A new annelation reaction in a series of cyclic Schiff's bases is described with examples of [3 + 3] cyclocondensation of 1-alkyl-3,4-dihydroquinolines and acetoacetic esters.

**Keywords:** azomethines, benzo[a]quinolizines, 3,4-dihydroisoquinolines, ketimines, β-keto esters, Schiff's bases, pyrido[2,1-a]isoquinolines, annelation, heterocyclization, cyclocondensation.

The multifunctionality of cyclic ketimines and derivatives of carbonyl compounds permits exceptionally wide possibilities for the synthesis of condensed nitrogen-containing heterocycles with an angular nitrogen atom [1-5], particularly alkaloids [6,7], and heterocyclic analogs of steroids (azasteroids) [3-5].

We previously studied the reaction of azomethines 1 with aminovinylcarbonyl (2, X = 2H) and dicarbonyl (2, X = O) compounds, leading to the condensed system 3 (Scheme 1) [5].

An additional stimulus for studying such reactions were the numerous data on the interaction of β-dicarbonyl compounds (1,3-dielectrophiles) with bifunctional nitrogen bases, such as hydrazine [8], hydroxylamine [9], and others [10].

Scheme 1

\[
\begin{align*}
\text{I} \quad \text{[H}^+\text{]} & \quad \text{NH} \\
R \quad \text{N} & \quad \text{R} \\
& \quad \text{X} \\
\end{align*}
\]

\[
\begin{align*}
\text{I} \quad \text{I} \quad \text{O} \\
\text{NH} \quad \text{NH} & \quad \text{R} \\
& \quad \text{X} \\
\end{align*}
\]

\[
\begin{align*}
\text{R} = \text{H, Alk; R}^' = \text{Alk, (CH}_2)_n; X = \text{2H, O}
\end{align*}
\]
In contemporary theory and practice of organic chemistry the enamine tautomers of Schiff’s bases are usually considered as C-nucleophiles [11-15]. However the results of theoretical investigations [16] and experimental data [5] enable these compounds to be considered as 1,3-dinucleophiles, capable of interacting with dielectrophiles. Paying attention to the results of the previous investigations [17,18], and also to the ability of 1-alkyl substituted 3,4-dihydroisoquinolines (cyclic ketimines) to act both as imine (4I) and as enamine (4E) tautomers [19], and the 1,3-dielectrophilic nature of β-keto esters, we have studied the interaction of 3,4-dihydroisoquinolines 4a,b with acetoacetic esters 5a-d. It was discovered that, as a result of these interactions, a previously unknown heterocyclization reaction is effected, leading to pyrido[2,1-a]isoquinolines (benzo[a]quinolizines, 6a-d). As a result of the interaction of the indicated substrates it is theoretically possible to expect the formation of both derivatives 6a-d and derivatives 7 isomeric with them. However the sole products of the interaction studied proved to be derivatives 6a-d.

![Scheme 2](image)

The condensation of 3,4-dihydroquinolines 4a,b with acetoacetic esters 5a-d was effected by heating mixtures of them at 140-220°C. The reaction products were isolated after cooling and were purified by crystallization. In individual cases flash chromatography (Silica gel L 40/5 µ from Chemapol, eluent chloroform) was used for isolation and purification of the product [20].

The enhanced tendency of derivatives 6a-d to form crystal hydrates should be noted. These are extremely stable and lose the water of crystallization with difficulty even on heating under reduced pressure over phosphoric anhydride. On the strength of this it is necessary to use anhydrous solvents to obtain samples without solvated water.

The structure ascribed to the product of interaction of 3,4-dihydroisoquinolines 4a,b with acetoacetic esters 5a-d was confirmed by data of physicochemical investigations, and for compound 6a also by data of X-ray structural analysis.

In the IR spectra of derivatives 6a-d intense broadened and asymmetric absorption bands (AB) were observed at 1590-1620, 1570-1585, and 1485-1550 cm⁻¹ caused by C=O and C=C stretching vibrations of the γ-pyridone C rings and the benzene A rings [21], and also AB at 1440-1470 cm⁻¹ which are caused by the C–H deformation vibrations of methylene and methyl groups [22].