Two methods of preparation have been proposed and the synthesis has been effectuated of a large series of \( \beta \)-N-acylhydrazides of 1-R-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acids. The possibility of using various condensing agents for converting them into the corresponding 1,3,4-oxadiazoloquinolines has been studied. Results are given of an investigation of the antitubercular activity of the synthesized compounds.

**Keywords:** acylhydrazines, 4-hydroxy-2-oxoquinoline-3-carboxylic acids, 1,3,4-oxadiazoles, antitubercular activity.

A characteristic feature of the search for new medicinal agents under modern conditions is purpose-directed synthesis based on developing, accumulating, and systematizing empirical data on the relation between chemical structure and the biological properties of substances. It is impossible in principle to develop rules of such a type from the example of any one compound. It is necessary to study a series of related structures [2]. The present communication is the investigation of just such a series, the aim of which is the definition in the structure of previously described benzylidenehydrazides of 1-R-4-hydroxy-2-oxo-1,2-dihydro-quinoline-3-carboxylic acids [3-5] of functional groups strengthening or, on the other hand, weakening the antitubercular activity of these substances.

To carry out the projected aim we obtained, and then subjected to microbiological screening, \( \beta \)-N-acylhydrazides of 1-R-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acids 1-4, which are formally derivatives of the acylhydrazones indicated above. The subjects of the investigation were synthesized by the two methods given in the scheme: by hydrazinolysis of the ethyl esters of quinoline-3-carboxylic acids 5 with subsequent acylation of the intermediate hydrazides 6 (method A) or by the direct reaction of esters 5 with previously obtained benzyldihydrzines (method B). Both methods are fairly simple in use, are readily reproduced, and give good yields of the desired 1,2-diacylhydrazines 1-4 (see Table 1). At first sight method B appears preferable since it is possible to form the final compounds in one step. At the same time each of the reactions in method A is distinguished by high

* For Communication 148 see [1].
efficiency. In fact the main criterion when selecting one or other of the methods of obtaining 1,2-diacylhydrazines 1-4 in each actual case is the availability of the respective reactants, viz. the presence of the prepared hydrazides of aromatic carboxylic acids using method B, or in the absence of them using the linear synthetic scheme A.

![Diagram of synthetic scheme](image)

\[
\begin{align*}
1\text{a–m}, & 5,6 \text{ a } R = \text{H, b } R = \text{Me, c } R = \text{Et, d } R = \text{Pr;} \\
1–4 \text{ a } R^1 = \text{H, b } R^1 = \text{2-F, c } R^1 = \text{2-Cl, d } R^1 = \text{3-Cl, e } R^1 = \text{2-Br, f } R^1 = \text{4-Br, g } R^1 = \text{2,4-Cl}_2, \\
h \text{ R }^1 = \text{2-NO}_2, i \text{ R }^1 = \text{3-NO}_2, j \text{ R }^1 = \text{4-NO}_2, k \text{ R }^1 = \text{3,5-(NO}_2)_2, l \text{ R }^1 = \text{3-Me, m } R^1 = \text{4-Me.}
\end{align*}
\]

All the synthesized 1,2-diacylhydrazines 1-4 (Table 1) were colorless crystalline substances practically insoluble in water and weakly soluble in alcohols. In their $^1$H NMR spectra (Table 2) signals of 7-9 protons close in properties were concentrated in the fairly narrow section from 7.25 to 8.18 ppm in the "aromatic" region of the spectrum. Consequently precise assignment was difficult if not impossible in the majority of cases without using special NMR procedures. Only in the spectra of the 3,5-dinitrobenzoyl derivatives 1k-4k, thanks to the two possessing the powerful magnetic anisotropy nitro groups, were the signals of the protons of the β-N-acyl residues strongly displaced towards low field and overlap with the signals of the quinolone protons was not observed.

The microbiological testing carried out showed that in vitro none of the obtained 1,2-diacylhydrazines 1-4 at a concentration of 6.25 µg/ml was capable of inhibiting to a significant degree the growth of Mycobacterium tuberculosis H37Rv ATCC 27294. The negative effect on antitubercular activity of replacing the azomethine grouping in benzylidenehydrazines of 1-R-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acids by an amide fragment similar in structure has therefore been confirmed experimentally.

![Diagram of synthetic scheme](image)

\[
\begin{align*}
8 \text{ a } R = \text{Et, b } R = \text{Pr.}
\end{align*}
\]