Some Imines and Azo Compounds Containing Furoxan Ring Synthesized from Methylisoeugenol

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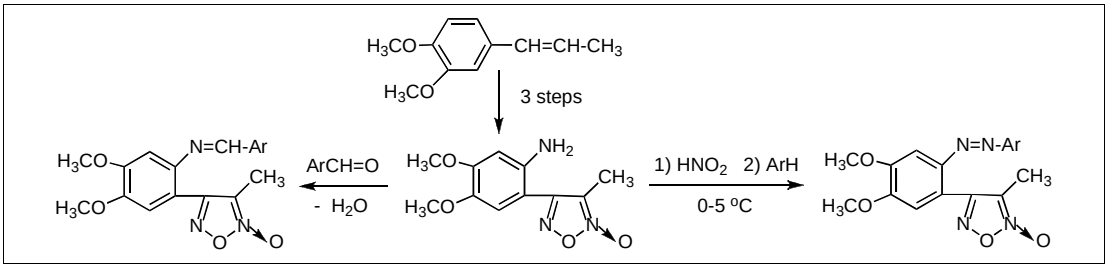

Some imines and azo compounds containing furoxan and benzene rings have been prepared starting from methylisoeugenol. The structure of reported compounds has been confirmed by elemental analysis, ms, uv, ir, and nmr spectroscopy. It is shown that, on treatment with $Na_2S_2O_4$, the nitro group on the benzene ring was reduced to an amino group, but the N→O group of furoxan ring was not. The ^{1}H- and ^{13}C nmr signals are assigned based on their spin-spin splitting patterns, in some cases, NOESY and HMBC spectra are used. The NOESY spectra indicate that the reported imines have *E*-configuration. Among 8 tested compounds, there are 5 compounds that exhibit anti-microbial activity toward Gr+ *S. aureus* at concentration 12.5μg /mL.

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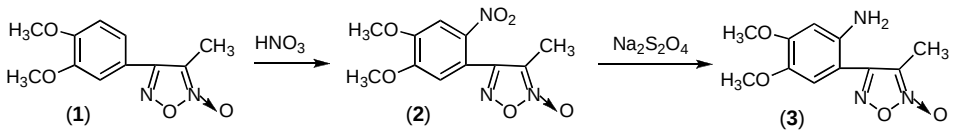
Introduction.

Furoxan derivatives display a variety of biological activities, their vasodilator activity and inhibition of platelet aggregation is well known [1,2,3]. Anti-parasitic properties, mutagenic, anticancer effects, anti-microbial, fulgicidal activities are listed [1,4]. These encouraged us to synthesize a few series of 4-aryl-3-methylfuroxans with a moiety of essential oil constituents and to find out if the resulting compounds have any biological action. In previous papers we reported on several imines and azo compounds containing a furoxan ring derived from anethole [5] and safrole [6]. Herein some analogous compounds synthesized from methylisoeugenol are described.

Results and Discussion.

A key intermediate for the title compounds, 4-(2-amino-3,4-dimethoxyphenyl)-3-methylfuroxan (**3**), was prepared from 4-(3,4-dimethoxyphenyl)-3-methylfuroxan as described in scheme I.

Scheme I



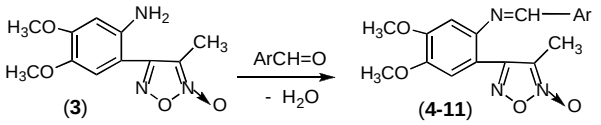
Although compound **1** has been prepared by reaction of methylisoeugenol with nitrous acid in 1894 year [7] nitro- and amino compounds **2** and **3** up to now were not described. The nitro compound **2** is obtained by nitration of **1** (see experimental). In the ^{1}H nmr spectrum of **1**, there are 3 signals of 3 aromatic protons: 7.30 (d, ^{4}J = 2 Hz); 7.32 (dd, ^{3}J=8, ^{4}J=2 Hz); 7.16 (d, ^{3}J=8 Hz). In the spectrum of **2** there are 2 singlets at 7.89 and 7.39 ppm, corresponding to the 2 aromatic protons at the *para*-position relative to one another. This indicates that, the nitro group is introduced into the *para*- position relative to the methoxy group (position 5, formula A).

When **2** is treated with iron, tin, zinc or tin(II) chloride in the presence of hydrochloric or acetic acids at 20 - 80 °C, we did not obtain the expected amine, hence, the starting nitro compound is not reduced under these conditions. Attempts to reduce **2** in toluene with sodium dithionite in alkaline medium

according to the reported procedure for its analogue [6] was unsuccessful. When anisole (methyl phenyl ether) was used as the solvent in place of toluene we receive **3** in 40% yield. This is acceptable since the furoxan ring was partially decomposed in strong alkaline medium. The ir spectrum of **3** shows two peaks at 3461 and 3359 cm^{-1} resulting from the N-H stretch of primary amine. The resonance of the NH_2-group appears as a broad singlet at 5.34 ppm. The EI ms spectrum of **3** shows its molecular weight is 251 (98.5%). These indicate that, when **2** is treated with $Na_2S_2O_4$, the nitro group on benzene ring is reduced and the N→O group on the furoxan ring is not.

The condensation of **3** with aromatic aldehydes was carried out in boiling ethanol for 8-10 h with or without acidic catalyst to give the imines **4-11** (scheme II).

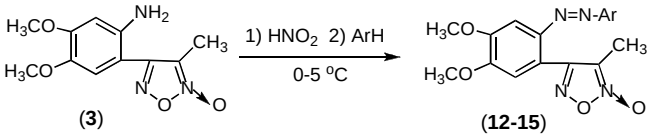
Scheme II



Ar: 4-$NO_2C_6H_4$ (**4**), 3-$NO_2C_6H_4$ (**5**), 3,4-$OCH_2OC_6H_3$ (**6**), 3-pyridyl (**7**), 2-ClC_6H_4 (**8**), 4-ClC_6H_4 (**9**), 4-FC_6H_4 (**10**), 4-$CH_3OC_6H_4$ (**11**).

Diazotizing **3** following reaction with phenols affords the azo compounds **12-15** (scheme III).

Scheme III



Ar: 3-CH_3-4-HOC_6H_3 (**12**), 3-Cl-4-HOC_6H_3 (**13**), 2-NO_2-4-HOC_6H_3 (**14**), 4-HOC_6H_4 (**15**).

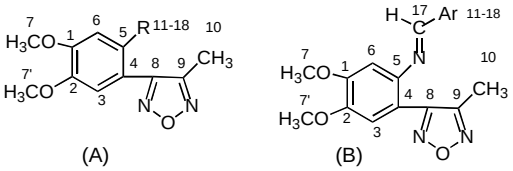
The obtained imines are yellow crystals, and the azo compounds are orange or red crystalline solids. The structures of the compounds were confirmed by uv-, ir-, ms- and nmr spectroscopy.

EI- ms data of the examined compounds agree with the expected molecular weight (see experimental). The peak corresponding to the loss of an oxygen atom, $[M-16]^{+\cdot}$, is very weak, while the peak corresponding to the loss of two NO molecules, $[M-60]^{+\cdot}$, is intense. These primary fragmentations are characterized for 3-methyl-4-arylfuroxans (scheme IV).

The compound **1** absorbs at 294 nm, while nitro-, amino-, and imine-derivatives (**2**, **3** and **4-11**) have a band in region near 338-358 nm (logε 3.8-4.7). This red shift is associated with the extension of conjugation in the molecules **2-11** compared with **1**. The azo compounds have bands in the visible region 393-455 nm (logε 3.9-4.6) due to the azo chromophore.

The NMR data of the examined compounds were most informative with respect to their structures. The numeration of the examined compounds especially for analysis of nmr spectra is shown as in formula A and B (Scheme V).

Scheme V



The resonances of 3-H-10–H are listed in Table 1, the resonances of 12-H-17–H are listed in Table 2. The assignment of the proton signals is based on their spin-spin splitting patterns, and in some cases, based also on NOESY- and HMBC spectra. For example, the NOESY spectrum of **9** (formula B, Ar = 4-ClC_6H_4) is presented in Figure 1.

The singlet at 8.82 ppm has been assigned to 17-H, its cross peak (*a)* shows that singlet at 7.27 ppm corresponds to 6-H, thus the next singlet (7.17 ppm) was assigned to 3-H. The cross peak (*b)* shows doublet at 7.83 ppm corresponding to 12-H, thus the next doublet (7.60 ppm) was assigned to 13-H. Since 6-H is adjacent to 7-H and 3-H is adjacent to 7'-H (formula B), the cross peaks (*c)* and (*d)* allow one to distinguish signals of 7-H and 7'-H. The cross peaks between 17-H (-CH=N-) and 6-H in the NOESY spectrum of **9** and of the other imines (formula B) also demonstrate that the imine group (-N=CH-) has *E*-configuration (formula B).

Scheme IV

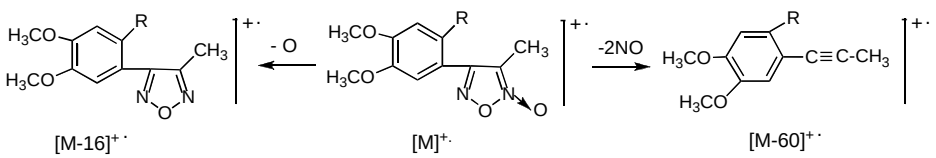


Table 1

Resonance signals from H-3-H-10 of examined compounds (formula A), δ, ppm, J Hz.

Compd	3-H	6-H	7-H	7'-H	10-H	Other
1	7.30; d; ^{4}J 2	7.16; d; ^{3}J 8	3.84; s	3.83; s	2.31; s	7.32; dd; 5-H
2	7.39; s	7.89;.s	3.97; s	3.94; s	2.01; s	-
3	6.81; s	6.50; s	3.75; s	3.67; s	2.17; s	5.34; s; NH_2
4	7.20; s	7.35; s	3.94; s	3.86; s	2.07; s	-
5	7.20; s	7.35; s	3.94; s	3.85; s	2.10; s	-
6	7.18; s	7.19; s	3.92; s	3.83; s	2.06; s	-
7	7.18; s	7.29; s	3.93; s	3.94; s	2.07; s	-
8	7.20; s	7.22; s	3.94; s	3.85; s	2.07; s	-
9	7.17; s	7.27; s	3.93; s	3.84; s	2.07; s	-
10	7.18; s	7.28; s	3.94; s	3.84; s	2.08; s	-
11	7.15; s	7.20; s	3.93; s	3.83; s	2.07; s	-
12	7.30; s	7.47; s	3.92; s	3.92; s	1.97; s	-
13	7.33; s	7.49; s	3.93; s	3.92; s	1.98; s	-
14	7.339; s	7.343; s	3.93; s	3.88; s	1.96; s	-
15	7.30; s	7.48; s	3.93; s	3.92; s	1.97; s	-

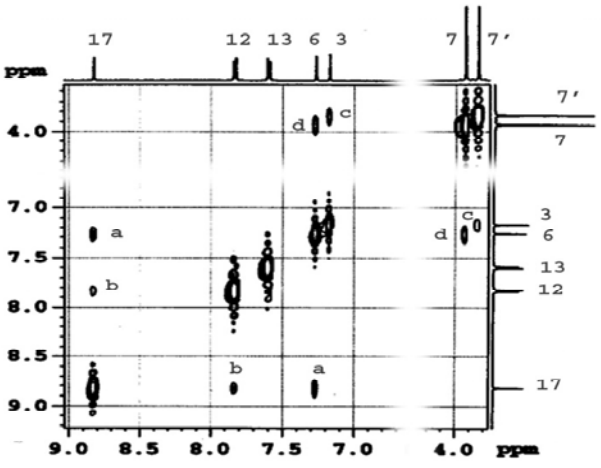


Figure 1. NOESY spectrum of compound **9**.

It is interesting that the NOESY spectrum of **1** yields cross peaks between the methyl group (10-H) and either of 3-H, 5-H. This demonstrates that the furoxan and the benzene rings rapidly rotate on the nmr time scale or two rings could not be coplanar.

Gasco and colleges [8] showed that the chemical shift of a ring methyl group adjacent to the N-oxide oxygen of furoxans occurs at 2.30-2.33 ppm, while a ring methyl group remote from it, at 2.50-2.53 ppm. The signal of the ring methyl group (10-H) of **1-15** appears as a singlet at 1.96-2.08 ppm (Table 1) indicating that the methyl group is at position 3 of the furoxan ring.

The ^{13}C NMR data are given in Tables 3 and 4. The assignment of the ^{13}C signals are based on their chemical shift and HMBC spectra of the examined compounds (**1,**

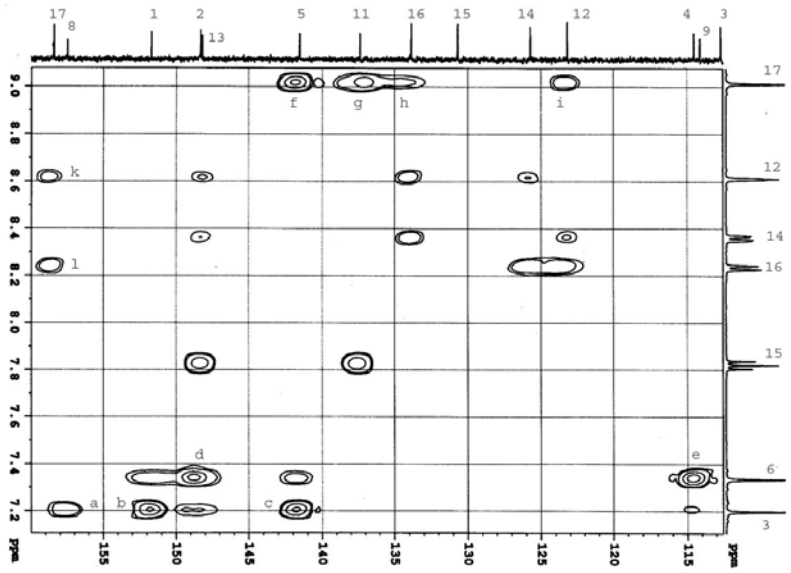
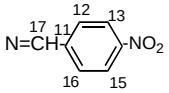
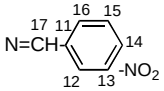
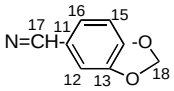
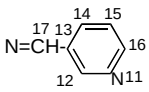
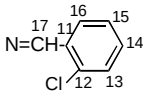
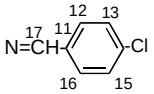
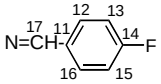
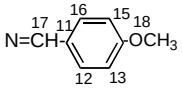
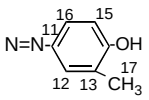
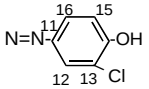
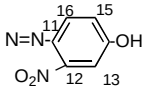
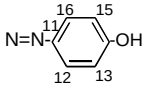


Figure 2. A part of HMBC spectrum of compound **5**.

Table 2

Resonance signals from 12-H-17–H of examined compounds (formula A), δ,ppm, J Hz

No	R	12-H	13-H	14-H	15-H	16-H	Others
4		8.06; d ^{3}J 8.5	8.37; d ^{3}J 8.5	-	8.37; d ^{3}J 8.5	8.06; d ^{3}J 8.5	8.99; s; 17-H
5		8.61; s	-	8.36; dt ^{3}J 8; ^{4}J 1.5	7.82; t ^{3}J 8	8.23; d ^{3}J 8	9.01; s; 17-H
6		7.27; d ^{4}J 1.5	-	-	7.07; d ^{3}J 8	8.37; dd ^{3}J8.5; ^{4}J1.5; ^{4}J1.5	8.68; s; 17-H 6.12; s; 18-H
7		8.96; d ^{4}J 1.5	-	8.16; d ^{3}J 7.5	7.55; dd ^{3}J 7.5; 5	8.69; dd ^{3}J5; ^{4}J 1.5	8.89; s; 17-H
8		-	7.59;dd ^{3}J 8; ^{4}J 1	7.55; td ^{3}J 8; ^{4}J1.5	7.48;t ^{3}J 8	7.92; dd ^{3}J 8; ^{4}J1.5	8.98; s; 17-H
9		7.83; d ^{3}J 8,5	7.60; d ^{3}J 8,5	-	7.60; d ^{3}J 8,5	7.83; d ^{3}J 8,5	8.82; s; 17-H
10		7.88; dd; ^{3}J 8.5; ^{4}J 6 (a)	7.37; t; ^{3}J 9 (b)	-	7.37; t ^{3}J 9 (b)	7.88; dd ^{3}J 8.5; ^{4}J 6 (a)	8.81; s; 17-H
11		7.77;d ^{3}J 8.5	7.08;d ^{3}J 8.5	-	7.08;d ^{3}J 8.5	7.77;d ^{3}J 8.5	8.71; s; 17-H 3.83; s; 18-H
12		7.56; d ^{4}J 2	-	-	6.94; d ^{3}J 8.5	7.47;dd ^{3}J 9; ^{4}J 2	2.19; s; 17-H 10.29; s; OH
13		7.75;d ^{4}J 2	-	-	7.15;d ^{3}J 8.5	7.63;dd ^{3}J8.5; ^{4}J2	11.16; s; OH
14		-	7.30;d ^{4}J 2	-	7.16;dd ^{3}J 9; ^{4}J 2	7.59;d ^{3}J 9	-
15		7.65;d ^{3}J 8,5	6.93;d ^{3}J 8,5		6.93;d ^{3}J 8,5	7.65;d ^{3}J 8,5	10.35; s; OH

2, 3, 4, 5, 7, 8, 9, 11, 12,13, 14, 15). For example, HMBC spectrum of **5** (formula B, Ar = 3-$O_2NC_6H_4$) is presented in Figure 2.

The signals of the protons 3-H, 6-H, 7-H, 10-H and 17-H are always assigned unambiguously. The signals of ring carbons are thus identified. For example, in Figure 2, three cross peaks of 3-H (*a, b, c*) show signals of 8-C (157.51), 1-C (151.44), 5-C (141.55); two cross peaks of 6-H (*d, e*) show signals of 2-C (148.33), 4-C (114.51); the cross peaks of 17-H (*f, g, h, i*) show signals of 5-C, 11-C, 12-C and 16-C; the cross peaks of 17-C (*k, l*), in turn, show signals of 12-H, 16-H; and so on.

Chemical shift of 1-C- 9–C significantly changed from **1** to **2** and **3,** but little changed from **4** to **15** (Table 3). Two carbon atoms of the furoxan ring show a remarkably large chemical shift difference in the ^{13}C nmr: δ (8–C) 157–158, δ(9–C) 113–114 ppm. Their assignment is based on HMBC spectra: both 9-C and 8-C give cross peaks with methyl protons 10-H but only 8-C forms cross peak with 3-H (peak a, Figure 2). The N-oxide group

Table 3

Resonance signals from 1-C - 10-C of examined compounds (formula A), δ, ppm.

Comp.	1-C	2-C	3-C	4-C	5-C	6-C	7-C	7'-C	8-C	9-C	10-C
1	151.11	149.13	110.43	118.54	120.78	111.99	55.67	55.67	157.06	112.91	9.01
2	153.34	150.34	114.06	114.29	140.23	108.46	56.77	56.46	156.43	113.70	7.57
3	152.24	140.18	113.74	99.90	142.57	100.19	55.22	56.40	157.02	113.60	9.07
4	151.72	148.55	112.71	114.85	141.61	102.14	55.98	56.00	157.52	114.19	8.77
5	151.71	148.33	112.68	114.51	141.55	102.19	55.96	55.96	157.51	114.11	8.80
7	151.78	148.16	112.69	114.28	142.08	102.19	56.00	56.00	157.65	114.25	8.84
8	151.71	148.08	112.70	114.02	142.36	102.40	55.93	55.93	157.44	113.82	8.72
9	151.70	147.90	112.62	114.15	142.11	102.15	55.89	55.89	157.62	114.01	8.76
10	151.79	147.81	112.70	114.22	142.40	102.24	55.95	55.95	157.74	113.88	8.83
11	151.76	147.35	112.61	113.46	142.85	102.10	55.84	55.34	157.88	114.22	8.84
12	151.52	151.14	112.40	118.66	143.68	98.29	56.10	55.69	157.36	114.30	8.52
13	151.71	151.51	112.46	119.41	143.40	98.33	56.20	55.78	157.07	114.28	8.50
14	152.36	151.42	112.63	120.11	143.53	98.34	56.27	55.63	156.69	114.12	8.37
15	151.53	151.26	112.43	118.89	143.62	98.24	56.12	55.72	157.30	114.32	8.49

exerts a shielding influence on 9-C and 10-C. Thus, the 9-C appears upfield of the 8-C by 42-44 ppm. These data are in good agreement with those of references [10,11].

It is interesting that the imine- (-N=CH-) and azo- (-N=N-) groups result in down-field shifts for 6-H of **4-15** as well as group -NO_2 - for 6-H of **3** (Table 1), but the same groups cause up-field shifts for 6-C of **4-15** as well as group -NH_2 - for 6-C of **3**. As expected, for **4-11**, the ^{13}C of imine group (17-C) resonated at the lowest field (Table 4).

Table 4

Resonance signals from 11-C - 18–C of examined compounds, (formula A), δ, ppm,J, Hz
(The numeration was shown in Table 2)

Com.	11-C	12-C	13-C	14-C	15-C	16-C	17-C	18-C
4	141.33	129.52	124.20	148.85	124.20	129.52	158.45	-
5	137.38	123.18	148.21	125.72	130.69	133.86	158.41	-
7	-	150.42	131.48	134.80	124.29	152.08	158.23	-
8	132.54	134.93	130.13	132.97	127.75	128.22	156.33	-
9	134.64	130.10	129.09	136.17	129.09	130.10	159.15	-
10	132.55 d $^4J_{F,C}$ 2.8	130.93 d $^3J_{F,C}$ 9.1	116.11 d $^2J_{F,C}$ 22	164.08 d $^1J_{F,C}$ 250	116.11 d $^2J_{F,C}$ 22	130.93 d $^3J_{F,C}$ 9.1	159.20	-
11	126.69	130.35	114.41	162.05	114.41	130.35	159.62	55.87
12	144.91	126.18	125.06	159.36	115.21	121.66	15.89	-
13	145.09	124.41	120.84	156.44	117.04	123.23	-	-
14	135.61	148.68	110.15	160.91	119.82	121.18	-	-
15	145.06	124.85	116.14	161.14	116.14	124.86	-	-

It is interesting that the imine- (-N=CH-) and azo- (-N=N-) groups result in down-field shifts for 6-H of **4-15** as well as group -NO_2 - for 6-H of **3** (Table 1), but the same groups cause up-field shifts for 6-C of

The compounds **7, 8, 9, 11, 12, 13, 14, 15** are tested for anti microbial activities. The results are listed in Table 5.

It is seen that the compounds 7, 8, 9, 11, and 14 showed high activity toward *Gr*$^+$ ***S. aureus***.

Table 5

The minimum inhibition concentration (MIC) (μg/ml) of examined compounds against some microorganism.

Compd.	*E.coli*	*B.subtillis*	*S.aureus*	*F.oxysprorum*	*C.albicans*
7	25	-	12.5	-	50
8	50	25	12.5	-	-
9	50	-	12.5	-	-
11	12.5	12.5	12.5	50	-
12	50	-	25	-	-
13	100	100	100	100	100
14	-	-	12.5	25	-
15	-	-	50	-	-

EXPERIMENTAL

IR spectra were recorded on a IMPACK- 410 NICOLET spectrometer in KBr discs at 400-4000 cm^{-1}. The uv spectra was recorded in ethanol at concentration 10^{-4}–10^{-5} *M* using uv-vis Cintra spectrometer. The EI mass spectra of examined compounds were recorded using 5989B Hewlett-Packard mass spectrometer. Nmr spectra were recorded on Bruker AVANCE 500 MHz spectrometer, all at 298-300 K, in d_6-DMSO with TMS as the internal standard. The antimicrobial activities toward *E. coli, B. subtillis, S. aureus, F. oxysprorum, C. albicans* were tested at the Experimental biological Lab - institute of Chemistry of natural compounds (in Hanoi), using the method "Vande Bergher and Vietlink " [9].

4-(3,4-Dimethoxyphenyl)-3-methylfuroxan (**1**).

Methylisoeugenol (17.8 g, 0.1 mol) was dissolved in 50 mL of acetic acid. To this solution $NaNO_2$ (15.1 g, 0.12 mol) was added in portions over 4 hours and stirred at 25-30 °C for an additional hour. The reaction mixture was poured into 100 mL of water. The organic layer was separated, washed with water. The residual was dissolved in 50 mL of hot ethanol and allowed to cool to room temperature. The resulting yellow precipitate was collected, recrystallized from ethanol and then from benzene to give light yellow needle crystals. The yield 20.3 g (86%), mp 118-119 °C (118 °C [1]). ir (KBr): 3088, 3013 (C-H), 1605, 1587 (ring); uv (ethanol), λmax, nm/logε: 294/3.8, 270/3.9, 208/4.2; ms: m/z 236(M^+), 220(M^+-O), 176(M^+-2NO); ^{1}H nmr and ^{13}C nmr see Table 1, 2, 3 and 4.

Anal. Calcd. for $C_{11}H_{12}N_2O_4$: C, 55.93; H, 5.08; N, 11.86. Found: C, 55.84; H, 4.98; N, 11.55.

4-(4,5-Dimethoxy-2-nitrophenyl)-3-methylfuroxan (**2**).

To a stirred solution of 11.8 g (0.05 mol) of **1** in 40 mL of acetic acid, at room temperature was slowly added a mixture of HNO_3 (12 mL, D = 1.41 g/mL) and H_2SO_4 (20 ml, D= 1.84 g/mL). The reaction mixture was stirred at 50-60 °C for 3 hours. The reaction mixture was allowed to cool to room temperature. The solid was collected and washed with water, with Na_2CO_3 solution, and then with water to neutralize. The resulting precipitate was recrystallized from ethanol. The yellow needle crystals were dried in vacuum at 50 °C for 2 hours. The yield 9.8 g (70%), mp 162-3 °C. ir (KBr): 3086, 3006(C-H), 1616,1576 (ring); uv (ethanol), λmax, nm/logε: 338/3.8, 250/4.3, 200/4.4; ms: m/z 281(M^+), 265(M^+-O), 221(M^+-2NO); ^{1}H- and ^{13}C nmr see Table 1, 2, 3 and 4.

Anal. Calcd. for $C_{11}H_{11}N_3O_6$: C, 46.97; H, 3.91; N, 14.94. Found: C, 46.62; H,4.05; N, 15.16.

4-(2-Amino-4,5-dimethoxyphenyl)-3-methylfuroxan (**3**).

To a vigorously stirred solution of 14.05 g (0.05 mol) of **2** in 150 mL of anisole, at 90°C was slowly added a solution of $Na_2S_2O_4$ (52.2 g, 0.3 mol) and NaOH (12 g, 0.3 mol). The reaction mixture was stirred at 90°C for 2 hours additional. The organic layer was extracted and allowed to cool to room temperature. The resulting precipitate was collected, recrystallized from ethanol and then from benzene to give light yellow needle crystals. The yield 3.89 g (31%), mp 175-176°C. ir (KBr): 3461, 3359, 1620 (NH_2), 3017, 2996 (C-H), 1597, 1528 (ring); uv (ethanol), λmax, nm/logε: 346/3.3, 253/3.9, 207/4.3; ms: m/z 251 (M^+), 235(M^+-O), 191 (M^+-2NO); ^{1}H- and ^{13}C nmr see Table 1, 2, 3 and 4.

Anal. Calcd. for $C_{11}H_{13}N_3O_4$: C, 52.59; H, 5.18; N, 16.73. Found: C, 52.42; H, 4.89; N, 17.11.

General Procedure for the Preparation of Imines **4**-**11**.

A solution of 1 mmol of **3** and 1 mmol of an aromatic aldehyde dissolved in 20 mL of ethanol (for the preparation of **6**, **9** and **11**, 2 drops of acetic acid was also added) was refluxed over 8-10 hours. Upon cooling the mixture to room temperature, the resulting yellow precipitate was collected and recrystallized.

3-Methyl-4-[2-(4-nitrobenzylyden)amino-4,5-dimethoxyphenyl]-furoxan (**4**).

This compound was obtained as yellow cristalline solid (from ethanol); The yield 0.27 g (70%), mp 216-7 °C. ir (KBr): 3029, 2973 (C-H), 1600, 1528, 1514 (ring); uv (ethanol), λmax, nm/logε: 345/4.7, 258/4.3, 207/4.2;x ms: m/z 323 (M^+), 307 (M^+-O), 293 (M^+-NO), 263 (M^+-2NO); ^{1}H- and ^{13}C nmr see Table 1, 2, 3 and 4.

Anal. Calcd. for $C_{18}H_{16}N_4O_6$: C, 56.27; H, 4.16; N, 14.57. Found: C, 55.92; H, 4.42; N, 14.18.

3-Methyl-4-[2-(3-nitrobenzylyden)amino-4,5-dimethoxyphenyl]-furoxan (**5**).

Yellow needles (from ethanol); the yield 0.25 g (65%), mp 219-220°C. ir (KBr): 3086, 3021, 2967 (C-H), 1611, 1521 (ring); uv (ethanol), λmax, nm/logε: 355/3.8, 257/4.3, 240/4.3, 206/4.29 ; ^{1}H- and ^{13}C nmr see Table 1, 2, 3 and 4.

Anal. Calcd. for $C_{18}H_{16}N_4O_6$: C, 56.27; H, 4.16; N, 14.57. Found: C, 55.97; H, 3.83; N,14.72.

3-Methyl-4-[2-(3,4-methylendioxybenzylyden)amino-4,5-di-methoxyphenyl]furoxan (**6**).

Yellow needles (from ethanol); the yield 0.23 g (60%), mp 220°C. ir (KBr): 3108, 2972, (C-H), 1605,1530 (ring); uv (ethanol), λmax, nm/logε: 350/4.1, 254/4.7,218/4.9 208/4.8; ^{1}H- and ^{13}C nmr see Table 1, 2, 3 and 4.

Anal. Calcd. for $C_{19}H_{17}N_3O_6$: C, 59.55; H, 4.44; N, 10.96. Found: C, 59.25; H, 4.22; N, 10.83.

3-Methyl-4-[2-(3-pyridymethylyden)amino-4,5-dimethoxyphen-yl]furoxan (**7**).

Yellow needles (from ethanol); The yield 0.30 g (90%), mp 213-4°C. ir (KBr): 3007, 2969, 22844 (C-H), 1611,1532 (ring); uv (ethanol), λmax, nm/logε: 357/3.6, 258/3.9; ^{1}H- and ^{13}C nmr see Table 1, 2, 3 and 4.

Anal. Calcd. for $C_{17}H_{16}N_4O_4$: C, 60.02; H, 4.70; N, 16.47. Found: C, 59.67; H, 4.67; N, 16.81.

3-Methyl-4-[2-(2-chlorobenzylyden)amino-4,5-dimethoxyphen-yl]furoxan (**8**).

Yellow needles (from ethanol); the yield 0.32 g (85%), mp 187-8 °C. ir (KBr): 3003, 2964, 2843, (C-H), 1604, 3164 (ring); uv (ethanol), λmax, nm/logε: 356/4.1, 263/4.5, 208/4.6; ^{1}H- and ^{13}C nmr see Table 1, 2, 3 and 4.

Anal. Calcd. for $C_{18}H_{16}N_3ClO_4$: C, 57.85; H, 4.28; N, 11.24. Found: C, 57.72; H, 4.41; N, 11.54

3-Methyl-4-[2-(4-chlorobenzylyden)amino-4,5-dimethoxyphen-yl]furoxan (**9**).

Yellow needles (from ethanol); the yield 0.33 g (89%), mp 184-5 °C. ir (KBr): 2994, 2947, 2844 (C-H), 1605, 1530, (ring);

uv (ethanol), λmax, nm/logε: 350/4.3, 267/4.6; ^{1}H- and ^{13}C nmr see Table 1, 2, 3 and 4.

Anal. Calcd. for $C_{18}H_{16}N_3ClO_4$: C, 57.85; H, 4.28; N, 11.24. Found: C, 57.69; H, 3.96; N, 11.60

3-Methyl-4-[2-(4-florobenzylyden)amino-4,5-dimethoxyphenyl]furoxan (**10**).

This compound was obtained as light-yellow needles (from ethanol); The yield 0.27 g (75%), mp 178-9°C. ir (KBr): 3017, 2945, 2845 (C-H), 1621, 1598, 1525 (ring); uv (ethanol), λmax, nm/logε: 348/3.9, 258/4.1, 213/4.2; ^{1}H- and ^{13}C nmr see Table 1, 2, 3 and 4.

Anal. Calcd. for $C_{18}H_{16}N_3FO_4$: C, 60.50; H, 4.48; N, 11.76. Found: C, 60.78; H, 4.31; N, 11.97

3-Methyl-4-[2-(4-methoxybenzylyden)amino-4,5-dimethoxyphenyl]furoxan (**11**).

Yellow needles (from ethanol); The yield 0.30 g (81%), mp 179-180°C. ir (KBr): 3004, 2955, 2857(C-H), 1605, 1569, 1530, (ring); uv (ethanol), λmax, nm/logε: 345/4.2, 280/4.3, 235/4.27; ^{1}H- and ^{13}C nmr see Table 1, 2, 3 and 4.

Anal. Calcd. for $C_{19}H_{19}N_3O_5$: C, 61.79; H, 5.15; N, 11.38. Found: C, 61.65; H, 5.05; N, 11.68

General Procedure for the Preparation of Azo Compounds **12-15**.

At 0-5 °C, 1.5 mL of 1 *M* $NaNO_2$ solution was slowly added to a solution of 1 mmol of **3** in 1 mL of 3 *M* HCl solution. The resulting solution was slowly added to a solution of 1 mmol of a phenol in 3 ml of 1.5 *M* NaOH solution. The mixture was neutralized with diluted HCl solution. The precipitate was collected and recrystallized.

3-Methyl-4-[2-(3-methyl-4-hydroxyphenyl)diazenyl-4,5-dimethoxyphenyl]furoxan (**12**).

This compound was obtained as orange needles (from etanol); the yield 0.29 g (79%), mp 205-6 °C. ir (KBr): 3400 (OH), 3100, 3040, 2950, 2860 (C-H), 1593, 1521 (ring); uv (ethanol), λmax, nm/logε: 425/shoulder, 394/4.3, 257/4.2, 207/4.1; ^{1}H- and ^{13}C nmr see Table 1, 2, 3 and 4.

Anal. Calcd. for $C_{18}H_{18}N_4O_5$: C, 58.38; H, 4.86; N, 15.13. Found: C, 58.67; H, 4.61; N, 15.39

3-Methyl-4-[2-(3-chloro-4-hydroxyphenyl)diazenyl-4,5-dimethoxyphenyl]furoxan (**13**).

This compound was obtained as yellow crystalline solid (from etanol); the yield 0.28 g (72%), mp 119-221°C. ir (KBr): 3439 (OH), 3090, 2943, 2844 (C-H), 1606, 1527, (ring); uv (ethanol), λmax, nm/logε: 425/shoulder, 393/4.6, 260/4.7, 200/4.8; ^{1}H- and ^{13}C nmr see Table 1, 2, 3 and 4.

Anal. Calcd. for $C_{17}H_{15}N_4O_5Cl$: C, 52.28; H, 3.84; N, 14.34. Found: C, 51.95; H, 3.92; N, 14.67

3-Methyl-4-[2-(2-nitro-4-hydroxyphenyl)diazenyl-4,5-dimethoxyphenyl]furoxan (**14**).

This compound was obtained as light red crystalline solid (from dioxane); the yield 0.25 g (62%), mp 221-3 °C. ir (KBr): 3441 (OH), 3092, 2951, 2843 (C-H), 1606, 1529 (ring); uv (ethanol), λmax, nm/logε: 455/shoulder, 398/3.8, 263/4.0, 205/4.5; ^{1}H- and ^{13}C nmr see Table 1, 2, 3 and 4.

Anal. Calcd. for $C_{17}H_{15}N_5O_7$: C, 50.87; H, 3.74; N, 17.45. Found: C, 51.16; H, 3.57; N, 17.67

3-Methyl-4-[2-(4-hydroxyphenyl)diazeny)-4,5-dimethoxyphenyl]furoxan (**15**).

This compound was obtained as orange crystalline solid (from ethanol); the yield 0.30 g (83%), mp 209-210 °C. ir (KBr): 3451(OH), 3105, 3062, 2951 (C-H), 1600, 1529 (ring); uv (ethanol), λmax, nm/logε: 425/shoulder, 392/4.4, 255/4.3; ^{1}H- and ^{13}C nmr see Table 1, 2, 3 and 4.

Anal. Calcd. for $C_{17}H_{16}N_4O_5$: C, 57.30; H, 4.49; N, 15.73. Found: C, 57.66; H, 4.61; N, 15.45.

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