Chemistry of Heterocyclic Compounds, Vol. 43, No. 7, 2007

4-HYDROXY-2-QUINOLONES

123*. AMIDATION OF 2-BROMOMETHYL-5-OXO-1,2-DIHYDRO-5H-OXAZOLO[3,2-*a*]-QUINOLINE-4-CARBOXYLIC ACID

I. V. Ukrainets[1], N. L. Bereznyakova[1], A. V. Turov[2], and S. V. Shishkina[3]

The reaction of 2-bromomethyl-5-oxo-1,2-dihydro-5H-oxazolo[3,2-a]quinoline-4-carboxylic acid with thionyl chloride is accompanied by a transformation of the oxazoloquinolone ring to give 4-chloro-1-(2,3-dichloropropyl)-2-oxo-1,2-dihydroquinoline-3-carboxylic acid chloride.

Keywords: oxazolo[3,2-*a*]quinoline, 4-chloro-2-quinolinone, amidation, ring closing, X-ray analysis.

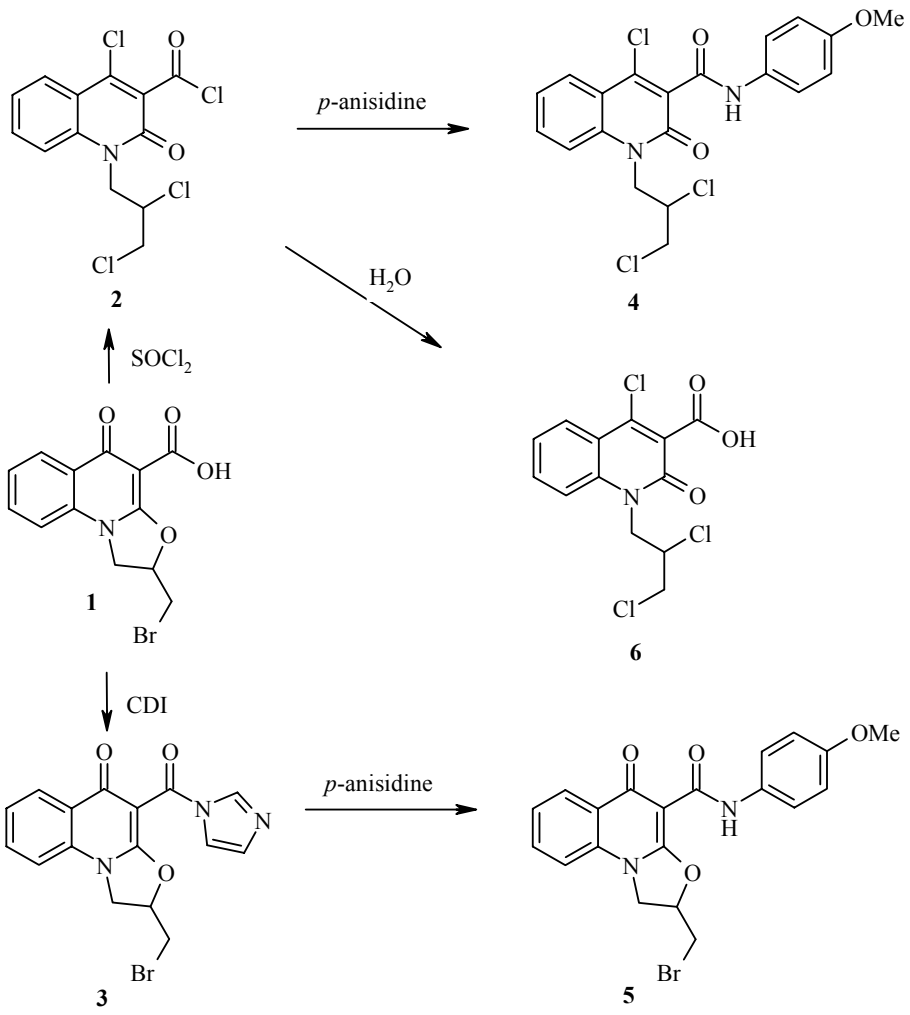
Using various methods, carboxylic acids can be converted to N-substituted amides which are potentially biologically active substances. None the less, only a few of these are widely used in preparative organic chemistry. The best known are the reaction of the acids to an acid chloride or to the imidazolide by treatment with thionyl chloride or N,N'-carbonyldiimidazole (CDI) respectively. We have studied the potential use of these methods for the amidation of the recently reported 2-bromomethyl-5-oxo-1,2-dihydro-5H-oxazolo[3,2-*a*]-quinoline-4-carboxylic acid (**1**).

It was found that the reaction of acid **1** with both thionyl chloride and CDI occurred without any obvious complication. Hence subsequent work up of the intermediate quinolones **2** and **3** with *p*-anisidine should theoretically have given the same 4-methoxyanilide of 2-bromomethyl-5-oxo-1,2-dihydro-5H-oxazolo[3,2-*a*]quinoline-4-carboxylic acid (**5**). However, the actual properties of the anilides **4** and **5** obtained proved to be different. It was initially proposed that, in the case of the use of CDI there might occur a nucleophilic substitution of the bromine in acid **1** for an imidazole residue but this was not correct since the corresponding imidazole signals were absent in the ^{1}H and ^{13}C NMR spectra. Further, a comparative analysis of the ^{1}H NMR spectra of the material obtained and of the synthetic precursor (acid **1**) showed that the thionyl chloride led to a marked change in the oxazoloquinolone skeleton whereas in the case of CDI the nature of the spectrum was little changed.

A similar conclusion was reached when looking at the ^{13}C NMR spectra of anilides **4** and **5** and after hydrolysis of the proposed acid chloride to form acid **6** which has properties and spectroscopic characteristics different to the starting acid.

* For Communication 122 see [1].

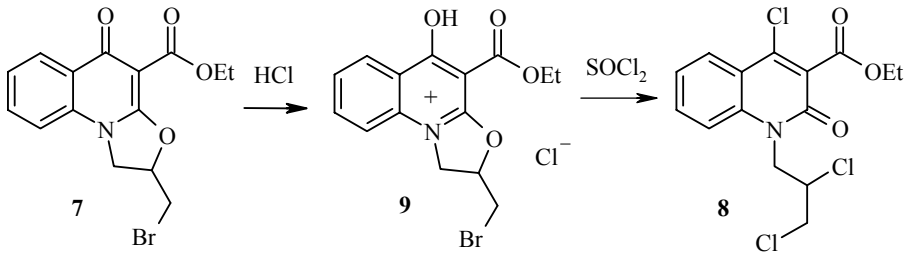
[1]National University of Pharmacy, Kharkiv 61002, Ukraine; e-mail: uiv@kharkov.ua. [2]Taras Shevchenko National University, Kiev 01033, Ukraine; e-mail: nmrlab@univ.kiev.ua. [3]STC Institute for Single Crystals, National Academy of Sciences, Kharkiv 61001 Ukraine; e-mail: sveta@xray.isc.kharkov.com.
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 1034-1042, July, 2007. Original article submitted March 23, 2006.



However, the question of what had occurred to acid **1** under these conditions remained open.

The answer to this problem was resolved after treatment of ethyl 2-bromomethyl-5-oxo-1,2-dihydro-5H-oxazolo[3,2-*a*]quinoline-4-carboxylate (**7**) with thionyl chloride.

It proved possible to grow a single crystal of the compound obtained suitable for X-ray analysis and this allowed us to identify it unambiguously as ethyl 4-chloro-1-(2,3-dichloropropyl)-2-oxo-1,2-dihydroquinoline-3-carboxylate (**8**). The initial stage of this unusual reaction is evidently addition of HCl, traces of which are always present in thionyl chloride. The 4-hydroxy derivative **9** then undoubtedly undergoes three reactions which are: nucleophilic aromatic substitution of the OH group, fission of an ether bond in the oxazolidine ring, and finally exchange of the bromine atom for chlorine. At this time it was not possible to prove unambiguously whether these processes occur simultaneously or in some particular kind of sequence.



From the X-ray data it was found that the bicyclic fragment and the $Cl_{(1)}$, $C_{(10)}$, $O_{(1)}$, and $C_{(13)}$ atoms of the ethyl ester **8** lie within a single plane to an accuracy of 0.01 Å (Figure 1, Tables 1, 2). A shortened intramolecular contact for $H_{(5)}\cdots Cl_{(1)}$ of 2.66 Å is found (sum of van der Waal radii 3.06 Å [2]). The ester substituent is twisted relative to the plane of the bicycle (torsional angle $C_{(7)}–C_{(8)}–C_{(10)}–O_{(2)}$ 89.3(5)º). The ethyl group occurs in an ap conformation relative to the $C_{(8)}–C_{(10)}$ bond and the $C_{(11)}–C_{(12)}$ bond is virtually perpendicular to the $C_{(10)}–O_{(3)}$ bond (torsional angles $C_{(11)}–O_{(3)}–C_{(10)}–C_{(8)}$ -179.5(3)º, $C_{(10)}–O_{(3)}–C_{(11)}–C_{(12)}$ -85.3(4)º). This positioning of the ethyl group leads to a shortened intramolecular contact $H_{(11a)}\cdots O_{(2)}$ 2.40 Å (2.46 Å).

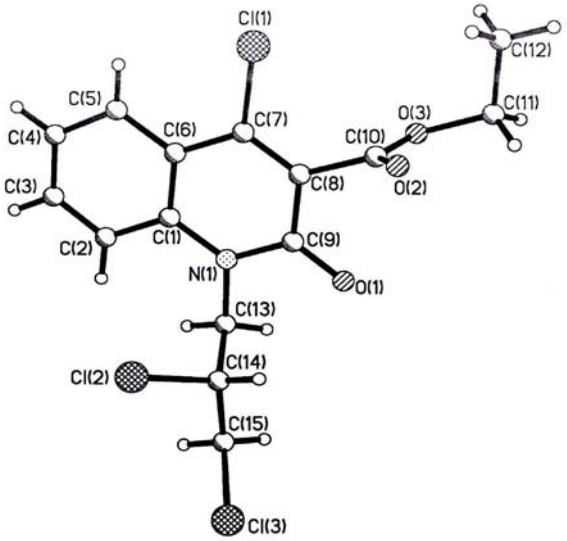


Fig. 1. Structure of the trichloro-substituted ester **8** molecule with atomic numbering.

There is a repulsion between the substituent on atom $N_{(1)}$, the neighboring carbonyl group, and the hydrogen in the *peri* position of the benzene ring [intramolecular shortened contacts $H_{(2)}\cdots C_{(13)}$ 2.60 (2.87), $H_{(2)}\cdots H_{(13a)}$ 1.95 (2.34), $H_{(13a)}\cdots C_{(2)}$ 2.51 (2.87), $H_{(13b)}\cdots O_{(2)}$ 2.38 (2.46), and $H_{(14)}\cdots C_{(9)}$ 2.84 Å (2.87 Å)] which results in the dichloropropyl substituent being almost perpendicular to the plane of the bicyclic fragment (torsional angle $C_{(9)}–N_{(1)}–C_{(13)}–C_{(14)}$ 78.1(3)º) and found in an ap conformation (torsional angle $N_{(1)}–C_{(13)}–C_{(14}–C_{(15)}$ -175.8(3)º). The chlorine atoms in it occur in a -*sc*-position relative to one another (torsional angle $Cl_{(2)}–C_{(14)}–C_{(15)}–Cl_{(3)}$ -65.1(3)º despite the shortened intramolecular contact $Cl_{(2)}\cdots C_{(1)}$ to 3.53 Å (3.61 Å).

TABLE 1. Bond Lengths (*l*) in the Trichloro-substituted Ester **8**

Bond	*l*, Å	Bond	*l*, Å
$Cl_{(1)}–C_{(7)}$	1.760(3)	$N_{(1)}–C_{(1)}$	1.386(4)
$N_{(1)}–C_{(9)}$	1.386(4)	$N_{(1)}–C_{(13)}$	1.467(4)
$O_{(1)}–C_{(9)}$	1.224(4)	$C_{(1)}–C_{(2)}$	1.409(5)
$C_{(1)}–C_{(6)}$	1.416(5)	$Cl_{(2)}–C_{(14)}$	1.827(3)
$O_{(2)}–C_{(10)}$	1.186(4)	$C_{(2)}–C_{(3)}$	1.352(6)
$Cl_{(3)}–C_{(15)}$	1.844(4)	$O_{(3)}–C_{(10)}$	1.321(4)
$O_{(3)}–C_{(11)}$	1.462(4)	$C_{(3)}–C_{(4)}$	1.393(8)
$C_{(4)}–C_{(5)}$	1.382(8)	$C_{(5)}–C_{(6)}$	1.388(5)
$C_{(6)}–C_{(7)}$	1.434(5)	$C_{(7)}–C_{(8)}$	1.321(5)
$C_{(8)}–C_{(9)}$	1.460(4)	$C_{(8)}–C_{(10)}$	1.499(4)
$C_{(11)}–C_{(12)}$	1.486(6)	$C_{(13)}–C_{(14)}$	1.520(5)
$C_{(14)}–C_{(15)}$	1.499(5)		

TABLE 2. Valence Angles (ω) in the Trichloro-substituted Ester **8**

Angle	ω, deg	Angle	ω, deg
$C_{(1)}$–$N_{(1)}$–$C_{(9)}$	123.0(2)	$C_{(1)}$–$N_{(1)}$–$C_{(13)}$	123.2(2)
$C_{(9)}$–$N_{(1)}$–$C_{(13)}$	113.7(2)	$N_{(1)}$–$C_{(1)}$–$C_{(2)}$	121.4(3)
$N_{(1)}$–$C_{(1)}$–$C_{(6)}$	120.4(3)	$C_{(2)}$–$C_{(1)}$–$C_{(6)}$	118.2(3)
$C_{(3)}$–$C_{(2)}$–$C_{(1)}$	120.7(4)	$C_{(10)}$–$O_{(3)}$–$C_{(11)}$	117.0(3)
$C_{(2)}$–$C_{(3)}$–$C_{(4)}$	121.7(4)	$C_{(5)}$–$C_{(4)}$–$C_{(3)}$	118.5(4)
$C_{(4)}$–$C_{(5)}$–$C_{(6)}$	121.4(5)	$C_{(5)}$–$C_{(6)}$–$C_{(1)}$	119.5(4)
$C_{(5)}$–$C_{(6)}$–$C_{(7)}$	124.5(4)	$C_{(1)}$–$C_{(6)}$–$C_{(7)}$	116.1(3)
$C_{(8)}$–$C_{(7)}$–$C_{(6)}$	123.6(3)	$C_{(8)}$–$C_{(7)}$–$Cl_{(1)}$	118.6(3)
$C_{(6)}$–$C_{(7)}$–$Cl_{(1)}$	117.8(2)	$C_{(7)}$–$C_{(8)}$–$C_{(9)}$	120.6(3)
$C_{(7)}$–$C_{(8)}$–$C_{(10)}$	125.1(3)	$C_{(9)}$–$C_{(8)}$–$C_{(10)}$	114.3(3)
$O_{(1)}$–$C_{(9)}$–$N_{(1)}$	121.3(3)	$O_{(1)}$–$C_{(9)}$–$C_{(8)}$	122.3(3)
$N_{(1)}$–$C_{(9)}$–$C_{(8)}$	116.3(2)	$O_{(2)}$–$C_{(10)}$–$O_{(3)}$	124.6(3)
$O_{(2)}$–$C_{(10)}$–$C_{(8)}$	123.8(3)	$O_{(3)}$–$C_{(10)}$–$C_{(8)}$	111.6(2)
$O_{(3)}$–$C_{(11)}$–$C_{(12)}$	111.2(3)	$N_{(1)}$–$C_{(13)}$–$C_{(14)}$	113.3(2)
$C_{(15)}$–$C_{(14)}$–$C_{(13)}$	108.8(3)	$C_{(15)}$–$C_{(14)}$–$Cl_{(2)}$	110.9(2)
$C_{(13)}$–$C_{(14)}$–$Cl_{(2)}$	111.7(2)	$C_{(14)}$–$C_{(15)}$–$Cl_{(3)}$	111.9(3)

The ester molecule **8** forms stacks in the crystal along the crystallographic (1 0 0) direction and these are mutually linked by weak intermolecular hydrogen bonds $C_{(13)}$–$H_{(13a)}$···$O_{(2')}$ (1+*x*, *y*, *z*) H···O 2.39 Å, C–H···O 133º, $C_{(15)}$–$H_{(15b)}$···$O_{(1')}$ (1-*x*, 2-*y*, 1-*z*) H···O 2.43 Å, C–H···O 162º. Shortened intermolecular contacts occur in the crystal as $H_{(4)}$···$Cl_{(3')}$ (*x*, *y*, *z*-1) 2.98 (3.06), $H_{(11b)}$···$Cl_{(2')}$ (*x*-1, *y*+1, *z*) 2.06 (3.06), $Cl_{(1)}$···$Cl_{(1')}$ (-*x*, 2-*y*, -*z*) 3.45 (3.80), $Cl_{(1)}$···$Cl_{(3')}$ (1-*x*, 1-*y*, 1-*z*) 3.58 (3.80), $Cl_{(2)}$···$C_{(9')}$ (1-*x*, 1-*y*, 1-*z*) 3.58 (3.61), $Cl_{(3)}$···$C_{(7')}$ (1-*x*, 1-*y*, 1-*z*) 3.57 Å (3.61 Å).

Based on the X-ray data obtained all of the NMR data fell into place. Hence the ^{13}C NMR spectrum of the anilide **4** fully agrees with its structure as the acyclic trichloro derivative. Pointing to this is the anomalously high field chemical shift for the $C_{(4)}$ atom in the quinoline fragment at 140.7 ppm. Such a position would in no way be possible for a corresponding carbonyl carbon atom. In addition, the β-carbon atom signal in the $N_{(1)}$-substituent also agrees fully with a -CHCl- group. For this compound the following carbon and proton chemical shifts were obtained.

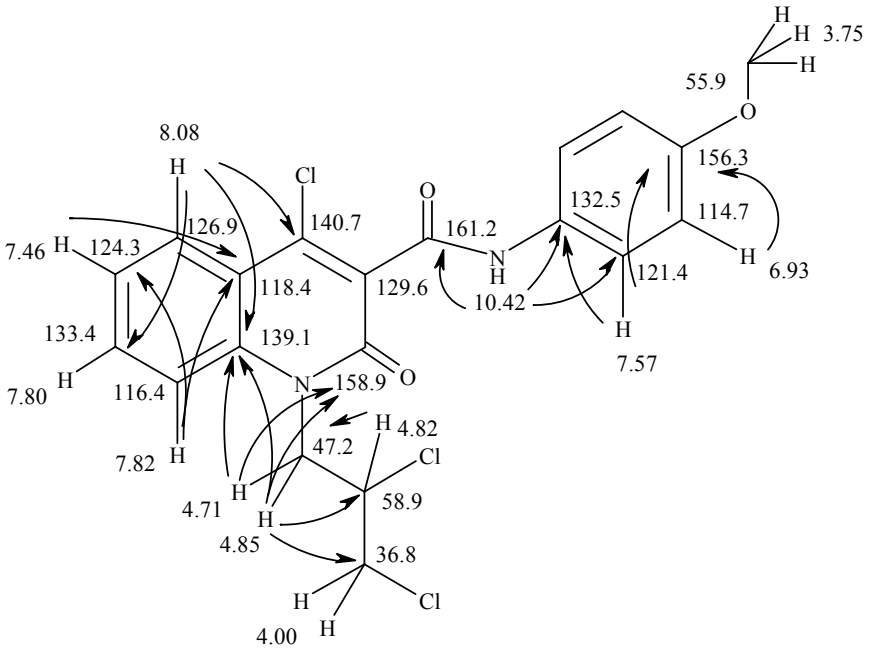


TABLE 3. Full Correlation List Found for the Anilide **4**

δ, ppm	HMQC	HMBC
10.42	—	161.2; 132.5; 121.4
8.08	126.9	140.7; 139.1; 133.4
7.82	116.4	139.1; 126.9; 124.3; 118.4
7.80	133.4	
7.57	121.4	156.30; 132.5; 121.4
7.46	124.3	118.4; 116.4
6.93	114.7	156.3; 132.5
4.85	47.2	58.9; 36.8; 158.9; 139.1
4.82	58.9	47.2
4.71	47.2	58.9; 36.8; 158.9; 139.1
4.00	36.8	58.98; 47.2
3.75	55.9	156.3

Assignment of the protonated carbon atoms was made on the basis of the HMQC spectra and that of the quaternary carbon atoms through correlation with HMBC spectra. Hence the assignment of the $C_{(8a)}$ carbon atom follows from its correlation with the H-5,7 proton and the N–CH_2 methylene group protons. Assignment of the chemical shift of the $C_{(4a)}$ atom was made from its correlation with the H-6 and H-8 protons. Atom $C_{(4)}$, which is bonded to the chlorine, has a strong correlation through three bonds with the H-5 proton and it can be specified with certainty. The carbonyl $C_{(2)}$ atom is assigned on the basis of its correlation with the N–CH_2 methylene group protons.

The signal for the amide carbonyl at $C_{(3)}$ was assigned from its correlation with the amide NH proton. The single carbon atom for which no proton correlation was found is the $C_{(3)}$ atom so is attributed by exclusion. The chemical shift of this atom is typical of conjugated systems. The most important HMBC correlations serving as the basis of the assignment are shown in the scheme and the full list is presented in Table 3.

Although it contains the same number of protons, the proton spectrum of the alternative anilide **5** differs markedly in chemical shifts. The signal assignments were made from their multiplicities and by the presence of cross peaks in the COSY spectrum. In the carbon spectrum of this compound the signal for the quinoline ring $C_{(5)}$ atom has a chemical shift of 177.7 ppm which is typical of a conjugated carbonyl group.

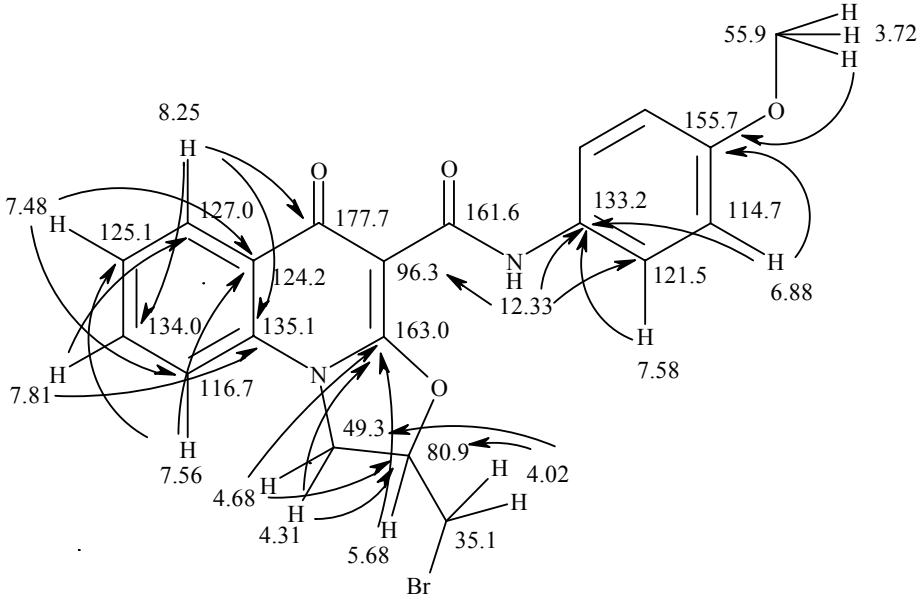


TABLE 4. Full Correlation List Found for the Oxazoloquinolone **5**

Δ, ppm	HMQC	HMBC
12.33	—	96.3; 121.5; 133.2
8.25	127.0	177.7; 135.1; 134.0
7.81	134.0	135.1; 127.0
7.58	121.5	155.7; 133.2; 121.5
7.56	116.7	125.1; 124.2
7.48	125.1	124.2; 116.7
6.88	114.7	155.7; 133.2; 114.7
5.68	80.9	163.0
4.68	49.3	163.0; 80.9; 35.1
4.31	49.3	163.0; 80.9; 35.1
4.02	35.1	80.9; 49.3
3.72	55.9	155.7

The $C_{(2)}$ atom of the oxazolidine ring has a chemical shift of 80.9 ppm which confirms its bonding to an oxygen atom. Assignment of the remaining signals follows from the observed HMBC and HMQC correlations. Hence the assignment of the 124.2 ppm signal to the bridging $C_{(5a)}$ atom follows from the presence of its correlation with atoms H-7 and H-9 and of the signal at 135.1 ppm to the $C_{(9a)}$ atom from its correlation through three bonds to the H-6 and H-8 atoms. The signal for the quinoline $C_{(3a)}$ atom was interpreted through its correlation with the methylene protons on the heterocyclic nitrogen atom and for the $C_{(4)}$ atom from its correlation with the amide NH group proton. The assignment of the signals in the oxazolidine ring also follows securely from the correlations found. Both the methylene protons and the CH proton have a correlation through three bonds with the quinoline $C_{(3a)}$ atom and this possibility is exclusive to a cyclic structure for the compound. It should be noted, however, that the correlation of the proton at 5.68 ppm (atom H-2 of the oxazolidine ring) and the quinoline ring $C_{(3a)}$ is extremely weak. It can only be observed by increasing the mixing time in the pulse sequence to 100 ms. When doing so the correlations with larger spin spin couplings become invisible. The assignments of the remaining signals are given in the scheme and in Table 4. Hence all of the data given agrees with the proposed anilide structures **4** and **5**.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra for the 4-methoxyanilides **4** and **5**, 2D ^{1}H NMR COSY experiments, homonuclear Overhauser effect NOESY-1D, and HMQC and HMBC heteronuclear correlation spectra were recorded on a Varian Mercury-400 (400 MHz) spectrometer (400 and 100 MHz respectively). All of the 2D experiments were carried out with a gradient selection of useful signals. The mixing times in the pulse sequences were $^1J_{CH}$ = 140 and $^{2,3}J_{CH}$ = 8 Hz respectively. The number of increments in the COSY and HMQC spectra was 128 and in the HMBC spectra 400. The mixing time in the NOESY-1D experiment was 500 ms. ^{1}H NMR spectra for the remaining compound were taken on a Varian Mercury VX-200 (200 MHz) instrument. In all cases the solvent was DMSO-d_6 and the internal standard TMS.

2-Bromomethyl-5-oxo-1,2-dihydro-5H-oxazolo[3,2-*a*]quinoline-4-carboxylic acid (**1**) and its ethyl ester **7** were prepared as in the method in [3]. The N,N'-carbonyldiimidazole and anhydrous DMF for peptide synthesis came from the Fluka company.

4-Chloro-1-(2,3-dichloropropyl)-2-oxo-1,2-dihydroquinoline-3-carboxylic Acid 4-Methoxyanilide (4). A mixture of 2-bromomethyl-5-oxo-1,2-dihydro-5H-oxazolo[3,2-*a*]quinoline-4-carboxylic acid (**1**) (3.24 g, 0.01 mol) and $SOCl_2$ (30 ml) was refluxed for 10 h. Excess $SOCl_2$ was distilled off *in vacuo*. The acid chloride **2**

formed was dissolved in dry acetone (15 ml) and the solution obtained was added to a mixture of *p*-anisidine (1.23 g, 0.01 mol) and triethylamine (1.4 ml, 0.01 mol) in dry acetone (20 ml) with cooling and vigorous stirring. After 5 h the reaction mixture was diluted with cold water. The precipitated anilide **4** was filtered off, washed with water, and dried. Yield 3.78 g (86%); mp 188-190ºC (acetone). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 10.42 (1H, s, NH); 8.08 (1H, d, *J* = 8.1, H-5); 7.82 (2H, m, H-7,8); 7.57 (2H, d, *J* = 8.7, H-2',6'); 7.46 (1H, t, *J* = 7.3, H-6); 6.93 (2H, d, *J* = 8.7, H-3',5'); 4.85 (1H, m, NCH); 4.82 (1H, m, $NCH_2C\underline{H}Cl$); 4.71 (1H, m, NCH); 4.00 (2H, m, CH_2Cl); 3.75 (3H, s, OCH_3). ^{13}C NMR spectrum, δ, ppm: 161.2 ($C_{(3)}$=O); 158.9 ($C_{(2)}$=O); 156.3 ($C_{(4')}$); 140.7 ($C_{(4)}$); 139.1 ($C_{(8a)}$); 133.4 ($C_{(7)}$); 132.5 ($C_{(1')}$); 129.6 ($C_{(3)}$); 126.9 ($C_{(5)}$); 124.3 ($C_{(6)}$); 121.4 ($C_{(2',6')}$); 118.4 ($C_{(4a)}$); 116.4 ($C_{(8)}$); 114.7 ($C_{(3',5')}$); 58. ($NCH_2\underline{C}HCl$); 55.9 (OCH_3); 47.2 ($NCH_{2)}$); 36.8 (CH_2Cl). Found, %: C 54.55; H 3.81; N 6.47. $C_{20}H_{17}Cl_3N_2O_3$. Calculated, %: C 54.63; H 3.90; N 6.37.

2-Bromomethyl-5-oxo-1,2-dihydro-5H-oxazolo[3,2-*a*]quinoline-4-carboxylic Acid 4-Methoxy-anilide (5). N,N'-Carbonyldiimidazole (1.62 g, 0.01 mol) was added to a solution of compound **1** (3.24 g, 0.01 mol) in anhydrous DMF (20 ml). The reaction mixture was stirred at 55-60ºC until CO_2 evolution had finished (about 2 h) with protection from atmospheric moisture. *p*-Anisidine (1.23 g, 0.01 mol) was added to the obtained imidazolide **3** and heating was continued for a further 3 h. The cooled reaction mixture was diluted with water. The precipitated anilide **5** was filtered off, washed with water, and dried. Yield 3.90 g (91%); mp 227-229ºC (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 12.33 (1H, s, NH); 8.25 (1H, d, *J* = 7.8, H-6); 7.81 (1H, t, *J* = 7.3, H-8); 7.58 (2H, d, *J* = 8.8, H-2',6'); 7.56 (1H, d, *J* = 8.5, H-9); 7.48 (1H, t, *J* = 7.3, H-7); 6.88 (2H, d, *J* = 8.8, H-3',5'); 5.68 (1H, m, $NCH_2C\underline{H}O$); 4.68 (1H, t, *J* = 9.8, NCH): 4.31 (1H, dd, *J* = 6.6 and 9.7, NCH); 4.02 (2H, m, CH_2Br); 3.72 (3H, s, OCH_3). ^{13}C NMR spectrum, δ, ppm: 177.7 ($C_{(5)}$=O); 163.0 ($C_{(3a)}$); 161.6 ($C_{(4)}$=O); 155.7 ($C_{(4)'}$); 135.1 ($C_{(9a)}$); 134.0 ($C_{(8)}$); 133.2 ($C_{(1')}$); 127.0 ($C_{(6)}$); 125.1 ($C_{(7)}$); 124.2 ($C_{(5a)}$); 121.5 ($C_{(2',6')}$); 116.7 ($C_{(9)}$); 114.7 ($C_{(3',5')}$); 96.3 ($C_{(4)}$); 80.9 ($NCH_2\underline{C}HO$); 55.9 (OCH_3); 49.3 (NCH_2); 35.1 (CH_2Br). Found, %: C 55.84; H 4.10; N 6.46. $C_{20}H_{17}BrN_2O_4$. Calculated, %: C 55.96; H 3.99; N 6.53.

4-Chloro-1-(2,3-dichloropropyl)-2-oxo-1,2-dihydroquinoline-3-carboxylic Acid (6). The obtained acid chloride **2** (see the above synthesis of anilide **4**) was treated with water (20 ml), thoroughly stirred, and left for 2-3 h at room temperature. The acid **6** formed was filtered off, washed with water, and dried. Yield 3.17 g (95%); mp 167-169ºC (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 12.11 (1H, br. s, COOH); 8.03 (1H, d, *J* = 8.0, H-5); 7.81-7.74 (2H, m, H-7,8); 7.44 (1H, t, *J* = 7.7, H-6); 4.90-4.53 (3H, m, NCH_2CH); 4.04 (2H, m, CH_2Cl). Found, %: C 46.76; H 3.13; N 4.10. $C_{13}H_{10}Cl_3NO_3$. Calculated, %: C 46.67; H 3.01; N 4.19.

Ethyl 4-Chloro-1-(2,3-dichloropropyl)-2-oxo-1,2-dihydroquinoline-3-carboxylate (8). A solution of ethyl 2-bromomethyl-5-oxo-1,2-dihydro-5H-oxazolo[3,2-*a*]quinoline-4-carboxylate **7** (3.52 g, 0.01 mol) and $SOCl_2$ (30 ml) was refluxed for 10 h. Excess $SOCl_2$ was distilled off *in vacuo*. The residue was treated with cold water. The precipitated ester **8** was filtered off, washed with water, and dried. Yield 3.26 g (90%); mp 84-86ºC (ether). ^{1}H NMR spectrum, δ, ppm (*J*. Hz): 8.03 (1H, d, *J* = 8.1, H-5); 7.83-7.76 (2H, m, H-7,8); 7.44 (1H, t, *J* = 7.6, H-6); 4.89-4.52 (3H, m, NCH_2CH); 4.34 (2H, q, *J* = 7.2, $COOCH_2$); 4.03 (2H, m, CH_2Cl); 1.29 (3H, t, *J* = 7.0, CH_3). Found, %: C 49.57; H 3.75; N 3.77. $C_{15}H_{14}Cl_3NO_3$. Calculated, %: C 49.68; H 3.89; N 3.86.

X-ray Structural Study. Crystals of the trichloro-substituted ester **8** (from diethyl ether) are triclinic, at 20ºC: *a* = 8.503(1), *b* = 9.109(1), *c* = 11.987(2) Å, α = 68.89(1), β = 79.20(1), γ = 73.48(1)º, *V* = 826.0(2) Å^3, M_r = 362.62, Z = 2, space group $P\bar{1}$, d_{calc} = 1.458 g/cm^3, μ(MoKα) = 0.565 mm^{-1}, *F*(000) = 372. The unit cell parameters and intensities of 7949 reflections (2277 independent, R_{int} = 0.017) were measured on an Xcalibur-3 diffractometer (MoKα, CCD detector, graphite monochromator, ω-scanning, $2\theta_{max}$ = 60º).

The structure was solved by a direct method using the SHELXTL program package [4]. The positions of the hydrogen atoms were revealed from electron density difference synthesis and refined using the *riding* model with $U_{iso} = nU_{eq}$ for a non-hydrogen atom bonded to the given hydrogen (*n* = 1.5 for a methyl group and *n* = 1.2 for remaining hydrogen atoms). The structure was refined using F^2 full matrix least squares analysis in the

anisotropic approximation for non-hydrogen atoms to wR_2 = 0.205 for 4648 reflections (R_1 = 0.075 for 2606 reflections with $F>4\sigma(F)$, S = 0.959). The complete crystallographic information has been placed in the Cambridge structural data bank (reference CCDC 604004). The interatomic distances and valence angles are given in Tables 1 and 2.

REFERENCES

1. I. V. Ukrainets, E. V. Mospanova, and L. V. Sidorenko, *Khim. Geterotsikl. Soedin.*, 1023 (2007). [*Chem. Heterocycl. Comp.*, **43**, 863 (2007)].
2. Yu. V. Zefirov, *Kristallografiya*, **42**, 936 (1997).
3. I. V.Ukrainets, L. V. Sidorenko, O. V. Gorokhova, S. V. Shishkina, and A. V. Turov, *Khim. Geterotsikl. Soedin.*, 736 (2007). [*Chem. Heterocycl. Comp.*, **43**, 617 (2007)].
4. G. M. Sheldrick, *SHELXTL PLUS PC Version. A System of Computer Programs for the Determination of Crystal Structure from X-ray Diffraction Data*, Revision 5.1 (1998).