Electronic Supplementary Information (ESI)

Regio- and Stereospecific *cis*-Hydrophenoxylation of Ynamides with Acidic Phenols

Ting Wang,[a,§] Yuyan Wan,[a,§] Mingyao Xu,[a] Yi Wang,[a] Xu-jia Hong,[a] Hui Gao,[a] Zhi Zhou,[a,*] Wei Yi[a,*]and Zhongyi Zeng[a,*]

[a]Guangzhou Municipal and Guangdong Provincial Key Laboratory of Molecular Target & Clinical Pharmacology, the NMPA and State Key Laboratory of Respiratory Disease, School of Pharmaceutical Sciences and the Fifth Affiliated Hospital, Guangzhou Medical University, Guangzhou, Guangdong 511436, P. R. China.
*E-mail: zzeng@gzhmu.edu.cn (Z. Zeng); yiwei@gzhmu.edu.cn (W. Yi); zhouzhi@gzhmu.edu.cn (Z. Zhou)
[§]These authors contributed equally to this work.

Table of Contents

1. General remarks

Ynamides were prepared according to our previous synthetic procedures.[1] Other chemicals were purchased from commercial suppliers, and were used without further purification. All the products obtained are analytically pure.

Nuclear magnetic resonance (NMR) spectra recorded on JEOL 400 MHz spectrometers at ambient temperature (25 °C) in either $CDCl_3$ or DMSO-d_6. Abbreviations for data quoted are s, singlet; brs, broad singlet; d, doublet; t, triplet; dd, doublet of doublets; m, multiplet. All NMR-data are reported in parts per million (ppm) relative to the solvent signal ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm; DMSO-d_6: δ_H = 2.50 ppm, δ_C = 39.52 ppm).

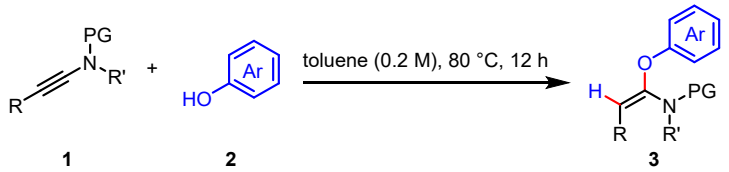
High-resolution mass spectrometry (HRMS) analyses were obtained on an agilent TOF-G6230B mass spectrometer and Thermo-DFS mass spectrometer with positive ion mode.

Thin layer chromatographies (TLC) were conducted on pre-coated silica gel 60 F254 plates (Merck). Silica gel 60H (200-300 mesh) and preparative TLC (200x200 mm, 0.2-0.25 mm in thickness) manufactured by Qingdao Haiyang Chemical Group Co. (China) were used for general chromatography.

Melting points were measured on a Mettler Hanon-MP450 and not uncorrected.

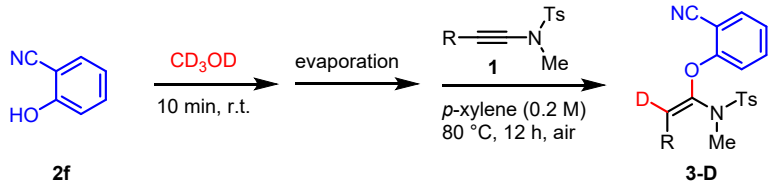
2. General Procedures

General procedure A for hydrophenoxylation reaction



A dry 5 mL vial equipped with a Teflon™-coated stirring bar, was charged with a solution of ynamides **1** (0.1 mmol, 1.0 equiv.) and phenols **2** (0.15 mmol, 1.5 equiv.) in toluene (0.5 mL). The vial was closed with a screw cap and stirred at 80 °C (oil bath) for 12 h under air. Once completed, aqueous NaOH (1 M, 0.15 mL) was added to neutralize the unreacted phenols. Then, the mixture was transferred a separatory funnel with water (10.0 mL) and was washed with EtOAc (3×3 mL). The aqueous phases were further extracted with EtOAc (2×5 mL). The combined organic phases were dried over anhydrous Mg_2SO_4, filtered, and the volatiles were removed under reduced pressure. The residue was purified by preparative TLC (eluent: petroleum ether/ethyl acetate), yielding the hydrophenoxylation products **3**.

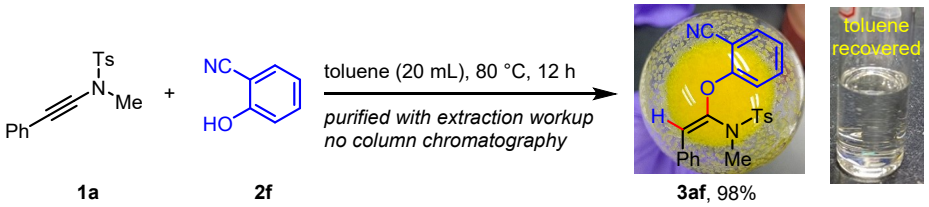
General procedure B for deuterophenoxylation reaction



A dry 5 mL vial equipped with a Teflon™-coated stirring bar, was charged with a solution of 2-cyanophenol (**2f**, 0.15 mmol, 1.5 equiv.) in CD_3OD (0.5 mL). The vial was closed with a screw cap and stirred at room temperature for 10 min under air. Then CD_3OD solvent was removed by a rotary evaporator under reduced pressure. Afterward, ynamides **1** (0.1 mmol, 1.0 equiv.) and dry *p*-xylene was added, and the resulting mixture was stirred at 80 °C (oil bath) for 12 h under air. Once completed, aqueous NaOH (1 M, 0.15 mL) was added to neutralize the unreacted phenols. Then, the mixture was transferred a separatory funnel with water (10.0 mL) and was washed with EtOAc (3×3 mL). The aqueous phases were further extracted with EtOAc (2×5 mL). The combined organic phases were dried over anhydrous Mg_2SO_4, filtered, and the volatiles were removed under reduced pressure. The residue was purified by preparative TLC (eluent: petroleum ether/ethyl acetate), yielding the deuterophenoxylation products **3-D**.

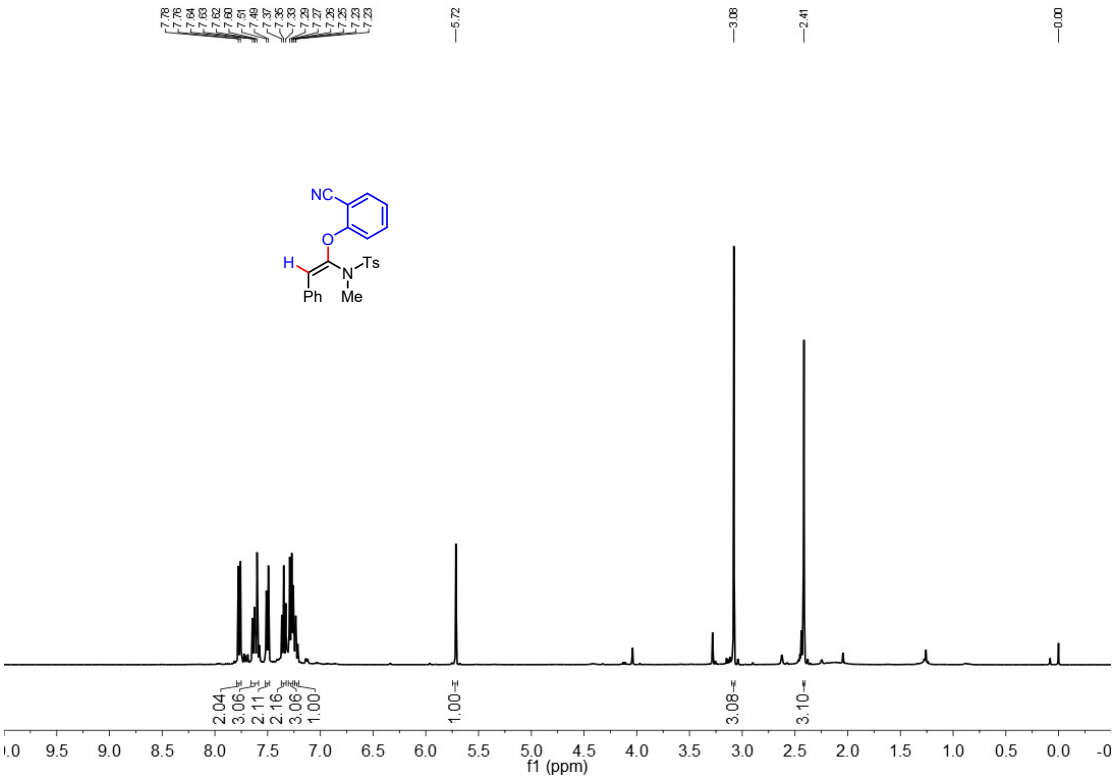
Note: To simplify the synthetic procedure and make it more practical, we performed these experiments without exclusion of air and moisture, which could be accounted for a slightly lower deuterium than 100%. It is also worth mentioning that here we used dry p-xylene instead of anhydrous toluene due to the accessibility issue of the latter solvent, and their comparable efficiency on this reaction has been demonstrated in Table 1)

3. Scale-up synthesis

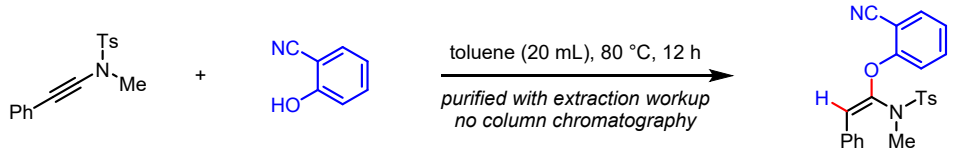


1a **2f** **3af**, 98%

A dry 50 mL round-bottom flask equipped with a Teflon™-coated stirring bar, was charged with a solution of ynamide **1a** (1.14 g, 4.0 mmol, 1.0 equiv.) and 2-cyanophenol (0.71 g, 6.0 mmol, 1.5 equiv.) in toluene (20 mL). The reaction mixture was stirred at 80 °C (oil bath) for 12 h under air. Once completed, toluene was removed by a rotary evaporator under reduced pressure and was recovered with a volume of 18 mL. Then, aqueous NaOH (1 M, 6 mL) was added to neutralize the unreacted phenol. The mixture was transferred a separatory funnel with water (10.0 mL) and was washed with EtOAc (3×5 mL). The aqueous phases were further extracted with EtOAc (2×15 mL). The combined organic phases were dried over anhydrous Mg_2SO_4, filtered, and the volatiles were removed under reduced pressure, leading to the analytically pure (see ^{1}H NMR spectrum below) product **3af** as yellow solid (1.58 g, 3.92 mmol, 98%).



4. Evaluation of green chemistry metrics



1a	**2f**	toluene recovered: 18 mL	**3af**
1.14 g, 4 mmol $C_{16}H_{15}NO_2S$: 285.08	**0.71 g**, 6 mmol C_7H_5NO: 119.04	actually used solvent: 2 mL, **1.74** g C_7H_8: 92.14	**1.58 g**, 3.92 mmol $C_{23}H_{20}N_2O_3S$: 404.12

Percentage Yield (%) $= \dfrac{\text{moles of product}}{\text{moles of limiting reactant}} \times 100 = \dfrac{3.84}{4} \times 100 =$ **98%**

Atom Economy (%) $= \dfrac{\text{molecular weight of product}}{\text{total molecular weight of reactants}} \times 100 = \dfrac{404.12}{285.08 + 119.04} \times 100 =$ **100%**

Atom Efficiency (%) = (% yield of product × % atom economy) × 100 = (98% × 100%) × 100 = **98%**

Carbon Efficiency (%) $= \dfrac{\text{amount of carbon in desired product}}{\text{total amount of carbon presented in all reactants}} \times 100 = \dfrac{23}{16 + 7} \times 100 =$ **100%**

Reaction Mass Efficiency (%) $= \dfrac{\text{mass of isolated product}}{\text{total mass of reactants}} \times 100 = \dfrac{1.58}{1.14 + 0.71} \times 100 =$ **85%**

E-factor $= \dfrac{\text{total waste}}{\text{total product}} = \dfrac{1.14 + 0.71 + 1.74}{1.58} =$ **2.3** kg waste/kg product (based on solvent recovery)

EcoScale = 100 – sum of individual penalties = 100 – 20 = **80** (>75, so it is an **excellent** synthesis)

Evaluation criteria of EcoScale:

EcoScale = 100 – sum of individual penalties
Score on EcoScale: > 75, excellent; > 50, acceptable; and < 50, inadequate

Ecoscale calculation of the current protocol:

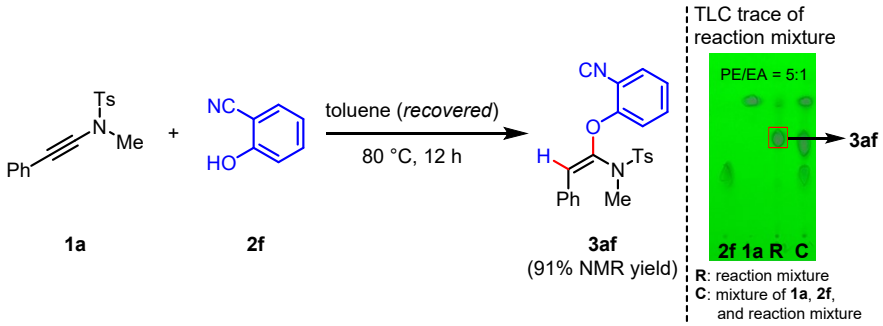
A. Calculation of penalty points

Parameters		Penalty points
1. Yield:	(100 – %yield)/2 = (100 – 98)/2	**1**
2. Price of reaction components (to obtain 10 mmol of the final product, **3af**)		
a. *N*,4-dimethyl-*N*-(phenylethynyl)benzenesulfonamide = 10.4 mmol		
Synthetic cost of required chemicals:		
① phenylacetylene = 10.6 mmol × 102 g/mol ÷ 0.93 g/cm^3 × \$120.6/100 mL = \$1.40		
② *N*-bromosuccinimide = 12.6 mmol × 178 g/mol × \$61.4/100 g = \$1.39		
③ silver nitrate = 0.53 mmol × 170 g/mol × \$821.1/100 g = \$0.74		
④ acetone = 35.1 mL × \$67.3/1000 mL = \$2.36		
⑤ *N*-methyl-*p*-toluenesulfonamide = 12.6 mmol × 185 g/mol × \$202.9/100 g = \$4.73		
⑥ copper(II) sulfate pentahydrate = 1.1 mmol × 250 g/mol × \$240.2/1000 g = \$0.07		
⑦ 1,10-phenanthroline = 2.1 mmol × 180 g/mol × \$474.6/100 g = \$0.18		
⑧ potassium carbonate = 26.3 mmol × 138 g/mol × \$215.7/1000 g = \$0.78		
⑨ toluene = 52.7 mL ×\$730.2/20 L = \$1.92		
b. 2-hydroxybenzonitrile = 15.63 mmol × 119 g/mol × \$207.1/25 g = \$15.4		
c. toluene = 52.1 mL × \$730.2/20 L = \$1.90		
Total cost of synthesis of **3af** = \$30.87 Thus expensive, since \$10 < (total cost of synthesis of **3af**) < \$50		**3**
3. Safety		
a. 2-hydroxybenzonitrile		**5**
b. toluene		**5**
4. Technical setup		
common setup		**0**
5. Temperature/time		
80 °C, 12 h (heating, > 1 h)		**3**
6. Workup and purification		
a. Removal of solvent with bp < 150 °C		**0**
b. Cooling to room temperature		**0**
c. Liquid-liquid extractione		**3**
Total penalty points:		**20**

B. Ecoscale calculation:

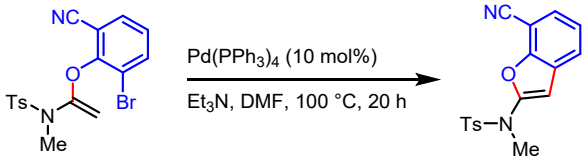
Ecoscale Score: **100** – **20** **=** **80** (>75, it is an **excellent** synthesis)

5. Recyclability of reaction solvent



A dry 5 mL vial equipped with a Teflon™-coated stirring bar, was charged with a solution of ynamide **1a** (28.5 mg, 0.1 mmol, 1.0 equiv.) and 2-cyanophenol (17.9 mg, 0.15 mmol, 1.5 equiv.) in the above *recovered* toluene (0.5 mL). The vial was closed with a screw cap and stirred at 80 °C (oil bath) for 12 h under air. Once completion (TLC trace shown as above), the reaction mixture was concentrated by a rotary evaporator under reduced pressure. The residue was subjected to ^{1}H NMR analysis with 1,3,5-trimethoxybenzene (5.6 mg, 0.03 mmol, 0.3 equiv.) as internal standard. The product **3af** was determined with 91% yield and > 20/1 *E/Z* selectivity.

6. Synthetic utilization



3rr **4**, 76%

A dry 10 mL sealed tube equipped with a Teflon™-coated stirring bar, was charged with a solution of **3rr** (40.6 mg, 0.1 mmol, 1.0 equiv.), $Pd(PPh_3)_4$ (11.6 mg, 0.01 mmol, 0.1 equiv.) and Et_3N (101.2 mg, 1.0 mmol, 10.0 equiv.) in DMF (1.0 mL). The reaction mixture was run at 100 °C (oil bath) for 20 h without exclusion of air and moisture. Once completed, water (5.0 mL) was added to quench the reaction. Then, the mixture was transferred a separatory funnel with water (5.0 mL) and was washed with EtOAc (3×3 mL). The aqueous phases were further extracted with EtOAc (2×5 mL). The combined organic phases were dried over anhydrous Mg_2SO_4, filtered, and the volatiles were removed under reduced pressure. The residue was purified by preparative TLC (eluent: petroleum ether/ethyl acetate = 5/1), delivering the desired 2-aminobenzofuran **4** as colorless oil (24.8 mg, 0.076 mmol, 76%).

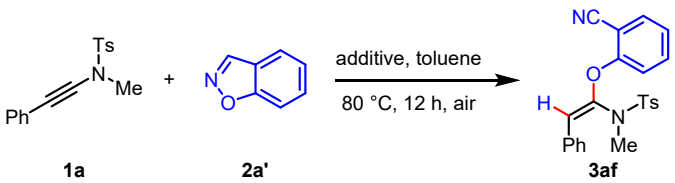
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.60 (d, *J* = 1.8 Hz, 1H), 7.47 – 7.45 (m, 1H), 7.26 – 7.23 (m, 1H), 6.66 – 6.65 (m, 1H), 3.27 (s, 1H), 2.37 (s, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 151.37, 145.01, 134.15, 130.09, 129.44, 128.03, 127.67, 126.02, 123.61, 114.91, 98.91, 95.97, 36.25, 21.74 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for Chemical Formula: $C_{17}H_{15}N_2O_3S$: 327.0798; Found: 327.0799.

7. Mechanistic investigation

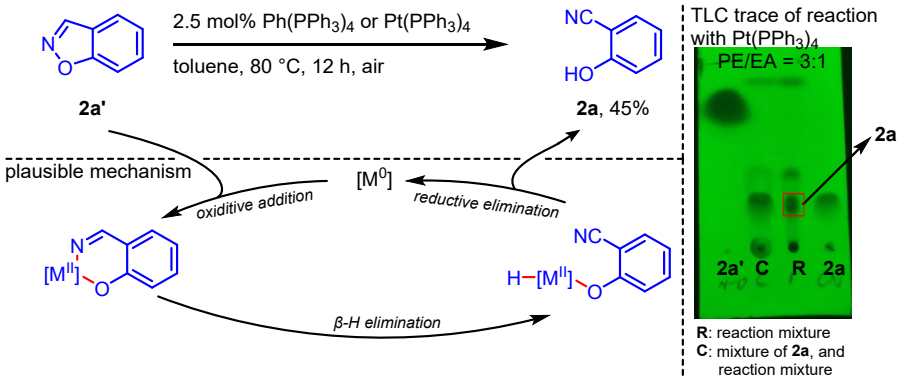
Use of 1,2-benzisoxazole for hydrophenoxylation



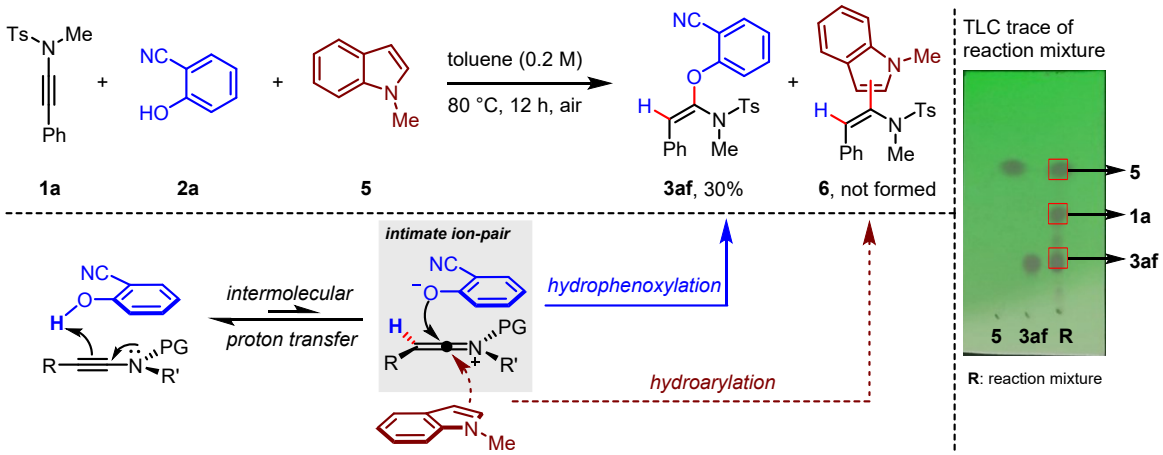
additive	**3af** (*E*:*Z*)
none	not formed
1 equiv. K_2CO_3	trace
2.5 mol% $Pd(PPh_3)_4$	94% (>20:1)
2.5 mol% $Pt(PPh_3)_4$	95% (>20:1)

A dry 5 mL vial equipped with a Teflon™-coated stirring bar, was charged with a solution of ynamide **1a** (28.5 mg, 0.1 mmol, 1.0 equiv.), 1,2-benzisoxazole (**2a**, 17.9 mg, 0.15 mmol, 1.5 equiv.) and indicated additive in toluene (0.5 mL). The vial was closed with a screw cap and stirred at 80 °C (oil bath) for 12 h under air. Once completion, the reaction mixture was concentrated by a rotary evaporator under reduced pressure. The residue was subjected to ^{1}H NMR analysis with 1,3,5-trimethoxybenzene (5.6 mg, 0.03 mmol, 0.3 equiv.) as internal standard.

Discussion: The above results shows that a catalytic amount of $Pd(PPh_3)_4$ or $Pt(PPh_3)_4$ could promoted the same hydrophenoxylation reaction with comparable efficiency. Control experiments (as below) reveals that both metal complexes can significantly mediate the isomeric ring opening of 1,2-benzisoxazole to release 2-cyanophenol through initial N–O oxidative addition, subsequent β-H elimination, and final reductive elimination.

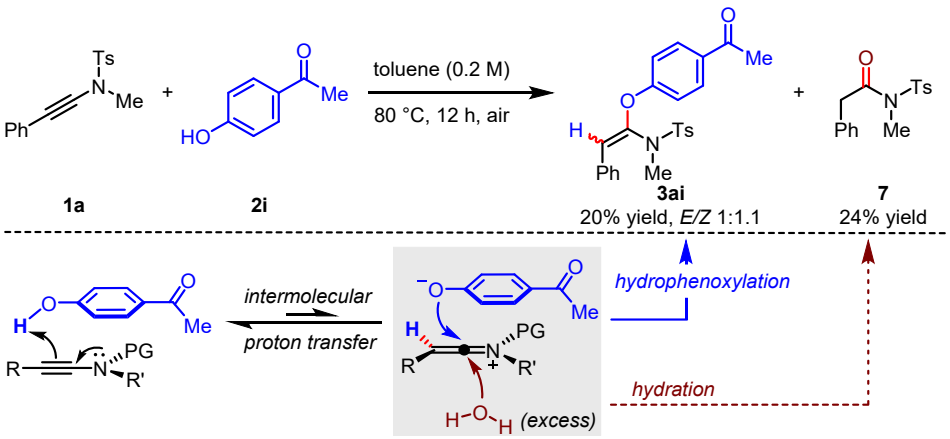


Nucleophilic competition reaction

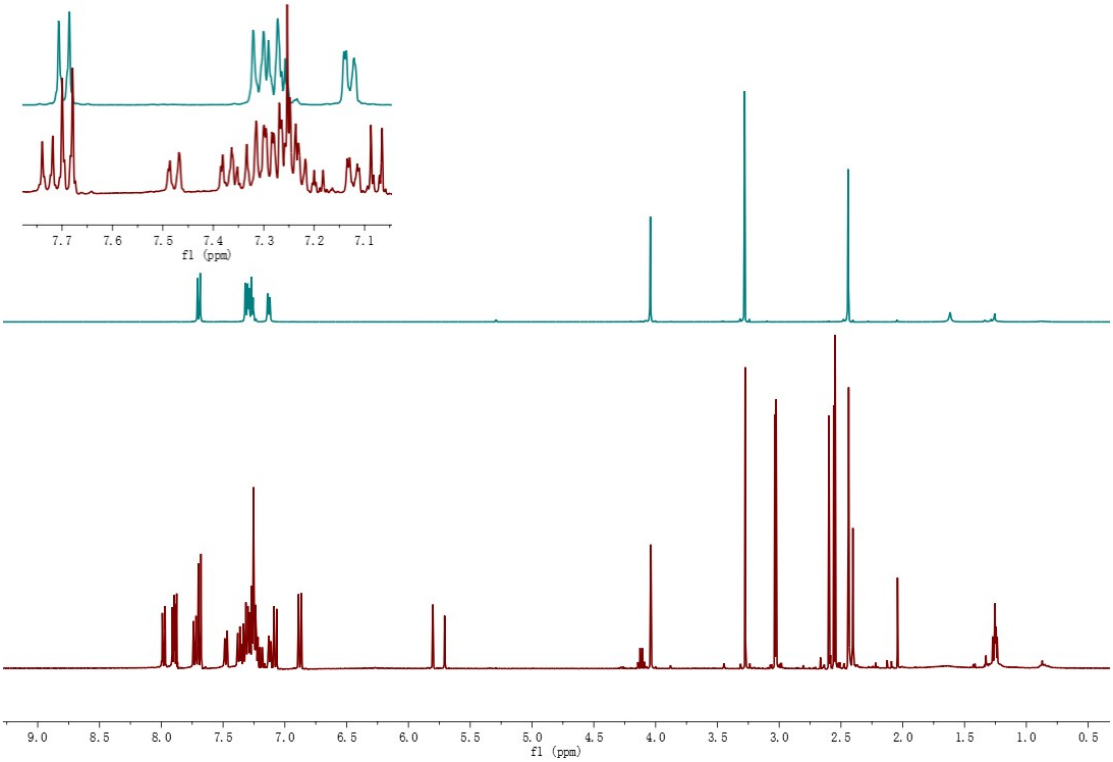


A dry 5 mL vial equipped with a Teflon™-coated stirring bar, was charged with a solution of ynamide **1a** (28.5 mg, 0.1 mmol, 1.0 equiv.), 2-cycnophenol (17.9 mg, 0.15 mmol, 1.5 equiv.), and *N*-methyl indole (**5**, 26.2 mg, 0.2 mmol, 2 equiv.) in toluene (0.5 mL). The vial was closed with a screw cap and stirred at 80 °C (oil bath) for 12 h under air. Once completion, TLC trace of the reaction mixture showed no formation of the hydroarylation product **6**. This result could be explained by the formation of intimate ion-pair between the phenolate anion and cationic keteniminium species through intermolecular proton transfer process. Thus, the nucleophilic attack of phenolate is highly favorable than indole attack.

Determination of by-product

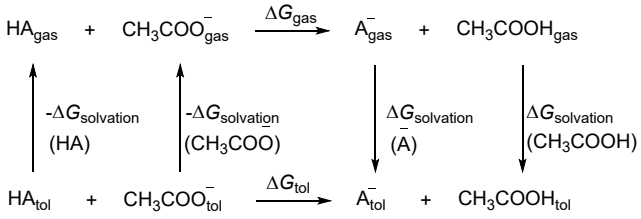


A dry 5 mL vial equipped with a Teflon™-coated stirring bar, was charged with a solution of ynamide **1a** (28.5 mg, 0.1 mmol, 1.0 equiv.) and 4-acetophenol **2i** (20.4 mg, 0.15 mmol, 1.5 equiv.) in toluene (0.5 mL). The vial was closed with a screw cap and stirred at 80 °C (oil bath) for 12 h under air. Once completed, aqueous NaOH (1 M, 0.15 mL) was added to neutralize the unreacted phenols. Then, the mixture was transferred a separatory funnel with water (10.0 mL) and was washed with EtOAc (3×3 mL). The aqueous phases were further extracted with EtOAc (2×5 mL). The combined organic phases were dried over anhydrous Mg_2SO_4, filtered, and the volatiles were removed under reduced pressure. The residue was purified by preparative TLC (eluent: petroleum ether/ethyl acetate), yielding a inseparable mixture of the hydrophenoxylated product **3ai** and the hydrated by-product **7,** which was determined by ^{1}H NMR analysis (red spectrum, below). *Note*: The green spectrum above is the ^{1}H NMR of authentic sample **7**.



8. pK_a Calculation

Thermodynamics cycles[2] shown in Scheme S1 were applied to calculate relative pK_a values of phenols in toluene. The introduction of CH_3COOH as the reference can avoid the difficulty of building a model for solvated proton theoretically. All calculations were performed with Gaussian 09 program.[3] Phenols and the corresponding anions were optimized using the B3LYP functional[4] with a standard 6-31G(d) basis set in gas phase. ΔG_{gas} is obtained by using the CBS-QB3[5] method. $\Delta G_{solvation}$ is calculated at the M05-2X level of density functional theory with a standard 6-31G(d) basis set using SMD solvation model (solvent = toluene).[6]



$\Delta G_{gas} = G_{gas}(\bar{A}) + G_{gas}(CH_3COOH) - G_{gas}(HA) - G_{gas}(CH_3\bar{C}OO)$

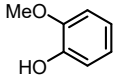
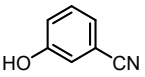
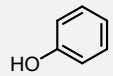
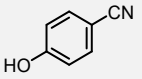
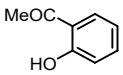
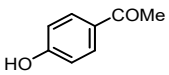
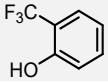
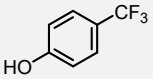
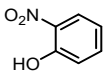
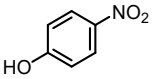
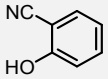
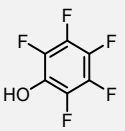
$\Delta G_{tol} = \Delta G_{gas} + \Delta G_{solvation}(\bar{A}) + \Delta G_{solvation}(CH_3COOH) - \Delta G_{solvation}(HA) - \Delta G_{solvation}(CH_3\bar{C}OO)$

relative pK_a = ΔG_{tol}/2.303RT

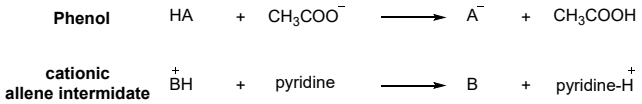
absolute pK_a = pK_a(CH_3COOH) + ΔG_{tol} / 2.303RT where R = 8.314 J/(mol*K), T = 298.15 K

Scheme S1 Thermodynamic cycle used to calculate relative pK_a values of phenols in toluene.

Table S1 Relative pK_a values of phenols to CH_3COOH in toluene.

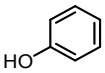
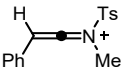
substrate	relative pK_a (in toluene)	substrate	relative pK_a (in toluene)
	8.0		-1.0
	4.5		-4.2
	2.68		-1.8
	-2.1		-1.6
	-1.6		-6.2
	-4.5		-7.9

Comparison of pK_a between phenols and the cationic keteniminium species: For cationic keteniminium species, the introduction of pyridine-H^+ as a reference, which is also a cationic acid, is required to reduce the error due to the unsymmetry in charge distribution.



Scheme S2 Calculation model for thermodynamic cycle.

Table S2 Absolute pK_a values of phenol and the cationic keteniminium species in DMSO and MeCN.

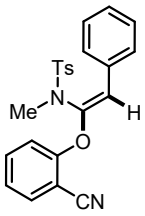
substrate	absolute pK_a		substrate	absolute pK_a	
	in DMSO	in MeCN		in DMSO	in MeCN
CH_3COOH	12.6[7]	22.3[8]	pyridine-H^+	3.4[7]	12.5[9]
	19.3[a]	29.9[a]		-5.8[a]	3.2[a]

[a]ΔG_{gas} is calculated at the level of B3LYP/6-31G(d)//B2PLYPD3[10]/6-311++G(d,p)

Our theoretical calculation indicates that the resulting cationic keteniminium is much more acidic than e.g., phenol (at least 10^{25} times in both solvents), which suggests that the initial proton transfer process between these two substrates seems highly unfavorable.

9. Synthesis and characterization of products

(*E*)-*N*-(1-(2-cyanophenoxy)-2-phenylvinyl)-*N*,4-dimethylben-zenesulfonamide (**3af**)



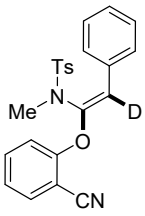
Compound **3af** was prepared following the General Procedure A with *N*,4-dimethyl-*N*-(phenylethynyl)benzenesulfonamide (**1a**, 28.5 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a light yellow solid (38.5 mg, 0.094 mmol, 94%). m.p.: 142–143 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 7.6 Hz, 2H), 7.67 – 7.55 (m, 3H), 7.49 (d, *J* = 7.3 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.30 – 7.17 (m, 4H), 5.70 (s, 1H), 3.06 (s, 3H), 2.40 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 157.28, 147.89, 144.32, 135.38, 134.82, 133.80, 132.37, 129.76, 128.81, 128.24, 128.13, 127.89, 124.56, 119.98, 115.62, 111.01, 104.92, 36.14, 21.70 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for Chemical Formula: $C_{23}H_{21}N_2O_3S$: 405.1267; Found: 405.1269.

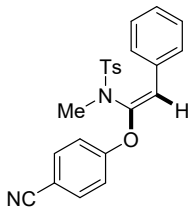
(*E*)-*N*-(1-(2-cyanophenoxy)-2-phenylvinyl-2-*d*)-*N,4*-dimethylbenzenesulfonamide (**3af-D**)



Compound **3af-D** was prepared following the General Procedure B with *N*,4-dimethyl-*N*-(phenylethynyl)benzenesulfonamide (**1a**, 28.5 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a light yellow solid (31.5 mg, 0.078 mmol, 78% with 91% D).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.66 – 7.59 (m, 3H), 7.52 – 7.48 (m, 2H), 7.35 (dd, *J* = 8.2, 6.9 Hz, 2H), 7.30 – 7.26 (m, 3H), 7.25 – 7.21 (m, 1H), 5.71 (s, 0.09H), 3.08 (s, 3H), 2.42 (s, 3H).

(*E*)-*N*-(1-(4-cyanophenoxy)-2-phenylvinyl)-*N*,4-dimethyl-benzenesulfonamide (**3ah**)



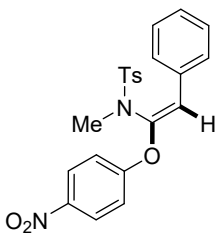
Compound **3ah** was prepared following the General Procedure A with *N*,4-dimethyl-*N*-(phenylethynyl)benzenesul-fonamide (**1a**, 28.5 mg, 0.1 mmol) and 4-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a light yellow solid (14.2 mg, 0.035 mmol, 35%). m.p.: 133–134 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 8.3 Hz, 2H), 7.67 – 7.63 (m, 2H), 7.48 (m, 2H), 7.37 – 7.22 (m, 7H), 5.74 (s, 1H), 3.03 (s, 3H), 2.41 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 159.33, 147.84, 144.30, 135.74, 134.41, 132.35, 129.65, 128.86, 128.16, 128.04, 127.91, 119.98, 118.69, 111.26, 107.59, 36.35, 21.70 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{23}H_{21}N_2O_3S$: 405.1267; Found: 405.1268.

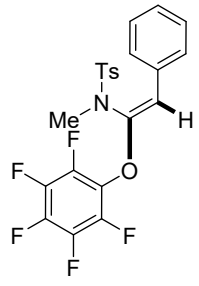
(*E*)-*N*,4-dimethyl-*N*-(1-(4-nitrophenoxy)-2-phenylvinyl)-benzenesulfonamide (**3ak**)



Compound **3ak** was prepared following the General Procedure A with *N*,4-dimethyl-*N*-(phenylethynyl)benzenesulfonamide (**1a**, 28.5 mg, 0.1 mmol) and 4-nitrophenol (20.9 mg, 0.15 mmol), and isolated as light yellow oil (27.2 mg, 0.064 mmol, 64%).

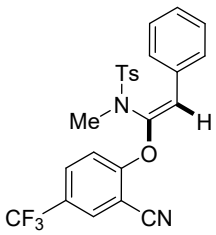
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 – 8.12 (m, 2H), 7.70 (m, 2H), 7.37 – 7.29 (m, 4H), 7.28 – 7.19 (m, 3H), 7.15 – 7.07 (m, 2H), 5.83 (s, 1H), 3.06 (s, 3H), 2.45 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$): δ 159.62, 144.63, 143.61, 143.10, 134.05, 132.46, 129.79, 128.74, 128.56, 128.18, 128.03, 125.86, 117.85, 113.24, 37.44, 21.72 ppm.
HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{22}H_{21}N_2O_5S$: 425.1166; Found: 425.1168.

(*E*)-*N*,4-dimethyl-*N*-(1-(perfluorophenoxy)-2-phenylvinyl)benzenesulfonamide (**3al**)



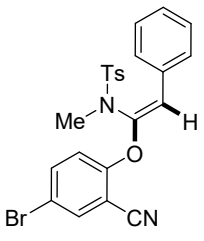
Compound **3al** was prepared following the General Procedure A with *N*,4-dimethyl-*N*-(phenylethynyl)benzenesulfonamide (**1a**, 28.5 mg, 0.1 mmol) and pentafluorophenol (27.6 mg, 0.15 mmol), and isolated as colorless oil (40.9 mg, 0.087 mmol, 87%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.1 Hz, 2H), 7.49 – 7.43 (m, 2H), 7.34 – 7.27 (m, 4H), 7.27 – 7.23 (m, 1H), 5.57 (s, 1H), 3.17 (s, 3H), 2.42 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$): δ 147.72, 144.38 (s), 143.09 – 142.95 (m), 140.58 – 140.39 (m), 139.72 – 139.41 (m), 138.16 – 137.86 (m), 137.19 – 136.90 (m), 135.24, 132.14, 129.65, 128.67, 128.42, 128.36, 127.88, 107.37, 35.88, 21.66 ppm.
^{19}F NMR (376 MHz, $CDCl_3$): δ -153.31 (d, *J* = 18.2 Hz, 2F), -158.37 (t, *J* = 21.9 Hz, 1F), -161.12 (t, *J* = 19.8 Hz, 2F).
HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{22}H_{17}F_5NO_3S$: 470.0844; Found: 470.0849.

(*E*)-*N*-(1-(2-cyano-4-(trifluoromethyl)phenoxy)-2-phenylvinyl)-*N*,4-dimethyl-benzenesulfonamide (**3am**)



Compound **3am** was prepared following the General Procedure A with *N*,4-dimethyl-*N*-(phenylethynyl)benzenesulfonamide (**1a**, 28.5 mg, 0.1 mmol) and 4-trifluoromethyl-2-cyanophenol (**2m**, 24.3 mg, 0.15 mmol), and isolated as a light yellow solid (39.3 mg, 0.083 mmol, 83%). m.p.: 138–139 °C
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 – 7.88 (m, 1H), 7.83 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.79 (m, 1H), 7.73 – 7.68 (m, 2H), 7.55 – 7.50 (m, 2H), 7.42 – 7.36 (m, 2H), 7.34 – 7.27 (m, 3H), 5.90 (s, 1H), 3.05 (s, 3H), 2.43 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$): δ 160.34, 146.37, 144.62, 135.20, 131.70 (q, J_{C-F} = 3.4 Hz), 131.64, 131.16 (q, J_{C-F} = 3.7 Hz), 129.89, 128.98, 128.48, 128.36, 127.91, 126.46 (q, J_{C-F} = 34.3 Hz), 122.95 (q, J_{C-F} = 271.8 Hz), 119.17 (s), 114.33 (s), 113.37 (s), 104.60 (s), 36.30 (s), 21.69 (s) ppm.
^{19}F NMR (376 MHz, $CDCl_3$): δ -62.27 (s, 3F) ppm.
HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{24}H_{20}F_3N_2O_3S$: 473.1141; Found: 473.1141.

(*E*)-*N*-(1-(4-bromo-2-cyanophenoxy)-2-phenylvinyl)-*N*,4-dimethylbenzenesul-fonamide (**3an**)



Compound **3an** was prepared following the General Procedure A with *N*,4-dimethyl-*N*-(phenylethynyl)benzenesulfonamide (**1a**, 28.5 mg, 0.1 mmol) and 4-bromo-2-cyanophenol (**2n**, 26.0 mg, 0.15 mmol), and isolated as a light yellow solid (38.2 mg, 0.079 mmol, 79%). m.p.: 122–

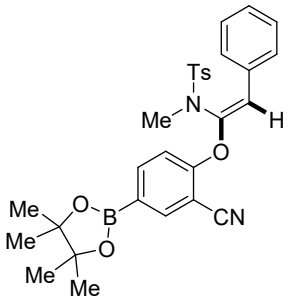
123 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 – 7.60 (m, 4H), 7.46 (d, *J* = 9.0 Hz, 1H), 7.43 – 7.39 (m, 2H), 7.29 (td, *J* = 6.8, 6.4, 1.6 Hz, 2H), 7.21 (d, *J* = 7.9 Hz, 3H), 5.67 (s, 1H), 2.98 (s, 3H), 2.35 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 156.66, 147.61, 144.47, 137.88, 135.88, 135.34, 132.00, 129.82, 128.89, 128.25, 128.13, 128.01, 121.41, 116.50, 114.23, 111.59, 106.44, 36.21, 21.71 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{23}H_{20}BrN_2O_3S$: 483.0373; Found: 483.0378.

(*E*)-*N*-(1-(2-cyano-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)-2-phenylvinyl)-*N*,4-dimethylbenzenesulfonamide (**3ao**)



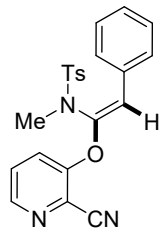
Compound **3ao** was prepared following the General Procedure A with *N*,4-dimethyl-*N*-(phenylethynyl)benzenesulfonamide (**1a**, 28.5 mg, 0.1 mmol) and 2-hydroxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (**2o**, 36.8 mg, 0.15 mmol), and isolated as a white solid (16.5 mg, 0.031 mmol, 31%). m.p.: 159–160 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, *J* = 1.5 Hz, 1H), 7.99 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.53 – 7.47 (m, 2H), 7.39 – 7.32 (m, 2H), 7.30 – 7.23 (m, 3H), 5.76 (s, 1H), 3.06 (s, 3H), 2.41 (s, 3H), 1.34 (s, 12H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 159.49, 147.13, 144.34, 140.93, 140.66, 135.33, 132.24, 129.78, 128.83, 128.30, 128.09, 128.01, 118.52, 115.54, 111.95, 104.29, 84.61, 36.16, 24.95, 21.69 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{29}H_{32}BN_2O_5S$: 531.2119; Found: 531.2126.

(*E*)-*N*-(1-((2-cyanopyridin-3-yl)oxy)-2-phenylvinyl)-*N*,4-dimethylbenzenesul-fonamide (**3ap**)



Compound **3ap** was prepared following the General Procedure A with *N*,4-dimethyl-*N*-(phenylethynyl)benzenesulfonamide (**1a**, 28.5 mg, 0.1 mmol) and 2-cyano-3-hydroxypyridine (**2p**, 18.0 mg, 0.15 mmol), and isolated as a white solid (26.8 mg, 0.066 mmol, 66%). m.p.: 122–123 °C

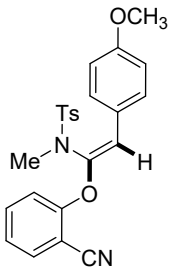
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 – 8.38 (m, 1H), 8.00 (dd, *J* = 8.7, 1.0 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.48 (ddt, *J* = 8.7, 4.5, 0.5 Hz, 1H), 7.45 – 7.41 (m, 2H), 7.35 – 7.27 (m, 2H), 7.25 – 7.21 (m, 3H), 5.71 (s, 1H), 2.98 (s, 3H), 2.36 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 155.68, 147.34, 146.23, 144.70, 135.20, 131.68, 129.91, 128.97, 128.38, 128.34, 128.27, 127.90, 127.37, 125.43, 114.53, 112.03, 36.31, 21.71.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{22}H_{20}N_3O_3S$: 406.1220; Found: 406.1217 ppm.

(*E*)-*N*-(1-(2-cyanophenoxy)-2-(4-methoxyphenyl)vinyl)-*N*,4-dimethylbenzenesul-fonamide (**3bf**)

Compound **3bf** was prepared following the General Procedure A with *N*-[2-(4-methoxyphenyl)ethynyl]-*N*,4-dimethylbenzenesulfonamide (**1b**, 131.5 mg, 0.1 mmol) and



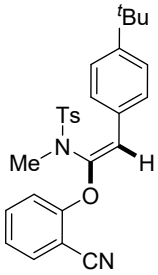
2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as light yellow oil (19.6 mg, 0.045 mmol, 45%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.64 – 7.53 (m, 3H), 7.45 (d, *J* = 8.7 Hz, 2H), 7.26 (d, *J* = 9.0 Hz, 2H), 7.22 – 7.15 (m, 1H), 5.71 (s, 2H), 3.80 (s, 1H), 3.06 (s, 3H), 2.40 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 159.34, 157.68, 146.04, 144.25, 135.40, 134.74, 133.78, 129.75, 129.59, 128.12, 124.70, 124.20, 119.48, 115.69, 114.27, 111.71, 104.61, 55.39, 35.99, 21.69 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{24}H_{23}N_2O_4S$: 435.1373; Found: 435.1378.

(*E*)-*N*-(2-(4-(*tert*-butyl)phenyl)-1-(2-cyanophenoxy)vinyl)-*N*,4-dimethylbenzene-sulfonamide (**3cf**)



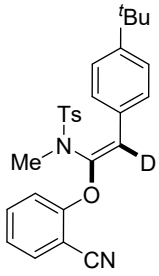
Compound **3cf** was prepared following the General Procedure A with *N*-[2-[4-(1,1-dimethylethyl)phenyl]ethynyl]-*N*,4-dimethylbenzenesulfonamide (**1c**, 34.1 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as white solid (39.2 mg, 0.085 mmol, 85%). m.p.: 124–125 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.1 Hz, 2H), 7.64 – 7.54 (m, 3H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.64 – 7.54 (m, 1H), 5.72 (s, 1H), 3.08 (s, 3H), 2.40 (s, 3H), 1.31 (s, 9H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 157.59, 151.09, 147.02, 144.25, 135.42, 134.73, 133.76, 129.75, 129.31, 128.15, 128.00, 125.79, 124.30, 119.64, 115.66, 111.58, 104.67, 36.11, 34.73, 31.33, 21.70 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{27}H_{29}N_2O_3S$: 461.1893; Found: 461.1918.

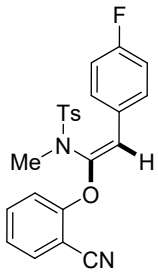
(*E*)-*N*-(2-(4-(*tert*-butyl)phenyl)-1-(2-cyanophenoxy)vinyl-2-*d*)-*N*,4-dimethylbenzenesulfonamide (**3cf-D**)



Compound **3cf-D** was prepared following the General Procedure B with *N*-[2-[4-(1,1-dimethylethyl)phenyl]ethynyl]-*N*,4-dimethylbenzenesulfonamide (34.1 mg, 0.1 mmol) and 2-cyanophenol-D (17.9 mg, 0.15 mmol), and isolated as a white solid (37.4 mg, 0.081 mmol, 81% with 76% D).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.65 – 7.57 (m, 3H), 7.49 – 7.45 (m, 2H), 7.41 – 7.36 (m, 2H), 7.30 – 7.26 (m, 2H), 7.24 – 7.18 (m, 1H), 5.73 (s, 0.24H), 3.09 (s, 3H), 2.42 (s, 3H), 1.32 (s, 9H).

(*E*)-*N*-(1-(2-cyanophenoxy)-2-(4-fluorophenyl)vinyl)-*N*,4-dimethylbenzenesul-fonamide (**3df**)

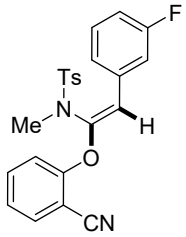


Compound **3df** was prepared following the General Procedure A with *N*-[2-(4-fluorophenyl)ethynyl]-*N*,4-dimethylbenzenesulfonamide (**1d**, 30.3 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a light yellow solid (18.6 mg, 0.044 mmol, 44%). m.p.: 119–120 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.4 Hz, 2H), 7.66 – 7.59 (m, 2H), 7.57 – 7.52 (m, 1H), 7.52 – 7.46 (m, 2H), 7.31 – 7.20 (m, 3H), 7.07 – 6.99 (m, 2H), 5.68 (s, 1H), 3.09 (d, *J* = 0.4 Hz, 3H), 2.41 (s, 3H) ppm.

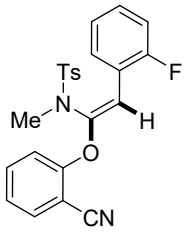
^{13}C NMR (100 MHz, $CDCl_3$): 162.22 (d, J_{C-F} = 248.1 Hz), 157.04, 147.73, 144.45, 135.19, 134.90, 133.89, 129.97 (d, J_{C-F} = 8.0 Hz), 129.81, 128.54 (d, J_{C-F} = 3.0 Hz), 128.16, 124.77, 120.05, 115.77 (d, J_{C-F} = 21.5 Hz), 115.56, 110.13, 105.08, 36.01, 21.69 ppm.
^{19}F NMR (376 MHz, $CDCl_3$): δ -90.53 – -130.22 (m) ppm.
HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{23}H_{20}FN_2O_3S$: 423.1173; Found: 423.1172.

(*E*)-*N*-(1-(2-cyanophenoxy)-2-(3-fluorophenyl)vinyl)-*N*,4-dimethylbenzenesul-fonamide (**3ef**)



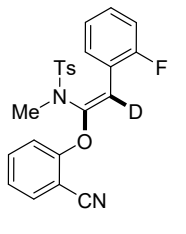
Compound **3ef** was prepared following the General Procedure A with *N*-[2-(3-fluorophenyl)ethynyl]-*N*,4-dimethylbenzenesulfonamide (**1e**, 30.3 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a white solid (30.0 mg, 0.071 mmol, 71%). m.p.: 130–131 °C.
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, 2H), 7.64 (s, 2H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.33 – 7.23 (m, 5H), 7.19 (d, *J* = 10.4 Hz,1H), 6.94 (t, *J* = 7.6 Hz, 1H), 5.62 (s, 1H), 3.11 (s, 3H), 2.41 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$): δ 162.95 (d, J_{C-F} = 245.2 Hz), 156.76, 149.03, 144.47, 135.17, 134.90, 134.70 (d, J_{C-F} = 8.2 Hz), 133.88, 130.19 (d, J_{C-F} = 8.5 Hz), 129.80, 128.17, 124.98, 124.01 (d, J_{C-F} = 2.1 Hz), 120.41, 115.46, 114.78 (d, J_{C-F} = 42.9 Hz), 114.77, 109.44, 105.30, 36.09, 21.70 ppm.
^{19}F NMR (376 MHz, $CDCl_3$): δ -112.65 – -112.69 (m) ppm.
HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{23}H_{20}FN_2O_3S$: 423.1173; Found: 423.1173.

(*E*)-*N*-(1-(2-cyanophenoxy)-2-(2-fluorophenyl)vinyl)-*N*,4-dimethylbenzenesul-fonamide (**3ff**)



Compound **3ff** was prepared following the General Procedure A with *N*-[2-(2-fluorophenyl)ethynyl]-*N*,4-dimethylbenzenesulfonamide (**1f**, 30.3 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a white solid (38.9 mg, 0.092 mmol, 92%). m.p.: 127–128 °C.
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (t, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 7.8 Hz, 2H), 7.64 (t, J_{C-F} = 8.3 Hz, 2H), 7.57 (d, *J* = 8.3 Hz, 1H), 7.32 – 7.14 (m, 5H), 7.01 (t, *J* = 9.2 Hz, 1H), 5.86 (s, 1H), 3.08 (s, 3H), 2.42 (s, 3H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$): δ 159.88 (d, J_{C-F} = 248.6 Hz), 156.88, 149.17, 144.38, 135.24, 134.83, 133.88, 129.76, 129.31 (d, J_{C-F} = 8.4 Hz), 128.81 (d, J_{C-F} = 1.2 Hz), 128.12, 124.85, 124.57 (d, J_{C-F} = 3.1 Hz), 120.54 (d, J_{C-F} = 12.2 Hz), 120.16, 115.48, 115.26, 105.15, 102.47 (d, J_{C-F} = 6.1 Hz), 36.13, 21.68 ppm.
^{19}F NMR (376 MHz, $CDCl_3$) δ -115.93 – -116.04 (m) ppm.
HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{23}H_{20}FN_2O_3S$: 423.1173; Found: 423.1187.

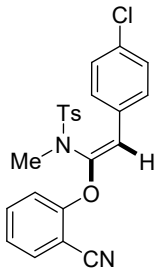
(*E*)-*N*-(1-(2-cyanophenoxy)-2-(2-fluorophenyl)vinyl-2-*d*)-*N*,4-dimethylbenzenesulfonamide(**3ff-D**)



Compound **3ff-D** was prepared following the General Procedure B with *N*-[2-(2-fluorophenyl)ethynyl]-*N*,4-dimethylbenzenesulfonamide (**1f**, 30.3 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a white solid (36.8 mg, 0.087 mmol, 87% with 84% D).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.76 (s, 2H), 7.61 (d, *J* = 26.9 Hz, 3H), 7.32 – 7.15 (m, 5H), 7.00 (s, 1H), 5.86 (s, 0.16H), 3.08 (s, 3H), 2.42 (s, 3H).

(*E*)-*N*-(2-(4-chlorophenyl)-1-(2-cyanophenoxy)vinyl)-*N*,4-dimethylbenzenesul-fonamide (**3gf**)



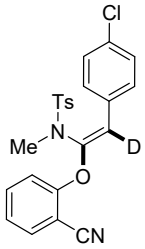
Compound **3gf** was prepared following the General Procedure with A *N*-[2-(4-chlorophenyl)ethynyl]-*N*,4-dimethylbenzenesulfonamide (**1g**, 32.0 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a white solid (32.5 mg, 0.074 mmol, 74%). m.p.: 108–109 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.1 Hz, 2H), 7.56 (t, *J* = 7.9 Hz, 2H), 7.47 (d, *J* = 8.3 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.25 – 7.13 (m, 5H), 5.56 (s, 1H), 3.01 (s, 3H), 2.34 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 156.85, 148.49, 144.47, 135.17, 134.90, 133.89, 133.46, 131.03, 129.80, 129.46, 128.94, 128.14, 124.91, 120.28, 36.04, 21.70 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{23}H_{20}ClN_2O_3S$: 439.0878; Found: 439.0901.

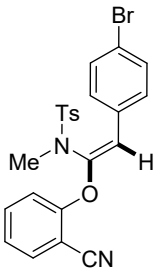
(*E*)-*N*-(2-(4-chlorophenyl)-1-(2-cyanophenoxy)vinyl-2-*d*)-*N*,4-dimethylbenzenesulfonamide (**3gf-D**)



Compound **3gf-D** was prepared following the General Procedure B with *N*-[2-(4-chlorophenyl)ethynyl]-*N*,4-dimethylbenzenesulfonamide (**1g**, 32.0 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a white solid (24.6 mg, 0.056 mmol, 56% with 76% D).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (dd, *J* = 5.7, 2.4 Hz, 2H), 7.69 – 7.61 (m, 2H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.30 (ddd, *J* = 13.4, 6.7, 4.7 Hz, 5H), 5.63 (d, *J* = 1.9 Hz, 0.24H), 3.09 (d, *J* = 2.2 Hz, 3H), 2.43 (d, *J* = 3.4 Hz, 3H).

(*E*)-*N*-(2-(4-bromophenyl)-1-(2-cyanophenoxy)vinyl)-*N*,4-dimethylbenzenesul-fonamide (**3hf**)



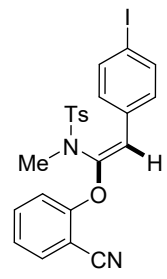
Compound **3hf** was prepared following the General Procedure A with *N*-[2-(4-bromophenyl)ethynyl]-*N*,4-dimethylbenzenesulfonamide (**1h**, 36.4 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a light yellow solid (39.8mg, 0.086 mmol, 86%). m.p.: 122–123 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 2H), 7.51 (d, *J* = 8.6 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.29 – 7.20 (m, 3H), 5.60 (s, 1H), 3.07 (s, 3H), 2.40 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 156.76, 148.51, 144.54, 135.09, 134.98, 134.49, 133.92, 133.12, 131.88, 131.52, 129.83, 129.76, 128.13, 125.00, 121.65, 120.56, 120.33, 115.50, 109.62, 105.20, 36.03, 21.72 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{23}H_{20}BrN_2O_3S$: 483.0373; Found: 483.0401.

(*E*)-*N*-(1-(2-cyanophenoxy)-2-(4-iodophenyl)vinyl)-*N*,4-dimethylbenzenesul-fonamide (**3if**)



Compound **3if** was prepared following the General Procedure A with *N*-[2-(4-iodophenyl)ethynyl]-*N*,4-dimethylbenzenesulfonamide (**1i**, 41.1 mg,

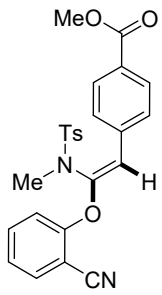
0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a white solid (41.5 mg, 0.075 mmol, 75%). m.p.: 126–127 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, J = 8.4 Hz, 2H), 7.66 – 7.59 (m, 2H), 7.56 – 7.50 (m, 1H), 7.46 – 7.42 (m, 2H), 7.37 – 7.32 (m, 2H), 7.30 – 7.22 (m, 3H), 5.60 (s, 1H), 3.07 (s, 3H), 2.41 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 156.83, 148.62, 144.47, 135.20, 134.90, 133.89, 131.90, 131.51, 129.80, 128.14, 124.93, 121.67, 120.34, 115.48, 109.56, 105.27, 36.05, 21.72 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{23}H_{20}IN_2O_3S$: 531.0234; Found: 531.0237.

(*E*)-4-(2-(2-cyanophenoxy)-2-((*N*,4-dimethylphenyl)-sulfonamido)vinyl)benzoate (**3jf**)



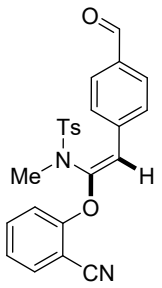
Compound **3jf** was prepared following the General Procedure A with methyl 4-[2-[methyl[(4-methylphenyl)sulfonyl]amino]ethynyl]benzoate (**1j**, 34.3 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a light yellow solid (36.6 mg, 0.079 mmol, 79%). m.p.: 118–119 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 – 7.96 (m, 2H), 7.79 (d, *J* = 6.9 Hz, 2H), 7.70 – 7.63 (m, 2H), 7.60 – 7.52 (m, 3H), 7.30 (d, *J* = 7.3 Hz, 3H), 5.67 (s, 1H), 3.92 (s, 3H), 3.12 (s, 3H), 2.42 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 166.96, 156.52, 149.86, 144.58, 137.44, 135.08, 135.03, 134.48, 133.94, 133.16, 130.01, 129.85, 128.95, 128.16, 128.08, 125.24, 120.67, 120.53, 115.43, 109.14, 105.41, 52.30, 36.14, 21.70 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{25}H_{23}N_2O_5S$: 463.1332; Found: 463.1346.

(*E*)-*N*-(1-(2-cyanophenoxy)-2-(4-formylphenyl)vinyl)-*N*,4-dimethylbenzenesul-fonamide (**3kf**)



Compound **3kf** was prepared following the General Procedure A with *N*-((4-formylphenyl)ethynyl)-*N*,4-dimethylbenzenesulfonamide (**1k**, 31.3 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a white solid (30.7 mg, 0.071 mmol, 71%). m.p.: 130–131 °C.

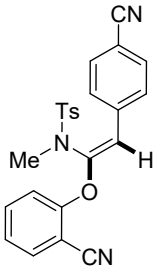
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.98 (s, 1H), 7.82 (dd, *J* = 20.1, 7.2 Hz, 4H), 7.71 – 7.61 (m, 4H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.30 (d, *J* = 5.9 Hz, 3H), 5.65 (s, 1H), 3.12 (s, 3H), 2.43 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 191.77, 156.33, 150.52, 144.64, 139.14, 135.21, 135.01, 133.97, 130.14, 129.85, 128.64, 128.18, 125.39, 120.81, 115.33, 108.74, 105.61, 36.14, 21.70 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{24}H_{21}N_2O_4S$: 433.1217; Found: 433.1234.

(*E*)-*N*-(1-(2-cyanophenoxy)-2-(4-cyanophenyl)vinyl)-*N*,4-dimethylbenzene-sulfonamide (**3lf**)

Compound **3lf** was prepared following the General Procedure A with *N*-((4-cyanophenyl)ethynyl)-*N*,4-dimethylbenzenesulfonamide (**1l**, 31.0 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as light yellow oil (27.5 mg, 0.064 mmol, 64%).



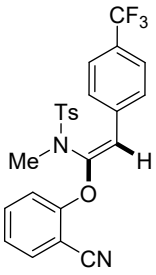
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.0 Hz, 2H), 7.68 (t, *J* = 7.9 Hz,

2H), 7.63 – 7.55 (m, 4H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.32 (t, *J* = 7.3 Hz, 3H), 5.58 (s, 1H), 3.12 (s, 3H), 2.44 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 156.10, 150.80, 144.77, 137.70, 135.08, 134.82, 134.04, 132.47, 129.90, 128.65, 128.21, 125.60, 120.96, 118.94, 115.28, 110.77, 108.11, 105.74, 36.08, 21.73 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{24}H_{20}N_3O_3S$: 430.1220; Found: 430.1221.

(*E*)-*N*-(1-(2-cyanophenoxy)-2-(4-(trifluoromethyl)phenyl)vinyl)-*N*,4-dimethyl-benzenesulfonamide (**3mf**)



Compound **3mf** was prepared following the General Procedure A with *N*,4-dimethyl-*N*-((4-(trifluoromethyl)phenyl)-ethynyl)benzenesulfonamide (**1m**, 35.3 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a light yellow solid (33.1 mg, 0.07mmol, 70%). m.p.: 138–139 °C.

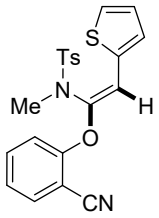
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 7.7 Hz, 2H), 7.64 (t, *J* = 8.2 Hz, 2H), 7.58 – 7.50 (m, 5H), 7.27 (d, *J* = 7.0 Hz, 3H), 5.63 (s, 1H), 3.09 (s, 3H), 2.40 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 156.48, 149.96, 144.57, 136.37, 135.07, 134.97, 133.94, 129.81, 129.37 (q, J_{C-F} = 32.6 Hz), 128.36, 128.15, 125.64 (q, J_{C-F} = 3.5 Hz), 125.25, 124.14 (q, J_{C-F} = 271.7 Hz), 120.70, 115.39, 108.70, 105.53, 36.11, 21.68 ppm.

^{19}F NMR (376 MHz, $CDCl_3$): δ -62.50 (s, 3F) ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{24}H_{20}F_3N_2O_3S$: 473.1141; Found: 473.1163.

(*E*)-*N*-(1-(2-cyanophenoxy)-2-(thiophen-2-yl)vinyl)-*N*,4-dimethylbenzenesul-fonamide (**3nf**)



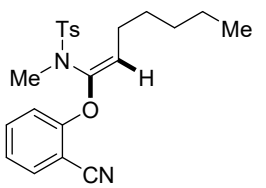
Compound **3nf** was prepared following the General Procedure with *N*,4-dimethyl-*N*-(thiophen-2-ylethynyl)benzenesulfonamide (**1n**, 29.1 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a light yellow solid (28.4 mg, 0.069 mmol, 69%). m.p.: 122–123 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 7.8 Hz, 2H), 7.63 (d, *J* = 5.8 Hz, 2H), 7.51 (d, *J* = 8.7 Hz, 1H), 7.34 – 7.22 (m, 4H), 6.98 (s, 2H), 6.01 (s, 1H), 3.18 (s, 3H), 2.42 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 156.98, 146.03, 144.44, 135.05, 134.91, 133.95, 129.76, 128.43, 128.29, 127.07, 126.76, 124.79, 119.85, 115.38, 107.67, 105.02, 35.83, 21.70 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{21}H_{19}N_2O_3S_2$: 411.0832; Found: 411.0832.

(*E*)-*N*-(1-(2-cyanophenoxy)hept-1-en-1-yl)-*N*,4-dimethyl-benzenesulfonamide (**3of**)



Compound **3of** was prepared following the General Procedure A with *N*-(hept-1-yn-1-yl)-*N*,4-dimethyl-benzenesulfonamide (**1o**, 27.9 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as light yellow oil (33.9 mg, 0.085 mmol, 85%).

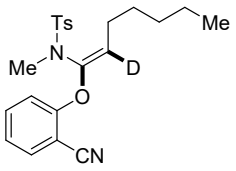
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.61 – 7.54 (m, 2H), 7.36 (d, *J* = 9.0 Hz, 1H), 7.30 – 7.24 (m, 2H), 7.18 (t, *J* = 7.6 Hz, 1H), 4.90 (t, *J* = 7.5 Hz, 1H), 3.07 (s, 3H), 2.40 (s, 3H), 2.26 (q, *J* = 7.4 Hz, 2H), 1.44 – 1.35 (m, 2H), 1.34

– 1.25 (m, 4H), 0.89 (t, *J* = 6.8 Hz, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 157.58, 146.02, 144.01, 135.30, 134.51, 133.81, 129.71, 128.04, 124.07, 119.34, 115.67, 114.23, 104.87, 36.07, 31.59, 28.84, 26.90, 22.52, 21.65, 14.13 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{22}H_{27}N_2O_3S$: 399.1737; Found: 399.1737.

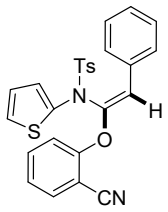
(*E*)-*N*-(1-(2-cyanophenoxy)hept-1-en-1-yl-2-*d*)-*N*,4-dimethylbenzenesulfonamide (**3of-D**)



Compound **3of-D** was prepared following the General Procedure B with *N*-(hept-1-yn-1-yl)-*N*,4-dimethyl-benzenesulfonamide (**1o**, 27.9 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as light yellow oil (33.9 mg, 0.085 mmol, 85% with 100% D).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.60 – 7.55 (m, 2H), 7.36 (dd, *J* = 9.1, 0.7 Hz, 1H), 7.29 – 7.25 (m, 2H), 7.20 – 7.15 (m, 1H), 3.06 (s, 3H), 2.40 (s, 3H), 2.30 – 2.22 (m, 2H), 1.42 – 1.28 (m, 6H), 0.89 (t, *J* = 6.8 Hz, 3H).

(*E*)-*N*-(1-(2-cyanophenoxy)-2-phenylvinyl)-4-methyl-*N*-(thiophen-2-yl)benzene-sulfonamide (**3pf**)



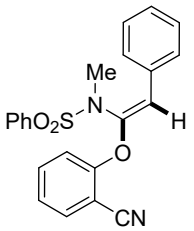
Compound **3pf** was prepared following the General Procedure A with 4-methyl-*N*-(phenylethynyl)-*N*-(thiophen-3-yl)benzenesulfonamide (**1p**, 35.3 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as a white solid (18.9 mg, 0.04 mmol, 40%). m.p.: 128–129 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.3 Hz, 1H), 7.66 (t, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 7.6 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.37 – 7.23 (m, 5H), 7.14 (d, *J* = 8.2 Hz, 3H), 7.05 (dd, 1H), 5.81 (s, 1H), 2.37 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 157.60, 147.18, 144.57, 135.89, 135.17, 134.98, 133.58, 132.00, 128.60, 128.51, 128.13, 128.04, 125.43, 125.11, 124.63, 120.68, 119.87, 115.70, 112.77, 104.93, 21.73 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{26}H_{21}N_2O_3S_2$: 473.0988; Found: 473.1002.

(*E*)-*N*-(1-(2-cyanophenoxy)-2-phenylvinyl)-*N*-methylbenzene-sulfonamide (**3qf**)



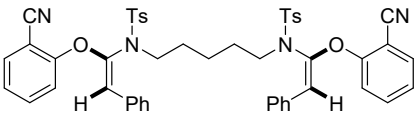
Compound **3qf** was prepared following the General Procedure A with *N*-methyl-*N*-(phenylethynyl)benzenesulfonamide (**1q**, 27.1 mg, 0.1 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as colorless oil (26.6 mg, 0.068 mmol, 68%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 – 7.86 (m, 2H), 7.67 – 7.57 (m, 4H), 7.50 (t, *J* = 7.1 Hz, 4H), 7.39 – 7.32 (m, 2H), 7.30 – 7.21 (m, 2H), 5.74 (s, 1H), 3.10 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 157.22, 147.72, 138.41, 134.83, 133.85, 133.40, 132.32, 129.17, 128.85, 128.26, 128.07, 127.97, 124.62, 119.92, 115.57, 111.10, 104.94, 36.25 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{22}H_{19}N_2O_3S$: 391.1111; Found: 391.1109.

N-((*E*)-1-(2-cyanophenoxy)-2-phenylvinyl)-*N*-(5-((*N*-((*E*)-1-(2-cyanophenoxy)-2-phenylvinyl)-4-methylphenyl)-sulfonamido)pentyl)-4-methylbenzenesulfonamide (**3rf**)



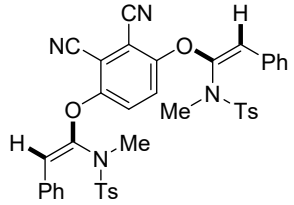
Compound **3rf** was prepared following the General Procedure A with *N*,*N*'-(pentane-1,5-diyl)bis(4-methyl-*N*-(phenylethynyl)benzene-sulfonamide) (**1r**, 30.7 mg, 0.05 mmol) and 2-cyanophenol (17.9 mg, 0.15 mmol), and isolated as light yellow oil (36.8 mg, 0.043 mmol, 87%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 7.7 Hz, 4H), 7.55 (d, *J* = 14.0 Hz, 6H), 7.41 (d, *J* = 7.2 Hz, 4H), 7.25 – 7.10 (m, 12H), 5.72 (s, 2H), 3.06 (t, *J* = 6.7 Hz, 4H), 2.31 (s, 6H), 1.47 – 1.05 (m, 4H), 0.94 – 0.69 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 157.29, 145.98, 144.27, 136.25, 134.88, 133.74, 132.36, 129.74, 128.67, 128.37, 128.18, 127.94, 124.60, 120.12, 115.57, 112.81, 105.15, 48.62, 27.36, 23.84, 21.68 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{49}H_{45}N_4O_4S_2$: 849.2775; Found: 849.2767.

N,*N*'-((1E,1'E)-((2,3-dicyano-1,4-phenylene)-bis(oxy))bis(2-phenylethene-1,1-diyl))bis(*N*,4-dimethylbenzenesulfonamide) (**3aq**)



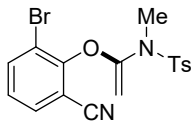
Compound **3aq** was prepared following the General Procedure A with *N*,4-dimethyl-*N*-(phenylethynyl)benzenesulfonamide (**1a**, 28.5 mg, 0.1 mmol) and 3,6-dihydroxyphthalonitrile (**1q**, 12.0 mg, 0.075 mmol), and isolated as a white solid (19 mg, 0.026 mmol, 26%). m.p.: 100–101 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (s, 1H), 7.69 – 7.65 (m, 2H), 7.41 – 7.37 (m, 2H), 7.31 – 7.19 (m, 6H), 5.73 (s, 1H), 2.96 (s, 3H), 2.38 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.34, 147.52, 144.70, 135.20, 131.58, 129.94, 128.95, 128.37, 128.26, 127.98, 126.15, 112.16, 111.94, 107.45, 36.28, 21.73 ppm.

HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{40}H_{35}N_4O_6S_2$: 731.1993; Found: 731.1987.

N-(1-(2-bromo-6-cyanophenoxy)vinyl)-*N*,4-dimethylbenzene-sulfonamide (**3rr**)



Compound **3rr** was prepared following the General Procedure A with *N*-ethynyl-*N*,4-dimethylbenzenesulfonamide (**1r**, 40.6 mg, 0.1 mmol) and 6-bromo-2-cyanophenol (**2r**, 17.9 mg, 0.15 mmol), and isolated as a light yellow solid (24.8 mg, 0.076 mmol, 76%). m.p.: 142–143 °C.

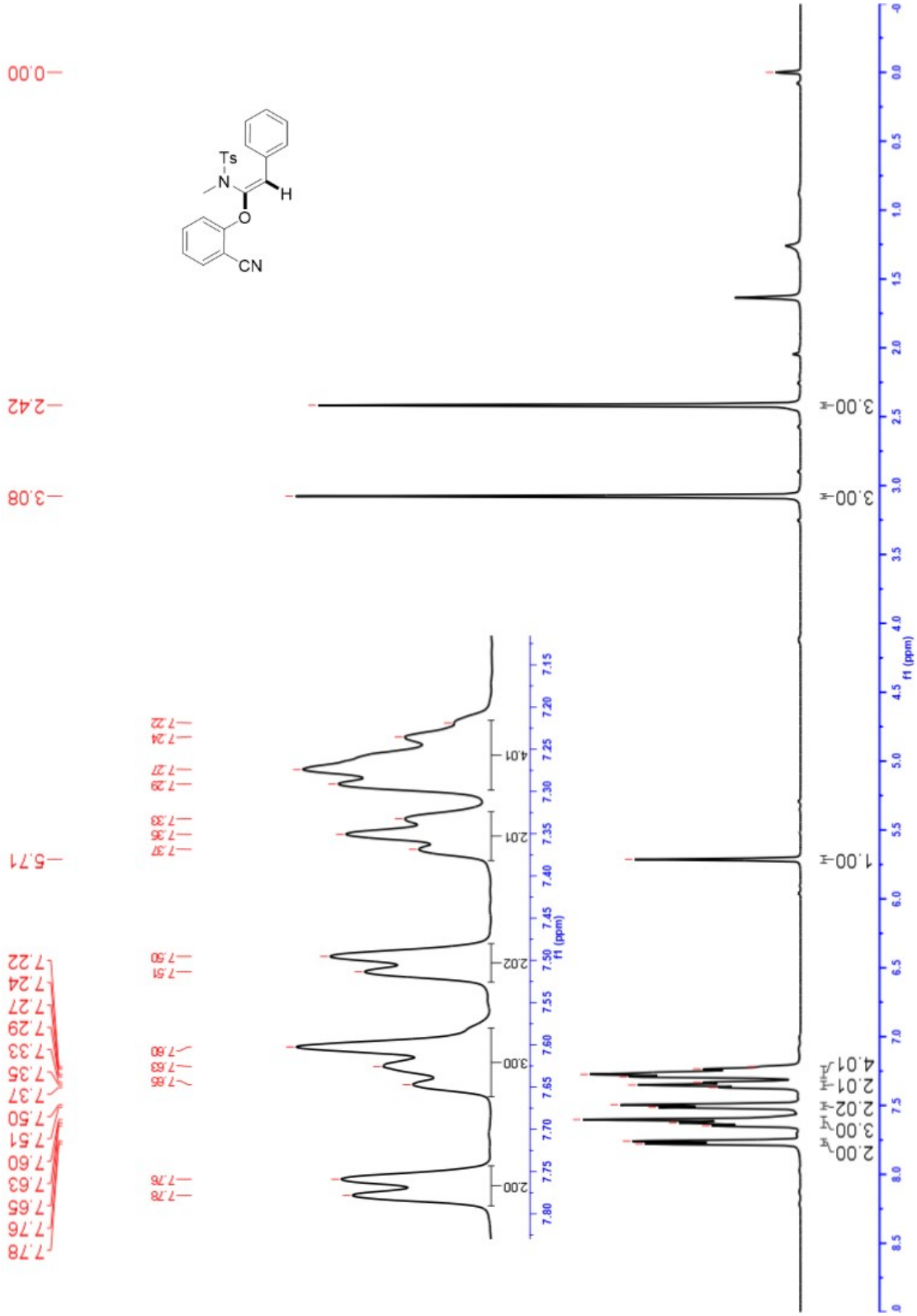
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, *J* = 8.0 Hz, 2H), 7.78 (ddd, *J* = 8.1, 1.5, 1.0 Hz, 1H), 7.56 (ddd, *J* = 7.7, 1.5, 1.0 Hz, 1H), 7.26 (d, *J* = 8.2 Hz, 2H), 7.14 (td, *J* = 8.1, 1.0 Hz, 1H), 4.55 (dd, *J* = 3.6, 1.0 Hz, 1H), 3.71 (dd, *J* = 3.6, 0.9 Hz, 1H), 3.24 (s, 3H), 2.36 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 152.07, 151.83, 144.10, 138.85, 135.16, 133.24, 129.75, 128.38, 127.38, 118.42, 114.71, 109.45, 89.21, 35.67, 21.70 ppm.

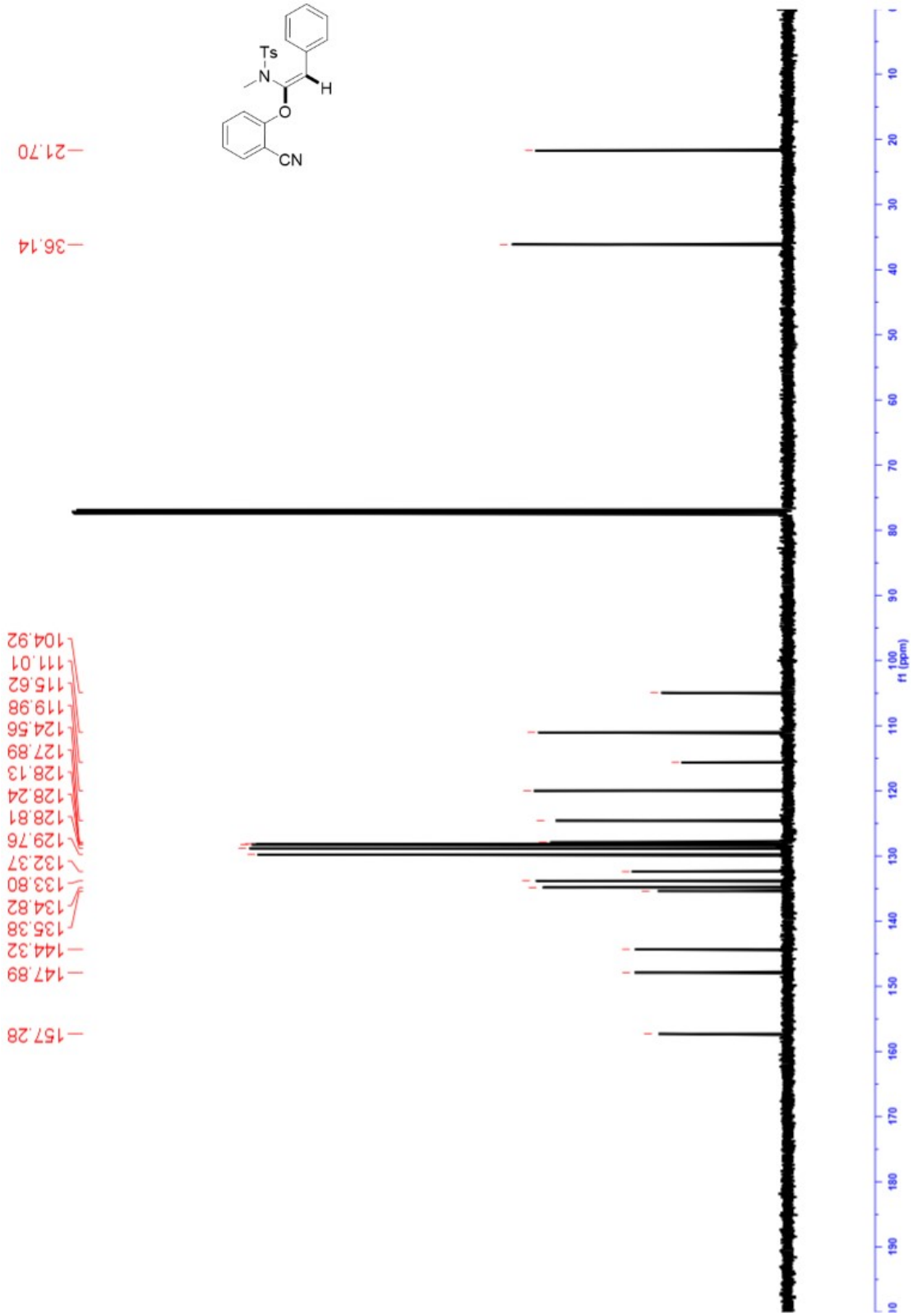
HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{17}H_{16}BrN_2O_3S$: 407.0060; Found: 407.0062.

10. Copies of NMR spectra

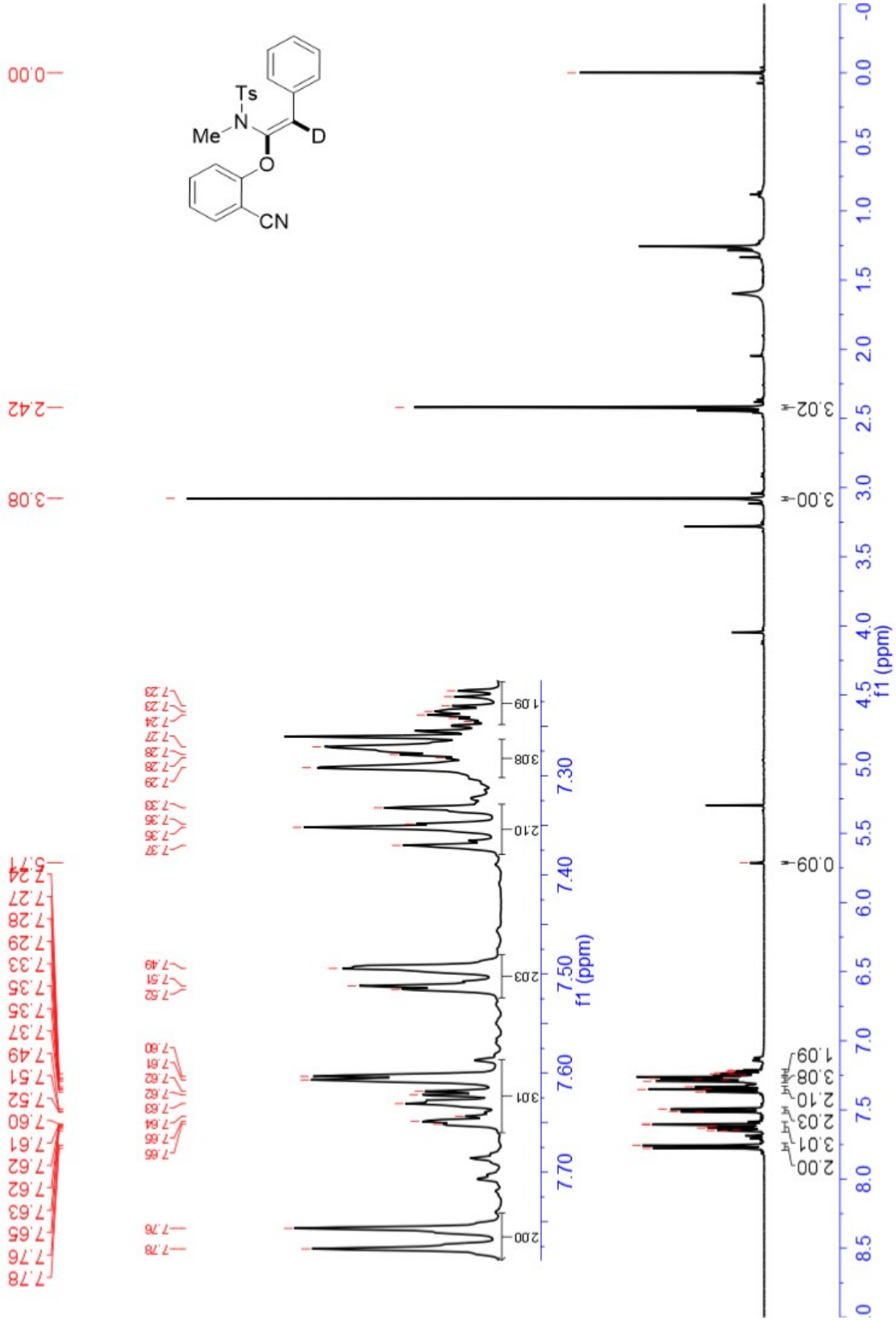
^{1}H NMR of 3af (400 MHz, $CDCl_3$)



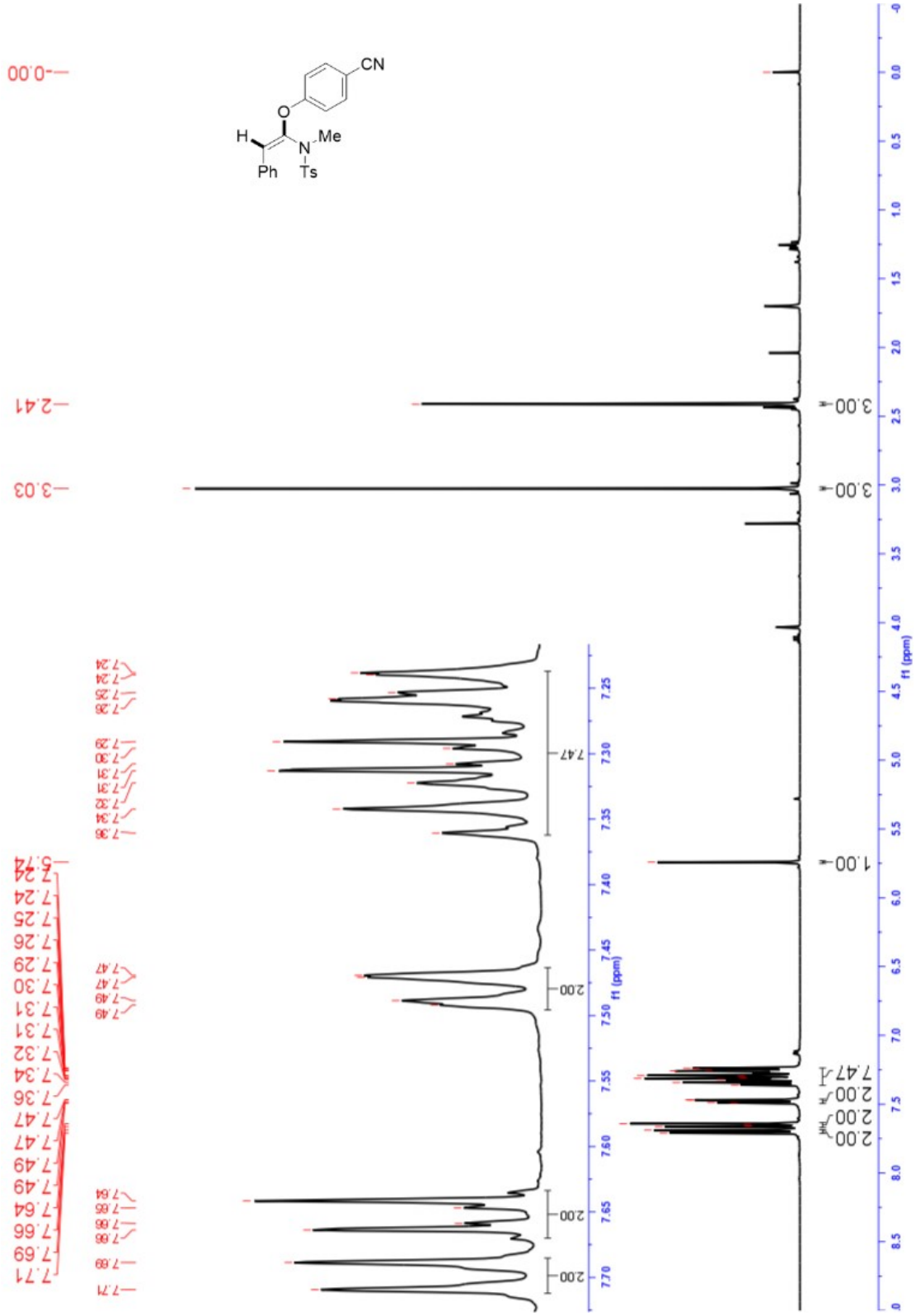
^{13}C NMR of 3af (100 MHz, $CDCl_3$)



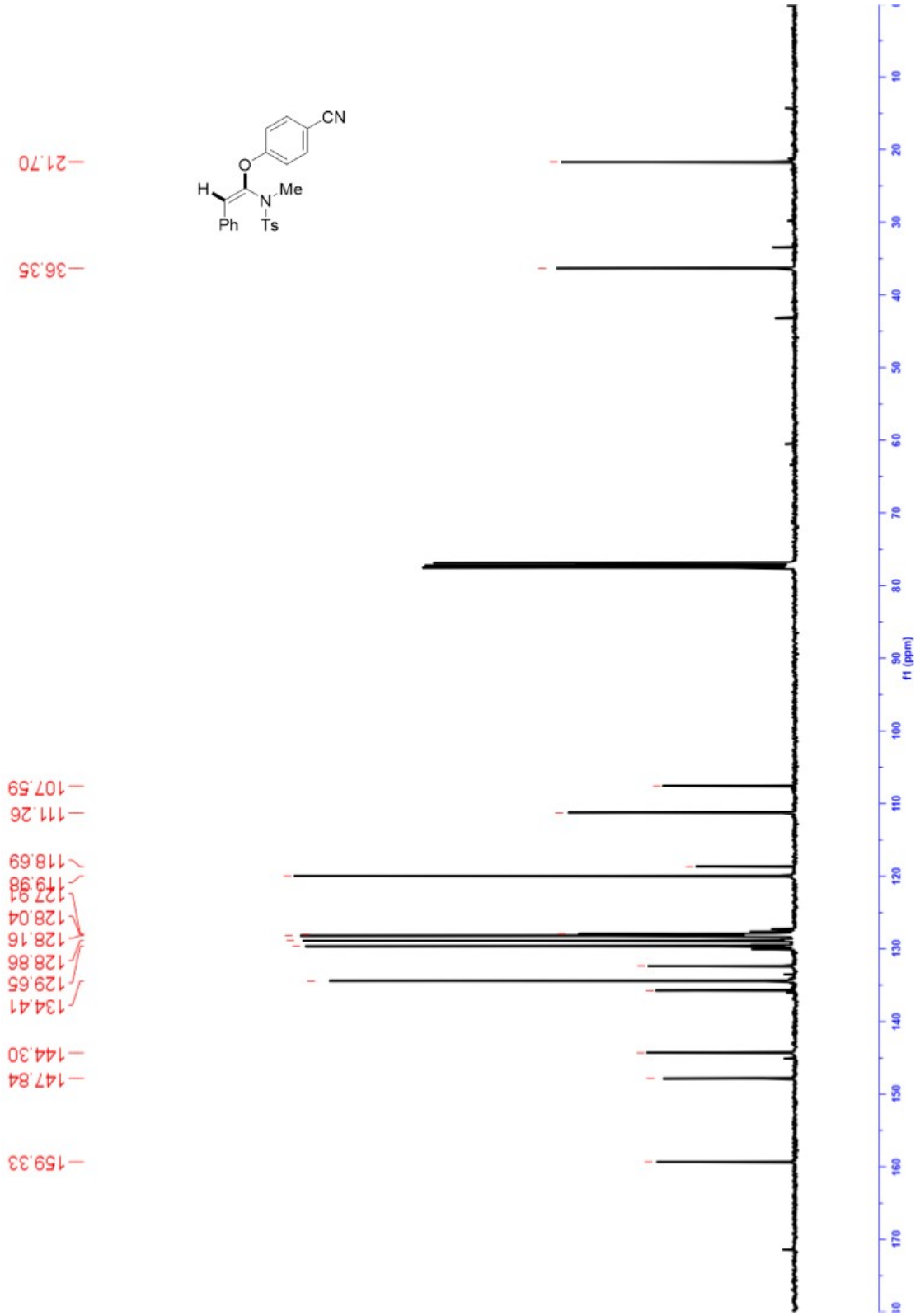
^{1}H NMR of 3af-D (400 MHz, $CDCl_3$)



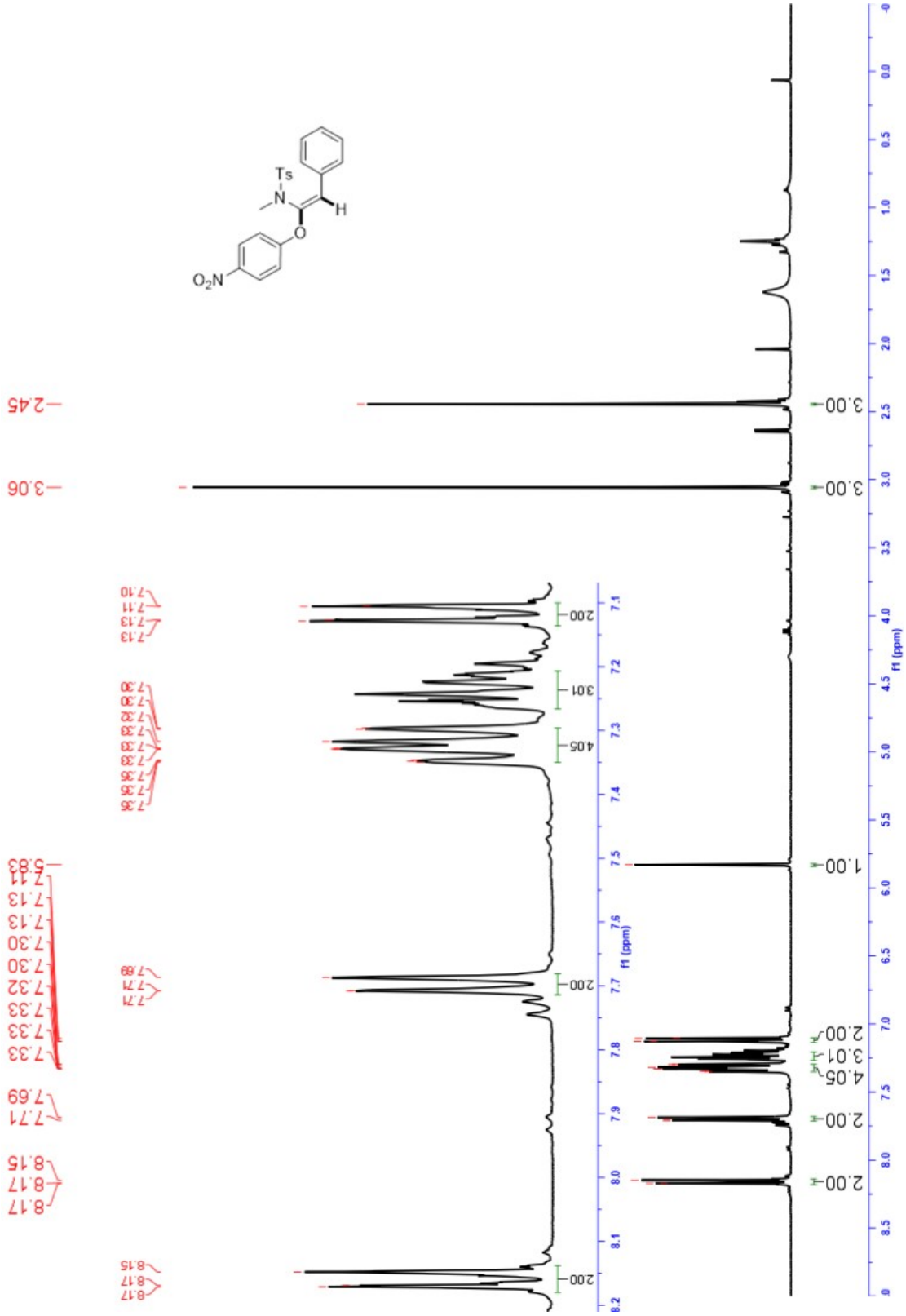
^{1}H NMR of 3ah (400 MHz, $CDCl_3$)



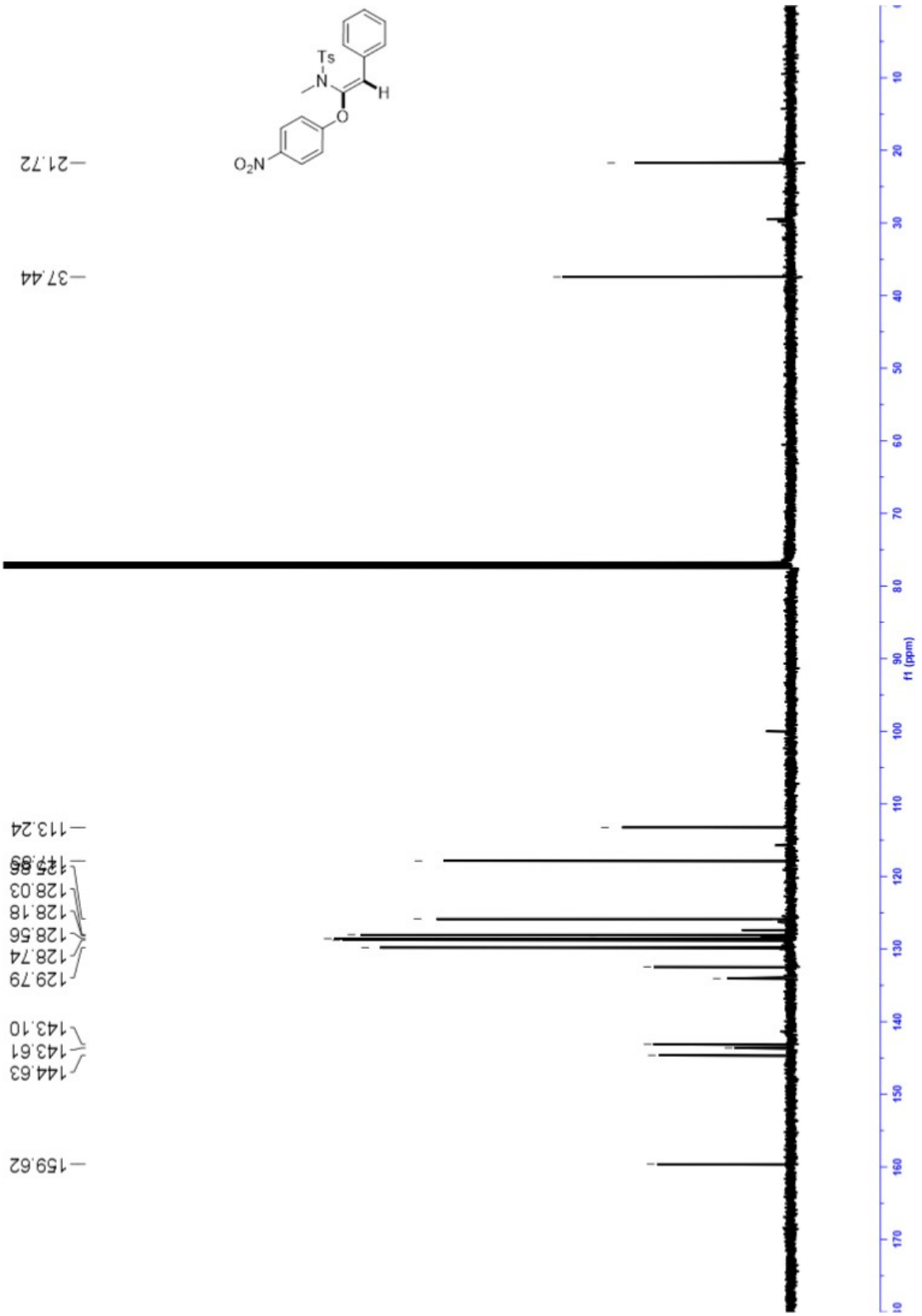
^{13}C NMR of 3ah (100 MHz, $CDCl_3$)



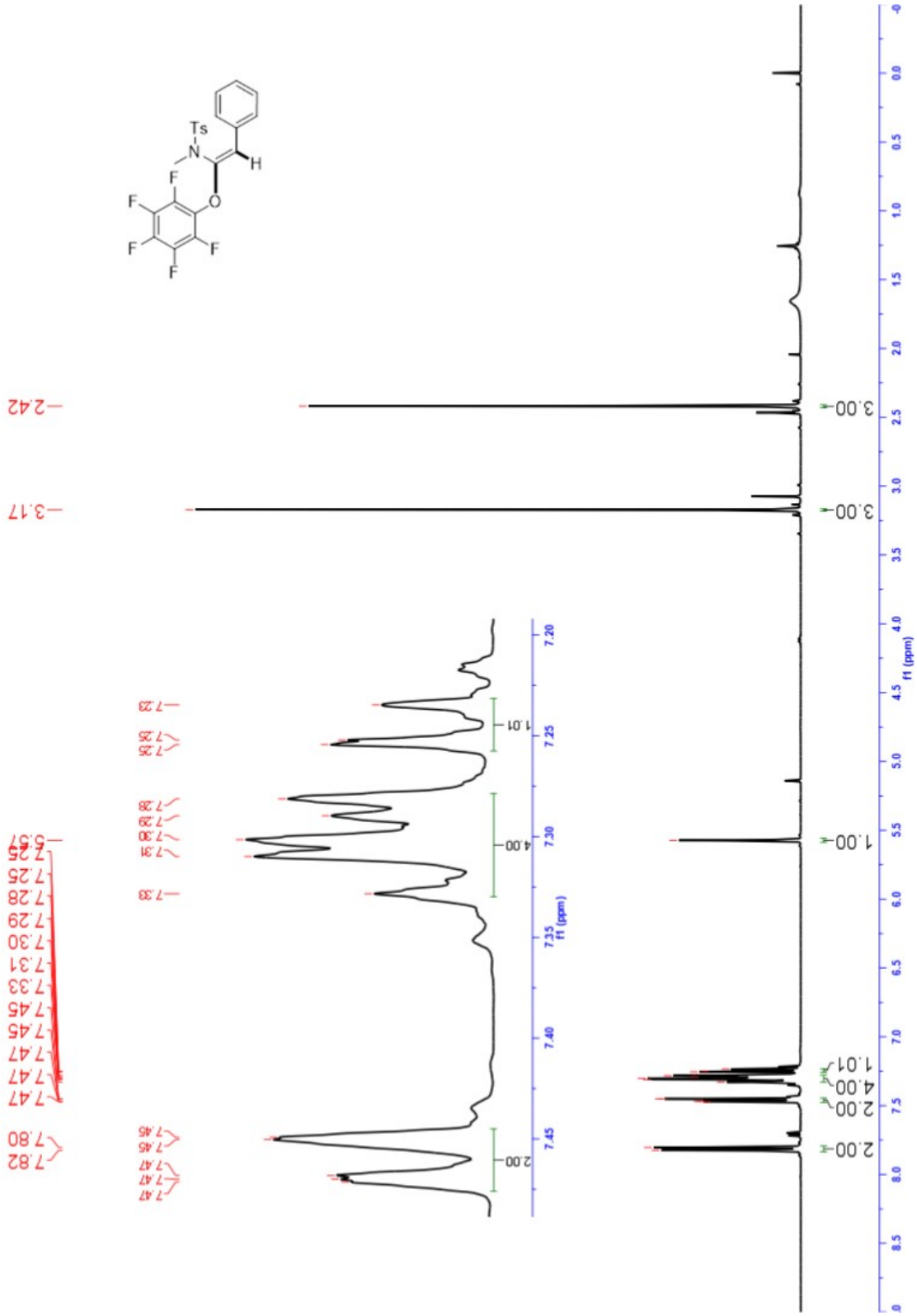
^{1}H NMR of 3ak (400 MHz, $CDCl_3$)



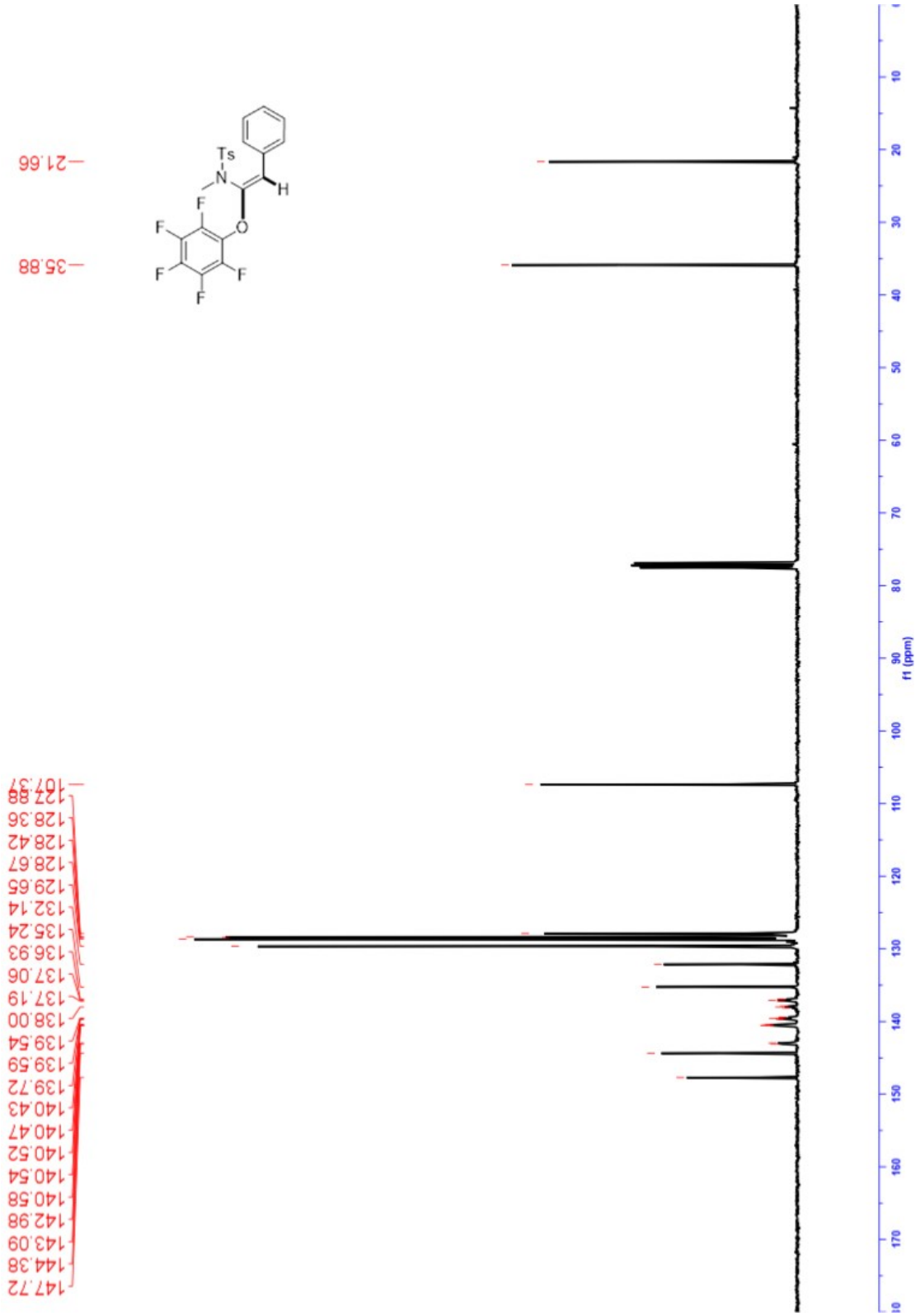
^{13}C NMR of 3ak (100 MHz, $CDCl_3$)



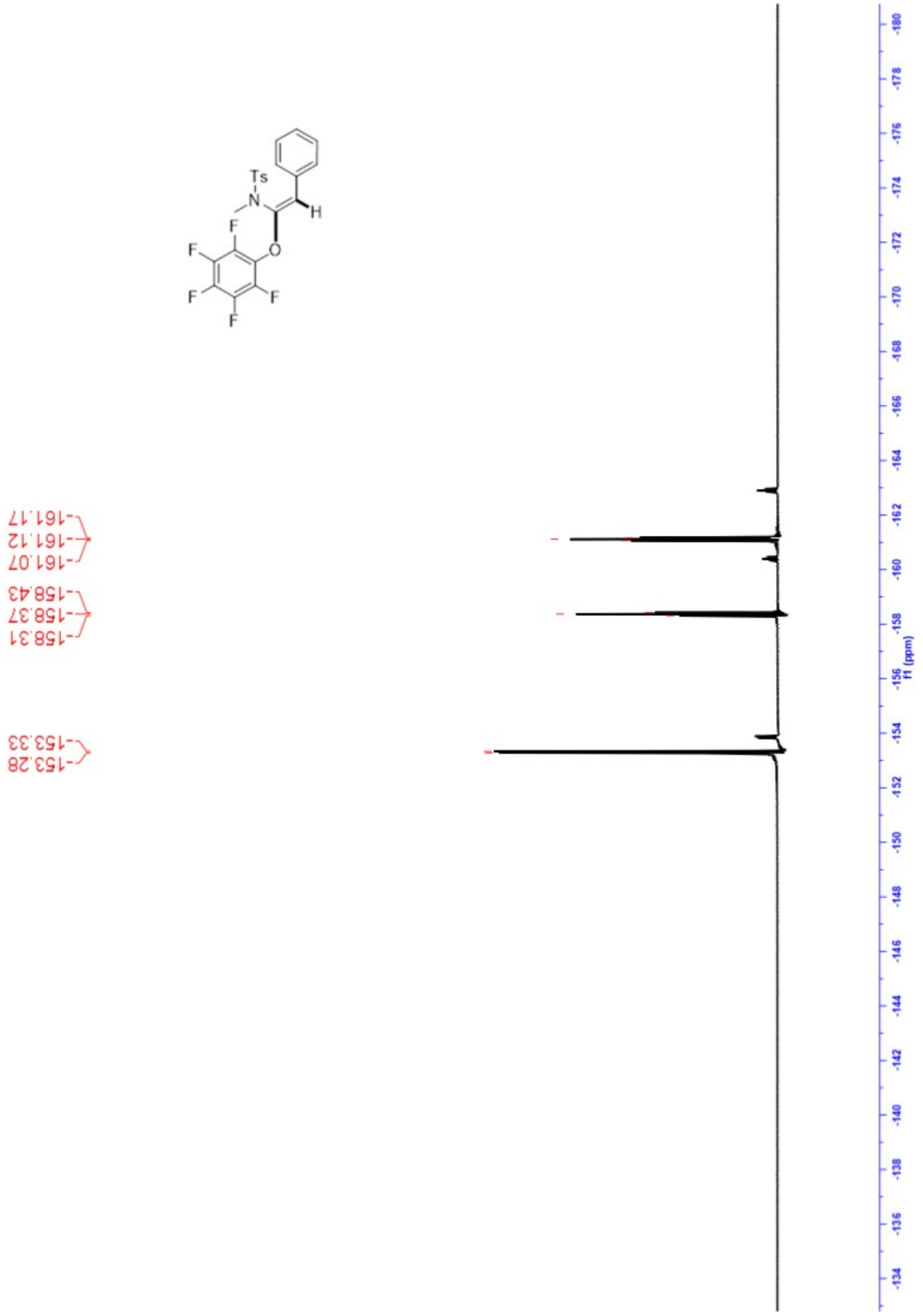
^{1}H NMR of 3al (400 MHz, $CDCl_3$)



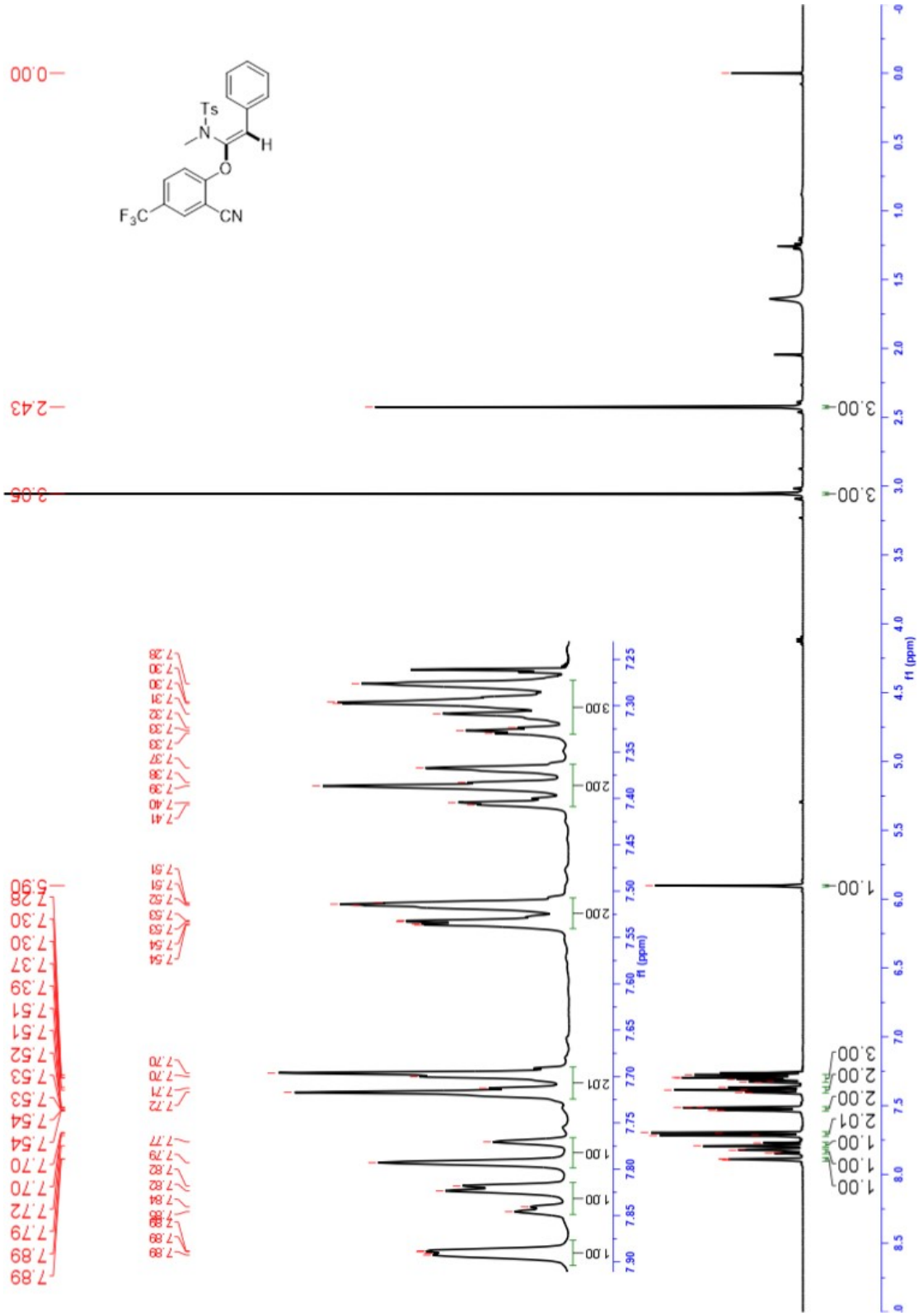
^{13}C NMR of 3al (100 MHz, $CDCl_3$)



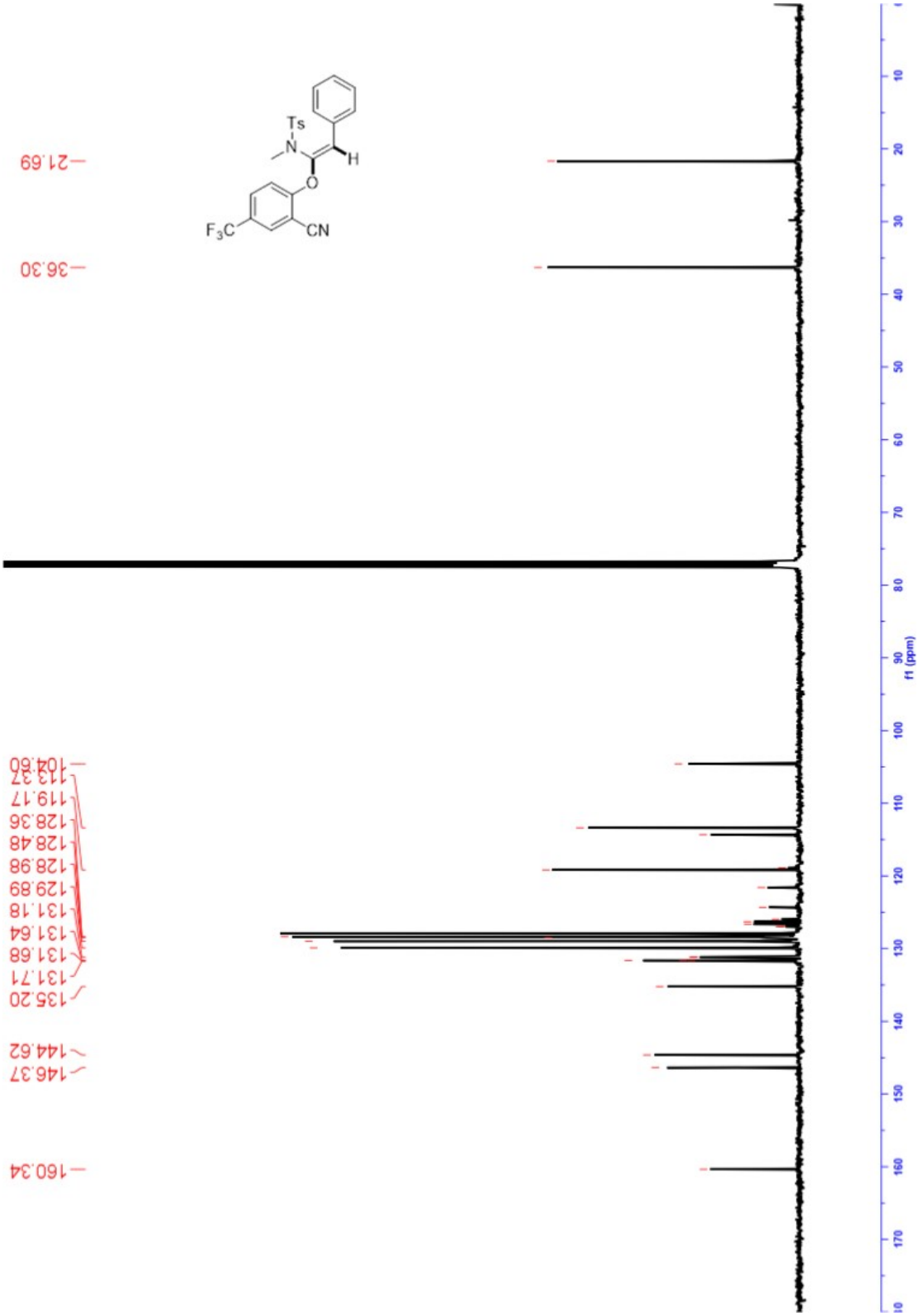
^{19}F NMR of 3al (376 MHz, $CDCl_3$)



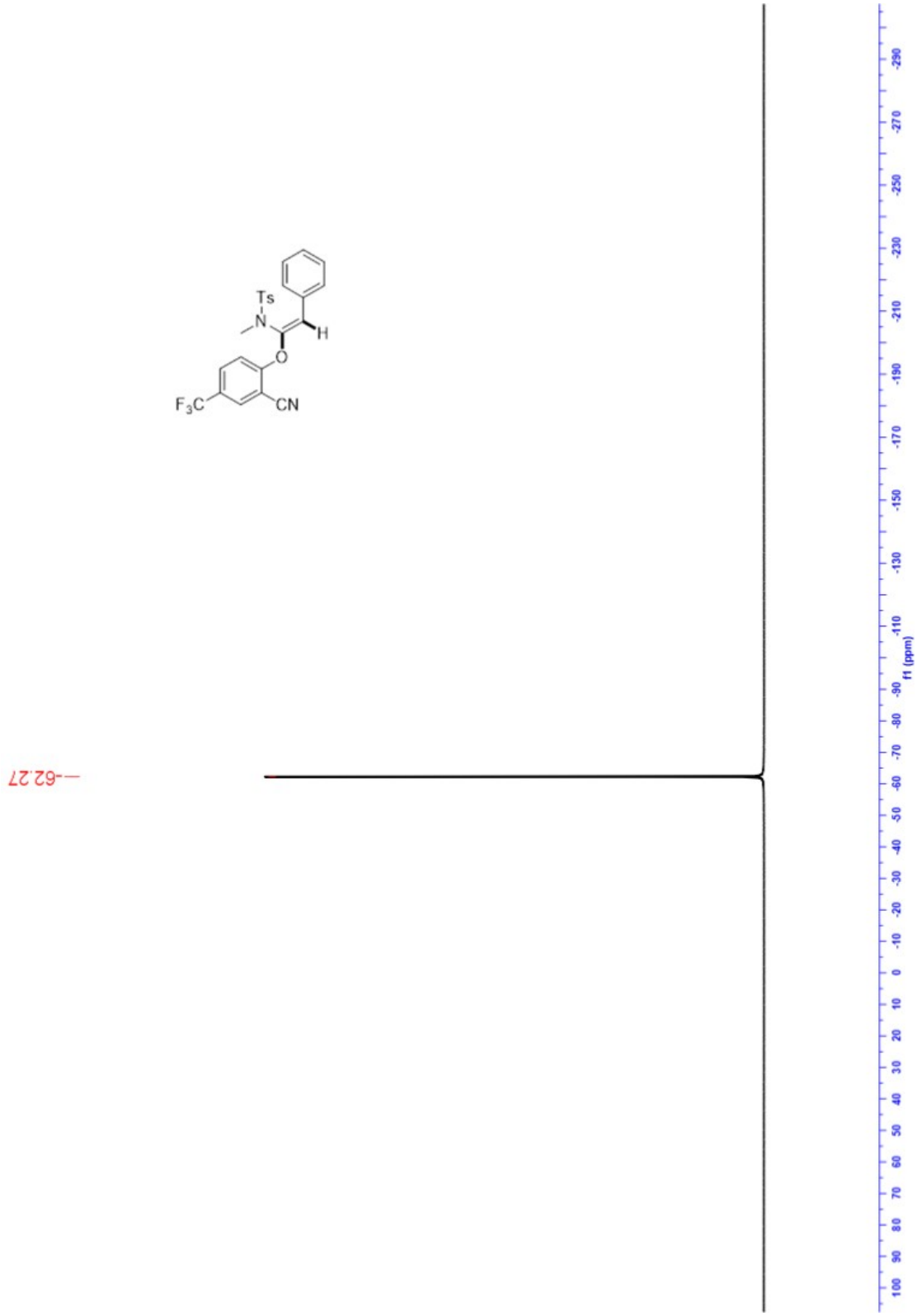
^{1}H NMR of 3am (400 MHz, $CDCl_3$)



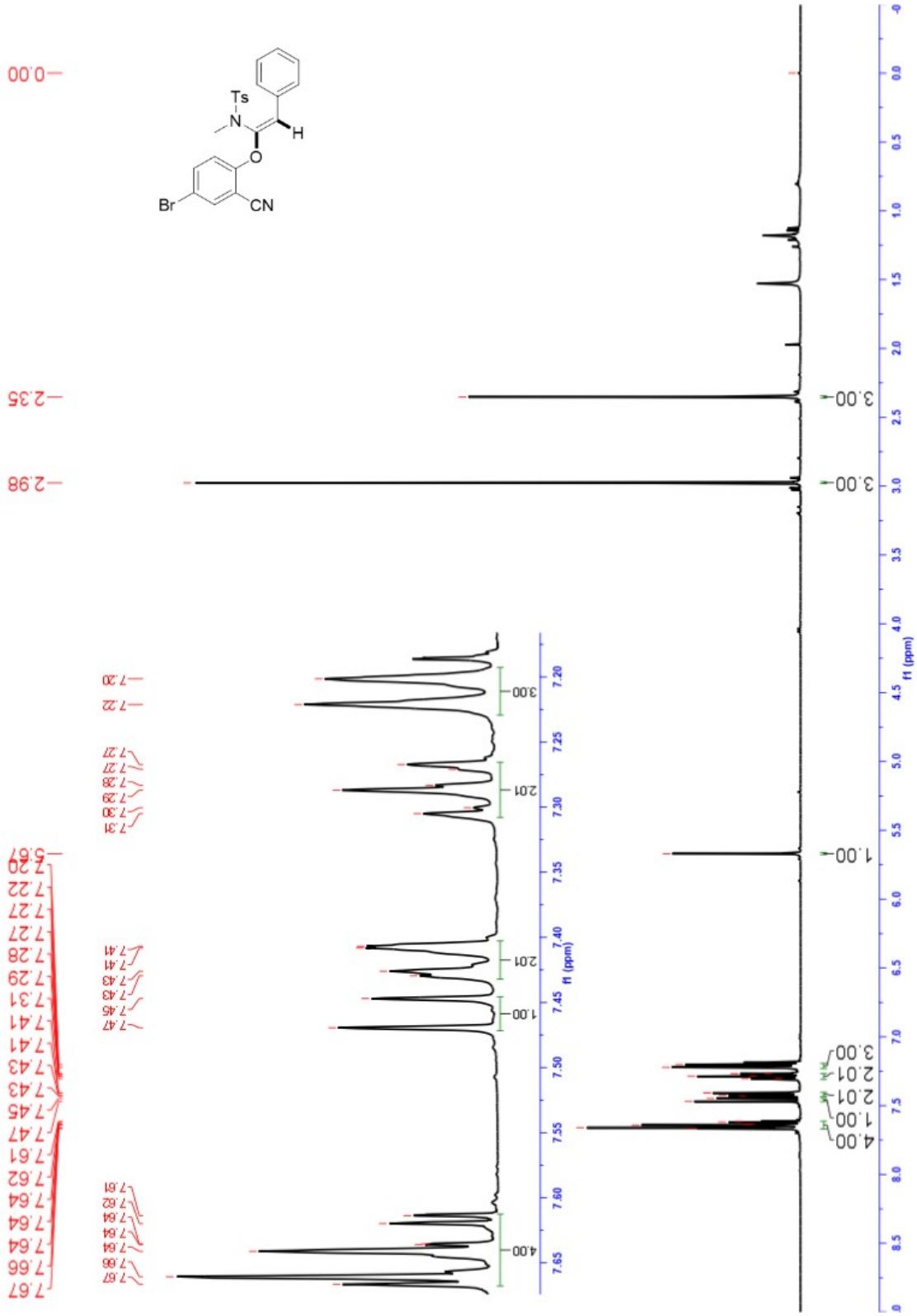
^{13}C NMR of 3am (100 MHz, $CDCl_3$)



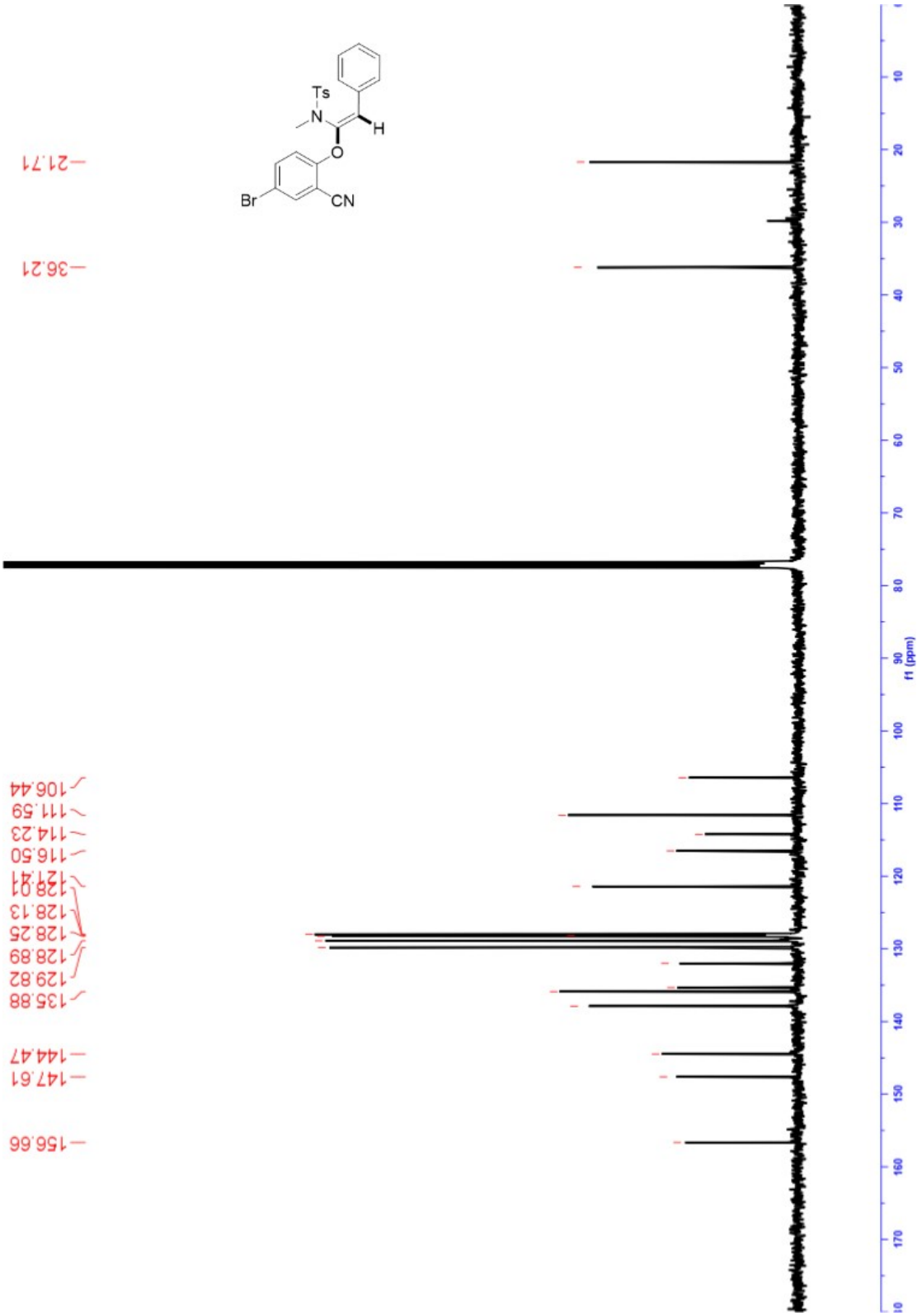
^{19}F NMR of 3am (376 MHz, $CDCl_3$)



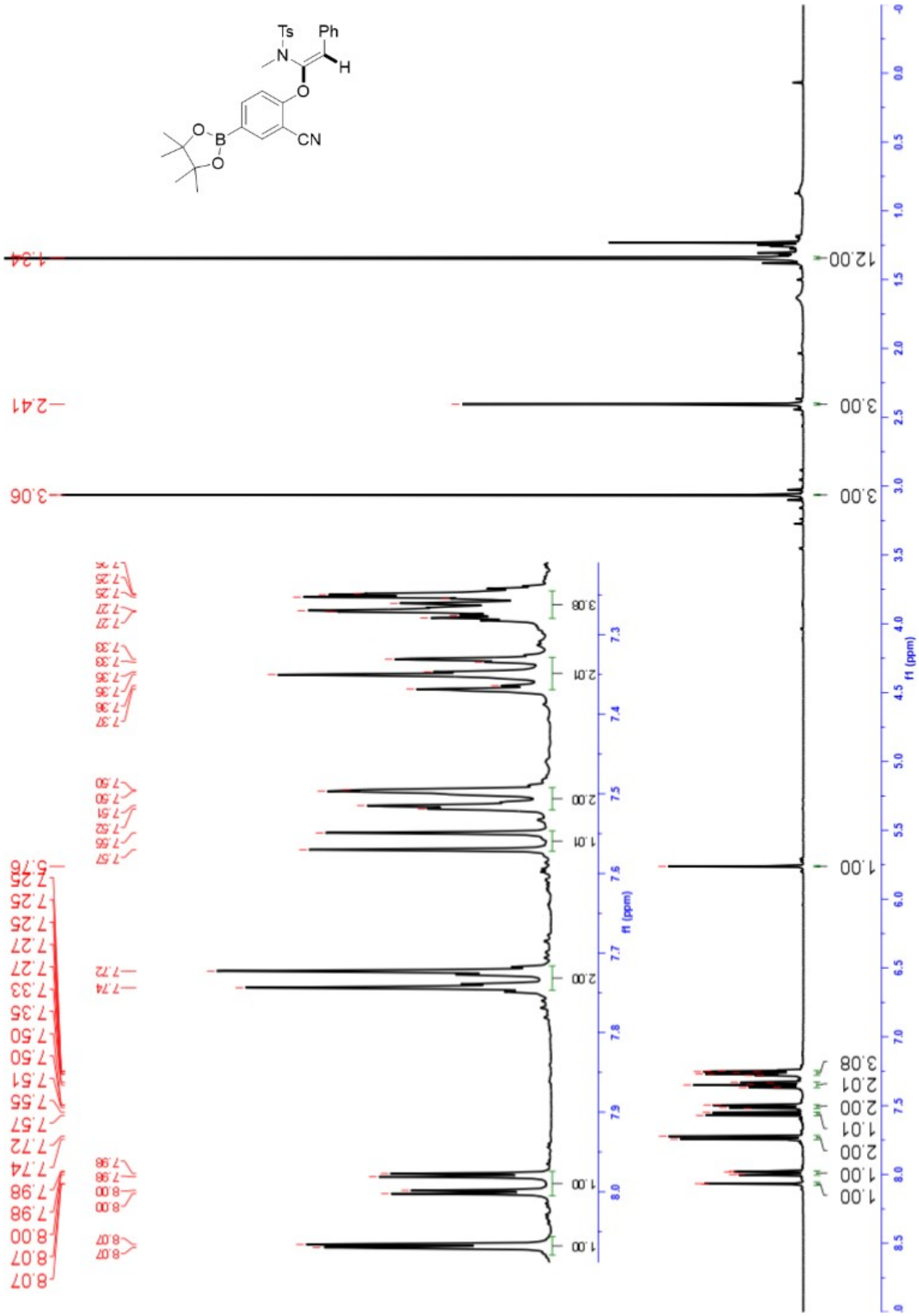
^{1}H NMR of 3an (400 MHz, $CDCl_3$)



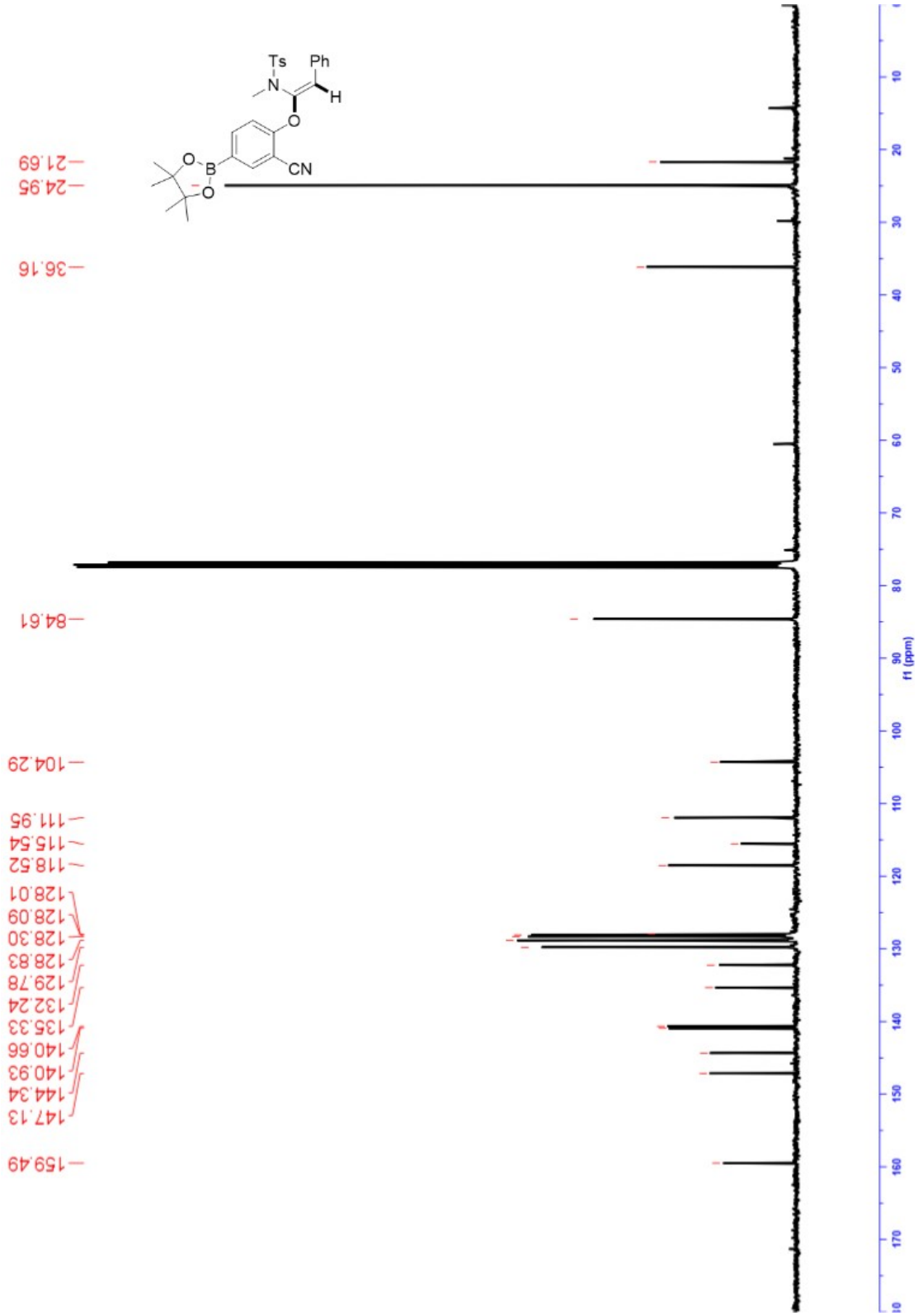
^{13}C NMR of 3an (100 MHz, $CDCl_3$)



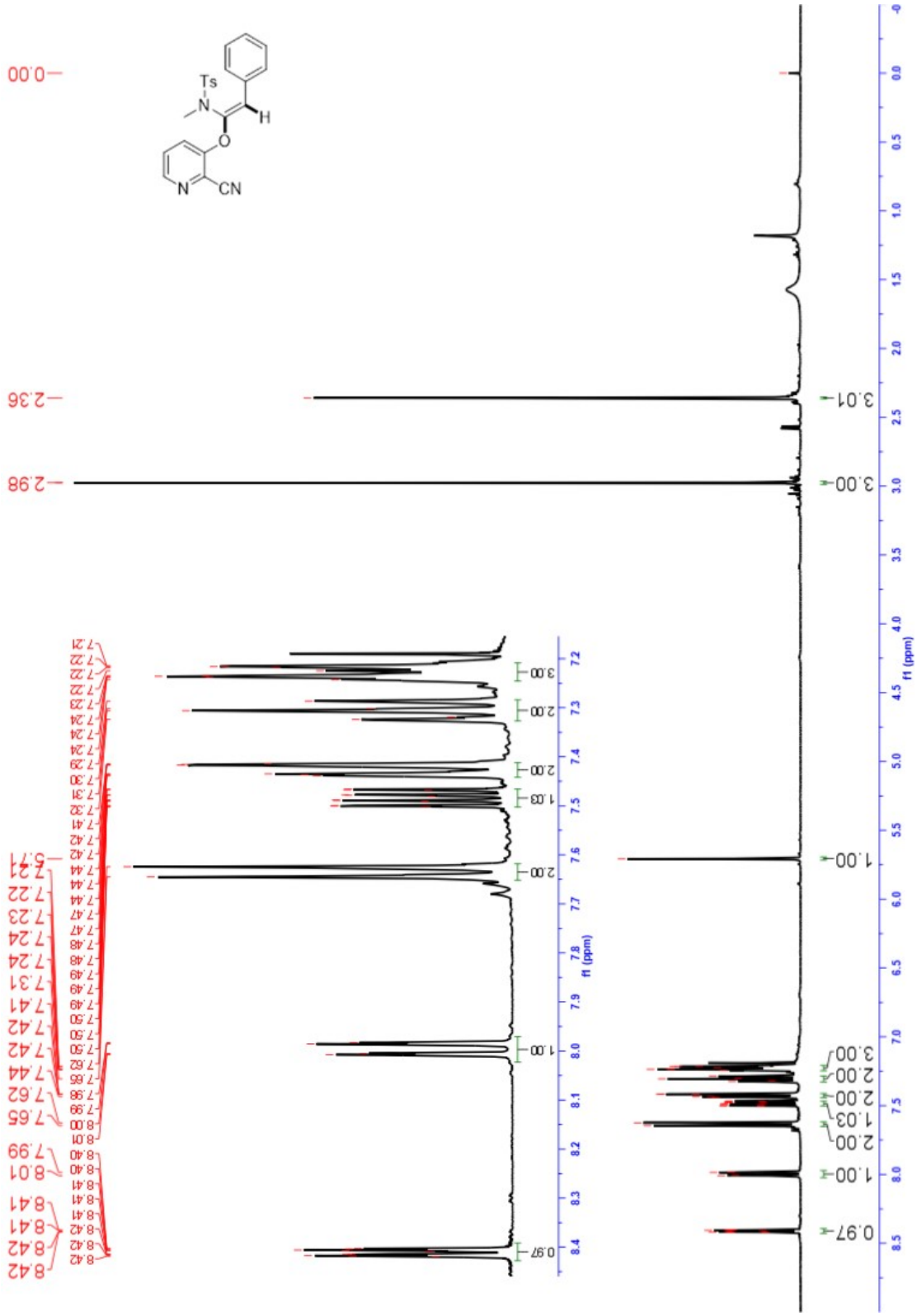
^{1}H NMR of 3ao (400 MHz, $CDCl_3$)



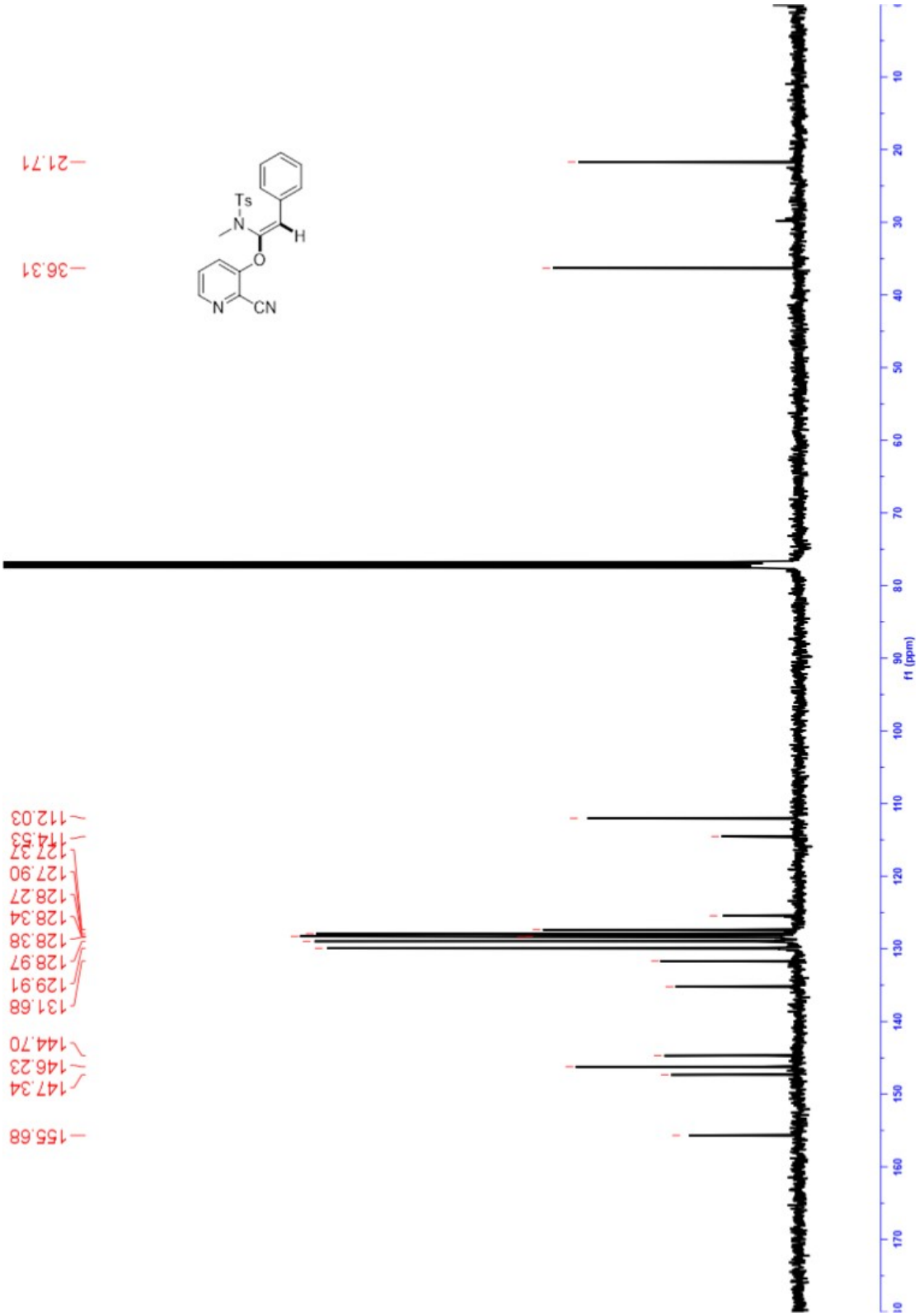
^{13}C NMR of 3ao (100 MHz, $CDCl_3$)



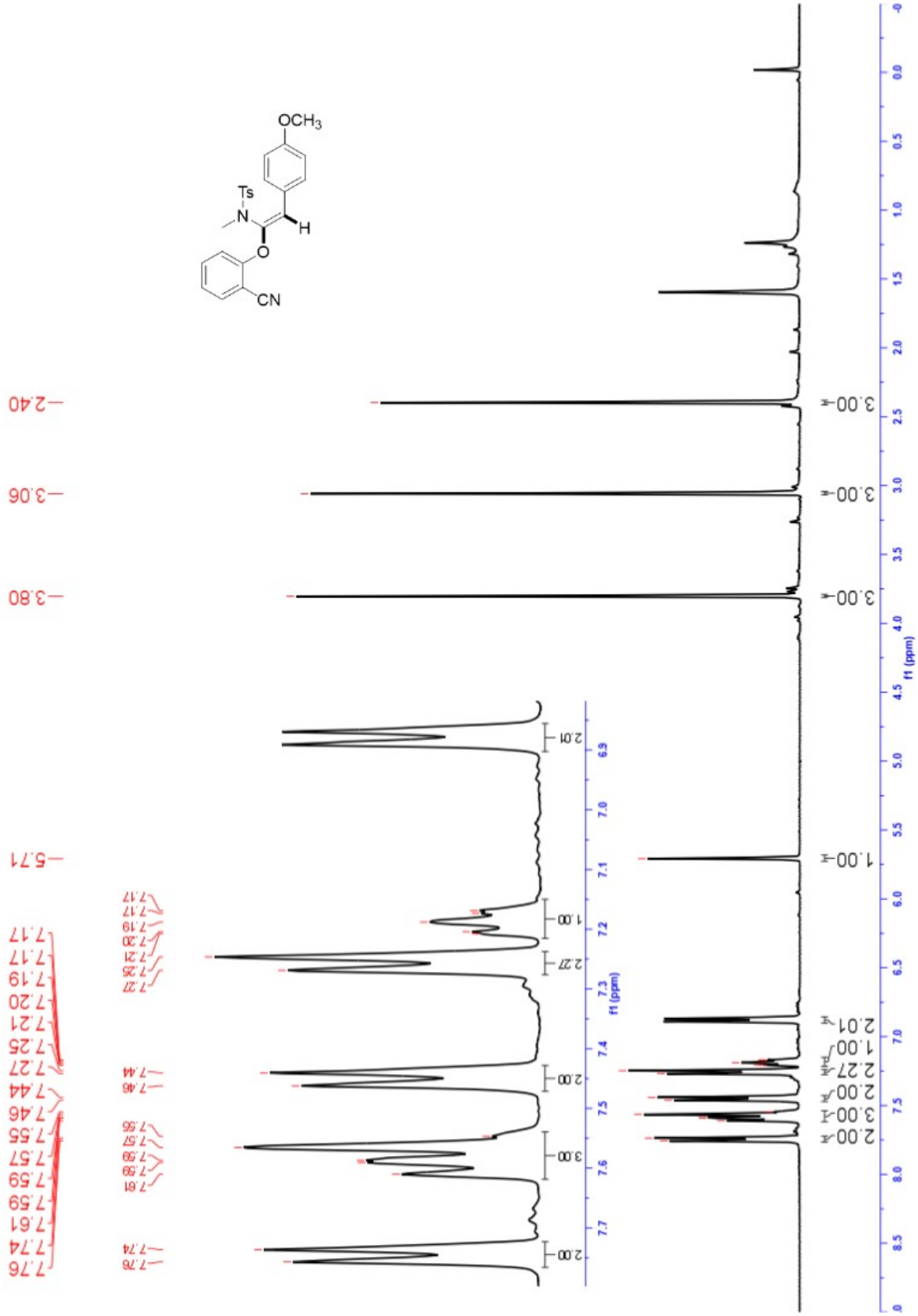
^{1}H NMR of 3ap (400 MHz, $CDCl_3$)



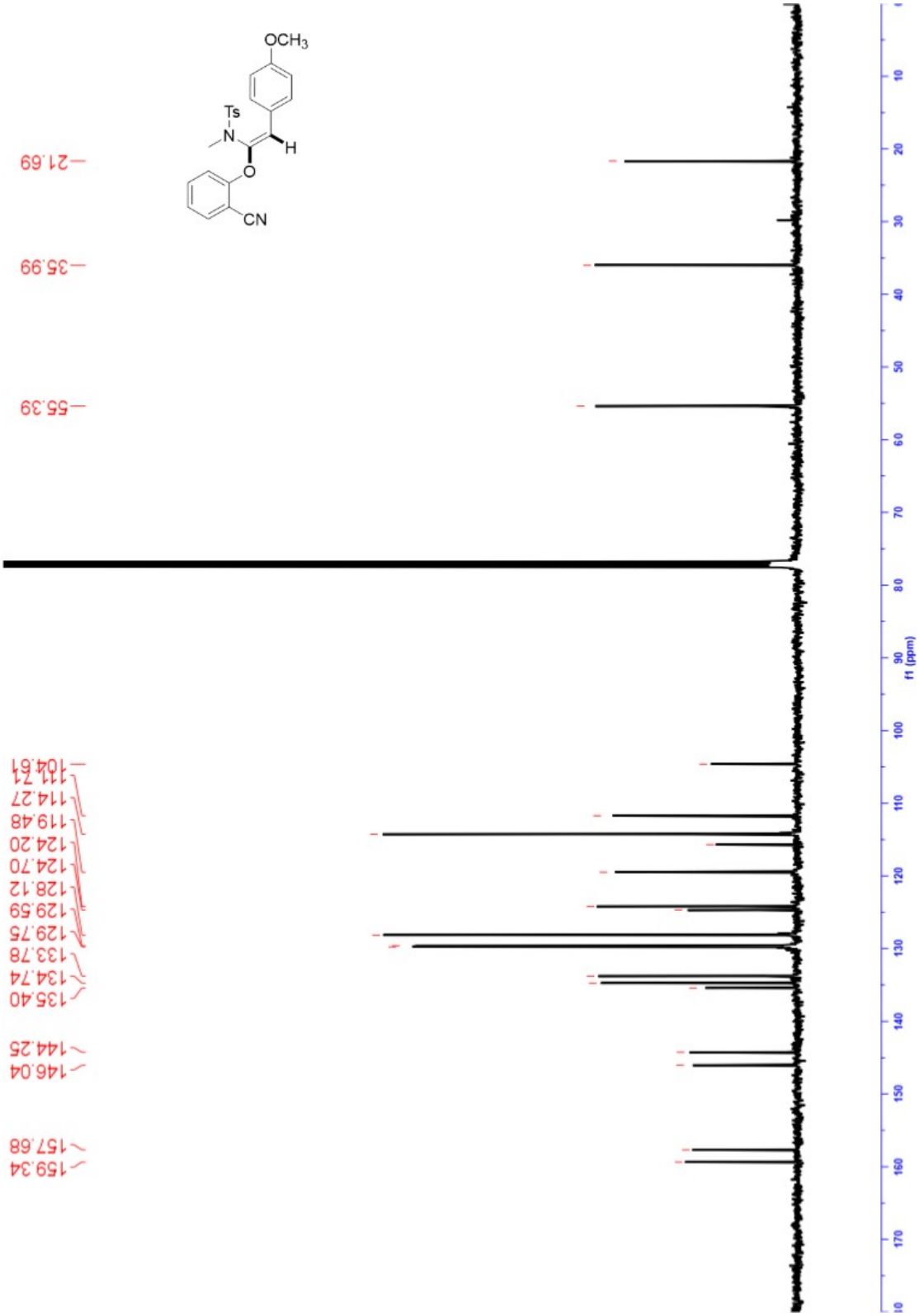
^{13}C NMR of 3ap (100 MHz, $CDCl_3$)



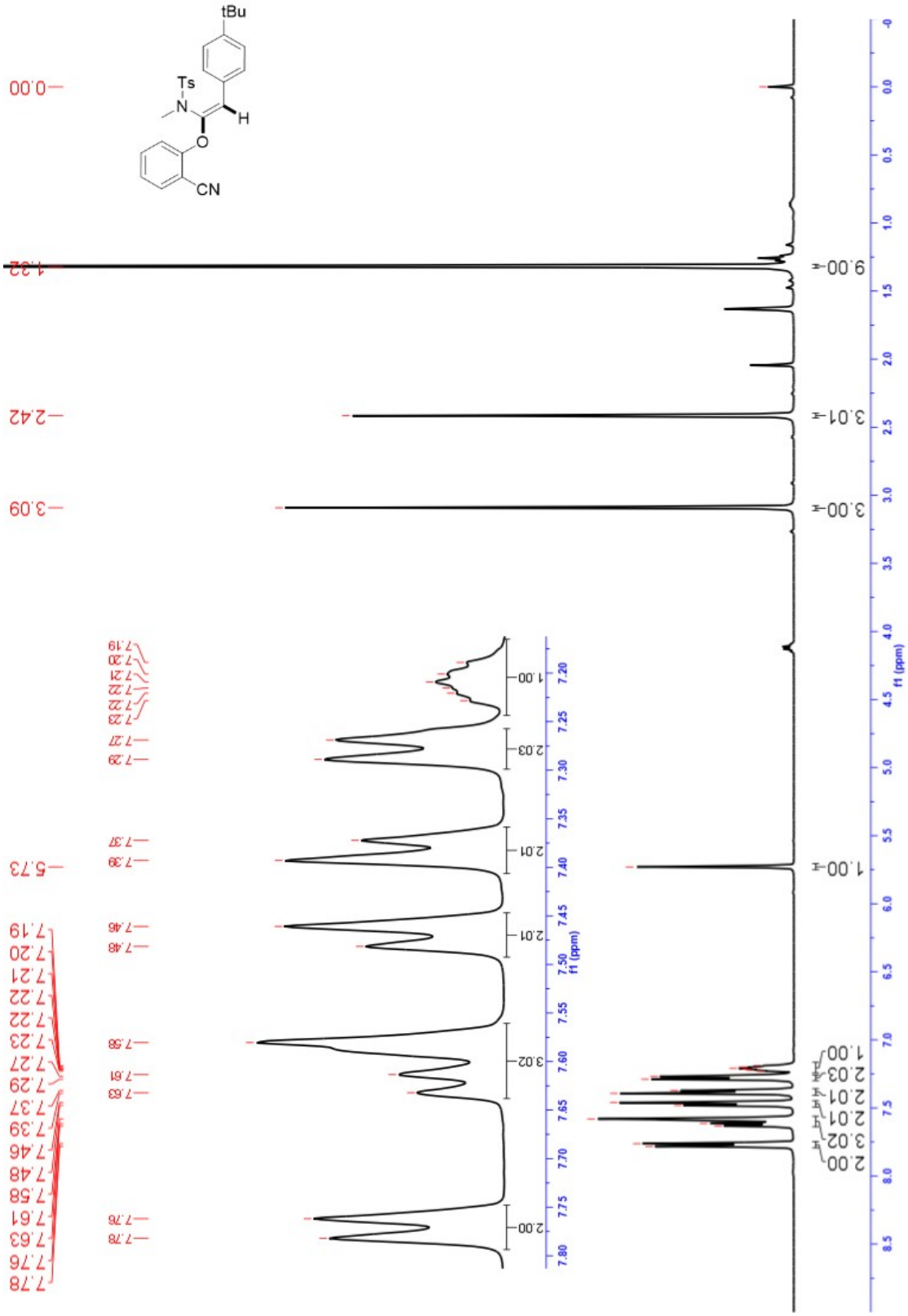
^{1}H NMR of 3bf (400 MHz, $CDCl_3$)



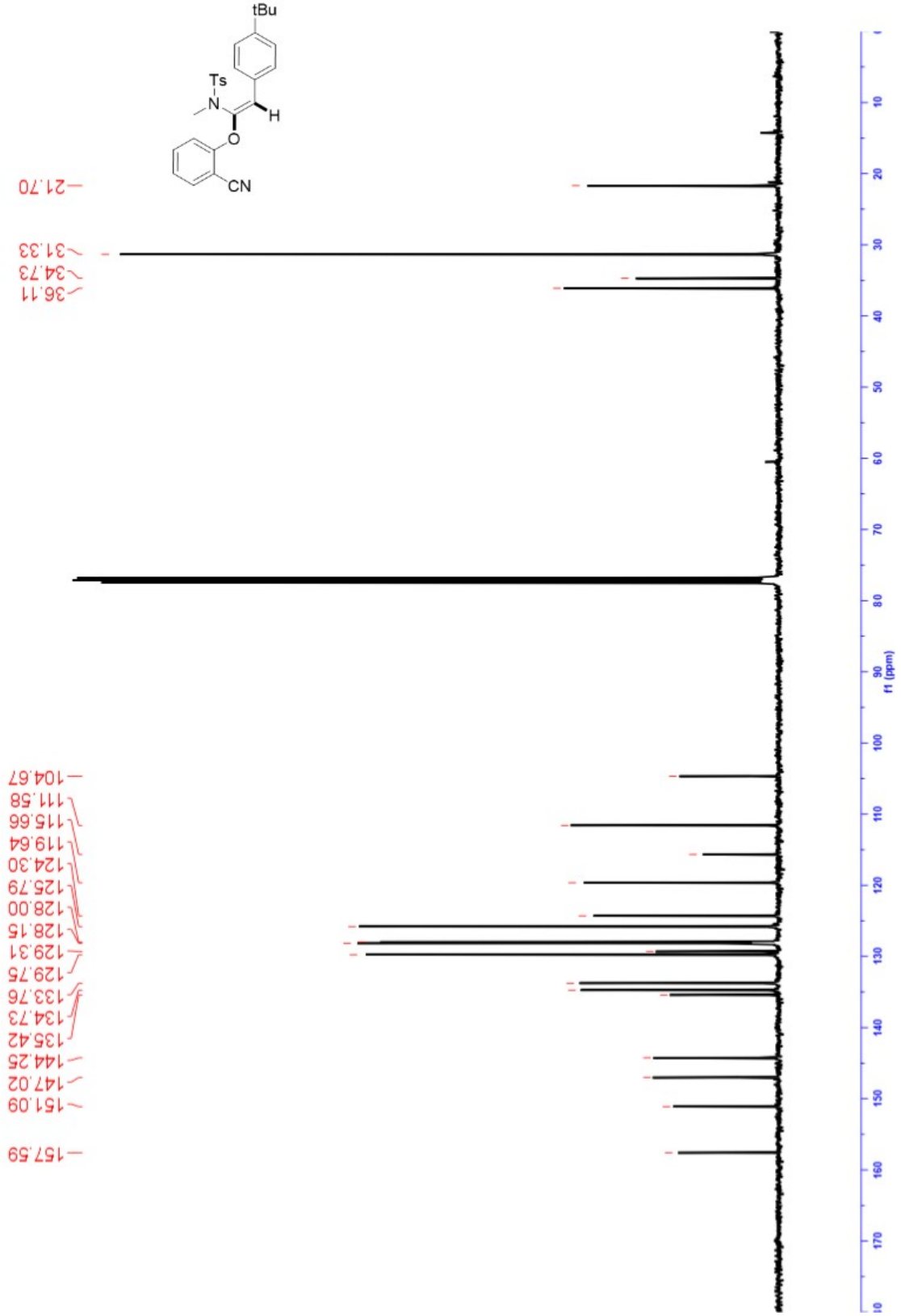
^{13}C NMR of 3bf (100 MHz, $CDCl_3$)



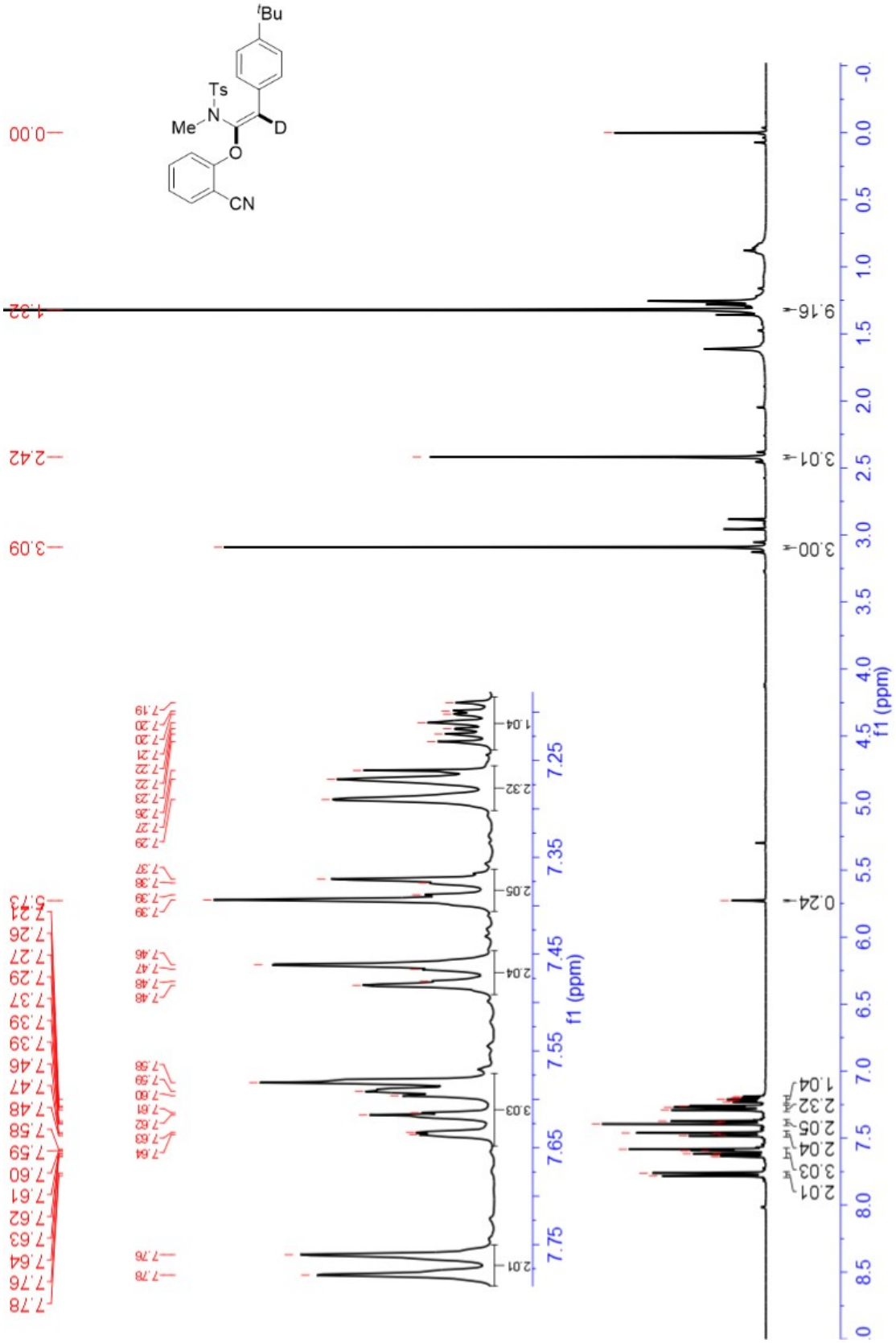
^{1}H NMR of 3cf (400 MHz, $CDCl_3$)



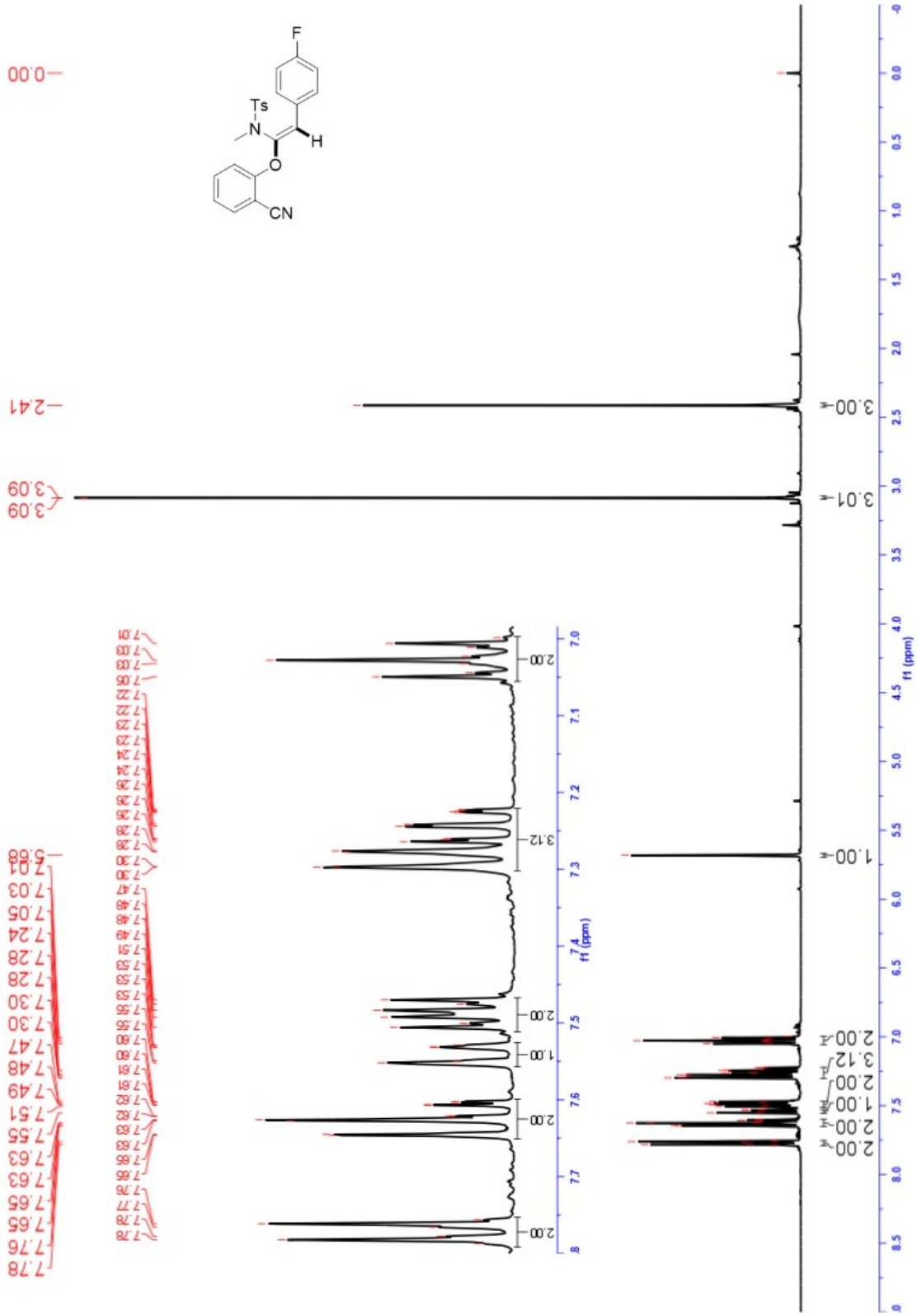
^{13}C NMR of 3cf (100 MHz, $CDCl_3$)



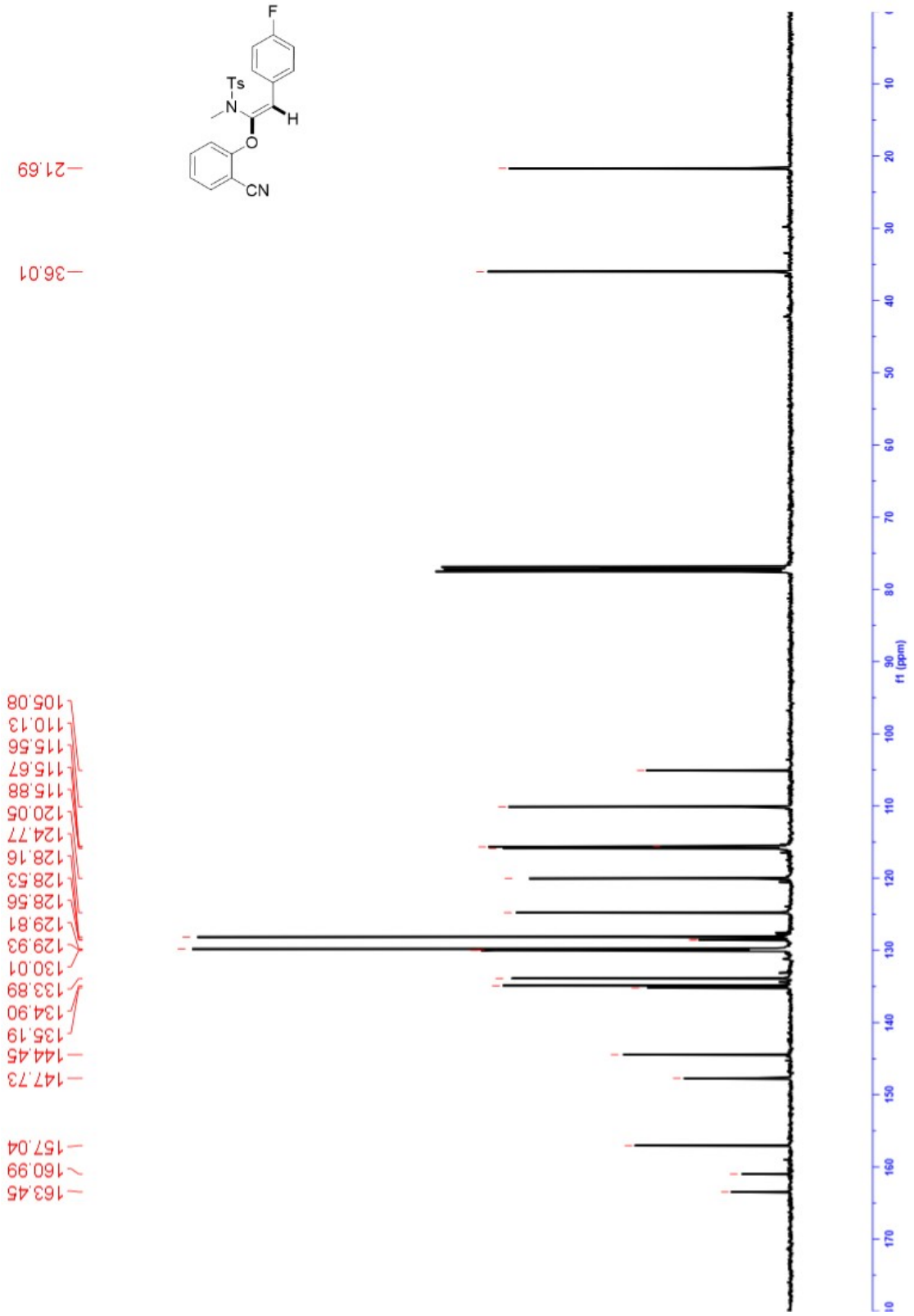
^{1}H NMR of 3cf-D (400 MHz, $CDCl_3$)



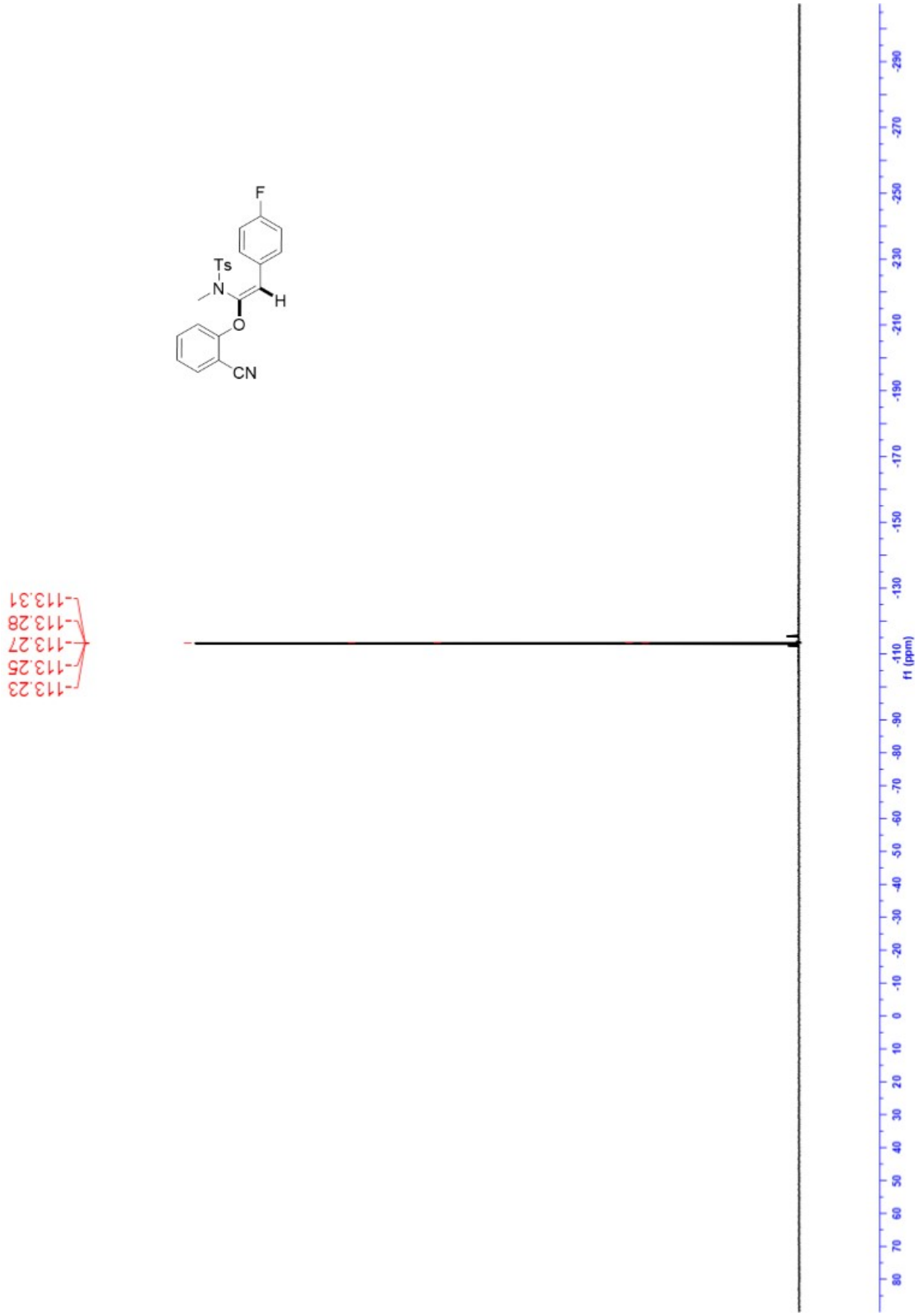
^{1}H NMR of 3df (400 MHz, $CDCl_3$)



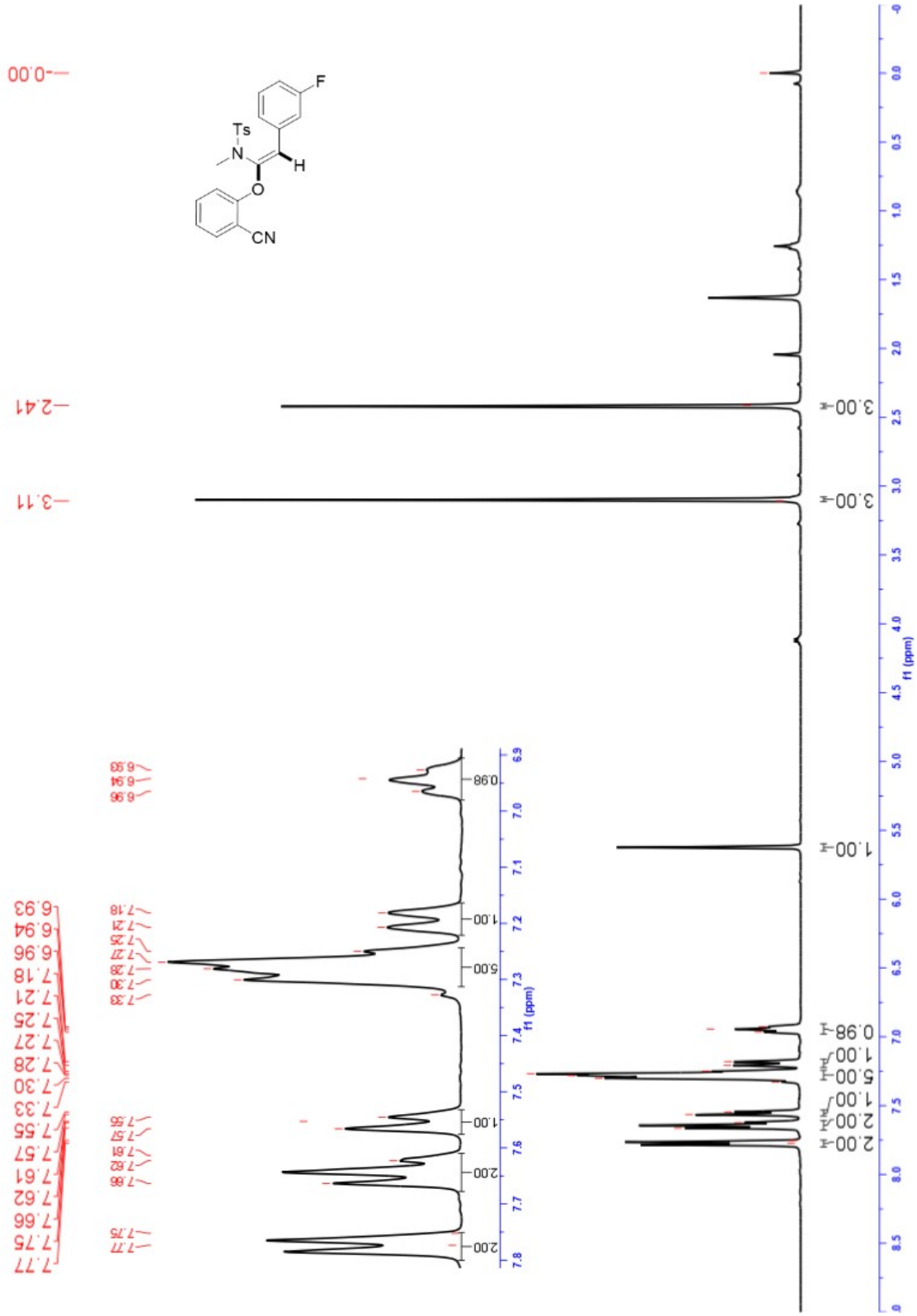
^{13}C NMR of 3df (100 MHz, $CDCl_3$)



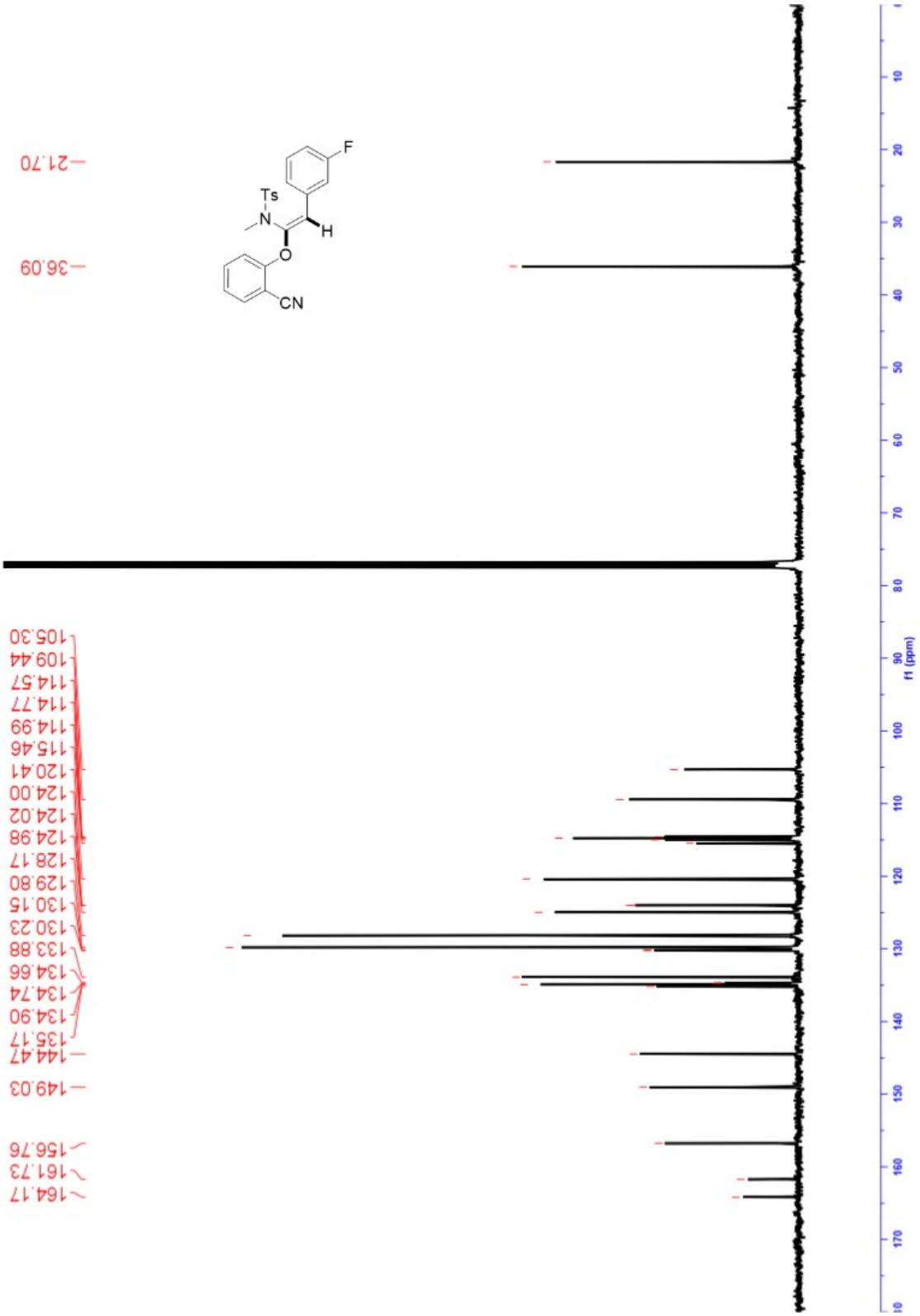
^{19}F NMR of 3df (376 MHz, $CDCl_3$)



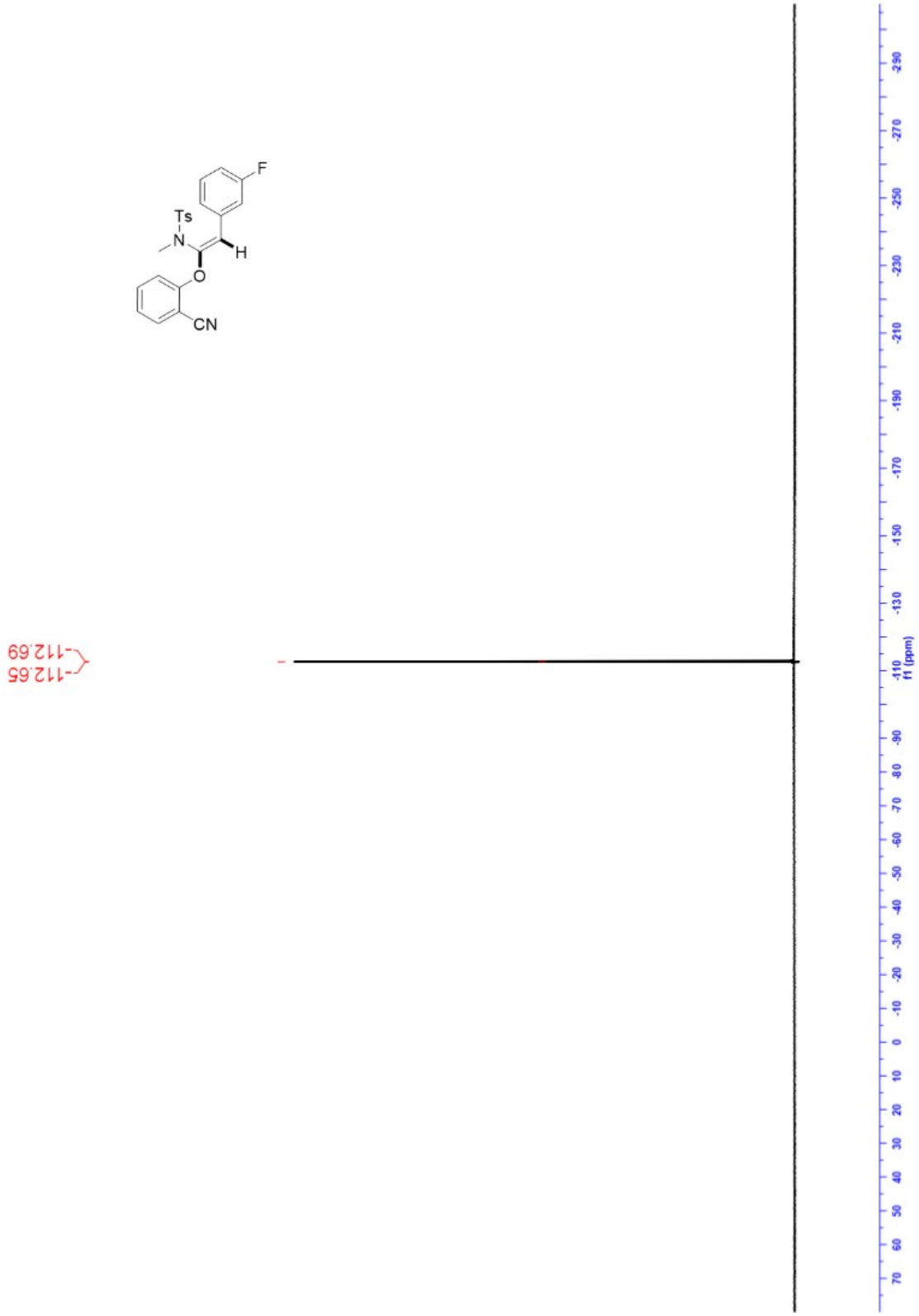
^{1}H NMR of 3ef (400 MHz, $CDCl_3$)



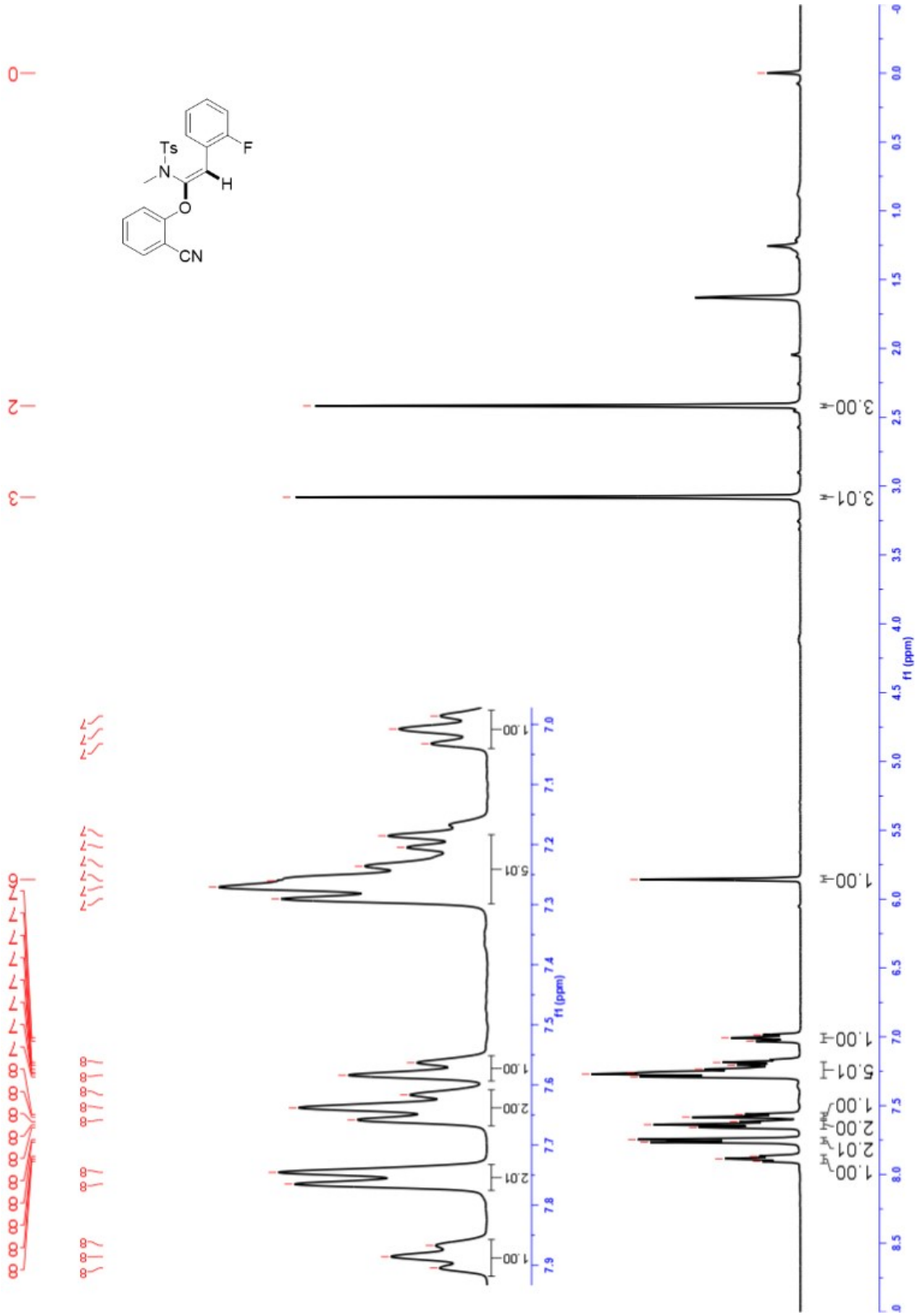
^{13}C NMR of 3ef (100 MHz, $CDCl_3$)



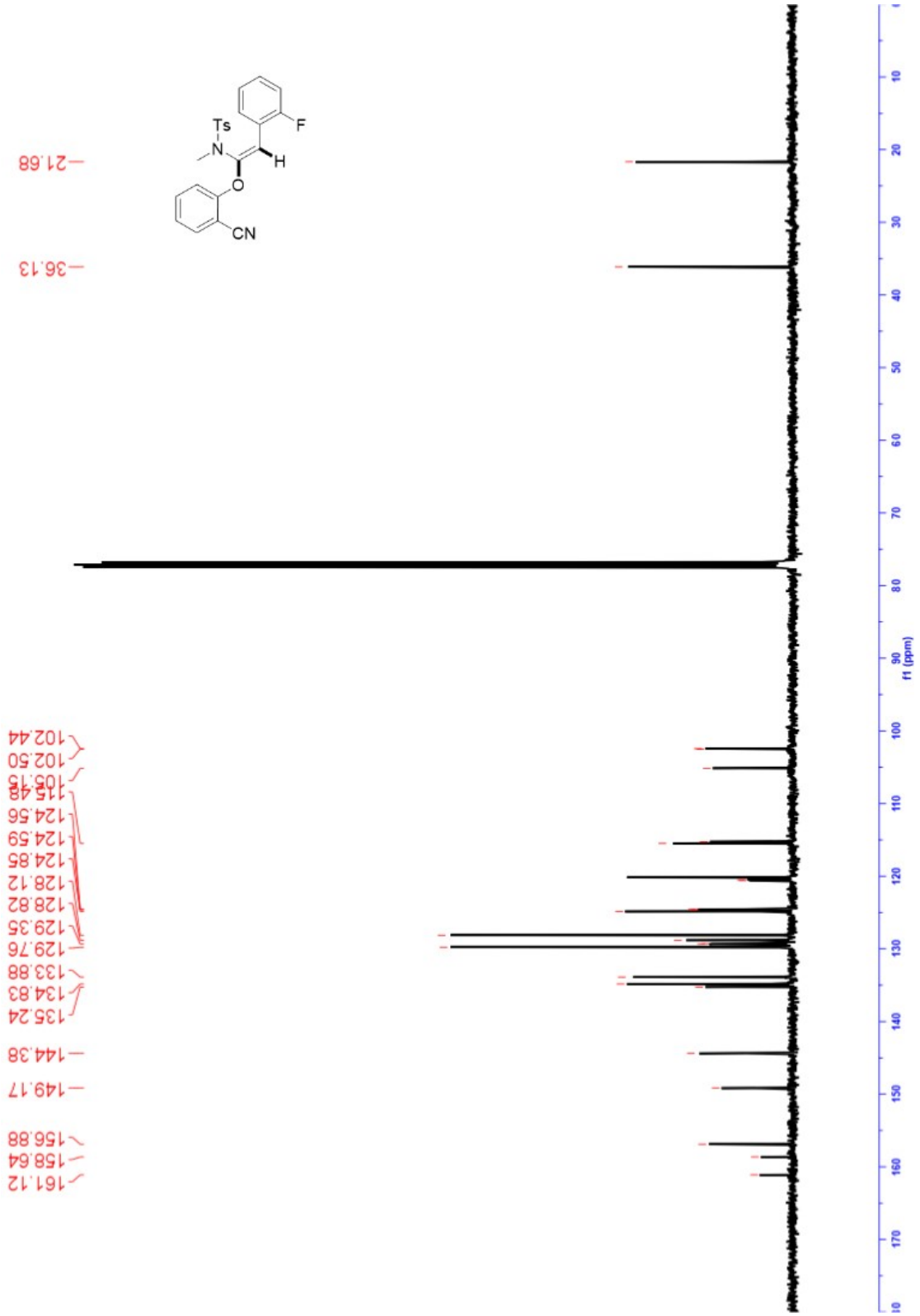
^{19}F NMR of 3ef (376 MHz, $CDCl_3$)



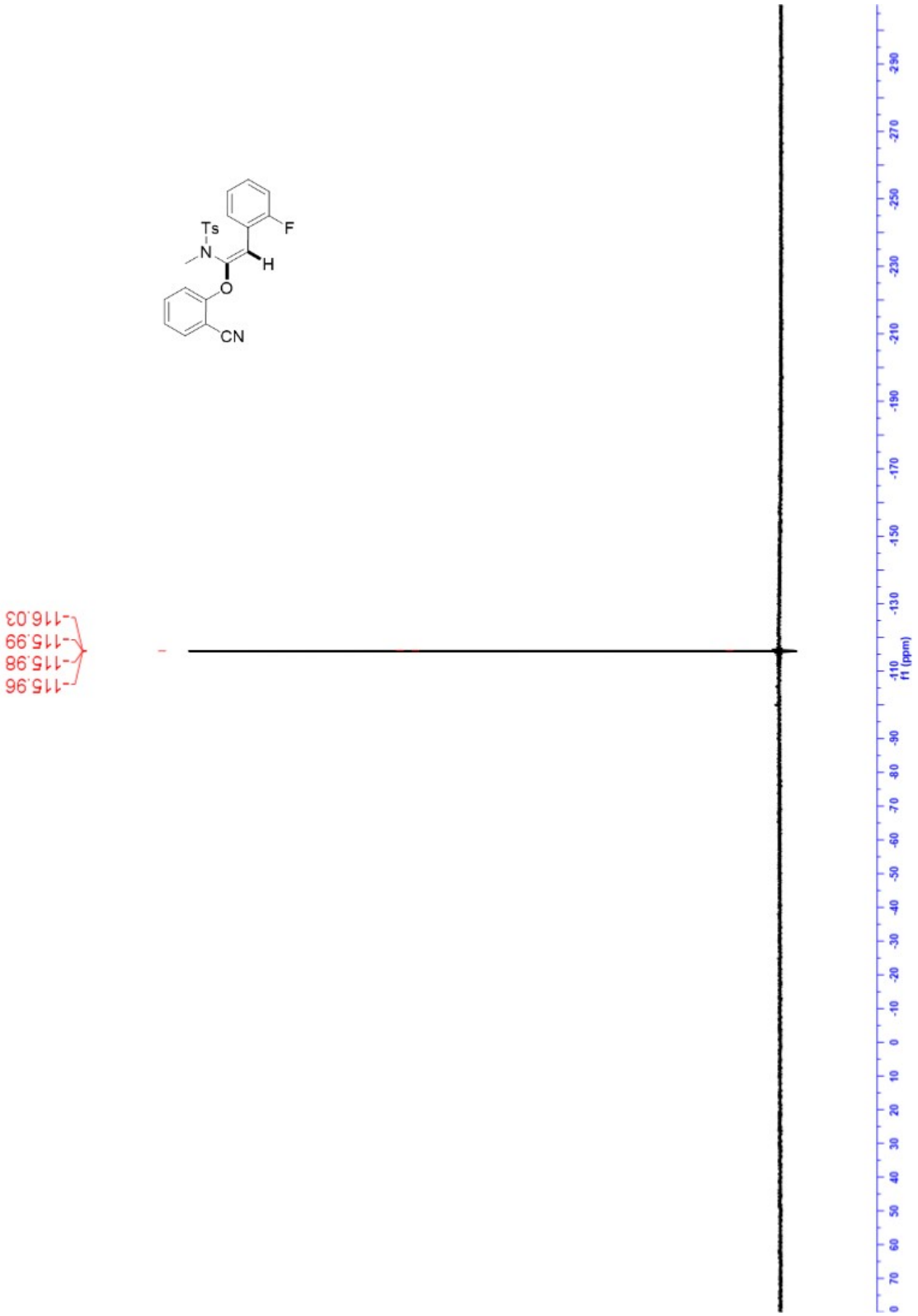
^{1}H NMR of 3ff (400 MHz, $CDCl_3$)



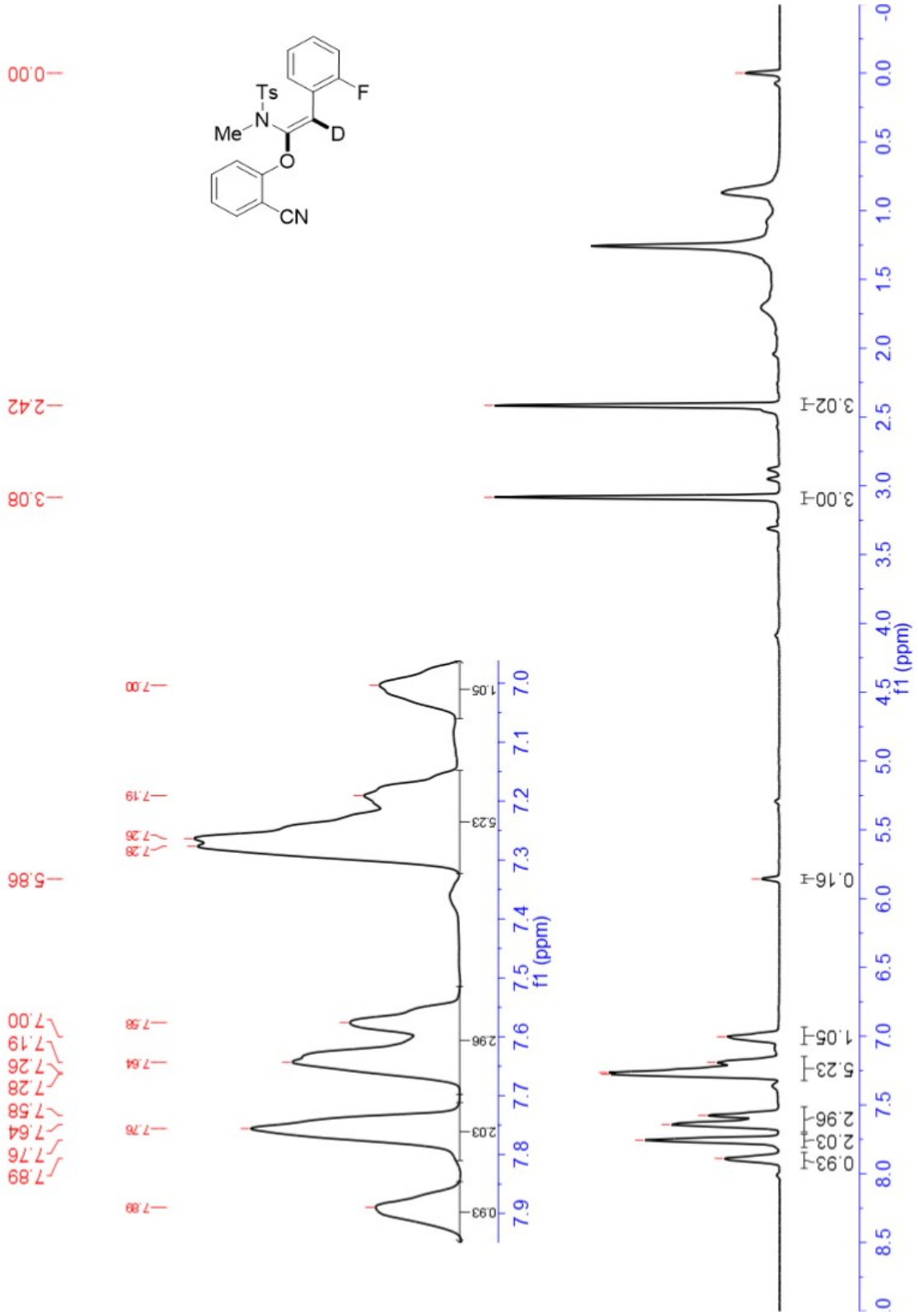
^{13}C NMR of 3ff (100 MHz, $CDCl_3$)



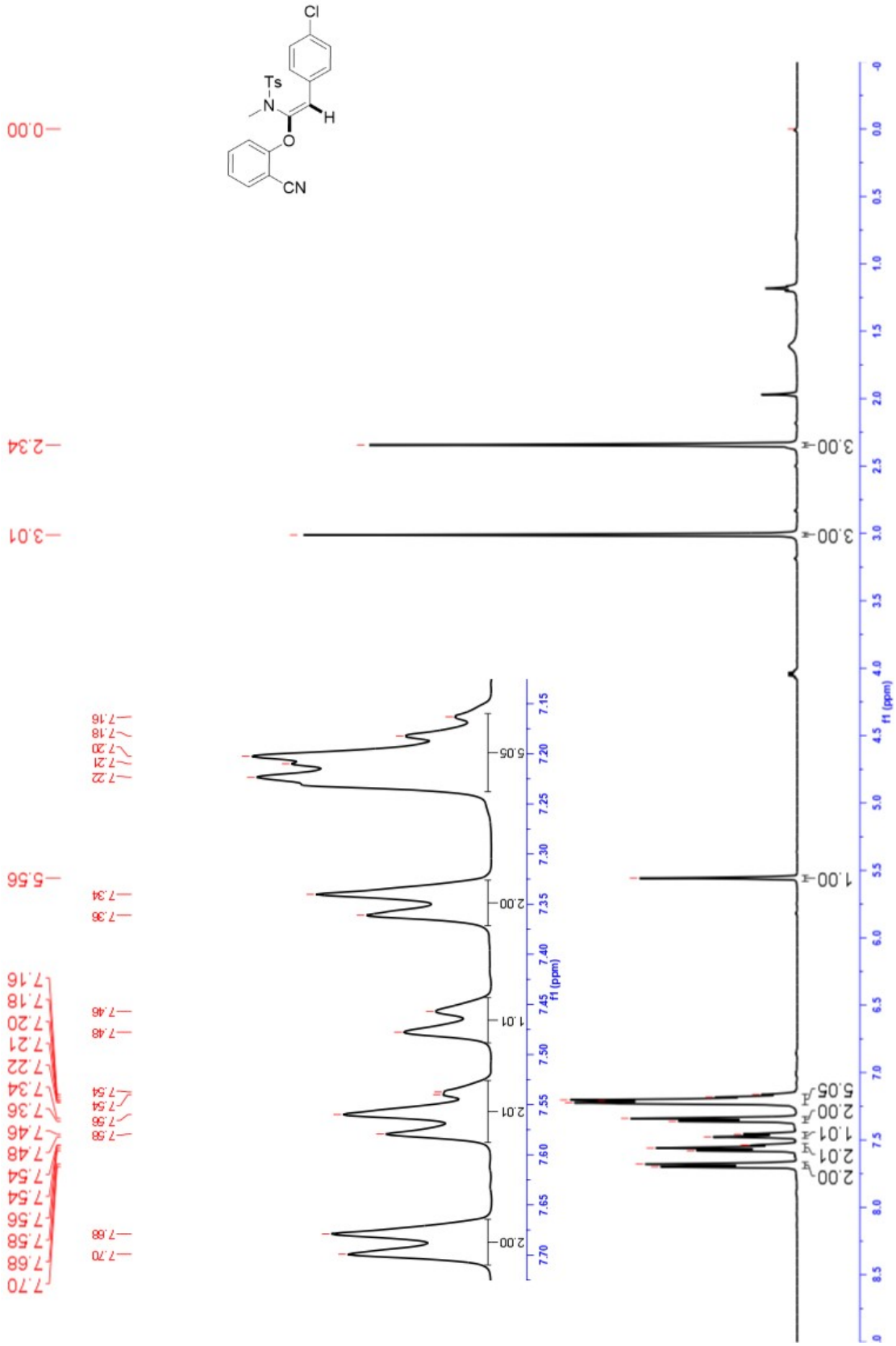
^{19}F NMR of 3ff (376 MHz, $CDCl_3$)



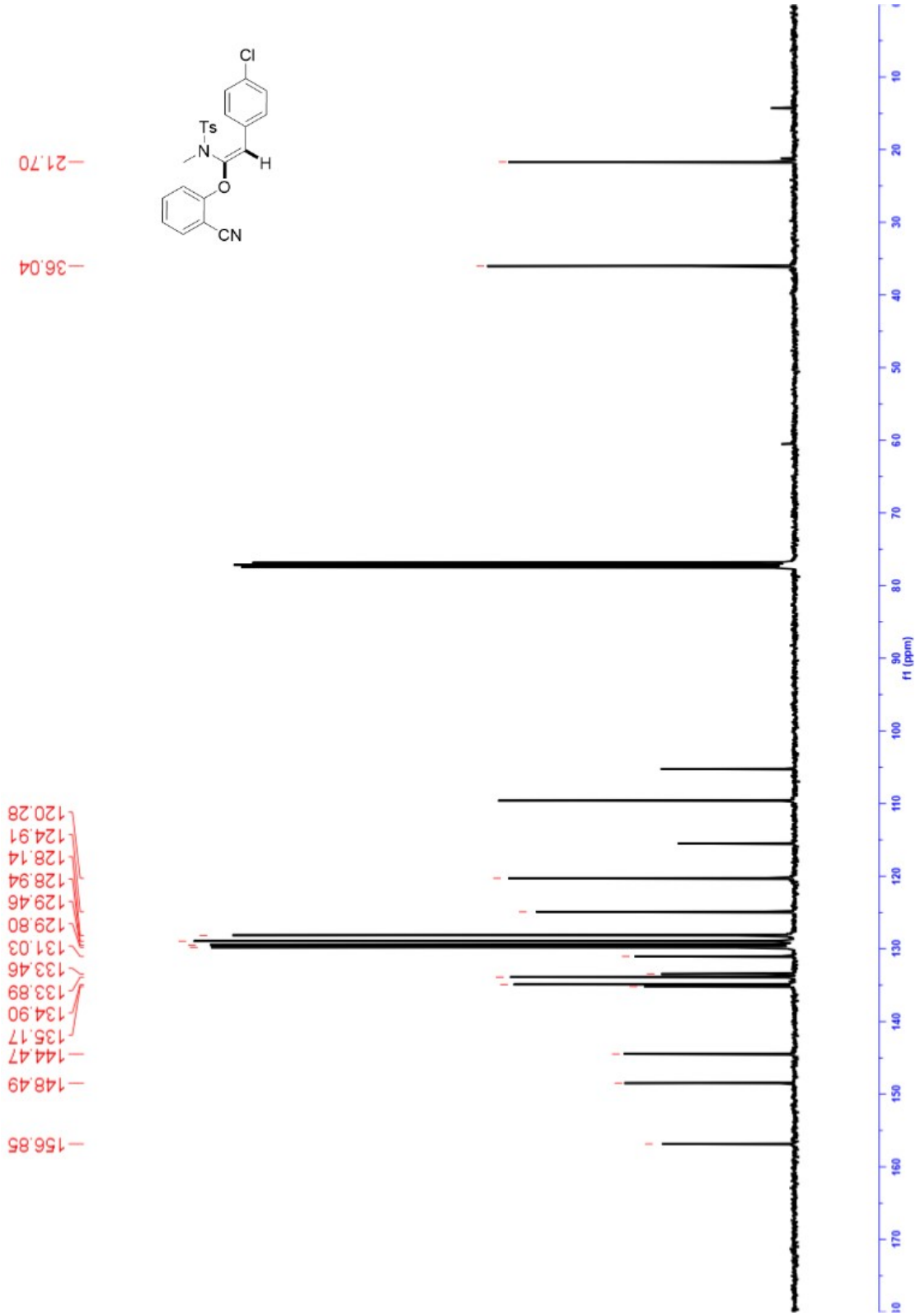
^{1}H NMR of 3ff-D (400 MHz, $CDCl_3$)



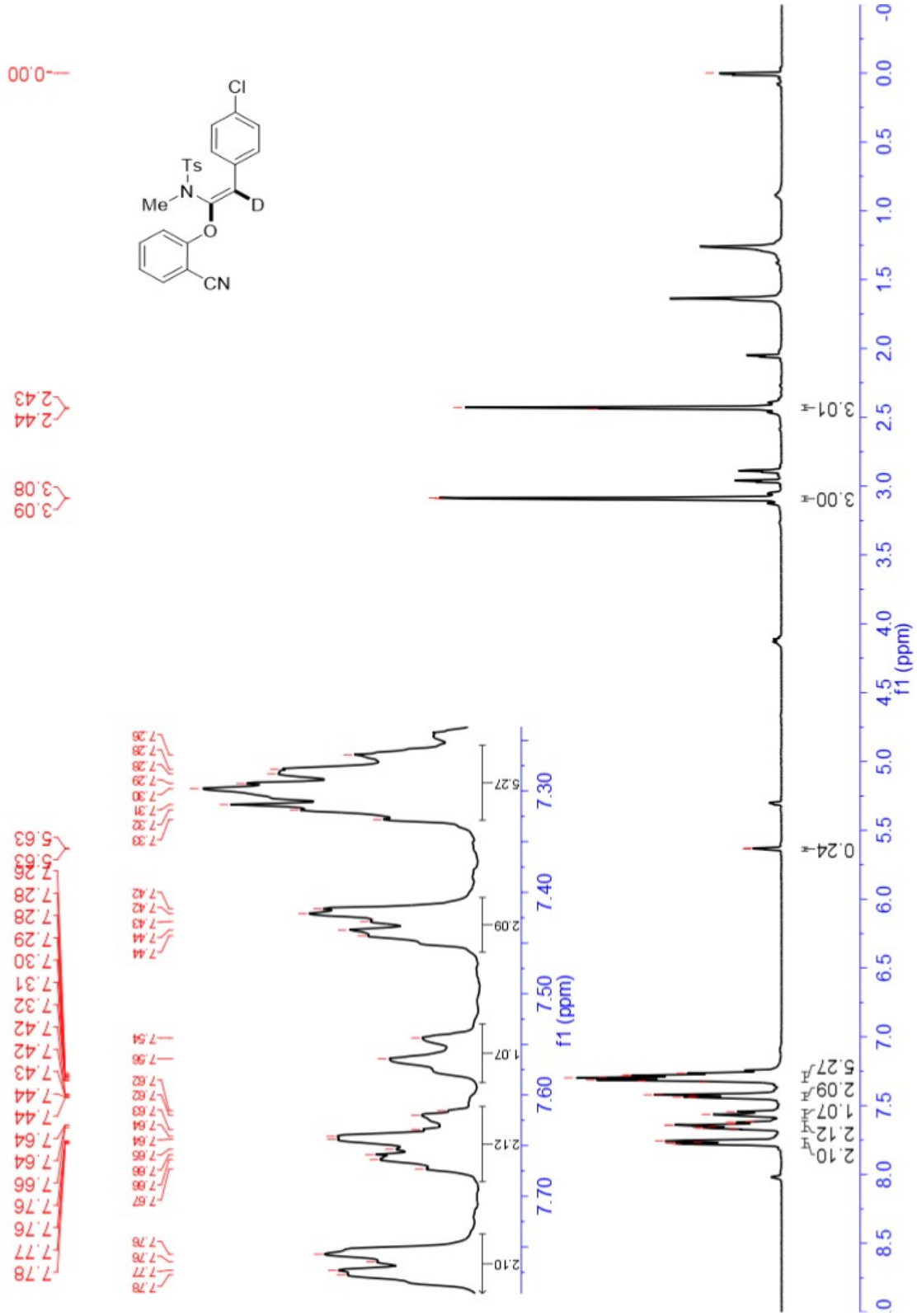
^{1}H NMR of 3gf (400 MHz, $CDCl_3$)



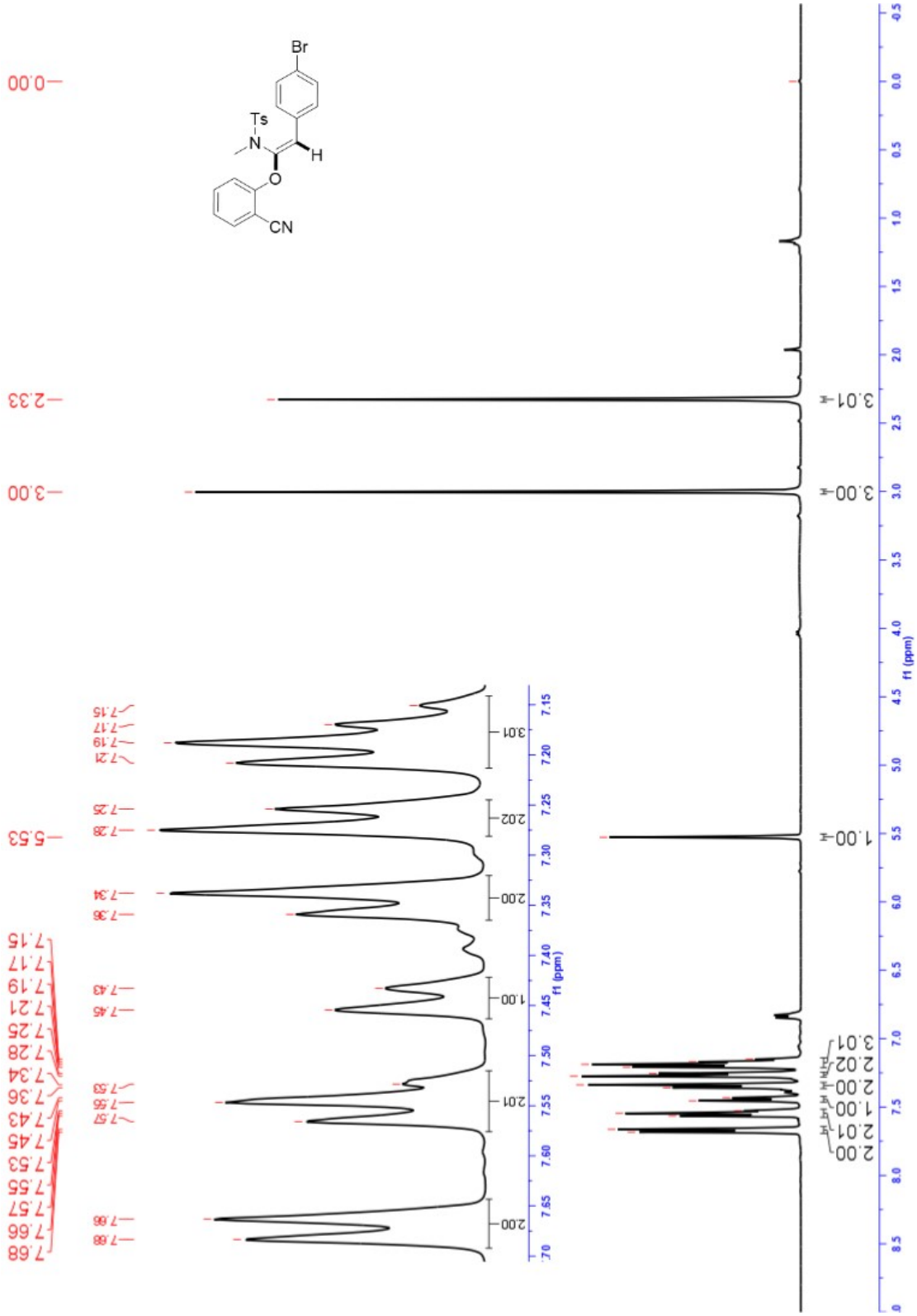
^{13}C NMR of 3gf (100 MHz, $CDCl_3$)



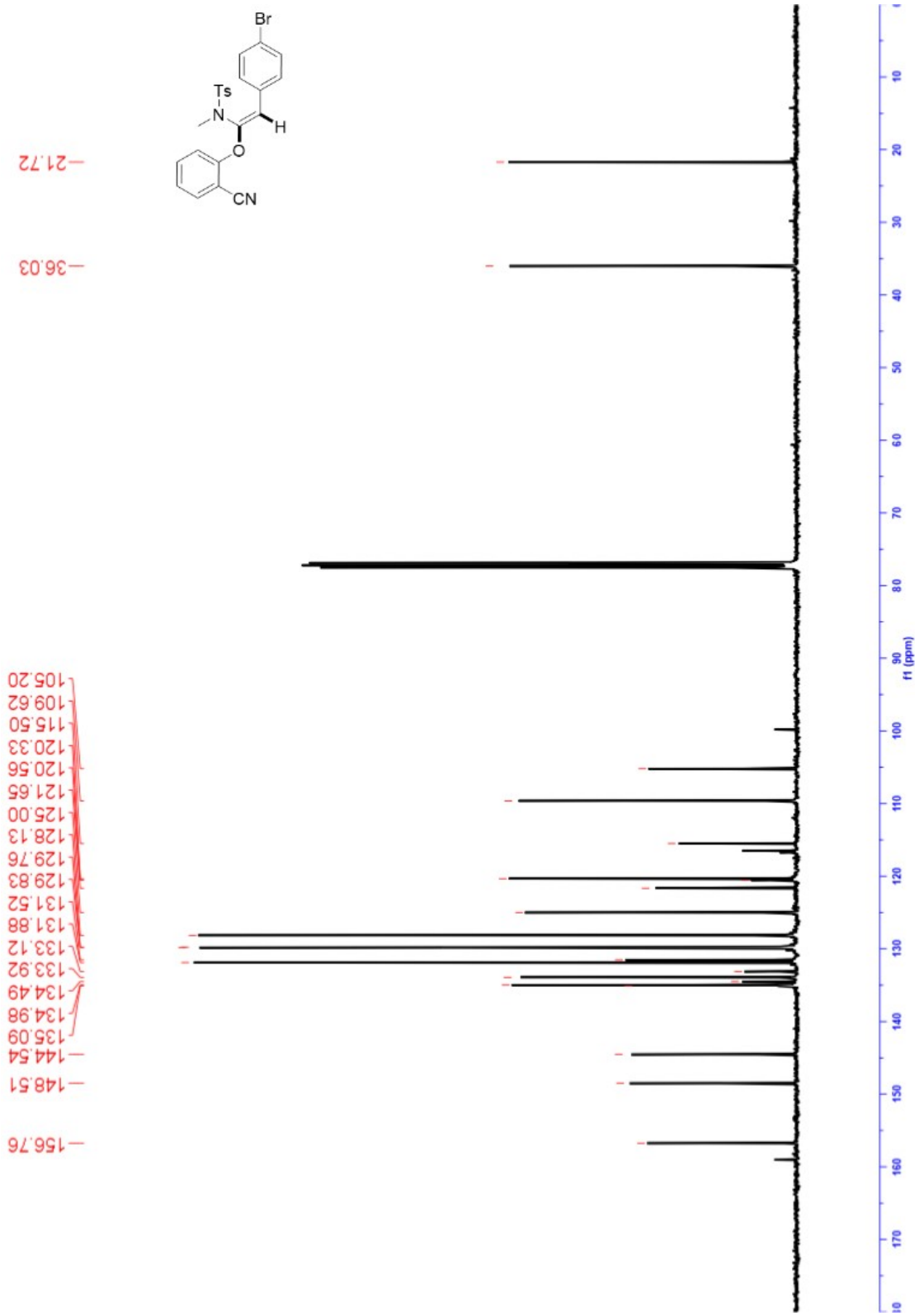
^{1}H NMR of 3gf-D (400 MHz, $CDCl_3$)



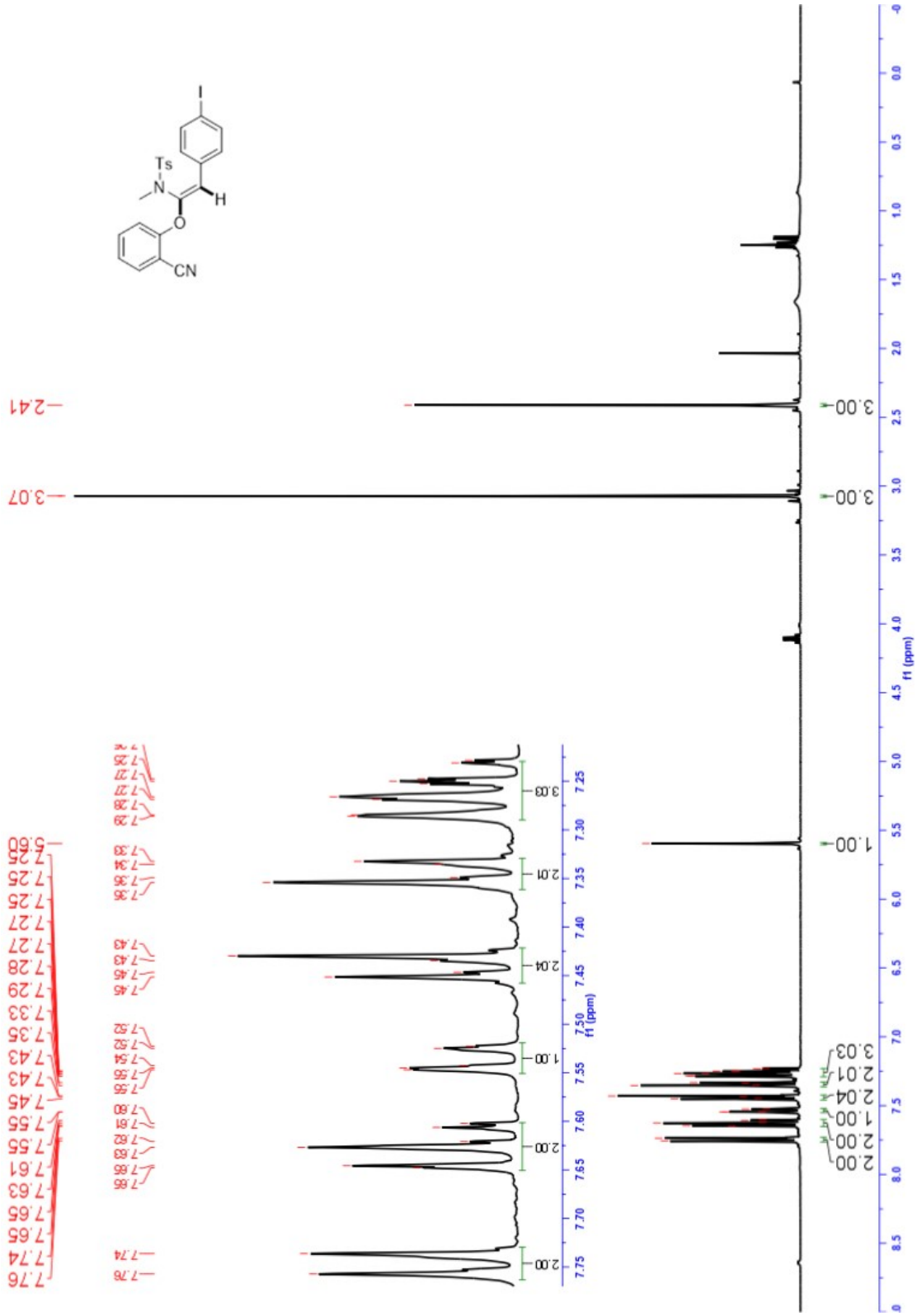
^{1}H NMR of 3hf (400 MHz, $CDCl_3$)



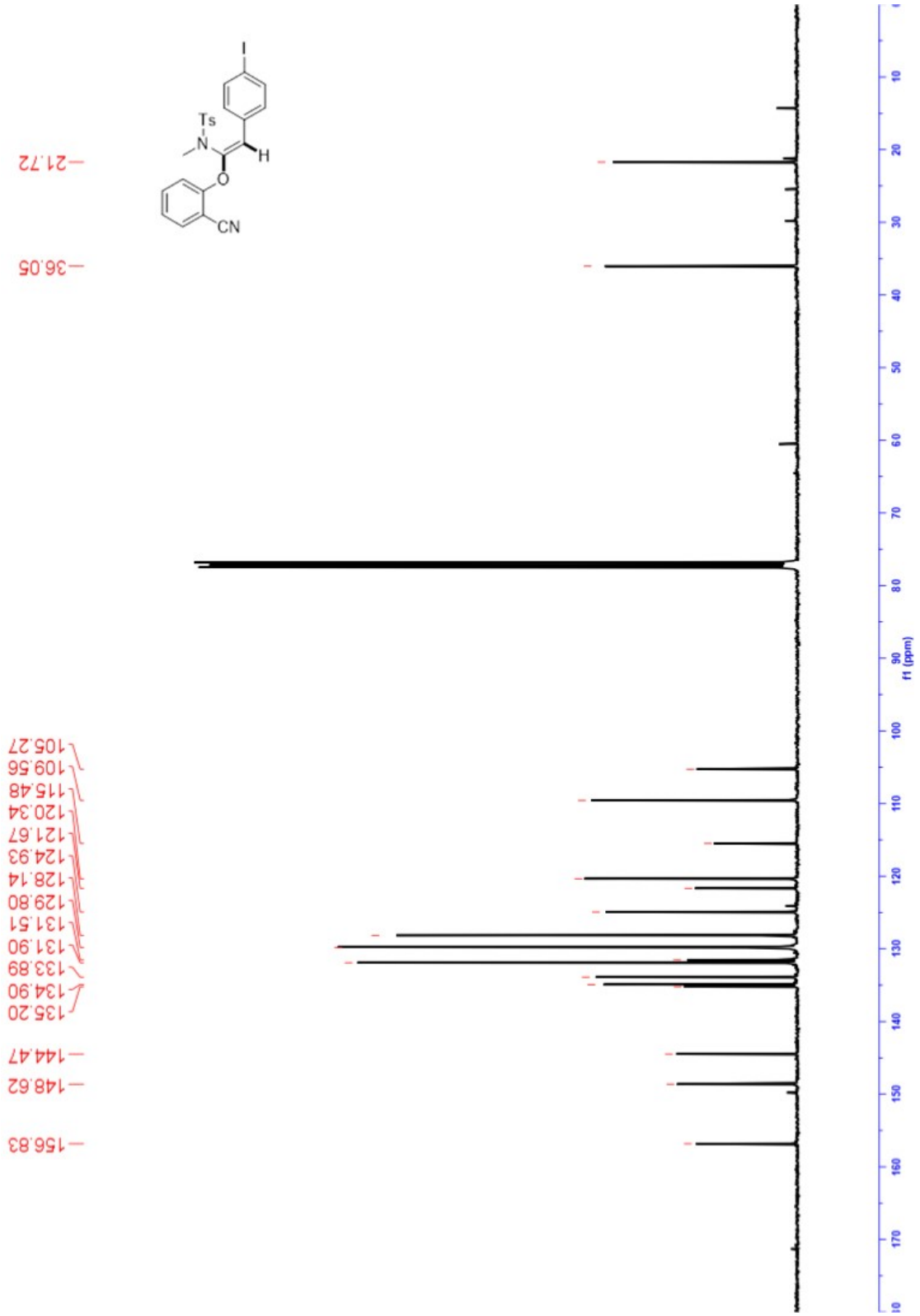
^{13}C NMR of 3hf (100 MHz, $CDCl_3$)



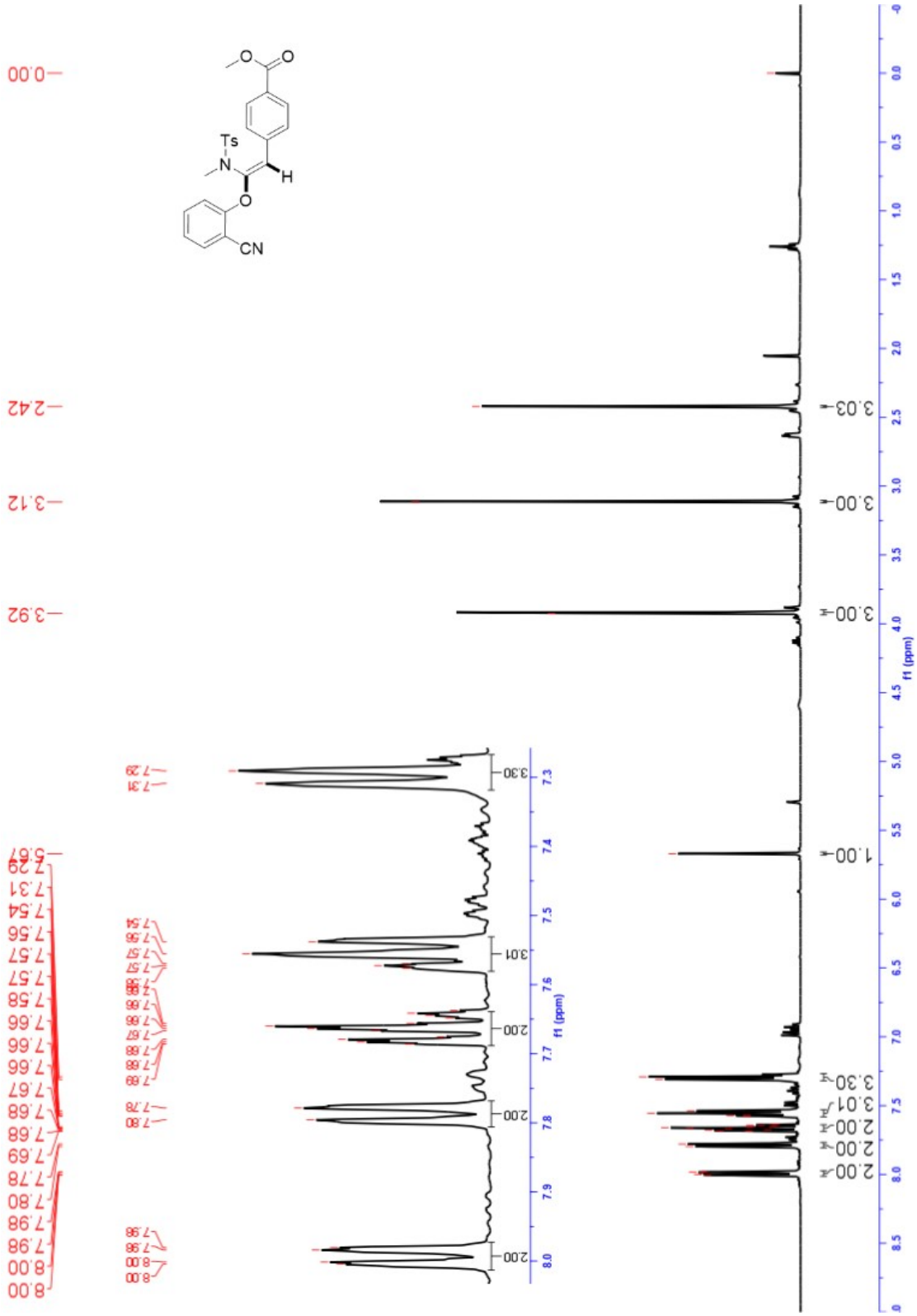
^{1}H NMR of 3if (400 MHz, $CDCl_3$)



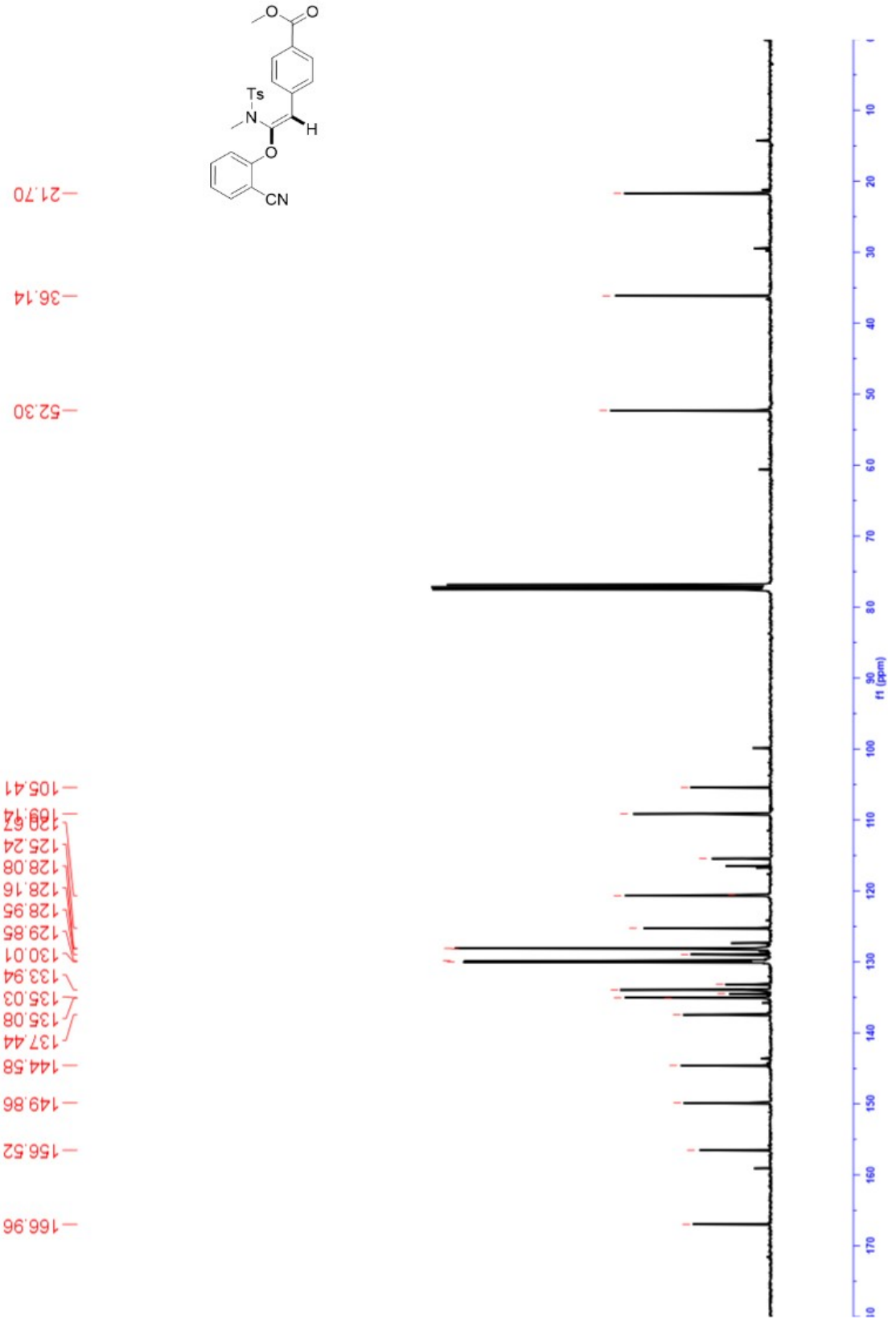
^{13}C NMR of 3if (100 MHz, $CDCl_3$)



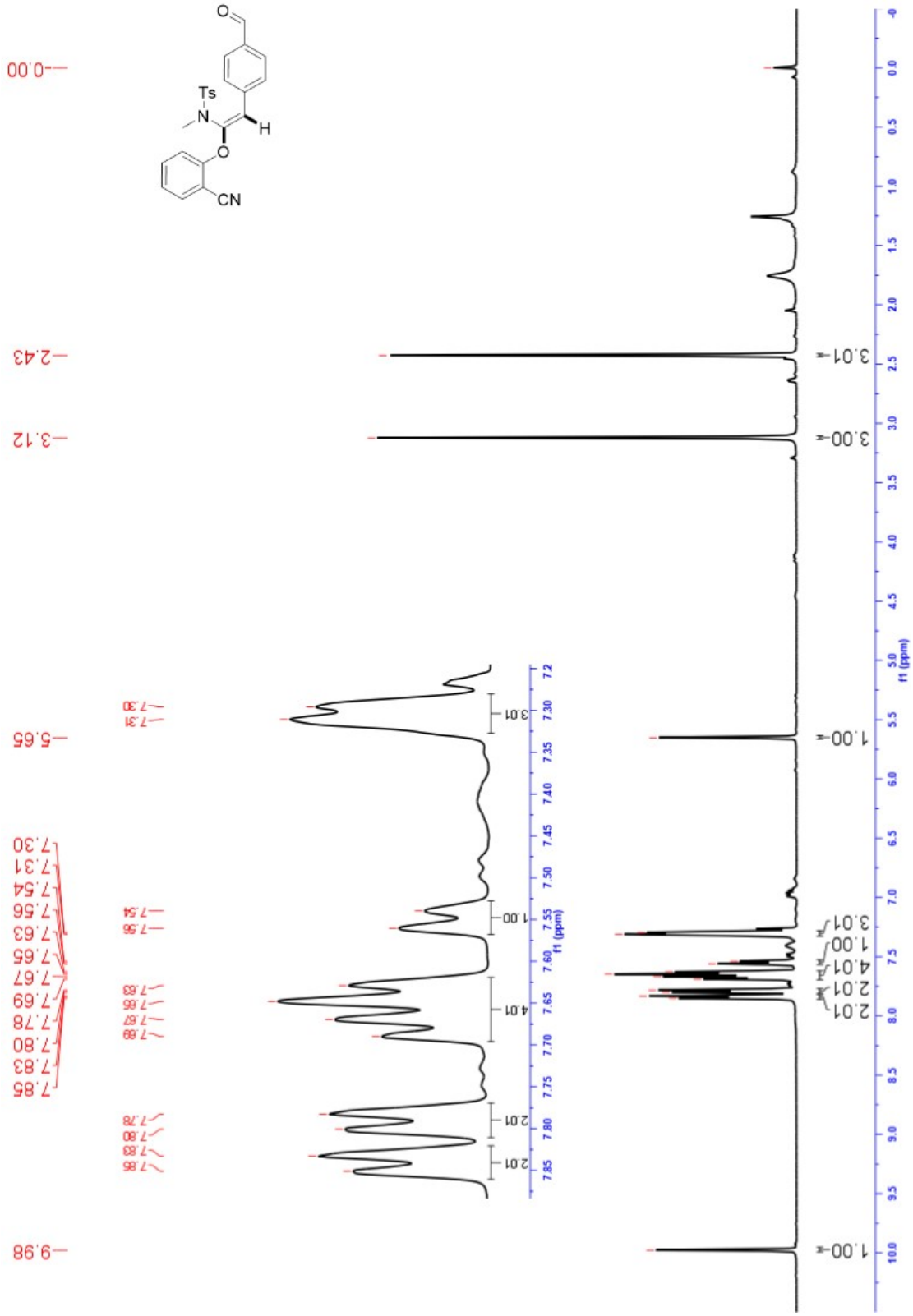
^{1}H NMR of 3jf (400 MHz, $CDCl_3$)



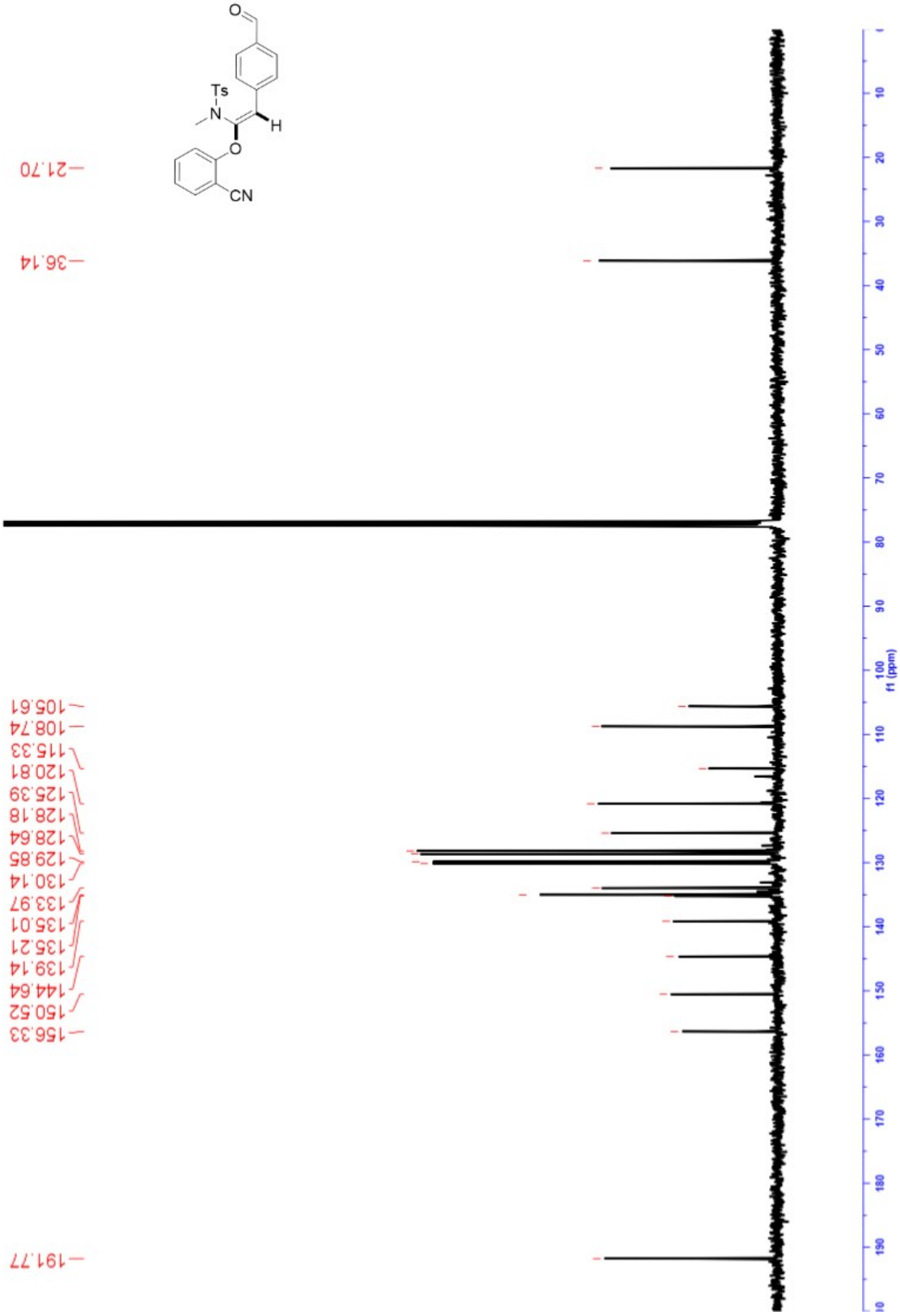
^{13}C NMR of 3jf (100 MHz, $CDCl_3$)



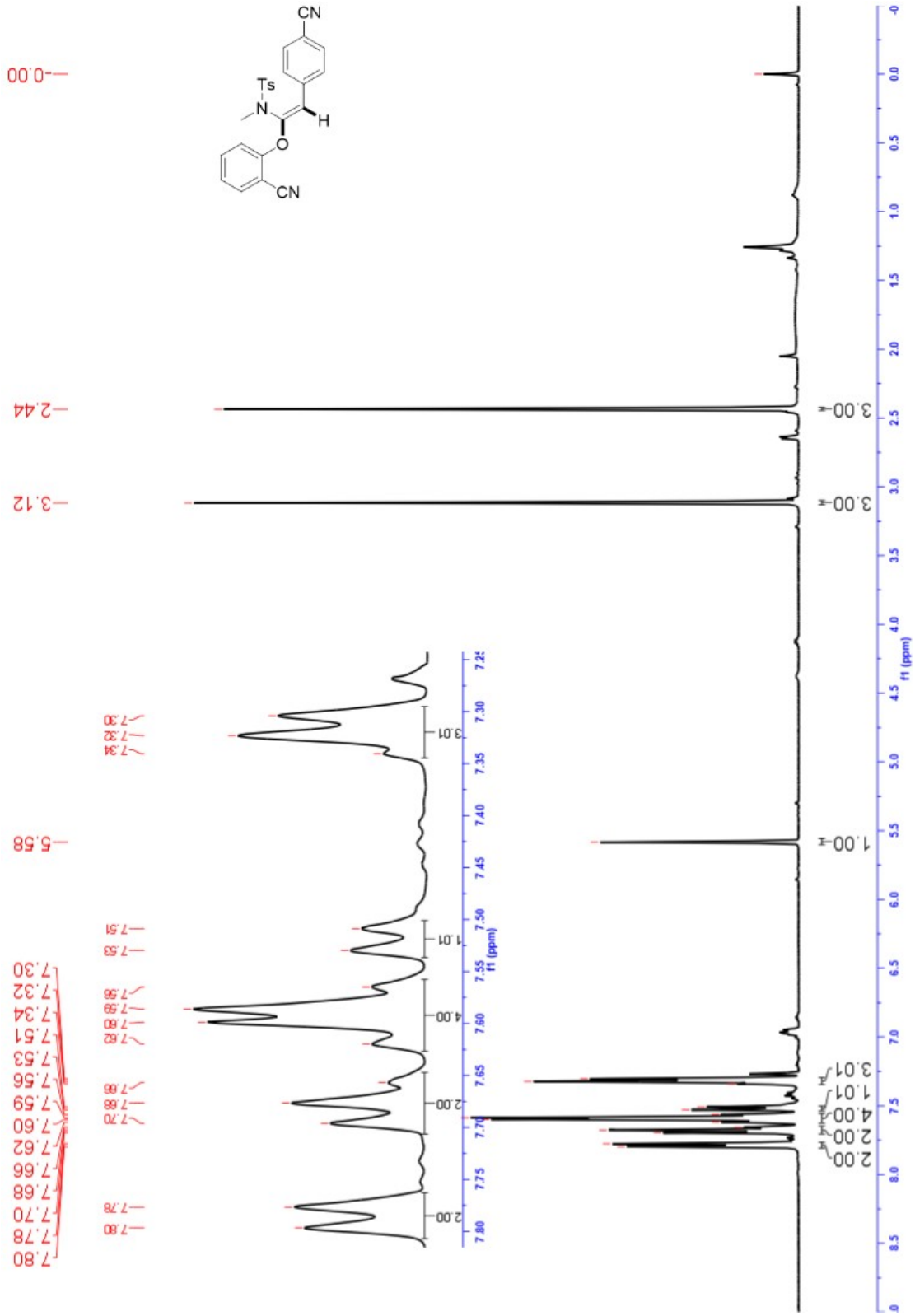
^{1}H NMR of 3kf (400 MHz, $CDCl_3$)



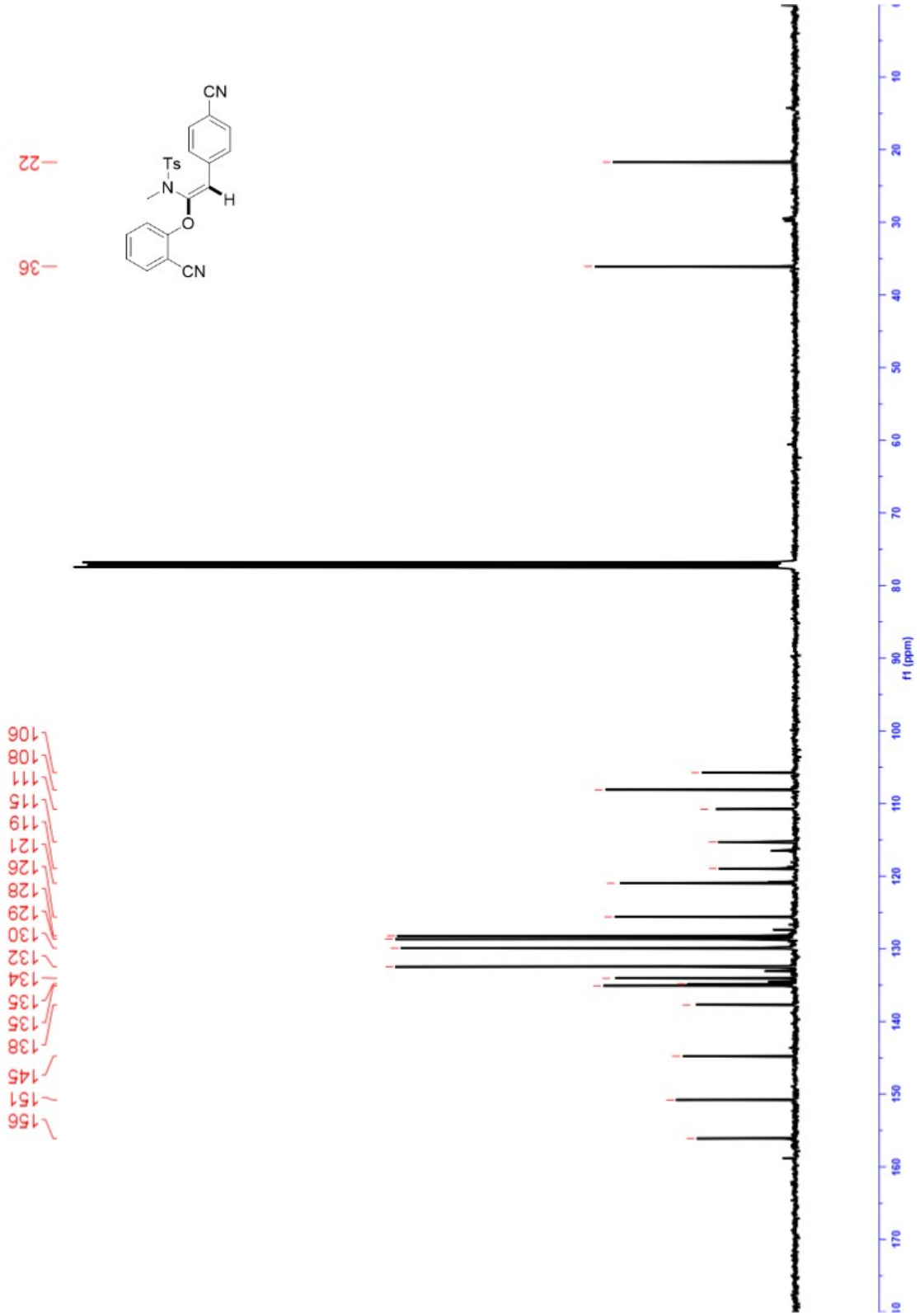
^{13}C NMR of 3kf (100 MHz, $CDCl_3$)



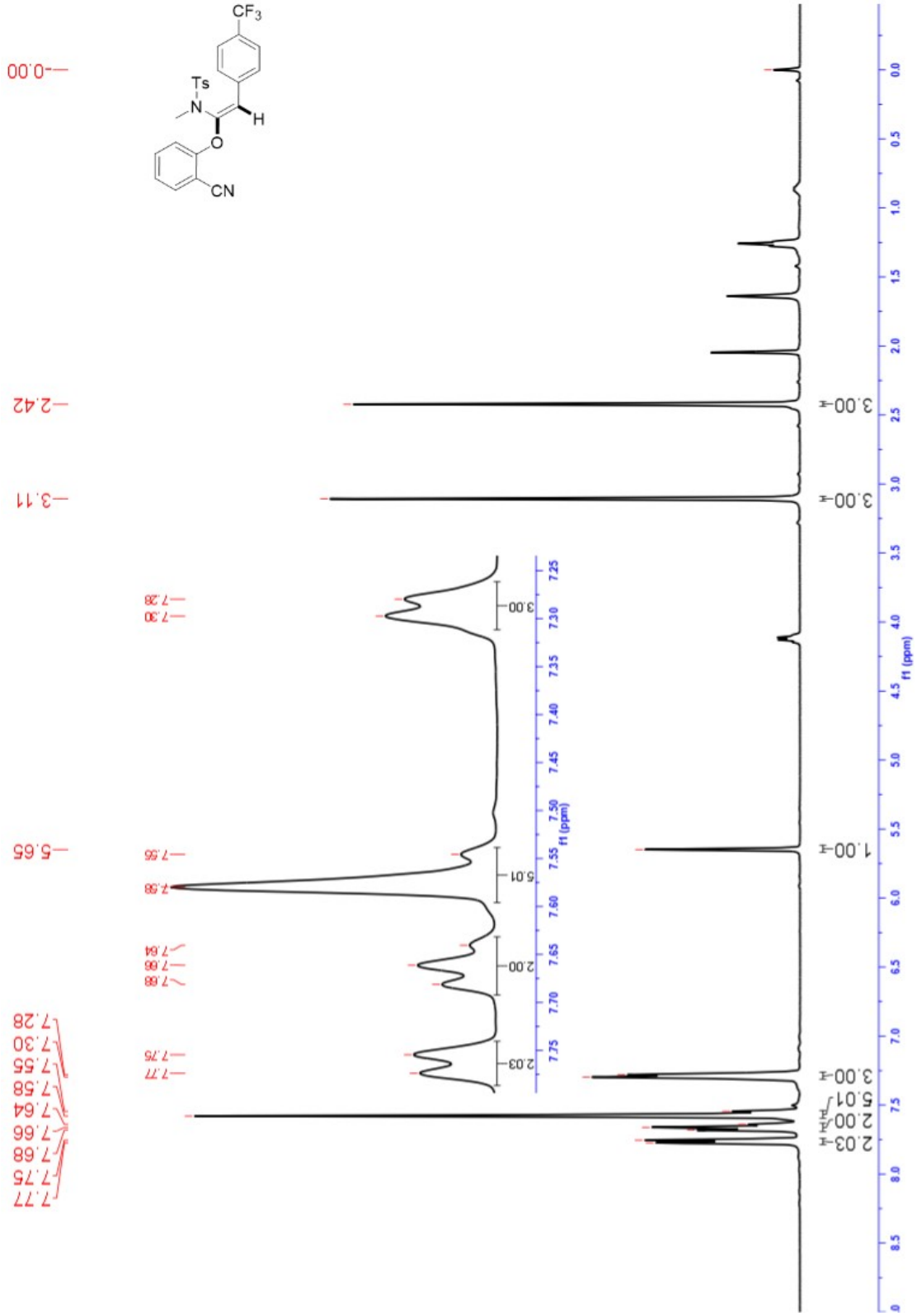
^{1}H NMR of 3lf (400 MHz, $CDCl_3$)



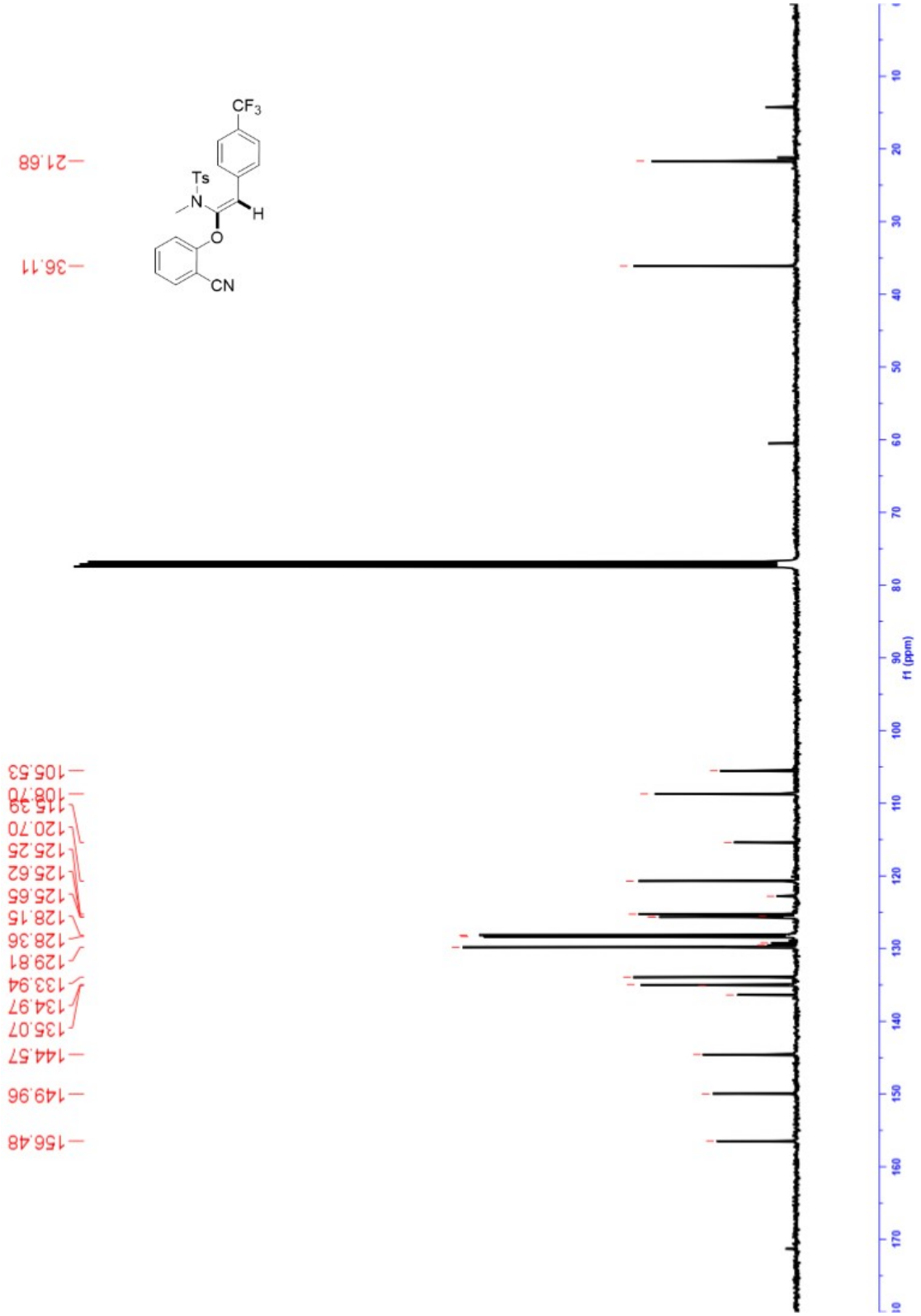
^{13}C NMR of 3lf (100 MHz, $CDCl_3$)



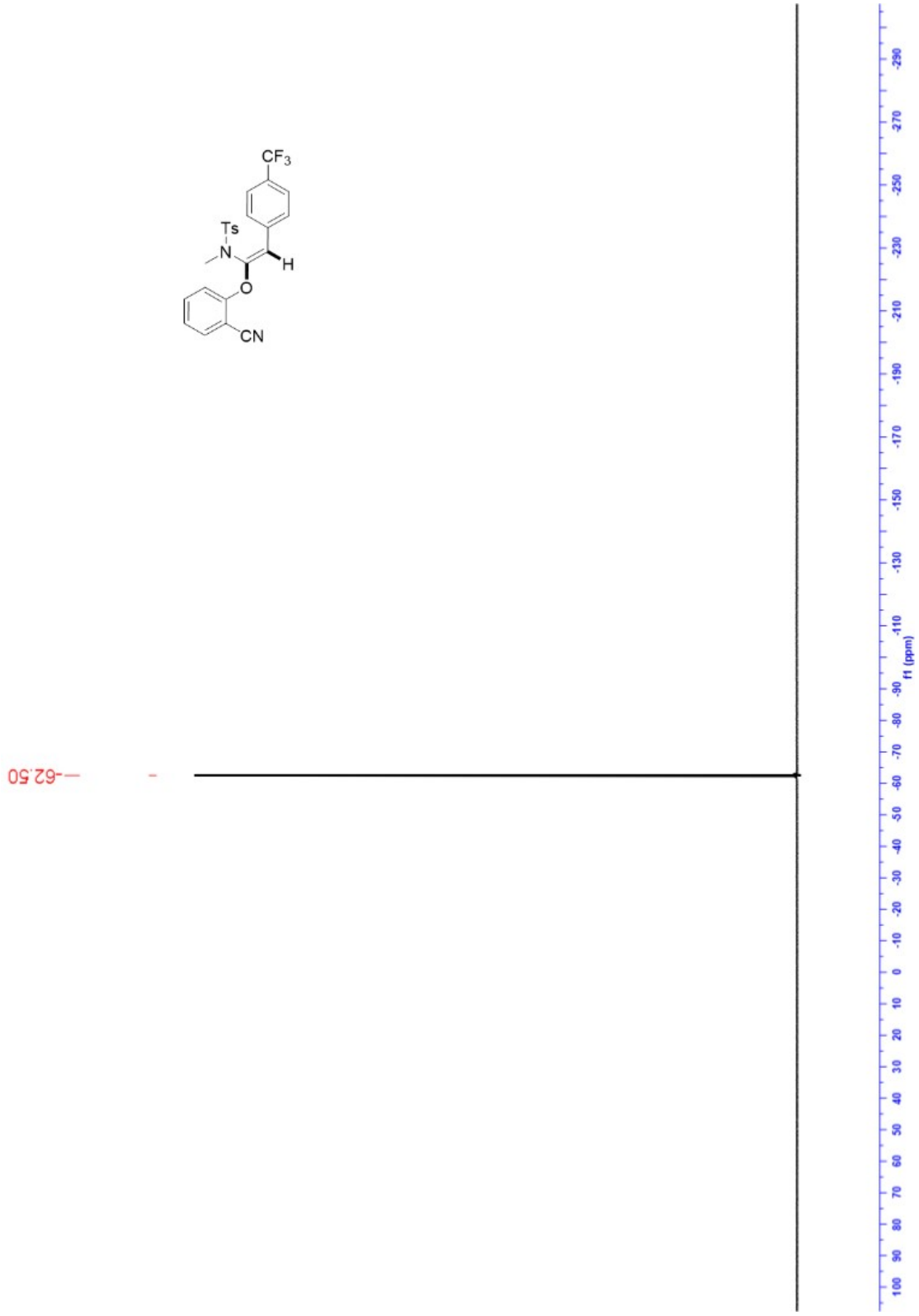
^{1}H NMR of 3mf (400 MHz, $CDCl_3$)



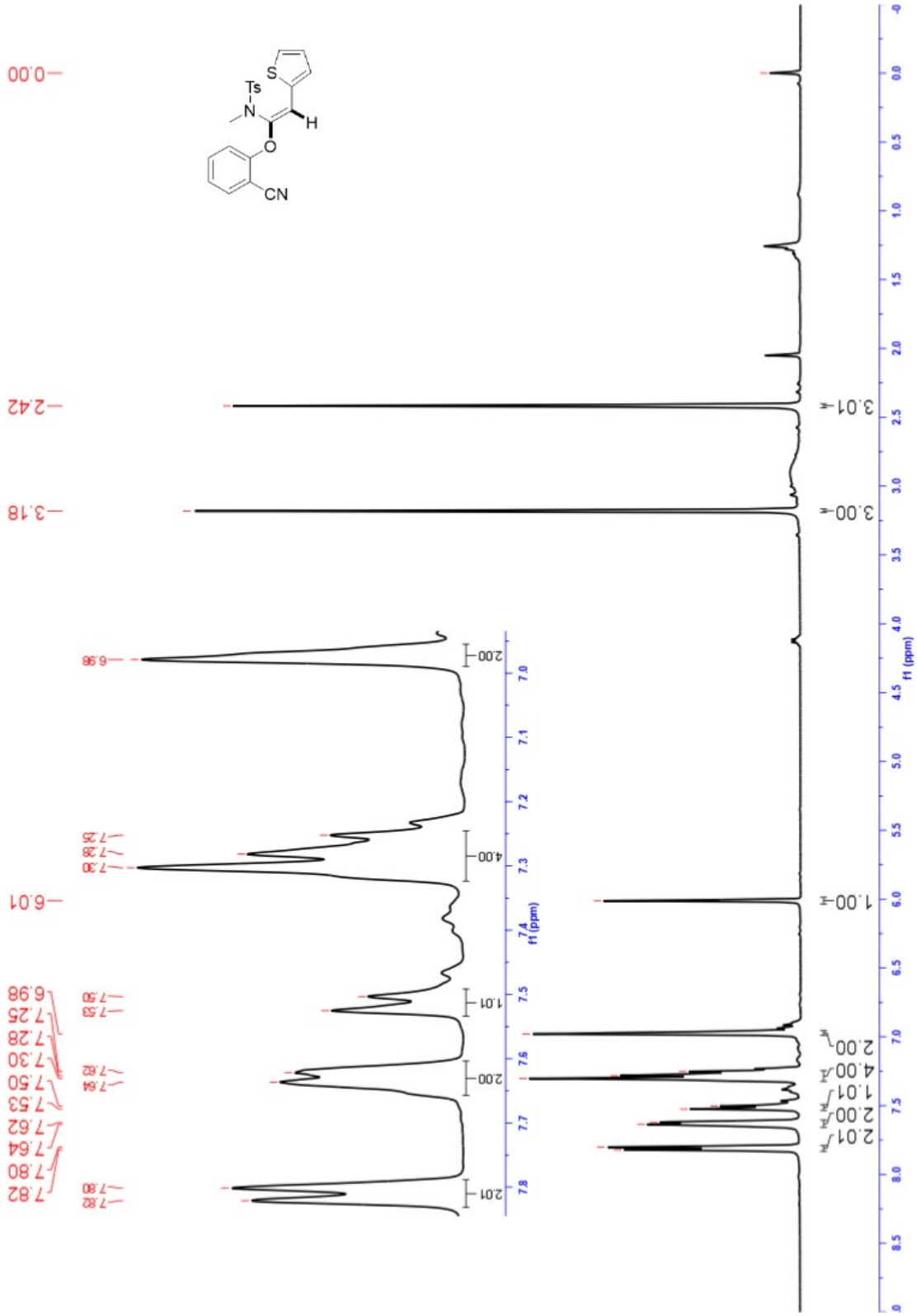
^{13}C NMR of 3mf (100 MHz, $CDCl_3$)



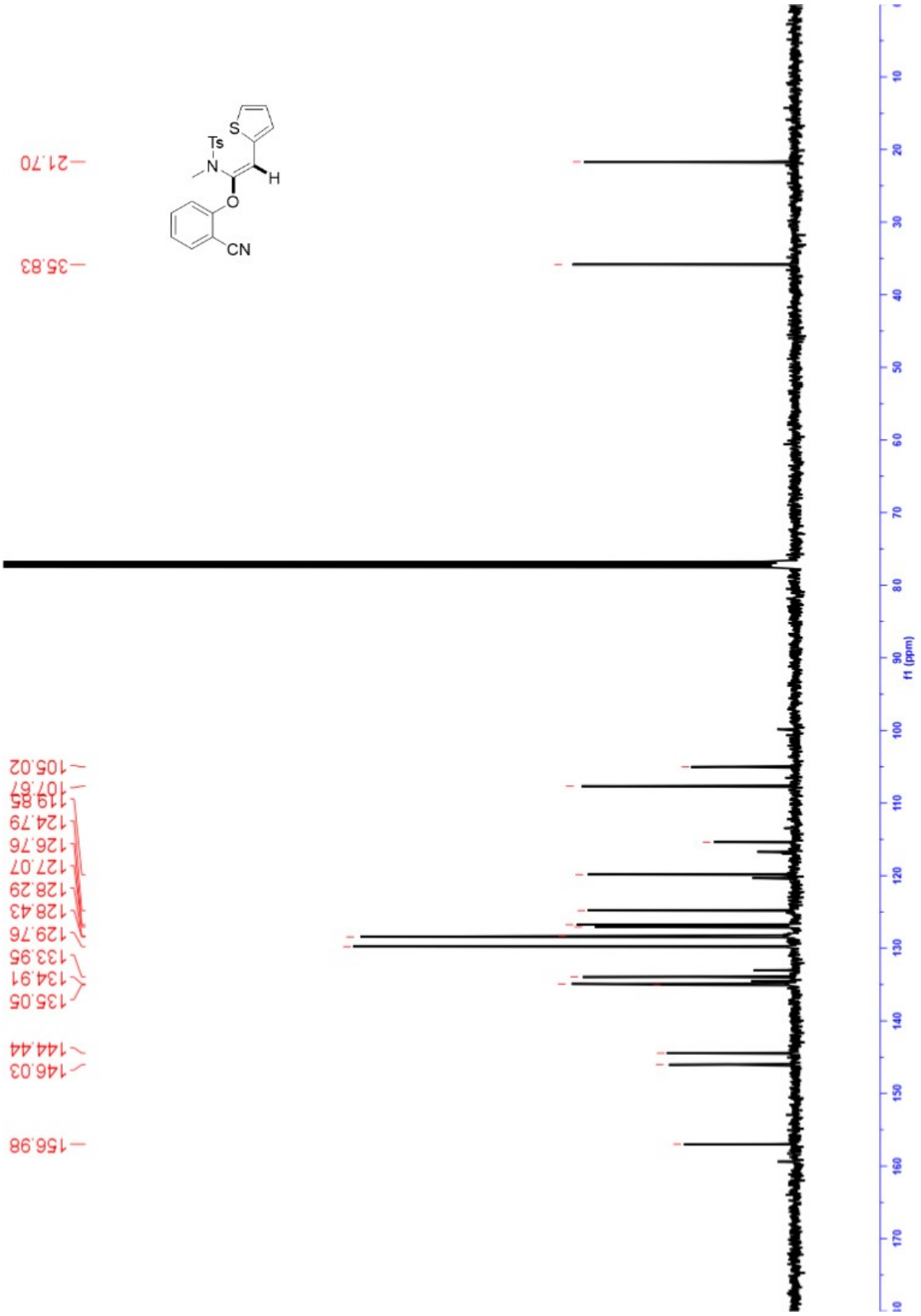
^{19}F NMR of 3mf (376 MHz $CDCl_3$)



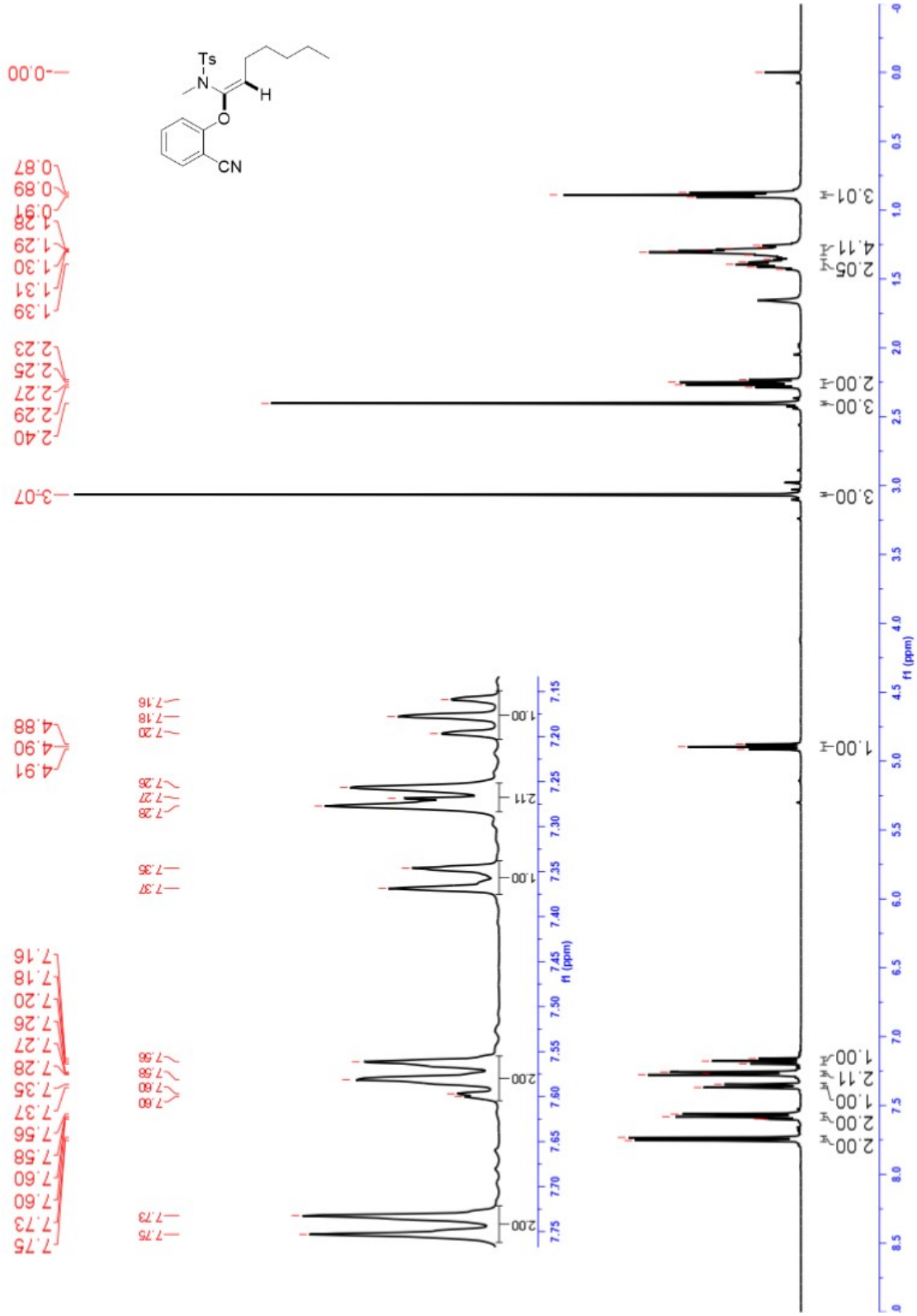
^{1}H NMR of 3nf (400 MHz, $CDCl_3$)



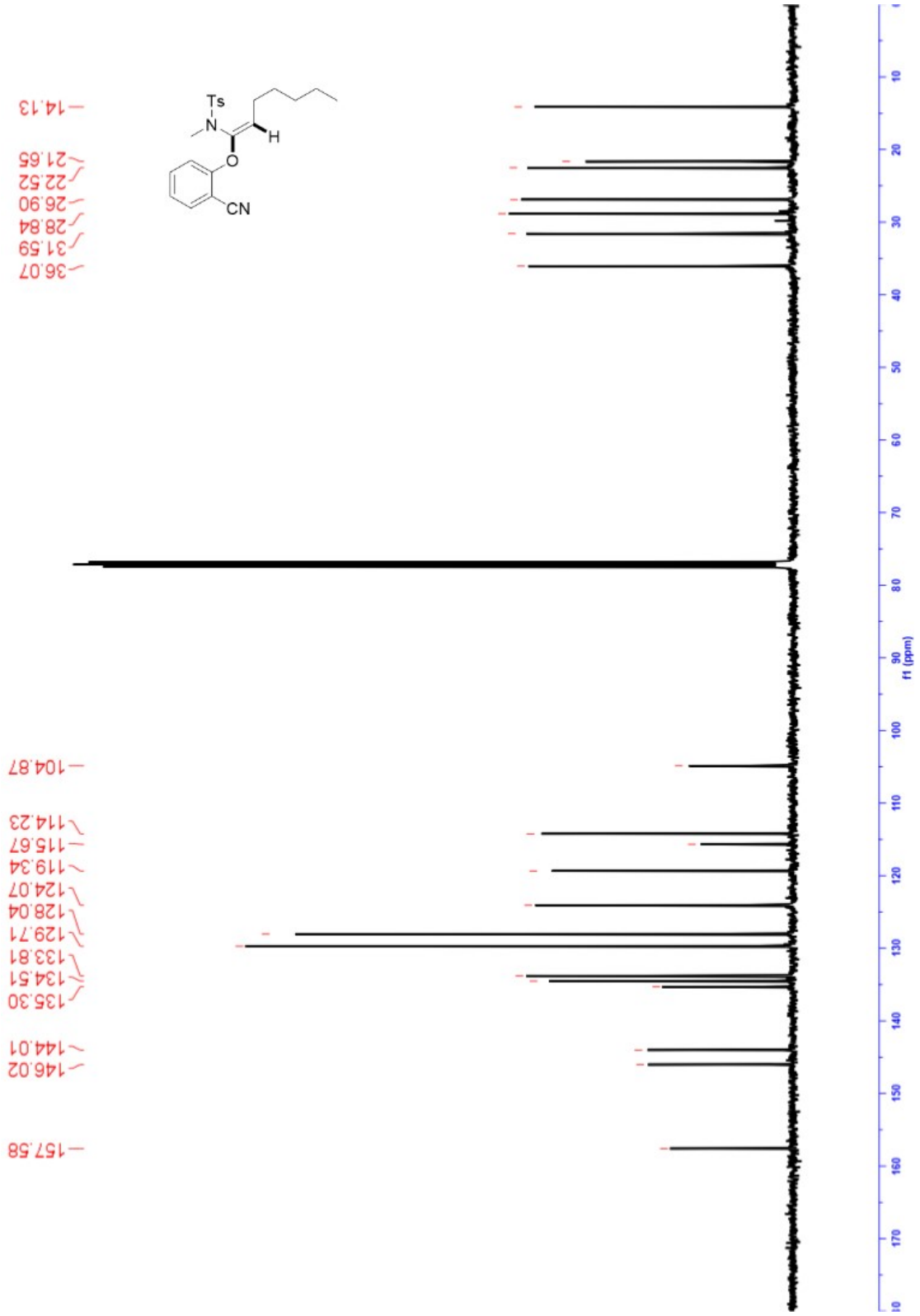
^{13}C NMR of 3nf (100 MHz, $CDCl_3$)



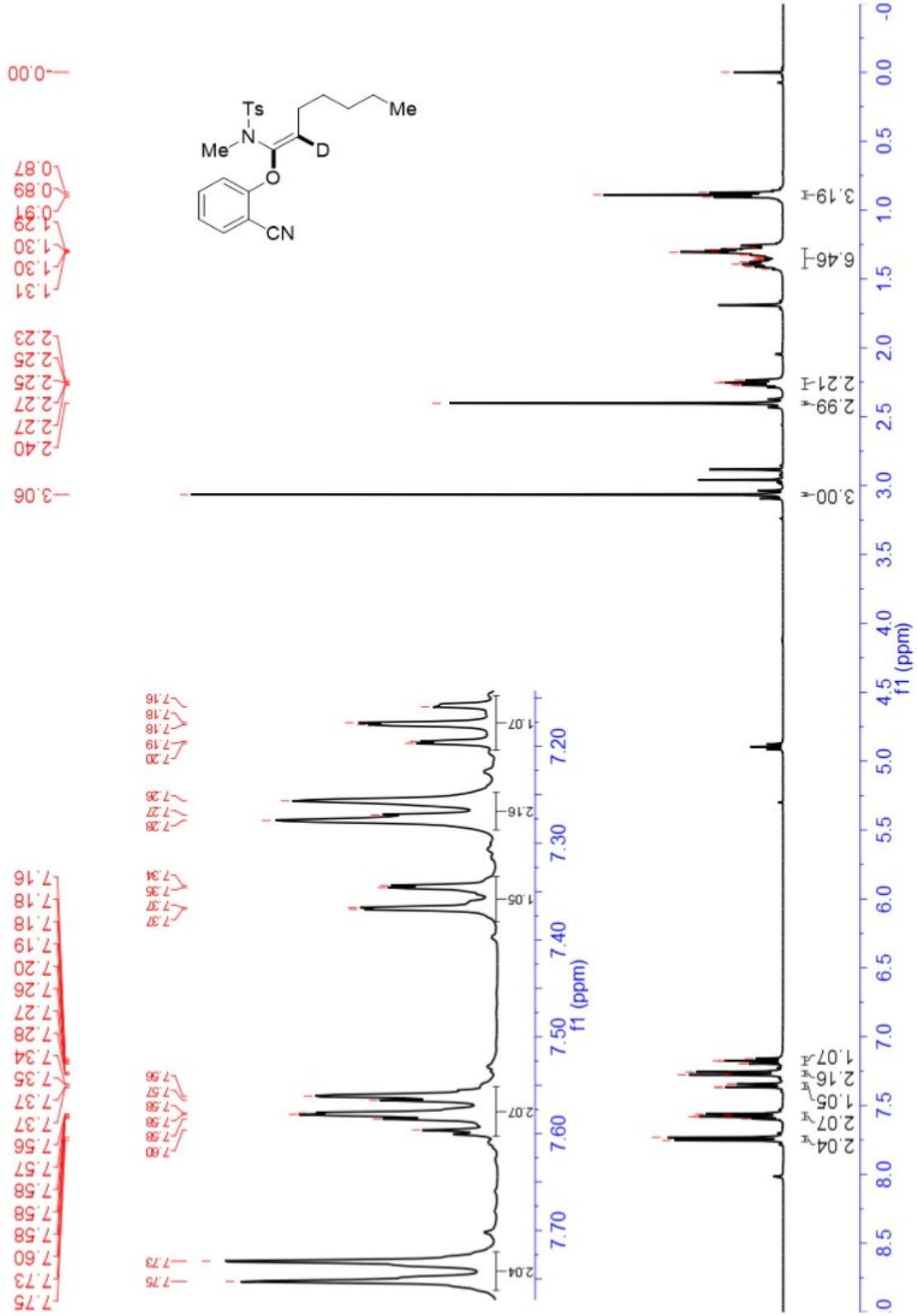
^{1}H NMR of 3of (400 MHz, $CDCl_3$)



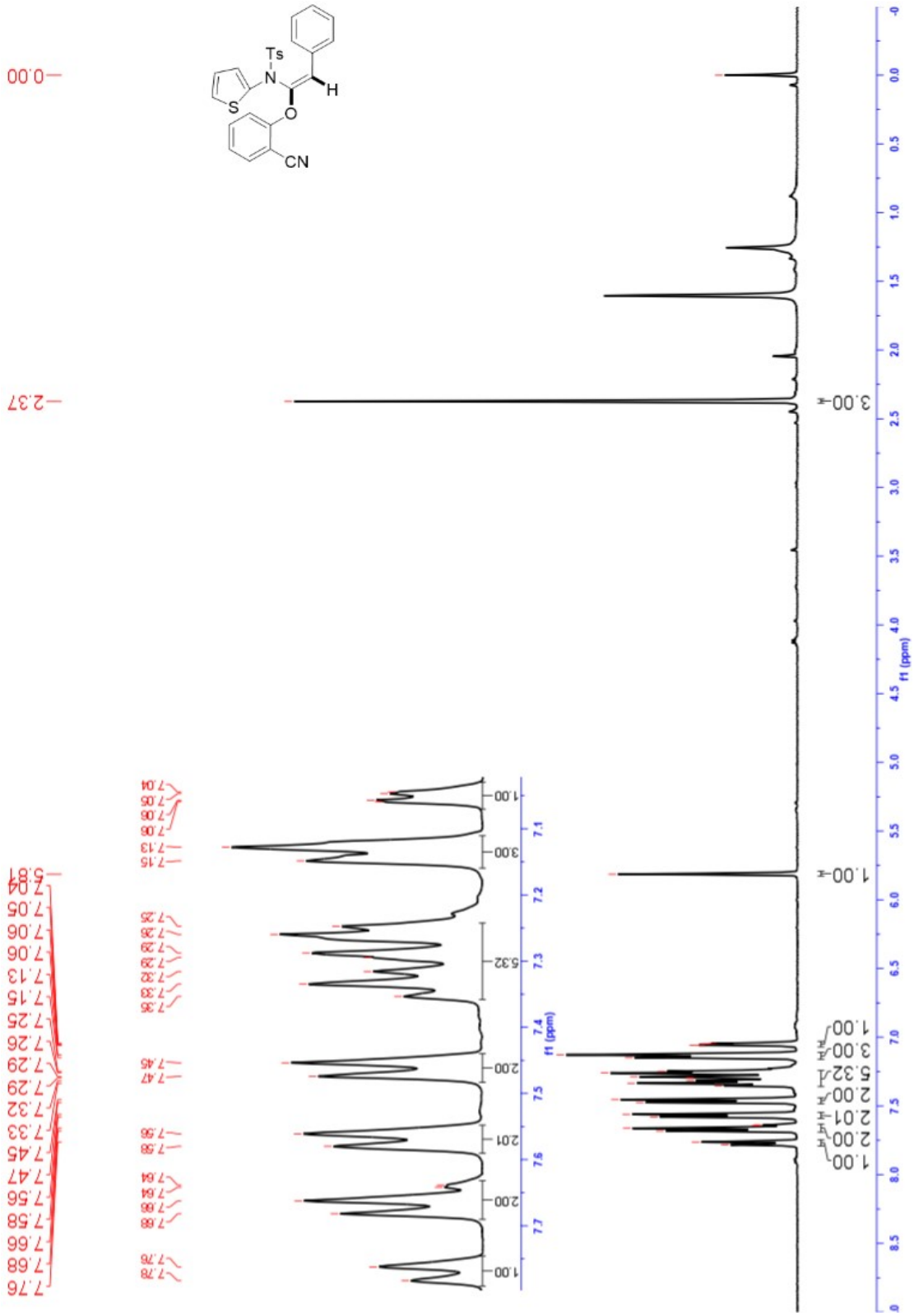
^{13}C NMR of 3of (100 MHz, $CDCl_3$)



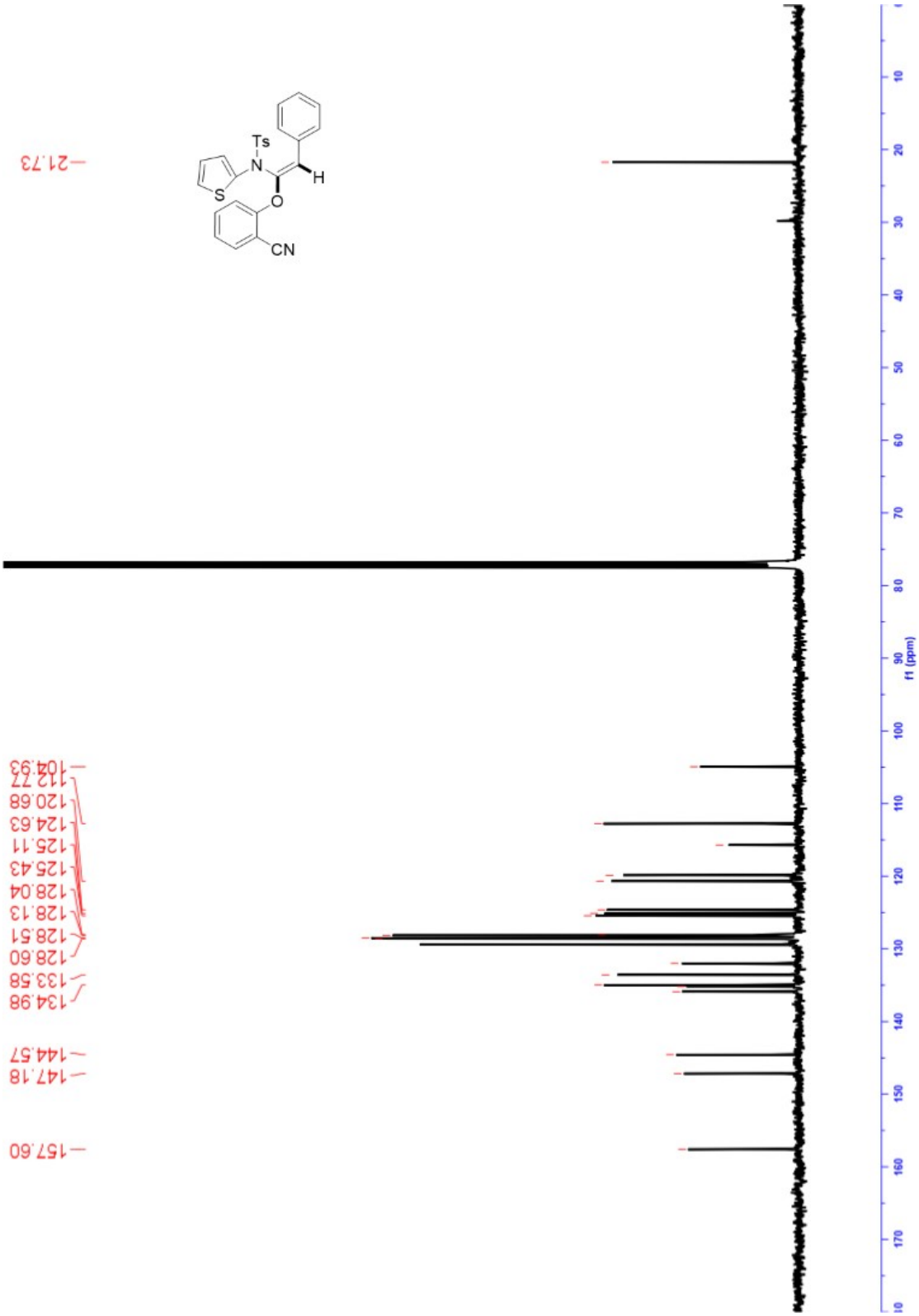
^{1}H NMR of 3of-D (400 MHz, $CDCl_3$)



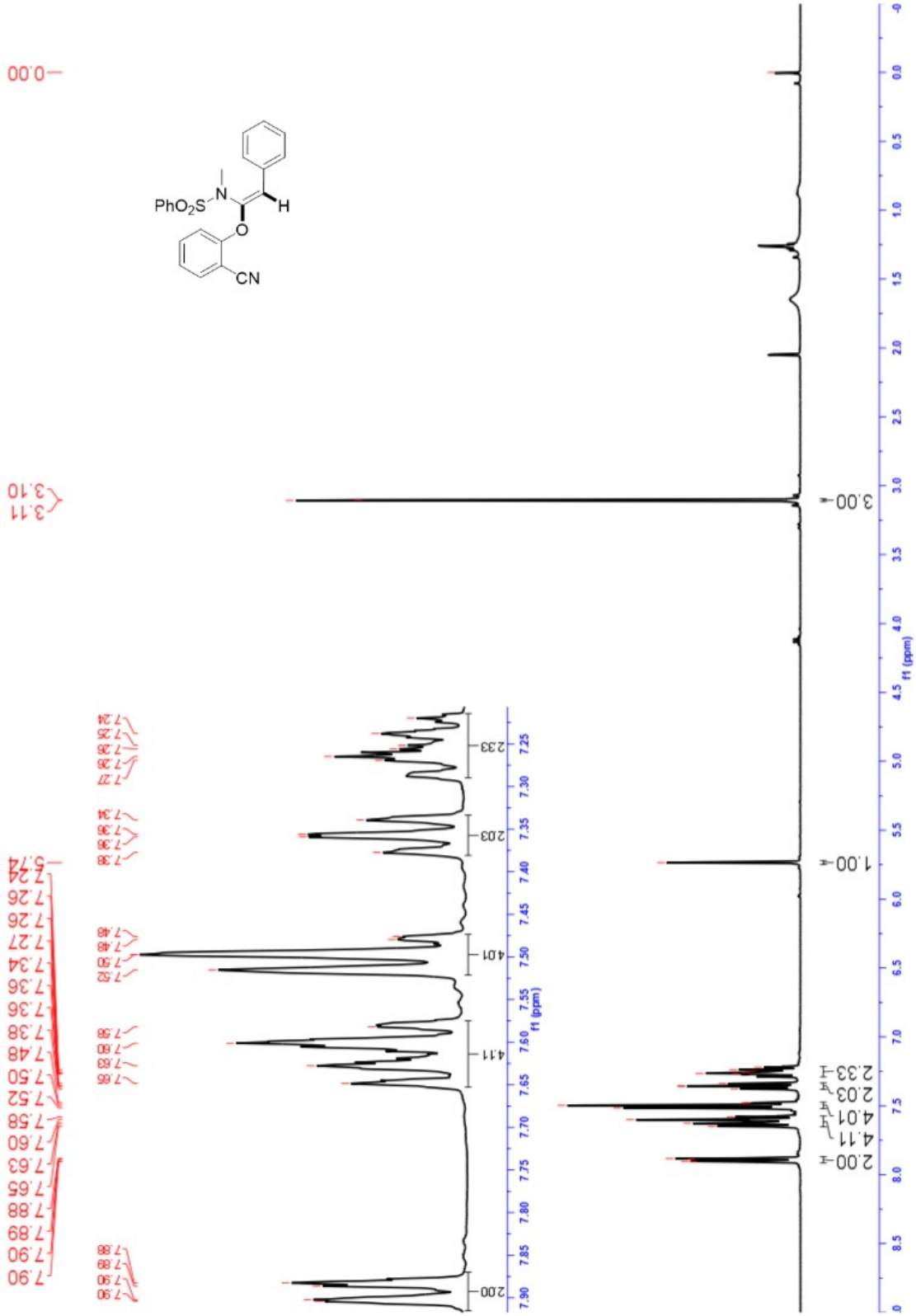
^{1}H NMR of 3pf (400 MHz, $CDCl_3$)



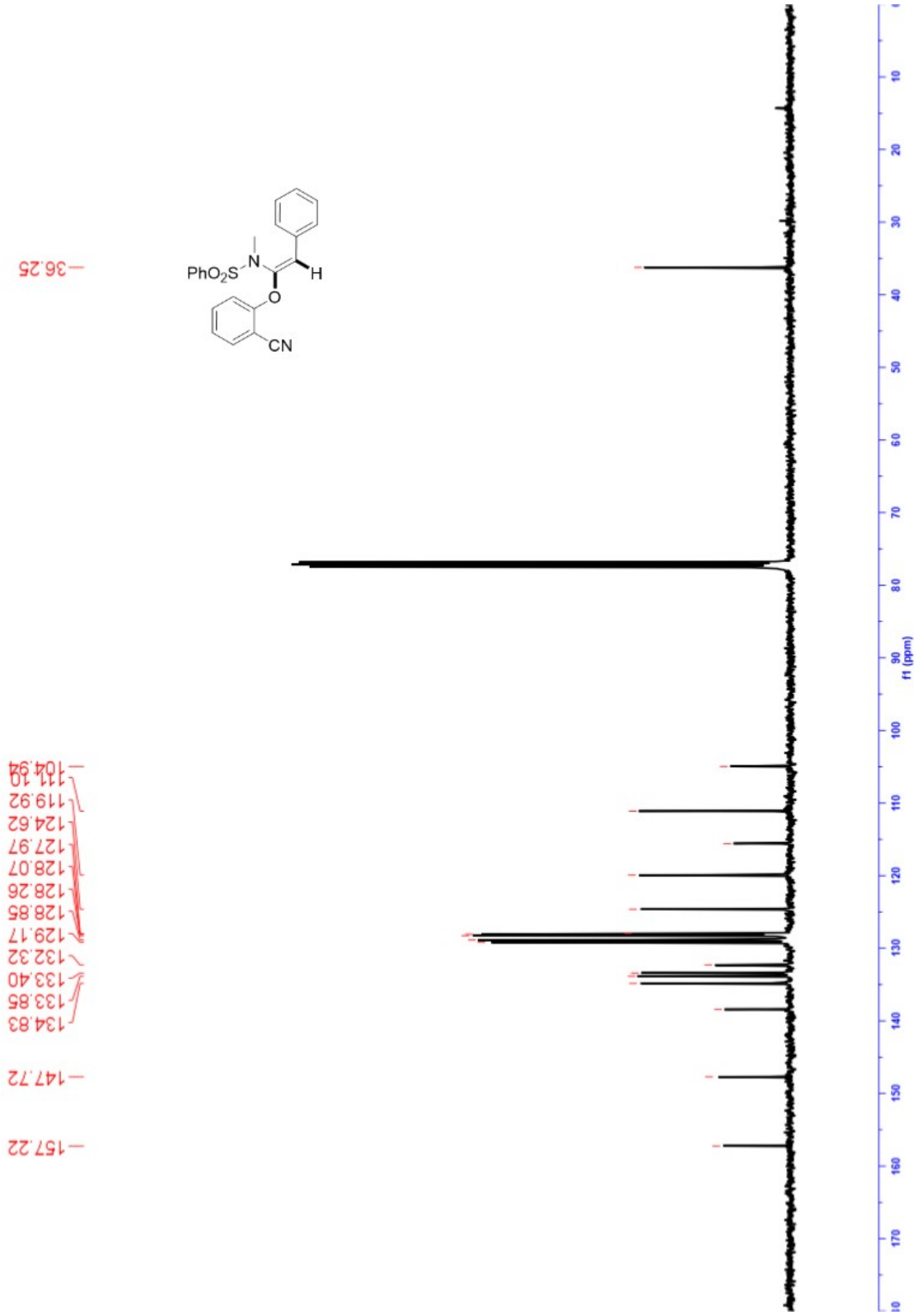
^{13}C NMR of 3pf (100 MHz, $CDCl_3$)



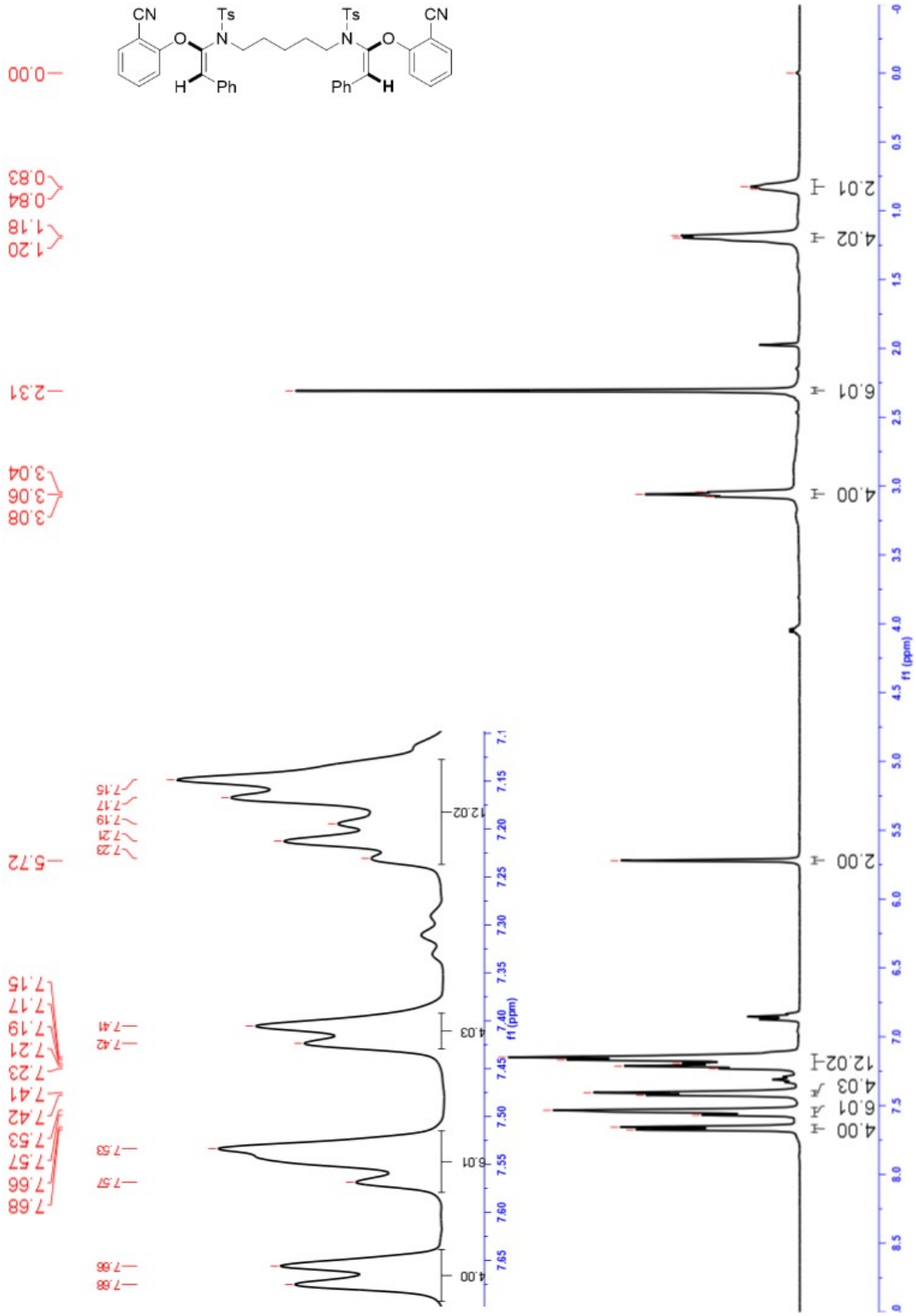
^{1}H NMR of 3qf (400 MHz, $CDCl_3$)



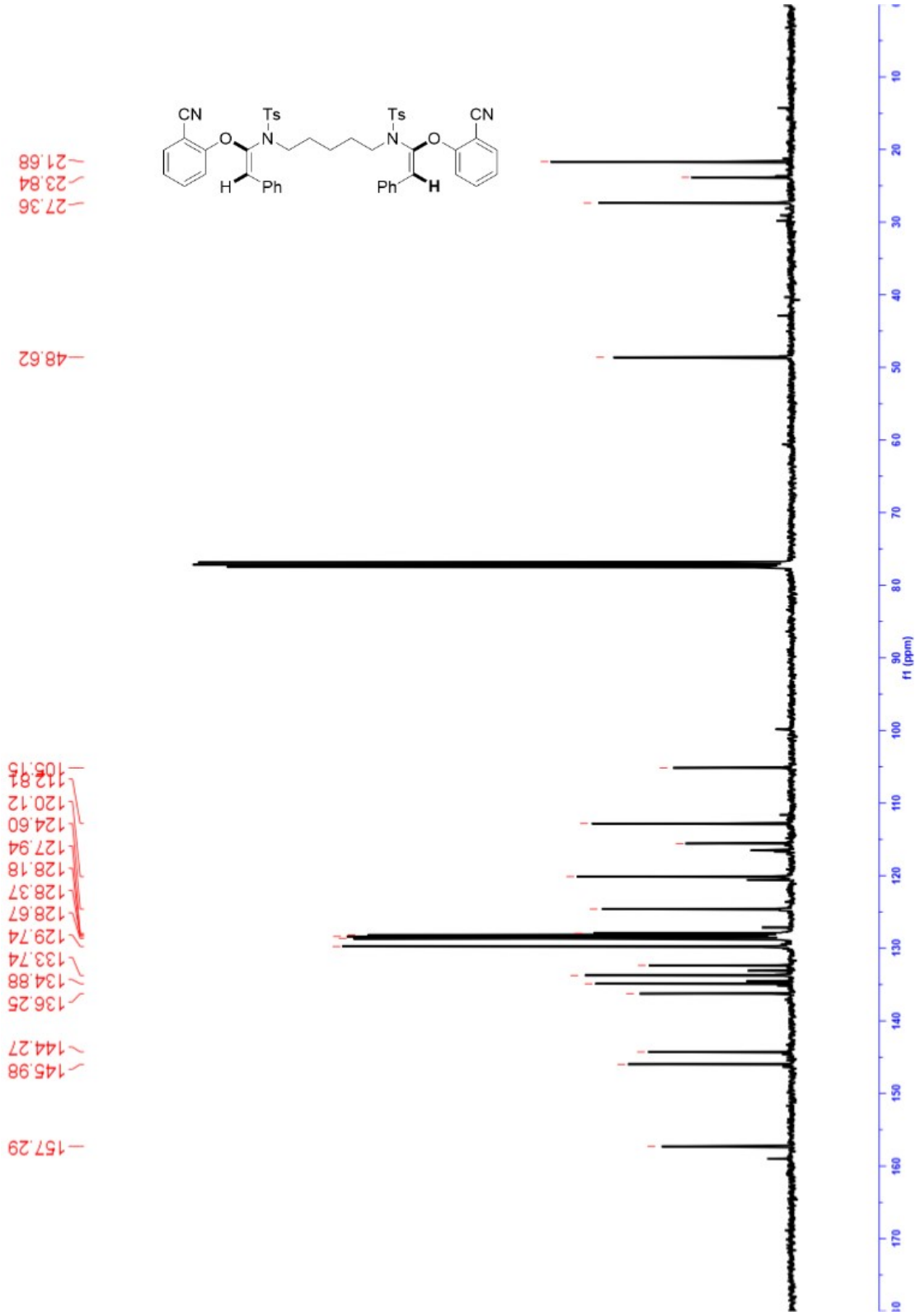
^{13}C NMR of 3qf (100 MHz, $CDCl_3$)



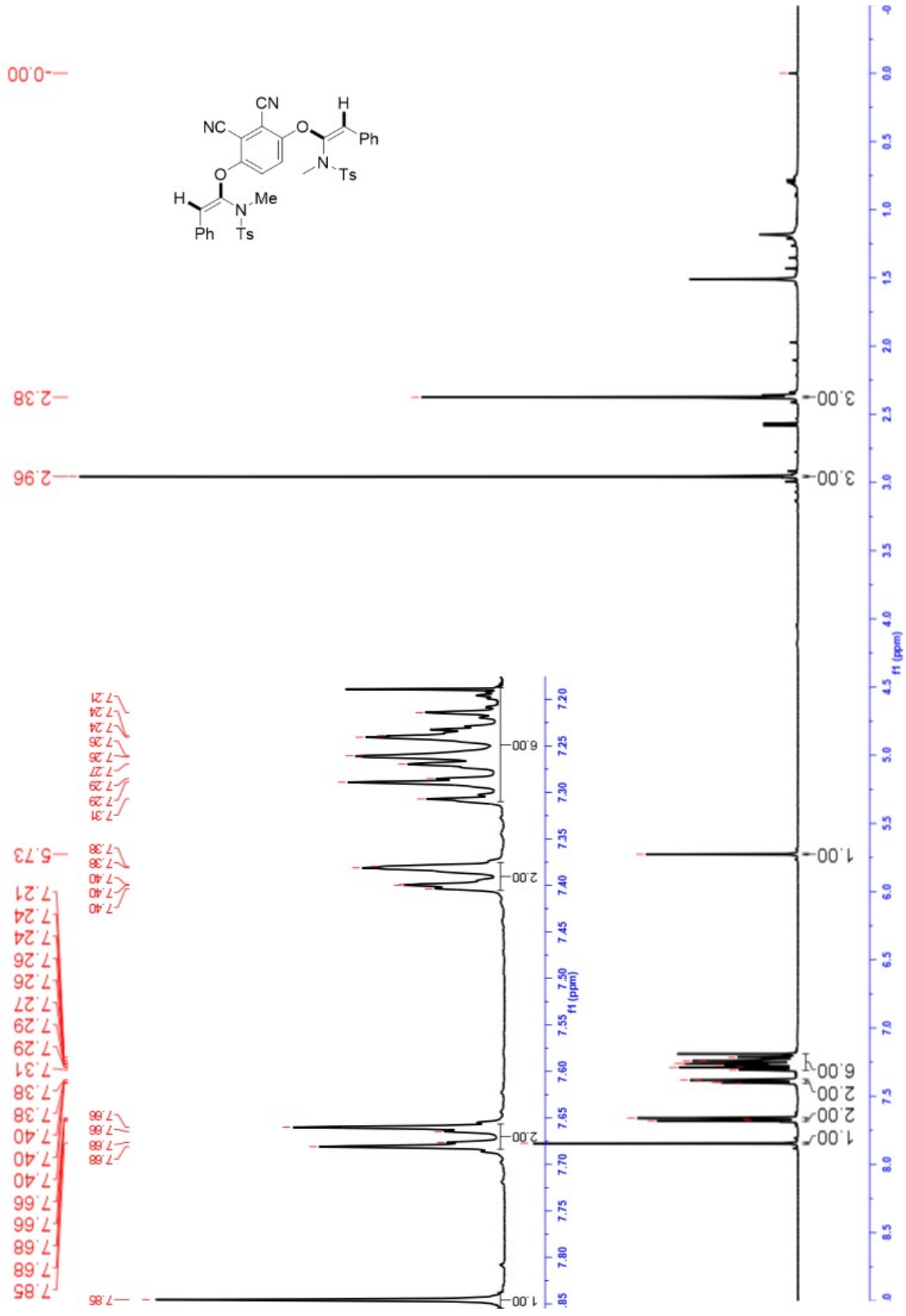
^{1}H NMR of 3rf (400 MHz, $CDCl_3$)



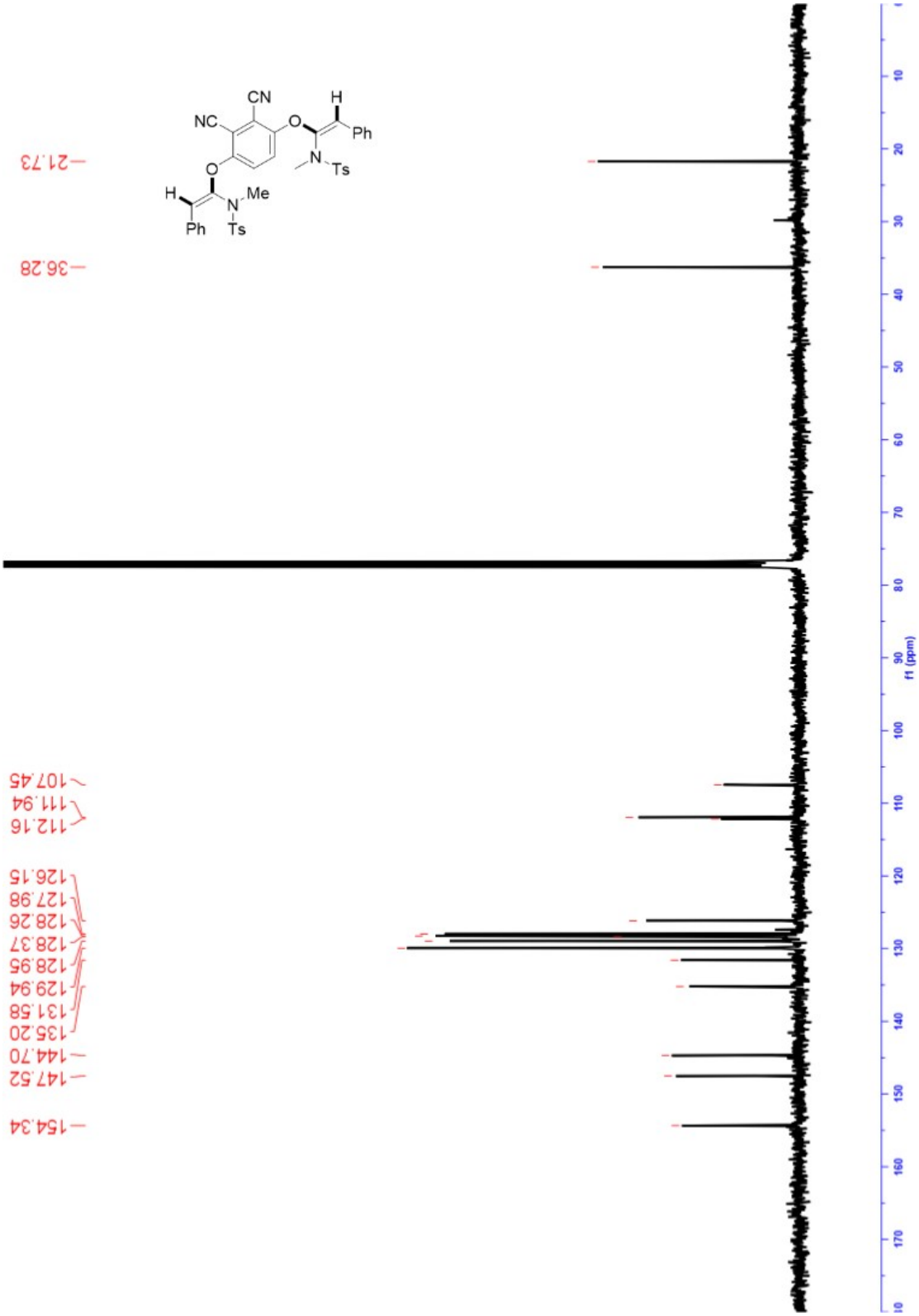
^{13}C NMR of 3rf (100 MHz, $CDCl_3$)



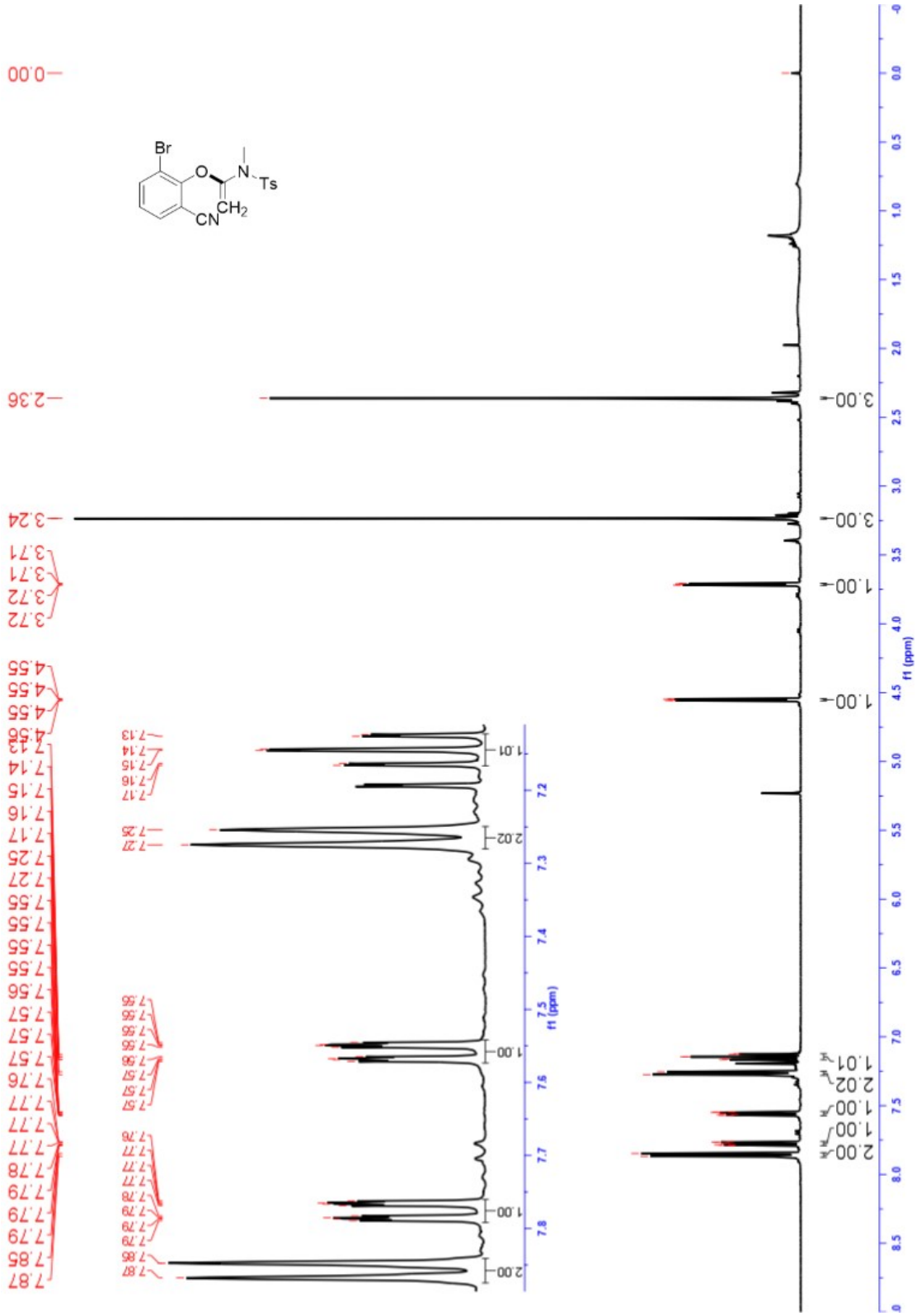
^{1}H NMR of 3aq (400 MHz, $CDCl_3$)



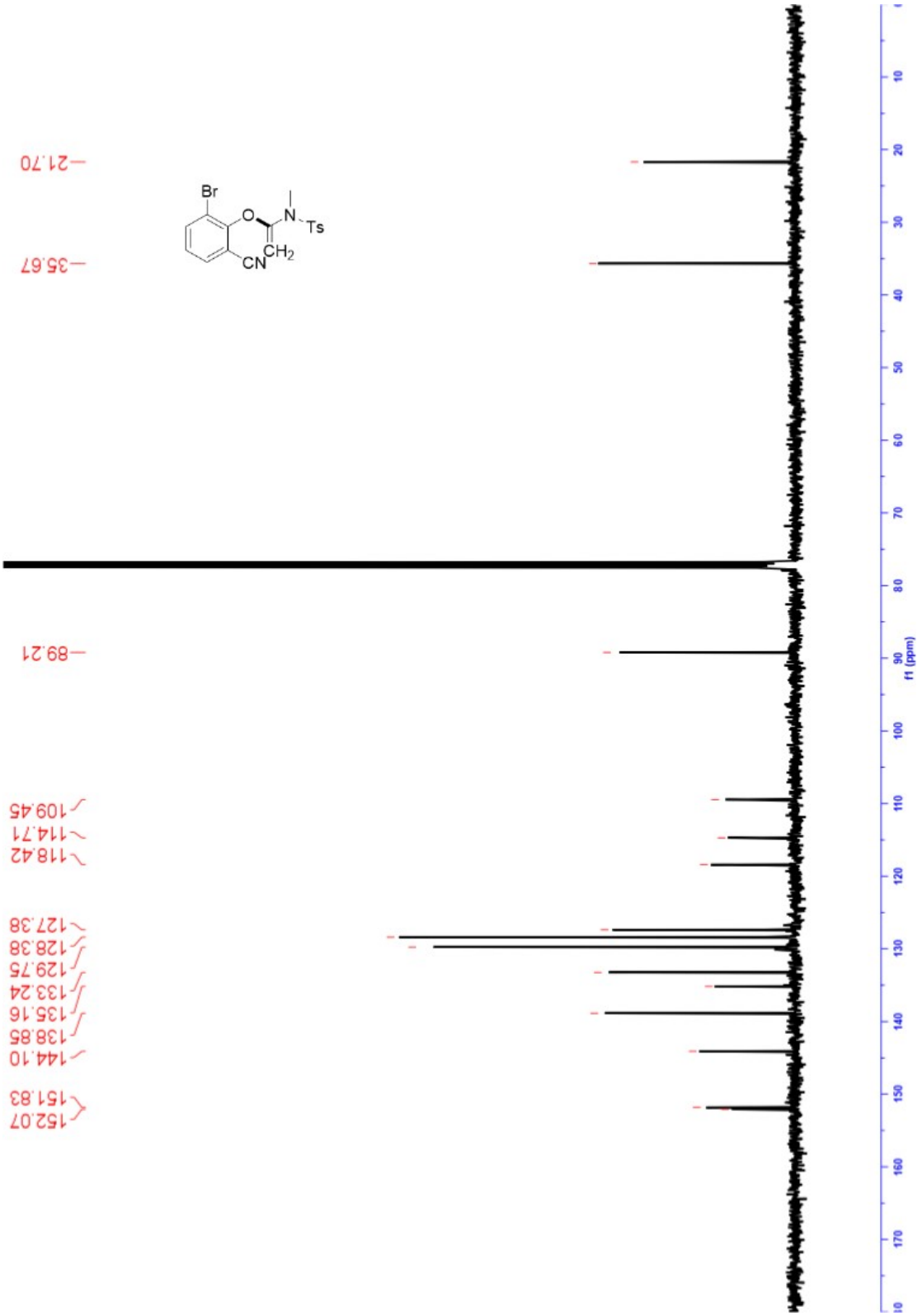
^{13}C NMR of 3aq (100 MHz, $CDCl_3$)



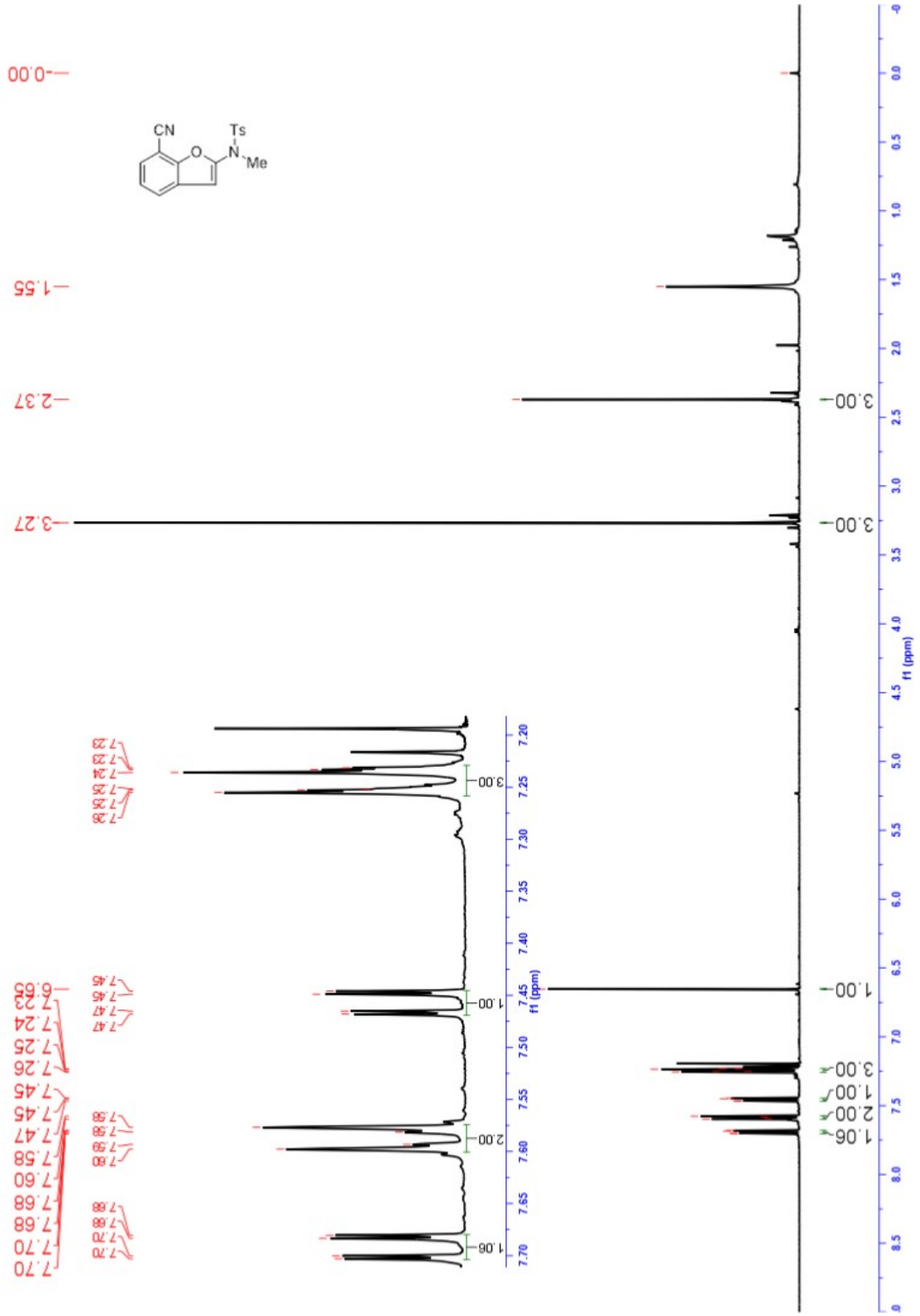
^{1}H NMR of 3rr (400 MHz, $CDCl_3$)



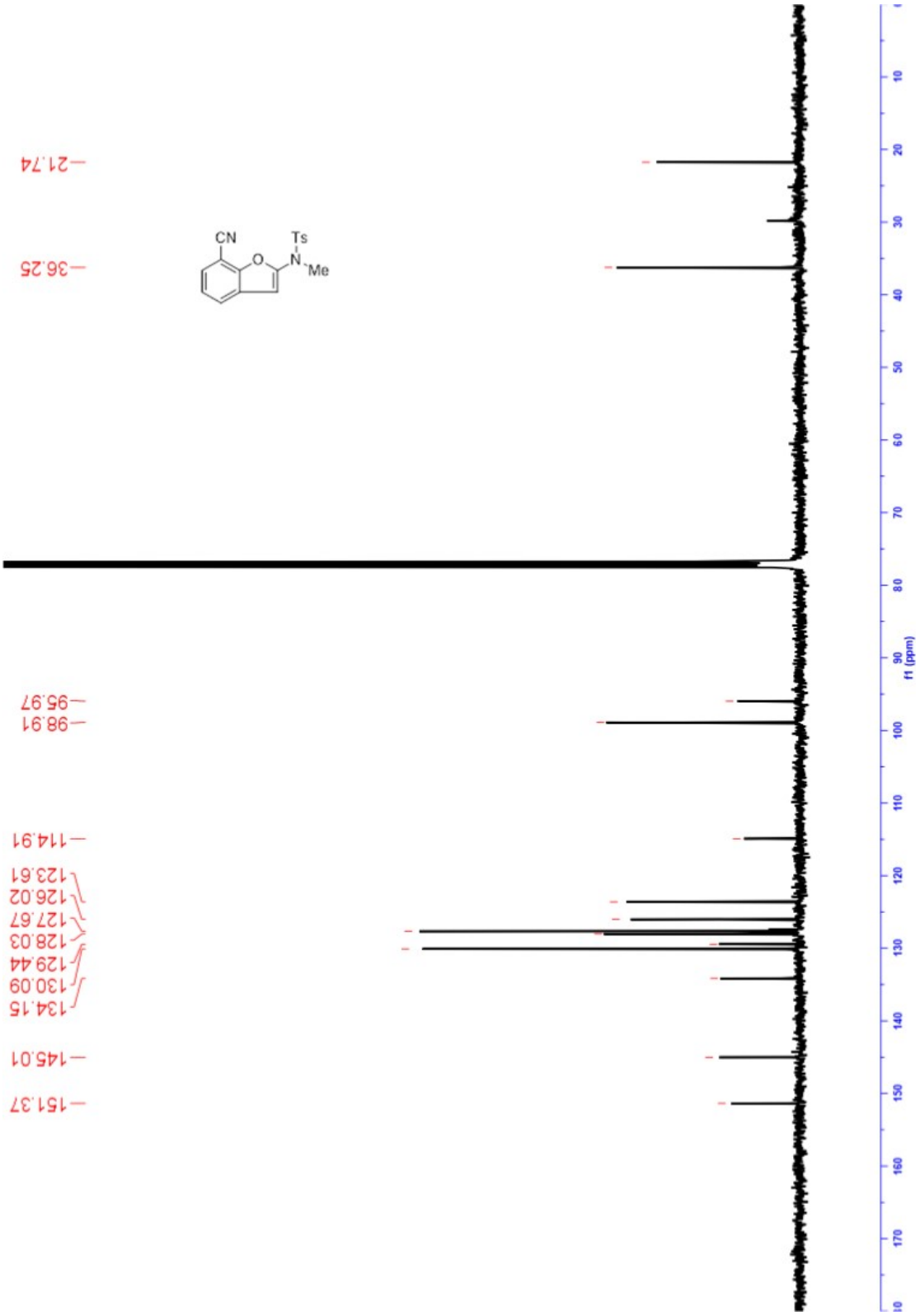
^{13}C NMR of 3rr (100 MHz, $CDCl_3$)



^{1}H NMR of 4 (400 MHz, $CDCl_3$)



^{13}C NMR of 4 (100 MHz, $CDCl_3$)



11. X-Ray crystallographic data

Single crystal growth: Compound **3af** was just dissolved in appropriate amount of EtOAc followed by the addition of petroleum ether to form a saturated solution. Then the solution was allowed to evaporate slowly at room temperature until the formation of a single crystal. A suitable crystal was selected and measured on a XtaLAB Synergy R, DW system, HyPix diffractometer. The crystal was kept at 100.00(10) K during data collection. Using Olex2, the structure was solved with the ShelXT structure solution program using Intrinsic Phasing and refined with the ShelXL refinement package using Least Squares minimisation. The crystallographic data have already been deposited at the Cambridge Crystallographic Data Centre (CCDC: 2217684), which can be acquired from www.ccdc.cam.ac.uk/data_request/cif.

The ellipsoid contour percent probability level is 50% for the image of the structure.

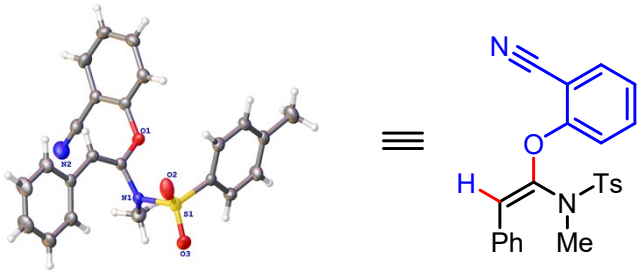


Table S3 Crystal data and structure refinement for **3af.**

Identification code	**3af**
Empirical formula	$C_{23}H_{20}N_2O_3S$
Formula weight	404.47
Temperature/K	249.97(10)
Crystal system	triclinic
Space group	P-1
a/Å	9.7863(9)
b/Å	10.1591(9)
c/Å	12.6200(8)
α/°	83.082(6)
β/°	68.299(7)
γ/°	63.337(9)
Volume/Å^3	1040.23(17)
Z	2
ρ_{calc}g/cm^3	1.291
μ/mm^{-1}	0.182
F(000)	424.0
Crystal size/mm^3	0.14 × 0.12 × 0.11
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.494 to 50

Index ranges	$-11 \leq h \leq 11$, $-12 \leq k \leq 9$, $-14 \leq l \leq 14$
Reflections collected	6733
Independent reflections	3659 [R_{int} = 0.0212, R_{sigma} = 0.0381]
Data/restraints/parameters	3659/0/264
Goodness-of-fit on F^2	1.029
Final R indexes [I>=2σ (I)]	R_1 = 0.0428, wR_2 = 0.1023
Final R indexes [all data]	R_1 = 0.0574, wR_2 = 0.1109
Largest diff. peak/hole / e $Å^{-3}$	0.18/-0.34

12. References

1 Zeng, Z.; Jin, H.; Xie, J.; Tian, B.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. *Org. Lett.* **2017**, *19*, 1020.

2 a) Ding, F.; Smith, J. M.; Wang, H. *J. Org. Chem*. **2009**, *74*, 2679; b) Xue, X.; Yang, C.; Li, X.; Cheng, J. *J. Org. Chem.* **2014**, *79*, 1166.

3 Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Y oung, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. *Gaussian 09 (Revision E.01)*, Gaussian, Inc.: Wallingford CT, 2013.

4 a) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B: Condens. Matter Mater. Phys.* **1988**, *37*, 785; b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

5 a) Montgomery, J. A.; Frisch, M. J.; Ochterski, J. W.; Petersson, G. A., *J. Chem. Phys*. **1999**, *110*, 2822; b) Montgomery, J. A.; Frisch, M. J.; Ochterski, J. W.; Petersson, G. A. *J. Chem. Phys.* **2000**, *112*, 6532.

6 a) Zhao, Y.; Schultz, N. E.; Truhlar, D. G. *J. Chem. Theory and Comput.* **2006**, *2*, 364; b) A. V. Marenich, C. J. Cramer; Truhlar D. G. *J. Phys. Chem. B* **2009**, *113*, 6378; c) Ho, J.; Klamt, A.; Coote, M. L. *J. Phys. Chem.* 2010, 114, 13442.

7 Bordwell, F. G. *Acc. Chem. Res*. **1988**, *21*, 456.

8 Kolthoff, I. M.; Chantooni, M. K. Jr. *J. Am. Chem. Soc.* **1975**, *97*, 1376

9 Kaljurand, I.; Kütt, A.; Sooväli, L.; Rodima, T.; Mäemets, V.; Leito, I.; Koppel, I. A. *J. Org. Chem*. **2005**, *70*, 1019.

10 L. Goerigk and S. Grimme. *J. Chem. Theory Comput.* **2011**, *7*, 291.