

Asymmetric [4+2]-Cycloaddition of Copper-Allenylidenes with Hexahydro-1,3,5-Triazines: Access to Chiral Tetrahydroquinazolines

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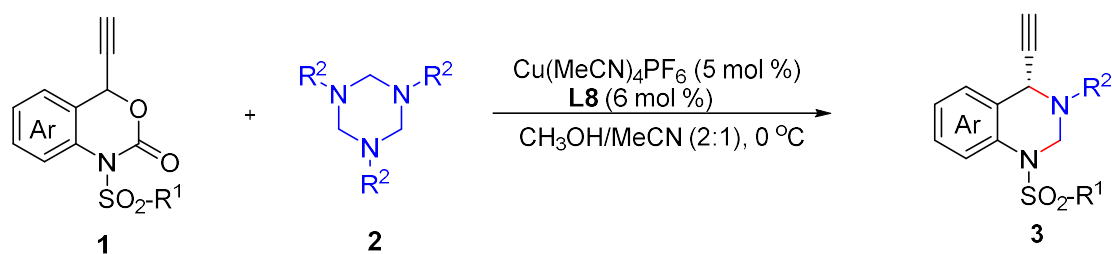
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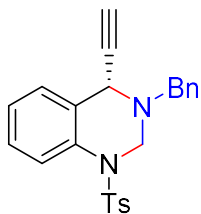
General information

All of the reactions were carried out in flame-dried tubes under argon atmosphere. Solvents were dried prior to use. For column chromatography, 200-300 mesh silica gel was used. ^1H NMR were recorded on Bruker 300 MHz, 400 MHz or 500 MHz spectrometer and ^{13}C NMR were recorded on Bruker 75 MHz, 100 MHz or 125 MHz spectrometer in CDCl_3 . HRMS were performed on Agilent 6540 Q-TOF mass spectrometer (ESI). Enantiomeric excesses (ee) values were determined by chiral HPLC analysis on Daicel Chiralpak IC, ID and IE column. Optical rotations were determined on a Rudolph Autopol IV polarimeter and reported as follows: $[\alpha]_{\text{D}}^{\text{T}}$ (c: g/100 mL, in solvent). The chiral ligands were purchased from Daicel Chiral Technologies (China) Co., Ltd. Melting points were determined on a SGW X-4B melting point apparatus. Ethynylbenzoxazinanes¹ and 1,3,5-hexahydro-1,3,5-triazines² were prepared according to the literature procedures.

General procedure of Scheme 2 for synthesis 3

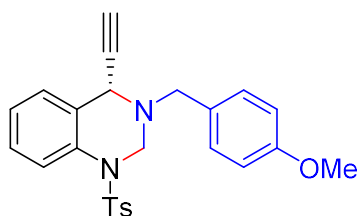


To a tube was added Cu(MeCN)₄PF₆ (3.7 mg, 5 mol %), **L8** (4.7 mg, 6 mol %) and MeOH/MeCN (2:1, 0.5 mL) under argon atmosphere, the resulting solution stirred at rt for 1 h. The reaction was cooled to 0 °C and added a solution of **1** (0.2 mmol) and **2** (0.07 mmol) in MeOH/MeCN (2:1, 1.5 mL). The reaction was stirred at 0 °C for 24 h. The reaction mixture was concentrated under vacuum, and the residue was purified by column chromatography (silica gel, eluted with EtOAc: Petroleum ether = 1:40-1:10) to give **3**.



***(S)*-3-benzyl-4-ethynyl-1-tosyl-1,2,3,4-tetrahydroquinazoline (3a):**

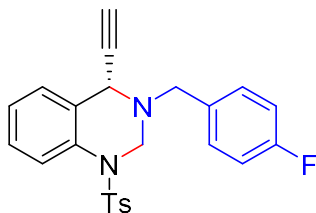
This compound was prepared via general procedure as a white solid (61.9 mg, yield: 77%); mp: 160-161 °C. 92% ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 80/20, flow rate 1.0 mL/min, λ = 254 nm, t_R = 10.11 min (major) and 11.09 min (minor). $[\alpha]_D^{20}$ = -4.0 (c = 0.10 in CH_2Cl_2). ^1H NMR (500 MHz, CDCl_3) δ 7.89 (d, J = 5.0 Hz, 1H), 7.50 (d, J = 10.0 Hz, 2H), 7.27 (s, 1H), 7.26-7.24 (m, 3H), 7.17 (d, J = 10.0 Hz, 2H), 7.12-7.06 (m, 2H), 7.01-7.00 (m, 2H), 4.93 (d, J = 15.0 Hz, 1H), 4.50 (d, J = 15.0 Hz, 1H), 4.25 (s, 1H), 3.73 (s, 2H), 2.41-2.40 (m, 4H). ^{13}C NMR (125 MHz, CDCl_3) δ 143.49, 136.71, 136.14, 134.88, 129.37, 129.18, 128.34, 128.31, 128.00, 127.66, 127.59, 126.81, 125.19, 123.90, 80.32, 75.19, 63.62, 55.31, 51.01, 21.56. HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{23}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$: 403.1475, found: 403.1473.



***(S)*-4-ethynyl-3-(4-methoxybenzyl)-1-tosyl-1,2,3,4-tetrahydroquinazoline (3b):**

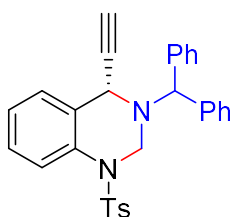
This compound was prepared via general procedure as a white solid (60.5 mg, yield: 70%); mp: 160-161 °C. 84% ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 85/15, flow rate 1.0 mL/min, λ = 254 nm, t_R = 16.33 min (major) and 17.94 min (minor). $[\alpha]_D^{20}$ = -6.0 (c = 0.10 in CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3) δ 7.87 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 1H), 7.17 (d, J = 8.0 Hz, 2H), 7.13-7.05 (m, 2H), 6.94 (d, J = 8.0 Hz, 2H), 6.79 (d, J = 8.0 Hz, 2H), 4.91 (d, J = 12.0 Hz, 1H), 4.48 (d, J = 12.0 Hz, 1H), 4.23 (s, 1H), 3.80 (s, 3H), 3.66 (s, 2H), 2.39 (s, 4H). ^{13}C NMR (125 MHz, CDCl_3) δ 159.06, 143.46, 136.70, 134.92, 130.39, 129.34, 128.34, 128.09, 127.96, 127.68, 126.87, 125.17, 123.87, 113.65, 80.43, 75.10,

63.52, 55.26, 54.68, 50.90, 21.57. HRMS (ESI) calcd. for C₂₅H₂₅N₂O₃S [M+H]⁺: 433.1580, found: 433.1583.



***(S)*-4-ethynyl-3-(4-fluorobenzyl)-1-tosyl-1,2,3,4-tetrahydroquinazoline (3c):**

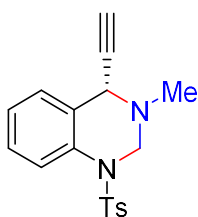
This compound was prepared via general procedure as a white solid (67.2 mg, yield: 80%); mp: 129-130 °C. 90% ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 85/15, flow rate 1.0 mL/min, λ = 254 nm, t_R = 9.61 min (major) and 10.86 min (minor). $[\alpha]_D^{20}$ = -26.7 (c = 0.1 in CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 7.87 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 8.0 Hz, 2H), 7.28-7.24 (m, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.13-7.07 (m, 2H), 6.99-6.91 (m, 4H), 4.91 (d, J = 12.0 Hz, 1H), 4.48 (d, J = 12.0 Hz, 1H), 4.21 (s, 1H), 3.73-3.65 (m, 2H), 2.41 (d, J = 4.0 Hz, 1H), 2.40 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 143.6, 136.8 (d, J = 193 Hz), 130.7 (d, J = 8.0 Hz), 129.4, 129.3, 129.1, 128.6, 128.4, 128.1, 127.6, 126.6, 125.3, 123.8 (d, J = 18.0 Hz), 115.2 (d, J = 21.0 Hz), 80.21, 75.32, 63.51, 54.53, 50.98, 21.59. HRMS (ESI) calcd. for C₂₄H₂₂FN₂O₂S [M+H]⁺: 421.1381, found: 421.1380.



***(S)*-3-benzhydryl-4-ethynyl-1-tosyl-1,2,3,4-tetrahydroquinazoline (3d):**

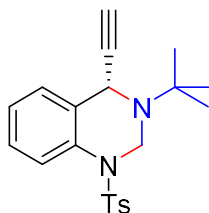
This compound was prepared via general procedure as a white solid (67.9 mg, yield: 71%); mp: 142-144 °C. 74% ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 85/15, flow rate 1.0 mL/min, λ = 254 nm, t_R = 12.06 min (major) and 14.14 min (minor). $[\alpha]_D^{20}$ = -30.0 (c = 0.1 in CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 7.81 (d, J = 8.0 Hz, 1H), 7.56 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 4.0 Hz, 4H), 7.26-7.20

(m, 8H), 7.07-6.99 (m, 3H), 4.93 (d, $J = 12.0$ Hz, 1H), 4.86 (s, 1H), 4.57 (s, 1H), 4.44 (d, $J = 12.0$ Hz, 1H), 2.45 (d, $J = 4.0$ Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 143.59, 140.72, 140.12, 136.99, 135.17, 129.39, 128.83, 128.67, 128.63, 128.45, 128.23, 128.18, 128.03, 127.96, 127.54, 125.53, 124.39, 121.74, 81.12, 75.72, 68.96, 60.97, 51.50, 21.61. HRMS (ESI) calcd. for $\text{C}_{30}\text{H}_{27}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$: 479.1788, found: 479.1792.



***(S)*-4-ethynyl-3-methyl-1-tosyl-1,2,3,4-tetrahydroquinazoline (3e):**

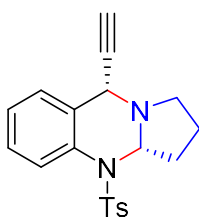
This compound was prepared via general procedure as a white solid (53.48 mg, yield: 82%); mp: 113-114 °C. 86% ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/*i*-PrOH = 80/20, flow rate 1.0 mL/min, $\lambda = 254$ nm, $t_R = 10.34$ min (major) and 12.23 min (minor). $[\alpha]_D^{20} = -10.0$ ($c = 0.1$ in CH_2Cl_2). ^1H NMR (300 MHz, CDCl_3) δ 7.77-7.75 (m, 1H), 7.53 (d, $J = 9.0$ Hz, 2H), 7.24-7.17 (m, 2H), 7.14-7.12 (m, 3H), 4.66 (d, $J = 12.0$ Hz, 1H), 4.48 (d, $J = 12.0$ Hz, 1H), 4.32 (d, $J = 3.0$ Hz, 1H), 2.38 (s, 3H), 2.34 (s, 3H), 2.33 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 143.45, 136.24, 134.80, 129.03, 128.12, 127.90, 127.76, 126.81, 125.23, 123.82, 74.04, 65.05, 54.35, 38.94, 29.71, 21.53. HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{19}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$: 327.1162, found: 327.1165.



***(S)*-3-(tert-butyl)-4-ethynyl-1-tosyl-1,2,3,4-tetrahydroquinazoline (3f):**

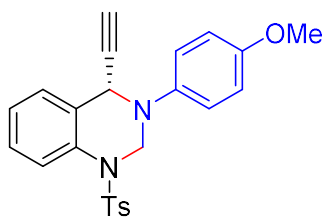
This compound was prepared via general procedure as a white solid (62.6 mg, yield: 85%), mp: 93-95 °C. 98% ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/*i*-PrOH = 80/20, flow rate 1.0 mL/min, $\lambda = 254$ nm, $t_R = 8.07$ min (major) and 9.58 min (minor). $[\alpha]_D^{20} = +72.0$ ($c = 0.1$ in CH_2Cl_2). ^1H NMR (300 MHz, CDCl_3) δ

7.70 (dd, $J = 9.0, 3.0$ Hz, 1H), 7.64 (d, $J = 12.0$, 2H), 7.20-7.12 (m, 4H), 7.05-7.00 (m, 1H), 5.42 (dd, $J = 12.0, 3.0$ Hz, 1H), 4.86 (s, 1H), 4.52 (d, $J = 12.0$ Hz, 1H), 2.41 (d, $J = 3.0$ Hz, 1H), 2.34 (s, 3H), 1.26 (s, 9H). ^{13}C NMR (125 MHz, CDCl_3) δ 143.48, 136.74, 135.56, 129.28, 128.18, 127.75, 127.50, 127.24, 124.06, 121.07, 84.72, 74.58, 59.50, 54.87, 48.42, 27.63, 21.51. HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{25}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$: 369.1631, found: 369.1628.



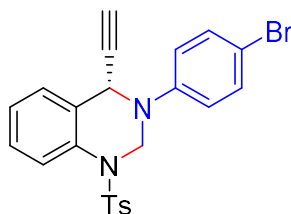
(3aS,9S)-9-ethynyl-4-tosyl-1,2,3,3a,4,9-hexahydropyrrolo[2,1-b]quinazoline (3g):

This compound was prepared via general procedure as a white solid (57.8 mg, yield: 65%), mp: 138-140 °C. 78% ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 95/5, flow rate 0.5 mL/min, $\lambda = 254$ nm, $t_R = 30.04$ min (minor) and 31.67 min (major). $[\alpha]_D^{20} = +83.3$ ($c = 0.1$ in CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3) δ 7.73 (d, $J = 8.0$ Hz, 1H), 7.50 (d, $J = 8.0$ Hz, 1H), 7.39-7.35 (m, 3H), 7.21 (t, $J = 8.0$ Hz, 1H), 7.16 (d, $J = 8.0$ Hz, 2H), 5.40-5.36 (m, 1H), 3.75 (s, 1H), 2.94-2.89 (m, 1H), 2.51 (d, $J = 4.0$ Hz, 1H), 2.46-2.41 (m, 1H), 2.37 (s, 3H), 2.32 (s, 1H), 2.19-2.07 (m, 2H), 1.72-1.65 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.86, 136.01, 134.87, 129.67, 129.26, 128.72, 126.99, 126.69, 126.46, 125.47, 78.00, 75.22, 48.47, 46.56, 35.28, 22.24, 21.80, 21.57. HRMS (ESI) calcd. for $\text{C}_{20}\text{H}_{21}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$: 353.1318, found: 353.1320.



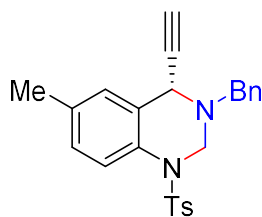
(S)-4-ethynyl-3-(4-methoxyphenyl)-1-tosyl-1,2,3,4-tetrahydroquinazoline (3h):

This compound was prepared via general procedure as a white solid (57.7 mg, yield: 69%); mp: 136-137 °C. 68% ee; determined by HPLC: Daicel Chiralpak IC column, n-hexane/i-PrOH = 90/10, flow rate 1 mL/min, λ = 254 nm, t_R = 28.34 min (minor) and 34.35 min (major). $[\alpha]_D^{20}$ = +40.0 (c = 0.1 in CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 7.87 (d, J = 12.0 Hz, 1H), 7.33-7.28 (m, 3H), 7.23-7.17 (m, 2H), 6.96 (d, J = 8.0 Hz, 2H), 6.89-6.83 (m, 4H), 5.62 (d, J = 12.0 Hz, 1H), 4.90 (s, 1H), 4.78 (d, J = 16.0 Hz, 1H), 3.81 (s, 3H), 2.28 (s, 3H), 2.26 (d, J = 4.0 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 154.79, 143.49, 139.78, 135.61, 135.12, 128.90, 128.12, 128.08, 127.85, 127.66, 125.94, 125.09, 119.43, 114.52, 81.44, 73.75, 61.61, 55.55, 51.53, 21.51. HRMS (ESI) calcd. for C₂₄H₂₃N₂O₃S [M+H]⁺: 419.1424, found: 419.1425.



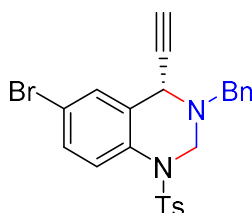
***(S)*-3-(4-bromophenyl)-4-ethynyl-1-tosyl-1,2,3,4-tetrahydroquinazoline (3i):**

This compound was prepared via general procedure as a white solid (71.8 mg, yield: 77%); mp: 167-169 °C. 80% ee; determined by HPLC: Daicel Chiralpak IC column, n-hexane/i-PrOH = 80/20, flow rate 1 mL/min, λ = 254 nm, t_R = 10.45 min (minor) and 13.62 min (major). $[\alpha]_D^{20}$ = +84.0 (c = 0.1 in CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 7.87 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 8.0 Hz, 2H), 7.36-7.28 (m, 2H), 7.25-7.20 (m, 3H), 6.90 (d, J = 8.0 Hz, 2H), 6.82 (d, J = 12.0 Hz, 2H), 5.80 (d, J = 12.0 Hz, 1H), 4.88 (s, 1H), 4.71 (d, J = 12.0 Hz, 1H), 2.28 (d, J = 4.0 Hz, 1H), 2.25 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 144.40, 143.73, 135.24, 135.13, 132.14, 128.91, 128.32, 128.08, 127.54, 127.22, 126.34, 125.43, 117.40, 112.99, 80.92, 73.61, 60.08, 49.35, 21.47. HRMS (ESI) calcd. for C₂₃H₂₀BrN₂O₂S [M+H]⁺: 467.0423, found: 467.0426.



***(S)*-3-benzyl-4-ethynyl-6-methyl-1-tosyl-1,2,3,4-tetrahydroquinazoline (3j):**

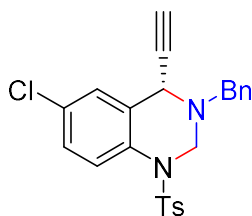
This compound was prepared via general procedure as a white solid (58.3 mg, yield: 70%); mp: 142-143 °C. 94% ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 85/15, flow rate 1 mL/min, λ = 254 nm, t_R = 13.56 min (major) and 14.77 min (minor). $[\alpha]_D^{20}$ = -25.0 (c = 0.1 in CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3) δ 7.77 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 8.0 Hz, 2H), 7.26-7.23 (m, 3H), 7.17 (d, J = 8.0 Hz, 2H), 7.06 (d, J = 8.0 Hz, 1H), 6.98-6.96 (m, 2H), 6.86 (s, 1H), 4.90 (d, J = 12.0 Hz, 1H), 4.47 (d, J = 12.0 Hz, 1H), 4.18 (s, 1H), 3.71 (s, 2H), 2.40 (s, 4H), 2.27 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 143.37, 136.77, 136.18, 135.01, 132.28, 129.36, 129.16, 128.89, 128.62, 128.27, 127.68, 127.55, 126.63, 123.93, 80.39, 75.05, 63.67, 55.29, 50.87, 21.58, 20.79. HRMS (ESI) calcd. for $\text{C}_{25}\text{H}_{25}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$: 417.1631, found: 417.1628.



***(S)*-3-benzyl-6-bromo-4-ethynyl-1-tosyl-1,2,3,4-tetrahydroquinazoline (3k):**

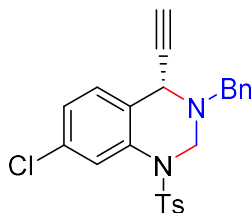
This compound was prepared via general procedure as a white solid (74.9 mg, yield: 78 %), mp: 105-106 °C. 93% ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 80/20, flow rate 1 mL/min, λ = 254 nm, t_R = 8.55 min (major) and 9.63 min (minor). $[\alpha]_D^{20}$ = -70.0 (c = 0.1 in CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3) δ 7.79 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 8.0 Hz, 2H), 7.36 (dd, J = 8.0, 4.0 Hz, 1H), 7.27 (s, 1H), 7.26-7.23 (m, 2H), 7.21-7.20 (m, 3H), 6.98-6.96 (m, 2H), 4.91 (d, J = 12.0 Hz, 1H), 4.46 (d, J = 12.0 Hz, 1H), 4.20 (s, 1H), 3.70 (s, 2H), 2.45 (d, J = 4.0 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 143.85, 136.31, 135.80, 134.07, 131.11, 129.56,

129.13, 128.75, 128.70, 128.39, 127.74, 127.65, 125.46, 118.29, 79.57, 75.89, 63.49, 55.21, 50.68, 21.61. HRMS (ESI) calcd. for $C_{24}H_{22}BrN_2O_2S$ $[M+H]^+$: 481.0580, found: 481.0582.



***(S)*-3-benzyl-6-chloro-4-ethynyl-1-tosyl-1,2,3,4-tetrahydroquinazoline (3l):**

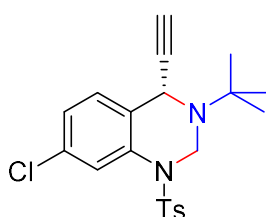
This compound was prepared via general procedure as a light yellow solid (68.0 mg, yield: 78 %); mp: 138-139 °C. 90% ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 80/20, flow rate 1 mL/min, λ = 254 nm, t_R = 8.29 min (major) and 9.27 min (minor). $[\alpha]_D^{20}$ = -365.0 (c = 0.1 in CH_2Cl_2). 1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 4.0 Hz, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.28-7.26 (m, 3H), 7.21 (d, J = 8.0 Hz, 2H), 7.07 (dd, J = 8.0, 4.0 Hz, 1H), 7.02-6.98 (m, 3H), 4.93 (d, J = 12.0 Hz, 1H), 4.47 (d, J = 12.0 Hz, 1H), 4.22 (s, 1H), 3.71 (d, J = 4.0 Hz, 2H), 2.43 (d, J = 4.0 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.90, 136.28, 135.96, 135.93, 133.60, 129.55, 129.39, 129.16, 128.39, 127.72, 127.68, 125.34, 125.08, 123.49, 79.87, 75.64, 63.41, 55.24, 50.71, 21.61. HRMS (ESI) calcd. for $C_{24}H_{22}ClN_2O_2S$ $[M+H]^+$: 437.1085, found: 437.1088.



***(S)*-3-benzyl-7-chloro-4-ethynyl-1-tosyl-1,2,3,4-tetrahydroquinazoline (3m):**

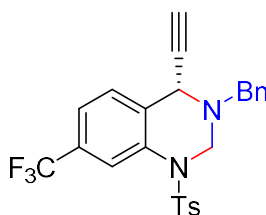
This compound was prepared via general procedure as a white solid (66.3 mg, yield: 76%); mp: 136-137 °C. 91% ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 85/15, flow rate 1 mL/min, λ = 254 nm, t_R = 11.31 min (major) and 12.40 min (minor). $[\alpha]_D^{20}$ = -15.0 (c = 0.1 in CH_2Cl_2). 1H NMR (400 MHz, $CDCl_3$) δ

7.94 (d, $J = 4.0$ Hz, 1H), 7.54 (d, $J = 8.0$ Hz, 2H), 7.28-7.26 (m, 3H), 7.21 (d, $J = 8.0$ Hz, 2H), 7.07 (dd, $J = 8.0, 4.0$ Hz, 1H), 7.02-6.98 (m, 3H), 4.93 (d, $J = 12.0$ Hz, 1H), 4.47 (d, $J = 12.0$ Hz, 1H), 4.22 (s, 1H), 3.71 (d, $J = 4.0$ Hz, 2H), 2.43 (d, $J = 4.0$ Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 143.90, 136.28, 135.96, 135.93, 133.60, 129.55, 129.39, 129.16, 128.39, 127.72, 127.68, 125.34, 125.09, 123.49, 79.87, 75.64, 63.41, 55.24, 50.71, 21.61. HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{22}\text{ClN}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$: 437.1085, found: 437.1086.



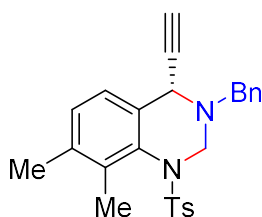
(S)-3-(tert-butyl)-7-chloro-4-ethynyl-1-tosyl-1,2,3,4-tetrahydroquinazoline (3n):

This compound was prepared via general procedure as a white solid (67.6 mg, yield: 84 %), mp: 140-141 °C. 91% ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 80/20, flow rate 1 mL/min, $\lambda = 254$ nm, $t_R = 6.69$ min (major) and 7.37 min (minor). $[\alpha]_D^{20} = +38.0$ ($c = 0.1$ in CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3) δ 7.76 (d, $J = 4.0$ Hz, 1H), 7.67 (d, $J = 8.0$ Hz, 2H), 7.21 (d, $J = 8.0$ Hz, 2H), 7.10 (d, $J = 8.0$ Hz, 1H), 6.99 (dd, $J = 8.0, 4.0$ Hz, 1H), 5.42 (dd, $J = 12.0, 4.0$ Hz, 1H), 4.83 (s, 1H), 4.48 (d, $J = 12.0$ Hz, 1H), 2.42 (d, $J = 4.0$ Hz, 1H), 2.37 (s, 3H), 1.25 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 143.90, 136.60, 136.21, 133.33, 129.48, 129.15, 127.50, 125.51, 124.12, 120.72, 84.17, 74.88, 59.41, 54.98, 48.07, 27.63, 21.57. HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{24}\text{ClN}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$: 403.1242, found: 403.1245.



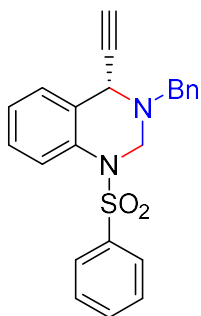
(S)-3-benzyl-4-ethynyl-1-tosyl-7-(trifluoromethyl)-1,2,3,4-tetrahydroquinazoline (3o):

This compound was prepared via general procedure as a white solid (76.2 mg, yield: 81 %), mp: 137-139 °C. 80% ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 90/10, flow rate 1 mL/min, λ = 254 nm, t_R = 8.23 min (major) and 9.27 min (minor). $[\alpha]_D^{20}$ = -28.0 (c = 0.1 in CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3) δ 8.20 (s, 1H), 7.52 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 1H), 7.32-7.28 (m, 3H), 7.21-7.18 (m, 3H), 7.05-7.02 (m, 2H), 4.98 (d, J = 12.0 Hz, 1H), 4.51 (d, J = 12.0 Hz, 1H), 4.30 (s, 1H), 3.74 (d, J = 4.0 Hz, 2H), 2.46 (d, J = 4.0 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 144.07, 136.07, 135.79, 135.46, 130.61, 130.18, 130.05, 129.57, 129.17, 129.05, 128.45, 127.81, 127.73, 121.81, 121.40, 120.69, 120.64, 100.00, 79.50, 76.07, 63.43, 55.25, 50.98, 21.61. HRMS (ESI) calcd. for $\text{C}_{25}\text{H}_{22}\text{F}_3\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$: 471.1349, found: 471.1355.



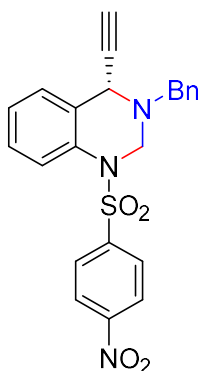
***(S)*-3-benzyl-4-ethynyl-7,8-dimethyl-1-tosyl-1,2,3,4-tetrahydroquinazoline (3p):**

This compound was prepared via general procedure as yellow oil (37 mg, yield: 43 %); 46% ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 80/20, flow rate 1 mL/min, λ = 254 nm, t_R = 8.91 min (major) and 9.48 min (minor). $[\alpha]_D^{20}$ = -35.0 (c = 0.1 in CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3) δ 7.26-7.24 (m, 6H), 7.12 (d, J = 8.0 Hz, 2H), 7.05 (d, J = 4.0 Hz, 1H), 6.84 (s, 2H), 4.82 (d, J = 12.0 Hz, 1H), 4.23 (d, J = 12.0 Hz, 1H), 4.05 (s, 1H), 3.60 (d, J = 12.0 Hz, 2H), 2.41 (d, J = 12.0 Hz, 6H), 2.38-2.36 (m, 1H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 143.00, 137.99, 137.55, 136.30, 135.90, 133.73, 129.52, 129.14, 128.34, 128.26, 128.14, 128.04, 127.37, 124.78, 80.14, 75.62, 64.59, 54.99, 50.39, 21.55, 20.49, 17.76. HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{27}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$: 431.1788, found: 431.1785.



***(S)*-3-benzyl-4-ethynyl-1-(phenylsulfonyl)-1,2,3,4-tetrahydroquinazoline (3q):**

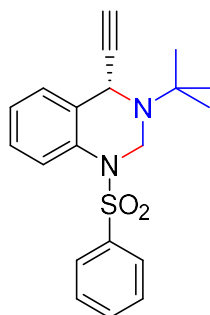
This compound was prepared via general procedure as a white solid (66.8 mg, yield: 86%); mp: 150-152 °C. 90 % ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 85/15, flow rate 1 mL/min, λ = 254 nm, t_R = 10.31 min (major) and 11.16 min (minor). $[\alpha]_D^{20}$ = -20.0 (c = 0.1 in CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3) δ 7.89 (d, J = 8.0 Hz, 1H), 7.61 (d, J = 8.0 Hz, 2H), 7.53 (t, J = 12.0 Hz, 1H), 7.37 (t, J = 16.0 Hz, 2H), 7.29-7.27 (m, 4H), 7.13-7.06 (m, 2H), 7.02-7.00 (m, 2H), 4.93 (d, J = 12.0 Hz, 1H), 4.52 (d, J = 12.0 Hz, 1H), 4.25 (s, 1H), 3.73 (s, 2H), 2.40 (d, J = 4.0 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 139.52, 136.05, 134.74, 132.66, 129.19, 128.77, 128.41, 128.37, 128.07, 127.67, 127.65, 126.92, 125.40, 123.95, 80.27, 75.27, 63.69, 55.36, 51.06. HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$: 389.1318, found: 389.1322.



***(S)*-3-benzyl-4-ethynyl-1-((4-nitrophenyl)sulfonyl)-1,2,3,4-tetrahydroquinazoline (3r):**

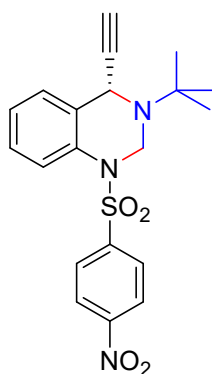
This compound was prepared via general procedure as a white solid (76.2 mg, yield: 88 %); mp: 105-106 °C. 96 % ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 85/15, flow rate 1 mL/min, λ = 254 nm, t_R = 10.83 min (major) and

11.62 min (minor). $[\alpha]_D^{20} = -14.0$ ($c = 0.1$ in CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3) δ 8.14 (d, $J = 8.0$ Hz, 2H), 7.87 (d, $J = 8.0$ Hz, 1H), 7.64 (d, $J = 8.0$ Hz, 2H), 7.33-7.27 (m, 4H), 7.20-7.19 (m, 1H), 7.13 (d, $J = 4.0$ Hz, 1H), 7.03-7.01 (m, 2H), 4.77 (d, $J = 12.0$ Hz, 1H), 4.57 (d, $J = 12.0$ Hz, 1H), 4.29 (s, 1H), 3.72 (q, $J = 12.0$ Hz, 2H), 2.40 (d, $J = 4.0$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 149.98, 144.73, 135.40, 133.99, 129.29, 129.07, 128.68, 128.55, 128.33, 128.05, 127.63, 126.42, 124.55, 123.72, 80.01, 75.25, 63.72, 55.59, 51.68. HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{20}\text{N}_3\text{O}_4\text{S}$ $[\text{M}+\text{H}]^+$: 434.1169, found: 434.1170.



(S)-3-(tert-butyl)-4-ethynyl-1-(phenylsulfonyl)-1,2,3,4-tetrahydroquinazoline (3s):

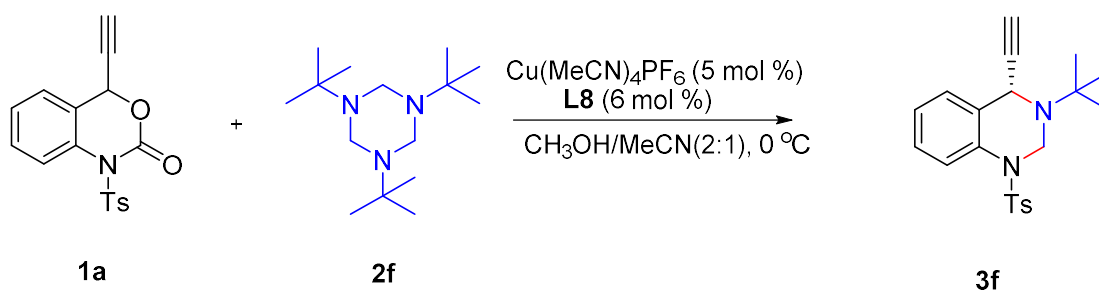
This compound was prepared via general procedure as a white solid (55.9 mg, yield: 79 %); mp: 103-104 °C. 92 % ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 80/20, flow rate 1 mL/min, $\lambda = 254$ nm, $t_R = 6.93$ min (major) and 7.98 min (minor). $[\alpha]_D^{20} = +24.0$ ($c = 0.1$ in CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3) δ 7.76-7.71 (m, 3H), 7.49-7.45 (m, 1H), 7.39-7.35 (m, 2H), 7.20-7.13 (m, 2H), 7.06-7.03 (m, 1H), 5.40 (dd, $J = 12.0, 4.0$ Hz, 1H), 4.86 (s, 1H), 4.52 (d, $J = 12.0$ Hz, 1H), 2.41 (d, $J = 4.0$ Hz, 1H), 1.25 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 149.95, 145.07, 134.47, 129.02, 128.68, 128.31, 128.12, 125.53, 123.66, 122.23, 84.18, 75.39, 59.67, 54.82, 48.59, 27.44. HRMS (ESI) calcd. for $\text{C}_{20}\text{H}_{23}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$: 355.1475, found: 355.1472.



***(S)*-3-(tert-butyl)-4-ethynyl-1-((4-nitrophenyl)sulfonyl)-1,2,3,4-tetrahydroquinazoline (**3t**):**

This compound was prepared via general procedure as a white solid (65.5 mg, yield: 82 %), mp: 115-116 °C. 78 % ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 80/20, flow rate 1 mL/min, λ = 254 nm, t_R = 7.81 min (major) and 8.95 min (minor). $[\alpha]_D^{20}$ = +34.0 (c = 0.1 in CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3) δ 8.18-8.16 (m, 2H), 7.90-7.88 (m, 2H), 7.77-7.75 (m, 1H), 7.24-7.20 (m, 2H), 7.14-7.10 (m, 1H), 5.31-5.27 (m, 1H), 4.82 (s, 1H), 4.53 (d, J = 12.0 Hz, 1H), 2.40 (d, J = 4.0 Hz, 1H), 1.25 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 139.66, 135.44, 132.70, 128.64, 128.20, 127.81, 127.48, 127.40, 124.28, 121.31, 84.63, 74.68, 59.52, 54.85, 48.40, 27.59. HRMS (ESI) calcd. for $\text{C}_{20}\text{H}_{22}\text{N}_3\text{O}_4\text{S}$ $[\text{M}+\text{H}]^+$: 400.1326, found: 400.1325.

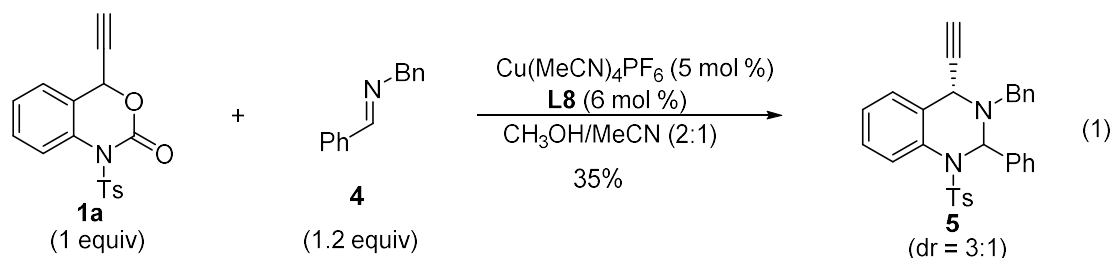
Large scale reaction



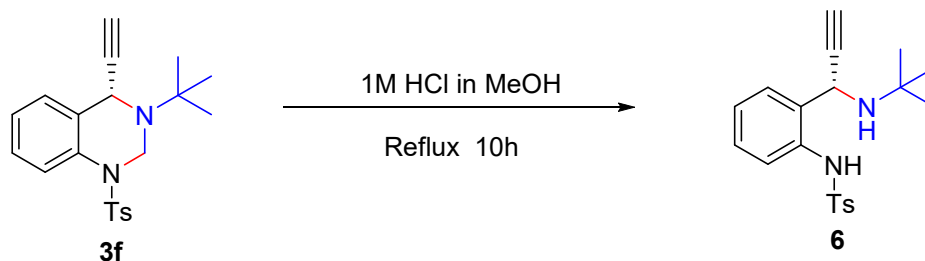
To a tube was added $\text{Cu}(\text{MeCN})_4\text{PF}_6$ (19 mg, 5 mol %), **L8** (24 mg, 6 mol %) and MeOH/MeCN (2:1, 5 mL) under argon atmosphere, the resulting solution stirred at rt for 1 h. The reaction was cooled to 0 °C and added a solution of **1a** (328 mg, 1 mmol) and **2f** (87 mg, 0.34 mmol) in MeOH/MeCN (2:1, 1.5 mL) quickly. The reaction was stirred at 0 °C for 24 h. The reaction mixture was concentrated under vacuum, the

residue was purified by column chromatography (silica gel, eluted with EtOAc: Petroleum ether = 1:40-1:10) to give **3f** (295 mg, Yield: 80 %, 95 % ee).

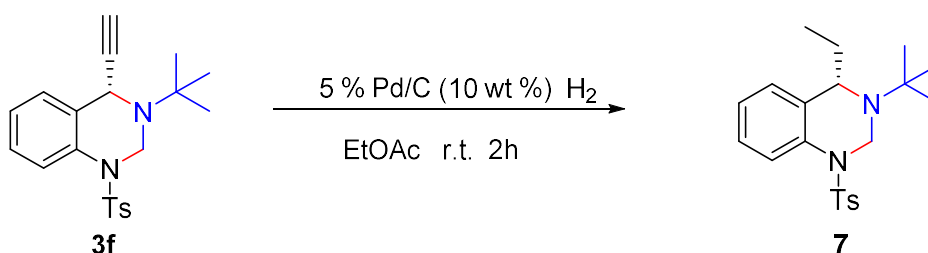
Further Exploration for Scheme 3



To a tube was added $\text{Cu}(\text{MeCN})_4\text{PF}_6$ (3.7 mg, 5 mol %), **L8** (4.7 mg, 6 mol %) and MeOH/MeCN (2:1, 2 mL) under argon atmosphere, the resulting solution stirred at rt for 1 h. The reaction was cooled to 0 °C and added a solution of **1a** (66 mg, 0.2 mmol) and **4** (115 mg, 0.24 mmol) in MeOH/MeCN (2:1, 3 mL) quickly. The reaction was stirred at 0 °C for 24 h. The reaction mixture was concentrated under vacuum, the residue was purified by column chromatography (silica gel, eluted with EtOAc: Petroleum ether = 1:40-1:10) to give **5** (unstable, a mixture of two isomers.) as a white solid (33 mg, 35 % yield, dr = 3:1). ^1H NMR (300 MHz, CDCl_3) δ 7.77 (dd, J = 9.0, 3.0 Hz, 1H), 7.68 (d, J = 9.0 Hz, 2H), 7.64-7.59 (m, 1H), 7.50-7.48 (m, 2H), 7.41-7.37 (m, 4H), 7.31-7.27 (m, 4H), 7.23-7.21 (m, 2H), 7.16-7.13 (m, 1H), 7.04-7.01 (m, 1H), 6.35 (s, 1H), 4.90 (d, J = 3.0 Hz, 1H), 4.36 (d, J = 12.0 Hz, 1H), 3.55 (d, J = 15.0 Hz, 1H), 2.42 (d, J = 3.0 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 144.04, 139.34, 138.30, 137.25, 135.27, 129.56, 129.17, 128.71, 128.63, 128.49, 128.33, 128.00, 127.77, 127.71, 127.40, 127.28, 123.23, 118.69, 80.58, 76.03, 75.22, 51.44, 49.21, 21.61.

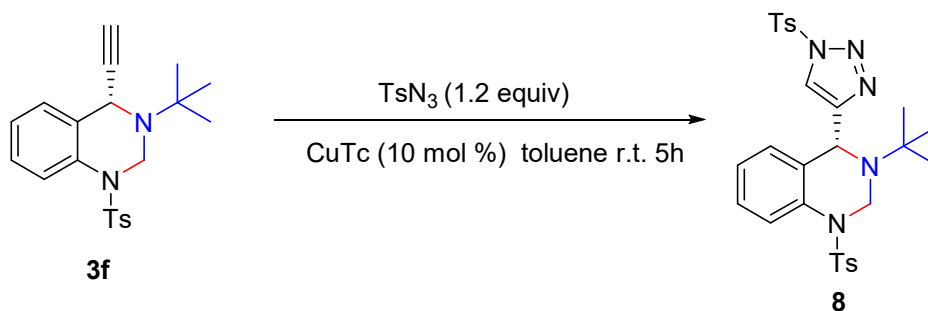


A solution of **3f** (0.2 mmol, 98% ee) in 1 M HCl/ MeOH (3 mL) was refluxed for 10 h. The reaction solution was cooled and added 1 M NaOH solution (20 mL), extracted three times with CH₂Cl₂. The combined organic phases were dried over Na₂SO₄ and the solvent was removed in vacuo and purified by column chromatography (EtOAc: Petroleum ether = 1:5) to afford **6** (51 mg, yield: 72 %) as a light yellow solid, mp: 131-132 °C. 94 % ee; determined by HPLC: Daicel Chiralpak IE column, n-hexane/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm, t_R = 78.55 min (minor) and 82.50 min (major). $[\alpha]_D^{20}$ = +26.0 (c = 0.1 in CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, J = 8.0 Hz, 2H), 7.49-7.43 (m, 2H), 7.22-7.19 (m, 3H), 7.00 (t, J = 12.0 Hz, 1H), 4.58 (s, 1H), 2.44 (s, 1H), 2.36 (s, 3H), 1.24 (s, 9H). ¹³C NMR (75 MHz, CDCl₃) δ 143.39, 137.60, 137.37, 129.51, 128.99, 128.41, 127.09, 124.05, 123.70, 120.05, 83.19, 75.58, 52.56, 47.51, 29.51, 21.53. HRMS (ESI) calcd. for C₂₀H₂₅N₂O₂S [M+H]⁺: 357.1631, found: 357.1630.

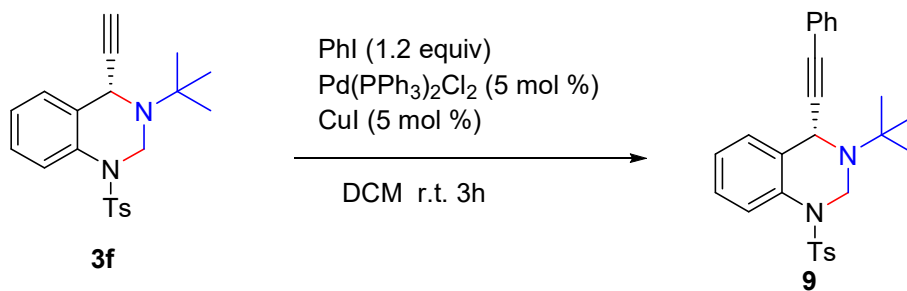


To a solution of **3f** (74 mg, 0.20 mmol, 98% ee) in EtOAc (5.0 mL) under argon was added 10% Pd/C (14 mg, 5 mol %). The reaction mixture was stirred under H₂ balloon at rt for 2 h. After the reaction was completed (monitored by TLC), the crude reaction mixture was filtrated with celite and washed with EtOAc. The solvents were removed under reduced pressure and purified by silica gel column chromatography (EtOAc: Petroleum ether = 1:20) to afford the desired product **7** (67 mg, yield: 90%) as yellow oil. 90 % ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 95/5, flow rate 1 mL/min, λ = 254 nm, t_R = 9.85 min (major) and 10.67 min (minor). $[\alpha]_D^{20}$ = +112.0 (c = 0.1 in CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 8.0 Hz, 1H), 7.26-7.25 (m, 2H), 7.05-7.01 (m, 2H), 6.92-6.89 (m, 1H), 5.58-5.55 (m, 1H), 4.52 (d, J = 12.0 Hz, 1H), 3.82-3.78 (m, 1H), 2.38 (s, 3H), 1.59-1.52

(m, 2H), 1.19 (s, 9H), 0.97 (t, $J = 12.0$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 143.53, 137.25, 136.63, 130.48, 129.77, 127.74, 126.81, 126.59, 122.26, 118.06, 59.85, 55.93, 54.77, 31.12, 28.44, 21.54, 11.50. HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{29}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$: 373.1944, found: 373.1947.



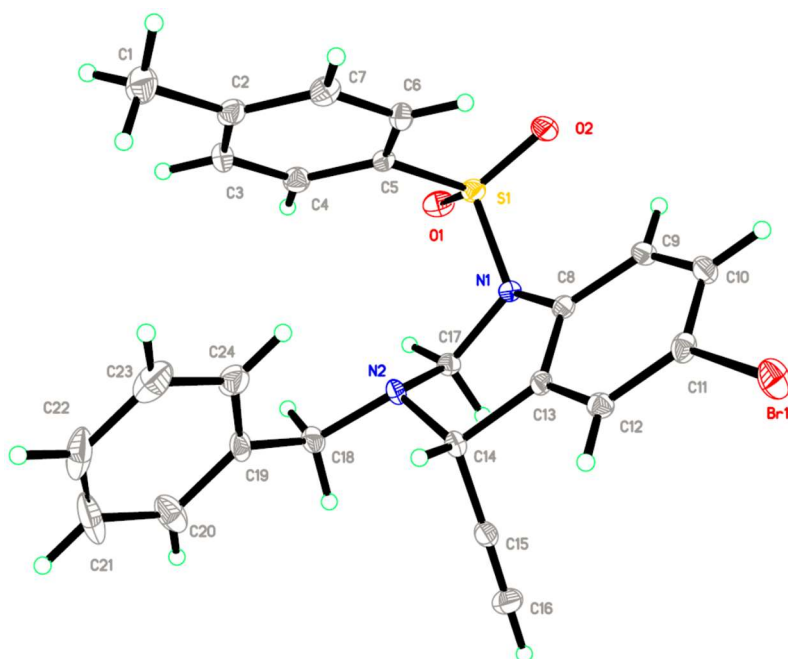
Under argon atmosphere, a flame-dried Schlenk tube was charged with **3f** (74 mg, 0.2 mmol, 98% ee), copper (I) thiophene-2-carboxylate (CuTc, 3.8 mg, 0.02 mmol, 10 mol%) and anhydrous toluene (3.0 mL). Subsequently, TsN_3 (47 mg, 0.24 mmol, 1.2 equiv) was added slowly, then the reaction mixture was stirred until completed (monitored by TLC). The reaction was quenched by saturated NH_4Cl aqueous solution (10 mL) and extracted with EtOAc (3×5 mL). The combined organic layers were dried over Na_2SO_4 , filtrated and concentrated under vacuum. Then the residue was purified by silica gel column chromatography (PE/EtOAc = 10/1) to afford the desired product **8** (101.0 mg, yield: 89%) as a white solid; mp: 70-71 °C. 97 % ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 50/50, flow rate 1 mL/min, $\lambda = 254$ nm, $t_R = 17.36$ min (major) and 23.82 min (minor). $[\alpha]_D^{20} = +82.0$ ($c = 0.1$ in CH_2Cl_2). ^1H NMR (300 MHz, CDCl_3) δ 7.96-7.93 (m, 2H), 7.69 (d, $J = 6.0$ Hz, 2H), 7.66-7.63 (m, 1H), 7.51 (d, $J = 3.0$ Hz, 1H), 7.38 (d, $J = 9.0$ Hz, 2H), 7.29-7.26 (m, 2H), 7.18-7.10 (m, 2H), 6.97-6.92 (m, 1H), 5.47-5.42 (m, 1H), 5.39 (s, 1H), 4.44 (d, $J = 15.0$ Hz, 1H), 2.45 (s, 3H), 2.41 (s, 3H), 1.25 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 151.79, 147.41, 144.08, 136.98, 136.93, 132.88, 130.42, 129.87, 128.94, 128.78, 127.80, 126.93, 125.34, 123.00, 121.60, 119.01, 60.43, 55.72, 51.47, 28.22, 21.89, 21.63. HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{32}\text{N}_5\text{O}_4\text{S}_2$ $[\text{M}+\text{H}]^+$: 566.1890, found: 566.1885.



Under argon atmosphere, a flame-dried Schlenk tube was charged with **3f** (74 mg, 0.20 mmol, 98% ee), iodobenzene (49 mg, 0.24 mmol, 1.2 equiv), Pd(PPh₃)₂Cl₂ (7.0 mg, 0.01 mmol), CuI (1.9 mg, 0.01 mmol), then anhydrous DCM (5 mL) and Et₃N (1 mL) were added. The resulting solution was stirred at room temperature for 3 h. The reaction was quenched by saturated NH₄Cl aqueous solution (10 mL) and extracted with CH₂Cl₂ (3×10 mL). The combined organic layers were washed with water and brine, then dried over Na₂SO₄, filtrated, and concentrated under vacuum. The residue was purified by silica gel column chromatography (PE/EtOAc = 20/1) to afford the desired product **9** (76 mg, yield: 85 %) as colorless oil; 92 % ee; determined by HPLC: Daicel Chiralpak ID column, n-hexane/i-PrOH = 80/20, flow rate 1 mL/min, λ = 254 nm, t_R = 7.76 min (major) and 11.50 min (minor). [α]_D²⁰ = +58.0 (c = 0.1 in CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃) δ 7.78-7.75 (m, 1H), 7.65 (d, *J* = 9.0 Hz, 2H), 7.33-7.27 (m, 3H), 7.26-7.23 (m, 3H), 7.17-7.11 (m, 3H), 7.07-7.01 (m, 1H), 5.43-5.38 (m, 1H), 5.06 (s, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 2.29 (s, 3H), 1.30 (s, 9H). ¹³C NMR (125 MHz, CDCl₃) δ 143.42, 136.70, 135.48, 131.43, 129.20, 128.44, 128.30, 128.27, 128.03, 127.64, 127.62, 124.23, 122.91, 121.44, 90.02, 86.45, 59.49, 54.71, 49.34, 27.69, 21.50. HRMS (ESI) calcd. for C₂₇H₂₉N₂O₂S [M+H]⁺: 445.1944, found: 445.1948.

X-ray structure of **3k**

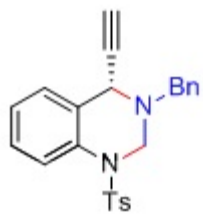
The crystal structures have been deposited at the Cambridge Crystallographic Data Centre (CCDC 1843737, **3k**). The data can be obtained free of charge via the internet at www.ccdc.cam.ac.uk/data_request/cif.



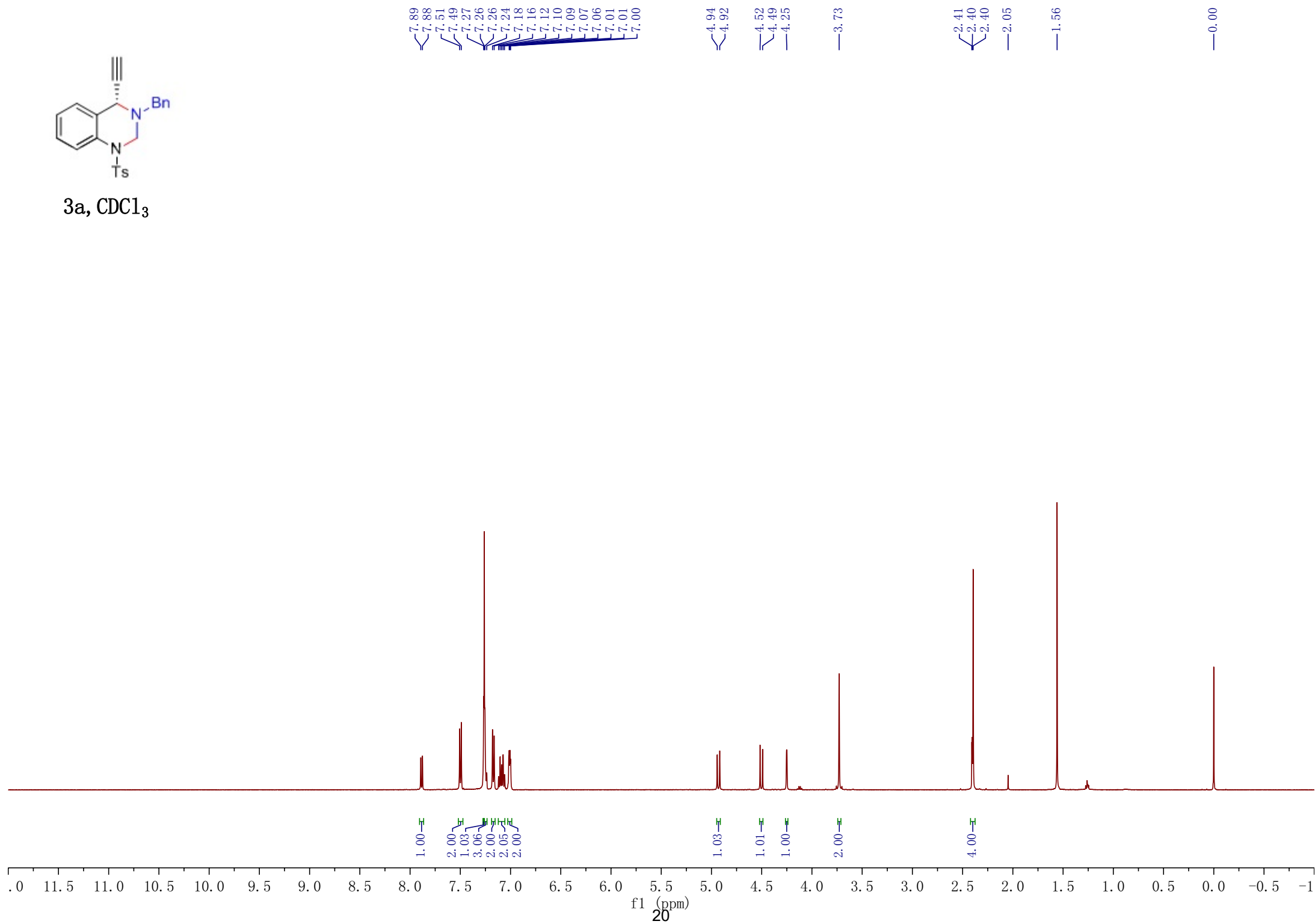
X-ray of **3k**

References

- [1] Wang, Q.; Li, T.-R.; Lu, L.-Q.; Li, M.-M.; Zhang, K.; Xiao, W.-J. *J. Am. Chem. Soc.* **2016**, *138*, 8360.
- [2] Zhu, C.; Xu, G.; Sun, J. *Angew. Chem. Int. Ed.* **2016**, *55*, 11867.

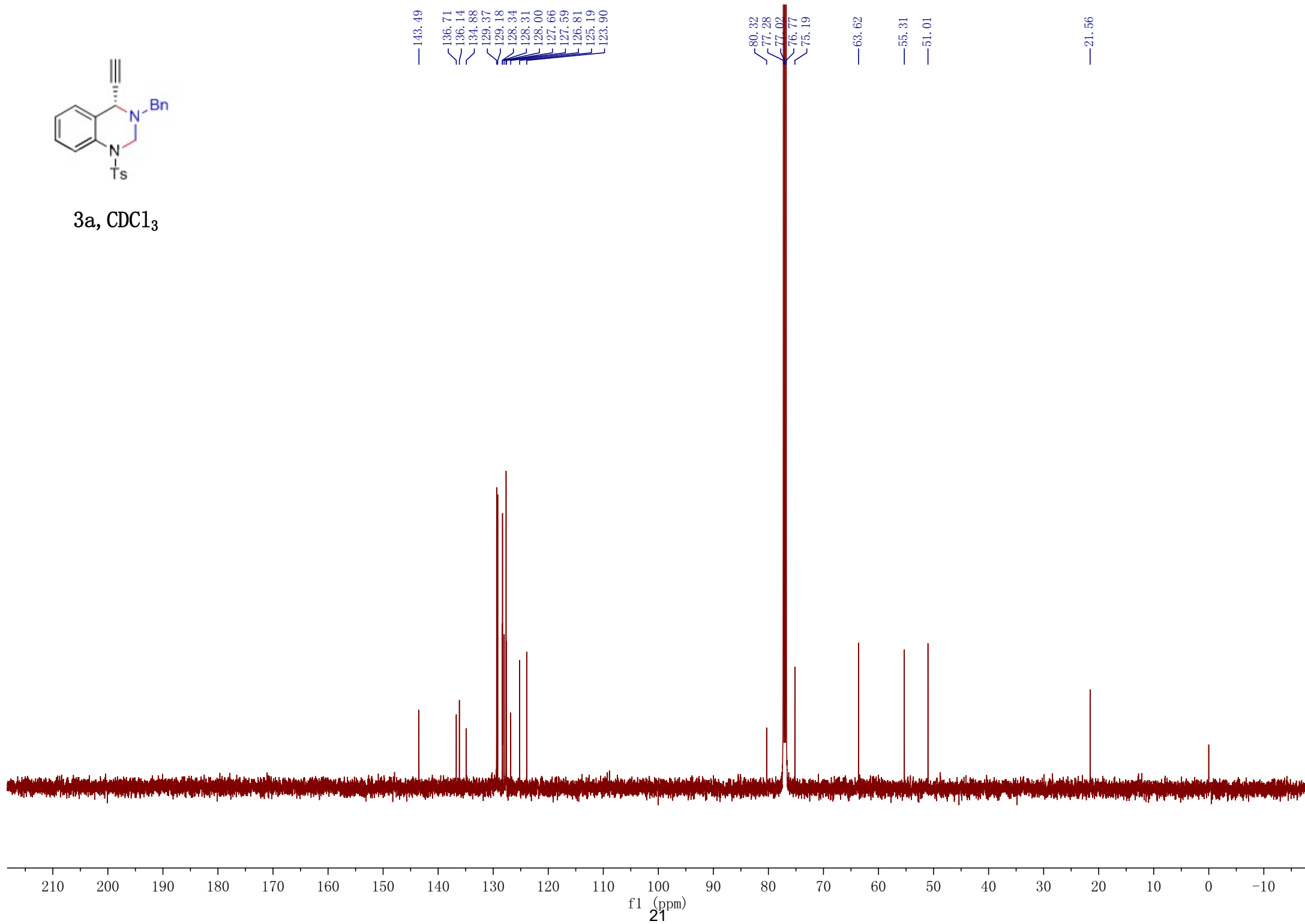


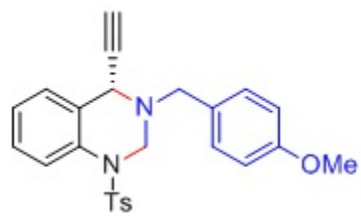
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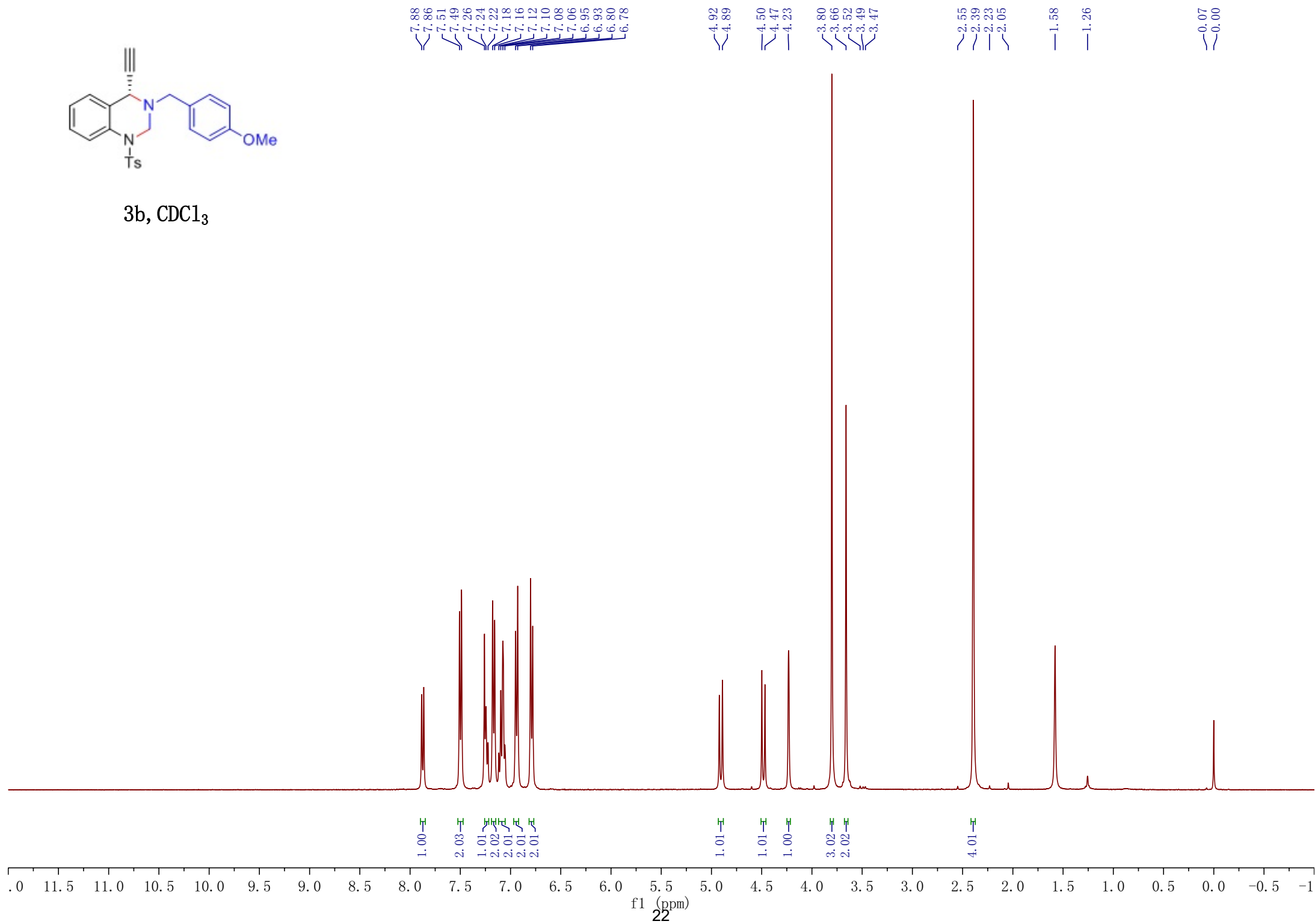


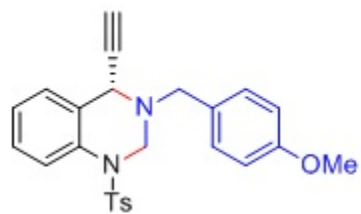
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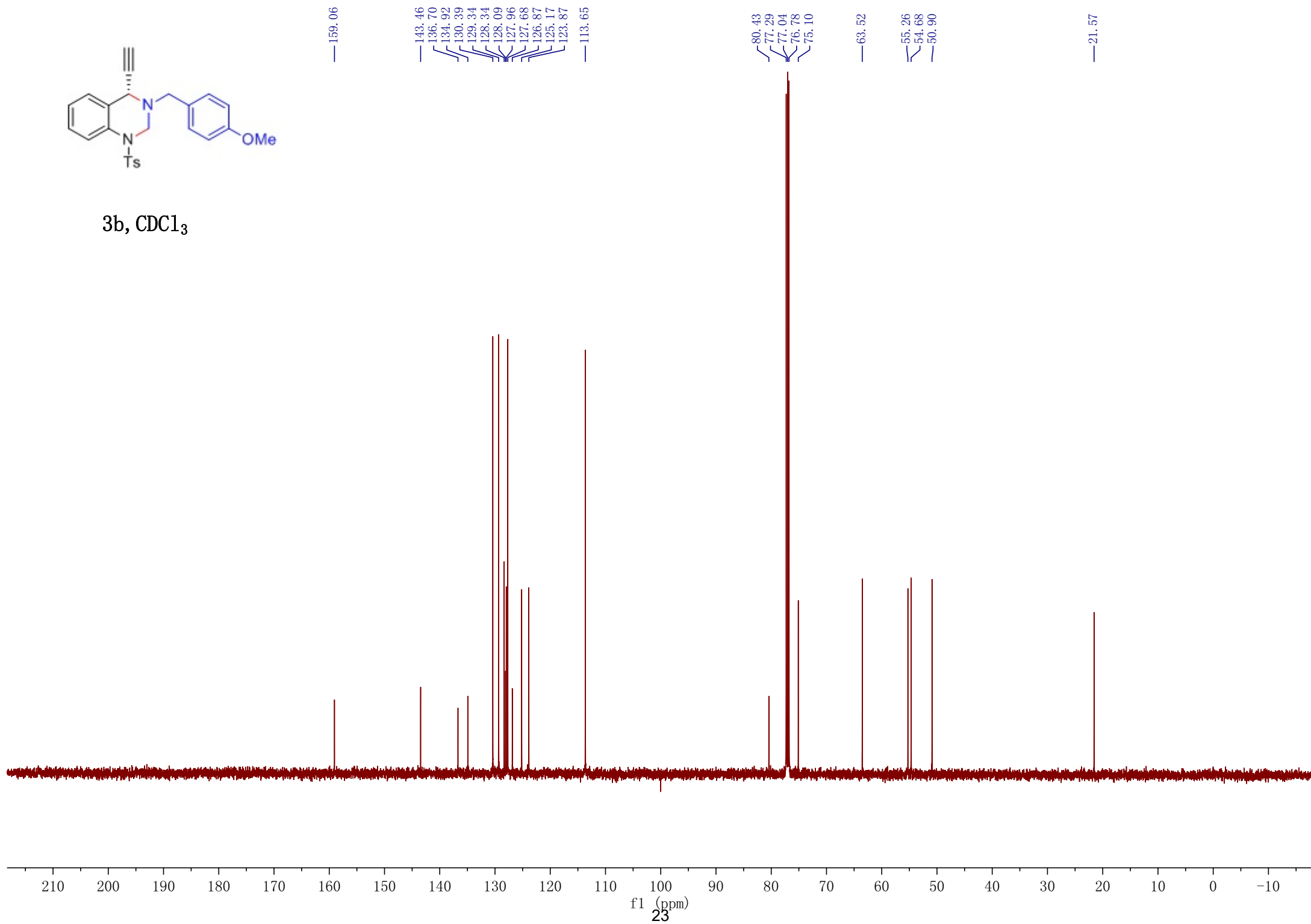


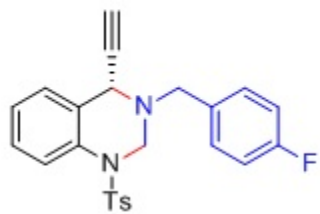
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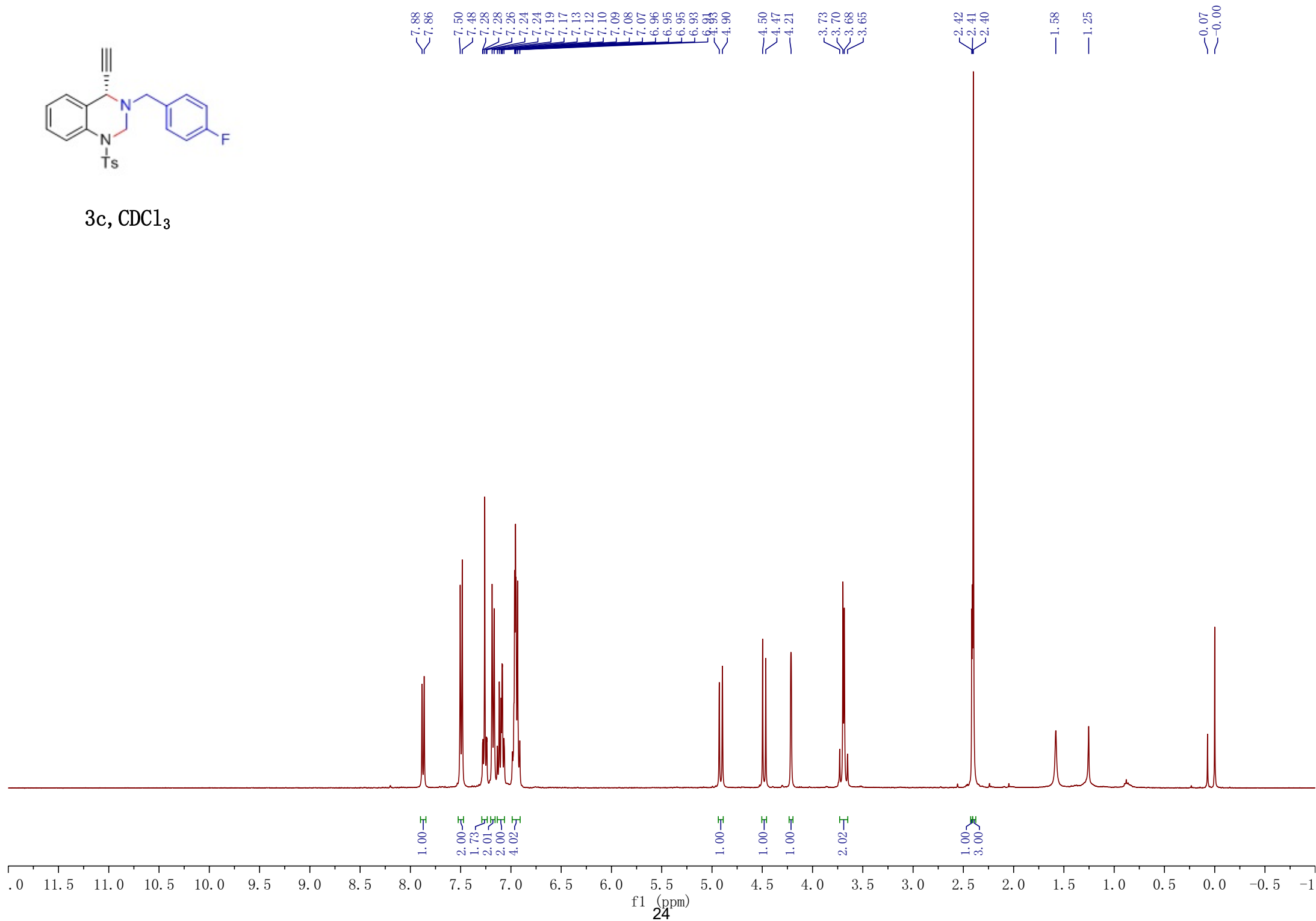


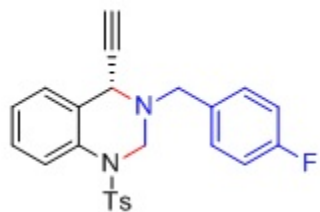
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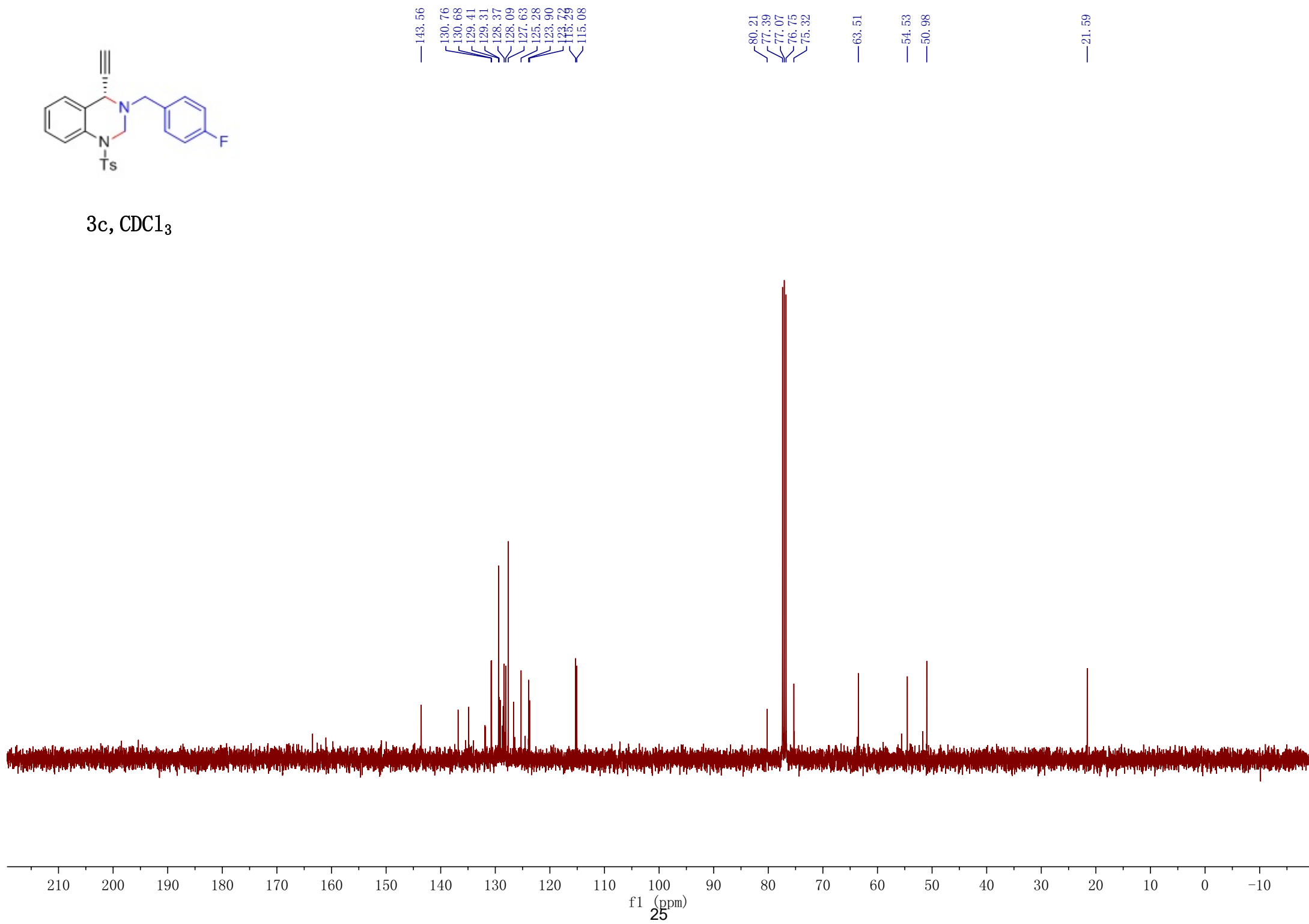


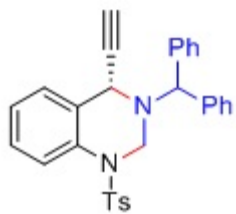
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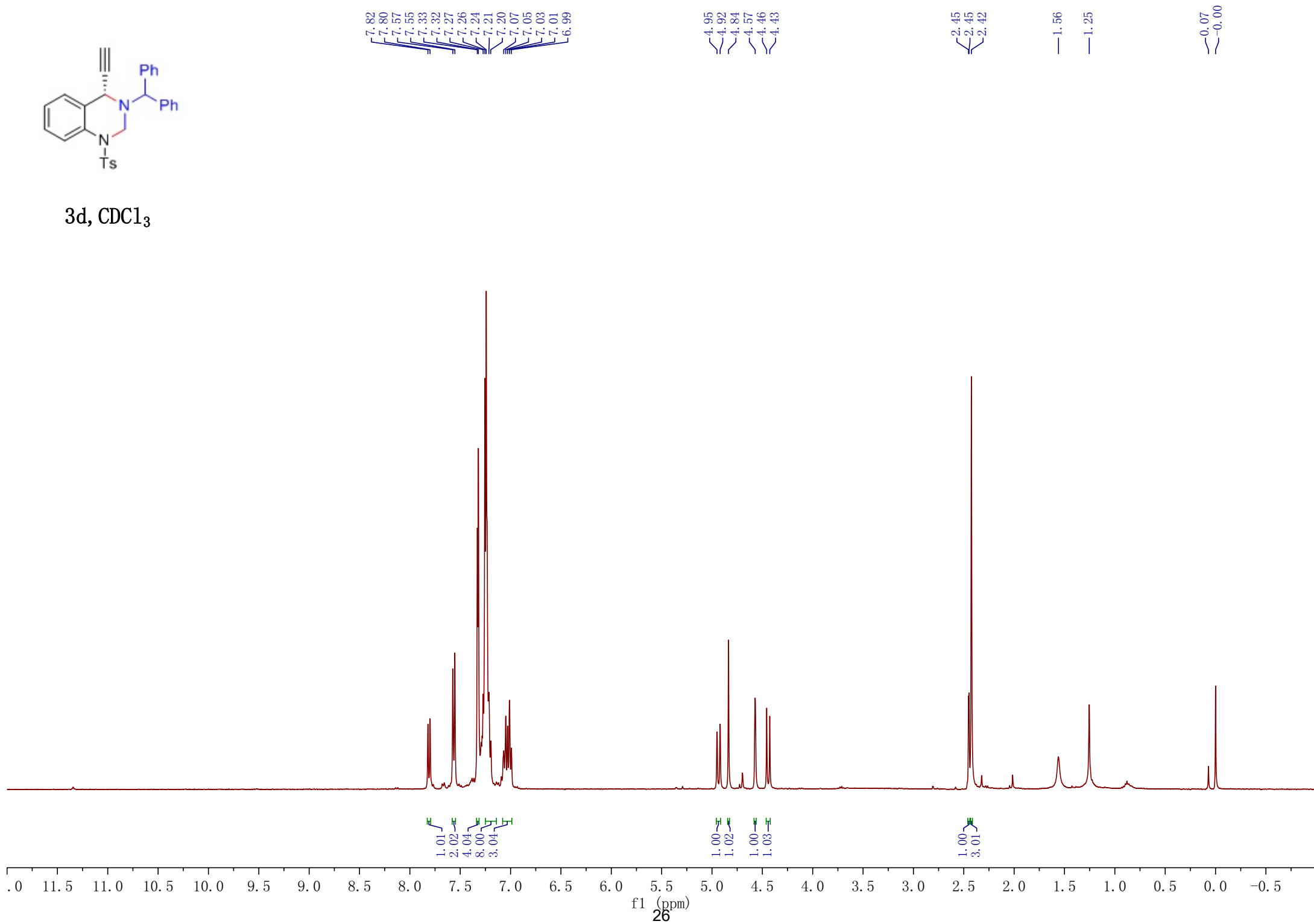


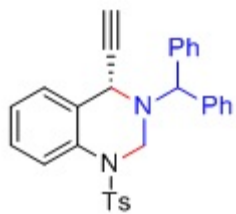
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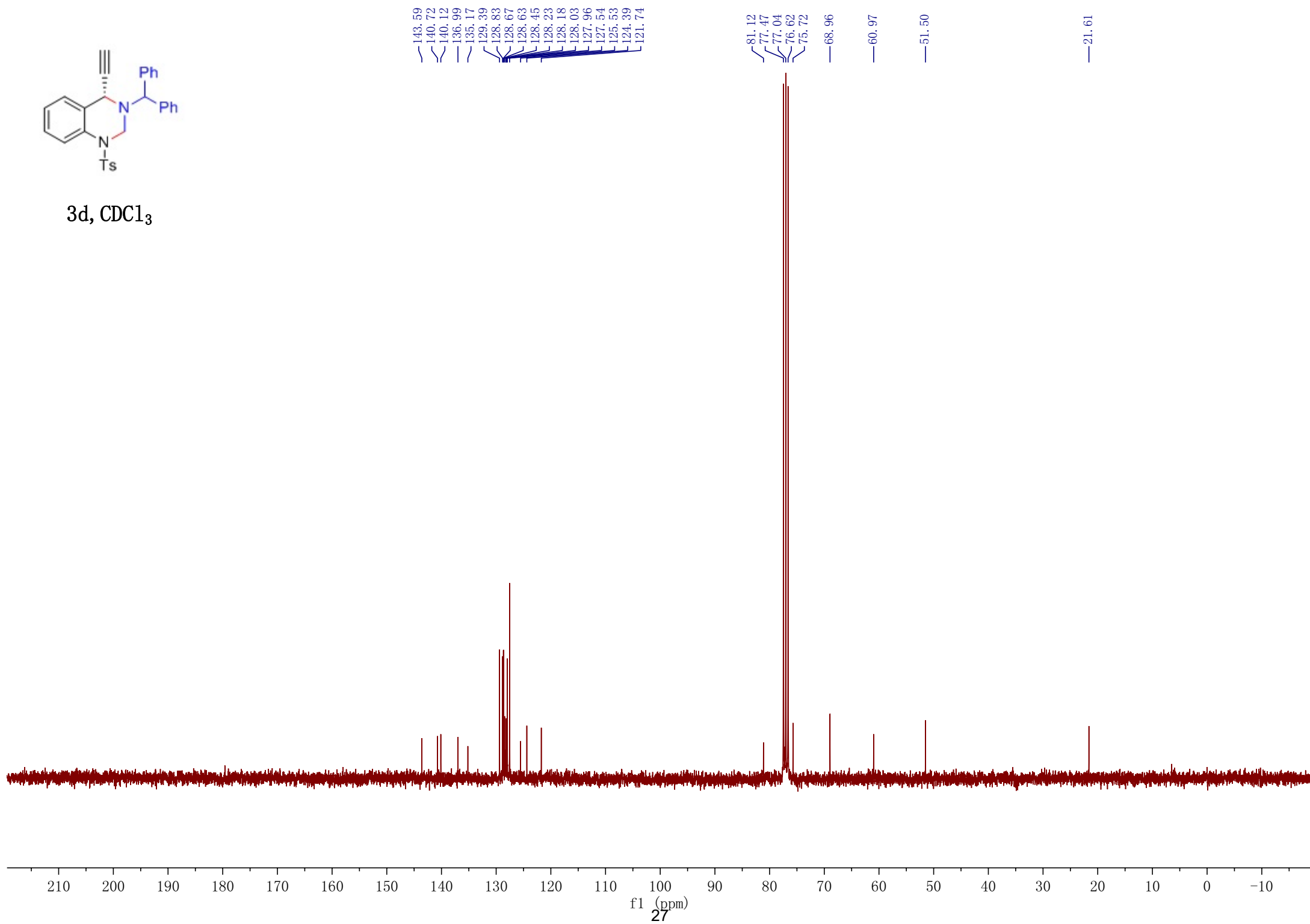


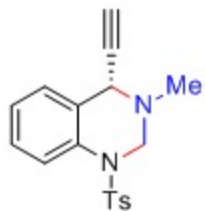
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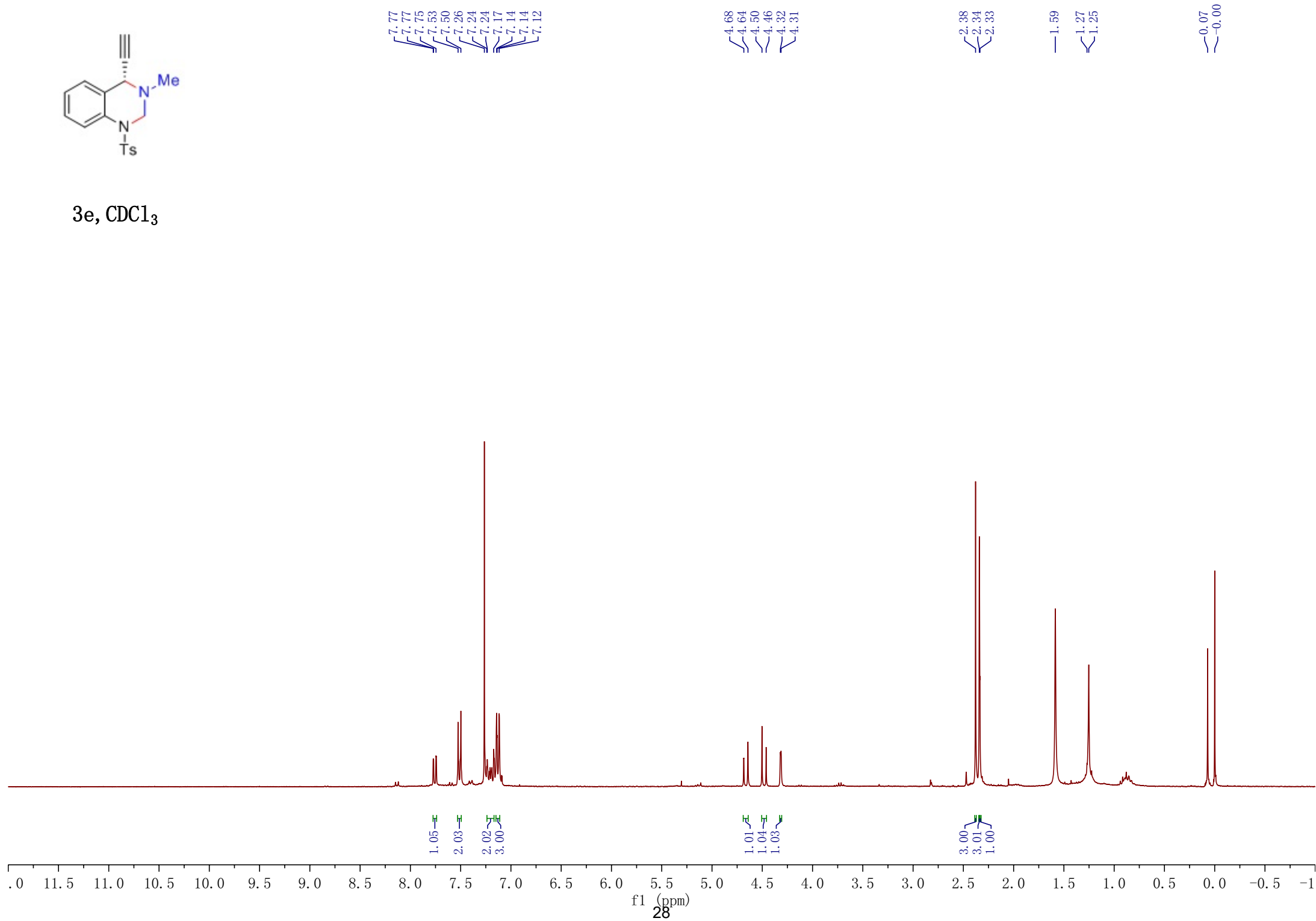


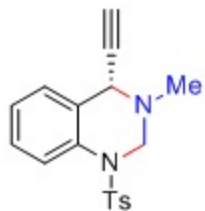
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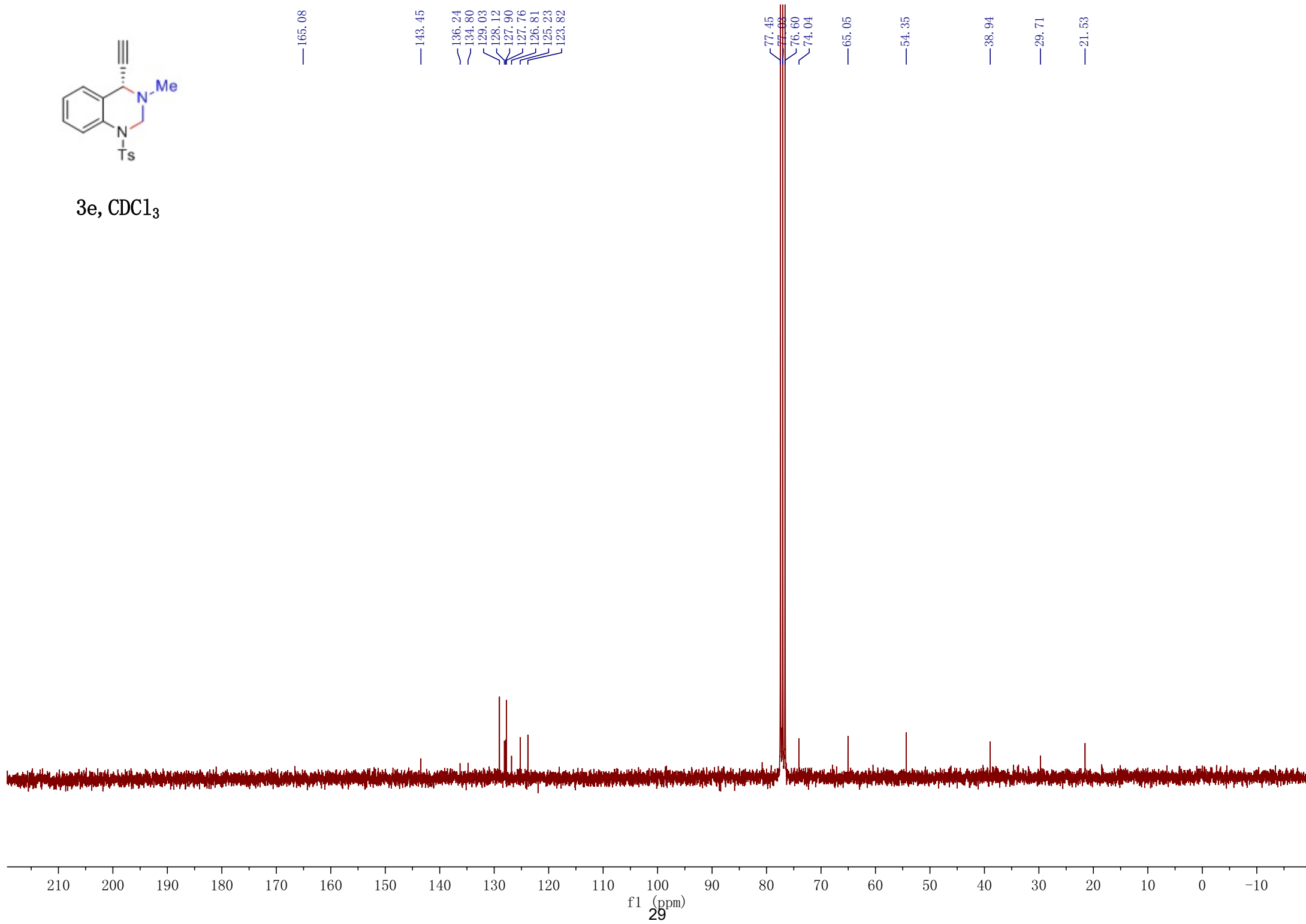


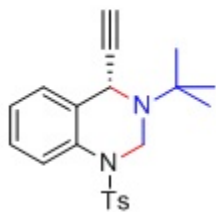
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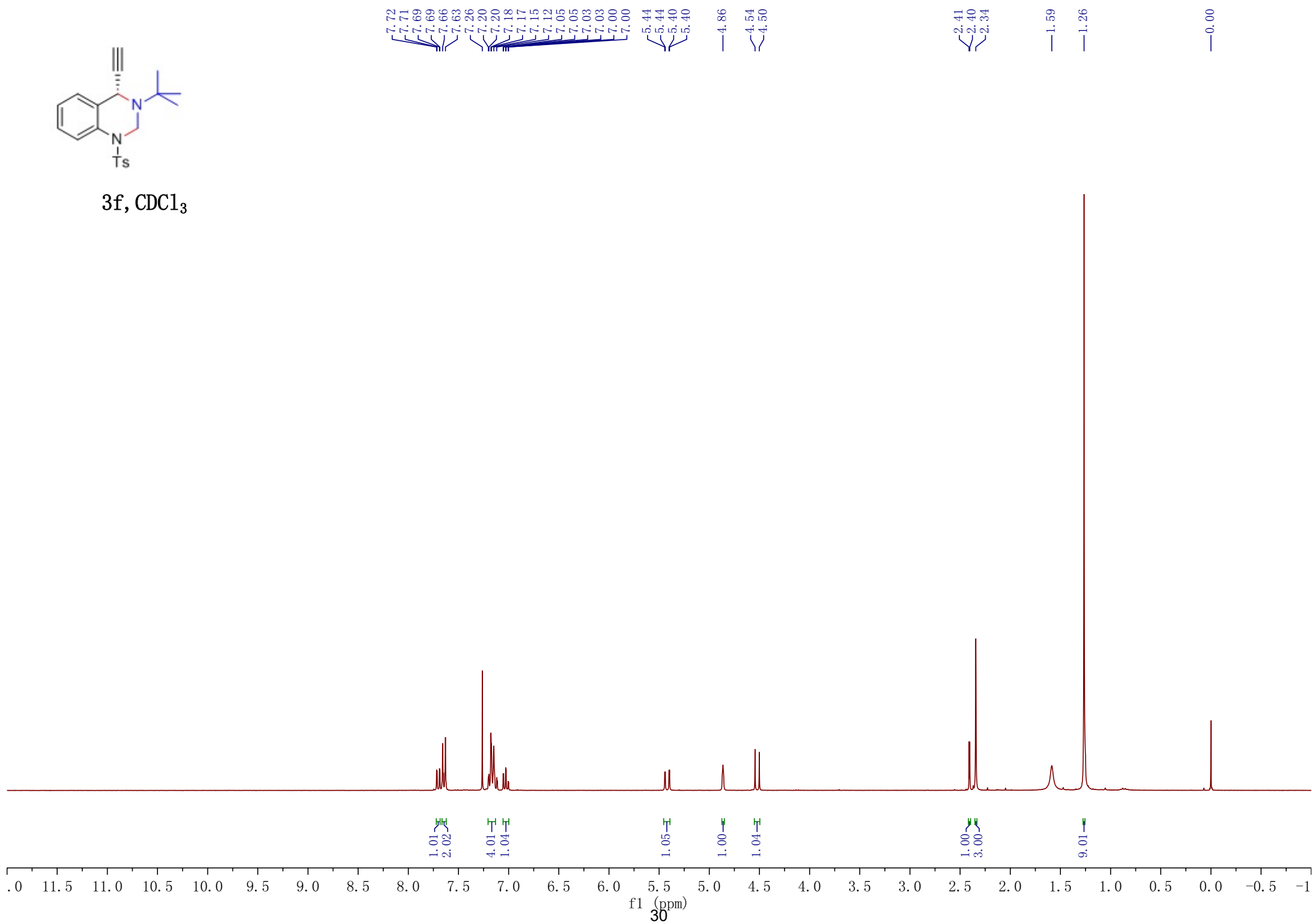


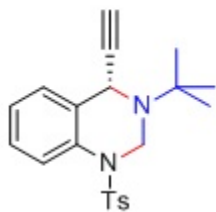
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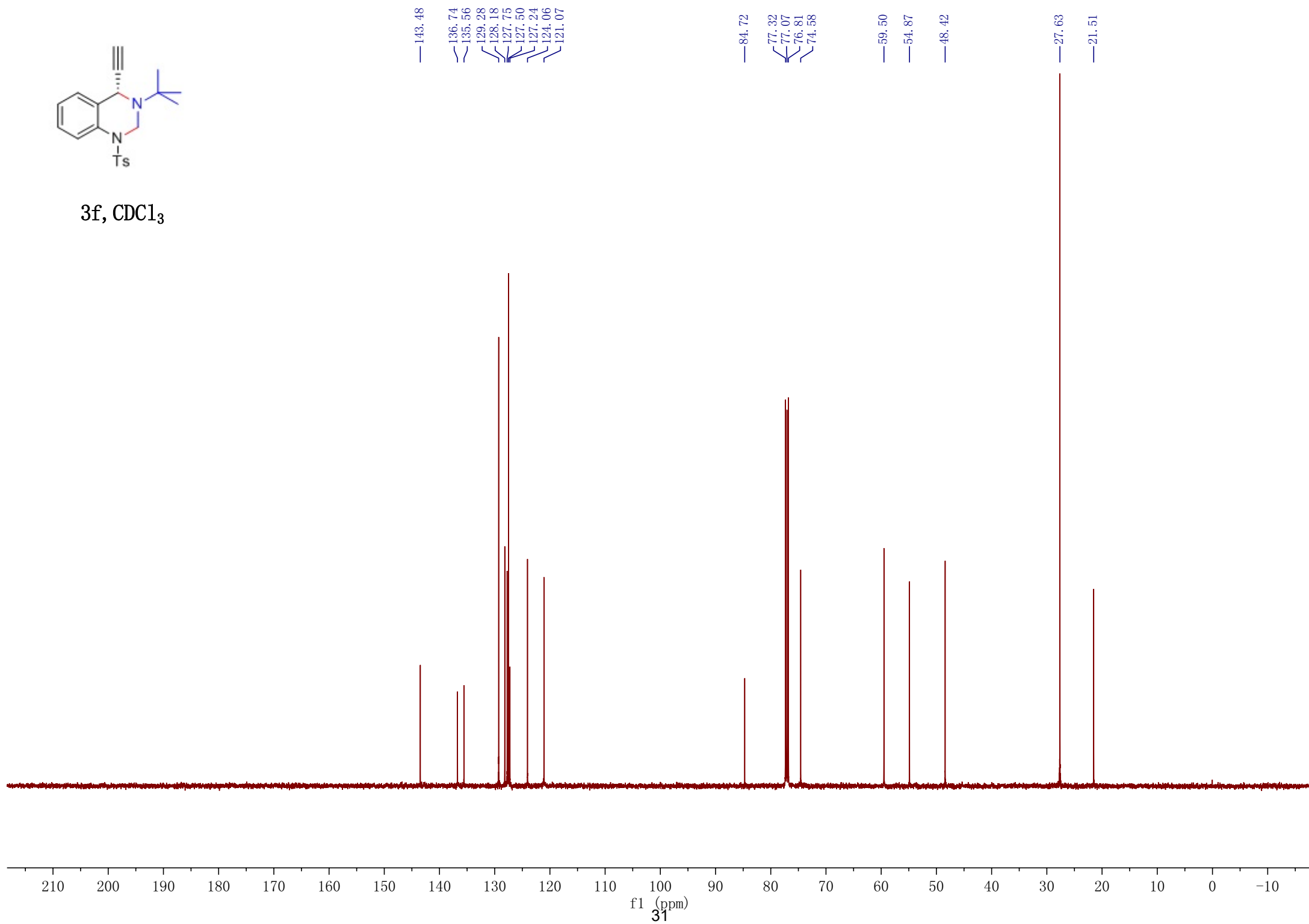


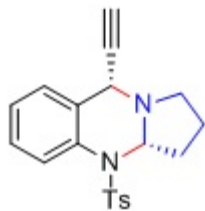
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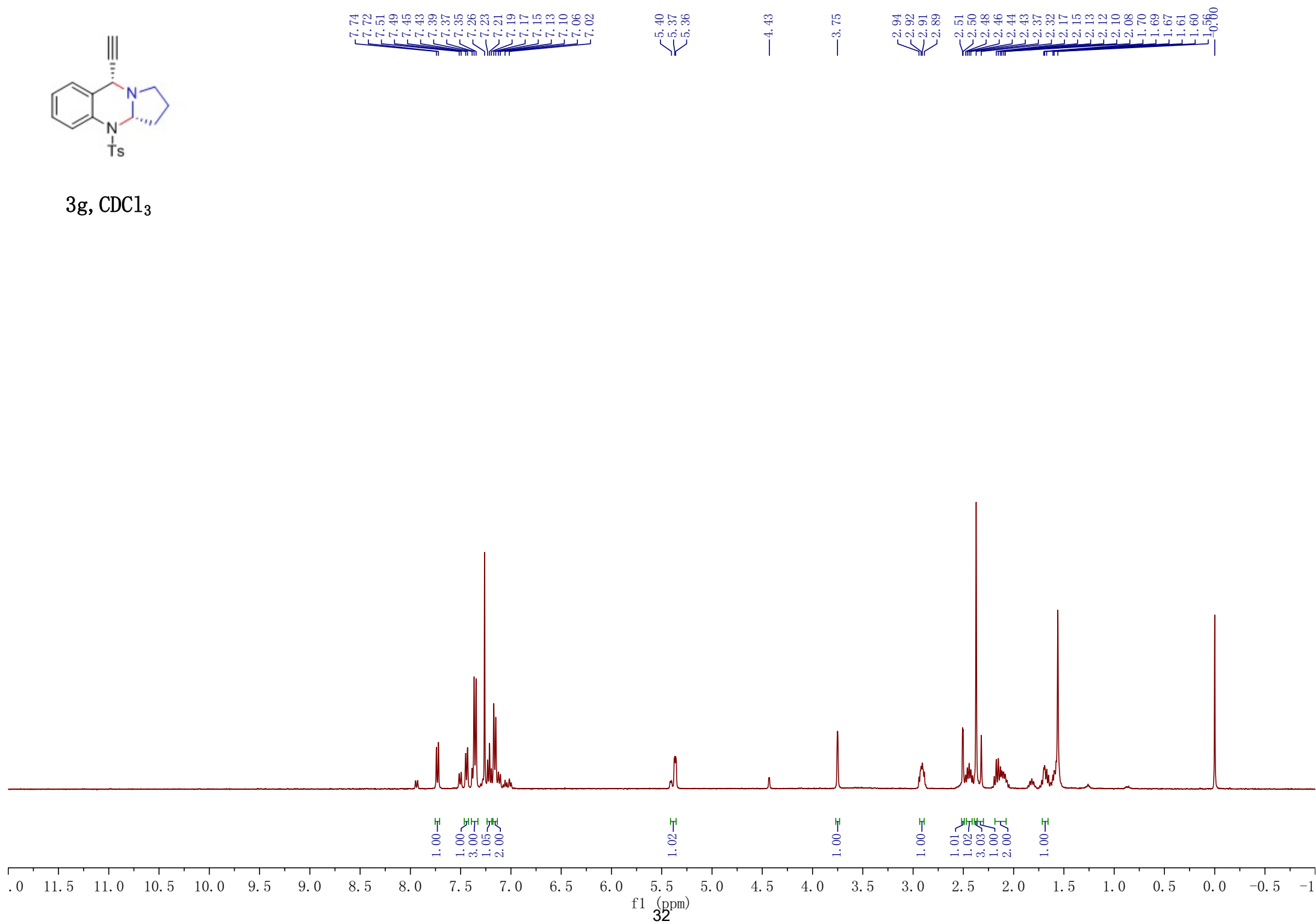


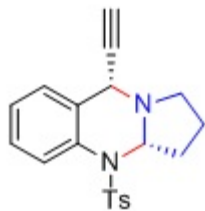
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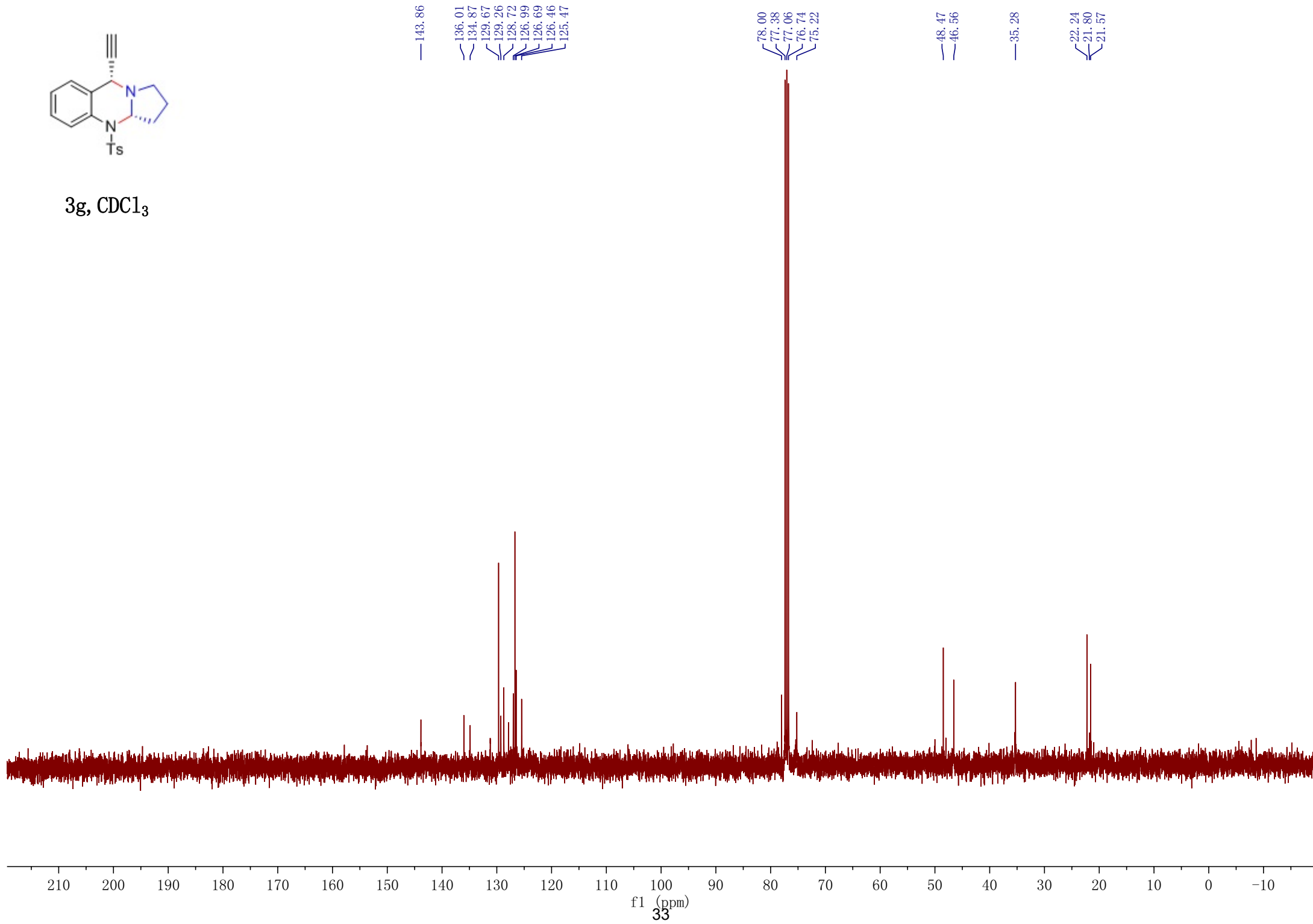


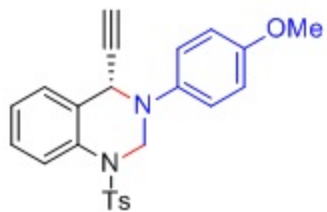
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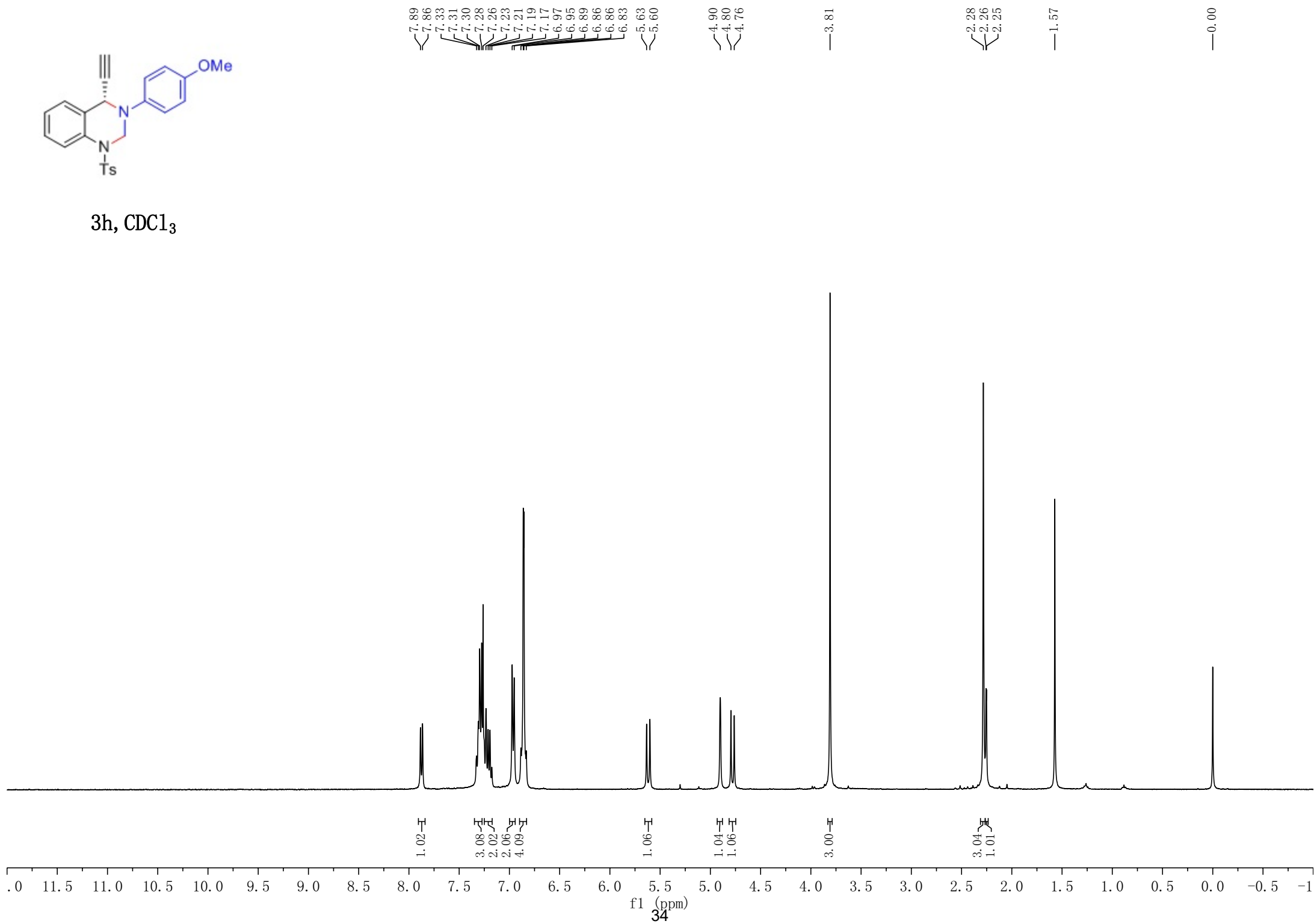


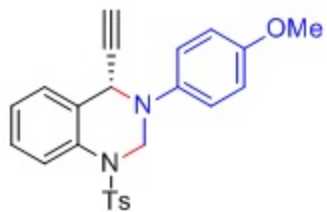
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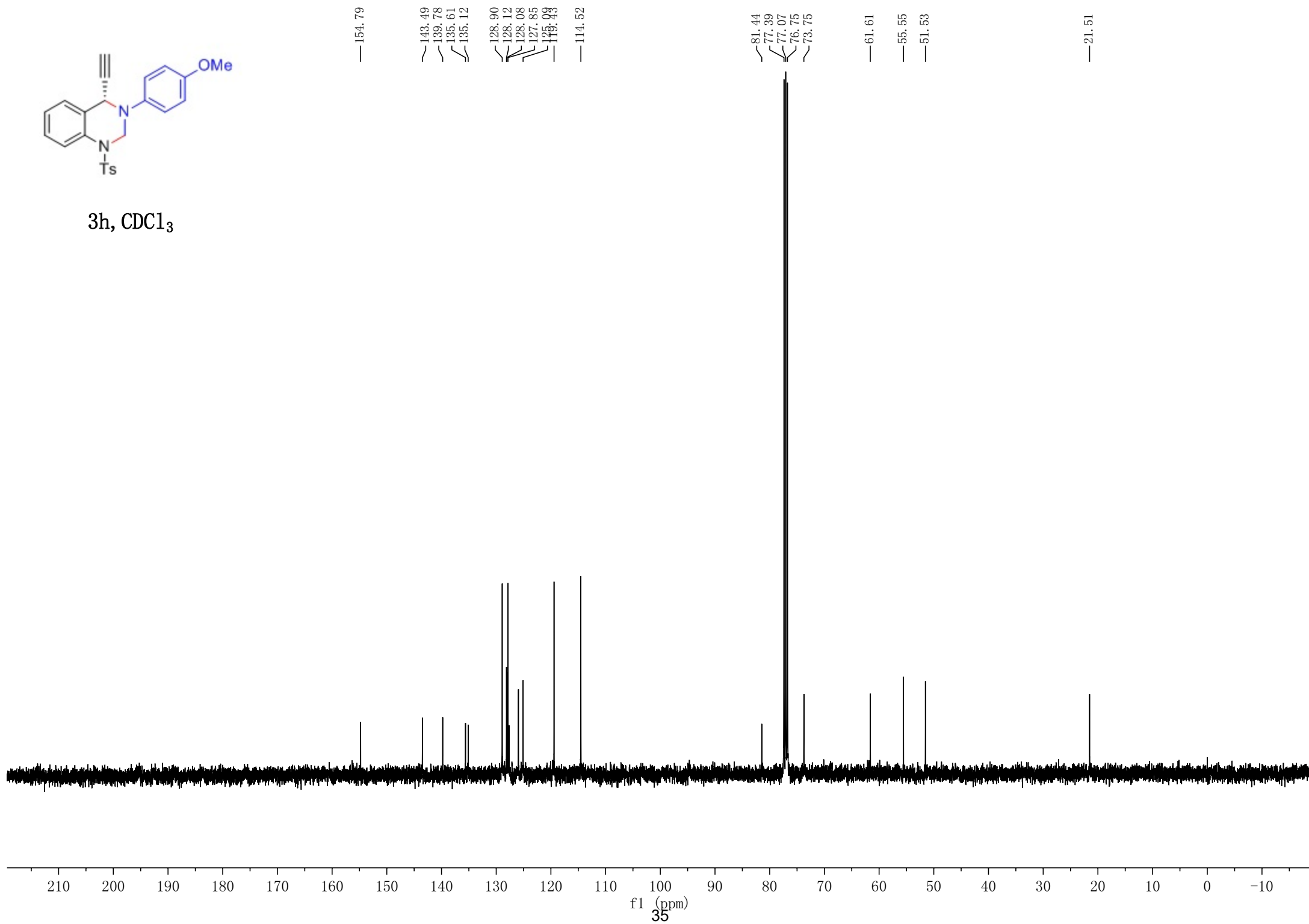


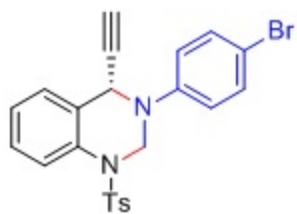
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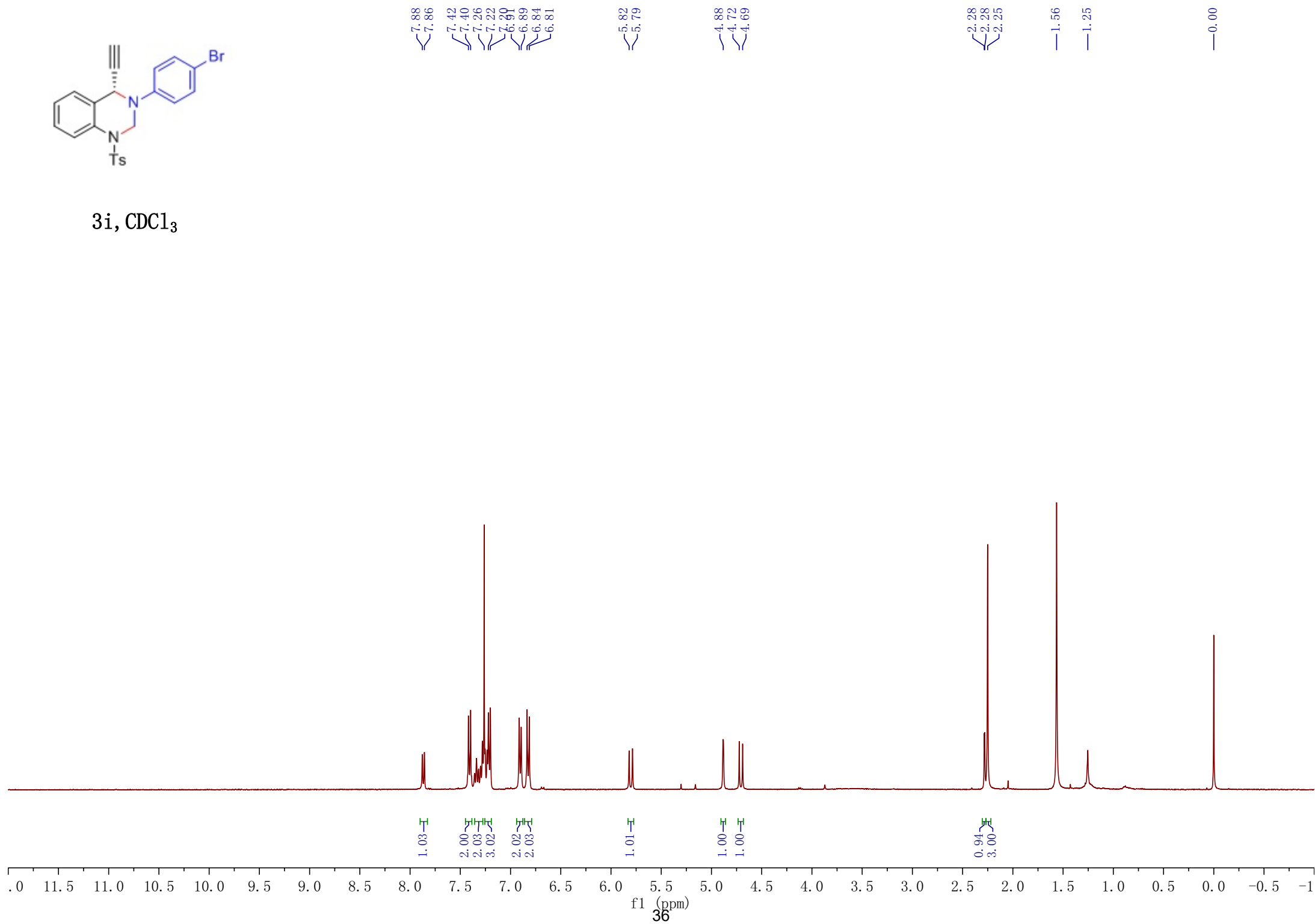


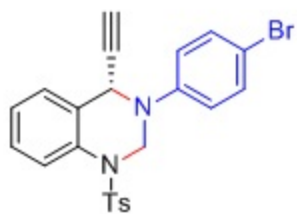
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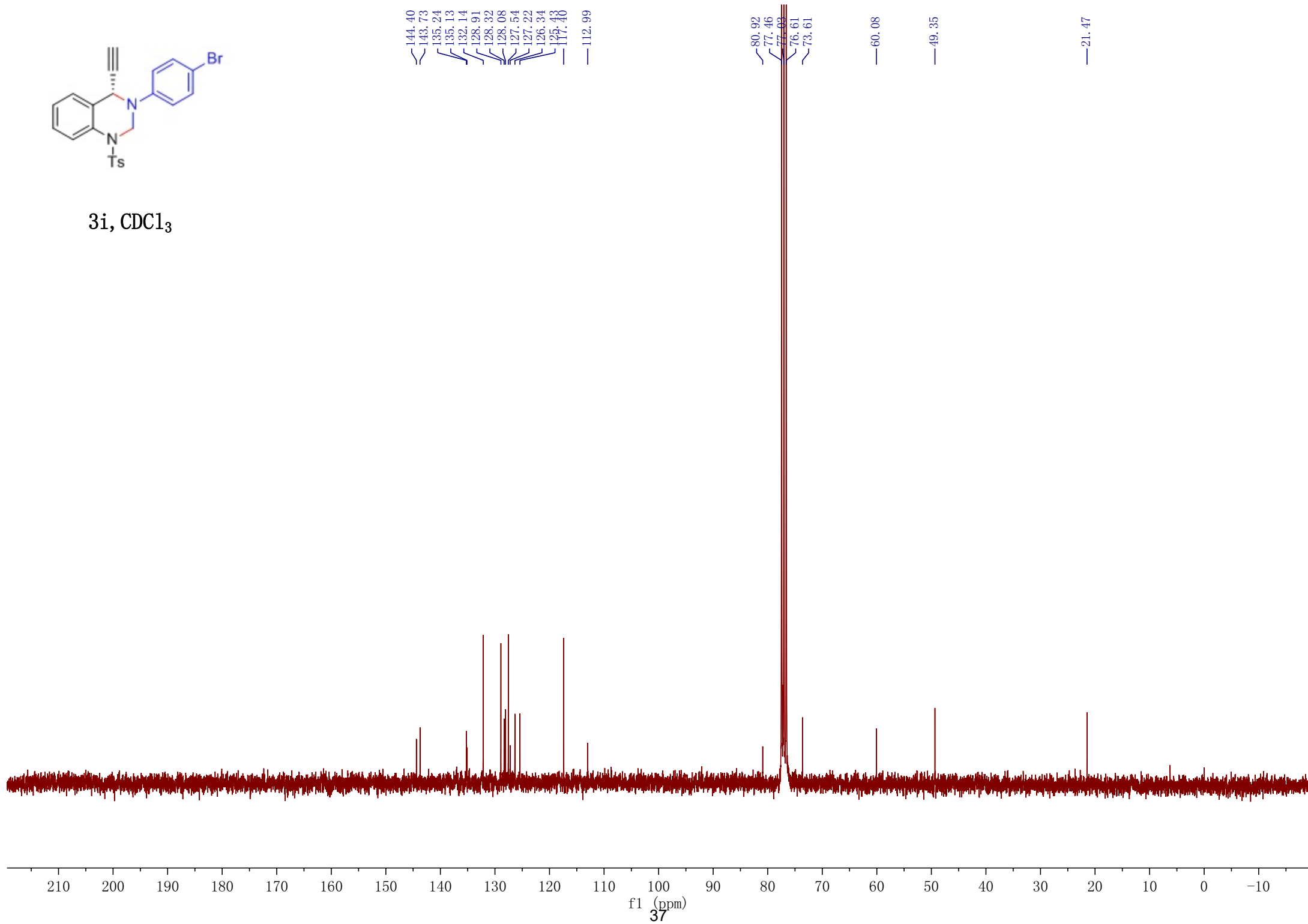


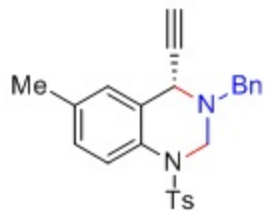
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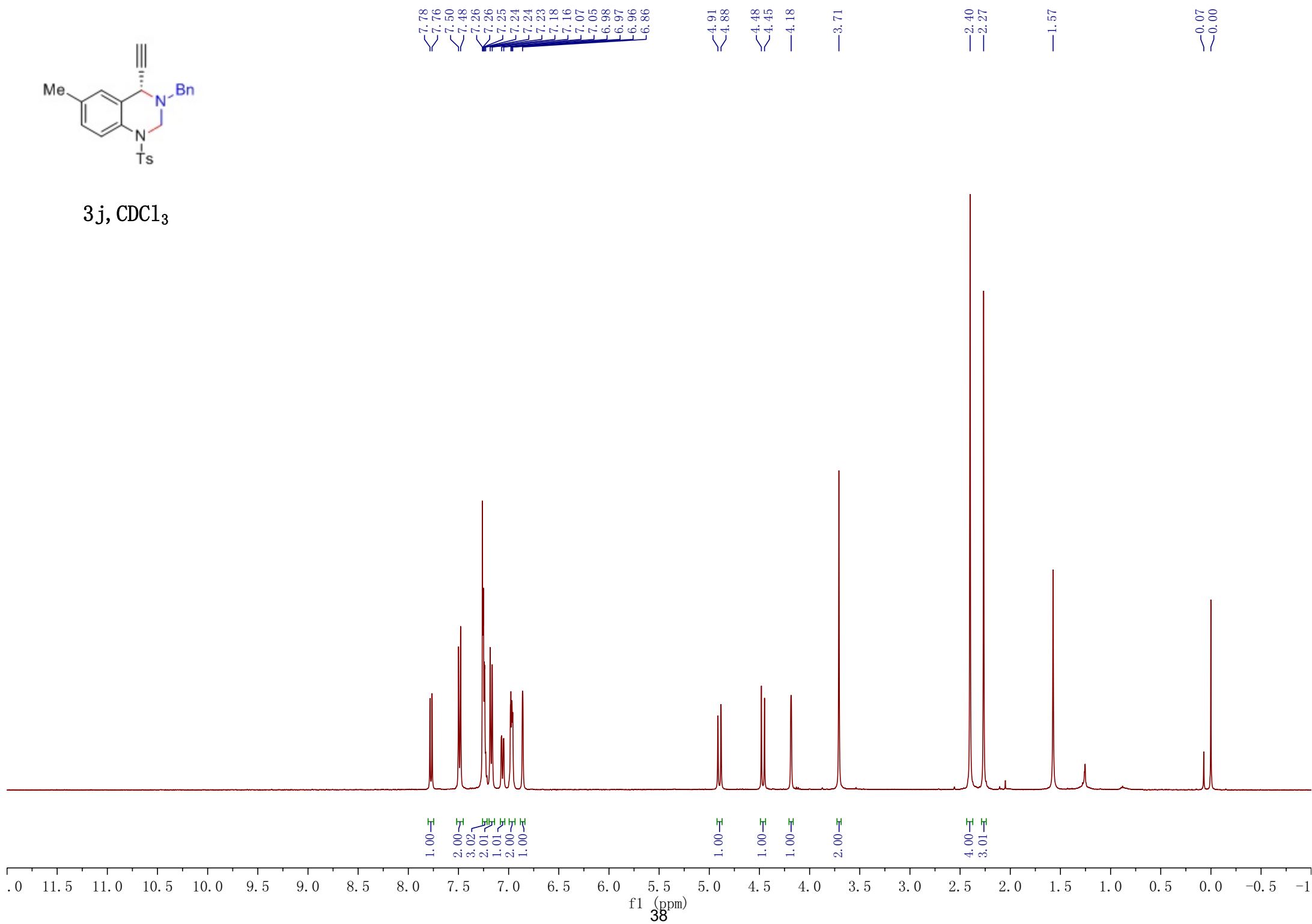


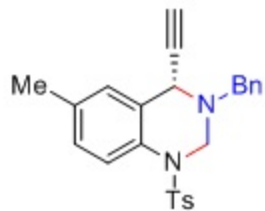
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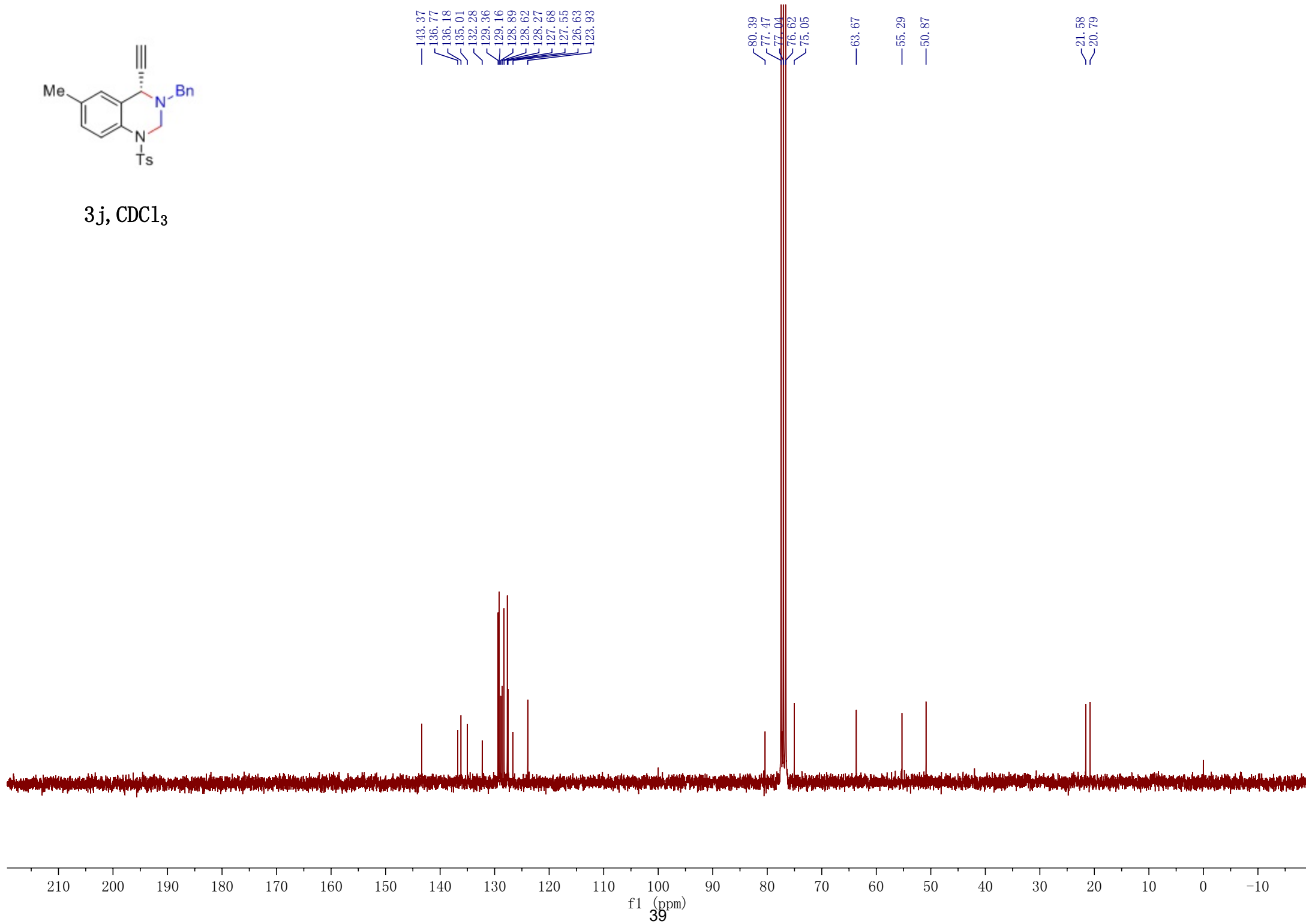


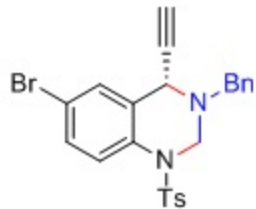
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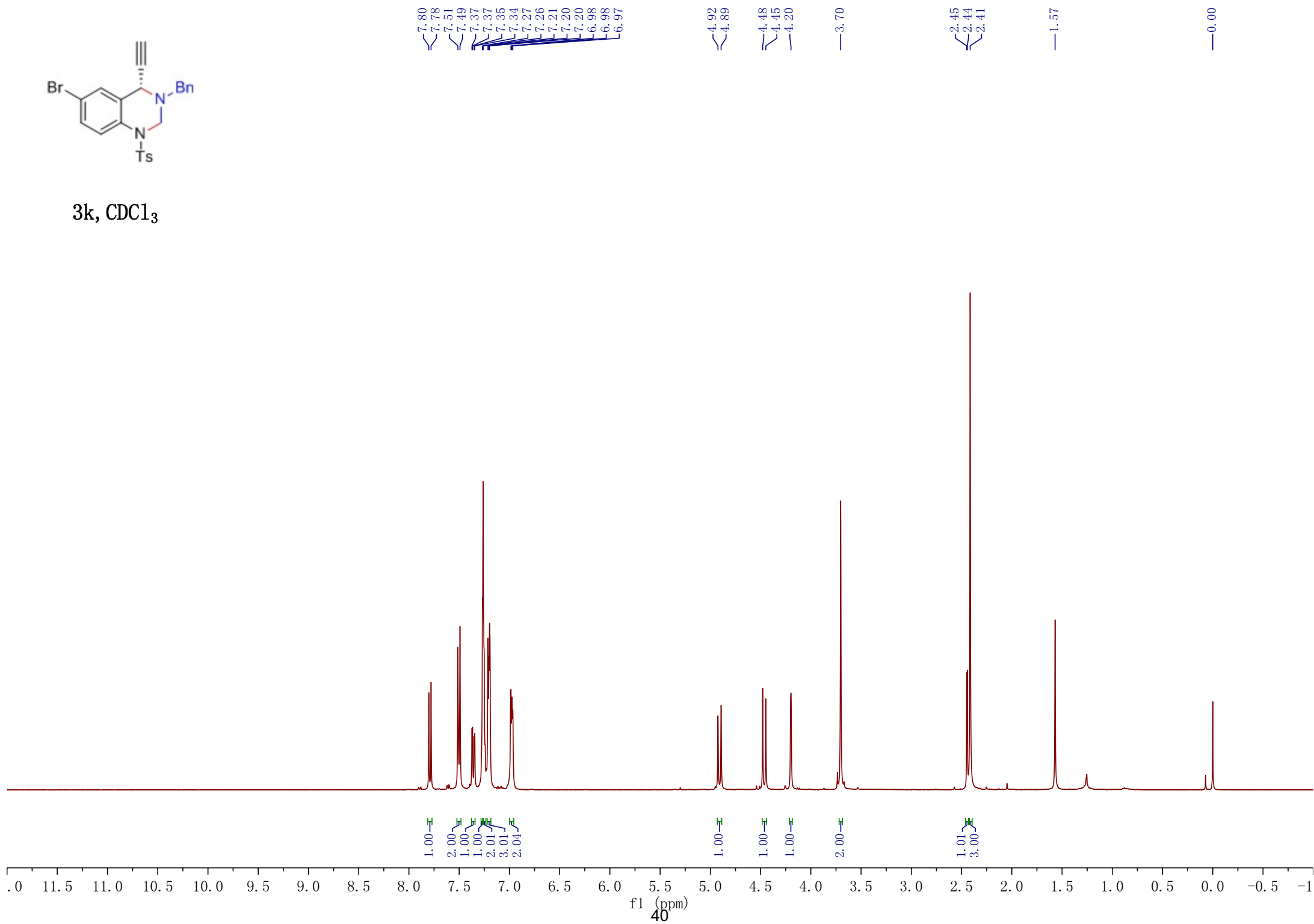


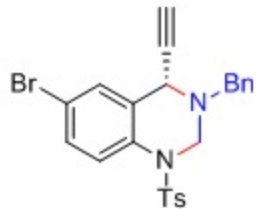
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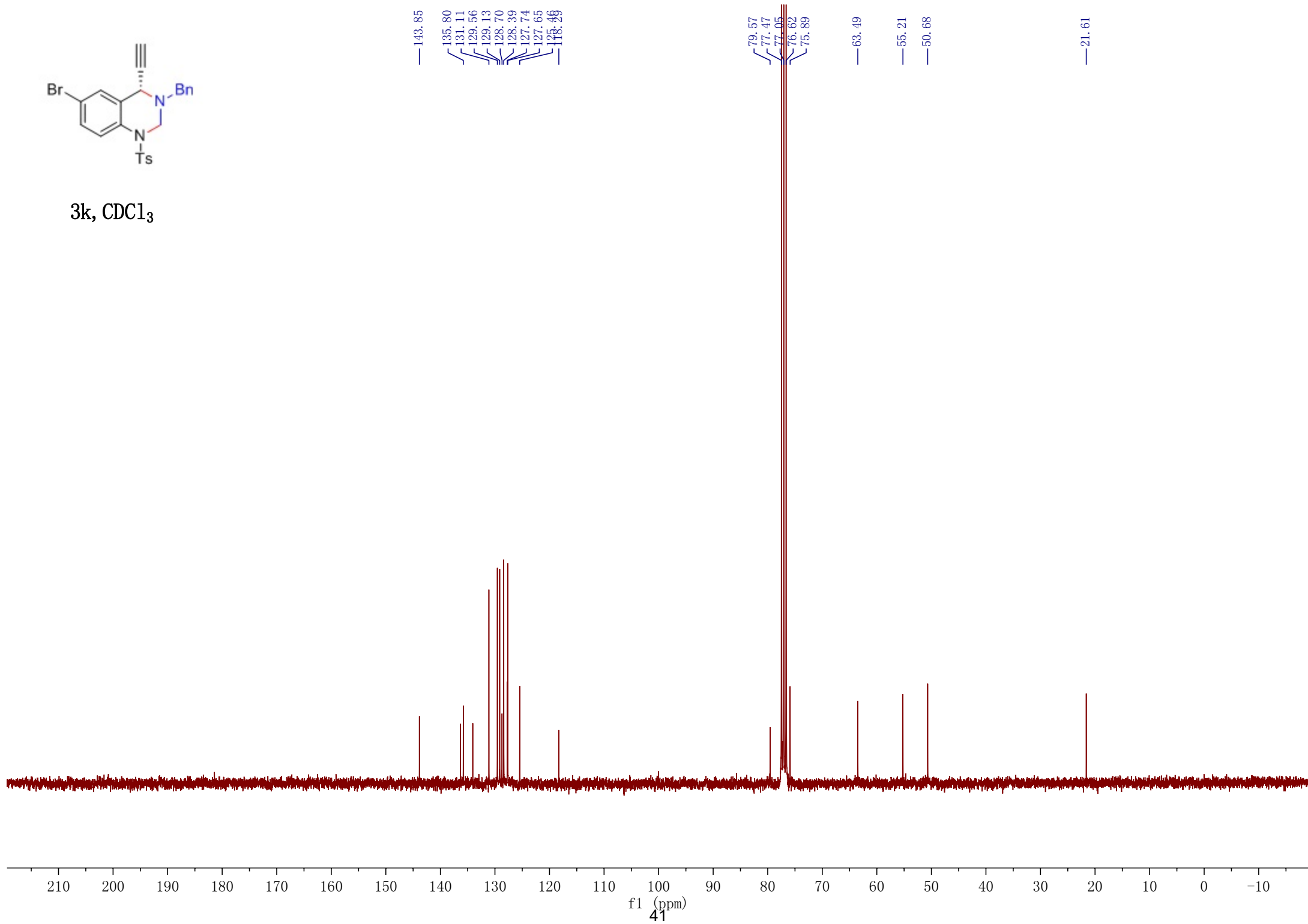


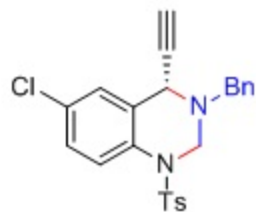
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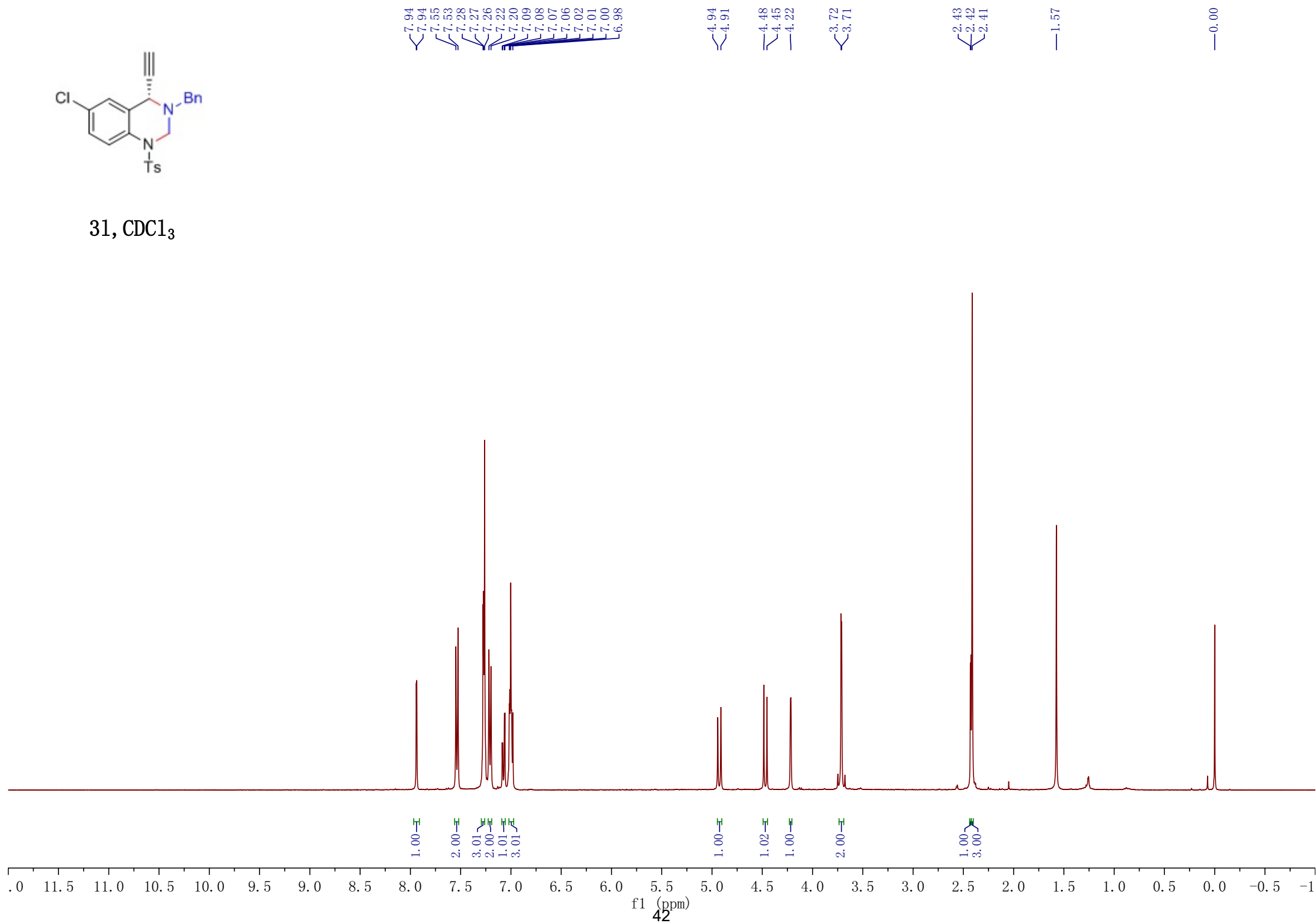


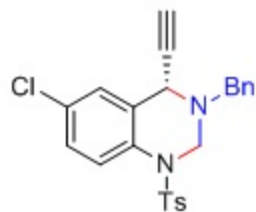
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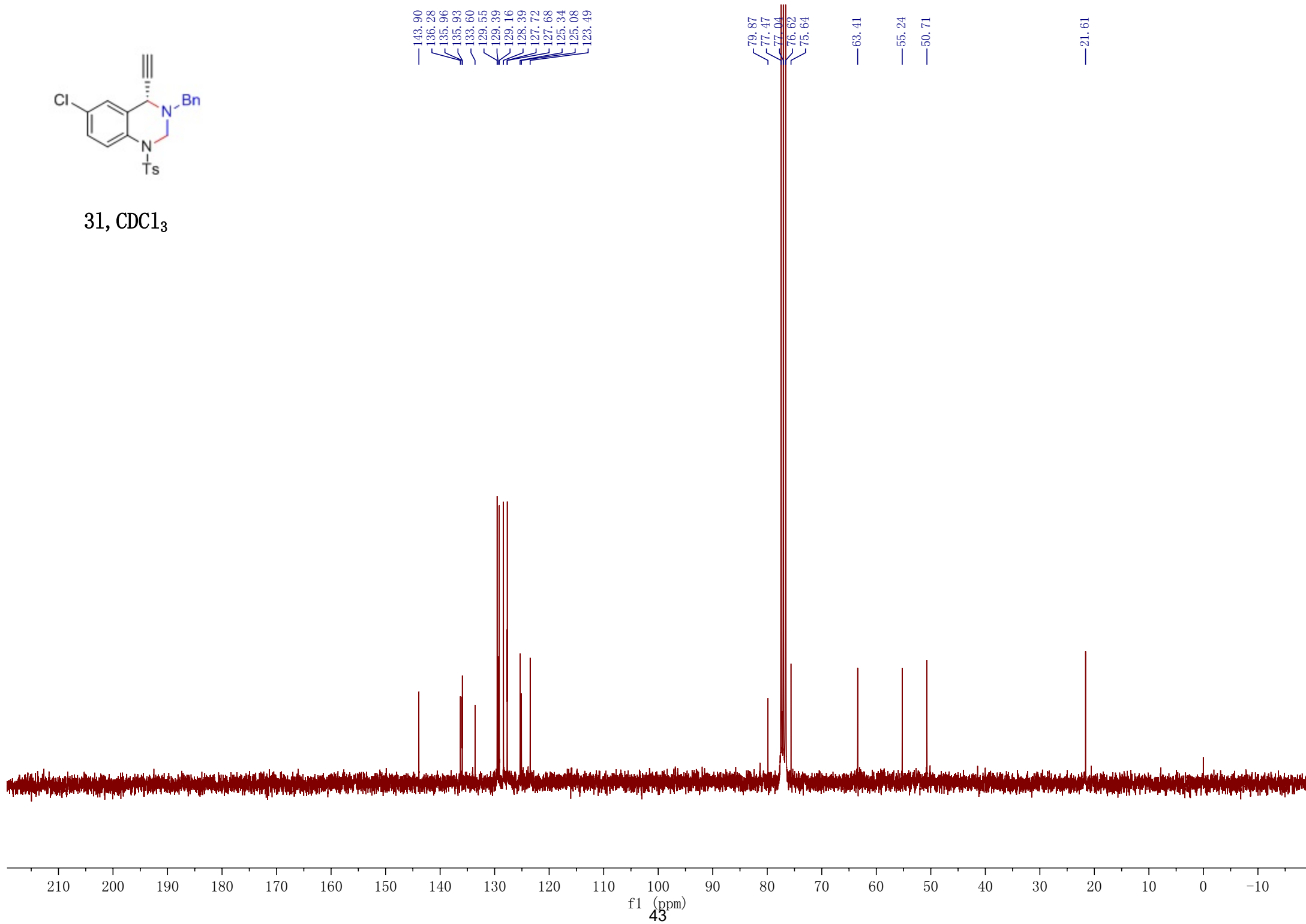


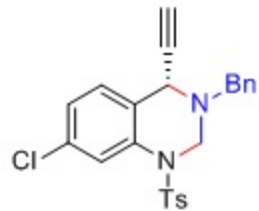
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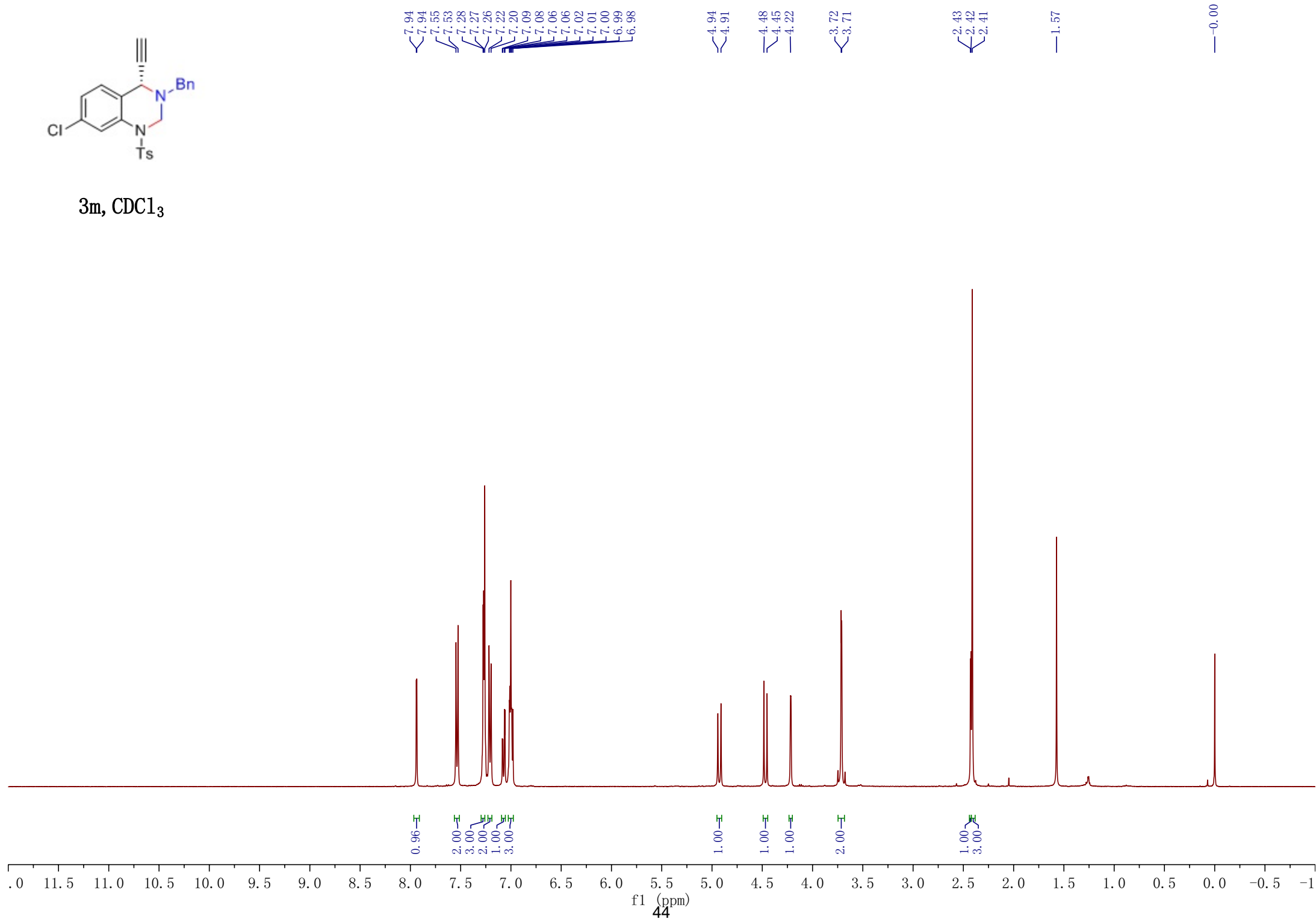


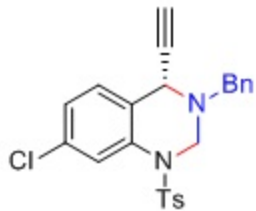
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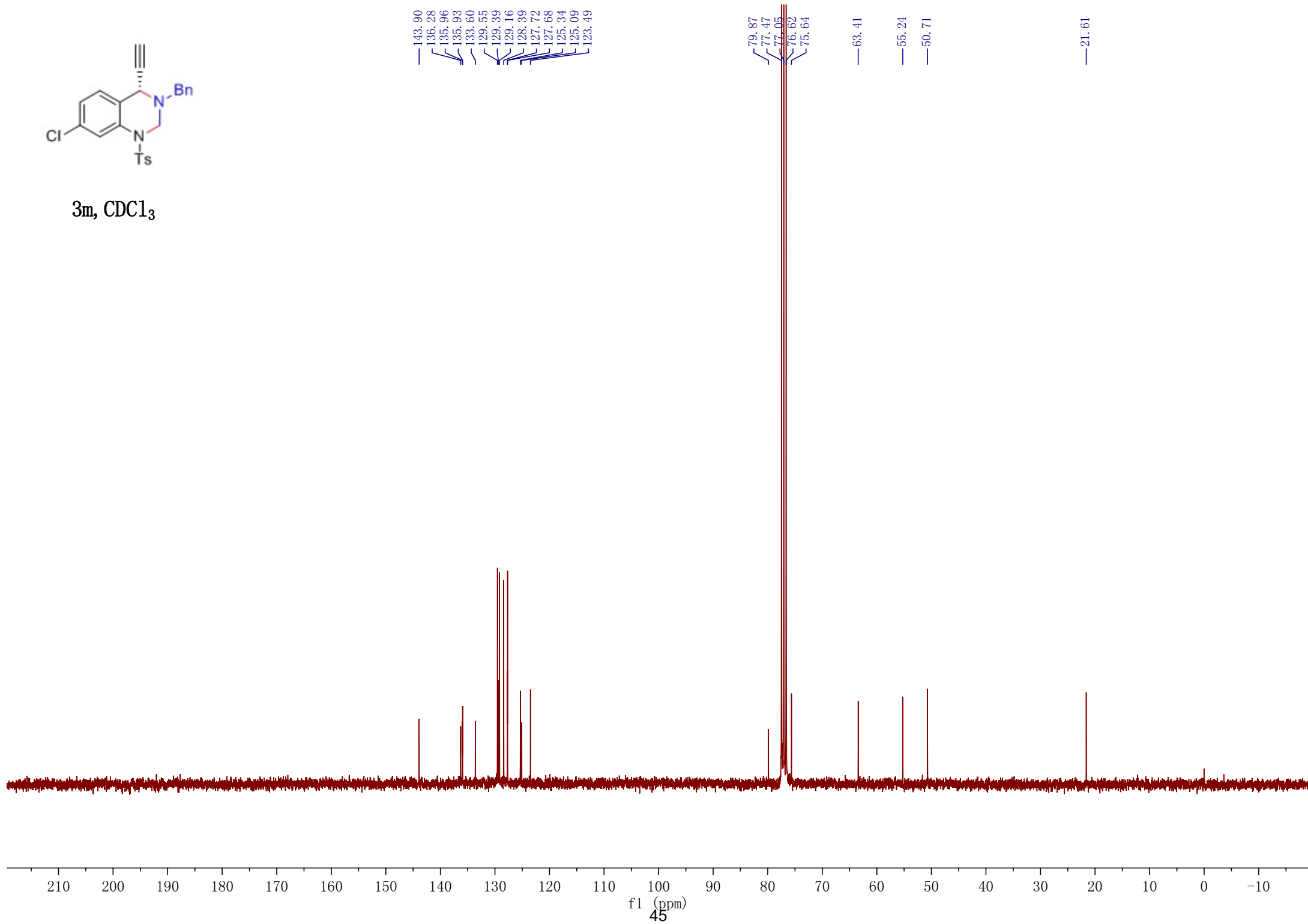


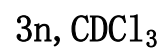
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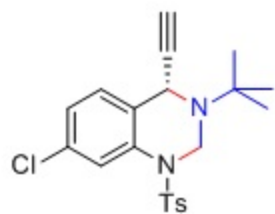




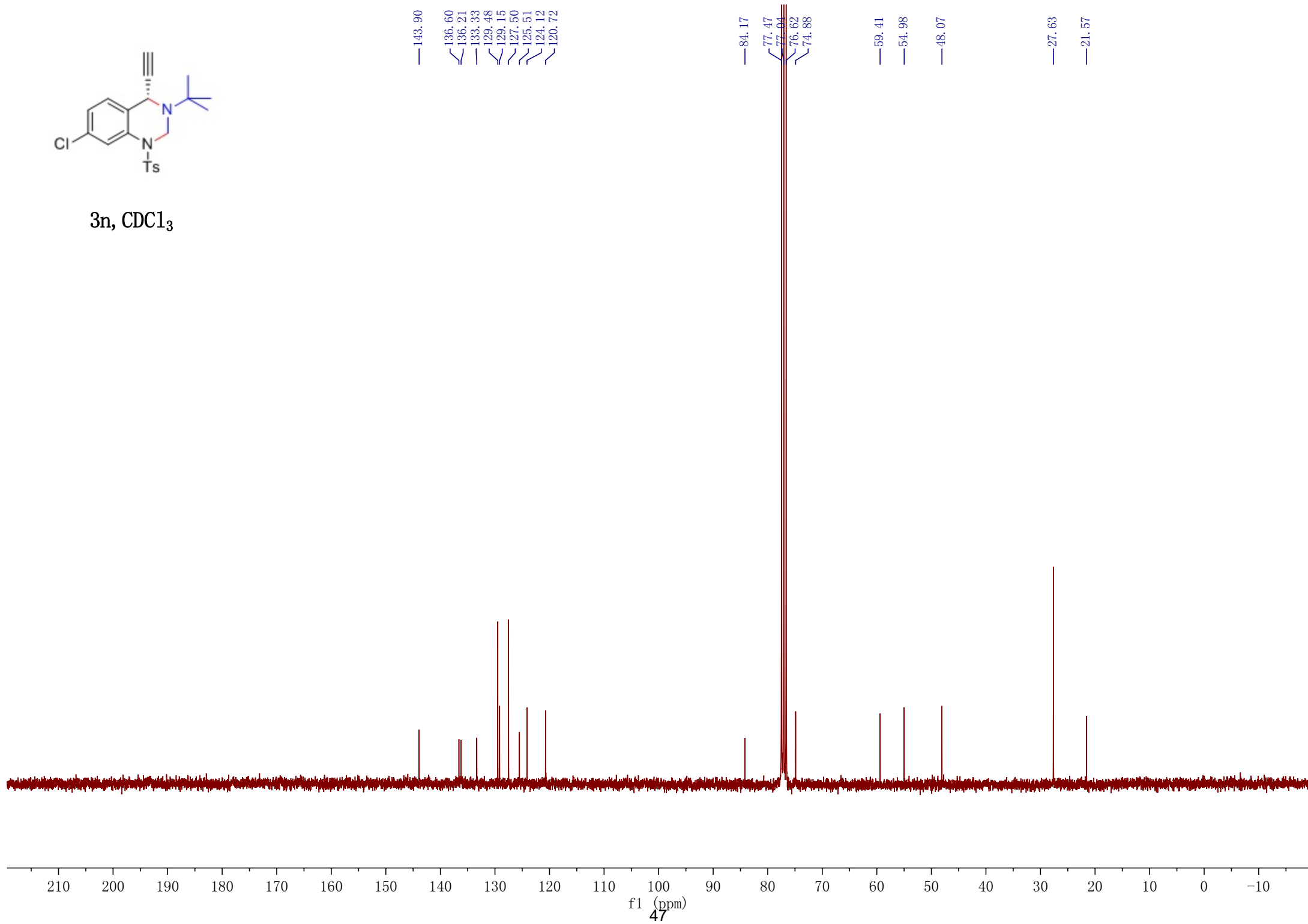
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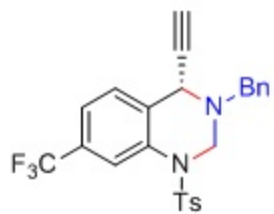




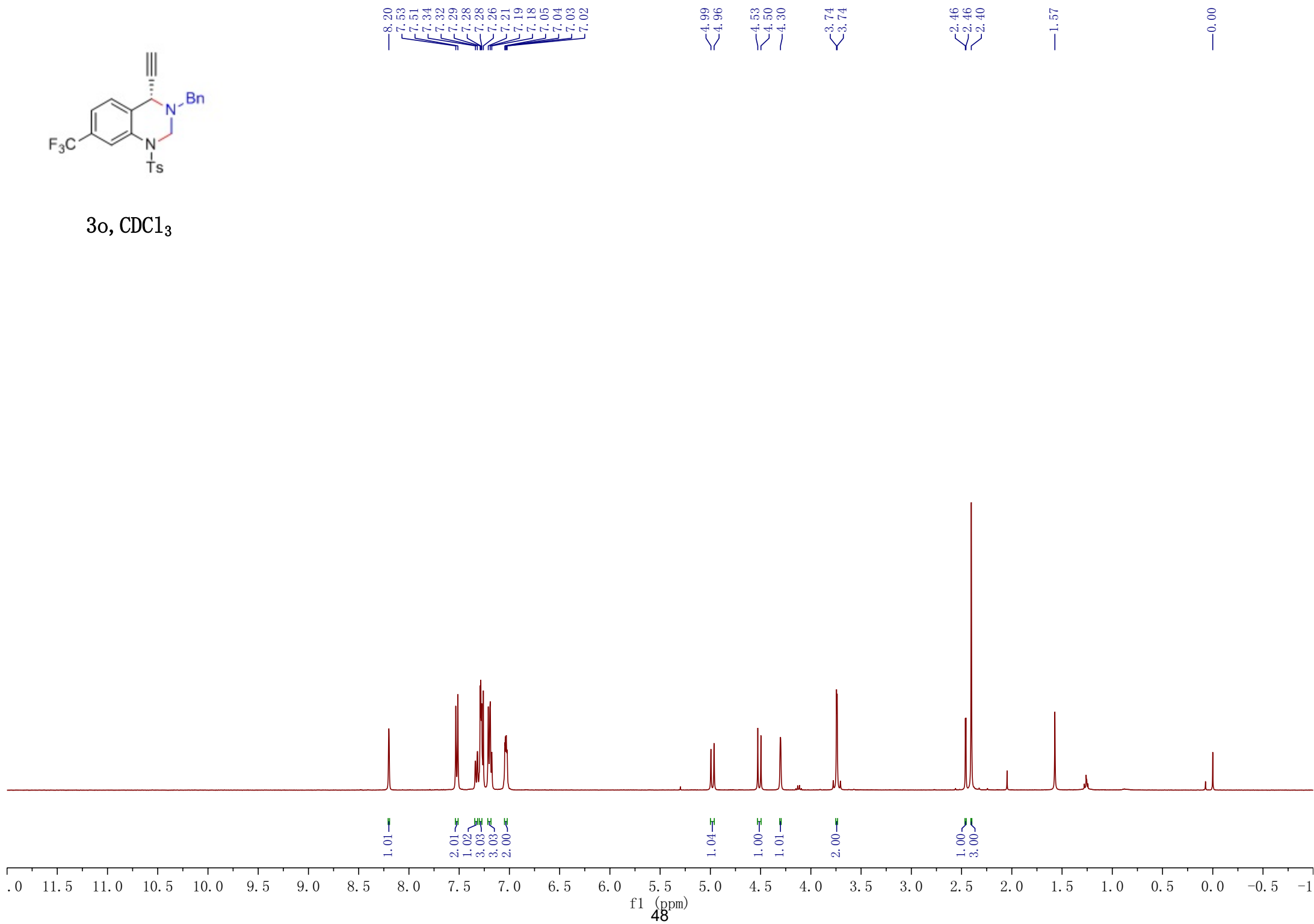


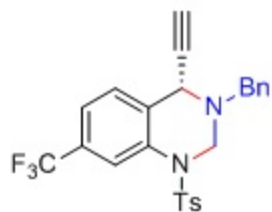
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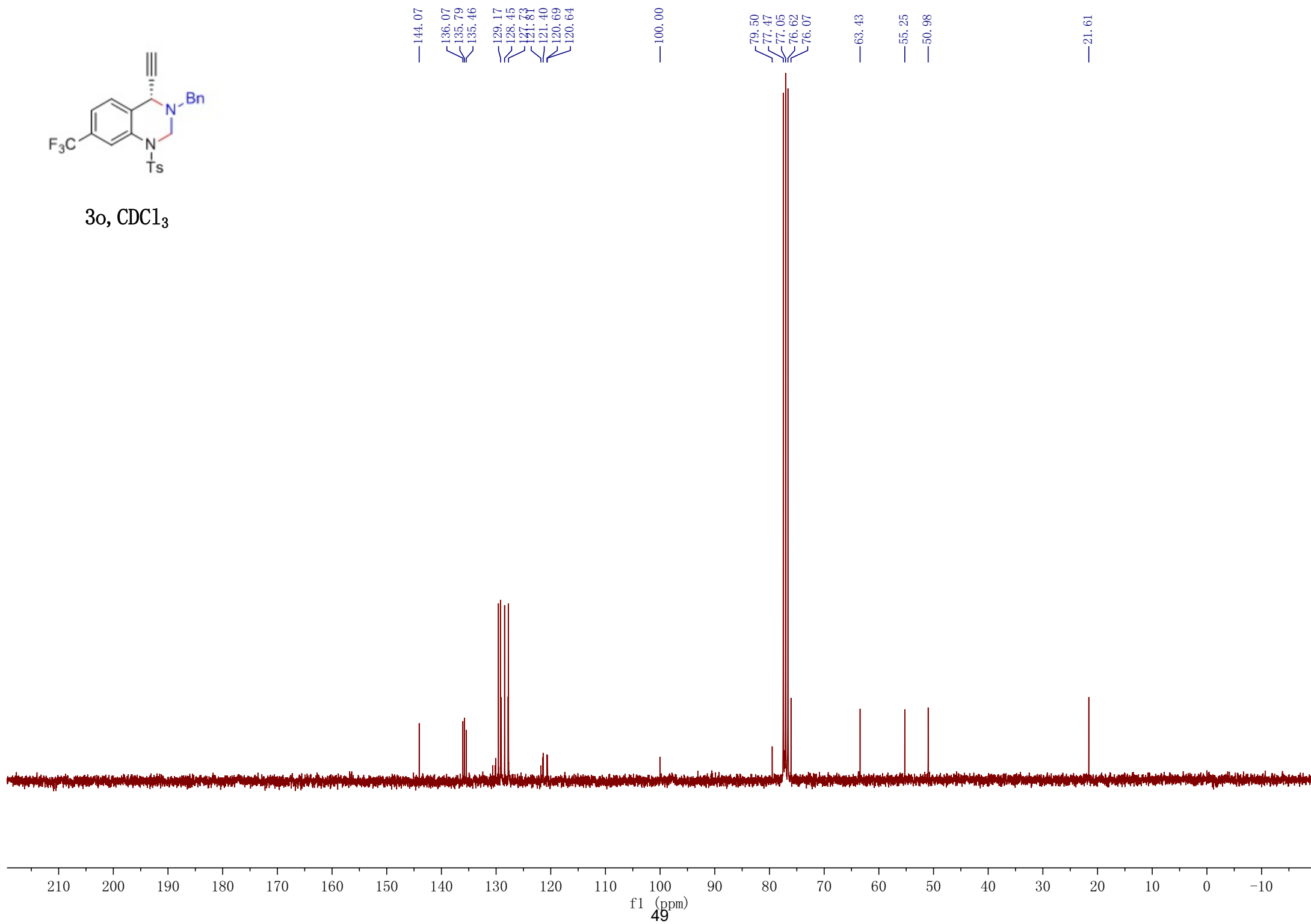


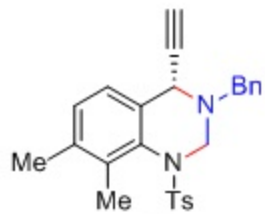
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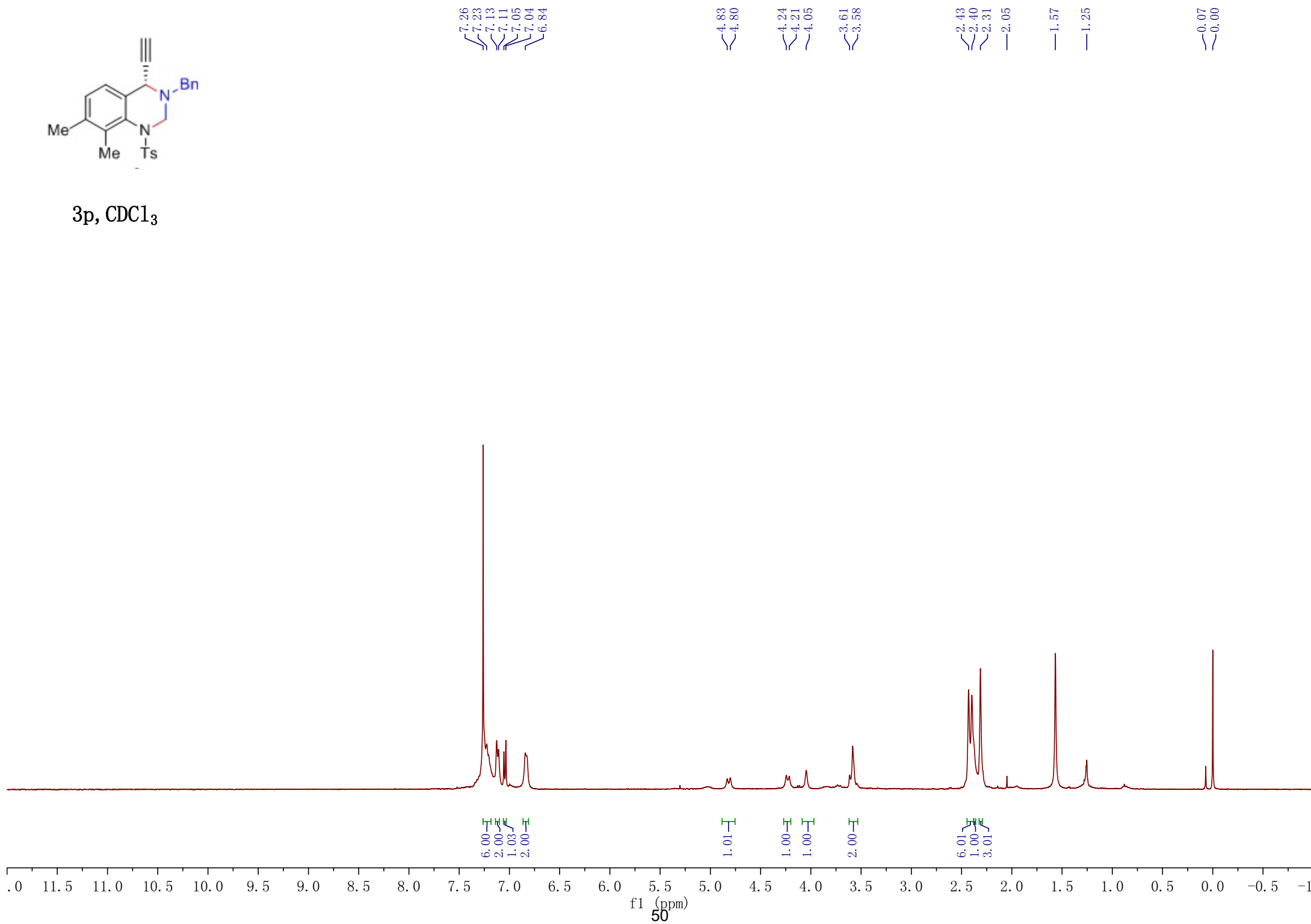


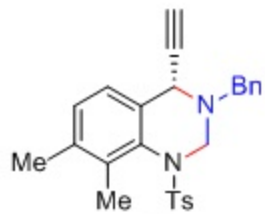
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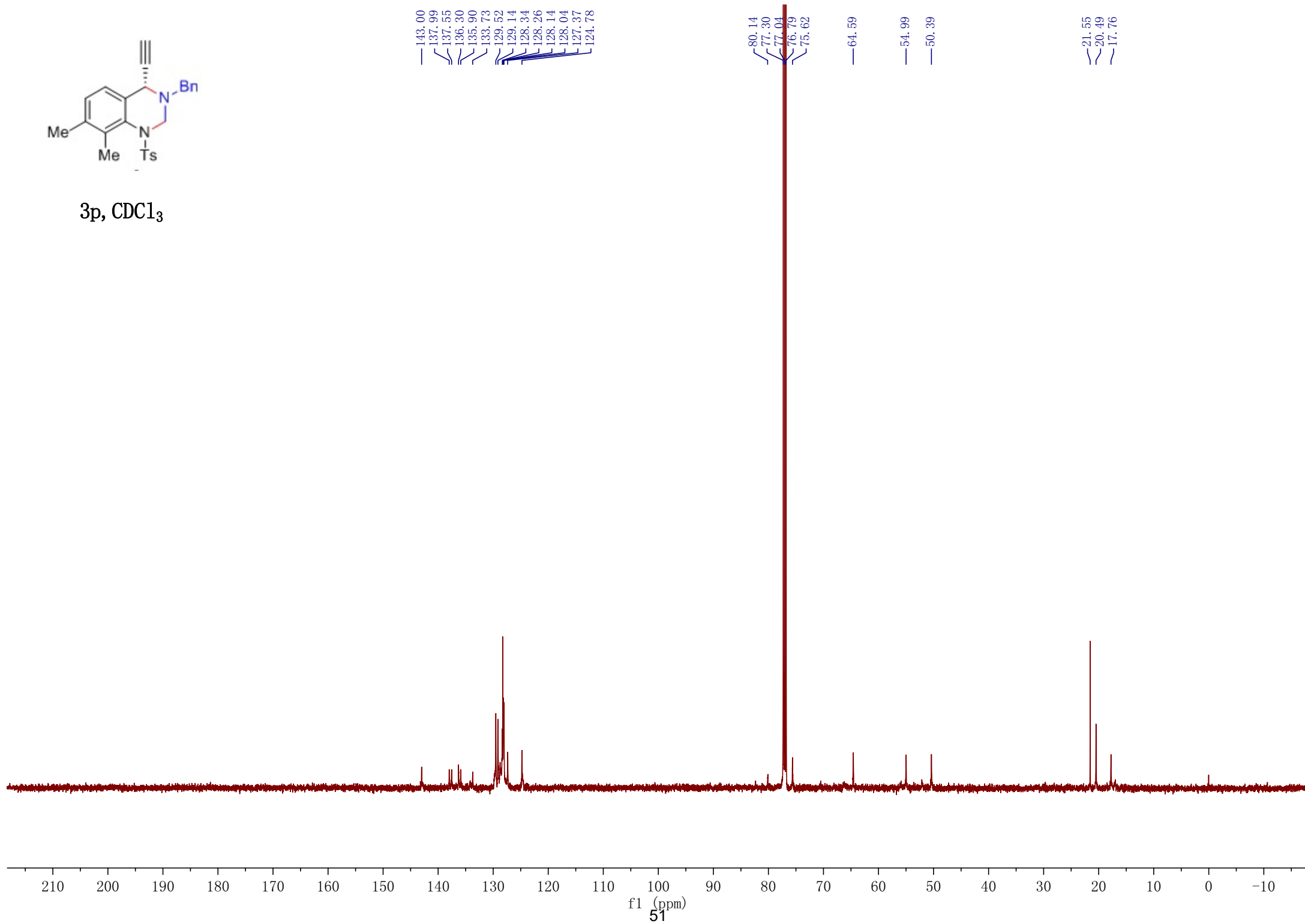


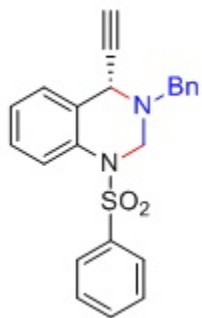
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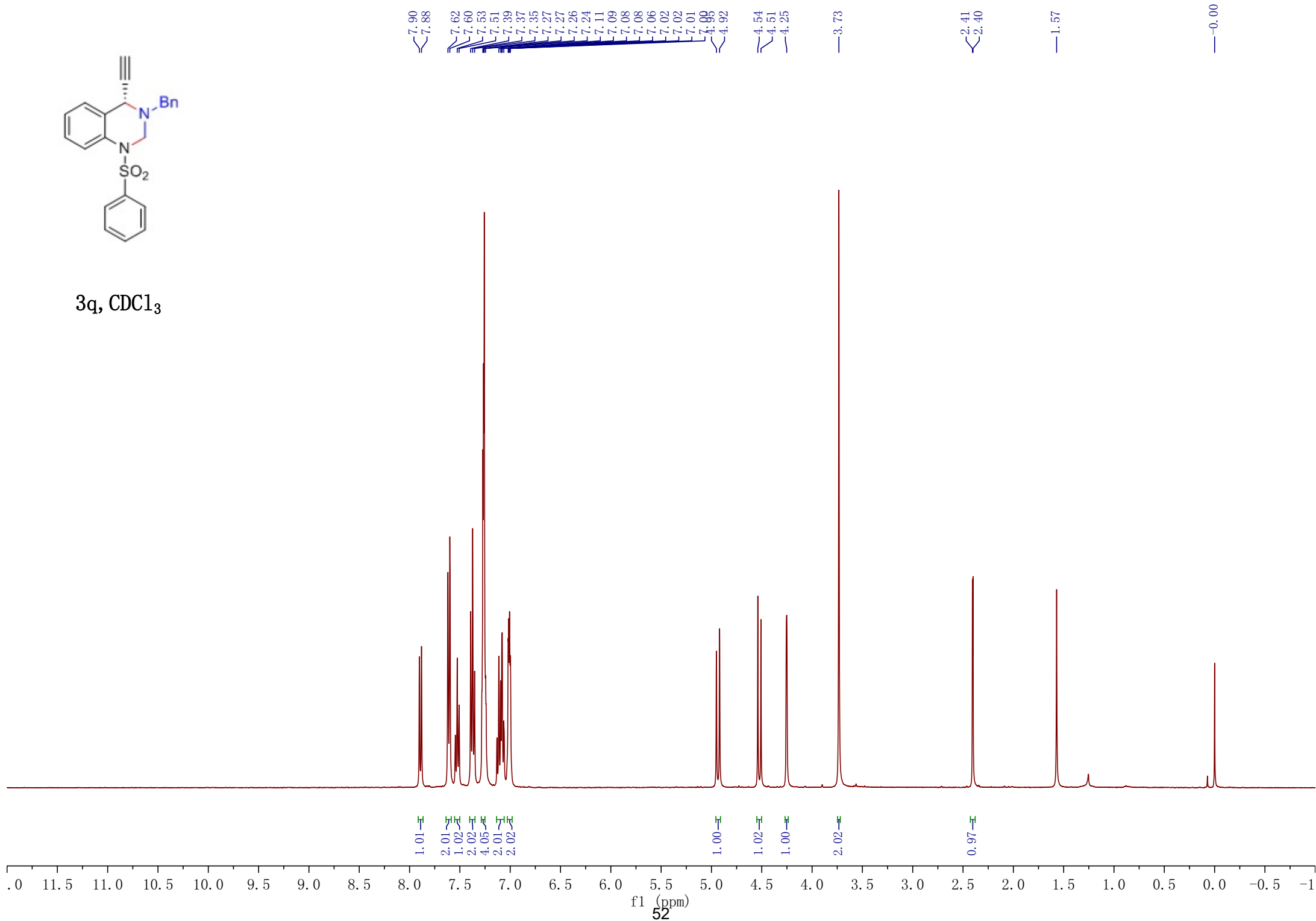


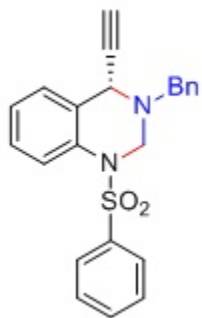
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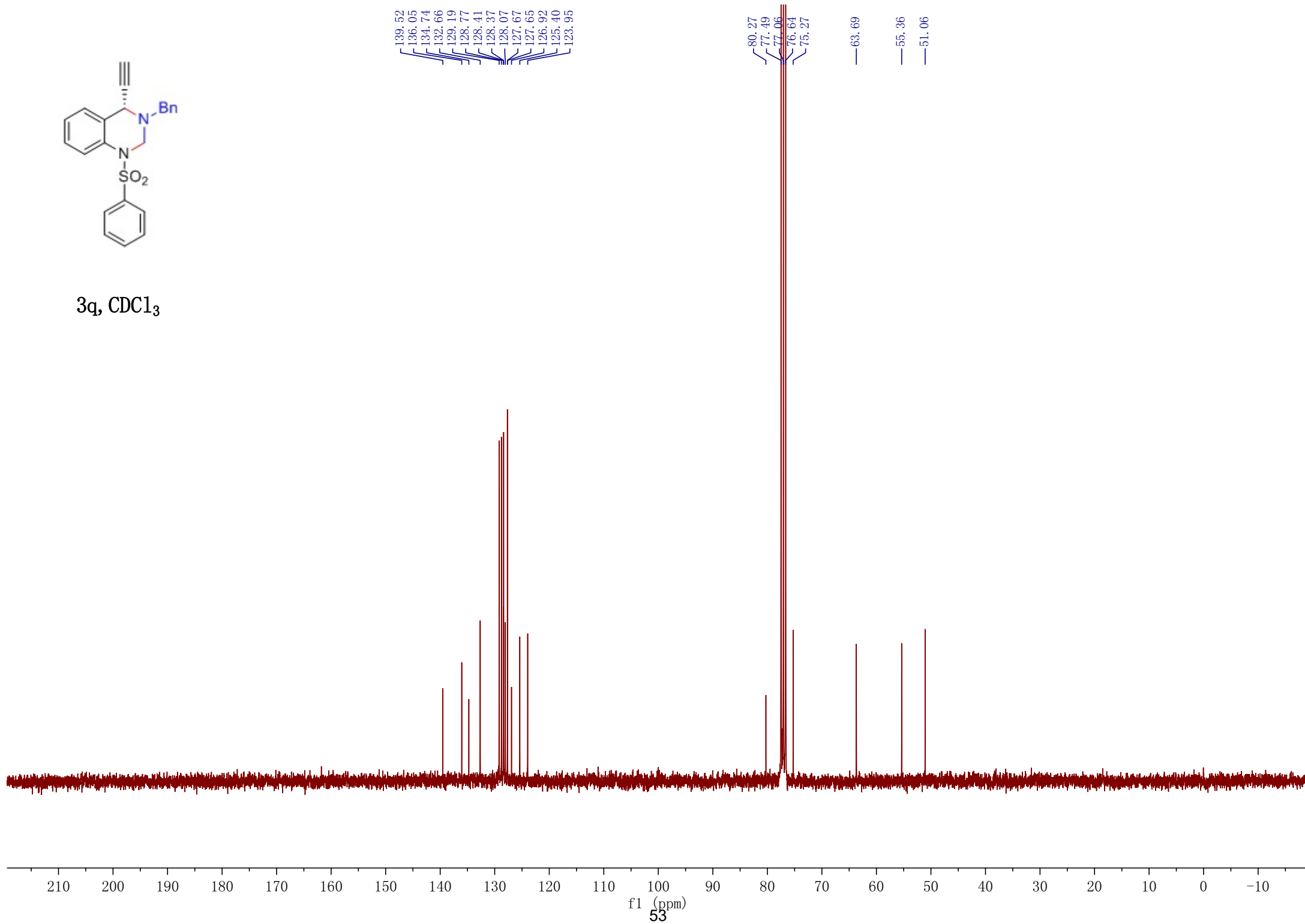


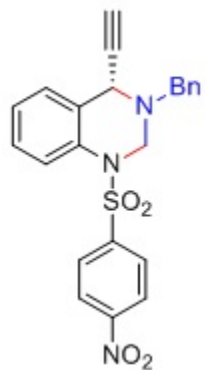
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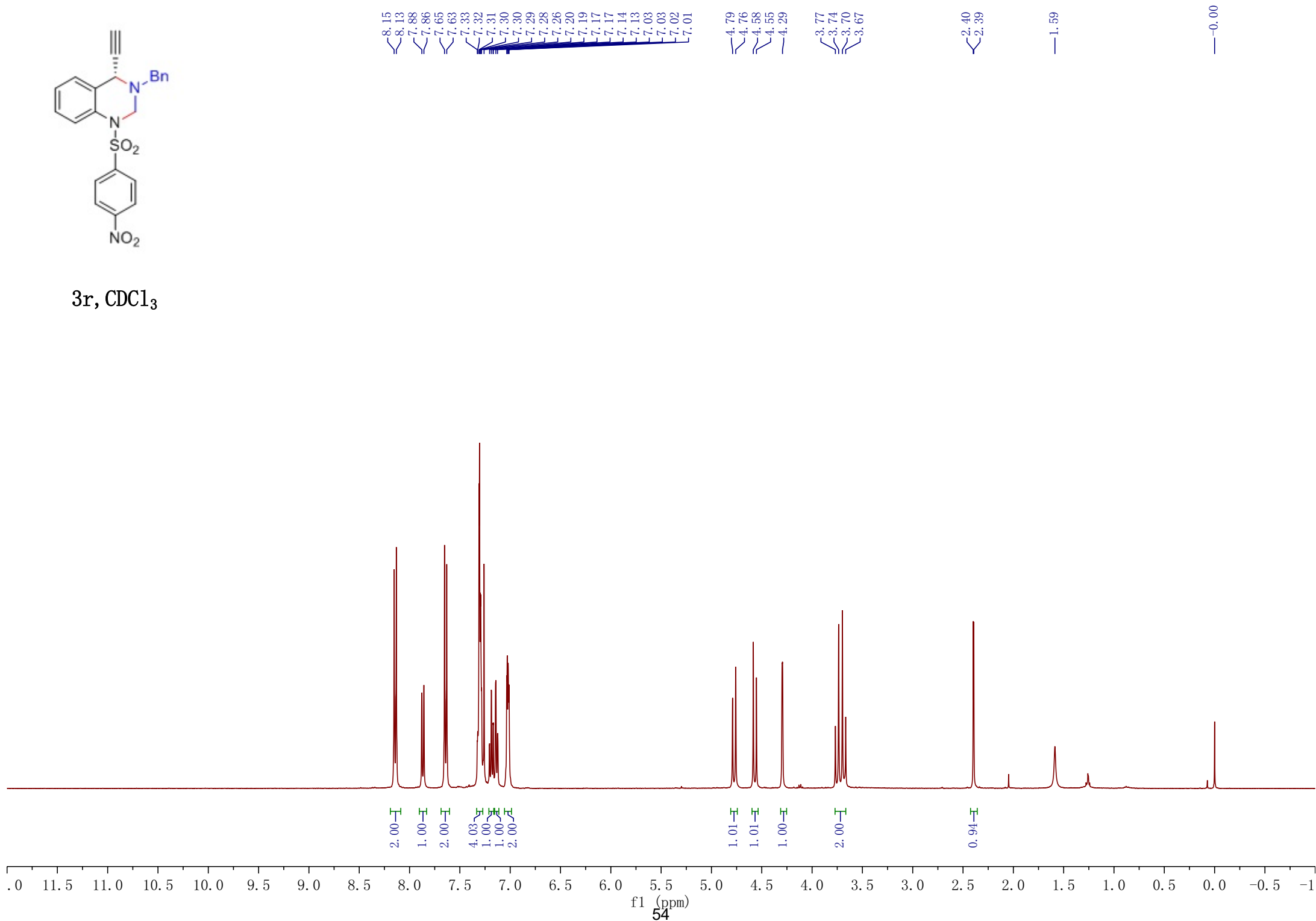


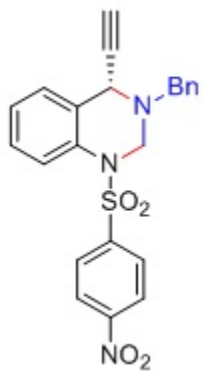
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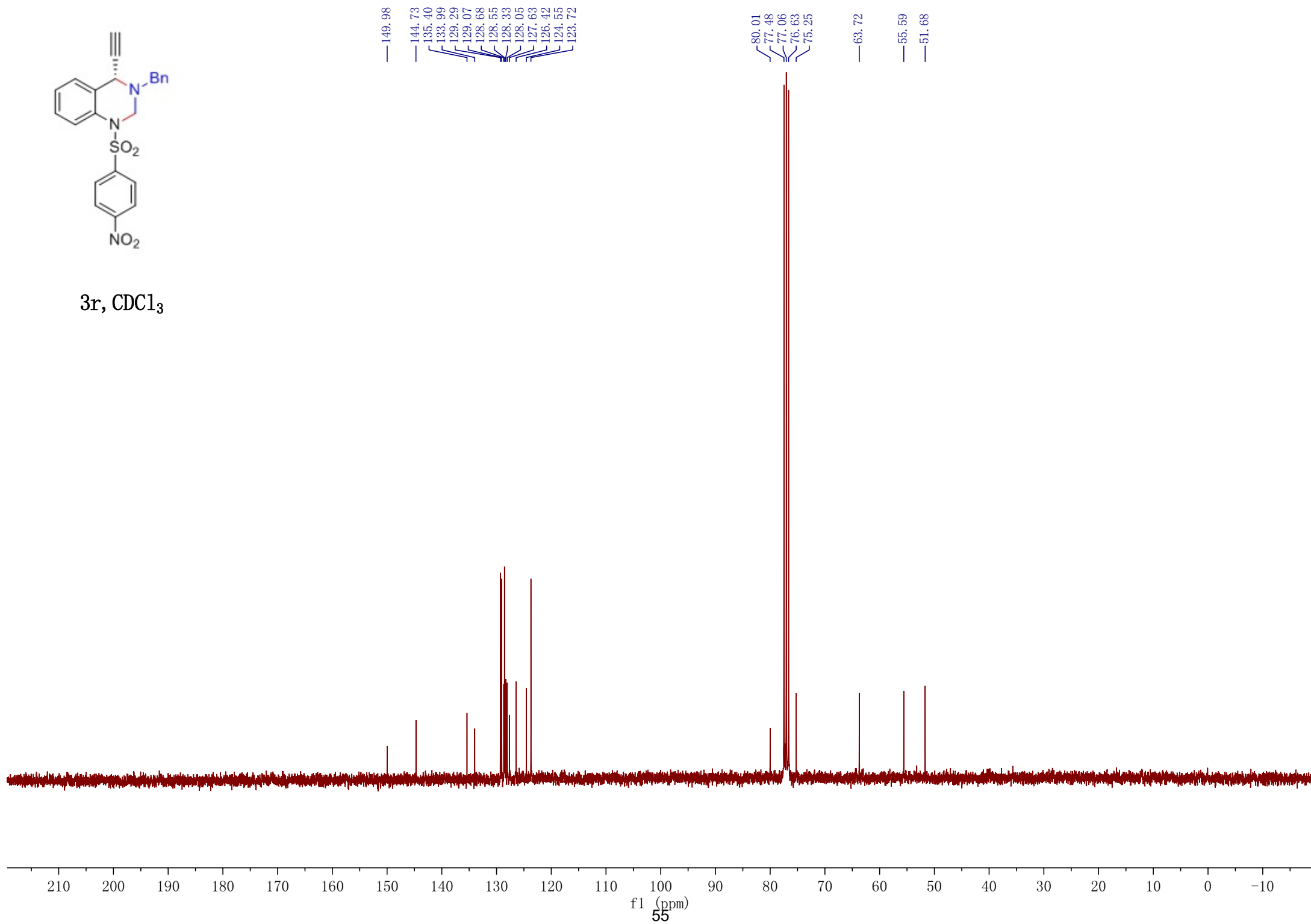


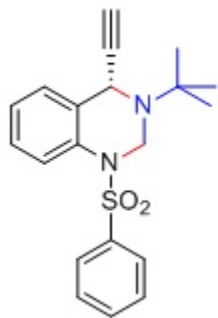
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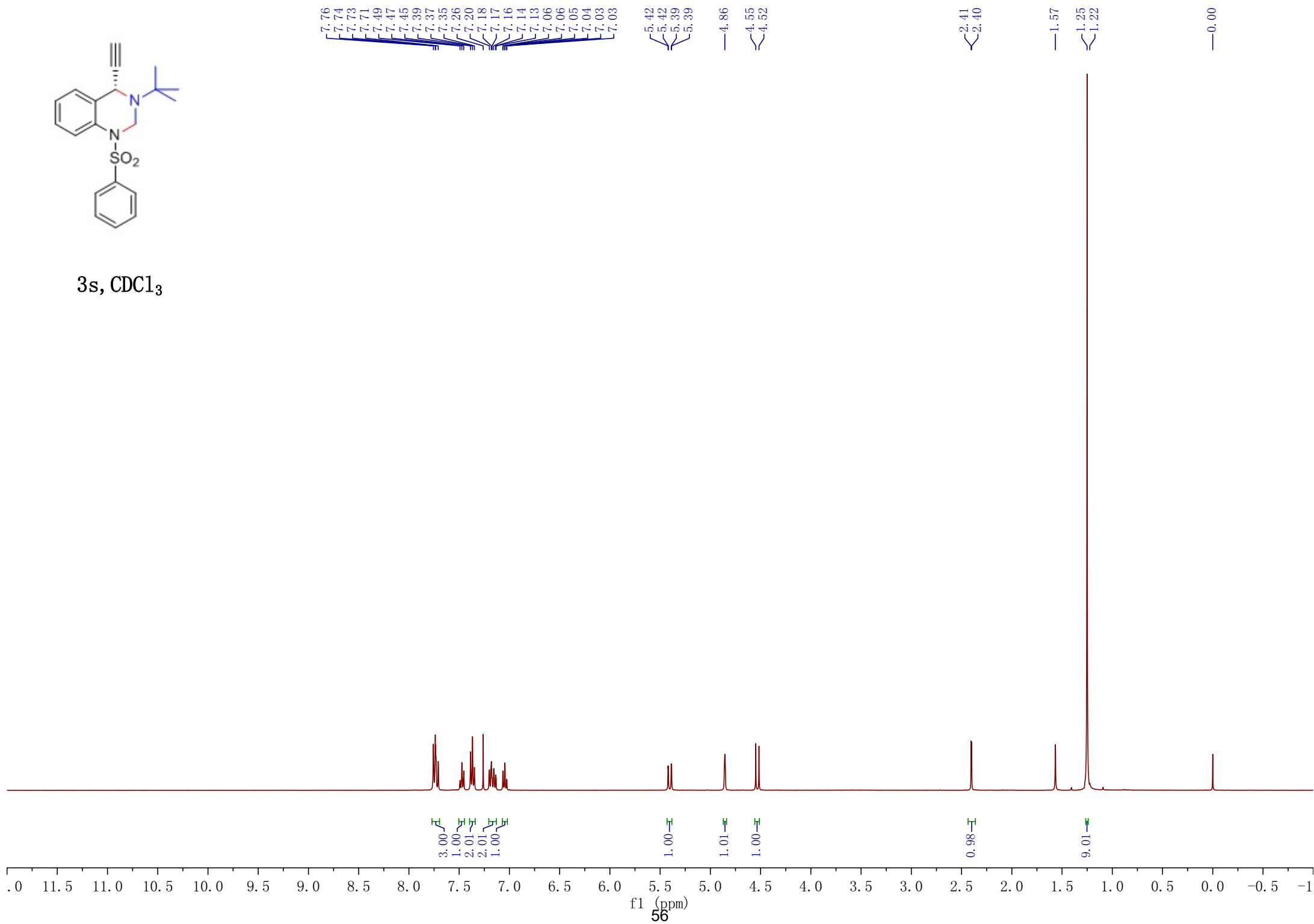


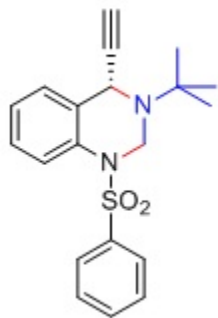
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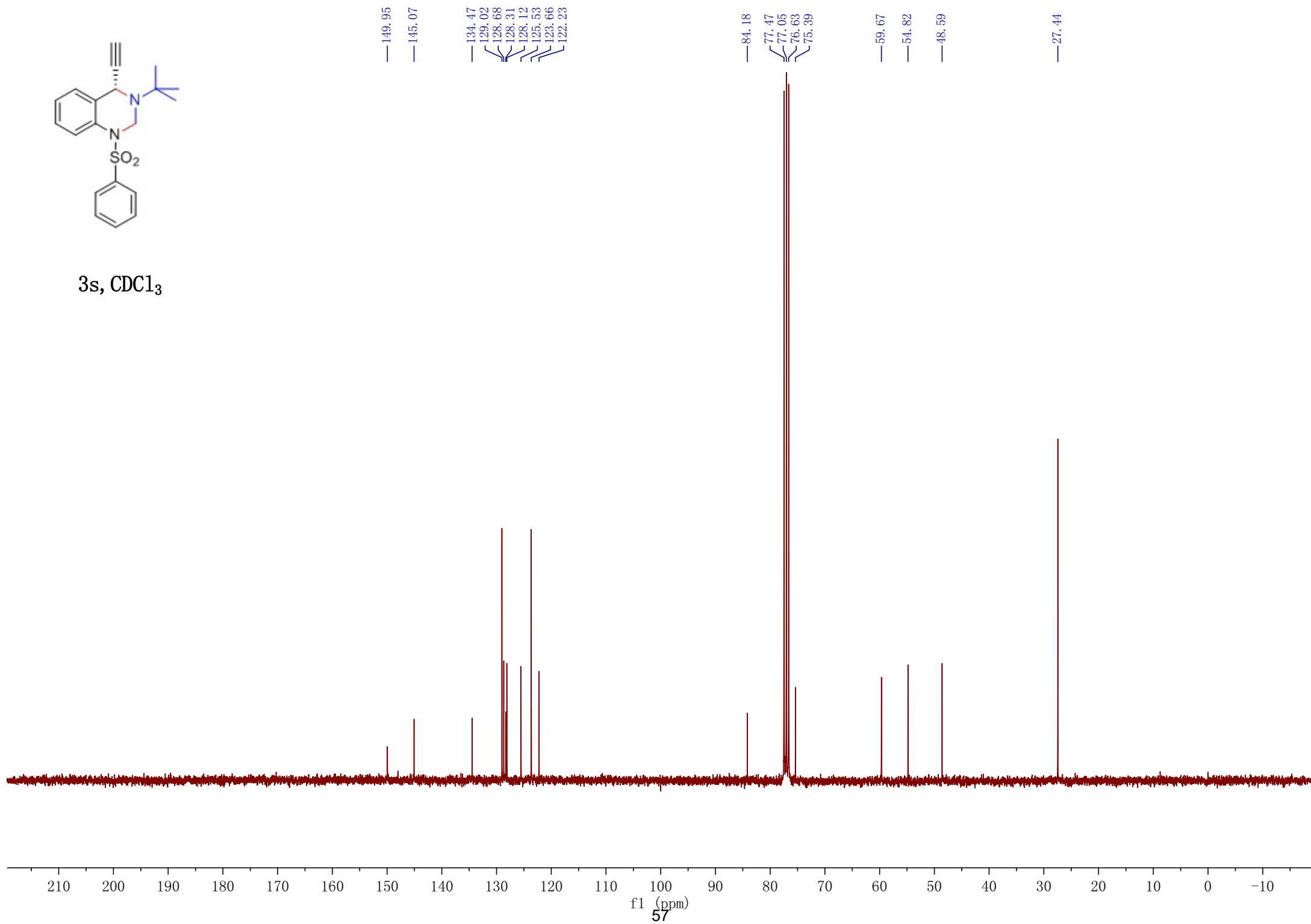


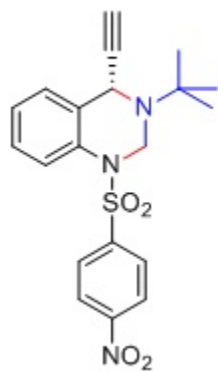
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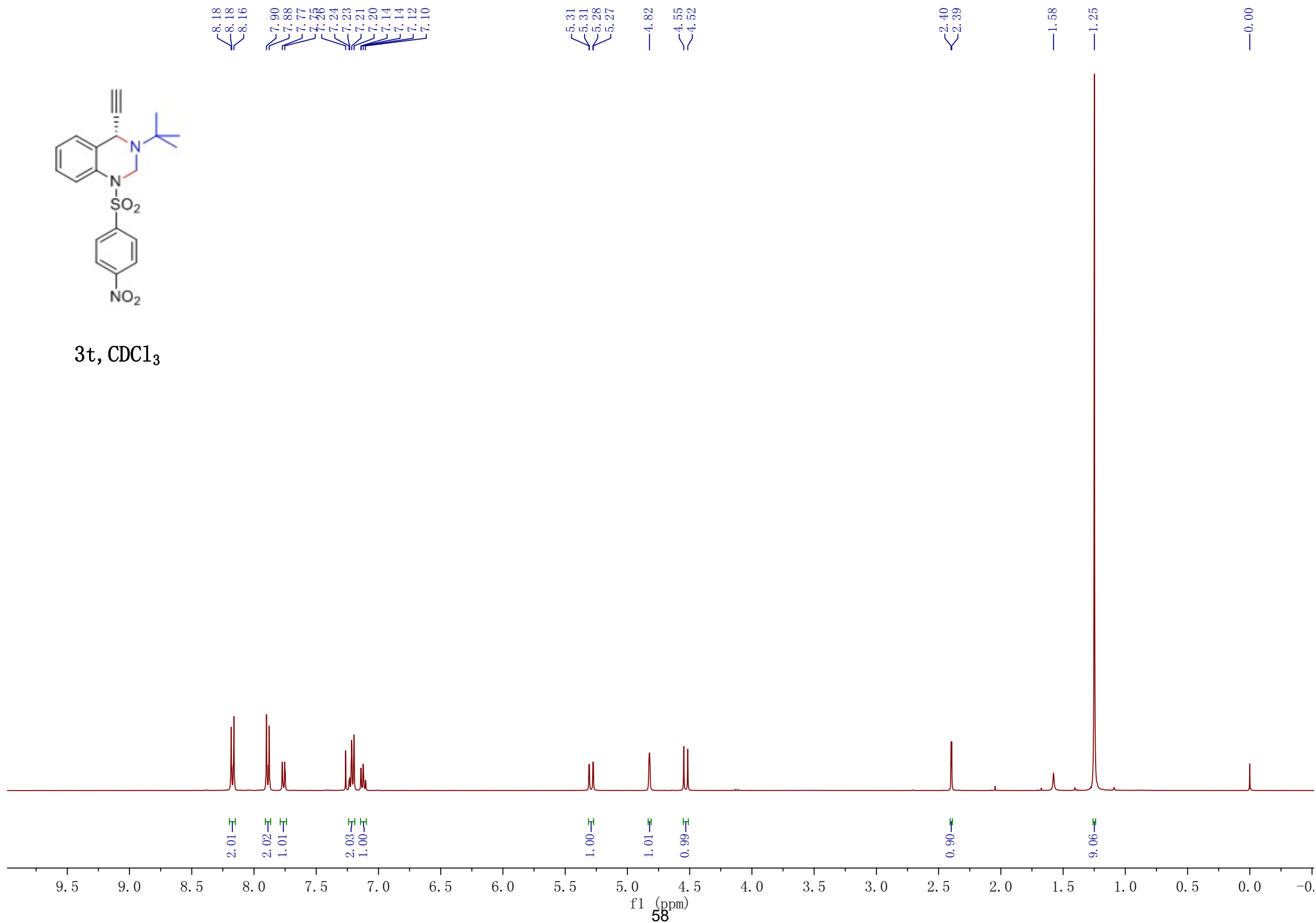


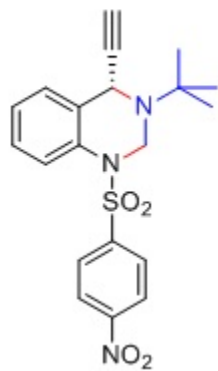
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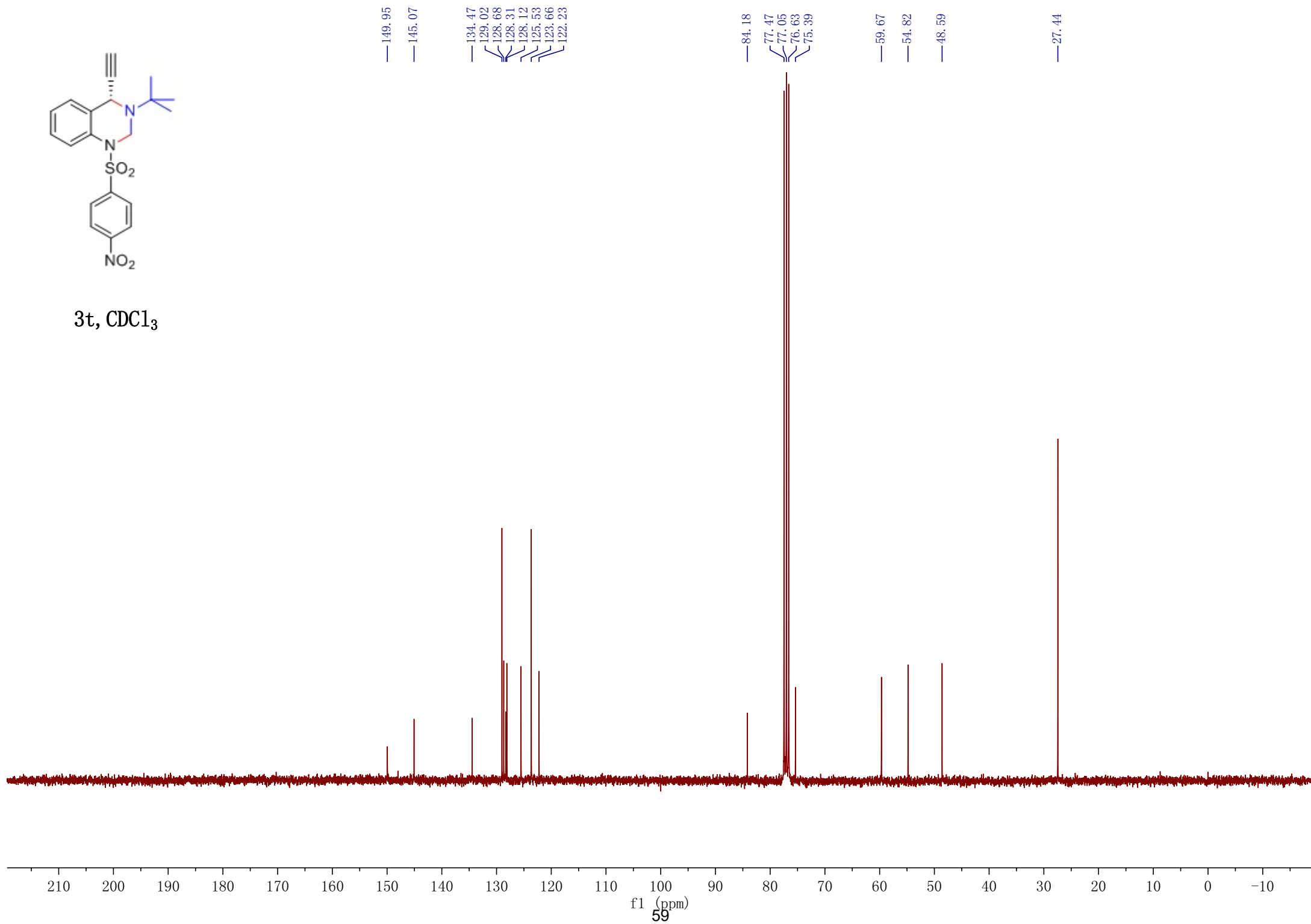


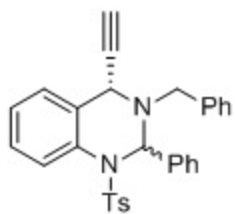
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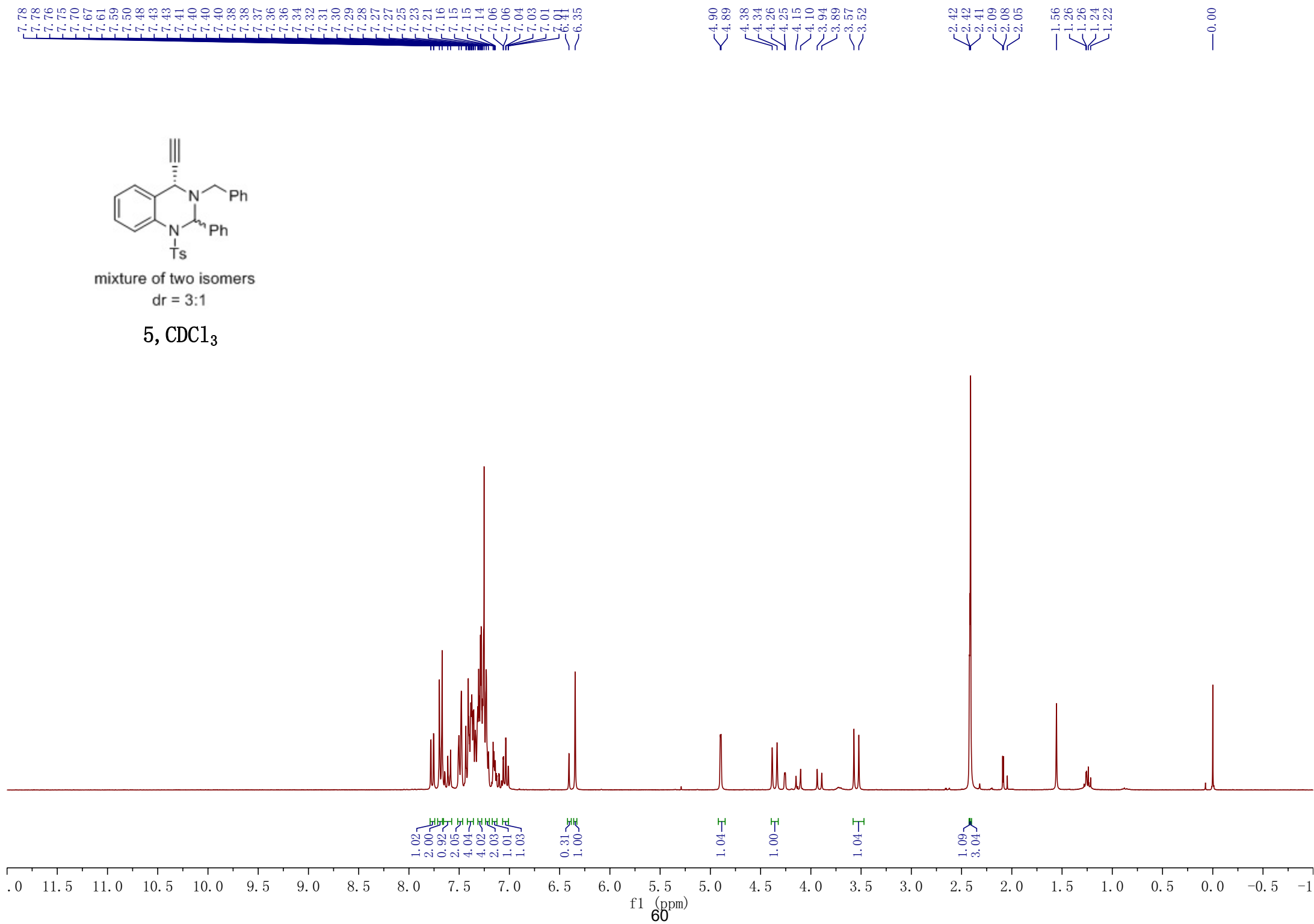
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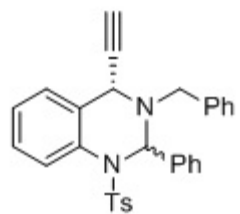




mixture of two isomers
dr = 3:1

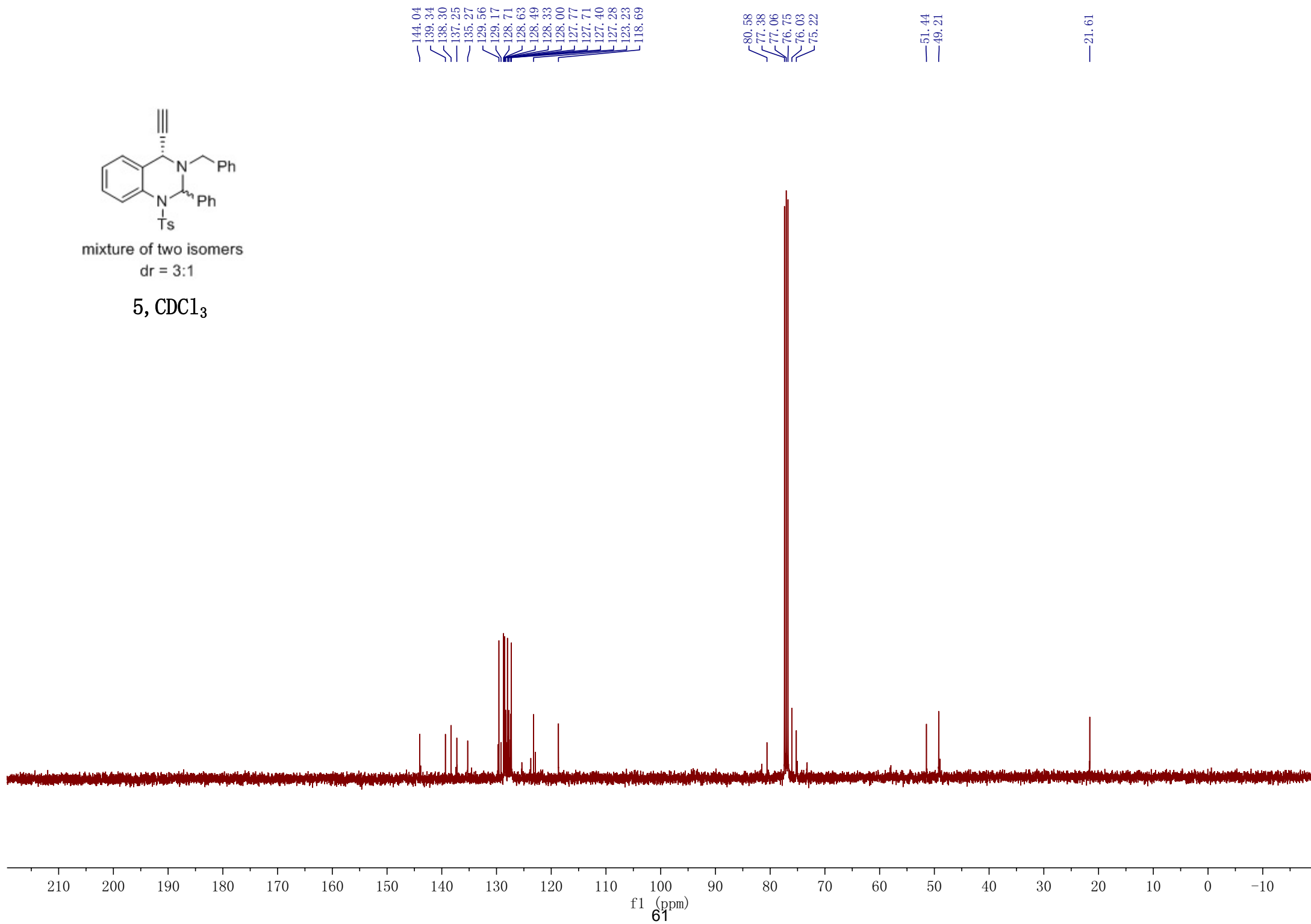
5, CDCl₃

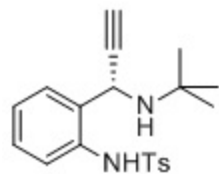




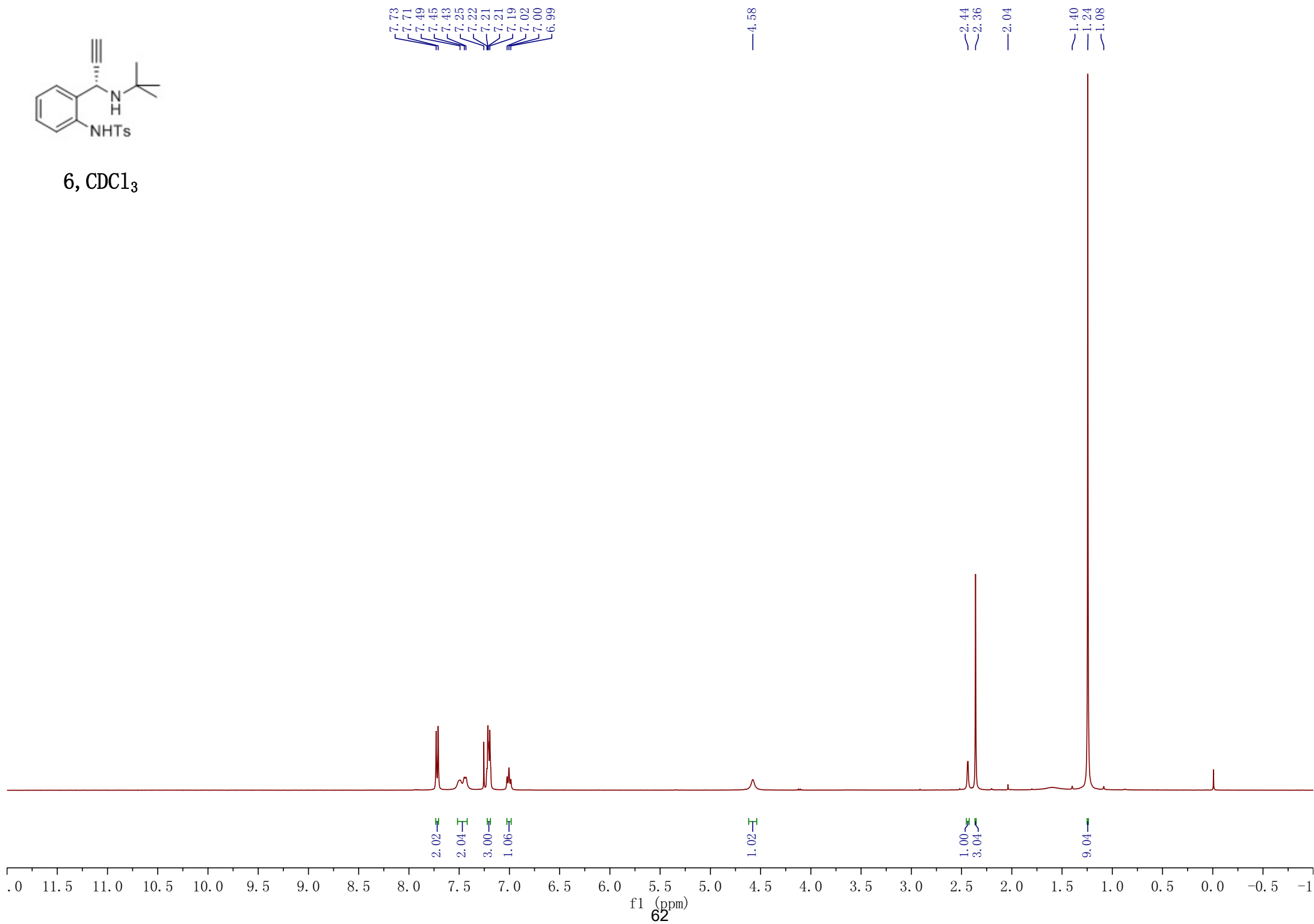
mixture of two isomers
dr = 3:1

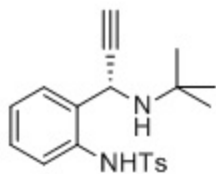
5, CDCl_3



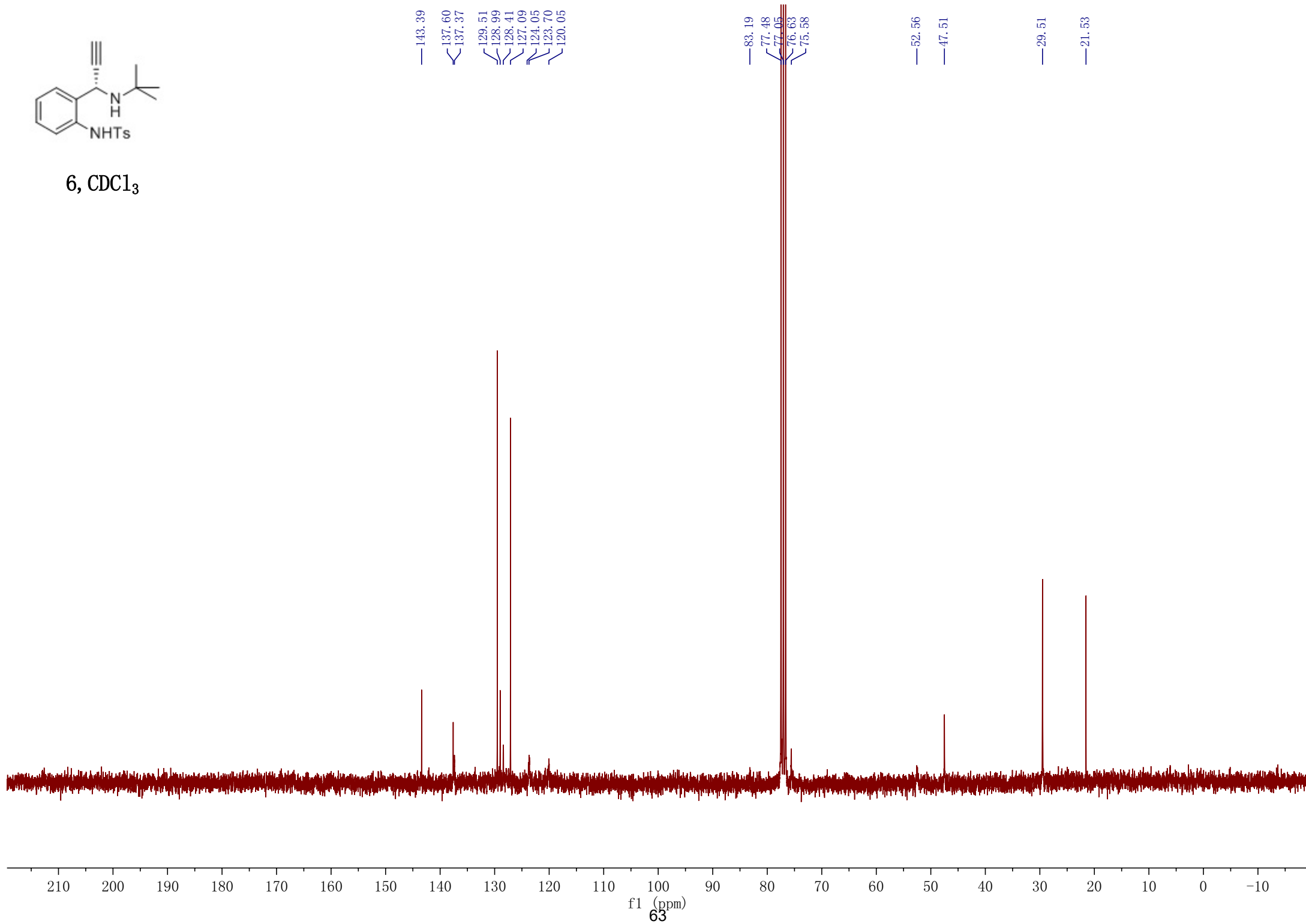


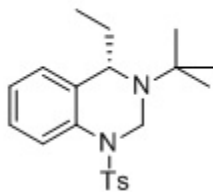
6, CDCl₃



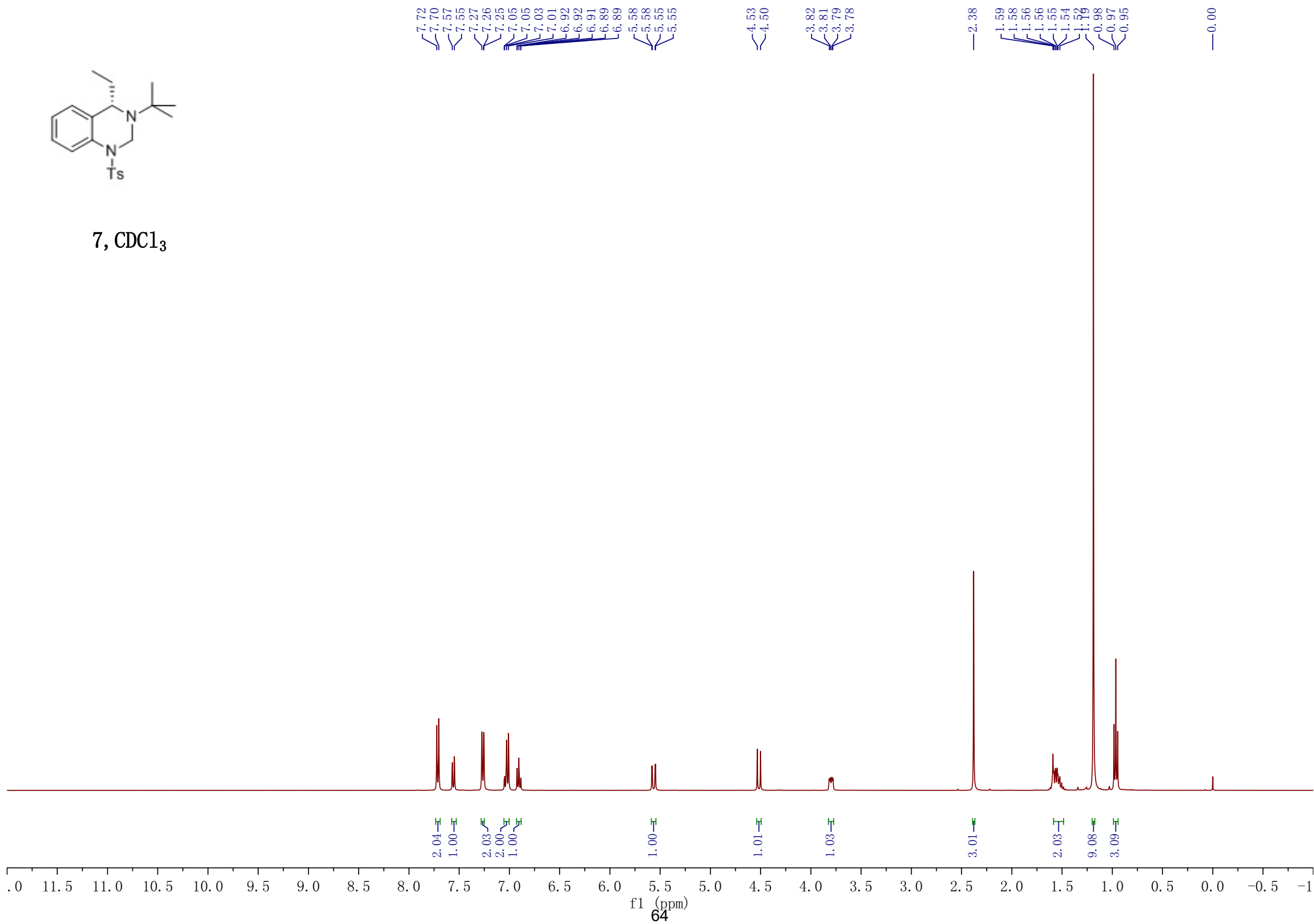


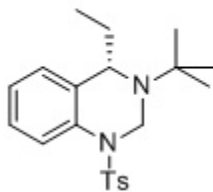
6, CDCl_3



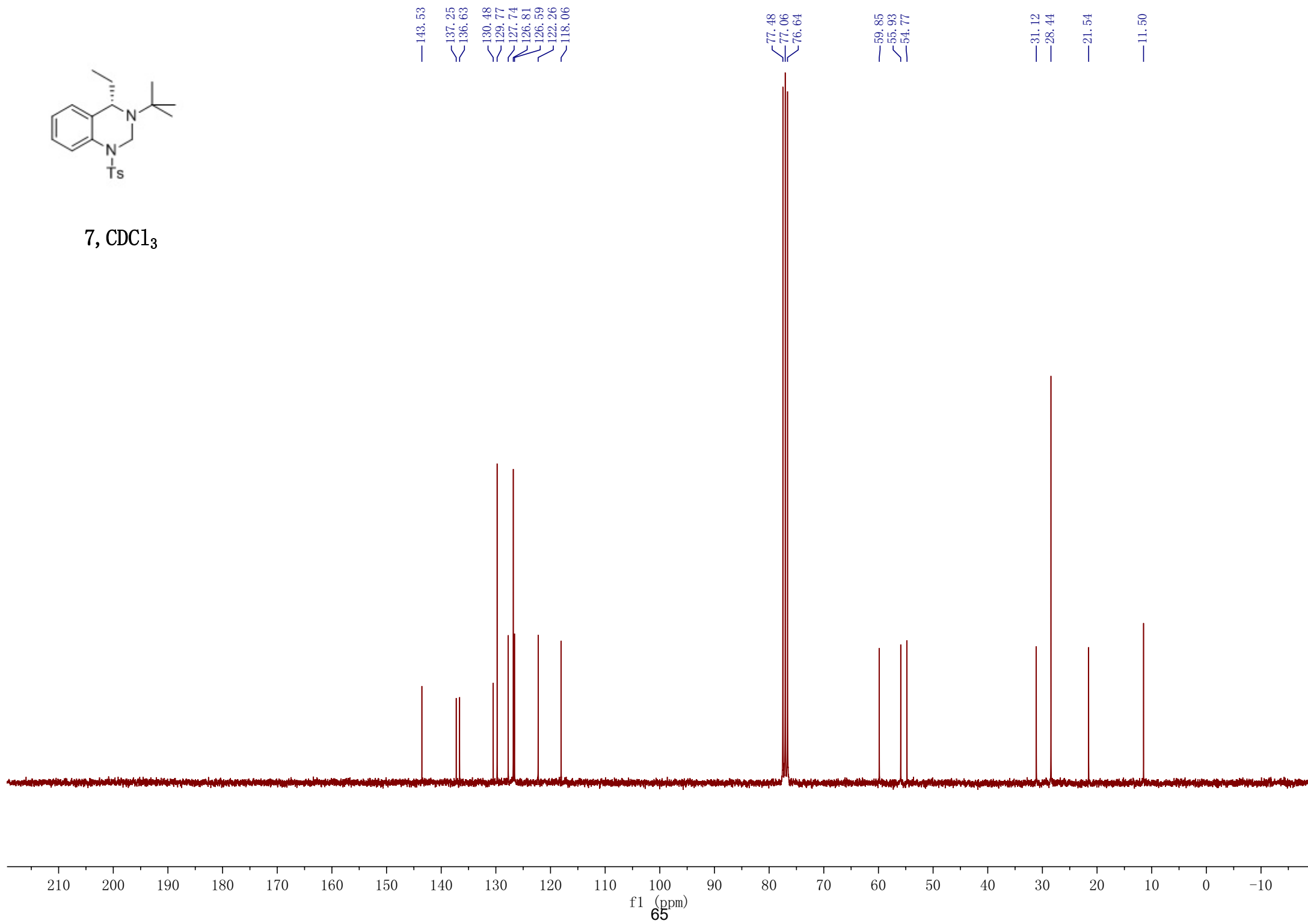


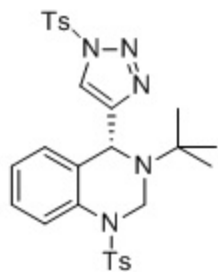
7, CDCl_3



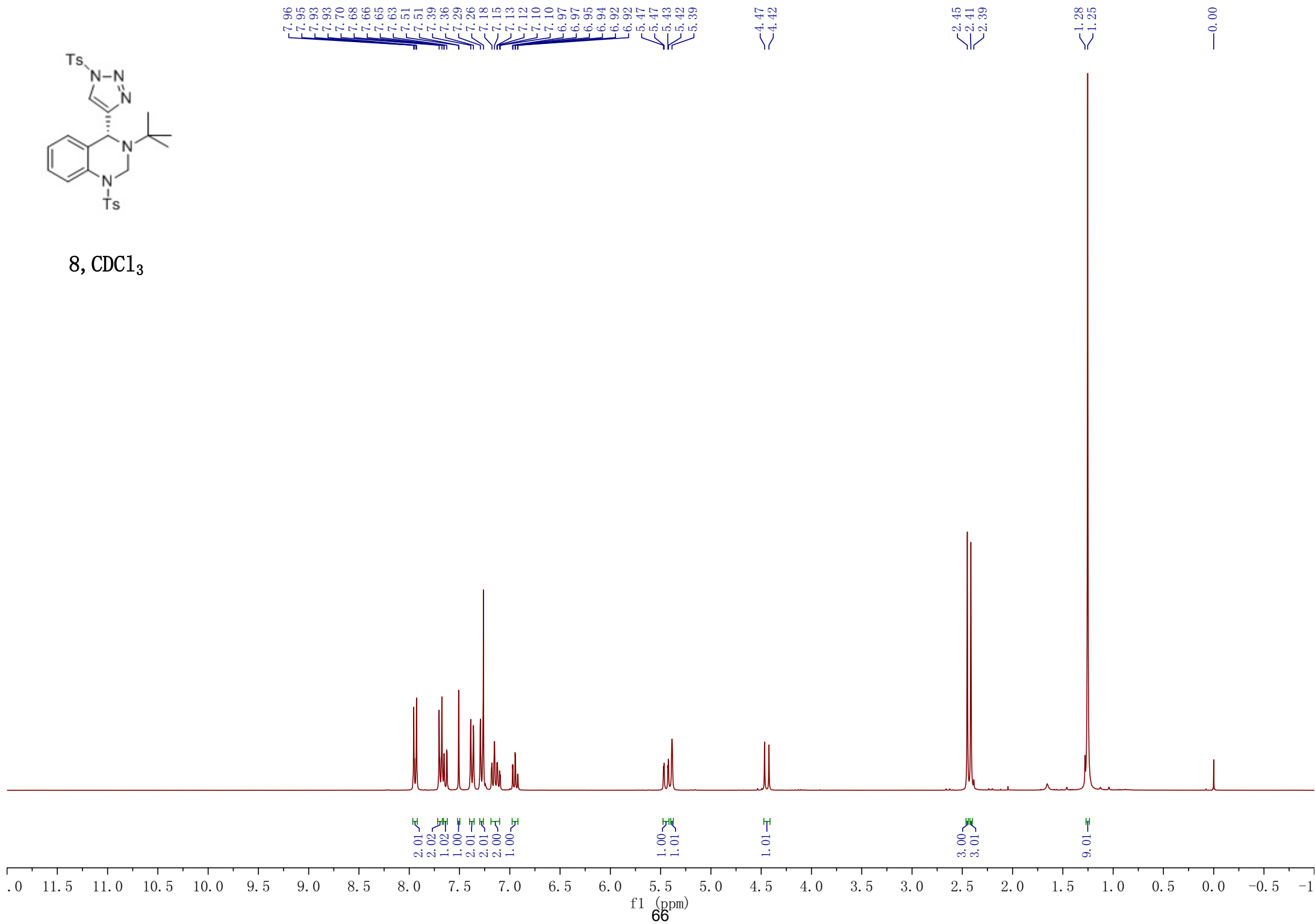


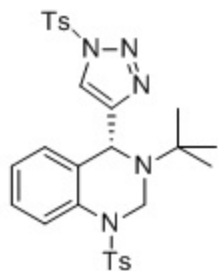
7, CDCl₃



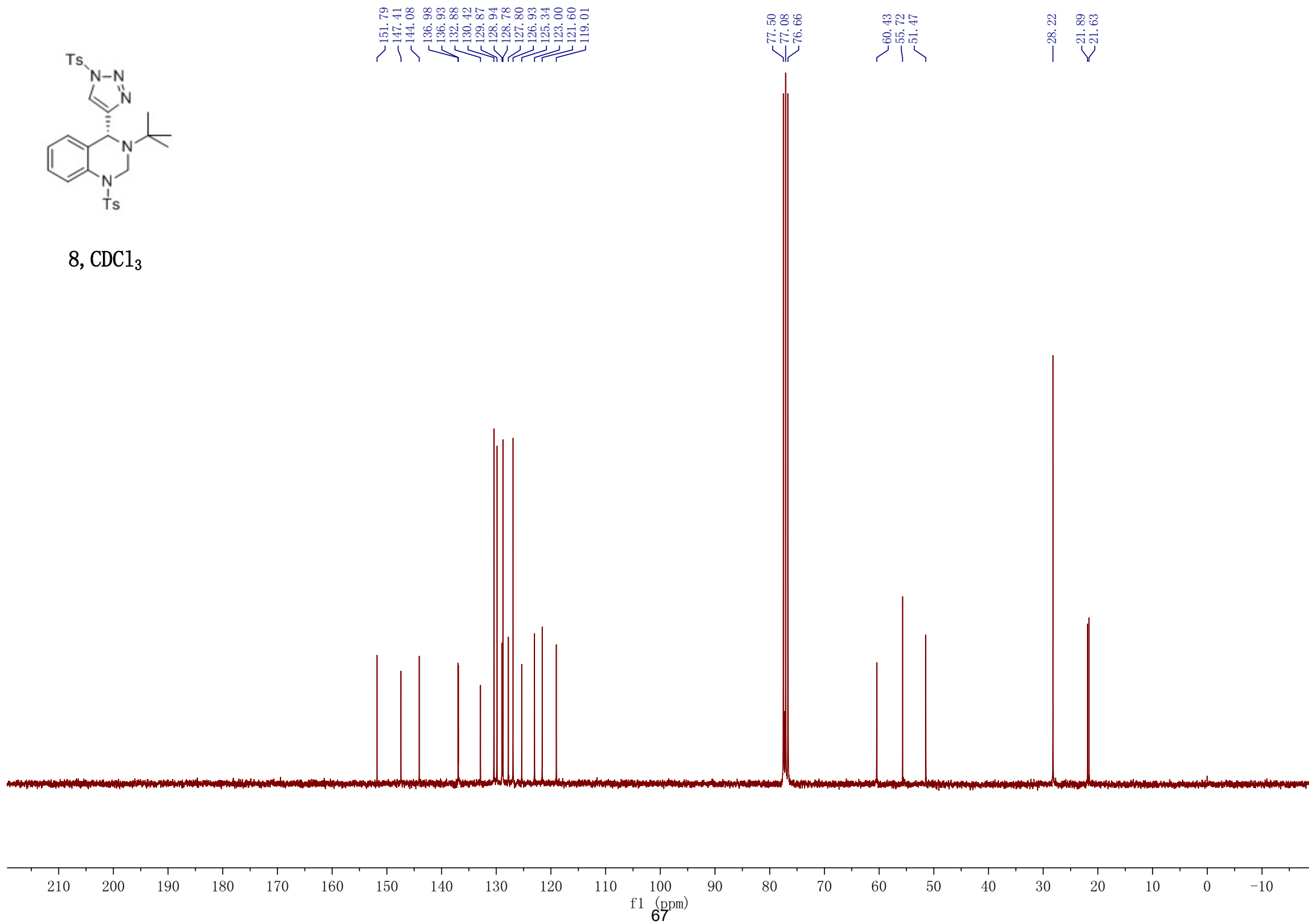


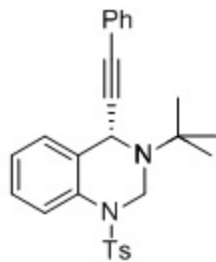
8, CDCl_3



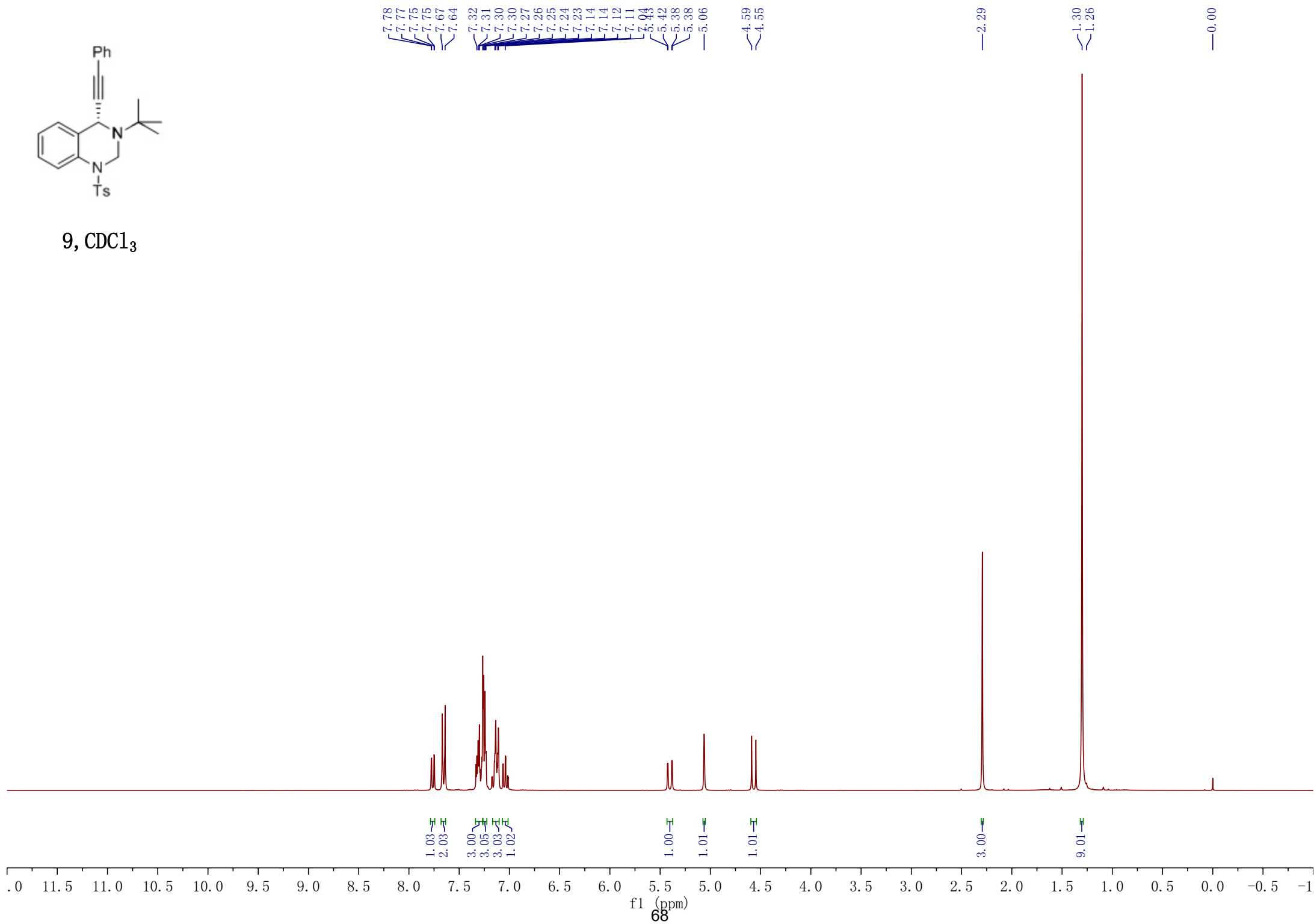


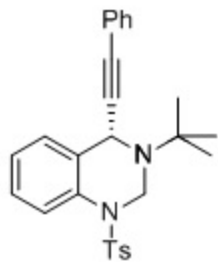
8, CDCl₃



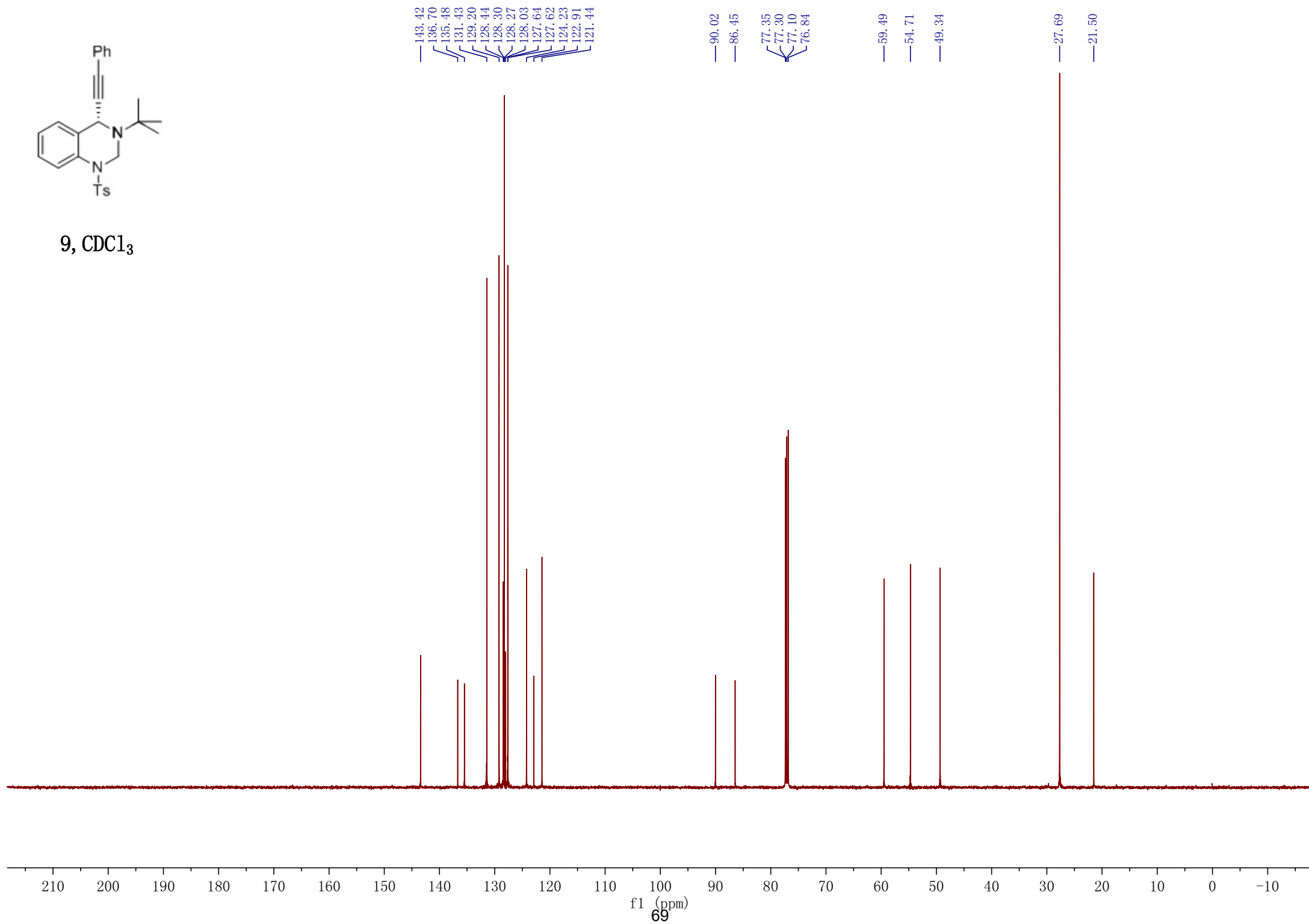


9, CDCl_3

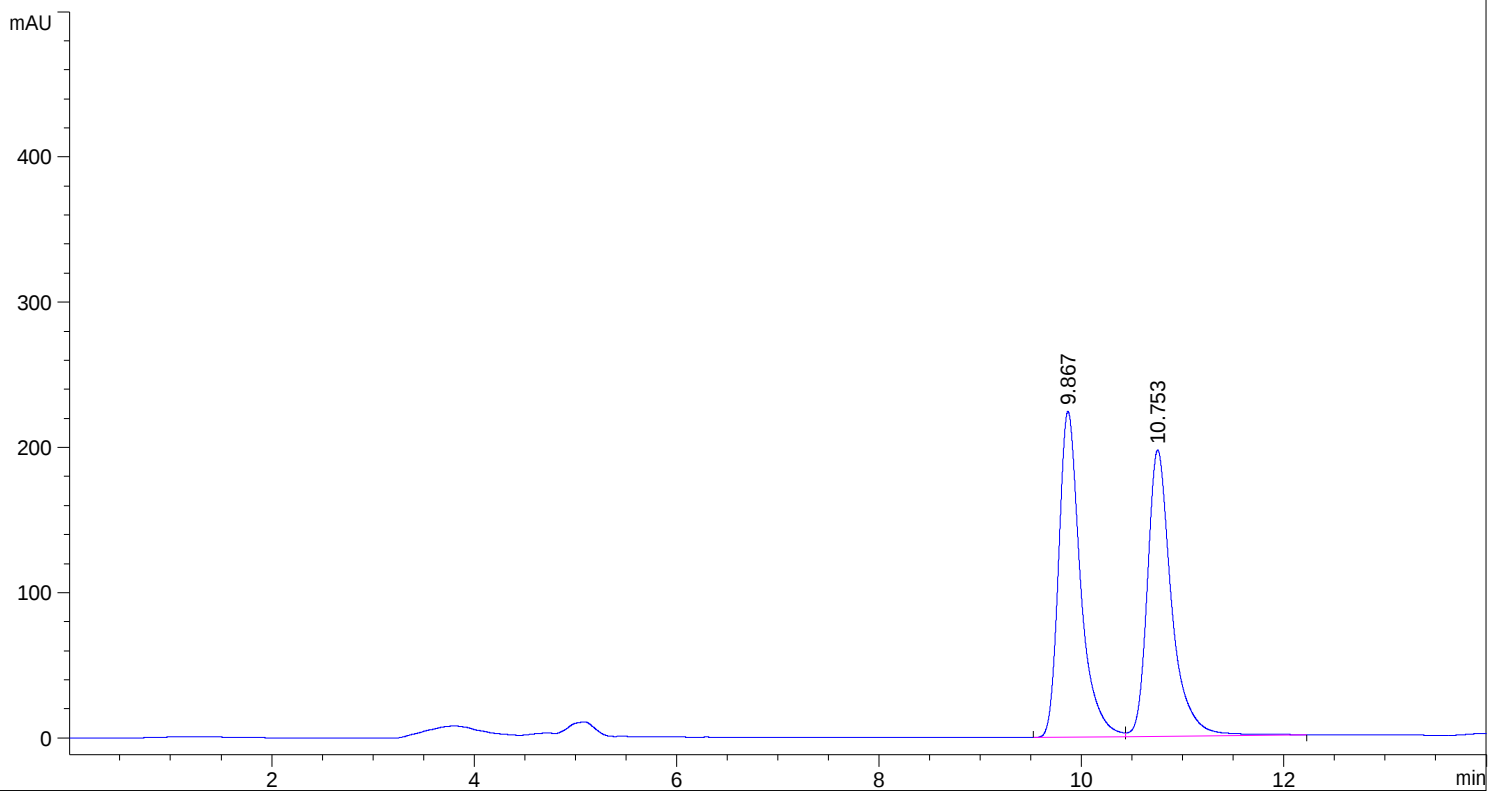




9, CDCl₃

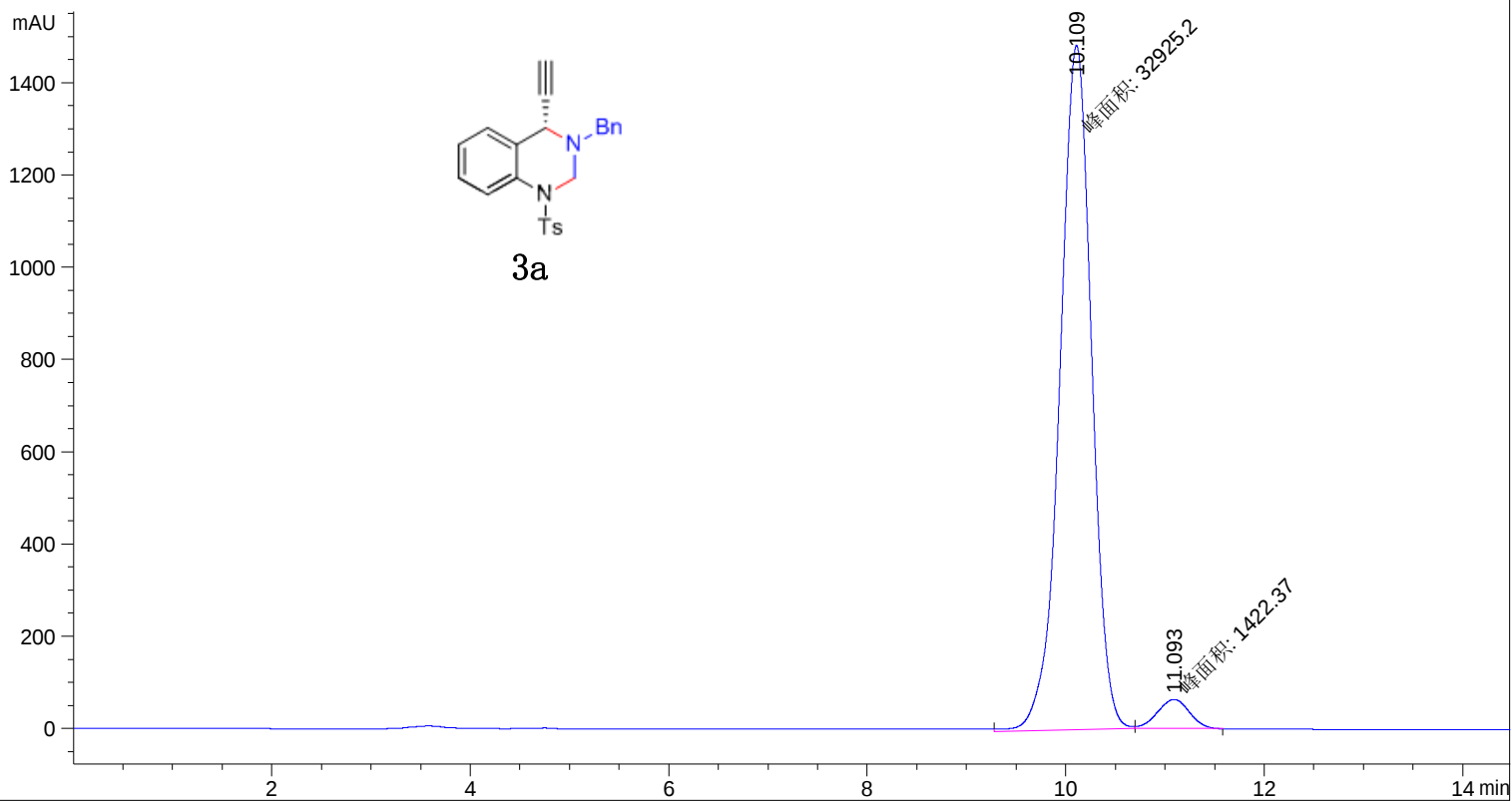


VWD1 A, Wavelength=254 nm



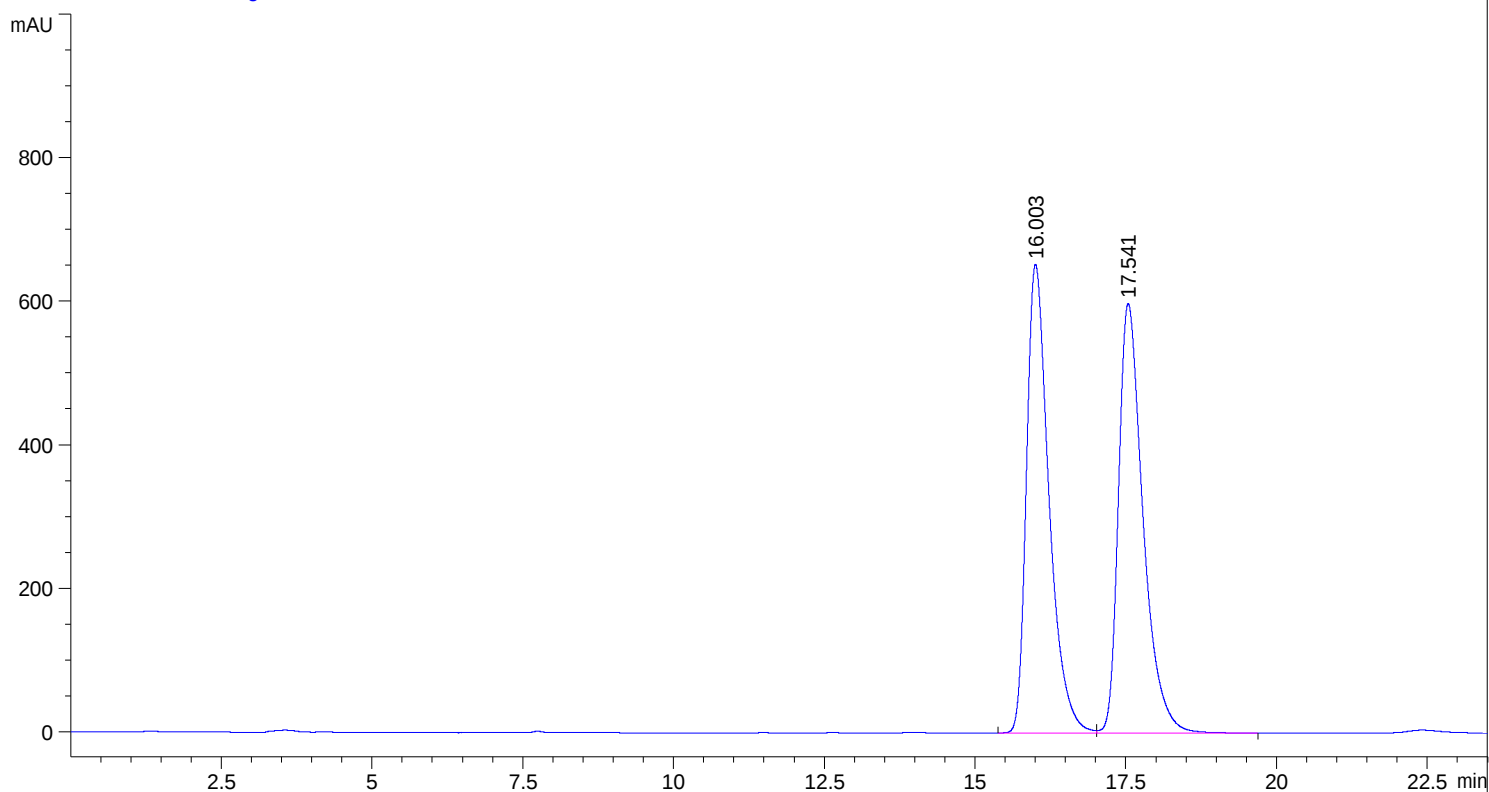
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	9.867	BV	0.2253	3363.58057	224.47545	50.7496
2	10.753	VB	0.2482	3264.21411	197.15384	49.2504

VWD1 A, Wavelength=254 nm



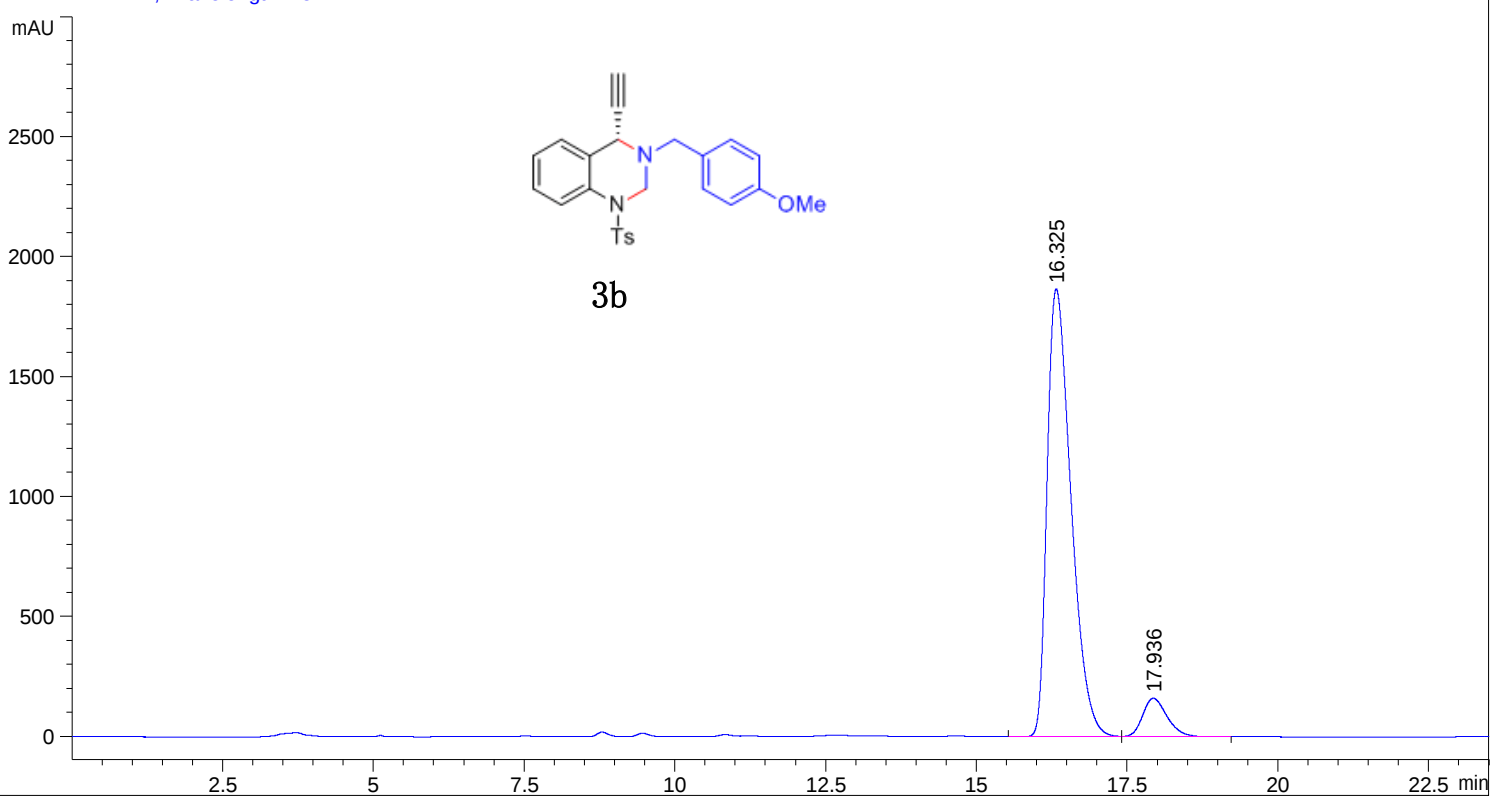
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	10.109	MM	0.3698	3.29252e4	1484.03845	95.8589
2	11.093	MM	0.3748	1422.36963	63.24511	4.1411

VWD1 A, Wavelength=254 nm



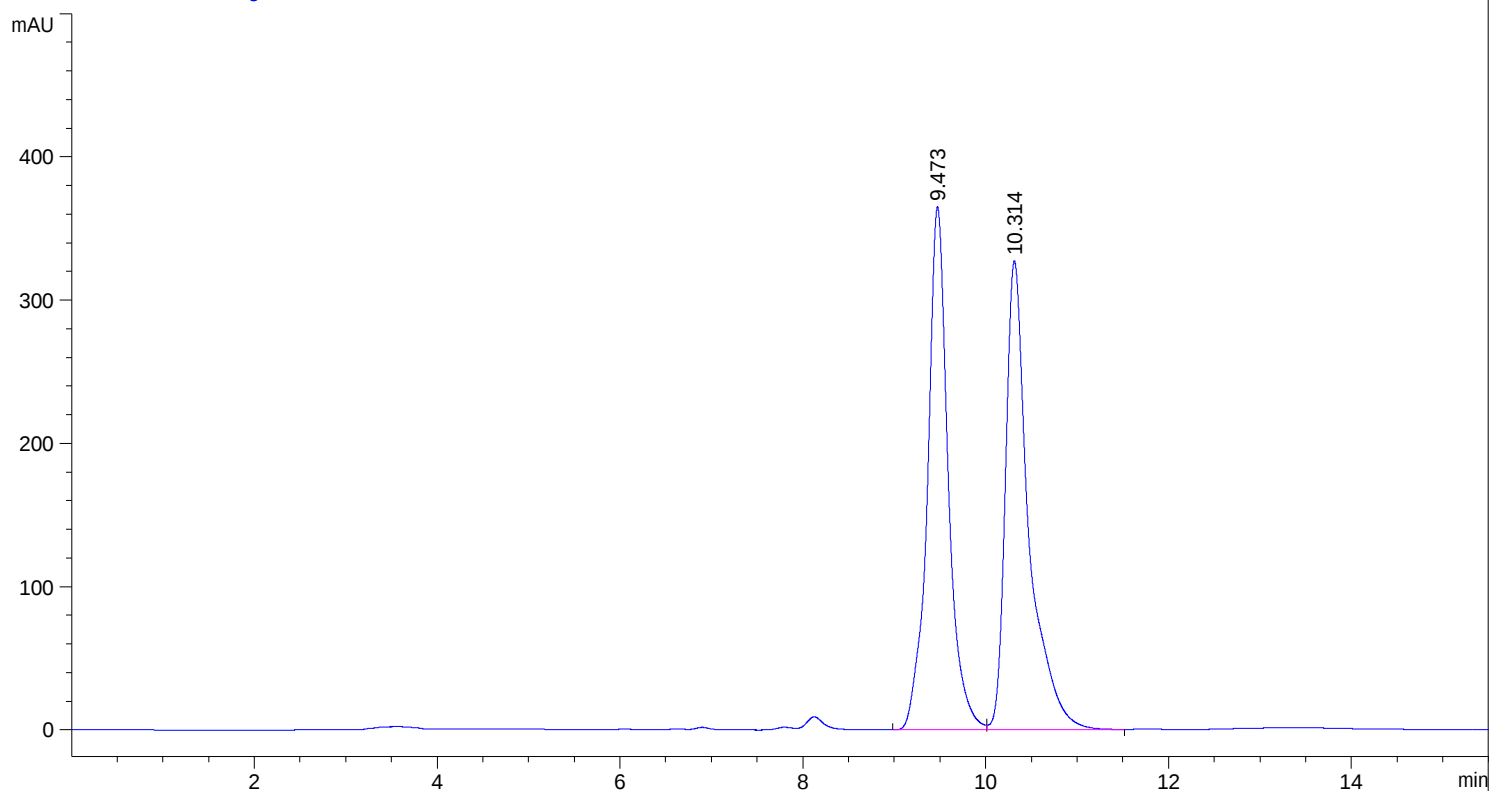
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	16.003	BV	0.3930	1.69241e4	652.68127	50.0049
2	17.541	VB	0.4296	1.69208e4	597.99634	49.9951

VWD1 A, Wavelength=254 nm



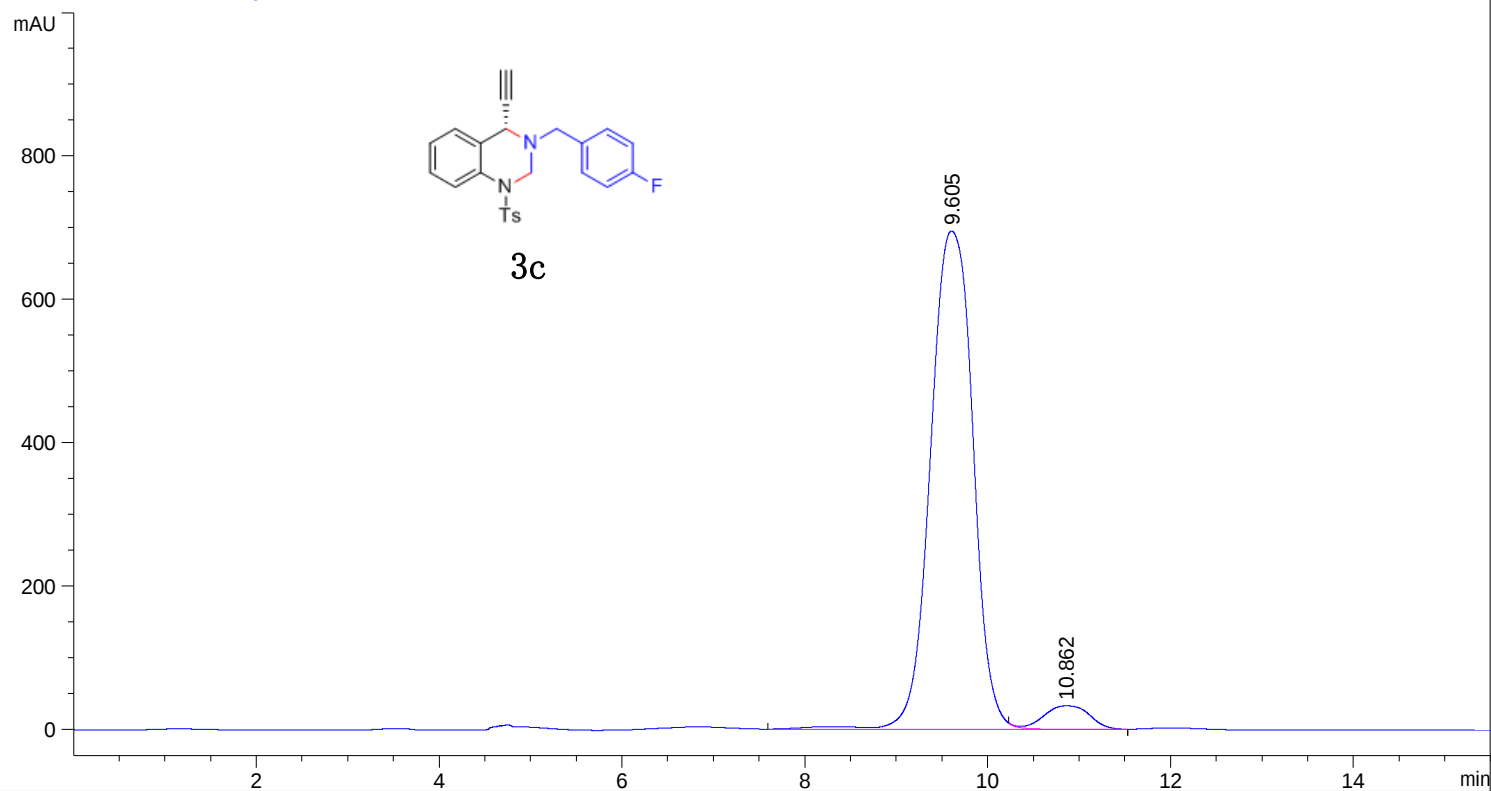
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	16.325	BV	0.4272	5.14197e4	1867.49121	91.8811
2	17.936	VB	0.4355	4543.58057	160.39514	8.1189

VWD1 A, Wavelength=254 nm



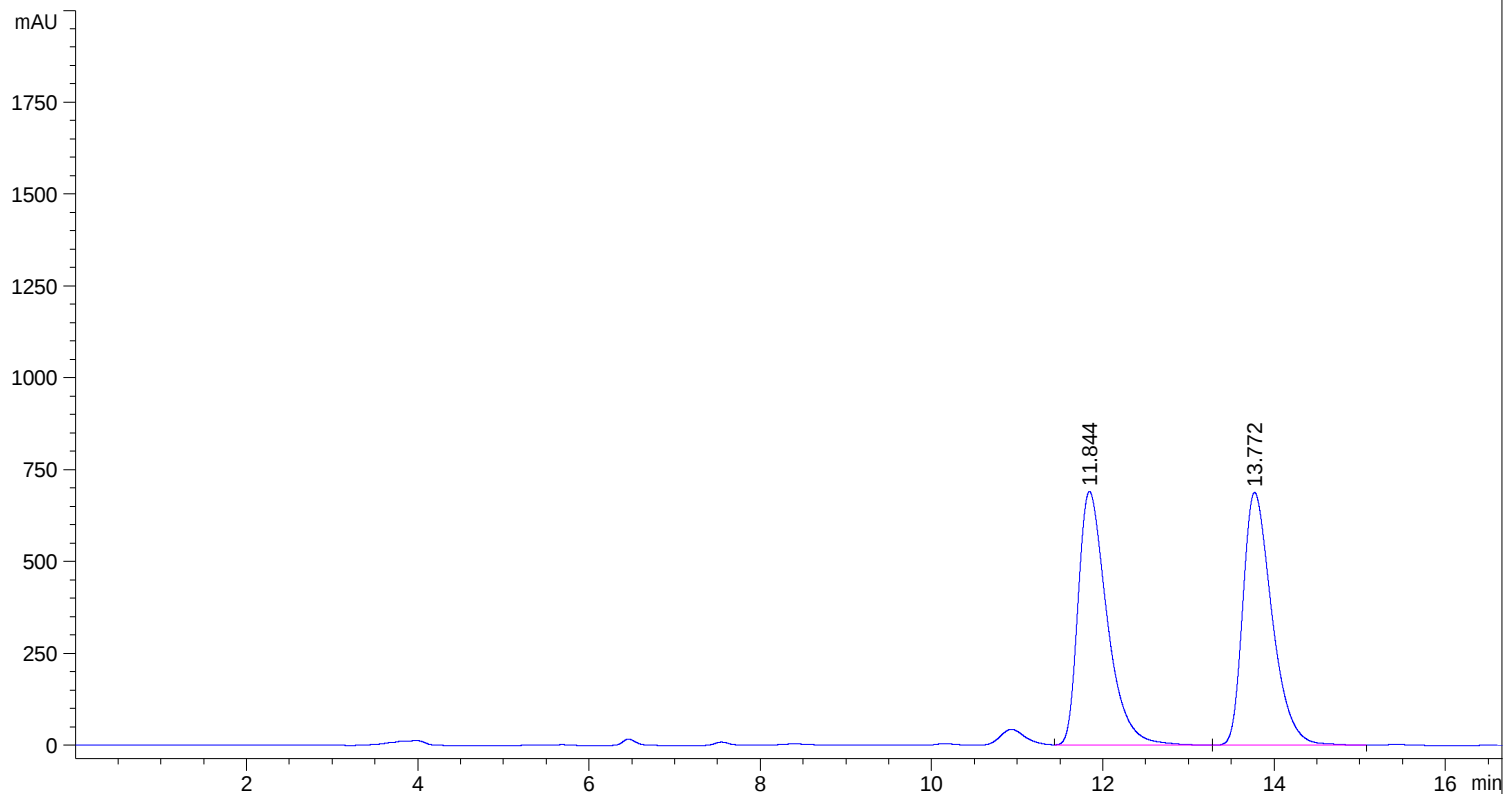
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	9.473	BV	0.2322	5764.08057	365.02237	49.8162
2	10.314	VB	0.2590	5806.62012	327.29303	50.1838

VWD1 A, Wavelength=254 nm



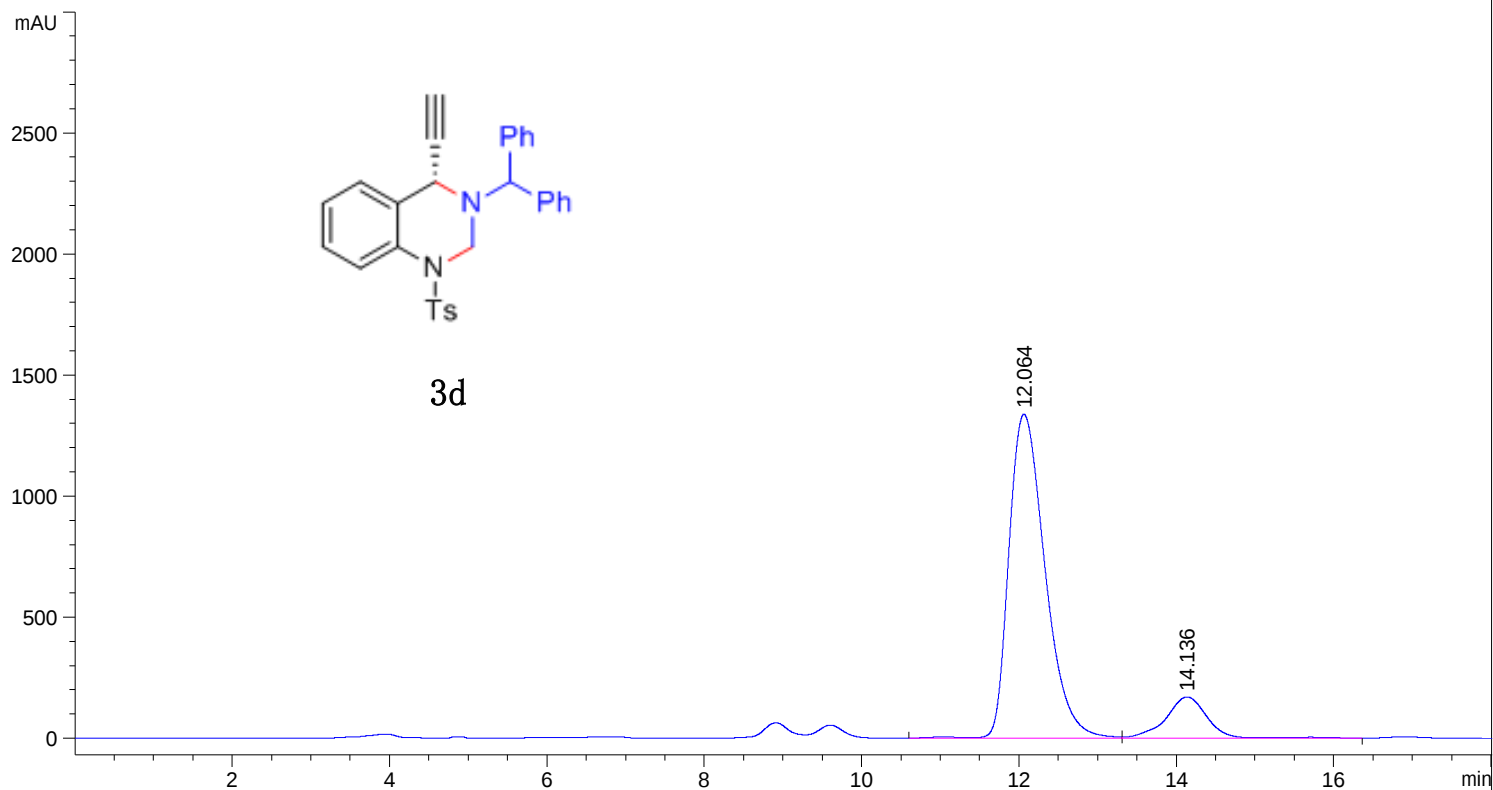
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	9.605	VV R	0.5146	2.24549e4	694.87036	95.2505
2	10.862	VB E	0.5551	1119.67065	32.61140	4.7495

VWD1 A, Wavelength=254 nm

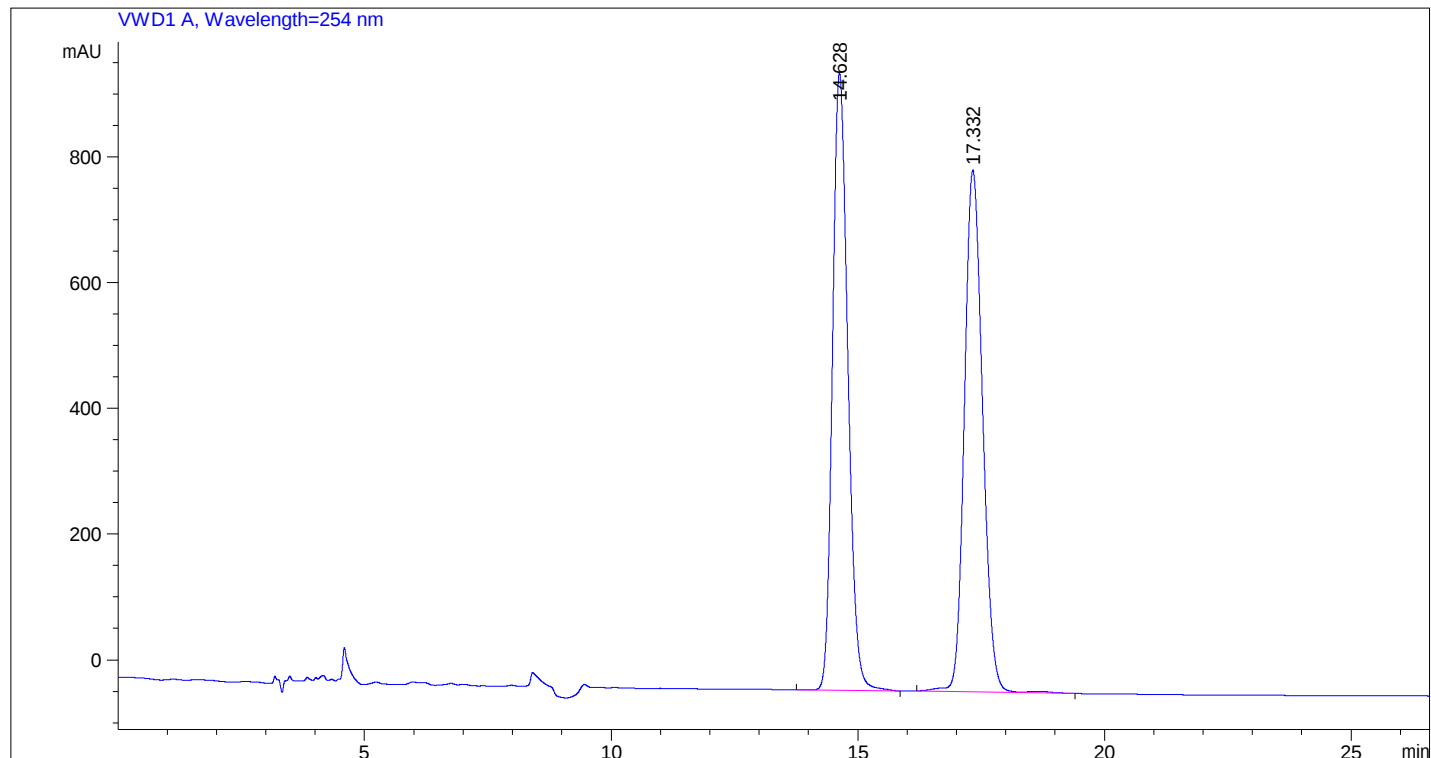


峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	11.844	VB	0.3605	1.62835e4	690.89148	50.0951
2	13.772	BB	0.3605	1.62216e4	688.22552	49.9049

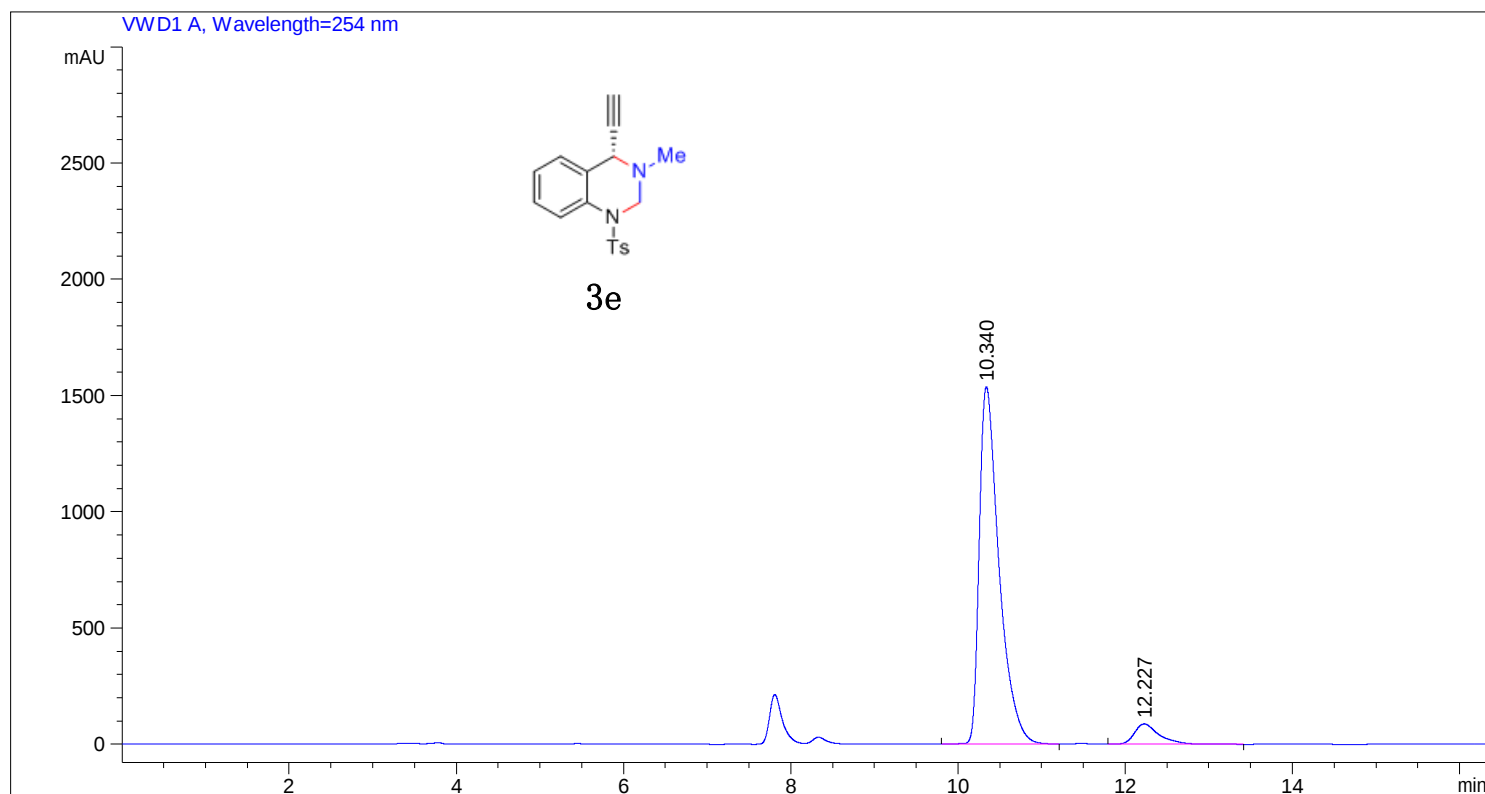
VWD1 A, Wavelength=254 nm



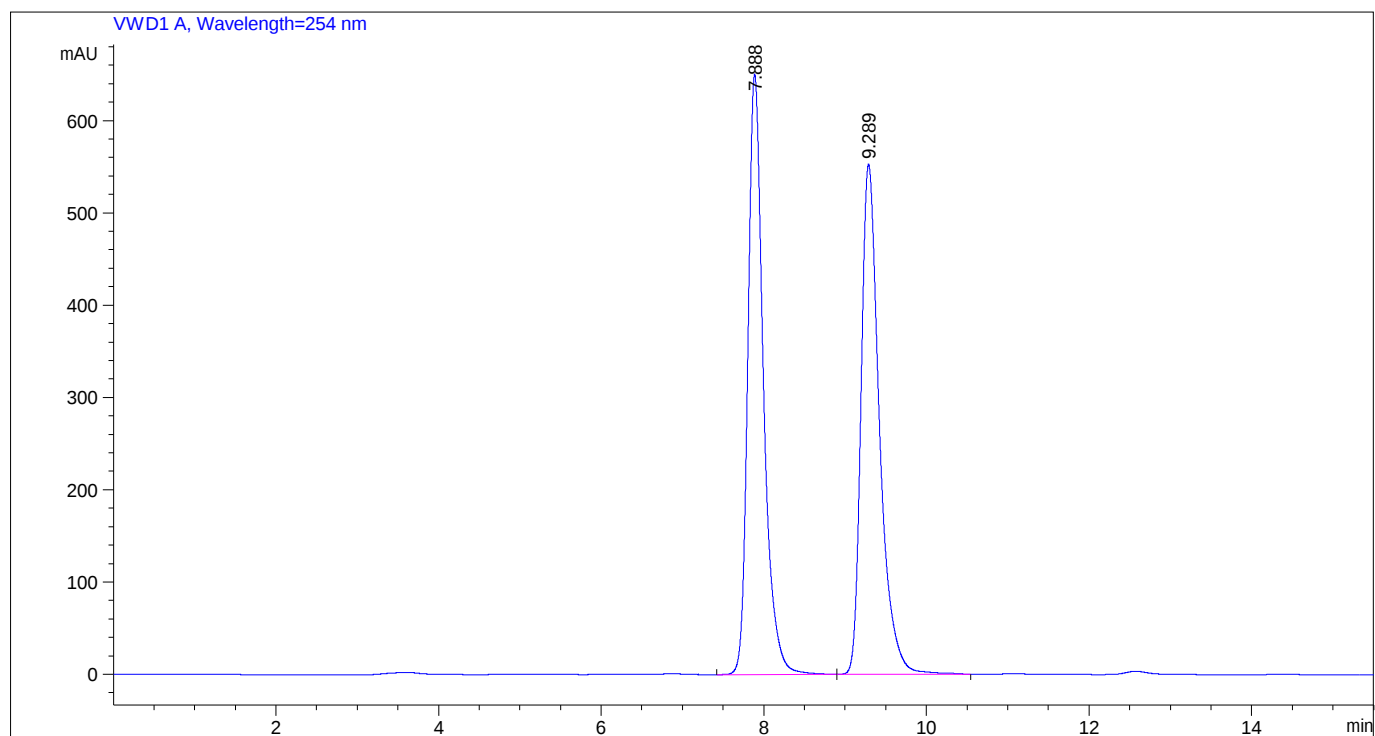
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	12.064	VV R	0.4961	4.25949e4	1337.59753	87.2460
2	14.136	VV R	0.5363	6226.68652	170.03209	12.7540



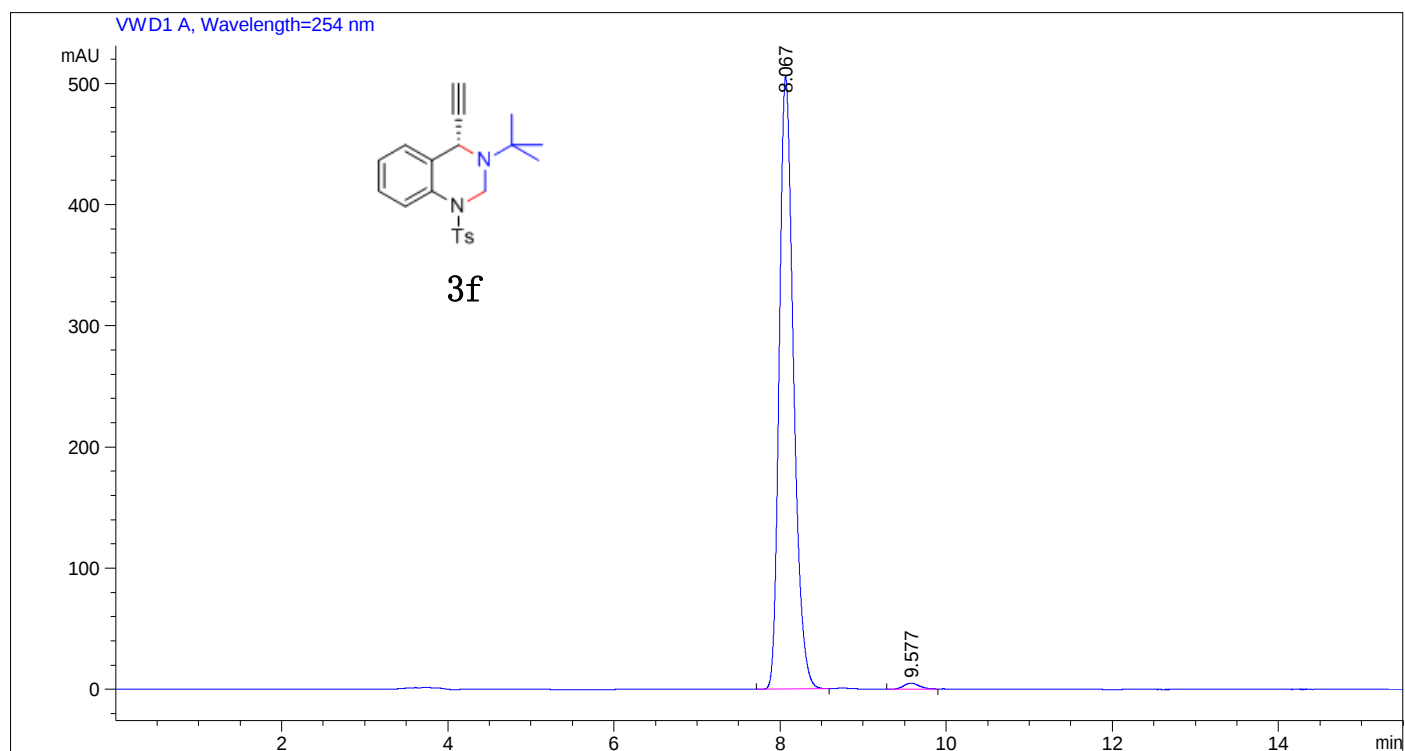
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	14.628	VB R	0.3362	2.12331e4	982.36255	49.9435
2	17.332	BV R	0.3979	2.12811e4	829.83038	50.0565



峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	10.340	BB	0.2473	2.52703e4	1537.42554	93.3908
2	12.227	BB	0.3032	1788.36023	87.39218	6.6092

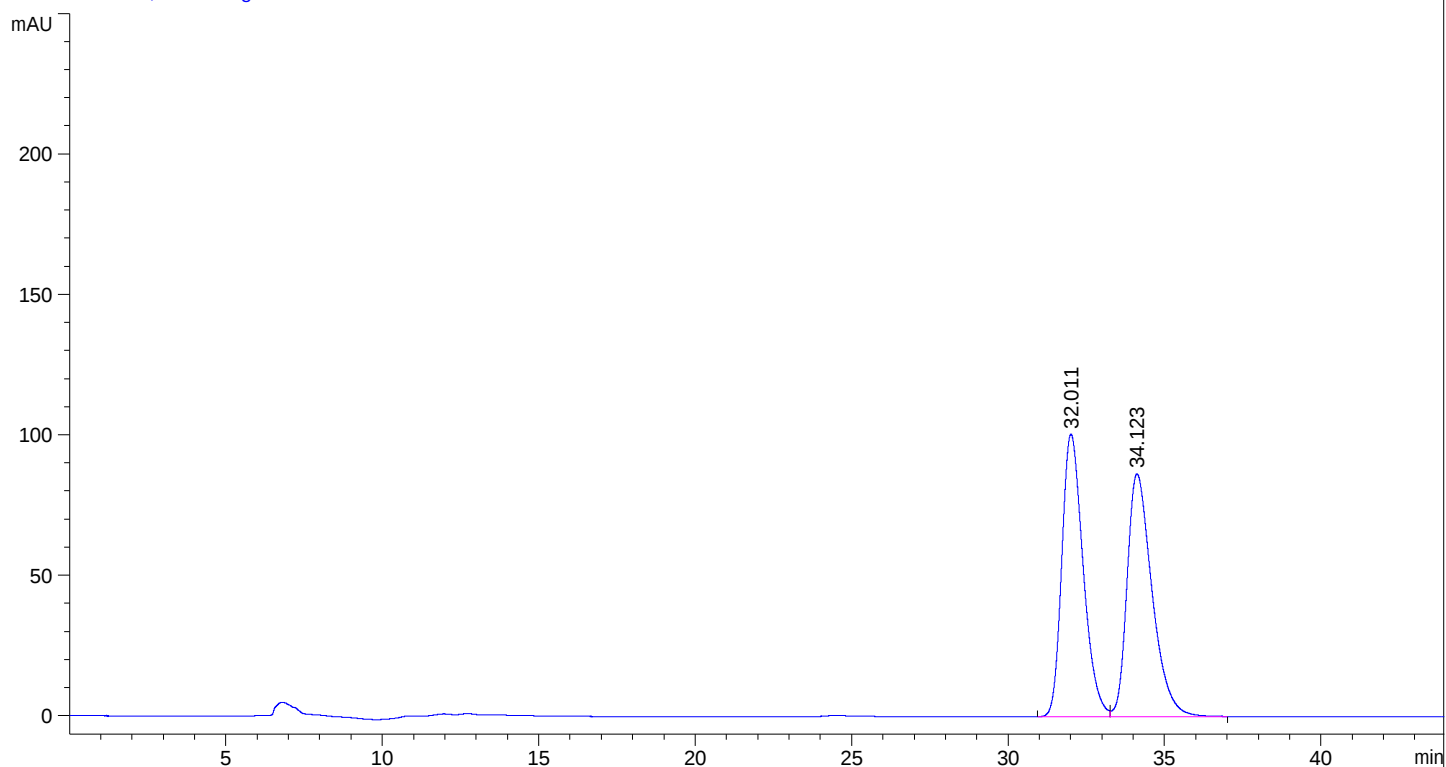


峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	7.888	BB	0.2015	8667.11230	650.45630	49.9498
2	9.289	BB	0.2378	8684.52051	552.62677	50.0502



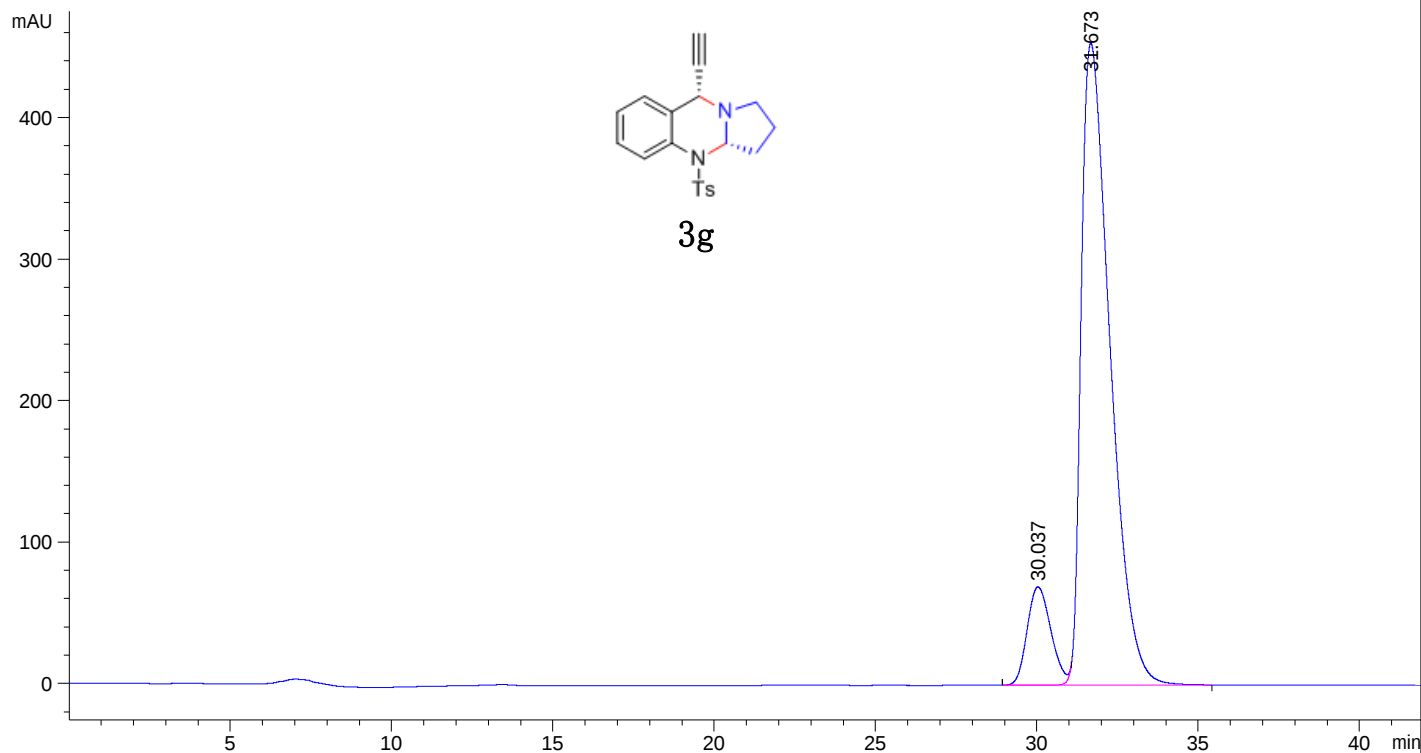
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.067	BB	0.1830	6028.90576	505.90189	98.9503
2	9.577	BB	0.1982	63.95896	4.91926	1.0497

VWD1 A, Wavelength=254 nm

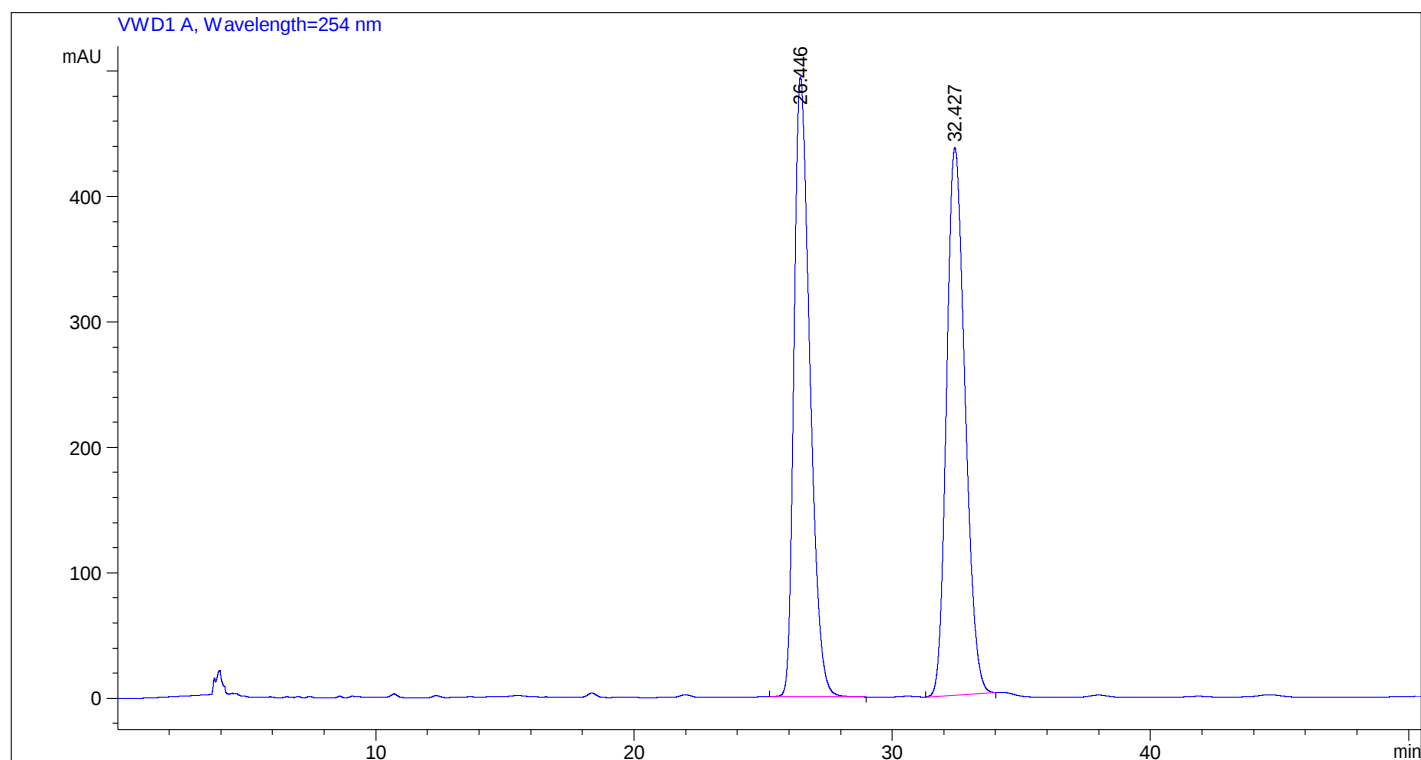


峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	32.011	BV	0.7181	4774.84912	100.62851	49.8557
2	34.123	VR	0.8191	4802.49707	86.45539	50.1443

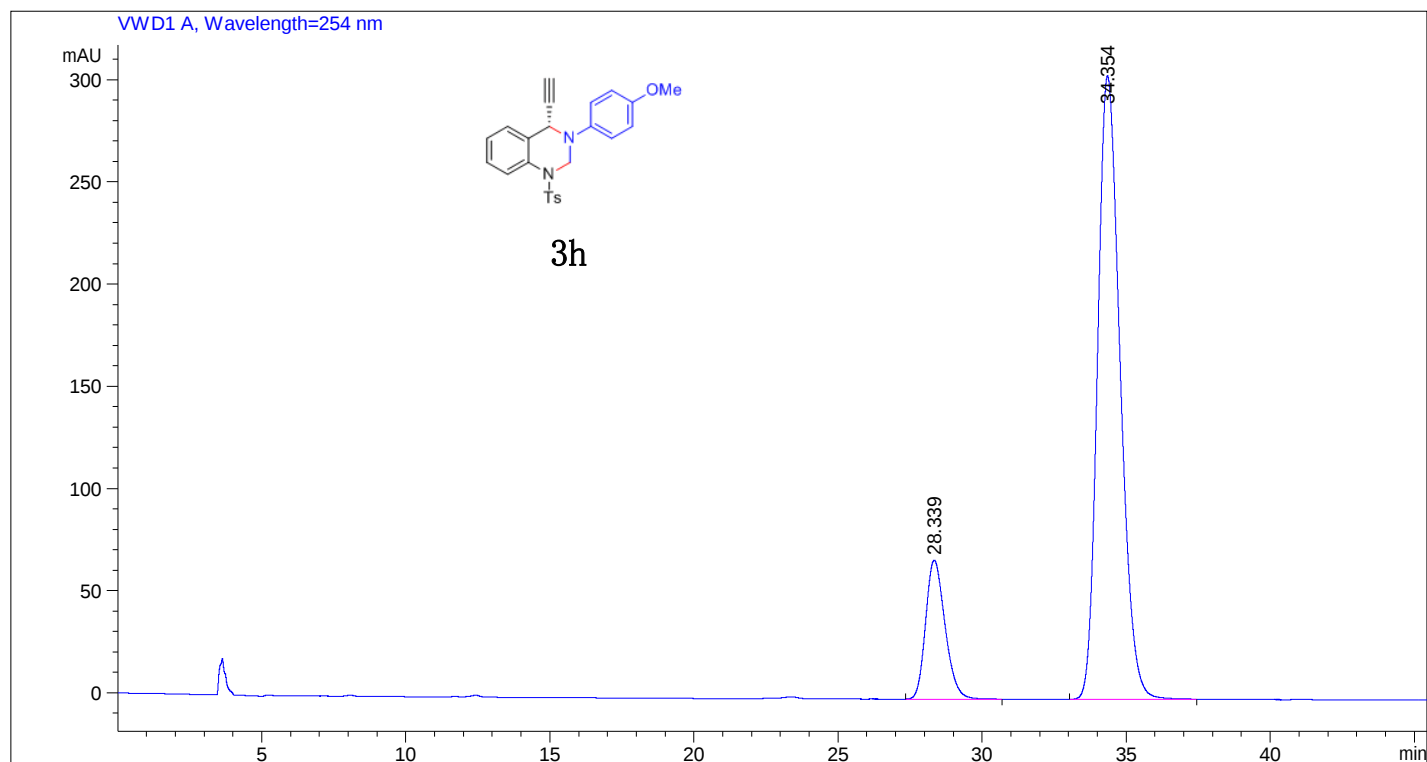
VWD1 A, Wavelength=254 nm



峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	30.037	BV E	0.7677	3545.44702	69.43201	11.1540
2	31.673	VB R	0.9441	2.82408e4	453.75208	88.8460

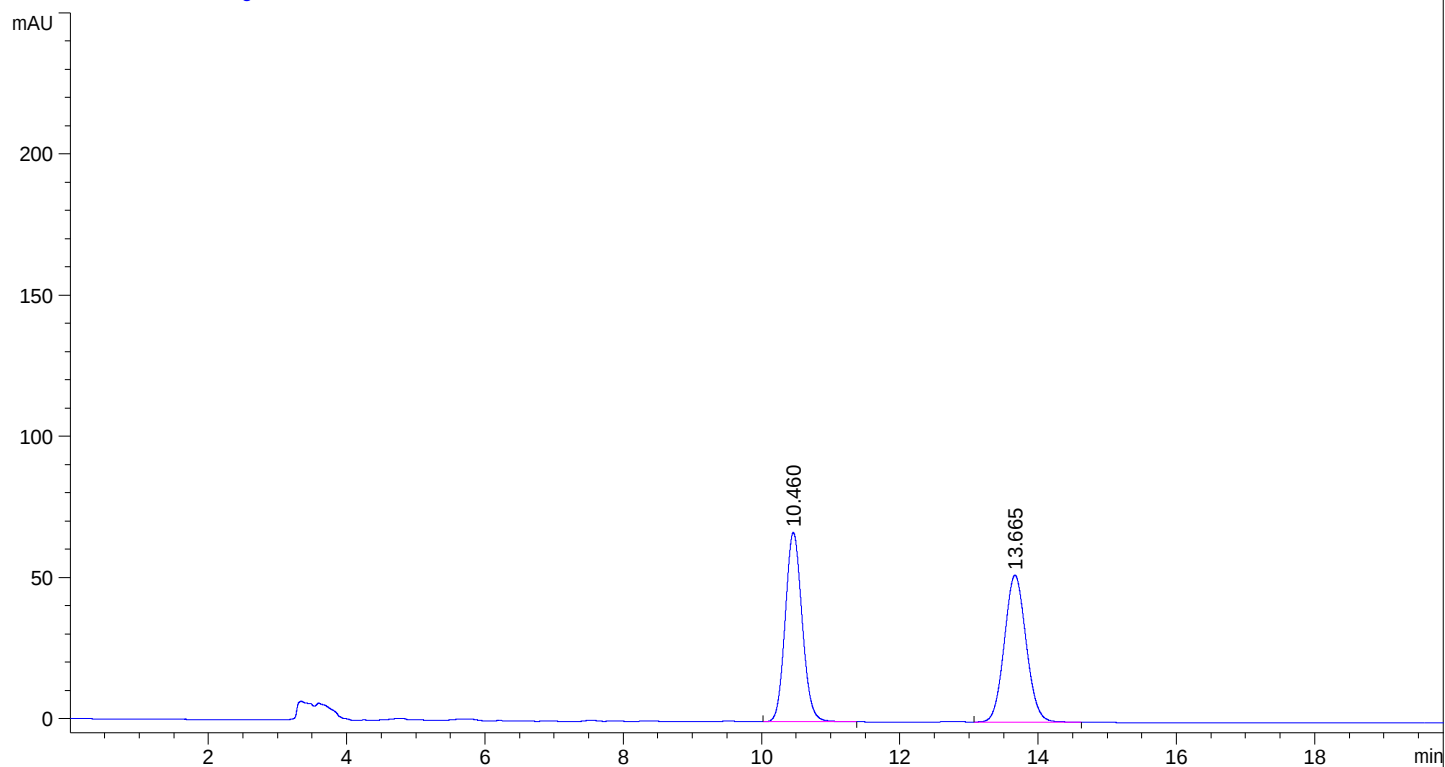


峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	26.446	BB	0.6603	2.11667e4	494.04630	49.3527
2	32.427	BB	0.7775	2.17219e4	436.56381	50.6473



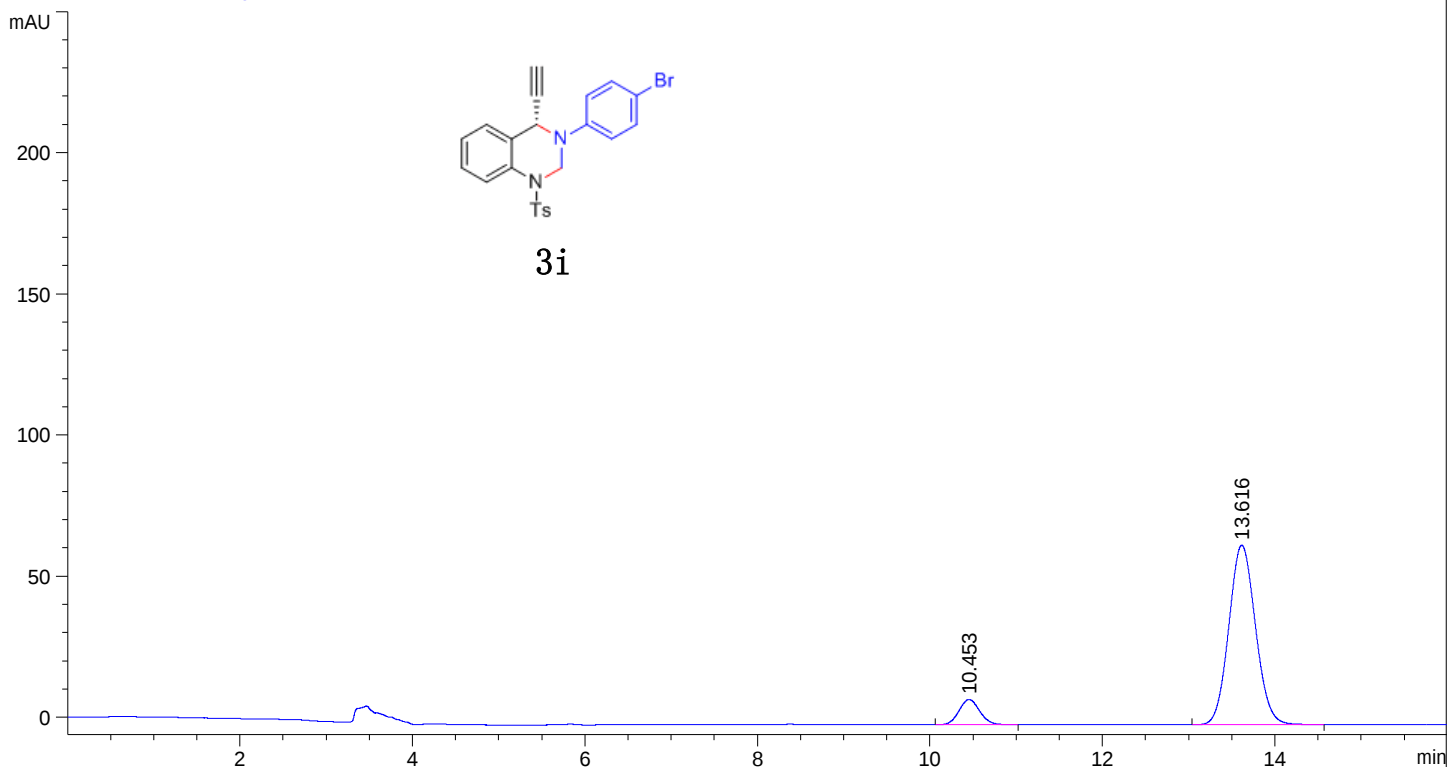
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	28.339	BB	0.7008	3181.15015	67.99416	16.1412
2	34.354	BB	0.8341	1.65271e4	305.04074	83.8588

VWD1 A, Wavelength=254 nm



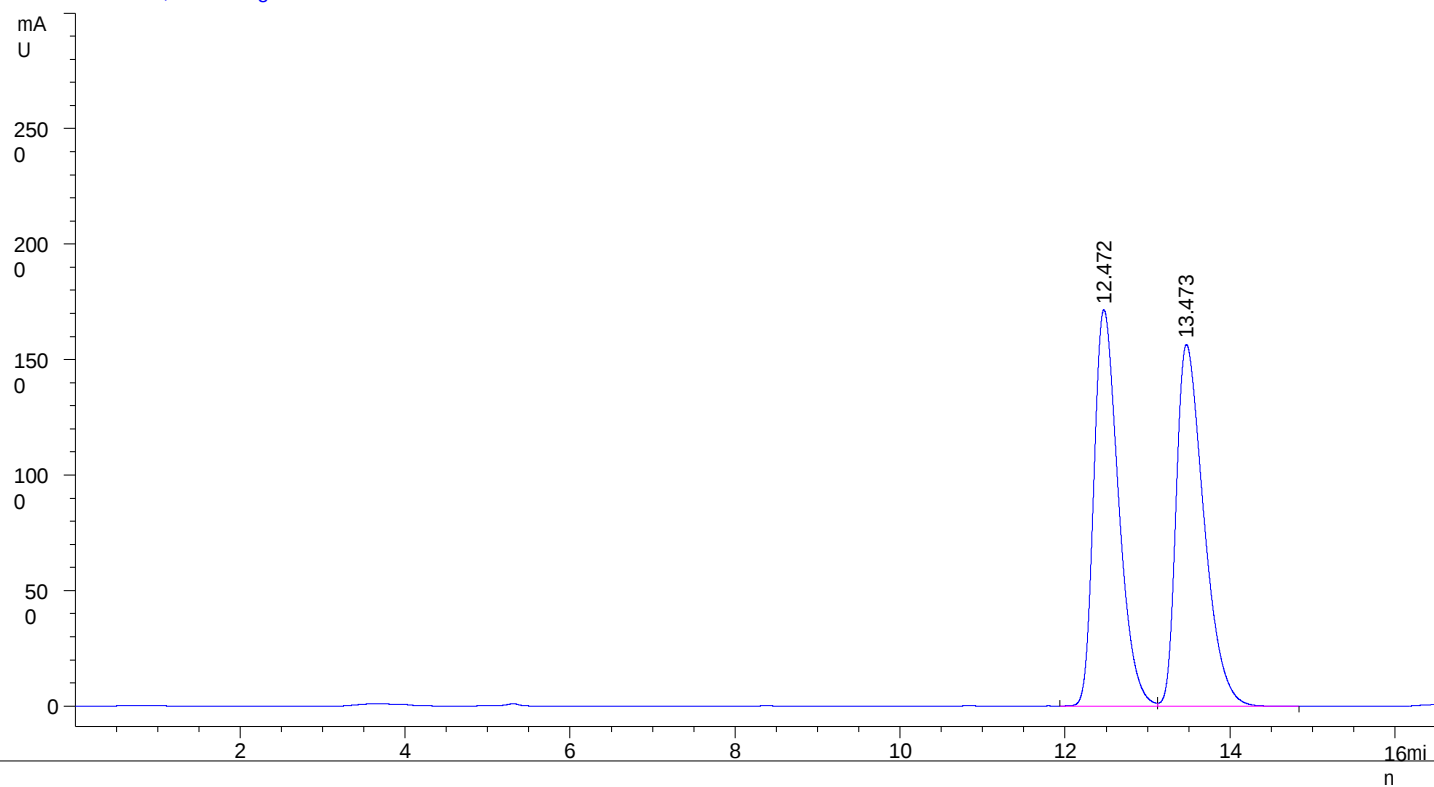
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	10.460	BB	0.2635	1141.42297	67.07532	50.0139
2	13.665	BB	0.3425	1140.78809	51.99844	49.9861

VWD1 A, Wavelength=254 nm



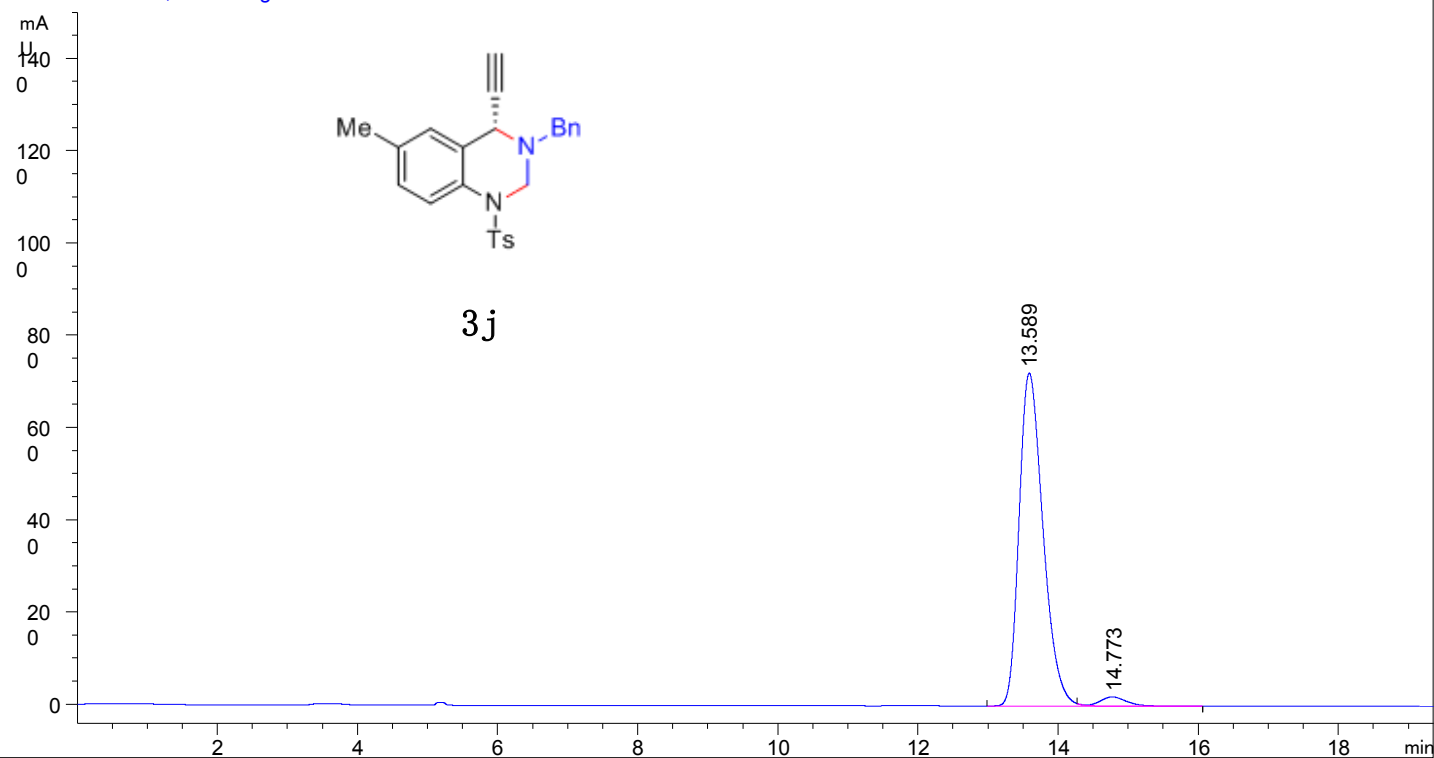
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	10.453	BB	0.2601	149.00162	8.93092	9.8315
2	13.616	BB	0.3341	1366.54480	63.62495	90.1685

VWD1 A, Wavelength=254 nm

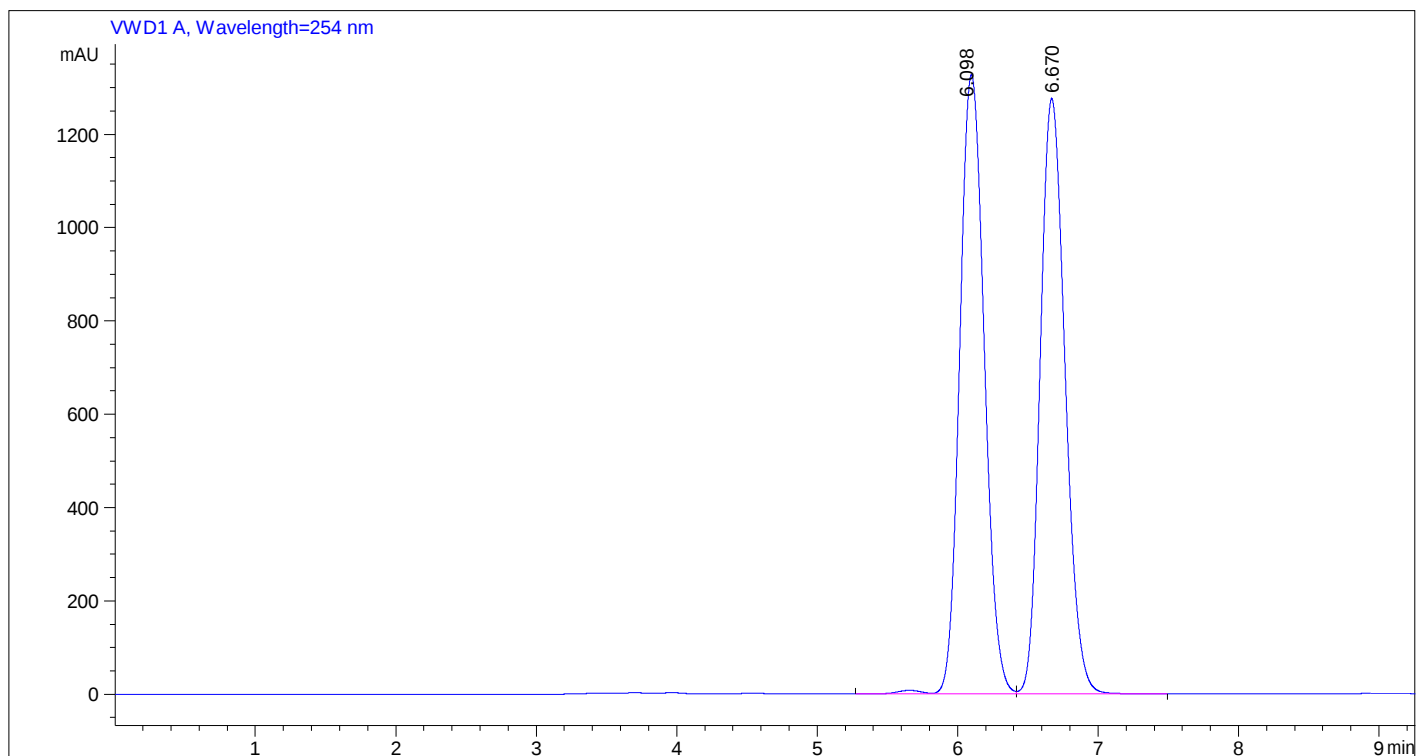


峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	12.472	BV	0.3205	3.55930e4	1715.87720	49.4332
2	13.473	VB	0.3562	3.64091e4	1566.04028	50.5668

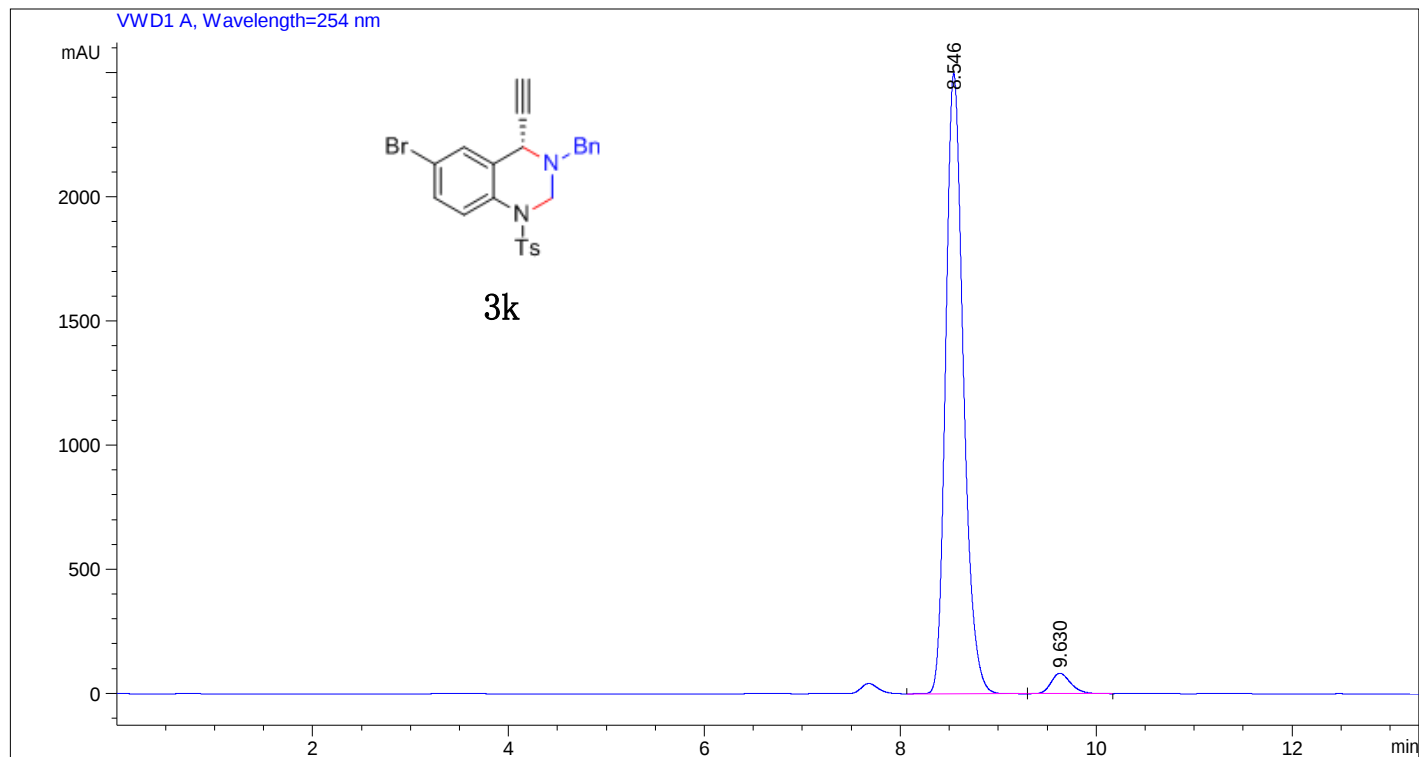
VWD1 A, Wavelength=254 nm



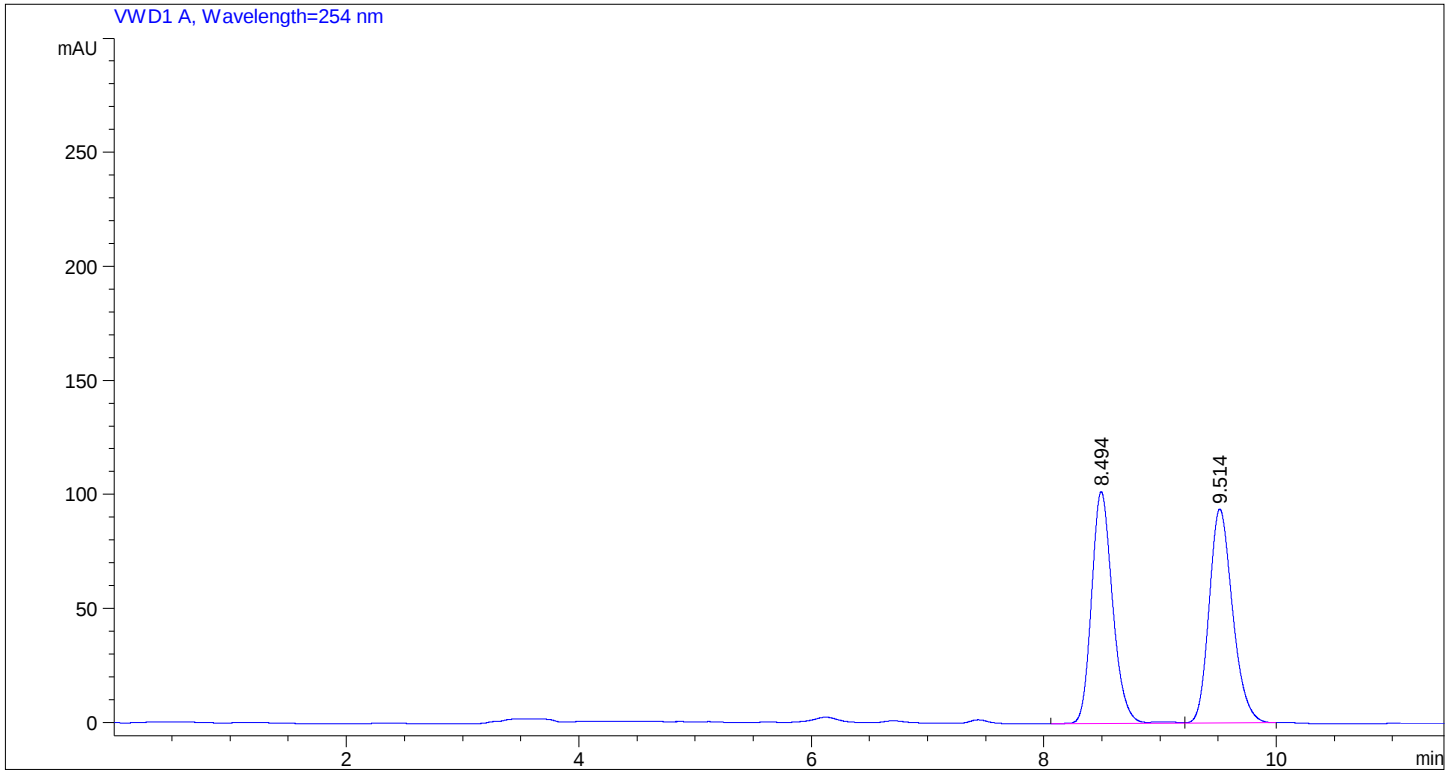
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	13.589	BV R	0.3667	1.71486e4	721.85675	97.0998
2	14.773	VB E	0.3850	512.20093	19.81999	2.9002



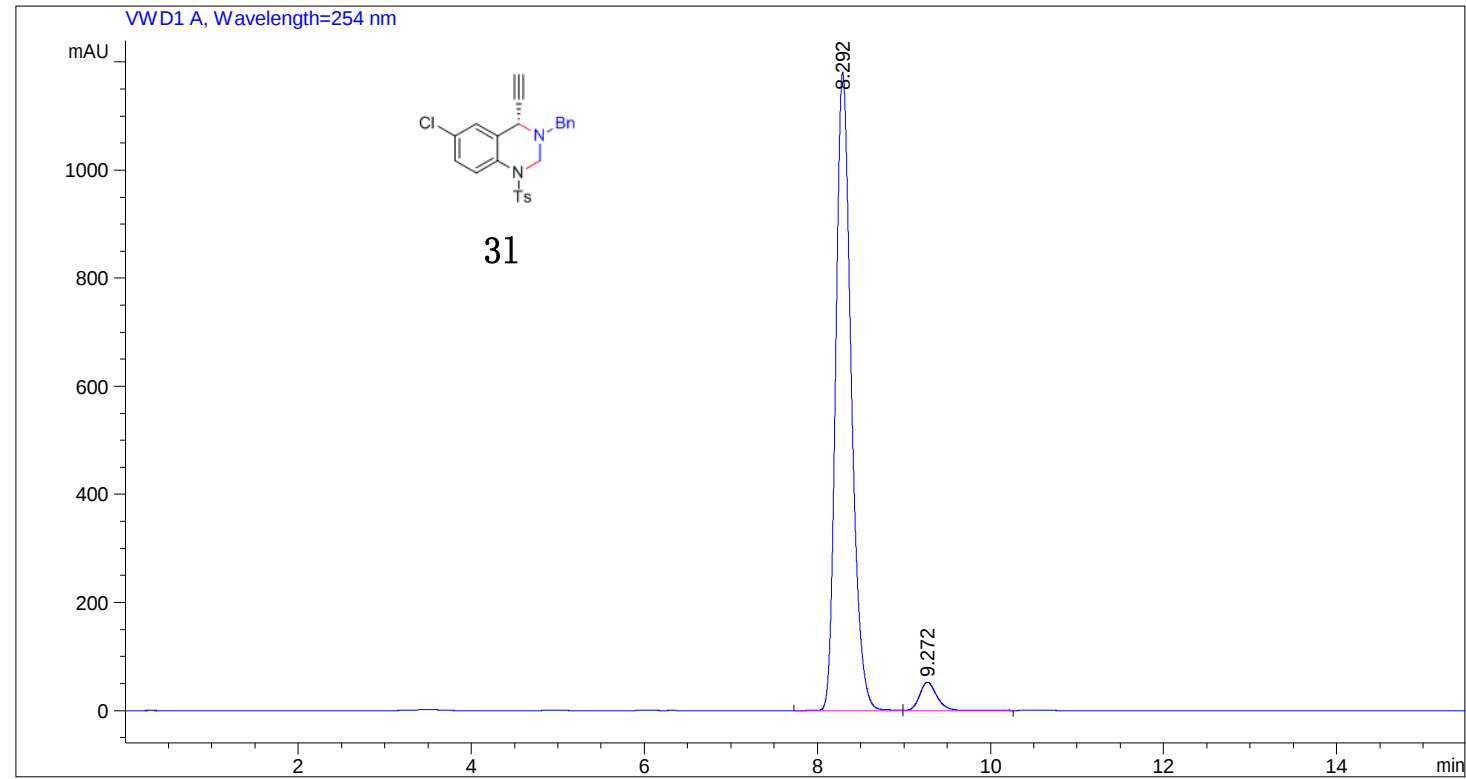
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	6.098	VV R	0.1910	1.61788e4	1326.94507	50.7084
2	6.670	VB	0.1937	1.57267e4	1276.59802	49.2916



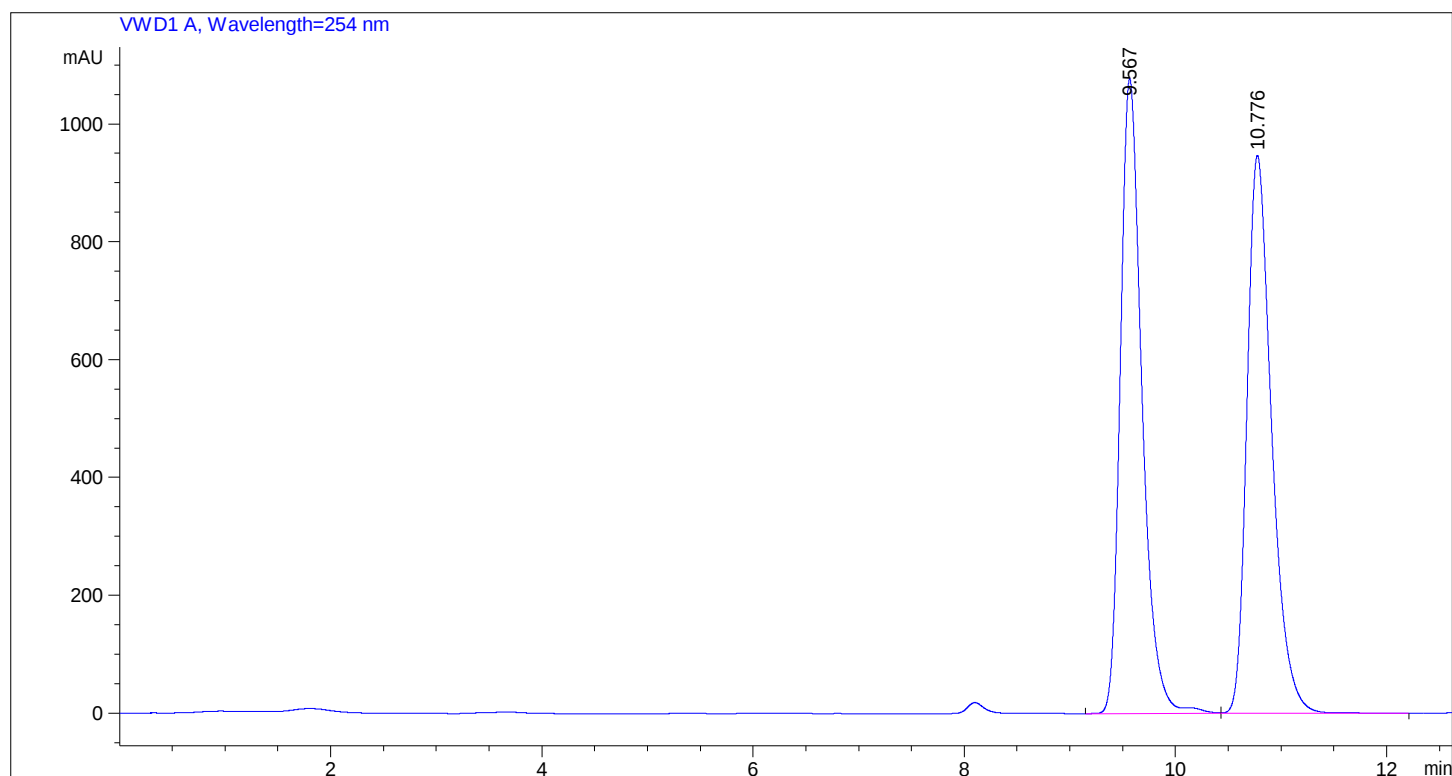
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.546	BB	0.1932	3.14332e4	2499.16797	96.4621
2	9.630	BB	0.2139	1152.84839	82.58139	3.5379



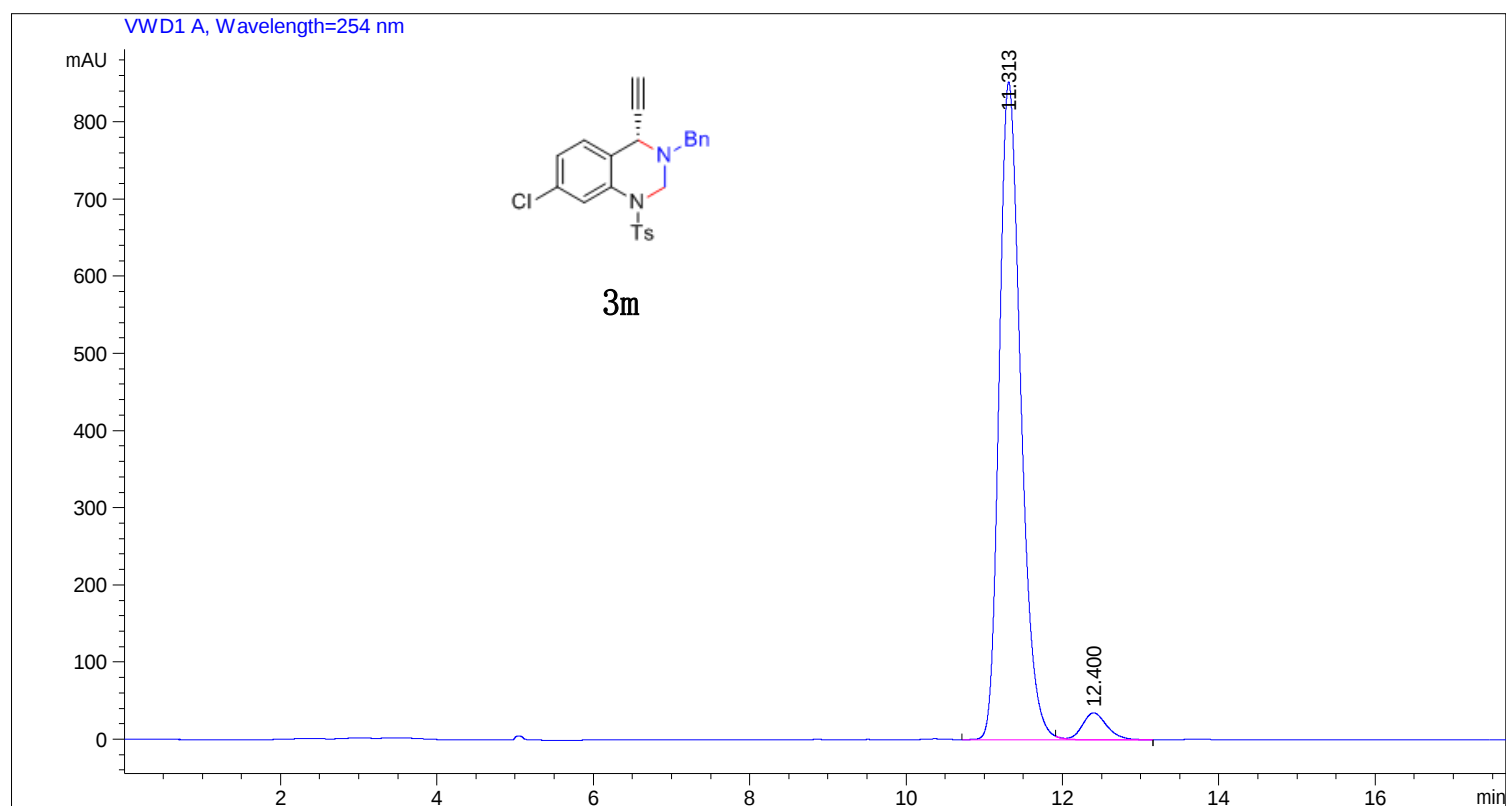
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.494	BV R	0.1933	1279.35486	101.69736	49.3146
2	9.514	VB	0.2154	1314.91797	93.86296	50.6854



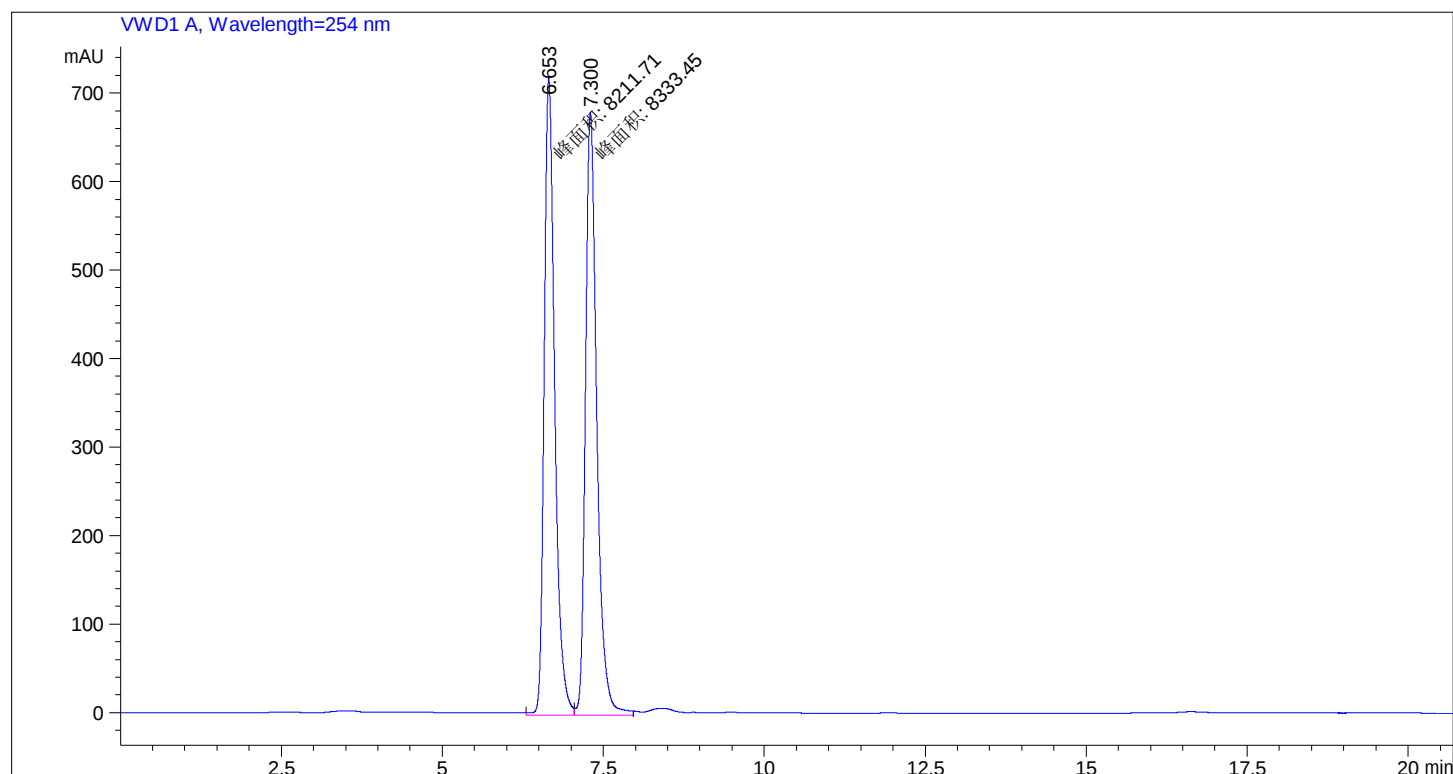
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.292	BV	0.1916	1.47423e4	1181.25208	95.2291
2	9.272	VV R	0.2127	738.57050	52.63773	4.7709



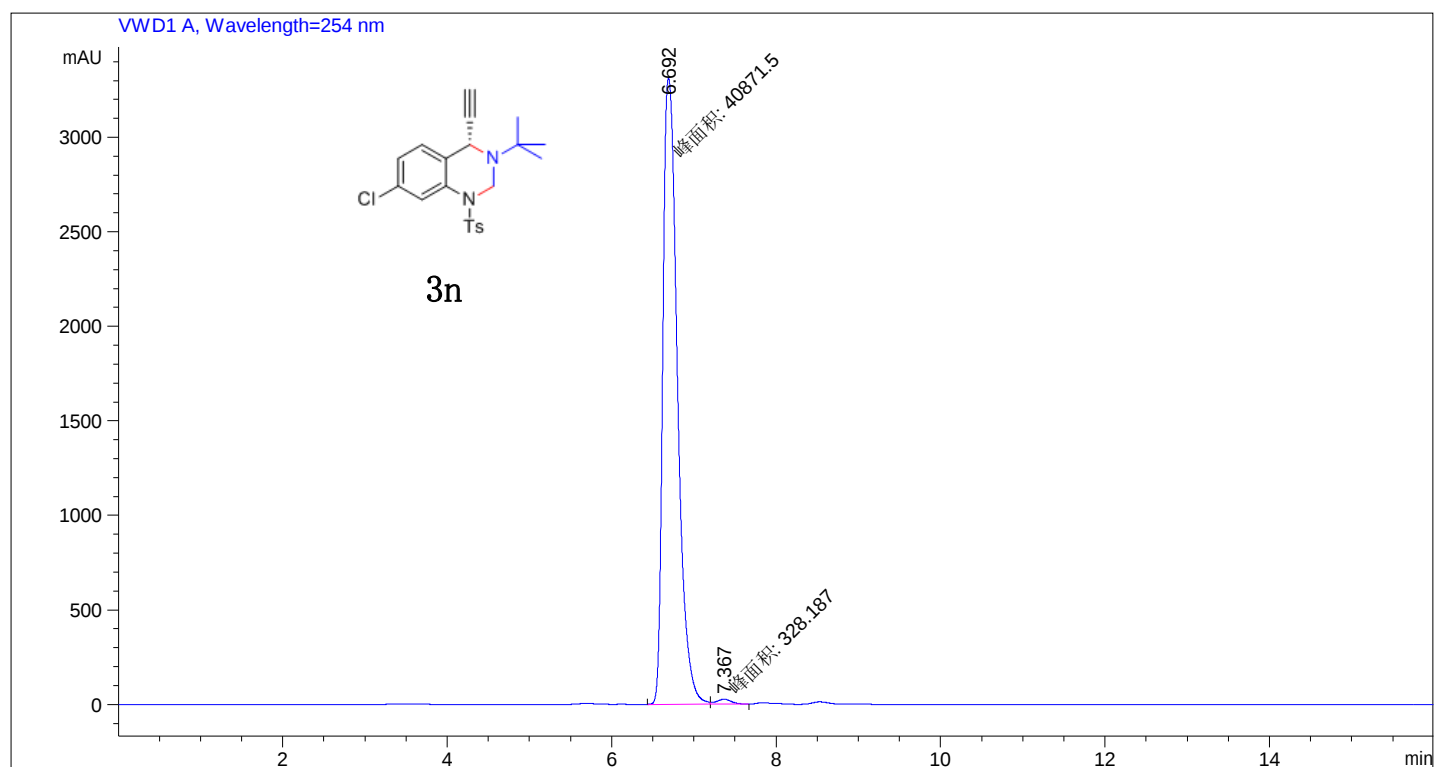
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	9.567	BV R	0.2159	1.53897e4	1077.71741	50.0105
2	10.776	VV R	0.2474	1.53833e4	947.47876	49.9895



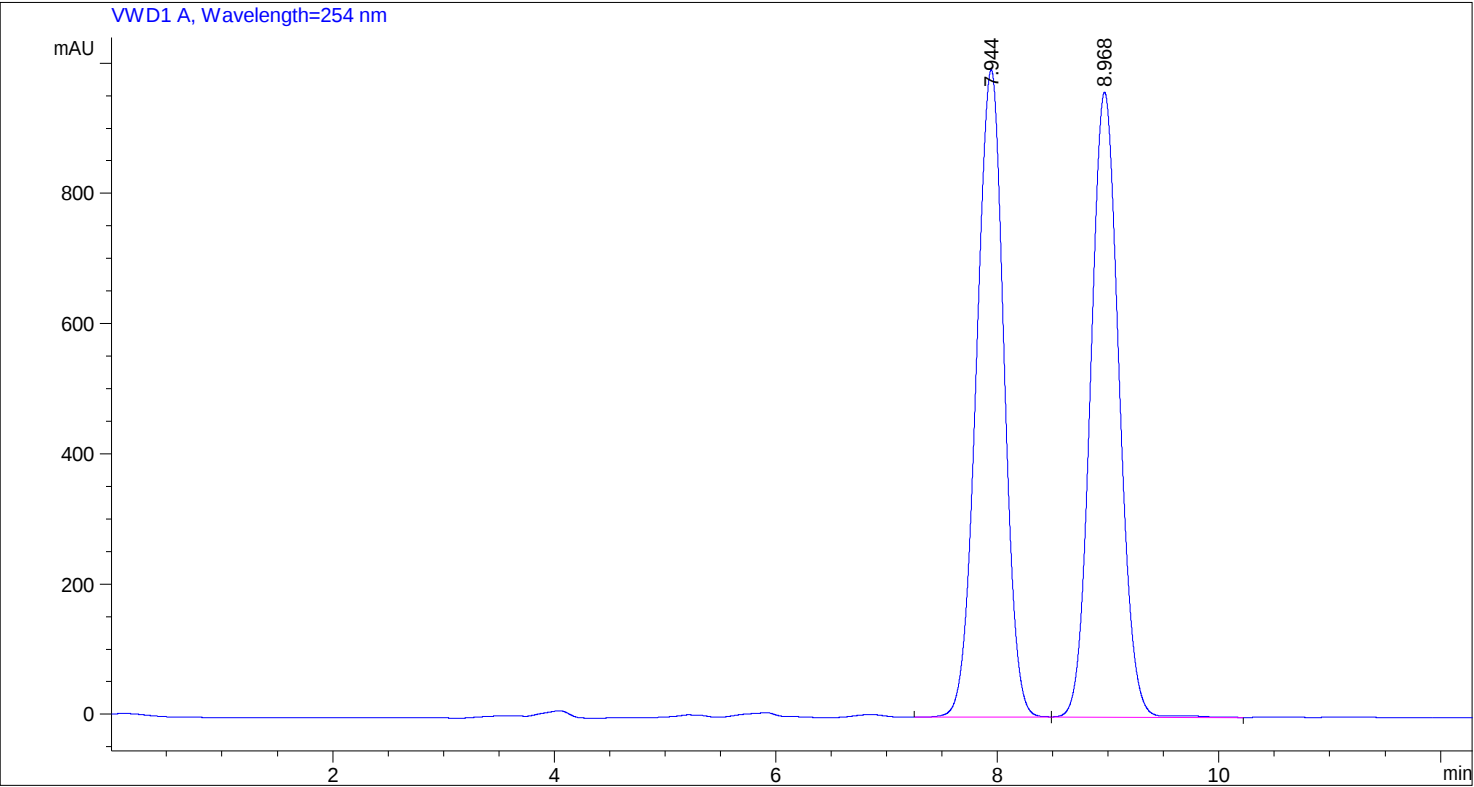
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	11.313	BV R	0.2971	1.63765e4	852.43652	95.5987
2	12.400	VB E	0.3300	753.96252	34.90228	4.4013



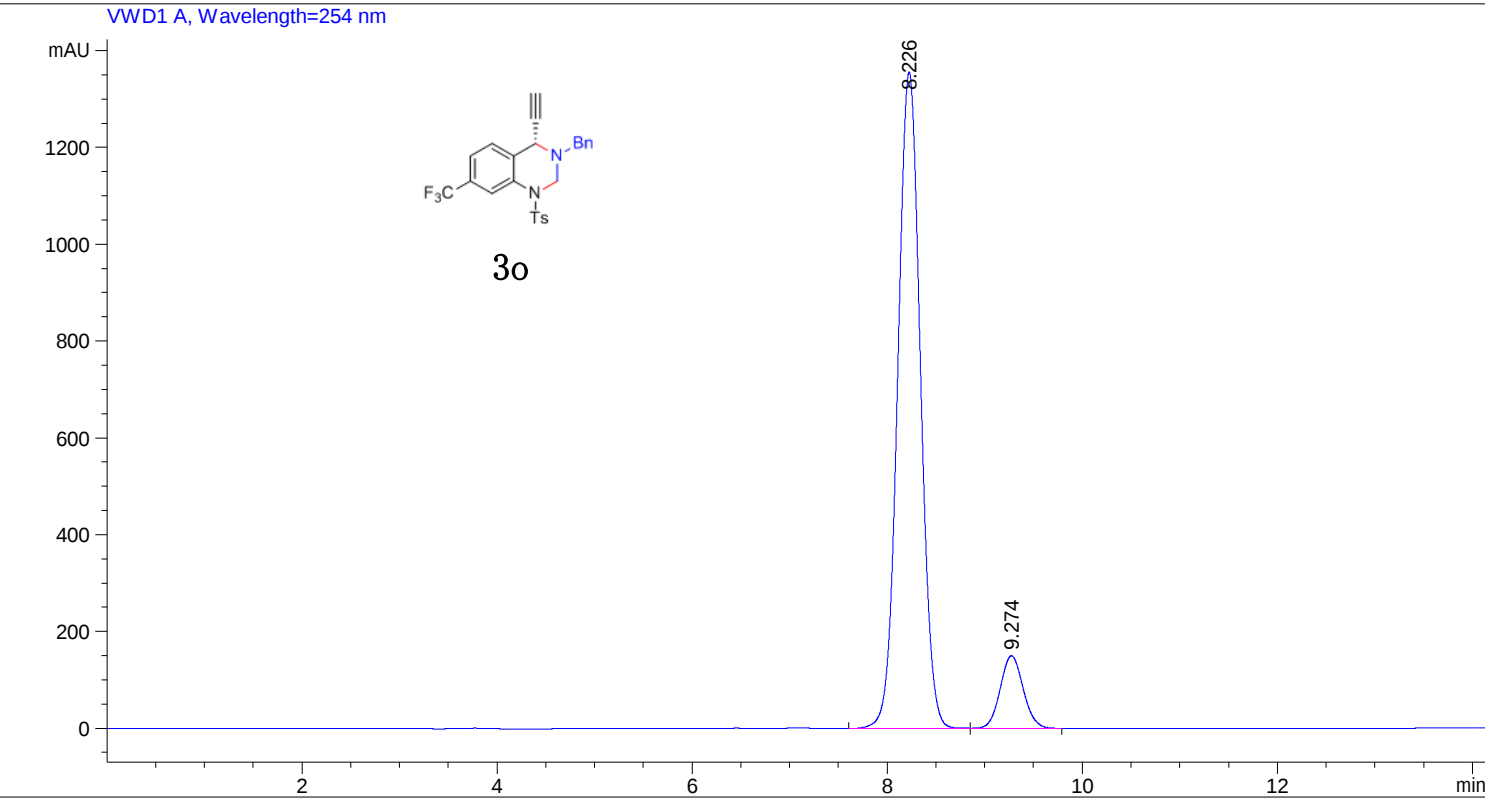
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	6.653	MM	0.1902	8211.71387	719.62555	49.6321
2	7.300	MM	0.2040	8333.44531	680.92206	50.3679



峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	6.692	MM	0.2056	4.08715e4	3313.92017	99.2034
2	7.367	MM	0.2065	328.18701	26.49206	0.7966

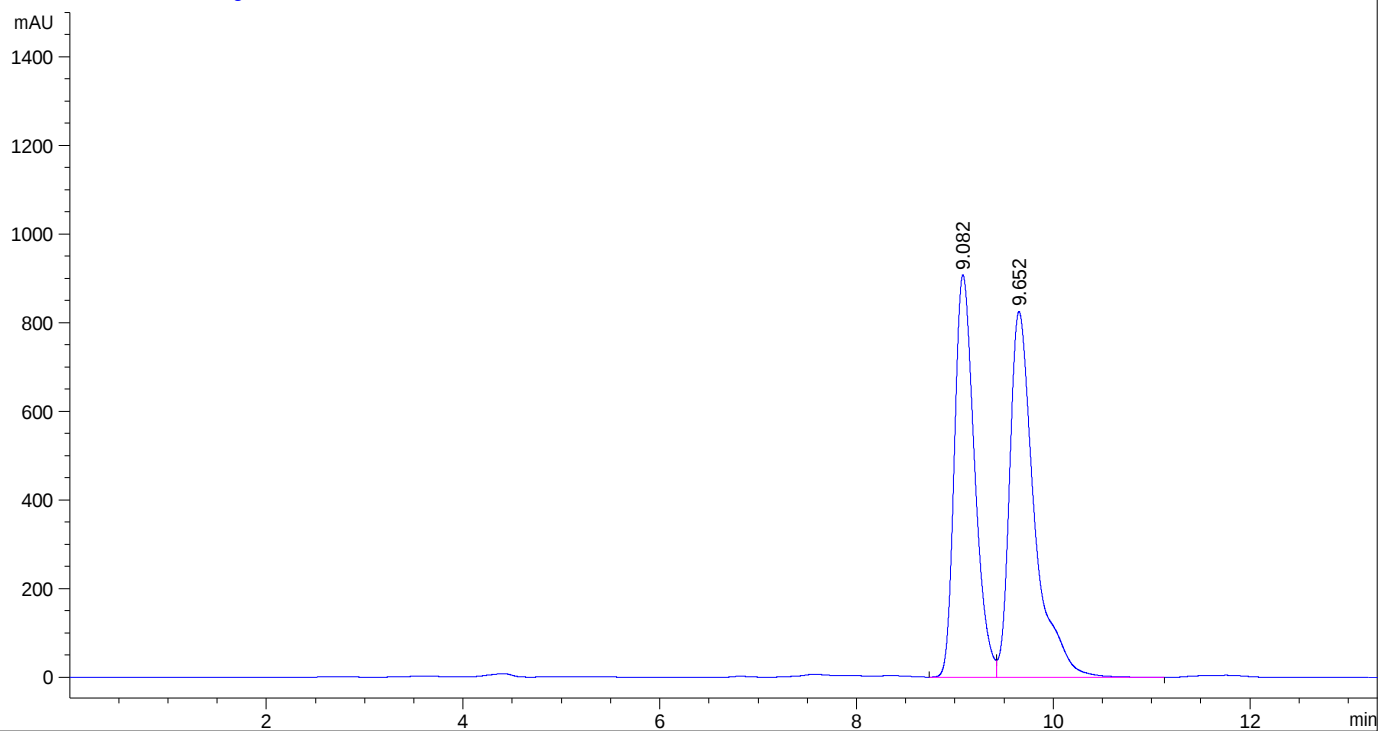


峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	7.944	BB	0.2716	1.71792e4	994.18805	50.1822
2	8.968	BV R	0.2772	1.70545e4	959.83246	49.8178



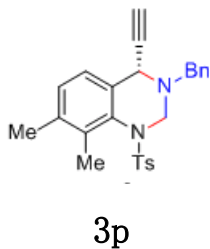
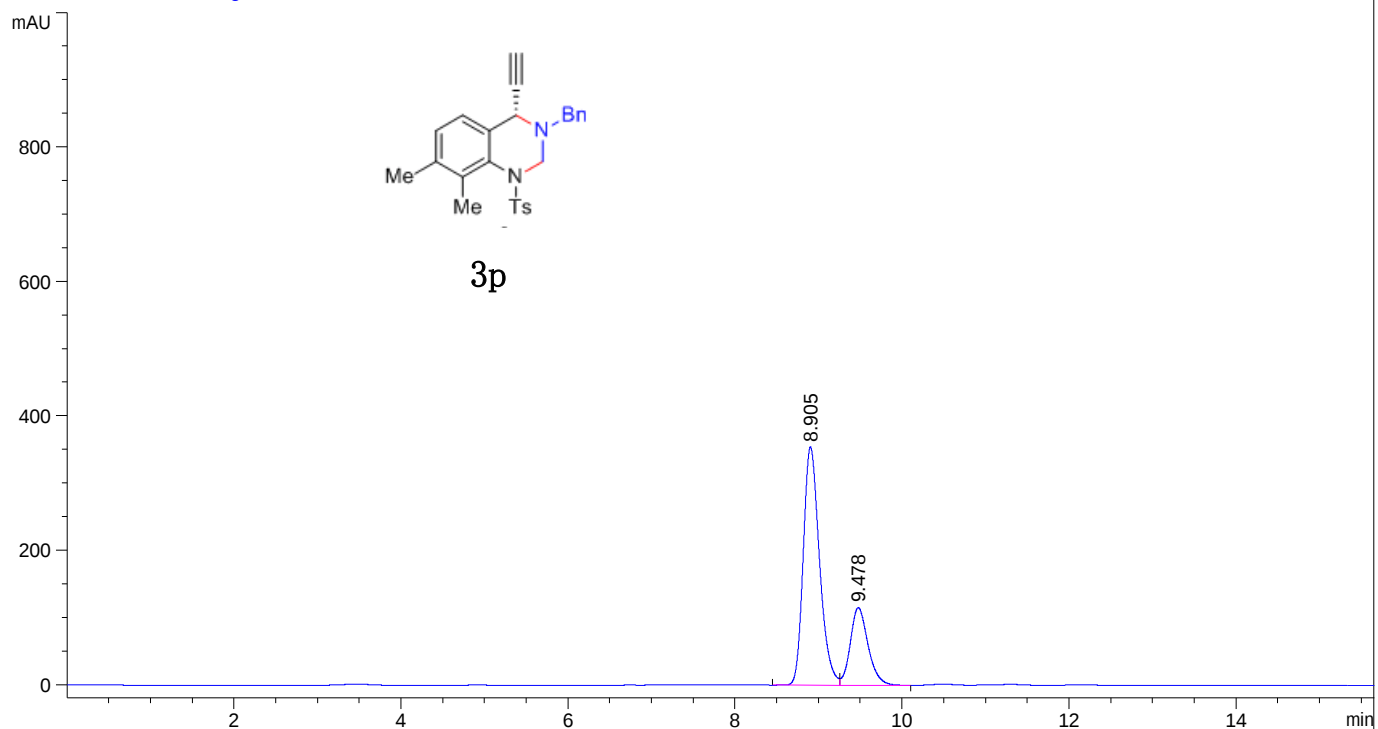
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.226	BB	0.2519	2.18382e4	1356.19958	89.9331
2	9.274	BB	0.2535	2444.51416	149.72130	10.0669

VWD1 A, Wavelength=254 nm



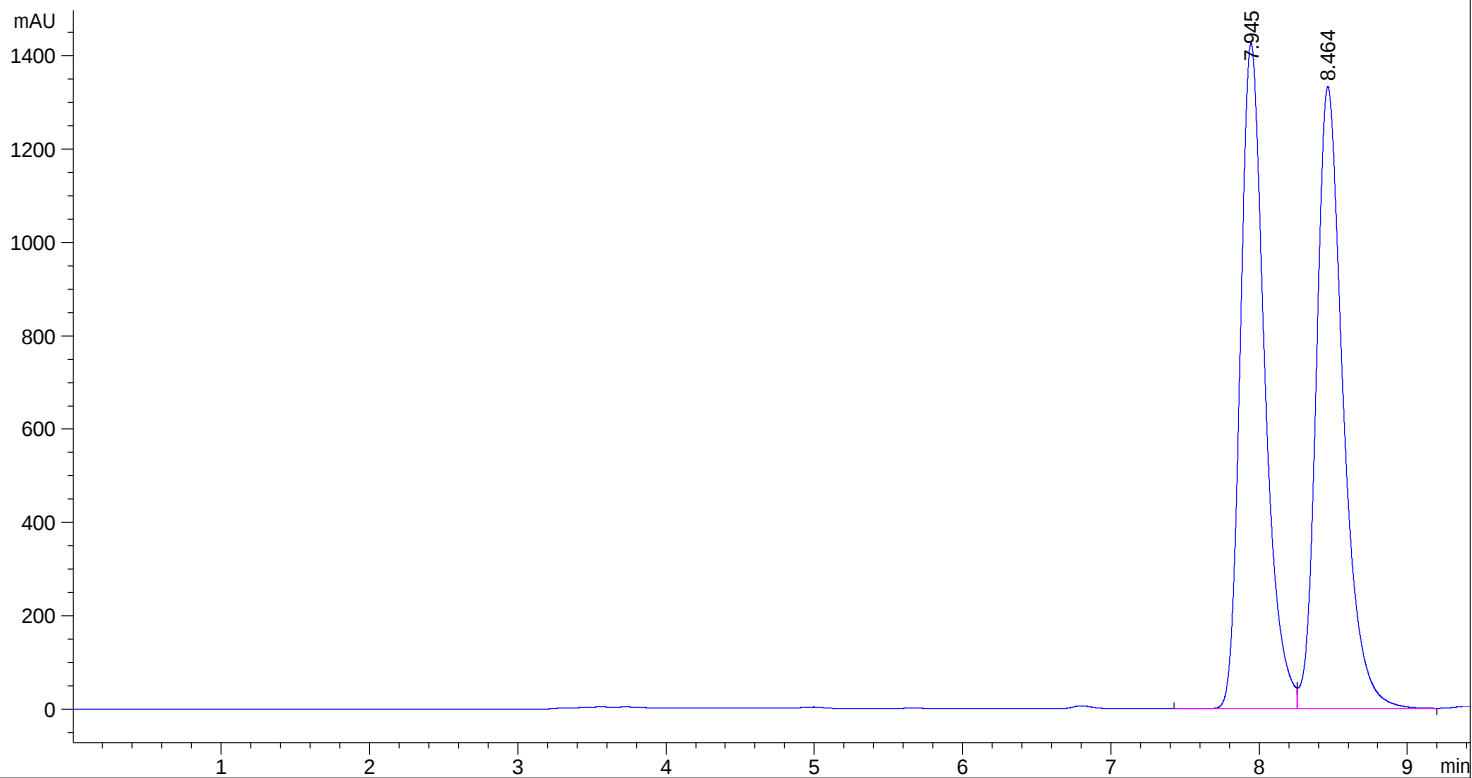
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	9.082	BV	0.2187	1.28905e4	907.65753	47.1559
2	9.652	VB	0.2633	1.44454e4	825.02460	52.8441

VWD1 A, Wavelength=254 nm



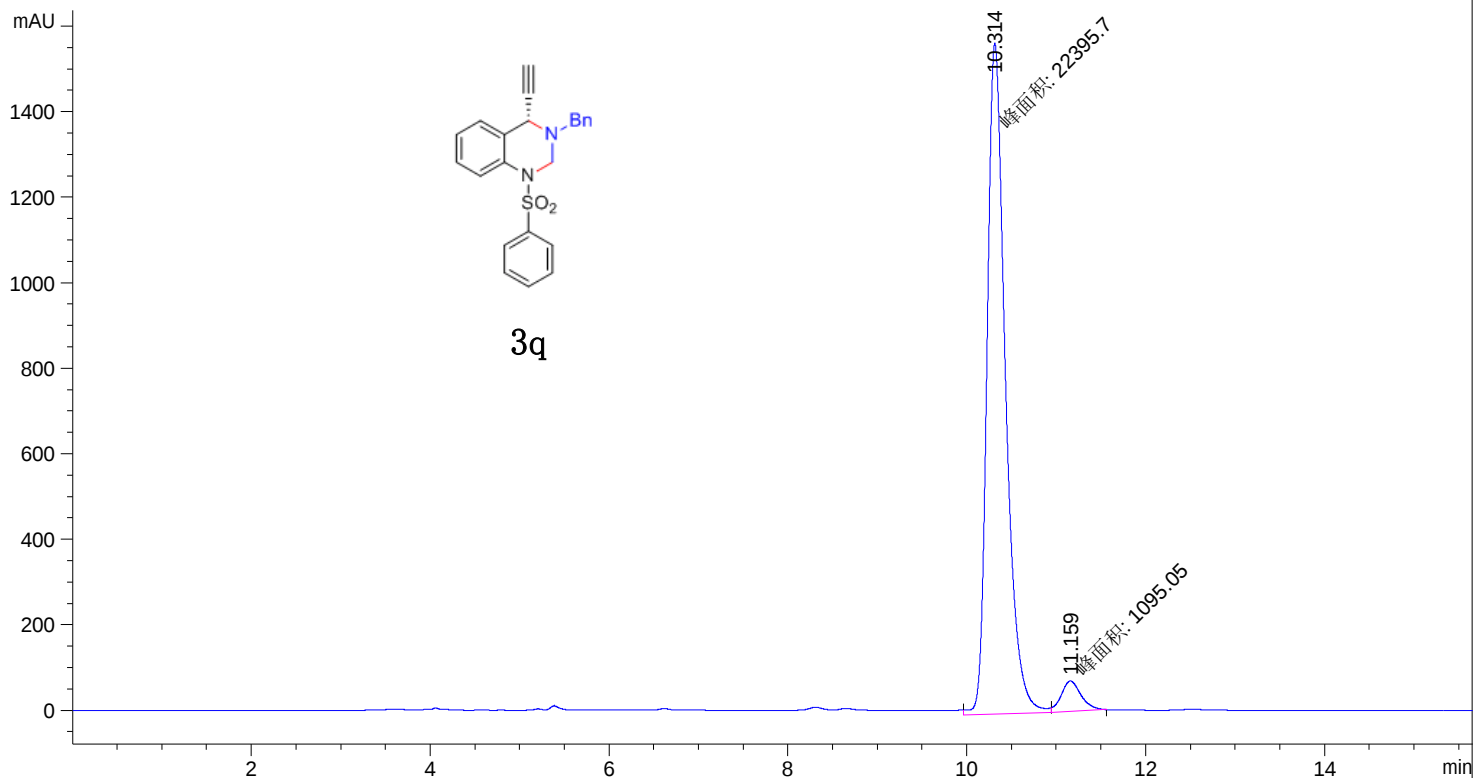
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.905	BV	0.2076	4784.94824	354.27237	73.7061
2	9.478	VB	0.2255	1706.97949	115.46147	26.2939

VWD1 A, Wavelength=254 nm



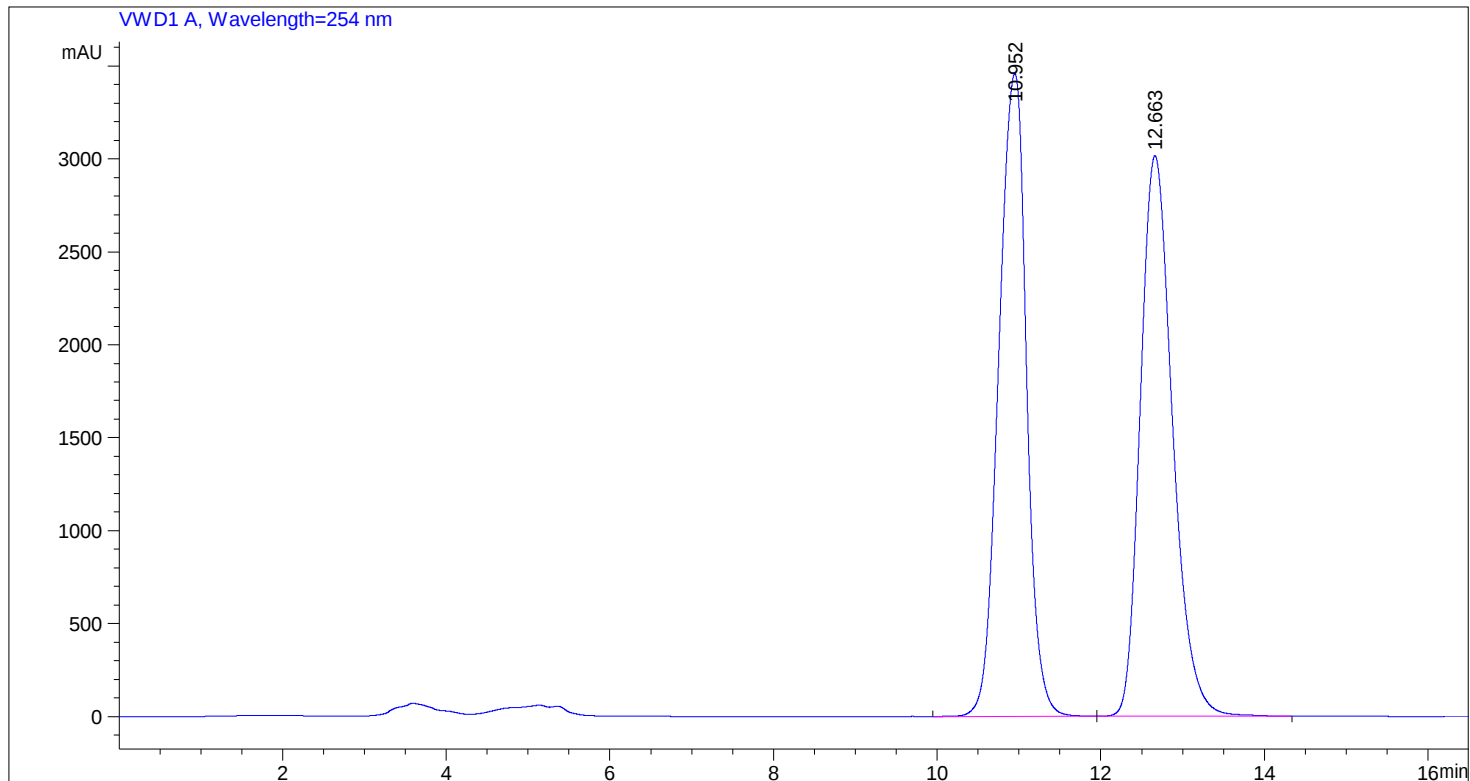
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	7.945	BV	0.1741	1.63380e4	1426.24072	49.4195
2	8.464	VB	0.1903	1.67218e4	1333.08936	50.5805

VWD1 A, Wavelength=254 nm



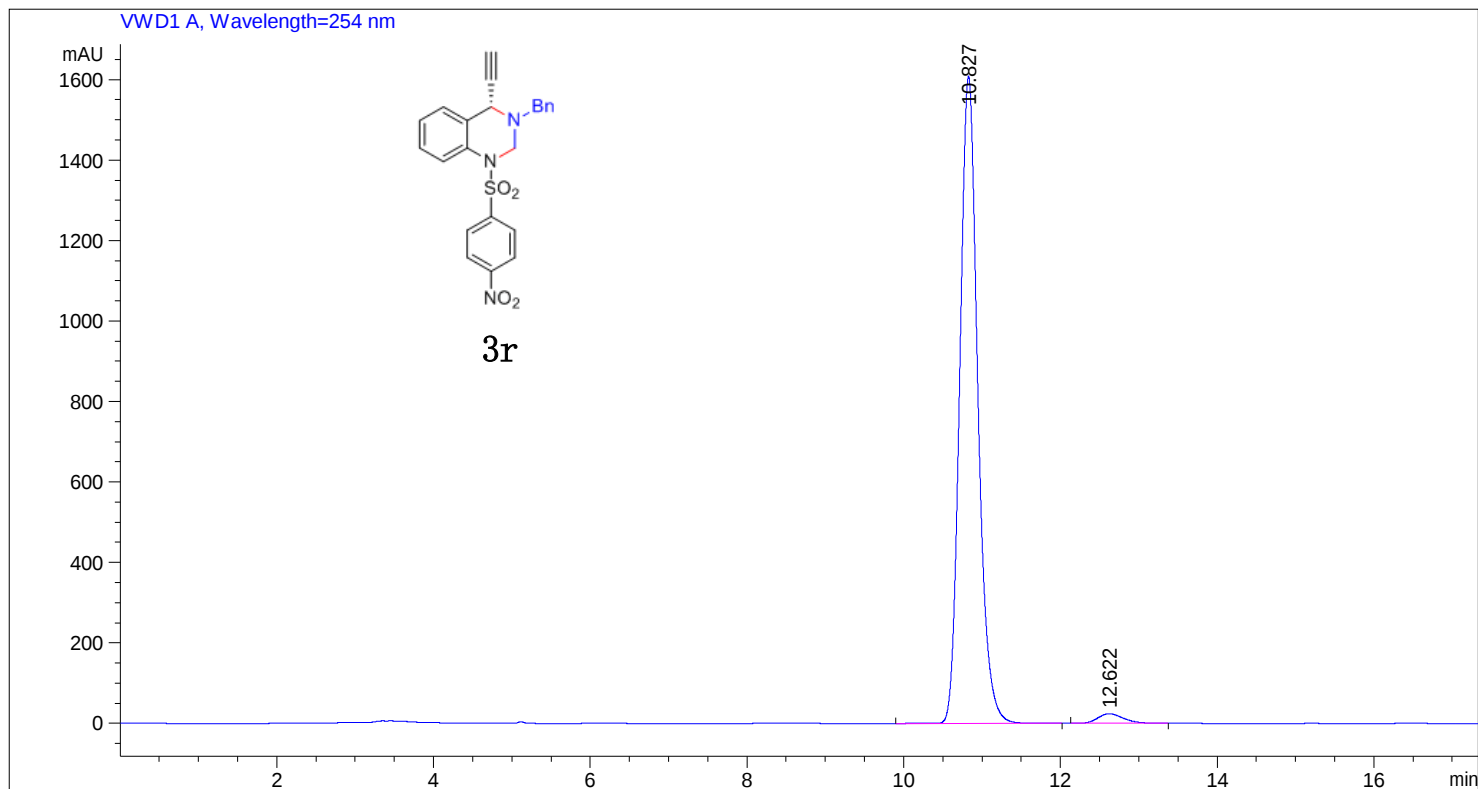
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	10.314	MM	0.2380	2.23957e4	1568.16797	95.3384
2	11.159	MM	0.2569	1095.04993	71.04025	4.6616

VWD1 A, Wavelength=254 nm

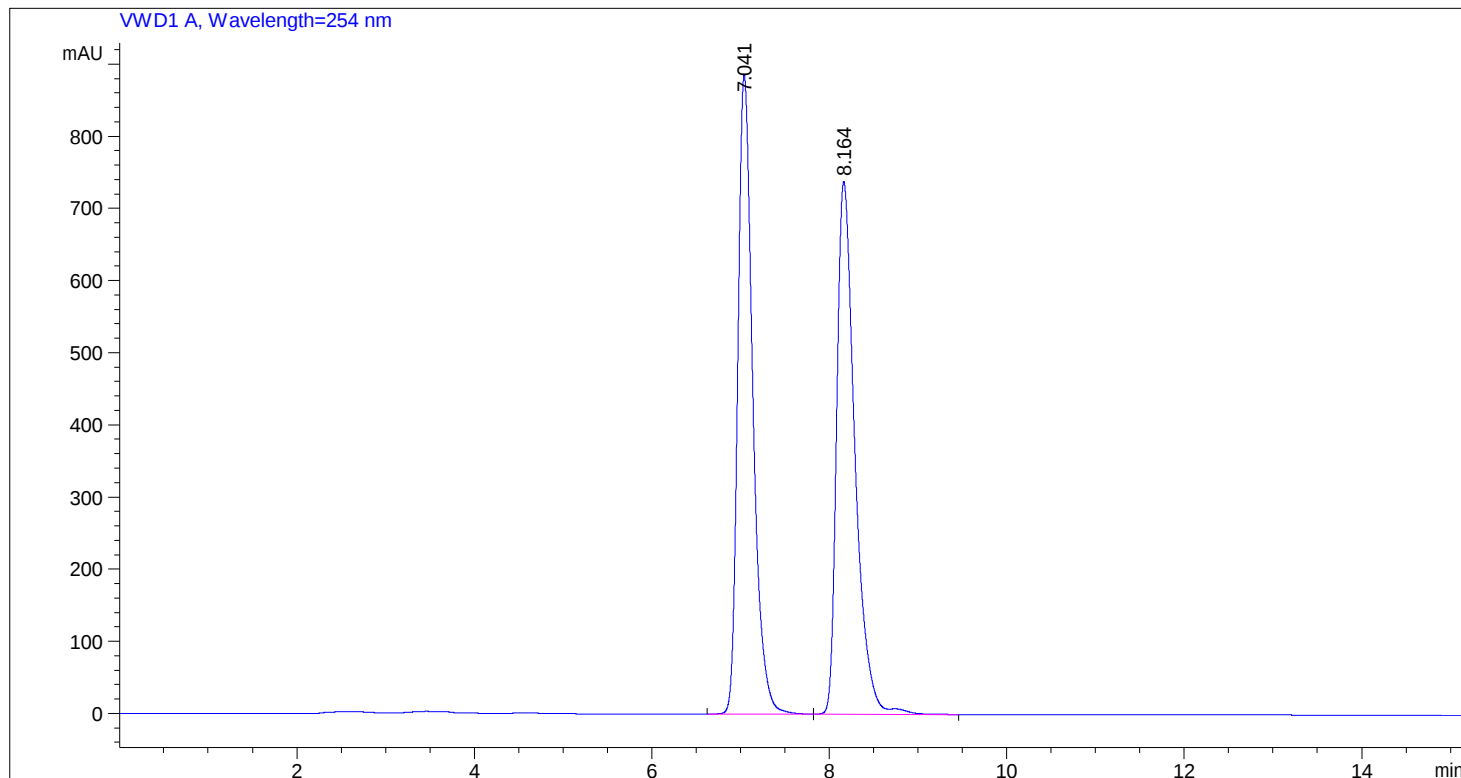


峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	10.952	BB	0.3729	8.14921e4	3458.49951	49.6923
2	12.663	BB	0.4236	8.25014e4	3016.66162	50.3077

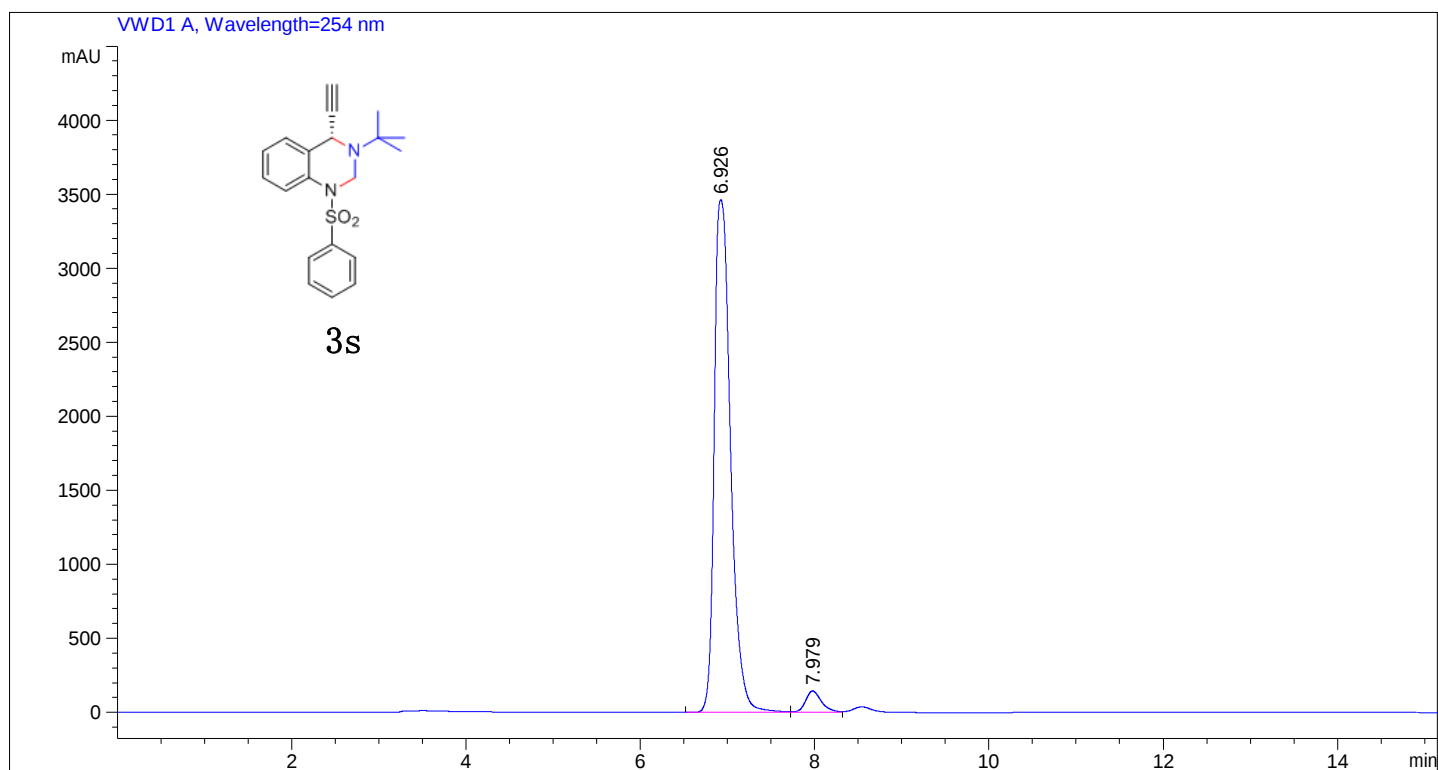
VWD1 A, Wavelength=254 nm



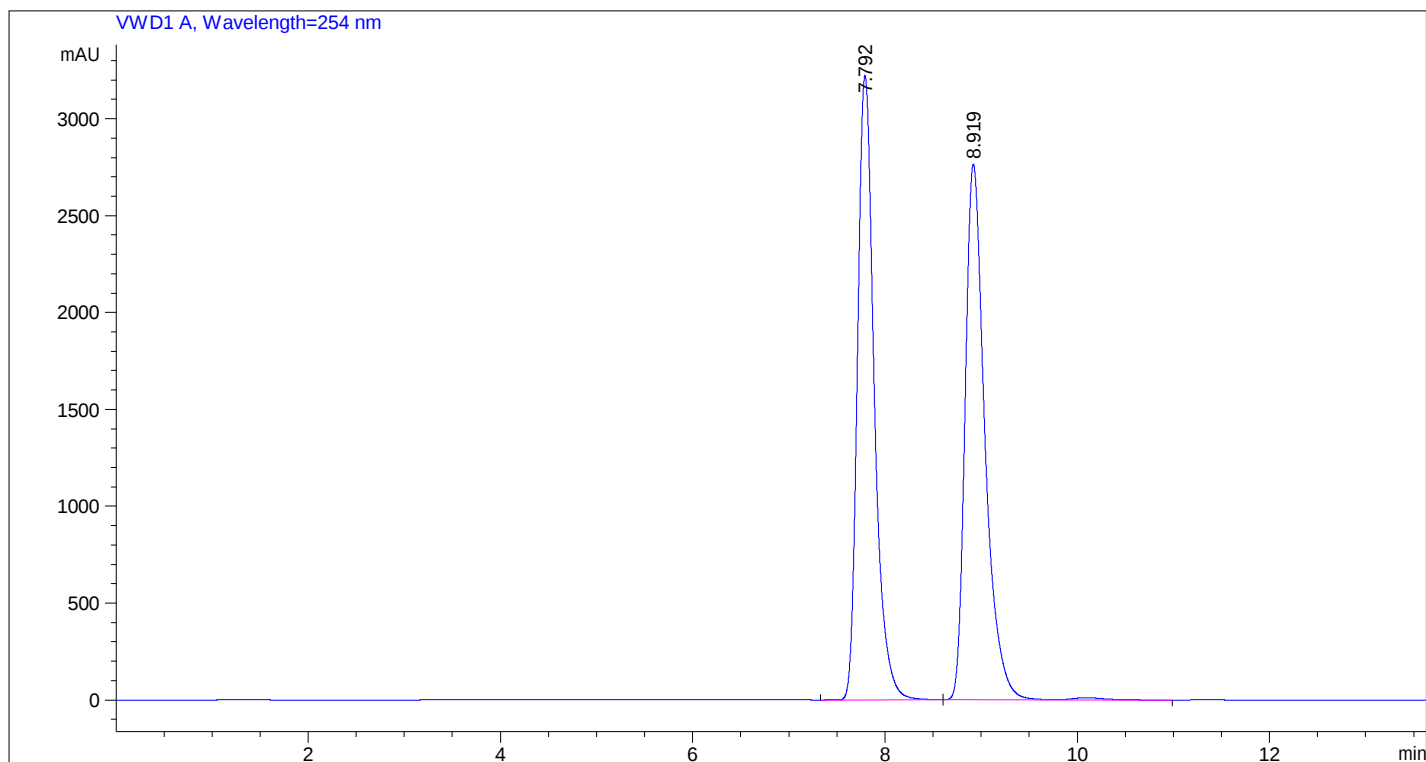
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	10.827	VB R	0.2442	2.56750e4	1608.50024	97.9017
2	12.622	BB	0.3481	550.29724	24.17424	2.0983



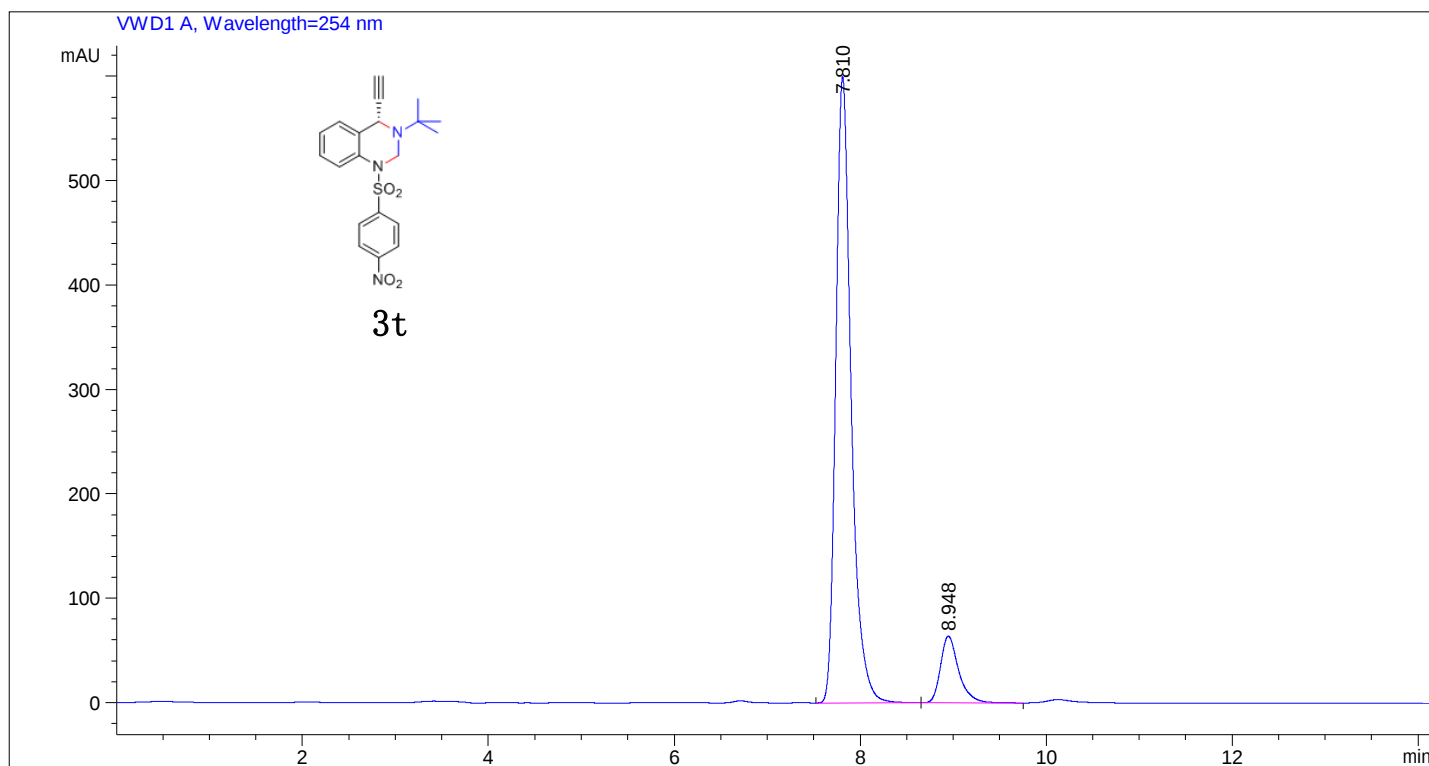
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	7.041	BB	0.1803	1.04278e4	886.37646	49.7581
2	8.164	BV R	0.2153	1.05292e4	738.17401	50.2419



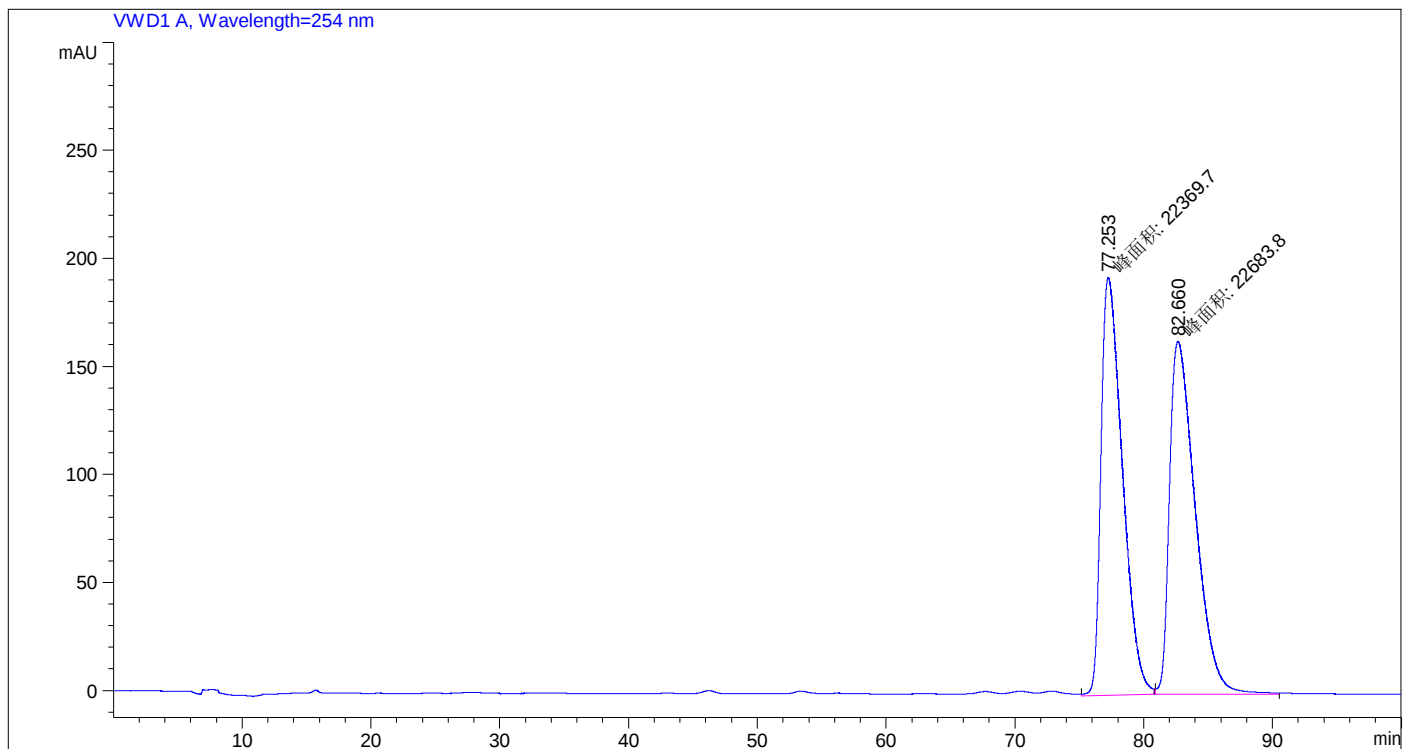
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	6.926	BV	0.1988	4.50466e4	3462.82959	95.9709
2	7.979	VV	0.1951	1891.15576	145.56007	4.0291



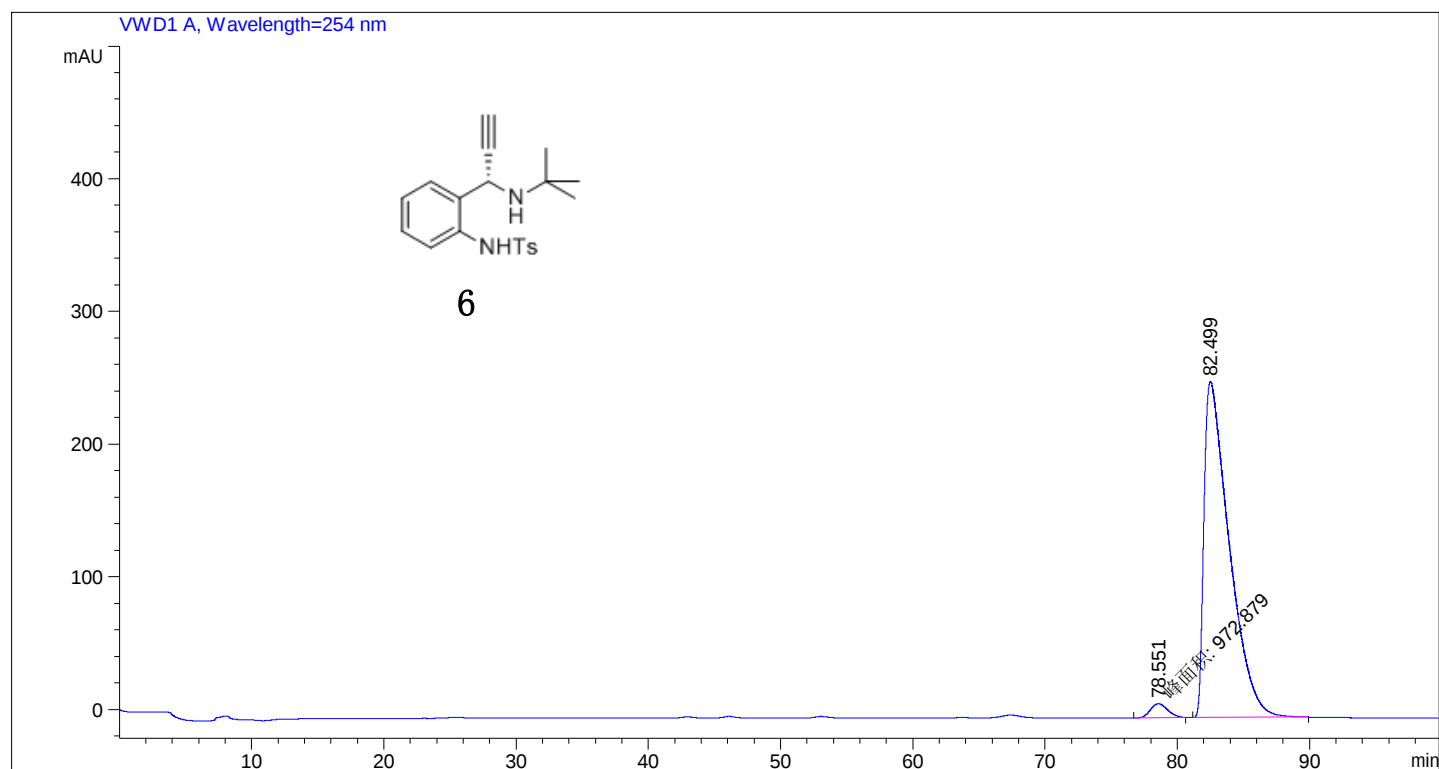
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	7.792	VB R	0.1848	3.90220e4	3222.25854	49.5742
2	8.919	BV R	0.2159	3.96923e4	2764.49878	50.4258



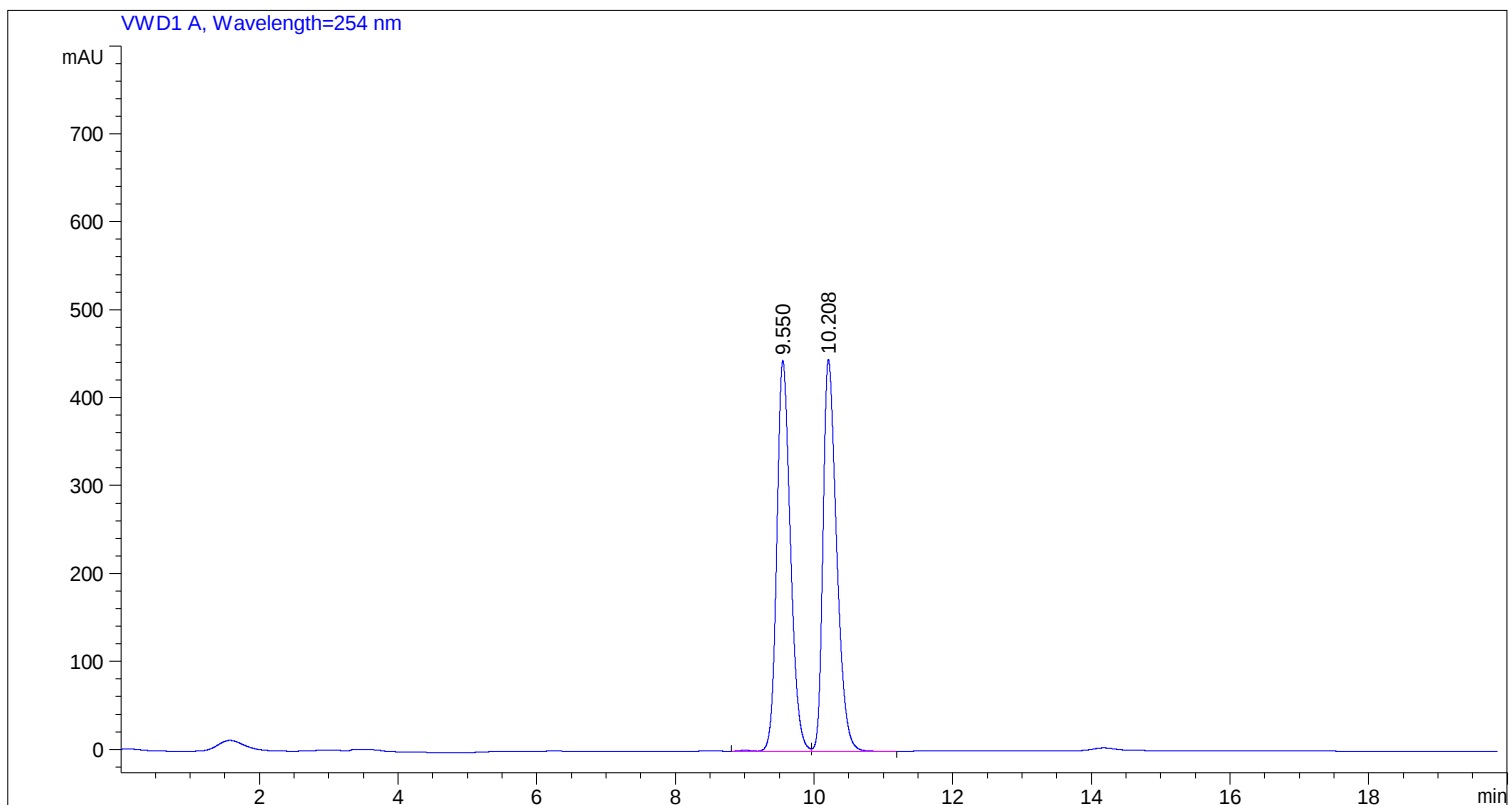
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	7.810	BB	0.1739	6883.34131	599.88135	88.8002
2	8.948	BB	0.2035	868.15454	64.10262	11.1998



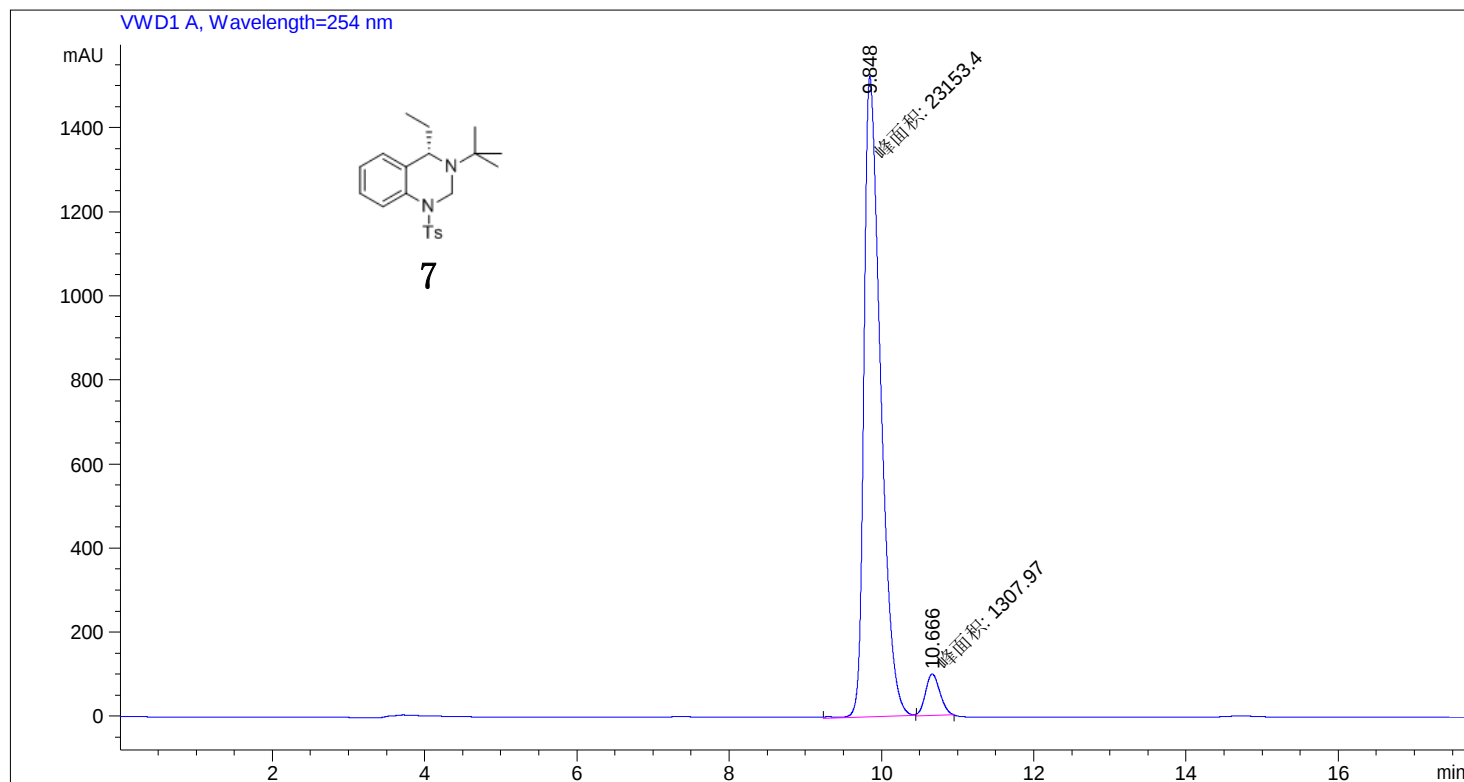
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	77.253	MM	1.9288	2.23697e4	193.29320	49.6513
2	82.660	MM	2.3176	2.26838e4	163.12752	50.3487



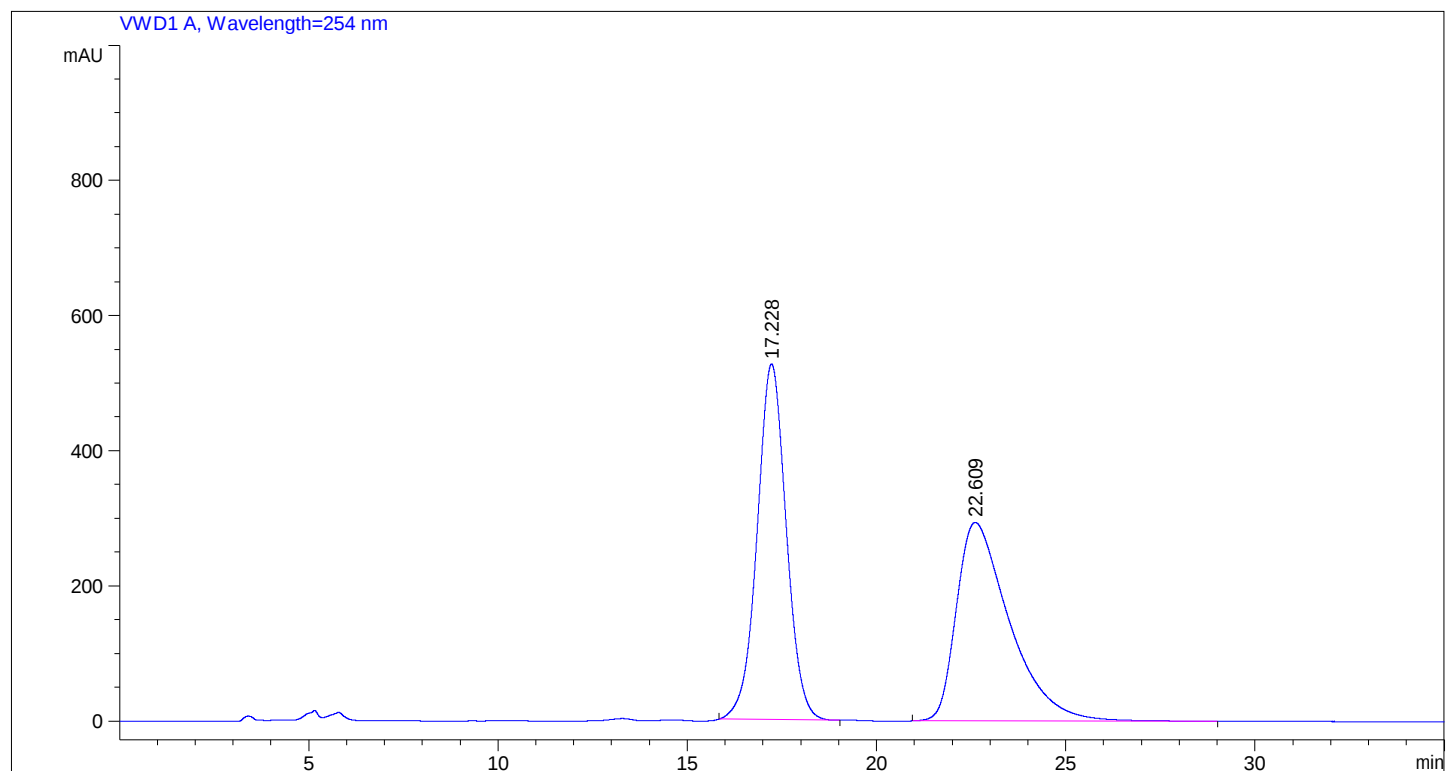
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	78.551	MM	1.5280	972.87927	10.61200	2.8209
2	82.499	BB	1.7581	3.35151e4	253.31650	97.1791



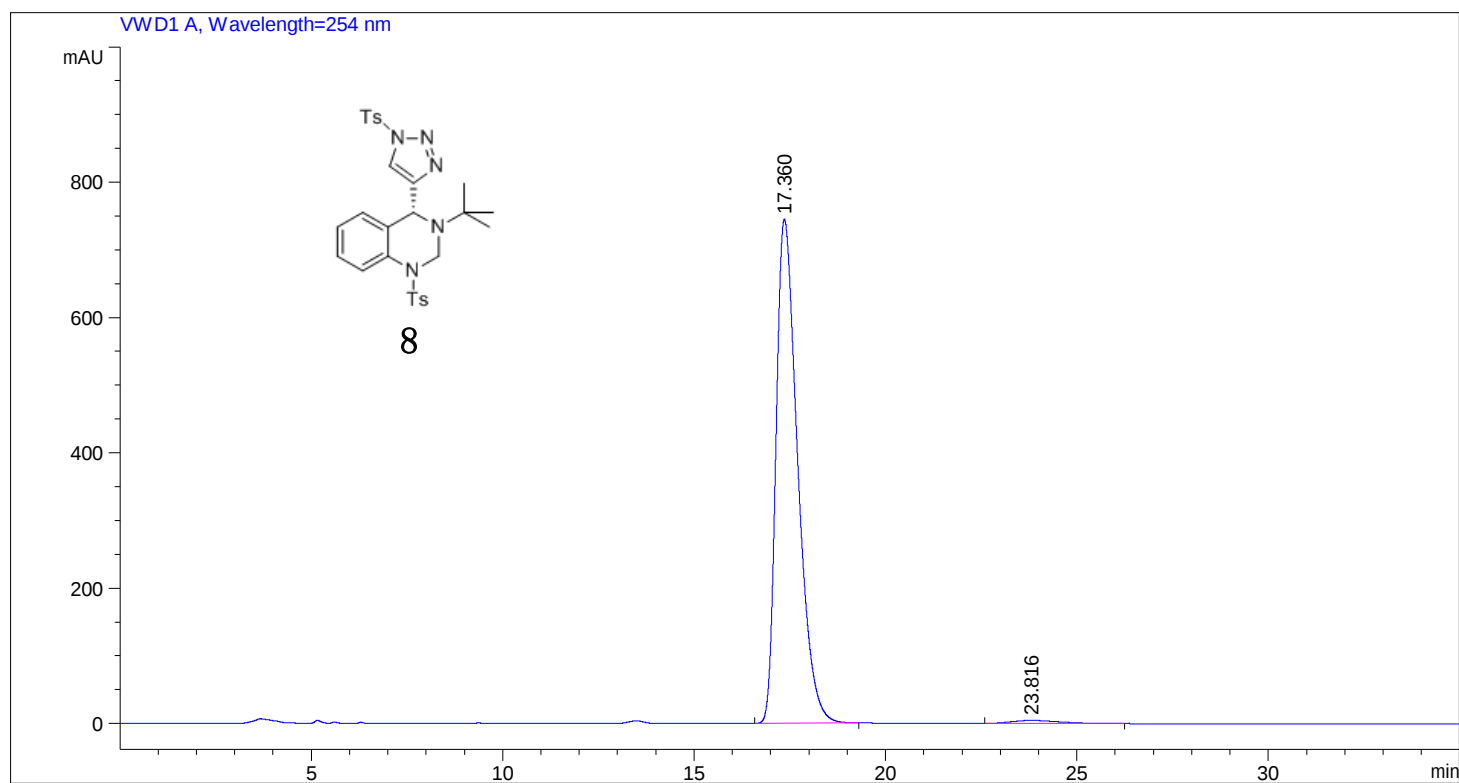
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	9.550	VV R	0.2094	6065.76270	444.04050	49.9585
2	10.208	VB	0.2085	6075.83984	445.71277	50.0415



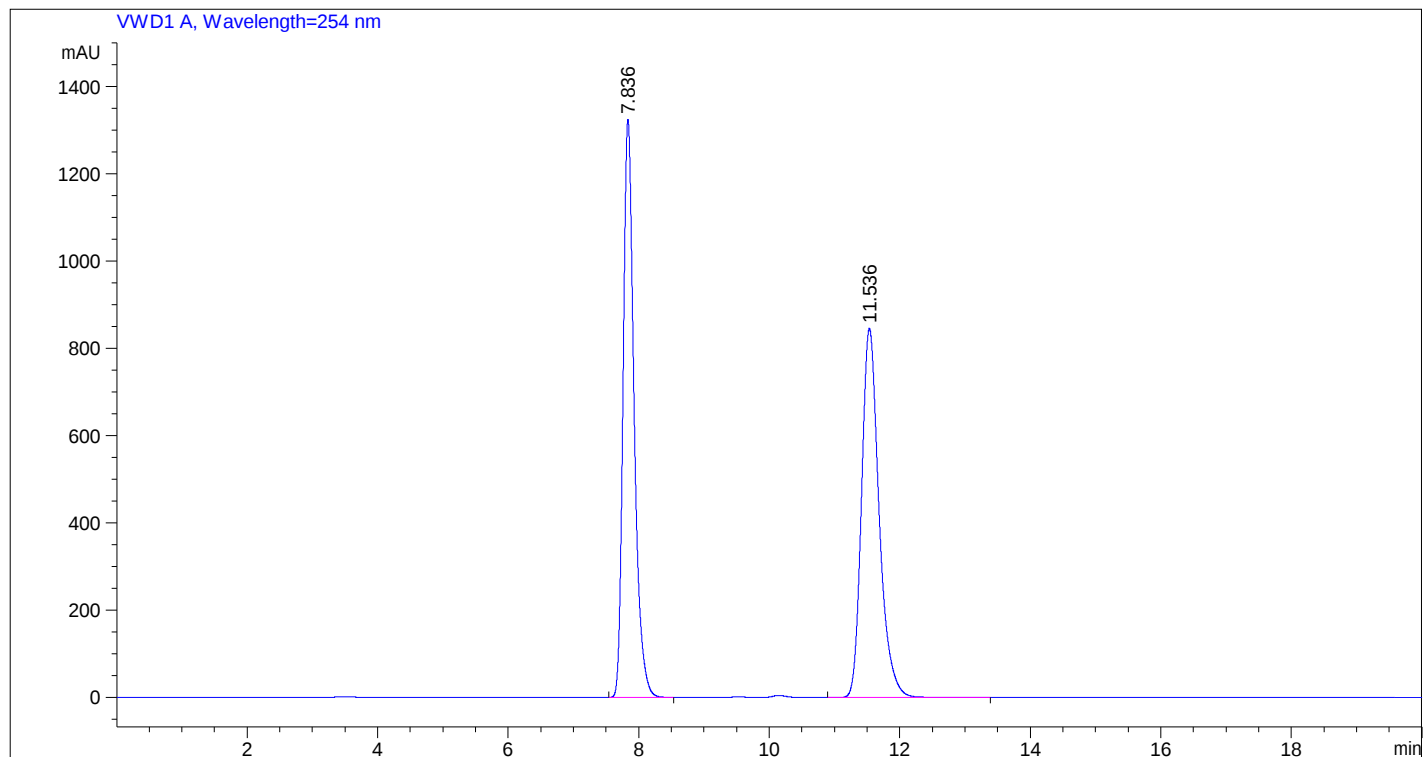
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	9.848	MM	0.2533	2.31534e4	1523.30676	94.6529
2	10.666	MM	0.2197	1307.97021	99.21782	5.3471



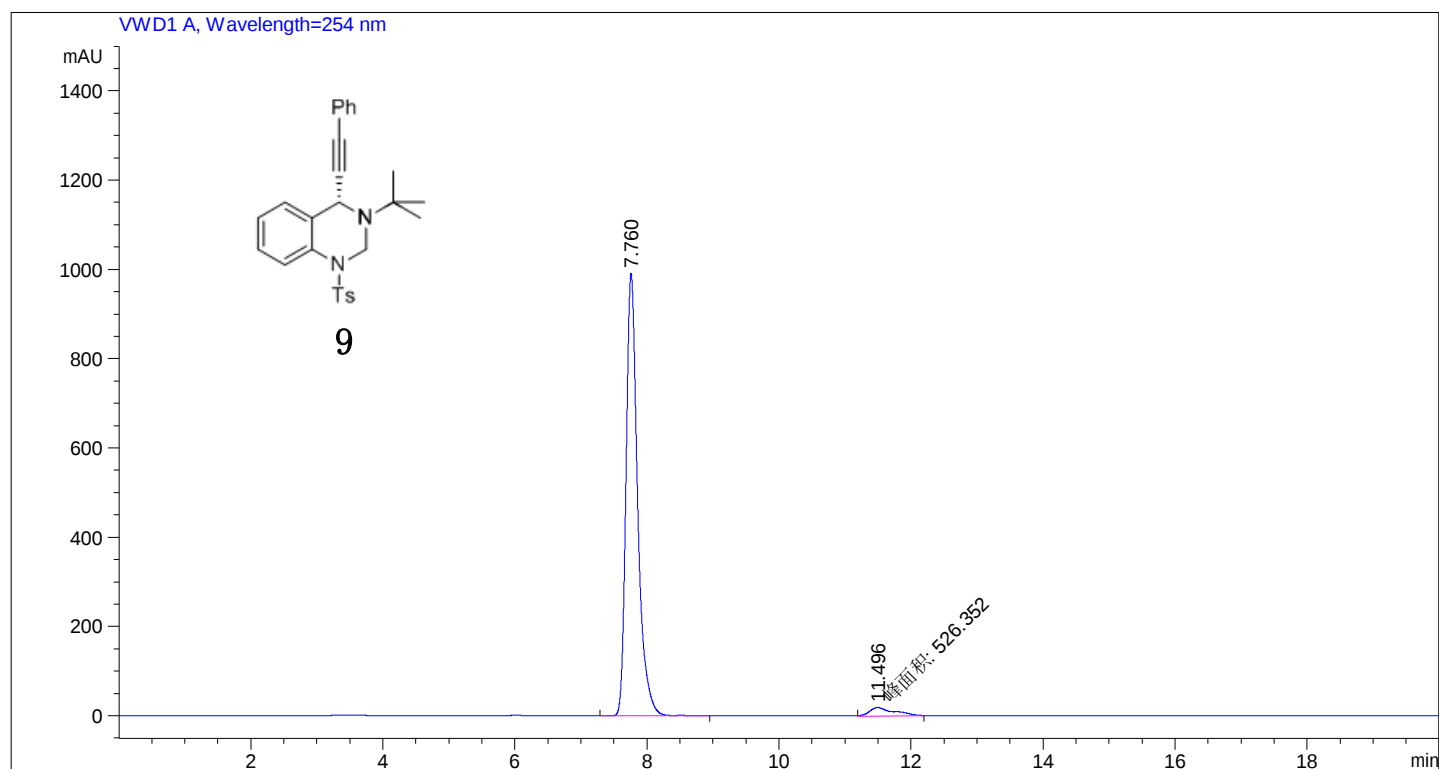
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	17.228	BB	0.8033	2.82186e4	526.51434	49.6077
2	22.609	BB	1.3321	2.86650e4	293.83835	50.3923



峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	17.360	BB	0.5967	2.91654e4	745.04846	98.6782
2	23.816	BB	1.0132	390.68149	4.51403	1.3218



峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	7.836	VB	0.1782	1.55137e4	1323.79175	49.5822
2	11.536	BB	0.2841	1.57751e4	845.74237	50.4178



峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	7.760	BV R	0.1844	1.20970e4	991.13800	95.8303
2	11.496	MM	0.4508	526.35162	19.46002	4.1697