

Supporting Information

for

AgOTf-catalyzed one-pot reactions of 2-alkynylbenzaldoximes with α,β -unsaturated carbonyl compounds

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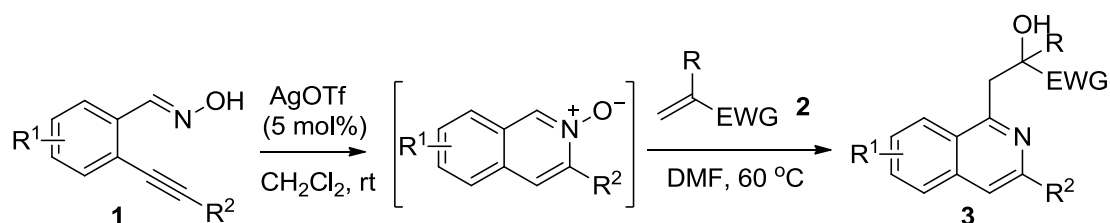
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Experimental part

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| 1. General procedure and characterization data for compounds 3 and 4 | S2–S13 |
| 2. NMR spectra of all compounds | S14–S33 |

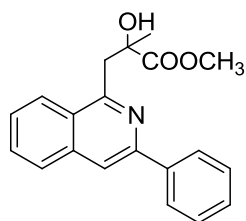
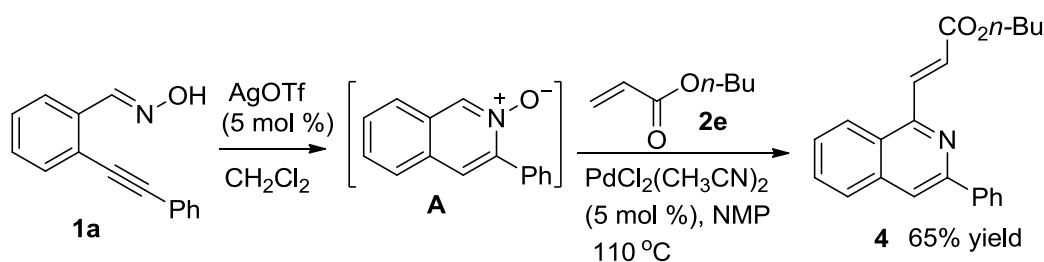
General procedure for the AgOTf-catalyzed one-pot reactions of 2-alkynylbenzaloximes **1** with α,β -unsaturated carbonyl compounds **2**: A mixture of 2-alkynylbenzaloximes **1** (0.3 mmol) and AgOTf (0.015 mmol, 5 mol %) in CH₂Cl₂ (2 mL) was stirred at room temperature for 2 h, until 2-alkynylbenzaloxime **1** was completely consumed. The solvent was removed under reduced pressure. Then, α,β -unsaturated carbonyl compound **2** (1.5 mmol, 5.0 equiv) in DMF (1 mL) was added to the residue, and allowed to stir at 60 °C overnight under a nitrogen atmosphere. After completion of the reaction as indicated by TLC, the reaction was quenched by water and extracted with ethyl acetate. The organic layers were dried with anhydrous MgSO₄, the solvent was evaporated under vacuum, and the residue was isolated by column chromatography with EtOAc/petroleum ether (1/5, v/v) as eluent to yield the desired products **3**.



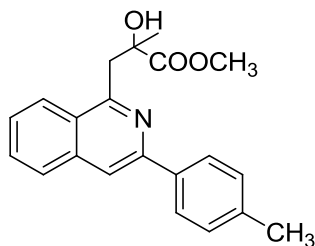
General procedure for palladium-catalyzed alkenylation reaction (Scheme 3):

A mixture of 2-alkynylbenzaloximes **1a** (0.3 mmol) and AgOTf (0.015 mmol, 5 mol %) in CH₂Cl₂ (2 mL) was stirred at room temperature for 2 h, until 2-alkynylbenzaloxime **1a** was completely consumed. The solvent was removed under reduced pressure. Then, butyl acrylate (**2e**, 192 mg, 1.5 mmol, 5.0 equiv), and PdCl₂(CH₃CN)₂ (3.9 mg, 5 mol %) in NMP (1 mL) was added to the residue, and

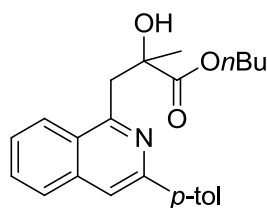
allowed to stir at 110 °C overnight under a nitrogen atmosphere. After completion of the reaction as indicated by TLC, the reaction was quenched by water and extracted with ethyl acetate. The organic layers were dried with anhydrous MgSO₄, the solvent was evaporated under vacuum, and the residue was isolated by column chromatography with EtOAc/petroleum ether (1/5, v/v) as eluent to yield the desired products **4**.



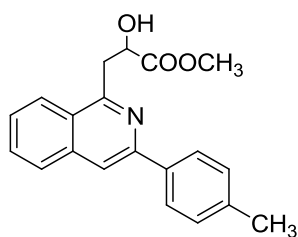
Methyl 2-hydroxy-2-methyl-3-(3-phenylisoquinolin-1-yl)propanoate **3a**: yield: 98%; white solid; R_f = 0.36; mp: 100–101 °C; ¹H NMR (400 MHz, CDCl₃) δ 1.69 (s, 3H), 3.48 (d, J = 16.8 Hz, 1H), 3.62 (s, 3H), 4.12 (d, J = 17.2 Hz, 1H), 6.53 (br, 1H), 7.38 (t, J = 7.2 Hz, 1H), 7.50–7.54 (m, 3H), 7.61 (t, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.90 (s, 1H), 8.04–8.07 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 26.8, 42.3, 52.3, 74.6, 115.7, 124.7, 126.3, 126.6, 127.4, 127.9, 128.8, 129.0, 130.7, 137.0, 138.7, 148.7, 158.3, 177.0; IR (KBr) ν /cm⁻¹: 3439, 2979, 2928, 1729, 1594, 1499; HRMS (ESI): m/z [M + H]⁺ calcd for C₂₀H₂₀NO₃: 322.1443; found: 322.1449.



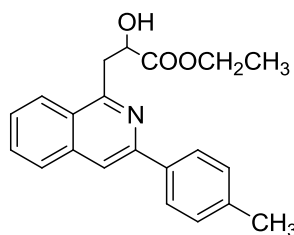
Methyl 2-hydroxy-2-methyl-3-(3-*p*-tolylisoquinolin-1-yl)propanoate (**3b**): yield: 70%; gray solid; $R_f = 0.39$; mp: 124–126 °C; ^1H NMR (400 MHz, CDCl_3) δ 1.70 (s, 3H), 2.40 (s, 3H), 3.49 (d, $J = 16.8$ Hz, 1H), 3.63 (s, 3H), 4.13 (d, $J = 17.2$ Hz, 1H), 6.60 (br, 1H), 7.29 (d, $J = 8.0$ Hz, 2H), 7.54 (t, $J = 7.2$ Hz, 1H), 7.65 (t, $J = 7.2$ Hz, 1H), 7.81 (d, $J = 8.0$ Hz, 1H), 7.92 (s, 1H), 7.97 (d, $J = 8.0$ Hz, 2H), 8.08 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.3, 26.8, 42.3, 52.3, 74.6, 115.2, 124.7, 126.2, 126.5, 127.2, 127.9, 129.7, 130.7, 135.9, 137.1, 138.8, 148.8, 158.2, 177.0; IR (KBr) ν/cm^{-1} : 3461, 2975, 2951, 1747, 1590, 1495; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{22}\text{NO}_3$: 336.1600; found: 336.1603.



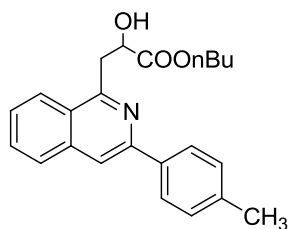
Butyl 2-hydroxy-2-methyl-3-(3-*p*-tolylisoquinolin-1-yl)propanoate (**3c**): yield: 81%; brown solid; $R_f = 0.50$; mp: 89–90 °C; ^1H NMR (400 MHz, CDCl_3) δ 0.64 (t, $J = 7.2$ Hz, 3H), 0.99–1.05 (m, 2H), 1.29–1.40 (m, 2H), 1.71 (s, 3H), 2.40 (s, 3H), 3.48 (d, $J = 16.8$ Hz, 1H), 3.93–3.98 (m, 1H), 4.01–4.05 (m, 1H), 4.14 (d, $J = 16.4$ Hz, 1H), 6.64 (br, 1H), 7.30 (d, $J = 8.0$ Hz, 2H), 7.53 (t, $J = 7.2$ Hz, 1H), 7.63 (t, $J = 8.0$ Hz, 1H), 7.79 (d, $J = 8.0$ Hz, 1H), 7.90 (s, 1H), 7.98 (d, $J = 8.0$ Hz, 2H), 8.08 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.4, 18.8, 21.3, 26.8, 30.5, 42.1, 64.8, 74.6, 115.2, 124.7, 126.1, 126.6, 127.1, 127.8, 129.6, 130.5, 136.0, 137.1, 138.6, 148.9, 158.4, 176.4; IR (KBr) ν/cm^{-1} : 3379, 2957, 2930, 1716, 1621, 1591; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{28}\text{NO}_3$: 378.2069; found: 378.2073.



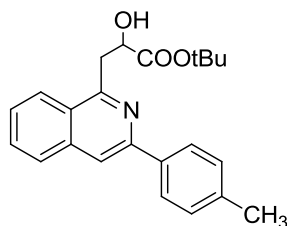
Methyl 2-hydroxy-3-(3-*p*-tolylisoquinolin-1-yl)propanoate (**3d**): yield: 50%; brown solid; $R_f = 0.27$; mp: 88–90 °C; ^1H NMR (400 MHz, CDCl_3) δ 2.41 (s, 3H), 3.75 (s, 3H), 3.85–3.87 (m, 2H), 4.95 (t, $J = 4.8$ Hz, 1H), 5.78 (br, 1H), 7.30 (d, $J = 8.0$ Hz, 2H), 7.56 (t, $J = 7.6$ Hz, 1H), 7.67 (t, $J = 8.0$ Hz, 1H), 7.83 (d, $J = 8.0$ Hz, 1H), 7.93 (s, 1H), 7.97 (d, $J = 8.0$ Hz, 2H), 8.07 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.3, 36.4, 52.3, 69.9, 115.4, 124.7, 126.2, 126.6, 127.2, 127.8, 129.7, 130.6, 136.1, 137.2, 138.7, 149.1, 157.9, 174.2; IR (KBr) ν/cm^{-1} : 3400, 2952, 2915, 1715, 1590, 1516; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{20}\text{NO}_3$: 322.1443; found: 322.1437.



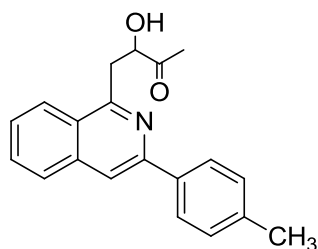
Ethyl 2-hydroxy-3-(3-*p*-tolylisoquinolin-1-yl)propanoate (**3e**): yield: 61%; brown solid; $R_f = 0.33$; mp: 102–103 °C; ^1H NMR (400 MHz, CDCl_3) δ 1.20 (t, $J = 7.2$ Hz, 3H), 2.43 (s, 3H), 3.84–3.90 (m, 2H), 4.21 (q, $J = 7.2$ Hz, 2H), 4.94 (t, $J = 4.8$ Hz, 1H), 5.78 (br, 1H), 7.31 (d, $J = 8.0$ Hz, 2H), 7.58 (t, $J = 7.6$ Hz, 1H), 7.69 (t, $J = 8.0$ Hz, 1H), 7.85 (d, $J = 8.0$ Hz, 1H), 7.95 (s, 1H), 7.99 (d, $J = 8.0$ Hz, 2H), 8.11 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.1, 21.3, 36.4, 61.3, 70.1, 115.4, 124.7, 126.2, 126.7, 127.2, 127.8, 129.6, 130.6, 136.1, 137.2, 138.7, 149.1, 157.9, 173.8; IR (KBr) ν/cm^{-1} : 3410, 2941, 2915, 1708, 1653, 1568; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{22}\text{NO}_3$: 336.1600; found: 336.1596.



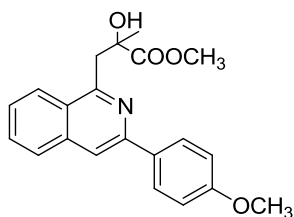
Butyl 2-hydroxy-3-(3-*p*-tolylisoquinolin-1-yl)propanoate (**3f**): yield: 98%; yellow solid; $R_f = 0.34$; mp: 66–67 °C; ^1H NMR (400 MHz, CDCl_3) δ 0.77 (t, $J = 7.2$ Hz, 3H), 1.16–1.22 (m, 2H), 1.47–1.53 (m, 2H), 2.42 (s, 3H), 3.82–3.92 (m, 2H), 4.10–4.15 (m, 2H), 4.93 (t, $J = 4.8$ Hz, 1H), 5.83 (br, 1H), 7.31 (d, $J = 8.0$ Hz, 2H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.68 (t, $J = 7.2$ Hz, 1H), 7.85 (d, $J = 8.4$ Hz, 1H), 7.94 (s, 1H), 7.98 (d, $J = 8.0$ Hz, 2H), 8.10 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.6, 19.0, 21.3, 30.6, 36.5, 65.1, 70.1, 115.4, 124.8, 126.2, 126.7, 127.2, 127.9, 129.6, 130.6, 137.2, 138.7, 149.2, 158.0, 173.9; IR (KBr) ν/cm^{-1} : 3406, 2959, 2927, 1716, 1591, 1517; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{26}\text{NO}_3$: 364.1913; found: 364.1918.



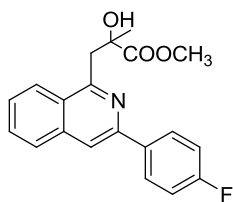
tert-Butyl 2-hydroxy-3-(3-*p*-tolylisoquinolin-1-yl)propanoate (**3g**): yield: 80%; yellow oil; $R_f = 0.38$; ^1H NMR (400 MHz, CDCl_3) δ 1.31 (s, 9H), 2.41 (s, 3H), 3.75 (dd, $J = 4.0, 16.8$ Hz, 1H), 3.88 (dd, $J = 5.6, 16.8$ Hz, 1H), 4.81 (t, $J = 4.8$ Hz, 1H), 5.58 (br, 1H), 7.30 (d, $J = 8.0$ Hz, 2H), 7.55 (t, $J = 7.2$ Hz, 1H), 7.66 (t, $J = 8.0$ Hz, 1H), 7.83 (d, $J = 8.0$ Hz, 1H), 7.92 (s, 1H), 8.00 (d, $J = 8.0$ Hz, 2H), 8.09 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.3, 27.8, 36.7, 70.4, 81.5, 115.2, 124.8, 126.2, 126.7, 127.1, 127.8, 129.6, 130.5, 136.1, 137.1, 138.6, 149.2, 158.2, 173.0; IR (KBr) ν/cm^{-1} : 3445, 2976, 2924, 1731, 1623, 1570; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{26}\text{NO}_3$: 364.1913; found: 364.1915.



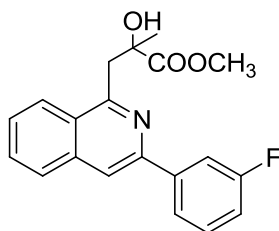
3-Hydroxy-4-(3-(*p*-tolyl)isoquinolin-1-yl)butan-2-one (**3h**): yield: 40%; yellow solid; R_f = 0.33; mp: 110–112 °C; ^1H NMR (400 MHz, CDCl_3) δ 2.41 (s, 3H), 2.42 (s, 3H), 3.71 (dd, J = 6.4, 16.4 Hz, 1H), 3.88 (dd, J = 3.2, 16.8 Hz, 1H), 4.73 (dd, J = 3.6, 6.4 Hz, 1H), 5.88 (br, 1H), 7.31 (t, J = 7.6 Hz, 2H), 7.56 (t, J = 7.6 Hz, 2H), 7.67 (t, J = 7.6 Hz, 1H), 7.83 (t, J = 8.4 Hz, 1H), 7.88 (d, J = 7.6 Hz, 1H), 7.91 (s, 1H), 8.12 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.2, 26.4, 35.7, 76.4, 115.7, 124.9, 126.3, 126.7, 127.2, 127.8, 129.6, 130.6, 136.2, 137.1, 138.7, 149.2, 158.2, 211.4; IR (KBr) ν / cm^{-1} : 3454, 3000, 2921, 1704, 1590, 1516; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{20}\text{NO}_2$: 306.1494; found: 306.1498.



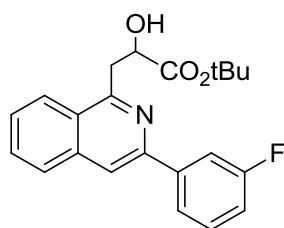
Methyl 2-hydroxy-3-(3-(4-methoxyphenyl)isoquinolin-1-yl)-2-methylpropanoate (**3j**): yield: 75%; yellow solid; R_f = 0.29; mp: 132–133 °C; ^1H NMR (400 MHz, CDCl_3) δ 1.69 (s, 3H), 3.49 (d, J = 16.8 Hz, 1H), 3.62 (s, 3H), 3.84 (s, 3H), 4.12 (d, J = 16.8 Hz, 1H), 6.57 (br, 1H), 7.01 (d, J = 8.8 Hz, 2H), 7.51 (t, J = 7.2 Hz, 3H), 7.62 (t, J = 7.2 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.84 (s, 1H), 8.02 (d, J = 8.8 Hz, 2H), 8.05 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 26.8, 42.3, 52.4, 55.4, 74.5, 114.3, 114.5, 124.7, 125.9, 127.0, 127.7, 127.9, 130.6, 131.3, 137.2, 148.5, 158.1, 160.2, 177.1; IR (KBr) ν / cm^{-1} : 3390, 2947, 2930, 1748, 1606, 1518; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{22}\text{NO}_4$: 352.1549; found: 352.1552.



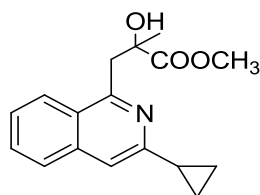
Methyl 3-(3-(4-fluorophenyl)isoquinolin-1-yl)-2-hydroxy-2-methylpropanoate (**3k**): yield: 48%; white solid; R_f = 0.31; mp: 126–127 °C; ^1H NMR (400 MHz, CDCl_3) δ 1.70 (s, 3H), 3.53 (d, J = 16.8 Hz, 1H), 3.62 (s, 3H), 4.12 (d, J = 16.8 Hz, 1H), 6.34 (br, 1H), 7.17 (t, J = 8.4 Hz, 2H), 7.58 (t, J = 8.0 Hz, 1H), 7.68 (t, J = 8.0 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 7.89 (s, 1H), 8.04 (dd, J = 5.6, 8.4 Hz, 2H), 8.09 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 26.8, 42.4, 52.3, 74.5, 115.4, 115.8 (d, $^2J_{\text{C-F}}$ = 22 Hz), 124.8, 126.2, 127.5, 127.8, 128.4 (d, $^2J_{\text{C-F}}$ = 8 Hz), 130.8, 134.9, 137.1, 147.8, 158.3, 163.3 (d, $^1J_{\text{C-F}}$ = 247 Hz), 176.9; IR (KBr) ν/cm^{-1} : 3373, 2986, 2979, 1727, 1601, 1587; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{19}\text{FNO}_3$: 340.1349; found: 340.1353.



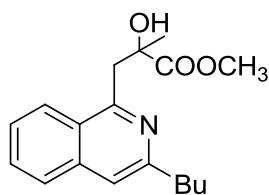
Methyl 3-(3-(3-fluorophenyl)isoquinolin-1-yl)-2-hydroxy-2-methylpropanoate (**3l**): yield: 83%; yellow solid; R_f = 0.36; mp: 127–129 °C; ^1H NMR (400 MHz, CDCl_3) δ 1.70 (s, 3H), 3.53 (d, J = 16.8 Hz, 1H), 3.67 (s, 3H), 4.13 (d, J = 16.8 Hz, 1H), 6.16 (br, 1H), 7.07 (dt, J = 2.0, 8.0 Hz, 1H), 7.41–7.46 (m, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.67 (t, J = 8.0 Hz, 1H), 7.76–7.79 (m, 1H), 7.82 (t, J = 8.0 Hz, 2H), 7.91 (s, 1H), 8.08 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 26.8, 42.6, 52.4, 74.5, 113.5 (d, $^2J_{\text{C-F}}$ = 23 Hz), 115.5 (d, $^2J_{\text{C-F}}$ = 21 Hz), 116.1, 122.1, 124.8, 126.5, 127.7, 127.9, 130.4 (d, $^3J_{\text{C-F}}$ = 8 Hz), 130.9, 136.9, 141.1 (d, $^3J_{\text{C-F}}$ = 7 Hz), 147.4, 158.4, 163.4 (d, $^1J_{\text{C-F}}$ = 244 Hz), 177.0; IR (KBr) ν/cm^{-1} : 3452, 2949, 2933, 1728, 1567, 1428; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{19}\text{FNO}_3$: 340.1349; found: 340.1355.



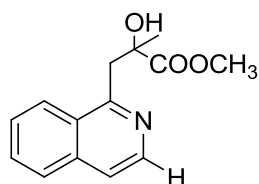
tert-Butyl 3-(3-(3-fluorophenyl)isoquinolin-1-yl)-2-hydroxypropanoate (**3m**): yield: 70%; brown solid; R_f = 0.34; mp: 96–98 °C; (*syn* + *anti*) ^1H NMR (400 MHz, CDCl_3) δ 1.32 (s, 7.2 H), 1.41 (s, 1.8 H), 3.78 (dd, J = 4.0, 16.4 Hz, 0.8 H), 3.88 (dd, J = 4.0, 16.4 Hz, 0.8 H), 4.30 (br, 0.2 H), 4.39 (dd, J = 4.8, 10.8 Hz, 0.2 H), 4.51 (dd, J = 4.8, 10.8 Hz, 0.2 H), 5.05 (br, 1H), 7.08 (dt, J = 1.2, 8.0 Hz, 1H), 7.42-7.47 (m, 1H), 7.60 (t, J = 7.6 Hz, 1H), 7.69 (t, J = 8.0 Hz, 1H), 7.79-7.90 (m, 3H), 7.94 (s, 0.8H), 7.98 (s, 0.2H), 8.07 (d, J = 8.8 Hz, 0.2H), 8.12 (d, J = 8.0 Hz, 0.8H); ^{13}C NMR (100 MHz, CDCl_3) (*anti*) δ 27.8, 37.1, 70.2, 81.8, 113.7 (d, $^2J_{\text{C-F}}$ = 23 Hz), 115.4 (d, $^2J_{\text{C-F}}$ = 21 Hz), 116.0, 122.4, 124.9, 126.7, 127.6, 127.9, 130.3 (d, $^3J_{\text{C-F}}$ = 8 Hz), 130.6, 136.9, 141.4 (d, $^3J_{\text{C-F}}$ = 8 Hz), 147.8, 158.3, 163.4 (d, $^1J_{\text{C-F}}$ = 243 Hz), 173.1; IR (KBr) ν / cm^{-1} : 3443, 2978, 2931, 1720, 1619, 1500; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{23}\text{FNO}_3$: 368.1662; found: 368.1666.



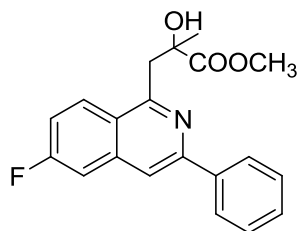
Methyl 3-(3-(cyclopropyl)isoquinolin-1-yl)-2-hydroxy-2-methylpropanoate (**3n**): yield: 80%; brown oil; R_f = 0.34; ^1H NMR (400 MHz, CDCl_3) δ 0.99-1.05 (m, 4H), 1.62 (s, 3H), 2.08-2.15 (m, 1H), 3.37 (d, J = 16.8 Hz, 1H), 3.63 (s, 3H), 4.00 (d, J = 16.8 Hz, 1H), 6.50 (br, 1H), 7.40 (s, 1H), 7.48 (t, J = 7.6 Hz, 1H), 7.62 (t, J = 8.0 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 8.02 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 9.0, 9.3, 16.7, 26.7, 41.6, 52.2, 74.6, 116.4, 124.7, 125.5, 126.2, 126.7, 130.4, 136.8, 153.7, 158.2, 176.8; IR (KBr) ν / cm^{-1} : 3397, 3002, 2951, 1747, 1592, 1498, 1404; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{17}\text{H}_{20}\text{NO}_3$: 286.1443; found: 286.1448.



Methyl 3-(3-butylisoquinolin-1-yl)-2-hydroxy-2-methylpropanoate (**3o**): yield: 35%; brown oil; $R_f = 0.50$; ^1H NMR (400 MHz, CDCl_3) δ 0.95 (t, $J = 7.6$ Hz, 3H), 1.34-1.40 (m, 2H), 1.64 (s, 3H), 1.72-1.79 (m, 2H), 2.82-2.87 (m, 2H), 3.39 (d, $J = 16.4$ Hz, 1H), 3.61 (s, 3H), 4.05 (d, $J = 16.4$ Hz, 1H), 6.88 (br, 1H), 7.33 (s, 1H), 7.53 (t, $J = 7.6$ Hz, 1H), 7.63 (t, $J = 7.2$ Hz, 1H), 7.72 (d, $J = 8.0$ Hz, 1H), 8.06 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.9, 22.3, 26.7, 31.6, 37.3, 41.5, 52.1, 74.8, 117.4, 124.7, 125.6, 126.5, 127.0, 130.3, 137.0, 153.2, 158.1, 176.8; IR (KBr) ν/cm^{-1} : 3418, 2955, 2871, 1747, 1625, 1499; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{24}\text{NO}_3$: 302.1756; found: 302.1763.

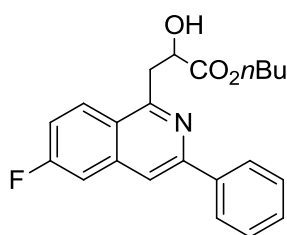


Methyl 2-hydroxy-2-methyl-3-(3-(trimethylsilyl)isoquinolin-1-yl)propanoate (**3p**): yield: 12%; brown solid; $R_f = 0.26$; mp: 69–71 °C; ^1H NMR (400 MHz, CDCl_3) δ 1.65 (s, 3H), 3.43 (d, $J = 16.4$ Hz, 1H), 3.60 (s, 1H), 4.06 (d, $J = 16.4$ Hz, 1H), 6.58 (br, 1H), 7.54 (d, $J = 5.6$ Hz, 1H), 7.63 (t, $J = 7.6$ Hz, 1H), 7.70 (t, $J = 7.6$ Hz, 1H), 7.82 (d, $J = 8.4$ Hz, 1H), 8.14 (d, $J = 8.4$ Hz, 1H), 8.34 (d, $J = 6.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 26.8, 41.8, 52.3, 74.8, 114.1, 119.9, 124.9, 127.4, 127.5, 130.4, 136.2, 140.5, 158.6, 176.8; IR (KBr) ν/cm^{-1} : 3439, 2925, 2854, 1702, 1619, 1459; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{14}\text{H}_{16}\text{NO}_3$: 246.1130; found: 246.1127.

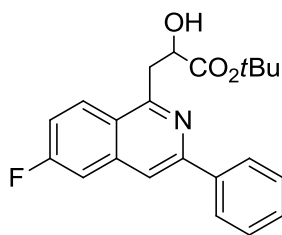


Methyl 3-(6-fluoro-3-phenylisoquinolin-1-yl)-2-hydroxy-2-methylpropanoate (**3q**): yield: 80%; yellow solid; $R_f = 0.32$; mp: 107–109 °C; ^1H NMR (400 MHz, CDCl_3) δ

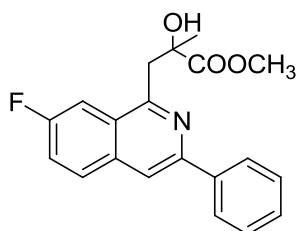
1.69 (s, 3H), 3.49 (d, $J = 16.8$ Hz, 1H), 3.64 (s, 3H), 4.09 (d, $J = 16.8$ Hz, 1H), 6.35 (br, 1H), 7.31 (dt, $J = 2.4, 8.8$ Hz, 1H), 7.41 (t, $J = 7.6$ Hz, 2H), 7.49 (t, $J = 7.6$ Hz, 2H), 7.88 (s, 1H), 8.04 (d, $J = 7.6$ Hz, 1H), 8.12 (dd, $J = 5.6, 8.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 26.3, 42.0, 51.9, 74.1, 110.5 (d, $^2J_{\text{C-F}} = 21$ Hz), 114.7, 117.1 (d, $^2J_{\text{C-F}} = 25$ Hz), 123.0, 126.2, 127.4 (d, $^3J_{\text{C-F}} = 9$ Hz), 127.5, 128.4, 128.5, 137.8, 138.3 (d, $^3J_{\text{C-F}} = 10$ Hz), 149.3, 157.7, 162.9 (d, $^1J_{\text{C-F}} = 252$ Hz), 176.4; IR (KBr) ν/cm^{-1} : 3423, 2990, 2953, 1708, 1602, 1521; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{19}\text{FNO}_3$: 340.1349; found: 340.1355.



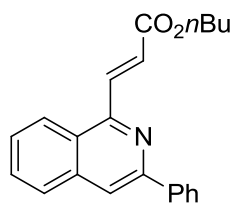
Butyl 3-(6-fluoro-3-phenylisoquinolin-1-yl)-2-hydroxypropanoate (**3r**): yield: 72%; yellow oil; $R_f = 0.31$; (*syn* + *anti*) ^1H NMR (400 MHz, CDCl_3) δ 0.78 (t, $J = 7.2$ Hz, 3H), 1.16-1.22 (m, 2H), 1.48-1.54 (m, 2H), 3.77-3.89 (m, 2H), 4.04-4.17 (m, 2H), 4.37-4.43 (m, 0.8H), 4.55 (dd, $J = 4.4, 10.4$ Hz, 0.4H), 4.71 (t, $J = 4.0$ Hz, 0.4H), 4.90 (t, $J = 4.4$ Hz, 0.6H), 5.44 (br, 0.6H), 7.31 (t, $J = 8.4$ Hz, 1H), 7.38-7.50 (m, 4H), 7.87 (s, 0.6H), 7.93 (s, 0.4H), 8.05 (d, $J = 7.2$ Hz, 2H), 8.10 (dd, $J = 5.2, 9.2$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ anti: 18.9, 30.5, 36.7, 63.3, 65.2, 69.9, 111.0 (d, $^2J_{\text{C-F}} = 20$ Hz), 115.3 (d, $^4J_{\text{C-F}} = 4$ Hz), 117.4, 117.7, 123.5, 126.9, 127.9 (d, $^3J_{\text{C-F}} = 10$ Hz), 128.9, 138.5, 138.9 (d, $^3J_{\text{C-F}} = 10$ Hz), 150.2, 158.0, 163.3 (d, $^1J_{\text{C-F}} = 251$ Hz), 173.9; Syn: 18.9, 30.5, 51.2, 63.3, 65.2, 69.9, 111.1 (d, $^2J_{\text{C-F}} = 20$ Hz), 115.9 (d, $^4J_{\text{C-F}} = 4$ Hz), 117.7, 117.9, 123.6, 126.8, 127.6 (d, $^3J_{\text{C-F}} = 9$ Hz), 129.0, 138.5, 139.1 (d, $^3J_{\text{C-F}} = 10$ Hz), 150.3, 156.8, 163.2 (d, $^1J_{\text{C-F}} = 251$ Hz), 171.2; IR (KBr) ν/cm^{-1} : 3454, 2959, 2932, 1738, 1503, 1455; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{23}\text{FNO}_3$: 368.1662; found: 368.1667.



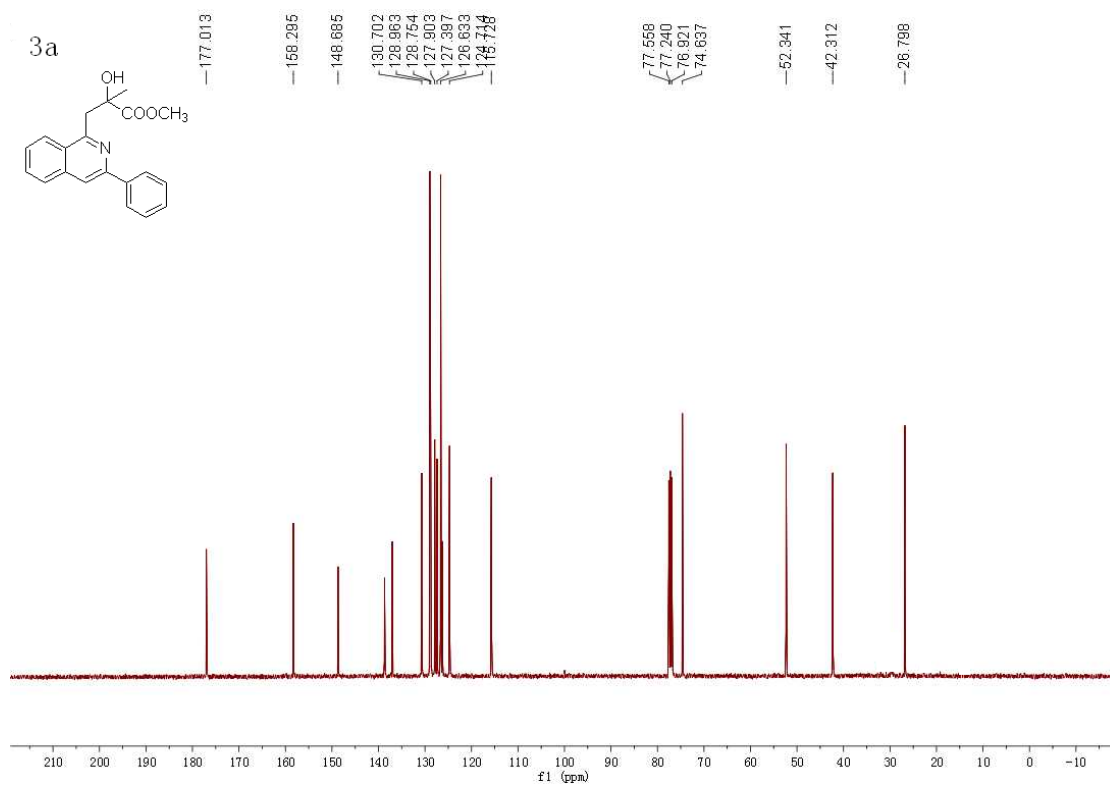
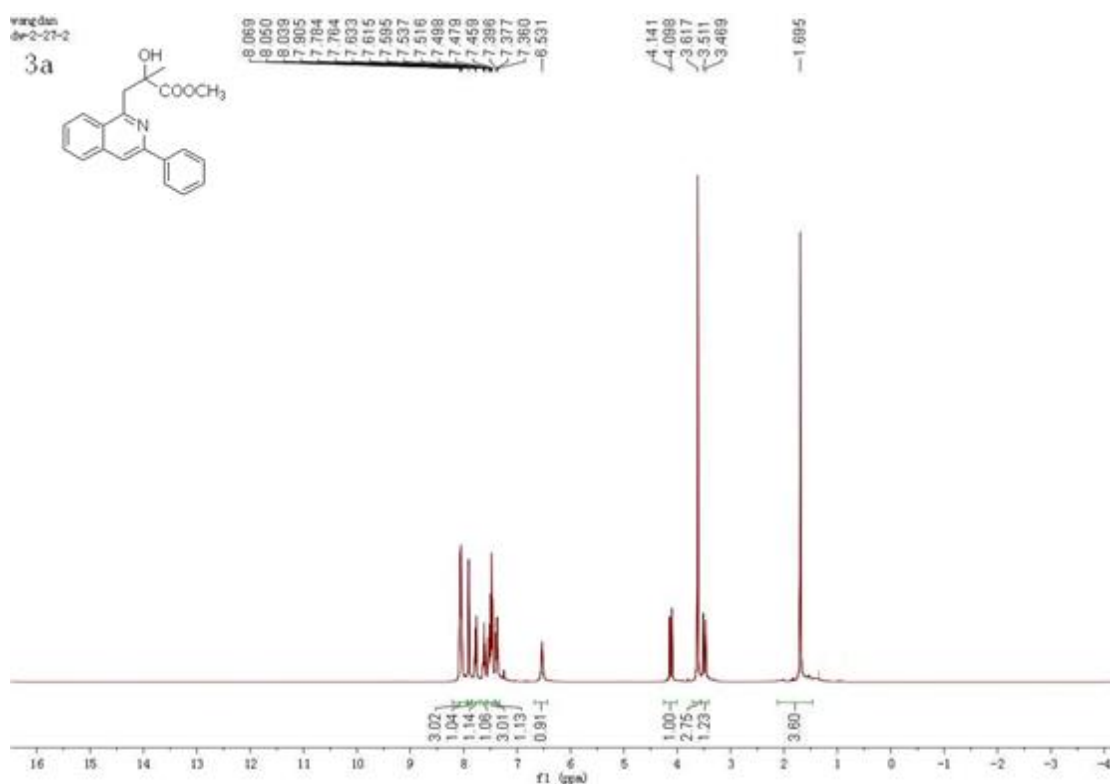
tert-Butyl 3-(6-fluoro-3-phenylisoquinolin-1-yl)-2-hydroxypropanoate (**3s**): yield: 71%; yellow oil; R_f = 0.34; (*syn* + *anti*) ^1H NMR (400 MHz, CDCl_3) δ 1.31 (s, 6.3H), 1.40 (s, 2.7H), 3.68 (s, 0.3H), 3.73 (dd, J = 4.0, 16.4 Hz, 0.7H), 3.85 (dd, J = 5.6, 16.4 Hz, 0.7H), 4.40 (dd, J = 4.8, 10.8 Hz, 0.3 H), 4.53 (dd, J = 4.8, 10.8 Hz, 0.3 H), 4.62 (t, J = 4.0 Hz, 0.3H), 4.80 (t, J = 4.4 Hz, 0.7H), 5.25 (br, 0.7H), 7.34 (t, J = 8.8 Hz, 1H), 7.39-7.52 (m, 4H), 7.89 (s, 0.7H), 7.94 (s, 0.3H), 8.06-8.15 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 27.9, 37.1, 70.3, 81.9, 111.0 (d, $^2J_{\text{C-F}}$ = 20 Hz), 115.3 (d, $^4J_{\text{C-F}}$ = 5 Hz), 117.5 (d, $^2J_{\text{C-F}}$ = 21 Hz), 123.6, 127.0, 128.1 (d, $^3J_{\text{C-F}}$ = 10 Hz), 128.9, 138.6, 138.8 (d, $^3J_{\text{C-F}}$ = 10 Hz), 150.2, 158.2, 163.3 (d, $^1J_{\text{C-F}}$ = 251 Hz), 172.9; IR (KBr) ν / cm^{-1} : 3444, 2924, 2853, 1730, 1573, 1504; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{23}\text{FNO}_3$: 368.1662; found: 368.1665.

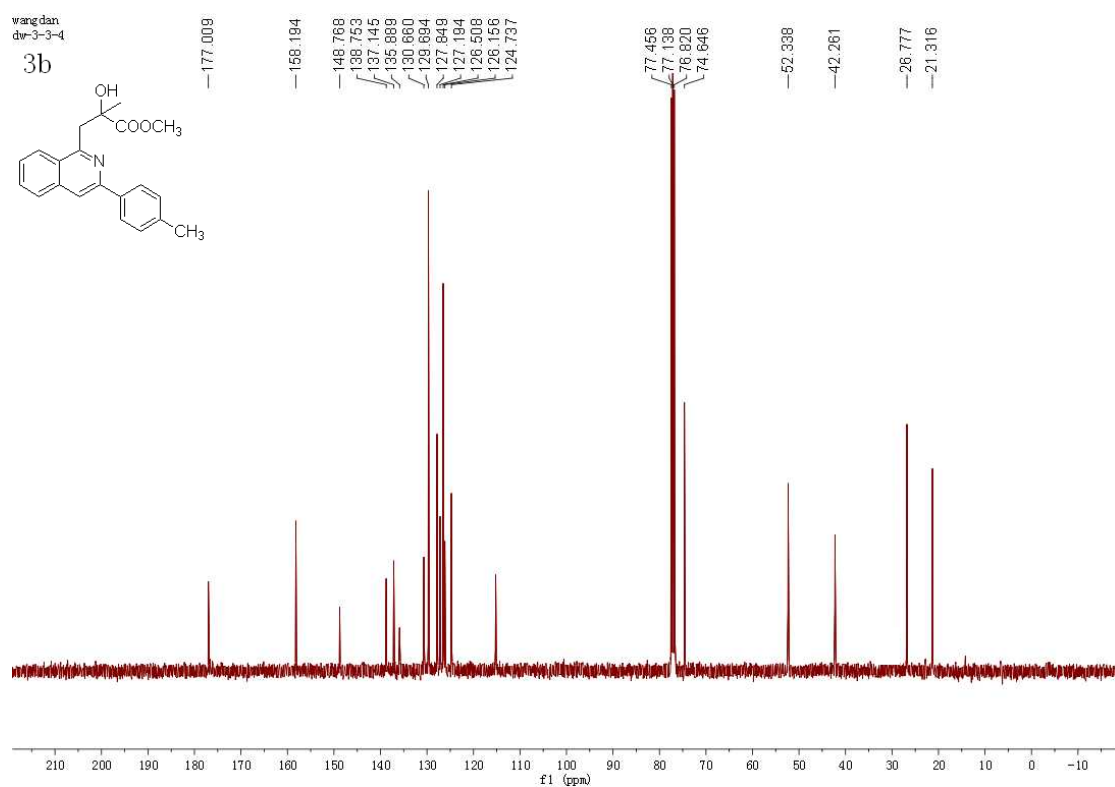
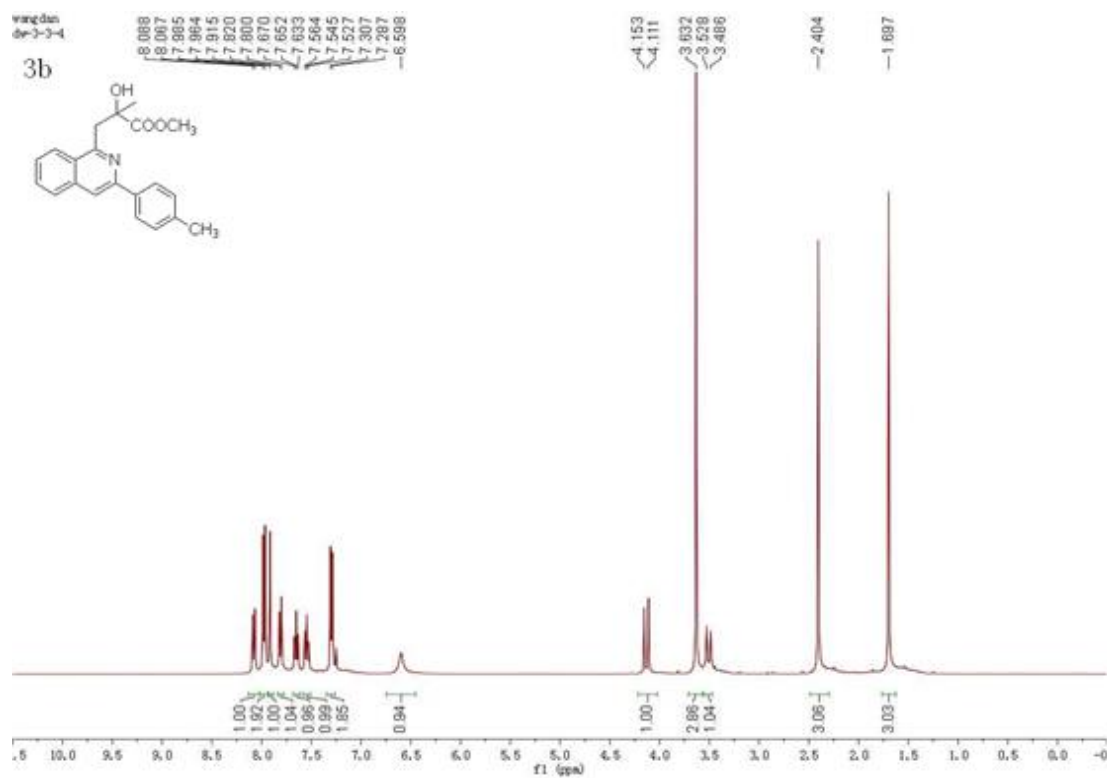


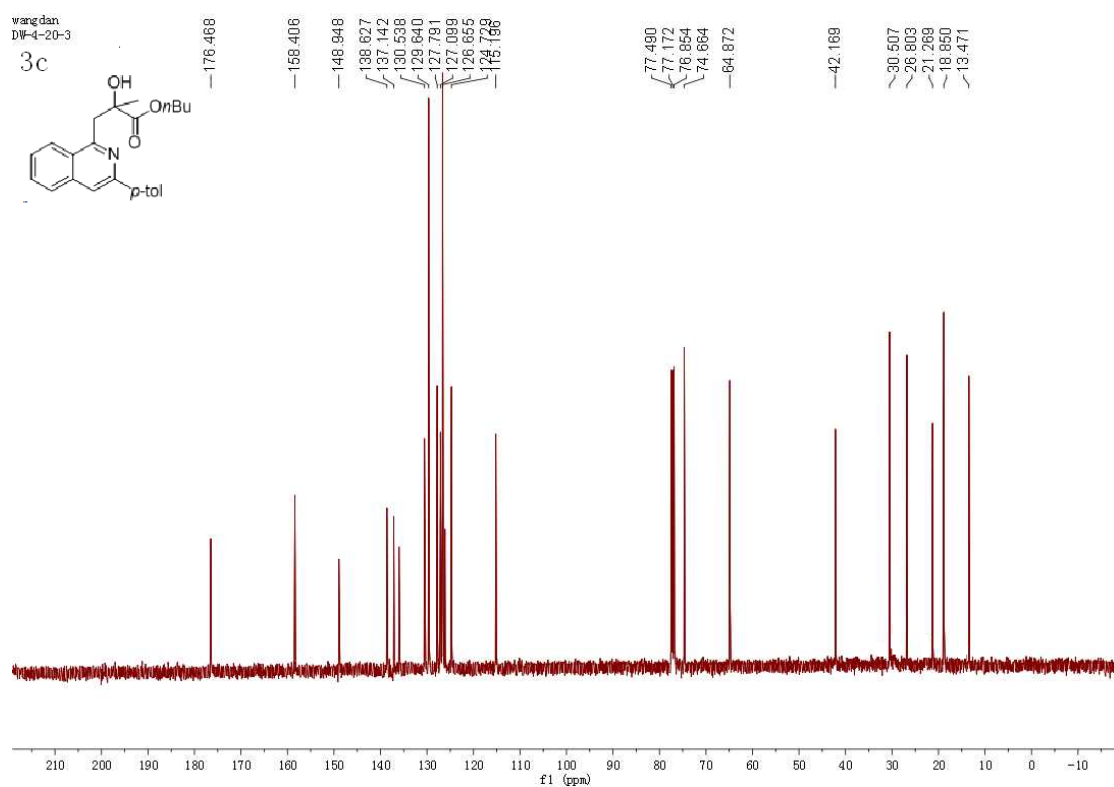
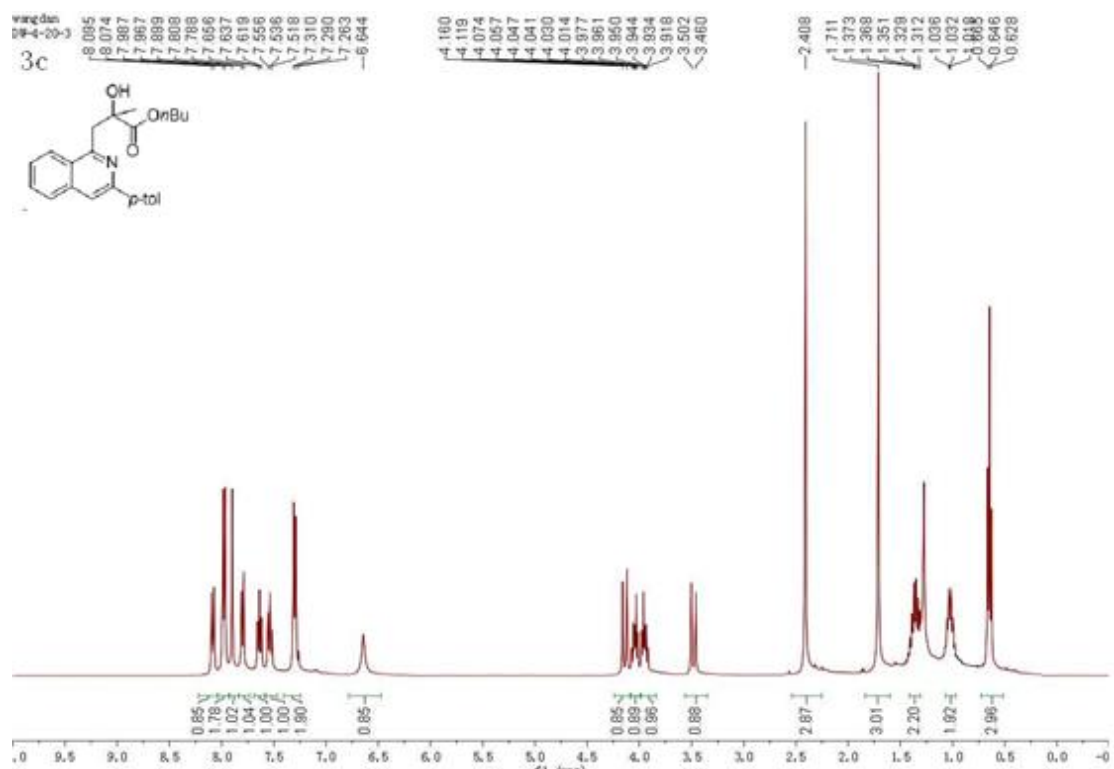
Methyl 3-(7-fluoro-3-phenylisoquinolin-1-yl)-2-hydroxy-2-methylpropanoate (**3t**): yield: 85%; yellow solid; R_f = 0.34; mp: 115–117 °C; ^1H NMR (400 MHz, CDCl_3) δ 1.70 (s, 3H), 3.44 (d, J = 16.8 Hz, 1H), 3.64 (s, 3H), 4.03 (d, J = 16.8 Hz, 1H), 6.30 (br, 1H), 7.37-7.50 (m, 4H), 7.67 (dd, J = 2.4, 9.6 Hz, 1H), 7.81 (dd, J = 5.6, 8.8 Hz, 1H), 7.91 (s, 1H), 8.03 (d, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 26.8, 42.5, 52.4, 74.5, 108.5 (d, $^2J_{\text{C-F}}$ = 21 Hz), 115.3, 121.2 (d, $^2J_{\text{C-F}}$ = 24 Hz), 126.5, 126.8 (d, $^3J_{\text{C-F}}$ = 8 Hz), 126.9, 128.8, 128.9, 130.5 (d, $^3J_{\text{C-F}}$ = 9 Hz), 134.1, 138.4, 148.5, 157.6 (d, $^4J_{\text{C-F}}$ = 6 Hz), 160.9 (d, $^1J_{\text{C-F}}$ = 248 Hz), 176.9; IR (KBr) ν / cm^{-1} : 3406, 2998, 2958, 1747, 1595, 1507; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{19}\text{FNO}_3$: 340.1394; found: 340.1399.

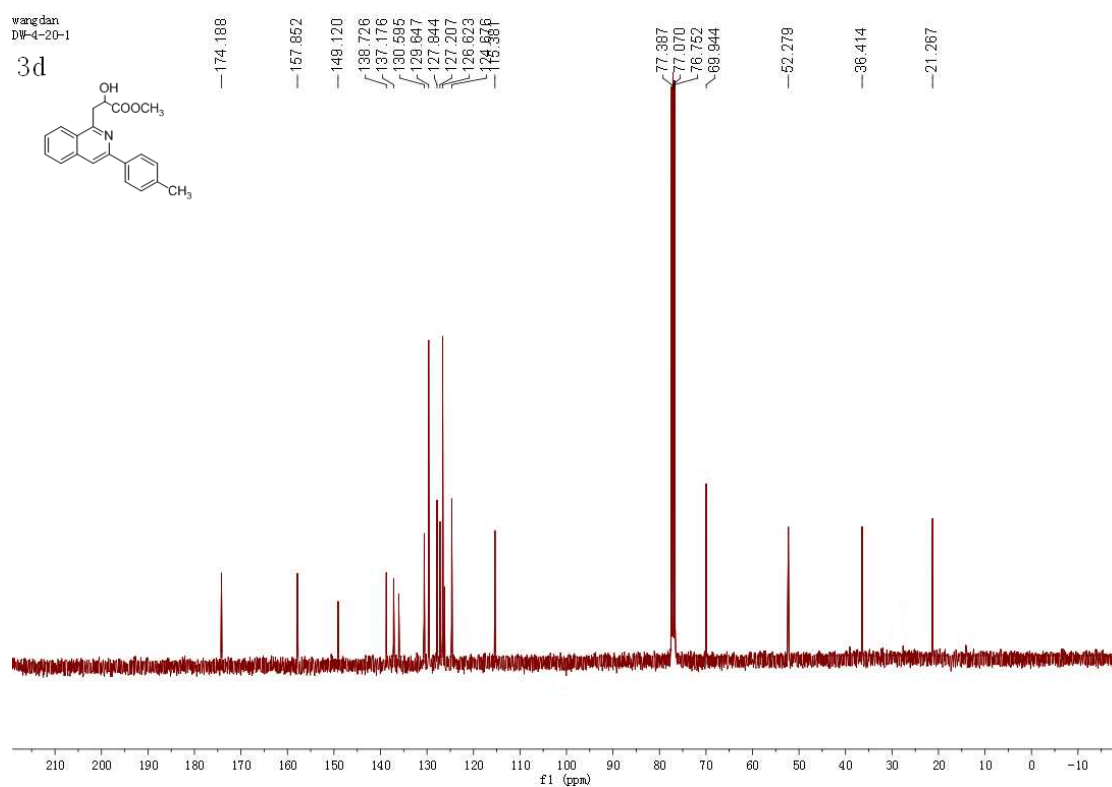
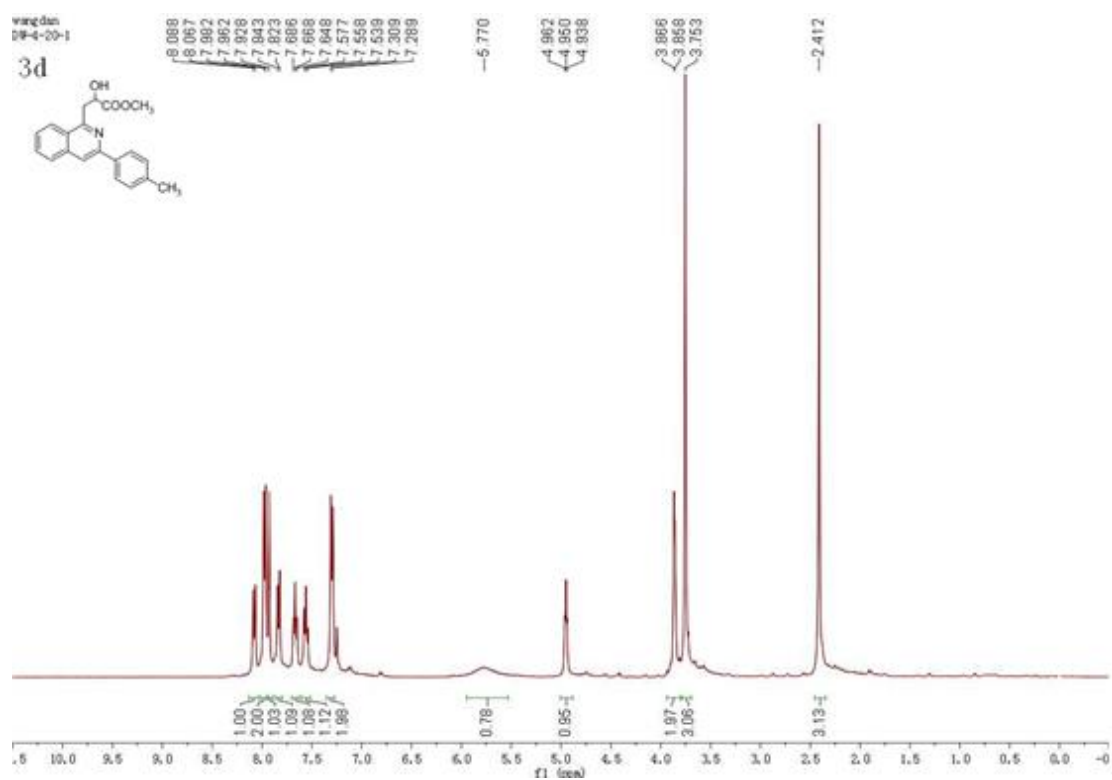


(*E*)-Butyl 3-(3-phenylisoquinolin-1-yl)-acrylate (**4**): yield: 65%; yellow solid; R_f = 0.75; mp: 58–59 °C; ^1H NMR (400 MHz, CDCl_3) δ 0.92 (t, J = 7.2 Hz, 3H), 1.35–1.42 (m, 2H), 1.64–1.69 (m, 2H), 4.22 (t, J = 6.4 Hz, 2H), 7.36 (t, J = 6.0 Hz, 2H), 7.51 (t, J = 7.2 Hz, 2H), 7.55 (t, J = 7.2 Hz, 1H), 7.63 (t, J = 7.2 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 8.04 (s, 1H), 8.15 (d, J = 7.6 Hz, 1H), 8.26 (d, J = 8.4 Hz, 1H), 8.50 (d, J = 15.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.8, 19.2, 30.9, 64.8, 117.8, 124.1, 125.2, 126.5, 127.0, 127.6, 127.8, 128.8, 130.3, 130.9, 132.4, 137.7, 138.3, 139.1, 150.3, 151.4, 167.1; IR (KBr) ν/cm^{-1} : 3472, 2959, 2931, 1717, 1661, 1573; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{22}\text{NO}_2$: 332.1651; found: 332.1657.



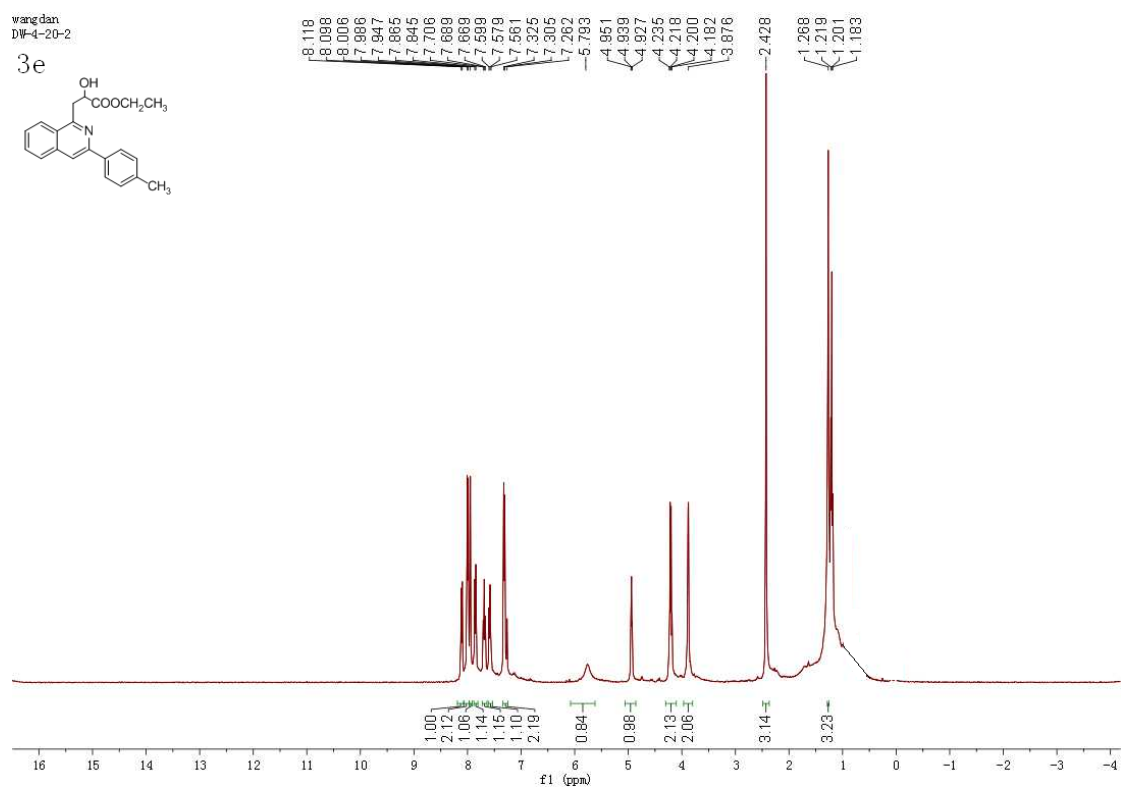
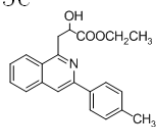






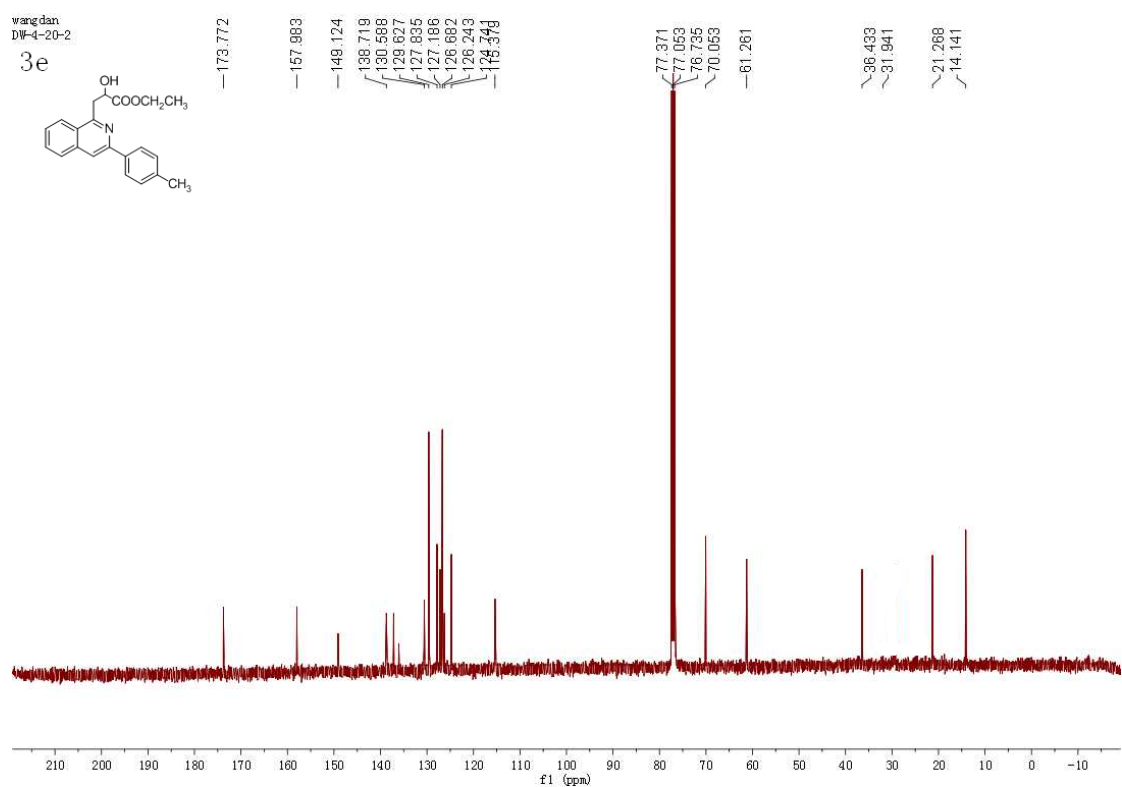
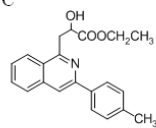
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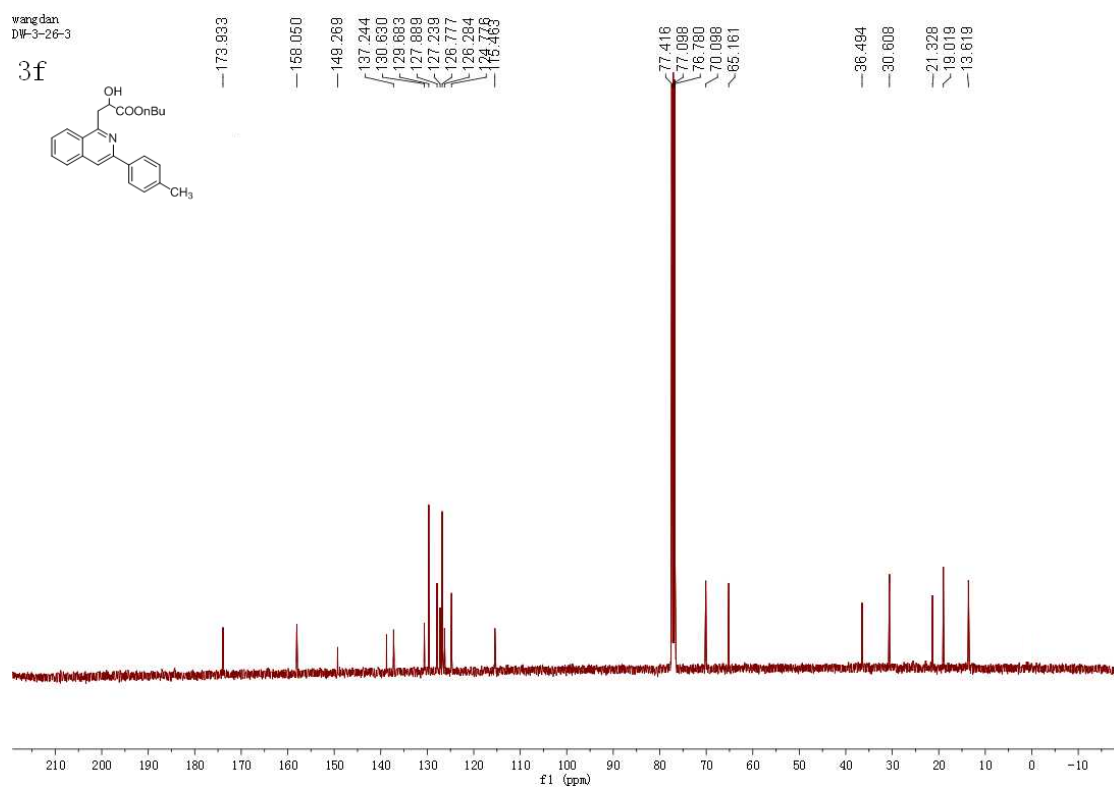
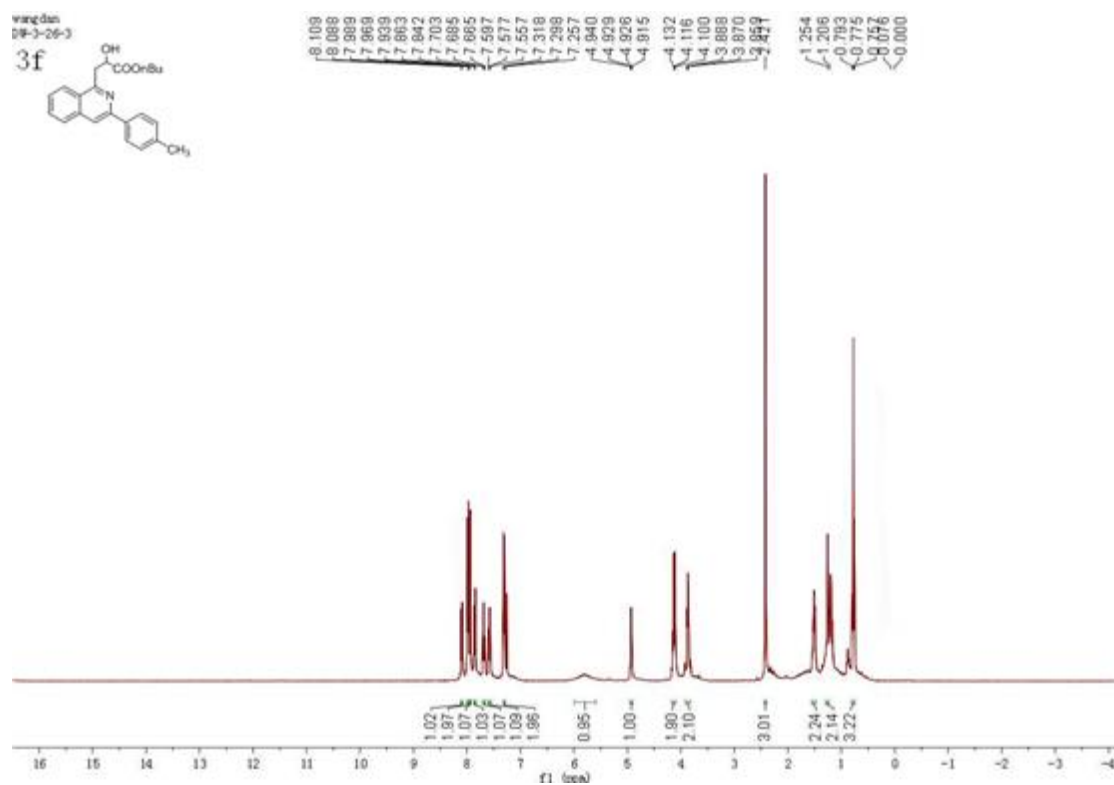
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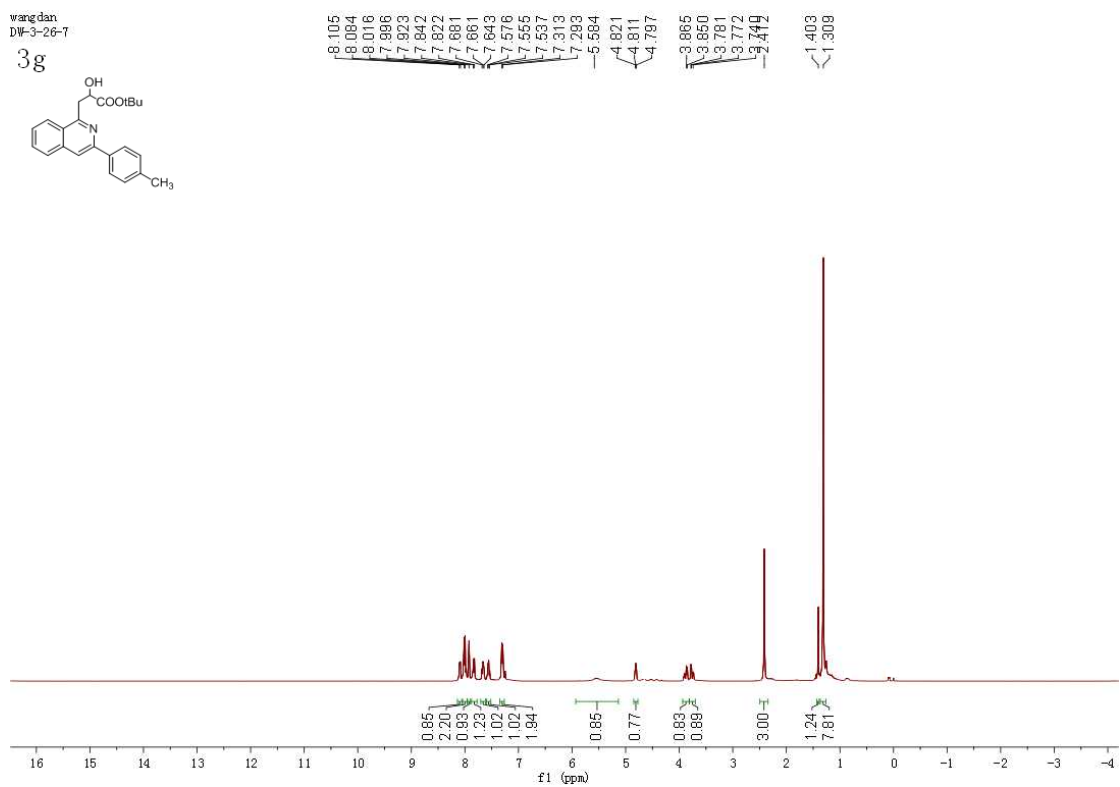
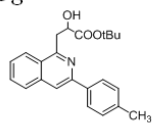
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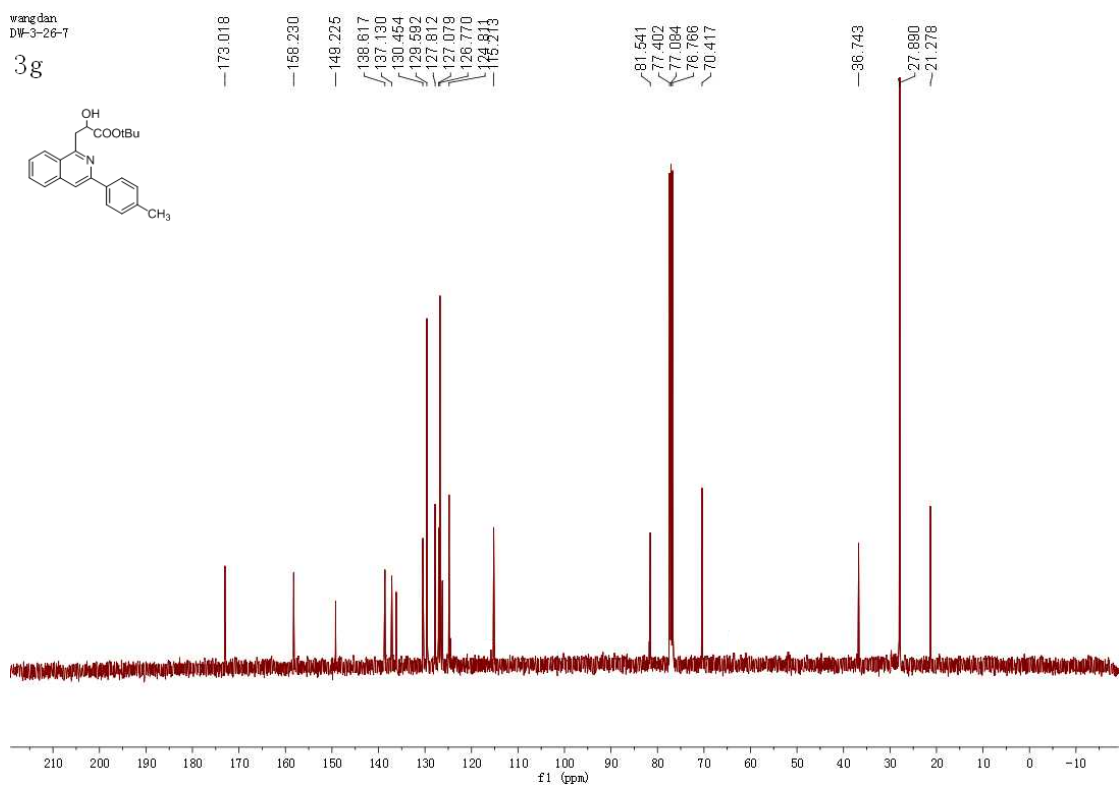
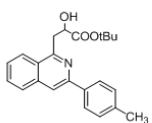
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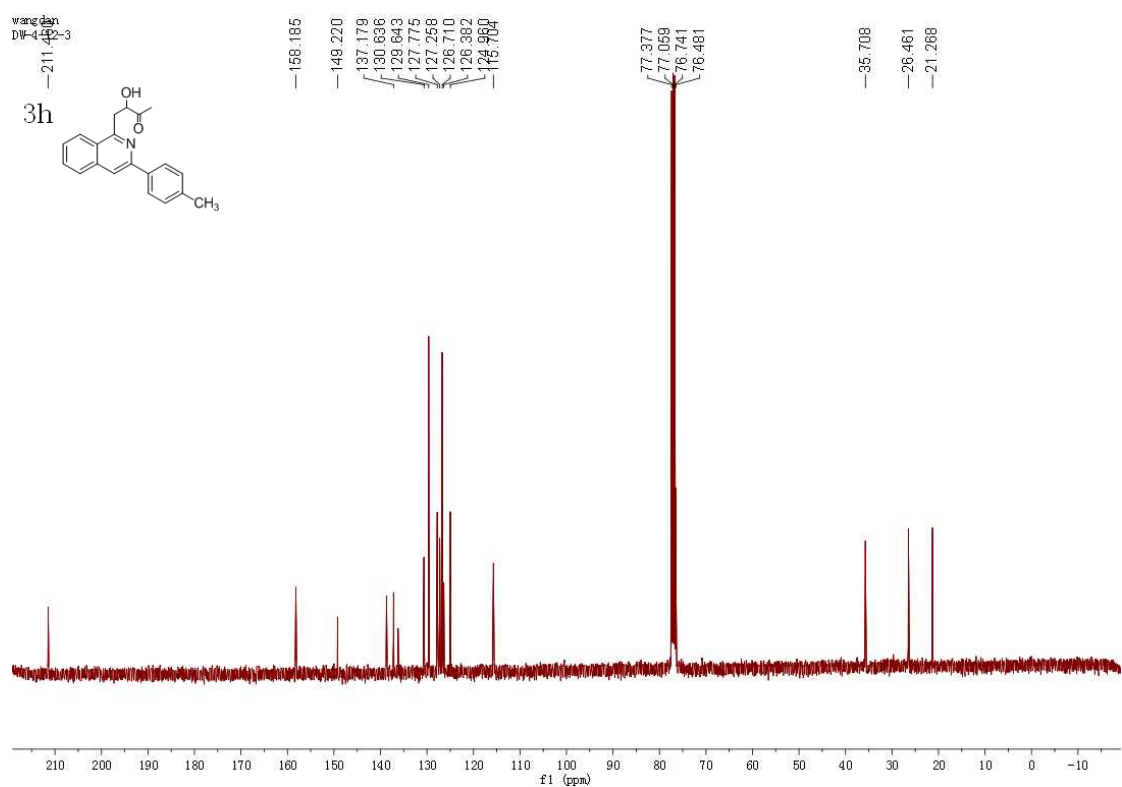
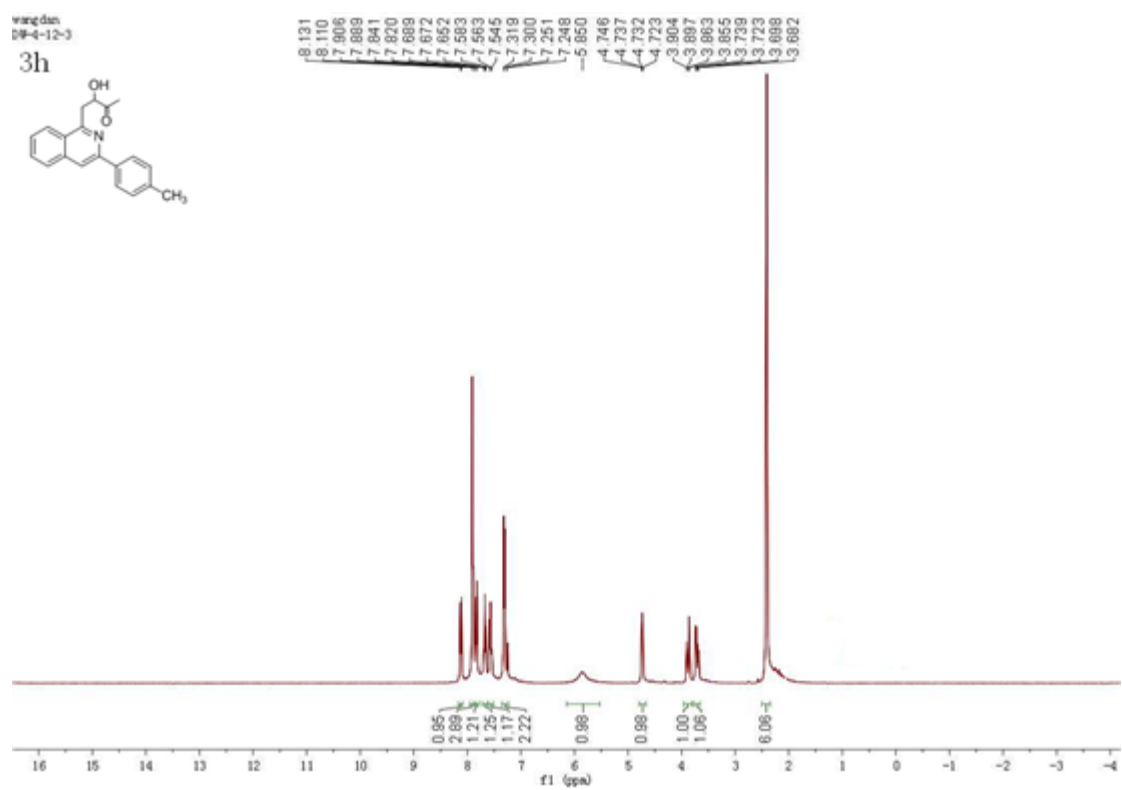
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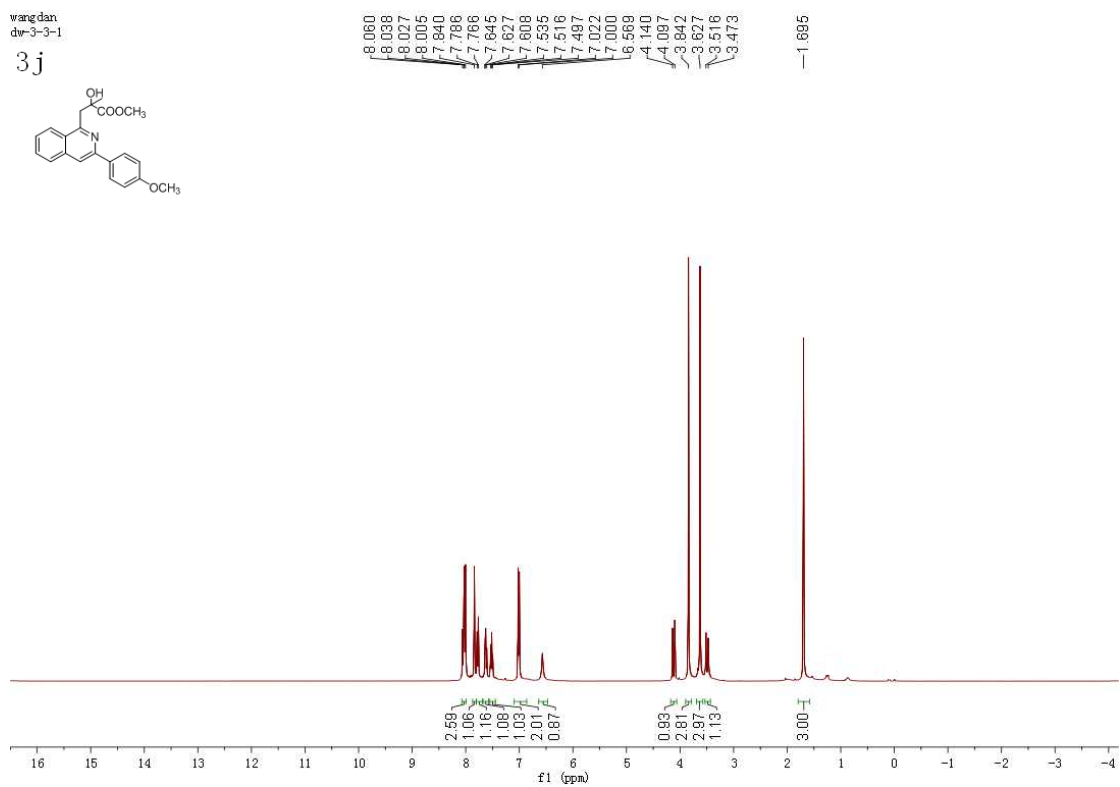
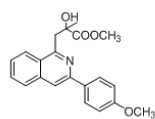
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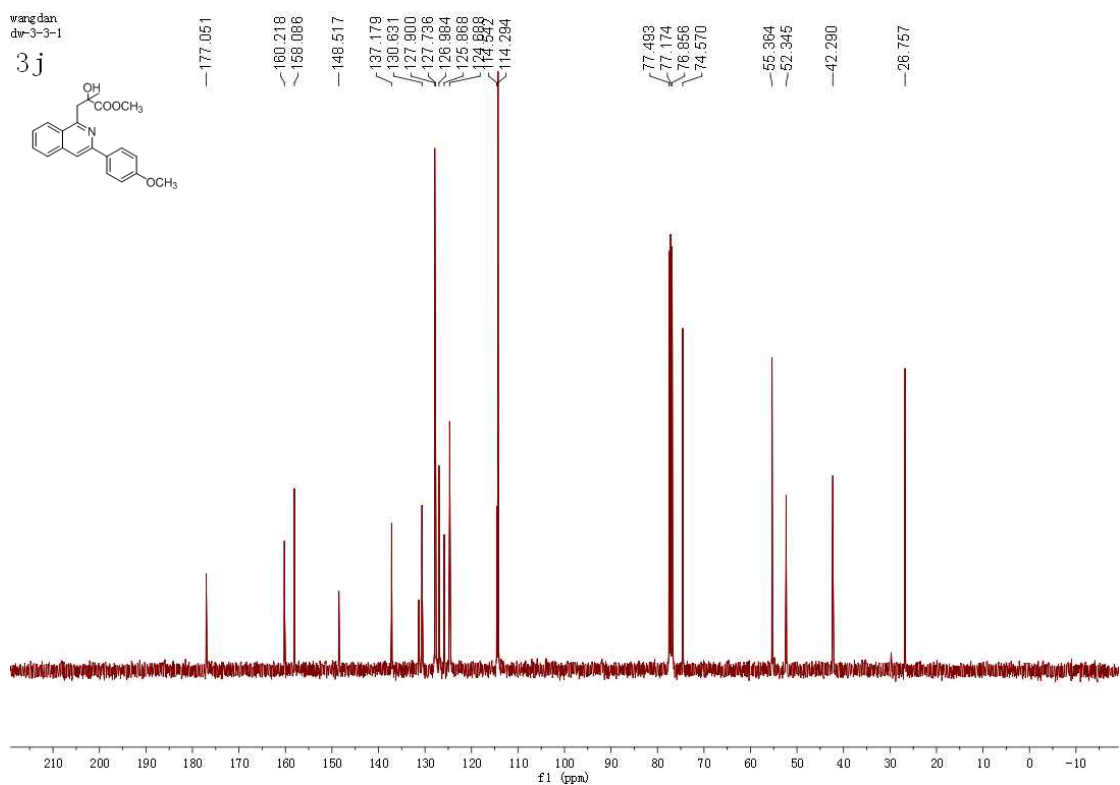
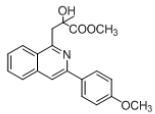
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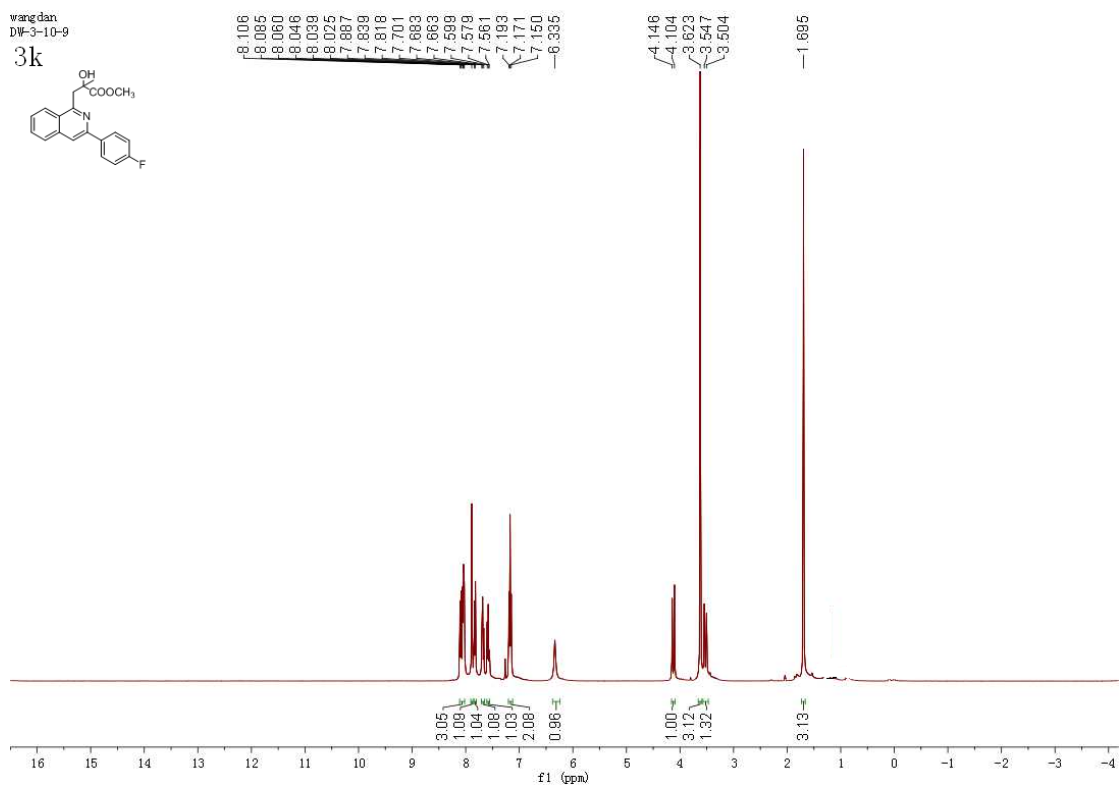
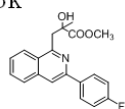
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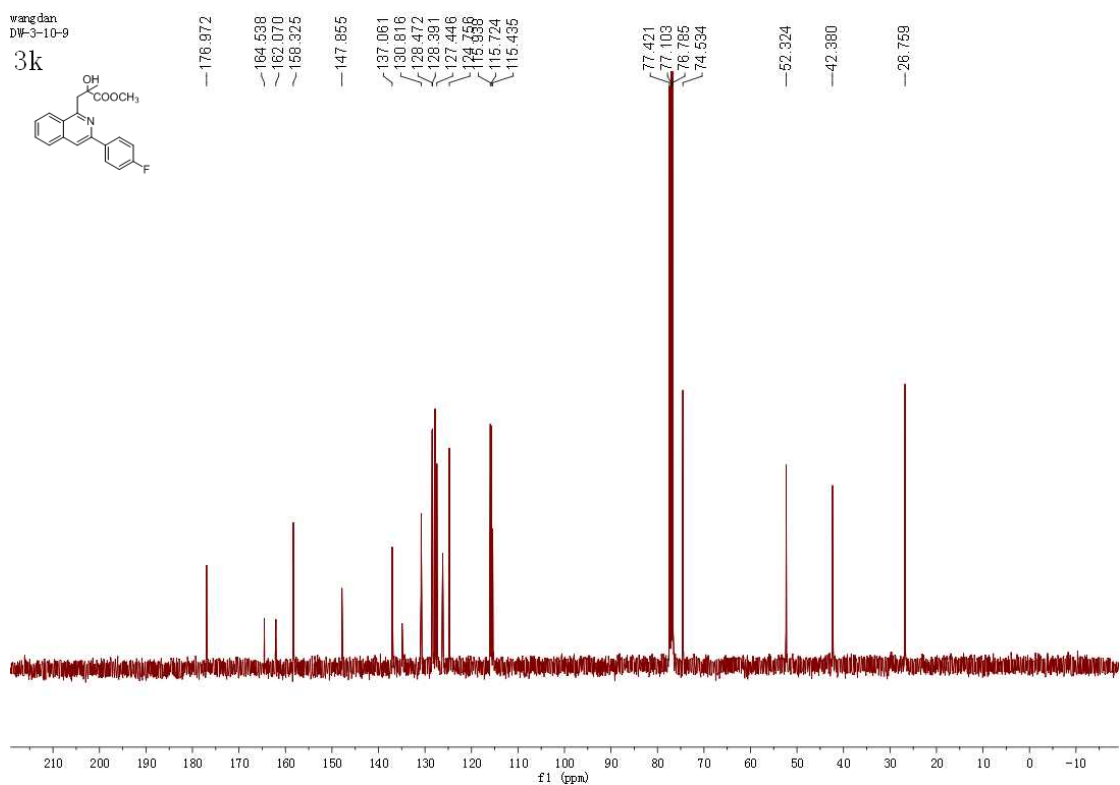
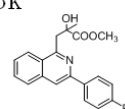
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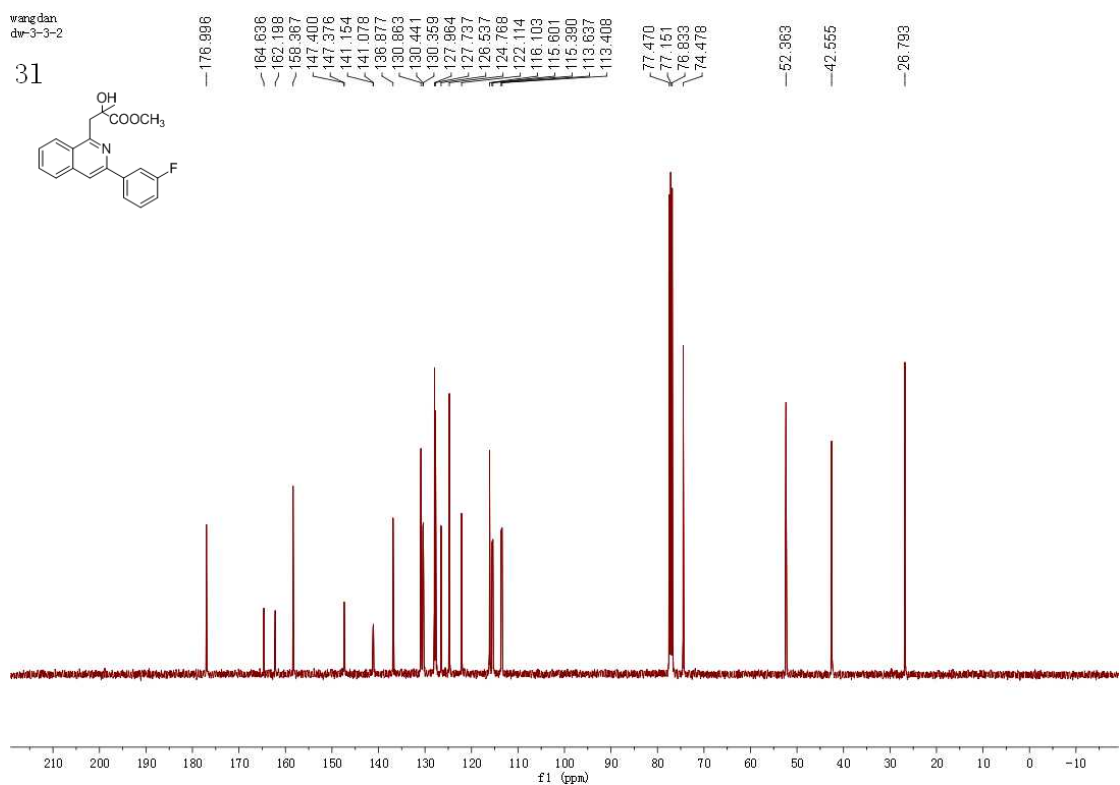
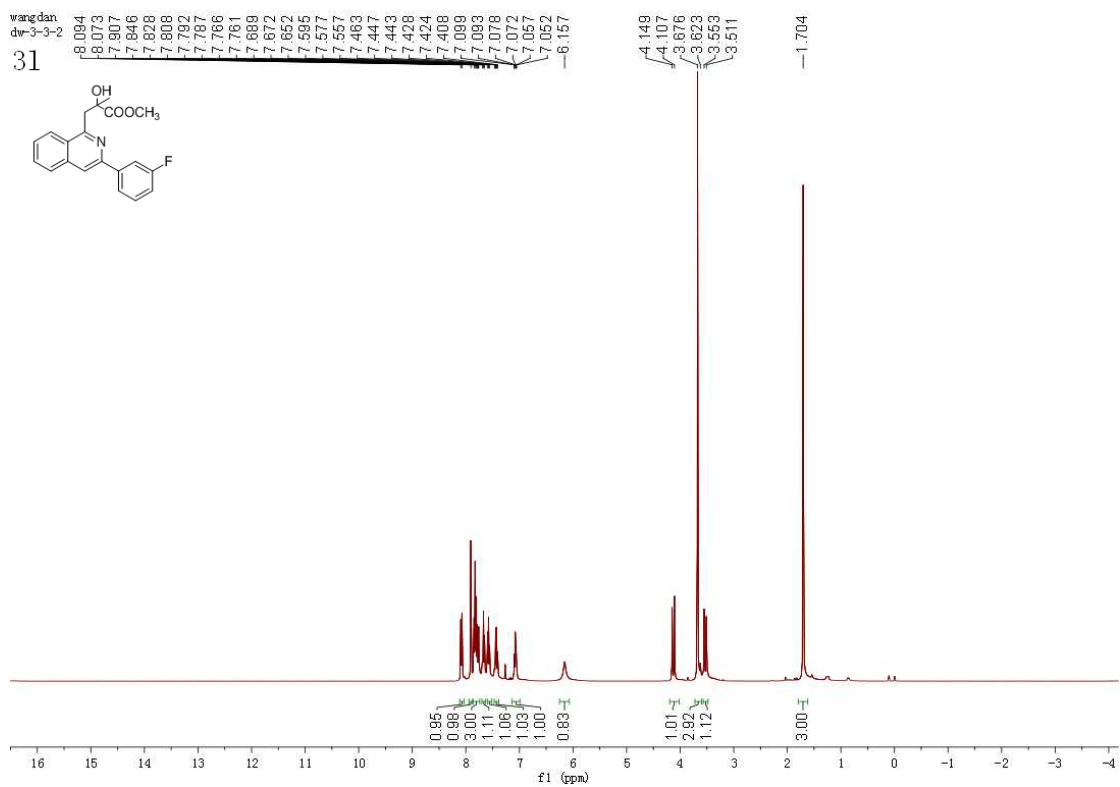
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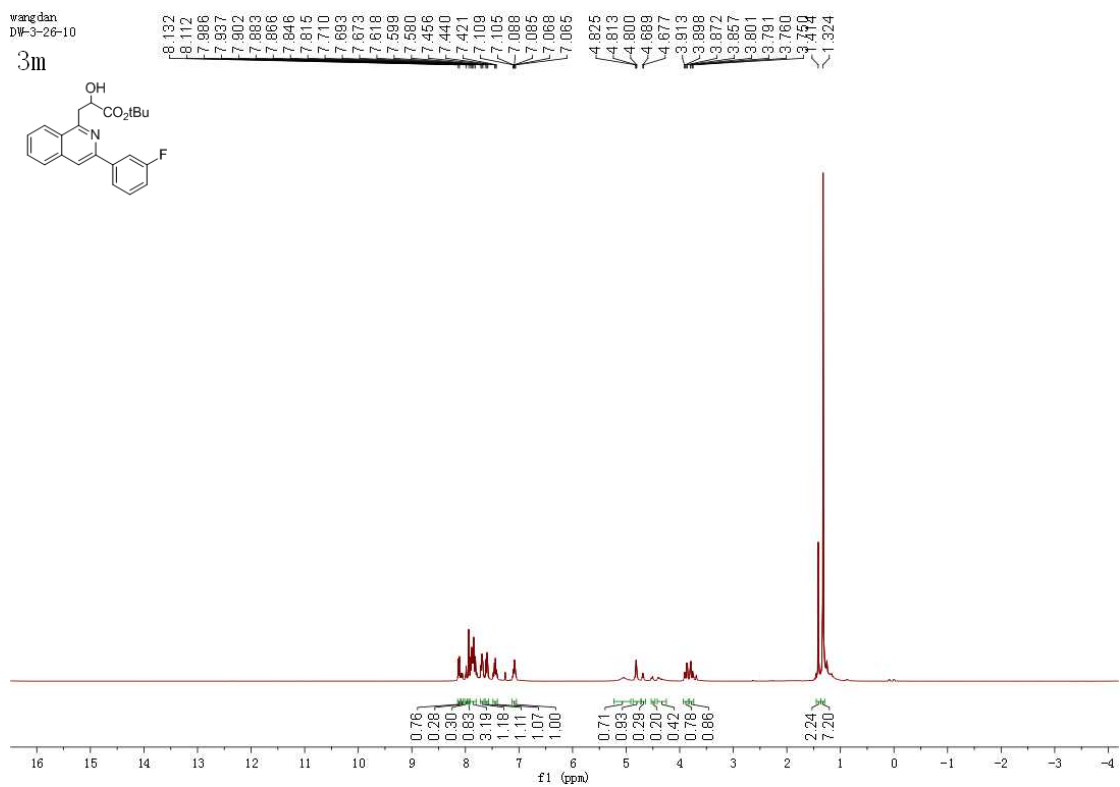
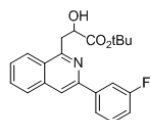
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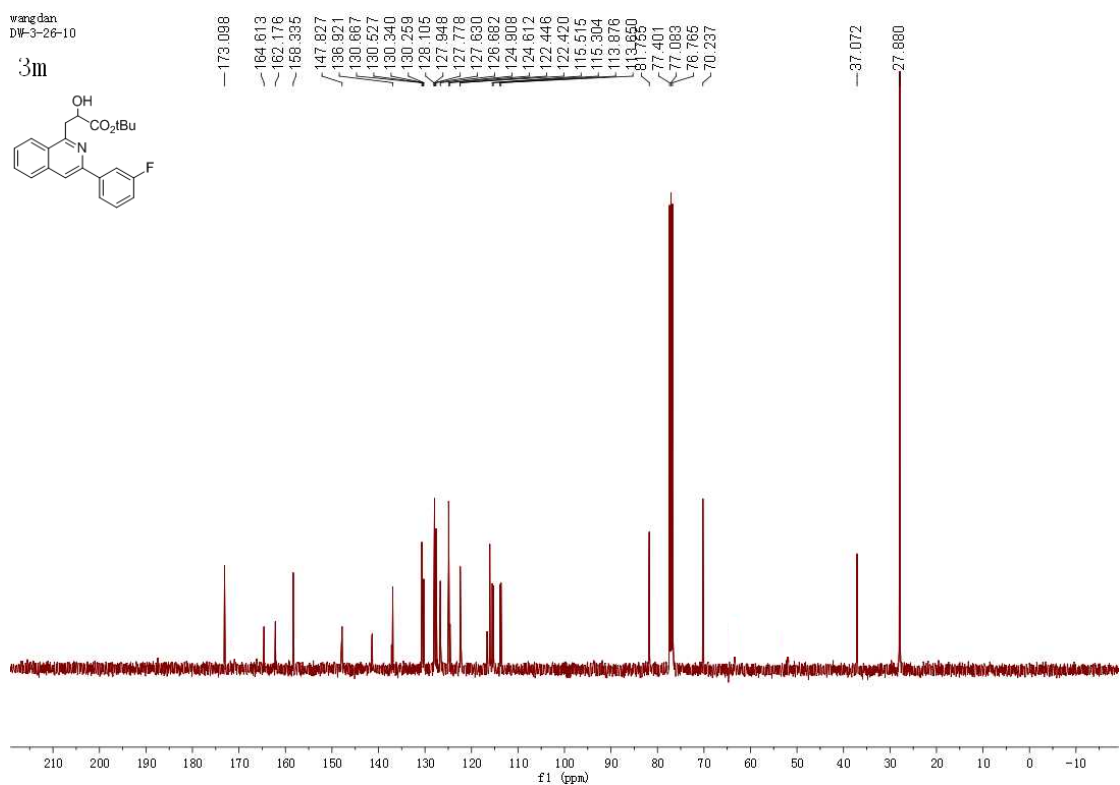
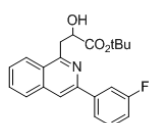
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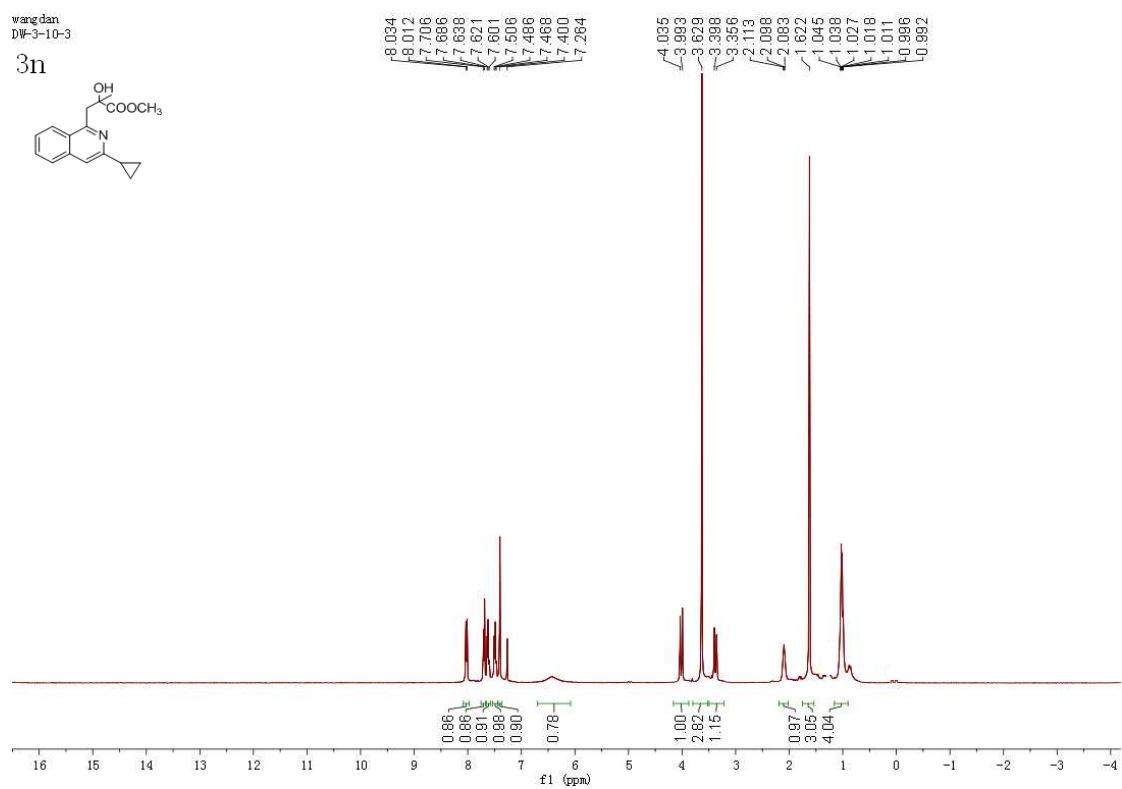
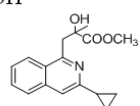
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DW-3-26-10

3m



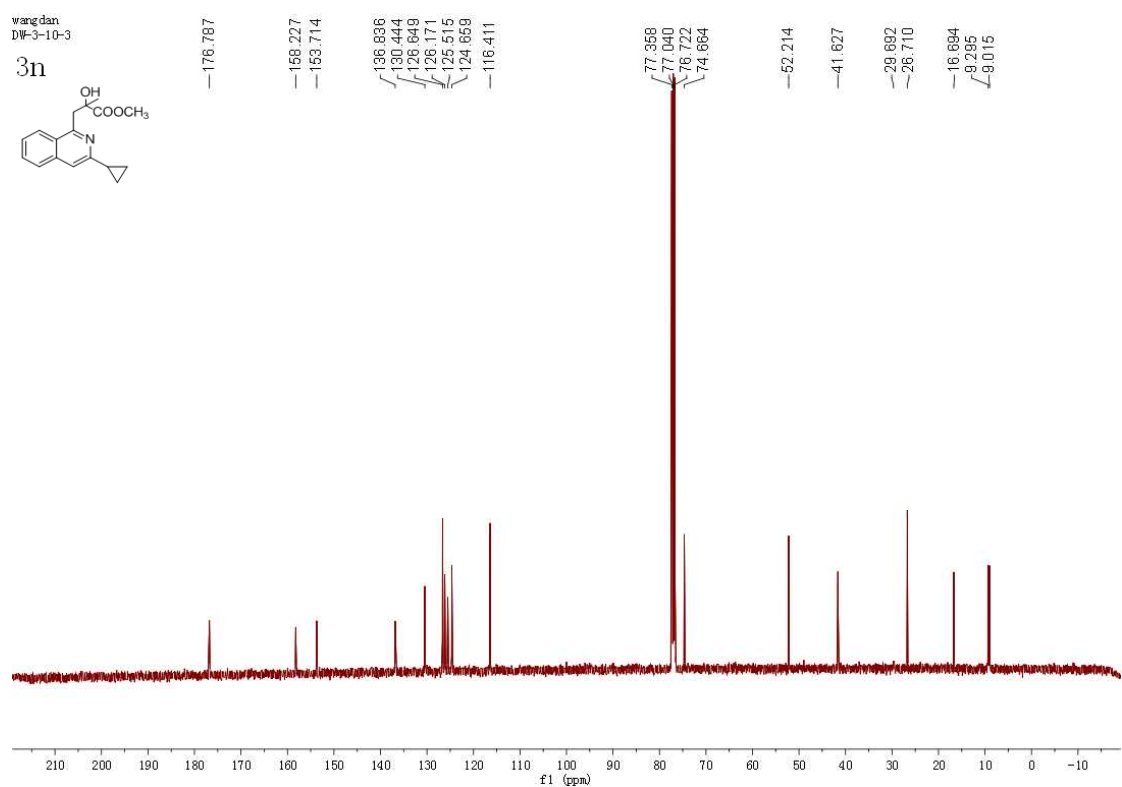
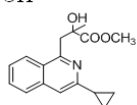
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3n

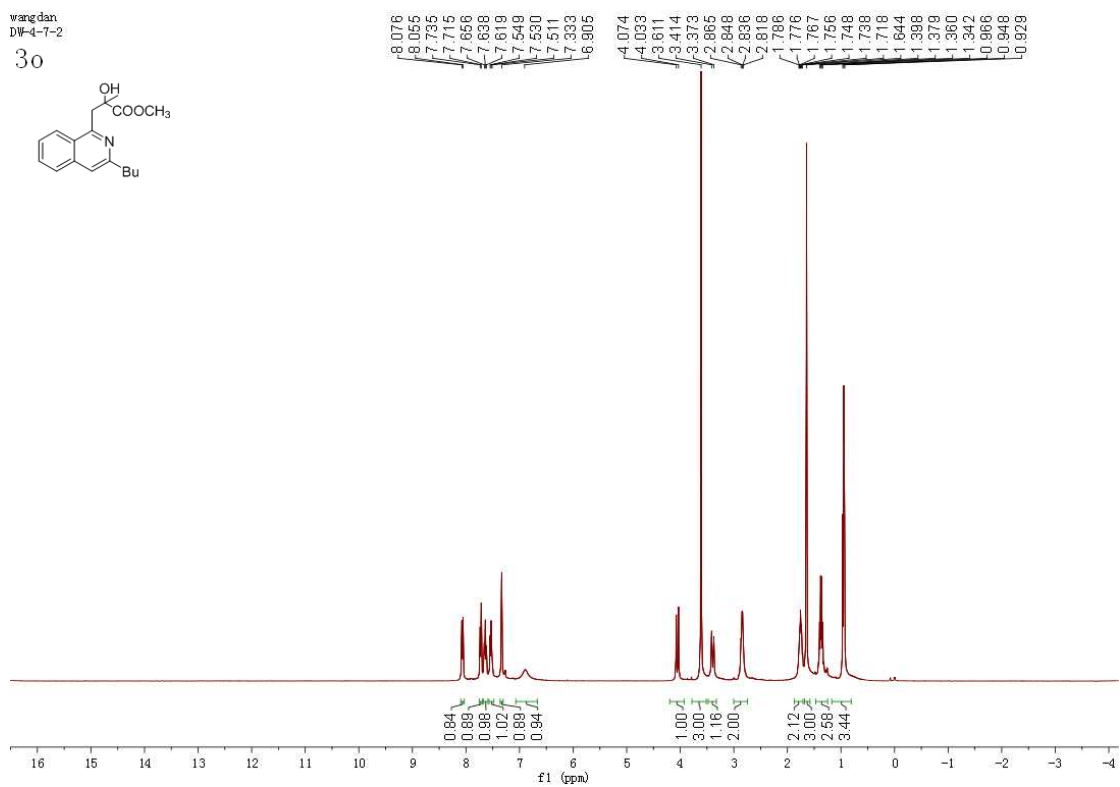
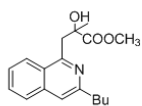


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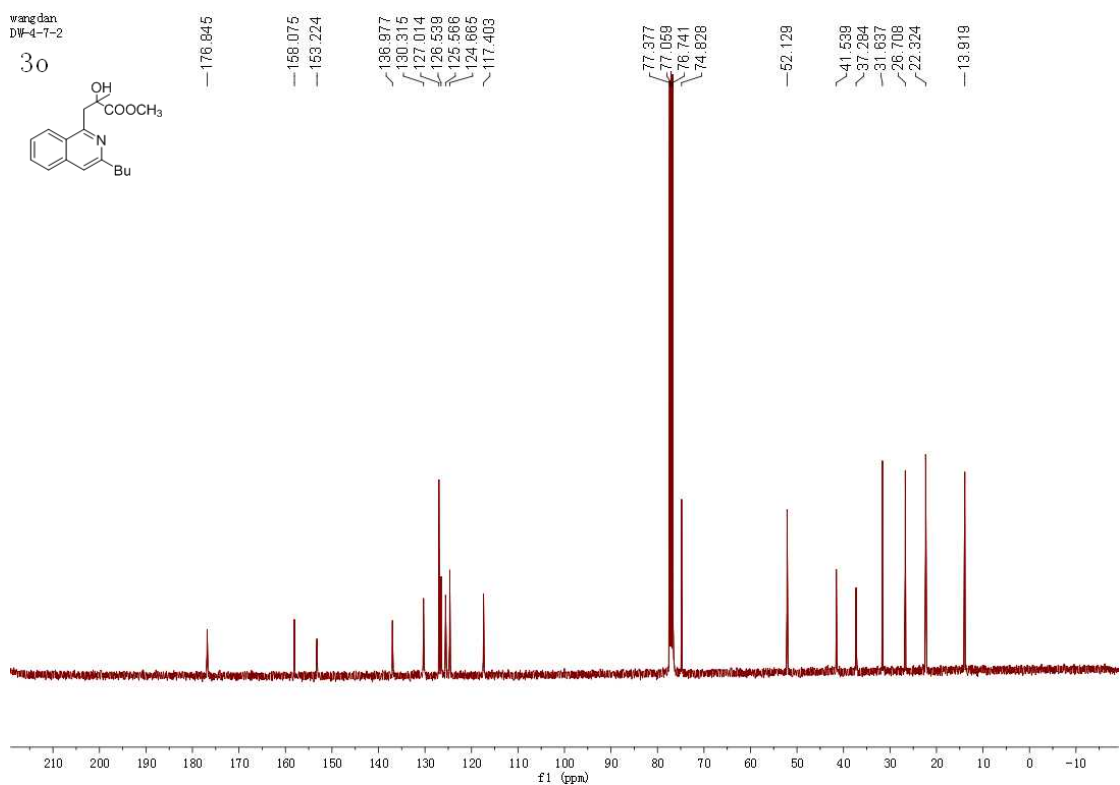
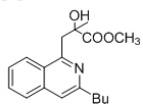
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wang dan
DW-4-7-2
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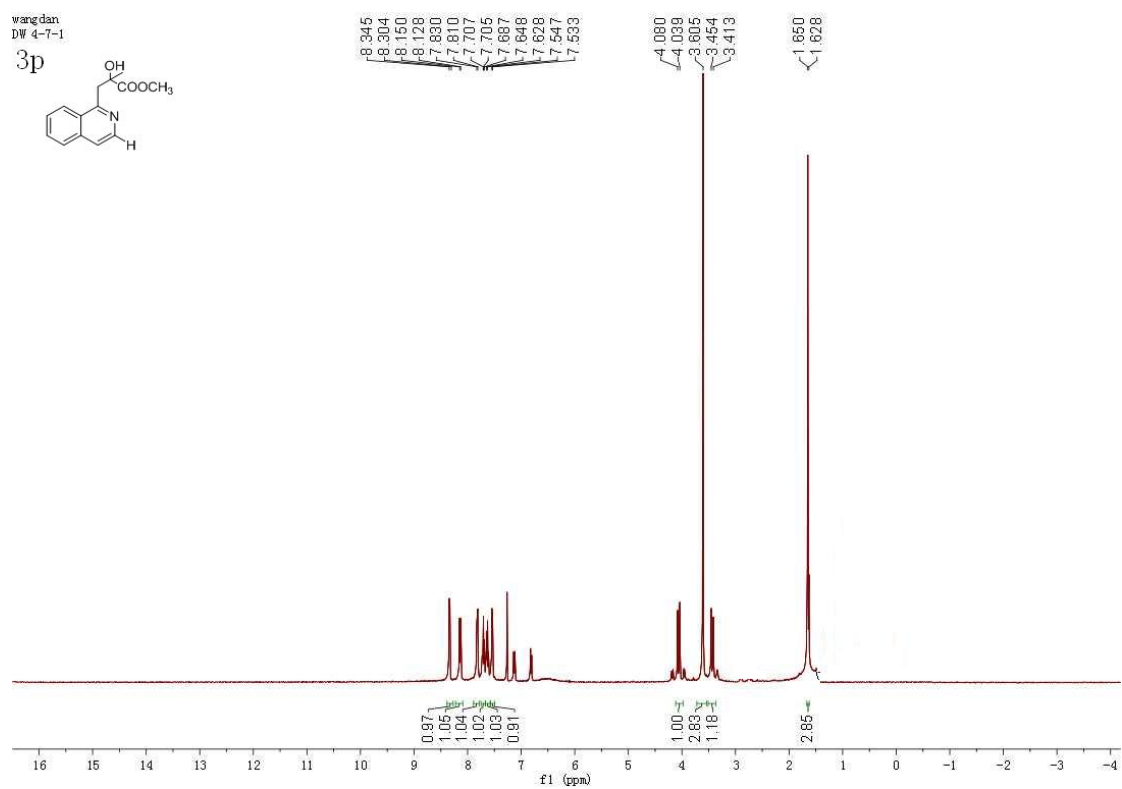
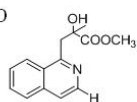


wang dan
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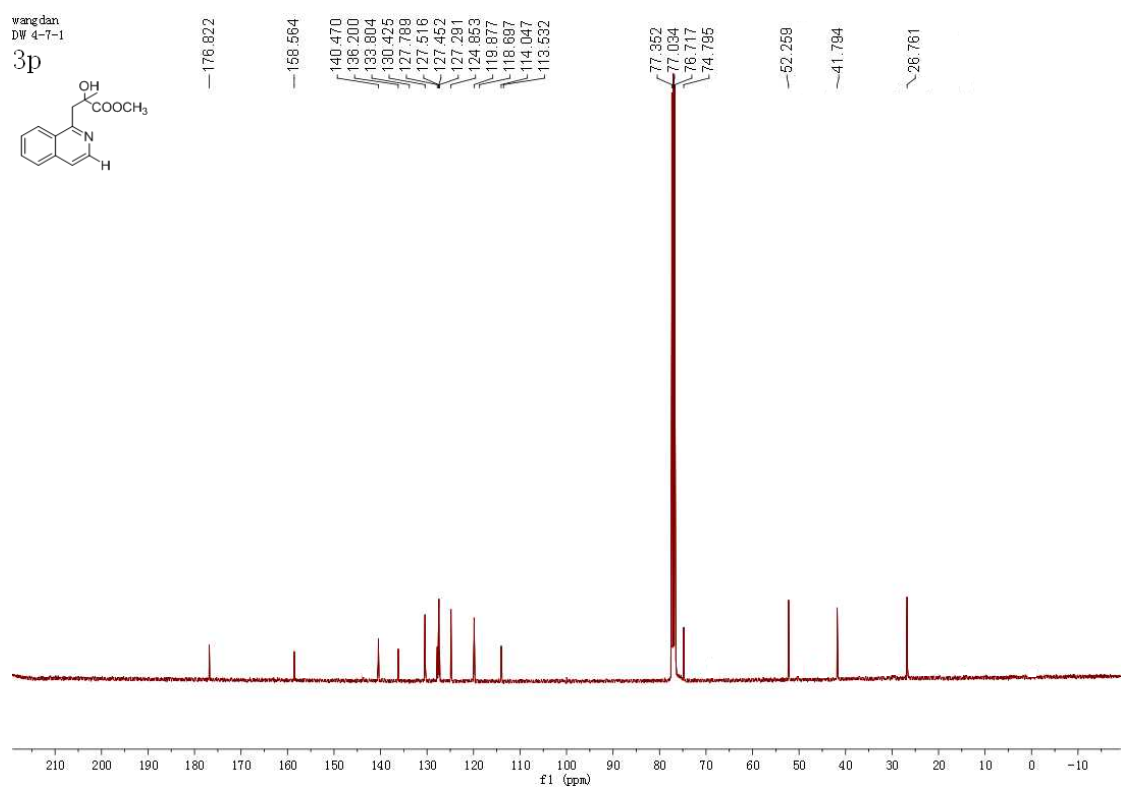
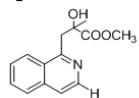
wangdan
DW 4-7-1

3p



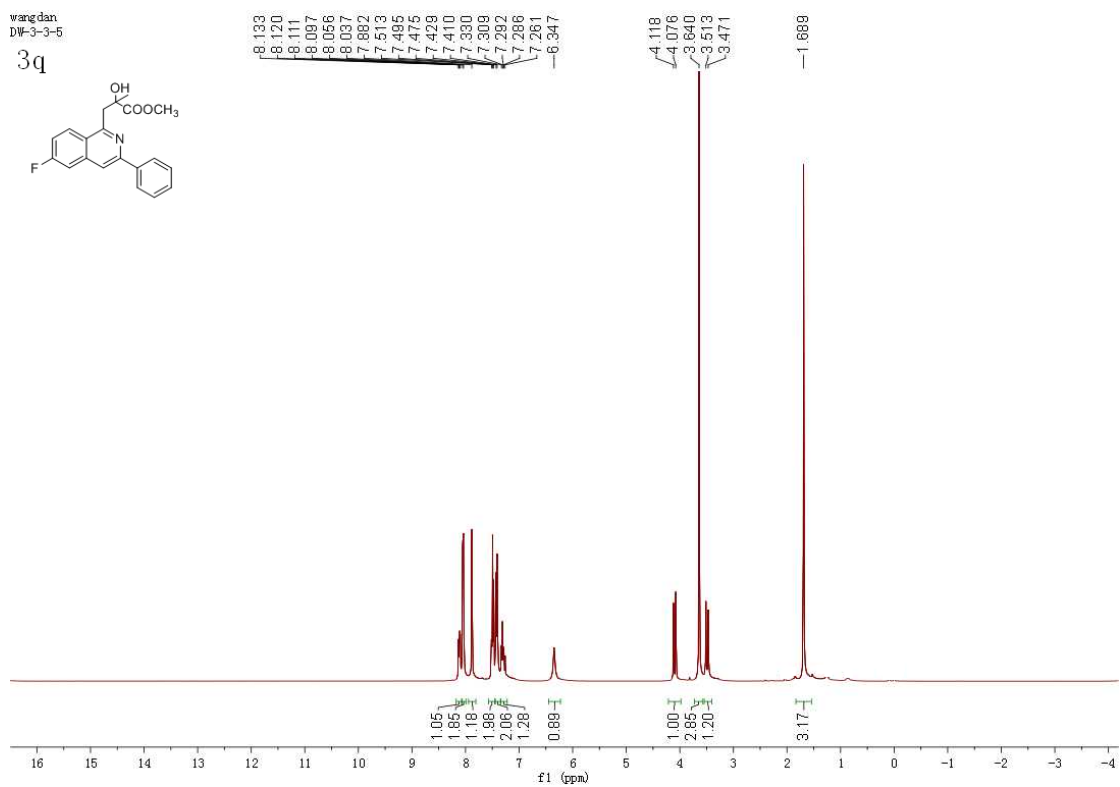
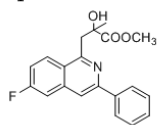
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DW 4-7-1

3p



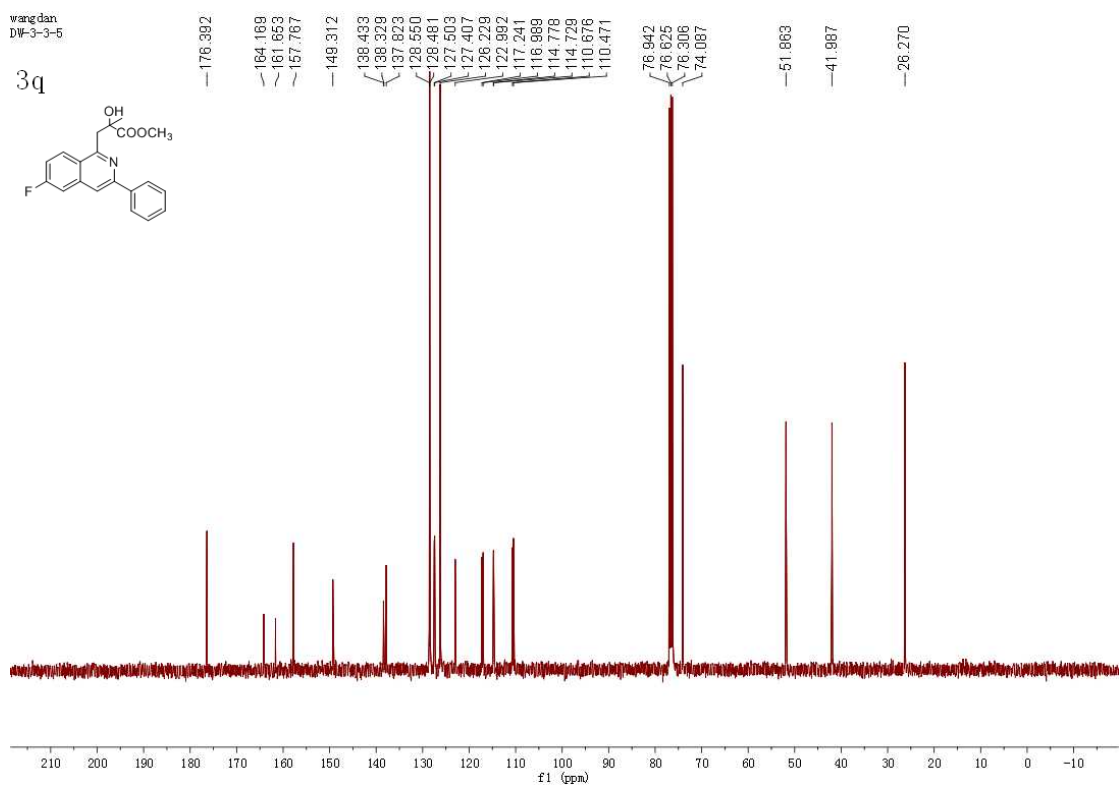
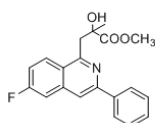
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3q



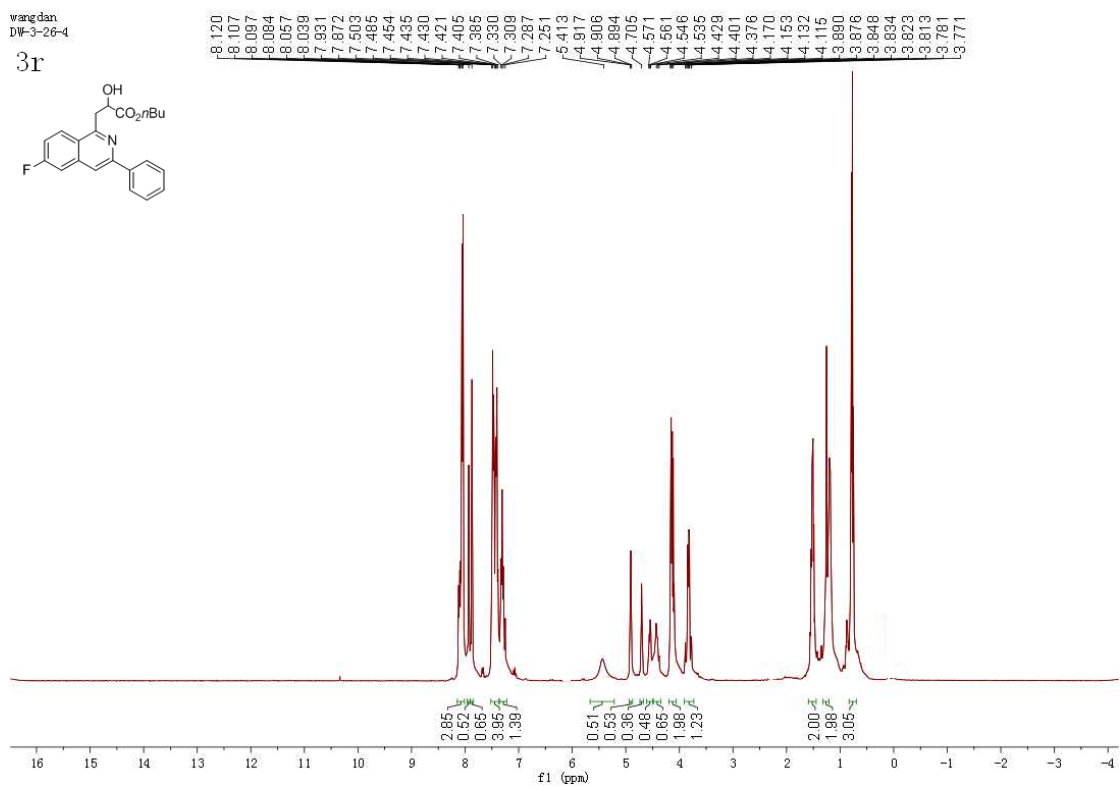
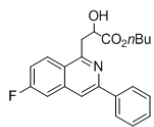
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DW-3-3-5

3q



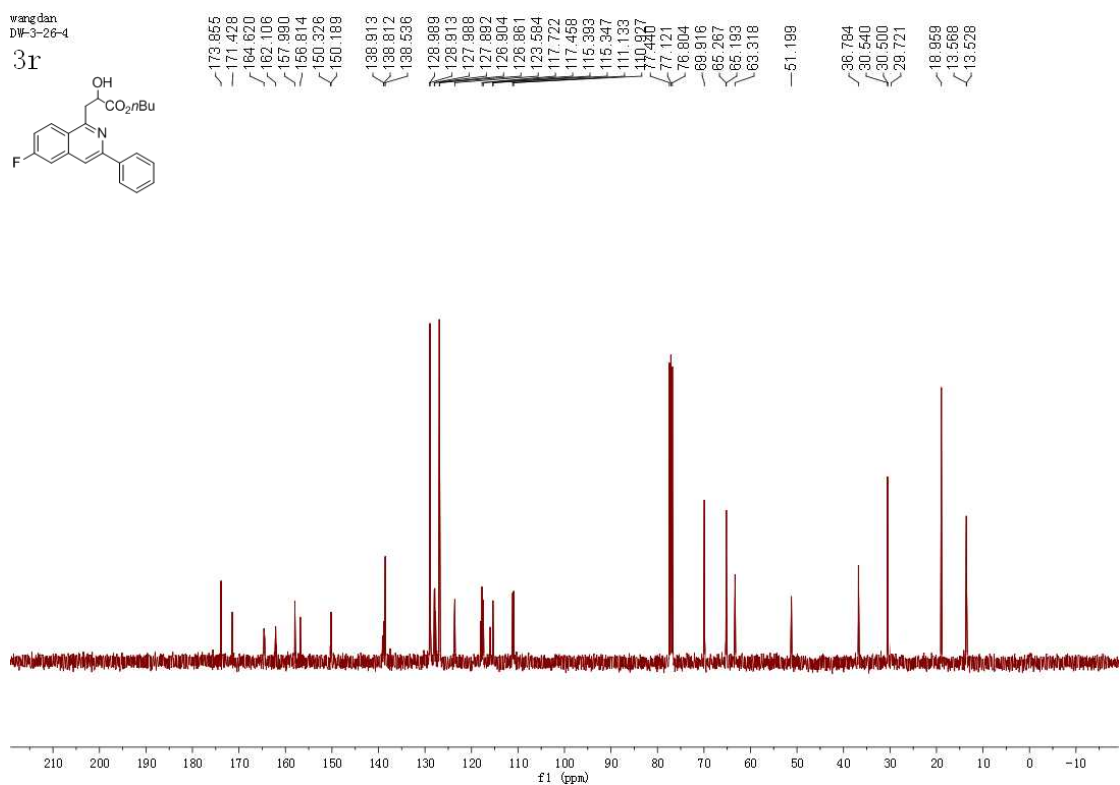
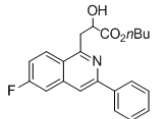
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DW-3-26-4

3r



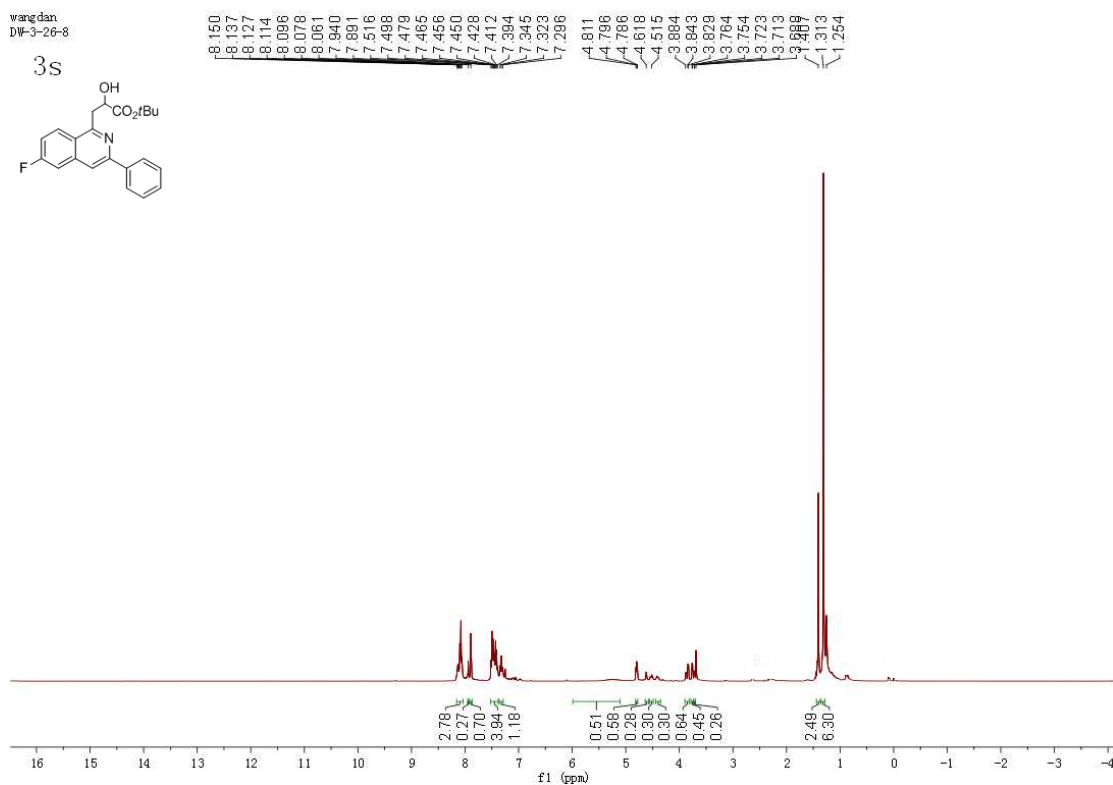
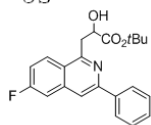
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DW-3-26-4

3r



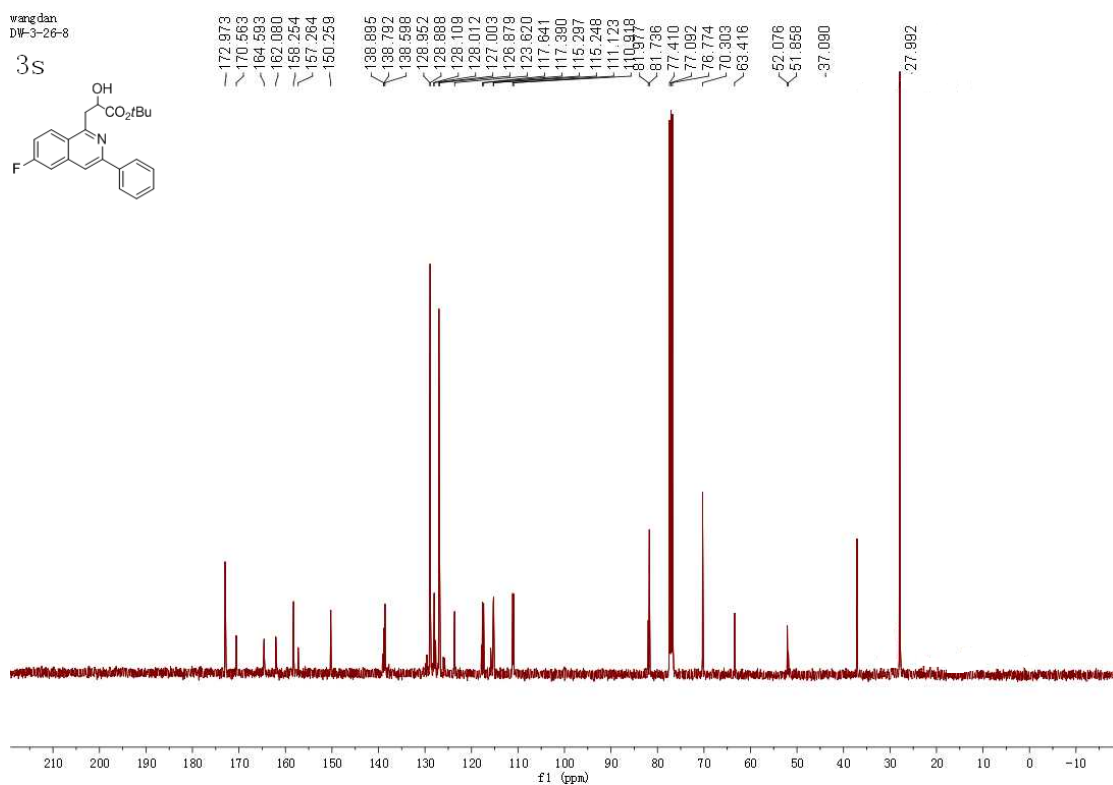
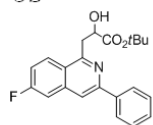
wangdan
DW-3-26-8

3S



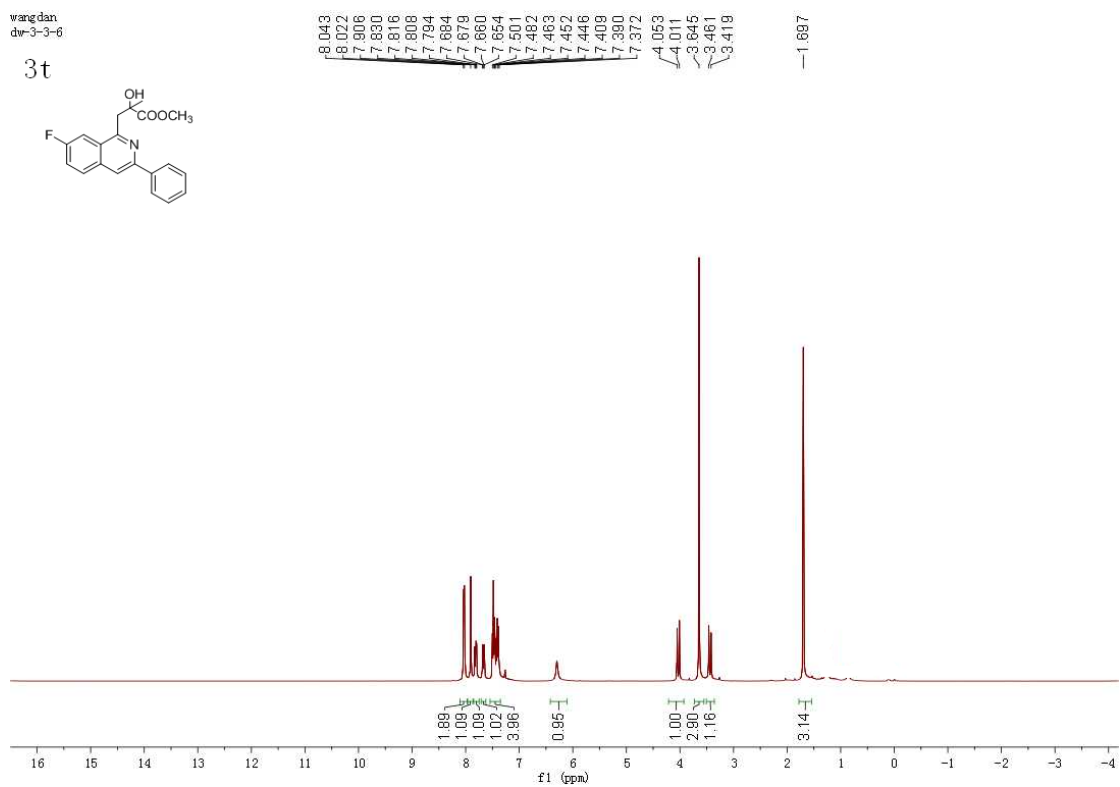
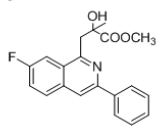
wangdan
DW-3-26-8

3S



wangdan
dw-3-3-6

3t



wangdan
dw-3-3-6

3t

