Chemistry of Heterocyclic Compounds, Vol. 41, No. 9, 2005

4-HYDROXYQUINOL-2-ONES. 87*. UNUSUAL SYNTHESIS OF 1-R-4-HYDROXY-2-OXO-1,2-DIHYDRO-QUINOLINE-3-CARBOXYLIC ACID PYRIDYLAMIDES

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4-Chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acids and their esters react with aminopyridines in refluxing DMF to give the corresponding 4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid pyridylamides. Their structures were proved by ^{1}H NMR and mass spectroscopy, counter synthesis, and by X-ray analysis. A possible mechanism is proposed for the indicated chemical reaction.

Keywords: aminopyridine, 4-chloro-2-oxoquinoline-3-carboxylic acids, amidation, X-ray analysis.

We have previously shown that 4-chloro-2-oxo-1,2-dihydroquinoline-3-carboxylate esters **1** react readily with primary and secondary amines to give high yields of the corresponding 4-N-substituted 3-carbalkoxy-1,2-dihydroquinolin-2-ones [2].

4-Chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acids **2** also form similar products of "normal" nucleophilic addition but with the difference that alternate compounds can be obtained depending on the reaction conditions. Hence when the reaction is carried out in ethanol the 4-alkyl(aryl)amino-substituted acids **3** are formed whereas the reaction in refluxing DMF gives 4-alkyl(aryl)aminoquinolin-2-ones **4**. In the latter case the decarboxylation evidently occurs after the formation of the 4-amino derivatives since 4-chloro-1,2-dihydroquinolin-2-ones, free from activation of the chlorine atom by electron-acceptor substituents in position 3 of the quinoline ring, are inert towards N-nucleophiles [3].

The reaction with aminopyridines, however, occurs quite differently. Thus the reaction of the 4-chloro-substituted acids **2** with α-, β-, or γ-aminopyridines under reflux in both anhydrous and ordinary DMF unexpectedly gave the corresponding 4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid pyridylamides **5**, whose structures were confirmed by ^{1}H NMR and mass-spectroscopic data and by chromatography-mass spectrometry. X-ray analysis was used also in the case of the pyridyl-4-amide **5c**.

The reaction of the aminopyridines with the 4-chloro esters **1** was just as unexpected. Hence the 4-hydroxy amides **5** are formed immediately in aqueous DMF. However, in anhydrous solvent the reaction stops at the stage of formation of the N-(3-alkoxycarbonyl-2-oxo-1,2-dihydroquinolin-4-yl)pyridinium chlorides **6** which can then be converted to the 4-hydroxy amides **5**. It was of interest that, in aqueous DMF, the 1-N-alkyl-

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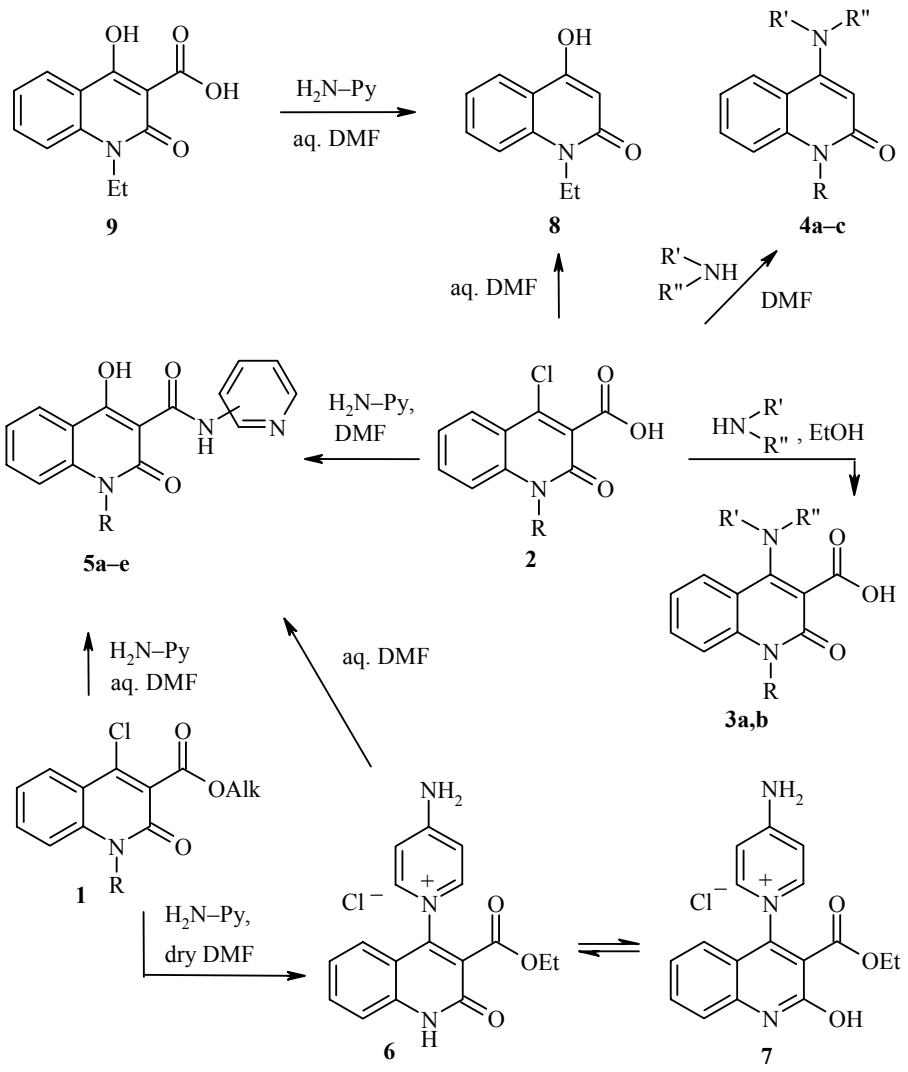
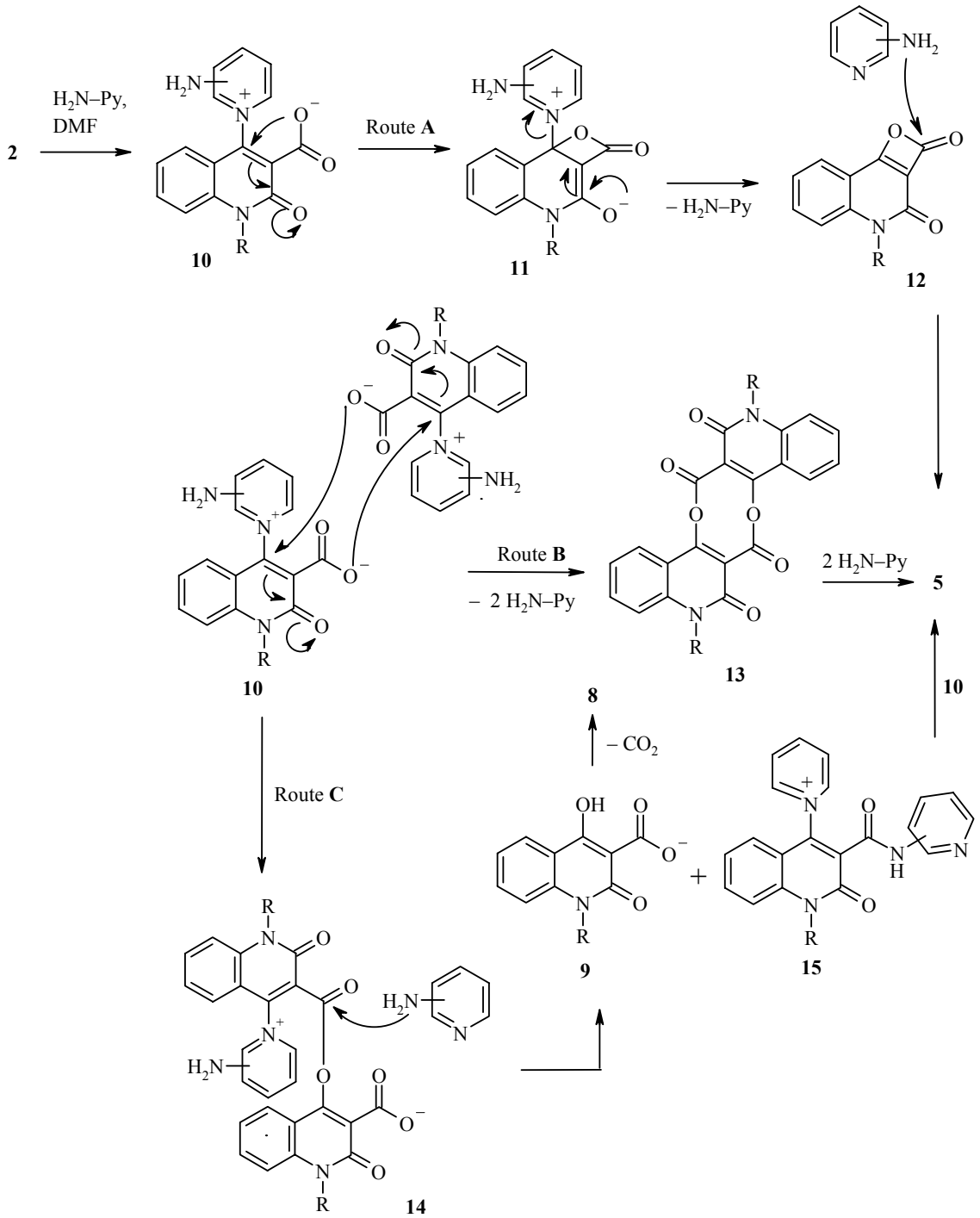


3 a R = R' = H, R'' = CH_2–Ph; **b** R = Pr, R' = H, R'' = 4-Cl-Ph; **4 a** R = R' = H, R'' = CH_2–Ph; **b** R = H, R' = R'' = Pr; **c** R = Pr, R' = H, R'' = 4-Cl–Ph; **5 a** R = H, 4-Py; **b** R = Et, 4-Py; **c** R = Pr, 4-Py; **d** R = Pr, 3-Py; **e** R = Pr, 2-Py

substituted esters **1** were converted to the amides **5** in the presence of the aminopyridines in the course of 30 min whereas the same reaction for the 1H derivative along with the 1H-pyridinium chloride **6** needs many hours reflux.

The 4-chloro acids **2** are hydrolyzed when simply worked up with refluxing aqueous DMF to the 4-hydroxy-1,2-dihydroquinolin-2-one **8**. None the less, the 4-hydroxyamides **5** should hardly be considered as a result of aminolysis by the aminopyridine acids **2** or their possible 4-hydroxy acid derivatives **9**. In the first place, as shown above, even with alkylamines (i.e. with stronger bases than the aminopyridines) the 4-chloro acids **2** form only the quinolin-2-ones **3** or **4**. In the second, 4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acids **9** are actually amidated in refluxing DMF but only using alkylamines [4]. Attempts to carry out such a reaction with anilines [5] or with 4-aminopyridine were unsuccessful. In other words, for the formation of the hetarylamides directly from the amines and acids **2** or **9**, the electrophilic properties of the latter are clearly insufficient. It undoubtedly needs some kind of activation of the carbonyls in their carboxyl groups.

Correlation of the data given allows us to conclude that the initial products of the reaction of the 4-chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acids **2** with the aminopyridines are the quaternary pyridinium salts **10**. The formation of the amides of the 4-hydroxy acids **5** in anhydrous DMF shows that the source of the 4-OH substituent can only be the carboxyl group in this instance. Hence the subsequent course of the reaction must include a nucleophilic attack of carboxylate ion at the carbon atom in position 4 of the quinolone ring (route **A**) which leads to the cyclic intermediate **11**. Following from this S_N2_{Ar} type reaction mode, fission of the bond to the leaving group liberates the aminopyridine which then reacts with lactone **12** to



give the final 4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carbalkoxylic acid pyridylamide **5**. It is likely that the 3-carbalkoxypyridinium chloride **6** is converted to the 4-hydroxyamide **5a** by a similar scheme after initial hydrolysis of the ester group since the reaction only occurs in the presence of water. A marked decrease in the rate of reaction in the case of the 1H-derivatives may be due to their ability to form the more hydrolytically stable aromatic 2-hydroxy tautomer **7** *via* lactam-lactim tautomerism. We have noted this feature during the alkylation in DMF of 4-hydroxy- [6] and 4-amino-1H-2-oxo-1,2-dihydroquinoline-3-carboxylate esters [1].

Of course, it is in principle impossible to exclude an intermolecular character for the reaction of the pyridinium salts **10** to the amides **5**. However, the realization of such a mechanism demands an additional condition for the successful occurrence of the reaction involving the formation of the symmetrical diester (route **B**) and coming about only as the result of a synchronous attack of the $C_{(4)}$ atoms by both carboxylate ions. Otherwise, the separated amine will react with the mono ester **14** (route **C**) thus liberating the 1-R-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acids **9** the participation of which in further chemical reactions is unlikely due to its high tendency towards decarboxylation under the described conditions. As a result the yield of the 4-hydroxyamide **5** would be markedly lowered due to the formation of the 4-hydroxyquinolin-2-one **8** and this does not agree with experimental data.

Hence comparison of the positive and negative aspects of each of the discussed variants of the formation of the 4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid pyridylamides **5** in the reactions of the 4-chloro acids **2** with the aminopyridines led us to conclude that route **A** appears to be preferred.

We have not considered inter- or intramolecular reaction of the pyridinium salts **10** involving acylation of a primary amino group as one possible route to the formation of the 4-hydroxyamides **5**. The pyridinium nitrogen atom is a powerful electron acceptor, exceeding the majority of other functional groups [7]. This leads to a marked lowering of the electron density and, consequently, to the reactivity of the amino group. ^{1}H NMR spectroscopic data is a persuasive confirmation of this. A singlet signal for the amino group protons in the

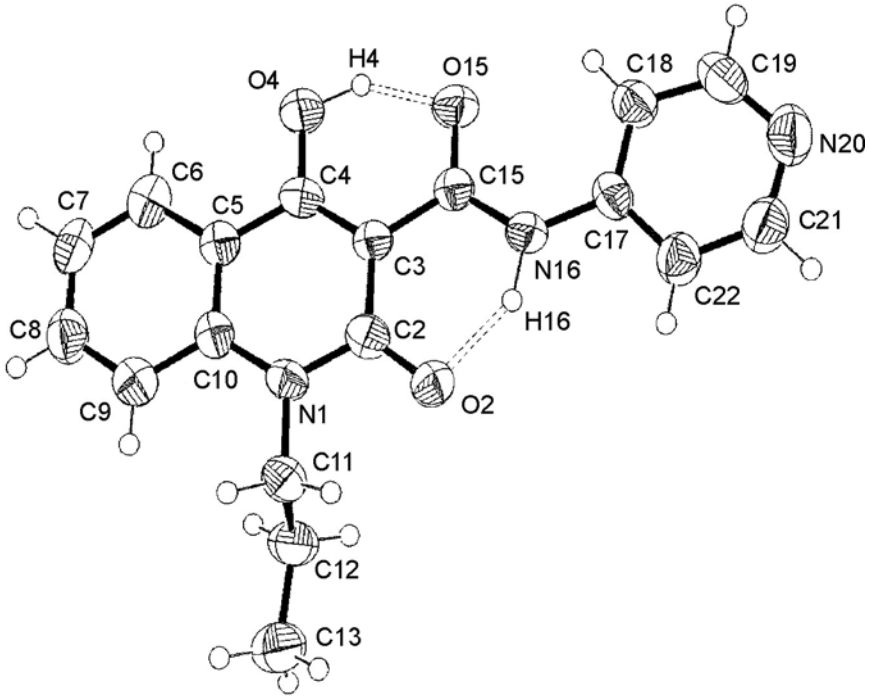


Fig. 1. Atomic numbering and spatial structure of the amide **5c** molecule. The thermal vibration ellipsoids are given with a 50% probability. The intramolecular hydrogen bonds are shown by dashed lines.

4-amino-1-(3-ethoxycarbonyl-2-oxo-1,2-dihydroquinolin-4-yl)pyridinium chloride (**6**) is found at 9.25 ppm. Such a chemical shift is typical of amides rather than amines [8]. Hence acylation of the amino group in the pyridinium salts **10** is not possible under these conditions.

TABLE 1. Specific Interatomic Distances (*d*) in the Structure of Compound **5c**

Bond	*d*, Å	Bond	*d*, Å	Bond	*d*, Å
$N_{(1)}$–$C_{(2)}$	1.389(4)	$C_{(5)}$–$C_{(10)}$	1.396(5)	$C_{(15)}$–$N_{(16)}$	1.350(4)
$N_{(1)}$–$C_{(10)}$	1.391(4)	$C_{(5)}$–$C_{(6)}$	1.397(4)	$N_{(16)}$–$C_{(17)}$	1.413(4)
$N_{(1)}$–$C_{(11)}$	1.453(4)	$C_{(6)}$–$C_{(7)}$	1.370(5)	$C_{(17)}$–$C_{(18)}$	1.368(4)
$C_{(2)}$–$O_{(2)}$	1.247(4)	$C_{(7)}$–$C_{(8)}$	1.380(5)	$C_{(17)}$–$C_{(22)}$	1.381(5)
$C_{(2)}$–$C_{(3)}$	1.438(4)	$C_{(8)}$–$C_{(9)}$	1.370(5)	$C_{(18)}$–$C_{(19)}$	1.383(5)
$C_{(3)}$–$C_{(4)}$	1.364(4)	$C_{(9)}$–$C_{(10)}$	1.410(5)	$C_{(19)}$–$N_{(20)}$	1.323(5)
$C_{(3)}$–$C_{(15)}$	1.465(4)	$C_{(11)}$–$C_{(12)}$	1.507(4)	$N_{(20)}$–$C_{(21)}$	1.329(5)
$C_{(4)}$–$O_{(4)}$	1.340(4)	$C_{(12)}$–$C_{(13)}$	1.515(4)	$C_{(21)}$–$C_{(22)}$	1.382(5)
$C_{(4)}$–$C_{(5)}$	1.445(5)	$C_{(15)}$–$O_{(15)}$	1.265(4)		

TABLE 2. Specific Valence Angles (ω) in the Structure of Compound **5c**

Angle	ω, deg.	Angle	ω, deg.
$C_{(2)}$–$N_{(1)}$–$C_{(10)}$	121.6(3)	$N_{(1)}$–$C_{(10)}$–$C_{(5)}$	120.8(4)
$C_{(2)}$–$N_{(1)}$–$C_{(11)}$	116.7(3)	$N_{(1)}$–$C_{(10)}$–$C_{(9)}$	120.9(4)
$C_{(10)}$–$N_{(1)}$–$C_{(11)}$	121.5(3)	$C_{(5)}$–$C_{(10)}$–$C_{(9)}$	118.4(4)
$O_{(2)}$–$C_{(2)}$–$N_{(1)}$	118.1(4)	$N_{(1)}$–$C_{(11)}$–$C_{(12)}$	112.4(3)
$O_{(2)}$–$C_{(2)}$–$C_{(3)}$	123.4(4)	$C_{(11)}$–$C_{(12)}$–$C_{(13)}$	112.8(3)
$N_{(1)}$–$C_{(2)}$–$C_{(3)}$	118.5(4)	$O_{(15)}$–$C_{(15)}$–$N_{(16)}$	122.0(4)
$C_{(4)}$–$C_{(3)}$–$C_{(2)}$	119.6(4)	$O_{(15)}$–$C_{(15)}$–$C_{(3)}$	119.9(4)
$C_{(4)}$–$C_{(3)}$–$C_{(15)}$	119.0(4)	$N_{(16)}$–$C_{(15)}$–$C_{(3)}$	118.1(4)
$C_{(2)}$–$C_{(3)}$–$C_{(15)}$	121.4(4)	$C_{(15)}$–$N_{(16)}$–$C_{(17)}$	128.5(4)
$O_{(4)}$–$C_{(4)}$–$C_{(3)}$	123.0(4)	$C_{(15)}$–$N_{(16)}$–$H_{(16)}$	109(2)
$O_{(4)}$–$C_{(4)}$–$C_{(5)}$	115.3(4)	$C_{(17)}$–$N_{(16)}$–$H_{(16)}$	123(2)
$C_{(3)}$–$C_{(4)}$–$C_{(5)}$	121.8(4)	$C_{(18)}$–$C_{(17)}$–$C_{(22)}$	118.8(4)
$C_{(4)}$–$O_{(4)}$–$H_{(4)}$	108(2)	$C_{(18)}$–$C_{(17)}$–$N_{(16)}$	124.9(4)
$C_{(10)}$–$C_{(5)}$–$C_{(6)}$	120.5(4)	$C_{(22)}$–$C_{(17)}$–$N_{(16)}$	116.3(4)
$C_{(10)}$–$C_{(5)}$–$C_{(4)}$	117.5(4)	$C_{(17)}$–$C_{(18)}$–$C_{(19)}$	117.5(4)
$C_{(6)}$–$C_{(5)}$–$C_{(4)}$	122.0(4)	$N_{(20)}$–$C_{(19)}$–$C_{(18)}$	126.2(4)
$C_{(7)}$–$C_{(6)}$–$C_{(5)}$	120.4(4)	$C_{(19)}$–$N_{(20)}$–$C_{(21)}$	114.3(4)
$C_{(6)}$–$C_{(7)}$–$C_{(8)}$	119.0(4)	$N_{(20)}$–$C_{(21)}$–$C_{(22)}$	125.3(4)
$C_{(9)}$–$C_{(8)}$–$C_{(7)}$	122.2(4)	$C_{(17)}$–$C_{(22)}$–$C_{(21)}$	118.0(4)
$C_{(8)}$–$C_{(9)}$–$C_{(10)}$	119.5(4)		

TABLE 3. Hydrogen Bonds in the Structure of the Studied Amide **5c***

D–H	*d* (*D*–H), Å	*d* (*D*···*A*), Å	*d* (H···*A*), Å	φ (*D*–H···*A*), deg.	*A*
$O_{(4)}$–$H_{(4)}$	1.02(4)	2.479(4)	1.57(4)	145(4)	$O_{(15)}$
$N_{(16)}$–$H_{(16)}$	1.00(4)	2.599(4)	1.70(3)	147(3)	$O_{(2)}$

* *D* = donor atom; *A* = acceptor atom; H = hydrogen atom, *d* = distance, φ = angle.

EXPERIMENTAL

^{1}H NMR spectra for the synthesized compounds were recorded on a Bruker WM-360 (360 MHz) instrument using DMSO-d_6 solvent and TMS internal standard. Mass spectra were recorded on a Finnigan MAT Incos 50 quadrupole spectrometer in the full scanning mode over the range 33-700 *m/z* with an electron ionization strength of 70 eV, direct introduction of the sample, and a heating rate of about 5°C/s. 4-Chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acids **2** and their esters were synthesized by a known method [6, 9].

4-Benzylamino-2-oxo-1,2-dihydroquinoline-3-carboxylic Acid (3a). Benzylamine (1.09 ml, 0.01 mol) was added to a solution of 4-chloro-2-oxo-1,2-dihydroquinoline-3-carboxylic acid (**2**, R = H, 2.23 g, 0.01 mol) in alcohol (15 ml) and refluxed for 2 h. The acid **3a** began to crystallized from the refluxing reaction mixture after just 20-30 min. After cooling, the crystals of the 4-benzylaminoacid **3a** were filtered off, washed with alcohol, and dried to give 2.79 g (95%); mp 246-248°C (decomp.). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 16.70 (1H, s, COOH); 12.00 (1H, s, NH); 11.42 (1H, t, *J* = 6.9, NH); 8.25 (1H, d, *J* = 8.0, H-5); 7.66 (1H, t, *J* = 7.2, H-7); 7.45-7.30 (6H, m, H-8 + C_6H_5); 7.21 (1H, t, *J* = 7.2, H-6); 5.10 (2H, d, *J* = 6.9, CH_2). Found, %: C 69.56; H 4.94; N 9.70. $C_{17}H_{14}N_2O_3$. Calculated, %: C 69.38; H 4.79; N 9.52.

4-(4-Chlorophenylamino)-2-oxo-1-propyl-1,2-dihydroquinoline-3-carboxylic Acid (3b). Obtained similarly. Yield 93%; mp 191-193°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 16.58 (1H, s, COOH); 11.97 (1H, s, NH); 7.73 (2H, m, H-5,7); 7.46 (1H, d, *J* = 7.9, H-8); 7.39 (2H, d, *J* = 8.0, H-3,5 C_6H_5); 7.18 (2H, d, *J* = 8.0, H-2,6 Ph); 7.09 (1H, t, *J* = 7.0, H-6); 4.24 (2H, t, *J* = 7.1, NCH_2); 1.67 (2H, m, C$\underline{H}_2$Me); 0.93 (3H, t, *J* = 7.1, CH_3). Found, %: C 63.84; H 4.70; N 7. 93. $C_{19}H_{17}ClN_2O_3$. Calculated, %: C 63.96; H 4.80; N 7.85.

4-Benzylamino-1H-quinolin-2-one (4a). Benzylamine (1.09 ml, 0.01 mol) was added to a solution of compound **2** (R = H, 2.23 g, 0.01 mol) in DMF (10 ml) and refluxed with a reflux condenser for 2 h. After cooling, the crystals of the aminoquinolone **4a** were filtered off, washed with water, and dried. Yield 1.85 g (74%); mp 250-251°C (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 10.77 (1H, s, NH); 8.00 (1H, d, *J* = 8.1, H-5); 7.65 (1H, t, *J* = 6.9, NH); 7.43 (1H, t, *J* = 7.3, H-7); 7.36-7.28 (5H, m, C_6H_5); 7.19 (1H, d, *J* = 7.6, H-8); 7.10 (1H, t, *J* = 7.3, H-6); 5.11 (1H, s, H-3); 4.44 (2H, d, *J* = 6.9, CH_2). Found, %: C 76.62; H 5.75; N 11.22. $C_{16}H_{14}N_2O$. Calculated, %: C 76.78; H 5.64; N 11.19.

Compounds 4b,c were prepared by the same method.

4-Dipropylamino-1H-quinolin-2-one (4b). Yield 77%; mp 133-135°C (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 11.20 (1H, s, NH); 7.67 (1H, d, *J* = 8.2, H-5); 7.41 (1H, t, *J* = 7.2, H-7); 7.25 (1H, d, *J* = 8.2, H-8); 7.11 (1H, t, *J* = 7.2, H-6); 5.80 (1H, s, H-3); 3.11 (4H, t, *J* = 7.0, $2NCH_2$); 1.50 (4H, m, 2C$\underline{H}_2$Me); 0.79 (6H, t, *J* = 7.0, $2CH_3$). Found, %: C 73.53; H 8.37; N 11.32. $C_{15}H_{20}N_2O$. Calculated, %: C 73.74; H 8.25; N 11.46.

4-(4-Chlorophenylamino)-1-propyl-1H-quinolin-2-one (4c). Yield 79%; mp 240-242°C (DMF). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.55 (1H, s, NH); 8.13 (1H, d, *J* = 7.8, H-5); 7.62 (1H, t, *J* = 7.1, H-7); 7.49 (1H, d, *J* = 7.8, H-8); 7.42 (2H, d, *J* = 8.2, H-3,5 Ph); 7.31 (2H, d, *J* = 8.2, H-2,6 Ph); 7.23 (1H, t, *J* = 7.1, H-6); 5.88 (1H, s, H-3); 4.14 (2H, t, *J* = 7.1, NCH_2); 1.60 (2H, m, C$\underline{H}_2$Me); 0.92 (3H, t, *J* = 7.1, CH_3). Found, %: C 69.24; H 5.53; N 8.90. $C_{18}H_{17}ClN_2O$. Calculated, %: C 69.12; H 5.48; N 8.96.

4-Hydroxy-2-oxo-1-propyl-1,2-dihydroquinoline-3-carboxylic Acid Pyrid-4-yl Amide (5c). 4-Aminopyridine (0.94 g, 0.01 mol) was added to a solution of 4-chloro-2-oxo-1-propyl-1,2-dihydroquinoline-3-carboxylic acid (**2**, R = Pr, 2.65 g, 0.01 mol) in dry or ordinary DMF (10 ml) and refluxed for 1 h. The reaction mixture was cooled and the separated amide **5c** was filtered off, washed with alcohol, and dried. Yield 2.74 g (85%); mp 190-192°C (DMF). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 16.48 (1H, s, OH); 12.94 (1H, s, NH); 8.44 (2H, d, *J* = 6.3, H-2,6 Py); 8.20 (1H, d, *J* = 7.9, H-5); 7.74 (1H, t, *J* = 7.9, H-7); 7.60 (2H, d, *J* = 6.3, H-3,5 Py); 7.50 (1H, d, *J* = 9.4, H-8); 7.33 (1H, t, *J* = 7.9, H-6); 4.33 (2H, t, *J* = 7.2, NCH_2); 1.70 (2H, m, C$\underline{H}_2$Me); 1.00 (3H, t, *J* = 7.2, CH_3). Mass spectrum, *m/z* (I_{rel}, %): 323 $[M]^+$ (100), 281 $[M–C_3H_6]^+$ (20), 230 $[M–NHPy]^+$ (25), 202 (1.2), 187 (77), 121 (0.9), 94 (26).

X-Ray Analysis of Amide 5c. The experimental intensities of the diffracted reflections were obtained at room temperature (293(2) K) on a CAD4 [10] diffractometer (MoKα irradiation, graphite monochromator, ω-scanning). The parameters for the unit cells were measured and refined for 25 reflexes in the range of θ angles 15-16°. The amide **5c** crystallized in the monoclinic crystal system with the space group $P2_1/n$ (a = 7.912(2), b = 10.274(2), c = 19.210(5) Å; β = 98.11(2)°; V = 1545.9(6) Å^3; Z = 4; d_{calc} = 1.389 g/cm^3; μ = 0.097 mm^{-1}). The diffraction experiment was carried out on a crystal with the linear dimensions 0.3 × 0.3 × 0.3 mm (2.14 ≤ θ ≤ 25.98°, index range h, k, l: -9 ≤ h ≤ 9, 0 ≤ k ≤ 12, 0 ≤ l ≤ 23). In all 3034 independent reflexes were collected (R_{int} = 0.0303). The number of refined parameters was 226. Results for the refined structure: GOF = 0.787, R_1/wR_2 [$I > 2\sigma(I)$] 0.0485 / 0.0460, R_1/wR_2 (all reflexes) 0.1909 / 0.0765, $\Delta\rho_{max}$ / $\Delta\rho_{min}$: 0.151 / -0.153 e·Å^{-3}.

Since the crystal of the investigated compound has a low linear absorption coefficient and small size a correction for absorption was not carried out. Initial treatment of the body of experimental data was performed using the WinGX program package [11]. All subsequent calculations were carried out using the SHELX97 program package [12]. The crystal structure was determined by a direct method with refinement of positional and thermal parameters then carried out in the anisotropic approximation for all non hydrogen atoms. The H atoms were calculated from geometric considerations and refined using the "riding atom" model. The hydrogens of the hydroxyl and amide group were excluded and they were directly localized from electron density difference synthesis. These hydrogen atoms were refined independently in the isotropic approximation. Individual interatomic distances and valence angles are presented in Tables 1 and 2. The parameters for the intramolecular hydrogen bonds are given in Table 3. The crystallographic information for the amide **5c** has been placed in the Cambridge Structural Database (reference CCDC No. 249895) [13]. The steric positioning of the atoms in the molecule of the compound studied with their numbering are shown in Figure 1 and were obtained using the ORTEP3 program [14]. The parameters for the H bonds were calculated using the PARST95 program [15].

The 1,2-dihydroquinoline system of the amide **5c** $N_{(1)}\cdots C_{(10)}$ is planar to an accuracy of 0.019(3) Å. The atoms $O_{(2)}$, $O_{(4)}$, $C_{(11)}$, and $C_{(15)}$ attached to it also lie in this plane. The amide group is virtually coplanar with the ring (torsional angle $C_{(4)}$–$C_{(3)}$–$C_{(15)}$–$O_{(15)}$ 0.7(6)°), the plane of the pyridine ring making a dihedral angle of 7.3(1)° with the plane of the hydroxydihydroquinoline bicycle. This amide substituent orientation is stabilized by a weak intramolecular hydrogen bond $O_{(15)}\cdots H_{(18)}$–$C_{(18)}$ (O···H 2.26 Å, O···H–C 120°) and a strong intramolecular hydrogen bond $O_{(15)}\cdots H_{(4)}$–$O_{(4)}$ (O···H 1.57 Å, O···H–O 145°).

The $C_{(4)}$–$O_{(4)}$ and $C_{(3)}$–$C_{(4)}$ bond lengths of 1.340(5) and 1.364(4) Å are typical of enols. The significant lengthening of the $C_{(15)}$–$O_{(15)}$ bond to 1.265(4) Å (mean value 1.202 Å [16]) is evidently due to the strong $O_{(15)}\cdots H_{(4)}$–$O_{(4)}$ intramolecular hydrogen bond.

The propyl substituent on the N_1 atom has an antiperiplanar conformation (torsional angle $N_{(1)}$–$C_{(11)}$–$C_{(12)}$–$C_{(13)}$ 172.7(3)°) and is turned almost perpendicularly to the plane of the quinoline ring (torsional angle $C_{(2)}$–$N_{(1)}$–$C_{(11)}$–$C_{(12)}$ 92.4(4)°). This position for the alkyl group is likely due to the intramolecular shortening of contact $H_{(11a)}\cdots H_{(9)}$ (1.85 Å) and the weak intramolecular hydrogen bond $O_{(2)}\cdots H_{(11b)}$–$C_{(11)}$ (O···H 2.26 Å, O···H–C 102°).

In the crystal the molecules of the amide **5c** form a stack along the crystallographic (1 0 0) axis. In each stack dimers are formed *via* interaction between the dihydroquinoline fragments with the dihydropyridine rings placed over the benzenes. The distance between the centers of the rings is 3.61 Å and the planes of the dihydropyridine and benzene rings subtend an angle of 1.3°. The dimers are orientated such that the pyridine ring amide fragments are placed over the benzene rings of the associated dimers with a distance of 3.79 Å between the centers of the rings and an angle between the planes of 7.2°.

Compounds 5d,e were prepared by the preceding method.

4-Hydroxy-2-oxo-1-propyl-1,2-dihydroquinoline-3-carboxylic Acid Pyrid-3-yl Amide (5d). Yield 89%; mp 161-163°C (DMF). ^{1}H NMR spectrum, δ, ppm (J, Hz): 16.55 (1H, s, OH); 13.02 (1H, s, NH); 8.74 (1H, s, H-2 Py); 8.30 (1H, d, J = 4.3, H-6 Py); 8.20 (2H, d, J = 8.3, H-5 + H-4 Py); 7.74 (1H, t, J = 7.6,

H-7); 7.52 (1H, d, J = 9.0, H-8); 7.33 (1H, t, J = 7.6, H-6); 7.30 (1H, t, J = 7.9, H-5 Py); 4.29 (2H, t, J = 7.2, NCH_2); 1.74 (2H, m, $C\underline{H}_2Me$); 1.09 (3H, t, J = 7.2, CH_3). Mass spectrum, *m/z* (I_{rel}, %): 323 $[M]^+$ (60), 281 $[M–C_3H_6]^+$ (12), 230 $[M–NHPy]^+$ (53), 187 (38), 94 (100).

4-Hydroxy-2-oxo-1-propyl-1,2-dihydroquinoline-3-carboxylic Acid Pyrid-2-yl Amide (5e). Yield 76%; mp 178-179°C (DMF). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 16.50 (1H, s, OH); 12.88 (1H, s, NH); 8.35 (1H, d, J = 5.0, H-6 Py); 8.24 (1H, d, J = 7.9, H-3 Py); 8.19 (1H, d, J = 7.9, H-5); 7.75 (1H, t, J = 7.6, H-7); 7.70 (1H, t, J = 8.2, H-4 Py); 7.45 (1H, d, J = 8.6, H-8); 7.30 (1H, t, J = 7.9, H-6); 7.08 (1H, t, J = 5.4, H-5 Py); 4.30 (2H, t, J = 7.2, NCH_2); 1.72 (2H, m, $C\underline{H}_2Me$); 1.01 (3H, t, J = 7.2, CH_3). Mass spectrum, *m/z* (I_{rel}, %): 323 $[M]^+$ (100), 281 $[M–C_3H_6]^+$ (75), 230 $[M–NHPy]^+$ (4.7), 202 (3.5), 187 (58), 121 (8), 94 (54).

4-Hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic Acid Pyrid-4-yl Amide (5a). Water (2 ml) was added to a suspension of compound **6** (3.45 g, 0.01 mol) in DMF (20 ml) and refluxed for 15 h. The reaction mixture was cooled and the precipitate was filtered off, washed several times on the filter with hot water to remove the starting pyridinium chloride **6**, and dried. Yield 1.60 g (57%); mp 360-362°C (DMR). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 16.43 (1H, s, OH); 12.91 (1H, s, NH–Py); 12.00 (1H, s, NH); 8.33 (2H, d, J = 4.8, H-2,6 Py); 8.16 (1H, d, J = 7.9, H-5); 7.63 (1H, t, J = 7.0, H-7); 7.52 (2H, d, J = 4.8, H-3,5 Py); 7.44 (1H, d, J = 7.9, H-8); 7.27 (1H, t, J = 7.0, H-6). Mass spectrum, *m/z* (I_{rel}, %): 281 $[M]^+$ (100), 188 $[M–NHPy]^+$ (70), 94 (37).

1-Ethyl-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic Acid Pyrid-4-yl Amide (5b). 4-Aminopyridine (0.94 g, 0.01 mol) and 2-3 drops of water were added to a solution of methyl 4-chloro-1-ethyl-2-oxo-1,2-dihydroquinoline-3-carboxylate (**1**, R = Et, Alk = Me, 2.65 g, 0.01 mol) in DMF (10 ml) and refluxed for 30 min. The reaction mixture was cooled and the precipitated amide **5b** was filtered off, washed on the filter with ethanol, and dried. Yield 2.53 g (82%); mp 187-189°C (DMF). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 16.56 (1H, s, OH); 12.97 (1H, s, NH); 8.45 (2H, d, J = 6.5, H-2,6 Py); 8.21 (1H, d, J = 8.3, H-5); 7.76 (1H, t, J = 7.9, H-7); 7.61 (2H, d, J = 6.5, H-3,5 Py); 7.53 (1H, d, J = 8.6, H-8); 7.34 (1H, t, J = 7.3, H-6); 4.35 (2H, q, J = 7.2, NCH_2); 1.31 (3H, t, J = 7.2, CH_3). Mass spectrum, *m/z* (I_{rel}, %): 309 $[M]^+$ (100), 281 $[M–C_2H_4]^+$ (18), 216 $[M–NHPy]^+$ (33), 187 (60), 94 (32).

A mixed sample of the pyridylamides **5a-e** with a known sample obtained by treating the ethyl 1R-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylates with the aminopyridines [17] did not cause a depression in melting points. The ^{1}H NMR and chromatography mass spectra for these materials were identical.

4-Amino-1-(3-ethoxycarbonyl-2-oxo-1,2-dihydroquinolin-4-yl)pyridinium Chloride (6). 4-Aminopyridine (0.94 g, 0.01 mol) was added to a solution of ethyl 4-chloro-2-oxo-1,2-dihydroquinoline-3-carboxylate (**1**, R = H, Alk = Et, 2.51 g, 0.01 mol) in anhydrous DMF (10 ml) and refluxed for 1 h. The reaction mixture was cooled and the precipitated pyridinium chloride **6** was filtered off, washed with acetone, and dried. Yield 3.11 g (90%); mp 290-292°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 12.91 (1H, s, NH); 9.25 (2H, s, NH_2); 8.32 (2H, d, J = 5.1, H-2,6 Py); 7.69 (1H, t, J = 7.2, H-7); 7.55 (1H, d, J = 7.8, H-8); 7.25 (1H, t, J = 7.2, H-6); 7.15-7.05 (3H, m, H-5 + H-3,5 Py); 4.10 (2H, q, J = 7.0, OCH_2); 1.00 (3H, t, J = 7.0, CH_3). Found, %: C 59.18; H 4.54; N 12.29. $C_{17}H_{16}ClN_3O_3$. Calculated, %: C 59.05; H 4.66; N 12.15.

1-Ethyl-4-hydroxy-1H-quinolin-2-one (8). A. A solution of 4-chloro-1-ethyl-2-oxo-1,2-dihydroquinoline-3-carboxylic acid (**2**, R = Et, 2.51 g, 0.01 mol) in aqueous DMF (10 ml) was refluxed for 2 h. After cooling, the reaction mixture was diluted with water. The precipitated solid was filtered off, washed with water, and dried. Yield 1.41 g (75%); mp 274-276°C (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 11.35 (1H, s, OH); 7.88 (1H, d, J = 8.0, H-5); 7.60 (1H, t, J = 7.1, H-7); 7.47 (1H, d, J = 8.0, H-8); 7.19 (1H, t, J = 7.1, H-6); 5.84 (1H, s, H-3); 4.19 (2H, q, J = 7.1, NCH_2); 1.12 (3H, t, J = 7.1, CH_3). Found, %: C 69.96; H 5.72; N 7.33. $C_{11}H_{11}NO_2$. Calculated, %: C 69.83; H 5.86; N 7.40.

B. A mixture of 1-ethyl-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid (**9**, 2.33 g, 0.01 mol) and 4-aminopyridine (0.94 g, 0.01 mol) in anhydrous DMF (10 ml) was treated by the method described above. Yield 1.51 g (80%).

A mixed sample with a sample of the quinolin-2-one **8** prepared by method A did not give a depression of melting point and the ^{1}H NMR spectra of the compounds were identical.

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