Electronic Supplementary Information

A CuBr-Mediated Expedient Synthesis of 4-Bromoisoquinolones from 2-Alkynylbenzaldehydes and Primary Amines under an O₂ atmosphere

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Electronic Supplementary Material (ESI) for Chemical Communications
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1. General

$^1$H NMR (400 MHz) spectra were recorded on a Bruker Avance 400 spectrometers in CDCl$_3$ [using (CH$_3$)$_3$Si (for $^1$H, $\delta$ = 0.00) as internal standard]. $^{13}$C NMR (100 MHz) spectra on a Bruker Avance 400 spectrometers in CDCl$_3$ [using CDCl$_3$ (for $^{13}$C, $\delta$ = 77.00) as internal standard]. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet, brs = broad singlet, brd = broad doublet. IR spectra were recorded on a Shimazu IR Prestige-21 FT-IR Spectrometer. High-resolution mass spectra were obtained with a Finnigan MAT 95 XP mass spectrometer (Thermo Electron Corporation). Melting points were uncorrected and were recorded on a Buchi B-54 melting point apparatus.

Flash column chromatography was performed using Merck silica gel 60 with distilled solvents. Benzene was used without further purification. CuBr·SMe$_2$ (99%) was purchased from Sigma-Aldrich Co., Inc. All amines 2 were purchased from Sigma-Aldrich Co., Inc. except for 2f, 2m$^2$ and 2n$^3$.

2. Synthesis of 2-alkynylbenzaldehyde derivatives

2.1. Preparation of 2-alkynylbenzaldehyde 1a-b & 1k-1s: a typical procedure for synthesis of 2-(2-phenylethynyl)benzaldehyde (1a).

To a solution of 2-bromobenzaldehyde (3.70 g, 20.0 mmol), PdCl$_2$(PPh$_3$)$_2$ (0.28 g, 0.40 mmol), and CuI (38 mg, 0.20 mmol) in 80 mL of NEt$_3$ was added phenylacetylene (2.08 g, 20.4 mmol). The resulting mixture was heated under nitrogen atmosphere at 50 °C. After the reaction was completed, the reaction mixture was quenched with distilled water and extracted with ethyl acetate (50 mL × 3). The combined extracts were washed with brine and dried over MgSO$_4$. Volatile materials were removed in vacuo and the resulting crude material was purified by flash column chromatography (Si gel, hexane : ethyl acetate = 95 : 5) to give 2-(2-phenylethynyl)benzaldehyde (1a) in 94% yield.

2-(2-Phenylethynyl)benzaldehyde (1a)$^4$

Brown oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.36-7.40 (3H, m), 7.45 (1H, tt, $J = 0.8, 7.6$ Hz), 7.55-7.60 (3H, m), 7.64 (1H, dd, $J = 0.8, 7.6$ Hz), 7.95 (1H, dd, $J = 0.8, 7.6$ Hz), 10.65 (d, $J = 0.4$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 84.8, 96.3, 122.3, 126.8, 127.2, 128.5, 128.6, 129.0, 131.6, 133.2, 133.7, 135.8, 191.7.

2-[2-(4-Methoxyphenyl)ethynyl]benzaldehyde (1b)$^5$

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Prepared from 2-bromobenzaldehyde and 1-ethynyl-4-methoxybenzene, and purified by by flash column chromatography (Si gel, hexane:ethyl acetate = 95:5) in quantitative yield; White solid; $^1$H NMR (400 MHz, CDCl$_3$) δ 3.84 (3H, s), 6.91 (2H, td, $J = 2.4, 8.8$ Hz), 7.42 (1H, dt, $J = 0.4, 7.2$ Hz), 7.50 (2H, td, $J = 2.4, 8.8$ Hz), 7.56 (1H, dt, $J = 1.6, 7.6$ Hz), 7.61 (1H, dd, $J = 0.8, 7.2$ Hz), 7.93 (1H, dd, $J = 0.8, 8.0$ Hz), 10.64 (1H, d, $J = 0.8$ Hz).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 55.3, 83.7, 96.6, 114.1, 114.3, 127.1, 127.3, 128.2, 133.0, 133.2, 133.7, 135.6, 160.2, 191.8.

2-(Hept-1-ynyl)benzaldehyde (1k)$^6$

Prepared from 2-bromobenzaldehyde and 1-heptyne and purified by by flash column chromatography (Si gel, hexane:ethyl acetate = 95:5) in 89% yield; Yellow oil; $^1$H NMR (400 MHz, CDCl$_3$) δ 0.93 (3H, t, $J = 7.2$ Hz), 1.32-1.49 (4H, m), 1.65 (2H, tt, $J = 6.8, 7.6$ Hz), 2.48 (2H, t, $J = 7.2$ Hz), 7.35-7.40 (1H, m), 7.48-7.55 (2H, m), 7.89 (1H, d, $J = 8.0$ Hz), 10.54 (1H, d, $J = 0.4$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 13.9, 19.5, 22.1, 28.2, 31.1, 76.3, 98.2, 126.8, 127.8, 127.9, 133.2, 133.6, 135.9, 192.2.

2-(Cyclohexylethynyl)benzaldehyde (1l)$^7$

Prepared from 2-bromobenzaldehyde and cyclohexylacetylene, and purified by by flash column chromatography (Si gel, hexane:ethyl acetate = 95:5) in quantitative yield; Yellow oil; $^1$H NMR (400 MHz, CDCl$_3$) δ 1.32-1.45 (3H, m), 1.46-1.61 (3H, m), 1.71-1.80 (2H, m), 1.87-1.95 (2H, m), 2.68 (1H, m), 7.35-7.40 (1H, m), 7.48-7.54 (2H, m), 7.88 (1H, d, $J = 7.6$ Hz), 10.56 (1H, d, $J = 0.8$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 24.8, 25.8, 29.8, 32.4, 76.2, 102.1, 126.8, 127.8, 128.0, 133.2, 133.6, 135.8, 192.2.

2-(2-Cyclopropylethynyl)benzaldehyde (1m)$^4$

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Prepared from 2-bromobenzaldehyde and cyclopropylacetylene, and purified by by flash column chromatography (Si gel, hexane:ethyl acetate = 95:5) in quantitative yield; Yellow oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 0.83-0.90 (2H, m), 0.90-0.98 (2H, m), 1.48-1.56 (1H, m), 7.36 (1H, t, $J$ = 7.6 Hz), 7.46-7.53 (2H, m), 7.87 (1H, d, $J$ = 8.0 Hz), 10.49 (1H, s); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 0.3, 8.9, 71.4, 101.2, 126.9, 127.7, 127.8, 133.2, 133.6, 136.0, 192.1.

3-Methyl-2-(phenylethynyl)benzaldehyde (1n)

Prepared from 2-bromo-3-methylbenzaldehyde and phenylacetylene, and purified by by flash column chromatography (Si gel, hexane:ethyl acetate = 95:5) in 96% yield; Brown solid; mp. 48–50 °C; IR (neat) 691, 756, 1242, 1489, 1682, 1701 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.59 (3H, s), 7.35 (1H, t, $J$ = 7.6 Hz), 7.38-7.42 (3H, m), 7.50 (1H, d, $J$ = 7.6 Hz), 7.56-7.60 (2H, m), 7.80 (1H, dd, $J$ = 0.4, 8.0 Hz), 10.69 (1H, d, $J$ = 0.8 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 20.5, 83.6, 100.8, 122.6, 124.6, 126.6, 128.1, 128.5, 129.0, 131.5, 134.8, 136.0, 141.5, 192.3; ESIHRMS: Found: m/z 221.0964. Calcd for C$_{16}$H$_{13}$O: (M+H)$^+$ 221.0966.

4,5-Dimethoxy-2-(2-phenylethynyl)benzaldehyde (1o)

Prepared from 6-bromo-1,3-benzodioxole-5-carboxaldehyde and phenylacetylene, and purified by flash column chromatography (Si gel, hexane:ethyl acetate = 95:5) in 93% yield; White solid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.10 (2H, s), 7.03 (1H, s), 7.37 (1H, s), 7.36-7.40 (3H, m), 7.52-7.56 (2H, m), 10.49 (1H, s); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 84.7, 95.1, 102.4, 106.1, 112.0, 122.3, 123.6, 128.5, 129.0, 131.6, 132.1, 148.7, 152.4, 190.0.

5-Methoxy-2-(phenylethynyl)benzaldehyde (1p)

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Prepared from 2-bromo-5-methoxybenzaldehyde and phenylacetylene, and purified by flash column chromatography (Si gel, hexane:ethyl acetate = 95:5) in 95% yield; Brown solid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.88 (3H, s), 7.14 (1H, dd, $J$ = 2.8, 8.8 Hz), 7.35-7.39 (3H, m), 7.43 (1H, d, $J$ = 2.8 Hz), 7.53-7.58 (3H, m), 10.62 (1H, s); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 55.6, 84.8, 94.8, 109.8, 119.6, 121.7, 122.6, 128.5, 128.7, 131.5, 134.5, 137.2, 159.8, 191.6.

5-Fluoro-2-(phenylethynyl)benzaldehyde (1q)$^5$

Prepared from 2-bromo-5-fluorobenzaldehyde and phenylacetylene, and purified by flash column chromatography (Si gel, hexane:ethyl acetate = 95:5) in 91% yield; Pale yellow solid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.30 (1H, dt, $J$ = 2.8, 8.0 Hz), 7.37-7.41 (3H, m), 7.54-7.57 (2H, m), 7.60-7.67 (2H, m), 10.60 (1H, d, $J$ = 3.2 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 83.8, 96.0, 113.7 (d, $J$ = 22.9 Hz), 121.3 (d, $J$ = 22.5 Hz), 122.1, 123.0 (d, $J$ = 3.6 Hz), 128.5, 129.1, 131.6, 135.2 (d, $J$ = 7.6 Hz), 137.7 (d, $J$ = 6.5 Hz), 162.3 (d, $J$ = 251.2 Hz), 190.4.

3-(Phenylethynyl)benzofuran-2-carbaldehyde (1r)

Prepared from 3-bromobenzofuran-2-carbaldehyde and phenylacetylene, and purified by flash column chromatography (Si gel, hexane:ethyl acetate = 95:5) in 96% yield; Brown solid; mp. 99–101 °C; IR (neat) 685, 748, 881, 1294, 1339, 1667 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.40-7.46 (4H, m), 7.58 (1H, dt, $J$ = 1.2, 8.8 Hz), 7.60-7.66 (3H, m), 7.89 (1H, d, $J$ = 8.0 Hz), 10.13 (1H, s); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 77.1, 100.1, 112.8, 115.9, 121.8, 122.5, 124.5, 127.5, 128.6, 129.6, 130.0, 131.9, 152.5, 155.4, 178.0; ESIHRMS: Found: m/z 247.0761. Calcd for C$_{17}$H$_{11}$O$_2$: (M+H)$^+$ 247.0759.

2-(Phenylethynyl)nicotinaldehyde (1s)$^5$

Prepared from 2-bromonicotinaldehyde and phenylacetylene, and purified by flash column chromatography (Si gel, hexane:ethyl acetate = 80:20) in 88% yield; Brown solid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.37-7.44 (4H, m), 7.64 (2H, d, $J$ = 6.8 Hz), 8.20 (1H, d, $J$ = 7.6 Hz), 8.81 (1H, d, $J$ = 4.4 Hz), 10.66 (1H, s); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 84.6, 95.9, 121.1, 123.1, 128.4, 129.7, 131.6, 132.0, 134.6, 145.8, 154.3, 190.6.
2.2. Preparation of 2-arylethynylbenzaldehyde 1c-1j: a typical procedure for the synthesis of 2-[2-(4-methylphenyl)ethynyl]benzaldehyde (1c)

To a solution of 2-ethynylbenzaldehyde\(^1\) (195 mg, 1.5 mmol), PdCl\(_2\)(PPh\(_3\))\(_2\) (21 mg, 0.03 mmol), and CuI (2.9 mg, 0.015 mmol) in 6 mL of NEt\(_3\) was added the 1-iodo-4-methylbenzene (393 mg, 1.8 mmol). The resulting mixture was heated under nitrogen atmosphere at 50 °C. After the reaction was completed, the reaction mixture was quenched with distilled water and extracted with ethyl acetate (50 mL × 3). Volatile materials were removed in vacuo and the crude material was purified by flash column chromatography (Si gel, hexane:ethyl acetate = 95:5) to give 2-[2-(4-methylphenyl)ethynyl]benzaldehyde (1c) in 85% yield.

2-[2-(4-Methylphenyl)ethynyl]benzaldehyde (1c)\(^8\)

Yellow solid; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 2.39 (3H, s), 7.19 (2H, d, \(J = 8.0\) Hz), 7.43 (1H, tt, \(J = 0.8, 7.2\) Hz), 7.46 (2H, d, \(J = 8.0\) Hz), 7.57 (1H, dt, \(J = 1.6, 7.6\) Hz), 7.63 (1H, dd, \(J = 0.8, 7.6\) Hz), 7.94 (1H, dd, \(J = 0.8, 7.6\) Hz), 10.65 (1H, d, \(J = 0.8\) Hz); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 21.6, 84.3, 96.6, 119.2, 127.1, 128.4, 129.3, 131.6 (overlapped), 133.1, 133.7, 135.7, 139.4, 191.8.

2-[2-(4-Fluorophenyl)ethynyl]benzaldehyde (1d)

Prepared from 2-ethynylbenzaldehyde and 4-fluoriodobenzene, and purified by flash column chromatography (Si gel, hexane:ethyl acetate = 95:5) in 82% yield; White solid; mp. 79–81 °C; IR (neat) 758, 829, 1233, 1506, 1591, 1684 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.08 (2H, tt, \(J = 2.0, 8.8\) Hz), 7.46 (1H, t, \(J = 7.6\) Hz), 7.53-7.61 (3H, m), 7.63 (1H, dd, \(J = 0.8, 7.6\) Hz), 7.95 (1H, dd, \(J = 0.8, 7.6\) Hz), 10.62 (1H, d, \(J = 0.4\) Hz); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 21.6, 84.6, 95.2, 155.9 (d, \(J = 21.9\) Hz), 118.4 (d, \(J = 3.5\) Hz), 126.6, 127.4, 128.7, 133.2, 133.6 (d, \(J = 8.5\) Hz), 133.8, 135.8, 162.9 (d, \(J = 249.6\) Hz), 191.5; ESIHRMS: Found: m/z 225.0711. Calcd for C\(_{15}\)H\(_{10}\)FO: (M+H)\(^+\) 225.0716.

Ethyl 4-((2-formylphenyl)ethynyl)benzoate (1e)\(^9\)

Prepared from 2-ethynylbenzaldehyde and ethyl 4-iodobenzoate, and purified by flash column chromatography (Si gel, hexane:ethyl acetate = 90:10) in 86% yield; Pale yellow solid; $^1$H NMR (400 MHz, CDCl$_3$) δ 1.42 (3H, t, J = 7.2 Hz), 4.40 (2H, q, J = 7.2 Hz), 7.50 (1H, t, J = 7.6 Hz), 7.59-7.65 (3H, m), 7.67 (1H, dd, J = 0.8, 7.2 Hz), 7.97 (1H, dd, J = 0.8, 7.6 Hz), 8.06 (2H, td, J = 1.6, 8.4 Hz), 10.64 (1H, s); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 14.3, 61.2, 87.6, 95.3, 126.1, 126.8, 127.5, 129.1, 129.6, 130.6, 131.5, 133.4, 133.8, 135.9, 165.9, 191.3.

2-[2-(4-Trifluoromethylphenyl)ethynyl]benzaldehyde (1f)$^5$

Prepared from 2-ethynylbenzaldehyde and 1-iodo-4-(trifluoromethyl)benzene, and purified by flash column chromatography (Si gel, hexane:ethyl acetate = 95:5) in 74% yield; Pale yellow solid; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.50 (1H, t, J = 7.6 Hz), 7.61 (1H, dt, J = 1.2, 7.6 Hz), 7.63-7.70 (5H, m), 7.97 (1H, dd, J = 1.2, 7.6 Hz), 10.62 (1H, d, J = 0.8 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 87.2, 94.5, 123.8 (q, J = 270.6 Hz), 125.5 (q, J = 3.7 Hz), 125.8, 126.1, 127.6, 129.2, 130.7 (q, J = 32.7 Hz), 131.9, 133.4, 133.8, 136.0, 191.2.

2-[2-(3-Methoxyphenyl)ethynyl]benzaldehyde (1g)$^10$

Prepared from 2-ethynylbenzaldehyde and 1-bromo-3-methoxybenzene, and purified by flash column chromatography (Si gel, hexane:ethyl acetate = 90:10) in 88% yield; Brown oil; $^1$H NMR (400 MHz, CDCl$_3$) δ 3.84 (3H, s), 6.95 (1H, ddd, J = 0.8, 2.4, 8.4 Hz), 7.08 (1H, q, J = 1.2 Hz), 7.16 (1H, d, J = 7.6 Hz), 7.29 (1H, t, J = 7.6 Hz), 7.45 (1H, t, J = 7.6 Hz), 7.58 (1H, dt, J = 1.2, 7.6 Hz), 7.65 (1H, d, J = 7.6 Hz), 7.95 (1H, dd, J = 0.8, 7.6 Hz), 10.65 (1H, s); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 55.3, 84.6, 96.2, 115.7, 116.3, 123.3, 124.2, 126.8, 127.2, 128.6, 129.6, 133.2, 133.8, 135.8, 159.4, 191.7.

2-[2-(2-Methoxyphenyl)ethynyl]benzaldehyde (1h)$^{11}$

Prepared from 2-ethynylbenzaldehyde and 1-bromo-2-methoxybenzene, and purified by by flash column chromatography (Si gel, hexane:ethyl acetate = 90:10) in 87% yield; Pale yellow solid; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.92 (3H, s), 6.92 (1H, d, \(J = 8.0\) Hz), 6.96 (1H, t, \(J = 7.2\) Hz), 7.35 (1H, dt, \(J = 1.6, 8.0\) Hz), 7.42 (1H, t, \(J = 7.6\) Hz), 7.51 (1H, dd, \(J = 1.6, 7.2\) Hz), 7.56 (1H, dt, \(J = 1.2, 7.6\) Hz), 7.65 (1H, dd, \(J = 0.4, 8.0\) Hz), 7.95 (1H, dd, \(J = 0.8, 7.6\) Hz), 10.74 (1H, d, \(J = 0.8\) Hz); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 55.8, 89.0, 93.0, 110.6, 111.6, 120.5, 126.9, 127.4, 128.3, 130.5, 132.9, 133.2, 133.6, 135.8, 160.4, 192.5.

2-[2-(2-Bromophenyl)ethynyl]benzaldehyde (1i)

Prepared from 2-ethynylbenzaldehyde and 2-bromoiodobenzene, and purified by flash column chromatography (Si gel, hexane:ethyl acetate = 95:5) in 94% yield; White solid; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.24 (1H, dt, \(J = 1.6, 7.6\) Hz), 7.34 (1H, dt, \(J = 1.2, 7.6\) Hz), 7.48 (1H, t, \(J = 7.6\) Hz), 7.58-7.63 (2H, m), 7.64 (1H, dd, \(J = 0.8, 8.0\) Hz), 7.70 (1H, dd, \(J = 0.8, 8.0\) Hz), 7.97 (1H, dd, \(J = 1.2, 8.0\) Hz), 10.76 (1H, s); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 89.3, 94.6, 124.6, 125.8, 126.4, 127.1, 127.2, 129.0, 130.1, 132.6, 133.4, 133.5, 133.8, 136.1, 191.9.

2-[2-(2-Naphthyl)ethynyl]benzaldehyde (1j)

Prepared from 2-ethynylbenzaldehyde and 2-iodonaphthalene, and purified by flash column chromatography (Si gel, hexane:ethyl acetate = 95:5) in 67% yield; White solid; mp. 73–75 °C; IR (neat) 743, 758, 1263, 1506, 1591, 1653, 1690 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.48 (1H, t, \(J = 7.6\) Hz), 7.51-7.56 (2H, m), 7.58-7.64 (2H, m), 7.70 (1H, dd, \(J = 0.8, 8.0\) Hz), 7.83-7.88 (3H, m), 7.98 (1H, dd, \(J = 0.8, 8.0\) Hz), 8.11 (1H, s), 10.73 (1H, d, \(J = 0.4\) Hz); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 85.2, 96.8, 119.5, 126.8, 126.9, 127.1, 127.3, 127.8, 127.9, 128.0, 128.2, 128.6, 131.9, 132.9,

3. CuBr-mediated synthesis of 4-bromoisoquinolones:

3.1. A typical procedure for synthesis of 3aa (Table 1, entry 6).

To a stirred solution of 2-alkynylbenzaldehyde (1a) (105.0 mg, 0.509 mmol), CuBr·SMe$_2$ (230.2 mg, 1.12 mmol) and SiO$_2$ (0.3 g) in 5 mL of solvent (benzene : pyridine = 5 : 1) at 80 °C under O$_2$ atmosphere were added benzylamine (2a) [(55 µL × 3), (0.509 × 3) mmol] three times at every 1 h interval, and the reaction mixture was allowed to stir for another 1 h. After cooled to room temperature, the reaction was quenched with pH 9 buffer and extracted with ethyl acetate (20 mL × 3). The combined extracts were washed with brine and dried over MgSO$_4$. Volatile materials were removed in vacuo, and the resulting crude material was purified by flash column chromatography (Si gel, hexane:ethyl acetate = 90:10) to give 2-benzyl-4-bromo-3-phenylisoquinolin-1(2H)-one (3aa) (158.0 mg, 0.405 mmol) in 80% yield.

2-Benzyl-4-bromo-3-phenylisoquinolin-1(2H)-one (3aa)
Sticky yellow oil; IR (neat) 694, 752, 1337, 1582, 1607, 1647 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 5.16 (2H, brs), 6.80-6.86 (2H, m), 7.06 (2H, d, $J$ = 7.2 Hz), 7.13-7.18 (3H, m), 7.35 (2H, dd, $J$ = 7.2, 7.6 Hz), 7.42 (1H, t, $J$ = 7.2 Hz), 7.58 (1H, dt, $J$ = 0.8, 7.6 Hz), 7.76 (1H, dt, $J$ = 1.2, 7.6 Hz), 8.00 (1H, d, $J$ = 8.0 Hz), 8.55 (1H, dd, $J$ = 0.8, 8.0 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 49.9, 102.8, 125.5, 126.5, 126.7, 127.0, 127.7, 128.2, 128.4, 128.5, 129.2, 133.3, 135.5, 135.6, 137.1, 142.2, 162.1; ESIHRMS: Found: m/z 390.0490. Calcd for C$_{22}$H$_{17}$NO$_7$Br: (M+H)$^+$ 390.0494.

Table 2
4-Bromo-2-(4-methoxybenzyl)-3-phenylisoquinolin-1(2H)-one (3ab)
Yellow oil; IR (neat) 748, 1032, 1177, 1246, 1510, 1582, 1607, 1647 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 3.74 (3H, s), 5.10 (2H, brs), 6.69 (2H, td, $J$ = 1.6, 8.8 Hz), 6.76 (2H, d, $J$ = 8.8 Hz), 7.09 (2H, d, $J$ = 7.2 Hz), 7.39 (2H, t, $J$ = 7.6 Hz), 7.45 (1H, t, $J$ = 7.6 Hz), 7.59 (1H, ddd, $J$ = 0.8, 7.2, 8.0 Hz), 7.78 (1H, ddd, $J$ = 1.2, 7.2, 8.0 Hz), 8.01 (1H, d, $J$ = 8.0 Hz), 8.55 (1H, dd, $J$ = 0.8, 8.0 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 49.4, 55.2, 102.8, 113.6, 125.6, 126.5, 127.7, 128.35, 128.41, 128.5, 129.2, 129.3, 129.6, 133.3, 135.6, 135.7, 142.2, 158.7, 162.2; ESIHRMS: Found: m/z 420.0599. Calcd for C$_{23}$H$_{19}$NO$_7$Br: (M+H)$^+$ 420.0599.
4-Bromo-2-(4-methylbenzyl)-3-phenylisoquinolin-1(2H)-one (3ac)

Yellow oil; IR (neat) 692, 907, 1034, 1246, 1510, 1647 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\) \(\delta\) 2.27 (3H, s), 5.11 (2H, brs), 6.73 (2H, d, \(J = 8.0\) Hz), 6.97 (2H, d, \(J = 8.0\) Hz), 7.09 (2H, d, \(J = 6.8\) Hz), 7.38 (2H, dd, \(J = 6.8, 7.6\) Hz), 7.44 (1H, tt, \(J = 1.2, 7.6\) Hz), 7.60 (1H, ddd, \(J = 1.2, 7.2, 7.6\) Hz), 7.78 (1H, ddd, \(J = 1.2, 7.2, 8.4\) Hz), 8.01 (1H, d, \(J = 8.0\) Hz), 8.55 (1H, dd, \(J = 0.8, 8.0\) Hz); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 21.0, 49.8, 102.7, 125.6, 126.5, 126.7, 127.7, 128.4, 128.5, 128.9, 129.2, 129.5, 133.2, 134.1, 135.5, 135.7, 136.6, 142.3, 162.1; ESIHRMS: Found: m/z 404.0650. Calcd for C\(_{23}\)H\(_{19}\)NO\(_7\)Br: (M+H\(^+\)) 404.0650.

4-Bromo-2-(4-fluorobenzyl)-3-phenylisoquinolin-1(2H)-one (3ad)

Yellow solid; mp. 149–151 °C; IR (neat) 750, 1219, 1335, 1508, 1582, 1638 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\) \(\delta\) 5.13 (2H, brs), 6.77–6.88 (4H, m), 7.07 (2H, d, \(J = 7.2\) Hz), 7.39 (2H, dd, \(J = 7.2, 8.0\) Hz), 7.46 (1H, tt, \(J = 1.2, 7.2\) Hz), 7.61 (1H, ddd, \(J = 0.8, 7.2, 8.0\) Hz), 7.79 (1H, ddd, \(J = 1.2, 7.2, 8.4\) Hz), 8.02 (1H, d, \(J = 8.4\) Hz), 8.55 (1H, dd, \(J = 0.8, 8.0\) Hz); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 49.2, 102.9, 115.0 (d, \(J = 21.4\) Hz), 125.5, 126.6, 127.8, 128.4, 128.5, 128.7 (d, \(J = 8.0\) Hz), 129.3, 129.5, 132.9 (d, \(J = 3.1\) Hz), 133.3, 135.51, 135.53, 141.9, 161.9 (d, \(J = 244.2\) Hz), 162.1; ESIHRMS: Found: m/z 408.0403. Calcd for C\(_{22}\)H\(_{16}\)NO\(_7\)Br: (M+H\(^+\)) 408.0399.

4-Bromo-2-phenethyl-3-phenylisoquinolin-1(2H)-one (3ae)

White solid; mp. 121–123 °C; IR (neat) 754, 1223, 1337, 1508, 1584, 1609, 1651 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\) \(\delta\) 2.83-2.90 (2H, m), 3.95–4.03 (2H, m), 6.86 (2H, d, \(J = 6.4\) Hz), 7.13–7.20 (3H, m), 7.27-7.32 (2H, m), 7.53-7.57 (3H, m), 7.60 (1H, dd, \(J = 7.2, 7.6\) Hz), 7.78 (1H, dd, \(J = 7.6, 8.0\) Hz), 8.00 (1H, d, \(J = 8.4\) Hz), 8.54 (1H, d, \(J = 8.0\) Hz); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 34.7, 49.1, 102.4, 125.6, 126.4, 126.5, 127.7, 128.1, 128.4, 128.7, 128.8, 129.3, 129.4, 133.2, 135.4, 136.0, 138.1, 142.0, 161.7; ESIHRMS: Found: m/z 404.0649. Calcd for C\(_{23}\)H\(_{19}\)NO\(_7\)Br: (M+H\(^+\)) 404.0650.

4-Bromo-2-(2,2-diphenylethyl)-3-phenylisoquinolin-1(2H)-one (3af)

S10
Yellow solid; mp. 159–161 °C; IR (neat) 698, 756, 1508, 1645, 1653 cm⁻¹;¹H NMR (400 MHz, CDCl₃) δ 4.52 (2H, brs), 4.60 (1H, t, J = 7.2 Hz), 6.72 (2H, brs), 6.90–6.97 (4H, m), 7.13–7.20 (6H, m), 7.36 (2H, dd, J = 7.2, 8.0 Hz), 7.44 (1H, tt, J = 1.2, 7.6 Hz), 7.57 (1H, ddd, J = 1.2, 6.8, 8.0 Hz), 7.75 (1H, ddd, J = 1.2, 7.2, 8.4 Hz), 7.95 (1H, d, J = 8.0 Hz), 8.50 (1H, dd, J = 0.8, 8.0 Hz);¹³C NMR (100 MHz, CDCl₃) δ 48.0, 52.0, 102.6, 125.6, 126.5, 126.6, 127.6, 128.2, 128.35, 128.43, 128.5, 129.1, 129.8, 133.1, 135.4, 135.6, 141.2, 142.3, 162.2; ESIHRMS: Found: m/z 480.0963. Calcd for C₂₉H₂₃NO₇Br: (M+H)⁺ 480.0963.

4-Bromo-2-pentyl-3-phenylisoquinolin-1(2H)-one (3ag)

Yellow oil; IR (neat) 762, 1092, 1339, 1474, 1582, 1647, 2930, 2955 cm⁻¹;¹H NMR (400 MHz, CDCl₃) δ 0.77 (3H, t, J = 6.8 Hz), 1.02–1.17 (4H, m), 1.56 (2H, tt, J = 7.2, 8.0 Hz), 3.79 (2H, t, J = 8.0 Hz), 7.33–7.37 (2H, m), 7.50–7.56 (3H, m), 7.57 (1H, ddd, J = 0.8, 7.2, 8.0 Hz), 7.75 (1H, ddd, J = 1.6, 7.2, 8.4 Hz), 7.98 (1H, d, J = 8.4 Hz), 8.50 (1H, dd, J = 0.8, 8.0 Hz);¹³C NMR (100 MHz, CDCl₃) δ 13.8, 21.9, 28.3, 28.8, 47.4, 102.3, 125.7, 126.4, 127.5, 128.2, 128.7, 129.25, 129.28, 133.0, 135.4, 136.2, 142.2, 161.6; ESIHRMS: Found: m/z 370.0814. Calcd for C₂₀H₂₁NO₇Br: (M+H)⁺ 370.0807.

4-Bromo-2-(2-(cyclohex-1-en-1-yl)ethyl)-3-phenylisoquinolin-1(2H)-one (3ah)

White solid; mp. 107–109 °C; IR (neat) 752, 1578, 1609, 1636, 1647, 2859, 2924 cm⁻¹;¹H NMR (400 MHz, CDCl₃) δ 1.40–1.52 (4H, m), 1.66 (2H, brs), 1.85 (2H, brs), 2.15 (2H, t, J = 8.0 Hz), 3.86 (2H, t, J = 8.0 Hz), 5.21 (1H, brs), 7.34–7.38 (2H, m), 7.51–7.58 (4H, m), 7.74 (1H, ddd, J = 1.2, 7.2, 8.4 Hz), 7.97 (1H, d, J = 8.0 Hz), 8.49 (1H, dd, J = 0.8, 8.0 Hz);¹³C NMR (100 MHz, CDCl₃) δ 22.1, 22.7, 25.1, 27.8, 36.9, 46.5, 102.3, 123.4, 125.6, 126.4, 127.5, 128.1, 128.7, 129.27, 129.34, 133.0, 134.1, 135.1, 135.3, 136.0, 142.0, 161.6; ESIHRMS: Found: m/z 408.0964. Calcd for C₂₃H₂₃NO₇Br: (M+H)⁺ 408.0963.

4-Bromo-2-(cyclohexylmethyl)-3-phenylisoquinolin-1(2H)-one (3ai)
Mixture Rotational isomer (1.00 : 0.22) at room temperature; White solid; mp. 140–145 °C; IR (neat) 1335, 1506, 1578, 1645, 1717, 2849, 2926 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, the major isomer’s spectra was shown) δ 0.73-0.84 (2H, m), 1.01-1.12 (3H, m), 1.37-1.43 (2H, m), 1.52-1.70 (4H, m), 3.78 (2H, brs), 7.30-7.36 (2H, m), 7.48-7.55 (3H, m), 7.57 (1H, ddd, J = 1.2, 6.8, 8.0 Hz), 7.75 (1H, ddd, J = 1.6, 7.2, 8.4 Hz), 7.99 (1H, d, J = 8.0 Hz), 8.50 (1H, dd, J = 0.8, 8.0 Hz); ¹³C NMR (100 MHz, CDCl₃, the major isomer’s spectra was shown) δ 25.8, 26.1, 30.7, 37.5, 52.6, 102.6, 125.6, 126.4, 127.5, 128.3, 128.5, 129.1, 129.9, 133.0, 135.4, 136.0, 142.4, 161.2; ESIHRMS: Found: m/z 396.0956. Calcd for C₂₂H₂₃NO⁷⁺Br (M+H)⁺ 396.0963.

4-Bromo-2-(cyclopropylmethyl)-3-phenylisoquinolin-1(2H)-one (3aj)

Orange solid; mp. 102–104 °C; IR (neat) 694, 764, 1474, 1607, 1645, 2851, 2924 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.16-0.22 (2H, m), 0.33-0.38 (2H, m), 0.92-1.03 (1H, m), 3.82 (2H, d, J = 6.8 Hz), 7.33-7.40 (2H, m), 7.48-7.56 (3H, m), 7.55 (1H, t, J = 7.2 Hz), 7.74 (1H, ddd, J = 1.2, 7.2, 8.4 Hz), 7.97 (1H, d, J = 8.0 Hz), 8.50 (1H, dd, J = 0.8, 8.0 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 4.2, 10.7, 50.8, 102.4, 125.7, 126.4, 127.5, 128.2, 128.6, 129.2, 129.7, 133.0, 135.4, 136.2, 142.0, 162.1; ESIHRMS: Found: m/z 354.0498. Calcd for C₁₉H₁₇NO⁷⁺Br: (M+H)⁺ 354.0494.

4-Bromo-2-(2-methoxyethyl)-3-phenylisoquinolin-1(2H)-one (3ak)

Yellow oil; IR (neat) 692, 760, 1103, 1115, 1580, 1647, 3003 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 3.18 (3H, s), 3.54 (2H, t, J = 6.0 Hz), 4.06 (2H, t, J = 6.0 Hz), 7.32-7.37 (2H, m), 7.50-7.55 (3H, m), 7.57 (1H, ddd, J = 1.2, 7.2, 8.0 Hz), 7.77 (1H, ddd, J = 1.2, 7.2, 8.0 Hz), 7.99 (1H, d, J = 8.0 Hz), 8.49 (1H, dd, J = 0.8, 8.0 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 46.4, 58.7, 69.4, 102.6, 125.5, 126.5, 127.6, 128.1, 128.7, 129.3, 129.7, 133.2, 135.6, 136.1, 142.4, 161.9; ESIHRMS: Found: m/z 358.0445. Calcd for C₁₈H₁₇NO₂⁷⁺Br (M+H)⁺ 358.0443.

4-Bromo-2-methyl-3-phenylisoquinolin-1(2H)-one (3al)
White solid; mp. 132–134 °C; IR (neat) 745, 756, 1117, 1474, 1636, 1645 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 3.32 (3H, s), 7.31-7.35 (2H, m), 7.50-7.59 (4H, m), 7.75 (1H, ddd, J = 1.2, 7.2, 8.4 Hz), 7.98 (1H, d, J = 8.4 Hz), 8.50 (1H, dd, J = 0.8, 8.0 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 35.1, 101.9, 125.3, 126.4, 127.6, 128.1, 128.98, 129.03, 129.3, 133.0, 135.4, 136.4, 142.2, 162.2; ESIHRMS: Found: m/z 314.0178. Calcd for C₁₆H₁₃NO₇Br: (M+H)+ 314.0181.

**2-Methyl-3-phenylisoquinolin-1(2H)-one (4al)**

White solid; ¹H NMR (400 MHz, CDCl₃) δ 3.43 (3H, s), 6.46 (1H, s), 7.39-7.43 (2H, m), 7.45-7.51 (6H, m), 7.63 (1H, dd, J = 7.2, 7.6 Hz), 8.46 (1H, d, J = 8.0 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 34.1, 107.5, 124.9, 125.8, 126.6, 127.8, 128.6, 128.7, 128.9, 132.2, 136.2, 136.3, 143.9, 163.3.

---Table 3---

**2-Benzyl-4-bromo-3-(4-methoxyphenyl)isoquinolin-1(2H)-one (3ba)**

Sticky yellow oil; IR (neat) 750, 1032, 1173, 1248, 1508, 1609, 1645 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 3.85 (3H, s), 5.18 (2H, brs), 6.84-6.90 (4H, m), 6.99 (2H, d, J = 8.4 Hz), 7.15-7.20 (3H, m), 7.59 (1H, ddd, J = 1.2, 7.2, 8.0 Hz), 7.78 (1H, ddd, J = 1.2, 7.2, 8.0 Hz), 8.01 (1H, d, J = 8.0 Hz), 8.55 (1H, dd, J = 0.8, 8.0 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 50.0, 55.3, 103.5, 113.8, 125.5, 126.6, 126.7, 127.0, 127.7, 128.1, 128.2, 128.6, 130.8, 133.3, 135.6, 137.3, 142.2, 160.0, 162.3; ESIHRMS: Found: m/z 420.0605. Calcd for C₂₃H₁₉NO₇Br: (M+H)+ 420.0599.

**2-Benzyl-4-bromo-3-(4-methylphenyl)isoquinolin-1(2H)-one (3ca)**

Sticky yellow oil; IR (neat) 1456, 1474, 1508, 1607, 1647, 3010 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.40 (3H, s), 5.16 (2H, brs), 6.84-6.89 (2H, m), 6.97 (2H, $J = 8.0$ Hz), 7.14-7.19 (3H, m), 7.56 (1H, ddd, $J = 1.2, 7.2, 8.0$ Hz), 7.77 (1H, ddd, $J = 1.2, 7.2, 8.4$ Hz), 8.01 (1H, d, $J = 8.0$ Hz), 8.54 (1H, dd, $J = 0.8, 8.0$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 21.4, 50.0, 102.9, 125.5, 126.5, 126.7, 127.0, 127.6, 128.2, 128.5, 129.1, 129.3, 132.8, 133.2, 135.6, 137.2, 139.2, 142.4, 162.2; ESIHRMS: Found: m/z 404.0656. Calcd for C$_{23}$H$_{19}$NO$_7$Br: (M+H)$^+$ 404.0650.

2-Benzyl-4-bromo-3-(4-fluorophenyl)isoquinolin-1(2H)-one (3da)

White solid; mp. 131–133 °C; IR (neat) 1223, 1238, 1373, 1506, 1636, 1717, 1734 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.17 (2H, brs), 6.80-6.85 (2H, m), 7.00-7.08 (4H, m), 7.16-7.20 (3H, m), 7.61 (1H, ddd, $J = 1.2, 7.2, 8.0$ Hz), 7.80 (1H, ddd, $J = 1.2, 7.2, 8.4$ Hz), 8.01 (1H, d, $J = 8.0$ Hz), 8.56 (1H, d, $J = 0.8, 8.0$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 49.9, 103.3, 115.6 (d, $J = 21.7$ Hz), 125.6, 126.59, 126.62, 127.2, 127.9, 128.3, 128.6, 131.5 (d, $J = 8.4$ Hz), 131.6 (d, $J = 3.8$ Hz), 133.4, 134.7, 141.2, 162.1, 162.9 (d, $J = 248.6$ Hz); ESIHRMS: Found: m/z 408.0392. Calcd for C$_{22}$H$_{16}$NO$_7$Br: (M+H)$^+$ 408.0399.

Ethyl 4-(2-benzyl-4-bromo-1-oxo-1,2-dihydroisoquinolin-3-yl)benzoate (3ea)

Yellow oil; IR (neat) 760, 1022, 1099, 1271, 1506, 1653, 1717 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.42 (3H, t, $J = 7.2$ Hz), 4.42 (2H, q, $J = 7.2$ Hz), 5.15 (2H, brs), 6.78-6.83 (2H, m), 7.12-7.20 (5H, m), 7.62 (1H, ddd, $J = 0.8, 7.2, 8.0$ Hz), 7.80 (1H, ddd, $J = 1.2, 7.2, 8.4$ Hz), 8.01 (1H, d, $J = 8.0$ Hz), 8.04 (2H, d, $J = 8.4$ Hz), 8.57 (1H, ddd, $J = 0.8, 8.0$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 49.9, 61.3, 102.6, 125.6, 126.59, 126.62, 127.2, 127.9, 128.3, 128.6, 131.5 (d, $J = 8.4$ Hz), 131.6 (d, $J = 3.8$ Hz), 133.4, 135.4, 141.2, 162.1, 165.8; ESIHRMS: Found: m/z 462.0703. Calcd for C$_{25}$H$_{21}$NO$_3$Br: (M+H)$^+$ 462.0705.

2-Benzyl-4-bromo-3-(4-trifluoromethylphenyl)isoquinolin-1(2H)-one (3fa)

Yellow oil; IR (neat) 760, 1067, 1128, 1167, 1321, 1647 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.14 (2H, brs), 6.75-6.81 (2H, m), 7.13-7.20 (5H, m), 7.59-7.66 (3H, m), 7.80 (1H, ddd, $J = 1.2, 7.2, 8.4$ Hz), 8.01 (1H, d, $J = 8.0$ Hz), 8.57 (1H, ddd, $J = 0.8, 8.0$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 49.9,
102.8, 123.7 (q, J = 270.6 Hz), 125.4 (q, J = 3.7 Hz), 125.7, 126.56, 126.63, 127.3, 128.2, 128.4, 128.7, 130.1, 131.3 (q, J = 3.7 Hz), 133.5, 135.3, 136.8, 139.0, 140.6, 162.1; ESIHRMS: Found: m/z 458.0359. Calcd for C_{23}H_{16}NOF_79Br: (M+H)^+ 458.0367.

2-Benzyl-4-bromo-3-(3-methoxyphenyl)isoquinolin-1(2H)-one (3ga)

Sticky oil; IR (neat) 1040, 1215, 1261, 1456, 1489, 1578, 1651 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.56 (3H, s), 4.94 (1H, brd, \(J = 14.8\) Hz), 5.38 (1H, brd, \(J = 15.2\) Hz), 6.46 (1H, s), 6.73 (1H, d, \(J = 7.6\) Hz), 6.83-6.90 (2H, m), 6.96 (1H, ddd, \(J = 0.8, 2.4, 8.4\) Hz), 7.16-7.21 (3H, m), 7.31 (1H, t, \(J = 8.0\) Hz), 7.60 (1H, ddd, \(J = 1.2, 7.6, 8.4\) Hz), 7.79 (1H, ddd, \(J = 1.2, 7.2, 8.4\) Hz), 8.02 (1H, d, \(J = 8.0\) Hz), 8.56 (1H, dd, \(J = 1.2, 8.0\) Hz); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 50.0, 55.0, 102.6, 114.3, 115.7, 121.5, 125.5, 126.5, 126.7, 127.0, 127.7, 128.3, 128.5, 133.3, 135.6, 136.6, 137.4, 142.0, 159.2, 162.2; ESIHRMS: Found: m/z 420.0602. Calcd for C_{23}H_{19}NO_2Br: (M+H)^+ 420.0599.

2-Benzyl-4-bromo-3-(2-methoxyphenyl)isoquinolin-1(2H)-one (3ha)

Yellow solid; mp. 108–110 °C; IR (neat) 758, 1256, 1495, 1578, 1599, 1636, 2965 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.55 (3H, s), 4.93 (1H, brd, \(J = 15.2\) Hz), 5.33 (1H, brd, \(J = 15.2\) Hz), 6.82-6.88 (2H, m), 6.88-6.95 (3H, m), 7.11-7.16 (3H, m), 7.40-7.46 (1H, m), 7.58 (1H, ddd, \(J = 1.2, 7.6, 8.4\) Hz), 7.77 (1H, ddd, \(J = 1.2, 7.2, 8.4\) Hz), 8.00 (1H, d, \(J = 8.0\) Hz), 8.56 (1H, dd, \(J = 1.2, 8.0\) Hz); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 49.8, 55.2, 103.3, 110.9, 120.4, 124.5, 125.6, 126.4, 126.9, 127.1, 127.5, 128.0, 128.5, 131.1, 133.1, 133.1, 135.7, 137.2, 139.7, 156.5, 162.4; ESIHRMS: Found: m/z 420.0598. Calcd for C_{23}H_{19}NO_2Br: (M+H)^+ 420.0599.

2-Benzyl-4-bromo-3-(2-bromophenyl)isoquinolin-1(2H)-one (3ia)

Yellow oil; IR (neat) 692, 752, 1026, 1327, 1472, 1607, 1647 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 4.49 (1H, d, \(J = 15.2\) Hz), 5.80 (1H, d, \(J = 15.6\) Hz), 6.80-6.87 (3H, m), 7.11-7.20 (4H, m), 7.30 (1H, dt, \(J = 1.6, 8.0\) Hz), 7.62 (1H, ddd, \(J = 1.2, 7.6, 8.4\) Hz), 7.69 (1H, dd, \(J = 1.2, 8.0\) Hz), 7.79 (1H, ddd, \(J = 1.2, 7.2, 8.4\) Hz), 8.01 (1H, d, \(J = 8.0\) Hz), 8.59 (1H, dd, \(J = 1.2, 8.0\) Hz); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 49.7, 103.4, 123.9, 125.8, 126.6, 127.0, 127.18, 127.22, 128.1, 128.2, 128.6,
130.9, 132.1, 132.7, 133.3, 135.4, 136.4, 136.9, 140.8, 162.2; ESIHRMS: Found: m/z 469.9583. Calcd for C_{22}H_{16}NO^{79}Br^{81}Br: (M+H)^{+} 469.9578.

2-Benzyl-4-bromo-3-(2-naphthyl)isoquinolin-1(2H)-one (3ja)

Yellow oil; IR (neat) 748, 1337, 1506, 1582, 1647 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 5.02 (1H, brd, \(J = 15.2\) Hz), 5.33 (1H, brd, \(J = 15.2\) Hz), 6.77 (2H, d, \(J = 6.8\) Hz), 7.07–7.20 (4H, m), 7.48–7.59 (3H, m), 7.62 (1H, ddd, \(J = 0.8, 7.2, 8.0\) Hz), 7.85 (1H, d, \(J = 8.4\) Hz), 7.89 (1H, d, \(J = 8.0\) Hz), 8.03 (1H, d, \(J = 8.4\) Hz), 8.59 (1H, dd, \(J = 0.8, 8.0\) Hz); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 50.1, 103.1, 125.6, 126.4, 126.57, 126.62, 126.8, 127.07, 127.13, 127.76, 127.81, 128.22, 128.24, 128.4, 128.6, 129.4, 132.6, 132.8, 133.1, 133.3, 135.6, 137.2, 142.1, 162.2; ESIHRMS: Found: m/z 440.0654. Calcd for C_{26}H_{19}NO^{79}Br: (M+H)^{+} 440.0650.

2-Benzyl-4-bromo-3-pentylisoquinolin-1(2H)-one (3ka)

Colorless crystal; mp. 109–111 \(^\circ\)C; IR (neat) 764, 1456, 1506, 1558, 1645, 1717 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 0.91 (3H, t, \(J = 6.8\) Hz), 1.30–1.42 (4H, m), 1.56–1.64 (2H, m), 2.90 (2H, t, \(J = 8.0\) Hz), 5.50 (2H, brs), 7.14 (2H, d, \(J = 7.2\) Hz), 7.25 (1H, t, \(J = 7.2\) Hz), 7.31 (2H, dd, \(J = 6.8, 7.6\) Hz), 7.51 (1H, ddd, \(J = 1.2, 7.2, 8.0\) Hz), 7.74 (1H, ddd, \(J = 1.2, 7.2, 8.4\) Hz), 7.98 (1H, d, \(J = 8.4\) Hz), 8.46 (1H, dd, \(J = 1.2, 8.0\) Hz); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 13.9, 22.2, 27.9, 31.7, 33.6, 48.1, 102.3, 124.6, 125.9, 126.1, 127.0, 127.3, 128.5, 128.8, 133.2, 135.8, 137.0, 142.4, 162.5; ESIHRMS: Found: m/z 384.0969. Calcd for C_{21}H_{23}NO^{79}Br: (M+H)^{+} 384.0963.

2-Benzyl-4-bromo-3-cyclohexylisoquinolin-1(2H)-one (3la)

White solid; mp. 126–128 \(^\circ\)C; IR (neat) 1339, 1456, 1506, 1576, 1607, 1636, 1653 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 0.92–1.50 (4H, m), 1.55–1.90 (4H, m), 2.53 (2H, ddd, \(J = 3.6, 12.4, 12.8\) Hz), 3.06 (1H, tt, \(J = 3.2, 12.0\) Hz), 5.57 (2H, brs), 7.19 (2H, d, \(J = 7.2\) Hz), 7.23–7.28 (1H, m), 7.32 (2H, dd, \(J = 7.2, 7.6\) Hz), 7.51 (1H, ddd, \(J = 1.2, 7.2, 8.0\) Hz), 7.72 (1H, ddd, \(J = 1.2, 7.2, 8.4\) Hz), 8.06
(1H, d, J = 8.0 Hz), 8.47 (1H, dd, J = 0.8, 8.0 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 25.4, 26.8, 27.9, 43.1, 48.6, 101.9, 124.6, 125.8, 126.2, 127.2, 127.3, 128.4, 128.7, 133.0, 136.2, 137.6, 145.2, 163.0; ESIHRMS: Found: m/z 396.0961. Calcd for C$_{22}$H$_{23}$NO$_7$Br: (M+H)$^+$ 396.0963.

2-Benzyl-4-bromo-3-cyclopropylisoquinolin-1(2H)-one (3ma)

![Structure Image]

White solid; mp. 120–122 °C; IR (neat) 696, 764, 1456, 1506, 1576, 1645, 1717 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 0.95−1.00 (2H, m), 1.23−1.29 (2H, m), 1.65 (1H, tt, J = 6.0, 8.4 Hz), 5.81 (2H, brs), 7.14 (2H, d, J = 7.2 Hz), 7.20−7.30 (3H, m), 7.52 (1H, ddd, J = 0.8, 7.2, 8.0 Hz), 7.73 (1H, ddd, J = 1.2, 7.2, 8.4 Hz), 8.02 (1H, d, J = 8.4 Hz), 8.46 (1H, dd, J = 0.8, 8.0 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 12.1, 15.3, 47.5, 105.5, 125.1, 126.0, 126.3, 127.0, 127.3, 128.3, 128.6, 133.0, 135.8, 137.6, 141.3, 162.5; ESIHRMS: Found: m/z 354.0497. Calcd for C$_{19}$H$_{17}$NO$_7$Br: (M+H)$^+$ 354.0494.

2-Benzyl-4-bromo-5-methyl-3-phenylisoquinolin-1(2H)-one (3na)

![Structure Image]

Yellow solid; mp. 141−143 °C; IR (neat) 694, 760, 1327, 1456, 1506, 1578, 1639 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 2.96 (3H, s), 5.11 (2H, brs), 6.78−6.84 (2H, m), 7.04 (2H, d, J = 7.2 Hz), 7.13−7.18 (3H, m), 7.32−7.42 (3H, m), 7.45 (1H, dd, J = 7.6, 8.0 Hz), 7.57 (1H, d, J = 7.2 Hz), 8.54 (1H, d, J = 8.0 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 12.1, 15.3, 47.5, 105.5, 125.1, 126.0, 126.3, 127.0, 127.3, 128.3, 128.6, 133.0, 135.8, 137.6, 141.3, 162.5; ESIHRMS: Found: m/z 404.0647. Calcd for C$_{23}$H$_{19}$NO$_7$Br: (M+H)$^+$ 404.0650.

6-Benzyl-8-bromo-7-phenyl-[1,3]dioxolo[4,5-g]isoquinolin-5(6H)-one (3oa)

![Structure Image]

Sticky yellow oil; IR (neat) 696, 1036, 1231, 1406, 1472, 1568, 1645 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 5.13 (2H, brs), 6.14 (2H, s), 6.79−6.85 (2H, m), 7.05 (2H, d, J = 6.8 Hz), 7.14−7.19 (3H, m), 7.35 (2H, dd, J = 6.8, 8.0 Hz), 7.42 (1H, s), 7.42 (1H, tt, J = 1.2, 8.0 Hz), 7.90 (1H, s); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 50.0, 102.1, 102.4, 105.1, 106.3, 121.2, 126.7, 127.0, 128.2, 128.4, 129.1, 129.5, 133.2, 135.8, 137.2, 141.0, 148.4, 152.8, 161.3; ESIHRMS: Found: m/z 434.0389. Calcd for C$_{23}$H$_{17}$NO$_3$ Br: (M+H)$^+$ 434.0392.
2-Benzyl-4-bromo-7-methoxy-3-phenylisoquinolin-1(2H)-one (3p)

Yellow solid; mp. 161–163 °C; IR (neat) 698, 939, 1038, 1406, 1474, 1645 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 3.97 (3H, s), 5.16 (2H, brs), 6.80–6.87 (2H, m), 7.07 (2H, d, J = 7.2 Hz), 7.14–7.19 (3H, m), 7.32–7.39 (3H, m), 7.42 (1H, t, J = 7.2 Hz), 7.94 (1H, d, J = 9.2 Hz), 7.96 (1H, d, J = 2.4 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 50.1, 55.8, 102.7, 108.4, 123.6, 126.7, 127.0, 128.2, 128.37, 128.40 (overlapped), 129.1, 129.6, 129.8, 135.7, 137.2, 139.7, 159.4, 161.9; ESIHRMS: Found: m/z 420.0599. Calcd for C₂₃H₁₉NO₂Br: (M+H)⁺ 420.0599.

2-Benzyl-4-bromo-7-fluoro-3-phenylisoquinolin-1(2H)-one (3q)

Yellow solid; mp. 104–106 °C; IR (neat) 696, 752, 941, 1341, 1489, 1585, 1647 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.15 (2H, brs), 6.79–6.85 (2H, m), 7.06 (2H, d, J = 6.8 Hz), 7.14–7.20 (3H, m), 7.37 (2H, dd, J = 7.2, 8.0 Hz), 7.44 (1H, tt, J = 1.2, 7.2 Hz), 7.51 (1H, ddd, J = 2.8, 8.0, 8.8 Hz), 8.04 (1H, dd, J = 4.8, 8.8 Hz), 8.21 (1H, d, J = 1.2, 9.2 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 50.2, 95.5, 112.8, 123.4, 123.5, 123.6, 127.0, 127.3, 128.5, 129.4 (d, J = 8.2 Hz), 129.5, 132.2 (d, J = 2.2 Hz), 135.4, 136.9, 141.5 (d, J = 2.8 Hz), 161.4 (d, J = 4.2 Hz), 162.0 (d, J = 247.9 Hz); ESIHRMS: Found: m/z 408.0405. Calcd for C₂₂H₁₆NOF₂Br⁻: (M+H)⁺ 408.0399.

2-Benzyl-4-bromo-3-phenylbenzofuro[2,3-c]pyridin-1(2H)-one (3r)

White solid; mp. 182–184 °C; IR (neat) 743, 1038, 1456, 1474, 1647, 1668 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.28 (2H, brs), 6.79–6.85 (2H, m), 7.05 (2H, d, J = 7.2 Hz), 7.13–7.19 (3H, m), 7.39 (2H, t, J = 7.6 Hz), 7.42–7.49 (2H, m), 7.62 (1H, ddd, J = 1.2, 7.2, 8.4 Hz), 7.75 (1H, d, J = 8.8 Hz), 8.45 (1H, dd, J = 0.4, 8.0 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 50.0, 95.5, 112.8, 123.4, 123.5, 123.6, 127.0, 127.3, 128.29, 128.32, 128.6, 129.3, 129.5, 129.8, 134.4, 136.7, 142.7, 143.3, 154.1, 156.9; ESIHRMS: Found: m/z 430.0437. Calcd for C₂₄H₁₇NO₂Br⁻: (M+H)⁺ 430.0443.

6-Benzyl-8-bromo-7-phenyl-1,6-naphthyridin-5(6H)-one (3s)
Yellow solid; mp. 138–140 °C; IR (neat) 698, 1435, 1456, 1541, 1558, 1638 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.17 (2H, brs), 6.80–6.87 (2H, m), 7.10 (2H, d, J = 7.2 Hz), 7.15–7.21 (3H, m), 7.39 (2H, dd, J = 6.8, 7.6 Hz), 7.46 (1H, tt, J = 1.2, 7.2 Hz), 7.54 (1H, dd, J = 4.8, 8.0 Hz), 8.81 (1H, dd, J = 1.6, 8.0 Hz), 9.09 (1H, dd, J = 1.6, 4.8 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 50.0, 104.7, 121.4, 122.6, 126.7, 127.2, 128.3, 128.5, 129.0, 129.4, 135.0, 136.6, 137.1, 146.2, 150.2, 155.1, 162.1; ESIHRMS: Found: m/z 391.0443. Calcd for C₂₁H₁₆N₂O₇Br: (M+H)⁺ 391.0446.

6-Benzyl-7-phenyl-1,6-naphthyridin-5(6H)-one (4a)

Yellow solid; mp. 113–115 °C; IR (neat) 704, 839, 1358, 1437, 1506, 1558, 1653 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.24 (2H, brs), 6.72 (1H, s), 6.87–6.93 (2H, m), 7.15–7.20 (3H, m), 7.23 (2H, d, J = 7.2 Hz), 7.36 (2H, dd, J = 7.2, 8.0 Hz), 7.41–7.46 (2H, m), 8.74 (1H, dd, J = 1.2, 8.0 Hz), 8.93 (1H, dd, J = 1.6, 4.8 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 48.6, 109.8, 120.9, 121.7, 126.8, 127.1, 128.3 (overlapped), 128.8, 129.2, 135.2, 136.6, 137.1, 147.8, 152.9, 154.8, 163.1; ESIHRMS: Found: m/z 313.1335. Calcd for C₂₁H₁₇N₂O: (M+H)⁺ 313.1341.

3.2. The reactions with CuCl and CuI

It was found that CuCl and CuI also showed the reactivity in the present reaction conditions, giving 4-chloro- and 4-iodoisoquinolones 3aa’ and 3aa”, respectively, while lower yields were observed.

![Scheme S1](image)

**Pyridine was used as a sole solvent.

2-Benzyl-4-chloro-3-phenylisoquinolin-1(2H)-one (3aa’)

S19
Synthesized from 2.2 equiv of CuCl; Yellow oil; IR (neat) 696, 752, 1477, 1495, 1585, 1611, 1647 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 5.15 (2H, brs), 6.80-6.86 (2H, m), 7.09 (2H, d, \(J = 6.8\) Hz), 7.14-7.18 (3H, m), 7.36 (2H, dd, \(J = 6.8, 7.6\) Hz), 7.43 (1H, t, \(J = 7.6\) Hz), 7.61 (1H, dt, \(J = 0.8, 7.6\) Hz), 7.79 (1H, dt, \(J = 1.2, 7.6\) Hz), 8.00 (1H, d, \(J = 8.0\) Hz), 8.57 (1H, dd, \(J = 0.8, 8.0\) Hz); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 49.5, 111.8, 123.8, 125.5, 126.8, 127.1, 127.8, 128.3, 128.5, 128.6, 129.2, 129.6, 133.1, 133.6, 134.7, 137.2, 140.5, 162.0; ESIHRMS: Found: m/z 346.1003. Calcd for C\(_{22}\)H\(_{17}\)NOCl: (M+H)\(^+\) 346.0999.

2-Benzyl-4-iodo-3-phenylisoquinolin-1(2H)-one (3aa’’)

Synthesized from 2.2 equiv of CuI in pyridine (0.1 M); White solid; IR (neat) 696, 762, 1030, 1339, 1587, 1603, 1647 cm\(^{-1}\); mp. 86–88 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 5.20 (2H, brs), 6.80-6.86 (2H, m), 7.02 (2H, d, \(J = 7.6\) Hz), 7.14-7.18 (3H, m), 7.35 (2H, dd, \(J = 7.2, 7.6\) Hz), 7.42 (1H, t, \(J = 7.2\) Hz), 7.57 (1H, t, \(J = 7.6\) Hz), 7.75 (1H, t, \(J = 7.6\) Hz), 7.96 (1H, d, \(J = 8.0\) Hz), 8.51 (1H, d, \(J = 8.0\) Hz); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 50.8, 79.9, 125.2, 126.7, 127.0, 127.8, 128.2, 128.4, 128.6, 129.3, 129.5, 131.7, 133.6, 137.2, 137.4, 139.3, 145.7, 162.5; ESIHRMS: Found: m/z 438.0354. Calcd for C\(_{22}\)H\(_{17}\)NOI: (M+H)\(^+\) 438.0355.
3.3. The reactions with β-alanine ethyl ester (2m) and propargylamine 2n

The reaction of β-alanine ethyl ester (2m) (as a hydrochloride salt) with 1a under the standard reaction conditions provided 4-bromoisoquinoline 5 and protonated isoquinoline 6 in 42% and 28% yields, respectively, with certain C-N bond cleavage, and no desired 4-bromoisoquinolone was formed at all (Scheme S2). Similarly, 3-phenylprop-2-yn-1-amine (2n) also delivered 4-bromoisoquinoline 5 without forming 4-bromoisoquinolone 3. It is noted that aromatic amines (anilines) did not work at all to provide any cyclized product under the present reaction conditions.

**Scheme S2.**

![Scheme S2](image)

4-Bromo-3-phenylisoquinoline (5)\(^{14}\)

![4-Bromo-3-phenylisoquinoline (5)](image)

White solid; \(^1H\) NMR (400 MHz, CDCl\(_3\)) \(\delta 7.41-7.53\ (3H, m), 7.66\ (1H, ddd, \(J = 0.8, 7.2, 8.0\) Hz), 7.71-7.76\ (2H, m), 7.82\ (1H, ddd, \(J = 1.2, 6.8, 8.4\) Hz), 7.98\ (1H, d, \(J = 8.0\) Hz), 8.31\ (1H, dd, \(J = 0.8, 8.8\) Hz), 9.22\ (1H, s); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \(\delta 118.2, 126.9, 127.7, 127.8, 127.9, 128.3, 128.5, 129.8, 131.8, 135.9, 140.7, 151.0, 152.3.\)

3-Phenylisoquinoline (6)\(^{15}\)

![3-Phenylisoquinoline (6)](image)

White solid; \(^1H\) NMR (400 MHz, CDCl\(_3\)) \(\delta 7.41\ (1H, tt, \(J = 1.2, 7.6\) Hz), 7.48-7.53\ (2H, m), 7.57\ (1H, ddd, \(J = 1.2, 6.8, 8.0\) Hz), 7.68\ (1H, ddd, \(J = 1.2, 6.8, 8.0\) Hz), 7.86\ (1H, d, \(J = 8.0\) Hz), 7.97

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4. Control experiments to elucidate the reaction mechanism

To elucidate the reaction mechanism for the formation of 4-bromoisoquinolone derivatives 3, especially pertaining to how N-C bond forming cyclization as well as formation of C=O and C-Br bonds could occur, several control experiments were conducted (Scheme S3). The reaction of N-benzylaldimines 7 under the standard reaction conditions afforded 4-bromoisoquinolone 3aa (Scheme S3-a), while cyclization of N-benzylamide 8 did not proceed at all (Scheme S3-b). With the fact that the reaction of benzaldehyde (9) and benzylamine (2a) under the present conditions gave only aldimine 10 derived from condensation of 9 and 2a as well as dimerization of 2a (Scheme S3-c), it could be expected that the N-C bond forming cyclization onto alkyne might occur prior to the C=O bond formation. Stahl reported a CuBr-catalyzed aerobic bromination of arenes in the presence of LiBr as a stoichiometric bromine atom source, where molecular bromine generated in situ underwent an electrophilic bromination. On the contrary, treatment of cyclooctene (11) under the present reaction conditions (2.2 equiv of CuBr•SMe₂, SiO₂, in benzene-pyridine under an O₂ atmosphere) did not afford any electrophilic bromination product (Scheme S3-d). This suggested that molecular bromine (or a precursor of bromonium cation) is not likely involved in the present 4-bromoisoquinolone formation. It is also noted that vinylic C-H bromination of isoquinolone 4aa did not proceed under the present reaction conditions (Scheme S3-e).

**standard conditions: CuBr•SMe₂ (2.2 equiv) in benzene-pyridine (5:1), SiO₂, 80 °C, under an O₂ atmosphere (1 atm).**

(1H, d, J = 8.0 Hz), 8.06 (1H, s), 8.10-8.15 (2H, m), 9.33 (1H, s); ¹³C NMR (100 MHz, CDCl₃) δ 116.5, 126.8, 126.9, 127.0, 127.5, 127.7, 128.4, 128.7, 130.4, 136.5, 139.5, 151.2, 152.3.
Preparation of N-benzyl-2-(2-phenylethynyl)benzaldimine (7):

To a solution of 2-(2-phenylethynyl)benzaldehyde (1a) (206 mg, 1.0 mmol) in 1 mL of CH₂Cl₂ were added benzylamine (2a) (107 mg, 1.0 mmol) and MS 4Å (20 mg). The reaction mixture was allowed to stir at room temperature for 24 h. After the completion of reaction, the mixture was filtered and volatile materials were removed in vacuo and the crude material was used for next reaction without further purification.

N-Benzyl-2-(2-phenylethynyl)benzaldimine (7)⁵
Brown oil; ¹H NMR (400 MHz, CDCl₃) δ 4.90 (2H, s), 7.36-7.40 (10H, m), 7.50-7.57 (3H, m), 8.14 (1H, d, J = 6.8 Hz), 8.99 (1H, s); ¹³C NMR (100 MHz, CDCl₃) δ 65.1, 86.4, 94.9, 122.9, 124.1, 126.4, 127.0, 128.1, 128.4, 128.5, 128.58, 128.63, 130.3, 131.5, 132.5, 136.7, 139.1, 160.5.

N-Benzyl-2-(phenylethynyl)benzamide (8)¹⁷

Prepared from N-benzyl-2-bromobenzamide and phenylacetylene by the same procedure with the section 2.1., and purified by flash column chromatography (Si gel, hexane:ethyl acetate = 80:20) in 95% yield; White solid; ¹H NMR (400 MHz, CDCl₃) δ 4.70 (2H, d, J = 5.6 Hz), 7.13 (2H, d, J = 7.2 Hz), 7.22-7.29 (5H, m), 7.30-7.40 (3H, m), 7.42-7.48 (2H, m), 7.56-7.61 (1H, m), 7.80 (1H, brs), 8.12-8.17 (1H, m); ¹³C NMR (100 MHz, CDCl₃) δ 44.5, 87.5, 95.8, 119.6, 121.8, 127.5, 128.2, 128.4, 128.75, 128.86, 128.92, 130.2, 130.6, 131.4, 133.6, 135.0, 137.8, 166.1.

Both imine 10 and isoquinolone 4aa were known compounds (see the references).

N-Benzyl-benzaldimine (10)¹⁸

2-Benzyl-3-phenylisoquinolin-1(2H)-one (4aa)¹⁹

¹⁸ L. G. Marinescu, C. M. Pedersen, M. Bols, Tetrahedron 2004, 61, 123.
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 1d (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 1d (100 MHz, CDCl$_3$)

[Diagram of carbonyl group and carbon atom labels]

ppm values:
- 191.54
- 164.16
- 161.66
- 135.78
- 133.68
- 133.59
- 133.15
- 128.66
- 126.59
- 118.40
- 115.99
- 115.77
- 95.16
- 84.65
- 77.32
- 77.00
- 76.68
4. $^1\text{H}$ and $^{13}\text{C}$ NMR spectrum of new compounds

$^1\text{H}$ NMR spectrum of 1j (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 1j (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 1n (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 1n (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 1r (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 1r (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3aa (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3aa (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3aa' (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3aa' (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3aa'' (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3aa" (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ab (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3ab (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ac (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3ac (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ad (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3ad (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ae (400 MHz, CDCl$_3$)

![NMR Spectrum Diagram](Image)
4. \(^1\)H and \(^{13}\)C NMR spectrum of new compounds

\(^{13}\)C NMR spectrum of 3ae (100 MHz, CDCl\(_3\))
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3af (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3af (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ag (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3ag (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ah (400 MHz, CDCl$_3$)
4. \( ^1H \) and \( ^{13}C \) NMR spectrum of new compounds

\( ^{13}C \) NMR spectrum of 3ah (100 MHz, CDCl\(_3\))
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ai (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3ai (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3aj (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3aj (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ak (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3ak (100 MHz, CDCl$_3$)
4. \(^1\)H and \(^{13}\)C NMR spectrum of new compounds

\(^1\)H NMR spectrum of 3al (400 MHz, CDCl\(_3\))
4. \(^1\)H and \(^{13}\)C NMR spectrum of new compounds

\(^{13}\)C NMR spectrum of 3al (100 MHz, CDCl\(_3\))
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ba (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3ba (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ca (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3ca (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3da (400 MHz, CDCl$_3$)

![NMR spectrum of 3da](image)
4. \(^1\)H and \(^{13}\)C NMR spectrum of new compounds

\(^{13}\)C NMR spectrum of 3da (100 MHz, CDCl\(_3\))
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ea (400 MHz, CDCl$_3$)

![NMR spectrum image]
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3ea (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3fa (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3fa (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ga (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3ga (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ha (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3ha (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ia (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3ia (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ja (400 MHz, CDCl$_3$)

![NMR spectrum of 3ja](image)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3ja (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ka (400 MHz, CDCl$_3$)
4. \(^1\)H and \(^{13}\)C NMR spectrum of new compounds

\(^{13}\)C NMR spectrum of 3ka (100 MHz, CDCl\(_3\))
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3la (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3la (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ma (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3ma (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3na (400 MHz, CDCl$_3$)

![NMR spectrum image]
4. \(^1\)H and \(^{13}\)C NMR spectrum of new compounds

\(^{13}\)C NMR spectrum of 3na (100 MHz, CDCl\(_3\))

![NMR spectrum of 3na](image_url)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3oa (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3oa (100 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3pa (400 MHz, CDCl$_3$)
4. \(^1\)H and \(^{13}\)C NMR spectrum of new compounds

\(^{13}\)C NMR spectrum of 3pa (100 MHz, CDCl\(_3\))
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3qa (400 MHz, CDCl$_3$)

![NMR Spectrum Image]
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3qa (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3ra (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3ra (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 3sa (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 3sa (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^1$H NMR spectrum of 4sa (400 MHz, CDCl$_3$)
4. $^1$H and $^{13}$C NMR spectrum of new compounds

$^{13}$C NMR spectrum of 4sa (400 MHz, CDCl$_3$)