

Copper-Catalyzed Cross-Dehydrogenative Coupling of Quinazoline-3-Oxides with Indoles

Qin Yang, Zhijian Yin, Lifang Zheng, Jianjun Yuan, Song Wei, Qiuping Ding,* YiyuanPeng*

^a Key Laboratory of Functional Small Organic Molecule, Ministry of Education, and Jiangxi Province's Key Laboratory of Green Chemistry, Jiangxi Normal University, Nanchang, Jiangxi, 330022, China

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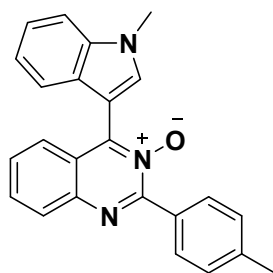
General experimental methods:

Unless otherwise stated, all commercial reagents were used as received. All solvents were dried and distilled according to standard procedures. Flash column chromatography was performed using silica gel (60-Å pore size, 32-63µm, standard grade). Analytical thin-layer chromatography was performed using glass plates pre-coated with 0.25 mm 230-400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Organic solutions were concentrated on rotary evaporators at ~20 Torr at 25-35°C. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale. ^1H and ^{13}C NMR spectra were recorded in CDCl_3 on a Bruker DRX-400 spectrometer operating at 400 MHz and 100 MHz, respectively. All chemical shift values are quoted in ppm and coupling constants quoted in Hz. High resolution mass spectrometry (HRMS) spectra were obtained on a micrOTOF II Instrument.

General experimental procedure:

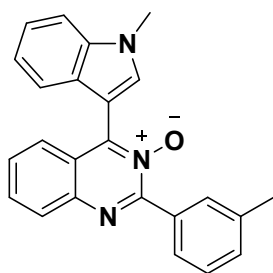
The quinazoline-3-oxide (0.2 mmol), indoles (0.3 mmol), CuCl_2 (0.02 mmol) and 2 mL CH_3OH were mixed in a dry reaction tube. The mixture was stirred at 60°C under air for 16 hours. After completion of the reaction (monitored by TLC), the mixture was concentrated in vacuum and the residue was purified by flash column chromatography on silica gel with petroleum ether-ethyl acetate as eluent to give the desired product.

Characterization data for the products:

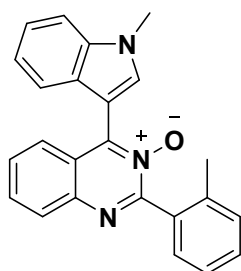


4-(1-methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3aa). Compound was obtained as a yellow solid: yield 78%; ^1H NMR (400 MHz, CDCl_3) δ 8.30 (s, 1H), 8.22 (d, $J = 8.0$ Hz, 2H), 8.04 (d, $J = 8.0$ Hz, 1H), 7.92 (d, $J = 8.4$ Hz, 1H), 7.69 (td, $J = 7.6, 1.2$ Hz, 1H), 7.52 - 7.40 (m, 3H), 7.36-7.27 (m, 3H), 7.19 (t, $J = 7.6$ Hz, 1H), 3.94 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 155.7, 147.1, 141.2, 140.7, 136.7, 135.5, 130.6, 130.5, 130.3, 128.7, 128.6, 128.0, 127.6, 126.5, 123.1, 122.5, 121.7, 121.0, 110.0, 102.6, 33.6, 21.6. HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for

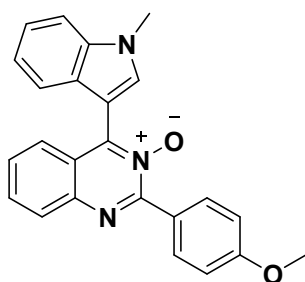
C₂₄H₂₀N₃O: 366.1606, found 366.1609.



4-(1-methyl-1H-indol-3-yl)-2-(*m*-tolyl)quinazoline 3-oxide (3ba). Compound was obtained as a yellow solid: yield 87%; ¹H NMR (400 MHz, CDCl₃) δ 8.32 (s, 1H), 8.12-7.85 (m, 3H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.71 (t, *J* = 7.2 Hz, 1H), 7.54-7.36 (m, 4H), 7.35-7.28 (m, 2H), 7.18 (t, *J* = 7.2 Hz, 1H), 3.95 (s, 3H), 2.43 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 156.0, 147.1, 141.2, 137.5, 136.7, 135.6, 133.3, 131.2, 130.65, 130.61, 128.8, 128.1, 127.9, 127.6, 127.4, 126.6, 123.2, 122.5, 121.6, 121.0, 110.0, 102.5, 33.6, 21.5. HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₄H₂₀N₃O: 366.1606, found 366.1607.

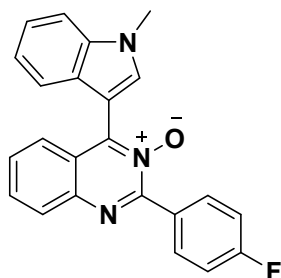


4-(1-methyl-1H-indol-3-yl)-2-(*o*-tolyl)quinazoline 3-oxide (3ca). Compound was obtained as a yellow solid: yield 71%; ¹H NMR (400 MHz, CDCl₃) δ 8.43 (s, 1H), 8.11 - 8.02 (m, 2H), 7.74 (td, *J* = 7.2, 1.2 Hz, 1H), 7.59 - 7.53 (m, 2H), 7.51 - 7.43 (m, 2H), 7.43 - 7.37 (m, 1H), 7.37 - 7.30 (m, 3H), 7.20 (t, *J* = 7.6 Hz, 1H), 3.92 (s, 3H), 2.35 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 157.8, 146.7, 140.9, 137.1, 136.8, 136.3, 134.1, 130.7, 130.2, 129.6, 128.8, 128.8, 128.3, 127.6, 126.7, 125.8, 123.2, 122.6, 121.7, 121.1, 110.1, 102.4, 33.6, 19.7. HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₄H₂₀N₃O: 366.1606, found 366.1611.



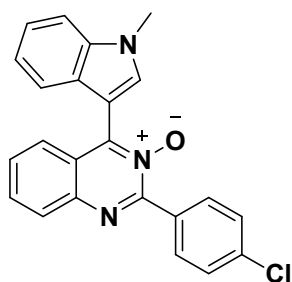
2-(4-methoxyphenyl)-4-(1-methyl-1H-indol-3-yl)quinazoline 3-oxide (3da). Compound was obtained as a yellow solid: yield 87%; ¹H NMR (400 MHz, CDCl₃) δ 8.46 - 8.37 (m, 2H), 8.28 (s, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.70 (td, *J* = 7.4, 1.2 Hz, 1H), 7.51 - 7.41 (m, 3H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.05 - 6.98 (m, 2H), 3.96 (s, 3H), 3.89 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 161.5, 155.1, 147.2, 141.3, 136.7, 135.3, 132.4, 130.6, 128.6, 127.8, 127.6,

126.5, 125.7, 123.0, 122.5, 121.7, 120.9, 113.3, 110.0, 102.7, 55.4, 33.6. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{24}H_{20}N_3O_2$: 382.1556, found 382.1555.



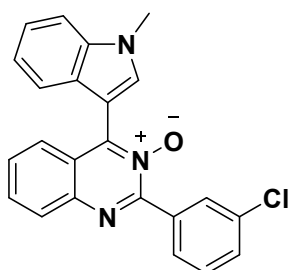
2-(4-fluorophenyl)-4-(1-methyl-1H-indol-3-yl)quinazoline 3-oxide (3ea).

Compound was obtained as a yellow solid: yield 83%; 1H NMR (400 MHz, $CDCl_3$) δ 8.45 - 8.35 (m, 2H), 8.30 (s, 1H), 8.05 (d, $J = 8.0$ Hz, 1H), 7.95 (d, $J = 8.0$ Hz, 1H), 7.73 (t, $J = 7.6$ Hz, 1H), 7.51 (t, $J = 7.6$ Hz, 1H), 7.49-7.41 (m, 2H), 7.34 (t, $J = 7.6$ Hz, 1H), 7.23-7.14 (m, 3H), 3.97 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2 (d, $J = 249.2$ Hz), 154.5, 141.2, 136.8, 135.5, 132.8 (d, $J = 8.5$ Hz), 129.4 (d, $J = 3.3$ Hz), 128.7, 128.2, 127.5, 126.6, 123.2, 122.6, 121.6, 121.1, 114.9 (d, $J = 21.6$ Hz), 110.1, 102.5, 33.6. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{23}H_{17}FN_3O$: 370.1356, found 370.1381.



2-(4-chlorophenyl)-4-(1-methyl-1H-indol-3-yl)quinazoline 3-oxide (3fa).

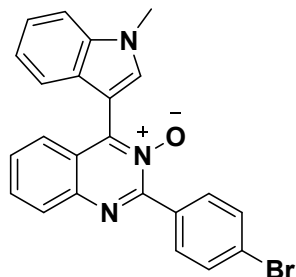
Compound was obtained as a yellow solid: yield 82%; 1H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, $J = 8.4$ Hz, 2H), 8.28 (s, 1H), 8.05 (d, $J = 8.0$ Hz, 1H), 7.95 (d, $J = 8.4$ Hz, 1H), 7.72 (t, $J = 7.2$ Hz, 1H), 7.55-7.41 (m, 5H), 7.34 (t, $J = 7.4$ Hz, 1H), 7.19 (t, $J = 7.4$ Hz, 1H), 3.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.4, 147.5, 141.2, 136.8, 136.6, 135.5, 131.9, 131.7, 130.9, 128.8, 128.3, 128.1, 127.5, 126.6, 123.2, 122.6, 121.6, 121.1, 110.1, 102.4, 33.6. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{23}H_{17}ClN_3O$: 386.1060, found 386.1075, and 388.1031, found 388.1044.



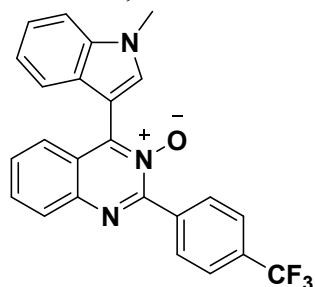
2-(3-chlorophenyl)-4-(1-methyl-1H-indol-3-yl)quinazoline 3-oxide (3ga).

Compound was obtained as a yellow solid: yield 83%; 1H NMR (400 MHz, $CDCl_3$) δ 8.35 (t, $J = 1.6$ Hz, 1H), 8.29 (s, 1H), 8.25 - 8.19 (m, 1H), 8.05 (d, $J = 8.4$ Hz, 1H), 7.95 (d, $J = 8.4$ Hz, 1H), 7.72 (t, $J = 7.6$ Hz, 1H), 7.56-7.40 (m, 5H), 7.33 (t, $J = 7.4$

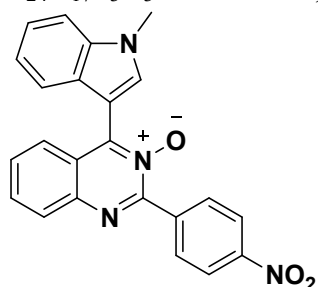
Hz, 1H), 7.19 (t, $J = 7.6$ Hz, 1H), 3.95 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 154.1, 147.5, 141.1, 136.8, 135.5, 135.0, 133.9, 130.9, 130.5, 130.4, 129.1, 128.9, 128.6, 128.5, 127.5, 126.6, 123.3, 122.6, 121.6, 121.1, 110.1, 102.4, 33.6. HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{17}\text{ClN}_3\text{O}$: 386.1060, found 386.1075, and 388.1031, found 388.1045.



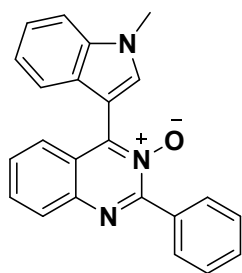
2-(4-bromophenyl)-4-(1-methyl-1H-indol-3-yl)quinazoline 3-oxide 3-oxide (3ha). Compound was obtained as a yellow solid: yield 76%; ^1H NMR (400 MHz, CDCl_3) δ 8.28 (s, 1H), 8.25 (d, $J = 8.4$ Hz, 2H), 8.05 (d, $J = 8.4$ Hz, 1H), 7.95 (d, $J = 8.4$ Hz, 1H), 7.73 (t, $J = 7.4$ Hz, 1H), 7.64 (d, $J = 8.8$ Hz, 2H), 7.52 (t, $J = 7.6$ Hz, 1H), 7.48-7.41 (m, 2H), 7.34 (t, $J = 7.6$ Hz, 1H), 7.20 (t, $J = 7.4$ Hz, 1H), 3.96 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 154.5, 147.5, 141.2, 136.8, 135.5, 132.2, 132.1, 131.1, 130.9, 128.8, 128.4, 127.5, 126.6, 125.1, 123.2, 122.6, 121.6, 121.1, 110.1, 102.4, 33.6. HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{17}\text{BrN}_3\text{O}$: 430.0555, found 430.0557, and 432.0535, found 432.0537.



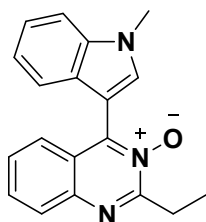
4-(1-methyl-1H-indol-3-yl)-2-(4-(trifluoromethyl)phenyl)quinazoline 3-oxide (3ia). Compound was obtained as a yellow solid: yield 93%; ^1H NMR (400 MHz, CDCl_3) δ 8.43 (d, $J = 8.0$ Hz, 2H), 8.31 (s, 1H), 8.07 (d, $J = 8.0$ Hz, 1H), 7.99 (dd, $J = 8.4, 0.4$ Hz, 1H), 7.77-7.73 (m, 3H), 7.55 (td, $J = 7.8, 1.2$ Hz, 1H), 7.46 (t, $J = 8.8$ Hz, 2H), 7.34 (td, $J = 7.8, 1.2$ Hz, 1H), 7.20 (t, $J = 7.8$ Hz, 1H), 3.96 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 154.2, 147.6, 141.2, 136.8, 135.7, 132.0 (q, $J = 32.3$ Hz), 131.0, 130.7, 128.9, 128.7, 127.4, 126.7, 124.8 (q, $J = 3.8$ Hz), 124.0 (q, $J = 207.7$ Hz), 123.4, 122.7, 121.6, 121.2, 110.1, 102.3, 33.6. HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{17}\text{F}_3\text{N}_3\text{O}$: 420.1324, found 420.1324.



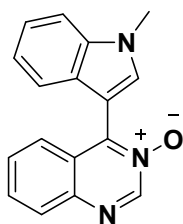
4-(1-methyl-1*H*-indol-3-yl)-2-(4-nitrophenyl)quinazoline 3-oxide (3ja). Compound was obtained as a yellow solid: yield 61%; ¹H NMR (400 MHz, CDCl₃) δ 8.58 - 8.50 (m, 2H), 8.38 - 8.29 (m, 3H), 8.08 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.60-7.55 (m, 1H), 7.60-7.55 (m, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.77 (td, *J* = 7.8, 1.2 Hz, 1H), 7.58 (td, *J* = 7.8, 1.2 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.35 (td, *J* = 7.6, 1.0 Hz, 1H), 7.21 (td, *J* = 7.6, 1.0 Hz, 1H), 3.98 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 153.3, 148.7, 141.3, 139.4, 136.8, 135.7, 131.5, 131.3, 129.01, 128.99, 127.4, 126.8, 123.4, 122.9, 122.8, 121.5, 121.3, 110.2, 102.2, 33.7. HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₃H₁₇N₄O₃: 397.1301, found 397.1276.



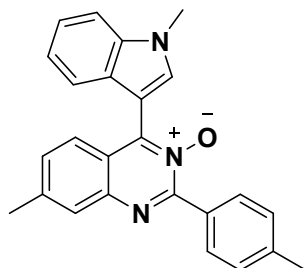
4-(1-methyl-1*H*-indol-3-yl)-2-phenylquinazoline 3-oxide (3ka). Compound was obtained as a yellow solid: yield 79%; ¹H NMR (400 MHz, CDCl₃) δ 8.37-8.22 (m, 3H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.71 (t, *J* = 7.1 Hz, 1H), 7.58 - 7.41 (m, 6H), 7.34 (t, *J* = 7.2 Hz, 1H), 7.20 (t, *J* = 7.2 Hz, 1H), 3.95 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 155.7, 147.1, 141.2, 136.7, 135.6, 133.4, 130.6, 130.4, 130.3, 128.8, 128.1, 127.9, 127.6, 126.6, 123.2, 122.5, 121.6, 121.0, 110.0, 102.5, 33.6. HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₃H₁₈N₃O: 352.1450, found 352.1437.



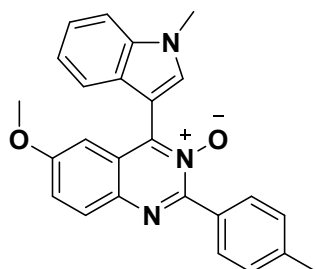
2-ethyl-4-(1-methyl-1*H*-indol-3-yl)quinazoline 3-oxide (3la). Compound was obtained as a yellow solid: yield 72%; ¹H NMR (400 MHz, CDCl₃) δ 8.22 (s, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.51 - 7.41 (m, 2H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.16 (t, *J* = 7.4 Hz, 1H), 3.94 (s, 3H), 3.34 (q, *J* = 7.2 Hz, 2H), 1.53 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 161.3, 145.8, 140.7, 136.7, 135.1, 130.4, 1228.2, 127.5, 126.5, 122.8, 122.5, 121.6, 120.9, 110.0, 102.5, 33.5, 26.3, 10.3. HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₉H₁₈N₃O: 304.1450, found 304.1456.



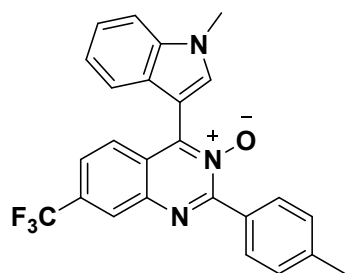
4-(1-methyl-1*H*-indol-3-yl)quinazoline 3-oxide (3ma). Compound was obtained as a yellow solid: yield 68%; ¹H NMR (400 MHz, CDCl₃) δ 9.10 (s, 1H), 8.26 (s, 1H), 8.14-7.89 (m, 2H), 7.70 (t, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 3.94 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 148.6, 141.5, 136.8, 135.4, 130.8, 128.8, 128.7, 127.2, 126.8, 123.2, 122.7, 121.5, 121.1, 110.1, 101.7, 33.6. HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₇H₁₄N₃O: 276.1137, found 276.1132.



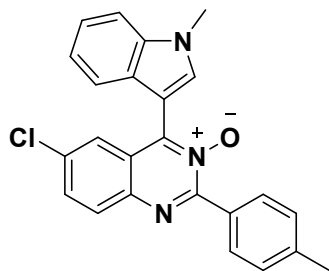
7-methyl-4-(1-methyl-1*H*-indol-3-yl)-2-(*p*-tolyl)quinazoline 3-oxide (3na). Compound was obtained as a yellow solid: yield 71%; ¹H NMR (400 MHz, CDCl₃) δ 8.31 (s, 1H), 8.22 (d, *J* = 8.0 Hz, 2H), 7.82 (d, *J* = 8.8 Hz, 2H), 7.45 (dd, *J* = 8.6, 1.8 Hz, 2H), 7.35 - 7.27 (m, 4H), 7.18 (t, *J* = 7.6 Hz, 1H), 3.95 (s, 3H), 2.56 (s, 3H), 2.43 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 155.6, 147.1, 141.6, 141.5, 140.6, 136.7, 135.5, 130.6, 130.3, 130.1, 128.5, 127.9, 127.6, 126.3, 122.4, 121.6, 121.1, 120.9, 110.0, 102.7, 33.6, 21.8, 21.6. HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₅H₂₂N₃O: 380.1763, found 380.1767.



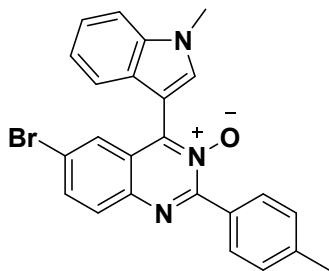
6-methoxy-4-(1-methyl-1*H*-indol-3-yl)-2-(*p*-tolyl)quinazoline 3-oxide (3oa). Compound was obtained as a yellow solid: yield 52%; ¹H NMR (400 MHz, CDCl₃) δ 8.37 (s, 1H), 8.18 (d, *J* = 8.0 Hz, 2H), 7.95 (d, *J* = 9.2 Hz, 1H), 7.50 - 7.43 (m, 2H), 7.37 - 7.27 (m, 4H), 7.22-7.16 (m, 2H), 3.96 (s, 3H), 3.67 (s, 3H), 2.43 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 158.9, 153.6, 146.0, 140.3, 137.3, 136.7, 135.5, 130.6, 130.3, 130.1, 128.6, 127.2, 124.1, 123.2, 122.4, 121.8, 120.6, 110.1, 104.6, 102.5, 55.7, 33.6, 21.6. HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₅H₂₂N₃O₂: 396.1712, found 396.1737.



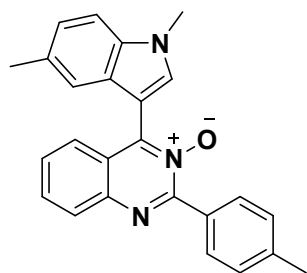
4-(1-methyl-1*H*-indol-3-yl)-2-(*p*-tolyl)-7-(trifluoromethyl)quinazoline 3-oxide (3pa). Compound was obtained as a yellow solid: yield 75%; ¹H NMR (400 MHz, CDCl₃) δ 8.37-8.32 (m, 2H), 8.26 (d, *J* = 8.0 Hz, 2H), 8.06 (d, *J* = 8.8 Hz, 1H), 7.64 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.37-7.30 (m, 3H), 7.21 (t, *J* = 7.6 Hz, 1H), 3.95 (s, 3H), 2.45 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 157.0, 147.0, 141.5, 140.2, 136.9, 136.0, 132.1 (q, *J* = 32.9 Hz), 130.5, 129.9, 128.8, 127.7, 127.4, 126.5 (q, *J* = 4.2 Hz), 124.6, 123.7 (q, *J* = 270.9 Hz), 123.6 (q, *J* = 3.0 Hz), 122.9, 121.45, 121.40, 110.3, 102.2, 33.7, 21.7. HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₅H₁₉F₃N₃O: 434.1480, found 434.1478.



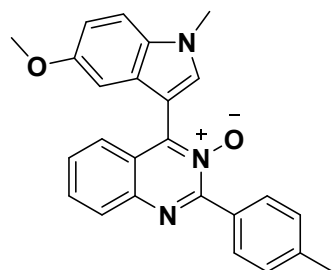
6-chloro-4-(1-methyl-1*H*-indol-3-yl)-2-(*p*-tolyl)quinazoline 3-oxide (3qa). Compound was obtained as a yellow solid: yield 83%; ¹H NMR (400 MHz, CDCl₃) δ 8.23 (d, *J* = 8.8 Hz, 3H), 7.97 (d, *J* = 8.8 Hz, 1H), 7.93 (d, *J* = 2.0 Hz, 1H), 7.62 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.46 (d, *J* = 8.8 Hz, 2H), 7.47-7.29 (m, 3H), 7.22 (t, *J* = 7.6 Hz, 1H), 3.96 (s, 3H), 2.44 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 155.9, 146.3, 141.1, 139.4, 136.8, 135.3, 134.0, 131.2, 130.3, 130.1, 131.2, 130.3, 130.1, 128.6, 127.2, 125.0, 124.0, 122.7, 121.4, 121.3, 110.1, 102.3, 33.6, 21.6. HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₄H₁₉ClN₃O: 400.1217, found 400.1219, and 402.1187, found 402.1188.



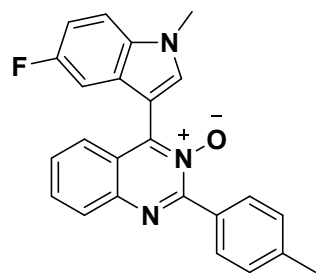
6-bromo-4-(1-methyl-1*H*-indol-3-yl)-2-(*p*-tolyl)quinazoline 3-oxide (3ra). Compound was obtained as a yellow solid: yield 84%; ¹H NMR (400 MHz, CDCl₃) δ 8.31 - 8.19 (m, 3H), 8.10 (d, *J* = 1.6 Hz, 1H), 7.90 (d, *J* = 8.8 Hz, 1H), 7.75 (dd, *J* = 8.8, 1.6 Hz, 3H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.37-7.28 (m, 3H), 7.23 (t, *J* = 7.6 Hz, 1H), 3.96 (s, 3H), 2.43 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 156.0, 146.3, 141.1, 139.7, 136.8, 135.3, 133.8, 130.34, 130.29, 130.1, 128.6, 128.3, 127.2, 124.4, 122.8, 122.0, 121.4, 121.3, 110.1, 102.3, 33.6, 21.6. HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₄H₁₉BrN₃O: 444.0711, found 444.0706, and 446.0691, found 446.0687.



4-(1,5-dimethyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3ab). Compound was obtained as a yellow solid: yield 76%; ^1H NMR (400 MHz, CDCl_3) δ 8.24 (s, 1H), 8.22 (d, $J = 8.4$ Hz, 2H), 8.05 (d, $J = 8.4$ Hz, 1H), 7.94 (d, $J = 8.4$ Hz, 1H), 7.71 (t, $J = 7.6$ Hz, 1H), 7.49 (t, $J = 7.8$ Hz, 1H), 7.34-7.30 (m, 3H), 7.22 (s, 1H), 7.14 (d, $J = 8.4$ Hz, 1H), 3.92 (s, 3H), 2.43 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 155.7, 147.3, 141.2, 140.7, 135.4, 135.2, 130.5, 130.4, 130.3, 128.7, 128.6, 127.8, 126.6, 124.1, 123.2, 121.3, 109.7, 102.1, 33.6, 21.63, 21.57. HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{25}\text{H}_{21}\text{N}_3\text{O}$: 380.1763, found 380.1762.

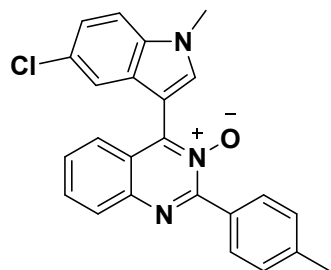


4-(5-methoxy-1-methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3ac). Compound was obtained as a yellow solid: yield 69%; ^1H NMR (400 MHz, CDCl_3) δ 8.29 (s, 1H), 8.27 - 8.18 (m, 2H), 8.05 (d, $J = 8.0$ Hz, 1H), 7.95 (d, $J = 8.4$ Hz, 1H), 7.71 - 7.67 (m, 1H), 7.50 - 7.46 (m, 1H), 7.34-7.30 (m, 3H), 6.97 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.86 (d, $J = 2.0$ Hz, 1H), 3.91 (s, 3H), 3.72 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 155.7, 155.1, 147.1, 141.2, 140.7, 135.8, 131.9, 130.6, 130.5, 130.3, 128.8, 128.6, 128.2, 127.7, 126.6, 122.9, 112.7, 110.7, 103.6, 102.3, 55.8, 33.7, 21.6. HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{25}\text{H}_{21}\text{N}_3\text{O}_2$: 396.1712, found 396.1712.



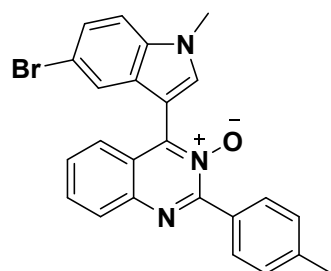
4-(5-fluoro-1-methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3ad). Compound was obtained as a yellow solid: yield 72%; ^1H NMR (400 MHz, CDCl_3) δ 8.28 (s, 1H), 8.22 (d, $J = 8.0$ Hz, 2H), 8.06 (d, $J = 8.4$ Hz, 1H), 7.88 (d, $J = 8.0$ Hz, 1H), 7.72 (t, $J = 7.4$ Hz, 1H), 7.52 (t, $J = 7.4$ Hz, 1H), 7.38-7.35 (m, 1H), 7.31 (d, $J = 7.8$ Hz, 2H), 7.15 - 7.01 (m, 2H), 3.94 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 158.5 (d, $J = 235.5$ Hz), 155.7, 146.7, 141.2, 140.9, 136.6, 133.4, 130.7, 130.3, 128.9, 128.6, 128.2, 128.0 (d, $J = 10.4$ Hz), 126.1, 123.0, 111.2, 110.9, 110.8

(d, $J = 9.8$ Hz), 107.0 (d, $J = 24.8$ Hz), 102.8, 33.8, 29.7, 21.6. HRMS (ESI): m/z [$M + H$]⁺ calcd for C₂₄H₁₈FN₃O: 384.1512, found 384.1501.



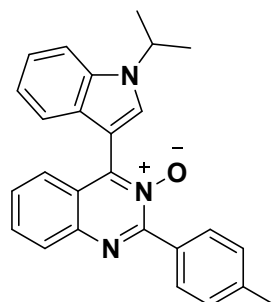
4-(5-chloro-1-methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3ae).

Compound was obtained as a yellow solid: yield 78%; ¹H NMR (400 MHz, CDCl₃) δ 8.22 (d, $J = 8.4$ Hz, 3H), 8.05 (d, $J = 8.0$ Hz, 1H), 7.84 (d, $J = 8.0$ Hz, 1H), 7.71 (t, $J = 7.2$ Hz, 1H), 7.52 (t, $J = 7.2$ Hz, 1H), 7.42 (s, 1H), 7.36 – 7.25 (m, 4H), 3.92 (s, 3H), 2.43 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 155.6, 146.5, 141.2, 140.9, 136.2, 135.2, 130.8, 130.3, 128.9, 128.6, 128.5, 128.3, 127.0, 126.0, 123.1, 123.0, 121.1, 111.0, 102.4, 33.7, 21.6. HRMS (ESI): m/z [$M + H$]⁺ calcd for C₂₄H₁₈ClN₃O: 400.1217, found 400.1219, and 402.1187, found 402.1188.



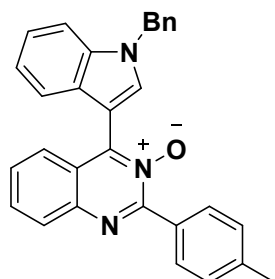
4-(5-bromo-1-methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3af).

Compound was obtained as a yellow solid: yield 87%; ¹H NMR (400 MHz, CDCl₃) δ 8.22 (d, $J = 8.0$ Hz, 1H), 8.19 (s, 1H), 8.05 (d, $J = 8.4$ Hz, 1H), 7.83 (d, $J = 8.0$ Hz, 1H), 7.71 (t, $J = 6.8$ Hz, 1H), 7.57 (s, 1H), 7.52 (t, $J = 7.2$ Hz, 1H), 7.40 (d, $J = 8.4$ Hz, 1H), 7.31 (d, $J = 8.0$ Hz, 3H), 3.92 (s, 3H), 2.43 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 155.6, 146.5, 141.2, 140.9, 136.1, 135.5, 130.8, 130.3, 129.1, 128.9, 128.6, 128.3, 126.0, 125.5, 124.1, 123.1, 114.5, 111.5, 102.4, 100.0, 33.7, 21.6. HRMS (ESI): m/z [$M + H$]⁺ calcd for C₂₃H₁₈BrN₃O: 444.0711, found 444.0710, and 446.0691, found 446.0690.

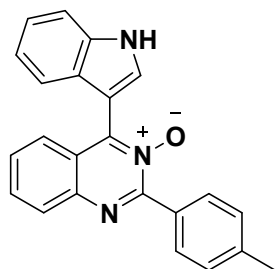


4-(1-isopropyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3ag). Compound was obtained as a yellow solid: yield 88%; ¹H NMR (400 MHz, CDCl₃) δ 8.46 (s, 1H),

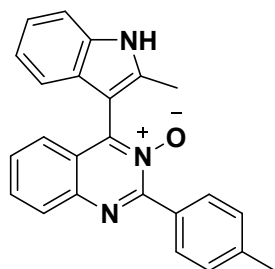
8.19 (d, $J = 8.0$ Hz, 2H), 8.05 (d, $J = 8.0$ Hz, 1H), 7.94 (d, $J = 8.4$ Hz, 1H), 7.70 (t, $J = 7.4$ Hz, 1H), 7.56-7.44 (m, 3H), 7.36-7.28 (m, 3H), 7.18 (t, $J = 7.4$ Hz, 1H), 4.90 - 4.75 (m, 1H), 2.44 (s, 3H), 1.67 (s, 3H), 1.65 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 155.9, 147.4, 141.3, 140.6, 135.7, 131.0, 130.61, 130.55, 130.2, 128.7, 128.6, 127.9, 127.8, 126.7, 123.2, 122.2, 121.9, 120.9, 110.3, 102.8, 48.1, 22.8, 21.6. HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{26}\text{H}_{24}\text{N}_3\text{O}$: 394.1919, found 394.1919.



4-(1-benzyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3ah). Compound was obtained as a yellow solid: yield 82%; ^1H NMR (400 MHz, CDCl_3) δ 8.33 (s, 1H), 8.22 (d, $J = 7.6$ Hz, 2H), 8.04 (d, $J = 8.4$ Hz, 1H), 7.92 (d, $J = 8.4$ Hz, 1H), 7.68 (t, $J = 7.4$ Hz, 1H), 7.47 (t, $J = 8.2$ Hz, 2H), 7.40 (d, $J = 8.0$ Hz, 1H), 7.37 – 7.21 (m, 7H), 7.17 (t, $J = 7.4$ Hz, 1H), 5.45 (s, 2H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 155.8, 147.0, 141.1, 140.7, 136.3, 134.8, 130.53, 130.47, 130.3, 129.0, 128.8, 128.6, 128.1, 128.0, 127.2, 126.4, 123.2, 122.6, 121.9, 121.1, 110.6, 103.4, 51.0, 21.6. HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{30}\text{H}_{24}\text{N}_3\text{O}$: 442.1919, found 442.1935.

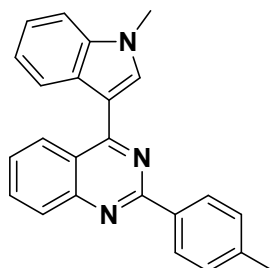


4-(1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3ai). Compound was obtained as a yellow solid: yield 83%; ^1H NMR (400 MHz, CDCl_3) δ 10.24 (s, 1H), 8.28 (d, $J = 7.2$ Hz, 2H), 8.05 (d, $J = 8.4$ Hz, 1H), 7.77 (d, $J = 8.4$ Hz, 1H), 7.71 (t, $J = 7.2$ Hz, 1H), 7.57-7.39 (m, 3H), 7.33 (d, $J = 7.6$ Hz, 2H), 7.08 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 155.5, 148.5, 141.5, 140.9, 136.1, 131.1, 131.0, 130.5, 130.4, 128.7, 128.6, 128.3, 126.6, 126.3, 123.5, 122.4, 121.4, 120.8, 112.3, 103.5, 21.6. HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{18}\text{N}_3\text{O}$: 352.1450, found 352.1447.



4-(2-methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3aj). Compound was obtained as a yellow solid: yield 58%; ^1H NMR (400 MHz, CDCl_3) δ 9.55 (s, 1H),

8.31 (d, $J = 8.0$ Hz, 2H), 8.06 (d, $J = 8.4$ Hz, 1H), 7.69 (t, $J = 7.6$ Hz, 1H), 7.56 (d, $J = 8.4$ Hz, 1H), 7.44 (t, $J = 7.6$ Hz, 1H), 7.32 (d, $J = 8.0$ Hz, 2H), 7.18 (d, $J = 7.7$ Hz, 1H), 7.05 (s, 3H), 2.43 (s, 3H), 2.04 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 155.7, 149.4, 141.03, 140.99, 139.7, 136.1, 130.8, 130.50, 130.45, 128.7, 128.5, 127.7, 126.6, 124.2, 121.4, 120.2, 119.5, 111.7, 101.3, 21.6, 13.7. HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{20}\text{N}_3\text{O}$: 366.1606, found 366.1602.



4-(1-methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline (4a). Compound was obtained as a off-white solid: yield 86%; ^1H NMR (400 MHz, CDCl_3) δ 8.64 (d, $J = 8.4$ Hz, 2H), 8.37 (d, $J = 8.4$ Hz, 2H), 8.11 (d, $J = 8.4$ Hz, 1H), 7.85 (td, $J = 7.0, 1.2$ Hz, 1H), 7.76 (s, 1H), 7.53 (td, $J = 7.6, 0.8$ Hz, 1H), 7.45 (d, $J = 7.6$ Hz, 1H), 7.42 – 7.31 (m, 4H), 3.94 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 163.1, 160.4, 152.1, 140.4, 137.6, 136.1, 133.0, 132.7, 129.3, 129.1, 128.6, 127.4, 126.8, 126.3, 123.0, 122.1, 121.8, 121.4, 113.4, 109.7, 33.4, 21.54. HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{19}\text{N}_3$: 350.1657, found 350.1656.

¹H and ¹³C NMR spectra of compounds

