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Halogenation Reactions in Position 3 of Quinoline-2,4-dione Systems by Electrophilic Substitution and Halogen Exchange [1]

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Summary. 3-Substituted 4-hydroxy-2(1 *H*)-quinolones **3**, **5**, **7** are halogenated with bromine or sulfuryl chloride to yield the quinolinediones **9** or **10**. Reaction of **3**, **5**, **7** with chloroform gives the dichloromethyl quinolinediones **11**. Halogen exchange leads from the chloro quinolinediones **10** to fluoro quinolinedones **12** and to azido quinolinediones **13**. Similarly the dichloro quinolinedione **10 an** reacts to the difluoro quinolinedione **14**, which is reduced to the 3-fluoro-4-hydroxyquinolone **16** and reacts again with sulfuryl chloride to give the mixed 3-chloro-3-fluoroquinolinedione **15**.

Keywords. Fluorination; 4-Hydroxy-2(1 *H*)-quinolones, 3-alkyl/3-aryl/3-fluoro; 1-Hydroxy-benzo[ij] quinolizine-3-ones, 2-alkyl/3-aryl; Quinoline-2,4(1 *H*,3 *H*)-diones, 3-azido-3-alkyl/3aryl, 3-bromo-3-alkyl/3-aryl, 3-chloro-3-alkyl/3-aryl, 3-fluoro-3-alkyl/3-aryl, 3-dichloromethyl-3-alkyl/3-aryl, 3-chloro-3-fluoro.

Halogenierungsreaktionen an der 3-Position von Chinolin-2,4-dion-systemen durch elektrophile Substitution und Halogenaustausch [1]

Zusammenfassung. 3-Substituierte 4-Hydroxy-2-chinolone **3**, **5**, **7** reagieren mit elementarem Brom oder Sulfurylchlorid zu den 3-Halogen-chinolindionen **9** oder **10**. Mit Chloroform reagieren die Hydroxychinolone **3**, **5**, **7** zu den 3-Dichlormethylchinolondionen **11**. Halogenaustausch an **10** führt zu den 3-Fluorchinolindionen **12** und zu 3-Azidochinolindionen **13**. Ähnlich reagiert 3,3-Dichlorochinolindion **10 an** zu 3,3-Fluorchinolindion **14**, das zum 3-Fluor-4-hydroxychinolon **16** reduziert werden kann und in weiterer Folge mit Sulfurylchlorid zum gemischten 3-Chlor-3-fluor-chinolindion **15** reagiert.

Introduction

3,3-Disubstituted quinoline-2,4-dione systems recently have found interest because of their biological activity (e. g. 1-substituted 3,3-diazido-quinolinediones as platelet aggregation inhibitors [2, 3], 3-hydroxy-3-alkylquinoline-2,4-diones as contents of

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bacteria with antibiotic activity [4 – 6]). Therefore 3-haloquinoline-2,4-diones with 3-alkyl- or 3-aryl substituents, which show similar structural properties in their active methylene group, have been synthesized in order to investigate their chemical and biological properties.

The introduction of a halogen atom in position 3 of a quinolinedione can be achieved either by electrophilic substitution at the keto-enol system of 4-hydroxy-2(1 *H*)-quinolones with halogens, or by a nucleophilic halogen exchange at the sp^3 methylene carbon of the 1,3-dicarbonyl system of the quinoline-2,4-dione.

Electrophilic substitution can be effected e. g. by action of gaseous chlorine, which is prepared in situ by reaction of hydrochloric acid and hydrogen peroxide [7]. Electron rich quinolones are chlorinated by this method in the benzo nucleus too, which restricts this method [7]. A simple reaction uses sulfuryl chloride as source of chloronium ions [3, 4, 7 – 9]. Another chlorination method was found by reaction of t-butyloxy chloride with carbocyclic 1,3-dicarbonyl compounds [10]. In most cases the bromination is carried out with bromine in acetic acid [4, 11]. Attention must be paid that excess of bromine and long reaction times again result in further bromination of the benzo part of the quinoline nucleus [4, 11].

The introduction of fluorine by direct electrophilic attack is not so simple. A literature survey reveals many possibilities and reagents to synthesize organo fluoro compounds, but a direct fluorination can be achieved only by elemental fluorine (e. g. in the CH group of dimedon silylether at – 78° in trifluoromethane [12]) or with strong fluorinating agents such as acetyl hypofluorite, N-fluoro sulfonamide or N-fluoro pyrimidinium salts [13, 14]. Alternatively nucleophilic halogen exchange reactions with fluorinating reagents (e. g. quarternary ammonium fluorides [15] or alkali fluorides supported by crown ether catalysis in aprotic dipolar solvents [16]) are described.

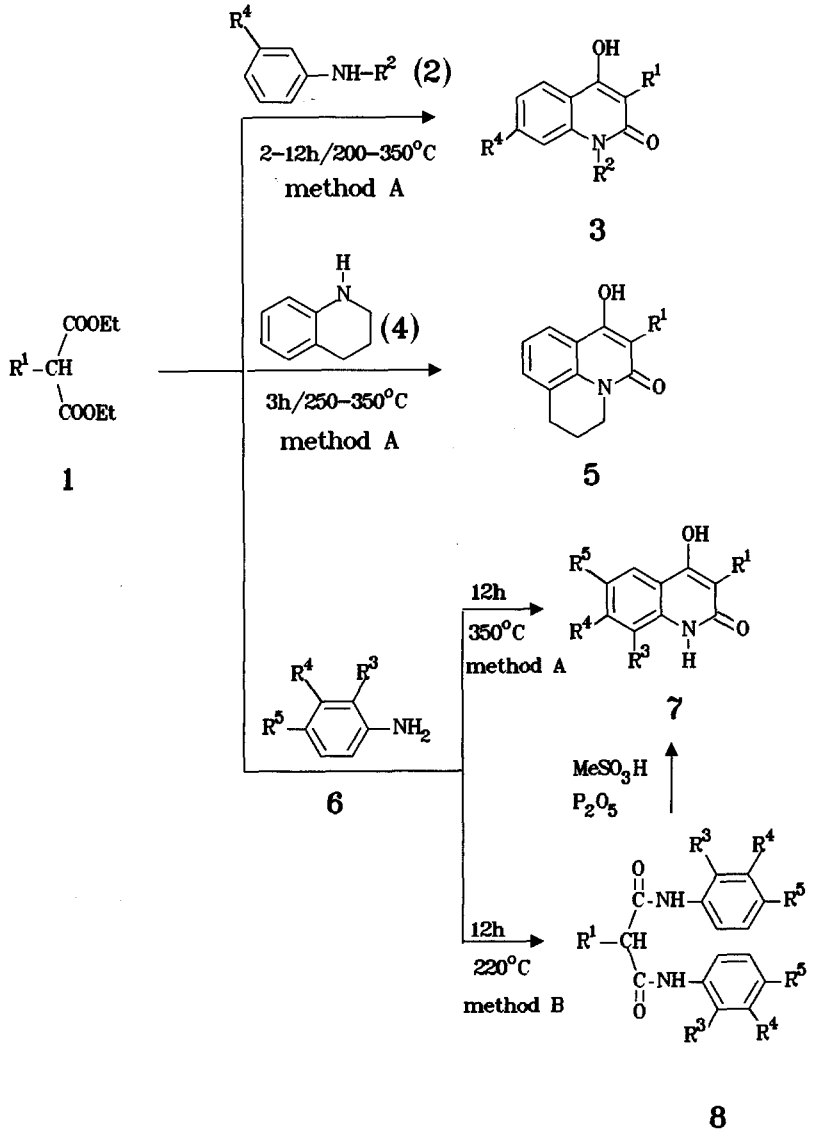
Similar conditions are found in the introduction of the azide anion, which can be considered as pseudo halogen and is known to undergo nucleophilic halogen exchange reactions also in aromatics like dinitro fluorobenzene [17].

In this paper the conditions should be investigated to synthesize azido-, bromo-, chloro- and fluoro derivatives of 3-substituted quinoline-2,4-diones, because some of these showed strong biological activity in preliminary tests.

Results and Discussion

4-Hydroxy-2(1 *H*)-quinolones **3** and **7** and the benzoquinolizinones **5** were synthesized from the substituted malonates **1** and the appropriate anilines **2** or **6**, resp., or 1,2,3,4-tetrahydroquinoline **4** in an 1 : 1 fusion reaction without solvent at temperatures between 250 – 350°C using an adapted literature method [17]. In some cases the ring closure of the intermediate malonesteranilide to the hydroxyquinolone took place only in very low yields, caused by the desactivating influence of chloro- or trifluoromethyl substituents in the benzo part of the anilines and prevented the synthesis of the hydroxyquinolones **7 d**, **e**, **f** and **i** in this way. Alternatively in these cases a two step method was used, where in the first step the malondianilides **8 d**, **e**, **f** and **i** were synthesized from the malonates **1** and the anilines **6 d**, **e**, **f** and **i** in a 1 : 2-ratio at 220°C, which could be cyclized in a second step to the hydroxyquinolones **7 d**, **e**, **f** and **i** at 150°C using phosphorous pentoxide in methanesulfonic acid [18].

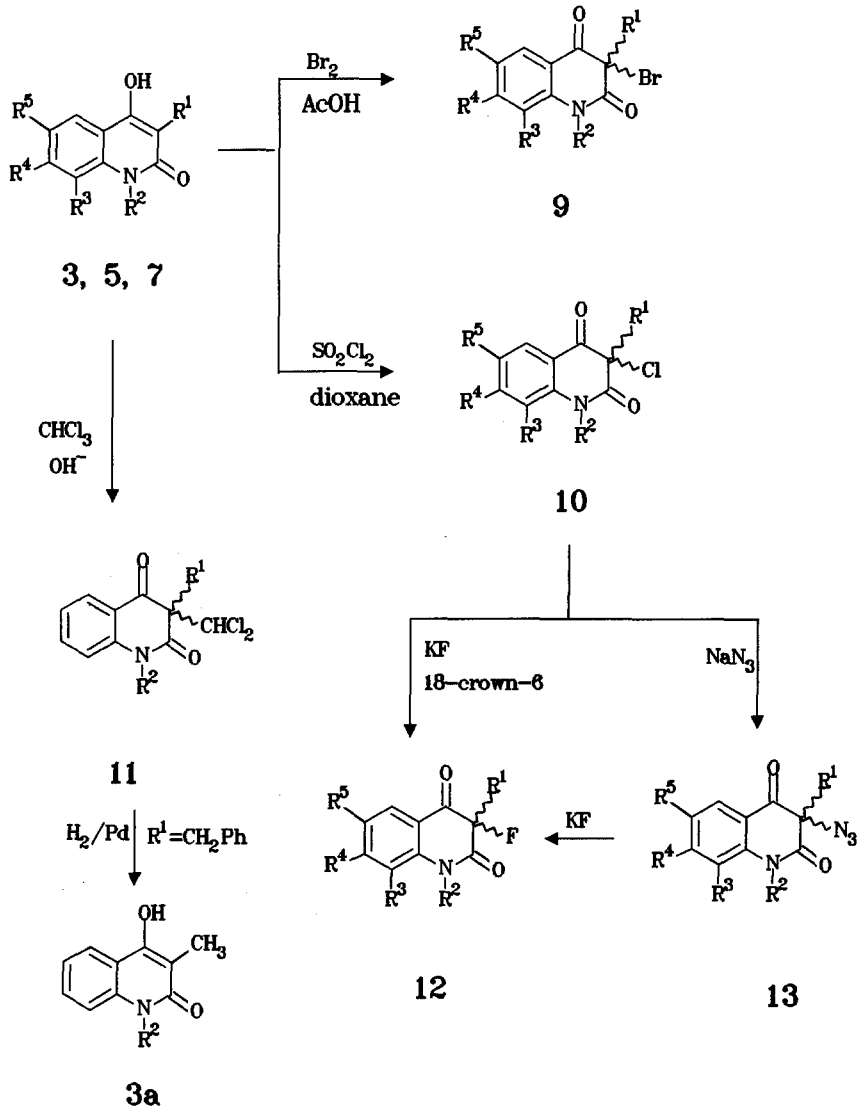
During the work-up of the hydroxyquinolones **3** the crude product is dissolved in sodium hydroxide solution and separated from uncyclized malondianilide and unreacted malonate by extraction with organic solvents. Using chloroform instead of toluene we observed by tlc monitoring that the chloroform layer contained a



Scheme 1 For the R-key of compounds **2**–**8** see Tables 1–4

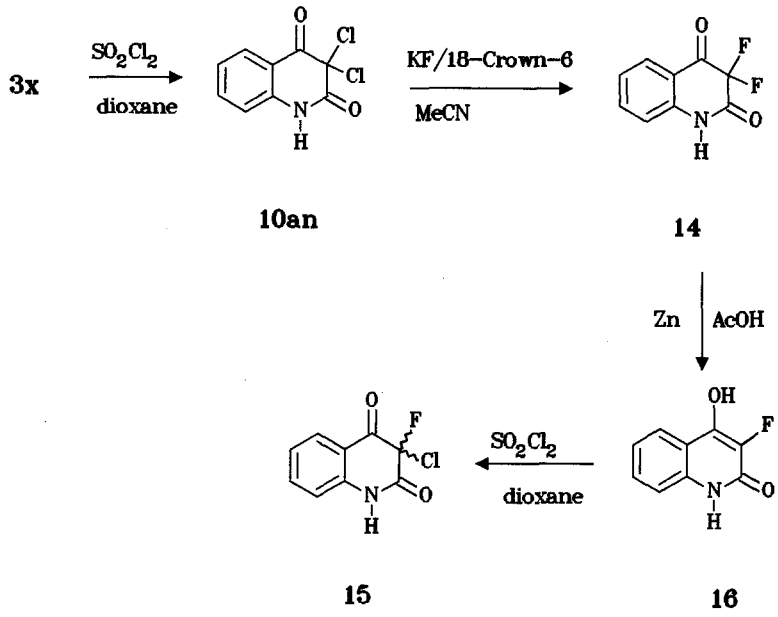
further compound (especially after long contact of the alkaline hydroxyquinolone solution and the chloroform layer) which was not present in the original crude product. The structure of this compound could be assigned to a 3-dichloromethyl quinolinedione **11**, a compound, which could be obtained on a preparative scale with about 40% yield by heating the 4-hydroxyquinolones **3** with aqueous sodium hydroxide solution and chloroform.

This reaction corresponds to the first step of a Reimer-Tiemann reaction. The reason why the reaction stops at the dichloromethyl step and no hydrolysis to the aldehyd occurs, has a simple explanation: in a typical aldehyde synthesis following the Reimer-Tiemann sequence, the primarily formed dichloromethyl compound is dissolved in the alkaline solution because of its phenolic character and can further be hydrolyzed to the aldehyde hydrate. In this way the 3-unsubstituted 4-hydroxy-2(1 *H*)-quinolone reacted to the corresponding 3-formyl-4-hydroxy-2(1 *H*)-quinolone [20]. In our



Scheme 2 For the R-key of compounds **9**–**13** see Tables 5–9

case, however, after dichloromethylation the formed quinolinedione **11** is not further soluble in alkaline solution but is extracted into the chloroform layer and protected against nucleophilic attacks of hydroxide ions. Other dichloromethyl intermediates of the Reimer-Tiemann synthesis have been isolated during the reaction of *p*-cresol and 1-methyl-2-naphthol [21]. Exchange of the chloro groups in **11** against fluoro or azide groups could not be performed because of the lack of the activating effect of the 1,3-dicarbonyl system. Also attempts to hydrolyse **11** showed a remarkable stability against hydroxide anions. In diluted sodium hydroxide solution no reaction took place, higher concentration led to a number of decomposition products which derived from ring opening reactions. Catalytic hydrogenation of the 3-benzyl-quinolinedione **11 a** with palladium in the presence of sodium acetate leads to the 4-hydroxy-3-methyl-2(1 *H*)-quinolone **3 a** by hydrogenolytic loss of the benzyl group and the chloro atoms of the dichloromethyl group. There are a few examples known where a cleavage of the C-C bond in 3,3-disubstituted quinolinediones [22, 23] occurs which show that benzyl groups are cleaved quantitatively, whereas allyl groups are partially reduced to a propyl group. Also



10an **14** **15** **16**

Scheme 3

the role of a basic co-catalyst is important [22]. In our case, the amount of sodium acetate has to be calculated to neutralize also the hydrochloric acid which is set free.

3-Bromo-quinoline-2,4(1 *H*,3 *H*)-diones **9** could be obtained by reaction of the 4-hydroxyquinolones **3**, **5** or **7**, resp., with elemental bromine in acetic acid. It was found that in the case of the methoxy substituted hydroxyquinolones **7j**, **l** only very short reaction times had to be used otherwise further bromination in the benzo part occurred. Nevertheless with the 7-methoxyderivative **7k** in all cases a further bromination took place, and only 3,6-dibromo-7-methoxyquinoline-2,4-dione **9g** was isolated.

The synthesis of the 3-chloro-quinoline-2,4-diones **10** was performed using sulfuryl chloride in a dioxane solution, which gave the best results and a simple isolation of the reaction product. Chloroquinolinediones with alkyl groups in both 1- and 3-position were isolated in most cases as an oil and had to be purified by column chromatography or filtration over silica gel. With the methoxyderivatives **7j**–**l** again the problem of multiple halogenation was observed. Whereas the 6- and 8-methoxyderivatives **7j** and **7l**, resp., at room temperature yielded the 3-monochloro quinolinediones **10aj** and **10am**, the 7-methoxyderivative **7k** reacted at 0°C with sulfuryl chloride to the 3,6-dichloroquinolinedione **10ak**; at 50°C the 3,6,8-trichloroquinolinedione **10al** was formed.

The introduction of a fluoro atom in 3-position of quinolinediones was assumed to be possible in an indirect way by halogen exchange. Among many attempts spray-dried potassium fluoride [19] was found to be an effective fluorinating agent, which led in dry acetonitrile in the presence of 18-crown-6 by exchange of the chloro atom of the quinolinediones **10** to the desired fluoro compounds **12**. In other aprotic solvents (e. g. *DMF*) the formation of **12** could be proved by tlc in small yields, but in most cases large amounts of byproducts were formed, and an isolation

was unsuccessful. Also in acetonitrile the reaction must be performed under dry conditions, otherwise the reaction time is increasing enormously. Use of an excess of crown ether allows to decrease the reaction time, but in this way byproducts are formed by hydrolytic effects, which render the isolation of pure **12** more difficult. In the absence of crown ether in dry acetonitrile, the reaction time increases considerably too.

In a similar way the 3-azidoquinolinediones **13** could be obtained from chloroquinolinediones **10** by reaction with the azide anion in *DMF* as solvent. In this reaction with sodium azide no catalyst is necessary, and the reactions in most cases could be performed at room temperature. The only problem, however, is to determine the end of the reaction, because of the similar tlc R_f-values of the educts **10** and the products **13**. Fluoroquinolinediones **12** too, react with sodium azide by halogen exchange and formation of the azidoquinolinediones **13**.

3,3-Dichloroquinolinedione **10 an**, prepared from 4-hydroxyquinolone (**3 x**) by chlorination with sulfurylchloride [3, 7 – 9], reacts with potassium fluoride and 18-crown-6 to 3,3-difluoroquinolinedione **14**. In this case good yields were obtained after heating for 12 h, whereas the 3-fluoroquinolinediones **12** only required 6 h. By mild reduction with zinc dust in acetic acid one fluoro atom was reduced selectively from the 3-position to yield 3-fluoro-4-hydroxy-2-quinolone **16**, which in turn could be chlorinated again with sulfuryl chloride to the mixed halogenide, the 3-chloro-3-fluoroquinolinedione **15**. Attempts to react 3,3,6- or 3,3,8-trichloroquinolinedione, resp., which are analogous to **10 an**, with potassium fluoride, were not successful: in these cases only decomposition products were obtained.

Halogenation of the 3-position of 3-substituted 4-hydroxyquinolones leads to a center of chirality; a separation into enantiomers was not attempted. In some ^{1}H-NMR spectra two sets of signals of groups adjacent to this center were observed, which can be explained by mixtures of enantiomers. The change from the 4-hydroxy quinolones to the quinolinediones is observed by the appearance of a second carbonyl band in the IR spectrum, where first only a broad amide carbonyl band at 1 640 – 1 660 cm^{-1} is visible, whereas in the spectra of the quinolinediones besides the sharper and intensive amide carbonyl band at about 1 680 cm^{-1} the 4-carbonyl group at 1 720 cm^{-1} appears. The 3-fluoroquinolinediones **12** show in the ^{1}H-NMR spectra an additional fluoro coupling with 3 – 7 Hz. The azidoquinolinediones **13** show a strong azide band around 2 100 cm^{-1}.

Experimental Part

Melting points were obtained on a Gallenkamp melting point apparatus, Mod. MFB-595 (open capillary tubes). IR spectra were recorded on a Perkin-Elmer 298 (KBr-pellets). ^{1}H-NMR- and ^{13}C-NMR spectra were recorded on a Varian Gemini 200 instrument (*TMS* as internal standard, δ-values in ppm, *DMSO-d_6* as solvent unless otherwise stated). Microanalyses werde performed on a C,H,N-Automat Carlo Erba 1106.

General Procedure for the Synthesis of the 1,3-Disubstituted 4-Hydroxy-2(1 H)-quinolones **3** *and* **7** *and the 2-Substituted 1-Hydroxy-5 H-6,7-dihydro-benzo[ij]quinolizin-3-ones* **5**

Method A (Direct Synthesis)

A mixture of the alkyl- or arylmalonates **1** (10 mmol) and the appropriate aniline **2** or **6**, resp., or the 1,2,3,4-tetrahydroquinoline **4** (10 mmol) was heated for 2 – 12 h to 200 – 350°C (time and temperature see Tables 1 – 3), while ethanol was liberated. After cooling, methanol (20 ml) was added to the semicrystalline residue and the product was filtered by suction. The crude hydroxyquinolones

Table 1. Experimental data of 1,3-disubstituted 4-hydroxy-2(1 *H*)-quinolones **3** *(following method A)

No.	R^1	R^2	R^4 Time	Yield (%) Temp.	M. p. (°C) Solvent	Molecular formula[a]
3a	methyl	H	H	Ref. [25]		
3b	methyl	ethyl	H	75	203	$C_{12}H_{13}NO_2$
			12	210	ethanol	203.2
3c	methyl	1-butyl	H	72	182	$C_{14}H_{17}NO_2$
			4	250	ethanol	231.3
3d	ethyl	H	H	Ref. [25]		
3e	ethyl	ethyl	H	74	166	$C_{13}H_{15}NO_2$
			8	250	ethanol	217.3
3f	ethyl	1-butyl	H	67	185	$C_{15}H_{19}NO_2$
			4	250	ethanol	245.3
3g	ethyl	phenyl	H	Ref. [25]		
3h	1-butyl	methyl	H	68	141	$C_{14}H_{17}NO_2$
			12	220	ethanol	231.3
3i	1-butyl	ethyl	H	69	128	$C_{15}H_{19}NO_2$
			4	250	ethanol	245.3
3j	1-butyl	1-butyl	H	74	138-41	$C_{17}H_{23}NO_2$
			4	300	ethanol	273.4
3k	1-butyl	phenyl	H	66	216	$C_{19}H_{14}NO_2$
			8	250	ethanol	288.3
3l	benzyl	H	H	Ref. [25]		
3m	benzyl	ethyl	H	64	228	$C_{18}H_{17}NO_2$
			4	250	ethanol	279.3
3n	benzyl	1-butyl	H	49	182-4	$C_{20}H_{21}NO_2$
			8	250	ethanol	307.4
3o	benzyl	benzyl	H	58	208	$C_{23}H_{19}NO_2$
			12	250	ethanol	341.4
3p	benzyl	phenyl	H	Ref. [25]		
3q	phenyl	H	H	Ref. [18]		
3r	phenyl	methyl	H	Ref. [18]		
3s	phenyl	ethyl	H	44	157	$C_{17}H_{15}NO_2$
			12	300	ethanol	265.3
3t	phenyl	1-butyl	H	68	186-8	$C_{19}H_{19}NO_2$
			12	250	ethanol	293.4
3u	phenyl	phenyl		Ref. [18]		
3v	phenyl	ethyl	methyl	28	163	$C_{18}H_{17}NO_2$
			12	270	ethanol	279.3
3w	ethyl	H	trifluormethyl	31	160 dec.	$C_{12}H_{10}F_3NO_2$
			12	250	*DMF*/H_2O	257.2
3x	H	H	H	Ref. [19]		

[a] satisfactory microanalyses obtained within ±0.4%

were dissolved in sodium hydroxide (0.5 N, 100 ml) and filtered to remove uncyclized malondianilides. The filtrate was extracted with toluene (2 × 100 ml) to remove unreacted malonate and alkaline insoluble byproducts and then cleared with charcoal. The nearly colorless filtrate was acidified with

Table 2. Experimental data of 2-substituted 1-hydroxy-6,7-dihydro-5*H*-benzo[ij]quinolizin-3-ones **5** (following method A)

No.	R^1 Time	Yield (%) Temp.	M. p. (°C) Solvent	Molecular formula[a]
5a	1-butyl	57	153	$C_{16}H_{19}NO_2$
	4	250	ethanol	257.3
5b	ethyl	Ref. [25]		
5c	benzyl	Ref. [25]		
5d	phenyl	Ref. [18]		

[a] satisfactory microanalyses obtained within ±0.4%

Table 3. Experimental data of 4-hydroxy-2(1*H*)-quinolones **7**

No.	R^1 Method	R^3	R^4	R^5 Time	Yield (%) Temp.	M. p. (°C) Solvent	Molecular formula[a]
7a	phenyl	H	H	fluoro	76	320 dec.	$C_{15}H_{10}FNO_2$
	A			1	280	*DMF*/H_2O	255.2
7b	phenyl	H	fluoro	H	89	330	$C_{15}H_{10}FNO_2$
	A			2	300	*DMF*/H_2O	255.2
7c	phenyl	fluoro	H	H	53	236	$C_{15}H_{10}FNO_2$
	A			2	280	*DMF*/H_2O	255.2
7d	phenyl	H	trifluoro-	H	42	220 dec.	$C_{16}H_{10}F_3NO_2$
	B		methyl	12	250	*DMF*/H_2O	305.3
7e	phenyl	H	H	chloro	76	335	$C_{15}H_{10}ClNO_2$
	B			2	280	*DMF*/H_2O	271.7
7f	phenyl	chloro	H	H	85	305 dec.	$C_{15}H_{10}ClNO_2$
	B			2	280	*DMF*/H_2O	271.7
7g	phenyl	H	chloro	chloro	64	290 dec.	$C_{15}H_9Cl_2NO_2$
	A			4	280	*DMF*/H_2O	306.1
7h	phenyl	chloro	chloro	H	90	300 dec.	$C_{15}H_9Cl_2NO_2$
	A			4	280	*DMF*/H_2O	306.1
7i	phenyl	chloro	H	chloro	Ref. [19]		
7j	phenyl	H	H	methoxy	Ref. [26]		
7k	phenyl	H	methoxy	H	Ref. [26]		
7l	phenyl	methoxy	H	H	Ref. [26]		
7m	phenyl	H	H	trifluor-	88	310	$C_{16}H_9FNO_2$
	A			methoxy	250	ethanol	266.3
7n	phenyl	H	H	methyl	Ref. [26]		
7o	phenyl	H	methyl	H	Ref. [26]		

[a] satisfactory microanalyses obtained within ±0.4%

hydrochloric acid (12 *N*, 30 ml), the solid was then isolated by filtration and washed several times with water to separate from sodium chloride. Experimental data: see Tables 1, 2, and 3. Spectral data: see Table 10.

Table 10. Spectral data of the 4-hydroxy-2-(1 *H*)-quinolones **3** and **7**, and 1-hydroxybenzo[ij]quinolizinones **5**

No.	IR (KBr)	^{1}H-NMR (*DMSO-d*$_6$), δ/ppm
3b	3 300-2 800 b, 1 625 m, 1 600 m, 1 570 s	0.8 (t, *J* = 7 Hz, butyl-CH_3), 1.0 – 1.8 (m, 2 butyl-CH_2), 4.2 (q, *J* = 7 Hz, 1-butyl-CH_2), 7.0 – 7.7 (m, 3 *Ar*H), 8.0 (dd, *J* = 2 + 7 Hz, 5-H), 10.1 (s, OH)
3e	3 300-2 850 b, 1 630 s, 1 600 s, 1 580 s	0.7 – 1.1 (m, ethyl-CH_3, butyl-CH_3), 1.2 – 1.8 (m, 2 butyl-CH_2), 2.6 (q, *J* = 7 Hz, ethyl-CH_2), 4.2 (t, *J* = 7 Hz, 1-butyl-CH_2), 7.0 – 7.7 (m, 3 *Ar*H), 8.0 (dd, *J* = 2 + 7 Hz, 5-H), 10.0 (s, OH)
3h	3 400-3 000 b, 2 950 m, 1 630 m, 1 605 s	
3i	3 300-2 860 b, 1 640 sh, 1 630 m, 1 605 m	0.7 – 0.9 (m, butyl-CH_3), 1.1 (t, *J* = 7 Hz, ethyl-CH_3), 1.2-1.5 (m, 2 butyl-CH2), 4.2 (q, ethyl-CH_2), 7.0 – 7.5 (m, 2 *Ar*H), 8.0 (dd, *J* = 2 + 7 Hz, H-5), 9.9 (s, OH)
3j	3 300-3 100 m, 2 900 m, 1 640 m, 1 605 m	0.7 – 1.0 (m, 2 butyl-CH_3), 1.1 – 2.0 (m, 4 butyl-CH_2), 2.4 – 2.8 (t, *J* = 7 Hz, 3-CH_2), 4.0 – 4.3 (t, *J* = 7 Hz, N-CH_2), 7.1 – 7.6 (m, 3 *Ar*-H), 8.0 (dd, *J* = 2 + 7 Hz, 5-H), 10.0 (s, OH)
3k	3 400-3 000 b, 2 950 m, 1 630 m, 1 605 s	
3n	3 300-2 850 m, 1 620 m, 1 600 s, 1 570 s	0.7 – 1.0 (t, *J* = 7 Hz, butyl-CH_3), 1.1 – 1.7 (m, 2 butyl-CH_2), 4.0 (s, benzyl-CH_2), 4.2 (t, N-CH_2), 7.0 – 7.7 (m, 8 *Ar*H), 8.1 (dd, *J* = 2 + 7 Hz, 5-H), 10.4 (s, OH)
3t	3 200-2 800 m, 1 615 sh, 1 610 s, 1 560 s	0.8 (t, *J* = 7 Hz, butyl-CH_3), 1.1 – 1.8 (m, 2 CH_2), 4.1 (t, *J* = 7 Hz, N-CH_2), 7.0 – 7.9 (m, 8 *Ar*H), 8.1 (dd, *J* = 2 + 7 Hz, 5-H)
3w	3 300-2 800 b, 1 640 s, 1 610 s, 1 560 sh	1.0 (t, *J* = 7 Hz, CH_3), 2.5 (q, *J* = 7 Hz, CH_2), 6.8 – 8.2 (m, 3 *Ar*H)
5a	3 400-3 000 b, 2 950 m, 1 630 m, 1 600 m, 1 580 s	
7d	3 200-2 800 b, 1 660 sh, 1 640 m, 1 620 s	
7e	3 300-2 800 m, 1 640 s, 1 605 m	
7m	3 300-2 600 b, 1 640 s, 1 615 s, 1 590 m	7.2 (s, 5 *Ar*H), 7.25 – 7.35 (m, 2 *Ar*H), 7.8 (d, *J* = 2 Hz, H-5)

Table 4. Experimental data of phenylmalondianilides **8**

No.	R^1	R^3	R^4	R^5 Time	Yield (%) Temp.	M. p. (°C) Solvent	Molecular formula[a]
8d	phenyl	H	trifluormethyl	H 2 h	78 250	182 ethanol	$C_{17}H_{12}F_6N_2O_2$ 390.3
8e	phenyl	H	H	chloro	Ref. [19]		
8f	phenyl	chloro	H	H	Ref. [19]		
8i	phenyl	chloro	H	chloro	Ref. [19]		

[a] satisfactory microanalyses obtained within ±0.4%

Table 5. Experimental data of 3-bromo quinoline-2,4(1 *H*,3 *H*)-diones **9**

No.	R^1	R^2	R^3	R^4	R^5	Yield (%) Starting material	M. p. (°C) Solvent	Molecular formula[a]
9a	phenyl	H	H	H	H	78 **3g**	173 ethanol	$C_{15}H_{10}BrNO_2$ 316.2
9b	phenyl	H	H	methyl	H	75 **7n**	196 ethanol	$C_{16}H_{12}BrNO_2$ 330.2
9c	phenyl	H	H	H	methyl	77 **7o**	177 ethanol	$C_{16}H_{12}BrNO_2$ 330 .2
9d	benzyl	ethyl	H	H	H	54 **3m**	86–88 ethanol	$C_{18}H_{16}BrNO_2$ 358 .2
9e	phenyl	H	H	H	methoxy	73 **7j**	160–63 toluene	$C_{16}H_{12}BrNO_3$ 346.2
9f	phenyl	H	methoxy	H	H	79 **7l**	191–92 toluene	$C_{16}H_{12}BrNO_3$ 346.2
9g	phenyl	H	H	methoxy	bromo	68 **7k**	151–55 acetic acid	$C_{18}H_{15}Br_2NO_3$ 453.1

[a] satisfactory microanalyses obtained within ±0.4%

Method B (2-Step Synthesis via the Appropriate Malondianilides **8***)*

Synthesis of the Malondianilides **8**. A mixture of the alkyl- or arylmalonates **1** (10 mmol) and the appropriate substituted anilines **6** was heated for 5 h in an oil bath to 220°C using a short air condenser to remove the liberated ethanol. When the reaction has ended, the melting is cooled, digested subsequently with methanol (20 ml) and petroleum ether (50 ml), the crystal pulp is filtered by suction and recrystallized from the solvents listed in Table 4.

Cyclization of the Dianilides **8** *to the 4-Hydroxy-2-quinolones* **7**. A suspension of the appropriate malondianilides **8** (10 mmol) in 100 ml methanesulfonic acid containing phosphorpentoxide (10%) was heated in an oil bath for 60 min to 150–170°C. After cooling, the mixture was poured on ice and filtered. Work up was performed as described in method A. Experimental data: Table 3. Spectral data: Table 10.

Table 11. Spectral data of the 3-bromoquinoline-2,4(1 *H*,3 *H*)-diones **9**

No.	IR (KBr)	^{1}H-NMR (*DMSO-d_6*), δ/ppm
9c	3200–2850 m, 1705 m, 1665 s, 1615 m	
9e		3.7 (s, OCH_3), 7.0–7.5 (m, 8 *Ar*H), 9.3 (s, NH)
9f		3.8 (s, OCH_3), 6.9–7.5 (m, 8 *Ar*H), 10.0 (s, NH)
9g		3.9 (s, OCH_3), 7.1 (s, 5 *Ar*H), 7.3 (s, 8-H), 7.7 (s, 5-H)

General Procedure for the Synthesis of the 3-Bromo-quinoline-2,4(1 H,3 H)-diones **9**

To a suspension of the hydroxyquinolone **3** or **7**, resp., (20 mmol) in glacial acetic acid (40 ml) at room temperature bromine (1.5 ml = 4.66 g, 29 mmol) is dropped under stirring. The solution obtained is stirred further 10 min, then ice/water (200 ml) is added to give a yellow precipitate, which is filtered. Experimental data: Table 5. Spectral data: Table 11.

General Procedure for the Synthesis of the 3-Chloro-quinoline-2,4(1 H,3 H)-diones **10**

A suspension or solution of the 4-hydroxy-2(1 *H*)-quinolone **3** or **7**, resp., or the 1-hydroxy-benzo[ij]quinolizin-3-one **5** (10 mmol) in dioxane (40 ml) was warmed to 40–50°C and then under vigorous stirring sulfurylchloride (2.0 ml, 24 mmol) was added dropwise, while the temperature should not exceed 60°C. After 10 min stirring the mixture was poured onto ice/water. The oily product was separated from the aqueous layer, subsequently washed with water (100 ml) and then filtered. **10b**, **e**, **g**, and **h** were isolated as oil, dissolved in diethylether (50 ml), dried with sodium sulfate and mixed with silicagel 60 (5 g, 70–230 mesh). After stirring for 10 min at room temperature, the adsorbens was removed by filtration and the solvent removed in vacuo. Experimental data: Table 6. Spectral data: Table 12.

General Procedure for the Synthesis of 3-Dichloromethyl-quinolin-2,4(1 H,3 H)-diones **11**

A solution of the appropriate 4-hydroxyquinolone **3** (0.01 mol) in water (30 ml), ethanol (20 ml) and sodium hydroxide (5 g, 0.125 mol) was treated with chloroform (10 ml) and tetramethylammoniumhydroxide (40%, 0.5 ml). The mixture was heated under reflux for 30 min, then another 15 ml of chloroform was added and the mixture heated again for 30 min. The cooled mixture was diluted with chloroform (50 ml) and water (50 ml), then the layers were separated and the aqueous layer acidified with 2 *N* HCl to yield about 40% of the starting material (**3**). The organic layer was washed with water, cleared with charcoal and after drying with sodium sulfate the solvent was evaporated in vacuo. The residue was triturated with cold methanol and recrystallized from the same solvent. Experimental data: Table 6. Spectral data: Table 13.

General Procedure for the Synthesis of the 3-Fluoro-quinoline-2,4(1 H,3 H)-diones **12**

A suspension of the appropriate 3-chloroquinoline-2,4-dione **10** (3 mmol), 18-crown-6 (0.1 g, 0.4 mmol) and spray-dried potassium fluoride [19] (0.23 g, 4 mmol) in dry acetonitrile (20 ml) was refluxed for 6 h. After cooling the potassium halides were filtered and most of the solvent removed in vacuo. The

Table 6. Experimental data of 3-chloro-quinoline-2,4(1 *H*,3 *H*)-diones **10**

No.	R^1	R^2	R^3	R^4	R^5	Yield (%) Starting material	M. p. (°C) Solvent	Molecular formula[a]
10a	methyl	H	H	H	H	93	172	$C_{10}H_8ClNO_2$
						3a	*Ac*OH/H_2O	209.6
10b	methyl	1-butyl	H	H	H	57	43	$C_{14}H_{16}ClNO_2$
						3c	[b]	265.7
10c	ethyl	H	H	H	H	90	106	$C_{11}H_{10}ClNO_2$
						3d	*Ac*OH/H_2O	223.7
10d	ethyl	ethyl	H	H	H	51	63	$C_{13}H_{14}ClNO_2$
						3e	*Ac*OH/H_2O	251.7
10e	ethyl	1-butyl	H	H	H	68	oil	$C_{15}H_{18}ClNO_2$
						3f	[b]	279.8
10f	ethyl	phenyl	H	H	H	73	163	$C_{17}H_{14}ClNO_2$
						3g	*Ac*OH/H_2O	299.8
10g	1-butyl	ethyl	H	H	H	56	oil	$C_{15}H_{18}ClNO_2$
						3i	[b]	279.8
10h	1-butyl	1-butyl	H	H	H	46	oil	$C_{17}H_{22}ClNO_2$
						3j	[b]	307.8
10i	1-butyl	phenyl	H	H	H	61	126	$C_{19}H_{18}ClNO_2$
						3k	*Et*OH/H_2O	327.8
10j	benzyl	H	H	H	H	97	181	$C_{16}H_{12}ClNO_2$
						3l	*Ac*OH/H_2O	285.7
10k	benzyl	ethyl	H	H	H	64	71	$C_{18}H_{16}ClNO_2$
						3m	*Et*OH/H_2O	313.8
10l	benzyl	1-butyl	H	H	H	71	86	$C_{20}H_{20}ClNO_2$
						3n	*Et*OH/H_2O	341.8
10m	benzyl	benzyl	H	H	H	59	96	$C_{23}H_{18}ClNO_2$
						3o	*Et*OH/H_2O	375.9
10n	benzyl	phenyl	H	H	H	83	121	$C_{22}H_{16}ClNO_2$
						3p	*Ac*OH/H_2O	361.8
10o	phenyl	H	H	H	H	Ref. [7]		
10p	phenyl	methyl	H	H	H	66	154	$C_{16}H_{12}ClNO_2$
						3r	ethanol	285.7
10q	phenyl	ethyl	H	H	H	93	117	$C_{17}H_{14}ClNO_2$
						3s	*Et*OH/H_2O	299.8
10r	phenyl	1-butyl	H	H	H	92	52	$C_{19}H_{18}ClNO_2$
						3t	ethanol	327.8
10s	phenyl	phenyl	H	H	H	Ref. [27]		
10t	ethyl	$-(CH_2)_2-$		H	H	Ref. [3]		
10u	1-butyl	$-(CH_2)_2-$		H	H	Ref. [3]		
10v	benzyl	$-(CH_2)_2-$		H	H	Ref. [25]		
10w	phenyl	$-(CH_2)_2-$		H	H	Ref. [25]		
10aa	phenyl	H	H	H	fluoro	52	179	$C_{15}H_9ClFNO_2$
						7a	*Et*OH	289.7
10ab	phenyl	H	H	fluoro	H	54	159	$C_{15}H_9ClFNO_2$
						7b	*Et*OH	289.7
10ac	phenyl	H	fluoro	H	H	68	164–166	$C_{15}H_9ClFNO_2$
						7c	*Et*OH	289.7

Table 6. *continued*

10 ad	phenyl	H	H	trifluor-methyl	H	39 **7 d**	168 – 170 ligroin	$C_{16}H_9ClF_3NO_2$ 339.7
10 ae	phenyl	H	H	H	chloro	Ref. [3]		
10 af	phenyl	H	chloro	H	H	72 **7 f**	150 – 152 *Et*OH	$C_{15}H_9Cl_2NO_2$ 306.1
10 ag	phenyl	H	H	chloro	chloro	58 **7 g**	244 – 246 *Me*OH	$C_{15}H_8Cl_3NO_2$ 340.9
10 ah	phenyl	H	chloro	chloro	H	79 **7 h**	162 – 164 acetic acid	$C_{15}H_8Cl_3NO_2$ 340.9
10 ai	phenyl	H	chloro	H	chloro	85 **7 i**	156 – 160 *Et*OH	$C_{15}H_8Cl_3NO_2$ 340.9
10 aj	phenyl	H	H	H	methoxy	73 **7 j**	168 – 172 *Et*OH	$C_{16}H_{12}ClNO_3$ 301.7
10 ak	phenyl	H	H	methoxy	chloro	36 **7 k**	236 *Ac*OH	$C_{16}H_{11}Cl_2NO_3$ 336.2
10 al	phenyl	H	chloro	methoxy	chloro	21 **7 k**	198 ligroin	$C_{16}H_{10}Cl_3NO_3$ 370.6
10 am	phenyl	H	methoxy	H	H	77 **7 l**	168 – 172 *Et*OH	$C_{16}H_{12}ClNO_3$ 285.3
10 an	chloro	H	H	H	H	Ref. [7 – 9]		

[a] satisfactory microanalyses obtained within ±0.4%
[b] Purified over silica gel

Table 12. Spectral data of the 3-chloroquinoline-2,4(1 *H*,3 *H*)-diones **10**

No.	IR (KBr)	^{1}H-NMR (*DMSO-d*$_6$), δ/ppm
10 d	2 980 – 2880 w, 1 705 s, 1 670 s, 1 600 s	0.95 (t, *J* = 7 Hz, ethyl-CH_3), 1.2 (t, *J* = 7 Hz, ethyl-CH_3), 2.3 (q, *J* = 7 Hz, 3-ethyl-CH_2), 4.1 (q, *J* = 7 Hz, 1-ethyl-CH_2), 7.3 (dt, *J* = 2 + 7 Hz, 7-H), 7.5 (dd, *J* = 2 + 7 Hz, 8-H), 7.8 (dt, *J* = 2 + 7 Hz, 6-H), 7.95 (dd, *J* = 2 + 7 Hz, 5-H)
10 f	3 080 – 2920 w, 1 710 s, 1 670 s, 1 630 w, 1 600 s	
10 i	2 950 – 2860 w, 1 710 s, 1 680 s, 1 600 s	1.85 s (t, *J* = 7 Hz, CH_3), 1.3 (m, 2 CH_2), 2.3 (q, *J* = 7 Hz, 3-CH_2), 6.4 (d, *J* = 7 Hz, 1 *Ar*H), 7.2 – 7.7 (m, 7 *Ar*H), 8.0 (dd, *J* = 2 + 7 Hz, 5-H)
10 k	3 060 – 2930 w, 1 700 s, 1 670 s, 1 600 s	1.1 (t, *J* = 7 Hz, ethyl-CH_2), 3.7 (d, *J* = 3 Hz, benzyl-CH_2), 4.1 (q, *J* = 7 Hz, ethyl-CH_2), 7.0 – 7.8 (m, 8 *Ar*H), 7.95 (dd, *J* = 2 + 7 Hz, 5-H)

Table 12. *continued*

No.	IR (KBr)	^{1}H-NMR (*DMSO-d_6*), δ/ppm
10l	3080−3020 w, 2980−2850 m, 1720 s, 1685 s, 1650 w, 1620 s, 1590 m	0.5-0.8 (m, CH_3), 1.0−1.6 (m, 2 CH_2), 3.5 (s, benzyl-CH_2), 3.7−4.0 (m, N-CH_2), 6.8−7.6 (m, 8 *Ar*H), 7.9 (dd, *J*=2+7 Hz, 5-H)
10n	1700 m, 1675 s, 1600 m	3.7 (s, CH_2), 6.7 (d, *J*=7 Hz, 1 *Ar*H), 7.05−7.7 (m, 7 *Ar*H), 8.0 (dd, *J*=2+7 Hz, 5-H)
10q	2980 w, 1710 s, 1680 s, 1600 s	
10r	3060 w, 2980−2860 w, 1710 s, 1675 s, 1600 s	
10aa	3300 s, 3080 m, 1740 s, 1700 s, 1630 s	
10ab	3220−2800 b, 1730 m, 1710 m, 1690 m, 1670 m, 1610 s	6.80−7.10 (m, 5-H, 6-H), 7.40 (s, 5 *Ar*H), 7.70−8.05 (m, 8-H), 11.55 (s, NH)
10ac	3200−2800 b, 1715 m, 1680 m, 1625 s	
10ad	3300−2700 b, 1720 m, 1700 s, 1630 m, 1600 m	7.40 (m, 7 *Ar*H), 8.10 (d, *J*=7 Hz, 5-H), 10.10 (s, NH)
10af	3360 s, 3240−3000 b, 1735 s, 1700 s, 1610 s	6.90 (m, 8 *Ar*H), 8.50 (b, NH)
10ag	3240−2900 b, 1725 m, 1700 s, 1610 s	7.30 (s, 6-H), 7.40 (s, 5 *Ar*H), 7.90 (s, 5-H), 11.40 (s, NH)
10ah	3250−3100 b, 1730 m, 1700 s, 1605 s	7.25−7.70 (m, 6 *Ar*H), 7.90 (d, *J*=7 Hz, 5-H), 8.65 (b, NH)
10ai	3350 s, 1730 s, 1700 s, 1595 s	7.35 (s, 5 *Ar*H), 7.6−7.9 (m, 5-H, 7-H)
10aj	3280 s, 1720 m, 1700 m, 1680 s	3.70 (s, OCH_3), 7.00−7.60 (m, 6 *Ar*H), 7.9 (d, *J*=7 Hz, 5-H), 8.65 (b, NH)
10ak	3300−2800 b, 1735 s, 1680 s, 1620 m, 1600 s	3.80 (s, OCH_3), 6.80 (s, 8-H), 7.30 (m, 5 *Ar*H), 7.8 (s, 5-H)
10al	3300−2800 b, 1735 s, 1680 s, 1620 m	4.00 (s, OCH_3), 7.50 (m, 5 *Ar*H), 7.80 (d, *J*=7 Hz, H-5)
10am	3280s, 1700 m, 1680 s	3.70 (s, OCH_3), 7.00−7.60 (m, 8 *Ar*H), 11.20 (s, NH)

Table 13. Spectral data of the 3-dichloromethyl-quinoline-2,4(1 *H*,3 *H*)-diones **11**

No.	IR (KBr)	^{1}H-NMR ($CDCl_3$), δ/ppm
11a	1690s, 1655 s, 1610 m, 1590 m	3.45 (s, CH_2), 6.2 (s, $CHCl_2$), 6.6−7.4 (m, 3 *Ar*H), 6.85 (s, C_6H_5), 7.7 (dd, *J*=2+8 Hz, 1 H, 5-H), 9.7 (s, br, NH)
11b	3100−2980 w, 1700 s, 1680 s, 1610 s	
11c	3280m, 1710 s, 1665 s, 1610 m, 1595 m	6.7 (s, $CHCl_2$), 6.65−7.5 (m, 8 *Ar*H), 7.75 (dd, *J*=2+8 Hz, 1 H, 5-H), 9.9 (s, b, NH)

Table 7. Experimental data of 3-dichloromethyl-quinoline-2,4(1 *H*,3 *H*)-diones **11**

No.	R^1	R^2	Yield (%) Starting material	M. p. (°C) Solvent	Molecular formula[a]
11a	benzyl	H	31 **3l**	171 methanol	$C_{17}H_{13}Cl_2NO_2$ 334.2
11b	phenyl	ethyl	34 **3s**	178 methanol	$C_{18}H_{15}Cl_2NO_2$ 348.2
11c	phenyl	H	36 **3q**	182 methanol	$C_{16}H_{11}Cl_2NO_2$ 320.2

[a] satisfactory microanalyses obtained within ±0.4%

Table 8. Experimental data of 3-fluoro-quinoline-2,4(1 *H*,3 *H*)-diones **12**

No.	R^1	R^2	R^3	R^4	R^5	Yield (%) Starting material	M. p. (°C) Solvent	Molecular formula[a]
12a	ethyl	H	H	H	H	76 **10c**	184 *Et*OH/H_2O	$C_{11}H_{10}FNO_2$ 207.3
12b	ethyl	ethyl	H	H	H	87 **10d**	98 ethanol	$C_{13}H_{14}FNO_2$ 235.3
12c	1-butyl	1-butyl	H	H	H	63 **10h**	62 *Et*OH/H_2O	$C_{17}H_{22}FNO_2$ 291.3
12d	benzyl	H	H	H	H	65 **10j**	193 *Me*OH/H_2O	$C_{16}H_{12}FNO_2$ 269.3
12e	benzyl	phenyl	H	H	H	68 **10n**	128 *Me*OH/H_2O	$C_{22}H_{16}FNO_2$ 345.4
12f	benzyl	ethyl	H	H	H	56 **10k**	125 *Me*OH/H_2O	$C_{18}H_{16}FNO_2$ 297.3
12g	benzyl	1-butyl	H	H	H	52 **10l**	120 *Me*OH/H_2O	$C_{20}H_{20}FNO_2$ 325.4
12h	phenyl	H	H	H	H	76 **10o**	196 ethanol	$C_{15}H_{10}FNO_2$ 255.2
12i	phenyl	methyl	H	H	H	86 **10p**	175 methanol	$C_{16}H_{12}FNO_2$ 269.3
12j	phenyl	ethyl	H	H	H	91 **10q**	175 *Me*OH/H_2O	$C_{17}H_{14}FNO_2$ 283.3
12k	phenyl	1-butyl	H	H	H	92 **10r**	112 ethanol	$C_{19}H_{18}FNO_2$ 311.3
12l	phenyl	phenyl	H	H	H	81 **10s**	198 methanol	$C_{21}H_{14}FNO_2$ 331.3
12m	ethyl	$-(CH_2)_3-$		H	H	65 **10t**	126 *Et*OH/H_2O	$C_{14}H_{14}FNO_2$ 247.3
12n	1-butyl	$-(CH_2)_3-$		H	H	77 **10u**	200−3 methanol	$C_{16}H_{18}FNO_2$ 275.2
12o	phenyl	H	H	H	fluoro	77 **10aa**	242−44 ethanol	$C_{15}H_9F_2NO_2$ 273.2

Table 8. *continued*

No.	R^1	R^2	R^3	R^4	R^5	Yield (%) Starting material	M. p. (°C) Solvent	Molecular formula[a]
12p	phenyl	H	H	fluoro	H	78 **10ab**	222–26 ethanol	$C_{15}H_9F_2NO_2$ 273.2
12q	phenyl	H	fluoro	H	H	71 **10ac**	226–29 ethanol	$C_{15}H_9F_2NO_2$ 273.2
12r	phenyl	H	H	trifluoro-methyl	H	46 **10ad**	214–15 ethanol	$C_{16}H_9F_4NO_2$ 323.2
12s	phenyl	H	H	H	chloro	74 **10ae**	270–72 acetic acid	$C_{15}H_9ClFNO_2$ 289.7
12t	phenyl	H	chloro	H	H	50 **10af**	160–62 ethanol	$C_{15}H_9ClFNO_2$ 289.7
12u	phenyl	H	H	chloro	chloro	75 **10ag**	264–66 acetic acid	$C_{15}H_8Cl_2FNO_2$ 324.1
12v	phenyl	H	chloro	chloro	H	67 **10ah**	208–210 ethanol	$C_{15}H_8Cl_2FNO_2$ 324.1
12w	phenyl	H	H	H	methoxy	98 **10aj**	248–50 acetic acid	$C_{16}H_{12}FNO_3$ 285.3
12x	phenyl	H	H	methoxy	chloro	78 **10ak**	250–53 acetic acid	$C_{16}H_{11}ClFNO_3$ 319.7
12y	phenyl	H	chloro	methoxy	H	72 **10al**	249–53 toluene	$C_{16}H_{10}ClFNO_3$ 319.7
12z	phenyl	H	methoxy	H	H	98 **10am**	229–30 acetic acid	$C_{16}H_{12}FNO_3$ 285.3

[a] satisfactory microanalyses obtained within ±0.4%

Table 14. Spectral data of the 3-fluoroquinoline-2,4(1 *H*,3 *H*)-diones **12**

No.	IR (KBr)	^{1}H-NMR (*DMSO-d*$_6$), δ/ppm ^{13}C-NMR (*DMSO-d*$_6$), δ/ppm
12a	3250–2870 m, 1710 m, 1680 s, 1610 m, 1600 m	0.8 (t, J=7 Hz, CH_3), 2.1–2.3 (m, 2H, CH_2), 6.9–7.2 (m, 2*Ar*H), 7.4–7.6 (m, 1*Ar*H), 7.8 (dd, J=2+7 Hz, 5-H), 11.1 (s, NH)
12b	2980 w, 1710 s, 1690 sh, 1675 s, 1600 m	0.95 (t, J, =7 Hz, 3-ethyl-CH_3), 1.3 (t, J=7 Hz, N-ethyl-CH_3), 1.85–2.35 (m, 3-ethyl-CH_2), 3.9–4.2 (m, N-ethyl-CH_2), 7.1–7.3 (m, 2*Ar*H), 7.6–7.8 (m, 1*Ar*H), 7.95 (dd, J=2+7 Hz, 5-H)
12c	2960–2860 s, 1710 s, 1680 s, 1600 s	0.5–0.95 (m, 2 CH_3), 1.0–1.8 (m, 4 CH_2), 1.8–2.2 (m, CH_2), 3.8 (q, J=7 Hz, N-CH_2), 7.0–7.4 (m, 2*Ar*H), 7.5–7.8 (m, 2*Ar*H)

Table 14. *continued*

12d	3200–2920 w, 1705 m, 1670 s, 1615 w, 1600 m	3.22+3.35 (2d, J=3 Hz, CH_2), 7.0–7.3 (m, 7*Ar*H), 7.6 (dd, J=2+7 Hz, 7-H), 7.8 (dd, J=2+7 Hz, 5-H), 11.1 (s, NH)
12e	3050–2980 w, 1720 s, 1695 m, 1600 m	3.37 und 3.52 (2d, J=7 Hz, CH_2), 7.05-7.7 (m, 13*Ar*H), 7.85 (dd, J=2+7 Hz, 5-H)
12f		0.9 (t, J=7 Hz, CH_3), 1.25–1.6 (m, 2 CH_2), 3.2+3.35 (2d, J=3 Hz, CH_2), 3.7–4.1 (m, N-CH_2), 6.9–7.0 (m, 2*Ar*H), 7.1–7.4 (m, 5*Ar*H), 7.65–7.8 (m, 2*Ar*H)
12g	2980–2850 w, 1705 s, 1670 s, 1600 s	0.85–1.1 (m, CH_3), 1.3–1.7 (m, 2 CH_2), 3.15+3.45 (2d, J=3 Hz, CH_2), 3.6–4.0 (m, N-CH_2), 6.9–7.4 (m, 7*Ar*H), 7.55–7.8 (m, 2*Ar*H)
12h	3280–3080 m, 1730 w, 1710 s, 1695 sh, 1675 m, 1615 m, 1595 m	
12k	2980 m, 2930 w, 2870 w, 1715 s, 1680 s, 1600 s	
12l	1715 s, 1680 s, 1600 s	6.5–6.7 (m, 8-H), 7.0–7.6 (m, 12*Ar*H), 8.0 (dd, J=2+7 Hz, 5-H). ^{13}C-NMR: 95.3 (C-3), 116.2 (8-C), 119–129 (*Ar*yl-C), 132.1 (1-C von 3-Phenyl), 136.2 (1-C von 1-Phenyl), 142.5 (8aC), 165.8 (2-C=O), 197.5 (4-C=O)
12o	3250 b, 1750 m, 1725 s, 1705 s, 1680 m, 1630 m	
12p	3200–2890 b, 1715 s, 1690 s, 1630 s, 1600 m	
12q	3240–2900 b, 1725 m, 1700 s, 1630 m	
12s	3240 s, 1745 s, 1720 s, 1695 s, 1670 m, 1610 s	
12t	3360 s, 1745 s, 1695 s, 1605 s	
12u	3200–2860 b, 1715 s, 1695 s, 1605 s	
12v	3220–302 b, 1725 s, 1690 s, 1610 s	
12w	3215 b, 1730 s, 1710 s, 1680 s, 1615 m	3.70 (s, OCH_3), 7.00–7.20 (m, 2*Ar*H), 7.40 (m, 6*Ar*H)
12x	3200–2900 b, 1715 s, 1680 s, 1615 s	
12y	3200 b, 1720 s, 1670 s, 1600 s	3.90 (s, OCH_3), 7.1 (d, J=7 Hz, H-6), 7.75 (d, J=7 Hz, H-5)
12z	3300–2900 b, 1720 s, 1685 s, 1615 m, 1595 m	3.75 (s, OCH_3), 7.00-7.20 (m, 2*Ar*H), 7.3 (m, 6*Ar*H), 10.40 (s, b, NH)

Table 9. Experimental data of 3-azido-quinoline-2,4(1 *H*,3 *H*)-diones **13**

No.	R^1	R^2	R^3	R^4	R^5	Yield (%) Starting material	M. p. (°C) Solvent	Molecular formula[a]
13a	ethyl	H	H	H	H	95 **10c**	115–17 cyclohexane	$C_{11}H_{10}N_4O_2$ 230.2
13b	ethyl	ethyl	H	H	H	59 **10d**	98 cyclohexane	$C_{13}H_{14}N_4O_2$ 258.3
13c	1-butyl	phenyl	H	H	H	65 **10i**	186 cyclohexane	$C_{19}H_{18}N_4O_2$ 334.4
13d	benzyl	H	H	H	H	89 **10j**	151 benzene	$C_{16}H_{12}N_4O_2$ 292.3
13e	phenyl	H	H	H	H	98 **10o**	169 toluene	$C_{15}H_{10}N_4O_2$ 278.3
13f	phenyl	methyl	H	H	H	55 **10p**	128 toluene	$C_{16}H_{12}N_4O_2$ 292.3
13g	phenyl	ethyl	H	H	H	67 **10q**	118–120 toluene	$C_{17}H_{14}N_4O_2$ 306.3
13h	phenyl	phenyl	H	H	H	93 **10s**	132–33 cyclohexane	$C_{21}H_{14}N_4O_2$ 345.3
13i	phenyl	H	H	H	chloro	92 **10ae**	177 cyclohexane	$C_{15}H_9ClN_4O_2$ 312.7
13j	phenyl	H	chloro	H	H	84 **10af**	182–84 toluene	$C_{15}H_9ClN_4O_2$ 312.7
13k	phenyl	H	H	H	methoxy	79 **10aj**	182–183 ethanol	$C_{16}H_{12}N_4O_3$ 308.3
13l	phenyl	H	H	methoxy	chloro	66 **10ak**	220 acetic acid	$C_{16}H_{11}ClN_4O_3$ 342.7
13m	phenyl	H	chloro	methoxy	chloro	57 **10al**	160 acetic acid	$C_{16}H_{10}Cl_2N_4O_3$ 376.2
13n	1-butyl	$-(CH_2)_3-$		H	H	67 **10u**	86 ethanol	$C_{16}H_{18}N_4O_2$ 298.3
13o	benzyl	$-(CH_2)_3-$		H	H	90 **10v**	93–95 cyclohexane	$C_{19}H_{16}N_4O_2$ 332.3
13p	phenyl	$-(CH2)_3-$		H	H	93 **10w**	96 benzene	$C_{18}H_{14}N_4O_2$ 318.3

[a] satisfactory microanalyses obtained within ±0.4%

residue was triturated with water (100 ml), stirred for 1 h and then filtered by suction. Experimental data: Table 8. Spectral data: Table 14.

General Procedure for the Synthesis of 3-Azido-quinolin-2,4(1 H,3 H)-diones **13**

A solution of the corresponding dichloro quinolinedione **10** (3 mmol) in dimethyl formamide (30 ml) was treated with sodium azide (0.3 g, 4.5 mol) in portions under ice cooling. The suspension was stirred for 1 h at 20°C, then diluted with ice/water (100 ml) and the resulting crystalline precipitate was filtered, washed with water and dried under vacuum at room temperature. Experimental data: Table 9. Spectral data: Table 15.

Table 15. Spectral data of the 3-azido-quinoline-2,4-(1 *H*,3 *H*)-diones **13**

No.	IR (KBr)
13a	3200 – 2880 w, 20 s, 1705 m, 1675 s, 1615 m, 1620 w
13b	2980 – 2880 w, 2105 s, 1710 s, 1670 s, 1600 s
13c	2960 – 2870 w, 2120 s, 1715 s, 1680 s, 1600 s
13d	3210 – 2920 b, 2110 s, 1760 w, 1705 s, 1680 s, 1610 m
13e	3150 – 2950 b, 2110 s, 1710 s, 1680 s, 1610 m
13f	2100 s, 1710 s, 1670 s, 1600 s
13g	2980 w, 2100 s, 1705 s, 1670 m, 1600 m
13h	2100 s, 1715 s, 1685 s, 1600 s
13i	3310 m, 2100 s, 1715 s, 1690 s, 1610 s
13j	3320 m, 2100 s, 1710 s, 1685 s, 1600 s
13k	3200 – 2920 m, 2120 s, 1710 m, 1670 s, 1625 w
13l	3200 – 2850 m, 2215 s, 1715 s, 1670 s, 1615 m
13m	3300 – 3080 m, 2120 s, 1730 m, 1690 s, 1600 m
13n	2960 – 2880 m, 2120 s, 2100 sh, 1705 s, 1665 s, 1590 s
13o	2929 s, 2100 s, 1690 s, 1650 s
13p	2100 s, 1705 s, 1670 s, 1595 s

3,3-Difluoro-quinolin-2,4(1 H,3 H)-dione (**14**)

A solution of the dichloroquinolinedione **10an** (18.4 g, 0.08 mol), spray-dried potassium fluoride [19] (13.9 g, 0.24 mol) and 18-crown-6 (0.5 g, 2 mmol) in dry acetonitrile (100 ml) was heated under reflux for 12 h. The solvent was removed in vacuo, the residue was treated with a small amount of icecold water to remove the excess of potassium fluoride, the formed potassium chloride and the crown ether, and then was filtered. Yield: 12.6 g (80%), dark yellow prisms, m. p. 156 – 158°C (ligroin). ^{13}C-NMR ($CDCl_3$): δ = 78.5 (3-CF_2), 118 – 142 (*Ar*-C), 162 (amide-C=O), 184 (4-C=O). $C_9H_5F_2NO_2$ (197.1): calcd. C 54.83, H 2.55, N 7.10; found C 54.90, H 2.59, N 7.01.

3-Chloro-3-fluoro-quinoline-2,4(1 H,3 H)-dione (**15**)

To a solution of 3-fluoro-4-hydroxyquinolone (**16**) (0.72 g, 4 mmol) in dioxane (10 ml), sulfurylchloride (0.4 ml, 4.9 mmol) was added slowly at room temperature. After the end of the exothermic reaction (about 10 min) the mixture was poured into ice/water (100 ml) and the resulting precipitate filtered by suction. Yield: 0.50 g (59%) yellow prisms, m. p. 194 – 195°C (toluene). IR: 3 250-2 920 m, 1 735 s, 1 700 s, 1 610 s. ^{1}H-NMR: δ = 6.9 – 7.1 (m, 2 *Ar*H), 7.5 (dd, *J* = 2 + 7 Hz, 1 *Ar*H), 7.8 (dd, *J* = 2 + 7 Hz, 1 H, 5-H), 11.5 (s, b, NH). ^{13}C-NMR: δ = 77 (CClF), 115 – 143 (*Ar*-C), 156 (amide-C=O), 175 (4-C=O). $C_9H_5ClFNO_2$ (213.6): calcd. C 50.60, H 2.31, N 6.55; found C 50.79, H 2.38, N 6.42.

3-Fluoro-4-hydroxy-2(1 H)-quinolone (**16**)

A hot solution of the difluoroquinolinedione **14** (1.0 g, 5 mmol) in glacial acetic acid (50 ml) was treated with zinc dust until the solution was decolorized. Then the hot solution was filtered from the insoluble residue, the resulting solution treated with water (100 ml) and the formed precipitate filtered by suction. Yield: 0.65 g (73%) pale yellowish needles, m. p. 281 – 282°C (ethanol). IR: 3 250 – 2 600 m, 1 650 s, 1 610 s. ^{1}H-NMR: δ = 7.2 – 7.6 (m, 3 *Ar*H), 8.0 (dd, *J* = 2 + 7 Hz, 1 H, 5-H), 11.7 (s, b, NH). $C_9H_6FNO_2$ (179.1): calcd. C 60.34, H 3.37, N 7.81; found C 60.42, H 3.44, N 7.70.

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