Convenient Synthesis of 1,6,7,8-Substituted 2-(3',4'-Substituted-phenyl)-4-quinolones *via* a 4-Ethoxyflavylium Salt

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Condensation of 2-hydroxyacetophenone with benzaldehyde in the presence of 70% perchloric acid in ethyl orthoformate gave the corresponding 4-ethoxyflavylium perchlorate, which was treated with aqueous ammonia or methylamine solution to afford 1,6,7,8-substituted 2-(3',4'-substituted-phenyl)-4-quinolone in fair to good yield.

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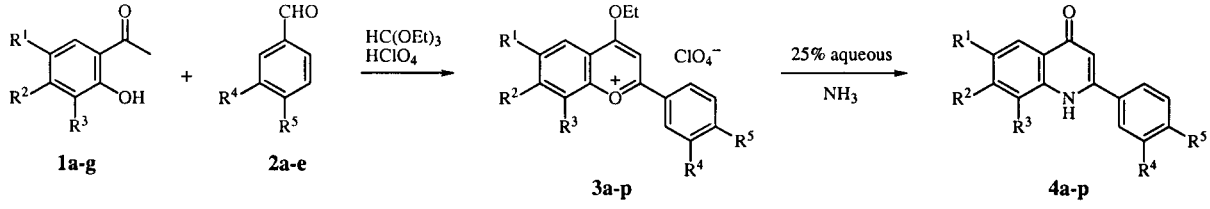
It has recently been reported that 2-phenyl-4-quinolone showed potential inhibition activity against a variety of human antitumor cell lines in concentration from nanomolar to micromolar [1] and the synthesis of many its derivatives as an antitumor agent was also done [1]. In their synthesis, versatile methods have been investigated, however almost by means of a condensation of an anirine derivative with a carbonyl compound and the subsequent thermal ring-closure reaction, or its modified method [1-5].

To synthesize 2-phenyl-4-quinolones bearing versatile substituents at the 1, 5, 6, 7, or 8 positions and at 2', 3', 4', 5', or 6' position of the 2-phenyl group, we undertook the development of a more convenient and efficient process. In the coarse of this study, it was found that 2-phenyl-4-quinolone could be easily synthesized by the reaction of the corresponding flavylium salt with 25% aqueous ammonia solution [6]. The flavylium salt was also easily synthesized by the mild three-component condensation reaction of acetophenone, benzaldehyde, and ethyl orthoformate in the presence of 70% perchloric acid at room temperature [7]. By this convenient two-step synthetic method using seven types of 4, 5, 6-substituted acetophenones and five types of 4- and 3,4-substituted benzaldehyde, as well as sixteen types of 2-phenyl-4-quinolones were synthesized (see Table). The overall yields were fair to good (42-93%) except for 6-hydroxy-2-phenyl-4-quinolone (entry 6, 24%). The reaction of aminoacetophenone afforded the corresponding favylium salt with a trifluoroacetyl protecting

Table

Synthesis of 2-Phenyl-4-quinolones *via* Flavylium Salt

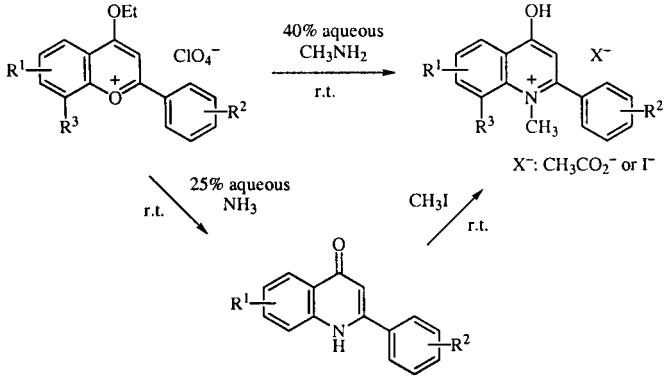


1a-g **2a-e** **3a-p** **4a-p**

Entry	R^1	R^2	R^3	R^4	R^5	Time (hours)	Product	Yield (%)	Time (hours)	Product	Yield (%)
1	CH_3	H	H	H	H	2	**3a**	60	3	**4a**	78
2	CH_3	H	H	H	OH	2	**b**	95	3	**b**	82
3	CH_3	H	H	OH	OH	2	**c**	71	3	**c**	82
4	CH_3	H	H	H	OCH_3	2	**d**	78	3	**d**	88
5	CH_3	H	H	OCH_3	OH	2	**e**	75	3	**e**	91
6	OH	H	H	H	H	4	**f**	58	16	**f**	42
7	OH	H	H	H	OCH_3	2	**g**	74	5	**g**	79
8	OCH_3	H	H	H	OH	2	**h**	55	7	**h**	95
9	OCH_3	H	H	OH	OH	3	**i**	64	12	**i**	76
10	OCH_3	H	H	OCH_3	OH	1.5	**j**	57	10	**j**	99
11	*t*-Bu	H	H	H	OH	3	**k**	62	5	**k**	95
12	*t*-Bu	H	H	OH	OH	2	**l**	55	14	**l**	85
13	*t*-Bu	H	H	OCH_3	OH	1	**m**	60	10	**m**	98
14	$NHCOCF_3$	H	H	H	OCH_3	4	**n**	50	5	**n**	84
15	H	H	$NHCOCF_3$	H	OCH_3	12	**o**	49	3	**o**	97
16	H	CH_3	H	H	OH	4	**p**	95	10	**p**	98

group (entries, 14 and 15). The reaction of 2-phenyl-4-quinolone with methyl iodide yielded the corresponding *N*-methylammonium iodides (see Scheme, compound **5d**, 72%). Furthermore, it was found that direct reaction of the flavylium perchlorate with 40% aqueous methylamine solution efficiently provided the corresponding *N*-methyl ammonium salts in better yield (compounds **5b**; 82% from **3b**, **5g**; 79% from **3g**, **5h**; 85% from **3h**).

Scheme



Thus, the earlier enumerated 6,7,8-substituted-2-(4'- and 3',4'-substituted-phenyl)-4-quinolones and 1-methylquinolinolium salts were synthesized by a simple two-step synthetic method *via* 4-ethoxyflavylium perchlorate under mild conditions (only stirring at room temperature). This method can be applied for the synthesis of the other 5,6,7,8-substituted 2-(2',3',4',5',6'-substituted-phenyl)-4-quinolone and its 1-alkyl or aryl quinolinolium salts. The inhibition-activity test against a human antitumor cell line is now in progress.

The authors are grateful to Takeyoshi Takahashi for elemental analyses and to Yutaka Kubota for infrared-spectra measurements.

EXPERIMENTAL

Melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. Elemental analyses were performed on a Perkin-Elmer PE 2400 II. The ^{1}H nmr spectra were measured at 60 MHz on a Hitachi H-60, a 270 MHz on a JOEL 270, and 200 MHz Varian 200 spectrometers. The ^{13}C nmr spectra were taken at 67.8 MHz on a JOEL 270 and at 50 MHz or on a Varian 200 spectrometers. The solvents were in deuteriochloroform or deuteriodimethyl sulfoxide or deuteriotrifluoroacetic acid for ethoxyflavylium salts. Chemical shifts are reported in δ (ppm) units relative to the internal reference tetramethylsilane. Infrared (ir) spectra were recorded on a Horiba IR spectrometer as potassium bromide pellets. Mass spectra (ms) data were obtained by Electron-Ionization (EI) method or Fast Atom Bombardment (FAB) method using 3-nitrobenzyl alcohol as a matrix on a JEOL HX 100 mass spectrometer. Flash chromatography was performed on silica gel (230-400 mesh, Fuji silysia Co. Ltd., BW-300) using ethyl acetate or a mixture of chloroform and methanol as eluents.

General Procedure.

Acetophenone libraries were prepared by the Fries rearrangement of its precursor, phenyl acetate. Substituted benzaldehydes and ethyl orthoformate were purchased and directly used.

1) Flavylium Perchlorate.

To a solution of 2-hydroxy-5-methylacetophenone (300 mg, 2.0 mmoles), *p*-hydroxybenzaldehyde (366 mg, 3.0 mmoles) in 7 ml of triethyl orthoformate, 70% perchlolic acid (430 mg, 3.0 mmoles) was added dropwise at room temperature. After confirming of the disappearance of the material by tlc monitoring (*ca.* 3 hours), the resulting precipitate was allowed to stand in a refrigerator overnight. The precipitate was filtered and washed with ethyl acetate and dried under reduced pressure to give flavylium perchlorate (720 mg, 95%) as blackish brown crystals, which were directly used to the next step without recrystalization.

4-Ethoxy-6-methyl-2-phenylflavylium Perchlorate (**3a**).

This compound was obtained as pale-yellow needles (from acetic acid), mp 249-250°; (EI) (m/z) 265 (M^+, 100); ir (potassium bromide): ν 3432, 2987, 1624, 1602, 1550, 1531, 1500, 1442, 1402, 1365, 1253, 1095 cm^{-1}; ^{1}H nmr (deuteriotrifluoroacetic acid): δ 1.29 (3H, t, J = 7.2 Hz, OCH_2CH_3), 2.45 (3H, s, CH_3), 4.45 (2H, q, J = 7.2 Hz, OCH_2CH_3), 7.3-7.9 (9H, m, ArH).

Anal. Calcd. for $C_{18}H_{17}ClO_6$: C, 59.27; H, 4.70. Found: C, 59.53; H, 4.63.

4-Ethoxy-6-methyl-2-(4'-methoxy)phenylflavylium Perchlorate (**3d**).

This compound was obtained as yellow needles (from acetic acid), mp 246-248° ms: (FAB) (m/z) 295 (M^+); ir (potassium bromide): ν 1599, 1546, 1247, and 1093 cm^{-1}; ^{1}H nmr (deuteriotrifluoroacetic acid): δ 1.22 (3H, t, J = 7.2 Hz, OCH_2CH_3) 2.08 (3H, s, CH_3), 3.48 (3H, s, OCH_3), 4.34 (2H, q, J = 7.2 Hz, OCH_2CH_3), 7.14 (1H, s, ArH), 7.60 (1H, s, ArH), 7.39 (2H, s, ArH), 7.75, 6.68 (each 2H, d, J = 8.0 Hz, *p*-substituted ArH).

Anal. Calcd. for $C_{19}H_{19}ClO_7$: C, 57.80; H, 4.85. Found: C, 57.88; H, 4.83.

6-*tert*-Buthyl-4-ethoxy-4'-hydroxyflavylium Perchlorate (**3k**).

This compound was obtained as yellow needles (from acetic acid), mp 227-230° ms: (FAB) (m/z) 323 (M^+); ir (potassium bromide): ν 3427, 3080, 2964, 1600, 1544, 1529, 1475, 1249, 1180, 1120, 1092 cm^{-1}; ^{1}H nmr (deuteriotrifluoroacetic acid): δ 1.07 (9H, s, *t*-Bu), 1.32 (3H, t, OCH_2CH_3), 4.49 (2H, q, OCH_2CH_3), 7.63 (8H, m, ArH).

Anal. Calcd for $C_{21}H_{23}ClO_7 \cdot 0.25C_2H_4O_2$: C, 58.97; H, 5.53. Found: C, 58.85; H, 5.64.

2) 2-Phenyl-4-quinolone.

To a stirred 25% aqueous ammonia solution, the flavylium perchlorate was added. The resulting suspension was vigorously stirred at room temperature until the disappearance of the material by aluminum oxide tlc monitoring (chloroform: methanol = 2:1) (for 3-16 hours), and the resulting precipitates were then filtered and washed with water to give the corresponding 2-phenyl-4-quinolone as orange crystals.

6-Methyl-2-phenyl-4-quinolone (**4a**).

This compound was obtained as pale-yellow needles (from ethyl acetate), mp 117°; ms: (EI) (m/z) 235(M^+, 100); ir (potassium bromide): ν 3183, 3058, 2919, 2861, 1637, 1564, 1494, 1222, 767, 688 cm^{-1}; ^{1}H nmr (deuteriodimethyl sulfoxide): δ

2.65 (3H, s, CH_3), 7.51 (1H, s, H-3), 7.68 (3H, m, H- 3',4', 5'), 7.88 (1H, d, J = 8.9 Hz, H-7), 8.06 (1H, d, J = 1.7, 8.9 Hz, H-7), 8.12-8.17 (2H, m, H-2', 6'); ^{13}C nmr (deuteriopyridine): δ 20.7, 106.0, 118.0, 122.0, 124.7, 126.0 (x2), 129.1 (x2), 130.7, 132.9, 133.3, 134.5, 152.1, 155.2, 160.1.

Anal. Calcd. for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.53; H, 5.52; N, 5.82.

6-Methyl-2-(4'-hydroxy)phenyl-4-quinolone (**4b**).

This compound was obtained as orange prisms from (methanol), mp 255-257°; ms: (FAB) (m/z) 252 $(M+H)^+$; ir (potassium bromide): ν 3407, 3031, 1614, 1587, 1552, 1471, 1344, 1261, 1165, 1080 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.39 (3H, s, $ArCH_3$), 6.68 (1H, s, ArH), 6.83 (2H, d, J = 8.8Hz, ArH), 7.44 (2H, m, ArH), 7.75 (2H, d, J = 8.8 Hz, ArH), 7.96 (1H, s, ArH).

Anal. Calcd. for $C_{16}H_{13}NO_2 \cdot 0.2CH_3OH$: C, 75.74; H, 5.34; N, 5.38. Found: C, 75.37; H, 5.24; N, 5.38.

6-Methyl-2-(3',4'-dihydroxy)phenyl-4-quinolone (**4c**).

This compound was obtained as brown prisms (from acetic acid), mp 270°; ms: (FAB) (m/z) 268 $(M+H)^+$; ir (potassium bromide): ν 3386, 3066, 1685, 1622, 1603, 1564, 1508, 1444, 1394, 1294 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.43 (3H, s, $ArCH_3$), 6.56 (1H, d, J = 8.8 Hz, ArH), 6.81 (1H, s, $ArCH_3$), 7.22 (2H, d, J = 2.3 Hz, ArH), 7.43 (1H, dd, J = 8.8 and 2.3 Hz, ArH), 7.64 (1H, s, ArH), 8.05 (1H, s, ArH).

Anal. Calcd. for $C_{16}H_{13}NO_3 \cdot 1.8CH_3CO_2H$: C, 62.71; H, 5.42; N, 3.73. Found: C, 62.62; H, 5.43; N, 3.62.

6-Methyl-2-(4'-methoxy)phenyl-4-quinolone (**4d**).

This compound was obtained as yellow needles (from ethyl acetate), mp 125-127° ms: (EI) (m/z) 265 (M^+, 100); ir (potassium bromide): ν 3197, 2972, 2925, 1637, 1562, 1512, 1489, 1332, 1263, 1184, 1024 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.43 (3H, s, CH_3), 3.87 (3H, s, OCH_3), 6.48 (1H, s, H-3), 6.98 (2H, d, J = 9.0 Hz, *p*-substituted ArH), 7.27 (1H, d, J = 8.1 Hz, H-8) 7.35 (1H, dd, J = 8.3, 1.6 Hz, H-7), 7.79 (2H, d, J = 9.0 Hz, *p*-substituted ArH), 7.93 (1H, d, J = 1.6 Hz, H-5); ^{13}C nmr (deuteriochloroform): δ 161.4, 160.9, 155.8, 151.7, 134.3, 133.0, 127.1 (x2), 124.7, 123.7, 120.8, 117.5, 114.1 (x2), 103.9, 55.3, 20.9.

Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 77.04; H, 5.78; N, 5.22.

6-Methyl-2-(4'-hydroxy-3'-methoxy)phenyl-4-quinolone (**4e**).

This compound was obtained as a brown powder (from acetic acid), mp 165-167° ms: (FAB) (m/z) 282$(M+H)^+$; ir (potassium bromide): ν 3409, 3068, 1660, 1620, 1593, 1564, 1508, 1469, 1346, 1276, 1134 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.42 (3H, s, CH_3), 6.90 (1H, d, J = 8.4 Hz, 2'-ArH), 7.09 (1H, s, ArH), 7.51 (1H, d, J = 2.2 Hz, 5'-ArH), 7.58 (1H, d, J = 8.4, 2.3 Hz, 6'-ArH), 7.76 (1H, s, ArH), 7.86 (1H, d, J = 9.0 Hz, ArH), 8.14 (1H, s, ArH).

Anal. Calcd. for $C_{17}H_{15}NO_3 \cdot CH_3CO_2H$: C, 66.85; H, 5.61; N, 4.10. Found: C, 66.81, H, 5.68; N, 4.07.

6-Hydroxy-2-phenyl-4-quinolone (**4f**).

This compound was obtained as a red powder (from acetic acid), mp 243-245° ms: (FAB) (m/z) 238 $(M+H)^+$; ir ν 3382, 3068, 1679, 1622, 1570, 1523, 1452, 1408, 1275, 1221, 1130, 1080 cm^{-1}; ^1H nmr (deoteriodimethyl sulfoxide): δ 6.81 (1H, s, H-3), 7.04 (1H, dd, J = 2.8 and 8.9 Hz, H-7), 7.39 (1H, d, J = 2.8 Hz, H-5), 7.45 (1H, d, J = 8.9 Hz, H-8), 7.54 (3H, m, ArH), 7.91 (2H, m, ArH).

Anal. Calcd. for $C_{15}H_{11}NO_2 \cdot 0.9CH_3CO_2H$: C, 69.27; H, 5.05; N, 4.81. Found: C, 69.14; H, 5.20; N, 4.53.

6-Hydroxy-2-(4'-methoxy)phenyl-4-quinolone (**4g**).

This compound was obtained as a red amorphous powder (from acetic acid), mp 223-225° ms: (FAB) (m/z) 266 $(M+H)^+$; ir (potassium bromide): ν 3074, 1606, 1552, 1506, 1304, 1261, 1182 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.44 (3H, s, CH_3), 6.56-7.93 (8H, m, ArH).

Anal. Calcd. for $C_{16}H_{13}NO_3 \cdot 1.1CH_3CO_2H$: C, 65.58; H, 5.26; N, 4.20. Found: C, 65.57; H, 5.25; N, 4.17.

6-Methoxy-2-(4'-hydroxy)phenyl-4-quinolone (**4h**).

This compound was obtained as an orange powder (from methanol), mp 280-283°; ms: (FAB) (m/z) 268 $(M+H)^+$; ir (potassium bromide): ν 3400, 3080, 1618, 1591, 1560, 1354, 1257, 1170 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 3.87 (3H, s, OCH_3), 6.69 (1H, s, H-4), 6.83 (2H, d, J = 8.8 Hz, *p*-substituted ArH), 7.24 (1H, dd, J = 3.2, 9.0 Hz, H-7), 7.46 (1H, d, J = 3.0 Hz, H- 5), 7.49 (1H, d, J = 9.0 Hz, H-8), 7.75 (2H, d, J = 8.8 Hz, *p*-substituted ArH).

Anal. Calcd. for $C_{16}H_{13}NO_3 \cdot 0.4CH_3OH$: C, 70.33; H, 5.24; N, 4.99. Found: C, 70.16; H, 4.86; N, 4.79.

6-Methoxy-2-(3',4'-dihydroxy)phenyl-4-quinolone (**4i**).

This compound was obtained as a brown powder (from acetic acid), mp >300°; ms: (FAB) (m/z) 284 $(M+H)^+$; ir (potassium bromide): ν 3080, 1674, 1622, 1564, 1508, 1444, 1400, 1321, 1292, 1251, 1228, 1122, 1078, 1030 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 3.90 (3H, s, OCH_3), 6.48 (1H, d, J = 8.4 Hz, *o*-ArH), 6.75 (1H, s, H-3), 7.18 (1H, d, J = 2.0 Hz, H-2'), 7.38 (1H, m, ArH), 7.41 (1H, m, ArH), 7.65 (1H, s, ArH), 7.70 (1H, d, J = 2.4 Hz, H-5).

Anal. Calcd. for $C_{16}H_{13}NO_4 \cdot 1.8CH_3CO_2H$: C, 60.15; H, 5.20; N, 3.58. Found: C, 60.21; H, 5.12; N, 3.34.

6-Methoxy-2-(4'-hydroxy-3'-methoxy)phenyl-4-quinolone (**4j**).

This compound was obtained as red prisms (from methanol-acetic acid), mp 156-158°; ms: (FAB) (m/z) 298 $(M+H)^+$; ir ν 3427, 3080, 1662, 1620, 1566, 1508, 1276, 1255, 1180, 1134, 1024 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 3.77 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 6.90 (1H, d, J = 8.4 Hz, H-5'), 7.09 (1H, s, ArH), 7.31 (1H, dd, J = 8.4 and 2.8 Hz, H-6'), 7.58 (3H, m, ArH), 7.81 (1H, d, J = 2.8 Hz, H-2').

Anal. Calcd. for $C_{17}H_{15}NO_4 \cdot 1.25CH_3CO_2H$: C, 62.89; H, 5.41; N, 3.76. Found: C, 63.16, H, 5.61; N, 3.83.

6-*tert*-Butyl-2-(4'-hydroxy)phenyl-4-quinolone (**4k**).

This compound was obtained as yellow prisms (from acetic acid-acetonitrile), mp 193-195°; ms: (FAB) (m/z) 294 $(M+H)^+$; ir (potassium bromide): ν 3419, 3072, 2964, 1622, 1604, 1560, 1506, 1388, 1294, 1261, 1174, 1033 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 1.34 (9H, s, *t*-Bu), 6.71 (1H, s, H-3), 6.81 (2H, d, J = 8.8 Hz, *p*-substituted ArH), 7.47 (1H, d, J = 8.8 Hz, H-8), 7.72 (1H, dd, J = 2.2, 8.8 Hz, H-7), 7.75 (2H, d, J = 8.8 Hz, *p*-substituted ArH), 8.14 (1H, d, J = 2.2 Hz, H-5).

Anal. Calcd. for $C_{19}H_{19}NO_2 \cdot 1.6CH_3CO_2H$: C, 68.46; H, 6.57; N, 3.60. Found: C, 68.46, H, 6.58; N, 3.58.

6-*tert*-Butyl-2-(3',4'-dihydroxy)phenyl-4-quinolone (**4l**).

This compound was obtained as brown prisms (from acetic acid), mp >300°; ms: (FAB) (m/z) 310$(M+H)^+$; ir (potassium

bromide): ν 3427, 3077, 2964, 1668, 1622, 1602, 1562, 1506, 1471, 1394, 1265, 1122 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 1.36 (9H, s, *t*-Bu), 6.44 (1H, d, J = 8.6 Hz, H-5'), 6.74 (1H, s, H-3), 7.16 (1H, d, J = 2.4 Hz, H-2'), 7.42 (1H, dd, J = 8.8, 2.4 Hz, H-6'), 7.62 (1H, d, J = 8.6 Hz, H-8), 7.84 (1H, dd, J = 8.6, 2.2 Hz, H-7), 8.17 (1H, d, J = 2.2 Hz, H- 5).

Anal. Calcd. for $C_{19}H_{19}NO_3 \cdot CH_3CO_2H$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.20; H, 6.33; N, 3.72.

6-*tert*-Butyl-2-(4'-hydroxy-3'-methoxy)phenyl-4-quinolone (**4m**).

This compound was obtained as a red amorphous powder (from methanol), mp 173-175°; ms: (FAB) (m/z) 324 $(M+H)^+$; ir (potassium bromide): ν 3425, 2962, 1616, 1591, 1560, 1506, 1473, 1363, 1344, 1271, 1232, 1122 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 1.36 (9H, s, *t*-Bu), 3.84 (3H, s, OCH_3), 6.75 (1H, d, J = 8.4 Hz, H-5), 6.89 (1H, s, H-3), 7.38 (1H, d, J = 2.2Hz, H-2'), 7.50 (1H, dd, J = 2.2, 8.4 Hz, H-6'), 7.63 (1H, d, J = 8.8 Hz, H-8), 7.84 (1H, dd, J = 8.8, 2.2 Hz, H-7), 8.21 (1H, d, J = 2.2 Hz, H-5).

Anal. Calcd. for $C_{20}H_{21}NO_3 \cdot 0.6CH_3OH$: C, 72.05; H, 6.94; N, 4.11. Found: C, 72.22; H, 6.87; N, 4.08.

6-Trifluoroacetylamino-2-(4'-methoxy)phenyl-4-quinolone (**4n**).

This compound was obtained as yellow needles (from acetic acid-methanol), mp 196-198°; ms: (FAB) (m/z) 363 $(M+H)^+$; ir (potassium bromide): ν 3400, 3074, 1720, 1630, 1606, 1510, 1261, 1182 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 3.86 (3H, s, OCH_3), 6.96 (1H, s, H-3), 7.15 (2H, d, J = 8.8 Hz, *p*-substituted ArH), 7.65 (1H, d, J = 9.0 Hz, H-8), 7.95 (2H, d, J = 8.8 Hz, *p*-substituted ArH), 8.03 (1H, dd, J = 2.1, 8.0 Hz, H-7), 8.36 (1H, d, J = 2.1 Hz, H-5), 10.3 (1H, br s, NH).

Anal. Calcd. for $C_{18}H_{13}F_3N_2O_3 \cdot 0.75CH_3CO_2H$: C, 57.49; H, 3.96; N, 6.88. Found: C, 57.28; H, 4.25; N, 6.65.

8-Trifluoroacetylamino-2-(4'-methoxy)phenyl-4-quinolone (**4o**).

This compound was obtained as yellow prisms (from acetic acid), mp 137°; ms: (FAB) (m/z) 363 $(M+H)^+$; ir (potassium bromide): ν 3429, 3082, 2846, 1726, 1676, 1626, 1604, 1570, 1508, 1263, 1184 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 3.89 (3H, s, OCH_3), 7.17 (2H, d, J = 8.8 Hz, *p*-substituted ArH), 7.21 (1H, s, H-3), 7.47 (1H, t, J = 8.0 Hz, H-6), 7.87 (2H, dt, J = 1.1, 8.0 Hz, H-5 and 7), 10.1 (1H, br.s, NH).

Anal. Calcd. for $C_{18}H_{13}F_3N_2O_3 \cdot 1.2CH_3CO_2H$: C, 56.40; H, 4.13; N, 6.45. Found: C, 56.15; H, 3.87; N, 6.60.

7-Methyl-2-(4-hydroxy)phenyl-4-quinolone (**4p**).

This compound was obtained as red prisms (from methanol), mp 161-163°; ms: (EI) (m/z) 251(M^+); ir (potassium bromide): ν 3419, 3062, 1630, 1581, 1483, 1331, 1261, 1165 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.42 (3H, s, CH_3), 6.66 (1H, s, H-3), 6.81 (2H, d, J = 9.0 Hz, *p*-substituted ArH), 7.20 (1H, dd, J = 1.3, 8.0 Hz, H-6), 7.35 (1H, d, J = 1.3 Hz, H-8), 7.74 (2H, d, J = 9.0 Hz, *p*-substituted ArH), 8.03 (1H, d, J = 8.0 Hz, H-5).

Anal. Calcd. for $C_{16}H_{13}NO_2 \cdot 0.25CH_3OH$: C, 75.27; H, 5.44; N, 5.40. Found: C, 75.38; H, 5.48; N, 5.35.

3) Methyl 2-Phenyl-4-quinolinolium Iodide.

To a solution of 6-methyl-2-(4'-methoxy)phenyl-4-quinolone **4d** (100 mg, 0.38 mmole) in 2-propanol (5 ml), 18 ml of methyl iodide (0.57 mmoles) was added and the mixture was refluxed for 2 hours. After standing at room temperature, the resulting crystals were filtered and washed with 2-propanol to give 110 mg (72%) of quinolinolium iodide **5d** as yellow prisms

Methyl 6-methyl-2-(4'-methoxy)phenyl-4-quinolinolium Iodide (**5d**).

This compound was obtained as yellow prisms (from ethanol), mp 254-256°; ms: (FAB) (m/z) $(M+H)^+$; ir (potassium bromide): ν 3429, 3089, 1624, 1600, 1558, 1431, 1259, 1182 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide+deuterium): δ 2.51 (3H, s, $ArCH_3$), 3.38 (3H, s, N-CH_3), 3.92 (3H, s, OCH_3), 7.21-8.38 (8H, m, ArH).

Anal. Calcd. for $C_{18}H_{18}INO_2$; C, 53.09; H, 4.46; N, 3.44. Found: C, 52.80; H, 4.34; N, 3.34.

4) Methyl 2-Phenyl-4-quinolinolium Acetate.

4'-Hydroxy-6-*tert*-butyl-4-ethoxyflavylium perchlorate **3g** (84 mg, 0.26 mmole) was dissolved in 5 ml of 40% aqueous methylamine solution. The resulting mixture was stirred at room temperature for 5 hours. The reaction mixture was evaporated under reduced pressure. The residual crystals were recrystallized from acetic acid to give 76 mg (79%) of methyl quinolinolium acetate **5g** as yellow prisms.

Methyl 6-methyl-2-(3',4'-dihydroxy)phenyl-4-quinolinolnium acetate (**5c**).

This compound was obtained as red prisms (from acetic acid-acetonitrile), mp >300° ms: (FAB) (m/z) 282 (M^+); ir (potassium bromide): ν 3410, 3085, 1626, 1560, 1275, 1120 cm^{-1}. ^1H nmr (deuteriodimethyl sulfoxide): δ 2.50 (3H, s, CH_3), 3.21 (3H, s, N-CH_3), 6.61 (2H, d, J = 8.8 Hz, H-5'), 7.36 (1H, s, ArH), 7.50 (3H, m, ArH), 7.93 (1H, s, ArH).

Anal. Calcd. for $C_{19}H_{19}NO_5 \cdot 0.25CH_3CO_2H$: C, 65.53; H, 5.64; N, 3.92. Found: C, 65.71; H, 5.82; N, 4.07.

Methyl 6-*tert*-Butyl-2-(4'-hydroxy)phenyl-4-quinolinolium Acetate (**5g**).

This compound was obtained as yellow prisms (from acetic acid-acetonitrile), mp 185-187°; ms: (FAB) (m/z) 308 (M^+); ir (potassium bromide): ν 3427, 3222, 3080, 2958, 1627, 1604, 1560, 1265, 1174 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.47 (3H, s, $ArCH_3$), 3.33 (3H, s, N-CH_3), 7.00 (2H, d, J = 8.8 Hz, *p*-substituted ArH), 7.37 (1H, s, H-3), 7.82 (2H, s, H-7, 8), 8.13 (1H, s, H-5), 8.20 (2H, d, J = 8.8 Hz, *p*-substituted ArH).

Anal. Calcd. for $C_{22}H_{25}NO_4 \cdot H_2O$: C, 68.55; H, 7.06; N, 3.63. Found: C, 68.47; H, 7.03; N, 3.75.

Methyl 6-*tert*-butyl-2-(3',4'-dihydroxy)phenyl-4-quinolinolium Acetate (**5h**).

This compound was obtained as brown prisms (acetic acid-acetonitrile), mp 233-236°; ms: (FAB) (m/z) 324 (M^+); ir (potassium bromide): ν 3427, 3209, 3081, 2960, 1627, 1602, 1564, 1265 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.39 (3H, s, $ArCH_3$), 3.21 (3H, s, N-CH_3), 6.61 (1H, d, J = 8.8 Hz, H-5'), 6.75 (1H, s, H-3), 7.36 (1H, s, H-2'), 7.48 (2H, br. s, H-7, 8), 7.50 (1H, br d, J = 8.8 Hz, H-6'), 7.94 (1H, br s, H-5).

Anal. Calcd. for $C_{22}H_{25}NO_5 \cdot 0.2H_2O$: C, 68.27; H, 6.62; N, 3.62. Found: C, 68.00; H, 6.47; N, 4.02.

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