Synthesis and Mass Spectral Fragmentation Patterns of some 2-Thiohydantoin, Salicyladazine and Pyradazine Derivatives

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Síntesis y patrones de fragmentación del espectro de masas de algunos derivados de 2-tiohidantoína, saliciladazina y piradazina

Síntesi i patrons de fragmentació de l'espectre de masses d'alguns derivats de 2-tiohidantoïna, saliciladazina i piradazina

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RESUMEN

Se preparan las 3-[(5-arilazo-2-hidroxibenziliden) amino]-2-tiohidantoínas **3a-c** por condensación de 5-arilazo-2-hidroxibenzaldehído **1** con tiosemicarbazida, seguido de ciclación de **2** con cloroacetato de etilo. La acetilación de **3** con anhídrido acético rinde los correspondientes diacetilderivados **6a-c**. La hidrazinólisis de los compuestos **3** y **6** con hidrato de hidrazina da los correspondientes 5-arilazosalicilaldehídos **5a-c**. La amonólisis de la benzoína **(7)** con amoníaco proporciona la correspondiente 2,3,5,6-tetrafenil-1,4-dihidropiradazina **(8)**. La acetilación del compuesto **8** con anhídrido acético da la correspondiente 1,4-diacetilpiradazina **9**. Los espectros de masas de ionización por impacto electrónico de las parejas de compuestos **3a** y **6a**, **3b** y **6b**, y **3c** y **6c** muestran el pico base a m/z 77, m/z 91 y m/z 111, respectivamente, resultado de la fragmentación. El pico base de los compuestos **5a**, **5b** y **5c** es en todos los casos el ión molecular.

Palabras clave: tiosemicarbazonas de hidroxibenzaldehído, espectro de masas, tiohidantoínas

ABSTRACT

3-[(5-Arylazo-2-hydroxybenzylidene)amino]-2-thiohydantoins **3a-c** were prepared via condensation of 5-arylazo-2-hydroxybenzaldehyde **1** with thiosemicarbazide, followed by cyclization of **2** with ethyl chloroacetate. Acetylation of **3** with acetic anhydride yielded the corresponding diacetyl derivatives **6a-c**. Hydrazinolysis of compounds **3** and **6** with hydrazine hydrate gave the corresponding 5-arylazosalicylaldehydes **5a-c**. Ammonolysis of benzoin **(7)** with ammonia afforded the corresponding 2,3,5,6-tetraphenyl-1,4-dihydropyradazine **(8)**. Acetylation of compound **8** with acetic anhydride gave the corresponding 1,4-diacetylpyradazine **9**. The electron impact ionization mass spectra of the compounds pairs **3a** and **6a**, **3b a**nd **6b,** and **3c** and **6c** show a base peak of m/z 77, m/z 91 and m/z 111 resulting from fragmentation. The base peak of compounds **5a**, **5b** and **5c** is the molecular ion for all these compounds.

Key words: hydroxybenzaldehyde thiosemicarbazones, mass spectra, thiohydantoins

RESUM

Es preparen les 3-[(5-arilazo-2-hidroxibenziliden)amino]-2-tiohidantoïnes **3a-c** per condensació de 5-arilazo-2-hidroxibenzaldehid **1** amb tiosemicarbazida, seguit de ciclització de **2** amb cloroacetat d'etil. L'acetilació de **3** amb anhídrid acètic rendeix els corresponents diacetilderivats **6a-c**. La hidrazinòlisi dels compostos **3** i **6** amb hidrat d'hidrazina dóna els corresponents 5-arilazosalicilaldehids **5a-c**. L'amonòlisi de la benzoïna **(7)** amb amoníac proporciona la corresponent 2,3,5,6-tetrafenil-1,4-dihidropiradazina **(8)**. L'acetilació del compost **8** amb anhídrid acètic dóna la corresponent 1,4-diacetilpiradazina **9**. Els espectres de masses de ionització per impacte electrònic de les parelles de compostos **3a** i **6a**, **3b** i **6b**, i **3c** i **6c** mostren el pic base a m/z 77, m/z 91 i m/z 111, respectivament, resultat de la fragmentació. El pic base dels compostos **5a**, **5b** i **5c** és en tots els casos el ió molecular.

Mots clau: tiosemicarbazones d'hidroxibenzaldehid, espectre de masses, tiohidantoïnes

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II- INTRODUCTION

In the course of recent investigations [1-6] involving 5-substituted-2-hydroxy benzaldehydes **(1)** and thiosemicarbazide, it was found that 5-substituted-2-hydroxybenzaldehyde thiosemicarbazones **(2)** is converted into 3-substituted-2-thiohydantoins **(3)** by the action of ethyl chloroacetate under reflux. The fact that only limited information is available on mass spectra of 3-substituted-2-thiohydantoins **(3)**, along with the preparation of a novel salicylaldazine derivative, has prompted us to report their synthesis and study their electron impact (EI) mass spectral fragmentation. The reactions studied and the products are depicted in Schemes 1,2 and 3.

III- RESULTS AND DISCUSSION

Chemistry

Condensation of 5-substituted-2-hydroxybenzaldehyde **(1a-c)** with thiosemicarbazide in boiling ethanol led to the formation of 5-substituted-2-hydroxybenzaldehyde thiosemicarbazones **(2a-c)**. Treatment of compound **2** with ethyl chloroacetate in the presence of fused sodium acetate in ethanol under reflux, yielded the corresponding 3-[(5-arylazo-2-hydroxybenzylidene) amino]-2-thiohydantoins **(3a-c)**.

Reaction of 3-[(5-arylazo-2-hydroxybenzylidene) amino]-2-thiohydantoins **(3a-c)** with hydrazine hydrate in ethanol under reflux was expected to give 6-substituted-1,2,5,6-tetrahydroimidazo-[2,3-b]-1,2,4,5-tetrazine-5-one **(4)**, but only 5-arylazo-salicyladazines (**5a-c**; Scheme 1)[7-9] was yielded, which may be formed by the nucleophilic attack both carbon atom in CH=N group in this compound **3** with elimination of 3-amino-2-thiohydantoin molecule as shown in Scheme 2.

The compound **5** was obtained via another way by acetylation of 3-[(5-arylazo-2-hydroxybenzylidene) amino]-2-thiohydantoins **(3a-c)** with acetic anhydride under reflux, led to the formation of diacetyl derivatives **(6a-c)**, followed by hydrazonolysis of **6** with hydrazine hydrate under reflux in ethanol.

Amonoloysis of benzoin **(7)** with ammonia form the ammonium acetate under fusion led to the formation of 2,3,5,6-tetraphenyl-1,4-dihydropyradazine **(8)**. The formation of compound **8** possibly takes place via the following mechanism as shown in Scheme 3.

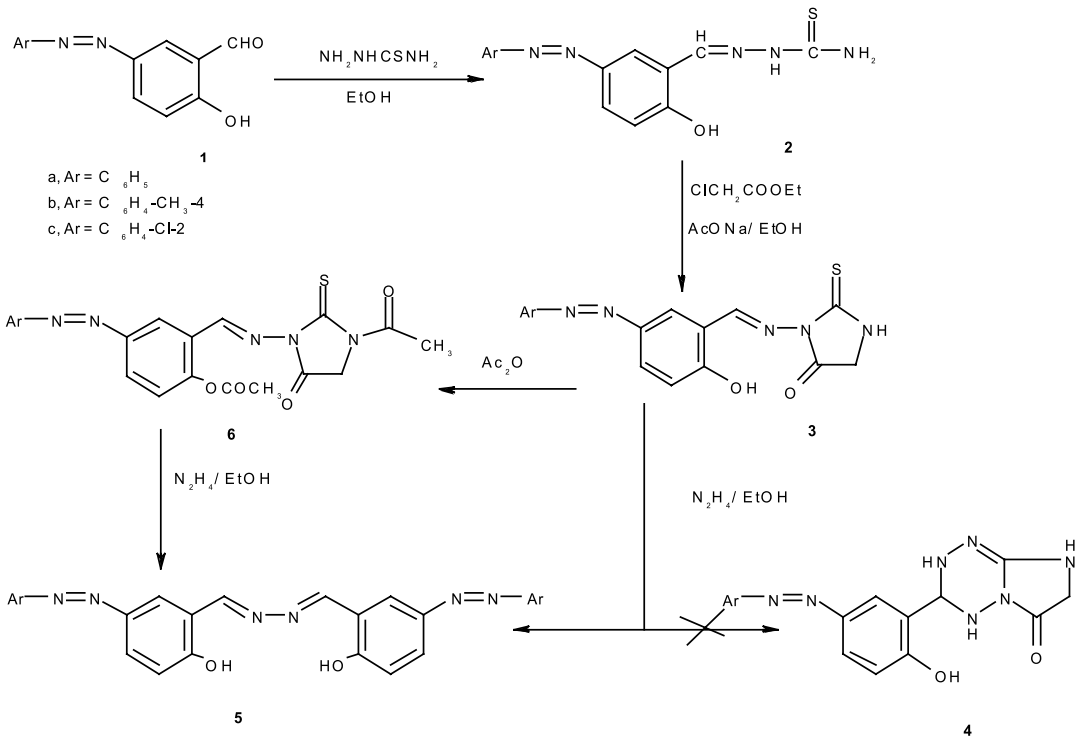
Acetylation of compound **8** with acetic anhydride under reflux yielded the corresponding to 1,4-diacetyl-2,3,5,6-tetraphenyl-1,4-dihydropyradazine **(9)**.

Mass spectroscopy

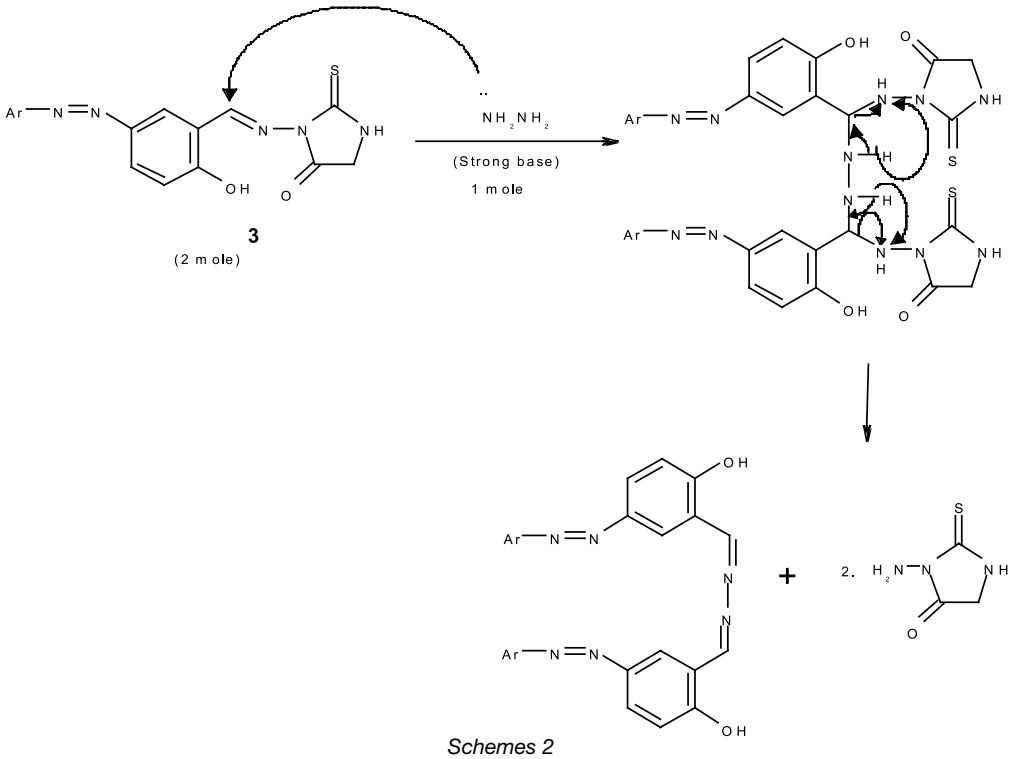
All the spectra showed characteristic common fragment ion, together with intense molecular ion peaks in most cases (Fig 1-4). Suggested fragmentation pathways are shown in Schemes 4, 5 and 6.

Compounds 3a-c and 6a-c

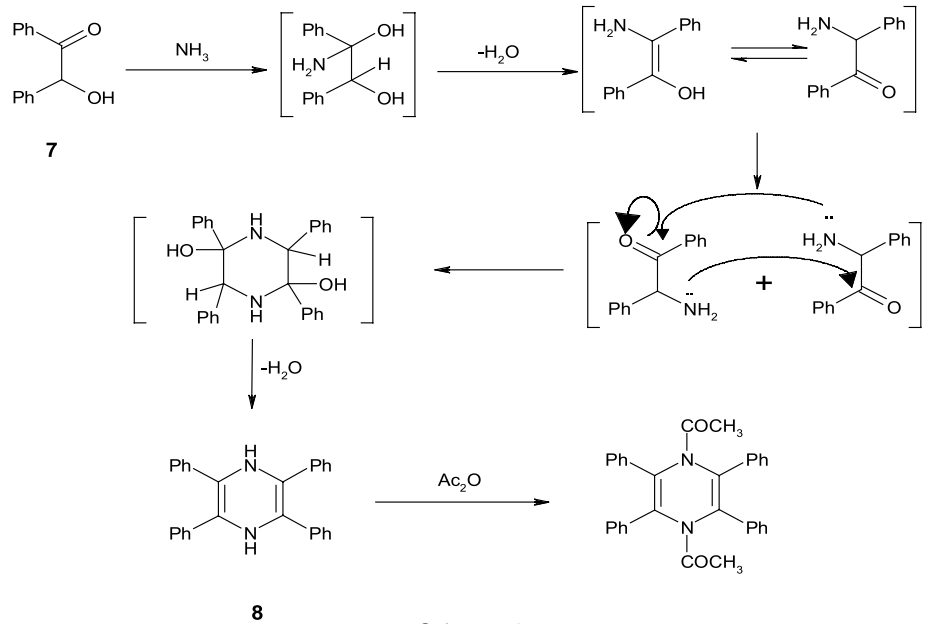
The mass spectra of compounds 3 and 6 are fully consistent with the assigned structures. In most cases, intense molecular ion peaks were observed. Thus, compounds **3a, 3b, 3c, 6a, 6b and 6c** showed an intense molecular ion peak m/z at 339, 353, 373, 423, 437 and m/z 457, corresponding to the molecular formula $C_{16}H_{13}N_5O_2S$, $C_{17}H_{15}N_5O_2S$, $C_{16}H_{12}N_5ClO_2S$, $C_{20}H_{17}N_5O_4S$, $C_{21}H_{19}N_5O_4S$ and $C_{20}H_{16}N_5ClO_4S$, respectively.



Schemes 1



Schemes 2



Schemes 3

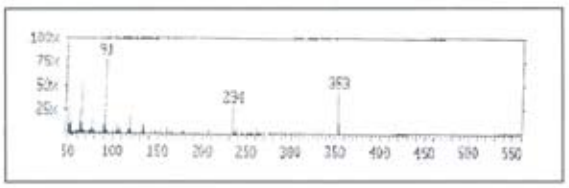


Figure 1: Mass spectra of compound (3b)

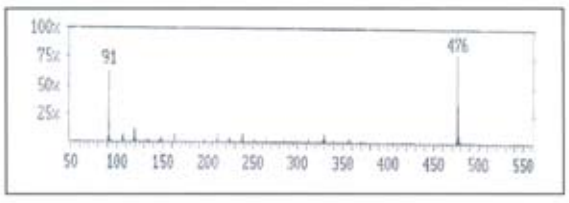


Figure 2: Mass spectra of compound (5b)

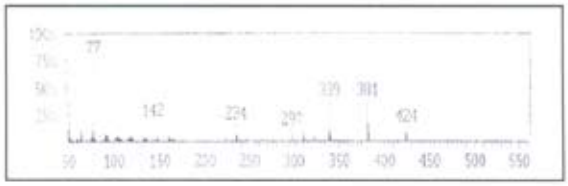


Figure 3: Mass spectra of compound (6a)

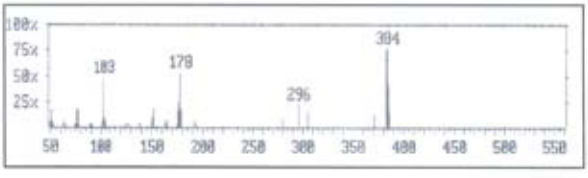
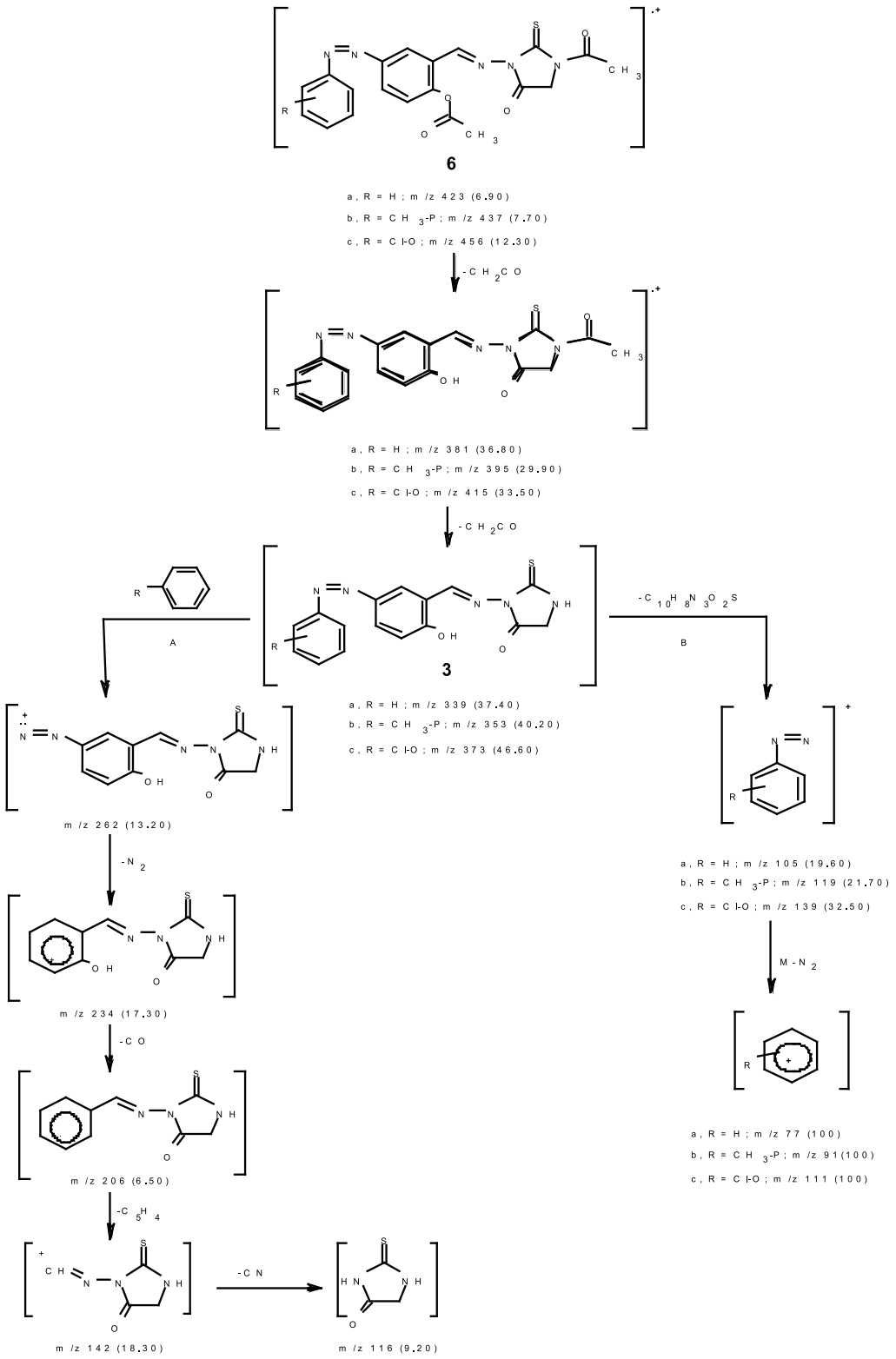


Figure 4: Mass spectra of compound (8)

From the studies of mass spectra of the compounds **6a-c**, it was found that the molecular ions (m/z 423, m/z 437 and m/z 457) for these compounds had fragmented to peaks at m/z 339, 353 and m/z 373, corresponding to the molecular ions of compounds **3a, 3b** and **3c** by losing two molecules of ketene (CH_2=C=O). The molecular ion of compound **3** and **6** fragmented further and involved two suggested pathways as illustrated in Scheme 4.

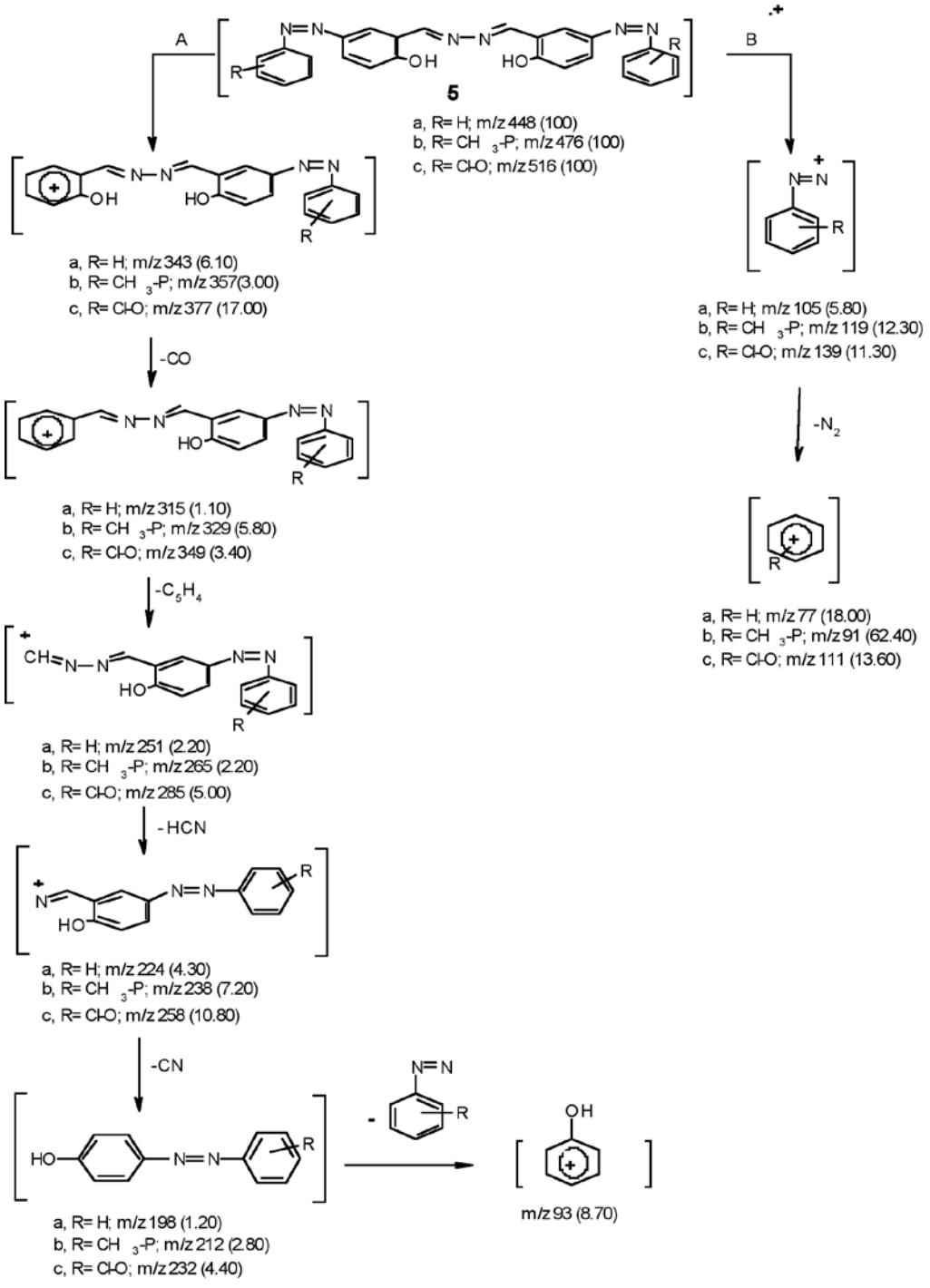


Scheme 4: *Main Fragmentation Pathway of compounds 3 and 6*

Compounds 5a-c

The mass spectra of compounds **5a, 5b** and **5c** are fully consistent with the assigned structures. In most cases, intense molecular ion peaks were observed. Thus compounds **5a, 5b** and **5c** showed an intense molecular ion peaks at m/z 448, m/z 516, corresponding to the molecular formula $C_{26}H_{20}N_6O_2$, $C_{28}H_{24}N_6O_2$ and $C_{26}H_{18}N_6Cl_2O_2$, respectively. From the study of the mass spectra of compounds **5a, 5b** and **5c**, it was found that the molecular ion for all these compounds fragmented further an involved two various pathways as illustrated by Scheme 5.

The molecular ions of m/z 476 fragment via the pathway A to give the m/z 357 by losing arylazo radical molecule. The m/z 357 fragmented to give the ion of m/z 329 by losing carbonyl group. This fragmentation led to ion of m/z 265, m/z 238, m/z 212 and ion of m/z 93, respectively. Subsequently, the molecular ion 476 was broken via pathway B to give the ion of m/z 119. The ion of m/z 119 broke to give an ion at m/z 91 which lost nitrogen molecule (N_2).



Scheme 5: Main Fragmentation pathways of compounds 5a-c

Compounds 8 and 9

The mass spectrum of compounds **8** and **9** showed intense molecular ion peaks at m/z 386 and m/z 470, corresponding to the molecular formula $C_{28}H_{22}N_2$ and $C_{32}H_{26}N_2O_2$, respectively. The loss of two molecules ketene (CH_2=C=O) from the molecular ion peak at m/z 470 of compound **9** gave a peak at m/z 386, corresponding to the molecular ion peak of compound **8**. The molecular ion of m/z 386 (Scheme 6) fragment via the pathway A give a stable peak at m/z 384 by losing hydrogen molecule (H_2). The ion of m/z 384 underwent fragmentation produce ion of m/z 103 by losing diphenyl acetylene. This fragmentation led to the ion of m/z 76. Accordingly, the same molecular ion of m/z 386 fragmented via the pathway B by cleavage NH group radical cation to give the peak at m/z 178. The ion of m/z 178 underwent loss of benzyn molecule radical cation to give peak at m/z 102.

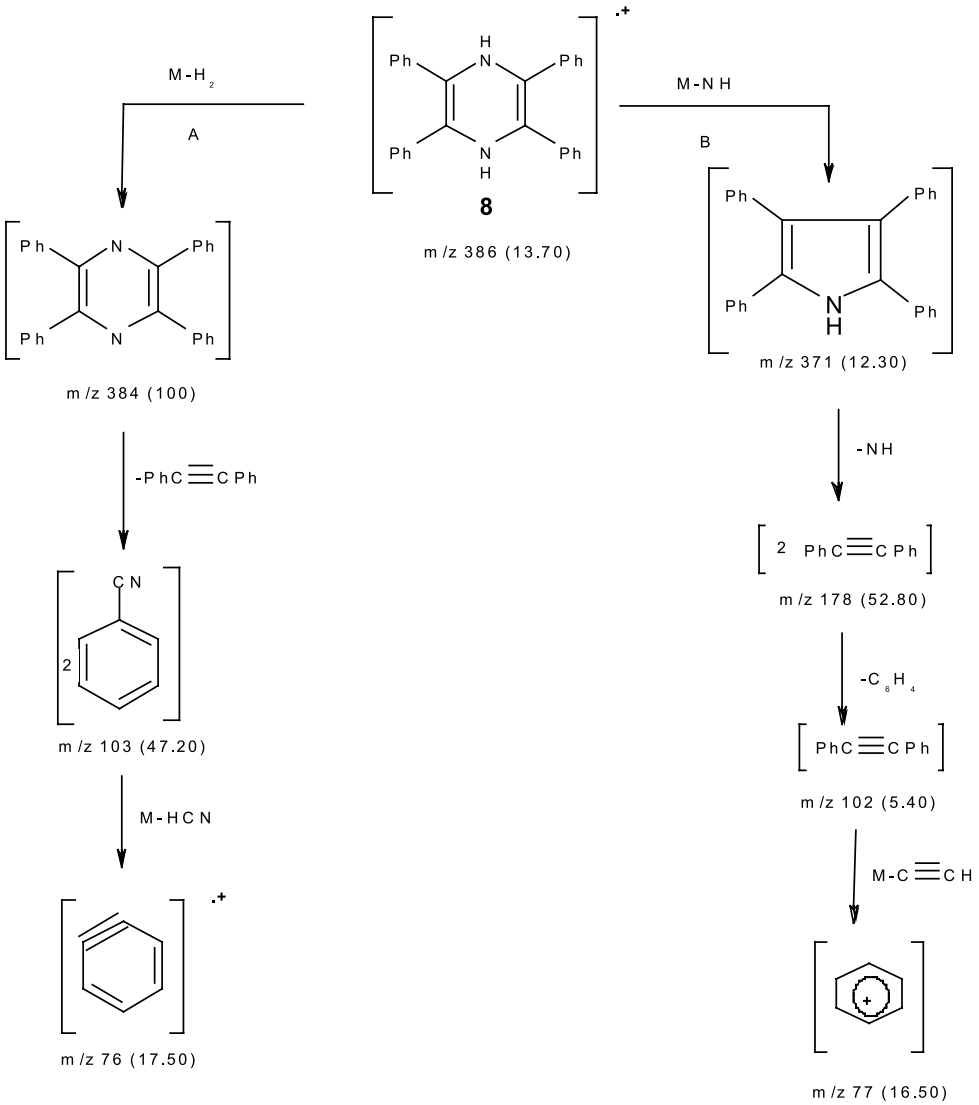
EXPERIMENTAL

Melting points were measured on a MEL-TEMPII apparatus and uncorrected. Infrared spectra were measured with Perkin-Elmer FT IR 410 spectrometer in KBr. The ^{1}HNMR spectra were performed on a VARIAN MERCURY 300 MHz spectrometer in DMSO-d_6 using TMS as an internal standard. Mass spectra were obtained on a JEOL JMS D-300 spectrometer operating at 70 eV. The elemental analyses were conducted using an elemental analyzer Heneaas CHN-OSRAPID 1106.

5 - Arylazo - 2 - hydroxybenzaldehyde thiosemicarbazones (2a-c)

A mixture of 5-arylazo-2-hydroxybenzaldehyde (0.01 mole) and thiosemicarbazide (0.01 mole) in ethanol (50 ml) was heated under reflux for 4hr, and then cooled. The resulting solid was filtered off dried and recrystallized from ethanol to give **2**.

5-Phenylazo-2-hydroxybenzaldehyde thiosemicarbazone **(2a)**, yield 78% (2.33 gm), mp: 299 °C, IR (KBr): 3340, 3168 (NH_2), 3245 (NH), 3383-2890 (br. OH), 1625 (C=N), 1607, 1580 (C=C), 1405 (C=S), 1120, 1034 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 6.31 (s, 2H, NH_2), 7.11-7.92 (m, 8H, ArH), 8.76 (s, 1H, CH=N), 10.35 (s, 1H, NH), 11.30-11.36 (br. S, 1H, OH) ppm. MS (m/z, %): 300 (M^++1, 14.40), 299 (M^+, 100), 298 (M^+-1, 3.30), 283 (3.40), 282 (11.30), 241 (1.10),



Scheme 6: Main Fragmentation Pathway of compound 8

240 (3.60), 223 (5.60), 222 (2.80), 207 (6.40), 205 (6.30), 196 (3.60), 194 (3.00), 178 (2.00), 177 (5.40), 168 (1.30), 167 (1.90), 160 (1.80), 148 (16.40), 147 (2.40), 146 (6.40), 136 (1.50), 135 (8.10), 118 (9.70), 105 (19.20), 102 (22.40), 93 (29.90), 77 (72.30), 76 (7.30), 60 (4.80), 59 (15.80). Anal. Calcd for $C_{14}H_{13}N_5OS$: C, 56.19; H, 4.35; N, 23.41; S, 10.70. Found: C, 56.00; H, 4.18; N, 23.14; S, 10.48.

5-(P-tolyl)azo-2-hydroxybenzaldehyde thiosemicarbazone **(2b)**, yield 79% (2.47 gm), mp: 270 °C, IR (KBr): 3343, 3175 (NH_2), 3221 (NH), 3381-2885 (br. OH), 1627 (C=N), 1605, 1585 (C=C), 1409 (C=S), 1135, 1067 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.31 (s, 3H, CH_3), 6.29 (s, 2H, NH_2), 7.11-7.93 (m, 7H, ArH), 8.78 (s, 1H, CH=N), 10.36 (s, 1H, NH), 11.32 (s, 1H, OH) ppm. MS (m/z, %): 314 (M^++1, 21.00), 313 (M^+, 97.10), 312 (M^+-1, 13.00), 297 (5.40), 296 (18.30), 254 (5.90), 238 (10.30), 237 (11.90), 223 (1.20), 222 (2.10), 207 (6.70), 206 (2.90), 205 (5.80), 195 (1.40), 194 (2.50), 178 (1.90), 177 (10.10), 176 (1.70), 160 (1.40), 150 (2.30), 148 (13.90), 146 (3.50), 136 (1.70), 135 (8.20), 120 (8.40), 119 (26.60), 102 (20.30), 92 (12.60), 91 (100), 77 (4.20), 76 (4.30), 65 (82.70), 60 (2.60), 59 (20.60). Anal. Calcd for $C_{15}H_{15}N_5OS$: C, 57.51; H, 4.79; N, 22.36; S, 10.22. Found: C, 57.33; H, 4.49; N, 22.03; S, 10.03.

5-(2-Chlorophenyl)azo-2-hydroxybenzaldehyde thiosemicarbazone **(2c)**, yield 78% (2.60 gm), mp: 278 °C, IR (KBr): 3339, 3181 (NH_2), 3212 (NH), 3401-2986 (br. OH), 1629 (C=N), 1603, 1592 (C=C), 1403 (C=S), 1215, 1067 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 6.28 (s, 2H, NH_2), 7.11-7.97 (m, 7H, ArH), 8.71 (s, 1H, CH=N), 10.36 (s, 1H, NH), 11.34 (s, 1H, OH) ppm. MS (m/z, %): 335 (M^++2, 34.60), 334 (M^++1, 11.70), 333 (M^+, 100), 318 (9.50), 316 (23.80), 258 (7.50), 257 (12.20), 222 (5.70), 207 (5.50), 206 (3.40), 205 (15.80), 194 (7.00), 178 (3.60), 177 (26.80), 176 (2.70), 160 (3.80), 150 (4.90), 148 (24.40), 146 (20.90), 139 (16.70), 135 (14.20), 129 (8.40), 127 (23.80), 118 (24.00), 111 (23.10), 108 (7.20), 103 (8.60), 102 (29.40), 91 (7.30), 77 (14.00), 76 (7.30), 59 (35.30). Anal. Calcd for $C_{14}H_{12}N_5ClOS$: C, 50.45; H, 3.60; N, 21.02; Cl, 10.66; S, 9.61. Found: C, 50.19; H, 3.41; N, 20.93; Cl, 10.42; S, 9.97.

3-[(5-Arylazo-2-hydroxybenzylidene) amino]-2-thiohydantoins (3a-c)

A mixture of **2** (0.01 mole) and ethyl chloroacetate (0.01 mole) in ethanol (60 ml) in presence of fused sodium acetate (0.03 mole) was heated 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**.

3-[(5-Phenyllazo-2-hydroxybenzylidene) amino]-2-thiohydantoin **(3a)**, yield 82% (2.78 gm), mp: 287 °C, IR (KBr): 3280 (NH), 3385-2961 (br. OH), 1698 (C=O), 1630 (C=N), 1609, 1583 (C=C), 1403 (C=S), 1225, 1070 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.93 (s, 2H, -CH_2N), 7.12-7.89 (m, 8H, ArH), 8.71 (s, 1H, CH=N), 10.21 (s, 1H, NH), 11.32 (s, 1H, OH) ppm. MS (m/z, %): 340 (M^++1, 5.30), 339 (M^+, 33.50), 234 (24.20), 136 (5.60), 135 (6.50), 116 (3.20), 114 (2.20), 105 (7.80), 91 (3.10), 77 (100), 65 (2.30), 64 (1.30), 63 (4.90), 51 (53.50). Anal. Calcd for $C_{16}H_{13}N_5O_2S$: C, 56.63; H, 3.83; N, 20.65; S, 9.44. Found: C, 56.32; H, 3.59; N, 20.45; S, 9.27.

3-[(5-Phenyllazo-2-hydroxybenzylidene) amino]-2-thiohydantoin **(3b)**, yield 83% (2.93 gm), mp: 294 °C, IR (KBr): 3385-2932 (br. OH), 3226 (NH), 1696 (C=O), 1629 (C=N), 1607, 1589 (C=C), 1401 (C=S), 1229, 1086 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.92 (s, 2H, $COCH_2$N), 7.11-7.87 (m, 7H, ArH), 8.61 (s, 1H, CH=N), 10.23 (s, 1H, NH), 11.29 (s, 1H, OH) ppm. MS (m/z, %): 354 (M^++1, 6.20), 353 (M^+, 36.20), 352 (9.70), 325 (11.30), 312 (2.60), 311 (12.80), 262 (6.50), 234 (15.20), 206 (1.30), 205 (1.30), 184 (2.10), 164 (3.20), 163 (3.50), 160 (4.10), 152 (3.80), 148 (2.60), 147 (2.80), 142 (6.50), 135 (4.60), 134 (2.80), 120 (4.30), 119 (27.20), 118 (5.30), 116 (2.50), 108 (1.60), 107 (3.20), 92 (22.30), 91 (100), 90 (13.20), 77 (10.70), 76 (9.50), 65 (45.20), 63 (12.30), 51 (11.20). Anal. Calcd for $C_{17}H_{15}N_5O_2S$: C, 57.80; H, 4.25; N, 19.83; S, 9.07. Found: C, 57.62; H, 4.08; N, 19.59; S, 8.87.

3-[(5-O-chlorophenyllazo-2-hydroxybenzylidene) amino]-2-thiohydantoin **(3c)**, yield 81% (3.02 gm), mp: 252 °C, IR (KBr): 3381-2952 (br. OH), 3251 (NH), 1697 (C=O), 1630 (C=N), 1605, 1591 (C=C), 1404 (C=S), 1216, 1055 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.91 (s, 2H, $COCH_2$N), 7.10-7.88 (m, 7H, ArH), 8.65 (s, 1H, CH=N), 10.25 (s, 1H, NH), 11.32 (s, 1H, OH) ppm. MS (m/z, %): 375 (M^++2, 28.90), 374 (M^++1, 11.20), 373 (M^+, 50.40), 353 (24.60), 352 (11.70), 336 (10.50), 325 (10.40), 311 (14.50), 262 (14.10), 261 (7.90), 260 (5.50), 235 (13.90), 234 (71.10), 207 (9.70), 206 (6.40), 179 (7.30), 165 (7.30), 164 (10.10), 160 (19.40), 142 (15.30), 141 (10.60), 139 (13.20), 135 (24.20), 134 (11.20), 120 (11.50), 119 (31.70), 116 (5.10), 113 (25.30), 111 (100), 106 (10.80), 105 (24.70), 75 (63.20), 63 (60.60), 51 (84.60). Anal. Calcd for $C_{16}H_{12}N_5ClO_2S$: C, 51.47; H, 3.22; N, 18.77; Cl, 9.52; S, 8.58. Found: C, 51.31; H, 3.03; N, 18.58; Cl, 9.33; S, 8.42.

1-Acetyl-3-[(5-arylazo-2-acetoxybenzylidene) amino]-2-thiohydantoins (6a-c)

A solution of **3** (0.01 mole) in acetic anhydride (25 ml) was heated under reflux for 2 he, then cooled and poured into ice-water. The resulting product was filtered off, washed with water, dried and purified by recrystallization with benzene to give **6**.

1-Acetyl-3-[(5-phenylazo-2-acetoxybenzylidene) amino]-2-thiohydantoin **(6a)**, yield 73% (3.09 gm), mp: 236 °C, IR (KBr): 1749 (C=O of ester); 1698 (C=O of ketone); 1631 (C=N), 1608, 1589 (C=C), 1227, 1060 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.13 (s, 3H, $COCH_3$), 2.29 (s, 3H, $OCOCH_3$), 3.98 (s, 2H, NCH_2CO), 7.13-7.81 (m, 8H, ArH), 8.73 (s, 1H, CH=N) ppm. MS (m/z, %): 423 (M^+, 6.90), 382 (15.10), 381 (36.80), 340 (7.90), 339 (37.40), 338 (7.90), 322 (5.70), 311 (7.80), 298 (5.20), 297 (10.10), 276 (5.00), 262 (10.92), 235 (5.10), 234 (15.10), 223 (5.50), 206 (1.70), 184 (7.30), 176 (2.10), 162 (2.80), 160 (4.60), 159 (4.80), 152 (2.90), 148 (2.30), 147 (5.30), 146 (4.90), 142 (17.40), 136 (2.90), 135 (4.70), 116 (2.30), 114 (10.70), 105 (19.60), 77 (100), 64 (10.20), 50 (11.50). Anal. Calcd for $C_{20}H_{17}N_5O_4S$: C, 56.74; H, 4.02; N, 16.55; S, 7.56. Found: C, 56.58; H, 3.92; N, 16.32; S, 7.43.

1-Acetyl-3-[(5-P-tolylazo-2-acetoxybenzylidene) amino]-2-thiohydantoin **(6b)**, yield 75% (3.28 gm), mp: 229 °C, IR (KBr): 1746 (C=O of ester); 1701 (C=O of ketone); 1629 (C=N), 1603, 1589 (C=C), 1401 (C=S), 1156, 1086 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.11 (s, 3H, $COCH_3$), 2.27 (s, 3H, $OCOCH_3$), 2.33 (s, 3H, Ar-CH_3), 4.10 (s, 2H, NCH_2CO), 7.11-7.81 (m, 7H, ArH), 8.69 (s, 1H, CH=N) ppm. MS (m/z, %): 438 (M^++1, 5.30), 437 (7.70), 396 (13.80), 395 (29.90), 353 (40.20), 352 (10.10), 325 (13.90), 312 (3.60), 311 (13.40), 262 (5.60), 234 (14.30), 206 (1.70), 205 (3.50), 184 (3.20), 164 (2.30), 163 (3.80), 160 (3.10), 152 (3.70), 148 (3.00), 147 (3.10), 142 (8.30), 135 (5.50), 134 (3.90), 120 (3.00), 119 (21.70), 118 (6.90), 116 (3.50), 108 (3.60), 107 (6.80), 92 (15.40), 91 (100), 90 (11.30), 77 (10.80), 76 (10.70), 65 (54.20), 52 (6.90). Anal. Calcd for $C_{21}H_{19}N_5O_4S$: C, 57.67; H, 4.35; N, 16.02; S, 7.32. Found: C, 57.48; H, 4.22; N, 15.87; S, 7.13.

1-Acetyl-3-[(5-(O-chlorophenylazo-2-acetoxybenzylidene) amino]-2-thiohydantoin **(6c)**, yield 74% (3.38 gm), mp: 211 °C, IR (KBr): 1751 (C=O of ester); 1699 (C=O of ketone); 1629 (C=N), 1609, 1591 (C=C), 1402 (C=S), 1216, 1095 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.10 (s, 3H, $COCH_3$), 2.28 (s, 3H, $OCOCH_3$), 4.08 (s, 2H, NCH_2CO), 7.12-7.89 (m, 7H, ArH), 8.70 (s, 1H, CH=N) ppm. MS (m/z, %): 459 (M^++2, 4.20), 457 (M^+, 12.30), 417 (12.20), 415 (33.50), 375 (17.20), 373 (46.60), 353 (22.20), 352 (10.20), 336 (17.10), 325 (11.50), 311 (16.30), 262 (13.20), 261 (6.20), 260 (5.30), 235 (10.20), 234 (17.30), 207 (3.90), 206 (6.20), 179 (8.50), 165 (7.10), 164 (12.70), 160 (21.30), 142 (18.30), 141 (13.20), 139 (32.50), 134 (11.30), 120 (11.30), 119 (27.80), 116 (9.20), 113 (27.80), 111 (100), 106 (11.60), 105 (3.90), 77 (2.30), 76 (4.30), 75 (62.30), 65 (23.20), 63 (59.60), 52 (17.80), 51 (33.50). Anal. Calcd for $C_{20}H_{16}N_5ClO_4S$: C, 52.52; H, 3.50; N, 15.32; Cl, 7.77; S, 7.00. Found: C, 52.35; H, 3.33; N, 15.17; Cl, 7.33; S, 6.89.

5-Arylazo-salicyladazines (5a-c)

A mixture of **3** and / or **6** (0.01 mole) and hydrazine hydrate (0.02 mole) in dimethyl formamide (30 ml) was heated under reflux for 2 hr, then cooled and poured into ice-water. The solid formed was filtered off, washed with water, dried and purified by recrystallization from butanol to give **5**.

5-Phenylazo-salicyladazine **(5a)**, yield 69% (3.09 gm), mp: 299 °C, IR (KBr): 3450 (OH), 1630 (C=N), 1606, 1583 (C=C), 1255, 1072 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 6.98-7.76 (m, 16H, ArH), 8.73 (s, 2H, 2×CH=N), 11.33 (s, 1H, 2×OH) ppm. MS (m/z, %): 449 (M^++1, 29.20), 448 (M^+, 100), 447 (28.90), 431 (1.70), 359 (2.60), 356 (1.90), 344 (1.80), 343 (6.10), 315 (1.10), 314 (1.20), 302 (5.20), 301 (3.00), 251 (2.20), 238 (1.50), 237 (1.20), 225 (2.40), 224 (4.30), 223 (1.10), 198 (1.20), 197 (1.10), 196 (5.00), 163 (4.10), 148 (2.40), 140 (1.30), 135 (1.40), 120 (4.00), 118 (1.40), 106 (1.20), 105 (5.80), 93 (4.50), 92 (1.50), 91 (1.30), 77 (18.00), 73 (2.90), 65 (1.00). Anal. Calcd for $C_{26}H_{20}N_6O_2$: C, 64.64; H, 4.46; N, 18.75. Found: C, 69.53; H, 4.37; N, 18.57.

5-(P-Tolyl)azo-salicyladazine **(5b)**, yield 67% (3.19 gm), mp: 353 °C, IR (KBr): 3465 (OH), 1632 (C=N), 1608, 1598 (C=C), 1215, 1205, 1057 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.31 (s, 6H, 2×CH_3), 6.89-7.78 (m, 14H, ArH), 8.73 (s, 2H, 2×CH=N), 11.34 (s, 2H, 2×OH) ppm. MS (m/z, %): 477 (M^++1, 33.90), 476 (M^+, 100), 475 (5.00), 370 (2.00), 357 (3.00), 355 (2.20), 330 (6.70), 329 (5.80), 328 (3.50), 313 (2.70), 312 (2.10), 265 (2.20), 252 (1.90), 251 (1.80), 239 (7.00), 238 (7.20), 224 (3.80), 223 (2.60), 212 (2.80), 211 (1.10), 210 (8.10), 197 (1.60), 196 (2.00), 163 (7.60), 148 (3.60), 135 (2.00), 120 (10.30), 119 (12.20), 118 (2.60), 107 (7.40), 93 (1.80), 91 (62.40), 65 (1.30), 51 (2.30). Anal. Calcd for $C_{28}H_{24}N_6O_2$: C, 70.54; H, 5.04; N, 17.65. Found: C, 70.41; H, 4.96; N, 17.51.

5-(2-Chlorophenyl)azo-salicyladazine **(5c)**, yield 68% (3.51 gm), mp: 302 °C, IR (KBr): 3466 (OH), 1632 (C=N), 1609, 1588 (C=C), 1215, 1205, 1057 (C-O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 6.91-7.83 (m, 14H, ArH), 8.75 (s, 2H, 2×CH=N), 11.34 (s, 2H, 2×OH) ppm. MS (m/z, %): 518 (M^++2, 60.50), 517 (M^++1, 33.40), 516 (M^+, 100), 515 (30.90), 499 (3.00), 395 (9.00), 390 (6.10), 379 (6.40), 378 (6.70), 377 (17.00), 372 (10.60), 370 (18.50), 369 (5.70), 349 (3.90), 285 (5.00), 260 (5.20), 258 (10.80), 232 (4.40), 230 (10.10), 224 (3.40), 222 (7.20), 210 (3.50), 197 (3.50), 163 (15.00), 141 (4.20), 139 (11.30), 113 (8.40), 111 (13.60), 106 (3.90), 93 (8.70), 80 (4.50), 77 (5.00). Anal. Calcd for $C_{26}H_{18}N_6Cl_2O_2$: C, 60.47; H, 3.49; N, 16.28; Cl, 13.75. Found: C, 60.33; H, 3.39; N, 16.16; Cl, 13.61.

2,3,5,6-Tetraphenyl-1,4-dihydropyradazine (8)

A mixture of benzoin (0.02 mole) and ammonium acetate (0.03 mole) was fused on a hot plate for 2 hr. The reaction mixture was cooled and poured into ice-water. The solid formed was filtered off, washed with water, dried and purified by recrystallization from dimethyl formamide to give **8** as yellow crystals, yield 78% (2.96 gm), mp: 265 °C, IR (KBr): 3225 (NH), 1605, 1588 (C=C) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 6.92-7.78 (m, 20H, ArH), 10.35 (s, 2H, 2×NH) ppm. MS (m/z, %): 386 (M^+, 13.70), 385 (M^+-1, 41.9), 384 (M^+-2, 100), 383 (93.30), 371 (12.30), 305 (14.60), 296 (22.00), 280 (8.00), 193 (2.80), 192 (6.50), 179 (18.10), 178 (52.80), 177 (14.90), 176 (25.10), 175 (2.90), 165 (6.70), 169 (2.30), 163 (5.30), 152 (18.20), 151 (10.50), 150 (6.00), 139 (4.00), 128 (3.60), 126 (4.10), 105 (5.40), 104 (9.70), 103 (47.20), 102 (5.90), 89 (4.80), 78 (2.90), 77 (16.80), 76 (17.50), 65 (1.60), 63 (7.10), 52 (6.20), 51 (17.00). Anal. Calcd for $C_{28}H_{22}N_2$: C, 87.05; H, 5.70; N, 7.25. Found: C, 86.98; H, 5.53; N, 7.02.

2,3,5,6-Tetraphenyl-1,4-diacetylpyradazine (9)

A solution of **8** (0.01 mole) in acetic anhydride (30 ml) was heated under reflux for 2 hr, then cooled and poured into ice-water. The resulting solid was filtered off, washed with water, dried and purified by recrystallization with ethanol to give **9** as pale yellow, yield 71% (3.33 gm), mp 178 °C, IR (KBr): 1705 (C=O), 1605, 1589 (C=C) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.21 (s, 6H, 2×$COCH_3$), 6.91-7.82 (m, 20H, ArH) ppm. MS (m/z, %): 471 (M^++1, 2.30), 470 (M^+, 12.60), 428 (9.80), 327 (12.30), 386 (13.20), 385 (32.10), 384 (100), 383 (72.10), 371 (10.50), 305 (16.40), 296 (27.20), 280 (7.30), 193 (1.80), 192 (5.60), 179 (17.30), 178 (16.30), 177 (11.30), 176 (35.10), 175 (3.80), 165 (5.30), 164 (3.00), 163 (6.30), 152 (20.10), 151 (12.50), 150 (5.30), 139 (3.60), 128 (2.30), 126 (5.10), 105 (6.30), 104 (8.60), 103 (49.80), 102 (5.60), 78 (3.30), 77 (26.80), 76 (16.50), 65 (1.60), 63 (9.50), 51 (10.30). Anal. Calcd for $C_{32}H_{26}N_2O_2$: C, 81.70; H, 5.53; N, 5.96. Found: C, 81.49; H, 5.35; N, 5.68.

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