Supporting Information

Enantioselective Friedel–Crafts Reaction between Phenols and *N*-Tosylaldimines Catalyzed by Leucine-Derived Bifunctional Catalyst

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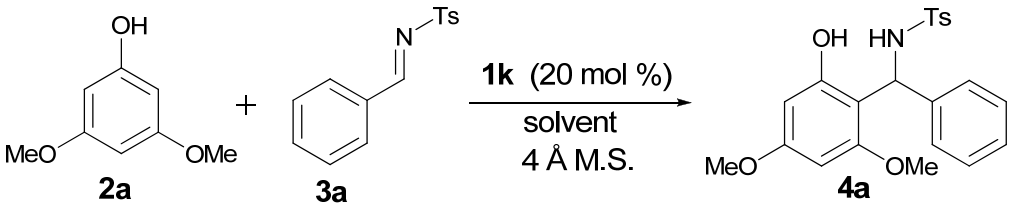
General information: All reagents were used as received without further purification. Solvents were purified according to the reported literature. Flash column chromatographies were performed using the indicated solvent system on Merck® silica gel (230–400 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on a 300 MHz or a 400 MHz NMR spectrometer. Peaks recorded are relative to internal standards: TMS ($\delta = 0.00$) for ^{1}H and $CDCl_3$ ($\delta = 77.00$) for ^{13}C spectra. High performance liquid chromatography (HPLC) analysis were conducted using Shimadzu LC–20AT with a UV detector SPD–20A and chiral column of Daicel CHIRALPAK AD–H (4.6 mm × 25 cm), CHIRALCEL OD–H (4.6 mm × 25 cm). Optical rotations were measured on Polarimeter Autopol IV-T Six Wavelength.

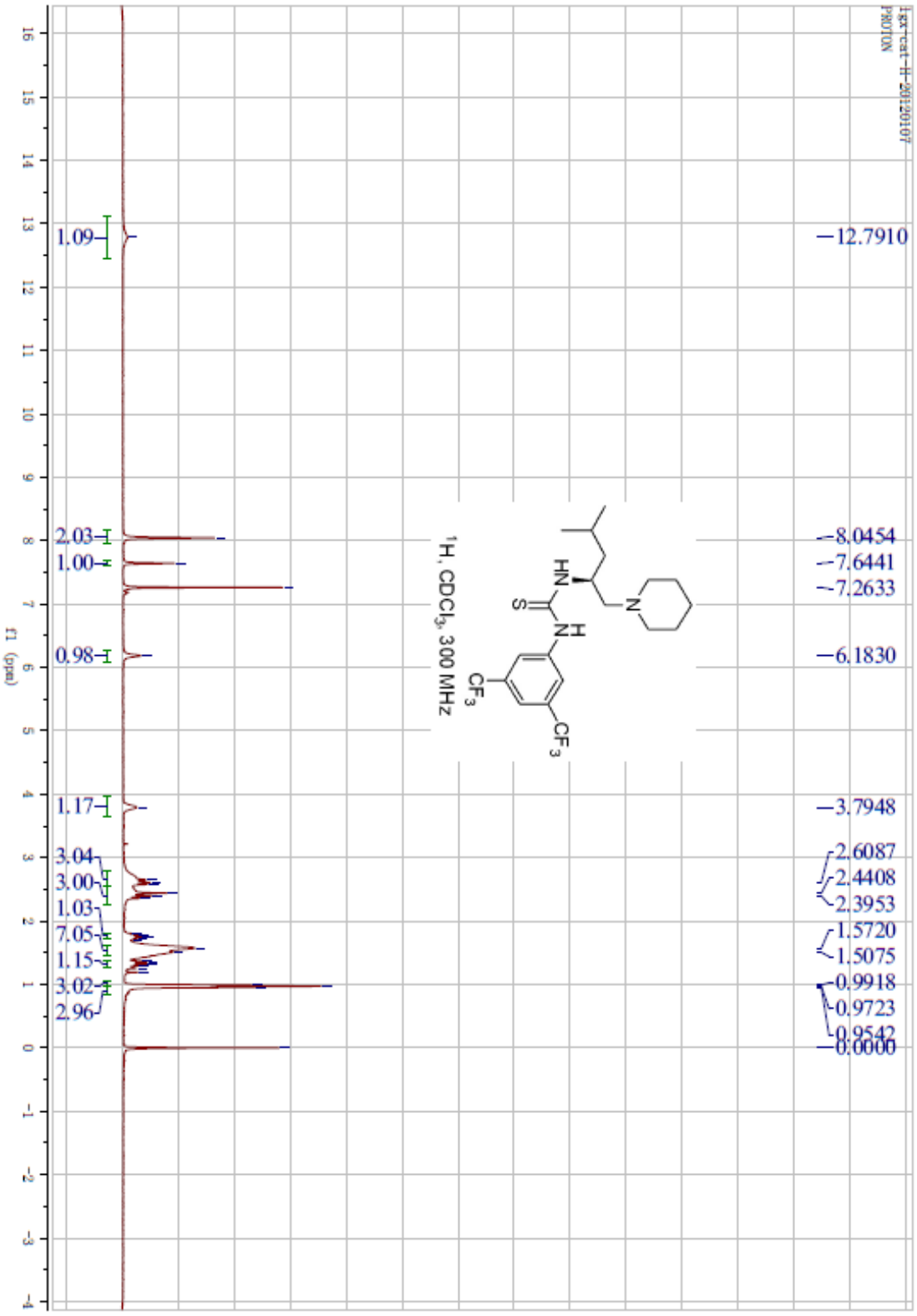
Condition Optimization for the Enantioselective Friedel–Crafts Reaction between **2a** and **3a** catalyzed by **1k** [a]

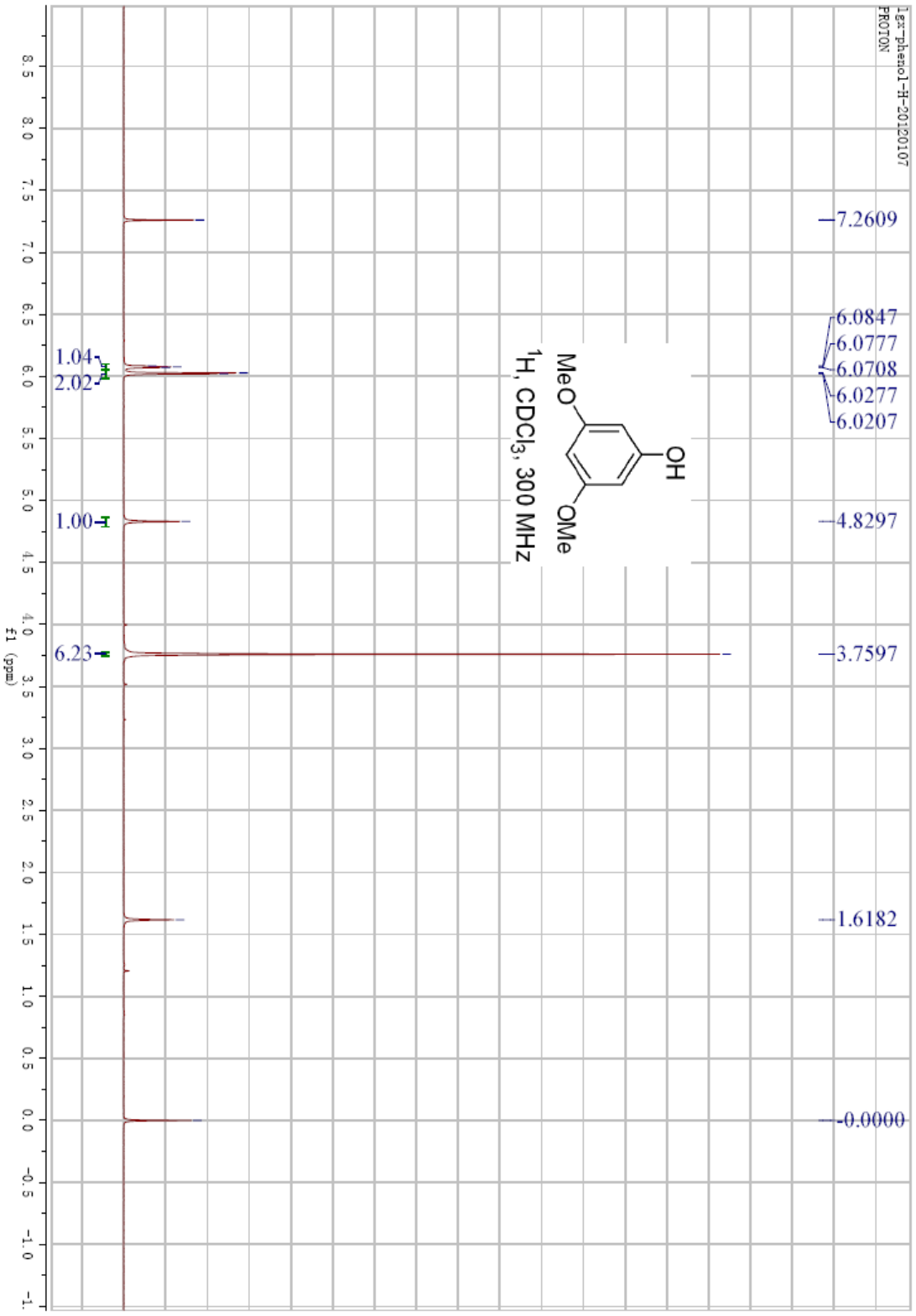


entry	solvent	temp. (°C)	time (h)	yield (%)[b]	ee (%)[c]
1	CH_2Cl_2	–30	48	92	74
2	trifluoromethylbenzene	–25	36	80	64
3	*m*-xylene[d]	–30	72	91	78
4	mesitylene[e]	–40	72	50	64
5	EtOAc	–30	72	N.R.	--
6	THF	–30	72	N.R.	--
7	Et_2O	–30	72	N.R.	--
8	$CHCl_3$	–50	72	68	74
9	toluene	–50	72	90	92

[a] Unless otherwise noted, reaction condition was: solution of **2a** (0.1 mmol) in 0.2 mL solvent was added dropwisely into the 1.0 mL of solution of **3a** (0.15 mmol) and catalyst **1k** (20 mol %). [b] Isolated yields. [c] Determined by HPLC analysis. [d] *m*-xylene: 1,3-dimethylbenzene. [e] mesitylene: 1,3,5-trimethylbenzene.

^{1}H NMR study of the interaction between catalyst 1k and 2a: No significant difference was found when the ^{1}H NMR spectrum of 1:1 mixture of catalyst **1k** and **2a** (in $CDCl_3$) was compared with the ^{1}H NMR spectra of **1k** or **2a** (in $CDCl_3$).

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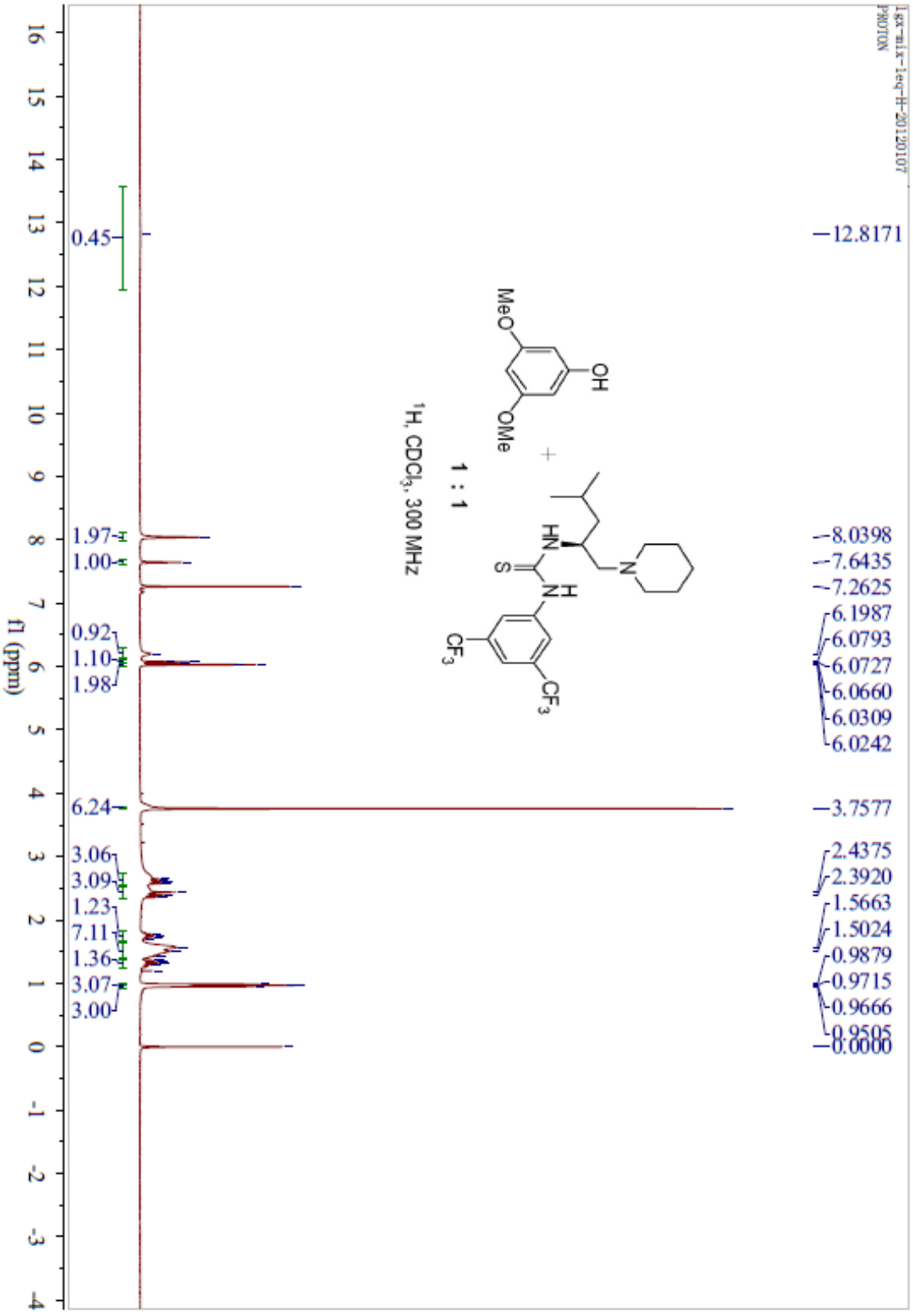
2.02
1.00
6.23
MeO
OMe
OH
^{1}H, CDCl$_3$, 300 MHz
f1 (ppm)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1.00
0.92
1.10
1.98
6.24
3.06
3.09
1.23
7.11
1.36
3.07
3.00
12.8171
8.0398
7.6435
7.2625
6.1987
6.0793
6.0727
6.0660
6.0309
6.0242
3.7577
2.4375
2.3920
1.5663
1.5024
0.9879
0.9715
0.9666
0.9505
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MeO
OH
OMe
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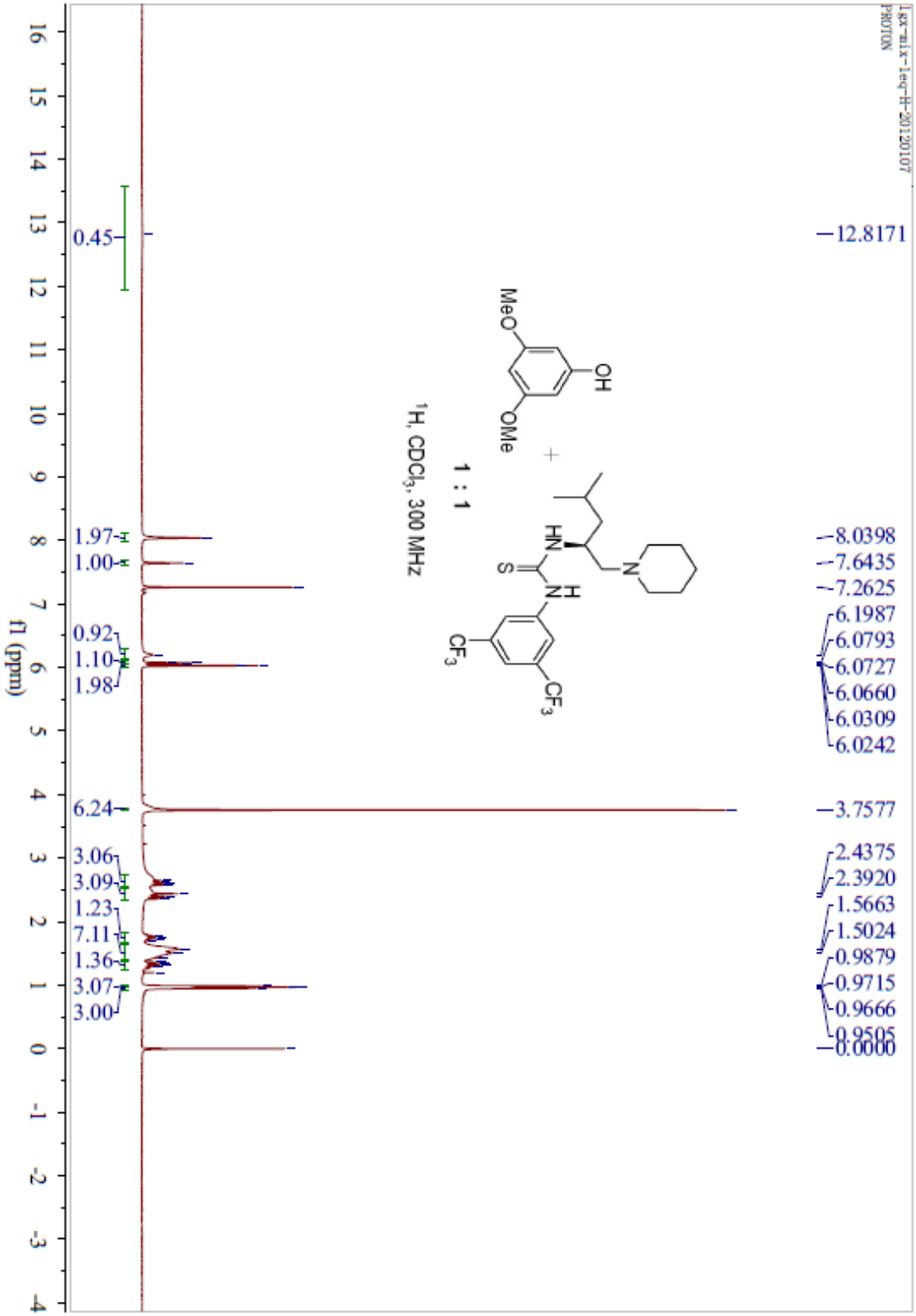
HN
S
N
H
N
CF$_3$
CF$_3$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6.0242
3.7577
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0.9666
0.9505
0.0000
0.45
1.97
1.00
0.92
1.10
1.98
6.24
3.06
3.09
1.23
7.11
1.36
3.07
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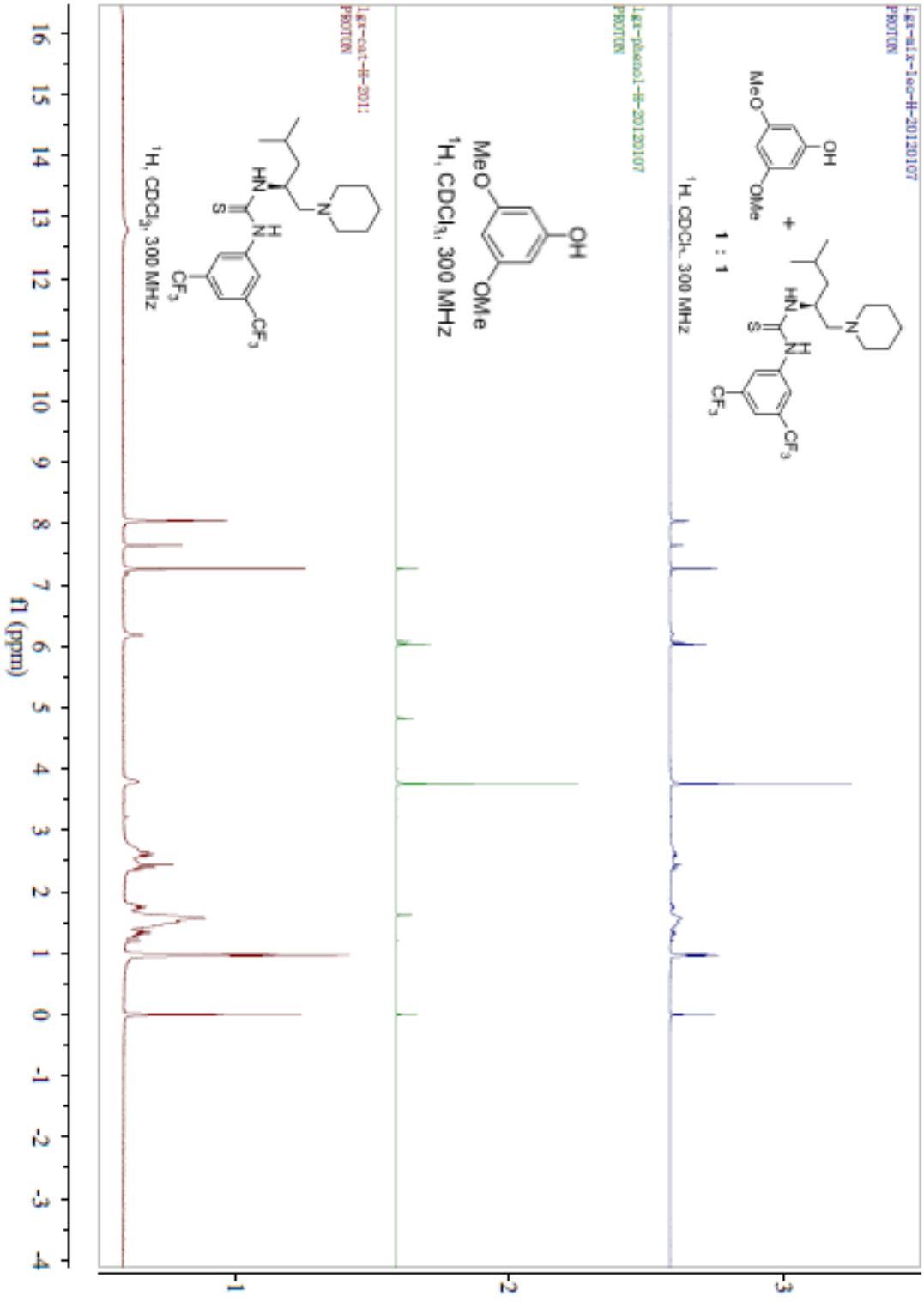
CF3
1 : 1
1H, CDCl3, 300 MHz
f1 (ppm)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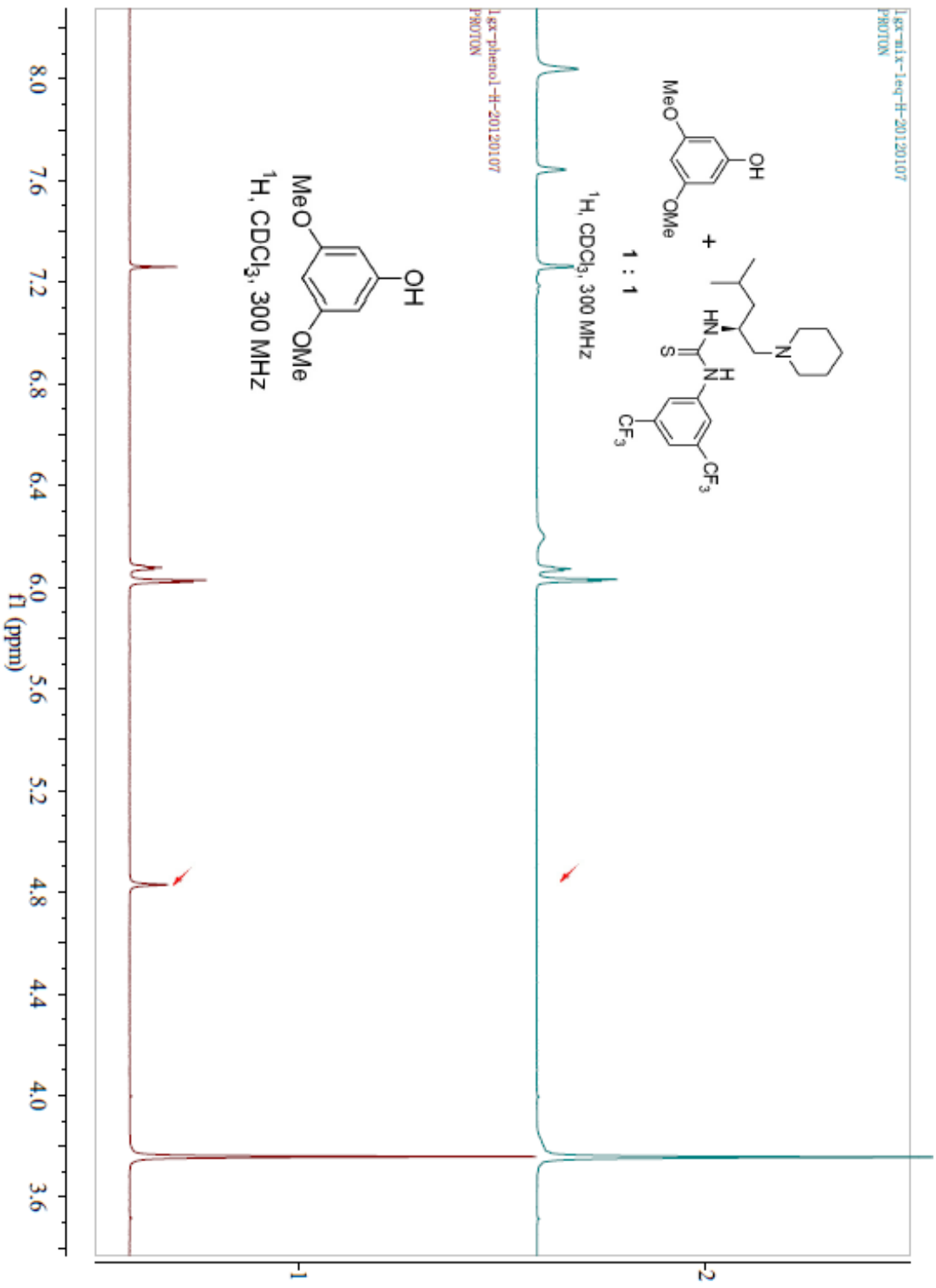
MeO
OMe
OH
^{1}H, CDCl$_3$, 300 MHz
^{1}H, CDCl$_3$, 300 MHz
f1 (ppm)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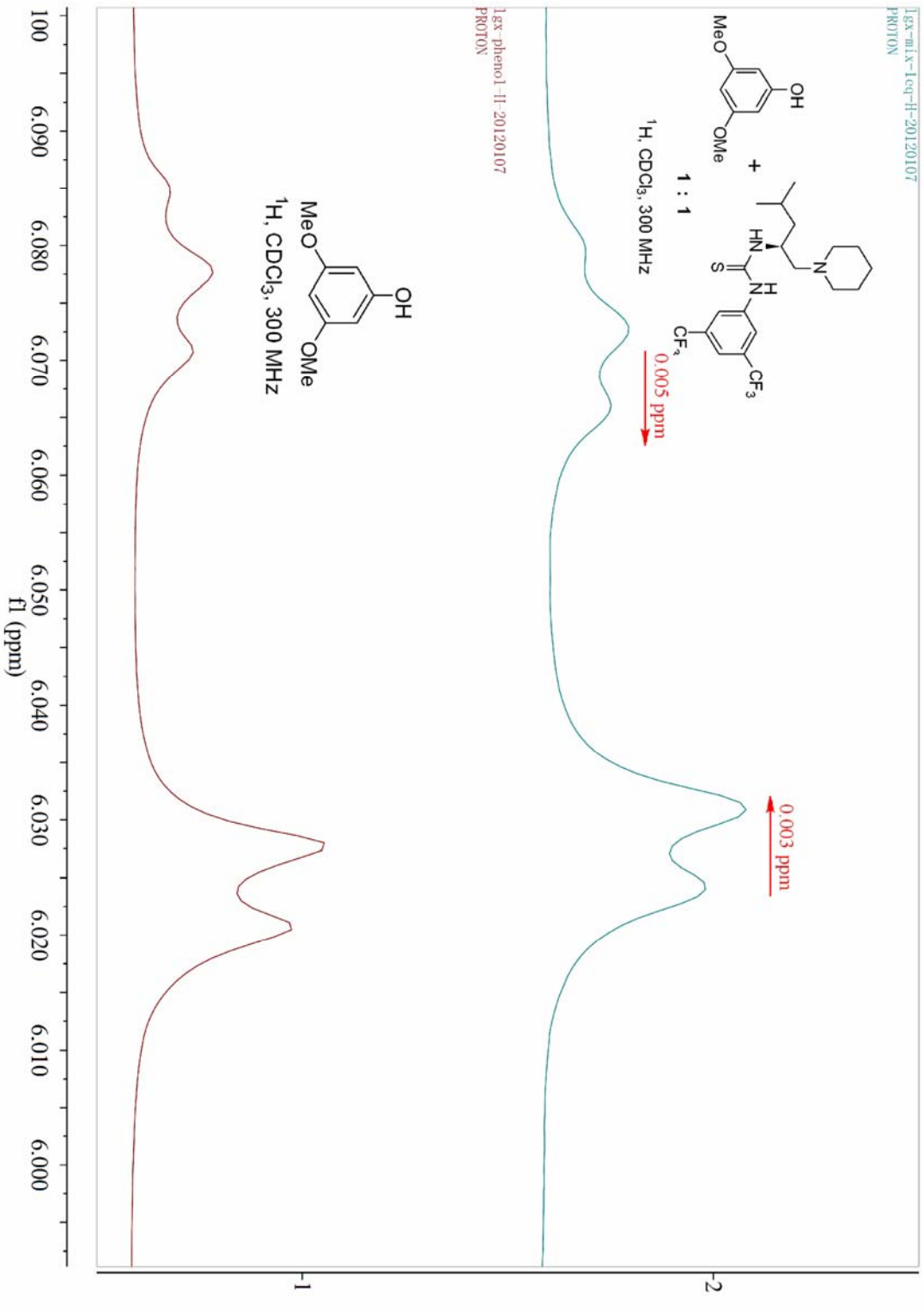
PROTON
OH
MeO
OMe
+
HN
S
N
H
N
CF3
CF3
1 : 1
1H, CDCl3, 300 MHz
lgx-phenol-H-20120107
PROTON
MeO
OH
OMe
1H, CDCl3, 300 MHz
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
f1 (ppm)
2
1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OH
MeO
OMe
+
HN
S
H
N
N
CF3
CF3
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0.003 ppm
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MeO
OH
OMe
1H, CDCl3, 300 MHz
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6.090
6.080
6.070
6.060
6.050
6.040
6.030
6.020
6.010
6.000
f1 (ppm)
-1
-2

Preparation and characterization data of catalysts 1a−1t:

Catalysts **1a**,[1] **1b**,[2] **1c**,[1] **1d**,[1] and **1e**[3] were prepared according to the literature procedure.

Catalyst 1a. White solid; m.p. 125−126 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.71 (d, *J* = 4.5 Hz, 1H), 8.04 (d, *J* = 9.3 Hz, 1H), 7.89 (s, 2H), 7.70−7.61 (m, 1H), 7.67 (s, 1H), 7.42 (dd, *J* = 9.2, 2.6 Hz, 1H), 7.31 (d, *J* = 4.5 Hz, 1H), 6.07–5.88 (m, 1H), 5.75−5.64 (m, 1H), 5.07 (d, *J* = 4.8 Hz, 1H), 5.03 (s, 1H), 3.98 (s, 3H), 3.54−3.44 (m, 2H), 3.25 (dd, *J* = 13.6, 10.3 Hz, 1H), 2.99−2.81 (m, 2H), 2.44−2.42 (m, 1H), 1.80−1.68 (m, 3H), 1.53−1.44 (m, 1H), 1.03−0.94 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 180.5, 158.1, 147.1, 144.2, 140.1, 139.6, 132.1 (d, *J* = 33.6 Hz), 130.8, 128.0, 123.4, 122.9 (q, *J* = 271.4 Hz), 122.2, 118.3, 115.5, 102.2, 60.4, 55.8, 54.5, 41.8, 38.4, 26.9, 26.8, 25.4.

Catalyst 1b. White solid; m.p. 139−141 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.70 (d, *J* = 3.9 Hz, 1H), 8.04 (d, *J* = 9.0 Hz, 1H), 7.85 (s, 2H), 7.69 (s, 1H), 7.51 (br s, 1H), 7.42 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.25 (s, 1H), 5.91−5.79 (m, 1H), 5.75−5.61 (m, 1H), 5.16 (d, *J* = 6.0 Hz, 1H), 5.12 (s, 1H), 3.97 (s, 3H), 3.31−3.14 (m, 1H), 3.04 (d, *J* = 8.7 Hz, 2H), 2.98−2.86 (m, 2H), 2.41−2.34 (m, 1H), 1.74−1.67 (m, 1H), 1.65−1.56 (m, 2H), 1.29−1.20 (m, 1H), 1.06−0.96 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 180.6, 157.9, 147.0, 144.2, 140.2, 139.8, 132.3 (d, *J* = 33.6 Hz), 130.8, 128.1, 123.4, 122.8 (q, *J* = 271.4 Hz), 122.3, 118.4, 115.0, 101.8, 60.7, 55.6, 48.4, 47.2, 38.6, 27.0, 26.0, 25.1.

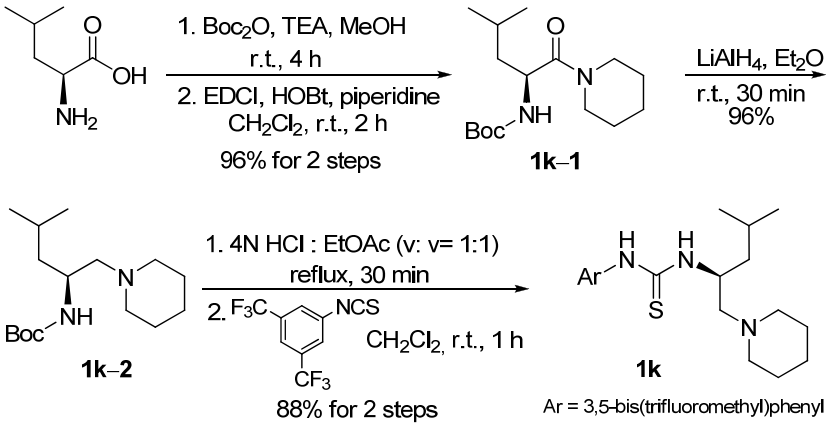
Catalyst 1c. White solid; m.p. 125−126 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.78 (d, *J* = 3.6 Hz, 1H), 8.36 (br s, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.80 (s, 2H), 7.77−7.71 (m, 1H), 7.70 (s, 1H), 7.66−7.61 (m, 1H), 7.25 (br s, 1H), 5.82−5.75 (m, 1H), 5.73−5.61 (m, 1H), 5.00 (d, *J* = 9.9 Hz, 1H), 4.95 (s, 1H), 3.33−3.23 (m, 2H), 3.15 (dd, *J* = 12.5, 10.5 Hz, 1H), 2.81−2.72 (m, 2H), 2.42−2.26 (m, 1H), 1.75−1.56 (m, 3H), 1.37−1.30 (m, 1H), 1.01−0.86 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 180.4, 149.6, 148.0, 140.6, 139.9, 132.3 (q, *J* = 33.4 Hz), 129.6, 129.4, 126.9, 123.7, 123.6, 122.8 (q, *J* = 271.2 Hz), 118.6, 114.8, 60.8, 54.6, 41.2, 39.0, 27.3, 27.0, 25.5.

Catalyst 1d. White solid; m.p. 124−126 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.87 (d, *J* = 3.0 Hz,

1H), 8.25 (br s, 1H), 8.17 (d, *J* = 8.4 Hz, 1H), 7.87 (s, 2H), 7.80−7.75 (m, 1H), 7.71−7.60 (m, 2H), 7.32 (d, *J* = 3.3 Hz, 1H), 5.85−5.64 (m, 2H), 5.16−5.09 (m, 2H), 3.37−3.15 (m, 1H), 3.08−2.92 (m, 2H), 3.01 (d, *J* = 9.0 Hz, 2H), 2.45−2.27 (m, 1H), 1.73−1.46 (m, 3H), 1.25−1.13 (m, 1H), 1.00−0.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.7, 149.7, 148.0, 140.0, 139.3, 132.2 (q, *J* = 33.7 Hz), 129.7, 129.4, 126.9, 126.8, 123.6, 123.4, 122.8 (q, *J* = 271.3 Hz), 118.4, 115.2, 61.1, 48.3, 46.9, 38.7, 27.0, 25.8, 24.7.

Catalyst 1e. White solid; m.p. 94−96 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (s, 2H), 7.62 (s, 1H), 3.88 (br s, 1H), 2.78−2.00 (m, 7H), 2.47 (td, *J* = 10.8, 3.0 Hz, 1H), 1.93 (d, *J* = 11.6 Hz, 1H), 1.85 (d, *J* = 11.6 Hz, 1H), 1.75 (d, *J* = 11.6 Hz, 1H), 1.31−1.14 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.2, 139.7, 132.1 (q, *J* = 33.7 Hz), 123.4, 122.8 (q, *J* = 271.0 Hz), 118.2, 66.5, 55.7, 39.8, 32.6, 24.6, 24.4, 21.1.

General procedure for the preparation of catalysts 1f−1p and 1t from amino acids:



(*S*)-*tert*-Butyl 4-methyl-1-oxo-1-(piperidin-1-yl)pentan-2-ylcarbamate (**1k-1**)[4]

To the solution of *L*-leucine (3.93 g, 30 mmol) in 80 mL of MeOH in a 150 mL flask was added triethylamine (3.03 g, 30 mmol). After stirring at room temperature for 15 min, Boc anhydride (Boc_2O, 13.08 g, 60 mmol) was added into the flask and was stirred for another 4 hours. The solvent was evaporated in *vacuo* and 80 mL of water and 20 mL of dichloromethane were added into the flask, and then followed by NaOH (1.60 g, 40 mmol) under stirring. The aqueous phase was separated and washed with dichloromethane (20 mL × 2). The aqueous phase and 50 mL of ethyl acetate were added into a 150 mL flask, acidified the aqueous phase with 0.5 N HCl (aq.) to

pH = 4.0–5.0 under vigorously stirring. The organic phase was separated and the aqueous phase was extracted with 100 mL of ethyl acetate for three times. The organic phase was combined and dried over Na_2SO_4. The solvent was evaporated in *vacuo* to get the product (6.93 g, 100% yield). The crude product was dissolved in 50 mL of CH_2Cl_2 in a 100 mL flask, HOBt (4.46 g, 33 mmol) and EDCI (6.30 g, 33 mmol) were added into the solution under stirring at 0 ^oC. After stirring at 0 ^oC for 15 min., piperidine (2.81 g, 33 mmol) was added into the flask dropwisely. The reaction was quenched with 0.5 mL of water after stirring for 2 hours. Evaporated the solvent in *vacuo* and the residue was dissolved in 100 mL of ethyl acetate. The organic phase was washed with 10 mL of 5% $KHSO_4$ (aq.), saturated aqueous $NaHCO_3$, water, and brine. The organic phase was dried over Na_2SO_4 and evaporated in *vacuo*. After flash column chromatography on silica gel (petrol ether/ethyl acetate (4:1)), the desired product was obtained as a colorless oil (8.58 g, 96% yield). ^1H NMR (400 MHz, $CDCl_3$): δ 5.35 (d, J = 8.8 Hz, 1H), 4.67 (td, J = 5.2, 3.6 Hz, 1H), 3.55 (t, J = 5.6 Hz, 2H), 3.50−3.41 (m, 2H), 1.78−1.69 (m, 1H), 1.69−1.60 (m, 4H), 1.58−1.52 (m, 3H), 1.43 (s, 9H), 1.39−1.32 (m, 1H), 1.00 (d, J = 6.4 Hz, 3H), 0.92 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 155.4, 79.0, 48.2, 46.2, 43.0, 42.9, 28.2, 26.2, 25.3, 24.4, 24.3, 23.3, 21.7..

(*S*)-*tert*-Butyl 4-methyl-1-(piperidin-1-yl)pentan-2-ylcarbamate (**1k-2**) [4]

1k–1 (7.45 g, 25 mmol) was dissolved in 100 mL of ethyl ether in a 150 mL flask, then $LiAlH_4$ (1.90 g, 50 mmol) was added into the solution portionly at 0 ^oC and stirred for another 30 min. at room temperature. Water (1 mL) was added carefully into the reaction solution at 0 ^oC to quench the reaction. Then 20 mL of saturated NH_4Cl (aq.) was added into the solution. The product was extracted from aqueous phase with 50 mL of ethyl ether for 3 times. The combined organic phase was dried over Na_2SO_4. The solvent was evaporated in vacuo to get the product as a colorless oil (6.82 g, 96% yield). ^1H NMR (400 MHz, $CDCl_3$): δ 4.53 (br s, 1H), 3.78−3.72 (m, 1H), 2.55−2.42 (m, 2H), 2.36−2.31 (m, 2H), 2.28−2.25 (m, 2H), 1.76−1.66 (m, 1H), 1.59−1.52 (m, 4H), 1.47 (s, 9H), 1.44−1.41 (m, 2H), 1.33 (t, J = 6.8 Hz, 2H), 0.94 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.8, 78.6, 63.6, 54.8, 46.4, 43.4, 28.4, 26.0, 24.7, 24.3, 23.1, 22.3.

(*S*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(4-methyl-1-(piperidin-1-yl)pentan-2-yl)thiourea (catalyst **1k**)

To the solution of **1k**–**2** (5.68 g, 20.0 mmol) in 50 mL of EtOAc in a 200 mL flask was added 50 mL of 4 N HCl (aq.). The reaction mixture was heated to reflux for 30 min. and then cooled to room temperature. Excessive concentrated aqueous ammonia was added into the mixture and separated the organic phase. The product was extracted with EtOAc (50 mL × 2) from the aqueous phase. The organic phase was combined and dried over Na_2SO_4. The organic phase was removed under reduced pressure and the product was used without further purification. To the solution of primary amine in 25 mL of dried CH_2Cl_2 was added 1-isothiocyanato-3,5-bis(trifluoromethyl)benzene (5.42 g, 20 mmol). The solution was stirred at room temperature for 1 hour. The solvent was removed under reduced pressure and the residue was underwent flash column chromatography on silica gel with CH_2Cl_2/MeOH (96:4) to afford the desired product as a colorless oil (8.02 g, 88% yield). $[\alpha]_D^{25} = -30.8$ (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.77 (br s, 1H), 8.05 (s, 2H), 7.63 (s, 1H), 6.54 (br s, 1H), 3.81 (br s, 1H), 2.85−2.58 (m, 3H), 2.58−2.29 (m, 3H), 1.84−1.70 (m, 1H), 1.59−1.46 (m, 7H), 1.36−1.26 (m, 1H), 0.98 (d, *J* = 6.2 Hz, 3H), 0.96 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.9, 141.8, 131.3 (q, *J* = 33.4 Hz), 124.4, 123.0 (q, *J* = 270.9 Hz), 117.6, 66.9, 54.8, 52.8, 42.1, 25.3, 24.6, 23.1, 22.4, 21.6; HRMS (ESI) for $C_{20}H_{27}F_6N_3S$: calcd $[M + H]^+$ *m*/*z* 456.1903, found 456.1910.

(*S*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-(dibutylamino)-3-phenylpropan-2-yl)thiou-rea (catalyst 1f).

Overall yield of 5 steps: 85%; colorless oil; $[\alpha]_D^{25} = -48.0$ (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.20 (br s, 1H), 7.99 (s, 2H), 7.60 (s, 1H), 7.37−7.33 (m, 2H), 7.29 (d, *J* = 7.2 Hz, 1H), 7.22 (d, *J* = 7.2 Hz, 2H), 6.73 (br s, 1H), 4.20−3.83 (m, 1H), 3.02 (d, *J* = 8.0 Hz, 1H), 2.82−2.59 (m, 5H), 2.56−2.44 (m, 2H), 2.39−2.32 (m, 2H), 1.47−1.23 (m, 4H), 1.22−1.15 (m, 4H), 0.82 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.2, 141.8, 136.5, 131.3 (q, *J* = 32.7 Hz), 129.0, 128.6, 126.9, 123.3, 123.0 (q, *J* = 271.1 Hz), 117.3, 60.3, 57.1, 54.1, 39.3, 27.7, 20.3, 13.4; HRMS (ESI) for $C_{26}H_{33}F_6N_3S$: calcd $[M + H]^+$ *m*/*z* 534.2372, found 534.2379.

(*S*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-(dibutylamino)-3-methylbutan-2-yl)thiour-ea (catalyst 1g).

Overall yield of 5 steps: 82%; colorless oil; $[\alpha]_D^{25} = -17.0$ (c = 1.0 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 13.15 (br s, 1H), 8.00 (s, 2H), 7.60 (s, 1H), 6.22 (br s, 1H), 3.60−3.56 (m, 1H), 2.74−2.64 (m, 3H), 2.58 (d, J = 13.6 Hz, 1H), 2.46 (td, J = 8.4, 4.0 Hz, 2H), 1.97−1.89 (m, 1H), 1.60−1.49 (m, 2H), 1.43−1.33 (m, 2H), 1.32−1.23 (m, 4H), 1.05 (d, J = 2.4 Hz, 3H), 1.03 (d, J = 2.4 Hz, 3H), 0.88 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.6, 141.7, 131.0 (q, J = 33.1 Hz), 123.2, 122.8 (q, J = 271.0 Hz), 116.8, 60.6, 59.2, 54.1, 31.0, 27.8, 20.2, 18.0, 17.9, 13.2; HRMS (ESI) for $C_{22}H_{33}F_6N_3S$: calcd $[M + H]^+$ m/z 486.2372, found 486.2381.

(*S*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-(dibutylamino)-4-methylpentan-2-yl)thiou-rea (catalyst 1h).

Overall yield of 5 steps: 86%; colorless oil; $[\alpha]_D^{25} = -70.6$ (c = 0.5 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 13.16 (br s, 1H), 8.00 (s, 2H), 7.60 (s, 1H), 6.15 (d, J = 3.2 Hz, 1H), 3.81−3.74 (m, 1H), 2.74−2.63 (m, 3H), 2.53−2.46 (m, 3H), 1.82−1.71 (m, 1H), 1.59−1.49 (m, 2H), 1.46−1.37 (m, 2H), 1.34−1.24 (m, 6H), 0.98 (d, J = 6.4 Hz, 3H), 0.96 (d, J = 6.4 Hz, 3H), 0.89 (t, J = 7.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.3, 141.8, 131.3 (q, J = 33.1 Hz), 112.9 (q, J = 270.9 Hz), 122.8, 116.6, 62.8, 54.7, 54.3, 41.5, 28.0, 24.4, 22.2, 21.1, 20.2, 13.2; HRMS (ESI) for $C_{23}H_{35}F_6N_3S$: calcd $[M + H]^+$ m/z 500.2529, found 500.2535.

(*S*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-(dibutylamino)-4,4-dimethylpentan-2-yl)th-ioure a (catalyst 1i).

Overall yield of 5 steps: 89%; white solid; m.p. 88−89 °C; $[\alpha]_D^{25} = -33.2$ (c = 1.0 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 13.09 (br s, 1H), 8.00 (s, 2H), 7.59 (s, 1H), 6.10 (d, J = 4.0 Hz, 1H), 3.86−3.82 (m, 1H), 2.78 (dd, J = 13.8, 10.4 Hz, 1H), 2.66 (td, J = 11.6, 4.8 Hz, 2H), 2.54 (td, J = 12.1, 4.8 Hz, 2H), 2.47 (d, J = 14.0 Hz, 1H), 1.58−1.49 (m, 2H), 1.47−1.36 (m, 4H), 1.33−1.24 (m, 4H), 1.02 (s, 9H), 0.89 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.6, 141.9, 131.4 (q, J = 33.2 Hz), 123.1 (q, J = 271.0 Hz), 123.0, 117.1, 64.4, 55.3, 54.4, 47.1, 30.5, 29.7, 28.3, 20.5, 13.6; HRMS (ESI) for $C_{24}H_{37}F_6N_3S$: calcd $[M + H]^+$ m/z 514.2685, found 514.2690.

(*S*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(4-methyl-1-(pyrrolidin-1-yl)pentan-2-yl)thio-urea (catalyst 1j).

Overall yield of 5 steps: 85%; colorless oil; $[\alpha]_D^{25} = -16.8$ (c = 1.0 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 13.34 (br s, 1H), 8.03 (s, 2H), 7.62 (s, 1H), 6.23 (br s, 1H), 3.82−3.79 (m, 1H), 2.99 (dd, J = 13.2, 9.2 Hz, 1H), 2.95−2.80 (m, 2H), 2.79−2.63 (m, 2H), 2.58 (d, J = 13.2 Hz, 1H), 1.96−1.85 (m, 4H), 1.84−1.74 (m, 1H), 1.52−1.45 (m, 1H), 1.41−1.34 (m, 1H), 1.01 (d, J = 6.4 Hz, 3H), 0.99 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.9, 142.2, 131.6 (q, J = 33.4 Hz), 123.2 (J = 271.0 Hz), 122.9, 117.4, 64.2, 54.4, 54.0, 42.6, 29.6, 24.9, 23.5, 22.6, 22.0; HRMS (ESI) for $C_{19}H_{25}F_6N_3S$: calcd $[M + H]^+$ m/z 442.1746, found 442.1752.

(*S*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(4-methyl-1-morpholinopentan-2-yl)thiourea (catalyst 1l).

Overall yield of 5 steps: 80%; white solid; m.p. 135−136 °C; $[\alpha]_D^{25} = -11.8$ (c = 1.0 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 13.31 (br s, 1H), 8.00 (s, 2H), 7.59 (s, 1H), 6.17 (br s, 1H), 3.80−3.73 (m, 1H), 2.96 (dd, J = 13.2, 9.2 Hz, 1H), 2.92−2.78 (m, 2H), 2.77−2.60 (m, 2H), 2.55 (d, J = 13.2 Hz, 1H), 1.94−1.82 (m, 4H), 1.80−1.73 (m, 1H), 1.49−1.42 (m, 1H), 1.38−1.31 (m, 1H), 0.98 (d, J = 6.4 Hz, 3H), 0.96 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.8, 141.2, 131.9 (q, J =30.0 Hz), 124.6, 122.9 (q, J = 271.0 Hz), 118.3, 66.4, 53.9, 52.4, 42.4, 24.7, 22.4, 21.8; HRMS (ESI) for $C_{19}H_{25}F_6N_3OS$: calcd $[M + H]^+$ m/z 458.1695, found 458.1698.

1-(3,5-Bis(trifluoromethyl)phenyl)-3-((2*S*)-1-(3,5-dimethylpiperidin-1-yl)-4-methylpen-tan-2-yl)thiourea (catalyst 1m).

Overall yield of 5 steps: 85%; colorless oil; $[\alpha]_D^{25} = -26.6$ (c = 1.0 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 12.68 (br s, 1H), 7.99 (s, 2H), 7.64 (s, 1H), 6.28 (br s, 1H), 3.88−3.69 (m, 1H), 3.03 (d, J = 6.0 Hz, 1H), 2.92 (d, J = 11.2 Hz, 1H), 2.65 (dd, J = 13.0, 8.8 Hz, 1H), 2.40 (d, J = 13.6 Hz, 1H), 1.81−1.73 (m, 3H), 1.71−1.59 (m, 1H), 1.57−1.42 (m, 3H), 1.35−1.28 (m, 1H), 0.99 (d, J = 6.4 Hz, 3H), 0.97 (d, J = 2.8 Hz, 3H), 0.88 (d, J = 6.4 Hz, 3H), 0.86 (d, J = 2.4 Hz, 3H), 0.63−0.54 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.2, 141.8, 131.4 (q, J = 32.8 Hz), 124.6, 123.1 (q, J = 271.0 Hz), 117.9, 66.6, 62.5, 61.1, 53.0, 42.4, 41.1, 31.1, 30.9, 24.7, 22.6, 21.8, 19.3, 19.2; HRMS (ESI) for $C_{22}H_{31}F_6N_3S$: calcd $[M + H]^+$ m/z 484.2216, found 484.2222.

(*S*)-1-(1-(Azocan-1-yl)-4-methylpentan-2-yl)-3-(3,5-bis(trifluoromethyl)phenyl)thioure-a

(catalyst 1n).

Overall yield of 5 steps: 86%; white solid; m.p. 126−127 ^{o}C; $[\alpha]_D^{25} = -36.2$ (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.12 (br s, 1H), 7.99 (s, 2H), 7.63 (s, 1H), 6.17 (d, *J* = 3.2 Hz, 1H), 3.82−3.79 (m, 1H), 3.15−2.79 (m, 4H), 2.77−2.64 (m, 2H), 1.81−1.70 (m, 1H), 1.68−1.42 (m, 11H), 1.36−1.28 (m, 1H), 0.98 (d, *J* = 6.0 Hz, 3H), 0.96 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.6, 141.9, 131.5 (q, *J* = 30.0 Hz), 123.8, 123.0 (q, *J* = 271.0 Hz), 117.7, 63.4, 53.2, 51.5, 42.3, 27.1, 25.0, 24.8, 24.5, 22.5, 21.8; HRMS (ESI) for $C_{22}H_{31}F_6N_3S$: calcd $[M + H]^+$ *m*/*z* 484.2224, found 484.2225.

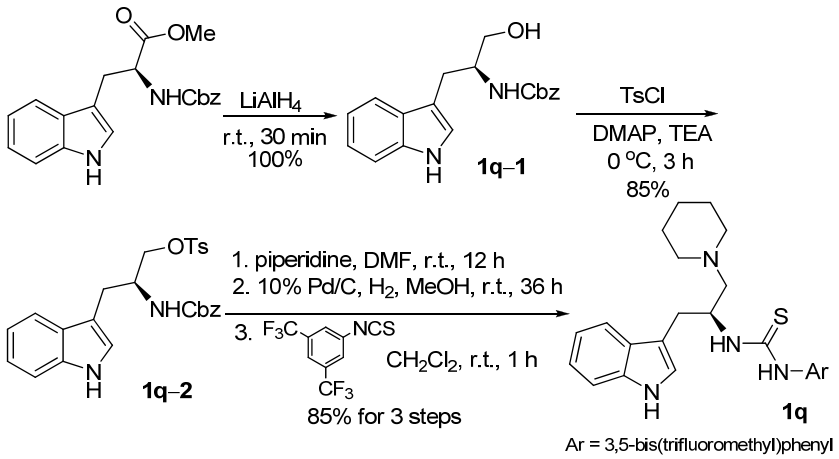
1-(3,5-Bis(trifluoromethyl)phenyl)-3-((*S*)-1-(adamantanamino)-4-methylpentan-2-yl)t-hioure a (catalyst 1o).

Overall yield of 5 steps: 81%; white solid; m.p. 56−58 ^{o}C; $[\alpha]_D^{25} = -31.6$ (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, CDCl3): δ 8.03 (s, 2H), 7.59 (s, 1H), 6.40 (br s, 1H), 3.83–3.67 (m, 1H), 2.90 (d, *J* = 12.6 Hz, 1H), 2.79–2.71 (m, 2H), 1.92–1.62 (m, 16H), 1.55−1.44 (m, 1H), 1.35−1.28 (m, 1H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.4, 141.8, 131.5 (q, *J* = 33.2 Hz), 123.5, 123.2 (q, *J* = 270.2 Hz), 117.7, 62.8, 56.5, 54.0, 42.3, 37.4, 31.9, 31.4, 31.1, 27.3, 27.1, 24.9, 22.8, 21.9; HRMS (ESI) for $C_{25}H_{33}F_6N_3S$: calcd $[M + H]^+$ *m*/*z* 522.2372, found 522.2378.

(*S*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-(isoindolin-2-yl)-4-methylpentan-2-yl)thio-urea (catalyst 1p).

Overall yield of 5 steps: 80%; colorless oil; $[\alpha]_D^{25} = -20.6$ (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.21 (br s, 1H), 7.55 (s, 2H), 7.39 (s, 1H), 7.31−7.20 (m, 4H), 6.57 (br s, 1H), 4.23 (d, *J* = 12.0 Hz, 2H), 4.08 (d, *J* = 11.2 Hz, 2H), 3.92−3.78 (m, 1H), 2.99−2.91 (m, 2H), 1.82−1.72 (m, 1H), 1.50−1.45 (m, 1H), 1.37−1.30 (m, 1H), 0.96 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.6, 141.8, 137.7, 131.3 (q, *J* = 33.3 Hz), 127.9, 122.8 (q, *J* = 271.0 Hz), 122.3, 121.9, 116.8, 62.7, 59.1, 54.2, 41.7, 29.6, 24.8, 22.1, 22.0; HRMS (ESI) for $C_{23}H_{25}F_6N_3S$: calcd $[M + H]^+$ *m*/*z* 490.1746, found 490.1753.

Preparation for Catalyst 1q



(*S*)-Benzyl 1-hydroxy-3-(1*H*-indol-3-yl)propan-2-ylcarbamate (1q-1)[5]

To the solution of (*S*)-methyl 2-(benzyloxycarbonylamino)-3-(1*H*-indol-3-yl)propanoate (750 mg, 2.13 mmol) in 20 mL of dry ethyl ether was added $LiAlH_4$ (162 mg, 4.26 mmol) portionwisely under stirring at 0 °C. The reaction mixture was stirred for another 30 min, then quenched the reaction with water carefully until no gas released. Another 20 mL of saturated NH_4Cl (aq.) was added into the flask. The product was extracted from the aqueous phase with ethyl ether (20 mL × 3). The organic phase was washed with brine (10 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure to get the product as a colorless oil without further purification (690 mg, 100% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (br s, 1H), 7.62 (d, *J* = 6.9 Hz, 1H), 7.39−7.23 (m, 7H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.11−7.06 (m, 1H), 6.91 (br s, 1H), 5.17 (d, *J* = 7.8 Hz, 1H), 5.06 (s, 2H), 4.03−4.01 (m, 1H), 3.64−3.51 (m, 2H), 2.96 (d, *J* = 6.3 Hz, 2H), 2.65 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.7, 136.3, 136.2, 128.5, 128.1, 128.0, 127.5, 122.8, 122.1, 119.5, 118.7, 111.4, 111.2, 66.8, 64.2, 53.3, 26.8; HRMS (ESI) for $C_{19}H_{20}N_2O_3$: calcd $[M + Na]^+$ *m*/*z* 347.1366, found 347.1368.

(*S*)-2-(Benzyloxycarbonylamino)-3-(1*H*-indol-3-yl)propyl 4-methylbenzenesulfonate (1q-2)

Compound **1q-1** (690 mg, 2.13 mmol) was dissolved in 10 mL of dried CH_2Cl_2, then DMAP (28 mg, 0.23 mmol), TEA (697 mg, 6.9 mmol), and TsCl (477 mg, 2.5 mmol) were added into the flask under stirring at 0 °C. The reaction mixture was stirred for 3 hours. Another 10 mL of CH_2Cl_2 was added into the flask to dilute the reaction mixture. The solution was washed with water (10 mL × 3) and brine. The organic phase was dried over Na_2SO_4. The solvent was evaporated in *vacuo*. The product was obtained as a colorless oil (796 mg, 85% yield) by flash

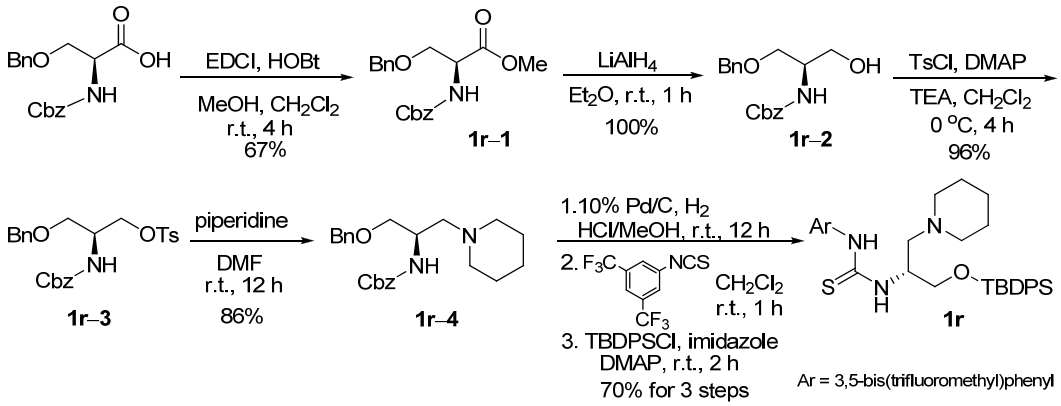
column chromatography on silica gel with petrol ether/ethyl acetate (4:1) as eluent. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.11 (br s, 1H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.37−7.31 (m, 6H), 7.27−7.22 (m, 2H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.12−7.05 (m, 1H), 6.92 (br s, 1H), 5.04 (s, 2H), 5.01 (br s, 1H), 4.17 (br s, 1H), 4.00 (d, *J* = 3.0 Hz, 2H), 3.07−2.92 (m, 2H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.7, 145.0, 136.2, 132.5, 129.9, 128.5, 128.1, 128.0, 127.9, 127.2, 123.1, 122.2, 119.6, 118.6, 111.2, 110.3, 69.9, 66.8, 50.3, 26.7, 21.6; HRMS (ESI) for $C_{26}H_{26}N_2O_5S$: calcd $[M + Na]^+$ *m*/*z* 501.1455, found 501.1458.

(*S*)-1-(1-(1*H*-indol-3-yl)-3-(piperidin-1-yl)propan-2-yl)-3-(3,5-bis(trifluoromethyl)phenyl)thiourea (catalyst 1q)

To the solution of compound **1q-2** (630 mg, 1.3 mmol) in 6 mL of dried DMF was added piperidine (553 mg, 6.5 mmol). The reaction mixture was stirred for 12 hours. The solution was diluted with 50 mL of brine. The product was extracted with ethyl ether (10 mL × 5). The organic phase was combined and dried over Na_2SO_4. The solvent was removed under reduced pressure to afford the crude chiral amine as a colorless oil (514 mg) which was used without further purification. 10% palladium on charcoal (60 mg, 100% w/w) was placed in a 10 mL flask. AcOH (2 mL) was added into the flask carefully under nitrogen atmosphere. The solution of the chiral amine (200 mg, 0.5 mmol) in 4 mL methanol was added dropwisely by a syringe. The flask was recharged with hydrogen. The reaction was stirred at room temperature for 36 hours. The reaction mixture was then filtered through a celite pad and the filtrate was evaporated to get the crude product which was used without further purification. To the solution of primary amine in 5 mL of dried CH_2Cl_2 was added 1-isothiocyanato-3,5-bis(trifluoromethyl)benzene (163 mg, 0.6 mmol). The solution was stirred at room temperature for 1 hour. The solvent was evaporated and the residue was underwent flash column chromatography on silica gel with CH_2Cl_2/methanol (95:5) as the eluent to get **1q** as a white solid (230 mg, 85% yield for 3 steps). m.p. 72−73 °C; $[\alpha]_D^{25}$ = −37.4 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.89 (br s, 1H), 8.38 (s, 1H), 7.97 (s, 2H), 7.61−7.56 (m, 2H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.23−7.12 (m, 2H), 7.06 (br s, 1H), 6.55 (br s, 1H), 4.11 (br s, 1H), 2.98 (d, *J* = 5.1 Hz, 2H), 2.74−2.57 (m, 4H), 2.45−2.22 (m, 2H), 1.56−1.34 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.1, 141.6, 136.4, 131.5 (q, *J* = 33.2 Hz), 126.9, 125.0, 123.1 (q, *J* = 271.0 Hz), 123.0, 122.4, 119.8, 118.2, 111.6, 110.1, 66.0, 54.7, 54.0, 29.6, 25.4, 23.3;

HRMS (ESI) for $C_{25}H_{26}F_6N_4S$: calcd $[M + H]^+$ *m*/*z* 529.1855, found 529.1862.

Preparation of catalyst 1r



(*S*)-Methyl 3-(benzyloxy)-2-(benzyloxycarbonylamino)propanoate (1r-1)[6]

To the solution of (*S*)-3-(benzyloxy)-2-(benzyloxycarbonylamino)propanoic acid (2.30 g, 7 mmol) in 30 mL of dried CH_2Cl_2 were added HOBt (1.04 g, 7.7 mmol) and EDCI (1.47 g, 7.7 mmol). The reaction mixture was stirred for 15 min. at 0 °C, then MeOH (336 mg, 10.5 mmol) was added dropwisely into the reaction mixture by a syringe. The reaction was stirred for another 4 hours at room temperature, then quenched with 0.5 mL of water. 50 mL of CH_2Cl_2 was added into the flask. The organic phase was washed with water (20 mL), brine, and dried over Na_2SO_4. The solvent was evaporated in *vacuo*. The desired product was obtained as a colorless oil (1.61 g, 67% yield) by flash column chromatography on silica gel with petrol ether/ethyl acetate (4:1) as eluent. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.31 (m, 7H), 7.28−7.23 (m, 3H), 5.73−5.56 (m, 1H), 5.12 (s, 2H), 4.55−4.46 (m, 3H), 3.88 (d, *J* = 9.2 Hz, 1H), 3.74 (s, 3H), 3.70 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 156.0, 137.4, 136.2, 128.5, 128.4, 128.1, 128.0, 127.8, 127.6, 73.2, 69.7, 67.0, 54.4, 52.5.

(*R*)-Benzyl 1-(benzyloxy)-3-hydroxypropan-2-ylcarbamate (1r-2)[7]

To the solution of (*S*)-methyl 3-(benzyloxy)-2-(benzyloxycarbonylamino)propanoate (1.50 g, 4.7 mmol) in 100 mL of dry ethyl ether was added $LiAlH_4$ (266 mg, 7.0 mmol) portionwisely at 0 °C. The reaction was stirred at room temperature for another 1 hour. Then the reaction was quenched with 1 mL of water carefully until no gas released. 50 mL of 0.5 N HCl was added into

the flask. The product was extracted from aqueous phase with ethyl ether (50 mL × 3). The organic phase was combined and dried over Na_2SO_4. The solvent was evaporated in *vacuo* to get the product as a colorless oil (1.48 g, 100% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37−7.27 (m, 10H), 5.44 (br s, 1H), 5.10 (s, 2H), 4.50 (s, 2H), 3.88−3.80 (m, 2H), 3.74−3.58 (m, 3H), 2.59 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.4, 137.5, 136.3, 128.5, 128.1, 128.0, 127.9, 127.6, 73.5, 70.5, 66.8, 63.6, 52.0.

(*S*)-3-(Benzyloxy)-2-(benzyloxycarbonylamino)propyl 4-methylbenzenesulfonate (1r-3)

To the solution of (*R*)-benzyl 1-(benzyloxy)-3-hydroxypropan-2-ylcarbamate **1r-2** (1.10 g, 3.5 mmol) in 50 mL of dry CH_2Cl_2, DMAP (43 mg, 0.35 mmol), TEA (1.06 g, 10.5 mmol), and TsCl (724 mg, 3.8 mmol) were added at 0 ^{o}C. The reaction mixture was stirred for 4 hours. The reaction mixture was washed with water (10 mL), brine and dried over Na_2SO_4. The solvent was removed under reduced pressure. The residue was underwent flash column chromatography on silica gel with petrol ether/ethyl acetate (5:1) as the eluent to get **1r-3** as a colorless oil (1.57 g, 96% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 7.6 Hz, 2H), 7.37−7.29 (m, 10H), 7.22 (d, *J* = 7.2 Hz, 2H), 5.06 (s, 2H), 5.10−5.02 (m, 1H), 4.42 (s, 2H), 4.16−4.09 (m, 2H), 4.09−4.00 (m, 1H), 3.58 (dd, *J* = 9.2, 2.0 Hz, 1H), 3.47 (dd, *J* = 8.8, 6.0 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.6, 145.0, 137.4, 136.1, 132.6, 129.9, 128.5, 128.4, 128.2, 128.1, 127.9, 127.8, 127.6, 73.3, 67.9, 67.7, 67.0, 49.5, 21.6.

(*R*)-Benzyl 1-(benzyloxy)-3-(piperidin-1-yl)propan-2-ylcarbamate (1r-4).

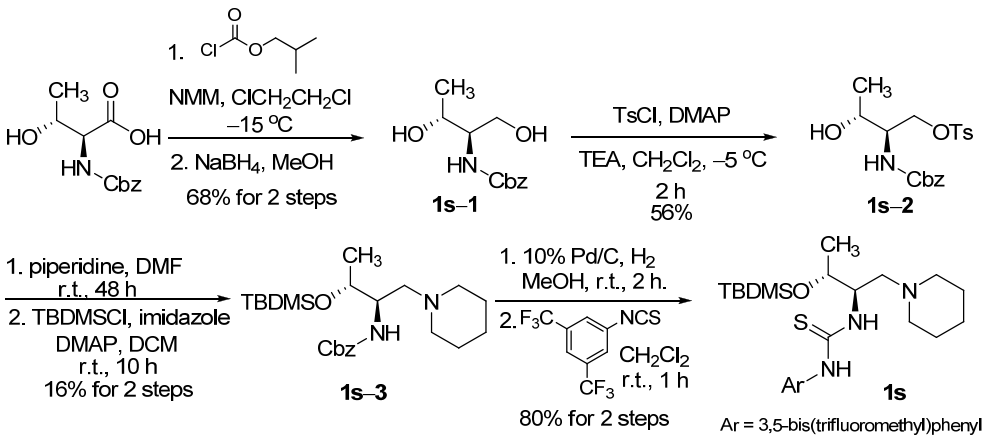
To the solution of compound **1r-3** (900 mg, 1.9 mmol) in 5 mL of dried DMF was added piperidine (816 mg, 9.6 mmol). The reaction mixture was stirred for 12 hours. 50 mL of brine was added into the reaction solution. The product was extracted with ethyl ether (5 mL × 5). The organic phase was combined and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was underwent flash column chromatography on silica gel with petrol ether/ethyl acetate (3:2) as the eluent to get **1r-4** as a colorless oil (625 mg, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.25 (m, 10H), 5.26 (br s, 1H), 5.10 (s, 2H), 4.55−4.46 (m, 2H), 3.86 (br s, 1H), 3.65 (d, *J* = 9.2 Hz, 1H), 3.54 (dd, *J* = 9.2, 4.0 Hz, 1H), 2.43 (d, *J* = 7.2 Hz, 2H), 2.41−2.29 (m, 4H), 1.53−1.47 (m, 4H), 1.41−1.37 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.2,

138.2, 136.6, 128.4, 128.3, 128.0, 127.6, 127.5, 73.2, 70.1, 66.5, 59.3, 54.9, 48.6, 26.0, 24.3; HRMS (ESI) for $C_{23}H_{30}N_2O_3$: calcd $[M + H]^+$ *m*/*z* 383.2329, found 383.2328.

(*R*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-(tert-butyldiphenylsilyloxy)-3-(piperidin-1-yl)propan-2-yl)thiourea (catalyst 1r).

10% Palladium on charcoal (400 mg, 100% w/w) was placed in a 50 ml flask. **1r-4** (390 mg, 1.02 mmol) dissolved in methanol (10 mL) was added to the reaction flask followed by the addition of 10% HCl in methanol (3 mL). The flask was recharged with H_2 with a hydrogen balloon. The reaction was stirred at room temperature for 12 hours. The reaction mixture was then filtered through a celite pad and the filtrate was evaporated to get the primary amine as its hydrochloride salt. The residue was dissolved in 20 mL of CH_2Cl_2, then 1-isothiocyanato-3,5-bis(trifluoromethyl)benzene (271 mg, 1.00 mmol) and TEA (404 mg, 4.00 mmol) were added into the solution. The reaction mixture was stirred for 1 hour at room temperature. The solvent was evaporated and the residue was dissolved in 50 mL of EtOAc. The organic phase was washed with water (10 mL), brine and dried over Na_2SO_4. The solvent was removed to get the crude alcohol product as a colorless oil (372 mg) which was dissolved in 15 mL of CH_2Cl_2. To the solution were added TBDPSCl (330 mg, 1.2 mmol), imidazole (102 mg, 1.5 mmol), and DMAP (6.0 mg, 0.05 mmol). The reaction mixture was stirred at room temperature for 2 hour. 30 mL of CH_2Cl_2 was added into the reaction mixture, then the organic phase was washed with water (10 mL), brine and dried over Na_2SO_4. The solvent was removed under reduced pressure. The residue was underwent flash column chromatography on silica gel with CH_2Cl_2/MeOH (97:3) to afford **1r** as a colorless oil (471 mg, 70% yield for 3 steps). $[\alpha]_D^{25}$ = −19.4 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.55 (br s, 1H), 8.02 (s, 2H), 7.67−7.64 (m, 5H), 7.49−7.39 (m, 6H), 6.75 (br s, 1H), 3.83−3.52 (m, 3H), 2.70−2.49 (m, 3H), 2.47−2.22 (m, 3H), 1.60−1.40 (m, 6H), 1.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.6, 141.6, 135.5, 132.4, 132.2, 131.6 (q, *J* = 34.0 Hz), 130.1, 128.0, 124.9, 123.1 (q, *J* = 271.0 Hz), 118.3, 64.3, 63.3, 55.2, 54.8, 29.6, 26.8, 25.4, 23.4, 19.1; HRMS (ESI) for $C_{33}H_{39}F_6N_3OSSi$: calcd $[M + H]^+$ *m*/*z* 668.2560, found 668.2562.

Preparation of catalyst 1s



Benzyl (2*R*,3*R*)-1,3-dihydroxybutan-2-ylcarbamate (1s-1)[8]

Yield: 68% for 2 steps, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.29 (m, 5H), 5.62 (d, *J* = 8.8 Hz, 1H), 5.09 (s, 2H), 4.14−4.09 (m, 1H), 3.76 (d, *J* = 4.0 Hz, 2H), 3.57−3.55 (m, 1H), 3.25−2.96 (br s, 2H), 1.18 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1, 136.2, 128.5, 128.2, 128.0, 68.5, 66.9, 64.6, 56.2, 20.2.

(2*R*,3*R*)-2-(Benzyloxycarbonylamino)-3-hydroxybutyl 4-methylbenzenesulfonate (1s-2)[9]

To the solution of **1s-1** (1.57 g, 6.57 mmol) in 50 mL of dried CH_2Cl_2 were added DMAP (81 mg, 0.66 mmol), TEA (1.99 g, 19.7 mmol), and TsCl (1.38 g, 7.22 mmol) at 0 °C. The reaction mixture was stirred for 2 hours. The reaction mixture was washed with water (10 mL) and brine. The organic phase was dried over Na_2SO_4. Removed the solvent under reduced pressure and the residue was underwent flash column chromatography on silica gel with petrol ether/ethyl acetate (1:1) as the eluent to get **1s-2** as a colorless oil (1.45 g, 56% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.1 Hz, 2H), 7.39−7.29 (m, 7H), 5.19 (d, *J* = 8.7 Hz, 1H), 5.06 (s, 2H), 4.13−4.01 (m, 3H), 3.80−3.72 (m, 1H), 2.44 (s, 3H), 2.29 (s, 1H), 1.18 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.4, 145.2, 136.1, 132.5, 130.0, 128.5, 128.2, 128.0, 127.9, 68.6, 67.1, 65.4, 54.5, 21.6, 19.9.

Benzyl (2*R*,3*R*)-3-(*tert*-butyldimethylsilyloxy)-1-(piperidin-1-yl)butan-2-ylcarbamate (1s-3).

To the solution of compound **1s-2** (750 mg, 1.91 mmol) in 10 mL of dried DMF was added piperidine (808 mg, 9.5 mmol) at room temperature. The reaction mixture was stirred for 48 hours. Brine (50 mL) was added into the reaction solution, then extracted the product with ethyl ether (5

mL × 5). Combined the organic phase and dried over Na_2SO_4. Removed the solvent under reduced pressure to get the crude chiral amine (269 mg) as a colorless oil which was dissolved in 15 mL of CH_2Cl_2. To the solution were added TBDMSCl (154 mg, 1.02 mmol), imidazole (88 mg, 1.3 mmol), and DMAP (10 mg, 0.085 mmol). The reaction mixture was stirred at room temperature for 10 hours. 30 mL of CH_2Cl_2 was added into the reaction mixture, the organic phase was then washed with water (10 mL) and brine. The organic phase was dried over Na_2SO_4. Removed the solvent under reduced pressure and the residue was underwent flash column chromatography on silica gel with petrol ether/ethyl acetate (7:3) to afford **1s3** as a colorless oil (128 mg, 16% yield for 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.31 (m, 5H), 5.15−5.07 (m, 2H), 5.01 (d, *J* = 8.4 Hz, 1H), 4.18−4.13 (m, 1H), 3.68−3.62 (m, 1H), 2.44−2.30 (m, 5H), 2.25 (dd, *J* = 12.0, 6.4 Hz, 1H), 1.55−1.46 (m, 4H), 1.45−1.34 (m, 2H), 1.13 (d, *J* = 6.0 Hz, 3H), 0.87 (s, 9H), 0.063 (s, 3H), 0.058 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.5, 136.8, 128.5, 128.1, 128.0, 66.8, 66.6, 60.2, 54.8, 53.6, 26.1, 25.9, 24.4, 20.9, 18.0, –4.2, –5.0; HRMS (ESI) for $C_{23}H_{40}N_2O_3Si$: calcd $[M + H]^+$ *m*/*z* 421.2881, found 421.2887.

1-(3,5-Bis(trifluoromethyl)phenyl)-3-((2*R*,3*R*)-3-(tert-butyldimethylsilyloxy)-1-(piperi-din-1-yl)butan-2-yl)thiourea (catalyst 1s).

10% palladium on charcoal (100 mg, 100% w/w) was placed in a 25 ml flask. **1s-3** (110 mg, 0.26 mmol) dissolved in methanol (10 mL) was added to the reaction flask. The flask was recharged with H_2 with a hydrogen balloon. The reaction was stirred at room temperature for 2 hours. The reaction mixture was then filtered through a celite pad and the filtrate was evaporated. The residue was dissolved in 10 mL of dried CH_2Cl_2, then 1-isothiocyanato-3,5-bis(trifluoromethyl)benzene (79 mg, 0.29 mmol) was added into the flask. The reaction was stirred for 1 hour at room temperature. Removed the solvent under reduced pressure and the residue was underwent flash column chromatography on silica gel with CH_2Cl_2/MeOH (97:3) to afford **1s** as a white solid (117 mg, 80% yield for 2 steps). m.p. 153−154 ^{o}C; $[\alpha]_D^{25} = -13.0$ (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.43 (br s, 1H), 8.05 (s, 2H), 7.63 (s, 1H), 6.67 (d, *J* = 3.9 Hz, 1H), 3.97−3.90 (m, 1H), 3.64−3.59 (m, 1H), 2.85−2.63 (m, 3H), 2.53−2.41 (m, 3H), 1.62−1.45 (m, 6H), 1.28 (d, *J* = 6.0 Hz, 3H), 0.91 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.0, 141.8, 131.5 (q, *J* = 33.0 Hz), 124.5, 123.2 (q, *J* = 270.0 Hz), 118.0, 69.5, 65.4,

59.7, 55.2, 25.7, 25.6, 23.4, 21.2, 17.9, –4.2, –5.0; HRMS (ESI) for $C_{24}H_{37}F_6N_3OSSi$: calcd [M + H]$^+$ *m*/*z* 558.2404, found 558.2411.

1-(3,5-bis(trifluoromethyl)phenyl)-3-((*S*)-3-methyl-2-((piperidin-1-yl)methyl)butyl)thiourea (catalyst 1t)

Overall yield of 5 steps: 80%; white solid; m.p. 100−102 °C; $[\alpha]_D^{25}$ = +12.0 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, CD_3OD): δ 8.11 (s, 2H), 7.67 (s, 1H), 4.03−3.78 (m, 1H), 3.53−3.38 (m, 1H), 2.73−2.46 (m, 2H), 2.44−2.22 (m, 4H), 1.97−1.65 (m, 2H), 1.61−1.37 (m, 6H), 1.00 (s, 3H), 0.98 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ 182.6, 143.3, 133.0 (q, *J* = 32.0 Hz), 127.4, 124.7 (q, *J* = 270.3 Hz), 117.8, 62.4, 56.1, 40.9, 30.2, 26.7, 25.2, 19.9; HRMS (ESI) for $C_{20}H_{27}F_6N_3S$: calcd [M + H]$^+$ *m*/*z* 456.1903, found 456.1908.

General Procedure for the Asymmetric Friedel−Crafts Reactions.

***N*-((2-Hydroxy-4,6-dimethoxyphenyl)(phenyl)methyl)-4-methylbenzenesulfonamide (4a).** To a dry 5 mL flask was added catalyst **1k** (9 mg, 0.02 mmol), *N*-Ts-aldimine **3a** (39 mg, 0.15 mmol), 1.0 mL of dried toluene, and 4 Å M.S. (20 mg). The flask was cooled to −50°C and stirred for 30 minutes. The solution of 3,5-dimethoxyphenol (**2a**) (15 mg, 0.10 mmol) in 0.2 mL of toluene was added into the flask with a syringe dropwisely within 15 minutes. The reaction mixture was stirred at −50°C for 72 hours. The reaction mixture was subjected to silica gel column chromatography with petrol ether/ethyl acetate (3:1) as the eluent to give the **4a** as a white solid (37 mg, yield 90%); m.p. 59−61°C; $[\alpha]_D^{25}$ = +11.7 (*c* = 0.5 in $CHCl_3$) for 92% ee; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.4 Hz, 2H), 7.28−7.26 (m, 2H), 7.23−7.15 (m, 3H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.31 (d, *J* =10.0 Hz, 1H), 6.13 (s, 1H), 6.08 (d, *J* = 10.0 Hz, 1H), 5.85 (d, *J* = 2.0 Hz, 1H), 5.81 (d, *J* = 2.0 Hz, 1H), 3.66 (s, 3H), 3.58 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.6, 158.0, 154.6, 142.8, 141.0, 136.9, 128.9, 128.0, 126.8, 126.7, 126.5, 107.3, 93.9, 91.2, 55.4, 55.2, 52.0, 21.3; HRMS (ESI) for $C_{22}H_{23}NO_5S$: calcd [M + H]$^+$ *m*/*z* 414.1370, found 414.1375; HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 85:15, flow rate = 0.5 mL/min, λ = 220 nm): t_1 = 26.5 min (minor), t_2 = 28.5 min (major).

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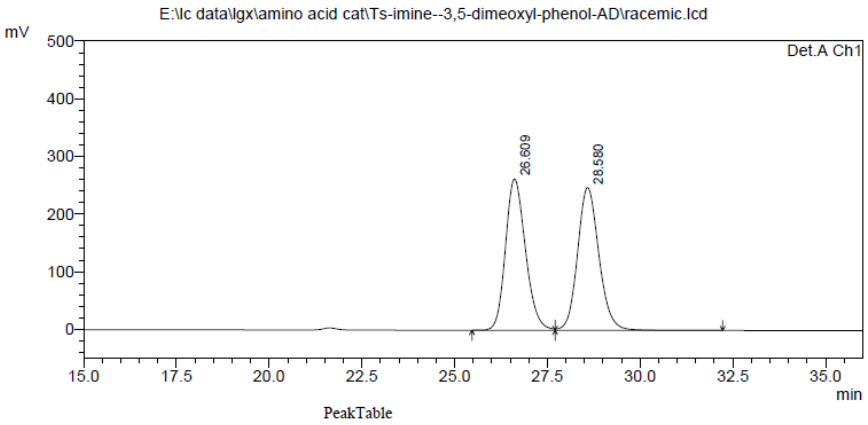

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.609	9847651	262624	49.734	51.445
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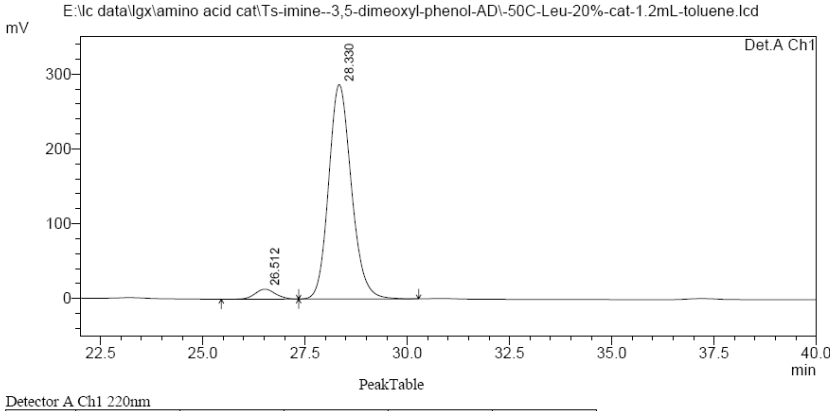

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.512	464847	13317	4.021	4.437
2	28.330	11095392	286835	95.979	95.563
Total		11560239	300151	100.000	100.000

Characterization of Products 4b−4l.

N-((3,5-Dimethylphenyl)(2-hydroxy-4,6-dimethoxyphenyl)methyl)-4-methylbenzenesulfonamide (**4b**) (Table 3, entry 2)

Yield: 95%; white solid; m.p. 72−74 ^{o}C; $[\alpha]_D^{25}$ = +4.9 (*c* = 0.5 in $CHCl_3$) for 85% ee; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.85 (s, 2H), 6.81 (s, 1H), 6.16 (d, *J* = 10.0 Hz, 1H), 6.01 (d, *J* = 9.6 Hz, 1H), 5.86 (br s, 1H), 5.85 (d, *J* = 2.0 Hz, 1H), 5.82 (d, *J* = 2.0 Hz, 1H), 3.68 (s, 3H), 3.59 (s, 3H), 2.31 (s, 3H), 2.20 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.4, 157.8, 154.6, 142.8, 140.6, 137.4, 136.7, 128.8, 128.5, 126.7, 124.3, 107.0, 93.7, 91.0, 55.4, 55.1, 52.0, 21.2; HRMS (ESI) for $C_{24}H_{27}NO_5S$: calcd $[M - H]^-$ *m*/*z* 440.1537, found

440.1545; HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 92:8, flow rate = 0.50 mL/min, λ = 220 nm): t_1 = 47.1 min (*R*, major), t_2 = 49.7 min (*S*, minor).

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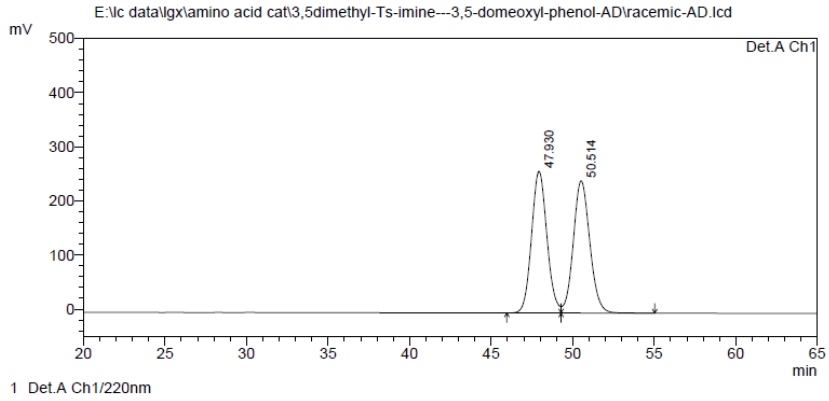

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	47.930	17157434	261945	49.956	51.734
2	50.514	17187431	244383	50.044	48.266
Total		34344865	506328	100.000	100.000

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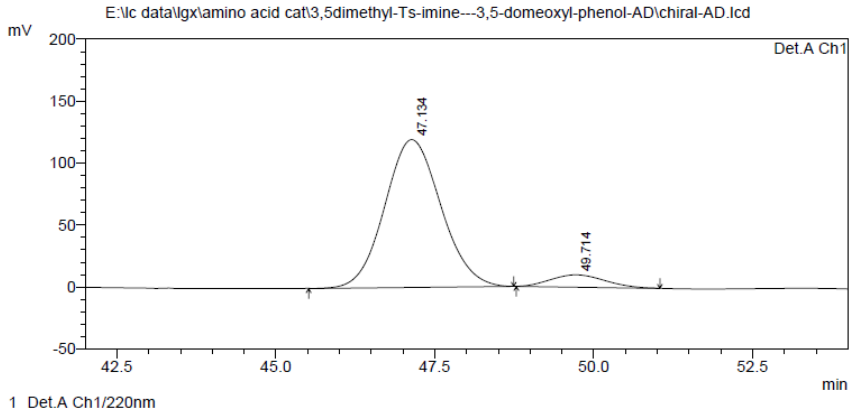

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	47.134	7349221	119347	92.509	92.297
2	49.714	595118	9960	7.491	7.703
Total		7944339	129307	100.000	100.000

N-((4-*tert*-Butylphenyl)(2-hydroxy-4,6-dimethoxyphenyl)methyl)-4-methylbenzenesulfonamide (**4c**) (Table 3, entry 3)

Yield: 94%; white solid; m.p. 62−65 °C; $[\alpha]_D^{25}$ = +1.4 (*c* = 0.5 in $CHCl_3$) for 84% ee; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, *J* = 8.0 Hz, 2H), 7.24−7.18 (m, 4H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.30 (d, *J* = 10.0 Hz, 1H), 6.18 (br s, 1H), 6.04 (d, *J* = 9.2 Hz, 1H), 5.86 (d, *J* = 1.6 Hz, 1H), 5.82 (d, *J* = 1.6 Hz, 1H), 3.66 (s, 3H), 3.59 (s, 3H), 2.30 (s, 3H), 1.26 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.5, 158.0, 154.6, 149.6, 142.7, 137.8, 137.1, 128.9, 126.9, 126.3, 125.0, 107.5, 94.1, 91.3, 55.5, 55.2, 52.0, 34.3, 31.3, 21.3; HRMS (ESI) for $C_{26}H_{31}NO_5S$: calcd $[M - H]^-$ *m*/*z* 468.1850, found

468.1847; HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 90:10, flow rate = 0.50 mL/min, λ = 220 nm): t_1 = 34.8 min (minor), t_2 = 37.0 min (major).

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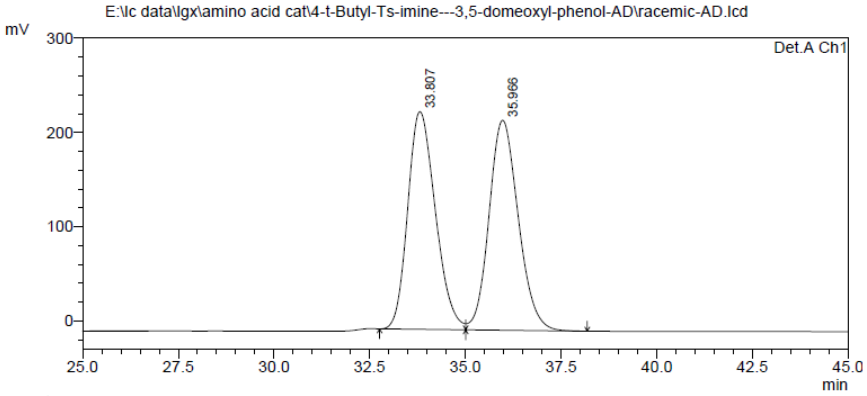

1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.807	11620449	231167	49.532	50.903
2	35.966	11840201	222970	50.468	49.097
Total		23460651	454138	100.000	100.000

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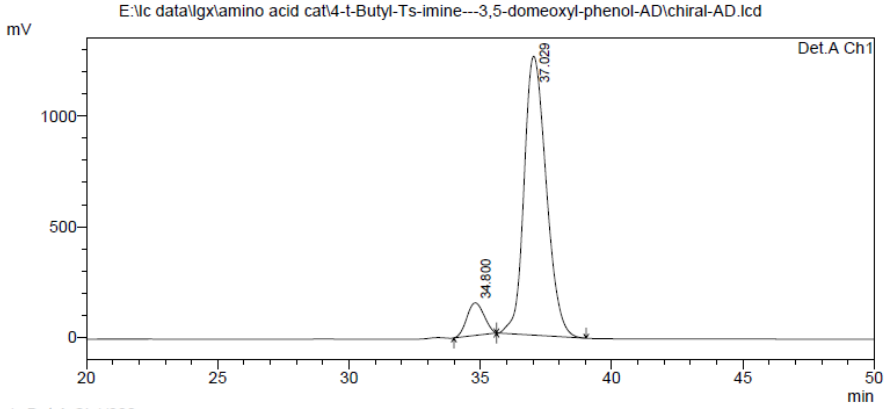

1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.800	6672930	147261	8.260	10.465
2	37.029	74109599	1259910	91.740	89.535
Total		80782529	1407171	100.000	100.000

N-((2-Hydroxy-4,6-dimethoxyphenyl)(3-phenoxyphenyl)methyl)-4-methylbenzenesulfonamide (**4d**) (Table 3, entry 4)

Yield: 97%; white solid; m.p. 50−52 °C; $[\alpha]_D^{25}$ = +12.0 (*c* = 0.5 in $CHCl_3$) for 84% ee; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.4 Hz, 2H), 7.32−7.27 (m, 2H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.09−7.03 (m, 4H), 6.96−6.94 (m, 1H), 6.94−6.92 (m, 1H), 6.92−6.90 (m, 1H), 6.77 (dd, *J* = 8.0, 2.4 Hz, 1H), 6.17 (d, *J* = 10.0 Hz, 1H), 6.06 (d, *J* = 10.0 Hz, 1H), 5.84 (d, *J* = 2.4 Hz, 1H), 5.81 (d, *J* = 2.4 Hz, 1H), 5.40 (br s, 1H), 3.68 (s, 3H), 3.59 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.6, 157.8, 157.1, 156.8, 154.5 143.4, 142.9, 136.8, 129.6, 129.2, 128.9, 126.8, 123.0,

121.6, 118.6, 117.4, 117.0, 107.2, 93.8, 91.2, 55.4, 55.2, 51.8, 21.3; HRMS (ESI) for $C_{28}H_{27}NO_6S$: calcd $[M - H]^-$ *m*/*z* 504.1486, found 504.1484; HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 85:15, flow rate = 0.50 mL/min, λ = 220 nm): t_1 = 29.7 min (minor), t_2 = 39.1 min (major).

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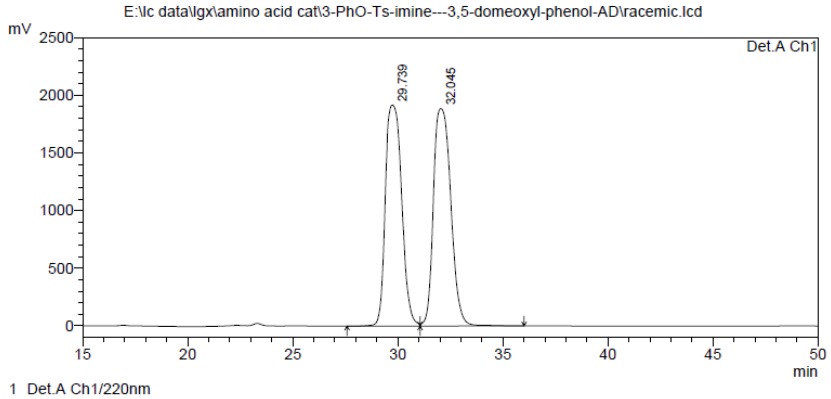

1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.739	103402004	1915538	48.772	50.390
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Total		212011111	3801455	100.000	100.000

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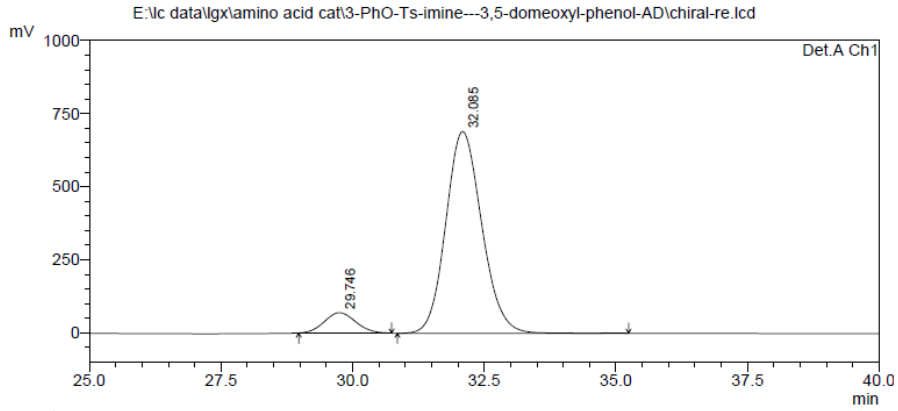


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

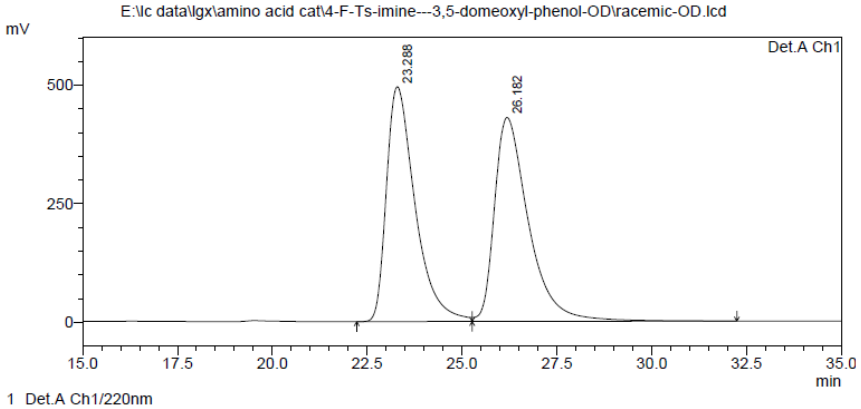
Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.746	2892060	69535	8.100	9.150
2	32.085	32813016	690408	91.900	90.850
Total		35705076	759943	100.000	100.000

N-((4-Fluorophenyl)(2-hydroxy-4,6-dimethoxyphenyl)methyl)-4-methylbenzenesulfonamide (**4e**) (Table 3, entry 5)

Yield: 90%; white solid, m.p. 47−49 °C; $[\alpha]_D^{25}$ = +14.1 (*c* = 0.5 in $CHCl_3$) for 92% ee; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.0 Hz, 2H), 7.22 (dd, *J* = 8.4, 5.6 Hz, 2H), 7.01 (d, *J* = 8.0 Hz, 2H), 6.89−6.84 (m, 2H), 6.42 (br s, 1H), 6.40 (br s, 1H), 6.03 (d, *J* = 10.0 Hz, 1H), 5.88 (d, *J* = 2.0

Hz, 1H), 5.80 (d, J = 2.0 Hz, 1H), 3.66 (s, 3H), 3.58 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7 (d, J = 243.1 Hz), 160.7, 157.9, 154.4, 143.0, 136.8, 136.7 (d, J = 2.9 Hz), 128.9, 128.2 (d, J = 7.9 Hz), 126.8, 114.7 (d, J = 21.3 Hz), 107.1, 93.9, 91.2, 55.5, 55.2, 51.4, 21.4; HRMS (ESI) for $C_{22}H_{22}FNO_5S$: calcd $[M + Na]^+$ m/z 454.1095, found 454.1097; HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 90:10, flow rate = 0.50 mL/min, λ = 220 nm): t_1 = 23.0 min (major), t_2 = 26.1 min (minor).

<Chromatogram>



1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.288	26047244	495644	49.190	53.534
2	26.182	26905023	430208	50.810	46.466
Total		52952267	925852	100.000	100.000

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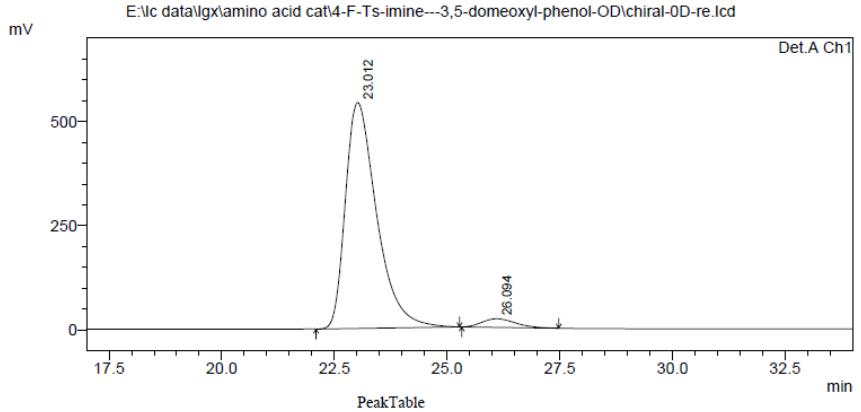

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.012	26231981	542769	96.135	96.325
2	26.094	1054714	20707	3.865	3.675
Total		27286695	563476	100.000	100.000

N-((3-Fluorophenyl)(2-hydroxy-4,6-dimethoxyphenyl)methyl)-4-methylbenzenesulfonamide (**4f**) (Table 3, entry 6)

Yield: 90%; white solid; m.p. 47−50 °C; $[\alpha]_D^{25}$ = +20.2 (c = 0.5 in $CHCl_3$) for 92% ee; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, J = 8.4 Hz, 2H), 7.18−7.12 (m, 1H), 7.06 (d, J = 8.0 Hz, 1H), 7.02

(d, J = 8.0 Hz, 2H), 6.97 (d, J =10.4 Hz, 1H), 6.84 (td, J = 8.0, 1.6 Hz, 1H), 6.43 (d, J =10.4 Hz, 1H), 6.36 (s, 1H), 6.05 (d, J = 10.4 Hz, 1H), 5.88 (d, J = 1.6 Hz, 1H), 5.80 (d, J =1.6 Hz, 1H), 3.65 (s, 3H), 3.58 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.7 (d, J = 243.5 Hz), 160.8, 157.9, 154.3, 143.9 (d, J = 7.1 Hz), 143.0, 136.8, 129.4 (d, J = 8.1 Hz), 129.0, 126.8, 122.1 (d, J = 2.5 Hz), 113.6 (d, J = 6.1 Hz), 113.4 (d, J = 7.4 Hz), 106.9, 93.8, 91.3, 55.5, 55.3, 51.5, 21.3; HRMS (ESI) for $C_{22}H_{22}FNO_5S$: calcd $[M + H]^+$ m/z 432.1275, found 432.1281; HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 90:10, flow rate = 0.50 mL/min, λ = 220 nm): t_1 = 47.7 min (minor), t_2 = 50.9 min (major).

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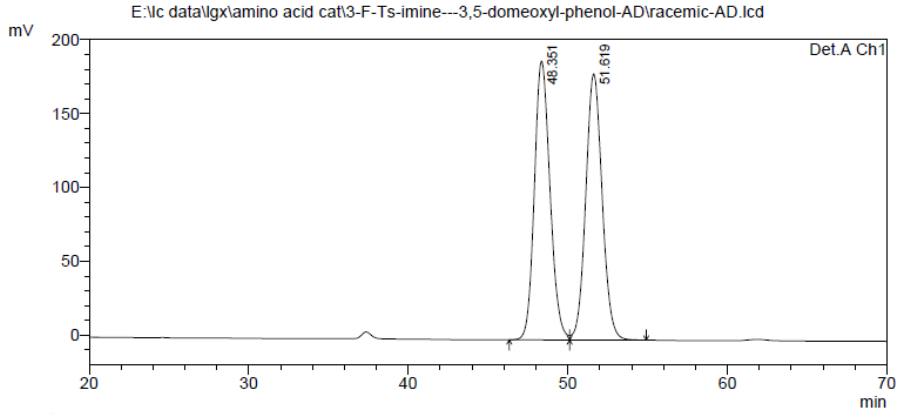


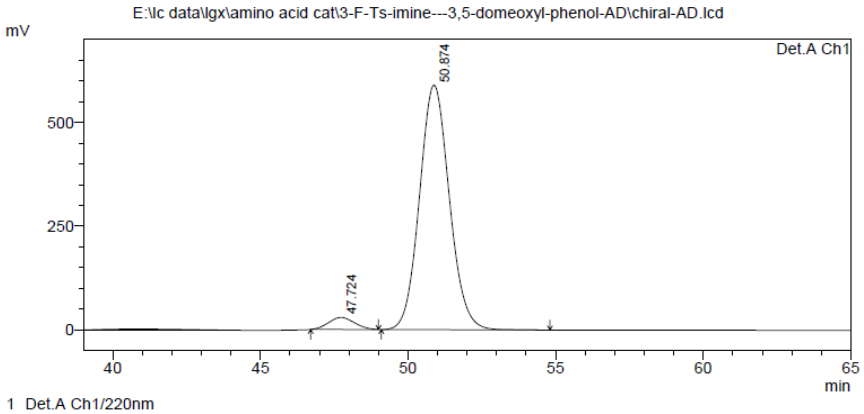
1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	48.351	12858593	188775	49.913	51.163
2	51.619	12903551	180190	50.087	48.837
Total		25762145	368966	100.000	100.000

<Chromatogram>



1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	47.724	1757387	28821	4.058	4.654
2	50.874	41548681	590424	95.942	95.346
Total		43306068	619245	100.000	100.000

N-((2-Fluorophenyl)(2-hydroxy-4,6-dimethoxyphenyl)methyl)-4-methylbenzenesulfonamide (**4g**) (Table 3, entry 7)

Yield: 93%; white solid; m.p. 152−154 °C; $[\alpha]_D^{25}$ = +3.5 (*c* = 0.5 in $CHCl_3$) for 91% ee; ^1H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, *J* = 8.4 Hz, 2H), 7.33 (td, *J* = 7.8, 1.6 Hz, 1H), 7.18−7.12 (m, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.98−6.94 (m, 1H), 6.93−6.89 (m, 1H), 6.43 (br s, 1H), 6.31 (d, *J* = 7.2 Hz, 1H), 6.25 (d, *J* = 8.4 Hz, 1H), 5.90 (d, *J* = 2.4 Hz, 1H), 5.84 (d, *J* = 2.0 Hz, 1H), 3.66 (s, 3H), 3.63 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.7, 160.0 (d, *J* = 246.9 Hz), 158.0, 154.8, 143.0, 136.6, 129.0 (d, *J* = 5.2 Hz), 128.98, 128.8 (d, *J* = 8.2 Hz), 127.6 (d, *J* = 13.1 Hz), 127.0, 123.6, 115.3 (d, *J* = 21.8 Hz), 106.1, 93.9, 91.4, 55.5, 55.2, 47.4, 21.4; HRMS (ESI) for $C_{22}H_{22}FNO_5S$: calcd $[M - H]^-$ *m/z* 430.1130, found 430.1135; HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 92:8, flow rate = 0.50 mL/min, λ = 220 nm): t_1 = 44.8 min (*R*, minor), t_2 = 57.1 min (*S*, major).

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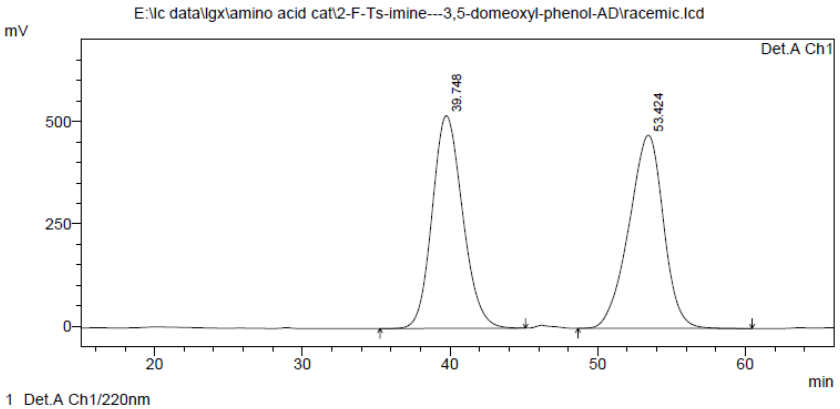

1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	39.748	74650170	519549	49.256	52.383
2	53.424	76905882	472271	50.744	47.617
Total		151556052	991820	100.000	100.000

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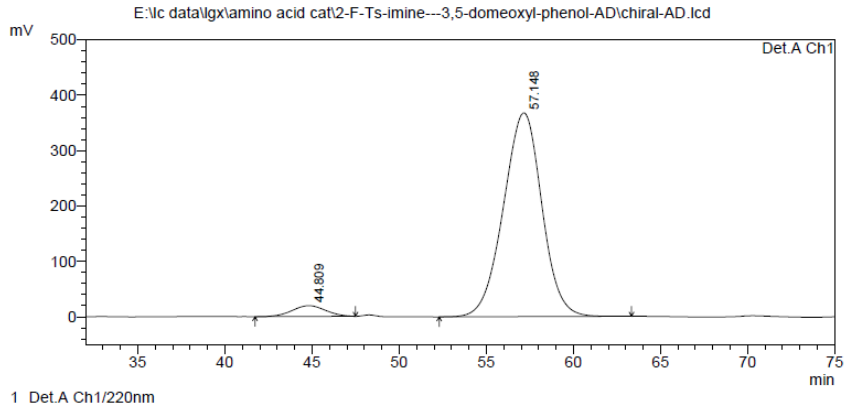

1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	44.809	2581902	19429	4.368	5.014
2	57.148	56533503	368064	95.632	94.986
Total		59115405	387492	100.000	100.000

N-((2-Hydroxy-4,6-dimethoxyphenyl)(4-(trifluoromethyl)phenyl)methyl)-4-methylbenzenesulfonamide (**4h**) (Table 3, entry 8)

Yield: 94%; white solid; m.p. 92−94 °C; $[\alpha]_D^{25}$ = +11.0 (*c* = 0.5 in $CHCl_3$) for 80% ee; ^1H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.34 (d, *J* = 10.4 Hz, 1H), 6.11 (d, *J* = 10.4 Hz, 1H), 5.86 (br s, 1H), 5.85 (s, 1H), 5.75 (br s, 1H), 3.69 (s, 3H), 3.61 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.9, 157.8, 154.3, 145.2, 143.1, 136.8, 129.0, 128.3 (q, *J* = 17.0 Hz), 128.2, 126.8, 124.9 (q, *J* = 3.5 Hz), 124.2 (q, *J* = 270.4 Hz), 106.8, 93.9, 91.2, 55.5, 55.3, 51.6, 21.3; HRMS (ESI) for $C_{23}H_{22}F_3NO_5S$: calcd $[M + H]^+$ *m*/*z* 482.1244, found 482.1240; HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 90:10, flow rate = 0.50 mL/min, λ = 220 nm): t_1 = 33.9 min (major), t_2 = 39.8 min (minor).

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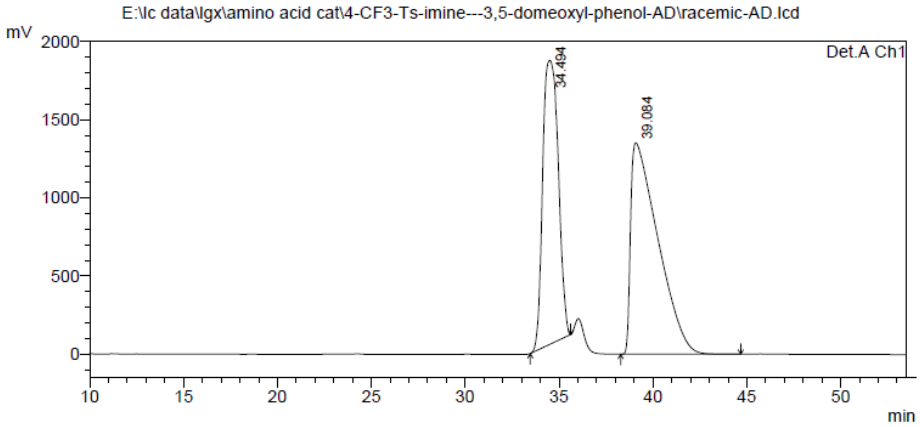

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.494	105263149	1820053	43.524	57.345
2	39.084	136586254	1353816	56.476	42.655
Total		241849404	3173869	100.000	100.000

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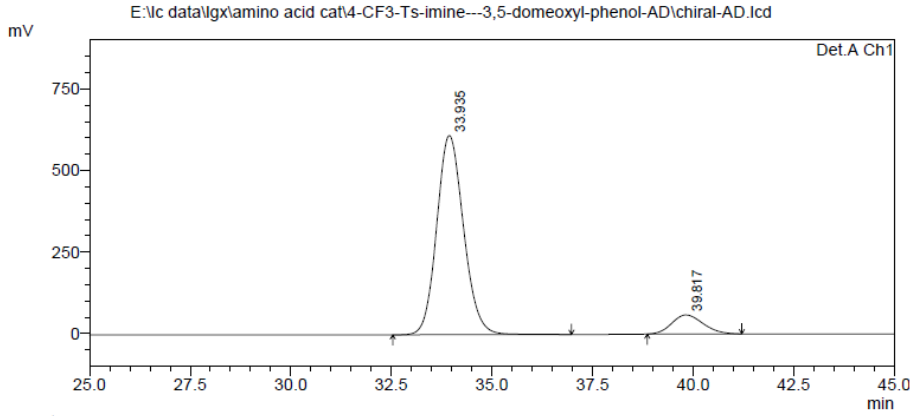

1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.935	28342144	611443	89.957	91.271
2	39.817	3164351	58475	10.043	8.729
Total		31506496	669918	100.000	100.000

Methyl 4-((2-hydroxy-4,6-dimethoxyphenyl)(4-methylphenylsulfonamido)methyl)benzoate (**4i**) (Table 3, entry 9)

Yield: 81%; white solid; m.p. 75−77 ^{o}C; 70% *ee*; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83 (d, *J* = 8.1 Hz, 2H), 7.53 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.00 (d, *J* = 8.1 Hz, 2H), 6.89 (s, 1H), 6.45 (d, *J* = 10.5 Hz, 1H), 6.10 (d, *J* = 10.5Hz, 1H), 5.90 (d, *J* = 1.8 Hz, 1H), 5.79 (d, *J* = 1.8, 1H), 3.88 (s, 3H), 3.63 (s, 3H), 3.57 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.4, 160.8, 154.6, 146.8, 142.9, 136.9, 129.3, 128.9, 128.3, 126.8, 126.5, 107.0, 93.9, 91.1, 55.5, 51.7, 21.3; HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 85:15, flow rate = 0.50 mL/min, λ = 220 nm): t_1 = 45.1 min (major), t_2 = 73.0 min (minor).

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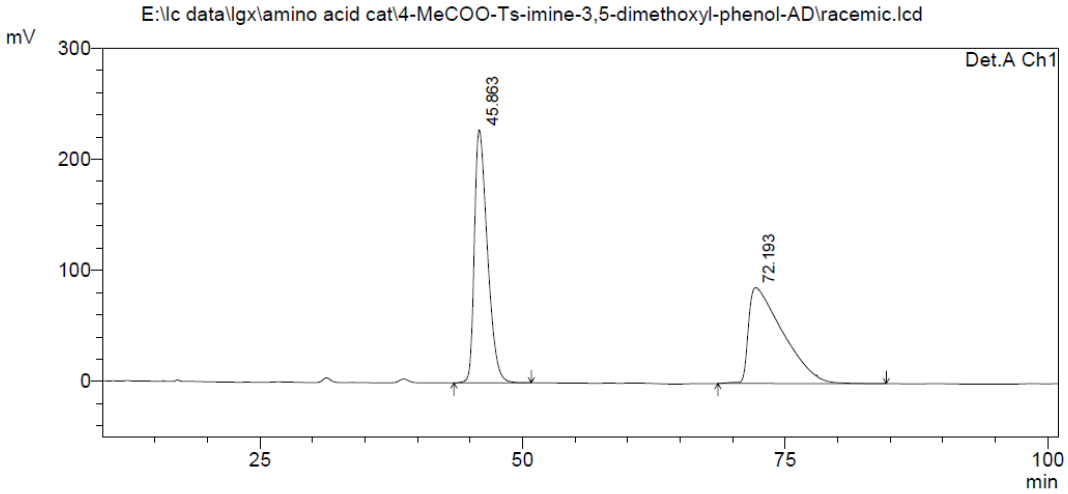

1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	45.863	19609998	227765	50.023	72.523
2	72.193	19591992	86293	49.977	27.477
Total		39201990	314058	100.000	100.000

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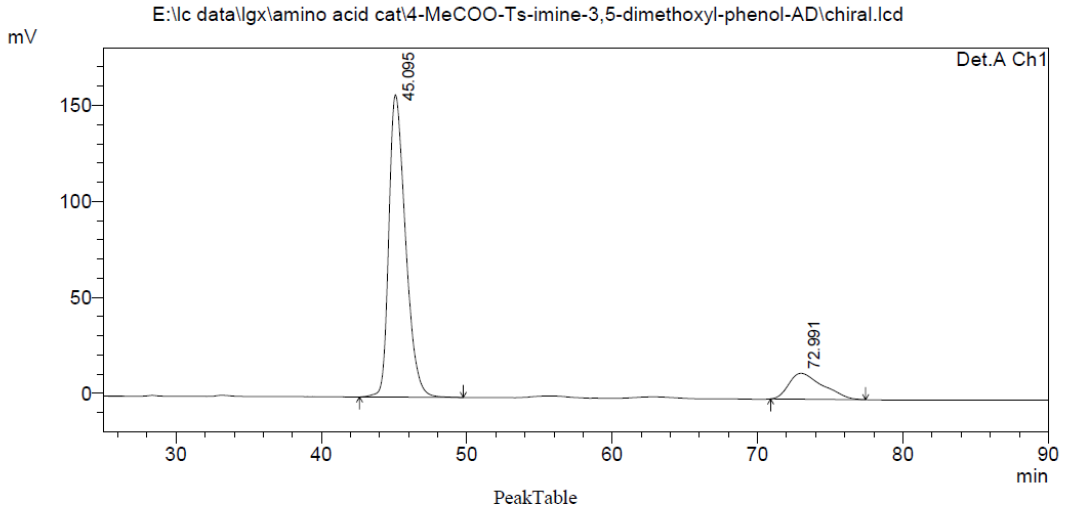

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	45.095	12556259	157495	85.164	92.128
2	72.991	2187356	13458	14.836	7.872
Total		14743615	170954	100.000	100.000

N-((2-Hydroxy-4,6-dimethoxyphenyl)(naphthalen-1-yl)methyl)-4-methylbenzenesulfonamide (**4j**) (Table 3, entry10)

Yield: 84%; white solid; m.p. 185−187 ^{o}C; $[\alpha]_D^{25} = -124.8$ (c = 0.5 in $CHCl_3$) for 95% ee; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.41 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 7.8 Hz, 1H), 7.76−7.73 (m, 1H), 7.58 (d, J = 8.4 Hz, 2H), 7.56−7.46 (m, 2H), 7.28 (s, 1H), 7.04 (d, J = 7.8 Hz, 2H), 6.83 (d, J = 8.1 Hz, 1H), 6.15 (br s, 1H), 5.84 (d, J = 2.1 Hz, 1H), 5.82 (d, J = 2.1 Hz, 1H), 5.79 (br s, 1H), 3.68 (s,

3H), 3.60 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.8, 158.2, 155.3, 143.1, 136.4, 134.4, 134.0, 131.2, 128.9, 128.7, 128.6, 127.0, 126.5, 125.8, 125.6, 125.0, 124.2, 105.7, 94.2, 91.5, 55.5, 55.2, 50.7, 21.3; HRMS (ESI) for $C_{26}H_{25}NO_5S$: calcd $[M + Na]^+$ *m*/*z* 486.1346, found 486.1351; HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 87:13, flow rate = 0.50 mL/min, λ = 220 nm): t_1 = 39.3 min (minor), t_2 = 41.9 min (major).

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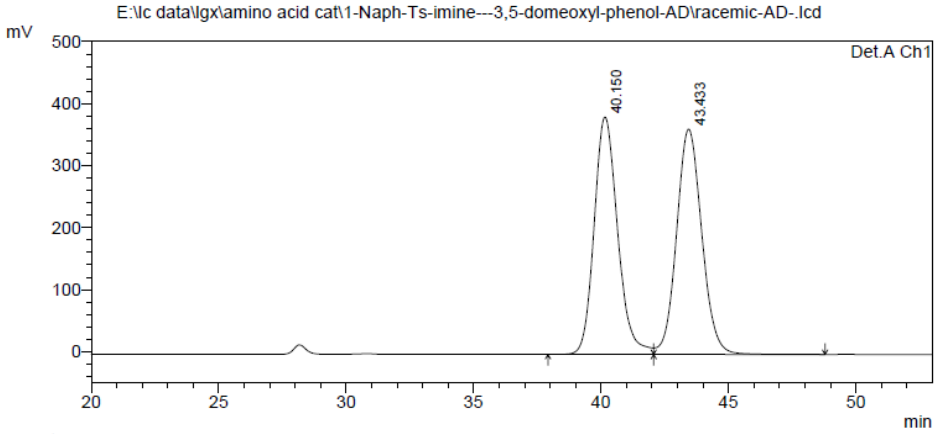

1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	40.150	24546368	382966	49.530	51.308
2	43.433	25012130	363436	50.470	48.692
Total		49558498	746401	100.000	100.000

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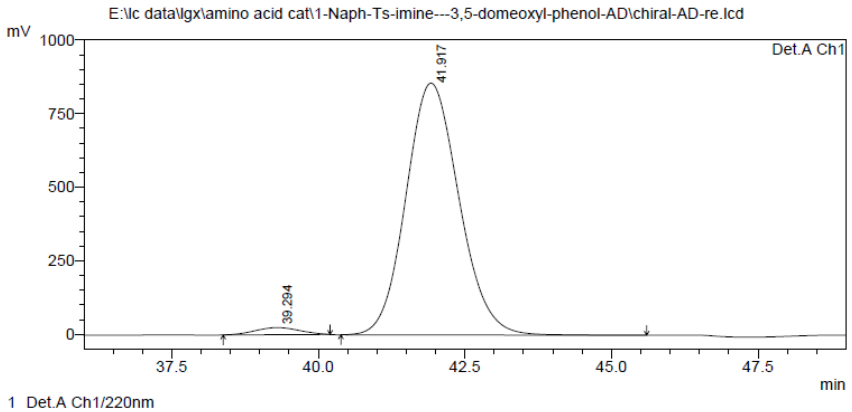

1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	39.294	1255055	24058	2.276	2.736
2	41.917	53879297	855373	97.724	97.264
Total		55134353	879431	100.000	100.000

N-((2-Hydroxy-4,6-dimethoxyphenyl)(naphthalen-2-yl)methyl)-4-methylbenzenesulfonamide (**4k**) (Table 3, entry 11)

Yield: 91%; white solid; m.p. 152−154 °C; $[\alpha]_D^{25}$ = +18.2 (*c* = 0.5 in $CHCl_3$) for 80% ee; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74−7.72 (m, 1H), 7.68−7.60 (m, 3H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.42

(d, J = 8.8 Hz, 1H), 7.39−7.35 (m, 2H), 6.92 (d, J = 8.0 Hz, 2H), 6.53 (d, J = 10.4 Hz, 1H), 6.49 (s, 1H), 6.22 (d, J = 10.4 Hz, 1H), 5.90 (d, J = 2.0 Hz, 1H), 5.80 (d, J = 2.0 Hz, 1H), 3.64 (s, 3H), 3.55 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.6, 158.0, 154.6, 142.9, 138.3, 136.8, 133.0, 132.4, 128.9, 128.0, 127.8, 127.4, 126.8, 125.8, 125.6, 125.2, 124.8, 107.1, 93.8, 91.2, 55.5, 55.2, 52.1, 21.3; HRMS (ESI) for $C_{26}H_{25}NO_5S$: calcd $[M + Na]^+$ m/z 486.1346, found 486.1349; HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 87:13, flow rate = 0.50 mL/min, λ = 220 nm): t_1 = 39.3 min (minor), t_2 = 41.9 min (major).

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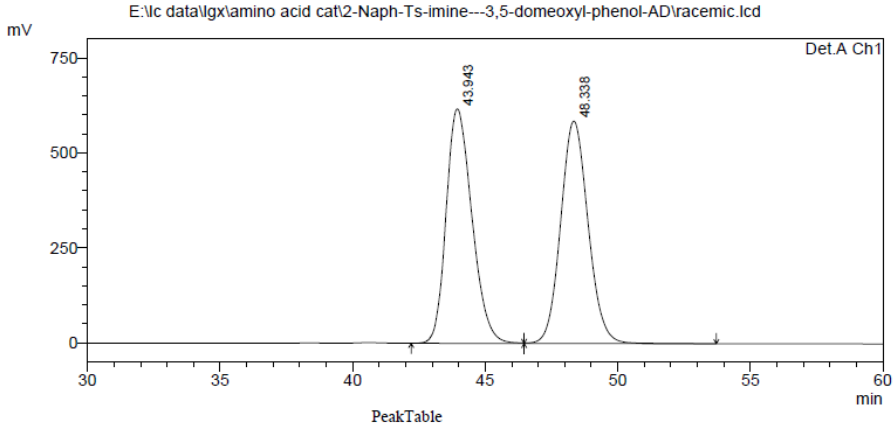
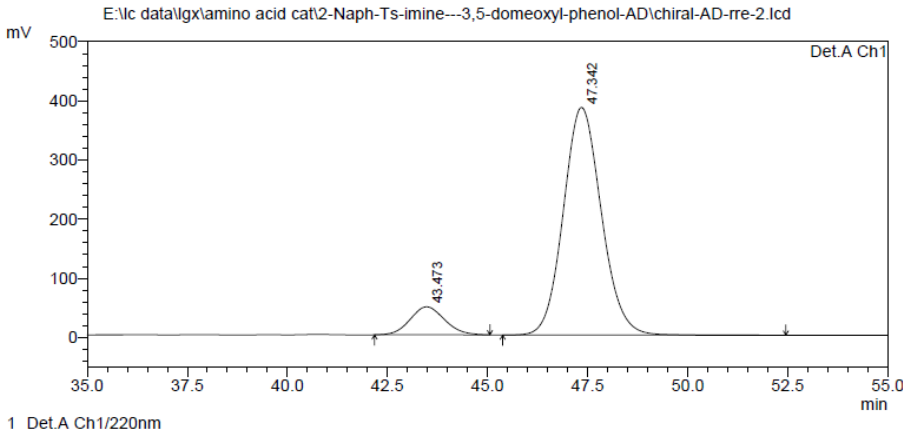


PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	43.943	41894680	617538	49.819	51.306
2	48.338	42199444	586106	50.181	48.694
Total		84094124	1203644	100.000	100.000

<Chromatogram>



1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	43.473	2828385	47316	9.999	10.947
2	47.342	25457439	384896	90.001	89.053
Total		28285825	432212	100.000	100.000

N-(Furan-2-yl(2-hydroxy-4,6-dimethoxyphenyl)methyl)-4-methylbenzenesulfonamide (**4l**) (Table 3, entry 12)

Yield: 93%; white solid; m.p. 46−48 °C; $[\alpha]_D^{25}$ = −15.2 (c = 0.5 in $CHCl_3$) for 88% ee; ^{1}H NMR

(400 MHz, $CDCl_3$): δ 7.59 (d, J = 8.4 Hz, 2H), 7.23 (s, 1H), 7.07 (d, J = 8.0 Hz, 2H), 6.60 (br s, 1H), 6.30 (d, J = 9.6 Hz, 1H), 6.19 (br s, 1H), 6.10 (d, J = 9.6 Hz, 1H), 6.00 (d, J = 2.8 Hz, 1H), 5.91 (d, J = 1.6 Hz, 1H), 5.83 (d, J = 1.6 Hz, 1H), 3.66 (s, 3H), 3.63 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8, 158.1, 155.0, 153.0, 143.0, 141.8, 136.8, 129.0, 126.9, 110.2, 106.9, 105.0, 93.9, 91.3, 55.6, 55.2, 47.2, 21.4; HRMS (ESI) for $C_{20}H_{21}NO_6S$: calcd $[M - H]^-$ m/z 402.1017, found 402.1012; HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 86:14, flow rate = 0.50 mL/min, λ = 220 nm): t_1 = 22.1 min (minor), t_2 = 24.7 min (major).

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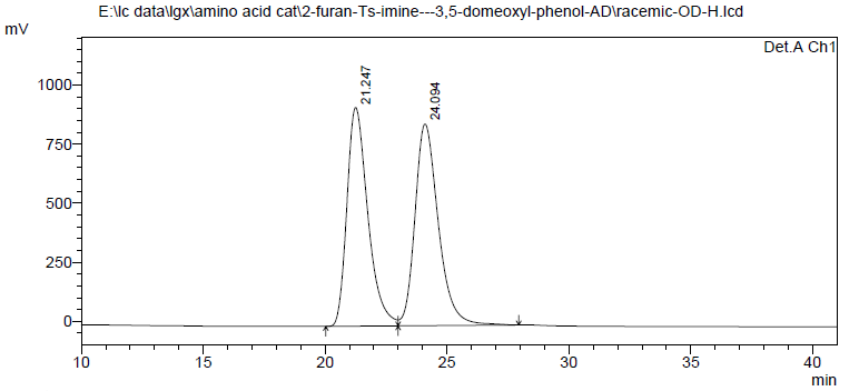

1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.247	55331697	925752	49.226	52.017
2	24.094	57072010	853967	50.774	47.983
Total		112403707	1779720	100.000	100.000

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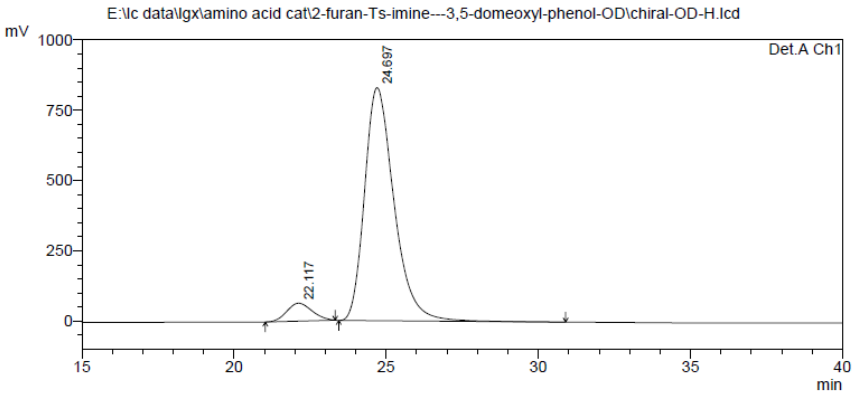


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.117	3685349	63867	6.183	7.152
2	24.697	55914958	829159	93.817	92.848
Total		59600307	893026	100.000	100.000

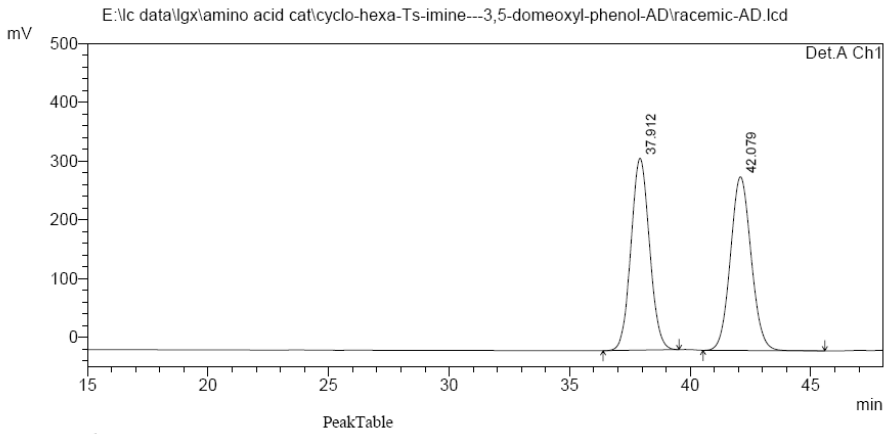
N-(Cyclohexyl(2-hydroxy-4,6-dimethoxyphenyl)methyl)-4-methylbenzenesulfonamide (**4m**)

(Table 3, entry 13)

Yield: 69%; white solid; m.p. 110−112 °C; $[\alpha]_D^{25}$ = −0.4 (c = 0.5 in $CHCl_3$) for 72% ee; ^1H

NMR (400 MHz, $CDCl_3$): δ 7.48 (d, J = 8.1 Hz, 2H), 6.99 (d, J = 7.8 Hz, 2H), 5.81 (br s, 1H), 5.75 (s, 2H), 4.45 (dd, J = 9.9, 9.6 Hz, 1H), 3.67 (s, 3H), 3.59 (s, 3H), 2.28 (s, 3H), 2.21−2.13 (m, 1H), 1.88−1.70 (m, 2H), 1.64−1.55 (m, 2H), 1.24−0.98 (m, 5H), 0.94−0.82 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.0, 154.6, 142.5, 128.8, 128.6, 126.8, 126.4, 107.0, 93.7, 90.3, 55.3, 55.2, 41.6, 30.4, 29.6, 26.4, 26.1, 26.0, 21.3; HRMS (ESI) for $C_{22}H_{29}NO_5S$: calcd $[M - H]^-$ m/z 418.1694, found 418.1693; HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 92:8, flow rate = 0.50 mL/min, λ = 220 nm): t_1 = 37.6 min (major), t_2 = 42.1 min (minor).

<Chromatogram>



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	37.912	17464737	326257	49.749	52.482
2	42.079	17641011	295403	50.251	47.518
Total		35105749	621660	100.000	100.000

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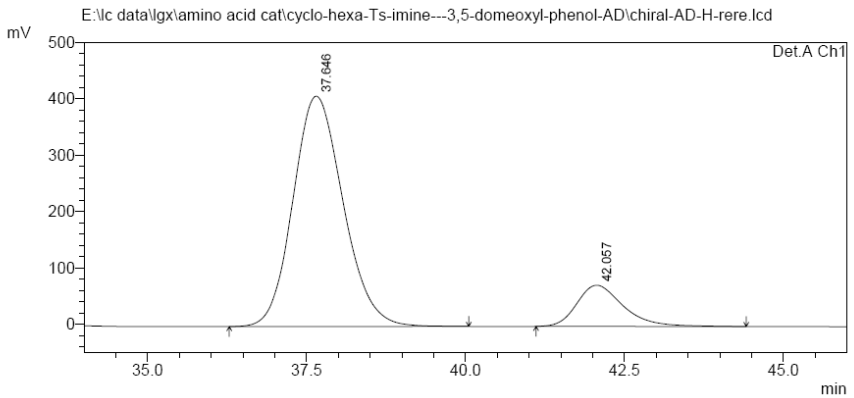

1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	37.646	22403195	408268	85.826	84.848
2	42.057	3699989	72910	14.174	15.152
Total		26103184	481177	100.000	100.000

N-(1-(2-Hydroxy-4,6-dimethoxyphenyl)pentyl)-4-methylbenzenesulfonamide (**4n**) (Table 3, entry 14)

Yield: 61%; white solid; m.p. 81−83 °C; *ee*: 53%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.53 (d, J =

8.1 Hz, 2H), 7.02 (d, J = 8.1 Hz, 2H), 5.90 (br s, 1H), 5.82 (br s, 1H), 5.80 (d, J = 2.4 Hz, 1H), 5.77 (d, J = 2.4 Hz, 1H), 4.81−4.73 (m, 1H), 3.66 (s, 3H), 3.64 (s, 3H), 2.30 (s, 3H), 1.86−1.73 (m, 1H), 1.72−1.59 (m, 1H), 1.38−1.09 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.9, 157.8, 154.6, 142.6, 137.0, 129.6, 128.7, 126.6, 126.3, 107.6, 93.6, 90.8, 55.2, 55.1, 49.8, 35.1, 28.2, 22.2, 21.2, 13.9; HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 92:8, flow rate = 0.50 mL/min, λ = 220 nm): t_1 = 34.9 min (minor), t_2 = 40.9 min (major).

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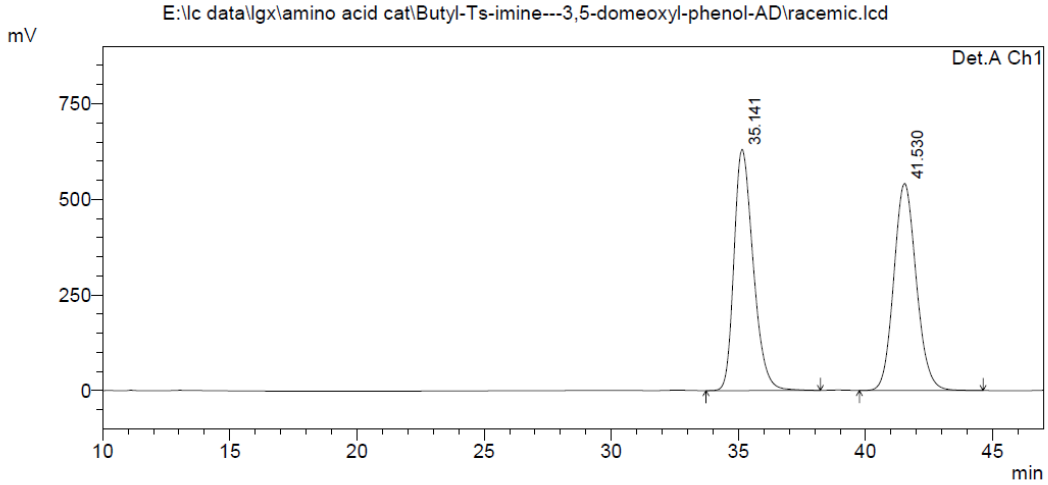

1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	35.141	33166291	630532	49.931	53.805
2	41.530	33257904	541348	50.069	46.195
Total		66424195	1171880	100.000	100.000

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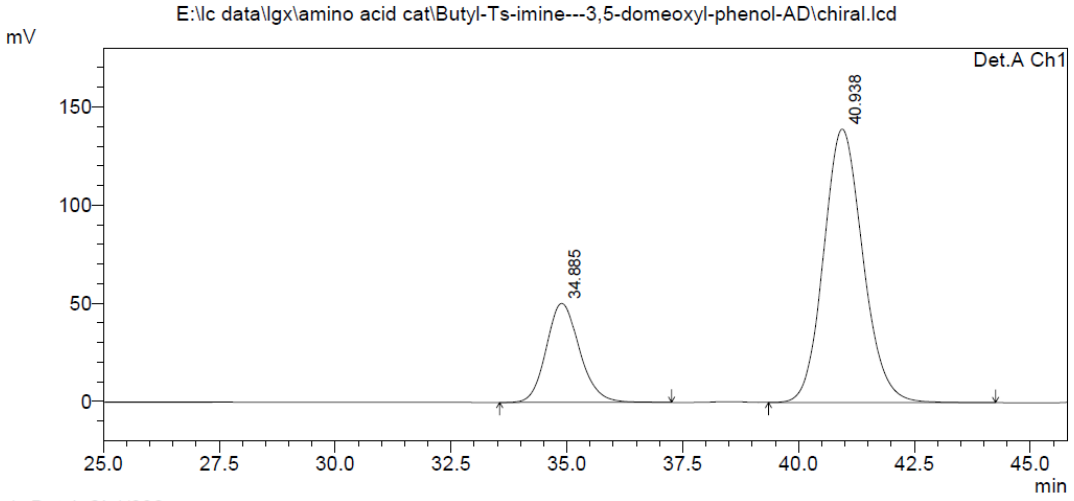

1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.885	2529230	50433	23.557	26.588
2	40.938	8207432	139252	76.443	73.412
Total		10736663	189685	100.000	100.000

Preparation of *N*-((2-hydroxy-4-methoxyphenyl)(phenyl)methyl)-4-methylbenzenesulfonamide (5a) (Table 3, entry 15)

To a dry 5 mL flask was added catalyst **1k** (9 mg, 0.02 mmol) and *N*-benzylidene-4-methylbenzenesulfonamide (52 mg, 0.2 mmol). Then 1.0 mL of dried toluene and 4 Å M.S. (20 mg) were added into the flask and the flask was cooled to 0 ^{o}C under stirring with a magnetic bar. After stirring for 30 minutes, the solution of 3-methoxyphenol (12 mg, 0.10 mmol) in 0.2 mL of toluene was added into the flask with a syringe dropwisely within 15 minutes. The reaction was stirred at 0 ^{o}C for 96 hours. The mixture was subjected to column chromatography on silica gel with petrol ether/ethyl acetate (4:1) as the eluent to give the desired product **5a** as a white solid (22 mg, 58%). m.p. 111−112 ^{o}C; $[\alpha]_D^{25}$ = +10.4 (*c* = 0.5 in $CHCl_3$) for 66% ee; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.4 Hz, 2H), 7.21−7.15 (m, 5H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.71 (d, *J* = 8.0 Hz, 1H), 6.29−6.26 (m, 2H), 6.00 (br s, 1H), 5.69 (d, *J* = 6.4 Hz, 1H), 5.60 (d, *J* = 5.2 Hz, 1H), 3.70 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.5, 154.3, 143.2, 139.8, 136.8, 130.2, 129.2, 128.3, 127.3, 127.1, 126.9, 118.5, 106.0, 102.6, 58.4, 55.3, 21.4; HRMS (ESI) for $C_{21}H_{21}NO_4S$: calcd $[M + H]^+$ *m*/*z* 384.1264, found 384.1270; HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 85:15, flow rate = 0.50 mL/min, λ = 210 nm): t_1 = 62.5 min (major), t_2 = 69.1 min (minor).

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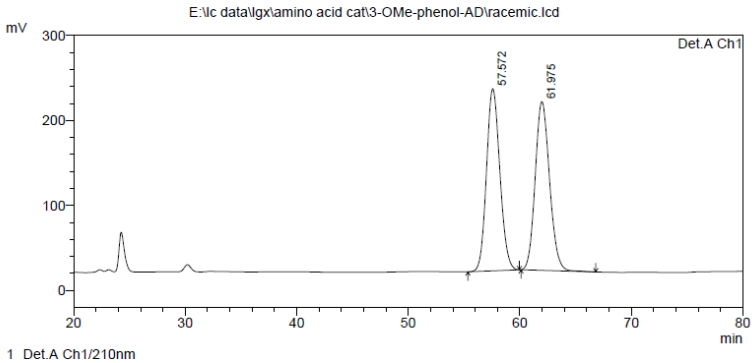


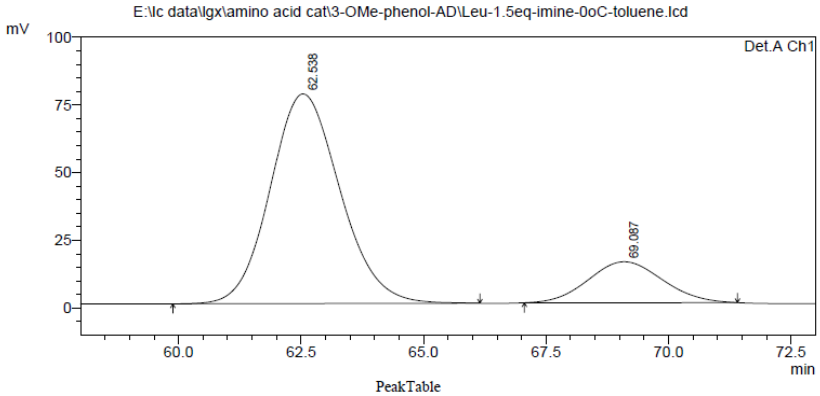
1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	57.572	17866597	214503	50.115	51.929
2	61.975	17784514	198567	49.885	48.071
Total		35651111	413070	100.000	100.000

<Chromatogram>



PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	62.538	7687559	77461	82.761	83.642
2	69.087	1601328	15149	17.239	16.358
Total		9288887	92610	100.000	100.000

Preparation of *N*-((4-tert-butyl-2-hydroxyphenyl)(phenyl)methyl)-4-methylbenzenesulfonamide (5b) (Table 3, entry 16)

To a dry 5 mL flask was added catalyst **1k** (27 mg, 0.06 mmol), 3-*tert*-butylphenol (90 mg, 0.60 mmol), *N*-benzylidene-4-methylbenzenesulfonamide (78 mg, 0.30 mmol). Then 0.5 mL of dried toluene was added into the flask. The reaction was stirred for 48 hours at 10 ^{o}C. The mixture was subjected to column chromatography on silica gel with petrol-ether/ethyl acetate (4:1) as the eluent to give the desired product **5b** as a white solid (104 mg, 85%). m.p. 126−129 ^{o}C; $[\alpha]_D^{25}$ = −0.9 (*c* = 0.5 in $CHCl_3$) for 28% ee; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.0 Hz, 2H), 7.25−7.11 (m, 5H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.71−6.65 (m, 3H), 6.15 (s, 1H), 6.11 (d, *J* = 9.2 Hz, 1H), 5.58 (d, *J* = 9.2 Hz, 1H), 2.27 (s, 3H), 1.19 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.7, 152.6, 142.8, 139.9, 136.8, 129.11, 129.07, 128.2, 127.2, 127.0, 126.9, 122.4, 117.4, 113.6, 59.1, 34.3, 31.1, 21.4. HRMS (ESI) for $C_{24}H_{27}NO_3S$: calcd $[M + H]^+$ *m*/*z* 410.1784, found 410.1786;

HPLC analysis (Daicel Chiralpak AD-H, hexane/2-propanol = 95:5, flow rate = 0.50 mL/min, λ = 220 nm): t_1 = 34.6 min (minor), t_2 = 43.0 min (major).

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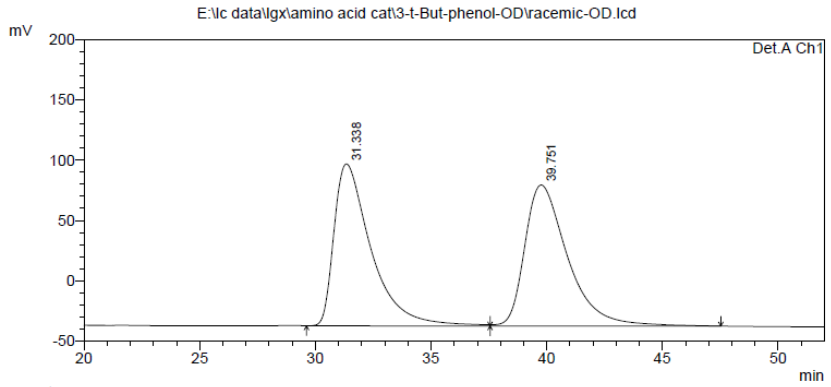

1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.338	14980010	134126	49.838	53.436
2	39.751	15077625	116875	50.162	46.564
Total		30057634	251001	100.000	100.000

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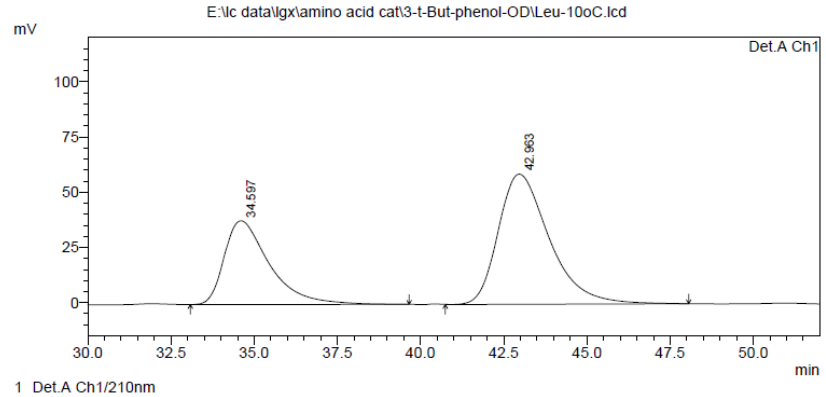

1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.597	3574841	37920	36.172	39.142
2	42.963	6308125	58958	63.828	60.858
Total		9882966	96878	100.000	100.000

Preparation of *N*-((1H-indol-3-yl)(phenyl)methyl)-4-methylbenzenesulfonamide

To a dry 5 mL flask was added catalyst **1k** (41 mg, 0.09 mmol), indole (211 mg, 1.8 mmol), *N*-benzylidene-4-methylbenzenesulfonamide (210 mg, 0.90 mmol). Then 0.6 mL of dried toluene was added into the flask and the flask was heated to 50 ^{o}C (oil bath). The reaction was stirred for 48 hours. The mixture was subjected to column chromatography on silica gel with petrol ether/ethyl acetate (4:1) as the eluent to give the desired product as a white solid (301 mg, 89%). m.p. 73−75 ^{o}C; $[\alpha]_D^{25}$ = −21.2 (*c* = 1.0 in $CHCl_3$) for 90% ee; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06 (s, 1H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.7 Hz, 2H), 7.19−7.08 (m, 6H), 7.03 (d, *J* = 8.1 Hz, 2H), 6.98−6.93 (m, 1H), 6.57 (d, *J* = 1.5 Hz, 1H), 5.81 (d, *J* = 7.2 Hz, 1H), 5.33 (br s, 1H), 2.32 (s,

3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.9, 140.2, 137.3, 136.5, 129.2, 128.2, 127.2, 127.1, 127.0, 125.3, 123.9, 122.3, 119.7, 119.1, 116.1, 111.3, 55.0, 21.4; HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 70:30, flow rate = 0.60 mL/min, λ = 254 nm): t_1 = 15.2 min (minor), t_2 = 25.5 min (major).

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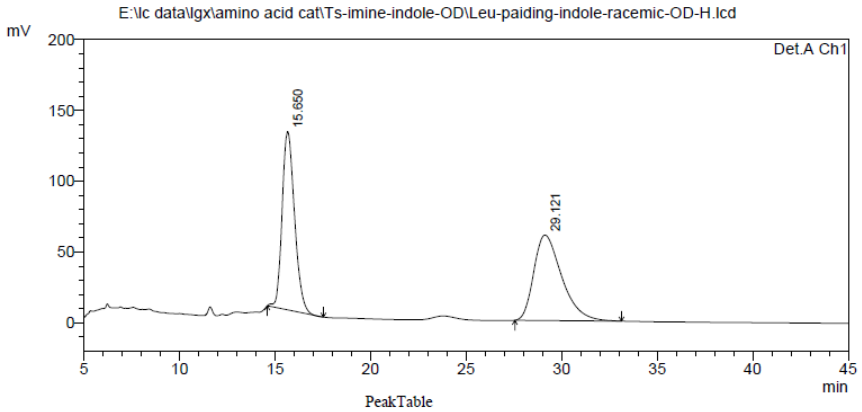
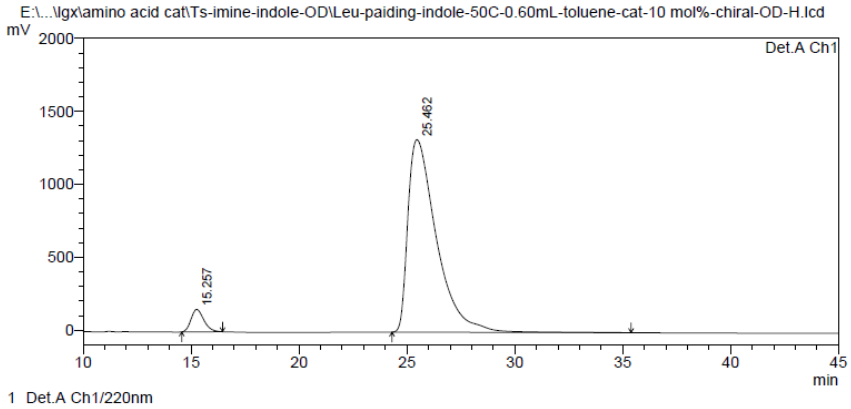


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.650	5695896	126073	48.128	67.625
2	29.121	6138897	60358	51.872	32.375
Total		11834792	186431	100.000	100.000

<Chromatogram>



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.257	6340633	153811	4.967	10.440
2	25.462	121315692	1319439	95.033	89.560
Total		127656325	1473250	100.000	100.000

General procedure for the preparation of *N*-Ts-aldimines:

Method A: To a 200 mL flask was added 80 mL of 1,2-dichloroethane, followed by 10 mmol of aldehyde and 10 mmol of 4-methylbenzenesulfonamide. The reaction mixture was heated to reflux when 1.2 mL of $TiCl_4$ was added into the flask dropwisely. Triethylamine (20 mmol) was added dropwisely at last. The reaction mixture was stirred at refluxing temperature for 10 minutes and then was cooled down to room temperature. The reaction mixture was diluted with 100 mL of

CH_2Cl_2. The organic phase was washed with diluted HCl (0.2 N, 2 x 20 mL), saturated $NaHCO_3$, water and brine, then dried over anhydrous Na_2SO_4. The organic solvent was evaporated in *vacuo* and the crude product was recrystallized in EtOAc/P.E. or benzene/P.E. to give pure aldimine as a solid.

Method B: To a 200 mL flask was added 80 mL of 1,2-dichloroethane, followed by 10 mmol of aldehyde and 10 mmol of 4-methylbenzenesulfonamide. The reaction mixture was heated when 1.2 mL of $TiCl_4$ was added into the flask dropwisely. Triethylamine (40 mmol) was added dropwisely at last. The reaction mixture was stirred at refluxing for 10 minutes and then was cooled to room temperature. The reaction mixture was diluted with 100 mL of CH_2Cl_2. The organic phase was washed with diluted HCl (0.2 N, 1 x 20 mL), saturated $NaHCO_3$, water and brine, then dried over anhydrous Na_2SO_4. Evaporate the organic solvent in vacuo. The crude product was recrystallized in EtOAc/P.E. or benzene/P.E. to give pure aldimine as a solid.

N-Benzylidene-4-methylbenzenesulfonamide (**3a**)[10]

Method A, yield: 50%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.03 (s, 1H), 7.93−7.88 (m, 4H), 7.63−7.58 (m, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.0, 144.5, 135.0, 134.9, 132.2, 131.2, 129.7, 129.0, 128.0, 21.5.

N-(3,5-Dimethylbenzylidene)-4-methylbenzenesulfonamide (**3b)**

Method A, yield: 52%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.96 (s, 1H), 7.88 (d, *J* = 8.0 Hz, 2H), 7.54 (s, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.24 (s, 1H), 2.44 (s, 3H), 2.35 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 144.4, 138.8, 136.7, 135.1, 132.2, 129.7, 129.0, 127.9, 21.5, 20.9; HRMS calcd ($M + H^+$) for $C_{16}H_{17}NO_2S$, 288.1053; found 288.1049.

N-(4-tert-Butylbenzylidene)-4-methylbenzenesulfonamide (**3c**)[11]

Method A, yield: 52%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.01 (s, 1H), 7.89−7.85 (m, 4H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 2.43 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 159.2, 144.3, 135.4, 131.2, 129.7, 127.9, 126.1, 35.4, 30.9, 21.5.

4-Methyl-*N*-(3-phenoxybenzylidene)benzenesulfonamide (**3d)**[12]

Method A, yield: 51%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.96 (s, 1H), 7.87 (d, *J* = 8.0 Hz, 2H), 7.63 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.57−7.51 (m, 1H), 7.44 (t, *J* = 8.0 Hz, 1H), 7.39−7.37 (m, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.28−7.23 (m, 1H), 7.20−7.13 (m, 1H), 7.00 (m, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, CDCl3): δ 169.4, 158.0, 156.0, 144.6, 134.8, 133.9, 130.4, 130.0, 129.7, 128.0, 126.2, 124.9, 124.1, 119.7, 119.2, 21.5.

N-(4-Fluorobenzylidene)-4-methylbenzenesulfonamide (**3e**)[13]

Method B, yield: 51%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.00 (s, 1H), 7.99−7.92 (m, 2H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 7.21−7.14 (m, 2H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.5, 166.8 (d, *J* = 257.1 Hz), 144.6, 135.0, 133.7 (d, *J* = 9.7 Hz), 129.8, 128.7 (d, *J* = 2.6 Hz), 128.0, 116.6 (d, *J* = 22.3 Hz), 21.6.

N-(3-Fluorobenzylidene)-4-methylbenzenesulfonamide (**3f**)[14]

Method B, yield: 36%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.00 (s, 1H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.69−7.63 (m, 2H), 7.51−7.44 (m, 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.30−7.27 (m, 1H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.6 (d, *J* = 2.3 Hz), 162.7 (d, *J* = 247.7 Hz), 144.8, 134.5 (d, *J* = 14.1 Hz), 130.8 (d, *J* = 7.8 Hz), 129.8, 128.1, 127.8 (d, *J* = 2.2 Hz), 121.8 (d, *J* = 21.5 Hz), 116.4 (d, *J* = 22.4 Hz), 21.5.

N-(2-Fluorobenzylidene)-4-methylbenzenesulfonamide (**3g**)[15]

Method B, yield: 58%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.36 (s, 1H), 8.10−8.06 (m, 1H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.64−7.58 (m, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.25−7.22 (m, 1H), 7.19−7.15 (m, 1H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.1 (d, *J* = 258.1 Hz), 163.4 (d, *J* = 1.1 Hz), 144.7, 137.0 (d, *J* = 9.2 Hz), 134.6, 129.7, 129.1, 128.0, 124.7 (d, *J* = 3.3 Hz), 120.2 (d, *J* = 8.7 Hz), 116.2 (d, *J* = 20.5 Hz), 21.5.

4-Methyl-*N*-(4-(trifluoromethyl)benzylidene)benzenesulfonamide (**3h**)[16]

Method B, yield: 54%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.08 (s, 1H), 8.05 (d, *J* = 8.1 Hz, 2H), 7.90 (d, *J* = 8.1 Hz, 2H), 7.74 (d, *J* = 8.1 Hz, 2H), 7.37 (d, *J* = 8.1 Hz, 2H), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.4, 145.0, 135.7 (q, *J* = 32.8 Hz), 135.3, 134.4, 131.3, 129.9, 128.2,

126.0 (q, J = 3.8 Hz), 123.3 (q, J = 271.3 Hz), 21.6.

Methyl 4-((tosylimino)methyl)benzoate (**3i**)[17]

This compound was prepared according to the reported literature. Yield: 35%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.07 (s, 1H), 8.18 (d, J = 8.4 Hz, 2H), 7.99 (d, J = 8.4 Hz, 2H), 7.90 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 3.95 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.8, 165.8, 144.9, 135.9, 135.3, 134.6, 131.0, 130.1, 129.9, 128.2, 52.6, 21.6.

N-(Tosylmethylene)naphthalen-1-amine (**3j**)[18]

Method A, yield: 66%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.59 (s, 1H), 8.97 (d, J = 8.8 Hz, 1H), 8.12 (d, J = 7.2 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.4 Hz, 2H), 7.89 (d, J = 8.0 Hz, 1H), 7.67−7.63 (m, 1H), 7.59−7.53 (m, 2H), 7.34 (d, J = 8.0 Hz, 2H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 144.5, 136.1, 135.4, 135.1, 133.7, 131.7, 129.8, 129.0, 128.8, 128.0, 127.5, 126.9, 125.0, 124.2, 21.6.

4-Methyl-*N*-(naphthalen-2-ylmethylene)benzenesulfonamide (**3k**)[19]

Method A, yield: 68%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.16 (s, 1H), 8.30 (s, 1H), 8.02 (dd, J = 8.7, 1.5 Hz, 1H), 7.94−7.91 (m, 3H), 7.85 (d, J = 8.7 Hz, 2H), 7.62 (td, J = 7.4, 1.2 Hz, 1H), 7.58−7.53 (m, 1H), 7.34 (d, J = 7.8 Hz, 2H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.0, 144.5, 136.4, 136.1, 135.2, 132.5, 130.0, 129.8, 129.4, 129.1, 128.04, 127.98, 127.2, 124.0, 21.6.

.

N-(Furan-2-ylmethylene)-4-methylbenzenesulfonamide (**3l**)[20]

Method B, yield: 36%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.82 (s, 1H), 7.88 (d, J = 8.0 Hz, 2H), 7.75 (s, 1H), 7.34 (d, J = 7.2 Hz, 2H), 7.33 (s, 1H), 6.65 (dd, J =2.0, 1.2 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.5, 149.7, 148.9, 144.5, 135.0, 129.7, 127.9, 124.9, 113.7, 21.5.

N-(Cyclohexylmethylene)-4-methylbenzenesulfonamide (**3m**)[21]

This compound was prepared according to the reported literature. Yield: 38%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.48 (d, J = 4.5 Hz, 1H), 7.80 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 2.44 (br s, 4H), 1.89−1.85 (m, 2H), 1.80−1.75 (m, 2H), 1.69−1.65 (m, 1H), 1.38−1.16 (m, 5H); ^{13}C NMR (75

MHz, $CDCl_3$): δ 181.0, 144.5, 134.8, 129.7, 128.0, 43.6, 28.3, 25.5, 25.0, 21.6.

4-Methyl-*N*-pentylidenebenzenesulfonamide (**3n**)[21]

This compound was prepared according to the reported literature. Yield: 89%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.60 (t, *J* = 4.5 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 2.54−2.48 (m, 2H), 1.65−1.55 (m, 2H), 1.41−1.29 (m, 2H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.5, 144.5, 134.3, 129.6, 127.8, 35.3, 26.3, 21.9, 21.3, 13.4.

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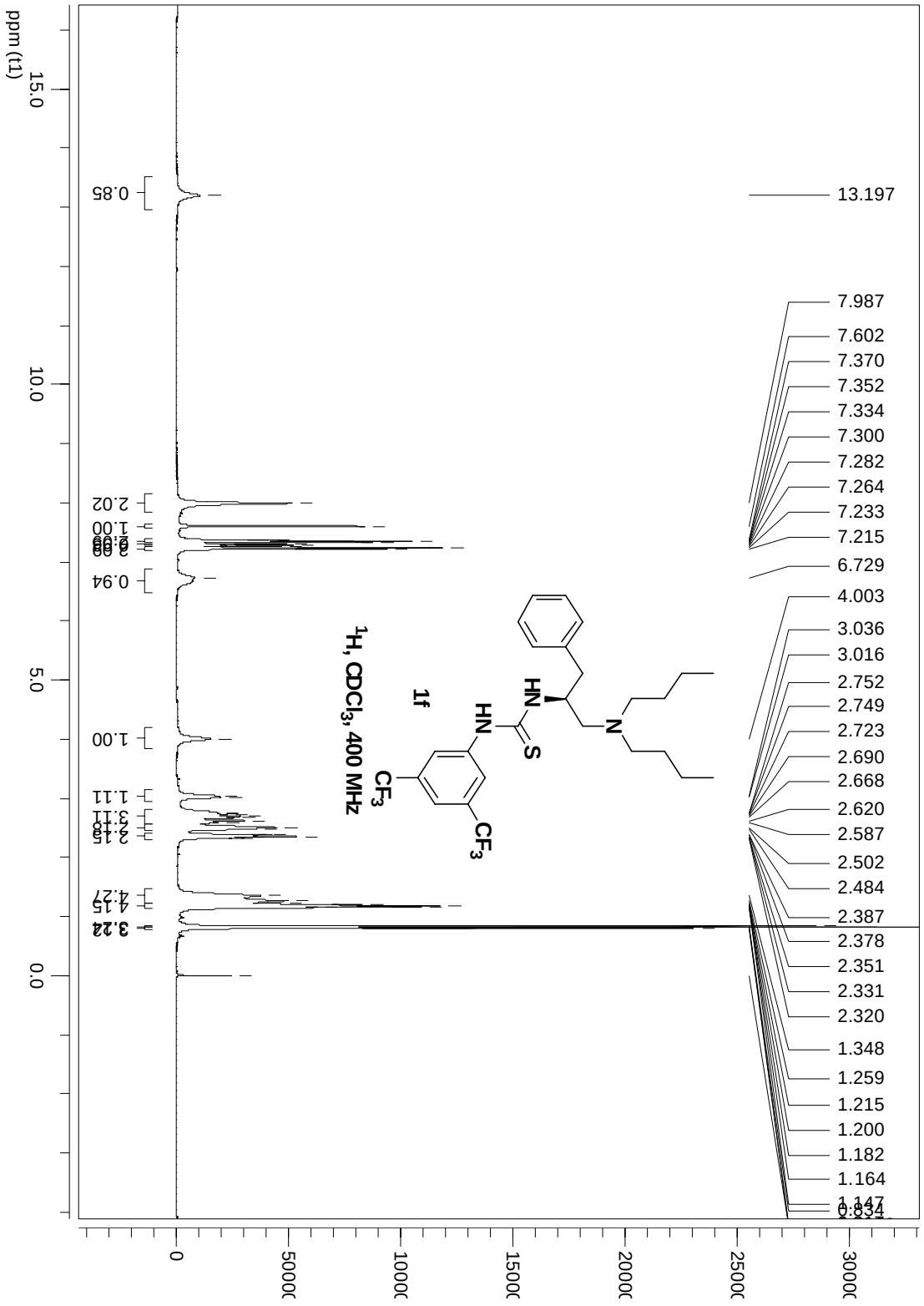
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1.00
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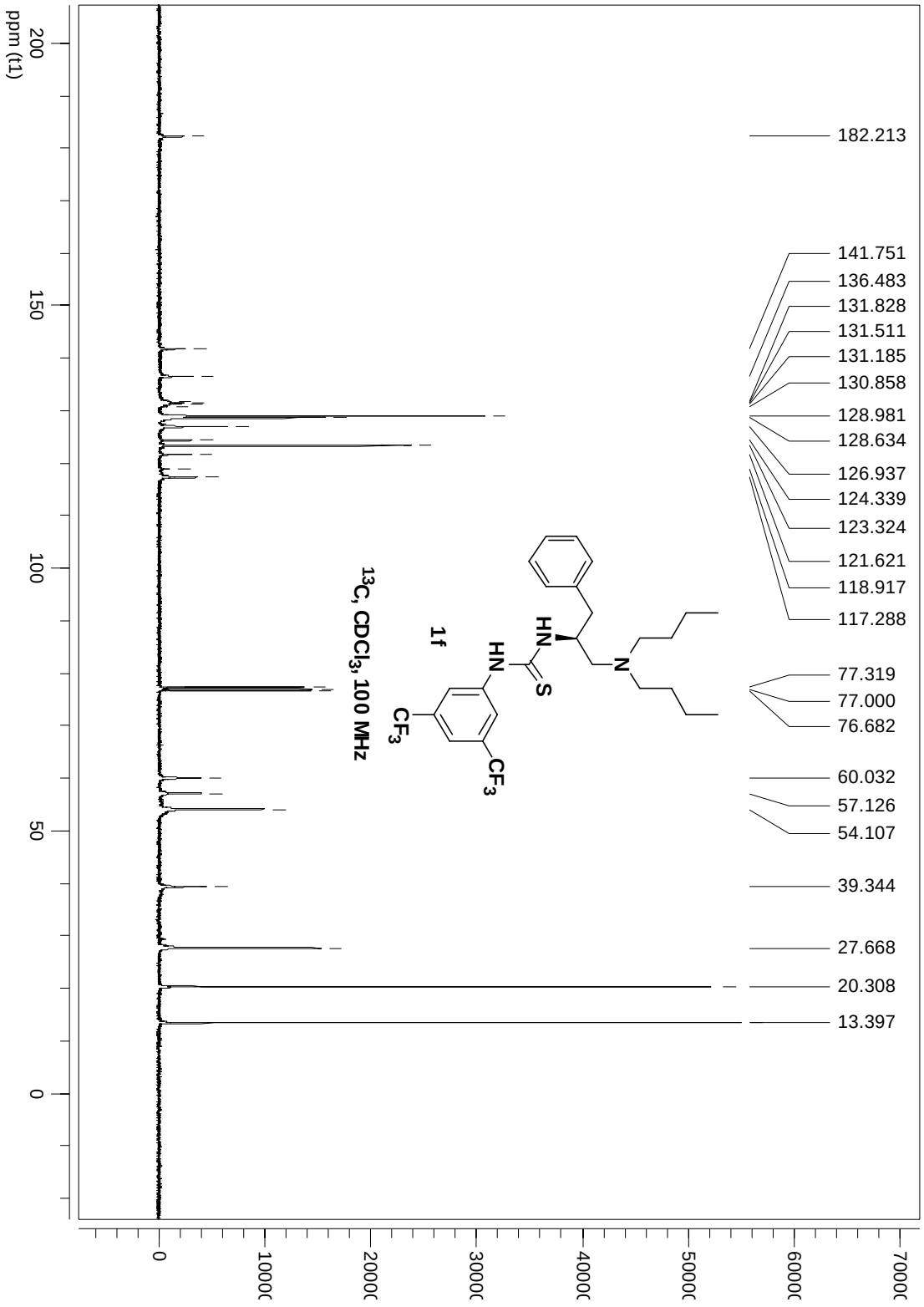
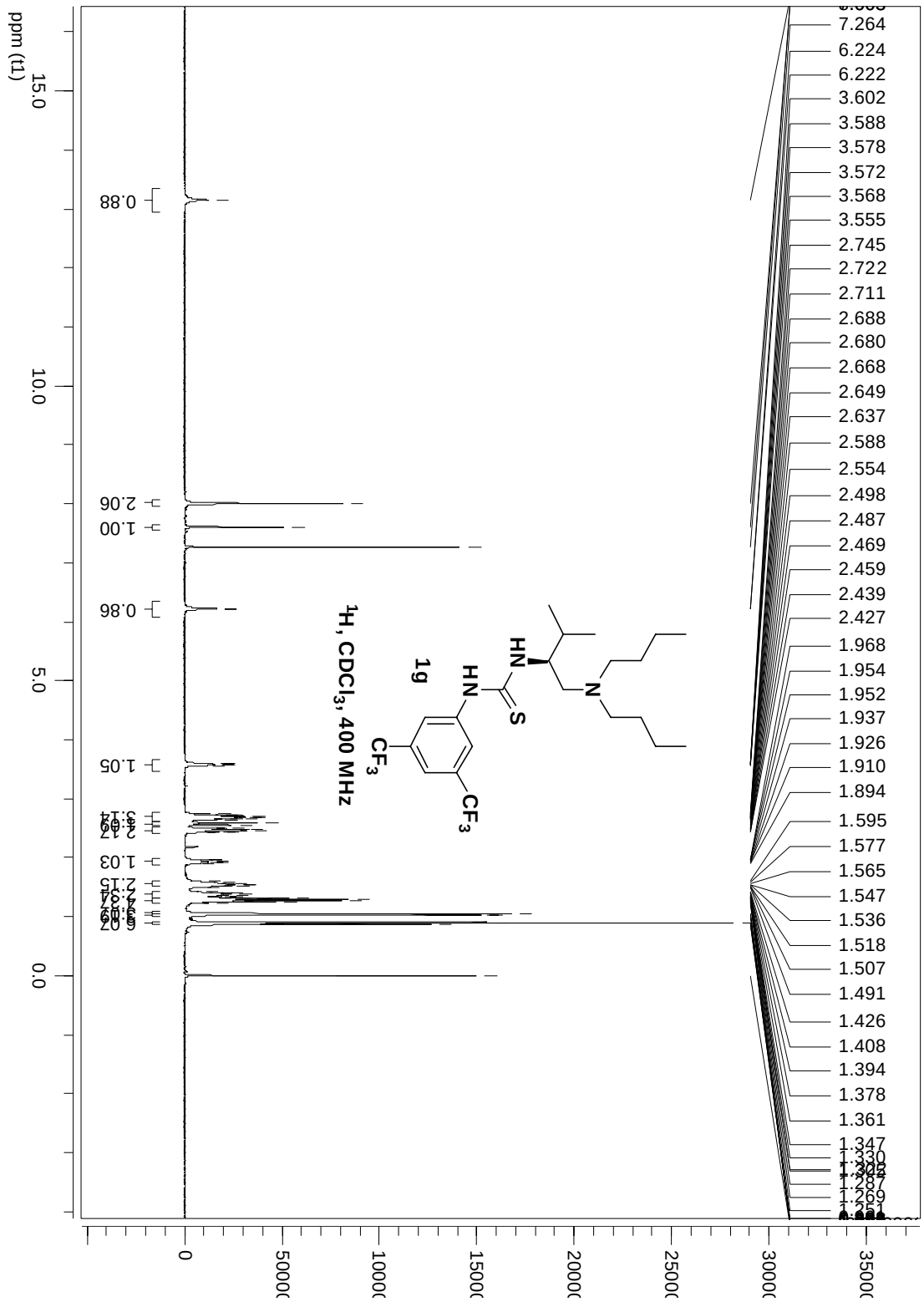
3.11
4.27
4.15
3.24
13.197
7.987
7.602
7.370
7.352
7.334
7.300
7.282
7.264
7.233
7.215
6.729
4.003
3.036
3.016
2.752
2.749
2.723
2.690
2.668
2.620
2.587
2.502
2.484
2.387
2.378
2.351
2.331
2.320
1.348
1.259
1.215
1.200
1.182
1.164
1.147
0.834
0
5000
10000
15000
20000
25000
30000
^{1}H, CDCl$_3$, 400 MHz
1f
HN
HN
S
N
CF$_3$
CF$_3$

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1.05
2.17
1.03
2.15
^{1}H, CDCl$_3$, 400 MHz
1g
HN
S
HN
N
CF$_3$
CF$_3$
7.264
6.224
6.222
3.602
3.588
3.578
3.572
3.568
3.555
2.745
2.722
2.711
2.688
2.680
2.668
2.649
2.637
2.588
2.554
2.498
2.487
2.469
2.459
2.439
2.427
1.968
1.954
1.952
1.937
1.926
1.910
1.894
1.595
1.577
1.565
1.547
1.536
1.518
1.507
1.491
1.426
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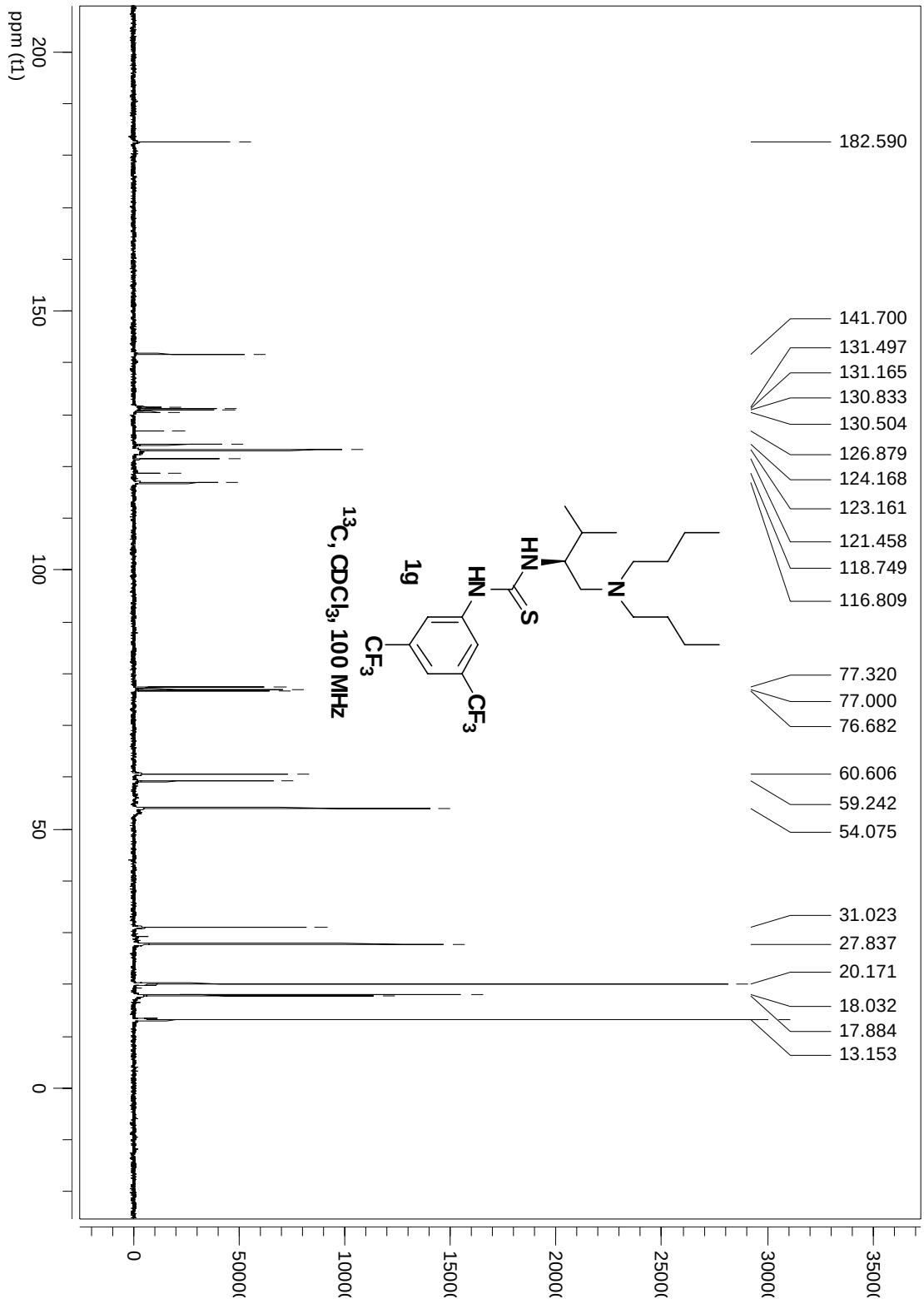
25000
30000
35000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130.504
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123.161
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116.809
77.320
77.000
76.682
60.606
59.242
54.075
31.023
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1g
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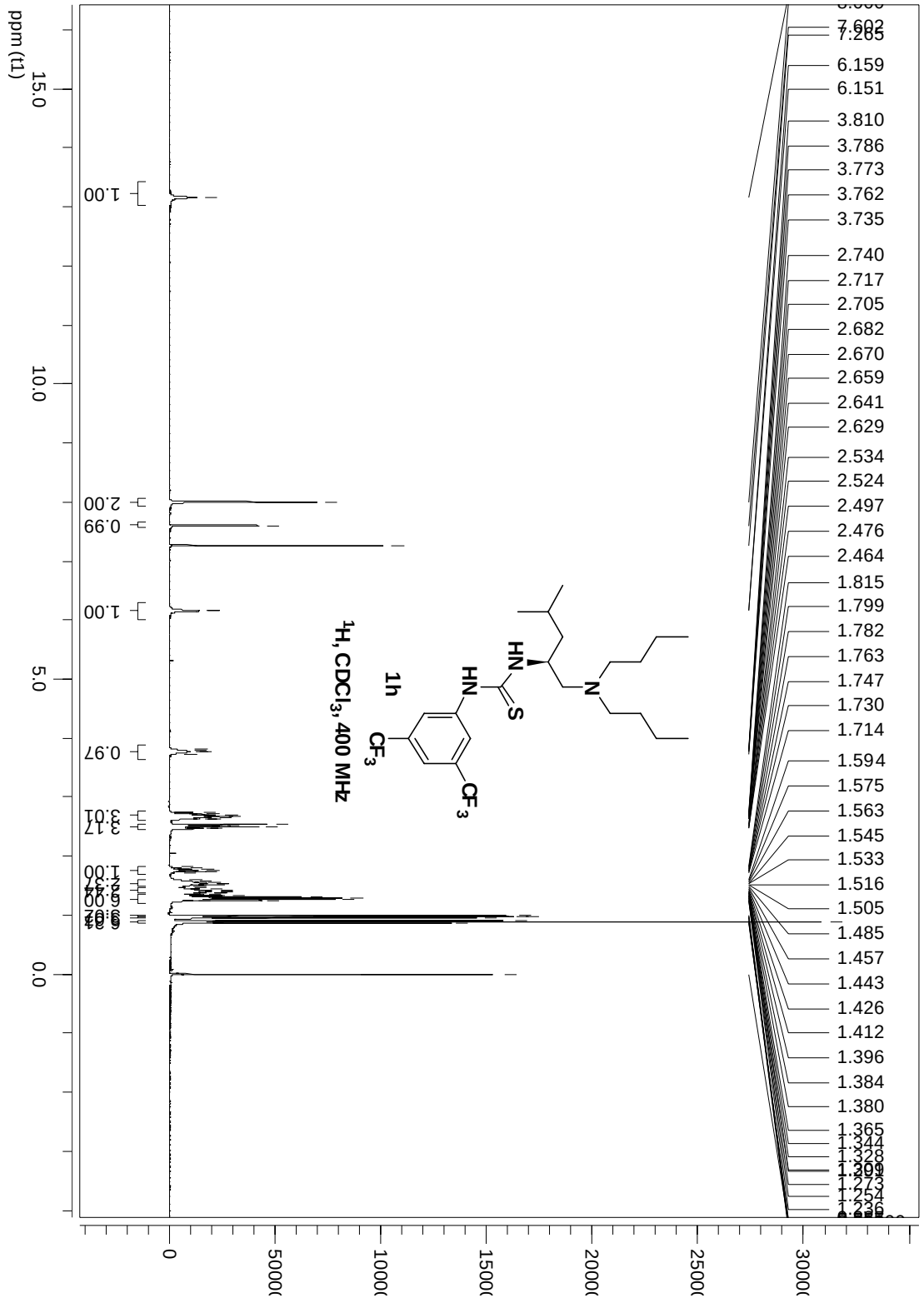
HN
S
N
CF3
CF3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HN
S
N
CF$_3$
CF$_3$
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5.0
0.0
1.00
2.00
0.99
1.00
0.97
3.01
3.17
1.00
6.00
7.602
7.265
6.159
6.151
3.810
3.786
3.773
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2.717
2.705
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2.641
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2.476
2.464
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1.799
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1.714
1.594
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1.563
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1.516
1.505
1.485
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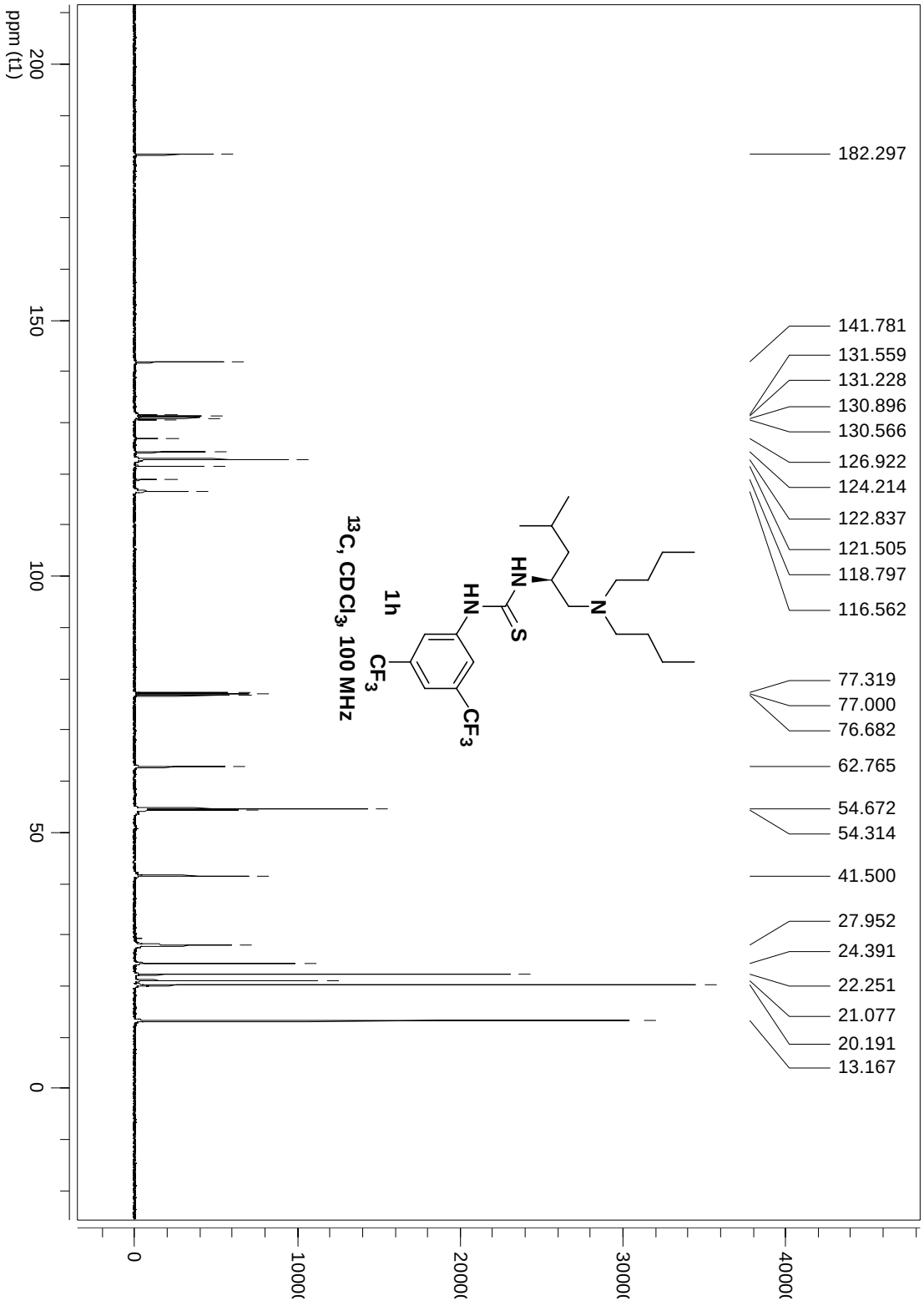
30000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124.214
122.837
121.505
118.797
116.562
77.319
77.000
76.682
62.765
54.672
54.314
41.500
27.952
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21.077
20.191
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13C, CDCl3, 100 MHz
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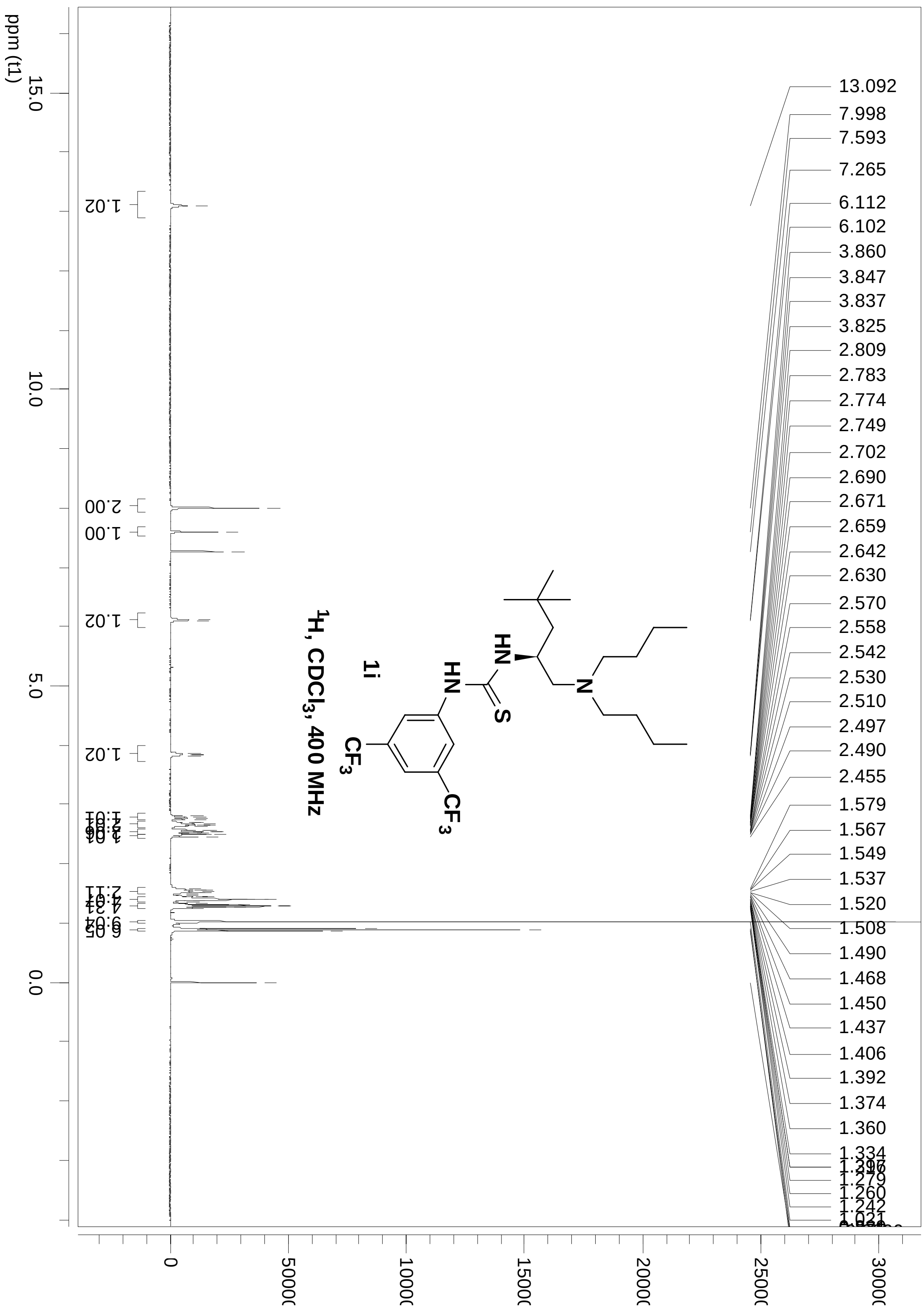
CF3
HN
HN
S
N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2.809
2.783
2.774
2.749
2.702
2.690
2.671
2.659
2.642
2.630
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2.558
2.542
2.530
2.510
2.497
2.490
2.455
1.579
1.567
1.549
1.537
1.520
1.508
1.490
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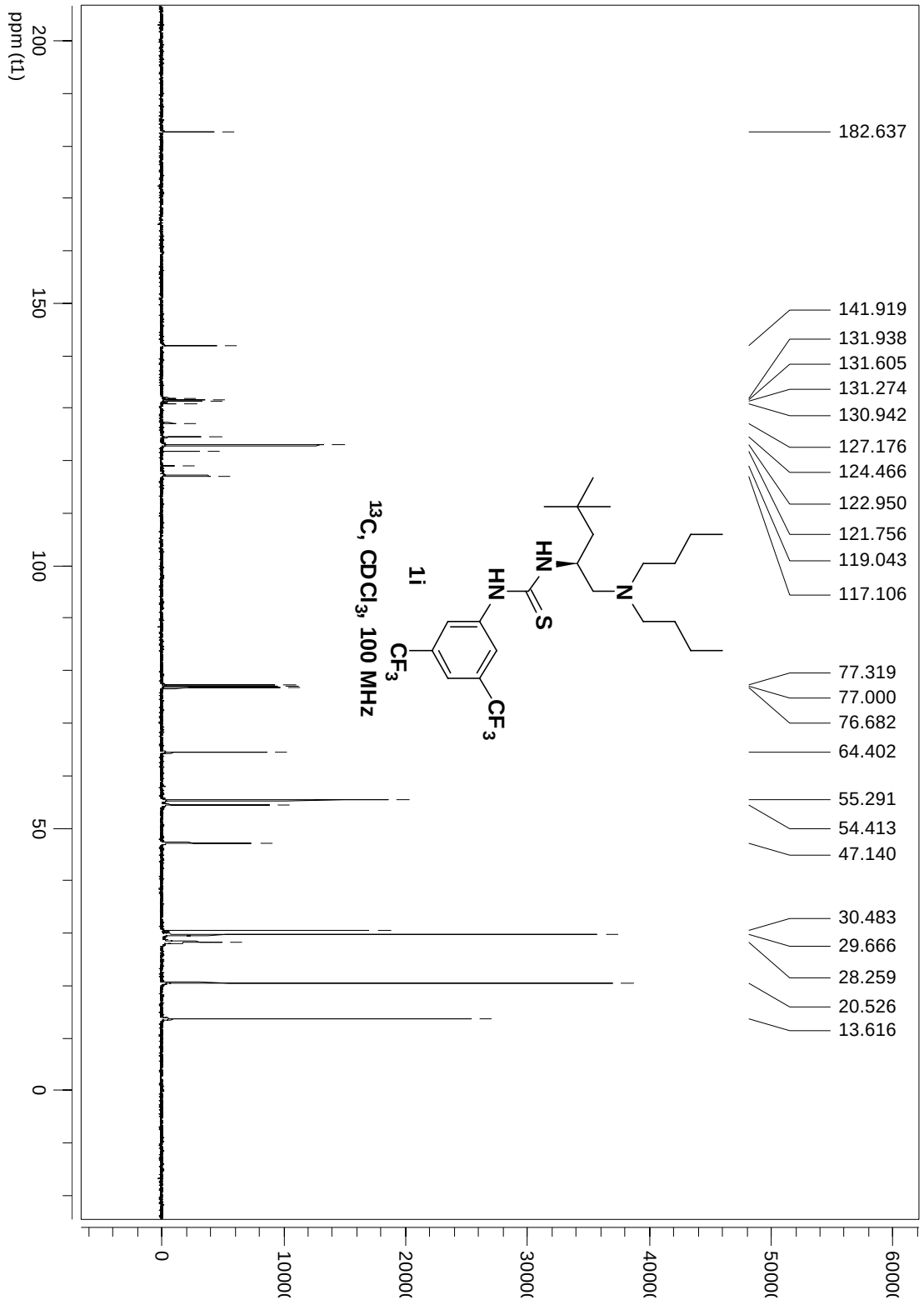
1.242
ppm (t1)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60000
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130.942
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121.756
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77.319
77.000
76.682
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47.140
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^{13}C, CDCl$_3$, 100 MHz
1i
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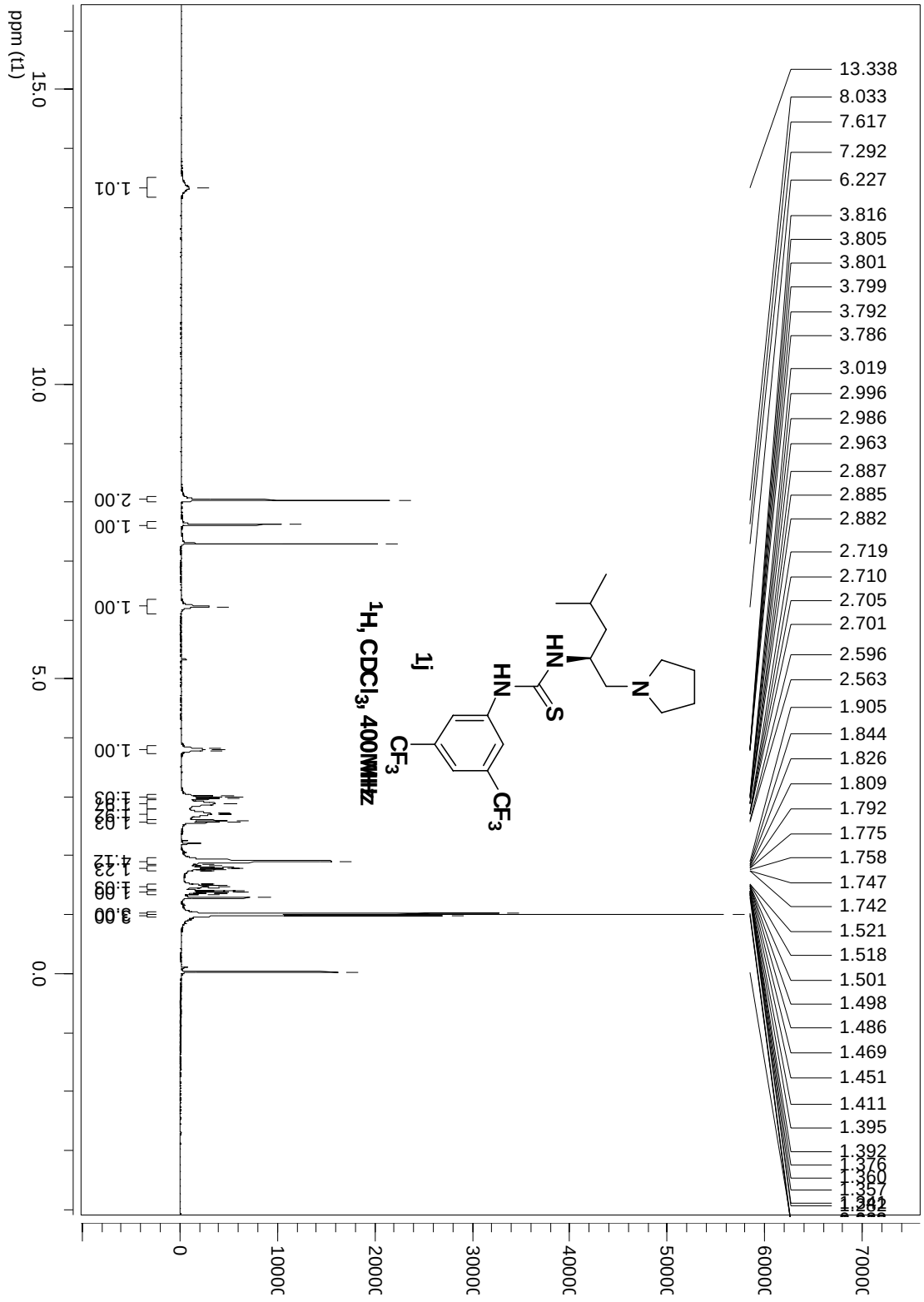
HN
S
N
CF$_3$
CF$_3$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3.816
3.805
3.801
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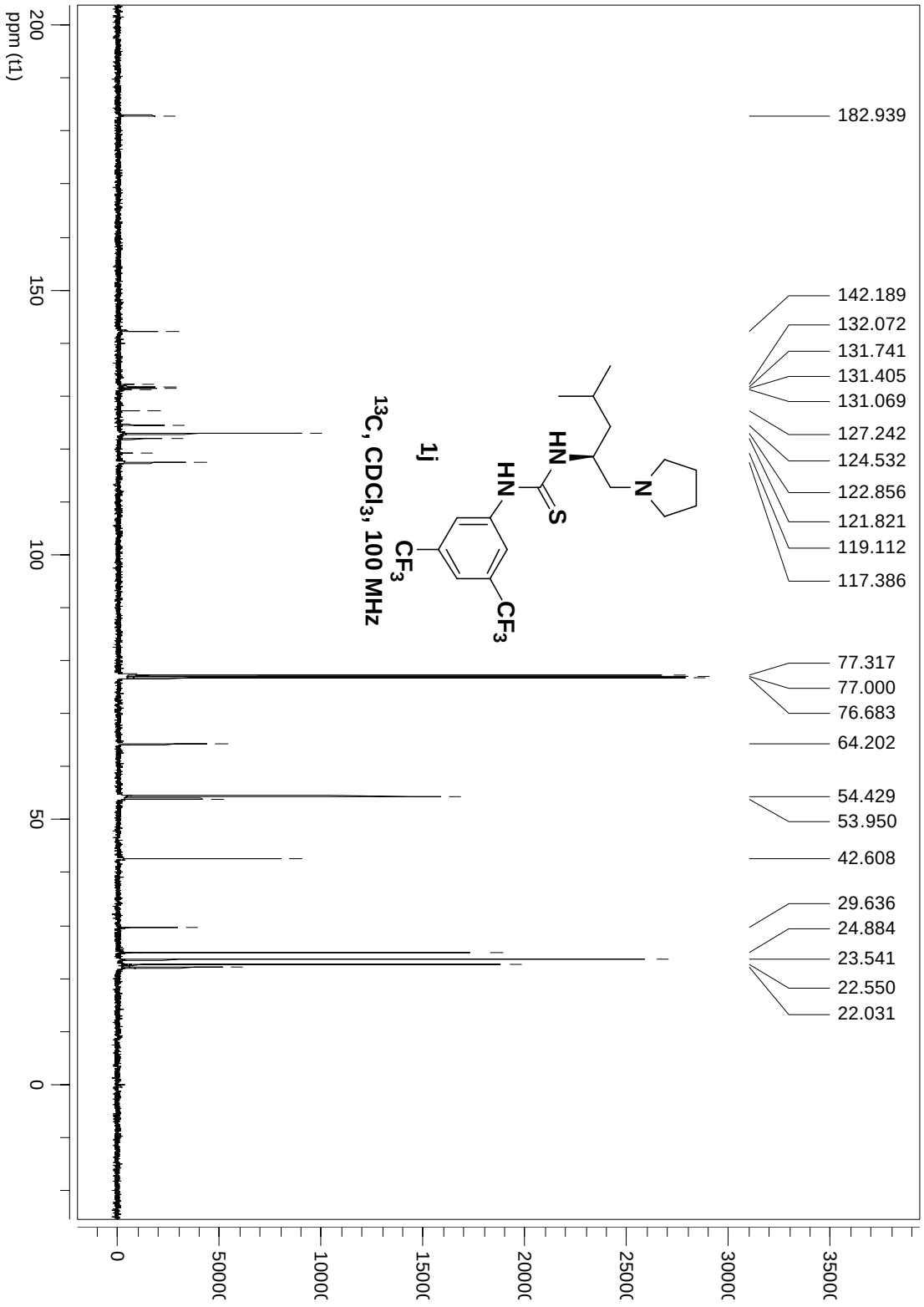
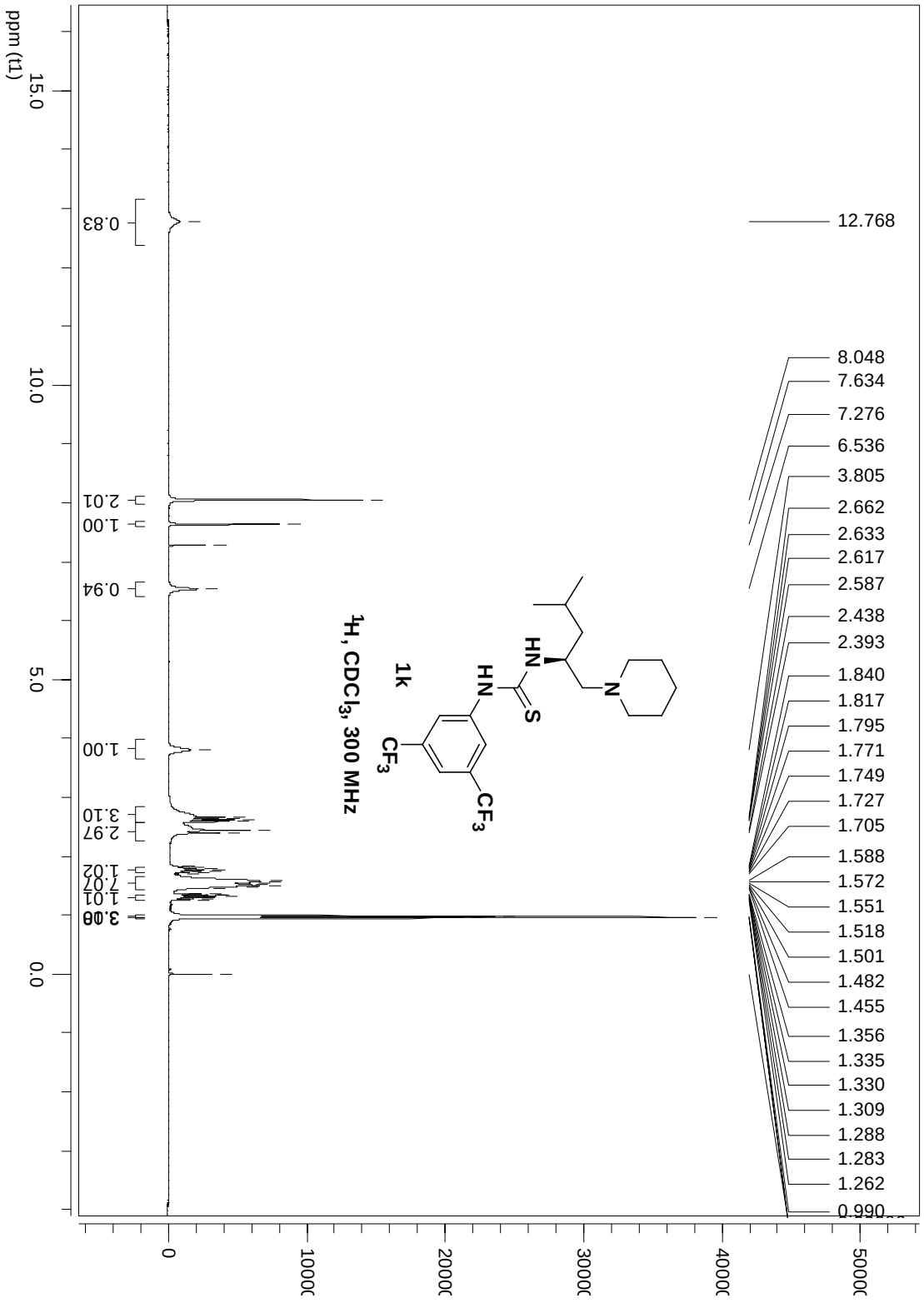
N
CF3
CF3

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1.01
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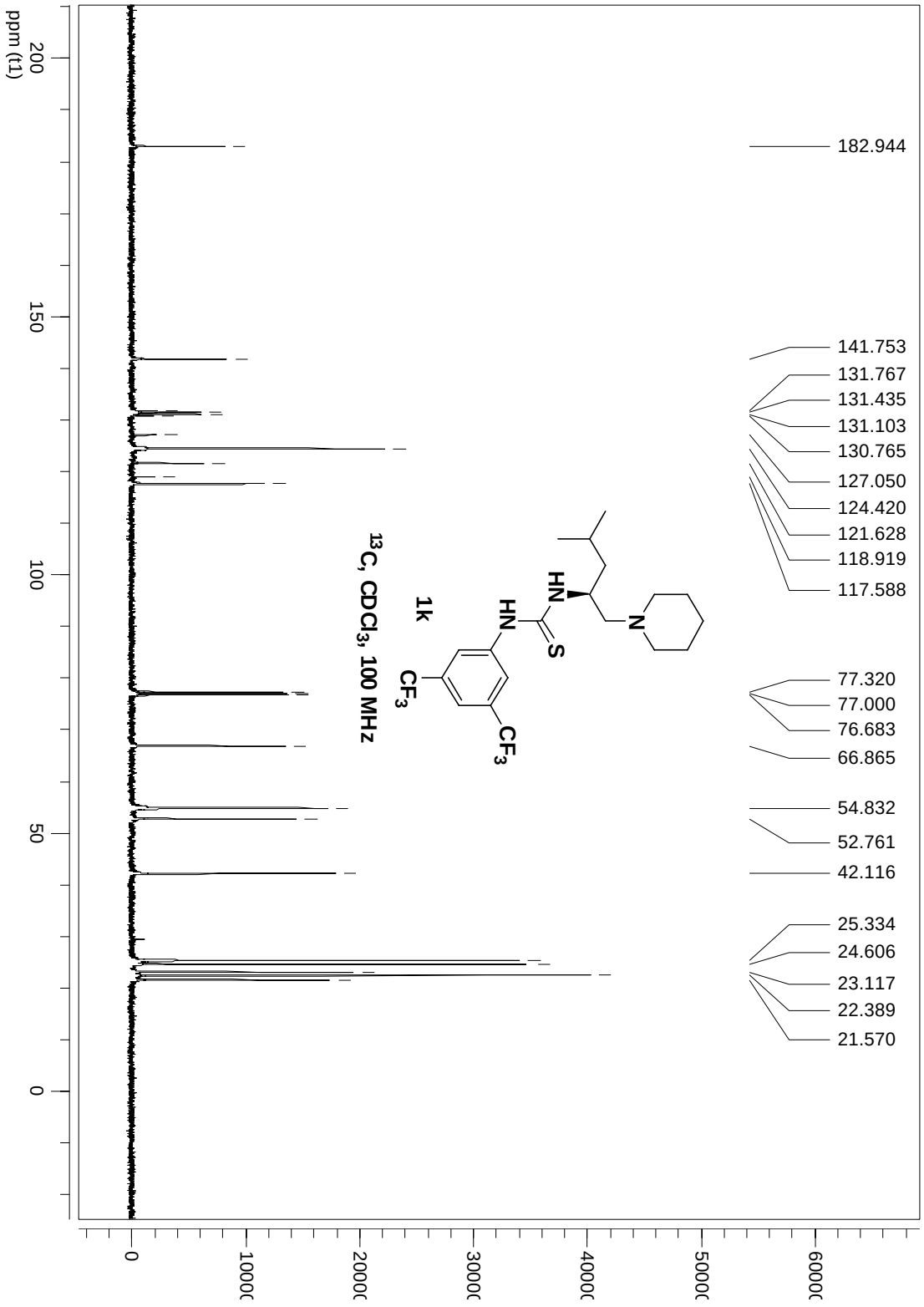
CF3
CF3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77.000
76.683
66.865
54.832
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42.116
25.334
24.606
23.117
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21.570
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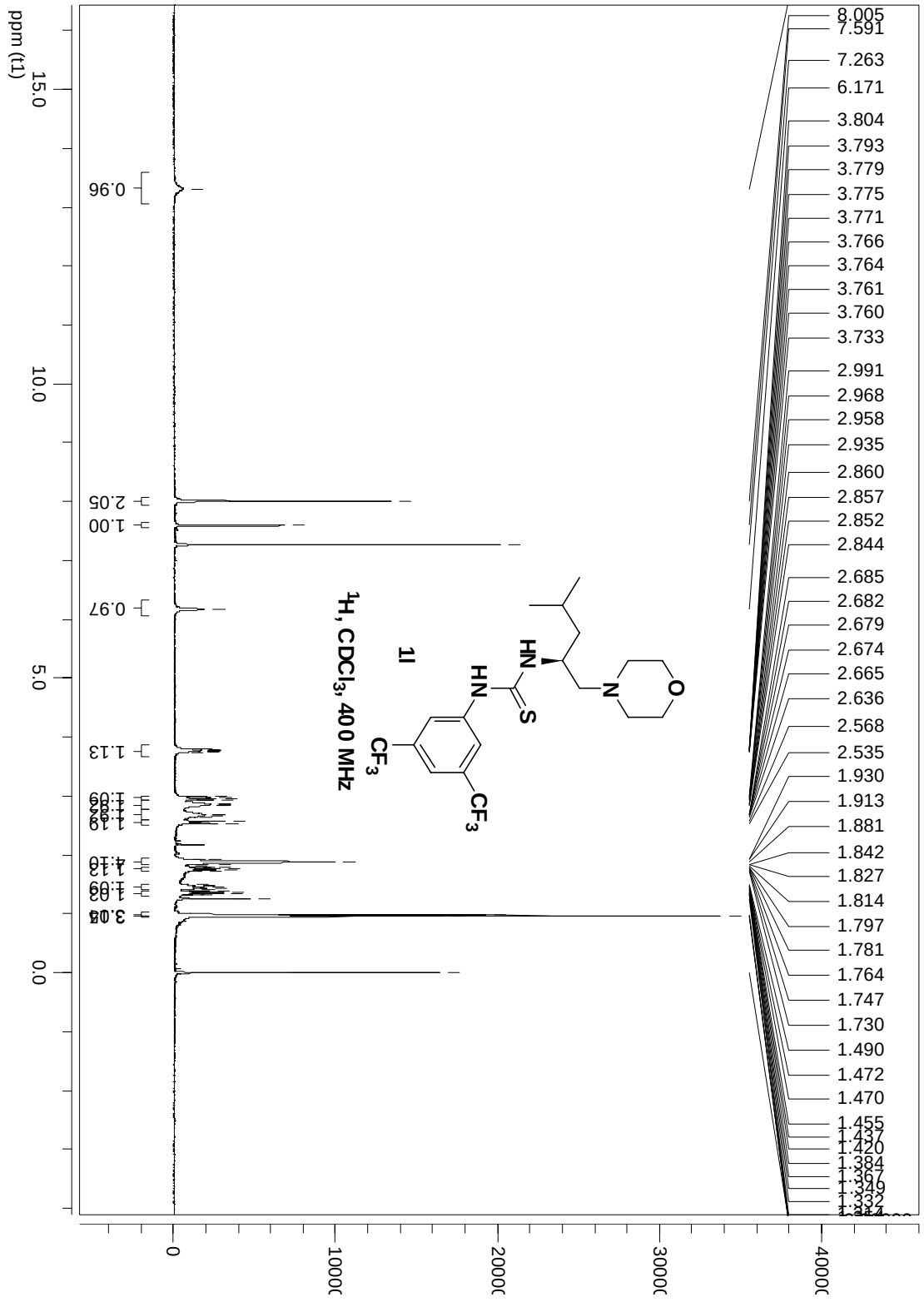
60000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4000
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N
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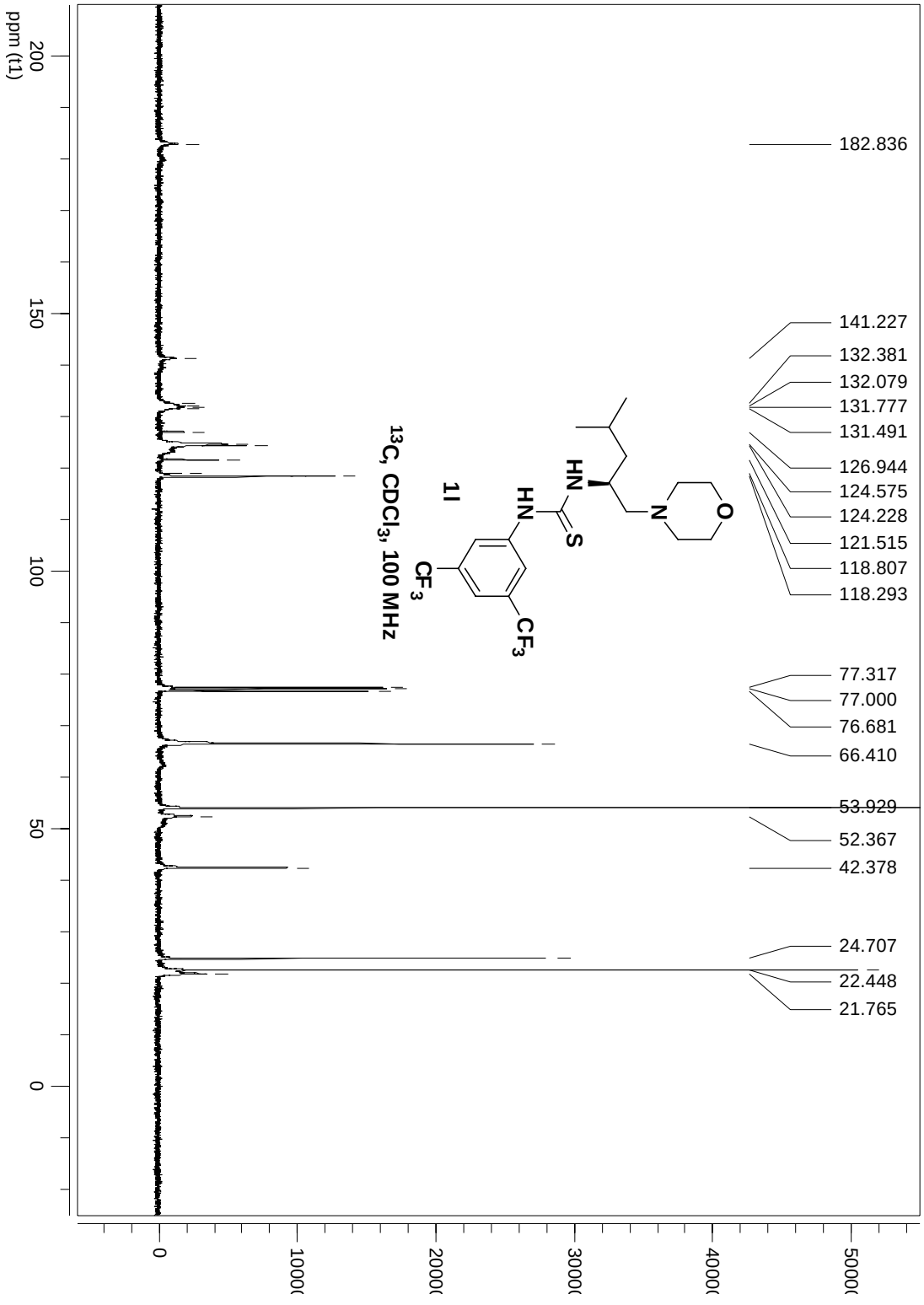
CF$_3$
CF$_3$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52.367
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24.707
22.448
21.765
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1l
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S
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N
O
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CF$_3$
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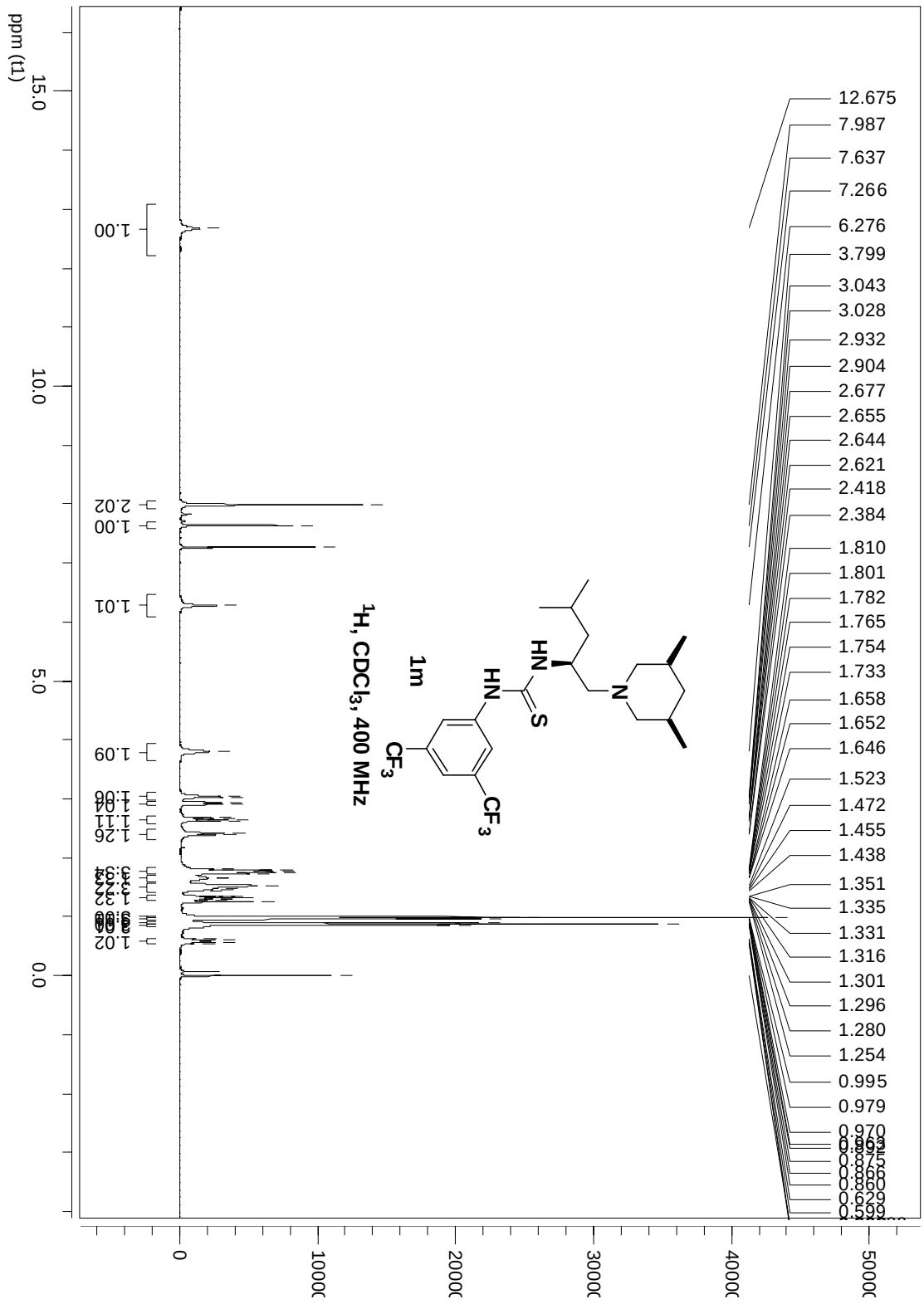
1000
2000
3000
4000
5000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1.11
1.26
1.02
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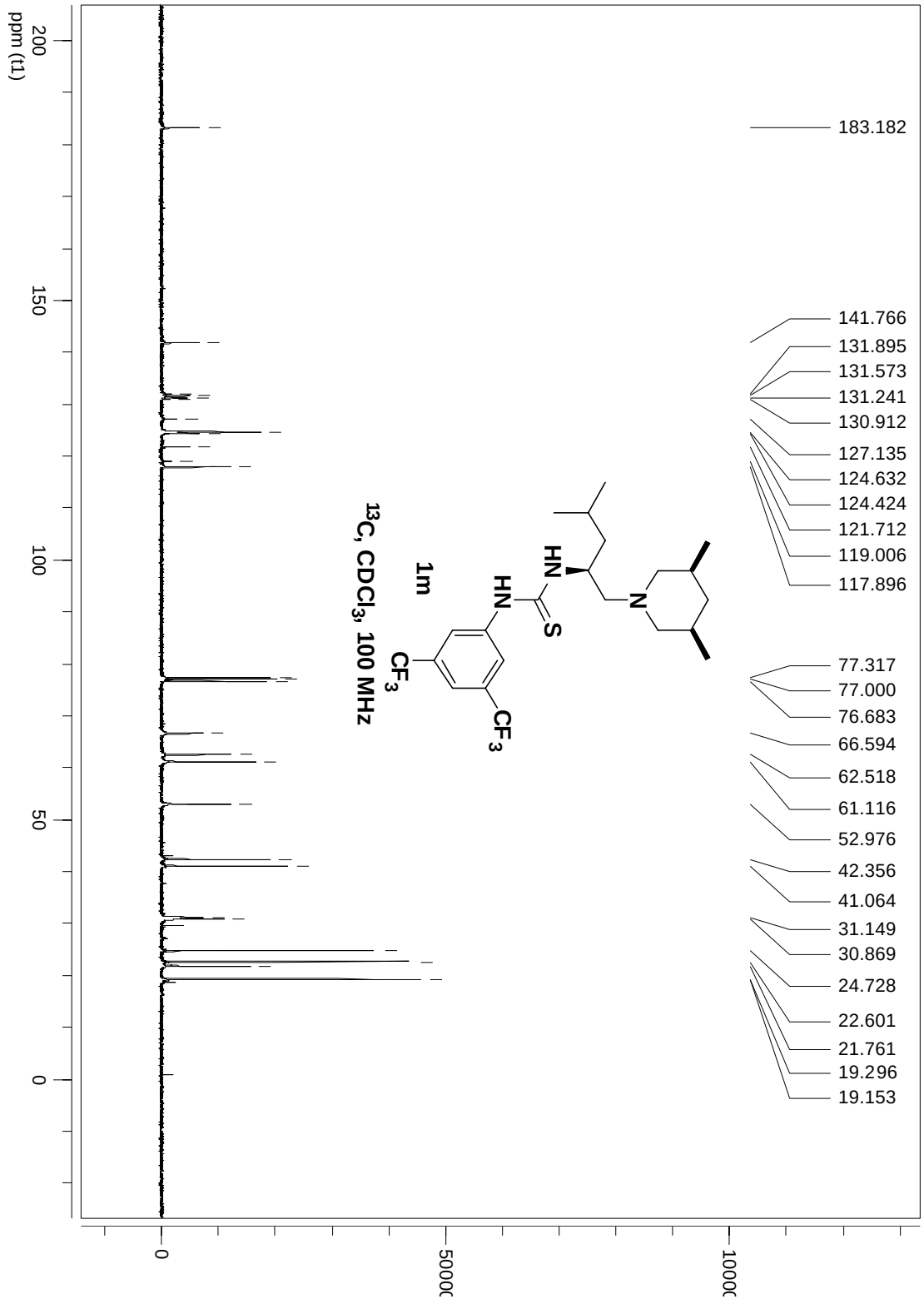
CF3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13C, CDCl3, 100 MHz
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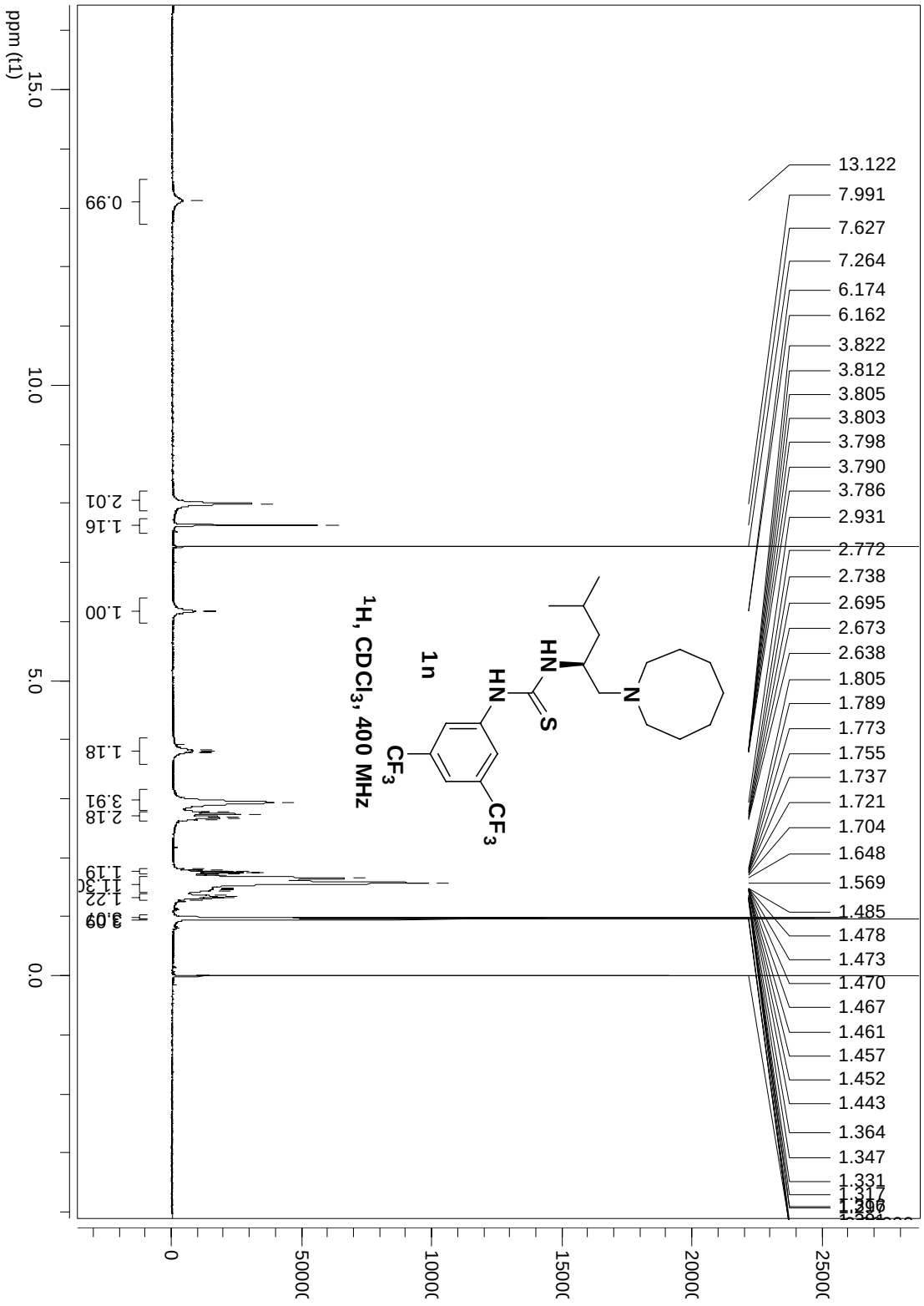
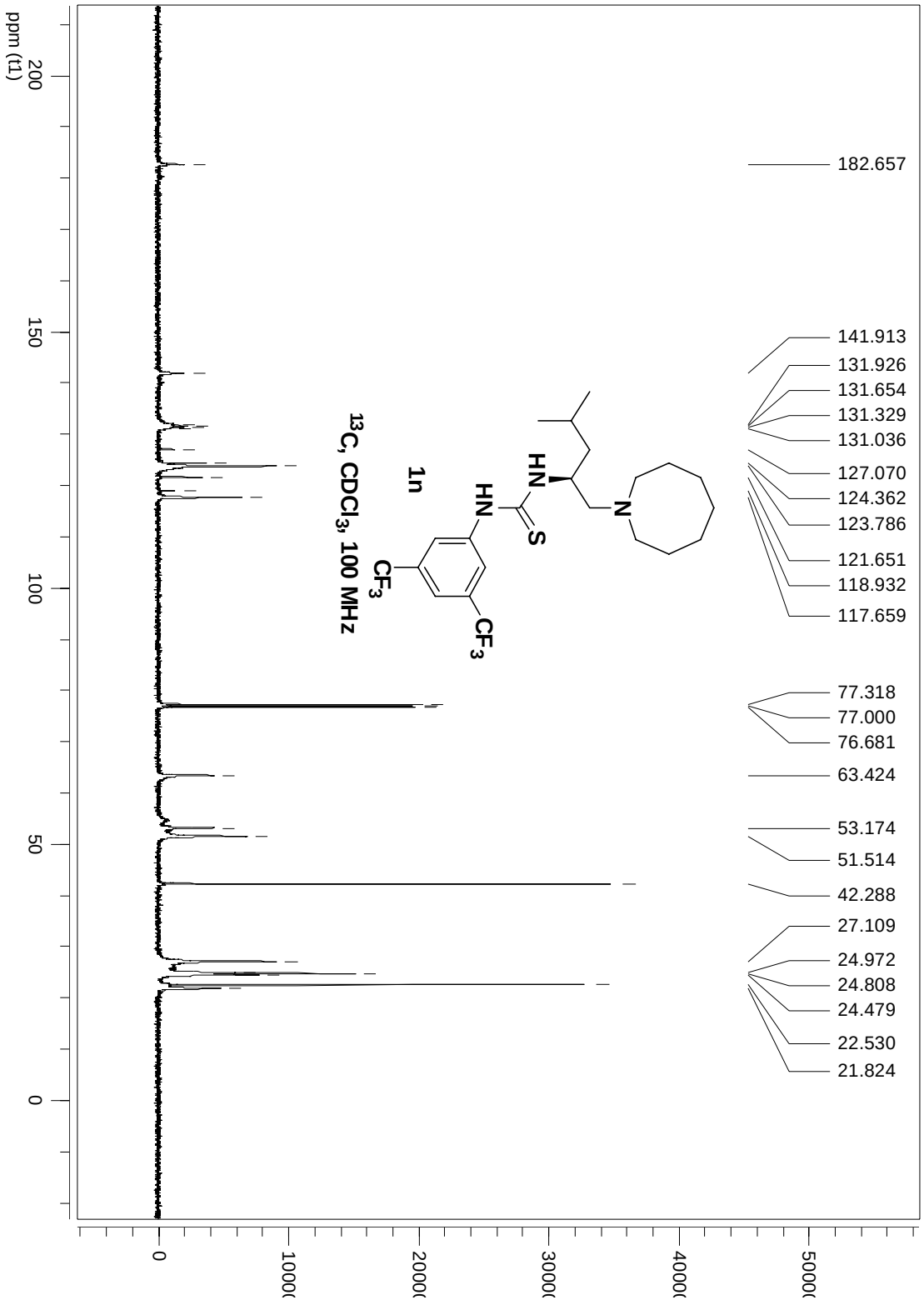
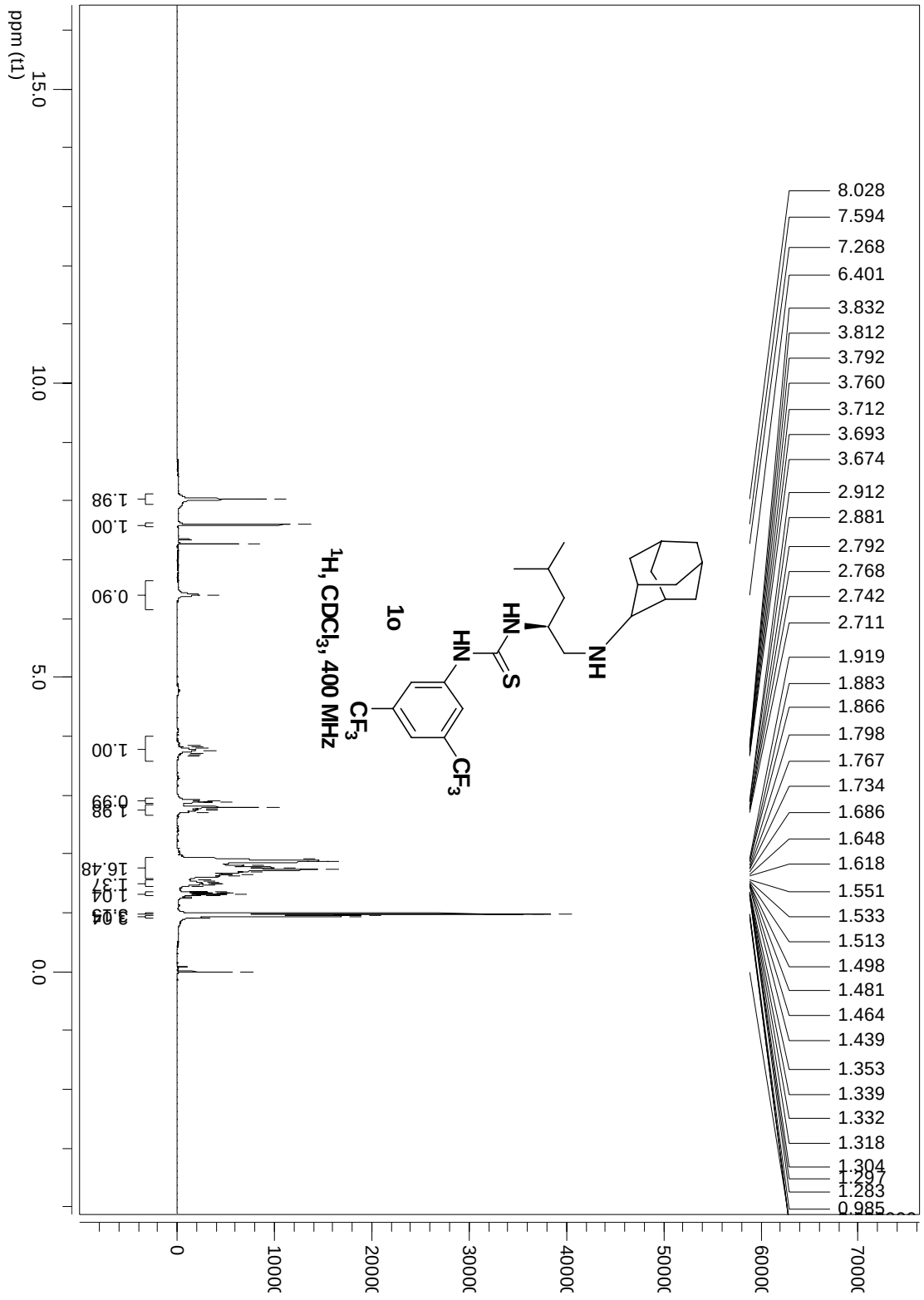
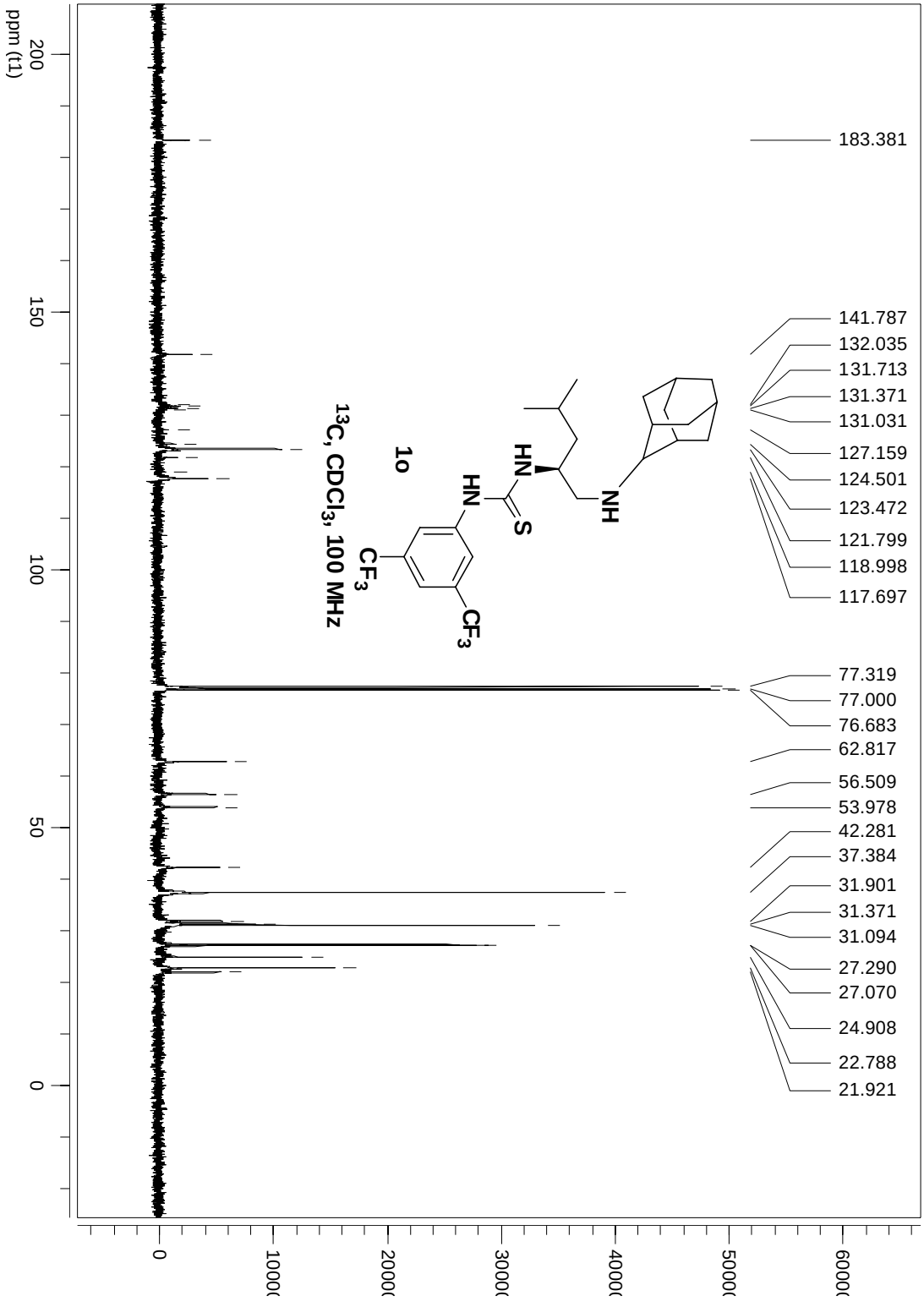
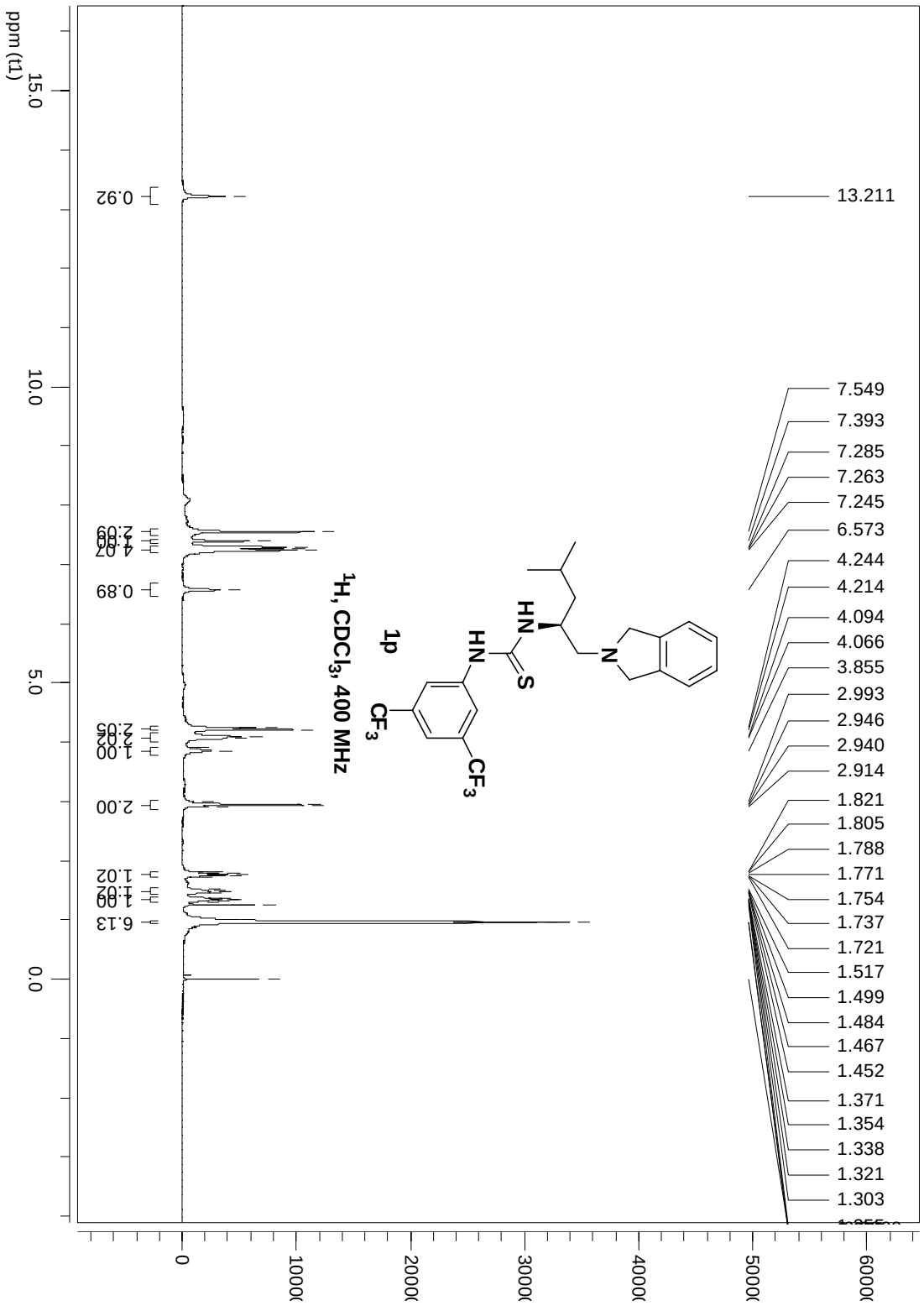
S
HN
N
CF3
CF3

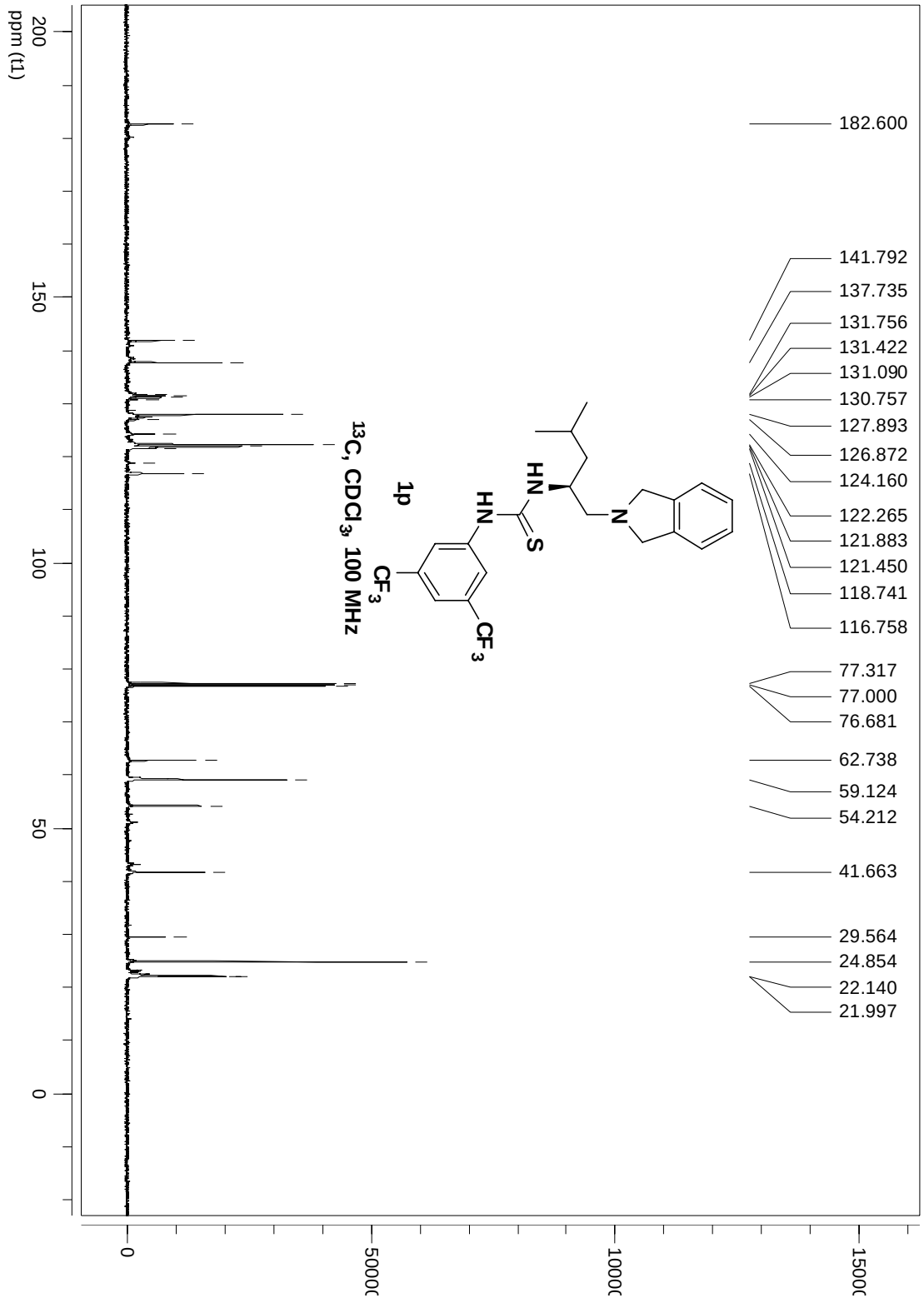

ppm (t1)
15.0
10.0
5.0
0.0
0.99
2.01
1.16
1.00
1.18
3.91
2.18
1.19
11.30
1.22
3.09
^{1}H, CDCl$_3$, 400 MHz
1n
HN
HN
S
N
CF$_3$
CF$_3$
13.122
7.991
7.627
7.264
6.174
6.162
3.822
3.812
3.805
3.803
3.798
3.790
3.786
2.931
2.772
2.738
2.695
2.673
2.638
1.805
1.789
1.773
1.755
1.737
1.721
1.704
1.648
1.569
1.485
1.478
1.473
1.470
1.467
1.461
1.457
1.452
1.443
1.364
1.347
1.331
0
5000
10000
15000
20000
25000

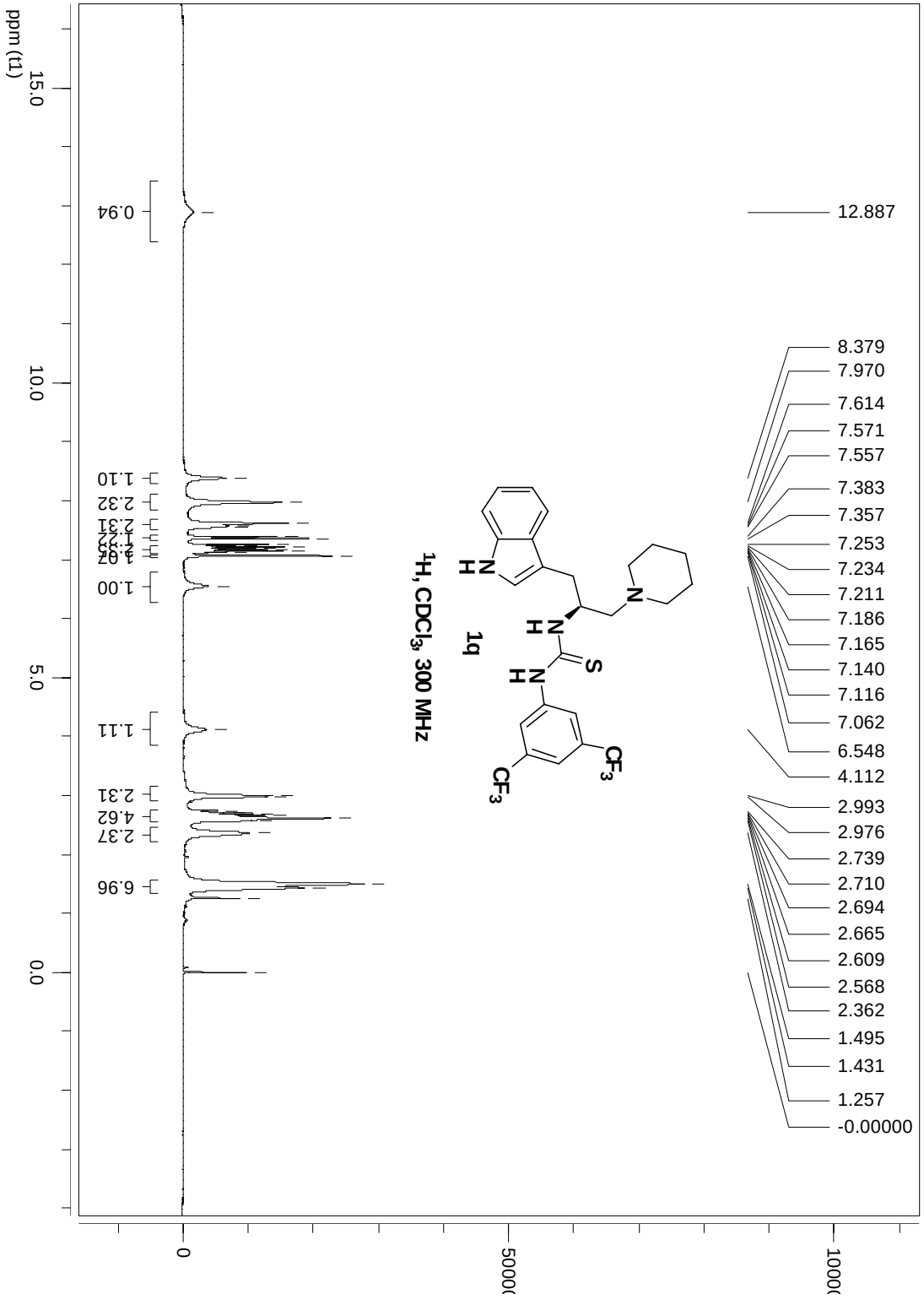

ppm (t1)
200
150
100
50
0
^{13}C, CDCl$_3$, 100 MHz
1n
HN
S
HN
N
CF$_3$
CF$_3$
182.657
141.913
131.926
131.654
131.329
131.036
127.070
124.362
123.786
121.651
118.932
117.659
77.318
77.000
76.681
63.424
53.174
51.514
42.288
27.109
24.972
24.808
24.479
22.530
21.824
0
10000
20000
30000
40000
50000

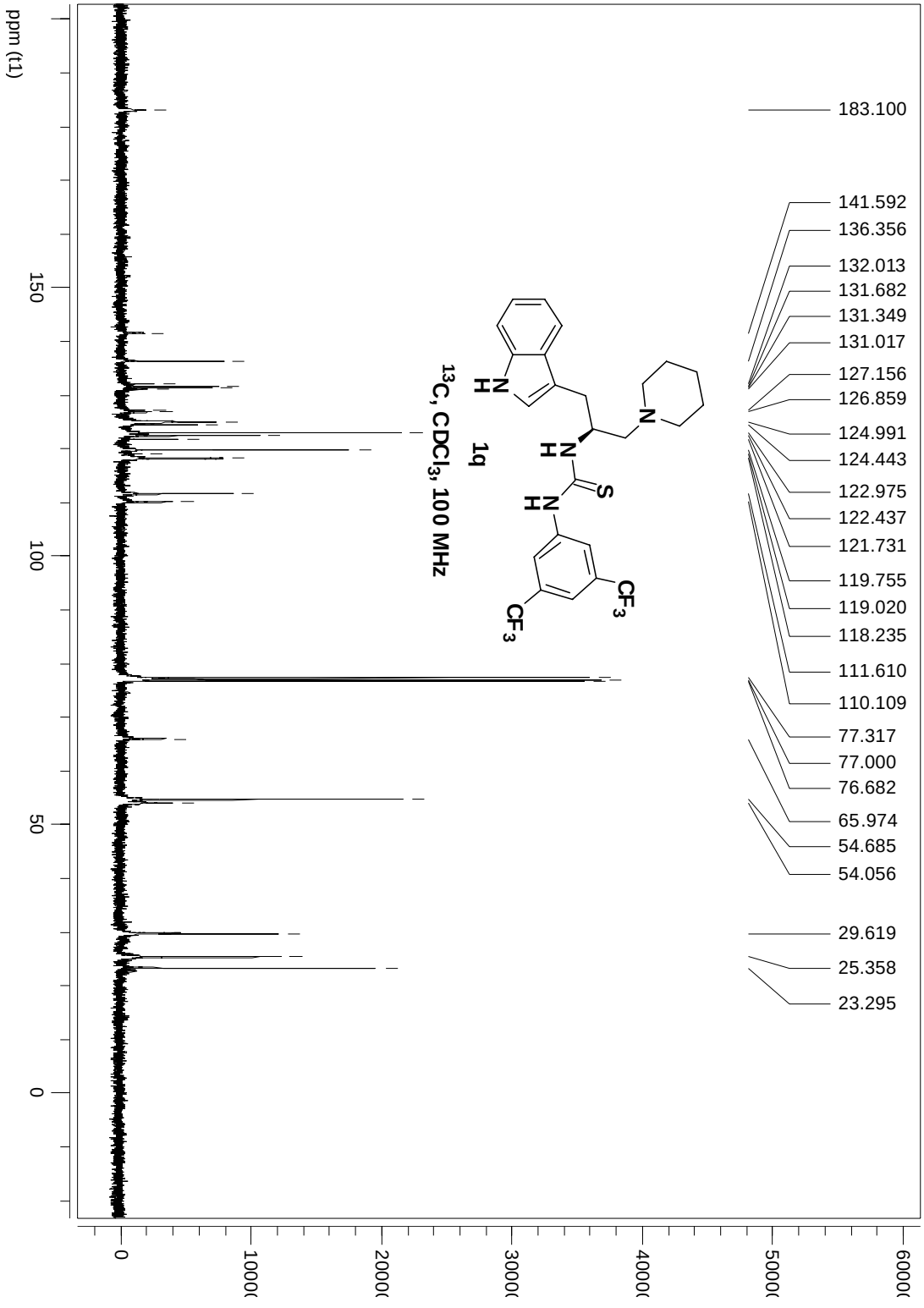

ppm (t1)
15.0
10.0
5.0
0.0
1.98
1.00
0.90
1.00
0.99
1.98
16.48
1.37
1.04
3.04
3.53
0
10000
20000
30000
40000
50000
60000
70000
8.028
7.594
7.268
6.401
3.832
3.812
3.792
3.760
3.712
3.693
3.674
2.912
2.881
2.792
2.768
2.742
2.711
1.919
1.883
1.866
1.798
1.767
1.734
1.686
1.648
1.618
1.551
1.533
1.513
1.498
1.481
1.464
1.439
1.353
1.339
1.332
1.318
1.304
1.297
1.283
0.985
^{1}H, CDCl$_3$, 400 MHz
1o
HN
S
HN
NH
CF$_3$
CF$_3$

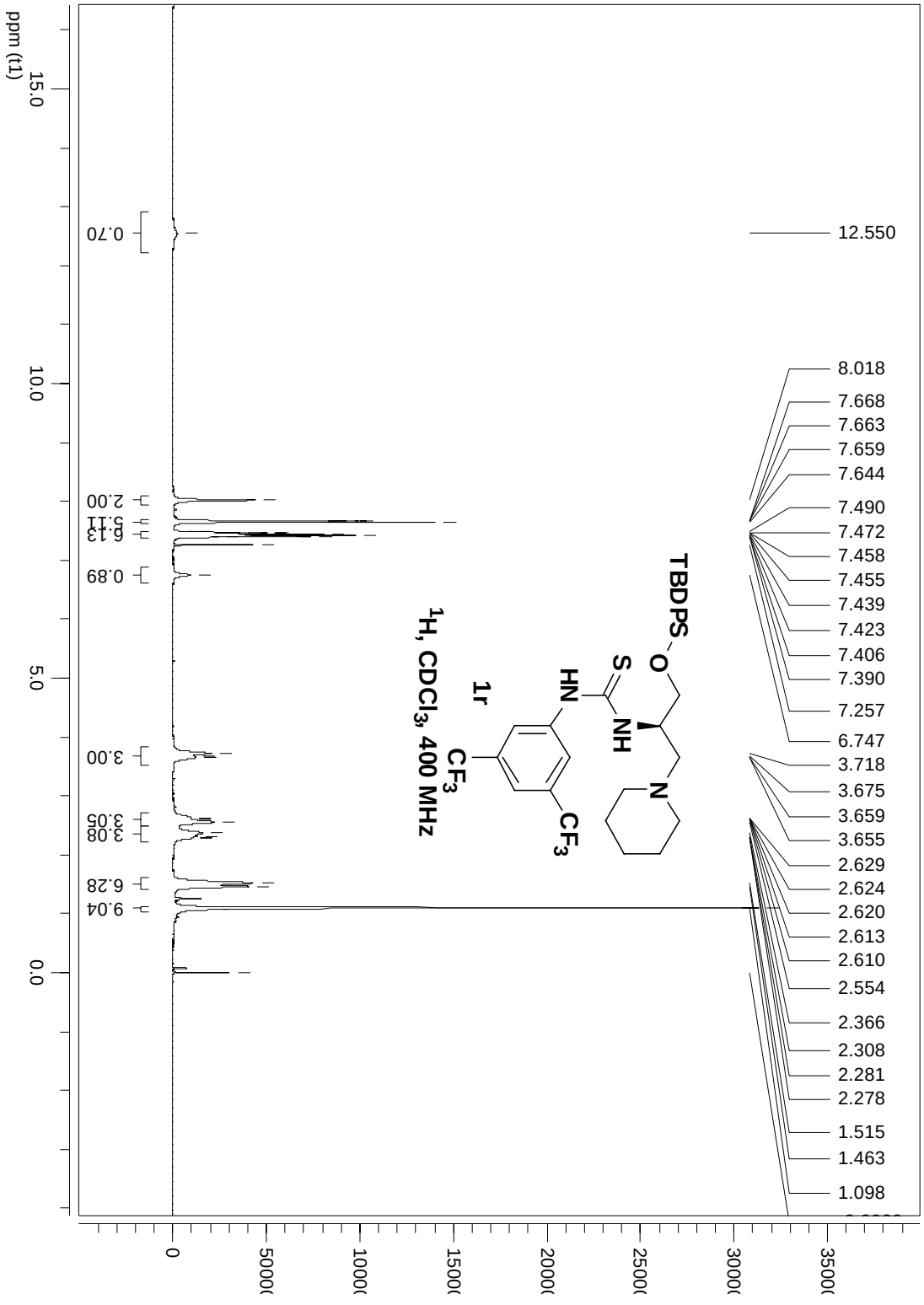

ppm (t1)
200
150
100
50
0
183.381
141.787
132.035
131.713
131.371
131.031
127.159
124.501
123.472
121.799
118.998
117.697
77.319
77.000
76.683
62.817
56.509
53.978
42.281
37.384
31.901
31.371
31.094
27.290
27.070
24.908
22.788
21.921
1o
13C, CDCl3, 100 MHz
HN
S
HN
NH
CF3
CF3
0
10000
20000
30000
40000
50000
60000

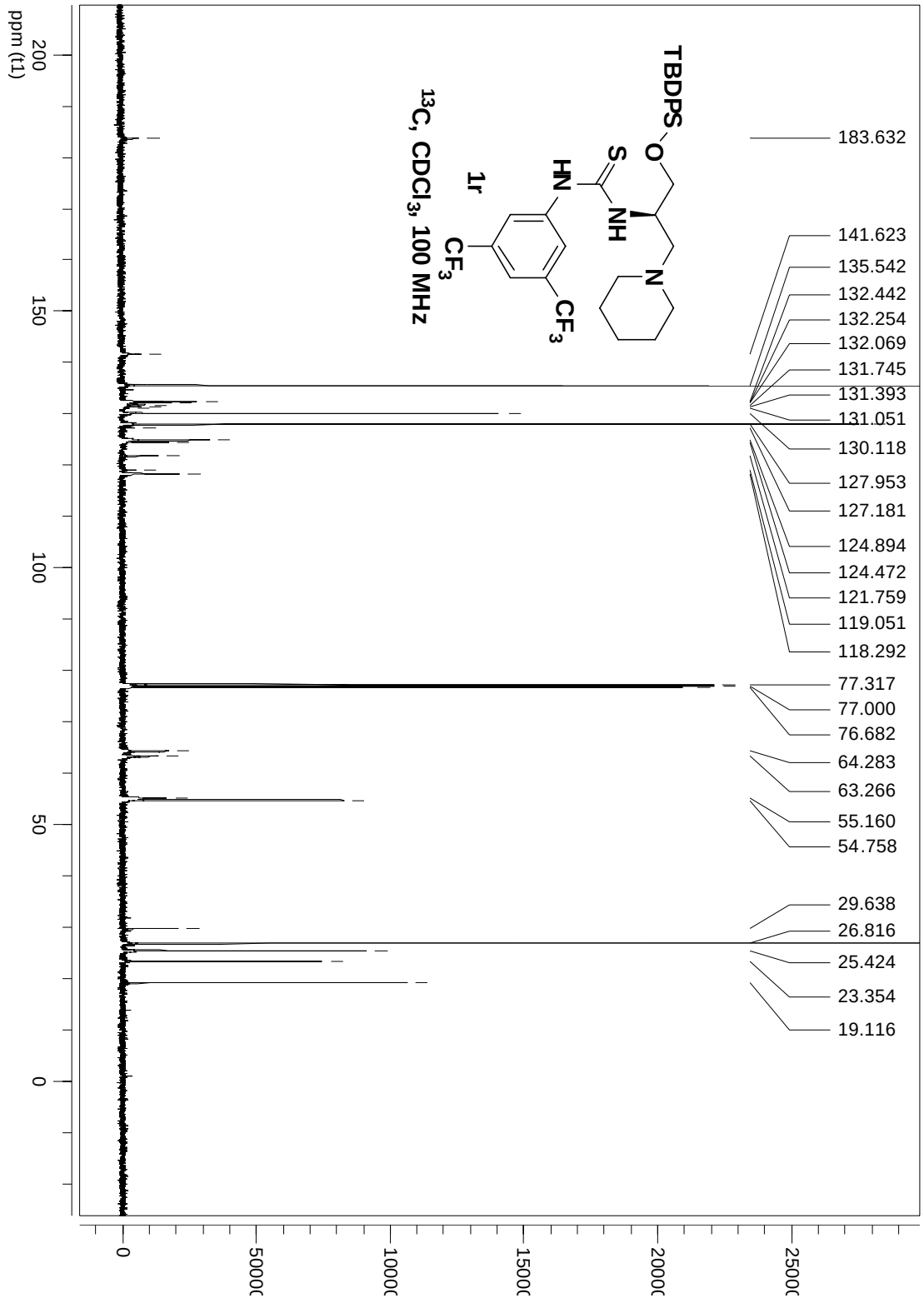

ppm (t1)
15.0
10.0
5.0
0.0
0.92
4.07
2.09
0.89
2.05
1.00
2.00
1.02
6.13
13.211
7.549
7.393
7.285
7.263
7.245
6.573
4.244
4.214
4.094
4.066
3.855
2.993
2.946
2.940
2.914
1.821
1.805
1.788
1.771
1.754
1.737
1.721
1.517
1.499
1.484
1.467
1.452
1.371
1.354
1.338
1.321
1.303
0
1000
2000
3000
4000
5000
6000
^{1}H, CDCl$_3$, 400 MHz
1p
HN
S
HN
N
CF$_3$
CF$_3$

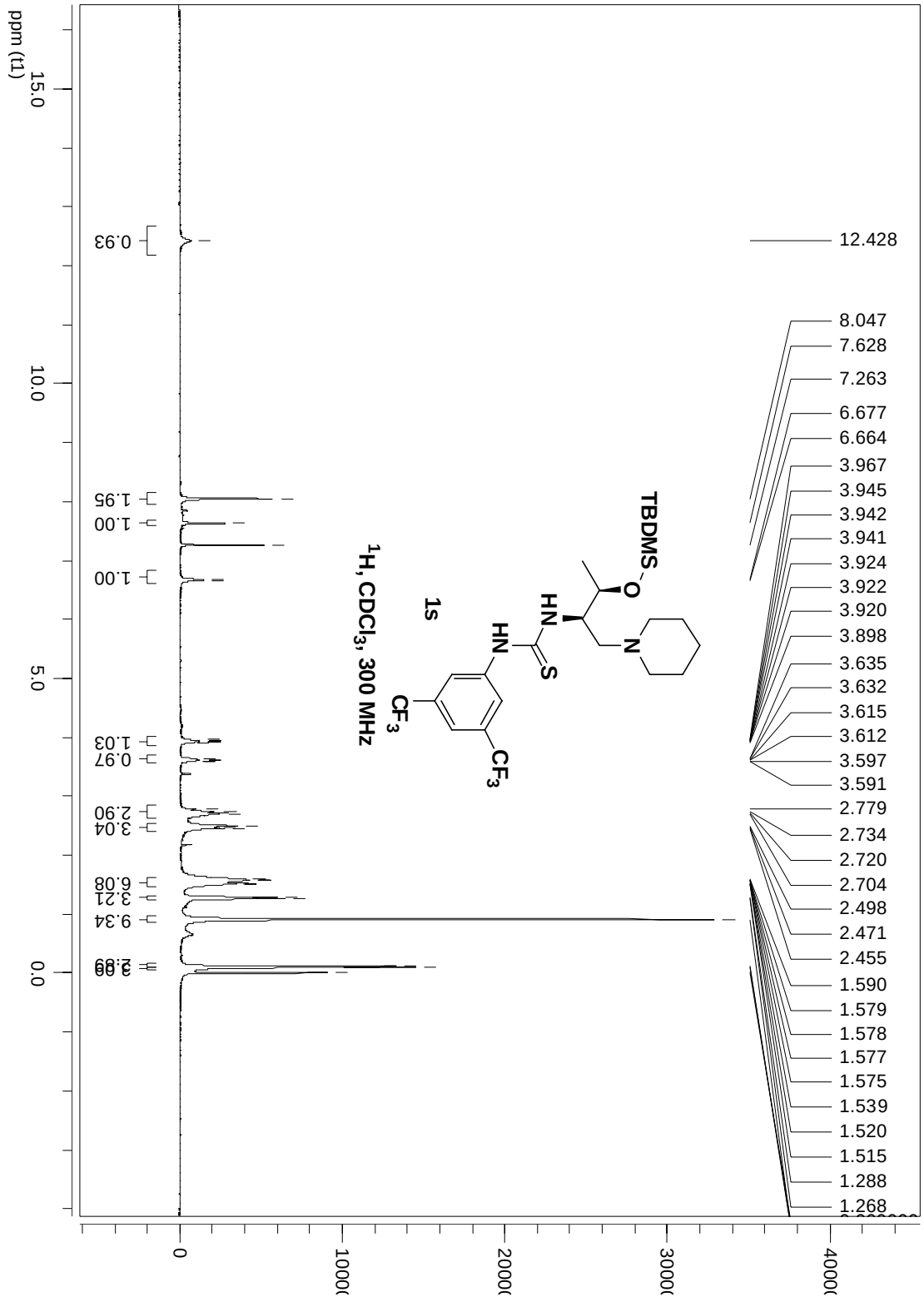

ppm (t1)
200
150
100
50
0
0
50000
100000
150000
182.600
141.792
137.735
131.756
131.422
131.090
130.757
127.893
126.872
124.160
122.265
121.883
121.450
118.741
116.758
77.317
77.000
76.681
62.738
59.124
54.212
41.663
29.564
24.854
22.140
21.997
13C, CDCl3, 100 MHz
1p
HN
S
HN
N
CF3
CF3

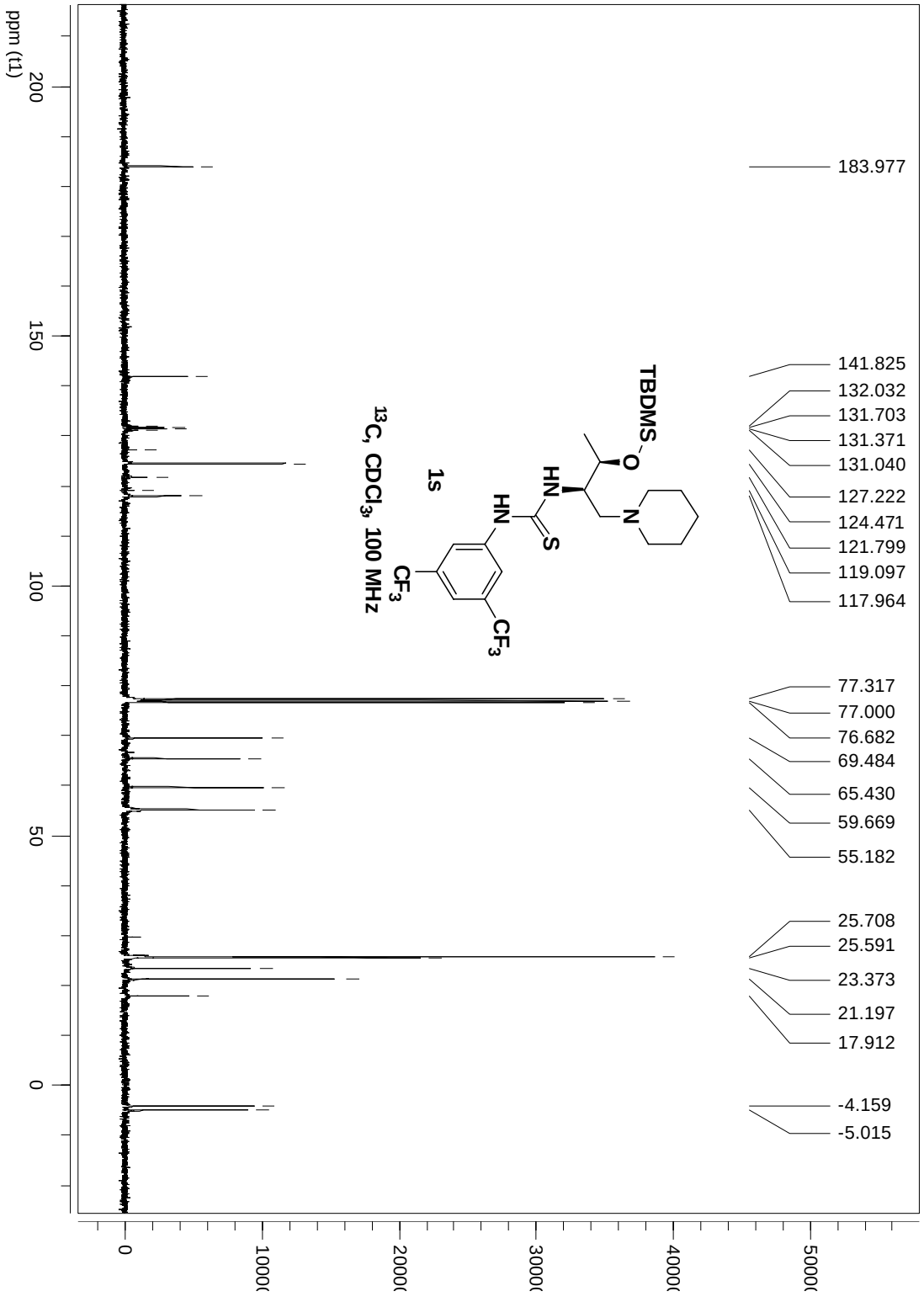

ppm (t1)
15.0
10.0
5.0
0.0
0.94
1.10
2.32
2.31
1.22
4.07
1.00
1.11
2.31
4.62
2.37
6.96
0
5000
10000
^{1}H, CDCl$_3$, 300 MHz
1q
12.887
8.379
7.970
7.614
7.571
7.557
7.383
7.357
7.253
7.234
7.211
7.186
7.165
7.140
7.116
7.062
6.548
4.112
2.993
2.976
2.739
2.710
2.694
2.665
2.609
2.568
2.362
1.495
1.431
1.257
-0.00000

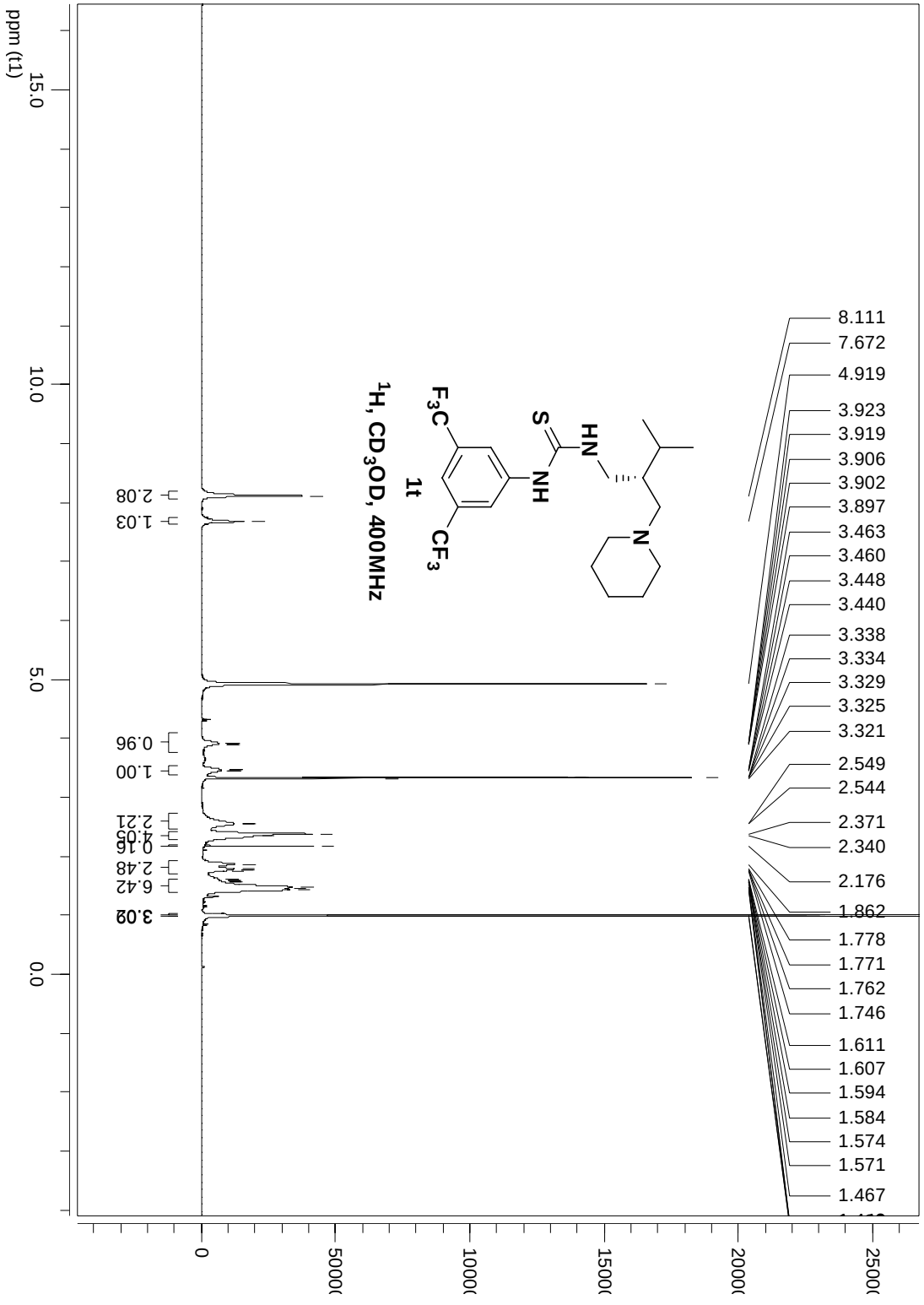

ppm (t1)
150
100
50
0
0
1000
2000
3000
4000
5000
6000
183.100
141.592
136.356
132.013
131.682
131.349
131.017
127.156
126.859
124.991
124.443
122.975
122.437
121.731
119.755
119.020
118.235
111.610
110.109
77.317
77.000
76.682
65.974
54.685
54.056
29.619
25.358
23.295
1q
13C, CDCl3, 100 MHz
N
H
N
H
S
N
H
CF3
CF3
N

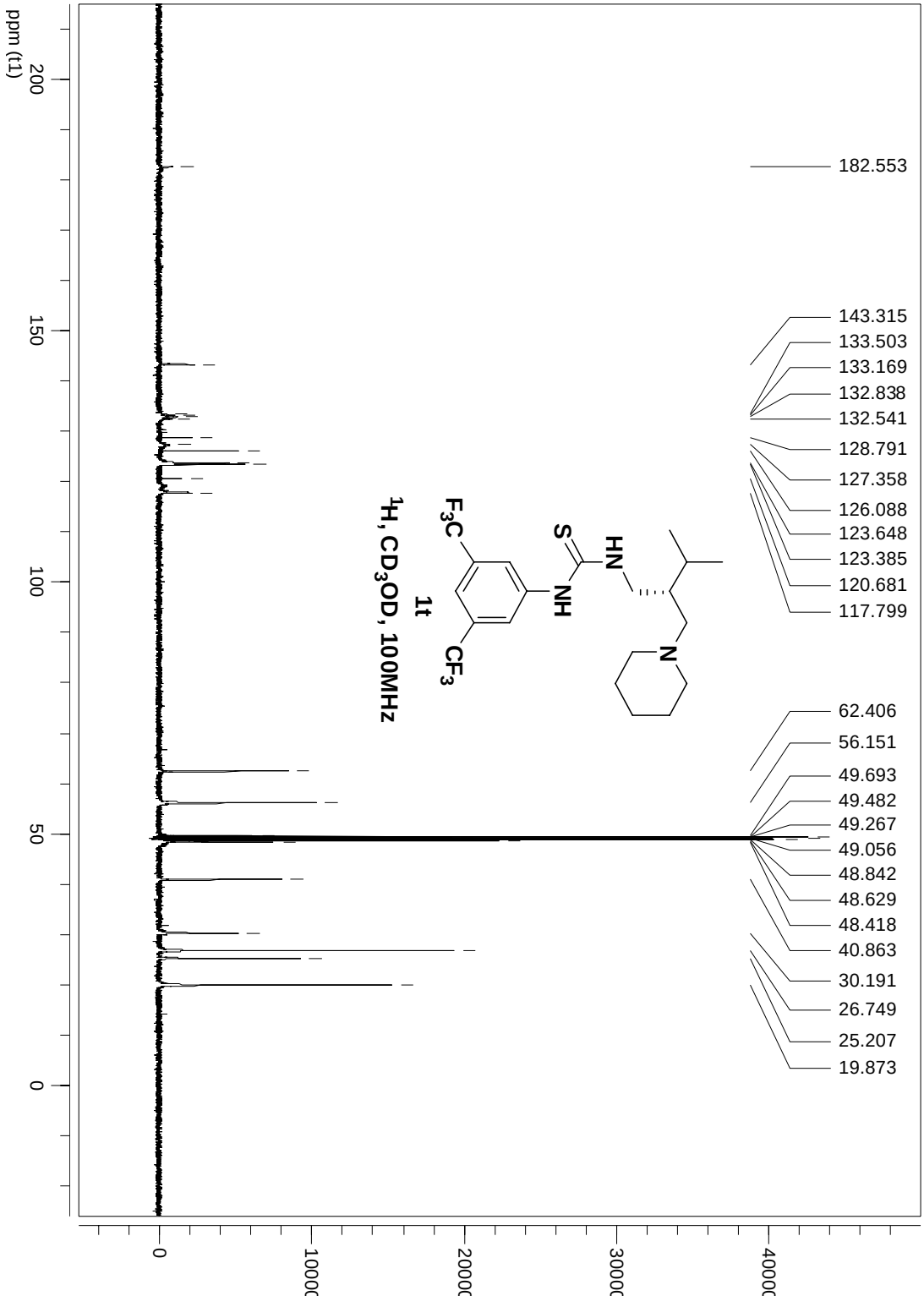

ppm (t1)
15.0
10.0
5.0
0.0
0.70
2.00
5.11
6.13
0.89
3.00
3.05
3.08
6.28
9.04
12.550
8.018
7.668
7.663
7.659
7.644
7.490
7.472
7.458
7.455
7.439
7.423
7.406
7.390
7.257
6.747
3.718
3.675
3.659
3.655
2.629
2.624
2.620
2.613
2.610
2.554
2.366
2.308
2.281
2.278
1.515
1.463
1.098
0
5000
10000
15000
20000
25000
30000
35000
^{1}H, CDCl$_3$, 400 MHz
1r
TBDPS
O
S
NH
HN
N
CF$_3$
CF$_3$

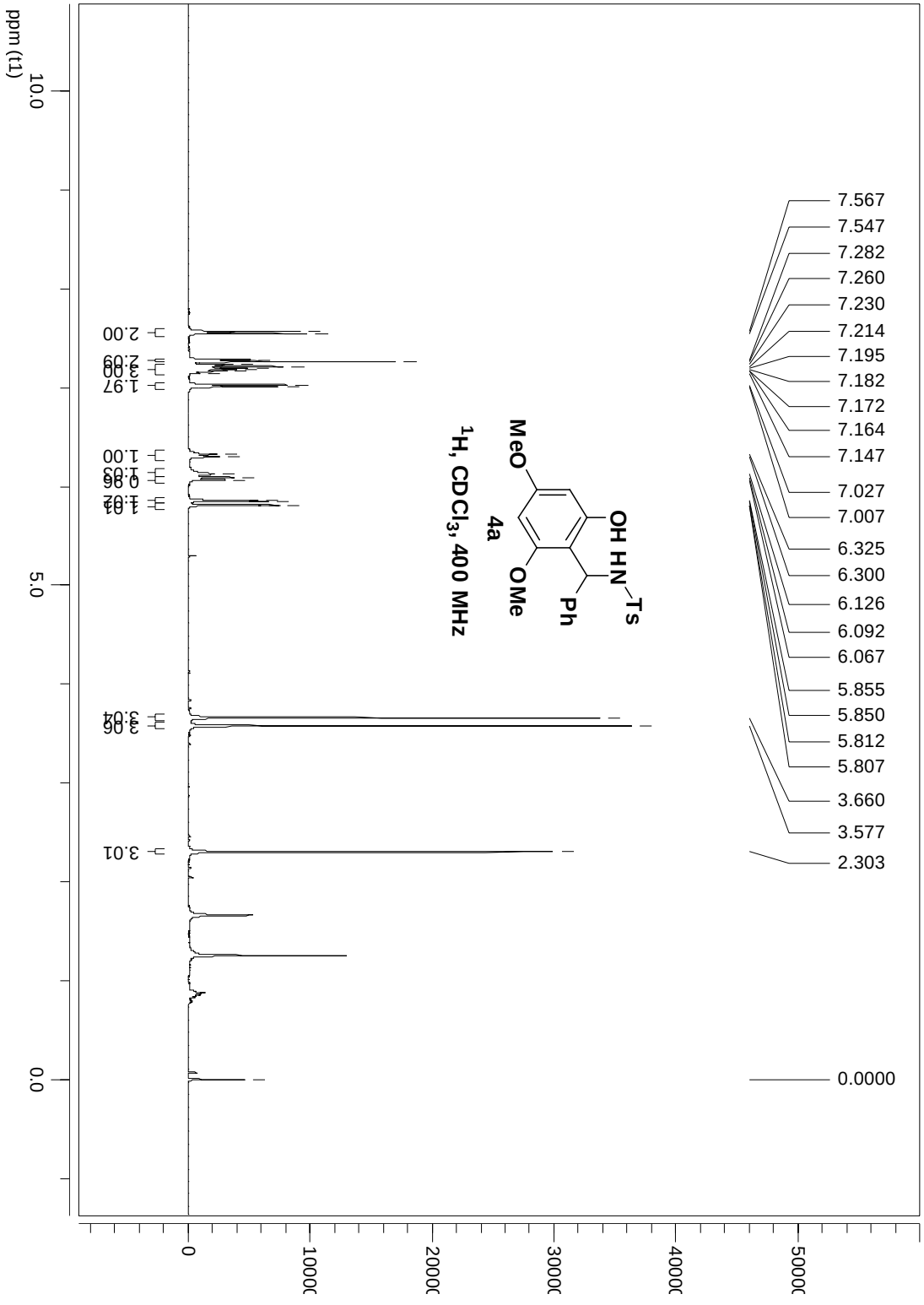

^{13}C, CDCl$_3$, 100 MHz
1r
TBDPSO
S
HN
NH
N
CF$_3$
CF$_3$
ppm (t1)
200
150
100
50
0
0
5000
10000
15000
20000
25000
183.632
141.623
135.542
132.442
132.254
132.069
131.745
131.393
131.051
130.118
127.953
127.181
124.894
124.472
121.759
119.051
118.292
77.317
77.000
76.682
64.283
63.266
55.160
54.758
29.638
26.816
25.424
23.354
19.116

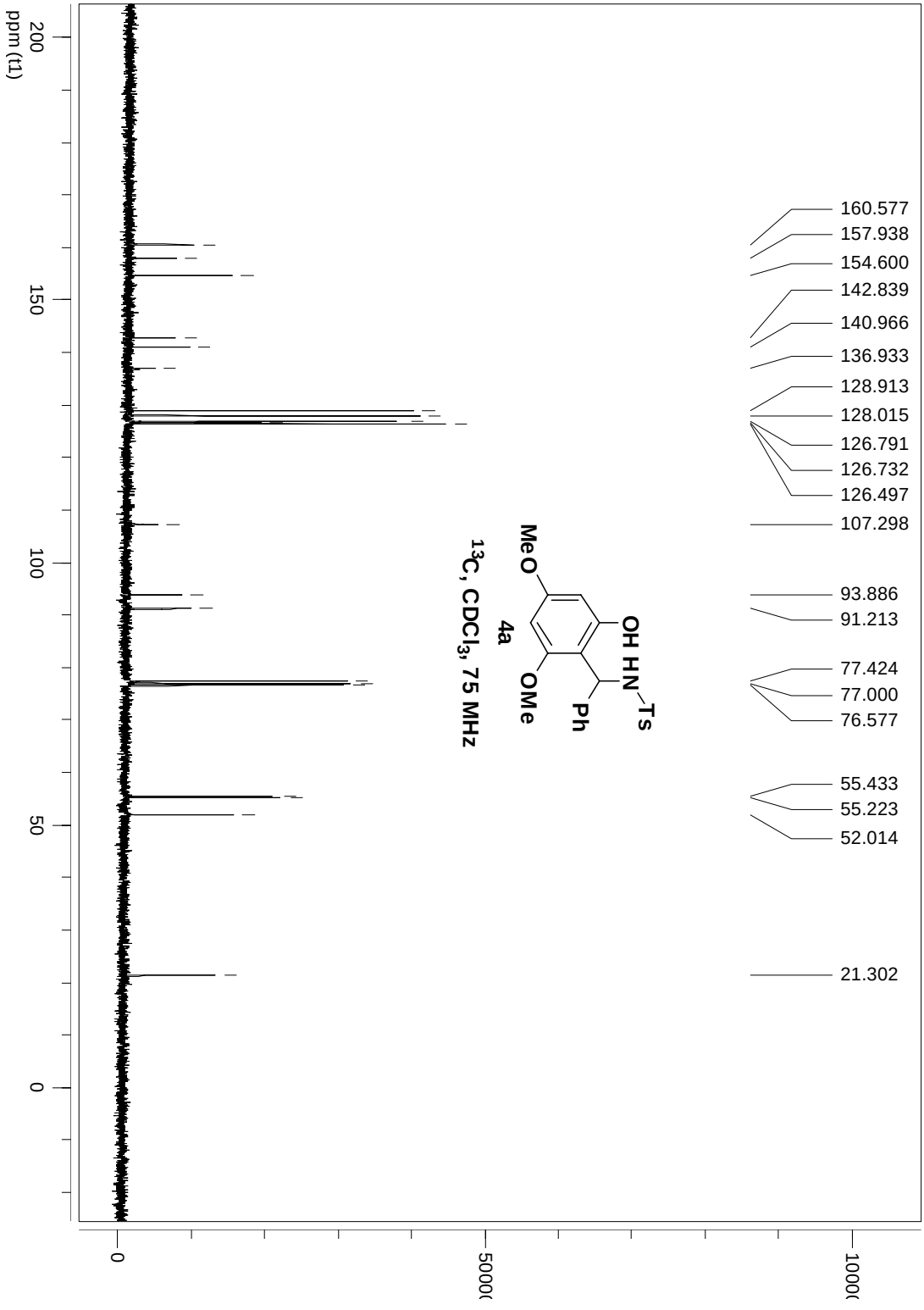

ppm (t1)
15.0
10.0
5.0
0.0
0
1000
2000
3000
4000
0.93
1.95
1.00
1.00
1.03
0.97
2.90
3.04
6.08
3.21
9.34
3.00
12.428
8.047
7.628
7.263
6.677
6.664
3.967
3.945
3.942
3.941
3.924
3.922
3.920
3.898
3.635
3.632
3.615
3.612
3.597
3.591
2.779
2.734
2.720
2.704
2.498
2.471
2.455
1.590
1.579
1.578
1.577
1.575
1.539
1.520
1.515
1.288
1.268
^{1}H, CDCl$_3$, 300 MHz
1s
TBDMS
O
HN
S
HN
N
CF$_3$
CF$_3$

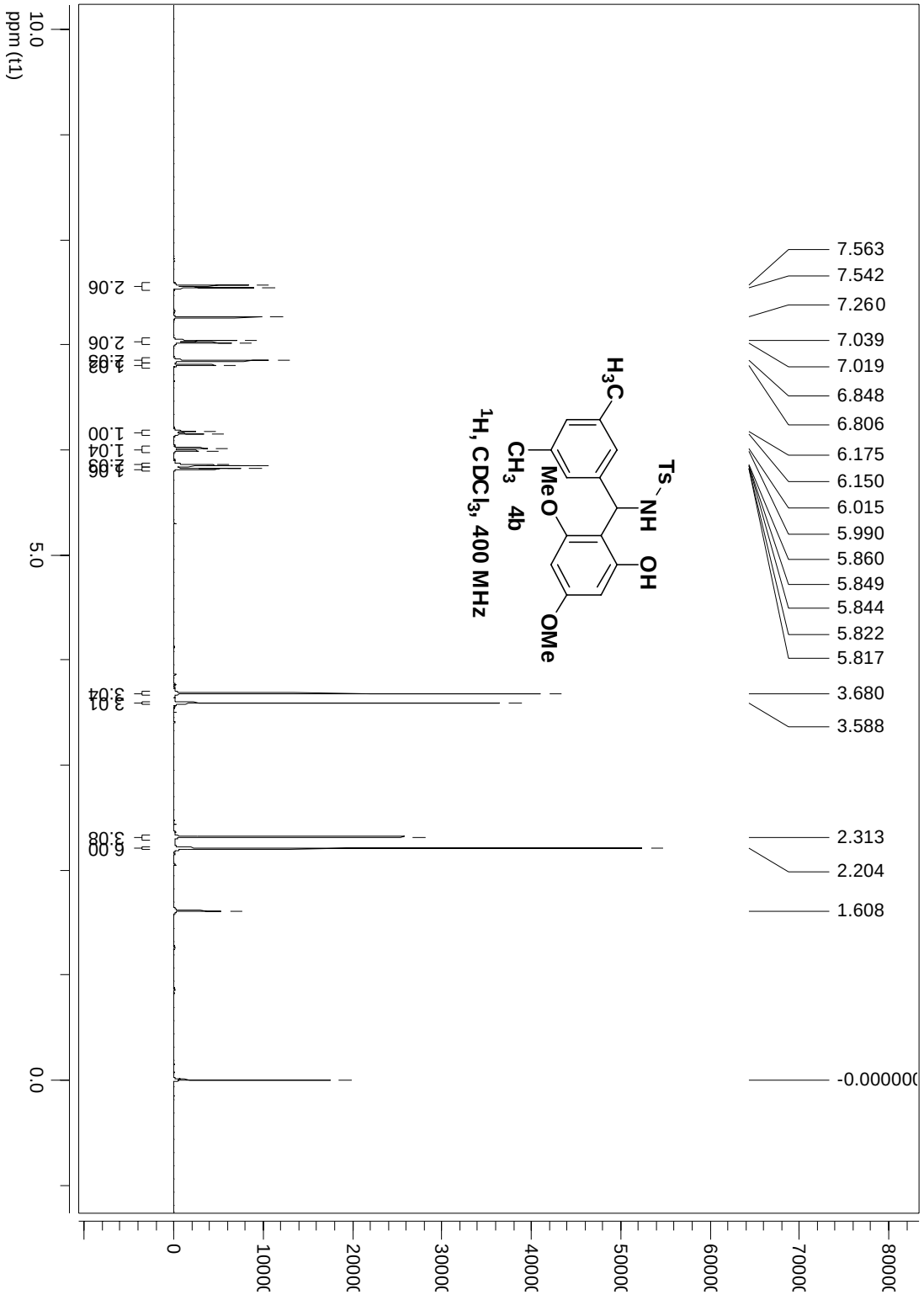

ppm (t1)
200
150
100
50
0
0
10000
20000
30000
40000
50000
183.977
141.825
132.032
131.703
131.371
131.040
127.222
124.471
121.799
119.097
117.964
77.317
77.000
76.682
69.484
65.430
59.669
55.182
25.708
25.591
23.373
21.197
17.912
-4.159
-5.015
1s
13C, CDCl3, 100 MHz
TBDMS
O
HN
S
HN
CF3
CF3
N

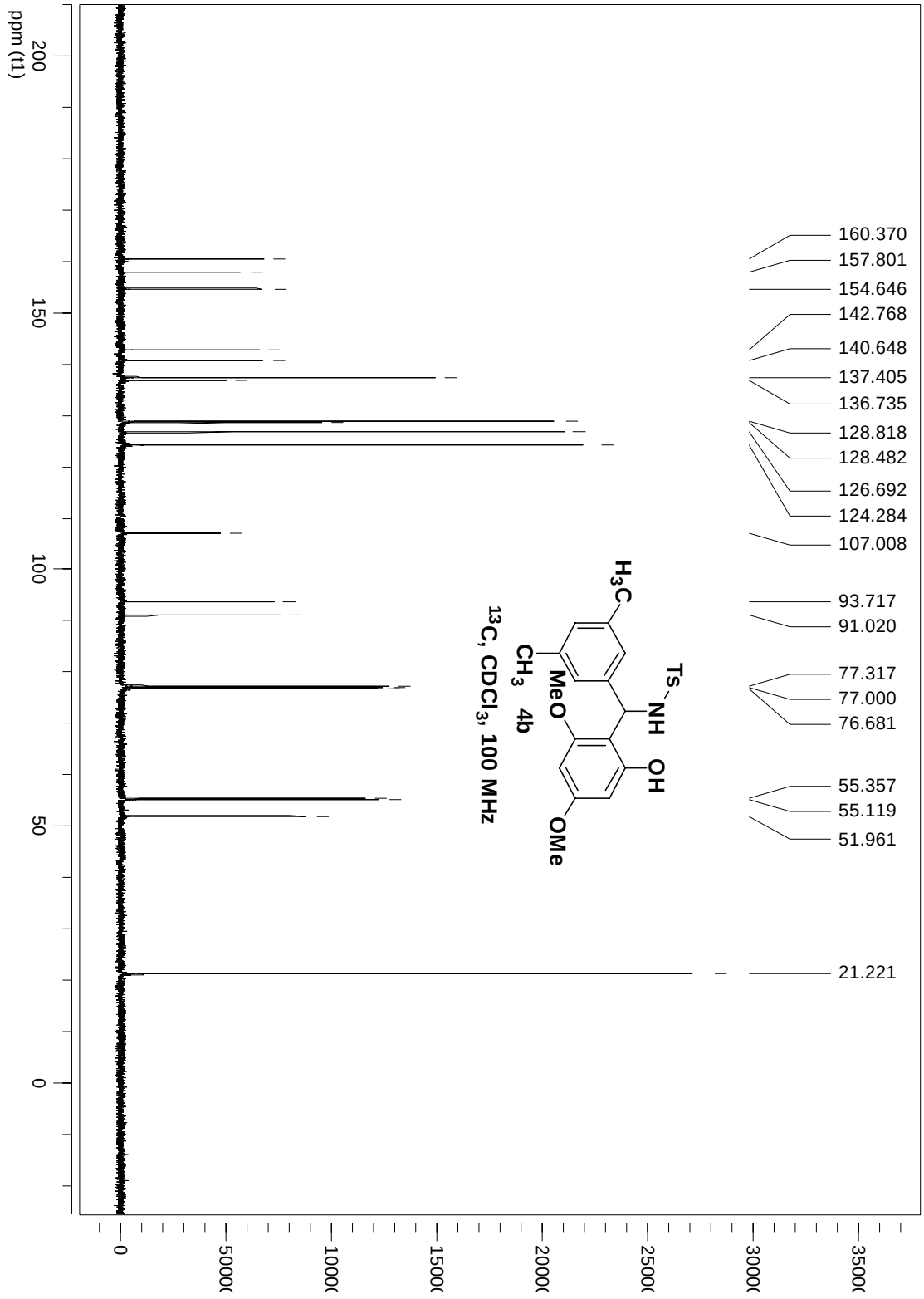

ppm (t1)
15.0
10.0
5.0
0.0
0
5000
10000
15000
20000
25000
^{1}H, CD$_3$OD, 400MHz
1t
F$_3$C
CF$_3$
S
NH
HN
N
2.08
1.03
0.96
1.00
2.21
4.05
0.16
2.48
6.42
3.09
8.111
7.672
4.919
3.923
3.919
3.906
3.902
3.897
3.463
3.460
3.448
3.440
3.338
3.334
3.329
3.325
3.321
2.549
2.544
2.371
2.340
2.176
1.862
1.778
1.771
1.762
1.746
1.611
1.607
1.594
1.584
1.574
1.571
1.467

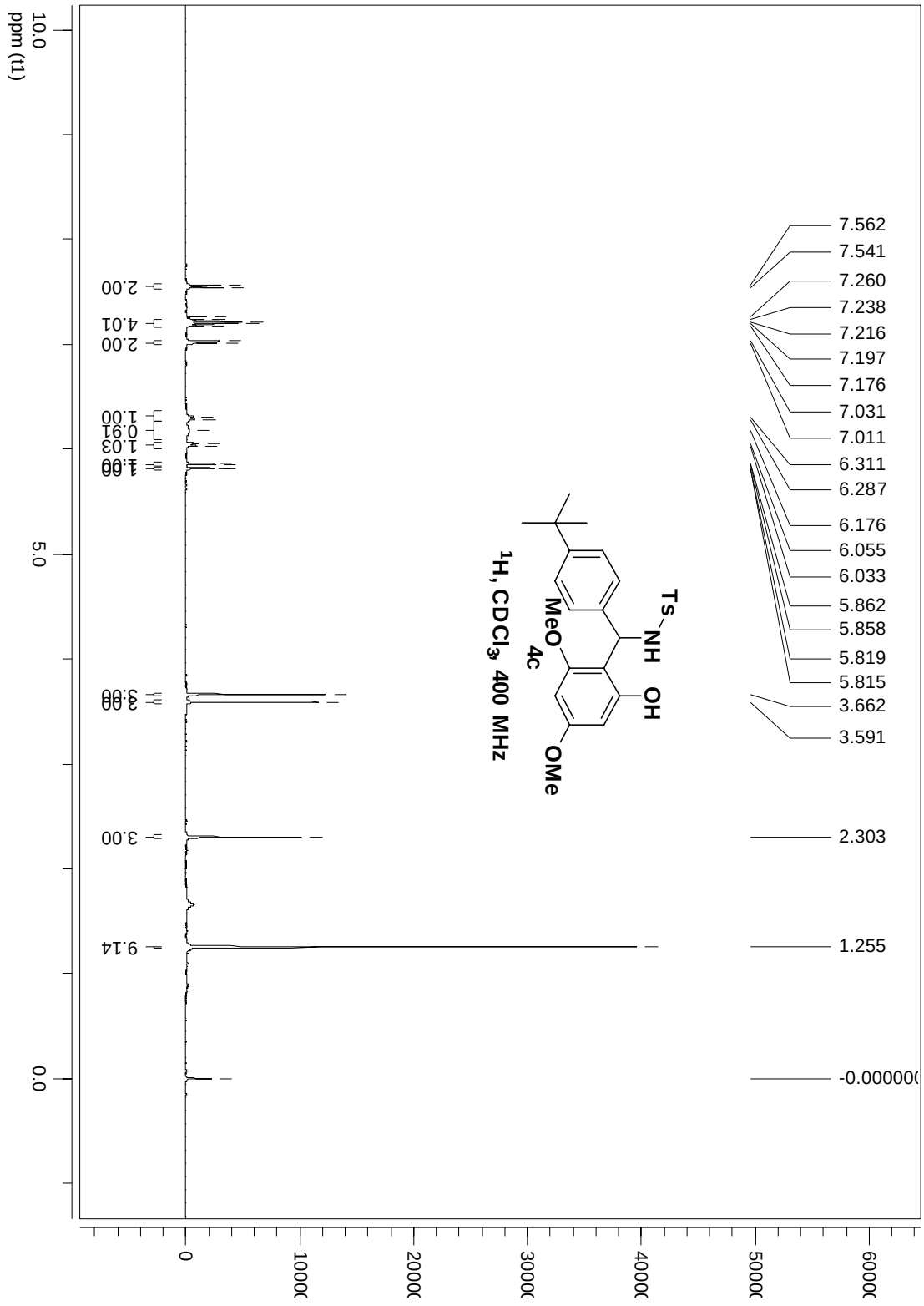

ppm (t1)
200
150
100
50
0
182.553
143.315
133.503
133.169
132.838
132.541
128.791
127.358
126.088
123.648
123.385
120.681
117.799
62.406
56.151
49.693
49.482
49.267
49.056
48.842
48.629
48.418
40.863
30.191
26.749
25.207
19.873
1t
^{1}H, CD$_3$OD, 100MHz
F$_3$C
CF$_3$
NH
S
HN
N
0
10000
20000
30000
40000

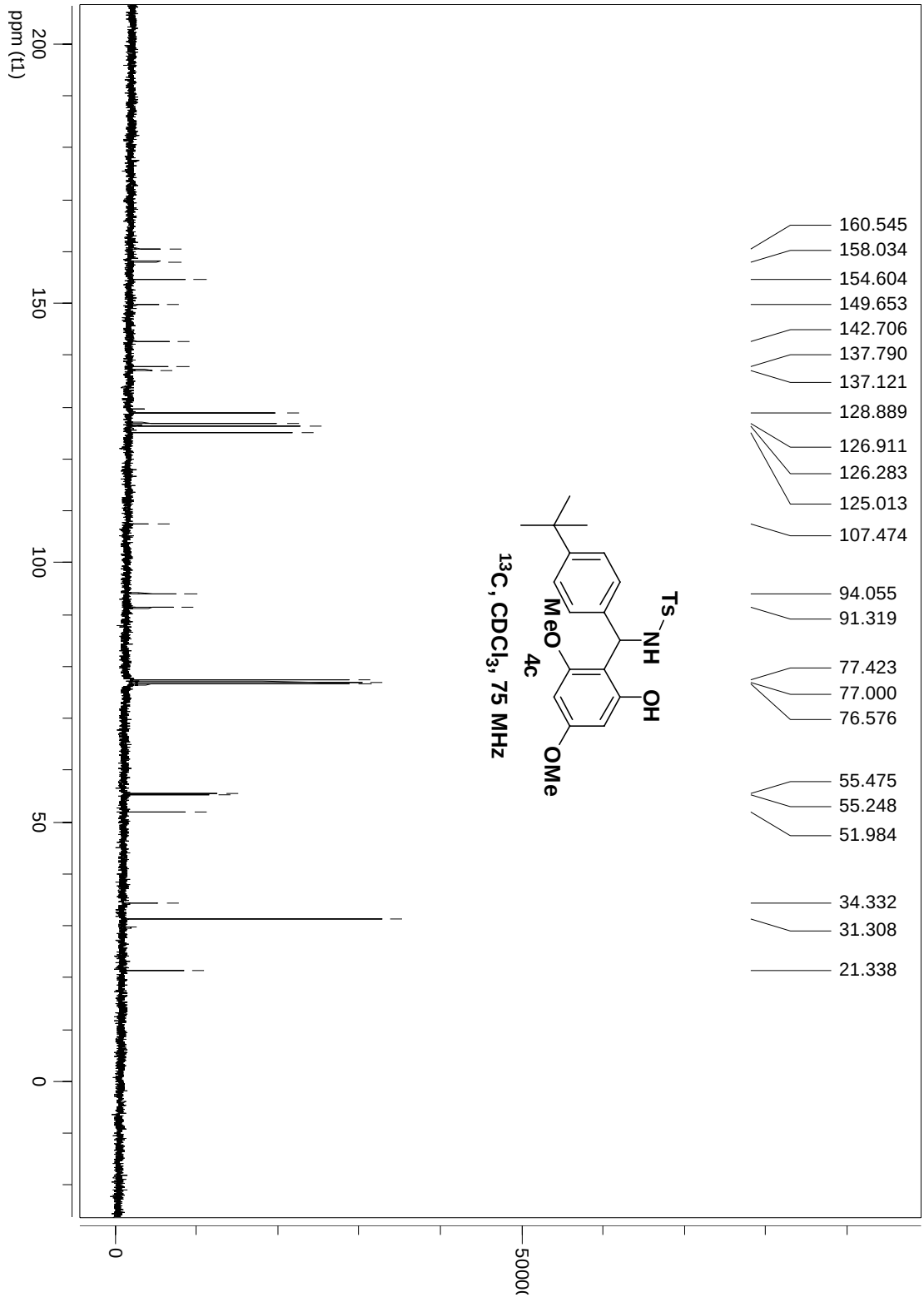

ppm (t1)
10.0
5.0
0.0
2.00
2.09
3.00
1.97
1.00
1.03
0.96
1.01
3.06
3.04
3.01
^{1}H, CDCl$_3$, 400 MHz
4a
MeO
OMe
Ph
OH HN
Ts
7.567
7.547
7.282
7.260
7.230
7.214
7.195
7.182
7.172
7.164
7.147
7.027
7.007
6.325
6.300
6.126
6.092
6.067
5.855
5.850
5.812
5.807
3.660
3.577
2.303
0.0000
0
10000
20000
30000
40000
50000

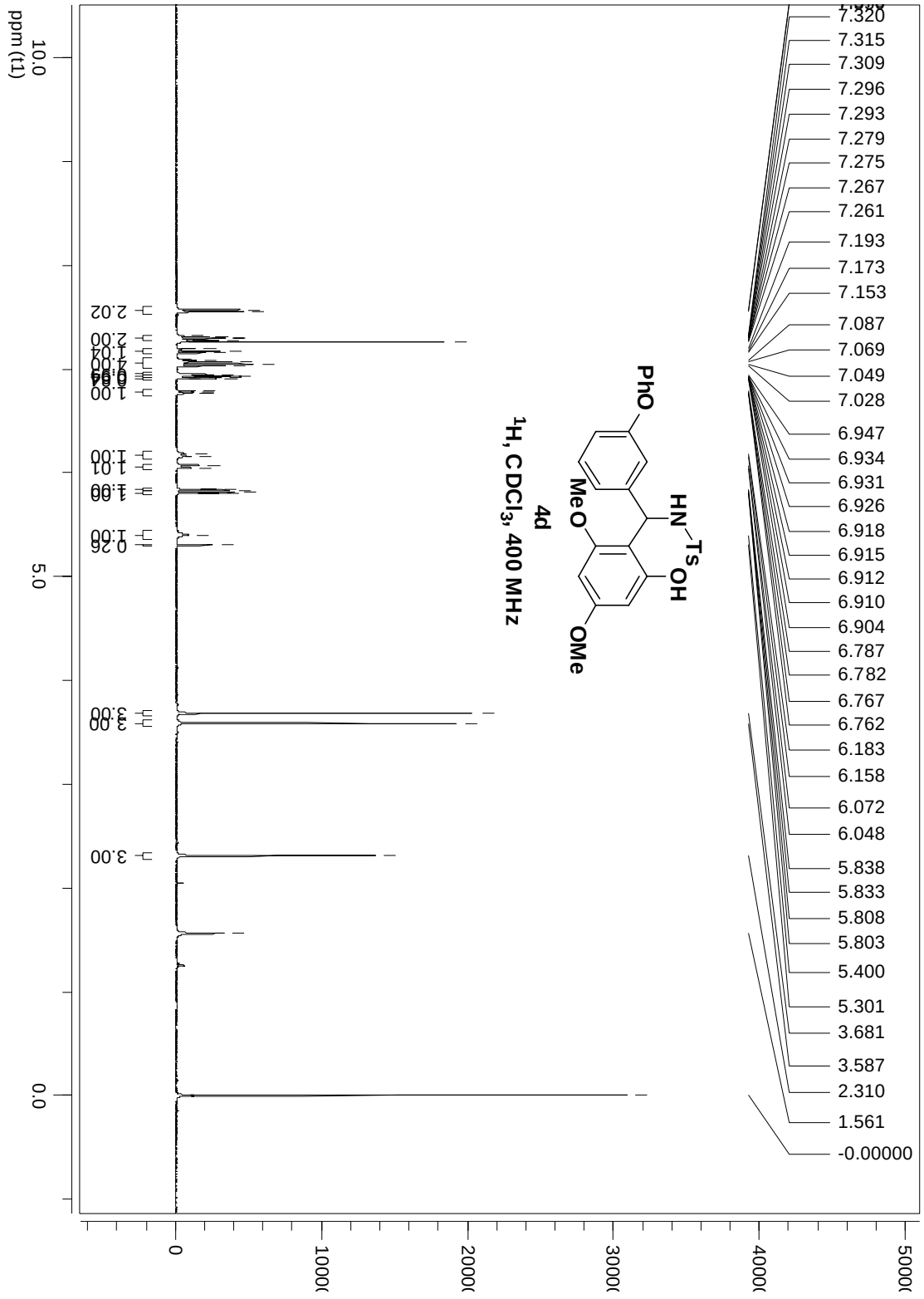

ppm (t1)
200
150
100
50
0
0
5000
10000
160.577
157.938
154.600
142.839
140.966
136.933
128.913
128.015
126.791
126.732
126.497
107.298
93.886
91.213
77.424
77.000
76.577
55.433
55.223
52.014
21.302
13C, CDCl3, 75 MHz
4a
MeO
OMe
OH HN
Ts
Ph

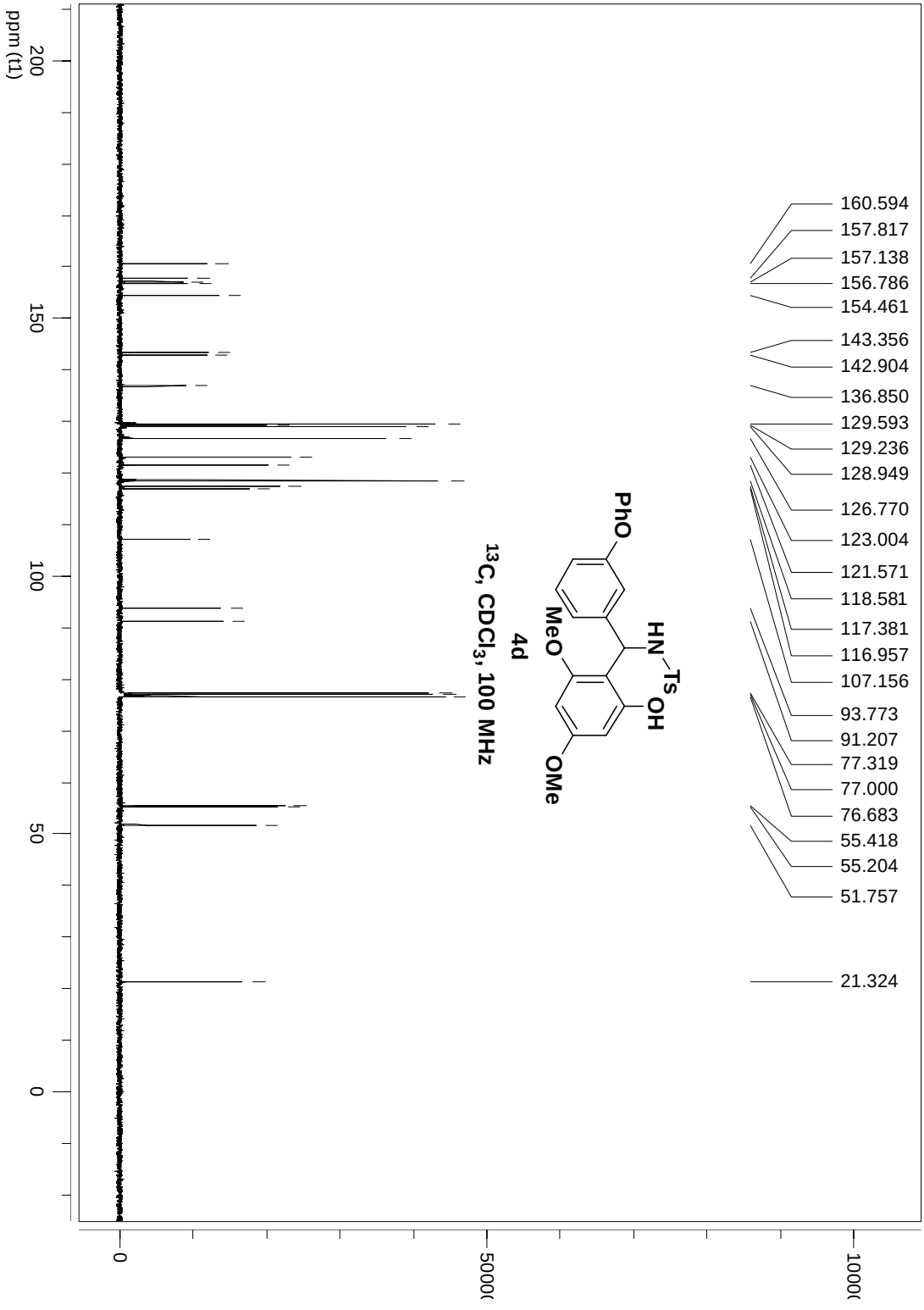

10.0
ppm (t1)
5.0
0.0
2.06
2.06
1.00
1.04
3.01
3.04
6.00
3.08
^{1}H, CDCl$_3$, 400 MHz
4b
CH$_3$
MeO
H$_3$C
Ts
NH
OH
OMe
7.563
7.542
7.260
7.039
7.019
6.848
6.806
6.175
6.150
6.015
5.990
5.860
5.849
5.844
5.822
5.817
3.680
3.588
2.313
2.204
1.608
-0.000000
0
10000
20000
30000
40000
50000
60000
70000
80000

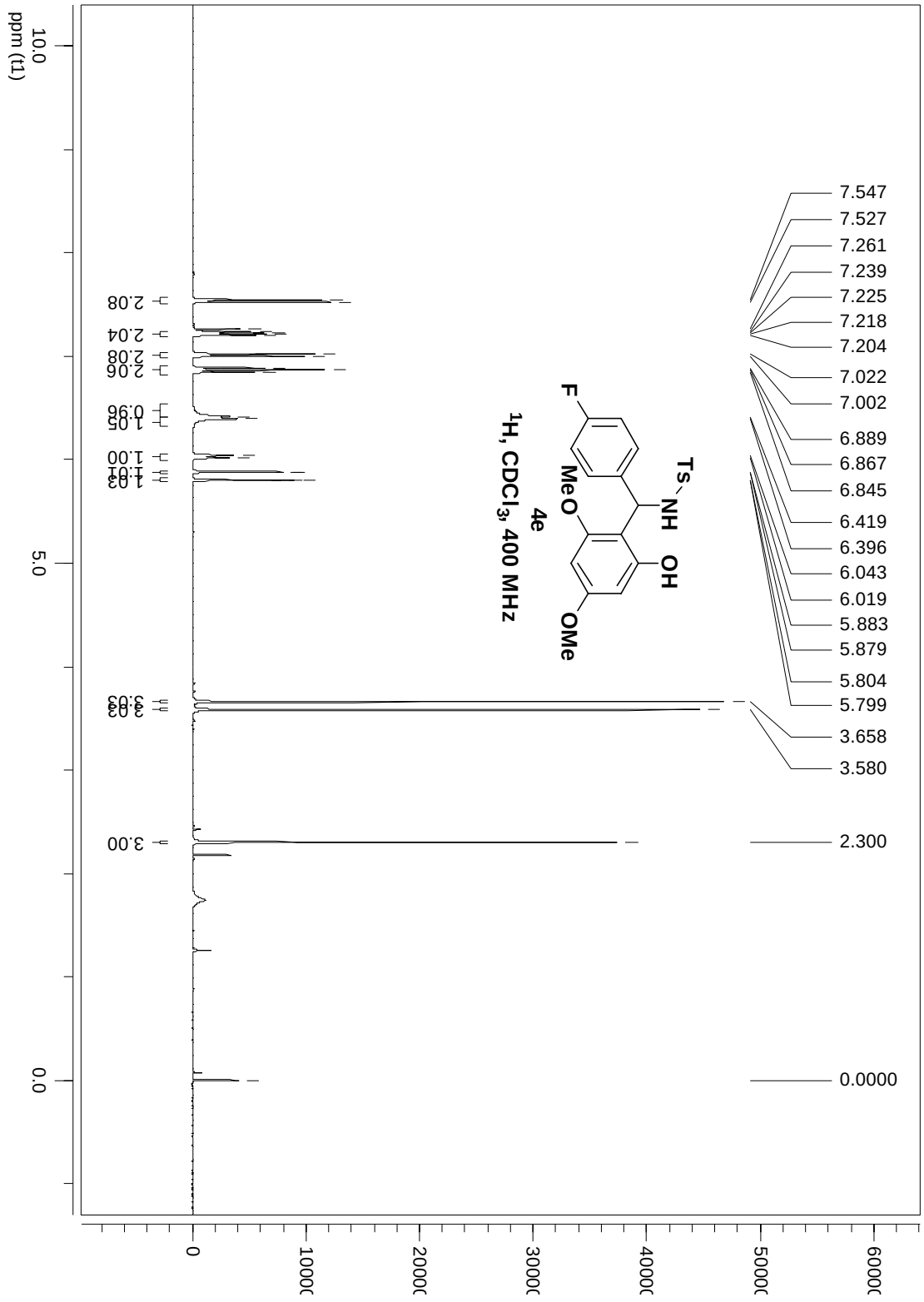

ppm (t1)
200
150
100
50
0
0
5000
10000
15000
20000
25000
30000
35000
160.370
157.801
154.646
142.768
140.648
137.405
136.735
128.818
128.482
126.692
124.284
107.008
93.717
91.020
77.317
77.000
76.681
55.357
55.119
51.961
21.221
13C, CDCl3, 100 MHz
4b
H3C
CH3
MeO
Ts
NH
OH
OMe

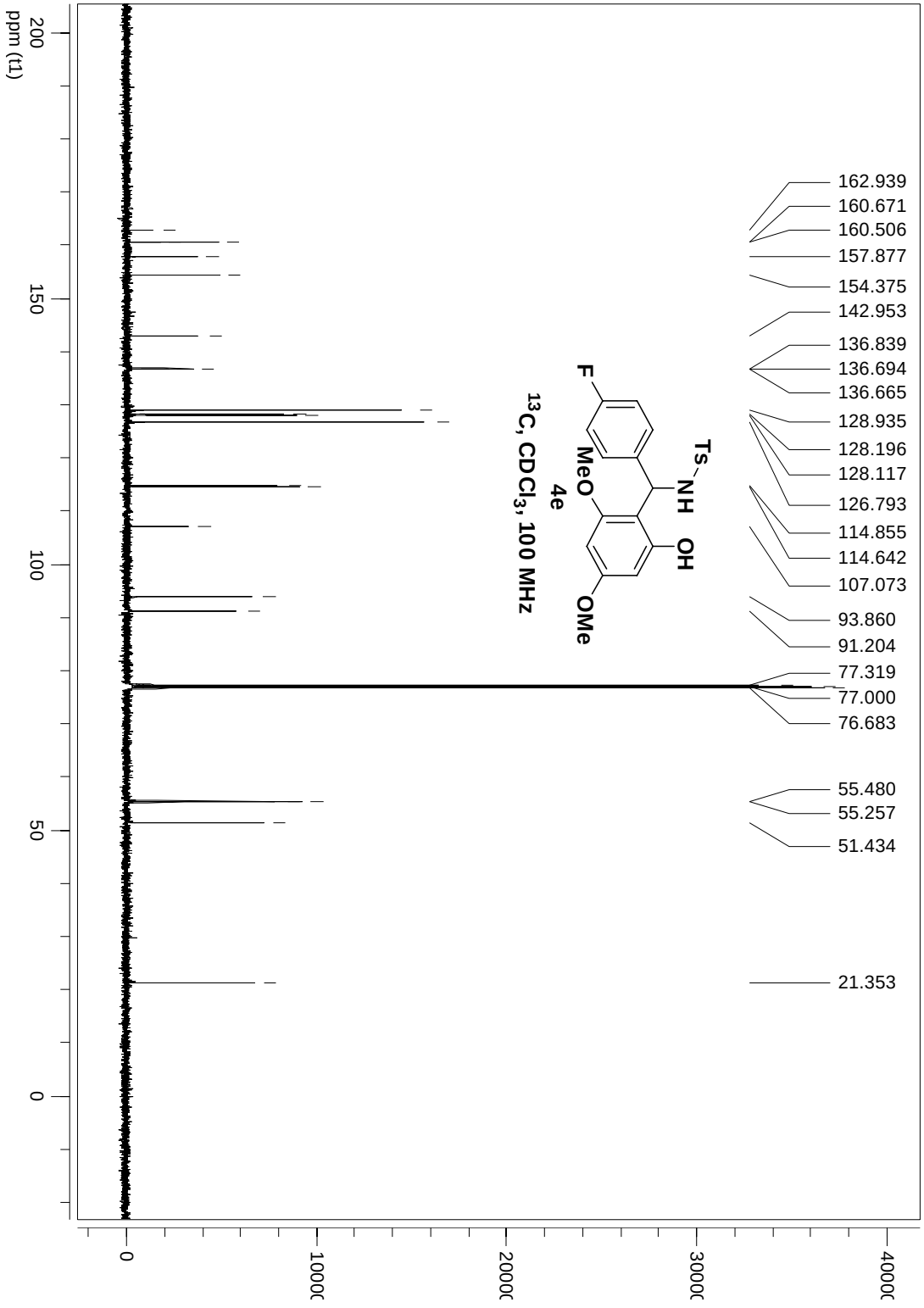

10.0
ppm (t1)
5.0
0.0
2.00
4.01
2.00
1.00
0.91
1.03
1.00
3.00
3.00
9.14
7.562
7.541
7.260
7.238
7.216
7.197
7.176
7.031
7.011
6.311
6.287
6.176
6.055
6.033
5.862
5.858
5.819
5.815
3.662
3.591
2.303
1.255
-0.000000
0
10000
20000
30000
40000
50000
60000
1H, CDCl3, 400 MHz
4c
MeO
OMe
NH
Ts
OH

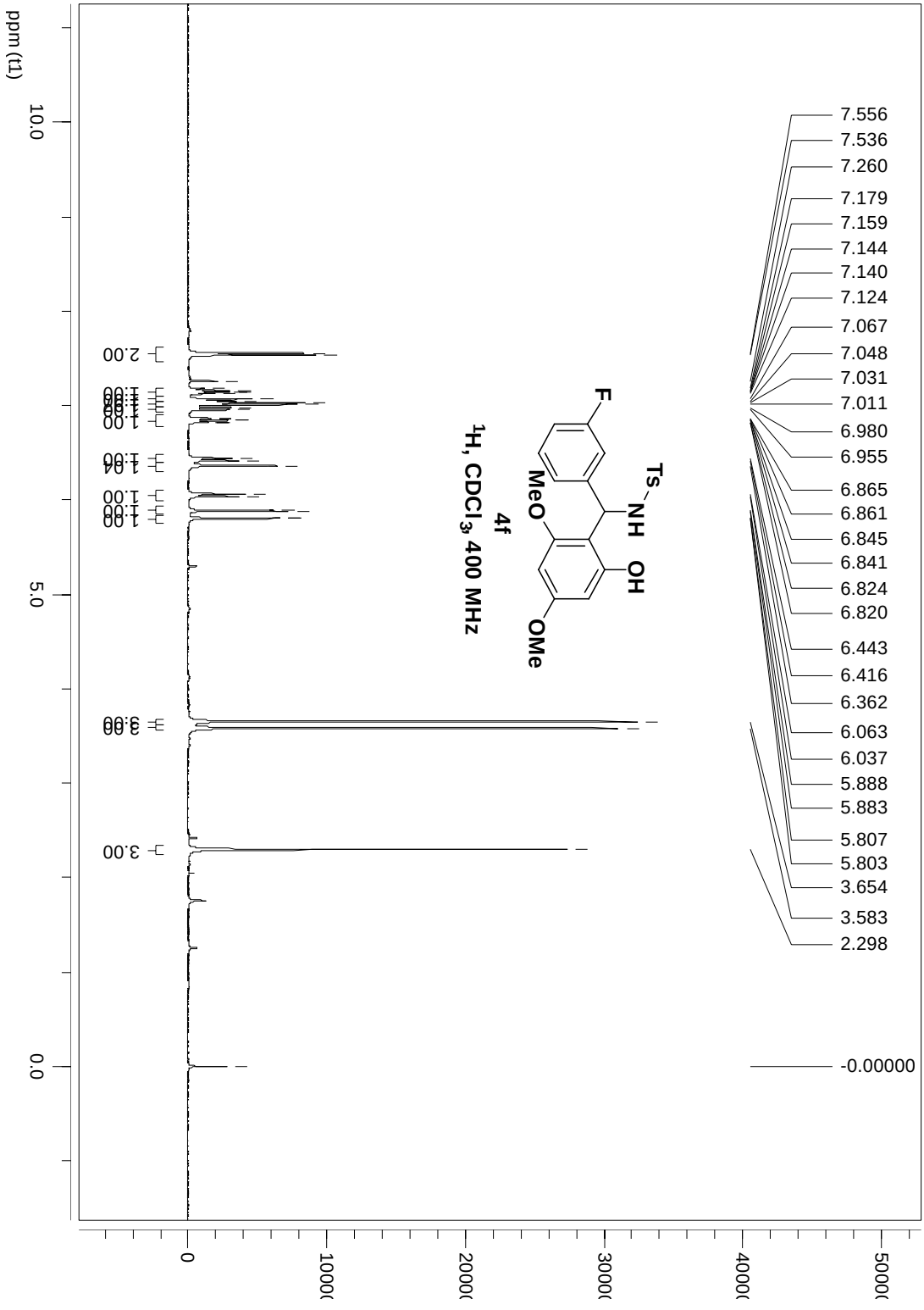

ppm (t1)
200
150
100
50
0
0
50000
160.545
158.034
154.604
149.653
142.706
137.790
137.121
128.889
126.911
126.283
125.013
107.474
94.055
91.319
77.423
77.000
76.576
55.475
55.248
51.984
34.332
31.308
21.338
13C, CDCl3, 75 MHz
4c
MeO
OMe
OH
NH
Ts

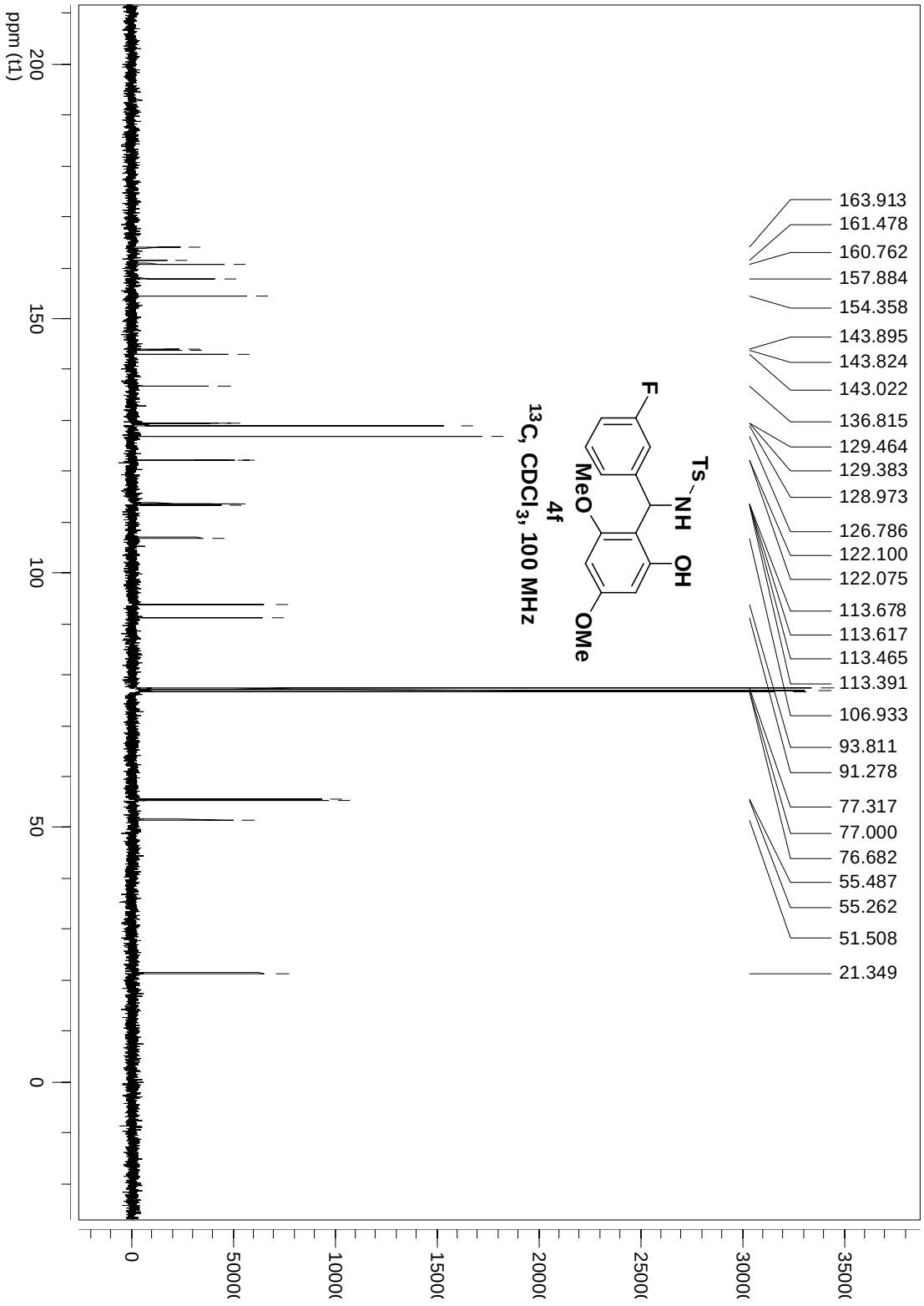

ppm (t1)
10.0
5.0
0.0
0
10000
20000
30000
40000
50000
7.320
7.315
7.309
7.296
7.293
7.279
7.275
7.267
7.261
7.193
7.173
7.153
7.087
7.069
7.049
7.028
6.947
6.934
6.931
6.926
6.918
6.915
6.912
6.910
6.904
6.787
6.782
6.767
6.762
6.183
6.158
6.072
6.048
5.838
5.833
5.808
5.803
5.400
5.301
3.681
3.587
2.310
1.561
-0.00000
2.02
2.00
1.02
1.00
1.01
1.00
1.00
0.26
1.00
3.00
3.00
3.00
PhO
HN
Ts
OH
MeO
OMe
4d
1H, CDCl3, 400 MHz

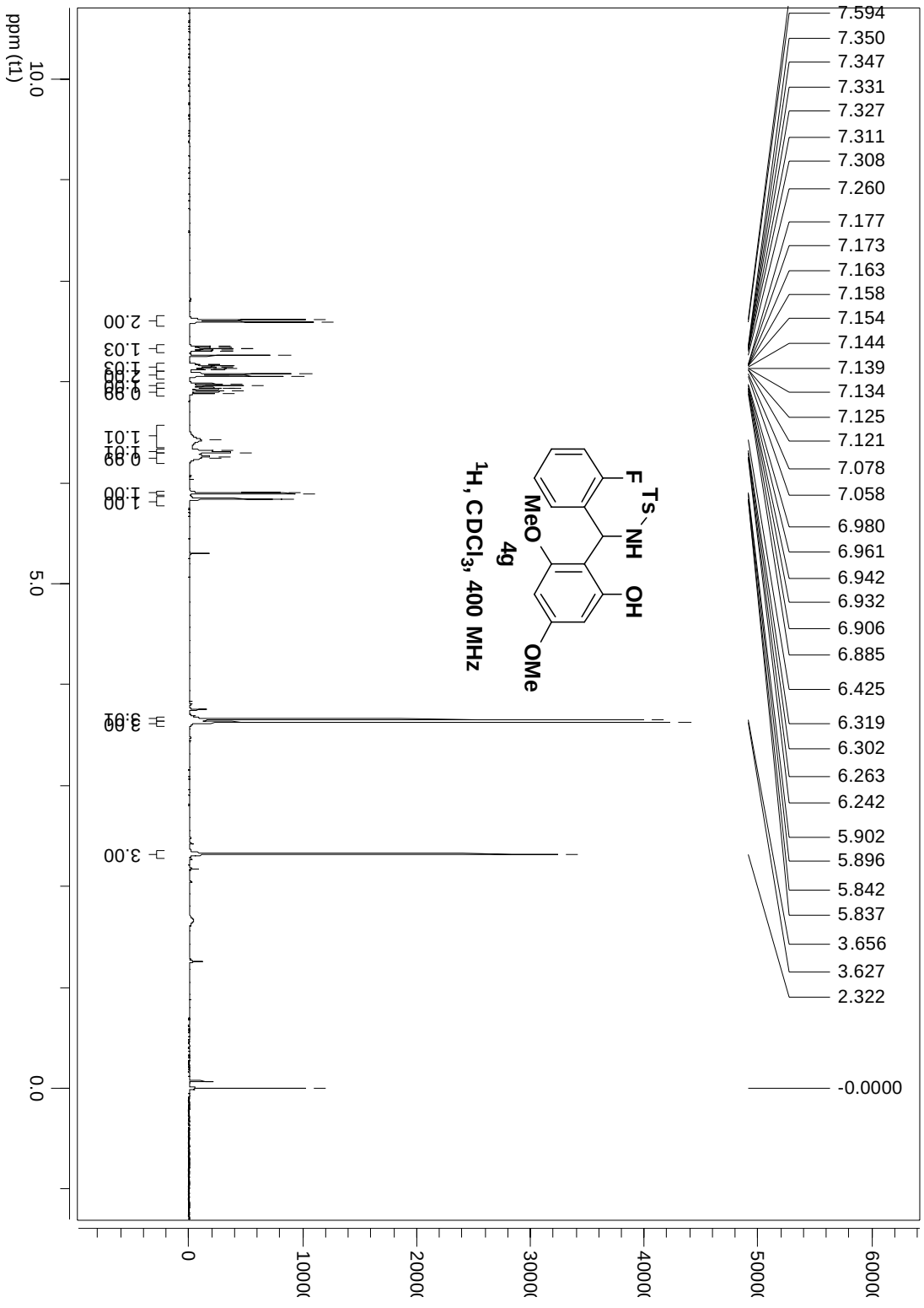

ppm (t1)
200
150
100
50
0
^{13}C, CDCl$_3$, 100 MHz
4d
PhO
HN
Ts
OH
MeO
OMe
160.594
157.817
157.138
156.786
154.461
143.356
142.904
136.850
129.593
129.236
128.949
126.770
123.004
121.571
118.581
117.381
116.957
107.156
93.773
91.207
77.319
77.000
76.683
55.418
55.204
51.757
21.324
0
5000
10000

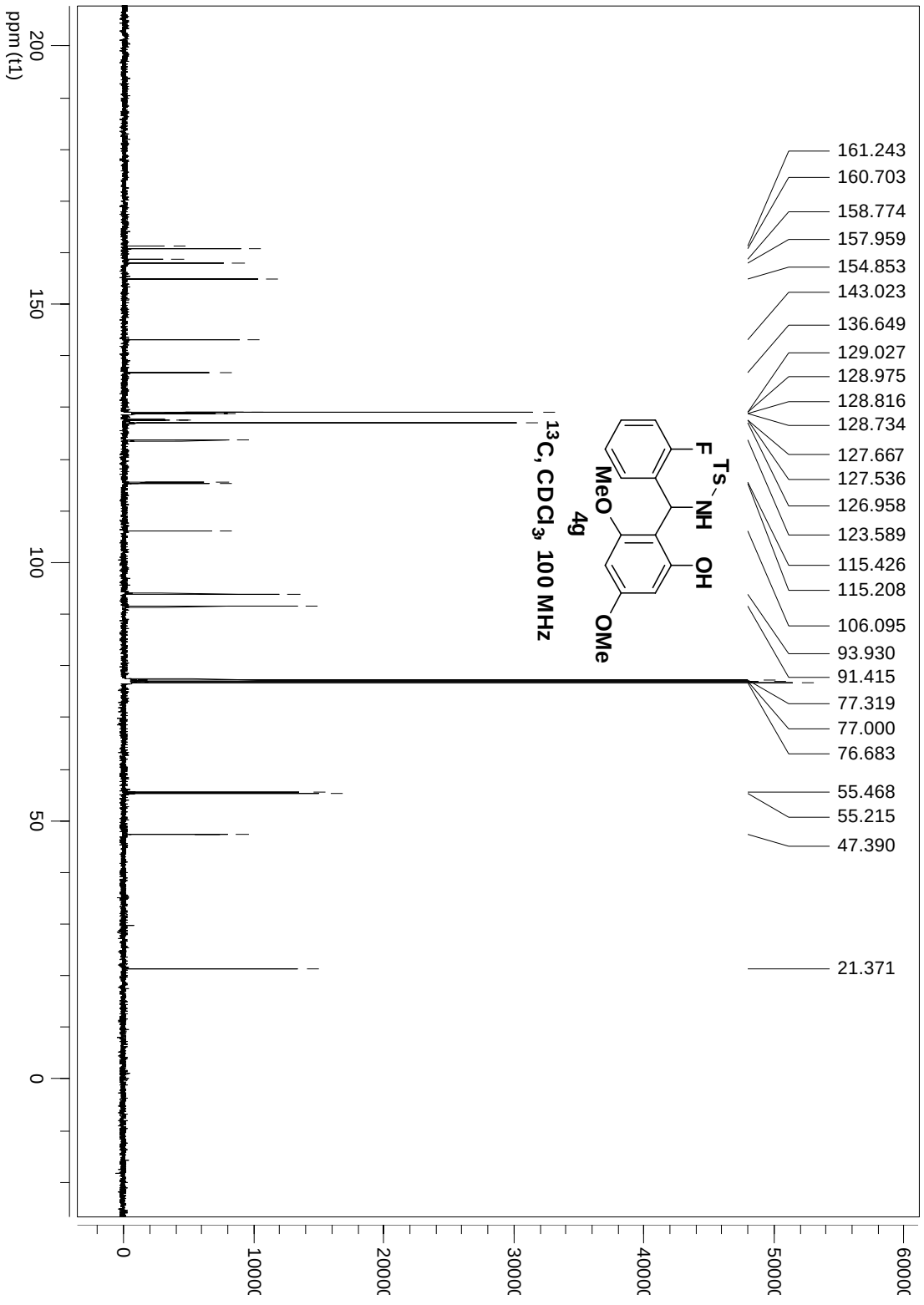

10.0
ppm (t1)
5.0
0.0
2.08
2.04
2.08
2.06
0.96
1.05
1.00
1.01
1.03
3.03
3.00
7.547
7.527
7.261
7.239
7.225
7.218
7.204
7.022
7.002
6.889
6.867
6.845
6.419
6.396
6.043
6.019
5.883
5.879
5.804
5.799
3.658
3.580
2.300
0.0000
F
MeO
OMe
NH
Ts
OH
4e
1H, CDCl3, 400 MHz
0
10000
20000
30000
40000
50000
60000

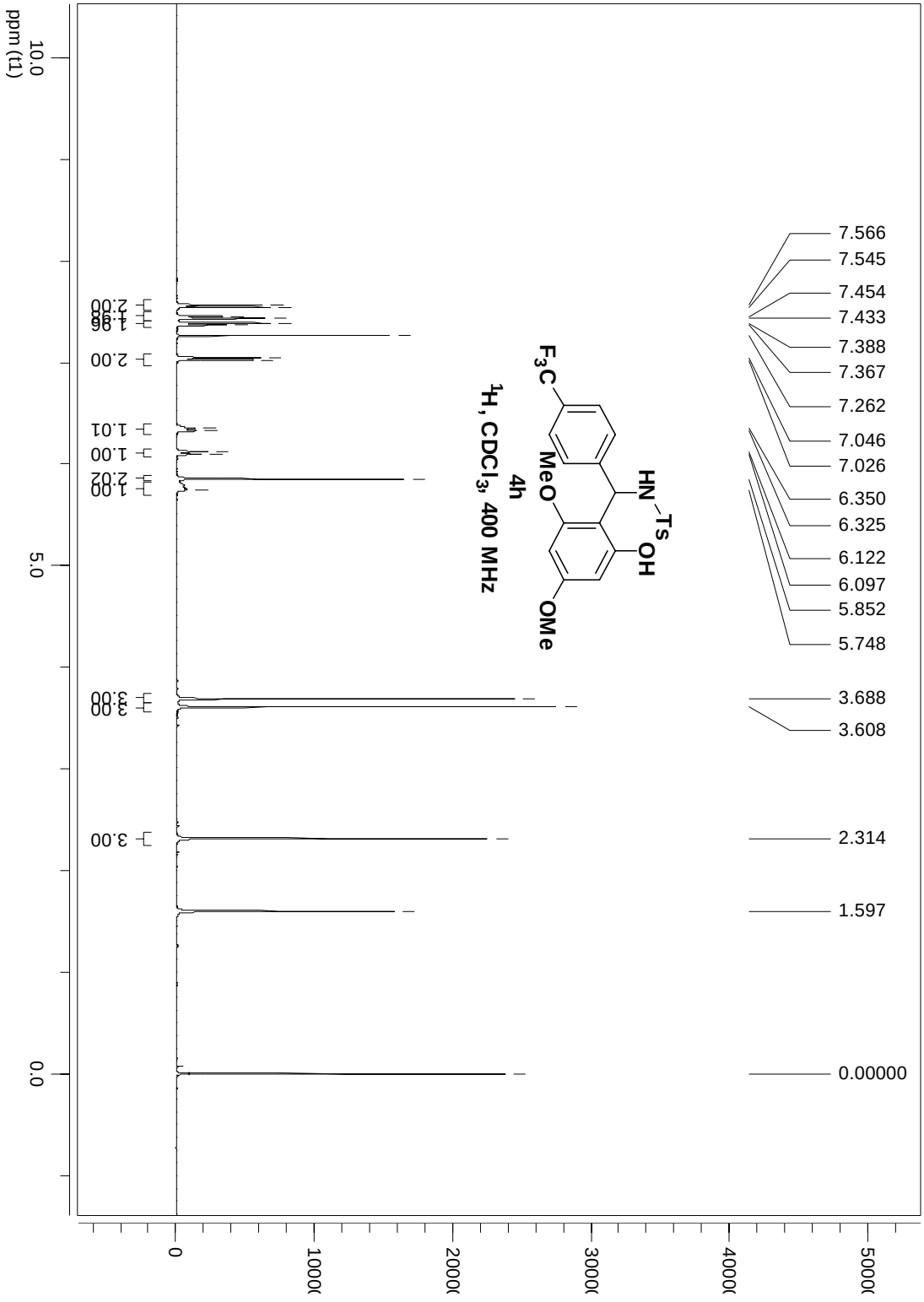

ppm (t1)
200
150
100
50
0
0
10000
20000
30000
40000
162.939
160.671
160.506
157.877
154.375
142.953
136.839
136.694
136.665
128.935
128.196
128.117
126.793
114.855
114.642
107.073
93.860
91.204
77.319
77.000
76.683
55.480
55.257
51.434
21.353
13C, CDCl3, 100 MHz
4e
F
MeO
OMe
NH
Ts
OH

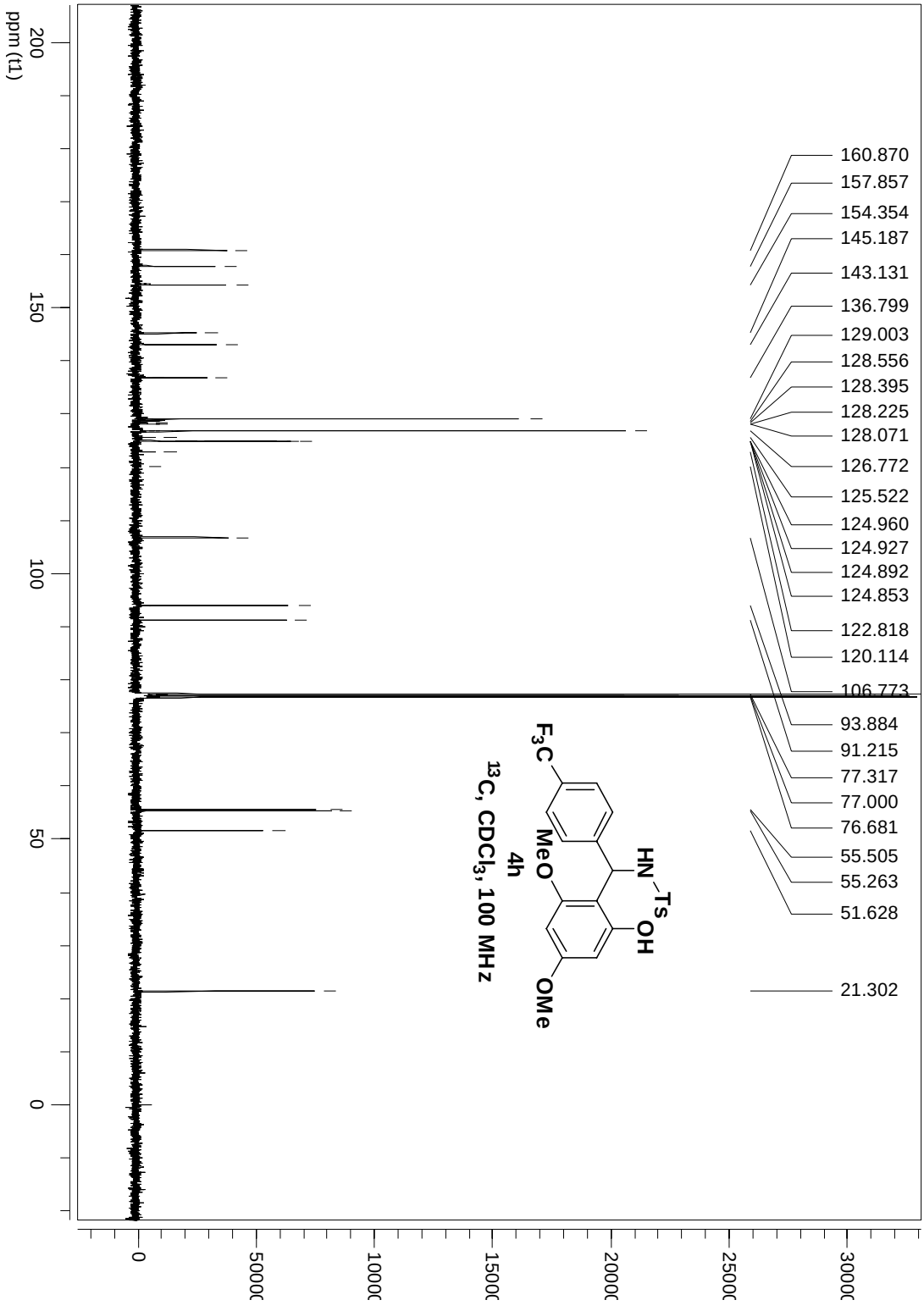

ppm (t1)
10.0
5.0
0.0
2.00
1.00
1.00
1.00
1.04
1.00
1.00
1.00
3.00
3.00
0
1000
2000
3000
4000
5000
7.556
7.536
7.260
7.179
7.159
7.144
7.140
7.124
7.067
7.048
7.031
7.011
6.980
6.955
6.865
6.861
6.845
6.841
6.824
6.820
6.443
6.416
6.362
6.063
6.037
5.888
5.883
5.807
5.803
3.654
3.583
2.298
-0.00000
F
Ts
NH
OH
MeO
OMe
4f
1H, CDCl3, 400 MHz

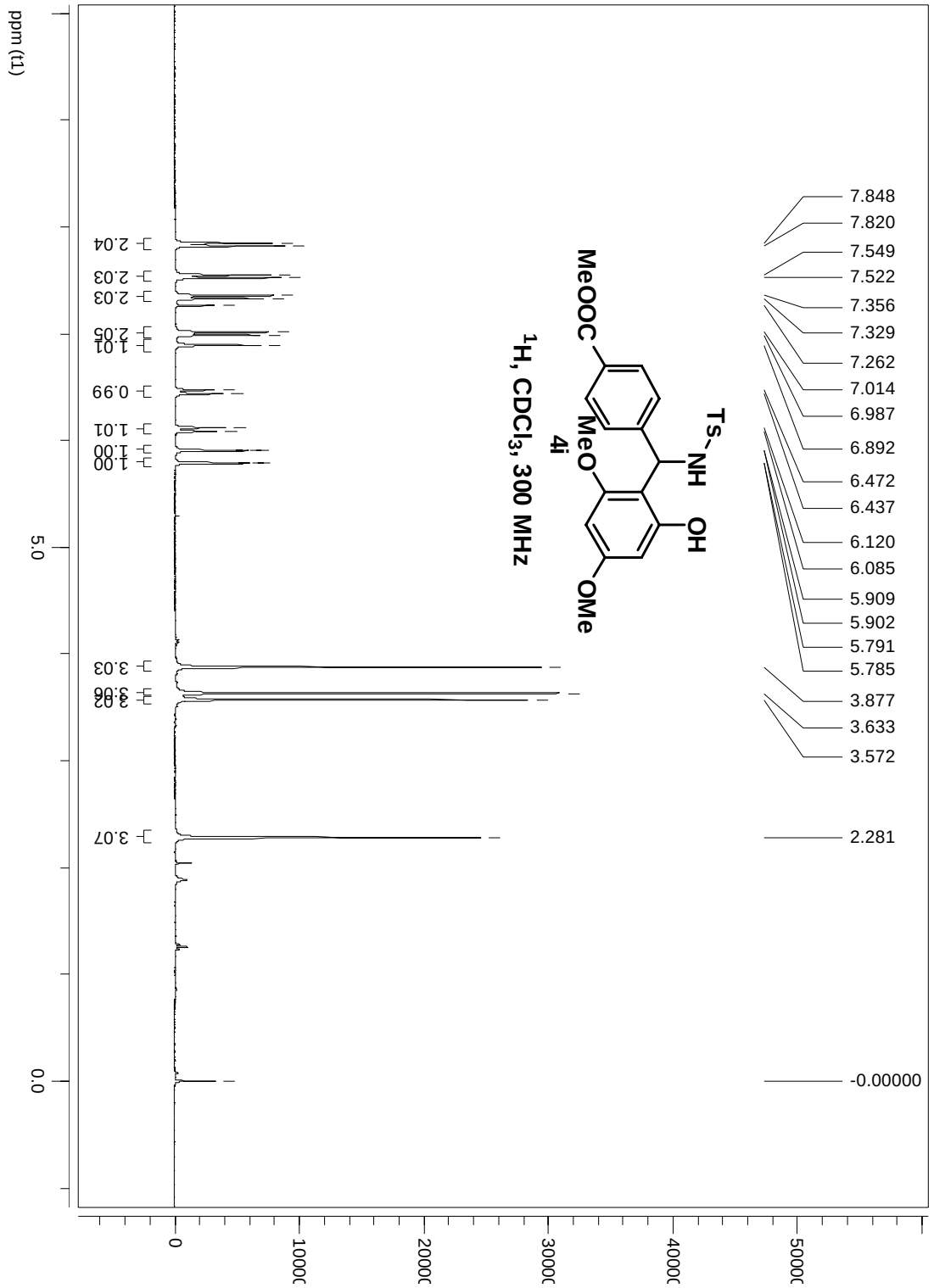


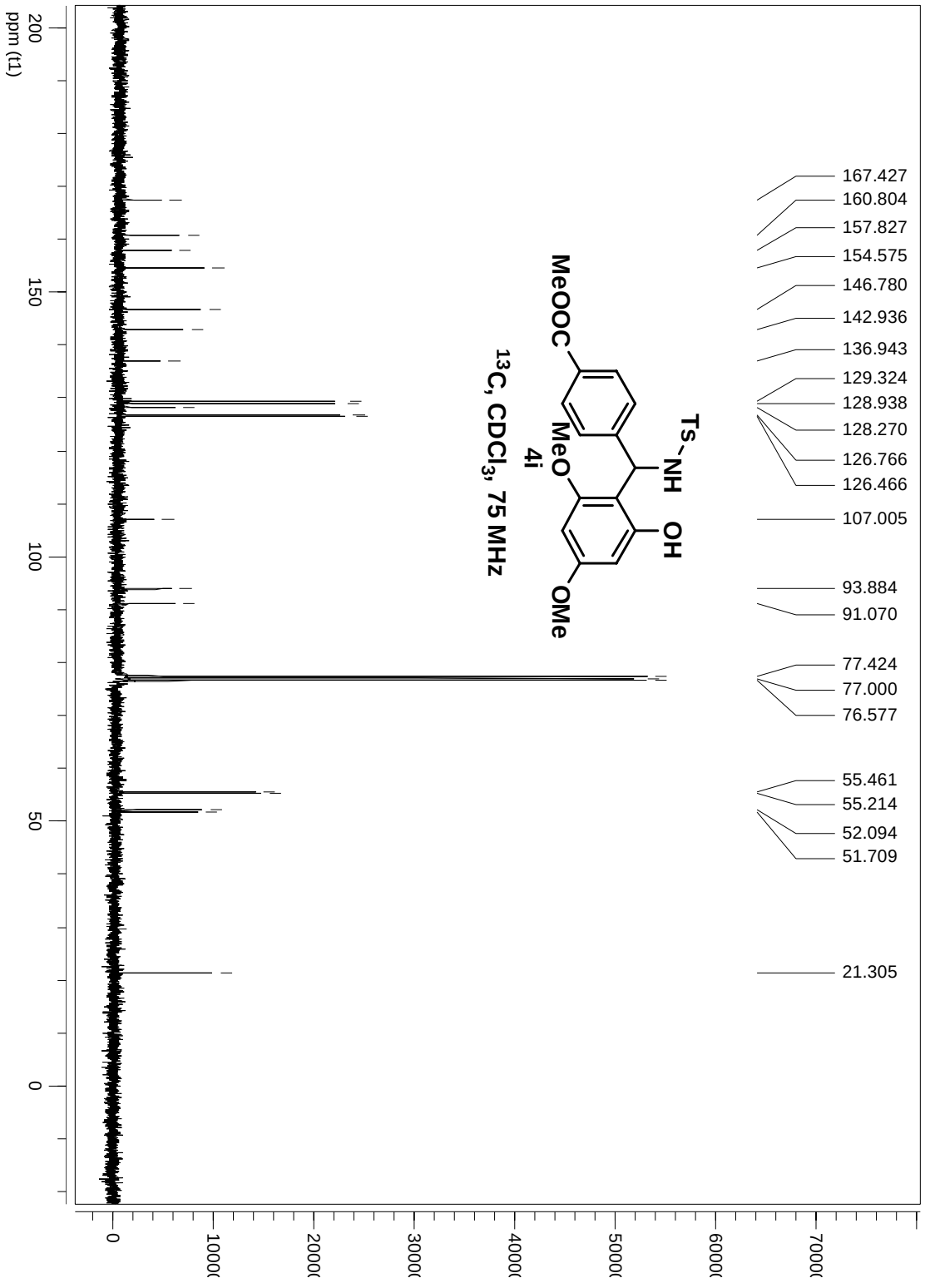

7.594
7.350
7.347
7.331
7.327
7.311
7.308
7.260
7.177
7.173
7.163
7.158
7.154
7.144
7.139
7.134
7.125
7.121
7.078
7.058
6.980
6.961
6.942
6.932
6.906
6.885
6.425
6.319
6.302
6.263
6.242
5.902
5.896
5.842
5.837
3.656
3.627
2.322
-0.0000
2.00
1.03
1.03
0.99
1.01
1.00
3.00
3.00
ppm (t1)
10.0
5.0
0.0
0
1000
2000
3000
4000
5000
6000
F
Ts
NH
OH
MeO
OMe
4g
^{1}H, CDCl$_3$, 400 MHz

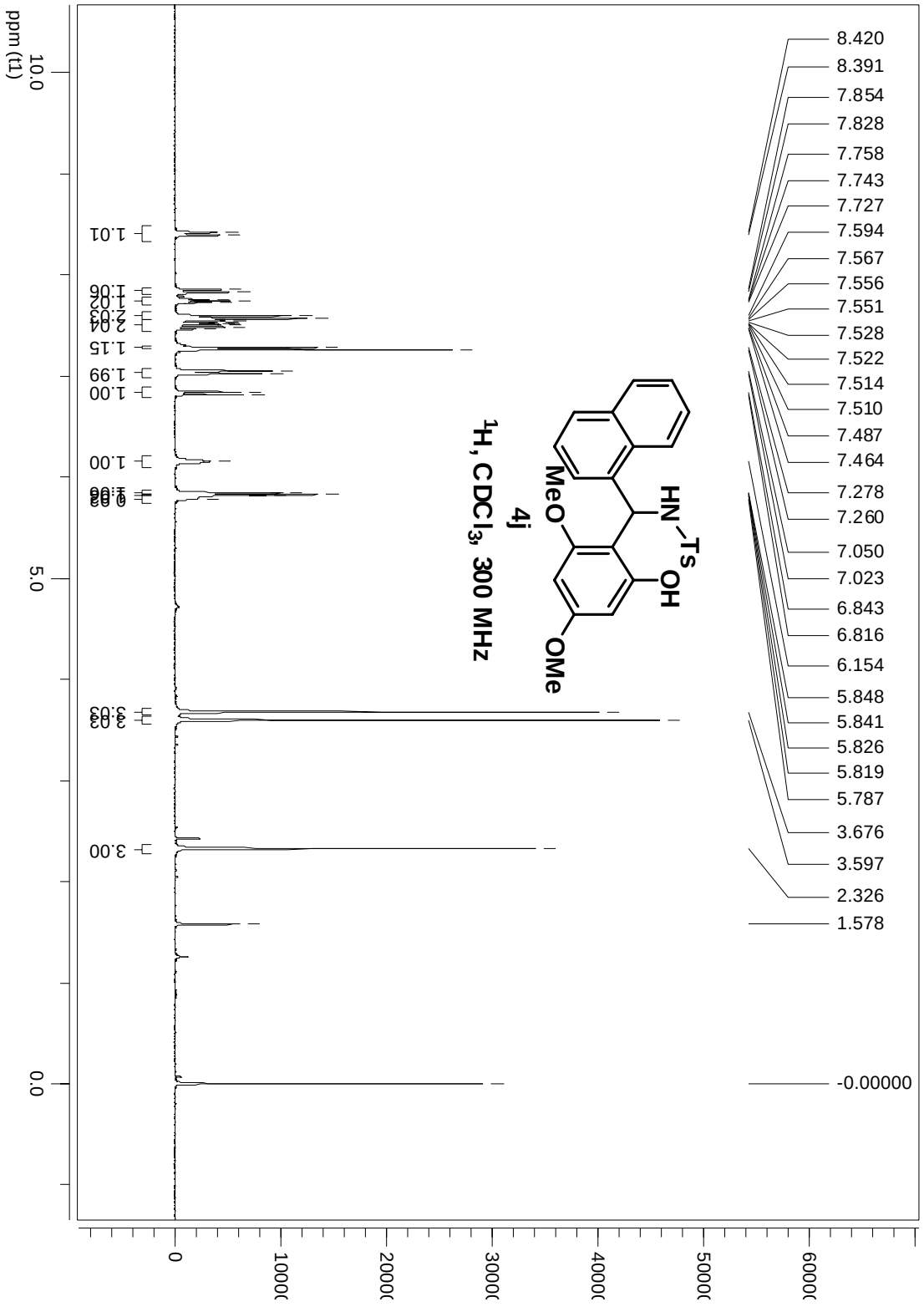

ppm (t1)
200
150
100
50
0
0
10000
20000
30000
40000
50000
60000
161.243
160.703
158.774
157.959
154.853
143.023
136.649
129.027
128.975
128.816
128.734
127.667
127.536
126.958
123.589
115.426
115.208
106.095
93.930
91.415
77.319
77.000
76.683
55.468
55.215
47.390
21.371
13C, CDCl3, 100 MHz
4g
MeO
OMe
NH
Ts
F
OH

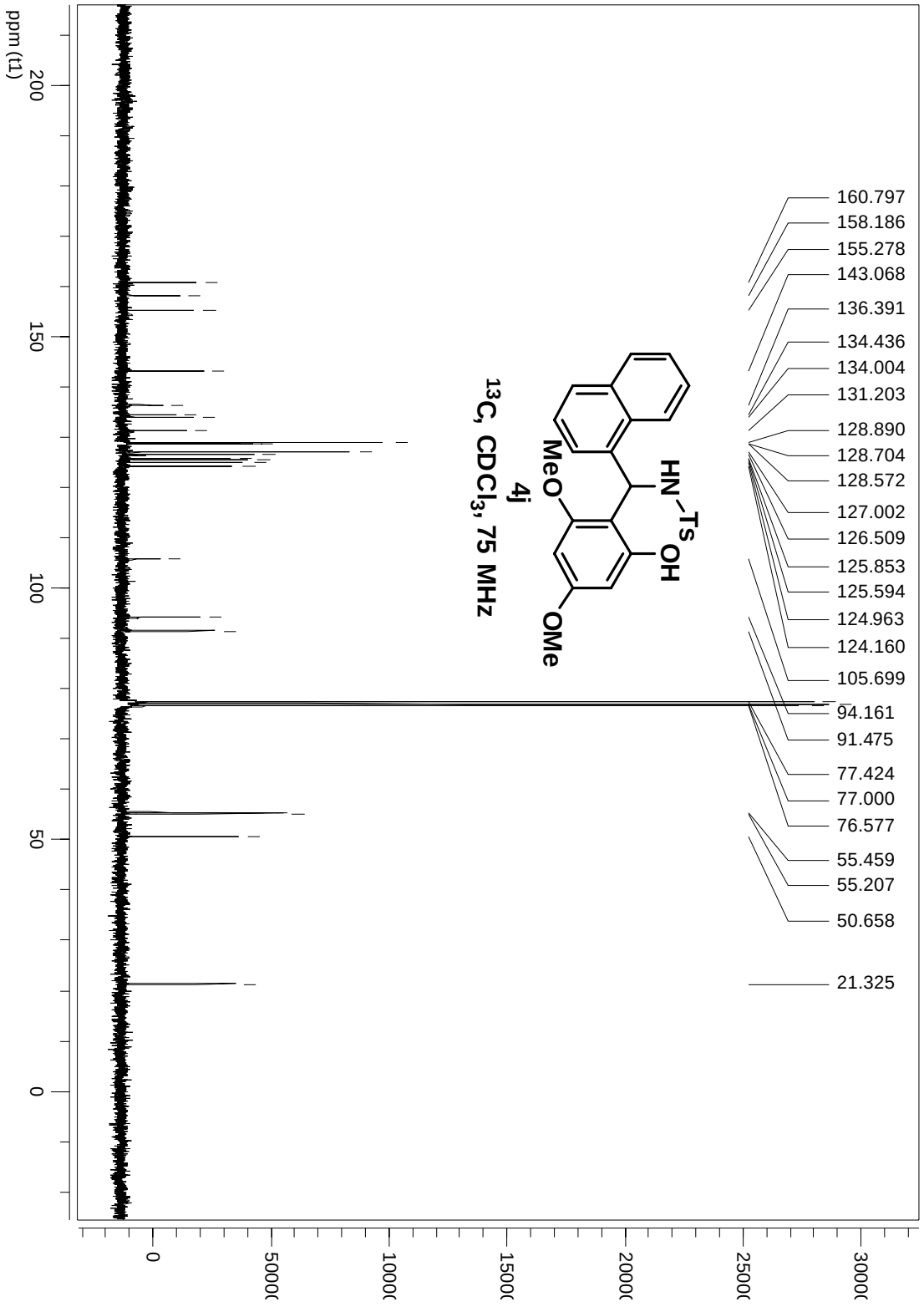

ppm (t1)
10.0
5.0
0.0
0
1000
2000
3000
4000
5000
7.566
7.545
7.454
7.433
7.388
7.367
7.262
7.046
7.026
6.350
6.325
6.122
6.097
5.852
5.748
3.688
3.608
2.314
1.597
0.00000
3.00
3.00
3.00
2.00
1.01
1.00
2.02
1.00
1.98
1.96
2.00
4h
1H, CDCl3, 400 MHz
F3C
MeO
OMe
HN
Ts
OH

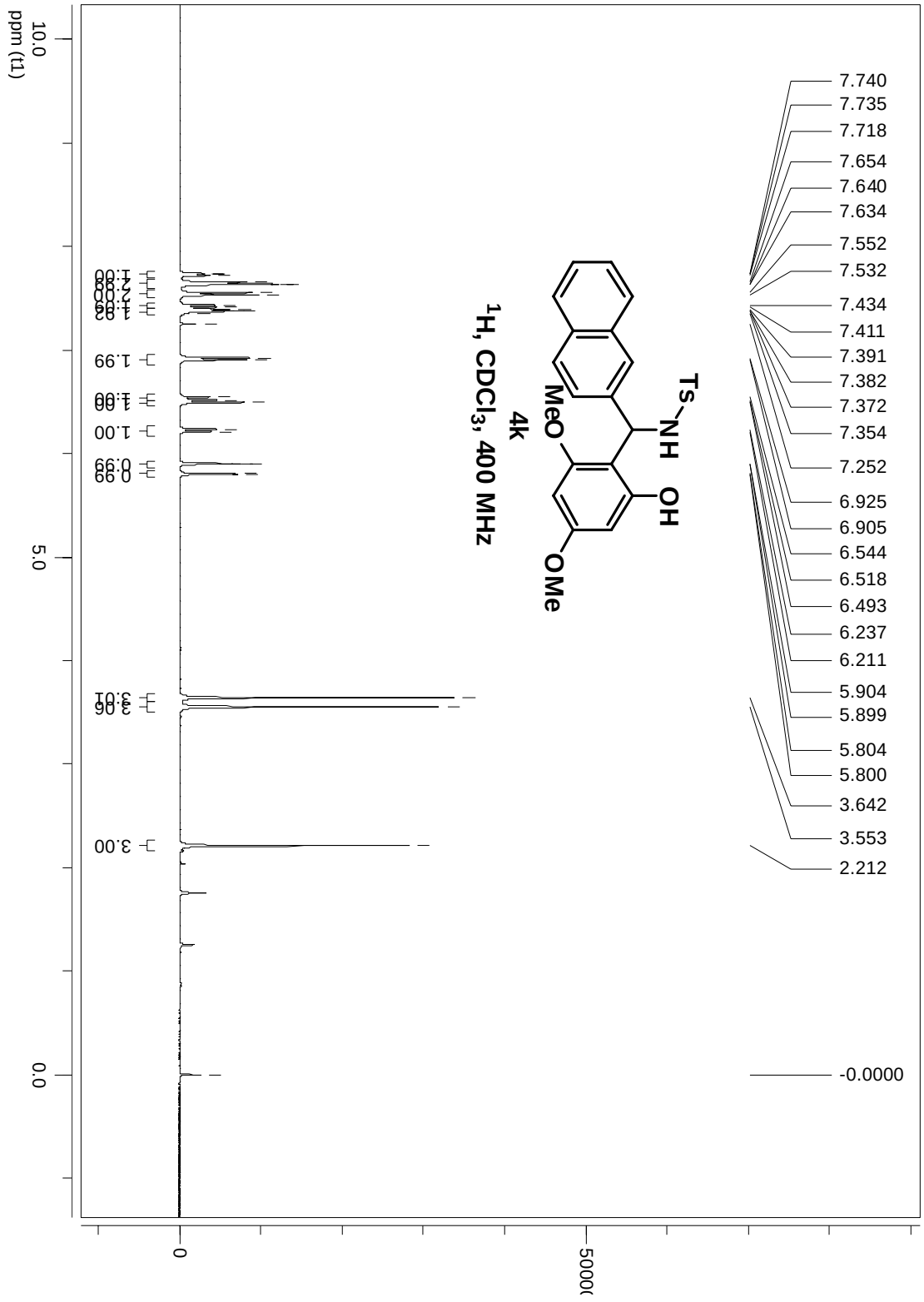

ppm (t1)
200
150
100
50
0
160.870
157.857
154.354
145.187
143.131
136.799
129.003
128.556
128.395
128.225
128.071
126.772
125.522
124.960
124.927
124.892
124.853
122.818
120.114
106.773
93.884
91.215
77.317
77.000
76.681
55.505
55.263
51.628
21.302
0
5000
10000
15000
20000
25000
30000
13C, CDCl3, 100 MHz
4h
F3C
MeO
HN
Ts
OH
OMe

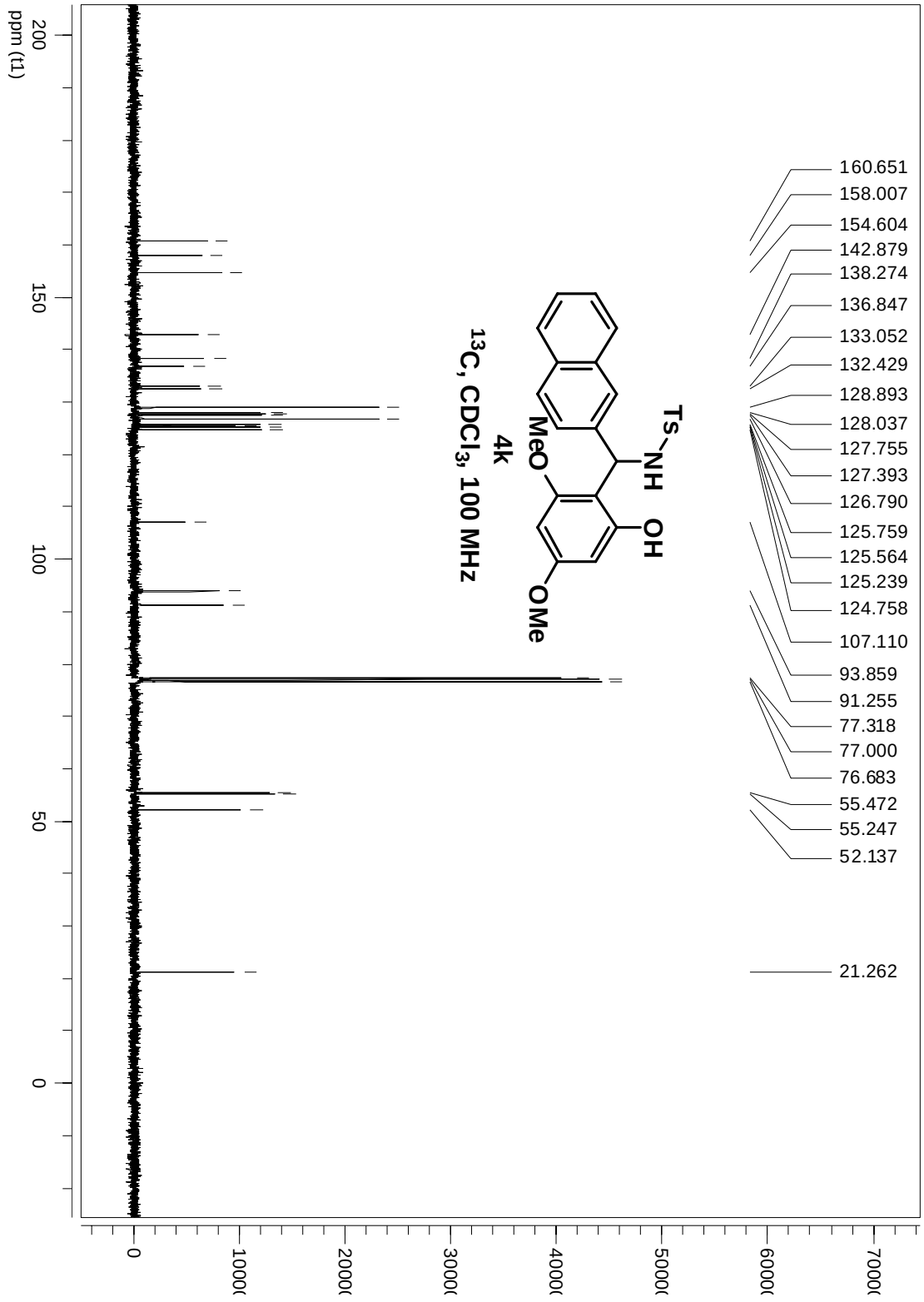

ppm (t1)
5.0
0.0
2.04
2.03
2.03
2.05
1.01
0.99
1.01
1.00
1.00
3.03
3.06
3.02
3.07
^{1}H, CDCl$_3$, 300 MHz
4i
MeOOC
MeO
OMe
NH
Ts
OH
7.848
7.820
7.549
7.522
7.356
7.329
7.262
7.014
6.987
6.892
6.472
6.437
6.120
6.085
5.909
5.902
5.791
5.785
3.877
3.633
3.572
2.281
-0.00000
0
10000
20000
30000
40000
50000

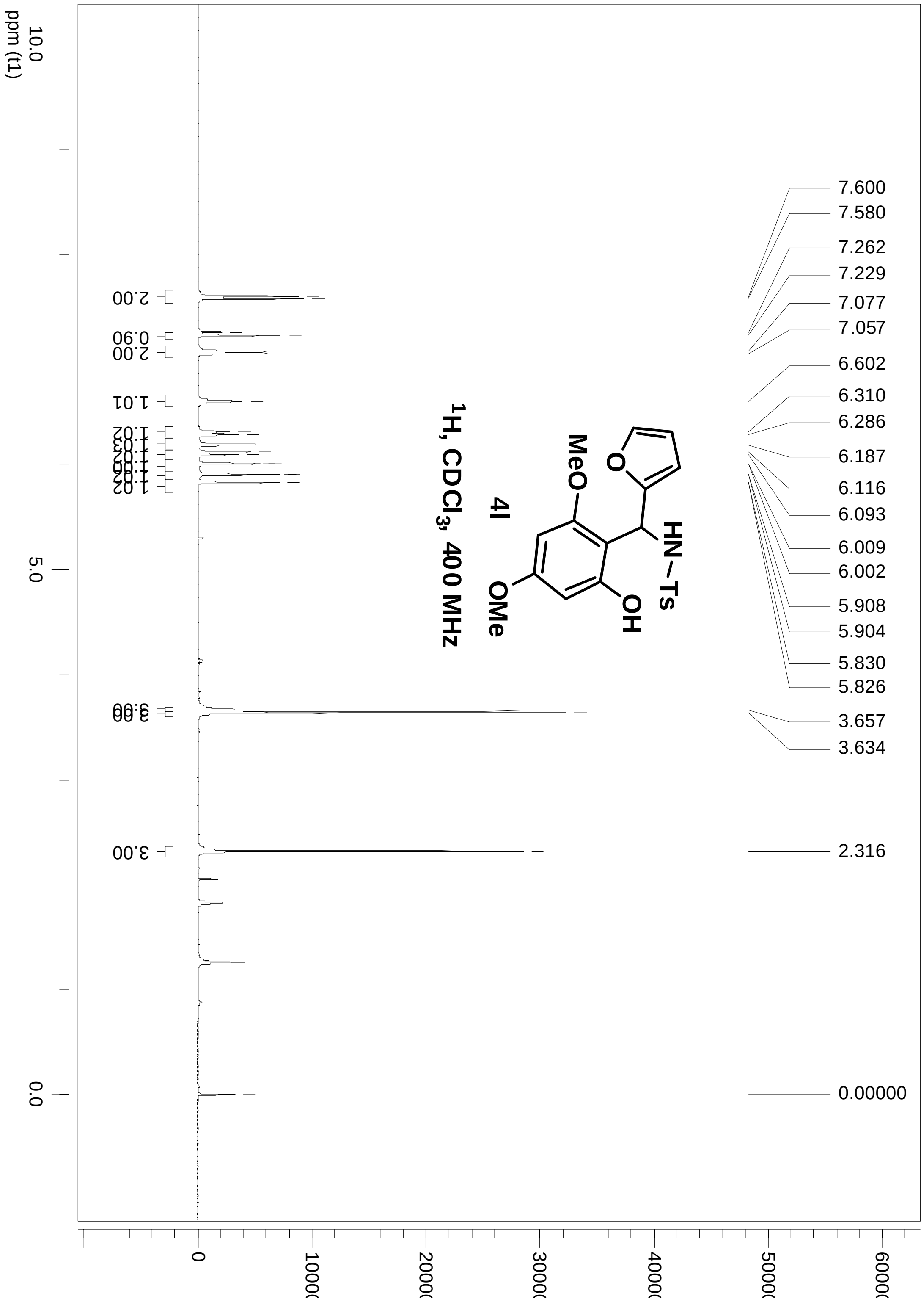

ppm (t1)
200
150
100
50
0
0
10000
20000
30000
40000
50000
60000
70000
MeOOC
MeO
OMe
OH
NH
Ts
4i
^{13}C, $CDCl_3$, 75 MHz
167.427
160.804
157.827
154.575
146.780
142.936
136.943
129.324
128.938
128.270
126.766
126.466
107.005
93.884
91.070
77.424
77.000
76.577
55.461
55.214
52.094
51.709
21.305

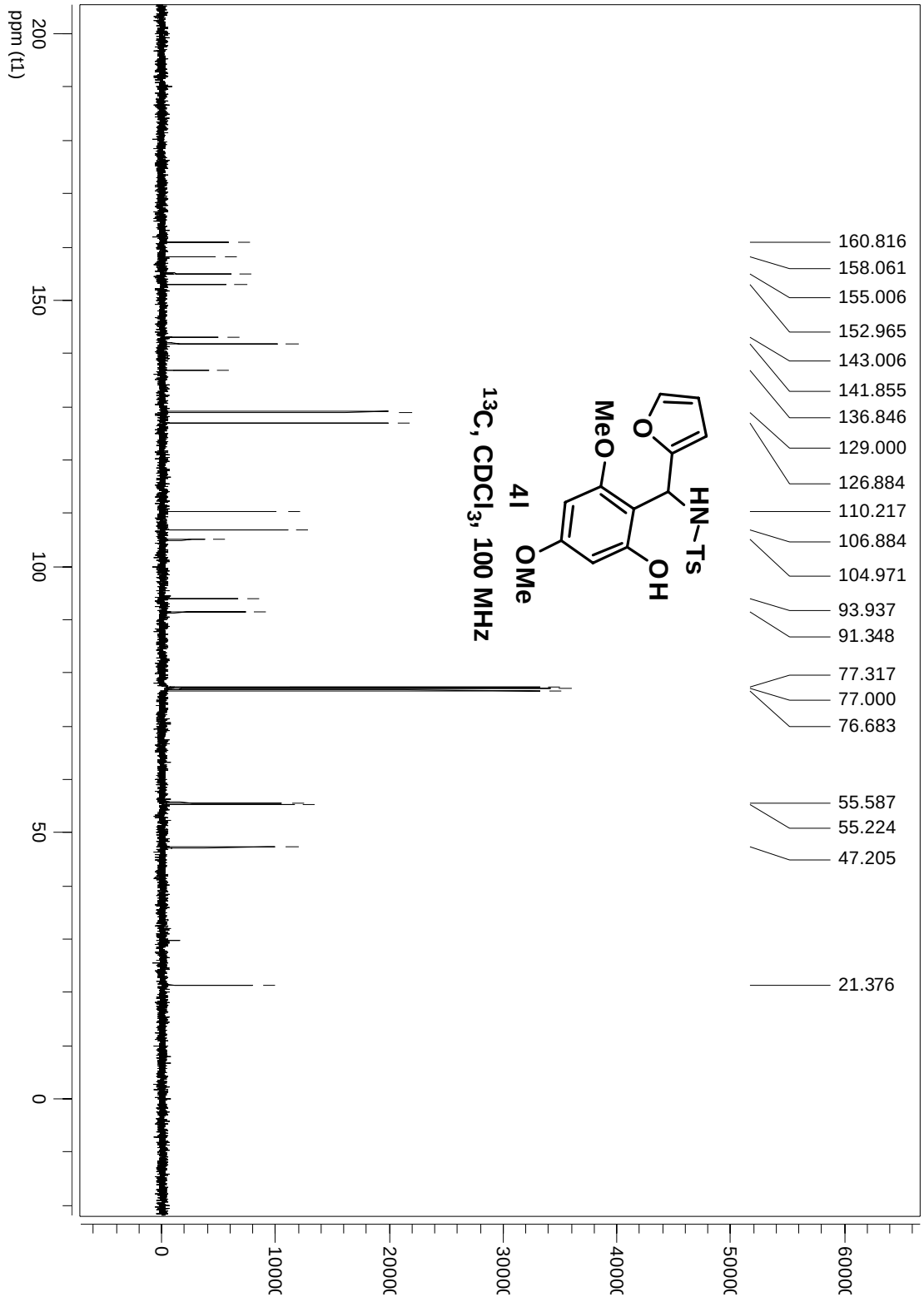

ppm (t1)
10.0
5.0
0.0
1.01
1.06
1.02
2.03
2.04
1.15
1.99
1.00
1.00
3.03
3.00
0
10000
20000
30000
40000
50000
60000
8.420
8.391
7.854
7.828
7.758
7.743
7.727
7.594
7.567
7.556
7.551
7.528
7.522
7.514
7.510
7.487
7.464
7.278
7.260
7.050
7.023
6.843
6.816
6.154
5.848
5.841
5.826
5.819
5.787
3.676
3.597
2.326
1.578
-0.00000
4j
^{1}H, CDCl$_3$, 300 MHz
MeO
OMe
HN
Ts
OH

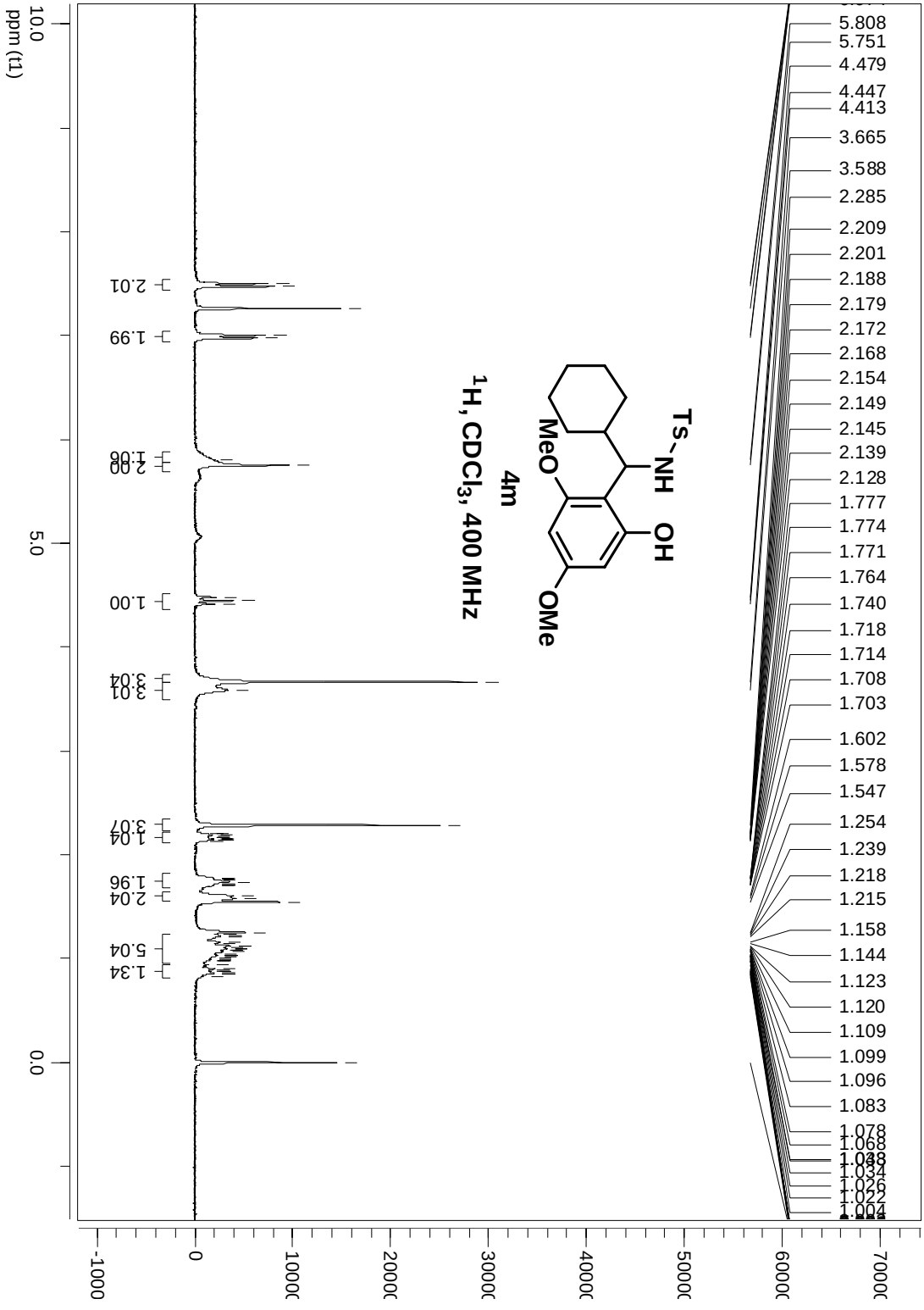

ppm (t1)
200
150
100
50
0
0
5000
10000
15000
20000
25000
30000
160.797
158.186
155.278
143.068
136.391
134.436
134.004
131.203
128.890
128.704
128.572
127.002
126.509
125.853
125.594
124.963
124.160
105.699
94.161
91.475
77.424
77.000
76.577
55.459
55.207
50.658
21.325
4j
13C, CDCl3, 75 MHz
MeO
OMe
HN
Ts
OH

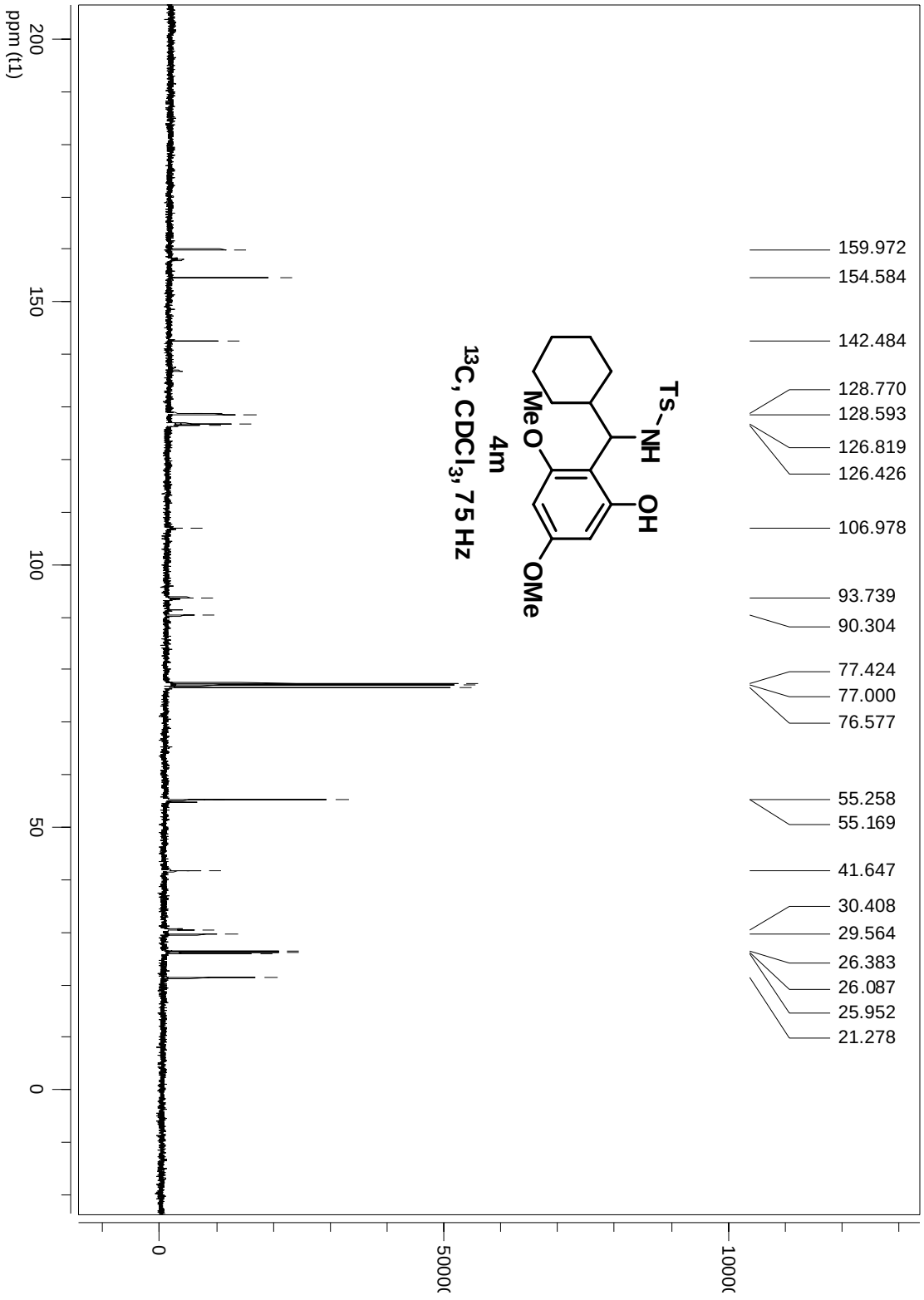

10.0
ppm (t1)
5.0
0.0
0
50000
1.00
1.99
1.00
1.00
0.99
3.01
3.00
7.740
7.735
7.718
7.654
7.640
7.634
7.552
7.532
7.434
7.411
7.391
7.382
7.372
7.354
7.252
6.925
6.905
6.544
6.518
6.493
6.237
6.211
5.904
5.899
5.804
5.800
3.642
3.553
2.212
-0.0000
4k
1H, CDCl3, 400 MHz
MeO
OMe
NH
Ts
OH

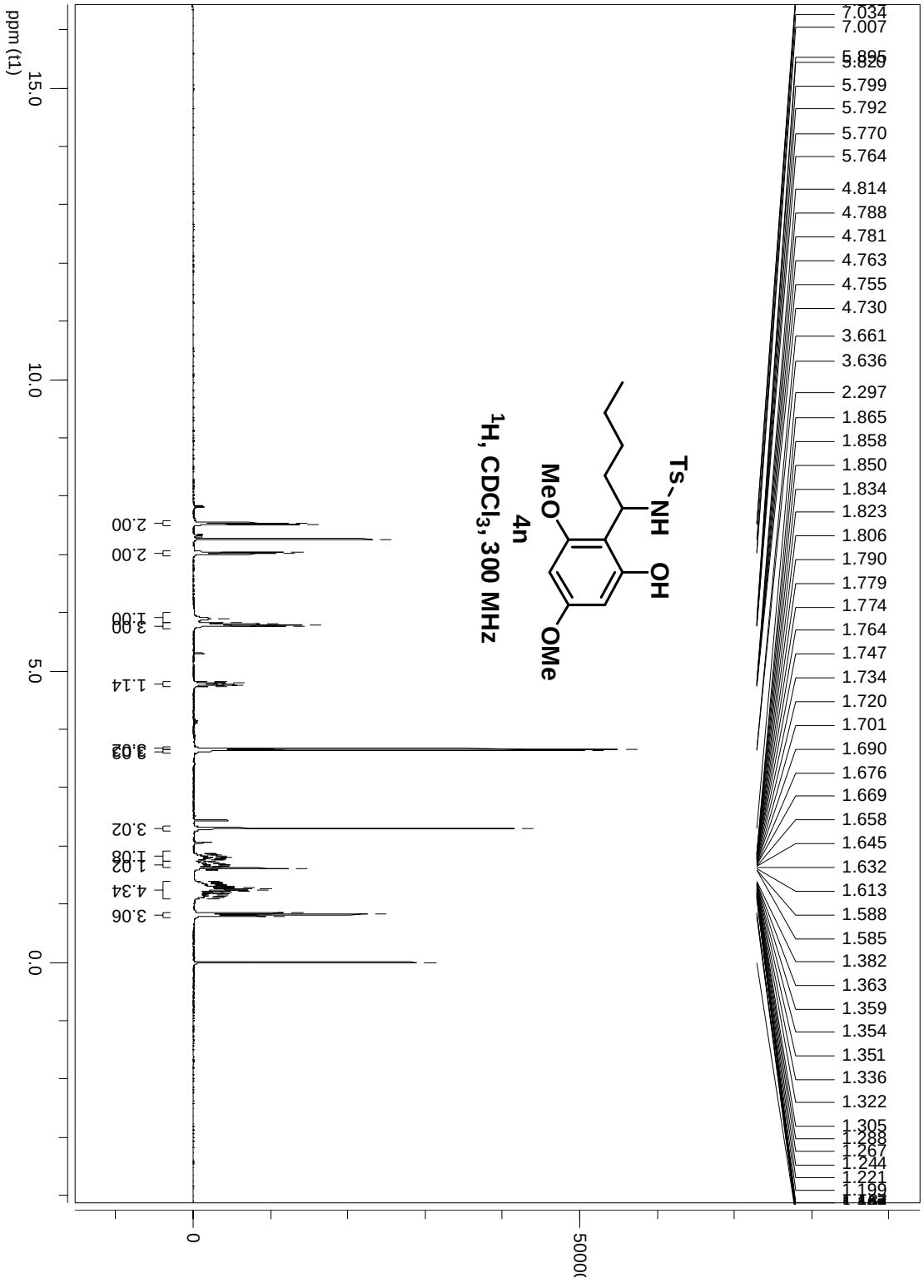

ppm (t1)
200
150
100
50
0
0
10000
20000
30000
40000
50000
60000
70000
160.651
158.007
154.604
142.879
138.274
136.847
133.052
132.429
128.893
128.037
127.755
127.393
126.790
125.759
125.564
125.239
124.758
107.110
93.859
91.255
77.318
77.000
76.683
55.472
55.247
52.137
21.262
4k
13C, CDCl3, 100 MHz
Ts
NH
OH
MeO
OMe

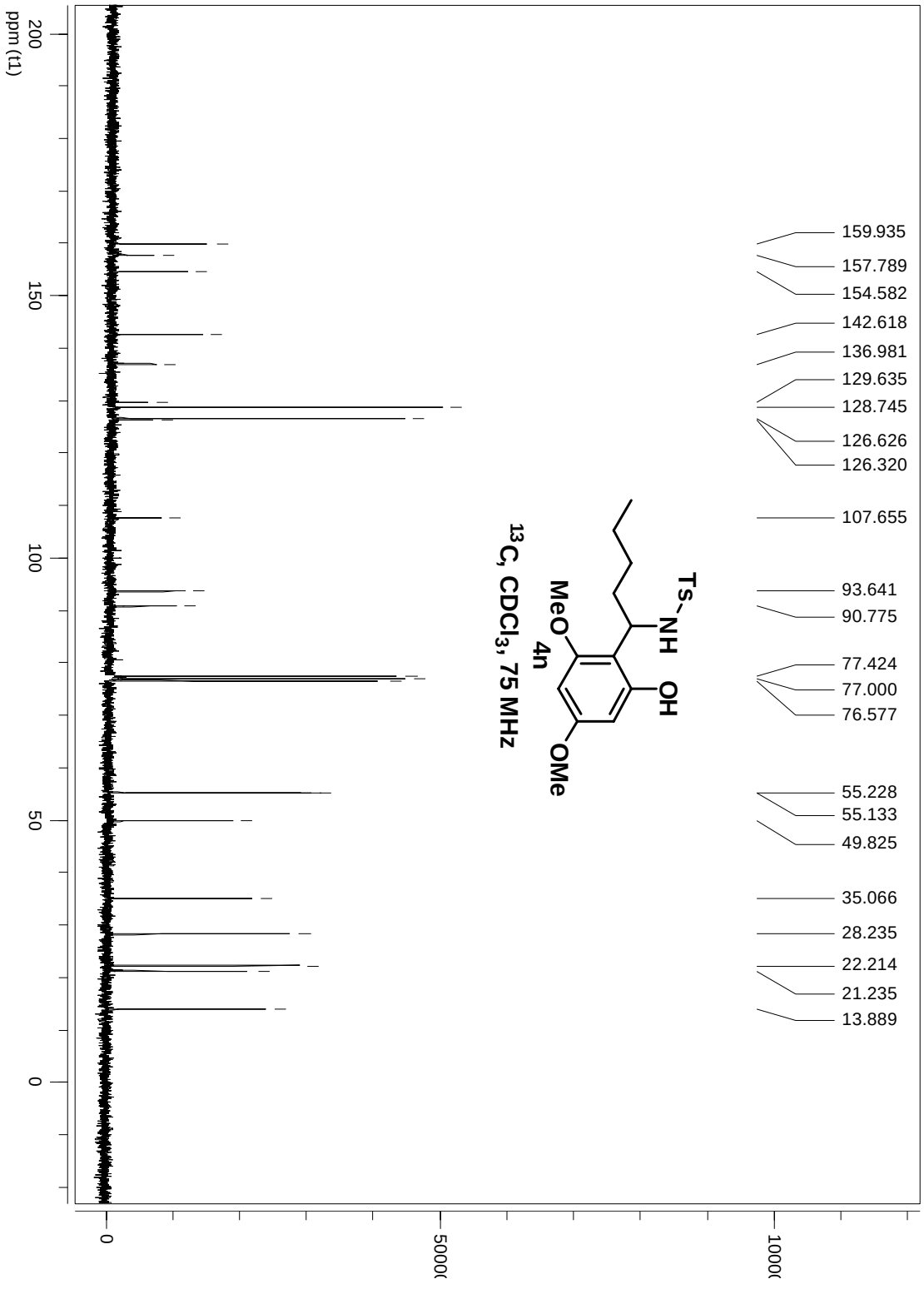

4l
1H, CDCl3, 400 MHz
MeO
OMe
OH
HN–Ts
O
7.600
7.580
7.262
7.229
7.077
7.057
6.602
6.310
6.286
6.187
6.116
6.093
6.009
6.002
5.908
5.904
5.830
5.826
3.657
3.634
2.316
0.00000
2.00
0.90
2.00
1.01
3.00
3.00
ppm (t1)
10.0
5.0
0.0

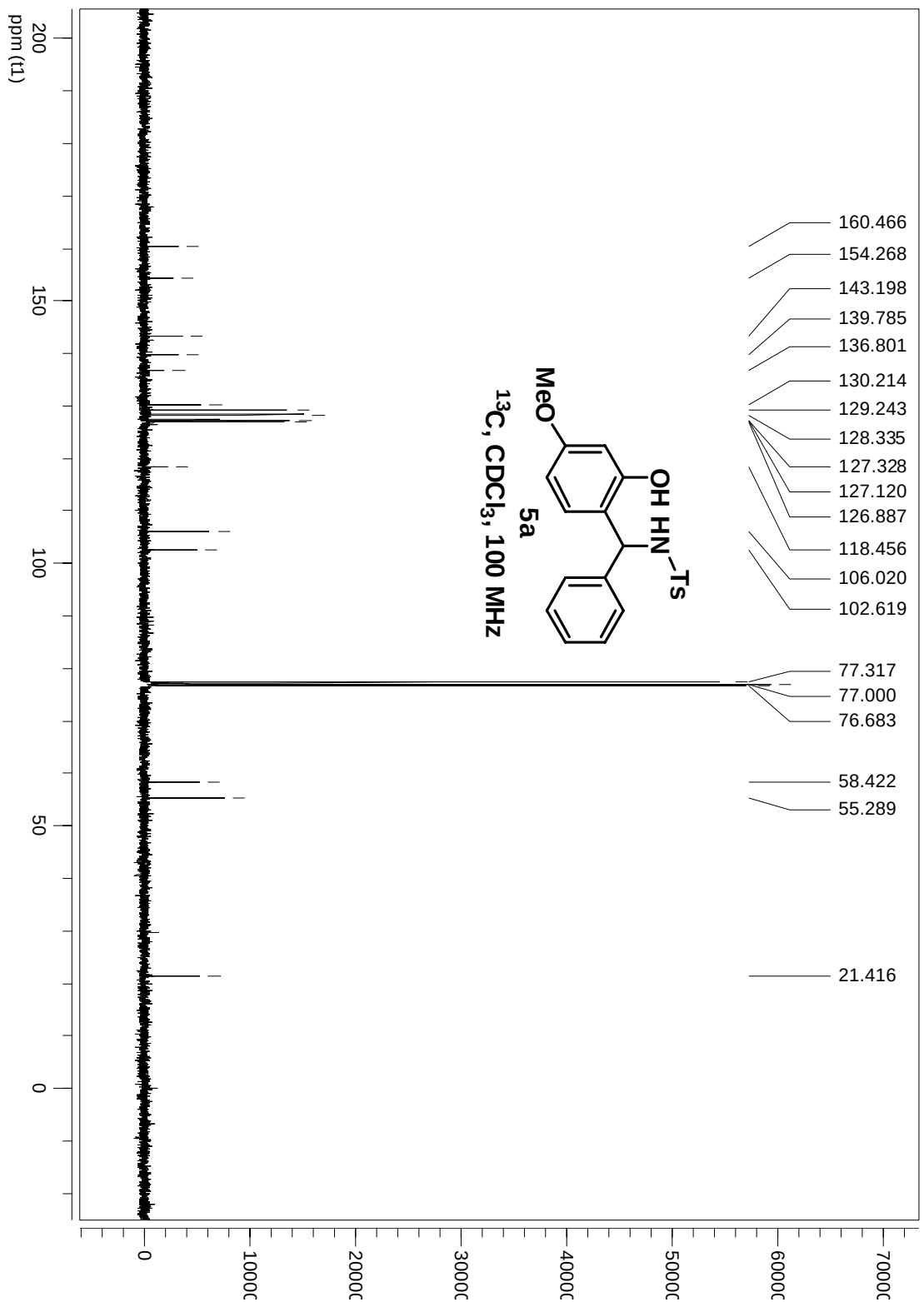


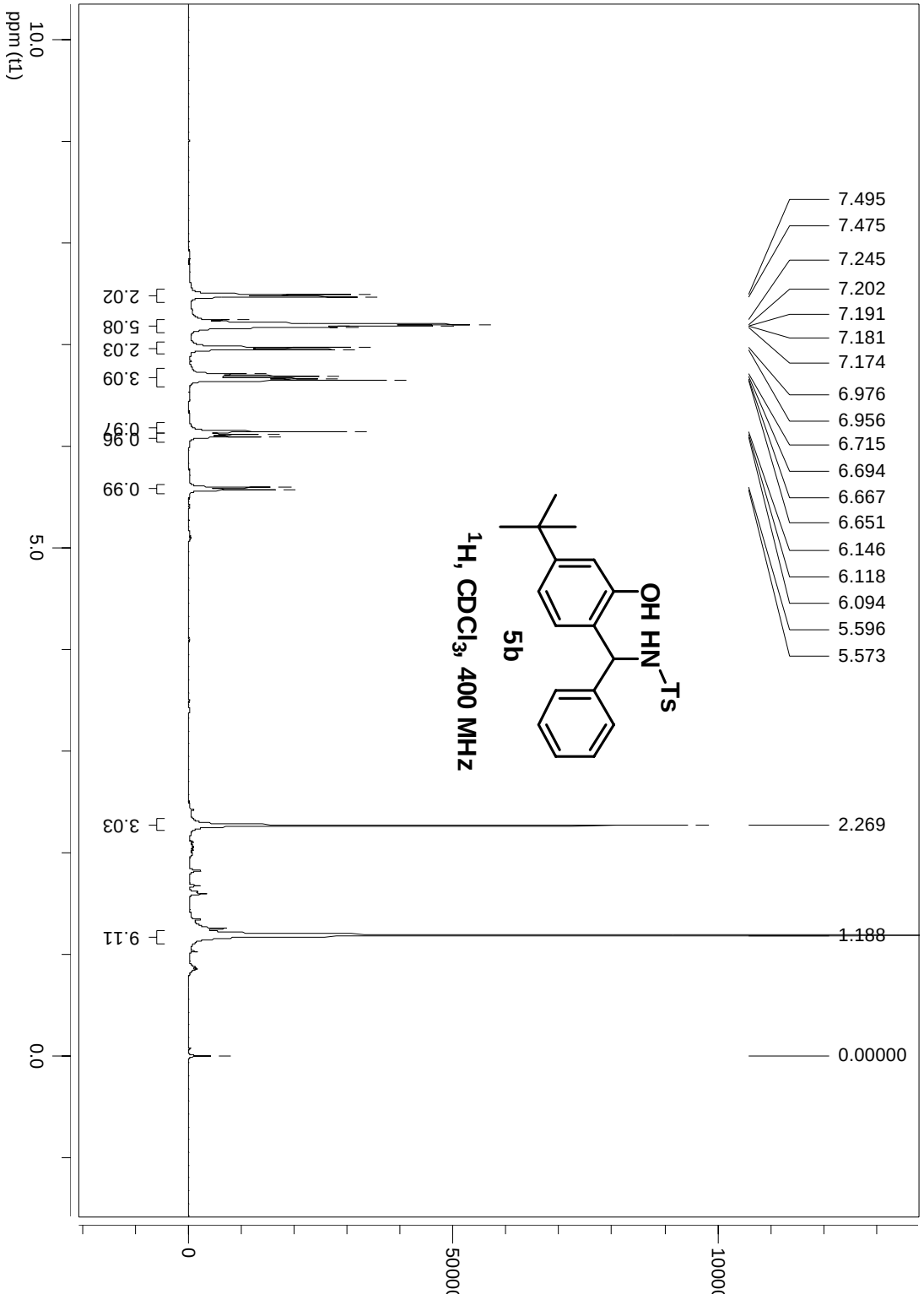

10.0
ppm (t1)
5.0
0.0
2.01
1.99
2.00
1.06
1.00
3.04
3.01
3.07
1.04
1.96
2.04
5.04
1.34
^{1}H, CDCl$_3$, 400 MHz
4m
MeO
OMe
OH
Ts
NH
5.808
5.751
4.479
4.447
4.413
3.665
3.588
2.285
2.209
2.201
2.188
2.179
2.172
2.168
2.154
2.149
2.145
2.139
2.128
1.777
1.774
1.771
1.764
1.740
1.718
1.714
1.708
1.703
1.602
1.578
1.547
1.254
1.239
1.218
1.215
1.158
1.144
1.123
1.120
1.109
1.099
1.096
1.083
1.078
1.068
1.034
1.026
1.022
1.004
-1000
0
1000
2000
3000
4000
5000
6000
7000

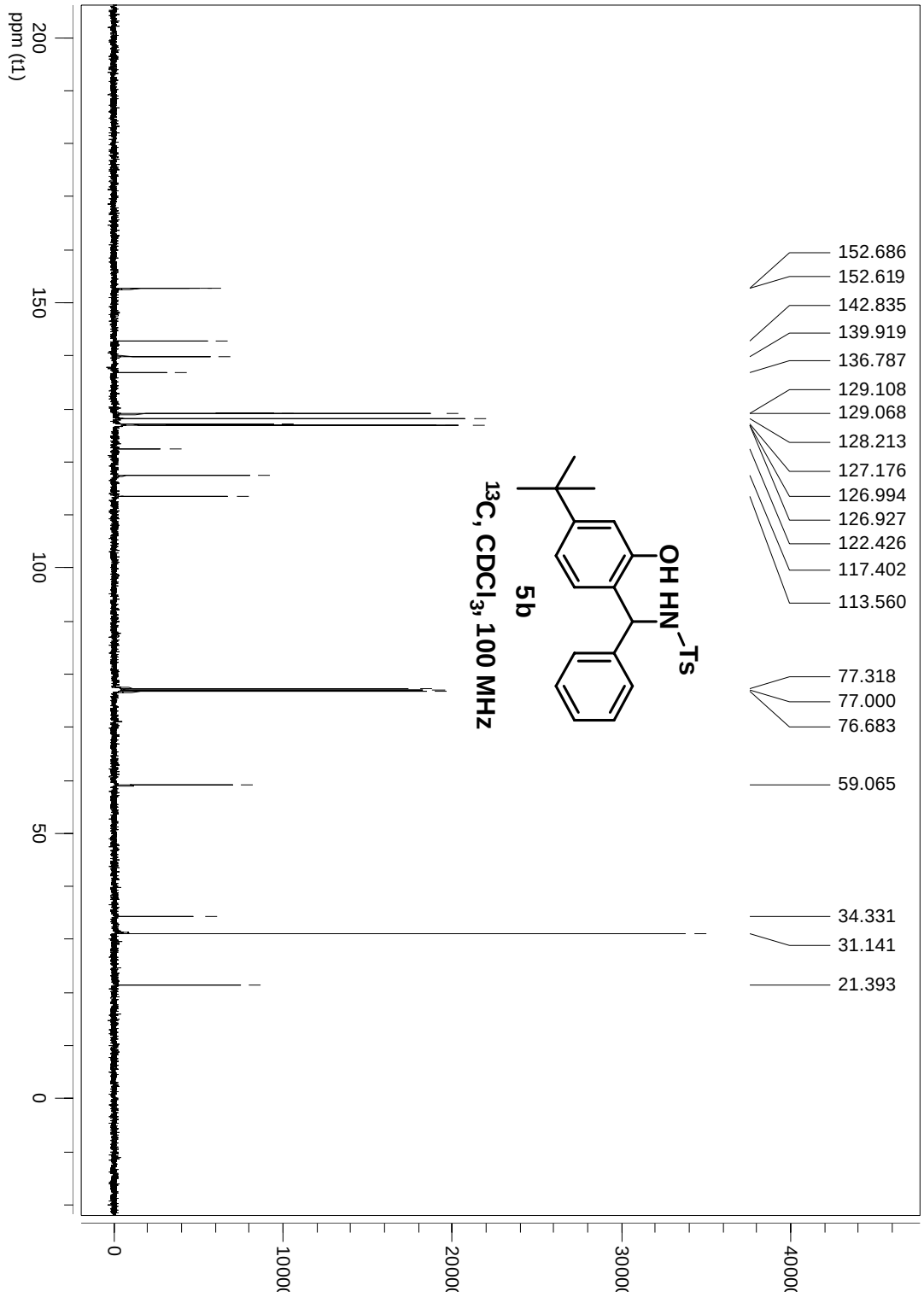

ppm (t1)
200
150
100
50
0
0
5000
10000
159.972
154.584
142.484
128.770
128.593
126.819
126.426
106.978
93.739
90.304
77.424
77.000
76.577
55.258
55.169
41.647
30.408
29.564
26.383
26.087
25.952
21.278
4m
13C, CDCl3, 75 Hz
MeO
OMe
OH
NH
Ts


ppm (t1)
15.0
10.0
5.0
0.0
0
50000
7.034
7.007
5.895
5.820
5.799
5.792
5.770
5.764
4.814
4.788
4.781
4.763
4.755
4.730
3.661
3.636
2.297
1.865
1.858
1.850
1.834
1.823
1.806
1.790
1.779
1.774
1.764
1.747
1.734
1.720
1.701
1.690
1.676
1.669
1.658
1.645
1.632
1.613
1.588
1.585
1.382
1.363
1.359
1.354
1.351
1.336
1.322
1.305
1.288
1.267
1.244
1.221
2.00
2.00
3.00
1.00
1.14
3.09
3.02
1.08
1.02
4.34
3.06
1H, CDCl3, 300 MHz
4n
MeO
OMe
NH
Ts
OH


ppm (t1)
200
150
100
50
0
0
5000
10000
159.935
157.789
154.582
142.618
136.981
129.635
128.745
126.626
126.320
107.655
93.641
90.775
77.424
77.000
76.577
55.228
55.133
49.825
35.066
28.235
22.214
21.235
13.889
^{13}C, CDCl$_3$, 75 MHz
4n
MeO
OMe
OH
NH
Ts

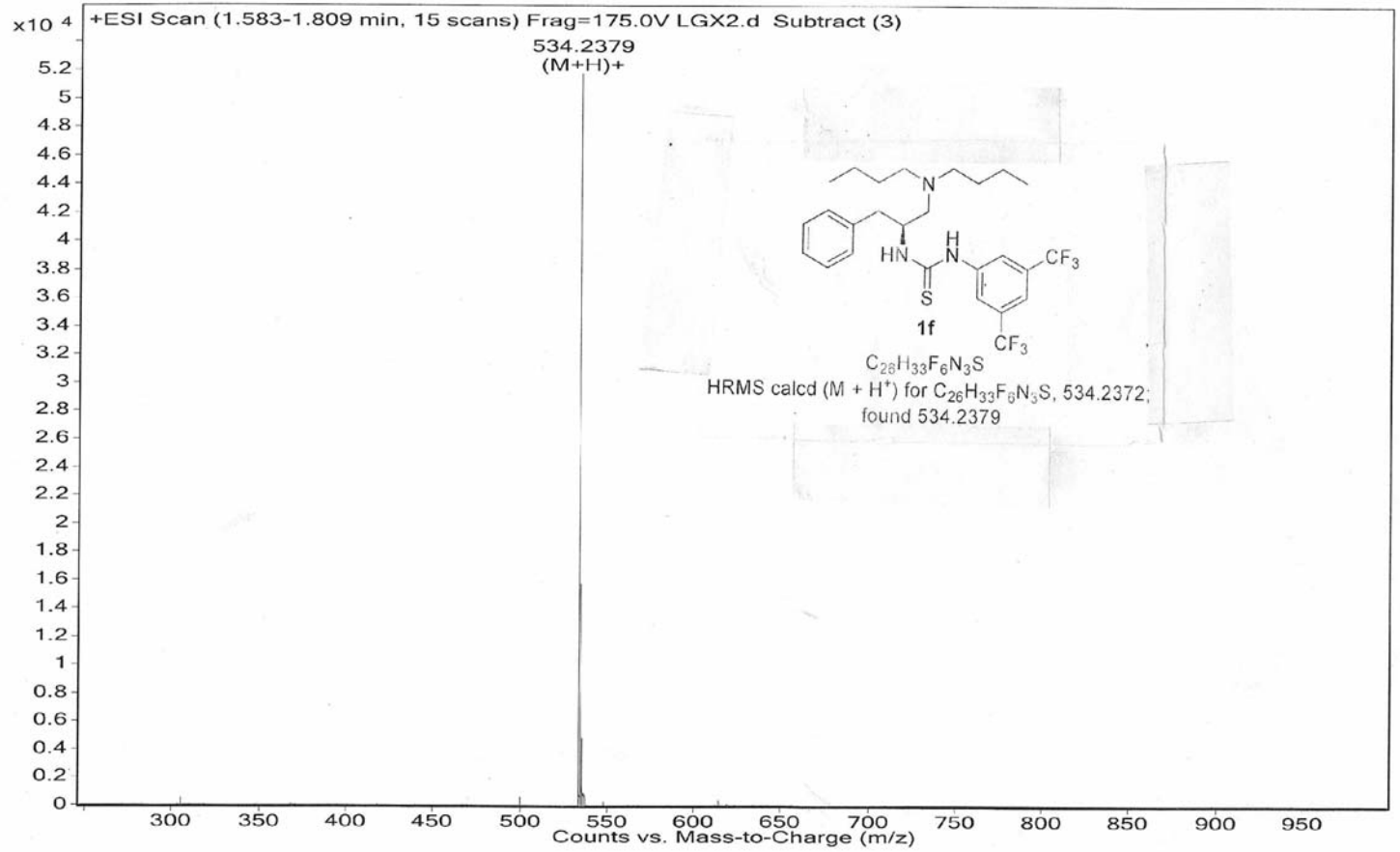

ppm (t1)
200
150
100
50
0
0
10000
20000
30000
40000
50000
60000
70000
160.466
154.268
143.198
139.785
136.801
130.214
129.243
128.335
127.328
127.120
126.887
118.456
106.020
102.619
77.317
77.000
76.683
58.422
55.289
21.416
MeO
OH HN
Ts
5a
13C, CDCl3, 100 MHz


ppm (t1)
10.0
5.0
0.0
2.02
5.08
2.03
3.09
0.97
0.96
0.99
3.03
9.11
7.495
7.475
7.245
7.202
7.191
7.181
7.174
6.976
6.956
6.715
6.694
6.667
6.651
6.146
6.118
6.094
5.596
5.573
2.269
1.188
0.00000
^{1}H, CDCl$_3$, 400 MHz
5b
OH HN
Ts
0
5000
10000


ppm (t1)
200
150
100
50
0
0
10000
20000
30000
40000
^{13}C, CDCl$_3$, 100 MHz
5b
OH HN
Ts
152.686
152.619
142.835
139.919
136.787
129.108
129.068
128.213
127.176
126.994
126.927
122.426
117.402
113.560
77.318
77.000
76.683
59.065
34.331
31.141
21.393

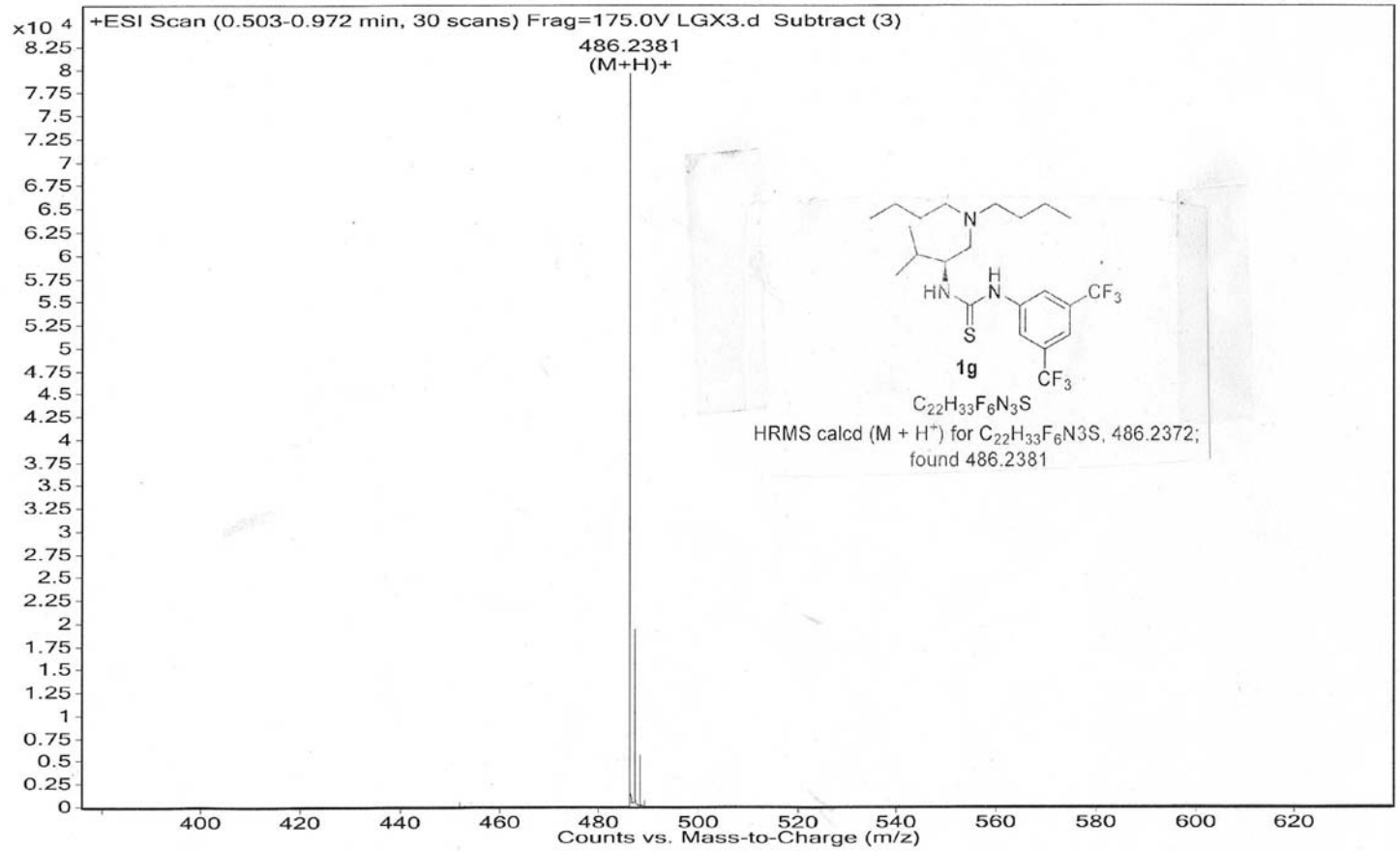
534.2372

Sample Name	LC/MS	**Position**	Vial 3	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Some Ions Missed
Data Filename	LGX2.d	**ACQ Method**		**Comment**		**Acquired Time**	5/6/2011 11:17:14 AM



486.2372

Sample Name	LC/MS	**Position**	Vial 3	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Some Ions Missed
Data Filename	LGX3.d	**ACQ Method**		**Comment**		**Acquired Time**	5/6/2011 11:21:10 AM



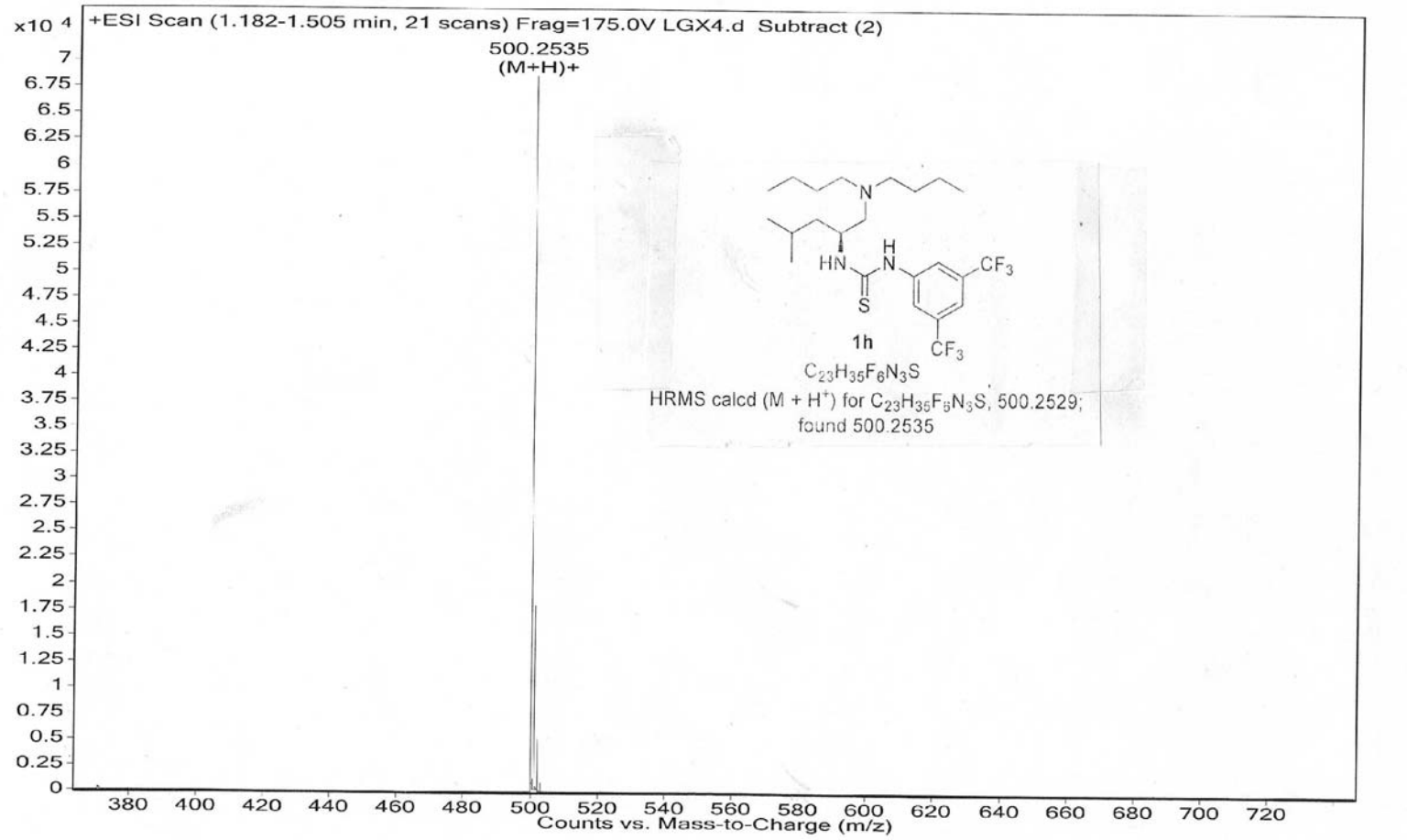
1g

$C_{22}H_{33}F_6N_3S$

HRMS calcd (M + H^+) for $C_{22}H_{33}F_6N3S$, 486.2372; found 486.2381

500.2529

Sample Name	LC/MS	**Position**	Vial 3	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Some Ions Missed
Data Filename	LGX4.d	**ACQ Method**		**Comment**		**Acquired Time**	5/6/2011 11:33:17 AM



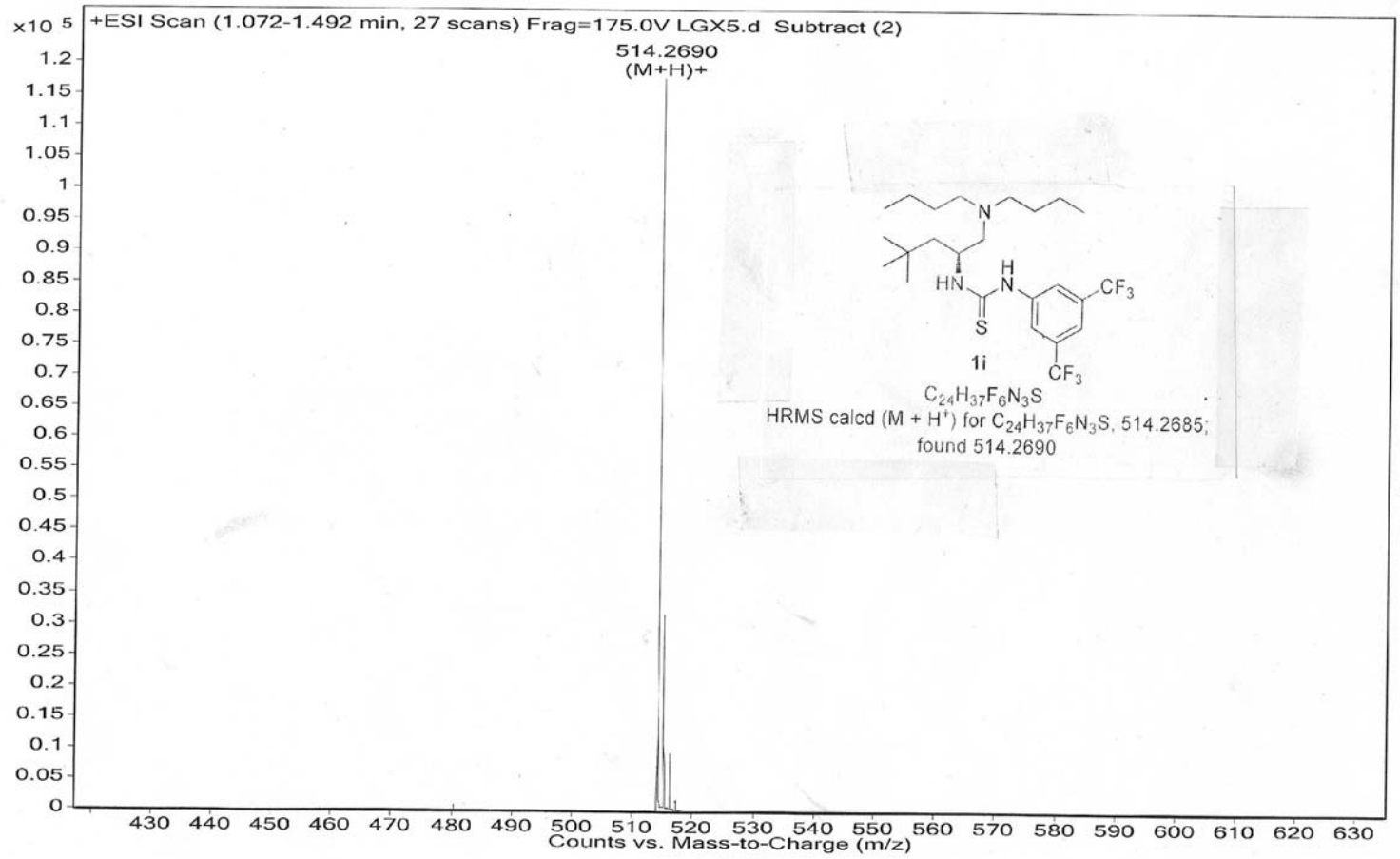
1h

$C_{23}H_{35}F_6N_3S$

HRMS calcd (M + H^+) for $C_{23}H_{35}F_6N_3S$, 500.2529; found 500.2535

514.2685

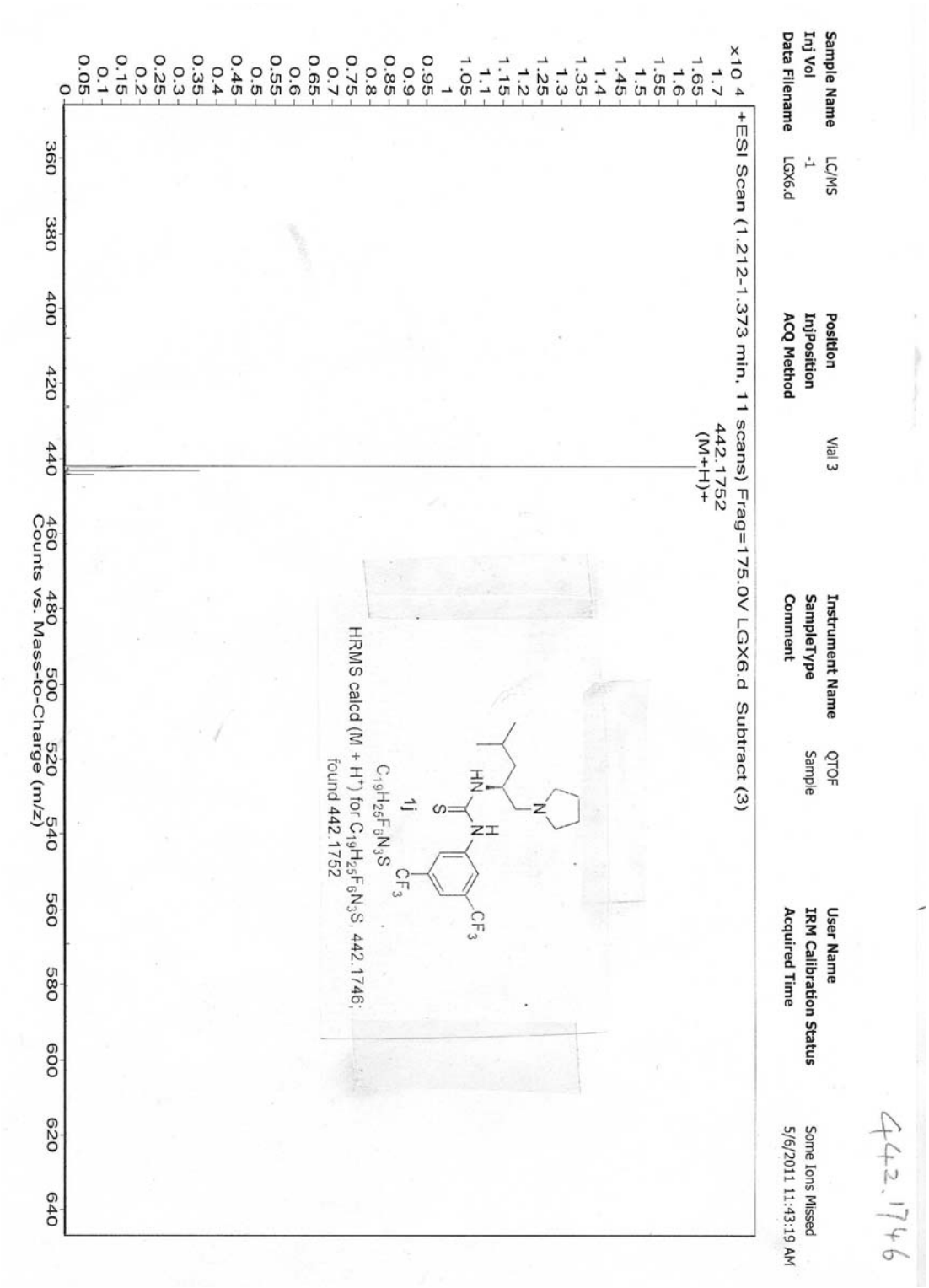
Sample Name	LC/MS	**Position**	Vial 3	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Some Ions Missed
Data Filename	LGX5.d	**ACQ Method**		**Comment**		**Acquired Time**	5/6/2011 11:36:25 AM

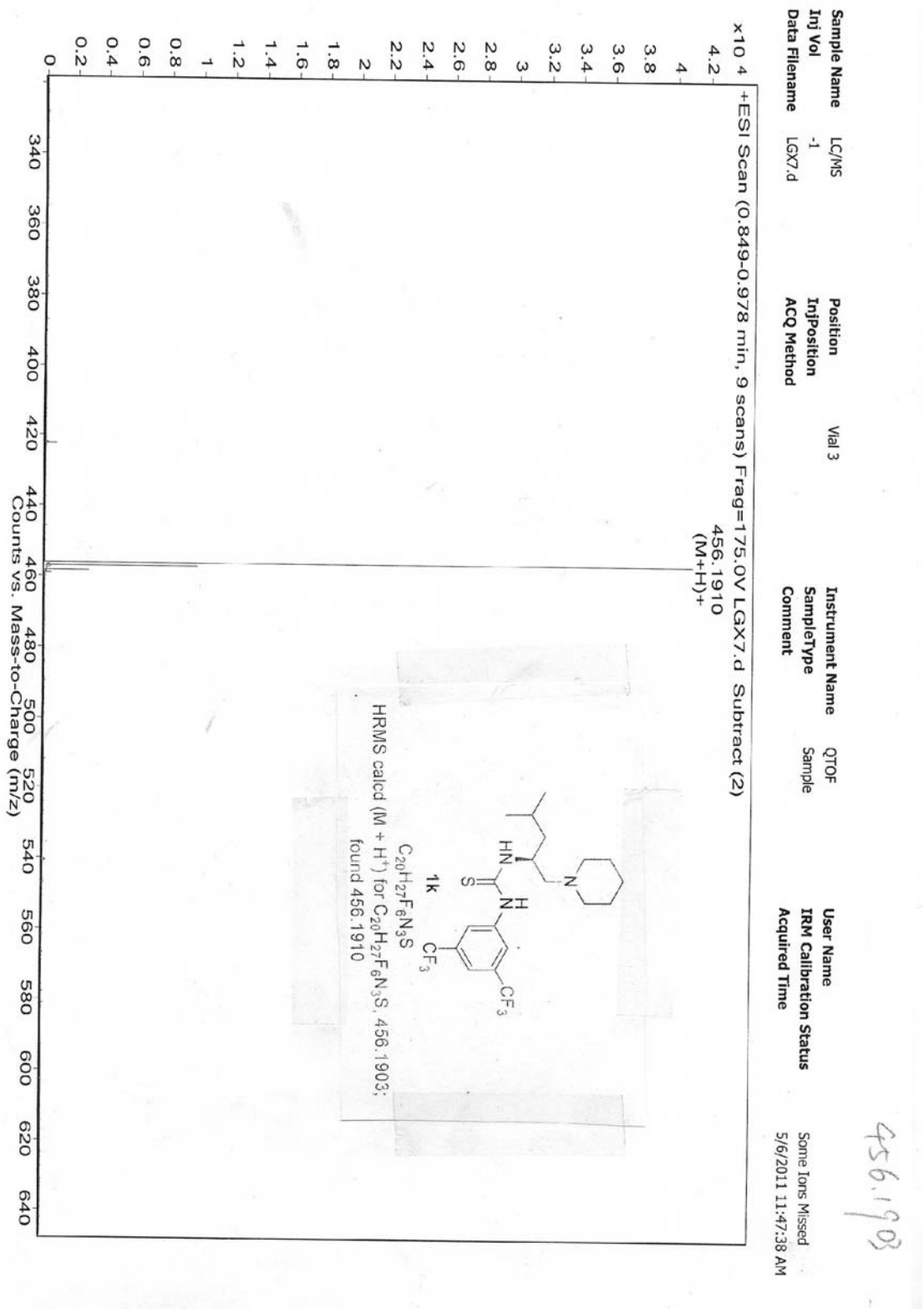


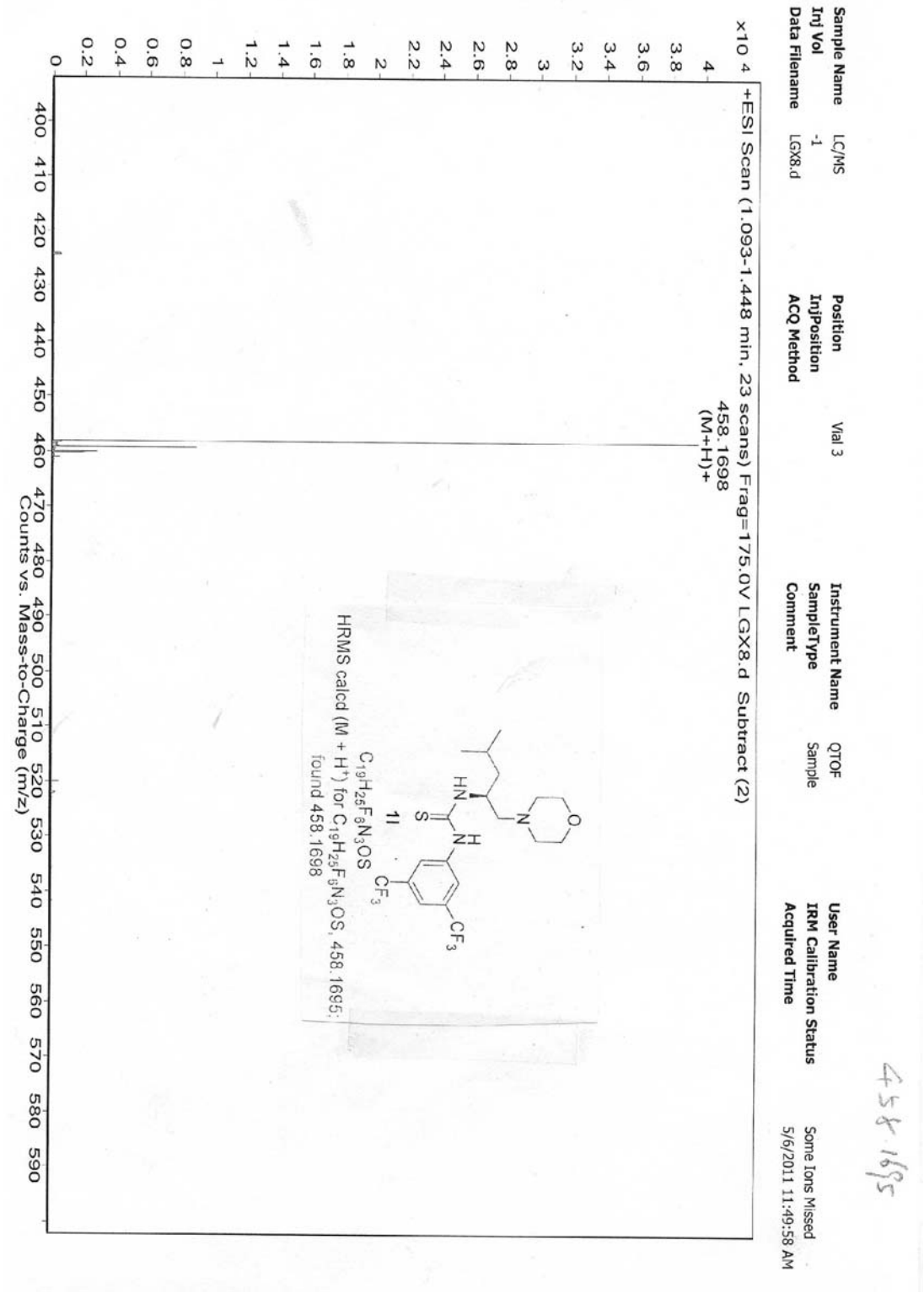
1i

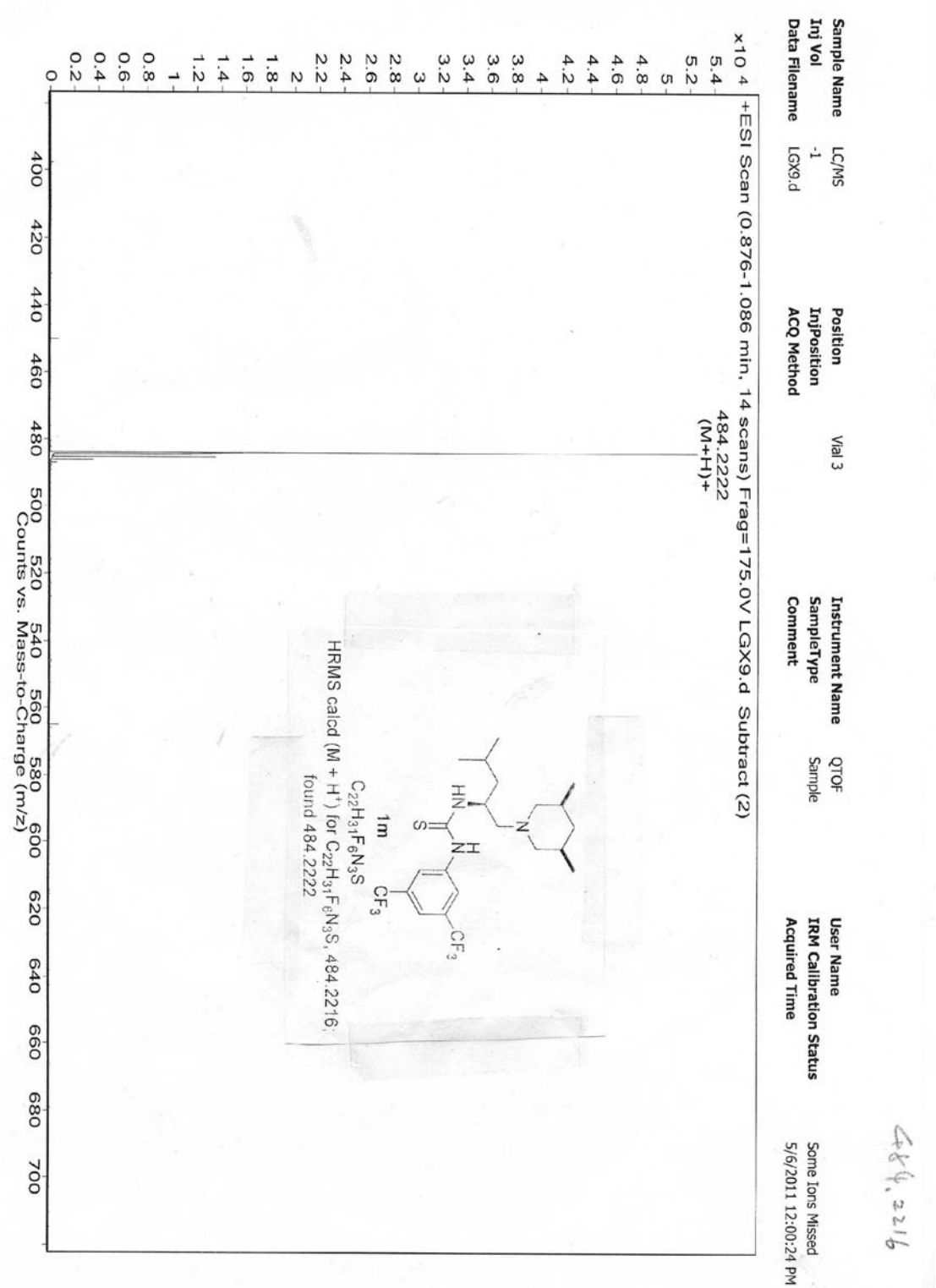
$C_{24}H_{37}F_6N_3S$

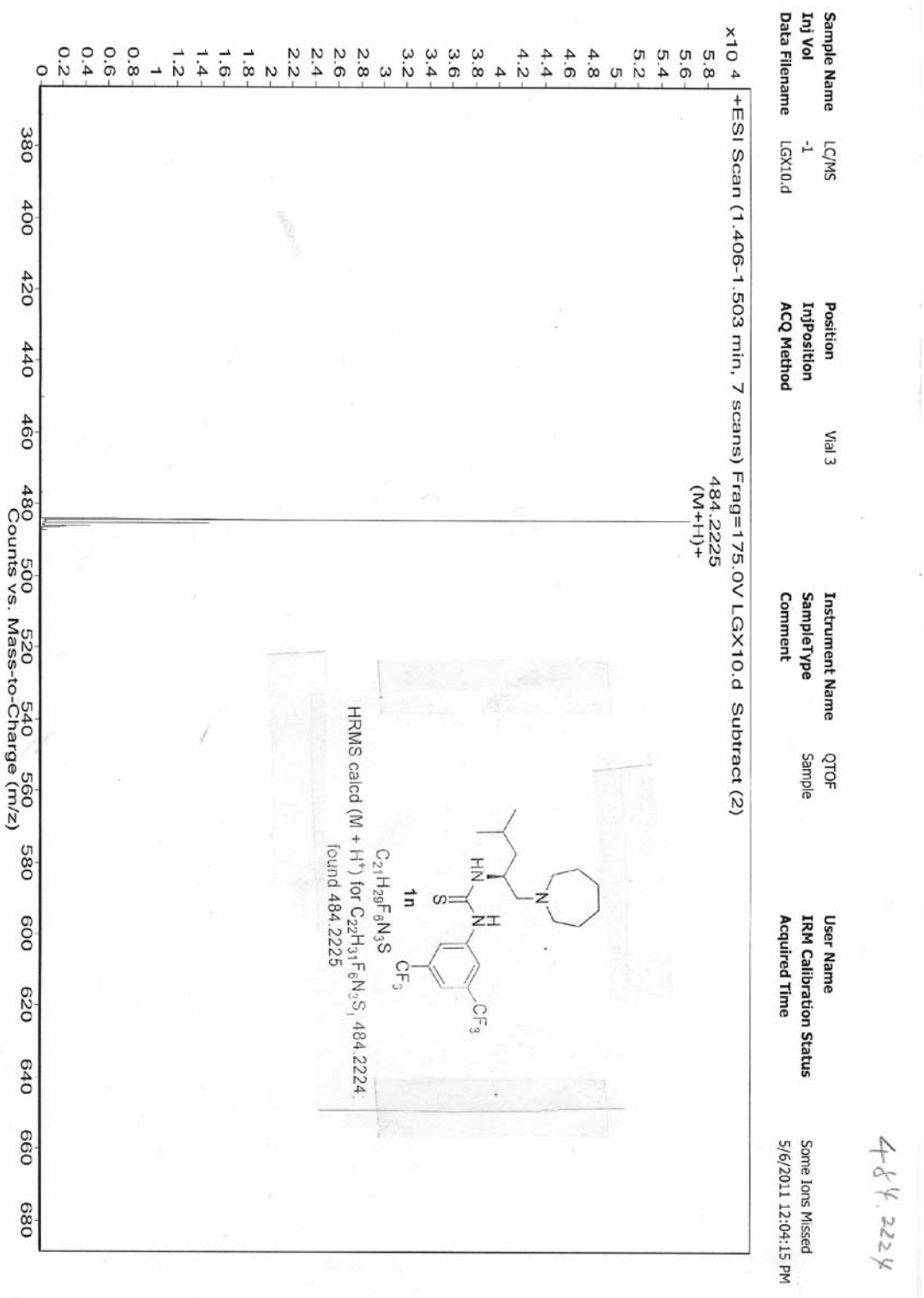
HRMS calcd (M + H^+) for $C_{24}H_{37}F_6N_3S$, 514.2685; found 514.2690


Sample Name LC/MS
Inj Vol -1
Data Filename LGX6.d
Position Vial 3
InjPosition
ACQ Method
Instrument Name QTOF
SampleType Sample
Comment
User Name
IRM Calibration Status
Acquired Time Some Ions Missed 5/6/2011 11:43:19 AM
442.1746
+ESI Scan (1.212-1.373 min, 11 scans) Frag=175.0V LGX6.d Subtract (3)
442.1752
(M+H)+
HN
N
H
N
S
CF3
CF3
1j
C19H25F6N3S
HRMS calcd (M + H+) for C19H25F6N3S, 442.1746;
found 442.1752
Counts vs. Mass-to-Charge (m/z)


Sample Name LC/MS
Inj Vol -1
Data Filename LGX7.d
Position Vial 3
InjPosition
ACQ Method
Instrument Name QTOF
SampleType Sample
Comment
User Name
IRM Calibration Status
Acquired Time Some Ions Missed 5/6/2011 11:47:38 AM
456.1903
+ESI Scan (0.849-0.978 min, 9 scans) Frag=175.0V LGX7.d Subtract (2)
456.1910
(M+H)+
x10 4
Counts vs. Mass-to-Charge (m/z)
1k
C20H27F6N3S
HRMS calcd (M + H+) for C20H27F6N3S, 456.1903;
found 456.1910

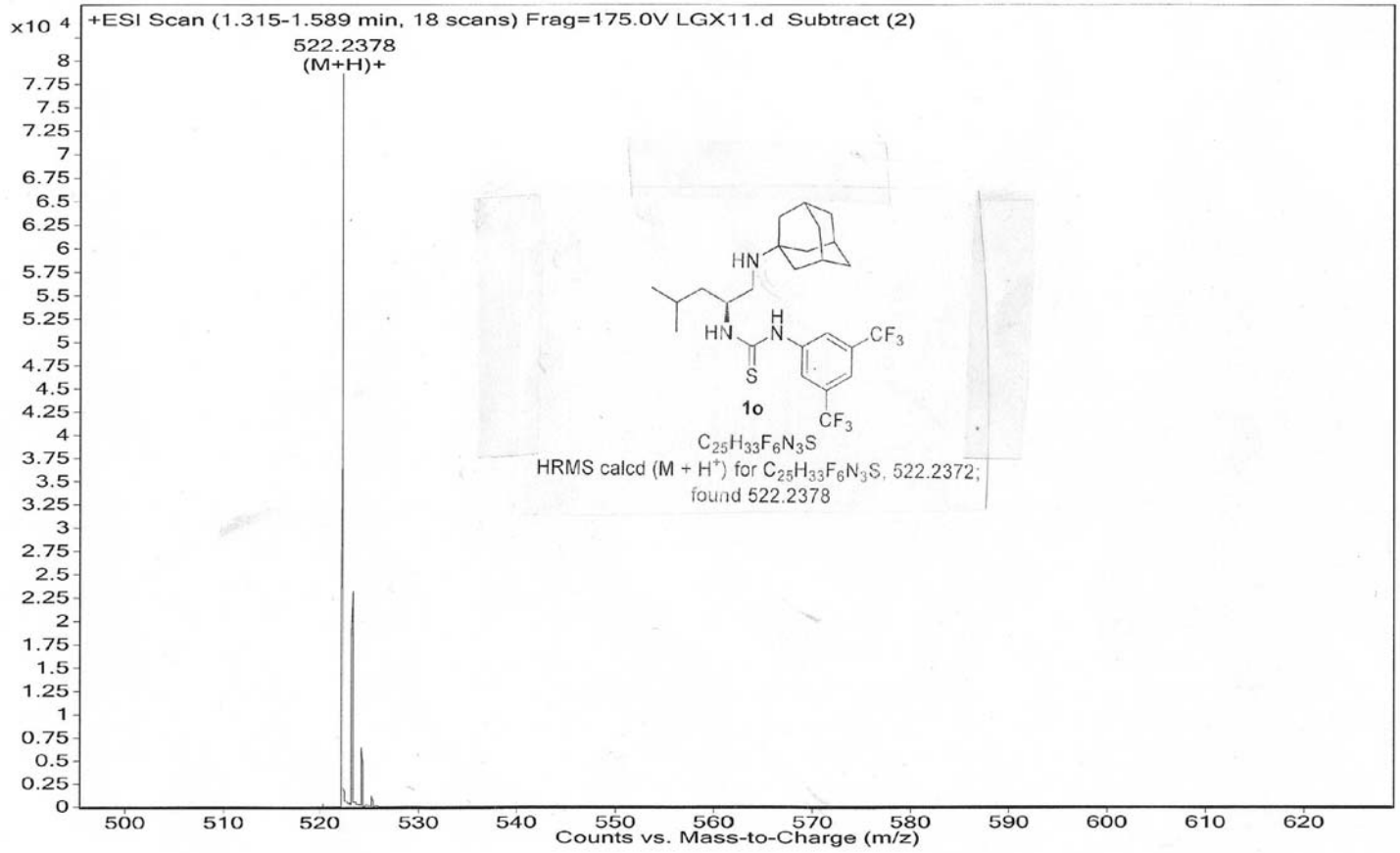

Sample Name LC/MS
Inj Vol -1
Data Filename LGX8.d
Position Vial 3
InjPosition
ACQ Method
Instrument Name QTOF
SampleType Sample
Comment
User Name
IRM Calibration Status
Acquired Time Some Ions Missed 5/6/2011 11:49:58 AM
458.1695
+ESI Scan (1.093-1.448 min, 23 scans) Frag=175.0V LGX8.d Subtract (2)
458.1698
(M+H)+
x10 4
Counts vs. Mass-to-Charge (m/z)
11
C19H25F6N3OS
HRMS calcd (M + H+) for C19H25F6N3OS, 458.1695;
found 458.1698


Sample Name LC/MS
Inj Vol -1
Data Filename LGX9.d
Position Vial 3
InjPosition
ACQ Method
Instrument Name QTOF
SampleType Sample
Comment
User Name
IRM Calibration Status Some Ions Missed
Acquired Time 5/6/2011 12:00:24 PM
484.2216
+ESI Scan (0.876-1.086 min, 14 scans) Frag=175.0V LGX9.d Subtract (2)
484.2222
(M+H)+
×10 4
Counts vs. Mass-to-Charge (m/z)
1m
$C_{22}H_{31}F_6N_3S$
HRMS calcd (M + H+) for $C_{22}H_{31}F_6N_3S$, 484.2216;
found 484.2222


Sample Name LC/MS
Inj Vol -1
Data Filename LGX10.d
Position Vial 3
InjPosition
ACQ Method
Instrument Name QTOF
SampleType Sample
Comment
User Name
IRM Calibration Status
Acquired Time Some Ions Missed 5/6/2011 12:04:15 PM
484.2224
+ESI Scan (1.406-1.503 min, 7 scans) Frag=175.0V LGX10.d Subtract (2)
484.2225
(M+H)+
1n
C21H29F6N3S
HRMS calcd (M + H+) for C22H31F6N3S, 484.2224;
found 484.2225
Counts vs. Mass-to-Charge (m/z)

522.2372

Sample Name	LC/MS	**Position**	Vial 3	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Some Ions Missed
Data Filename	LGX11.d	**ACQ Method**		**Comment**		**Acquired Time**	5/6/2011 12:09:47 PM

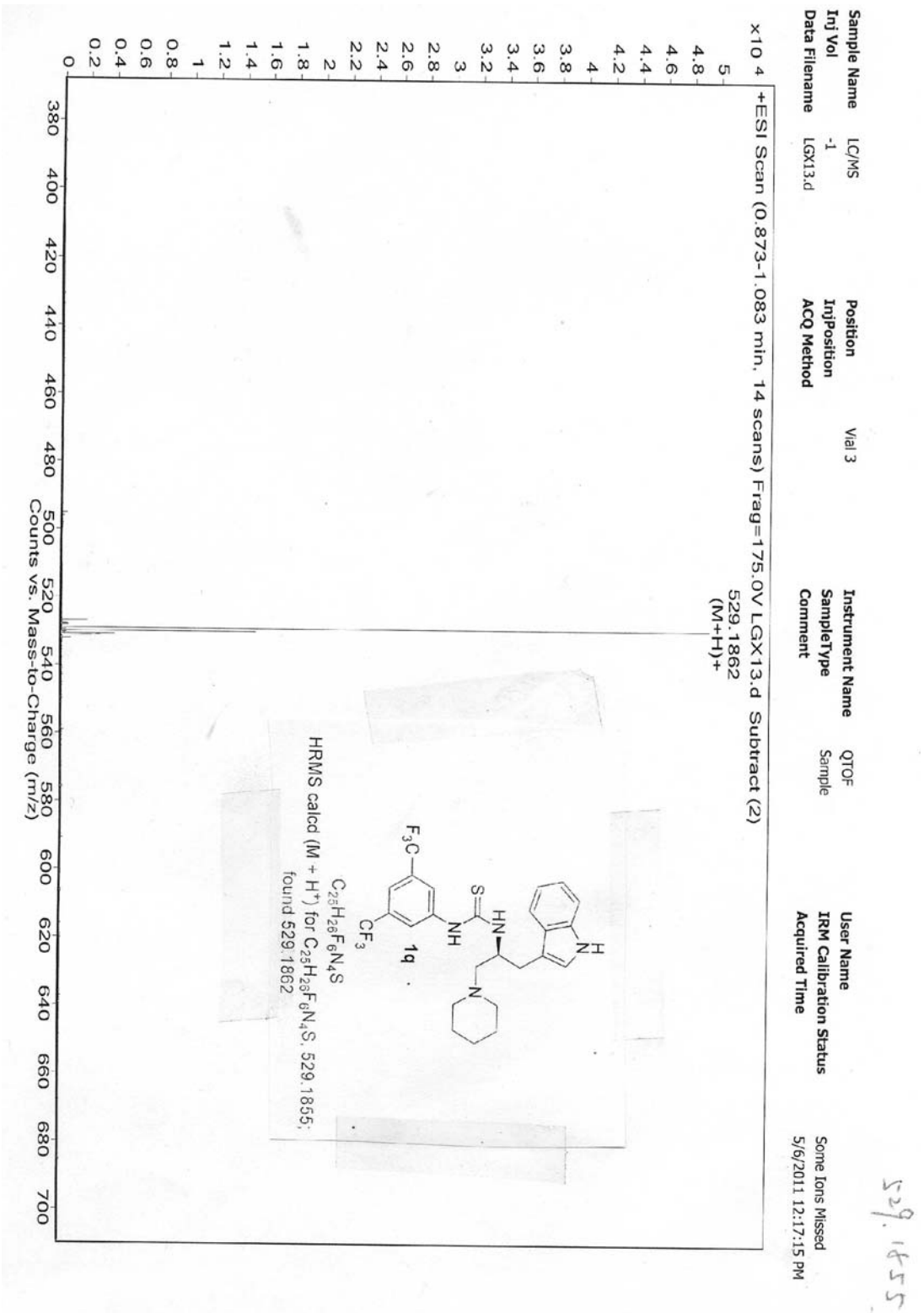


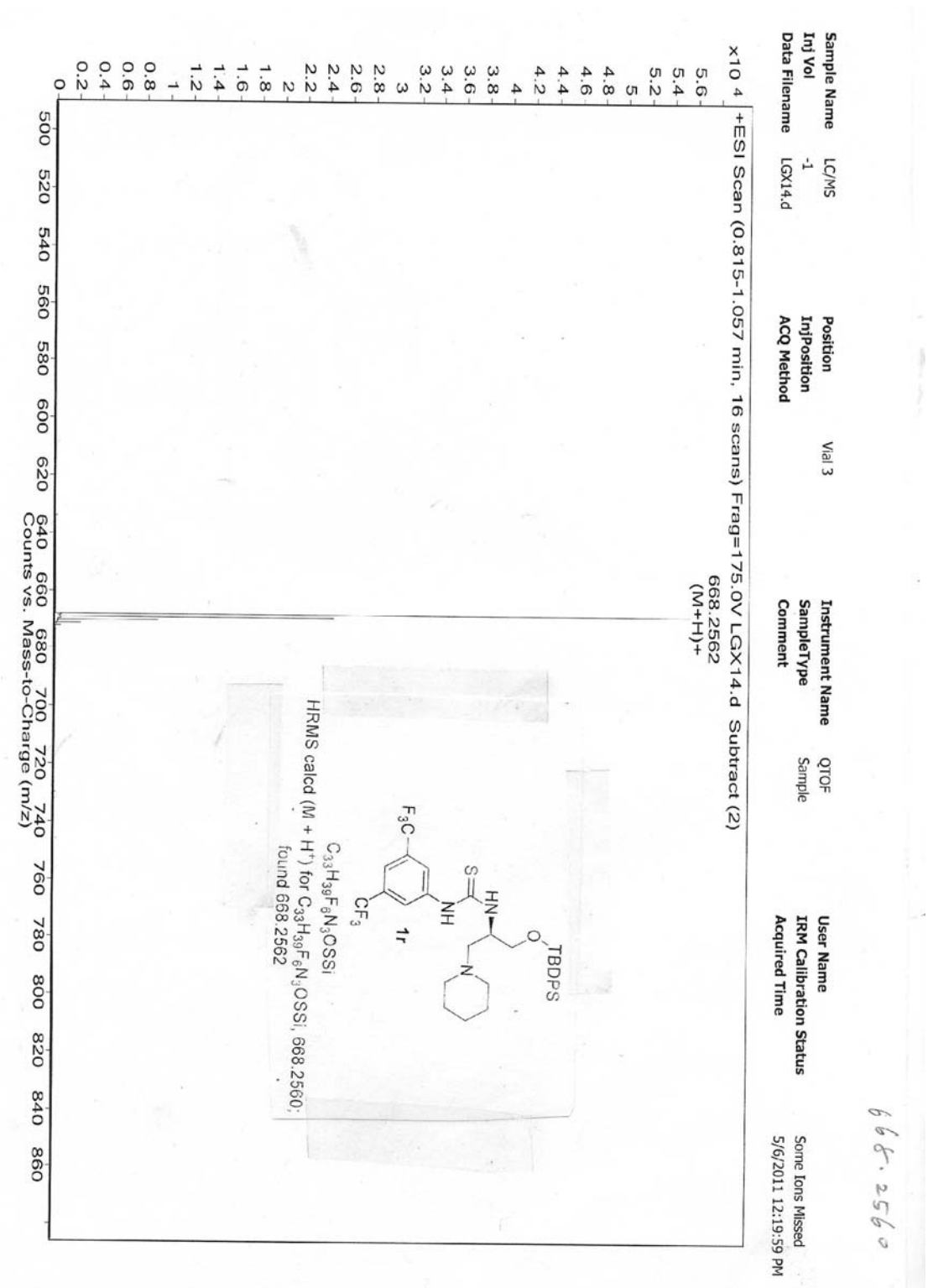
1o

$C_{25}H_{33}F_6N_3S$

HRMS calcd (M + H^+) for $C_{25}H_{33}F_6N_3S$, 522.2372; found 522.2378

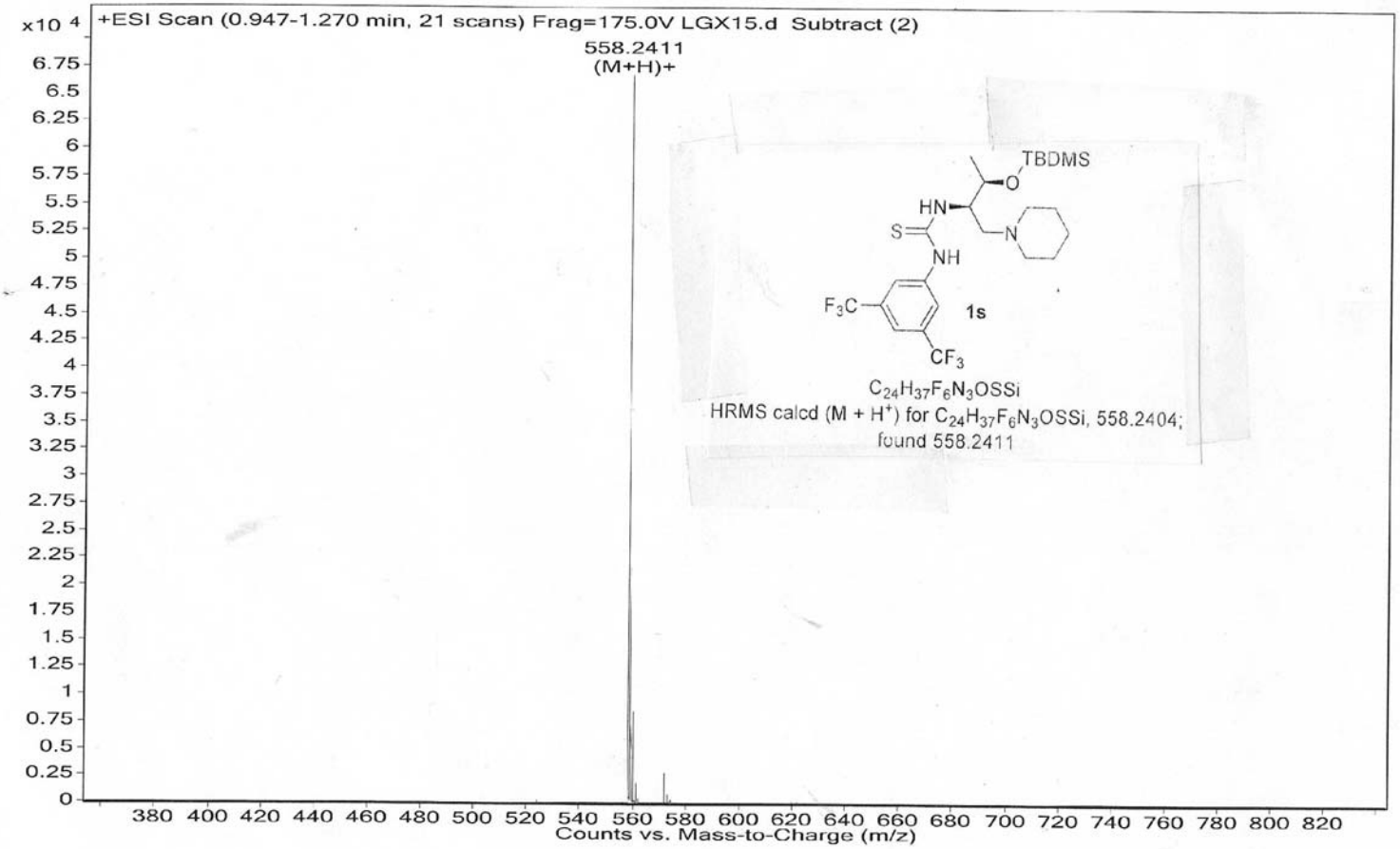
Sample Name LC/MS
Inj Vol -1
Data Filename LGX12.d
Position Vial 3
InjPosition
ACQ Method
Instrument Name QTOF
SampleType Sample
Comment
User Name
IRM Calibration Status
Acquired Time Some Ions Missed 5/6/2011 12:13:28 PM
490.1746
+ESI Scan (1.165-1.392 min, 15 scans) Frag=175.0V LGX12.d Subtract (2)
490.1753
(M+H)+
×10 4
Counts vs. Mass-to-Charge (m/z)
1p
HRMS calcd (M + H+) for C23H25F6N3S, 490.1746;
found 490.1753


Sample Name LC/MS
Inj Vol -1
Data Filename LGX13.d
Position Vial 3
InjPosition
ACQ Method
Instrument Name QTOF
SampleType Sample
Comment
User Name
IRM Calibration Status
Acquired Time Some Ions Missed 5/6/2011 12:17:15 PM
×10 4
+ESI Scan (0.873-1.083 min, 14 scans) Frag=175.0V LGX13.d Subtract (2)
529.1862
(M+H)+
Counts vs. Mass-to-Charge (m/z)
1q
C25H26F6N4S
HRMS calcd (M + H+) for C25H26F6N4S, 529.1855;
found 529.1862
529.1855


Sample Name LC/MS
Inj Vol -1
Data Filename LGX14.d
Position Vial 3
InjPosition
ACQ Method
Instrument Name QTOF
SampleType Sample
Comment
User Name
IRM Calibration Status
Acquired Time Some Ions Missed 5/6/2011 12:19:59 PM
668.2562
+ESI Scan (0.815-1.057 min, 16 scans) Frag=175.0V LGX14.d Subtract (2)
668.2562
(M+H)+
TBDPS
HN
S
NH
N
O
F3C
CF3
1r
C33H39F6N3OSSi
HRMS calcd (M + H+) for C33H39F6N3OSSi, 668.2560;
found 668.2562
Counts vs. Mass-to-Charge (m/z)

558.2404

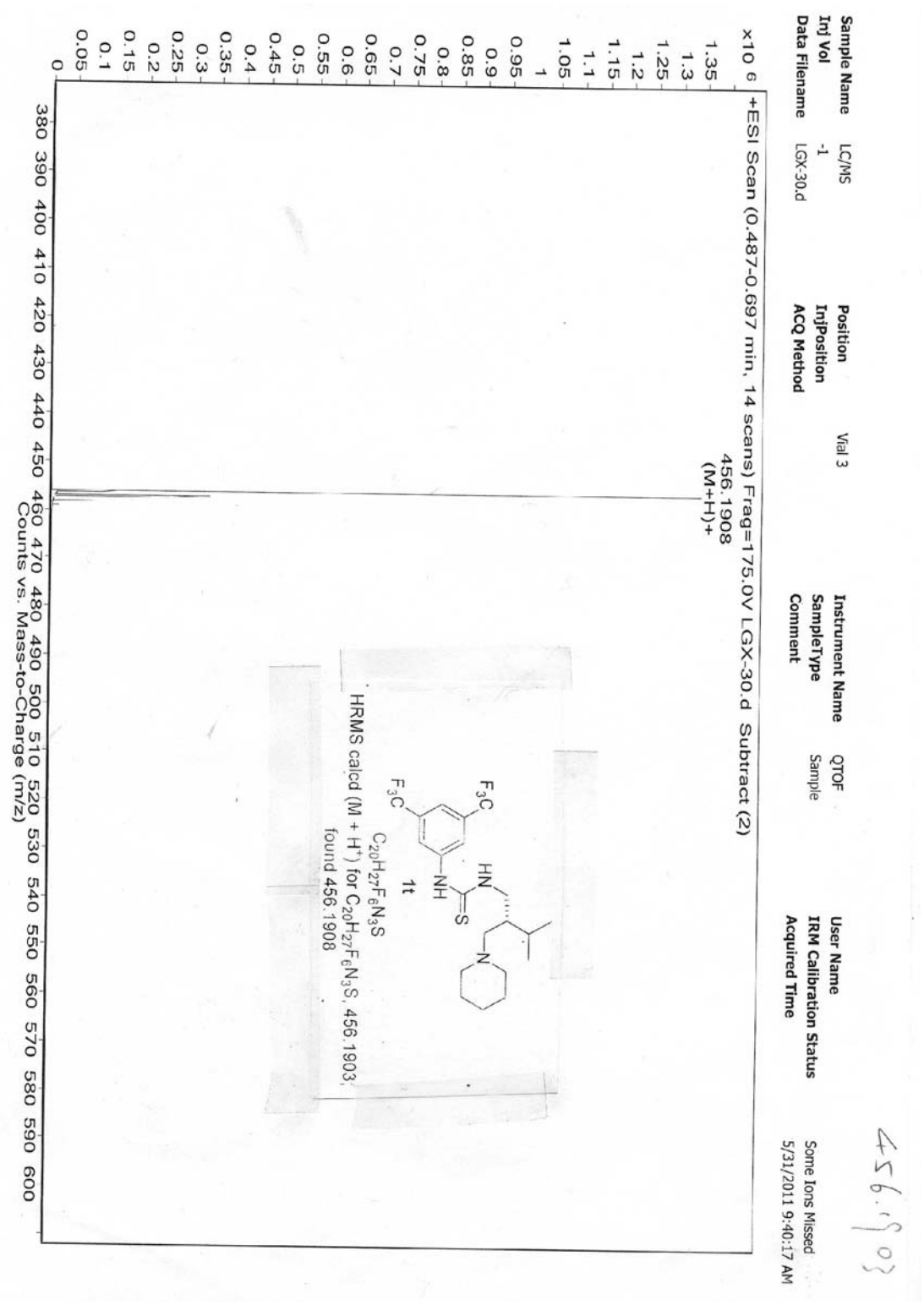
Sample Name	LC/MS	**Position**	Vial 3	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Some Ions Missed
Data Filename	LGX15.d	**ACQ Method**		**Comment**		**Acquired Time**	5/6/2011 12:22:43 PM

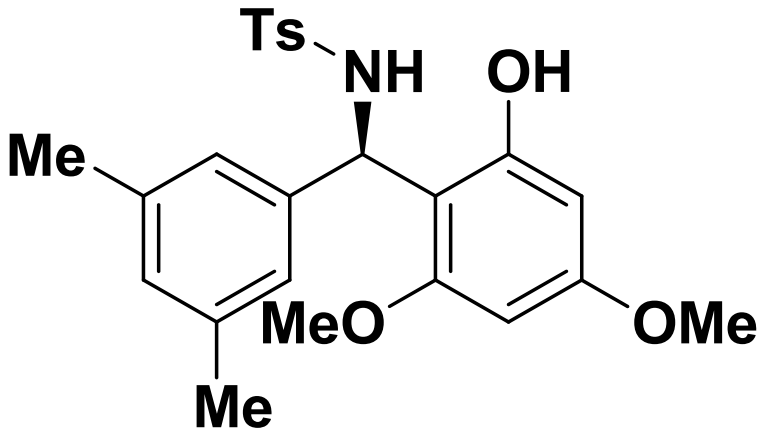


1s

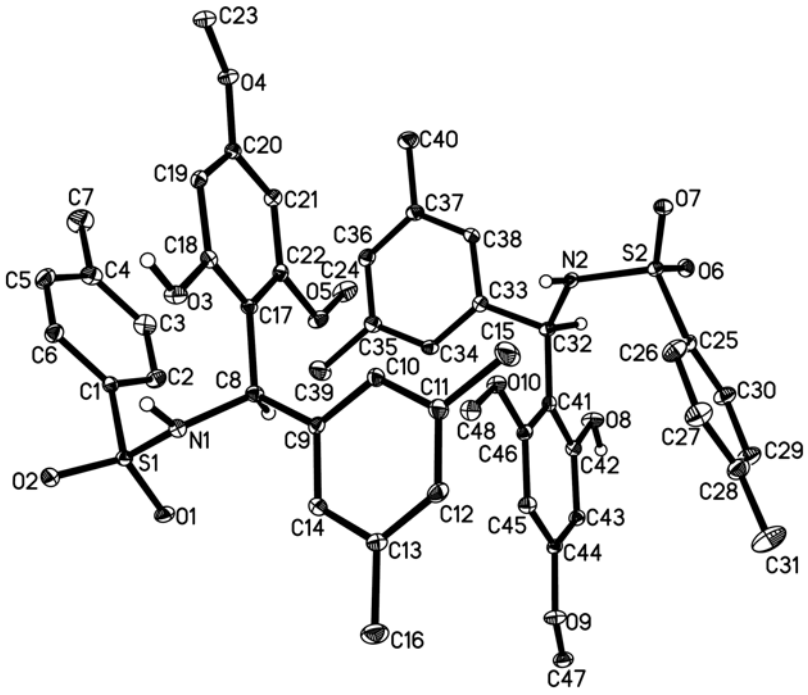
$C_{24}H_{37}F_6N_3OSSi$

HRMS calcd (M + H^+) for $C_{24}H_{37}F_6N_3OSSi$, 558.2404; found 558.2411

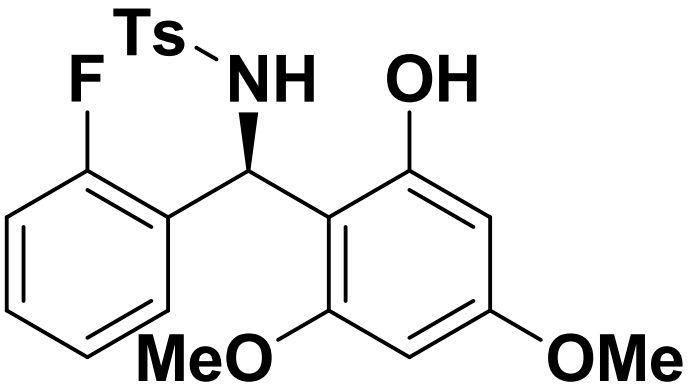

Sample Name LC/MS
Inj Vol -1
Data Filename LGX-30.d
Position Vial 3
InjPosition
ACQ Method
Instrument Name QTOF
SampleType Sample
Comment
User Name
IRM Calibration Status
Acquired Time Some Ions Missed 5/31/2011 9:40:17 AM
456.1908
+ESI Scan (0.487-0.697 min, 14 scans) Frag=175.0V LGX-30.d Subtract (2)
456.1908
(M+H)+
×10 6
Counts vs. Mass-to-Charge (m/z)
F3C
HN
NH
S
N
F3C
1t
C20H27F6N3S
HRMS calcd (M + H+) for C20H27F6N3S, 456.1903,
found 456.1908



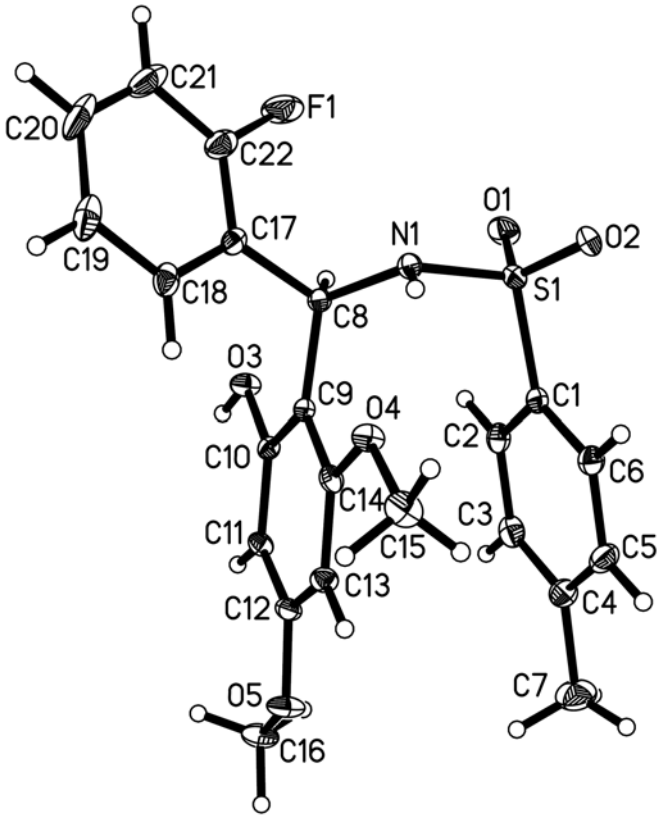
Product (*R*)-**4b**



X-ray structure of product (*R*)-**4b** (partial H atoms are omitted for clarity, 20% probability)



Product (*S*)-**4g**



X-ray structure of product (*S*)-**4g** (30% probability)