Supporting Information

Expeditious Synthesis of Multisubstituted Quinolinone Derivatives Based on Ring Recombination Strategy

Kazuma Yokoo,[†] and Keiji Mori[†]*

[†]Department of Applied Chemistry, Graduate School of Engineering, Tokyo University of Agriculture and Technology, 2-24-16 Nakacho, Koganei, Tokyo 184-8588, Japan.

k_mori@cc.tuat.ac.jp

Supporting Information

Table of contents	S 1
General experimental procedures	S2
Procedure and spectral data	S 3
Scanned images of ¹ H-, ¹³ C-NMR of new compounds	S19

General experimental procedures

All reactions utilizing air- and moisture-sensitive reagents were performed in dried glassware under an atmosphere of dry nitrogen. Anhydrous ethereal solvents (THF, Et_2O) were purchased from Kanto Chemical Co., INC., and used directly. Dichloromethane and 1,2-dichloroethane were distilled over CaH₂. Benzene and toluene were distilled over CaH₂, and stored over 4A molecular sieves. *N*,*N*-Dimethylformamide (DMF) was distilled over CaH₂, and stored over 4A molecular sieves.

For thin-layer chromatography (TLC) analysis, Merck pre-coated plates (silica gel 60 F_{254} , Art 5715, 0.25 mm) were used. Column chromatography and preparative TLC (PTLC) were performed on Silica Gel 60N (spherical, neutral), Kanto Chemical Ltd. and Wakogel B-5F, Wako Pure Chemical Industries, respectively.

Melting point (mp) determinations were performed by using a AS ONE ATM-01 instrument and are uncorrected. ¹H NMR, ¹³C NMR, ¹⁹F NMR were measured on a AL-300 MR (JEOL Ltd., 300 MHz), ECX-400 (JEOL Ltd., 400 MHz), and ECA-500 (JEOL Ltd., 500 MHz) spectrometers. Chemical shifts are expressed in parts per million (ppm) downfield from internal standard (tetramethylsilane for ¹H, and C₆F₆ for ¹⁹F, 0.00 ppm), and coupling constants are reported as hertz (Hz). Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; m, multiplet. Infrared (IR) spectra were recorded on a FTIR-8600PC instrument (Shimadzu Co.). Elemental analysis (EA) was carried out on Flash2000 instrument (Amco Inc.).

1. Preparation of starting materials.

Scheme S1. Preparation of starting materials **3**. Preparation of **3a** was shown as a representative example.¹



Synthesis of 2-(benzyl(methyl)amino)benzaldehyde (3a):

To a solution of commercially available, 2-fluorobenzaldehyde (s1) (810 mg, 3.99 mmol) in DMF (4.0 mL) were successively added dibenzyl amine (0.92 mL, 4.8 mmol) and K_2CO_3 (770 mg, 5.57 mmol), then heated at reflux. After heating for 17 h, the reaction was stopped by adding H₂O. The crude products were extracted with EtOAc (x3) and the combined organic extracts were washed with brine, dried (Na₂SO₄), and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 10/1) to give **3a** (450 mg, 31%) as yellow oil.

IR (neat) 3063, 3029, 2988, 2946, 2848, 2804, 2739, 1683, 1596, 1568, 1484, 1453, 1422, 1385, 1361, 1277, 1223, 1191, 1174, 1103, 1086, 1044, 1029, 946 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 2.81 (s, 3H), 4.33 (s, 2H), 7.02–7.14 (m, 2H), 7.24–7.37 (m, 5H), 7.47 (ddd, 1H, *J* = 1.8, 7.5, 7.5 Hz), 7.82 (dd, 1H, *J* = 1.8, 7.5 Hz), 10.39 (s, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 42.3, 62.3, 119.4, 121.6, 127.4, 127.9, 128.5, 130.1, 134.6, 137.3, 155.6, 191.3.

Anal. Calcd for C₁₅H₁₅NO: C, 79.97; H, 6.71; N, 6.22. Found: C, 80.03; H, 6.56; N, 6.46. (MW: 225.21)

2-(Methyl(4-methylbenzyl)amino)benzaldehyde (**3b**). Yellow oil.

Yield: 263 mg (46%, synthesized from s1).

IR (neat) 3022, 2947, 2922, 2850, 2736, 1685, 1596, 1514, 1483, 1454, 1423, 1383, 1359, 1277, 1225, 1211, 1190, 1117, 1083, 1044, 951 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 2.33 (s, 3H), 2.80 (s, 3H), 4.29 (s, 2H), 7.01–7.24 (m, 6H), 7.47 (ddd, 1H, J = 2.4, 7.5, 7.5 Hz), 7.82 (dd, 1H, J = 2.4, 7.5 Hz), 10.39 (s, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 21.0, 42.1, 62.1, 119.4, 121.5, 127.9, 128.0, 129.1, 130.0, 134.2, 134.6, 137.0, 155.7, 191.3.

Anal. Calcd for C₁₆H₁₇NO: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.16; H, 7.24; N, 5.67. (MW: 239.13)

2-(Methyl(4-methylbenzyl)amino)benzaldehyde (3c).

Yellow oil.

Yield: 148 mg (56%, synthesized from s1).

IR (neat) 2996, 2953, 2905, 2836, 1684, 1610, 1596, 1512, 1483, 1454, 1425, 1384, 1362, 1301, 1279, 1249, 1174, 1107, 1-84, 1035, 947 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 2.78 (s, 3H), 3.78 (s, 3H), 4.25 (s, 2H), 6.81–6.88 (m, 2H), 7.05 (dd, 1H, J = 8.1, 8.1 Hz), 7.07 (d, 1H, J = 8.1 Hz), 7.12–7.20 (m, 2H), 7.46 (ddd, 1H, J = 1.8, 8.1, 8.1 Hz), 7.81 (dd, 1H, J = 1.8, 8.1 Hz), 10.38 (s, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 42.0, 55.2, 61.8, 113.8, 119.6, 121.6, 128.2, 129.2, 129.3, 130.0, 134.6, 155.6, 158.9, 191.3.

Anal. Calcd for C₁₆H₁₇NO₂: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.42; H, 6.97; N, 5.20. (MW: 255.13)



2-((4-Bromobenzyl)(methyl)amino)benzaldehyde (**3d**). Yellow oil.

Yield: 385 mg (47%, synthesized from s1).

IR (neat) 3064, 3036, 2987, 2950, 2849, 2739, 1682, 1596, 1486, 1454, 1423, 1403, 1385, 1361, 1283, 1225, 1191, 1173, 1103, 1070, 1044, 1011, 952 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 2.79 (s, 3H), 4.27 (s, 2H), 7.03–7.19 (m, 4H), 7.40–7.54 (m, 3H), 7.81 (dd, 1H, *J* = 1.5, 7.8 Hz), 10.36 (s, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 42.4, 61.5, 119.5, 121.2, 121.9, 128.1, 129.7, 130.4, 131.6, 134.7, 136.3, 155.2, 191.0.

Anal. Calcd for C₁₅H₁₄BrNO: C, 59.23; H, 4.64; N, 4.60. Found: C, 59.05; H, 4.85; N, 4.52. (MW: 303.03)



2-(Methyl(naphthalen-1-ylmethyl)amino)benzaldehyde (3e).

Yellow solid.

Mp. 138-140 °C.

Yield: 206 mg (64%, synthesized from s1).

IR (KBr) 3063. 2989, 2951, 2847, 2740, 1682, 1658, 1596, 1569, 1508, 1485, 1453, 1422, 1384, 1322, 1285, 1244, 1227, 1187, 1166, 1116, 1101, 1046, 941 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 2.83 (s, 3H), 4.74 (s, 2H), 7.05 (dd, 1H, *J* = 8.1, 8.1 Hz), 7.21 (d, 1H, *J* = 8.1 Hz), 7.37–7.53 (m, 5H), 7.76–7.93 (m, 4H), 10.24 (s, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 43.7, 59.0, 119.4, 121.5, 123.3, 125.2, 125.7, 126.1, 126.2, 128.1, 128.3, 128.7, 129.9, 131.7, 132.9, 133.8, 134.6, 155.8, 191.2.

Anal. Calcd for C₁₉H₁₇NO: C, 82.88; H, 6.22; N, 5.09. Found: C, 82.75; H, 6.10; N, 4.89. (MW: 275.13)

Scheme S2. Preparation of starting materials 3 with dibenzylamine or diethyl group nitrogen atom. Preparation of 3f was shown as a representative example.²



Synthesis of 2-(Dibenzylamino)benzaldehyde (3f):

To a solution of *o*-bromoaniline **s2** (2.78 g, 16.2 mmol) in DMF (32.3 mL) was added K_2CO_3 (11.2 g, 80.8 mmol) and BnBr (7.69 mL, 64.6 mmol) at room temperature, followed by heating at 120 °C. After stirring for 48 h at 120 °C, the reaction was stopped by adding Et₂NH (4.20 mL, 40.4 mmol) at 0 °C. The crude products were extracted with Ether (x4) and the combined organic extracts were washed with brine, dried (Na₂SO₄) and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 30/1) to afford dibenzyl aniline **s3** (5.70 g, quant.) as a colorless oil.

To a solution of **s3** (5.70 g, 16.2 mmol) in THF (83.7 mL) was added *n*-BuLi (1.59 M in Hexane, 13.3 mL, 21.0 mmol) at -78 °C for 5 min. After stirring for 5 min at -78 °C, DMF (2.51 mL, 32.4 mmol) was added to the reaction mixture, and the reaction was stopped by adding saturated aqueous NaHCO₃ at -78 °C. The crude products were extracted with CH₂Cl₂ (x4) and the combined organic extracts were washed with brine, dried (Na₂SO₄) and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 30/1) to afford aldehyde **3f** (2.77 g, 57%) as yellow solid.

¹H NMR (300 MHz, CDCl₃) δ 4.27 (s, 4H), 7.04 (d, 1H, *J* = 7.8 Hz), 7.10 (dd, 1H, *J* = 7.8, 7.8 Hz), 7.12–7.34 (m, 10H), 7.43 (ddd, 1H, *J* = 2.4, 7.8, 7.8 Hz), 7.83 (dd, 1H, *J* = 2.4, 7.8 Hz), 10.54 (s, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 58.6, 122.3, 122.8, 127.3, 128.3, 128.5, 129.5, 129.7, 134.3, 137.0, 154.3, 191.2.

¹H and ¹³C NMR were coincided with those of the reported data.²

2-(Diethylamino)benzaldehyde (3g).

Yellow oil.

Yield: 175 mg (38%, synthesized from s2).

IR (neat) 2973, 2933, 2838, 1686, 1595, 1483, 1451, 1379, 1330, 1289, 1275, 1242, 1190, 1176, 1145, 1092, 1063, 1044, 1009, 829 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 1.06 (t, 6H, J = 7.2 Hz), 3.19 (q, 4H, J = 7.2 Hz), 7.08

(dd, 1H, *J* = 7.5, 7.5 Hz), 7.17 (d, 1H, *J* = 7.5 Hz), 7.49 (ddd, 1H, *J* = 1.5, 7.5, 7.5 Hz), 7.81 (dd, 1H, *J* = 1.5, 7.5 Hz), 10.36 (s, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 12.3, 48.9, 121.7, 122.3, 128.8, 130.8, 134.2, 154.6, 192.1.

Anal. Calcd for C₁₁H₁₅NO: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.28; H, 8.30; N, 8.13. (MW: 177.12)

2-(Dibenzylamino)-5-methylbenzaldehyde (**3h**).¹

Yellow oil.

Yield: 337 mg (61%, synthesized from commercially available, 2-bromo-4-methylaniline)

IR (neat) 3085, 3061, 3028, 2922, 2846, 2734, 1682, 1608, 1569, 1495, 1454, 1410, 1385, 1367, 1322, 1278, 1223, 1205, 1159, 1104, 1078, 1029, 955 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 2.30 (s, 3H), 4.21 (s, 4H), 6.97 (d, 1H, *J* = 8.1 Hz), 7.13–7.32 (m, 11H), 7.61 (d, 1H, *J* = 2.1 Hz), 10.54 (s, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 20.5, 59.0, 122.6, 127.3, 128.3, 128.6, 129.2, 130.0, 132.8, 135.3, 137.3, 152.2, 191.6.

Anal. Calcd for C₂₂H₂₁NO: C, 83.78; H, 6.71; N, 4.44. Found: C, 83.96; H, 6.48; N, 4.58. (MW: 315.16)



2-(Dibenzylamino)-5-methoxybenzaldehyde (3i).¹

Red oil.

Yield: 157 mg (36%, synthesized from commercially available, 2-bromo-4-methoxyaniline).

IR (neat) 3085, 3061, 3029, 3004, 2938, 2838, 1682, 1605, 1574, 1495, 1454, 1418,

1369, 1314, 1277, 1245, 1227, 1191, 1160, 1092, 1074, 1042, 1029, 934 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 3.77 (s, 3H), 4.16 (s, 4H), 7.00–7.34 (m, 13H), 10.55 (s, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 55.5, 59.6, 110.1, 122.3, 124.9, 127.3, 128.3, 128.9, 131.9, 137.3, 148.2, 156.0, 191.4.

Anal. Calcd for C₂₂H₂₁NO₂: C, 79.73; H, 6.39; N, 4.23. Found: C, 79.86; H, 6.63; N, 4.04. (MW: 331.16)

2-(Dibenzylamino)-4-methylbenzaldehyde (**3j**).¹

Yellow oil.

Yield: 386 mg (40%, synthesized from commercially available, 2-bromo-5-methylaniline).

IR (neat) 3085, 3061, 3029, 2923, 2849, 1682, 1602, 1566, 1494, 1454, 1415, 1367, 1277, 1230, 1200, 1157, 1103, 1078, 1028, 959 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 2.31 (s, 3H), 4.25 (s, 4H), 6.85 (s, 1H), 6.92 (d, 1H, J = 7.8 Hz), 7.13–7.35 (m, 10H), 7.73 (d, 1H, J = 7.8 Hz), 10.47 (s, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 22.0, 58.5, 122.8, 124.0, 127.4, 128.4, 128.6, 129.7, 137.2, 145.6, 154.6, 191.0.

Anal. Calcd for C₂₂H₂₁NO: C, 83.78; H, 6.71; N, 4.44. Found: C, 83.65; H, 6.79; N, 4.17. (MW: 315.16)

3-(Dibenzylamino)-2-naphthaldehyde (**3k**).¹

Yellow solid.

Mp. 108–111 °C.

Yield: 226 mg (47%, synthesized from commercially available,

3-iodonaphthalen-2-amine).

IR (KBr) 3085, 3060, 3028, 2927, 2845, 1693, 1624, 1591, 1496, 1454, 1395, 1374, 1334, 1173, 1153, 1104, 1078, 1029, 954, 909 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 4.30 (s, 4H), 7.13–7.33 (m, 11H), 7.38 (dd, 1H, *J* = 7.5, 7.5 Hz), 7.48 (dd, 1H, *J* = 7.5, 7.5 Hz), 7.64 (d, 1H, *J* = 7.5 Hz), 7.87 (d, 1H, *J* = 7.5 Hz), 8.37 (s, 1H), 10.69 (s, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 58.3, 119.5, 125.3, 126.9, 127.4, 128.4, 128.6, 128.7, 129.2, 129.7, 129.9, 131.7, 136.5, 137.0, 149.2, 191.8.

Anal. Calcd for C₂₅H₂₁NO: C, 85.44; H, 6.02; N, 3.99. Found: C, 85.25; H, 5.92; N, 4.15. (MW: 351.16)

2. Synthesis of quinolinone derivatives.

General procedure for the formation of quinolinone derivatives from tetrahydroquinolines.

A solution of tetrahydroquinoline **5a** (0.10 mmol) in ClCH₂CH₂Cl (1.0 mL) was added heated a solution of BF₃•OEt₂ (0.10 M in ClCH₂CH₂Cl, 1.0 μ mol), then heated (heat block) at reflux for 12 h. After cooling to room temperature, the reaction was stopped by adding saturated aqueous NaHCO₃. The crude products were extracted with EtOAc (x3) and the combined organic extracts were washed with brine, dried (Na₂SO₄), and concentrated in vacuo. The residue was purified by preparative TLC to give quinolinone derivatives **4a**.

General procedure for the formation of quinolinone derivatives (one-pot procedure).

A solution of *ortho*-amino benzaldehyde derivative **3** (0.10 mmol) and Meldrum's acid (0.10 mmol) in ClCH₂CH₂Cl (1.0 mL) was heated (heat block) at reflux for 12 h. After cooling to room temperature, a solution of BF₃•OEt₂ (0.10 M in ClCH₂CH₂Cl, 1.0 μ mol) was added to the reaction mixture, and then heated (heat block) at reflux for 12 h. After cooling to room temperature, DBU (0.10 mmol) was added to the reaction mixture. After being stirred for 1 h at room temperature, the reaction was stopped by adding saturated aqueous NaHCO₃. The crude products were extracted with EtOAc (x3) and the combined organic extracts were washed with brine, dried (Na₂SO₄), and concentrated in vacuo. The residue was purified by preparative TLC to give quinolinone derivatives **4**.

Gram-scale reaction.

A solution of *ortho*-dibenzylamino benzaldehyde **3a** (1.07 g, 4.74 mmol) and Meldrum's acid (683 mg, 4.74 mmol) in ClCH₂CH₂Cl (47.4 mL) was heated (oil bath) at reflux for 12 h. After cooling to room temperature, a solution of BF₃•OEt₂ (0.10 M in ClCH₂CH₂Cl, 474 μ L, 47.4 μ mol) was added to the reaction mixture, and then heated (oil bath) at reflux for 12 h. After cooling to room temperature, DBU (0.71 mL, 4.74 mmol) was added to the reaction mixture, and then heated (oil bath) at reflux for 12 h. After cooling to room temperature, DBU (0.71 mL, 4.74 mmol) was added to the reaction mixture. After being stirred for 1 h at room temperature, the reaction was stopped by adding saturated aqueous NaHCO₃. The crude products were extracted with EtOAc (x3) and the combined organic extracts were

washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by preparative TLC to give quinolinone derivatives **4a** (955 mg, 81%).



1',2,2-Trimethyl-2'-phenyl-2',4'-dihydro-1'*H*-spiro[[1,3]dioxane-5,3'-quinoline]-4,6-dion e (**5a**).

Yellow solid.

Mp. 135–137 °C.

Yield: 34.4 mg (98%).

IR (KBr) 3065, 3030, 3001, 2915, 2878, 2825, 1739, 1605, 1583, 1500, 1455, 1433, 1392, 1381, 1355, 1268, 1204, 1133, 1102, 1046, 1003, 969 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 1.02 (s, 3H), 1.62 (s, 3H), 2.83 (s, 3H), 3.17 (d, 1H, *J* = 15.3 Hz), 3.62 (d, 1H, *J* = 15.3 Hz), 4.87 (s, 1H), 6.74 (ddd, 1H, *J* = 1.2, 7.5, 7.5 Hz), 6.86 (d, 1H, *J* = 7.5 Hz), 6.99 d, 1H, *J* = 7.5 Hz), 7.16–7.38 (m, 6H).

¹³C NMR (75 MHz, CDCl₃) δ 27.9, 29.6, 35.9, 37.9, 53.7, 67.3, 105.3, 112.4, 117.4, 118.5, 127.9, 128.0, 128.6, 128.9, 128.9, 136.8, 145.9, 163.8, 168.5.

Anal. Calcd for C₂₁H₂₁NO₄: C, 71.78; H, 6.02; N, 3.99. Found: C, 71.56; H, 5.91; N, 4.19. (MW: 351.15)

Ph NO

3-Benzyl-1-methylquinolin-2(1*H*)-one (4a).

Colorless oil.

Yield: 22.2 mg (89%).

IR (neat) 3083, 3060, 3027, 3002, 2921, 1646, 1625, 1596, 1575, 1495, 1463, 1417, 1387, 1301, 1223, 1165, 1128, 1091, 1076, 1041, 1030, 996 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 3.75 (s, 3H), 3.98 (s, 2H), 7.18 (dd, 1H, *J* = 7.6, 7.6 Hz), 7.21–7.28 (m, 1H), 7.29–7.37 (m, 6H), 7.44 (dd, 1H, *J* = 1.6, 7.6 Hz), 7.50 (ddd, 1H, *J* = 1.6, 7.6, 7.6 Hz).

¹³C NMR (100 MHz, CDCl₃) δ 29.8, 37.0, 113.8, 120.5, 122.0, 126.3, 128.2, 128.5,

129.4, 129.6, 133.4, 135.8, 139.0, 139.1, 162.3.

Anal. Calcd for C₁₇H₁₅NO: C, 81.90; H, 6.06; N, 5.62. Found: C, 82.15; H, 6.32; N, 5.38. (MW: 249.12)

1-Methyl-3-(4-methylbenzyl)quinolin-2(1*H*)-one (**4b**).

White solid.

Mp. 49–51 °C.

Yield: 22.8 mg (83%).

IR (KBr) 3021, 2920, 1646, 1597, 1574, 1514, 1499, 1462, 1417, 1387, 1299, 1272, 1223, 1183, 1166, 1128, 1109, 1090, 1040, 947 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 2.33 (s, 3H), 3.74 (s, 3H), 3.93 (s, 2H), 7.10–7.24 (m, 5H), 7.27–7.36 (m, 2H), 7.42–7.54 (m, 2H).

¹³C NMR (75 MHz, CDCl₃) δ 21.0, 29.7, 36.6, 113.8, 120.6, 121.9, 128.2, 129.2, 129.3, 129.5, 133.6, 135.6, 135.8, 135.9, 139.0, 162.3.

Anal. Calcd for C₁₈H₁₇NO: C, 82.10; H, 6.51; N, 5.32. Found: C, 81.89; H, 6.73; N, 5.17. (MW: 263.13)



3-(4-Methoxybenzyl)-1-methylquinolin-2(1H)-one (4c).

Yellow oil.

Yield: 26.8 mg (90%).

IR (neat) 3033, 2997, 1935, 2834, 1644, 1595, 1513, 1463, 1417, 1387, 1301, 1246, 1177, 1128, 1108, 1090, 1036, 949, 913 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 3.74 (s, 3H), 3.80 (s, 3H), 3.91 (s, 2H), 6.84–6.92 (m, 2H), 7.14–7.35 (m, 5H), 7.42–7.54 (m, 2H).

¹³C NMR (75 MHz, CDCl₃) δ 29.2, 36.1, 55.2, 113.8, 113.9, 120.6, 121.9, 128.2, 129.5, 130.3, 131.0, 133.7, 135.5, 138.9, 158.1, 162.3.

Anal. Calcd for C₁₈H₁₇NO₂: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.14; H, 5.96; N, 4.86. (MW: 279.13)

3-(4-Bromobenzyl)-1-methylquinolin-2(1*H*)-one (4d).

Yellow oil.

Yield: 28.4 mg (82%).

IR (neat) 3039, 2920, 2849, 1645, 1597, 1574, 1486, 1462, 1417, 1403, 1387, 1300, 1224, 1090, 1070, 1011, 840 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 3.75 (s, 3H), 3.92 (s, 2H), 7.16–7.25 (m, 3H), 7.34 (d, 1H, J = 8.0 Hz), 7.36 (s, 1H), 7.41–7.57 (m, 4H).

¹³C NMR (100 MHz, CDCl₃) δ 29.8, 36.6, 113.9, 120.2, 120.4, 122.1, 128.3, 129.8, 131.1, 131.6, 132.7, 135.9, 138.2, 139.1, 162.1.

Anal. Calcd for C₁₇H₁₄BrNO: C, 62.21; H, 4.30; N, 4.27. Found: C, 62.46; H, 4.15; N, 3.98. (MW: 327.03)



1-Methyl-3-(naphthalen-1-ylmethyl)quinolin-2(1*H*)-one (**4e**).

Yellow solid.

Mp. 138-140 °C.

Yield: 26.6 mg (90%).

IR (KBr) 3044, 2938, 1645, 1595, 1575, 1509, 1500, 1462, 1416, 1397, 1389, 1314, 1290, 1274, 1222, 1166, 1128, 1091, 1040, 1017, 994 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 3.81 (s, 2H), 4.43 (s, 2H), 6.92 (s, 1H), 7.07 (dd, 1H, J = 7.5, 7.5 Hz), 7.20 (d, 1H, J = 7.5 Hz), 7.32 (d, 1H, J = 7.5 Hz), 7.36–7.54 (m, 5H), 7.82 (d, 1H, J = 7.5 Hz), 7.89 (d, 2H, J = 7.5 Hz).

¹³C NMR (75 MHz, CDCl₃) δ 29.8, 33.8, 113.8, 120.5, 121.9, 124.4, 125.6, 125.6, 126.1, 127.4, 128.0, 128.2, 128.6, 129.5, 132.2, 132.7, 133.9, 135.04.9, 135.7, 138.7, 162.3. Anal. Calcd for C₂₁H₁₇NO: C, 84.25; H, 5.72; N, 4.68. Found: C, 84.10; H, 5.54; N, 4.38. (MW: 299.13)



1,3-Dibenzylquinolin-2(1*H*)-one (**4f**).

Colorless oil.

Yield: 30.1 mg (89%).

IR (neat) 3084, 3061, 3028, 3006, 2924, 2853, 1645, 1596, 1573, 1496, 1454, 1392, 1369, 1300, 1222, 1210, 1179, 1156, 1102, 1076, 1029, 985 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 4.04 (s, 2H), 5.58 (s, 2H), 7.13 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.17–7.39 (m, 13H), 7.43 (dd, 1H, *J* = 1.2, 8.0 Hz).

¹³C NMR (100 MHz, CDCl₃) δ 37.0, 46.3, 114.7, 120.8, 122.1, 126.4, 126.6, 127.2, 128.3, 128.6, 128.7, 129.5, 129.6, 133.4, 136.3, 136.5, 138.4, 139.0, 162.5.

Anal. Calcd for C₂₃H₁₉NO: C, 84.89; H, 5.89; N, 4.30. Found: C, 84.73; H, 6.14; N, 4.54. (MW: 325.15)

1,3-Diethylquinolin-2(1*H*)-one (**4g**).

Colorless oil.

Yield: 10.5 mg (29%, 4g/s4 = 1/1, the ratio was determined after hydrogenolysis).

IR (neat) 3077, 3039, 2968, 2933, 2873, 1644, 1598, 1496, 1462, 1396, 1370, 1344, 1299, 1244, 1220, 1175, 1098, 1091, 1063, 1042, 1030, 946 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 1.27 (t, 3H, *J* = 7.6 Hz), 1.37 (t, 3H, *J* = 7.6 Hz), 2.69 (dq, 2H, *J* = 0.8, 7.6 Hz), 4.39 (q, 2H, *J* = 7.6 Hz), 7.20 (ddd, 1H, *J* = 1.2, 8.4, 8.4 Hz), 7.36 (d, 1H, *J* = 8.4 Hz), 7.46–7.58 (m, 2H).

¹³C NMR (100 MHz, CDCl₃) δ 12.5, 12.7, 23.8, 37.5, 113.7, 121.1, 128.2, 129.2, 133.8, 135.4, 137.8, 161.7.

Anal. Calcd for C₁₃H₁₅NO: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.30; H, 7.40; N, 7.14. (MW: 201.12)

1,3-Diethyl-3,4-dihydroquinolin-2(1*H*)-one (s4).

Colorless oil.

Yield: 11.0 mg (29%, **4g/s4** = 1/1, the ratio was determined after hydrogenolysis). IR (neat) 2966, 2934, 2875, 1668, 1602, 1496, 1462, 1379, 1350, 1300, 1251, 1201, 1187, 1134, 1101, 1089, 1055, 967 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 0.99 (t, 3H, *J* = 7.2 Hz), 1.25 (t, 3H, *J* = 7.2 Hz), 1.37–1.50 (m, 1H), 1.77–1.90 (m, 1H), 2.38–2.50 (m, 1H), 2.68 (dd, 1H, *J* = 8.8, 15.2 Hz), 2.98 (dd, 1H, *J* = 5.6, 15.2 Hz), 3.98 (q, 2H, *J* = 7.2 Hz), 6.95–7.04 (m, 2H), 7.16 (d, 1H, *J* = 8.0 Hz), 7.24 (dd, 1H, *J* = 8.0, 8.0 Hz).

¹³C NMR (100 MHz, CDCl₃) δ 11.5, 12.8, 22.5, 30.2, 37.5, 42.1, 114.2, 122.5, 125.7, 127.3, 128.3, 139.2, 172.1.

Anal. Calcd for C₁₃H₁₇NO: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.56; H, 8.26; N, 7.02. (MW: 203.13)



1,3-Dibenzyl-6-methylquinolin-2(1*H*)-one (**4h**).

Colorless oil.

Yield: 31.5 mg (89%).

IR (neat) 3061, 3028, 2921, 1646, 1604, 1573, 1497, 1454, 1436, 1389, 1305, 1235, 1210, 1177, 1124, 1076, 1029, 989 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 2.32 (s, 3H), 4.03 (s, 2H), 5.57 (s, 2H), 7.07–7.42 (m, 14H).

¹³C NMR (75 MHz, CDCl₃) δ 20.5, 37.0, 46.3, 114.6, 120.8, 126.4, 126.6, 127.1, 128.2, 128.6, 128.7, 129.5, 130.8, 131.6, 133.4, 136.1, 136.5, 136.6, 139.1, 162.4.

Anal. Calcd for C₂₄H₂₁NO: C, 84.92; H, 6.24; N, 4.13. Found: C, 84.69; H, 6.50; N, 4.33. (MW: 339.16)

1,3-Dibenzyl-6-methoxyquinolin-2(1*H*)-one (4i).

Pale red oil.

Yield: 34.2 mg (98%).

IR (neat) 3060, 3027, 2932, 2835, 1648, 1626, 1604, 1574, 1499, 1464, 1454, 1434, 1355, 1296, 1242, 1207, 1175, 1161, 1076, 1047, 1029, 991 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 3.77 (s, 3H), 4.04 (s, 2H), 5.57 (s, 2H), 6.88 (dd, 1H, J = 2.7 Hz), 6.97 (dd, 1H, J = 2.7, 9.0 Hz), 7.12–7.43 (m, 12H).

¹³C NMR (75 MHz, CDCl₃) δ 37.0, 46.4, 55.6, 110.0, 116.0, 118.3, 121.5, 126.4, 126.6, 127.2, 128.6, 128.7, 129.6, 132.9, 134.0, 135.8, 136.6, 139.1, 154.6, 162.0.

Anal. Calcd for C₂₄H₂₁NO₂: C, 81.10; H, 5.96; N, 3.94. Found: C, 80.95; H, 5.77; N, 4.08. (MW: 355.16)



1,3-Dibenzyl-7-methylquinolin-2(1*H*)-one (**4j**).

Colorless oil.

Yield: 30.2 mg (91%).

IR (neat) 3084, 3060, 3028, 2920, 1645, 1604, 1563, 1495, 1453, 1395, 1361, 1301, 1217, 1184, 1076, 1030, 919 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 2.34 (s, 3H), 4.01 (s, 2H), 5.56 (s, 2H), 6.95 (dd, 1H, J = 0.9, 7.8 Hz), 7.04 (s, 1H), 7.18–7.37 (m, 12H).

¹³C NMR (75 MHz, CDCl₃) δ 22.1, 36.9, 46.3, 114.8, 118.6, 123.5, 126.3, 126.6, 127.1, 128.2, 128.5, 128.7, 129.5, 132.2, 136.2, 136.6, 138.6, 139.2, 140.1, 162.6.

Anal. Calcd for C₂₄H₂₁NO: C, 84.92; H, 6.24; N, 4.13. Found: C, 85.05; H, 6.07; N, 4.16. (MW: 339.16)



1,3-Dibenzylbenzo[g]quinolin-2(1*H*)-one (**4**k).

Colorless oil.

Yield: 32.8 mg (91%).

IR (neat) 3060, 3028, 2923, 1650, 1621, 1590, 1512, 1495, 1472, 1454, 1372, 1358, 1308, 1226, 1187, 1146, 1076, 1027, 908 cm⁻¹.

¹H NMR (300 MHz, CDCl₃) δ 4.07 (s, 2H), 5.65 (s, 2H), 7.18–7.49 (m, 13H), 7.56 (s, 1H), 7.72 (d, 1H, *J* = 8.1 Hz), 7.81 (d, 1H, *J* = 8.1 Hz), 7.94 (s, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 37.0, 46.5, 110.9, 121.3, 124.8, 126.5, 126.6, 127.1, 127.2, 127.4, 127.7, 127.7, 128.6, 128.8, 128.8, 129.6, 133.6, 133.8, 136.1, 136.5, 138.9, 162.7.

Anal. Calcd for C₂₇H₂₁NO: C, 86.37; H, 5.64; N, 3.73. Found: C, 86.55; H, 5.40; N, 3.48. (MW: 375.16)

Ph NO

3-Benzyl-1-methyl-3,4-dihydroquinolin-2(1*H*)-one (8).

Yellow oil.

Yield: 18.5 mg (71%, hydrogenolysis of **4a**).

IR (neat) 3061, 3027, 2923, 2855, 1671, 1603, 1497, 1472, 1415, 1371, 1339, 1272, 1257, 1122, 754 cm⁻¹.

¹H NMR (400 MHz, CDCl₃) δ 2.50–2.66 (m, 2H), 2.75–2.85 (m, 2H), 3.31 (dd, 1H, *J* = 3.6, 13.6 Hz), 3.40 (s, 3H), 6.95–7.04 (m, 2H), 7.07 (d, 1H, *J* = 6.8 Hz), 7.15–7.38 (m, 6H).

¹³C NMR (75 MHz, CDCl₃) δ 29.3, 29.8, 35.5, 42.4, 114.4, 122.8, 125.1, 126.3, 127.4, 128.2, 128.4, 129.1, 139.1, 140.2, 172.1.

Anal. Calcd for C₁₇H₁₇NO: C, 81.24; H, 6.82; N, 5.57. Found: C, 80.95; H, 6.70; N, 5.75. (MW: 251.13)

References

- 1) Mori, K.; Ehara, K.; Kurihara, K.; Akiyama, T. J. Am. Chem. Soc. 2011, 133, 6166.
- 2) Mori, K.; Ohshima, Y.; Ehara, K.; Akiyama, T. Chem. Lett. 2009, 38, 524.

¹H NMR spectrum of **3a**.



¹³C NMR spectrum of **3a**.



¹H NMR spectrum of **3b**.



¹³C NMR spectrum of **3b**.



¹H NMR spectrum of **3c**.



¹³C NMR spectrum of **3c**.



¹H NMR spectrum of **3d**.



¹³C NMR spectrum of **3d**.



¹H NMR spectrum of **3e**.



¹³C NMR spectrum of **3e**.



¹H NMR spectrum of **3f**.



¹³C NMR spectrum of **3f**.



¹H NMR spectrum of **3g**.



¹³C NMR spectrum of **3g**.



¹H NMR spectrum of **3h**.



¹³C NMR spectrum of **3h**.



¹H NMR spectrum of **3i**.



¹³C NMR spectrum of **3i**.



¹H NMR spectrum of **3**j.



¹³C NMR spectrum of **3**j.



¹H NMR spectrum of **3k**.







¹H NMR spectrum of **5a**.



¹³C NMR spectrum of **5a**.



¹H NMR spectrum of **4a**.



¹³C NMR spectrum of **4a**.



¹H NMR spectrum of **4b**.



¹³C NMR spectrum of **4b**.



¹H NMR spectrum of **4c**.



¹³C NMR spectrum of **4c**.



¹H NMR spectrum of **4d**.



¹³C NMR spectrum of **4d**.



¹H NMR spectrum of **4e**.



¹³C NMR spectrum of **4e**.



¹H NMR spectrum of **4f**.





S54

¹H NMR spectrum of **4g**.



¹³C NMR spectrum of **4g**.



¹H NMR spectrum of **s4**.



¹³C NMR spectrum of **s4**.



¹H NMR spectrum of **4h**.



¹³C NMR spectrum of **4h**.



¹H NMR spectrum of **4i**.



¹³C NMR spectrum of **4i**.



¹H NMR spectrum of **4**j.



¹³C NMR spectrum of **4**j.

auto Thu Aug 01 09:43:1 13C BCM sec usec KHz Hz MHz sec ppm Hz Hz υ 5-MeQuinoC.ALS 75.45 M 124.00 F 1840.00 F 32768 32768 512 512 1.6097 1.6097 5.50 u 77.00 0.10 25 29.0 CDCL3 H DFILLE COMNT DATIM OBNUC OBBUC OBBERQ OBSET OBFIN POLINT FREQU SCANS SCANS SCANS PD PU IRNUC CTEMP PD RGAIN RGAIN Mdo ノン合成データ¥5-MeQuinoC.ALS 22.119 25 36. 899 46.263 50 76. 581 77. 427 77. 427 77. 427 1 75 auto C:¥Users¥mori_lab¥Desktop¥NMR¥300MHz¥yokoo¥*÷*, 00 125 150 175 200

¹H NMR spectrum of **4k**.







¹H NMR spectrum of **8**.



¹³C NMR spectrum of **8**.

