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4-HYDROXY-2-QUINOLONES. 202*. SYNTHESIS, CHEMICAL AND BIOLOGICAL PROPERTIES OF 4-HYDROXY-6,7-DIMETHOXY-2-OXO-1,2-DIHYDROQUINOLINE-3-CARBOXYLIC ACID ALKYLAMIDES

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In continuation of the search for potential analgesics amongst 4-hydroxyquinol-2-one derivatives we have proposed and carried out a preparative method of synthesis of 4-hydroxy-6,7-dimethoxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid alkylamides. It has been shown that bromination of 4-hydroxy-6,7-dimethoxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid allylamide using an equivalent of molecular bromine occurs with a conventional addition of the halogen to the allyl double bond and not with halocyclization. The results of the study of the analgesic properties of the compounds prepared are presented.

Keywords: 4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxamides, amidation, analgesic activity, bromination.

Pain is one of the most widespread symptoms for which people seek medical advice. Hence, it is not surprising that analgesic agents are one of the most popular types of medicines [2-4]. Nonetheless, the current medicinal arsenal of medications of this pharmacological group are regrettably far from perfect [5-7]. For this reason, the search for substances with the ability to arrest pain and the creation of novel analgesics within contemporary demands of effectiveness and safety is one of the most important tasks of medicinal chemistry.

Pronounced analgesic properties have recently been discovered in 1-allyl-4-hydroxy-6,7-dimethoxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid alkylamides [8]. The chemical modification of these compounds is undoubtedly of interest for development of this new pharmaceutical direction of 4-hydroxy-2-quinolone

*For Communication 201, see [1].

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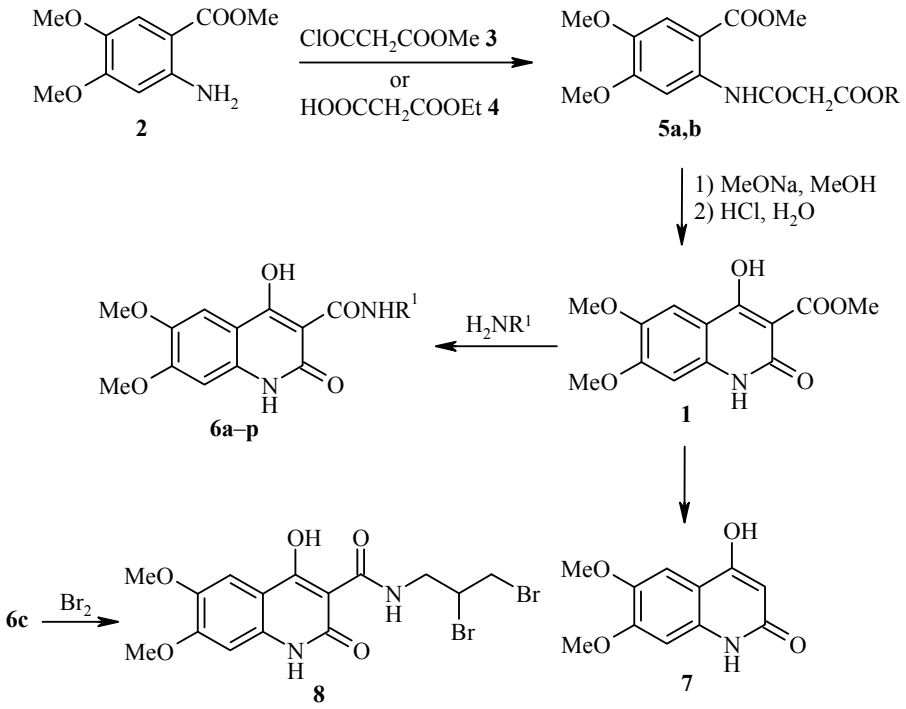
derivatives. At least the results of such a study can provide the structure-activity relationships theoretically important for subsequent research. In the case of good luck (an element of chance is always present in similar studies), it would be quite possible to reveal novel and promising lead structures having practical value in resolving the problems indicated above.

Many variants of the chemical transformation of 1-allyl-4-hydroxy-6,7-dimethoxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid alkylamides can, of course, be proposed. In our view, however, most rationally is to start with the simplest one, namely, with the removal of the 1-*N*-allyl substituent from the basic molecule.

The basis of the whole synthetic scheme is methyl 4-hydroxy-6,7-dimethoxy-2-oxo-1,2-dihydroquinoline-3-carboxylate (**1**), which can be prepared by acylation of the commercially available 4,5-dimethoxymethylanthranilate (**2**) using methyl malonyl chloride (**3**) in the presence of triethylamine or using monoethyl malonate (**4**) in the presence of *N*,*N*'-dicyclohexylcarbodiimide with subsequent heterocyclization of the intermediate anilides **5a,b** under base-catalyzed ester condensation. Immediately it should be noted that the use of sodium methylate in methanol as the main catalyst in the cyclization of ethyl 4,5-dimethoxy-2-[(3-methoxy-3-oxopropanoyl)amino]benzoate (**5b**) causes transesterification. Thus, independently of the acylating agent used, the final reaction product is the same methyl ester **1**. Preference should be given, however, to the monoester **4** since the carbodiimide method ensures not only a higher yield of ester **1**, but also such a high purity (see Experimental) so that no additional purification is needed.



5 a R= Me, **b** R = Et; **6 a** R^1 = Me, **b** R^1 = Et, **c** R^1 = All, **d** R^1 = Pr, **e** R^1 = 2-Pr, **f** R^1 = Bu, **g** R^1 = *i*-Bu, **h** $R^1 = C_5H_{11}$, **i** $R^1 = i\text{-}C_5H_{11}$, **j** $R^1 = C_6H_{13}$, **k** $R^1 = C_7H_{15}$, **l** $R^1 = C_8H_{17}$, **m** $R^1 = C_9H_{19}$, **n** $R^1 = C_{10}H_{21}$, **o** $R^1 = C_{11}H_{23}$, **p** $R^1 = C_{12}H_{25}$

The 4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylates are highly reactive [9, 10], therefore, their conversion to different *N*-R-amides usually does not cause any difficulty. That is why the problems arising upon amidation of the dimethoxy-substituted ester **1** using primary alkylamines appeared to be rather unexpected. Hence, when carrying out the reaction in refluxing DMF (used because of the low solubility of ester **1** in other organic solvents) a significant amount of the 4-hydroxy-6,7-dimethoxy-1*H*-quinolin-2-one (**7**) was found in addition to the target alkylamides **6**. The former was readily identified by the characteristic singlet at 5.59 ppm for the H-3 proton in the ^{1}H NMR spectrum. This was our first experience of such a marked

TABLE 1. Characteristics of Alkylamides **6a-p**

Compound	Empirical formula	Found, % / Calculated, %			Mp, °C (DMF)	Yield, %	Analgesic activity*
		C	H	N			
6a	$C_{13}H_{14}N_2O_5$	56.23 / 56.11	5.15 / 5.07	9.94 / 10.07	323-325	98	18.8
6b	$C_{14}H_{16}N_2O_5$	57.62 / 57.53	5.61 / 5.52	9.47 / 9.58	270-272	96	22.6
6c	$C_{15}H_{16}N_2O_5$	59.32 / 59.21	5.43 / 5.30	9.14 / 9.21	276-278	96	36.5
6d	$C_{15}H_{18}N_2O_5$	58.74 / 58.82	5.81 / 5.92	9.08 / 9.15	281-283	93	60.6
6e	$C_{15}H_{18}N_2O_5$	58.90 / 58.82	5.83 / 5.92	9.26 / 9.15	255-257	88	24.2
6f	$C_{16}H_{20}N_2O_5$	60.11 / 59.99	6.38 / 6.29	8.85 / 8.74	242-244	92	32.9
6g	$C_{16}H_{20}N_2O_5$	60.06 / 59.99	6.35 / 6.29	8.83 / 8.74	280-282	93	28.5
6h	$C_{17}H_{22}N_2O_5$	60.94 / 61.07	6.55 / 6.63	8.30 / 8.38	246-248	90	25.1
6i	$C_{17}H_{22}N_2O_5$	61.15 / 61.07	6.52 / 6.63	8.27 / 8.38	259-261	88	48.1
6j	$C_{18}H_{24}N_2O_5$	62.18 / 62.05	7.01 / 6.94	7.95 / 8.04	243-245	91	14.4
6k	$C_{19}H_{26}N_2O_5$	63.09 / 62.97	7.30 / 7.23	7.84 / 7.73	238-240	85	43.9
6l	$C_{20}H_{28}N_2O_5$	63.72 / 63.81	7.43 / 7.50	7.36 / 7.44	234-236	89	28.5
6m	$C_{21}H_{30}N_2O_5$	64.74 / 64.60	7.85 / 7.74	7.11 / 7.17	230-232	90	32.9
6n	$C_{22}H_{32}N_2O_5$	65.40 / 65.32	8.08 / 7.97	7.02 / 6.93	228-230	86	35.1
6o	$C_{23}H_{34}N_2O_5$	65.94 / 66.01	8.06 / 8.19	6.58 / 6.69	225-227	92	44.3
6p	$C_{24}H_{36}N_2O_5$	66.52 / 66.64	8.30 / 8.39	6.36 / 6.48	222-224	94	41.9
Metamizole sodium		—	—	—	—	—	35.1

* Decrease in the amount of "acetic acid writhing" when compared with control, %.

tendency of 3-alkoxycarbonyl-4-hydroxy-2-oxo-1,2-dihydroquinolines to decomposition under rather mild conditions. It was interesting that the presence in the reaction mixture of the base in the form of alkylamine was not at all necessary for the loss of the carbomethoxy group from ester **1**. It has been found that the decomposition occurs after refluxing in DMF for only a few minutes (two solvents grades were used: the "pure" and the anhydrous for peptide synthesis, i.e. practically free from amines and with the water content not more than 0.02%). It seems doubtful that the effect observed is caused specifically by DMF since a totally similar transformation of ester **1** occurs in refluxing, dry bromobenzene or xylene.

On the basis of these data it is hard to give an unambiguous explanation of the unusual behavior of dimethoxy-substituted ester **1** when heated in high boiling solvents.

This problem arising in the preparation of alkylamides **6c-p** was solved quite simply. The undesirable decomposition of ester **1** to quinolone **7** can be avoided by carrying out the amidation at a lower temperature. In practice, this can be achieved in several ways, e.g. by holding the reaction mixture temperature in the range of 80-100ºC or simply by carrying out the reaction in a refluxing mixture of solvents containing DMF and about 15% methanol.

TABLE 2. ^{1}H NMR Spectra of 4-Hydroxy-6,7-dimethoxy-2-oxo-1,2-dihydroquinoline-3-carboxylic Acid Alkylamides (**6a-p**)

Compound	Chemical shifts, δ, ppm (*J*, Hz)							
	4-OH (1H, s)	1-NH (1H, s)	NH–R (1H)	H Ar		6,7-(OMe)$_2$		R
				H-5 (1H, s)	H-8 (1H, s)	(3H, s)	(3H, s)	
6a	17.13	11.53	10.13 (q, *J* = 4.8)	7.27	6.86	3.84	3.81	2.87 (3H, d, *J* = 4.8, CH_3)
6b	17.15	11.47	10.27 (t, *J* = 5.0)	7.26	6.87	3.84	3.81	3.37 (2H, quin., *J* = 7.1, NCH_2); 1.16 (3H, t, *J* = 7.1, CH_3)
6c	16.89	11.32	10.40 (t, *J* = 5.6)	7.26	6.87	3.84	3.81	5.94 (1H, m, CH); 5.22 (1H, dq, *J* = 17.7, *J* = 1.5, *trans*-NCH_2CH=C$\underline{H}$); 5.14 (1H, dq, *J* = 10.9, *J* = 1.5, *cis*-NCH_2CH=C$\underline{H}$); 3.99 (2H, tt, *J* = 5.6, *J* = 1.5, N$\underline{H}_2$CH=CH_2)
6d	17.14	11.49	10.31 (t, *J* = 5.4)	7.26	6.86	3.84	3.80	3.31 (2H, q, *J* = 6.6, NCH_2); 1.56 (2H, m, $NCH_2C\underline{H}_2$); 0.91 (3H, t, *J* = 7.3, CH_3)
6e	17.13	11.45	10.23 (d, *J* = 7.5)	7.25	6.87	3.84	3.81	4.08 (1H, m, CH); 1.21 (6H, d, *J* = 6.8, $2CH_3$)
6f	17.14	11.49	10.28 (t, *J* = 5.6)	7.27	6.87	3.84	3.81	3.35 (2H, q, *J* = 6.3, NCH_2); 1.55 (2H, quin., *J* = 7.0, $C\underline{H}_2CH_2CH_3$); 1.36 (2H, m, $C\underline{H}_2CH_3$); 0.91 (3H, t, *J* = 7.3, CH_3)
6g	17.12	11.48	10.40 (t, *J* = 5.8)	7.26	6.87	3.83	3.80	3.18 (2H, t, *J* = 6.4, NCH_2); 1.84 (1H, m, CH); 0.92 (6H, d, *J* = 6.8, $2CH_3$)
6h	17.14	11.47	10.29 (t, *J* = 5.8)	7.26	6.87	3.84	3.81	3.33 (2H, q, *J* = 6.5, NCH_2); 1.55 (2H, quin., *J* = 6.8, $NCH_2C\underline{H}_2$); 1.38-1.26 (4H, m, $(C\underline{H}_2)_2CH_3$); 0.87 (3H, t, *J* = 6.8, CH_3)
6i	17.11	11.45	10.28 (t, *J* = 5.7)	7.25	6.86	3.83	3.80	3.36 (2H, q, *J* = 6.8, NCH_2); 1.63 (1H, m, CH); 1.44 (2H, q, *J* = 7.1, $NCH_2C\underline{H}_2$); 0.91 (6H, d, *J* = 6.4, $2CH_3$)
6j	17.14	11.47	10.30 (t, *J* = 5.6)	7.26	6.86	3.84	3.80	3.33 (2H, q, *J* = 6.3, NCH_2); 1.54 (2H, quin., *J* = 6.7, $NCH_2C\underline{H}_2$); 1.36-1.22 (6H, m, $(C\underline{H}_2)_3CH_3$); 0.86 (3H, t, *J* = 6.7, CH_3)
6k	17.14	11.47	10.29 (t, *J* = 5.5)	7.27	6.87	3.84	3.81	3.33 (2H, q, *J* = 6.3, NCH_2); 1.54 (2H, quin., *J* = 6.4, $NCH_2C\underline{H}_2$); 1.36-1.21 (8H, m, $(C\underline{H}_2)_4CH_3$); 0.85 (3H, t, *J* = 6.4, CH_3)
6l	17.14	11.47	10.28 (t, *J* = 5.6)	7.30	6.89	3.85	3.82	3.35 (2H, q, *J* = 6.4, NCH_2); 1.56 (2H, quin., *J* = 6.8, $NCH_2C\underline{H}_2$); 1.35-1.22 (10H, m, $(C\underline{H}_2)_5CH_3$); 0.85 (3H, t, *J* = 6.7, CH_3)
6m	17.15	11.47	10.30 (t, *J* = 5.6)	7.27	6.87	3.84	3.81	3.33 (2H, q, *J* = 6.4, NCH_2); 1.54 (2H, quin., *J* = 6.8, $NCH_2C\underline{H}_2$); 1.32-1.21 (12H, m, $(C\underline{H}_2)_6CH_3$); 0.84 (3H, t, *J* = 6.6, CH_3)
6n	17.15	11.48	10.30 (t, *J* = 5.4)	7.27	6.87	3.84	3.81	3.33 (2H, q, *J* = 6.6, NCH_2); 1.54 (2H, quin., *J* = 6.7, $NCH_2C\underline{H}_2$); 1.31-1.20 (14H, m, $(C\underline{H}_2)_7CH_3$); 0.83 (3H, t, *J* = 6.6, CH_3)
6o	17.15	11.47	10.30 (t, *J* = 5.4)	7.27	6.87	3.84	3.81	3.33 (2H, q, *J* = 6.4, NCH_2); 1.54 (2H, quin., *J* = 6.5, $NCH_2C\underline{H}_2$); 1.30-1.19 (16H, m, $(C\underline{H}_2)_8CH_3$); 0.83 (3H, t, *J* = 6.4, CH_3)
6p	17.15	11.47	10.30 (t, *J* = 5.5)	7.27	6.87	3.84	3.81	3.34 (2H, q, *J* = 6.3, NCH_2); 1.54 (2H, quin., *J* = 6.5, $NCH_2C\underline{H}_2$); 1.30-1.18 (18H, m, $(C\underline{H}_2)_9CH_3$); 0.83 (3H, t, *J* = 6.5, CH_3)

As a result, the target alkylamides **6a-p** can be prepared in high yields and purity (Table 1). They are all colorless, crystalline materials with narrow melting point ranges, being moderately soluble in DMF and DMSO at room temperatures, but virtually insoluble in water. The structure of the compounds synthesized was confirmed by their ^{1}H NMR spectra (Table 2).

Their ability to exist in different tautomeric forms and thus their far from predictable behavior in common reactions served as a stimulus for involving 4-hydroxyquinol-2-ones in various chemical processes. Attention is mostly attracted to reactions, which lead to the effective formation of novel heterocycles. Bromination of 1-*N*- and 3-*C*-allyl-substituted derivatives occurring through halocyclization to oxazolo- [11] or furoquinolones [12], respectively, can be an example. We have attempted to find out how it is reflected in this reaction where the allyl and quinolone fragments are separated by a carbamide group by examining the bromination of 4-hydroxy-6,7-dimethoxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid allylamide (**6c**).

The brown color disappears almost immediately after addition of an equivalent of molecular bromine to the solution of allylamide **6c** in glacial acetic acid. After dilution of the reaction mixture with water, a colorless product has been obtained, which ^{1}H NMR spectrum shows that all of the changes occur exclusively in the allyl part of the molecule. In other words, the presence of the carbamide bridge between the allyl group and the 4-hydroxyquinolin-2-one ring blocks a potential halocyclization reaction. As a result, the bromination occurs just as in the classical addition of a halogen to an olefinic bond and ends with the formation of 4-hydroxy-6,7-dimethoxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid 2,3-dibromopropylamide (**8**).

The analgesic properties of the alkylamides **6a-p** obtained were studied on the standard "acetic acid writhing" test [13, 14] reported by us in detail before [15]. Experiments were carried out on non-pedigree white mice with the weight of 18-23 g by the introduction of the compound orally in the dose of 20 mg/kg. The classical analgesic metamizole sodium [6] was used as a reference drug by the same administration method in the dose of 55 mg/kg (corresponding to the ED_{50} of this compound on the "acetic acid writhing model" [16]).

A comparative analysis of the results of these biological experiments for alkylamides **6a-p** (Table 1) and their allyl-substituted analogs [8] has shown that the removal of the 1-*N*-allyl fragment undertaken by us, quite naturally leads in certain cases to some increase in analgesic effects (amides **6d,i,k,n-p**) and, conversely, in others to their decrease (amides **6a,h**). However, in our opinion, the observation that complete or at least a marked loss of activity has not been recorded in a single case is more interesting. Hence, there is every reason to suggest that a substituent on the quinoline nitrogen atoms has only a weak effect on the analgesic properties of 4-hydroxy-6,7-dimethoxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid amides. Their biological effect depends to a much greater extent on the structure of the *N*-R-amide fragment.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Varian Mercury VX-200 spectrometer (200 MHz) (alkylamides **6a-p**) and on a Varian Mercury-400 spectrometer (400 MHz) (methyl ester **1**). DMSO-d_6 was used as a solvent and TMS as internal standard for all compounds. The analysis of purity of the methyl ester **1** samples prepared by different methods was performed by HPLC on a Waters Alliance 2690 liquid chromatograph with a Waters PAD 996 photodiode array detector. The chromatographic conditions were: Symmetry C8 (Nova Pak C8) column, size 3.9×150 mm, mobile phase flow rate 1 ml/min, column temperature 40ºC, injection volume 20 µl, and detection wavelength 232 nm. The composition of the mobile phase was 65% acetonitrile and 35% aqueous ammonium perchlorate solution (5 ml 70% perchloric acid and 25% ammonia solution to pH 2.5-3.0 per 1 l of the solution).

Methyl 4-Hydroxy-6,7-dimethoxy-2-oxo-1,2-dihydroquinoline-3-carboxylate (1). A. Triethylamine (1.54 ml, 11 mmol) was added to a solution of methyl 2-amino-4,5-dimethoxybenzoate (**2**) (2.11 g, 10 mmol) in CH_2Cl_2 (20 ml). Methyl malonyl chloride (**3**) (1.18 ml, 11 mol) was then added dropwise with cooling and stirring and left at room temperature for 5 h. The reaction mixture was diluted with cold water and vigorously

stirred. The organic layer was separated, dried over $CaCl_2$, and the solvent was distilled off (finally under reduced pressure). The residue of anilide **5a** was treated with a solution of sodium methylate (prepared from metallic sodium (0.69 g, 30 mmol) and absolute MeOH (15 ml)), taken to reflux, and then left for 10-12 h at room temperature. The reaction mixture was diluted with cold water and acidified with diluted HCl (1:1) to pH 4.5-5.0. The precipitated ester **1** was filtered off, washed with water, and dried. Yield 2.23 g (81%). According to HPLC, the content of the main substance in the crude product was 93.2%. Mp after recrystallization from MeOH was 245ºC (decomp.). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 13.94 (1H, s, OH); 11.28 (1H, s, NH); 7.24 (1H, s, H-5); 6.74 (1H, s, H-8); 3.92 (3H, s, OCH_3); 3.89 (3H, s, OCH_3); 3.85 (3H, s, OCH_3). Found, %: C 55.80; H 4.55; N 4.93. $C_{13}H_{13}NO_6$. Calculated, %: C 55.92; H 4.69; N 5.02.

B. Monoethyl malonate (**4**) (1.32 g, 10 mmol) was added dropwise with stirring and cooling to a solution of methyl 2-amino-4,5-dimethoxybenzoate (**2**) (2.11 g, 10 mmol) and *N*,*N*'-dicyclohexylcarbodiimide (2.06 g, 10 mmol) in CH_2Cl_2 (30 ml) and left at room temperature for 6-8 h. The precipitated *N*,*N*'-dicyclohexylurea was removed by filtration and washed on the filter with CH_2Cl_2. The solvent from the filtrate was distilled off on a water bath (finally under reduced pressure). The residue of anilide **5b** was treated with the solution of sodium methylate (prepared from metallic sodium (0.69 g, 30 mmol) and absolute MeOH (15 ml)), taken to reflux, and left for 10-12 h at room temperature. The cooled reaction mixture was diluted with cold water (60 ml). A small amount of *N*,*N*'-dicyclohexylurea admixture remained as an insoluble material. The solution was purified using carbon and filtered. The filtrate was acidified with dilute (1:1) HCl to pH 4.5-5.0. The precipitated ester **1** was filtered off, washed with water, and dried. Yield 2.59 g (93%). The content of the main product was 99.4%.

^{1}H NMR spectra of the samples of methyl ester **1** prepared by different methods were identical.

4-Hydroxy-6,7-dimethoxy-2-oxo-1,2-dihydroquinoline-3-carboxylic Acid Methylamide (6a). A suspension of methyl ester **1** (2.79 g, 0.01 mol) in DMF (20 ml) was saturated with gaseous methylamine (the precipitate was rapidly dissolved) and left at room temperature for 3 h. The reaction mixture was diluted with cold water and acidified with dilute HCl (1:1) to pH 4.5-5.0. The precipitated amide **6a** was filtered off, washed with water, and dried.

Ethylamide 6b was synthesized similarly.

4-Hydroxy-6,7-dimethoxy-2-oxo-1,2-dihydroquinoline-3-carboxylic Acid Alkylamides 6c-p (General Method). The corresponding alkylamine (11 mmol) was added to a mixture of methyl ester **1** (2.79 g, 10 mmol), DMF (30 ml) and MeOH (5 ml) and refluxed for 3 h using a reflux condenser (in the case of the isopropylamine the reaction time was increased to 6 h). The subsequent treatment of the reaction mixture and separation of the final product was carried out as in the procedure for compound **6a**.

4-Hydroxy-6,7-dimethoxy-1*H*-quinolin-2-one (7). A solution of 4-hydroxy-6,7-dimethoxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid [17] (2.65 g, 0.01 mol) in DMF (15 ml) was refluxed until evolution of CO_2 ceased (about 10 min), cooled, and diluted with cold water. The precipitated quinolinone **7** was filtered off, washed with water, and dried. Yield 2.07 g (94%); mp 403-405ºC (DMF–EtOH, 1:5). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 11.11 (1H, s, OH); 10.95 (1H, s, NH); 7.13 (1H, s, H-5); 6.78 (1H, s, H-8); 5.59 (1H, s, H-3); 3.77 (3H, s, OCH_3); 3.75 (3H, s, OCH_3). Found, %: C 59.67; H 4.94; N 6.25. $C_{11}H_{11}NO_4$. Calculated, %: C 59.73; H 5.01; N 6.33.

4-Hydroxy-6,7-dimethoxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid 2,3-Dibromopropylamide (8). A solution of bromine (0.52 ml, 0.01 mol) in glacial acetic acid (5 ml) was added with vigorous stirring to a solution of 4-hydroxy-6,7-dimethoxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acid allylamide (**6c**) (3.04 g, 0.01 mol) in the same solvent (50 ml). The brown color of the bromine disappeared instantly. The reaction mixture was diluted with cold water and the colorless precipitate of 2,3-dibromopropylamide **8** was filtered off, washed with water, and dried. Yield 3.80 g (82%); mp 255-257ºC (DMF). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 16.63 (1H, s, OH); 11.67 (1H, s, NH); 10.65 (1H, t, J = 6.2, $NHCH_2$); 7.25 (1H, s, H-5); 6.87 (1H, s, H-8); 4.64 (1H, m, NCH_2CH); 3.95 (4H, m, $NCH_2CH(Br)CH_2Br$); 3.84 (3H, s, OCH_3); 3.80 (3H, s, OCH_3). Found, %: C 38.73; H 3.35; N 5.91. $C_{15}H_{16}Br_2N_2O_5$. Calculated, %: C 38.82; H 3.47; N 6.04.

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