RESEARCH ON ARYLHYDRAZONES OF SUBSTITUTED GLYOXYLIC ACIDS

X. Arylhydrazones of the Hydrazide and Acetylhydrazide of Cyanoglyoxylic Acid, and their Cyclization Products*

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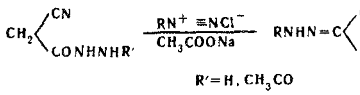
Reaction of the hydrazides and acetylhydrazides of cyanoacetic acid with aryldiazonium chlorides gives arylhydrazones of the hydrazide and acetylhydrazide of cyanoglyoxylic acid. 2-Acetyl-3-imino-4-arylpyrazol-5-ones and 3-imino-4-arylazopyrazol-5-ones are obtained by cyclizing the arylhydrazones.

A previous paper [1] described arylhydrazones of chloromethylglyoxylyl chloride. It was of interest to investigate the hitherto unknown arylhydrazones of the hydrazide and acetylhydrazide of cyanoacetic acid.

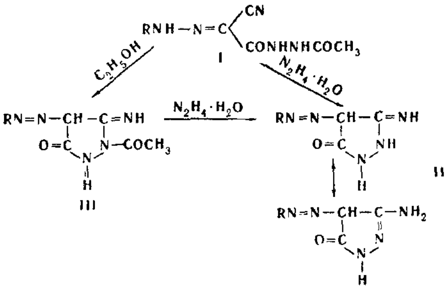
In recent years hydrazides of carboxylic acids have been attracting the attention of research workers, since they include compounds with valuable physiological activities, and some have been found applicable in practical medicine [2]. Treatment of the hydrazide and acetylhydrazide of cyanoacetic acid [3] with aryldiazonium salts in aqueous ethanol solution in the presence of sodium acetate gave the corresponding arylhydrazones [4] (Table 1).



Good yields of arylhydrazones of the hydrazide and acetylhydrazide of cyanoacetic acid were obtained, forming pale yellow crystals, which were soluble in organic solvents. It is to be noted that, no matter what the coupling conditions, only arylhydrazones of the hydrazide of cyanoacetic acid with electron-accepting substituents in the phenyl rings can be isolated.

Up to the present it has not been possible to convert cyanoacetyl hydrazide to the pyrazolone derivative isomeric with it [3]. It was of interest to carry out the cyclization of the arylhydrazones of the hydrazide and acetylhydrazide cyanoglyoxilic acid already prepared. Treatment of arylhydrazones of the acetylhydrazide of cyanoglyoxylic acid (I) with nucleophilic reagents, e.g. hydrazine hydrate, diethylamine and aniline, leads to cyclization with splitting off of the acetyl group and formation of 3-imino-4-arylazopyrazol-5-one (II).

Refluxing arylhydrazones of the acetylhydrazide of cyanoacetic acid in ethanol for two hours gives 2-acetyl-3-imino-4-arylazopyrazol-5-ones (III). If the resultant products are then boiled in the presence of hydrazine hydrate, diethylamine, or other nucleophilic reagents, an acetyl group is split off, and the products II are identical with those obtained in the above condensation of arylhydrazones with acetylhydrazides of cyanoglyoxylic acid (undepressed mixed up [5]).



The pyrazole derivatives (Table 2) were red or cherry red crystalline compounds with a metallic glitter.

The 3-imino-4-arylazopyrazol-5-ones synthesized are identical with the cyclization products obtained by the action of hydrazine hydrate on arylhydrazones of ethyl cyanoglyoxylate [6, 7].

We thank P. S. Kel'kis for his interest in the work.

EXPERIMENTAL

Phenylhydrazone of the hydrazide of cyanoglyoxylic acid. 0.9 g (0.01 mole) of aniline was dissolved in 15 ml 17% HCl, and diazotized with 0.8 g $NaNO_2$ dissolved in 2 ml water (temperature not over 0–5°). The phenyldiazonium chloride solution was neutralized with NaOAc to pH 7. The resultant solution of phenyldiazonium acetate was added slowly to a mixture of 1.4 g (0.01 mole) cyanoacetyl hydrazide in 17 ml aqueous EtOH (1:1), and 10 g NaOAc. A light yellow precipitate formed immediately. Stirring was continued for 30 min more. The precipitate was filtered off, and washed with water, then with EtOH. Yield 1 g, crystallized from EtOH.

The compounds of Table 1 were prepared similarly.

2-Acetyl-3-imino-4-phenylazopyrazol-5-one. 2.45 g (0.01 mole) cyanoglyoxylyl acetylhydrazide phenylhydrazone was suspended in 20 ml EtOH and refluxed for 2 hr. On cooling a dark cherry red precipitate with a metallic glitter formed. It was filtered off and washed with EtOH, yield 1.7 g, recrystallized from EtOH.

The p-bromo derivative was prepared similarly.

3-Imino-4-(o-chlorophenylazo)pyrazol-5-one. 2.8 g (0.01 mole) cyanoglyoxylyl acetylhydrazide o-chlorophenylhydrazone was suspended in 5 ml EtOH. 5 ml hydrazone hydrate was added, and the mixture refluxed for 2 hr. The solid was filtered off and washed with EtOH, yield 1.2 g, recrystallized from EtOH. The rest of the non-acetylated pyrazolones were prepared similarly.

Refluxing 2-acetyl-3-imino-4-(p-bromophenylazo)pyrazol-5-one in EtOH in the presence of hydrazine hydrate for 2 hr led to quantitative conversion to 3-imino-4-(p-bromophenylazo)pyrazol-5-one.

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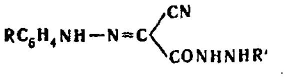
*For Part IX see [1].

Table 1

Arylhydrazones of Cyanoglyoxylyl Hydrazide and Acetylhydrazide



$$RC_6H_4NH{-}N{=}C\begin{matrix}\diagup CN\\ \diagdown CONHNHR'\end{matrix}$$

R	R'	Mp, °C	Formula	Found, %		Calculated, %		Yield, %
				N	Cl	N	Cl	
H	H	103—104	$C_9H_9N_5O$	34.46 34.51		34.48		50
o-Cl		123—124	$C_9H_8N_5OCl$		14.71 14.68		14.94	46
p-Cl		134—136	$C_9H_8N_5OCl$		15.21 15.30		14.94	42
m-NO_2		256—258	$C_9H_8N_6O_3$	33.91 34.10		33.87		44
2-OCH_3 5-NO_2		110—112	$C_{10}H_{10}N_6O_4$	29.89 29.93		30.21		43
H	CH_3CO	207—208	$C_{11}H_{11}N_5O_2$	28.53 28.31		28.57		97
o-CH_3*		219—220	$C_{12}H_{13}N_5O_2$					96
m-CH_3		212—213	$C_{12}H_{13}N_5O_2$	27.48 27.53		27.02		92
p-CH_3		206—207	$C_{12}H_{13}N_5O_2$	26.80 26.79		27.02		78
o-CH_3O		234—235	$C_{12}H_{13}N_5O_3$	25.30 25.27		25.45		84
o-C_2H_5O		212—214	$C_{13}H_{15}N_5O_3$	23.97 23.92		24.22		86
p-NO_2**		236—237	$C_{11}H_{10}N_6O_4$					96
o-Cl		195—197	$C_{11}H_{10}N_5O_2Cl$		12.40 12.31		12.73	93
m-Cl		231—232	$C_{11}H_{10}N_5O_2Cl$	24.74 24.81		25.04		93
p-Br***		191—193	$C_{11}H_{10}N_5BrO_2$					55

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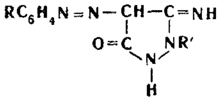
*Found: C 55.86, 55.81; H 5.09, 5.20%; calculated: C 55.59, H 5.02%.

**Found: C 45.72, 45.73, H 3.45, 3.57%; calculated: C 45.51, H 3.45%.

***Found: Br 25.27, 25.41%; calculated: Br 24.69%.

Table 2

3-Imino-4-arylazopyrazolo-5-one



<table>
<tr><th rowspan="2">R</th><th rowspan="2">R′</th><th rowspan="2">Mp, °C</th><th rowspan="2">Formula</th><th colspan="2">N, %</th><th rowspan="2">Catalyst used</th><th rowspan="2">Yield %</th></tr>
<tr><th>Found</th><th>Calculated</th></tr>
<tr><td>H</td><td>$COCH_3$</td><td>203—204</td><td>$C_{11}H_{11}N_5O_2$</td><td>28.50
28.31</td><td>28.57</td><td>EtOH</td><td>70</td></tr>
<tr><td>p-Br</td><td></td><td>223—224</td><td>$C_{11}H_{10}N_5BrO_2$</td><td>21.50
21.43</td><td>21.60</td><td>EtOH*</td><td>70</td></tr>
<tr><td>H</td><td>H</td><td>248 (decomp.)</td><td>$C_9H_9N_5O$</td><td>34.31
34.27</td><td>34.48</td><td>Hydrazine hydrate**</td><td>66</td></tr>
<tr><td></td><td></td><td></td><td>$C_9H_9N_5O$</td><td>34.35
34.14</td><td></td><td>Diethylamine</td><td>66</td></tr>
<tr><td>p-C_2H_5O</td><td></td><td>191—192</td><td>$C_{11}H_{13}N_5O_2$</td><td>28.35
28.47</td><td></td><td>Hydrazine hydrate</td><td>65</td></tr>
<tr><td></td><td></td><td></td><td></td><td>27.91
28.07</td><td>28.34</td><td>Diethylamine</td><td>59</td></tr>
<tr><td></td><td></td><td></td><td></td><td>28.14
28.20</td><td></td><td>Aniline</td><td>59</td></tr>
<tr><td>p-Br</td><td></td><td>229—230</td><td>$C_9H_8N_5BrO$</td><td>25.15
25.03</td><td>24.83</td><td>Hydrazine hydrate***</td><td>51</td></tr>
<tr><td>o-Cl</td><td></td><td>219—220</td><td>$C_9H_8N_5OCl$</td><td>29.23
29.19</td><td>29.47</td><td>Hydrazine hydrate</td><td>50</td></tr>
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*Found: C 40.45, 40.31, H 3.06, 3.18%; calculated: C 40.74, H 3.08%.

**Found: C 52.80, 52.95, H 4.45, 4.64%; calculated: C 53.20, H 4.43%.

***Found: C 37.91, 38.02, H 3.31, 3.47%; calculated: C 38.29, H 2.83%.

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