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SYNTHESIS SOME IMINES AND AZO COMPOUNDS DERIVED FROM 4-(2-AMINO-3,4-DIMETHOXYPHENYL)-3-METHYLFUROXAN

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SUMMARY

Some imines and azo compounds containing furoxan and benzene rings has been prepared starting from 4-(2-amino-3,4-dimethoxyphenyl)-3-methylfuroxan. The structure of reported compounds has been confirmed by UV, IR, a NMR spectroscopy.

I - INTRODUCTION

The furoxan derivatives have been shown to possess pharmacological activities. Some are depressants of the central nervous system, or of frog flesor muscle reflexes, or are reported as potential antitrypanosomal drugs [1], hypoxic cytotoxins [2, 3], vasodilatory activities [4 - 7]. These compounds have been shown to possess NO - mimetic pharmacological activities [8, 9]. In previous paper [10] we reported on the preparation and structure of 4-(2-amino-3,4-dimethoxyphenyl)-3-methylfuroxan starting from eugenol, herein some imines and azo compounds derived from this amine are described.

II - EXPERIMENT

1. Physical measurements

IR spectra were recorded on a IMPACK-410 NICOLET spectrometer in KBr discs at 400 ÷ 4000 cm^{-1}.

The UV spectra are recorded in ethanol at concentration 10^{-4} — 10^{-5} M using UV-Vis Cintra 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.

2. Preparation

General procedure for the preparation of imines ***1 ÷ 5***

A solution of 1 mmol of 4-(2-amino-3,4-dimethoxyphenyl)- 3-methylfuroxan (Am) and 1 mmol of an aromatic aldehyde dissolved in 20 ml of ethanol was refluxed over 8-10 hours. The mixture was allowed to stand at room temperature. The resulting yellow precipitate was collected and recrystallized from etanol.

The preparation of azo compounds ***6*** *and* ***7***

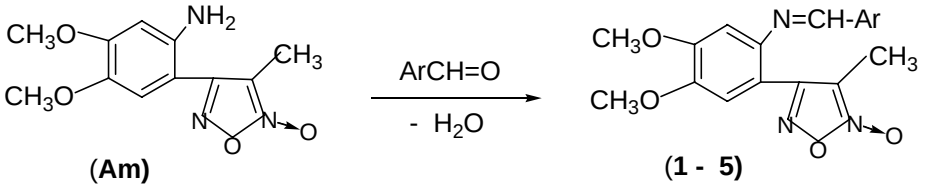
4-(2-amino-3,4-dimethoxyphenyl)-3-methylfuroxan (Am), 1 mmol in 1 ml HCl (1:3), was diazotized by 1 ml of 1M $NaNO_2$ solution at 0°C . The obtained solution was added to a solution of 1.2 mmol of phenol compound in 3 ml 1.5 M NaOH solution at 0 - 5°C. The resulting precipitate was collected and recrystallized from etanol: dioxane 1:1.

*The preparation of azo compounds **8** and **9***

4-(2-amino-3,4-dimethoxyphenyl)-3-methylfuroxan (Am), 1 mmol in 1ml HCl (1:3), was diazotized by 1 ml of 1M $NaNO_2$ solution at 0°C . The obtained solution was added to a solution of 1.2 mmol of aromatic amine in 3 ml 1.5 M acetic acid solution at 0 - 5°C during 30 minutes. After that, the mixture was heated at 60 °C during 20 minutes and then allowed to stand at room temperature. The resulting precipitate was filtered with suction and recrystallized from etanol : dioxane 1:1.

III - RESULTS AND DISCUSSION

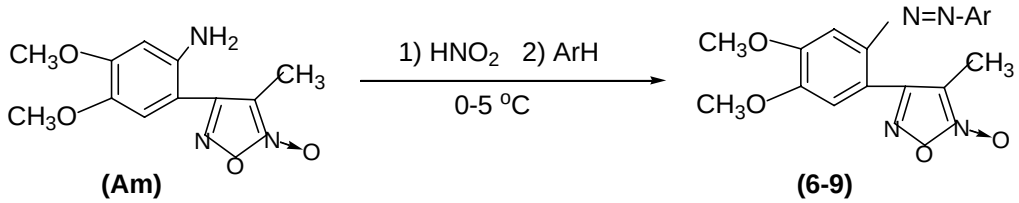
The imines have been prepared by condensation of 4-(2-amino-3,4-dimethoxy-phenyl)- 3-methylfuroxan (Am) with aromatic aldehydes:



(**Am**) (**1 - 5**)

Ar: 2-FC_6H_4(**1**); 2-$NO_2C_6H_4$ (**2**); 2-HOC_6H_4 (**3**); 2,4-$(HO)_2C_6H_3$ (**4**); 3-CH_3O-4-HOC_6H_3 (**5**)

The azo compounds have been synthesized as following:



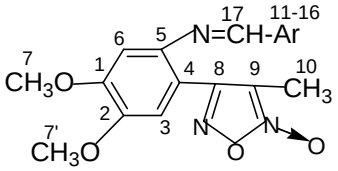
(Am) **(6-9)**

Ar: 3-NO_2-4-HOC_6H_3 (**6**); 4-$HOC_{10}H_6$ (4-hydroxynapht-1-yl) (**7**), 3-CH_3-4-$H_2NC_6H_3$ (**8**), 4-$H_2NC_{10}H_6$ (4-aminonapht-1-yl) (**9**)

The obtained imines are yellow crystals, and the azo compounds are orange or red crystalline solids. The imine-derivatives (**1 - 5**) have a band in region near 338 - 358 nm ($\log\varepsilon$ = 3.8 - 4.6). The azo compounds (**6 - 9**) have bands in the visible region 393 - 455 nm ($\log\varepsilon$ = 3.9 - 4.5) due to the azo chromophore. The main IR- absorption bands of the compounds are listed in Table 1.

In IR spectra of the examined compounds (table 1) there are several absorption bands at 1480 - 1612 cm^{-1}, characterized for C=N and C=C of imine group, benzene and furoxane ring. In spectra of **3-7** there is a broad O-H stretching band of phenol (~ 3400 cm^{-1}). The spectra of **8, 9,** each show a pair shape of N-H stretching bands of primary amine.

The ^1H NMR data of the examined compounds are listed in table 2. The assignment of the proton signals based on their spin-spin splitting patterns and on a comparison with proton signals of analogous compounds [10, 11]. The numeration of the examined compounds especially for analysis NMR spectra is shown as following:



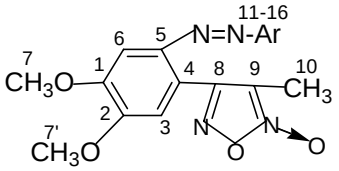


Table 1: The yield, melting point and IR-absorption of the synthesized compounds

Com.	Yield %	mp, °C	IR, cm^{-1}			
			ν_{OH} , ν_{NH}	ν_{CH}	$\nu_{C=N}$, $\nu_{C=C}$	ν_{NO}
1	69	155 - 156	-	3076, 2999, 2966	1612, 1550, 1496	1453
2	80	220 - 221	-	3067, 3002, 2938	1603, 1523, 1492	1446
3	70	194	3400	3002, 2945, 2845	1607, 1532, 1496	1454
4	70	208.5 - 209	3433, 3353	3010, 2938, 2845	1607, 1550, 1496	1449
5	20	190 - 191	3454, 3354	3060, 2988, 2945	1596, 1520, 1490	1450
6	76	192 -193	3448	3i20, 2940, 2843	1604, 1528, 1490	1459
7	79	196 - 197	3447	3088, 3072, 2937	1609, 1525, 1488	1456
8	80	200 - 201	3300, 3254	3090, 3024, 2902	1601, 1517, 1491	1465
9	85	194 -195	3379, 3240	3064, 3010, 2906	1597, 1505, 1489	1468

Table 2: ^{1}H NMR signals of examined compounds (δ, ppm; J, Hz)

	1	**2**	**3**	**4**	**5**	**8**
H3	7.18; s	7.19; s	7.21; s	7.16; s	7.14; s	7.16; s
H6	7.28; s	7.20; s	7.40; s	7.33; s	7.18; s	7.27; s
H7	3.94; s	3.91; s	3.95; s	3.94; s	3.92; s	3.92; s
H7'	3.84; s	3.89; s	3.84; s	3.82; s	3.82; s	3.81; s
H10	2.08; s	2.02; s	2.03; s	2.00; s	2.09; s	2.05; s
H12	-	-	-	-	7.34; d; 1.5	7.56; d;1.5
H13	7.36; t; 9.0	8.04; dd; 1.0; 8.0	6.92; d; 8.0	6.26; d; 2.2	-	-
H14	7.59; ddd; 7.5;6.5;1.5	7.76; td; 1.5; 8.0	7.40; td; 1.5; 8.0	-	-	-
H15	7.345; t; 7.5	7.85; t; 8.0	6.99; td; 1.3; 7.5	6.42; dd; 2.5; 8.5	6.89; d; 8.5	6.72; d; 8.0
H16	7.86; ddd; 8.5;7.5;1.5	7.98; dd; 2,0; 8.0	7.63; dd; 1.5; 7.5	7.43; d; 8.5	7.27; dd; 1.5; 8.5	7.56; dd; 1.5; 8.5
H17	8.94; s;	8.96; s;	9.09; s;	8.93; s;	8.64; s;	-
Other				12.8;s;(OH) 10.3;s;(OH)	3.79; (OCH_3)	2.14; (CH_3) 5.90; (NH_2)

Gasco and colleges [12] 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 (H-10) of examined compounds appears as a singlet at 2.00 - 2.09 ppm (Table 2) indicating that the methyl group is at position 3 of the furoxan ring.

The ^{13}C NMR spectra of compounds 4 and 5 are recorded. The assignment of the ^{13}C signals are based on their chemical shift and based on a comparison with ^{13}C-NMR spectra of analogous compounds [10, 11]. The data are given in table 3.

For the imines **4** and **5**, chemical shift of C1 ÷ C10 little changed from one to another, while chemical shift of C11 ÷ C17 are lager changed (table 3).

Table 3: The ^{13}C-NMR signals of imines **4** and **5** (δ, ppm)

	Imine 4	**Imine 5**		**Imine 4**	**Imine 5**
C1	151.77	151.83	C10	8.34	8.99
C2	147.54	147.97	C11	134.38	127.70
C3	112.72	112.62	C12	162.67	110.70
C4	113.83	113.50	C13	102.35	147.30
C5	140.28	142.83	C14	162.45	150.80
C6	102.40	101.96	C15	108.12	115.61
C7; C7'	55.98; 55.98	55.93; 55.88	C16	112.11	123.69
C8	157.09	158.03	C17	162.07	159.56
C9	112.90	114.29	Other	-	55.32

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