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Synthesis and Characterization of New Mono- and Bis-Schiff Bases

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New Schiff base derivatives were prepared by the condensation of 3,4-dihydroxybenzaldehyde and 2,4,5-trihydroxybenzaldehyde with 4-amino-1,2-dihydro-1,5-dimethyl-2-phenyl-3H-pyrazole-3-one (4-amino-phenazone, 4-aminoantipyrine, 4-AAP) (**4** and **5**). 2,2′-[1,2-Phenylenebis(methyleneoxy)]dibenzaldehyde (**3**) was prepared by the reaction of 1,2-bis(bromomethyl)benzene and salicylaldehyde. Condensation reactions between the dialdehyde (**3**) with 4-aminoantipyrine and 2-aminomethylfuran (furfurylamine) yielded the new Schiff base ligands **6** and **7**. The structures of these compounds were confirmed on the basis of elemental analyses, IR, ^{1}H and ^{13}C NMR and mass spectroscopic data.

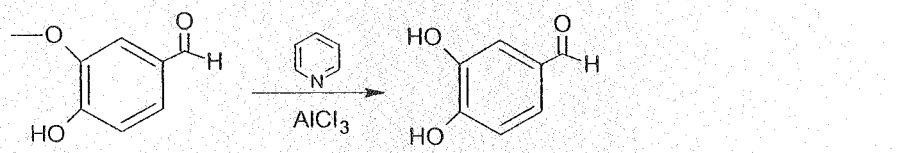
Key Words: Schiff bases, 4-Aminoantipyrine, NMR studies, Mass spectra.

INTRODUCTION

Schiff base ligands are the basis of an extensive class in the coordination chemistry of transition and main group elements[1–4]. Schiff bases and their metal complexes exhibit wide applications in biological and industrial systems[5, 6]. The characterization[7–9], thermodynamic[10], theoretical[11] and catalytic aspect[12] of this class of compounds have been extensively investigated. The Schiff bases of 4-aminoantipyrine have attracted the attention in research groups[13, 14] because of their potential biological[15], clinical[16], pharmoacological[17] and analytical[18] activities. This originated from the fact that the 4-aminoantipyrine derivatives and their metal complexes have been investigated for bioactivity and analgesic[19], antimicrobial[20] and anticancer activity[21] have been reported. The aim of this work is to study some new 4-aminoantipyrine Schiff bases. In the present paper we report the preparation of some new Schiff bases (**4–7**). These Schiff bases (**4–7**) have been characterized by the spectral data (IR, ^{1}H, ^{13}C NMR and ms). The dialdehyde (**3**) is the starting material of compounds **6** and **7** and they have also been prepared and characterized. The structures of the starting compounds and Schiff bases are given in **Scheme-1**.

EXPERIMENTAL

The starting compounds, 3,4-dihydroxybenzaldehyde[22] (**1**), 1,2,4-triacetoxybenzene[23], 1,2,4-trihydroxybenzene[24] and 2,4,5-trihydroxybenzaldehyde[24] (**2**) and 1,2-bis(bromomethyl) benzene[25] were prepared according to literature.



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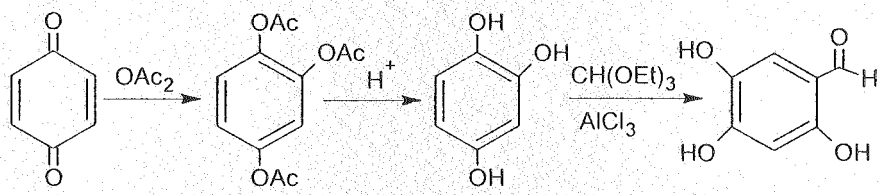

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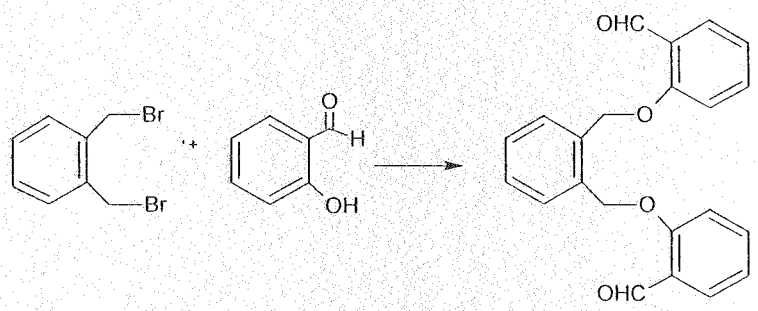

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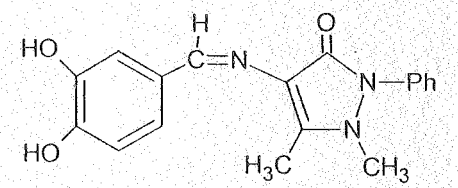

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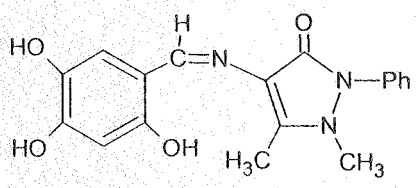

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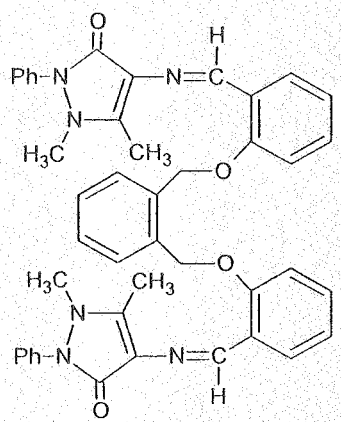

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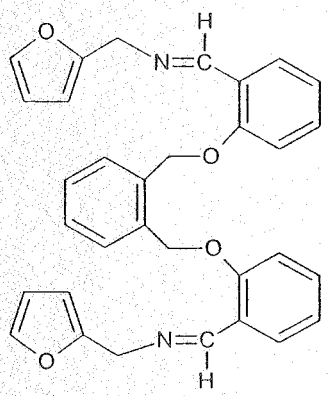

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Scheme 1. Structures of the starting compounds (1–3) and Schiff bases (4–5).

Melting points were measured on a Gallencamp apparatus using a capillary tube. Elemental analyses were performed on a LECO CHNS-932C instrument. IR spectra were recorded with a Mattson 1000 FTIR spectrometer in KBr discs. ^{1}H and ^{13}C NMR (400 MHz) spectra were measured on a Bruker DPX FT-NMR spectrometer. Mass spectra were recorded on an Agilent 1100 MSD spectrometer according to APCI. Furfurylamine, 4-aminoantipyrine and 3-methoxy-4-hydroxybenzaldehyde were purchased from Aldrich. Unless otherwise stated, commercial grade chemicals were used without further purification.

2,2′-[1,2-Phenylenebis(methyleneoxy)]dibenzaldehyde (3): An aqueous NaOH solution (1.21 g, 30 mmol) was added dropwise at room temperature and with stirring, over 5 min to an ethanolic solution of salicylaldehyde (3.70 g, 30 mmol). The reaction mixture immediately turned to a yellow coloured solid and the mixture was heated. The 25 mL ethanolic solution of 1,2-bis(bromomethyl)-benzene (4.00 g, 15 mmol) was added. The mixture was refluxed for 2 h and then allowed to come to ambient temperature. The white precipitate formed was filtered.

4-{[(3,4-Dihydroxyphenyl)methylene]amino}-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (4): A solution of 3,4-dihydroxybenzaldehyde (**1**) (2.50 g, 18 mmol) in dry ethanol (50 mL) was added dropwise to a solution of 4-aminoantipyrine (3.67 g, 18 mmol) in ethanol (20 mL). The solution was refluxed for 1 h and then allowed to reach ambient temperature. White powder was formed and recrystallized from ethanol.

1,5-Dimethyl-2-phenyl-4-{[(2,4,5-trihydroxyphenyl)methylene]amino}-1,2-dihydro-3H-pyrazol-3-one (5): To a solution of 2,4,5-trihydroxybenzaldehyde (**2**) (2.77 g, 18 mmol) in dry methanol (50 mL) was added dropwise a solution of 4-aminoantipyrine (3.65 g, 18 mmol) in dry methanol (20 mL) with constant stirring. The reaction mixture immediately turned to yellow colour. The mixture was refluxed for 1 h and then allowed to come to ambient temperature. A bright yellow product was formed.

2,2′-[1,2-Phenylenebis(methyleneoxy)]dibenzaldehyde (3) with 4-Amino-antipyrine Schiff Base (6): To a solution of 2,2′-[1,2-phenylenebis(methylene-oxy)]dibenzaldehyde (**3**) (1.73 g, 5 mmol) in dry methanol (20 mL) was added dropwise a solution of 4-aminoantipyrine (2.03 g, 10 mmol) in methanol (20 mL). The mixture was refluxed for 1 h, then allowed to come to ambient temperature. The formed pale yellow solid residue was filtered and recrystallized from aceto-nitrile.

2,2′-[1,2-Phenylenebis(methyleneoxy)]dibenzaldehyde (3) with furfuryl-amine Schiff Base (7): To a solution of 2,2′-[1,2-phenylenebis(methylene-oxy)]dibenzaldehyde (**3**) (1.73 g, 5 mmol) in dry methanol (20 mL) was added dropwise a solution of furfurylamine (0.97 g, 10 mmol) in dry methanol (20 mL) with stirring for 1 h. The solvent was evaporated and the oily products were recrystallized from *n*-heptane and a pale yellow product was formed.

RESULTS AND DISCUSSION

The compound **3** was synthesized from salicylaldehyde with 1,2-bis(bromomethyl)benzene in the presence of NaOH. The condensation of the appropriate amines and aldehydes gave the mono- and bis-imine compounds **4–7**. Yields, elemental analysis and physical data for all new compounds are given in Table-1.

TABLE-1
PHYSICAL CHARACTERIZATION AND ANALYTICAL DATA OF THE SCHIFF BASES

Compd.	m.f.	Colour	m.p. (°C)	Yield (%)	Elemental Analyses(%) Found (Calcd.)			M(M^++1) Calcd. (Found)
					C	H	N	
3.	$C_{22}H_{18}O_4$	White	110	78	76.63 (76.30)	5.39 (5.20)	–	–
4.	$C_{18}H_{17}N_3O_3$	White	*	83	66.74 (66.87)	5.32 (5.26)	12.87 (13.00)	–
5.	$C_{18}H_{17}N_3O_4$	Yellow	*	57	63.81 (63.72)	4.79 (5.01)	12.31 (12.39)	339 (340)
6.	$C_{44}H_{40}N_6O_4{\cdot}H_2O$	Pale yellow	218	73	72.20 (71.93)	5.60 (5.44)	11.28 (11.44)	716 (717)
7.	$C_{32}H_{28}N_2O_4$	Pale yellow	81	62	76.00 (76.19)	5.14 (5.56)	5.25 (5.55)	504 (505)

* Decomposition for compound **4** < 250°C and for compound **5** < 200°C.

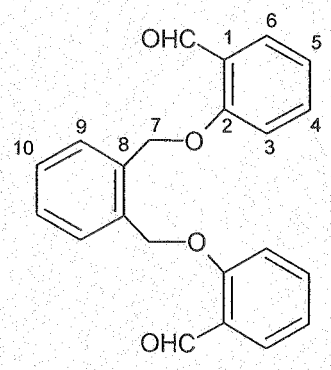
Infrared spectra: Characteristic IR data for the Schiff bases are given in Table-2. In the IR of compound **3** the aldehyde (C—H) and (C=O) peaks were detected at 2761 and 1695 cm^{-1}. The characteristic imine (C=N) stretching bands attributable to the azomethine group (CH=N) were observed at 1603, 1610, 1617, 1624 and 1635 cm^{-1} for compounds **4–7**, respectively.

TABLE-2
KEY IR BANDS (cm^{-1}) OF THE SCHIFF BASES

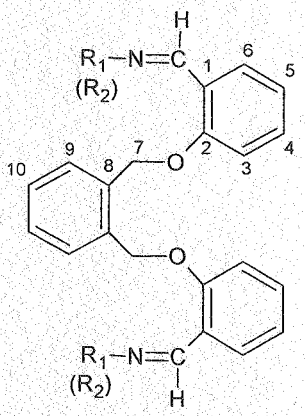
Compd.	ν(C=N)	$\nu(C—H)_{aliph.}$	ν(C=C)	$\nu(C—OC)_{arom.}$	ν(OH)	ν(HC=O)	ν(C—O)
3	–	2916; 2856	1599	1296; 1235	–	2761	–
4	1592	2945	1560	–	3491	–	1278
5	1617	2878	1560	–	3485	–	1290
6	1624	2919; 2887	1595	1299; 1245	–	–	–
7	1635	2922; 2880	1600	1293; 1235	–	–	–

A strong band observed around 1278 and 1290 cm^{-1} for the Schiff bases **4** and **5** has been assigned to phenolic C—O stretching. Furthermore, the very strong band observed in the region 3491–3485 cm^{-1} is attributable to the stretching vibration of the free phenolic hydroxy group. All other characteristic bands are also present in the expected region.

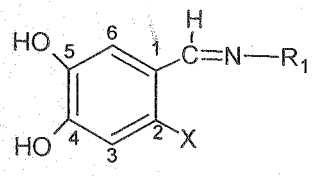
NMR spectra: The ^1H NMR data of the compounds **3–7** are listed in Table-3. In the ^1H NMR spectra, the integral ratio of the aliphatic and aromatic protons for compounds **3**, **6** and **7** indicates the molecules to be symmetric. The characteristic aldehyde proton (—CHO) of compound **3** was detected at 10.47 ppm. The azomethine protons were observed as singlets at 9.39, 9.48, 10.12 and 8.69 ppm for the Schiff bases **(4–7)**. The ^1H NMR spectra show that the aromatic protons are highly complicated in the region 7.06–7.86, 6.96–8.27 and 6.87–7.95 ppm for compounds **3, 6** and **7**. The aliphatic protons (—CH_2) of the dialdehyde **(3)** and Schiff bases **6** and **7** were seen at 5.34, 5.33 and 5.17 ppm, respectively. Phenazone's methyl groups (H_{14} and H_{15}) were detected as singlets at 2.43, 3.10 for compound **4**, 2.35, 3.15 for compound **5** and 2.51, 3.15 ppm for compound **6**. Two and three phenolic OH protons were observed as singlet and broad singlet at 8.84 and 9.65 in compound **4**, 8.70, 9.75 and 12.62 ppm in compound **5**. Aromatic protons of H_3 and H_6 were seen as singlet at 6.75 and 6.30 ppm in compound **5** but in other similar compound **4** these peaks were not observed because of overlapping with other aromatic protons.



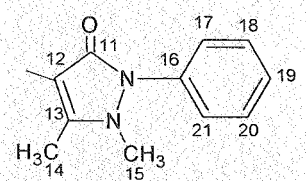
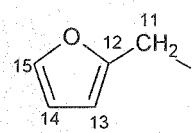
(3)



(6), (7)



(4), (5)

Compd.	X	R_1	R_2
4	H		
5	OH		
6	–		
7	–		

Numbering of the compound carbons and protons for NMR spectra

The ^{13}C NMR data of the compounds **3, 5–7** are listed in Table-4.

TABLE-3
^{1}H NMR SPECTRAL DATA. CHEMICAL SHIFTS (δ: ppm) ARE REPORTED IN ppm (s: SINGLET, s: MULTIPLET, bs: BROAD SINGLET).

Compd.	O=CH	N=CH	Ar-H	H_3	H_6	H_7	H_{11}	H_{13}	H_{14}	H_{15}	OH
3[b]	10.47 (s, 1H)	–	7.06–7.86 (m,12H)	[a]	[a]	5.34 (s, 4H)	–	–	–	–	–
4[c]	–	9.39 (s, 1H)	6.77–7.84 (m, 8H)	[a]	[a]	–	–	–	2.43 (s, 3H)	3.10 (s, 3H)	9.65 (s, 1H), 8.84 (s, 1H)
5[d]	–	9.48 (s, 1H)	7.37–7.55 (m, 5H)	6.75 (s, 1H)	6.30 (s, 1H)	–	–	–	2.35 (s, 3H)	3.15 (s, 3H)	12.62 (s, 1H), 9.75 (bs, 1H) 8.70 (bs, 1H)
6[b]	–	10.12 (s, 2H)	6.96–8.27 (m, 22H)	[a]	[a]	5.33 (s, 4H)	–	–	2.51 (s, 6H)	3.15 (s, 6H)	–
7[b]	–	8.69 (s, 2H)	6.87–7.95 (m, 14H)	[a]	[a]	5.17 (s,4H)	4.65 (s,4H)	6.16 (m,2H)	[a]	6.24 (m, 2H)	–

[a]Overlapping with other Ar-H peaks. [b]In $CDCl_3$, [c]In $CDCl_3$ + d_6-DMSO, [d]in d_6-DMSO.

TABLE-4
SELECTED ^{13}C-NMR SPECTRAL DATA (δ: ppm).

Compd.	O=CH	N=CH	C_7	$C_{(arom)}$[a]	C_{11}	C_{14}	C_{15}
3[c]	189.36	–	68.62	160.67; 136.05; 134.26; 129.27; 129.00; 128.95; 125.10; 121.30; 112.80	–	–	–
5[d]	–	154.97	–	159.97; 158.49; 150.54; 150.05; 138.77; 134.90; 129.62; 127.38; 124.95; 116.85; 115.49; 111.76; 103.72	b	10.29	35.93
6[C]	–	160.46	68.44	158.50; 154.24; 136.25; 134.75; 134.59; 134.33; 132.95; 129.24; 128.60; 128.41; 127.02; 124.86; 124.60; 121.26; 120.76; 113.40; 112.79	189.69	10.70	35.76
7[C]	–	158.72	68.45	157.85; 152.47; 142.14; 134.78; 132.31; 129.31; 128.99; 127.83; 124.66; 121.36; 112.32; 110.35; 107.44	57.44	b	b

[a]For compound **3**, $C_{1-6,\ 8-10}$; compound **4**, $C_{1-6,\ 12,\ 13,\ 16-21}$; compound **6**, $C_{1-6,\ 8-10,\ 12,\ 13,\ 16-21}$ and compound **7** $C_{1-6,8-10,12-15}$; [b]Overlapping with aromatic carbons; [c]in $CDCl_3$; [d]in D_6-DMSO.

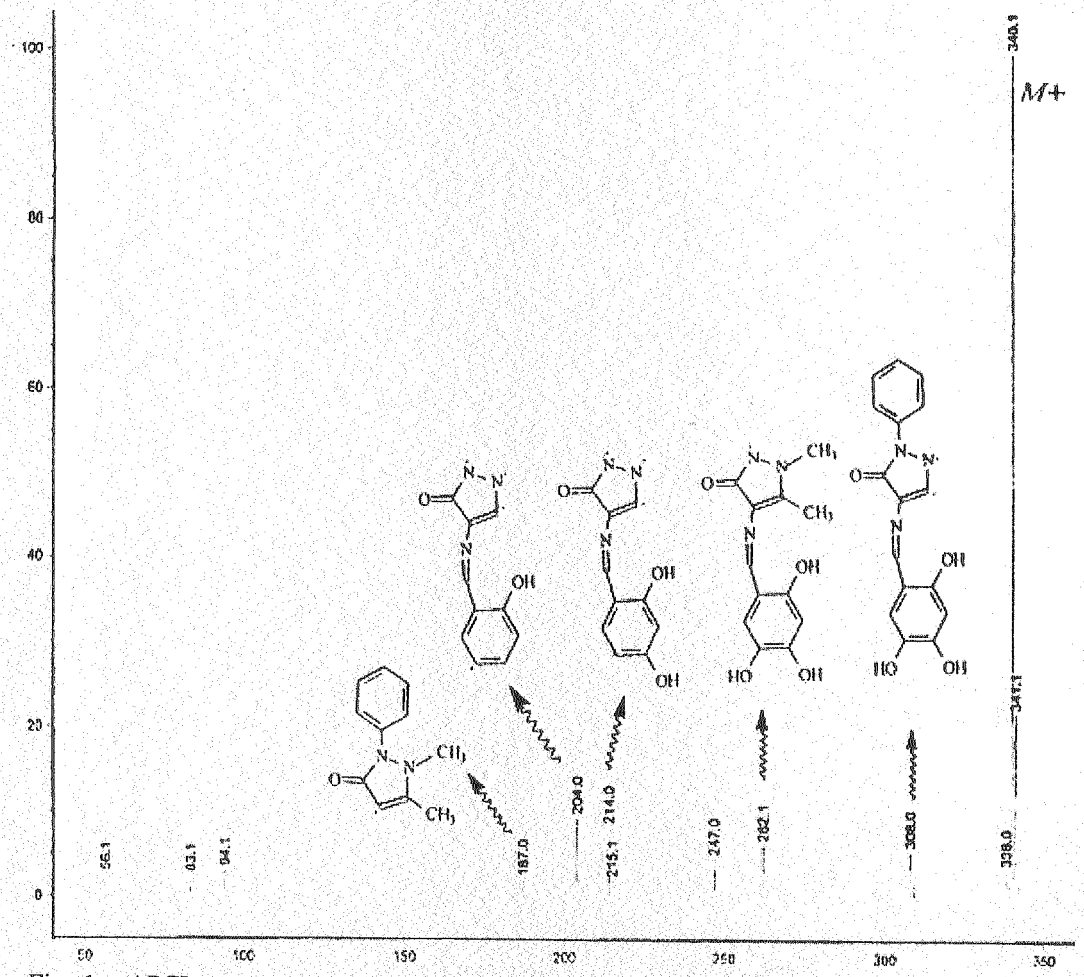


Fig. 1. APCI ms spectrum of compound **5**. Important fragments were found at m/z 308.0 (309.1 – 1); 262.1; 214.0 (215 – 1); 204.0 (201 + 3) and 187.

The signals of the aromatic carbons are equal to the number in the proposed symmetric structure of compounds **3, 6** and **7**. The aldehyde carbon (—CHO) of compound **(3)** was observed at 189.36 ppm. The characteristic aliphatic —$CH_2(C_7)$ carbons are detected at 68.62, 68.44 and 68.45 ppm for compounds **3, 6** and **7**, respectively. The other aliphatic carbons —CH_3 (C_{14} and C_{15}) of the compounds **5** and **6** are observed at 10.29, 35.93 and 10.70, 35.76 ppm, respectively. Although a total of 15 peaks were expected for the compound **5**, only 13 peaks were observed due to H_{17}, H_{18} with H_{20} and H_{21} symmetric carbons. For the compound **7** aliphatic $CH_2(C_{11})$ carbon was detected at 57.44 ppm. Aromatic carbons of all the compounds **3, 5–7** were detected in the expected region.

Mass spectra: In the APCI mass spectra of the mono- and bis-Schiff bases **(5, 6** and **7)** (Table-1) the respective molecular ion peaks ($M^+ + 1$) are observed at 340 (main in multiplet, 100%), 717 and 505 (highest peak in multiplet, 90% and 22%), respectively. Figs. 1–3 show only the important fragments of the

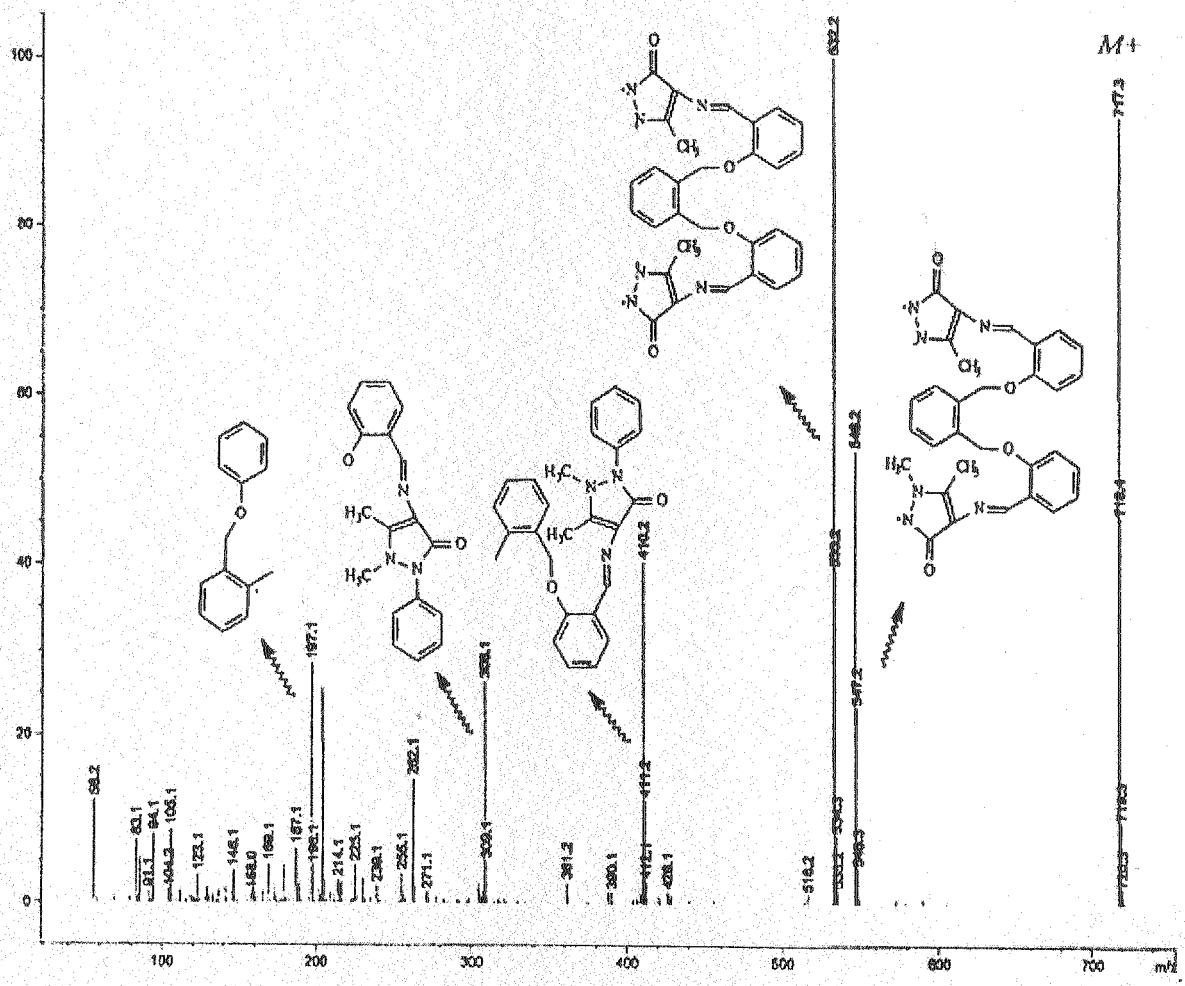


Fig. 2. APCI ms spectrum of compound **6**. Important fragments were found at m/z 547.2, 532.2, 411.2, 308.1 (306 + 2) and 197.1

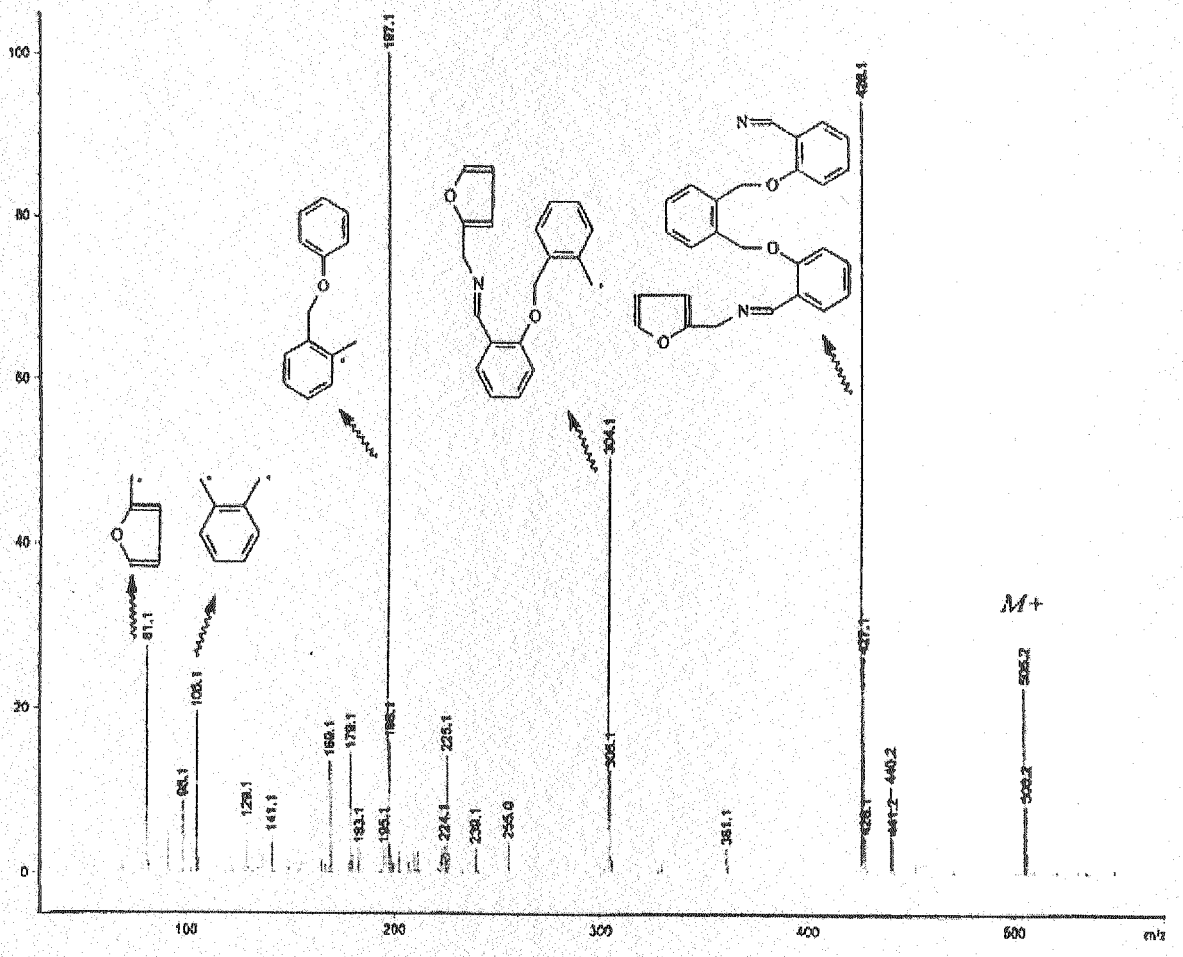


Fig. 3. APCI ms spectrum of compound **7**. Important fragments were found at m/z 426.1 (423 + 3), 304.1, 197.1, 105.1 (104 + 1) and 81.1

corresponding MS spectra obtained for compounds **5, 6** and **7**, respectively. The important fragments of compound **5** were found at m/z 308.0, 262.1, 214.0, 204.0 and 187, compound **6** at 547.2, 532.2, 410.2, 308.1 and 197.1 corresponding to loss of phenazone's methyl (—CH_3) and phenyl groups. The fragmentation pattern shows that the etheric chains are fragile under the experimental conditions in compound **6** and **7**[26]. The molecular ion peaks (M^+ + 1) and fragments of the compounds **5–7** support the proposed structures.

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