SYNTHESESOMEIMINESANDAZOCOMPOUNDS
DERIVED FROM 4-(2-AMINO-3,4-DIMETHOXYPHENYL)-3-
METHYLEFURXAN

Received 23 August 2007
NGUYEN HUU DINH, NGUYEN VAN KIEN, MAI THI THANH HUONG
Department of Chemistry, Hanoi University of Education

SUMMARY
Some imines and azo compounds containing furoxan and benzene rings have 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 antitypanosomal 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
÷ 4,000 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 D₂O-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 ethanol.
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 NaNO₂
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 ethanol: 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 NaNO₂ 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-dimethoxyphenyl)-3-methylfuroxan (Am) with aromatic aldehydes:

\[
\text{NH}_2 \quad \text{N} \quad \text{O} \\
\text{CH}_3 \\
\text{CH}_3 \text{O} \\
\text{CH}_3 \text{O}
\]

\[
\text{CH}_3 \text{O} - \text{ArCH}=O \quad \text{N=CH-Ar}
\]

Ar: 2-FC₆H₄ (1); 2-NO₂C₆H₄ (2); 2-HOC₆H₄ (3); 2,4-(HO)₂C₆H₄ (4); 3-CH₃O-4-HOC₆H₄ (5)

The azo compounds have been synthesized as following:

\[
\text{NH}_2 \quad \text{N} \quad \text{O} \\
\text{CH}_3 \\
\text{CH}_3 \text{O} \\
\text{CH}_3 \text{O}
\]

\[
\text{CH}_3 \text{O} - \text{ArCH}=O \quad \text{N=N-Ar}
\]

Ar: 3-NO₂-4-HOC₆H₄ (6); 4-HOC₁₀H₆ (4-hydroxynapht-1-yl) (7); 3-CH₃-4-H₂NC₆H₃ (8); 4-H₂NC₁₀H₆ (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 ε = 3.8 - 4.6). The azo compounds (6 - 9) have bands in the visible region 393 - 455 nm (log ε = 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 ‘H 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

<table>
<thead>
<tr>
<th>Com.</th>
<th>Yield %</th>
<th>mp, °C</th>
<th>IR, cm⁻¹</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>νOH, νNH</td>
<td>νCH</td>
<td>νC=N, νC=C</td>
<td>νNO</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>69</td>
<td>155 - 156</td>
<td>-</td>
<td>3076, 2999, 2966</td>
<td>1612, 1550, 1496</td>
<td>1453</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>80</td>
<td>220 - 221</td>
<td>-</td>
<td>3067, 3002, 2938</td>
<td>1603, 1523, 1492</td>
<td>1446</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>70</td>
<td>194</td>
<td>3400</td>
<td>3002, 2945, 2845</td>
<td>1607, 1532, 1496</td>
<td>1454</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>70</td>
<td>208.5 - 209</td>
<td>3433, 3353</td>
<td>3010, 2938, 2845</td>
<td>1607, 1550, 1496</td>
<td>1449</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>190 - 191</td>
<td>3454, 3354</td>
<td>3060, 2988, 2945</td>
<td>1596, 1520, 1490</td>
<td>1450</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>76</td>
<td>192 - 193</td>
<td>3348</td>
<td>3120, 2940, 2843</td>
<td>1604, 1528, 1490</td>
<td>1459</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>79</td>
<td>196 - 197</td>
<td>3447</td>
<td>3088, 3072, 2937</td>
<td>1609, 1525, 1488</td>
<td>1456</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>80</td>
<td>200 - 201</td>
<td>3300, 3254</td>
<td>3090, 3024, 2902</td>
<td>1601, 1517, 1491</td>
<td>1465</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>85</td>
<td>194 - 195</td>
<td>3379, 3240</td>
<td>3064, 3010, 2906</td>
<td>1597, 1505, 1489</td>
<td>1468</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: 'H NMR signals of examined compounds (δ, ppm; J, Hz)

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>H3</td>
<td>7.18; s</td>
<td>7.19; s</td>
<td>7.21; s</td>
<td>7.16; s</td>
<td>7.14; s</td>
<td>7.16; s</td>
</tr>
<tr>
<td>H6</td>
<td>7.28; s</td>
<td>7.20; s</td>
<td>7.40; s</td>
<td>7.33; s</td>
<td>7.18; s</td>
<td>7.27; s</td>
</tr>
<tr>
<td>H7</td>
<td>3.94; s</td>
<td>3.91; s</td>
<td>3.95; s</td>
<td>3.94; s</td>
<td>3.92; s</td>
<td>3.92; s</td>
</tr>
<tr>
<td>H7'</td>
<td>3.84; s</td>
<td>3.89; s</td>
<td>3.84; s</td>
<td>3.82; s</td>
<td>3.82; s</td>
<td>3.81; s</td>
</tr>
<tr>
<td>H10</td>
<td>2.08; s</td>
<td>2.02; s</td>
<td>2.03; s</td>
<td>2.00; s</td>
<td>2.09; s</td>
<td>2.05; s</td>
</tr>
<tr>
<td>H12</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>7.34; d; 1.5</td>
<td>7.56; d; 1.5</td>
<td>-</td>
</tr>
<tr>
<td>H13</td>
<td>7.36; t; 9.0</td>
<td>8.04; dd; 1.0; 8.0</td>
<td>6.92; d; 8.0</td>
<td>6.26; d; 2.2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>H14</td>
<td>7.59; ddd; 7.5;6.5;1.5</td>
<td>7.76; td; 1.5; 8.0</td>
<td>7.40; td; 1.5; 8.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>H15</td>
<td>7.345; t; 7.5</td>
<td>7.85; t; 8.0</td>
<td>6.99; td; 1.3; 7.5</td>
<td>6.42; dd; 2.5; 8.5</td>
<td>6.89; d; 8.5</td>
<td>6.72; d; 8.0</td>
</tr>
<tr>
<td>H16</td>
<td>7.86; ddd; 8.5;7.5;1.5</td>
<td>7.98; dd; 2.0; 8.0</td>
<td>7.63; dd; 1.5; 7.5</td>
<td>7.43; d; 8.5</td>
<td>7.27; dd; 1.5; 8.5</td>
<td>7.56; dd; 1.5; 8.5</td>
</tr>
<tr>
<td>H17</td>
<td>8.94; s; 8.96; s</td>
<td>9.09; s; 8.93; s; 8.64; s</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>12.8; s(CH(OH)</td>
<td>10.3; s(OH)</td>
<td>3.79; (OCH₃)</td>
</tr>
</tbody>
</table>
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 larger changed (table 3).

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

<table>
<thead>
<tr>
<th></th>
<th>Imine 4</th>
<th>Imine 5</th>
<th>Imine 4</th>
<th>Imine 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>151.77</td>
<td>151.83</td>
<td>8.34</td>
<td>8.99</td>
</tr>
<tr>
<td>C2</td>
<td>147.54</td>
<td>147.97</td>
<td>134.38</td>
<td>127.70</td>
</tr>
<tr>
<td>C3</td>
<td>112.72</td>
<td>112.62</td>
<td>162.67</td>
<td>110.70</td>
</tr>
<tr>
<td>C4</td>
<td>113.83</td>
<td>113.50</td>
<td>102.35</td>
<td>147.30</td>
</tr>
<tr>
<td>C5</td>
<td>140.28</td>
<td>142.83</td>
<td>162.45</td>
<td>150.80</td>
</tr>
<tr>
<td>C6</td>
<td>102.40</td>
<td>101.96</td>
<td>108.12</td>
<td>115.61</td>
</tr>
<tr>
<td>C7; C7'</td>
<td>55.98; 55.98</td>
<td>55.93; 55.88</td>
<td>112.11</td>
<td>123.69</td>
</tr>
<tr>
<td>C8</td>
<td>157.09</td>
<td>158.03</td>
<td>162.07</td>
<td>159.56</td>
</tr>
<tr>
<td>C9</td>
<td>112.90</td>
<td>114.29</td>
<td>Other</td>
<td>55.32</td>
</tr>
</tbody>
</table>

REFERENCES


