SYNTHESIS AND STRUCTURAL ELUCIDATION OF SOME NOVEL PYRAZOLIN-5-ONES

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ABSTRACT

A new series of Pyrazolin-5-ones were synthesized. The structures for all the compounds have been established by elemental analysis, IR spectral, 1H NMR spectral and Mass spectral studies.

Keywords: Pyrazolin-5-ones, characterization, elemental analysis, IR Spectral data, 1H NMR spectral data, mass spectral data.

INTRODUCTION

In modern medicinal chemistry, the approach of pharmacophore hybrid for the exploration of novel and highly active compounds is an effective and commonly used direction. Pyrazolines have been found to possess broad-spectrum of biological activities\(^1\).\(^2\). The chemistry of pyrazolone derivatives has received much attention, because of their interesting structural properties and applications to diverse areas\(^3\). Pyrazolin-5-ones are very important class of heterocycles, due to their potential pharmacological and biological applications\(^3\)\(^6\). It is well known fact that they have been used as therapeutic agents, such as anti-inflammatory\(^7\), antibacterial\(^8\), antifungal\(^9\), analgesic\(^9\), antipyretic\(^11,12\), anti-oxidant\(^13\), insecticidal\(^14\), molluscicidal\(^7\), antidepressant\(^15\), antituberular\(^16\), anti HIV\(^17\), antimalarial\(^18\), anti cancer\(^19,20\), and cerebral infarction (Free radical Scavenger)\(^21\)-\(^24\). The diversified applications of pyrazolin-5-ones in different fields have inspired the authors to synthesize the new pyrazolin-5-ones.

EXPERIMENTAL

Instruments and Chemicals employed: pH measurements were made using the ELICO Private Limited, Hyderabad, India. IR Spectral details were obtained from a Perkin-Elmer 283 spectrometer. All reagents used were of analytical grade procured from Merck, India. The working solutions were prepared using double distilled water. The Britton-Robinson buffer was prepared from appropriate amounts of 0.04M o-phosphoric acid, 0.04M Boric acid and 0.04M acetic acid. The solutions of desired pH values were prepared by the addition of an appropriate volume of 0.2M sodium hydroxide solution.

Synthesis of N-(Benzene sulfonyl)-3-methyl-4-(2’-substituted aryl hydrazono)-pyrazolin-5-ones: The synthesis involves the following steps:

1. **Synthesis of Benzene sulfonyl hydrazide**

   A solution of benzene sulfonyl chloride in acetone and an appropriate amount of hydrazine hydrate were treated with 5% NaOH solution. The mixture is shaken vigorously for 10 minutes, cooled and poured into 1:1 HCl. The precipitate is filtered off, washed with water and recrystallized from methanol. Melting point of the compound is 104-106°C.
2. **Synthesis of aryl diazonium chloride**
The required amount of substituted aryl amine was dissolved in a suitable volume of dilute HCl. The solution obtained is cooled to 0°C a little amount of an aqueous solution of sodium nitrite was added slowly. The addition of an excess of sodium nitrite solution stabilizes the diazonium chloride.

3. **Synthesis of aryl diazonium aceto acetic ester**
The appropriate diazonium chloride solution was added to an ice cold solution of the mixture of sodium acetate and aceto acetic acid solutions in methanol. The addition of corresponding diazonium chloride was continued till yellow crystals were separated out, the crystals were filtered, washed with water and dried. It was recrystallized from 1:1 DMF. Yield is 3.9 g.

4. **Synthesis of N-(Benzene sulfonyl)-3-methyl-4-(2’-substituted aryl hydrazono)-pyrazolin-5-ones**
A mixture of appropriate amounts of diazonium acetoacetic ester and benzene sulfonyl chloride was refluxed for 4 hours and cooled. The crystalline solid separated was filtered, washed with water, dried and recrystallized from 1:1 DMF.

**RESULTS AND DISCUSSION**
The melting points of the synthesized compounds are presented in Table-1.

**Elemental Analysis Data**
The compounds are analyzed for carbon, hydrogen, nitrogen and sulfur and the results are presented in Table-1.

| Table-1: Analytical Data for the compounds synthesized |
| Sample Number | Substituent | Color  | Melting Point (°C) | Elemental Analysis |
|               |             |        |                   | Found (Cal) %       |
|               |             |        |                   | C   | H    | N    | S    |
| I             | -H          | Orange | 117-120           | 56.14 (55.89)       |
|               |             |        |                   | 4.09 (4.81)         |
|               |             |        |                   | 16.37 (16.01)       |
|               |             |        |                   | 9.35 (9.19)         |
| II            | 2’-CH₃      | Yellow | 243-245           | 57.30 (57.00)       |
|               |             |        |                   | 4.49 (4.21)         |
|               |             |        |                   | 15.73 (15.40)       |
|               |             |        |                   | 8.90 (8.71)         |
| III           | 2’-OCH₃     | Yellow | 215-217           | 54.83 (54.51)       |
|               |             |        |                   | 4.84 (4.59)         |
|               |             |        |                   | 15.05 (57.00)       |
|               |             |        |                   | 8.60 (14.70)        |
| IV            | 2’-OH       | Black  | 260-263           | 53.63 (53.31)       |
|               |             |        |                   | 4.47 (4.21)         |
|               |             |        |                   | 15.64 (15.31)       |
|               |             |        |                   | 8.94 (8.73)         |
| V             | 2’-Cl       | Yellow | 210-212           | 50.99 (50.62)       |
|               |             |        |                   | 3.98 (3.71)         |
|               |             |        |                   | 14.87 (14.51)       |
|               |             |        |                   | 8.50 (8.30)         |
| VI            | 2’-NO₂      | Orange | 224-226           | 49.61 (49.27)       |
|               |             |        |                   | 3.36 (3.12)         |
|               |             |        |                   | 18.09 (17.70)       |
|               |             |        |                   | 8.27 (8.01)         |

**Table-2: IR Spectral data for the Compounds (I to VI)**

<table>
<thead>
<tr>
<th>S. No</th>
<th>Group</th>
<th>ν (cm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>I</td>
</tr>
<tr>
<td>1</td>
<td>-N-H</td>
<td>3452</td>
</tr>
<tr>
<td>2</td>
<td>C-H (Aromatic)</td>
<td>3050</td>
</tr>
<tr>
<td>3</td>
<td>C=O (in pyrazolin ring)</td>
<td>1689</td>
</tr>
<tr>
<td>4</td>
<td>C---C(in aromatic nucleus)</td>
<td>1656, 1654, 1650, 1640, 1540, 1614, 1545, 1575, 1453, 1501</td>
</tr>
</tbody>
</table>
### Infrared Spectral Studies

The infrared spectral data for N-(Benzene sulfonyl)-3-methyl-4-(2'-substituted aryl hydrazono)-pyrazolin-5-ones were recorded. It is revealed from the study of infrared spectral data that a weak $\text{>C=N}$ stretching frequency band is present in the compounds around 1565 cm$^{-1}$. The characteristic absorption band for –NH-- group in –NH-N=C< is observed in the region 3448 cm$^{-1}$. Sulphone (O=S=O) group noticed in the region of 1270 cm$^{-1}$ and 1165-1685 cm$^{-1}$. The (cyclic) C=O group is observed in the region 1686-1701 cm$^{-1}$.

The detailed IR data pertaining to different compounds are given in the Table-2.

<p>| | | | | | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>5</td>
<td>$\text{&gt;C=N}$</td>
<td>1569</td>
<td>1565</td>
<td>1560</td>
<td>1559</td>
</tr>
<tr>
<td>6</td>
<td>C-H (def)</td>
<td>1439</td>
<td>1436</td>
<td>1433</td>
<td>1431</td>
</tr>
<tr>
<td>7</td>
<td>N------O (stre)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>S=O (sym &amp; Asym)</td>
<td>1269,1167</td>
<td>1270,1169</td>
<td>1269,1165</td>
<td>1260,1170</td>
</tr>
<tr>
<td>9</td>
<td>S-aryl</td>
<td>1088,1045</td>
<td>1086,1040</td>
<td>1087,1040</td>
<td>1080,1030</td>
</tr>
<tr>
<td>10</td>
<td>C-H (def) (mono substituted)</td>
<td>757,726</td>
<td>759,724</td>
<td>751,725</td>
<td>748,721</td>
</tr>
<tr>
<td>11</td>
<td>C-H (def)</td>
<td>762</td>
<td>759</td>
<td>752</td>
<td>749</td>
</tr>
<tr>
<td>12</td>
<td>C---- (def) (out of plane ring)</td>
<td>685</td>
<td>683</td>
<td>680</td>
<td>668</td>
</tr>
<tr>
<td>13</td>
<td>C-Cl (stre) (Aromatic ring)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Fig.-1: IR Spectrum of compound I
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*Fig.-2: IR Spectrum of compound III*

*Fig.-3: IR Spectrum of compound V*

**1H NMR spectral data:** The $^1$H NMR spectra were recorded for all the synthesized compounds (I to VI). The chemical shift for N-H proton is observed at 13.4 ppm. The –CH$_3$ group (in pyrazolone) is appeared at 1.4 ppm, phenyl group in –SO$_2$C$_6$H$_5$ is observed at 7.1 to 7.8 ppm. The results relating to $^1$H NMR data is presented in Table-3.

<table>
<thead>
<tr>
<th>Compound</th>
<th>–CH$_3$ (singlet)</th>
<th>–CH$_3$/–OCH$_3$/–OH attached to the aromatic ring</th>
<th>–C$_6$H$_4$(-R) (multiplet)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1.4</td>
<td>6.9-7.1</td>
<td>7.4-8.1</td>
</tr>
<tr>
<td>II</td>
<td>1.4</td>
<td>2.4</td>
<td>7.1-7.3</td>
</tr>
<tr>
<td>III</td>
<td>1.4</td>
<td>4.0</td>
<td>6.8-7.2</td>
</tr>
<tr>
<td>IV</td>
<td>1.4</td>
<td>5.2</td>
<td>7.1-7.4</td>
</tr>
</tbody>
</table>

Table-3: $^1$H NMR spectral data for the compounds I to VI (δ ppm)
Mass Spectral Data
Mass spectral studies for N-(Benzene sulfonyl)-3-methyl-4-(2’-substituted aryl hydrazono)-pyrazolin-5-ones were recorded. Molecular ion peaks (M+) were present in all compounds (Compounds I to VI) (Figures-6 and 7). Major fragmentation patterns observed are due to loss of C_{6}H_{5}-SO_{2}, N_{2}, CO, C_{6}H_{5}. 

<table>
<thead>
<tr>
<th></th>
<th>1.4</th>
<th></th>
<th>7.0-7.4</th>
<th>7.6-8.2</th>
<th>13.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>V</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VI</td>
<td>1.4</td>
<td></td>
<td>7.3-7.7</td>
<td>8.0-8.3</td>
<td>13.4</td>
</tr>
</tbody>
</table>

Fig.-4: 1H NMR spectrum of compound II

Fig.-5: 1H NMR spectrum of compound V
CONCLUSIONS

On the basis of elemental analysis, IR, $^1$H-NMR and mass spectral studies, the structure was proposed for N-(Benzene sulfonyl)-3-methyl-4-(2’-substituted aryl hydrazono)-pyrazolin-5-ones (Compounds I to VI).

REFERENCES


[RJC-1411/2016]