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Use of salicylaldehyde in the synthesis of 2-thioxoimidazolidinone and salicyladazine derivatives

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ABSTRACT

5-arylazo-2- hydroxybenzaldehyde thiosemicarbazones (2a-c) and 2-[(5-arylazo-2-hydroxybenzylidene)-amino]-benzoic acids (3a-c) were prepared via condensation of 5- arylazo-2- hydroxybenzaldehyde (1) with thiosemicarbazide and 2-amino benzoic acid. 3-substituent- imidazolidinones (4a-c) were synthesized by the reaction of 2 with ethyl chloro acetate in presence of fused sodium acetate. Bezoylation and acetylation of 3-substituent- imidazolidinones (4a-c) with benzoyl chloride and acetic anhydride in presence or absence of fused sodium acetate led to the formation of bezoyl derivatives (7) and acetyl derivatives (5, 6). 5-aryl salicyladazines (8 a-c) were obtained by hydrazonlysis of 3, 5 and 6 with hydrazine hydrate. The electron impact mass spectra of both of the above some series of compounds have also recorded and their fragmentation pattern is discussed.

Keywords: salicylaldehyde, synthesis, 2-thioxoimidazolidinone, salicyladazine derivatives.

INTRODUCTION

Schiff bases are well known to have pronounced biological activities[1-4], and a form a class of important compounds in medicinal and pharmaceutical field. It has been suggested that azomethine linkage might be responsible for the biological activities of Schiff bases[5]. Some azopyrazoles and azocoumarins have been synthesized[6-8] and they were found to be highly active against bacteria. In course of investigations[9], involving salicylaldehyde and aryl diazonium salt, it was found that 5-arylazo-2-hydroxylbenzaldehydes (1a-c) is converted into Schiff bases (2 and 3) by the action of thiosemicarbazide and anthranilic acid. The fact that only limited information is available on the mass spectra of Schiff bases (2 and 8), along with the preparation of 2-thioxoimidazoldinones and salicylaldazine derivatives, has prompted us to report their synthesis and study their electron impact (EI) mass spectral fragmentation.

MATERIALS AND METHODS

NMR spectra were recorded on a General Electric QE 300 instrument and chemical shifts were given with respect to TMS. IR spectra were recorded on a Perkin – Elmer 1420 spectrometer and a Biorad FTS7 (kBr). Mass spectra were recorded on GC/MS with CI(Chemical Ionization) and a Hewlett- Packerd MS-Engine Thermospray and ionization by electron impact to 70 eV. The accelerating voltage was 6 kV, the temperature of the ion source was ≈ 200 °C and the emission current 100 mA. Microanalyses were conducted using an elemental analyzer 1106. Melting points were determined on MEL- TEMP II malting point apparatus and uncorrected.

2- [(5-arylazo-2-hydrxybenzylidene)amino]-benzoic acid (3a-c)

A mixture of 1 (0.01mol) and anthranilic acid (0.01 mol) in ethanol (50ml) in presence of acetic acid (2ml) was heated under reflux for 4 hrs, and then cooled. The solid formed was filtered off, dried and re- crystallized from ethanol to give 3.

2-[(5-phenylazo-2-hydroxybenzylidene)amino]- benzoic acid (3a) as yellow crystals, yield 78%, mp 300°C, IR (KBr): 1719(C=O), 1620(C=N), 3380-2850(br-OH), 1615,1603,1578(C=C), 1212,1075(C-O) cm^{-1} .^{1}H-NMR (DMSO-d_6): δ 11.35(br.s, 1H, OH), 10.55(br.s, 1H, OH), 8.35 (s, 1H, CH=N), 7.12 – 7.81(m, 12H, Ar-H) ppm. Anal. Calcd for $C_{20}H_{15}N_3O_3$: C,69.57, H,4-35, N,12.17. Found: C,69.43, H,4.26, N,12.06.

2-[(5-p-tolylazo -2-hydrorybinzylidene) amino]- benzoic acid (3b) as deep yellow crystals, yield 79% , m.p.280 °C. IR (KBr) 3400-2820 (br-OH), 1720, (C=O), 1623(C=N), 1605,1588(C=C), 1122, 1078(C-O)cm^{-1} ^{1}H-NMR (DMSO-d_6): δ 2.33 (s, 3H, CH_3),(m, 11H, Ar-H), 8.33 (s, 1H, CH=N), 10.56(br. s, 1H, OH), 11.43(br. s, 1H, OH) ppm. Anal. Calad for $C_{21}H_{17}N_3O_3$: C,70.19; H,4.74; N,11.70. Found: C,70.08; H,4.26; N,11.57.

2- [(5-O-chlorophenylazo-2-hydrorybenzylidene)amino] benzoic acid (3c) as yellow crystals, yield 77%, m.p.320°C. IR (KBr):1723(C=O), 1625(C=N) , 1605, 1585(C=C), 1122, 1075(C - O) cm^{-1} . ^{1}H-NMR (DMSO-d_6): δ 7.4 -7.83(m, 11H, Ar-H) , 8.33(s, 1H, CH=N) , 10.83(br.s, 1H, OH) ,11.83(br.s, 1H, OH) ppm. Anal. Calcd for $C_{20}H_{14}N_3ClO_3$: C,63.32; H,3.69; N,11.08; Cl,9.37. Found C,63.24; H,3.60; N,10.87; Cl,9.25

3- [(5-arylazo-2-hydroxybenzylidene)amino]-2-thioxo-imidazolidin-4-anes (4a-c)
A mixture of 2 (0.01 mol), ethyl chloroacetate (0.01mol) and fused sodium acetate (0.03 mol) in dimethyl formamide (30 ml) was heated under reflux for 4 hrs. The reaction mixture was cooled and poured into water. The resulting solid was filtered off, washed with hot water dried and purified by suitable solvent to give 4.

3- [(5-phenylozo-2-hydroxybenzylidene)amino]-2- thioxo- imidazolidine- 4- one (4a) as yellow crystals, yield 82%, m.p. 287 °C. IR (KBr): 3390-2887(br. OH), 3280(NH), 1698(C=O), 1631(C=N), 1610, 1558(C=C), 1403(C=S), 1225 (C– O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.93(s, 2H,-CH_2N), 7.13-7.98(m, 8H, Ar-H), 8.71(s, 1H, CH=N), 10.21(s, 1H, NH), 11.31(s, 1H, OH) ppm. 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-p-tolylazo-2-hydroxybenzylidene)amino]-2-thioxo-imidazolidine-4- one (4b) as yellow crystals, yield 83%, m.p. 294 °C. IR (KBr): 3380-2915 (br. OH), 3285 (NH), 1695 (C=O), 1629(C=N), 1615, 1583(C=C), 1410 (C=S), 1210, 1073 (C – O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.31 (s, 3H, CH_3), 3.91(s, 2H, CH_2N), 7.11-7.90(m, 7H, Ar-H), 8.35(s, 1H, CH=N), 10.23(s, 1H, NH), 11.29 (s, 1H, OH) ppm. 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-chlorophenylazo-2-hydroxybenzylidone)amino]-2-thioxo- imidazolidin- 4-one (4c) as yellow crystals, yield 81%, m.p.255°C. IR(KBr) : 3389 - 2933(br. OH), 3285(NH),1699 (C=O), 1629(C=N), 1605,1589 (C=C), 1411(C=S), 1220,1078(C – O) cm^{-1} . ^{1}H-NMR (DMSO-d_6): δ 3.91 (s, 2H, CH_2N) 7.10 - 7.81 (m, 7H, Ar-H), 8.71(s, 1H, CH=N) , 10.25(s,1H,NH) , 11.30 (s, 1H, OH) ppm. Anal.Calcd for $C_{16}H_{12}N_5ClO_2S$: C, 51.47; H,3.22; N,18.77; Cl,9.25; 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-thioxo- imidazolidin-4-one (5a-c)
A solution of 4 (0.01mol) in acetic anhydride (25 ml) was heated under reflux for 2hr, then cooled and poured onto ice water. The resulting solid was filtered off, washed with water, dried and purified by recrystallization from benzene to give 5.

1-Acetyl-3-[(5-phenylazo-2- a cetoxybenzylidene)amino]-2-thioxo–imidazolidin-4-one (5a) as pale yellow crystals , yield 73% , m.p. 236°C. IR (KBr): 1750 (C=O) of ester, 1705-1695 (C=O) of ketone, 1632(C=N), 1608,1587 (C=C), 1227, 1103(C=O) cm^{-1} . ^{1}H-NMR ($CDCl_3$): δ 2.13 (s,3H, $COCH_3$) , 2.29(s, 3H, $OCOCH_3$), 4.11(s, 2H, NCH_2CO), 7.12-7.89(m, 8H, Ar-H), 8.73(s, 1H, CH=N) ppm. 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-acetoxybenzylideme)amino]-2-thioxo– imidazolidin–4- one (5b) as pale yellow, yield 75% , m.p. 229 °C. IR (KBr): 1752(C= O) of ester, 1707, 1698 (CO of ketone), 1630 (C=N) , 1609 , 1577(C=C), 1220, 1108 (C – O) cm^{-1} . ^{1}H-NMR (DMSO-d_6): δ 2.11(s, 3H, $COCH_3$), 2.27 (s, 3H, $OCOCH_3$), 2.31(s, 3H, CH_3-Ar), 4.15 (s, 2H, NCH_2CO), 7.11-7.88 (m, 7H, Ar-H), 8.70 (s, 1H, CH=N) ppm. Anal. Colcd 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,4.32; N,15.87; S, 7.13.

1-Acetyl-3-[(5-o-chlorophenylazo-2-acetoxybenzylidene)amino]-2- thioxo–imidazolidine-4-one (5c) as pale yellow, yield 74% , m.p. 211 °C. IR (KBr): 1748(C=O) of ester, 1703, 1697(C=O) of ketone, 1631(C=N), 1608, 1583(C=C), 1202, 1048(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), 7.11 -7.89(m, 7H, Ar-H), 8.72(s, 1H, CH=N) ppm. 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.

1-Acetyl-3-[(5-arylazo-2-acetoxybanzylidene)amino]-5-acetyl-2-thioxo-imidazolidin-4-ones (6a-c).
A mixture of 4 (0.01 mol) and fused sodium acetate (0.03 mol) in acetic anhydride (25ml) was heated under reflux for 4hr, then cooled and poured onto water. The solid formed was filtered off, washed with hot water, dried and purified by recrystallization for benzene to give 6.

1-Acetyl-3-[(5-phenyl azo-2-acetoxybenzylidene)amino]-5-acetyl-2- thioxo- imidazolidin-4- one (6a) as pale yellow, yield 68% , m.p. 168°C. IR (KBr): 1756 (C=O) of ester, 1703, 1697(C=O) of ketone, 1631 (C=N), 1607, 1588(C=C), 1212, 1078(C – O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 2.11 – 2.21(br.s, 6H, 2 x $COCH_3$) 2.32 (s, 3H, $OCOCH_3$), 5.81 (s, 1H, $NCH(CO)_2$) , 7.13-7.81(s, 8H, Ar-H), 8.71(s, 1H, CH=N) ppm. Anal. Calcd for $C_{22}H_{19}N_5O_5S$: C, 56.77; H, 4.08; N, 15.05; S, 6.88. Found: C, 56.57; H, 3.98; N, 15.01; S, 6.66.

1-Acetyl-3-[(5-p-totylazo-2-acetoxybenzylidene)amino]-5-acetyl-2-thioxo –imidazolidin-4-one (6b) as yellow , yield 71% , m.p. 173°C. IR (KBr) : 1753 (C=O)of ester, 1703, 1696(C=O) of ketone, 1632(C=N), 1605, 1583(C=C), 1213, 1079 (C – O) cm^{-1} . ^{1}H-NMR ($CDCl_3$): δ 2.01 -2.12 (br.s, 6H, 2 x $COCH_3$), 2.30 (s, 3H, $OCOCH_3$), 2.33(s, 3H, Ar-CH_3), 5.73(s, 1H, $NCH(CO)_2$), 7.12-7.80(m, 7H, Ar-H) , 8.70(s, 1H, CH=N) ppm. Anal.Calcd for $C_{23}H_{21}N_5O_5$: C, 57-62; H, 4.38; N, 14.61; S, 6.68. Found: C, 57.42; H, 4.23; N, 14.51; S, 6.49.

1-Acetyl-3-[(5-o-chlorophenylazo-2-acetoxybenzylidene)amino]-5- acetyl -2- thioxo-imidazolidin-4-one (6c) as yellow , yield 73%, m.p. 162°C. IR (KBr): 1752 (C=O) of ester, 1702 (C=O) of ketone, 1624(C=N), 1603, 1581(C=C), 1212, 1079 (C – O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.01-2.12(b.s, 6H, 2 x $COCH_3$), 2.29(s, 3H, $OCOCH_3$), 5.74(s, 1H, $NCH(CO)_2$), 7.12 - 7.79(m, 7H, Ar-H), 8.73(s, 1H, CH=N) ppm. Anal. Calcd for $C_{22}H_{18}N_5ClO_5S$: C, 52.91; H, 3.61; N, 14.03; Cl, 7.11; S, 6.41. Found: C, 52.73; H, 3.48; N, 13.98; Cl ,7.01; S, 2.26.

1-Benoyl-3-[(5-arylazo-2-benzoyloxybenzylidene)amino)-2-thioxo- imidazolidin-4-one (7a,b)
A mixture of 4 (0.01 mol) and benzoyl chloride (0.01 mol) in pyridine (20ml) was heated under reflux for 2 hr, then cooled and poured into ice – dilute hydrochloric acid (3%). The crude obtained was filtered of, washed with water, dried and re crystallized from acetic acid to give 7.

1-Benzoyl-3-[(5-phenylazo-2-benzyloxybenzylidene)amino)-2-thioxo- imidazolidin-4-one (7a) as yellow, yield 67%, m.p. 236°C. IR (KBr): 1745(C=O) of ester, 1698(C=O) of ketone, 1628(C=N) 1603, 1585(C=C), 1120, 1087(C – O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.98(s, 2H, NCH_2CO), 6.81-7.78(m, 18H, Ar-H), 8.72(s, 1H, CH=N) ppm. Anal. Calcd for $C_{30}H_{21}N_5O_4S$: C, 65.81; H, 3.84; N, 12.79; S, 5.85. Found: C, 65.67; H, 3.76; N, 12.63; S, 5.66.

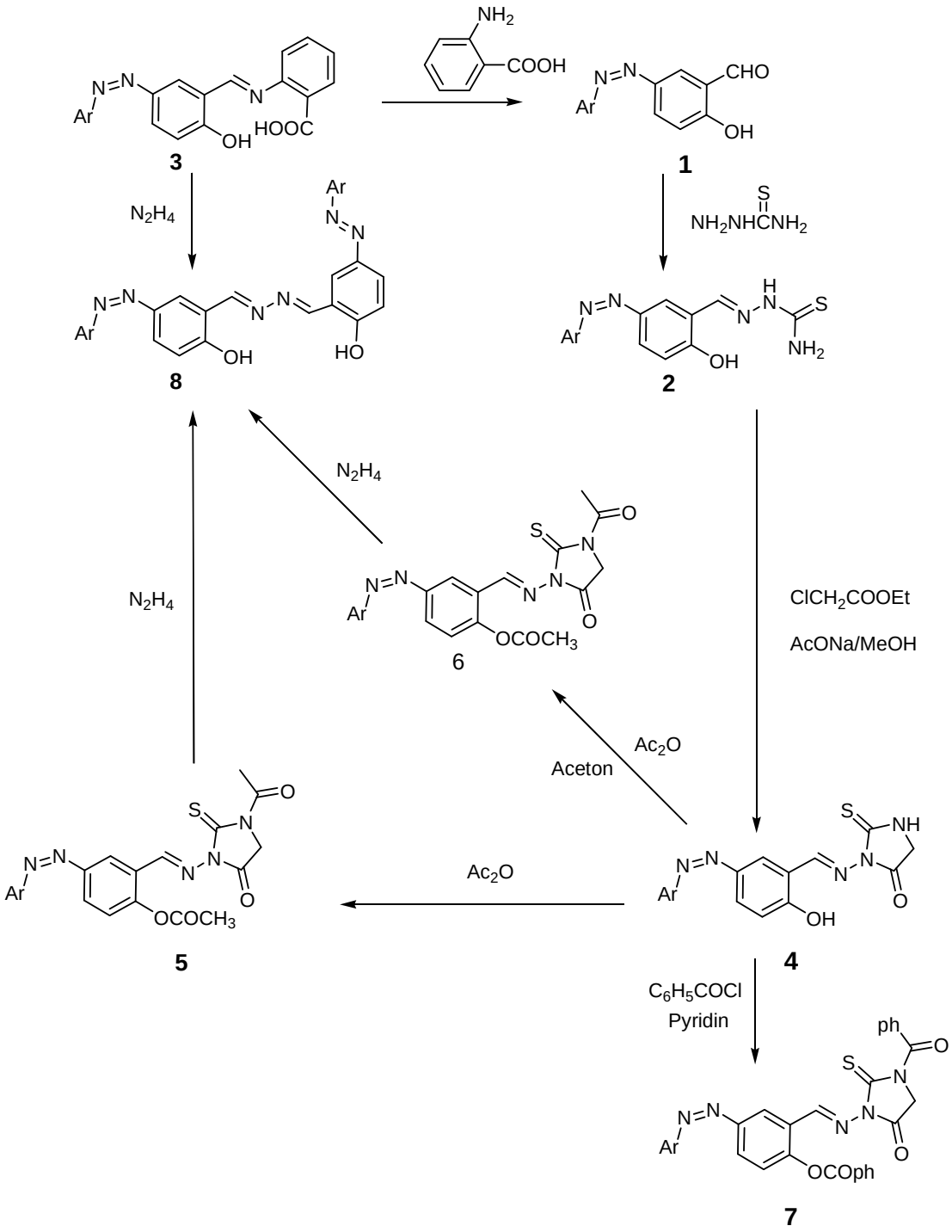
1-Benzoyl-3-[(5-p-tolylazo-2-benzoyloxybenzylidene)amino]-2-thioxo- imidazolidin-4-one(7b) as yellow, yield 72%, m.p. 228°C. IR (KBr): 1746(C=O) of ester, 1701, 1689(C=O) of ketone, 1629(C=N), 1605, 1583(C=C), 1210, 1073(C – O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.32(s, 3H, CH_3), 4.01(s, 2H, NCH_2CO), 6.89 – 7.78(m, 17H, Ar-H), 8.71 (s, 1H, CH=N) ppm. Anal. Calcd for $C_{31}H_{23}N_5O_4S$: C, 66.31; H, 4.10; N, 12.48; S, 5.70. Found: C, 66.19; H, 4.01; N, 12.26; S, 5.51.

5-arylazosalicyladazines (8a-c)
A mixture of 3 or acetyl derivatives (5 and 6) (0.01 mol) and hydrazine hydrate (0.02 mol) in dimethylformamide (30 ml) was heated under reflux for 2hrs, then cooled and poured into ice –water . The resulting solid was filtered off, washed with water, dried and purified by re crystallization with dimethylformamide to give 8.

5- phenylazosalicyladazine (8a) as yellow, yield 68% , m.p . 299 °C. IR (KBr): 3450 (OH), 1632 (C=N), 1605, 1582 (C=C), 1078, 1020(C – O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 6.98 - 7.76(m, 16H, Ar – H), 8.73(s, 2H, 2x CH=N), 11.33(s, 2H, 2x OH) ppm. Anal. Calcd for $C_{26}H_{20}N_6O_2$: C, 69.64; H, 4.46; N, 18.75. Found: C, 69.53; H, 4.37; N, 18.57.

5-(p-tolyl)azosalicyladazine (8b) as yellow , yield 67% , m.p. 353°C. IR (KBr): 3432(OH), 1630(C=N), 1604, 1595 (C=C), 1095, 1035(C – O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.30 (s, 6H, 2x CH_5), 6.89-7.78(m, 14H, Ar–H) 8.73(s, 2H, 2x CH=N), 11.32(s, 2H, 2x OH) ppm. 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-(o-chlorophenyl)azosalicyladzine (8 c) as yellow, yield 68% , m.p 302°C. IR (KBr): 3443(OH), 1634(C=N), 1607, 1583(C=C), 1095, 1015(C –O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 6.91-7.81(m, 14H, Ar-H), 8.73(s, 2H, 2x CH=N), 11.34 (s, 2H, 2x OH) ppm. 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.



Where Ar = C_6H_5 -, 4-CH_3-C_6H_4 , 2-ClC_6H_4 -

Scheme 1

RESULTS AND DISCUSSION

Chemistry

In view of this 5-arylazo-2-hydroxybenzaldehyde thiosemicarbazones (2a-c) and 2-[(5-arylazo-2-hydroxybenzylidene)amino]-benzoic acid (3a-c) were prepared from the reaction of 5-arylazo-2-hydroxybenzaldehyde (1a-c) with thiosemicarbazide and 2- aminobenzoic acid in presence of acetic acid .

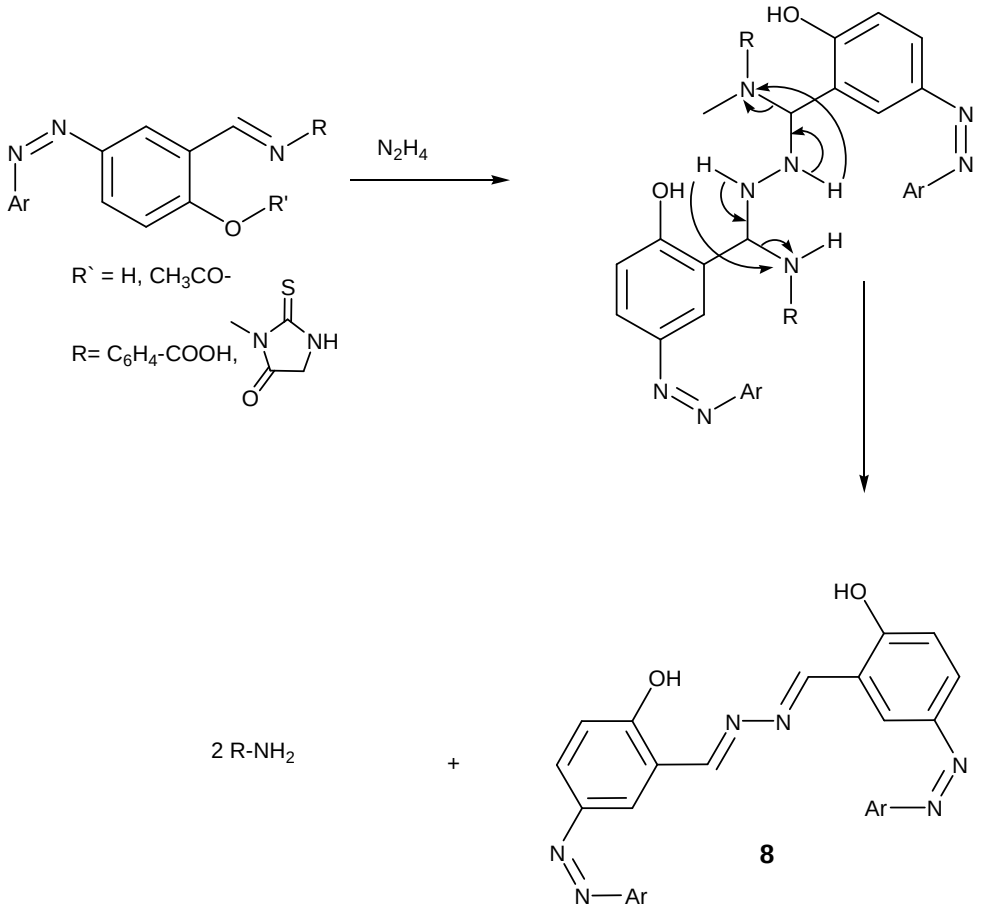
Treatment[10] of 5-arylazo-2-hydroxybenzaldehyde (1a-c) with ethyl chloroacetate in presence of fused sodium acetate in dimethyl formamide under reflux yielded the corresponding to 3-[(5-arylazo-2-hydroxybenzylidene) amino]-2-thioxo imidazolidin-4-enes (4a-c, scheme) .

Acetylation[11] of 4 with acetic anhydride afforded the corresponding to 1-acetyl-3-[5-arylazo-2-actoxy-benzylidene]-amino-2-thioxo-imidazolidin-4-ones (5a-c), while the acetylation of 4 with acetic anhydride in presence of fused sodium acetate gave the corresponding to 1-acetyl-3-[(5-arylazo-2-actoxybenzylidene)-amino]-5-acetyl-2-thioxo-imidazolidin-4-ones (6a-c).

Benzoylation of compound 4 with benzoyl chloride in pyridine under reflux yielded the corresponding to 1-benzoyl-3-[(5-arylazo-2-benzoyloxy benzylidene)-amino]-2-thioxo-imidazoldin-4-one (7a,b, scheme 1)

5-arylazosalicylaldazines (8a-c) were prepared via the reaction of 2- thioxo–imidazolidiones derivatives (5 and 6) and 2-[(5-arylazo-2-hydroxybenzylidene)amino]-benzoic acid (3) with hydrazine hydrate in dimethyl formamide.

Structure 8 which may be formed by the nucleophilic attack at methane amino (- CH = N -) by one mole from hydrazine hydrate with two moles of compound 3 and/or 6 as shown in scheme 2.



Where Ar =C_6H_5-, C_6H_4-CH_3, C_6H_4-Cl

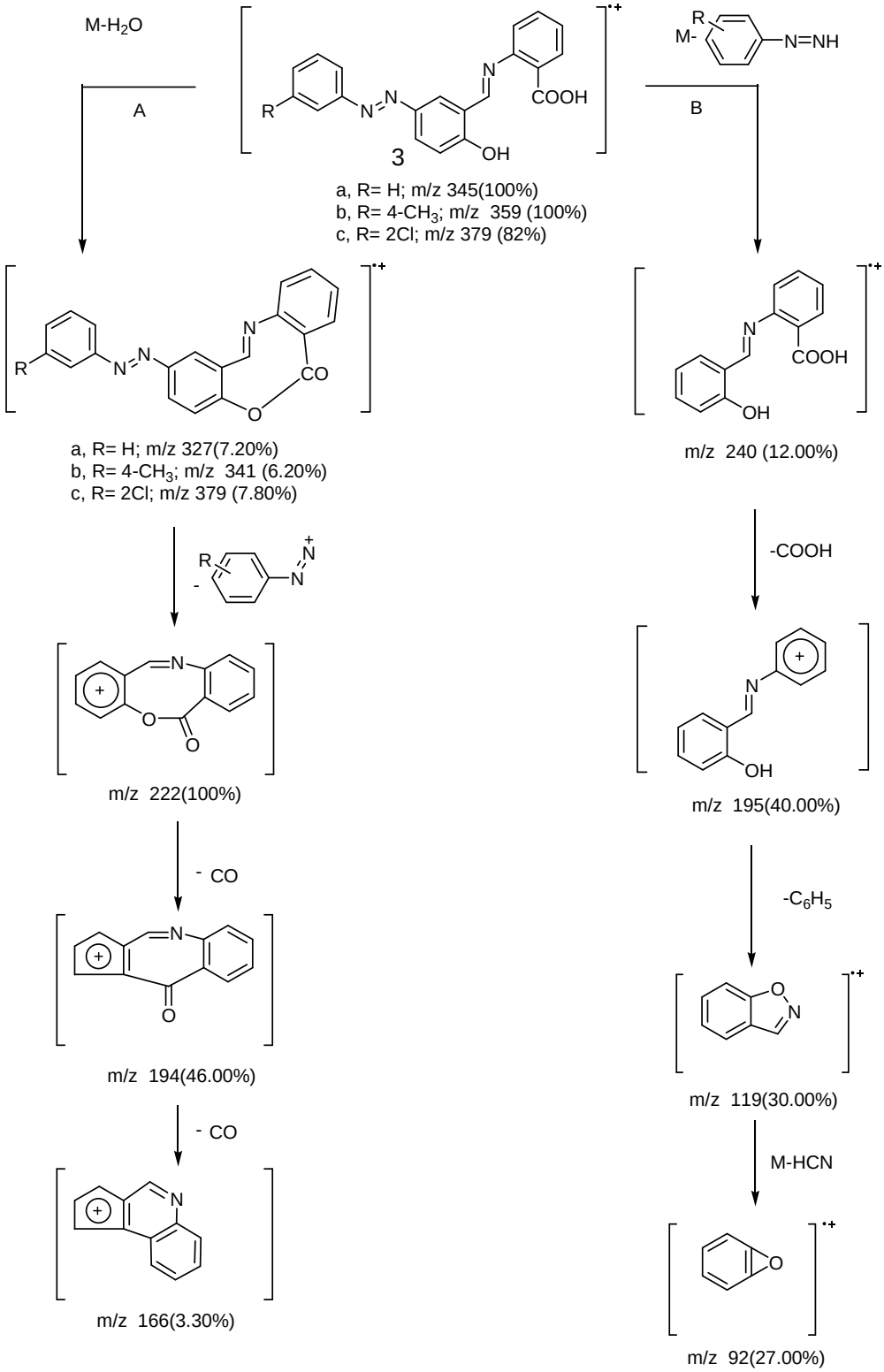
Scheme 2

Mass spectrometry

The mass spectral decomposition modes [12-14] of various nitrogen compounds containing arylazo substituents have been suggested and investigated.

Table 1 list the *m/z* (relative abundance, %) values of the principle fragment of the synthesized compounds. The electron impact ionization of the compounds (3a-c), it was found that the molecular ion for all these compounds is a base peak, while the base peak of compound 3c is *m/z* 222.

Mass spectra of three compounds (6a-c) belonging to this series were recorded and all the spectra showed characteristic common fragmentation pathways as shown in scheme 3.



Scheme 3: Main fragmentation pathway of compound 3

Compounds 4, 5 and 6

All the spectra showed characteristic common fragmentation pathways with intense molecular ion peaks in most cases. From the study of the mass spectra of compounds 4, 5 and 6 , it was found that the molecular ion for all these compounds fragmented further and involved two various pathways as illustrated by scheme 4 as representative examples. The molecular ion of compound 4b underwent fragmentation via pathway *A* to produce peak at *m/z* 262 by losing methyl phenyl radical cation (CH_3-C_6H_4-) ion of *m/z* 262 was broken to give the ion of *m/z* 234 by losing nitrogen molecule. This fragmentation led to the ion of *m/z* 206, 142 and *m/z* 116 respectively.

Finally, the same ion of *m/z* 353 was broken via pathway *B* to give an ion of *m/z* 119, which lost 3-[(2-hybroxybenzylidene)–amino] -2- thioxo- imidazolidin-4-one cation radical. The ion of *m/z* 119 was broken to give the stable ion of *m/z* 91 by losing nitrogen molecule.

From study the mass spectra of compounds 5a-c, it was found that the molecular ion for all these compounds had fragmented to ions of *m/z* 339, 353 and 373, corresponding to the molecular ion of compounds 4a-c by losing two molecules from the ketene (CH_2CO), while the molecular ion of compounds 6a-c were broken to give an ions of *m/z* 339, 353 and *m/z* 373, corresponding to the molecular ion of compounds 4a-c by losing three molecules from the ketene. The ion of m/z 353 has further broken via similar way of compound 4b.

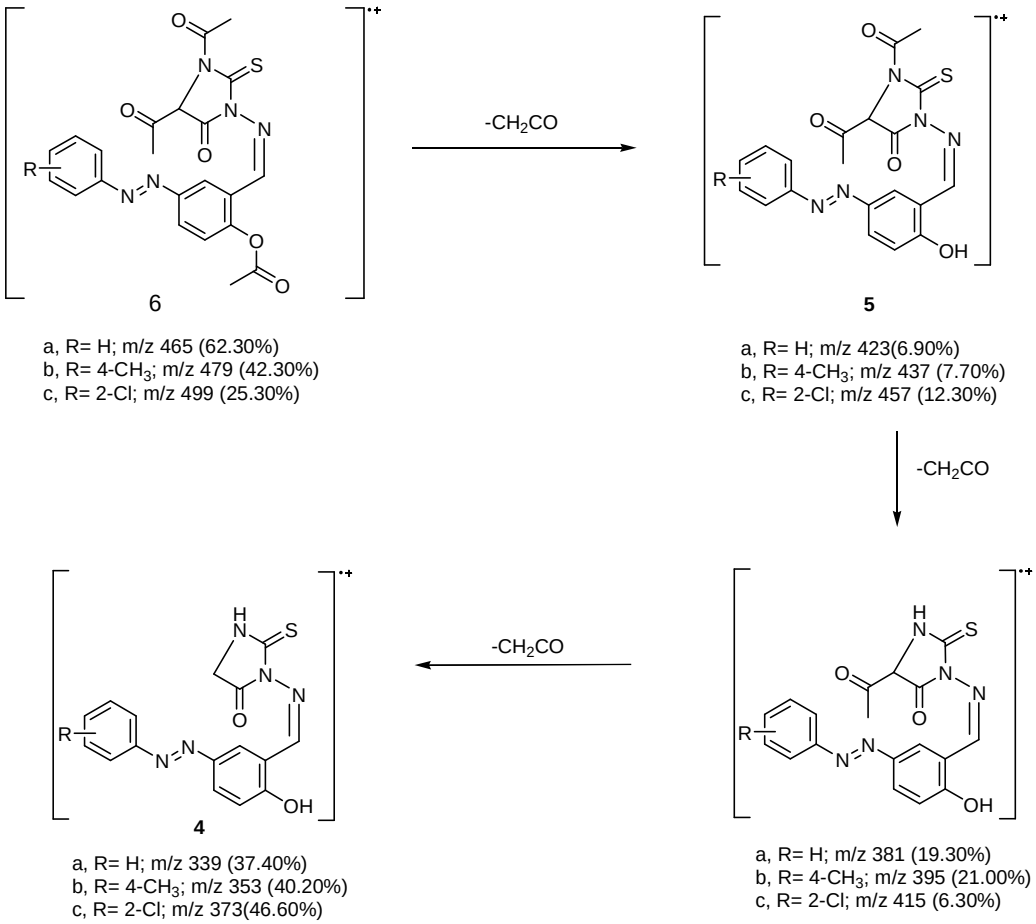
Compounds 8a-c

The mass spectra of compounds 8a-c are fully consistent with the assigned structures. In most cases, intense molecular ion peaks were observed.

Thus compounds 8a-c showed an intense molecular ion peaks at *m/z* 448, 476 and *m/z* 516, corresponding to the molecular formula $C_{26}H_{20}N_60_2$, $C_{28}H_{24}N_6O_2$ and $C_{26}H_{18}N_6Cl_2O_2$, respectively.

The molecular ion of compounds 8a-c fragmented further and involved two possible pathways as illustrated in scheme 5.

The electron impact ionization mass spectra of compounds 8a-c, it was found that the molecular ion for these three compounds is a base peak.



6

a, R= H; m/z 465 (62.30%)
b, R= 4-CH_3; m/z 479 (42.30%)
c, R= 2-Cl; m/z 499 (25.30%)

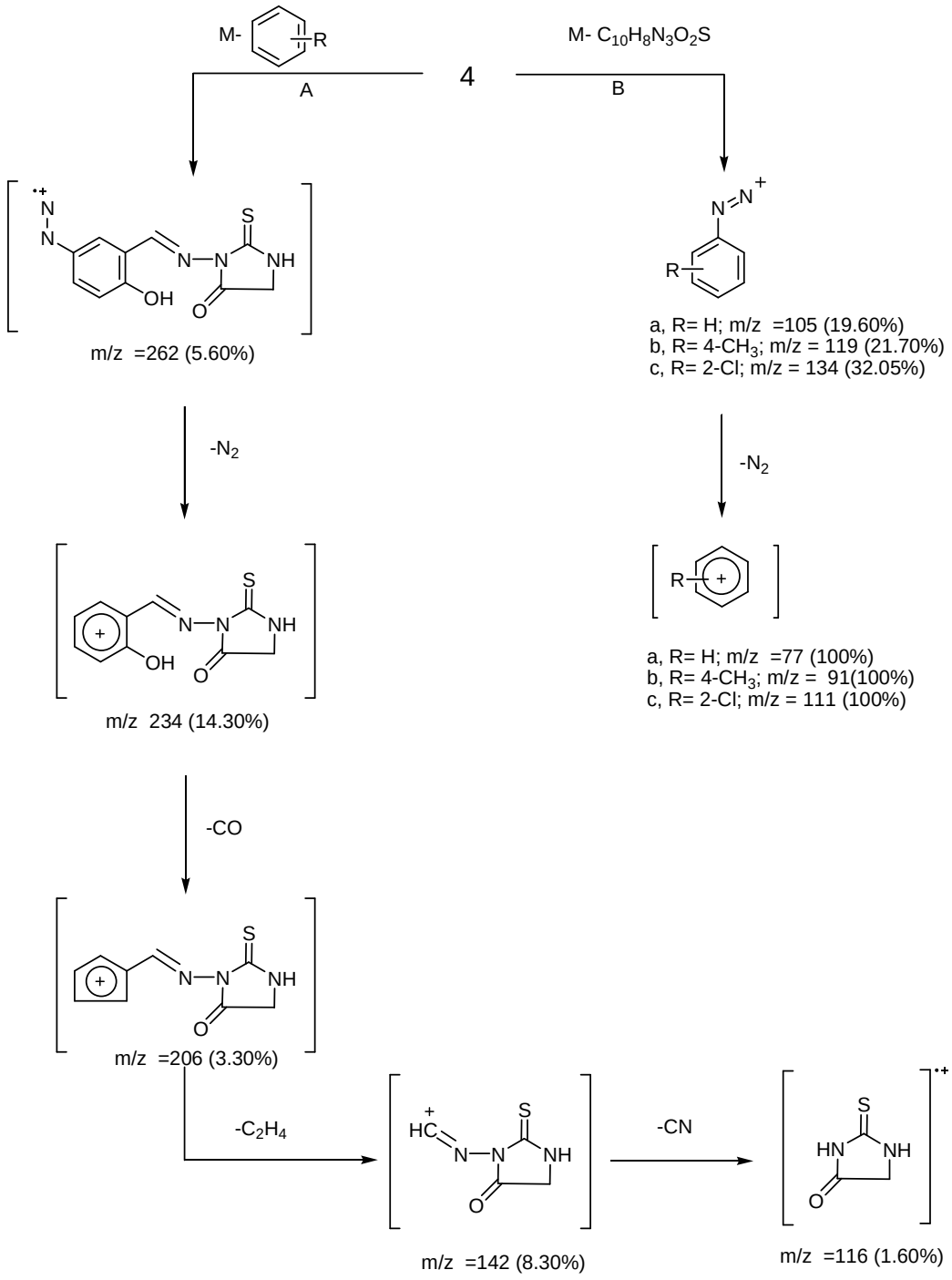
5

a, R= H; m/z 423(6.90%)
b, R= 4-CH_3; m/z 437 (7.70%)
c, R= 2-Cl; m/z 457 (12.30%)

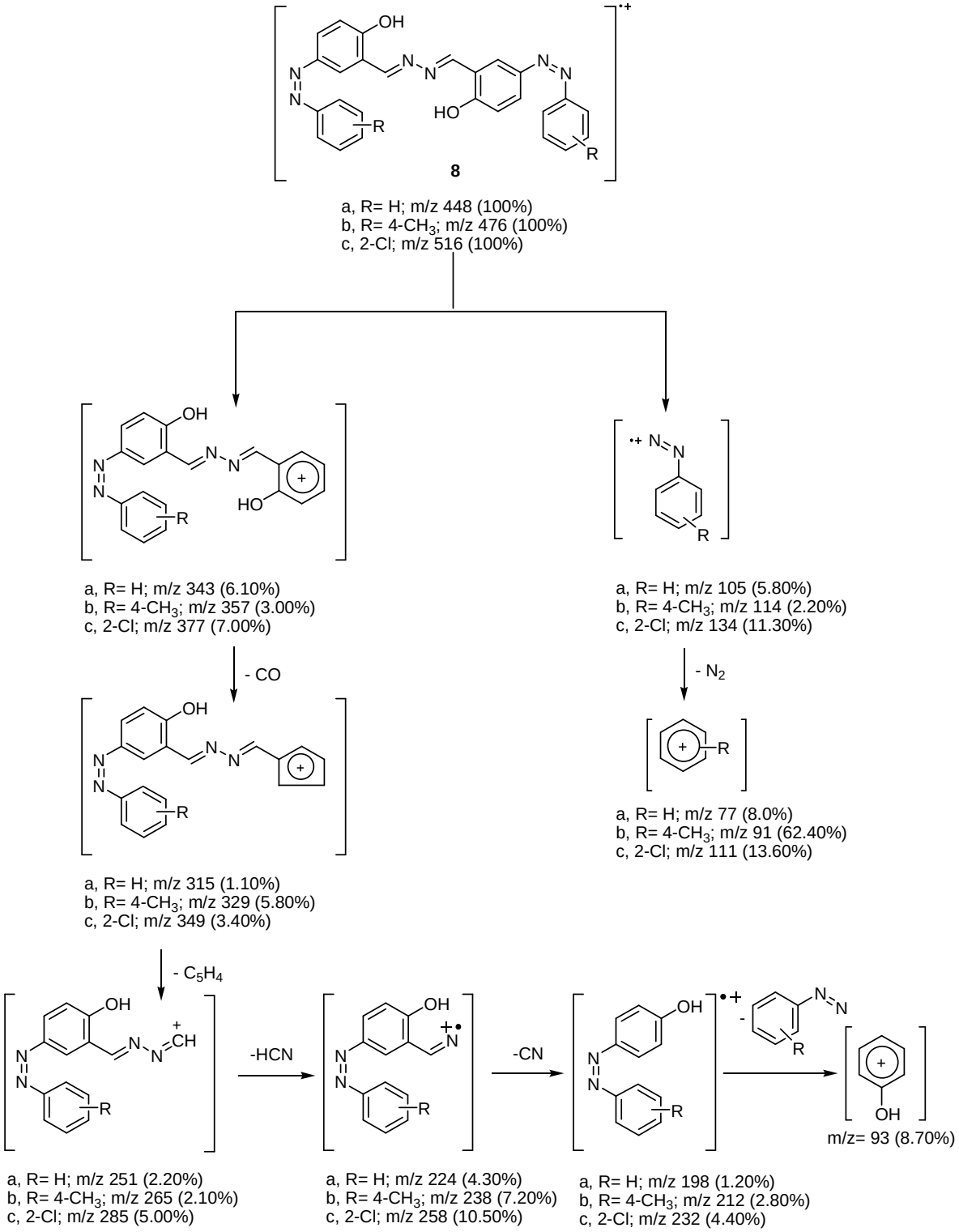
a, R= H; m/z 381 (19.30%)
b, R= 4-CH_3; m/z 395 (21.00%)
c, R= 2-Cl; m/z 415 (6.30%)

4

a, R= H; m/z 339 (37.40%)
b, R= 4-CH_3; m/z 353 (40.20%)
c, R= 2-Cl; m/z 373(46.60%)



Scheme 4: Main fragmentation pathway of compound 4, 5 and 6



Scheme 5: Main fragmentation pathway of compound 8_{a-c}

Table (1) EI Mass Spectra (70 eV) of Compounds 3, 4, 5, 6 and 8 m/z

Comp d	M^+	Pathway A		Pathway B		Other ions
		-M	m/z	-M	m/z	
3a	$[C_{20}H_{15}N_3O_3]^+$ 345 (100)	H_2O C_6H_5 N_2 CO CO	$[C_{20}H_{13}N_3O_2]^+$ 327 (7.20) $[C_{14}H_8N_3O_2]^+$ 250 (1.00) $[C_{14}H_8NO_2]^+$ 222 (26.30) $[C_{13}H_8NO]^+$ 194(11.50) $[C_{12}H_8N]^+$ 166(3.20)	$C_6H_5N_2$ H, CO_2 C_6H_4 HCN	$[C_{14}H_{10}NO_3]^+$ 240(11.00) $[C_{13}H_9NO]^+$ 195(8.20) $[C_7H_5NO]^+$ 119(4.30) $[C_6H_4O]^+$ 92 (2.30)	345 (M^++l, 20.50), 328(1.80), 326(1.90), 302(1.40), 301(6.10), 271(1.10), 268(2.80), 253(2.90), 250(1.00), 241(2.20), 239(2.30), 223(4.50), 221(1.50), 214(3.10), 212(1.20), 196(8.90), 178(1.40), 170(3.10), 168(1.40), 148(1.50), 137(5.20), 120(3.20), 105(6.40), 93(21.10), 77(21.10),
3b	$[C_{21}H_{17}N_3O_3]^+$ 359 (100)	H_2O C_7H_7H,N_2 CO CO	$[C_{21}H_{15}N_3O_2]^+$ 341(6.20) $[C_{14}H_8NO_2]^+$ 222 (25.30) $[C_{13}H_8NO]^+$ 194 (9.30) $[C_{12}H_8N]^+$ 166 (1.70)	$C_7H_7N_2$ H,CO_2 C_6H_4 HCN	$[C_{14}H_{10}NO_3]^+$ 240 (9.70) $[C_{13}H_9NO]^+$ 195 (7. 80) $[C_7H_5NO]^+$ 119 (10.20) $[C_6H_4O]^+$ 92(6.90)	360(M^++l, 23.80), 358(4.70), 345(4.80), 268(4.80), 253(5.20), 241(3.40), 239(3.80), 223(6.90), 214(1.60), 196(6.90), 170(6.00), 137(4.10,) 120(3.10), 107(6.40), 91(32.80)

Comp d	M^+	Pathway A		Pathway B		Other ions
		-M	m/z	-M	m/z	
3c	$[C_{20}H_{14}N_3ClO_3]^+$ 379(82.00)	H_2O C_6H_4Cl,N_2 CO CO	$[C_{20}H_{12}N_3ClO_3]$+ 361(7.80) $[C_{14}H_8NO_2]^+$ 222(100) $[C_{13}H_8NO]^+$ 194 (46.00) $[C_{12}H_8N]^+$ 166(8.30)	$C_6H_4ClN_2$ CO_2,H C_6H_4 HCN	$[C_{14}H_{14}NO3]^+$ 240(12.00) $[C_{13}H_9NO]^+$ 195(40.00) $[C_7H_5NO]^+$ 119(3.00) $[C_6H_4O]^+$ 92 (40.00)	381 (M^++2, 34.00), 224(2.00), 223(22.00), 196(26.00), 127(26.00), 111(32.00)
4a	$[C_{16}H_{13}N_5O_2S]^+$ 339 (37.40)	C_6H_5 N_2 CO C_5H_4 CN	$[C_{10}H_8N_5O_2S]^+$ 262(6.30) $[C_{10}H_8N_3O_2S]^+$ 234 (14.30) $[C_9H_8N_3OS]^+$ 206 (3.30) $[C_4H_4N_3OS]^+$ 142(8.30) $[C_3H_4NOS]^+$ 166 (1.80)	$C_{10}H_8N_3O_2S$ N_2 C_2H_2	$[C_6H_5N_5]^+$ 105(19.60) $[C_6H_5]^+$ 77(100) $[C_4H_3]^+$ 51(53.30)	340 (M^++l, 11.20), 338(6.90), 322(6.70), 311(8.70), 298(6.30), 297(11.20), 176(7.10), 235(6.20), 223(6.30), 184(8.10), 176(3.30), 162(3.80), 160(5.30), 148(3.20), 147(4.30), 146(6.30), 136(3.90), 135(5.30), 134(3.40), 114(10.70), 104(5.30), 64(11.30), 50(12.30)
4b	$[C_{17}H_{15}N_5O_2S]^+$ 353 (40.20)	C_7H_7 N_2 CO C_5H_4 CN	$[C_{10}H_8N_5O_2S]^+$ 262(9.30) $[C_{10}H_8N_3O_2S]^+$ 234 (43.20) $[C_9H_8N_3OS]^+$ 206 (5.30) $[C_4H_4N_3OS]^+$ 142(7.60) $[C_3H_4NOS]^+$ 166 (9.80)	$C_{10}H_8N_3O_2S$ N_2 C_2H_2	$[C_7H_7N_5]^+$ 119(21.70) $[C_7H_7]^+$ 91(100) $[C_5H_5]^+$ 65(34.30)	354 (M^++l, 16.20), 352(11.20), 325(11.90), 312(4.60), 311(16.10), 205(4.50), 184(3.30), 164(3.20), 163(4.20), 160(3.50), 152(4.30), 148(4.20), 120(4.10), 118(7.90), 108(3.50), 107(6.50), 921(6.30), 901(3.30), 76(9.70), 65(23.30), 63(11.10), 52(7.60)

Comp d	M^+	Pathway A		Pathway B		Other ions
		-M	m/z	-M	m/z	
4c	$[C_{16}H_{12}N_5ClO_2S]^+$ 373(50.40)	C_6H_4Cl N_2 CO C_5H_4 CN	$[C_{10}H_8N_5O_3S]+$ 264(14.10) $[C_{10}H_8N_3O_2S]^+$ 234(71.10) $[C_9H_8N_3OS]^+$ 206(6.40) $[C_4H_4N_3OS]^+$ 142(15.30) $[C_3H_4N_2OS]^+$ 116(5.10)	$C_{10}H_8N_3O_2S$ N_2 HCl C_2H	$[C_6H_4ClN_2]^+$ 139(13.20) $[C_6H_4Cl]^+$ 111(100) $[C_6H_3]^+$ 75(63.20) $[C_4H_2]^+$ 50(31.20)	375 (M^++2, 28.90), 374(M^++1, 11.20), 353(24.60), 352(11.70), 336(10.50), 325(10.40), 311(14.50), 261(7.90), 260(5.50), 235(13.90), 207(9.70), 179(7.30), 165(7.30), 164(10.10), 160(19.40), 141(10.60), 135(24.20), 134(11.20), 120(11.50), 119(31.70), 113(25.30), 106(10.80), 105(24.70), 63(60.60), 51(84.60)
5a	$[C_{20}H_{17}N_5O_4S]^+$ 423 (6.90)	CH_2CO CH_2CO C_6H_4 CO C_5H_4 CN	$[C_{18}H_{15}N_5O_3S]^+$ 381(36.80) $[C_{16}H_{13}N_5O_2S]^+$ 334 (37.40) $[C_{10}H_8N_5O_2S]^+$ 262 (10.90) $[C_{10}H_8N_3O_2S]^+$ 234(15.10) $[C_4H_4N_3OS]^+$ 206(1.70) $[C_4H_4N_2OS]^+$ 116(2.30)	CH_2CO CH_2CO $C_{10}H_8N_3O_2S$ N_2 C_2H_2	$[C_{18}H_{15}N_5O_3S]^+$ 381(36.80) $[C_{18}H_{15}N_5O_3S]^+$ 339(37.40) $[C_{18}H_{15}N_5O_3S]^+$ 105(19.60) $[C_6H_5]^+$ 77(100) $[C_4H_3]^+$ 51(39.10)	424 (M^++l, 1.30), 382(15.10), 340(7.90), 338(7.90), 322(5.70), 311(7.80), 298(5.20), 297(10.10), 276(5.00), 235(5.10), 223(5.50), 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), 136(2.90), 135(4.70), 134(4.70), 114(10.70), 104(4.40), 64(10.20), 50(11.50)

Comp d	M^+	Pathway A		Pathway B		Other ions
		-M	m/z	-M	m/z	
5b	$[C_{21}H_{19}N_5O_4S]^+$ 437(7. 70)	CH_2CO CH_2CO C_7H_7 N_2 CO C_5H_4 CN	$[C_{19}H_{17}N_5O_3S]^+$ 395(29.90) $[C_{17}H_{15}N_5O_2S]^+$ 353(40.20) $[C_{10}H_8N_5O_2S]^+$ 262(5.60) $[C_{10}H_8N_3O_2S]^+$ 234(14.30) $[C_9H_8N_3OS]^+$ 206(1.70) $[C_4H_4N_3OS]^+$ 142(8.30) $[C_3H_4N_2OS]^+$ 116(3.50)	CH_2CO CH_2CO $C_{10}H_8N_3OS$ N_2 CH_2 CH_2	$[C_{19}H_{17}N_5O_3S]^+$ 395(29.90) $[C_{17}H_{15}N_5O_2S]^+$ 353(40.20) $[C_7H_7N_2]^+$ 119(21.70) $[C_7H_7]^+$ 91(100) $[C_6H_5]^+$ 77(10.80) $[C_4H_3]^+$ 51(12.80)	375 (M^++2, 28.90), 374(M^++1, 11.20), 353(24.60), 352(11.70), 336(10.50), 325(10.40), 311(14.50), 261(7.90), 260(5.50), 235(13.90), 207(9.70), 179(7.30), 165(7.30), 164(10.10), 160(19.40), 141(10.60), 135(24.20), 134(11.20), 120(11.50), 119(31.70), 113(25.30), 106(10.80), 105(24.70), 63(60.60), 51(84.60)
5c	$[C_{20}H_{16}N_5ClO_4S]^+$ 457 (12.30)	CH_2CO CH_2CO C_6H_4Cl,N_2 CO C_5H_4 CN	$[C_{18}H_{14}N_5ClO_3S]^+$ 415(33.50) $[C_{16}H_{12}N_5ClO_2S]^+$ 373 (46.60) $[C_{10}H_8N_3O_2S]^+$ 234 (17.30) $[C_9H_8N_3OS]^+$ 206(6.20) $[C_4H_4N_3OS]^+$ 192(18.30) $[C_3H_4N_2OS]^+$ 116(9.20)	CH_2CO CH_2CO $C_{10}H_8N_3O_2S$ N_2 HCl	$[C_{18}H_{14}N_5ClO_3S]^+$ 415(33.50) $[C_{16}H_{12}N_5ClO_2S]^+$ 373 (46.60) $[C_8H_4N_2Cl]^+$ 139(32.50) $[C_6H_4Cl]^+$ 111(100) $[C_6H_3]^+$ 75(62.30)	459 (M^++2, 1.30), 417(12.20), 375(17.20), 353(22.20), 352(10.20), 326(17.10), 325(11.50), 311(16.30), 262(13.30), 261(6.20), 260(5.30), 235(10.20), 207(3.40), 179(8.50), 165(7.10), 164(12.70), 160(21.30), 141(13.20), 134(11.30), 120(11.30), 119(27.80), 113(27.80), 106(11.60), 105(3.90), 77(2.30), 76(4.30), 65(23.20), 63(59.60), 52(17.80), 51(33.50)

Comp d	M^+	Pathway A		Pathway B		Other ions
		-M	m/z	-M	m/z	
6a	$[C_{22}H_{19}N_5O_5S]^+$ 465(62.30)	CH_2CO CH_2CO CH_2CO C_6H_5 N_2 CO C_5H_4 CN	$[C_{20}H_{17}N_5O_4S]^+$ 423(13.50) $[C_{18}H_{15}N_5O_3S]^+$ 381(42.30) $[C_{16}H_{13}N_5O_2S]^+$ 339(28.50) $[C_{10}H_8N_5O_2S]^+$ 262(13.30) $[C_{10}H_8N_3O2S]^+$ 234(19.50) $[C_9H_8N_3OS]^+$ 206(2.30) $[C_4H_4N_3OS]^+$ 142(19.20) $[C_4H_4N_2OS]^+$ 116(6.20)	CH_2CO CH_2CO CH_2CO $C_{10}H_8N_3OS$ N_2 CH_2	$[C_{20}H_{17}N_5O_4S]^+$ 423(13.50) $[C_{18}H_{15}N_5O_3S]^+$ 381(42.30) $[C_{16}H_{13}N_5O_2S]^+$ 339(28.50) $[C_6H_5N_2]^+$ 105(23.30) $[C_6H_5]^+$ 77(100) $[C_4H_3]^+$ 51(43.30)	466(M^++1, 7.20), 424(6.30), 382(10.10), 340(4.70), 338(11.20), 322(7.50), 311(8.70), 298(6.30), 297(13.10), 276(7.20), 235(6.30), 223(7.30), 184(17.20), 176(3.30), 162(3.20), 160(5.60), 159(3.80), 152(4.20), 148(3.50), 147(6.5), 146(5.90), 136(4.20), 135(4.30), 143(6.30), 114(11.80), 104(5.30), 64(12.20), 50(13.50)
6b	$[C_{23}H_{21}N_5O_5S]^+$ 479 (42.61)	CH_2CO CH_2CO CH_2CO C_7H_7 N_2 CO C_5H_4 CN	$[C_{21}H_{19}N_5O_4S]^+$ 437(9.30) $[C_{19}H_{17}N_5O_3S]^+$ 395 (23.30) $[C_{17}H_{15}N_5O_2S]^+$ 353 (43.20) $[C_{10}H_8N_5O_2S]^+$ 262(7.30) $[C_{10}H_8N_3O_2S]^+$ 234(16.40) $[C_9H_8N_3OS]^+$ 206(3.20) $[C_4H_4N_3OS]^+$ 142(12.30) $[C_3H_4N_2OS]^+$ 116(4.30)	CH_2CO CH_2CO CH_2CO $C_{10}H_8N_3O_2S$ N_2 C_2H_2	$[C_{21}H_{19}N_5O_4S]^+$ 437(9.30) $[C_{19}H_{17}N_5O_3S]^+$ 395 (23.30) $[C_{17}H_{15}N_5O_2S]^+$ 353 (43.20) $[C_7H_7N_2]^+$ 119(43.20) $[C_7H_7]^+$ 91(100) $[C_5H_5]^+$ 65(43.20)	480 (M^++1, 6.20), 438(4.20), 396(14.20), 352(11.30), 325(16.80), 312(4.30), 311(17.30), 205(6.30), 184(7.20), 164(3.20), 163(4.80), 160(5.10), 152(4.30), 148(5.00), 120(4.10), 118(7.90), 108(4.60), 107(7.80), 92(42.30), 90(21.30), 77(11.30), 76(11.80), 63(23.20), 52(7.90), 51(13.80)

Comp d	M^+	Pathway A		Pathway B		Other ions
		-M	m/z	-M	m/z	
6c	$[C_{22}H_{16}N_5ClO_5S]^+$ 499(32.20)	CH_2CO CH_2CO CH_2CO C_6H_4Cl N_2 CO C_5H_4 CN	$[C_{20}H_{16}N_5ClO_4S]^+$ 457(11.30) $[C_{18}H_{14}N_5ClO_3S]^+$ 415(23.30) $[C_{16}H_{12}N_5ClO_2S]^+$ 373(36.20) $[C_{10}H_8N_5O_2S]^+$ 262(7.60) $[C_{10}H_8N_3O_2S]^+$ 234(19.50) $[C_9H_8N_3OS]^+$ 206(2.30) $[C_4H_4N_3OS]^+$ 142(19.20) $[C_4H_4N_2OS]^+$ 116(6.20)	CH_2CO CH_2CO CH_2CO $C_{10}H_8N_3O_2S$ N_2 CH_2	$[C_{20}H_{16}N_5ClO_4S]^+$ 457(11.30) $[C_{18}H_{14}N_5ClO_3S]^+$ 415(23.30) $[C_{16}H_{12}N_5ClO_2S]^+$ 373(36.20) $[C_6H_5N_2Cl]^+$ 139(43.30) $[C_6H_4Cl]^+$ 111(100) $[C_6H_3]^+$ 75(61.30)	501(M^++2, 5.30), 459(6.30), 417(6.30), 375(10.20), 353(11.20), 352(8.20), 336(19.30), 325(13.50), 311(19.20), 261(5.60), 260(7.30), 235(9.80), 207(4.90), 179(8.30), 165(6.50), 164(11.80), 160(19.50), 141(11.30), 134(12.30), 120(13.20), 119(28.70), 113(26.10),106(13.60), 105(4.80), 77(2.50), 76(8.30), 65(22.50), 63(51.20), 52(18.20), 51(34.30)
8a	$[C_{26}H_{20}N_6O_2]^+$ 448 (100)	$C_6H_5N_2$ CO C_5H_4 HCN CN $C_6H_5N_2$	$[C_{20}H_{15}N_4O_2]^+$ 343(6.10) $[C_{19}H_{15}N_4O]^+$ 315 (1.10) $[C_{14}H_{11}N_4O]^+$ 251(2.20) $[C_{13}H_{10}N_3O]^+$ 224(4.30) $[C_{12}H_{10}N_2O]^+$ 198(1.20) $[C_6H_5O]^+$ 93(4.50)	$C_{20}H_{15}N_4O_2$ N_2 C_2H_2	$[C_6H_5N_2]^+$ 105(9.30) $[C_6H_5]^+$ 77 (18.00) $[C_4H_3]^+$ 51 (13.20)	449 (M^++1, 6.20), 447(28.90), 431(1.70), 359(2.60), 356(1.90), 344(1.80), 314(1.20), 302(5.20), 301(3.00), 238(1.50), 237(1.20), 255(2.40), 223(1.10), 197(1.10), 196(5.00), 163(4.10), 148(2.40), 142(1.30), 135(1.40), 120(4.30), 118(1.40), 106(1.30), 92(1.50), 91(1.30), 73(2.40), 65(1.00), 52(3.20)

Comp d	M^+	Pathway A		Pathway B		Other ions
		-M	m/z	-M	m/z	
8b	$[C_{28}H_{24}N_6O_2]^+$ 476(100)	$C_7H_7N_2$ CO C_5H_4 HCN CN $C_7H_7N_2$	$[C_{21}H_{17}N_4O_2]^+$ 357(3.00) $[C_{20}H_{17}N_4O]^+$ 329(5.80) $[C_{15}H_{13}N_4]^+$ 265(2.20) $[C_{10}H_8N_5O_2S]^+$ 238(7.20) $[C_{13}H_{12}N_2O]^+$ 212(2.80) $[C_6H_5O]^+$ 93(1.80)	$C_{21}H_{17}N_4O_2$ N_2 C_2H_2 $C_{10}H_8N_3O_2S$ N_2 CH_2	$[C_7H_7N_2]^+$ 119(12.20) $[C_7H_7]^+$ 41 (62.40) $[C_5H_5]^+$ 65(1.30)	477(M^++1, 33.20), 475(5.00), 370(2.00), 357(3.00), 355(2.20), 330(6.70), 328(3.50), 313(2.70), 312(2.10), 252(1.90), 251(1.80), 239(7.00), 237(3.50), 224(3.80), 223(2.60), 211(1.10), 210(8.10), 197(1.60), 196(2.00), 163(7.60), 148(3.60), 135(2.00), 120(10.30), 118(2.60), 107(7.40), 92(11.30), 90(30.10), 77(11.20), 76(10.30), 63(13.20), 52(11.20), 51(13.10)
8c	$[C_{26}H_{18}N_6Cl_2O_2]^+$ 516 (100)	$C_6H_4ClN_2$ CO C_5H_4 HCN CN $C_6H_4ClN_2$	$[C_{20}H_{14}N_4ClO_2]^+$ 377(17.00) $[C_{19}H_{14}N_4ClO]^+$ 349 (3.40) $[C_{14}H_{10}N_4ClO]^+$ 285(5.00) $[C_{13}H_9N_3ClO]^+$ 258(10.80) $[C_{12}H_9N_2ClO]^+$ 232(4.40) $[C_6H_5O]^+$ 93(8.70)	$C_{20}H_{14}N_4ClO_2$ N_2 HCl	$[C_6H_4ClN_2]^+$ 193(11.30) $[C_6H_4Cl]^+$ 111 (13.60) $[C_6H_3]^+$ 75(6.70)	518 (M^++2, 60.50),517(M^++1,33.40), 515(30.90), 499(3.00), 395(9.00), 390(6.10), 379(6.40), 378(6.70), 372(10.60), 370(18.50), 369(5.70), 260(5.20), 230(10.10), 224(3.40), 222(7.20), 210(3.50), 197(3.50), 163(15.00), 141(4.20), 113(8.40), 106(3.90), 80(4.50), 77(5.00), 51(6.30)

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