Reactions of Isomeric Arylchloropyruvates and Glycidates with Hydrazines

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Abstract—Reactions of arylchloropyruvic acids esters with aryl- and hetarylhydrazines give rise to pyrazolinedione hydrazones as a result of a tandem condensation of the substituted hydrazines with arylchloropyruvates. In contrast to this process in reaction with hydrazine hydrate a ready reduction unexpectedly occurs by Kizhner–Wolff mechanism affording 3-hydroxydihydrocinnamic acid hydrazide as the principal product. The isomeric arylglycidate reacts along the same pattern.

The condensations of α-halocarbonyl compounds with hydrazines often occur in a complex way affording several products. The main reason of this is the instability of unsubstituted and monosubstituted hydrazones of carbonyl compounds [1] containing a halogen atom in the α-position [1, 2]. Therefore even in the course of the corresponding hydrazone preparation 1,4-elimination frequently takes place affording an azoolefin molecule [3, 4]. In many cases further reaction pathway is governed by the reactivity of the intermediate formed azoolefin that undergoes isomerization into hydrazones of α,β-unsaturated carbonyl compounds which in their turn get involved into versatile 1,4-cycloadditions. The addition of an arylhydrazine may furnish a diazoolefin, osazone, and their reaction product [5]. Besides in some cases the azoolefins suffer dimerization by Diels–Alder reaction [6]. When the intermediate azoolefin contains in its structure both a diene and dienophile fragments an intramolecular cyclization may also occur by the same mechanism [7]. The azoolefins unsubstituted at the nitrogen are prone to nitrogen elimination giving an olefin, similarly to Kizhner reduction [8]. The various concurrent reactions proceeding in the system chloropyruvate Ia, Ib–hydrazine or phenylhydrazine commonly prevent isolation of individual products and their identification at the use of equimolar reagents ratio since the hydrazine and many among its derivatives show abnormal high nucleophilic activity with respect to the sp²-hybridized carbon atom linked to the corresponding leaving groups [1, 9]. On the other hand, condensation of hydrazine and its derivatives with carbonyl compounds affording hydrazones is well known and is widely used for aldehydes and ketones identification [10]. At the same time the hydrazines alkylation occurs usually at the more substituted nitrogen. With a bulky alkylating agent the attack may be directed also on the other nitrogen atom [11].

The above mentioned concise analysis of the published data reveals that the reactions of hydrazones even with the simplest representatives of the α-haloketones, like α-haloacetophenones and α-chloroacetone, take multiple routes affording cyclic and non-cyclic compounds of various types. The number of probable and sometimes unpredictable reactions with nucleophilic reagents increases even more due to the possible processes involving additional functional groups introduced into the structure of the α-haloketones [8, 9, 12, 13]. In this connection we deemed it interesting to study the behavior in the condensation with various hydrazines of functionalized α-chloroketones: methyl phenyl- (Ia) and 3-nitrophenoxychloropyruvates (Ib), and of one among the chloroepoxides isomeric to the above esters, methyl 3-(3-nitrophenoxy)-2-chloroglycidate (II) (the precursor of the chloropyruvate). These compounds might act either like functionally-substituted α-chloroketones, or like unsubstituted ketones, or like esters of β-chlorocarboxylic acids.
The study of reaction between arylchloropyruvates \textbf{Ia} and \textbf{Ib} and hydrazines revealed that the best results were obtained in the process carried out in a boiling methanol solution at the molar reagents ratio of 1:3. From the products of reaction between compound \textbf{Ia} and hydrazine hydrate we isolated a substance whose spectral characteristics did not fit to those of azoolefin \textbf{III} \[2\] and/or olefin \textbf{IV} \[1, 2\], the expected products of these reactions. The presence in the H$_1$NMR spectrum signals from protons of the CH$_2$CH group in the form of an ABX system, and also the lack of the methoxy group signal and appearance of broadened singlets with the intensity ratio 2:1 in the region 4.17 and 9.28 ppm belonging to the protons of a hydrazide moiety suggest that the reaction of chloropyruvate \textbf{Ia} with hydrazine hydrate occurs involving all electrophilic sites, namely, with the reduction of the cabonyl group by Kizhner–Wolff reaction \[1\], the hydrazinolysis of the ester group, and the hydrolysis of the benzylhalide fragment resulting in 3-phenyl-3-hydroxypropionic acid hydrazide (\textbf{V}) (Scheme 1).

The standard reaction products of \(\alpha\)-chloroketones and hydrazines are commonly azoolefins that further are converted into olefins \[12\]. In the event described here the expected products were azoocompound \textbf{III} and methyl cinnamate \textbf{IV}. But inasmuch as the reaction of the latter with the hydrazine hydrate does not afford compound \textbf{V} (resulting from the hydration of the olefin bond and the hydrazinolysis) but a dihydrocynamic acid hydrazide (\textbf{VI}) (a product of the olefin bond reduction followed by hydrazinolysis) and 3-pyrazolidone (\textbf{VII}) (Scheme 2), it is presumable that the keto function in the phenylchloropyruvate \textbf{I} is reduced into a methylene group before the 1,4-elimination of HCl from the intermediate hydrazone \textbf{IIIa} to give azoolefin \textbf{III} which should have provided methyl ester \textbf{IV} and further the dihydrocynamic acid hydrazide; most likely, the hydrazone intermediate \textbf{IIIa} undergoes the Kizhner–Wolff reduction and then hydrazinolysis and hydrolysis of the \(\alpha\)-chlorobenzyl function leading finally to hydrazide \textbf{V}.

The Kizhner–Wolff reduction under these mild conditions is a remarkable fact for this reaction usually requires high temperature (200–230°C) and a presence of strong bases \[1, 14\].

The reaction of methyl arylchloropyruvates \textbf{Ia} and \textbf{Ib} with phenylhydrazine, weaker base than hydrazine (pK$_a$ 5.27 and 7.95 respectively \[15\]), in the boiling methanol gave rise to crystalline substances of light-orange (\textbf{VIIIa}) and bright-red (\textbf{VIIIb}) color depending on the initial chloropyruvates \textbf{Ia} and \textbf{Ib}. Based on the analytical and spectral data we assigned these reaction products isomeric structures \textbf{VIII} and \textbf{IX}. 

\begin{enumerate}
  \item Scheme 1.
  \item Scheme 2.
\end{enumerate}