

Supporting information for

**Symmetry in Cascade Chirality-Transfer Processes: A Catalytic
Atroposelective Direct Arylation Approach to BINOL**

Derivatives

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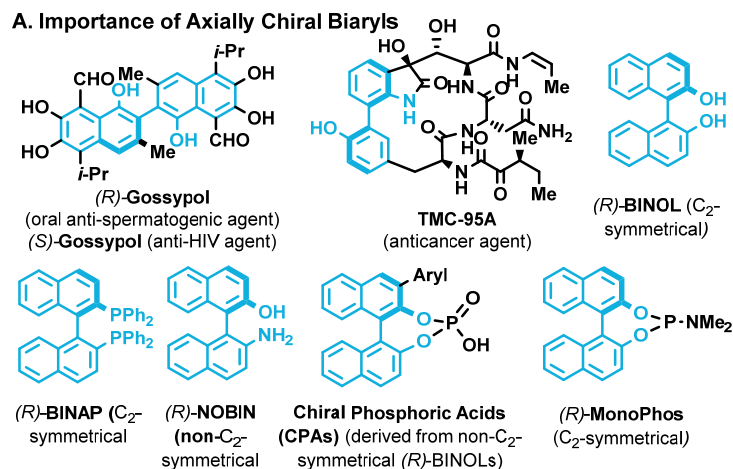
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Table of contents

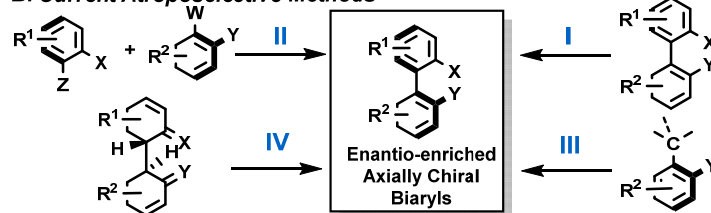
General Methods.....	S2
Figure 1 and Figure 4.....	S3
Optimization of the reaction conditions.....	S4
Explanation of substrate stereocontrol.....	S5
General procedure for synthesis of substrate 6	S6
General procedure for the enantioselective synthesis of biaryls.....	S9
General procedure for synthesis of chiral CPA 7i and used as a catalyst.....	S23
General procedure for synthesis of compound 9ea *.....	S24
References.....	S24
Copies of NMR and HPLC spectra.....	S25

General Methods.

All reactions were carried out in oven-dried glassware under air with magnetic stirring. All Naphthol compounds were purchased from Sigma-Aldrich Co. and used without further purification. Reactions were monitored by TLC on silica gel 60 F254 plates. Column chromatography was carried out on silica gel (200-300 mesh). Proton (^1H) and carbon (^{13}C) NMR spectra were recorded on an ACF* 300Q Bruker spectrometer operating at 300 MHz (or 500 MHz) for proton and 75 MHz (or 151 MHz) for carbon nuclei using CDCl_3 [or $(\text{CD}_3)_2\text{SO}$] as solvent, respectively. Chemical shifts are expressed as parts per million (δ , ppm) and are referenced to 7.26 (CDCl_3) or 2.50 $(\text{CD}_3)_2\text{SO}$ for ^1H NMR and 77.23 (CDCl_3) or 39.51 $(\text{CD}_3)_2\text{SO}$ for ^{13}C NMR. Data for ^1H NMR are recorded as follows: chemical shift (δ , ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br s = broad singlet, coupling constant (s) in Hz, integration). Data for ^{13}C NMR are reported in terms of chemical shift (δ , ppm). High Resolution Mass Spectrometry was performed on a Agilent Technologies 6230 TOF LC/MS under the conditions of electrospray ionization (ESI) in both positive and negative mode. Optical rotations were measured using a 2-mL cell with a 10-cm path length on Rudolph Autopol[®] IV automatic polarimeter, and concentrations (c) were reported in $\text{g}\times(100\text{ mL})^{-1}$. Analytical HPLC was recorded on a HPLC machine equipped with SHIMADZU LC-20AT HPLC Pump and SHIMADZU SPD-20A Photodiode Array Detector (SHIMADZU HPLC machine). The chiral stationary phase was Daicel Chiralpak AD-H or IA, IA-3 column ($\text{Ø} = 0.46\text{ cm}$, length = 25.0 cm). Melting points were recorded on Tianjin Analysis Instrument Factory RY-1.



B. Current Atroposelective Methods



I: Traditional resolution, catalytic kinetic resolution or desymmetrization via dynamic kinetic resolution; II: Direct atroposelective biaryl coupling (via metal-catalyzed cross-coupling or oxidation); III: Atroposelective biaryl synthesis by *de novo* construction of an aromatic ring (via cycloaddition or aldol condensation); IV: Central-to-axial chirality exchange (oxidative dimerization, Michael addition or sigmatropic rearrangement).

C. THIS WORK: Organocatalytic Atroposelective Direct Arylation

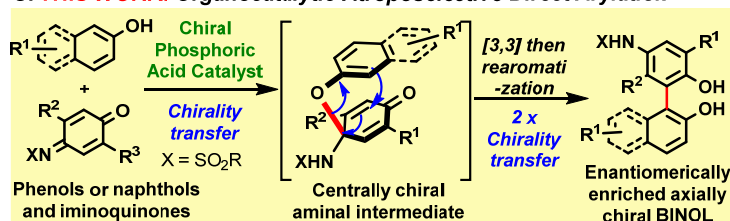


Figure 1. Organocatalytic atroposelective direct arylation of hydroxyarenes to afford non- C_2 -symmetrical BINOLs.

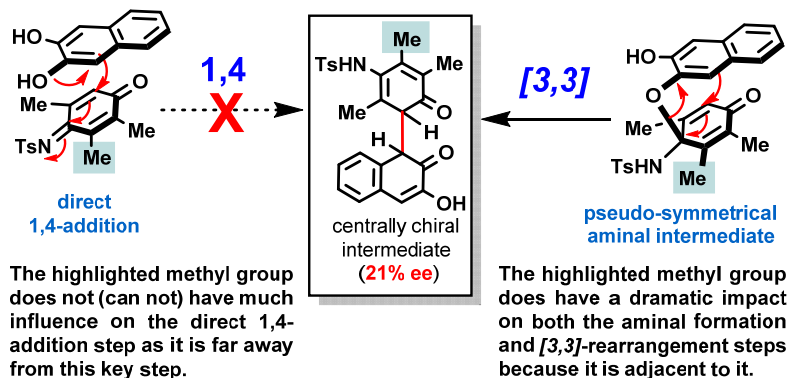
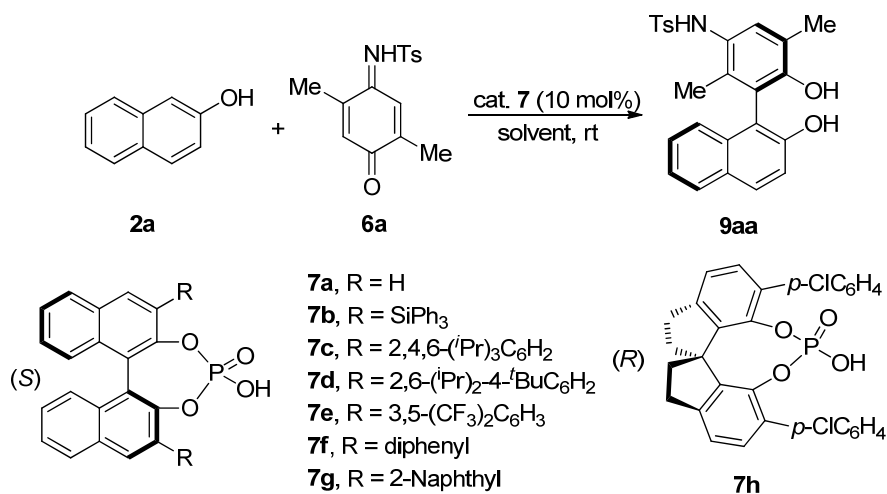


Figure 4. The case is made for the aminal-formation/[3,3]-rearrangement sequence as opposed to a 1,4-direct addition.

Optimization of the reaction conditions for the conversion of 2a + 6a

→ 9aa.

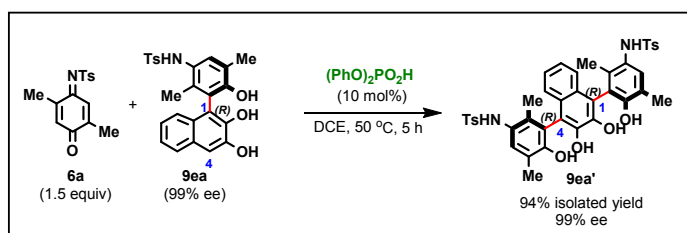


entry	cat.	solvent	time (h)	ee (%) ^b
1	7a	CH ₂ Cl ₂	48	25
2	7b	CH ₂ Cl ₂	48	49
3	7c	CH ₂ Cl ₂	48	77
4	7d	CH ₂ Cl ₂	48	44
5	7e	CH ₂ Cl ₂	8	25
6	7f	CH ₂ Cl ₂	8	30
7	7g	CH ₂ Cl ₂	8	46
8	7h	CH ₂ Cl ₂	8	41
9	7c	CH ₃ CN	48	53
10	7c	toluene	48	72
11	7c	DCE	48	88
12	7c	THF	48	5
13	7c	CHCl ₃	48	81
14	7c	chlorobenzene	84	94
15	7c	1,3-di-CF ₃ -benzene	60	86
16 ^c	7c	DCE	24	88
17 ^c	7c	chlorobenzene	48	92
18 ^d	7c	DCE	8	82
19 ^{c,e}	7c	DCE	100	77

^a Reaction conditions: **2a** (0.075 mmol), **6a** (0.05 mmol), cat. (10 mol%), solvent (1 mL). ^b Determined by HPLC analysis. ^c Reacted at 50 °C. ^d Reacted at 80 °C. ^e Using 5 mol% **7c**.

Explanation of substrate stereocontrol.

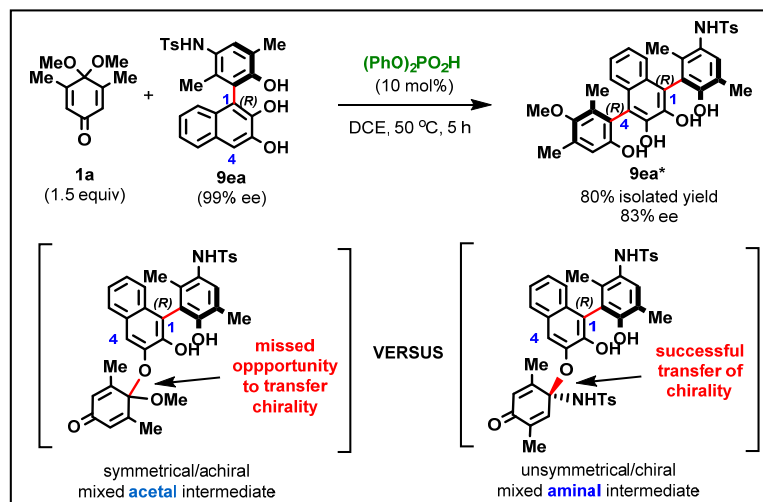
The description about **9ea'** refers to the possibility that once the first axis of chirality was established in position #1 of the 2,3-dihydroxynaphthalene nucleus, the now existing axially chiral stereocenter would exert significant influence over the stereoselectivity of the second aryl-aryl bond-forming step in position #4. To demonstrate that this substrate control is truly operational and completely independent of the chirality of the acid catalyst, we conducted a control experiment (see scheme at



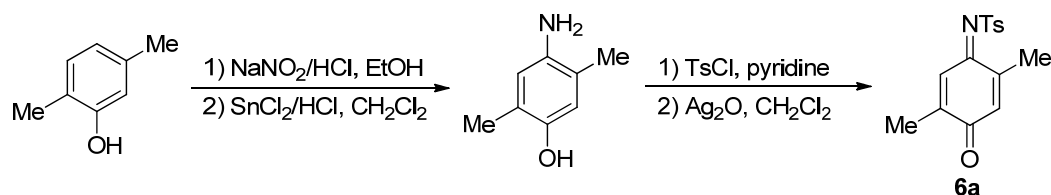
left) in which enantiomerically pure biaryl **9ea** was reacted with slight excess of iminoquinone **6a** (1.5

equivalents) at 50 °C in DCE using 10 mol% of the achiral diphenylphosphoric acid as catalyst. Indeed the product **9ea'** was obtained in excellent isolated yield and also as a single enantiomer (99% *ee*; the stereochemistry at the two chiral axes were determined to be *R,R* using X-ray crystallography). Not even traces of the *meso* diastereomer (*R,S*) were observed using LC/MS analysis.

Moreover, the coupling reaction between symmetrical quinone monoacetal **1a** and enantiomerically pure biaryl **9ea** was also successful (see scheme below) and gave rise to enantiomerically enriched terphenyl **9ea*** in 83% *ee*. Clearly substrate stereocontrol was operational in this case but to a lesser extent than during the formation of terphenyl **9ea'**. Since only a symmetrical acetal intermediate could be formed the system “*missed an opportunity*” to transfer chirality in the first step and the stereoselectivity of the second aryl-aryl bond-forming step (i.e., via the *[3,3]*-sigmatropic rearrangement) could not be perfectly controlled by the substrate.



General procedure for synthesis of the substrates 6. ^[1]

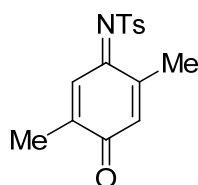


The phenol (50.0 mmol) was dissolved in HCl (33 mL, 12 mol/L) and 95% ethanol (30 mL). NaNO_2 (5.0 g) was slowly added at 0 °C (5 min) maintaining the stirring for 1 h at 0 °C. Ethanol (10 mL) was then added and the stirring was maintained for a further hour at room temperature. The reaction mixture was diluted with water (300 mL) and extracted with ethyl ether. The organic phase was extracted with 10% aqueous Na_2CO_3 solution. The carbonate solution on acidification with HCl (3 mol/L) yielded a precipitate, wash the precipitate with hexane to eliminate soluble impurities. To an eggplant shaped bottle para-benzoquinone mono-oxime (10.0 mmol) was dissolved in CH_2Cl_2 (100 mL), then concentrated HCl (2 mL) was added. The solution was heated to reflux, then SnCl_2 (5.7 g, 30.0 mmol) was added. The mixture was heated to reflux for 24 h. Then remove the CH_2Cl_2 under reduced pressure, and the residue was dissolved in ethyl acetate and washed with concentrated aqueous NaHCO_3 . Filter off the precipitate and the organic layer was dried over anhydrous Na_2SO_4 and the filtrate was concentrated under reduced pressure to afford the solid amino phenols.

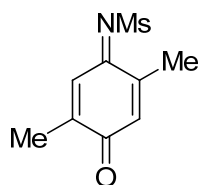
Then the para-amino-phenol (5.0 mmol) was dissolved in dry pyridine (6 mL) and

cooled to 0 °C. Para-toluenesulfonyl chloride (1.14 g, 6.0 mmol) was added in small portions. The mixture was warmed to room temperature and stirred under nitrogen for 24 h. The reaction mixture was diluted with EtOAc and washed with HCl (10 mol/L), the organic layer was dried over anhydrous MgSO₄, filtered, and concentrated to yield the crude sulfonamide.

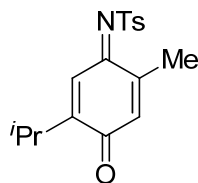
The N-tosyl-para-aminophenol (4.0 mmol) was dissolved in dry CH₂Cl₂ (15 mL) and Ag₂O (8.0 mmol) was added, and stirred. The reaction was monitored by TLC. When the reaction was completed, the solution was filtered through celatom. The organic layer was concentrated to yield the crude product. The product **6** was purified by silica gel column using petroleum ether/ acetone (20:1) as eluent. 35-45% yields (4 steps).



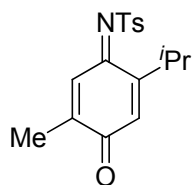
6a, yellow solid (920 mg, 45% yield). ¹H NMR (500 MHz, DMSO-*d*₆) δ 7.91 (d, *J* = 8.2 Hz, 2H), 7.83 (s, 1H), 7.51 (d, *J* = 8.2 Hz, 2H), 6.75 (s, 1H), 2.46 (s, 3H), 2.07 (s, 3H), 2.00 (s, 3H).



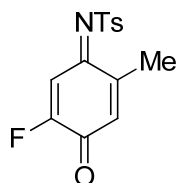
6b, brown solid (620 mg, 40% yield). ¹H NMR (500 MHz, DMSO-*d*₆) δ 7.64 (s, 1H), 6.75 (s, 1H), 3.40 (s, 3H), 2.10 (s, 3H), 2.03 (s, 3H).



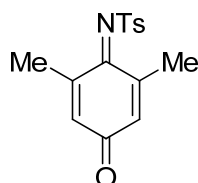
6c, yellow solid (420 mg, 35% yield). ¹H NMR (500 MHz, DMSO-*d*₆) δ 7.90 (d, *J* = 8.0 Hz, 2H), 7.74 (s, 1H), 7.51 (d, *J* = 7.6 Hz, 2H), 6.74 (s, 1H), 3.02-2.97 (m, 1H), 2.45 (s, 3H), 2.01 (s, 3H), 1.11 (d, *J* = 6.8 Hz, 6H).



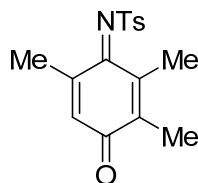
6d, yellow solid (470 mg, 38% yield). $^1\text{H NMR}$ (500 MHz, $\text{DMSO-}d_6$) δ 7.92-7.85 (m, 3H), 7.51 (d, $J = 7.2$ Hz, 2H), 6.60 (s, 1H), 3.00-2.92 (m, 1H), 2.45 (s, 3H), 2.07 (s, 3H), 1.05 (d, $J = 7.2$ Hz, 6H).



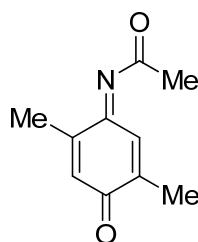
6e, brown solid (350 mg, 36% yield). $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.92-7.89 (m, 3H), 7.39 (d, $J = 8.0$ Hz, 2H), 6.60-6.57 (m, 1H), 2.48 (s, 3H), 2.11 (s, 3H).



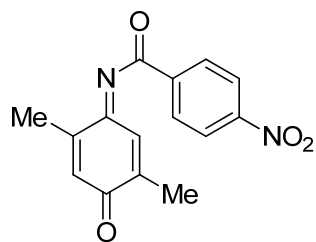
6f, orange solid (210 mg, 18% yield). $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.80 (s, $J = 8.3$ Hz, 2H), 7.28 (d, $J = 8.2$ Hz, 2H), 6.42 (s, 2H), 2.39 (s, 3H), 2.25 (s, 6H).



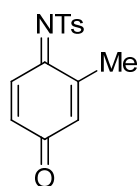
6g, orange solid (235 mg, 22% yield). $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.88 (d, $J = 8.1$ Hz, 2H), 7.35 (d, $J = 8.0$ Hz, 2H), 6.48 (s, 1H), 2.47 (s, 3H), 2.37 (s, 3H), 2.23 (s, 3H), 2.05 (s, 3H).



6h, yellow solid (450 mg, 40% yield). $^1\text{H NMR}$ (500 MHz, $\text{DMSO-}d_6$) δ 6.88 (s, 1H), 6.62 (s, 1H), 2.30 (s, 3H), 2.09 (s, 3H), 1.95 (s, 3H).



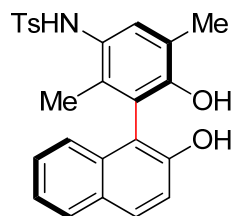
6i, yellow solid (380 mg, 38% yield). $^1\text{H NMR}$ (500 MHz, $\text{DMSO-}d_6$) δ 8.38 (d, $J = 8.4$ Hz, 2H), 8.17 (d, $J = 8.4$ Hz, 2H), 6.85 (s, 1H), 6.75 (s, 1H), 2.25 (s, 3H), 1.91 (s, 3H).



6j, brown solid (280 mg, 34% yield). $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 8.19-8.15 (m, 1H), 7.89 (d, $J = 7.9$ Hz, 2H), 7.36 (d, $J = 8.0$ Hz, 2H), 6.63-6.55 (m, 2H), 2.48 (s, 3H), 2.06 (s, 3H).

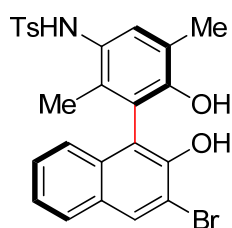
General procedure for the enantioselective synthesis of biaryls.

To a stirred solution of **2a** (32.5 mg, 0.225 mmol) and **6a** (43.5 mg, 0.15 mmol) in DCE or chlorobenzene (3 mL), cat. CPA **7c** (11.2 mg, 10 mol%) was added in one portion at room temperature, and it was stirred at rt or 50 °C until the reaction was completed. Solvent was removed under reduced pressure and the crude residue was purified by column chromatography on silica-gel (petroleum ether/acetone = 8:1 to 1:1) to give pure product **9aa** (63.0 mg, 97% yield).

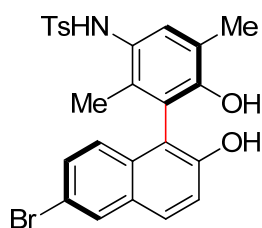


9aa, white solid, 97% yield (63.0 mg), 88% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; $t_R = 15.32$ (minor), 50.88 (major) min]. $[\alpha]_D^{20} = -82.7$ ($c = 0.3$, CH_3OH). $^1\text{H NMR}$ (500 MHz, $\text{DMSO-}d_6$) δ 9.22 (br s, 1H), 9.14 (br s, 1H), 7.77 (d, J

= 7.9 Hz, 1H), 7.73 (d, $J = 8.8$ Hz, 1H), 7.50 (d, $J = 6.4$ Hz, 2H), 7.49 (s, 1H), 7.32 (d, $J = 8.0$ Hz, 2H), 7.29-7.19 (m, 3H), 6.88 (s, 1H), 6.83 (d, $J = 8.2$ Hz, 1H), 2.31 (s, 3H), 2.12 (s, 3H), 1.21 (s, 3H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 152.45, 151.96, 142.45, 137.76, 133.50, 133.32, 131.54, 129.56, 129.41, 128.67, 128.08, 127.84, 126.67, 125.94, 125.86, 123.77, 122.26, 121.52, 118.51, 116.09, 21.00, 16.55, 14.36. HRMS (ESI-TOF): Exact mass calcd. for $\text{C}_{25}\text{H}_{23}\text{NO}_4\text{S}$ $[\text{M}+\text{Na}]^+$ 456.1240, Found: 456.1240. MP 139-141 $^\circ\text{C}$.

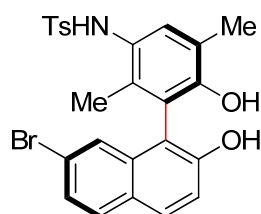


9ba, brown solid, 87% yield (66.9 mg), 92% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; $t_{\text{R}} = 11.38$ (major), 16.62 (minor) min]. $[\alpha]_{\text{D}}^{20} = -56.0$ (c = 0.3, CH_3OH). ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 9.19 (br s, 1H), 8.39 (br s, 1H), 8.17 (s, 1H), 7.78 (dd, $J = 3.5, 6.2$ Hz, 1H), 7.50 (d, $J = 8.2$ Hz, 2H), 7.38-7.25 (m, 4H), 6.95 (s, 1H), 6.80-6.73 (m, 1H), 2.30 (s, 3H), 2.14 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 152.66, 148.98, 142.85, 138.05, 133.68, 132.86, 131.56, 130.70, 129.80, 129.35, 127.42, 127.09, 126.80, 126.50, 124.39, 123.94, 122.83, 122.39, 119.60, 114.23, 21.39, 16.99, 14.74. HRMS (ESI-TOF): Exact mass calcd. for $\text{C}_{25}\text{H}_{22}\text{BrNO}_4\text{S}$ $[\text{M}+\text{Na}]^+$ 534.0345, Found: 534.0360. MP 113-115 $^\circ\text{C}$.

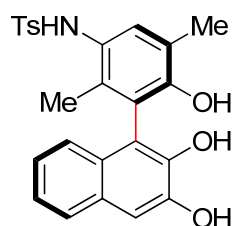


9ca, Brown solid, 88% yield (67.6 mg), 78% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; $t_{\text{R}} = 11.53$ (major), 14.36 (minor) min]. $[\alpha]_{\text{D}}^{20} = -71.0$ (c = 0.3,

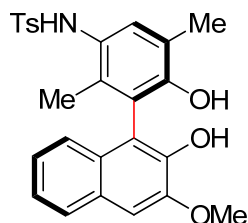
CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.41 (br s, 1H), 9.16 (br s, 1H), 8.03 (s, 1H), 7.74 (d, *J* = 8.9 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.41 (dd, *J* = 1.6, 8.8 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 8.9 Hz, 1H), 6.91 (s, 1H), 6.74 (d, *J* = 8.9 Hz, 1H), 2.32 (s, 3H), 2.12 (s, 3H), 1.16 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 153.39, 152.33, 142.82, 138.09, 133.62, 132.57, 130.18, 129.89, 129.83, 129.69, 129.20, 128.34, 127.08, 126.51, 126.29, 123.58, 122.09, 120.11, 116.91, 115.49, 21.37, 16.93, 14.67. HRMS (ESI-TOF): Exact mass calcd. for C₂₅H₂₂BrNO₄S [M+Na]⁺ 534.0345, Found: 534.0351. MP 113-115 °C.



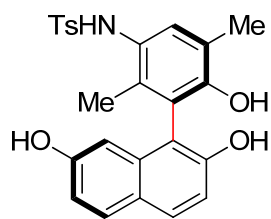
9da, brown solid, 84% yield (64.6 mg), 81% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; *t_R* = 11.60 (minor), 21.28 (major) min]. [α]_D²⁰ = -52.0 (c = 0.3, CH₃OH). ¹H NMR (300 MHz, CDCl₃) δ 7.83 (d, *J* = 8.9 Hz, 1H), 7.69 (d, *J* = 8.7 Hz, 1H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.44 (dd, *J* = 1.9, 11.2 Hz, 1H), 7.36 (s, 1H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.25 (s, 1H), 7.16 (d, *J* = 1.7 Hz, 1H), 6.14 (br s, 1H), 4.99 (br s, 1H), 4.60 (br s, 1H), 2.39 (s, 3H), 2.29 (s, 3H), 1.37 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 153.49, 151.86, 142.45, 137.84, 134.93, 133.23, 130.25, 129.86, 129.28, 128.79, 126.49, 126.00, 125.17, 125.08, 123.06, 121.74, 119.69, 119.09, 115.68, 20.92, 16.47, 14.27. HRMS (ESI-TOF): Exact mass calcd. for C₂₅H₂₂BrNO₄S [M+Na]⁺ 534.0345, Found: 534.0340. MP 129-131 °C.



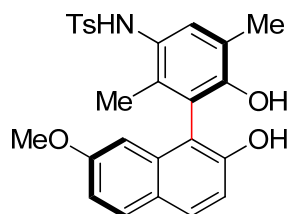
9ea, white solid, 80% yield (54.0 mg), 96% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 25.50 (minor), 43.86 (major) min]. $[\alpha]_D^{20} = -86.3$ (c = 0.3 CH₃OH). ¹H NMR (300 MHz, CD₃OD) δ 7.60-7.55 (m, 3H), 7.29 (d, J = 7.9 Hz, 2H), 7.23-7.18 (m, 2H), 7.10 (t, J = 7.3 Hz, 1H), 7.00 (s, 1H), 6.85 (d, J = 8.2 Hz, 1H), 2.35 (s, 3H), 2.18 (s, 3H), 1.33 (s, 3H). ¹³C NMR (75 MHz, CD₃OD) δ 153.47, 147.47, 145.79, 144.75, 138.97, 135.39, 131.59, 131.19, 130.66, 129.70, 128.45, 127.80, 127.37, 125.00, 124.65, 124.58, 124.02, 123.79, 117.09, 110.65, 21.63, 16.55, 15.00. HRMS (ESI-TOF): Exact mass calcd. for C₂₅H₂₃NO₅S [M+Na]⁺ 472.1189, Found: 472.1197. MP 138-140 °C.



9fa, white solid, 89% yield (61.9 mg), 85% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 31.69 (major), 35.00 (minor) min]. $[\alpha]_D^{20} = -58.3$ (c = 0.3, CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.15 (br s, 1H), 8.58 (br s, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.50 (br s, 1H), 7.48 (d, J = 7.9 Hz, 2H), 7.34 (s, 1H), 7.30 (d, J = 7.9 Hz, 2H), 7.24 (t, J = 7.1 Hz, 1H), 7.15 (t, J = 7.1 Hz, 1H), 6.88 (s, 1H), 6.75 (d, J = 8.0 Hz, 1H), 3.95 (s, 3H), 2.31 (s, 3H), 2.11 (s, 3H), 1.20 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 151.79, 148.41, 144.17, 142.35, 137.71, 133.14, 129.51, 129.32, 128.47, 128.37, 126.57, 126.51, 125.75, 123.49, 123.42, 122.83, 121.44, 116.79, 105.68, 55.51, 20.95, 16.46, 14.29. HRMS (ESI-TOF): Exact mass calcd. for C₂₆H₂₅NO₅S [M+Na]⁺ 486.1347. Found: 486.1352. MP 129-131 °C.

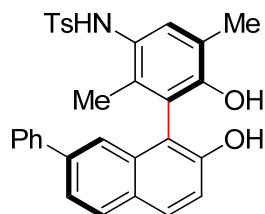


9ga, brown solid, 78% yield (52.6 mg), 85% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 16.30 (minor), 25.72 (major) min]. $[\alpha]_D^{20} = +105.3$ (c = 0.3, CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.40 (s, 1H), 9.12 (s, 1H), 9.05 (s, 1H), 7.59 (t, *J* = 8.3 Hz, 2H), 7.50 (d, *J* = 8.1 Hz, 2H), 7.41 (s, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 1H), 8.86 (s, 1H), 6.80 (dd, *J* = 1.8, 8.8 Hz, 1H), 6.23 (d, *J* = 1.7 Hz, 1H), 2.27 (s, 3H), 2.12 (s, 3H), 1.15 (s, 3H). ¹³C NMR (125 MHz, DMSO-*d*₆) δ 155.52, 152.72, 151.83, 142.29, 137.94, 135.28, 133.39, 129.61, 129.32, 128.44, 126.58, 125.92, 124.12, 122.84, 121.32, 115.04, 114.74, 114.34, 105.49, 20.91, 16.47, 14.07. HRMS (ESI-TOF): Exact mass calcd. for C₂₅H₂₃NO₅S [M+Na]⁺ 472.1189, Found: 472.1186. MP 128-130 °C.

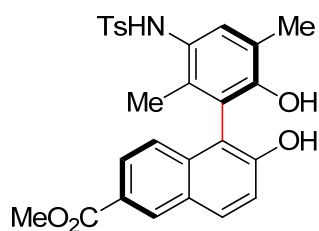


9ha, brown solid, 87% yield (60.5 mg), 89% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 11.92 (minor), 22.11 (major) min]. $[\alpha]_D^{20} = -25.0$ (c = 0.3, CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.21 (br s, 1H), 9.16 (br s, 1H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.67 (d, *J* = 8.8 Hz, 1H), 7.52 (br s, 1H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 8.8 Hz, 1H), 6.94 (dd, *J* = 2.1, 8.8 Hz, 1H), 6.70 (s, 1H), 6.28 (s, 1H), 3.64 (s, 3H), 2.32 (s, 3H), 2.07 (s, 3H), 1.39 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 159.34, 152.73, 151.90, 144.14, 136.91, 134.36, 133.15, 131.19, 130.97, 130.25, 129.75, 127.43, 127.33, 124.84, 123.75, 118.80, 115.66, 115.23,

111.33, 103.45, 55.46, 21.75, 16.16, 14.60. HRMS (ESI-TOF): Exact mass calcd. for $C_{26}H_{25}NO_5S$ $[M+Na]^+$ 486.1346, Found: 486.1339. MP 124-126 °C.

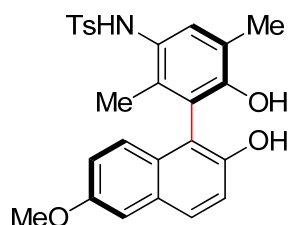


9ia, white solid, 90% yield (69.0 mg), 87% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 14.11 (minor), 33.44 (major) min]. $[\alpha]_D^{20}$ = -110.33 (c = 0.3, CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.40 (br s, 1H), 9.24 (s, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.79 (d, *J* = 8.8 Hz, 1H), 7.67 (br s, 1H), 7.60-7.45 (m, 5H), 7.43-7.35 (m, 3H). 7.23 (d, *J* = 8.9 Hz, 1H), 7.13 (s, 1H), 6.93 (d, *J* = 8.1 Hz, 2H), 6.78 (s, 1H), 2.14 (s, 3H), 2.11 (s, 3H), 1.30 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 152.86, 152.02, 142.28, 140.93, 137.88, 137.64, 133.79, 133.58, 129.74, 129.02, 128.98, 128.66, 128.38, 127.40, 127.34, 126.77, 126.44, 125.89, 123.71, 121.57, 121.53, 121.35, 118.70, 116.54, 20.82, 16.49, 14.62. HRMS (ESI-TOF): Exact mass calcd. for $C_{31}H_{27}NO_4S$ $[M+Na]^+$ 532.1553, Found: 532.1543. MP 86-88 °C.

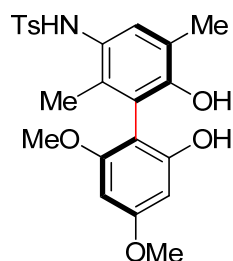


9ja, white solid, 62% yield (45.7 mg), 85% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 11.44 (major), 16.66 (minor) min]. $[\alpha]_D^{20}$ = -92.3 (c = 0.3, CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.79 (br s, 1H), 9.17 (s, 1H), 8.50 (s, 1H), 7.96 (d, *J* = 8.9 Hz, 1H), 7.77 (dd, *J* = 1.4, 8.9 Hz, 1H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 9.0 Hz, 1H), 6.92 (s, 1H), 6.86 (d, *J* = 8.9 Hz, 1H),

3.89 (s, 3H), 2.31 (s, 3H), 2.13 (s, 3H), 1.16 (s, 3H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 166.98, 155.41, 152.35, 142.85, 138.06, 136.44, 133.56, 131.19, 130.87, 130.18, 129.81, 127.37, 127.10, 126.29, 125.36, 124.55, 123.65, 123.56, 122.13, 119.89, 116.94, 52.36, 21.35, 16.94, 14.71. HRMS (ESI-TOF): Exact mass calcd. for $\text{C}_{27}\text{H}_{25}\text{NO}_6\text{S}$ $[\text{M}+\text{Na}]^+$ 514.1295, Found: 514.1291. MP 119-121 °C.

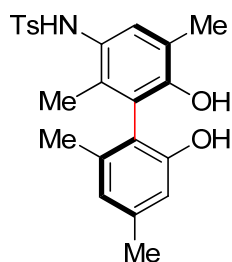


9ka, white solid, 99% yield (69.2 mg), 83% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_{R} = 14.64 (major), 17.57 (minor) min]. $[\alpha]_{\text{D}}^{20}$ = -63.7 (c = 0.3, CH_3OH). ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 9.21 (s, 1H), 9.06 (s, 1H), 7.65 (d, J = 8.8 Hz, 1H), 7.56 (s, 1H), 7.49 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 7.9 Hz, 2H), 7.21-7.16 (m, 2H), 6.99 (d, J = 7.6 Hz, 1H), 6.92 (s, 1H), 6.73 (d, J = 9.1 Hz, 1H), 3.82 (s, 3H), 2.31 (s, 3H), 2.13 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 154.86, 151.85, 150.67, 142.38, 137.67, 133.19, 129.46, 129.37, 128.82, 128.65, 127.37, 126.62, 125.76, 125.29, 123.86, 121.45, 118.83, 118.18, 116.30, 106.47, 55.08, 21.00, 16.54, 14.31. HRMS (ESI-TOF): Exact mass calcd. for $\text{C}_{26}\text{H}_{25}\text{NO}_5\text{S}$ $[\text{M}+\text{Na}]^+$ 486.1346, Found: 486.1340. MP 200-202 °C.

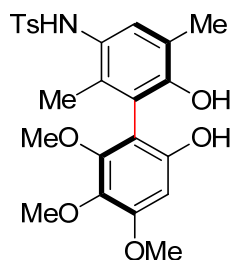


9la, brown solid, 64% yield (42.6 mg), 76% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_{R} = 50.36 (minor), 55.42 (major) min]. $[\alpha]_{\text{D}}^{20}$ = -7.7 (c = 0.3, CH_3OH). ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 9.07 (s, 1H), 9.04 (s, 1H), 7.48 (d, J = 8.3

Hz, 2H), 7.32-7.28 (m, 3H), 6.58 (s, 1H), 6.06 (dd, $J = 2.2, 8.3$ Hz, 2H), 3.69 (s, 3H), 3.52 (s, 3H), 2.34 (s, 3H), 1.99 (s, 3H), 1.37 (s, 3H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 160.10, 158.67, 156.25, 151.81, 142.27, 138.30, 133.84, 129.24, 128.67, 126.59, 125.40, 122.46, 120.63, 104.68, 93.72, 89.86, 55.20, 54.80, 20.94, 16.40, 14.59. HRMS (ESI-TOF): Exact mass calcd. for $\text{C}_{23}\text{H}_{25}\text{NO}_6\text{S}$ $[\text{M}+\text{Na}]^+$ 466.1295, Found: 466.129. MP 97-98 °C.

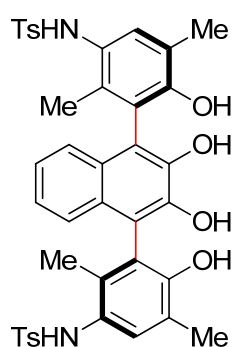


9ma, brown solid, 49% yield (30.0 mg), 75% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; $t_{\text{R}} = 9.42$ (minor), 77.47 (major) min]. $[\alpha]_{\text{D}}^{20} = +12.67$ ($c = 0.3$, CH_3OH). ^1H NMR (300 MHz, DMSO- d_6) δ 9.09 (s, 1H), 9.72 (s, 1H), 7.45-7.41 (m, 3H), 7.29 (d, $J = 8.1$ Hz, 2H), 6.71 (s, 1H), 6.49 (s, 2H), 2.35 (s, 3H), 2.18 (s, 3H), 2.06 (s, 3H), 1.66 (s, 3H), 1.30 (s, 3H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 154.63, 151.18, 142.51, 136.81, 129.39, 128.98, 125.80, 121.34, 120.75, 113.46, 21.00, 20.93, 19.27, 16.50, 14.34. HRMS (ESI-TOF): Exact mass calcd. for $\text{C}_{23}\text{H}_{25}\text{NO}_4\text{S}$ $[\text{M}+\text{Na}]^+$ 434.1367, Found: 434.1395. MP 119-121 °C.

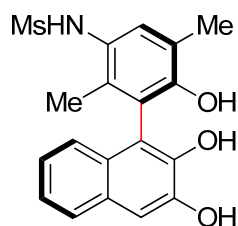


9na, brown solid, 97% yield (69.4 mg), 21% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; $t_{\text{R}} = 10.10$ (minor), 54.73 (major), min]. $[\alpha]_{\text{D}}^{20} = +5.7$ ($c = 0.3$,

CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.07 (s, 1H), 8.86 (br s, 1H), 7.49 (br s, 1H), 7.49 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.64 (s, 1H), 6.31 (s, 1H), 3.74 (s, 3H), 3.64 (s, 3H), 3.35 (s, 3H), 2.34 (s, 3H), 2.04 (s, 3H), 1.48 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 152.59, 151.90, 151.83, 151.09, 142.41, 138.09, 134.53, 133.57, 129.31, 128.99, 126.66, 125.45, 122.51, 120.85, 109.82, 95.76, 60.43, 59.82, 55.39, 20.96, 16.50, 14.92. HRMS (ESI-TOF): Exact mass calcd. for C₂₄H₂₇NO₇S [M+Na]⁺ 496.1400, Found: 496.1403. MP 58-60 °C.

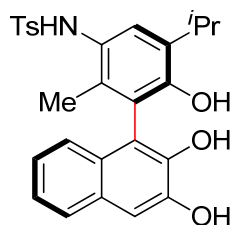


9ea', white solid, 90% yield (100.0 mg), 99% ee. [Daicel CHIRALPAK IC (0.46 cm x 25 cm); *n*-hexane/2-propanol = 60/40; flow rate = 1.0 mL/min; detection wavelength = 230 nm; *t*_R = 29.12 (major), 55.25 (minor) min]. [α]_D²⁰ = +85.0 (c = 0.3, CH₃OH). ¹H NMR (500 MHz, DMSO-*d*₆) δ 9.18 (s, 2H), 8.41 (br s, 2H), 7.65-7.56 (m, 6H), 7.36-7.38 (m, 4H), 7.09-7.00 (m, 4H), 6.74 (s, 2H), 2.35 (s, 6H), 2.18 (s, 6H), 1.34 (s, 6H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 152.05, 143.80, 142.33, 137.88, 133.70, 129.60, 129.32, 128.10, 126.59, 125.88, 123.69, 123.21, 122.42, 121.41, 116.25, 20.99, 16.46, 14.56. HRMS (ESI-TOF): Exact mass calcd. for C₄₀H₃₈N₂O₈S₂ [M+Na]⁺ 761.1962, Found: 761.1975. MP 251-253 °C.

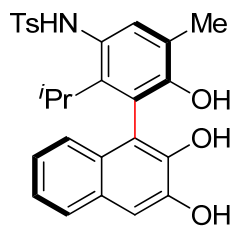


9eb, white solid, 98% yield (54.9 mg), 87% ee. [Daicel CHIRALPAK AD-H (0.46 cm

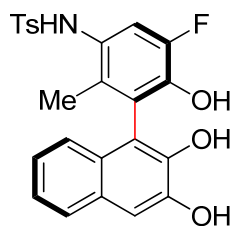
x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 16.45 (minor), 22.31 (major), min]. $[\alpha]_D^{20}$ = -2.3 (c = 0.3, CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.75 (br s, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.19-7.14 (m, 2H), 7.07-7.03 (m, 2H), 6.89 (d, *J* = 8.3 Hz, 1H), 2.92 (s, 3H), 2.18 (s, 3H), 1.73 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 152.40, 146.74, 144.89, 134.08, 129.61, 129.29, 128.35, 126.82, 126.32, 124.25, 123.86, 123.25, 123.09, 122.10, 117.40, 109.16, 40.24, 16.89, 15.64. HRMS (ESI-TOF): Exact mass calcd. for C₁₉H₁₉NO₅S [M+Na]⁺ 396.0876, Found: 396.0860. MP 127-129 °C.



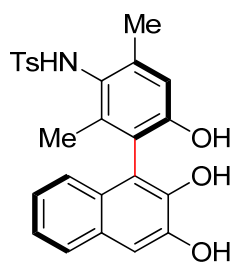
9ec, brown solid, 68% yield (48.7 mg), 91% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 17.88 (major), 20.24 (minor) min]. $[\alpha]_D^{20}$ = -32.3 (c = 0.3, CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.07 (br s, 1H), 9.07 (s, 1H), 8.45 (br s, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.27 (s, 1H), 7.20-7.06 (m, 3H), 6.73 (d, *J* = 8.2 Hz, 1H), 6.64 (s, 1H), 3.15-3.08 (m, 1H), 2.34 (s, 3H), 1.40 (s, 3H), 1.02 (d, *J* = 6.7 Hz, 6H). ¹³C NMR (125 MHz, DMSO-*d*₆) δ 150.47, 146.13, 144.57, 142.38, 137.51, 133.39, 131.66, 129.23, 128.80, 127.90, 126.80, 126.06, 125.75, 124.51, 123.59, 123.32, 122.73, 122.55, 116.43, 108.72, 25.71, 22.51, 22.41, 20.87, 14.53. HRMS (ESI-TOF): Exact mass calcd. for C₂₇H₂₇NO₅S [M+Na]⁺ 500.1502, Found: 500.1482. MP 159-161 °C.



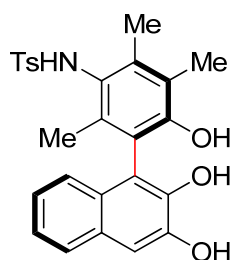
9ed, brown solid, 63% yield (45.1 mg), 73% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 11.98 (minor), 18.16 (major) min]. $[\alpha]_D^{20} = -17.7$ ($c = 0.3$, CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.07 (br s, 1H), 8.94 (s, 1H), 8.41 (br s, 1H), 7.71 (d, $J = 8.2$ Hz, 2H), 7.58 (d, $J = 8.1$ Hz, 1H), 7.43 (d, $J = 8.1$ Hz, 2H), 7.30 (s, 1H), 7.18-7.14 (m, 2H), 7.05 (t, $J = 8.2$ Hz, 1H), 6.84 (d, $J = 8.3$ Hz, 1H), 6.40 (s, 1H), 2.73-2.68 (m, 1H), 2.41 (s, 3H), 1.94 (s, 3H), 0.88 (d, $J = 7.1$ Hz, 3H), 0.77 (d, $J = 6.9$ Hz, 3H). ¹³C NMR (125 MHz, DMSO-*d*₆) δ 157.06, 151.14, 149.78, 148.86, 147.43, 144.48, 134.93, 134.41, 133.93, 133.62, 131.82, 130.96, 130.69, 129.06, 128.50, 127.60, 127.38, 126.08, 122.17, 113.67, 34.67, 26.93, 26.83, 25.98, 21.30. HRMS (ESI-TOF): Exact mass calcd. for C₂₇H₂₇NO₅S [M+Na]⁺ 500.1502, Found: 500.1483. MP 115-117 °C.



9ee, yellow solid, 56% yield (38.1 mg), 78% ee. [Daicel CHIRALPAK IA-3 (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 17.85 (minor), 33.92 (major) min]. $[\alpha]_D^{20} = -42.33$ ($c = 0.3$, CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.02 (s, 1H), 9.37 (s, 1H), 8.95 (s, 1H), 8.48 (s, 1H), 7.56 (d, $J = 7.6$ Hz, 1H), 7.48 (d, $J = 8.0$ Hz, 2H), 7.33 (d, $J = 7.8$ Hz, 2H), 7.18-7.04 (m, 3H), 6.88 (d, $J = 11.8$ Hz, 1H), 6.65 (d, $J = 8.1$ Hz, 1H), 2.30 (s, 3H), 1.21 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 150.39, 147.25, 146.10, 143.94, 142.71, 141.66, 137.25, 131.36, 129.49, 128.57, 127.41, 126.56, 125.79, 125.41, 123.19, 122.80 (d, $J = 12.0$ Hz), 114.25, 114.03 (d, $J = 6.0$ Hz), 108.62, 20.96, 13.99. HRMS (ESI-TOF): Exact mass calcd. for C₂₄H₂₀FNO₅S [M+Na]⁺ 476.0938, Found: 476.0918. MP 109-111 °C.

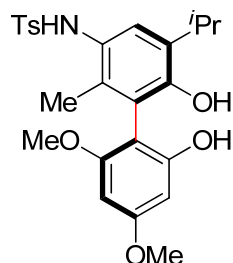


9ef, white solid, 31% yield (21.0 mg), 4% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 27.42 (minor), 31.95 (major) min]. $[\alpha]_D^{20} = +1.0$ (c = 0.1, CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.07 (br s, 1H), 8.98 (s, 1H), 8.82 (br s, 1H), 8.28 (br s, 1H), 7.57-7.52 (m, 3H), 7.32 (d, J = 8.1 Hz, 2H), 7.09-7.18 (m, 3H), 6.87 (d, J = 1.9 Hz, 1H), 6.62 (s, 1H), 2.30 (s, 3H), 2.08 (s, 3H), 1.26 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 154.08, 146.14, 143.79, 142.26, 138.85, 138.30, 137.54, 129.44, 128.58, 127.82, 126.52, 125.67, 124.48, 123.71, 122.55, 121.28, 117.88, 114.63, 108.23, 20.92, 18.95, 15.42. HRMS (ESI-TOF): Exact mass calcd. for C₂₅H₂₃NO₅S [M+Na]⁺ 472.1189, Found: 472.0672. MP 167-169 °C.

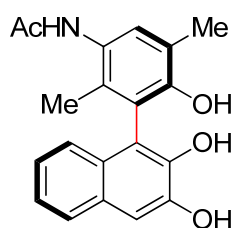


9eg, yellow solid, 68% yield (47.3 mg), 21% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 19.42 (major), 21.77 (minor) min]. $[\alpha]_D^{20} = +14.7$ (c = 0.3, CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.94 (br s, 1H), 9.03 (s, 1H), 8.35 (br s, 1H), 7.58 (d, J = 8.2 Hz, 1H), 7.52 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 7.8 Hz, 2H), 7.18 (t, J = 7.6 Hz, 1H), 7.12 (s, 2H), 6.85 (d, J = 7.8 Hz, 1H), 2.29 (s, 3H), 2.09 (s, 3H), 1.18 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 151.55, 146.17, 142.13, 136.59, 134.66, 134.38, 129.40, 128.78, 127.99, 126.55, 125.75, 124.93, 123.62, 122.72, 122.58, 121.09, 120.70, 116.82, 108.62, 20.92, 16.33, 15.37, 12.97. HRMS

(ESI-TOF): Exact mass calcd. for $C_{26}H_{25}NO_5S$ $[M+Na]^+$ 486.1346, Found: 486.1334.
MP 134-136 °C.

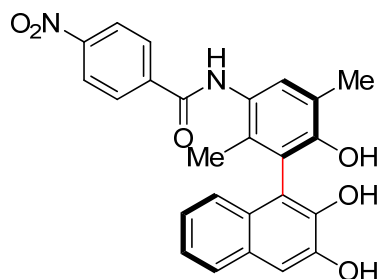


9lc, brown solid, 48% yield (34.0 mg), 83% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 13.93 (minor), 47.81 (major), min]. $[\alpha]_D^{20}$ = -6.0 (c = 0.3, CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.08 (br s, 1H), 8.97 (s, 1H), 7.54 (d, *J* = 7.7 Hz, 2H), 7.35 (d, *J* = 7.7 Hz, 2H), 7.02 (br s, 1H), 6.36 (s, 1H), 6.11 (d, *J* = 7.2 Hz, 2H), 3.73 (s, 3H), 3.57 (s, 3H), 3.08-3.04 (m, 1H), 2.38 (s, 3H), 1.63 (s, 3H), 0.93 (m, 6H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 160.75, 159.34, 156.90, 151.10, 142.87, 138.60, 134.68, 131.37, 129.72, 127.39, 126.25, 124.27, 122.95, 104.91, 94.33, 90.56, 55.78, 55.31, 26.17, 23.00, 22.91, 21.41, 15.39. HRMS (ESI-TOF): Exact mass calcd. for $C_{25}H_{29}NO_6S$ $[M+Na]^+$ 494.1608, Found: 494.1593. MP 206-208 °C.

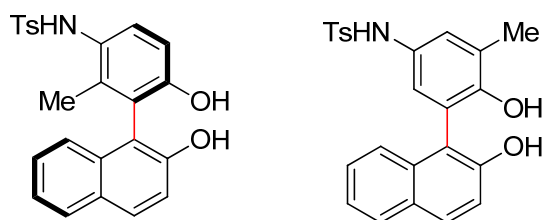


9eh, white solid, 98% yield (49.6 mg), 76% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 80/20; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 8.64 (minor), 12.96 (major), min]. $[\alpha]_D^{20}$ = -3.7 (c = 0.3, CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.09 (s, 1H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.20-7.15 (m, 2H), 7.08-7.04 (m, 2H), 6.93 (d, *J* = 8.4 Hz, 1H), 2.17 (s, 3H), 2.00 (s, 3H), 1.62 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 167.98, 150.56, 146.24, 144.44, 130.41, 128.78, 128.04, 127.88, 127.44, 125.81, 123.64, 123.25, 122.61, 120.97,

117.19, 108.55, 23.03, 16.49, 14.73. HRMS (ESI-TOF): Exact mass calcd. for $C_{20}H_{19}NO_4$ $[M+H]^+$ 338.1387, Found: 338.1382. MP 129-131 °C.



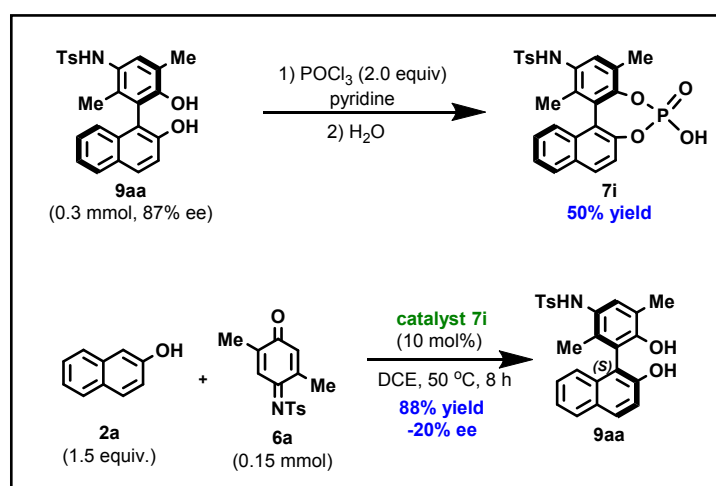
9ei, yellow solid, 69% yield (45.7 mg), 58% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 6.57 (minor), 11.19 (major) min]. $[\alpha]_D^{20} = +1.0$ (c = 0.3, CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.07 (s, 1H), 8.35 (d, *J* = 8.6 Hz, 2H), 8.21 (d, *J* = 8.5 Hz, 2H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.21-7.07 (m, 4H), 6.99 (d, *J* = 8.2 Hz, 1H), 2.24 (s, 3H), 1.68 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 163.71, 151.47, 149.00, 146.23, 144.55, 140.56, 131.87, 128.95, 128.80, 128.23, 128.04, 127.08, 125.85, 123.61, 123.56, 123.49, 122.71, 122.64, 121.36, 116.98, 108.64, 16.45, 14.85. HRMS (ESI-TOF): Exact mass calcd. for $C_{25}H_{20}N_2O_6$ $[M+Na]^+$ 467.1214, Found: 467.1204. MP 103-105 °C.



9aj and **9aj'**, white solid, 99% yield (63 mg), 82% ee for **9aj**. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 19.59 (minor), 30.77 (major) min]. $[\alpha]_D^{20} = -42.7$ (c = 0.3, CH₃OH). ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.16 (br s, 1H), 8.92 (br s, 1H), 7.75-7.68 (m, 2H), 7.51 (d, *J* = 7.9 Hz, 2H), 7.32-7.15 (m, 6H), 6.70 (s, 1H), 6.42 (s, 1H), 2.21 (s, 3H), 2.08 (s, 3H). HRMS (ESI-TOF): Exact mass calcd. for $C_{24}H_{21}NO_4S$ $[M+Na]^+$ 442.1084, Found: 442.1089. MP 89-91 °C.

General procedure for synthesis of chiral CPA **7i** and used as a catalyst.

The **9aa** (0.15 mmol, 87% ee) was dissolved in dry pyridine in a three-necked flask. Under the argon condition, POCl₃ (0.3 mmol) was added dropwise. The mixture was allowed to stir at room temperature for 3 h and the reaction. Then the mixture was cooled to 0 °C, add water (0.5 mL) slowly and stirred at room temperature for 30 min. Add CH₂Cl₂ to dissolve the mixture completely, wash the organic phase using 1N HCl. Then the organic phase was dried over anhydrous Na₂SO₄ and the filtrate was concentrated under reduced pressure. The product was purified column chromatography on silica-gel (AcOEt : MeOH = 25:1 to 7:1) to give the white solid. Dissolved the solid to CH₂Cl₂ and washed with 1N HCl, The organic phase was dried over anhydrous Na₂SO₄ and the filtrate was concentrated under reduced pressure. **7i**, white solid, 50% yield (74 mg). ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.46 (s, 1H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.43-7.30 (m, 5H), 6.70-6.96 (m, 2H), 2.41 (s, 3H), 2.24 (s, 3H), 1.42 (s, 3H). ³¹P NMR (75 MHz, DMSO-*d*₆) δ 2.74. HRMS (ESI-TOF): Exact mass calcd. for C₂₅H₂₂NO₆PS [M+Na]⁺ 518.0798, Found: 518.0794.



The novel non-C₂-symmetrical CPA **7i** proved to be a viable catalyst for the coupling of **2a** and **6a** and afforded functionalized biaryl **9aa** in 88% isolated yield. The level of enantio-induction was poor (-20%, giving rise to the (*S*)-enantiomer) which was

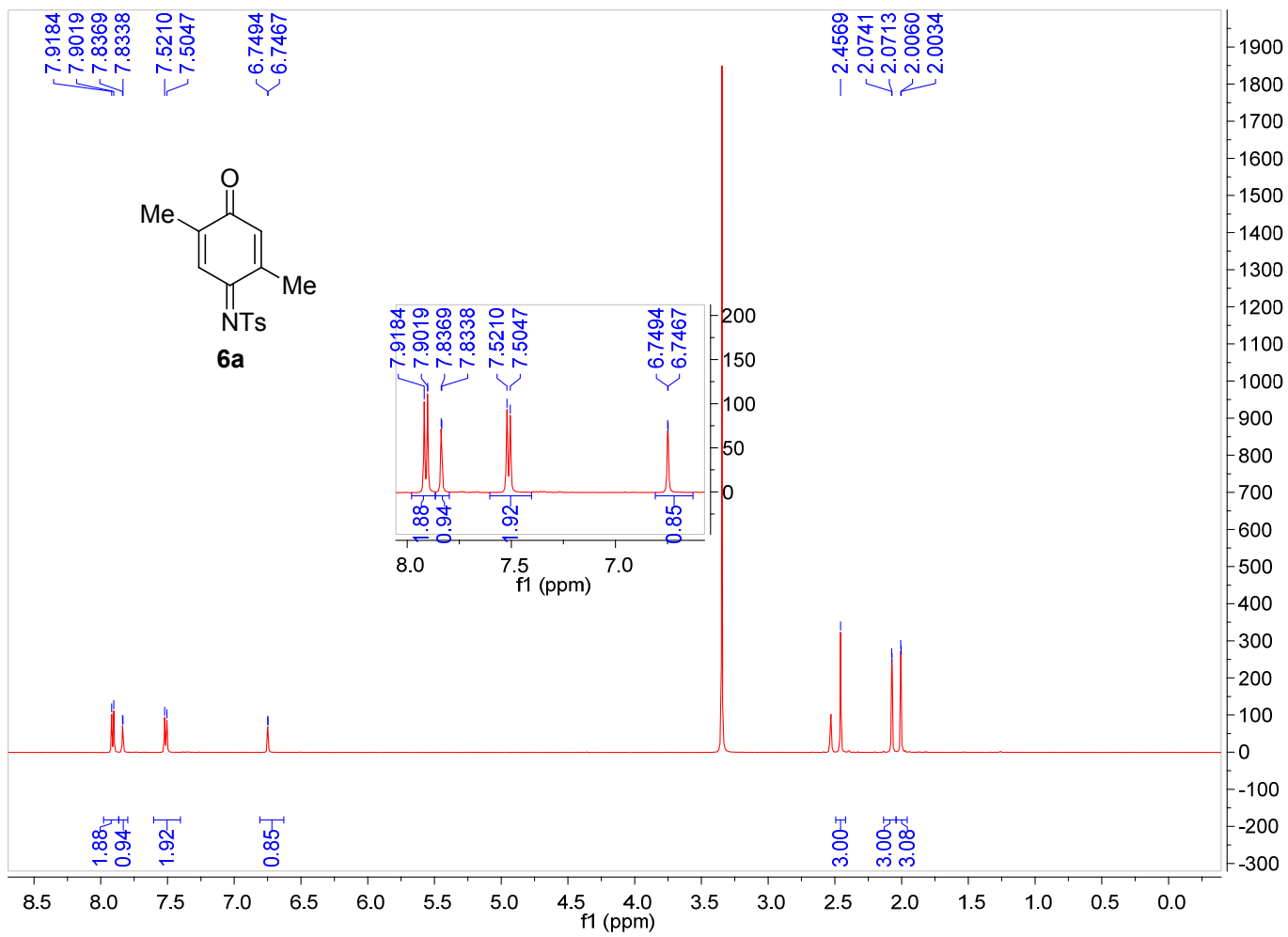
not surprising as no steric modifier is present in **7i** in the 2'-position of the naphthalene nucleus that plays a huge role in determining the stereoselectivity of the reactions in our manuscript.

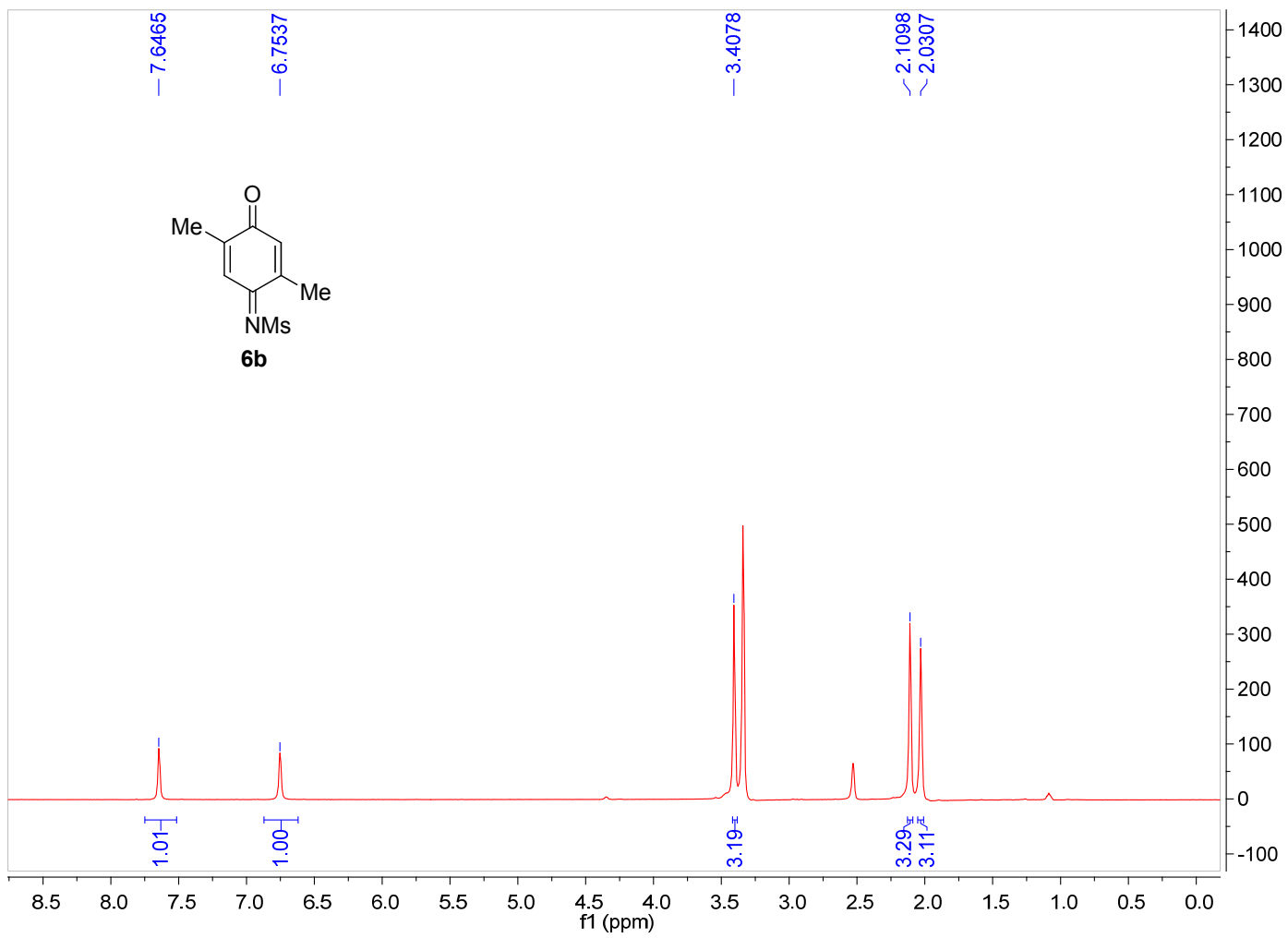
General procedure for synthesis of compound **9ea***

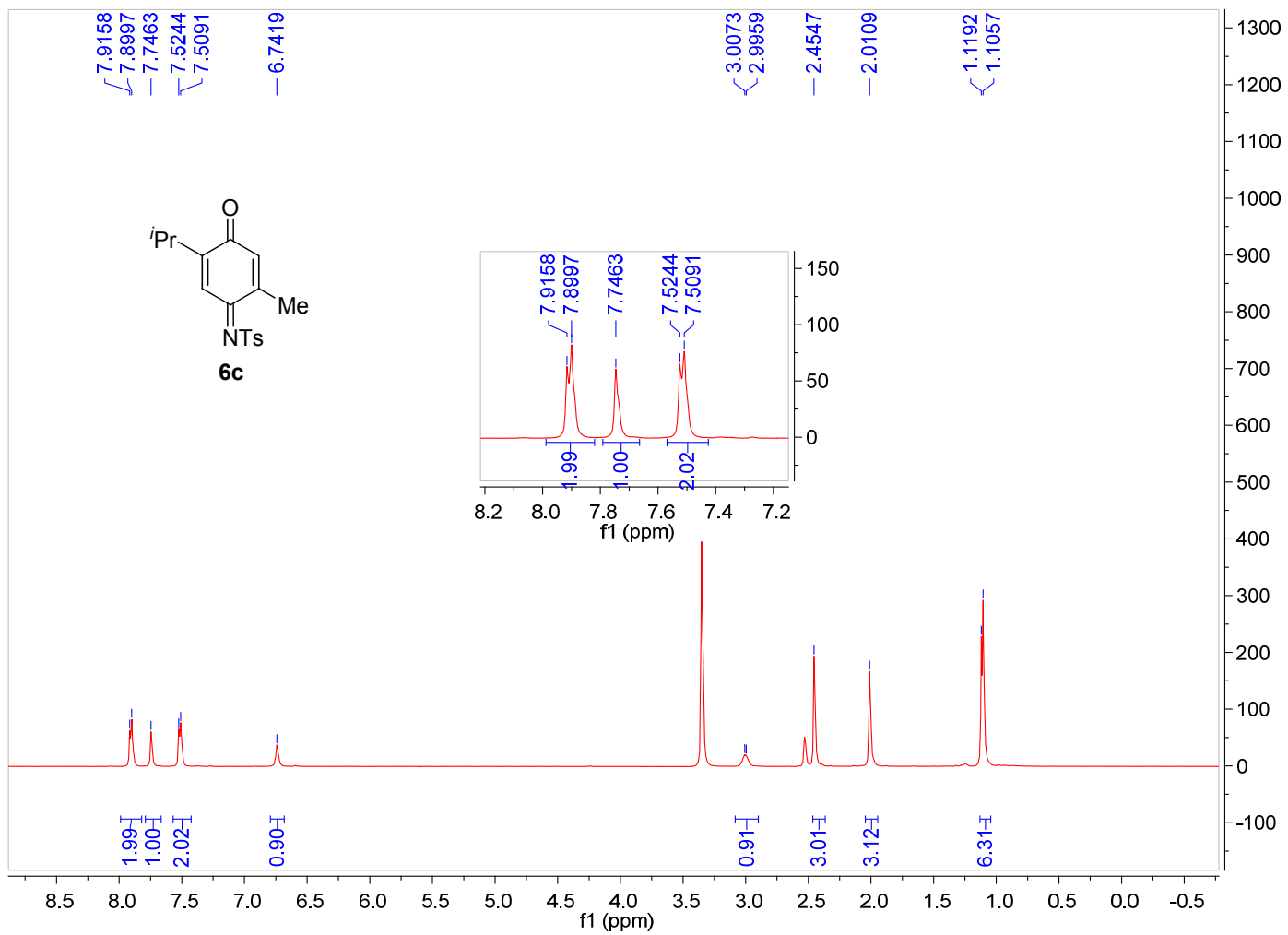
To a stirred solution of **9ea** (45 mg, 0.1 mmol) and **6k** (27 mg, 0.15 mmol) in toluene or DCE (3 mL), TFA (1.2 mg, 0.8 μ L, 0.01 mmol) or (PhO)₂PO₂H was added in one portion at room temperature, and it was stirred at 100 °C for 3-8 hours. Solvent was removed under reduced pressure and the crude residue was purified by column chromatography on silica-gel (hexane/ethyl acetate = 5:1 to 1:1) to give pure product **9ea*** (48 mg, 80% yield), 83% ee. [Daicel CHIRALPAK AD-H (0.46 cm x 25 cm); *n*-hexane/2-propanol = 70/30; flow rate = 1.0 mL/min; detection wavelength = 230 nm; t_R = 9.73 (minor), 46.05 (major) min]. ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.18 (s, 1H), 8.38 (br s, 3H), 7.65 (br s, 1H), 7.53 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.07-7.03 (m, 2H), 7.02-6.97 (m, 2H), 6.76-6.73 (m, 2H), 6.64 (s, 1H), 3.65 (s, 3H), 2.33 (s, 3H), 2.27 (s, 3H), 2.16 (s, 3H), 1.82 (s, 3H), 1.31 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 152.97, 152.25, 150.16, 144.75, 144.27, 143.31, 138.75, 134.36, 132.24, 130.26, 130.37, 130.25, 129.04, 128.85, 127.49, 126.79, 124.94, 124.59, 124.47, 123.33, 123.26, 122.38, 121.68, 118.15, 116.88, 115.54, 60.34, 21.90, 17.38, 16.89, 15.50, 14.11. MP 165-167 °C. HRMS (ESI-TOF): Exact mass calcd. for C₃₄H₃₃NO₇S [M+Na]⁺ 622.1870, Found: 622.1862.

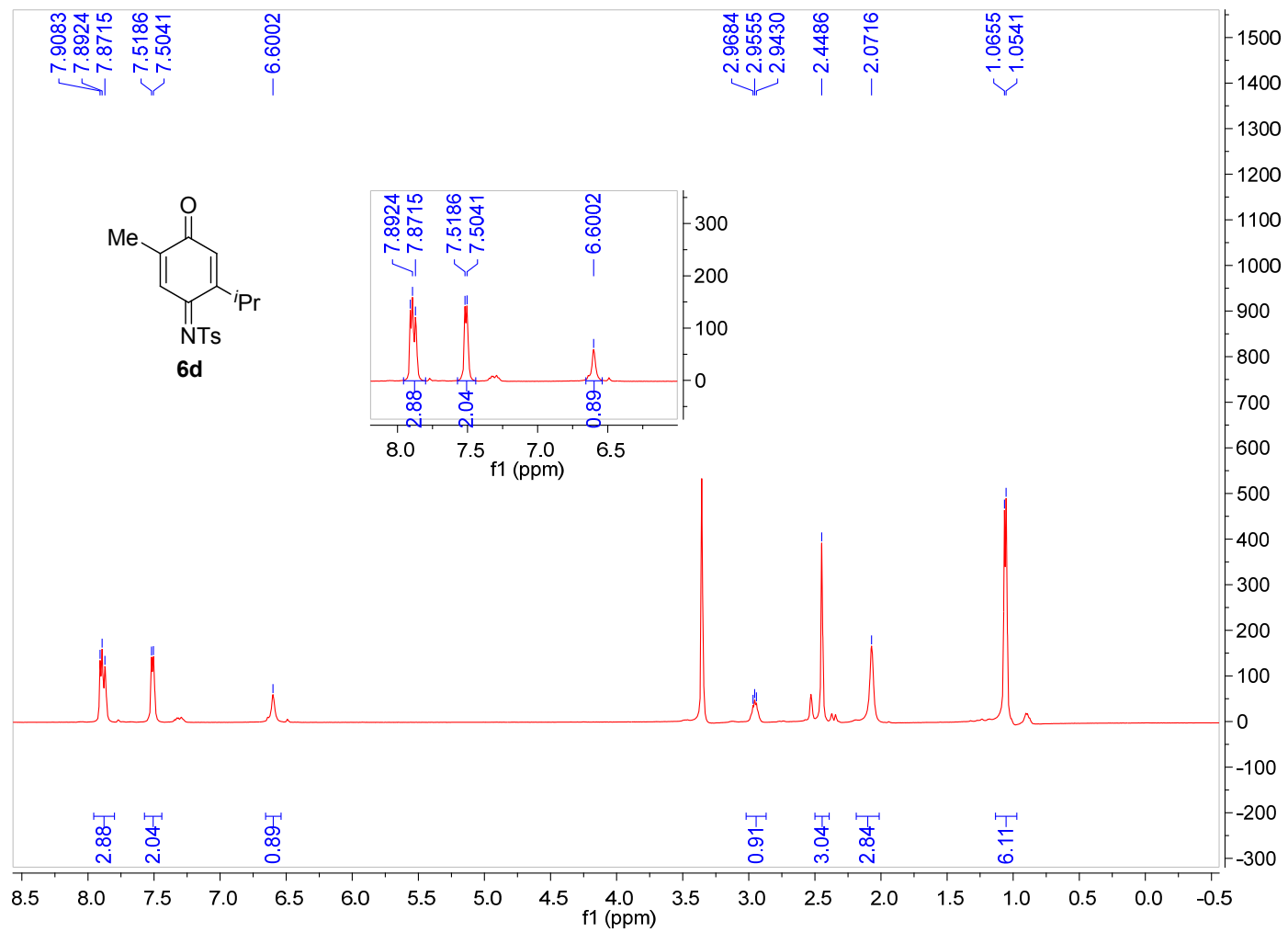
Reference:

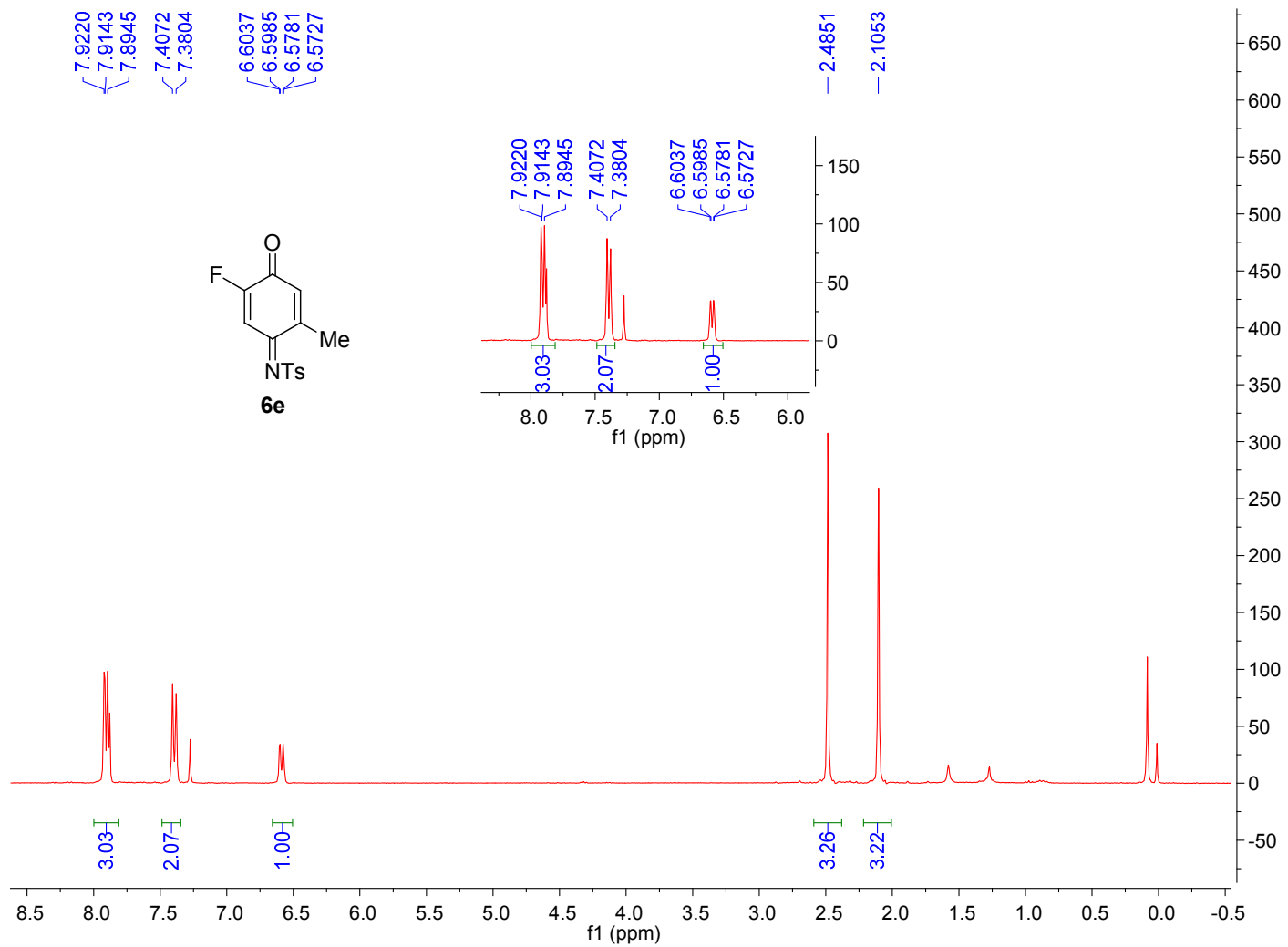
[1] Uliana, M. P.; Servilha, B. M.; Alexopoulos, O.; de Oliveira, K. T.; Tormena, C. F.; Ferreira, M. A. B.; Brocksom, T. J. *Tetrahedron* **2014**, *70*, 6963.

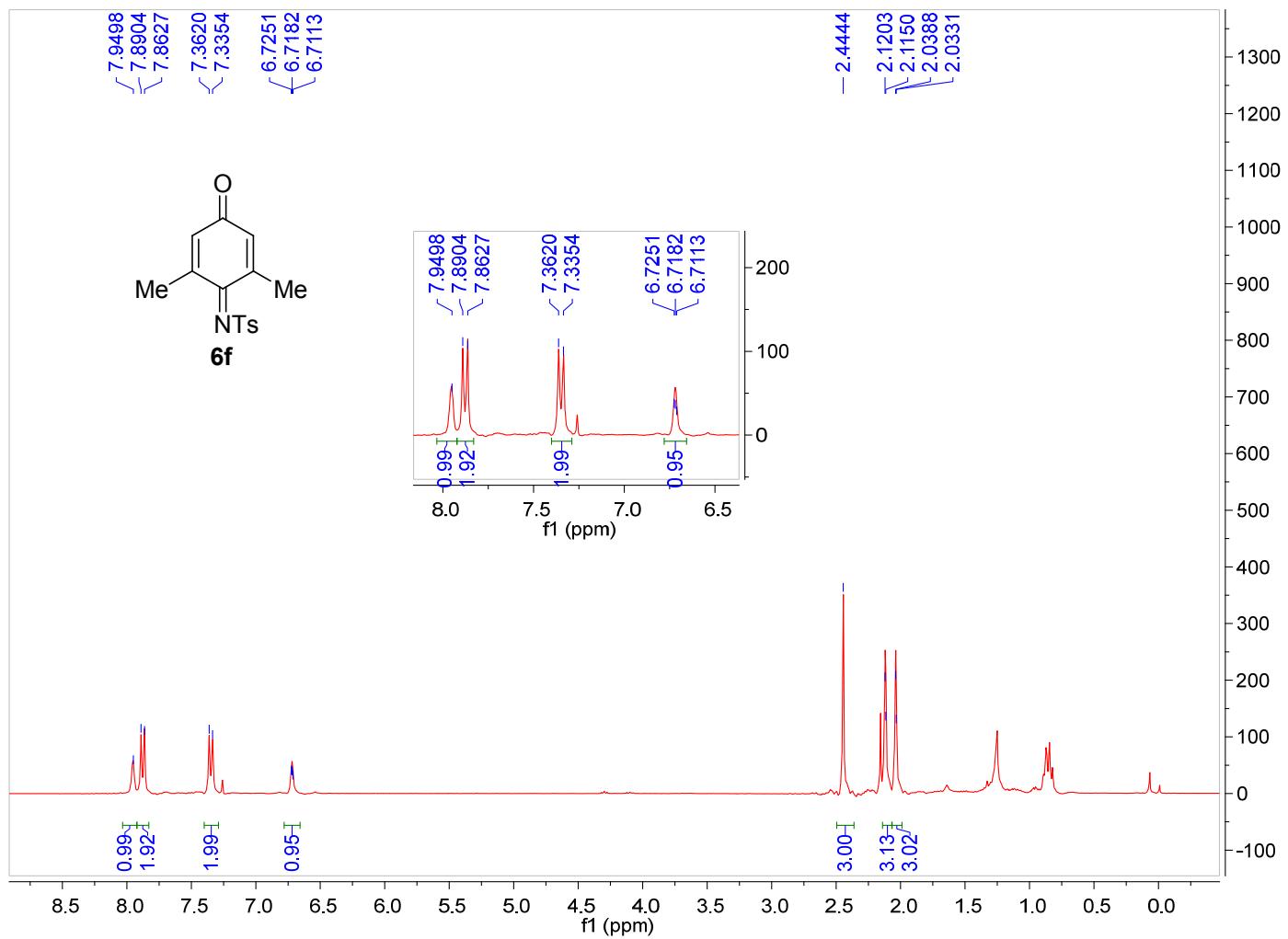


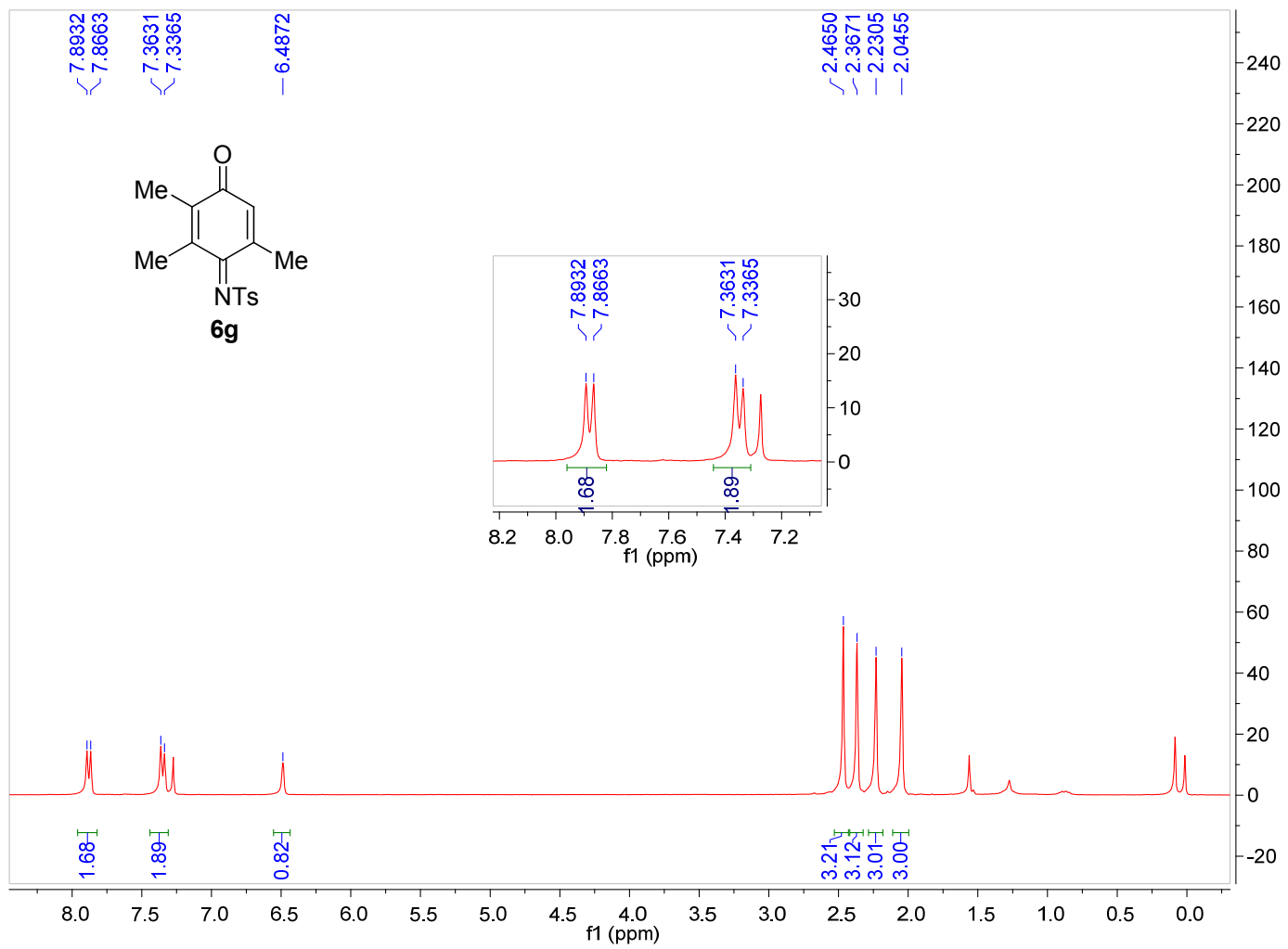


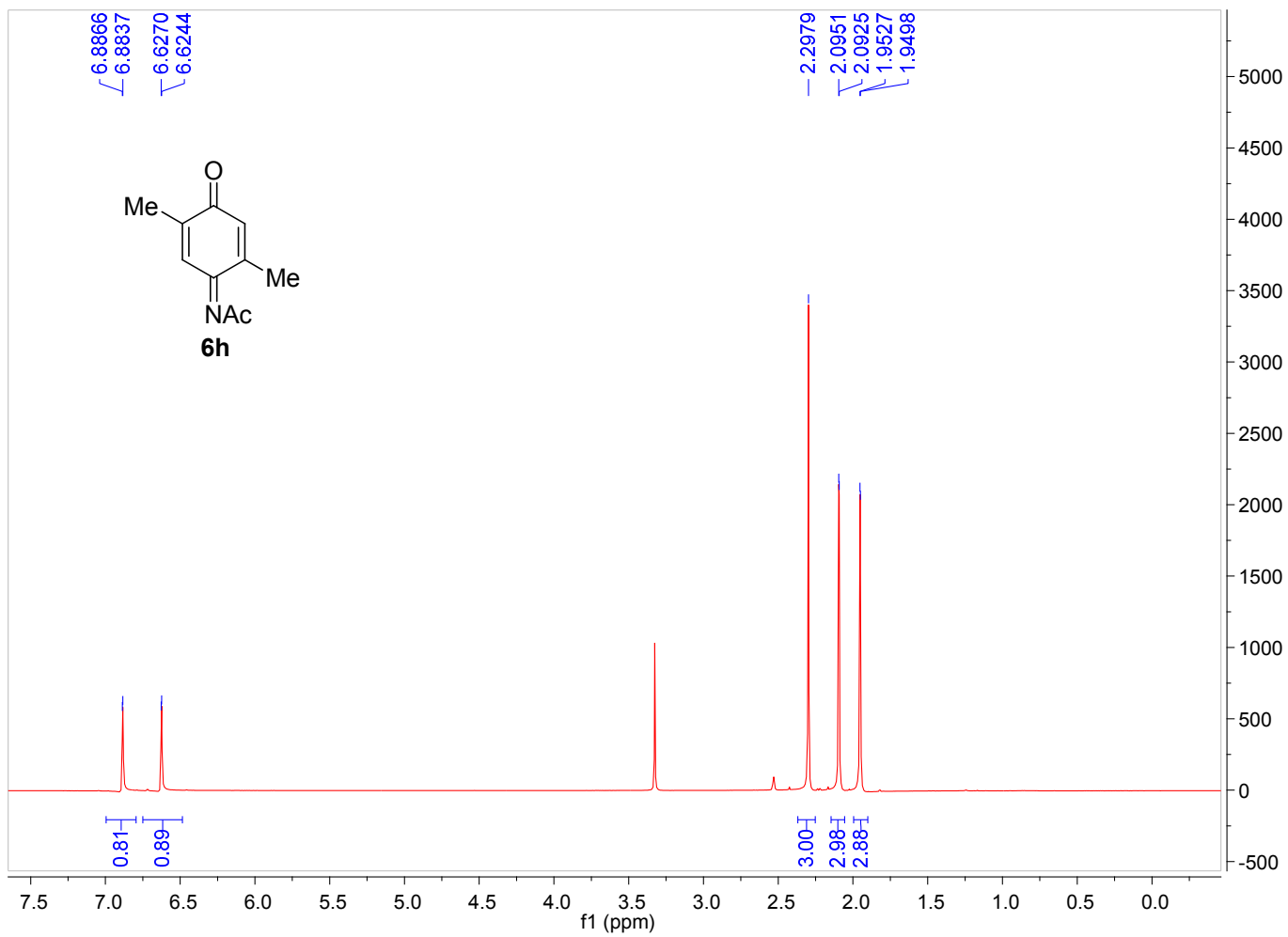


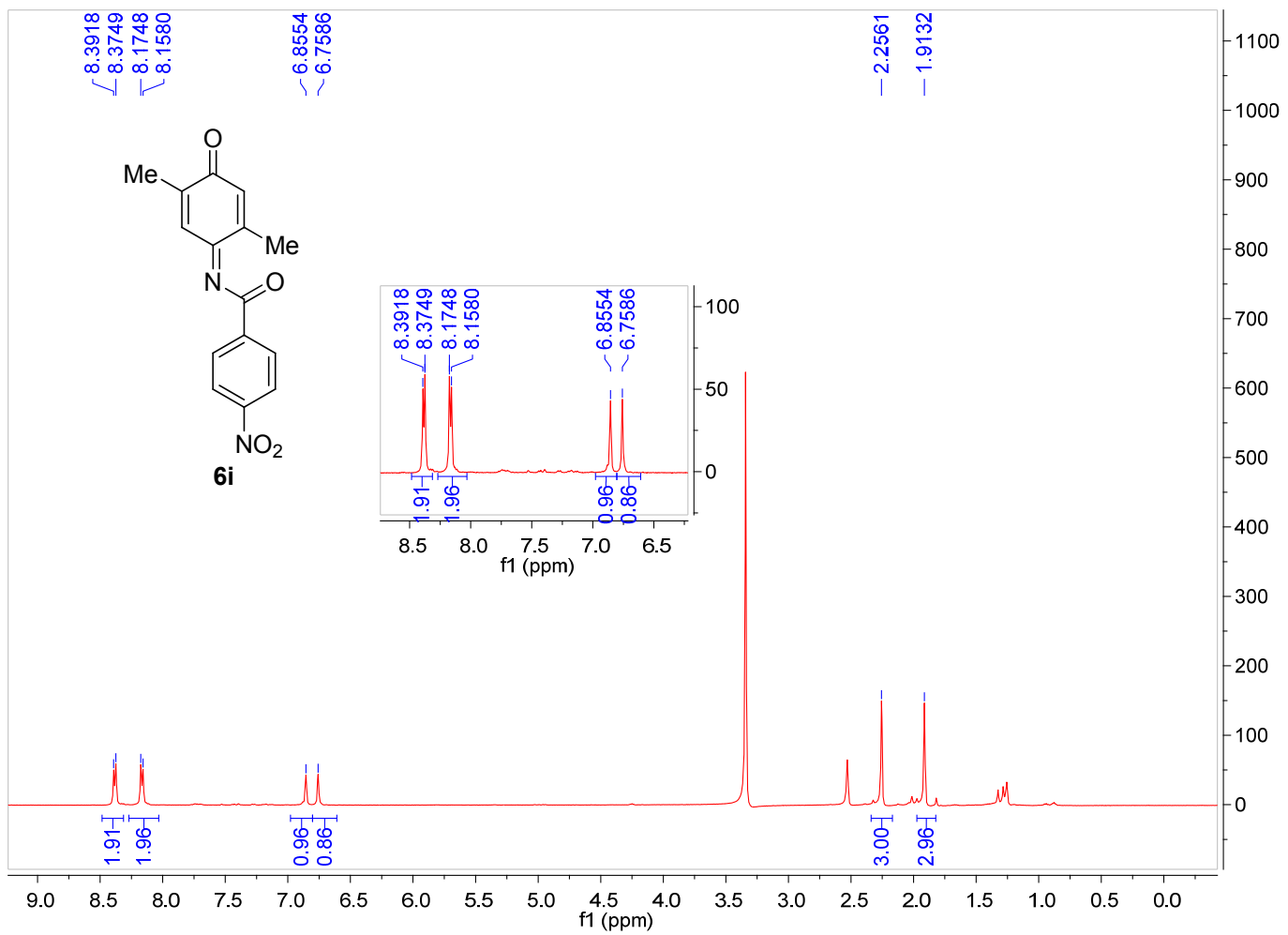


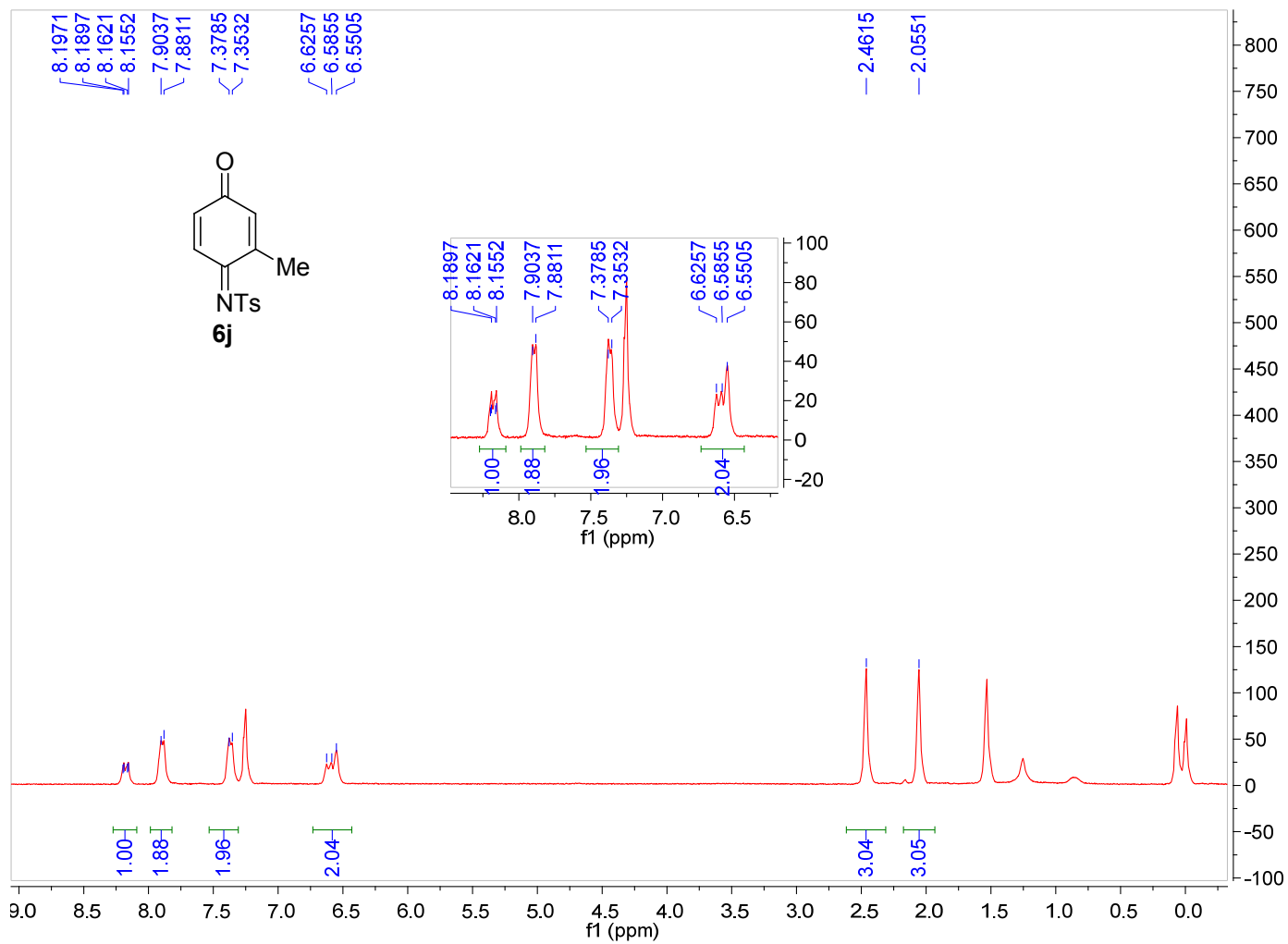


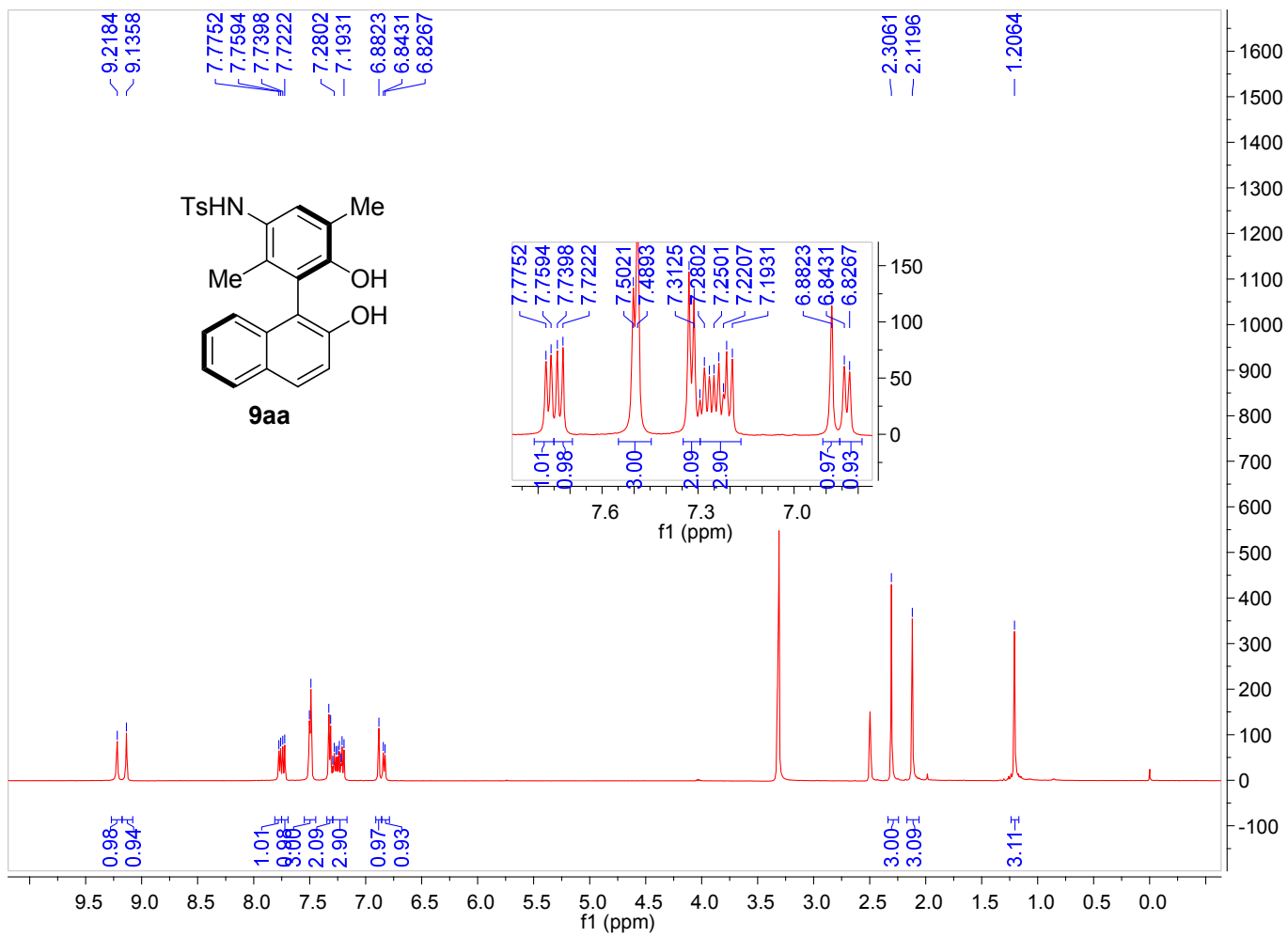


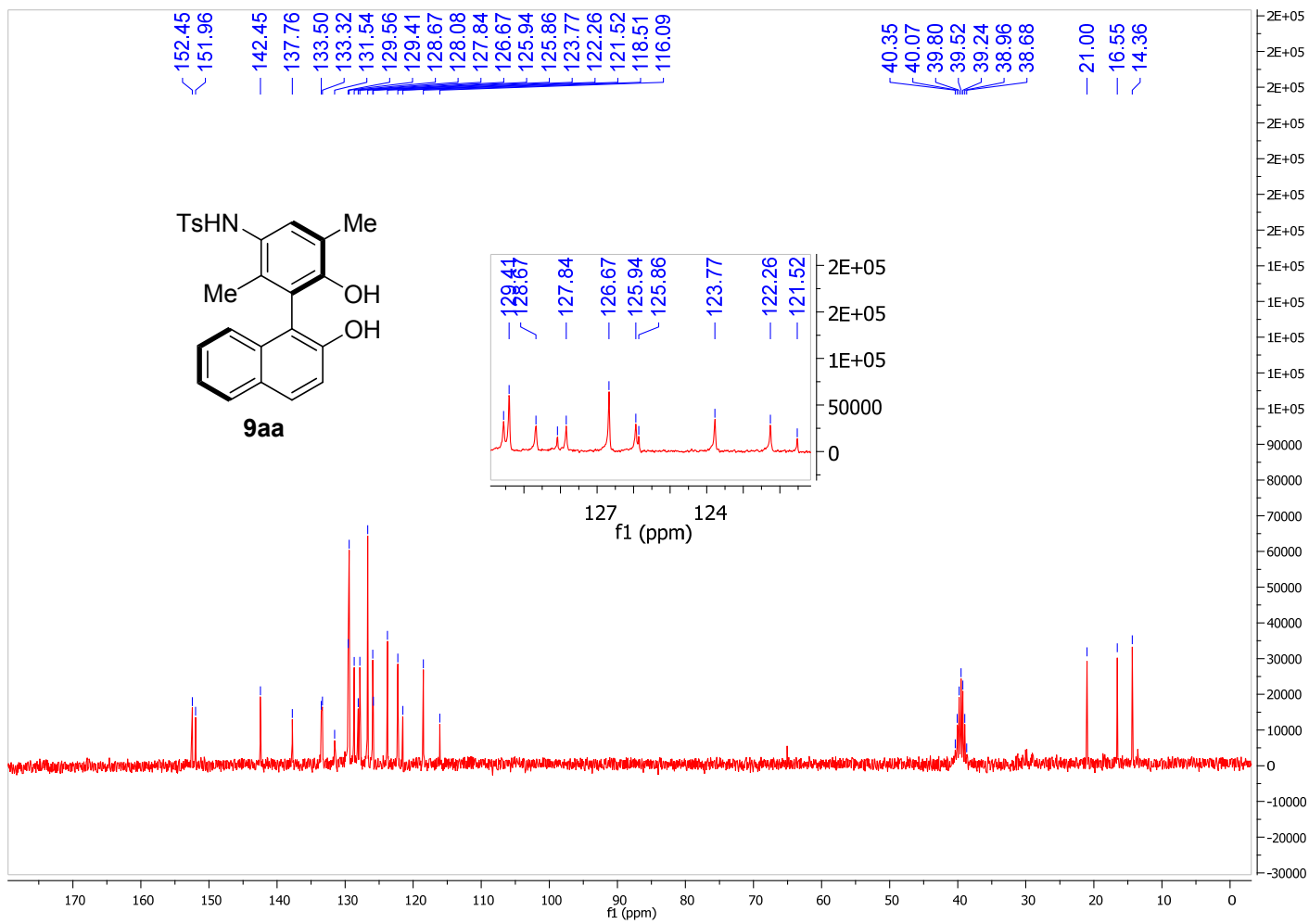


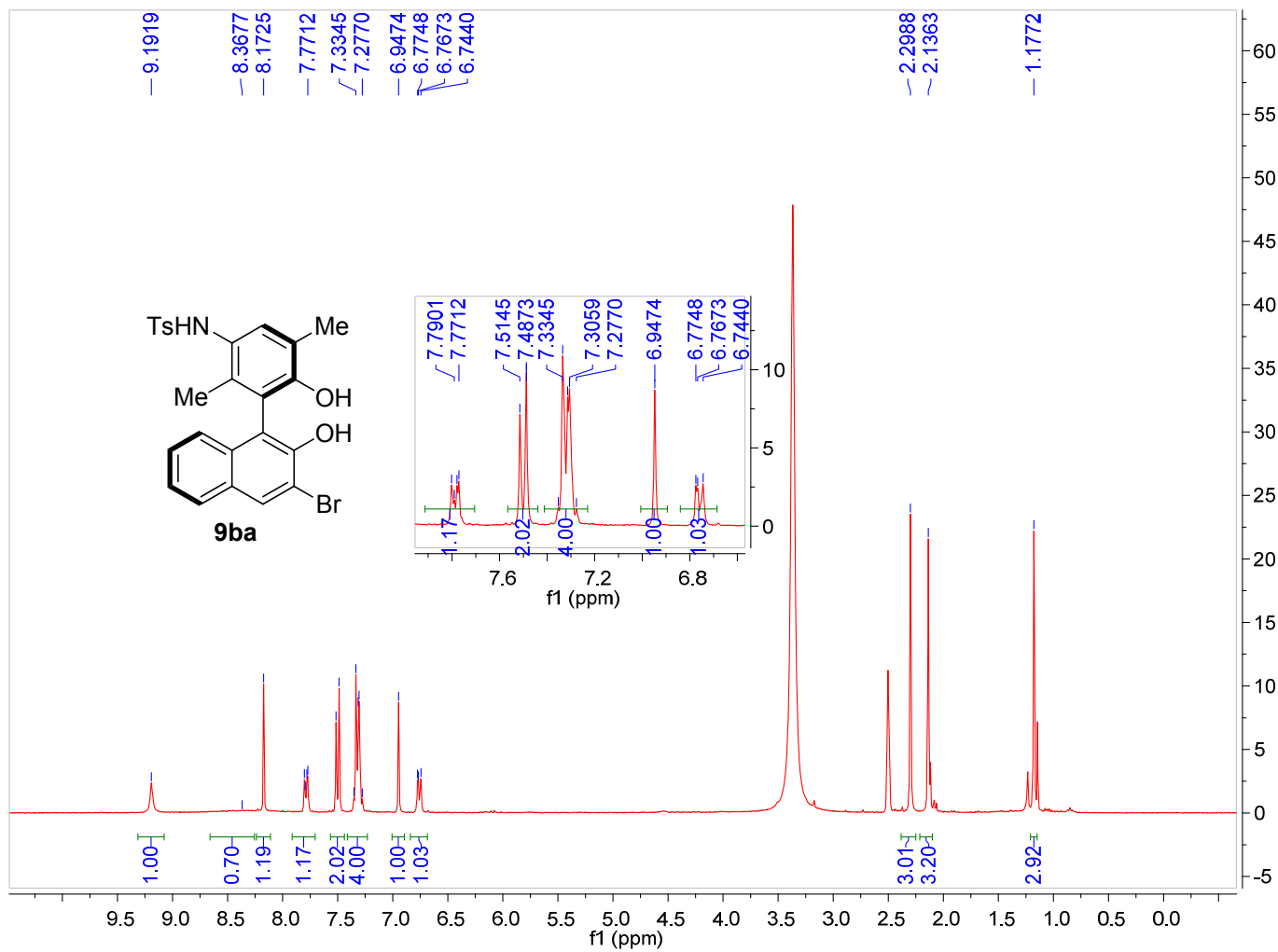


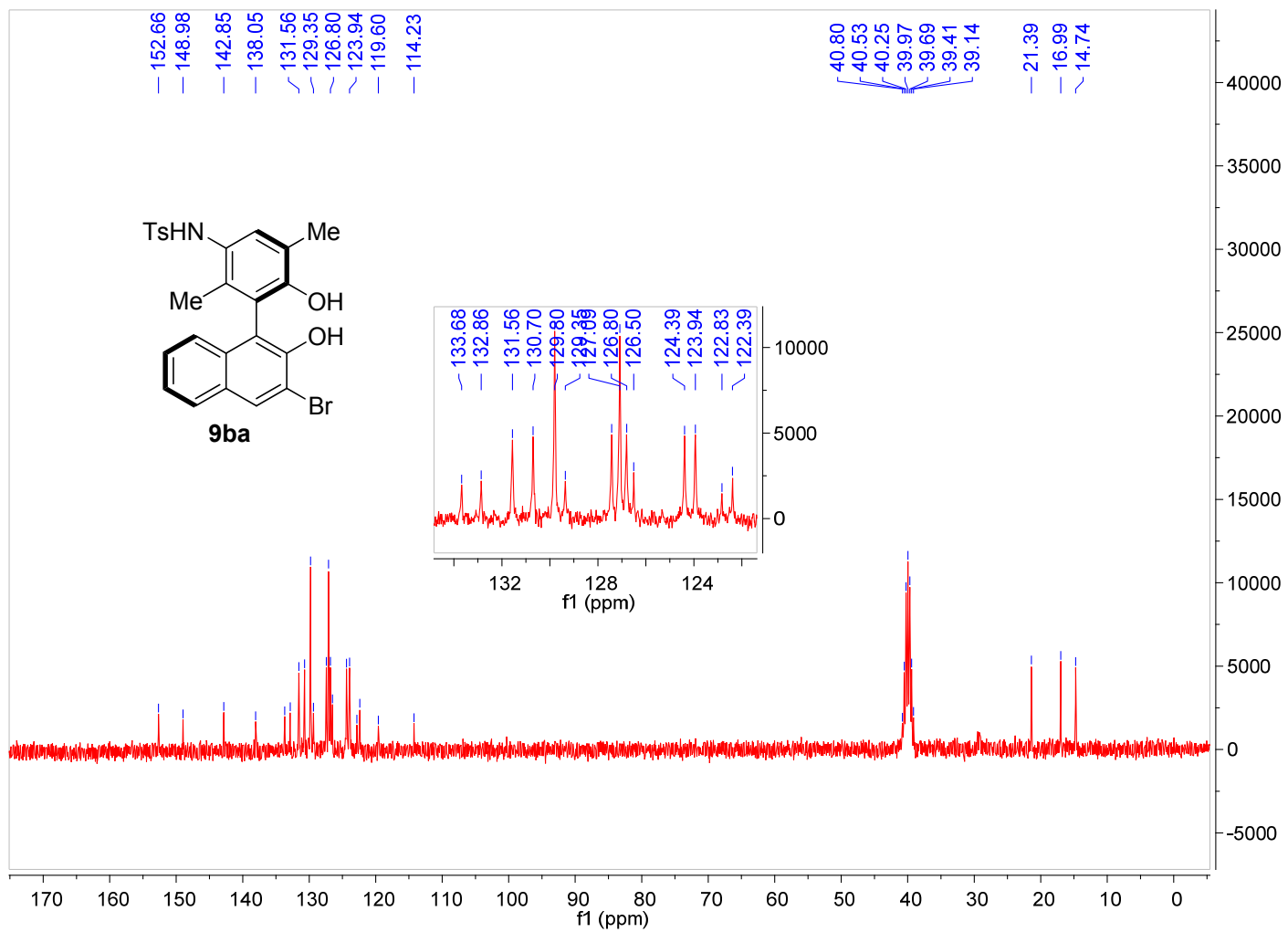


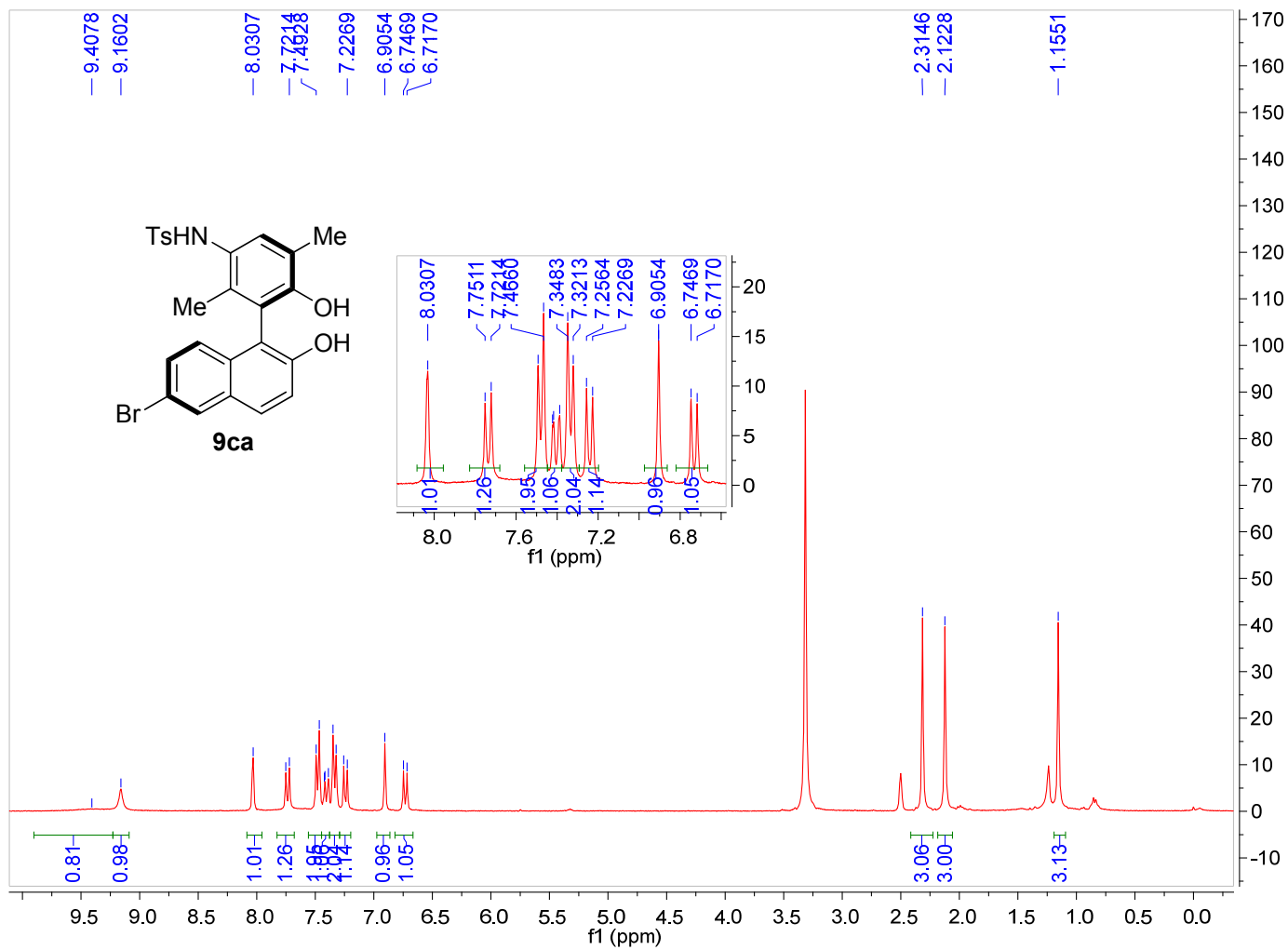


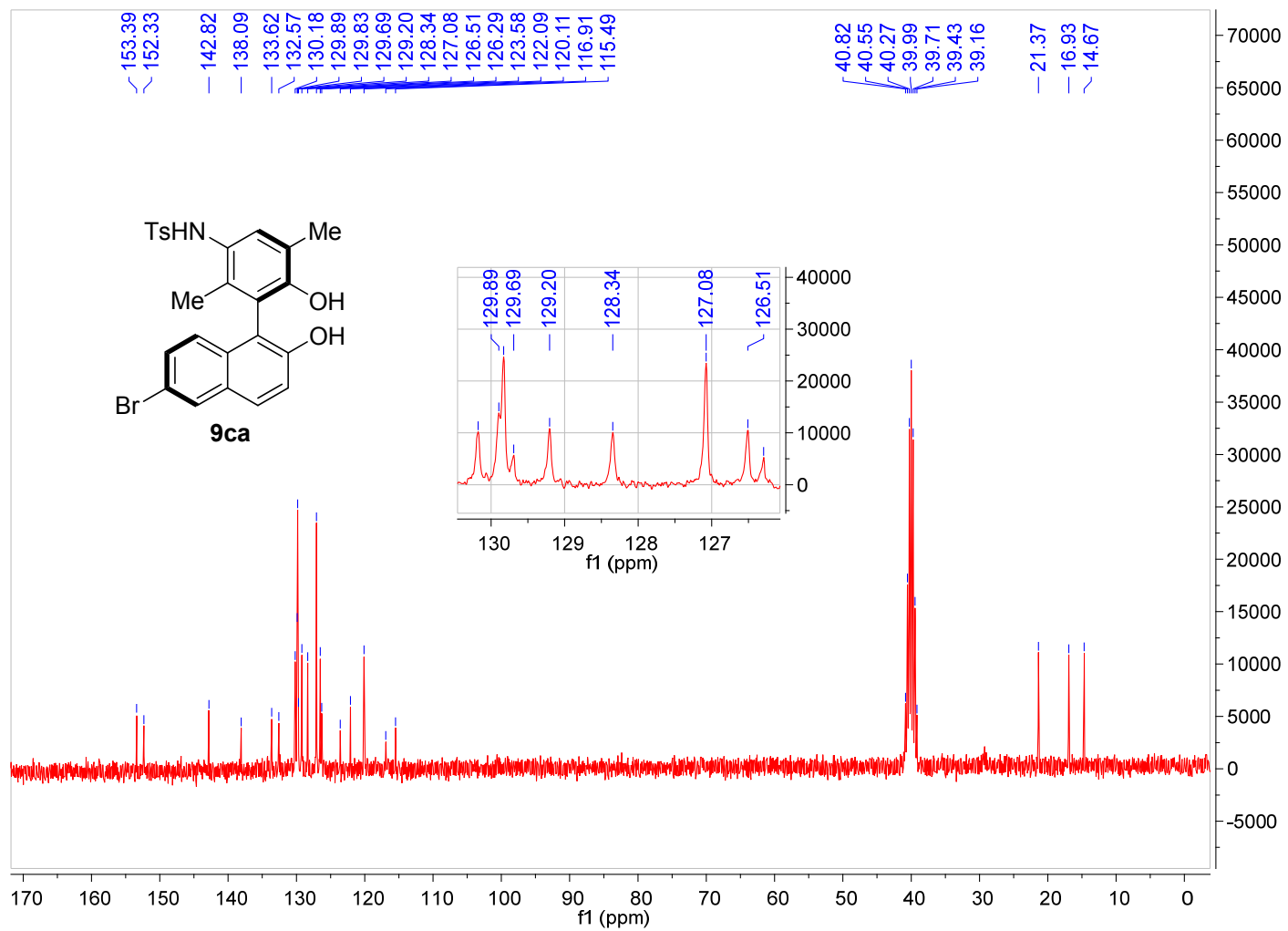


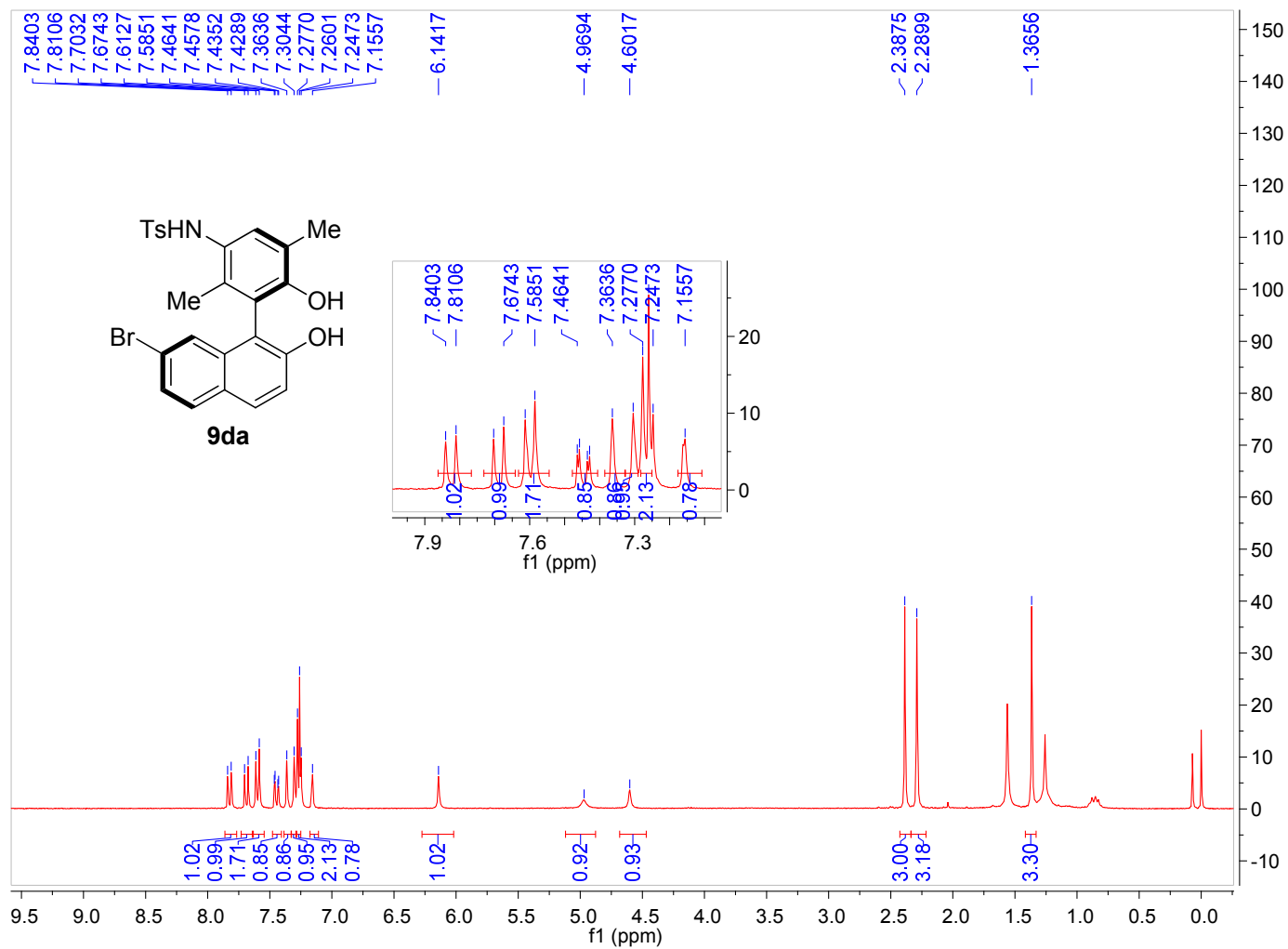


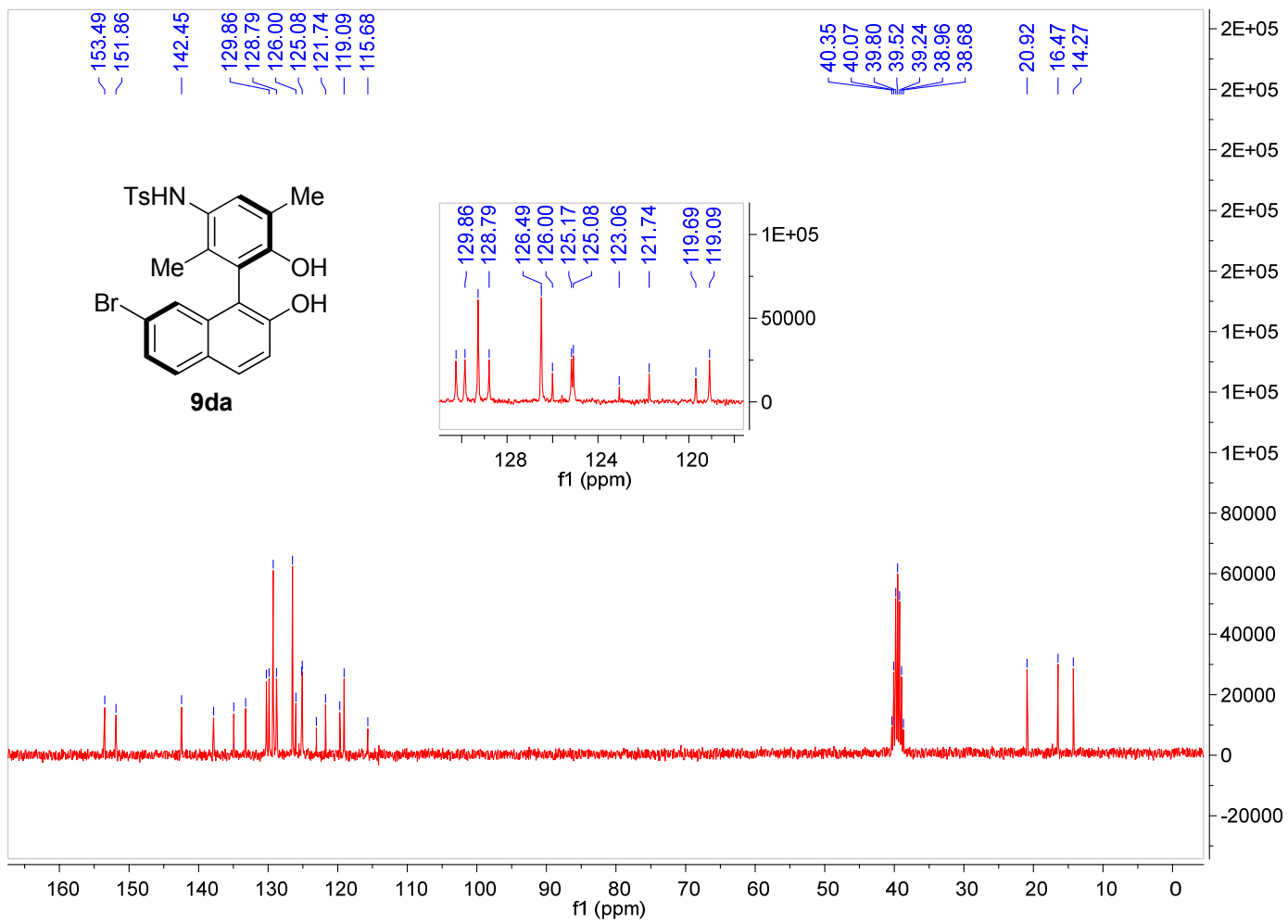


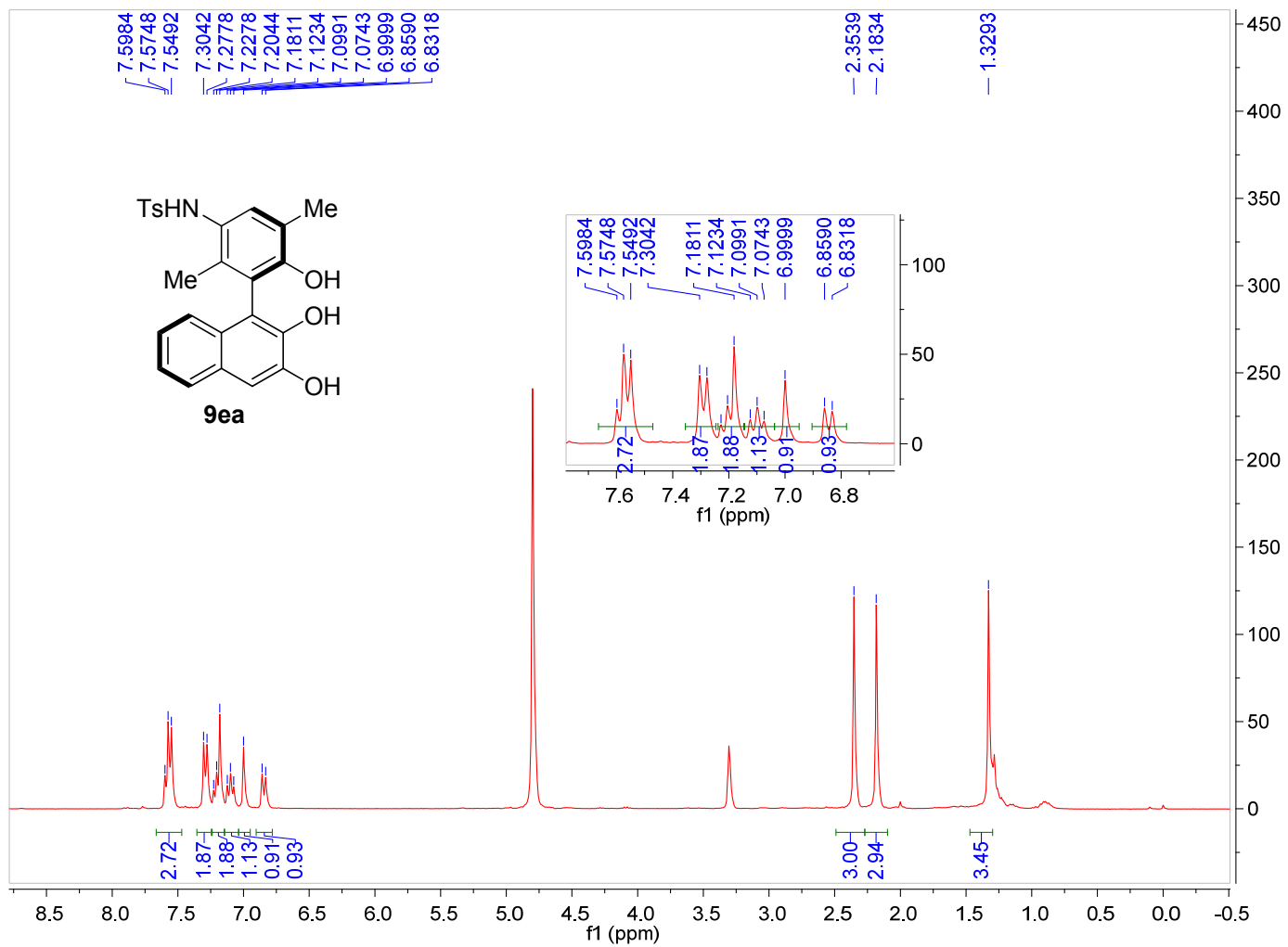


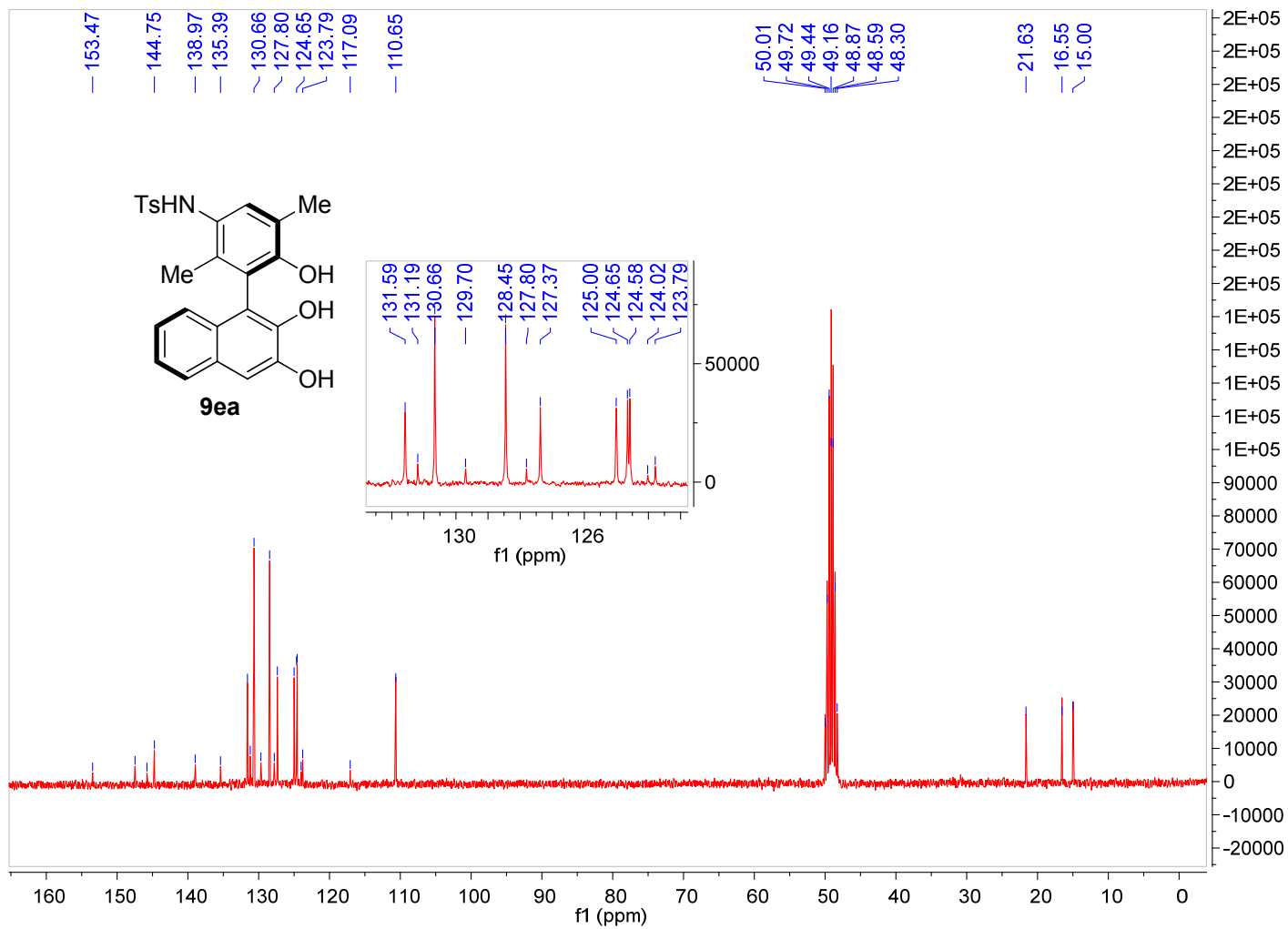


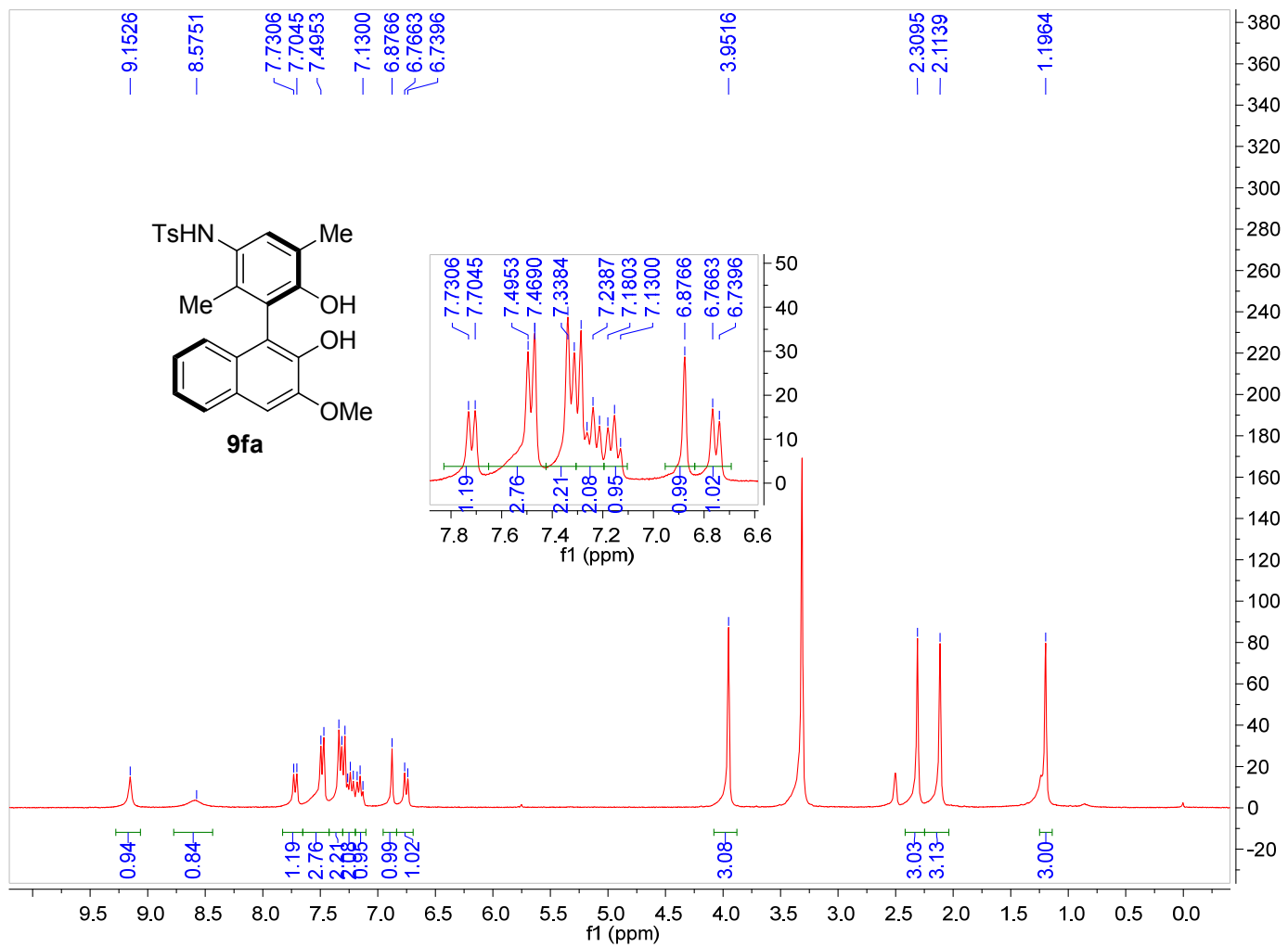


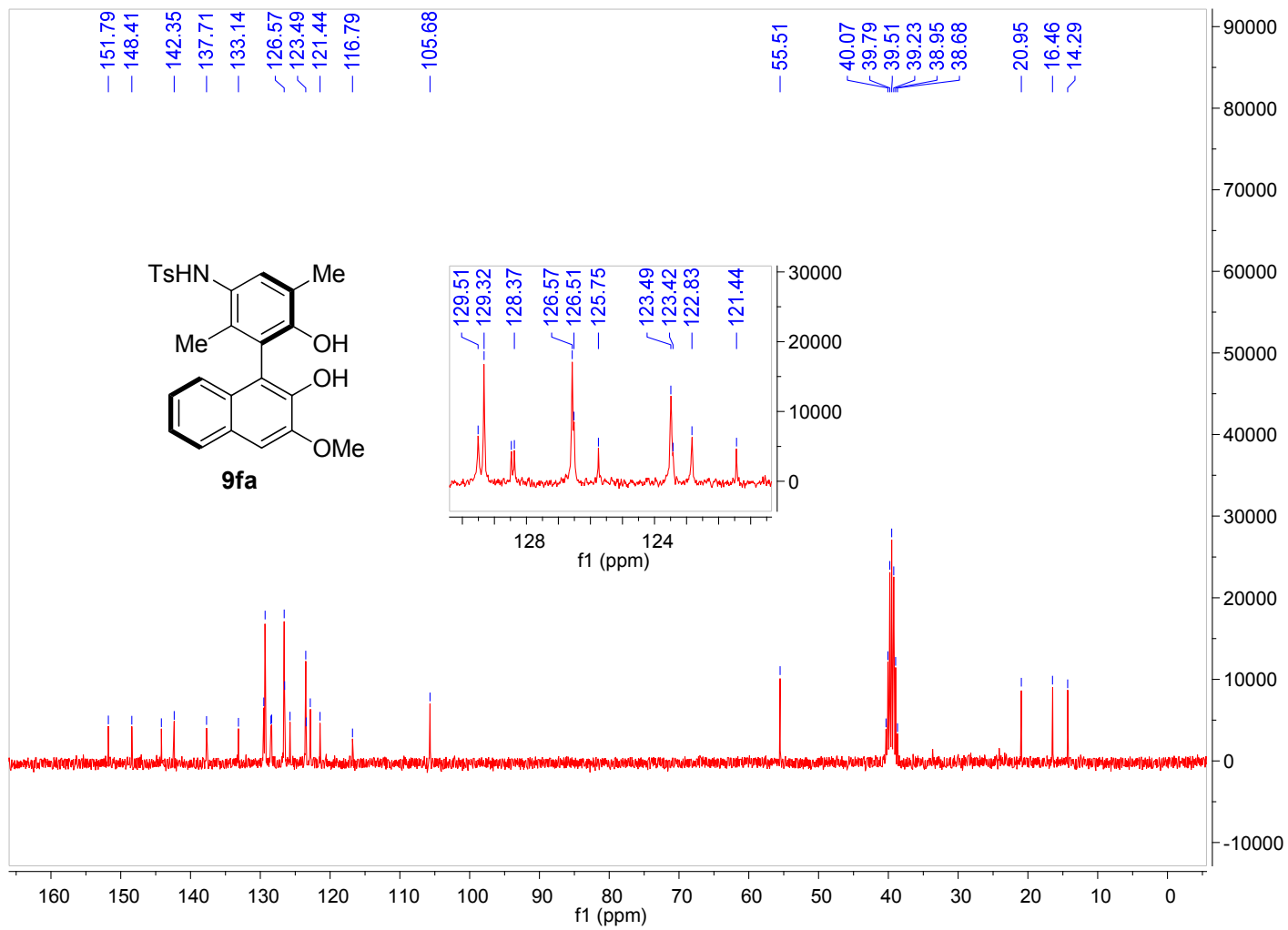


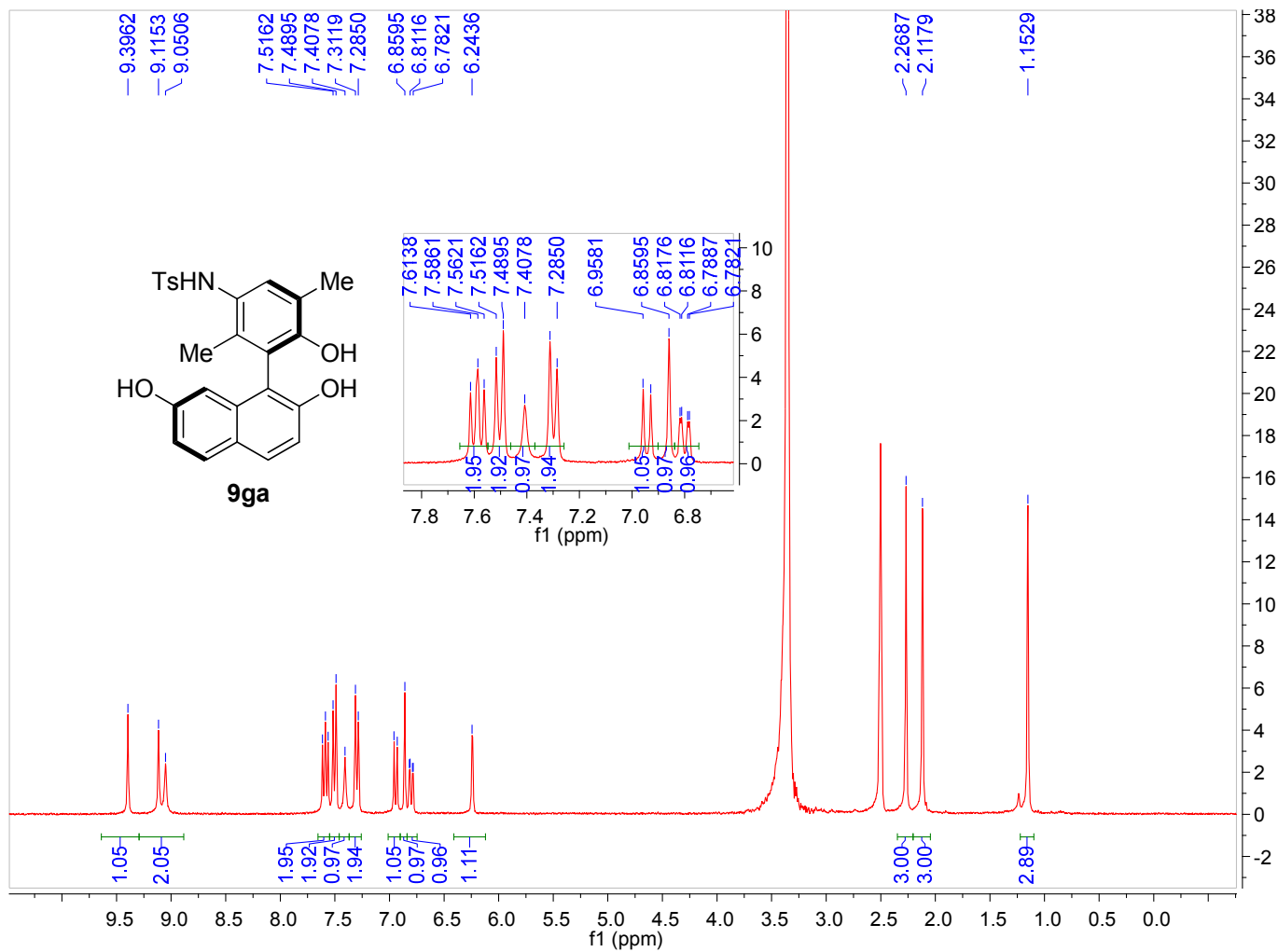


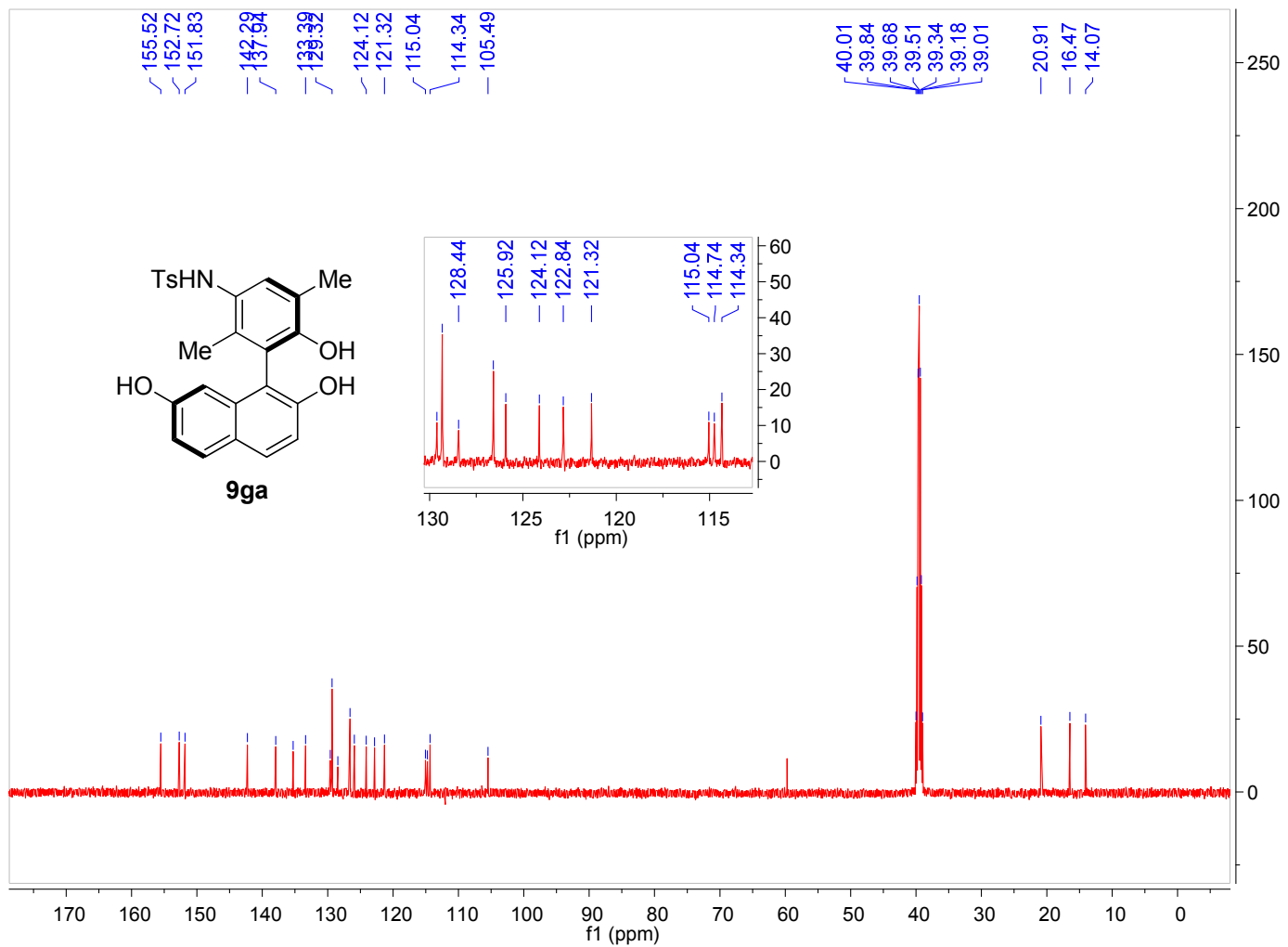


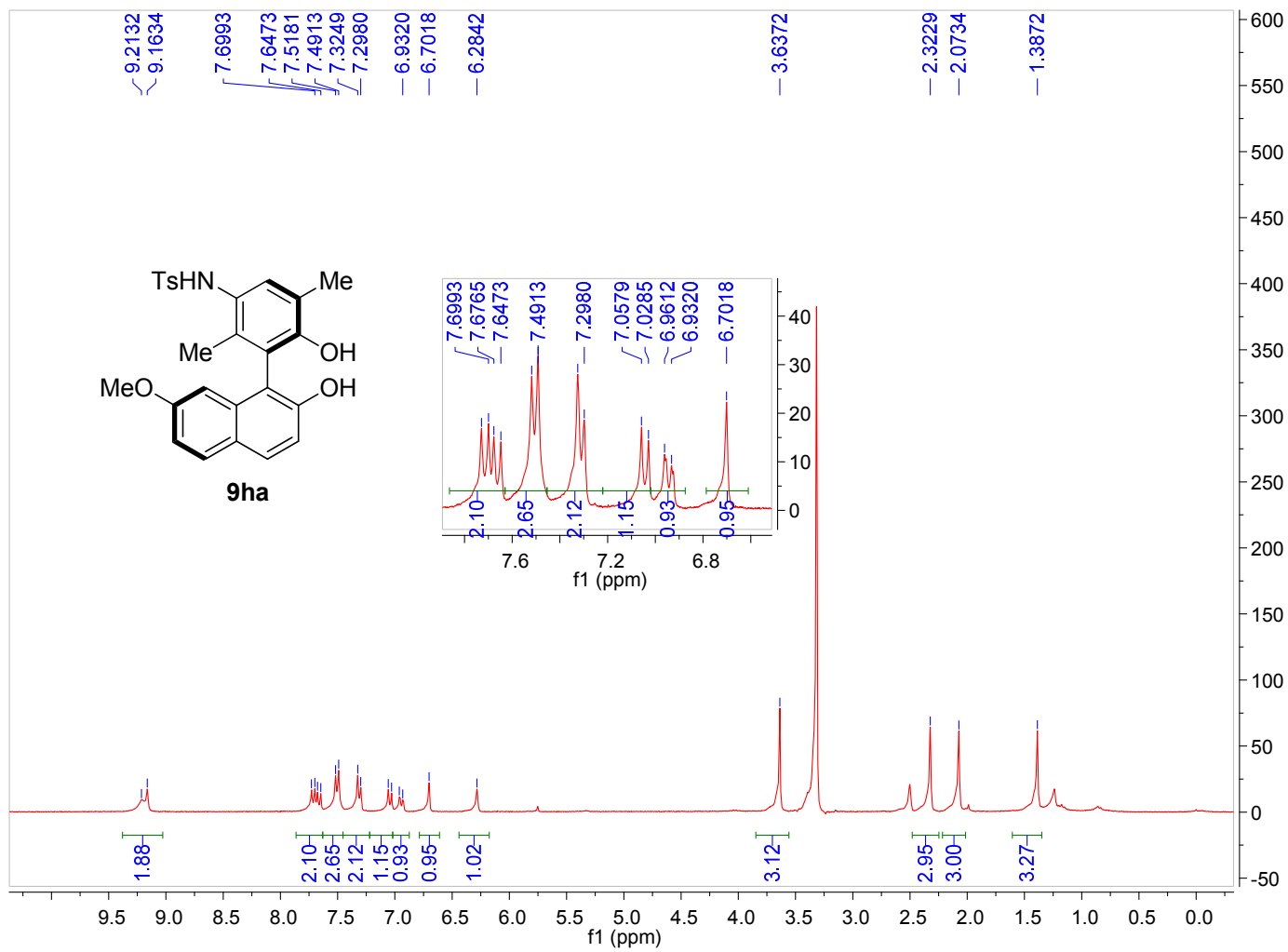


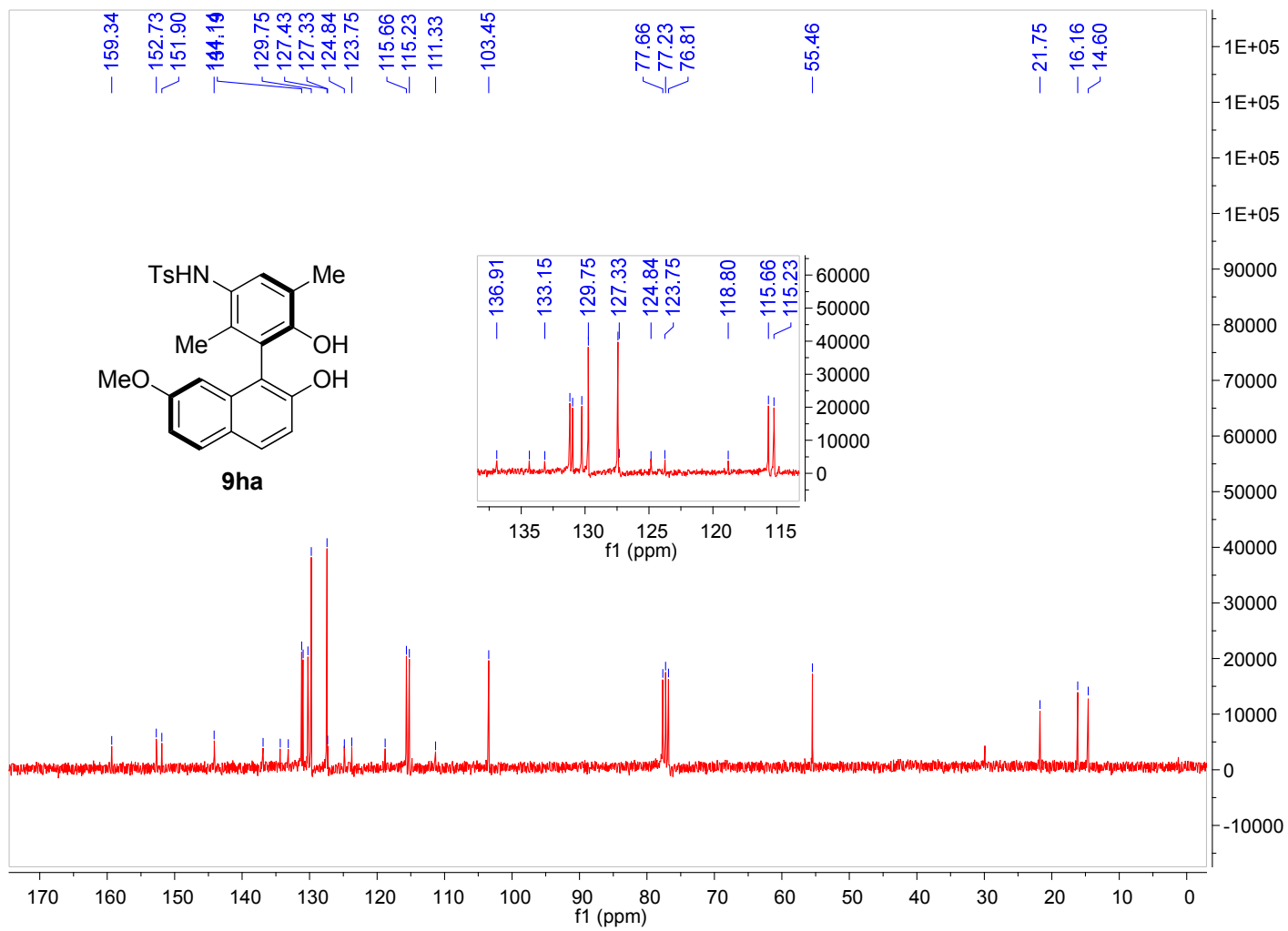


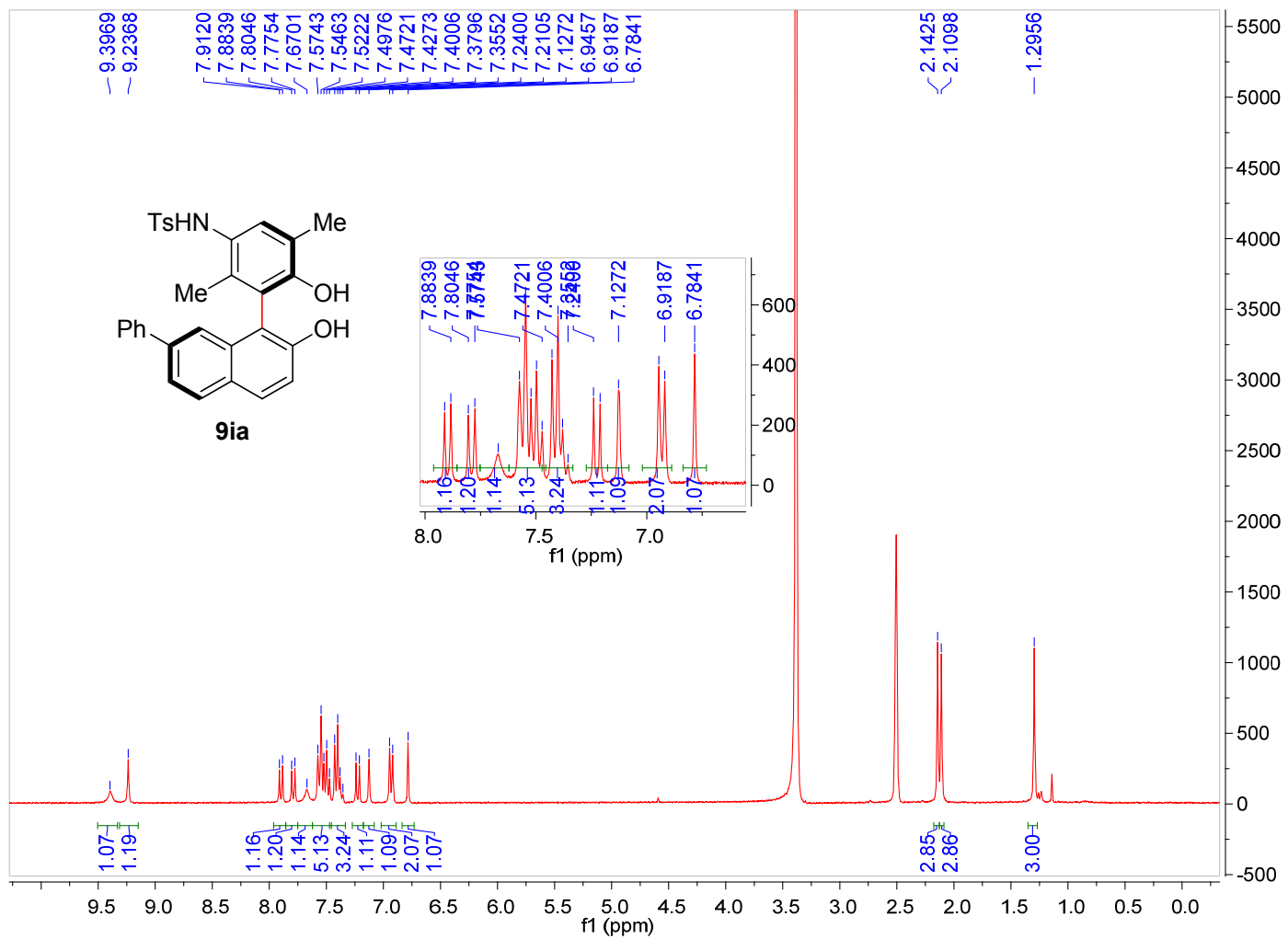


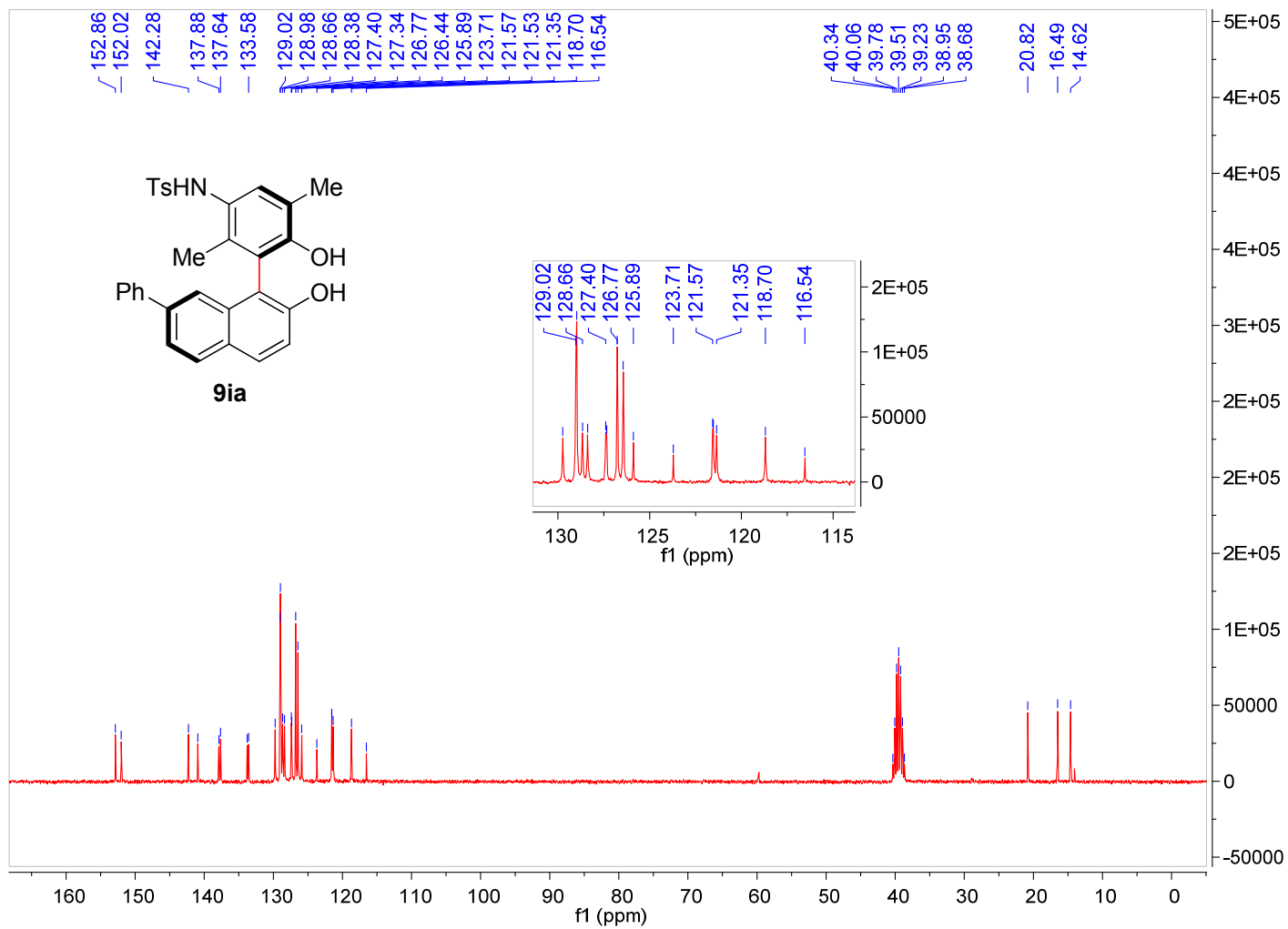


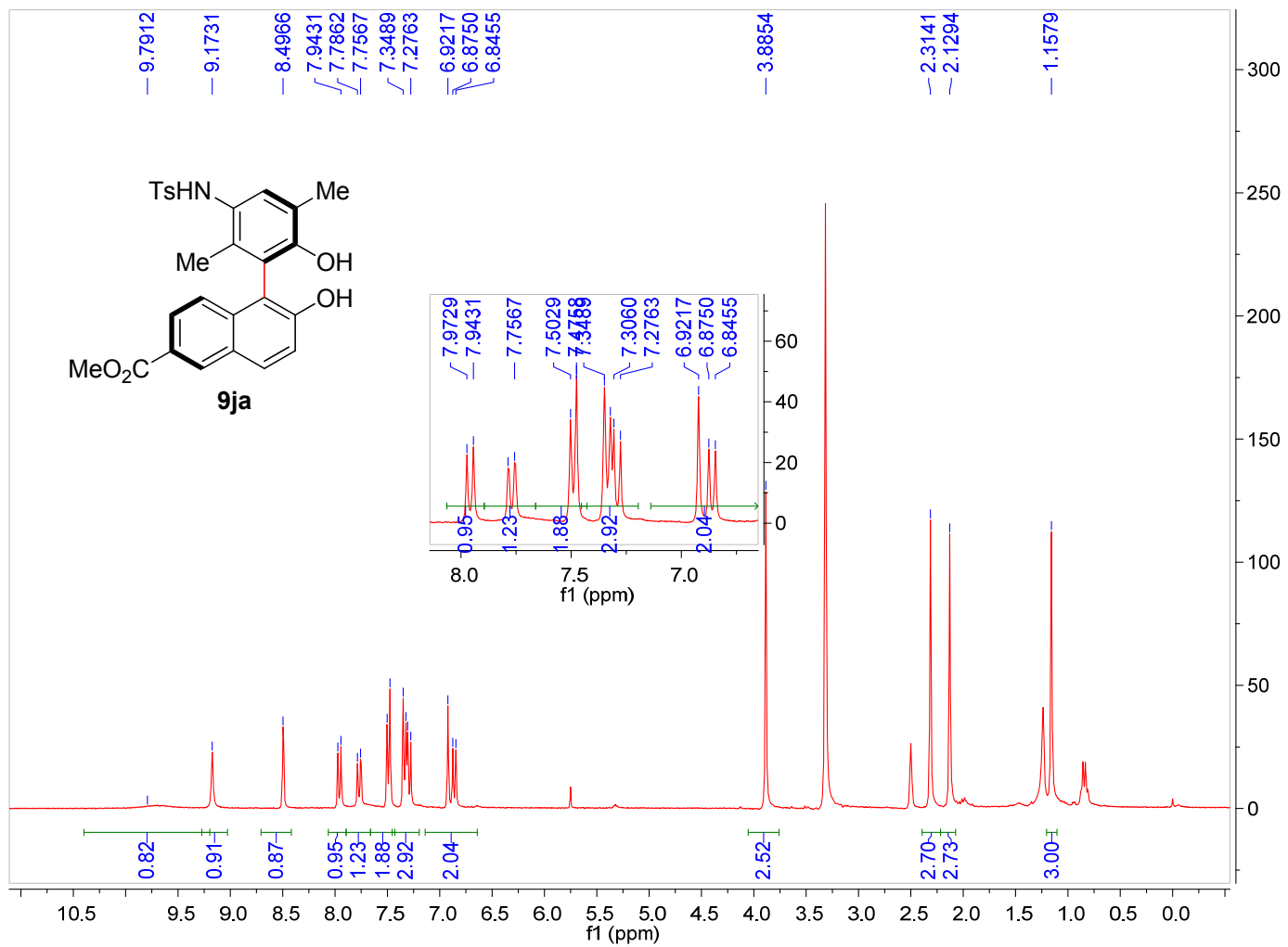


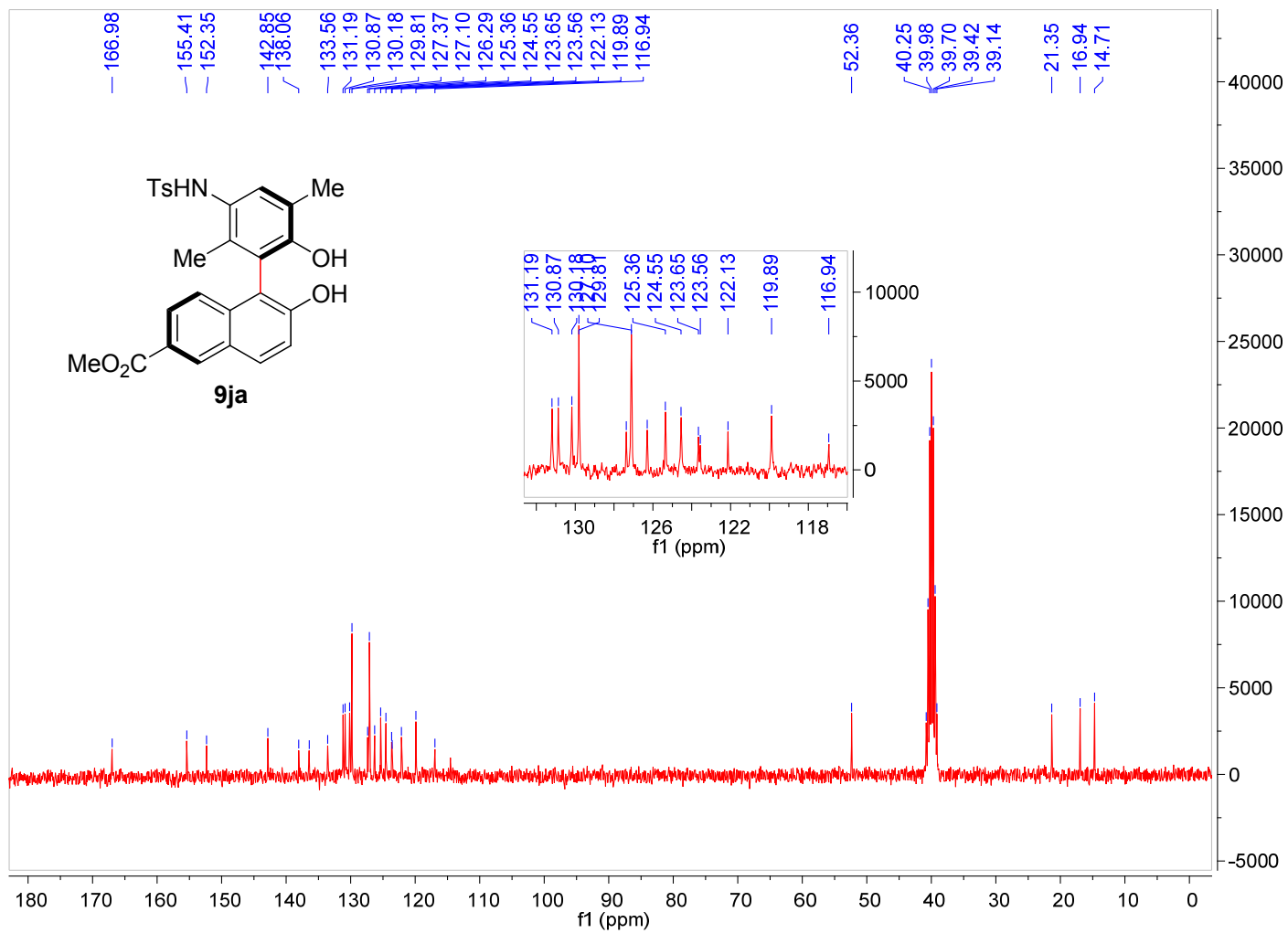


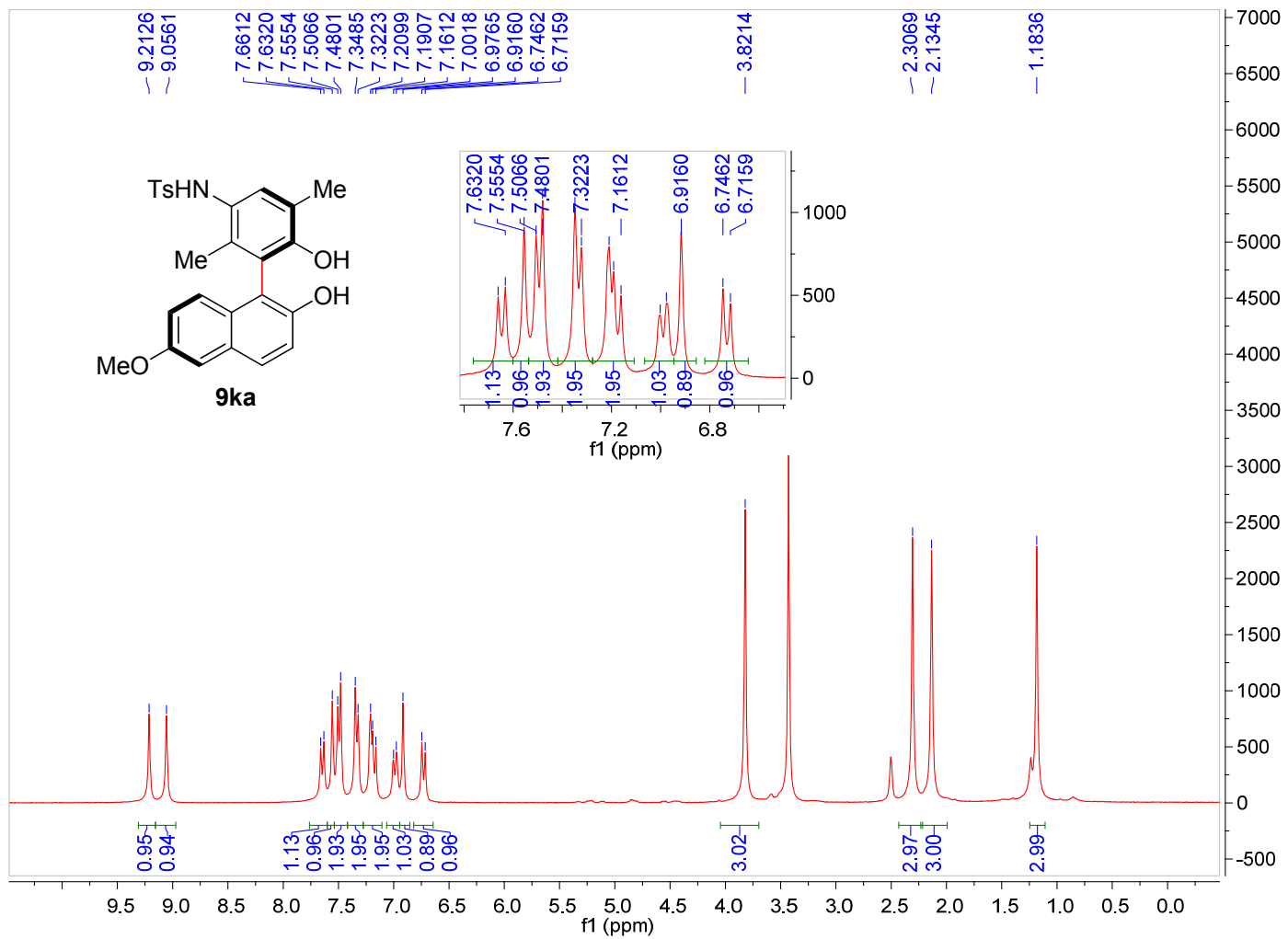


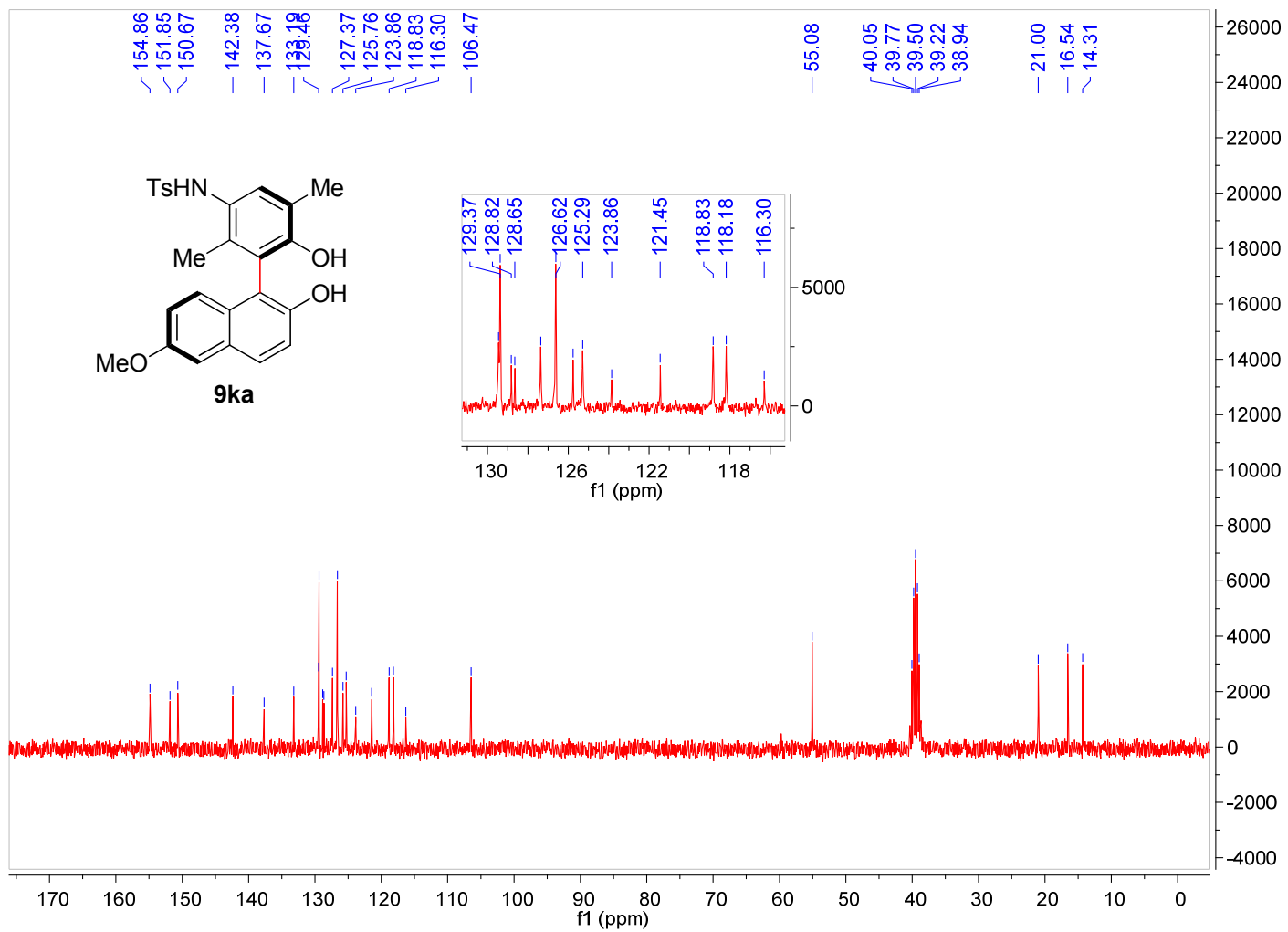


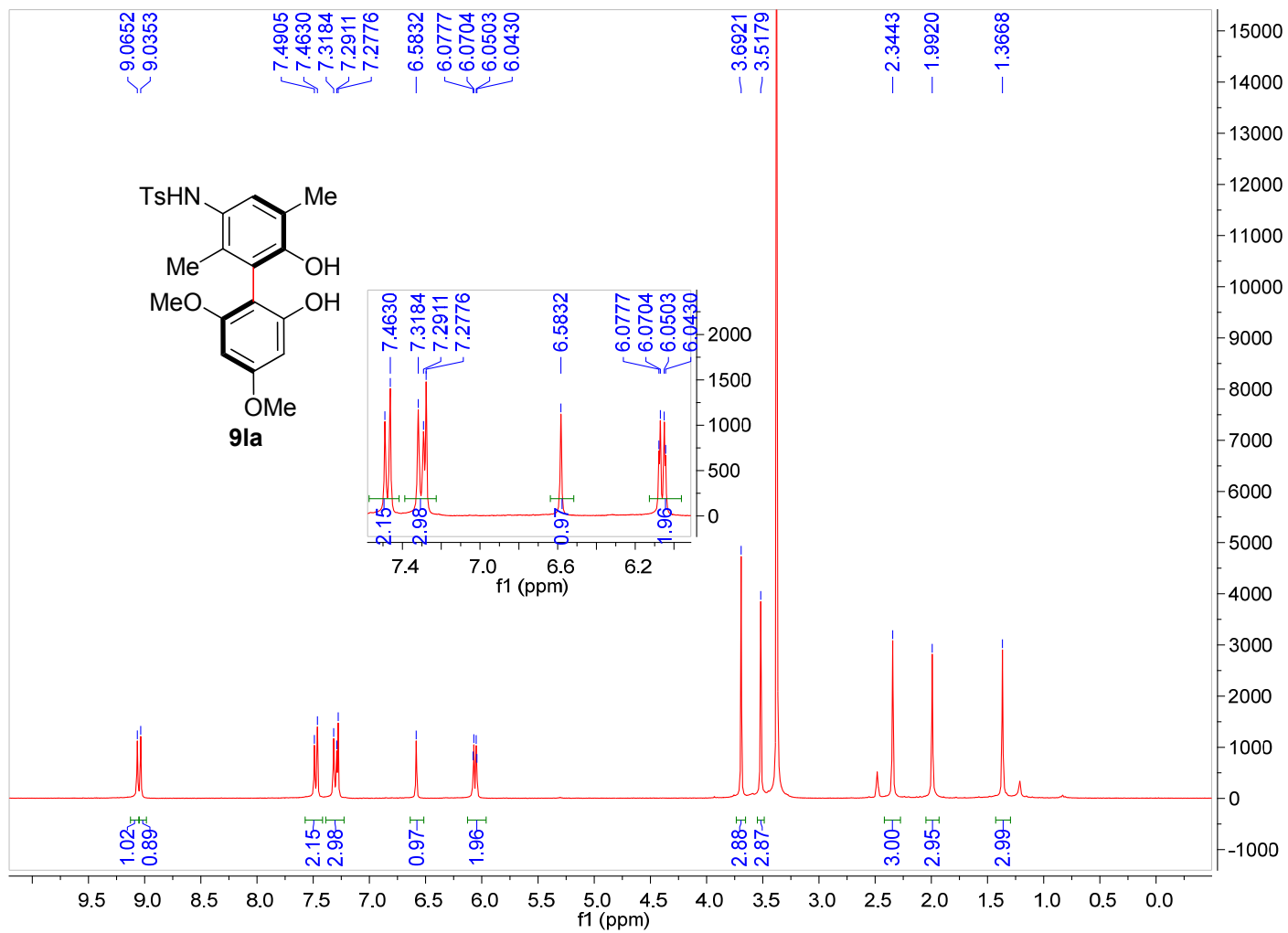


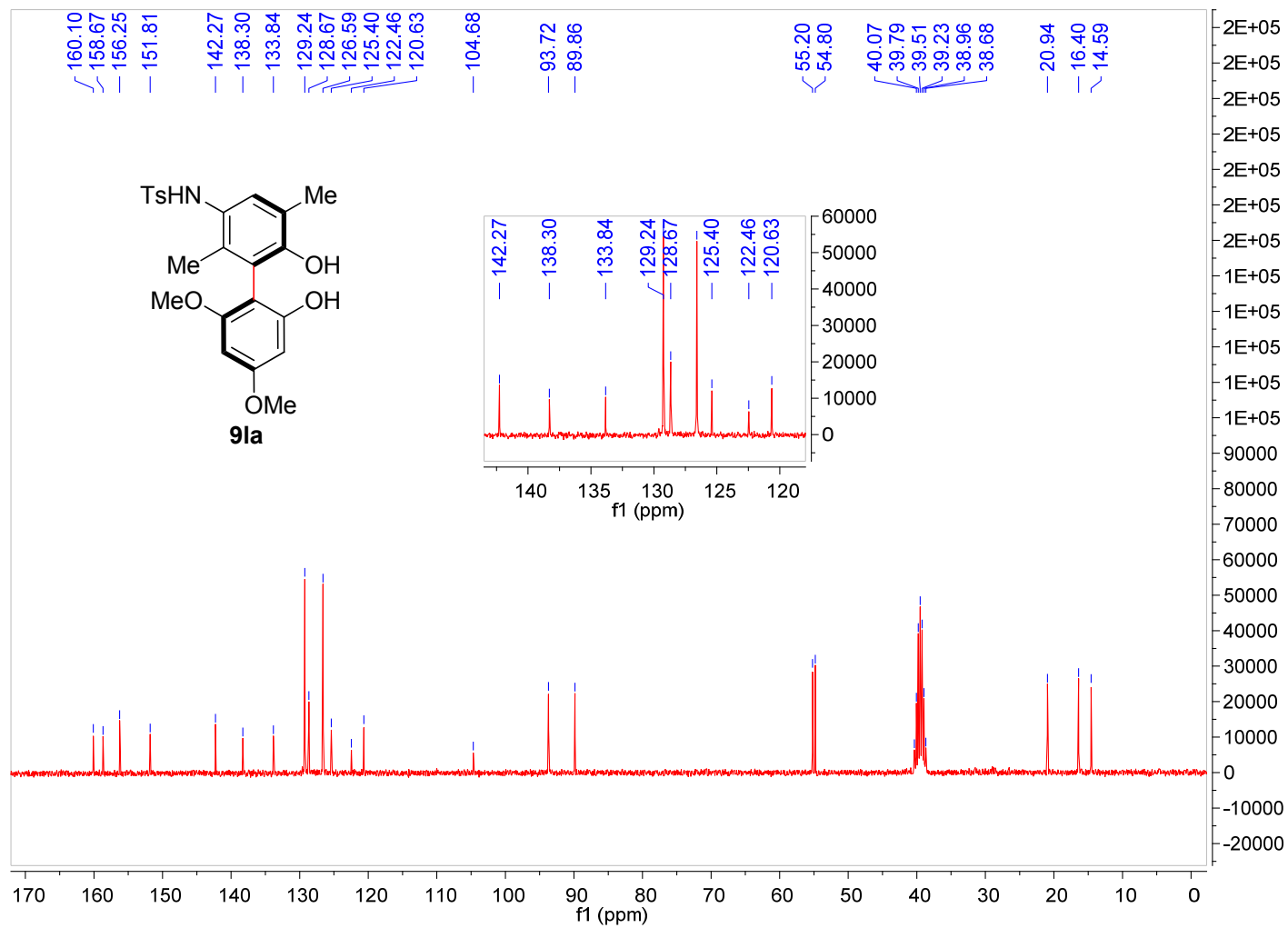


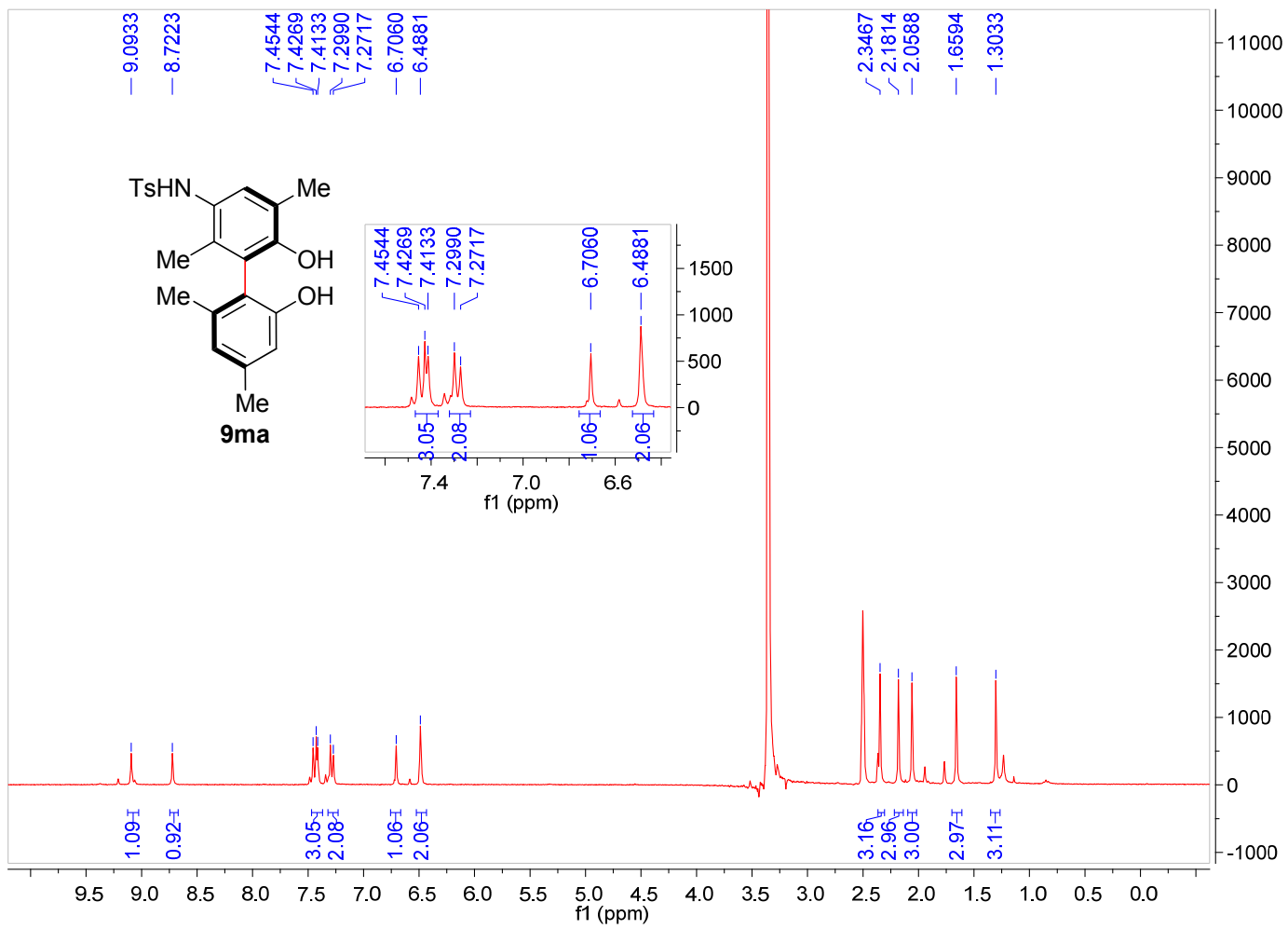


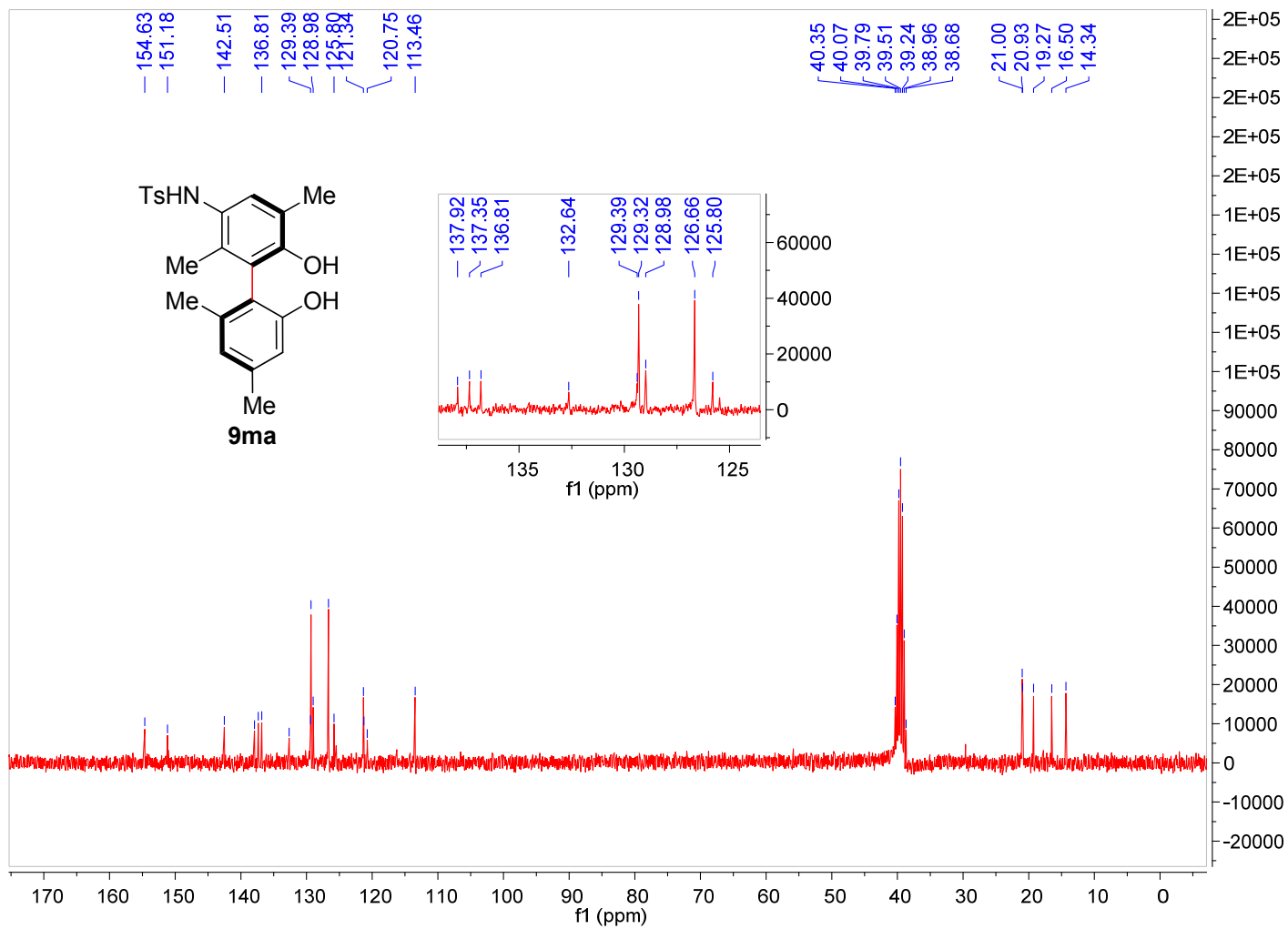


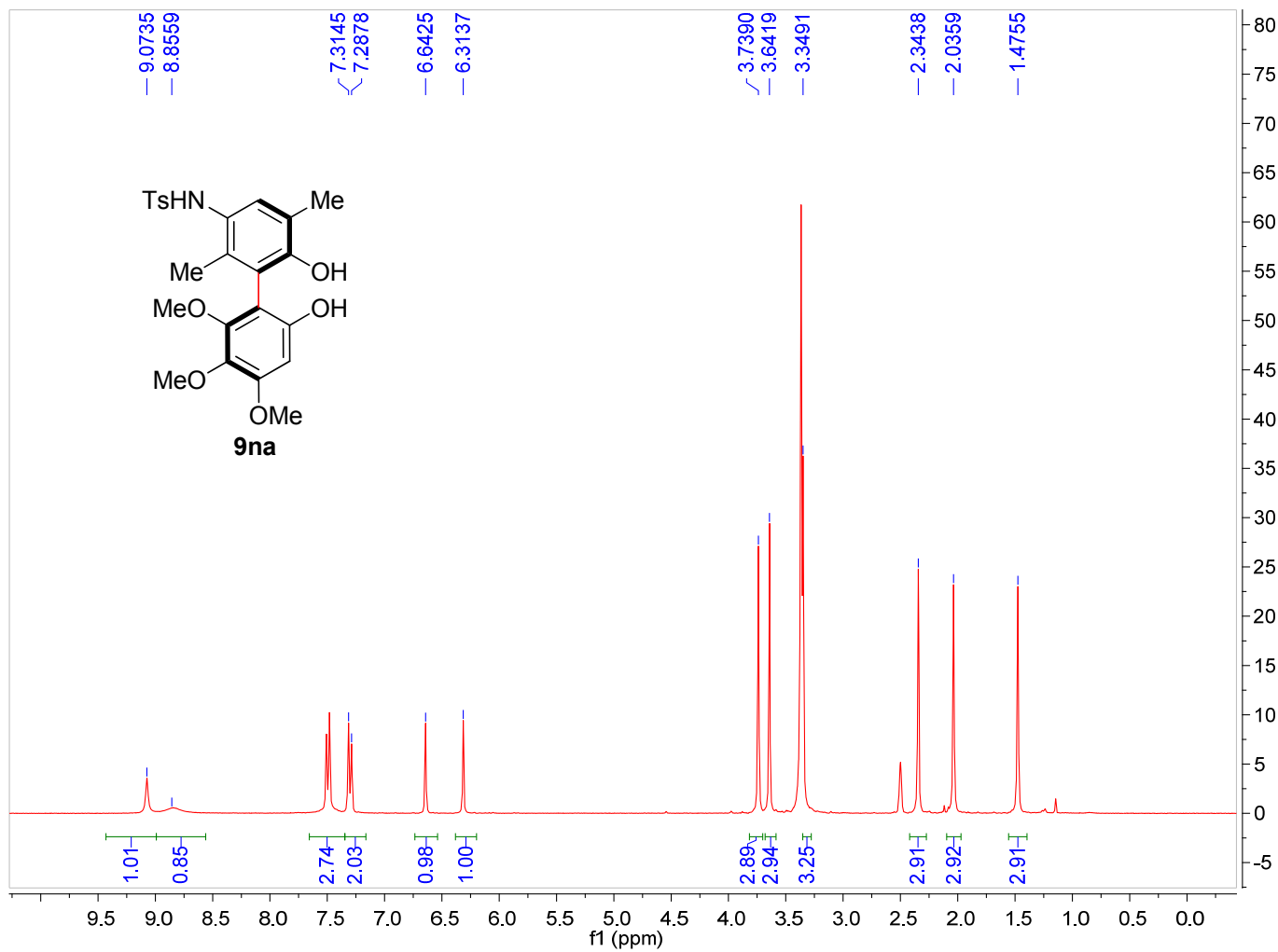


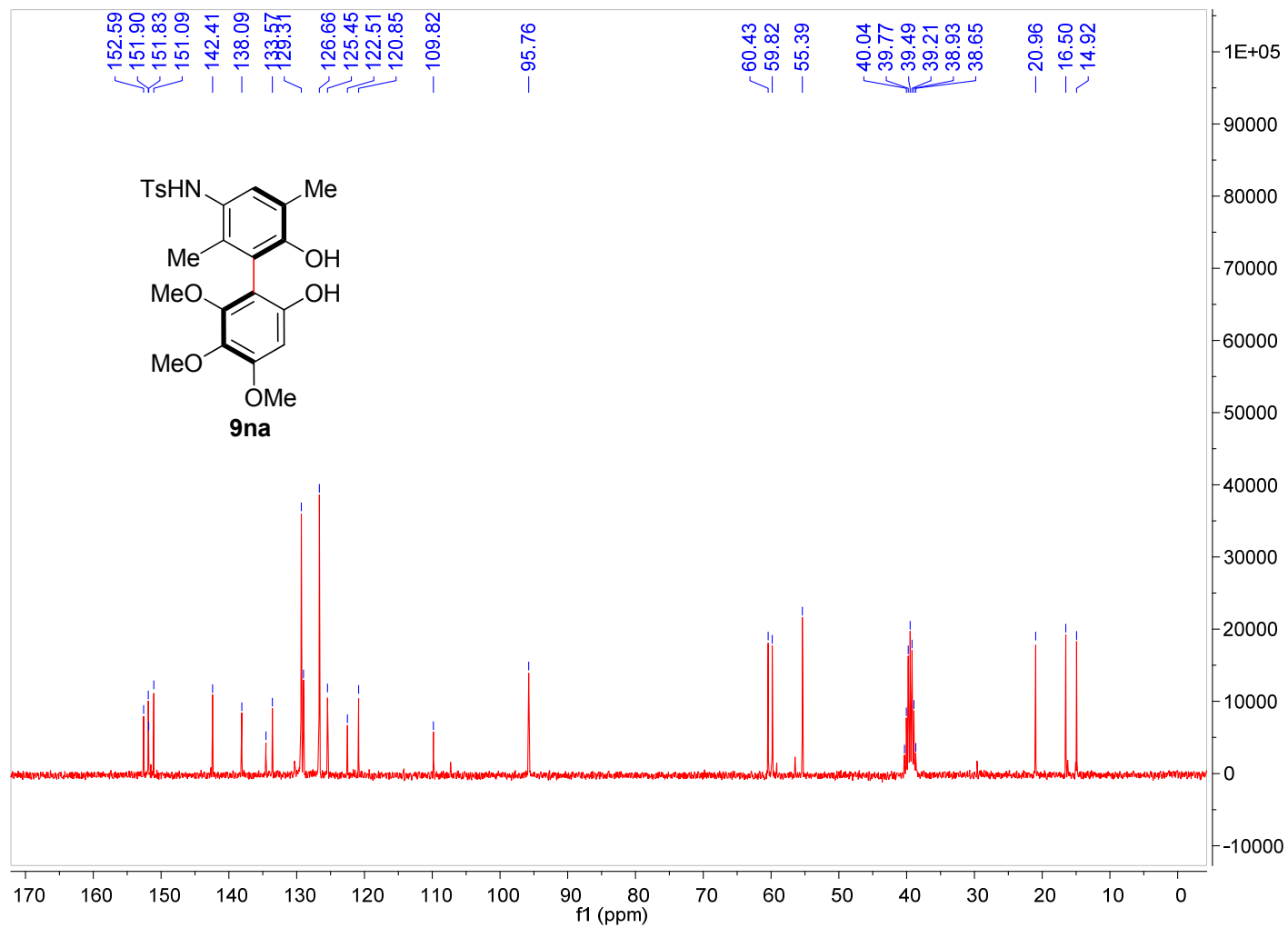


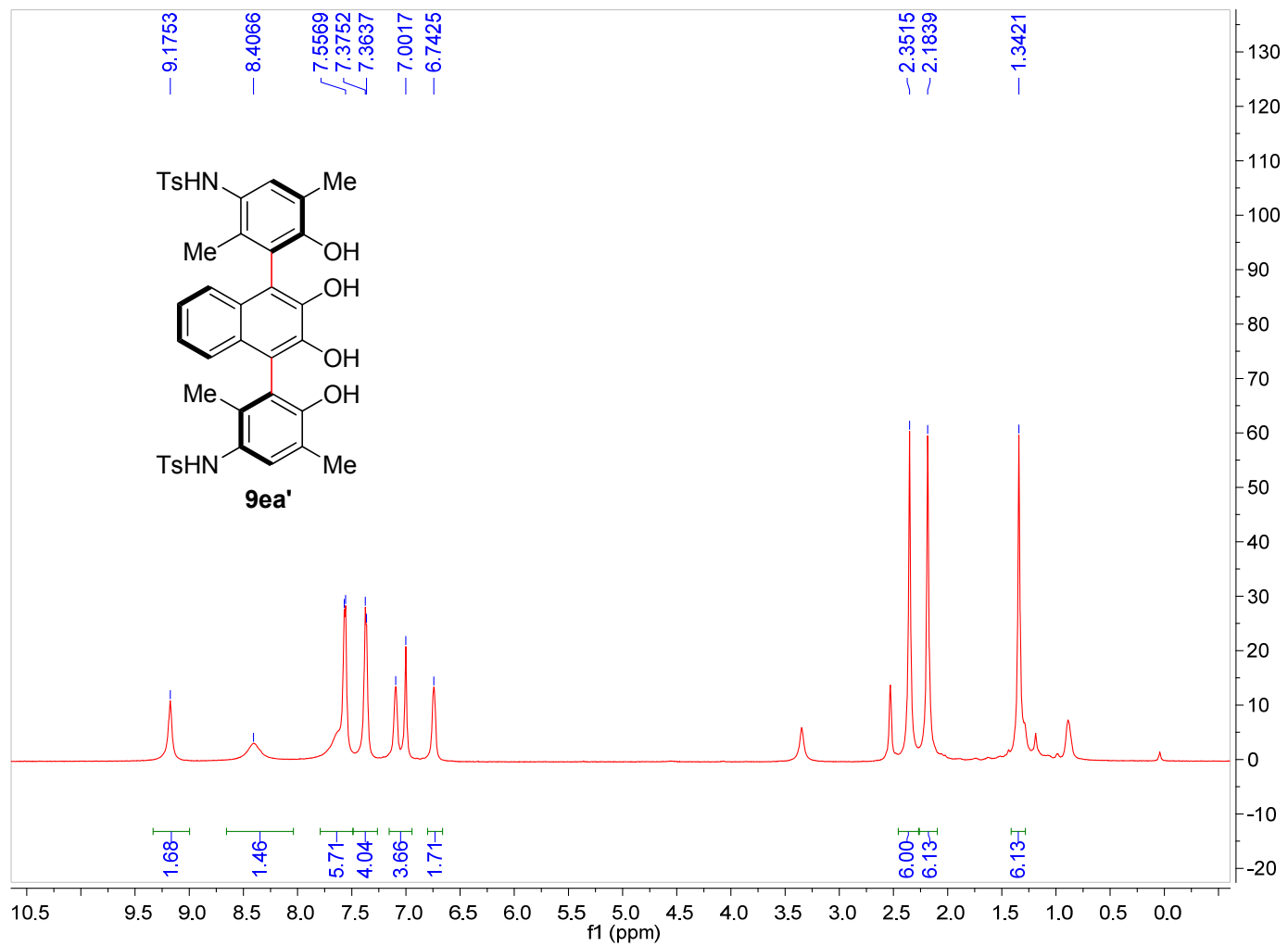


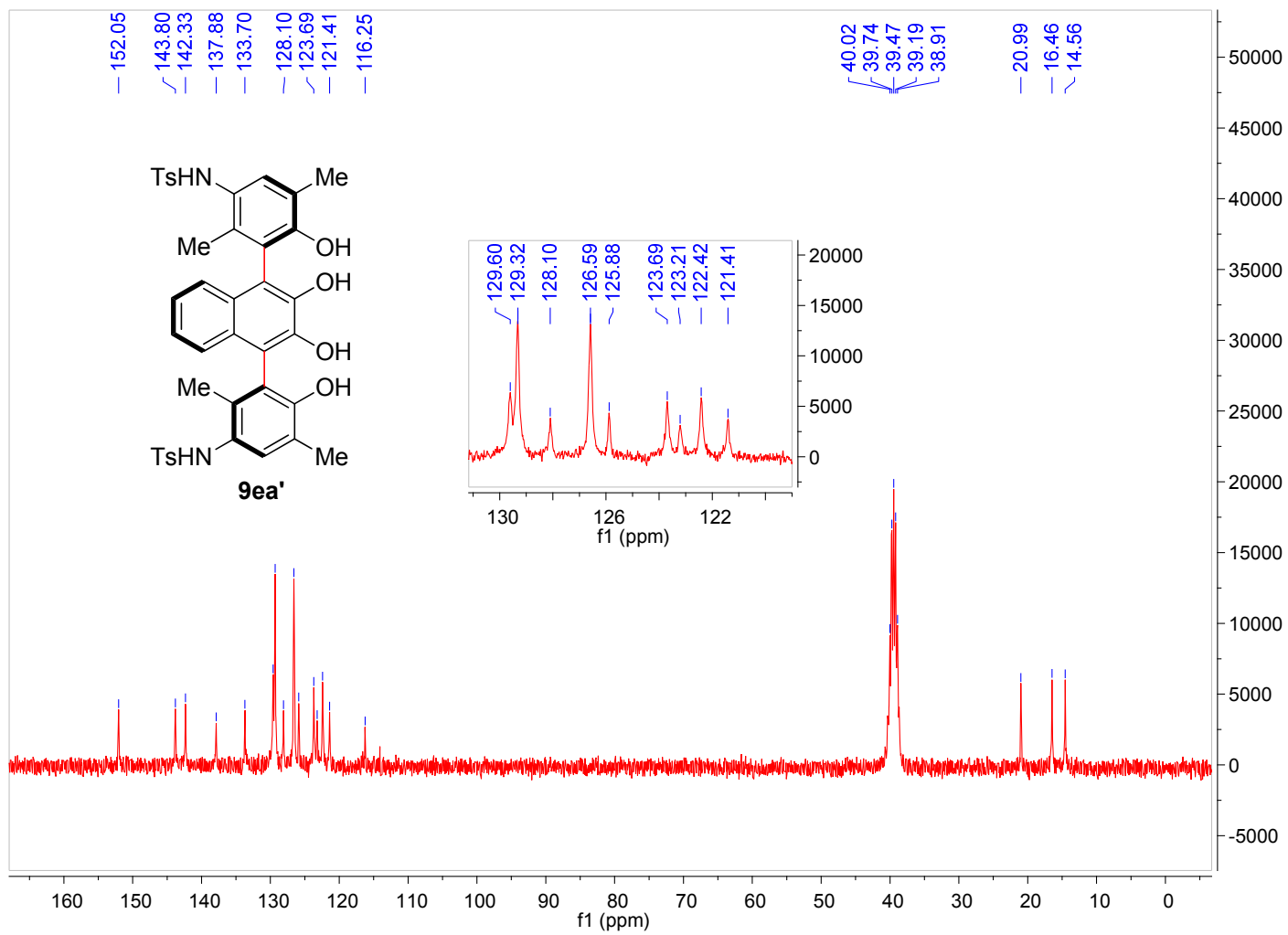


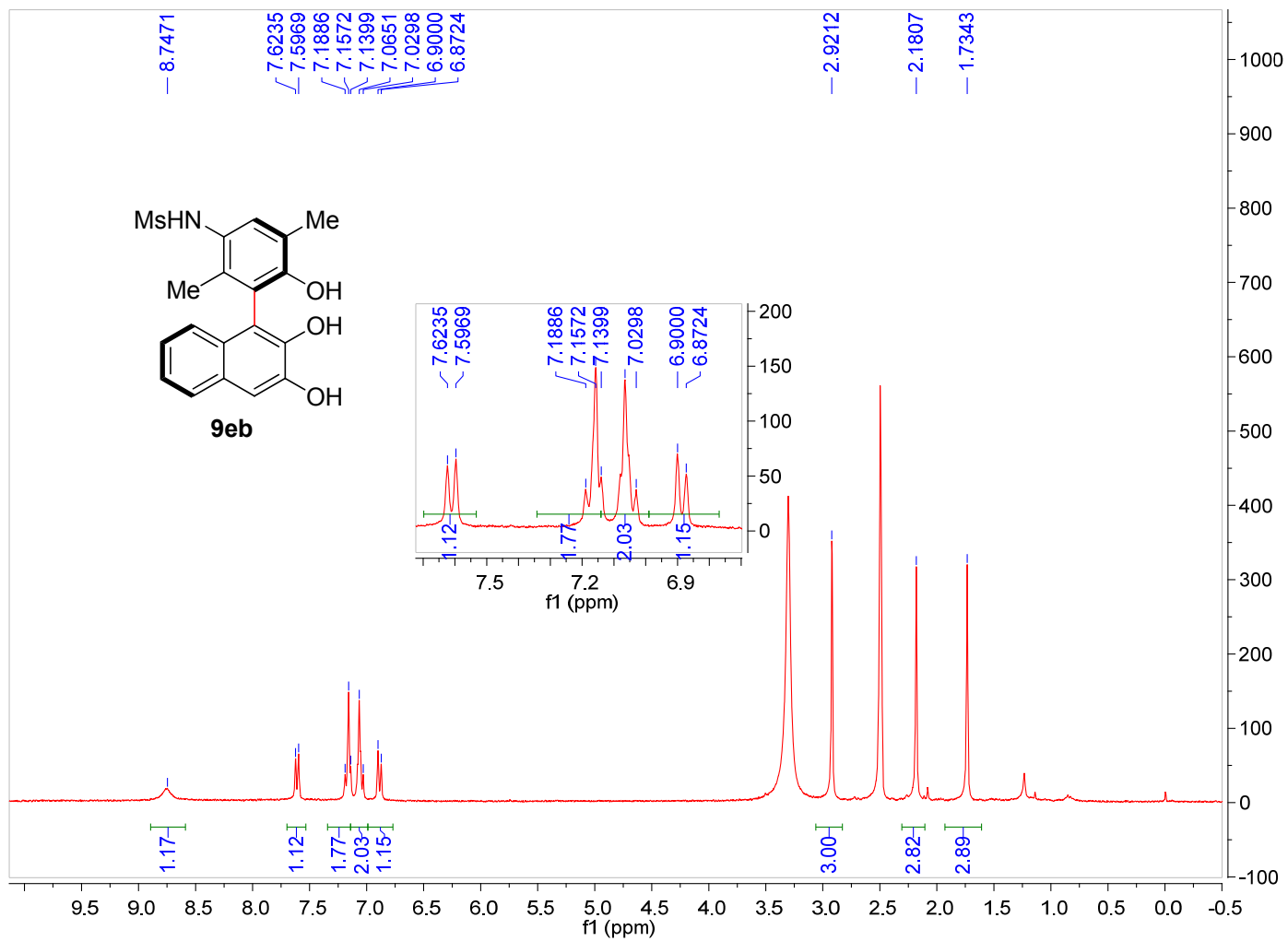


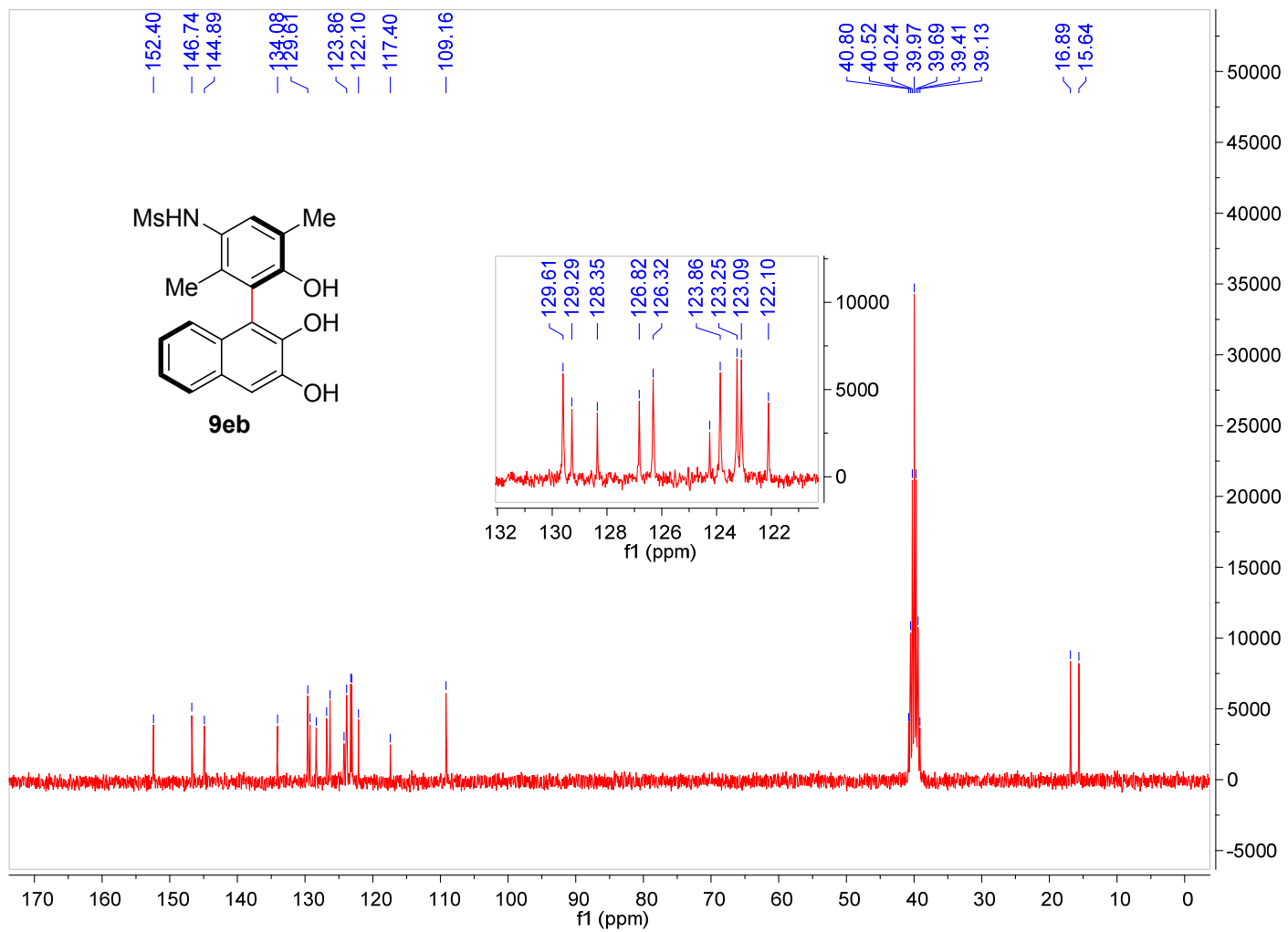


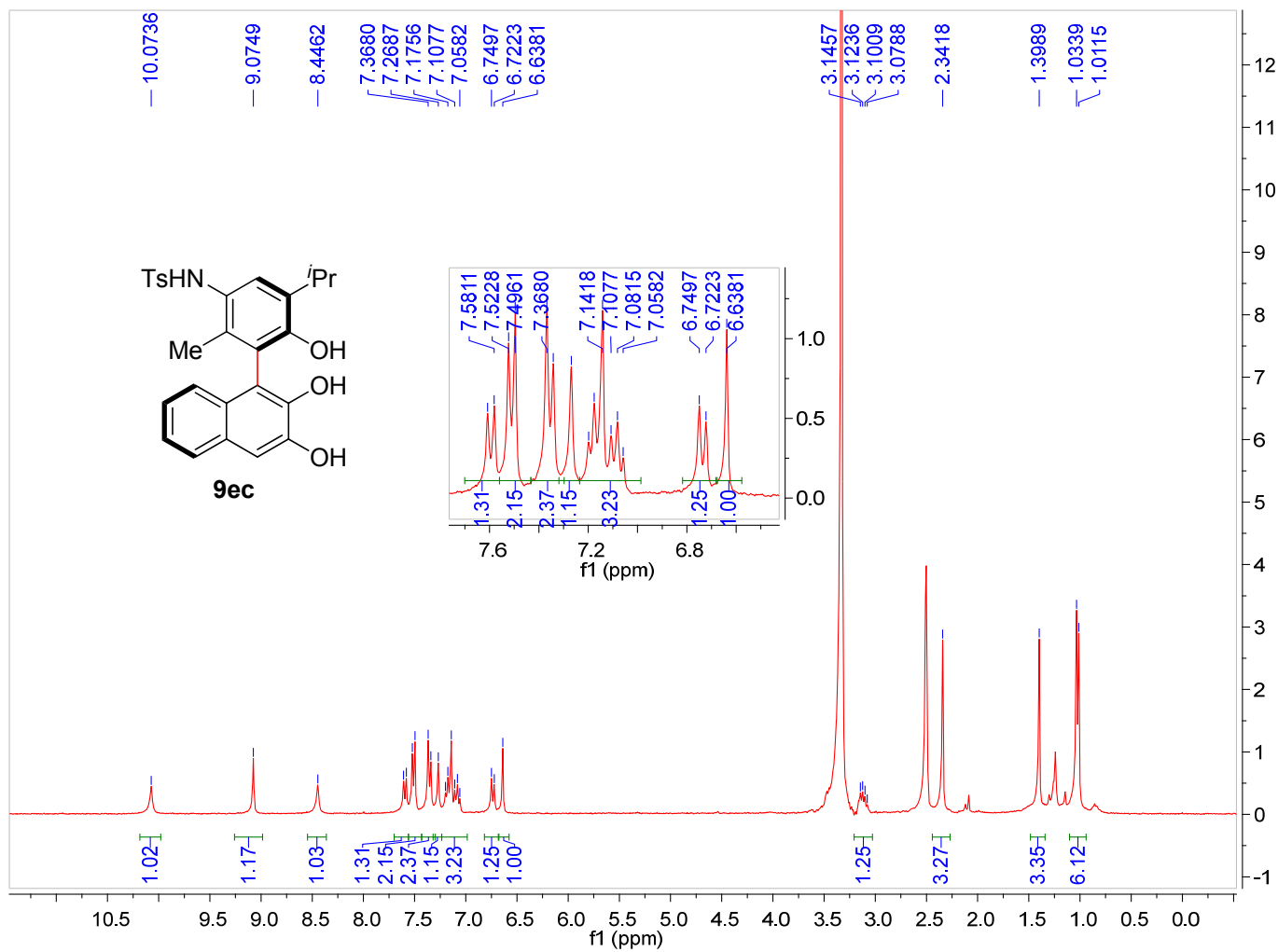


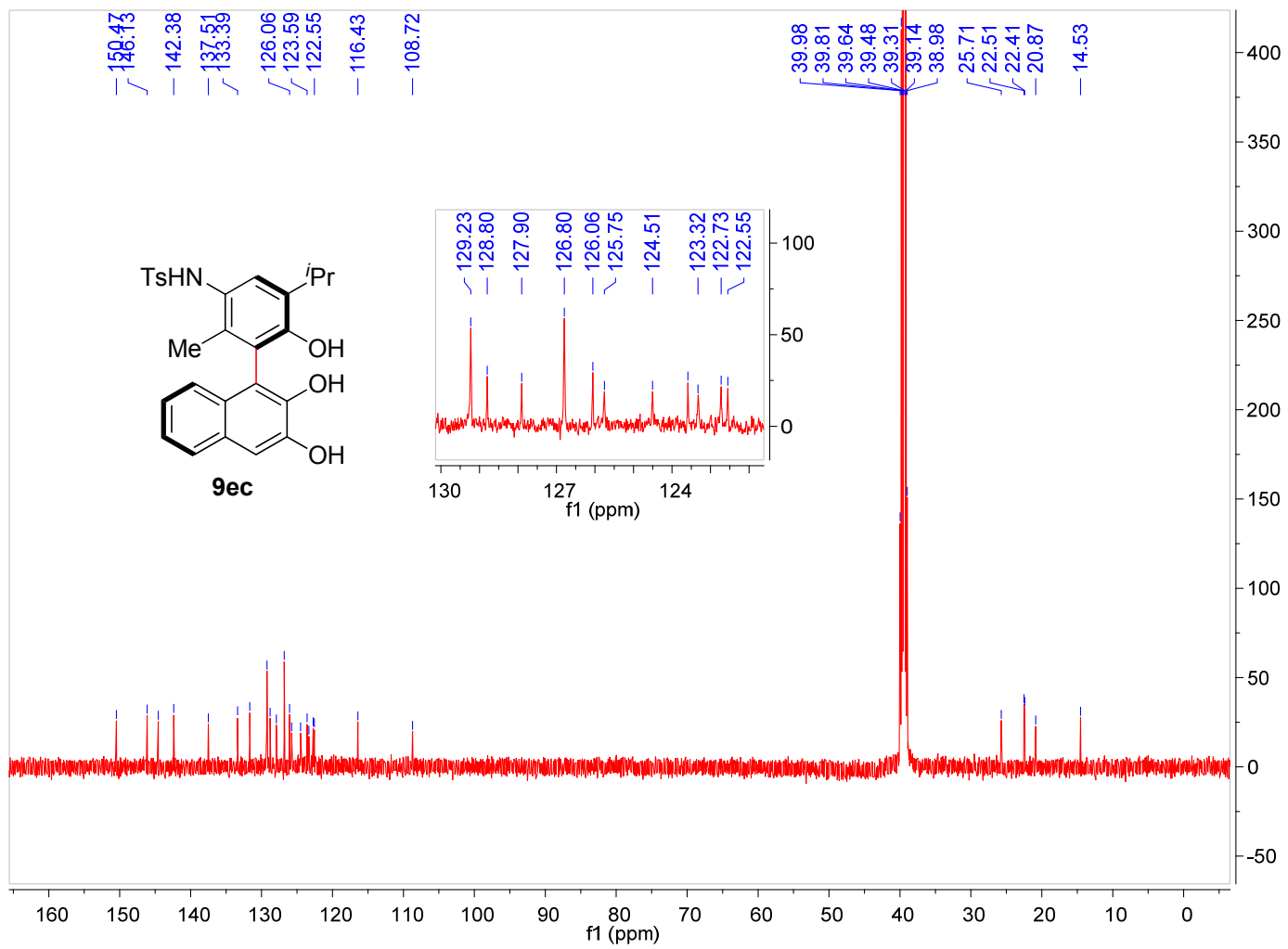


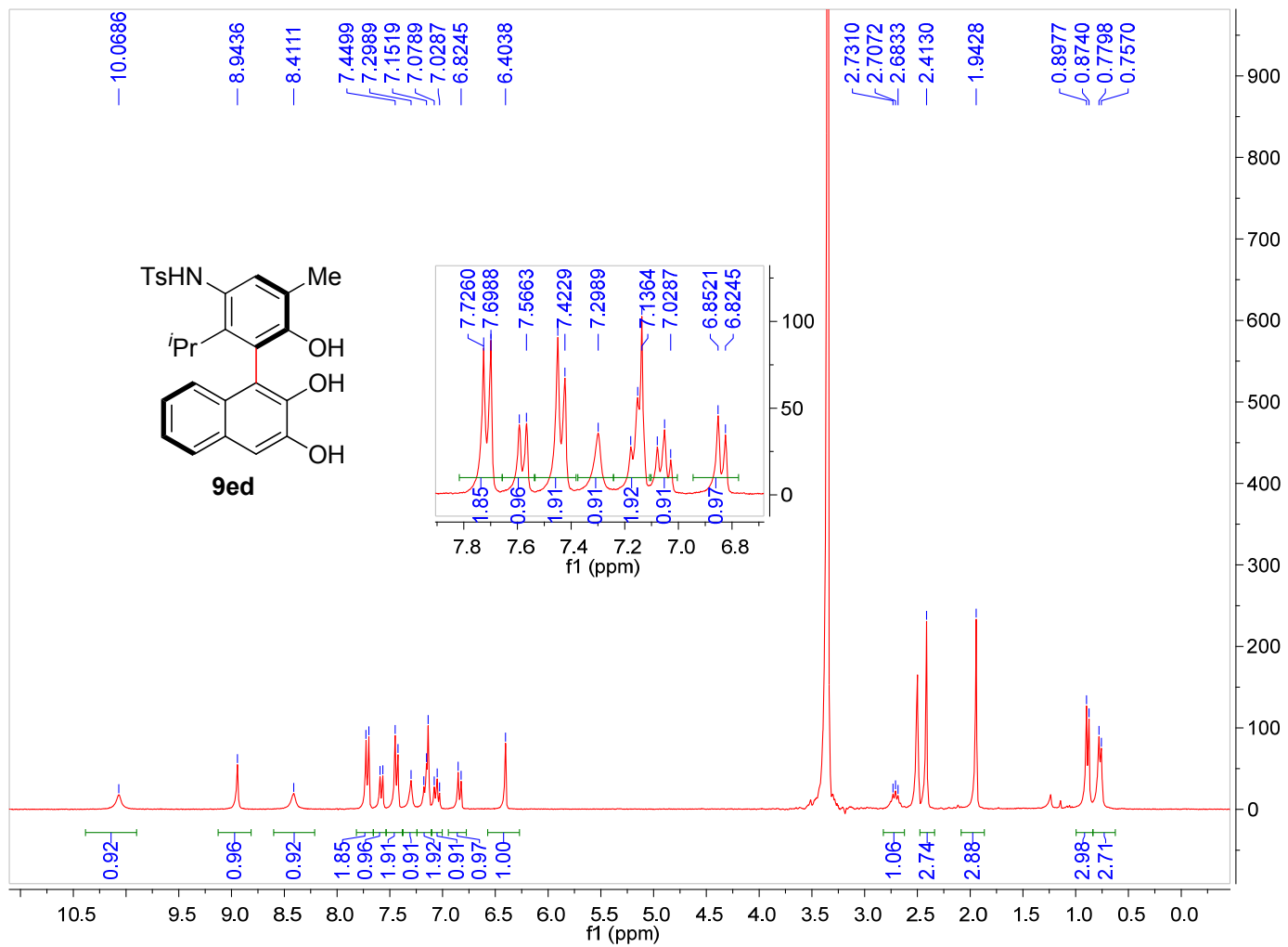


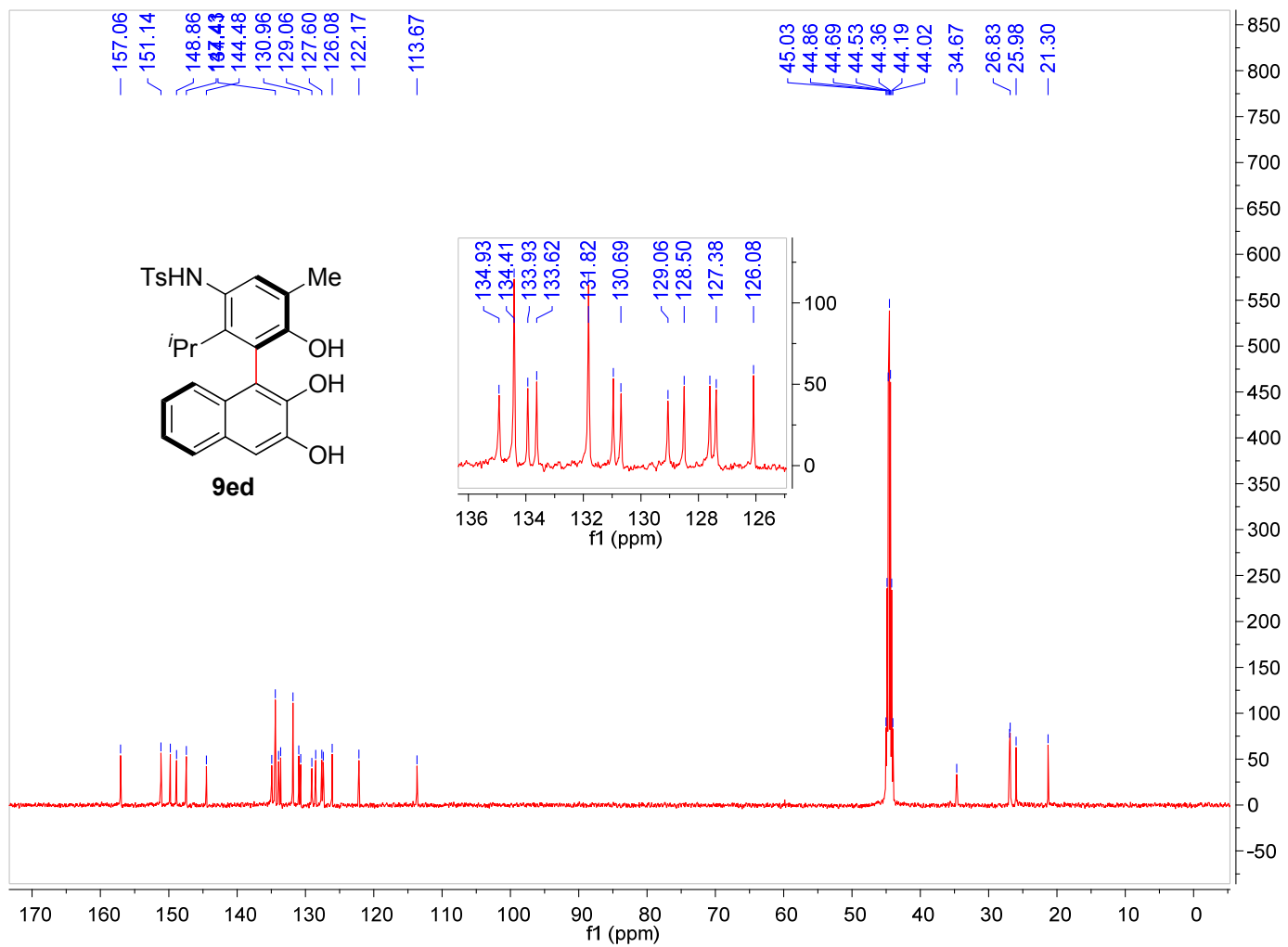


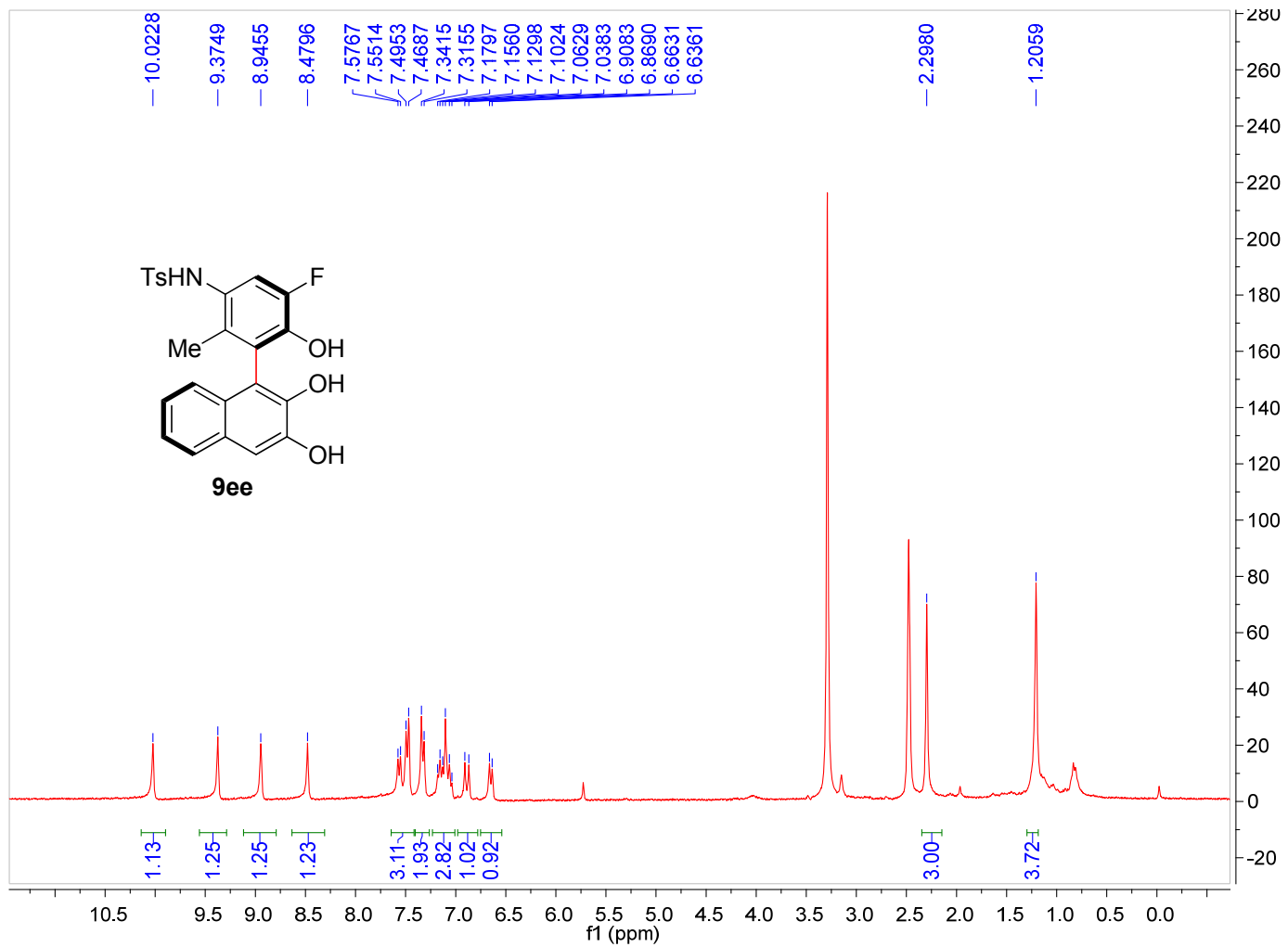


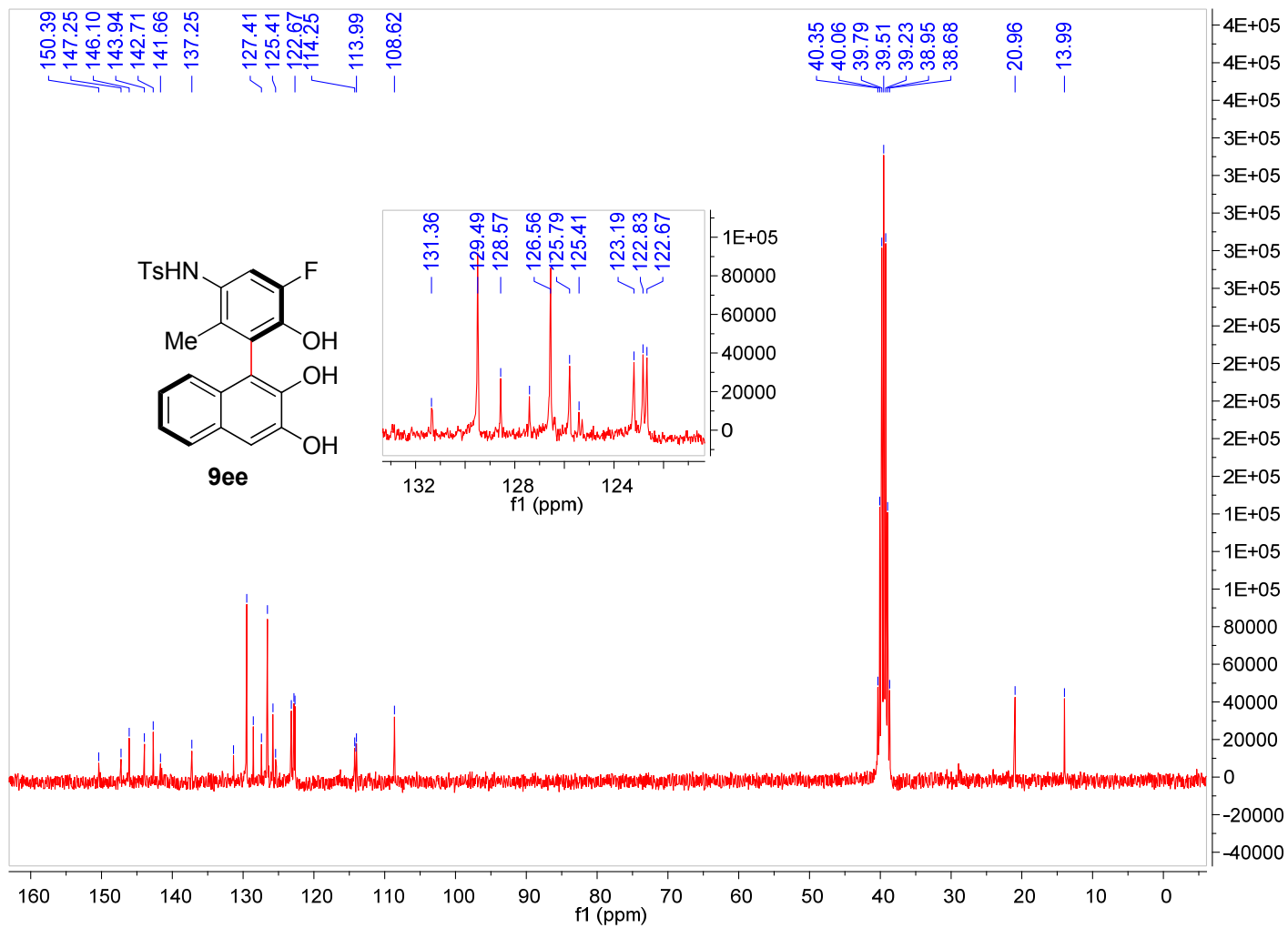


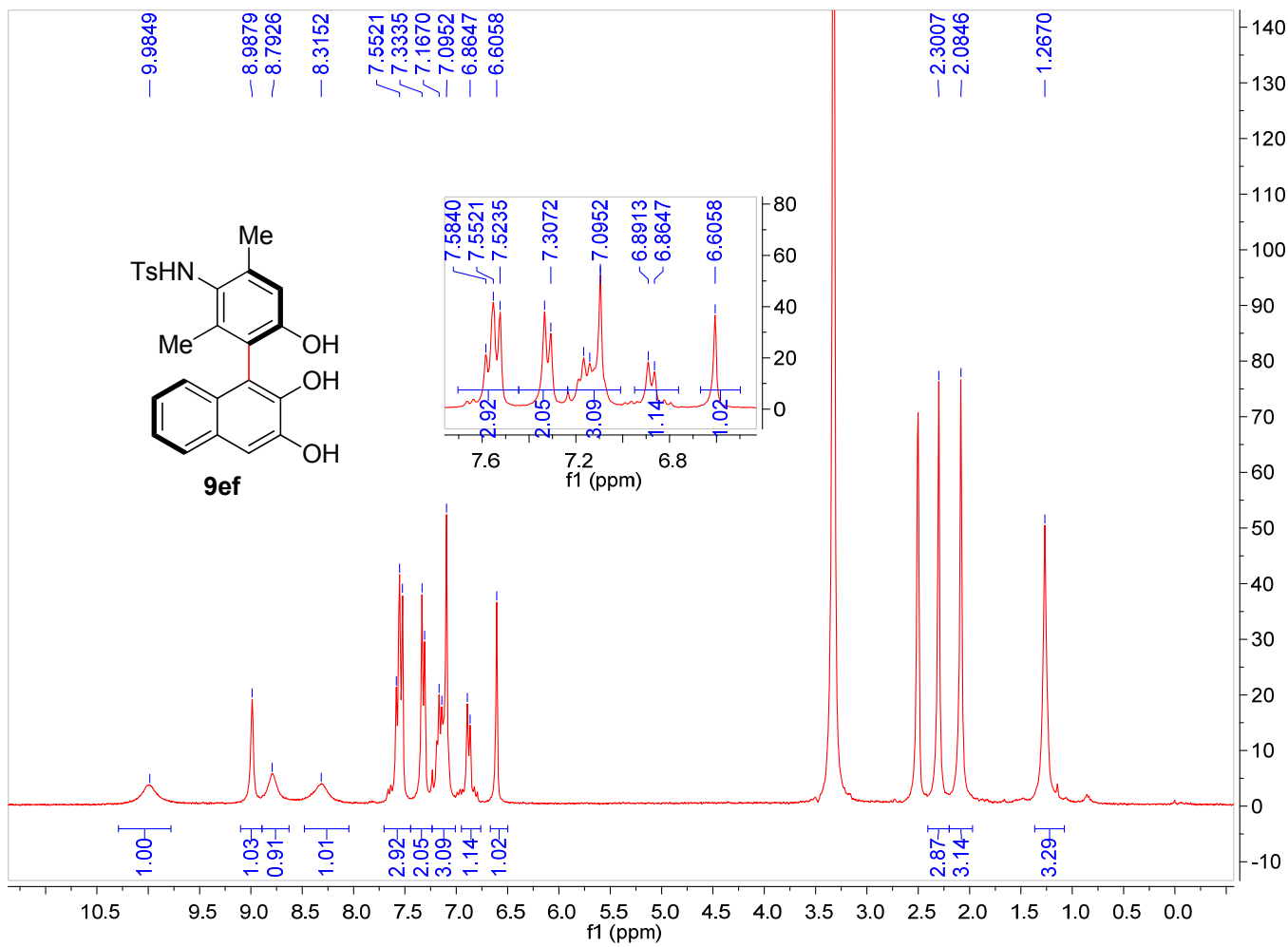


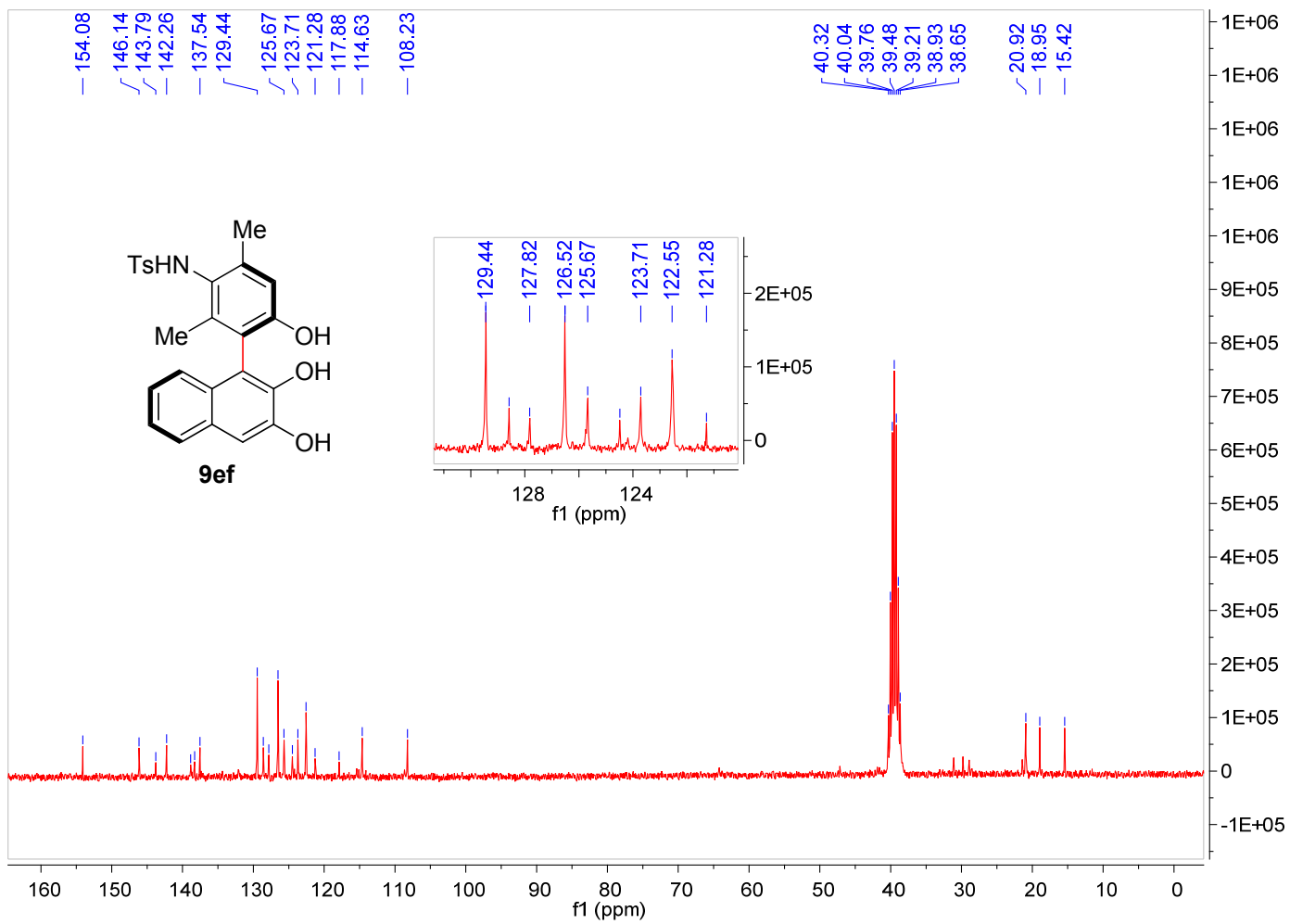


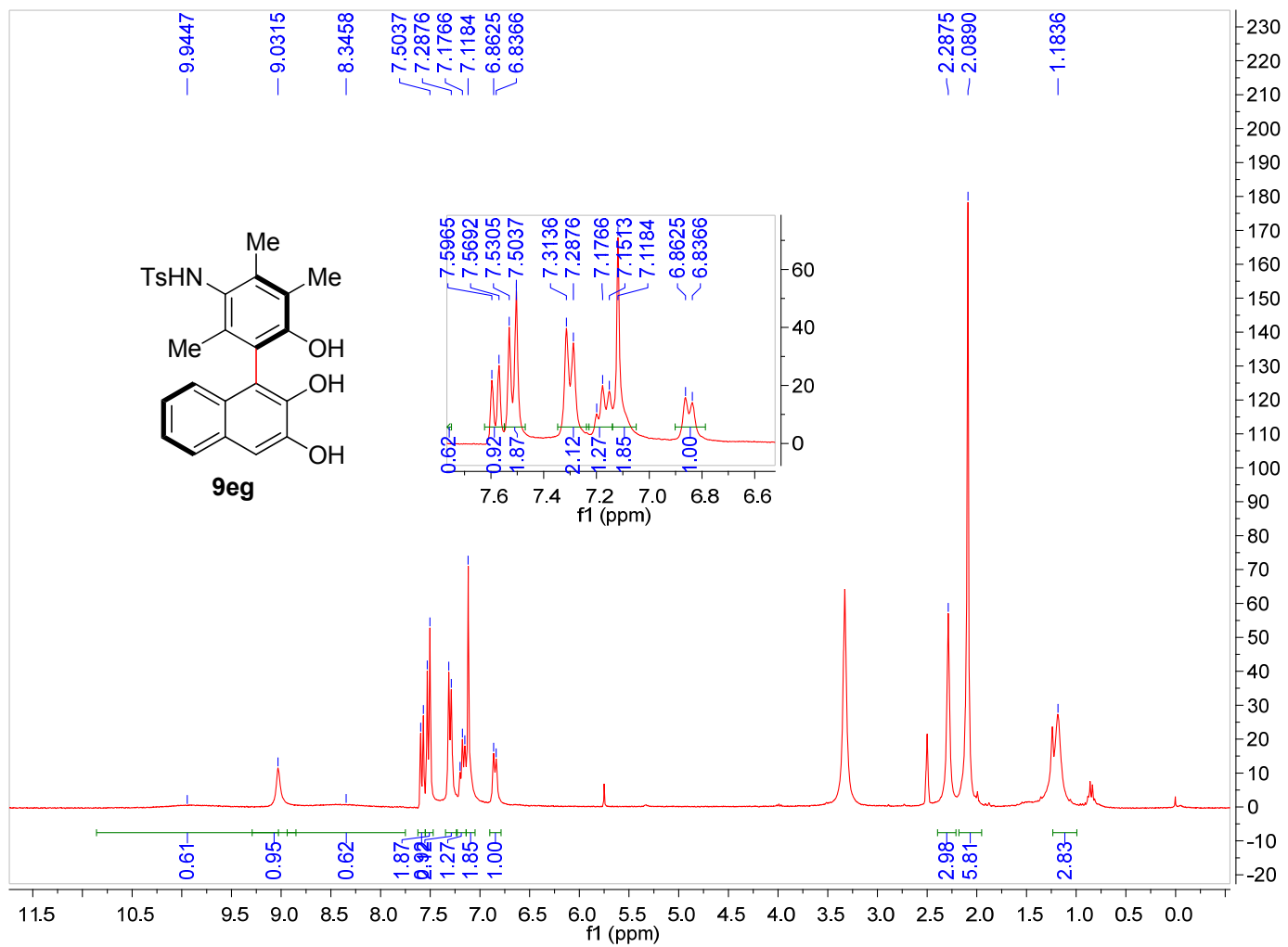


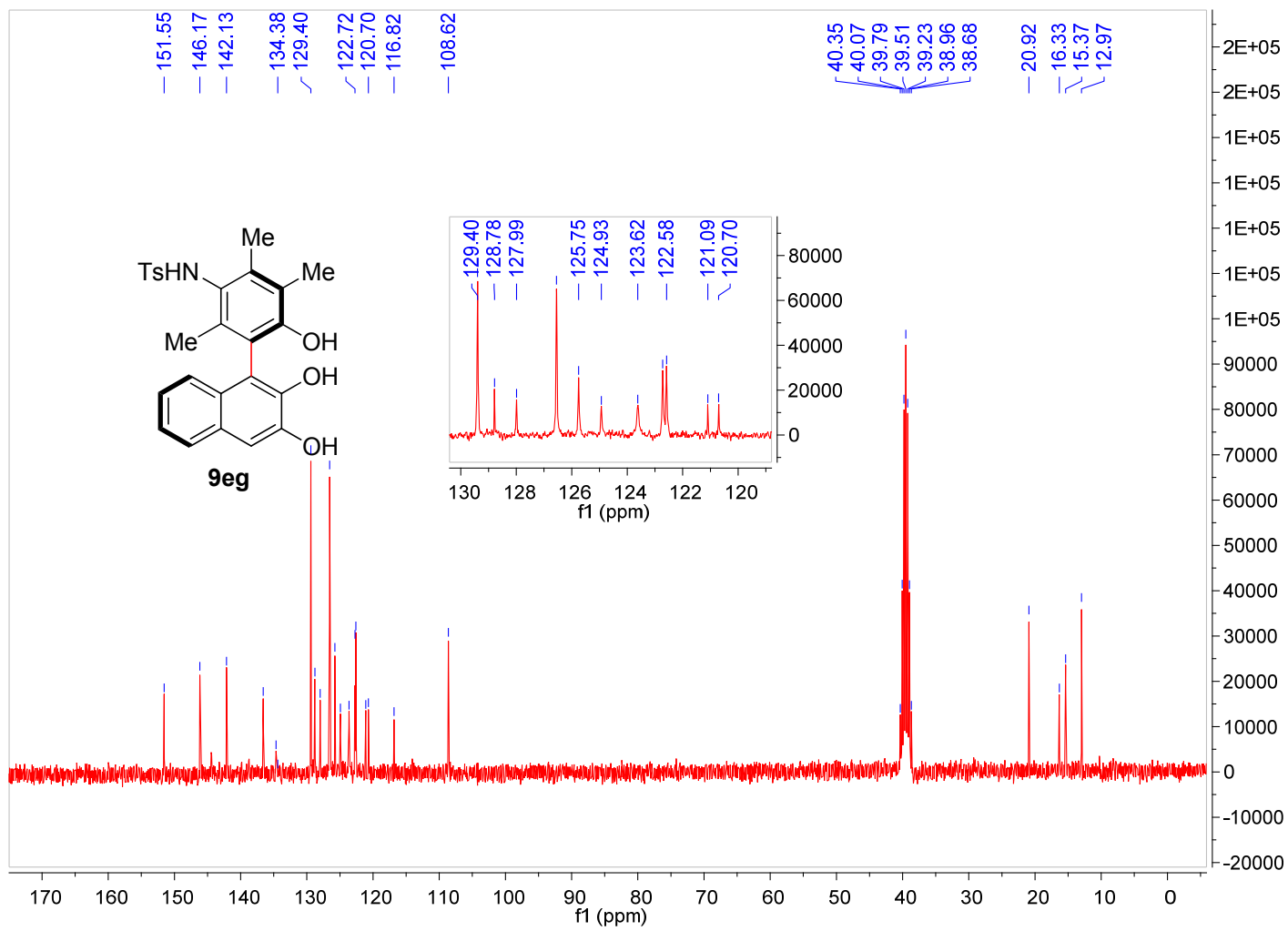


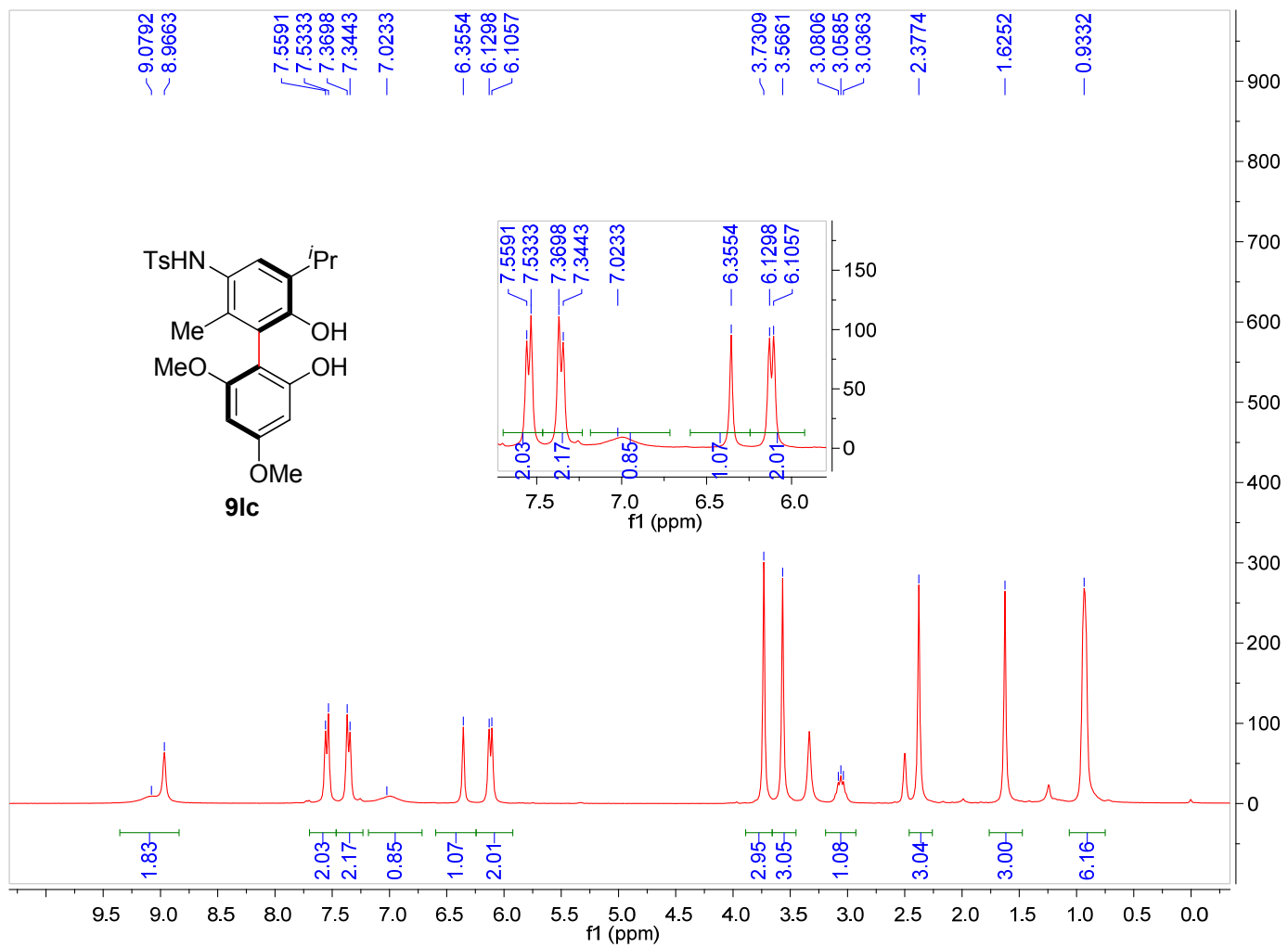


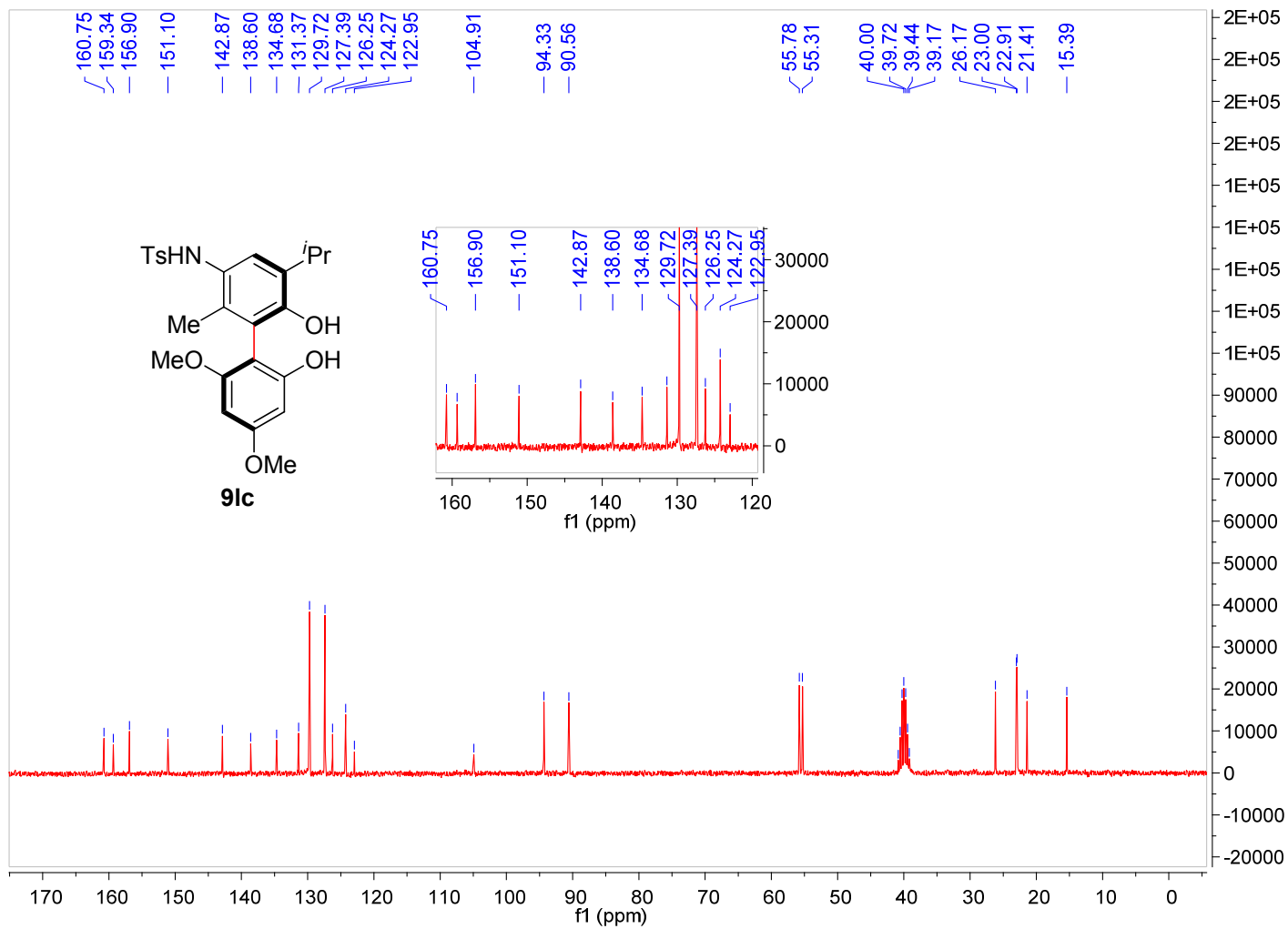


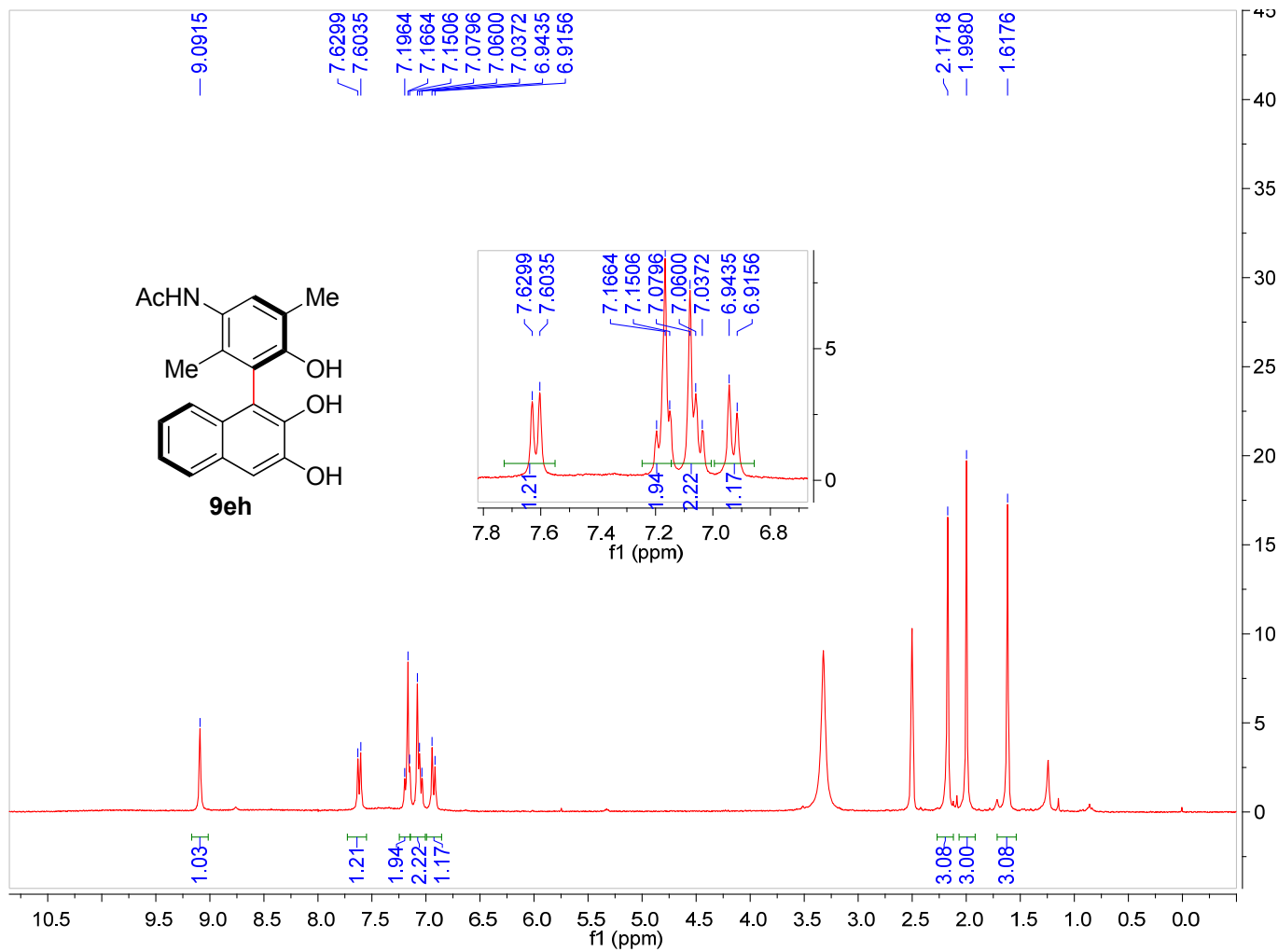


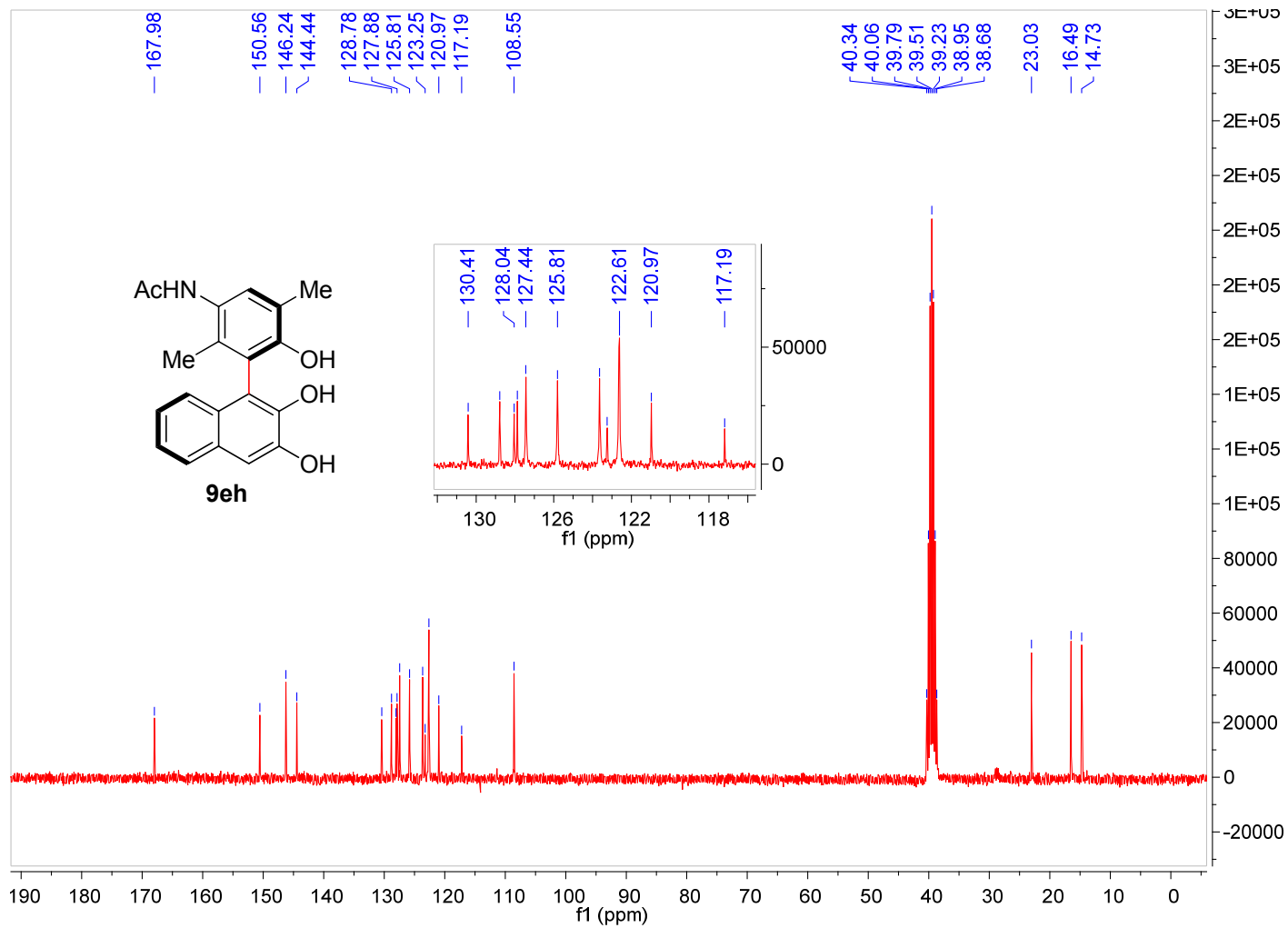


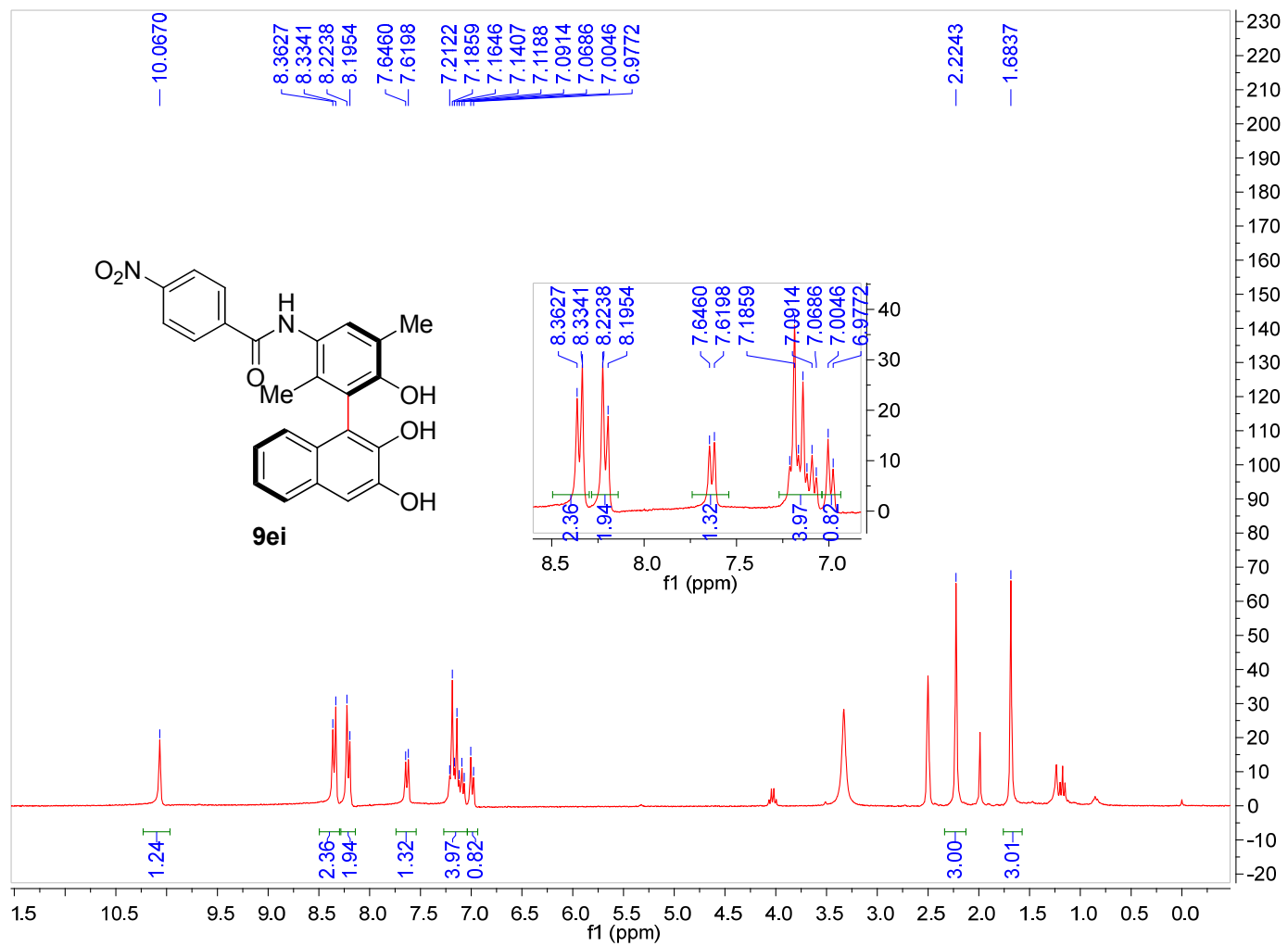


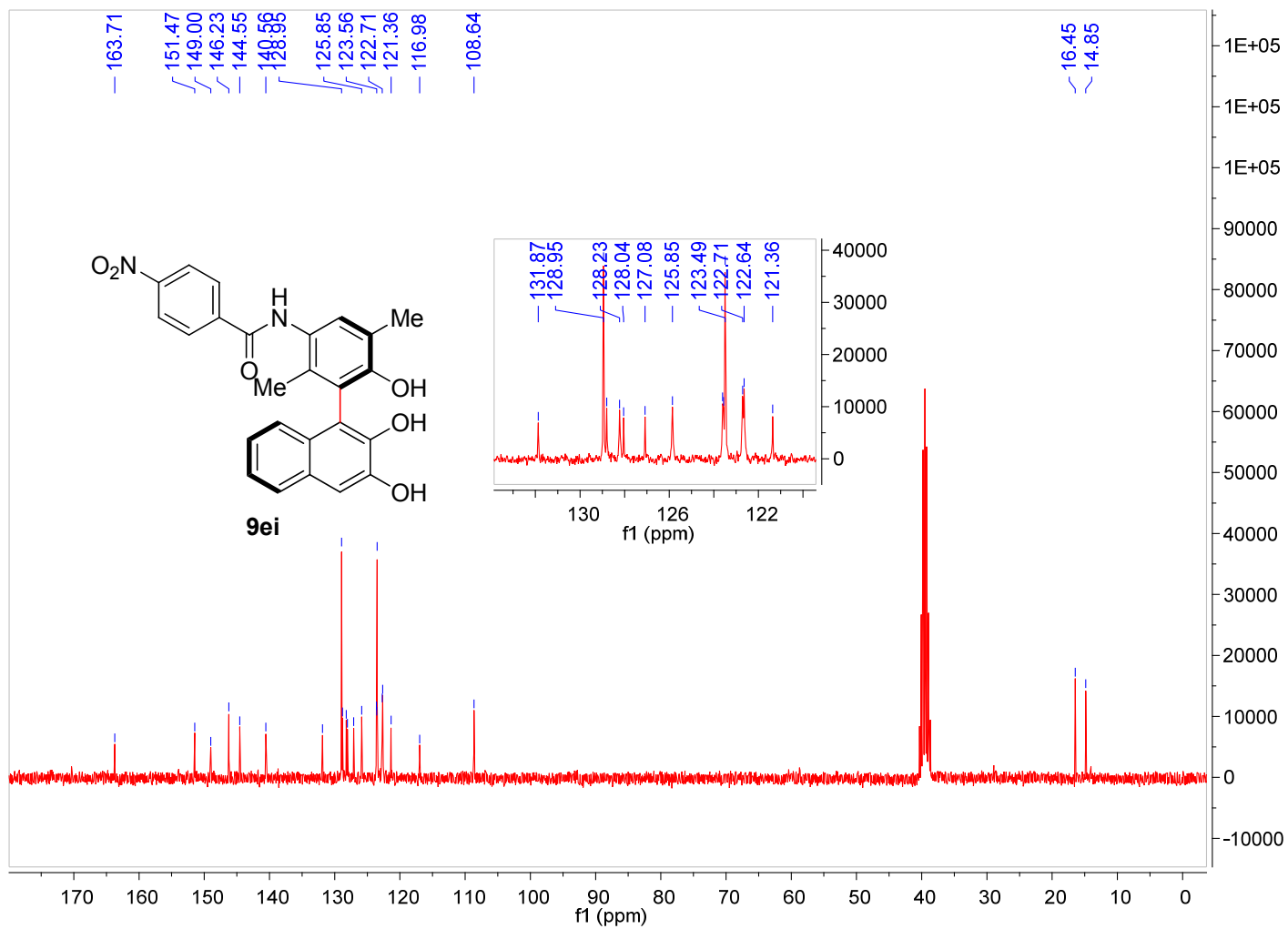


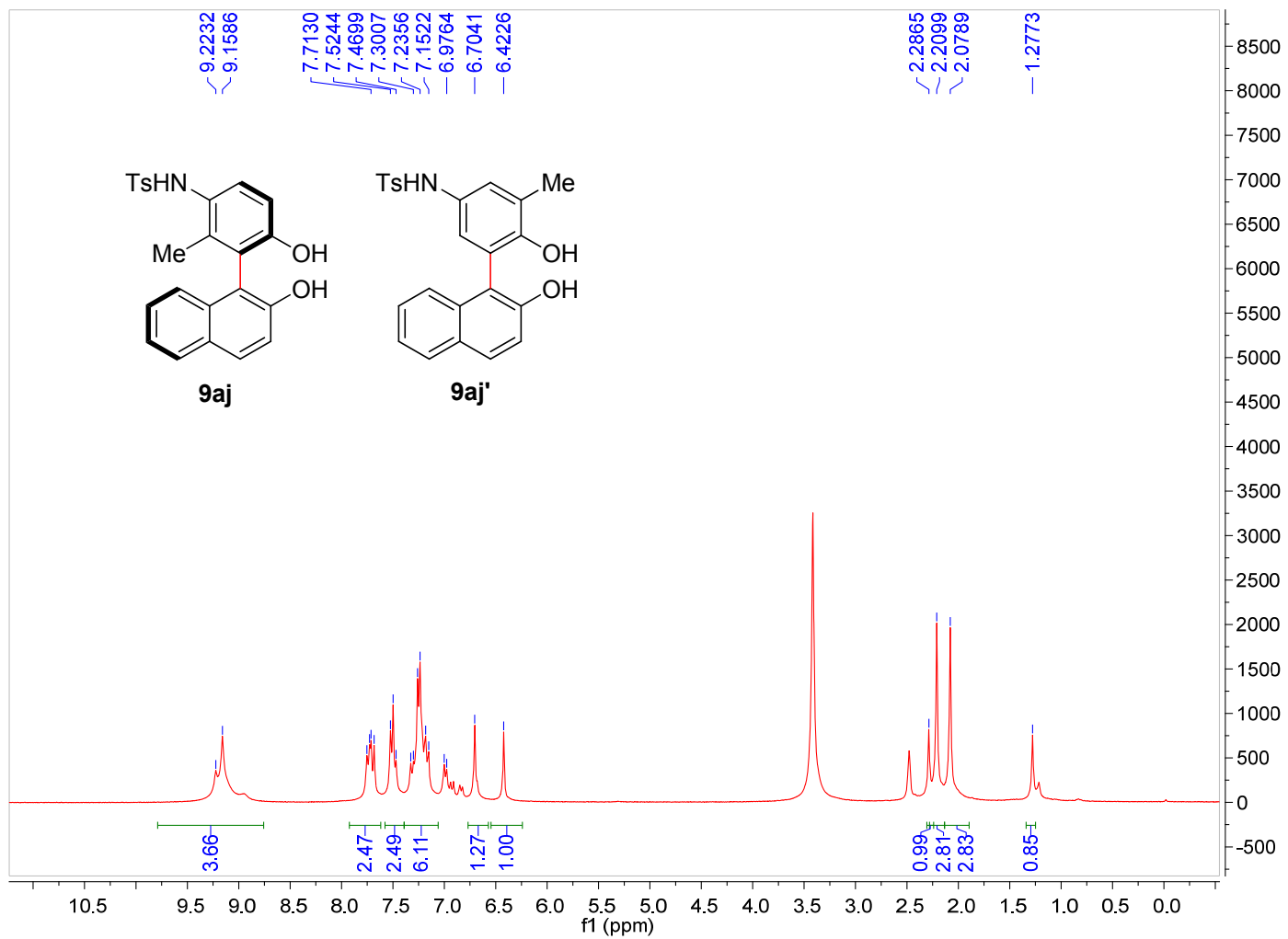


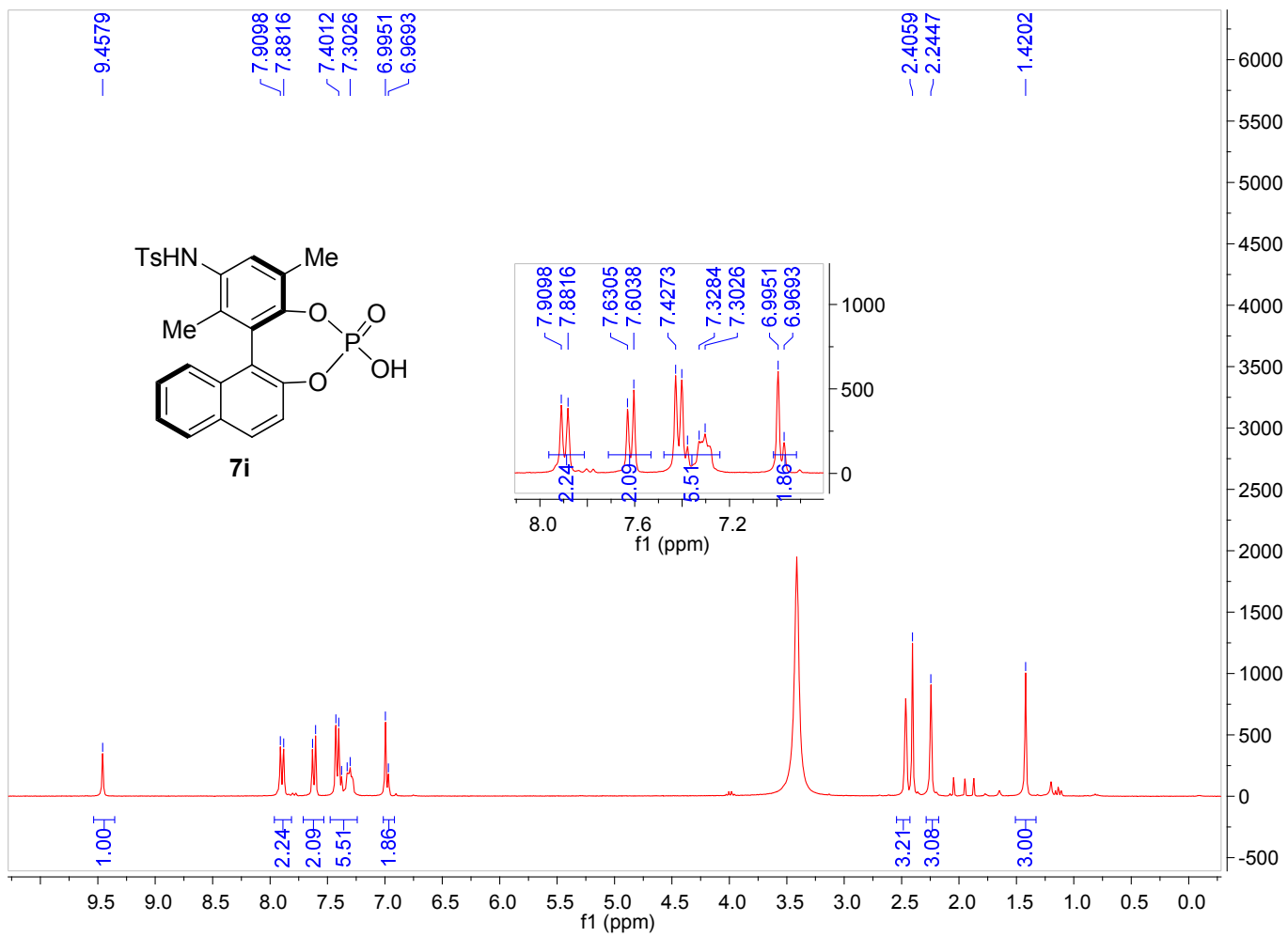


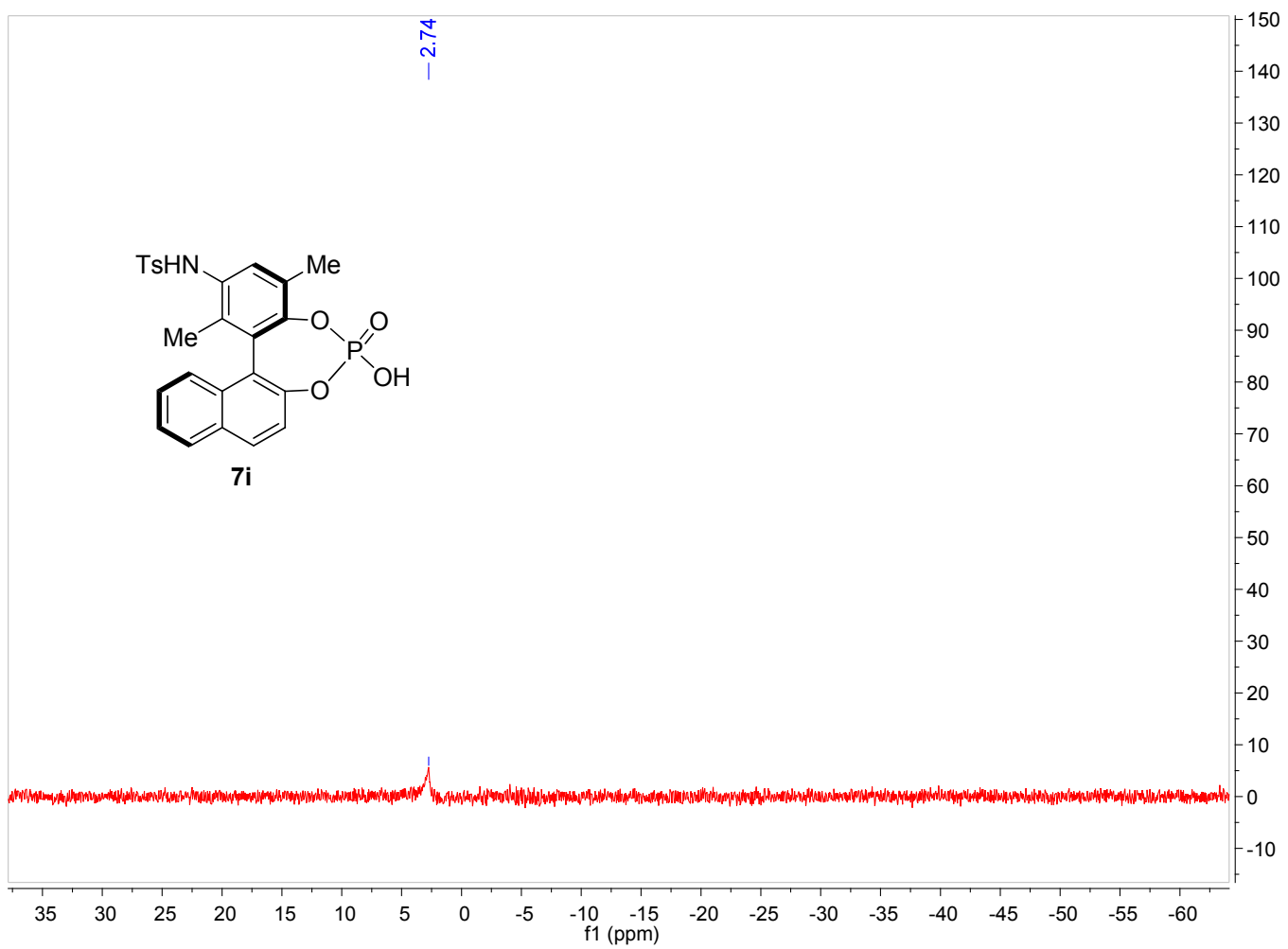




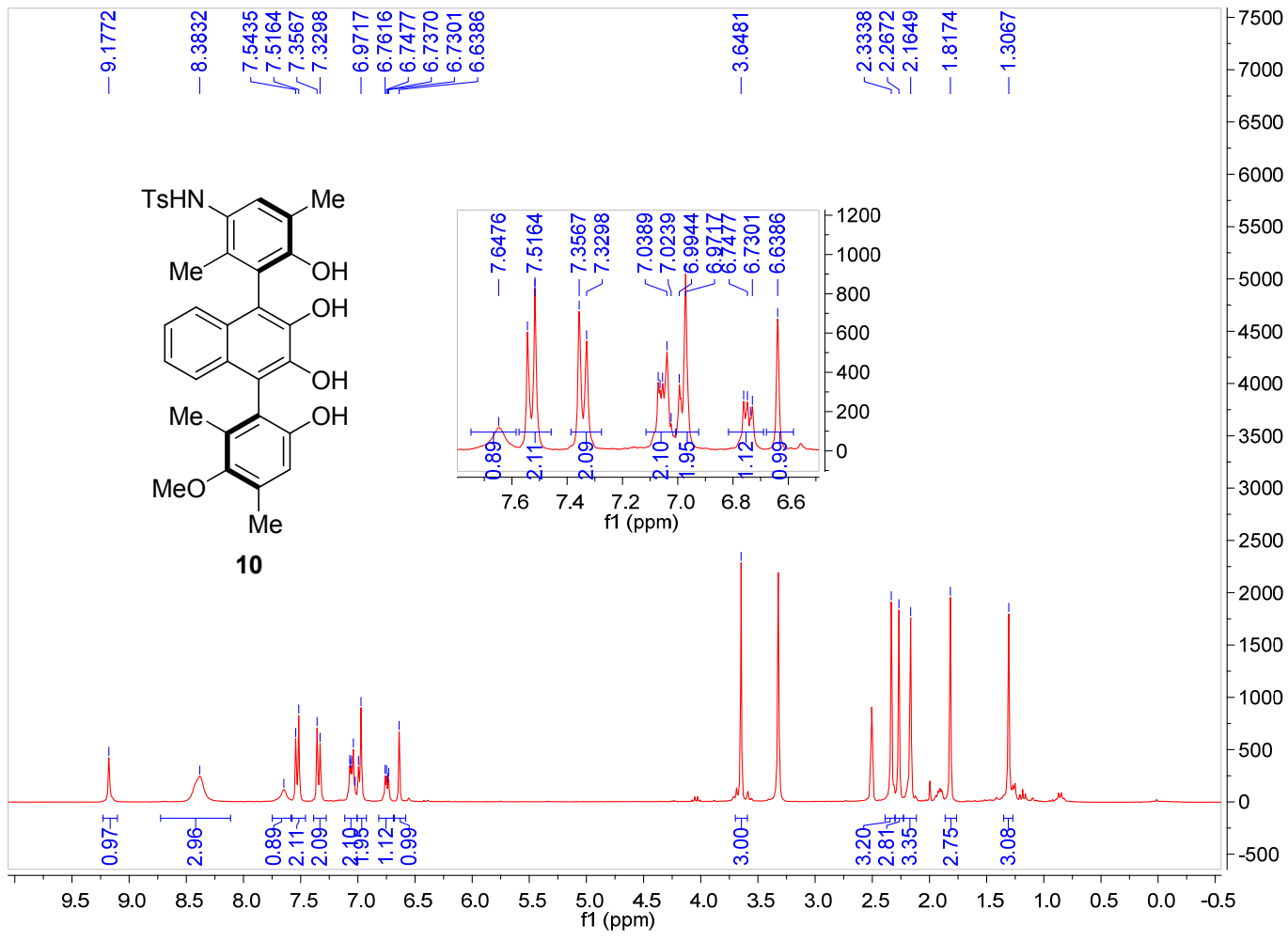


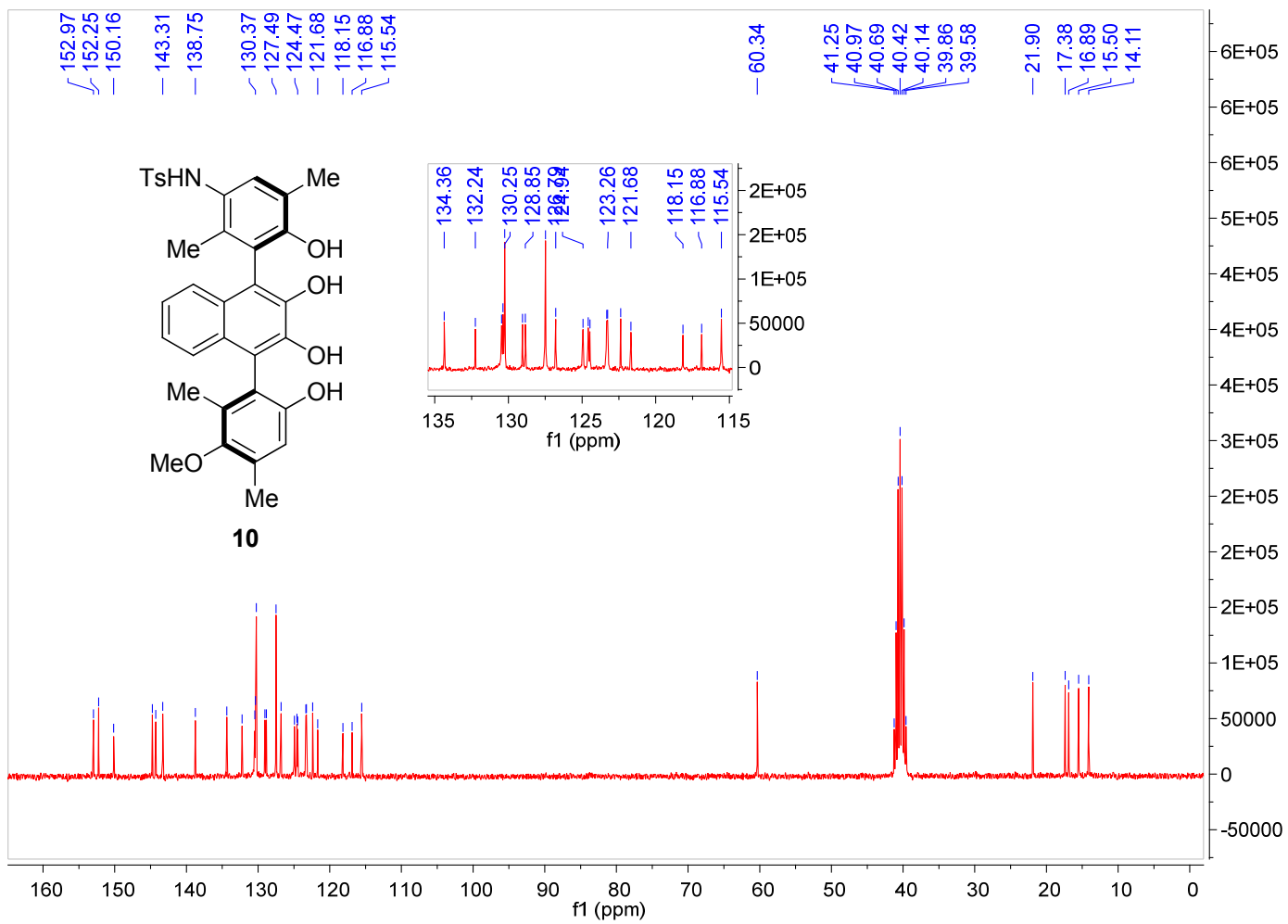


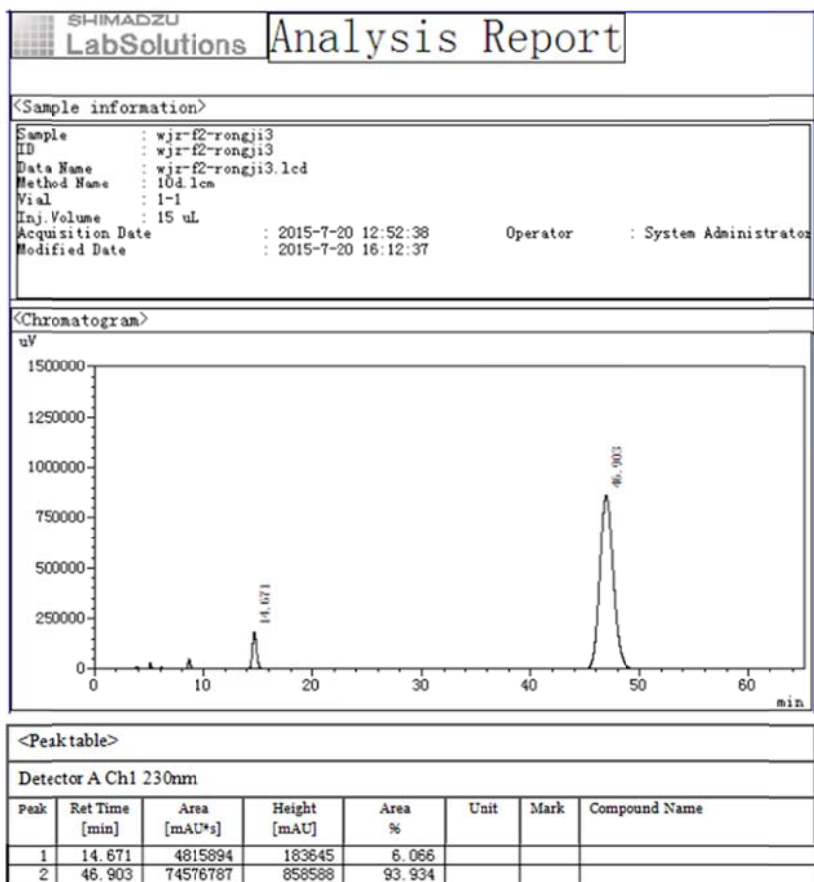
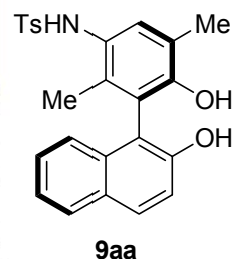
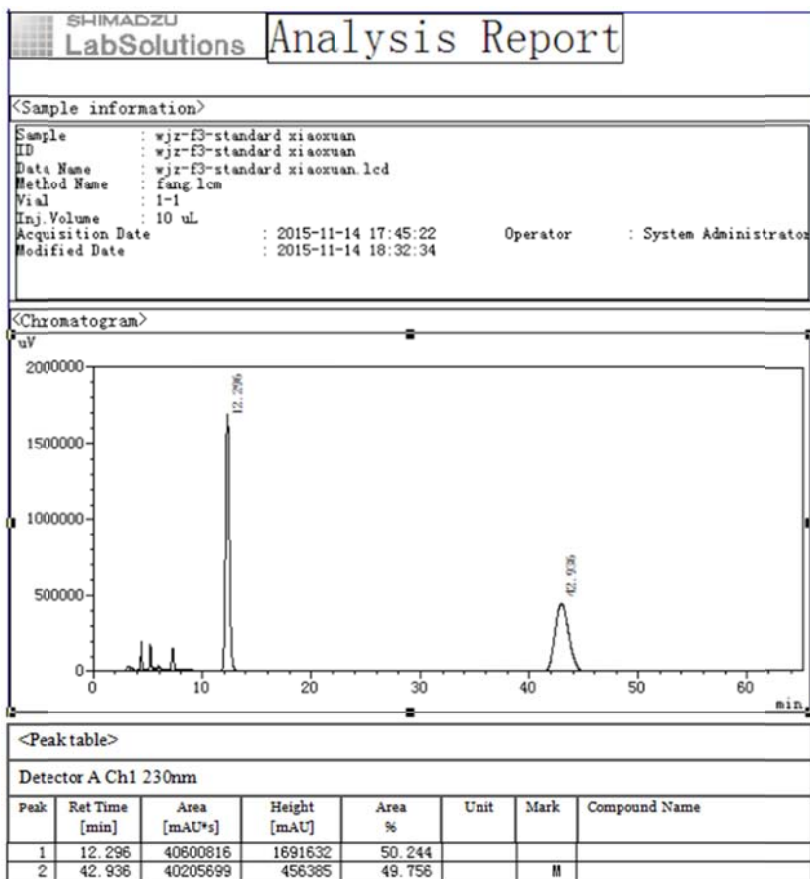


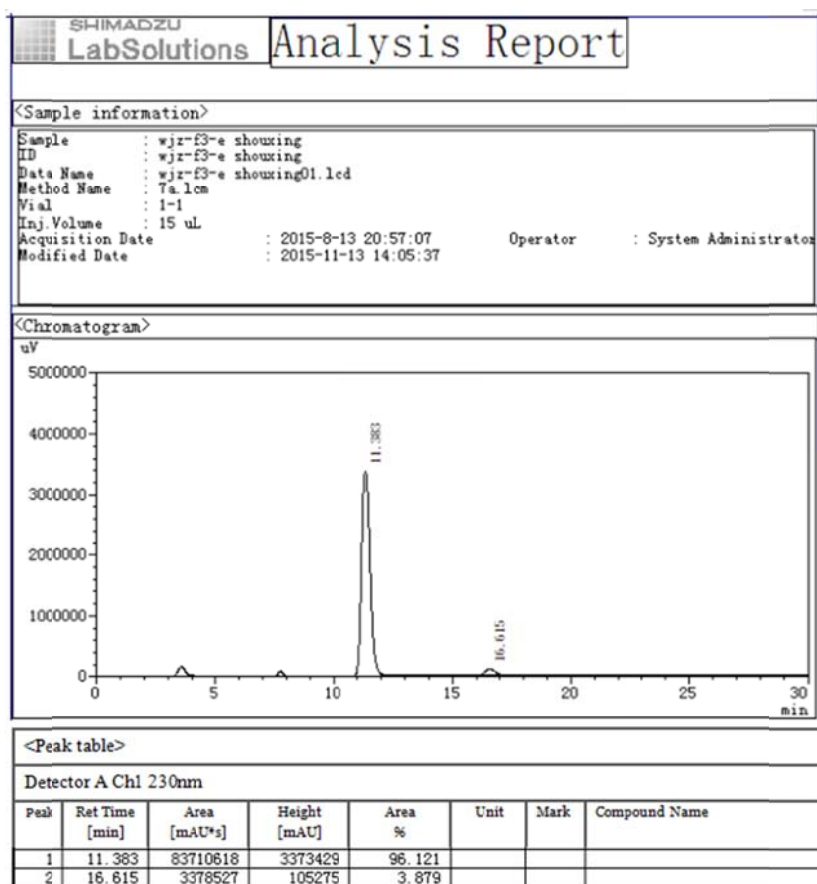
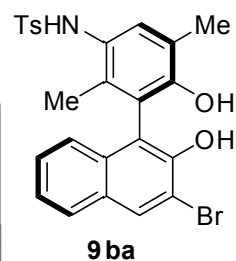
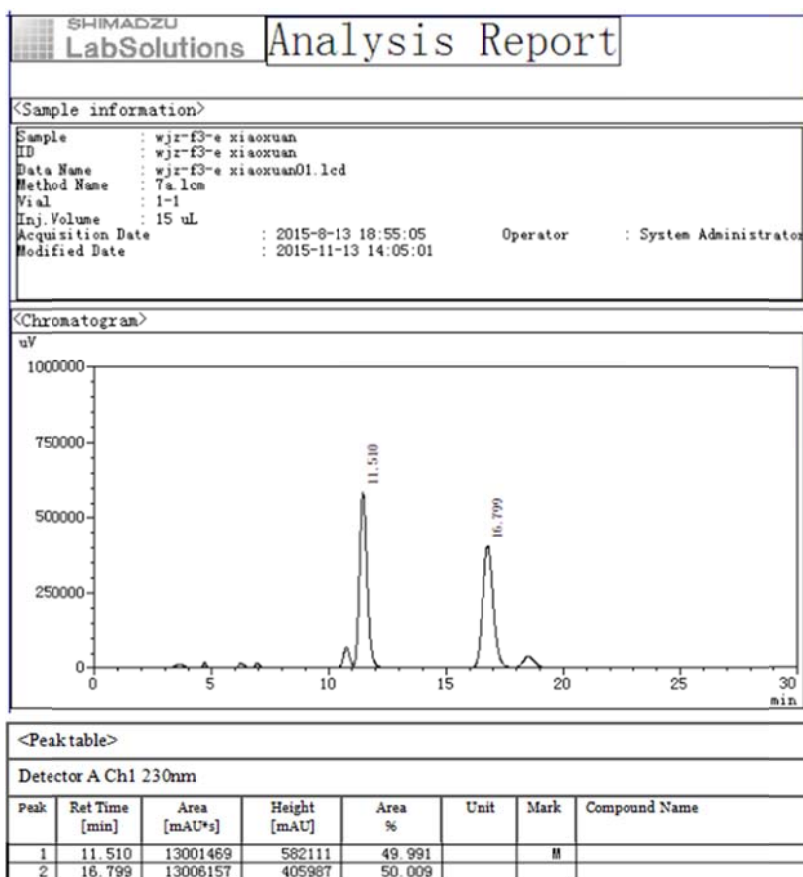


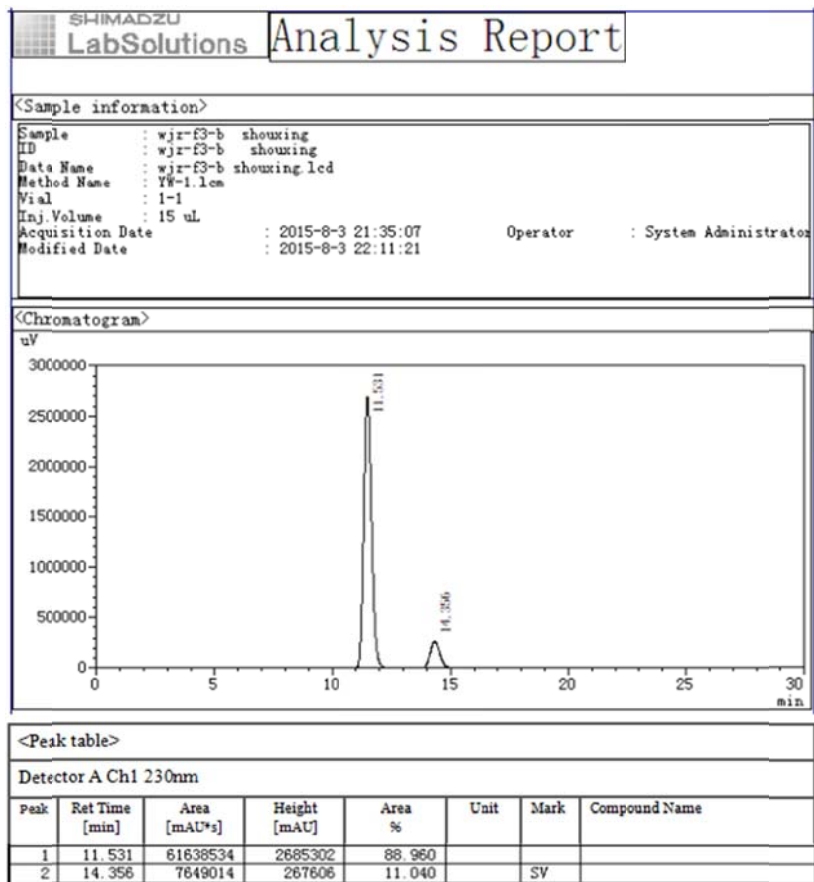
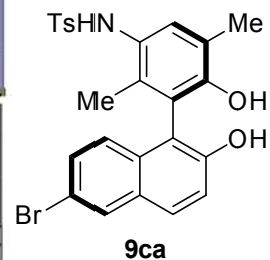
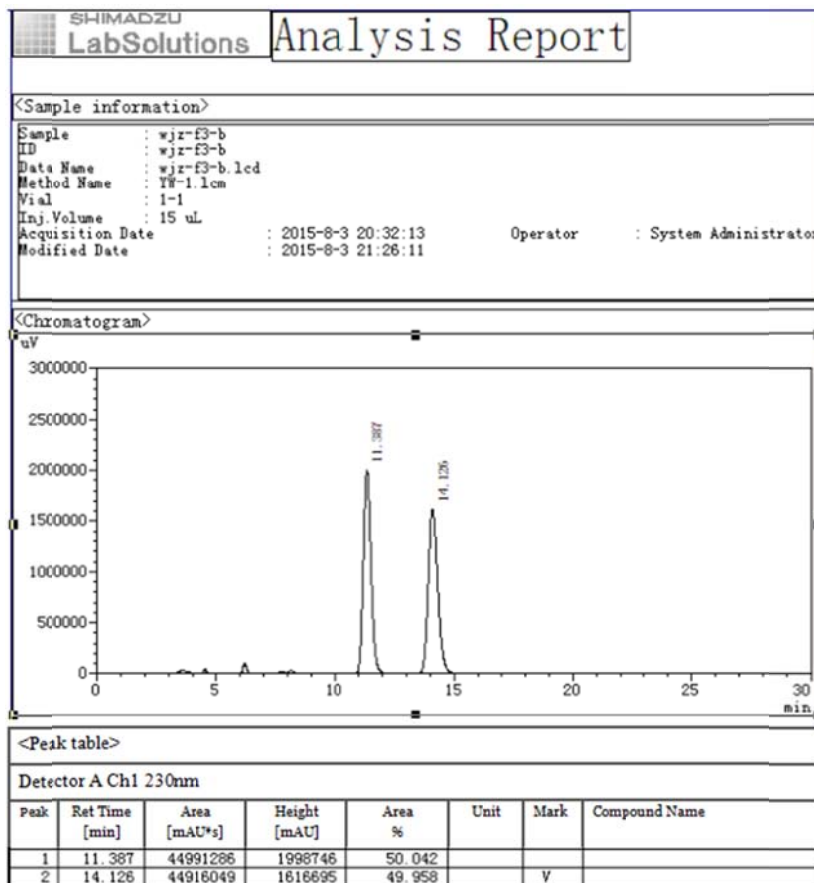
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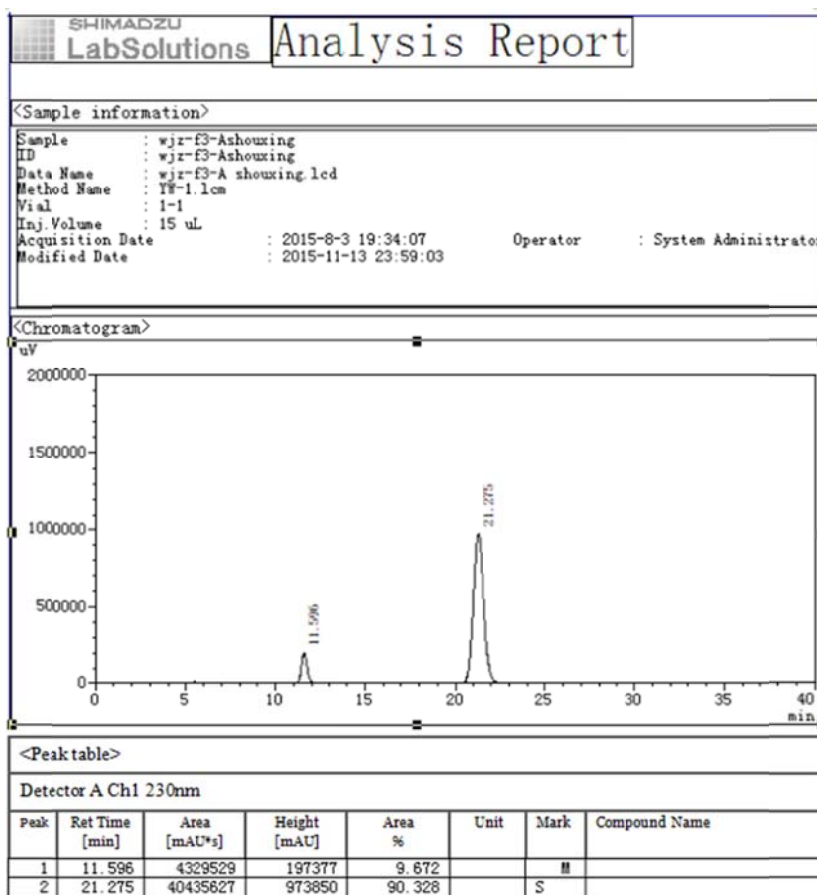
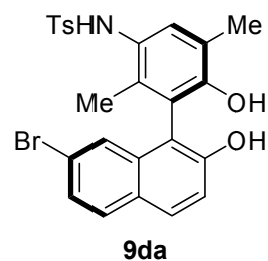
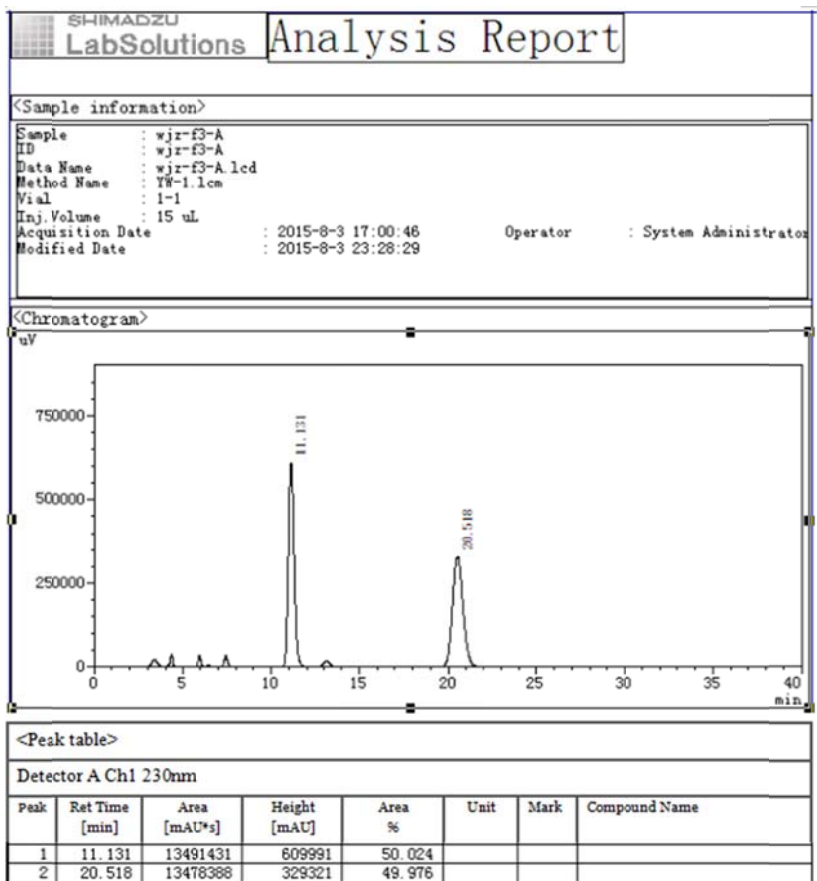


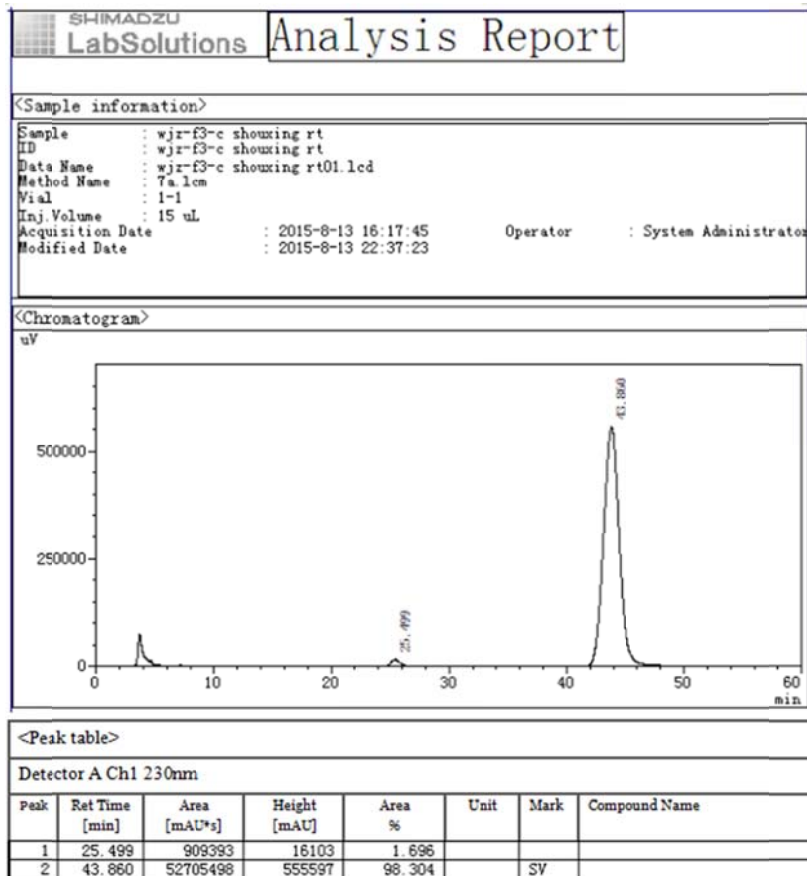
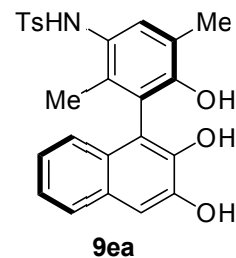
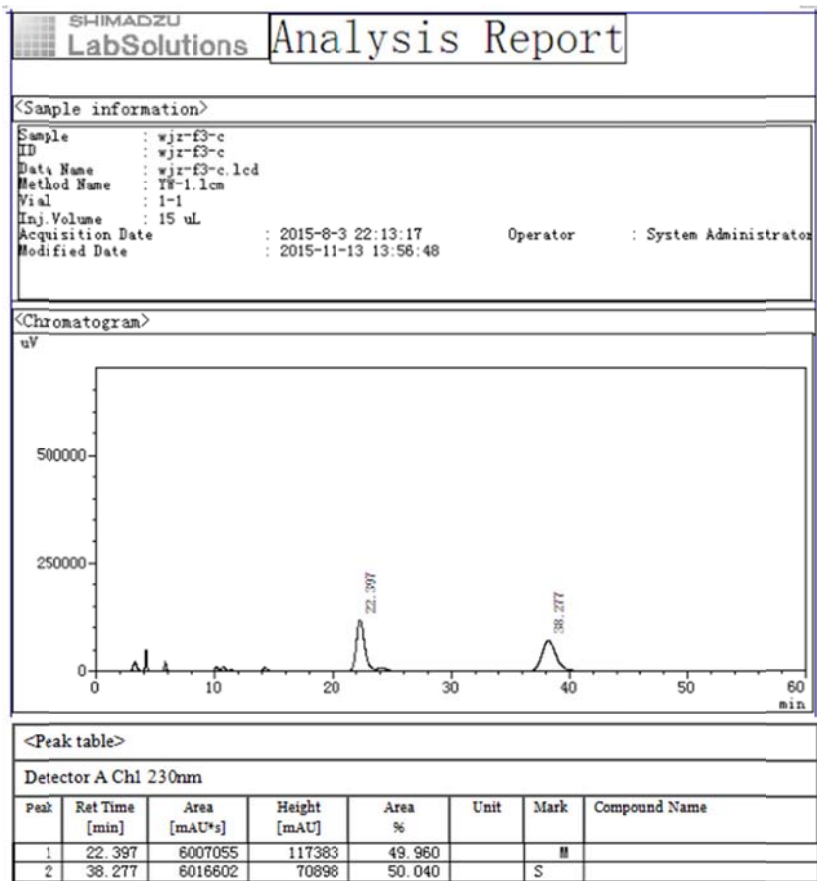


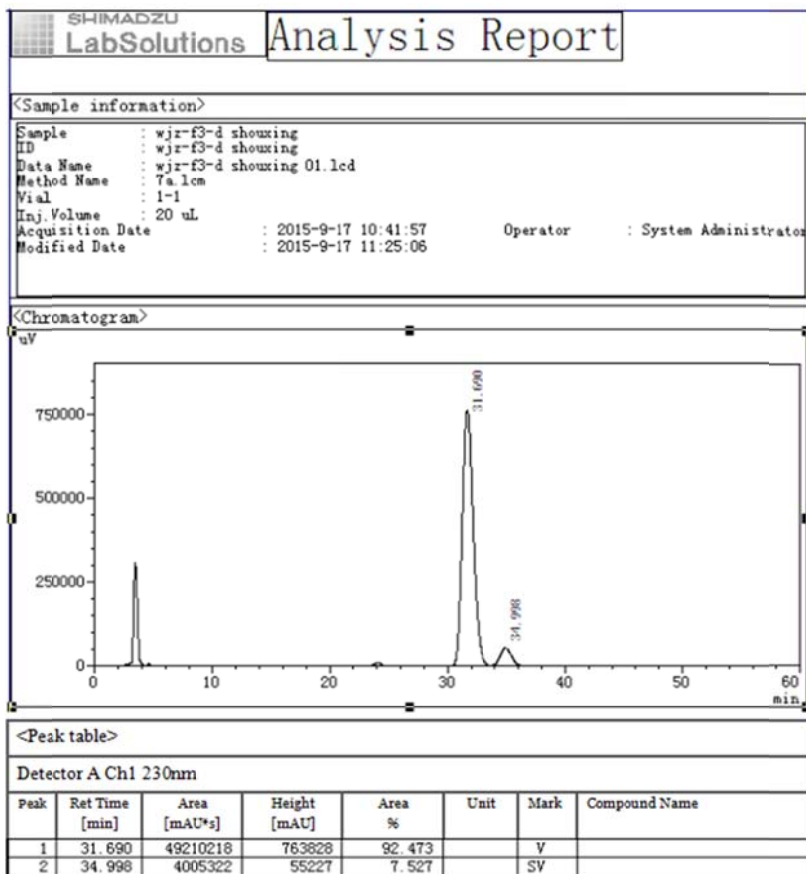
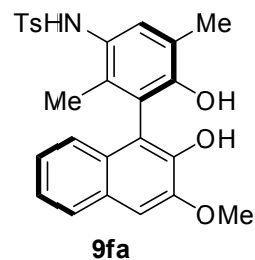
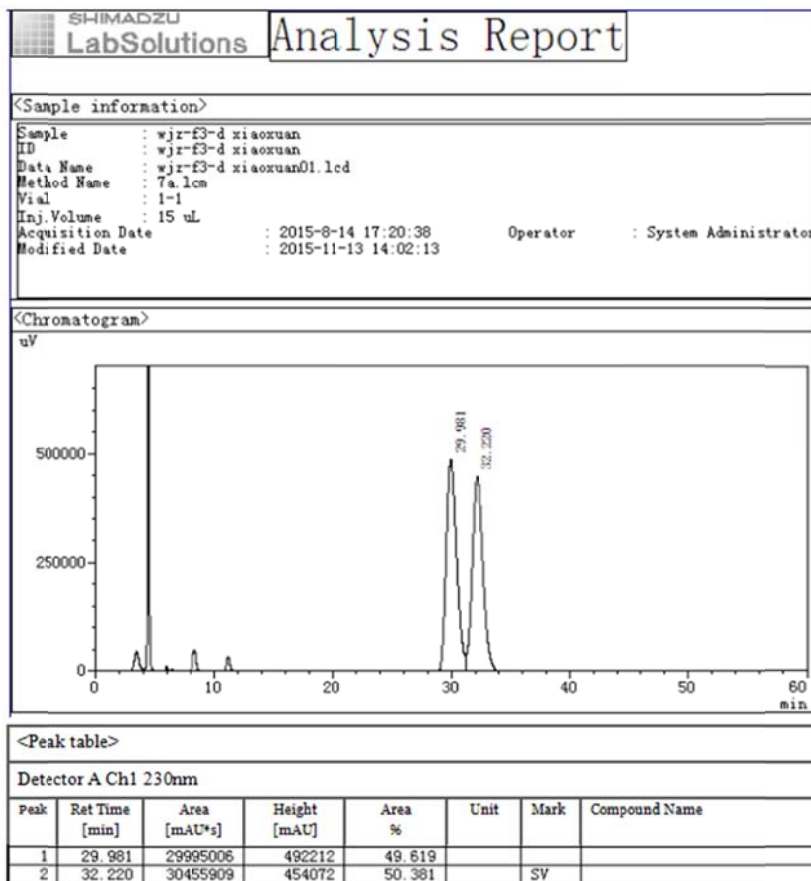


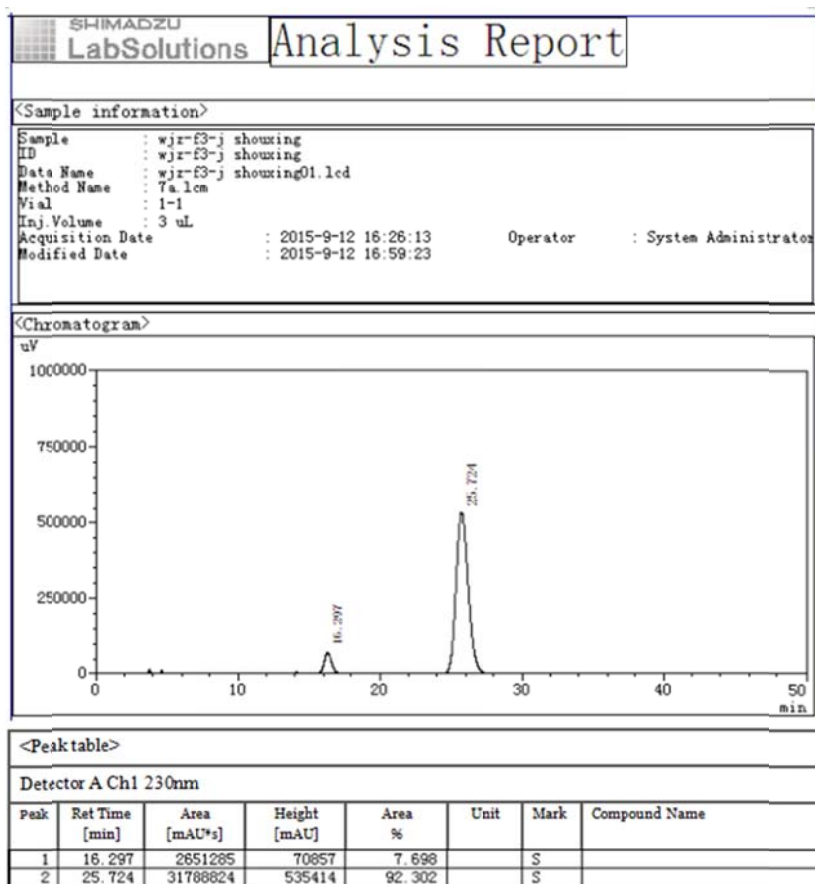
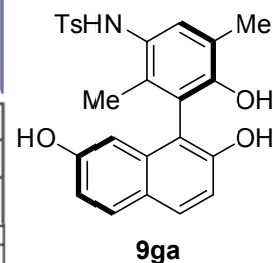
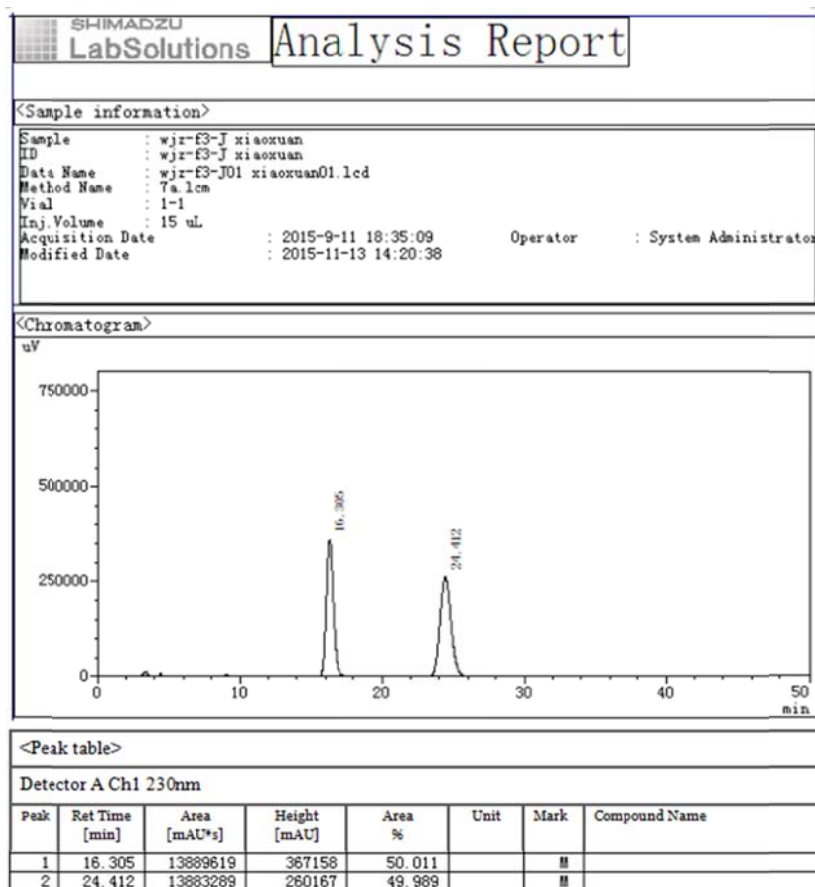










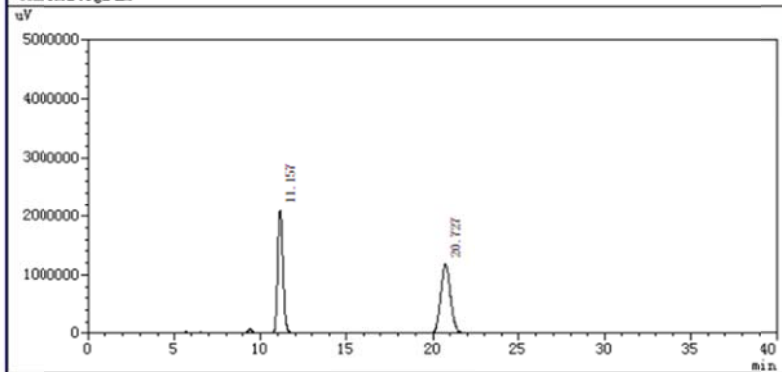


SHIMADZU LabSolutions Analysis Report

<Sample information>

Sample : wjz-f3-fxiaoxuan
 ID : wjz-f3-f xiaoxuan
 Data Name : wjz-f3-fxiaoxuan01.lcd
 Method Name : 7a.1cm
 Vial : 1-1
 Inj. Volume : 12 uL
 Acquisition Date : 2015-9-5 17:15:13 Operator : System Administrator
 Modified Date : 2015-11-13 14:07:18

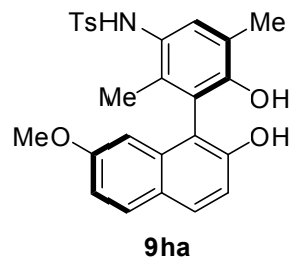
<Chromatogram>



<Peak table>

Detector A Ch1 230nm

Peak	Ret Time [min]	Area [mAU*s]	Height [mAU]	Area %	Unit	Mark	Compound Name
1	11.157	45785530	2118290	49.909		#	
2	20.727	45952860	1172845	50.091		#	

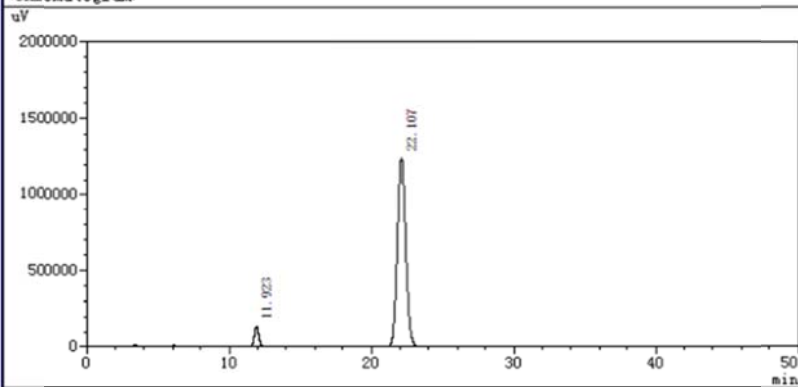


SHIMADZU LabSolutions Analysis Report

<Sample information>

Sample : wjz-f3-f shouxing
 ID : wjz-f3-f shouxing
 Data Name : wjz-f3-f shouxing01.lcd
 Method Name : 7a.1cm
 Vial : 1-1
 Inj. Volume : 12 uL
 Acquisition Date : 2015-9-5 19:13:54 Operator : System Administrator
 Modified Date : 2015-10-11 17:17:17

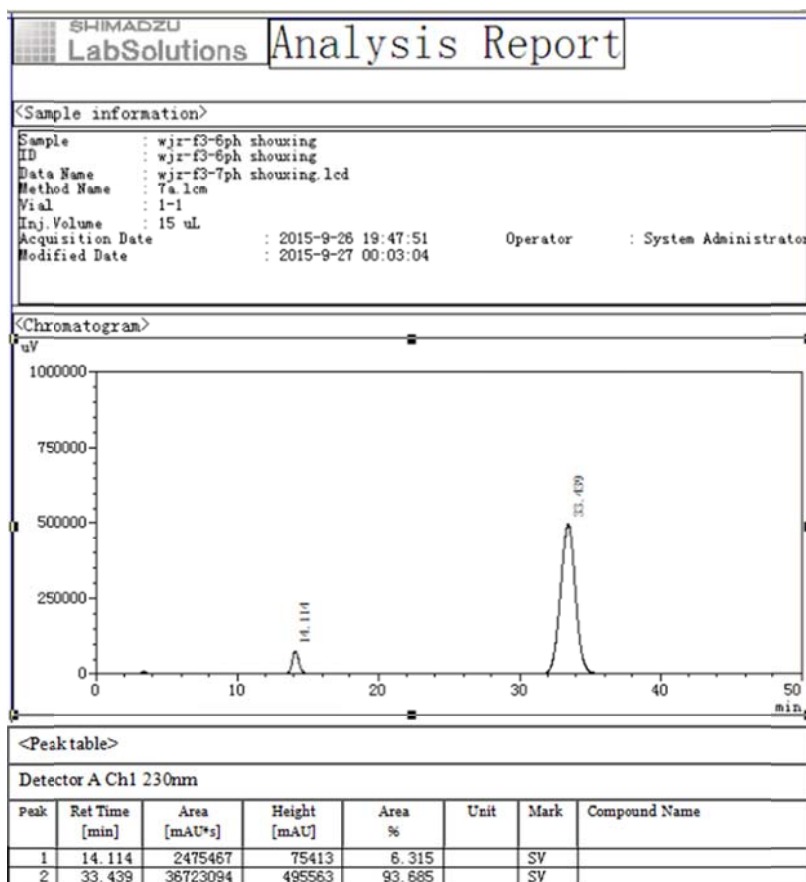
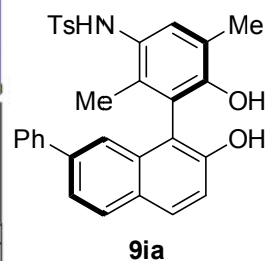
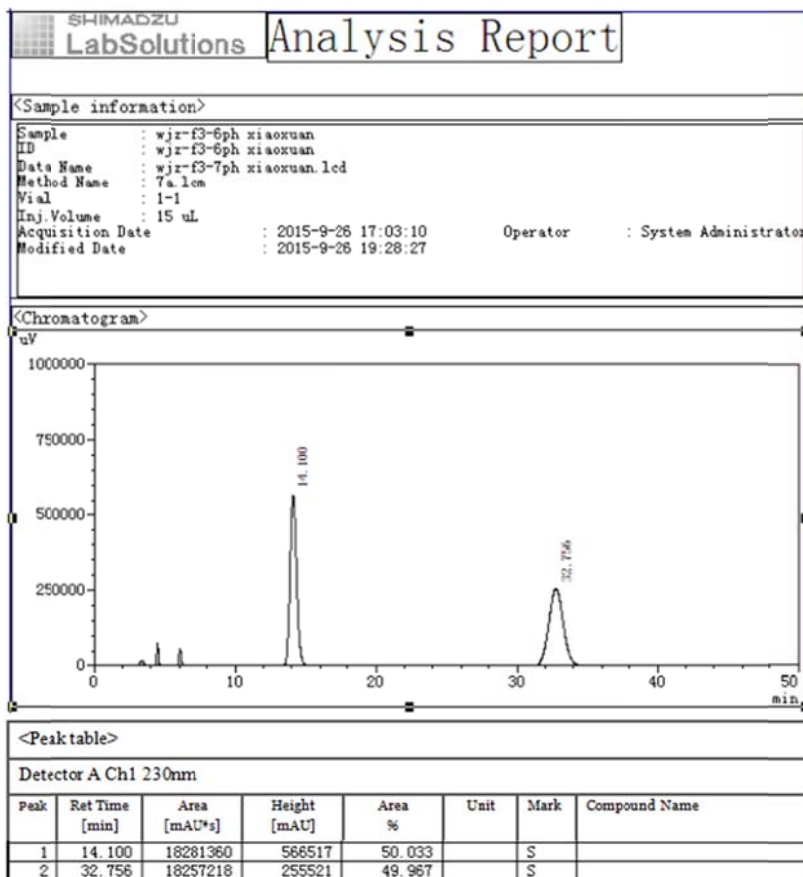
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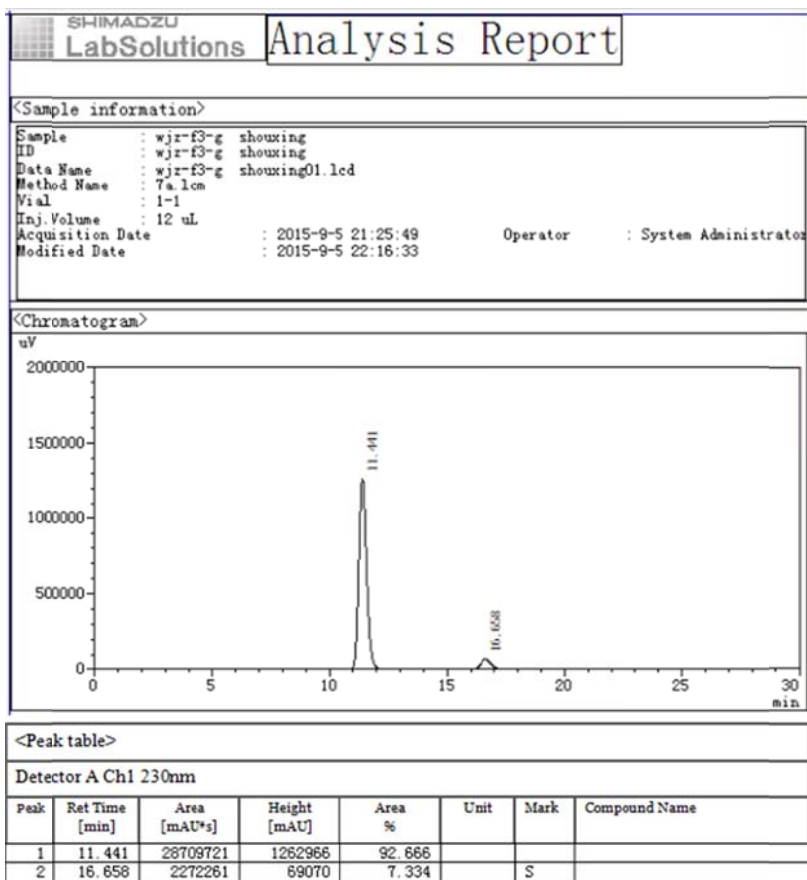
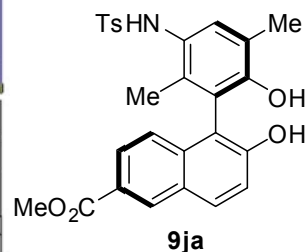
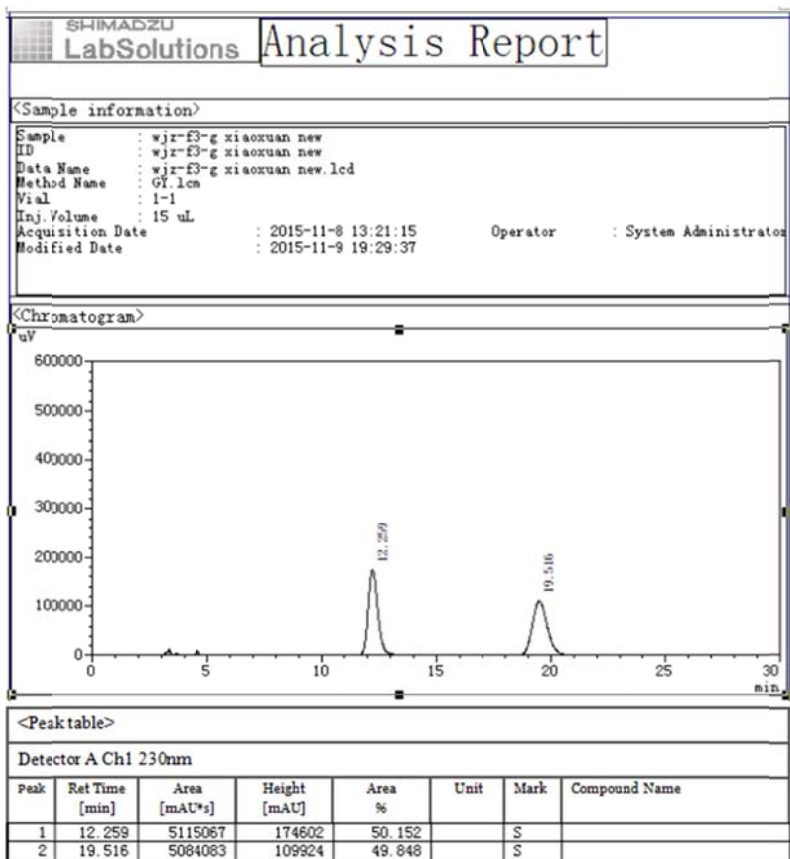


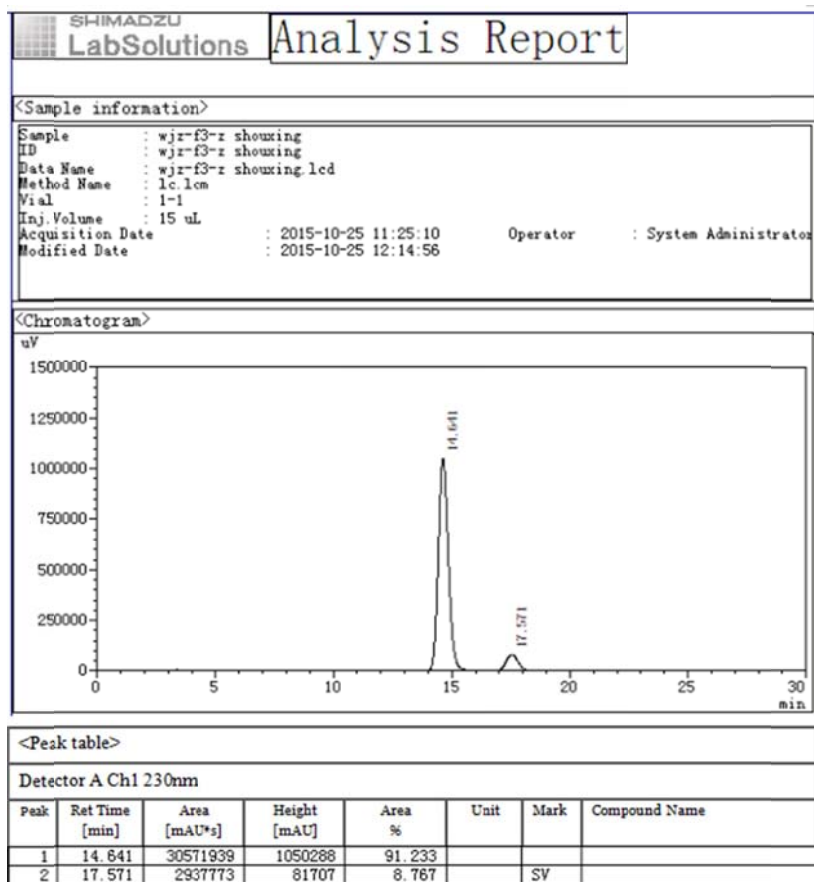
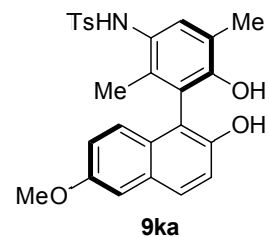
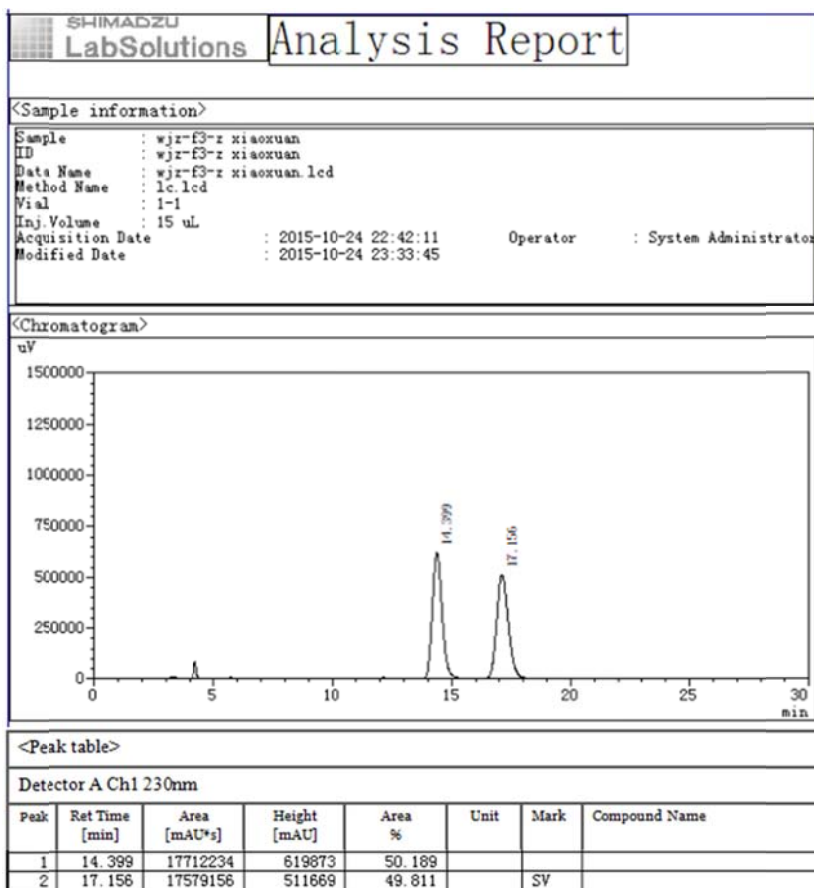
<Peak table>

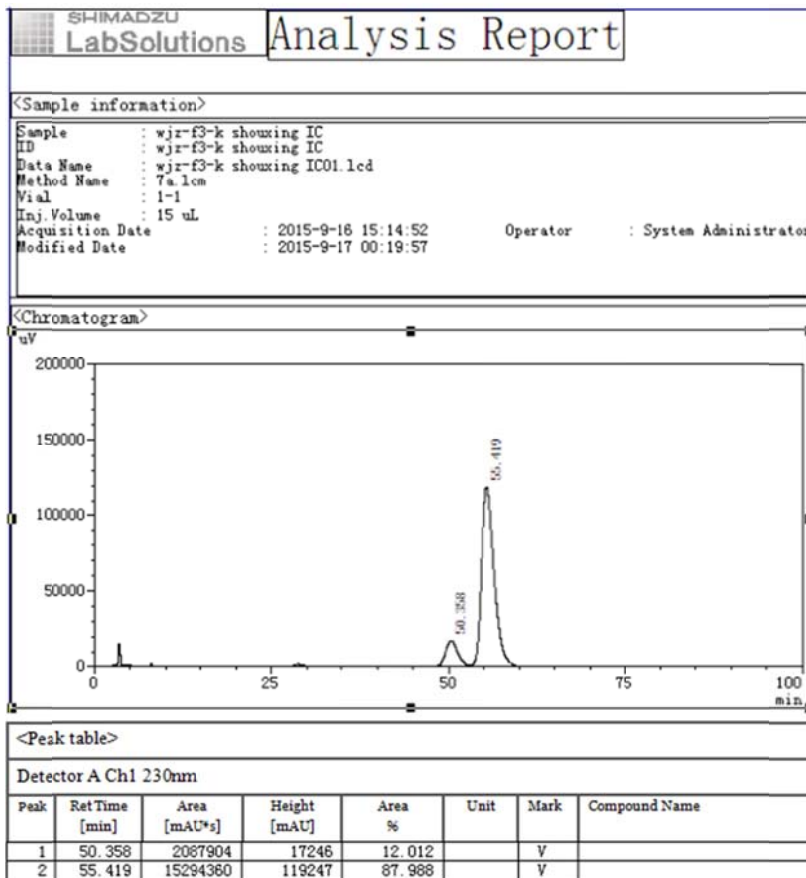
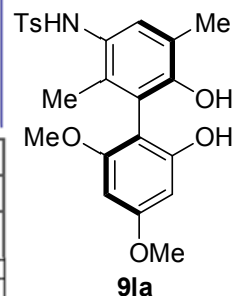
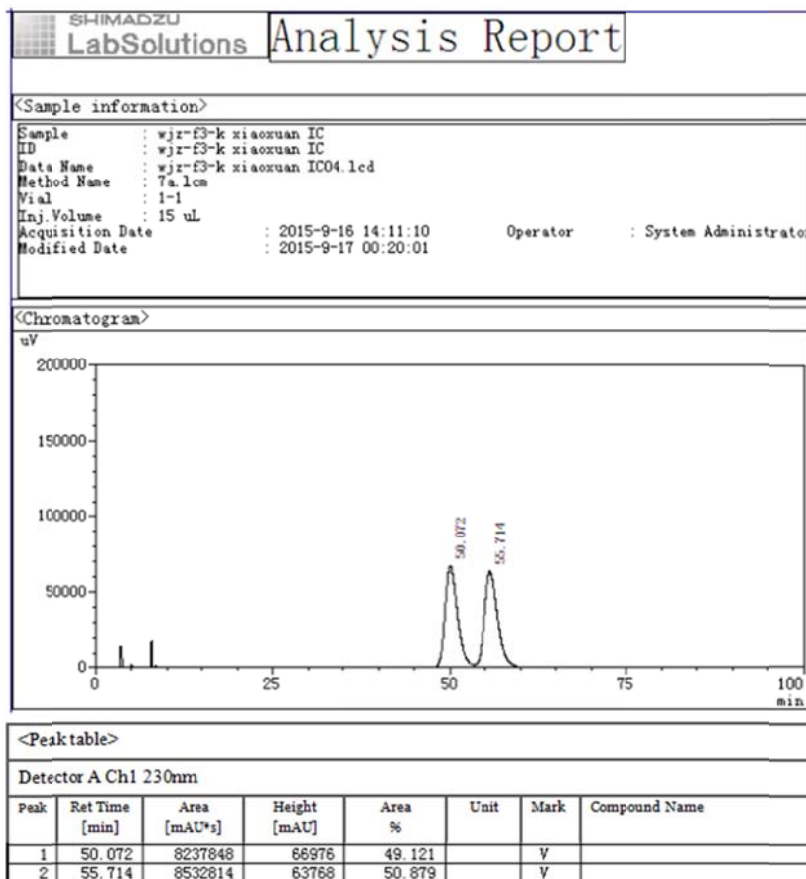
Detector A Ch1 230nm

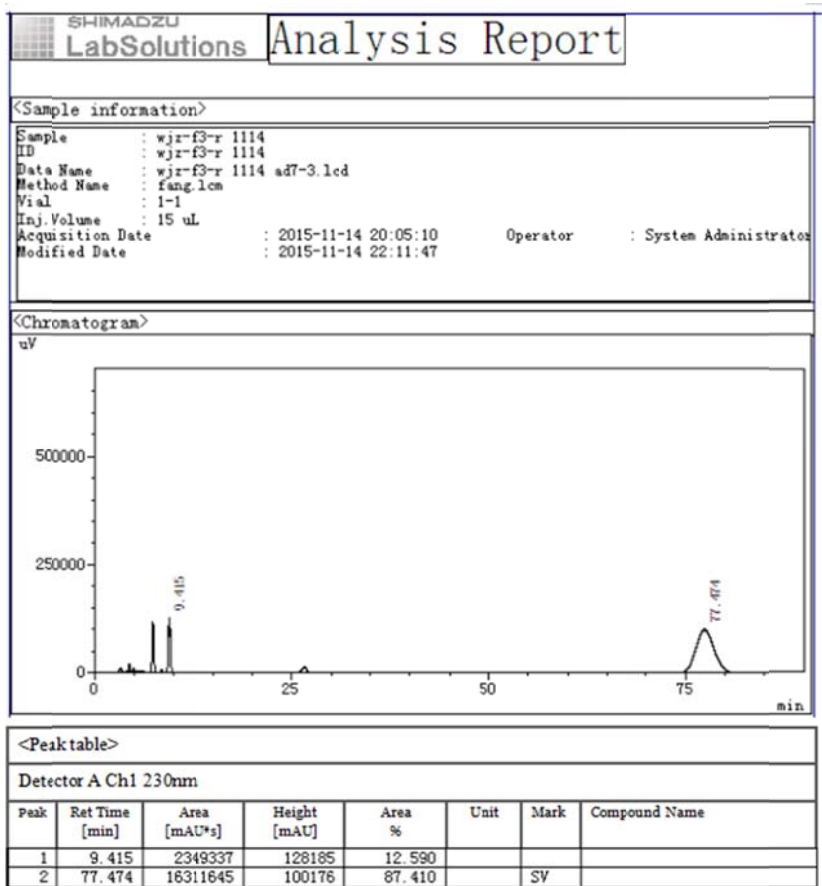
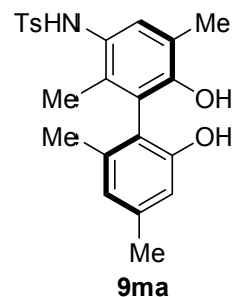
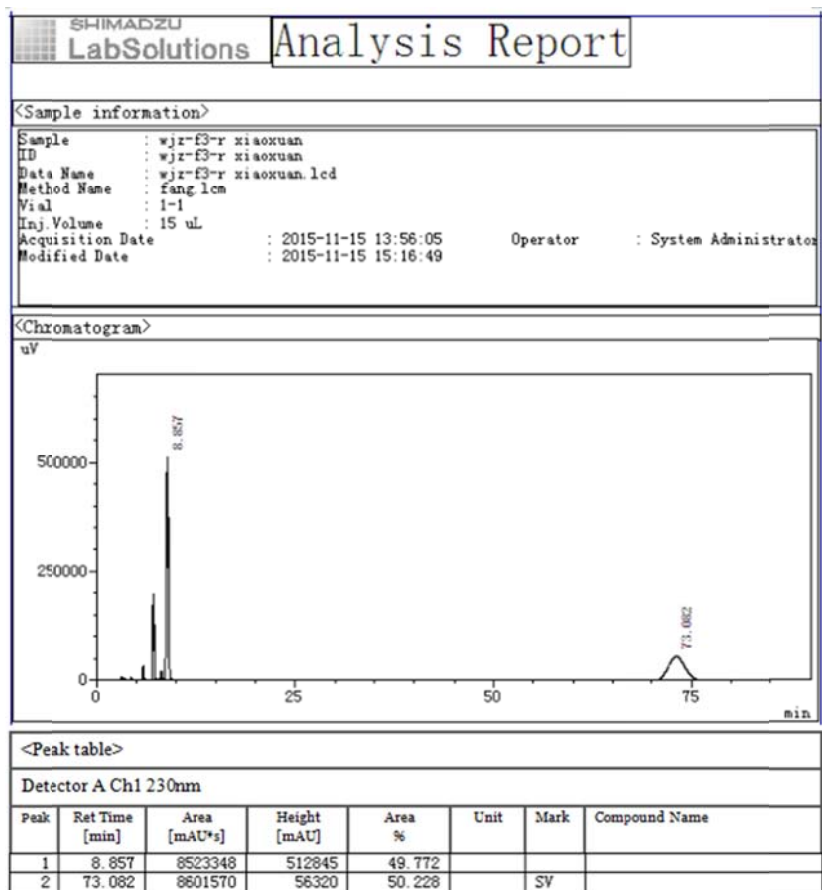
Peak	Ret Time [min]	Area [mAU*s]	Height [mAU]	Area %	Unit	Mark	Compound Name
1	11.923	2888610	135419	5.363		#	
2	22.107	50935775	1241832	94.637		S #	

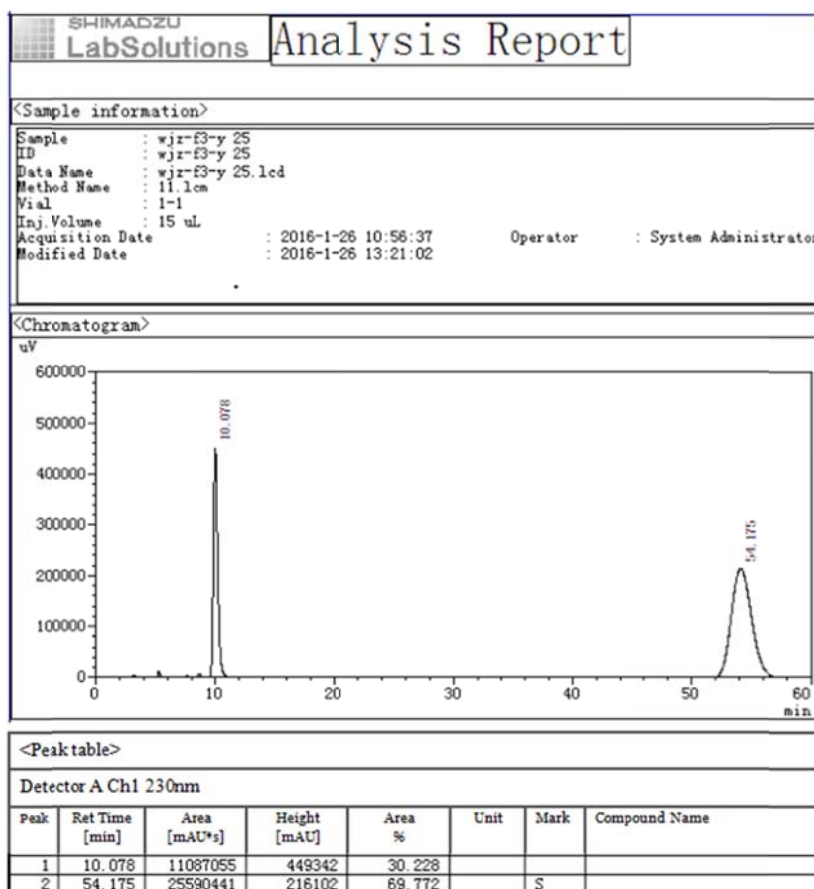
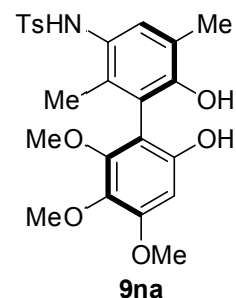
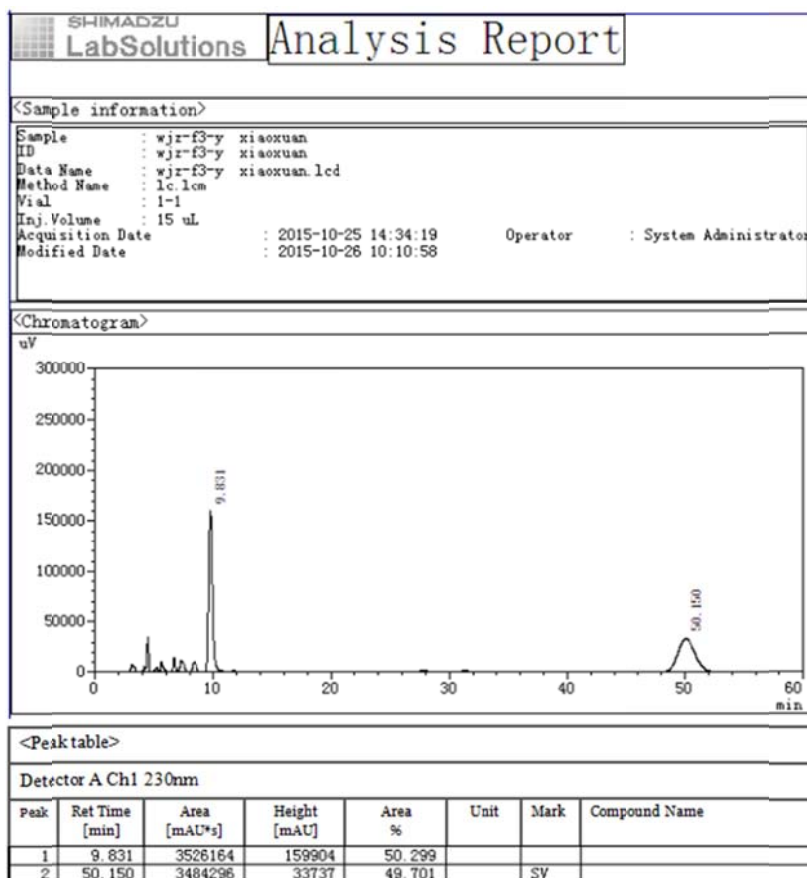






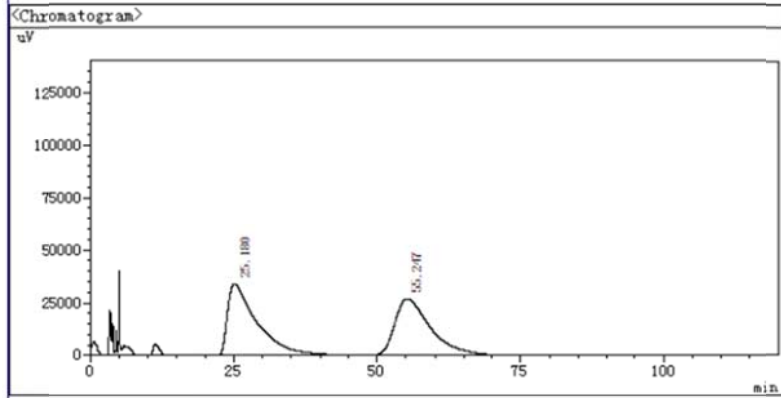






SHIMADZU LabSolutions Analysis Report

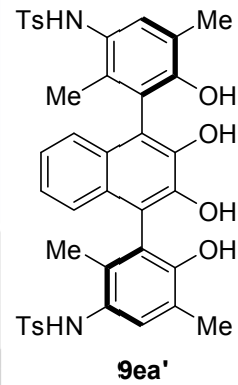
<Sample information>
 Sample : wjr-f3-h xiaoxuan chun ic
 ID : wjr-f3-h xiaoxuan chun ic
 Data Name : wjr-f3-h xiaoxuan chun ic6-4(2).lcd
 Method Name : GF.1cm
 Vial : 1-1
 Inj. Volume : 15 uL
 Acquisition Date : 2015-10-29 12:45:16 Operator : System Administrator
 Modified Date : 2015-10-29 20:40:05



<Peak table>

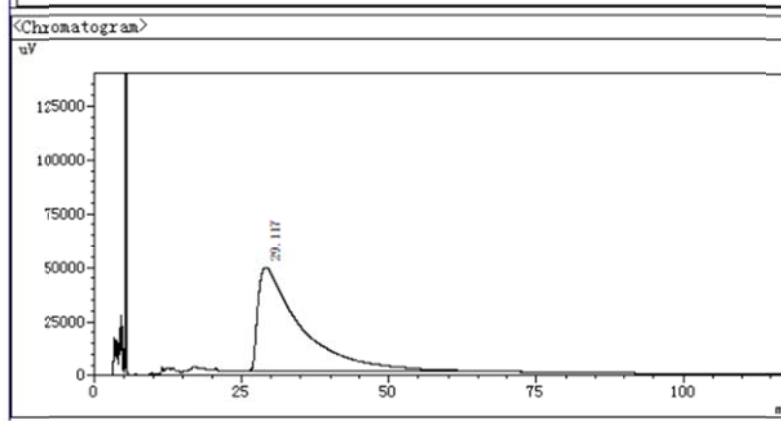
Detector A Ch1 230nm

Peak	Ret Time [min]	Area [mAU*s]	Height [mAU]	Area %	Unit	Mark	Compound Name
1	25.189	12431027	34580	50.636		#	
2	55.247	12118816	26944	49.364		#	



SHIMADZU LabSolutions Analysis Report

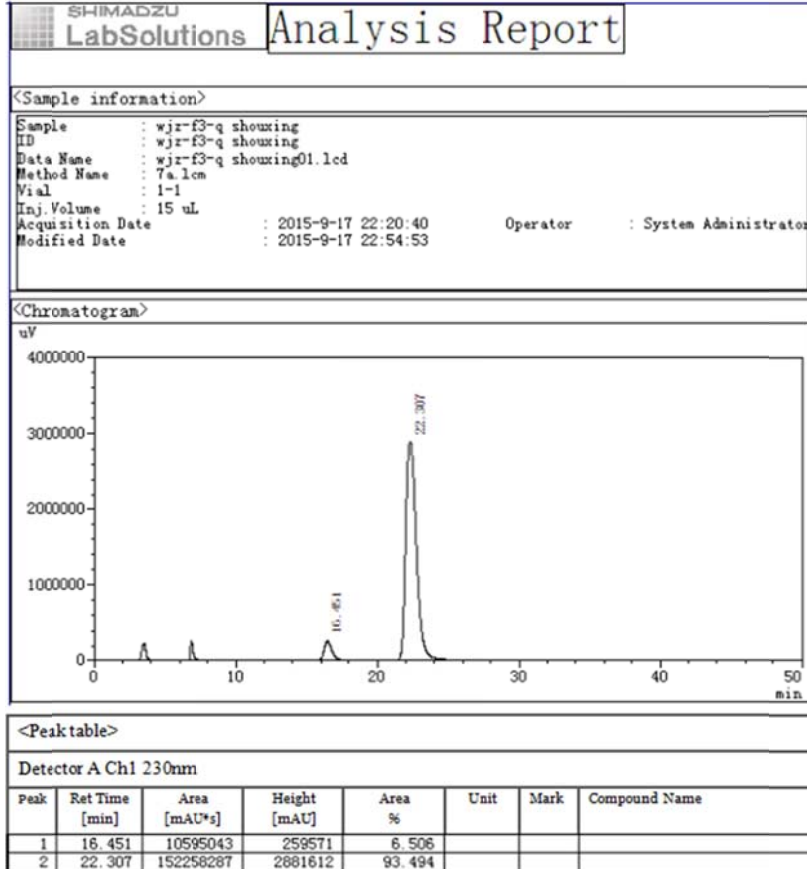
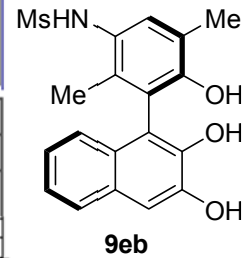
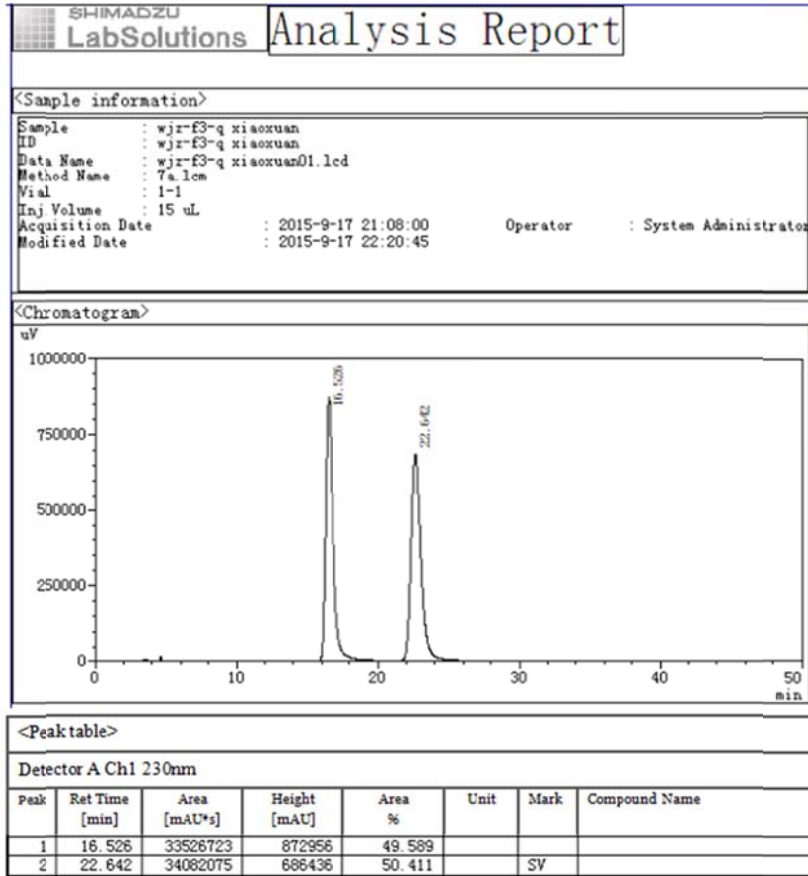
<Sample information>
 Sample : wjz-f3-h shouxing chun ic6-4
 ID : wjz-f3-h shouxing chun ic6-4
 Data Name : wjz-f3-h shouxing chun ic6-4.lcd
 Method Name : GF.1cm
 Vial : 1-1
 Inj. Volume : 15 uL
 Acquisition Date : 2015-11-10 09:11:39 Operator : System Administrator
 Modified Date : 2015-11-10 12:03:11

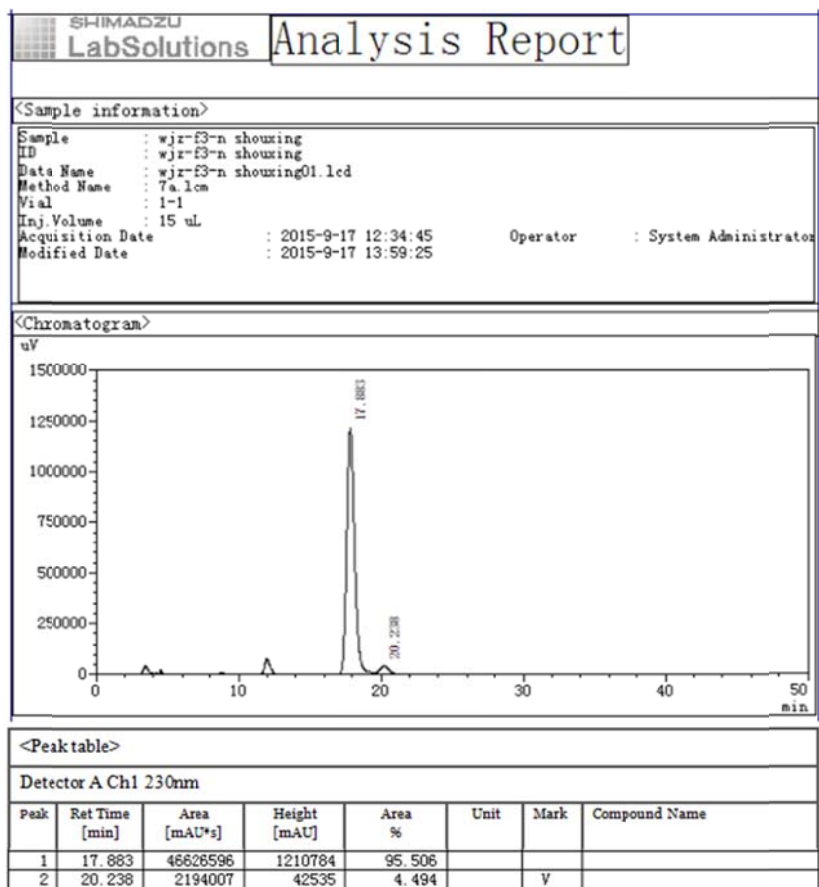
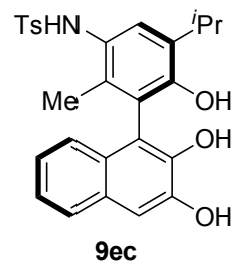
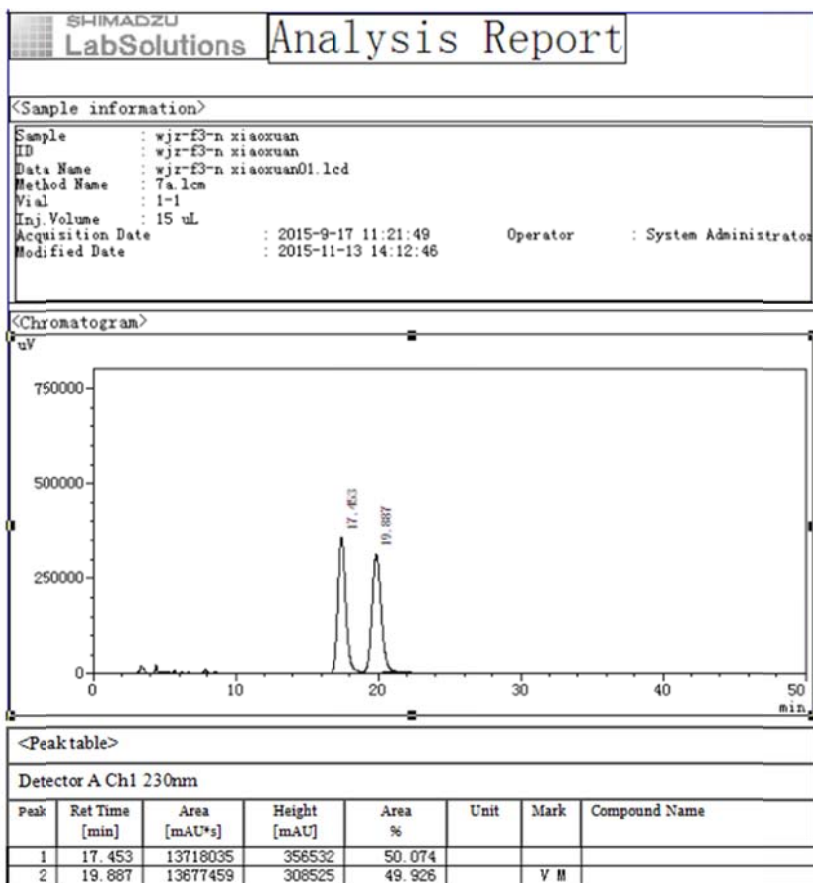


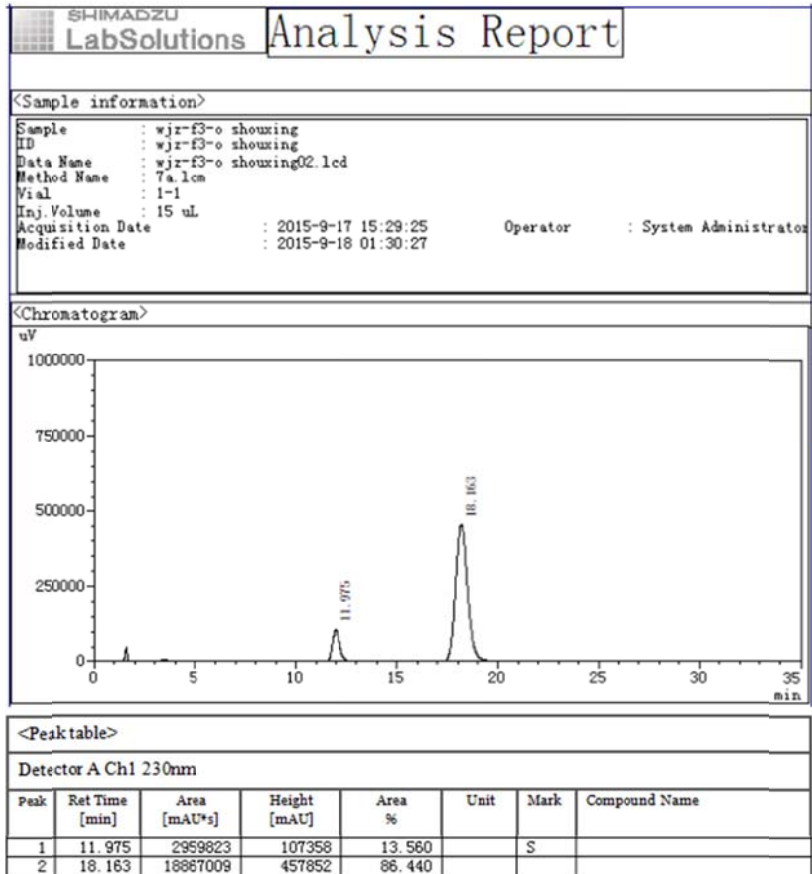
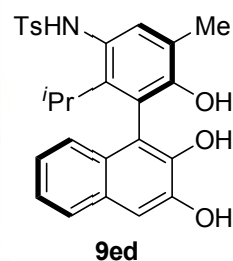
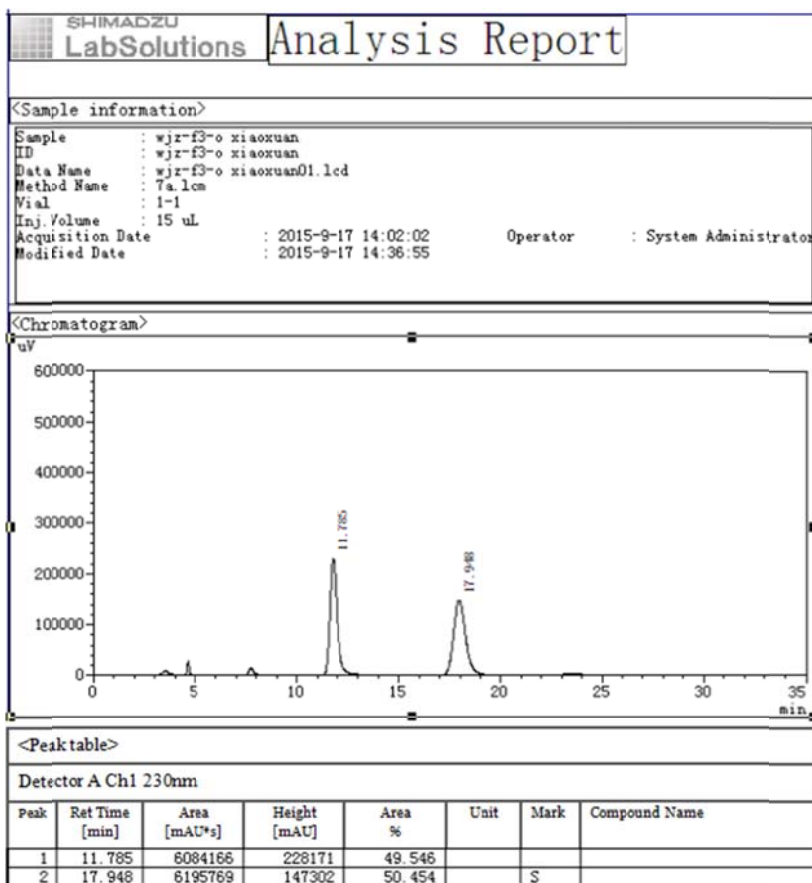
<Peak table>

Detector A Ch1 230nm

Peak	Ret Time [min]	Area [mAU*s]	Height [mAU]	Area %	Unit	Mark	Compound Name
1	29.117	24479780	47788	100.000		#	





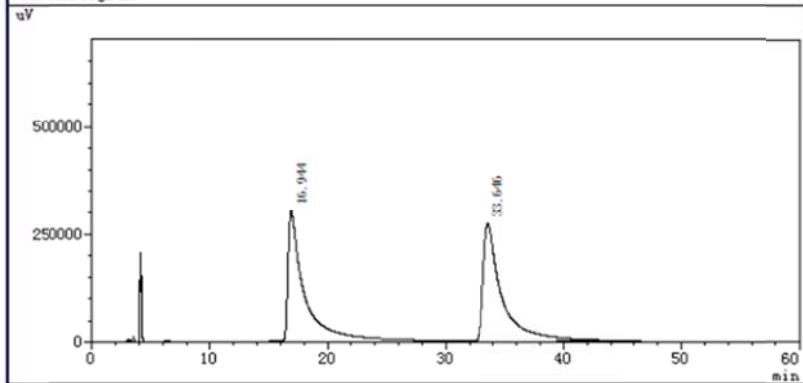


SHIMADZU LabSolutions Analysis Report

<Sample information>

Sample : wjr-f3-p ia xiaoxuan
 ID : wjr-f3-p ia xiaoxuan
 Data Name : wjr-f3-p ia xiaoxuan02.lcd
 Method Name : 74.lcm
 Vial : 1-1
 Inj. Volume : 20 uL
 Acquisition Date : 2015-9-18 16:20:30 Operator : System Administrator
 Modified Date : 2015-9-18 17:09:03

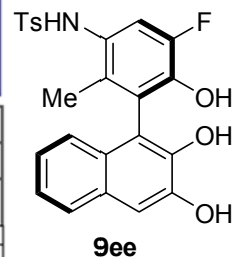
<Chromatogram>



<Peak table>

Detector A Ch1 230nm

Peak	Ret Time [min]	Area [mAU*s]	Height [mAU]	Area %	Unit	Mark	Compound Name
1	16.944	31249922	300070	50.350		SV	
2	33.646	30815848	270879	49.650		V	

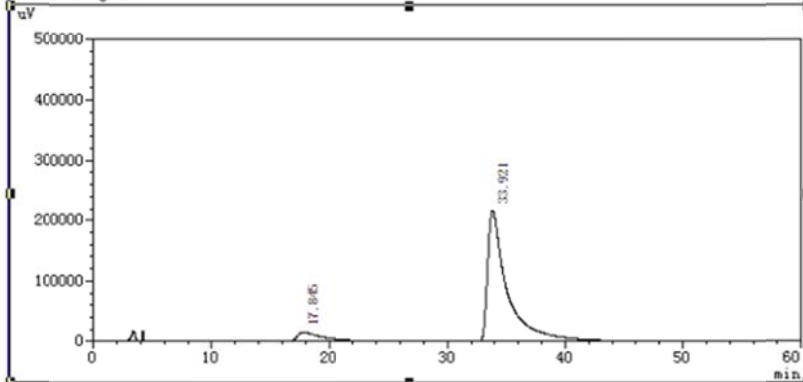


SHIMADZU LabSolutions Analysis Report

<Sample information>

Sample : wjr-f3-p ia showing
 ID : wjr-f3-p ia showing
 Data Name : wjr-f3-p ia showing01.lcd
 Method Name : 74.lcm
 Vial : 1-1
 Inj. Volume : 20 uL
 Acquisition Date : 2015-9-18 17:09:03 Operator : System Administrator
 Modified Date : 2015-9-18 18:16:36

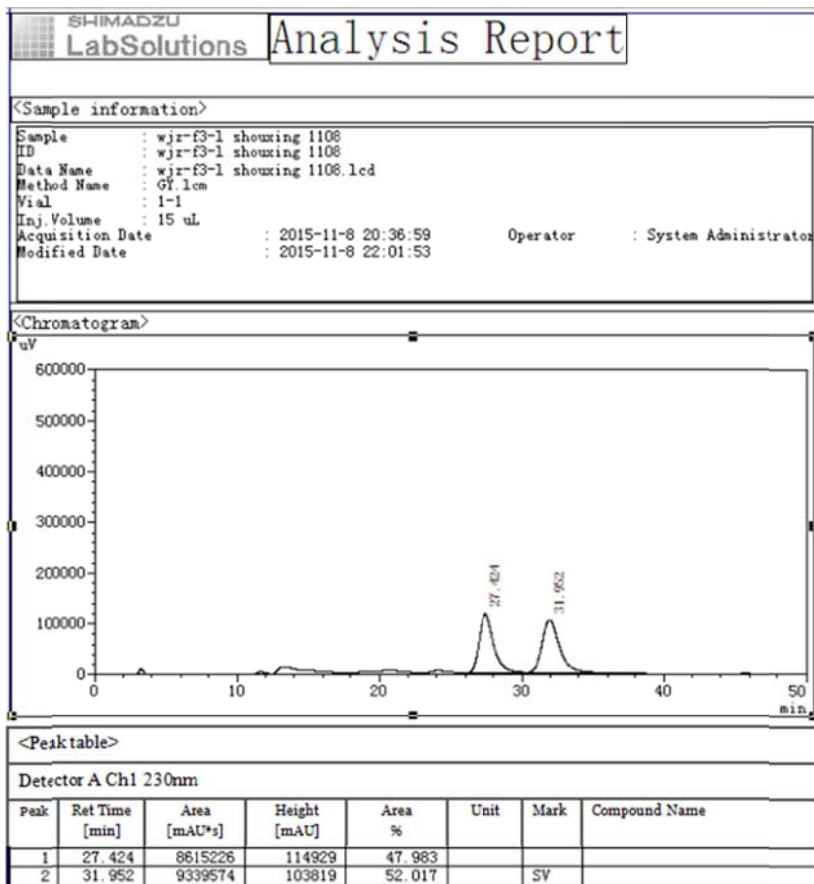
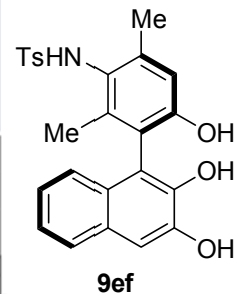
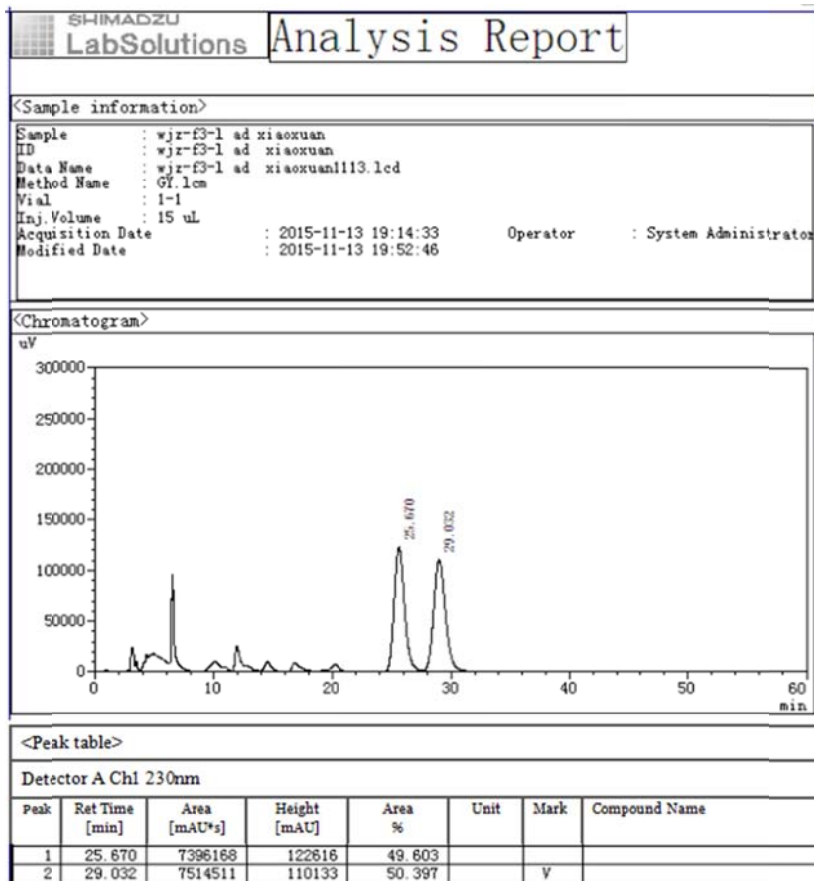
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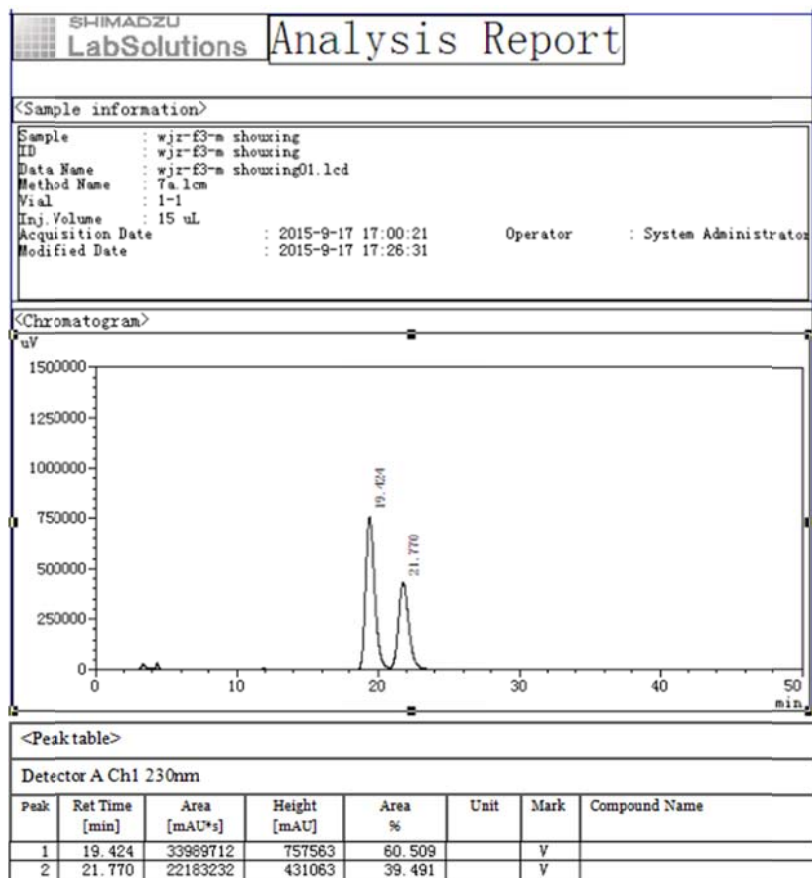
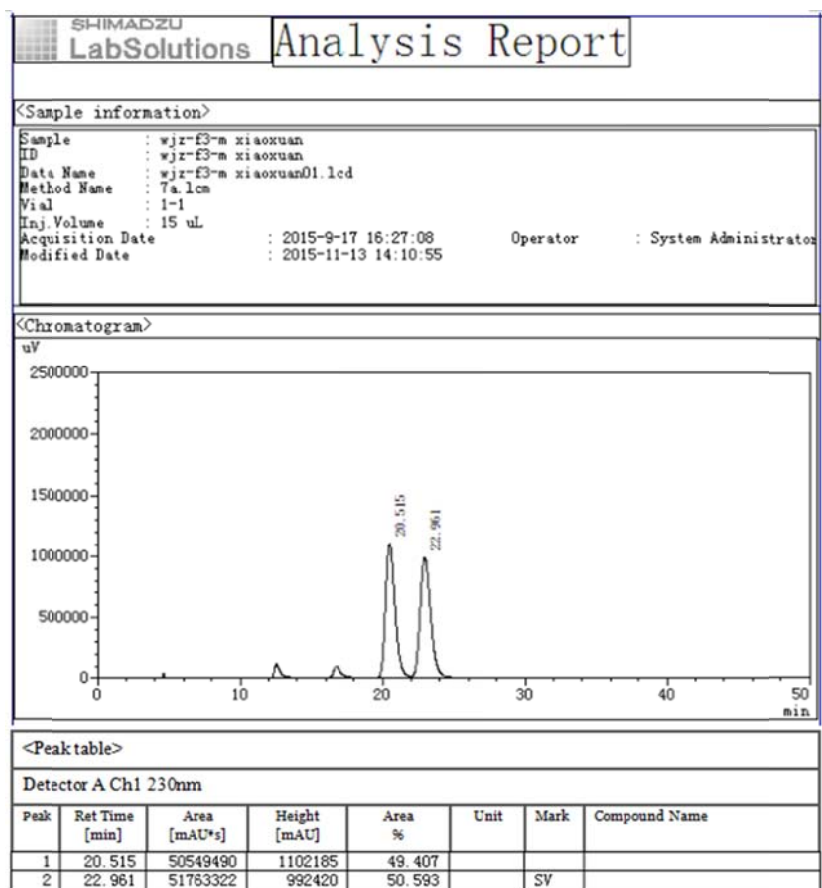


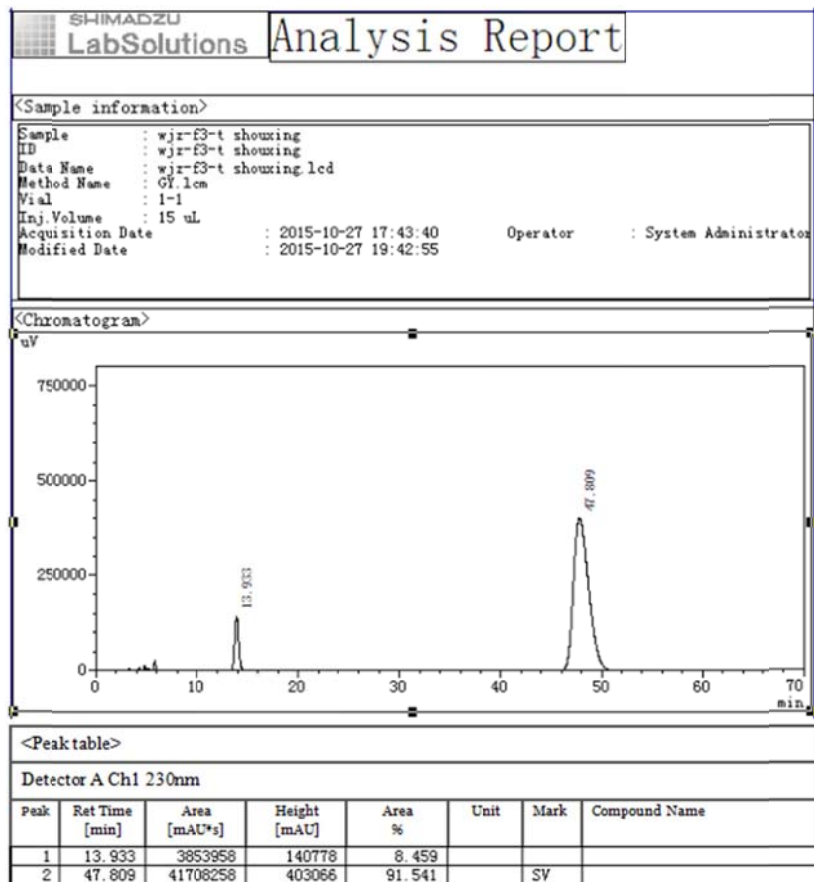
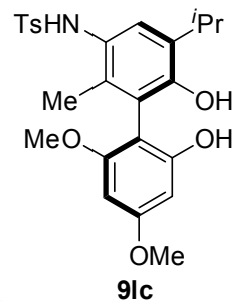
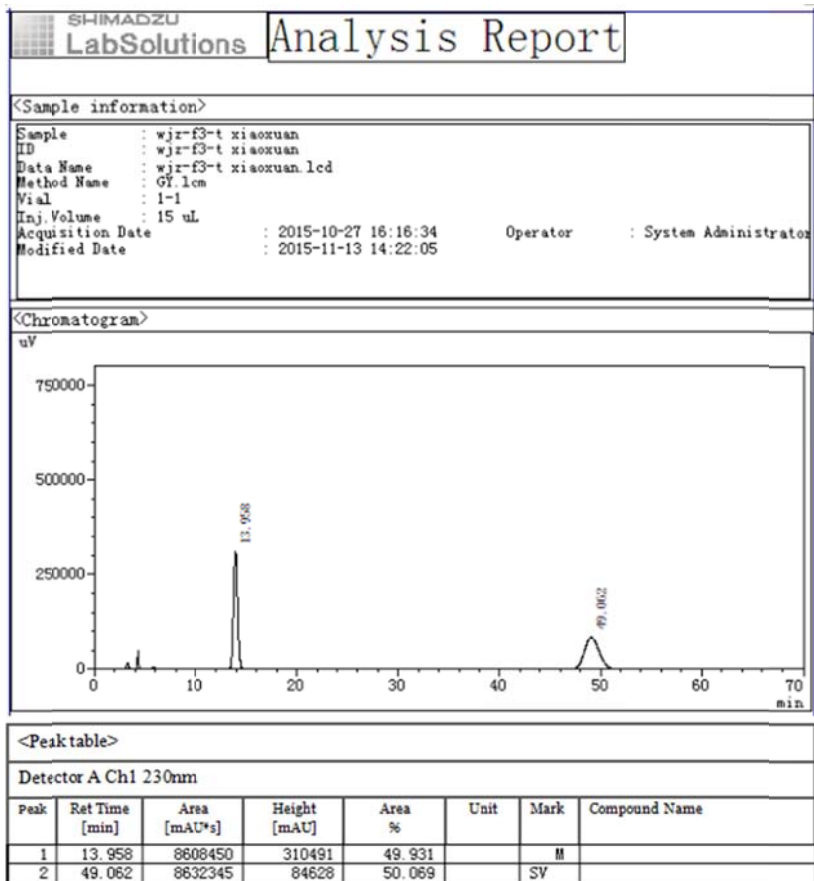
<Peak table>

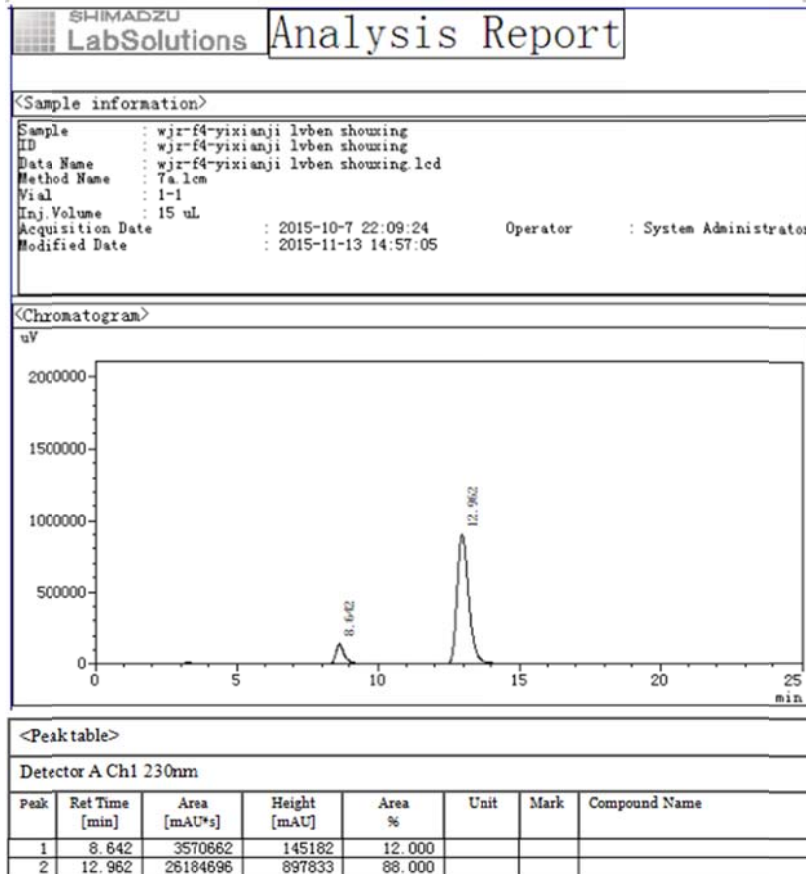
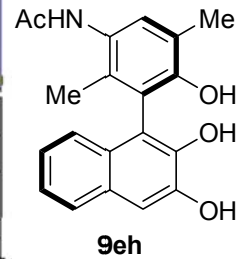
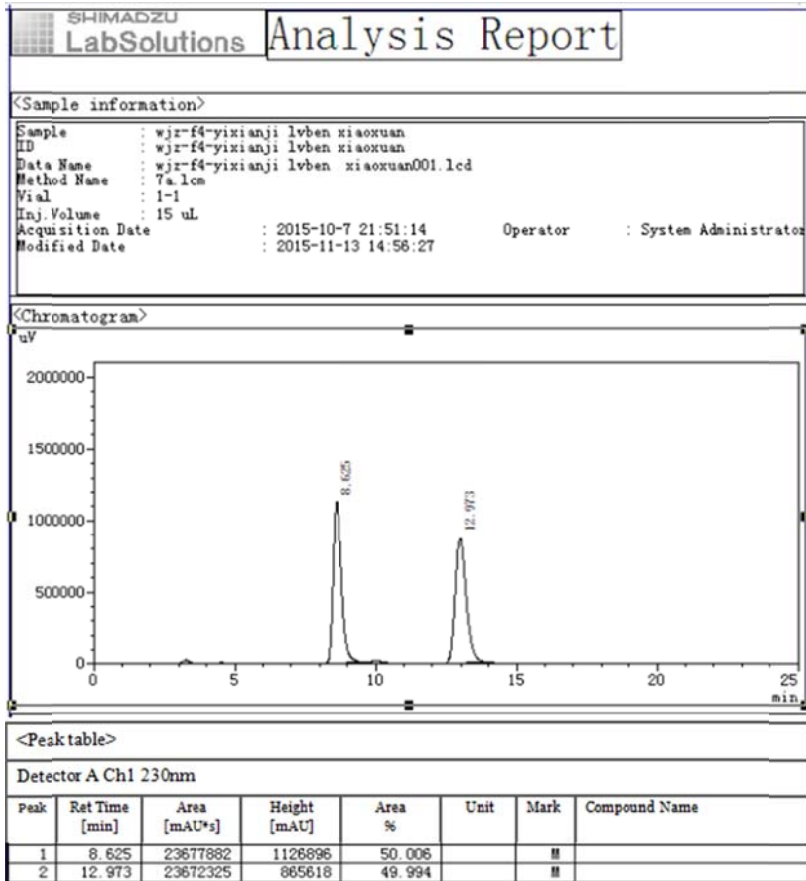
Detector A Ch1 230nm

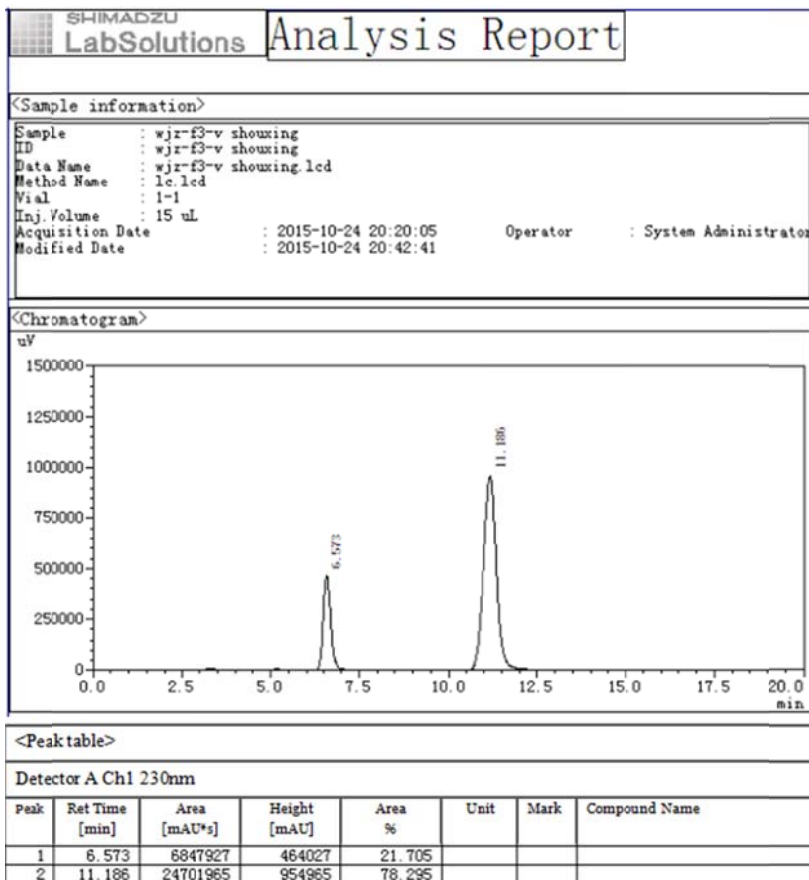
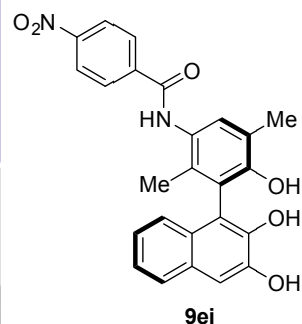
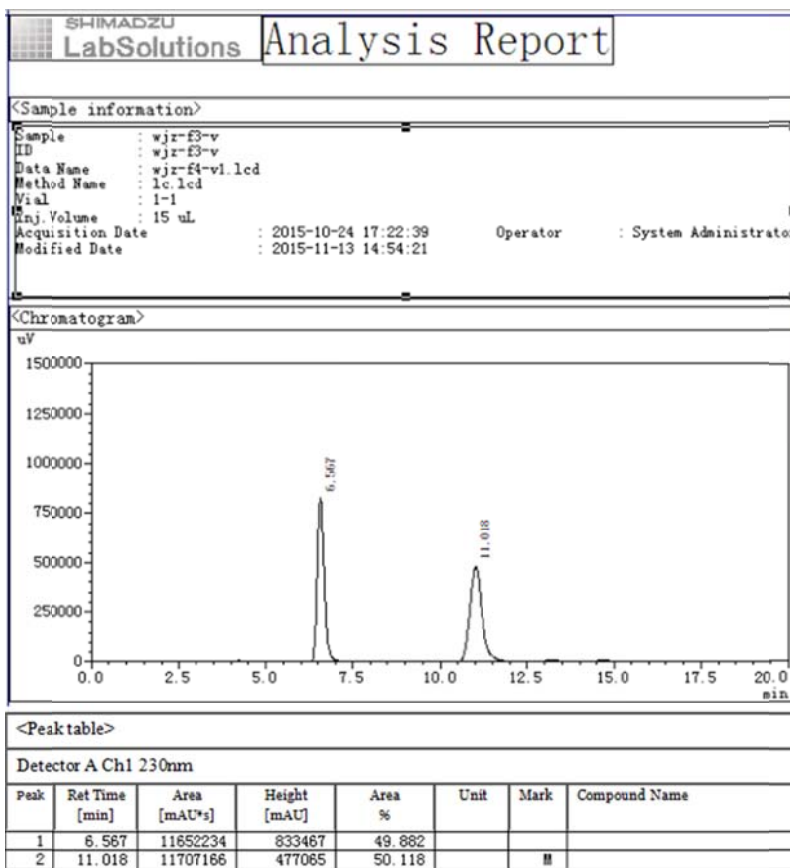
Peak	Ret Time [min]	Area [mAU*s]	Height [mAU]	Area %	Unit	Mark	Compound Name
1	17.845	3361594	16804	11.030		S	
2	33.921	27114589	218677	88.970		S	









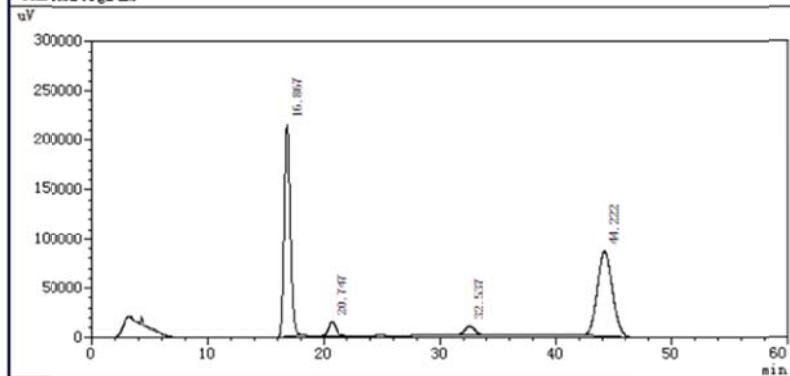


SHIMADZU LabSolutions Analysis Report

<Sample information>

Sample : wjr-E3-w chun xiaozuan
 ID : wjr-E3-w chun xiaozuan
 Data Name : wjr-E3-w chun xiaozuan.lcd
 Method Name : lc.lcm
 Vial : 1-1
 Inj. Volume : 15 uL
 Acquisition Date : 2015-10-25 10:12:57 Operator : System Administrator
 Modified Date : 2015-11-14 18:37:33

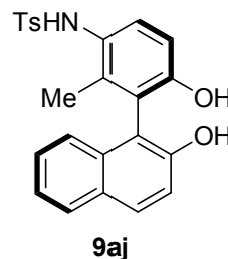
<Chromatogram>



<Peak table>

Detector A Ch1 230nm

Peak	Ret Time [min]	Area [mAU*s]	Height [mAU]	Area %	Unit	Mark	Compound Name
1	16.867	7700196	214099	46.852		M	
2	20.747	597240	13886	3.634			
3	32.537	564178	8663	3.433		S	
4	44.222	7573541	85046	46.081		V	

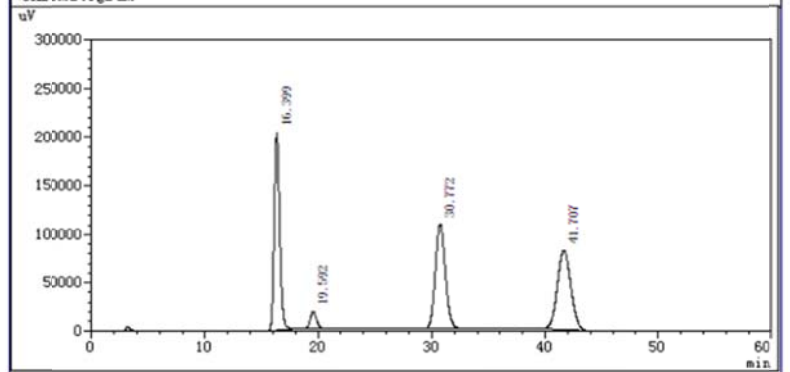


SHIMADZU LabSolutions Analysis Report

<Sample information>

Sample : wjr-E3-w shouxing
 ID : wjr-E3-w shouxing
 Data Name : wjr-E3-w shouxing.lcd
 Method Name : lc.lcm
 Vial : 1-1
 Inj. Volume : 15 uL
 Acquisition Date : 2015-10-24 21:42:25 Operator : System Administrator
 Modified Date : 2015-11-14 18:37:29

<Chromatogram>



<Peak table>

Detector A Ch1 230nm

Peak	RetTime [min]	Area [mAU*s]	Height [mAU]	Area %	Unit	Mark	Compound Name
1	16.399	6902582	203325	33.141			
2	19.592	615548	16500	2.955		M	
3	30.772	6507723	107811	31.245		M	
4	41.707	6802365	81909	32.659		V	

