Quinoline Title

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Supporting Information

SI-I-X

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General Experimental Procedures

Materials: Common abbreviations.[2] Starting materials were purchased from commercial vendors and used without purification unless noted.[3]

General Experimental Techniques: Unless otherwise noted, all reactions were carried out using flame-dried glassware and standard syringe, cannula, and septa techniques, when necessary.[4] Tetrahydrofuran (THF), diethyl ether (Et_2O), hexanes, dichloromethane (CH_2Cl_2), and toluene ($PhCH_3$) were dried by passage through a column of activated alumina on an mBraun SPS.[5] Triethylamine (Et_3N), *N,N*-dimethylformamide (DMF), and acetonitrile (ACN) were dried by passage through a column of activated alumina on an Innovative Technologies system. Trimethylsilyl chloride and Hunig's base were distilled from calcium hydride under argon. Pyridine was distilled from potassium hydroxide under nitrogen. 2-methyl-4-hydroxyquinoline was purchased from Combi-Blocks in San Diego, CA. All boronic acids were purchased from either Combi-Blocks or Oakwood Chemicals in Georgia. Analytical thin layer chromatography was performed using Sorbent Technologies 250 μm glass-backed UV254 silica gel plates. The plates were first visualized by fluorescence upon 254 nm irradiation then by iodine chamber. The plates were then dipped in one of the following stains followed by heating: *p*-anisaldehyde, phosphomolybdic acid, vanillin, ceric ammonium molybdate, potassium iodoplatinate, ninhydrin or bromocresol green.[6] Flash column chromatography was performed using Sorbent Technologies 40-63 μm, pore size 60 Å silica gel with solvent systems indicated. Solvent removal was effected using a Buchi R3 rotary evaporator with a V900 diaphragm pump (~ 10 mmHg). All yields refer to isolated material that is chromatographically (TLC or HPLC) and spectroscopically (^{1}H NMR) homogenous.

Characterization: All melting points were taken with a Thomas Hoover melting point apparatus and are uncorrected. Infrared spectra were recorded on a Nicolet Nexus 470 FTIR spectrometer as neat liquids, oils, solids or as thin films formed from evaporation of NMR solvent over the ATR plate. HPLC were recorded on an Agilent 1260 Infinity using a Poroshell 120 EC-C18 (3.0 x 50 mm, 2.7 micron) column with a binary gradient of 0.1%TFA in H_2O (**A**) and 0.1%TFA in CH_3CN (**B**): [0 min: **A** (95%), **B** (5%); 7 min: **A** (5%), **B** (95%); 8 min: **A** (5%), **B** (95%)] monitoring 214, 254, and 280 nm. All final compounds were demonstrated to have ≥90% purity. Low-resolution mass spectra were recorded on a ThermoFinnigan LXQ ESI-LCMS by use of chemical ionization (CI). High-resolution mass spectra were recorded either at the Old Dominion University College of Science Major Instrumentation Center (COSMIC) on a Bruker 12 Tesla APEX-Qe FTICR-MS with an Apollo II ion source or The Ohio State University Campus Chemical Instrumentation Center (CCIC). Combustion analysis was performed at Atlanitic Microlabs on samples taken from the bulk of the material.

NMR Parameters: Proton nuclear magnetic resonance spectra were recorded on a Bruker UltraShield Plus 400 MHz spectrometer and are recorded in parts per million from internal chloroform (7.26 ppm), methanol, benzene, or dimethylsulfoxide on the δ scale and are reported as follows: chemical shift [multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, qu=quintet, m=multiplet), coupling constant(s) in hertz, integration,

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[2] (a) For a general overview of organic chemistry acronyms see: Daub, G. H.; Leon, A. A.; Silverman, I. R.; Daub, G. W.; Walker, S. B. "The Use of Acronyms in Organic Chemistry." *Aldrichimica Acta* **1984**, 17(*1*), 13-23.

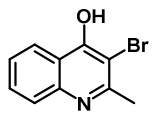
[3] For general purification procedures see: Armarego, W. L. F.; Perrin, D. D. "Purification of Laboratory Chemicals." 4th Ed. 1996, Butterworth-Heinemann.

[4] For general laboratory techniques see: (a) Furniss, B. S.; Hannaford, A. J.; Smith, P. W. G.; Tatchell, A. R. "Vogel's, Textbook of Practical Organic Chemistry." 5th Ed. **1989**, Longman. (b) "Handling Air-Sensitive Reagents" Aldrich Technical Bulletin AL-134, revised 12/94; (d) "Handling Pyrophoric Reagents" Aldrich Technical Bulletin, revised 06/95.

[5] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.

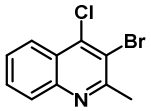
[6] TLC Stains

interpretation].[7] ^{13}C NMR data were recorded on a Bruker UltraShield Plus 400 MHz spectrometer and are reported as follows: chemical shift (multiplicity as determined from DEPT (CH, CH_3 up and CH_2 down)) and/or HSQC experiments.



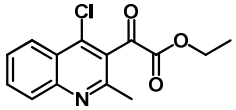
NGJ-7-011

3-bromo-2-methylquinolin-4-ol: To a 100 mL roundbottom flask was added 2-methylquinolin-4-ol (1.2 g, 7.5 mmol), N-bromosuccinimide (1.3 g, 7.5 mmol), and acetic acid (34 mL, 7.5 mmol). The reaction was stirred at 60 °C and within 15 minutes the white slurry obtained a yellow tint and increased in viscosity. The reaction was determined complete after 30 minutes via HPLC and TLC, was cooled to ambient temperature, and diluted with cold distilled water (20 mL). This mixture was filtered through a Hirsch funnel and the precipitate was washed with cold water (10 mL), saturated sodium bicarbonate (10 mL), and acetone (20 mL). The precipitate was dried by pulling air for 15 minutes and was collected to afford 3-bromo-2-methylquinolin-4-ol (1.6 g, 92%) as a yellow solid. No further purification was performed. mp >260 ºC; IR (solid) cm^{-1} 2731 (br); ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.10 (dd, J = 8.1, 1.2 Hz, 1H), 7.67 (ddd, J = 8.4, 7.0, 1.5 Hz, 1H), 7.56 (d, J = 8.1 Hz, 1H), 7.35 (ddd, J = 8.0, 7.0, 1.0 Hz, 1H), 2.56 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 171.4 (s), 149.3 (s), 139.4 (s), 132.2 (d), 125.7 (d) 124.0 (d), 123.3 (s), 118.6 (d), 106.4 (s), 22.0 (q).



NGJ-7-012

3-bromo-4-chloro-2-methylquinoline (4): To a 50 mL roundbottom flask was added 3-bromo-2-methylquinolin-4-ol (13.1 g, 55 mmol) and phosphorus oxychloride (25.6 mL, 275 mmol). The reaction was stirred at 80 °C for 2 hours before determining complete with HPLC. The reaction was cooled to ambient temperature and was slowly poured into a 250 mL beaker full of ice (~100 g). The residual material in the flask was rinsed with water and was added to the beaker. The beaker was maintained at 0 °C while the solution was neutralized with sodium hydroxide pellets and vigorous stirring. Slow addition was required to prevent extreme exotherms. Once neutral, the solution contained a yellow precipitate. The slurry was stirred for an additional three hours at ambient temperature then filtered through a Buchner funnel. The precipitate was collected and dried under vacuum overnight to afford 3-bromo-4-chloro-2-methylquinoline (13.8 g, 98%) as a yellow solid. No further purification was performed. mp 54-56 ºC; IR (solid) cm^{-1} 2913; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.14 (d, J = 8.1 Hz, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.72 (ddd, J = 8.3, 6.7, 1.2 Hz, 1H), 7.51 (dd, J = 7.4 Hz, 1H), 2.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 158.2 (s), 146.4 (s), 142.0 (s), 130.3 (d), 129.1 (d) 127.5 (d), 125.9 (s), 124.5 (d), 119.8 (s), 27.4 (q).

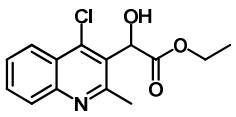


NGJ-7-018

ethyl 2-(4-chloro-2-methylquinolin-3-yl)-2-oxoacetate: To a flame dried 50 mL 3-neck round bottom flask equipped with a low temperature thermometer was added 3-bromo-4-chloro-2-methylquinoline (1.0 g, 4 mmol), copper(I) bromide-dimethyl sulfide complex (41 mg, 0.20 mmol), and tetrahydrofuran (7 mL). The solution was cooled to 0□C in an ice bath. Isopropylmagnesium chloride lithium chloride complex (7.7 mL, 10 mmol, 1M in THF) was added dropwise over 30 minutes via syringe pump. During addition, the solution changed from a clear, light yellow to a green/yellow solution to black. The reaction was stirred at 0°C for an additional five minutes following complete addition. An additional 100 mL 3-neck round bottom flask was prepared with ethyl 2-chloro-2-oxoacetate (0.728 mL, 8 mmol) and tetrahydrofuran (7 mL) and was cooled to 0 °C. The Grignard cuprate was added to the 100 mL flask via cannula at a rate that kept the solution temperature below 10 °C. The reaction was stirred at 0 °C for 15 minutes before determining complete via HPLC. The reaction was quenched with saturated ammonium chloride (10 mL) and was stirred for 15 minutes then transferred to a separatory funnel and the aqueous phase was removed. The organic phase was washed with saturated sodium bicarbonate (10 mL). The combined aqueous phase was extracted with ethyl acetate (10 mL). The combined organic phase was washed with brine (10 mL), dried over magnesium sulfate, vacuum filtered and concentrated in vacuo to afford a brown oil. The residue was chromatographed via automated purification over 40 g of silica gel eluted with hexanes-ethyl acetate using a linear gradient. Product rich fractions were pooled and evaporated to afford ethyl 2-(4-chloro-2-methylquinolin-3-yl)-2-oxoacetate (700 mg, 47%) as a yellow oil. IR (thin film) 1723 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.21 (dd, J = 8.4, 0.9 Hz, 1H), 8.07 (d, J = 8.4, 1H), 7.84 (ddd, J = 8.4, 7.0, 1.4 Hz, 1H), 7.66 (ddd, J = 8.2, 7.0, 1.0 Hz, 1H), 4.44 (q, J = 7.1 Hz, 2H),

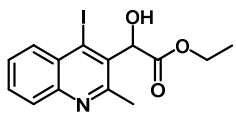
[7] For an overview of NMR analysis see : (a) Hoye, T. R.; Hanson, P. R. ; Vyvyan, J. R. « A Practical Guide to First-Order Multiplet Analysis in ^1H NMR Spectroscop. « *J. Org. Chem.* **1994**, *59*, 4096-4103.

2.69 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 187.2 (s), 160.7 (s), 155.5 (s), 148.5 (s), 140.8 (s), 132.0 (d), 129.2 (d), 129.1 (s), 127.8 (d), 124.0 (d), 123.8 (s), 63.3 (t), 23.8 (q), 13.9 (q).



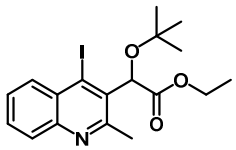
NGJ-7-027

ethyl 2-(4-chloro-2-methylquinolin-3-yl)-2-hydroxyacetate (5): To a 25 mL roundbottom flask was added ethyl 2-(4-chloro-2-methylquinolin-3-yl)-2-oxoacetate (525 mg, 1.9 mmol), tetrahydrofuran (5 mL), and ethanol (50 µL). The solution was cooled to 0 °C then sodium borohydride (71 mg, 1.9 mmol) was added. The reaction was stirred at 0 °C for 30 minutes before observing complete conversion by HPLC. The reaction was diluted with water (5 mL) and was neutralized with 1N HCl (1-2 mL). The aqueous phase was extracted with dichloromethane (two 3 mL portions). The organic phase was washed with brine (5 mL), dried over sodium sulfate, gravity filtered, and concentrated in vacuo to afford a yellow oil. The residue was chromatographed via automated purification over 12 g of silica gel eluted with a linear gradient of hexanes-ethyl acetate. Product rich fractions were pooled and evaporated to afford ethyl 2-(4-chloro-2-methylquinolin-3-yl)-2-hydroxyacetate (409 mg, 77%) as a yellow solid. mp 54-56 ºC IR (thin film) 3074, 1745 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.24 (dd, J = 8.4, 0.9 Hz, 1H), 8.07 (d, J = 8.4, 1H), 7.77 (ddd, J = 8.3, 6.9, 1.3 Hz, 1H), 7.62 (ddd, J = 8.2, 7.0, 1.0 Hz, 1H), 6.00 (s, 1H, O-H), 4.28 (dq, J = 10.8, 7.1; 1H), 2.80 (s, 3H), 1.22 (t, J = 7.1, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 173.0 (s), 158.3 (s), 147.1 (s), 143.5 (s), 130.9 (d), 128.5 (d), 128.0 (s), 127.3 (d), 125.2 (s), 124.7 (d), 69.3 (d), 62.9 (t), 23.9 (q), 14.0 (q).



NGJ-7-046

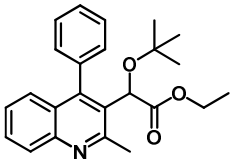
ethyl 2-hydroxy-2-(4-iodo-2-methylquinolin-3-yl)acetate (6): To a 25 mL roundbottom flask was added ethyl 2-(4-chloro-2-methylquinolin-3-yl)-2-hydroxyacetate (409 mg, 1.5 mmol) and tetrahydrofuran (5.0 mL). Hydrochloric acid (1.5 mL, 6.141 mmol, 4 M in dioxane) was added to the flask and the reaction was stirred at ambient temperature for 40 minutes. The solution was concentrated in vacuo and the residue was diluted in acetonitrile (5.0 mL) then transferred to a 10-20 mL microwave vial. Sodium iodide (4.4 g, 29.2 mmol) was added and the vial was sealed. The reaction was heated to 90°C and monitored via HPLC. After 3 hours the reaction was cooled to ambient temperature and the solvent was removed in vacuo. The red residue was diluted with ethyl acetate (10 mL) and was washed with saturated sodium bicarbonate (6 mL), 10% sodium thiosulfate (6 mL), and brine (6 mL). The organic phase was dried over magnesium sulfate, vacuum filtered, and concentrated in vacou to afford a yellow oil (693 mg). The product was utilized in the proceeding reaction without purification. The reaction was determined complete via LRMS [m/z (I) = 280, m/z (VI) = 372]. The MS solution used was a 50/50 THF/MeOH solvent with trace NaCl and the samples were analyzed using the LXQ-ESI with direct injection. IR (thin film) 3061, 1741 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.24 (dd, J = 8.4, 0.9 Hz, 1H), 8.07 (d, J = 8.4, 1H), 7.77 (ddd, J = 8.3, 6.9, 1.3 Hz, 1H), 7.62 (ddd, J = 8.2, 7.0, 1.0 Hz, 1H), 6.00 (s, 1H, O-H), 4.28 (dq, J = 10.8, 7.1; 1H), 2.80 (s, 3H), 1.22 (t, J = 7.1, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 173.0 (s), 158.3 (s), 147.1 (s), 143.5 (s), 130.9 (d), 128.5 (d), 128.0 (s), 127.3 (d), 125.2 (s), 124.7 (d), 69.3 (d), 62.9 (t), 23.9 (q), 14.0 (q).



NGJ-7-070

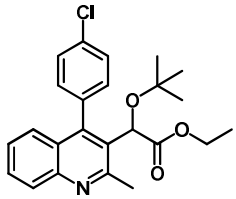
ethyl 2-(tert-butoxy)-2-(4-iodo-2-methylquinolin-3-yl)acetate (7): To a 5.0 mL conical vial was added ethyl 2-hydroxy-2-(4-iodo-2-methylquinolin-3-yl)acetate (91 mg, 0.25 mmol) and tert-butyl acetate (817 µL, 0.25 mmol). Perchloric acid (44 µL, 0.74 mmol) was then added to the vial and the reaction was stirred at ambient temperature. After a total of 3 hours, the reaction was quenched with water (1 mL) and was neutralized to pH 7.0 with saturated sodium bicarbonate. The solution was extracted with ethyl acetate (three 1-mL portions) and the combined organic phase was washed with saturated sodium bicarbonate (1 mL) and brine (1 mL), dried over sodium sulfate, gravity filtered, and concentrated in vacou to afford a yellow oil (110 mg). The residue was chromatographed over 4 g of silica gel eluted with hexanes-ethyl acetate (25 mL 4:1→ 25 mL 2:1→ 25 mL 1:1) in 5 mL fractions. Product rich fractions were pooled and evaporated to afford ethyl 2-(tert-butoxy)-2-(4-iodo-2-methylquinolin-3-yl)acetate (78 mg, 74%) as a yellow oil. IR (thin film) 1750 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.12 (dd, J = 8.4, 1.0 Hz, 1H), 7.95 (dd, J = 8.3, 0.8, 1H), 7.69 (ddd, J = 8.3, 6.9, 1.3 Hz, 1H), 7.56 (ddd, J = 8.3, 7.0, 1.2 Hz, 1H), 5.93 (s, 1H), 4.18 (dq, J = 10.8, 7.1 Hz; 1H), 2.83 (s, 3H), 1.26 (s, 9H), 1.18 (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 171.3 (s), 158.8 (s), 146.7 (s), 136.9 (s), 133.2 (d), 130.1 (d), 129.4 (s), 128.8 (d), 127.5 (d), 120.5 (s), 80.2 (d), 76.7 (s), 61.6 (t), 28.3 (q), 24.7 (q), 14.1 (q).

General Procedure for the Preparation of 4-Aryl Quinolines (8-10,14): To a 0.5-2.0 mL microwave vial was added ethyl 2-(tert-butoxy)-2-(4-iodo-2-methylquinolin-3-yl)acetate (100 mg, 0.25 mmol), boronic acid (0.50 mmol), potassium carbonate (0.70 mmol), and tetrakis(triphenylphosphine)palladium(0) (0.05 mmol). The vial was immediately sealed then evacuated and charged with nitrogen three times. Dimethylformamide (800 µL) and water (80 µL) were then added via syringe. The reaction was heated to 90 ºC for a total of 3-16 hours and were monitored via HPLC and TLC. The reaction was cooled to ambient temperature then diluted with water (1 mL) and ethyl acetate (2 mL). The aqueous phase was removed, and the organic phase was filtered through a Celite® plug. The filtrate was washed with water (five 1 mL portions), dried over magnesium sulfate, gravity filtered, and concentrated to afford a crude oil. The residue was chromatographed over 12 g of silica gel eluted with hexanes-acetone (9:1→4:1→2:1). Product rich fractions were pooled and evaporated to isolate the 4-aryl quinoline products.



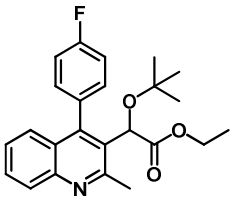
NGJ-9-018

ethyl 2-(tert-butoxy)-2-(2-methyl-4-phenylquinolin-3-yl)acetate (8a): yellow oil; IR (thin film) cm^{-1} 1749; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.05 (d, J = 8.4 Hz, 1H), 7.64 (ddd, J = 8.3, 4.4, 3.8 Hz, 1H), 7.55-7.48 (m, 4H), 7.34-7.31 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 172.6 (s), 159.4 (s), 146.8 (s), 146.5 (s), 136.2 (s), 130.7 (d), 129.9 (d), 129.6 (s), 129.2 (d), 128.5 (d), 128.45 (d), 128.4 (d), 128.0 (d), 126.7 (d), 126.3 (s), 125.7 (d), 76.0 (s), 70.8 (d), 61.3 (t), 28.1 (q), 24.9 (q), 14.1 (q).



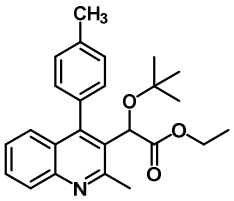
NGJ-7-059

ethyl 2-(tert-butoxy)-2-(4-(4-chlorophenyl)-2-methylquinolin-3-yl)acetate (8b): Yellow oil; IR (thin film) 1750 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.05 (d, J = 8.1 Hz, 1H), 7.66 (ddd, J = 8.3, 6.8, 1.4 Hz, 1H), 7.53 (m, 2H), 7.46 (m, 1H), 7.37 (ddd, 8.3, 6.8, 1.2 Hz, 1H), 7.29-7.26 (m, 2H), 5.10 (s, 1H), 4.19 (dq, J = 10.8, 7.2 Hz, 2H), 2.85 (s, 3H), 1.23 (t, J = 7.1, 3H), 1.00 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 172.4 (s), 159.4 (s), 146.8 (s), 145.2 (s), 134.7 (s), 134.6 (s), 132.3 (d), 131.2 (d), 129.6 (s), 129.3 (d), 128.8 (d), 128.7 (d), 128.3 (d), 126.3 (d), 126.1 (s), 125.9 (d) 76.1 (s), 70.8 (d), 61.4 (t), 28.1 (q), 24.9 (q), 14.1 (q).



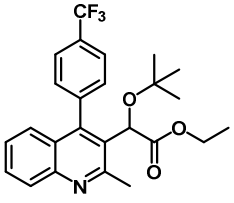
NGJ-8-098

ethyl 2-(tert-butoxy)-2-(4-(4-fluorophenyl)-2-methylquinolin-3-yl)acetate (8c): yellow oil; IR (thin film) 1752 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.04 (d, J = 8.3 Hz, 1H), 7.66 (ddd, J = 8.3, 6.7, 1.5 Hz, 1H), 7.50 (m, 1H), 7.37 (ddd, J = 8.3, 6.7, 1.5 Hz, 1H), 7.32-7.29 (m, 2H), 7.25-7.21 (m, 2H), 5.12 (s, 1H), 4.19 (qd, J = 10.8, 7.1 Hz, 2H), 2.85 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H), 0.99 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 172.5 (s), 163.9 (s), 161.5 (s), 159.4 (s), 146.8 (s), 145.5 (s), 132.6 (d, ^3J = 8 hz), 132.1 (s), 131.6 (d, ^3J = 8.0 hz), 128.5 (s, ^1J = 350 Hz), 129.3 (d), 128.6 (d), 126.4 (d), 125.9 (d), 115.6 (d, ^2J = 21 Hz), 115.1 (d, ^2J = 21 Hz), 76.1 (s), 70.8 (d), 61.4 (t), 28.1 (q), 24.9 (q), 14.1 (q).



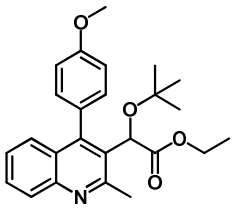
NGJ-9-019

ethyl 2-(tert-butoxy)-2-(2-methyl-4-(p-tolyl)quinolin-3-yl)acetate (8d): Yellow oil; IR (solid) 1750 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.03 (d, J = 8.4 Hz, 1H), 7.64 (ddd, J = 8.3, 6.2, 2.1 Hz, 1H), 7.39-7.32 (m, 5H), 7.22-7.20 (m, 1H), 5.19 (s, 1H), 4.19 (dq, J = 10.7, 7.1 Hz, 2H), 2.84 (s, 3H), 2.49 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H), 0.98 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 172.7 (s), 159.4 (s), 146.8 (s), 146.7 (s), 138.2 (s), 133.1 (s), 130.6 (d), 129.8 (d), 129.7 (s), 129.2 (d), 129.1 (d), 128.6 (d), 128.5 (d), 126.8 (d), 126.5 (s), 125.6 (d), 76.0 (s), 70.8 (d), 61.3 (t), 28.1 (q), 24.8 (q), 21.4 (q), 14.1 (q).



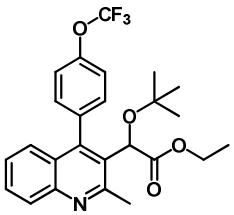
NGJ-9-020

ethyl 2-(tert-butoxy)-2-(2-methyl-4-(4-(trifluoromethyl)phenyl)quinolin-3-yl)acetate (8e): Yellow oil; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.07 (d, J = 8.4 Hz, 1H), 7.82 (m, 2H), 7.68 (m, 2H), 7.49 (m, 1H), 7.38 (ddd, J = 8.0, 6.4, 0.8 Hz, 1H), 7.22 (d, J = 8.2 Hz, 1H), 5.03 (s, 1H), 4.20 (dq, J = 10.8, 7.1 Hz, 2H), 2.87 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H), 1.00 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 172.2 (s), 159.4 (s), 146.7 (s), 145.0 (s), 140.2 (s), 131.4 (d), 130.7 (s, ^2J = 32 Hz), 130.2 (d), 129.5 (d), 127.6 (s, ^1J = 370 Hz), 128.6 (d), 126.2 (d), 125.8 (s), 125.5 (d, ^3J = 3.6 Hz), 124.9 (d, ^3J = 3.6 Hz), 76.2 (s), 70.8 (d), 61.5 (t), 28.0 (q), 24.8 (q), 14.1 (q).



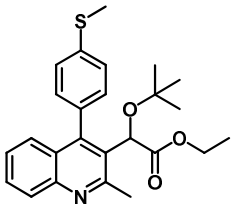
JDH-1-141

ethyl 2-(tert-butoxy)-2-(4-(4-methoxyphenyl)-2-methylquinolin-3-yl)acetate (8f): Yellow oil; ^{1}H NMR (CDCl3, 400MHz) δ: 8.04 (d, J = 8.3, 1H), 7.65 (ddd, J = 1.9, 6.3, 8.7 Hz, 1H), 7.31-7.46 (m, 3H), 7.23-7.27 (m, 1H), 7.03-7.09 (m, 2H), 5.21 (s, 1H), 4.19 (m, 1H), 3.92 (s, 3H), 2.83(s, 3H), 1.23 (t, J = 7.1 Hz, 3H) 0.98 (s, 9H)); ^{13}C NMR (CDCl3, 100MHz) δ: 172.7 (s), 159.6 (s), 159.5 (s), 146.8 (s), 146.4 (s), 132.0 (d), 131.2 (m), 129.1 (d), 128.5 (d),128.2 (2), 126.8 (d), 126.7 (s), 125.7 (d), 113.7 (d), 113.6 (d), 78.0 (s), 70.8 (d), 61.3 (t), 55.4 (q), 28.1 (q), 24.8 (q), 14.1 (q).



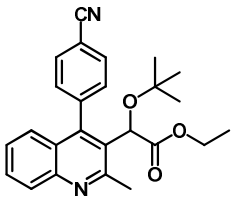
JDH-1-137

ethyl 2-(tert-butoxy)-2-(2-methyl-4-(4-(trifluoromethoxy)phenyl)quinolin-3-yl)acetate (8g): Yellow oil, IR (thin film) 1751 cm^{-1}; ^{1}H NMR (CDCl3, 400MHz) δ: 8.06 (d, J = 8.4 Hz, 1H), 7.67 (dd, J = 7.7, 8.4 Hz, 1H), 7.57 (dd, J = 1.6, 8.4 Hz, 1H), 7.34 – 7.44 (m, 4H), 7.29 (d, J = 8.4Hz, 1H), 5.07 (s, 1H), 4.19 (m, 2H), 2.86 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H), 0.99 (s, 9H); ^{13}C NMR (CDCl3, 100MHz) δ: 172.4 (s), 159.4 (s), 149.3 (s), 146.7 (s), 145.1 (s), 134.9 (s), 132.4 (d), 131.4 (d), 129.7 (s), 129.4 (d), 128.6 (d), 126.3 (d), 126.1 (d), 121.8 (s), 120.8 (d), 120.4 (d), 119.2 (s), 76.1 (s), 70.7 (d), 61.5 (t), 28.0 (q), 24.8 (q), 14.1 (q).



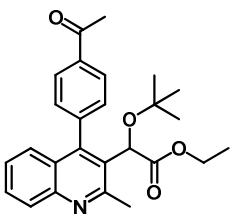
JDH-1-149

ethyl 2-(tert-butoxy)-2-(2-methyl-4-(4-(methylthio)phenyl)quinolin-3-yl)acetate (8h): Yellow oil, ^{1}H NMR ($CDCl_3$, 400MHz) δ: 8.04 (d, J = 8.4 Hz, 1H), 7.65 (ddd, J = 4.7, 4.1, 4.2, 4.2 Hz, 1H), 7.22 - 7.45 (m, 6H), 5.18 (s, 1H), 4.19 (m, 1H), 2.84 (s, 3H), 2.59 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H), 0.99 (s, 9H); ^{13}C NMR (CDCl3, 100MHz) δ: 172.6 (s), 159.5 (s), 146.8 (s), 146.0 (s), 139.3 (s), 132.6 (s), 131.2 (d), 130.3 (d), 129.8 (s), 129.2 (d), 128.6 (d), 126.6 (d), 126.4 (s), 125.9 (d), 125.8 (d), 125.5 (d), 76.1 (s), 70.8 (d), 61.4 (t), 29.7 (s), 28.1 (q), 24.8 (q), 15.4 (q), 14.2 (q).



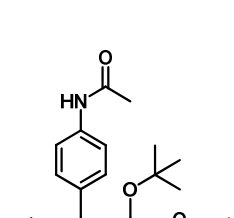
NGJ-8-078

ethyl 2-(tert-butoxy)-2-(4-(4-cyanophenyl)-2-methylquinolin-3-yl)acetate (8i): Black oil; IR (thin film) 2230, 1747 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.07 (d, J = 8.4 Hz, 1H), 7.86 (dd, J = 5.1, 1.1 Hz, 2H), 7.71-7.65 (m, 3H), 7.47-7.45 (m, 1H), 7.38 (dd, J = 8.1, 0.9 Hz, 1H), 4.98 (s, 1H), 4.19 (dq, J = 10.8, 7.1 Hz, 2H), 2.87 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H), 0.99 (s, 9H); ^{13}C NMR (DMSO-d6, 100 MHz) δ: 172.1 (s), 159.3 (s), 146.8 (s), 144.4 (s), 141.4 (s), 132.2 (d), 131.9 (d), 131.7 (d), 130.6 (d), 129.6 (d), 129.2 (s), 128.8 (d), 127.9 (d), 126.3 (d), 125.4 (s), 118.4 (s), 112.6 (s), 76.2 (s), 70.8 (d), 61.6 (t), 28.0 (q), 24.9 (q), 14.1 (q).



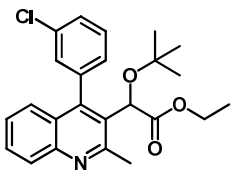
NGJ-8-072

ethyl 2-(4-(4-acetylphenyl)-2-methylquinolin-3-yl)-2-(tert-butoxy)acetate (8j): White Solid; IR (thin film) 1750, 1684 cm^{-1}; mp 135-137ºC; ^{1}H NMR (CDCl3, 400 MHz) δ: 8.14 (dd, J = 7.3, 1.3 Hz, 2H), 8.06 (d, J = 8.5 Hz, 1H), 7.67 (ddd, J = 8.2, 6.9, 1.3 Hz, 1H), 7.63 (dd, J = 8.8, 1.7 Hz, 1H), 7.45 (dd, 8.7, 1.5 Hz, 1H), 7.36 (ddd, J = 8.2, 6.8, 1.1 Hz, 1H), 7.23 (dd, J = 8.4, 0.7 Hz, 1H), 5.05 (s, 1H), 4.19 (qd, J = 10.8, 7.1 Hz, 2H), 2.85 (s, 3H), 2.73 (s, 3H), 1.24 (t, J = 7.1, 3H), 0.98 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 197.6 (s), 172.3 (s), 159.4 (s), 146.8 (s), 145.3 (s), 141.4 (s), 136.9 (s), 131.3 (d), 130.2 (d), 129.4 (d), 129.3 (s), 128.7 (d), 128.4 (d), 127.9 (d), 126.2 (d), 126.0 (d), 125.7 (s), 76.1 (s), 70.8 (d), 61.5 (t), 28.1 (q), 26.7 (q), 24.9 (q), 14.2 (q).



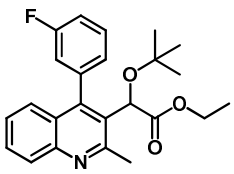
NGJ-8-082

ethyl 2-(4-(4-acetamidophenyl)-2-methylquinolin-3-yl)-2-(tert-butoxy)acetate (8k): yellow oil; IR (thin film) 1747, 1673 cm^{-1}; ^{1}H NMR (CDCl3, 400 MHz) δ: 8.04 (d, J = 8.4, 1H), 7.93 (s, 1H, N-H), 7.76 (d, J = 8.7, 2H), 7.64 (ddd, J = 8.3, 5.4, 3.1 Hz, 1H), 7.46 (dd, J = 9.3, 2.2 Hz, 1H), 7.36-7.34 (m, 2H), 7.28 (d, J = 2.1, 1H), 5.19 (s, 1H), 4.19 (dq, 10.8, 7.1, 2H), 2.84 (s, 3H), 2.25 (s, 3H), 1.22 (t, J = 7.1, 3H), 0.97 (s, 9H); ^{13}C NMR (DMSO-d6, 100 MHz) δ: 172.6 (s), 168.8 (s), 159.4 (s), 146.7 (s), 146.2 (s), 138.5 (s), 131.6 (s), 131.4 (d), 130.6 (d), 129.8 (s), 129.3 (d), 128.3 (d), 126.7 (d), 126.4 (s), 125.8 (d), 119.3 (d), 118.9 (d), 76.1 (s), 70.8 (d), 61.4 (t), 28.1 (q), 24.72 (q), 24.70 (q), 14.1 (q).



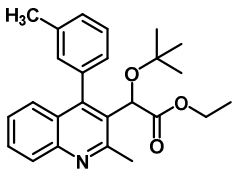
AH-3-39

ethyl 2-(tert-butoxy)-2-(4-(3-chlorophenyl)-2-methylquinolin-3-yl)acetate (9b): The product was isolated as an 1:0.80 mixture of atropisomers using the peaks at 2.86 and 2.85 ppm. Orange-red oil. IR (thin film) 1640 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.04 (d, J = 7.2 Hz, 1H), 7.67 (m,1H), 7.52 (m, 1H), 7.49 (m, 1H), 7.44 (m, 1H), 7.38 (m, 1H) 7.38 (m, 1H), 7.30 (m, 1H), 5.07 (minor), 5.06 (major) (s, 1H), 4.19 (m, 2H), 2.86 (major), 2.85 (minor) (s, 3H), 1.23 (dt, J = 7.2, 16.7 Hz, 3H), 1.01 (minor), 1.00 (major) (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [172.39, 172.06] (s), 159.51 (s), 146.75 (s), 145.01 (s), 138.10 (s), [134.58, 134.11] (s), 131.07 (d), [129.85, 129.79] (d), [129.55, 129.48] (s), [129.42, 129.28] (d), 129.03 (d), [128.65, 128.62] (d), 127.85 (d), 126.34 (d), [126.07, 126.01] (d), [125.97, 125.88] (s), 76.13 (s), 70.76 (d), [61.52, 61.42] (t), [28.07, 28.03] (q), [24.90, 24.83] (q).



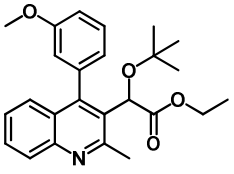
AH-3-44

ethyl 2-(tert-butoxy)-2-(4-(3-fluorophenyl)-2-methylquinolin-3-yl)acetate (9c): The product was isolated as an 1:0.78 mixture of atropisomers using the peaks at 2.86 and 2.85 ppm. Orange-red oil. IR (thin film) 1751 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.05 (d, J = 8.4 Hz, 1H), 7.67 (m, 1H), 7.49 (m, 1H), 7.32 (m, 1H), 7.32 (m, 1H), 7.32 (m, 1H), 7.32 (m, 1H), 7.09 (m, 1H), 5.12 (minor), 5.10 (major) (s, 1H), 4.19 (m, 2H), 2.86 (major), 2.85 (minor) (s, 3H), 1.23 (q, J = 6.4, 3H), 1.00 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [172.40, 172.17] (s), [163.86, 163.42, 161.40, 160.95] (s), [159.44, 159.43] (s), 146.70 (s), [145.16, 145.10] (s), [138.46, 138.39, 138.38, 138.32] (s), [133.83, 133.64] (d), [132.15, 132.06, 132.02, 131.99] (d), [130.27, 130.18, 130.13, 129.70, 129.62, 129.43] (d), [129.51, 129.49] (s), [128.70, 128.60, 128.56, 128.53, 128.47, 128.45] (d), [126.68, 126.65, 126.06, 126.01] (d), [126.38, 126.36, 125.61, 125.58] (s), [125.61, 125.58] (s), [118.32, 118.10, 115.63, 115.59, 115.42, 115.38] (d), [117.13, 116.92] (d), [76.15, 76.11] (s), [70.77, 70.76] (d), [61.51, 61.43] (t), 28.06 (q), [24.82, 24.80] (q), [14.13, 14.10] (q).



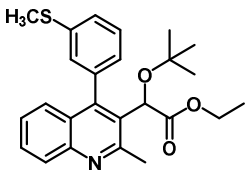
AH-3-59

ethyl 4,6-dihydroxy-2-methylquinoline-3-carboxylate (9d): The product was isolated as a 1:0.91 mixture of atropisomers using the peaks at 5.16 and 5.15. Yellow Oil; IR (thin film) 1749 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.04 (d, J = 8.4 Hz, 1H), 7.64 (m, 1H), 7.48-7.26 (m, 4H), 7.15-7.04 (m, 2H), 5.16 major, 5.15 minor (s, 1H), 4.15 (m, 2H), 2.86 major, 2.85 minor (s, 3H), 2.43 major, 2.42 minor (s, 3H), 1.24 major, 1.21 minor (t, J = 7.1 Hz, 3H), 0.99 major, 0.98 minor (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [172.64, 172.51] (s), [159.47, 159.44] (s), [146.93, 146.65] (s), 138.04 (s), 137.58 (s), [136.09, 136.06] (s), 131.38 (d), 130.47 (d), 129.70 (s), [129.28, 129.23] (d), [129.19, 129.09] (d), [128.34, 128.32] (d), [127.85, 127.75] (d), [126.86, 126.82] (d), [126.41, 126.35] (s), 125.72 (d), 76.03 (s), [70.87, 70.82] (d), [61.37, 61.20] (t), [28.10, 28.01] (q), [24.75, 24.69] (q), [21.53, 21.42] (q), [14.23, 14.13] (q).



AH-3-27

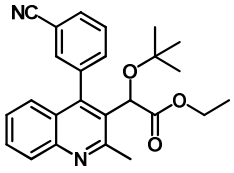
ethyl 2-(tert-butoxy)-2-(4-(3-methoxyphenyl)-2-methylquinolin-3-yl)acetate (9f): The product was isolated as an 1:0.72 mixture of atropisomers using the peaks at 0.98 and 0.96 ppm. Orange Oil; IR (thin film) 1749 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.45 (d, J = 8.4 Hz, 1H), 7.65 (m, 1H), 7.45 (m, 4H), 7.37 (m, 1H), 7.06 (m, 1H), 5.20 (major), 5.19 (minor) (s, 1H), 4.19 (q, J = 7.2 Hz, 2H), 3.84 (major) 3.82 (minor) (s, 3H), 2.85 (s, 3H), 1.22 (dt, J = 7.2, 5.4 Hz, 3H), 1.01 (minor), 1.00 (major) (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ:[172.62, 172.57] (s), [159.57, 159.45, 159.43, 159.06] (s), [146.64, 146.63, 146.58, 146.50] (s), [137.45, 137.44] (s), [132.15, 132.06] (s), 129.93 (s), [129.61, 129.53, 129.50] (d), [129.28, 129.06] (d), [128.60, 128.48, 128.35, 128.33] (d), [126.78, 126.75, 125.83, 125.80] (d), [126.78, 126.75] (d), 126.20 (s), [125.83, 125.80] (d), [123.15, 122.22] (d), [116.31, 115.36] (d), [114.28, 114.13] (d), 76.07 (s), [70.89, 70.83] (d), [61.42, 61.35] (t), [55.35, 55.28] (q), [28.12, 28.10] (q), [24.72, 24.71] (q), [14.18, 14.13] (q).



AH-3-60

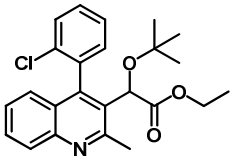
ethyl 2-(tert-butoxy)-2-(2-methyl-4-(3-(methylthio)phenyl)quinolin-3-yl)acetate (9h): The product was isolated as a 1:0.76 mixture of atropisomers using the peaks at 5.16 and 5.14.. Yellow Oil; IR (thin film) 1748 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.04 (d, J = 8.5 Hz, 1H), 7.65 (m, 1H), 7.49-7.22 (m, 5H), 7.20-7.05 (m, 1H), [5.16, 5.14] (s, 1H), 4.15 (m, 2H), [2.85, 2.84] (s, 3H), [2.50, 2.47] (s, 3H), 1.23 (m, 3H), [1.00, 0.99] (s, 9H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ: [172.50, 172.49] (s), 159.43 (s), [146.85, 146.72] (s), [139.30, 138.64] (s), [136.92, 136.80] (s), [131.39, 130.48] (d), [129.54, 129.50] (s), [129.30, 129.17] (d), [129.09, 129.06] (d), [128.48, 128.40] (d), [128.31, 128.20] (d), [126.84, 126.66] (d), [126.36, 126.27] (d), [126.40, 126.14] (s), [125.84, 125.68] (d), [76.11, 76.08] (s), [70.87, 70.84] (d), [61.47, 61.36] (t), [28.10, 28.01] (q), [24.83, 24.78] (q), [21.53, 21.42] (q), [14.22, 14.13] (q).



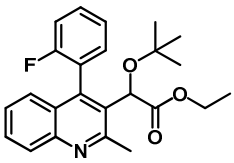
AH-3-41

ethyl 2-(tert-butoxy)-2-(4-(3-cyanophenyl)-2-methylquinolin-3-yl)acetate (9i): The product was isolated as an 1:0.79 mixture of atropisomers using the peaks at 4.99 and 4.97 ppm. Orange-red oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.07 (d, J = 8.3 Hz, 1H), 7.84 (m, 1H), 7.84 (m, 1H), 7.68 (dt, J = 7.7, 1.4 Hz, 1H), 7.66 (m, 1H), 7.61 (m, 1H), 7.40 (m, 1H), 7.17 (m, 1H), 4.99 (minor), 4.97 (major) (s, 1H), 4.17 (m, 2H), 2.88 (major), 2.27 (minor) (s, 3H), 1.25 (dt, J = 14.4, 7.2 Hz, 3H), 1.00 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [172.14, 171.48] (s), [159.34, 159.26] (s), [146.73, 146.71] (s), [144.04, 143.98] (s), [137.80, 137.77] (s), [135.40, 133.98] (d), 134.52 (d), 133.12 (s), 129.68 (s) 129.43 (d), [128.94, 128.75] (d), [126.42, 126.36] (d), [125.88, 125.85] (d), [118.28, 118.19] (s), [112.91, 112.44] (s), [76.26, 76.22] (s), [70.70, 70.66] (d), [61.68, 61.57] (t), [28.03, 28.01] (d), [24.85, 24.81] (q), [14.15, 14.14] (q).



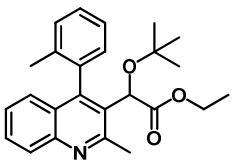
KM-1-65

ethyl 2-(tert-butoxy)-2-(4-(2-chlorophenyl)-2-methylquinolin-3-yl)acetate (10b): The product was isolated as an 1:0.97 mixture of atropisomers using the peaks at 5.11 and 5.08. Orange Oil: IR (thin film) 1748 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.05 (d, J = 8.4 Hz, 1H), 7.64 (td, J = 6.8, 1.2 Hz, 1H), 7.61-7.28 (m, 5H), 7.28-7.10 (m, 1H), 5.11 major, 5.08 minor (s, 1H), 4.10 (m, 2H), 3.00 major, 2.90 minor (s, 3H), 1.22 major, 1.15 minor (t, J = 7.1 Hz, 3H), 1.11 major, 1.05 minor (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [172.50, 171.82] (s), [159.61, 159.55] (s), [146.67, 146.58] (s), [144.36, 144.92] (s), [137.25, 137.14] (s), [134.99, 134.96] (s), [133.84, 133.64] (d), [130.18, 129.94] (d), [129.88, 129.86] (d), [129.46, 129.37] (d), [129.43, 129.34] (s), [128.61, 128.53] (d), [126.66, 126.56] (d), [126.28, 125.95] (d), [126.11, 126.10] (d), [125.77, 127.35] (d), [76.27, 75.84] (s), [71.26, 70.84] (d), [61.34, 61.18] (t), [28.16, 27.95] (q), [25.32, 24.97] (q), [14.13, 13.99] (q).



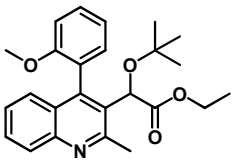
AH-3-70

ethyl 2-(tert-butoxy)-2-(4-(2-fluorophenyl)-2-methylquinolin-3-yl)acetate (10c): The product was isolated as an 1:0.66 mixture of atropisomers using the peaks at 2.95 and 2.86. Orange Oil: IR (thin film) 1749 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.05 (d, J = 8.4 Hz, 1H), 7.66 (ddt, J = 8.4, 6.7, 1.6 Hz, 1H), 7.58-7.43 (m, 2H), 7.42-7.16 (m, 4H), 5.14 major, 5.13 minor (s, 1H), 4.13 (m, 2H), 2.95 minor, 2.86 major (s, 3H), 1.23 major, 1.13 minor (t, J = 7.1 Hz, 3H), 1.08 minor, 1.01 major (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [172.40, 171.78] (s), [161.81, 160.57, 159.33, 158.11] (s), [159.71, 159.38] (s), [146.71 146.48] (s), [141.11, 140.92] (s), [132.86, 132.83] (d), [131.04, 130.31] (d), [130.98, 130.90, 130.76, 130.67] (d), [130.37, 130.31] (s), [129.43, 129.39] (d), [128.67, 128.61] (d), [126.29, 125.76] (s), [126.15, 126.06, 125.96, 125.91] (d), [124.25, 124.22, 123.88, 123.85] (d), [124.10, 123.79, 123.63] (s), [116.10, 115.99, 115.88, 115.77] (d), [76.19, 75.88] (s), [71.20, 70.80] (d), [61.42, 61.22] (t), [28.09, 27.82] (q), [25.17, 24.81] (q), [14.13, 13.82] (q).



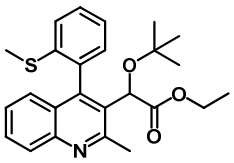
AH-3-64

ethyl 2-(tert-butoxy)-2-(2-methyl-4-(o-tolyl)quinolin-3-yl)acetate (10d): The product was isolated as an 1:0.78 mixture of atropisomers using the peaks at 5.14 and 5.12. Yellow Oil: IR (thin film) 1750 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.07 (d, J = 8.4 Hz, 1H), 7.63 (ddd, J = 8.3, 6.8, 1.4 Hz, 1H), 7.48-7.28 (m, 3H), 7.25-6.98 (m, 3H), 5.14 major, 5.12 minor (s, 1H), 4.14 (m, 2H), 2.93 minor, 2.89 major (s, 3H), 1.97 minor, 1.90 major (s, 3H), 1.22 major, 1.15 minor (t, J = 7.1 Hz, 3H), 1.11 minor, 1.00 major (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [172.85, 172.48] (s), [159.94, 159.91] (s), [147.29, 146.65] (s), [146.38, 146.27] (s), [137.86, 137.41] (s), [135.68, 135.37] (s), [130.38, 130.31] (d), [129.55, 129.44] (d), [129.49, 129.33] (s), [128.79, 128.69] (d), [128.31, 128.15] (d), 126.83 (d), [126.54, 126.39] (d), [126.17, 125.81] (s), [126.13, 126.08] (d), [125.71, 125.54] (d), [76.37, 75.65] (s), [71.26, 70.69] (d), [61.29, 61.20] (t), [28.44, 27.06] (q), [24.77, 24.53] (q), [20.37, 19.85] (q), [14.11, 14.01] (q).



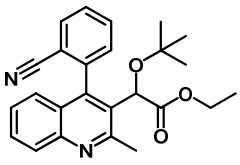
AH-3-66

methyl 2-(tert-butoxy)-2-(4-(2-methoxyphenyl)-2-methylquinolin-3-yl)acetate (10f): The product was isolated as an 1:0.84 mixture of atropisomers using the peaks at 5.16 and 5.09. Yellow Oil: IR (thin film) 1744 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.03 (dd, J = 8.4, 5.4 Hz, 1H), 7.61 (m, 1H), 7.50 (m, 1H), 7.29 (m, 3H), 7.10 (t, J = 7.4 Hz, 1H), 7.04 (t, J = 7.8 Hz, 1H), 5.16 major, 5.14 minor (s, 1H), 4.15 (m, 2H), 3.60 minor, 3.58 major (s, 3H), 2.96 minor, 2.85 major (s, 3H), 1.21 major, 1.20 minor (t, J = 7.1 Hz, 3H), 1.02 minor, 0.99 major (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [172.65, 171.72] (s), [159.82, 159.50] (s), [157.62, 156.44] (s), [146.94, 146.40] (s), [144.29, 143.93] (s), [132.28, 131.14] (d), [130.29, 130.22] (d), [129.97, 129.69] (s), [129.05, 128.95] (d), [128.44, 128.40] (d), [126.66, 126.47] (d), [126.43, 126.23] (s), 125.54 (d), [124.85, 124.66] (s), [120.44, 120.24] (d), [110.84, 110.54] (d), [76.23, 75.67] (s), [71.73, 70.94] (d), [61.25, 60.96] (t), [55.04, 54.83] (q), [28.18, 27.75] (q), [25.39, 24.80] (q), [14.13, 14.09] (q).



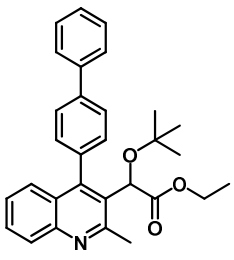
AH-3-67

ethyl 2-(tert-butoxy)-2-(2-methyl-4-(2-(methylthio)phenyl)quinolin-3-yl)acetate (10h): The product was isolated as an 1:0.84 mixture of atropisomers using the peaks at 5.16 and 5.09. Yellow-Orange Oil: IR (thin film) 1743 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.03 (d, J = 8.4 Hz, 1H), 7.63 (ddt, J = 8.2, 6.8, 1.4 Hz, 1H), 7.50 (tdd, J = 8.0, 3.5, 1.6 Hz, 1H), 7.42-7.2 (m, 4H), 7.13 (m, 1H), 5.09 minor, 5.08 major (s, 1H), 4.13 (m, 2H), 2.98 minor, 2.90 major (s, 3H), 2.29 minor, 2.28 major (s, 3H), 1.21 major, 1.16 minor (t, J = 7.1 Hz, 3H), 1.09 minor, 1.05 major (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [172.69, 171.77] (s), [159.96, 159.82] (s), [146.80, 146.64] (s), [145.37, 144.38] (s), [139.86, 138.75] (s), 131.43 (d), [129.60, 129.29] (d), [129.52, 129.19] (s), [129.28, 129.12] (d), [128.68, 128.58] (d), 126.65 (d), 126.22 (d), [125.84, 125.58] (s), [125.79, 125.77] (d), [76.32, 75.76] (s), [71.55, 70.88] (d), [61.19, 61.04] (t), [28.29, 27.94] (q), [25.46, 25.01] (q), [16.04, 15.41] (q), [14.10, 14.02] (q).



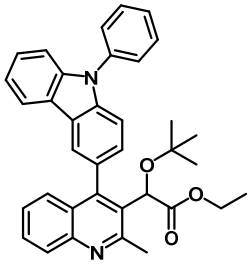
KM-1-67

ethyl 2-(tert-butoxy)-2-(4-(2-cyanophenyl)-2-methylquinolin-3-yl)acetate (10i): The product was isolated as an 1:0.67 mixture of atropisomers using the peaks at 5.10 and 4.99. Orange Oil: IR (thin film) 1748 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.07 minor, 8.06 major (d, J = 8.4 Hz, 1H), 7.90-7.83 (m, 1H), 7.80-7.59 (m, 3H), 7.45-7.29 (m, 2H), 7.12 minor, 7.03 major (dd, J = 8.4, 0.8, 1H), 5.10 minor, 4.99 major (s, 1H), 4.15 (m, 2H), 2.99 major, 2.91 minor (s, 3H), 1.23 major, 1.17 minor (t, J = 7.1 Hz, 3H), 1.12 major, 1.05 minor (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [172.17, 171.63] (s), [159.25, 159.62] (s), [146.76, 146.73] (s), [143.12, 142.42] (s), [140.72, 139.98] (s), [132.85, 132.45] (d), [132.44, 132.21] (d), 129.92 (d), [129.74, 129.70] (d), 129.61 (s), [129.16, 128.97] (d), [128.86, 128.77] (d), [126.59, 126.56] (d), [125.41, 125.26] (d), [177.54, 117.16] (s), [115.28, 113.90] (s), [76.75, 76.06] (s), [70.81, 70.67] (d), [61.52, 61.39] (t), [27.92, 27.91] (q), [25.12, 24.960] (q), [14.11, 14.06] (q).



NGJ-8-084

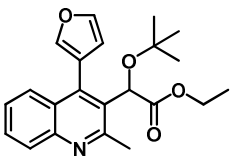
ethyl 2-(4-([1,1'-biphenyl]-4-yl)-2-methylquinolin-3-yl)-2-(tert-butoxy)acetate (14a): Yellow oil; IR (thin film) 1747, 1721 cm^{-1}; ^1H NMR (CDCl3, 400 MHz) δ: 8.06 (d, J = 8.4 Hz, 1H), 7.79-7.77 (m, 2H), 7.74 (m, 2H), 7.66 (ddd, J = 8.2, 6.6, 1.5, 1H), 7.58 (m, 1H), 7.53-7.49 (m, 2H), 7.44-7.35 (m, 4H), 5.22 (s, 1H), 4.21 (dq, J = 10.8, 7.1 Hz, 2H), 2.86 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H), 0.99 (s, 9H); ^{13}C NMR (DMSO-d6, 100 MHz) δ: 172.6 (s), 159.5 (s), 146.8 (s), 146.3 (s), 140.3 (s), 135.2 (s), 131.2 (d), 130.4 (d), 129.7 (s), 129.2 (d), 129.0 (d), 128.6 (d), 127.8 (d), 127.1 (d), 127.0 (d), 126.7 (d), 126.5 (d), 126.3 (s), 125.8 (d), 76.1 (s), 70.9 (d), 61.4 (t), 28.1 (q), 24.9 (q), 14.2 (q).



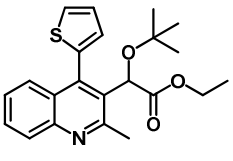
NGJ-9-025

ethyl 2-(tert-butoxy)-2-(2-methyl-4-(9-phenyl-9H-carbazol-3-yl)quinolin-3-yl)acetate (14b): The product was isolated as an 1.0:0.8 of atropisomers using peaks at 5.36 and 5.32 ppm; Yellow oil; IR (thin film) 1747 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.30 (d, J = 1.3 Hz, 1H), 8.10-8.06 (m, 2H), 7.68-7.62 (m, 5H), 7.56-7.45 (m, 5H), 7.40-7.30 (m, 3H) 5.36 (major), 5.32 (minor) (s, 1H), 4.30 (minor), 4.19 (major) (dq, J = 10.7, 7.1 Hz, 2H), 2.91 (major), 2.89 (minor) (s, 3H), 1.35 (major), 1.22 (minor) (t, J = 7.1 Hz, 3H), 0.98 (minor), 0.96 (major) (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [172.8, 172.7] (s), [159.6,

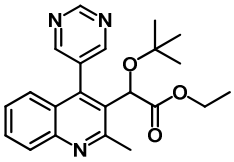
159.5] (s), 147.4 (s), [146.9, 146.8] (s), [141.5, 141.4] (s), [140.6, 140.5] (s), [137.5, 137.4] (s), 130.2 (s), 130.1 (d), 129.1 (d), 128.54 (d), 128.52 (d), 127.84 (d), [127.82, 127.79] (d), [127.61, 127.59] (s), [127.15, 127.12] (d), [126.56, 126.54] (d), [125.7, 125.6] (d), 123.4 (s), 123.1 (s), 122.9 (s) 122.8 (d), 129.1 (d), 120.4 (d), [120.35, 120.32] (d), [110.20, 110.17] (d), 109.7 (d), 109.2 (d), [76.10, 75.98] (s), [71.0, 70.9] (d), [61.4, 61.3] (t), [28.18, 28.17] (q), [25.0, 24.9] (q), [14.4, 14.2] (q).


AH-3-33

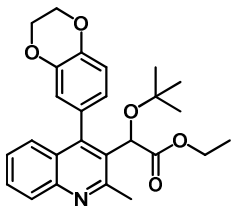
ethyl 4,6-dihydroxy-2-methylquinoline-3-carboxylate (14c): Orange oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.02 (d, J = 8.2 Hz, 1H), 7.49 (m, 1H), 7.49 (m, 1H), 7.49 (m, 1H), 7.37 (m, 1H), 7.37 (m, 1H), 6.62 (s, 1H), 5.45 (s, 1H), 4.22 (dq, J = 10.8, 7.2 Hz, 1H), 4.17 (dq, J = 10.8, 7.2 Hz, 1H), 2.82 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H), 1.02 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 172.5 (s), 159.3 (s), 146.7 (s), 143.3 (d), 132.2 (s), 130.8 (d), 129.3 (d), 128.6 (s), 128.4 (d), 126.3 (d), 125.9 (d), 119.8 (s), 113.0 (d), 76.1 (s), 70.7 (d), 61.4 (t), 28.0 (q), 24.8 (q), 14.2 (q).


AH-3-49

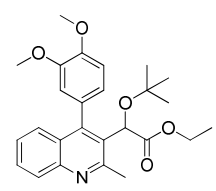
ethyl 2-(tert-butoxy)-2-(2-methyl-4-(thiophen-2-yl)quinolin-3-yl)acetate (14d): The product was isolated as an 1:0.13 mixture of atropisomers using the peaks at 2.85 and 2.83. Red-Orange Oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.10 (d, J = 8.4 Hz, 1H), 7.95 (d, J = 8.3 Hz, 1H), 7.67 (m, 1H), 7.67 (m, 1H), 7.54 (m, 1H), 7.46 (m, 1H), 7.33 (m, 1H), 5.93 (s, 1H), 4.18 (m, 2H), 2.85 (minor), 2.83 (major) (s, 3H), 1.28 (minor), 1.25 (major) (s, 9H), 1.18 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 171.30 (s), 158.78 (s), 146.68 (s), 137.23 (s), 136.85 (s), [133.83, 133.63] (d), 133.18 (d), 133.02 (s), [132.15, 132.05, 131.97, 131.94] (d), 130.09 (d), 129.38 (s), [128.78, 128.70] (d), [128.57, 128.52, 128.45] (d), 127.46 (d), 80.26 (s), [70.79, 70.36] (d), [61.56, 61.38] (t), [28.34,28.11] (q), 24.69 (q), 14.08 (q).


NGJ-9-003

ethyl 2-(tert-butoxy)-2-(2-methyl-4-(pyrimidin-5-yl)quinolin-3-yl)acetate (14e): yellow oil; IR (thin film) 1743 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 9.40 (s, 1H), 8.90 (d, J = 2.8 Hz, 1H), 8.69 (d, J = 2.8, 1H), 8.10 (d, J = 8.4 Hz, 1H), 7.73 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 7.44 (ddd, J = 8.5, 6.9, 1.2 Hz, 1H), 7.20 (d, J = 8.4 Hz, 1H), 5.04 (s, 1H), 4.16 (dq, 10.9, 7.1, 2H), 2.91 (t, J = 7.1, 3H), 1.23 (s, 3H), 1.04 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 171.7 (s), 158.7 (s), 158.5 (d), 158.4 (d), 156.8 (d), 146.8 (s), 139.3 (s), 130.7 (s), 130.6 (s), 129.9 (d), 129.0 (d), 126.7 (d), 126.1 (s), 125.3 (d), 76.5 (s), 70.5 (d), 61.7 (t), 28.0(q), 24.9 (q), 14.1 (q).


NGJ-8-099

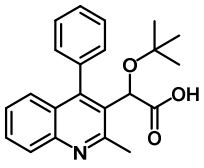
ethyl 2-(tert-butoxy)-2-(4-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-2-methylquinolin-3-yl)acetate (14f): The product was isolated as an indistinguishable mixture of atropisomers. Yellow oil; IR (thin film) 1747, 1673 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.03 (d, J = 8.3, 1H), 7.64 (dt, J = 6.9, 1.4 Hz, 1H), 7.47-7.35 (m, 2H), 7.04-6.96 (m, 2H), 6.84-6.78 (m, 1H), 5.25 (s, 1H), 4.38-4.30 (m, 4H) 4.24-4.11 (m, 2H), 2.83 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H), 1.01 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [172.7, 172.5] (s), 159.4 (s), 146.8 (s), 146.1 (s), [143.7, 143.6] (s), 143.5 (s), 143.0 (s), 129.8 (s), [129.2, 129.1] (d), [128.47, 128.46] (d), [126.82, 126.78] (d), [126.55, 126.46] (s), [125.68, 125.64] (d), 124.0 (d), 123.1 (d), 120.0 (d), [119.95, 119.77] (d), 118.95 (d), [117.45, 117.29] (d), 116.7 (d), 115.5 (d), [76.02, 75.98] (s), [70.83, 70.80] (d), [64.49, 64.47] (t), [64.44, 64.36] (t), [61.38, 61.31] (t), 28.1 (q), 24.8 (q), 14.13 (q).


NGJ-9-091

ethyl 2-(tert-butoxy)-2-(4-(3,4-dimethoxyphenyl)-2-methylquinolin-3-yl)acetate (14g): The product was isolated as an 1:1 mixture of atropisomers using the peaks at 3.95 and 3.92 ppm. Brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.04 (d, J = 8.5 Hz, 1H), 7.65 (ddd, J = 9.4, 6.8, 1.2 Hz,1H), 7.44 (dd, J = 8.5, 1.1 Hz, 1H), 7.37 (ddd, J = 9.8, 6.7, 1.4, 1H), 7.11-7.02 (m, 2H), 6.96-6.84 (m, 1H), 5.25-5.26 (s, 1H), 4.20 (dq, J = 10.3, 7.1, 2H), 4.00 (s, 3H), 3.95-3.92 (s, 1H), 3.86-3.83 (s, 3H), 2.84 (s, 3H), 1.24 (s, 3H), 1.01-0.99 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [172.9, 172.7] (s), [159.5, 159.4] (s), [149.1, 148.3]

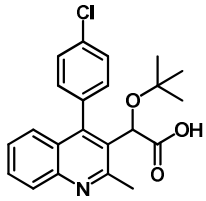
(s), [149.0, 148.9] (s), [148.8, 148.4] (s), [146.84, 146.78] (s), [146.5, 146.3] (s), [129.89, 129.86] (s), [129.2, 129.1] (d), [128.6, 128.45] (s), [128.6, 128.51] (d), [126.8, 126.7] (d), [126.6, 126.5] (s), [125.74, 125.70] (d), [123.3, 122.5] (d), [114.1, 113.3] (d), [111.5, 110.4] (d), [111.0, 110.5] (d), [76.04, 75.97] (s), [70.9, 70.8] (d), [61.4, 61.3] (t), [56.00, 55.98] (q), [55.94, 5.88] (q), [28.13, 28.09] (q), [24.86, 24.82] (q), [14.25, 14.16] (q).

General Procedure for Ethyl Ester Hydrolysis (11-13,15): To a solution of ethyl ester quinoline (1.0 equiv.) and ethanol (3.5 mL) was added aqueous 50% sodium hydroxide (3 equiv.). The reaction was heated to 60 ºC and was stirred until 100% conversion was observed by HPLC. The solution was cooled to ambient temperature and was neutralized with 1N HCl to pH 5. The solution was extracted with chloroform-d_6 (two 0.5-mL portions) and the combined organic phase was dried over magnesium sulfate, filtered, and examined via ^{1}H-NMR. Carboxylic acid products requiring purification were chromatographed over 4g of silica gel eluted with dichloromethane-methanol (0% methanol→5% methanol→10% methanol). Product rich fractions were pooled and evaporated to afford desired acids (10-13, and 15).



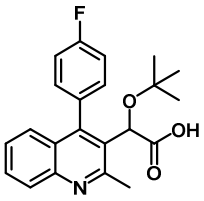
NGJ-9-021

2-(tert-butoxy)-2-(2-methyl-4-phenylquinolin-3-yl)acetic acid (11a): yellow oil; IR (thin film) 1719 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.96 (s, 1H, O-H), 8.11 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 6.7 Hz, 1H), 7.66 (ddd, J = 8.3, 6.3, 2.0 Hz, 1H), 7.58-7.51 (m, 3H), 7.41-7.33 (m, 3H), 5.29 (s, 1H), 2.88 (s, 3H), 0.97 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 173.2 (s), 158.5 (s), 148.2 (s), 146.1 (s), 135.6 (s), 131.3 (d), 129.77 (d), 129.75 (d), 129.2 (s), 128.8 (d), 128.7 (d), 127.9 (d), 127.8 (d), 126.8 (d), 126.3 (s), 126.2 (d), 70.7 (d), 28.1 (q), 24.1 (q).



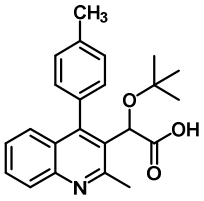
NGJ-7-060

2-(tert-butoxy)-2-(4-(4-chlorophenyl)-2-methylquinolin-3-yl)acetic acid (11b): white solid; mp 122-125 ºC, IR (thin film) 1730, 3060 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.16 (d, J = 8.3 Hz, 1H), 7.71 (ddd, J = 8.3, 6.8, 1.4 Hz, 1H), 7.68 (m, 1H), 7.56 (dd, J = 9.2, 2.1, 1H), 7.54 (dd, J = 9.2, 2.1, 1H), 7.43 (ddd, J = 8.3, 6.7, 0.8, 1H), 7.37 (dd, 8.3, 0.8 Hz, 1H), 7.29 (dd, J = 8.1, 2.2, 1H), 5.24 (s, 1H), 2.89 (s, 3H), 1.02 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 172.1 (s), 158.2 (s), 147.5 (s), 135.2 (s), 133.8 (s), 132.8 (d), 130.9 (d), 130.3 (d), 129.3 (s), 128.8 (s), 128.3 (d), 127.7 (d), 126.7 (d), 126.5 (d), 126.0 (s) 77.9 (s), 70.6 (d), 28.2 (q), 24.1 (q); Exact mass calcd for $C_{22}H_{22}ClNO_3$ $[M+H]^+$, 384.136098. Found 384.136414.



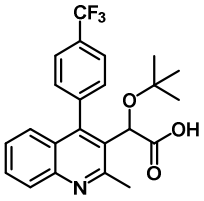
NGJ-8-100

2-(tert-butoxy)-2-(4-(4-fluorophenyl)-2-methylquinolin-3-yl)acetic acid (11c): yellow oil; IR (thin film) 1730 1724 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.17 (d, J = 8.2 Hz, 1H), 7.75 (dd, J = 5.7 Hz, 1H), 7.66 (ddd, J = 8.0, 5.5, 1.6 Hz), 7.41-7.22 (m, 5H), 5.22 (s, 3H), 2.93 (s, 3H), 0.99 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 174.0 (s), 164.1 (s), 161.7 (s), 159.0 (s), 147.5 (s), 144.8 (s), 133.2 (d), 131.5 (d), 131.4 (s), 130.8 (s), 130.1 (d), 126.9 (d), 126.6 (d), 115.9 (d), 115.1 (d), 76.7 (s), 70.7 (d), 28.1 (q), 23.4 (q); HRMS (ESI+): Exact mass calcd for $C_{22}H_{22}FNO_3$ $[M+H]^+$, 368.165648. Found 368.165826.



NGJ-9-022

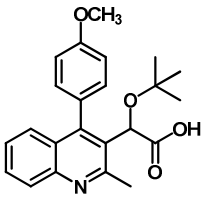
2-(tert-butoxy)-2-(2-methyl-4-(p-tolyl)quinolin-3-yl)acetic acid (11d): clear, colorless oil; IR (solid) 3313, 1607 cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz) δ: 7.83 (d, J = 8.1 Hz, 1H), 7.69 (m, 1H), 7.51 (ddd, J = 8.4, 6.8, 1.5 Hz, 1H), 7.35 (dd, J = 8.4, 1.0 Hz, 1H), 7.27-7.24 (m, 3H), 7.12 (m, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 178.0 (s), 160.2 (s), 146.5 (s), 145.6 (s), 138.0 (s), 133.9 (s), 133.3 (s), 131.2 (d), 130.2 (d), 128.7 (d), 128.4 (d), 127.8 (d), 126.56 (d), 126.61 (s), 126.4 (d), 125.3 (d), 74.6 (s), 72.3 (d), 27.3 (q), 23.4 (q), 20.0 (q); Exact mass calcd for $C_{23}H_{25}NO_3$ $[M+H]^+$, 364.190720. Found 364.191012.



NGJ-9-023

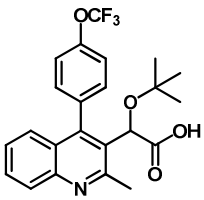
2-(tert-butoxy)-2-(2-methyl-4-(4-(trifluoromethyl)phenyl)quinolin-3-yl)acetic acid (11e): yellow oil; IR (thin film) 1730 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 10.33 (s, 1H, O-H), 8.18 (d, J = 8.4 Hz, 1H), 7.90-7.82 (m, 3H), 7.70 (ddd, J = 8.2, 7.0, 1.3 Hz, 1H), 7.50 (d, J = 7.6 Hz, 1H), 7.41 (t, J = 8.2 Hz, 1H), 7.28 (d, J = 8.0 Hz, 1H), 5.14 (s, 1H), 2.94 (s, 3H), 1.00 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 173.3 (s), 158.8 (s), 146.9 (s), 145.3 (s), 139.5 (s), 131.8 (d), 131.0 (s, ^{2}J = 32 Hz), 130.3 (d), 130.0 (d), 129.9 (s), 127.2 (d), 126.8 (d), 126.3

(d), 125.9 (s), 125.8 (d, ^3J = 3.5 Hz), 125.3 (s), 124.9 (d, ^3J = 3.5 Hz), 123.9 (s, ^1J = 270 Hz), 77.2 (s), 70.7 (d), 28.1 (q), 23.7 (q); Exact mass calcd for $C_{23}H_{22}F_3NO_3$ $[M+H]^+$, 418.162455. Found 418.162948.



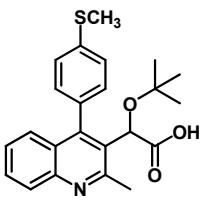
JDH-1-145

2-(tert-butoxy)-2-(4-(4-mehtoxyphenyl)-2-methylquinolin-3-yl)acetic acid (11f): White white solid, mp 152-153 ºC; IR (thin film) 1716 cm^{-1},^{1}H NMR ($CDCl_3$,400 MHz,) δ: 8.05 (d, J = 8.2 Hz, 1H), 7.74-7.59 (m, 2H), 7.45 (d, J = 8.0 Hz, 1H), 7.38 (dd, J = 7.0, 7.3 Hz, 1H), 7.31-7.21 -(m, 1H) 7.07 (dd, J = 6.8, 6.9 Hz, 2H), 5.37 (s, 1H), 3.92 (s, 3H), 2.83 (s, 3H), 0.97 (s, 9H); ^{13}C (100MHz, $CDCl_3$) δ: 172.8 (s) 159.9 (s), 158.2 (s), 146.8 (s), 132.7 (d), 131.1 (d), 129.6 (d), 128.8 (d), 128.3 (d), 127.6 (s), 126.8 (d), 126.5 (s), 126.0 (s), 113.8 (d), 113.7 (d), 77.8 (s), 70.8 (d), 55.4 (q), 29.7 (s), 28.1 (q), 24.6 (q).



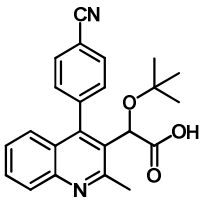
JDH-1-140

2-(tert-butoxy)-2-(4-(4-trifluoromethyoxy)phenyl)quinolin-3-yl)acetic acid (11g): White white solid, mp > 260 ºC; IR (thin film) 1721 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 8.11 (d, J=8.4Hz, 1H), 7.80 (d, J=7.6 Hz, 1H), 7.68 (ddd, J=1.4, 5.6, 8.3 Hz, 1H), 7.30-7.46 (m, 5H), 5.18 (s, 1H), 2.89 (s, 3H), 0.98 (s, 9H); ^{13}C NMR ($CDCl_3$,100 MHz) δ: 173.5 (s), 158.6 (s), 149.5 (s), 146.7 (s), 145.9 (s), 134.3 (s), 133.0 (d), 131.3 (d), 130.0 (d), 129.7 (s) 127.8 (d), 126.5 (d), 126.4 (d), 126.0 (s), 121.1 (d), 120.5 (s, J = 260 Hz) 120.3 (d), 77.8 (s), 70.7 (d), 28.1 (q), 24.1 (q).



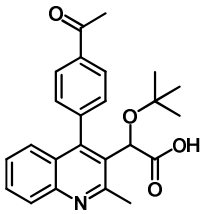
JDH-1-151

2-(tert-butoxy)-2-(2-methyl-4-(4-(methylthio)phenyl)quinolin-3-yl)acetic acid (11h): Yellow solid, mp 119-120 ºC; IR (thin film) 1754 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08 (d, 8.0Hz, 1H), 7.64 (d, 5.8 Hz,2H), 7.53-7.28 (m, 4H), 7.23 (d, J=6.8 Hz), 5.26 (s, 1H), 2.86 (s, 3H), 2.55 (s, 3H), 0.94 (s, 9H); ^{13}C NMR (100MHz, $CDCl_3$) δ: 173.9 (s), 158.7 (s), 147.5 (s), 146.0 (s), 139.7 (s), 131.97 (s), 131.7 (d), 130.2 (d), 129.6 (d),127.8 (d), 126.7 (d), 126.3 (s),126.14 (d), 126.11 (s), 126.0 (d), 125.3 (d), 77.2 (s), 71.0 (d), 28.1 (q), 24.2 (q), 15.3 (q); Exact mass calcd for $C_{23}H_{25}NO_3S$ $[M+H]^+$, 396.162791. Found 396.163099.



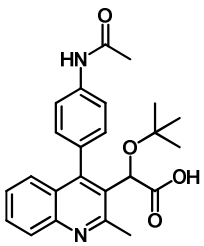
NGJ-8-094

2-(tert-butoxy)-2-(4-(4-cyanophenyl)-2-methylquinolin-3-yl)acetic acid (11i): white solid; mp 202-207 ºC; IR (solid) 3073, 2226, 1713 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.12 (d, J = 8.4 Hz, 1H), 7.85-7.83 (m, 3H), 7.70 (dd, J = 7.4 Hz, 1H), 7.47 (d, J = 7.7 Hz, 1H), 7.41 (dd, 7.7 Hz, 1H), 7.22 (d, J = 8.3 Hz, 1H), 5.07 (s, 3H), 2.89 (s, 3H), 0.98 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 172.1 (s), 158.6 (s), 145.9 (s), 140.8 (s), 132.5 (d), 132.3 (d), 131.7 (d), 130.5 (d), 130.2 (d), 129.5 (s), 127.8 (d), 126.8 (d), 125.9 (d), 125.5 (s), 118.3 (s), 112.9 (s), 77.2 (s), 70.7 (d), 28.1 (q), 24.1 (q); Exact mass calcd for $C_{23}H_{22}N_2O_3$ $[M+H]^+$, 375.170319. Found 375.170547.



NGJ-8-092

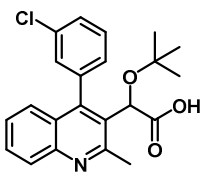
2-(4-(4-acetylphenyl)-2-methylquinolin-3-yl)-2-(tert-butoxy)acetic acid (11j): Yellow oil; IR (thin film) 1678 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.16-8.11 (m, 3H), 7.85 (d, J = 7.2 Hz, 1H), 7.69 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.47 (m, 1H), 7.39 (ddd, J = 8.0, 6.9, 1.0 Hz, 1H), 7.29 (d, J = 7.8 Hz, 1H), 5.19 (s, 1H), 2.89 (s, 3H), 2.72 (s, 3H), 1.01 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 198.0 (s), 172.5 (s), 158.4 (s), 147.0 (s), 146.3 (s), 140.7 (s), 137.2 (s), 131.8 (d), 130.0 (d), 128.9 (d), 128.7 (s), 128.1 (d), 127.7 (d), 126.5 (d), 126.3 (d), 125.7 (s), 77.7 (s), 70.7 (d), 28.2 (q), 26.7 (q), 24.3 (q); Exact mass calcd for $C_{24}H_{25}NO_4$ $[M+H]^+$, 392.185626. Found 392.185845.



NGJ-8-088

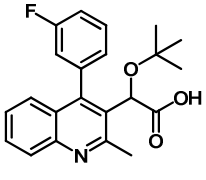
2-(4-(4-acetamidophenyl)-2-methylquinolin-3-yl)-2-(tert-butoxy)acetic acid (11k): yellow solid; mp 205-207ºC; IR (solid) 3313, 1684, 1598, 1534 cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz) δ: 7.99 (d, J = 8.4, 1H), 7.84 (dd, J = 8.3, 2.2 Hz, 1H), 7.79 (dd, J = 8.3, 2.1, 1H), 7.73 (dd, J = 8.3, 4.1 Hz, 1H), 7.59 (dd, J = 8.3, 2.0 Hz, 1H), 7.46 (dd, J = 4.4, 0.8, 1H), 7.32 (dd, J = 8.3, 2.0, 1H), 5.26 (s, 1H), 2.83 (s, 3H), 2.20 (s, 3H), 0.97 (s, 9H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 174.7 (s), 170.5 (s), 159.1 (s), 147.7 (s), 145.4 (s), 139.4 (s), 131.0 (d), 130.8 (s), 130.5 (d), 129.7 (d), 126.6 (d), 126.4 (s), 126.3 (d), 119.4 (d), 119.0 (d), 75.9 (s), 70.5

(d), 27.0 (q), 22.7 (q), 22.5 (q); Exact mass calcd for $C_{24}H_{26}N_2O_4$ $[M+H]^+$, 407.196534. Found 407.196903.



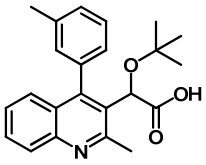
NGJ-9-024

ethyl 2-(tert-butoxy)-2-(4-(3-chlorophenyl)-2-methylquinolin-3-yl)acetate (12b): The product was isolated as an 1.0:0.9 mixture of atropisomers using the peaks at 5.20 and 5.17 ppm; Yellow oil; IR (thin film) 1640 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 10.00 (s, 1H, OH) 8.13 (d, J = 8.4 Hz, 1H), 7.78 (s,1H), 7.69-7.61 (m, 2H), 7.54-7.46 (m, 2H), 7.43-7.30 (m, 2H), 7.22 (d, J = 7.3 Hz, 1H), 5.2 major, 5.17 minor (s, 1H), 2.94 major, 2.90 minor (s, 3H), 0.99 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 173.7 (s), [158.9, 158.8] (s), [146.6, 146.5] (s), [145.5, 145.4] (s), [137.6, 137.5] (s), 134.0 (s), 131.2 (d), [130.3, 129.9] (s), [130.2, 129.2] (d), [130.1, 130.0] (d), [129.6, 129.5] (d), [129.0, 128.9] (d), 127.9 (d), [127.4, 127.3] (d), [126.6, 126.5] (d), 126.4 (d), [126.1, 125.9] (s), [77.2, 76.9] (s), 70.7 (d), [28.14, 28.07] (q), [23.8, 23.7] (q). Exact mass calcd for $C_{22}H_{22}ClNO_3$ $[M+H]^+$, 384.136098. Found 384.136358.



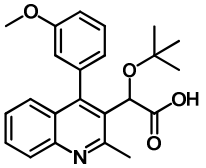
AH-3-52

2-(tert-butoxy)-2-(4-(3-fluorophenyl)-2-methylquinolin-3-yl)acetic acid (12c): The product was isolated as an indistinguishable mixture of atropisomers. White Solid; mp 110-115ºC; IR (thin film) 1730 cm^{-1}; ^1H NMR (MeOH-d4, 400 MHz) δ: 8.06 (d, J = 8.4 Hz, 1H), 7.68 (t, J = 6.9 Hz, 1H), 7.61-7.18 (m, 5H), 7.09 (m, 1H), 5.24 (s, 1H), 2.84 (s, 3H), 1.00 (s, 9H); ^{13}C NMR (MeOH-d4, 100 MHz) δ: 177.26 (s), [158.95, 157.20] (s), [146.05, 144.62] (s), 137.05 (s), 132.68 (s), [132.13, 132.08, 132.06, 132.03] (d), [131.83, 131.51, 131.65] (s), [130.11, 129.78] (s) 129.87 (d), 129.87 (s), [129.15, 129.00] (d), [128.63, 128.17] (d), 126.71 (d), [125.36, 125.35, 125.30] (s), 119.04 (d), 116.20 (d), 116.16 (d) [75.71, 75.60] (s), 72.83 (d), [27.91, 27.79] (q), 24.66 (q); Exact mass calcd for $C_{23}H_{22}FNO_4$ $[M+H]^+$, 368.165648. Found 368.165782.



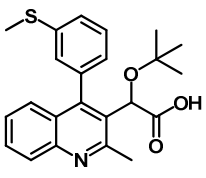
AH-3-61

2-(tert-butoxy)-2-(2-methyl-4-(m-tolyl)quinolin-3-yl)acetic acid (12d): The product was isolated as a 1:0.79 mixture of atropisomers using the peaks at 5.33 and 5.32. Yellow Oil; IR (thin film) 1726 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.06 (d, J = 8.4 Hz, 1H), 7.67 (ddt, J = 2.2, 6.6, 8.4 Hz, 1H), 7.52-7.30 (m, 5H), 7.15-7.08 (m, 1H), [5.33, 5.32] (s, 1H), 2.84 (s, 3H), 2.44 (s, 3H), [1.01, 1.00] (s, 9H); Exact mass calcd for $C_{23}H_{25}NO_3$ $[M+H]^+$, 364.190720. Found 364.190736.



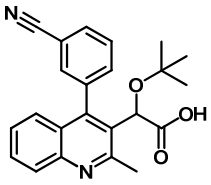
AH-3-42

2-(tert-butoxy)-2-(4-(3-methoxyphenyl)-2-methylquinolin-3-yl)acetic acid (12f): The product was isolated as a 1:0.72 mixture of atropisomers using the peaks at 3.84 and 3.83. Yellow Oil; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.22 (m, 1H), 7.71 (t, J = 7.6 Hz, 1H), 7.45 (m, 3H), 7.29 (m, 1H), 7.08 (dtd, J = 0.8, 3.5, 8.3 Hz, 1H), 6.90 (m, 1H), 5.33 minor, 5.32 major (s, 1H), 3.84 minor, 3.83 major (s, 3H), 2.91 (s, 3H), 1.02 minor, 1.01 major (s, 9H); 13C NMR ($CDCl_3$, 100 MHz) δ: [172.35, 172.25] (s), [159.81, 159.04], [158.31, 158.18] (s), 149.11 (s), [136.52, 136.44] (s), [132.17, 132.12] (d), [130.37, 130.12] (d), 129.09 (s), [128.62, 128.50] (d), 126.93 (d), 126.68 (d), 126.15 (s), [123.58, 121.69] (d), 115.86 (s), 115.34 (d), [115.60, 114.49] (d), [77.90, 77.72] (s), [70.68, 70.50] (d), [55.43, 55.21] (q), 28.13 (q), 23.79 (q).

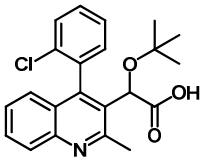


AH-3-62

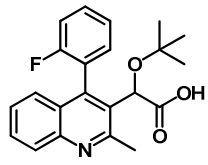
2-(tert-butoxy)-2-(2-methyl-4-(3-(methylthio)phenyl)quinolin-3-yl)acetic acid (12h): The product was isolated as a 1:0.78 mixture of atropisomers using the peaks at 5.30 and 5.27. Yellow Oil; IR (thin film) 1729 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.13 (m, H), 7.66 (m, 1H), 7.52-7.29 (m, 5H), 7.16-7.02 (m, 1H), 5.31 minor, 5.28 major (s, 1H), 2.89 (s, 3H), 2.48 major, 2.44 minor (s, 3H), 1.02 major, 1.00 minor (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [173.01, 172.81] (s), [158.48, 158.45] (s), [148.92, 148.90] (s), [145.89, 145.82] (s), [138.64, 137.55] (s), [136.30, 135.39] (s), 131.74 (d), [129.97, 129.95] (d), [129.57, 128.74] (s), 129.30 (s), [128.27, 128.08] (d), [127.83, 127.78] (d), [127.67, 127.59] (d), [126.72, 126.64] (d), 126.10 (s), 125.75 (d), [77.56, 77.42] (s), 70.69 (d), [28.75, 28.06] (q), [24.01, 23.81] (q), [21.57, 21.42] (q); Exact mass calcd for $C_{23}H_{25}NO_3S$ $[M+H]^+$, 396.162791. Found 396.163160.


AH-3-47

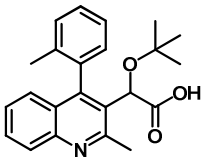
2-(tert-butoxy)-2-(4-(3-cyanophenyl)-2-methylquinolin-3-yl)acetic acid (12i): The product was isolated as a 1:0.95 mixture of atropisomers using the peaks at 5.06 and 4.97. Yellow Oil; ^{1}H NMR (MeOH-d4, 400 MHz) δ: 8.16-7.90 (m, 3H), 7.71-7.29 (m, 5H), 5.06 major, 4.97 minor (s, 1H), 2.90 minor, 2.87 major (s, 3H), 0.92 minor, 0.89 major (s, 9H); ^{13}C NMR (MeOH-d4, 100 MHz) δ:178.09 (s), 160.13 (s), [146.45, 145.61] (s), [145.55, 145.48] (s), [137.11, 136.73] (s), [135.93, 135.73] (s), [133.88, 133.81] (s), 133.04 (d), 132.83 (s), 131.30 (d), [128.91, 128.75] (d), [128.53, 128.30] (d), [127.46,127.12] (d), 126.77 (d), 126.55 (d), 126.40 (s), [125.73, 125.49] (d), 74.75 (s), [72.40, 72.32] (d), [27.33, 27.25] (q), [23.44, 23.39] (q); Exact mass calcd for $C_{23}H_{22}N_2O_4 \bullet H_2O$ $[M+Na]^+$, 415.162828. Found 415.163184.


AH-3-73

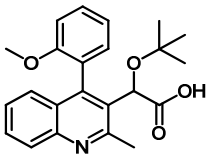
2-(tert-butoxy)-2-(4-(2-chlorophenyl)-2-methylquinolin-3-yl)acetic acid (13b): The product was isolated as a 1:0.97 mixture of atropisomers using the peaks at 5.34 and 5.19. White Solid; mp 109-115 ºC; IR (thin film) 1729 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.13 (d, J = 8.5 Hz, 1H), 7.73-7.62 (m, 2H), 7.81-7.50 (m, 1H), 7.50-7.32(m, 3H), 7.22-7.15 (m, 1H), 5.34 major, 5.19 minor (s, 1H), 3.04 major, 2.93 minor (s, 3H), 1.16 major, 1.08 minor (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [173.68, 172.97] (s), [159.35, 158.43] (s), [145.98, 145.54] (s), [145.24, 145.08] (s), [135.64, 134.64] (s), [134.57, 133.53] (s), 133.35 (d), [132.18, 132.08] (d), [130.57, 130.33] (d), 130.04 (s), [129.82, 129.72] (d), [128.59, 128.47] (d), [127.84, 127.70] (d), [126.95, 126.66] (d), [126.41, 125.89] (d), [126.24, 125.41] (s), 76.51 (s), [70.72, 70.39] (d), [28.04, 27.80] (q), [24.32, 24.09] (q); Exact mass calcd for $C_{22}H_{22}ClNO_3$ $[M+H]^+$, 384.136098. Found 384.136256.


AH-3-72

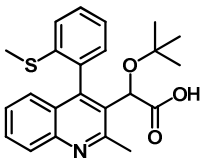
2-(tert-butoxy)-2-(4-(2-fluorophenyl)-2-methylquinolin-3-yl)acetic acid (13c): The product was isolated as a 1:0.56 mixture of atropisomers using the peaks at 2.93, and 2.85. White Solid; mp 140-144 ºC; IR (thin film) 1722 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.02 (d, J = 8.4 Hz, 1H), 7.80-7.71 (m, 1H), 7.71-7.57 (m, 2H), 7.52-7.22 (m, 4H), 5.23 minor, 5.21 major (s, 1H), 2.93 minor 2.85 major (s, 3H), 1.08 minor, 0.99 major (s, 9H); ^{13}C NMR (CD_3OD, 100 MHz) δ: [178.09, 177.45] (s), [165.63, 164.45, 63.18, 162.00] (s), [163.22, 162.94] (s), [149.42, 149.02] (s), [146.52, 146.23] (s), [136.45, 136.23] (d), [135.41, 135.33, 134.91, 134.83] (d), 135.18 (s), 133.90 (d), [130.60, 130.52] (d), 130.38 (d), [129.80, 129.63] (d), 129.70 (s), [128.31, 128.28, 127.02, 127.83] (d), [127.60, 127.43, 127.02, 126.86] (s), [119.73, 119.63, 119.52, 119.42] (d), [80.07, 79.70](s), [74.51, 74.28] (d), [30.90, 30.71] (q), [27.09, 26.74] (q); Exact mass calcd for $C_{23}H_{22}FNO_4$ $[M+H]^+$, 368.165648. Found 368.165878.


AH-3-65

2-(tert-butoxy)-2-(2-methyl-4-(o-tolyl)quinolin-3-yl)acetic acid (13d): The product was isolated as a 1:1 mixture of atropisomers using the peaks at 5.34 and 5.24.White Solid, mp 220-226 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.13 (d, J = 8.4 Hz, 1H), 7.64 (m, 1H), 7.50-7.28 (m, 4H), 7.24 (m, 2H) 5.34, 5.24 (s, 1H), 2.92, 2.90 (s, 3H), 2.06, 1.91 (s, 3H), 1.15, 1.05 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [173.97, 173.33] (s), [159.25, 159.01] (s), [148.92, 148.33] (s), [145.29, 144.92] (s), 136.12 (s) [135.23, 134.67] (s), [130.94, 130.62] (d), [130.38, 130.11] (d), 129.95 (s) [128.92, 128.86] (d), [127.15, 126.98] (d), [126.68, 126.62] (d), [126.55, 126.42] (d), 126.40 (s), 125.41 (d), 120.28 (d), 76.64 (s), [71.05, 70.62] (d), [28.38, 27.98] (q), [23.89, 23.65] (q), [20.44, 20.05] (q); Exact mass calcd for $C_{23}H_{25}NO_3$ $[M+H]^+$, 364.190720. Found 364.191025.

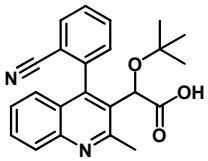

AH-3-69

2-(tert-butoxy)-2-(4-(2-methoxyphenyl)-2-methylquinolin-3-yl)acetic acid (13f): The product was isolated as a 1:0.38 mixture of atropisomers using the peaks at 3.67 and 3.61. Yellow Solid; mp 115-120 ºC; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.37 (m, 1H), 7.72 (m, 1H), 7.62-7.49 (m, 2H), 7.42 (m, 1H), 7.34 (m, 1H), 7.22-7.03 (m, 2H), 5.28 major, 5.08 minor (s, 1H), 3.67 minor, 3.61 major (s, 3H), 3.07 minor, 3.02 major (s, 3H), 1.02 minor, 1.01 major (s, 9H); Exact mass calcd for $C_{23}H_{25}NO_4$ $[M+H]^+$, 380.185635. Found 380.185964.



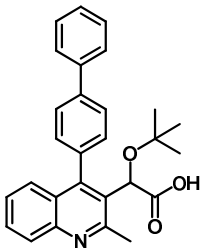
AH-3-68

2-(tert-butoxy)-2-(2-methyl-4-(2-(methylthio)phenyl)quinolin-3-yl)acetic acid (13h): The product was isolated as a 1:0.64 mixture of atropisomers using the peaks at 1.10, and 1.03. Yellow Oil; IR (thin film) 1734 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ:7.97 minor, 7.96 major (d, J = 8.0 Hz, 1H), 7.72 (m, 1H), 7.60-7.10 (m, 6H), 5.14 minor, 5.19 major (s, 1H), 2.99 minor 2.89 major (s, 3H), 2.32 major, 2.31 minor (s, 3H), 1.10 minor, 1.03 major (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [175.06, 173.60] (s), [159.66, 159.54] (s), [147.03, 146.41] (s), [145.04, 144.92] (s), 138.83 (s) [134.77, 133.54] (s), 131.10 (d), [129.69, 129.62] (d), 129.44 (d) [129.19, 129.12] (d), [126.88, 126.43] (d), [126.35, 126.30] (d), [126.23, 125.83] (d), [124.49, 124.20] (d), [76.17, 75.49] (s), [71.07, 70.71] (d), [27.21, 27.09] (q), [23.61, 22.99] (q), [14.23, 14.27] (q); Exact mass calcd for $C_{23}H_{25}NO_3S$ $[M+H]^+$, 396.162791. Found 396.163143.



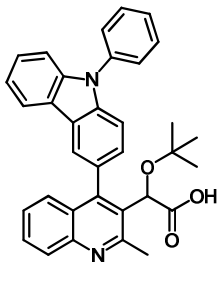
AH-3-75

2-(tert-butoxy)-2-(4-(2-cyanophenyl)-2-methylquinolin-3-yl)acetic acid (13i): The product was isolated as a 1:0.63 mixture of atropisomers using the peaks at 5.3, and 5.06. White Solid; mp >260ºC; IR (thin film) 2904, 1704 cm^{-1}; 1H NMR ($CDCl_3$, 400 MHz) δ: 8.14 (t, J = 7.7 Hz, 1H), 7.93-7.82 (m, 2H), 7.79-7.56 (m, 3H), 7.40 (m, 1H), 7.18-7.06 (m, 1H), 5.37 major, 5.06 minor (s, 1H), 3.04 major 2.91 minor (s, 3H), 1.17 major, 1.06 minor (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [173.41, 172.83] (s), [158.84, 156.73] (s), [146.16, 145.84] (s), [143.96, 143.81] (s), [140.39, 139.30] (s), [132.98, 132.94] (d), [132.61, 132.52] (d), [132.18, 132.09] (d), [130.26,129.45] (d), 130.14 (s), 129.93 (d), [128.24, 128.09] (d), [127.07, 126.97] (d), [126.41, 125.33] (s), [125.54, 125.11] (d), [117.91, 117.24] (s), [115.04, 113.65] (s), [77.72, 77.57] (s), [70.66, 69.96] (d), [28.07, 27.62] (q), [24.25, 24.09] (q); Exact mass calcd for $C_{23}H_{22}N_2O_3$ $[M+H]^+$, 375.170319. Found exact mass not observed.



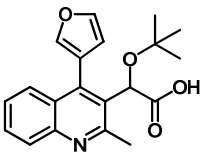
NGJ-8-090

2-(4-([1,1'-biphenyl]-4-yl)-2-methylquinolin-3-yl)-2-(tert-butoxy)acetic acid (15a): white solid, mp 198-200ºC; IR (solid) 3356, 1600 cm^{-1}; ^1H NMR (CD_3OD, 400 MHz) δ: 8.00 (d, J = 8.1, 1H), 7.95 (m, 1H), 7.85 (dd, J = 5.7, 1.6 Hz, 1H), 7.83 (dd, J = 5.7, 1.6 Hz, 1H), 7.75 (d, J = 7.1 Hz, 2H), 7.68 (ddd, J = 8.3, 6.8, 1.4 Hz, 1H), 7.52-7.37 (m, 6H), 5.22 (s, 1H), 2.92 (s, 3H), 0.97 (s, 9H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 177.0 (s), 159.9 (s), 146.6 (s), 145.5 (s), 141.2 (s), 140.2 (s), 135.1 (s), 133.0 (s), 131.6 (d), 130.8 (d), 128.9 (d), 128.6 (d), 127.9 (s), 127.4 (d), 126.7 (d), 126.6 (d), 126.4 (d), 125.9 (d), 125.7 (d), 75.1 (s), 71.8 (d), 27.3 (q), 23.2 (q); Exact mass calcd for $C_{28}H_{27}NO_3$ $[M+H]^+$, 426.206370. Found 426.207036.



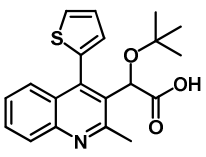
NGJ-9-028

2-(tert-butoxy)-2-(2-methyl-4-(9-phenyl-9H-carbazol-3-yl)quinolin-3-yl)acetic acid (15b): The product was isolated as an 1.0:1.0 mixture of atropisomers using the peaks at 5.53 and 5.43 ppm. Yellow oil. IR (thin film) 1732 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 10.09 (s, 1H, O-H), 8.61 (s, 1H), 8.32 (t, J = 8.9 Hz,1H), 8.16 (d, J = 7.7 Hz, 1H), 8.12 (d, J = 7.7 Hz, 1H), 7.81 (dd, J = 8.4, 1.3 Hz, 1H), 7.70-7.26 (m, 14H), [5.53, 5.43] (s, 1H), [3.05, 3.04] (s, 3H), [0.96, 0.95] (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [173.81, 173.78] (s), [158.9, 158.8] (s), [150.5, 150.4] (s), [141.5, 141.4] (s), [140.9, 140.8] (s), [137.4, 137.2] (s), 132.2 (d), [132.13, 132.11] (d), [131.2, 131.1] (s), [130.4, 130.3] (d), 130.1 (d), 128.9 (d), [128.6, 128.5] (d), 127.9 (d), [127.8, 127.7] (d), [127.41, 127.39] (d), 127.2 (s), [127.11, 127.09] (d), [126.67, 126.56] (d), [126.63, 126.59] (s), 123.6 (s), 123.4 (d), [123.1, 123.0] (s), 122.8 (s), 121.7 (d), 121.0 (d), [120.50, 120.45] (d), 120.40 (d), [110.3, 110.0] (d), [110.1, 109.2] (d), [77.00, 76.98] (s), [70.9, 70.8] (d), [28.24, 28.20] (q), [23.2, 23.1] (q); Exact mass calcd for $C_{34}H_{30}N_2O_3$ $[M+H]^+$, 515.232919. Found 515.233267.



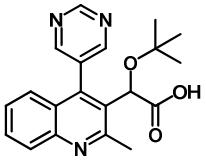
AH-3-46

2-(tert-butoxy)-2-(4-(furan-3-yl)-2-methylquinolin-3-yl)acetic acid (15c): Yellow solid; mp >260ºC; IR (thin film) 3352, 1595 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.93 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 9.0 Hz, 1H), 7.78 (s, 1H), 7.69-7.50 (m, 3H), 7.44 (t, J = 7.8 Hz, 1H), 5.35 (s, 1H), 2.86 (s, 3H), 0.97 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.99 (s), 169.06 (d), 159.97 (s), 145.43 (s), 143.03 (d), 138.35 (s), 134.84 (s), [132.44, 132.41] (d), [131.72, 131.62] (d), [128.63, 128.54] (d), 126.74 (d), 126.50 (s), [125.91, 125.59] (d), 119.90 (s), 74.75 (s), 72.14 (d), 27.22 (q), 23.38 (q).



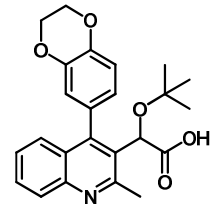
AH-3-55

2-(tert-butoxy)-2-(2-methyl-4-(thiophen-2-yl)quinolin-3-yl)acetic acid (15d): The product was isolated as an 1:0.42 mixture of atropisomers using the peaks at 6.02 and 5.32. Red-Orange solid; mp >260 °C: IR (thin film) 1732 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.09 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 8.3 Hz, 1H), 7.72-7.56 (m, 2H), 7.54 (m, 1H) 7.49-7.38 (m, 2H), 6.02 (major), 5.32 (minor) (s, 1H), 2.88 (minor), 2.83 (major) (s, 3H), 1.25 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: [173.15, 173.38] (s), [157.97, 156.24] (s), 137.16 (s), 134.19 (s), 133.35 (s), [132.24, 132.21, 132.16, 132.06] (d), 131.10 (d), 130.89 (s), 129.57 (d), [128.66, 128.59] (s), 128.11 (d), 127.38 (d), 127.01 (d), 123.46 (d), [77.58, 76.91] (s), [80.26, 70.52] (d), [28.37, 28.12] (q), [23.72, 20.57] (q); Exact mass calcd for $C_{20}H_{21}NO_3S$ $[M+H]^+$, 356.131491. Found 356.131781.



NGJ-9-005

2-(tert-butoxy)-2-(2-methyl-4-(pyrimidin-5-yl)quinolin-3-yl)acetic acid (15e): yellow oil; IR (thin film) 1734 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 9.29 (s, 1H), 9.00 (s, 1H), 8.73 (s, 1H), 8.13 (d, J = 8.4 Hz, 1H), 7.72 (dd, J = 7.6 Hz, 1H), 7.42 (dd, J = 7.9 Hz, 1H), 7.15 (d, J = 8.4, 1H), 5.26 (s, 1H), 3.03 (s, 3H), 1.06 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 173.1 (s), 159.6 (d), 155.6 (d), 146.5 (s), 139.8 (s), 130.8 (s), 130.1 (d), 128.7 (d), 126.9 (d), 126.5 (s), 125.1 (d), 77.2 (s), 69.7 (d), 28.0 (q), 24.5 (q); Exact mass calcd for $C_{20}H_{21}N_3O_3$ $[M+H]^+$, 352.165568. Found 352.165853.



NGJ-9-002

2-(tert-butoxy)-2-(4-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-2-methylquinolin-3-yl)acetic acid (15f): The product was isolated as an indistinguishable mixture of atropisomers. Yellow oil; IR (thin film) 1717 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.22-8.20 (m, 1H), 7.67-7.63 (m, 1H), 7.54-7.31 (m, 3H), 7.05-7.00 (m, 1H), 6.89-6.78 (m, 1H), 5.35 (s, 1H), 4.37-4.34 (m, 4H) 2.94 (s, 3H), 1.00 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 173.7 (s), 158.9 (s), 148.5 (s), [144.05, 144.00] (s), 143.6 (s), 143.0 (s), [132.2, 132.1] (d), [130.9, 130.6] (s), 130.1 (d), [128.6, 128.5] (d), [128.4, 128.3] (s), [126.96, 126.93] (d), [126.7, 126.6] (s), [126.5, 126.4] (d), 124.5 (d), 122.9 (d), 120.3 (d), 119.8 (d), [118.9, 118.8] (d), [117.6, 117.4] (d), [116.9, 116.8] (d), 115.5 (d), 76.9 (s), [70.77, 70.74] (d), [64.50, 64.48] (t), [64.46, 64.44] (t), [28.19, 28.16] (q), [23.23, 23.17] (q); Exact mass calcd for $C_{24}H_{25}NO_5$ $[M+H]^+$, 408.180549. Found 408.180636.

Recombinant Proteins and IN Multimerization Assay.

Recombinant wild type HIV-1 IN proteins containing either a N-terminal 6xHis or a FLAG tag were expressed in E. coli and purified as previously described.[8] The HTRF-based assay used to monitor the inhibitor induced aberrant multimerization of IN was performed as previously reported.[8,9] Briefly, two separate preparations of His-tagged and FLAG-tagged IN proteins were mixed in presence of increasing concentration of the test compounds and incubated for 2.5 h at room temperature. Anti-His6-XL665 and anti-FLAG-EuCryptate antibodies (Cisbio, Inc., Bedford, MA) were then added to the reaction and incubated at room temperature for 3 h. The IN multimerization HTRF signal was recorded using a PerkinElmer EnSpire multimode plate reader and dose-response curves were fitted using Origin software (v9.4).

Dynamic Light Scattering Assay.

DLS experiments were performed as previously described (refs). Briefly, each test compound was added at 10 μM final to 200 nM IN in a buffer containing 50 mM HEPES, at pH 7.4, 2 mM DTT, 2 mM MgCl2, and 1 M NaCl. DLS signals were recorded after 30 minutes incubations at RT (25 °C) using a Malvern Nano series zetasizer instrument, and particle size distributions were calculated.

[8] Kessl, J.J., et al. Multimode, cooperative mechanism of action of allosteric HIV-1 integrase inhibitors. The Journal of biological chemistry 287, 16801-16811 (2012).

[9] Kessl, J.J., Sharma, A. & Kvaratskhelia, M. Methods for the Analyses of Inhibitor-Induced Aberrant Multimerization of HIV-1 Integrase. Methods Mol Biol 1354, 149-164 (2016).