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Syntheses of 3-Acyl-4-hydroxy-2(1H)quinolones

Thomas Kappe, Rudolf Aigner [1], Peter Hohengassner [2] and Wolfgang Stadlbauer

Graz/Austria, Institute of Organic Chemistry, Karl-Franzens-University

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Abstract. 3-Acyl-4-hydroxy-2(1H)-quinolones **5** are obtained by hydrolytic ring opening and subsequent decarboxylation from the corresponding pyrano[3,2-c]quinolin-2,5(6H)-diones **4**, which in turn are easily obtained from 1:2 condensation of anilines **1** with diethyl malonate **2a** or 1:1 condensation of diethyl alkyl- or arylmalonates **2b–e** with 4-hydroxy-2(1H)-quinolones **3**. Nitropyranoquinolinediones **6** furnish after ringopening 3-nitroacetyl-4-hydroxy-2(1H)quinolones **8**. Pyranoquinolines **7** and **9** with acetyl- or aminosubstituents are hydrolyzed during basic ringopening to yield **5**.

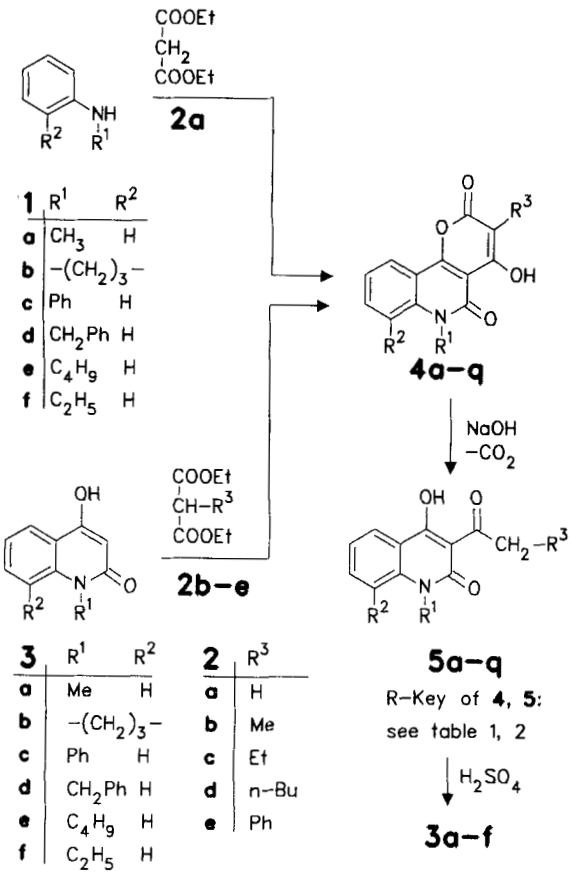
In the last years 4-hydroxyquinolines, 4-hydroxycoumarins, 4-hydroxy-2-pyridones and 4-hydroxy-2-pyrones with aliphatic acyl groups in position 3 have found much interest because of their biological properties [3]. Most methods to introduce acyl groups start from aliphatic carboxylic acids [4] or their reactive derivatives like carboxylic acid chlorides [5] and anhydrides [4c, 6]. Depending on the acylating agent and the catalyst (e.g. phosphoryl chloride, polyphosphoric acid, pyridine and others) the acylation takes place either directly at the 3-position of the heterocycle which is to be acylated, or an intermediate 4-O-acyl product is obtained [3a, 4g, 5–7], which can be rearranged to the 3-C-acyl compound thermically or by Fries rearrangement. Other methods use ring closure reactions with building blocks containing acyl substituents [8].

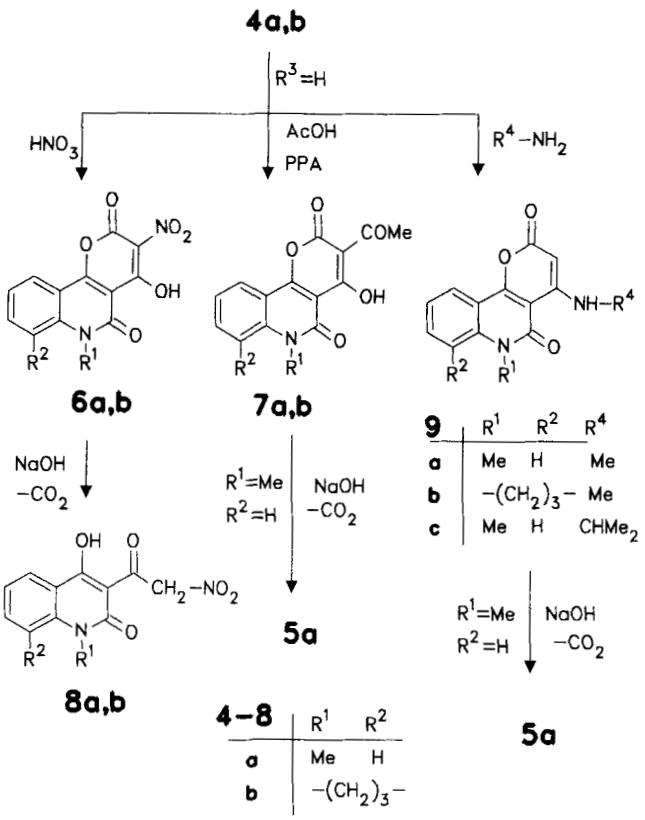
Another approach to 3-acetyl-4-hydroxy-2-quinolones and related heterocycles uses a two-step reaction sequence *via* pyrono compounds obtained easily from 1:2 condensation of anilines with malonates [9]. This method has the advantage to start from easily obtainable starting materials and avoids 4-acetoxy products which have to be rearranged. In a second step 3-acetyl compounds are obtained by alkaline hydrolysis of the lacton ring and subsequent decarboxylation of the resulting β-oxo-carboxylate [9]. Recently we have improved this method to raise both yield and purity [10].

In order to obtain 3-acetyl-4-hydroxy-2-quinolones **5d–f** we have adopted the methods described for **5a–c** [10] starting from N-alkylanilines **1d–f** and diethylmalonate **2a** to yield pyranoquinolines **4d–f**. Degradation of **4d–f** in sodium hydroxide afforded 3-acetylquinolones **5d–f** in good yields. Cleavage of the 3-acetyl group with sulfuric acid resulted in the formation of 3-unsubstituted quinolones **3a–f**.

3-Acyl-quinolones of type **5g–q** with longer alkyl chains or arylalkyl substituents are described to be prepared by aldol condensation of 3-acetyl-quinolones with aldehydes followed by reduction of the alkenyl substituents to alkyl substituents [11], because direct introduction of long-chain or substituted acyl groups often causes low yields [4, 9g]. We developed another approach to obtain this type of compounds: The reaction step of anilines **1** to pyranoquinolines **4** as described before was divided into two single steps: first the 3-unsubstituted 4-hydroxyquinolones **3a–c** were prepared according to known procedures [9, 10], and in a second step diethyl alkyl- and arylmalonates **2b–e** were condensed in a 1:1 reaction with the 1,3-dinucleophilic 4-hydroxy-quinolones **3a–c** in refluxing diphenylether to afford pyranoquinolones **4g–q** having a substituent in position 3. Experiments using nitrobenzene as high boiling solvent or carrying out the reaction without solvent were not successful because of lower yields and purity. The pyranoquinolines **4g–q** were treated with conc. sodium hydroxide in 1,2-ethandiole to cleave the pyrano ring and yielded 3-acyl-4-hydroxyquinolones **5g–q** with longer alkyl chains or arylalkyl substituents.

Infrared spectral data of pyranoquinolines **4** show two typical carbonyl frequencies, the lactone signal at 1720–1740 cm ^{1} and the lactam signal at 1640–1680 cm^{-1}. 3-Acylquinolones **5** show in most cases carbonyl frequencies in the region of 1640–1660 cm^{-1}. Comparison of ^{1}H-NMR data of **4** and **5** indicates the appearance of additional aliphatic signals in **5** caused by the formation of the acyl-CH_2-group adjacent to the C=O group which is formed by ring opening and decarboxylation of the pyrano ring followed by tautomerization of the hydroxy group to the keto moiety. So **4d** having no substituent in the 3-pyrano position, shows an olefinic proton at δ = 6.1 ppm, which disappears in **5d** to change into an methyl group at δ = 2.1 ppm. Similar, **4i** with a 3-methyl group at δ = 2.5 ppm changes to **5i** with an ethyl signal at 1.15 ppm (t, J = 7 Hz) and 3.25 (q, J = 7 Hz).





Since the variation of the acyl group depends on the substituent in position 3 of the pyranoquinolines **4**, another possibility to obtain new acyl substituents is the electrophilic substitution of the pyranoquinolines **4**, which is known to attack the CH-acidic position of the cyclic β-dicarbonyl system of compounds of type **4**.

Nitration of pyranoquinolines **4a, b** at 70–90 °C with conc. nitric acid and sulfuric acid afforded 3-nitropyranoquinolines **6a, b** in good yields. Hydrolytic cleavage of nitropyranoquinolines **6a, b** using aqueous sodium hydroxide led to 3-nitroacetylquinolones **8a, b**. Attempts to synthesize the corresponding nitroso compounds with sodium nitrite in glacial acetic or by basic catalyzed reaction with iso-amylnitrite were not successful.

Introduction of an acetyl group into the 3-position of pyranoquinolines **4a, b** should be possible by the same general methods mentioned in the introduction [3a, 4g, 5–7]. Attempts to obtain 4-acetoxy-pyranoquinolines, which could be rearranged to 3-acetyl-pyranoquinolines, were not successful, because always a mixture of products was isolated, which could not be separated in a satisfactory manner to get considerable amounts of acetoxy product. Best results were obtained by direct C-acetylation of **4a, b** with acetic acid in polyphosphoric acid according to known methods [4], and 3-acetyl-pyranoquinolines **7a, b** were obtained in good yields. Ring opening, however, did not yield the desired 3-acetoacetyl-4-hydroxy-quinolines. When the pyrano ring of **7a** was opened in alkaline medium as shown before, the acetyl group was cleaved by a retro-Claisen reaction and the only product which could be isolated was the 3-acetyl-4-hydroxy-quinoline **5a**. Attempts to achieve the ring cleavage of **7a** in an acidic medium in order to obtain 3-acetoacetyl-quinolones failed too but rearrangement reactions have been observed [2].

Attempts to react urea with pyranoquinolines **4a, b** were not successful. With 1,3-dimethylurea methylamino-pyranoquinolines **9a, b** were obtained in low yields, which probably derive from degradation of 1,3-dimethylurea by formation of methylamine. Better yields of methylamino-pyranoquinolines **9a, b** could be obtained when methylammonium chloride was added as methylamine source. Isourea formation of **4a** with 1,3-diisopropylcarbodiimide was unsuccessful too, and the only reaction product was again the corresponding 4-isopropylamino-pyranoquinoline **9c**. When the pyrone ring of **9a** was cleaved under alkaline conditions, the amino group was hydrolyzed too which resulted again in the formation of the 3-acetyl-4-hydroxyquinolone **5a**.

Experimental

Melting points were obtained on a Gallenkamp Melting Point Apparatus, Mod. MFB-595 in open capillary tubes. ^{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 was DMSO-d_6 unless otherwise stated. Microanalyses were performed on a Carlo Erba 1106 analyzer. Infrared spectra were taken on a Perkin-Elmer 298 spectrophotometer in potassium bromides pellets.

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 F-254 (Merck) plates using uv light (254 and 366 nm) for detection.

4-Hydroxy-quinolin-2(1H)-ones (**3a, c**) *and 1-Hydroxy-6,7-dihydro-5H-benzo[ij]quinolizin-3-one* (**3b**)

4-Hydroxy-1-methyl-2(1*H*)-quinolone (**3a**) is commercially available [12] or was prepared according to ref. [10a]. 1-Hydroxy-6,7-dihydro-5*H*-benzo[ij]quinolizin-3-one (**3b**) and 4-hydroxy-1-phenyl-2(1H)-quinolone (**3c**) were prepared according to ref. [10b].

1-Benzyl-4-hydroxy-2(1H)-quinolone (**3d**)

A solution of N-benzylaniline (**1d**) (9.2 g, 0.02 mol) and malonic acid (6.3 g, 0.025 mol) in phosphorylchloride (30 ml) is heated to 90 °C for 1 h. Then the reaction mixture is poured into ice/water, filtered by suction and washed with water. The precipitate is dissolved in 1 N sodium hydroxide (300 ml), filtered from insoluble material, acidified with conc. hydrochloric acid and then filtered by suction. Yield: 3.6 g (72 %), colorless prisms, m.p. 279 °C (lit. m.p. 283–84 °C [13]).

1-Butyl-4-hydroxy-2(1H)-quinolone (**3e**)

A solution of the acetylquinolone **5e** (9.5 g, 0.044 mol) in 90 % sulfuric acid (40 ml) is heated for 15 min at 140 °C. Then the solution was poured into 100 ml of ice/water and the obtained suspension filtered after standing for 12 h. The precipitate was washed several times with water. Yield: 6.3 g (66 %) colorless prisms, m.p. 245 °C (ethanol); IR: 3100–2700 m, b, 1640 s, 1610 w, 1590 cm^{-1}, m; ^{1}H-NMR: δ = 0.85 (t, J = 7 Hz, 3 H, CH_3), 1.0–2.0 (m, 4 H, 2 CH_2), 4.1 (t, J = 7 Hz, N-CH_2), 5.95 (s, 1 H, 3-H), 7.0–78.7 (m, 3 H, Ar-H), 7.95 (dd, J = 2 + 7 Hz, 1 H, 5-H), 11.0 (s, b, 1 H, OH).

$C_{13}H_{15}NO_2$	Calcd.: C 71.87	H 6.96	N 6.45
(217.3)	Found: C 71.99	H 7.36	N 6.77

1-Ethyl-4-hydroxy-2(1H)-quinolone (**3f**)

From 3-acetyl-1-ethyl-4-hydroxy-2-quinolone (**5f**) (80 g, 0.35 mol) in 90 % conc. sulfuric acid (160 ml) according to the method described for **3e**. Yield: 63 g (95 %) colorless prisms, m.p. 258–260 °C (ethanol); IR: 3040–2810 m, b, 1645 s, 1610 w, 1595 cm^{-1}, m.

$C_{11}H_{11}NO_2$	Calcd.: C 69.83	H 5.86	N 7.40
(217.3)	Found: C 70.14	H 5.67	N 7.37

4-Hydroxy-6-methyl-, 4-Hydroxy-6-phenyl-pyrano[3,2-c]quinoline-2,5(6H)-dione (**4a, c**) *and 9-Hydroxy-5,6-dihydro-4H-benzo[ij]pyrano[2,3-b]quinolizine-8,11-dione* (**4b**)

Preparation was performed according to ref. [10].

General Procedure for the Synthesis of 4-Hydroxy-pyrano[3,2-c]quinoline-2,5(6H)-diones (4d–f)

A mixture of the appropriate aniline (**1d–f**) (0.2 mol) and diethylmalonate (**2a**) (64 g, 0.4 mol) in diphenylether (100 g) is refluxed in a distillation apparatus equipped with a 20 cm-Vigreux-column. During 5 hours, the liberated ethanol (about 44 ml) is distilled. Then the mixture is allowed to cool to about 100 °C and treated with dioxane (50 ml). After about 12 h the precipitate was filtered by suction and washed with dioxane and diethyl ether to remove the diphenyl ether. Experimental and analytical data: Table 1.

General Procedure for the Synthesis of 3-Substituted 4-Hydroxy-pyrano[3,2-c]quinoline-2,5(6H)-diones and 10-Substituted 9-Hydroxy-5,6-dihydro-4H-benzo[ij]pyrano[2,3-b]quinolizine-8,11-diones (4g–q)

A solution of the corresponding 4-hydroxy-2(1H)-quinolone **3a, c** or 1-hydroxy-6,7-dihydro-5H-benzo[ij]quinolizine-3-one **3b** (0.04 mol) and the appropriate substituted diethyl malonate **2b–e** (0.08 mol) in diphenylether (80 ml) is heated to 220–280 °C for about 30 min in a distillation apparatus equipped with a 20 cm-Vigreux-column. The end of the reaction is determined by distillation of the resulting reaction alcohol. After cooling the mixture is diluted with diethyl ether (100 ml) and the precipitate filtered by suction. Experimental and analytical data: Table 1.

3-Acetyl-4-hydroxy-1-methyl-, 3-Acetyl-4-hydroxy-1-phenyl-quinolin-2(1H)-one (**5a, c**) and *2-Acetyl-1-hydroxy-6,7-dihydro-5H-benzo[ij]quinolizin-3-one* (**5b**)

Method a) From **1a–c** and **2a** according to ref. [10].
Method b) From **7a**: Acetyl-pyranoquinolinedione **7a** (0.57 g, 2 mmol) is heated under reflux in 2 N aqueous sodium hydroxide solution (10 ml) for 6 h. After filtration from the insoluble residue the filtrate is cooled to 5 °C and precipitated by addition of 2 N hydrochloric acid to pH = 1. Yield: 0.27 g (62 %), m.p. 144–145 °C (ethanol); lit. m.p. 141–142.5 °C (ref. [10a]).

Method c) From **9a**: Methylamino-pyranoquinolinedione **9a** (1.03 g, 4 mmol) is heated under reflux in 5 N aqueous potassium hydroxide solution (40 ml) until the solution is clear. After cooling to 10 °C crystals precipitate, which are dissolved by adding water. Then the product is precipitated by acidification with 2 N hydrochloric acid to pH = 1. Yield: 0.72 g (83 %), m.p. 144–146 °C (ethanol).

General Procedure for the Synthesis of 3-Acyl-4-hydroxy-2(1H)-quinolones and 2-Acyl-1-hydroxy-6,7-dihydro-5H-benzo[ij]quinolizin-3-ones (5d–g)

A suspension of the appropriate pyrano-quinolinedione **4** (0.08 mol) in 1,2-dihydroxyethane (250 ml) and of sodium hydroxide (16 g, 0.4 mol) in water (25 ml) is heated to gentle boiling for 90 min and then poured into ice/water (700 ml). The obtained solution is slowly acidified with conc. hydrochloric acid (40 ml) to precipitate the product (attention: strong foaming because of liberated carbon dioxide). The precipitate is filtered, washed subsequently with water and dried at 80 °C. Experimental and analytical data: Table 2.

Table 1 Experimental and Analytical Data of 3-Substituted 4-Hydroxy-pyrano[3,2-c]quinoline-2,5(6H)-diones and 10-Substituted 9-Hydroxy-5,6-dihydro-4H-benzo[ij]pyrano[2,3-b]quinolizine-8,11-diones (**4d–q**)

Nr.	R^1	R^2	R^3	yield (%)	m.p. [°C] solvent	molecular formula (mol.mass)	Calcd. Found C	H	N
4d	CH_2Ph	H	H	57	239–240	$C_{19}H_{13}NO_4$	71.47	4.10	4.39
					toluene	(319.3)	71.59	4.48	4.11
4e	C_4H_9	H	H	55	228–230	$C_{16}H_{15}NO_4$	67.36	5.30	4.91
					toluene	(285.3)	67.60	5.18	5.04
4f	C_2H_5	H	H	70	234–236	$C_{14}H_{11}NO_4$	65.37	4.31	5.45
					toluene	(257.2)	65.12	4.47	5.26
4g	Me	H	Me	64	280–282	$C_{14}H_{11}NO_4$	65.36	4.31	5.45
					1-butanol	(257.2)	65.48	4.50	5.27
4h	$-(CH_2)_3-$		Me	65	255–256	$C_{16}H_{13}NO_4$	67.84	4.62	4.96
					1-butanol	(283.3)	68.03	4.59	5.05
4i	Ph	H	Me	51	325–327	$C_{19}H_{13}NO_4$	71.46	4.10	4.38
					1-butanol	(319.3)	71.84	4.25	4.33
4j	Me	H	Et	70	250–252	$C_{17}H_{13}NO_4$	66.41	4.83	5.16
					ethanol	(271.3)	66.21	4.71	5.35
4k	$-CH_2)_3-$		Et	67	209–210	$C_{17}H_{15}NO_4$	68.67	5.09	4.71
					ethanol	(297.3)	68.33	5.14	4.68
4l	Ph	H	Et	68	250–251	$C_{20}H_{15}NO_4$	72.06	4.54	4.20
					1-butanol	(333.3)	72.00	4.60	4.15
4m	Me	H	C_4H_9	70	170–172	$C_{17}H_{17}NO_4$	68.21	5.73	4.68
					ethanol	(299.3)	67.91	5.77	4.63
4n	$-(CH_2)_3)-$		C_4H_9	75	190–192	$C_{19}H_{19}NO_4$	70.13	5.89	4.30
					ethanol	(325.4)	69.89	5.78	4.21
4o	Me	H	Ph	87	232–234	$C_{19}H_{13}NO_4$	71.47	4.10	4.39
					ethanol	(319.3)	71.63	4.20	4.42
4p	$-(CH_2)_3-$		Ph	86	264–66	$C_{21}H_{15}NO_4$	73.03	4.38	4.05
					DMF	(345.3)	73.06	4.42	4.15
4q	Ph	H	Ph	42	273–275	$C_{24}H_{15}NO_4$	75.58	3.69	3.67
					ethanol	(381.4)	75.35	3.97	3.56

4-Hydroxy-6-methyl-3-nitro-pyrano[3,2-c]quinoline-2,5(6H)-dione (**6a**)

A solution of the pyranoquinolindione **4a** (4.86 g, 0.02 mol) in glacial acetic acid (40 ml) is warmed up to 70 °C under stirring and reacted with a mixture of conc. nitric acid (2.0 ml) and conc. sulfuric acid (2.4 ml). Immediately a precipitate is formed, the mixture is poured into ice/water and filtered by suction. Yield: 5.20 g (90 %), yellow needles, m.p. 241 °C, dec. (glacial acetic acid); IR: 1760 s, 1660 s, 1610 m, 1570 s, 1325 cm^{-1} s.

$C_{13}H_8N_2O_6$	Calcd.: 54.17	H 2.80	N 9.72
(288.2)	Found: 53.78	H 2.87	N 9.54

9-Hydroxy-10-nitro-5,6-dihydro-4H-benzo[ij]pyrano[2,3-b]quinolizine-8,11-dione (**6b**)

A solution of benzopyranoquinolizindione **4b** (5.38 g, 0.02 mol) in glacial acetic acid (350 ml) is reacted with conc. nitric acid (2.0 ml) and conc. sulfuric acid (2.4 ml) as described for **6a**. Yield: 5.00 g (80 %) yellow prisms, m.p. 253 °C, dec. (glacial acetic acid); IR: 1615 s, 1555 s, 1500 m, 1340 cm^{-1}, m.

$C_{15}H_{10}N_2O_6$	Calcd.: C 57.33	H 3.21	N 8.92
(314.3)	Found: C 57.34	H 3.40	N 8.67

3-Acetyl-4-hydroxy-6-methyl-pyrano[3,2-c]quinoline-2,5(6H)-dione (**7a**)

A solution of the pyranoquinolinedione **4a** (4.86 g, 0.02 mol) in refluxing glacial acetic acid (120 ml) is treated with polyphosphoric acid (30 ml) and then heated under reflux for 15 min. The hot mixture is poured onto ice, where a yellow precipitate is formed. Yield: 5.24 g (92 %), dark yellow needles, m.p. 257 °C (glacial acetic acid); IR: 1750 s, 1660 cm ^{1}, s; ^{1}H-NMR (CF_3COOH): δ = 2.97 (s, 3 H, CH_3), 4.2 (s, 3 H, N-CH_3), 7.7–8.4 (m, 3 H, ArH), 8.63 (dd, J = 2+8 Hz, 10-H).

$C_{15}H_{11}NO_5$	Calcd.: C 63.16	H 3.89	N 4.91
(285.3)	Found: C 63.15	H 3.98	N 4.89

10-Acetyl-9-hydroxy-5,6-dihydro-4H-benzo[ij]pyrano[2,3-b]quinolizine-8,11-dione (**7b**)

Benzopyranoquinolizindione **4b** (5.38 g, 0.02 mol) in refluxing glacial acetic acid (200 ml) is treated with polyphosphoric acid (30 ml) as described for **7a**. Yield: 4.90 g (79 %), yellow needles, m.p. 225–227 °C (xylene).

$C_{17}H_{13}NO_5$	Calcd.: C 65.59	H 4.21	N 4.50
(311.3)	Found: C 65.84	H 4.33	N 4.44

Table 2 Experimental and Analytical Data of 3-Acyl-4-hydroxy-2(1H)-quinolones and 2-Acyl-1-hydroxy-6,7-dihydro-5H-benzo[ij]quinolizin-3-ones (**5d–q**)

Nr.	R^1	R^2	R^3	yield (%)	m.p. [°C] solvent	molecular formula (mol.mass)	Calcd. Found C	H	N
5d	CH_2Ph	H	H	92	158–160	$C_{18}H_{15}NO_3$	73.71	5.15	4.78
					toluene	(293.3)	73.70	4.95	4.82
5e	C_4H_9	H	H	96	107	$C_{15}H_{17}NO_3$	69.48	6.61	5.40
					ethanol	(259.3)	69.58	6.49	5.42
5f	C_2H_5	H	H	89	156	$C_{13}H_{13}NO_3$	67.52	5.67	6.06
					ethanol	(231.3)	67.89	5.45	5.78
5g	Me	H	Me	97	134–136	$C_{13}H_{13}NO_3$	67.49	5.66	6.05
					ethanol	(231.2)	67.45	5.80	6.03
5h	$-(CH_2)_3-$		Me	94	155–156	$C_{15}H_{15}NO_3$	70.02	5.88	5.44
					ethanol	(257.3)	70.32	5.57	5.40
5i	Ph	H	Me	97	175–176	$C_{18}H_{15}NO_3$	73.70	5.15	4.78
					ethanol	(293.3)	74.01	5.22	4.77
5j	Me	H	Et	92	97–98	$C_{14}H_{15}NO_3$	68.54	6.16	5.71
					ethanol	(245.3)	68.36	6.10	5.63
5k	$-(CH_2)_3-$		Et	92	>350	$C_{16}H_{17}NO_3$	70.83	6.32	5.16
					ethanol	(271.3)	70.55	6.23	5.01
5l	Ph	H	Et	73	126–128	$C_{19}H_{17}NO_3$	74.25	5.58	4.56
					ethanol	(307.3)	74.15	5.57	4.48
5m	Me	H	C_4H_9	85	>350	$C_{16}H_{19}NO_3$	70.33	7.01	5.13
					ethanol	(273.3)	70.14	6.98	5.18
5n	$-(CH_2)_3-$		C_4H_9	92	>350	$C_{18}H_{21}NO_3$	72.32	7.07	4.68
					ethanol	(299.3)	72.26	7.04	4.59
5o	Me	H	Ph	92	>350	$C_{18}H_{15}NO_3$	73.68	5.15	4.77
					ethanol	(293.4)	73.61	5.23	4.69
5p	$-(CH_2)_3-$		Ph	85	>350	$C_{20}H_{17}NO_3$	75.22	5.37	4.39
					ethanol	(319.4)	75.03	5.29	4.42
5q	Ph	H	Ph	77	151–152	$C_{23}H_{17}NO_3$	77.73	4.82	3.94
					ethanol	(355.4)	76.90	4.86	3.84

4-Hydroxy-1-methyl-3-nitroacetyl-quinolin-2(1H)-one (**8a**)

A suspension of the nitropyranoquinolinedione **6a** (0.63 g, 2.2 mmol) in 2 N aqueous sodium hydroxide (22 ml) is heated under reflux until a clear solution is formed. After cooling to 0 °C the product is precipitated with 2 N hydrochloric acid. Yield: 0.43 g (75 %), pale yellow needles, m.p. 180–185 °C, dec. (ethanol); IR: 1760 s, 1670 s, 1610 s, 1580 s, 1530 s, 1320 cm^{-1}, s.

$C_{12}H_{10}N_2O_5$	Calcd.: C 54.96	H 3.84	N 10.69
(262.2)	Found: C 55.05	H 3.91	N 10.61

1-Hydroxy-2-nitroacetyl-6,7-dihydro-5H-benzo[ij]quinolizin-3-one (**8b**)

Nitrobenzopyranoquinolizinedione **6b** (2.83 g, 9 mmol) in 2 N aqueous sodium hydroxide (90 ml) is reacted as described for **6a**. Yield: 1.97 g (76 %), pale yellow needles, m.p. 189 °C, dec. (dioxane); IR: 2960 w, 1620 s, 1590 s, 1555 s, 1375 cm^{-1}, m.

$C_{14}H_{12}N_2O_5$	Calcd.: C 58.33	H 4.20	N 9.72
(288.3)	Found: C 57.95	H 4.51	N 9.93

6-Methyl-4-methylamino-pyrano[3,2-c]quinolin-2,5(6H)-dione (**9a**)

A mixture of the pyranoquinolindione **4a** (2.43 g, 0.1 mol), 1,3-dimethylurea (0.015 mol) and methylammoniumchloride (1.01 g, 0.015 mol) are fused by heating during 1 h up to 230 °C. The still hot melting is treated carefully with methanol to obtain a yellow precipitate. Yield: 1.33 g (52 %) pale yellow needles, m.p. 278 °C (ethanol); IR: 3255 m, 1700 s, 1650 s, 1615 sh, 1585 cm^{-1}, m; ^{1}H-NMR: δ = 2.9 (s, 3 H, N-CH_3), 3.7 (s, 3 H, ring-N-CH_3), 5.0 (s, 1 H, 3-H), 7.3–8.1 (m, 4 H, ArH).

$C_{14}H_{12}N_2O_3$	Calcd.: C 65.61	H 4.72	N 10.93
(256.3)	Found: C 65.52	H 4.80	N 10.78

9-Methylamino-5,6-dihydro-4H-benzo[ij]pyrano[2,3-b]quinolizin-8,11-dione (**9b**)

Benzopyranoquinolizininedione **4b** (2.69 g, 0.01 mol), 1,3-dimethylurea (1.1 g, 0.0125 mol) and methylammoniumchloride (0.85 g, 0.0125 mol) are reacted and worked up as described for **9a**. Yield: 1.50 g (53 %). colorless prisms, m.p. 274 °C, dec. (ethanol);

IR: 3260 m, 2960–2860 b, m, 1700 s, 1650 s, 1610 cm^{-1}, m; ^{1}H-NMR (CF_3COOH): δ = 1.95–2.5 (m, 2 H, CH_2), 3.1 (t, J

= 6 Hz, 2 H, Ar-CH_2), 3.2 (s, N-CH_3), 4.3 (t, J = 7 Hz, 2 H, N-CH_2), 5.8 (s, 1 H, 10-H), 7.2–7.9 (m, 2 H, ArH), 8.13 (dd, J = 2+7 Hz, 1 H, 1-H).

$C_{16}H_{14}N_2O_3$	Calcd.:	C 68.07	H 5.00	N 9.93
(282.3)	Found:	C 68.12	H 4.94	N 9.88

4-Isopropylamino-6-methyl-pyrano[3,2-c]quinoline-2,5(6H)-dione (**9c**)

A solution of the pyranoquinoline **4a** (1.46 g, 0.006 mol) and N,N-diisopropylcarbodiimide (0.90 g, 0.0072 mol) in abs. dimethylformamide (25 ml) is heated under reflux for 17 h. After cooling the product is precipitated by addition of water. Yield: 1.01 g (59 %), yellowish needles, m.p. 221–227 °C (acetic acid/water); IR: 3270–2860 b, 1705 s, 1650 s, 1620 cm^{-1} m; ^{1}H-NMR (CF_3COOH): δ = 1.38 (d, J = 6 Hz, 6 H, isopropyl-CH_3), 3.8–4.1 (q, J = 6 Hz, 1 H, isopropyl-CH), 3.87 (s, 3 H, N-CH_3), 5.7–6.0 (s, b, 1 H, 3-H), 7.4–8.05 (m, 3 H, ArH), 8.32 (dd, J = 2+7 Hz, 1-H).

$C_{16}H_{16}N_2O_3$	Calcd.:	C 67.59	H 5.67	N 9.86
(284.3)	Found:	C 67.04	H 5.50	N 9.53

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Address for correspondence:
Univ. Prof. Dr. Thomas Kappe
Abteilung for Organische Chemie
Institut für Organische Chemie
Karl-Franzens-Universität Graz
Heinrichstraße 28
A-8010 Graz, Austria