Synthesis of Benzo-halogenated 4-Hydroxy-2(1*H*)-quinolones

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Malondianilides **3** derived from dichloro substituted anilines **2** undergo cyclization to afford 4-hydroxy-2(1*H*)-quinolones **4** in very good yields using methane sulfonic acid-phosphorus pentoxide as catalyst. 3,4-Dichloro anilines **5** can be shown to yield two isomers, **7** and **8**, whereas 3-substituted anilines **9** afford merely 7-substituted 4-hydroxy-2(1*H*)-quinolones **11**.

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Since 4-hydroxy-2-quinolones are useful intermediates for many industrial products (*e.g.* dye stuffs [1-3], herbicides [4,5]) and contents of natural products [6], several methods for their synthesis have been developed. Four methods have been established for a wide range of derivatives of 4-hydroxy-2-quinolones: Cyclization of *N*-acetylanthranilic acid derivatives [6,7], condensation of malonates with anilines [8-10], cyclization of malondianilides with alumina trichloride [11,12] or poly phosphoric acid [13], and reactions of carbanions with isatoic anhydrides [14-19].

There has been continued interest in our laboratory in the synthesis of 4-hydroxy-2-quinolones especially from malonates. In this course we found that quinolones having more than one chlorine atom in the benzo moiety of the molecule could be synthesized only in poor or moderate yields by the existing methods [8-13]. Therefore we have developed an improved cyclization step of malondianilides.

Malondianilides **3** are readily available in good yields from the suitable substituted anilines **1** and the corresponding malonates **2**. Cyclization with alumina trichloride [12] or poly phosphoric acid [13] afforded the corresponding quinolones **4** in poor to moderate yields,

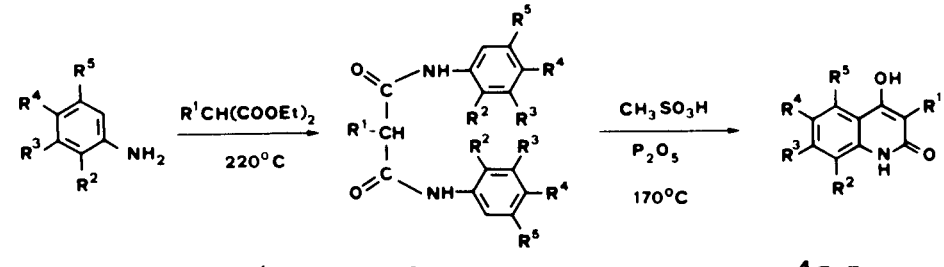
Table 1

Comparison of the yields of some 4-Hydroxyquinolin-2(1*H*)-ones

Compound No.	Catalysts (yields in %) PPA	$AlCl_3$	$MeSO_3H/P_2O_5$
3a	30	55	92
3b	27	66	90
3c	25	35	91
3d	28	48	96
3e	29	65	95
3m	29	66	92
7d/8d	– –	65	93

and in some cases the reaction failed to give a product (Table 1). The best results in this cyclization step were obtained with another catalyst, namely methane sulfonic acid containing 10% of phosphorus pentoxide [20]. Using this reaction, the cyclization could be performed in more than 90% yield and the procedure allows a simple and quick workup. The malondianilide is heated up to 140-170° and the resulting reaction mixture is then poured on ice yielding a crude product which is pure enough for further reactions. In this way all the 4-hydroxy-

Scheme 1



1	R	R	R^3	R^4
a	Cl	H	H	Cl
b	Cl	H	Cl	H
c	OMe	Cl	H	H

2	R^1
a	H
b	Ph
c	Me
d	Et
e	nBu
f	CH_2Ph
g	Cyclohexyl
h	$CH_2CH=CH_2$

R - Key: Table 2 and 4

Table 2

Malondianilides **3a-n**

Compound	R^1	R^2	R^3	R^4	R^5	Yield %	Mp (°C) solvent	Molecular Formula Molweight	Analysis Calcd./Found C	H	N	Cl
3a	H	Chloro	H	H	Chloro	24	208-15 1-propanol	$C_{15}H_{10}Cl_4N_2O_2$ 392.1	45.95 46.20	2.57 2.51	7.15 6.99	36.17 35.89
3b	Phenyl	Chloro	H	H	Chloro	24	199 1-propanol	$C_{21}H_{14}Cl_4N_2O_2$ 468.2	53.88 54.06	3.01 2.98	5.98 5.86	30.29 30.18
3c	Methyl	Chloro	H	H	Chloro	34	240-45 1-propanol	$C_{16}H_{12}Cl_4N_2O_2$ 4.06.1	47.32 47.31	2.98 3.01	6.90 6.77	34.92 34.62
3d	Ethyl	Chloro	H	H	Chloro	32	216-20 1-propanol	$C_{17}H_{14}Cl_4N_2O_2$ 420.1	48.60 48.90	3.36 3.25	6.67 6.57	33.75 33.98
3e	*n*-Butyl	Chloro	H	H	Chloro	30	185-90 1-propanol	$C_{19}H_{18}Cl_4N_2O_2$ 448.2	50.92 50.70	4.05 4.20	6.25 5.94	31.64 31.26
3f	Benzyl	Chloro	H	H	Chloro	30	208 1-propanol	$C_{22}H_{16}Cl_4N_2O_2$ 482.2	54.80 55.02	3.34 3.52	5.81 5.64	29.41 29.10
3g	Cyclohexyl	Chloro	H	H	Chloro	32	250 DMF-water	$C_{21}H_{20}Cl_4N_2O_2$ 474.2	53.19 53.17	4.25 4.24	5.91 5.88	29.90 29.72
3h	Allyl	Chloro	H	H	Chloro	22	215 DMF	$C_{16}H_{14}Cl_4N_2O_2$ 432.1	50.03 49.98	3.27 3.41	6.48 6.28	32.82 32.91
3i	H	Chloro	H	Chloro	H	24	218 DMF	$C_{15}H_{10}Cl_4N_2O_2$ 392.1	45.95 45.88	2.57 2.63	7.15 35.86	36.17
3j	Phenyl	Chloro	H	Chloro	H	24	210 1-propanol	$C_{21}H_{14}Cl_4N_2O_2$ 468.2	53.88 53.67	3.01 3.05	5.98 5.84	30.29 29.92
3k	Methyl	Chloro	H	Chloro	H	35	225 DMF-water	$C_{16}H_{12}Cl_4N_2O_2$ 406.1	47.32 47.42	2.98 2.87	6.90 6.82	34.92 34.54
3l	Ethyl	Chloro	H	Chloro	H	35	214 DMF	$C_{17}H_{14}Cl_4N_2O_2$ 420.1	48.60 48.88	3.36 3.45	6.67 6.72	33.75 33.87
3m	*n*-Butyl	Chloro	H	Chloro	H	33	204 DMF-water	$C_{19}H_{18}Cl_4N_2O_2$ 448.2	50.92 50.77	4.05 4.32	6.25 6.34	31.64 31.78
3n	Phenyl	Methoxy	Chloro	H	H	89	172 ethanol	$C_{21}H_{20}Cl_2N_2O_4$ 435.3	57.94 58.08	4.63 4.51	6.44 6.28	16.29 15.95

Table 3

Spectral Data of Malondianilides **3**

Compound	IR [cm^{-1}] NH	C=O	^{1}H-NMR (δ ppm)
3a	3280s	1690s	3.7 (s, CH_2), 7.1 + 7.3 (dd, H-4, J = 8 + 2 Hz), 7.0 (d, H-3, J = 8 Hz), 7.9 (2d, H-6, J = 2 Hz), 10.0 (s, NH)
3b	3280s	1690s	5.1 (s, CH), 7.1-7.7 (m, 9 ArH), 7.9 (2d, H-6, J = 2 Hz), 10.2 (s, NH)
3c	3260s	1690s	
3d	3260s	1690s	1.0 (t, Me, J = 7 Hz), 2.2 (q, CH_2, J = 7 Hz), 3.7 (t, CH, J = 7 Hz), 7.1 + 7.4 (dd, H-4, J = 8 + 2 Hz), 7.6 (d, H-3, J = 8 Hz), 7.9 (d, H-6, J = 2 Hz)
3e	3300s	1690s	0.7-2.1 (m, butyl), 3.7 (t, CH, J = 7 Hz), 7.1 + 7.3 (dd, H-4, J = 8 + 2 Hz), 7.4 (d, H-3, J = 8 Hz), 7.9 (d, H-6, J = 2 Hz), 1.1 (s, NH)
3f	3220s	1680s	
3g	3320s	1690s	
3h	3350s	1690s	3.9 (m, CH_2 + CH), 4.95 (d, CH_2=, J = 7 Hz), 5.5-5.7 (m, Allyl-CH), 7.1 + 7.3 (dd, H-4, J = 8 + 2 Hz), 7.9 (d, H-6, J = 2 Hz)
3i	3285s	1690s	
3j	3280s	1690s	
3k	3300s	1690s	
3l	3250s	1685s	
3m	3300s	1690s	
3n	3250s	1680s	

2-quinolones **4a-m** could be synthesized in excellent yields. A comparison of some yields with other catalysts is listed in Table 1.

Scheme 2

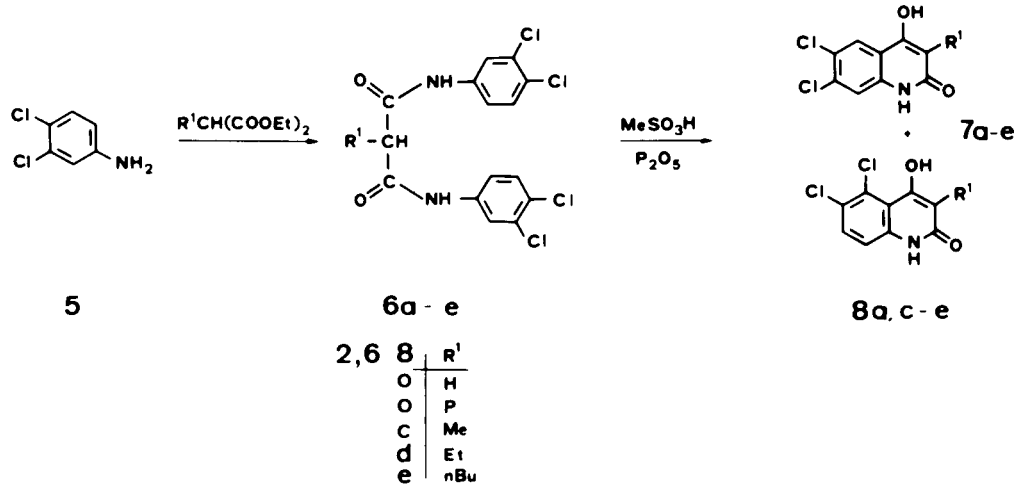


Table 4

4-Hydroxy-2(1*H*)-quinolones **4**

Compound	R^1	R^2	R^3	R^4	R^5	Yield %	Mp (°C) solvent	Molecular Formula Molweight	Analysis Calcd./Found C	H	N	Cl
4a	H	Chloro	H	H	Chloro	92	310 1-Propanol	$C_9H_5Cl_2NO_2$ 230.1	46.99 46.85	2.19 2.20	6.09 5.83	30.82 30.81
4b	Phenyl	Chloro	H	H	Chloro	90	210-15 1-Propanol	$C_{15}H_9Cl_2NO_2$ 306.1	58.85 59.18	2.96 3.15	4.58 4.36	23.16 22.90
4c	Methyl	Chloro	H	H	Chloro	96	198-204 Methanol	$C_{10}H_7Cl_2NO_2$ 244.1	49.21 49.11	2.89 2.68	5.74 5.76	29.05 28.89
4d	Ethyl	Chloro	H	H	Chloro	95	150 Methanol	$C_{11}H_9Cl_2NO_2$ 258.1	51.19 51.33	3.51 3.34	5.43 5.43	27.47 27.56
4e	*n*-Butyl	Chloro	H	H	Chloro	76	148-150 Methanol	$C_{13}H_{13}Cl_2NO_2$ 286.2	54.57 54.30	4.58 4.56	4.89 4.87	24.78 24.64
4f	Benzyl	Chloro	H	H	Chloro	91	212-216 1-Propanol	$C_{16}H_{11}Cl_2NO_2$ 320.2	60.02 59.83	3.46 3.37	4.37 4.30	22.15 22.46
4g	Cyclohexyl	Chloro	H	H	Chloro	76	227.5 DMF	$C_{15}H_{15}Cl_2NO_2$ 312.2	57.71 57.44	4.84 4.73	4.49 4.76	22.71 22.99
4h	Allyl	Chloro	H	H	Chloro	99	207 DMF	$C_{12}H_9Cl_2NO_2$ 270.1	53.36 53.46	3.36 3.26	5.19 5.21	26.25 26.46
4i	H	Chloro	H	Chloro	H	93	285 DMF	$C_9H_5Cl_2NO_2$ 230.1	46.99 47.13	2.19 2.25	6.09 5.94	30.82 31.12
4j	Phenyl	Chloro	H	Chloro	H	92	295 DMF-water	$C_{15}H_9Cl_2NO_2$ 306.1	58.85 58.55	2.96 2.92	4.58 4.83	23.16 23.11
4k	Methyl	Chloro	H	Chloro	H	92	275 DMF-water	$C_{10}H_7Cl_2NO_2$ 244.1	49.21 49.07	2.89 2.76	5.74 5.91	29.05 29.14
4l	Ethyl	Chloro	H	Chloro	H	95	242 Methanol	$C_{11}H_9Cl_2NO_2$ 258.1	51.19 51.20	3.51 3.41	5.43 5.35	27.47 27.12
4m	*n*-Butyl	Chloro	H	Chloro	H	95	220-227 Methanol	$C_{13}H_{13}Cl_2NO_2$ 286.2	54.57 54.82	4.58 4.46	4.89 4.88	24.78 24.34
4n	Phenyl	Methoxy	Chloro	H	H	71	172 Ethanol	$C_{16}H_{12}ClNO_3$ 301.7	63.69 63.87	4.01 3.89	4.64 4.52	11.75 12.02

Table 5

Spectral Data of the 4-Hydroxy-(1*H*)-quinolones **4**

Compound	IR [cm^{-1}] NH	C=O	^{1}H-NMR (δ ppm)
4a	3600s	1650s	5.85 (s, H-3), 7.0 + 7.6 (2d, H-6 + H-7, J = 8 Hz)
4b	3300b	1625s	7.35 (s, 5 ArH), 7.2 + 7.7 (2d, H-6 + H-7, J = 8 Hz)
4c	3320w	1655s	2.25 (s, Me), 7.5 + 7.8 (2d, H-6 + H-7, J = 8 Hz) [a]
4d	3400s	1645s	1.25 (t, Me, J = 7 Hz), 2.9 (q, CH_2, J = 7 Hz), 7.5 + 7.8 (2d, H-6 + H-7, J = 8 Hz) [a]
4e	3450s	1645s	0.9 (t, Me, J = 7 Hz), 1.3-1.6 (m, 2 CH_2), 2.8-2.9 (m, CH_2), 7.5 + 7.8 (2d, H-6 + H-7, J = 8 Hz) [a]
4f	3500s	1630s	3.95 (s, CH_2), 7.1-7.3 (m, 5 ArH + H-7), 7.6 (d, H-6, J = 8 Hz)
4g	3490s	1640s	
4h	3180w	1675s	3.8 (d, CH_2, J = 7 Hz), 4.9 (d, CH_2=, J = 7 Hz), 5.4-5.7 (m, Allyl-CH), 7.5 + 7.9 (2d, H-6 + H-7, J = 8 Hz) [a]
4i	3550s	1645s	
4j	3280w	1640s	
4k	3420s	1640s	2.0 (s, Me), 7.6 + 7.8 (2d, H-5 + H-7, J = 2 Hz)
4l	3360s	1640s	1.0 (t, Me, J = 7 Hz), 2.7 (q, CH_2, J = 7 Hz), 7.6-7.8 (2d, H-5 + H-7, J = 2 Hz)
4m	3360s	1635s	0.7-1.6 (m, butyl-H), 2.8 (t, CH_2), 7.5 + 7.8 (2d, H-5 + H-7, J = 2 Hz)
4n	3100b	1630s	3.8 (s, MeO), 5.0 (bs, NH), 7.0 (s, H-6, 7.3 (s, 5 ArH), 7.8 (d, H-5, J = 8 Hz)

[a] Recorded in trifluoro acetic acid.

Also 7-chloro-4-hydroxy-8-methoxy-3-phenylquinolone (**4n**) which could not be obtained by one step thermal condensation [8] from diethyl phenylmalonate **2b** and the 3-chloro-2-methoxyaniline **1c**, was prepared in this manner.

In the course of these investigations we found the malon-bis-3,4-dianilides **6** to cyclize to a mixture of two isomer quinolones **7** and **8**, with the exception of the phenylmalondianilide **6b**, which gave only the 6,7-dichloro isomer **7b**.

Table 6

Malondianilides **6** and 4-Hydroxy-2(1*H*)-quinolones **7**, **8**

Compound	R^1	Yield %	MP (°C) solvent	Molecular Formula Molweight	Analysis Calcd./Found C	H	N	Cl	IR [cm^{-1}] ^{1}H-NMR (δ ppm)
6a	H	24	224 DMF	$C_{15}H_{10}Cl_4N_2O_2$ 392.1	45.95 46.20	2.57 2.67	7.15 7.36	36.17 35.96	3285 s, 1690 s, 1585 s, 1530 s
6b	Phenyl	24	223 DMF	$C_{21}H_{14}Cl_4N_2O_2$ 468.2	53.88 53.54	3.01 3.25	5.98 6.13	30.29 29.76	3285 s, 1690 s, 1590 s, 1525 a
6c	Methyl	36	235 DMF	$C_{16}H_{12}Cl_4N_2O_2$ 406.1	47.32 47.68	2.98 3.04	6.90 6.73	34.92 35.12	3260 s, 3090 w, 2980 s, 1690 s, 1580 s
6d	Ethyl	34	225 DMF	$C_{17}H_{14}Cl_4N_2O_2$ 420.1	48.60 48.92	3.36 3.34	6.67 6.52	33.75 33.87	3245 s, 2980 s, 1690 s, 1585 s, 1525 m
6e	*n*-Butyl	33	202 DMF	$C_{19}H_{18}Cl_4N_2O_2$ 448.2	50.92 50.64	4.05 4.11	6.25 5.94	31.64 31.79	3300 s, 3260 s, 2960 s, 1690 s, 1590 s
7a + 8a	H	96	335 DMF-water	$C_9H_5Cl_2NO_2$ 230.1	46.99 46.88	2.19 2.23	6.09 6.11	30.82 30.45	3160 w, 1650 s, 1600 w, 1570 m 5.8 (s, H-3), 7.1 + 7.6 (2d, J = 8 Hz, H-7 + H-8), 7.3 + 7.5 (2s, H-5 + H-8)
7b	Phenyl	96	320 DMF-water	$C_{15}H_9Cl_2NO_2$ 306.1	58.85 58.49	2.96 2.98	4.58 4.80	23.16 23.24	3300-2900 m, 1640 s, 1570 m, 1495 s 7.3-7.6 (m, 5 ArH), 7.9 + 8.3 (2s, H-8 + H-5)
7c + 8c	Methyl	96	286 DMF-water	$C_{10}H_7Cl_2NO_2$ 244.1	49.21 49.05	2.89 3.05	5.74 5.94	29.05 28.87	3300 w, 1635 s, 1600 m, 1580 s 1.8 (s, Me), 7.1 + 7.6 (2d, H-7 + H-8, J = 8 Hz), 7.5 + 7.9 (2s, H-8 + H-5)
7d + 8d	Ethyl	92	218-220 Methanol	$C_{11}H_9Cl_2NO_2$ 258.1	51.19 50.85	3.51 3.49	5.43 5.39	27.47 27.13	3500-2980 b, 1640 s, 1600 m, 1570 m, 1.1 (t, Me, J = 7 Hz), 2.8 (q, Me, J = 7 Hz), 7.2 + 7.6 (2d, H-7 + H-8, J = 8 Hz), 7.4 + 7.9 (2s, H-8 + H-5)
7e + 8e	*n*-Butyl	96	185 DMF-water	$C_{13}H_{13}Cl_2NO_2$ 286.2	54.57 54.35	4.58 4.58	4.89 5.01	24.78 24.41	3300-2940 b, 1645 s, 1600 m, 1575 s 0.7-1.5 (m, Butyl-CH_2), 7.2 + 7.6 (2d, H-7 + H-8, J = 8 Hz), 7.4 + 7.9 (2s, H-8 + H-5)

Alkyl malondianilides **6c-e** and the 3-unsubstituted malondianilide **6a** afforded an 1:1 mixture of the 6,7-dichloro- and the 5,6-dichloro-4-hydroxy-2-quinolone **7a**, **c-d** and **8a**, **c-d**. These mixtures could not be separated even by tlc, but the aromatic signals of the proton nmr spectra can be assigned clearly to the corresponding isomers.

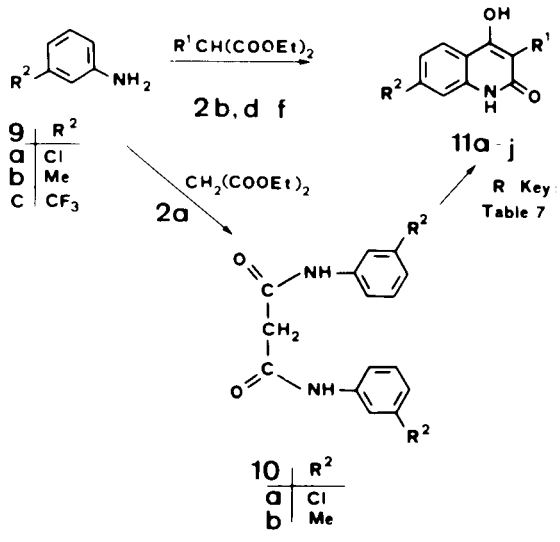
To study the range of this electrophilic attack of the amide towards the aromatic ring, some meta-monosubstituted anilines (**9**, with chlorine, methyl or trifluoromethyl as the substituent) were reacted with malonates either in one step under thermal conditions to the quinolones **11b-d**, **f-j** or *via* the malonanilides **10a,b** with methane sulfonic acid - phosphorous pentoxide catalysis to yield **11a,e**.

Table 7

Malondianilides **10** and 7-Substituted 4-Hydroxy-2-quinolones **11**

Compound	R^1	R^2	Yield %	Mp (°C) solvent	Molecular Formula Molweight	Analysis Calcd./Found C	H	N	Cl	IR [cm^{-1}] ^{1}H-NMR (δ ppm)
10a	H	Chloro	93	235 ethanol	$C_{15}H_{12}Cl_2N_2O_2$ 323.2	55.75 55.96	3.74 3.55	8.67 8.56	21.94 22.28	3280 s, 1640 s 3.4 (s, CH_2), 6.9-7.3 (m, 6 ArH), 7.7 (dd, H-2, J = 2 Hz), 8.8 (s, NH)
10b	Methyl	H	91	141 [Lit?]						
11a	H	Chloro	86	340 DMF	$C_9H_6ClNO_2$ 195.6	55.26 55.43	3.09 2.94	7.16 7.03	18.12 17.89	1670 s, 1605 s 6.3 (s, H-3), 7.1 (d, H-8, J = 2 Hz), 7.25 (dd, H-6, J = 2 + 7 Hz), 7.6 (d, H-5, J = 7 Hz), 11.8 (s, NH)
11b	Ethyl	Chloro	78	238 ethanol	$C_{11}H_{10}ClNO_2$ 223.7	59.07 58.76	4.51 4.65	6.26 6.34	15.85 16.12	3300-2180 b, 1640 s, 1600 sh, 1585 s 1.0 (t, Me, J = 7 Hz), 2.6 (q, CH_2, J = 7 Hz), 7.1 (dd, H-6, J = 7 + 1 Hz), 7.3 (d, C-8, J = 1 Hz), 7.8 (d, J = 7 Hz, C-5), 11.2 (s, NH)
11c	Benzyl	Cholor	89	246 ethanol	$C_{16}H_{12}ClNO_2$ 285.7	67.26 67.51	4.23 4.29	4.90 5.07	12.41 12.74	3140 s, 1650 s 3.9 (s, CH_2), 7.1 (dd, H-6, J = 1 + 7 Hz), 7.25 (d, H-8, J = 1 Hz), 7.9 (d, H-5, J = 7 Hz), 11.5 (NH)
11d	Phenyl	Chloro	91	315 ethanol	$C_{15}H_{10}ClNO_2$ 271.7	66.31 66.57	3.71 3.65	5.16 5.31	13.05 12.82	3300-2800 b, 1660 s, 1630 sh, 1590 s 7.1 (dd, H-6, J = 1 + 7 Hz), 7.2-7.6 (m, Ph), 7.8 (d, H-8, J = 1 Hz), 7.9 (d, H-5, J = 7 Hz)
11e	H	Methyl	86	305 DMF	$C_{10}H_9NO_2$ 175.2	68.56 68.43	5.18 5.27	8.00 8.31		3200-2920 m, 1645 s, 1605 w 2.4 (s, Me), 6.2 (s, H-3), 7.1 (dd, J = 1 + 7 Hz, H-6), 7.2 (d, H-8, J = 1 Hz), 7.8 (d, H-5, J = 7 Hz)
11f	Ethyl	Methyl	69	231 ethanol	$C_{12}H_{13}NO_2$ 203.2	70.92 71.14	6.45 6.57	6.89 6.71		3300-2800 m, 1635 s, 1620 sh, 1590 s 1.0 (t, J = 7 Hz, Me), 2.3 (s, Me), 2.5 (q, CH_2), 7.0 (dd, H-6, J = 1 + 7 Hz), 7.1 (d, J = 1 Hz, H-8), 7.8 (d, J = 7 Hz, H-5), 10.0 (s, NH)
11g	Benzyl	Methyl	78	254 ethanol	$C_{17}H_{15}NO_2$ 265.3	76.96 77.19	5.70 5.87	5.28 5.12		3200-2900 m, 1640 s, 1605 m 4.0 (s, CH_2), 7.0 (dd, J = 1 + 7 Hz, H-6), 7.2 (d, J = 1 Hz, H-8), 7.8 (d, J = 7 Hz, H-5), 10.5 (s, NH)
11h	Phenyl	Methyl	78	340 DMF	$C_{16}H_{13}NO_2$ 267.3	76.48 76.62	5.21 5.38	5.57 5.35		3200-2800 b, 1640 s, 1600 sh 2.3 (s, Me), 7.0-7.2 (m, C-6 + C-8), 7.3 (s, Ph), 7.8 (d, J = 1 + 7 Hz, H-5)
11i	Ethyl	CF_3	24	167 ethanol	$C_{12}H_{10}F_3NO_2$ 257.2	56.04 55.67	3.92 3.72	5.45 5.67		3300-2800 b, 1640 s, 1610 s 1.0 (t, Me, J = 7 Hz), 2.5 (q, CH_2, J = 7 Hz), 5.5 (s, b, NH), 7.0 (d, J = 1 Hz, H-8), 7.3 (dd, J = 1 + 7 Hz, H-6), 8.2 (d, J = 7 Hz, H-5)
11j	Phenyl	CF_3	28	224 acetic acid	$C_{16}H_{10}F_3NO_2$ 305.3	62.96 62.76	3.30 3.68	4.59 4.33		3200-2800 b, 1660 sh, 1640 m, 1610 s 7.1 (d, J = 7 Hz, H-8), 7.3 (dd, J = 1 + 7 Hz, H-6), 8.1 (d, J = 7 Hz, H-5)

Scheme 3



Although in these cases also two isomers could be expected, only one isomer was obtained, the structure of which could be unequivocal assigned to the 7-substituted 4-hydroxy-2-quinolones **11a-j** on the basis of pmr spectra.

EXPERIMENTAL

Melting points were determined on a Gallenkamp Melting point Apparatus Model MFB-595 in open capillary tubes. Infrared spectra were taken in potassium bromide pellets on a Perkin Elmer 298 spectrophotometer; the ^{1}H nmr spectra were recorded either on a Varian EM 360 or a Varian XL 200 spectrometer, respectively. Chemical shifts are reported in ppm from internal tetramethylsilane and are given in δ-units. The solvent for nmr spectra was deuterio dimethyl sulfoxide unless otherwise stated. Elemental analyses were performed on a C,H,N-automatic Carl Erba 1106 and are within 0.4 of the theoretical percentages. 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 for detection.

General Method for the Preparation of the Malondianilides **3a-n**, **6a-c** and **10**.

A mixture of the appropriate substituted aniline, **1**, **5** or **9** (0.12 mole) with the corresponding malonate **2a-h** (0.05 moles) was heated for 15-20 hours in an oil bath to 220° using a short air condenser to remove the resulting reaction alcohol. After cooling the mixture was digested with methanol, petroleum ether or ether, filtered by suction and recrystallized from the solvent listed in Table 2. Spectral data are listed in Table 3.

General Method for the Preparation of the 4-Hydroxyquinolin-2(1*H*)-ones **4a-n**, **7a-e**, **8a-e**, **11a** and **11e**.

The appropriate malondianilide, **3**, **6** or **10**, (0.1 mole) was dissolved in 60 ml of methanesulfonic acid, which contains 10% of phosphorus pentoxide, and was then heated in an oil bath for 60-80 minutes at 150-170°. After cooling the reaction mixture was poured on ice and filtered. Then the crude product was dissolved in 0.5 *N* sodium hydroxide, the alkaline solution was extracted with 100 ml of toluene and precipitated with concentrated hydrochloric acid. After filtration, the precipitate was recrystallized from the appropriate solvent (Table 4). Spectral data are listed in Table 5.

General Method for the Preparation of the 4-Hydroxyquinolin-2(1*H*)-ones **11b-d** and **11f-j**.

A mixture of the appropriate 7-substituted aniline **9a-c** (0.1 mole) and the corresponding malonate **2b**, **d-f** (0.1 mole) was heated for 3 hours to 250° using a short air condenser to remove the reaction alcohol. Then the temperature was raised to 350° for 30 minutes. After cooling, the residue was digested with methanol, the crude product filtered and dissolved in 0.5 *N* sodium hydroxide. The alkaline solution was treated with charcoal and extracted with 100 ml of toluene. Then the quinolone was precipitated with concentrated hydrochloric acid, filtered and recrystallized form the appropriate solvent (Table 6).

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