

Supporting Information

Silver Triflate and Triflic Anhydride-Promoted Expedient Synthesis of Acylated 1-Aminoisoquinolines

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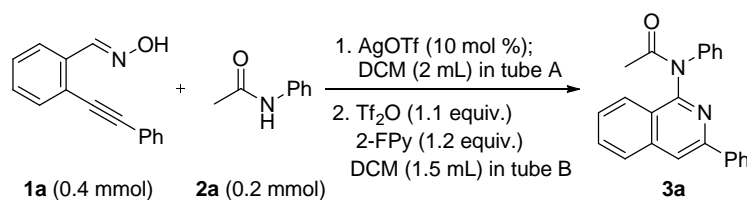
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General Information

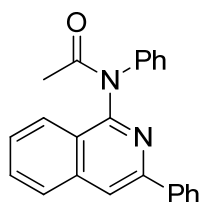
Unless otherwise stated, all commercial reagents were used as received. All solvents were dried and distilled according to standard procedures. Flash column chromatography was performed using silica gel (60-Å pore size, 32-63µm, standard grade). Analytical thin-layer chromatography was performed using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

General experimental procedure for the reaction of N'-(2-alkynylbenzylidene)benzenesulfonylhydrazide 1a with amide 2a:



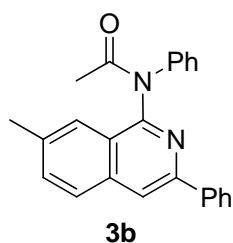
The mixture of 2-alkynylbenzaloxime **1a** (0.20 mmol) and silver triflate (0.02 mmol, 5.1 mg) in dichloromethane (2.0 mL) was stirred at room temperature for 2-3 h in one reaction tube A, the reaction was monitored via TLC. Meanwhile, in another reaction tube B, *N*-phenylacetamide **2a** (0.30 mmol) and 2-fluoropyridine (0.36 mmol) were stirred in dichloromethane (1.5 mL) and cooled to -78 °C under N_2 , then trifluoromethanesulfonic anhydride (0.33 mmol) was added slowly *via* a microsyringe during a period of 15 min. The reaction mixture was stirred at -78°C for further 5-10 min. Then upon completion of the reaction in reaction tube A, the reaction solution in

tube A was carefully transferred into tube B via a syringe. After stirring at -78°C for about 5 min, the resulting reaction mixture in tube B was allowed to warm to room temperature, and kept stirred at room temperature for 4 h. Upon completion of the reaction as indicated by TLC, triethylamine (100 μL) was added to quench, and the reaction mixture was diluted by dichloromethane (10 mL), washed with brine (10 mL), and the layers were extracted with dichloromethane (2×5 mL). The combined organic layers were dried over Na_2SO_4 . The residue was purified by column chromatography on silica gel (eluted with petroleum ether/ether acetate = 20:1) to provide the acylated 1-aminoisoquinolines **3a**.



N-Phenyl-*N*-(3-phenylisoquinolin-1-yl)acetamide (**3a**).

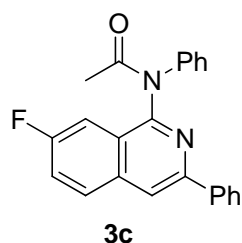
^1H NMR (400 MHz, CDCl_3): δ 8.15-8.10 (m, 4H), 7.88 (d, $J = 8.4$ Hz, 1H), 7.65 (t, $J = 7.4$ Hz, 1H), 7.55-7.48 (m, 5H), 7.43-7.41 (m, 1H), 7.34-7.32 (m, 2H), 7.23 (s, 1H), 2.10 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.18, 153.56, 150.09, 141.56, 139.52, 138.50, 130.89, 129.09, 128.96, 128.87, 128.79, 128.26, 127.68, 126.89, 124.97, 124.50, 117.01, 23.80; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}$ ($\text{M}+\text{H}$) $^+$: 339.1497; found, 339.1499.



N-(7-Methyl-3-phenylisoquinolin-1-yl)-*N*-phenylacetamide (**3b**).

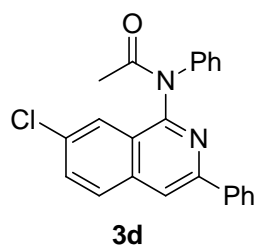
^1H NMR (400 MHz, CDCl_3): δ 8.14-8.07 (m, 3H), 7.86 (s, 1H), 7.80 (d, $J = 8.4$ Hz, 1H), 7.54-7.48 (m, 5H), 7.41 (d, $J = 6.7$ Hz, 1H), 7.34-7.33 (m, 1H), 7.24-7.20 (m, 1H), 2.51 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.1, 167.6, 152.7,

149.2, 138.5, 137.8, 133.1, 132.9, 130.8, 128.9, 128.7, 127.4, 126.7, 124.6, 123.5, 116.8, 22.1, 19.1; HRMS (ESI) calcd. for C₂₄H₂₁N₂O (M+H)⁺: 353.1654; found, 353.1606.



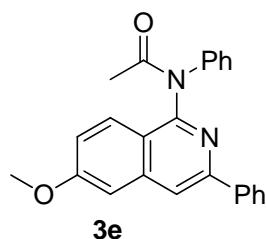
N-(7-Fluoro-3-phenylisoquinolin-1-yl)-*N*-phenylacetamide (**3c**).

¹H NMR (400 MHz, CDCl₃): δ 8.04-8.00 (m, 3H), 7.83 (dd, *J* = 8.9, 5.3 Hz, 1H), 7.62 (d, *J* = 8.9 Hz, 1H), 7.44-7.39 (m, 4H), 7.38-7.34 (m, 2H), 7.30-7.27 (m, 2H), 7.17 (s, 1H), 2.05 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 171.15, 161.5 (d, ¹*J* = 250.9 Hz), 153.12, 149.77, 149.75, 130.36, 130.27, 129.22, 128.98, 128.87, 126.8, 125.3, 125.2, 116.5, 108.6 (d, ²*J* = 22.0 Hz), 22.7; HRMS (ESI) calcd. for C₂₃H₁₈FN₂O (M+H)⁺: 357.1403; found, 357.1363.



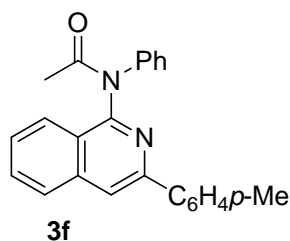
N-(7-Chloro-3-phenylisoquinolin-1-yl)-*N*-phenylacetamide (**3d**).

¹H NMR (400 MHz, CDCl₃): δ 8.11-8.08 (m, 3H), 7.84 (d, *J* = 8.8 Hz, 1H), 7.71 (dt, *J* = 6.2, 3.1 Hz, 1H), 7.60 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.54-7.47 (m, 3H), 7.44 (d, *J* = 7.3 Hz, 1H), 7.41-7.35 (m, 2H), 7.30-7.25 (m, 2H), 2.13 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 171.3, 167.7, 152.7, 150.5, 138.1, 137.7, 133.9, 132.4, 132.0, 130.9, 129.3, 129.2, 128.9, 128.9, 126.9, 125.1, 124.0, 116.5, 23.8; HRMS (ESI) calcd. for C₂₃H₁₇ClN₂NaO (M+Na)⁺: 395.0927; found, 395.0908.



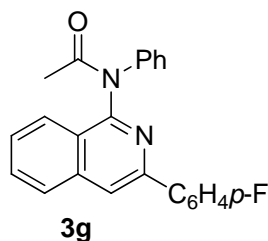
N-(6-Methoxy-3-phenylisoquinolin-1-yl)-*N*-phenylacetamide (**3e**).

^1H NMR (400 MHz, CDCl_3): δ 8.14 (d, $J = 5.6$ Hz, 2H), 8.04-7.95 (m, 2H), 7.73-7.70 (m, 1H), 7.53-7.50 (m, 4H), 7.35-7.32 (m, 1H), 7.30-7.21 (m, 2H), 7.20-7.16 (m, 2H), 3.94 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.1, 167.7, 161.3, 153.2, 150.7, 141.6, 138.6, 132.4, 130.9, 129.0, 128.9, 128.8, 126.9, 126.79, 121.3, 120.0, 116.3, 105.2, 55.6, 23.8; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{21}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}$) $^+$: 369.1603; found, 369.1560.



N-Phenyl-*N*-(3-(*p*-tolyl)isoquinolin-1-yl)acetamide (**3f**).

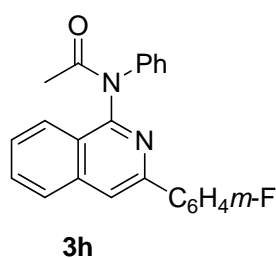
^1H NMR (400 MHz, CDCl_3): δ 8.00-7.97 (m, 4H), 7.77 (d, $J = 8.2$ Hz, 1H), 7.54 (t, $J = 7.5$ Hz, 1H), 7.45-7.44 (m, 2H), 7.24-7.20 (m, 4H), 7.14-7.09 (m, 2H), 2.32 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.1, 153.3, 151.8, 150.1, 139.4, 138.8, 135.60, 130.7, 129.6, 129.5, 129.2, 128.9, 127.9, 127.5, 126.6, 124.8, 124.2, 116.3, 22.6, 21.2; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{21}\text{N}_2\text{O}$ ($\text{M}+\text{H}$) $^+$: 353.1654; found, 353.1605.



N-(3-(4-Fluorophenyl)isoquinolin-1-yl)-*N*-phenylacetamide (**3g**).

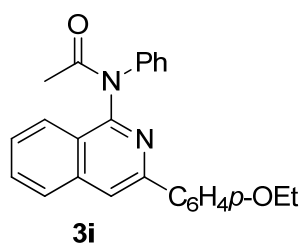
^1H NMR (400 MHz, CDCl_3): δ 8.02-8.00 (m, 3H), 7.93 (s, 1H), 7.78 (d, $J = 7.9$ Hz, 1H), 7.56 (t, $J = 7.1$ Hz, 1H), 7.46-7.44 (m, 3H), 7.30-7.19 (m, 2H), 7.14-7.07 (m,

3H), 2.01 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.1, 163.4 (d, $J = 248.6$ Hz), 153.5, 149.0, 139.4, 134.6, 130.9, 129.7, 129.0, 128.59, 128.51, 128.2, 127.5, 124.9, 124.3, 116.5, 115.6 (d, $J = 21.6$ Hz), 18.3; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{18}\text{FN}_2\text{O}$ ($\text{M}+\text{H}$) $^+$: 357.1403; found, 357.1393.



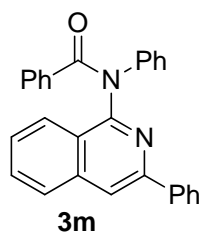
N-(3-(3-Fluorophenyl)isoquinolin-1-yl)-*N*-phenylacetamide (**3h**).

^1H NMR (400 MHz, CDCl_3): δ 8.09-8.00 (m, 2H), 7.88-7.73 (m, 3H), 7.64-7.54 (m, 1H), 7.54-7.39 (m, 3H), 7.39-7.31 (m, 1H), 7.31-7.19 (m, 2H), 7.18-7.08 (m, 1H), 7.06-6.96 (m, 1H), 2.02 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.2, 163.4 (d, $^1J = 245.3$ Hz), 153.7, 148.62, 148.6, 140.8, 139.4, 131.1, 130.3, 130.26, 129.2, 128.6, 127.8, 125.0, 124.8, 122.30, 122.28, 117.3, 115.7 (d, $^2J = 21.6$ Hz), 113.8 (d, $^2J = 23.0$ Hz), 23.7; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{18}\text{FN}_2\text{O}$ ($\text{M}+\text{H}$) $^+$: 357.1403; found, 357.1423.



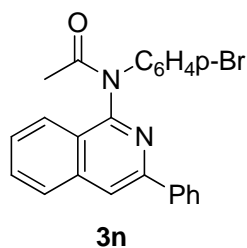
N-(3-(4-Ethoxyphenyl)isoquinolin-1-yl)-*N*-phenylacetamide (**3i**).

^1H NMR (400 MHz, CDCl_3): δ 8.10-8.06 (m, 3H), 8.01 (s, 1H), 7.86 (d, $J = 8.2$ Hz, 1H), 7.64 (t, $J = 7.5$ Hz, 1H), 7.57-7.48 (m, 3H), 7.33 (t, $J = 7.0$ Hz, 2H), 7.24-7.16 (m, 1H), 7.01 (d, $J = 8.6$ Hz, 2H), 4.10 (q, $J = 6.9$ Hz, 2H), 2.09 (s, 3H), 1.45 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.2, 167.7, 159.8, 153.3, 149.9, 141.5, 139.6, 130.8, 130.7, 129.0, 128.1, 127.7, 127.4, 124.8, 124.0, 115.7, 114.7, 63.5, 23.7, 14.8; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{22}\text{N}_2\text{NaO}$ ($\text{M}+\text{Na}$) $^+$: 405.1579; found, 406.1603.



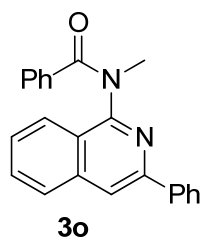
N-Phenyl-*N*-(3-phenylisoquinolin-1-yl)benzamide (**3m**).

^1H NMR (400 MHz, CDCl_3): δ 8.14-8.01 (m, 2H), 7.71 (dd, $J = 5.7, 3.3$ Hz, 1H), 7.51 (dd, $J = 5.7, 3.3$ Hz, 1H), 7.48-7.28 (m, 7H), 7.23-7.15 (m, 3H), 7.12-7.07 (m, 3H), 6.99-6.97 (m, 1H), 6.74-6.72 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 170.6, 167.7, 152.0, 141.0, 135.8, 132.4, 131.34, 131.28, 130.9, 129.8, 129.1, 128.86, 128.82, 128.7, 128.6, 128.5, 128.2, 128.0, 125.9, 125.7, 123.1, 121.8; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{21}\text{N}_2\text{O}$ ($\text{M}+\text{H}$) $^+$, 401.1654; found, 401.1625.



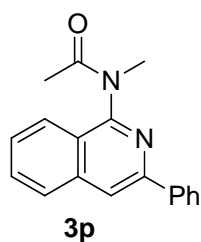
N-(4-Bromophenyl)-*N*-(3-phenylisoquinolin-1-yl)acetamide (**3n**).

^1H NMR (400 MHz, CDCl_3): δ 8.14-8.00 (m, 3H), 7.91 (d, $J = 7.9$ Hz, 1H), 7.79 (d, $J = 8.1$ Hz, 1H), 7.58-7.54 (m, 1H), 7.41-7.38 (m, 3H), 7.37-7.30 (m, 5H), 1.97 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 170.9, 152.9, 150.1, 140.3, 139.5, 138.1, 132.0, 131.0, 129.0, 128.8, 128.4, 127.8, 127.7, 126.7, 124.5, 124.2, 117.1, 23.8; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{18}\text{BrN}_2\text{O}$ ($\text{M}+\text{H}$) $^+$: 417.0603; found, 417.0613.



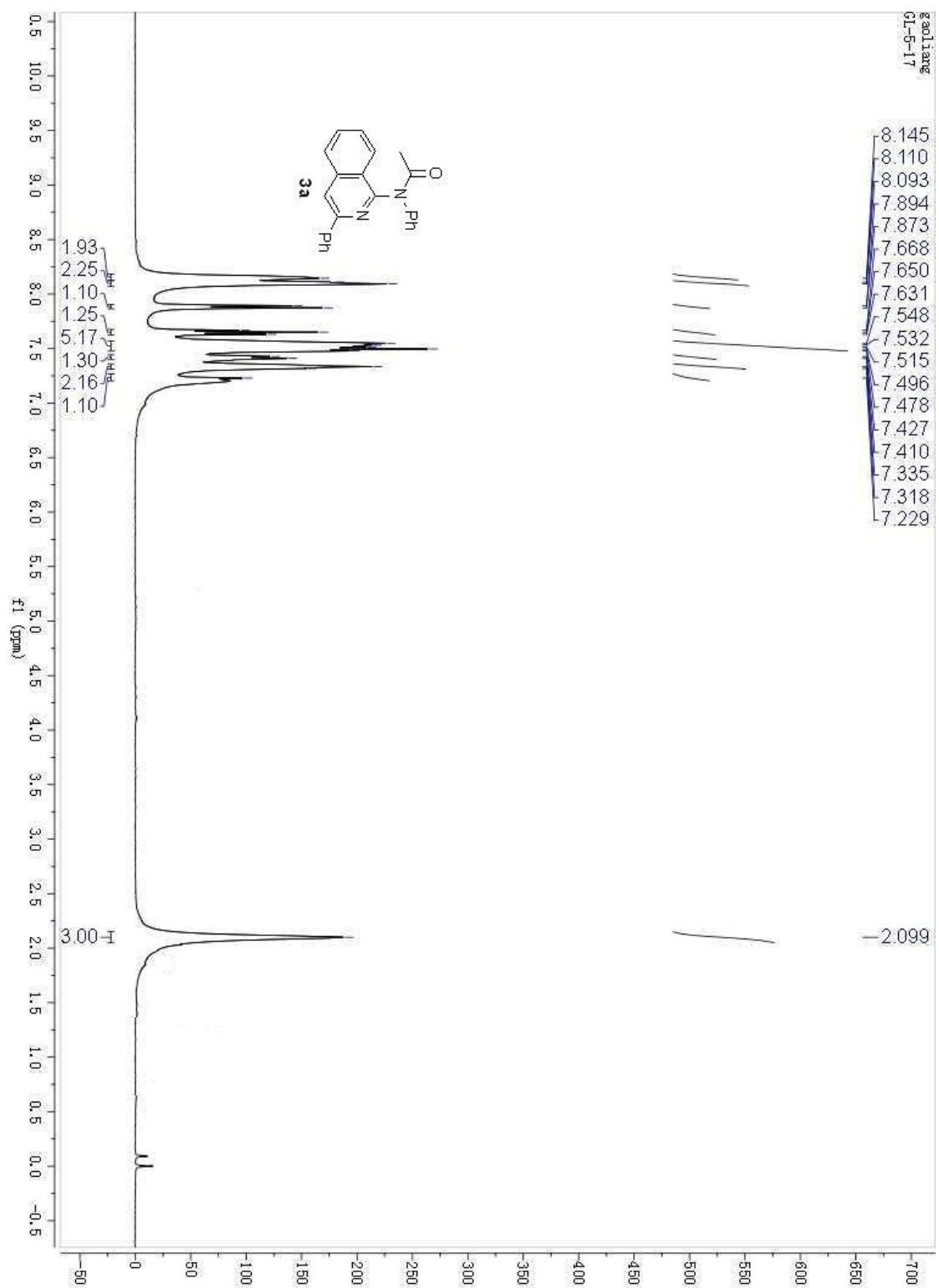
N-Methyl-*N*-(3-phenylisoquinolin-1-yl)benzamide (**3o**).

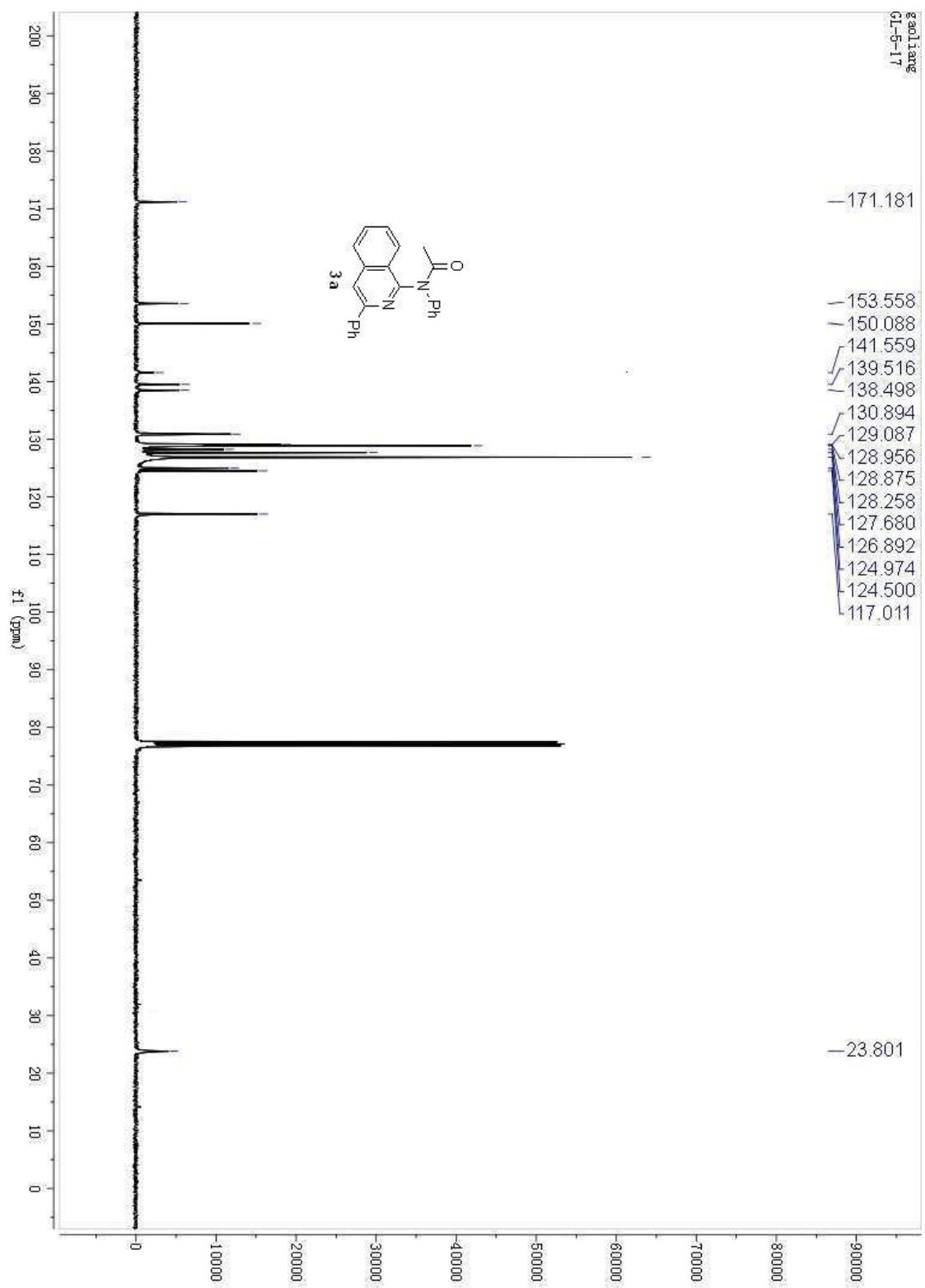
^1H NMR (400 MHz, CDCl_3): δ 8.00 (d, $J = 8.4$ Hz, 1H), 7.92-7.90 (m, 3H), 7.82 (d, $J = 8.2$ Hz, 1H), 7.65-7.61 (m, 1H), 7.57-7.53 (m, 1H), 7.47-7.43 (m, 2H), 7.41-7.35 (m, 3H), 7.10-7.08 (m, 1H), 7.04-7.02 (m, 2H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 172.2, 155.6, 149.8, 139.1, 138.5, 136.5, 130.7, 129.9, 128.8, 128.76, 128.0, 127.9, 127.7, 127.6, 126.8, 124.6, 123.6, 116.3, 37.2; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}$ ($\text{M}+\text{H}$) $^+$: 339.1497; found, 339.1471.

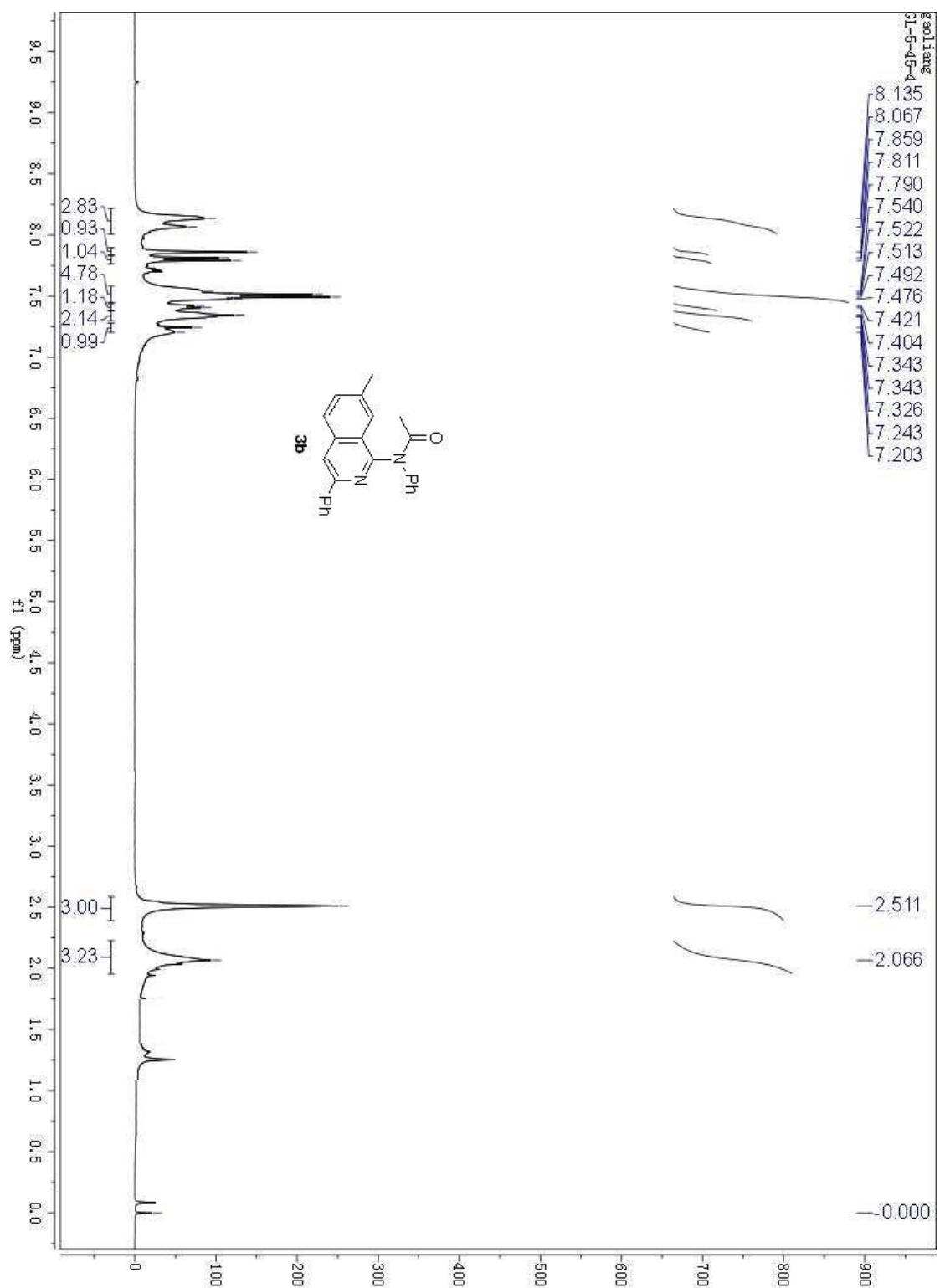


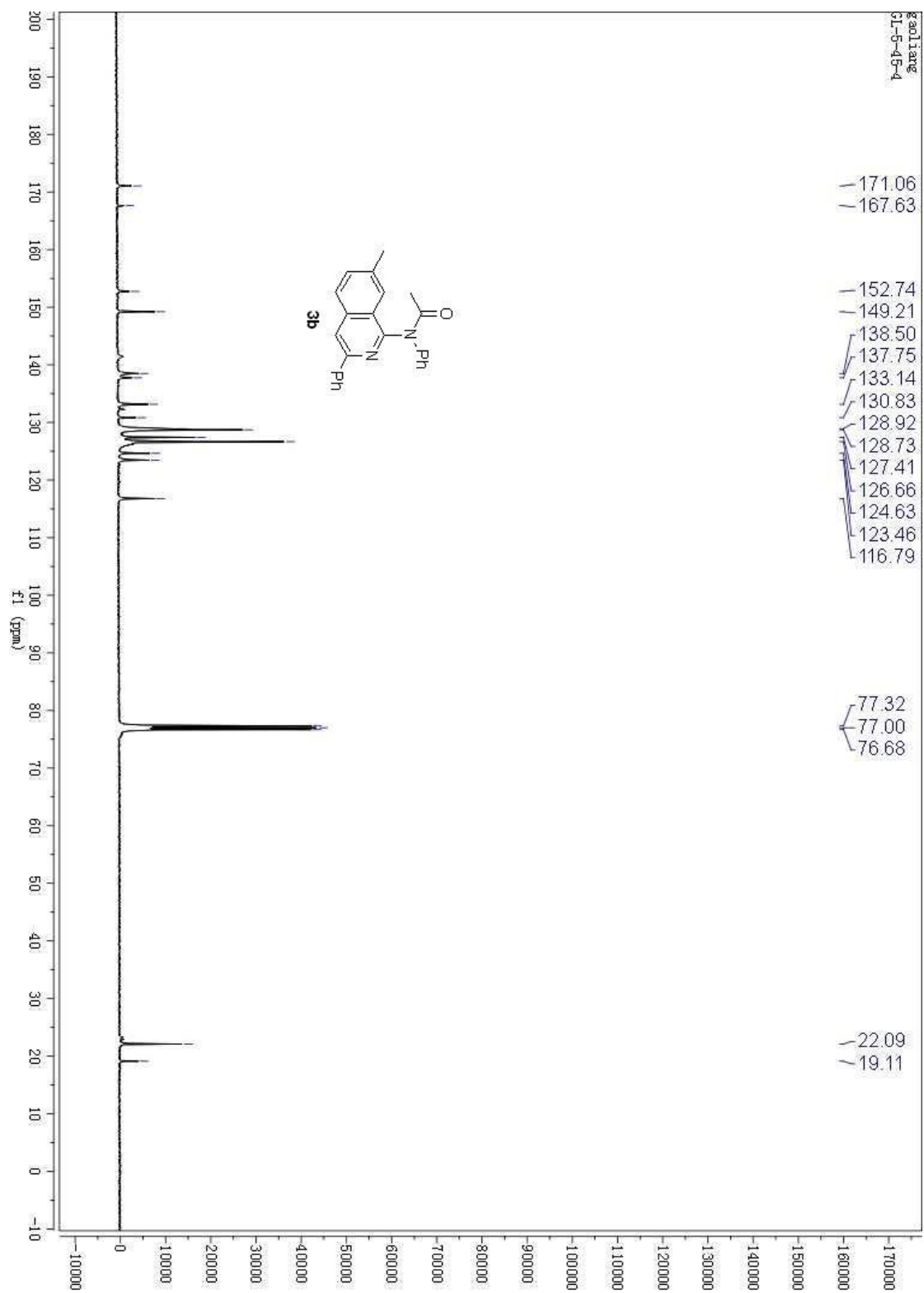
N-Methyl-*N*-(3-phenylisoquinolin-1-yl)acetamide (**3p**).

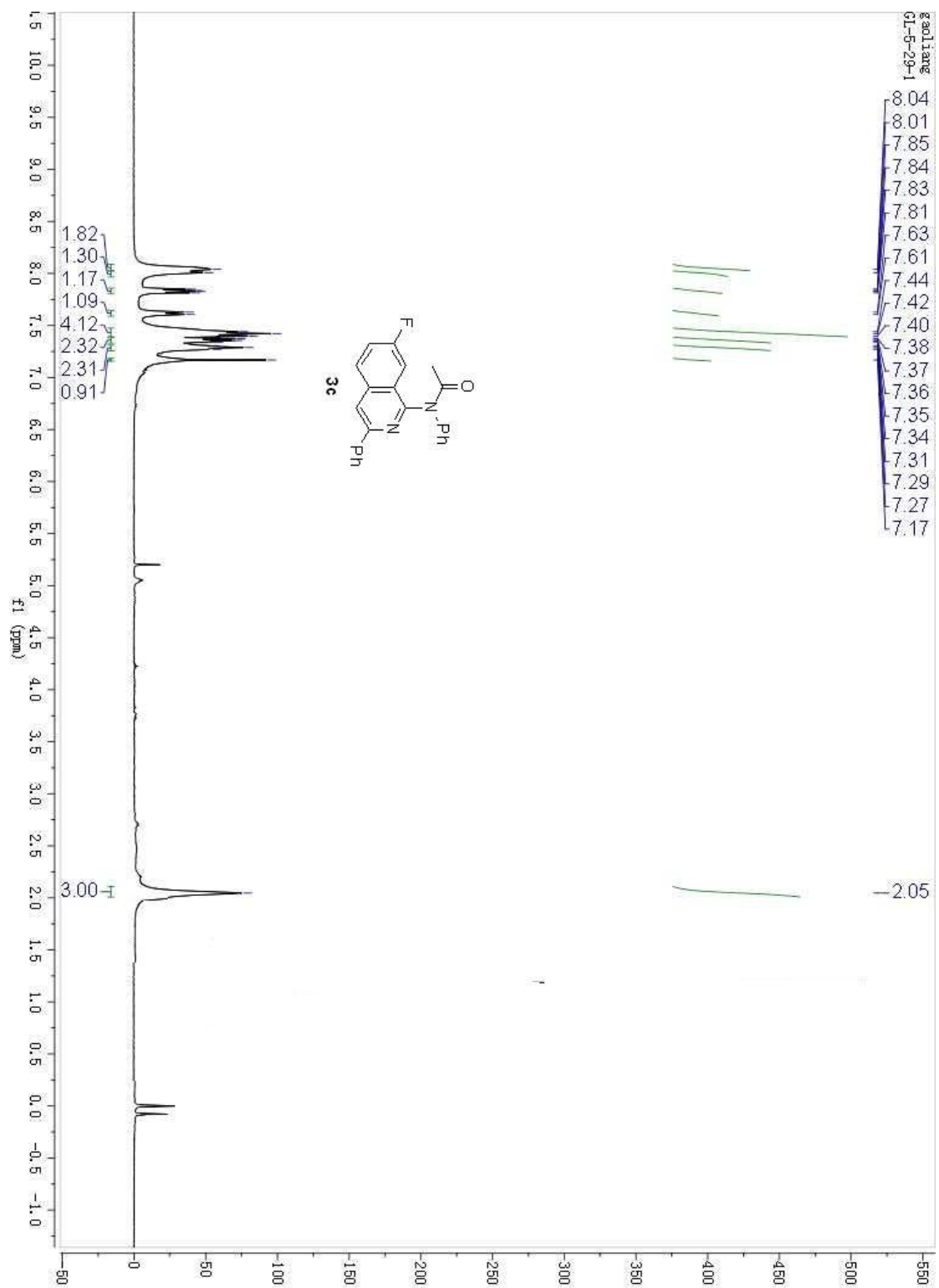
^1H NMR (400 MHz, CDCl_3): δ 8.14-8.12 (m, 3H), 7.98-7.94 (m, 2H), 7.76 (t, $J = 7.4$ Hz, 1H), 7.66-7.62 (m, 1H), 7.52 (t, $J = 7.4$ Hz, 2H), 7.45 (d, $J = 7.2$ Hz, 1H), 3.46 (s, 3H), 1.88 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.4, 154.9, 150.3, 139.4, 138.4, 131.2, 129.0, 128.9, 128.3, 127.7, 126.9, 124.4, 123.8, 116.9, 35.7, 22.6; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{16}\text{KN}_2\text{O}$ ($\text{M}+\text{K}$) $^+$: 315.0900; found, 315.0881.



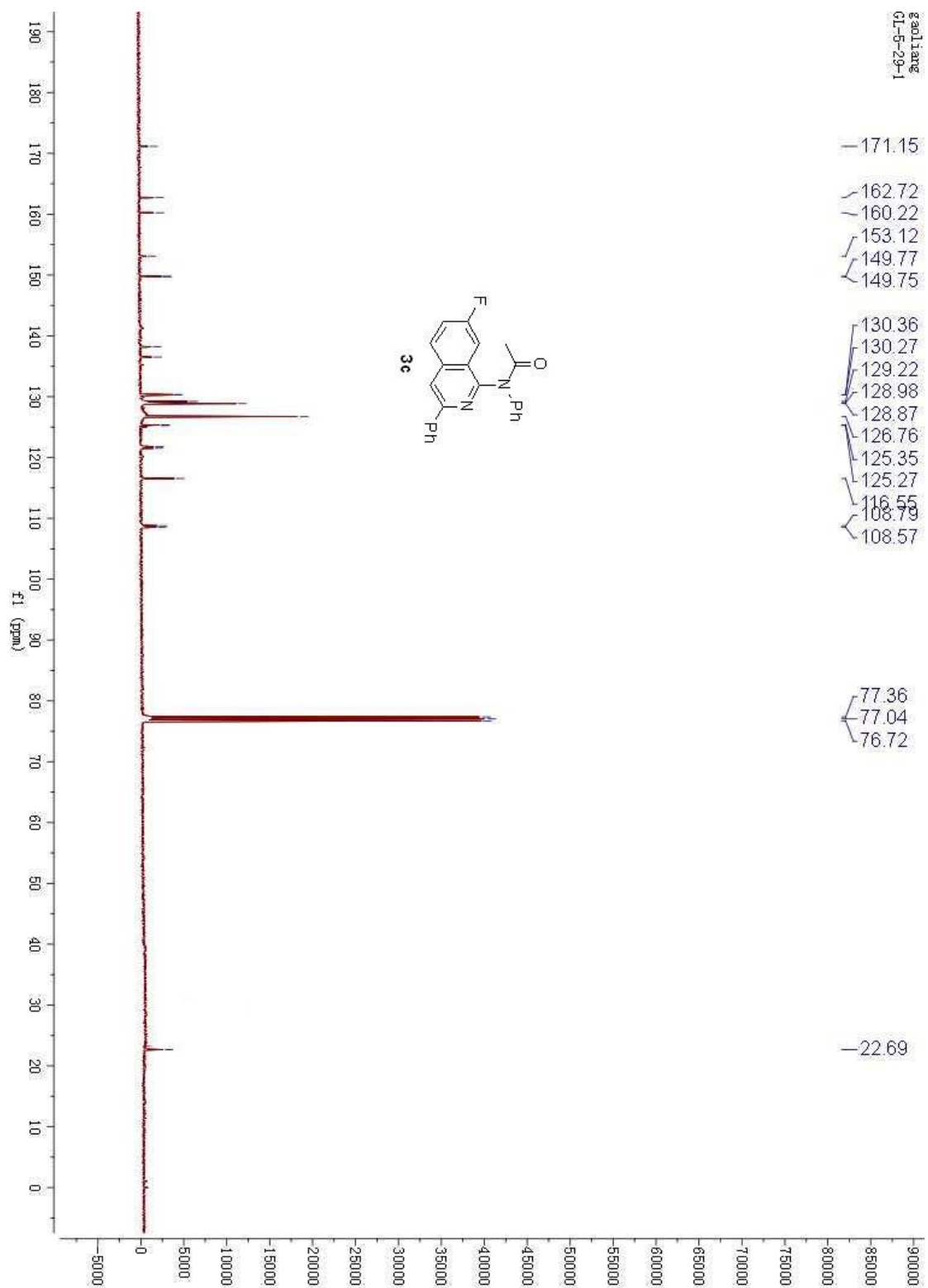


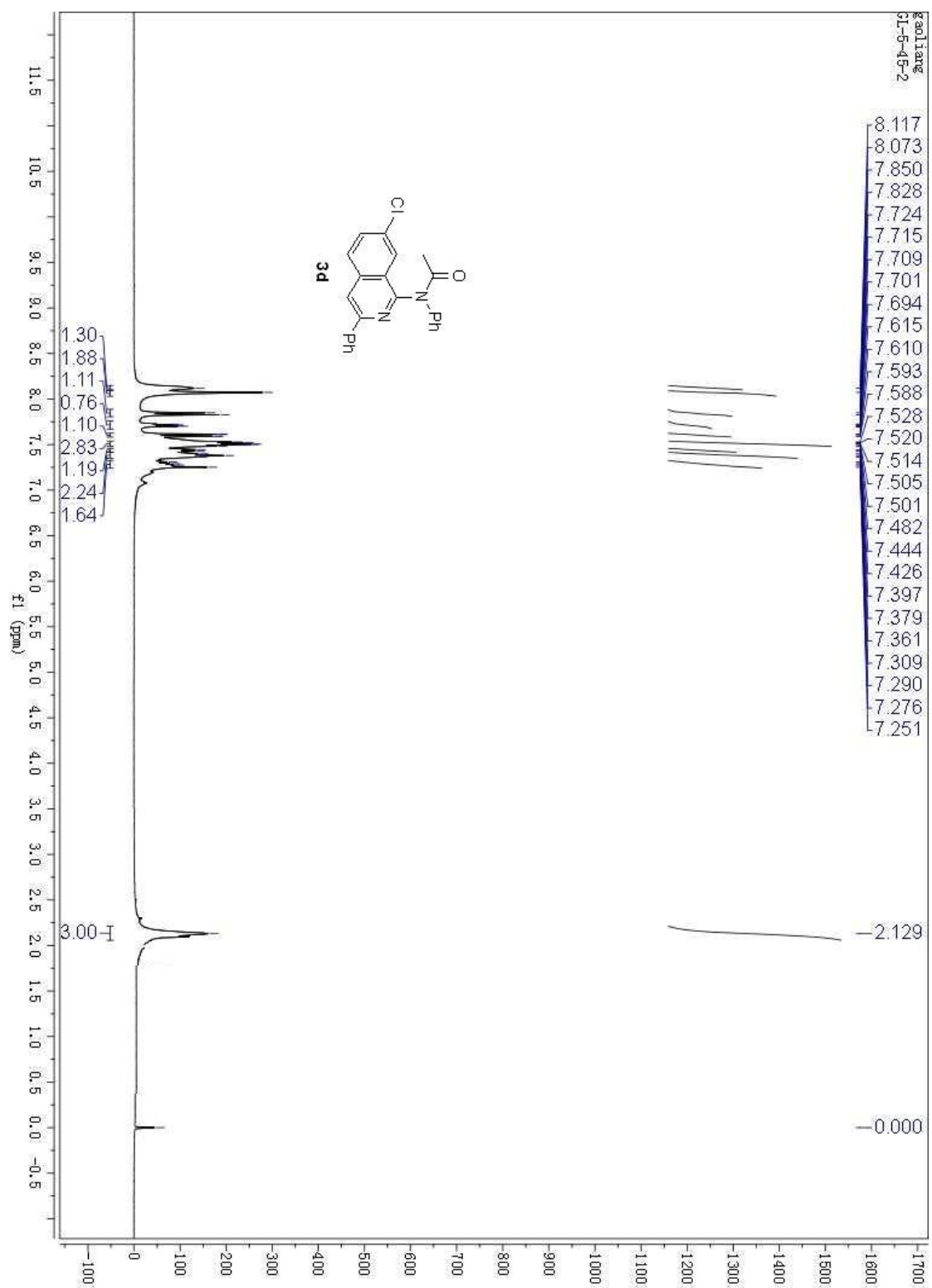


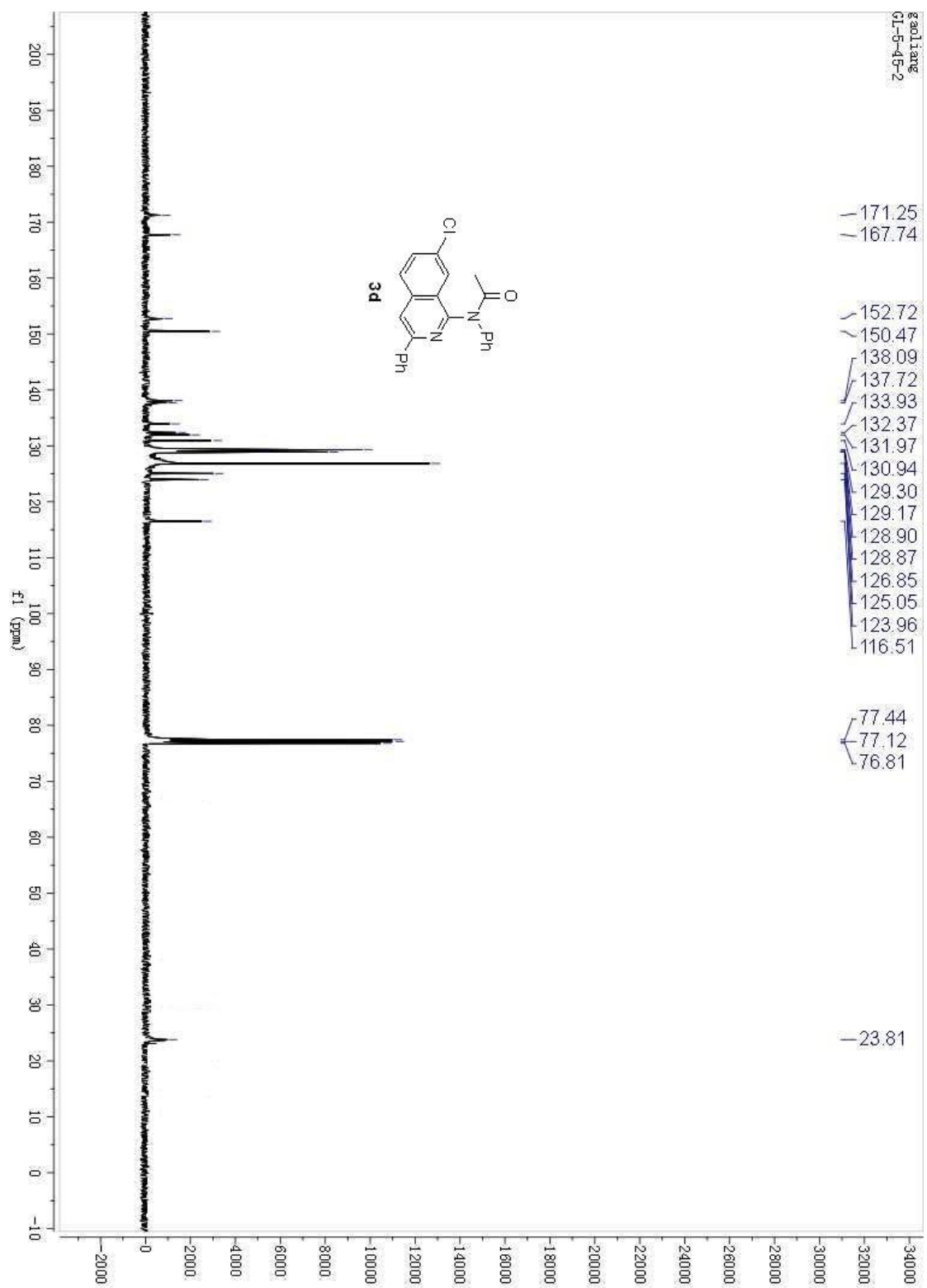


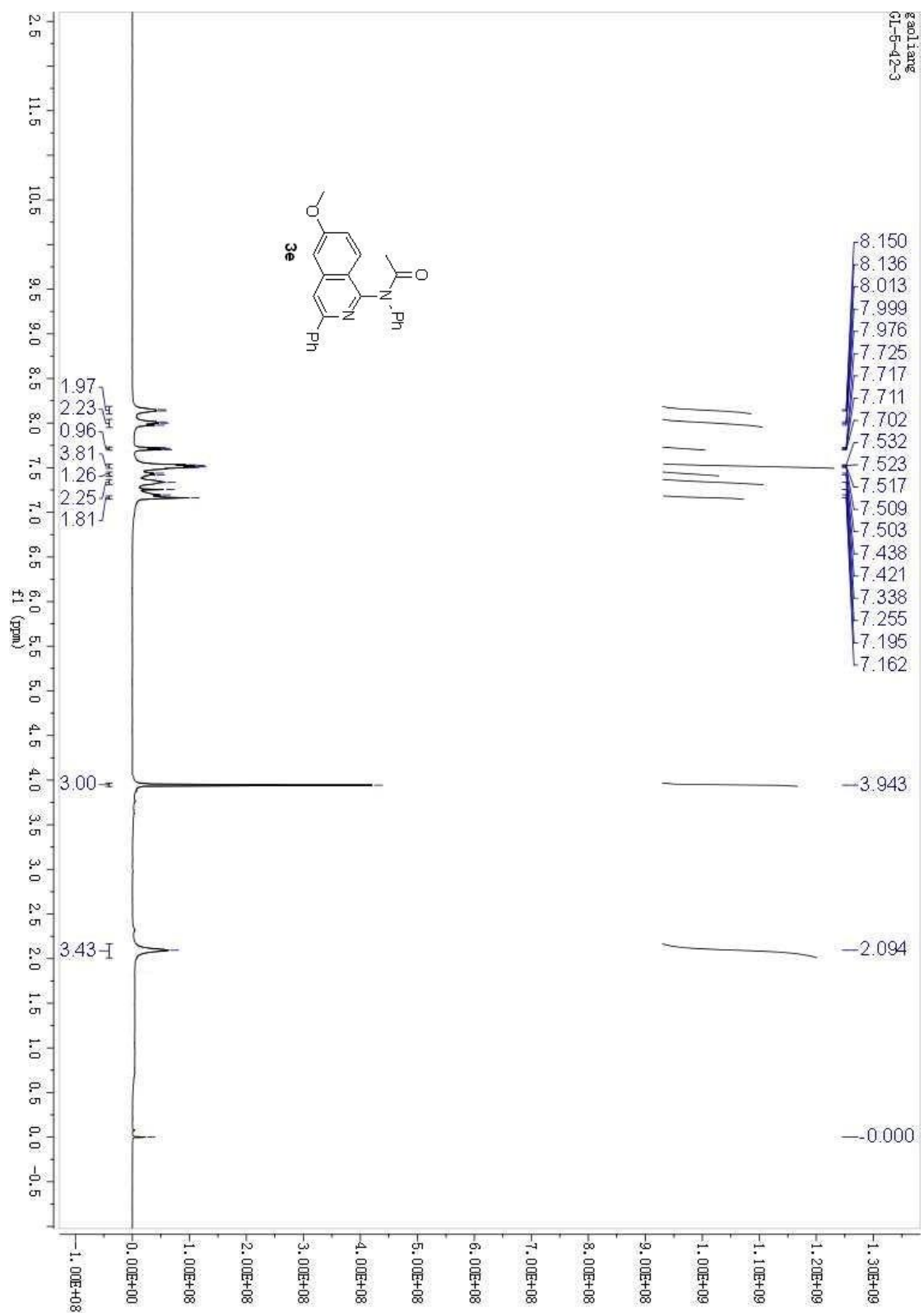


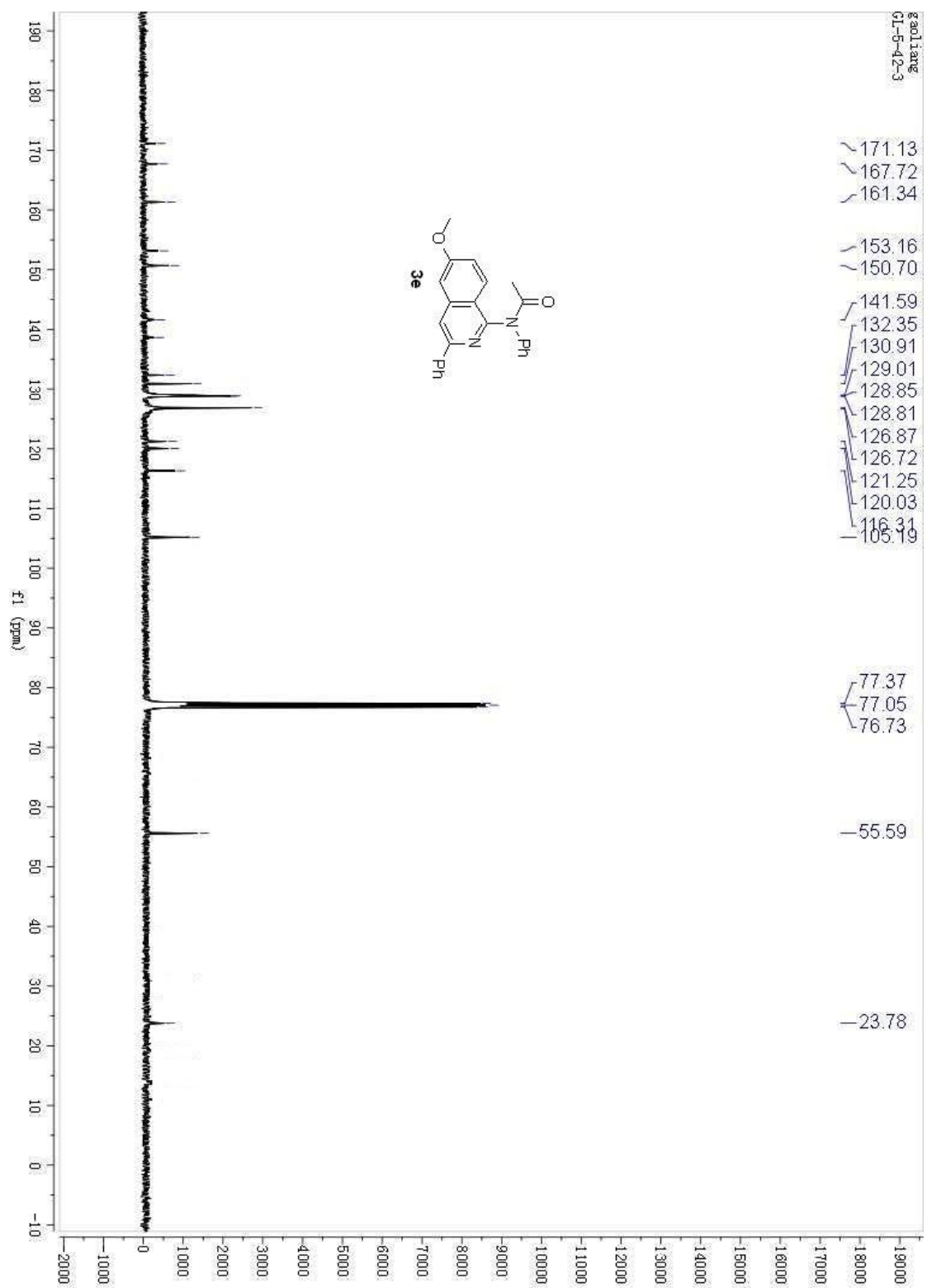
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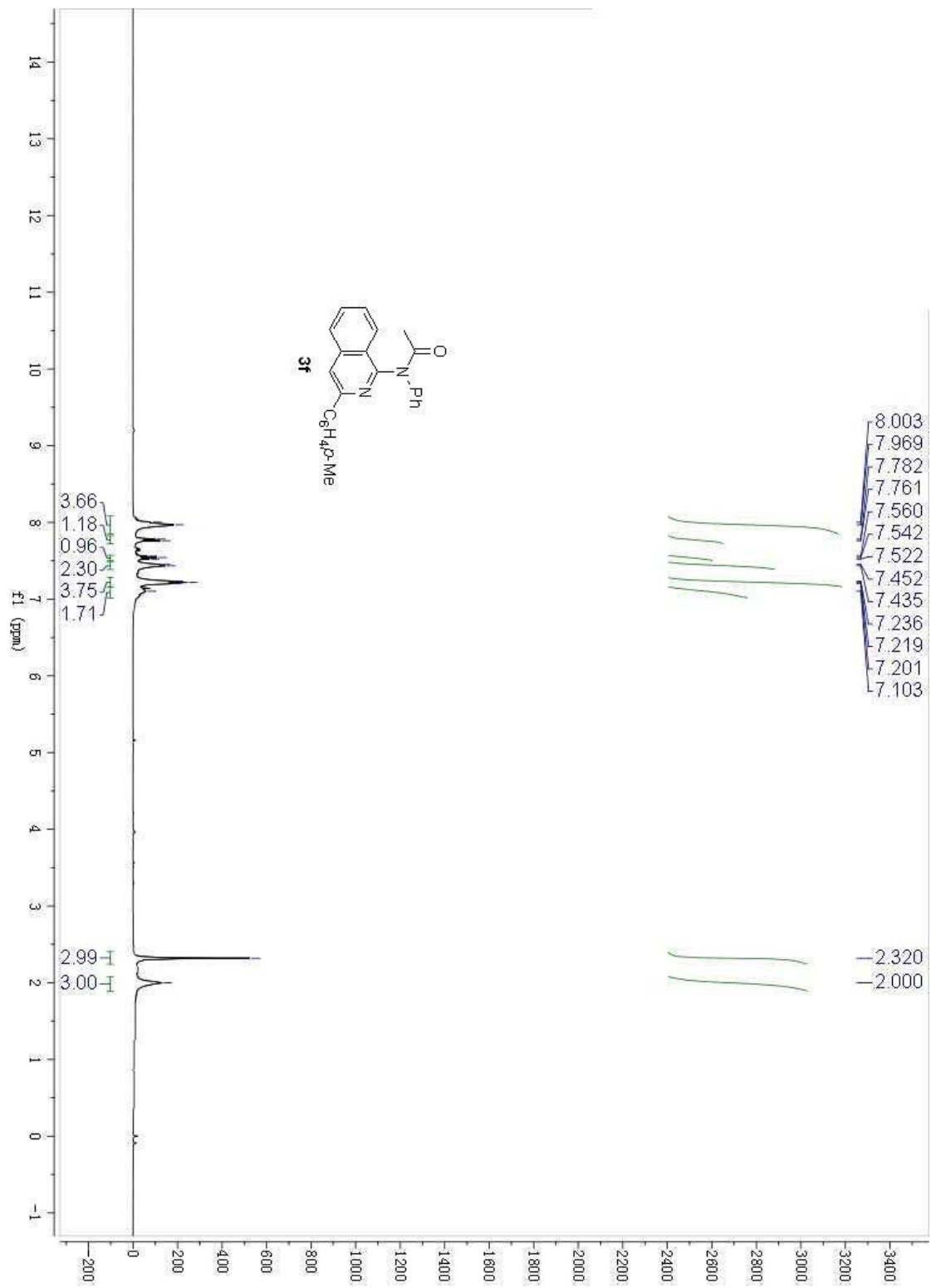


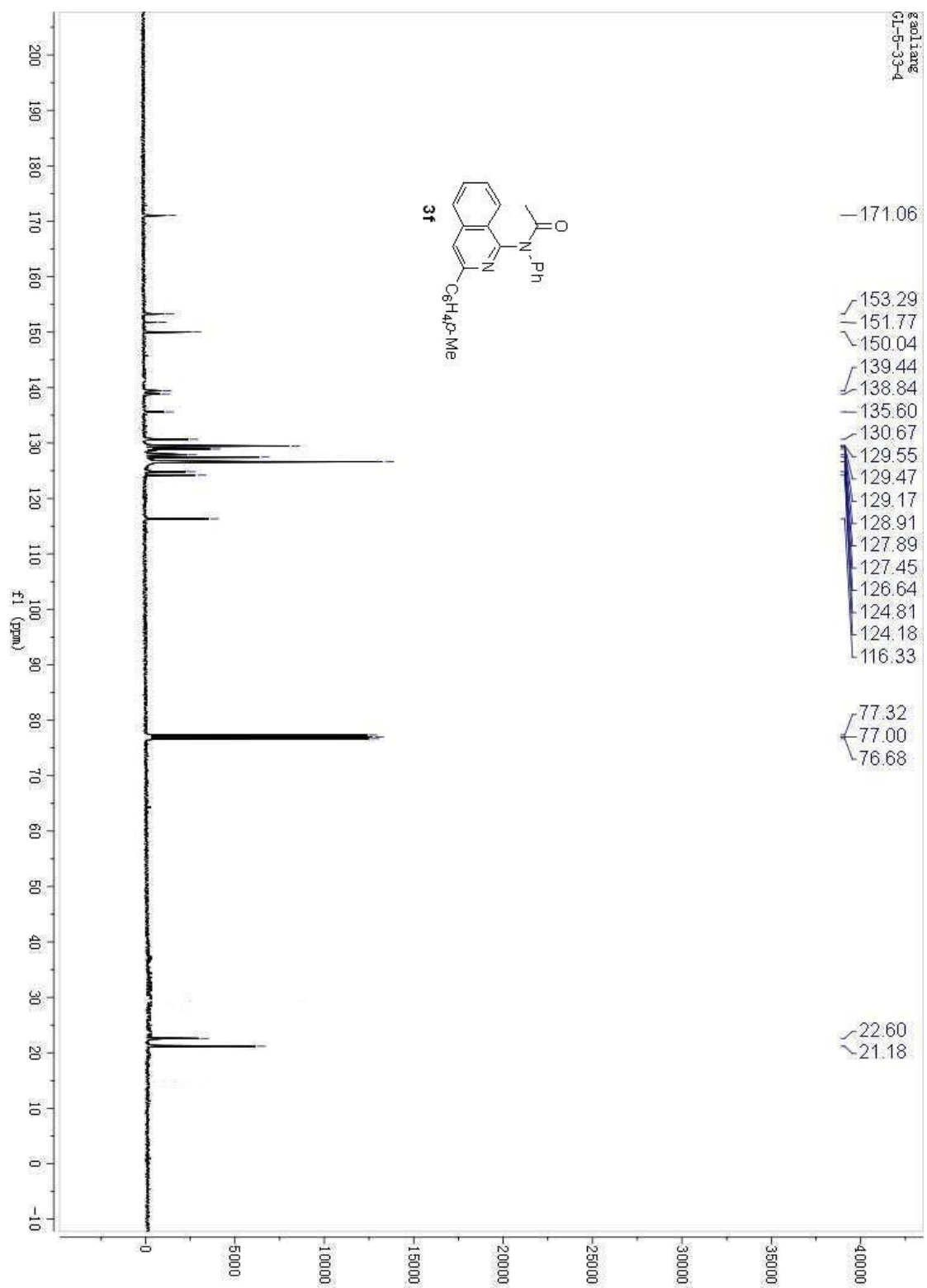




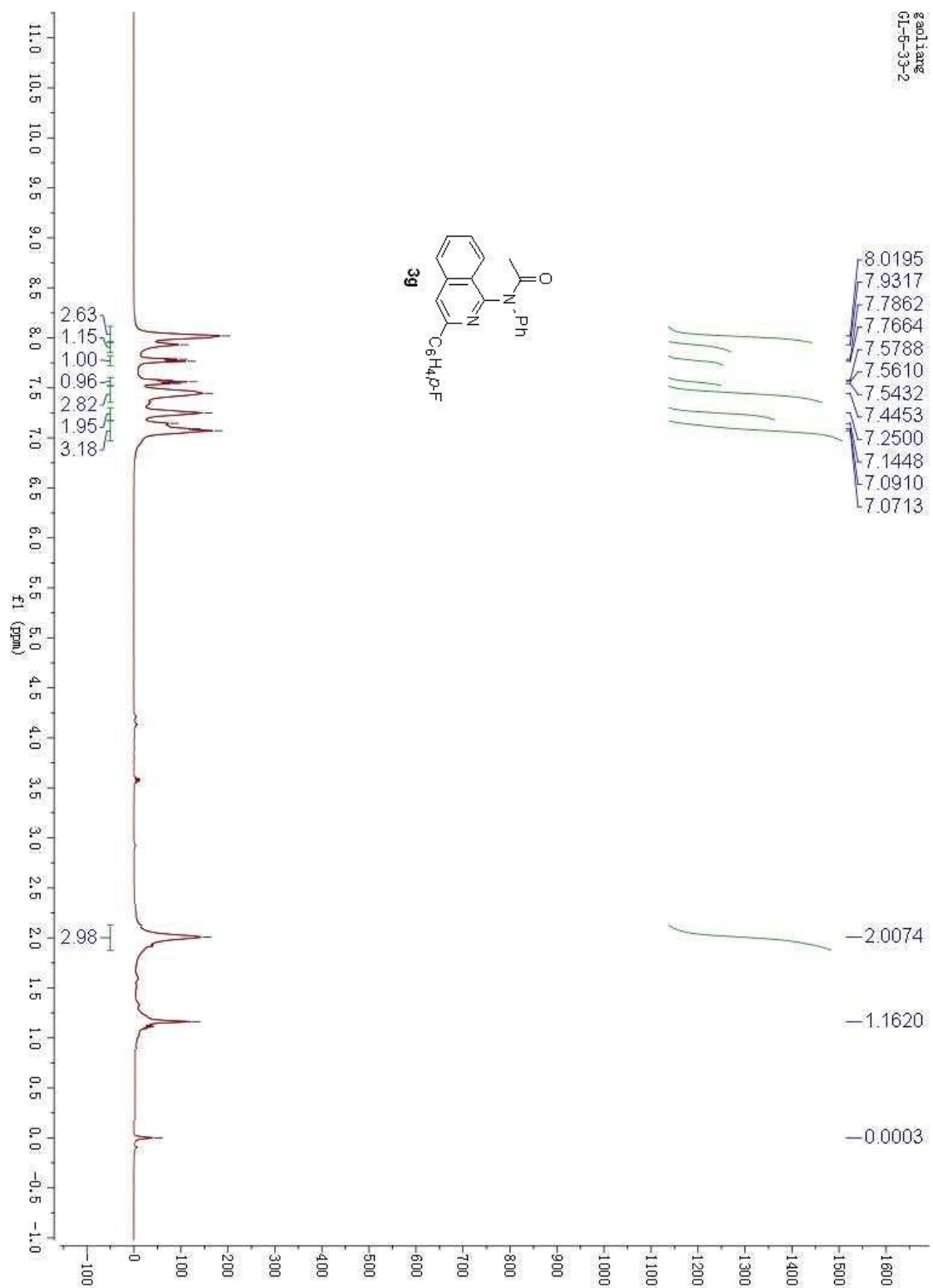




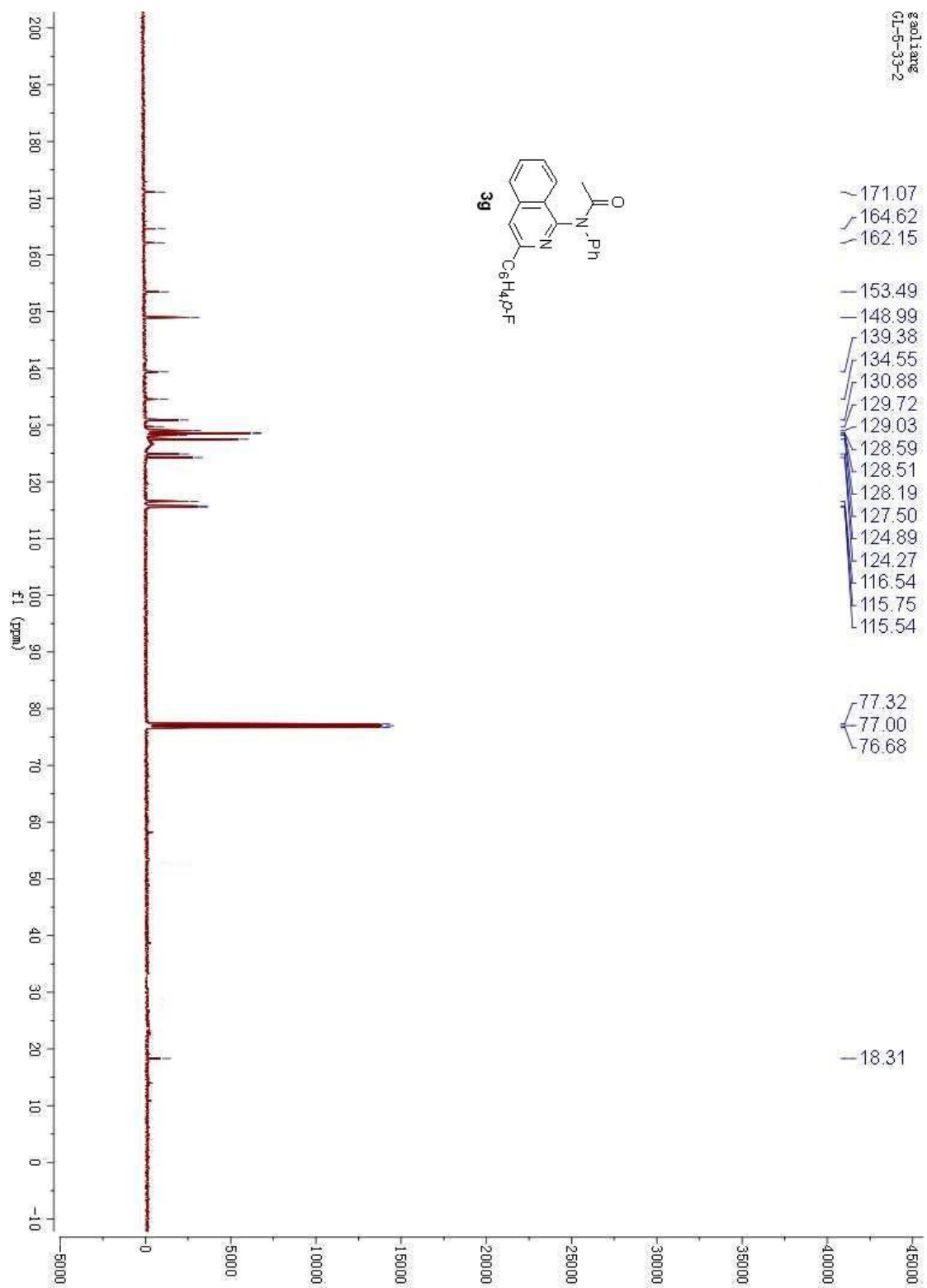




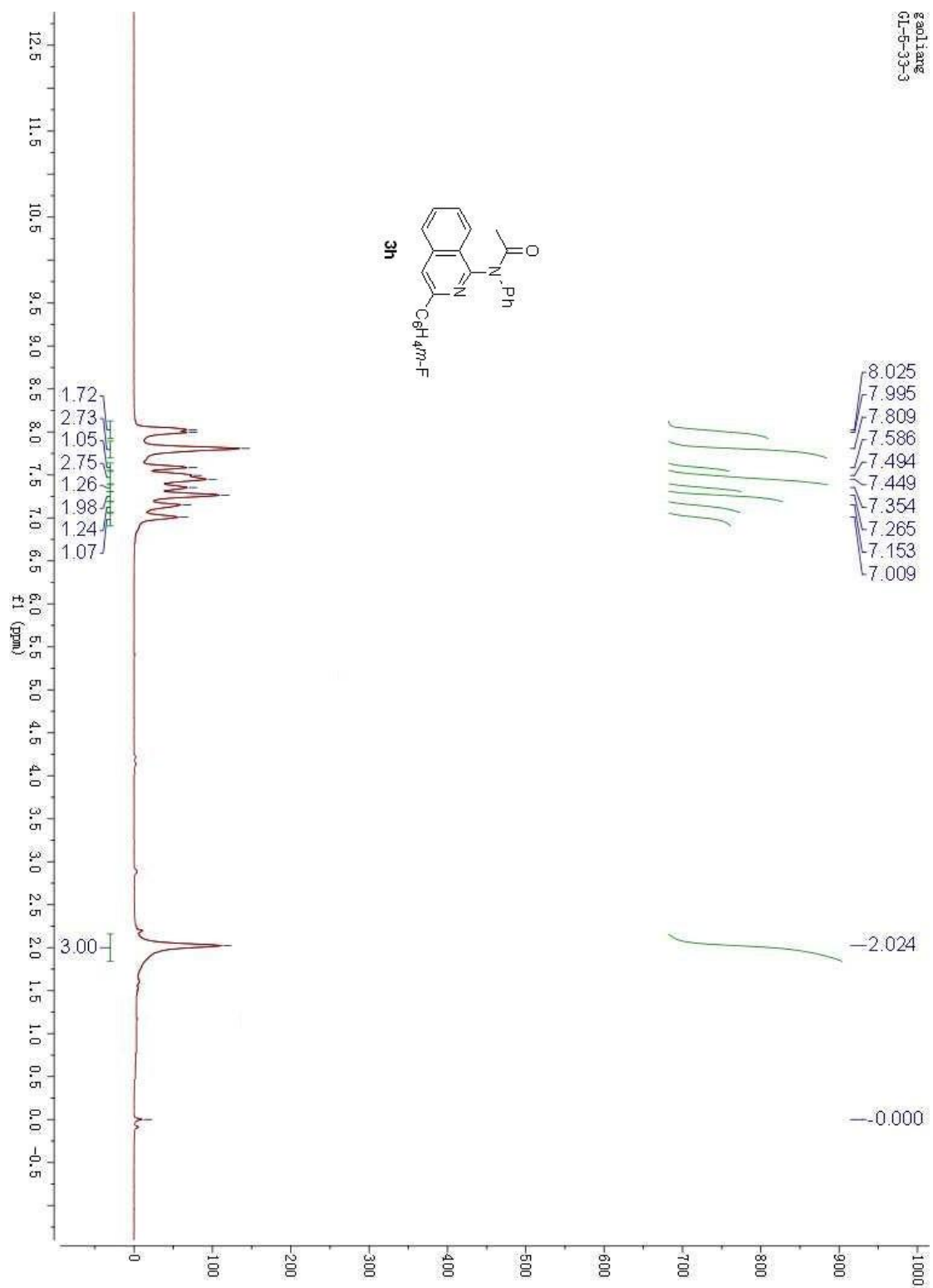
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