Chemistry of Heterocyclic Compounds, Vol. 44, No. 12, 2008

4-HYDROXY-2-QUINOLONES 150*. EFFICIENT SYNTHESIS, STRUCTURE, AND BIOLOGICAL ACTIVITIES OF 4-METHYL-2-OXO-1,2-DIHYDROQUINOLINE-3-CARBOXYLIC ACID ALKYL AMIDES

I. V. Ukrainets, N. L. Bereznyakova, V. A. Parshikov, and O. V. Gorokhova

A simple and efficient method for preparing 4-methyl-2-oxo-1,2-dihydroquinoline-3-carboxylic acid alkyl amides is proposed. The results of a study of the diuretic activity of the compounds synthesized are reported.

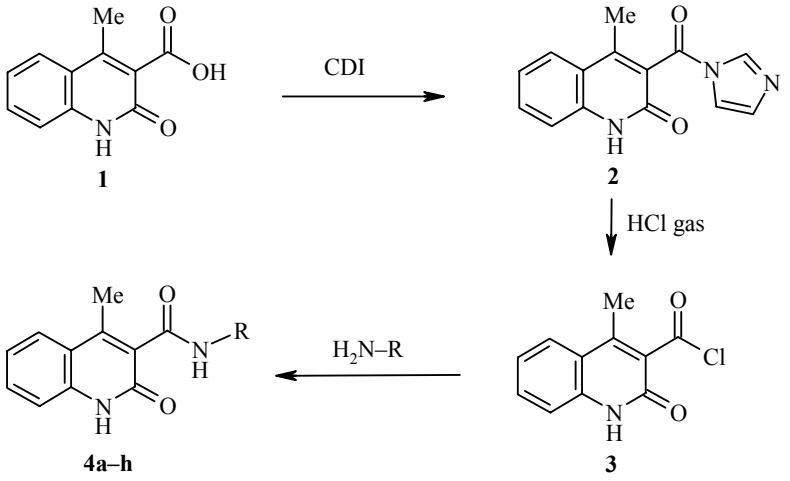
Keywords: diuretics, 4-methyl-2-oxo-1,2-dihydroquinoline-3-carboxylic acid, amidation, X-ray structural analysis.

Neither 4-methyl-2-oxo-1,2-dihydroquinoline-3-carboxylic acid (**1**) nor its readily available lower alkyl esters can unfortunately be directly amidated by primary and secondary amines. For this reason the synthesis of the corresponding N-R-amides (which are of interest as potentially biologically active substances) is only possible after additional activation of the carbonyl carbon atom of the carboxyl group. As is known, the most obvious, convenient, and widely used practical method of achieving this is through conversion of the acids to acid chlorides. None the less, treatment of acid **1** with thionyl chloride (phosphorus halides readily convert 1,2-dihydroquinolin-2-ones to aromatic 2-chloroquinolines [2] and are therefore unsuitable in this case) appears at first glance to be a trivial synthesis but is complicated by the formation of brightly colored cyanine dyes which can strongly contaminate the final products [3] even at low concentrations. With this in mind it was proposed to carry out amidation of acid **1** not *via* the acid chloride but by its conversion to the intermediate 4-methyl-2-oxo-1,2-dihydroquinoline-3-carboxylic acid imidazolide (**2**) using N,N'-carbonyldiimidazole (CDI). The use of this route suppresses the formation of the colored side products but a further synthetic problem arises. The reactivity of imidazolide **2** proved unusually low for such a class of compound. Although prolonged treatment with the anilines in anhydrous high boiling solvents gave the corresponding anilides [4], the scope of the practical use of the method of preparing the amides is significantly limited overall by the need to use only those amines which are thermally stable with quite high boiling points. Low boiling, and more so gaseous, amines react very slowly under normal conditions with imidazolide **2**. However, a method has long been known for the simple and efficient preparation of even very unstable acid chlorides consisting of the passage of dry hydrogen chloride into a solution of the imidazolide in an inert organic solvent [5]. The synthesis is carried out

* For communication 149 see [1].

National University of Pharmacy, Kharkiv 61002, Ukraine; e-mail: uiv@kharkov.ua. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1841-1848, December, 2008. Original article submitted September 28, 2007.

with cooling which reduces to zero virtually all side products. In fact, by applying this method to the imidazolide **2** we were able to prepare the colorless 4-methyl-2-oxo-1,2-dihydroquinoline-3-carboxylic acid chloride (**3**) which then gave the target alkyl amides **4a-h** in high overall yield (Table 1).



4 a R = Me, **b** R = Et, **c** R = Pr, **d** R = *i*-Pr, **e** R = *cyclo*-Pr, **f** R = Bu, **g** R = *i*-Bu, **h** R = *s*-Bu

The ^{1}H NMR spectra of the synthesized alkyl amides **4a-h** were not complicated by superposition hence the presence of all of the proton-containing functional groups were readily confirmed by the corresponding chemical shifts, intensities, and multiplicities of the signals (Table 2).

Steric structural features were studied by X-ray analysis for the *sec*-butylamide **4h** (see Figure 1 and Tables 3 and 4). It was found that two molecules (**A** and **B**) were found in the independent part of the unit cell

TABLE 1. Characteristics of the 4-Methyl-2-oxo-1,2-dihydroquinoline-3-carboxylic Acid Alkyl Amides **4a-h**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %	Diuretic activity*, % of control
		C	H	N			
4a	$C_{12}H_{12}N_2O_2$	66.76 / 66.65	5.68 / 5.59	13.03 / 12.95	297-299	96	-14
4b	$C_{13}H_{14}N_2O_2$	67.90 / 67.81	6.23 / 6.13	12.12 / 12.17	274-276	93	+32
4c	$C_{14}H_{16}N_2O_2$	68.74 / 68.83	6.67 / 6.60	11.56 / 11.47	220-222	92	-21
4d	$C_{14}H_{16}N_2O_2$	68.89 / 68.83	6.71 / 6.60	11.58 / 11.47	283-285	87	+8
4e	$C_{14}H_{14}N_2O_2$	69.35 / 69.41	5.72 / 5.82	11.47 / 11.56	308-310	79	+17
4f	$C_{15}H_{18}N_2O_2$	69.66 / 69.74	6.95 / 7.02	10.73 / 10.84	206-208	90	+20
4g	$C_{15}H_{18}N_2O_2$	69.70 / 69.74	7.05 / 7.02	10.88 / 10.84	259-261	93	+11
4h	$C_{15}H_{18}N_2O_2$	69.81 / 69.74	7.10 / 7.02	10.92 / 10.84	245-247	85	-35
	Hypothiazide	—	—	—	—	—	+61

* Increase (+) or inhibition (-) of diuresis relative to the control taken as 100%.

TABLE 2. ^{1}H NMR Spectra of Compounds **4a-h**

Compound	Chemical shifts, δ, ppm (*J*, Hz)							
	NH (1H, s)	NHR (1H)	Quinolone ring				4-CH_3 (3H, s)	R
			H-5 (1H, dd)	H-7 (1H, td)	H-8 (1H, dd)	H-6 (1H, td)		
4a	11.97	8.19 (q, *J* = 4.7)	7.76 (*J* = 8.1 and 1.2)	7.51 (*J* = 7.6 and 1.3)	7.29 (*J* = 8.2 and 1.1)	7.19 (*J* = 7.5 and 1.2)	2.33	2.72 (3H, d, *J* = 4.7, NCH_3)
4b	11.83	8.26 (t, *J* = 5.5)	7.75 (*J* = 8.2 and 1.1)	7.51 (*J* = 7.6 and 1.2)	7.28 (*J* = 8.2 and 1.0)	7.20 (*J* = 7.4 and 1.2)	2.34	3.21 (2H, q, *J* = 7.1, NCH_2); 1.08 (3H, t, *J* = 7.2, CH_3)
4c	11.80	8.25 (t, *J* = 5.1)	7.76 (*J* = 8.2 and 1.2)	7.50 (*J* = 7.7 and 1.3)	7.29 (*J* = 8.2 and 1.1)	7.20 (*J* = 7.4 and 1.3)	2.34	3.14 (2H, q, *J* = 6.1, NCH_2); 1.49 (2H, m, $C\underline{H}_2CH_3$); 0.90 (3H, t, *J* = 7.4, CH_3)
4d	11.79	8.16 (d, *J* = 7.6)	7.75 (*J* = 8.1 and 1.0)	7.50 (*J* = 7.8 and 1.2)	7.29 (*J* = 8.2 and 1.0)	7.19 (*J* = 7.6 and 1.2)	2.33	3.98 (1H, m, NCH); 1.11 (6H, d, *J* = 6.5, $2CH_3$)
4e	11.81	8.32 (d, *J* = 4.5)	7.74 (*J* = 8.2 and 1.1)	7.50 (*J* = 7.6 and 1.3)	7.28 (*J* = 8.3 and 1.1)	7.19 (*J* = 7.5 and 1.3)	2.34	2.76 (1H, m, NCH); 0.67 (2H, m, CH_2); 0.45 (2H, m, CH_2)
4f	11.79	8.23 (t, *J* = 5.6)	7.75 (*J* = 8.1 and 1.1)	7.51 (*J* = 7.7 and 1.3)	7.30 (*J* = 8.3 and 1.0)	7.20 (*J* = 7.4 and 1.3)	2.34	3.18 (2H, q, *J* = 6.2, NCH_2); 1.40 (4H, m, $(C\underline{H}_2)_2CH_3$); 0.89 (3H, t, *J* = 7.0, CH_3)
4g	11.80	8.28 (t, *J* = 5.7)	7.75 (*J* = 8.2 and 1.1)	7.51 (*J* = 7.7 and 1.2)	7.29 (*J* = 8.1 and 1.1)	7.20 (*J* = 7.5 and 1.2)	2.35	3.02 (2H, t, *J* = 6.4, NCH_2); 1.77 (1H, m, $C\underline{H}(CH_3)_2$); 0.90 (6H, d, *J* = 6.7, $2CH_3$)
4h	11.76	8.07 (d, *J* = 8.1)	7.75 (*J* = 8.1 and 1.2)	7.49 (*J* = 7.7 and 1.2)	7.29 (*J* = 8.2 and 1.0)	7.19 (*J* = 7.6 and 1.3)	2.34	3.82 (1H, m, NCH); 1.43 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 1.08 (3H, d, *J* = 6.8, $CHC\underline{H}_3$); 0.89 (3H, t, *J* = 7.3, $CH_2C\underline{H}_3$)

of the compound studied and that they differed in several geometrical parameters. The bicyclic quinolone fragment and the atoms $O_{(1)}$, $C_{(10)}$, and $C_{(15)}$ lie in a single plane within 0.02 Å for both molecules despite the marked repulsion between the 4-methyl group, the neighboring substituent at $C_{(8)}$, and the aromatic ring atoms.

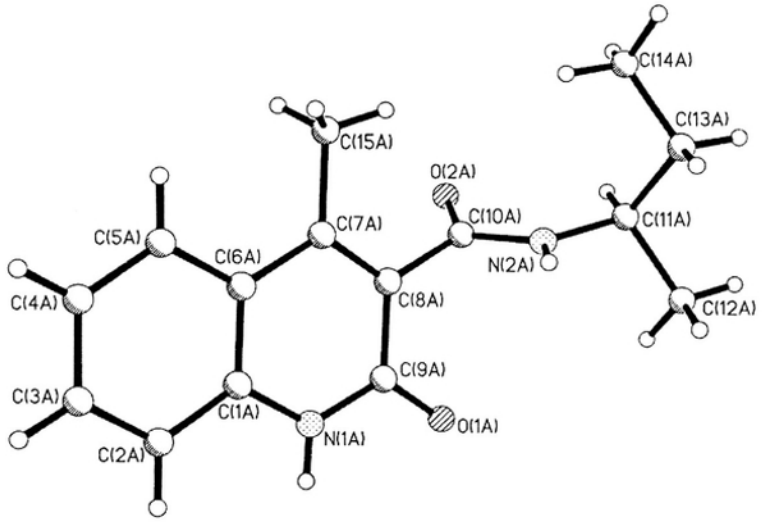


Fig. 1. Structure of the *sec*-butylamide molecule **4h** with atomic numbering.

This is shown in molecule **A** by the shortened intramolecular contacts $H_{(15a)}\cdots C_{(5a)}$ of 2.79 (sum of van der Waal radii 2.87 Å) [6], $H_{(15a)}\cdots H_{(5)}$ 2.30 (2.34), and $H_{(15b)}\cdots C_{(10)}$ 2.47 Å (2.87 Å) and in molecule **B** the shortened intramolecular contact $H_{(15f)}\cdots C_{(10b)}$ of 2.53 Å (2.87 Å). The carbamide fragment is twisted relative to the plane of bicycle (torsional angle $C_{(7)}$–$C_{(8)}$–$C_{(10)}$–$O_{(2)}$ -74.1(4)º in **A** and 69.0(4)º in **B**). The *sec*-butyl substituent is found in an *ap*-conformation relative to the $C_{(8)}$–$C_{(10)}$ bond (torsional angle $C_{(11)}$–$N_{(2)}$–$C_{(10)}$–$H_{(8)}$ 167.8(3)º in **A**

TABLE 3. Bond Lengths (*l*) in the *sec*-Butylamide **4h** Structure

Bond	*l*, Å	Bond	*l*, Å
$O_{(1A)}$–$C_{(9A)}$	1.244(4)	$O_{(2A)}$–$C_{(10A)}$	1.245(3)
$N_{(1A)}$–$C_{(9A)}$	1.346(4)	$N_{(1A)}$–$C_{(1A)}$	1.362(4)
$N_{(2A)}$–$C_{(10A)}$	1.334(4)	$N_{(2A)}$–$C_{(11A)}$	1.463(4)
$C_{(1A)}$–$C_{(2A)}$	1.396(5)	$C_{(1A)}$–$C_{(6A)}$	1.413(5)
$C_{(2A)}$–$C_{(3A)}$	1.353(5)	$C_{(3A)}$–$C_{(4A)}$	1.384(6)
$C_{(4A)}$–$C_{(5A)}$	1.362(5)	$C_{(5A)}$–$C_{(6A)}$	1.398(5)
$C_{(6A)}$–$C_{(7A)}$	1.449(4)	$C_{(7A)}$–$C_{(8A)}$	1.359(4)
$C_{(7A)}$–$C_{(15A)}$	1.517(5)	$C_{(8A)}$–$C_{(9A)}$	1.455(4)
$C_{(8A)}$–$C_{(10A)}$	1.487(4)	$C_{(11A)}$–$C_{(13A)}$	1.493(4)
$C_{(11A)}$–$C_{(12A)}$	1.563(4)	$C_{(13A)}$–$C_{(14A)}$	1.488(5)
$O_{(1B)}$–$C_{(9B)}$	1.268(4)	$O_{(2B)}$–$C_{(10B)}$	1.227(3)
$N_{(1B)}$–$C_{(9B)}$	1.348(4)	$N_{(1B)}$–$C_{(1B)}$	1.396(4)
$N_{(2B)}$–$C_{(10B)}$	1.325(4)	$N_{(2B)}$–$C_{(11B)}$	1.443(4)
$C_{(1B)}$–$C_{(2B)}$	1.390(5)	$C_{(1B)}$–$C_{(6B)}$	1.428(5)
$C_{(2B)}$–$C_{(3B)}$	1.406(6)	$C_{(3B)}$–$C_{(4B)}$	1.401(6)
$C_{(4B)}$–$C_{(5B)}$	1.354(5)	$C_{(5B)}$–$C_{(6B)}$	1.425(5)
$C_{(6B)}$–$C_{(7B)}$	1.453(5)	$C_{(7B)}$–$C_{(8B)}$	1.380(5)
$C_{(7B)}$–$C_{(15B)}$	1.535(5)	$C_{(8B)}$–$C_{(9B)}$	1.479(5)
$C_{(8B)}$–$C_{(10B)}$	1.503(4)	$C_{(11B)}$–$C_{(13B)}$	1.504(4)
$C_{(11B)}$–$C_{(12B)}$	1.532(4)	$C_{(13B)}$–$C_{(14B)}$	1.498(4)

and -174.6(3)º in **B**) and is twisted in such a way that the methyl group occurs in a *-ac*-conformation relative to the $C_{(10)}$–$N_{(2)}$ bond (torsional angle $C_{(10)}$–$N_{(2)}$–$C_{(11)}$–$C_{(12)}$ -115.8(5)º in molecule **A** and -119.0(4)º in **B**). The ethyl group occurs in an *ac*-conformation relative to the bond $C_{(10)}$–$N_{(2)}$ and is twisted relative to the $N_{(2)}$–$C_{(11)}$ bond (torsional angle $C_{(10)}$–$N_{(2)}$–$C_{(11)}$–$C_{(13)}$ 122.6(5)º in **A** and 118.2(5)º in **B**); $N_{(2)}$–$C_{(11)}$–$C_{(13)}$–$C_{(14)}$ -67.3(6)º in **A** and -52.6(7)º in **B**). Such an orientation of the *sec*-butyl substituent leads to the shortened intramolecular contacts: in molecule **A** $H_{(11a)}$···$H_{(14c)}$ 2.30 (2.34) and $H_{(14b)}$···$N_{(2a)}$ 2.53 (2.67) and in molecule **B** $H_{(11b)}$···$O_{(2b)}$ 2.41 Å (2.46 Å).

The crystals of the *sec*-butylamide molecule **4h** form dimers *via* the intermolecular hydrogen bonds $N_{(1a)}$–$H_{(1Na)}$…$O_{1(b')}$ (1-*x*, 0.5+*y*, 0.5-*z*, H···O 1.95 Å, N–H···O 170º) and $N_{(1b)}$–$H_{(1Nb)}$ ···$O_{(1a)'}$ (1-*x*, -0.5+*y*, 0,5-*z*, H···O 2.05 Å, N–H···O 174º). In turn, thanks to the intermolecular hydrogen bonds $N_{(2a)}$–$H_{(2Na)}$···$O_{(2b)}$ (H···O 2.09 Å, N–H···O 158º) and $N_{(2b)}$–$H_{(2Nb)}$···$O_{(2a')}$ (1+*x*, *y*, *z*, H···O 2.11 Å, N–H···O 160º) these dimers are grouped in infinite chains along the crystallographic (1 0 0) direction. In addition, formation of the intermolecular hydrogen bonds likely leads to lengthening of the $O_{(1)}$–$C_{(9)}$ bond to 1.244(4) in molecule **A** and to 1.268(4) Å in molecule **B** and the $O_{(2)}$–$C_{(10)}$ bond to 1.245(3) in **A** and to 1.227(3) Å in **B** when compared with their mean value of 1.210 Å [7].

The theoretical reason for studying the diuretic properties of the alkyl amides **4a-h** is the clear ability to increase the urinary function of the kidneys in several of the closely structurally related 1-hydroxy-3-oxo-5,6-dihydro-3H-pyrrolo[3,2,1-*ij*]quinoline-2-carboxylic acid alkyl amides discovered by us before [8]. Biological studies were carried out on white, non-pedigree male mice of weight 180-200 g by a known method [9] in comparison with hypothiazide. The synthesized compounds **4a-h** were introduced orally in a dose of 40 mg/kg (the effective dose for hypothiazide), after which the experimental animals were placed in a "metabolic cage". The volume of urea was recorded over 4 h, taking the control as 100%. The experimental data

TABLE 4. Valence Angles (ω) in the *sec*-Butylamide **4h** Structure

Valence angle	ω, deg	Valence angle	ω, deg
$C_{(9A)}$–$N_{(1A)}$–$C_{(1A)}$	124.2(3)	$C_{(10A)}$–$N_{(2A)}$–$C_{(11A)}$	125.1(3)
$N_{(1A)}$–$C_{(1A)}$–$C_{(2A)}$	119.2(3)	$N_{(1A)}$–$C_{(1A)}$–$C_{(6A)}$	119.2(3)
$C_{(2A)}$–$C_{(1A)}$–$C_{(6A)}$	121.6(3)	$C_{(3A)}$–$C_{(2A)}$–$C_{(1A)}$	118.2(4)
$C_{(2A)}$–$C_{(3A)}$–$C_{(4A)}$	121.2(4)	$C_{(5A)}$–$C_{(4A)}$–$C_{(3A)}$	121.5(4)
$C_{(4A)}$–$C_{(5A)}$–$C_{(6A)}$	119.7(4)	$C_{(5A)}$–$C_{(6A)}$–$C_{(1A)}$	117.7(3)
$C_{(5A)}$–$C_{(6A)}$–$C_{(7A)}$	123.2(3)	$C_{(1A)}$–$C_{(6A)}$–$C_{(7A)}$	119.0(3)
$C_{(8A)}$–$C_{(7A)}$–$C_{(6A)}$	118.8(3)	$C_{(8A)}$–$C_{(7A)}$–$C_{(15A)}$	121.8(3)
$C_{(6A)}$–$C_{(7A)}$–$C_{(15A)}$	119.4(3)	$C_{(7A)}$–$C_{(8A)}$–$C_{(9A)}$	121.2(3)
$C_{(7A)}$–$C_{(8A)}$–$C_{(10A)}$	121.1(3)	$C_{(9A)}$–$C_{(8A)}$–$C_{(10A)}$	117.7(3)
$O_{(1A)}$–$C_{(9A)}$–$N_{(1A)}$	120.0(3)	$O_{(1A)}$–$C_{(9A)}$–$C_{(8A)}$	122.5(3)
$N_{(1A)}$–$C_{(9A)}$–$C_{(8A)}$	117.5(3)	$O_{(2A)}$–$C_{(10A)}$–$N_{(2A)}$	124.4(3)
$O_{(2A)}$–$C_{(10A)}$–$C_{(8A)}$	121.3(3)	$N_{(2A)}$–$C_{(10A)}$–$C_{(8A)}$	114.3(3)
$N_{(2A)}$–$C_{(11A)}$–$C_{(13A)}$	110.6(4)	$N_{(2A)}$–$C_{(11A)}$–$C_{(12A)}$	108.6(3)
$C_{(13A)}$–$C_{(11A)}$–$C_{(12A)}$	110.6(5)	$C_{(14A)}$–$C_{(13A)}$–$C_{(11A)}$	106.6(5)
$C_{(9B)}$–$N_{(1B)}$–$C_{(1B)}$	123.4(3)	$C_{(10B)}$–$N_{(2B)}$–$C_{(11B)}$	124.2(3)
$C_{(2B)}$–$C_{(1B)}$–$N_{(1B)}$	119.0(3)	$C_{(2B)}$–$C_{(1B)}$–$C_{(6B)}$	120.6(4)
$N_{(1B)}$–$C_{(1B)}$–$C_{(6B)}$	120.4(3)	$C_{(1B)}$–$C_{(2B)}$–$C_{(3B)}$	118.7(4)
$C_{(4B)}$–$C_{(3B)}$–$C_{(2B)}$	120.9(4)	$C_{(5B)}$–$C_{(4B)}$–$C_{(3B)}$	120.8(4)
$C_{(4B)}$–$C_{(5B)}$–$C_{(6B)}$	120.3(4)	$C_{(5B)}$–$C_{(6B)}$–$C_{(1B)}$	118.7(3)
$C_{(5B)}$–$C_{(6B)}$–$C_{(7B)}$	122.7(3)	$C_{(1B)}$–$C_{(6B)}$–$C_{(7B)}$	118.7(3)
$C_{(8B)}$–$C_{(7B)}$–$C_{(6B)}$	118.0(3)	$C_{(8B)}$–$C_{(7B)}$–$C_{(15B)}$	122.6(3)
$C_{(6B)}$–$C_{(7B)}$–$C_{(15B)}$	119.4(3)	$C_{(7B)}$–$C_{(8B)}$–$C_{(9B)}$	122.6(3)
$C_{(7B)}$–$C_{(8B)}$–$C_{(10B)}$	121.9(3)	$C_{(9B)}$–$C_{(8B)}$–$C_{(10B)}$	115.4(3)
$O_{(1B)}$–$C_{(9B)}$–$N_{(1B)}$	119.6(3)	$O_{(1B)}$–$C_{(9B)}$–$C_{(8B)}$	123.6(3)
$N_{(1B)}$–$C_{(9B)}$–$C_{(8B)}$	116.8(3)	$O_{(2B)}$–$C_{(10B)}$–$N_{(2B)}$	123.2(3)
$O_{(2B)}$–$C_{(10B)}$–$C_{(8B)}$	120.0(3)	$N_{(2B)}$–$C_{(10B)}$–$C_{(8B)}$	116.7(3)
$N_{(2B)}$–$C_{(11B)}$–$C_{(13B)}$	111.5(3)	$N_{(2B)}$–$C_{(11B)}$–$C_{(12B)}$	110.2(3)
$C_{(13B)}$–$C_{(11B)}$–$C_{(12B)}$	110.3(4)	$C_{(14B)}$–$C_{(13B)}$–$C_{(11B)}$	120.4(5)

given in Table 1 shows that the investigated compounds demonstrate approximately the same structure-activity relationship as do the corresponding 1-hydroxy-3-oxo-5,6-dihydro-3H-pyrrolo[3,2,1-*ij*]quinoline-2-carboxylic acid alkyl amides [8] and, depending of the structure of the amide fragment, can either increase or inhibit diuresis in the experimental animals. However, the strength of the experimental effects proved small and, on this basis, our search for potentially diuretic medicinal substances amongst 4-methyl-2-oxo-1,2-dihydro-quinoline-3-carboxylic acid alkyl amides shows little promise.

EXPERIMENTAL

^{1}H NMR spectra for the synthesized compounds were recorded on a Varian Mercury VX-200 (200 MHz) instrument using DMSO-d_6 as solvent and TMS as internal standard. The imidazolide **2** was prepared by a known method [4].

4-Methyl-2-oxo-1,2-dihydroquinoline-3-carboxylic Acid Methylamide (4a). A stream of dry HCl gas was passed for 15 min through a suspension of finely powdered imidazolide **2** (2.53 g, 0.01 mol) in anhydrous CCl_4 (70 ml) cooled to -20ºC. The product was tightly sealed and left at about 5ºC for 3 days. The main amount of excessive HCl was removed from the reaction mixture by bubbling through dry argon, after which the reaction vessel with the acid chloride **3** obtained was placed in an ice bath and saturated with gaseous methylamine. After 3-4 h the solvent was evaporated to dryness *in vacuo*. The residue was treated with cold water and acidified with dilute (1:1) HCl to pH 5. The precipitated methylamide **4a** was filtered off, washed with cold water, dried, and crystallized from ethanol.

The ethyl amide **4b** was prepared similarly.

Two variants of the amidation of the acid chloride **3** as obtained in the preceding example are possible to yield the amides **4c-h**. The cheap and available alkylamine are added with cooling and stirring to the acid chloride in a 3-fold molar excess. In the case of the expensive amines a 1:2 mixture of the amine with triethylamine is used. Subsequent separation of the reaction products is the same in all cases (see the example of the synthesis of methyl amide **4a**).

X-ray Structural Investigation. Crystals of *sec*-butylamide **4h** are monoclinic (ethanol), at 20ºC: a = 9.477(2), b = 14.898(2), c = 20.949(6) Å, β = 101.98(2)º, V = 2893(1) Å^3, M_r = 258.31, Z = 8, space group $P2_1/c$, d_{calc} = 1.186 g/cm^3, μ(MoKα) = 0.080 mm^{-1}, F(000) = 1104. The unit cell parameters and intensities of 17467 reflections (5017 independent, R_{int} = 0.067) were measured on an Xcalibur-3 diffractometer (MoKα radiation, CCD detector, graphite monochromator, ω scanning to $2\theta_{max}$ = 50º).

The structure was solved by a direct method using the SHELXTL program package [10]. In refinement of the structure limits were imposed on the bond lengths in the *sec*-butyl fragment $C_{(sp3)}$–$C_{(sp3)}$ = 1.53 Å. The positions of the hydrogen atoms were revealed in electron density difference synthesis and refined using the "riding" model with $U_{iso} = nU_{eq}$ for the non-hydrogen atom bound with the given hydrogen (n = 1.5 for methyl groups and n = 1.2 for remaining hydrogen atoms). The structure was refined in F^2 full-matrix least-squares analysis for non-hydrogen atoms to wR_2 = 0.179 for 4881 reflections (R_1 = 0.069 for 2174 reflections with $F > 4\sigma$ (F), S = 0.845). The full crystallographic information has been placed in the Cambridge structural data bank as CCDC 672204. Interatomic distances and valence angles are given in Tables 3 and 4.

REFERENCES

1. I. V. Ukrainets, A. A. Tkach, and Liu Yang Yang, *Khim. Geterotsikl. Soedin.*, 1655 (2008). [*Chem. Heterocycl. Comp.*, **44**, 1347 (2008)].

2. I. V. Ukrainets, O. V. Gorokhova, and L. V. Sidorenko, *Khim. Geterotsikl. Soedin.*, 1195 (2005). [*Chem. Heterocycl. Comp.*, **41**, 1019 (2005)].
3. I. V. Ukrainets, N. L. Bereznyakova, V. A. Parshikov, and V. N. Kravchenko, *Khim. Geterotsikl. Soedin.*, 78 (2008). [*Chem. Heterocycl. Comp.*, **44**, 64 (2008)].
4. I. V. Ukrainets, N. L. Bereznyakova, V. A. Parshikov, and O. I. Naboka, *Khim. Geterotsikl. Soedin.*, 239 (2008). [*Chem. Heterocycl. Comp.*, **44**, 178 (2008)].
5. L. F. Fieser and M. Fieser, *Reagents for Organic Synthesis* [Russian translation], Vol. 2, Mir, Moscow (1970), p. 120.
6 Yu. V. Zefirov, *Kristallografiya*, **42**, 936 (1997).
7. H. -B. Burgi and J. D. Dunitz, *Structural Correlation*, Vol. 2, VCH, Weinheim (1994), p. 741.
8. I. V. Ukrainets, N. L. Bereznyakova, and E. V. Mospanova, *Khim. Geterotsikl. Soedin.*, 1015 (2007). [*Chem. Heterocycl. Comp.*, **43**, 856 (2007)].
9. L. N. Sernov and V. V. Gatsura, *Elements of Experimental Pharmacology* [in Russian], Moscow (2000), p. 103.
10. G. M. Sheldrick, *SHELXTL PLUS. PC Version. A System of Computer Programs for the Determination of Crystal Structure from X-ray Diffraction Data*, Rev. 5.1 (1998).