Available online at www.derpharmachemica.com

Scholars Research Library

Der Pharma Chemica, 2012, 4(5):1923-1934
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

Synthesis and mass spectra of some new 3-substituted coumarin derivatives

Jehan A. Hasanen

Chemistry Department, Faculty of Science, Suez Canal University, Ismailia, Egypt

---

ABSTRACT

Reaction of 3-acetylcoumarin (1) with thiosemicarbazide gave the corresponding 3-acetylcoumarin thiosemicarbazone (2). Treatment of 2 with acetic anhydride, benzoyl chloride, ethyl chloroacetate, ω-bromomethylketones and dicarbonyl compounds afforded the corresponding diacetyl- and- dibenzoyl thiosemicarbazone derivatives (3,4), 3-(Coumarin-3-ylethylidene)amino-2-thioxo-imidazolidin-4-one (5) , 5-Aryl-2-[(coumarin-3-ylethylidene)-hydrazino]-thiazole (7) and 1-(Coumarin-3-ylethylidene) amino-2-thioxopyrimidine derivatives (8 and 9), respectively. The mass spectral fragmentation patterns of some prepared compounds have been investigated in order to elucidate the structure of the synthesized compounds.

Key words: Synthesis, Mass spectra, Thiosemicarbazone, Coumarin,Thiazole, imidazolidinone.

INTRODUCTION

Various substituted nitrogen heterocycles containing coumarin moiety have recently received significant importance because of their diverse pharmacological properties. These included analgesic, antiasthmatic divretic, antihypertensive, anticholinergic and anti-inflammatory properties[1-5], As an extension of our previous work[6-10], this paper reported the preparation of some thiosemicarbazone, thiohydantoin and pyrimidine derivatives containing coumarin moiety using 3-acetylcoumarin (1) as a key starting material which was obtainable in the reaction of 2-hydroxy- benzaldhyde with ethylacetoacetate.

The electron impact (EI) imization mass spectral fragmentation patterns of some synthesized compounds are described.

MATERIALS AND METHODS

Melting points were determined in capillaries with a Thomas uni-melt apparatus uncorrected. NMR spectra were recorded on a general electric QE 300 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 JMS D-300 spectrometer operating at 70 ev. Microanalyses were conducted using an elemental analyzer 1106.

3-Acetylcoumarin thiosemicarbazone (2)
A mixture of 1 (0.01 mole), thiosemicarbazide (0.01 mole) and acetic acid (3 ml) in methanol (30 ml) was heated under reflux for 2 hr, then cooled. The solid formed was filtered off, dried and purified by recrystallization from ethanol to give 2 as yellow crystals, yield 86%, m.p. 220^{o}C. IR(KBr): 3414, 3150(NH_2), 3230(NH), 1720(C=O), 1632(C=N), 1610, 1585(C=S), 1381(C=S), 1120,1095(C-O)cm^{-1}.

^{1}H-NMR(DMSO-d6):δ 3.20(S, 3H, CH_3), 7.21-7.89(m, 4H, Ar-H), 8.32(S, 1H, pyran-H), 9.23(S, 2H, NH_2), 10.98(S, 1H, NH)ppm. MS: m/z (%) 262(M^++1, 6.90), 261(M^+, 15.10) 246(46.50), 245(47.80), 244(40.30), 243(26.40), 219(15.70), 218(13.80), 228(8.80), 227(12.60), 203(9.40), 202(34.60), 201(74.20), 200(78.00),

199(24.50), 188(14.50), 187(35.80), 186(47.80), 185(39.00), 184(30.80), 173(18.20), 172(37.10), 171(34.00), 147(13.20), 146(38.40), 145(34.00), 144(28.30), 131(23.30), 130(15.70), 129(17.00), 119(13.80), 118(38.40), 117(20.10), 116(32.10), 115(86.20), 114(34.00), 103(28.30), 102(22.60), 101(24.50), 91(23.90), 90(40.30), 89(96.90), 88(51.60), 87(20.80), 77(28.90), 76(20.80), 75(35.20), 64(23.30), 63(100), 62(48.40), 60(37.70), 59(79.90), 58(42.80, 51(56.60), 50(35.20). And Found: C, 55.01; H, 4.05; N, 15.98; S, 12.02. $C_{12}H_{11}N_3O_2S$ requires: C, 55.17; H, 4.21; N, 16.09; S, 12.26.

3-Acetylcoumarin-2, 4-diacetyl thiosemicarbazone (3)
A solution of 2 (0.01 mol) in acetic anhydride (10 ml) was refluxed for 2hr, then cooled and poured onto ice water. The solid obtained was filtered off, washed with water, dried and purified by recrystallization with ethanol to give 3 as pole yellow crystals, yield 56%, m.p 200^{o}C.

IR(KBr): 3225(NH), 1721, 1705(C=O), 1631(C=N), 1605, 1583(C=C), 1398(C=S), 1125, 1085(C-O) cm^{-1}. ^{1}H-NMR(DMSO-d6): δ 2.01(S, 3H, $COCH_3$), 2.25(S, 3H, $COCH_3$), 3.15(S, 3H, CH_3), 7.36-7.93(m, 4H, Ar-H), 8.31(S, 1H, pyran-H), 11.60(S, 1H, NH)ppm. MS: m/z(%) 346(M^++1, 2.80), 345(M^+, 12.70), 344(M^+-1, 10.50), 330(2.10), 304(3.10), 303(14.20), 302(13.20), 289(15.70), 288(100), 287(91.80), 261(0.90), 260(1.40), 248(2.60), 247(6.10), 246(39.30), 245(38.60), 229(4.70), 228(3.90), 227(3.40), 218(4.40), 217(4.30), 202(3.80), 201(16.70), 200(19.10), 188(3.70), 187(6.20), 186(11.40), 185(9.10), 173(13.30), 172(12.10), 171(14.00), 170(11.20), 158(8.10), 157(6.60), 146(3.60), 145(5.00), 144(9.40), 143(9.80), 131(4.30), 130(3.90), 128(6.40), 127(7.30), 118(5.90), 117(9.70), 116(15.50), 115(39.30), 103(3.40), 102(5.80), 101(4.90), 91(6.30), 90(9.50), 89(24.60), 88(10.90), 77(7.20), 76(4.50), 75(10.60), 64(3.40), 63(18.70), 62(9.20), 51(11.60), 50(6.60). Anal. Found: C, 55.46; H, 4.23; N, 12.03; S, 9.09. $C_{16}H_{15}N_3O_4S$ requires: C, 55.65; H, 4.35; N, 12.17; S, 9.27.

3-Acetylcoumarin-2, 4-dibenzoyl thiosemicarbazone (4)
A mixture of 2 (0.01 mol) and benzoyl chloride (0.02 mole) in acetic acid (20 ml) was heated under refluex for hr, then cooled and poured into water. The resulting solid was filtered off, washed with water, dried and purified by recrystallization from methanol to give 4 as pale yellow, yield 63.90, m.p. 183^{o}C. IR(KBr): 3222(NH), 1718, 1698(C=O), 1625(C=N), 1602, 1589(C=C), 1389(C=S), 1230, 1090(C-O) cm^{-1}. ^{1}H-NMR(DMSO-d6): δ 3.21(S, 3H, CH_3), 7.15-7.98(m, 14H, Ar-H), 8.23(S,1H, pyran-H), 11.10(S, 1H, NH)ppm. Anal. Found: C, 66.35; H, 4.01; N, 8.82; S, 6.67. $C_{26}H_{19}N_3O_4S$ requires: C, 66.52; H, 4.05; N, 8.95; S, 6.82.

3-(Coumarin-3-ylethylidene)amino-2-thioxo-imidiazolidin-4-one (5)
5-Aryl-2-[(coumarin-3-ylethylidene)-hydrazino]-thiazole (7)
A mixture of 2(0.01 mole), ethyl chloroacetate and ω-bromomethyl arylketones (such as phenacyl bromide and 4-methylphenacylbromide) (0.01 mole) in ethanol (30 ml) in presence of fused sodium acetate (0.03 mole) was heated under reflux for 4hr, then cooled and poured into water. The solid formed was filtered off, washed with water, dried and purified by recrystallization from a suitable solvent to give 5 and 7.

Compound 5 as pale yellow crystals; yield 63%, m.p 200^{o}C. IR(KBr): 3225(NH), 1721, 1698(C=O), 1623(C=N), 1603, 1583(C=C), 1389(C=S), 1030(C-O) cm^{-1}. ^{1}H-NMR (DMSO-d6): δ 3.21(S, 3H, CH_3), 3.81(S, 2H, NCH_2CO), 7.20-7.89(m, 4H, Ar-H), 8.20(S, 1H, pyran-H), 9.95(S, 1H, NH)ppm. MS: m/z(%) 302(M^++1, 13.80), 301(M^+, 31.20), 300(M^+-1, 39.10), 286(12.30), 285(8.70), 284(12.30), 283(11.60), 274(5.10), 273(11.60), 272(7.20), 258(14.50), 254(15.20), 247(10.90), 246(9.90), 227(13.80), 226(13.80), 225(10.90), 203(7.20), 202(15.90), 201(34.80), 200(52.40), 199(44.90), 188(13.80), 187(27.50), 186(26.10), 185(22.50), 184(23.90), 178(37.70), 177(33.30), 170(34.10), 169(15.90), 160(13.00), 159(23.20), 158(24.60), 157(11.60), 146(50.0), 145(33.30), 144(55.80), 143(42.80), 132(15.90), 131(24.00), 130(100), 129(59.40), 122(29.0), 121(28.30), 120(34.30), 119(15.20), 118(35.50), 117(24.60), 116(27.50), 115(94.90), 114(29.00), 111(23.90), 109(15.20), 103(18.10), 102(34.80), 101(24.60), 100(27.50), 98(83.30), 97(65.20), 96(21.70), 91(16.70), 90(24.0), 89 (71.90), 88(69.60), 87(34.80), 86(25.40), 78(37.70), 77(47.80), 76(29.0), 75(33.30), 65(31.90), 64(25.40), 63(60.10), 62(47.10), 61(33.30), 60 (23. 90), 59(31.90), 51(63.00), 50(42.00). Anal. Found: C, 65.03; H, 3.55; N, 13.79; S, 10.49. $C_{14}H_{11}N_3O_3S$ requires: C, 65.12; H, 3.65; N, 13.95; S, 10.63.

5-Phenyl-2-[(coumarin-3-ylethylidene)-hydrazino]-thiazole (7a) as pale yellow crystals, yield 71%, m.p. 131^{o}C. IR (KBr): 3250(NH), 1721(C=O), 1625(C=N), 1602, 1586(C=C), 1125, 1083(C-O) cm-1. ^{1}H-NMR (DMSO-d6): δ 3.21(S, 3H, CH_3), 6.95-7.89(m, 10H, Ar-H and thiazol-H), 8.25(S, 1H, pyran-H), 10.30(S, 1H, NH)ppm. MS: m/z (%) 326(M^++1, 11.20), 361(M^+, 1810), 187(11.20), 186(13, 20), 176920.10), 175(31.50), 172(11.20), 186(13.20), 176(20.10), 175(31.10), 172(11.20), 171(8.20), 145(3.20), 144(6.80), 143(2.10), 135(20.10), 134(31.20), 129(11.20), 119(100), 118(35.50), 116(20.20), 92(13.20), 91(78.70), 90(16.20), 78(1.20), 77.(76.10), 65(12.10), 64(11.20), 63(24.20), 51(11.20), 50(16.20). Anal. Found: C, 68.08; H, 4.37; N, 12.30; S, 9.83. $C_{20}H_{15}N_3O_2S$ requires: C, 68.18; H, 4.26; N, 11.93; S, 9.94

5-(4-Methylphenyl)-2-[(coumarin-3-ylethylidene)-hydrazino]-thiazde(7b).
As pale yellow crystals, yield 65%, , m.p. 124°C. IR(KBr): 3235(NH), 1719(C=O), 1627(C=N), 1601, 1589(C=C), 1210, 1095(C-O) cm^{-1}. ^{1}H-NMR (DMSO-d6): δ 2.35(S, 3H, CH_3), 3.21(S, 3H, CH_3), 7.25-7.89(m, 4H, Ar-H and thiazole-H), 8.35(S, 1H, pyran-H), 10.35(S, 1H, NH)ppm. MS: m/z(%) 376(M^++1, 4.30), 375(M^+, 17.10), 374 (M^+-1, 14.60), 373(31.10), 372(56.70), 357(14.60), 356(11.00), 355(15.20), 346(6.10), 343(15.20), 315(13.40), 314(12.20), 304(10.40), 302(5.50), 301(8.50), 286(7.30), 284(15.90), 278(11.60), 272(14.00), 271(44.50), 270(44.50), 247(5.50), 243(13.40), 242(6.10), 225(6.70), 224(10.40), 221(13.40), 220(11.00), 216(15.20), 215(16.50), 206(10.40), 205(13.40), 199(11.30), 196(12.80), 191(13.40), 190(24.40), 189(25.60), 188(17.10), 186(14.00), 178(9.10), 176(6.10), 175(23.20), 174(15.90), 172(9.10), 161(10.40), 160(8.50), 159(15.90), 148(28.00), 147(39.00), 146(24.40), 145(11.60), 143(14.60), 135(23.80), 134(21.30), 130(3.70), 128(9.80), 127(14.60), 126(12.20), 120(10.40), 119(100), 117(15.90), 116(31.10), 115(28.70), 114(43.90), 107(15.20), 104(17.10), 102(11.60), 100(12.80), 95(6.10), 94(14.60), 92(10.40), 91(78.70), 90(17.10), 89(18.90), 88(13.40), 87(11. 60), 81(10.40), 80(10.40), 78(9.80), 77(23.20), 65(29.90), 63(23. 20), 62(25.00), 53(101.60), 52(9.10), 51(22.60), 50(11.60). And. Found: C, 67.02; H, 4.33; N, 11.01; S, 8.38. $C_{21}H_{17}N_3O_2S$ requires: C, 67.20; H, 4.53; N, 11.20; S, 8.53.

1-Actetyl-3-(Coumerin – 3-Ylethylidene) amino-2-thioxo-imidazolidin-4-one (6).
A solution of 5 (0.01 mole) in acetic anhydride (20ml) was heated under reflux for 2 hr, then cooled and poured into ice-water. The solid obtained was filtered off, washed with water, dried and purified by re-crystallization with benzene to give 6 pale yellow crystals, yield 57%, m.p. 163°C. IR(KBr).1721, 1701-1698 (C= O), 1625 (C=N), 1602, 1595 (C=C), 1389 (C=S), 1020 (C – O) cm^{-1}. ^{1}H-NMR(DMSO-d_6) : δ 2.01(S, 3H, $COCH_3$), 3.20(S, 3H, CH_3), 3.81(S, 2H, NCH_2CO), 7.21-7.89(m, 4H, Ar-H), 8.31(S, 1H, pyran-H)ppm- MS: m/z(%) 344(M^++1, 6.30), 434(M^+, 17.60), 302(16.80), 301(100), 300(57.10), 286(11.30), 285(9.70), 284(13.20), 283(10.50), 274(6.30), 273(12.30), 272(6.20), 258(13.30), 254(16.30), 247(10.90), 246(8.30), 227(12.70), 226(14.20), 225(11.80), 203(6.30), 202(15.90), 201(36.70), 200(54.50), 199(43.80), 188(12.30), 187(37.60), 186(36.10), 185(11.20), 184(21.20), 178(36.50), 177(31.60), 170(43.10), 169(13.80), 160(11.01), 159(31.20), 158(14.20), 157(11.60), 146(49.00), 145(30.30), 144(53.50),143(45.20), 132(13.20), 131(19.50), 130(53.20), 129(33.20), 122(17.80), 121(30.20), 120(23.20), 119(13.50), 118(45.50), 117(21.40), 116(28.10), 115(89.80), 114(25.30), 111(26.10), 109(13.20), 103(19.20), 102(32.20), 101(24.60), 100(26.50), 98(71.30), 97(63.20), 96(19.20), 91(15.60), 90(31.20), 89(61.20), 88(69.20), 87(33.20), 86(23.50), 78(39.30), 77(49.20), 76(28.10), 75(31.30), 65(30.80), 64(26.20), 63(61.20), 62(46.10), 61(35.20), 60(26.80), 59(21.80), 51(63.20), 50(46.30), Anal. Found: C, 55.81; H, 3.69; N, 12.17; S, 9.11. $C_{16}H_{13}N_3O_4S$ requires: C, 55.98; H, 3.79; N, 12.24; S, 9.33.

4,6-disubstituted-1-(coumarin-3-ylethylidene)aminopyrimidines(8 and 9).
A mixture of 2 (0.01 mole) and dicarbonyl compounds(namely ethyl acetoacetate and dietaylmalonate) (0.01mole) in acetic acid (25ml) was heated under reflux for 3hr, then cooled and poured into water. The resulting product was filtered off, washed with water, dried and purified by recrystallization from ethanol to give 8 and 9 respectively.

6-Methyl-1-(Coumarin-3-ylethylidene)amino-2-thioxo-pyrimidin-4-one (8)
As yellow crystals, yield 62%, m.p. 170°C. IR(KBr): 3275(NH), 1721, 1698(C=O), 1628(C=N), 1603, 1585(C=C), 1389(C=S), 1125(C-O) cm^{-1}. ^{1}H-NMR(DMSO-d_6) : δ 2.57 (S, 3H, CH_3), 3.20(S, 3H, CH_3),7.35-7.91(m, 4H, Ar-H), 8.36(S, 1H, pyran-H), 8.63(S, 1H, pyrimidin-H), 10.40(S, 1H, NH)ppm. MS: m/z (%): 328(M^++1, 25.40), 327(M^+, 40.70), 326(M^+-1, 20.30), 305(16.90), 304(10.20), 303(11.90), 298(11.90), 288(22.00), 252(11.90), 249(11.90), 248(25.40), 247(79.70), 246(47.50), 231(13.60), 227(16.90), 225(20.30), 219(10.20), 218(15.30), 217(35.60), 216(39.00), 202(44.10), 201(52.50), 200(45.80), 199(27.10), 190(16.90), 189(35.60), 186(25.40), 185(27.10), 184(25.40), 171(42.90),170(33.90), 169(10.20), 164(15.30), 159(15.30), 158(13.60), 147(11.90), 146(16.90), 144(32.20), 143(39.00), 132(16.90), 131(20.30), 130(28.80), 128(18.60), 127(27.10), 126(16.90), 123(15.30), 121(16.90), 116(28.80), 115(74.60), 114(76.30), 109(40.70), 107(23.70), 106(15.30), 103(22.00), 102(45.80), 98(74.60), 97(59.30), 95(32.20), 94(22.00), 91(44.10), 90(10.20), 87(30.50), 85(28.80), 84(22.00), 83(37.30), 77(20.30), 76(39.00), 75(33.90), 69(42.40), 68(35.60), 67(44.10), 65(22.00), 60(50.80), 59(100.00), 58(33.90), 53(25.40), 52(20.30), 51(25.40), 50(16.90). Anal. Found: C, 58.62; H, 3.79; N, 12.63; S, 9.63. $C_{16}H_{13}N_3O_3S$ requires: C, 58.72; H, 3.97; N, 12.84; S, 9.78.

4,6-Dihydroxy-1-(coumarin-3-ylethylidene)aminopyrimidin-2-thione(9) As yellow crystals, yield 58%, m.p. 165°c. IR(KBr): 3350-3330(br-OH), 1719(C=O), 1632(C=N), 1605, 1589(C=C), 1401(C=S), 1120, 1098(C-O) cm^{-1}. ^{1}H-NMR(DMSO-d_6) : δ 3.11(S, 3H, CH3), 7.31-7.89(m, 4H, Ar-H), 8.21(S, 1H, pyran-H), 8.71(S, 1H, pyrimidin-H), 11.35(br-S, 2H, OH)ppm. MS: m/z(%): 330(M^++1, 13.50), 329(27.30), 328(M^+-1, 32.20), 253(61.50), 252(41.00), 247(28.20), 235(10.30), 234(15.40), 227(12.80), 226(38.50), 225(48.70), 218(15.40), 217(28.20), 196(12.80), 189(30.80), 185(35.90), 146(25.60), 142(10.30), 141(23.10), 140(38.50), 137(20.50), 135(28.20), 134(25.60),

131(46.20), 129(30.80), 128(23.10), 126(35.90), 123(30.80), 116(30.80), 115(48.70), 114(66.70), 106(25.60), 105(30.80), 102(51.30), 99(20.50), 98(41.00), 97(71.80), 96(30.80), 87(17.90), 82(17.90), 78(48.70), 77(41.00), 76(30.80), 73(33.30), 71(12.80), 70(30.80), 68(35.90), 67(46.20), 65(20.50), 60(64.10), 59(100.00), 55(25.60), 54(48.70), 53(35.90). Anal. Found: C, 54.31; H, 3.22; N, 12.58; S, 9.61.
$C_{15}H_{11}N_3O_4S$ requires: C, 54.71; H, 3.34; N, 12.76; S, 9.73.

RESULTS AND DISCUSSION

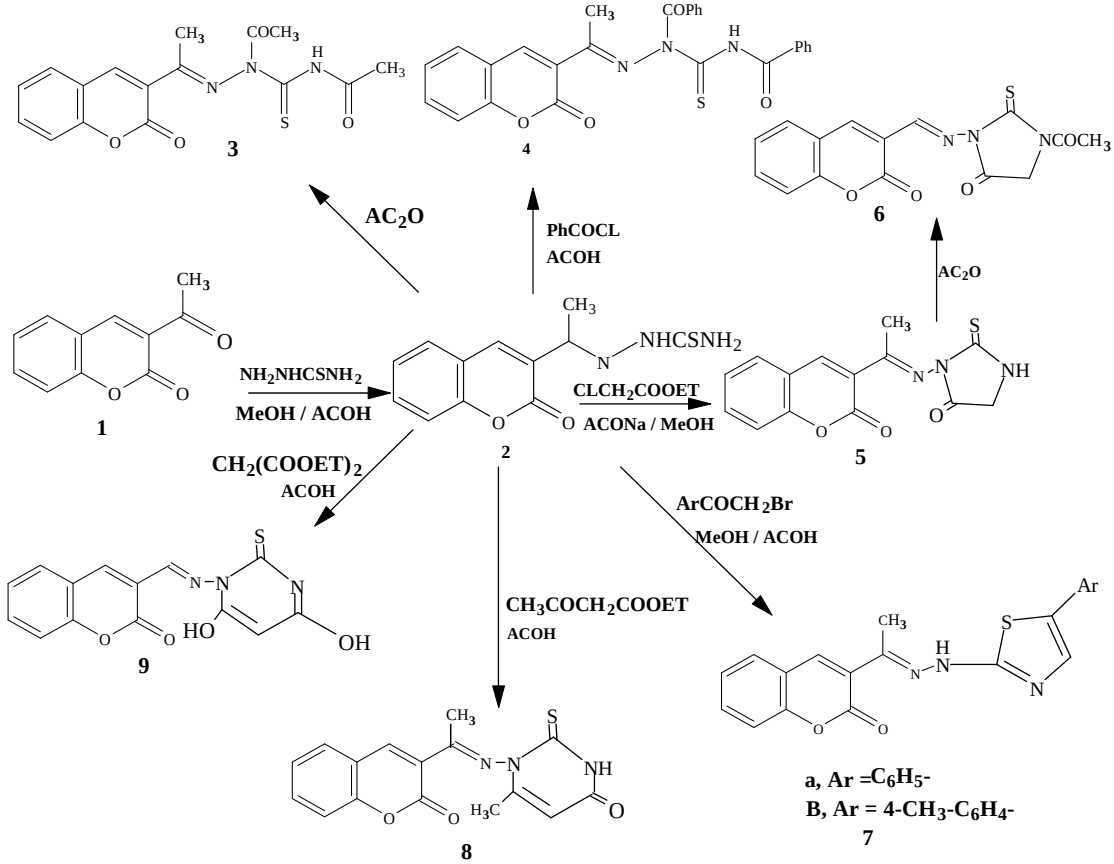
Chemistry

Condensation of 3-acetylcoumarin with thiosemicarbazide in presence of acid medium in methanol under reflux, yielded the corresponding 3-acetylcoumarin thiosemicarbazone (2, scheme 1).

Acetylation and benzoylation of compound 2 with acetic anhydride and benzoyl chloride under reflux led to the formation of 3- acetylcoumarin-2, 4-Diacetyl thiosemicarbazone (3) and 3- Acetylcoumarin-2,4-dibenzoyl thiosemicarbazone(4).The reaction[11]of compound 2 with ethyl chloroacetate in presence of fused sodium acetate in methanol afforded the corresponding 3-(Coumarin-3-ylethylidene)amino-2-thioxo-imidazolidin-4-one(5,scheme1).

Acetylation[12] of compound 5 with acetic anhydride under reflux yielded the corresponding 1-acetyl-3-(coumarin-3-ylethylidene) amino-2-thioxo-imidazolidin-4-one (6).
Treatment of compound 2 with ω-bromomethyl arylketones (such as phenacyl bromide and 4-methylphenacyl bromide) in presence of fused sodium acetate in methanol under reflux led to the formation of 5-aryl-2-[(coumarin-3-ylethylidene)-hyrazino]-thiazole (7).

Condensation of compound 2 with dicarbonyl compounds (namely ethylacetoacetate and diethyl malonate) in acetic acid under reflux gave the corresponding 6-methyl-1-(coumarin-3-ylethylidene) amino-2-thioxo-pyrimidin-4-one (8) and 4, 6-dihydroxy-1-(Coumarin-3-ylethylidene) amino-pyrimidin-2-thione (9,scheme 1), respectively.



Scheme 1

Mass Spectrometry

The mass spectral decomposition modes of the prepared thiosemi- carbazone derivatives and nitrogen heterocyclic compounds containing coumarin ring have been investigated. The mass spectra of compound 2 (Fig. 1) showed an intense molecular ion peak at m/z 261 corresponding to the molecular formula $C_{12}H_{11}N_3O_2S$. The molecular ion of 2 (Scheme 2) underwent fragmentation to produce a peak at m/z 246 by losing NH_2 group. The loss of NCS group from the ion with m/z 245 resulted in an ion at m/z 187. The ion at m/z 187 underwent loss of H, CH_3 radical, HCN radical and CO to give peaks at m/z 186, 171, 144 and m/z 116, respectively.

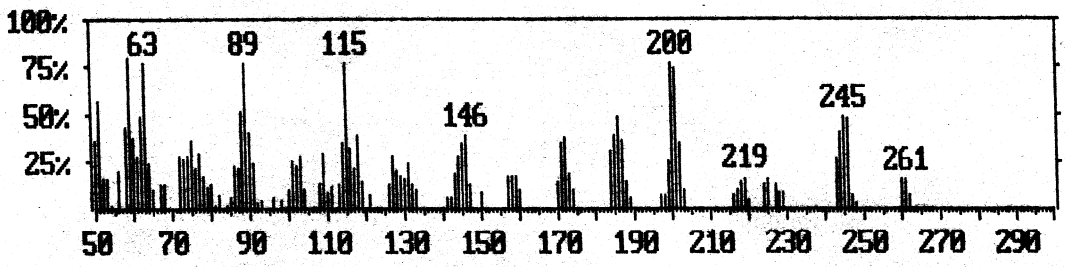


Fig. 1

Also the molecular ion at m/z 261 undergoes fragmentation to produce the ion at m/z 246 by losing NH group. It further underwent loss of CHS, H, N_2 and C_2H_2 to give peaks at m/z 201, 200, 172 and m/z 146, respectively. The ion at m/z 146 underwent loss of CO and CHO to give peak at m/z 118 and m/z 89.

The loss of acetylene molecule (C_2H_2) from the ion with m/z 89 gives a stable fragment at m/z 63.

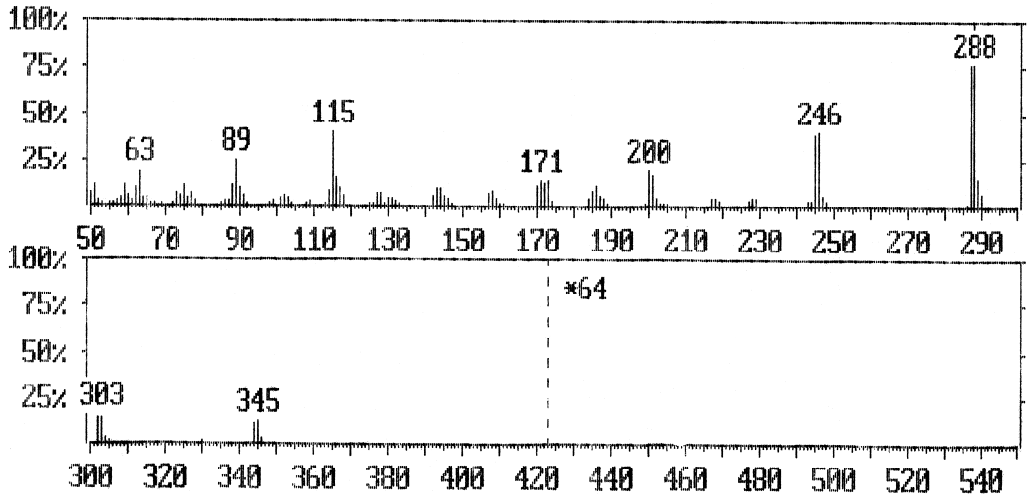
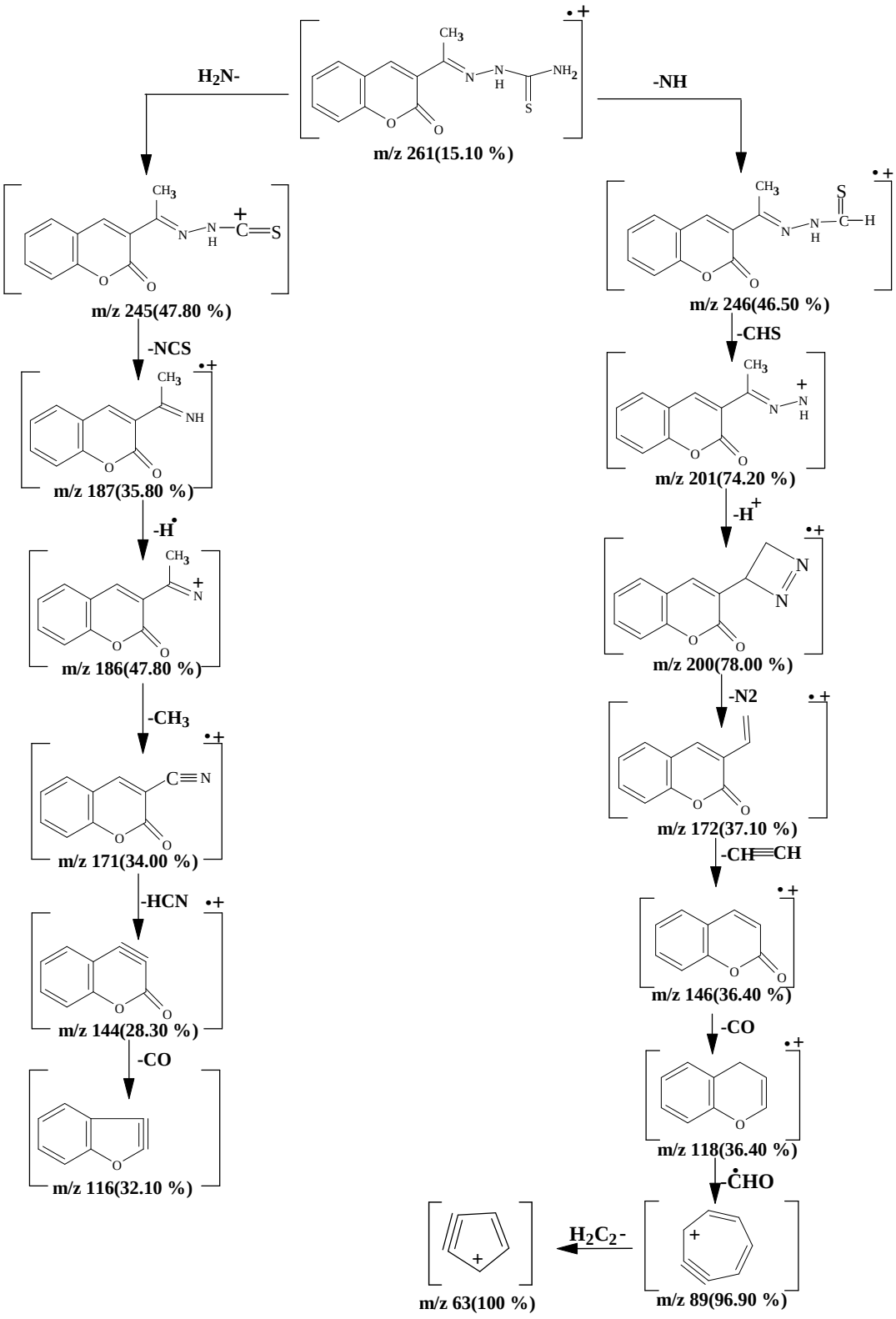
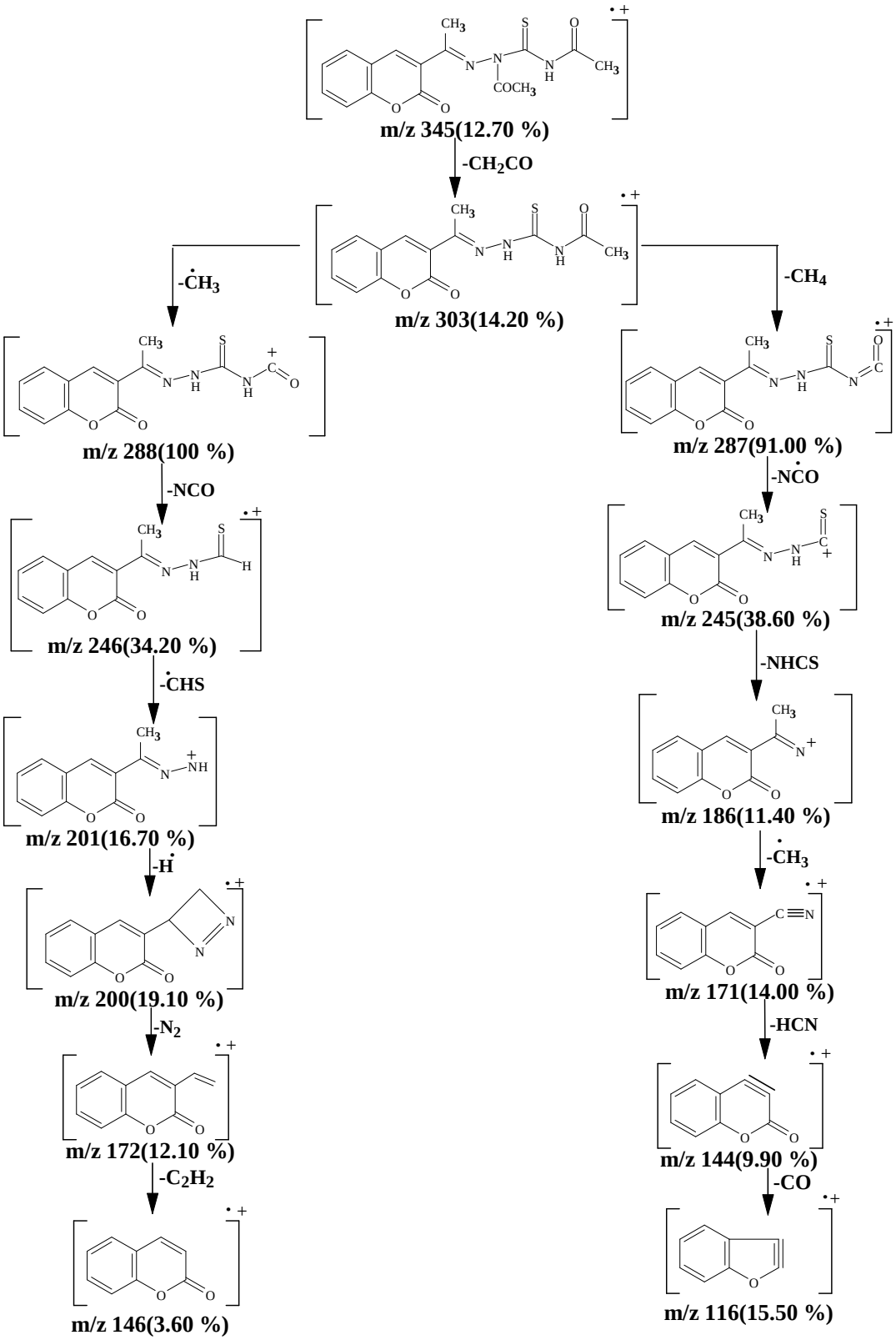


Fig. 2

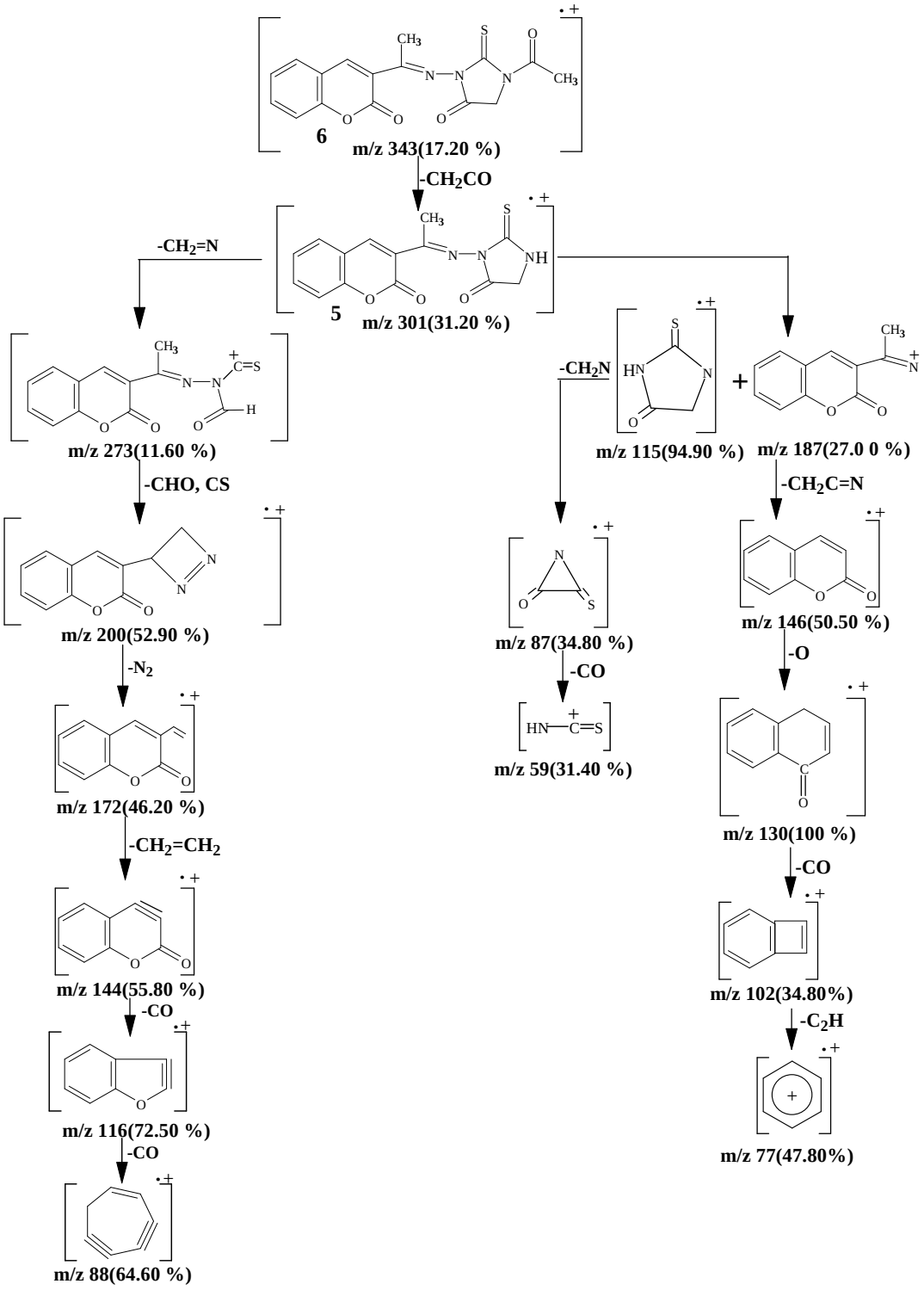
The molecular ion peak of compound 3 (Fig. 2) was observed at m/z 345 corresponding to the molecular formula $C_{16}H_{15}N_3O_4S$. the loss ketene molecule (CH_2CO) from the molecular ion peak at m/z 345 gave a peak at m/z 303. The common peak at m/z 288 was also observed in this case which is attributed to an ion obtained by the loss of methyl group from the ion at m/z 303. The suitable fragment ion at m/z 288 underwent loss of NCO to give peak at m/z 246 (Scheme 3).



Scheme 2: Main fragmentation pathway of compound 2



Scheme 3: Main fragmentation pathway of compound 3



Scheme 4: Main fragmentation pathway of compounds 5 and 6

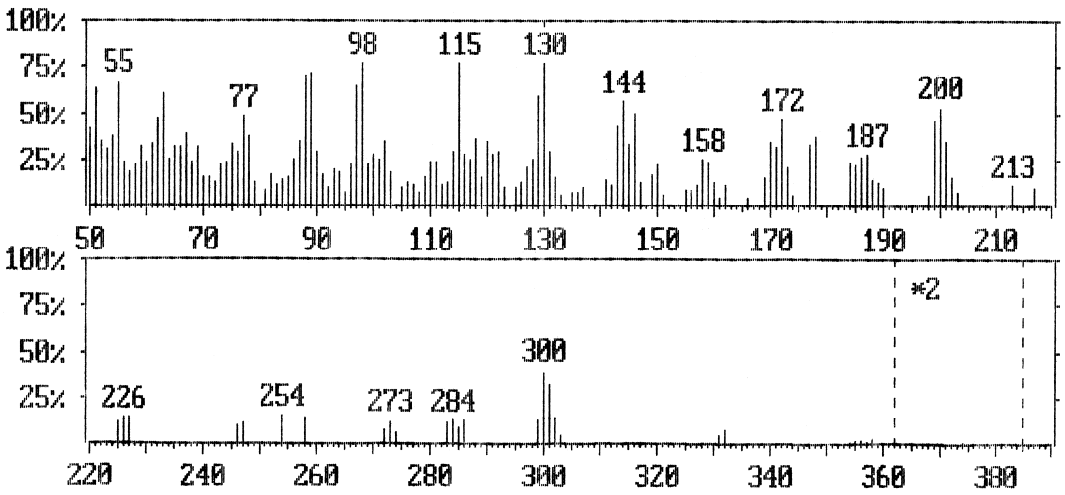


Fig. 3

Also the ion m/z 303 underwent loss of CH4 and NCO to give peak at m/z 287 and 245, respectively. The fragment ions of m/z 287 and 245, respectively. The fragmentations ions of m/z 246 and m/z 245, which have further broken via pathway similar to compound 2.

From the mass spectrum of compound 6, it was concluded that the molecular ion was at m/z 345. The ion of m/z 343 under went fragmentation to produce a peak at m/z 301 by losing ketene molecule (CH_2CO), Corresponding to the molecular ion of compound 5(Fig. 3). The fragment ion of m/z 301 further broke via different pathways are summarized in (Scheme 4).
The electron impact ionization mass spectrum of compound 5 shows a bases peak at m/z 130, while compound 6 is a molecular ion at m/z 301.

The mass spectra of compounds 7a, b (Fig. 4) are fully consistent with the assigned structures. In most cases, intense molecular ion peaks were observed. Thus, compounds 7a, b showed intense molecular ion peaks at m/z 361 and 375, consistent with the molecular formula $C_{20}H_{15}N_3O_2S$ and $C_{21}H_{17}N_3O_2S$, respectively. The molecular ions of compounds 7a and 7b (Scheme 5)underwent fragmentations to produce peaks at m/z 175 and m/z 189, corresponding to the 5- substituted 2- aminothiazole radical cation. It further underwent loss of HN=C=N and CH=C=S to give peaks at m/z 134, 148 and 77, 91 respectively. Also found to undergo fragmentation to produce the ion of m/z 186. The ion at m/z 186 underwent loss of N, CO and CH=C to give peaks at m/z 172, 144 and stable fragment ion at m/z 119.

The mass spectra of compound 8 and 9 show relatively strong molecular ions and peaks typical of a cleavage and rearrangement processes type fragmentation. Thus, compounds 8 and 9 showed an intense molecular ion peak at m/z 327 and 329, corresponding to the molecular formula $C_{16}H_{13}N_3O_3S$ and $C_{15}H_{11}N_3O_4S$. From a study of the mass of compound 8 (Fig. 5), it was found that the molecular ion of these compound fragmented further and involved two various possible pathways as illustrated by (Scheme 5) showing representative example.

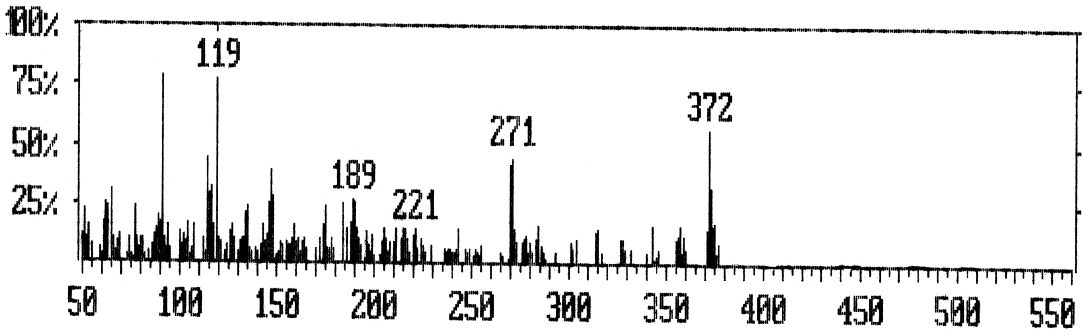
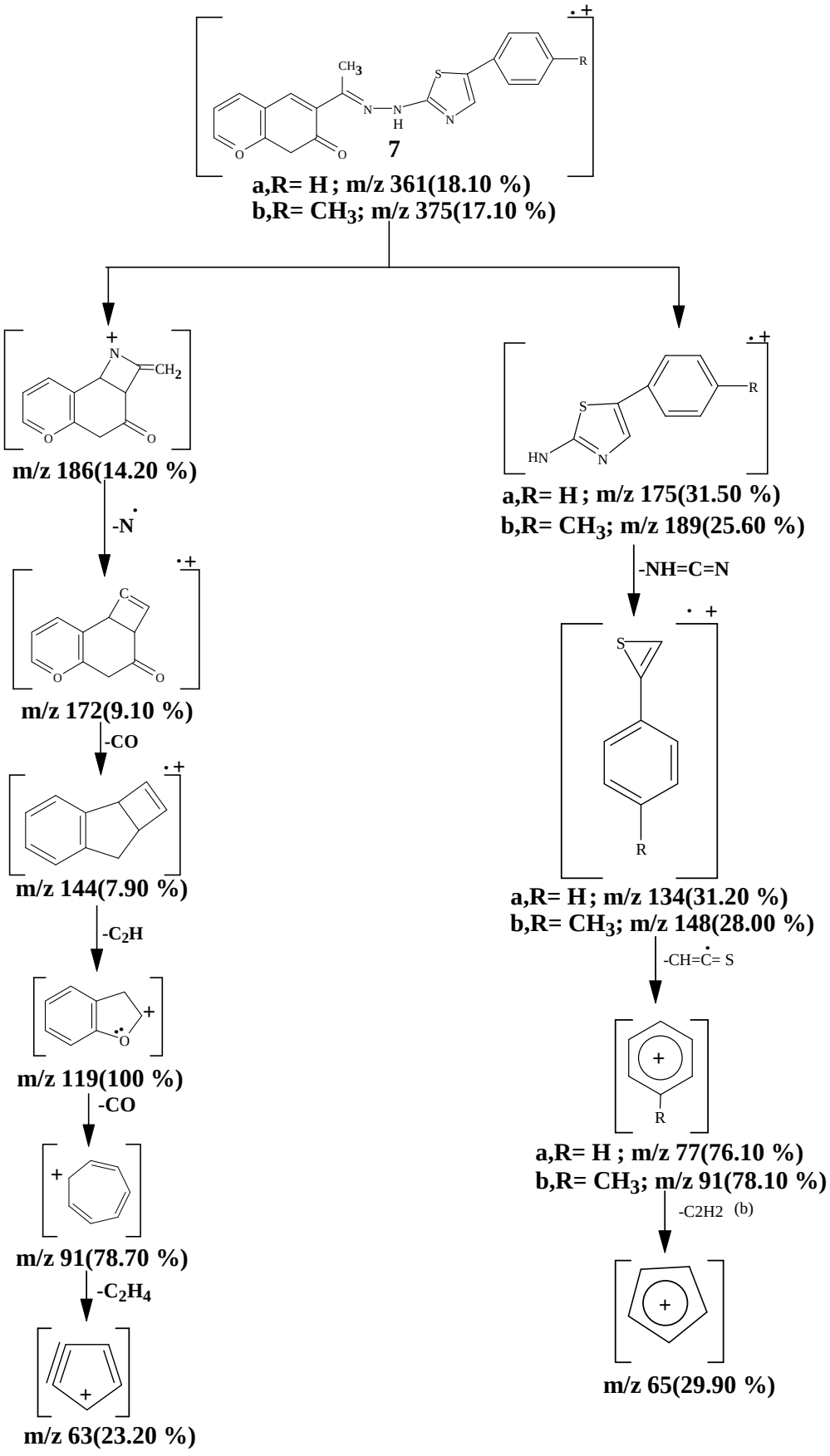
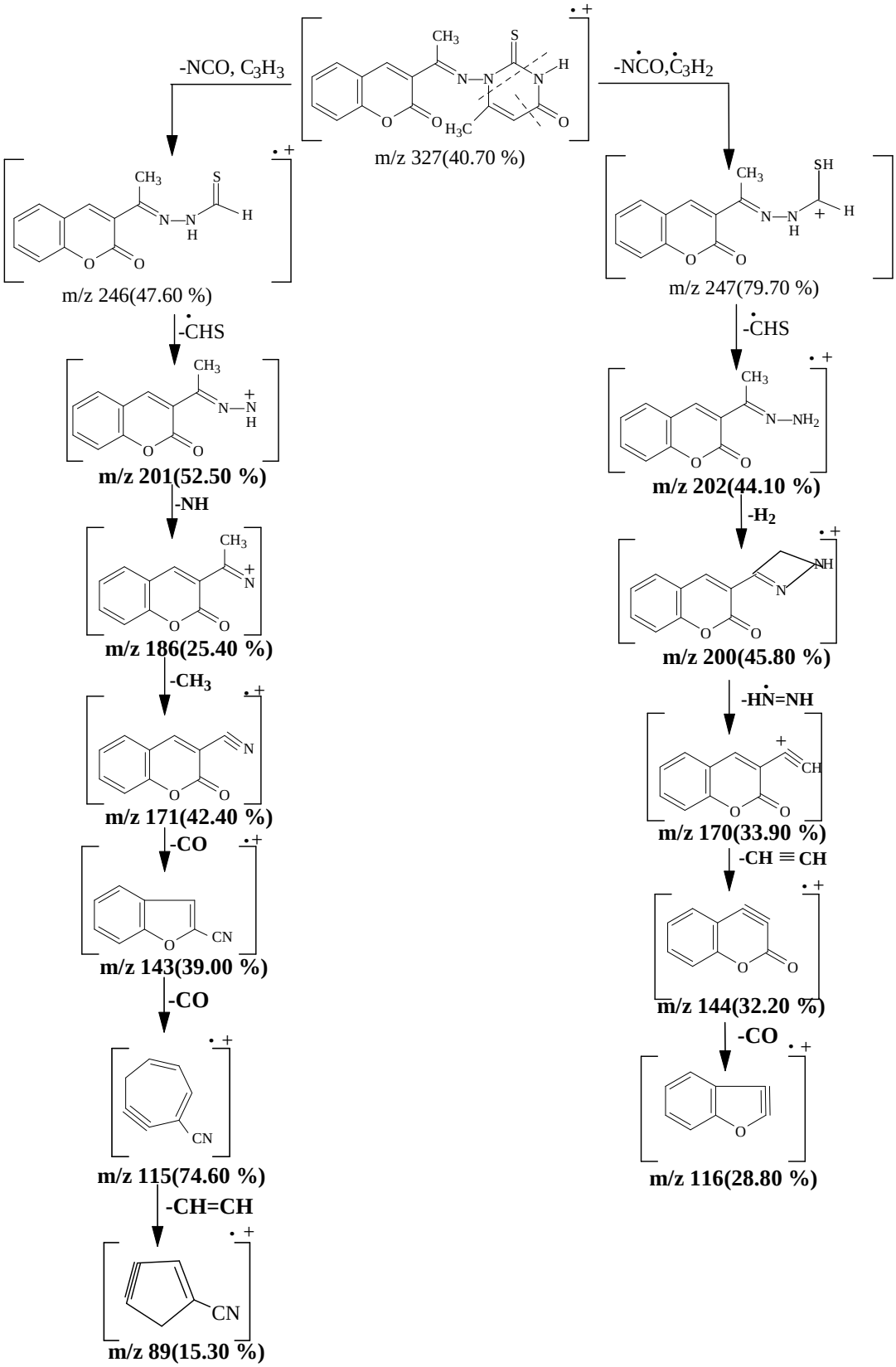


Fig. 4



Scheme 5: Main fragmentation pathway of compounds 7a,b



Scheme 6: Main fragmentation pathway of compound 8.

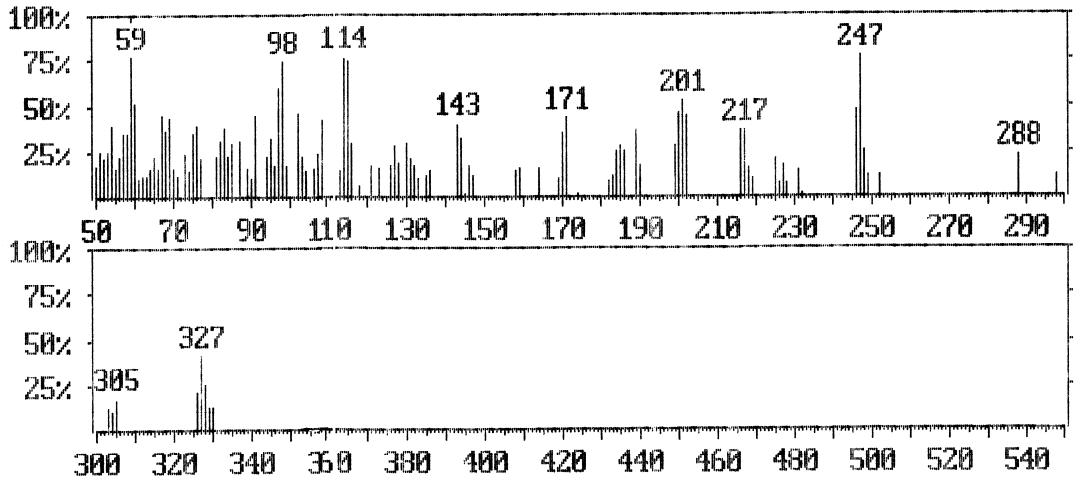


Fig.5

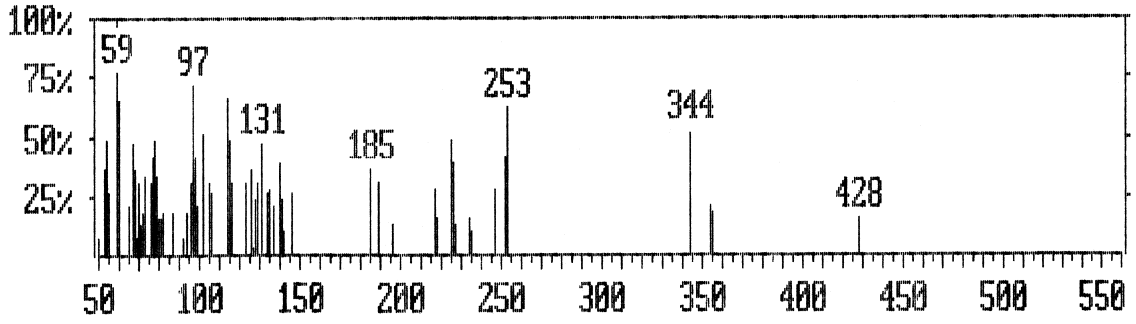


Fig.6

REFERENCES

[1] Takashi, O.Yasuhisa, X. and Hiroshi, N. *PCT Int. lat Appl*., (2002)[chem.. Abstr., 137, 154943(**2002**)].
[2] Baraldi, P.G., U.S. Pat., (2002), 11, US 6358964 *Chem. Abstr*. 136, 247601, (**2002**)]
[3] Bedoya, M.L.; Beltrain, M; Sancho, R.; Olmedo, A.D.; Sanchez-Palamino, S.; Oinia, F.O., Loper-Perez, J.I.; Munoz, F.; Felicino, A.S. and Alcami, J.; *Bioorg. Med. Chem. Lett*. 15, 4447(**2005**).
[4] Marquez, N.; Sancho, R.; Bedoya, L.M.; Alcami, J.; Loper-Perez, J.L.; Felicino, A.S.; Fiebich, B.L. and Munrioz, E.; *Antiviral research*, 66, 137(**2005**).
[5] Bailly, F.; Queffelec, C.; Mbemba, G.; Fram-Mouscadet, J.F. and Cotenc, P.; *Bioorg. Med. Chem. Lett*., 15, 5053(**2005**).
[6] Ibrahim,H.K. and Hasanen, J.A.; Afinidad, 64(527), 60(**2007**).
[7] El-Deen, I.M. and Ibrahim, H.K.; *Phosphorous, Sulfur, Silicon Relat. Elem.*, 179, 195(**2001**).
[8] El-Deen, I.M. and Ibrahim, H.K.; *Chem. Pap*., 58, 200(**2004**).
[9] El-Deen, I.M., Ibrahim, H.K. and Mahmoud, F.F.; *Chin.J. Chem.*, 18,590(**2000**).
[10] El-Deen, I.M.; Al-Wakeel, S.I and Fl-Mawal, A.G.; *Bull-Korean Chem. Soc*., 23, 610(**2002**).
[11] Barot, V.M.; Oriental J. Chem., 12, 91(**1996**).
[12] Mohamed, S.M.; Unis, M. and Abd El-Hady, H.; *Egypt. J. Chem*., 49, 209(**2006**).