SYNTHESIS OF 2(1*H*)-QUINOLINONEQUINONES AND 2-ALKOXYQUINOLINEQUINONES USING OXIDATIVE DEMETHYLATION WITH CERIUM (IV) AMMONIUM NITRATE

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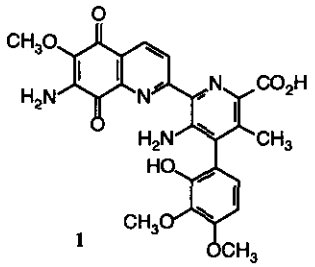
Abstract —— 2,5,8(1*H*)-Quinolinetriones (**12**), 2,5,6(1*H*)-quinolinetriones (**13**), 2-alkoxy-5,8-quinolinediones (**14**), 2,8-dimethoxy-5,6-quinolinedione (**15**), and 2,6-dimethoxy-7,8-quinolinediones (**16**) were synthesized by oxidative demethylation of the corresponding 2(1*H*)-quinolinones (**7**) and 2-alkoxyquinolines (**11**) *with cerium (IV) ammonium nitrate.*

Streptonigrin (**1**), a highly substituted 5,8-quinolinedione, was first reported as an antitumor antibiotic produced by *Streptomyces flocculus*.[1] It was later found to be one of the most potent inhibitors of avian myeloblastosis virus reverse transcriptase (AMV-RT), but its remarkable cytotoxic activity seemed to be disadvantageous with respect to a specific inhibitor of retrovirus.[2] Recently, we observed that synthetic 6-methoxy-5,8-quinolinediones (**2a**, **b**) and 8-methoxy-5,6-quinolinediones (**2c**, **d**) were much less toxic than **1**, while the activity of **2a-d** against AMV-RT was comparable to that of **1**.[3] Furthermore, we examined the inhibition of AMV-RT by a series of quinolinequinones, isoquinolinequinones, and quinoxalinequinones.[3] We wish to report here the synthesis of various 2(1*H*)-quinolinonequinones and 2-alkoxyquinolinequinones.



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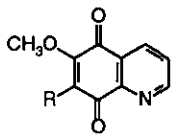
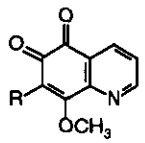


2a: R=H
b: R=CH_3

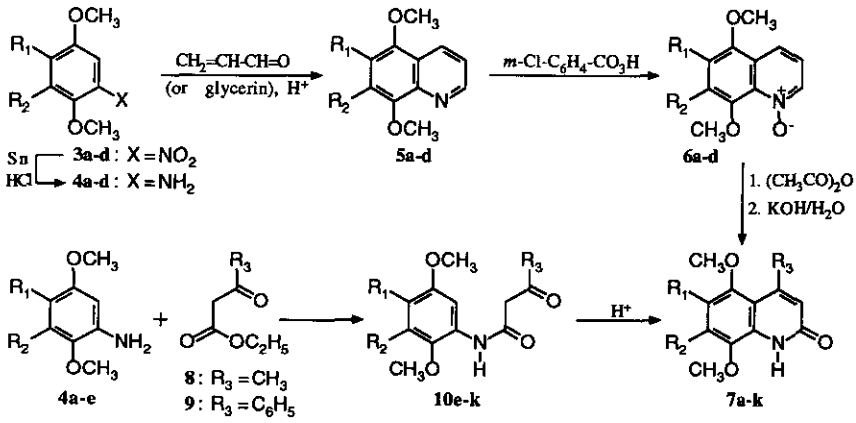


2c: R=H
d: R=CH_3

5,7,8-Trimethoxyquinoline (**5a**) and 5,6,8-trimethoxyquinolines (**5b-d**) prepared from the corresponding trimethoxyanilines (**4a-d**), were oxidized with *m*-chloroperoxybenzoic acid to give **6a-d**. The *N*-oxides (**6a-d**) were treated with acetic anhydride followed by aqueous potassium hydroxide to furnish the 2(1*H*)-quinolinones (**7a-d**). On the other hand, condensation of trimethoxyanilines (**4a-d**) and ethyl acetoacetate (**8**) in refluxing

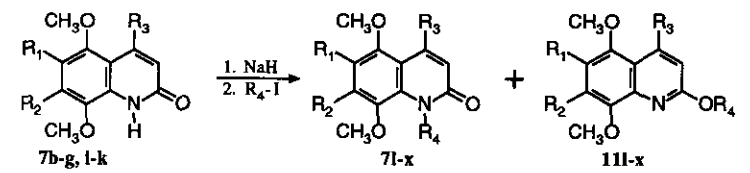
toluene containing a catalytic amount of pyridine afforded the corresponding β-ketoanilides (**10e-h**). Acid catalyzed cyclization of **10e-h** gave 4-methyl-2(1*H*)-quinolinones (**7e-h**). Furthermore, 4-phenyl-2(1*H*)-quinolinones (**7i-k**) were prepared from the anilines (**4e, a, c**) and ethyl benzoylacetate (**9**), respectively.

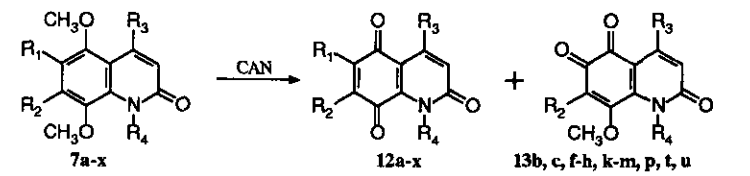
Treatment of the 2(1*H*)-quinolinones (**7b-g, i-k**) with sodium hydride followed by methyl iodide afforded the corresponding *N*-methyl-2(1*H*)-quinolinones (**7l-t**, 49-84% yield) and 2-methoxyquinolines (**11l-t**, 14-34%

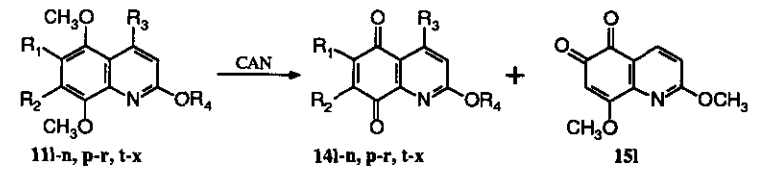


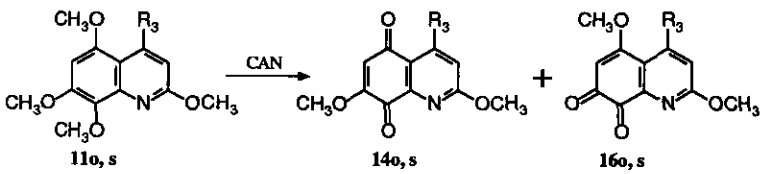
3-6

	R_1	R_2
a	H	OCH_3
b	OCH_3	H
c	OCH_3	CH_3
d	OCH_3	C_2H_5
e	H	H









7, 10-14, 16

	R_1	R_2	R_3	R_4
a	H	OCH_3	H	H
b	OCH_3	H	H	H
c	OCH_3	CH_3	H	H
d	OCH_3	C_2H_5	H	H
e	H	OCH_3	CH_3	H
f	OCH_3	H	CH_3	H
g	OCH_3	CH_3	CH_3	H
h	OCH_3	C_2H_5	CH_3	H
i	H	H	C_6H_5	H
j	H	OCH_3	C_6H_5	H
k	OCH_3	CH_3	C_6H_5	H
l	OCH_3	H	H	CH_3
m	OCH_3	CH_3	H	CH_3
n	OCH_3	C_2H_5	H	CH_3
o	H	OCH_3	CH_3	CH_3
p	OCH_3	H	CH_3	CH_3
q	OCH_3	CH_3	CH_3	CH_3
r	H	H	C_6H_5	CH_3
s	H	OCH_3	C_6H_5	CH_3
t	OCH_3	CH_3	C_6H_5	CH_3
u	OCH_3	H	CH_3	C_2H_5
v	OCH_3	CH_3	CH_3	C_2H_5
w	H	H	C_6H_5	C_2H_5
x	OCH_3	CH_3	C_6H_5	C_2H_5

yield). In contrast, ethylation of 2-quinolinones (**7f, g, i, k**) with ethyl iodide gave the corresponding *N*-ethyl-2(1*H*)-quinolinones (**7u-x**, 16-41% yield), but the major product was 2-ethoxyquinolines (**11u-x**, 45-80% yield). Oxidative demethylation of 5,8-dimethoxy-2(1*H*)-quinolinones (**7i, r, w**) and 5,7,8-trimethoxy-2(1*H*)-quinolinones (**7a, e, j, o, s**) with cerium (IV) ammonium nitrate (CAN) in aqueous acetonitrile containing suspended pyridine-2,6-dicarboxylic acid *N*-oxide[4] afforded the corresponding *p*-quinones (**12i, r, w, a, e, j, o, s**) in 24-78% yields; but no *o*-quinones. In contrast, 5,6,8-trimethoxy-2(1*H*)-quinolinones unsubstituted at N_1 or C_7 (**7b, c, f-h, k, l, p, u**) were oxidized with CAN under the same conditions to furnish the corresponding quinones (45-92% yield), which consisted of *p*-quinones (**12b, c, f-h, k, l, p, u**, 28-84% yield) and *o*-quinones (**13b, c, f-h, k, l, p, u**, 6-31% yield). Other 5,6,8-trimethoxy-2(1*H*)-quinolinones (**7d, m, n, q, t, v, x**) gave *p*-quinones (**12d, m, n, q, t, v, x**) and/or *o*-quinones (**13m, t**) in 7-36% yields.

In order to confirm the *p*-quinone structure for **12a, e, j**, we examined oxidation of 5,8-diethoxy-7-methoxy-2(1*H*)-quinolinones (**7a', e', j'**), prepared by the same method used for the corresponding 5,7,8-trimethoxy-2(1*H*)-quinolinones (**7a, e, j**). The 2(1*H*)-quinolinones (**7a', e', j'**) were oxidized with CAN to give the corresponding 7-methoxy-2,5,8(1*H*)-quinolinetriones, which were identical to the quinones (**12a, e, j**) from 5,7,8-trimethoxy-2(1*H*)-quinolinones (**7a, e, j**), respectively.

Finally, we examined oxidative demethylation of 2-alkoxyquinolines (**11l-x**) with CAN. 5,6,8-Trimethoxyquinoline (**11l**) and 5,7,8-trimethoxyquinolines (**11o, s**) furnished the corresponding *p*-quinones (**14l, o, s**, 37-62% yield) and *o*-quinones (**15l, 16o, s**, 11-31% yield). Other 2-alkoxyquinolines (**11m, n, p-r, t-x**) gave only *p*-quinones (**14m, n, p-r, t-x**) in 57-89% yields. The spectral data of 2(1*H*)-quinolinonequinones (**12, 13**) and 2-alkoxyquinolinequinones (**14-16**) are given in Table I.

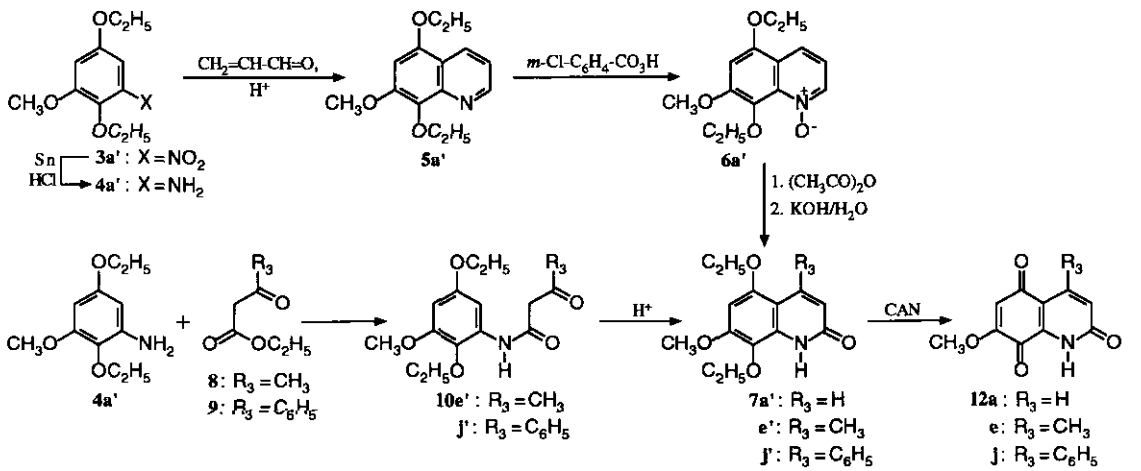


TABLE I. 2-Quinolinonequinones and 2-Alkoxyquinolinequinones

	Yield[a] (%)	Appearance (Recrystn. solv.)	mp (°C)	Formula	Analysis or Hrms[b] Calcd (Found) C	H	N	Ms *m/z* (%)	Ir (KBr) (cm^{-1})	^{1}H-Nmr (270 MHz)[c] δ ($CDCl_3$, *J* = Hz)
2,5,8(1*H*)-Quinolinetriones										
12a	31 [56]	Yellow needles (CH_2Cl_2-ether)	*ca.* 270	$C_{10}H_7NO_4$	205.0375 (205.0372)			205 (M^+, 100)	1650	3.98 (3H, s, OCH_3), 6.34 (1H, s, C_6-H), 7.22 (1H, d, *J* = 9.2, C_3-H), 8.32 (1H, d, *J* = 9.2, C_4-H)
12b	28	Red needles (CH_2Cl_2-ether)	>300	$C_{10}H_7NO_4$	58.54 (58.21	3.44 3.49	6.83 6.66)	205 (M^+, 100) 176 (62)	1676 1654	3.98 (3H, s, OCH_3), 6.23 (1H, s, C_7-H), 7.07 (1H, d, *J* = 9.6, C_3-H), 8.23 (1H, d, *J* = 9.6, C_4-H)
12c	31	Red needles (CH_3OH-$CHCl_3$-ether)	*ca.* 260 (decomp.)	$C_{11}H_9NO_4$	60.28 (60.22	4.14 4.16	6.39 6.27)	219 (M^+, 100) 191 (32)	1712 1666	2.03 (3H, s, C_7-CH_3), 4.20 (3H, s, OCH_3), 6.79 (1H, d, *J* = 9.6, C_3-H), 7.91 (1H, d, *J* = 9.6, C_4-H), 9.60 (1H, br, NH)
12d	36	Orange needles (ether)	173-176	$C_{12}H_{11}NO_4$	61.80 (61.59	4.75 4.73	6.01 5.85)	233 (M^+, 100) 218 (95) 190 (57)	1682 1658 1620	1.08 (3H, t, *J* = 7.6, CH_2CH_3), 2.54 (2H, q, *J* = 7.6, CH_2CH_3), 4.20 (3H, s, OCH_3), 6.79 (1H, d, *J* = 9.6, C_3-H), 7.91 (1H, d, *J* = 9.6, C_4-H), 9.47 (1H, br, NH)
12e	37 [73]	Orange prisms (CH_2Cl_2-hexane)	*ca.* 250	$C_{11}H_9NO_4$	60.28 (60.12	4.14 4.16	6.39 6.32)	219 (M^+, 100)	1640	2.59 (3H, d, *J* = 1.0, C_4-CH_3), 3.89 (3H, s, OCH_3), 5.98 (1H, s, C_6-H), 6.63 (1H, q, *J* = 1.0, C_3-H), 9.20 (1H, br, NH)
12f	69	Orange needles (CH_2Cl_2-hexane)	260-262	$C_{11}H_9NO_4$	60.28 (59.92	4.14 3.95	6.39 6.35)	219 (M^+, 100) 204 (25)	1678 1666	2.59 (3H, d, *J* = 1.2, C_4-CH_3), 3.93 (3H, s, OCH_3), 6.05 (1H, s, C_7-H), 6.56 (1H, q, *J* = 1.2, C_3-H), 9.48 (1H, br, NH)
12g	38	Orange prisms (CH_2Cl_2-ether)	213-215	$C_{12}H_{11}NO_4$	61.80 (61.77	4.75 4.66	6.01 5.88)	233 (M^+, 100) 205 (26)	1638	2.02 (3H, s, C_7-CH_3), 2.57 (3H, d, *J* = 1.0, C_4-CH_3), 4.16 (3H, s, OCH_3), 6.55 (1H, q, *J* = 1.0, C_3-H), 9.56 (1H, br, NH)
12h	39	Orange needles (CH_2Cl_2-hexane)	194-195	$C_{13}H_{13}NO_4$	63.15 (62.99	5.30 5.27	5.67 5.66)	247 (M^+, 100) 232 (77) 204 (58)	1656 1626	1.08 (3H, t, *J* = 7.6, CH_2CH_3), 2.52 (2H, q, *J* = 7.6, CH_2CH_3), 2.57 (3H, d, *J* = 1.0, C_4-CH_3), 4.15 (3H, s, OCH_3), 6.55 (1H, q, *J* = 1.0, C_3-H), 9.56 (1H, br, NH)
12i	49	Orange needles (CH_2Cl_2-hexane)	195-198 (decomp.)	$C_{15}H_9NO_3$	71.71 (71.39	3.61 3.32	5.58 5.57)	251 (M^+, 100) 250 (88)	1660 1650	6.68 (1H, s, C_3-H), 6.78 and 6.93 (each 1H, d, *J* = 10.2, C_6-H, C_7-H), 7.2-7.5 (5H, m, C_6H_5), 9.59 (1H, br, NH)
12j	24 [27]	Orange needles (CH_2Cl_2-hexane)	>290	$C_{16}H_{11}NO_4$	281.0688 (281.0712)			281 (M^+, 100) 280 (77)	1638	3.81 (3H, s, OCH_3), 6.01 (1H, s, C_6-H), 6.43 (1H, s, C_3-H), 7.2-7.5 (5H, m, C_6H_5), 10.69 (1H, br, NH)
12k	29	Orange needles (CH_2Cl_2-hexane)	219-220	$C_{17}H_{13}NO_4$ ·1/2CH_2Cl_2	62.23 (62.20	4.18 4.00	4.15 4.16)	295 (M^+, 100) 266 (47)	1656 1640	2.03 (3H, s, C_7-CH_3), 4.05 (3H, s, OCH_3), 6.60 (1H, s, C_3-H), 7.2-7.5 (5H, m, C_6H_5), 9.72 (1H, br, NH); 5.30 (1H, 1/2 CH_2Cl_2)
12l	69	Red needles (CH_2Cl_2-ether)	190-191	$C_{11}H_9NO_4$	60.28 (60.01	4.14 4.15	6.39 6.34)	219 (M^+, 100) 204 (51)	1676 1648	3.90 and 3.93 (each 3H, s, NCH_3, OCH_3), 6.02 (1H, s, C_7-H), 6.84 (1H, d, *J* = 9.6, C_3-H), 8.04 (1H, d, *J* = 9.6, C_4-H)
12m	14	Red needles ($CHCl_3$-ether)	172-173	$C_{12}H_{11}NO_4$	61.80 (61.70	4.75 4.77	6.01 5.96)	233 (M^+, 100) 218 (61)	1696 1656	2.03 (3H, s, C_7-CH_3), 3.89 (3H, s, NCH_3), 4.14 (3H, s, OCH_3), 6.82 (1H, d, *J* = 9.6, C_3-H), 7.97 (1H, d, *J* = 9.6, C_4-H)
12n	7	Orange needles (ether-hexane)	90-93	$C_{13}H_{13}NO_4$	247.0844 (247.0844)			247 (M^+, 100) 232 (86)	1662 1622	1.08 (3H, t, *J* = 7.6, CH_2CH_3), 2.54 (2H, q, *J* = 7.6, CH_2CH_3), 3.90 (3H, s, NCH_3), 4.14 (3H, s, OCH_3), 6.82 (1H, d, *J* = 8.9, C_3-H), 7.97 (1H, d, *J* = 8.9, C_4-H)
12o	24	Red needles (CH_2Cl_2-hexane)	187-188	$C_{12}H_{11}NO_4$	61.80 (61.67	4.75 4.73	6.01 5.92)	233 (M^+, 100) 204 (21)	1678 1630	2.57 (3H, d, *J* = 1.0, C_4-CH_3), 3.85 and 3.87 (each 3H, s, NCH_3, OCH_3), 5.93 (1H, s, C_6-H), 6.69 (1H, q, *J* = 1.0, C_3-H)
12p	82	Orange needles (CH_2Cl_2-ether)	211-212	$C_{12}H_{11}NO_4$	61.80 (61.80	4.75 4.66	6.01 5.93)	233 (M^+, 100) 218 (48)	1666 1628	2.57 (3H, d, *J* = 1.0, C_4-CH_3), 3.87 and 3.89 (each 3H, s, NCH_3, OCH_3), 5.99 (1H, s, C_7-H), 6.62 (1H, q, *J* = 1.0, C_3-H)

12q	19	Orange needles (CH_2Cl_2-hexane)	138-139	$C_{13}H_{13}NO_4$	63.15 (63.12	5.30 5.27	5.67 5.64)	247 (M^+, 100) 232 (58)	1686 1650	2.01 (3H, s, C_7-CH_3), 2.55 (3H, d, J = 1.0, C_4-CH_3), 3.84 (3H, s, NCH_3), 4.08 (3H, s, OCH_3), 6.60 (1H, q, J = 1.0, C_3-H)
12r	78	Orange needles (CH_2Cl_2-hexane)	186-188	$C_{16}H_{11}NO_3$	72.45 (72.30	4.18 4.30	5.28 5.13)	265 (M^+, 100) 264 (90)	1644	3.93 (3H, s, NCH_3), 6.71 (1H, s, C_3-H), 6.70 and 6.83 (each 1H, d, J = 10.2, C_6-H, C_7-H), 7.1-7.5 (5H, m, C_6H_5)
12s	39	Orange needles (CH_2Cl_2-hexane)	244-246	$C_{17}H_{13}NO_4$	295.0844 (295.0828)			295 (M^+, 100) 294 (93)	1662 1630	3.86 and 3.93 (each 3H, s, NCH_3, OCH_3), 5.84 (1H, s, C_6-H), 6.72 (1H, s, C_3-H), 7.1-7.5 (5H, m, C_6H_5)
12t	13	Orange prisms (CH_2Cl_2-hexane)	178-180	$C_{18}H_{15}NO_4$	69.89 (69.63	4.89 5.00	4.53 4.45)	309 (M^+, 100) 294 (63)	1654 1630	2.02 (3H, s, C_7-CH_3), 3.91 and 3.97 (each, 3H, s, NCH_3, OCH_3), 6.64 (1H, s, C_3-H), 7.2-7.5 (5H, m, C_6H_5)
12u	84	Orange needles (CH_2Cl_2-hexane)	152-154	$C_{13}H_{13}NO_4$	63.15 (63.02	5.30 5.31	5.67 5.61)	247 (M^+, 100) 232 (90) 204 (40)	1654 1626	1.40 (3H, t, J = 6.9, CH_2CH_3), 2.56 (3H, d, J = 1.0, C_4-CH_3), 3.88 (3H, s, OCH_3), 4.51 (2H, q, J = 6.9, CH_2CH_3), 5.98 (1H, s, C_7-H), 6.61 (1H, q, J = 1.0, C_3-H)
12v	19	Orange needles (ether-hexane)	114-115	$C_{14}H_{15}NO_4$	64.36 (64.09	5.79 5.83	5.36 5.29)	261 (M^+, 100) 246 (97)	1692 1660 1632	1.41 (3H, t, J = 6.9, CH_2CH_3), 2.01 (3H, s, C_7-CH_3), 2.54 (3H, d, J = 0.7, C_4-CH_3), 4.08 (3H, s, OCH_3), 4.43 (2H, q, J = 6.9, CH_2CH_3), 6.59 (1H, q, J = 0.7, C_3-H)
12w	61	Orange prisms (CH_2Cl_2-hexane)	122-123	$C_{17}H_{13}NO_3$	73.11 (72.99	4.69 4.55	5.02 4.96)	279 (M^+, 100) 278 (87) 264 (18)	1672 1656	1.45 (3H, t, J = 6.9, CH_2CH_3), 4.54 (2H, q, J = 6.9, CH_2CH_3), 6.68 and 6.82 (each 1H, d, J = 10.2, C_6-H, C_7-H), 6.69 (1H, s, C_3-H), 7.1-7.5 (5H, m, C_6H_5)
12x	15	Yellow powder (hexane)	114-116	$C_{19}H_{17}NO_4$	70.58 (70.42	5.30 5.35	4.33 4.26)	323 (M^+, 93) 308 (100)	1656 1628	1.46 (3H, t, J = 6.9, CH_2CH_3), 2.02 (3H, s, C_7-CH_3), 3.97 (3H, s, OCH_3), 4.52 (2H, q, J = 6.9, CH_2CH_3), 6.62 (1H, s, C_3-H), 7.1-7.5 (5H, m, C_6H_5)
2,5,6(1*H*)-Quinolinetriones										
13b	31	Orange needles (CH_2Cl_2-ether)	275-278	$C_{10}H_7NO_4$	205.0375 (205.0374)			205 (M^+, 26) 177 (M^+-CO, 100) 148 (43)	1686 1666 1650	4.16 (3H, s, OCH_3), 6.17 (1H, s, C_7-H), 6.94 (1H, d, J = 9.6, C_3-H), 8.20 (1H, d, J = 9.6, C_4-H)
13c	26	Red prisms (CH_3OH-$CHCl_3$-ether)	230-232 (decomp.)	$C_{11}H_9NO_4$	60.28 (60.23	4.14 4.18	6.39 6.24)	219 (M^+, 33) 191 (M^+-CO, 100) 176 (54)	1686 1640	2.17 (3H, s, C_7-CH_3), 4.18 (3H, s, OCH_3), 6.59 (1H, d, J = 9.6, C_3-H), 7.95 (1H, d, J = 9.6, C_4-H), 10.05 (1H, br, NH)
13f	16	Orange needles (CH_2Cl_2-hexane)	275-277 (decomp.)	$C_{11}H_9NO_4$	60.28 (60.12	4.14 4.16	6.39 6.33)	219 (M^+, 25) 191 (M^+-CO, 100) 162 (51)	1674 1658 1622	2.59 (3H, d, J = 0.9, C_4-CH_3), 4.05 (3H, s, OCH_3), 6.00 (1H, s, C_7-H), 6.45 (1H, q, J = 0.9, C_3-H), 9.38 (1H, br, NH)
13g	23	Red needles (CH_2Cl_2-ether)	260-261	$C_{12}H_{11}NO_4$	61.80 (61.50	4.75 4.67	6.01 5.88)	233 (M^+, 29) 205 (M^+-CO, 100) 190 (47) 176 (53)	1688 1654 1628	2.15 (3H, s, C_7-CH_3), 2.56 (3H, d, J = 1.0, C_4-CH_3), 4.14 (3H, s, OCH_3), 6.37 (1H, q, J = 1.0, C_3-H), 9.65 (1H, br, NH)
13h	14	Orange needles (CH_2Cl_2-hexane)	243-245	$C_{13}H_{13}NO_4$	63.15 (62.98	5.30 5.22	5.67 5.51)	247 (M^+, 17) 219 (M^+-CO, 64) 204 (100)	1654	1.18 (3H, t, J = 7.6, CH_2CH_3), 2.57 (3H, d, J = 1.0, C_4-CH_3), 2.62 (2H, q, J = 7.6, CH_2CH_3), 4.14 (3H, s, OCH_3), 6.37 (1H, q, J = 1.0, C_3-H), 10.04 (1H, br, NH)
13k	16	Orange needles (CH_2Cl_2-ether)	260-262	$C_{17}H_{13}NO_4$	69.15 (68.78	4.44 4.23	4.74 4.60)	295 (M^+, 13) 267 (M^+-CO, 100) 252 (32) 238 (44)	1686 1662 1640	2.17 (3H, s, C_7-CH_3), 4.19 (3H, s, OCH_3), 6.43 (1H, s, C_3-H), 7.2-7.5 (5H, m, C_6H_5), 9.93 (1H, br, NH)

TABLE I. (Continued)

	Yield (%)	Appearance (Recrystn. solv.)	mp (°C)	Formula	Analysis or Hrms Calcd (Found) C	H	N	Ms *m/z* (%)	Ir (KBr) (cm^{-1})	^{1}H-Nmr (270 MHz) δ ($CDCl_3$, *J* = Hz)
13l	9	Red powder (CH_2Cl_2-ether)	235-240 (decomp.)	$C_{11}H_9NO_4$	60.28 (60.09	4.14 4.15	6.39 6.11)	219 (M^+, 17) 191 (M^+-CO, 100) 162 (21) 134 (32)	1666 1650	3.84 (3H, s, NCH_3), 4.04 (3H, s, OCH_3), 5.99 (1H, s, C_7-H), 6.71 (1H, d, *J* = 9.6, C_3-H), 8.00 (1H, d, *J* = 9.6, C_4-H)
13m	5	Dark red needles ($CHCl_3$-ether)	196.5-198	$C_{12}H_{11}NO_4$	61.80 (61.75	4.75 4.79	6.01 5.93)	233 (M^+, 24) 205 (M^+-CO, 100) 190 (62)	1684 1648	2.10 (3H, s, C_7-CH_3), 3.81 and 3.91 (each 3H, s, NCH_3, OCH_3), 6.61 (1H, d, *J* = 9.6, C_3-H), 7.92 (1H, d, *J* = 9.6, C_4-H)
13p	10	Red needles (CH_2Cl_2-ether)	260-262	$C_{12}H_{11}NO_4$	61.80 (61.50	4.75 4.77	6.01 5.92)	233 (M^+, 14) 205 (M^+-CO, 100)	1672 1650	2.55 (3H, s, C_4-CH_3), 3.77 (3H, s, NCH_3), 4.02 (3H, s, OCH_3), 5.99 (1H, s, C_7-H), 6.50 (1H, s, C_3-H)
13t	9	Red prisms (CH_2Cl_2-hexane)	184-186	$C_{18}H_{15}NO_4$	309.1001 (309.1016)			309 (M^+, 4) 281 (M^+-CO, 100) 266 (26)	1646	2.09 (3H, s, C_7-CH_3), 3.81 and 3.93 (each, 3H, s, NCH_3, OCH_3), 6.46 (1H, s, C_3-H), 7.1-7.5 (5H, m, C_6H_5)
13u	6	Red prisms (CH_2Cl_2-hexane)	213-215	$C_{13}H_{13}NO_4$	247.0844 (247.0849)			247 (M^+, 14) 219 (M^+-CO, 100) 191 (38) 162 (68)	1656	1.45 (3H, t, *J* = 6.9, CH_2CH_3), 2.53 (3H, d, *J* = 1.3, C_4-CH_3), 4.03 (3H, s, OCH_3), 4.33 (2H, q, *J* = 6.9, CH_2CH_3), 5.99 (1H, s, C_7-H), 6.49 (1H, q, *J* = 1.3, C_3-H)
2-Alkoxy-5,8-quinolinediones										
14l	62	Yellow needles (CH_2Cl_2-ether)	211-212	$C_{11}H_9NO_4$	60.28 (59.97	4.14 4.13	6.39 6.32)	219 (M^+, 100) 189 (37)	1676 1664	3.92 (3H, s, C_6-OCH_3), 4.16 (3H, s, C_2-OCH_3), 6.24 (1H, s, C_7-H), 7.03 (1H, d, *J* = 8.6, C_3-H), 8.30 (1H, d, *J* = 8.6, C_4-H)
14m	64	Yellow needles ($CHCl_3$-hexane)	163-164	$C_{12}H_{11}NO_4$	61.80 (61.74	4.75 4.79	6.01 5.99)	233 (M^+, 100) 218 (49)	1668	2.11 (3H, s, C_7-CH_3), 4.13 and 4.14 (each 3H, s, $2OCH_3$), 7.00 (1H, d, *J* = 8.6, C_3-H), 8.22 (1H, d, *J* = 8.6, C_4-H)
14n	57	Yellow needles (ether)	94-96	$C_{13}H_{13}NO_4$	63.15 (63.10	5.30 5.33	5.67 5.62)	247 (M^+, 73) 232 (100) 204 (33)	1664 1620	1.12 (3H, t, *J* = 7.6, CH_2CH_3), 2.62 (2H, q, *J* = 7.6, CH_2CH_3), 4.14 (6H, s, $2OCH_3$), 7.00 (1H, d, *J* = 8.6, C_3-H), 8.21 (1H, d, *J* = 8.6, C_3-H)
14o	47	Yellow needles (CH_2Cl_2-hexane)	214-215	$C_{12}H_{11}NO_4$	61.80 (61.63	4.75 4.82	6.01 5.96)	233 (M^+, 100) 203 (35)	1696 1640 1622	2.72 (3H, d, *J* = 1.0, C_4-CH_3), 3.89 (3H, s, C_7-OCH_3), 4.11 (3H, s, C_2-OCH_3), 6.05 (1H, s, C_6-H), 6.83 (1H, q, *J* = 1.0, C_3-H)
14p	89	Yellow needles (CH_2Cl_2-hexane)	216-217	$C_{12}H_{11}NO_4$	61.80 (61.57	4.75 4.76	6.01 5.95)	233 (M^+, 100) 218 (28) 203 (31)	1672 1656	2.72 (3H, d, *J* = 0.7, C_4-CH_3), 3.90 (3H, s, C_6-OCH_3), 4.13 (3H, s, C_2-OCH_3), 6.19 (1H, s, C_7-H), 6.81 (1H, q, *J* = 0.7, C_3-H)
14q	79	Yellow needles (CH_2Cl_2-hexane)	191-192	$C_{13}H_{13}NO_4$	63.15 (63.04	5.30 5.31	5.67 5.61)	247 (M^+, 100) 232 (48) 219 (31) 204 (30)	1660 1632	2.09 (3H, s, C_7-CH_3), 2.70 (3H, s, C_4-CH_3), 4.08 and 4.11 (each 3H, s, $2OCH_3$), 6.78 (1H, s, C_3-H)
14r	89	Yellow prisms (CH_2Cl_2-hexane)	137-139	$C_{16}H_{11}NO_3$	72.45 (72.27	4.18 4.31	5.28 5.32)	265 (M^+, 100) 264 (69)	1680 1662	4.18 (3H, s, OCH_3), 6.89 (1H, s, C_3-H), 6.81 and 7.00 (each 1H, d, *J* = 10.2, C_6-H, C_7-H), 7.2-7.5 (5H, m, C_6H_5)

14s	37	Yellow needles (CH_2Cl_2-hexane)	241-242	$C_{17}H_{13}NO_4$	69.15 (68.96	4.44 4.49	4.74 4.70)	295 (M^+, 100) 294 (94)	1692 1642 1622	3.88 (3H, s, C_7-OCH_3), 4.17 (3H, s, C_2-OCH_3), 5.96 (1H, s, C_6-H), 6.86 (1H, s, C_3-H), 7.2-7.5 (5H, m, C_6H_5)
14t	57	Yellow prisms (CH_2Cl_2-hexane)	155-156	$C_{18}H_{15}NO_4$	69.89 (69.82	4.89 4.78	4.53 4.46)	309 (M^+, 100) 294 (30) 280 (50)	1658 1630	2.09 (3H, s, C_7-CH_3), 3.98 (3H, s, C_6-OCH_3), 4.17 (3H, s, C_2-OCH_3), 6.81 (1H, s, C_3-H), 7.2-7.5 (5H, m, C_6H_5)
14u	77	Yellow needles (CH_2Cl_2-hexane)	177-180	$C_{13}H_{13}NO_4$	63.15 (63.06	5.30 5.33	5.67 5.60)	247 (M^+, 70) 232 (54) 219 (100) 203 (57)	1660	1.42 (3H, t, J = 6.9, CH_2CH_3), 2.71 (3H, d, J = 0.7, C_4-CH_3), 3.90 (3H, s, OCH_3), 4.59 (2H, q, J = 6.9, CH_2CH_3), 6.18 (1H, s, C_7-H), 6.78 (1H, q, J = 0.7, C_3-H)
14v	73	Yellow needles (CH_2Cl_2-hexane)	135-136	$C_{14}H_{15}NO_4$	64.36 (64.15	5.79 5.77	5.36 5.32)	261 (M^+, 100) 246 (82) 233 (82) 217 (49) 205 (57)	1664 1630	1.41 (3H, t, J = 7.3, CH_2CH_3), 2.08 (3H, s, C_7-CH_3), 2.69 (3H, s, C_4-CH_3), 4.08 (3H, s, OCH_3), 4.57 (2H, q, J = 7.3, CH_2CH_3), 6.75 (1H, s, C_3-H)
14w	84	Yellow prisms (CH_2Cl_2-hexane)	145-146	$C_{17}H_{13}NO_3$	73.11 (73.14	4.69 4.51	5.02 5.02)	279 (M^+, 100) 264 (42) 251 (63) 250 (94) 234 (43)	1676 1660	1.45 (3H, t, J = 7.3, CH_2CH_3), 4.64 (2H, q, J = 7.3, CH_2CH_3), 6.80 and 6.99 (each 1H, d, J = 10.2, C_6-H, C_7-H), 6.86 (1H, s, C_3-H), 7.2-7.5 (5H, m, C_6H_5)
14x	65	Yellow needles (ether-hexane)	124-125	$C_{19}H_{17}NO_4$	70.58 (70.50	5.30 5.36	4.33 4.29)	323 (M^+, 100) 308 (50) 295 (48)	1658 1638	1.44 (3H, t, J = 7.3, CH_2CH_3), 2.09 (3H, s, C_7-CH_3), 3.98 (3H, s, OCH_3), 4.63 (2H, q, J = 7.3, CH_2CH_3), 6.79 (1H, s, C_3-H), 7.2-7.5 (5H, m, C_6H_5)
2-Alkoxy-5,6-quinolinedione and 2-Alkoxy-7,8-quinolinediones										
15l	31	Yellow needles (CH_2Cl_2-ether)	*ca.* 250	$C_{11}H_9NO_4$	60.28 (60.08	4.14 4.17	6.39 6.36)	219 (M^+, 13) 191 (M^+-CO, 100) 190 (45) 162 (65)	1692 1648	4.04 and 4.11 (each 3H, s, $2OCH_3$), 6.05 (1H, s, C_7-H), 6.90 (1H, d, J = 8.9, C_3-H), 8.25 (1H, d, J = 8.9, C_4-H)
16o	11	Red needles (CH_2Cl_2-hexane)	252-255	$C_{12}H_{11}NO_4$	61.80 (61.60	4.75 4.77	6.01 5.93)	233 (M^+, 4) 205 (M^+-CO, 100) 204 (52) 175 (27)	1706 1640	2.61 (3H, s, C_4-CH_3), 4.00 and 4.07 (each 3H, s, $2OCH_3$), 5.90 (1H, s, C_6-H), 6.81 (1H, s, C_3-H)
16s	16	Orange needles (CH_2Cl_2-hexane)	185-187	$C_{17}H_{13}NO_4$	295.0844 (295.0836)			295 (M^+, 18) 294 (15) 267 (M^+-CO, 100)	1708 1652 1640	3.47 (3H, s, C_5-OCH_3), 4.13 (3H, s, C_2-OCH_3), 5.81 (1H, s, C_6-H), 6.84 (1H, s, C_3-H), 7.1-7.5 (5H, m, C_6H_5)

a) Yields from 5,8-diethoxy-2(1*H*)-quinolinones (**7a'**, **e'**, **j'**) in blackets. *b*) High-resolution ms. *c*) Measured in $CDCl_3$-CF_3CO_2D (**12a**, **b**, **13b**) and dimethyl sulfoxide-d_6 (**12j**).

EXPERIMENTAL

All melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. ^{1}H-Nmr spectra were measured at 270 MHz in $CDCl_3$ (unless otherwise noted) with tetramethylsilane as an internal standard. All reactions were run with magnetic stirring. Anhydrous sodium sulfate was used for drying organic solvent extracts, and the solvent was removed with a rotary evaporator and finally under high vacuum. Column chromatography (flash chromatography)[5] was performed with silica gel 60 (230-400 mesh).

1,2,4-Trimethoxy-3-methyl-5-nitrobenzene (3c) and 3-Ethyl-1,2,4-trimethoxy-5-nitrobenzene (3d) Concentrated HNO_3 (*d* 1.38, 20 ml) was added dropwise to a solution of 1,2,4-trimethoxy-3-methylbenzene[6] (or 3-ethyl-1,2,4-trimethoxybenzene[7]) (50 mmol) in acetic acid (200 ml) for 5 min. The resulting solution was left for 1 h, poured into water (1000 ml), and extracted with CH_2Cl_2 (3 x 300 ml). The extract was washed with saturated aqueous $NaHCO_3$ solution and water, dried, and evaporated. The residue was chromatographed (eluting with CH_2Cl_2) to afford **3c** (or **3d**).

3c: Yield 96%. mp 47-48°C (hexane). Ms *m/z* (%): 227 (M^+, 100). *Anal.* Calcd for $C_{10}H_{13}NO_5$: C, 52.86; H, 5.77; N, 6.16. Found: C, 52.80; H, 5.80; N, 6.10. ^{1}H-Nmr δ: 2.22 (3H, s, C_3-CH_3), 3.84 (3H, s, OCH_3), 3,89 (6H, s, $2OCH_3$), 7.30 (1H, s, C_6-H).

3d: Yield 94%. oil. Ms *m/z* (%): 241 (M^+, 100). High-resolution ms Calcd for $C_{11}H_{15}NO_5$: 241.0950. Found: 241.0962. ^{1}H-Nmr δ: 1.18 (3H, t, *J* = 7.6 Hz, CH_2CH_3), 2.72 (2H, q, *J* = 7.6 Hz, CH_2CH_3), 3.87, 3.89, 3.93 (each 3H, s, $3OCH_3$), 7.37 (1H, s, C_6-H).

2,5-Diethoxy-1-methoxy-3-nitrobenzene (3a') A solution of 40% KOH (175 ml) was added dropwise to 2,5-dihydroxy-1-methoxy-3-nitrobenzene[8] (25.15 g, 135 mmol) and diethyl sulfate (124 ml, 0.95 mol) in ethanol (300 ml) at 70°C. The resulting solution was heated at 70°C for 30 min, then cooled, diluted with water (800 ml), and extracted with with CH_2Cl_2 (3 x 800 ml). The extract was washed with 5% NaOH solution (2 x 500 ml) and water, dried, and evaporated. The residue was chromatographed (eluting with ethyl acetate-hexane 2:8) to afford **3a'** (27.67 g, 84%). mp 58-59°C (ethyl acetate). Ms *m/z* (%): 241 (M^+, 82), 213 (100), 185 (73). *Anal.* Calcd for $C_{11}H_{15}NO_5$: C, 54.77; H, 6.27; N, 5.81. Found: C, 54.68; H, 6.17; N, 5.75. ^{1}H-Nmr δ: 1.38, 1.42 (each 3H, t, *J* = 6.9 Hz, $2CH_2CH_3$), 3.87 (3H, s, OCH_3), 4.02, 4.12 (each 2H, q, *J* = 6.9 Hz, $2CH_2CH_3$), 6.66 (1H, d, *J* = 3.0 Hz, C_6-H), 6.79 (1H, d, *J* = 3.0 Hz, C_4-H).

2,4,5-Trimethoxy-3-methylaniline (4c), 3-Ethyl-2,4,5-trimethoxyaniline (4d), and 2,5-Diethoxy-3-methoxyaniline (4a') A mixture of **3c** (or **3d**, **3a'**) (25 mmol), Sn (23.7 g, 0.2 mol) and concentrated HCl (60 ml) was heated at 60-70°C for 1 h. The reaction mixture was cooled, adjusted to pH 9–10 with 10% NaOH solution, and extracted with CH_2Cl_2 (3 x 100 ml). The extract was washed with water, dried, and evaporated to afford **4c** (or **4d**, **a'**).

4c: Yield 77%. mp 55-56°C (hexane). Ms *m/z* (%): 197 (M^+, 58), 182 (100). *Anal.* Calcd for $C_{10}H_{15}NO_3$: C, 60.90; H, 7.67; N, 7.10. Found: C, 60.64; H, 7.81; N, 7.04. ^{1}H-Nmr δ: 2.20 (3H, s, C_3-CH_3), 2.7-3.7 (2H, br, NH_2), 3.71, 3.73, 3.79 (each 3H, s, $3OCH_3$), 6.30 (1H, s, C_6-H).

4d: Yield 94%. oil. Ms *m/z* (%): 211 (M^+, 54), 196 (100). High-resolution ms Calcd for $C_{11}H_{17}NO_3$: 211.1208. Found: 211.1169. ^{1}H-Nmr δ: 1.19 (3H, t, *J* = 7.6 Hz, CH_2CH_3), 2.5–3.5 (2H, br, NH_2), 2.64 (2H, q, *J* = 7.6 Hz, CH_2CH_3), 3.73, 3.76, 3.79 (each 3H, s, $3OCH_3$), 6.24 (1H, s, C_6-H).

4a': Yield 70%. mp 49.5-51.5°C (ether-hexane). Ms *m/z* (%): 211 (M^+, 51), 182 (100), 154 (72). High-resolution ms Calcd for $C_{11}H_{17}NO_3$: 211.1208. Found: 211.1207. ^{1}H-Nmr δ: 1.35, 1.38 (each 3H, t, *J* = 6.9

Hz, $2CH_2CH_3$), 3.79 (3H, s, OCH_3), 3.82 (2H, br, NH_2), 3.94, 3.97 (each 2H, q, J = 6.9 Hz, $2CH_2CH_3$), 5.93, 5.94 (each 1H, d, J = 2.6 Hz, C_4-H, C_6-H).

5,7,8-Trimethoxyquinoline (5a), 7-Ethyl-5,6,8-trimethoxyquinoline (5d), and 5,8-Diethoxy-7-methoxyquinoline (5a') Acrolein (1.74 g, 30 mmol) was added dropwise to a refluxing solution of 2,3,5-trimethoxyaniline[8] (**4a**) (or 3-ethyl-2,4,5-trimethoxyaniline (**4d**), 2,5-diethoxy-3-methoxyaniline (**4a'**)) (5 mmol) in 6 N HCl (50 ml), and the resulting solution was refluxed for an additional 30 min. The reaction mixture was cooled, diluted with water (100 ml), basified with 10% NaOH solution, and extracted with CH_2Cl_2 (3 x 100 ml). The extract was washed with water, dried, and evaporated. The residue was chromatographed (eluting with ethyl acetate-hexane 2:8-3:7) to afford the quinoline (**5a, d, a'**).

5a: Yield 55%. mp 88-90°C (ethyl acetate). Ms *m/z* (%): 219 (M^+, 47), 204 (100). *Anal.* Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.47; H, 5.99; N, 6.27. ^{1}H-Nmr δ: 4.00, 4.04, 4.05 (each 3H, s, $3OCH_3$), 6.69 (1H, s, C_6-H), 7.26 (1H, dd, J = 8.5, 4.3 Hz, C_3-H), 8.47 (1H, dd, J = 8.5, 1.7 Hz, C_4-H), 8.92 (1H, dd, J = 4.3, 1.7 Hz, C_2-H).

5d: Yield 43%. oil. Ms *m/z* (%): 247 (M^+, 38), 232 (100). High-resolution ms Calcd for $C_{14}H_{17}NO_3$: 247.1208. Found: 247.1195. ^{1}H-Nmr δ: 1.26 (3H, t, J = 7.3 Hz, CH_2CH_3), 2.90 (2H, q, J = 7.3 Hz, CH_2CH_3), 3.97, 4.01, 4.11 (each 3H, s, $3OCH_3$), 7.36 (1H, dd, J = 8.5, 4.3 Hz, C_3-H), 8.42 (1H, dd, J = 8.5, 1.7 Hz, C_4-H), 8.85 (1H, dd, J = 4.3, 1.7 Hz, C_2-H).

5a': Yield 48%. mp 78-79°C (ethyl acetate). Ms *m/z* (%): 247 (M^+, 33), 232 (100), 218 (31), 190 (83). High-resolution ms Calcd for $C_{14}H_{17}NO_3$: 247.1208. Found: 247.1208. ^{1}H-Nmr δ: 1.47, 1.55 (each 3H, t, J = 6.9 Hz, $2CH_2CH_3$), 4.03 (3H, s, OCH_3), 4.20, 4.29 (each 2H, q, J = 6.9 Hz, $2CH_2CH_3$), 6.69 (1H, s, C_6-H), 7.27 (1H, dd, J = 8.3, 4.3 Hz, C_3-H), 8.55 (1H, dd, J = 8.3, 1.7 Hz, C_4-H), 8.94 (1H, dd, J = 4.3, 1.7 Hz, C_2-H).

5,6,8-Trimethoxy(-7-methyl)quinoline (5b, c) Concentrated H_2SO_4 (3 ml) was added to a mixture of 2,4,5-trimethoxy(-3-methyl)aniline (**4b**,[9] **c**) (5 mmol), glycerin (20 ml), *m*-nitrobenzenesulfonic acid (1.52 g, 7.5 mmol), H_3BO_3 (0.5 g), and $FeSO_4 \cdot 7H_2O$ (0.3 g). The whole was heated at 140-150°C for 15 min. The reaction mixture was cooled, diluted with ice-water (75 ml), basified with 10% NaOH solution, and extracted with CH_2Cl_2 (3 x 50 ml). The extract was washed with water, dried, and evaporated. The residue was chromatographed (eluting with ethyl acetate-hexane 3:7-7:3) to afford the quinoline (**5b, c**).

5b: Yield 70%. mp 84-85°C (ether). Ms *m/z* (%): 219 (M^+, 52), 204 (100). *Anal.* Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.50; H, 5.98; N, 6.29. ^{1}H-Nmr δ: 3.94, 4.04, 4.10 (each 3H, s, $3OCH_3$), 6.88 (1H, s, C_7-H), 7.43 (1H, dd, J = 8.6, 4.3 Hz, C_3-H), 8.42 (1H, dd, J = 8.6, 1.7 Hz, C_4-H), 8.82 (1H, dd, J = 4.3, 1.7 Hz, C_2-H).

5c: Yield 57%. oil. Ms *m/z* (%): 233 (M^+, 48), 218 (100). High-resolution ms Calcd for $C_{13}H_{15}NO_3$: 233.1052. Found: 233.1045. ^{1}H-Nmr δ: 2.43 (3H, s, C_7-CH_3), 3.97, 3.98. 4.06 (each 3H, s, $3OCH_3$), 7.37 (1H, dd, J = 8.6, 4.3 Hz, C_3-H), 8.43 (1H, dd, J = 8.6, 1.7 Hz, C_4-H), 8.87 (1H, dd, J = 4.3, 1.7 Hz, C_2-H).

5,7,8-Trimethoxyquinoline *N*-Oxide (6a), (7-Alkyl-)5,6,8-trimethoxyquinoline *N*-Oxide (6b-d), and 5,8-Diethoxy-7-methoxyquinoline *N*-Oxide (6a') *m*-Chloroperoxybenzoic acid (80% purity, 270 mg, 1.25 mmol) was added to a solution of quinoline (**5a-d, a'**) (1 mmol) in CH_2Cl_2 (5 ml). The resulting mixture was left for 16 h, and the precipitated crystals were filtered off. The filtrate was washed with saturated aqueous $NaHCO_3$ solution (3 x 10 ml) and water, dried, concentrated, and chromatographed. Elution with ethyl acetate

was discarded, and further elution with ethyl acetate-CH_3OH (100:1-7:3) afforded *N*-oxide (**6a-d, a'**) as a solid, which was used without further purification.

6a: Yield 39%. ^{1}H-Nmr δ: 3.99, 4.00, 4.03 (each 3H, s, $3OCH_3$), 6.74 (1H, s, C_6-H), 7.09 (1H, dd, *J* = 8.6, 5.9 Hz, C_3-H), 8.09 (1H, dd, *J* = 8.6, 1.0 Hz, C_4-H), 8.55 (1H, dd, *J* = 5.9, 1.0 Hz, C_2-H).

6b: Yield 40%. ^{1}H-Nmr δ: 3.92, 4.02, 4.04 (each 3H, s, $3OCH_3$), 6.92 (1H, s, C_7-H), 7.24 (1H, dd, *J* = 8.9, 5.9 Hz, C_3-H), 8.04 (1H, dd, *J* = 8.9, 1.3 Hz, C_4-H), 8.32 (1H, dd, *J* = 5.9, 1.3 Hz, C_2-H).

6c: Yield 72%. ^{1}H-Nmr δ: 2.40 (3H, s, C_7-CH_3), 3.95, 3.96, 3.97 (each 3H, s, $3OCH_3$), 7.17 (1H, dd, *J* = 8.6, 5.9 Hz, C_3-H), 7.96 (1H, dd, *J* = 8.6, 1.3 Hz, C_4-H), 8.40 (1H, dd, *J* = 5.9, 1.3 Hz, C_2-H).

6d: Yield 73%. ^{1}H-Nmr δ: 1.23 (3H, t, *J* = 7.6 Hz, CH_2CH_3), 2.87 (2H, q, *J* = 7.6 Hz, CH_2CH_3), 3.95, 3.97, 4.01 (each 3H, s, $3OCH_3$), 7.15 (1H, dd, *J* = 8.6, 5.9 Hz, C_3-H), 7.91 (1H, dd, *J* = 8.6, 1.0 Hz, C_4-H), 8.36 (1H, dd, *J* = 5.9, 1.0 Hz, C_2-H).

6a': Yield 23%. ^{1}H-Nmr δ: 1.48, 1.55 (each 3H, t, *J* = 6.9 Hz, $2CH_2CH_3$), 4.01 (3H, s, OCH_3), 4.16, 4.20 (each 2H, q, *J* = 6.9 Hz, $2CH_2CH_3$), 6.73 (1H, s, C_6-H), 7.05 (1H, dd, *J* = 8.6, 5.9 Hz, C_3-H), 8.08 (1H, dd, *J* = 8.6, 1.0 Hz, C_4-H), 8.43 (1H, dd, *J* = 5.9, 1.0 Hz, C_2-H).

5,7,8-Trimethoxy-2(1*H*)-quinolinone (7a), (7-Alkyl-)5,6,8-trimethoxy-2(1*H*)-quinolinone (7b-d), and 5,8-Diethoxy-7-methoxy-2(1*H*)-quinolinone (7a') A solution of *N*-oxide (**6a-d, a'**) (5 mmol) in acetic anhydride (7 ml) was left for 30 min. The reaction mixture was added dropwise to ice-water (100 ml), and extracted with $CHCl_3$ (3 x 30 ml). The extract was successively washed with water (3 x 60 ml), saturated aqueous $NaHCO_3$ solution (60 ml) and brine, dried, and evaporated. The residue was dissolved in CH_3OH (8 ml), and water (2 ml) and 10% KOH in CH_3OH (10 ml) were added. The whole was left for 15 min, diluted with water (60 ml), and extracted with ethyl acetate (or CH_2Cl_2) (3 x 30 ml). The extract was washed with water (60 ml) and brine, dried, and evaporated. The residue was chromatographed (eluting with CH_2Cl_2-ethyl acetate) to give 2(1*H*)-quinolinone (**7a-d, a'**).

7a: Yield 42%. mp 190-194°C (CH_2Cl_2). Ms *m/z* (%): 235 (M^+, 77), 220 (100), 192 (48). *Anal.* Calcd for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.95. Found: C, 61.28; H, 5.67; N, 5.74. Ir (KBr): 1646 cm^{-1} (C=O). ^{1}H-Nmr δ: 3.87, 3.92, 3.97 (each 3H, s, $3OCH_3$), 6.28 (1H, s, C_6-H), 6.42 (1H, d, *J* = 9.6 Hz, C_3-H), 8.02 (1H, d, *J* = 9.6 Hz, C_4-H), 9.09 (1H, br, NH).

7b: Yield 62%. mp 172-173°C (CH_2Cl_2-ether). Ms *m/z* (%): 235 (M^+, 86), 220 (100). *Anal.* Calcd for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.95. Found: C, 61.11; H, 5.54; N, 5.91. Ir (KBr): 1646 cm^{-1} (C=O). ^{1}H-Nmr δ: 3.91, 3.93, 3.97 (each 3H, s, $3OCH_3$), 6.71 (1H, d, *J* = 9.6 Hz, C_3-H), 6.76 (1H, s, C_7-H), 8.09 (1H, d, *J* = 9.6 Hz, C_4-H), 9.44 (1H, br, NH).

7c: Yield 61%. mp 156-157°C ($CHCl_3$-hexane). Ms *m/z* (%): 249 (M^+, 94), 234 (100), 206 (23), 191 (20). *Anal.* Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.56; H, 6.04; N, 5.57. Ir (KBr): 1656 cm^{-1} (C=O). ^{1}H-Nmr δ: 2.33 (3H, s, C_7-CH_3), 3.82, 3.85, 3.95 (each 3H, s, $3OCH_3$), 6.61 (1H, d, *J* = 9.6 Hz, C_3-H), 8.01 (1H, d, *J* = 9.6 Hz, C_4-H), 9.34 (1H, br, NH).

7d: Yield 52%. mp 164-165°C (ethyl acetate). Ms *m/z* (%): 263 (M^+, 73), 248 (100). *Anal.* Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.63; H, 6.46; N, 5.26. Ir (KBr): 1666 cm^{-1} (C=O). ^{1}H-Nmr δ: 1.25 (3H, t, *J* = 7.6 Hz, CH_2CH_3), 2.78 (2H, q, *J* = 7.6 Hz, CH_2CH_3), 3.87, 3.90, 3.95 (each 3H, s, $3OCH_3$), 6.66 (1H, d, *J* = 9.6 Hz, C_3-H), 8.10 (1H, d, *J* = 9.6 Hz, C_4-H), 9.65 (1H, br, NH).

7a': Yield 48%. mp 179-181°C (ethyl acetate). Ms *m/z* (%): 263 (M^+, 75), 234 (99), 206 (100). *Anal.* Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.75; H, 6.46; N, 5.28. Ir (KBr): 1696 cm^{-1} (C=O).

^{1}H-Nmr δ: 1.39, 1.49 (each 3H, t, J = 6.9 Hz, $2CH_2CH_3$), 3.93 (3H, s, OCH_3), 4.09, 4.12 (each 2H, q, J = 6.9 Hz, $2CH_2CH_3$), 6.27 (1H, s, C_6-H), 6.41 (1H, dd, J = 9.6, 2.0 Hz, C_3-H), 8.05 (1H, d, J = 9.6 Hz, C_4-H), 8.92 (1H, br, NH).

***N*-(2,3,5-Trimethoxyphenyl)-3-oxobutyramide (10e), *N*-(2,4,5-Trimethoxyphenyl)-3-oxobutyramide (10f-h), and *N*-(2,5-Diethoxy-3-methoxyphenyl)-3-oxobutyramide (10e')** A solution of aniline (**4a-d, a'**) (10 mmol), ethyl acetoacetate (2.60 g, 20 mmol) and pyridine (0.2 ml) in toluene (20 ml) was refluxed for 3 h. The reaction mixture was evaporated and the residue was chromatographed (eluting with ethyl acetate-hexane 3:7-7:3) to afford anilide (**10e-h, e'**).

10e: Yield 64% (from **4a**). mp 56-57°C (ether-hexane). Ms *m/z* (%): 267 (M^+, 81), 168 (100). *Anal.* Calcd for $C_{13}H_{17}NO_5$: C, 58.42; H, 6.41; N, 5.24. Found: C, 58.32; H, 6.40; N, 5.15. Ir (KBr): 3280 cm^{-1} (NH); 1708, 1654 cm^{-1} (C=O). ^{1}H-Nmr δ: 2.34 (3H, s, CH_3CO), 3.61 (2H, s, CH_2), 3.79, 3.84, 3.86 (each 3H, s, $3OCH_3$), 6.27 (1H, d, J = 3.0 Hz, C_4-H), 7.63 (1H, d, J = 3.0 Hz, C_6-H), 9.45 (1H, br, NH).

10f: Yield 86% (from **4b**). mp 92-93°C (ether-hexane). Ms *m/z* (%): 267 (M^+, 100), 209 (39), 168 (73). *Anal.* Calcd for $C_{13}H_{17}NO_5$: C, 58.42; H, 6.41; N, 5.24. Found: C, 58.39; H, 6.38; N, 5.15. Ir (KBr): 3284 cm^{-1} (NH); 1720, 1648 cm^{-1} (C=O). ^{1}H-Nmr δ: 2.33 (3H, s, CH_3CO), 3.58 (2H, s, CH_2), 3.86, 3.87, 3.89 (each 3H, s, $3OCH_3$), 6.56 (1H, s, C_3-H), 8.06 (1H, s, C_6-H), 9.08 (1H, br, NH).

10g: Yield 85% (from **4c**). mp 98-99°C (ether-hexane). Ms *m/z* (%): 281 (M^+, 89), 266 (11), 182 (100). *Anal.* Calcd for $C_{14}H_{19}NO_5$: C, 59.78; H, 6.81; N, 4.98. Found: C, 59.60; H, 6.75; N, 4.88. Ir (KBr): 3240 cm^{-1} (NH); 1706, 1656 cm^{-1} (C=O). ^{1}H-Nmr δ: 2.23 (3H, s, C_3-CH_3), 2.34 (3H, s, CH_3CO), 3.61 (2H, s, CH_2), 3.76, 3.77, 3.85 (each 3H, s, $3OCH_3$), 7.90 (1H, s, C_6-H), 9.43 (1H, br, NH).

10h: Yield 91% (from **4d**). mp 85-86°C (ether-hexane). Ms *m/z* (%): 295 (M^+, 99), 280 (14), 196 (100). *Anal.* Calcd for $C_{15}H_{21}NO_5$: C, 61.00; H, 7.17; N, 4.74. Found: C, 60.93; H, 7.12; N, 4.65. Ir (KBr): 3272 cm^{-1} (NH); 1708, 1670 cm^{-1} (C=O). ^{1}H-Nmr δ: 1.20 (3H, t, J = 7.6 Hz, CH_2CH_3), 2.34 (3H, s, CH_3CO), 2.68 (2H, q, J = 7.6 Hz, CH_2CH_3), 3.62 (2H, s, $COCH_2$), 3.79, 3.81, 3.85 (each 3H, s, $3OCH_3$), 7.89 (1H, s, C_6-H), 9.43 (1H, br, NH).

10e': Yield 93% (from **4a'**). mp 70-72°C (ethyl acetate). Ms *m/z* (%): 295 (M^+, 75), 266 (79), 182 (100), 154 (53). *Anal.* Calcd for $C_{15}H_{21}NO_5$: C, 61.00; H, 7.17; N, 4.74. Found: C, 60.79; H, 7.08; N, 4.66. Ir (KBr): 3228 cm^{-1} (NH); 1710, 1682 cm^{-1} (C=O). ^{1}H-Nmr δ: 1.39, 1.45 (each 3H, t, J = 6.9 Hz, $2CH_2CH_3$), 2.33 (3H, s, CH_3CO), 3.60 (2H, s, $COCH_2$), 3.82 (3H, s, OCH_3), 4.02, 4.05 (each 2H, q, J = 6.9 Hz, $2CH_2CH_3$), 6.27 (1H, d, J = 3.0 Hz, C_4-H), 7.63 (1H, d, J = 3.0 Hz, C_6-H), 9.52 (1H, br, NH).

***N*-(2,5-Dimethoxyphenyl)-3-phenyl-3-oxopropionamide (10i), *N*-(2,3,5-Trimethoxyphenyl)-3-phenyl-3-oxopropionamide (10j), *N*-(2,4,5-Trimethoxy-3-methylphenyl)-3-phenyl-3-oxopropionamide (10k), and *N*-(2,5-Diethoxy-3-methoxyphenyl)-3-phenyl-3-oxopropionamide (10j')** A solution of aniline (**4e, a, c, a'**) (10 mmol), ethyl benzoylacetate (2.31 g, 12 mmol) and pyridine (0.2 ml) in toluene (20 ml) was refluxed for 5 h. The reaction mixture was evaporated, and the residue was chromatographed (eluting with ethyl acetate-hexane 1:4-3:7) to afford anilide (**10i-k, j'**).

10i: Yield 97% (from **4e**). mp 49-51°C (CH_2Cl_2-hexane). Ms *m/z* (%): 299 (M^+, 100), 179 (66), 153 (46), 138 (57), 105 (29). *Anal.* Calcd for $C_{17}H_{17}NO_4$: C, 68.22; H, 5.72; N, 4.68. Found: C, 68.06; H, 5.82; N, 4.57. Ir (KBr): 3268 cm^{-1} (NH); 1672 cm^{-1} (C=O). ^{1}H-Nmr δ: 3.78, 3.90 (each 3H, s, $2OCH_3$), 4.13 (2H, s, CH_2), 6.59 (1H, dd, J = 8.9, 2.9 Hz, C_4-H), 6.81 (1H, d, J = 8.9 Hz, C_3-H), 7.4-8.1 (5H, m, C_6H_5), 8.09 (1H, d, J = 2.9 Hz, C_6-H), 9.42 (1H, br, NH).

10j: Yield 76% (from **4a**). mp 102-105°C (CH_2Cl_2). Ms *m/z* (%): 329 (M^+, 86), 314 (23), 209 (24), 194 (31), 183 (24), 168 (100), 105 (31). *Anal.* Calcd for $C_{18}H_{19}NO_5$: C, 65.64; H, 5.82; N, 4.25. Found: C, 65.62; H, 5.80; N, 4.19. Ir (KBr): 3268 cm^{-1} (NH); 1680, 1660 cm^{-1} (C=O). ^{1}H-Nmr δ: 3.79, 3.84, 3.87 (each 3H, s, $3OCH_3$), 4.14 (2H, s, CH_2), 6.28 (1H, d, *J* = 2.6 Hz, C_4-H), 7.4-8.1 (5H, m, C_6H_5), 7.65 (1H, d, *J* = 2.6 Hz, C_6-H), 9.58 (1H, br, NH).

10k: Yield 59% (from **4c**). mp 89-90°C (CH_2Cl_2-hexane). Ms *m/z* (%): 343 (M^+, 95), 223 (44), 182 (100), 105 (33). *Anal.* Calcd for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16; N, 4.08. Found: C, 66.30; H, 6.18; N, 3.99. Ir (KBr): 3336 cm^{-1} (NH); 1694, 1672 cm^{-1} (C=O). ^{1}H-Nmr δ: 2.24 (3H, s, C_3-CH_3), 3.77, 3.78, 3.85 (each 3H, s, $3OCH_3$), 4.14 (2H, s, CH_2), 7.4-8.1 (5H, m, C_6H_5), 7.92 (1H, s, C_6-H), 9.57 (1H, br, NH).

10j': Yield 83% (from **4a'**). mp 145-146°C (CH_2Cl_2). Ms *m/z* (%): 357 (M^+, 94), 328 (69), 208 (23), 182 (100), 154 (34), 105 (44). *Anal.* Calcd for $C_{20}H_{23}NO_5$: C, 67.21; H, 6.49; N, 3.92. Found: C, 67.09; H, 6.47; N, 3.88. Ir (KBr): 3288 cm^{-1} (NH); 1686, 1664 cm^{-1} (C=O). ^{1}H-Nmr δ: 1.39, 1.47 (each 3H, t, *J* = 6.9 Hz, $2CH_2CH_3$), 3.82 (3H, s, OCH_3), 4.02, 4.06 (each 2H, q, *J* = 6.9 Hz, $2CH_2CH_3$), 4.12 (2H, s, CH_2), 6.27 (1H, d, *J* = 2.6 Hz, C_4-H), 7.4-8.1 (5H, m, C_6H_5), 7.65 (1H, d, *J* = 2.6 Hz, C_6-H), 9.61 (1H, br, NH).

5,7,8-Trimethoxy-4-methyl-2(1*H*)-quinolinone (7e), 5,7,8-Trimethoxy-4-phenyl-2(1*H*)-quinolinone (7j), 5,8-Diethoxy-7-methoxy-4-methyl-2(1*H*)-quinolinone (7e'), and 5,8-Diethoxy-7-methoxy-4-phenyl-2(1*H*)-quinolinone (7j') A solution of anilide (**10e, j, e', j'**) (5 mmol) in concentrated HCl–dioxane (1:5, 30 ml) was heated at 90°C for 60 min. The reaction mixture was cooled, poured into ice-water (100 ml) and extracted with CH_2Cl_2 (3 x 50 ml). The extract was washed with water, dried and evaporated. The residue was chromatographed (eluting with ethyl acetate-hexane 1:9-3:7) to afford 2(1*H*)-quinolinone (**7e, j, e', j'**).

7e: Yield 84%. mp 189-192°C (CH_2Cl_2-hexane). Ms *m/z* (%): 249 (M^+, 76), 234 (100), 206 (33). *Anal.* Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.34; H, 6.03; N, 5.60. Ir (KBr): 1636 cm^{-1} (C=O). ^{1}H-Nmr δ: 2.60 (3H, d, *J* = 1.0 Hz, , C_4-CH_3), 3.87, 3.89, 3.97 (each 3H, s, $3OCH_3$), 6.23 (1H, br s, C_3-H), 6.28 (1H, s, C_6-H), 9.31 (1H, br, NH).

7j: Yield 92%. mp 196-198°C (CH_2Cl_2-hexane). Ms *m/z* (%): 311 (M^+, 83), 296 (100), 268 (31). *Anal.* Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.31; H, 5.55; N, 4.49. Ir (KBr): 1640 cm^{-1} (C=O). ^{1}H-Nmr δ: 3.41 (3H, s, C_5-OCH_3), 3.92, 3.96 (each 3H, s, C_7-OCH_3, C_8-OCH_3), 6.23 (1H, s, C_6-H), 6.27 (1H, d, *J* = 2.0 Hz, C_3-H), 7.2-7.4 (5H, m, C_6H_5), 9.23 (1H, br, NH).

7e': Yield 71%. mp 190-192°C (CH_2Cl_2-hexane). Ms *m/z* (%): 277 (M^+, 73), 248 (100), 220 (97), 192 (30). *Anal.* Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 64.81; H, 6.85; N, 5.01. Ir (KBr): 1640 cm^{-1} (C=O). ^{1}H-Nmr δ: 1.40, 1.50 (each 3H, t, *J* = 6.9 Hz, $2CH_2CH_3$), 2.63 (3H, s, C_4-CH_3), 3.93 (3H, s, OCH_3), 4.08, 4.09 (each 2H, q, *J* = 6.9 Hz, $2CH_2CH_3$), 6.23 (1H, s, C_3-H), 6.27 (1H, s, C_6-H), 9.14 (1H, br, NH).

7j': Yield 68%. mp 227-229°C (CH_2Cl_2). Ms *m/z* (%): 339 (M^+, 77), 310 (90), 282 (100), 254 (24). *Anal.* Calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24; N, 4.13. Found: C, 70.51; H, 6.23; N, 4.14. Ir (KBr): 1646 cm^{-1} (C=O). ^{1}H-Nmr δ: 0.69 (3H, t, *J* = 6.9 Hz, C_5-CH_2CH_3), 1.44 (3H, t, *J* = 6.9 Hz, C_8-CH_2CH_3), 3.67 (2H, q, *J* = 6.9 Hz, C_5-CH_2CH_3), 3.92 (3H, s, OCH_3), 4.14 (2H, q, *J* = 6.9 Hz, C_8-CH_2CH_3), 6.20 (1H, s, C_6-H), 6.26 (1H, d, *J* = 2.3 Hz, C_3-H), 7.2-7.4 (5H, m, C_6H_5), 9.31 (1H, br, NH).

(7-Alkyl-)5,6,8-trimethoxy-4-methyl-2(1*H*)-quinolinone (7f-h) A mixture of anilide (**10f-h**) (5 mmol) and polyphosphoric acid (25 ml) was heated at 150°C for 10 min. The reaction mixture was cooled, poured into ice-water (50 ml), neutralized with 28% ammonia solution, and extracted with CH_2Cl_2 (4 x 50 ml). The extract was

washed with water, dried and evaporated. The residue was chromatographed (eluting with ethyl acetate) to afford **7f-h**.

7f: Yield 43%. mp 150-152°C (ethyl acetate-hexane). Ms *m/z* (%): 249 (M^+, 96), 234 (100), 206 (30). *Anal.* Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.37; H, 6.06; N, 5.60. Ir (KBr): 1644 cm^{-1} (C=O). ^{1}H-Nmr δ: 2.68 (3H, d, J = 1.0 Hz, C_4-CH_3), 3.84, 3.93, 3.96 (each 3H, s, 3OCH_3), 6.49 (1H, br s, C_3-H), 6.78 (1H, s, C_7-H), 9.39 (1H, br, NH).

7g: Yield 63%. mp 169-170°C (CH_2Cl_2-hexane). Ms *m/z* (%): 263 (M^+, 100), 248 (98), 220 (28). *Anal.* Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.87; H, 6.62; N, 5.29. Ir (KBr): 1646 cm^{-1} (C=O). ^{1}H-Nmr δ: 2.32 (3H, s, C_7-CH_3), 2.65 (3H, s, C_4-CH_3), 3.80, 3.83, 3.89 (each 3H, s, 3OCH_3), 6.40 (1H, s, C_3-H), 9.09 (1H, br, NH).

7h: Yield 42%. mp 185-187°C (CH_2Cl_2-hexane). Ms *m/z* (%): 277 (M^+, 90), 262 (100), 234 (25). *Anal.* Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 64.98; H, 7.03; N, 5.04. Ir (KBr): 1656 cm^{-1} (C=O). ^{1}H-Nmr δ: 1.25 (3H, t, J = 7.6 Hz, CH_2CH_3), 2.65 (3H, s, C_4-CH_3), 2.76 (2H, q, J = 7.6 Hz, CH_2CH_3), 3.83, 3.87, 3.88 (each 3H, s, 3OCH_3), 6.40 (1H, s, C_3-H), 9.08 (1H, br, NH).

5,8-Dimethoxy-4-phenyl-2(1*H*)-quinolinone (7i) and 5,6,8-Trimethoxy-7-methyl-4-phenyl-2(1*H*)-quinolinone (7k) A mixture of anilide (**10i, k**) (5 mmol) and 80% sulfuric acid (20 ml) was heated at 75°C for 30 min. The reaction mixture was cooled, poured into ice-water (100 ml), and extracted with CH_2Cl_2 (3 x 50 ml). The extract was washed with water, dried and evaporated. The residue was chromatographed (eluting with ethyl acetate-hexane 3:7-1:1) to afford 2(1*H*)-quinolinone (**7i, k**).

7i: Yield 89%. mp 184-186°C (CH_2Cl_2-hexane). Ms *m/z* (%): 281 (M^+, 100), 266 (99). *Anal.* Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.43; H, 5.28; N, 5.21. Ir (KBr): 1642 cm^{-1} (C=O). ^{1}H-Nmr δ: 3.38 (3H, s, C_5-OCH_3), 3.96 (3H, s, C_8-OCH_3), 6.48 (1H, s, C_3-H), 6.50, 6.94 (each 1H, d, J = 8.9 Hz, C_6-H, C_7-H), 7.2-7.4 (5H, m, C_6H_5), 9.49 (1H, br, NH).

7k: Yield 68%. mp 227-229°C (CH_2Cl_2-hexane). Ms *m/z* (%): 325 (M^+, 100), 310 (75), 282 (38). *Anal.* Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.31. Found: C, 70.01; H, 5.82; N, 4.27. Ir (KBr): 1644 cm^{-1} (C=O). ^{1}H-Nmr δ: 2.34 (3H, s, C_7-CH_3), 3.17 (3H, s, C_5-OCH_3), 3.76, 3.86 (each 3H, s, C_6-OCH_3, C_8-OCH_3), 6.43 (1H, s, C_3-H), 7.3-7.5 (5H, m, C_6H_5), 9.29 (1H, br, NH).

Alkylation of 2(1*H*)-Quinolinones (7b-g, i-k) Sodium hydride (180 mg, 7.5 mmol) was added to a solution of **7b-g, i-k** (5 mmol) in *N,N*-dimethylformamide (60 ml) with stirring. The whole was left for 30 min, and methyl iodide (or ethyl iodide) (15 mmol) was added dropwise. The mixture was left for 30 min, quenched with water (300 ml), and extracted with CH_2Cl_2 (3 x 100 ml). The extract was washed with water, dried, and evaporated. The residue was chromatographed. Elution with ethyl acetate-hexane (1:9-3:7) afforded the less polar 2-alkoxyquinoline (**11l-x**), and further elution with ethyl acetate-hexane (1:1-7:3) afforded the more polar *N*-alkylquinolinone (**7l-x**).

7l: Yield 84% (from **7b**). mp 83-84°C (ether). Ms *m/z* (%): 249 (M^+, 100), 234 (74). *Anal.* Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.48; H, 6.07; N, 5.55. Ir (KBr): 1652 cm^{-1} (C=O). ^{1}H-Nmr δ: 3.88, 3.89, 3.92, 3.93 (each 3H, s, NCH_3, 3OCH_3), 6.74 (1H, d, J = 9.6 Hz, C_3-H), 6.80 (1H, s, C_7-H), 8.00 (1H, d, J = 9.6 Hz, C_4-H).

7m: Yield 53% (from **7c**). mp 69-70°C ($CHCl_3$-hexane). Ms *m/z* (%): 263 (M^+, 100), 248 (88), 218 (22), 205 (23). *Anal.* Calcd for $C_{14}H_{17}NO_4$: C, 63.86; H, 6.51; N, 5.32. Found: C, 63.63; H, 6.46; N, 5.21. Ir (KBr):

1662 cm^{-1} (C=O). ^{1}H-Nmr δ: 2.34 (3H, s, C_7-CH_3), 3.63, 3.86, 3.92, 3.93 (each 3H, s, NCH_3, $3OCH_3$), 6.65 (1H, d, J = 9.6 Hz, C_3-H), 7.98 (1H, d, J = 9.6 Hz, C_4-H).

7n: Yield 49% (from **7d**). oil. Ms *m/z* (%): 277 (M^+, 97), 262 (100). High-resolution ms Calcd for $C_{15}H_{19}NO_4$: C, 277.1314. Found: 277.1316. Ir (KBr): 1660 cm^{-1} (C=O). ^{1}H-Nmr δ: 1.25 (3H, t, J = 7.6 Hz, CH_2CH_3), 2.78 (2H, q, J = 7.6 Hz, CH_2CH_3), 3.64 (3H, s, NCH_3), 3.90 (6H, s, $2OCH_3$), 3.93 (3H, s, OCH_3), 6.65 (1H, d, J = 9.6 Hz, C_3-H), 7.98 (1H, d, J = 9.6 Hz, C_4-H).

7o: Yield 77% (from **7e**). mp 175-176°C (CH_2Cl_2-hexane). Ms *m/z* (%): 263 (M^+, 86), 248 (100), 233 (28). *Anal.* Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.70; H, 6.48; N, 5.23. Ir (KBr): 1644 cm^{-1} (C=O). ^{1}H-Nmr δ: 2.58 (3H, d, J = 1.0 Hz, C_4-CH_3), 3.68, 3.87, 3.89, 3.98 (each 3H, s, NCH_3, $3OCH_3$), 6.42 (1H, br s, C_3-H), 6.41 (1H, s, C_6-H).

7p: Yield 56% (from **7f**). mp 130-131°C (CH_2Cl_2-hexane). Ms *m/z* (%): 263 (M^+, 100), 248 (45), 233 (18), 220 (30). *Anal.* Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.71; H, 6.58; N, 5.25. Ir (KBr): 1658 cm^{-1} (C=O). ^{1}H-Nmr δ: 2.63 (3H, s, C_4-CH_3), 3.81, 3.82, 3.86, 3.92 (each 3H, s, NCH_3, $3OCH_3$), 6.51 (1H, s, C_3-H), 6.83 (1H, s, C_7-H).

7q: Yield 65% (from **7g**). mp 81-82°C (hexane). Ms *m/z* (%): 277 (M^+, 100), 262 (67), 247 (15), 234 (22). *Anal.* Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 64.84; H, 7.12; N, 5.00. Ir (KBr): 1656 cm^{-1} (C=O). ^{1}H-Nmr δ: 2.32 (3H, s, C_7-CH_3), 2.61 (3H, s, C_4-CH_3), 3.56, 3.81, 3.83, 3.87 (each 3H, s, NCH_3, $3OCH_3$), 6.46 (1H, s, C_3-H).

7r: Yield 82% (from **7i**). mp 119-120°C (CH_2Cl_2-hexane). Ms *m/z* (%): 295 (M^+, 100), 280 (76). *Anal.* Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.17; H, 5.74; N, 4.99. Ir (KBr): 1648 cm^{-1} (C=O). ^{1}H-Nmr δ: 3.32 (3H, s, C_5-OCH_3), 3.87, 3.94 (each 3H, s, NCH_3, C_8-OCH_3), 6.50 (1H, s, C_3-H), 6.57, 7.07 (each 1H, d, J = 8.9 Hz, C_6-H, C_7-H), 7.2-7.5 (5H, m, C_6H_5).

7s: Yield 76% (from **7j**). mp 143-144°C (hexane). Ms *m/z* (%): 325 (M^+, 83), 310 (100). *Anal.* Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.31. Found: C, 70.10; H, 5.92; N, 4.26. Ir (KBr): 1638 cm^{-1} (C=O). ^{1}H-Nmr δ: 3.37 (3H, s, C_5-OCH_3), 3.75, 3.96, 3.97 (each 3H, s, NCH_3, C_7-OCH_3, C_8-OCH_3), 6.34 (1H, s, C_6-H), 6.43 (1H, s, C_3-H), 7.1-7.4 (5H, m, C_6H_5).

7t: Yield 62% (from **7k**). oil. Ms *m/z* (%): 339 (M^+, 100), 324 (67). High-resolution ms Calcd for $C_{20}H_{21}NO_4$: 339.1470. Found: 339.1483. Ir (KBr): 1658 cm^{-1} (C=O). ^{1}H-Nmr δ: 2.34 (3H, s, C_7-CH_3), 3.14 (3H, s, C_5-OCH_3), 3.63, 3.75, 3.91 (each 3H, s, NCH_3, C_6-OCH_3, C_8-OCH_3), 6.48 (1H, s, C_3-H), 7.2-7.5 (5H, m, C_6H_5).

7u: Yield 36% (from **7f**). mp 84-85°C (CH_2Cl_2-hexane). Ms *m/z* (%): 277 (M^+, 100), 262 (37), 234 (45). *Anal.* Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 64.78; H, 7.03; N, 4.87. Ir (KBr): 1644 cm^{-1} (C=O). ^{1}H-Nmr δ: 1.37 (3H, t, J = 6.9 Hz, CH_2CH_3), 2.61 (3H, s, C_4-CH_3), 3.81, 3.91, 3.93 (each 3H, s, $3OCH_3$), 4.45 (2H, q, J = 6.9 Hz, CH_2CH_3), 6.51 (1H, s, C_3-H), 6.82 (1H, s, C_7-H).

7v: Yield 16% (from **7g**). oil. Ms *m/z* (%): 291 (M^+, 100), 276 (62), 262 (30), 248 (37). High-resolution ms Calcd for $C_{16}H_{21}NO_4$: 291.1470. Found: 291.1499. Ir (KBr): 1646 cm^{-1} (C=O). ^{1}H-Nmr δ: 1.19 (3H, t, J = 6.9 Hz, CH_2CH_3), 2.33 (3H, s, C_7-CH_3), 2.60 (3H, d, J = 1.0 Hz, C_4-CH_3), 3.59, 3.84, 3.87 (each 3H, s, $3OCH_3$), 4.59 (2H, q, J = 6.9 Hz, CH_2CH_3), 6.45 (1H, q, J = 1.0 Hz, C_3-H).

7w: Yield 41% (from **7i**). mp 117-118°C (CH_2Cl_2-hexane). Ms *m/z* (%): 309 (M^+, 100), 280 (53), 266 (49). *Anal.* Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.57; H, 6.19; N, 4.53. Ir (KBr): 1642 cm^{-1} (C=O). ^{1}H-Nmr δ: 1.44 (3H, t, J = 6.9 Hz, CH_2CH_3), 3.31 (3H, s, C_5-OCH_3), 3.91 (3H, s, C_8-OCH_3),

4.59 (2H, q, J = 6.9 Hz, CH_2CH_3), 6.49 (1H, s, C_3-H), 6.56, 7.06 (each 1H, d, J = 8.9 Hz, C_6-H, C_7-H), 7.2-7.4 (5H, m, C_6H_5).

7x: Yield 16% (from **7k**). mp 187-188°C (ether-hexane). Ms *m/z* (%): 353 (M^+, 100), 338 (61). *Anal.* Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.29; H, 6.55; N, 3.92. Ir (KBr): 1648 cm^{-1} (C=O). ^{1}H-Nmr δ: 1.28 (3H, t, J = 6.9 Hz, CH_2CH_3), 2.35 (3H, s, C_7-CH_3), 3.14 (3H, s, C_5-OCH_3), 3.66, 3.75 (each 3H, s, C_6-OCH_3, C_8-OCH_3), 4.65 (2H, q, J = 6.9 Hz, CH_2CH_3), 6.44 (1H, s, C_3-H), 7.2-7.5 (5H, m, C_6H_5).

11l: Yield 14% (from **7b**). mp 101-102.5°C (ether-hexane). Ms *m/z* (%): 249 (M^+, 76), 234 (100). *Anal.* Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.65; H, 6.12; N, 5.58. ^{1}H-Nmr δ: 3.92, 3.99, 4.06, 4.10 (each 3H, s, 4OCH_3), 6.85 (1H, s, C_7-H), 6.93 (1H, d, J = 8.9 Hz, C_3-H), 8.27 (1H, d, J = 8.9 Hz, C_4-H).

11m: Yield 27% (from **7c**). oil. Ms *m/z* (%): 263 (M^+, 64), 248 (100). High-resolution ms Calcd for $C_{14}H_{17}NO_4$: 263.1158. Found: 263.1158. ^{1}H-Nmr δ: 2.37 (3H, s, C_7-CH_3), 3.91, 3.96, 4.08, 4.09 (each 3H, s, 4OCH_3), 6.85 (1H, d, J = 9.2 Hz, C_3-H), 8.24 (1H, d, J = 9.2 Hz, C_4-H).

11n: Yield 29% (from **7d**). oil. Ms *m/z* (%): 277 (M^+, 60), 262 (100). High-resolution ms Calcd for $C_{15}H_{19}NO_4$: C, 277.1314. Found: 277.1309. ^{1}H-Nmr δ: 1.24 (3H, t, J = 7.6 Hz, CH_2CH_3), 2.85 (2H, q, J = 7.6 Hz, CH_2CH_3), 3.94, 3.95, 4.08, 4.15 (each 3H, s, 4OCH_3), 6.85 (1H, d, J = 8.9 Hz, C_3-H), 8.24 (1H, d, J = 8.9 Hz, C_4-H).

11o: Yield 22% (from **7e**). mp 74-75°C (hexane). Ms *m/z* (%): 263 (M^+, 57), 248 (100). *Anal.* Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.80; H, 6.50; N, 5.27. ^{1}H-Nmr δ: 2.74 (3H, d, J = 1.0 Hz, C_4-CH_3), 3.90, 4.01, 4.03, 4.07 (each 3H, s, 4OCH_3), 6.49 (2H, br s, C_3-H, C_6-H).

11p: Yield 26% (from **7f**). mp 116-117°C (CH_2Cl_2-hexane). Ms *m/z* (%): 263 (M^+, 80), 248 (100). *Anal.* Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.76; H, 6.57; N, 5.24. ^{1}H-Nmr δ: 2.80 (3H, d, J = 1.0 Hz, C_4-CH_3), 3.84, 3.97, 4.04, 4.07 (each 3H, s, 4OCH_3), 6.69 (1H, q, J = 1.0 Hz, C_3-H), 6.87 (1H, s, C_7-H).

11q: Yield 34% (from **7g**). oil. Ms *m/z* (%): 277 (M^+, 64), 262 (100). High-resolution ms Calcd for $C_{15}H_{19}NO_4$: 277.1314. Found: 277.1310. ^{1}H-Nmr δ: 2.36 (3H, s, C_7-CH_3), 2.78 (3H, d, J = 0.9 Hz, C_4-CH_3), 3.88, 3.89, 4.04, 4.05 (each 3H, s, 4OCH_3), 6.61 (1H, br s, C_3-H).

11r: Yield 14% (from **7i**). mp 142-143°C (CH_2Cl_2-hexane). Ms *m/z* (%): 295 (M^+, 76), 280 (100). *Anal.* Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.23; H, 5.72; N, 5.00. ^{1}H-Nmr δ: 3.41 (3H, s, C_5-OCH_3), 4.05, 4.15 (each 3H, s, C_2-OCH_3, C_8-OCH_3), 6.74 (1H, s, C_3-H), 6.62, 7.00 (each 1H, d, J = 8.2 Hz, C_6-H, C_7-H), 7.2-7.5 (5H, m, C_6H_5).

11s: Yield 23% (from **7j**). mp 142-143°C (ether-hexane). Ms *m/z* (%): 325 (M^+, 78), 310 (100). *Anal.* Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.31. Found: C, 69.97; H, 5.92; N, 4.30. ^{1}H-Nmr δ: 3.44 (3H, s, C_5-OCH_3), 4.01, 4.09, 4.13 (each 3H, s, C_2-OCH_3, C_7-OCH_3, C_8-OCH_3), 6.47, 6.56 (each 1H, s, C_3-H, C_6-H), 7.2-7.4 (5H, m, C_6H_5).

11t: Yield 33% (from **7k**). mp 122-124°C (CH_2Cl_2-hexane). Ms *m/z* (%): 339 (M^+, 82), 324 (100). *Anal.* Calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24; N, 4.13. Found: C, 70.83; H, 6.27; N, 4.08. ^{1}H-Nmr δ: 2.38 (3H, s, C_7-CH_3), 3.17 (3H, s, C_5-OCH_3), 3.81 (3H, s, OCH_3), 4.11 (6H, s, 2OCH_3), 6.66 (1H, s, C_3-H), 7.3-7.5 (5H, m, C_6H_5).

11u: Yield 45% (from **7f**). mp 66-67°C (hexane). Ms *m/z* (%): 277 (M^+, 100), 262 (84), 234 (48). *Anal.* Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 64.92; H, 6.89; N, 4.98. ^{1}H-Nmr δ: 1.44 (3H, t, J = 6.9 Hz, CH_2CH_3), 2.81 (3H, d, J = 0.7 Hz, C_4-CH_3), 3.84, 3.97, 4.04 (each 3H, s, 3OCH_3), 4.55 (2H, q, J = 6.9 Hz, CH_2CH_3), 6.71 (1H, br s, C_3-H), 6.88 (1H, s, C_7-H).

11v: Yield 78% (from **7g**). oil. Ms *m/z* (%): 291 (M^+, 82), 276 (100), 262 (16), 248 (45). High-resolution ms Calcd for $C_{16}H_{21}NO_4$: 291.1470. Found: 291.1469. ^{1}H-Nmr δ: 1.44 (3H, t, J = 6.9 Hz, CH_2CH_3), 2.36 (3H, s, C_7-CH_3), 2.78 (3H, d, J = 1.0 Hz, C_4-CH_3), 3.88, 3.89, 4.03 (each 3H, s, 3OCH_3), 4.53 (2H, q, J = 6.9 Hz, CH_2CH_3), 6.61 (1H, q, J = 1.0 Hz, C_3-H).

11w: Yield 49% (from **7i**). mp 96-97°C (CH_2Cl_2-hexane). Ms *m/z* (%): 309 (M^+, 100), 294 (59), 280 (85), 266 (35). *Anal.* Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.63; H, 6.14; N, 4.48. ^{1}H-Nmr δ: 1.45 (3H, t, J = 6.9 Hz, CH_2CH_3), 3.40 (3H, s, C_5-OCH_3), 4.04 (3H, s, C_8-OCH_3), 4.61 (2H, q, J = 6.9 Hz, CH_2CH_3), 6.73 (1H, s, C_3-H), 6.61, 6.99 (each 1H, d, J = 8.6 Hz, C_6-H, C_7-H), 7.2-7.4 (5H, m, C_6H_5).

11x: Yield 80% (from **7k**). mp 79-80°C (hexane). Ms *m/z* (%): 353 (M^+, 100), 338 (97), 324 (24), 310 (39). *Anal.* Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.28; H, 6.60; N, 3.91. ^{1}H-Nmr δ: 1.46 (3H, t, J = 6.9 Hz, CH_2CH_3), 2.38 (3H, s, C_7-CH_3), 3.17 (3H, s, C_5-OCH_3), 3.81, 4.09 (each 3H, s, C_6-OCH_3, C_8-OCH_3), 4.58 (2H, q, J = 6.9 Hz, CH_2CH_3), 6.65 (1H, s, C_3-H), 7.3-7.5 (5H, m, C_6H_5).

Oxidative Demethylation of 2(1*H*)-Quinolinones (7a-x, a', e', j') and 2-Alkoxyquinolines (11l-x) A solution of CAN (1370 mg, 2.5 mmol) in acetonitrile-water (1:1, 7.5 ml) was added dropwise to **7a-x, a', e', j'** or **11l-x** (0.5 mmol) dissolved in acetonitrile-water (4:1, 25 ml) containing pyridine-2,6-dicarboxylic acid *N*-oxide (458 mg, 2.5 mmol) at 0-5°C. The mixture was kept at 0-5°C for 30 min, diluted with water (65 ml), and extracted with CH_2Cl_2 (3 x 25 ml). The extract was washed with brine, dried and evaporated. The residue was chromatographed (eluting with ethyl acetate-hexane, ethyl acetate-methanol, or ethyl acetate-CH_2Cl_2) to afford the corresponding *p*-quinones (**12** or **14**) and/or *o*-quinones (**13**, **15** or **16**).

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