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Nucleophilic Chlorination of 3-Formyl-4-hydroxy-quinolin-2(1H)-ones

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Abstract. Chlorination of 1-substituted 3-formyl-4-hydroxy-2-quinolones (**1a, b**) with phosphorylchloride leads to 4-chloro-3-dichloromethylquinolones (**2**), which can be hydrolyzed to 4-chloro-3-formylquinolones (**4**). From the anilinomethylene quinolinediones (**3**), at low temperatures the formylquinolones **4** can be obtained directly, whereas at high temperatures cleavage of the tautomeric azomethine moiety followed by subsequent ring closure to the naphthyridines (**7**) takes place. With 1-unsubstituted 3-formyl-4-hydroxy-2-quinolones (**1d**) either the 3-dichloromethylquinolone (**2d**) or the 2,4-dichloro-3-dichloromethylquinoline (**10**) is obtained depending on the reaction conditions. Similar results are obtained with the 1-unsubstituted anilinomethylene compounds (**3**). Attempts to obtain the 3-formyl-2,4-dichloroquinoline (**11**) were unsuccessful because in all experiments the 2-chloro-group was converted to an oxygen function.

Quinoline- and benzopyran-3-carbaldehydes having chloro atoms in position 2 or 4 have been investigated during the last years [1], used as first step for ring closure reactions [2], or have been studied because of their biological activity [3].

In the course of our investigations of the ring closure reactions of 3-acylquinolines having ortho-azido substituents [2c, 4] we found that 4-hydroxy-2-quinolones, which were chosen as starting materials for azido-formylquinolines, could not be formylated and chlorinated using the Vilsmeier formylation as shown in the coumarin chemistry [1a, 2a, 3a]. Kinetic experiments showed, that in the quinolone series the chlorination in position 4 proceeded more rapidly than the introduction of the 3-formyl group and the resulting intermediate 4-chloroquinolone did not react in terms of a Vilsmeier reaction. Known one step procedures for **1** [5] by using a Reimer-Tiemann synthesis are working with very low yields (less than 40 %).

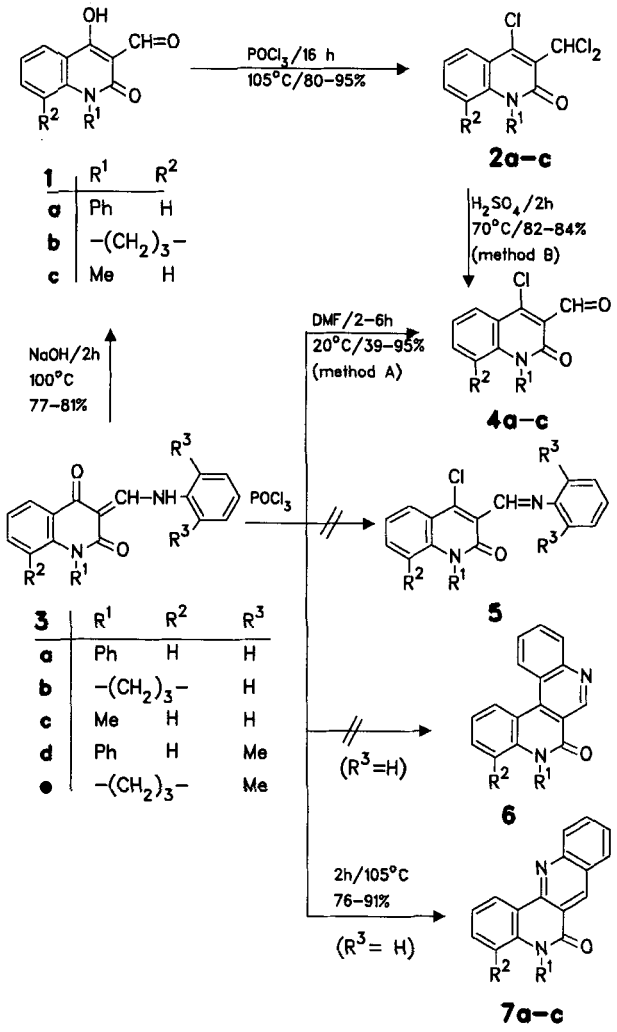
Results and Discussion

Our synthetic approach to chlorinated quinoline-3-carbaldehydes started from the aryl-aminomethylene quinolinediones **3** bearing a tautomerized azomethine moiety, which were hydrolyzed to the corresponding 3-formyl-4-hydroxyquinolones **1** by using an improved literature method [6] in overall yields of more than 70 %. Chlorination of the aldehydes **1** with phosphoryl chloride which is known to substitute hydroxy groups by a nucleophilic displacement reaction did not stop at the desired 4-chloro-3-formyl intermediates **4**, but reacted in a further halogenation step to give the 3-dichloromethyl quinolones **2**. Acid catalyzed hydrolysis of **2** yielded in turn the 4-chloro-3-formylquinolones **4a – c**.

Fruitless attempts to synthesize 4-chloro-quinoline-3-azomethines **5** for further ring closure experiments [4c] resulted in a much quicker procedure for the desired 4-chloro-3-formylquinolones **4** by reacting the phenylaminomethylene quinolinediones **3** directly with phosphorylchloride in DMF at room temperature without preparing the intermediate carbaldehyde **1**. In this case the 4-chloro-3-formylquinolones **4a – c** were obtained in a one step reaction in good yields.

Using higher reaction temperatures furnished in the case of the phenylaminomethylene compounds **3a – c** with no substituent at the phenylamino moiety (R^3 = H) in moderate yields a compound which derived from **3a – c** by elimination of water. The structure of these cyclization products could be shown to correspond with **7a – c**.

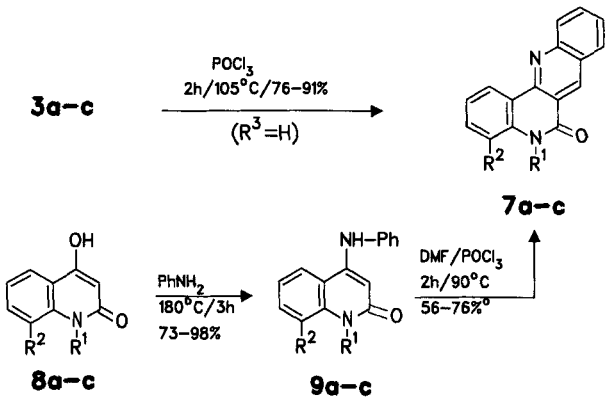
The expected structure of these cyclized products was a dibenzo[c,f][2,7]naphthyridinone **6**. Because the spectral data were not unequivocal, isomeric dibenzo[b,h][1,6]naphthyridinones **7** were prepared to check the possibility of the formation of these compounds. They were obtained by amination of the 4-hydroxyquinolones **8a – c** with aniline according to ref.



1	R^1	R^2
a	Ph	H
b	$-(CH_2)_3-$	
c	Me	H

3	R^1	R^2	R^3
a	Ph	H	H
b	$-(CH_2)_3-$		H
c	Me	H	H
d	Ph	H	Me
e	$-(CH_2)_3-$		Me

Scheme 1



Scheme 2

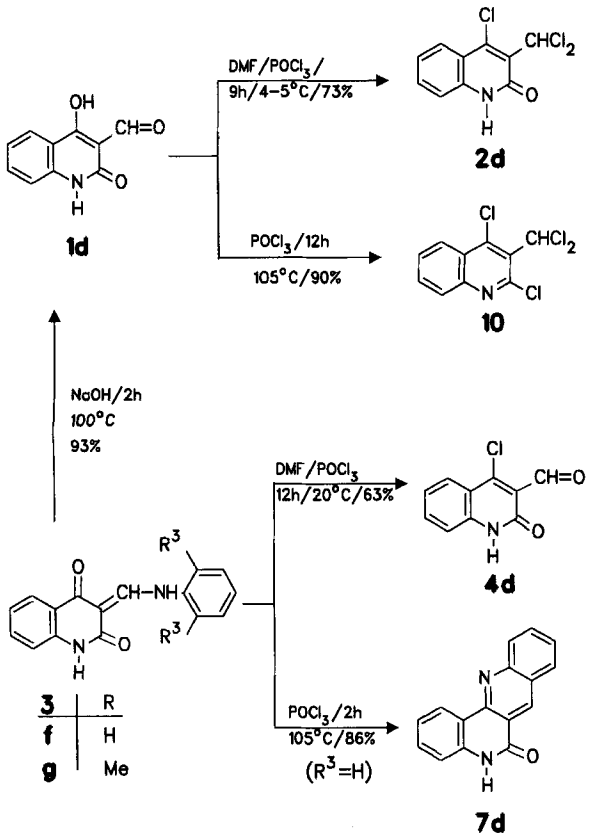
[7] followed in a second step by a Vilsmeier formylation of the anilinoquinolines **9a–c** with phosphoryl chloride/DMF and subsequent cyclization between the formyl and the anilino part to yield **7a–c** similar to results obtained in the coumarin chemistry [8]. Surprisingly, all physical and spectral data, including the i.r. spectra in its fingerprint area, showed complete identity with the data of the compounds obtained from **3a–c**. So it is evident that the reaction step **3**→**7** includes a migration of the phenylamino group from the azomethine moiety to the 4-position of the quinoline nucleus followed by a cyclization step (formally by dehydration). Addition of anilinium chloride was found to increase the yield and to accelerate the reaction rate significantly, which could be a hint to an intermolecular migration of the phenylamino group.

We tried to apply these reactions to the 1-unsubstituted 4-hydroxyquinolones in order to obtain the 4-chloro-3-formyl-2-quinolone **4d**. We started from 3-formyl-4-hydroxy-2-quinolone **1d** which was prepared from the phenylaminomethylene quinolinediones **3f, g**. Chlorination of **1d** by using boiling phosphoryl chloride as a solvent, yielded the 2,4-dichloro-3-dichloromethylquinoline **10**, in which all oxygen functions were exchanged against chloro substituents, caused by the possibility of a tautomeric 2,4-dihydroxyquinoline. Using DMF/phosphoryl chloride to achieve a more selective chlorination, we found that only at temperatures below 5 °C one product could be obtained which was shown to be the 4-chloro-3-dichloromethylquinolone **2d**. The isomeric 4-quinolone structure is excluded because the infrared spectrum shows significantly an amide carbonyl function at 1670 cm^{-1}, whereas 4-quinolones are known to have carbonyl absorptions below 1600 cm^{-1} [9]. When higher reaction temperatures were used, in every case a mixture of compounds was obtained. Attempts to use phosphoryl chloride with catalytical amounts of water, a reagent which was introduced as a selective chlorination agent in the barbituric acid and uracil chemistry [10], were not successful, because many products without a significant main product were formed. So it was evident, that we always obtained by direct chlorination of **1d** the compounds **2d** or **10**, in which the aldehyd group was converted to the dichloromethyl group.

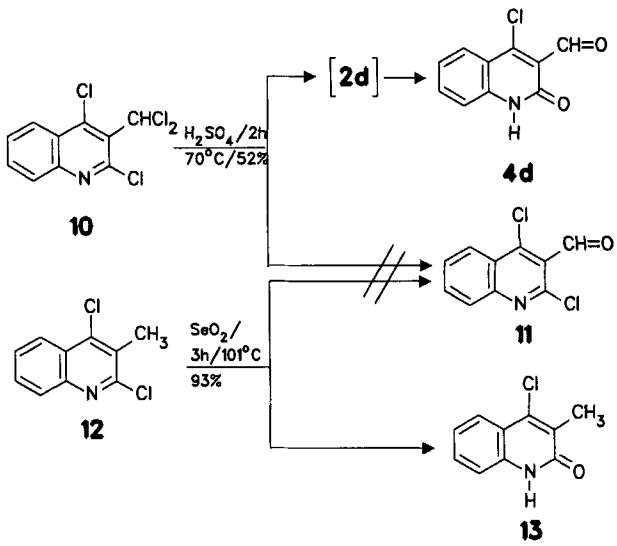
Using the method to chlorinate the phenylaminomethylene quinolinediones **3f, g** at room temperature, we were able to obtain in one step the 1-unsubstituted 4-chloro-3-formyl-2-quinolone **4d**, a target compound for use in cyclization reactions [4c]. The formation of a possible other isomer of **4d** having a 4-quinolone structure can be excluded [9].

When the chlorination reaction of **3** was performed in boiling phosphoryl chloride, in the case of **3f** (having an unsubstituted anilinomethylene group) we obtained again the dibenzonaphthyridinone **7d**, whereas **3g** with a (2,6-dimethylphenyl)aminomethylene moiety yielded a mixture of compounds, which were not separated.

Another approach to the chloro aldehyde **4d** was found by acid catalyzed hydrolysis of the tetrachloro compound **10** in conc. sulfuric acid. All attempts to



Scheme 3



Scheme 4

find a selective hydrolysis method leading from **10** to the dichloro aldehyde **11**, which would be of interest in our study of nucleophilic displacement in dichloroquinolines [13], failed. Kinetic experiments showed, that the first hydrolytic attack takes place at the quinoline nucleus followed by the transformation of the dichloromethyl group to the aldehyde group. So in no case it was possible by changing reaction parameters to obtain the aldehyde before the quinoline chloro atom was hydrolyzed. Changing the reaction conditions, e.g. from acidic to alkaline hydrolysis had no effects. These findings are similar to results obtained with other chloroquinoline carbaldehydes [1b, 11].

Another possibility to obtain the dichloro aldehyde **11** by conversion of a nitro group into the aldehyde [12] failed. Also the oxidation of the methyl group in the 2,4-dichloro-3-methylquinoline **12** by selenium dioxide was not successful, but the 2-chloro function was converted into the oxo group of the lactame structure in **13**; the 3-methyl group remained unchanged.

All experiments have shown that the two chloro atoms in 2,4-dichloroquinoline-3-carbaldehyde are strongly different in their behaviour against nucleophilic displacement reactions in protic solvents. Only the chloro atom in position 2, which is part of a cyclic imidoylchloride structure, reacts with the hydroxide anion to give the 2-quinolone structure, whereas the 4-chloro atom which represents a vinylogous (hetero)-carbonylchloride structure is stable against nucleophilic attacks. In aprotic solvents this behaviour is changed and the first attack is directed to the carbon atom in 4-position [13]. The chloro atoms in the dichloromethyl group range in their reactivity between the two ring chloro atoms in positions 2 and 4 of the ring system.

Experimental

Melting points were determined on a Gallenkamp Melting Point Apparatus Mod. MFB-595 in open capillary tubes and are uncorrected. ^{1}H-NMR-spectra (200 MHz) were obtained on a Varian Gemini 200 instrument. Chemical shifts are reported in ppm from internal tetramethylsilane standard and are given in δ-units. The solvent for NMR spectra was DMSO-d_6 unless otherwise stated. Microanalyses were performed on a Carlo Erba 1106 analyzer and are within 0.4 of the theoretical percentages. Infrared spectra were taken in potassium bromide pellets on a Perkin-Elmer 298 spectrophotometer. Common reagent-grade chemicals are either commercially available and were used without further purification or prepared by standard literature procedures. All reactions were monitored by thin layer chromatography, carried out on 0.2 mm silica gel 60 F-254 (Merck) plates using uv light (254 and 366 nm) for detection.

General Procedure for the Synthesis of 3-Formyl-4-hydroxy-2(1H)-quinolones (**1a – d**)

A solution of 50 mmole of the corresponding phenylaminomethylene quinolone (**3**) in 650 ml of 2N sodium hydroxide and 350 ml of dioxane was subjected to steam-distillation for 2 hours to remove the formed aniline. After filtration, the solution was cooled to 10 °C and acidified with conc. hydrochloric acid to pH 1. The resulting precipitate was filtered. Experimental and analytical data: table 1, spectral data: table 5.

Table 1 Experimental and Analytical Data of 3-Formyl-4-hydroxy-2(1H)-quinolones (**1a – d**)

Nr.	R^1	R^2	yield (%)	m.p. [°C] solvent	molecular formula mol.mass	Calcd. Found C	H	N
1a	Ph	H	81	242 – 243 toluene	$C_{16}H_{11}NO_3$ (265.3)	72.44 72.83	4.18 4.45	5.28 5.24
1b	$-(CH_2)_3-$		77	151 toluene	$C_{13}H_{11}NO_3$ (229.3)	68.11 67.73	4.84 4.70	6.11 5.97
1c	Me	H	81	176 (ref. [1b] 175 – 178)				
1d	H	H	93	> 300 (ref. [6a] 300)				

4-Chloro-3-dichloromethyl-1-phenyl-quinolin-2(1H)-one (**2a**)

A solution of **1a** (2.5 g, 9.5 mmole) in 100 ml of phosphorylchloride was heated under reflux for 16 hours. Then the excess of phosphorylchloride was removed i. vac. and the residue was poured on 200 g of crushed ice. The product was collected and dried after neutralisation with sodium hydroxide. Yield: 3.02 g (95 %), m.p. 197 – 198.5 °C (1-propanol); IR: 1660 m, 1640 s, 1605 s, 1590 m, 1565 cm^{-1} m; ^{1}H-NMR: δ = 6.70 (d, J = 9 Hz, 1H, aryl-H), 7.35 – 7.50 (m, 3H, aryl-H), 7.60 – 7.75 (m, 5H, aryl-H, and C**H**Cl_2), 8.20 (dd, J = 7 Hz and 1.5 Hz, 1H, 5-H).

$C_{16}H_{10}Cl_3NO$	Calcd.:	C 56.74	H 2.98	N 4.14
(338.6)	Found:	C 56.53	H 3.32	N 4.12

1-Chloro-2-dichloromethyl-6,7-dihydro-5H-benzo[i,j] quinolizin-3-one (**2b**)

From **1b** (8.2 g, 36 mmoles) according to **2a**. Yield: 8.1 g (79 %), m.p. 214 °C dec. (toluene); IR: 1620 s, 1590 m, 1585 cm^{-1}, sh; ^{1}H-NMR: δ = 2.05 (q, J = 7 Hz, 2H, CH_2), 3.0 (t, J = 7 Hz, 2H, Ar-C**H**$_2$), 4.15 (t, J = 7 Hz, 2H, N-C**H**$_2$), 7.35, 7.40 (2d, J = 7 Hz, 1H, 8-H), 7.60 (dd, J = 7 and 1.5 Hz, 1H, 7-H), 7.75 (s, 1H, C**H**Cl_2), 8.0 (dd, J = 7 and 1.5 Hz, 1H, 9-H).

$C_{13}H_{10}Cl_3NO$	Calcd.:	C 51.59	H 3.33	N 4.63
(302.6)	Found:	C 51.83	H 3.46	N 4.43

4-Chloro-3-dichloromethyl-1-methylquinolin-2(1H)-one (**2c**)

From **1c** (5.3 g, 26 mmoles) according to **2a**. Yield: 3.5 g (48 %), m.p. 180 °C dec. (toluene); lit. m.p. 179 – 180 °C [2c].

4-Chloro-3-dichloromethyl-quinolin-2(1H)-one (**2d**)

A solution of **1d** (1.5 g, 8 mmole) in 30 ml of DMF was cooled to 4 – 5 °C and 10 ml phosphorylchloride were added dropwise. The solution was stirred for 9 hours. Then the reaction mixture was poured into 350 ml of ice water and the formed precipitate filtered by suction. The product was carefully washed with water, filtered and dried. Yield 1.52 g (73 %), m.p. 259.3 °C (glacial acetic acid); IR: 3010 – 2750 w, br, 1655 s, 1600 cm^{-1} w; ^{1}H-NMR: δ = 7.40 – 7.80 (m, 4H, aryl-H and C**H**Cl_2), 8.05 (dd, J = 7 and 1.5 Hz, 1H, 5-H), 12.60 (s, br, 1H, NH).

$C_{10}H_7Cl_3NO$	Calcd.:	C 45.58	H 2.68	N 5.32
(263.5)	Found:	C 45.96	H 2.55	N 5.21

General Procedure for the Synthesis of 3-Phenylamino-methylene-quinoline-2,4-diones (**3a – g**)

A mixture of 0.5 mole of the corresponding 4-hydroxy-quinolone **8** with 0.5 mole of triethyl orthoformiate and 0.5 mole of aniline in 10 ml of ethyleneglycole was heated under stirring until the formation of ethanol started. The temperature was increased during 2 hours to 190 °C until the formation of ethanol stopped. The reaction mixture was cooled to room temperature and treated with 100 ml of ethanol. The precipitate was filtered and washed with ethanol. Experimental and analytical data: table 2, spectral data: table 6.

General Procedure for the Synthesis of 4-Chloro-3-formyl-quinolones (**4a – d**)

Method A: To a solution of **3** (20 mmole) in 50 ml of dimethylformamide 2.5 ml of phosphorylchloride were added slowly and the solution was stirred at 20 °C for the time given in table 3. Then the mixture was poured into 500 ml of ice water and the precipitate was filtered by suction.

Method B: A solution of **2** (2 mmole) in 10 ml of conc. sulfuric acid was heated to 70 °C for 2 hours while a slow stream of nitrogen was bubbled through the solution. Then the reaction mixture was poured onto 150 g of crushed ice and neutralized with sodium hydroxide. The product was filtered and dried. Experimental and analytical data: table 3, spectral data: table 7.

Method C: (leading to **4d**) From **10** (0.4 g, 1.4 mmole) in 10 ml of conc. sulfuric acid according to method B.

General Procedure for the Synthesis of Dibenzo[b,h][1,6] naphthyridinones (**7a – d**)

Method A: A solution of the anilinomethylene compound **3** (6 mmole) in 40 ml of phosphorylchloride was refluxed for 2 hours. The excess of phosphorylchloride was removed by distillation and the residue poured onto 200 g of crushed ice. Then the solution was neutralized with sodium hydroxide and the product collected by suction.

Method B: A solution of phenylaminoquinolones **9** (9 mmole) in 50 ml of dimethylformamide and 3.0 ml of phosphorylchloride was heated to 90 – 95 °C for 2 hours. Then it was poured into 150 ml of ice water, the precipitate filtered and washed with water. Experimental and analytical data: table 4, spectral data: table 8.

Table 2 Experimental and Analytical Data of 3-Phenylaminomethylene-quinoline-2,4(1H,3H)-diones (**3a – g**)

Nr.	R^1	R^2	R^3	yield (%)	m.p. [°C] solvent	molecular formula (mol.mass)	Calcd. Found C	H	N
3a	Ph	H	H	66	184 (ref. [6b] 178)				
3b	$-(CH_2)_3-$		H	69	168 ligroin	$C_{19}H_{16}N_2O_2$ (304.3)	74.98 74.79	5.30 5.25	9.21 9.08
3c	Me	H	H	62	154 (ref. [6b] 152)				
3d	Ph	H	Me	30	217 (dec.) 1-propanol	$C_{24}H_{21}N_2O_2$ (369.4)	78.02 77.62	5.73 5.58	7.58 7.19
3e	$-(CH_2)_3-$		Me	49	181.3 – 181.5 toluene	$C_{21}H_{20}N_2O_2$ (332.4)	75.88 76.15	6.06 5.78	8.43 8.08
3f	H		H	91	269 (ref. [6b] 248)				
3g	H		Me	77	238 toluene	$C_{18}H_{16}N_2O_2$ (292.3)	73.95 73.78	5.52 5.48	9.56 9.41

Table 3 Experimental and Analytical Data of 4-Chloro-3-formyl-2(1H)-quinolinones (**4a – d**)

Nr.	R^1	R^2	method: yield (%)/ reaction time [h]	m.p. [°C] solvent	molecular formula (mol.mass)	Calcd. Found C	H	N
4a	Ph	H	a: 65/6 b: 84	237 – 238 toluene	$C_{16}H_{10}ClNO_2$ (283.7)	67.73 68.05	3.55 3.79	4.94 4.86
4b	$-(CH_2)_3-$		a: 39/6 b: 82	133 – 134 toluene	$C_{13}H_{10}ClNO_2$ (247.7)	63.04 63.29	4.07 4.33	5.66 5.95
4c	Me	H	a: 95 b: 90	168 – 169 (ref. [2c] 166 – 167)				
4d	H	H	a: 63/12 c: 52	251 xylene	$C_{10}H_6ClNO_2$ (207.6)	57.84 57.75	2.91 3.26	6.74 6.45

Table 4 Experimental and Analytical Data for Dibenzo[b,h][1,6]naphthyridinones (**7a – d**)

Nr.	R^1	R^2	method: yield (%)	m.p.[°C] solvent	molecular formula (mol.mass)	Calcd. Found C	H	N
7a	Ph	H	a: 91 b: 56	266 – 267 DMF	$C_{22}H_{14}N_2O$ (322.4)	81.97 81.89	4.38 4.38	8.69 8.78
7b	$-(CH_2)_3-$		a: 88 b: 76	181 – 183 toluene	$C_{19}H_{14}N_2O$ (286.3)	79.70 79.78	4.93 4.97	9.79 9.65
7c	Me	H	a: 24 (81)[a] b: 90	225 (ref. [2c] 211 – 223)				
7d	H	H	a: 86	374 – 375 DMF	$C_{16}H_{10}N_2O$ (246.3)	78.03 77.76	4.09 4.40	11.38 11.44

[a] yield in brackets: obtained by addition of anilinium chloride

4-Phenylamino-1-phenyl-quinolin-2(1H)-one (**9a**)

A mixture of 4-hydroxy-1-phenyl-quinolin-*2(1H)*-one (**8a**) (2.4 g, 10 mmole) and aniline hydrochloride (1.3 g, 10 mmole) was treated with aniline (9.3 g, 100 mmole) according to ref. [7]. Yield: 3.1 g (98 %), m.p. 256.5 – 256.8 °C (ethanol); ^{1}H-NMR: $\delta = 5.7$ (s, 1H, 3-H), 6.5 (d, $J = 7$ Hz, 1H, aryl-H), 7.15 – 7.70 (m, 12H, aryl-H), 8.25 (d, $J = 7$ Hz, 1H, 5-H), 8.8 (s, 1H, NH).

$C_{21}H_{16}N_2O$	Calcd.:	C 80.74	H 5.16	N 8.97
(312.4)	Found:	C 81.00	H 5.18	N 8.89

Table 5 Spectral data of 3-Formyl-4-hydroxy-quinoline-2(1H)-ones (**1a, b, d**)

Nr.	IR (KBr) [cm^{-1}]	^{1}H-NMR (DMSO-d_6), δ values
1a	3060 w, 1660 s, 1640 s, 1570 s, 1495 s.	6.55 (d, J = 10 Hz, 1H, OH), 7.30 – 7.45 (m, 4H, aryl-H), 7.55 – 7.75 (m, 4H, aryl-H), 8.15 (dd, J = 7 and 1.5 Hz, 1H, 5-H), 10.1 (s, 1H, CHO).
1b	2930 w, 2870 w, 1640 s, sh, 1630 s, 1590 – 1610 m, 1570 m.	2.0 (m, 2H, CH_2), 2.95 (t, J = 7 Hz, 2H, Ar-CH_2), 4.0 (t, J = 7 Hz, 2H, N-CH_2), 7.25 (t, J = 10 Hz, 1H, 8-H), 7.60 (dd, J = 7 Hz and 1.5 Hz, 1H, 7-H), 7.90 (dd, J = 7 Hz and 1.5 Hz, 1H, 9-H), 10.1 (s, 1H, CHO).
1d	3200 – 2700 m, br, 1690 s, 1670 s, 1640 s, 1615 s, 1605 s, 1550 m.	7.20 – 7.40 (m, 2H, aryl-H); 7.70 (t, J = 7 Hz, 1H, 6-H), 8.0 (dd, J = 7 Hz and 1.5 Hz, 1H, 5-H), 10.0 (s, 1H, CHO), 11.75 (s, br, 1H, NH).

Table 6 Spectral Data of 3-Phenylaminomethylene-quinoline-2,4(1H,3H)-diones (**3b, d, e, g**)

Nr.	IR (KBr) [cm^{-1}]	^{1}H-NMR (DMSO-d_6), δ values
3b	2980 – 2920 w, br, 1670 m, sh, 1650 m, 1590 m, 1580 m, 1560 m, sh.	1.95 (m, 2H, CH_2), 2.90 (t, J = 7 Hz, 2H, Ar-CH_2), 4.0 (t, J = 7 Hz, 2H, N-CH_2), 7.0 – 7.65 (m, 8H, aryl-H), 7.90 (dd, J = 7 Hz and 1.5 Hz, 1H, 9-H), 8.90 (s, br, 1H, NH).
3d	1660 s, 1610 s, 1590 s, 1575 m, 1555 m.	2.25 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 6.40 (t, J = 7 Hz, 1H, =CH-N), 7.10 – 7.70 (m, 12H, aryl-H), 8.10 (d, J = 7 Hz, 1H, 5-H).
3e	2980 – 2880 w, br, 1655 m, sh, 1650 s, 1610 s, 1580 s, 1550 m.	1.95 (m, 2H, CH_2), 2.25 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 2.90 (t, J = 7 Hz, 2H, Ar-CH_2), 4.0 (t, J = 7 Hz, 2H, N-CH_2), 7.10 (t, J = 7 Hz, 1H, 7-H), 7.20 (s, 3H, aryl-H), 7.45 (d, J = 7 Hz, 1H, 8-H), 7.90 (d, J = 7 Hz, 1H, 9-H), 8.35, 8.45 (2d, J = 11 Hz, 1H, =CH-N), 12.15 (s, br. 0.5H, D_2O exch., NH), 13.15 (s, br. 0.5H, D_2O exch., NH).
3g	3200 – 2900 w, br, 1660 s, 1600 s, 1585 s, 1500 m.	2.25 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 7.10 – 7.30 (m, 5H, aryl-H), 7.55 (t, J = 7 Hz, 1H, 6-H), 8.0 (t, J = 7 Hz, 1H, 5-H), 8.4 (s, 1H, NH), 10.85 (d, J = 17 Hz, 1H, NH).

Table 7 Spectral Data of 4-Chloro-3-formyl-2(1H)-quinolinones (**4a, b, d**)

Nr.	IR (KBr) [cm^{-1}]	^{1}H-NMR (DMSO-d_6), δ values
4a	1700 m, 1640 s, 1600 m, 1530 m.	6.6 (d, J = 10 Hz, 1H, aryl-H), 7.35 – 7.50 (m, 3H, aryl-H), 7.55 – 7.75 (m, 4H, aryl-H), 8.30 (dd, J = 7 Hz and 1.5 Hz, 1H, 5-H), 10.30 (s, 1H, CHO).
4b	1700 m, 1685 m, 1635 s, 1600 m, 1580 m, 1545 m.	2.0 (m, 2H, CH_2), 2.95 (t, J = 7 Hz, 2H, Ar-CH_2), 4.05 (t, J = 7 Hz, 2H, N-CH_2), 7.30 (t, J = 7 Hz, 1H, 8-H), 7.60 (dd, J = 7 Hz and 1.5 Hz, 1H, 7-H), 8.0 (dd, J = 7 Hz and 1.5 Hz, 1H, 9-H), 10.30 (s, 1H, CHO).
4d	3060 – 2200 w, br, 1705 s, 1660 s, 1655 m, 1590 m.	7.30 – 7.75 (m, 3H, aryl-H), 8.10 (d, J = 7 Hz, 1H, 5-H), 10.30 (s, 1H, CHO), 12.40 (s, 1H, NH).

Table 8 Spectral Data of Dibenzo[b,h][1,6]-naphthyridinones (**7a, b, d**)

Nr.	IR (KBr) [cm^{-1}]	^{1}H-NMR (DMSO-d_6), δ values
7a	3060 w, 1660 s, 1620 m, 1600 s, 1595 s, sh, 1500 m, 1495 m.	6.60 (d, J = 10 Hz, 1H, aryl-H), 7.35 – 7.80 (m, 8H, aryl-H), 8.05 – 8.33 (m, 2H, aryl-H), 9.0 (dd, J = 7 Hz and 1.5 Hz, 1H, 1-H), 9.4 (s, 1H, 7-H).
7b	1655 s, 1650 s, 1620 m, 1595 m.	2.10 (m, 2H, CH_2), 2.95 (t, J = 7 Hz, 2H, Ar-CH_2), 4.20 (t, J = 7 Hz, 2H, N-CH_2), 7.20 – 8.35 (m, 6H, aryl-H), 8.75 (dd, J = 7 Hz and 1.5 Hz, 1H, 1-H), 9.30 (s, 1H, 8-H).
7d	1585 m, 1560 w, 1500 m.	7.20 – 8.35 (m, 7H, aryl-H), 8.80 (dd, J = 7 Hz and 1.5 Hz, 1H, 1-H), 9.35 (s, 1H, 7-H), 11.75 (s, 1H, NH).

1-Phenylamino-6,7-dihydro-5H-benzo[i,j]quinolizin-3-one (**9b**)

From 1-hydroxy-6,7-dihydro-5H-benzo[i,j]quinolizine-3-one (**8b**, 4.0 g, 20 mmole) and aniline hydrochloride (2.6 g, 20 mmole) in aniline (18.6 g, 200 mmole) according to ref. [7]. Yield: 4.0 g (72.7 %), m.p. 227.8 – 228.3 °C (ethanol); ^{1}H-NMR: δ = 2.0 (m, 2H, -CH_2-), 2.95 (t, J = 7 Hz, 2H, Ar-CH_2), 4.05 (t, J = 7 Hz, 2H, N-CH_2), 5.80 (s, 1H, 2-H), 7.10 – 7.50 (m, 7H, aryl-H), 8.0 (d, J = 7 Hz, 1H, 9-H), 8.6 (s, 1H, NH).

$C_{18}H_{16}N_2O$	Calcd.:	C 78.23	H 5.84	N 10.14
(276.3)	Found:	C 78.01	H 5.83	N 10.12

1-Methyl-4-phenylamino-2(1H)-quinolone (**9c**)

From 4-hydroxy-2-quinolone (**8c**) (3.50 g, 20 mmole) and aniline hydrochloride (2.6 g, 20 mmole) in aniline (9.3 g, 100 mmole) according to ref. [7]. Yield: 4.75 g (95 %), m.p. 202 °C (ethanol); lit. m.p. 199 – 201 °C [2c].

2,4-Dichloro-3-dichloromethyl-quinoline (**10**)

A solution of **1d** (4.4 g, 23.3 mmole) in 50 ml of phosphorylchloride was refluxed for 12 hours. Then the excess of phosphorylchloride was removed i. vac. and the residue was treated with 100 g of crushed ice. The solution was brought to pH 4 – 5 with sodium hydroxide, the precipitate was filtered by suction and dried. Yield 4.73 g (90 %), m.p. 124.9 – 125.5 °C (ethanol); IR: 1705 w, 1660 s, 1615 m, 1555 cm^{-1} s; ^{1}H-NMR: δ = 7.84 – 8.10 (m, 4H, aryl-H and C**H**Cl_2).

$C_{10}H_5Cl_4N$	Calcd.:	C 42.75	H 1.79	N 4.99
(281.0)	Found:	C 42.66	H 1.89	N 4.97

4-Chloro-3-methyl-quinoline-2(1H)-one (**13**)

A solution of 2,4-dichloro-3-methyl-quinoline (**12**) (1.9 g, 8.9 mmole) in 50 ml of dry dioxane was heated under reflux with selenium dioxide (1.1 g, 9 mmole) for 3.5 hours. The reaction mixture was filtered from inorganic material, cooled to room temperature and the precipitate was filtered and dried. Yield 1.51 g (93 %), m.p. 266.7 – 267.7 °C (toluene); IR: 3180 – 2280 m, br, 1660 s, 1600 m, 1570 m, 1500 m, 1485 cm^{-1} m; ^{1}H-NMR: δ = 2.2 (s, 3H, CH_3), 7.20 – 7.55 (m, 3H, aryl-H), 7.85 (d, J = 7 Hz, 1H, 5-H), 12.05 (s, 1H, NH).

$C_{10}H_8ClNO$	Calcd.:	C 62.02	H 4.16	N 7.23
(193.6)	Found:	C 61.84	H 4.19	N 7.16

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