Synthesis of New 4-Arylhydrazono-3-methyl-2-pyrazolin-5-one Derivatives and their Reactivity towards Active Methylene Components and Grignard Reagents

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4-Arylhydrazono-3-methyl-2-pyrazolin-5-one, Grignard Reagents

Treatment of 4-arylhydrazono-3-methyl-2-pyrazolin-5-ones (1a-e) with dimethyl sulphate afforded the N-methyl derivatives (2a-e) which on treatment with phenylmagnesium bromide gave the carbinol (3). The hydroxy pyrazolones (4a-e) were reacted with ethyl acetocetate and diethyl malonate to give the a-N-methyl derivatives (5 and 6a-e). The hitherto unknown 4-arylhydrazono-3-methyl-1-benzenesulphonyl-2-pyrazolin-5-ones (7a-e) were now obtained and upon treatment with Grignard reagent gave 4-arylhydrazono-3-methyl-3,5,5-triphenylpyrazolines (7a, e, d).

Previous work on the reactions of 4-arylazo1-12, and 4-arylhydrazono13,2-pyrazolin-5-ones, showed the validity of these compounds in the preparation of dyes and the reactivity of the pyrazolin ring.

In the present paper we studied the synthesis and reactivity of 4-arylhydrazono-3-methyl-2-pyrazolin-5-ones (1a-e) towards methylation and the behaviour of N-methyl derivatives (2a-e) towards Grignard reagents, and chlorosulphonation. Also we studied the reactivity of the N-hydroxymethyl derivatives (4a-e) towards condensation with active methylene compounds, and the behaviour of the N-benzenesulphonyl derivatives (7a, e, d) towards the action of organomagnesium compounds.

Results and Discussion

Heating 4-arylhydrazono-3-methyl-2-pyrazolin-5-ones (1a-e) with dimethyl sulphate, afforded the N-methyl derivatives (2a-e), which show endocyclic carbonyl stretching vibration in their infrared spectra at 1635 cm⁻¹.

The behaviour of some 4-substituted 3-pyrazolin-5-ones towards organomagnesium compounds has been reported1. In extension to this study we investigated the behaviour of 2a towards Grignard reagents. Thus, when 2a was treated with Grignard reagent the carbinol (3) was obtained. Their IR spectra do not show the carbonyl absorption band. Furthermore two absorption maxima appear at 1600 and 3600 cm⁻¹ attributable to the C=N and free OH group, respectively.

It was reported that treatment of 4-arylhydrazono-3-methyl-2-pyrazolin-5-ones (1a-e) with formaldehyde in methanol afforded the N-hydroxymethyl derivatives (6a-e)13. Thus, when (4a-e) were treated with ethyl acetocetate and diethyl malonate in presence of concentrated sulphuric acid, the a-N-methyl derivatives (5 and 6a-e) were obtained. Their IR spectra show the regular absorption bands at 1630, 1660, and 1675 cm⁻¹, attributable to the amide carbonyl, carbonyl of the ketone group and carbonyl of the ester group respectively.

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The hitherto unknown 4-arylhydrazono-3-methyl-1-benzenesulphonyl-2-pyrazolin-5-ones (7a, c-e) were now obtained by two alternative methods, either by treatment of the appropriate arylazo derivative of ethyl acetoacetate with benzenesulphonhydrazide in ethanol, or by treatment of the 4-arylhydrazono-3-methyl-2-pyrazolin-5-ones (1a-e) with benzenesulphonyl chloride in pyridine at low temperatures.

The benzenesulphonyl radical in (7a) was readily eliminated upon treatment with either alcoholic potassium hydroxide or piperidine to give the arylhydrazonopyrazolone (1).

The behaviour of 4-arylazo-3-methyl-1-phenyl-2-pyrazolin-5-ones and the 4-arylazo derivatives of antipyrene towards the action of organo-magnesium compounds has been reported. In extension to this work, we have investigated the reactivity of 7 toward the same reagents. Thus, when 7a, c and d) were treated with phenylmagnesium bromide, 4-arylhydrazono-3-methyl-3,5,5-triphenylpyrazolines (8a, c and d) were isolated.

The carbonyl absorption band disappeared in the IR spectra of these compounds. The formation of 8 involved three molecules of the Grignard reagent effecting the hetero-ring openings followed by recyclisation and addition to the endocycle C=N group activated by conjugation with the hydrazono group in position 4. The stability of the benzenesulphonyl group to the action of the Grignard reagent is in contrast to the ready elimination of the aminomethyl group in the N-Mannich base with the same reagent. However, when the Grignard product (8a) was refluxed with alcoholic potassium hydroxide, the benzenesulphonyl group was readily eliminated, followed by atmospheric oxidation affording 4-phenylhydrazono-3-methyl-3,5,5-triphenyl-1-pyrazoline (10). The absence of the absorption characteristics of the hydrazo linkage is in support of structure 10 and not the intermediate structure 9. Moreover, similar auto-oxidation has been reported for the tetrahydrophthalazines and pyridazines.

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**Experimental**

All melting points are uncorrected. Infrared spectra were determined by the KBr waffer technique on a Unicam SP 1000 Infrared Spectrophotometer.

1,3-Dimethyl-4-arylhydrazono-2-pyrazolin-5-ones (2a–e)

Compounds 1a–e (0.01 mole) were heated with dimethyl sulphate (0.02 mole) for 5 min, cooled, poured onto ice-cold sodium hydroxide solution (30%). The products that separated were filtered and crystallized from dilute methanol.

The results are given in Table I.

**Action of phenylmagnesium bromide on 2a. Formation of 3a**

General procedure: To an etheral solution of phenylmagnesium bromide (prepared from 0.9 g magnesium, 8.0 g bromobenzene and 40 ml dry ether), was added a solution of 2a (1.0 g) in dry...
ether (50 ml). The reaction mixture was heated under reflux on a steam bath for two hours, set aside at room temperature overnight, and then decomposed with a cold, saturated aqueous ammonium chloride solution. The reaction mixture was extracted with ether. The ethereal layer was dried and allowed to evaporate slowly at room temperature. The oily residue was triturated with hot petroleum ether (b.p. 40–60 °C) and crystallised from ethyl alcohol.

The Grignard product (3a) formed a brown solid powder, m.p. 120 °C, yield 60%.

Analysis: C_{23}H_{24}N_{4}O (372)
Caled C 74.19 H 6.45 N 15.05
Found C 75.05 H 6.40 N 15.11.

Condensation of 4a–e with ethyl acetoacetate and diethyl malonate. Formation of 5a–e, 6a–e

**General procedures:** To a cooled mixture of 4a–e (1.0 g) and ethyl acetoacetate or diethyl malonate (1.0 ml), concentrated sulphuric acid (10 ml) was added and left to stand overnight at room temperature. The reaction mixture was poured onto ice. The solid product that separated, was filtered and crystallised from ethanol. The results are given in Table II.

**4-Arylhydrazono-1-benzenesulphonyl-3-methyl-2-pyrazolin-5-ones (8a, c–e)**

**General procedures:** a) A mixture of the arylazo derivatives of ethyl acetoacetate (1.17 g) and...
benzenesulphonhydrazide (1.7 g) in ethanol was refluxed for three hours, set aside at room temperature overnight. The precipitated solid was filtered and crystallised from ethanol. The results are given in Table III.

b) To an ice-cold solution of compounds (1a, c-e) (1.0 g) in pyridine (10 ml), benzenesulphonyl chloride (1 ml) was added dropwise with stirring, and the reaction mixture left to stand overnight. The product that separated proved to be identical with compounds 7a, c-e (m.p. and mixed m.p.).

Action of alcoholic potassium hydroxide or pyridine on 7a, c-e. Formation of 1a

Compound 8a (0.5 g) was refluxed with 4% alcoholic potassium hydroxide solution (10 ml) or pyridine (10 ml) for one hour, diluted with water and acidified with hydrochloric acid, the product obtained proved to be 1a (m.p. 135 °C and mixed m.p. 135 °C).

Action of phenylmagnesium bromide on 8a, c and d

To an etheral solution of phenylmagnesium bromide (prepared from 0.9 g magnesium 8.0 g bromobenzene and 40 ml dry ether (50 ml) was added a solution of 7a, c and d in ether and the reaction mixture was heated under reflux on a steam bath for two hours, set aside at room temperature overnight, and then decomposed with a cold saturated aqueous ammonium chloride solution. The reaction mixture was extracted with ether; the etheral layer dried and then allowed to evaporate slowly at room temperature. The oily residue was triturated with hot petroleum ether (b.p. 40–60 °C) and crystallised from ethyl alcohol. The results are given in Table IV.

Action of alcoholic potassium hydroxide on 8a. Formation of 10

A suspension of 8a (0.5 g) in 4% alcoholic potassium hydroxide solution (20 ml) was refluxed for one hour, diluted with water, and acidified with hydrochloric acid. The product that separated, was filtered off and crystallised from acetone as brown-red crystals, m.p. 185 °C, yield 60%.

Analysis: C$_{28}$H$_{34}$N$_4$ (416)

Caled C 80.74 H 5.80 N 13.45,

Found C 80.80 H 5.70 N 13.50.

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<th>Compound</th>
<th>m.p. [°C]</th>
<th>Yield [%]</th>
<th>Formula (mol. wt.)</th>
<th>Carbon [%] Found</th>
<th>Caled</th>
<th>Hydrogen [%] Found</th>
<th>Caled</th>
<th>Nitrogen [%] Found</th>
<th>Caled</th>
<th>Sulphur [%] Found</th>
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<tr>
<td>7a</td>
<td>135</td>
<td>91</td>
<td>C$<em>{16}$H$</em>{14}$N$_2$SO$_3$ (342)</td>
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<td>56.28</td>
<td>4.1</td>
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<td>16.0</td>
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<td>125</td>
<td>89</td>
<td>C$<em>{17}$H$</em>{16}$N$_3$S$_2$ (356)</td>
<td>57.3</td>
<td>57.29</td>
<td>4.6</td>
<td>4.52</td>
<td>16.1</td>
<td>15.72</td>
<td>9.1</td>
<td>8.99</td>
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<td>7d</td>
<td>158</td>
<td>93</td>
<td>C$<em>{17}$H$</em>{18}$N$_3$S$_2$ (372)</td>
<td>55.0</td>
<td>54.83</td>
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<td>4.33</td>
<td>14.9</td>
<td>15.04</td>
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<tr>
<td>7e</td>
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<td>90</td>
<td>C$<em>{17}$H$</em>{18}$N$_3$S$_2$ (372)</td>
<td>54.9</td>
<td>54.83</td>
<td>4.1</td>
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<td>15.1</td>
<td>15.04</td>
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Table III. The N-benzenesulphonyl derivatives (7a, e-e).

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<th>Compound</th>
<th>m.p. [°C]</th>
<th>Yield [%]</th>
<th>Formula (mol. wt.)</th>
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<th>Caled</th>
<th>Hydrogen [%] Found</th>
<th>Caled</th>
<th>Nitrogen [%] Found</th>
<th>Caled</th>
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<tr>
<td>8a</td>
<td>170</td>
<td>65</td>
<td>C$<em>{24}$H$</em>{20}$N$_4$S$_2$ (558)</td>
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<td>73.09</td>
<td>5.2</td>
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<td>10.03</td>
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<tr>
<td>8c</td>
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<td>70</td>
<td>C$<em>{23}$H$</em>{22}$N$_4$S$_2$ (572)</td>
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<td>73.39</td>
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<td>9.7</td>
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<tr>
<td>8d</td>
<td>135</td>
<td>63</td>
<td>C$<em>{23}$H$</em>{22}$N$_4$S$_2$ (588)</td>
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<td>71.40</td>
<td>5.5</td>
<td>5.47</td>
<td>9.4</td>
<td>9.51</td>
<td>5.3</td>
<td>5.44</td>
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Table IV. Action of phenylmagnesium bromide on 7a, c and d.
9. L. Knor, Ann. 238, 183 [1887].
dron 20, 531 [1964].