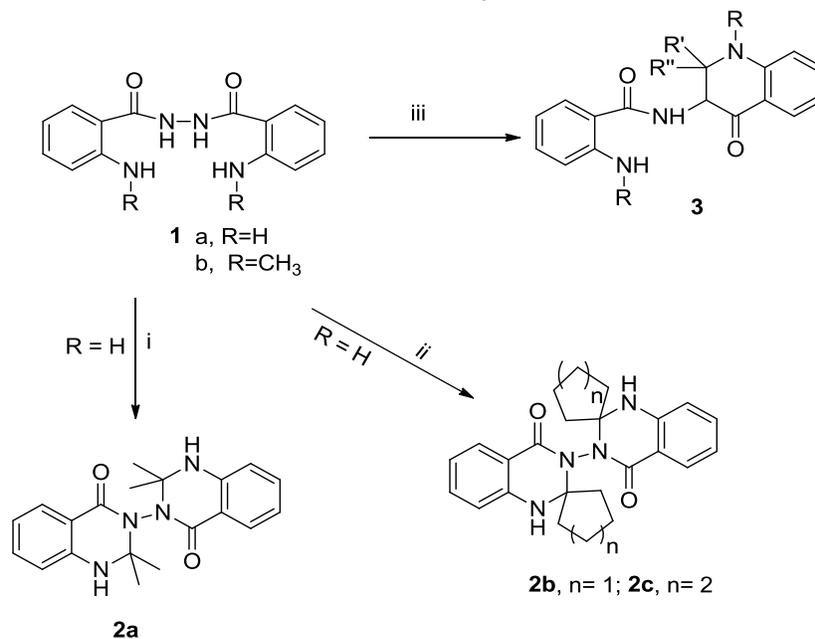
## **Computational work**

Semi-empirical PM3 method belonging to NDDO approximation is used to study the stabilities of bisazaheterocycles, 2,2-tetrasubstituted-tetrahydro-3,3'-bisquinazolin-4,4'-diones(2a-c), 2-amino-N-[1,2-disubstituted-1,2-dihydro-4-oxo-3-(4H)-quinazolinyl]benzamides (3a-c) and 2-methylamino-N-[1,2-dimethyl-2'-ethyl-1,2-dihydro-4-oxo-3-(4H)-quinazolinyl]-benzamide(4). All molecules were geometrically optimized and the molecular orbital calculations were performed using PM3 method.

## RESULTS AND DISCUSSION

The compounds **2a-c**, **3a-c** and **4** were synthesized according to the procedure reported earlier from our laboratory, from **1a/1b** with appropriate ketones in methanol in the presence of p-TsOH under reflux for 6 – 8 h (Scheme 1).

Scheme 1: The reaction of **1a/1b** with ketones



i) H<sub>3</sub>CCOCH<sub>3</sub>, p-TsOH, MeOH, Δ, 6h; ii) , p-TsOH, MeOH, Δ, 6h; iii) ketone, p-TsOH, MeOH, Δ, 6 – 8h

### Mass spectral fragmentation of 2,2,2',2'-Tetrasubstituted-tetrahydro-3,3'-bisquinazolin-4,4'-dione (**2a-c**)

The partial Electron Impact induced mass spectral fragmentation of **2a** (Fig. 1, Scheme 2) and **2b-c** (Scheme 3) indicate that the molecular ion  $M^+$  is recorded with low intensity. These compounds have shown distinct and intense  $M^+/2$  ion peaks corresponding to the 2,2'-disubstituted-dihydro-4(3H)-quinazolinonylcations arising by N-N bond cleavage in  $M^+$  ion. These ions further give fragments via retro Diels-Alder path. The  $M^+$  ion in **2a** gives the ion at  $m/z$  335 due to the loss of methyl radical. The molecular ion of **2a** seems to undergo 1,2-elimination reaction to form the ion at  $m/z$  160 as the base peak. In **2b** and **2c** loss of H, methylene and ethylene radicals in  $M^+/2$  ion is noticed from 2-cycloalkane moiety. The detailed mass spectral fragmentation pattern for **2a-c** is shown in Schemes 2 and 3.

Scheme 2: Partial Mass spectral fragmentation pattern of 2a

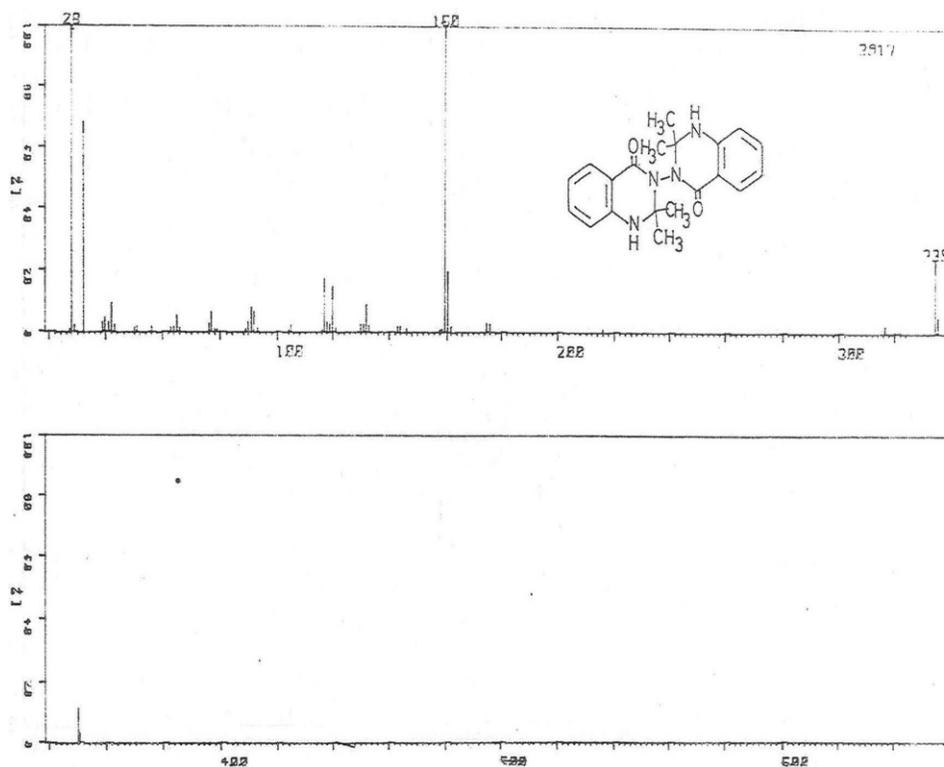
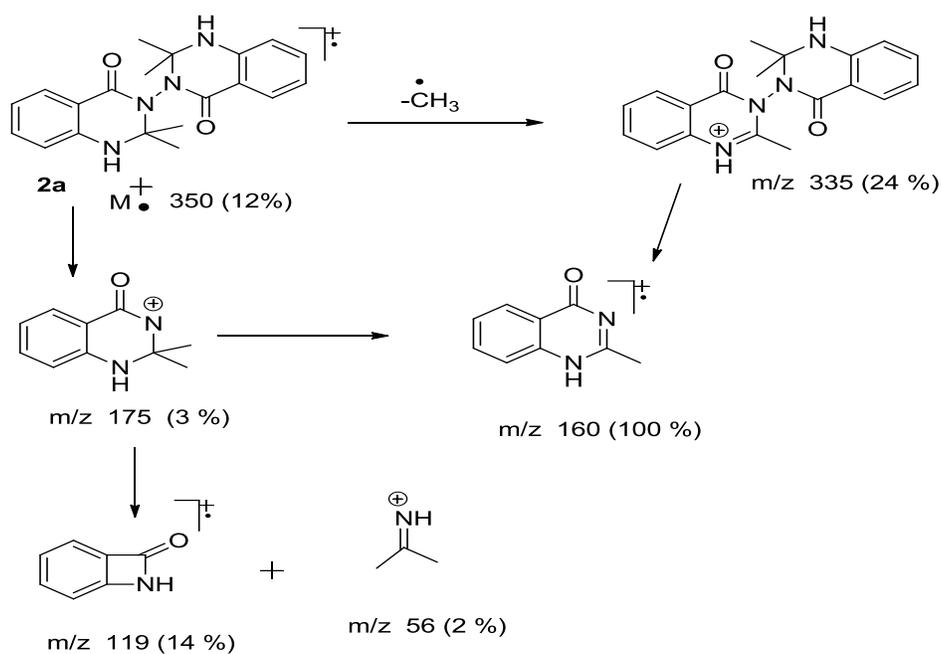
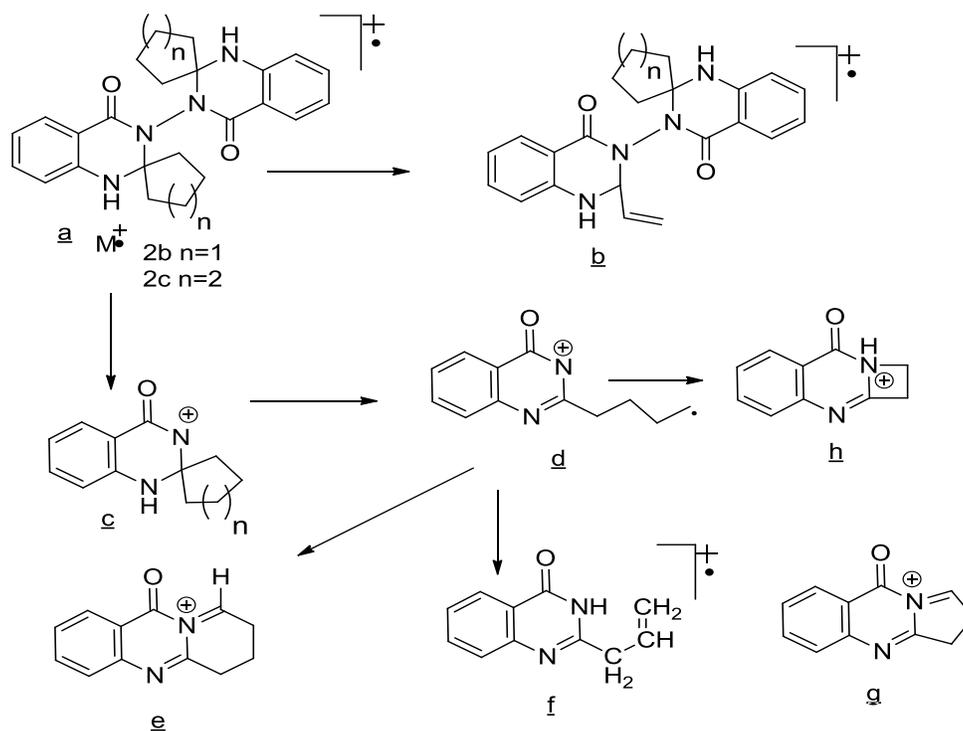


Fig. 1: Mass spectrum of 2,2,2',2'-tetramethyl-tetrahydro-3,3'-bisquinazolin-4,4'-dione (2a)

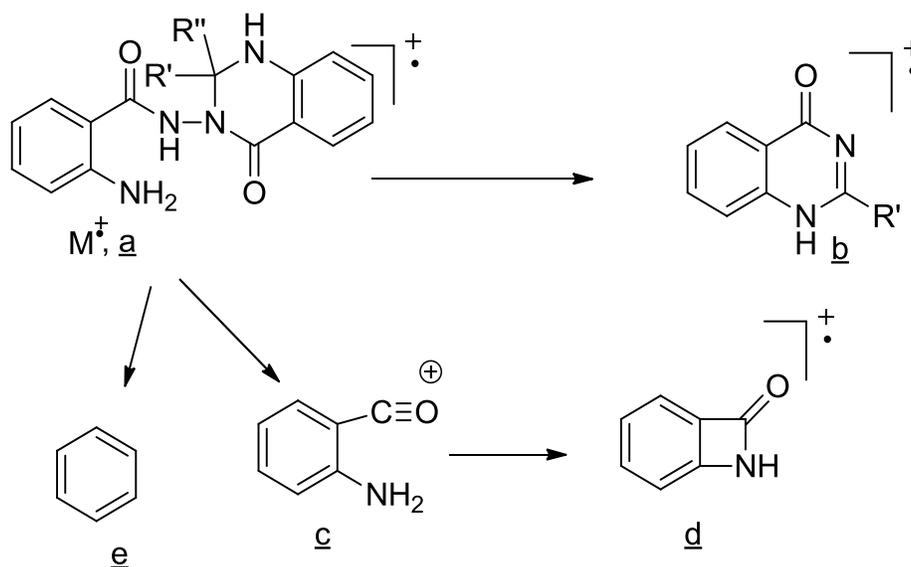
**Scheme 3: Partial Mass spectral fragmentation pattern of 2b and 2c**


compound	Ion (m/z rel. Int., %)							
	a	b	c	d	e	f	g	h
<b>2b</b>	402 (16)	373 (6)	201 (60)	200 (200)	199 (10)	186 (100)	185 (24)	173 (40)
<b>2c</b>	430 (18)	387 (10)	215 (80)	200 (80)	199 (30)	186 (22)	185 (24)	173 (70)

### Mass spectral fragmentation pattern of 2-amino-N-[1,2-disubstituted-1,2-dihydro-4-oxo-3-(4H)-quinazolinyl]benzamides (3a-c)

The partial Electron impact induced mass spectral fragmentation of **3a-c** (Fig.2, Scheme 4) indicates that the molecular ion  $M^+$  a is recorded with low intensity. The peaks arising from N-N bond cleavage in  $M^+$  are prominent. The ion b underwent retro Diels-Alder path to give d ion. In **3a** 2-aminobenzoyl cation c at m/z 120 is the base peak. In **3b** and **3c** benzene radical ion e at m/z 78 is the base peak.

Scheme 4: Partial Mass spectral fragmentation pattern of 3a-c



compound	Ion (m/z rel. Int., %)				
	<u>a</u>	<u>b</u>	<u>c</u>	<u>d</u>	<u>e</u>
<b>3a</b>	324 (7)	174 (23)	120 (100)	119 (7)	78 (7)
<b>3b</b>	372 (2)	222 (12)	120 (16)	119 (7)	78 (100)
<b>3c</b>	-	234 (2)	120 (9)	119 (2)	78 (100)

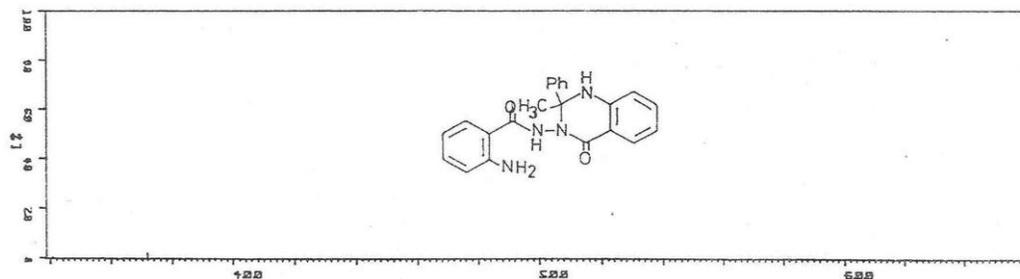
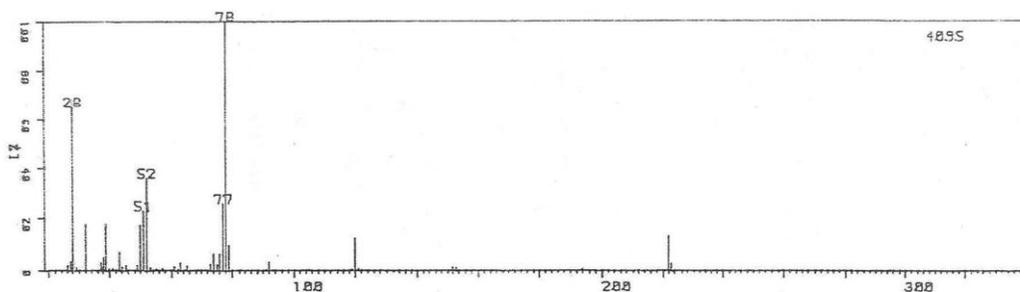
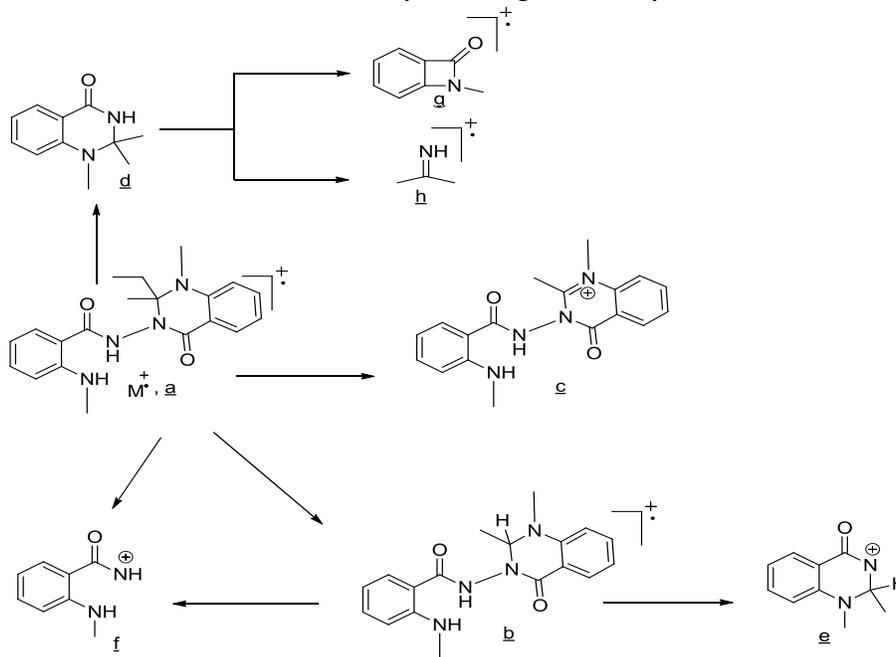


Fig. 2 : Mass spectrum of 2-amino-N-[2-methyl-2'-phenyl-1,2-dihydro-3(4H)-quinazolinyl]-benzamide (3b)

Mass spectral fragmentation pattern of 2-methylamino-N-[1,2-dimethyl-2'-ethyl-1,2-dihydro-4-oxo-3-(4H)-quinazoliny]benzamide (4)

Scheme 5: Partial Mass spectral fragmentation pattern of 4



compound	Ion (m/z rel. Int., %)							
	a	b	c	d	e	f	g	h
4	352 (6)	324 (5)	323 (12)	203 (1)	173 (13)	149 (10)	134 (100)	70 (10)

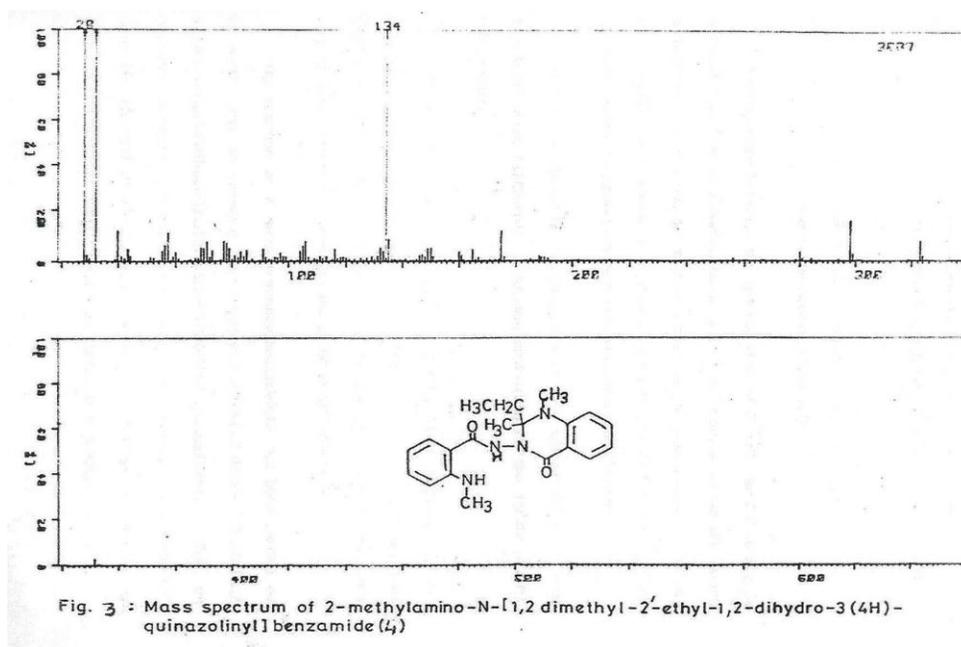


Fig. 3 : Mass spectrum of 2-methylamino-N-[1,2 dimethyl-2'-ethyl-1,2-dihydro-3 (4H)-quinazoliny] benzamide (4)

Electron impact induced mass spectral fragmentation studies of **4** (Fig.3, Scheme 5) has shown the molecular ion  $M^+_{a}$  at  $m/z$  352 with low intensity. The cleavage of N-N bond in the molecular ion results in cations  $d$  and  $f$ . The loss of ethylene and ethyl radicals in the molecular ion is noticed to give the ions  $b$  and  $c$ . The formation of cation  $e$  from cation  $b$  by N-N bond cleavage is also noticed.

### Computational studies of 2a-c, 3a-c and 4

The ball and stick model, distribution of electron density mapped with electrostatic potential for the ground state and the structures of HOMO and LUMO of N,N-linked bisquinazolinones **2a-c** (**2a**, Fig 4,5,6) and 2-methylamino-N-quinazolinonlybenzamide **4** (Fig. 7,8,9) are displayed. The reactive sites on the molecules along with the potential donor atoms are revealed by the electron density mapped with electrostatic potential. Total energy values, binding energies, dipole moments ( $\mu$ ),  $\log p$  and heat of formation values were calculated for bisazaheterocycles **2a-c**, 2-aminobenzamide derivatives **3a-c** and 2-methylaminobenzamide derivative **4** (Table 1). The calculated total energies suggest that in **2a-c**, the compound **2c** is quite stable than the other two. The compound **3a** and **4** are stable than **3b** and **3c**. The  $\log p$  values state that the **2c** is more biologically active, **3c** is moderately active and the remaining compounds are biologically inactive.

**Table 1: Details of PM3 calculations - Total energy (TE), Binding Energy(E), Heat of formation, Dipole moment ( $\mu$ ) and  $\log p$  values.**

S.No	Compound	TE(kcal/mol)	BE(kcal/mol)	Heat of formation (kcal/mol)	Dipole moment ( $\mu$ )	$\log p$
1	2a	-90961.85	-5143.89	-8.727	2.96	0.41
2	2b	-97103.73	-4643.18	55.31	1.65	1.09
3	2c	-110209.28	-6589.06	-11.74	4.10	2.47
4	3a	-84782.13	-4697.27	-8.04	3.33	-0.5
5	3b	-95687.29	-5342.13	30.60	3.32	-0.1
6	3c	-116931.55	-6822.01	59.57	2.11	0.97
7	4	-91662.89	-5241.98	-2.62	2.83	0.27

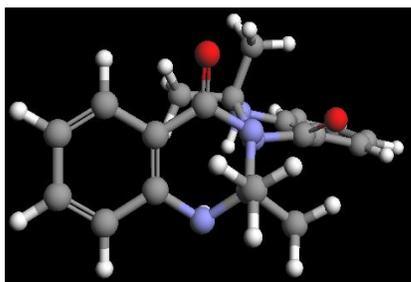


Fig. 4: (2a) Ball & stick diagram

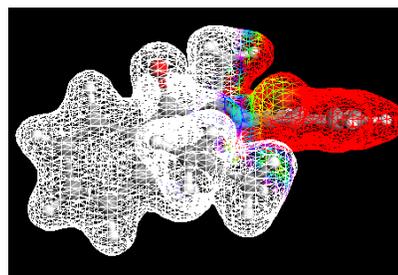


Fig. 5: (2a) Electrostatic Potential map

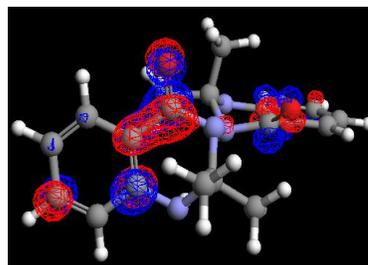
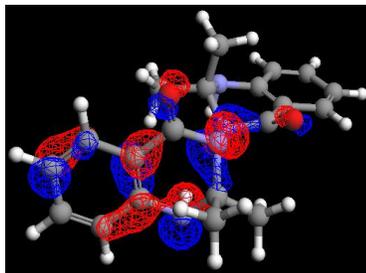


Fig. 6: (2a) Homo ↔ Lumo

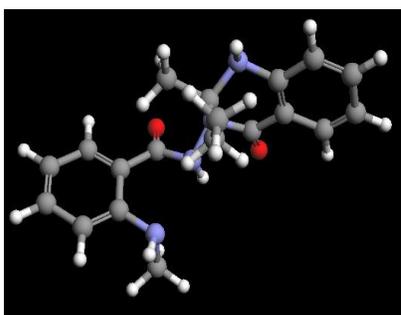


Fig. 7: (4) Ball &amp; Stick diagram

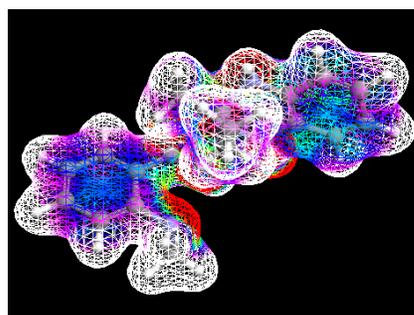


Fig. 8: (4) Electrostatic Potential map

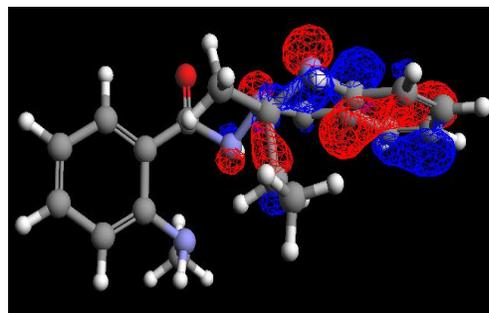
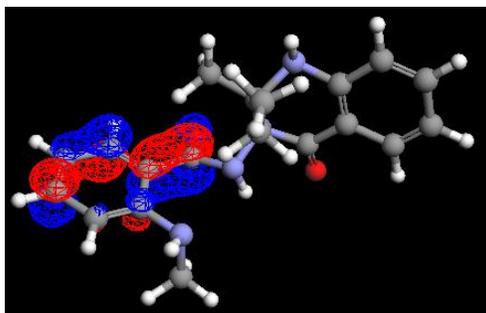


Fig. 9: (4) Homo ↔ Lumo

## CONCLUSION

EI induced partial mass spectral fragmentation pattern of 2,2-tetrasubstituted-tetrahydro-3,3'-bisquinazolin-4,4'-diones (**2a-c**), 2-amino-N-[1,2-disubstituted-1,2-dihydro-4-oxo-3-(4H)-quinazoliny]benzamides (**3a-c**) and 2-methylamino-N-[1,2-dimethyl-2'-ethyl-1,2-dihydro-4-oxo-3-(4H)-quinazoliny]-benzamide (**4**) is studied and the results are presented. The fragmentation pattern pathways, indicate that the molecular ion is recorded with low intensity and the N,N-bond is more susceptible for cleavage and is a potent source for nitrogen centered free radicals.

The retro Diels-Alder fragmentation path is also noticed in the mass spectral fragmentation of the compounds. The semiempirical pm3 method is used to study the stability, electron density and molecular geometry of the compounds. Further, less stability of the compounds is also indicated by the computational studies using semi empirical parametric method PM3.

### REFERENCES

- [1] Mounir AK, Mahmoud ED, Alexandria J. *Pharma Sci* 1989; 3: 190.
- [2] Trevedi PB, Undavia NK, Dave AM, Bhatt KN, Desai NC. *Indian J Chem* 1993; 32B: 497.
- [3] William JW, Rémy CL, Lee C, Aesop C, Thomas ER. *Biorog Med Chem Lett* 2004; 14(20): 5133.
- [4] Papp o, Szasz G, Orfi L, hermecz I. *J Chromatogr* 1991; 537(6): 371.
- [5] Fisnerova I, Grimova J, Roubal z, Brunova B. *Czech* 1987; 3pp CS 249493, B1 19871215.
- [6] Rao AD, Shanker CR, Rao AB, Reddy VM. *Indian J Chem* 1986; 25B: 665.
- [7] Allen EE, Kevin N, Rivero RA, Glinka TW. *Eur Pat Appl* 1992; 155pp. EP 510812, A1 19921028.
- [8] Archana, Srivastava VK, Kumar A. *Eur J Org Chem* 2002; 37(11): 873.
- [9] Capan G, Ergenic N, Buyuktimkin S, Yulug N. *Scientia Pharmaceutica* 1993; 61(4): 243.
- [10] Jean L, Laurent L, Christine L, Gerard D, Phosphorous Sulfur Silicon *Relat Elem* 1995; 102(1140): 155.
- [11] El-Feky SA, El-Sami ZKA. *Pharmazie* 1995; 50(5); 341.
- [12] Sheng-Li C, Yu-Ping F, Yu-Yang J, Shi-Ying L, Guo-Yu D, Run-Tao L. *Biorog Med Chem Lett* 2005; 15: 1915.
- [13] Stephen T, Stephen H. *J Chem Soc* 1956; 4178.
- [14] Mohamed YA, Aziziamohensen AE, SalmaFM, Akfity AM. *J Serb Chem Soc* 1992; 57(10): 629.
- [15] Takekoshi T. *US Pat* 1970; 3541,054.
- [16] Deshmukh MB, Deshmukh DS. *J. Indian Chem Soc* 1995; 72(12): 847.
- [17] Srivastava VK, Singh KS, Gulati A, Shanker K. *Indian J Chem* 1987; 26B: 652.
- [18] Mounir AK, Mahmoud, ED. *Alexandria J Pharma Sci* 1989; 3: 190.
- [19] Komatsu M, Yamamoto S, Ohshiro Y, Agawa T. *Heterocycles* 1985; 23: 677.
- [20] Alcaide B, Miranda M, Perez-Castells J, Polanco C, Sierra M A. *J Org Chem* 1994; 59: 8003.
- [21] Shethna YI, Wilson PW, Beinert H. *Biochim Biophys Acta* 1966; 258: 4051; b) Wang JH. *Science* 1970; 25: 167; c) Wang J H. *Biochem* 1970; 9: 21505.
- [22] Mukai K, Hatanaka T, Senba N, Nakayashiki T, Misaki Y, Tanaka K, Ueda K, Sugimoto T, Azuma N. *Inorg Chem* 2002; 41(20): 5006.
- [23] Hallvest B, Gutteridge JMC. *Free Rad Biol Med* 1985; 38.
- [24] Wengenack NL, Rusnak F. *Biochem* 2001; 40: 8990.
- [25] Cibra K, Gerestenberger M R C, Hass A, Kirste B. *J Heterocycl Chem* 1985; 22: 1689;
- [26] Ziegler FE, Berlin MY. *Tetrahedron Lett* 1998; 39: 2455. (a) Ziegler FE, Belema M. *J. Org. Chem* 1997; 62: 1083; (b) Bowman WR, Elsegood RJ, Stein T, Weaver W. *Org Biomol Chem*. 2007; 5: 103.
- [27] Bhavani AKD, Reddy PSN. *Org. Prep Procedures Int* 1992; 24(1): 125.



- [28] Bogentoft C, Ericsson O, Danielsson B. Acta Chem Succ 1974; 11: 513; (a) Turecek F, Svetlik J. Org Mass Spectrum 1981;16:285. (c) Rao V B, Reddy PSN, Ratnam C V. Org Mass Spectra 1983 18(7): 317.
- [29] Thomas B, Karl J. Theoret Chem Acc 2005; 113(1): 1.