Supporting Information

Solvent Controlled Radical Cyclization of Propargylamines
for Multi-Iodinated Quinoline Formation


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1. General information
Commercially available reagents were used as received without purification. Column chromatography was carried out on silica gel (300–400 mesh). Analytical thin-layer chromatography was performed on glass plates of Silica Gel GF–254 with detection by UV. Infrared spectroscopy was measured by Agilent Cary 630 FTIR Spectrometer. $^1$H and $^{13}$C NMR spectra were recorded on a 400M Bruker spectrometer. The chemical shift references were as follows: $^1$H NMR (CDCl$_3$) 7.26 ppm. $^{13}$C NMR (CDCl$_3$) 77.0 ppm. HRMS spectra were carried out on TOF MS EI$^+$ and ESI. Melting point determination was taken on a Melt–Temp apparatus (X-4) and was uncorrected.

2. Synthesis of propargylamines 1 following reported procedures (J. Am. Chem. Soc., 2002, 124, 5638; J. Org. Chem. 2006, 71, 2064-2070; Org. Lett. 2006, 8, 2405-2408; Tetrahedron, 2014, 70, 3134-3140.) The mixture of aldehyde (0.2 mmol), phenylacetylene (0.3 mmol), aniline (0.24 mmol) and copper (I) chloride (10 mol %) was heated at 60°C for two hours. The mixture in water was extracted with diethyl ether. The organic layer was washed with water and dried over anhydrous MgSO$_4$. The solvent was removed in vacuo. After flash column chromatography on silica gel with EtOAc/hexane as eluent, the product was isolated as a yellow oil.

3. General procedure
Propargylamine 1 (0.1 mmol) and N-iodosuccinimide (0.12 mmol) were stirred in 1,4-dioxane (2 ml) at room temperature for 6h to give a red-brown solution. The solution was evaporated to dryness and the crude product was purified by column chromatography to afford pure product 2. Propargylamine 1 (0.1 mmol) and N-iodosuccinimide (0.3 mmol) were stirred in methanol (2 ml) at 60 °C for 6h to give a brown solution. The solution was evaporated to dryness and the crude product purified by column chromatography with EtOAc/hexane as eluent to obtain the final product 3.

4. Characterization data
3-iodo-2,4-diphenylquinoline (2a): White solid, mp 121-122 °C. Yield: 27.3 mg (67%). IR $\nu_{max}$
3-iodo-5,7-dimethyl-2,4-diphenylquinoline (2b): White solid. mp 157-158 °C. Yield: 27.8 mg (64%). IR ν max cm⁻¹ (KBr disc): 2967, 1534, 1492, 1384, 1261, 1291, 1285, 1280, 1271, 1218, 98.4, 35.0, 31.0. HRMS (ESI): Calcd. for C₂²H₁₉INO (M+H)+ 436.0562, found 436.0557.

3-iodo-6-methoxy-2,4-diphenylquinoline (2d): White solid. Melting point: 137-138 °C. Yield: 32.8 mg (75%). IR ν max cm⁻¹ (KBr disc): 2967, 2950, 1562, 1498, 1346, 1276, 1252, 1134, 1028, 954. ¹H NMR (CDCl₃, 400 MHz) δ 8.06 (d, J = 9.2 Hz, 1H), 7.65 – 7.41 (m, 8H), 7.38 (m, 1H), 7.33 – 7.27 (m, 2H), 6.63 (m, 1H), 3.69 (s, 3H).

6-(tert-butyl)-3-iodo-2,4-diphenylquinoline (2e): White solid. Melting point: 252-253 °C. Yield: 34.6 mg (72%). IR ν max cm⁻¹ (KBr disc): 3067, 2957, 2868, 1539, 1507, 1157, 1084, 1013, 978. ¹H NMR (CDCl₃, 400 MHz) δ 8.08 (m, 1H), 7.83 (m, 1H), 7.67 – 7.49 (m, 5H), 7.35 – 7.26 (m, 5H), 2.43 (s, 3H), 1.26 (s, 9H). ¹F NMR (CDCl₃, 100 MHz) δ -113.1. HRMS (ESI): Calcd. for C₂₅H₂₂FIN (M+H)+ 482.0781, found 482.0781.

6-chloro-3-iodo-2,4-diphenylquinoline (2f): White solid. Melting point: 244-245 °C. Yield: 36.3 mg (76%). IR ν max cm⁻¹ (KBr disc): 3054, 2950, 1535, 1440, 1087, 1027, 749, 697, 609. ¹H NMR (CDCl₃, 400 MHz) δ 7.65 – 7.41 (m, 8H), 7.38 (m, 1H), 7.33 – 7.27 (m, 2H), 6.63 (m, 1H), 3.69 (s, 3H). ¹³C NMR (CDCl₃) δ 150.4, 145.3, 142.2, 141.0, 138.4, 139.3, 138.2, 129.3, 129.0, 128.8, 128.6, 128.5, 128.4, 128.0, 127.1, 121.9, 115.1, 114.9 (d, J = 8.3 Hz), 129.2, 129.1, 128.8, 128.6, 128.5, 128.4, 128.0, 122.5, 104.9, 99.1, 55.4. HRMS (ESI): Calcd. for C₂₅H₂₁INO (M+H)+ 478.1032, found 478.1028.
(CDCl₃, 400 MHz) δ 8.13–8.06 (m, 1H), 7.69–7.45 (m, 9H), 7.38 (m, 1H), 7.30–7.26 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 162.2, 154.0, 145.4, 143.4, 141.5, 133.2, 131.1, 129.2, 129.0, 128.9, 128.8, 128.0, 127.9, 125.6, 99.8. HRMS (ESI): Calcd. for C₁₄H₁₄ClIN (M+H)+ 441.9859, found 441.9851.

3-iodo-2,4-diphenyl-6-(trifluoromethyl)quinoline (2i): White solid. Melting point: 245-246 °C. Yield: 33.8 mg (71%). IR νmax cm⁻¹ (KBr disc): 3066, 1625, 1560, 1441, 1336, 1383, 1314, 1293, 977, 900. ¹H NMR (CDCl₃, 400 MHz) δ 8.27 (m, 1H), 7.90 (m, 1H), 7.71 (s, 1H), 7.68 – 7.45 (m, 8H), 7.30 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 164.2, 154.8, 147.9, 143.2, 141.2, 130.7, 129.2, 129.1, 129.0, 128.9, 128.6, 128.1, 126.3, 125.8 (q, J = 2.9 Hz) 125.1, 124.8 (q, J = 4.5 Hz), 122.4, 100.1. ¹⁹F NMR (CDCl₃, 100 MHz) δ -62.4. HRMS (ESI): Calcd. for C₁₂H₁₄F₃I₂N (M+H)+ 476.0123, found 476.0118.

3,6-diiodo-2,4-diphenylquinoline (3a): White solid, yield: 40.5 mg (76%), mp 223-225 °C. IR νmax cm⁻¹ (KBr disc): 3056, 2344, 1528, 1441, 1328, 1025, 971, 883, 827, 743. ¹H NMR (CDCl₃, 400 MHz) δ 7.97 (m, 1H), 7.87 (m, 1H), 7.76 (s, 1H), 7.67 – 7.43 (m, 9H), 7.32 – 7.27 (m, 1H). ¹³C NMR (CDCl₃, 101 MHz) δ 165.3, 153.7, 145.9, 143.4, 141.4, 139.0, 135.5, 131.1, 129.2, 129.1, 129.0, 128.9, 128.8, 128.7, 128.0, 99.6, 93.3. HRMS (ESI): calcd for C₁₂H₁₂I₂N (M+H)+ 533.9216, found 533.9211.

7-fluoro-3,6-diiodo-2,4-diphenylquinoline (3b): Yellow solid, yield: 34.7 mg (63%), mp 201-202 °C. IR νmax cm⁻¹ (KBr disc): 3062, 1556, 1463, 1338, 1180, 1085, 885, 747, 693, 557. ¹H NMR (CDCl₃, 400 MHz) δ 7.85 (d, J = 6.7 Hz, 1H), 7.78 (d, J = 8.7 Hz, 1H), 7.65 – 7.55 (m, 5H), 7.52 – 7.46 (m, 3H), 7.29 – 7.25 (m, 2H). ¹³C NMR (CDCl₃, 101 MHz) δ 163.6, 162.7, 160.2, 153.7, 153.7, 147.7 (d, J = 11.8 Hz), 143.2, 141.3, 138.2, 138.2, 129.2, 129.0, 128.9, 128.1, 125.8, 113.18 (d, J = 23.7 Hz), 98.4, 84.0 (d, J = 28.6 Hz). ¹⁹F NMR (CDCl₃, 100 MHz) δ -90.6. HRMS (ESI): calcd for C₁₂H₁₁F₂I₂N (M+H)+ 551.9121, found 551.9120.

3,6-diiodo-5,7-dimethyl-2,4-diphenylquinoline (3c): White solid, yield 41.5 mg (74%), mp 201-202 °C. IR νmax cm⁻¹ (KBr disc): 3056, 1491, 1437, 1157, 1028, 988, 971, 848, 704. ¹H NMR (CDCl₃, 400 MHz) δ 7.94 (s, 1H), 7.77 – 7.56 (m, 2H), 7.56 – 7.36 (m, 6H), 7.25 – 7.22 (m, 2H), 2.66 (s, 3H), 2.14 (s, 3H). ¹³C NMR (CDCl₃, 101 MHz) δ 162.0, 153.1, 147.3, 146.7, 143.8, 143.6, 138.5, 129.6, 129.2, 128.7, 128.6, 128.5, 128.0, 127.6, 125.0, 113.4, 100.9, 31.9, 31.1. HRMS (ESI): calcd for C₁₂H₁₂I₂N (M+H)+ 561.9529, found 561.9563.

2-[(1,1'-biphenyl)-4-yl]-3,6-diiodo-4-phenylquinoline (3d): White solid, yield 37.1 mg (61%), mp 307-308 °C, IR νmax cm⁻¹ (KBr disc): 3028, 1327, 1243, 1086, 1057, 971, 885, 831, 695, 611. ¹H NMR (CDCl₃, 400 MHz) δ 7.97 (m, 1H), 7.88 (m, 1H), 7.79 – 7.53 (m, 10H), 7.47 (m, 2H), 7.37 (m, 1H), 7.29 (m, 2H). ¹³C NMR (CDCl₃, 101 MHz) δ 162.2, 153.7, 146.0, 142.3, 141.7, 141.5, 140.7, 139.0, 135.5, 131.1, 129.8, 129.1, 129.0, 128.9, 128.8, 128.7, 127.6, 127.3, 126.8, 99.4, 93.3. HRMS (ESI): Calcd. for C₁₂H₁₁I₂N (M+H)+ 609.9529, found 609.9581.

3,6-diiodo-2-(4-(trifluoromethyl)phenyl)quinoline (3e) White solid, yield: 41.5 mg (69%), mp 297-298 °C. IR νmax cm⁻¹ (KBr disc): 3069, 1588, 1467, 1318, 1124, 1018, 972, 887, 831, 699. ¹H NMR (CDCl₃, 400 MHz) δ 7.99 (dd, J = 8.8, 1.9 Hz, 1H), 7.85 (d, J = 8.8 Hz, 1H), 7.80 – 7.74 (m, 5H), 7.63 – 7.54 (m, 3H), 7.28 (m, 2H). ¹³C NMR (CDCl₃, 101 MHz) δ 161.1, 154.0, 146.7, 145.9, 141.1, 139.3, 135.6, 131.1, 129.8, 129.1, 129.0, 128.9, 125.1 (q, J = 3.7 Hz), 98.5, 93.9. ¹⁹F NMR (CDCl₃, 100 MHz) δ -62.6. HRMS (ESI): Calcd. for C₁₂H₁₂F₃I₂N (M+H)+ 610.9089, found 610.9086.

2-(4-chlorophenyl)-3,6-diiodo-4-phenylquinoline (3f) White solid, yield 37.9 mg (67%), mp
300-301°C. IR νmax cm⁻¹ (KBr disc): 3024, 1655, 1459, 1325, 1090, 973, 885, 823. ¹H NMR (400 MHz, CDCl₃) δ 7.97 (m, 1H), 7.84 (m, 1H), 7.76 (m, 1H), 7.58 (m, 5H), 7.47 (m, 2H), 7.33 – 7.25 (m, 2H). ¹³C NMR (CDCl₃, 101 MHz) δ 161.3, 153.9, 145.9, 141.7, 141.3, 139.2, 135.5, 135.0, 131.0, 130.8, 129.0, 128.9, 128.8, 128.3, 99.1, 93.6. HRMS (ESI): calcd for C₂₁H₁₃I₂N (M+H)⁺ 567.8826, found 567.8823.

2-(4-(tert-butyl)phenyl)-3,6-diiodo-4-phenylquinoline (3g) White solid, yield 44.2 mg (75%), mp 214-216 °C. IR νmax cm⁻¹ (KBr disc): 2954, 2860, 1523, 1508, 1459, 1323, 1109, 971, 829, 747. ¹H NMR (CDCl₃, 400 MHz) δ 7.95 (m, 1H), 7.86 (m, 1H), 7.75 (m, 1H), 7.55 (m, 7H), 7.27 (m, 2H), 1.37 (s, 9H). ¹³C NMR (CDCl₃, 101 MHz) δ 162.6, 153.6, 151.8, 145.9, 141.6, 140.5, 138.9, 135.5, 131.1, 129.1, 128.9, 128.8, 128.7, 125.0, 99.7, 93.1, 34.8, 31.4. HRMS (ESI): calcd for C₂₅H₂₁I₂N (M+H)⁺ 589.9842, found 589.9838.

4-(3-fluorophenyl)-3,6-diiodo-2-phenylquinoline (3h) White solid, yield 32.5 mg (59%), mp 218-219 °C. IR νmax cm⁻¹ (KBr disc): 3065, 1578, 1467, 1435, 1329, 1211, 993, 885, 826, 764. ¹H NMR (CDCl₃, 400 MHz) δ 7.96 (m, 1H), 7.86 (m, 1H), 7.73 (m, 1H), 7.65–7.43 (m, 7H), 7.24 (m, 1H), 7.08–6.97 (m, 2H). ¹³C NMR (CDCl₃, 101 MHz) δ 162.5, 152.2, 152.1, 145.9, 143.2, 139.2, 135.1, 131.2, 130.8 (d, J = 8.4 Hz), 129.2, 128.9, 128.4, 128.1, 125.0, 116.5 (d, J = 22.3 Hz), 116.0 (d, J = 20.9 Hz), 99.3, 93.6. ¹⁹F NMR (CDCl₃, 100 MHz) δ -111.4. HRMS (ESI): Calcd for C₂₁H₁₃F₂I₂N (M+H)⁺ 551.9121, found 551.9121.

4-(4-chlorophenyl)-3,6-diiodo-2-phenylquinoline (3i) White solid, yield 39.7 mg (70%), mp 279-280 °C. IR νmax cm⁻¹ (KBr disc): 3051, 2344, 1587, 1459, 1396, 1329, 1176, 1088, 972, 885. ¹H NMR (CDCl₃, 400 MHz) δ 7.98 (m, 1H), 7.87 (m, 1H), 7.74 (m, 1H), 7.66–7.42 (m, 7H), 7.25–7.20 (m, 2H). ¹³C NMR (CDCl₃, 101 MHz) δ 152.4, 145.9, 143.2, 139.7, 139.1, 135.1, 135.0, 131.2, 130.6, 129.3, 129.2, 128.9, 128.5, 128.1, 99.5, 93.6. HRMS (ESI): Calcd. for C₂₁H₁₃ClI₂N (M+H)⁺ 567.8826, found 567.8821.

2,3,4,6-tetraphenylquinoline (4a): 6-diiodo-5,7-diphenylquinoline 3a (0.267g, 0.5 mmol), sodium carbonate (0.106g, 1 mmol), phenylboroic acid (0.183g, 1.5 mmol), Pd(PPh₃)₄ (0.029g, 0.0025mmol) in the molar ratio of 1:2:3:0.05 were stirred in the 1:1 mixture of THF and H₂O (12 ml) at 70 °C for 12h to give a brown solution. The reaction mixture was allowed to cool to room temperature after which water (10 mL) was added. The mixture was then extracted with dichloromethane (3×10 mL) and the organic extracts dried (Na₂SO₄), filtered and concentrated in vacuo. Purification by flash chromatography furnished the pure cross-coupled product as a white liquid (0.156 g, 72%). IR νmax cm⁻¹ (KBr disc): 3027, 2343, 1545, 1442, 1351, 1075, 1019, 926, 852, 755. ¹H NMR (400 MHz, CDCl₃) δ 8.33 (m, 1H), 8.00 (m, 1H), 7.77 (m, 1H), 7.66 – 7.42 (m, 7H), 7.25–7.20 (m, 2H). ¹³C NMR (CDCl₃, 101 MHz) δ 159.0, 147.9, 146.8, 141.2, 140.7, 140.2, 139.3, 138.4, 136.9, 133.4, 131.4, 130.2, 130.0, 129.2, 128.9, 127.9, 127.7, 127.6, 127.5, 127.4, 126.9, 126.4, 124.4. HRMS (ESI): Calcd. for C₃₃H₂₄N (M+H)⁺ 567.8826, found 567.8821.

2,4-diphenyl-3,6-bis(phenylethynyl)quinoline (4b): 6-diiodo-5,7-diphenylquinoline 3a (0.267g, 0.5 mmol), Cul (0.1 mmol), (PPh₃)₂PdCl₂ (0.05 mmol) and potassium carbonate (1.5 mmol) was charged in a dry and argon-flushed Schlenk-flask. Then phenylacetylene (1.5 mmol) and dry DMF (3.0 mL) were added and the mixture was stirred at 120 °C for 18 h. The reaction mixture was allowed to cool to room temperature after which water (20 mL) was added. The mixture was then extracted with dichloromethane (3×10 mL) and the organic phase was dried with Na₂SO₄, filtered and concentrated in vacuo. Purification by flash chromatography furnished the pure cross-
coupling product as a white solid (0.171 g, 71%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.17 (d, \(J = 9.1\) Hz, 1H), 8.09 (d, \(J = 7.4\) Hz, 2H), 7.82 (d, \(J = 7.2\) Hz, 2H), 7.57 (ddd, \(J = 24.7, 13.3, 7.3\) Hz, 10H), 7.39 – 7.30 (m, 3H), 7.24 – 7.17 (m, 3H), 6.96 (d, \(J = 7.7\) Hz, 2H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 159.9, 151.6, 146.2, 139.9, 136.7, 132.7, 131.7, 131.1, 130.2, 129.6, 129.4, 129.1, 128.7, 128.0, 127.9, 125.6, 122.9, 121.9, 116.2, 98.8, 90.9, 89.3, 87.6. HRMS (ESI): Calcd. for C\(_{37}\)H\(_{23}\)NH\((\text{M+H})^+\) 482.1909, found 482.1906.
4. $^1$H NMR and $^{13}$C NMR Spectra of iodoquinolines 2-4

3-iodo-2,4-diphenylquinoline (2a)
3-iodo-5,7-dimethyl-2,4-diphenylquinoline (2b)
6-(tert-butyl)-3-iodo-2,4-diphenylquinoline (2c)
3-iodo-6-methoxy-2,4-diphenylquinoline (2d)
6-(tert-butyl)-2-(4-fluorophenyl)-3-iodo-4-phenylquinoline (2e)
6-(tert-butyl)-3-iodo-4-phenyl-2-(p-tolyl)quinolone (2f)
6-(tert-butyl)-3-iodo-2-phenyl-4-(p-tolyl)quinolone (2g)
6-chloro-3-iodo-2,4-diphenylquinoline (2h)
3-ido-2,4-diphenyl-6-(trifluoromethyl)quinolone (2i)
3,6-diodo-2,4-diphenylquinoline (3a)
7-fluoro-3,6-diodo-2,4-diphenylquinoline (3b)
3,6-diiodo-5,7-dimethyl-2,4-diphenylquinoline (3c)
2-((1,1'-biphenyl)-4-yl)-3,6-diodo-4-phenylquinoline (3d)
3,6-diiodo-4-phenyl-2-(4-(trifluoromethyl)phenyl)quinolone (3e)
2-(4-chlorophenyl)-3,6-diiodo-4-phenylquinoline (3f)
2-(4-(tert-butyl)phenyl)-3,6-diiodo-4-phenylquinoline (3g)
4-(3-fluorophenyl)-3,6-diiodo-2-phenylquinoline (3h)
4-(4-chlorophenyl)-3,6-diiodo-2-phenylquinoline (3i)
2,3,4,6-tetraphenylquinoline (4a)
2, 4-diphenyl-3, 6-bis(phenylethynyl)quinoline (4b)