

Synthesis, Investigation of Mass Spectra and Antimicrobial Activity of 2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione and its Derivatives

Mohamed A. Zein

Chemistry Department, Faculty of Science, Damanhour University, Damanhour, Egypt

mf_mohanad@yahoo.com

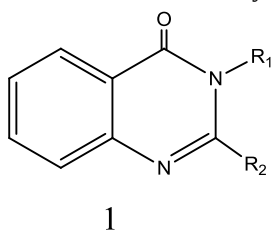
Abstract: Treatment of Anthranilic acid with chloroacetylchloride in presence of sodium acetate gave 2-(chloromethyl)-4H-benzo[d][1,3]oxazin-4-one (1), that fused with ammonium acetate to give 2-(aminomethyl)quinazolin-4(3H)-one (2). The compounds 2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [3] was prepared from cyclization of (2) with ethyl chloroacetate in presence of fused sodium acetate. Treatment of (3) with acetic anhydride and/or with acetic anhydride in presence of fused sodium acetate yielded the corresponding 2-acetyl-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione (4) and 1,2,3-triacetyl-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione (5) respectively. The reaction of (3) with diazonium chloride gave 1,3-bis((aryl)diazenyl)-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione (6) which can be acetylated with acetic anhydride to give 2-acetyl-1,3-bis((aryl)diazenyl)-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione (7). The electron impact mass spectra of the above series of compounds have also been recorded and their fragmentation pattern is discussed. The prepared compounds also exhibited antimicrobial activity.

[Mohamed A. Zein. **Synthesis, Investigation of Mass Spectra and Antimicrobial Activity of 2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione and its Derivatives.** J Am Sci 2012; 8(10): [213-221]. (ISSN: 1545-1003); Impact Factor: 1.32 <http://www.americanscience.org>.

Keywords: benzo[d][1,3]oxazinone, pyrazine, quinazolin-4,6-dione, Antimicrobial activity

1. Introduction

Heterocyclic chemistry comprises at least half of all organic chemistry research worldwide. In particular, heterocyclic structures form the basis of many pharmaceutical, agrochemical and veterinary products. 4(3H) Quinazolinones **1** and related quinazolines **2** are classes of fused Heterocycles that



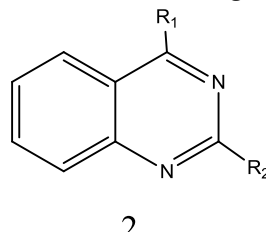
The electron impact (EI) ionization mass spectral fragmentations of some synthesized compounds were described.

2- Experimental section:

Melting points were determined in Capillaries with a Thomas Uni-melt apparatus uncorrected. NMR spectra were recorded on a general electric QE300 instrument and chemical shifts are given with respect to TMS. IR spectra were recorded on a Perkin-Elmer 1420 spectrometer and a Biorad FTS7 (KBr). Mass spectra were obtained on a Jeol JMSD-300 spectrometer operating at 70 eV. Microanalyses were conducted using an elemental analyzer 1106.

2-(chloromethyl)-4H-benzo[d][1,3]oxazin-4-one [1]

are of considerable interest because of the diverse range of their biological properties, for example, anticancer, diuretic, anti-inflammatory, anticonvulsant and antihypertensive activities.¹⁻¹⁸ Many of the literature synthetic methods for elaboration of this simple ring structure are, however, time consuming, tedious and often low yielding.¹⁹⁻²⁶



A mixture of Anthranilic acid (0.01 mol), chloroacetylchloride (0.01 mol) in presence of sodium acetate (0.02mol) was heated under reflux for 2 hr, and then cooled. The solid formed was filtered off, dried and purified by recrystallization with ethanol to give [1] as colorless crystals, yield 87%, m.p: 165°C; IR (KBr): 1722(C=O), 1630(C=N), 1605, 1592(C=C), 1120, 1075(C-O) cm⁻¹. ¹H-NMR (DMSO-d₆): δ2.91(s, 2H, CH₂), 7.25-7.33(d, 1H, Ar-H), 7.46-7.55(t, 1H, Ar-H), 7.72-7.83(t, 1H, Ar-H), 7.91-8.10(d, 2H, Ar-H) ppm. MS (m/z,%): 197(M⁺, 6.1), 196(M⁺, 14.2), 195(M⁺, 51.3), 191(17.4), 160(48.7), 147(25.8), 146(17.0), 103(100), 92(25.2), 91(37.4), 90(14.8), 77(45.2), 63(22.6), 51(27.8). Anal. Calcd. For C₉H₆ClNO₂: C, 55.26; H,

3.09; Cl, 18.13; N, 7.16 Found: C, 55.11; H, 2.89; Cl, 17.93; N, 7.12

2-(aminomethyl)quinazolin-4(3H)-one [2]

A mixture of [1] (0.01 mol) and ammonium acetate (0.02) was heated until fusion. The crude product was cooled, washed with water, filtered off and purified by ethanol to give [2] as white crystals, yield 75%, m.p: 245°C; IR (KBr): 3320-3300(NH₂), 3296(NH), 1722(C=O), 1630(C=N), 1605, 1592(C=C) cm⁻¹. ¹H-NMR (DMSO-d₆): δ 2.75(s, 2H, CH₂), 7.45-7.72(m, 4H, Ar-H), 8.2(s, 2H, NH₂), 8.9(s, 1H, NH) ppm. MS (m/z,%): 176(M⁺, 15.9), 175(M⁺, 31.1), 159(31.1), 145(100), 105(35.6), 91(45.9), 77(83.8), 50(32.4). Anal. Calcd. For C₉H₆N₃O: C, 61.70; H, 5.18; N, 23.99 Found: C, 61.48; H, 4.98; N, 23.68

2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [3]

The reaction of [2] (0.01 mol) and ethylchloroacetate under reflux in presence of sodium acetate gave [3], pale yellow crystals yield 68%, m.p: 261°C; IR (KBr): 3229(NH), 1685-1710(C=O), 1630(C=N), 1585(C=C) cm⁻¹. ¹H-NMR (DMSO-d₆): δ 2.46(s, 2H, CH₂C=N), δ 3.31(s, 2H, CH₂C=O), 7.71-7.83(m, 4H, Ar-H), 8.4(s, 1H, NH) ppm. MS (m/z,%): 215(M⁺, 62.3), 187(59.9), 173(53.2), 145(100), 105(31.3), 91(40.6), 77(81.1), 50(26.9). Anal. Calcd. for C₁₁H₉N₃O₂: C, 61.39; H, 4.22; N, 19.53 Found: C, 61.12; H, 4.08; N, 19.22

2-acetyl-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [4]

1,2,3-triacetyl-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [5]

The reaction of [3] (0.01 mol) with acetic anhydride (0.01 mol) by fusion and/or with acetic anhydride under reflux in presence of sodium acetate gave [4] and [5] respectively.

Compound 4 as pale yellow crystals yield 75%, m.p: 180 °C; IR (KBr): 1710-1667(C=O), 1642(C=N), 1550(C=C) cm⁻¹. ¹H-NMR (DMSO-d₆): δ 2.30(s, 3H, CH₃), δ 4.33(s, 2H, CH₂C=N), 4.89(s, 2H, CH₂C=O), 7.22-7.78(m, 4H, Ar-H) ppm. MS (m/z,%): 258(M⁺, 13.2), 257(M⁺, 65.1), 242(45.1), 214(57.6), 187(100), 173(29.3), 145(45.0). Anal. Calcd. for C₁₃H₁₁N₃O₃: C, 60.70; H, 4.31; N, 16.33 Found: C, 60.53; H, 4.11; N, 16.28

Compound 5 as white crystals yield 66%, m.p: 210 °C; IR (KBr): 1725-1685(C=O), 1630(C=N), 1585(C=C) cm⁻¹. ¹H-NMR (DMSO-d₆): δ 2.21(s, 9H, CH₃), δ 4.01(s, 1H, CHC=N), 4.76(s, 1H, CHC=O), 7.30-7.71(m, 4H, Ar-H) ppm. MS (m/z,%): 342(M⁺, 13.2), 341(M⁺, 53.2), 298(57.8), 255(45.0), 212(41.6), 173(43.3), 145(100), 105(33.9), 91(31.9), 77(43.1), 51(22.2). Anal. Calcd. for C₁₇H₁₅N₃O₅: C, 59.82; H, 4.43; N, 12.31 Found: C, 59.54; H, 4.29; N, 12.10

1,3-bis((aryl)diazenyl)-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [6a,b,c]

Solution of [3] (0.01 mol) in aqueous sodium hydroxide (50ml, 10%) was chilled in ice to (0-5°C), A cold aqueous solution of the diazonium salt (0.02 mol) was added drop wise with stirring during 45 min. After addition the mixture was stirred for further 30 min and then left for 2hr, in refrigerator. The precipitated product was collected, washed with water, dried and purified by recrystallization with ethanol to give [6a,b,c].

Compound [6a] as pale yellow crystals yield 81%, m.p: 173 °C; IR (KBr): 3310(NH), 1687-1718(C=O), 1677(N=N), 1625(C=N), 1578(C=C) cm⁻¹. ¹H-NMR (DMSO-d₆): δ 2.33(s, 1H, CHC=N), δ 3.11(s, 1H, CHC=O), 7.23-7.88(m, 14H, Ar-H), 8.6(s, 1H, NH) ppm. MS (m/z,%): 423(M⁺, 38.1), 346(27.2), 318(45.3), 241(38.3), 213(44.2), 187(39.6), 173(42.1), 145(100), 105(67.3), 91(87.1), 77(62), 50(53.1). Anal. Calcd. for C₂₃H₁₇N₇O₂: C, 65.24; H, 4.05; N, 23.16 Found: C, 65.10; H, 3.97; N, 22.89

Compound [6b] as pale yellow crystals yield 77%, m.p: 186 °C; IR (KBr): 3315(NH), 1650-1702(C=O), 1641(N=N), 1612(C=N), 1591(C=C) cm⁻¹. ¹H-NMR (DMSO-d₆): δ 1.87(s, 6H, CH₃), δ 2.41(s, 1H, CHC=N), δ 3.33(s, 1H, CHC=O), 7.11-8.01(m, 12H, Ar-H), 8.7(s, 1H, NH) ppm. MS (m/z,%): 451(M⁺, 33.1), 436(21.5), 360(41.2), 332(51.6), 317(22.8), 241(67.2), 213(32.5), 187(21.8), 173(100), 145(84.3), 105(21.5), 91(67.5), 77(75.6), 50(54.8). Anal. Calcd. for C₂₅H₂₁N₇O₂: C, 66.51; H, 4.69; N, 21.72 Found: C, 66.23; H, 4.42; N, 21.55

Compound [6c] as pale yellow crystals yield 81%, m.p: 205 °C; IR (KBr): 3280(NH), 1644-1728(C=O), 1612(N=N), 1592(C=N), 1575(C=C), 1215-1111(C-O-C) cm⁻¹. ¹H-NMR (DMSO-d₆): δ 2.13(s, 1H, CHC=N), δ 3.25(s, 1H, CHC=O), δ 4.10(s, 6H, CH₃), 7.24-8.12(m, 12H, Ar-H), 9.2(s, 1H, NH) ppm. MS (m/z,%): 483(M⁺, 28.6), 463(32.5), 452(49.3), 376(22.5), 348(52.3), 333(67.3), 317(42.5), 241(32.5), 213(28.9), 187(54.6), 173(77.2), 145(100), 105(81.3), 91(87.6), 77(64.2), 50(55.8). Anal. Calcd. for C₂₅H₂₁N₇O₄: C, 62.11; H, 4.38; N, 20.28 Found: C, 61.99; H, 4.19; N, 20.11

2-acetyl-1,3-bis((aryl)diazenyl)-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [7a,b,c]

Acetylation of [6a,b,c] (0.01 mol) by fusion with acetic anhydride (0.01mol), The crude product was filtered off, washed with water, dried and purified by ethanol to give compounds [7a,b,c] respectively.

Compound [7a] as yellow crystals yield 75%, m.p: 196 °C; IR (KBr): 1672-1709(C=O), 1665(N=N), 1616(C=N), 1556(C=C) cm⁻¹. ¹H-NMR (DMSO-d₆): δ 1.74 (s, 3H, CH₃), δ 2.41(s, 1H, CHC=N), δ 3.67(s, 1H, CHC=O), 7.19-7.97(m, 14H, Ar-H) ppm. MS (m/z,%): 465(M⁺, 33.2), 450(19.5), 422(37.5),

345(66.8), 317(48.2), 240(43.2), 212(50.3), 187(52.3), 173(61.5), 145(100), 105(67.5), 91(54.6), 77(59.8), 50(48.6). Anal.Calcld. for $C_{25}H_{19}N_7O_3$: Elemental Analysis: C, 64.51; H, 4.11; N, 21.06 Found: C, 64.12; H, 4.09; N, 20.87

Compound [7b] as yellow crystals yield 80%, m.p: 218 °C; IR (KBr): 1645-1711(C=O), 1635(N=N), 1606(C=N), 1573(C=C) cm^{-1} . 1H -NMR (DMSO- d_6): δ 1.93(s, 3H, CH_3CO), δ 2.17(s, 6H, CH_3), δ 2.53(s, 1H, $CHC=N$), δ 3.86(s, 1H, $CHC=O$), 7.22-8.11(m, 12H, Ar-H) ppm. MS (m/z,%): 493(M^+ , 30.2), 478(38.9), 450(52.6), 435(64.3), 359(54.3), 331(44.2), 316(32.8), 240(41.5), 212(45.9), 187(29.7), 173(100), 145(87.2), 105(67.5), 91(56.2), 77(41.1), 50(51.5). Anal.Calcld. for $C_{27}H_{23}N_7O_3$: C, 65.71; H, 4.70; N, 19.87 Found: C, 65.55; H, 4.65; N, 19.76

Compound [7c] as yellow crystals yield 65%, m.p: 227 °C; IR (KBr): 1654-1712(C=O), 1632(N=N), 1581(C=N), 1574(C=C), 1220-1100(C-O-C) cm^{-1} . 1H -NMR (DMSO- d_6): δ 1.9(s, 3H, CH_3CO), δ 2.2(s, 1H, $CHC=N$), 2.91(s, 6H, CH_3O), δ 3.45(s, 1H, $CHC=O$), 7.28-8.10(m, 12H, Ar-H) ppm. MS (m/z,%): 525(M^+ , 28.1), 510(38.4), 482(50.3), 467(56.7),

451(29.4), 375(48.2), 347(58.1), 332(54.2), 316(29.1), 240(31.2), 212(64.5), 187(33.9), 173(48.3), 145(100), 105(64.2), 91(33.5), 77(61.5), 50(54.5). Anal.Calcld. for $C_{27}H_{23}N_7O_5$: C, 61.71; H, 4.41; N, 18.66 Found: C, 61.59; H, 4.36; N, 18.39

3- Antimicrobial activity

In vitro antibacterial screening

Applying the agar plate diffusion technique^{30,31} all of the compounds were screened *in Vitro* for antibacterial activity against *Bacillus subtilis*, *Streptococcus Penumonia*, *Staphylococcus aureas*, *E. coli* and *Pseudomonas solanarium*. The compounds were tested at (10mg, 50mg and 100mg) concentrations and the activity was determined by measuring the zone of inhibition. The screening results given in table (1) where, the activities of compounds were compared with *Streptomycin* as antibacterial standard. The compound (7c) showed maximum antibacterial potency. Compounds 6a, 6b, 6c, 7a, 7b and 7c have more activity, Compounds 3, 4 and 5 have nearly activity and compounds 1 and 2 have less activity compared with *streptomycin* against all bacterial organisms.

Table(1) Antibacterial Activity

Comp.	Gram Positive Bacteria									Gram Negative Bacteria					
	<i>Bacillus subtilis</i>			<i>Streptococcus penumonia</i>			<i>Staphylococcus aureas</i>			<i>E.coli</i>			<i>Pseudomonas Sp.</i>		
	10 mg	50 mg	100 mg	10 mg	50mg g	100 mg	10mg g	50mg g	100mg g	10mg g	50 mg	100 mg	10 mg	50 mg	100 mg
1		1	5		3	6			5			3			1
2		6	9		5	10			9		1	8		1	8
3	1	7	14	1	10	15	2	9	16	3	12	20	5	11	22
4	5	7	18	4	14	19	7	11	18	5	14	19	7	10	25
5	5	9	19	6	13	18	6	18	21	5	17	22	6	13	24
6a	9	11	25	8	18	22	9	21	33	10	19	29	11	19	33
6b	10	10	29	11	15	27	10	27	34	11	21	31	14	20	38
6c	12	15	36	15	20	33	11	28	37	13	25	33	15	28	35
7a	10	18	38	16	18	35	13	29	39	15	29	37	15	30	41
7b	10	11	26	9	19	28	9	28	41	9	23	40	9	21	38
7c	13	23	31	10	28	42	21	37	43	18	30	42	10	33	45
Streptomycin	3	7	18	2	11	17	4	16	20	8	17	22	6	12	27

In vitro antifungal screening

The compounds were evaluated for their *in vitro* antifungal activity against *Aspergillus Nigaer*, *Candia albicans*, and *Penicillium Sp.* using an agar dilution method³². The screening results given in table (2) where, the activities of compounds were compared

with *Ketoconazole* as antifungal standard. The compound (7c) showed maximum antifungal potency. Compounds 6a, 6b, 6c, 7a, 7b and 7c have more activity, Compounds 3, 4 and 5 have nearly activity and compounds 1 and 2 have less activity compared with *Ketoconazole* against all Fungal organisms.

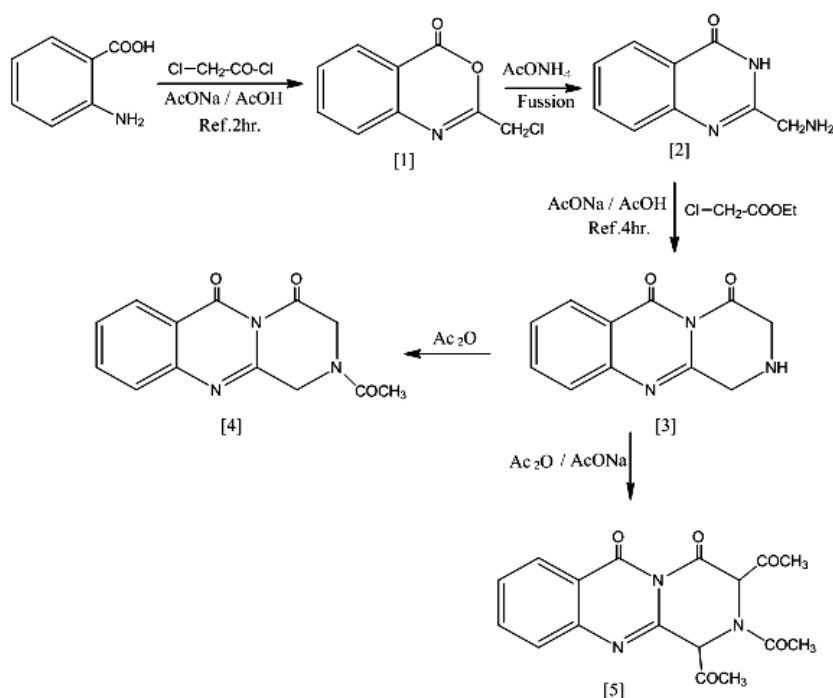
Table (2) Antifungal Activity

Comp.									
	<i>Aspergillus nigaer</i>			Penicillium Sp.			<i>Candia albicans</i>		
	10 mg	50mg	100mg	10mg	50mg	100mg	10mg	50mg	100mg
1					1	3			3
2		1	5		7	9		1	9
3	7	11	16	5	15	19	5	15	18
4	5	12	17	7	13	20	7	14	20
5	5	13	18	6	17	20	6	16	19
6a	13	20	33	12	19	28	15	21	32
6b	11	18	31	14	26	30	15	28	35
6c	14	16	31	10	22	27	10	23	29
7a	11	17	29	12	21	29	9	29	33
7b	10	19	38	14	20	30	11	27	31
7c	19	23	41	19	30	39	18	31	43
ketoconazole	8	13	18	7	17	21	6	17	21

4- Result and Discussion**4.1 Chemistry**

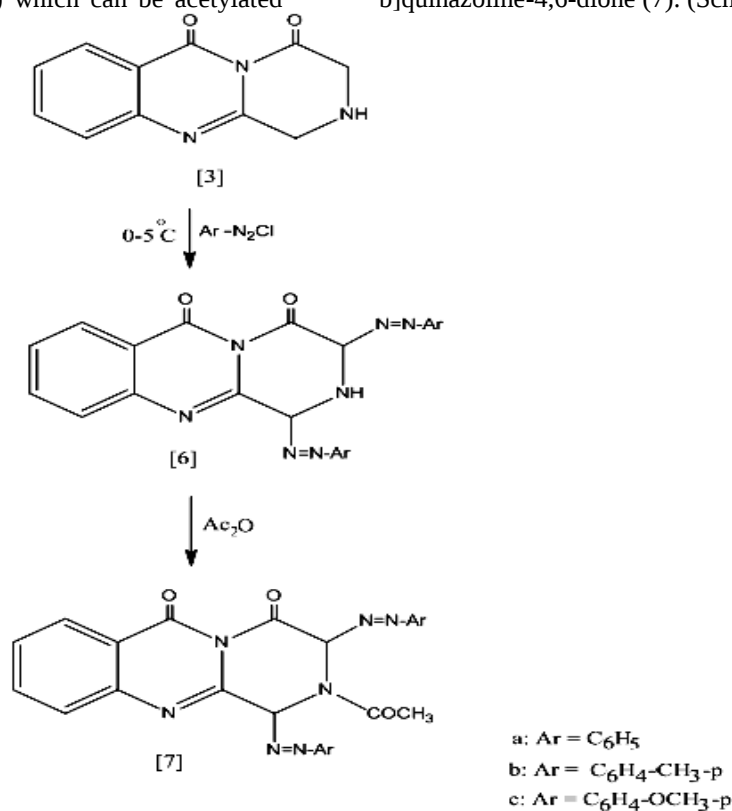
The reaction of Anthranilic acid with chloroacetylchloride in presence of sodium acetate under reflux gave the corresponding 2-(chloromethyl)-4H-benzo[d][1,3]oxazin-4-one [1]. A monolysis of 2-chloromethyl-4-oxo-3,1-benzoxazinone(1) with ammonia from ammonium acetate and/or formamide under fusion led to the formation of 2-aminomethyl-4-oxo-quinazolinone

(2). Cyclization of 2 with ethyl chloroacetate in presence of fused sodium acetate gave 2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione (3). Treatment of 3 with acetic anhydride and/or with acetic anhydride in presence of fused sodium acetate yielded the corresponding 2-acetyl-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione (4) and 1,2,3-triacetyl-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione (5) respectively. (Scheme I)

**Scheme I**

Treatment of [3] with diazonium chloride gave 1,3-bis((aryl)diazenyl)-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione (6) which can be acetylated

with acetic anhydride to give 2-acetyl-1,3-bis((aryl)diazenyl)-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione (7). (Scheme II)



Scheme II

4.2 Mass spectrometry:

All the spectra of synthesized compounds show relatively small molecular ions and peaks typical of a cleavage and rearrangement process type fragmentation²⁷⁻²⁹. The molecular ions of [1]; (Fig.1), [2]; (Fig.2), [3]; (Fig.3), [4]; (Fig.4) and [5] (Fig.5) fragmented further and involved pathway as illustrated in Scheme III, Where the molecular ion of [5] at m/z 341 fragmented to give the molecular ion

of [4] at m/z 263 by losing 2CH₂CO that broken and lose C₂O to give the molecular ion of [2] at m/z 175 which fragmented to give the fragment of m/z 159 by losing NH₂. The fragment of m/z 159, which broken to give the fragment of m/z 145 (the base peak) by losing CH=NH. The fragment of m/z 145 was broken to give an ion of m/z 105 which further broke to give an ion at m/z 77. The later loss CH₂=CH to form the fragment of m/z 50.

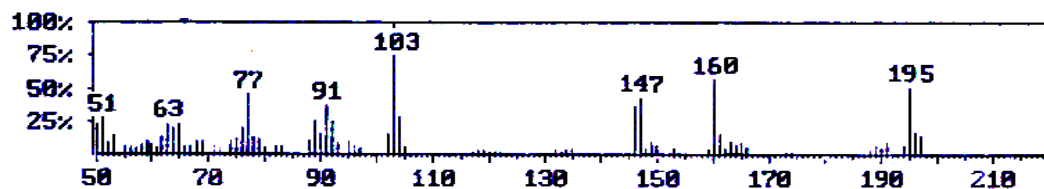


Fig.1 70 eV mass spectrum of compound [1]

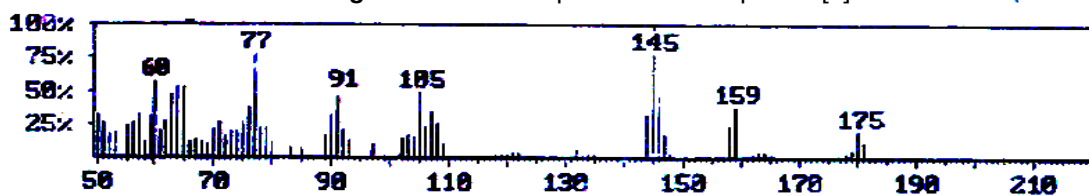


Fig.2 70 eV mass spectrum of compound [2]

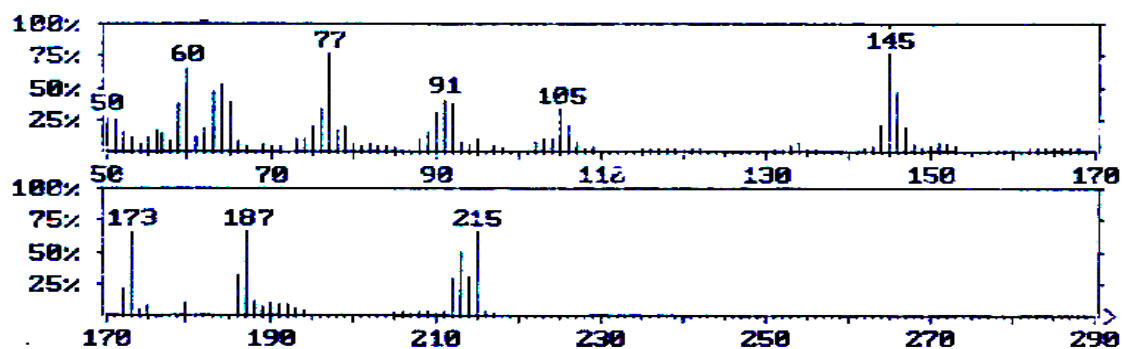


Fig.3 70 eV mass spectrum of compound [3]

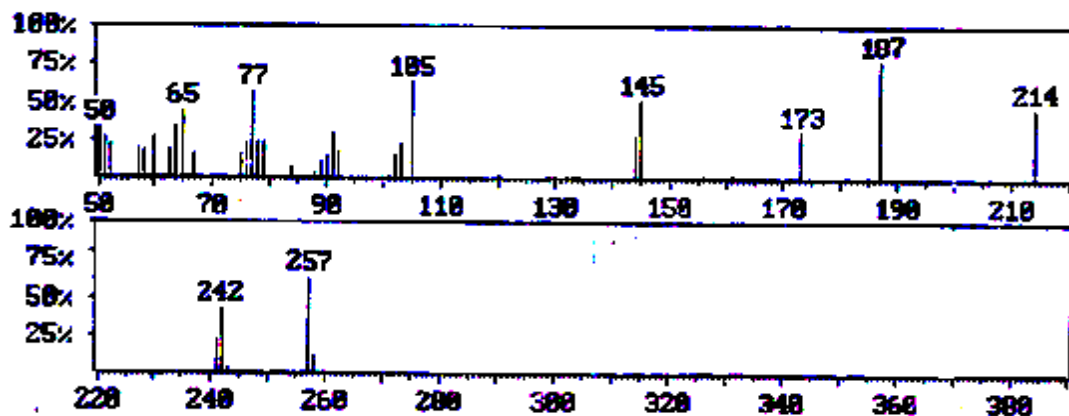


Fig.4 70 eV mass spectrum of compound [4]

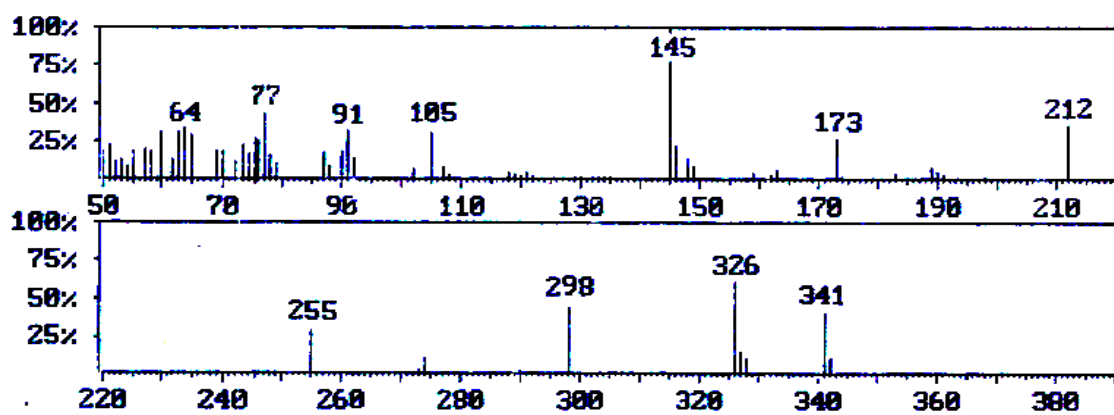
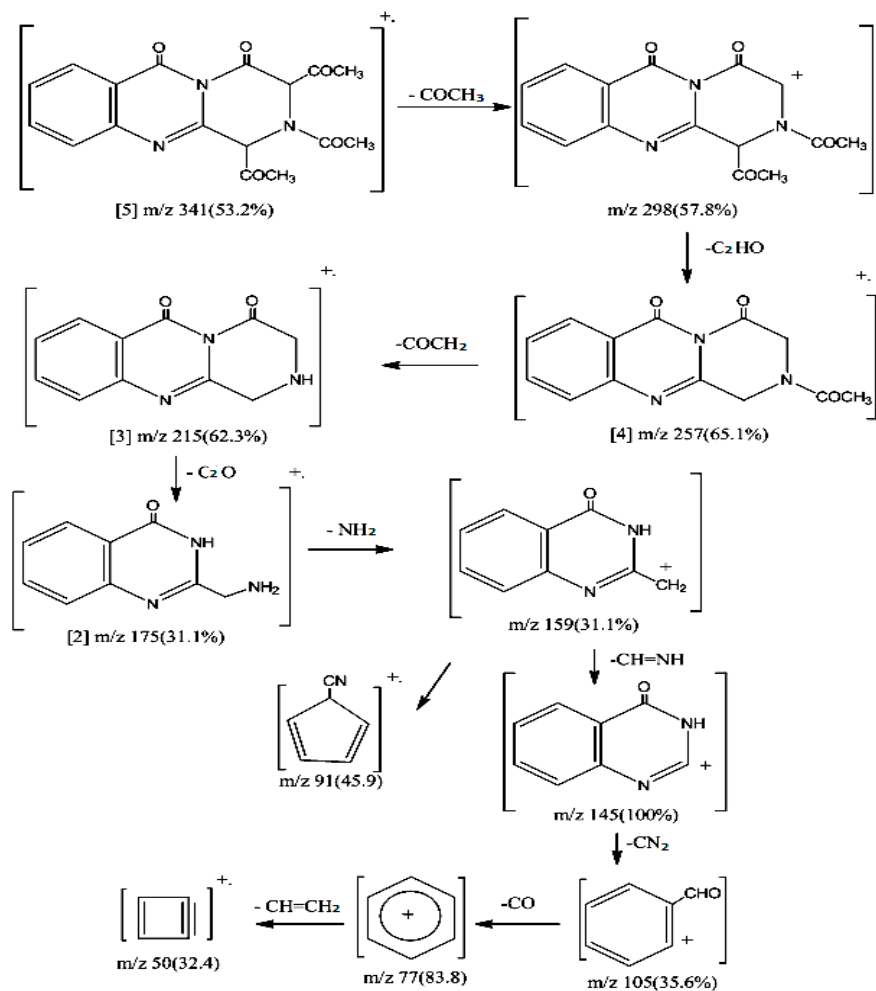


Fig.5 70 eV mass spectrum of compound [5]



Scheme III. Main fragmentation pathway of compounds [2],[3],[4]and [5].

The molecular ions of [3]; (Fig.3),[6a];(Fig.6) and [7a] (Fig.7) fragmented further and involved pathway as illustrated in Scheme IV, Where the molecular ion of [7a] at m/z 465 fragmented to give the molecular ion of [6a] at m/z 423 by losing CH_2CO that broken and lose $2\text{C}_6\text{H}_4\text{N}_2$ to give the molecular ion of [3] at m/z 215 which fragmented to give the

fragment of m/z 187 by losing CO . The fragment of m/z 187, which broken to give the fragment of m/z 145 (the base peak) by losing $\text{CH}_2\text{-CH=NH}$. The fragment of m/z 145 was broken to give an ion of m/z 105 which further broke to give an ion at m/z 77. The later loss $\text{CH}_2=\text{CH}$ to form the fragment of m/z 50.

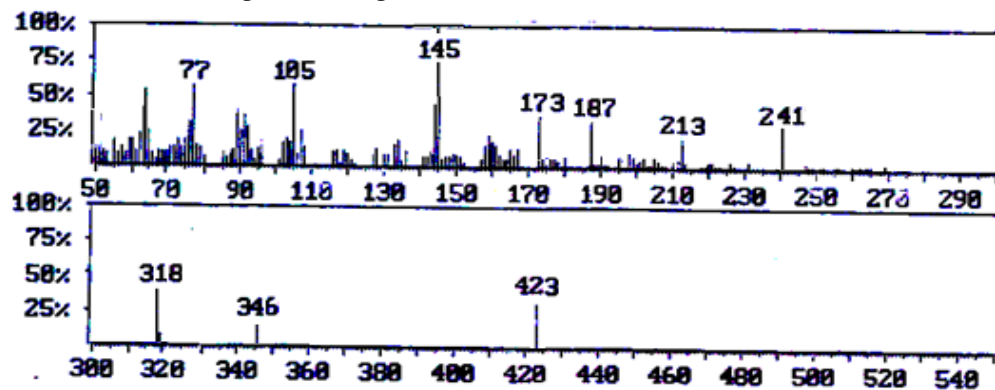


Fig.6 70 eV mass spectrum of compound [6a]

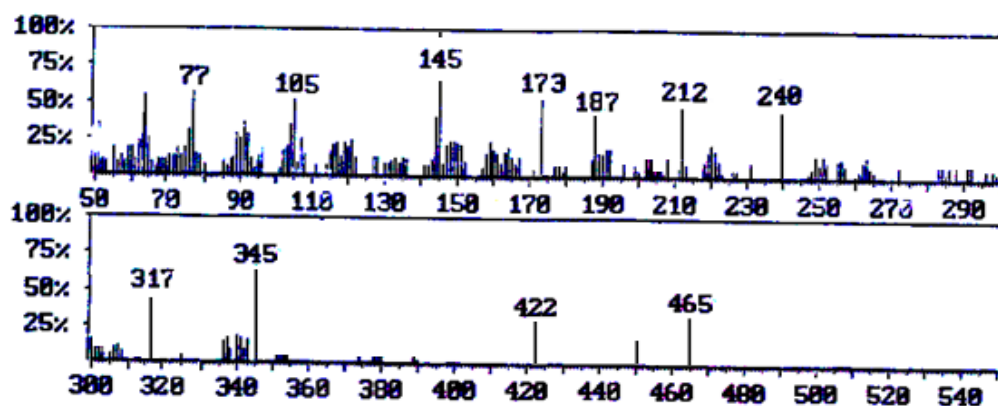
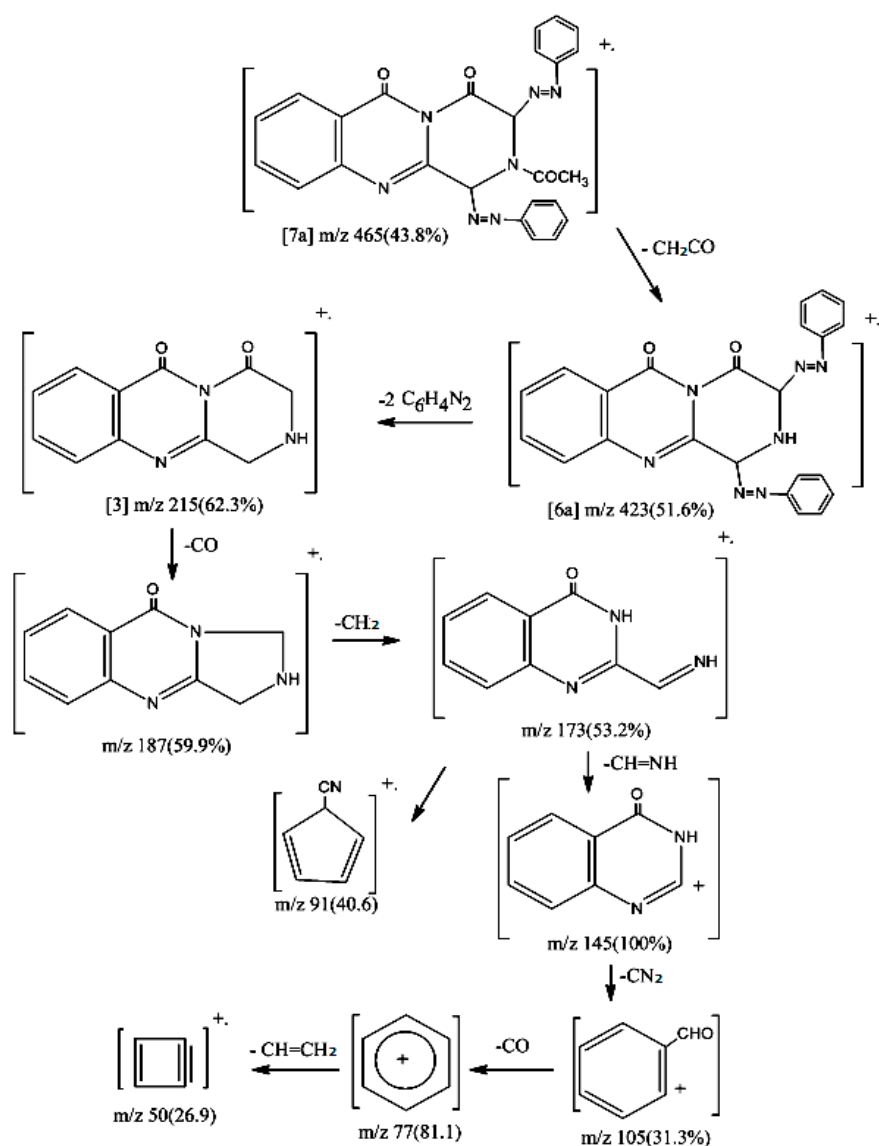


Fig.7 70 eV mass spectrum of compound [7a]



Scheme IV. Main fragmentation pathway of compounds [3], [6a] and [7a].

Corresponding authors**Mohamed Abd Ellatif Zein**

Chemistry Department, Faculty of Science,
Damanhour University, Damanhour, Egypt
mf_mohanad@yahoo.com

References:

- 1-David J. Connolly, Declan Cusack, and Patrick J. Guiry, Synthesis of quinazolinones and quinazolines; Tetrahedron 61 (2005) 10153–10202
2. Chan, J. H.; Hong, J. S.; Kuyper, L. F.; Jones, M. L.; Baccanari, D. P.; Tansik, R. L.; Boytos, C. M.; Rudolph, S. K.; Brown, A. D. 2-Phenylquinazolin-4-yl)oxy-1,2,3-triazol-1-yl ; j. Heterocycl. Chem. 1997, 34, 145.
3. Gackenheimer, S. L.; Schaus, J. M.; Gehlert, D. R. quinazolin-4-yl)oxy-1,2,3-triazol-1-yl)butan-1-ol; J. Pharmacol. Exp. Ther. 1996, 732: 113.
4. Dempcy, R. O.; Skibo, E. B., base interactions in some isoquinoline and quinazolines derivatives, Biochemistry 1991, 30, 8480.
5. Nordisk-Droge. , synthesis of Quinazolinethiones ,18113; Patent, N. A. Ed.; Nordisk Drogeand Kemi-Kalieforretning AIS: Netherlands, 1965.
6. Bogert, M. T.; Hand, W. F., synthesis of 4(3H)-quinazolinones under solvent-free condition, J. Am. Chem. Soc. 1902, 24, 1031.
7. Bogert, M. T.; Hand, W. F, A Metal-Free Approach for the Synthesis of 2-Phenylquinazolines, J. Am. Chem. Soc. 1903, 25, 935.
8. Taylor, E. C.; Knopf, R. J.; Borrer, A. L., synthesis of 4(3H)-quinazolinones under solvent free conditions, J. Am. Chem. Soc. 1960, 82, 3152.
9. Irwin, W. J.; Wibberly, D. G., synthesis of imidazopyridodiazepines from peri annulation in imidazo[1,2-a]pyridine, J. Chem. Soc., Chem. Commun. 1965, 4240.
10. Jiang, J. B.; Hesson, D. P.; Dusak, B. A.; Dexter, D. L.; Kang, G. L.; Hamel, E. imidazolidinones, J. Med. Chem. 1990, 33, 1721–1728.
11. Bandgar, B. P. triazol, Synth. Commun. 1997, 27, 2065–2068.
12. Batvetsias, V. Synthesis of quinazolinones, Synth. Commun. 1998, 28, 4547–4559.
13. Showell, G. A Quinazolines Synth. Commun. 1980, 10, 241–243.
14. Zentmyer, D. T.; Wagner, E. C. J. Org. Chem. 1949, 14, 967.
15. Errede, L. A.; McBrady, J. J.; Oien, H. T. J. Org. Chem. 1977, 42, 656.
16. Armarego, W. L. F. Fused Pyrimidines, Part 1: Quinazolines; Interscience: New York, 1967.
17. Undheim, K.; Benneche, T. In Comprehensive Heterocyclic Chemistry II, Vol. 6; Pergamon: Oxford, 1998.
18. Gilchrist, T. L. J. Chem. Soc., Perkin Trans. 1 2001, 2491–2515.
19. Gilchrist, T. L. J. Chem. Soc., Perkin Trans. 1 1999, 2849–2866.
20. Xia, Y.; Yang, Z.-Y.; Hour, M.-J.; Kyo, S.-C.; Xia, P.; Bastow, K. F.; Nakanishi, Y.; Nampoothiri, P.; Hackl, T.; Hamel, E.; Lee, K.-H. Bioorg. Med. Chem. Lett. 2001, 11, 1193–1196.
21. Rad-Moghadam, K.; Mohseni, M. J. Chem. Res. (S) 2003, 487.
22. Koerner, M. J. Prakt. Chem. 1887, 36, 155.
23. Bergman, J.; Brynolf, A. Tetrahedron Lett. 1990, 46, 1295–1310.
24. Witt, A.; Bergman, J. Tetrahedron 2000, 56, 7245–7253.
25. Hattori, K. J. Med. Chem. 2004, 47, 4151–4154.
26. Reddy, P. S. N.; Nagaraju, C. Synth. Commun. 1991, 21, 173–181.
27. I. M. El-Deen, and M. E. Abd El-Fattah; Bull. Korean Chem. Soc., 24, 473 (2003).
28. I. M. El-Deen, and H. K. Ibrahim; Chem. Pap., 58, 200 (2004).
29. M. E. Abd El-Fattah ; Indian Journal of chemistry, V45 B, 2523–2533 (2006)
30. Bauer A W, Kirby W M, Sherris J C and Turck M, Am J Clin Pathol, 1966, 39(5), 493–496.
31. Robert G Petersdorf and John C Sherris, Am J Med., 1965, 39(5), 766–779.
32. Gillespie S H, Medical Microbiology-Illustrated, Butterworth Heinemann: London, 1994, 234–247.

9/5/2012