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4-HYDROXY-2-QUINOLONES. 93*. SYNTHESIS AND BIOLOGICAL PROPERTIES OF 2-HYDROXY-4-IMINO-1,4-DIHYDROQUINOLINE-3-CARBOXYLIC ACID N-R-AMIDES

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Various methods of synthesizing amides of 2-hydroxy-4-imino-1,4-dihydroquinoline-3-carboxylic acids have been studied. Results of investigations on the antitubercular and antiinflammatory activity of the obtained compounds are discussed.

Keywords: 4-chloro-2-oxo-1,2-dihydroquinolines, 2-hydroxy-4-imino-1,4-dihydroquinolines, amidation, intramolecular cyclization, enamine–imine tautomerism, antitubercular and anti-inflammatory activity.

Amides are a class of organic compounds which are rightfully considered to be most convenient for carrying out investigations devoted to the search for rules on structure–pharmacological activity links. The basis for such a conclusion is the fact that the amide group is an important component of many biologically active substances, both natural and synthetic. The enormous variety of methods and procedures used in the synthesis of amides, and also the practically unlimited selection of starting materials, enables systematic changes to be introduced into the structure of the final compounds, thereby purposefully changing their physicochemical and biological properties.

Proceeding from this, one of the stages of our investigations was devoted to the amide of 4-amino-2-oxoquinoline-3-carboxylic acids. As one of the proposed variants of obtaining such compounds we studied the possibility of synthesizing amides of 1H-4-chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acid **1**, which then might be transformed into the 4-amino derivative by any suitable method.

Previous attempts to obtain amides **1** by the reaction of 4-chloro acid **2a** with amines in the presence of N,N'-dicyclohexylcarbodiimide were unsuccessful [2]. Activation of the acid component of acid **2a** with N,N'-carbonyldiimidazole (CDI) also gave no positive result. It turned out that on interacting 4-chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acid (**2a**) with N,N'-carbonyldiimidazole in anhydrous DMF the vigorous evolution of CO_2 characteristic of this reaction was observed, obviously indicating the formation of acylimidazole **3** (Scheme 1).

* For Part 92 see [1].

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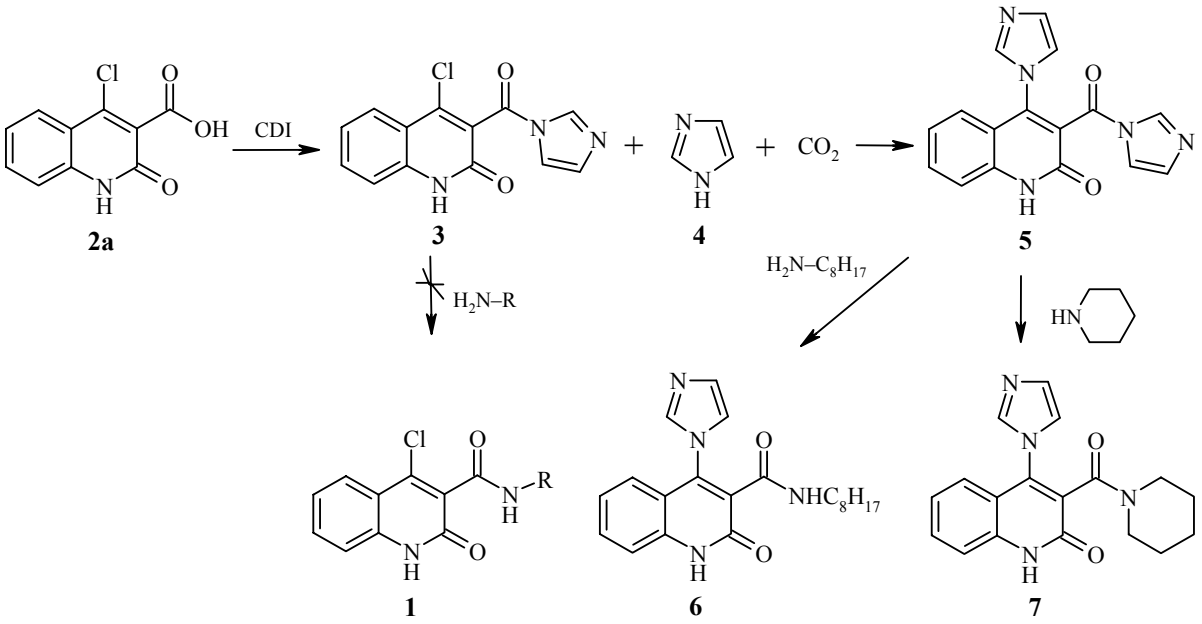
Scheme 1



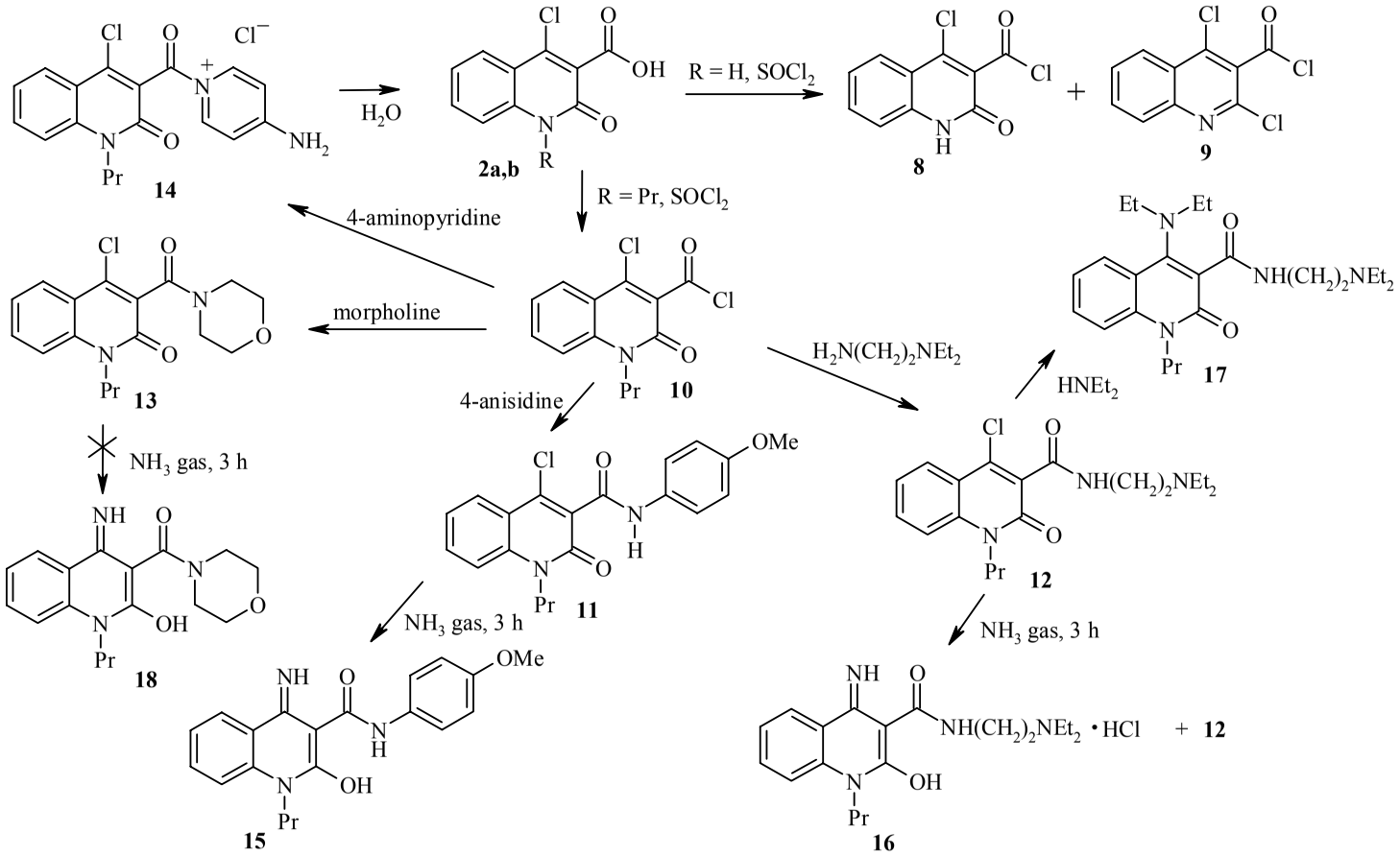
It was assumed that further treatment of it with N-nucleophiles must lead to the corresponding amide of 1H-4-chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acid **1**. On the basis of the attempts made, it was shown that the acylimidazole obtained as a result of the reaction of 4-chloro acid **2a** with N,N'-carbonyldiimidazole in reality reacts smoothly with primary and with secondary aliphatic amines. However it was established by methods of ^{1}H NMR spectroscopy and chromato-mass spectrometry that the compounds synthesized in this way are not the expected N-R-amides of 1H-4-chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acid **1** but are alkyl and dialkyl amides of 1H-4-(1-imidazolyl)-2-oxo-1,2-dihydroquinoline-3-carboxylic acid **6** and *7* respectively. It follows from this that the chlorine atom of the initially formed imidazide **3** is readily substituted under the synthesis conditions by a residue of liberated imidazole **4**, which leads to the imidazolide of 1H-4-(1-imidazolyl)-2-oxo-1,2-dihydroquinoline-3-carboxylic acid (**5**) and finally to amides **6** and **7**.

Attempts to activate the carbonyl of the carboxyl group of 4-chloro acid **2a** by converting it to an acid halide were also unjustified. By the action of an excess of thionyl chloride 1H-4-chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acid chloride (**8**) is indisputably formed, but regrettably the reaction failed to stop at this stage, since in acid chloride **8** the 2-C=O group (more precisely its hydroxy tautomer) is also fairly readily exchanged by chlorine, showing the activating influence of the neighboring acid chloride grouping. The extreme ease of exchange of the 2-C=O group by halogen (which is exchanged first) was also noted for 1H-3-ethoxycarbonyl-4-hydroxy-2-oxo-1,2-dihydroquinoline in [3]. As a result, the final product of the described reaction is in fact a mixture of the acid chlorides of 4-chloro-2-oxo- and 2,4-dichloroquinoline-3-carboxylic acids **8** and **9** respectively (Scheme 2). For this reason the acid chloride method of obtaining 1H-4-chloro-2-oxo-1,2-dihydro-quinoline-3-carboxamides also has no practical value.

It is understandable that the corresponding acid chlorides **10** are synthesized without complications from 1-substituted 4-chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acids (for example, **2b** R = Pr), since the possibility of forming 2-hydroxy forms with subsequent replacement of the hydroxy group by halogen is excluded in such cases.

As was expected, acid chloride **10** readily acylates primary aromatic, aliphatic, and secondary amines and the corresponding amides **11-13** are formed as a result. Reaction occurs with aminopyridines somewhat unusually, at first sight. Thus, after interaction of the acid chloride of 4-chloro-2-oxo-1-propyl-1,2-

Scheme 2


Cl
O
Cl⁻
N
+
NH2
Pr
14
H2O
OH
R
2a,b
R = H, SOCl2
8
9
R = Pr, SOCl2
4-aminopyridine
morpholine
13
10
Et
N
Et
NH(CH2)2NEt2
17
H2N(CH2)2NEt2
HNEt2
4-anisidine
OMe
11
12
NH3 gas, 3 h
18
15
16
NH(CH2)2NEt2 · HCl
+ 12

dihydroquinoline-3-carboxylic acid (**10**) with 4-aminopyridine in dry acetone, maintaining the reaction mixture for 10 h at room temperature, and subsequently diluting with water, the initial 4-chloro-2-oxo-1-propyl-1,2-dihydroquinoline-3-carboxylic acid (**2b**) was isolated. The obtained result is undoubtedly due to the formation not of the amide but of the N-acylpyridylammonium salt **14**. Such behavior on acylation with acid chlorides is characteristic of many azaheterocyclic amines, including aminopyridines [4], although usually salts of the type of **14** are far less stable and are rapidly rearranged into the corresponding acylamino derivatives, i.e. amides. Aminopyridines, existing predominantly in the aromatic form, are acylated at the heteroatom in neutral medium, since it is the nucleophilic center in just those conditions. This fact is explained from the position of the principle of hard and soft acids and bases. An acid chloride is a relatively soft electrophile, consequently it attacks a more soft reaction center bearing a more negative charge, i.e. the pyridine nitrogen atom [5].

Unlike the ethyl esters of 1-R-4-chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acids [6] the chlorine atom in methoxyanilide **11** is readily exchanged by an amino group with the formation of the 4-imino derivative **15** on reaction with gaseous ammonia at normal pressure, although it would be more logical to expect a reduction in reactivity, since the carbonyl in amides is superseded by ester in its activating effect [7]. A similar effect, although less marked, is also observed in the case of diethylaminoethylamide **12**. According to ^{1}H NMR data, after treatment of this compound with ammonia under the same conditions and for the same time (Scheme 2), the exchange of halogen by an amino group occurs only to 60%, although this reaction goes readily with diethylamine and the 4-diethylamino derivative **17** is formed practically quantitatively.

It is interesting that with other amines, the basicity of which is significantly less than ammonia (for example, with anilines), the esters of 4-chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acids react without any complications [1]. The same may be said about sterically hindered amines (isopropylamine, 1-phenylethylamine) [8]. In reality the selective inertness noticed previously in [6] of the ethyl esters of 1-R-4-chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acids in relation just to ammonia is caused not by the mobility of the chlorine atom, but by other reasons, obstructing the specific mutual orientation of the reacting molecules and thereby not permitting them to approach fairly close to one another. One of such reasons may be, for example, the formation of complexes of 4-chloroquinoline-3-carboxylic acid ester with ammonia, as a result of which access to the carbon atom in position 4 of the quinoline for nucleophilic attack becomes impossible.

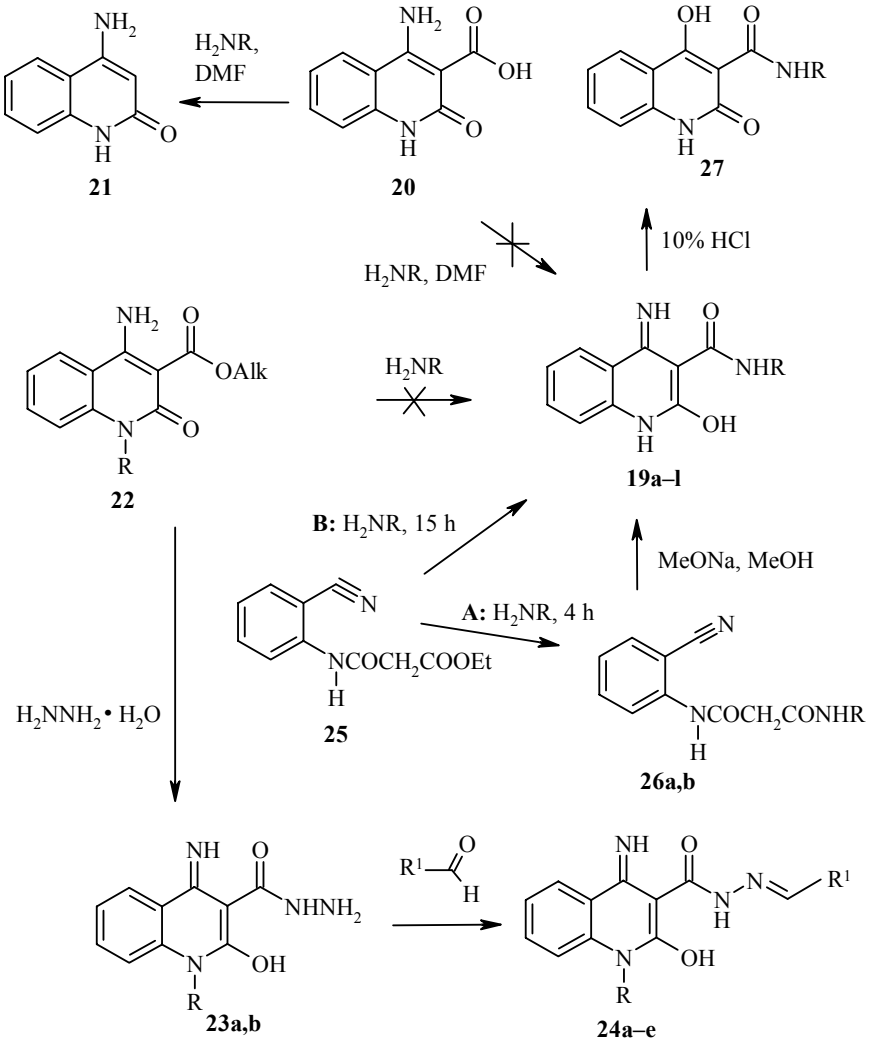
A distinctive special feature of the structure of primary amides of 1-R-2-oxo-1,2-dihydroquinoline-3-carboxylic acids [9-12], among them probably their 4-chloro substituted analogs **11** and **12**, is the formation of a stable intramolecular hydrogen bond 2-C=O···H-N(R)–$CO_{(3)}$, which evidently also prevents the formation of unreactive compounds with ammonia. Confirmation of this conclusion is the fact that like the ester the secondary amides of 1-R-4-chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acids (for example **13**), in which the formation of the indicated intramolecular hydrogen bond is impossible, do not react with ammonia at normal pressure.

It follows from the results presented that 1-R-4-chloro-2-oxo-1,2-dihydro-quinoline-3-carboxylic acids are expedient for use only in the synthesis of 1-substituted 2-hydroxy-4-imino-1,4-dihydroquinoline-3-carboxamides. The 1-H-derivative **19** regrettably was not successfully obtained by any of the methods considered. The amidation of 1-H-4-amino-2-oxo-1,2-dihydroquinoline-3-carboxylic acid (**20**, Scheme 3) was also unsuccessful. Boiling equimolar quantities of acid and amine in DMF, used successfully in the synthesis of alkylamides of 1-H-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid [13], was accompanied in this case by the decarboxylation of the 4-aminoacid **20** with the formation of 1-H-4-amino-2-oxo-1,2-dihydroquinoline (**21**).

Esters of 4-amino-2-oxo-1,2-dihydroquinoline-3-carboxylic acids **22** also do not react with alkylamines. At the same time hydrazinolysis of these compounds was effected and hydrazides of 1-R-2-hydroxy-4-imino-1,4-dihydroquinoline-3-carboxylic acids **23** may be isolated in good yield. Subsequent treatment of them with aromatic aldehydes gives the corresponding arylidenehydrazides **24a-e**.

Concerning the alkylamides of 1H-2-hydroxy-4-imino-1,4-dihydroquinoline-3-carboxylic acid **19**, a different synthetic scheme to obtain them is completely justified, by forming the aminoquinolone nucleus just to carry out amidation. As it turned out the ethyl ester of 2-cyanomalonic acid (**25**) is amidated fairly simply, and the alkylamides **26** formed in this way may be obtained in the pure state or, after treatment with sodium methylate in anhydrous methyl alcohol, are converted into the desired 1-H-2-hydroxy-4-imino-1,4-dihydroquinoline-3-carboxamides **19a-l** in high yield and without isolation from the reaction mixture (Table 1, method A).

Scheme 3



19 a R = $CH_2CH{=}CH_2$, **b** R = Pr, **c** R = *i*-Bu, **d** R = *i*-C_5H_{11}, **e** R = C_6H_{13}, **f** R = C_8H_{17}, **g** R = CH_2Ph, **h** R = 2-picolyl, **i** R = 3-picolyl, **j** R = 4-picolyl, **k** R = furfuryl, **l** R = $CH_2CH_2NMe_2$; **23 a** R = H, **b** R = C_7H_{15}; **24 a** R = H, R^1 = 2-FC_6H_4, **b** R = H, R^1 = 3-FC_6H_4, **c** R = C_7H_{15}, R^1 = 2-pyridyl, **d** R = C_7H_{15}, R^1 = 3-pyridyl, **e** R = C_7H_{15}, R^1 = 4-pyridyl; **26 a** R = *i*-Bu, **b** R = CH_2Ph

TABLE 1. Characteristics of Alkylamides of 1-H-2-Hydroxy-4-imino-1,4-dihydroquinoline-3-carboxylic Acid **19a-l**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %*
		C	H	N		
19a	$C_{13}H_{13}N_3O_2$	64.31 / 64.19	5.25 / 5.39	17.12 / 17.27	254-256	83
19b	$C_{13}H_{15}N_3O_2$	63.78 / 63.66	6.14 / 6.16	17.24 / 17.13	247-249	80
19c	$C_{14}H_{17}N_3O_2$	64.70 / 64.85	6.57 / 6.61	16.10 / 16.20	244-246	77
19d	$C_{15}H_{19}N_3O_2$	65.79 / 65.91	7.15 / 7.01	15.43 / 15.37	243-245	78
19e	$C_{16}H_{21}N_3O_2$	66.73 / 66.88	7.23 / 7.37	14.66 / 14.62	240-241	80
19f	$C_{18}H_{25}N_3O_2$	68.42 / 68.54	7.86 / 7.99	13.21 / 13.32	250-252	79
19g	$C_{17}H_{15}N_3O_2$	69.70 / 69.61	5.02 / 5.15	14.39 / 14.33	255-257	83
19h	$C_{16}H_{14}N_4O_2$	65.21 / 65.30	4.67 / 4.79	19.17 / 19.04	224-226	77
19i	$C_{16}H_{14}N_4O_2$	65.15 / 65.30	4.88 / 4.79	19.11 / 19.04	266-268	82
19j	$C_{16}H_{14}N_4O_2$	65.28 / 65.30	4.71 / 4.79	19.09 / 19.04	293-295	81
19k	$C_{15}H_{13}N_3O_3$	63.53 / 63.60	4.50 / 4.63	14.92 / 14.83	245-247	84
19l	$C_{14}H_{18}N_4O_2$	61.37 / 61.30	6.54 / 6.61	20.65 / 20.42	218-220	70

* Yield is given for method A (compounds **19a-k**) and B (compound **19l**).

Being bases, alkylamines in principle are capable not only of amidating the acyclic ester **25**, but also of catalyzing its intramolecular cyclization. However the ethyl (or methyl as a possible product of transesterification after carrying out the synthesis in methanol) ester of 4-amino-2-oxo-1,2-dihydroquinoline-3-carboxylic acid was not detected in the reaction mixture. Nonetheless partial closure of the ring occurs, but after amidation, which is indicated by the cyclic *iso*-butylamide **19c** isolated after treatment of ester **25** with *iso*-butylamine (method B). With the usual aliphatic amines the cyclization of amides of 2-cyanomalonanilic acid **26** occurs fairly slowly, consequently to reduce the reaction time the need also arises to apply stronger bases, such as sodium methylate. But on using alkylamines containing more basic groupings than a primary aliphatic amino group (such as the tertiary amino group of dimethylaminoethylamine) the synthesis of the corresponding cyclic compound **19l** is effected efficiently and without adding sodium alcoholates.

A characteristic special feature of the ^{1}H NMR spectra of acyclic alkylamides of 2-cyanomalonanilic acid **26** is the singlet signal of the malonic acid methylene group protons of intensity 2H at 3.4 ppm. On closing the quinoline ring this signal routinely disappears. A more detailed analysis of the ^{1}H NMR spectra of cyclic alkylamides and hydrazides **19**, **23**, **24** shows that, unlike 4-amino-2-oxo-1,2-dihydroquinoline-3-carboxylic acids and their esters, the amidated derivatives exist in the 2-hydroxy-4-imino form (Table 2). The imino group is displayed in the spectrum by a broadened singlet forming, with the doublet of the aromatic quinoline H-5 proton, a general signal of integrated intensity 2H. The 2-hydroxy-4-imino-1,4-dihydroquinoline structure of amides **19** is also confirmed by their chemical properties. On treatment with 10% HCl solution these compounds are converted quantitatively into 4-hydroxy derivatives **27**. It is necessary to take this circumstance into account when isolating amides **19** and in order to avoid hydrolysis of the 4-amino group mineral acids are not used to neutralize the excess of basic catalyst. Dilute acetic acid is completely suitable for this purpose.

TABLE 2. ^{1}H NMR Spectra of Alkylamides of 1-H-2-Hydroxy-4-imino-1,4-dihydroquinoline-3-carboxylic Acid **19a-l**

Compound	Chemical shifts, δ, ppm. (*J*, Hz)*						
	2-OH (1H, s)	NH-Alk (1H, t)	H arom.				R
			H-5+ HN= (2H, d)	H-7 (1H, t)	H-8 (1H, d)	H-6 (1H, t)	
19a	10.85	10.68 (*J* = 5.0)	8.11 (*J* = 8.1)	7.56 (*J* = 7.0)	7.29 (*J* = 7.8)	7.18 (*J* = 7.0)	5.90 (1H, m, CH=); 5.15 (2H, m, =CH_2); 3.91 (2H, t, *J* = 5.8, NCH_2)
19b	10.90	10.57 (*J* = 5.0)	8.10 (*J* = 8.0)	7.64 (*J* = 7.1)	7.28 (*J* = 8.1)	7.16 (*J* = 7.1)	3.23 (2H, q, *J* = 6.8, NCH_2); 1.56 (2H, m, $NCH_2C\underline{H}_2$); 0.89 (3H, t, *J* = 6.8, CH_3)
19c	10.81	10.63 (*J* = 5.4)	8.09 (*J* = 8.1)	7.55 (*J* = 7.0)	7.26 (*J* = 7.9)	7.17 (*J* = 7.0)	3.10 (2H, t, *J* = 6.1, NCH_2); 1.78 (1H, m, CH); 0.90 (6H, d, *J* = 6.9, $2CH_3$)
19d	10.84	10.52 (*J* = 5.1)	8.10 (*J* = 7.9)	7.59 (*J* = 7.0)	7.27 (*J* = 8.0)	7.18 (*J* = 7.0)	3.26 (2H, q, *J* = 6.2, NCH_2); 1.48 (1H, m, CH); 1.42 (2H, q, *J* = 6.8, $NCH_2C\underline{H}_2$); 0.91 (6H, d, *J* = 6.8, $2CH_3$)
19e	10.88	10.54 (*J* = 5.0)	8.09 (*J* = 8.0)	7.58 (*J* = 7.1)	7.29 (*J* = 8.0)	7.19 (*J* = 7.1)	3.23 (2H, q, *J* = 6.4, NCH_2); 1.30 (8H, m, $(C\underline{H}_2)_4CH_3$); .86 (3H, t, *J* = 7.2, CH_3)
19f	10.80	10.55 (*J* = 5.1)	8.10 (*J* = 7.9)	7.56 (*J* = 7.0)	7.28 (*J* = 8.0)	7.18 (*J* = 7.0)	3.24 (2H, q, *J* = 6.4, NCH_2); 1.26 (12H, m, $(C\underline{H}_2)_6CH_3$); 0.84 (3H, t, *J* = 7.2, CH_3)
19g	10.79	10.95 (*J* = 5.4)	8.11 (*J* = 8.1)	7.58 (*J* = 7.1)	7.40-7.13 (7H, m, H-8,6 + C_6H_5)		4.51 (2H, d, *J* = 6.1, NCH_2); C_6H_5 - see H arom.
19h	10.71	11.10 (*J* = 5.0)	8.11 (*J* = 8.0)	7.59 (*J* = 7.0)	7.44-7.10 (4H, m, H-8,6 + H-3',5'-Py)		8.54 (1H, d, *J* = 5.0, H-6'); 7.81 (1H, t, *J* = 7.1, H-4'); H-3',5'-Py see H arom.; 4.61 (2H, d, *J* = 5.4, NCH_2)
19i	10.71	11.02 (*J* = 5.4)	8.12 (*J* = 8.2)	7.58 (*J* = 7.1)	7.47-7.06 (3H, m, H-8,6 + H-5'-Py)		8.58 (1H, s, H-2'); 8.45 (1H, d, *J* = 5.0, H-6'); 7.73 (1H, d, *J* = 7.9, H-4'); H-5'-Py see H arom.; 4.53 (2H, d, *J* = 6.1, NCH_2)
19j	10.67	11.06 (*J* = 5.4)	8.13 (*J* = 8.0)	7.58 (*J* = 7.1)	7.36 (3H, m, H-8+H-3',5')	7.19 *J* = 7.1	8.51 (2H, d, *J* = 4.9, H-2',6'); H-3',5'-Py see H arom.; 4.54 (2H, d, *J* = 6.1, NCH_2)
19k	10.70	10.87 (*J* = 5.0)	8.12 (*J* = 8.0)	7.56 (2H, m, H-7+H-5')	7.30 (*J* = 8.2)	7.20 (*J* = 7.2)	H-5' - see H arom. 6.39 (1H, t, *J* = 2.0, H-4'); 6.28 (1H, d, *J* = 3.6, H-3'); 4.49 (2H, d, *J* = 6.1, NCH_2)
19l	10.82	10.55 (*J* = 6.1)	8.09 (*J* = 8.0)	7.55 (*J* = 7.1)	7.29 (*J* = 8.2)	7.18 (*J* = 7.1)	3.35 (2H, q, *J* = 6.1, NCH_2); 2.42 (2H, t, *J* = 6.1, $C\underline{H}_2N(CH_3)_2$); 2.20 (6H, s, $N(CH_3)_2$)

* Signals of the NH group protons of the quinolone fragments have the form of a singlet at 10.09-11.23 ppm.

The mass spectra of alkylamides of 1-H-2-hydroxy-4-imino-1,4-dihydroquinoline-3-carboxylic acid **19** were interesting for the investigation, particularly in comparison with the mass spectra of their synthetic precursors, the amides of 2-cyanomalonanilic acid **26**, since they are isomers and their molecular masses are identical. Under the action of electron impact the cyclic amides **19** form molecular ions, but the intensity of the peaks did not exceed 10%. Further fragmentation is accompanied by fission of the amide bond and the formation of two fragments, the peak of one of which has the maximum intensity in the spectrum, although for amides with branched alkyl chains (such as *iso*-butylamide **19c**) initial loss of an *iso*-propyl fragment is also possible.

Comparison of the mass spectra of isomeric *iso*-butylamides of 2-cyano-malonanilic (**26a**) and 1-H-2-hydroxy-4-imino-1,4-dihydroquinoline-3-carboxylic (**19c**) acids showed that they are practically identical, differing only in the intensity of peaks of certain ions. Evidently in the mass spectrometer (rapid heating in vacuum) the acyclic amide **26a** is subject to intramolecular condensation and in fact the spectrum recorded is of the already cyclic amide **19c**, since such behavior at increased temperatures is characteristic of many active-methylene nitriles having the structural prerequisites for this.

The structural similarity with derivatives of 4-hydroxy-2-oxo-1,2-dihydro-quinoline-3-carboxylic acids which display marked antimycobacterial properties in experiments *in vitro* [15], served as a theoretical basis for studying the antitubercular activity of some of the compounds synthesized by us, particularly the hydrazides and arylidenehydrazides of 1-R-2-hydroxy-4-imino-1,4-dihydroquinoline-3-carboxylic acids **23** and **24**. The microbiological screening was carried out at the National Institute of Allergy and Infectious Diseases in the USA within the framework of the TAACF (Tuberculosis Antimicrobial Acquisition & Coordinating Facility) program in relation to *Mycobacterium tuberculosis* H37Rv ATCC 27294 using nutrient medium BACTEC 12B and the radiometric system BACTEC 460 [16-19]. Analysis of the experimental data obtained showed that replacement of the 4-hydroxy-2-oxo-1,2-dihydroquinoline nucleus by 2-hydroxy-4-imino-1,4-dihydroquinoline leads practically to complete loss of antimycobacterial properties, and in the plan of searching for new agents useful for combating tuberculosis, such a modification is not expedient.

As a result of investigations of the anti-inflammatory activity of amides **19a-l** carried out on the carrageenan paw edema model in white rats [20], it was established that in the character of the action on the course of the inflammatory reaction they were like the 2-oxo-1,2-dihydro-4-quinolinylaminocarboxylic acids described previously in [1]. Intraperitoneal injection of these substances aids reduction of the inflammation, but only for 1-2 h, after which a drop in activity and even the appearance of an inflammatory effect follows.

EXPERIMENTAL

The mass spectra of the synthesized compounds were recorded on a Kratos MS 890A magnetic mass spectrometer, ionizing by electron impact (EI) at 70eV with direct insertion of samples, heating the coupling for direct insertion with a heating chamber at 250°C, or on a Hewlett Packard 5890/5972 instrument in total scanning mode for the range 35-700 *m/z*, ionization by electron impact (EI) at 70 eV; chromatographic column Hewlett Packard 5MS, length 25 m, internal diameter 0.2 mm, stationary phase was a polysiloxane film (5% diphenylpolysiloxane, 95% dimethylpolysiloxane) of thickness 0.33 μm, carrier gas helium. The ^{1}H NMR spectra were obtained on a Bruker WM 250 (250 MHz) instrument in DMSO-d_6, internal standard was TMS. 4-Chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acids **2** were obtained by the known procedure of [21]. Anhydrous DMF for peptide synthesis from Fluka was used in the synthesis of amides **6**, **7**, and **15**.

Octylamide of 1-H-4-(1-Imidazolyl)-2-oxo-1,2-dihydroquinoline-3-carboxylic Acid (6). N,N'-Carbonyldiimidazole (1.78 g, 0.011 mol) was added to a solution of acid **2a** (2.23 g, 0.01 mol) in anhydrous DMF (20 ml) and, while protected from the moisture of the air by a $CaCl_2$ tube, was maintained for ~1 h at 90°C until CO_2 evolution ceased. Octylamine (1.65 ml, 0.01 mol) was added, the reaction mixture was heated to 90°C and maintained at this temperature for 2 h, after which the reaction mixture was cooled, and

diluted with water. The solid amide **6** which separated was filtered off, washed with water, and dried. Yield 3.11 g (85%); mp 193-195°C (ethanol). Mass spectrum, *m/z* (I_{rel}, %): 366 (5) $[M]^+$, 298 (17) $[M\text{-imidazole}]^+$, 280 (93), 237 (37) $[M\text{-}NHC_8H_{17}]^+$, 223 (82), 209 (100) $[M\text{-}NHC_8H_{17}\text{-CO-H}]^+$, 154 (51), 127 (48), 68 (84). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 12.41 (1H, t, *J* = 6.1, N<u>H</u>CH_2); 11.20 (1H, s, NH); 8.21 (1H, s, H-2 imidazole); 8.16 (1H, d, *J* = 8.9, H-5 quinolone); 7.64 (1H, d, *J* = 2.0, H-5 imidazole); 7.50 (1H, t, *J* = 7.2, H-7 quinolone); 7.20 (1H, d, *J* = 8.4, H-8 quinolone); 7.09 (1H, t, *J* = 7.2, H-6 quinolone); 7.04 (1H, d, *J* = 2.0, H-4 imidazole); 2.92 (2H, q, *J* = 6.1, NCH_2); 1.49 (2H, m, $NCH_2C\underline{H}_2$); 1.12 [10H, m, $NCH_2CH_2(C\underline{H}_2)_5$]; 0.82 (3H, t, *J* = 6.1, CH_3). Found, %: C 68.70; H 7.37; N 15.41. $C_{21}H_{26}N_4O_2$. Calculated, %: C 68.83; H 7.15; N 15.29.

Piperidide of 1-H-4-(1-Imidazolyl)-2-oxo-1,2-dihydroquinoline-3-carboxylic Acid (7) was obtained by the procedure of the previous experiment. Yield 80%; mp 262-264°C (ethanol). Mass spectrum, *m/z*, (I_{rel}, %): 322 (11) $[M]^+$, 255 (100) $[M\text{-imidazole}]^+$, 237 (22), 225 (23), 68 (73). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 11,79 (1H, s, CONH); 8.33 (1H, s, H-2 imidazole); 7.83 (1H, d, *J* = 8.0, H-5 quinolone); 7.73 (1H, d, *J* = 1.9, H-5 imidazole); 7.59 (1H, t, *J* = 7.1, H-7 quinolone); 7.36 (1H, d, *J* = 7.3, H-8 quinolone); 7.25 (1H, t, *J* = 7.1, H-6 quinolone); 7.07 (1H, d, *J* = 1.9, H-4 imidazole); 3.00 [4H, s, $N(CH_2)_2$]; 1.60 [6H, s, $NCH_2(C\underline{H}_2)_3$]. Found, %: C 67.22; H 5.50; N 17.47. $C_{18}H_{18}N_4O_2$. Calculated, %: C 67.07; H 5.63; N 17.38.

4-Methoxyanilide of 4-Chloro-2-oxo-1-propyl-1,2-dihydroquinoline-3-carboxylic Acid (11). Thionyl chloride (1.4 ml, 0.02 mol) was added to a solution of 4-chloro-2-oxo-1-propyl-1,2-dihydroquinoline-3-carboxylic acid (**2b**) (2.65 g, 0.01 mol) in CH_2Cl_2 (40 ml) and the mixture boiled under reflux until cessation of HCl evolution (about 3 h). The reflux condenser was changed to a condenser set for distillation and the solvent and excess of $SOCl_2$ were distilled off. The acid chloride **10** obtained was dissolved in dry acetone (20 ml) and a solution of *p*-anisidine (1.23 g, 0.01 mol) and triethylamine (1.4 ml, 0.01 mol) in acetone (50 ml) was added dropwise with stirring and cooling. After 4-5 h the reaction mixture was diluted with water, the separated solid anilide **11** was filtered off, washed with water, and dried. Yield 3.07 g (83%); mp 207-209°C (ethanol). Mass spectrum, *m/z* (I_{rel}, %): 370 (34) $[M]^+$, 248 (100), 206 (44), 162 (17), values of *m/z* are given only for the ^{35}Cl isotope. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 13.80 (1H, s, NH); 8.04 (1H, d, *J* = 8.1, H-5 quinolone); 7.78 (1H, t, *J* = 7.6, H-7 quinolone); 7.71 (1H, d, *J* = 8.2, H-8 quinolone); 7.56 (2H, d, *J* = 8.0, *J* = 8.6, H-3, 5 anilide); 7.42 (1H, t, *J* = 7.6, H-6 quinolone); 6.90 (2H, d, *J* = 8.6, H-2, 6 anilide); 4.22 (2H, t, *J* = 7.1, NCH_2); 3.71 (3H, s, OCH_3); 1.62 (2H, m, $C\underline{H}_2CH_3$); 0.93 (3H, t, *J* = 7.1, $CH_2C\underline{H}_3$). Found, %: C 64.60; H 5.28; N 7.43. $C_{20}H_{19}ClN_2O_3$. Calculated, %: C 64.78; H 5.16; N 7.55.

Compounds **12** and **13** were obtained by an analogous procedure.

2-Diethylaminoethylamide of 4-Chloro-2-oxo-1-propyl-1,2-dihydroquinoline-3-carboxylic Acid (12). Yield 74%; mp 112-113°C (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*,Hz): 8.31 (1H, t, *J* = 6.1, NH); 8.00 (1H, d, *J* = 8.0, H-5); 7.75 (1H, t, *J* = 7.7, H-7); 7.66 (1H, d, *J* = 8.2, H-8); 7.39 (1H, t, *J* = 7.7, H-6); 4.20 (2H, t, *J* = 7.1, $NC\underline{H}_2CH_2CH_3$); 3,26 (2H, q, *J* = 6.2, $NHC\underline{H}_2$); 2.58 [6H, m, $N(C\underline{H}_2)_3$]; 1.64 (2H, m, $NCH_2C\underline{H}_2CH_3$); 0.95 [9H, t, *J* = 7.6, $NCH_2CH_2C\underline{H}_3$ + $N(CH_2C\underline{H}_3)_2$]. Found, %: C 62.82; H 7.43; N 11.40. $C_{19}H_{26}ClN_3O_2$. Calculated, %: C 62.71; H 7.20; N 11.55.

Morpholide of 4-Chloro-2-oxo-1-propyl-1,2-dihydroquinoline-3-carboxylic Acid (13). Yield 80%; mp 97-99°C (ethanol). Mass spectrum, *m/z* (I_{rel}, %): 334 (4) $[M]^+$, 299 (54), 248 (50), 221 (47), 86 (100), values of *m/z* are given only for the ^{35}Cl isotope. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.02 (1H, d, *J* = 7.9, H-5); 7.78 (1H, t, *J* = 7.5, H-7); 7.70 (1H, d, *J* = 8.1, H-8); 7.43 (1H, t, *J* = 7.5, H-6); 4.23, (2H, t, *J* = 7.1, $NC\underline{H}_2CH_2CH_3$); 3.64 (8H, m, 4$C\underline{H}_2$ morpholine); 1.65 (2H, m, $NCH_2C\underline{H}_2CH_3$); 0.95 (3H, t, *J* = 7.1, $NCH_2CH_2C\underline{H}_3$). Found, %: C 60.85; H 5.76; N 8.44. $C_{17}H_{19}ClN_2O_3$. Calculated, %: C 60.99; H 5.72; N 8.37.

4-Methoxyanilide of 2-Hydroxy-4-imino-1-propyl-1,4-dihydroquinoline-3-carboxylic Acid (15). A solution of compound **11** (3.7 g, 0.01 mol) in anhydrous DMF (20 ml) was heated to 90-100°C and a stream of dry ammonia was passed through for 3 h. The reaction mixture was cooled, and diluted with water. The precipitated solid anilide **14** was filtered off, washed with water, and dried. Yield 3.07 g (83%); mp 143-145°C (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 12.89 (1H, s, CONH); 10.72 (1H, s, OH); 8.25 (2H, d, *J* = 8.1,

H-5 quinolone + 4-NH); 7.73 (1H, t, J = 7.1, H-7 quinolone); 7.56 (3H, d, J = 8.5, H-8 quinolone + H-3, 5 anilide); 7.33 (1H, t, J = 7.1, H-6 quinolone); 6.88 (2H, d, J = 8.5, H-2, 6 anilide); 4.20 (2H, t, J = 7.0, NCH_2); 3.74 (3H, s, OCH_3); 1.65 (2H, m, $C\underline{H}_2CH_3$); 0.96 (3H, t, J = 7.0, $CH_2C\underline{H}_3$). Found, %: C 68.48; H 6.17; N 11.82. $C_{20}H_{21}N_3O_3$. Calculated, %: C 68.36; H 6.02; N 11.96.

2-Diethylaminoethylamide of 4-Diethylamino-2-oxo-1-propyl-1,2-dihydroquinoline-3-carboxylic Acid (17). Diethylamine (1.65 ml, 0.025 mol) was added to a solution of compound **12** (3.63 g, 0.01 mol) in ethyl alcohol (30 ml) and the mixture was boiled under reflux for 5 h. The excess of diethylamine and the solvent were distilled off under reduced pressure. Water (50 ml) was added to the residue, and then a solution of Na_2CO_3 to pH 8. The solid amide **17** was filtered off, washed with water, and dried. Yield 3.76 g (94%); mp 72-73°C (hexane–2-propanol). ^{1}H NMR spectrum, δ, ppm (J, Hz): 7.95 (1H, t, J = 6.1, NH); 7.90 (1H, d, J = 7.9, H-5); 7.58 (1H, t, J = 7.3, H-7); 7.49 (1H, d, J = 8.0, H-8); 7.23 (1H, t, J = 7.3, H-6); 4.21 (2H, t, J = 7.1, $NC\underline{H}_2CH_2CH_3$); 3.23 (2H, q, J = 6.2, $NHC\underline{H}_2$); 3.16 [4H, q, J = 6.0, $4\text{-}N(C\underline{H}_2CH_3)_2$]; 2.45 [6H, m, $C\underline{H}_2N(C\underline{H}_2CH_3)_2$]; 1.61 (2H, m, $NCH_2C\underline{H}_2CH_3$); 0.90-1.06 (15H, m, $5CH_3$). Found, %: C 68.80; H 9.14; N 13.83. $C_{23}H_{36}N_4O_2$. Calculated, %: C 68.97; H 9.06; N 13.99.

4-Amino-2-oxo-1,2-dihydroquinoline (21). Benzylamine (1.09 ml, 0.01 mol) was added to a solution of 4-amino-2-oxo-1,2-dihydroquinoline-3-carboxylic acid (**20**) (2.04 g, 0.01 mol) in DMF (20 ml) and the mixture was boiled under reflux for 4 h. The reaction mixture was cooled, diluted with water, and acidified with AcOH. The separated crystals were filtered off, washed with water, and dried. Yield 1.52 g (95%); mp 299-300°C (aqueous ethanol). Mass spectrum, m/z (I_{rel}, %): 160 (100) $[M]^+$, 132 (38) $[M\text{-}CO]^+$, 118 (12), 104 (24), 77 (17). ^{1}H NMR spectrum, δ, ppm (J, Hz): 10.78 (1H, s, NH); 7.86 (1H, d, J = 8.0, H-5); 7.43 (1H, t, J = 7.8, H-7); 7.22 (1H, d, J = 8.3, H-8); 7.08 (1H, t, J = 7.8, H-6); 6.56 (2H, s, NH_2); 5.44 (1H, s, H-3). Found, %: C 67.63; H 5.22; N 17.36. $C_9H_8N_2O$. Calculated, %: C 67.49; H 5.03; N 17.49.

Hydrazide of 1H-2-Hydroxy-4-imino-1,4-dihydroquinoline-3-carboxylic Acid (23a). Hydrazine hydrate (0.011 mole: calculated on the actual content) was added to a solution of the ethyl ester of 4-amino-2-oxo-1,2-dihydroquinoline-3-carboxylic acid (**22**, R = H) [22] (2.32 g, 0.01 mol) in ethyl alcohol (20 ml), and the mixture boiled under reflux for 5 h. After cooling, the solid hydrazide **23a** was filtered off, washed with water, and dried. Yield 1.91 g (88%); mp 313-315°C (DMF). ^{1}H NMR spectrum, δ, ppm (J, Hz): 13.85 (1H, s, NH); 11.16 (1H, s, NH); 10.60 (1H, s, OH); 8.10 (2H, d, J = 8.1, H-5 + 4-NH); 7.57 (1H, t, J = 7.2, H-7); 7.30 (1H, d, J = 8.3, H-8); 7.19 (1H, t, J = 7.2, H-6); 4.57 (2H, s, NH_2). Found, %: C 55.15; H 4.53; N 25.80. $C_{10}H_{10}N_4O_2$. Calculated, %: C 55.04; H 4.62; N 25.67.

Hydrazide of 1-Heptyl-2-hydroxy-4-imino-1,4-dihydroquinoline-3-carboxylic Acid (23b) was obtained analogously from the methyl ester of 4-amino-1-heptyl-2-oxo-1,2-dihydroquinoline-3-carboxylic acid (**22**, R = C_7H_{15}) [6]. Yield 90%; mp 154-156°C (ethanol). ^{1}H NMR spectrum, δ, ppm (J, Hz): 11.19 (1H, s, NH); 10.62 (1H, s, OH); 8.18 (2H, d, J = 8.0, H-5 + 4-NH); 7.69 (1H, t, J = 7.1, H-7); 7.47 (1H, d, J = 8.3, H-8); 7.26 (1H, t, J = 7.1, H-6); 4.48 (2H, s, NH_2); 4.17 (2H, t, J = 7.2, $NC\underline{H}_2$); 1.54 (2H, q, J = 6.9, $NHCH_2C\underline{H}_2$); 1.30 [8H, m, $(C\underline{H}_2)_4CH_3$]; 0.84 (3H, t, J = 6.9, CH_3). Found, %: C 64.41; H 7.52; N 17.84. $C_{17}H_{24}N_4O_2$. Calculated, %: C 64.53; H 7.65; N 17.71.

2-Fluorobenzylidenehydrazide of 1H-2-hydroxy-4-imino-1,1-dihydro-quinoline-3-carboxylic Acid (24a). 2-Fluorobenzaldehyde (1.25 ml, 0.012 mol) was added to a solution of hydrazide **23a** (2.18 g, 0.01 mol) in DMF (20 ml), and the mixture boiled under reflux for 2 h. After cooling, the solid hydrazide **24a** was filtered off, washed with water, and dried. Yield 2.75 g (85%); mp >340°C (DMF). ^{1}H NMR spectrum, δ, ppm (J, Hz): 13.92 (1H, s, NH); 11.37 (1H, s, NH); 10.60 (1H, s, OH); 8.40 (1H, s, CH=); 7.11-8.16 (9H, m, H arom. + 4-NH). Found, %: C 62.84; H 4.16; N 17.17. $C_{17}H_{13}FN_4O_2$. Calculated, %: C 62.96; H 4.04; N 17.28.

Compounds **24b-e** were obtained by an analogous method.

3-Fluorobenzylidenehydrazide of 1H-2-Hydroxy-4-imino-1,4-dihydro-quinoline-3-carboxylic Acid (24b). Yield 92%; mp >340°C (DMF). ^{1}H NMR spectrum, δ, ppm (J, Hz): 13.91 (1H, s, NH); 11.38 (1H, s, NH); 10.64 (1H, s, OH); 8.33 (1H, s, CH=); 7.15-8.18 (9H, m, H arom. + 4-NH). Found, %: C 62.87; H 4.09; N 17.20. $C_{17}H_{13}FN_4O_2$. Calculated, %: C 62.96; H 4.04; N 17.28.

2-Pyridylmethylidenehydrazide of 1-Heptyl-2-hydroxy-4-imino-1,4-dihydroquinoline-3-carboxylic Acid (24c). Yield 90%; mp 236-238°C (DMF). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 13.87 (1H, s, NH); 10.55 (1H, s, OH); the proton of the 4-imino group is displayed in the spectrum as a broad singlet in the region of 8-9 ppm; 8.60 (1H, d, *J* = 5.0, H-6 Py); 8.26 (1H, s, CH=); 8.19 (1H, d, *J* = 8.3, H-5 quinoline); 7.95 (1H, d, *J* = 7.9, H-3 Py); 7.87 (1H, t, *J* = 8.4, H-5 Py); 7.73 (1H, t, *J* = 7.9, H-7 quinoline); 7.54 (1H, d, *J* = 9.0, H-8 quinoline); 7.41 (1H, t, *J* = 7.5, H-4 Py); 7.32 (1H, t, *J* = 7.9, H-6 quinoline); 4.20 (2H, t, *J* = 7.1, NCH_2); 1.55 (2H, q, *J* = 7.0, $NHCH_2C\underline{H}_2$); 1.31 [8H, m, $(C\underline{H}_2)_4CH_3$]; 0.80 (3H, t, *J* = 7.0, CH_3). Found, %: C 68.22; H 6.63; N 17.34. $C_{23}H_{27}N_5O_2$. Calculated, %: C 68.13; H 6.71; N 17.27.

3-Pyridylmethylidenehydrazide of 1-Heptyl-2-hydroxy-4-imino-1,4-dihydroquinoline-3-carboxylic Acid (24d). Yield 92%; mp 217-219°C (DMF). ^{1}H NMR spectrum, δ, ppm (*J,* Hz): 13.90 (1H, s, NH); 10.61 (1H, s, OH); the proton of the 4-imino group is displayed in the spectrum as a broad singlet in the 8-9 ppm region; 8.83 (1H, s, H-2 Py); 8.57 (1H, d, *J* = 4.7, H-6 Py); 8.40 (1H, s, CH=); 8.23 (1H, d, *J* = 8.3, H-5 quinoline); 8.09 (1H, d, *J* = 7.9, H-4 Py); 7.71 (1H, t, *J* = 7.9, H-7 quinoline); 7.53 (1H, d, *J* = 8.3, H-8 quinoline); 7.46 (1H, t, *J* = 6.1, H-5 Py); 7.31 (1H, t, *J* = 7.9, H-6 quinoline); 4.18 (2H, t, *J* = 7.1, NCH_2); 1.53 (2H, q, *J* = 7.1, $NHCH_2C\underline{H}_2$); 1.30 [8H, m, $(C\underline{H}_2)_4CH_3$]; 0.81 (3H, t, *J* = 7.1, CH_3). Found, %: C 68.05; H 6.66; N 17.38. $C_{23}H_{27}N_5O_2$. Calculated, %: C 68.13; H 6.71; N 17.27.

4-Pyridylmethylidenehydrazide of 1-Heptyl-2-hydroxy-4-imino-1,4-dihydroquinoline-3-carboxylic Acid (24e). Yield 95%; mp 224-226°C (DMF). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 14.00 (1H, s, NH); 10.63 (1H, s, OH); the proton of the 4-imino group is displayed in the spectrum as a broad singlet in the 8-9 ppm region; 8.61 (2H, d, *J* = 5.4, H-2, 6 Py); 8.35 (1H, s, CH=); 8.24 (1H, d, *J* = 7.9, H-5 quinoline); 7.72 (1H, t, *J* = 6.8, H-7 quinoline); 7.63 (2H, d, *J* = 5.4, H-3, 5 Py); 7.52 (1H, d, *J* = 8.6, H-8 quinoline); 7.30 (1H, t, *J* = 6.8, H-6 quinoline); 4.17 (2H, t, *J* = 7.1, NCH_2); 1.57 (2H, q, *J* = 7.1, $NHCH_2C\underline{H}_2$); 1.33 [8H, m, $(C\underline{H}_2)_4CH_3$]; 0.80 (3H, t, *J* = 7.1, CH_3). Found, %: C 68.27; H 6.77; N 17.38. $C_{23}H_{27}N_5O_2$. Calculated, %: C 68.13; H 6.7; N 17.27.

***iso*-Butylamide of 2-Cyanomalonanilic Acid (26a).** *iso*-Butylamine (1.1 ml, 0.011 mol) was added to a solution of the ethyl ester of 2-cyanomalonanilic acid (**25**) [22] (2.32 g, 0.01 mol) in absolute methyl alcohol (20 ml) and the mixture was boiled under reflux for 4 h. The reaction mixture was then poured into water (100 ml), and acidified with HCl to pH 4. The solid amide **26a** was filtered off, washed with water, and dried. Yield 2.12 g (82%). Colorless crystals of mp 110-112°C (ethanol). Mass spectrum, *m/z* (I_{rel}, %): 259 (11) $[M]^+$, 216 (25) $[M\text{-}C_3H_7\text{-}i]^+$, 187 (60) $[M\text{-}C_4H_9NH]^+$, 145 (36), 118 (100), 72 (40). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 10.50 (1H, s, NH-Ar); 8.12 (1H, t, *J* = 5.1, NH-Alk); 7.21-7.86 (4H, m, H arom.); 3.40 (2H, s, $COCH_2CO$); 2.90 (2H, t, *J* = 5.8, NCH_2); 1.69 (1H, m, CH); 0.92 (6H, d, *J* = 6.4, $2CH_3$). Found, %: C 64.71; H 6.73; N 16.33. $C_{14}H_{17}N_3O_2$. Calculated, %: C 64.85; H 6.61; N 16.20.

Benzylamide of 2-Cyanomalonanilic Acid (26b) was obtained analogously. Yield 87%. Colorless crystals of mp 117-119°C (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz); 10.49 (1H, s, NH-Ar); 8.64 (1H, t, *J* = 5.4, NH-Alk); 7.23-7.90 (9H, m, H arom.); 4.32 (2H, d, *J* = 6.1, NCH_2); 3.45 (2H, s, $COCH_2CO$). Found, %: C 69.74; H 5.22; N 14.21. $C_{17}H_{15}N_3O_2$. Calculated, %: C 69.61; H 5.15; N 14.33.

***iso*-Butylamide of 1-H-2-Hydroxy-4-imino-1,4-dihydroquinoline-3-carboxylic Acid (19c).** A. *iso*-Butylamine (1.1 ml, 0.011 mol) was added to a solution of compound **25** (2.32 g, 0.01 mol) in absolute methyl alcohol (20 ml) and the mixture was boiled under reflux for 4 h. A solution of sodium methylate [from metallic sodium (0.23 g, 0.01 mol) and absolute methyl alcohol (10 ml)] was added, the reaction mixture was boiled for 1 h on a water bath, after which the heating was stopped, and the mixture left for 7-8 h at room temperature, The reaction mixture was diluted with water, and acidified with dilute acetic acid. The solid amide **19c** was filtered off, washed with water, and dried. The product was crystallized from DMF. Mass spectrum, *m/z* (I_{rel}, %): 259 (9) $[M]^+$, 216 (57) $[M\text{-}C_3H_7\text{-}i]^+$, 187 (100) $[M\text{-}C_4H_9NH]^+$, 145 (12), 118 (33), 72 (8).

Amides **19a-k** (Table 1) were obtained analogously.

B. *iso*-Butylamine (2.2 ml, 0.22 mol) was added to a solution of compound **25** (2.32 g, 0.01 mol) in absolute methyl alcohol (20 ml) and the mixture boiled for 15 h. The reaction mixture was diluted with water and acidified with dilute acetic acid. The solid which separated was filtered off, dried, and then treated with boiling ethanol (30 ml) and filtered hot. Amide **19c** (0.72 g, 28%) was obtained on the filter. The acyclic amide **26a** was isolated from the filtrate by dilution with water.

A mixing test of samples of amide **19c** obtained by the various methods gave no depression of melting point. Their ^{1}H NMR spectra were identical.

Equimolar quantities of ester **25** and dimethylaminoethylamine were used when obtaining dimethylaminoethylamide **19l**. After completion of amidation and cyclization the reaction mixture was cooled without acidification, the precipitated crystals of amide **19l** were filtered off, washed with water, and dried.

Propylamide of 1-H-4-Hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid (27). After dilution with water (see example of obtaining amide **19c**, method A) the reaction mixture was acidified with dilute HCl to pH 3-4 and left at room temperature for 4-5 h. The solid amide **27**, which precipitated, was filtered off, washed with water, and dried. Yield 89%; mp 209-210°C (DMF). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 17.37 (1H, s, OH); 11.84 (1H, s, NH); 10.35 (1H, t, *J* = 5.4, NH-Alk); 7.97 (1H, d, *J* = 7.9, H-5); 7.70 (1H, t, *J* = 7.2, H-7); 7.40 (1H, d, *J* = 8.0, H-8); 7.31 (1H, t, *J* = 7.2, H-6); 3.37 (2H, q, *J* = 6.5, $NHC\underline{H}_2$); 1.62 (2H, m, $NCH_2C\underline{H}_2CH_3$); 0.93 (3H, t, *J* = 6.8, CH_3).

A mixing test with a sample of amide **27** obtained by amidation of the ethyl ester of 1-H-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid with propylamine [13] gave no depression of melting point. The ^{1}H NMR spectra of these compounds were identical.

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