Synthesis of Novel Halogenated 4(1*H*)-Quinolones by Thermolysis of Arylaminomethylene-1,3-dioxane-4,6-diones

Sven Rotzoll,[a] Helmut Reinke,[a] Christine Fischer,[b] Peter Langer*[a,b]

[a] Institut für Chemie, Universität Rostock, Albert-Einstein-Str. 3a, 18059 Rostock, Germany
Fax +49(381)4986412; E-mail: peter.langer@uni-rostock.de

[b] Leibniz-Institut für Katalyse e.V. an der Universität Rostock, Albert-Einstein-Str. 29a, 18059 Rostock, Germany

Received 13 July 2008

Abstract: A variety of novel 4(1*H*)-quinolone derivatives were prepared by thermolysis of aminomethylene Meldrum's acid derivatives.

Key words: N-heterocycles, quinolones, cyclizations

Quinolone alkaloids are widespread in nature. For example, 4(1*H*)-quinolones **A** and **B** (Figure 1) occur in marine sponges, such as *Verongia aerophoba*[1] or *Dendrilla membranosa*,[2] in bacteria (e.g., in *Pseudomonas aeruginosa*)[3] or in terrestrial plants, such as *Galipea officinales*.[4]

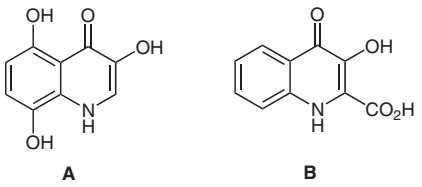


Figure 1 4(1*H*)-Quinolone alkaloids from *Verongia aerophoba*

4(1*H*)-Quinolones also constitute an important class of antibiotics (Figure 2). The activity relies on the inhibition of topoisomerase II (Gyrase-A subunit).[5,6] In addition, 4(1*H*)-quinolones represent important intermediates in organic synthesis.[7]

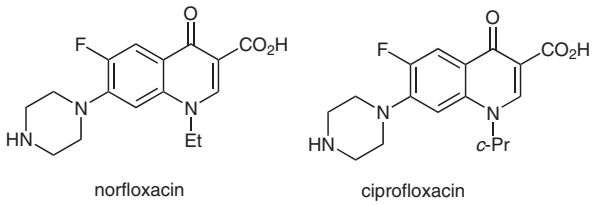


Figure 2 Antimicrobial 4(1*H*)-quinolones norfloxacin (Norfluxx®) and ciprofloxacin (Ciprobay®)

Classic syntheses of 4(1*H*)-quinolones rely on the addition of (ethoxymethylene)malonates with anilines and subsequent cyclization[8] and on the addition of maleates to *o*-aminobenzoates and subsequent cyclization.[9] However, these methods are not suitable for the synthesis of 2,3-unsubstituted 4(1*H*)-quinolones as the ester groups present at these positions have to be removed in several steps. Heindel et al. reported[10] and elegant approach to 4(1*H*)-quinolones by nucleophilic addition of anilines to methyl acetylenecarboxylate and subsequent cyclization. Some drawbacks of this method are the low yields and long reaction times in the case of electron-poor anilines. An efficient approach to 4(1*H*)-quinolones relies on the thermolysis of arylaminomethylene-1,3-dioxane-4,6-diones available from Meldrum's acid.[11,12] This method has been applied so far to the synthesis of nitro- and methoxy-substituted 4(1*H*)-quinolones. Herein, we report what is, to the best of our knowledge, the first application to the synthesis of various halogenated 4(1*H*)-quinolones. The products represent potentially useful synthetic building blocks in medicinal chemistry.

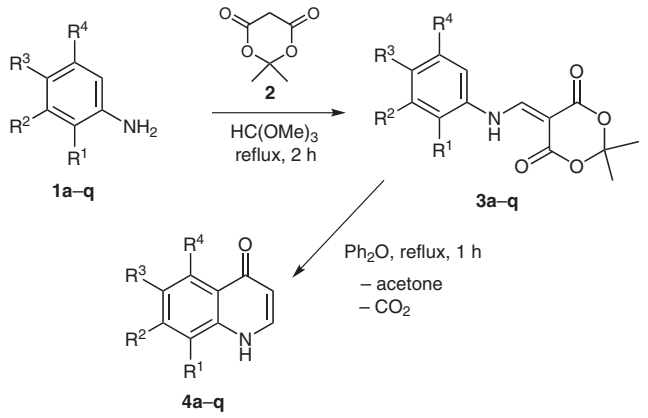
The reaction of anilines **1a–q** with Meldrum's acid (**2**) afforded arylaminomethylene-1,3-dioxane-4,6-diones **3a–q** (Table 1). Reflux of a diphenyl ether solution of the latter afforded the novel 4(1*H*)-quinolones **4a–q**. All reactions proceeded in good to excellent yields. This includes a number of chloride- and bromide-substituted 4(1*H*)-quinolones, derived from the corresponding electron-poor anilines, which could also be prepared in good yields. The method is limited to the use of symmetrical or *ortho*-substituted anilines. The thermolysis of **3l**, derived from 3-chloroaniline, resulted in the formation of a mixture of regioisomeric 4(1*H*)-quinolones.

The structures of all products were established by spectroscopic methods. The structures of **3d** and **4o** were independently confirmed by X-ray crystal structure analyses (Figure 3 and Figure 4).[13] Products **3** contain an intramolecular hydrogen bond N–H···O, which can be detected in solution (low field signal in the ^{1}H NMR spectrum) and in the solid state (crystal structure analysis of **3d**). Products **4** can exist as 4(1*H*)-quinolones or as tautomeric 4-hydroxyquinolines. All products show only one set of NMR signals. In the solid state **4o** exists in the 4(1*H*)-quinolone tautomeric form with intermolecular hydrogen bonds between the NH and O4 (the hydrogen position could be elucidated from the difference map and was refined freely).

N-Protected 4(1*H*)-quinolones represent important synthetic building blocks.[14] The reaction of 4(1*H*)-quinolones **4** with methyl, ethyl, allyl, and benzyl chloroformate **5a–d** afforded the N-protected 4(1*H*)-quinolones **6a–h**

SYNTHESIS 2009, No. 1, pp 0069–0078
Advanced online publication: 01.12.2008
DOI: 10.1055/s-0028-1083237; Art ID: C04108SS

Table 1 Synthesis of Novel 4(1*H*)-Quinolones



Products **3**,**4**	R^1	R^2	R^3	R^4	Yield (%)[a] of **3**	Yield (%)[a] of **4**
a	-$(CH)_4$-		H	H	78	61
b	Ph	H	H	H	83	75
c	H	H	*t*-Bu	H	75	55
d	Me	H	H	Me	96	67
e	H	Me	H	Me	69	76
f	Me	H	Me	Me	82	90
g	Me	H	Cl	H	73	69
h	Cl	H	Me	H	76	72
i	CF_3	H	H	H	78	84
j	H	H	I	H	53	83
k	Br	H	H	H	72	70
l	H	Br	H	H	58	73[b]
m	Br	H	Br	H	68	54
n	Cl	H	Cl	H	80	78
o	Cl	Cl	H	H	45	62
p	Cl	H	H	Cl	84	61
q	Cl	H	Cl	Cl	75	71

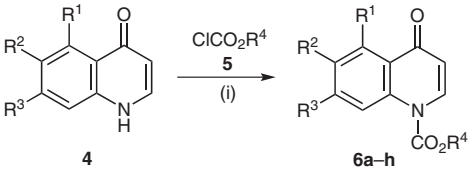
[a] Isolated yields.
[b] Mixture of regioisomeric 5- and 7-bromoquinolone (ratio 1:1.6).

(Table 2). The structure of **6c** was independently confirmed by X-ray crystal structure analysis (Figure 5).[13]

In conclusion, we have reported the synthesis of a variety of novel protected and unprotected 4(1*H*)-quinolones based on the thermolysis of aminomethylene Meldrum's acids.

All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. For ^1H and ^{13}C NMR spectra the deuterated solvents indicated were used. Mass spectrometric data were obtained by electron ionization (EI, 70 eV), chemical ionization (CI, H_2O), or electrospray ionization (ESI). For preparative-

Table 2 Synthesis of N-Protected 4(1*H*)-Quinolones **6**[a]



Product **6**	R^1	R^2	R^3	R^4	Yield (%)[b]
a	H	Cl	H	Me	71
b	H	Br	H	Me	84
c	H	Br	H	Et	70
d	H	F	H	Me	63
e	Cl	H	Cl	Me	66
f	Me	H	Me	allyl	79
g	H	F	H	allyl	84
h	H	*t*-Bu	H	Bn	45

[a] Reaction conditions: (i) **4** (1.0 equiv), NaH (2.6 equiv), $ClCO_2R^4$ (2.6 equiv), THF, 20 °C, 48 h.
[b] Isolated yields.

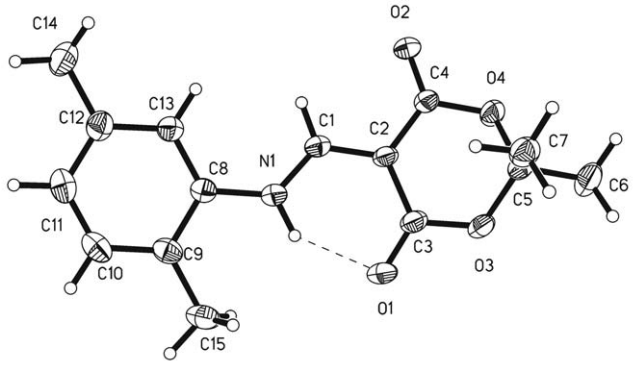


Figure 3 ORTEP plot of **3d** (50% probability level)

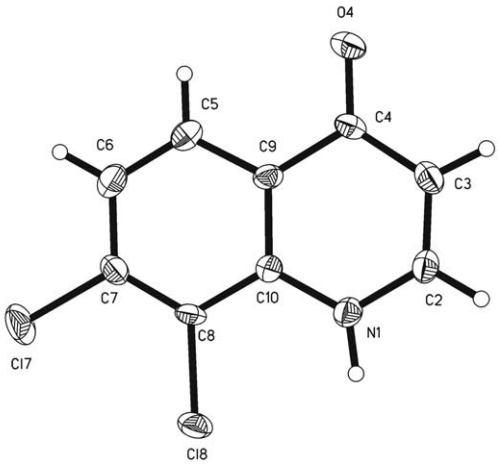


Figure 4 ORTEP plot of **4o** (50% probability level)

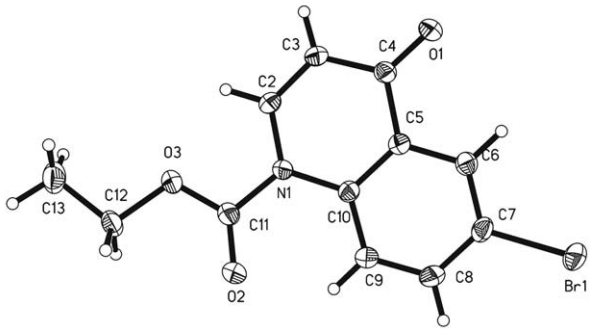


Figure 5 ORTEP plot of **6c** (50% probability level)

scale chromatography, silica gel (60–200 mesh) was used. Melting points are uncorrected.

Arylaminomethylene-1,3-dioxane-4,6-diones 3a–q; General Procedure

A solution of Meldrum's acid **2** (1.5 equiv) and trimethyl orthoformate (25.0 equiv) was heated under reflux for 2 h under argon. The solution was cooled to r.t., the appropriate aniline **1a–q** (1.0 equiv) was added and the mixture was heated under reflux for 2 h. The precipitated product was washed with MeOH (10 mL) and dried. For products that did not precipitate, the solvent was removed in vacuo and the residue was washed with MeOH (10 mL) and dried.

2,2-Dimethyl-5-[(naphthalen-1-ylamino)methylene]-1,3-dioxane-4,6-dione (3a)

Starting from Meldrum's acid **2** (7.30 g, 50.60 mmol), trimethyl orthoformate (95.7 mL, 875.00 mmol), and 1-naphthylamine (**1a**; 5.00 g, 34.90 mmol), **3a** was isolated as a yellow solid (8.11 g, 78%); mp 148 °C.

IR (KBr): 3058 (m), 2994 (m), 2939 (m), 1724 (s), 1683 (br, s), 1634 (br, s), 1594 (br, s), 1574 (br, m), 1279 (br, s), 1205 (br, s), 1010 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.79 (s, 6 H, 2 × CH_3), 7.39–7.50 (m, 2 H, Ar), 7.54–7.64 (m, 2 H, Ar), 7.77–7.99 (m, 3 H, Ar), 8.72 (d, ^3J = 13.9 Hz, 1 H, =CH), 11.95 (br d, ^3J = 13.9 Hz, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.1 (2 × CH_3), 80.0 (O*C*CH_3), 105.3 (C), 114.9, 120.2 (CH_{Ar}), 125.4 (C), 125.6, 127.2, 127.5, 127.6, 128.8 (CH_{Ar}), 134.1 (C), 154.4 (=CH), 163.5, 166.1 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 297 ($[M]^+$, 18), 239 (55), 195 (63), 167 (100), 139 (26), 127 (20), 115 (9).

Anal. Calcd for $C_{17}H_{15}NO_4$ (297.31): C, 68.68; H, 5.09; N, 4.71.; Found: C, 68.57; H, 5.08; N, 4.52.

5-[(Biphenyl-2-ylamino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione (3b)

Starting from Meldrum's acid **2** (4.32 g, 30.00 mmol), trimethyl orthoformate (56.6 mL, 517.50 mmol), and 2-phenylaniline (**1b**; 3.50 g, 20.70 mmol), **3b** was isolated as a yellow solid (5.79 g, 83%); mp 122 °C.

IR (KBr): 3187 (br, m), 3089 (m), 2999 (m), 1730 (s), 1685 (br, s), 1631 (br, s), 1605 (br, s), 1441 (br, s), 1267 (br, s), 1118 (br, s), 1008 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.68 (s, 6 H, 2 × CH_3), 7.35–7.53 (m, 9 H, Ar), 8.65 (d, ^3J = 14.2 Hz, 1 H, =CH), 11.37 (br d, ^3J = 14.2 Hz, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.1 (2 × CH_3), 87.5 (O*C*CH_3), 105.0 (C), 116.1, 126.7, 128.7, 129.2, 129.2, 129.4, 131.4 (CH_{Ar}), 133.8, 135.3, 136.3 (C), 152.1 (=CH), 163.7, 165.1 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 323 ($[M]^+$, 26), 265 (85), 220 (57), 193 (100), 180 (63), 167 (20), 152 (23).

Anal. Calcd for $C_{19}H_{17}NO_4$ (323.34): C, 70.58; H, 5.30; N, 4.33. Found: C, 70.67; H, 5.25; N, 4.20.

5-{[(4-*tert*-Butylphenyl)amino]methylene}-2,2-dimethyl-1,3-dioxane-4,6-dione (3c)

Starting from Meldrum's acid **2** (7.00 g, 48.60 mmol), trimethyl orthoformate (91.5 mL, 837.80 mmol), and 4-*tert*-butylaniline (**1c**; 5.00 g, 33.50 mmol), **3c** was isolated as a yellow solid (7.62 g, 75%); mp 148 °C.

IR (KBr): 3190 (br, m), 3059 (w), 2962 (m), 2870 (w), 1733 (s), 1682 (br, s), 1623 (br, s), 1579 (s), 1456 (br, s), 1272 (br, s), 1141 (m), 1003 (m), 992 cm^{-1} (m).

^1H NMR (250 MHz, $CDCl_3$): δ = 1.32 (s, 9 H, 3 × CH_3), 1.74 (s, 6 H, 2 × CH_3), 7.17 (d, ^3J = 8.8 Hz, 2 H, Ar), 7.43 (d, ^3J = 8.8 Hz, 2 H, Ar), 8.62 (d, ^3J = 14.5 Hz, 1 H, =CH), 11.23 (br d, ^3J = 14.5 Hz, 1 H, NH).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 27.0 (2 × CH_3), 31.2 (3 CH_3), 34.6 (*C*CH_3), 86.8 (O*C*CH_3), 105.1 (C), 117.7, 127.0 (CH_{Ar}), 135.2, 150.3 (C), 152.5 (=CH), 163.6, 165.7 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 303 ($[M]^+$, 3), 245 (7), 201 (25), 186 (100), 160 (29), 144 (34), 117 (10).

Anal. Calcd for $C_{17}H_{21}NO_4$ (303.35): C, 67.31; H, 6.98; N, 4.62. Found: C, 67.15; H, 6.84; N, 4.46.

5-{[(2,5-Dimethylphenyl)amino]methylene}-2,2-dimethyl-1,3-dioxane-4,6-dione (3d)

Starting from Meldrum's acid **2** (5.88 g, 40.80 mmol), trimethyl orthoformate (85.6 mL, 783.80 mmol), and 2,5-dimethylaniline (**1d**; 3.80 g, 31.40 mmol), **3d** was isolated as a yellow solid (8.35 g, 96%); mp 163 °C.

IR (KBr): 3162 (br, w), 3061 (m), 2985 (m), 1725 (s), 1669 (br, s), 1636 (s), 1608 (br, s), 1444 (s), 1275 (br, s), 1022 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.76 (s, 6 H, 2 × CH_3), 2.36 (s, 6 H, 2 × CH_3), 6.99 (d, ^3J = 7.6 Hz, 1 H, Ar), 7.13 (s, 1 H, Ar), 7.14 (d, ^3J = 7.6 Hz, 1 H, Ar), 8.64 (d, ^3J = 13.9 Hz, 1 H, =CH), 11.38 (br d, ^3J = 13.9 Hz, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.9, 21.1 (CH_3), 27.1 (2 × CH_3), 87.2 (O*C*CH_3), 105.1 (C), 117.0 (CH_{Ar}), 125.0 (C), 127.6, 131.4 (CH_{Ar}), 136.3, 137.7 (C), 152.8 (=CH), 163.7, 165.8 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 275 ($[M]^+$, 14), 217 (49), 173 (30), 158 (100), 144 (36), 130 (33), 103 (10).

Anal. Calcd for $C_{15}H_{17}NO_4$ (275.30): C, 65.44; H, 6.22; N, 5.09. Found: C, 65.33; H, 6.26; N, 5.00.

5-{[(3,5-Dimethylphenyl)amino]methylene}-2,2-dimethyl-1,3-dioxane-4,6-dione (3e)

Starting from Meldrum's acid **2** (5.88 g, 40.80 mmol), trimethyl orthoformate (85.6 mL, 783.80 mmol), and 3,5-dimethylaniline (**1e**; 3.80 g, 31.40 mmol), **3e** was isolated as a yellow solid (5.93 g, 69%); mp 168 °C.

IR (KBr): 3165 (br, m), 3062 (m), 2988 (m), 1722 (s), 1672 (br, s), 1633 (br, s), 1595 (br, s), 1483 (s), 1283 (br, s), 1205 (br, s), 1013 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.75 (s, 6 H, 2 × CH_3), 2.34 (s, 6 H, 2 × CH_3), 6.88 (s, 2 H, Ar), 6.90 (s, 1 H, Ar), 8.63 (d, ^3J = 14.3 Hz, 1 H, =CH), 11.15 (br d, ^3J = 14.3 Hz, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.3 (2 × CH_3), 27.1 (2 × CH_3), 86.9 (O*C*CH_3), 105.1 (C), 115.8, 128.6 (CH_{Ar}), 137.7, 140.1 (C), 152.5 (=CH), 163.7, 165.5 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 275 ([M]$^+$, 37), 217 (84), 172 (39), 158 (100), 145 (63), 130 (49), 103 (10).

Anal. Calcd for $C_{15}H_{17}NO_4$ (275.30): C, 65.44; H, 6.22; N, 5.09. Found: C, 65.29; H, 6.26; N, 4.93.

2,2-Dimethyl-5-{[(2,4,5-trimethylphenyl)amino]methylene}-1,3-dioxane-4,6-dione (3f)

Starting from Meldrum's acid **2** (6.90 g, 47.88 mmol), trimethyl orthoformate (90.0 mL, 824.09 mmol), and 2,4,5-trimethylaniline (**1f**; 4.37 g, 32.32 mmol), **3f** was isolated as a yellow solid (7.40 g, 82%); mp 175 °C.

IR (ATR): 3003 (w), 2945 (w), 1721 (m), 1663 (m), 1606 (br, m), 1432 (br, m), 1264 (br, m), 1198 (br, m), 929 (m), 773 cm^{-1} (m).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.75 (s, 6 H, 2 CH_3), 2.23 (s, 3 H, CH_3), 2.26 (s, 3 H, CH_3), 2.32 (s, 3 H, CH_3), 7.00 (s, 1 H, Ar), 7.07 (s, 1 H, Ar), 8.59 (d, ^3J = 14.3 Hz, 1 H, =CH), 11.35 (br d, ^3J = 14.3 Hz, 1 H, NH).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 16.7, 19.2, 19.5 (CH_3), 27.0 (2 × CH_3), 86.7 (O*C*CH_3), 105.1 (C), 117.7 (CH_{Ar}), 125.3 (C), 132.6 (CH_{Ar}), 134.1, 135.5, 136.1 (C), 152.8 (=CH), 163.8, 165.9 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 289 ([M]$^+$, 15), 231 (33), 187 (51), 172 (100), 158 (15), 144 (23), 91 (7).

Anal. Calcd for $C_{16}H_{19}NO_4$ (289.23): C, 66.42; H, 6.62; N, 4.84. Found: C, 66.32; H, 6.46; N, 4.76.

5-{[(4-Chloro-2-methylphenyl)amino]methylene}-2,2-dimethyl-1,3-dioxane-4,6-dione (3g)

Starting from Meldrum's acid **2** (7.37 g, 51.20 mmol), trimethyl orthoformate (96.4 mL, 882.50 mmol), and 4-chloro-2-methylaniline (**1g**; 5.00 g, 35.30 mmol), **3g** was isolated as a yellow solid (7.59 g, 73%); mp 185 °C.

IR (KBr): 3197 (br, m), 3058 (m), 2992 (m), 1724 (s), 1677 (br, s), 1623 (br, s), 1595 (s), 1463 (s), 1300 (br, s), 1200 (s), 1007 cm^{-1} (m).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.75 (s, 6 H, 2 × CH_3), 2.38 (s, 3 H, CH_3), 7.25 (m, 3 H, Ar), 8.58 (d, ^3J = 14.0 Hz, 1 H, =CH), 11.39 (br d, ^3J = 14.0 Hz, 1 H, NH).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 17.2 (CH_3), 27.1 (2 × CH_3), 87.8 (O*C*CH_3), 105.3 (C), 117.6, 127.7 (CH_{Ar}), 129.9 (C), 131.4 (CH_{Ar}), 132.0, 135.2 (C), 152.5 (=CH), 163.3, 165.8 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 295 ([M]$^+$, 29), 237 (100), 193 (68), 178 (59), 165 (46), 158 (29), 130 (38).

Anal. Calcd for $C_{14}H_{14}ClNO_4$ (295.72): C, 56.86; H, 4.77; N, 4.74: Found: C, 56.85; H, 4.70; N, 4.58.

5-{[(2-Chloro-4-methylphenyl)amino]methylene}-2,2-dimethyl-1,3-dioxane-4,6-dione (3h)

Starting from Meldrum's acid **2** (7.37 g, 51.20 mmol), trimethyl orthoformate (96.4 mL, 882.50 mmol), and 2-chloro-4-methylaniline (**1h**; 5.00 g, 35.30 mmol), **3h** was isolated as a yellow solid (7.92 g, 76%); mp 139 °C.

IR (KBr): 3187 (br, w), 3060 (w), 2986 (m), 2937 (w), 1728 (s), 1680 (br, s), 1615 (br, s), 1441 (br, s), 1270 (br, s), 1051 (m), 993 (m), 930 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.76 (s, 6 H, 2 × CH_3), 2.36 (s, 3 H, CH_3), 7.16 (d, ^3J = 8.3 Hz, 1 H, Ar), 7.28 (s, 1 H, Ar), 7.29 (d, ^3J = 8.3 Hz, 1 H, Ar), 8.62 (d, ^3J = 14.0 Hz, 1 H, =CH), 11.62 (br d, ^3J = 14.0 Hz, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.8 (CH_3), 27.2 (2 × CH_3), 88.2 (O*C*CH_3), 105.3 (C), 116.7 (CH_{Ar}), 124.4 (C), 129.1, 130.8 (CH_{Ar}), 132.6, 137.8 (C), 151.7 (=CH), 163.6, 165.3 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 295 ([M]$^+$, 34), 237 (100), 193 (83), 178 (80), 165 (66), 130 (62), 117 (25).

Anal. Calcd for $C_{14}H_{14}ClNO_4$ (295.72): C, 56.86; H, 4.77; N, 4.74. Found: C, 56.96; H, 4.76; N, 4.66.

2,2-Dimethyl-5-{([(2-(trifluoromethyl)phenyl]amino}methylene)-1,3-dioxane-4,6-dione (3i)

Starting from Meldrum's acid **2** (6.48 g, 45.00 mmol), trimethyl orthoformate (84.9 mL, 776.40 mmol), and 2-(trifluoromethyl)aniline (**1i**; 5.00 g, 31.10 mmol), **3i** was isolated as a yellow solid (7.64 g, 78%); mp 128 °C.

IR (KBr): 3162 (br, m), 3052 (m), 2978 (m), 1736 (s), 1678 (br, s), 1623 (s), 1590 (s), 1435 (br, s), 1270 (br, s), 1200 (br, s), 1009 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.79 (s, 6 H, 2 × CH_3), 7.42–7.53 (m, 2 H, Ar), 7.69–7.76 (m, 2 H, Ar), 8.65 (d, ^3J = 13.4 Hz, 1 H, =CH), 11.74 (br d, ^3J = 13.4 Hz, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.2 (2 × CH_3), 89.4 (O*C*CH_3), 105.4 (C), 119.4 (CH), 121.3 (q, $^1J_{F,C}$ = 246 Hz, CF_3), 122.0, 124.7 (C), 126.6, 127.3, 133.8 (CH_{Ar}), 136.3 (C), 153.6 (=CH), 163.2, 165.2 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 315 ([M]$^+$, 19), 257 (100), 229 (75), 212 (65), 192 (15), 165 (29), 145 (29).

Anal. Calcd for $C_{14}H_{12}F_3NO_4$ (315.24): C, 53.34; H, 3.84; N, 4.44. Found: C, 53.37; H, 3.84; N, 4.36.

5-{[(4-Iodophenyl)amino]methylene}-2,2-dimethyl-1,3-dioxane-4,6-dione (3j)

Starting from Meldrum's acid **2** (4.77 g, 33.10 mmol), trimethyl orthoformate (63.3 mL, 570.00 mmol), and 4-iodoaniline (**1j**, 5.00 g, 22.80 mmol), **3j** was isolated as a yellow solid (4.51 g, 53%); mp 208–210 °C.

IR (KBr): 3213 (br, w), 3090 (w), 2993 (w), 1716 (m), 1671 (br, s), 1611 (br, s), 1573 (br, s), 1448 (br, s), 1262 (br, s), 1200 (br, s), 1661 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.76 (s, 6 H, 2 × CH_3), 7.02 (d, ^3J = 6.9 Hz, 2 H, Ar), 7.75 (d, ^3J = 6.9 Hz, 2 H, Ar), 8.60 (d, ^3J = 14.2 Hz, 1 H, =CH), 11.21 (br d, ^3J = 14.2 Hz, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.1 (2 × CH_3), 87.2 (O*C*CH_3), 90.7, 105.4 (C), 119.7 (2 CH_{Ar}), 137.6 (C), 139.1 (2 CH_{Ar}), 152.2 (=CH), 163.4, 165.6 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 373 ([M]$^+$, 38), 315 (100), 271 (76), 245 (17), 203 (14), 144 (44), 116 (62).

Anal. Calcd for $C_{13}H_{12}INO_4$ (373.14): C, 41.84; H, 3.24; N, 3.75. Found: C, 41.82; H, 3.16; N, 3.71.

5-{[(2-Bromophenyl)amino]methylene}-2,2-dimethyl-1,3-dioxane-4,6-dione (3k)

Starting from Meldrum's acid **2** (6.08 g, 42.20 mmol), trimethyl orthoformate (79.4 mL, 726.80 mmol), and 2-bromoaniline (**1k**; 5.00 g, 29.10 mmol), **3k** was isolated as a yellow solid (6.84 g, 72%); mp 160 °C.

IR (KBr): 3191 (br, w), 3069 (w), 2997 (m), 2942 (w), 1729 (s), 1690 (br, s), 1611 (br, s), 1438 (s), 1277 (br, s), 1020 (m), 751 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.77 (s, 6 H, 2 × CH_3), 7.12–7.18 (m, 1 H, Ar), 7.41–7.43 (m, 2 H, Ar), 7.64–7.67 (m, 1 H, Ar), 8.64 (d, ^3J = 14.0 Hz, 1 H, =CH), 11.64 (br d, ^3J = 14.0 Hz, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.2 (2 × CH_3), 88.7 (O*C*CH_3), 105.4, 114.6 (C), 117.1, 127.5, 129.1, 133.8 (CH_{Ar}), 136.4 (C), 151.9 (=CH), 163.4, 165.2 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 325 ([M]$^+$, ^{79}Br, 19), 269 (100), 239 (15), 224 (59), 195 (58), 171 (16), 155 (15), 116 (71), 76 (11).

Anal. Calcd for $C_{13}H_{12}BrNO_4$ (326.14): C, 47.87; H, 3.71; N, 4.29. Found: C, 47.78; H, 3.26; N, 4.16.

5-{[(3-Bromophenyl)amino]methylene}-1,3-dioxane-4,6-dione (3l)

Starting from Meldrum's acid **2** (4.20 g, 30.53 mmol), trimethyl orthoformate (55.0 mL, 499.90 mmol), and 3-bromoaniline (**1l**; 2.20 mL, 20.35 mmol), **3l** was isolated as a yellow solid (3.79 g, 58%); mp 164–165 °C.

IR (ATR): 3211 (br, w), 2988 (w), 1724 (m), 1673 (br, s), 1617 (s), 1574 (s), 1459 (s), 1196 (br, s), 1070 (m), 1010 cm^{-1} (br, m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.76 (s, 6 H, 2 CH_3), 7.17–7.21 (m, 1 H, Ar), 7.28–7.34 (m, 1 H, Ar), 7.39–7.45 (m, 2 H, Ar), 8.60 (d, ^3J = 14.1 Hz, 1 H, =CH), 11.20 (br d, ^3J = 14.1 Hz, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.1 (2 × CH_3), 81.1 (O*C*CH_3), 105.4 (C), 116.7, 121.1 (CH_{Ar}), 123.8 (C), 129.7, 131.4 (CH_{Ar}), 139.1 (C), 152.4 (=CH), 163.3, 165.4 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 327 (M$^+$, ^{81}Br, 18), 325 (M$^+$, ^{79}Br, 18), 269 (95), 267 (95), 224 (100), 222 (98), 197 (44), 171 (12), 155 (18), 116 (54), 89 (21).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{12}BrNO_4$ ([M]$^+$, ^{79}Br) 324.99442; found: 324.99343.

5-{[(2,4-Dibromophenyl)amino]methylene}-2,2-dimethyl-1,3-dioxane-4,6-dione (3m)

Starting from Meldrum's acid **2** (4.15 g, 28.90 mmol), trimethyl orthoformate (54.0 mL, 498.20 mmol), and 2,4-dibromoaniline (**1m**; 5.00 g, 19.90 mmol), **3m** was isolated as a colorless solid (5.48 g, 68%); mp 184 °C.

IR (KBr): 3096 (m), 3067 (m), 2987 (m), 1725 (s), 1677 (br, s), 1601 (br, s), 1435 (br, s), 1389 (m), 1279 (br, s), 1199 (br, s), 999 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.77 (s, 6 H, 2 × CH_3), 7.29 (d, ^3J = 8.5 Hz, 1 H, Ar), 7.54 (dd, ^3J = 8.5 Hz, ^4J = 2.1 Hz, 1 H, Ar), 7.79 (d, ^4J = 2.1 Hz, 1 H, Ar), 8.59 (d, ^3J = 13.8 Hz, 1 H, =CH), 11.60 (br d, ^3J = 13.8 Hz, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.2 (2 × CH_3), 89.2 (O*C*CH_3), 105.5, 115.1 (C), 118.0 (CH_{Ar}), 119.6 (C), 132.1 (CH_{Ar}), 135.7 (C), 136.0 (CH_{Ar}), 151.5 (=CH), 163.2, 165.2 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 403 ([M]$^+$, 10), 347 (96), 303 (98), 275 (63), 251 (33), 222 (100), 194 (54), 169 (14), 115 (43).

Anal. Calcd for $C_{13}H_{11}Br_2NO_4$ (405.04): C, 38.55; H, 2.74; N, 3.46: Found: C, 38.44; H, 2.59; N, 3.38.

5-{[(2,4-Dichlorophenyl)amino]methylene}-2,2-dimethyl-1,3-dioxane-4,6-dione (3n)

Starting from Meldrum's acid **2** (6.45 g, 44.80 mmol), trimethyl orthoformate (85.0 mL, 772.50 mmol), and 2,4-dichloroaniline (**1n**; 5.00 g, 30.90 mmol), **3n** was isolated as a colorless solid (7.81 g, 80%); mp 193 °C.

IR (KBr): 3148 (br, m), 3075 (m), 2999 (br, w), 1724 (s), 1685 (br, s), 1618 (br, s), 1443 (br, s), 1289 (br, s), 1206 (s), 1103 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.77 (s, 6 H, 2 × CH_3), 7.37 (m, 2 H, Ar), 7.51 (s, 1 H, Ar), 8.62 (d, ^3J = 13.8 Hz, 1 H, =CH), 11.64 (br d, ^3J = 13.8 Hz, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.2 (2 × CH_3), 89.4 (O*C*CH_3), 105.5 (C), 117.5 (CH_{Ar}), 125.3 (C), 128.7, 130.3 (CH_{Ar}), 132.0, 133.9 (C), 151.5 (=CH), 163.2, 165.2 (C=O).

MS (CI, pos.): *m*/*z* (%) = 316 ([M + H]$^+$, 100).

Anal. Calcd for $C_{13}H_{11}Cl_2NO_4$ (316.14): C, 49.39; H, 3.51; N, 4.43. Found: C, 49.16; H, 3.46; N, 4.32.

5-{[(2,3-Dichlorophenyl)amino]methylene}-2,2-dimethyl-1,3-dioxane-4,6-dione (3o)

Starting from Meldrum's acid **2** (6.45 g, 44.80 mmol), trimethyl orthoformate (85.0 mL, 772.50 mmol), and 2,3-dichloroaniline (**1o**; 5.00 g, 30.90 mmol), **3o** was isolated as a colorless solid (4.44 g, 45%); mp 159 °C.

IR (KBr): 3157 (br, w), 3087 (m), 2997 (w), 1724 (s), 1686 (br, s), 1618 (br, s), 1417 (s), 1291 (br, s), 1010 cm^{-1} (br, m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.77 (s, 6 H, 2 × CH_3), 7.29–7.39 (m, 3 H, Ar), 8.64 (d, ^3J = 13.8 Hz, 1 H, =CH), 11.72 (br d, ^3J = 13.8 Hz, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.2 (2 × CH_3), 89.4 (O*C*CH_3), 105.5 (C), 114.7 (CH_{Ar}), 123.5 (C), 127.6, 128.3 (CH_{Ar}), 134.7, 136.8 (C), 151.7 (=CH), 163.2, 165.2 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 315 ([M]$^+$, 12), 257 (61), 213 (100), 185 (93), 145 (25), 123 (17).

Anal. Calcd for $C_{13}H_{11}Cl_2NO_4$ (316.14): C, 49.39; H, 3.51; N, 4.43. Found: C, 49.24; H, 3.37; N, 4.33.

5-{[(2,5-Dichlorophenyl)amino]methylene}-2,2-dimethyl-1,3-dioxane-4,6-dione (3p)

Starting from Meldrum's acid **2** (6.45 g, 44.80 mmol), trimethyl orthoformate (85.0 mL, 772.50 mmol), and 2,5-dichloroaniline (**1p**; 5.00 g, 30.90 mmol), **3p** was isolated as a colorless solid (8.15 g, 84%); mp 186 °C.

IR (KBr): 3135 (br, w), 3091 (w), 3063 (m), 3000 (w), 1727 (s), 1690 (br, s), 1625 (br, s), 1442 (s), 1202 (br, s), 1101 (s), 826 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.77 (s, 6 H, 2 × CH_3), 7.18 (d, ^3J = 8.6 Hz, 1 H, Ar), 7.42 (d, ^3J = 8.6 Hz, 1 H, Ar), 7.44 (s, 1 H, Ar), 8.61 (d, ^3J = 13.8 Hz, 1 H, =CH), 11.62 (br d, ^3J = 13.8 Hz, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.2 (2 × CH_3), 89.6 (O*C*CH_3), 105.6 (C), 116.9 (CH_{Ar}), 122.7 (C), 126.9, 131.4 (CH_{Ar}), 134.4, 136.0 (C), 151.3 (=CH), 163.1, 165.1 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 315 ([M]$^+$, 12), 257 (50), 212 (80), 178 (100), 150 (27), 123 (17).

Anal. Calcd for $C_{13}H_{11}Cl_2NO_4$ (316.14): C, 49.39; H, 3.51; N, 4.43. Found: C, 49.39; H, 2.96; N, 4.34.

2,2-Dimethyl-5-{[(2,4,5-trichlorophenyl)amino]methylene}-1,3-dioxane-4,6-dione (3q)

Starting from Meldrum's acid **2** (4.41 g, 30.60 mmol), trimethyl orthoformate (60.4 mL, 552.50 mmol), and 2,4,5-trichloroaniline (**1q**; 4.34 g, 22.10 mmol), **3q** was isolated as a colorless solid (5.80 g, 75%); mp 225 °C.

IR (KBr): 3125 (w), 3081 (w), 3053 (m), 3003 (m), 1724 (s), 1675 (br, s), 1625 (br, s), 1434 (s), 1287 (br, s), 917 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.77 (s, 6 H, 2 × CH_3), 7.56 (s, 1 H, Ar), 7.60 (s, 1 H, Ar), 8.58 (d, ^3J = 13.4 Hz, 1 H, =CH), 11.59 (br d, ^3J = 13.4 Hz, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.2 (2 × CH_3), 90.0 (O*C*CH_3), 105.7 (C), 118.0 (CH_{Ar}), 123.1, 130.2 (C), 131.5 (CH_{Ar}), 132.9, 134.6 (C), 151.1 (=CH), 163.0, 165.1 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 351 ([M]$^+$, 11), 293 (51), 248 (80), 212 (100), 184 (20), 157 (11).

Anal. Calcd for $C_{13}H_{10}Cl_3NO_4$ (350.58): C, 44.54; H, 2.88, N, 4.00. Found: C, 44.62; H, 2.83; N, 3.83.

4(1*H*)-Quinolones 4a–q; General Procedure

A mixture of the respective starting material **3a–q** (1.0 equiv) and diphenyl ether (2 mL per 1 mmol of **3**) was heated under reflux for 1 h. The solution was allowed to cool to r.t. and hexane (1 mL per 1 mmol of **3**) was added. The precipitate formed was collected by filtration, washed with hexane (50 mL), and dried in vacuo.

Benzo[*h*]quinolin-4(1*H*)-one (4a)

Starting from **3a** (5.00 g, 16.82 mmol) and diphenyl ether (34 mL), **4a** was isolated as a brownish solid (2.02 g, 61%); mp 246–249 °C.

IR (KBr): 3225 (br, m), 3175 (br, m), 3051 (br, m), 1629 (br, s), 1560 (br, s), 1528 (br, s), 1426 (s), 1255 (m), 1185 (m), 807 cm^{-1} (br, m).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 6.30 (br s, 1 H, CH), 7.71–7.76 (m, 3 H, Ar), 8.01–8.15 (m, 3 H, Ar), 8.69 (br s, 1 H, CH), 12.20 (br s, 1 H, NH).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 118.6, 121.6, 122.0 (CH), 122.5, 123.4 (C), 123.5, 126.8 (CH), 128.4 (C), 128.6, 130.0 (CH), 134.2 (C), 138.4 (CH), 176.6 (C).

MS (EI, 70 eV): *m*/*z* (%) = 195 ([M]$^+$, 100), 167 (30), 149 (6), 139 (16), 127 (7), 97 (14), 84 (26).

HRMS (EI): *m*/*z* calcd for $C_{13}H_9NO$ ([M]$^+$): 195.06787; found: 195.06752.

8-Phenylquinolin-4(1*H*)-one (4b)

Starting from **3b** (1.50 g, 4.64 mmol) and diphenyl ether (10 mL), **4b** was isolated as a brownish solid (0.77 g, 75%); mp 201–203 °C.

IR (KBr): 3173 (br, m), 3060 (m), 3029 (m), 1619 (m), 1560 (br, m), 1441 (br, m), 1337 (br, m), 1179 (m), 751 (s), 695 cm^{-1} (s).

^{1}H NMR (300 MHz, acetone-d_6): δ = 6.07 (d, ^3J = 7.5 Hz, 1 H, CH), 7.39 (dd, ^3J = 7.5 Hz, ^3J = 7.5 Hz, 1 H, Ar), 7.46–7.54 (m, 6 H, Ar), 7.79 (d, ^3J = 7.5 Hz, 1 H, CH), 8.25 (dd, ^3J = 7.5 Hz, ^4J = 1.6 Hz, 1 H, Ar), 9.97 (br s, 1 H, NH).

^{13}C NMR (75 MHz, acetone-d_6): δ = 110.0, 123.6, 126.0 (CH), 127.7 (C), 129.2, 130.1, 130.4 (CH), 132.4 (C), 133.3 (CH), 137.9 (C), 139.9 (CH), 178.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 221 ([M]$^+$, 100), 193 (35), 165 (13), 139 (6), 95 (9), 83 (7).

Anal. Calcd for $C_{15}H_{11}NO$ (221.25): C, 81.43; H, 5.01; N, 6.33. Found: C, 81.52; H, 5.08; N, 6.05.

6-*tert*-Butylquinolin-4(1*H*)-one (4c)

Starting from **3c** (3.50 g, 11.54 mmol) and diphenyl ether (24 mL), **4b** was isolated as a brownish solid (1.28 g, 55%); mp 290–297 °C.

IR (KBr): 3054 (br, w), 2960 (m), 2867 (m), 1637 (m), 1595 (br, m), 1542 (br, m), 1486 (br, s), 1362 (br, m), 1203 (br, m), 1157 (m), 824 cm^{-1} (br, s).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.33 (s, 9 H, 3CH_3), 6.02 (d, ^3J = 7.4 Hz, 1 H, CH), 7.50 (d, ^3J = 8.8 Hz, 1 H, Ar), 7.75 (dd, ^3J = 8.8 Hz, ^4J = 2.2 Hz, 1 H, Ar), 7.87 (d, ^3J = 7.4 Hz, 1 H, CH), 8.06 (d, ^4J = 2.2 Hz, 1 H, Ar), 11.73 (br s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 31.0 (3 CH_3), 34.4 (CCH_3), 108.4, 118.1, 119.9 (CH), 125.3 (C), 129.7 (CH), 138.0 (C), 139.0 (CH), 145.5, 176.9 (C).

MS (EI, 70 eV): *m*/*z* (%) = 201 ([M]$^+$, 29), 186 (100), 170 (6), 158 (12), 146 (7), 115 (4).

Anal. Calcd for $C_{13}H_{15}NO$ (201.26): C, 77.58; H, 7.51; N, 6.96. Found: C, 77.55; H, 7.60; N, 6.74.

5,8-Dimethylquinolin-4(1*H*)-one (4d)

Starting from **3d** (5.00 g, 16.16 mmol) and diphenyl ether (36 mL), **4d** was isolated as a brownish solid (2.18 g, 67%); mp 208–210 °C.

IR (KBr): 3173 (br, w), 3104 (br, m), 2972 (br, m), 1608 (m), 1560 (br, s), 1519 (br, s), 1450 (m), 1209 (s), 1021 (m), 805 cm^{-1} (s).

^{1}H NMR (400 MHz, CD_3OD): δ = 2.42 (s, 3 H, CH_3), 2.83 (s, 3 H, CH_3), 6.22 (d, ^3J = 7.3 Hz, 1 H, CH), 6.92 (d, ^3J = 7.4 Hz, 1 H, Ar), 7.26 (d, ^3J = 7.4 Hz, 1 H, Ar), 7.75 (d, ^3J = 7.3 Hz, 1 H, CH).

^{13}C NMR (100 MHz, CD_3OD): δ = 17.5, 24.1 (CH_3), 111.7 (CH), 125.0, 125.5 (C), 127.2, 133.4 (CH), 139.1 (C), 139.5 (CH), 141.6, 183.7 (C).

MS (EI, 70 eV): *m*/*z* (%) = 173 ([M]$^+$, 100), 158 (14), 144 (19), 130 (39), 115 (7), 103 (6), 87 (57).

Anal. Calcd for $C_{11}H_{11}NO$ (173.21): C, 76.28; H, 6.40; N, 8.08. Found: C, 75.38; H, 6.38; N, 7.73.

5,7-Dimethylquinolin-4(1*H*)-one (4e)

Starting from **3d** (5.00 g, 16.16 mmol) and diphenyl ether (36 mL), **4e** was isolated as a brownish solid (2.39 g, 76%); mp 183–189 °C.

IR (KBr): 3066 (br, w), 2915 (br, m), 2810 (br, m), 1614 (s), 1556 (s), 1511 (s), 1423 (m), 1240 (m), 1116 (m), 829 cm^{-1} (s).

^{1}H NMR (300 MHz, CD_3OD): δ = 2.39 (s, 3 H, CH_3), 2.84 (s, 3 H, CH_3), 6.17 (d, ^3J = 7.3 Hz, 1 H, CH), 6.91 (s, 1 H, Ar), 7.10 (s, 1 H, Ar), 7.72 (d, ^3J = 7.3 Hz, 1 H, CH).

^{13}C NMR (75 MHz, CD_3OD): δ = 21.5, 23.9 (CH_3), 111.4, 116.7 (CH), 123.5 (C), 129.4, 139.5 (CH), 141.1, 143.5, 183.2 (C).

MS (EI, 70 eV): *m*/*z* (%) = 173 ([M]$^+$, 100), 158 (9), 143 (20), 130 (13), 115 (19), 102 (7), 86 (63).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{11}NO$ ([M]$^+$): 173.08352; found: 173.08385.

5,6,8-Trimethylquinolin-4(1*H*)-one (4f)

Starting with **3f** (11.80 g, 40.79 mmol) and diphenyl ether (72 mL), **4f** was isolated as a brownish solid (6.10 g, 90%); mp 153 °C.

IR (ATR): 3067 (br, m), 2966 (m), 2917 (br, m), 1556 (br, m), 1485 (m), 1231 (br, m), 746 (br, m), 688 cm^{-1} (br, m).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.24 (s, 3 H, CH_3), 2.37 (s, 3 H, CH_3), 2.74 (s, 3 H, CH_3), 5.95 (d, ^3J = 7.5 Hz, 1 H, CH), 7.26 (s, 1 H, Ar), 7.64 (d, ^3J = 7.5 Hz, 1 H, CH), 10.65 (br s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 17.1, 17.2, 19.8 (CH_3), 110.6 (CH), 122.5, 124.2, 130.5 (C), 134.2 (CH), 134.4 (C), 137.3 (CH), 138.5 (C), 180.2 (C).

MS (EI, 70 eV): *m*/*z* (%) = 187 ([M]$^+$, 100), 172 (34), 158 (8), 144 (12), 115 (6), 91 (5).

Anal. Calcd for $C_{12}H_{13}NO$ (187.24): C, 76.98; H, 7.00; N, 7.48. Found: C, 76.69; H, 7.11; N, 7.23.

6-Chloro-8-methylquinolin-4(1*H*)-one (4g)

Starting from **3g** (3.50 g, 11.86 mmol) and diphenyl ether (24 mL), **4g** was isolated as a brownish solid (1.58 g, 69%); mp 285–295 °C.

IR (KBr): 3079 (br, m), 2969 (br, m), 2909 (br, m), 1549 (br, s), 1511 (br, s), 1455 (s), 1429 (s), 1256 (m), 1192 (s), 791 cm^{-1} (br, s).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.52 (s, 3 H, CH_3), 6.12 (d, ^3J = 7.4 Hz, 1 H, CH), 7.57 (d, ^4J = 2.5 Hz, 1 H, Ar), 7.86 (d, ^3J = 7.4 Hz, 1 H, CH), 7.90 (d, ^4J = 2.5 Hz, 1 H, Ar), 11.29 (br s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 16.9 (CH_3), 109.0, 121.6 (CH), 126.7, 127.3, 129.7 (C), 131.9 (CH), 137.4 (C), 139.8 (CH), 175.9 (C).

MS (EI, 70 eV): *m*/*z* (%) = 193 ([M]$^+$, 100), 165 (15), 158 (26), 130 (30), 102 (10), 77 (8).

Anal. Calcd for $C_{10}H_8ClNO$ (193.63): C, 62.03; H, 4.16; N, 7.23. Found: C, 62.22; H, 4.11; N, 6.97.

8-Chloro-6-methylquinolin-4(1*H*)-one (4h)
Starting from **3h** (3.50 g, 11.86 mmol) and diphenyl ether (24 mL), **4h** was isolated as a brownish solid (1.66 g, 72%); mp 240–243 °C.

IR (KBr): 3105 (br, m), 3044 (m), 2941 (br, m), 2839 (br, m), 1602 (s), 1562 (br, s), 1510 (br, s), 1402 (m), 1349 (m), 1310 (s), 1222 (s), 800 (br, m), 534 cm^{-1} (m).

^1H NMR (300 MHz, CD_3OD): δ = 2.45 (s, 3 H, CH_3), 6.33 (d, ^3J = 7.4 Hz, 1 H, CH), 7.64 (d, ^4J = 1.5 Hz, 1 H, Ar), 7.93 (d, ^3J = 7.4 Hz, 1 H, CH), 7.96 (d, ^4J = 1.5 Hz, 1 H, Ar).

^{13}C NMR (75 MHz, CD_3OD): δ = 21.0 (CH_3), 110.2 (CH), 123.0 (C), 124.7 (CH), 127.9 (C), 134.6 (CH), 135.9, 136.2 (C), 141.4 (CH), 180.1 (C).

MS (EI, 70 eV): *m*/*z* (%) = 193 ($[M]^+$, 100), 164 (20), 130 (36), 102 (10), 77 (9), 64 (10).

Anal. Calcd for $C_{10}H_8ClNO$ (193.63): C, 62.03; H, 4.16; N, 7.23. Found: C, 61.85; H, 4.10; N, 7.01.

8-(Trifluoromethyl)quinolin-4(1*H*)-one (4i)
Starting from **3i** (3.00 g, 9.28 mmol) and diphenyl ether (20 mL), **4i** was isolated as a brownish solid (1.72 g, 84%); mp 170–172 °C.

IR (KBr): 3187 (br, m), 3077 (br, m), 3036 (br, m), 1631 (m), 1579 (br, m), 1520 (m), 1448 (br, m), 1304 (br, m), 1104 (s), 1084 (s), 748 (s), 716 cm^{-1} (s).

^1H NMR (300 MHz, acetone-d_6): δ = 6.29 (d, ^3J = 7.6 Hz, 1 H, CH), 7.49–7.54 (m, 1 H, Ar), 8.02 (d, ^3J = 7.6 Hz, 1 H, CH), 8.06–8.09 (m, 1 H, Ar), 8.54–8.58 (m, 1 H, Ar), 10.65 (br s, 1 H, NH).

^{13}C NMR (75 MHz, acetone-d_6): δ = 111.0 (CH), 119.7 (q, $^1J_{F,C}$ = 245 Hz, CF_3), 123.2 (CH), 126.9, 128.1 (C), 130.6, 131.6 (CH), 137.8 (C), 141.2 (CH), 178.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 213 ($[M]^+$, 100), 193 (65), 184 (5), 165 (87), 138 (13), 114 (4), 83 (10).

Anal. Calcd for $C_{10}H_6F_3NO$ (213.16): C, 56.35; H, 2.84; N, 6.57. Found: C, 56.51; H, 2.79; N, 6.33.

6-Iodoquinolin-4(1*H*)-one (4j)
Starting from **3j** (4.50 g, 12.05 mmol) and diphenyl ether (25 mL), **4j** was isolated as a brownish solid (2.71 g, 83%); mp 275–281 °C.

IR (KBr): 3055 (br, m), 2955 (br, m), 2805 (br, m), 1600 (br, m), 1544 (br, s), 1501 (br, s), 1460 (br, s), 1392 (m), 1199 (br, s), 1142 (m), 807 cm^{-1} (s).

^1H NMR (300 MHz, DMSO-d_6): δ = 6.08 (d, ^3J = 7.4 Hz, 1 H, CH), 7.37 (d, ^3J = 8.7 Hz, 1 H, Ar), 7.91 (dd, ^3J = 8.7 Hz, ^4J = 2.0 Hz, 1 H, Ar), 7.94 (d, ^3J = 7.4 Hz, 1 H, CH), 8.37 (d, ^4J = 2.0 Hz, 1 H, Ar), 11.91 (br s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 109.1 (CH), 118.6 (C), 120.8 (CH), 127.5, 130.0 (C), 133.4 139.6, 139.8 (CH), 175.4 (C).

MS (EI, 70 eV): *m*/*z* (%) = 271 ($[M]^+$, 100), 144 (32), 116 (20), 105 (16), 97 (11), 77 (14).

Anal. Calcd for C_9H_6INO (271.05): C, 39.88; H, 2.23; N, 5.17. Found: C, 39.88; H, 2.20; N, 4.94.

8-Bromoquinolin-4(1*H*)-one (4k)
Starting from **3k** (6.00 g, 18.40 mmol) and diphenyl ether (38 mL), **4k** was isolated as a brownish solid (2.89 g, 70%); mp 174 °C.

IR (KBr): 3150 (m), 3080 (m), 2934 (m), 1626 (m), 1605 (s), 1556 (br, s), 1516 (s), 1433 (m), 1335 (m), 798 cm^{-1} (br, m).

^1H NMR (300 MHz, DMSO-d_6): δ = 6.13 (d, ^3J = 7.4 Hz, 1 H, CH), 7.26 (dd, ^3J = 7.8 Hz, ^3J = 7.9 Hz, 1 H, Ar), 7.86 (d, ^3J = 7.4 Hz, 1 H, CH), 7.98 (dd, ^3J = 7.9 Hz, ^4J = 1.4 Hz, 1 H, Ar), 8.11 (d, ^3J = 7.8 Hz, ^4J = 1.4 Hz, 1 H, Ar), 11.15 (br s, 1 H, NH).

^{13}C NMR (75 MHz, CD_3OD): δ = 110.5 (CH), 112.9 (C), 125.7, 126.2 (CH), 128.1 (C), 137.0 (CH), 139.1 (C), 141.9 (CH), 180.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 223 ($[M]^+$, 100), 195 (51), 169 (2), 116 (48), 89 (27), 63 (16).

Anal. Calcd for C_9H_6BrNO (224.05): C, 48.25; H, 2.70; N, 6.25. Found: C, 48.55; H, 2.57; N, 6.15.

7-Bromoquinolin-4(1*H*)-one (4l-A) and 5-Bromoquinolin-4(1*H*)-one (4l-B)
Starting from **3l** (4.00 g, 12.31 mmol) and diphenyl ether (25 mL), a mixture of **4l-A** und **4l-B** (1.6:1) was isolated as a brownish solid (2.00 g, 73%).

4l-A
^1H NMR (300 MHz, DMSO-d_6): δ = 6.07 (d, ^3J = 7.4 Hz, 1 H, CH), 7.44 (dd, ^3J = 8.6 Hz, ^4J = 1.8 Hz, 1 H, Ar), 7.75 (d, ^4J = 1.8 Hz, 1 H, Ar), 7.93 (d, ^3J = 7.4 Hz, 1 H, CH), 8.00 (d, ^3J = 8.6 Hz, 1 H, Ar), 11.80 (br s, 1 H, NH).

4l-B
^1H NMR (300 MHz, DMSO-d_6): δ = 6.03 (d, ^3J = 7.4 Hz, 1 H, CH), 7.42–7.55 (m, 3 H, Ar), 7.84 (d, ^3J = 7.4 Hz, 1 H, CH), 11.80 (br s, 1 H, NH).

6,8-Dibromoquinolin-4(1*H*)-one (4m)
Starting from **3m** (5.00 g, 12.35 mmol) and diphenyl ether (26 mL), **4m** was isolated as a brownish solid (2.02 g, 52%); mp 291 °C.

IR (KBr): 3066 (br, m), 2920 (br, m), 1586 (br, s), 1547 (br, s), 1507 (br, s), 1427 (s), 1299 (m), 1188 (s), 1116 (m), 802 cm^{-1} (br, s).

^1H NMR (300 MHz, DMSO-d_6): δ = 6.28 (d, ^3J = 7.5 Hz, 1 H, CH), 8.00 (d, ^3J = 7.5 Hz, 1 H, CH), 8.28 (d, ^4J = 2.3 Hz, 1 H, Ar), 8.33 (d, ^4J = 2.3 Hz, 1 H, Ar), 11.43 (br s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 109.6 (CH), 112.9, 115.4 (C), 127.2 (CH), 127.8, 136.8 (C), 136.9, 140.7 (CH), 175.2 (C).

MS (EI, 70 eV): *m*/*z* (%) = 303 ($[M]^+$, 100), 275 (40), 222 (19), 194 (27), 131 (25), 115 (57).

Anal. Calcd for $C_9H_5Br_2NO$ (302.95): C, 35.68; H, 1.66; N, 4.62. Found: C, 35.75; H, 1.49; N, 4.60.

6,8-Dichloroquinolin-4(1*H*)-one (4n)
Starting from **3n** (5.40 g, 15.41 mmol) and diphenyl ether (32 mL), **4n** was isolated as a brownish solid (2.56 g, 78%); mp 290 °C.

IR (KBr): 3140 (w), 3083 (m), 2928 (w), 1620 (br, m), 1560 (br, s), 1511 (s), 1337 (s), 1213 (s), 1080 cm^{-1} (m).

^1H NMR (400 MHz, DMSO-d_6): δ = 6.18 (d, ^3J = 7.5 Hz, 1 H, CH), 7.90 (d, ^3J = 7.5 Hz, 1 H, CH), 8.00 (d, ^4J = 2.4 Hz, 1 H, Ar), 7.01 (d, ^4J = 2.4 Hz, 1 H, Ar), 11.55 (br s, 1 H, NH).

^{13}C NMR (125 MHz, DMSO-d_6/CD_3OD): δ = 108.7, 122.6 (CH), 126.4, 127.1 (C), 130.6 (CH), 134.7 (C), 139.7 (CH), 177.5 (C).

MS (EI, 70 eV): *m*/*z* (%) = 213 ($[M]^+$, 100), 185 (55), 150 (21), 123 (14), 93 (9).

Anal. Calcd for $C_9H_5Cl_2NO$ (214.05): C, 50.50; H, 2.35; N, 6.54. Found: C, 50.45; H, 2.30; N, 6.48.

7,8-Dichloroquinolin-4(1*H*)-one (4o)
Starting from **3o** (3.77 g, 10.77 mmol) and diphenyl ether (22 mL), **4o** was isolated as a brownish solid (1.43 g, 62%); mp 303 °C.

IR (KBr): 3126 (w), 3071 (m), 2934 (w), 1623 (br, m), 1600 (s), 1588 (s), 1552 (br, s), 1335 (m), 1189 cm^{-1} (s).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 6.17 (d, ^3J = 7.5 Hz, 1 H, CH), 7.54 (d, ^3J = 8.7 Hz, 1 H, Ar), 7.89 (d, ^3J = 7.5 Hz, 1 H, CH), 8.06 (d, ^3J = 8.7 Hz, 1 H, Ar), 11.25 (br s, 1 H, NH).

^{13}C NMR (125 MHz, DMSO-d_6/CD_3OD): δ = 110.3 (CH), 120.4 (C), 124.6, 125.6 (CH), 130.3, 135.8, 138.2 (C), 140.9 (CH), 177.1 (C).

MS (EI, 70 eV): *m*/*z* (%) = 213 ([M]$^+$, 100), 185 (83), 150 (23), 123 (17), 93 (14).

Anal. Calcd for $C_9H_5Cl_2NO$ (214.05): C, 50.50; H, 2.35; N, 6.54. Found: C, 50.34; H, 2.29; N, 6.42.

5,8-Dichloroquinolin-4(1*H*)-one (4p)
Starting from **3p** (6.00 g, 18.98 mmol) and diphenyl ether (38 mL), **4p** was isolated as a brownish solid (2.52 g, 61%); mp 268 °C.

IR (KBr): 3092 (m), 3046 (m), 2953 (m), 1625 (s), 1590 (br, s), 1559 (s), 1502 (s), 1396 (m), 1205 (s), 808 cm^{-1} (m).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.10 (d, ^3J = 7.5 Hz, 1 H, CH), 7.27 (d, ^3J = 8.4 Hz, 1 H, Ar), 7.74 (d, ^3J = 8.4 Hz, 1 H, Ar), 7.77 (d, ^3J = 7.5 Hz, 1 H, CH), 11.25 (br s, 1 H, NH).

NMR (75 MHz, DMSO-d_6): δ = 111.8 (CH), 120.6, 122.6 (C), 125.6, 131.4 (CH), 138.7 (C), 138.8 (CH), 175.8 (C).

MS (EI, 70 eV): *m*/*z* (%) = 213 ([M]$^+$, 100), 185 (51), 150 (19), 123 (13), 93 (10).

Anal. Calcd for $C_9H_5Cl_2NO$ (214.05): C, 50.50; H, 2.35; N, 6.54. Found: C, 50.45; H, 2.09; N, 6.48.

5,6,8-Trichloroquinolin-4(1*H*)-one (4q)
Starting from **3q** (5.80 g, 16.54 mmol) and diphenyl ether (34 mL), **4q** was isolated as a brownish solid (2.88 g, 71%); mp 318 °C.

IR (KBr): 3084 (m), 3015 (br, m), 2949 (m), 2887 (m), 1625 (br, m), 1601 (br, s), 1566 (br, s), 1497 (s), 1427 (s), 1210 (s), 1086 (m), 803 cm^{-1} (m).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.16 (d, ^3J = 7.5 Hz, 1 H, CH), 7.81 (d, ^3J = 7.4 Hz, 1 H, CH), 8.18 (s, 1 H, Ar), 11.30 (br s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 112.2 (CH), 124.4, 127.2 129.0 (C), 131.8 (CH), 137.6 (C), 138.8 (CH), 175.1 (C).

MS (EI, 70 eV): *m*/*z* (%) = 247 ([M]$^+$, 100), 219 (25), 184 (13), 142 (12), 111 (8), 97 (12).

Anal. Calcd for $C_9H_4Cl_3NO$ (248.49): C, 43.50; H, 1.62; N, 5.64. Found: C, 43.57; H, 1.59; N, 5.22.

1-Alkoxycarbonyl-4-quinolones 6a–h; General Procedure
To a suspension of NaH (2.6 equiv) in THF (4.5 mL per 1 mmol of **4**) was added portionwise the quinolone **4** (1.0 equiv) at 0 °C. The mixture was stirred for 30 min at 50 °C and the chloroformate (2.6 equiv) was subsequently added dropwise. The solution was allowed to cool to r.t. and stirred for 48 h. To the mixture was added aq 2 M HCl (50 mL). The organic and the aqueous layer were separated and the latter was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes–EtOAc, 1:1).

6-Chloro-1-methoxycarbonyl-4-quinolone (6a)
Starting from 6-chloroquinolin-4(1*H*)-one (0.637 g, 3.55 mmol), NaH (0.221 g, 9.22 mmol), THF (17.0 mL), and methyl chloroformate (0.858 g, 9.10 mmol), **6a** was isolated as a colorless solid (600 mg, 71%); mp 140–141 °C.

IR (KBr): 3438 (br, w), 3106 (w), 3073 (w), 2955 (w), 1750 (s), 1662 (s), 1639 (s), 1599 (s), 1557 (m), 1469 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.09 (s, 3 H, OCH_3), 6.28 (d, ^3J = 8.5 Hz, 1 H, CH), 7.61 (dd, ^4J = 2.5 Hz, ^3J = 9.4 Hz, 1 H, Ar), 8.33 (d, ^4J = 2.5 Hz, 1 H, Ar), 8.36 (d, ^3J = 8.5 Hz, 1 H, CH), 8.65 (d, ^3J = 9.4 Hz, 1 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 112.6, 121.9, 126.0 (CH), 127.8, 131.8 (C), 133.0 (CH), 136.8 (C), 138.4 (CH), 151.7 (NCO), 177.7 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 239 (M$^+$, ^{37}Cl, 16), 237 (M$^+$, ^{35}Cl, 53), 193 (59), 178 (17), 150 (100), 123 (52).

Anal. Calcd for $C_{11}H_8ClNO_3$ (237.02): C, 55.60; H, 3.39; N, 5.89. Found: C, 55.70; H, 3.38; N, 5.74.

6-Bromo-1-methoxycarbonyl-4-quinolone (6b)
Starting from 6-bromoquinolin-4(1*H*)-one (0.835 g, 3.73 mmol), NaH (0.233 g, 9.70 mmol), THF (17.0 mL), and methyl chloroformate (0.900 g, 9.50 mmol), **6b** was isolated as a colorless solid (882 mg, 84%); mp 143–144 °C.

IR (KBr): 3438 (br, w), 3100 (m), 3071 (m), 2952 (m), 1750 (s), 1662 (s), 1640 (s), 1593 (s), 1554 (w), 1267 (s), 1432 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.08 (s, 3 H, OCH_3), 6.26 (d, ^3J = 8.5 Hz, 1 H, CH), 7.73 (dd, ^3J = 9.5 Hz, ^4J = 2.4 Hz, 1 H, Ar), 8.35 (d, ^3J = 8.5 Hz, 1 H, CH), 8.46 (d, ^4J = 2.4 Hz, 1 H, Ar), 8.56 (d, ^3J = 9.5 Hz, 1 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 112.6 (CH), 119.5 (C), 122.0 (CH), 127.9 (C), 129.1 135.8 (CH), 137.2 (C), 138.4 (CH), 151.6 (NCO), 177.5 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 283 (M$^+$, ^{81}Br, 97), 281 (M$^+$, ^{79}Br, 100), 239 (17), 237 (17), 211 (12), 209 (14), 196 (20), 194 (20), 130 (11), 128 (8).

Anal. Calcd for $C_{11}H_8BrNO_3$ (280.97): C, 46.84; H, 2.86; N, 4.97. Found: C, 46.77; H, 2.87; N, 4.72.

6-Bromo-1-ethoxycarbonyl-4-quinolone (6c)
Starting from 6-bromoquinolin-4(1*H*)-one (1.000 g, 4.50 mmol), NaH (0.280 g, 11.70 mmol), THF (20.0 mL), and ethyl chloroformate (1.250 g, 11.50 mmol), **6c** was isolated as a yellow solid (920 mg, 70%); mp 104–106 °C.

IR (ATR): 3057 (br, w), 2977 (w), 1753 (s), 1629 (br, s), 1466 (s), 1402 (m), 1213 (br, s), 1190 (br, s), 1152 (br, s), 820 (s), 757 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.50 (t, ^3J = 7.1 Hz, 3 H, CH_3), 4.54 (q, ^3J = 7.1 Hz, 2 H, CH_2), 6.28 (d, ^3J = 8.6 Hz, 1 H, CH), 7.73 (dd, ^3J = 9.4 Hz, ^4J = 2.6 Hz, 1 H, Ar), 8.37 (d, ^3J = 8.6 Hz, 1 H, CH), 8.46 (d, ^4J = 2.6 Hz, 1 H, Ar), 8.56 (d, ^3J = 9.4 Hz, 1 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 (CH_3), 65.4 (OCH_2), 112.4 (CH), 119.4 (C), 122.1 (CH), 128.0 (C), 129.1 135.7 (CH), 137.3 (C), 138.5 (CH), 151.1 (NCO), 177.6 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 297 (M$^+$, ^{81}Br, 98), 295 (M$^+$, ^{79}Br, 99), 238 (46), 223 (100), 197 (19), 172 (9), 144 (24), 116 (43), 89 (13).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{10}BrNO_4$ ([M]$^+$, ^{79}Br): 294.98386; found: 294.98376.

6-Fluoro-1-methoxycarbonyl-4-quinolone (6d)
Starting from 6-fluoroquinolin-4(1*H*)-one (0.735 g, 4.50 mmol), NaH (0.280 g, 11.70 mmol), THF (25.0 mL), and methyl chloroformate (1.09 g, 11.70 mmol), **6d** was isolated as a yellow solid (625 mg, 63%); mp 122–123 °C.

IR (KBr): 3206 (br, w), 3117 (m), 2959 (w), 1750 (s), 1664 (s), 1617 (s), 1480 (s), 1275 (br, s), 1242 (br, s), 1149 (m), 831 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.10 (s, 3 H, OCH_3), 6.27 (d, ^3J = 8.5 Hz, 1 H, CH), 7.40 (m, 1 H, Ar), 8.01 (m, 1 H, Ar), 8.39 (d, ^3J = 8.5 Hz, 1 H, CH), 8.73 (m, 1 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 115.5 (d, $^2J_{C,F}$ = 23 Hz, CH_{Ar}), 111.9 (CH), 120.9 (d, $^2J_{C,F}$ = 24 Hz, CH_{Ar}), 122.7 (d, $^3J_{C,F}$ = 8 Hz, CH_{Ar}), 128.6 (d, $^3J_{C,F}$ = 7 Hz, C_{Ar}), 134.8 (C_{Ar}), 138.4 (CH), 151.8 (NCO), 159.9 (d, $^1J_{C,F}$ = 247 Hz, C_{Ar}), 178 (d, $^4J_{C,F}$ = 2 Hz, C=O).

MS (EI, 70 eV): *m*/*z* (%) = 221 ([M]$^+$, 100), 177 (21), 162 (10), 148 (21), 134 (34), 107 (24), 97 (6).

Anal. Calcd for $C_{11}H_8FNO_3$ (221.18): C, 59.73; H, 3.65; N, 6.33. Found: C, 59.91; H, 3.53; N, 6.28.

5,7-Dichloro-1-methoxycarbonyl-4-quinolone (6e)

Starting from 5,7-dichloroquinolin-4(1*H*)-one (1.430 g, 6.75 mmol), NaH (0.420 g, 17.25 mmol), THF (25.0 mL), and methyl chloroformate (1.630 g, 17.25 mmol), **6e** was isolated as a yellow solid (1.200 g, 66%); mp 147–148 °C.

IR (KBr): 3131 (w), 3090 (w), 2971 (w), 1749 (br, s), 1666 (br, s), 1584 (s), 1249 (br, s), 1262 (m), 957 cm^{-1} (br, m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.09 (s, 3 H, CH_3), 6.19 (d, ^3J = 8.6 Hz, 1 H, CH), 7.42 (d, ^4J = 2.0 Hz, 1 H, Ar), 8.19 (d, ^3J = 8.6 Hz, 1 H, CH), 8.59 (d, ^4J = 2.0 Hz, 1 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.5 (OCH_3), 114.4, 119.2 (CH), 121.8 (C), 128.9 (CH), 135.2 (C), 136.5 (CH), 137.8, 140.8 (C), 151.5 (NCO), 177.0 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 271 ([M]$^+$, ^{37}Cl, 100), 227 (27), 199 (29), 184 (27), 149 (12), 121 (15), 91 (9).

Anal. Calcd for $C_{11}H_7Cl_2NO_3$ (272.08): C, 48.56; H, 2.59; N, 5.15. Found: C, 46.69; H, 2.55; N, 4.96.

1-Allyloxycarbonyl-5,7-dimethyl-4-quinolone (6f)

Starting from 5,7-dimethylquinolin-4(1*H*)-one (**4e**; 0.571 g, 3.30 mmol), NaH (0.210 g, 8.60 mmol), THF (17.0 mL), and allyl chloroformate (0.9 mL, 8.60 mmol), **6f** was isolated as a yellow solid (667 mg, 79%); mp 72–74 °C.

IR (KBr): 3138 (w), 2962 (m), 2921 (m), 1745 (br, s), 1645 (br, s), 1607 (s), 1456 (s), 1241 (br, s), 1202 (br, s), 1099 (s), 961 cm^{-1} (br, s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.41 (s, 3 H, CH_3), 2.82 (s, 3 H, CH_3), 4.89 (m, 2 H, OCH_2), 5.40 (m, 1 H, CH=CH_2), 5.46 (m, 1 H, CH=CH_2), 6.00 (m, 1 H, CH=CH_2), 6.27 (d, ^3J = 8.5 Hz, 1 H, CH), 6.99 (s, 1 H, Ar), 8.16 (d, ^3J = 8.5 Hz, 1 H, CH), 8.19 (s, 1 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.1, 23.9 (CH_3), 69.0 (OCH_2), 114.2, 118.2 (CH), 120.5 (=CH_2), 123.2 (C), 130.2, 130.6, 136.3 (CH), 140.2, 141.0, 142.2 (C), 151.6 (NCO), 181.2 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 257 ([M]$^+$, 44), 172 (100), 144 (15), 115 (8), 91 (4).

Anal. Calcd for $C_{15}H_{15}NO_3$ (257.11): C, 70.02; H, 5.88; N, 5.44. Found: C, 69.59; H, 5.87; N, 5.32.

1-Allyloxycarbonyl-6-fluoro-4-quinolone (6g)

Starting from 6-fluoroquinolin-4(1*H*)-one (0.540 g, 3.30 mmol), NaH (0.210 g, 8.60 mmol), THF (25.0 mL), and allyl chloroformate (0.9 mL, 8.60 mmol), **6g** was isolated as a yellow solid (681 mg, 84%); mp 74–78 °C.

IR (KBr): 3150 (m), 3076 (m), 2986 (w), 1752 (br, s), 1640 (br, s), 1617 (s), 1476 (s), 1225 (br, s), 1196 (br, s), 1138 (s), 924 (s), 525 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.94 (m, 2 H, OCH_2), 5.42 (m, 1 H, CH=CH_2), 5.49 (m, 1 H, CH=CH_2), 6.04 (m, 1 H, CH=CH_2), 6.27 (d, ^3J = 8.6 Hz, 1 H, CH), 7.39 (m, 1 H, Ar), 8.00 (m, 1 H, Ar), 8.39 (d, ^3J = 8.6 Hz, 1 H, CH), 8.73 (m, 1 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 69.5 (OCH_2), 111.5 (d, $^2J_{C,F}$ = 23 Hz, CH_{Ar}), 111.9 (CH), 120.9 (d, $^2J_{C,F}$ = 22 Hz, CH_{Ar}), 121.1 (=CH_2), 122.7 (d, $^3J_{C,F}$ = 7 Hz, CH_{Ar}), 128.5 (d, $^3J_{C,F}$ = 8 Hz, C_{Ar}), 130.3 (CH), 134.8 (d, $^4J_{C,F}$ = 2 Hz, C_{Ar}), 138.4 (CH), 151.0 (NCO), 159.8 (d, $^1J_{C,F}$ = 247 Hz, C_{Ar}), 178.0 (d, $^4J_{C,F}$ = 2 Hz, C=O).

MS (EI, 70 eV): *m*/*z* (%) = 247 ([M]$^+$, 39), 203 (21), 163 (11), 134 (19), 107 (19), 97 (8), 41 (100).

Anal. Calcd for $C_{13}H_{10}FNO_3$ (247.22): C, 63.16; H, 4.08; N, 5.67. Found: C, 63.10; H, 4.00; N, 5.73.

1-Benzyloxycarbonyl-*tert*-butyl-4-quinolone (6h)

Starting from 6-*tert*-butylquinolin-4(1*H*)-one (**4c**; 1.000 g, 5.00 mmol), NaH (0.500 g, 60% suspension in mineral oil, 12.90 mmol), THF (25.0 mL), and benzyl chloroformate (2.200 g, 12.90 mmol), **6h** was isolated as a yellow oil (751 mg, 45%).

IR (neat): 3031 (m), 2958 (br, s), 1755 (br, s), 1646 (br, s), 1607 (s), 1486 (br, s), 1217 (br, s), 1115 (m), 1022 (s), 828 (s), 699 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.38 (s, 9 H, 3 × CH_3), 5.46 (s, 2 H, CH_2), 6.24 (d, ^3J = 8.5 Hz, 1 H, CH), 7.33–7.50 (m, 5 H, Ar), 7.72 (dd, ^3J = 9.2 Hz, ^4J = 2.6 Hz, 1 H, Ar), 8.34 (d, ^3J = 8.5 Hz, 1 H, CH), 8.36 (d, ^4J = 2.6 Hz, 1 H, Ar), 8.61 (d, ^3J = 9.2 Hz, 1 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.0 (3 × CH_3), 34.7 (CCH_3), 70.4 (OCH_2), 112.4, 119.8, 122.4 (CH), 126.2 (C), 128.5, 128.5, 128.6, 130.1 (CH), 136.3 (C), 137.9 (CH), 141.0, 148.7 (C), 151.3 (NCO), 179.3 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 335 ([M]$^+$, 23), 291 (46), 276 (60), 201 (33), 186 (78), 158 (9), 91 (100).

HRMS (EI): *m*/*z* calcd for $C_{21}H_{21}NO_3$ ([M]$^+$): 335.15160; found: 335.15111.

Anal. Calcd for $C_{21}H_{21}NO_3$ (335.40): C, 75.26; H, 6.31; N, 4.18. Found: C, 75.60; H, 6.74; N, 4.04.

References

(1) Cimino, G.; de Rosa, S.; deStefano, S.; Spinelli, A.; Sodano, G. *Tetrahedron Lett.* **1984**, *25*, 2925.
(2) Molinski, T. F.; Faulkner, D. J. *Tetrahedron Lett.* **1988**, *29*, 2137.
(3) Royt, P. W.; Honeychuk, R. V.; Ravich, V.; Ponnaluri, P.; Pannel, L. K.; Buyer, J. S.; Chandhoke, V.; Stalick, W. M.; de Sesso, L. C.; Donohue, S.; Ghei, R.; Releya, J. D.; Ruiz, R. *Bioorg. Chem.* **2001**, *29*, 387.
(4) Jaquemond-Collet, I.; Bessiere, J. M.; Hannedouche, S.; Bertrand, C.; Fouraste, I.; Moulis, C. *Phytochem. Anal.* **2001**, *12*, 312.
(5) Wentland, M. P.; Perni, R. B.; Dorff, P. H.; Brundage, R. P.; Castaldi, M. J.; Bailey, T. R.; Carabateas, P. M.; Bacon, E. R.; Young, D. C.; Woods, M. G.; Rosi, D.; Drozd, M. L.; Kullnig, R. K.; Dutko, F. J. *J. Med. Chem.* **1993**, *36*, 1580.
(6) Schmidt, R. D. *Taschenatlas der Biotechnologie und Gentechnik*; Wiley-VCH Verlag: Weinheim, **2002**.
(7) (a) Legros, J. Y.; Primault, G.; Fiaud, J. C. *Tetrahedron* **2001**, *57*, 2507. (b) Walker, S. D.; Barder, T.; Martinelli, J. R.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2004**, *43*, 1871. (c) Wolf, C.; Kovi, K. E. *Eur. J. Org. Chem.* **2006**, 1917. (d) Graf, G. I.; Hastreiter, D.; da Silva, L. E.; Rebelo, R. A.; Montalban, A. G.; McKillop, A. *Tetrahedron* **2002**, *58*, 9095.
(8) Price, C. C.; Roberts, R. M. *J. Am. Chem. Soc.* **1946**, *68*, 1204.
(9) Biere, H.; Seelen, W. *Liebigs Ann. Chem.* **1976**, 1972.
(10) Heindel, N. D.; Kennewell, P. D.; Fish, V. B. *J. Heterocycl. Chem.* **1969**, *6*, 77.
(11) Sterling Drug Inc. British Patent 1147760, **1969**; *Chem. Abstr.* **1969**, *71*, 49967a.

(12) Cassis, R.; Tapia, R.; Valderrama, J. A. *Synth. Commun.* **1985**, *15*, 125.
(13) CCDC-695059 (**3d**), CCDC-695060 (**4o**) and CCDC-695061 (**6c**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
(14) (a) Beifuss, U.; Schniske, U.; Feder, G. *Tetrahedron* **2001**, *57*, 1005. (b) Kocienski, P. J. *Protecting Groups*; Thieme: Stuttgart, **1994**.