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STUDY THE BIOLOGICAL EFFECT ACETOPHENONE THIOSEMICARBAZONE

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Abstract: The Study of the biological activity of Some Compounds Which prepared by the reactions of acetophenone-thiosemicarbazone (1) with ω-bromo- methylaryl ketones, acetic anhydride, ethyl chloroacetate, diethyl oxalate and benzyl chloride yielded the corresponding imidazolidine derivatives (**3**a, b, **5** and **9**), N-diacetyl and N-benzyl acetophenone-thiosemicarbazons (**5** and **10**) respectively. 3-(1-phenyl-ethylidene)-amino-2-thioxo-2, 3-dihydro-imidazo-lidin-4-one (**8**) was prepared via bromination of **6** with bromine to give bromo derivatives (**7**), followed by dehydrobromination of **7** with boiling acetic acid and sodium acetate. The mass spectral fragmentation patterns of some prepared compounds are described. The bioactive compounds can be used as new Antibacterial drugs

Keywords: Synthesis, Mass spectrum, Imidazolidine, Thioxo-imidazolidine

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INTRODUCTION

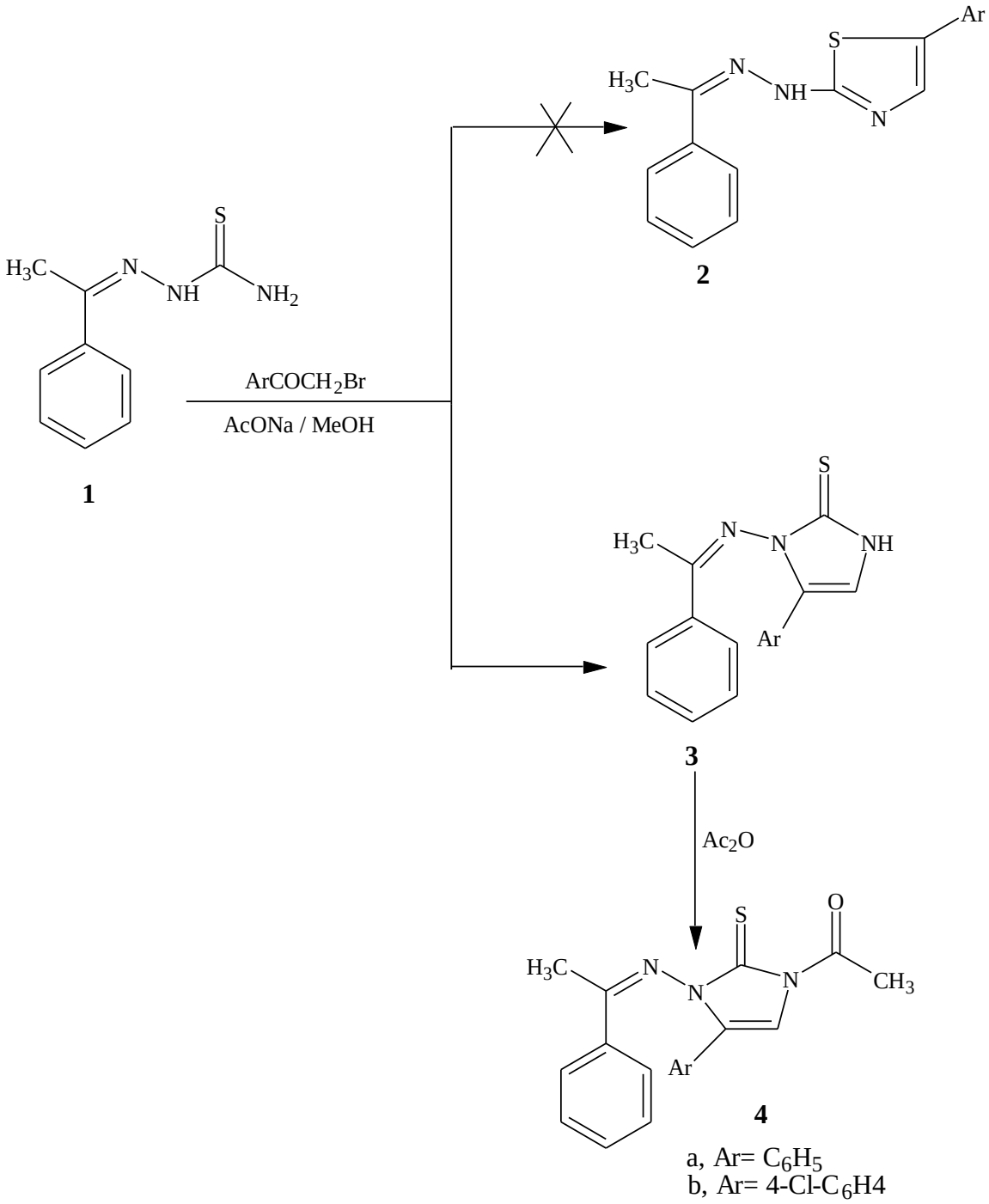
Imidazolidine derivatives constitute an important class of heterocycles in medicinal chemistry because many derivatives have been identified as molecules which may interact with a broad range of biological targets[1-4].In the course of recent investigations[5-7]. Involving acetophenone and thiosemicarbzide, it was found that acetophenone thiosemicarbazone (**1**) is converted into 2-thioxo-imidazolidine derivatives by the action of ω-bromo-methylaryl ketones, ethyl chloroacetate and diethyl oxalate under different conditions. The electron impact (EI) mass spectral fragmentation patterns of some synthesized imidazolidine derivatives are described.

RESULTS AND DISCUSSIONS

CHEMISTRY

Acetophenone thiosemicarbazone (**1**) was prepared via the condensation of acetophenone with thiosemicarbazide under reflux in methanol[5]. Treatment of compound **1** with ω-bromomethylaryl ketones (such as phenacyl bromide and 4-chlorophenacyl bromide in methanol in presence of fused sodium acetate gave the corresponding 4-aryl-3-(1-phenyl-ethylidene) amino-1, 3-dihydro-imidazolidin-2-thiones (**3**a,b),which does not give the expected structure (Scheme 1). Acylation[8] of compound **3** with acetic anhydride under reflux led to the formation of 1-acetyl-3-(1-phenylethylidene) amino-4-aryl-imidazolidin-2-thiones (**4**a,b).

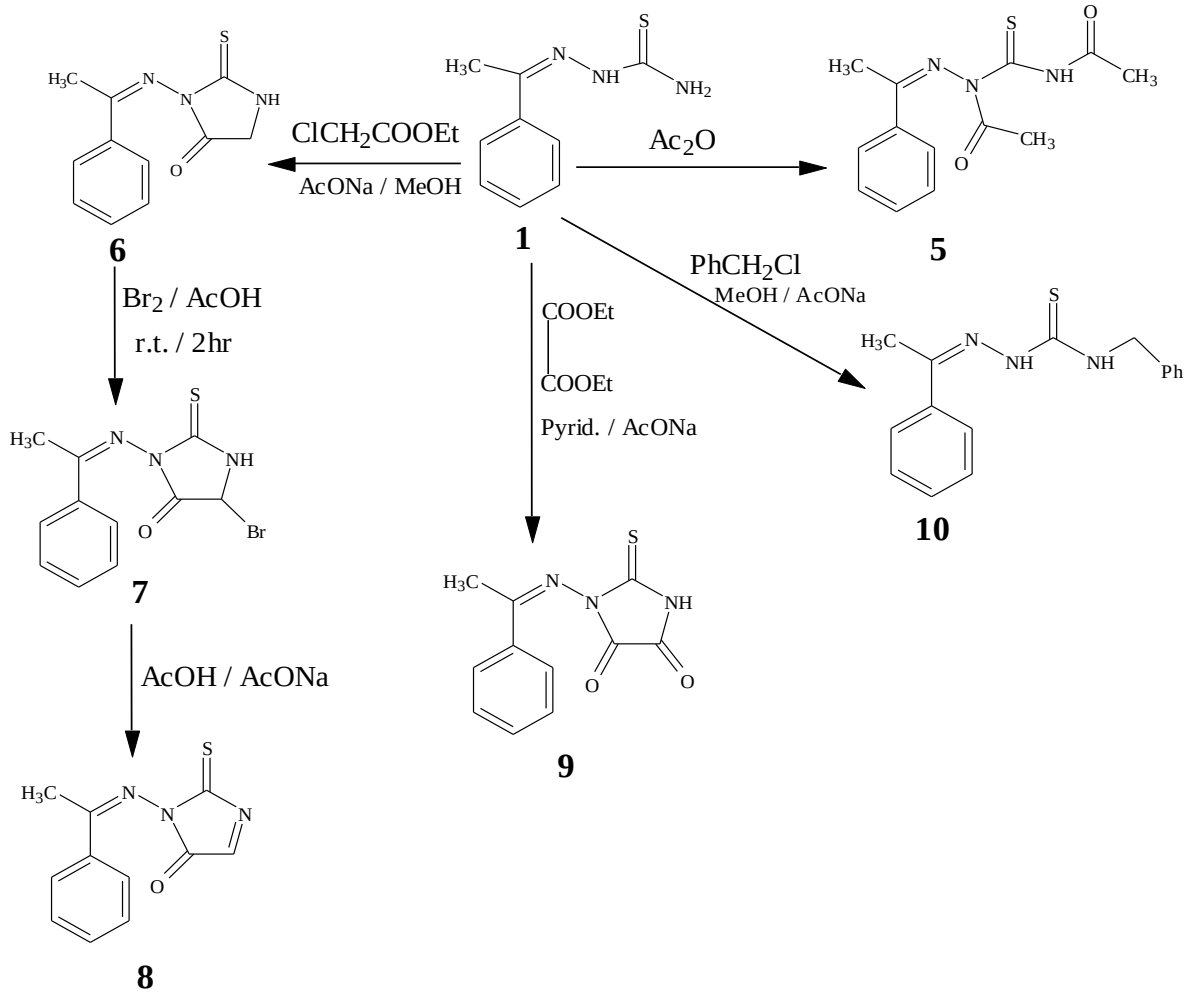
The reaction of acetophenone-thiosemicarbazone (**1**) with acetic anhydride under reflux yielded the corresponding 2, 4-diacetylacetophenone thiosemi- carbazone (**5**). Treatment of compound **1** with ethyl chloroacetate in the presence of fused sodium acetate in methanol under reflux afforded the corresponding 3-(1-phenylethylidene) amino-2-thioxo-imidazolidin-4-one (**6**, Scheme 2).


Ar
S
N
H3C
NH
N
2
S
H3C
N
NH
NH2
ArCOCH2Br
AcONa / MeOH
1
S
H3C
N
N
NH
Ar
3
Ac2O
S
O
H3C
N
N
N
CH3
Ar
4
a, Ar= C6H5
b, Ar= 4-Cl-C6H4

Scheme 1

Bromination[9] of 3-(1-phenylethylidene) amino-2-thioxo-imidazolidin-4-one (**6**) with one mole from the bromine in glacial acetic acid at room temperature gave the corresponding 5-bromo-3-(1-phenylethylidene) amino-2-thioxo-imidazolidin-4-one (**7**).

Dehydrobromination of compound **7** with boiling acetic acid in the presence of fused sodium acetate gave the corresponding 3-(1-phenylethylidin) amino-2-thioxo-2,3-dihydro-imidazolidin-4-one (**8**, Scheme 2).



Scheme 2

Treatment of acetophenone thiosemicarbazone (**1**) with diethyl oxalate in presence of fused sodium acetate in pyridine afforded the corresponding 3-(1-phenylethylidene) amino-2-thioxo-imidazolidin-4,5-dione (**9**).

Alkylation of compound 1 with benzyl chloride in presence of fused sodium acetate in methanol yielded the corresponding 4-benzyl acetophenone thiosemicarbazone (**10**, Scheme 2).

Mass Spectrometry

The mass spectral[6,7] decomposition modes of various imidazolidine and thiosemicarbazone derivatives containing (1-phenylethylidene) amino substituents have been suggested and investigated. Mass spectra of five compounds **3**b, **4**b, **5**, **6** and **7** (Figures 1-5) belonging to this series were recorded and all the spectra showed characteristic common suggested fragmentation pathways, as shown in Schemes 3,4 and 5.

Compounds 3b and 4b

The mass spectra of compounds **3**b and **4**b are fully consistent with the assigned structures. In most cases, intense molecular ion peaks were observed. Thus, compound 3**b** showed an intense molecular ion peak at 327 corresponding to the molecular formula $C_{17}H_{14}N_3ClS$. The M+2 was observed along with the molecular ion peak due to the presence of isotopes chlorine atom present in the compound. The formation of ion m/z 312 could be explained due to lose of NH radical from the molecular ion peak (M-15).

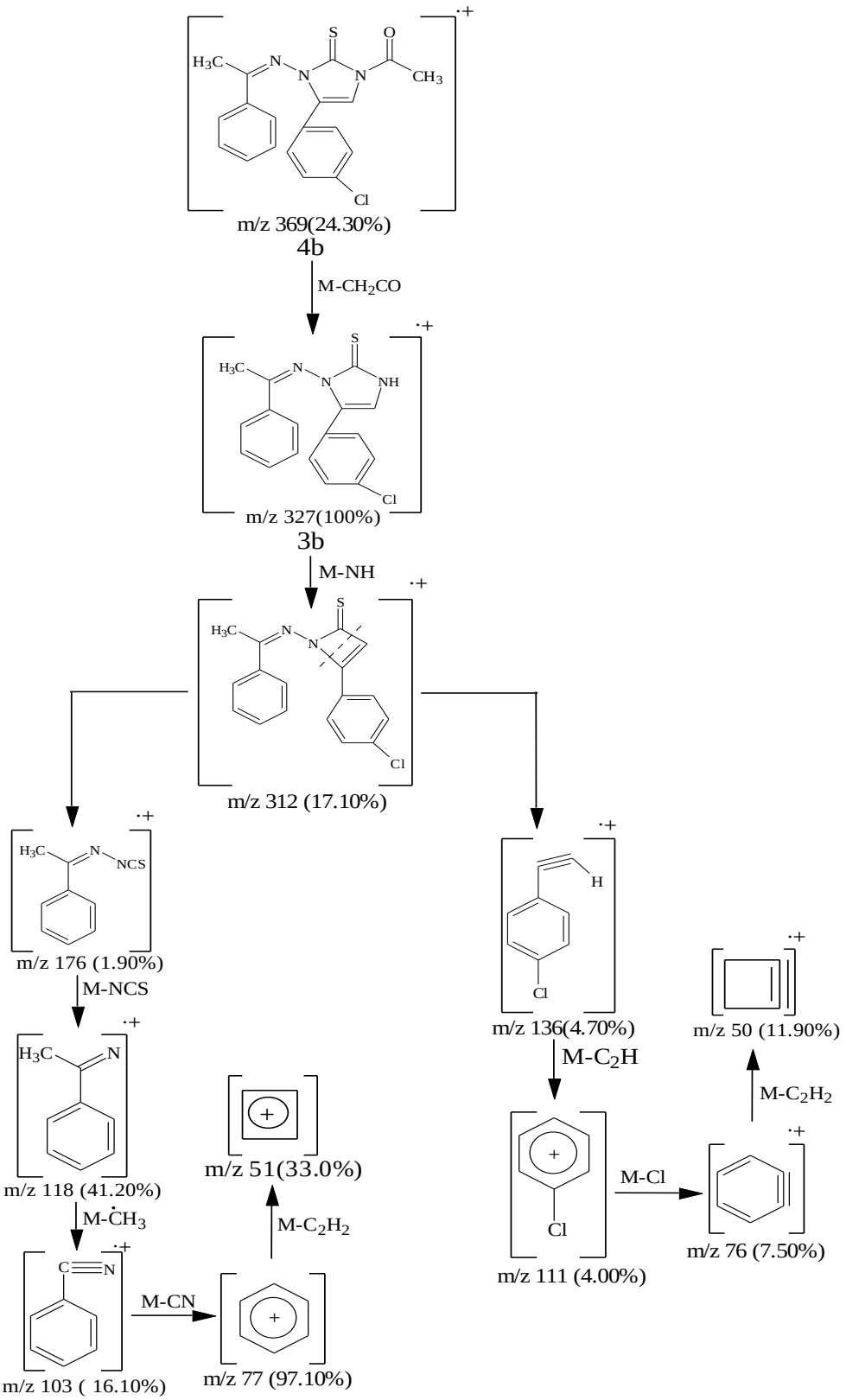
The ion of m/z 312 underwent fragmentation to produce peaks at m/z 176 and m/z 136, corresponding to the molecular ion of (1-phenylethylidene) amino-isothiocyanate and 4-chlorophenylacetylene.

The ion of m/z 176 underwent loss of NCS to give peak at m/z 118 which is a characteristic of (1-phenylethylidene) amino radical cation. It further underwent loss of CH_3, CN and C_2H_2 to give peaks at m/z 103, m/z 77 and m/z 51 respectively. The ion of m/z 136 underwent loss of C_2H, Cl and C_2H_2 to give peaks at m/z 111, m/z 76 and m/z 50 respectively.

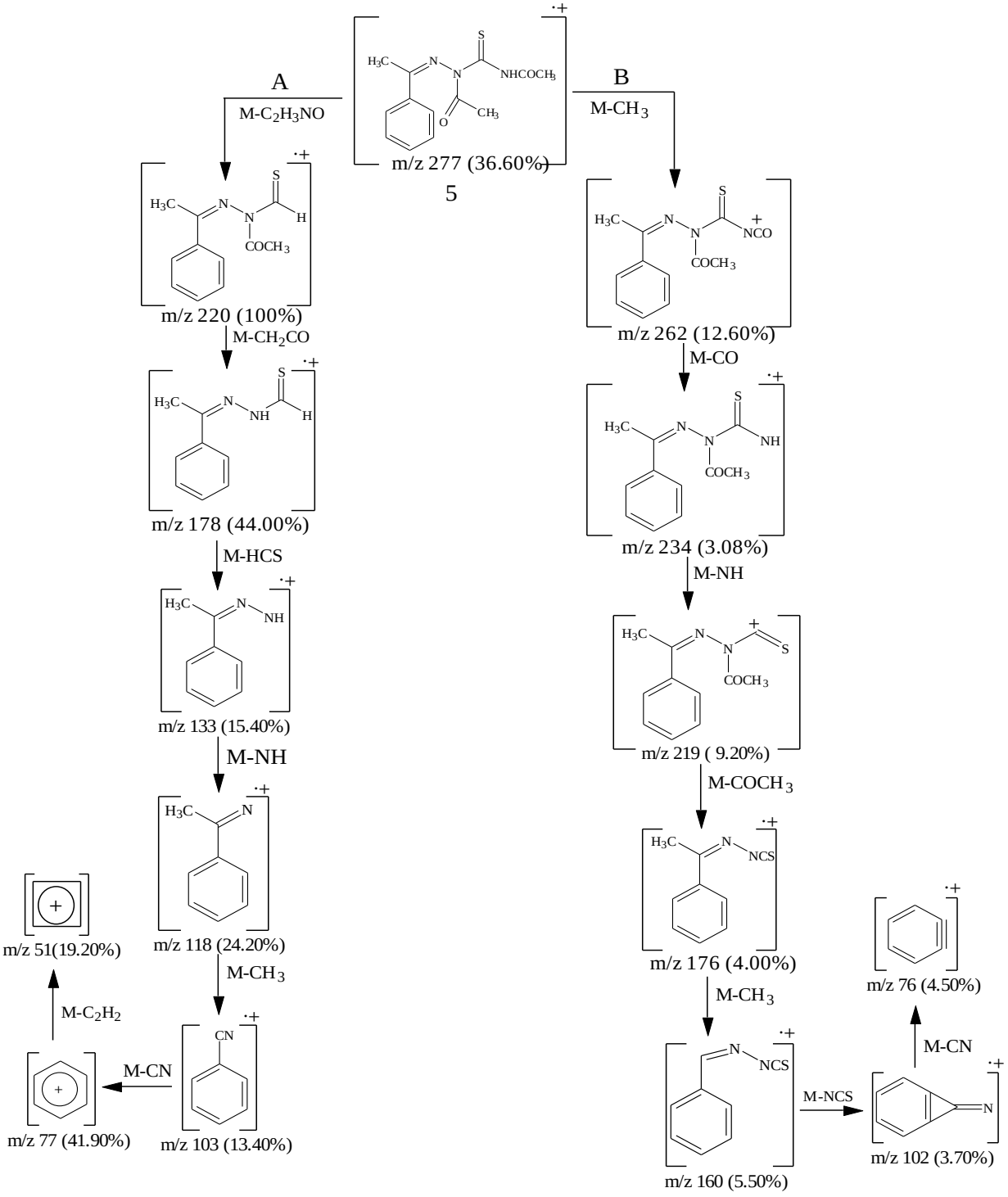
The compound **4**b showed an intense molecular ion peak at m/z 369 corresponding to the molecular formula $C_{19}H_{16}N_3ClOS$. The M+2 peak was also observed at m/z 371. The formation of fragment ion at m/z 327, which was also found to be the base peak and corresponding to the molecular formula of compound **3**b could be explained by loss of CH_2CO molecule from the molecular ion peak (m/z = 369). The ion of m/z 327 was broken via pathway in the same fragmentation processes which was observed for compound (3**b**, Scheme 3).

The compound **5** showed an intense molecular ion peak at m/z 277 corresponding to the molecular formula $C_{13}H_{15}N_3O_2S$. The molecular ion of m/z 277 fragmented further and involved two various possible pathways as illustrated by Scheme 4. However, the molecular ion of m/z 277 fragmented via the pathway A to give the stable ion of m/z 220, which fragmented further to give ion of m/z 178 by losing CH_2CO. The ion of m/z 178 was broken to give the ion of m/z

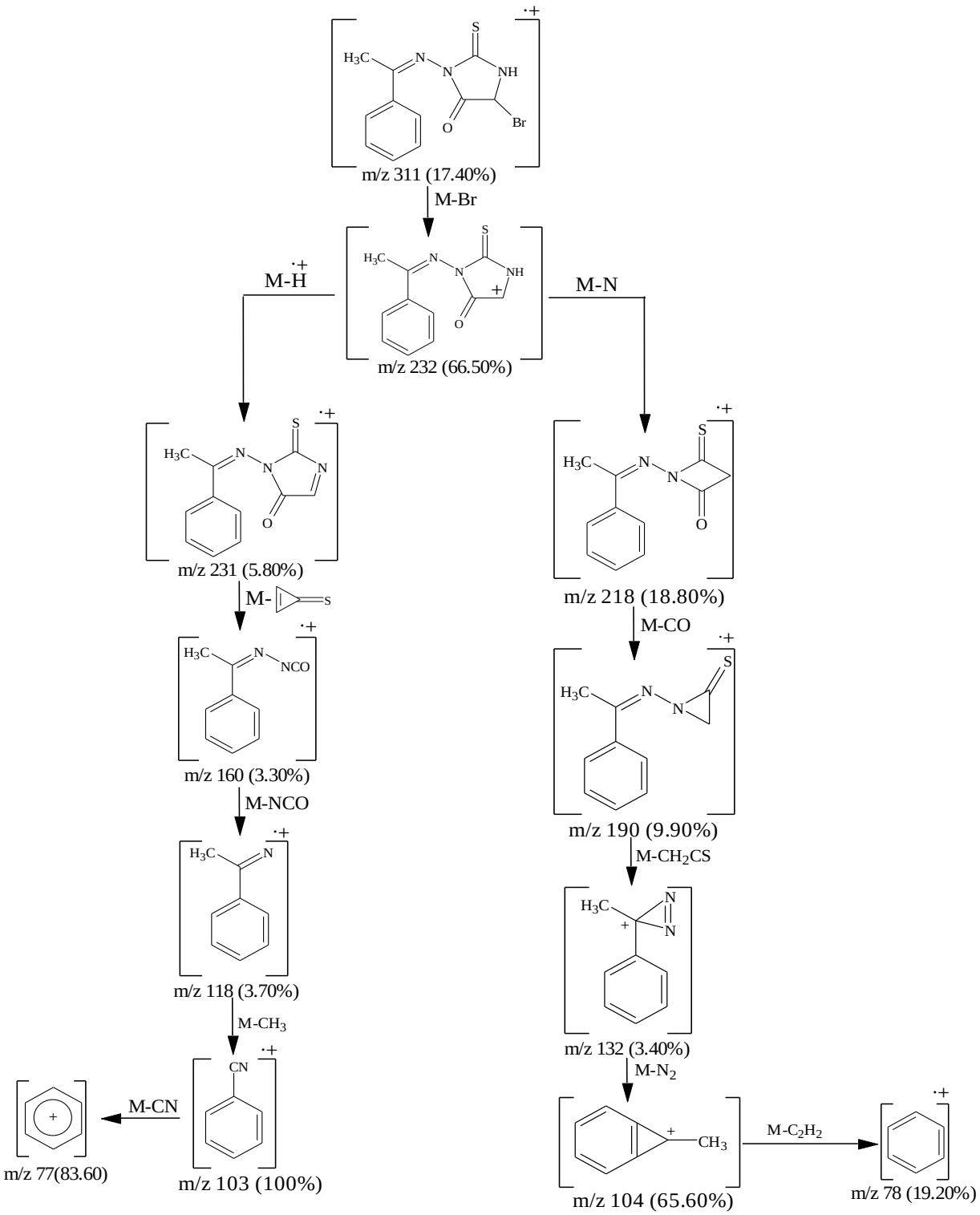
133 by losing HCS group. The loss of NH group from the ion of m/z 133 gave a ion of m/z 118 and subsequent loss of methyl group from this ion resulted in the formation of ion at m/z 103. This fragmentation led to the fragment of m/z 77 and 51 by losing CN group and acetylene molecule.



Scheme 3: Mass fragmentation pattern of imidazolidin dervatives (3b and 4b)



Scheme 4: Mass fragmentation pattern of compound 5



Scheme 5: Mass fragmentation pattern of compound 7

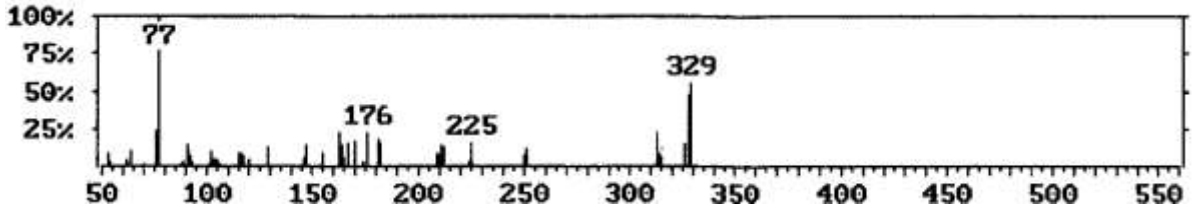


Figure 1: 70 eV mass spectrum of 3b

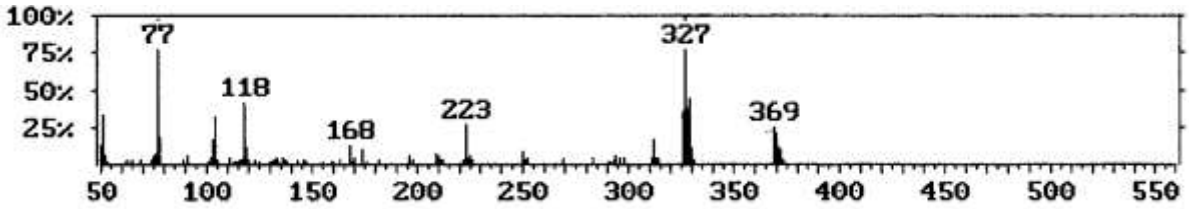


Figure 2: 70 eV mass spectrum of 4b

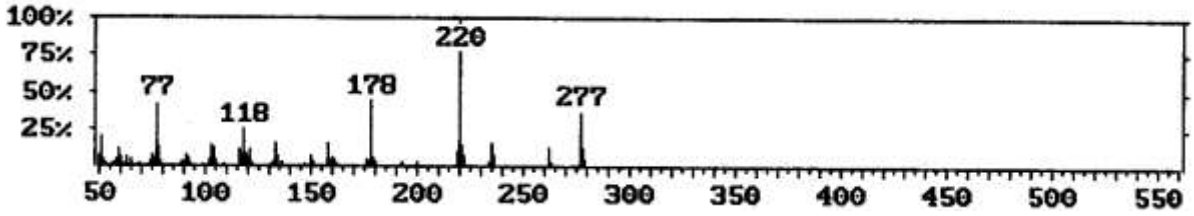


Figure 3: 70 eV mass spectrum of 5

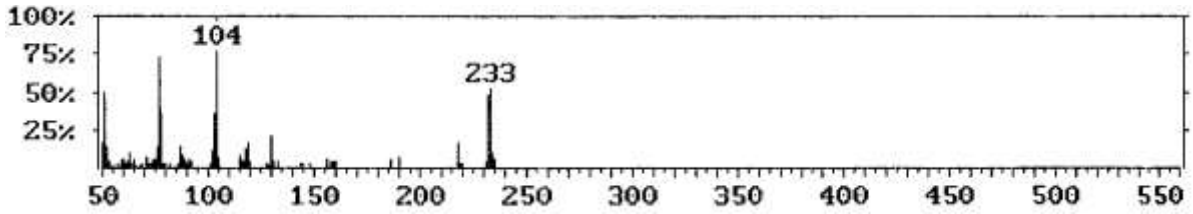


Figure 4: 70 eV mass spectrum of 6

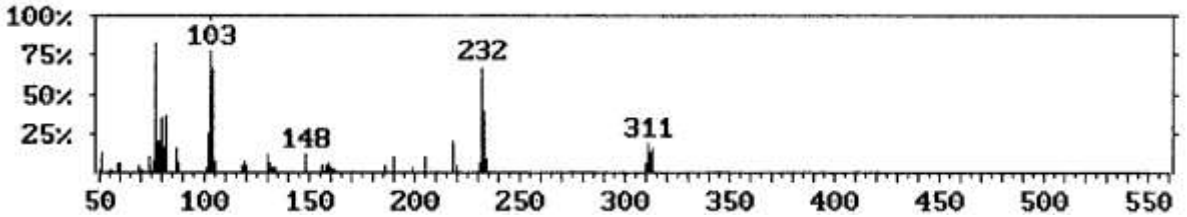


Figure 5: 70 eV mass spectrum of 7

Compound 5

The mass spectra of the 2, 4-diacetylacetophenone thiosemicarbazone (**5**) showed intense molecular ion peak at m/z 277, constituent with the molecular formula $C_{13}H_{15}N_3O_2S$. The molecular ion of m/z 277 fragmented further and involved two various possible pathways as illustrated by Scheme 4. However, the molecular ion of m/z 277 fragmented via the pathway A to give the stable ion of m/z 220, which fragmented further to give ion of m/z 178 by losing CH_2CO. The ion of m/z 178 was broken to give the ion of m/z 133 by losing HCS group. The loss of NH group from the ion of m/z 133 gave a ion of m/z 118 and subsequent loss of methyl group from this ion resulted in the formation of an ion at m/z 103. This fragmentation led to the ions of m/z 77 and m/z 51 by losing CN group and acetylene molecule.

Accordingly, the same molecular ion of m/z 277 fragmented via pathway B to give a fragmented of m/z 262 by losing methyl group. This fragmentation led to the ions of m/z 234, 219, 176, 161, 103 and m/z 76 respectively.

Compounds 6 and 7

The mass spectra of compound **6** and **7** are fully consistent with the assigned structures in most cases, intense molecular ion peaks were observed. Thus compound 6 showed intense molecular ion peak at m/z 233 corresponding to the molecular formula $C_{11}H_{11}N_3OS$. The formation of ion at m/z 232 could be explained due to the loss of hydrogen atom radial from the molecular ion peak (M-1).

The loss of CH_2CO, N_2, CS and CH_3 from the molecular ion resulted in a base peak at m/z 104.

The molecular ion peak of compound **7** was observed at m/z 311/313 corresponding to the molecular formula $C_{11}H_{10}N_3BrOS$. The M+2 was observed along with the molecular ion peak due to the presence of isotopes bromine atom present in the compound.

The mass fragmentation pattern of 5- bromo- 3-(1-phenylethylidene) amino-2-thioxo-imidazolidin-4-one (**7**) was summarized in Scheme 5

Experimental

Melting points were determined in capillaries with a MEL-TEMP II apparatus and uncorrected. Infrared spectra were taken on a Perkin-Elmer 337 spectrophotometer using KBr Wafers. Proton NMR spectra were obtained on a Varian EM 360 spectrometer using solution in hexadeuteriodimethyl sulfoxide with tetramethylsillane as the internal standared. Mass spectra were recorded on a VG Autspec GEI FAB^+ and a Hewlett Packard MS-Engine thermo spray and ionization by electron impact 70 eV. The accelerating Voltage was 6 Kv. The temperature of the

source was ~ 200°C, and the emission current ~ 100 mA. Microanalyses were conducted using on a Perkin-Elmer 2408 CHN analyzer.

Acetophenone-thiosemicarbazone (1)

A mixture of acetophenone (0.01mol) and thiosemicarbazide (0.01 mol) in methanol (50 ml) was heated under reflux for 4 hr, and then cooled. The resulting solid was filtered off, washed with methanol, dried and recrystallized from methanol to give **1** as colourless, yield 87%, m.p.: 131°C, IR (KBr): 3325, 3175(NH_2), 3221(NH), 1632(C=N), 1605, 1585(C=C), 1345(C=S), cm^{-1}, ^{1}H-NMR (DMSO-d_6): δ 2.01 (s, 3H, CH_3), 6.81 (s, 2H, NH_2), 7.20-7.71 (m, 5H, ArH), 10.10 (s, 1H, NH) ppm. MS (m/z, %); 194(M^++1, 18.90), 193(M^+, 75.30), 192(M^+-1, 83.10), 180(7.00), 179(18.00), 178(73.30), 177(99.10), 176(7.60), 175(5.50), 162(9.30), 161(7.80), 160(7.30), 159(7.80), 151(8.40), 149(11.00), 136(7.80), 135(7.00), 134(16.00), 133(33.40), 132(41.100),119(20.90), 118(45.30), 117(35.50), 116(14.20), 115(17.20), 104(20.60), 103(36.30), 102(21.80), 92(21.50), 91(12.20), 78(8.70), 77(69.50), 76(100), 65(20.10), 64(17.70), 60(31.70), 59(59.60), 58(28.80), 51(42.20), 50(43.60). Anal. Calcd for $C_9H_{11}N_3S$: C, 55.96; H, 5.70; N, 21.76; S, 16.58. Found: C, 55.82; H, 5.59; N, 21.61; S, 16.43.

4-Aryl-3-(1-phenylethylidene) amino-1,3-dihydro-imidazolidin-2-thione (3a, b)

3-(1-Phenylethylidene) amino-2-thioxo-imidazlidin-4-one (6)

A mixture of **1** (0.01 mol) and aryl bromomethyl ketones (such as chlorophenacyl bromide and 4-Chlorophenacyl bromide) (0.01mol) and / or ethyl Chloroacetate (0.01 mol) in methanol (50 ml) in presence of fused sodium acetate (0.03 mol) was heat under reflux for 5 hr. The reaction mixture was cooled and poured into water. The resulting solid was filtered off, washed with hot water, dried and recrystallized from ethanol to give **3** and **6**.

*4-Phenyl-3-(1-phenylethylidene)amino-1,3-dihydro-imidazolidin-2-thione (3**a**),* as pale yellow, yield 63%, m.p.: 205°C; IR (KBr): 3221(NH), 1632(C=N), 1610, 1589(C=C), 1349(C=S) cm^{-1}, ^{1}H-NMR (DMSO-d_6): δ 2.01(s, 3H, CH_3), 6.99-7.81(m, 11H, ArH and olefinic proton of imidazolidine ring), 11.35(s, 1H, NH) ppm. MS (m/z, %) 244(M^++1, 17.20), 243(M^+, 22.50), 279 (9.20), 278(13.30), 250(6.20), 249(16.30), 178(2.30), 177(6.20), 176 (23.20), 161(2.20), 160(3.90), 132(2.10), 131(1.20), 120 (2.30), 119(6.20), 118(38.30), 117(29.30), 116(9.20), 105(2.30), 104(33.20), 103(48.50), 102 (21.20), 101(7.20), 91(2.30), 90(6.20), 78(16.20), 77(100), 76(9.50), 65 (2.10), 6493.20), 63(6.80), 51(36.30), 50(23.30).

Anal. Calcd for $C_{17}H_{15}N_3S$: C, 69.62; H, 5.12; N, 14.33; S, 10.92. Found: C, 69.36; H, 5.00; N, 14.03; S, 10.71.

*4-(p-Chloro)-phenyl-3-(1-phenylethylidene)amino-1, 3-dihydro-imidazolidi-n-2-thione (**3**b)*, as yellow crystals, yield 66%; m.p.: 189°C; IR (KBr): 3224(NH), 1632(C=N), 1609, 1593(C=C), 1349(C=S) cm^{-1}, ^{1}H-NMR (DMSO-d_6): δ 2.10(s, 3H, CH_3), 6.99-7.89(m, 10H, ArH and oelfinic proton of imidazolidin ring), 11.52(s, 1H, NH) ppm. MS (m/z, %): 329(M^++2, 55.70), 327(M^+, 47.00), 326(M^+-1, 15.10), 315(5.40), 314(8.60), 313(21.60), 251(11.40), 250(6.50), 225(15.70), 224(2.70), 212(13.00), 211(4.10), 210(7.60), 209(8.60),182(15.10), 181(18.40), 176(22.70), 174(3.20), 170(17.30), 167(15.10), 165(5.90), 164(14.60). 163(22.20), 155(8.60), 147(13.50), 146(5.90), 129(12.40), 120(3.80), 117(6.50). 116(8.60), 115(8.60), 105(4.30), 104(4.30), 103(4.90), 102(10.30), 92(7.60), 91(4.60), 89(3.20), 88(1.600, 77(100), 76(23.80), 64(9.20), 63(3.80), 54(2.70), 53(8.10).Anal. Calcd for $C_{17}H_{14}N_3ClS$: C, 62.38; H, 4.28; N, 12.84; Cl, 10.86; S, 9.78. Found: C, 62.08; H, 4.17; N, 12.63; Cl, 10.62; S, 9.56.

*3-(1-Phenylethylidene)amino-2-thioxo-imidazolidin-4-one (**6**)*, as yellow crystals, yield 73%, m.p.: 151°C, IR (KBr): 3143(NH), 1699(C=O), 1620(C=N), 1610, 1584(C=C), 1354(C=S) cm^{-1}, ^{1}H-NMR (DMSO -d_6): δ 2.01(s, 3H, CH_3), 3.88(s, 2H, CH_2CO), 7.20-7.73(m, 5H, ArH), 11.30(s, 1H, NH) ppm. MS (m/z, %): 234(M^++1, 9.40), 233(M^+, 51.70), 232(M^+-1, 47.70), 219(3.10), 218(16.10), 190(6.80), 186(6.30), 160(3.70), 159(4.10), 158(4.80), 156(5.10), 148(2.30), 145(3.00), 144(2.70), 133(4.60), 131(3.80), 130(20.60), 128(2.50), 120(4.30), 119(16.70), 118(12.80), 117(4.70), 105(7.70), 104(100), 103(36.10), 102(11.80), 92(4.40), 91(6.10), 89(6.20), 87(14.40), 78(35.70), 77(73.00), 76(13.70), 64(3.10), 63(9.30), 60(5.60), 52(13.80), 51(49.000, 50(16.20). Anal. Calcd for$C_{11}H_{11}N_3OS$: C, 56.65; H, 4.72; N, 18.03; S, 13.73. Found: C, 56.49; H, 4.63; N, 17.97; S, 13.58.

1-Acetyl-3-(1-phenylethylidene)amino-4-aryl-1,3-dihydro-imidazolidin-2-thions (4a,b)

2, 4-Diacetylacetatophenone thiosemicarbazone (5)

A solution of **3** (0.01 mol) and / or **1** (0.01 mol) in acetic anhydride(25 ml) was heated under reflux for 2 hr, then cooled and poured into ice –water. The resulting product was filtered off, washed with water, dried and recrystallized from ethanol to give **4** and **5**.

*1-Acetyl-3-(1-phenylethylidene) amino-4-phenyl-1,3-dihydro-imidazolidin-2-thione(**4**a)*, as pale yellow crystals, yield, 62%, m.p.: 123°C. IR (KBr): 1699(CO), 1625(C=N), 1608, 1599(C=C), 1349(C=S) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 2.01(s, 3H, CH_3), 2.36(s, 3H, $COCH_3$), 6.99-7.78(m, 11H, ArH and olefinic proton of imidazolidin ring) ppm.

MS (m/z,%), 336(M^++1, 19.20),335(M^+, 27.50), 294(32.200, 293(100), 292(15.20), 279(6.30), 278(11.70), 250(4.30), 249(11.30), 177(6.20), 176(28.60), 161(1.92), 160(4.20), 133(1.30), 132(3.30), 131(2.20), 120(3.60), 119(7.50), 118(48.30), 117(27.60), 116(8.50), 105(3.60), 104(33.50), 103(42.20), 102(22.10), 101(9.60), 91(3.20), 90(6.80), 78(28.30), 77(87.50),

76(16.20), 75(6.60), 74(3.50), 65(5.50), 64(6.10), 63(9.30), 51(42.30), 50(23.50).Anal. Calcd for $C_{19}H_{17}N_3OS$: C, 68.06; H, 5.07; N, 12.54; S, 9.55. Found: C, 67.89; H, 4.97; N, 12.29; S, 9.31.

*1-Acetyl-3-(1-phenylethylidene) amino-4-(p-Cloro)-phenyl-1,3-dihydro-imi- dazolidin-2-thione (4**b**),* as pale yellow crystals, yield 63%, m.p.: 126°C. IR (KBr): 1689(CO), 1623(C=N), 1610, 1585(C=C), 1349(C=S) cm^{-1}.^{1}H-NMR ($CDCl_3$): δ 2.03(s, 3H, CH_3), 2.35(s, 3H, $COCH_3$), 6.98-7.79(m, 10H,ArH and olefinic proton of imidazolidine ring) ppm. MS (m/z, %): 371(M^++2, 10.60), 369 (M^+, 24.30), 329(43.70), 327(100), 326(35.70), 314(4.90), 312(17.10), 298(4.80), 296(3.70), 294(6.20), 226(2.50), 225(5.80), 224(4.50), 223(25.90), 210(5.20), 209(7.40), 198(3.40), 196(6.20), 182(2.90), 176(1.90), 174(9.50), 169(1.80), 168(12.30), 147(2.10), 136(4.70), 134(2.10), 133(4.90), 120(3.40), 119(10.60), 118(41.20), 117(2.60), 111(4.00), 105(3.30), 104(31.20), 103(16.10), 91(6.10), 90(1.30), 89(3.10), 78(17.50), 77(97.10), 76(7.50), 75(5.90), 69(2.40), 65(2.70), 63(3.50), 52(5.10), 51(23.00), 50(11.90). Anal. Calcd for $C_{19}H_{16}N_3ClOS$: C, 61.79; H, 4.34; N, 11.38; Cl, 9.62; S, 8.67. Found: C, 61.58; H, 4.17; N, 11.23; S, 8.47.

*2, 4-Diacetyl-acetophenone-thiosemicarbazone (**5**)*, as colourless crystals, yield 71%, m.p.: 225°C. IR (KBr): 3221(NH), 1699-1687(br. CO), 1621(C=N), 1607, 1589(C=C), 1348(C=S) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.01(s, 3H, CH_3), 2.35-2.38(s, 6H, 2 x $COCH_3$), 7.01-7.78(m, 5H, ArH), 10.35(s, 1H, NH) ppm. MS (m/z, %): 278 (M^++1 ,13.00), 277(M^+, 36.30)263(2.70), 262(12.60), 236(7.70), 235(14.90), 234(3.00), 222(7.30), 221(13.60), 220(100), 219(9.20), 193(2.90), 192(2.20), 179(5.20), 178 (44.00), 177(3.60), 160(5.50), 159(2.50), 158(15.30), 151(3.30), 134(6.60), 133 (15.90), 132(2.50), 121(11.80), 120(5.60), 119(8.70), 118(24.20), 117 (6.50), 116(10.60), 105(4.20), 104(13.20), 103(13.40), 92(6.10), 91(6.60), 78(11.90), 77(41.90), 76(4.50), 65(4.80), 63(5.20), 51(19.20), 50(7.40). Anal. Calcd for $C_{13}H_{15}N_3O_2S$: C, 56.32; H, 5.41; N, 15.16; S, 11.55. Found: C, 56.13; H, 5.22; N, 14.97; S, 11.31.

5-Bromo-3-(1-phenylethylidene) amino-2-thioxo-imidazolidin-4-one (7)

A solution of **6** (0.01 mol) in glacial acetic acid (30 ml) was added to a solution of bromine (0.01 mol) in glacial acetic acid (10 ml) with stirring at room temperature for 2 hr. The solid obtained was filtered off, washed with water, dried and recrystallized from toluene to give **7** as pale orange crystals, yield 68%, m.p.: 185°C. IR(KBr): 3229(NH), 1689(C=O), 1608, 1347(C=S) cm^{-1}.^{1}H-NMR(DMSO-d_6): δ 2.02(s, 3H, CH_3), 6.31(s, 1H, NCHBr), 7.01-7.79(m, 5H, ArH), 11.35(s, 1H, NH) ppm. MS (m/z, %) 313(M^++2, 15.80), 311(M^+, 17.40), 310(5.20), 233(38.30), 232(66.50), 231(5.80), 220(3.80), 218(18.80), 205(9.90), 190(9.90), 186(4.90), 162(2.00), 160(3.30), 159(5.30), 158(4.40), 156(4.60), 148(10.50), 134(3.10), 132(3.40), 131(6.30), 130(11.40), 119 (7.10), 118(3.70), 105(7.70), 104(65.60), 103(100), 102(24.30), 87(15.10), 82(35.20), 81(15.80), 80(34.90), 79(20.00), 78(19.20), 77(83.10), 76(6.90), 51(13.10), 50(1.50). Anal. Calcd for

$C_{11}H_{10}N_3BrOS$: C, 42.44; H, 3.22; N 13.50; Br, 25.40; S, 10.29. Found: C, 42.19; H, 3.01; N, 13.23; Br, 25.27; S, 10.10.

3-(1-Phenylethylidene) amino-2-thioxo-2,3-dihydro-imidazolidin-4-one (8)

A solution of **7** (0.01 mol) in acetic acid (30 ml) in presence of fused sodium acetate (0.03 mol) was heated under reflux for 2-3 hr. The reaction mixture was cooled and poured into water. The resulting product was filtered off, washed with hot water, dried and recrystallized from ethanol to give **8** as pale-yellow crystals, yield 62%, and m.p.: 145°C. IR (KBr): 1698(CO), 1632(C=N), 1605, 1593(C=C), 1348(C=S) cm^{-1}.

^{1}H-NMR ($CDCl_3$): δ 2.01(s, 3H, CH_3), 7.01-7.79 (m, 5H, ArH), 8.35 (s, 1H, CH=N) ppm. MS (m/z, %): 232(M^++1, 13.20), 231(M^+, 60.20), 218(22.60), 193(2.00), 192(3.40), 190(14.00), 186(7.30), 161(3.10), 160(7.80), 158(4.60), 156(4.20), 148(8.40), 144(2.90), 143(5.70), 134(3.40), 133(9.40), 132(3.50), 130(21.13), 120(3.10), 119(13.20), 118(21.90), 117(6.50), 104(100), 103(55.10), 102(10.70), 92(3.90), 91(5.50), 88(10.10), 87(16.60), 78(57.20), 77(94.80), 76(9.80), 64(2.60), 63(13.70), 62(4.00), 51(46.20), 50(17.60). Anal. Calcd for $C_{11}H_{19}H_3OS$: C, 57.14; H, 3.90; N, 18.18; S, 13.85. Found: C, 57.01; H, 3.62; N, 17.93; S, 13.58.

3-(1-Phenylethylidene) amino-2-thioxo-imidazolidin-4,5-dione (9)

A mixture of **1** (0.01 mol), diethyl oxalate (0.01 mol) and fused sodium acetate (0.03 mol) in pyridine (30 ml) was heated under reflux for 6 hr. The reaction mixture was cooled and poured into ice-HCl. The solid obtained was filtered off, washed with water, dried and recrystallized from ethanol to give **9** as pale-yellow crystals, yield 63%, m.p.: 250°C. IR (KBr): 3245(NH), 1698-1687(br.CO), 1625(C=N), 1607, 1589(C=C), 1346(C=S) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.10(s, 3H, CH_3) 7.1-7.78(m, 5H, ArH), 11.57(s, 1H, NH) ppm. MS (m/z, %): 248(M^++1, 13.20), 247(M^+, 33.20), 246(27.30), 232(18.35), 231(10.20), 205(6.90), 204(16.30), 178(4.90), 177(28.20), 176(3.10), 120(2.90), 119(12.90), 118(35.70), 117(2.50), 104(22.60), 103(16.30), 92(2.30), 91(3.90), 78(21.00), 77(100), 76(8.60), 63(4.20), 51(36.20), 50(11.50). Anal. Calcd for $C_{11}H_9N_3O_2S$: C, 53.44; H, 3.64; N, 17.00; S, 12.96. Found: C, 53.19; H, 3.51; N, 16.82; S, 12.79.

4-Benzylacetophenone-thiosemicarbazone (10)

A mixture of **1**(0.01 mol), benzyl chloride (0.01 mol) and fused sodium acetate (0.03 mol) in methanol (50 ml) was heated under reflux for 6 hr. The solid formed after cooling was filtered off, washed with methanol, dried and recrystallized from ethanol to give **10** as colourless crystals, yield 71%, m.p.:172°C. IR (KBr); 3275(NH), 1623(C=N), 1607, 1587(C=C), 1350(C=S) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 2.10(s, 3H, CH_3), 3.52(s, 2H, NCH_2Ar), 7.12-7.79(m, 10H, ArH), 9.21(s, 1H, NH), 10.30(s, 1H, NH) ppm. MS (m/z,%): 284(M^++1, 11.30), 283(M^+, 22.30), 192(3.20), 176(3.50), 164 (6.30), 163(2.30), 135(2.30), 134(23.20), 118(32.40), 117(7.500, 116(12.30),

107(2.10), 106(13.50), 105(11.30), 104(16.20), 103(21.20), 92(32.30), 91 (100), 90(2.11), 78(11.90), 77(51.20), 76(6.30), 66(2.10), 65(36.90), 64 (10.20), 51(17.20), 50(11.70). Anal. Calcd for $C_{16}H_{17}N_3S$: C, 67.84; H, 6.01; N, 14.84; S, 11.31. Found: C, 67.62; H, 5.89; N, 14.61; S, 11.03.

Biological assay

Antimicrobial activity

The Antimicrobial activities of the synthesized compounds 4 , 7, 8,9 and10 were determined by agar well diffusion method [10, 11]. The compounds were evaluated for antibacterial activity against *Bacillus subtilis* (RCMBOO107) and *Streptococcus pneumonia* (RCMBOO105) as Gram - Positive bacteria, and *Escherichia coli* (RCMBO-O103) and *Pseudomonas Sp.* (ATCC9027) as Gram - negative bacteria.

Antifungal [12] some Fungi (*Aspergillus Niger* and *Penicillium sp.*). The following Tables 1 and 2 Show the results in which of this compound have higher effect and can be used as antibacterial drug.

Table: 1 Antimicrobial activity of prepared compounds.

Compounds	Gram-Positive Bacteria						Gram-negative Bacteria					
	Bacillus Subtilis			*Streptococcus pneumonia*			*Escherichia Coli*			*Pseudomonas Sp.*		
	10 mg	50 mg	100mg	10mg	50mg	100mg	10mg	50mg	100mg	10mg	50mg	100mg
6	-	+	++	-	++	++	-	+	++	-	+	++
7	+	+	++	-	++	+++	+	++	+++	+	++	++
8	++	+++	+++	++	+++	+++	++	++	+++	+	+++	+++
9	+	+	+++	+	++	+++	++	++	+++	+	++	+++
10	++	+++	+++	++	+++	+++	+	++	+++	++	++	+++
Streptomycin	++	++	+++	+	++	+++	+	+	+++	+	++	+++
Clotrimazole	-	-	-	-	-	-	-	-	-	-	-	-

- Inactive, + slightly active, ++ moderately active, +++ highly active

Table: 2 Antifungal activity of prepared compounds.

Compounds	Fungi					
	Aspergillus niger			*Penicillium Sp.*		
	10 mg	50 mg	100mg	10mg	50mg	100mg
6	-	+	+	-	++	++
7	+	++	++	-	++	+
8	++	+++	+++	++	++	+++
9	++	++	++	+	++	+++
10	++	+++	+++	++	+++	+++
Streptomycin	-	-	-	-	-	-
Clotrimazole	++	++	+++	+	++	+++

- Inactive, + slightly active, ++ moderately active, +++ highly active

CONCLUSIONS

A series of Acetophenone thiosemicarbazone were synthesized, and their antimicrobial activity was compared with that of a standard drug. Compounds 7,8,9 and 10 wer found to exhibit the highest antimicrobial activity.

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