

Supporting Information

**Pd-catalyzed sp^3 C-H alkoxy carbonylation of 8-methylquinolines using
 $\text{Mo}(\text{CO})_6$ as CO surrogate**

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General Information. Pd(OAc)₂ (≥99.9%), benzoquinone, Mo(CO)₆, NaOAc, Ag₂CO₃ (99%), 8-methylquinoline, 5-methylquinoxaline, benzylmercaptan and alcohols were purchased from Aldrich and used as received. The substituted 8-MQs **1b-i**, 8-ethyl-4-phenylquinoline **1j** and 4-methylbenzo[d]oxazole **1l** were prepared according to literature.¹ Merck silica gel G/GF 254 plates were used for analytical TLC and Rankem silica gel (60-120 mesh) was used for column chromatography. NMR (¹H and ¹³C) spectra were recorded in Bruker Avance III 400 and 600 spectrometers using CDCl₃ as solvent and TMS as an internal standard. Chemical shifts (δ) and spin-spin coupling constant (*J*) are reported in ppm and in Hz, respectively, and other data are reported as follows: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, m = multiplet and q = quartet. Melting points were determined using a Büchi B-540 apparatus and are uncorrected. IR spectra were collected on a PerkinElmer Fourier transform infrared (FT-IR) spectrometer. Quadrupole time-of-flight electrospray ionization (ESI) mass spectrometer (model HAB 273) was used for mass analysis.

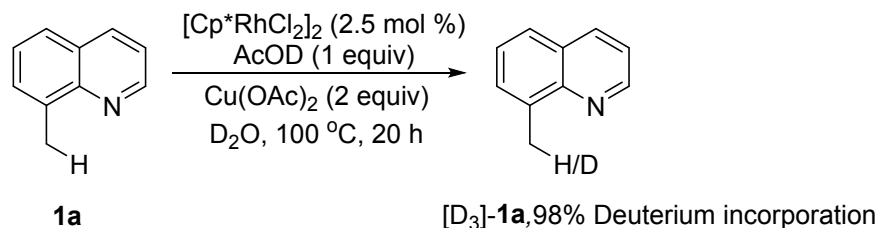
General Procedure for the sp³ C-H Alkoxy carbonylation of 8-MQs. 8-MQ **1** (0.2 mmol), alcohol **2** (2 mmol), Pd(OAc)₂ (10 mol %, 4.4 mg), BQ (0.2 mmol, 21.2 mg), Mo(CO)₆ (0.2 mmol, 52.8 mg) and Ag₂CO₃ (0.3 mmol, 83 mg) were stirred at 100 °C for 24 h in 1,2-dichloroethane (2 mL) in a sealed tube. The mixture was diluted with dichloromethane (10 mL) and passed through a short pad of celite. The organic layer was washed with brine (5 mL) and water (5 mL). Drying (Na₂SO₄) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane/EtOAc (10:2) as eluent to afford the desired **3**.

Scale-up Synthesis of 3aa. 8-Methylquinoline **1a** (5 mmol, 715 mg), EtOH **2** (50 mmol, 2.3 g), Pd(OAc)₂ (10 mol %, 110 mg), BQ (5 mmol, 530 mg), Mo(CO)₆ (5 mmol, 1.32 g) and Ag₂CO₃ (7.5 mmol, 2 g) were subjected to the above described standard reaction condition. The mixture was diluted with dichloromethane (20 mL) and passed through a celite pad and washed with brine (5 mL) and water (5 mL). The organic layer was dried over Na₂SO₄ and the solvent was evaporated to produce a residue, which was purified by column chromatography on silica gel using *n*-hexane/EtOAc (10:2) as eluent to afford **3aa** in 54% (580 mg) yield.

Synthesis of 4aa.² 3-Chloroperbenzoic acid (0.2 mmol, 34.5 mg) was added to a stirred solution of ethyl 2-(quinolin-8-yl)acetate **3aa** (0.2 mmol, 43 mg) in CH₂Cl₂ (1 mL) at 0 °C. The reaction mixture was allowed to stir at room temperature for 24 h and then treated with an aqueous

NaHCO₃. The resultant mixture was extracted with CH₂Cl₂ (10 mL) and the organic phase was washed with brine (3 mL) and water (3 mL). The organic layer was dried over Na₂SO₄ and the solvent was evaporated under reduced pressure to give the residue, which was purified by column chromatography on silica gel using EtOAc /MeOH (8:1) as an eluent.

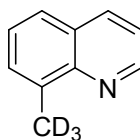
Synthesis of [D₃]-1a. 8-MQ **1a** (0.3 mmol, 43.0 mg), [RhCp*Cl₂]₂ (2.5 mol %, 4.6 mg), AcOD (0.9 mmol, 54.1 mg), Cu(OAc)₂ (0.6 mmol, 109.0 mg) and D₂O (1 mL) were stirred at 100 °C for 20 h. The resultant mixture was extracted with EtOAc (10 mL) and the organic layer was dried over Na₂SO₄. Evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane/EtOAc (10:1) to afford [D₃]-**1a** in 90% yield. The deuterium incorporation was determined using 400 MHz ¹H NMR as 98%.



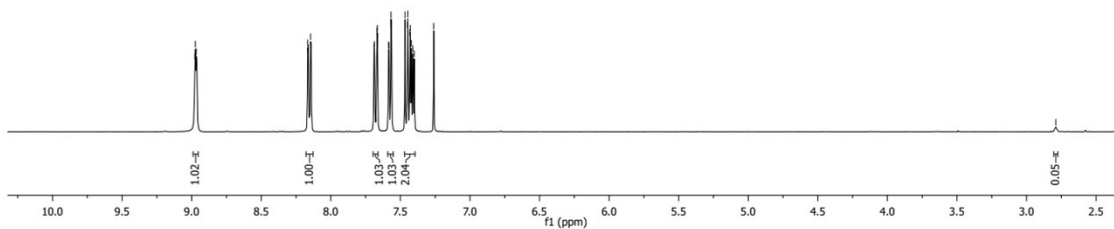
KT-211-N



— 2.789

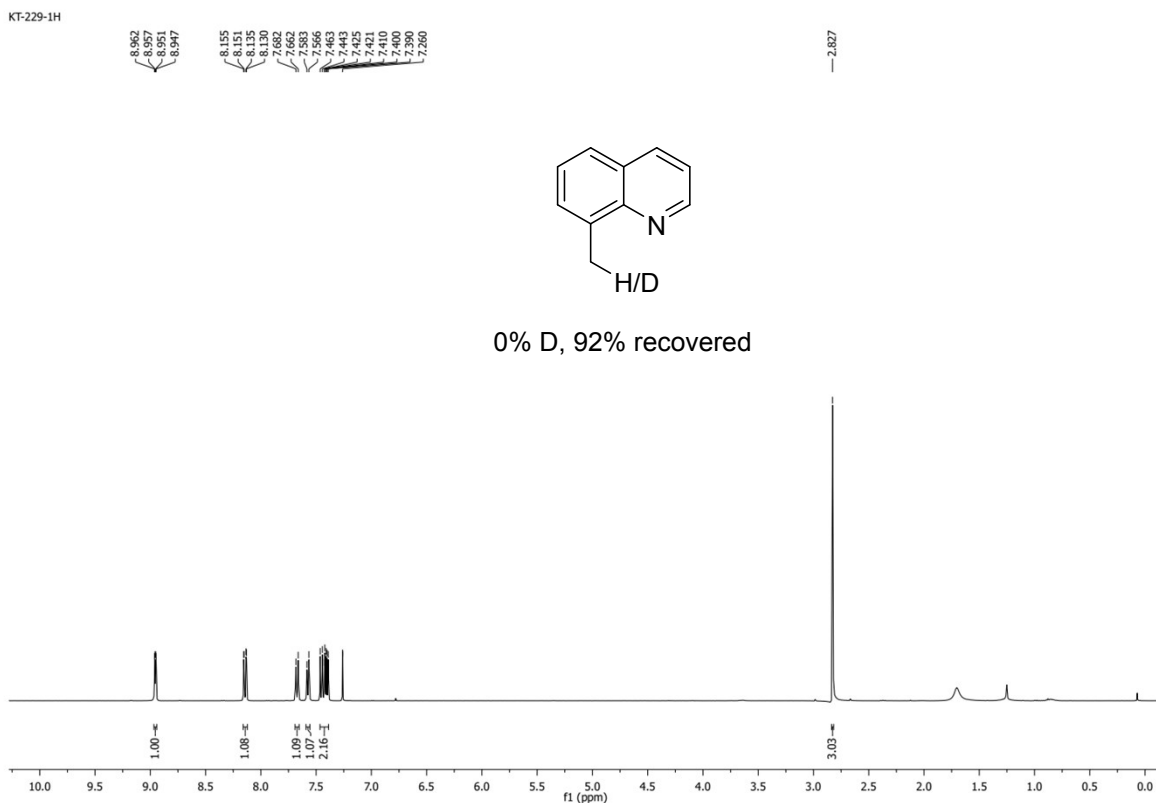


[D₃]-**1a**, 98% Deuterium incorporation



Mechanistic Investigations

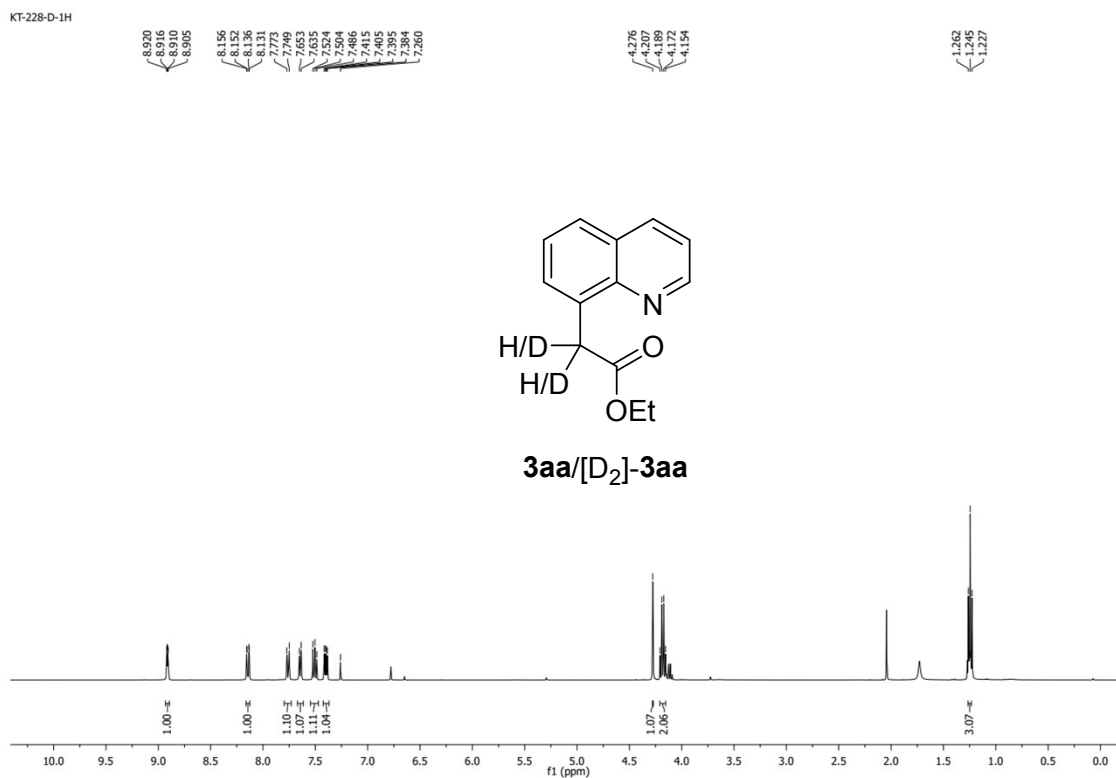
H/D Exchange Experiment with D₂O. 8-MQ **1a** (0.2 mmol, 28.6 mg), Pd(OAc)₂ (10 mol %, 4.4 mg), BQ (0.2 mmol, 21.2 mg), Mo(CO)₆ (0.2 mmol, 52.8 mg), Ag₂CO₃ (0.3 mmol, 83 mg) and D₂O (2 mmol) were stirred in 1,2-dichloroethane at 100 °C for 24 h in a sealed tube. The work-up and purification were performed as described in the general procedure. 400 MHz ¹H NMR spectrum of the product showed no deuterium incorporation.



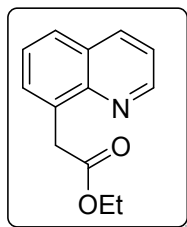
H/D Exchange Experiment with D₂O in Presence of Alcohol. 8-Methylquinoline **1a** (0.2 mmol, 28.6 mg), EtOH (2 mmol, 92 mg), Pd(OAc)₂ (10 mol %, 4.4 mg), BQ (0.2 mmol, 21.2 mg), Mo(CO)₆ (0.2 mmol, 52.8 mg), Ag₂CO₃ (0.3 mmol, 83 mg) and D₂O (2 mmol) were stirred in 1,2-dichloroethane at 100 °C for 24 h. The work-up and purification was performed as above, and the 400 MHz ¹H NMR spectrum of the product revealed no deuterium incorporation.



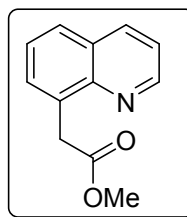
Kinetic Isotope Effect Experiment. A mixture of 8-Methylquinoline **1a** (0.2 mmol, 28.6 mg) and $[D_3]$ -**1a** (0.2 mmol, 29.2 mg) was reacted with EtOH **2a** (2 mmol, 92 mg) for 2 h under standard reaction conditions. The reaction mixture was diluted with DCM (5 mL), and passed through a short pad of celite using DCM (3 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent on vacuo produced a residue, which was purified on silica gel column chromatography on silica gel using *n*-hexane and EtOAc (10:2) as eluent to afford **3aa**/ $[D_2]$ -**3aa**. The intermolecular k_H/k_D was found to be 1.13, based on the 400 MHz 1H NMR spectroscopy.



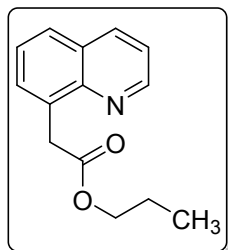
Characterization data



Ethyl 2-(quinolin-8-yl)acetate 3aa. Yellow liquid; yield 76% (33 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.91 (q, $J = 2.4$ Hz, 1H), 8.15 (dd, $J = 8.4$ Hz, 6.4 Hz, 1H), 7.77 (d, $J = 8.0$ Hz, 1H), 7.65 (d, $J = 6.8$ Hz, 1H), 7.50 (t, $J = 7.6$ Hz, 1H), 7.40 (q, $J = 4.0$ Hz, 1H), 4.27 (s, 2H), 4.19 (q, $J = 7.2$ Hz, 2H), 1.24 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.4, 149.7, 146.8, 136.3, 133.6, 130.4, 128.4, 127.5, 126.3, 121.2, 60.8, 37.3, 14.3; FT-IR (neat) 2980, 2924, 2852, 1729, 1499, 1367, 1026, 830, 797 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{14}\text{NO}_2^+$: 216.1019, found: 216.1025.

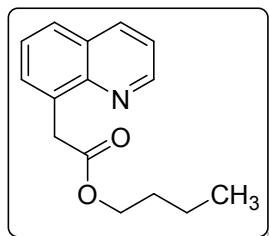


Methyl 2-(quinolin-8-yl)acetate 3ab. Yellow liquid; yield 73% (29 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.92 (q, $J = 2.4$ Hz, 1H), 8.15 (dd, $J = 8.0$ Hz, 6.4 Hz, 1H), 7.78 (d, $J = 8.4$ Hz, 1H), 7.65 (d, $J = 7.2$ Hz, 1H), 7.51 (t, $J = 8.0$ Hz, 1H), 7.41 (q, $J = 4.0$ Hz, 1H), 4.29 (s, 2H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.8, 149.8, 146.8, 136.3, 133.5, 130.4, 128.5, 127.6, 126.3, 121.3, 52.1, 37.0; FT-IR (neat) 2952, 2921, 2852, 1734, 1499, 1259, 1171, 1014, 794, 733 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{12}\text{NO}_2^+$: 202.0863, found: 202.0868.

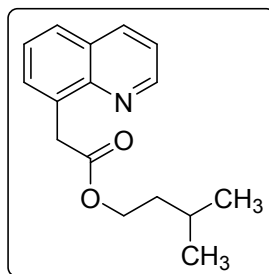


Propyl 2-(quinolin-8-yl)acetate 3ac. Yellow liquid; yield 71% (32 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.91 (q, $J = 2.8$ Hz, 1H), 8.15 (dd, $J = 8.0$ Hz, 6.4 Hz, 1H), 7.77 (d, $J = 8.4$ Hz, 1H), 7.65 (d, $J = 7.2$ Hz, 1H), 7.50 (t, $J = 7.6$ Hz, 1H), 7.40 (q, $J = 4.0$ Hz, 1H), 4.29 (s, 2H), 4.07 (t, $J = 6.8$ Hz, 2H), 1.66-1.58 (m, 2H), 0.85 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz,

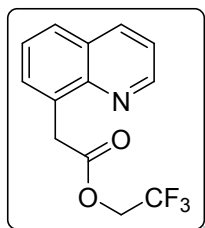
CDCl₃) δ 172.4, 149.7, 146.9, 136.3, 133.7, 130.3, 128.4, 127.4, 126.3, 121.2, 66.4, 37.3, 22.0, 10.4; FT-IR (neat) 2965, 2934, 2877, 1730, 1499, 1336, 1153, 1059, 794, 762 cm⁻¹; HRMS (ESI) m/z [M+H]⁺ calcd for C₁₄H₁₆NO₂⁺: 230.1176, found: 203.1175.



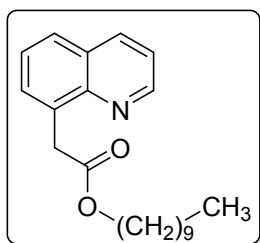
Butyl 2-(quinolin-8-yl)acetate 3ad. Yellow liquid; yield 74% (36 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.91 (q, J = 2.4 Hz, 1H), 8.15 (dd, J = 8.0 Hz, 6.4 Hz, 1H), 7.77 (d, J = 9.2 Hz, 1H), 7.65 (d, J = 7.2 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.40 (q, J = 4.0 Hz, 1H), 4.27 (s, 2H), 4.11 (t, J = 6.8 Hz, 2H), 1.61-1.54 (m, 2H), 1.33-1.25 (m, 2H), 0.86 (t, J = 7.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 172.5, 149.7, 146.9, 136.3, 133.7, 130.3, 128.4, 127.4, 126.3, 121.2, 64.7, 37.3, 30.7, 19.1, 13.8; FT-IR (neat) 2958, 1730, 1499, 1338, 1258, 1172, 1061, 794, 763 cm⁻¹; HRMS (ESI) m/z [M+H]⁺ calcd for C₁₅H₁₈NO₂⁺: 244.1332, found: 244.1337.



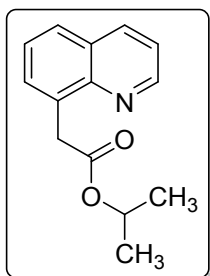
Isopentyl 2-(quinolin-8-yl)acetate 3ae. Yellow liquid; yield 70% (36 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.91 (q, J = 2.4 Hz, 1H), 8.15 (dd, J = 8.0 Hz, 6.4 Hz, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.64 (d, J = 6.8 Hz, 1H), 7.50 (t, J = 8.0 Hz, 1H), 7.40 (q, J = 4.0 Hz, 1H), 4.27 (s, 2H), 4.14 (t, J = 6.8 Hz, 2H), 1.61-1.53 (m, 1H), 1.49 (q, J = 6.8 Hz, 2H), 0.85 (s, 3H), 0.83 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 172.4, 149.7, 146.9, 136.3, 133.7, 130.3, 128.4, 127.5, 126.3, 121.2, 63.5, 37.4, 25.1, 22.5; FT-IR (neat) 2956, 1731, 1499, 1367, 1258, 1154, 1049, 981, 794, 761 cm⁻¹; HRMS (ESI) m/z [M+H]⁺ calcd for C₁₆H₂₀NO₂⁺: 258.1489, found: 258.1493.



2,2,2-Trifluoroethyl 2-(quinolin-8-yl)acetate 3af. Colorless liquid; yield 75% (40 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.90 (q, $J = 2.4$ Hz, 1H), 8.16 (dd, $J = 8.4$ Hz, 6.4 Hz, 1H), 7.80 (d, $J = 8.0$ Hz, 1H), 7.65 (d, $J = 6.4$ Hz, 1H), 7.51 (t, $J = 8.0$ Hz, 1H), 7.42 (q, $J = 4.0$ Hz, 1H), 4.52 (q, $J = 7.6$ Hz, 2H), 4.36 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.8, 149.8, 146.7, 136.3, 132.5, 130.4, 128.4, 127.9, 126.3, 124.5 (q, $J_{\text{C-F}} = 275.7$), 121.4, 60.8 (q, $J_{\text{C-F}} = 36.3$), 36.7; ^{19}F NMR (377 MHz, CDCl_3) δ -73.6; FT-IR (neat) 2921, 2852, 1716, 1595, 1401, 1279, 979, 812, 764 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{11}\text{F}_3\text{NO}_2^+$: 270.0736, found: 270.0740.

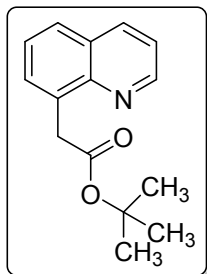


Decyl 2-(quinolin-8-yl)acetate 3ag. Yellow liquid; yield 68% (44 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.91 (q, $J = 2.4$ Hz, 1H), 8.15 (dd, $J = 8.4$ Hz, 6.4 Hz, 1H), 7.77 (d, $J = 8.4$ Hz, 1H), 7.65 (d, $J = 6.8$ Hz, 1H), 7.50 (t, $J = 7.6$ Hz, 1H), 7.40 (q, $J = 4.0$ Hz, 1H), 4.27 (s, 2H), 4.10 (t, $J = 6.8$ Hz, 2H), 1.59-1.54 (m, 1H), 1.31-1.28 (m, 15H), 0.88 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.4, 149.7, 146.9, 136.3, 133.8, 130.3, 128.4, 127.4, 126.3, 121.2, 65.0, 37.3, 32.0, 29.6, 29.4, 29.3, 28.7, 25.9, 22.8, 14.2; FT-IR (neat) 2923, 2853, 1734, 1595, 1338, 1171, 1028, 795, 783 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{30}\text{NO}_2^+$: 328.2271, found: 328.2287.

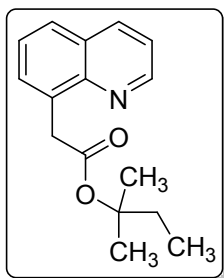


Isopropyl 2-(quinolin-8-yl)acetate 3ah. Yellow liquid; yield 67% (31 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.90 (q, $J = 2.4$ Hz, 1H), 8.14 (dd, $J = 8.4$ Hz, 6.4 Hz, 1H), 7.76 (d, $J = 8.0$ Hz, 1H), 7.64 (d, $J = 6.8$ Hz, 1H), 7.50 (t, $J = 8.0$ Hz, 1H), 7.39 (q, $J = 4.4$ Hz, 1H), 5.11-5.01

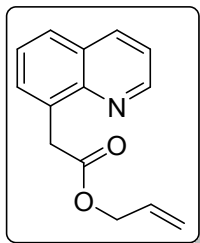
(m, 1H), 4.24 (s, 2H), 1.24 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.9, 149.6, 146.8, 136.2, 133.9, 130.3, 128.4, 127.4, 126.3, 121.2, 68.1, 37.6, 21.9; FT-IR (neat) 2978, 2934, 1725, 1499, 1372, 1241, 1104, 957, 794, 763 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{14}\text{H}_{16}\text{NO}_2^+$: 230.1176, found: 230.1181.



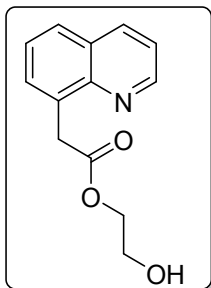
tert-Butyl 2-(quinolin-8-yl)acetate 3ai. Yellow liquid; yield 62% (30 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.91 (q, $J = 2.4$ Hz, 1H), 8.14 (dd, $J = 8.0$ Hz, 6.4 Hz, 1H), 7.75 (d, $J = 8.0$ Hz, 1H), 7.64 (d, $J = 7.2$ Hz, 1H), 7.49 (t, $J = 7.6$ Hz, 1H), 7.40 (q, $J = 4.4$ Hz, 1H), 4.19 (s, 2H), 1.44 (s, 9H); ^{13}C NMR (150 MHz, CDCl_3) δ 171.7, 149.6, 146.9, 136.3, 134.2, 130.3, 128.4, 127.3, 126.3, 121.2, 80.7, 38.5, 28.2; FT-IR (neat) 2977, 1731, 1499, 1392, 1345, 1367, 1256, 797 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{18}\text{NO}_2^+$: 244.1332, found: 244.1329.



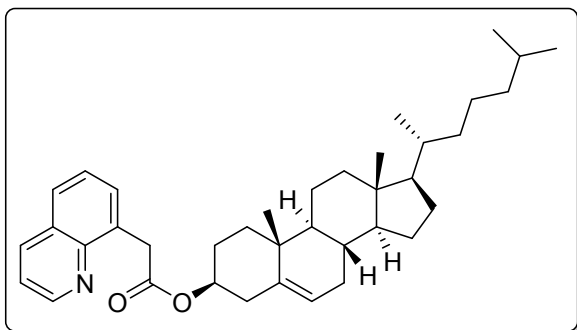
tert-Pentyl 2-(quinolin-8-yl)acetate 3aj. Yellow liquid; yield 64% (33 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.90 (q, $J = 2.0$ Hz, 1H), 8.14 (dd, $J = 8.4$ Hz, 6.8 Hz, 1H), 7.75 (d, $J = 7.2$ Hz, 1H), 7.63 (d, $J = 7.2$ Hz, 1H), 7.49 (t, $J = 7.2$ Hz, 1H), 7.39 (q, $J = 4.0$ Hz, 1H), 4.19 (s, 2H), 1.72 (q, $J = 7.2$ Hz, 2H), 1.40 (s, 6H), 0.78 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.6, 149.6, 146.9, 136.2, 134.3, 130.3, 128.4, 127.2, 126.3, 121.2, 83.0, 38.5, 33.6, 25.6, 8.1; FT-IR (neat) 2973, 2925, 2855, 1726, 1499, 1196, 1142, 1060, 949, 829, 762 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{16}\text{H}_{20}\text{NO}_2^+$: 258.1489, found: 258.1486.



Allyl 2-(quinolin-8-yl)acetate 3ak. Yellow liquid; yield 63% (28 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.91 (q, $J = 2.4$ Hz, 1H), 8.15 (dd, $J = 8.0$ Hz, 6.8 Hz, 1H), 7.77 (d, $J = 8.0$ Hz, 1H), 7.66 (d, $J = 7.2$ Hz, 1H), 7.50 (t, $J = 8.0$ Hz, 1H), 7.41 (q, $J = 4.0$ Hz, 1H), 5.95-5.86 (m, 1H), 5.29-5.24 (m, 1H), 5.20-5.16 (m, 1H), 4.64-4.62 (m, 2H), 4.32 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.0, 149.8, 146.8, 136.3, 133.4, 132.4, 130.4, 128.4, 127.6, 126.3, 121.3, 118.0, 65.4, 37.2; FT-IR (neat) 2926, 2854, 1731, 1499, 1365, 1239, 1150, 987, 828, 794, 764 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{14}\text{H}_{14}\text{NO}_2^+$: 228.1019, found: 228.1020.

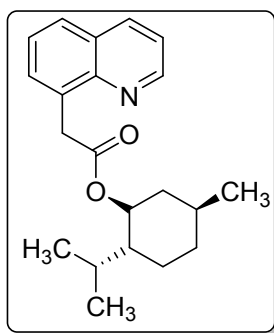


2-Hydroxyethyl 2-(quinolin-8-yl)acetate 3al. Yellow liquid; yield 68% (31 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.90 (q, $J = 2.8$ Hz, 1H), 8.18 (dd, $J = 8.4$ Hz, 6.4 Hz, 1H), 7.80 (d, $J = 8.0$ Hz, 1H), 7.66 (d, $J = 7.2$ Hz, 1H), 7.51 (t, $J = 8.0$ Hz, 1H), 7.43 (q, $J = 4.0$ Hz, 1H), 4.29 (t, $J = 4.4$ Hz, 2H), 4.26 (s, 2H), 3.79 (t, $J = 4.4$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.6, 149.9, 146.6, 136.7, 133.3, 130.8, 128.6, 127.8, 126.5, 121.4, 66.4, 61.2, 37.9; FT-IR (neat) 3406, 2924, 2854, 1732, 1500, 1259, 1173, 1077, 794, 765 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{14}\text{NO}_3^+$: 232.0968, found: 232.0976.



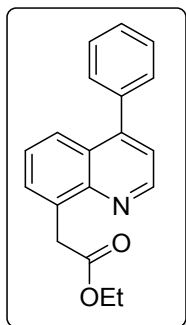
(3S,8S,9S,10R,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-

cyclopenta[*a*]phenanthren-3-yl 2-(quinolin-8-yl)acetate 3an. Colorless solid; mp 155-157 °C; yield 51% (57 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.91 (q, *J* = 2.4 Hz, 1H), 8.15 (dd, *J* = 8.4 Hz, 6.4 Hz, 1H), 7.76 (d, *J* = 6.8 Hz, 1H), 7.65 (d, *J* = 6.8 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.40 (q, *J* = 4.4 Hz, 1H), 5.35 (d, *J* = 5.2 Hz, 1H), 4.70-4.62 (m, 1H), 4.25 (s, 2H), 2.34-2.30 (m, 2H), 2.04-1.97 (m, 2H), 1.92-1.77 (m, 3H), 1.60-1.57 (m, 4H), 1.54-1.51 (m, 2H), 1.47-1.41 (m, 4H), 1.33-1.32 (m, 2H), 1.25 (s, 1H), 1.15-1.03 (m, 7H), 0.99 (s, 4H), 0.91 (d, *J* = 4.8 Hz, 3H), 0.86 (dd, *J* = 6.8 Hz, 4.8 Hz, 6H), 0.66 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 171.8, 149.6, 146.9, 139.9, 136.2, 133.9, 130.3, 128.4, 127.4, 126.3, 122.6, 121.2, 74.4, 56.8, 56.2, 50.1, 42.4, 39.8, 39.6, 38.1, 37.6, 37.1, 36.7, 36.3, 35.9, 32.05, 32.00, 28.3, 28.1, 27.8, 24.4, 23.9, 22.9, 22.7, 21.1, 19.4, 18.8, 12.0; FT-IR (neat) 2933, 2867, 2852, 1732, 1499, 1260, 1172, 1028, 796, 764, 703 cm⁻¹; HRMS (ESI) *m/z* [M+H]⁺ calcd for C₃₈H₅₄NO₂⁺: 556.4149, found: 556.4149.

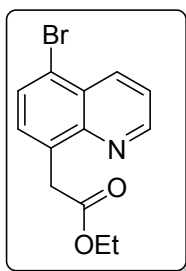


(1R,2S,5S)-2-Isopropyl-5-methylcyclohexyl 2-(quinolin-8-yl)acetate

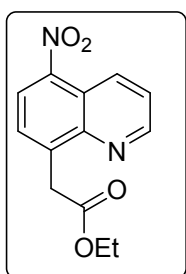
3ao. Yellow solid; mp 85-87 °C; yield 40% (26 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.88 (q, *J* = 2.8 Hz, 1H), 8.17 (dd, *J* = 8.0 Hz, 6.4 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 6.8 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.40 (q, *J* = 4.0 Hz, 1H), 4.72-4.65 (m, 1H), 4.23 (s, 2H), 1.66-1.59 (m, 3H), 1.34-1.25 (m, 3H), 0.97 (q, *J* = 6.0 Hz, 1H), 0.91 (t, *J* = 6.0 Hz, 2H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.79 (d, *J* = 6.8 Hz, 3H), 0.67 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 172.0, 149.6, 146.9, 136.2, 134.0, 130.2, 128.4, 127.3, 126.3, 121.2, 74.6, 47.1, 40.9, 38.0, 34.4, 31.5, 26.0, 23.5, 22.1, 20.8, 16.4; FT-IR (neat) 2953, 2925, 2868, 1729, 1499, 1368, 1259, 1173, 985, 811, 795 cm⁻¹; HRMS (ESI) *m/z* [M+H]⁺ calcd for C₂₁H₂₈NO₃⁺: 326.2115, found: 326.2116.



Ethyl 2-(4-phenylquinolin-8-yl)acetate 3ba. Yellow liquid; yield 58% (34 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.39 (d, $J = 4.4$ Hz, 1H), 7.86 (d, $J = 7.6$ Hz, 1H), 7.65 (d, $J = 6.8$ Hz, 1H), 7.52-7.47 (m, 6H), 7.33 (d, $J = 4.4$ Hz, 1H), 4.31 (s, 2H), 4.22 (q, $J = 7.2$ Hz, 2H), 1.28 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 172.4, 149.1, 148.6, 147.1, 138.2, 133.8, 130.2, 129.5, 128.5, 128.3, 126.8, 126.1, 125.5, 121.4, 60.7, 37.6, 14.2; FT-IR (neat) 2918, 2849, 1731, 1490, 1396, 1252, 1154, 1030, 853, 765 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{18}\text{NO}_2^+$: 292.1332, found: 292.1334.

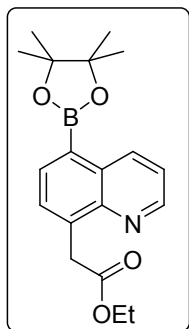


Ethyl 2-(5-bromoquinolin-8-yl)acetate 3ca. Yellow solid; mp 104-106 $^\circ\text{C}$; yield 66% (39 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.92 (q, $J = 2.8$ Hz, 1H), 8.54 (dd, $J = 8.4$ Hz, 6.8 Hz, 1H), 7.80 (d, $J = 7.6$ Hz, 1H), 7.52-7.49 (m, 2H), 4.22 (s, 2H), 4.18 (q, $J = 6.8$ Hz, 2H), 1.23 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.9, 150.3, 147.5, 135.8, 133.8, 130.6, 130.1, 127.8, 122.3, 121.2, 60.9, 37.2, 14.3; FT-IR (neat) 2978, 2988, 2937, 1718, 1568, 1496, 1343, 1179, 1028, 934, 847, 789 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{13}\text{BrNO}_2^+$: 294.0124, found: 294.0131.



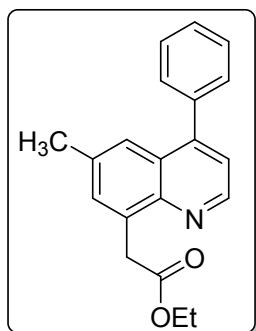
Ethyl 2-(5-nitroquinolin-8-yl)acetate 3da. Yellow solid; mp 66-67 $^\circ\text{C}$; yield 76% (39 mg); ^1H NMR (400 MHz, CDCl_3) δ 9.04-9.00 (m, 2H), 8.36 (d, $J = 7.6$ Hz, 1H), 7.75 (d, $J =$

8.0 Hz, 1H), 7.65 (q, $J = 4.4$ Hz, 1H), 4.33 (s, 2H), 4.19 (q, $J = 7.2$ Hz, 2H), 1.24 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.1, 150.7, 146.6, 144.9, 141.7, 132.3, 128.6, 124.4, 124.0, 121.3, 61.2, 37.9, 14.3; FT-IR (neat) 2930, 2854, 1734, 1521, 1336, 1275, 1176, 1028, 815, 764 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{13}\text{N}_2\text{O}_4^+$: 261.0870, found: 261.0882.



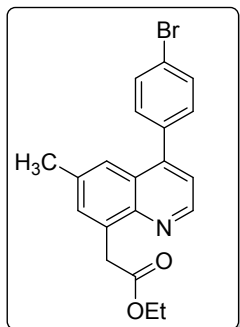
Ethyl 2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinolin-8-yl)acetate

3ea. Yellow liquid; yield 60% (41 mg); ^1H NMR (400 MHz, CDCl_3) δ 9.11 (dd, $J = 8.4$ Hz, 2.8 Hz, 1H), 8.89 (q, $J = 2.4$ Hz, 1H), 8.09 (d, $J = 7.2$ Hz, 1H), 7.63 (d, $J = 6.8$ Hz, 1H), 7.43 (q, $J = 4.4$ Hz, 1H), 4.28 (s, 2H), 4.16 (q, $J = 7.2$ Hz, 2H), 1.41 (s, 12H), 1.21 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.2, 149.2, 146.7, 137.2, 137.0, 135.9, 132.2, 130.4, 129.6, 121.4, 84.0, 60.8, 37.8, 25.1, 14.3; FT-IR (neat) 2979, 2927, 2854, 1733, 1502, 1368, 1259, 1111, 1029, 976, 856, 795 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{25}\text{BNO}_4^+$: 342.1871, found: 342.1886.

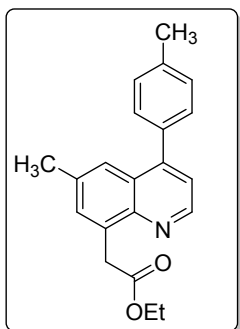


Ethyl 2-(6-methyl-4-phenylquinolin-8-yl)acetate 3fa. Yellow liquid; yield

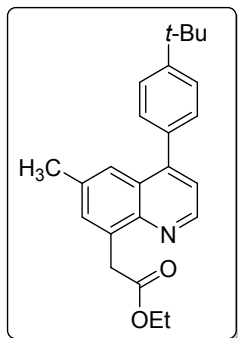
70% (43 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.86 (d, $J = 4.4$ Hz, 1H), 7.59 (s, 1H), 7.55-7.47 (m, 6H), 7.28 (d, $J = 4.4$ Hz, 1H), 4.27 (s, 2H), 4.22 (q, $J = 6.4$ Hz, 2H), 2.44 (s, 3H), 1.28 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.6, 148.3, 147.9, 145.8, 138.6, 136.0, 133.5, 132.6, 129.6, 128.6, 128.3, 126.9, 124.3, 121.6, 60.8, 37.7, 21.9, 14.3; FT-IR (neat) 2980, 2919, 2849, 1731, 1491, 1366, 1253, 1160, 1031, 867, 764 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{20}\text{NO}_2^+$: 306.1489, found: 306.1486.



Ethyl 2-(4-(4-bromophenyl)-6-methylquinolin-8-yl)acetate 3ga. Yellow liquid; yield 72% (55 mg); $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.85 (d, $J = 4.2$ Hz, 1H), 7.66 (d, $J = 8.4$ Hz, 2H), 7.51 (d, $J = 13.2$ Hz, 2H), 7.35 (d, $J = 7.8$ Hz, 2H), 7.24 (d, $J = 4.2$ Hz, 1H), 4.26 (s, 2H), 4.21 (q, $J = 7.2$ Hz, 2H), 2.44 (s, 3H), 1.28 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ 172.5, 148.2, 146.6, 145.8, 137.4, 136.4, 133.7, 132.8, 131.8, 131.2, 126.6, 123.9, 122.7, 121.4, 60.9, 37.7, 21.9, 14.3; FT-IR (neat) 2978, 2924, 2865, 1731, 1485, 1387, 1160, 1009, 827, 764, 749 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{19}\text{BrNO}_2^+$: 384.0594, found: 384.0595.

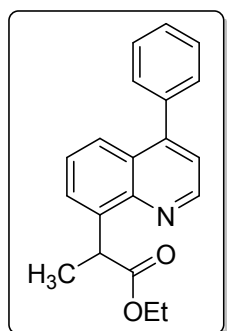


Ethyl 2-(6-methyl-4-(*p*-tolyl)quinolin-8-yl)acetate 3ha. Yellow liquid; yield 55% (35 mg); $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.84 (d, $J = 4.4$ Hz, 1H), 7.62 (s, 1H), 7.48 (s, 1H), 7.39-7.32 (m, 4H), 7.27 (d, $J = 4.4$ Hz, 1H), 4.26 (s, 2H), 4.22 (q, $J = 7.2$ Hz, 2H), 2.47 (s, 3H), 2.44 (s, 3H), 1.28 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 172.6, 148.3, 148.0, 145.8, 138.2, 135.9, 135.6, 133.5, 132.5, 129.5, 129.3, 127.1, 124.4, 121.6, 60.8, 37.7, 21.9, 21.4, 14.3; FT-IR (neat) 2980, 29128, 2850, 1731, 1498, 1439, 1386, 1159, 1029, 908, 867, 817, 729 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{22}\text{NO}_2^+$: 320.1645, found: 320.1659.



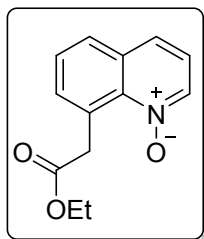
Ethyl 2-(4-(4-(tert-butyl)phenyl)-6-methylquinolin-8-yl)acetate 3ia.

Yellow liquid; yield 68% (49 mg); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.77 (d, $J = 4.4$ Hz, 1H), 7.59 (s, 1H), 7.48 (d, $J = 8.4$ Hz, 2H), 7.41 (s, 1H), 7.36 (d, $J = 8.4$ Hz, 2H), 7.19 (t, $J = 4.4$ Hz, 1H), 4.19 (s, 2H), 4.15 (q, $J = 7.2$ Hz, 2H), 2.38 (s, 3H), 1.34 (s, 9H), 1.21 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ 172.7, 151.4, 148.3, 147.9, 145.8, 135.9, 135.6, 133.4, 132.6, 129.4, 127.0, 125.5, 124.5, 121.6, 60.8, 37.7, 34.8, 31.5, 21.9, 14.3; FT-IR (neat) 2961, 2906, 2867, 1733, 1498, 1365, 1254, 1160, 1031, 834, 750 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{28}\text{NO}_2^+$: 362.2115, found: 362.2116.



Ethyl 2-(4-phenylquinolin-8-yl)propanoate 3ja. Colorless liquid; yield 32%

(19 mg); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.94 (d, $J = 4.4$ Hz, 1H), 7.83 (dd, $J = 8.4$ Hz, 2.4 Hz, 1H), 7.67 (dd, $J = 6.8$ Hz, 1.2 Hz, 1H), 7.52-7.44 (m, 6H), 7.33 (d, $J = 4.4$ Hz, 1H), 5.08 (q, $J = 7.2$ Hz, 1H), 4.18 (q, $J = 6.8$ Hz, 2H), 1.66 (d, $J = 7.2$ Hz, 3H), 1.19 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 175.8, 149.0, 146.3, 140.4, 138.4, 129.7, 128.6, 128.4, 127.3, 127.0, 126.4, 125.1, 121.5, 60.7, 40.4, 18.5, 14.3; FT-IR (neat) 2977, 2922, 2850, 1730, 1490, 1395, 1189, 1096, 855, 767 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{20}\text{NO}_2^+$: 306.1489, found: 306.1489.

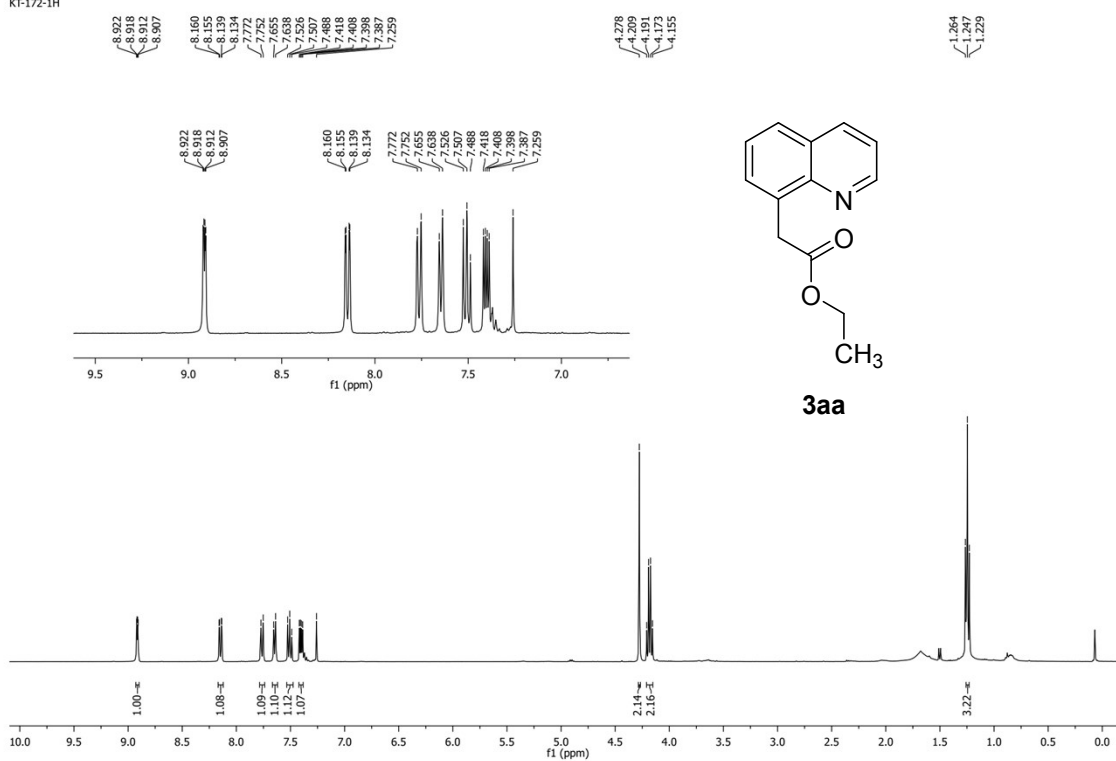


8-(2-Ethoxy-2-oxoethyl)quinoline 1-oxide 4aa. Brown solid; 109-110 °C; yield 81% (37 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.38 (d, $J = 6.0$ Hz, 1H), 7.78 (d, $J = 8.0$ Hz, 1H), 7.68 (d, $J = 8.4$ Hz, 1H), 7.51 (t, $J = 8.0$ Hz, 1H), 7.42 (d, $J = 6.8$ Hz, 1H), 7.22 (q, $J = 2.4$ Hz, 1H), 4.39 (s, 2H), 4.23 (q, $J = 7.2$ Hz, 2H), 1.28 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.7, 149.7, 137.2, 134.7, 132.5, 129.4, 128.6, 128.2, 126.5, 121.1, 60.7, 43.5, 14.4; FT-IR (neat) 3415, 3070, 2983, 2905, 1730, 1575, 1370, 1301, 1228, 1180, 1024, 817, 762 cm^{-1} ; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{14}\text{NO}_3^+$: 232.0968, found: 232.0982.

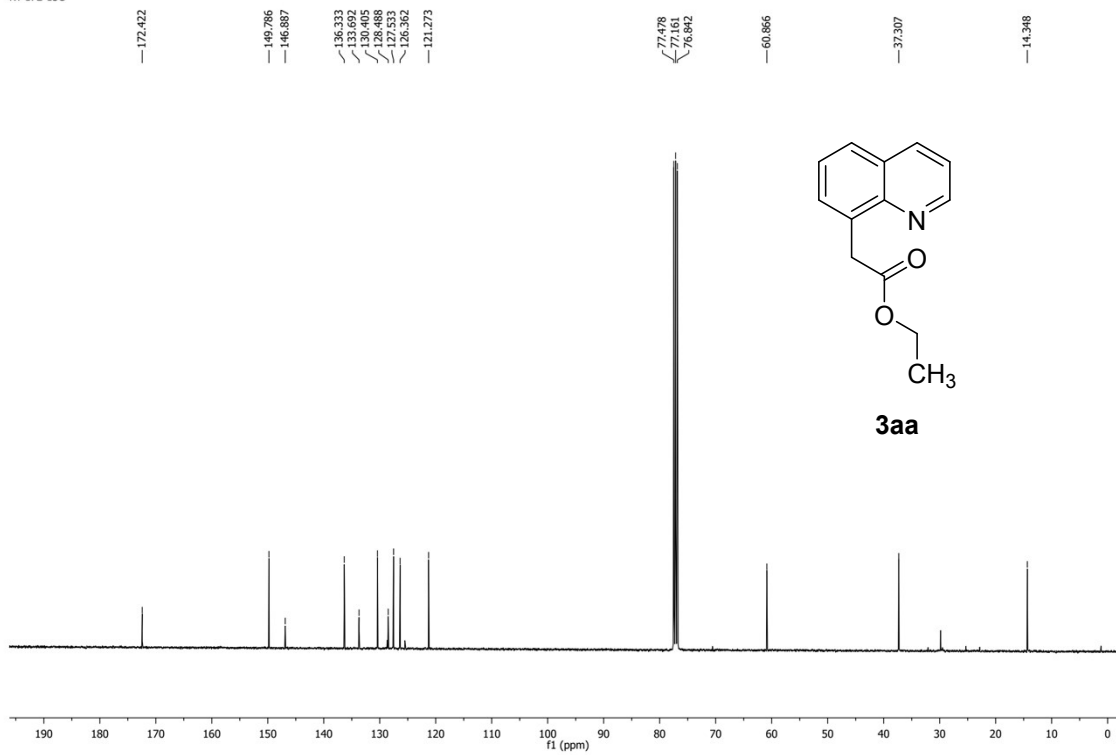
References

1. (a) X. Xu, Y. Yang, X. Zhang and W. Yi, *Org. Lett.*, 2018, **20**, 566; (b) S. Fukagawa, M. Kogima, T. Yoshino and S. Matsunaga, *Angew. Chem. Int. Ed.*, 2019, **58**, 18154; (c) S. H. Cho, J. Y. Kim, S. Y. Lee and S. Chang, *Angew. Chem. Int. Ed.*, 2009, **48**, 9127.
2. J. Zhao, P. Li, C. Xia and F. Li, *RSC Adv.* 2015, **5**, 32835.
3. S. Kim, S. Han, J. Park, S. Sharma, N. K. Mishra, H. Oh, J. H. Kwak and I. S. Kim, *Chem. Commun.*, 2017, **53**, 3006.

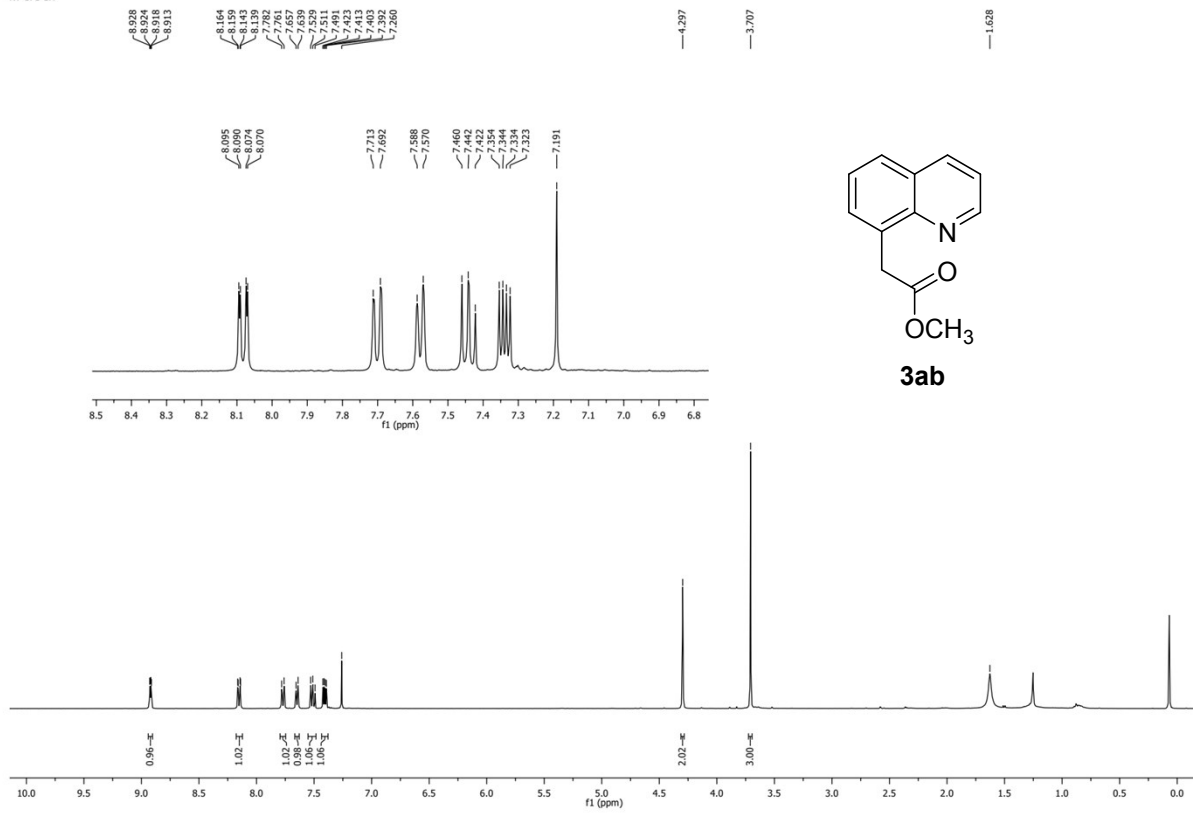
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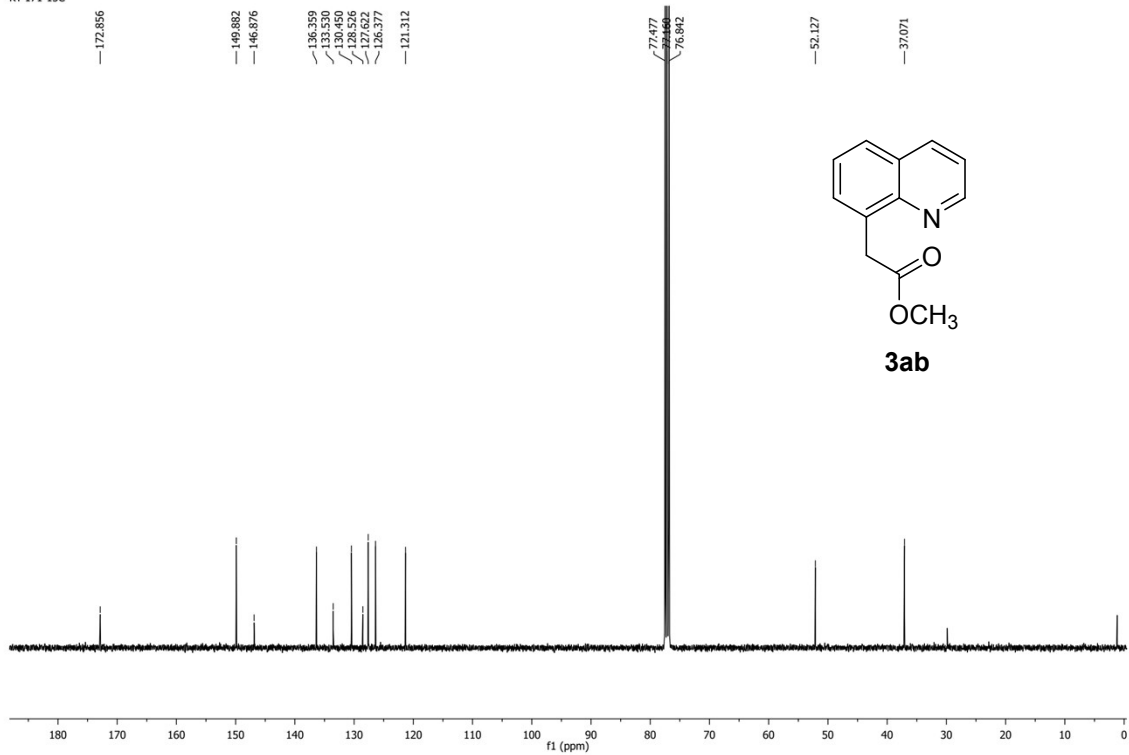
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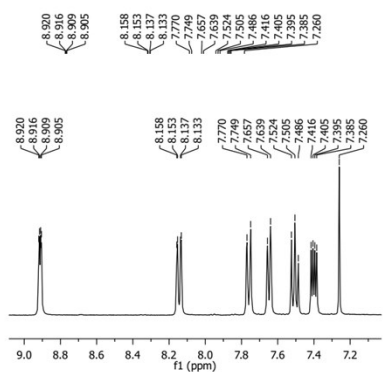
KT-171-1H



KT-171-13C

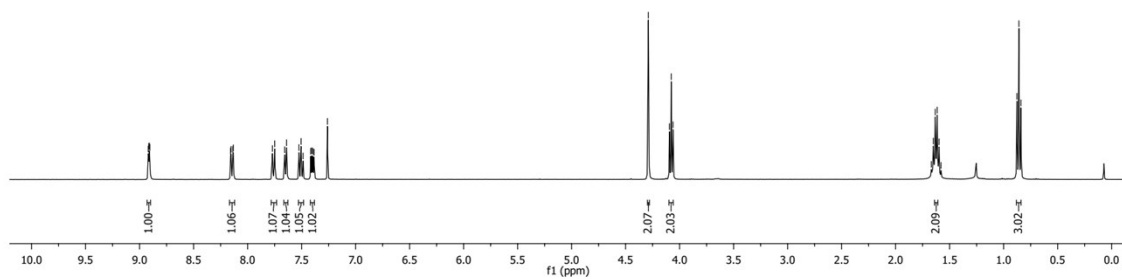
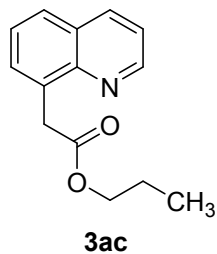


KT-176-1H

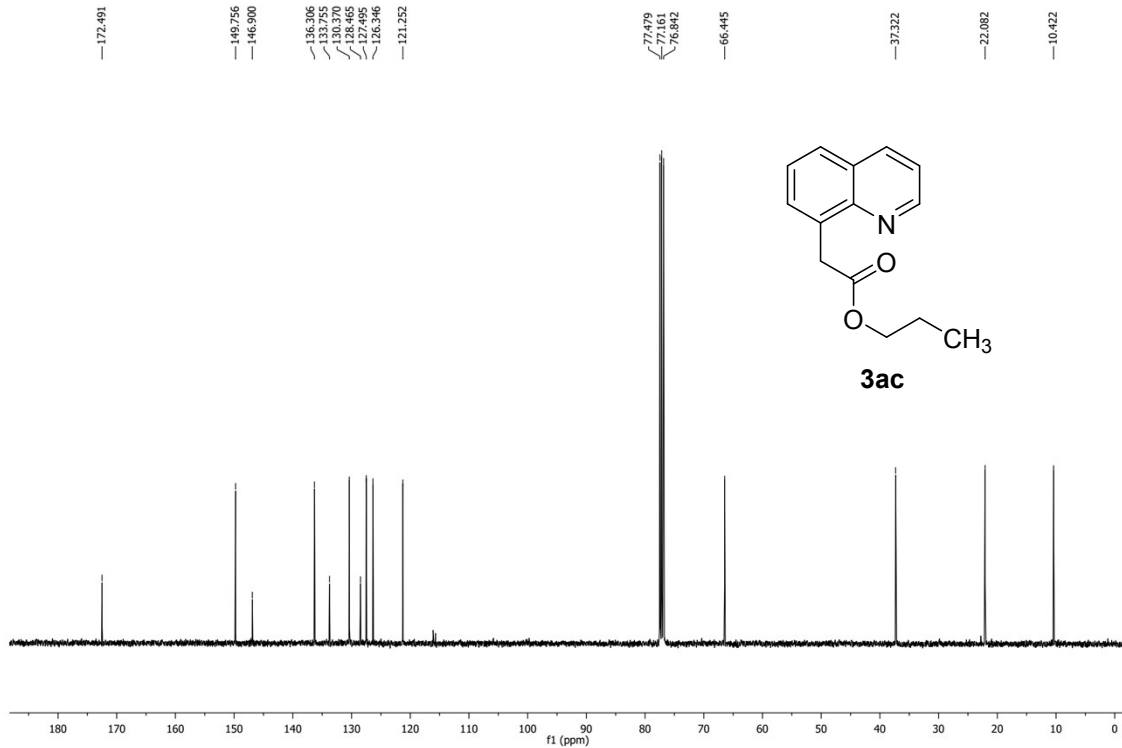


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3.978
1.001

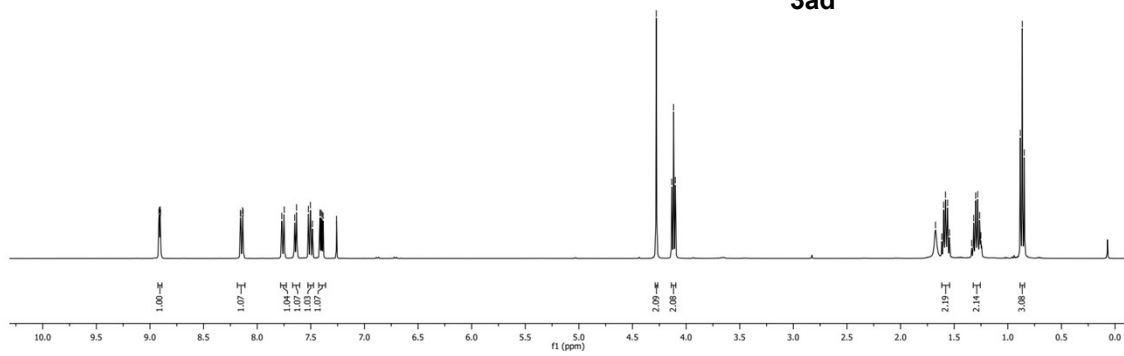
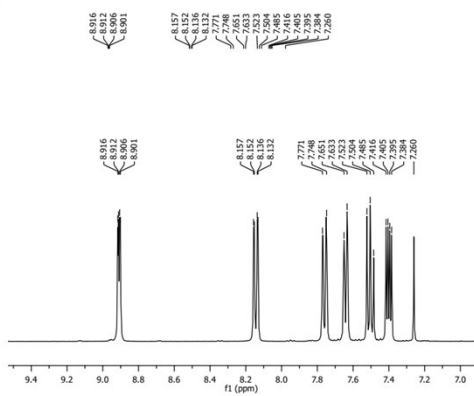
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0.860



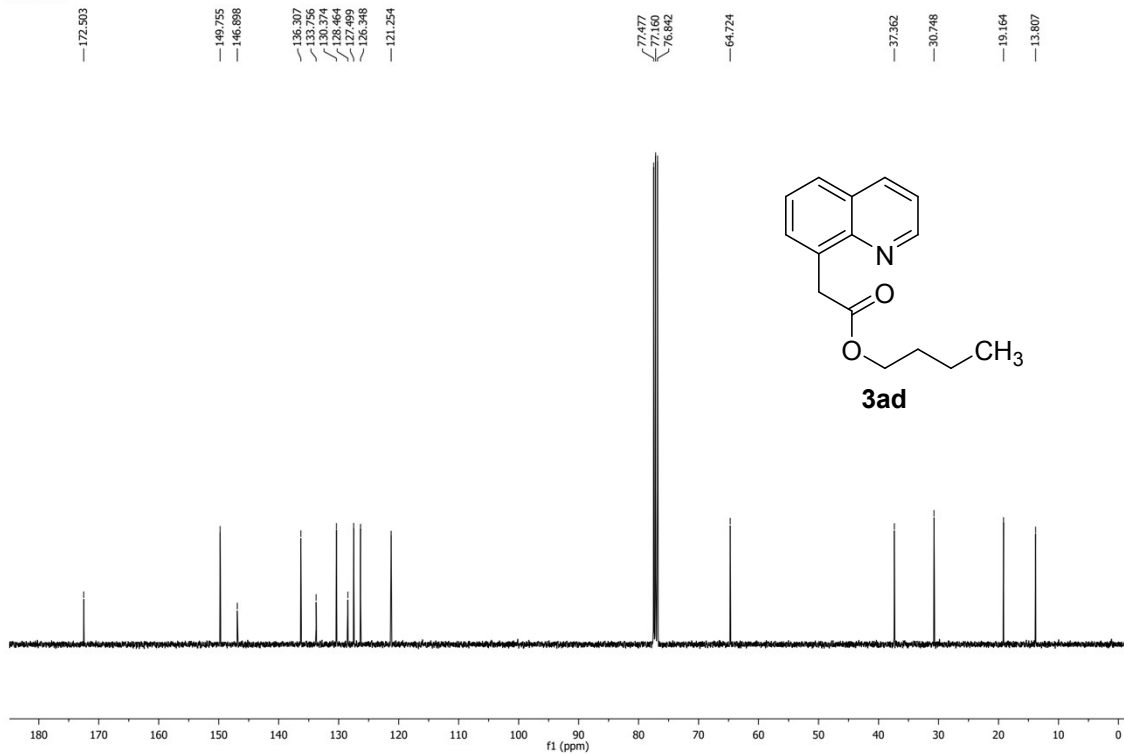
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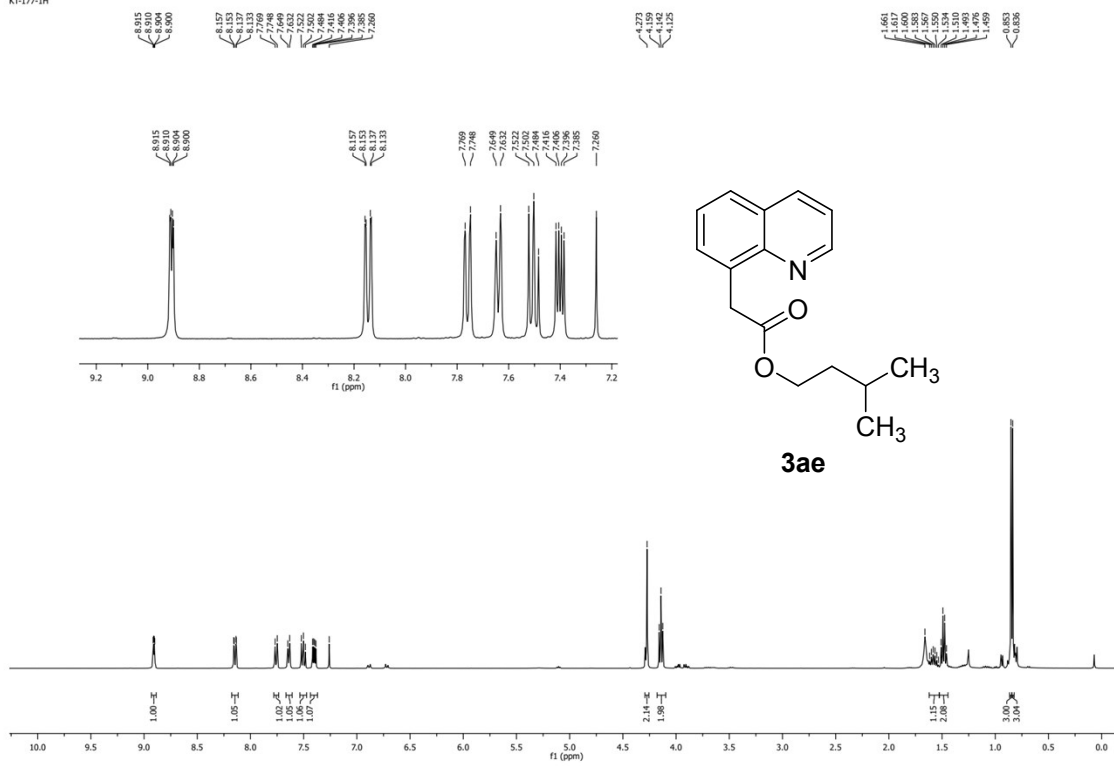
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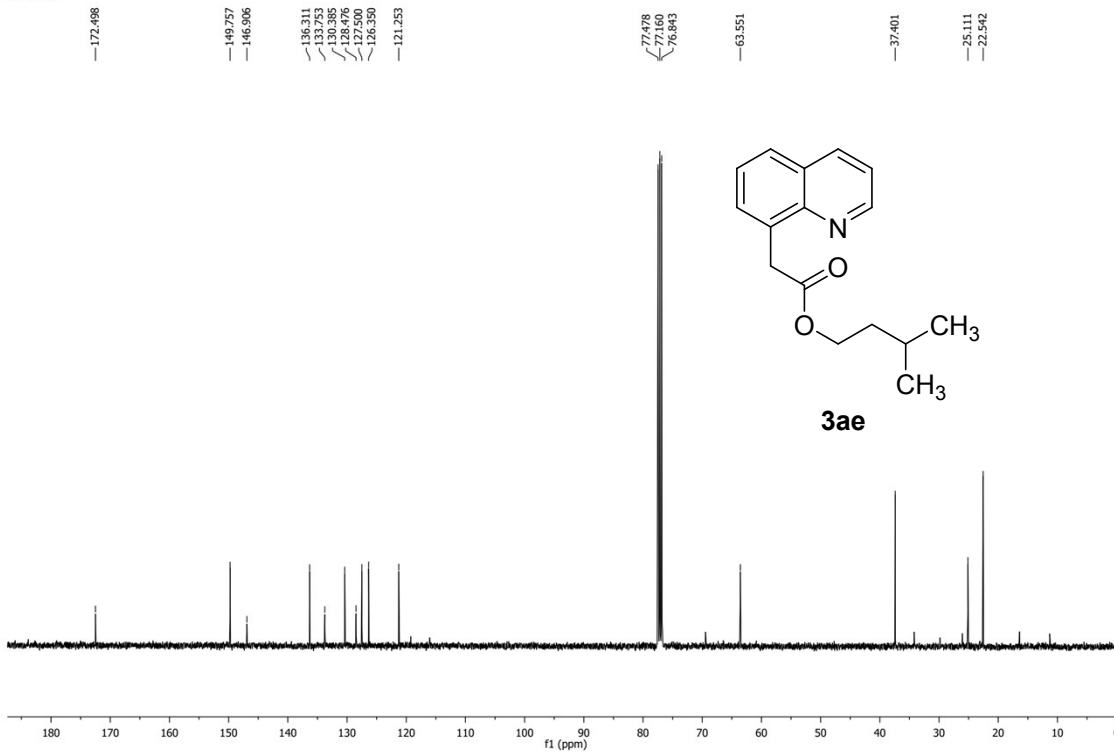
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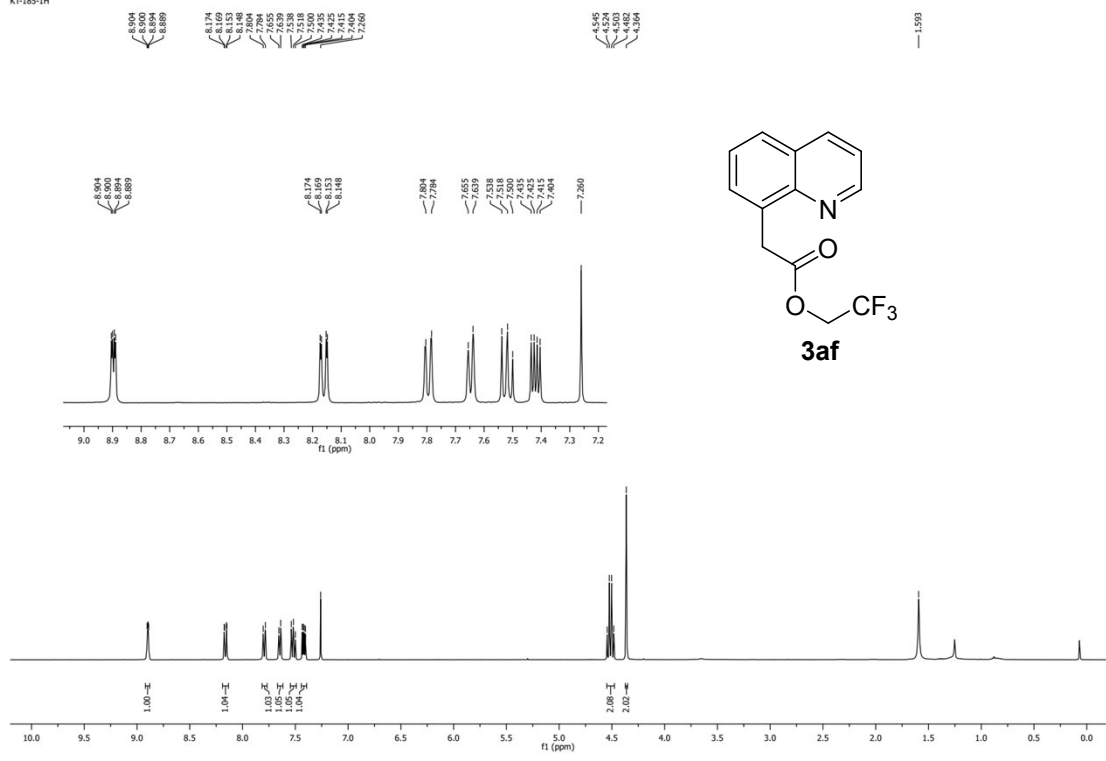
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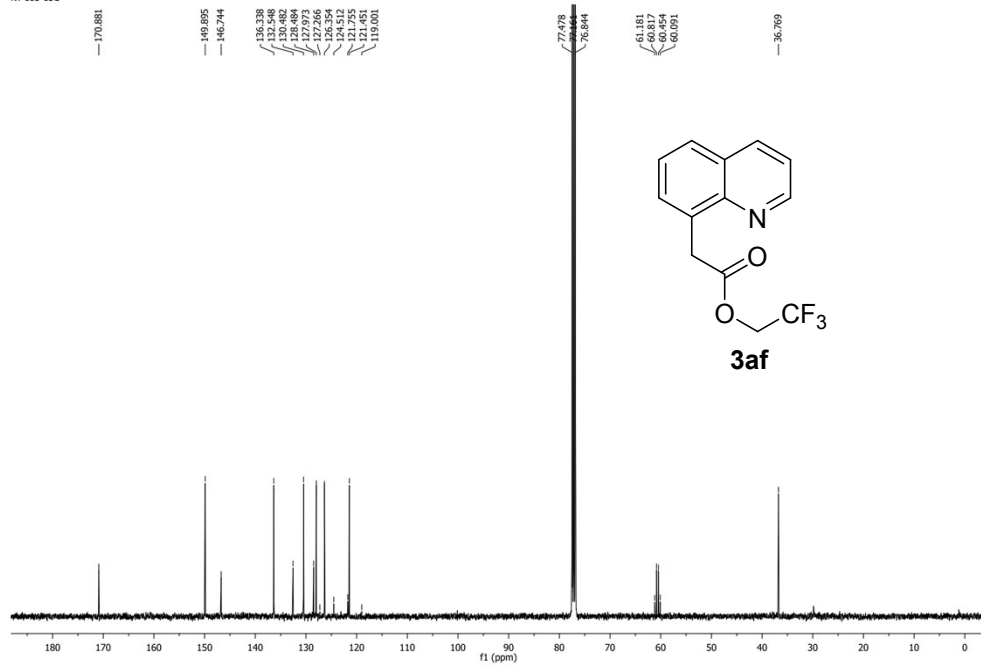
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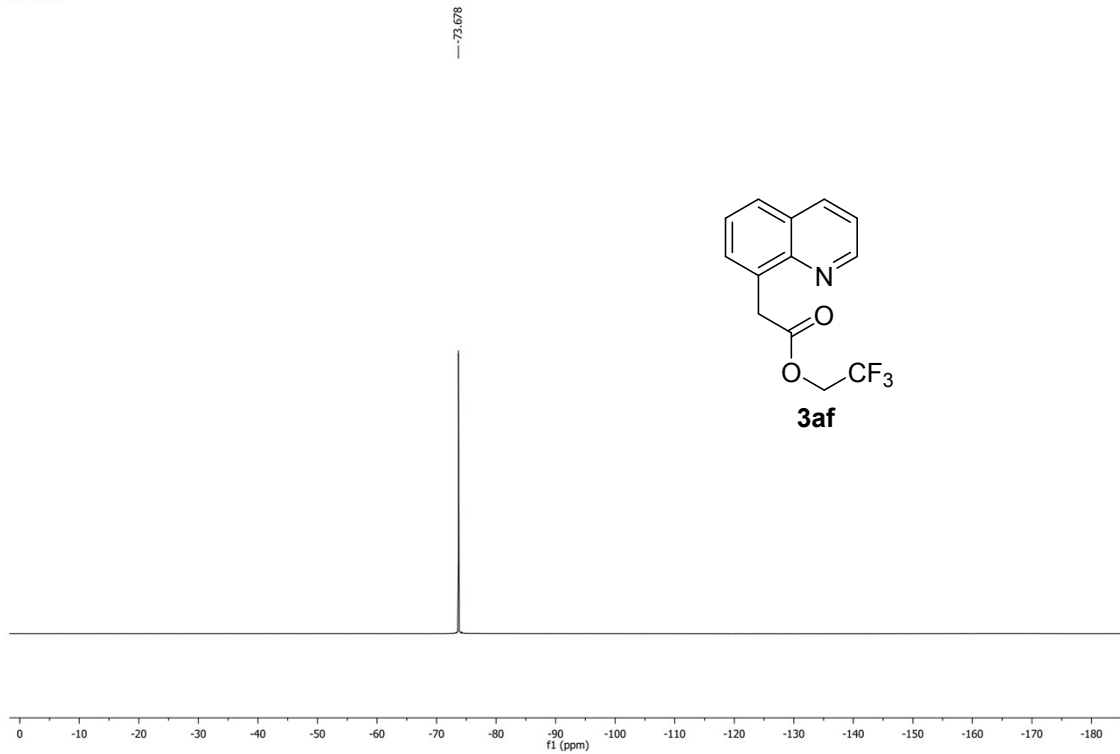
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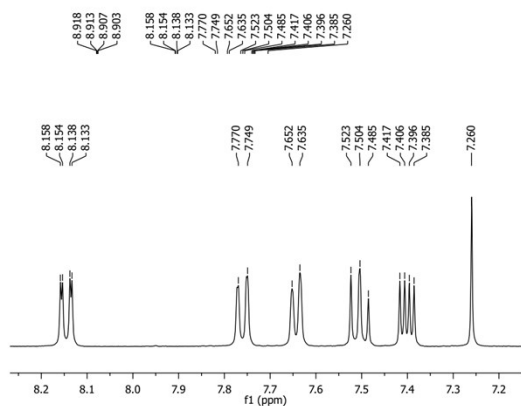
KT-185-13C



KT-185-19F

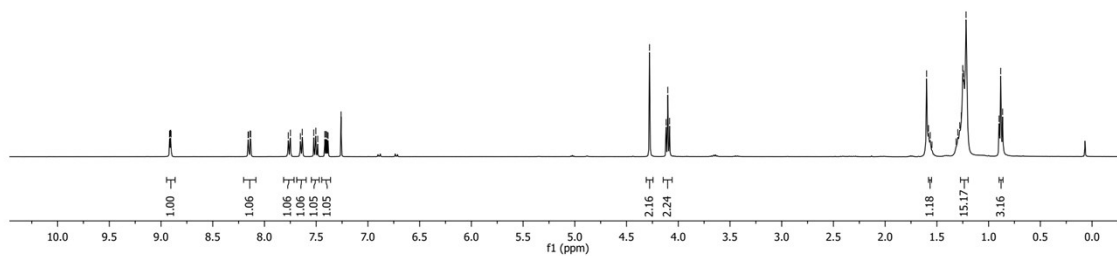
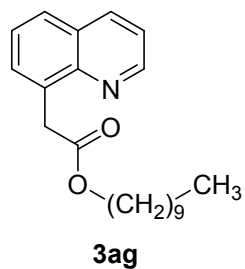


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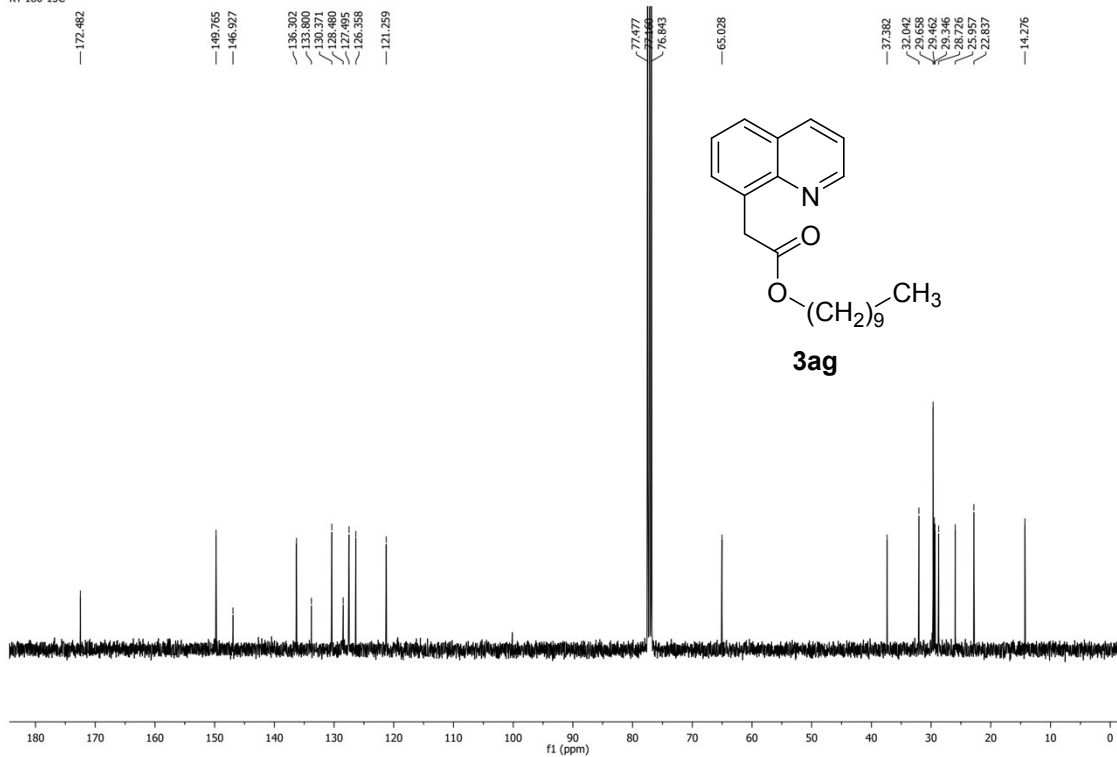


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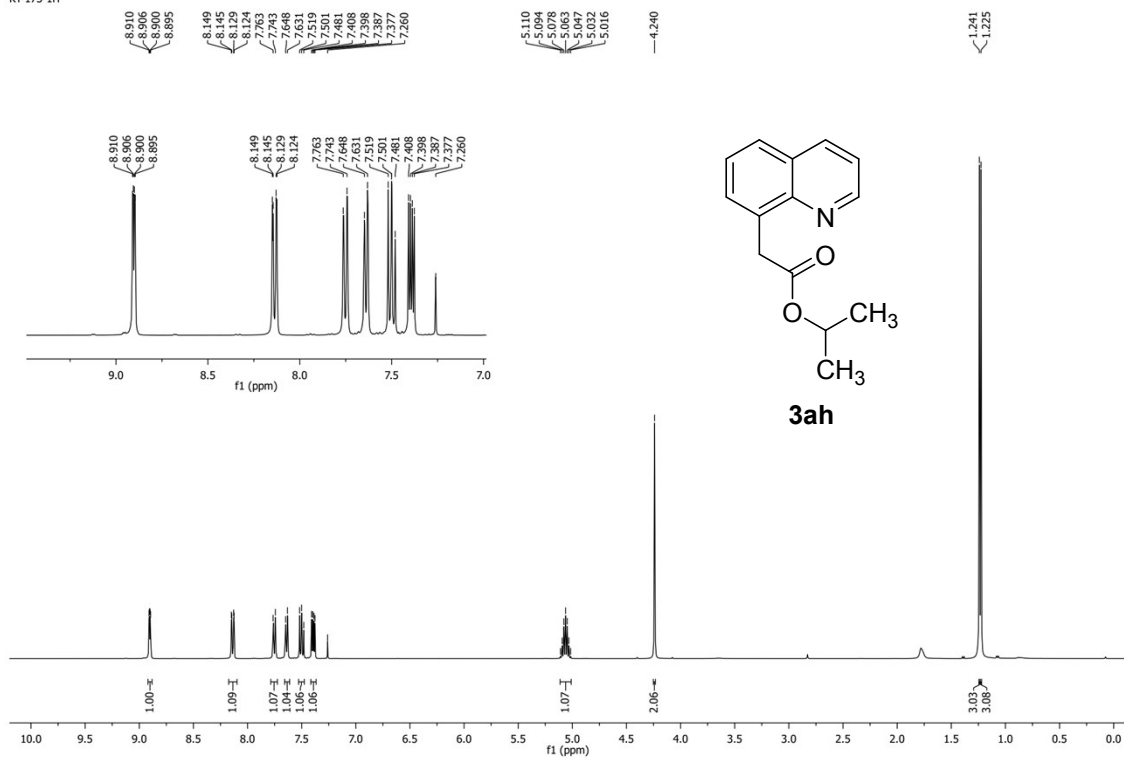
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0.885



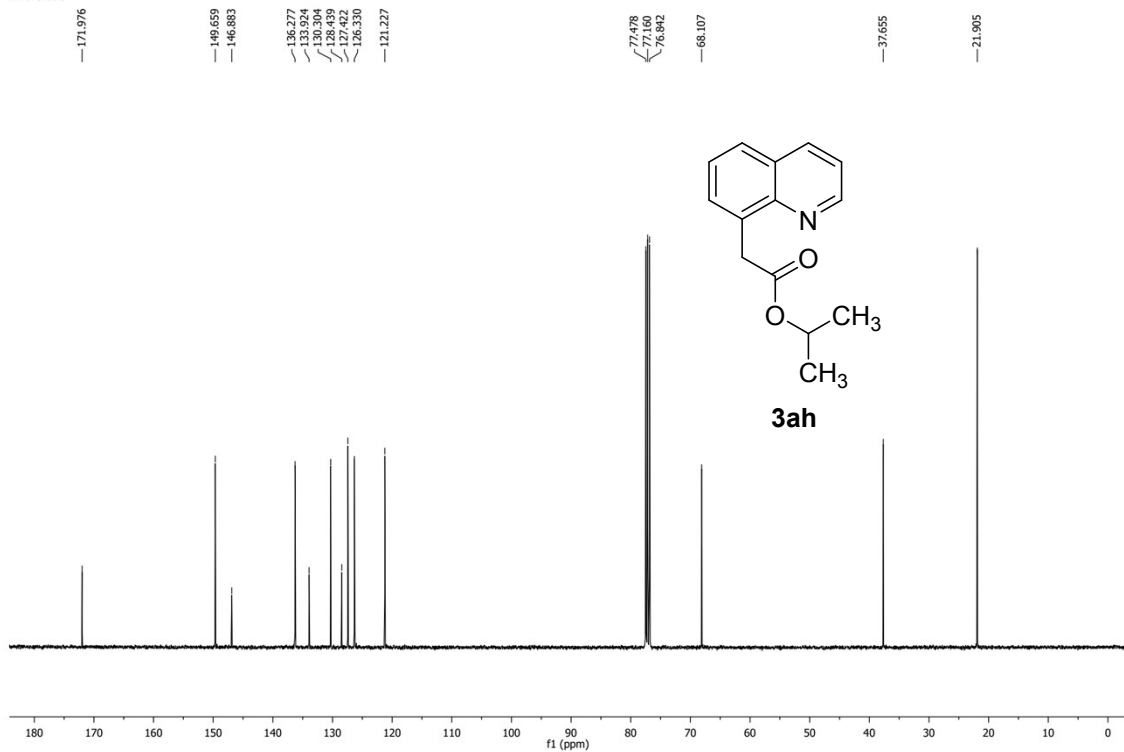
KT-180-13C



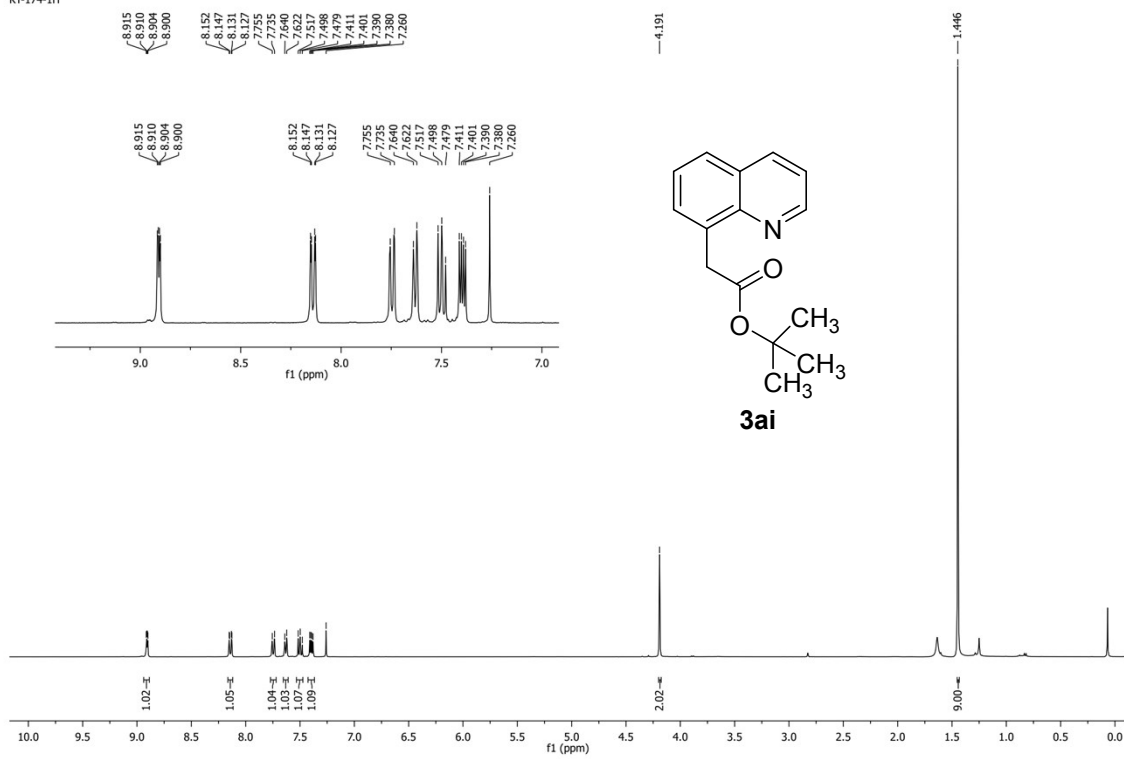
KT-173-1H



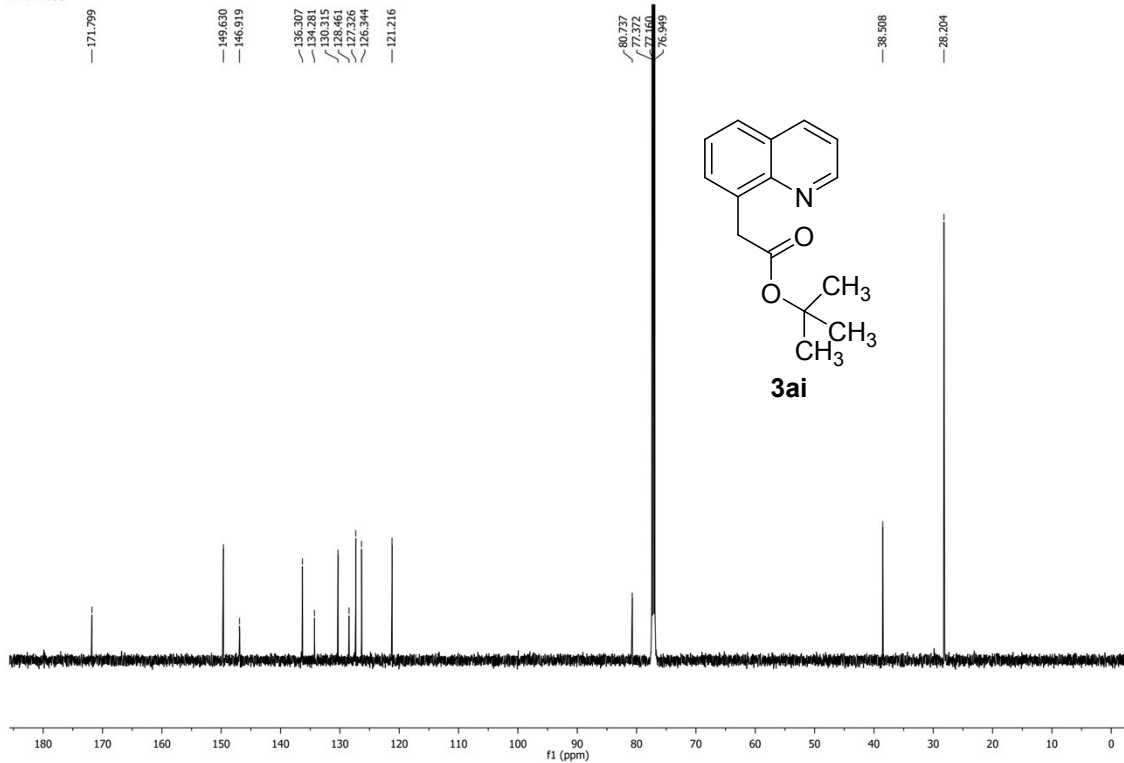
KT-173-13C



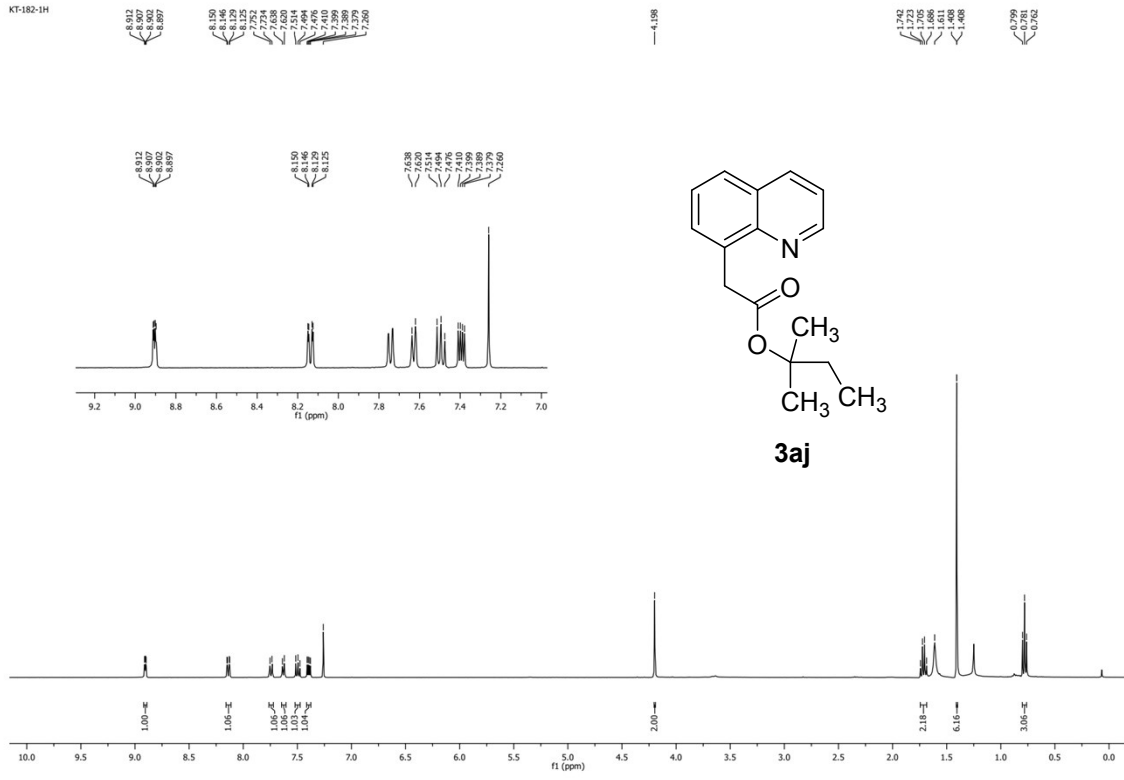
KT-174-1H



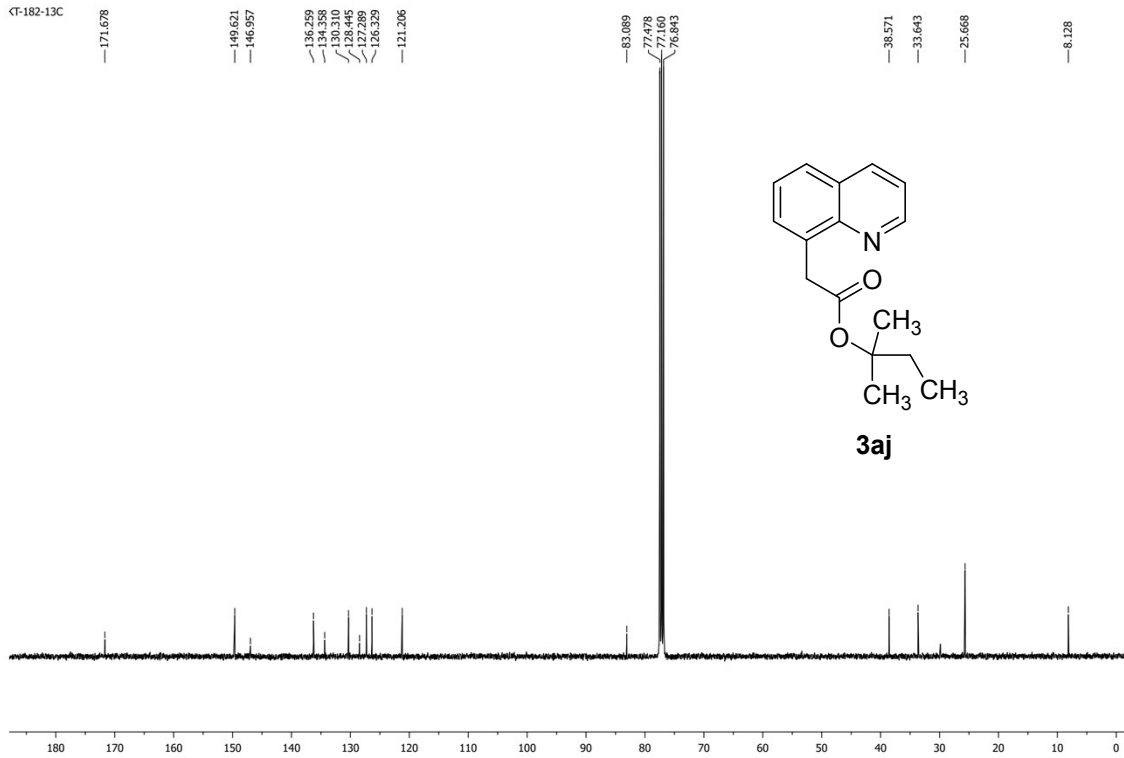
KT-174-13C



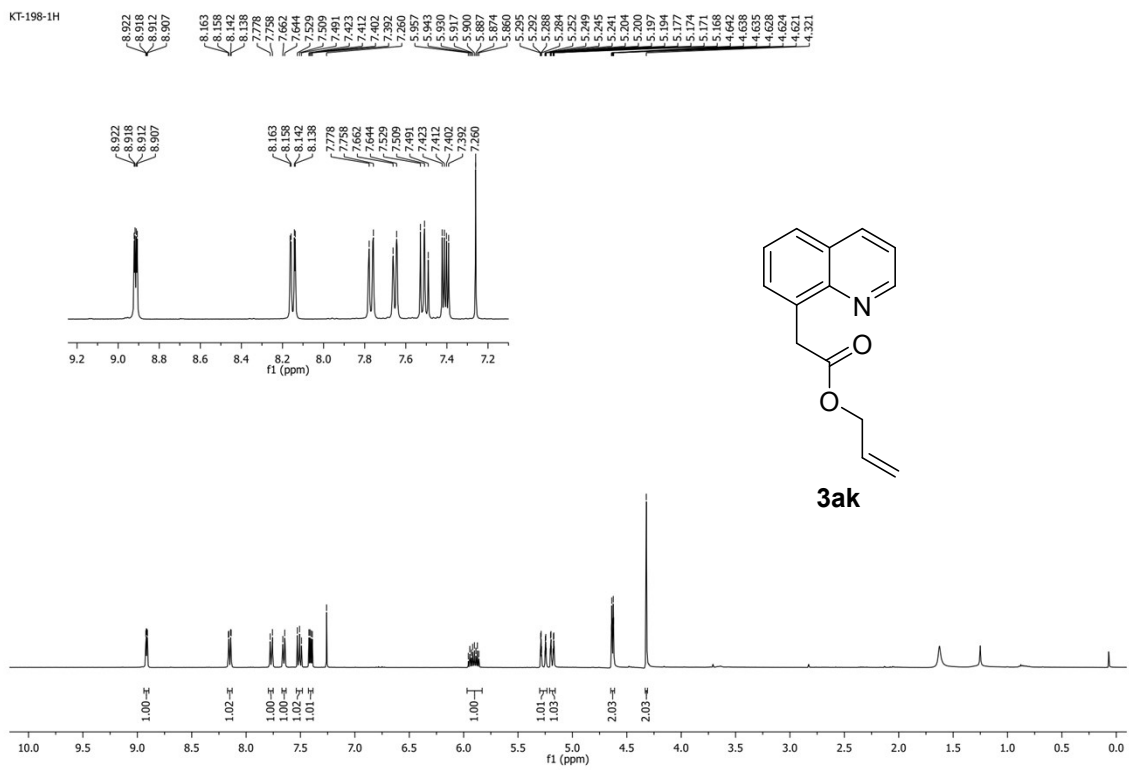
KT-182-1H



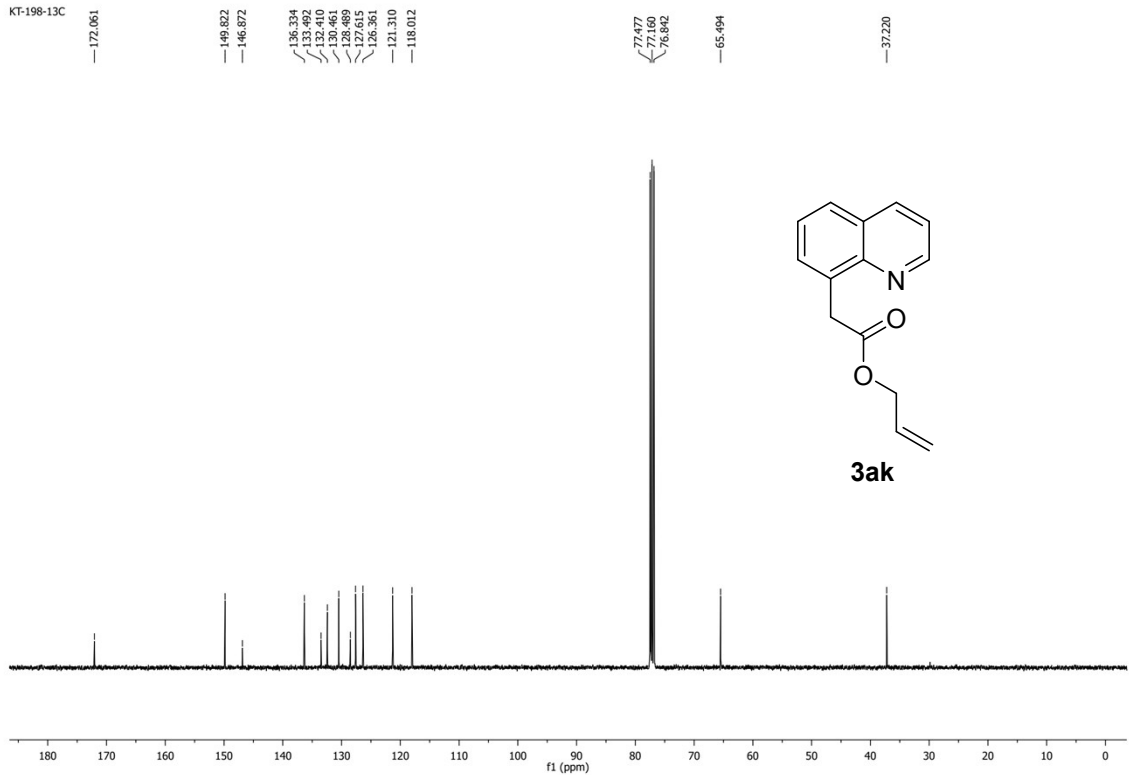
KT-182-13C



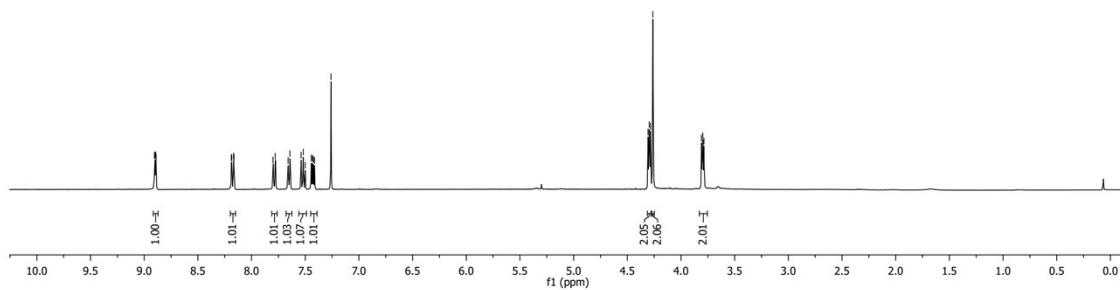
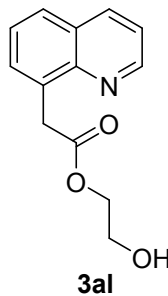
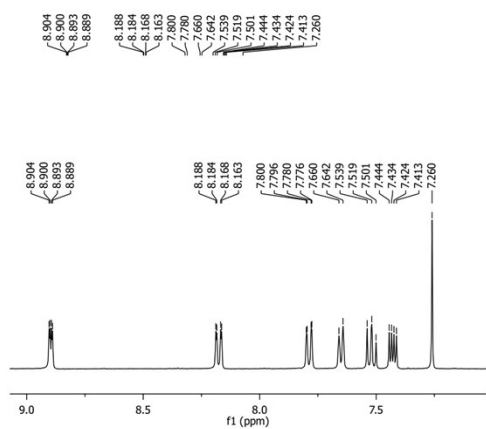
KT-198-1H



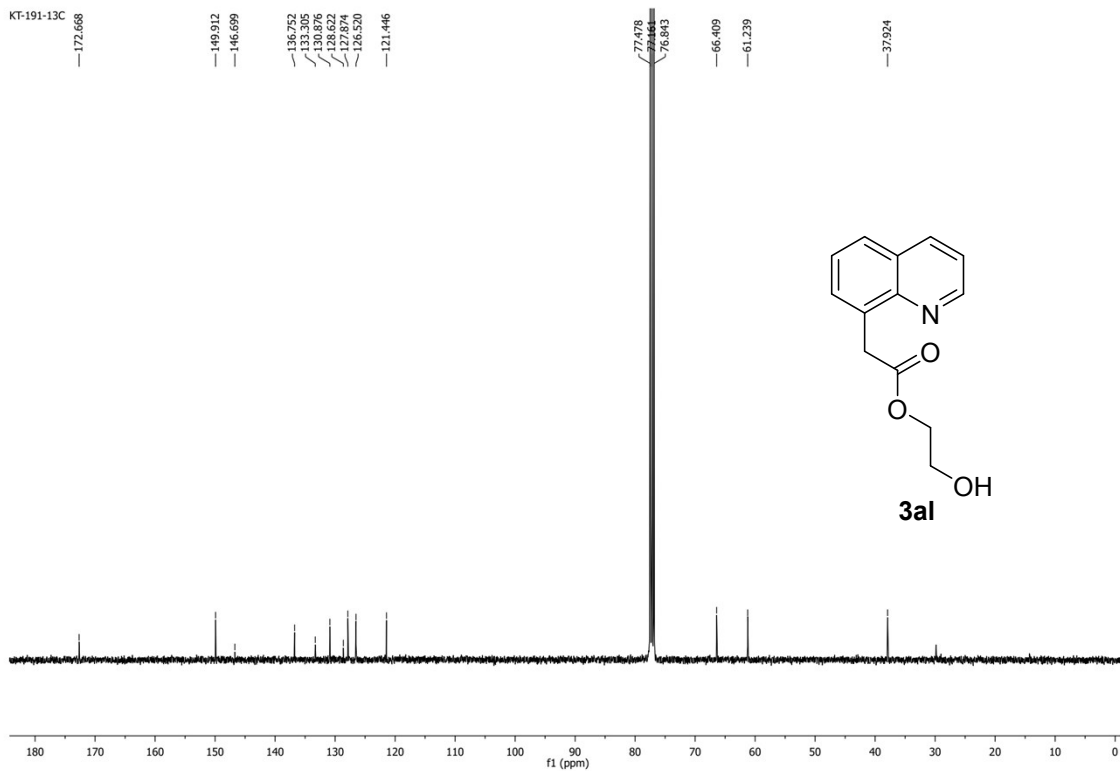
KT-198-13C



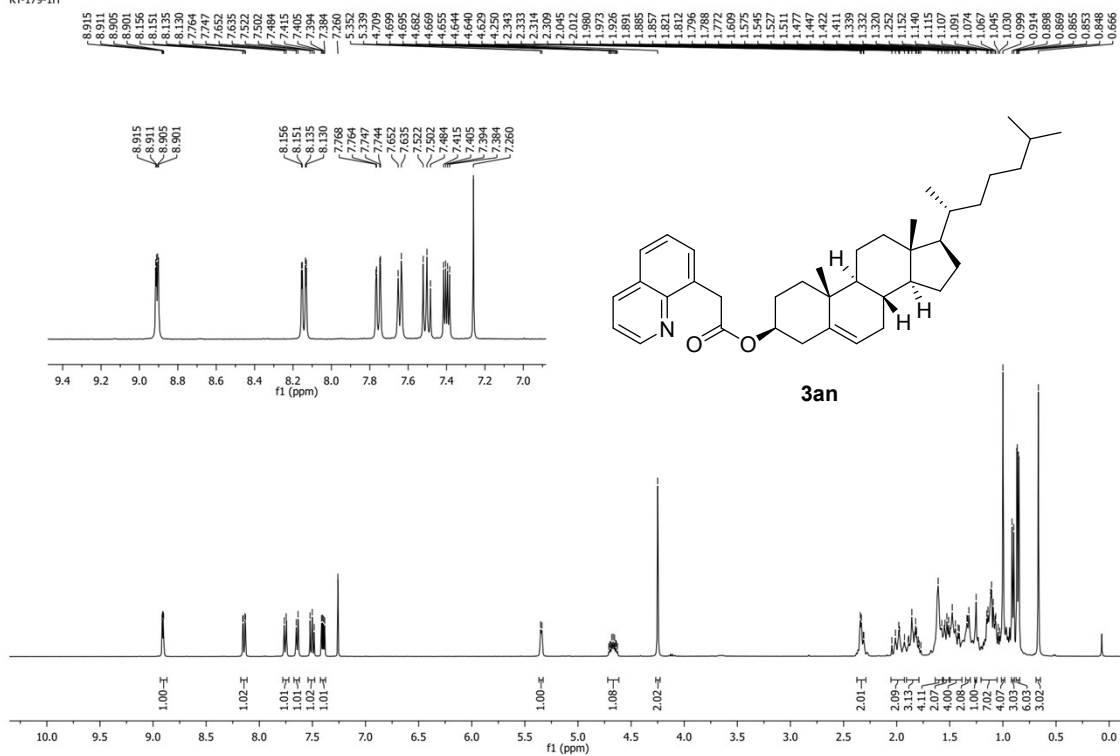
KT-191-1H



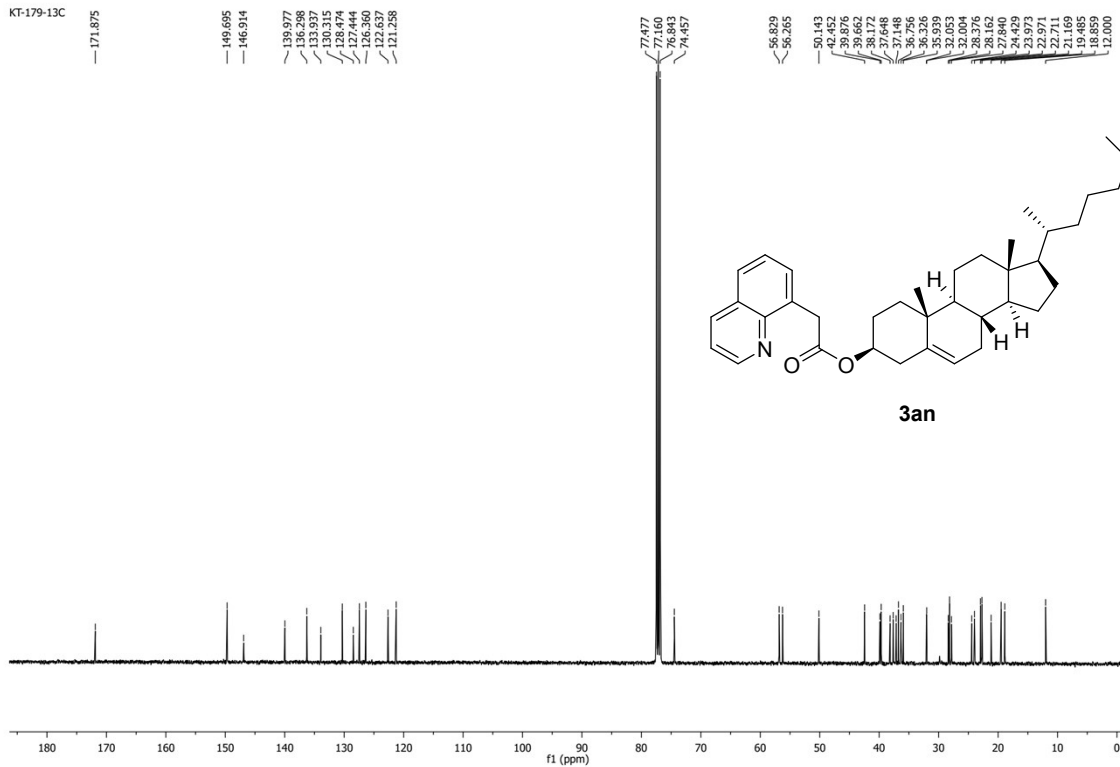
KT-191-13C



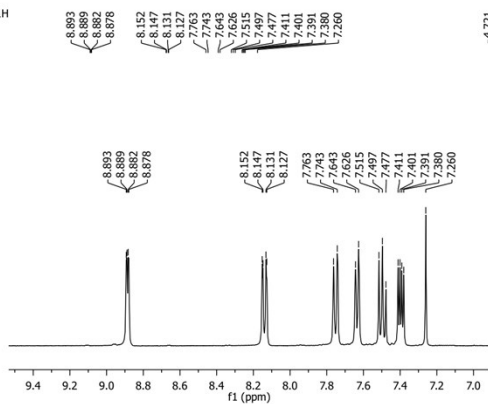
KT-179-1H



KT-179-13C

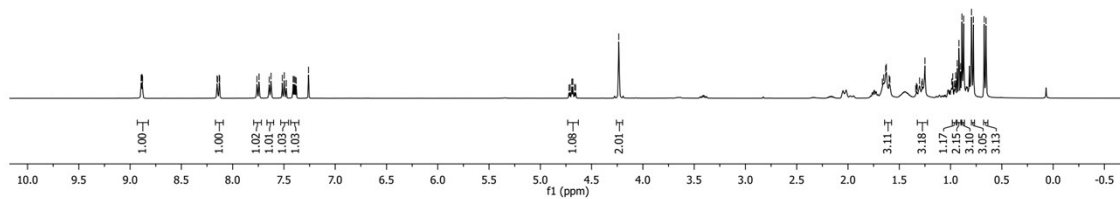


KT-184-1H

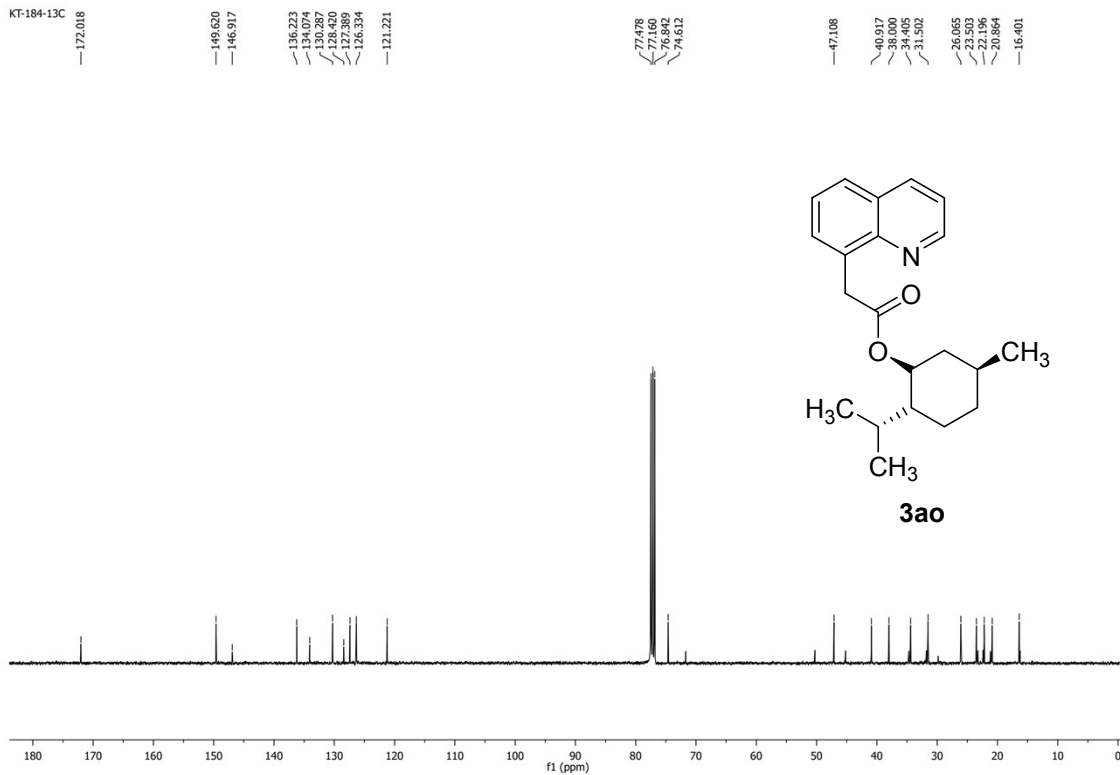


8.893
8.889
8.882
8.878
8.152
8.147
8.141
8.127
7.763
7.743
7.643
7.636
7.626
7.497
7.477
7.411
7.401
7.391
7.380
7.260
4.771
4.770
4.683
4.682
4.666
4.655
4.235

1.665
1.652
1.633
1.626
1.598
1.591
1.581
1.340
1.332
1.325
1.303
1.300
1.274
1.250
0.988
0.978
0.968
0.950
0.935
0.918
0.903
0.889
0.872
0.778
0.672
0.654



KT-184-13C



172.018

149.620
146.917

136.223
134.074
130.287
128.420
127.599
126.334
121.221

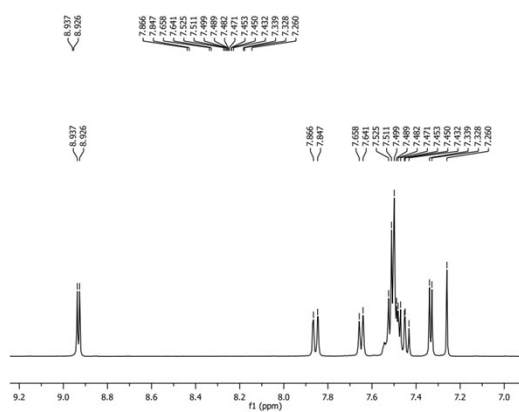
77.478
77.160
76.642
74.612

47.108

40.917
38.000
35.005
31.902

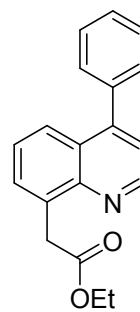
26.065
21.105
20.105
22.106
20.864
16.401

KT-217-N-1H

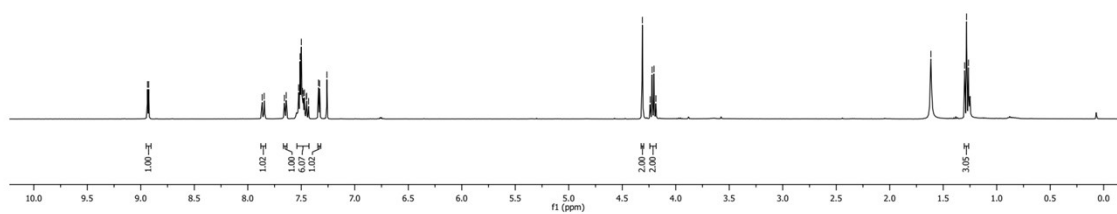


4.312
4.329
4.320
4.185

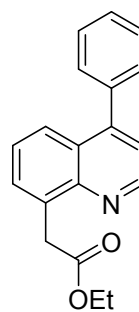
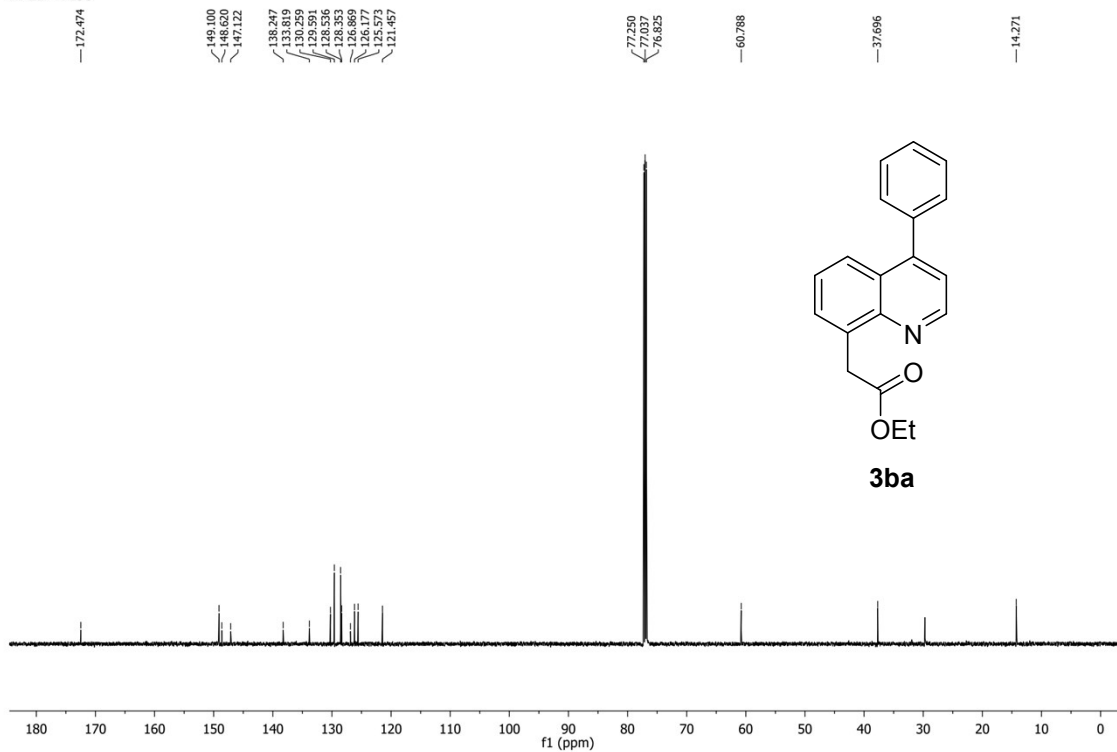
1.615
1.360
1.264



3ba

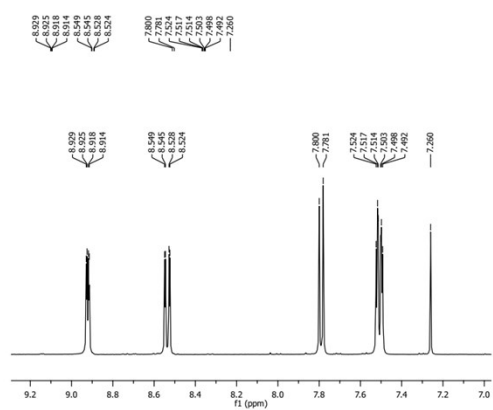


KT-217-N-13C



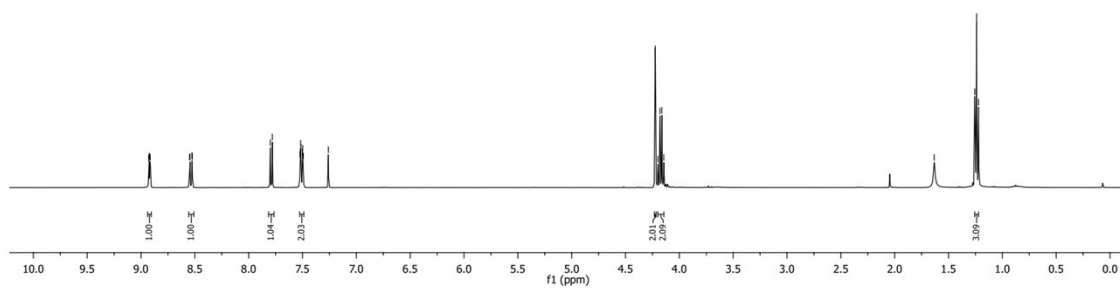
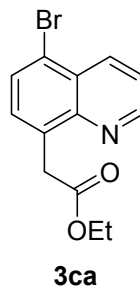
3ba

KT-196-1H



4.223
4.181
4.133
4.115

1.633
1.256
1.239
1.221



KT-196-13C

171.941

150.334
147.514

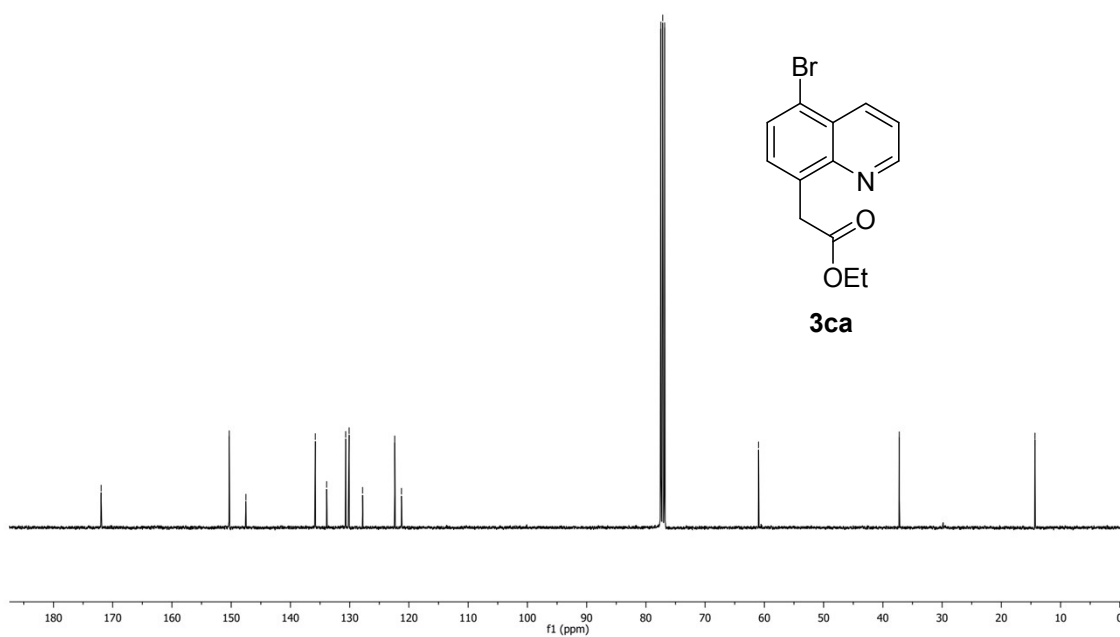
135.803
133.875
130.675
130.100
127.815
122.387
121.259

77.478
77.160
76.843

60.980

37.234

14.334

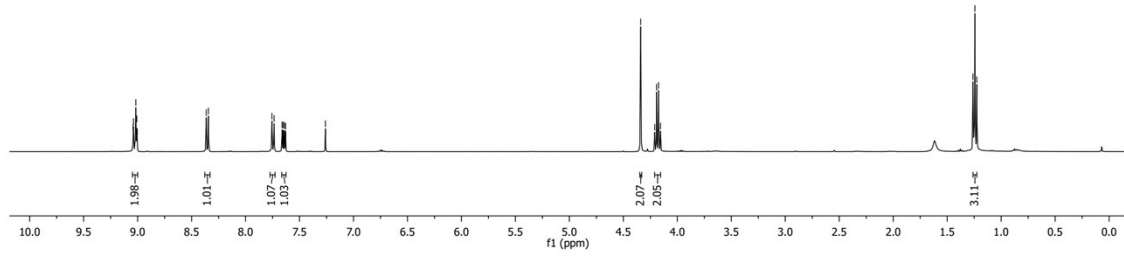
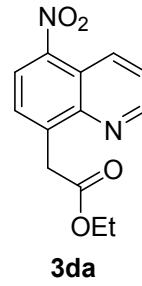
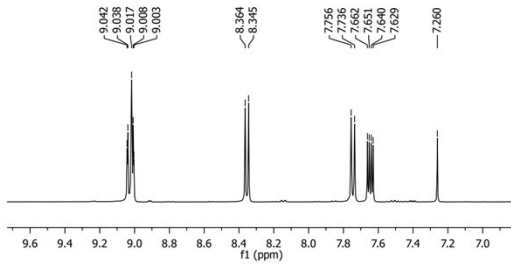


KT-203-1H

9.042
9.038
9.017
9.008
9.003
8.364
8.345
7.756
7.662
7.651
7.640
7.629
7.260

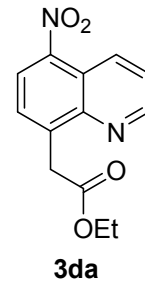
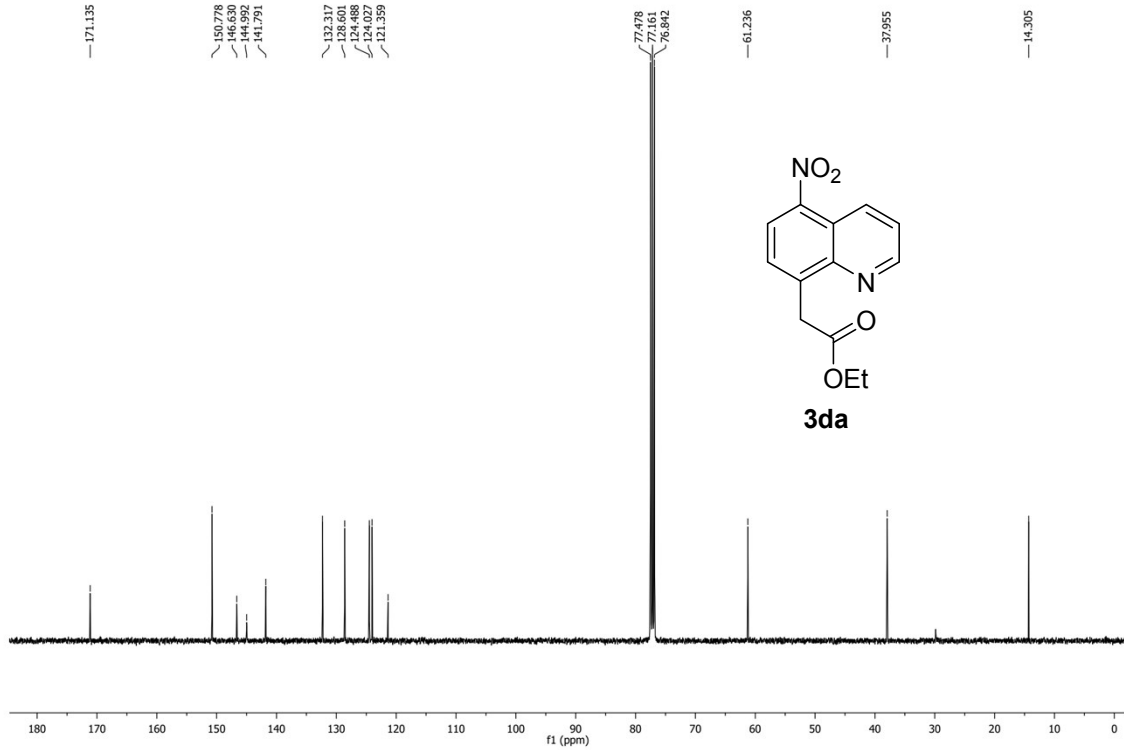
4.339
4.309
4.282
4.174
4.156

1.261
1.243
1.226

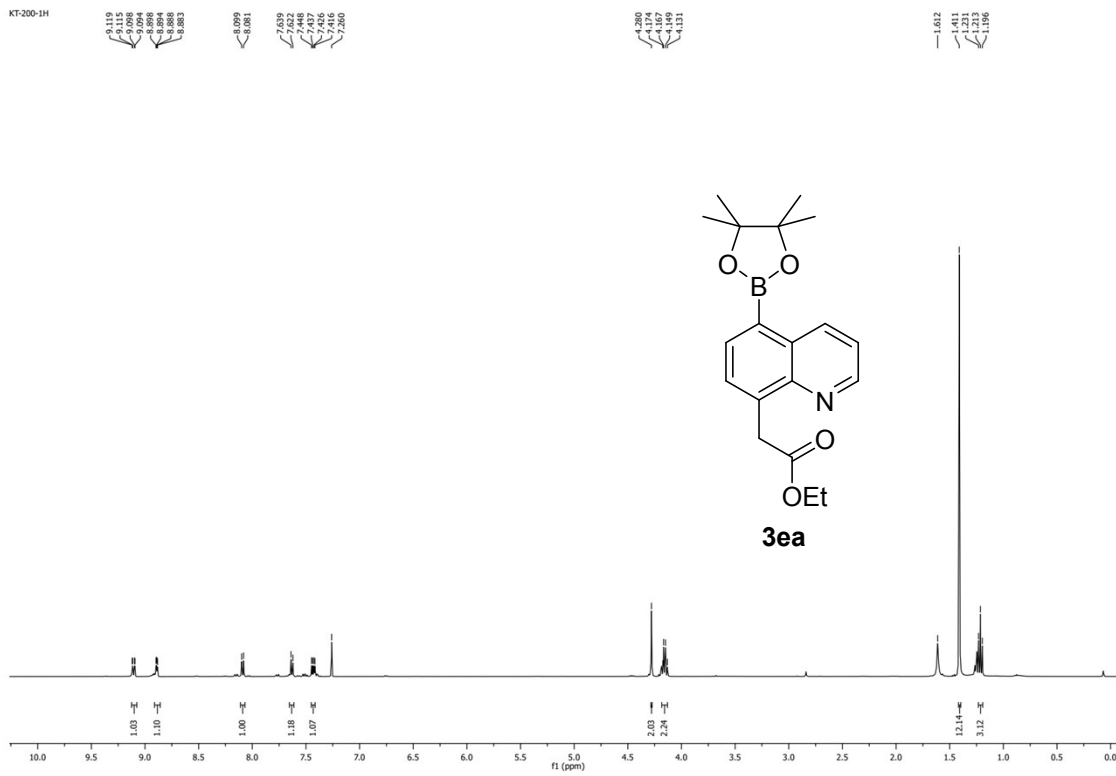


KT-203-13C

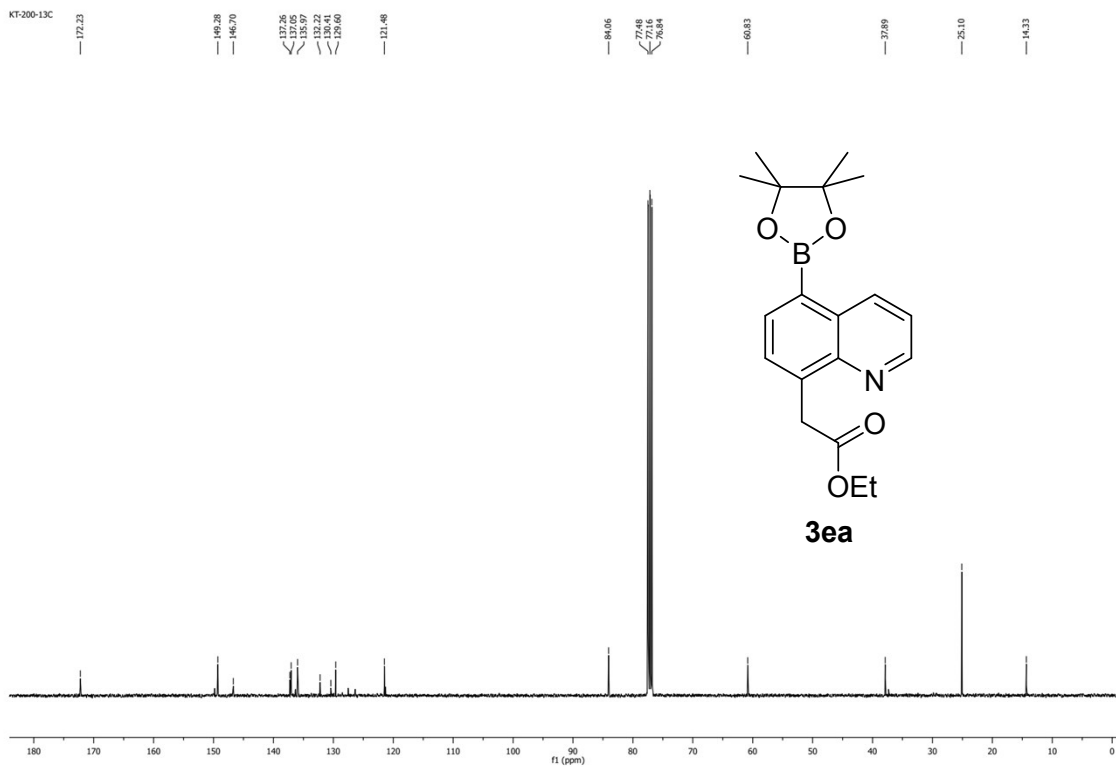
171.135
160.776
146.630
144.992
141.791
132.317
128.601
124.488
124.027
121.359
77.478
77.161
76.842
61.236
37.955
14.305



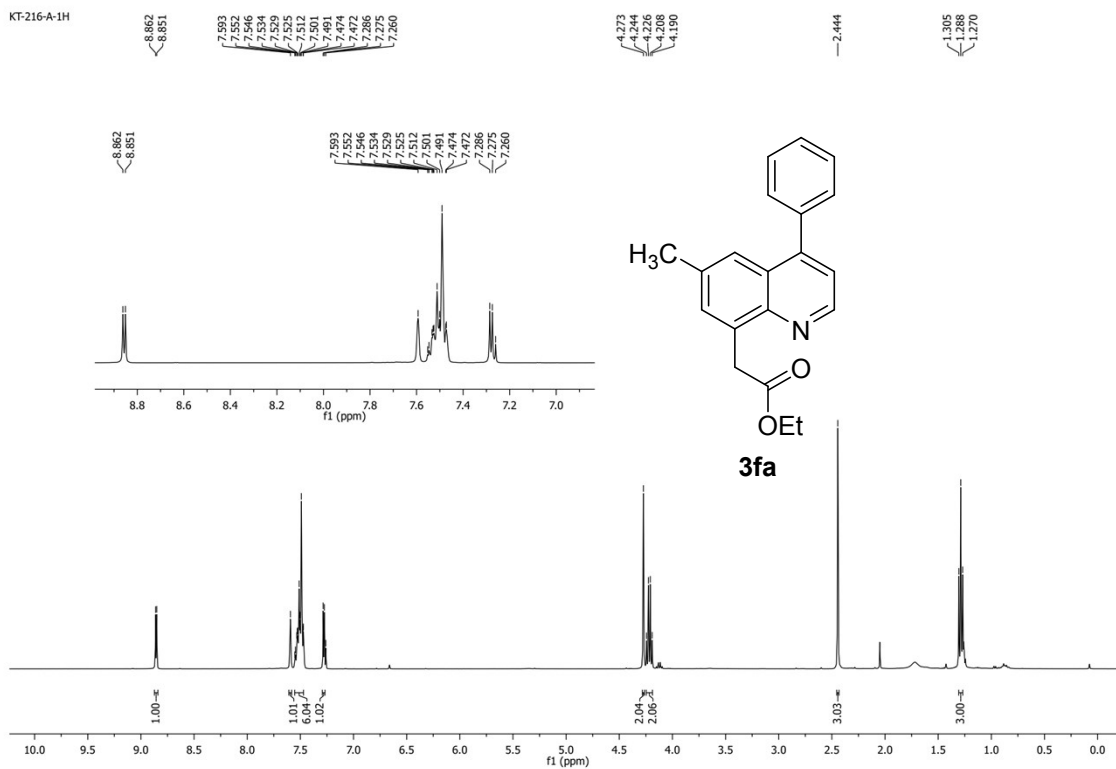
KT-200-1H



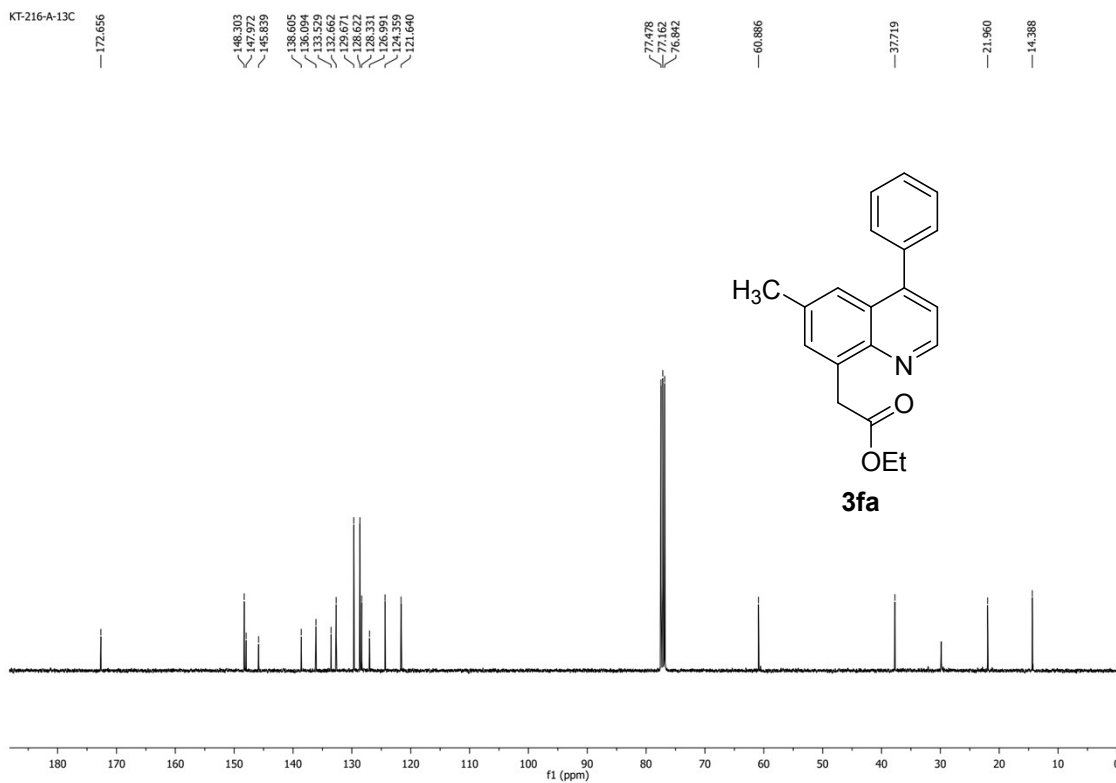
KT-200-13C



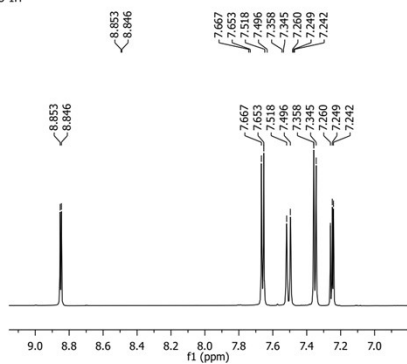
KT-216-A-1H



KT-216-A-13C



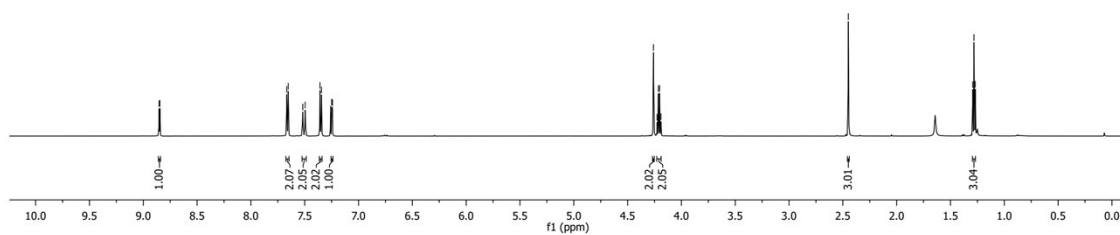
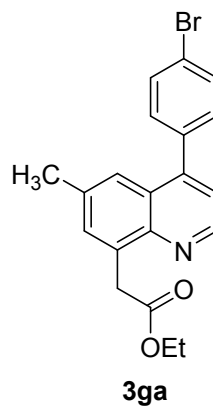
KT-225-1H



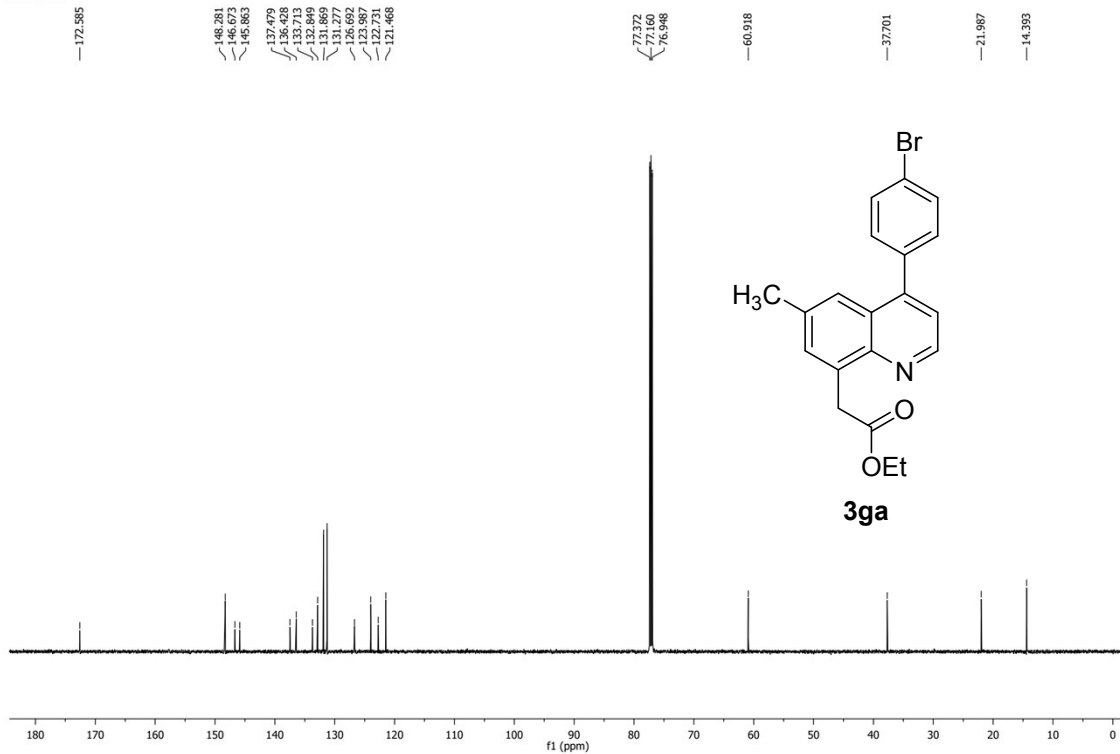
4.260
4.226
4.214
4.202
4.191

2.449

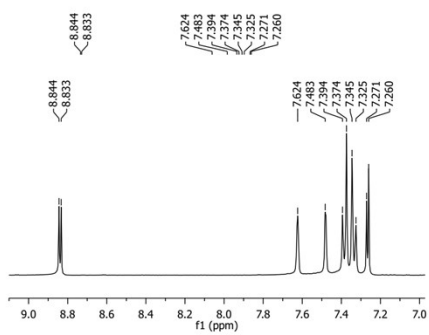
1.294
1.282
1.270



KT-225-13C



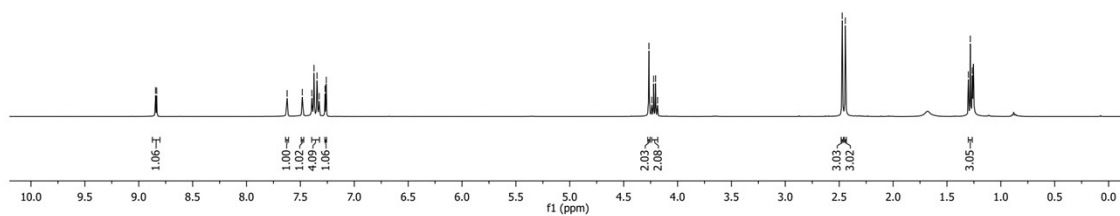
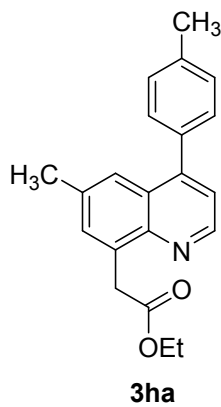
KT-231-1H



4.266
4.239
4.222
4.205
4.188

2.472
2.443

1.301
1.286
1.266



KT-231-13C

172.677

148.321
148.212
145.860

138.238
135.964
135.684
133.502
132.866
129.343
127.109
124.440
121.629

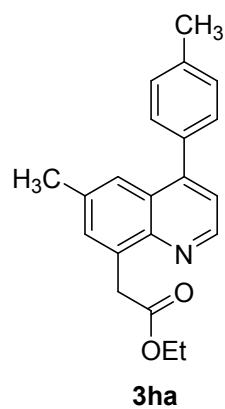
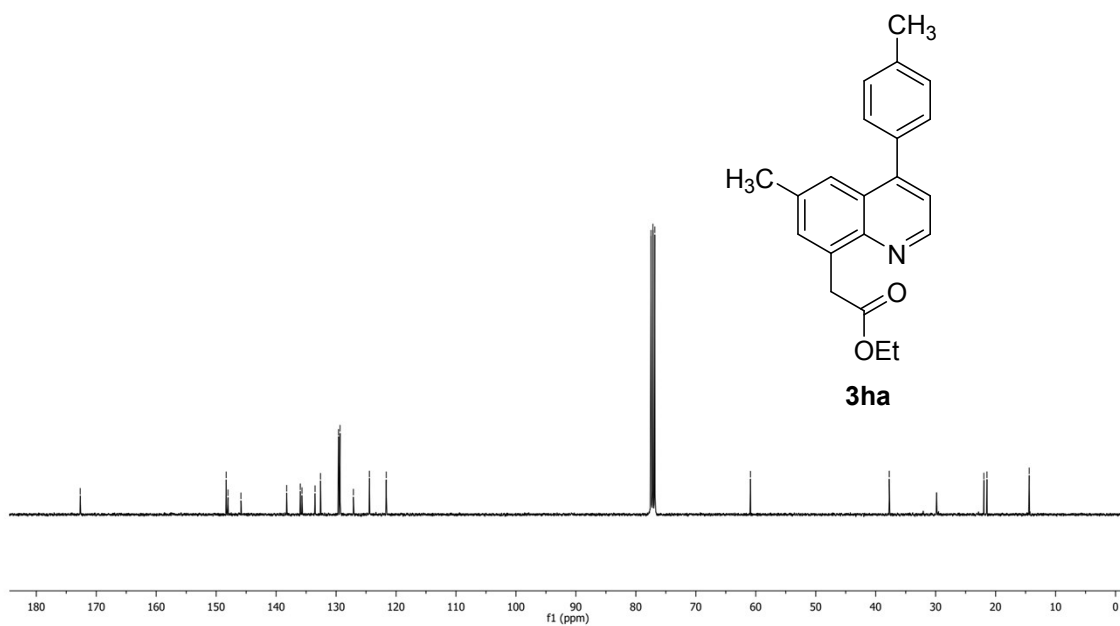
77.477
77.160
76.842

60.875

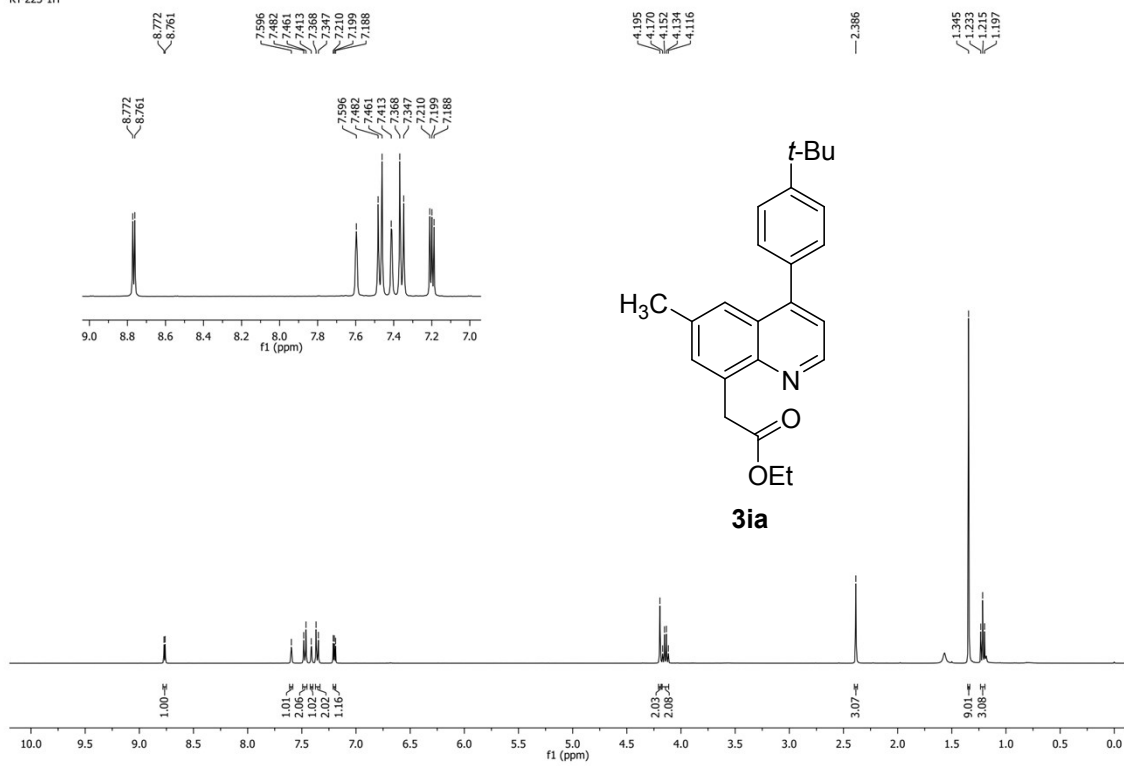
37.734

21.956
21.451

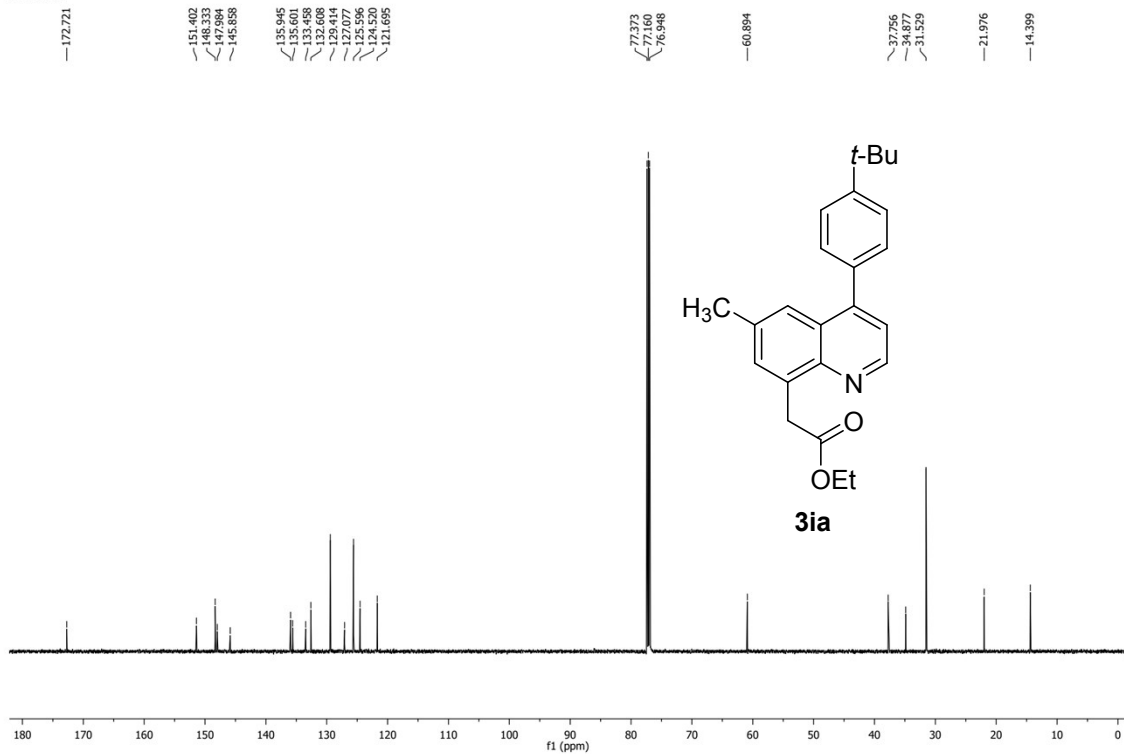
14.395



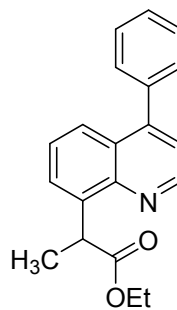
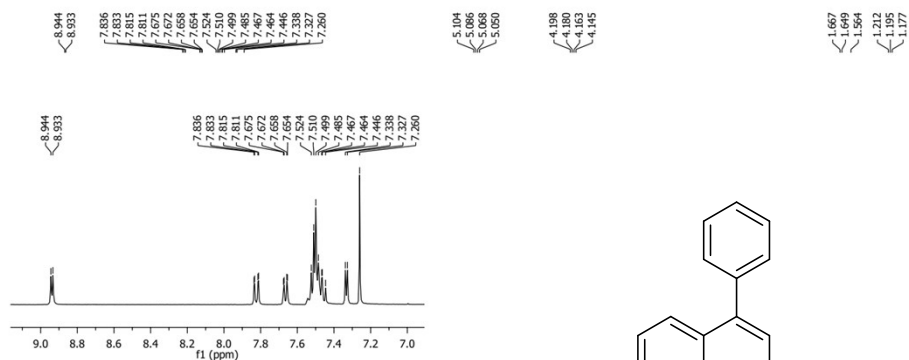
KT-223-1H



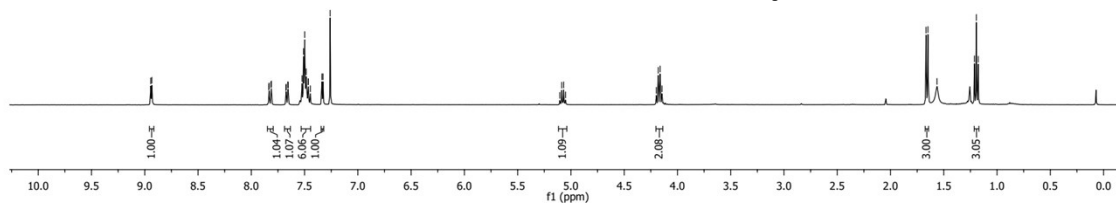
KT-223-13C



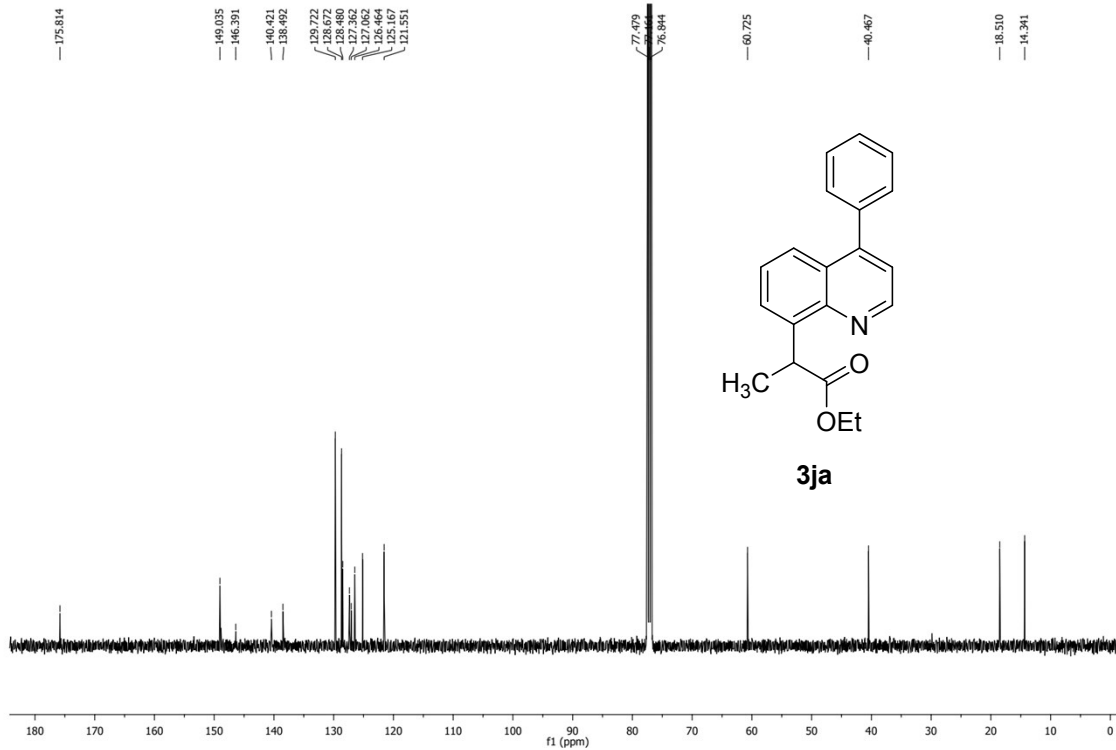
KT-249-1H



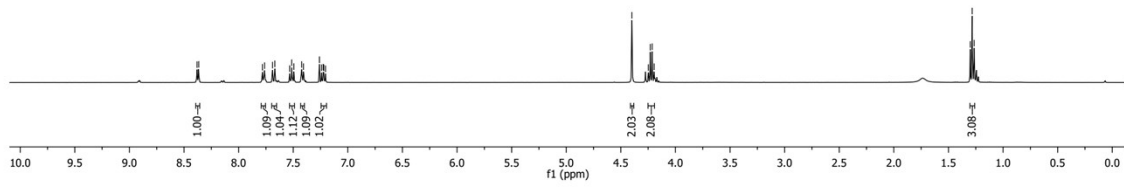
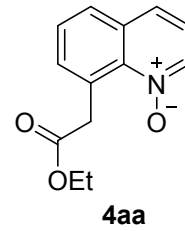
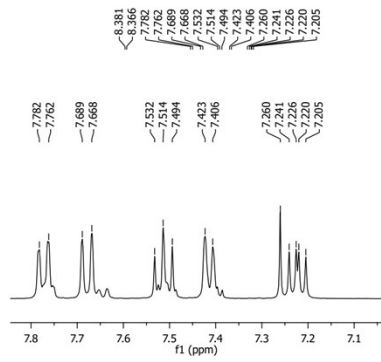
3ja



KT-249-13C



KT-235-1H



KT-235-13C

