SUPPORTING INFORMATION

Diversity Synthesis of Complex Pyridines Yields a Probe of a Key Neurotrophic Signaling Pathway

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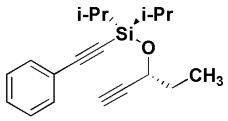
General techniques. Except as otherwise noted, reactions were carried out under nitrogen with dry, freshly purified solvents. Tetrahydrofuran was purified by passage through a column of activated alumina (A-2) and supported copper redox catalyst (Q-5 reactant). All other solvents were obtained from Aldrich. All solvents were degassed by vigorous bubbling of a stream of argon for 20 min immediately prior to use, or alternatively, by repeated freeze-pump-thaw cycles in liquid nitrogen under an atmosphere of argon. NMR spectra were recorded at 500 or 300 MHz for all compounds using Varian I-500 and Bruker Biospin 300 instruments. ^{1}H NMR chemical shifts are reported relative to residual $CHCl_3$ (7.26 ppm). ^{13}C NMR data were recorded at 125 or 75 MHz for all compounds using Varian 1-500 or Bruker Biospin 300 MHz instruments, respectively. ^{13}C chemical shifts are reported relative to the central line of $CDCl_3$ (77.0 ppm). Infrared spectra were recorded using a Perkin-Elmer FT-IR spectrometer (thin film or neat, as indicated). Mass spectra were obtained with JEOL AX 505, JEOL SX-102 and Micromass ESI-LCT spectrometers. Nitriles were obtained from Aldrich and used as received. NMO, TMAO, triphenylphosphine, dppp, and cyclooctadiene were obtained from Aldrich and used as received. Cyclopentadienylcobalt dicarbonyl was obtained from Strem Chemicals and stored at – 10 ºC under argon in the dark. All other catalysts were obtained commercially and used as received.

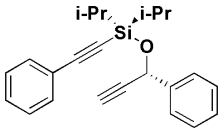
Representative procedure for silyl ether formation:
1-octyne (1.00 g, 9.07 mmol) was weighed into a flame-dried round-bottom flask equipped with magnetic stirrer and dissolved in THF (9.0 ml). The solution was cooled to – 78 °C and a 2.5 M *n*-BuLi solution in hexanes (3.62 ml, 9.07 mmol) was introduced dropwise. After 45 min, chlorodi*iso*propylsilane (1.55 ml, 9.07 mmol) was added dropwise, and the mixture warmed to ambient temperature. After 20 hours, the solution was diluted with Et_2O (9.0 ml) and quenched with a saturated soltuion of NH_4Cl (18.0 ml). Extraction was carried out using Et_2O, and combined organics were washed using saturated aqueous NaCl and H_2O. Drying over $MgSO_4$ and concentration afforded diisopropyl(oct-1-ynyl)silane (1.97 g, 8.78 mmol, 97%) which was used without further purification. Diisopropyl(oct-1-ynyl)silane (250 mg, 1.11 mmol) was moved to a tapered flask equipped with magnetic stirrer and dissolved in CH_2Cl_2 (2.5 ml). N-bromosuccinimide (198 mg, 1.11 mmol) was slowly introduced in 10-15 mg portions to the rapidly stirring solution, giving a pale yellow solution that was maintained under argon for 30 min and then added to a stirring solution of (*R*)-1-phenylprop-2-yn-1-ol (132 mg, 1.00 mmol), triethylamine (155 μl, 1.10 mmol), and 4-dimethylaminopyridine (13 mg, 0.10 mmol, 10 mol %) in CH_2Cl_2 (2.0 ml). After 12 h, the solution was concentrated and the crude mixture purified by silica chromatography using an *Isco Combiflash* 40 g

column with 20:1 hexanes:EtOAc as eluant to give (*R*)-diisopropyl(oct-1-ynyl)(1-phenylprop-2-ynyloxy)silane (249 mg, 0.70 mmol, 63%) as a clear oil. Other diynes used in this study were prepared by replacing 1-octyne with with desired acetylene and (*R*)-1-phenylprop-2-yn-1-ol with the desired alcohol.

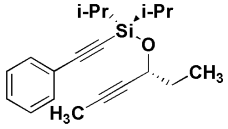
Characterization data for diyne substrates:



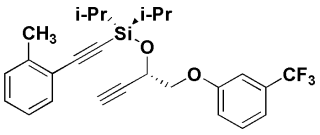
Diisopropyl(pent-1-yn-3-yloxy)(phenylethynyl)silane (I). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51-7.49 (m, 2 H); 7.37-7.30 (m, 3 H); 4.63 (dt, *J* = 6.50, 2.50, 1 H); 2.42 (d, *J* = 2.05, 1 H); 1.81-1.75 (m, 2 H); 1.17-1.06 (m, 14 H); 1.03 (t, *J* = 7.00, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.1, 128.8, 128.6, 128.3, 122.8, 107.4, 88.3, 85.1, 72.0, 65.3, 31.4, 18.5, 18.3, 17.3, 17.2, 17.1, 17.1, 13.6, 13.2, 12.9, 10.9, 9.3; IR (film): 3308, 2944, 2896, 2868, 2154, 1490, 1462, 1351, 1225, 1113, 1064, 1022, 987, 882, 826, 764, 694, 659, 540 cm^{-1}



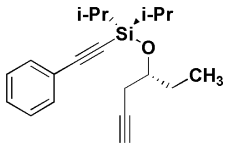
(*R*)-diisopropyl(2-phenylethynyl)(1-phenylprop-2-ynyloxy)silane (II). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58-7.56 (m, 2 H); 7.50-7.49 (m, 2 H); 7.37-7.29 (m, 6 H); 5.80 (d, *J* = 1.76, 1 H); 2.60 (d, *J* = 2.05, 1 H); 1.20 (br s, 6 H); 1.13-1.08 (m, 2 H); 1.03-1.02 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 132.1, 128.9, 128.3, 127.9, 126.5, 122.6, 108.0, 88.0, 84.3, 73.8, 65.9, 17.2, 17.1, 17.1, 13.5, 13.0; IR (film): 3308, 2951, 2860, 2154, 1484, 1456, 1064, 987, 959, 882, 826, 764, 700, 652, 526, 463 cm^{-1}



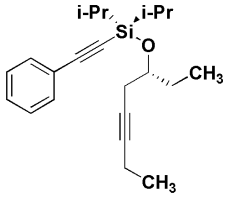
(hex-4-yn-3-yloxy)diisopropyl(2-phenylethynyl)silane (III). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 7.91, 1.46, 2 H); 7.36-7.30 (m, 3 H); 4.60-4.57 (m, 1 H); 1.84 (dd, *J* = 6.74, 2.05, 3 H); 1.77-1.71 (m, 2 H); 1.16 (d, *J* = 4.93, 6 H); 1.14-1.08 (m, 8 H); 1.01 (t, *J* = 7.32, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.1, 128.7, 128.2, 122.9, 107.0, 88.6, 80.5, 80.1, 65.7, 31.8, 17.2, 17.2, 17.1, 13.6, 12.9, 9.5, 3.6; IR (film): 3322, 3077, 3035, 2937, 2868, 2176, 2120, 1700, 1602, 1462, 1386, 1281, 1197, 1064, 987, 924, 882, 833, 736, 694 cm^{-1}



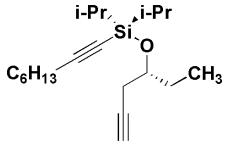
diisopropyl(2-*o*-tolylethynyl)(1-(3-(trifluoromethyl)phenoxy)but-3-yn-2-yloxy)silane (IV). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.32, 1 H); 7.32 (t, *J* = 7.81, 1 H); 7.26-7.08 (m, 6 H); 5.10-5.07 (m, 1 H); 4.20-4.13 (m, 2 H); 2.50 (s, 1 H); 2.45 (s, 3 H); 1.16-1.15 (m, 6 H); 1.11-1.09 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 140.8, 132.6, 129.9, 129.4, 129.0, 125.5, 122.3, 118.1, 117.7, 117.7, 111.6, 111.6, 106.9, 91.4, 81.8, 73.8, 71.9, 63.1, 20.8, 17.1, 17.0, 17.0, 13.4, 13.0; IR (film): 3309, 2948, 2891, 2865, 2148, 1591, 1491, 1448, 1330, 1300, 1243, 1170, 1117, 1065, 1048, 996, 970, 883, 848, 791, 756, 696, 661, 522, 456 cm^{-1}



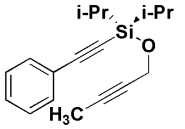
(hex-5-yn-3-yloxy)diisopropyl(phenylethynyl)silane (V). NMR (500 MHz, $CDCl_3$) δ 7.51-7.48 (m, 2 H); 7.36-7.30 (m, 3 H); 4.07-4.03 (m, 1 H); 2.53 (ddd, *J* = 16.50, 4.25, 2.50, 1 H); 2.44 (ddd, *J* = 16.75, 7.00, 3.00, 1 H); 1.98 (t, *J* = 2.50, 1 H); 1.82-1.74 (m, 1 H); 1.70-1.62 (m, 1 H); 1.17-1.04 (m, 14 H); 0.96 (t, *J* = 8.00, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.1, 128.7, 128.3, 122.9, 107.1, 89.0, 81.5, 73.2, 69.8, 29.7, 28.8, 26.3, 18.5, 18.3, 17.3, 17.3, 17.2, 13.4, 10.9, 9.3; IR (neat): 3309, 2965, 2952, 2896, 2865, 2157, 1496, 1465, 1391, 1365, 1252, 1226, 1113, 1070, 1035, 996, 943, 922, 887, 826, 761, 691, 648, 530 cm $^{-1}$



diisopropyl(oct-5-yn-3-yloxy)(phenylethynyl)silane (VI). NMR (500 MHz, $CDCl_3$) δ 7.50 (app dd, *J* = 7.75, 1.50, 2 H); 7.35-7.30 (m, 3 H); 4.02-3.97 (m, 1 H); 2.50-2.46 (m, 1 H); 2.39-2.34 (m, 1 H); 2.16-2.12 (m, 2 H); 1.79-1.72 (m, 2 H); 1.66-1.59 (m, 3 H); 1.12-1.08 (m, 14 H); 0.96 (t, *J* = 8.00, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.1, 128.6, 128.2, 123.0, 106.9, 89.3, 83.1, 73.8, 29.0, 26.7, 18.5, 18.3, 17.3, 17.3, 17.3, 14.2, 13.9, 13.4, 13.2, 12.5, 10.9, 9.3; IR (neat): 2965, 2935, 2874, 2161, 1487, 1461, 1383, 1317, 1248, 1209, 1109, 1070, 1030, 991, 926, 883, 830, 756, 687, 648, 535, 487 cm $^{-1}$



(hex-5-yn-3-yloxy)diisopropyl(oct-1-ynyl)silane (VII). NMR (500 MHz, $CDCl_3$) δ 3.98-3.95 (m, 1 H); 2.48 (ddd, *J* = 16.50, 4.50, 3.00, 1 H); 2.38 (ddd, *J* = 16.88, 7.50, 3.00, 1 H); 2.26 (t, *J* = 7.00, 2 H); 1.96 (t, *J* = 3.00, 1 H); 1.77-1.72 (m, 1 H); 1.64-1.59 (m, 1 H); 1.56-1.50 (m, 2 H); 1.45-1.39 (m, 2 H); 1.33-1.27 (m, 4 H); 1.10-1.02 (m, 14 H); 0.93 (t, *J* = 7.00, 3 H); 0.89 (t, *J* = 7.00, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.2, 128.8, 128.2, 122.8, 107.5, 88.0, 81.1, 53.2, 17.2, 17.1, 13.2, 3.6; IR (neat): 3317, 2965, 2930, 2865, 2174, 1470, 1387, 1248, 1113, 1078, 1030, 1009, 987, 935, 887, 839, 813, 739, 678, 635 cm $^{-1}$

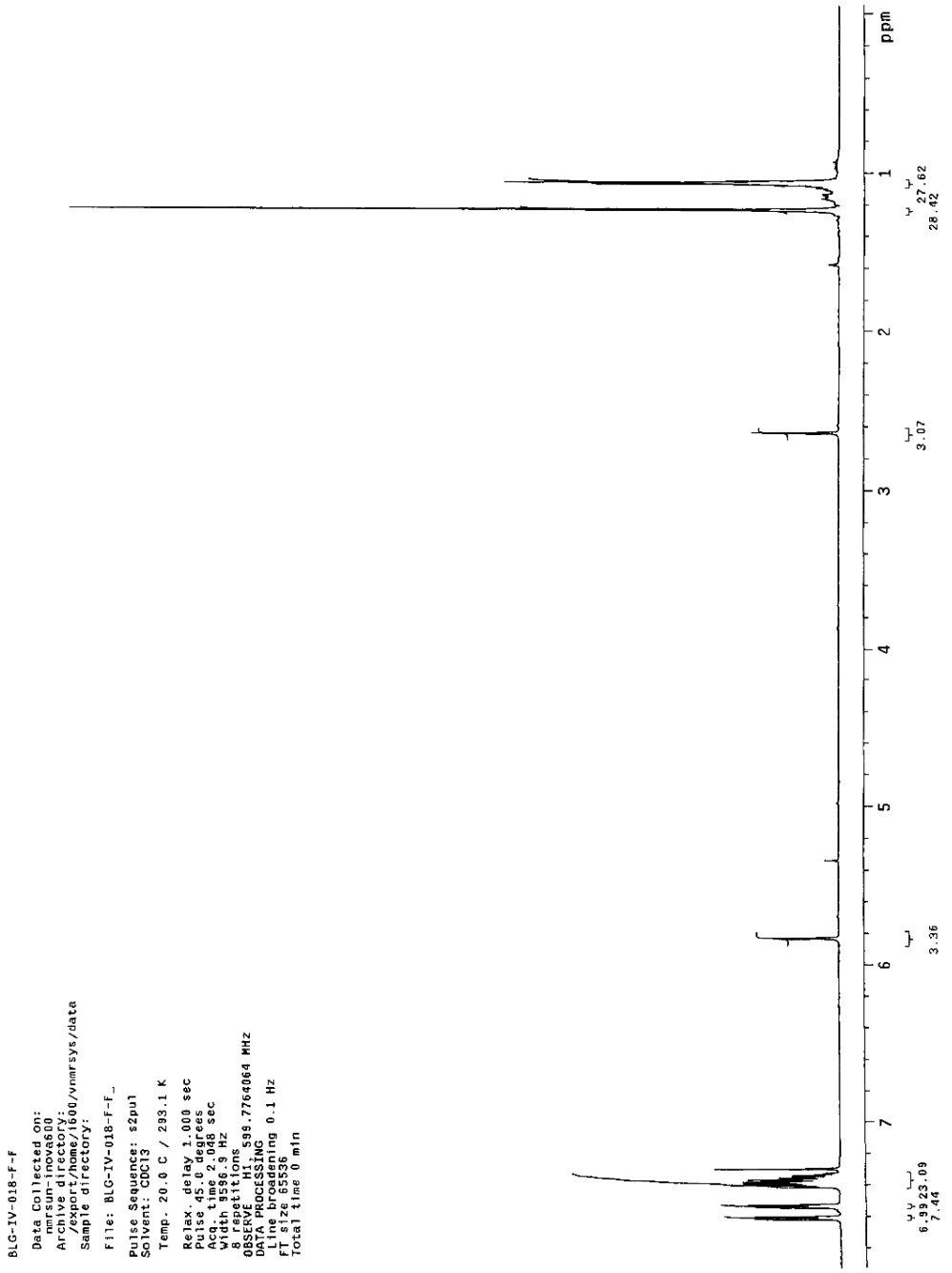


(but-2-ynyloxy)diisopropyl(phenylethynyl)silane (VIII). NMR (500 MHz, $CDCl_3$) δ 7.51-7.50 (m, 2 H); 7.35-7.32 (m, 3 H); 4.47-4.46 (m, 2 H); 1.85 (t, *J* = 2.00, 3 H); 1.15-1.05 (m, 14 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.2, 128.8, 128.2, 122.8, 107.5, 88.0, 81.1, 53.2, 17.3, 17.2, 17.1, 16.9, 13.2, 3.6; IR (neat): 2952, 2926, 2900, 2870, 2157, 1496, 1461, 1370, 1222, 1252, 1148, 1065, 1000, 930, 874, 835, 752, 691, 657, 530 cm $^{-1}$

Representative 1-H & 13-C NMR Spectra for Diyne Substrates:
*Spectra for compounds **II, III, & IV**:*

^{1}H and ^{13}C NMR spectra for silyl ether substrates:

page	subst	spectrum	page	subst	spectrum
5	**II**	1H	8	**III**	13C
6	**II**	13C	9	**IV**	1H
7	**III**	1H	10	**IV**	13C


BLG-IV-018-F-F
Data Collected on:
nmrsun-inova600
Archive directory:
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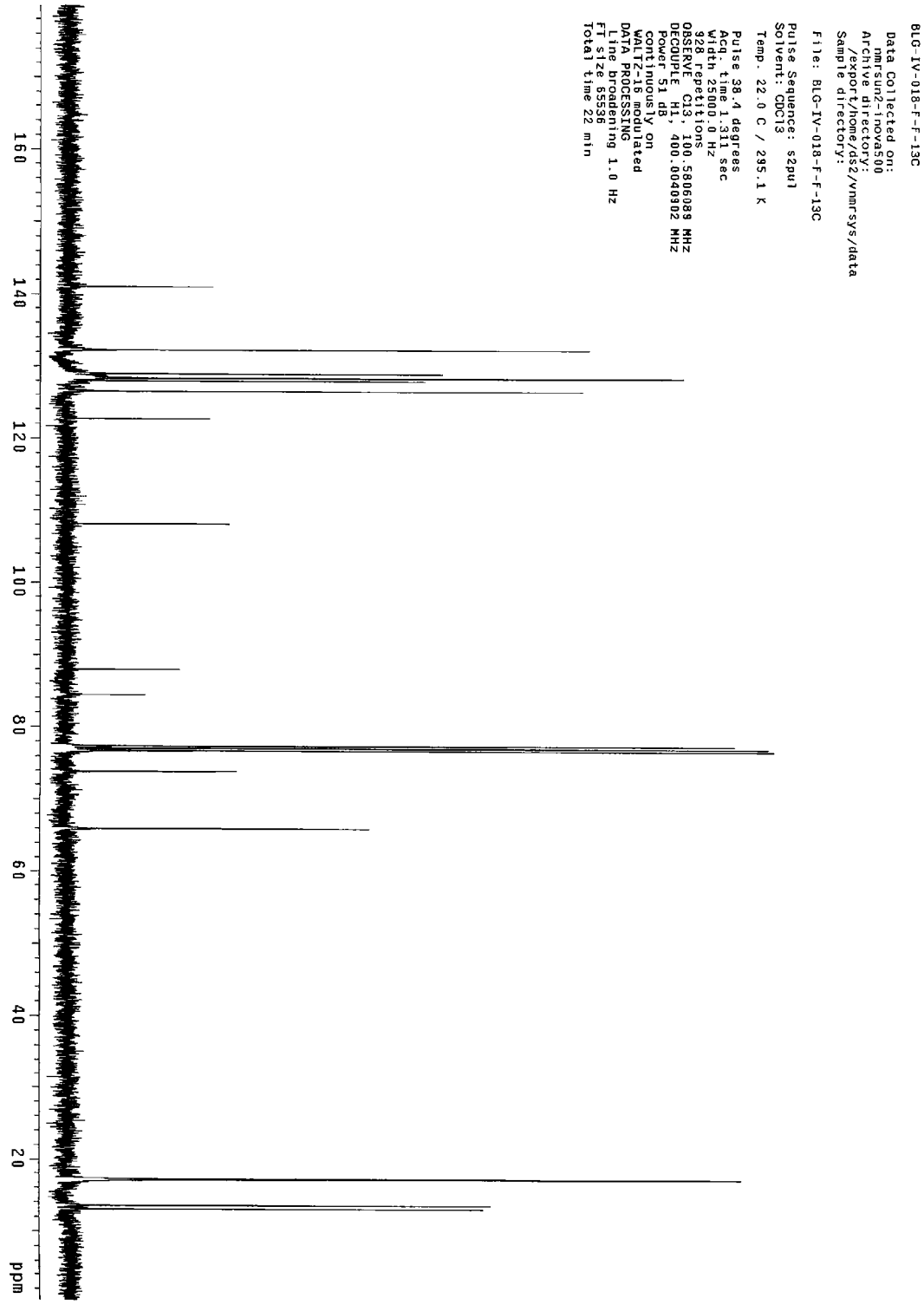
Sample directory:
File: BLG-IV-018-F-F_
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 20.0 C / 293.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 9596.9 Hz
8 repetitions
OBSERVE H1, 599.7764064 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 0 min
6.99
23.09
7.44
3.36
3.07
27.62
28.42
ppm


BLG-IV-018-F-F-13C
Data Collected on:
nmrsun2-inova500
Archive directory:
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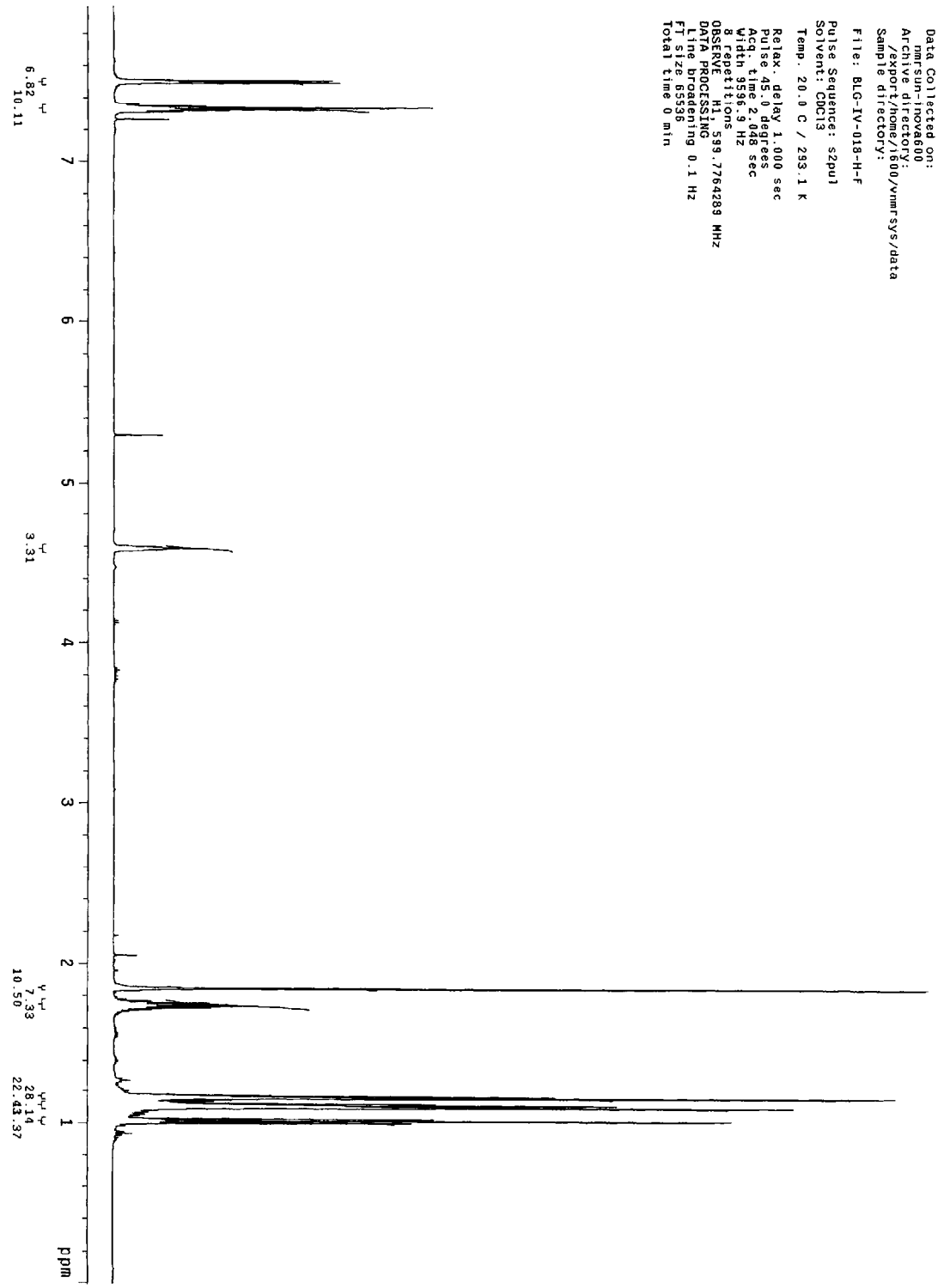
Sample directory:
File: BLG-IV-018-F-F-13C
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 22.0 C / 295.1 K
Pulse 38.4 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
928 repetitions
OBSERVE C13, 100.5806089 MHz
DECOUPLE H1, 400.0040902 MHz
Power 51 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 22 min
160
140
120
100
80
60
40
20
ppm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File: BLG-IV-018-H-F
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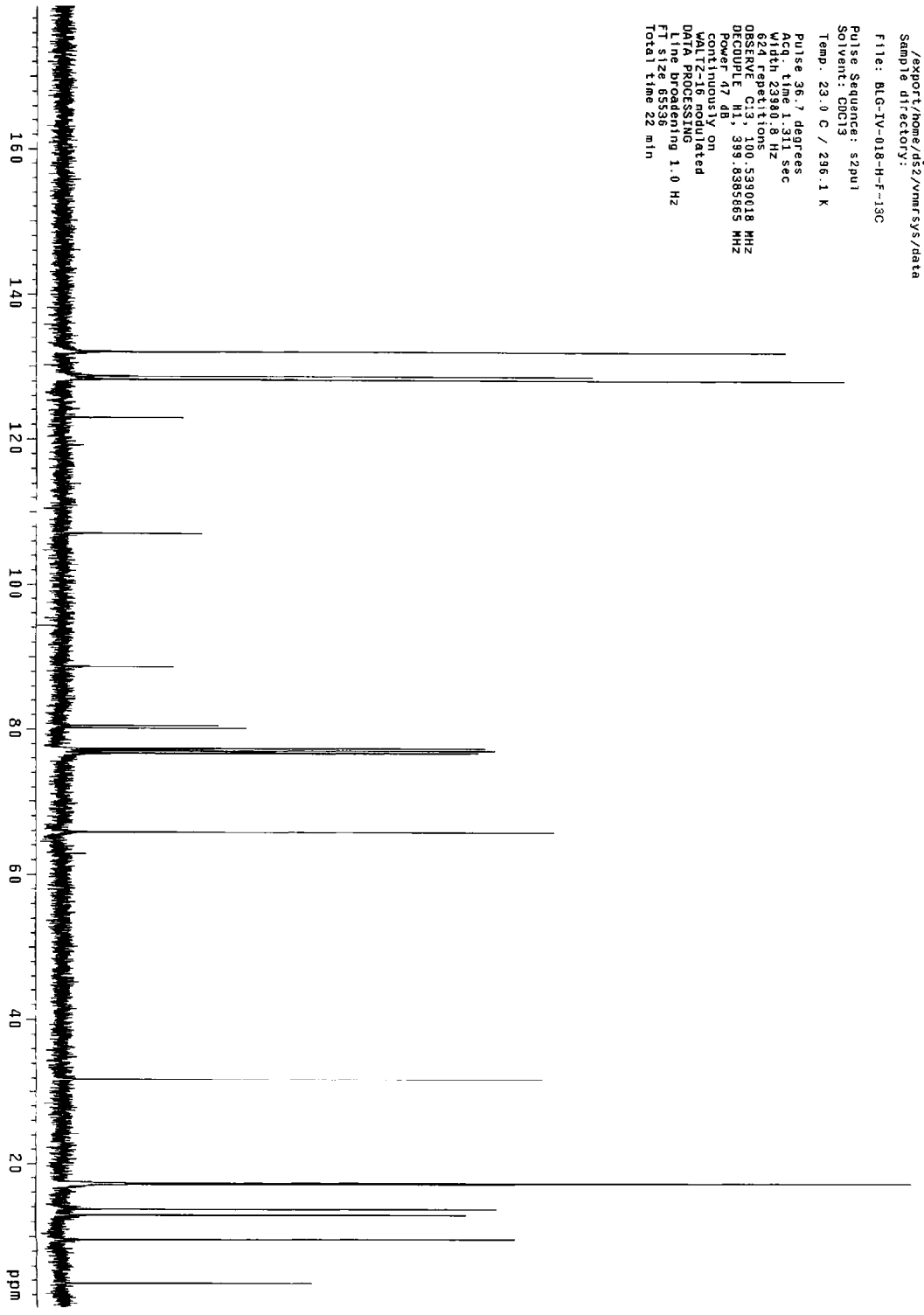
Solvent: CDCl3
Temp. 20.0 C / 293.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 9596.9 Hz
8 repetitions
OBSERVE H1 599.7764289 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 0 min
6.82
10.11
3.31
7.33
10.50
28.14
22.43
37
7
6
5
4
3
2
1
ppm


BLG-IV-018-H-F-13C
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nmrsun2-inova500
Archive directory:
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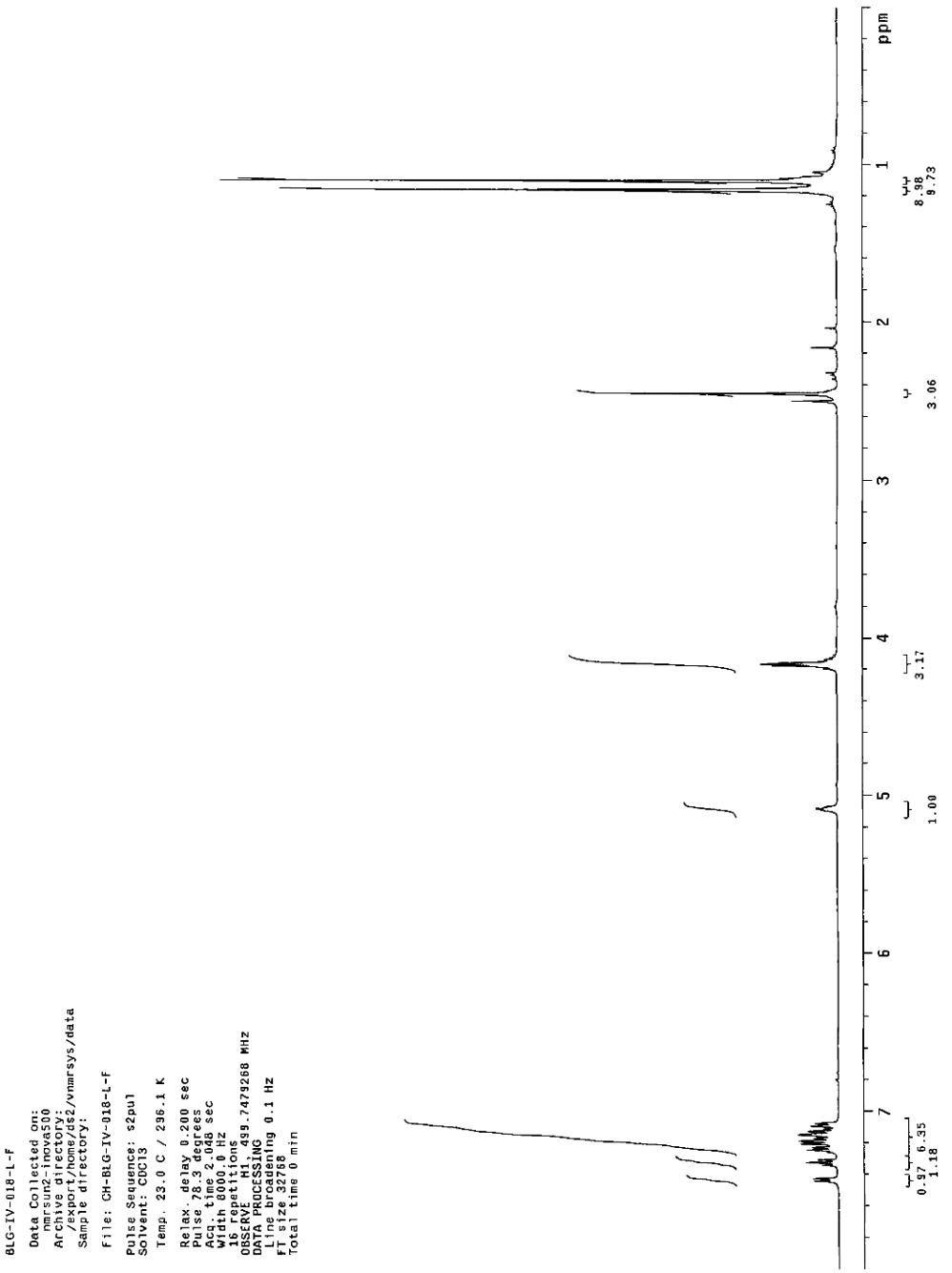
Sample directory:
File: BLG-IV-018-H-F-13C
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 23.0 C / 296.1 K
Pulse 36.7 degrees
Acq. time 1.311 sec
Width 23981.8 Hz
64 repetitions
OBSERVE C13, 100.5390018 MHz
DECOUPLE H1, 399.8388385 MHz
Power 17 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 22 min
160
140
120
100
80
60
40
20
ppm


BLG-IV-018-L-F
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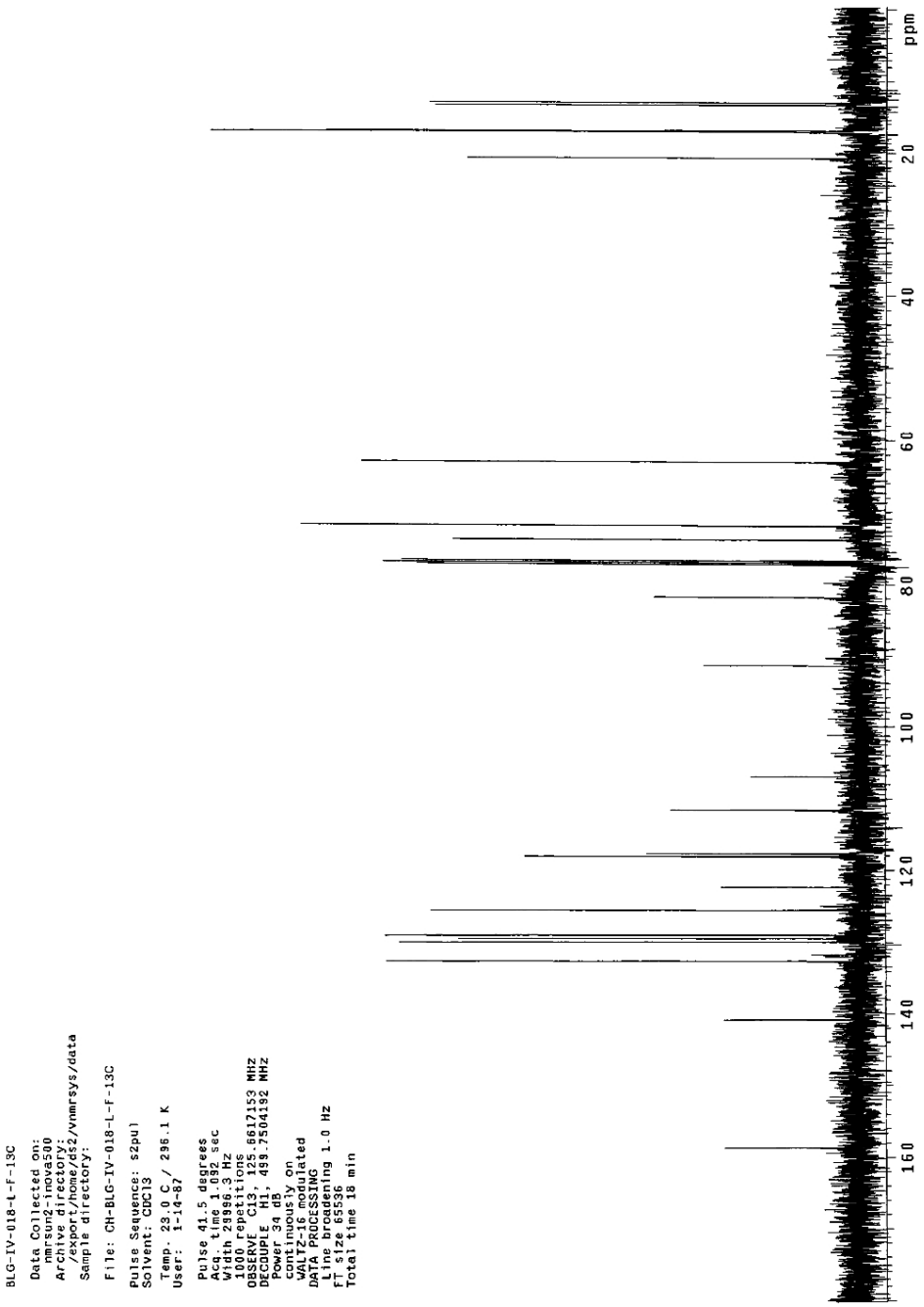
Archive directory:
/export/home/ds2/vnmrsys/data
Sample directory:
File: CH-BLG-IV-018-L-F
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 23.0 C / 296.1 K
Relax. delay 8.200 sec
Pulse 78.3 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7479268 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 0 min
ppm
0.97 6.35
1.18
1.00
3.17
3.06
8.98
9.73


BLG-IV-018-L-F-13C
Data Collected on:
nmrsun2-inova500
Archive directory:
/export/home/ds2/vnmrsys/data
Sample directory:
File: CH-BLG-IV-018-L-F-13C
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 23.0 C / 296.1 K
User: 1-id-87
Pulse 41.5 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
1000 repetitions
OBSERVE C13, 125.6817153 MHz
DECOUPLE H1, 499.7504192 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 18 min
160
140
120
100
80
60
40
20
ppm

Procedure for optimization of cycloisomerization (Table I):

Diisopropyl(pent-1-yn-3-yloxy)(phenylethynyl)silane **1** (10.0 mg, 0.033 mmol) was placed into an oven-dried sealed tube equipped with magnetic stirrer and dissolved in degassed solvent (0.67 ml). 5-methoxy-2-pyridinecarbonitrile (6.7 mg, 0.05 mmol) was added as a solid to the stirring solution. Additives/ligands (0.017 mmol, 50 mol %) were introduced either as solids or minimal solutions in xylenes. After complete dissolution, a solution of cyclopentadienylcobalt(I) dicarbonyl in degassed xylenes (50 μl) was introduced by syringe, giving a pale yellow solution. The sealed tube was immediately submerged into an oil bath preheated to 140 °C. After 24 h, the dark brown solution was cooled to ambient temperature and loaded onto a 4 g silica plug. Filtration was performed using an *Isco Combiflash* system using a gradient starting with hexanes and ending with 1/1 hexanes/ethyl acetate (total volume of approximately 40 ml), which effectively removed insoluble cobalt byproducts. Pooled fractions were concentrated *in vacuo* and assayed for conversion by ^{1}H NMR. Purification was performed by silica gel chromatography using an *Isco Combiflash* 12 g column with 20:1 hexanes:EtOAc as eluant, providing 3-ethyl-1,1-diisopropyl-5-(6-methoxypyridin-3-yl)-7-phenyl-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridine **5** as a clear oil.

Optimized procedure for cycloisomerization (Results from Table I):
*Reaction sequence used for the generation of **5***:

Diisopropyl(pent-1-yn-3-yloxy)(phenylethynyl)silane **1** (10.0 mg, 0.033 mmol) was placed into an oven-dried sealed tube equipped with magnetic stirrer and dissolved in degassed THF (0.67 ml). 5-methoxy-2-pyridinecarbonitrile (6.7 mg, 0.05 mmol) was added as a solid to the stirring solution. After complete dissolution, a solution of cyclopentadienylcobalt(I) dicarbonyl (1.5 mg, 0.0083 mmol, 25 mol %) in degassed xylenes (50 μl) was introduced by syringe, giving a pale yellow solution. The sealed tube was immediately submerged into an oil bath preheated to 140 °C. After 24 h, the dark brown solution was cooled to ambient temperature and loaded onto a 4 g silica plug. Filtration was performed using an *Isco Combiflash* system using a gradient starting with hexanes and ending with 1/1 hexanes/ethyl acetate (total volume of approximately 40 ml), which effectively removed insoluble cobalt byproducts. Pooled fractions were concentrated *in vacuo* and assayed for conversion by ^{1}H NMR. Purification was performed by silica gel chromatography using an *Isco Combiflash* 12 g column with 20:1 hexanes:EtOAc as eluant, providing 3-ethyl-1,1-diisopropyl-5-(6-methoxypyridin-3-yl)-7-phenyl-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridine **5** (8.8 mg, 0.020 mmol, 61%) as a clear oil.

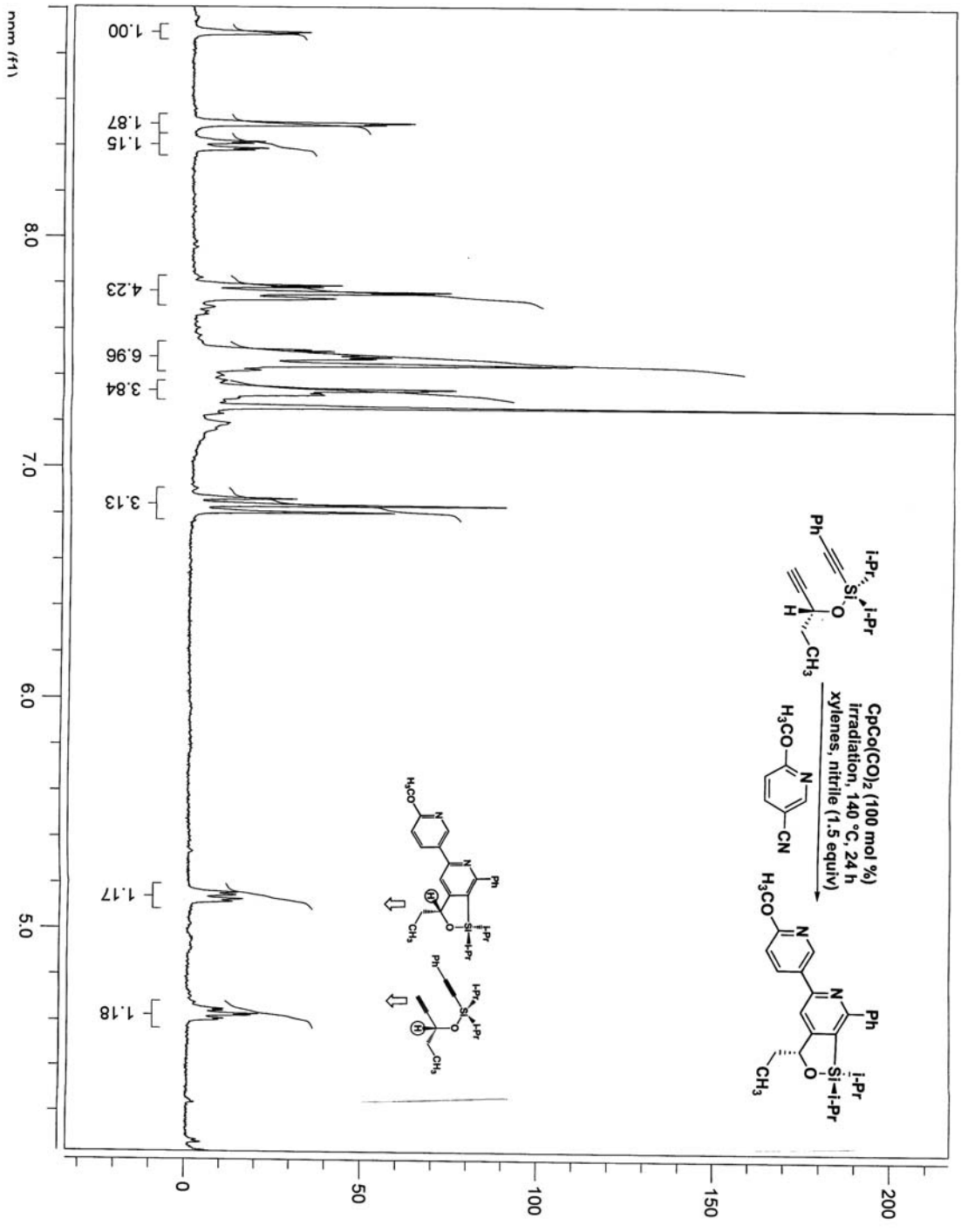
Spectral data for reaction optimization experiments (Table I):
^{1}H NMR spectra for entries 1-20:

page	*table 1 entry*	*reaction conditions*	*Conversion*
S-13	1	$CpCo(CO)_2$ (100 mol %), xylenes, 140 ºC, hυ	50%
S-14	2	$CpCo(CO)_2$ (25 mol %), xylenes, 140 ºC, hυ	17%
S-15	3	$CpCo(CO)_2$ (25 mol %), dimethoxyethane, 140 ºC, hυ	29%
S-16	4	$CpCo(CO)_2$ (25 mol %), dichloroethane, 140 ºC, hυ	69%
S-17	5	$CpCo(CO)_2$ (25 mol %), 1,4-dioxane, 140 ºC, hυ	<2%
S-18	6	$CpCo(CO)_2$ (25 mol %), chlorobenzene, 140 ºC, hυ	18%
S-19	7	$CpCo(CO)_2$ (25 mol %), dichlorobenzene, 140 ºC, hυ	8%
S-20	8	$CpCo(CO)_2$ (25 mol %), pyridine, 140 ºC, hυ	<2%
S-21	9	$CpCo(CO)_2$ (25 mol %), lutidene, 140 ºC, hυ	8%
S-22	10	$CpCo(CO)_2$ (25 mol %), trichloroethane, 140 ºC, hυ	13%
S-23	11	$CpCo(CO)_2$ (25 mol %), dimethylacetamide, 140 ºC, hυ	<2%
S-24	12	$CpCo(CO)_2$ (25 mol %), 2-methyltetrahydrofuran, 140 ºC, hυ	80%
S-25	13	$CpCo(CO)_2$ (25 mol %), THF, 140 ºC, hυ	82%
S-26	14	$CpCo(CO)_2$ (25 mol %), xylenes, NMO (50 mol %), 140 ºC, hυ	37%
S-27	15	$CpCo(CO)_2$ (25 mol %), xylenes, TMAO (50 mol %), 140 ºC, hυ	57%
S-28	16	$CpCo(CO)_2$ (25 mol %), xylenes, PPh_3 (50 mol %), 140 ºC, hυ	54%
S-29	17	$CpCo(CO)_2$ (25 mol %), xylenes, dppp (50 mol %), 140 ºC, hυ	40%

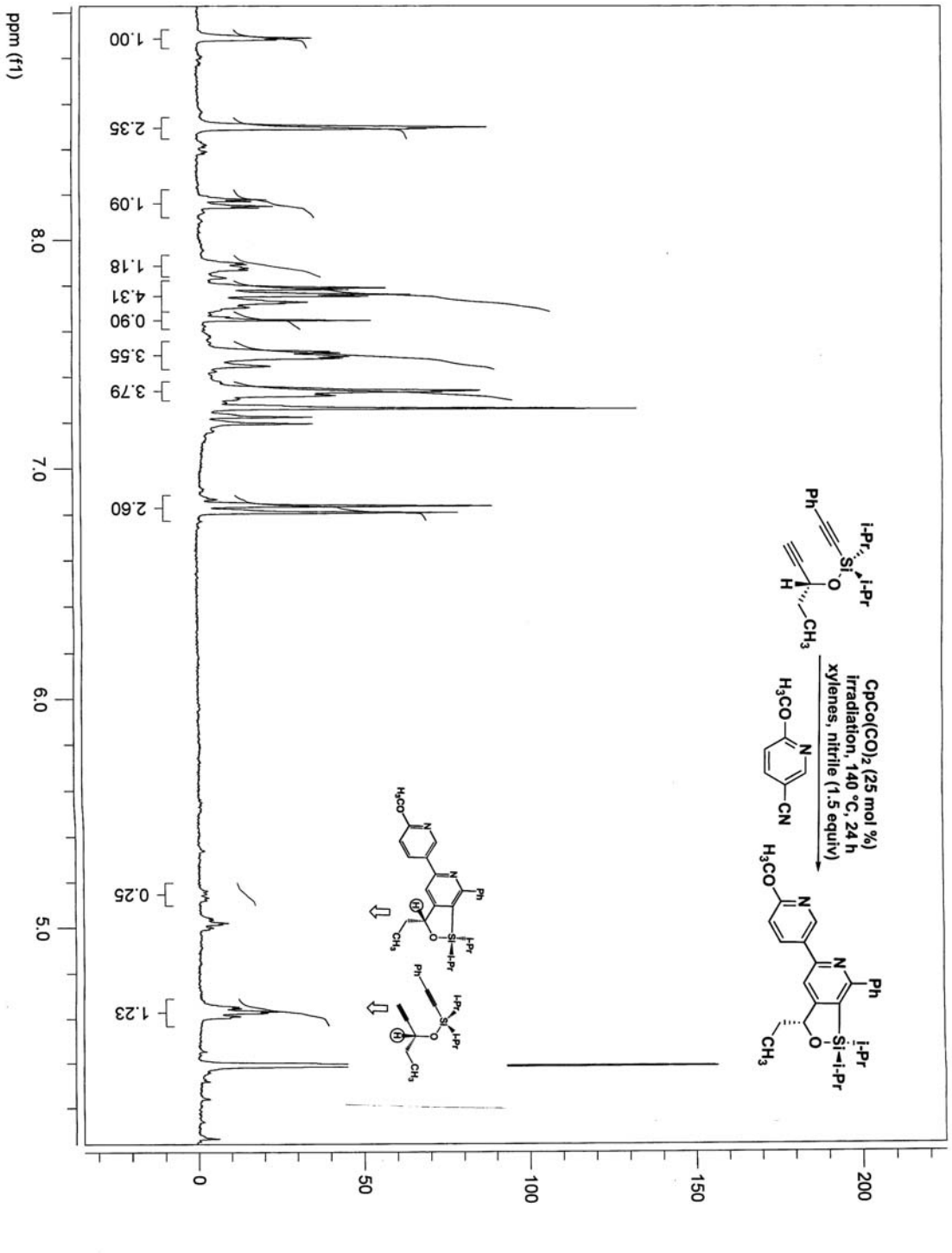
S-30	18	$CpCo(CO)_2$ (25 mol %), xylenes, cod (50 mol %), 140 ºC, hυ	41%
S-31	19	$CpCo(CO)_2$ (25 mol %), THF, 140 ºC	>95%
S-32	20	$CpCo(CO)_2$ (25 mol %), THF, 70 ºC	<2%

Conversions were determined on the basis of integration between the methine proton H(A) at 4.6 ppm in diisopropyl(pent-1-yn-3-yloxy)(phenylethynyl)silane **1** and the equivalent methine proton H(A) at 5.0 ppm in 3-ethyl-1,1-diisopropyl-5-(6-methoxypyridin-3-yl)-7-phenyl-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridine **5**.

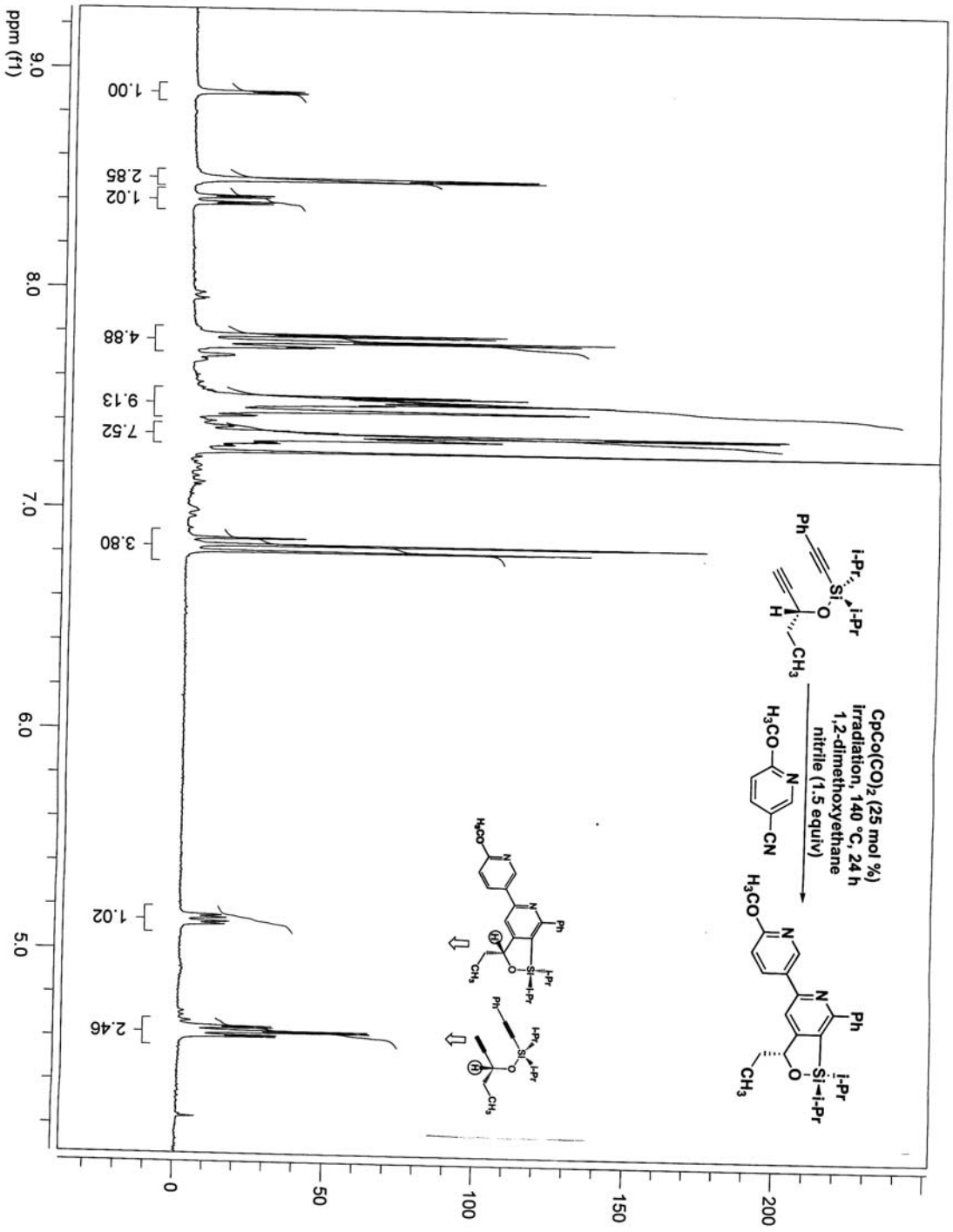
Solvent: $CDCl_3$ – Frequency: 300 MHz



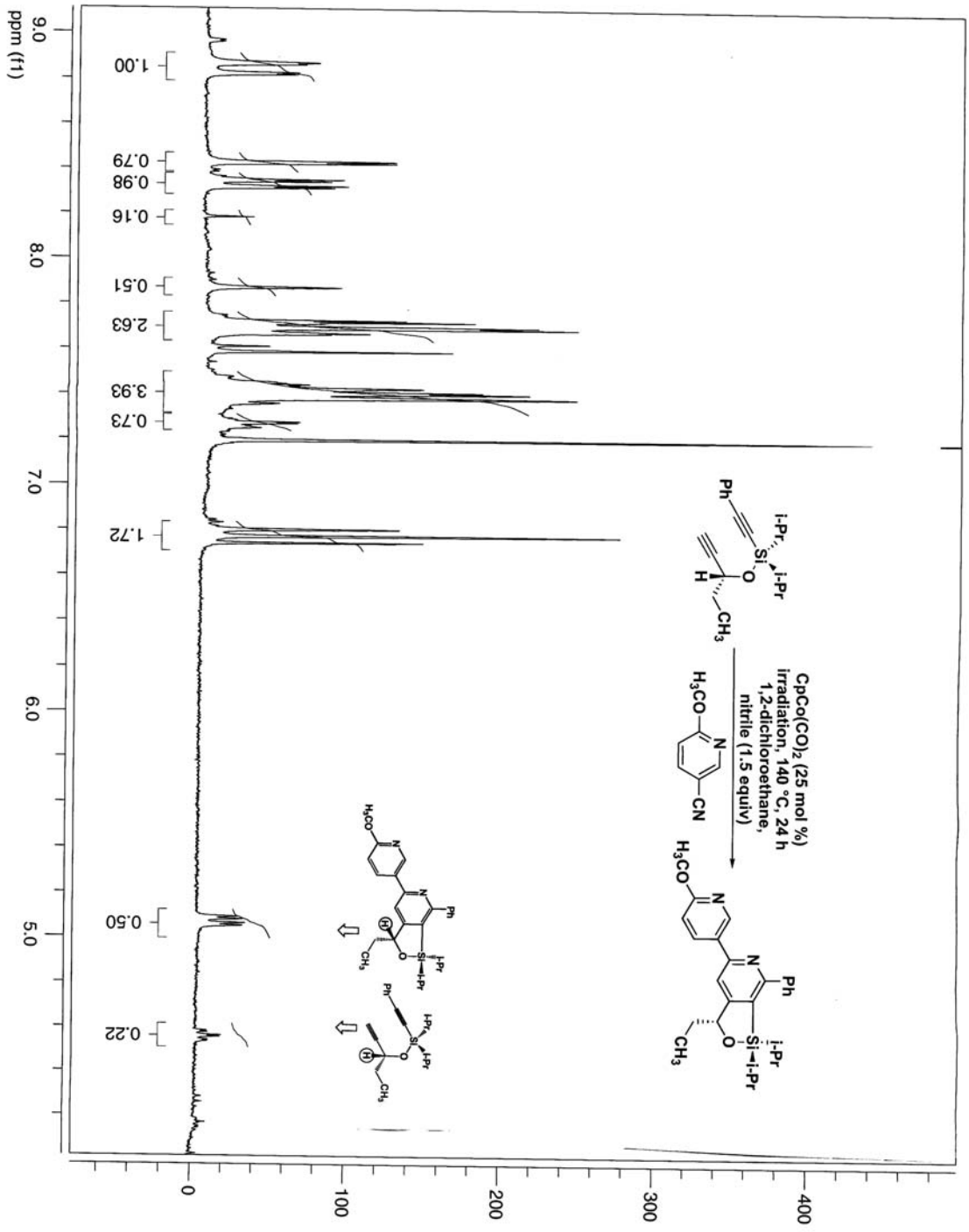
Solvent: $CDCl_3$ – Frequency: 300 MHz



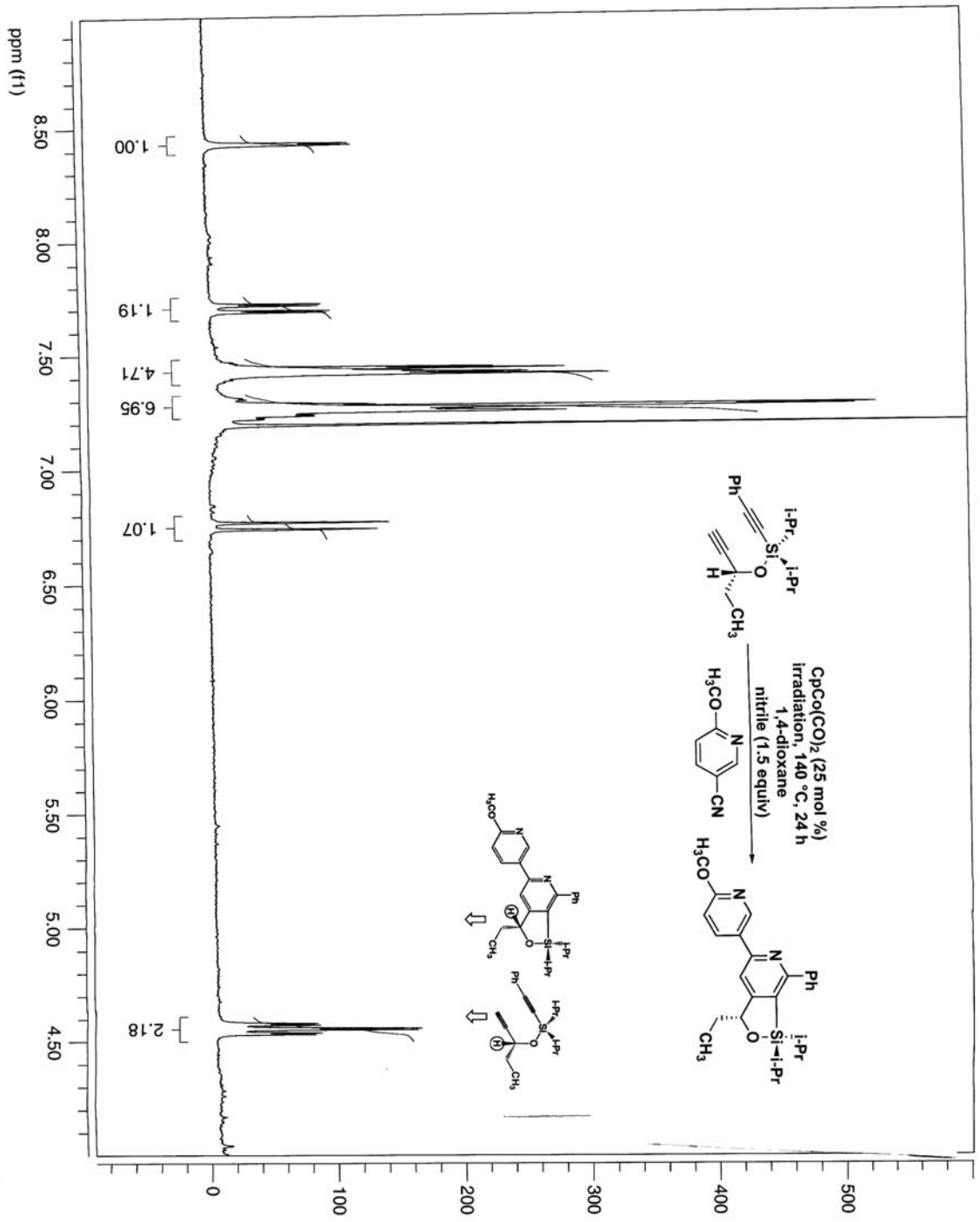
Solvent: $CDCl_3$ – Frequency: 300 MHz



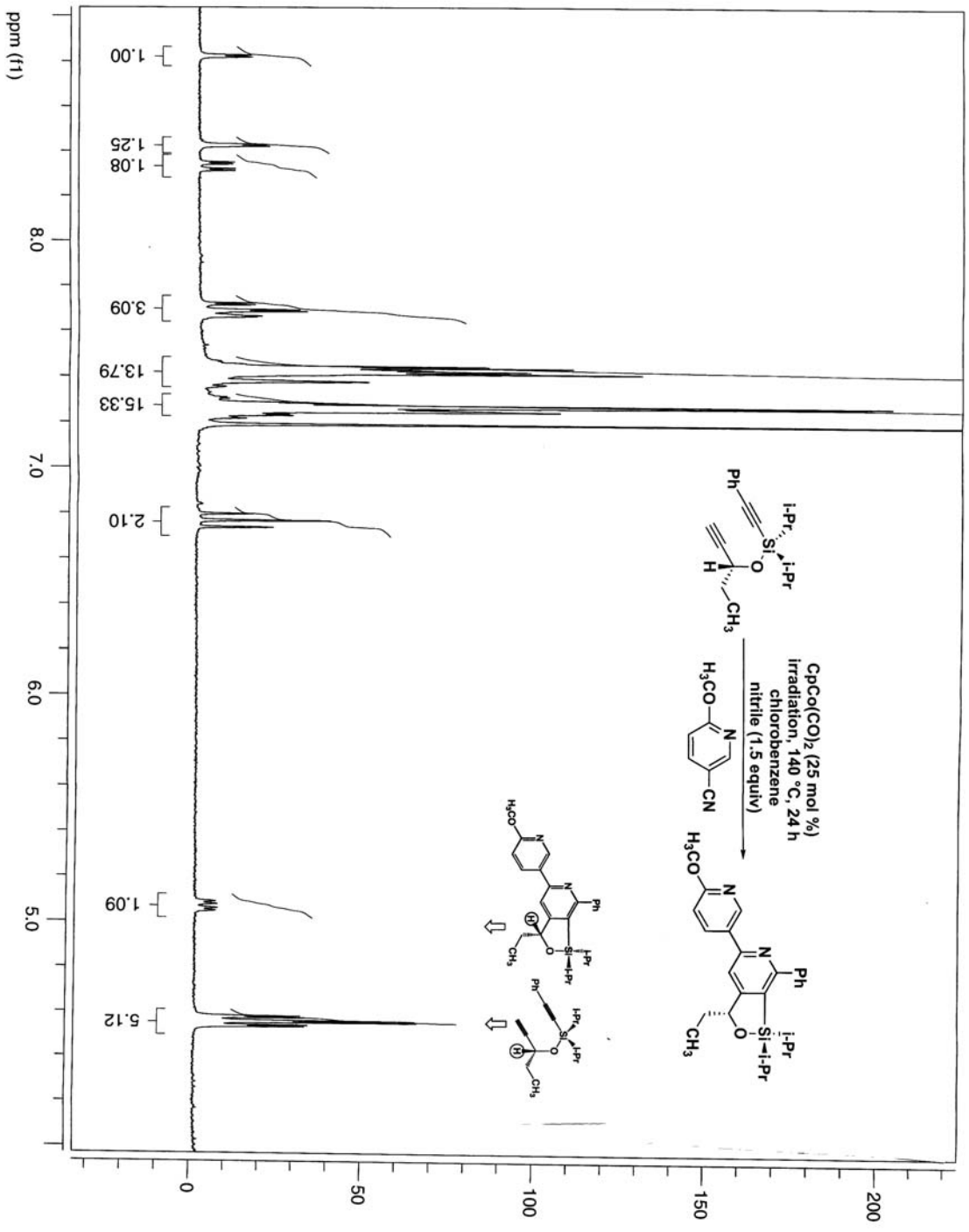
Solvent: $CDCl_3$ – Frequency: 300 MHz



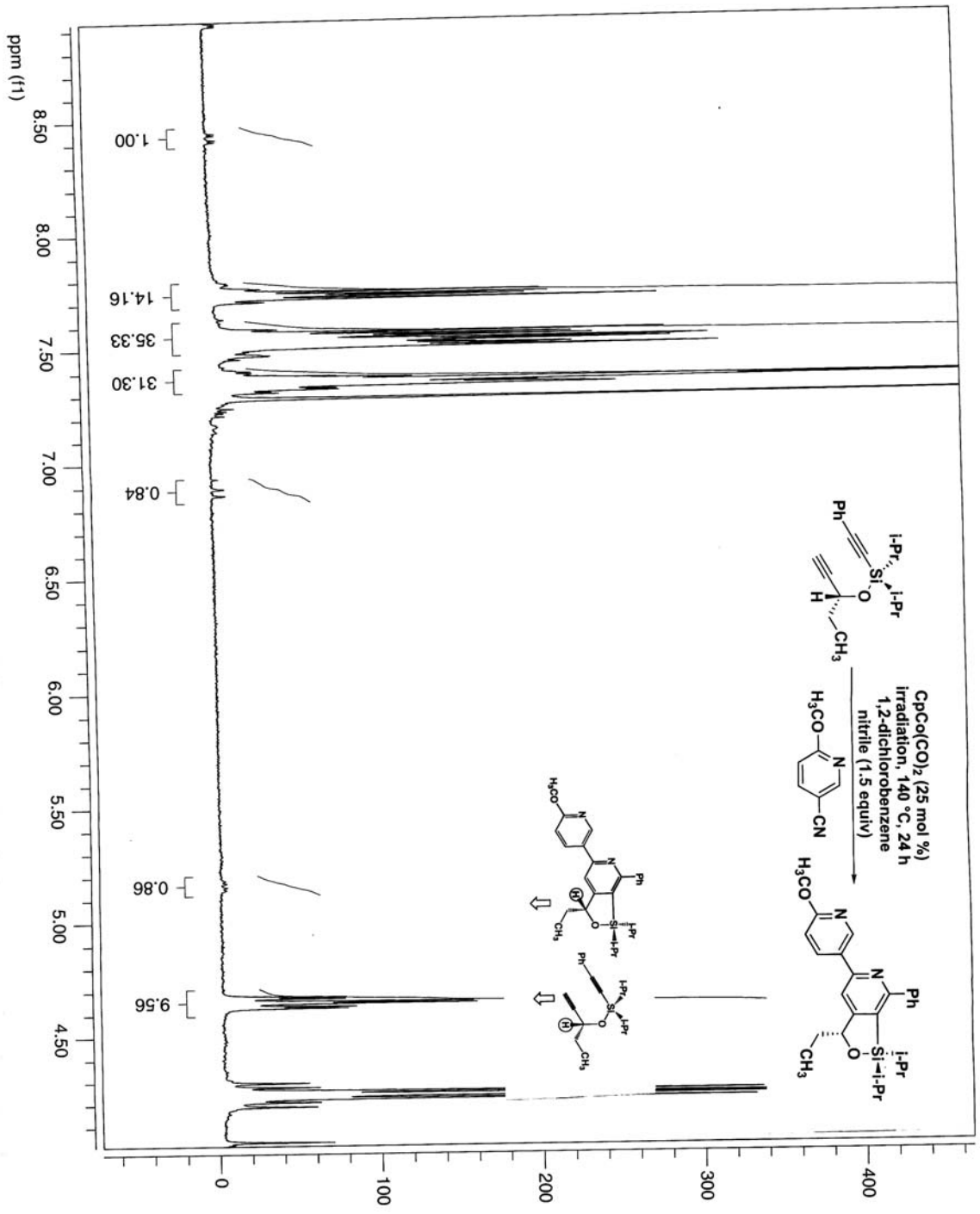
Solvent: $CDCl_3$ – Frequency: 300 MHz



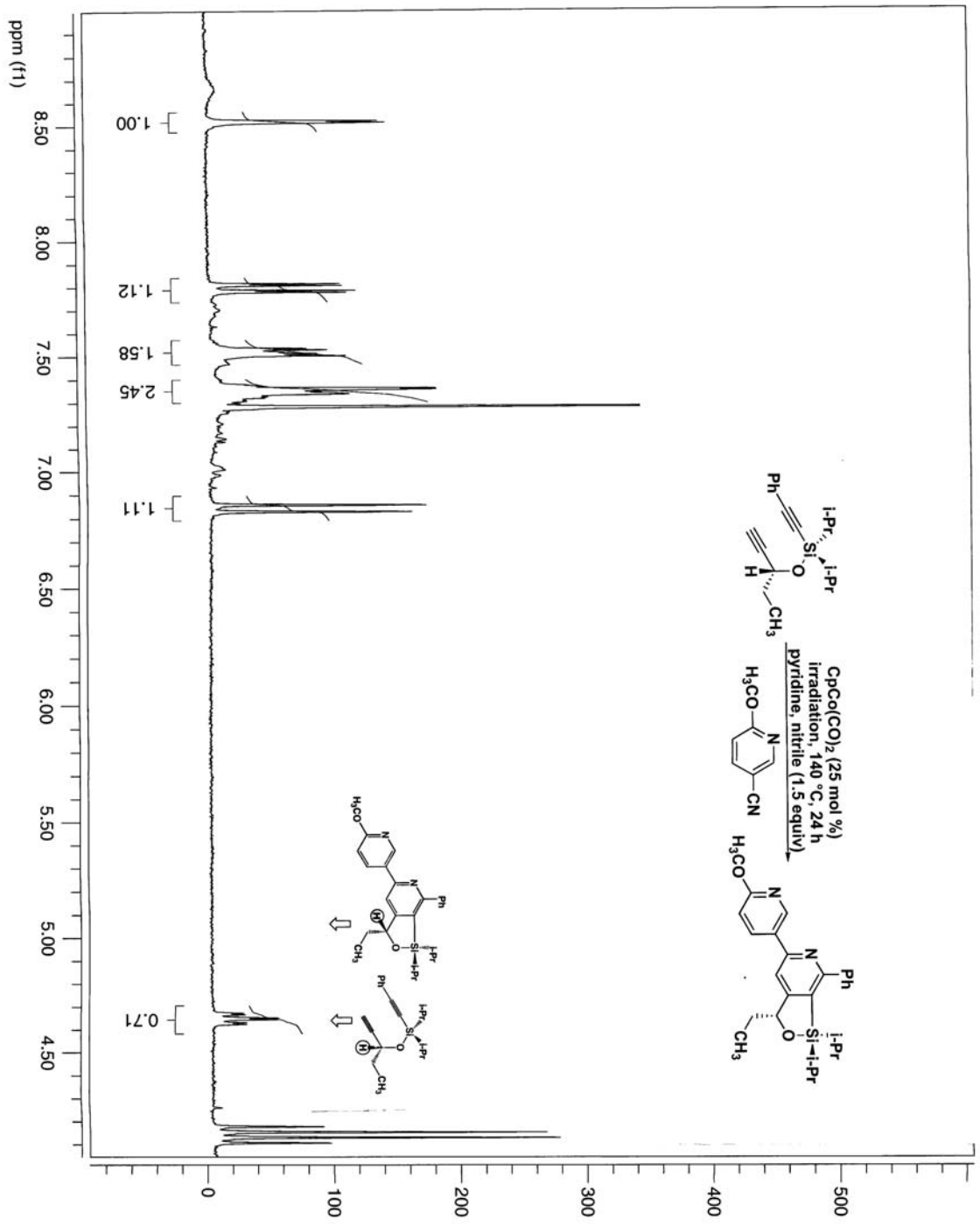
Solvent: $CDCl_3$ – Frequency: 300 MHz



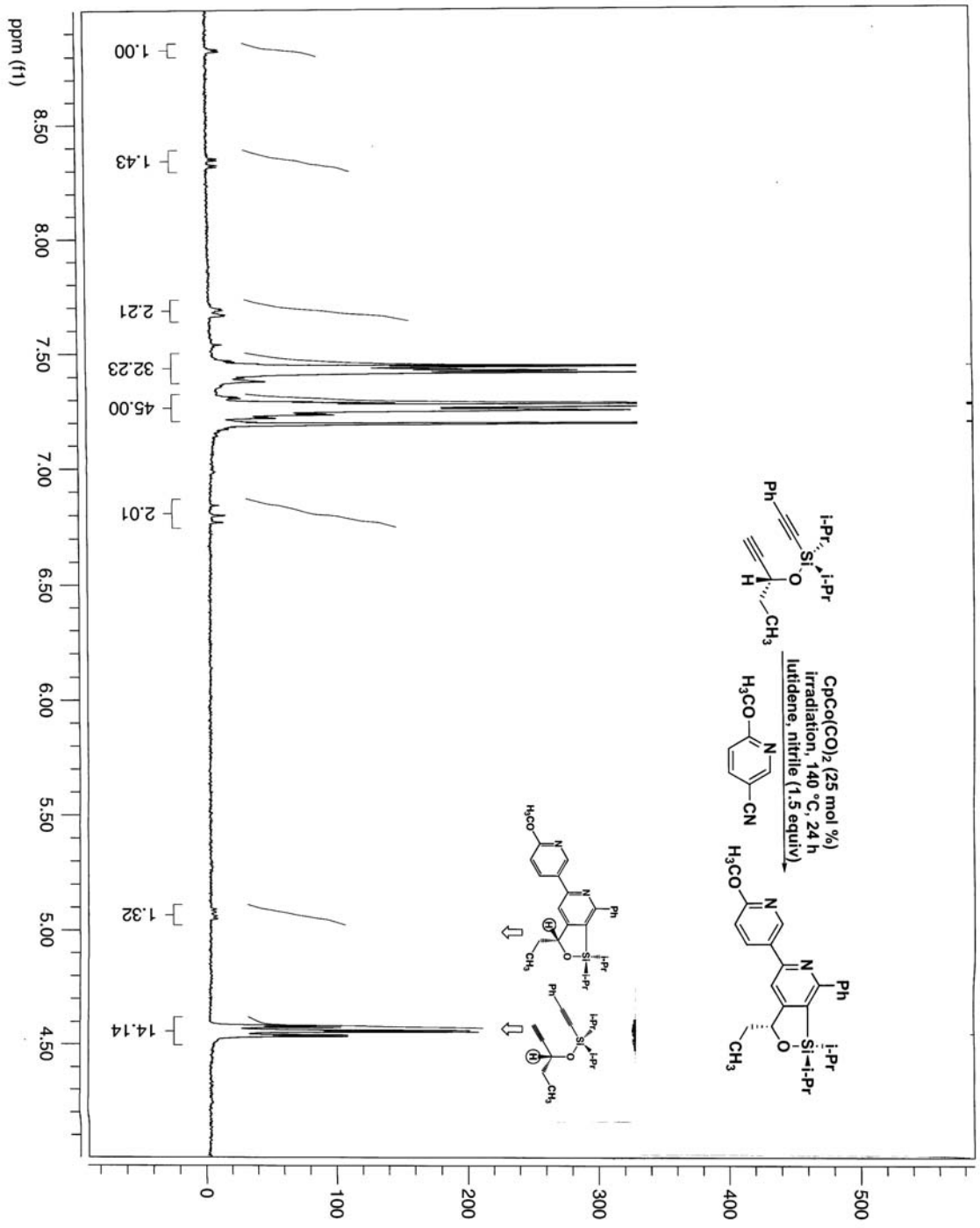
Solvent: $CDCl_3$ – Frequency: 300 MHz



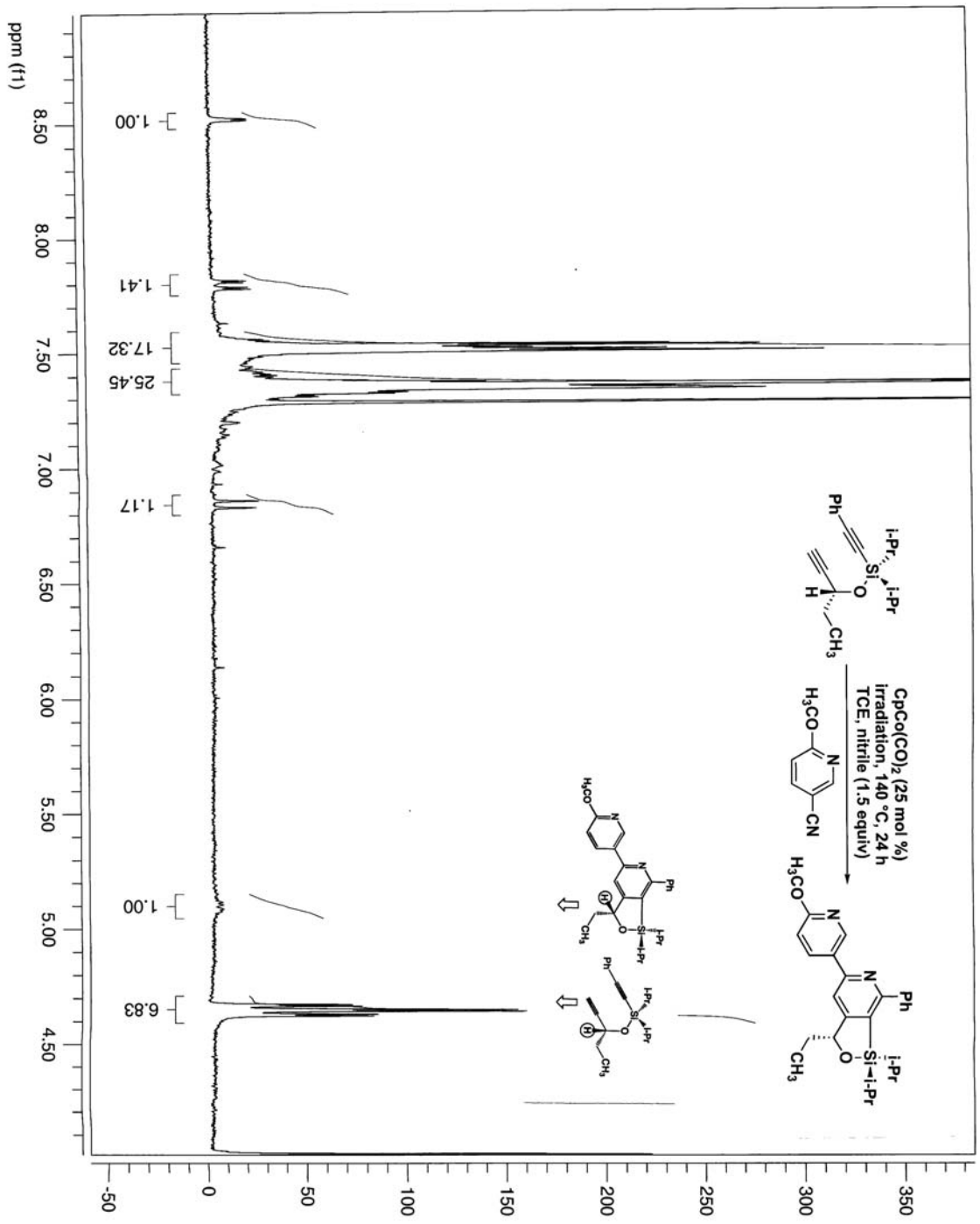
Solvent: $CDCl_3$ – Frequency: 300 MHz



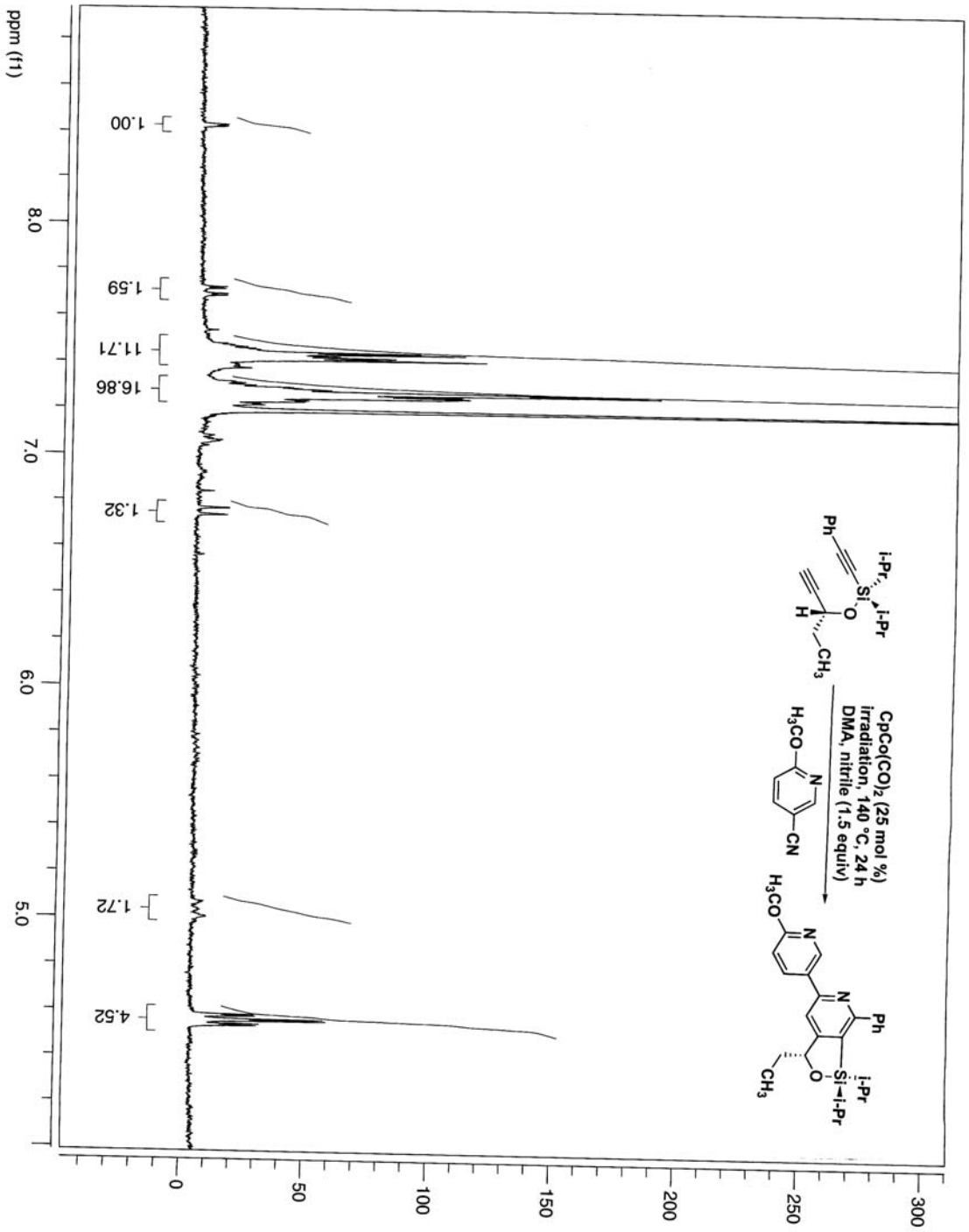
Solvent: $CDCl_3$ – Frequency: 300 MHz



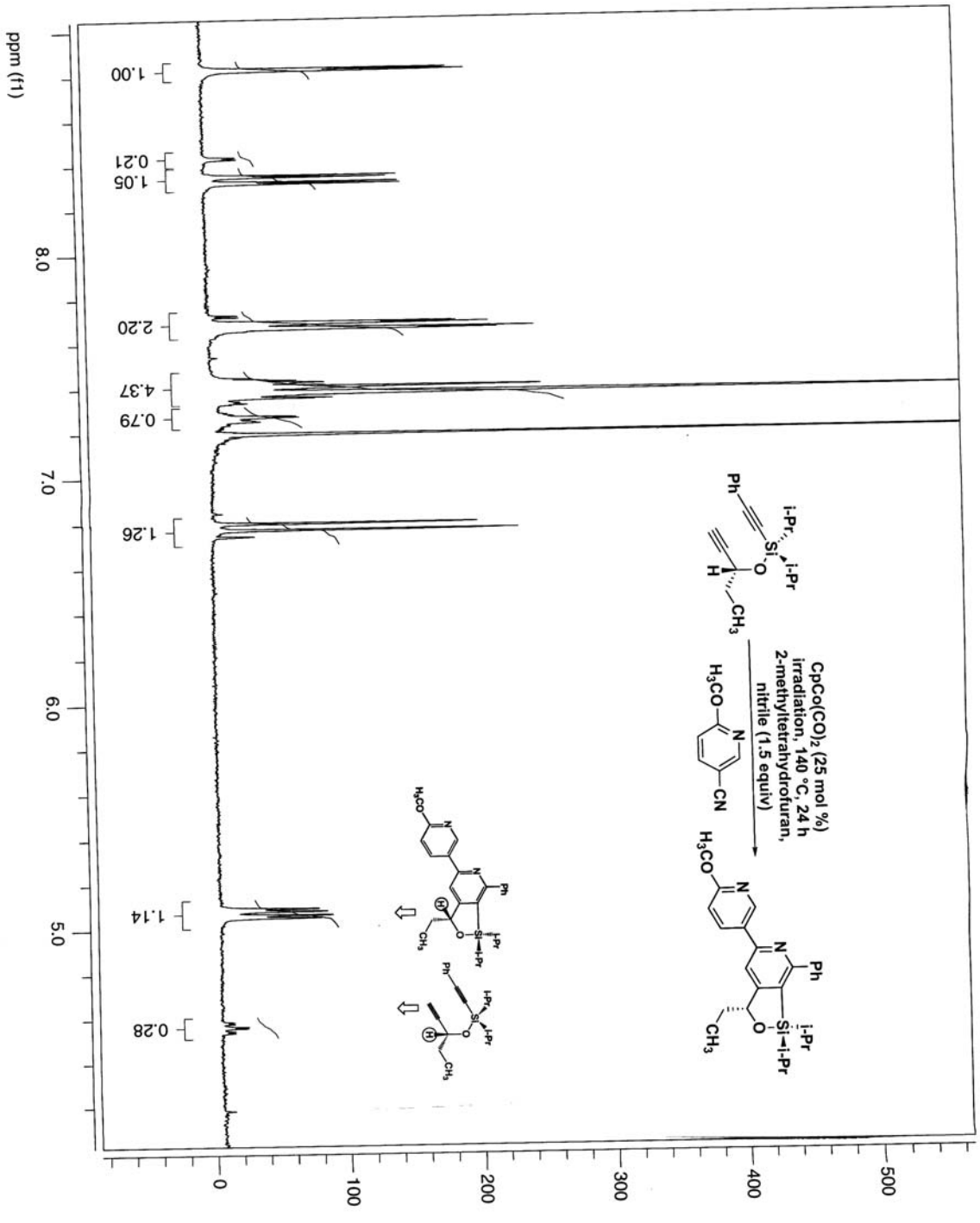
Solvent: $CDCl_3$ – Frequency: 300 MHz



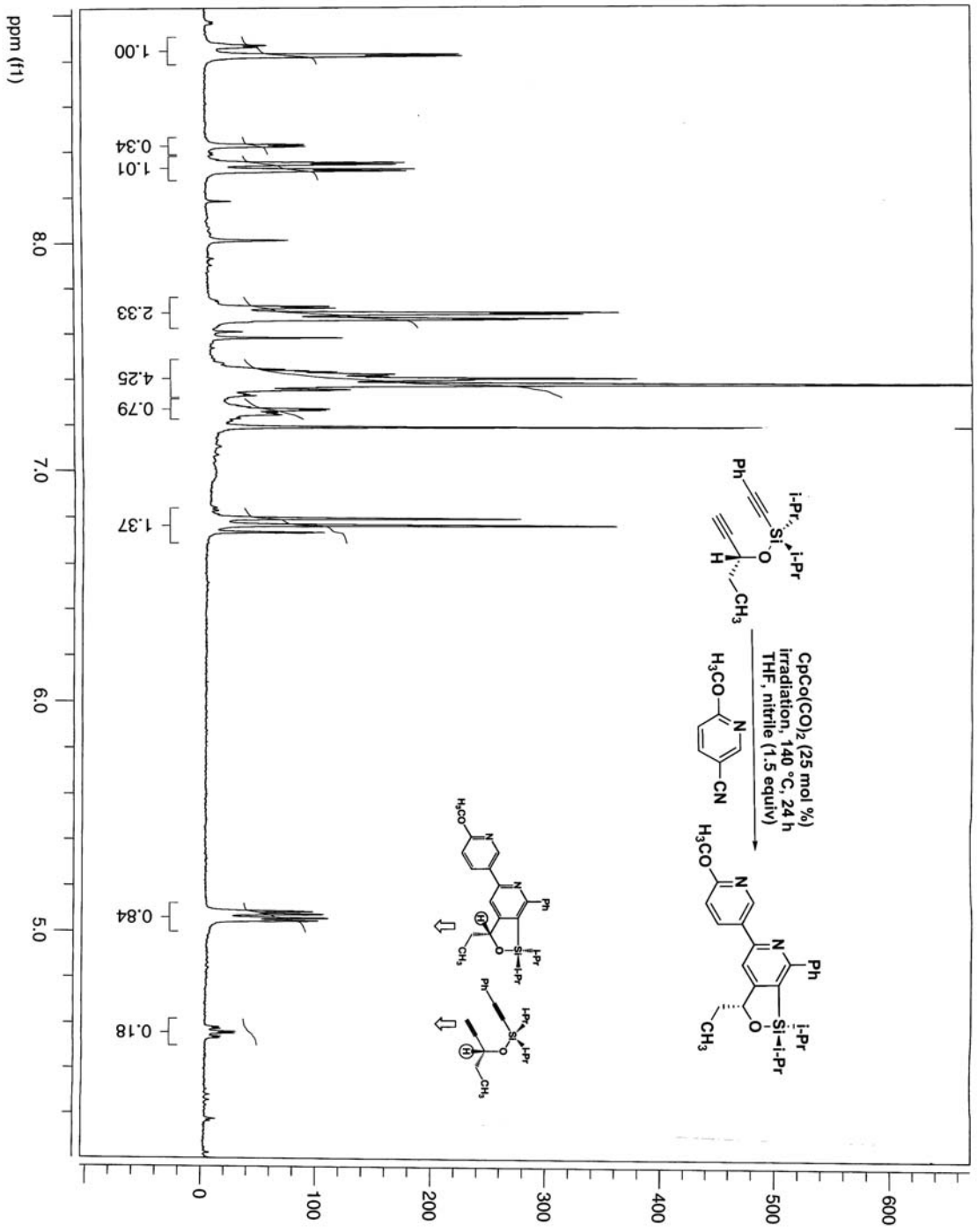
Solvent: $CDCl_3$ – Frequency: 300 MHz



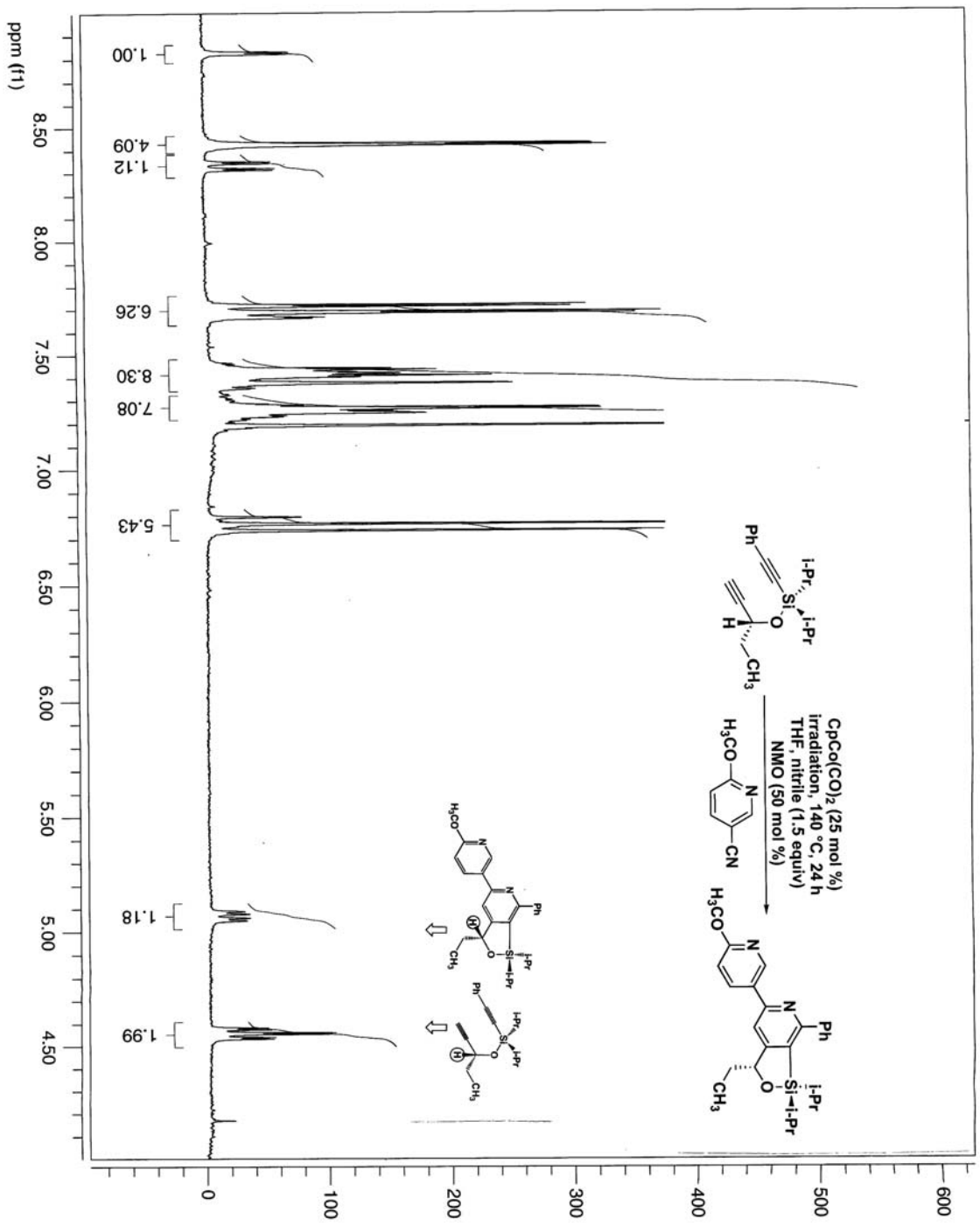
Solvent: $CDCl_3$ – Frequency: 300 MHz



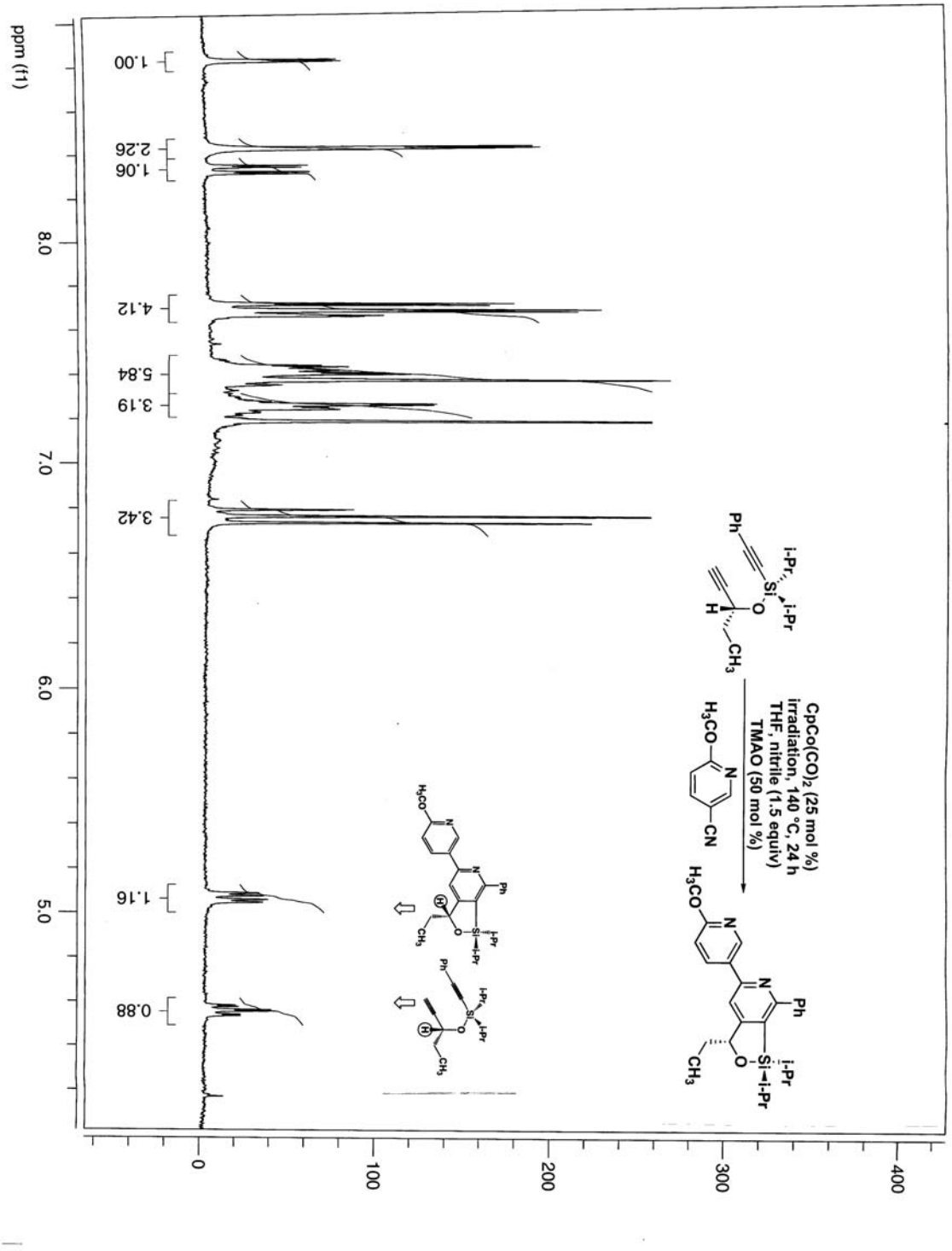
Solvent: $CDCl_3$ – Frequency: 300 MHz



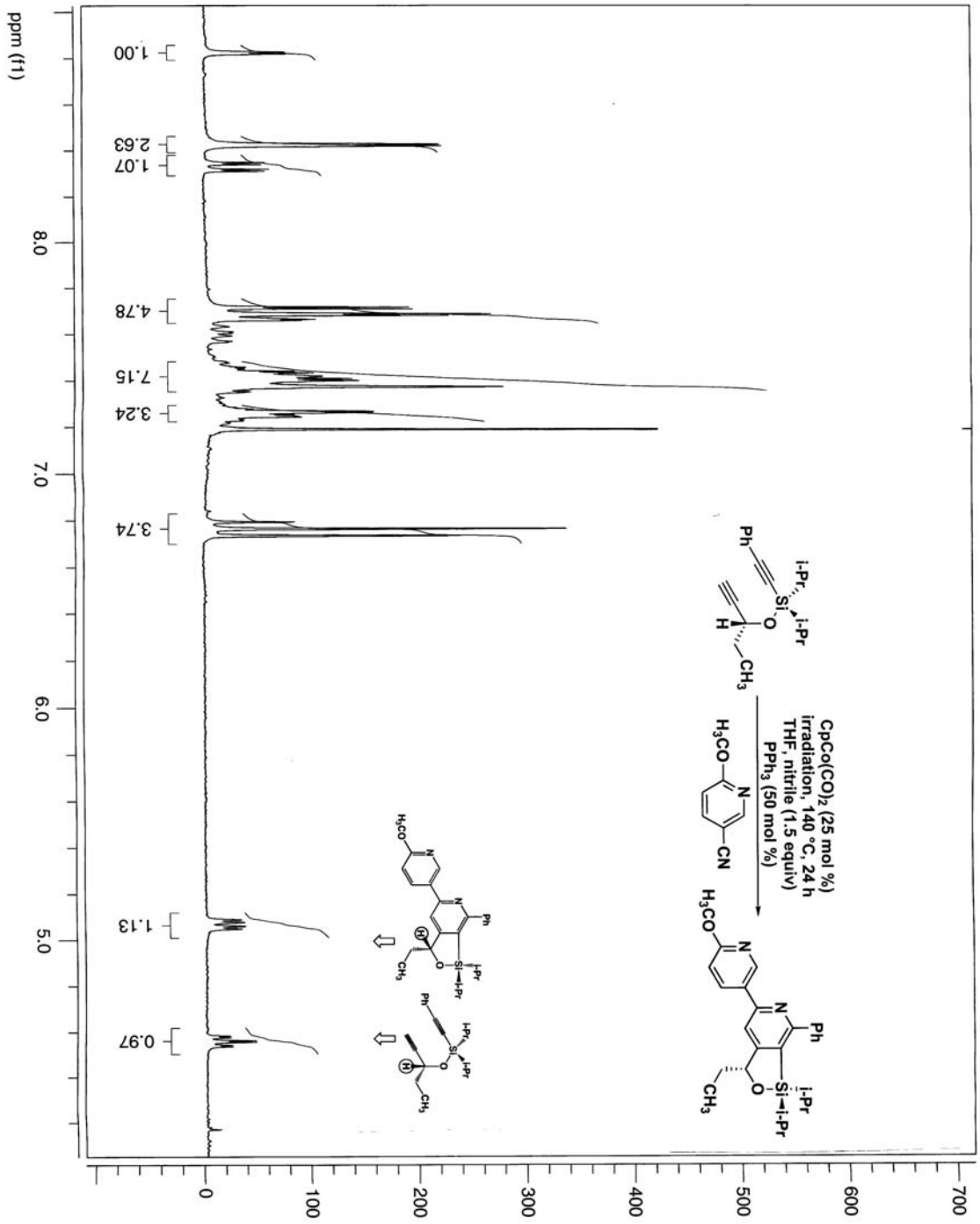
Solvent: $CDCl_3$ – Frequency: 300 MHz



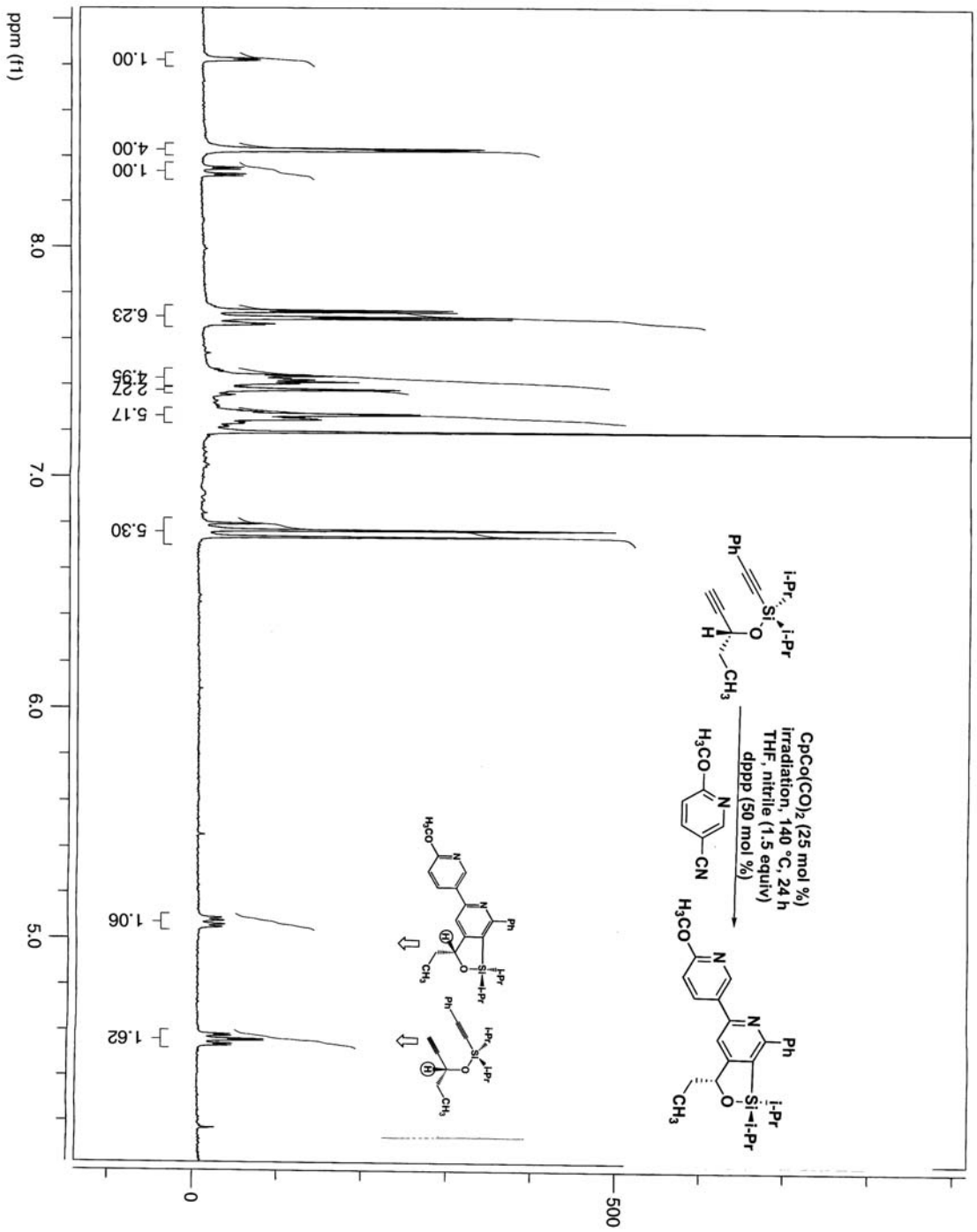
Solvent: $CDCl_3$ – Frequency: 300 MHz



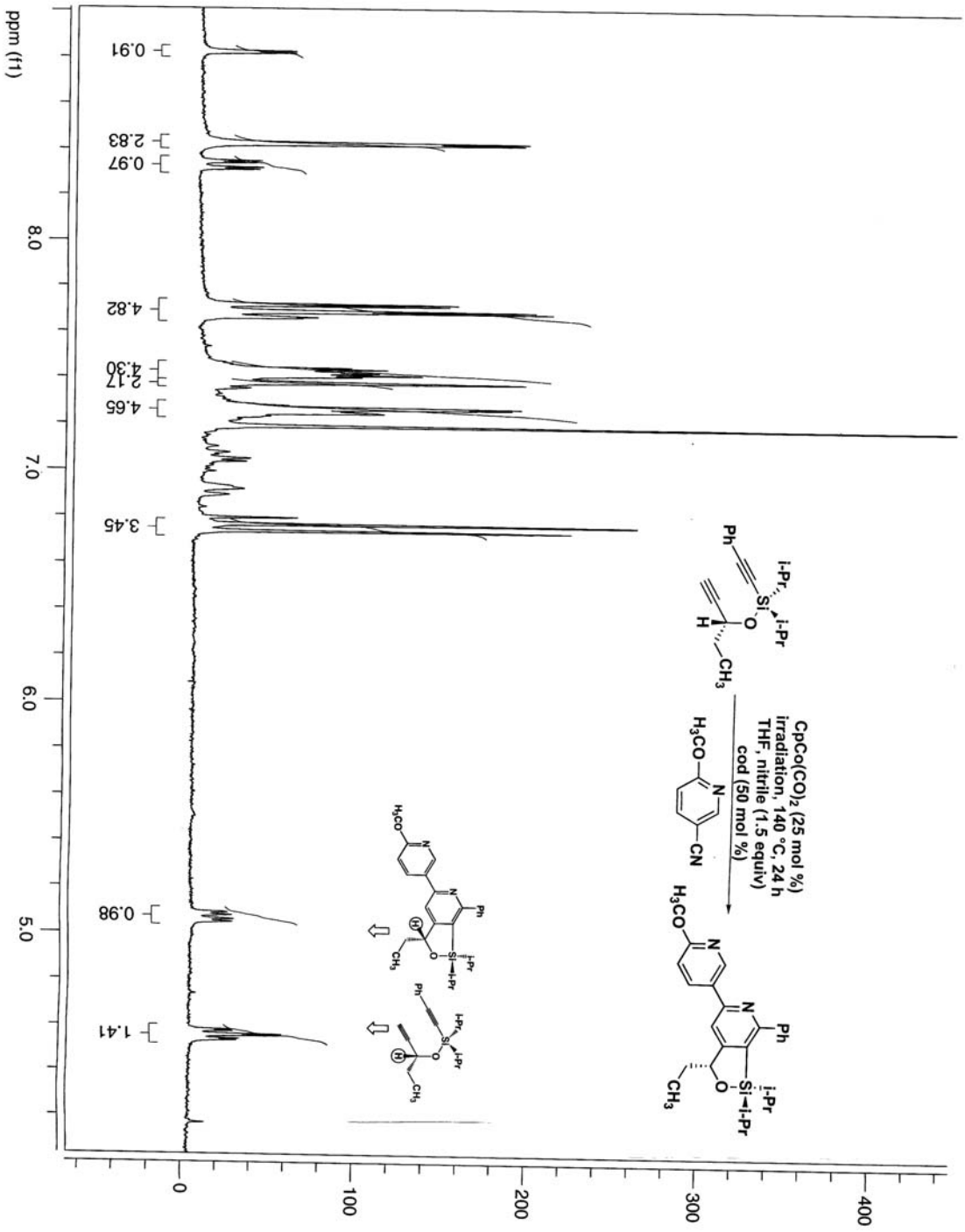
Solvent: $CDCl_3$ – Frequency: 300 MHz



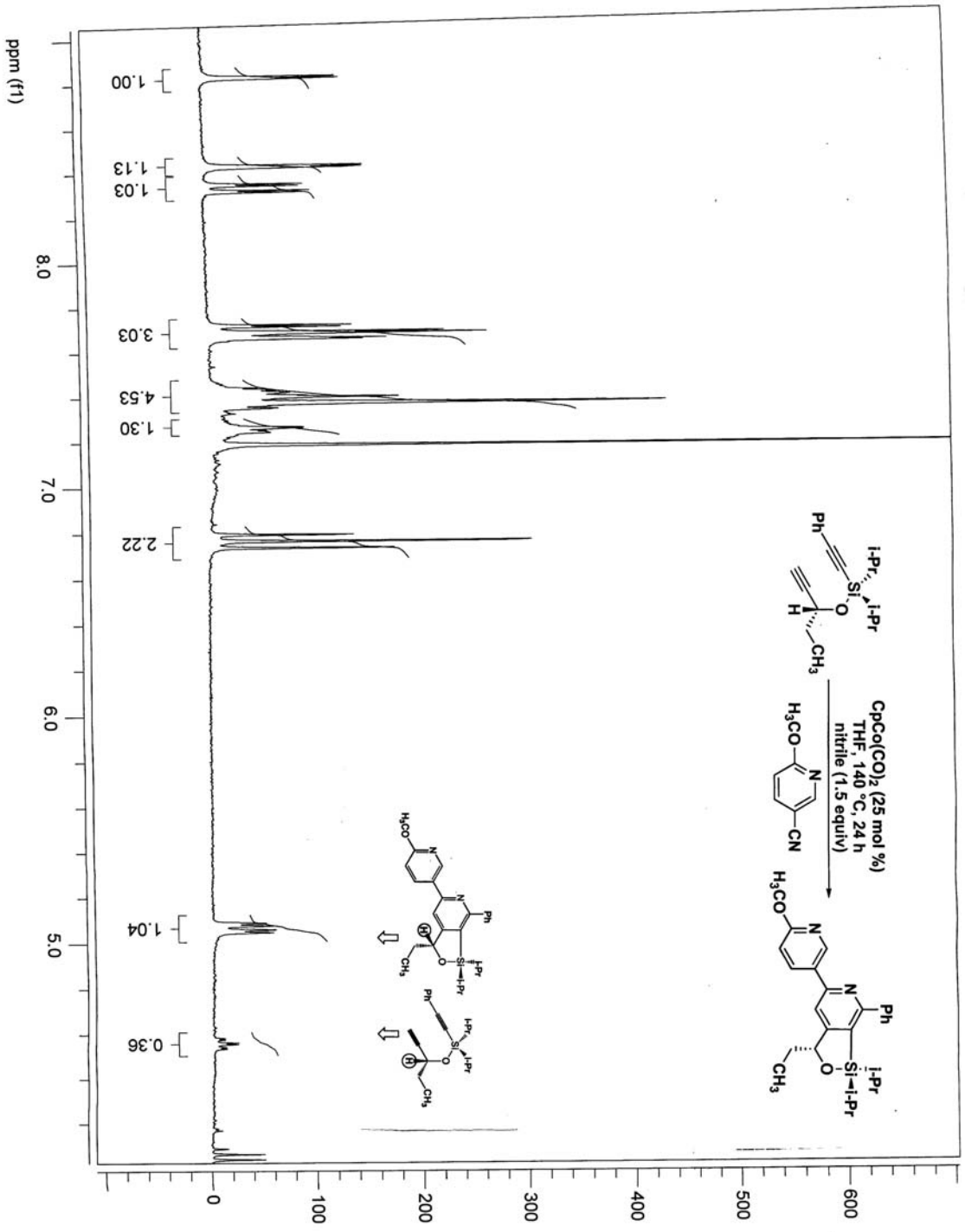
Solvent: $CDCl_3$ – Frequency: 300 MHz



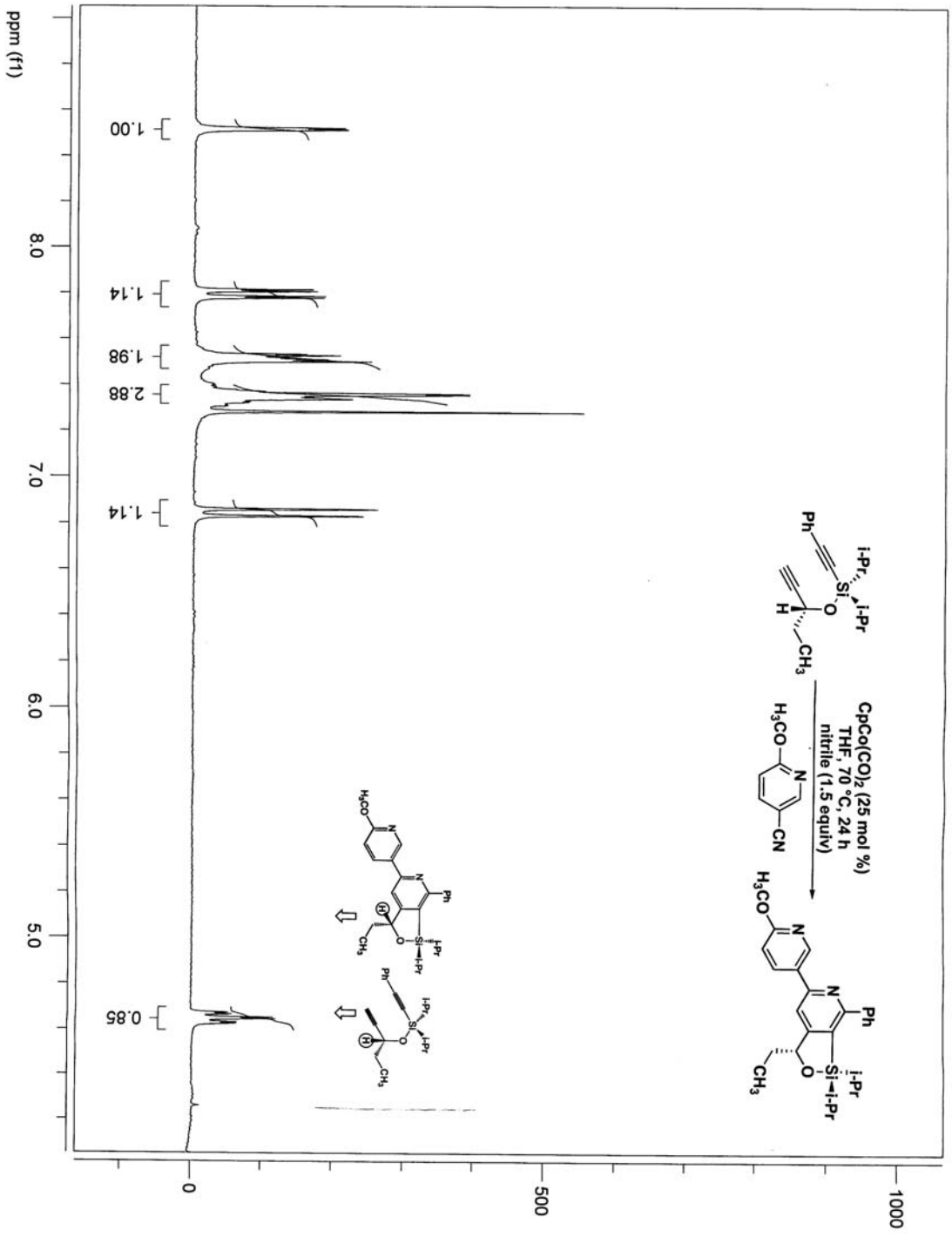
Solvent: $CDCl_3$ – Frequency: 300 MHz



Solvent: $CDCl_3$ – Frequency: 300 MHz



Solvent: $CDCl_3$ – Frequency: 300 MHz



Representative procedure for nitrile screening (Table II):

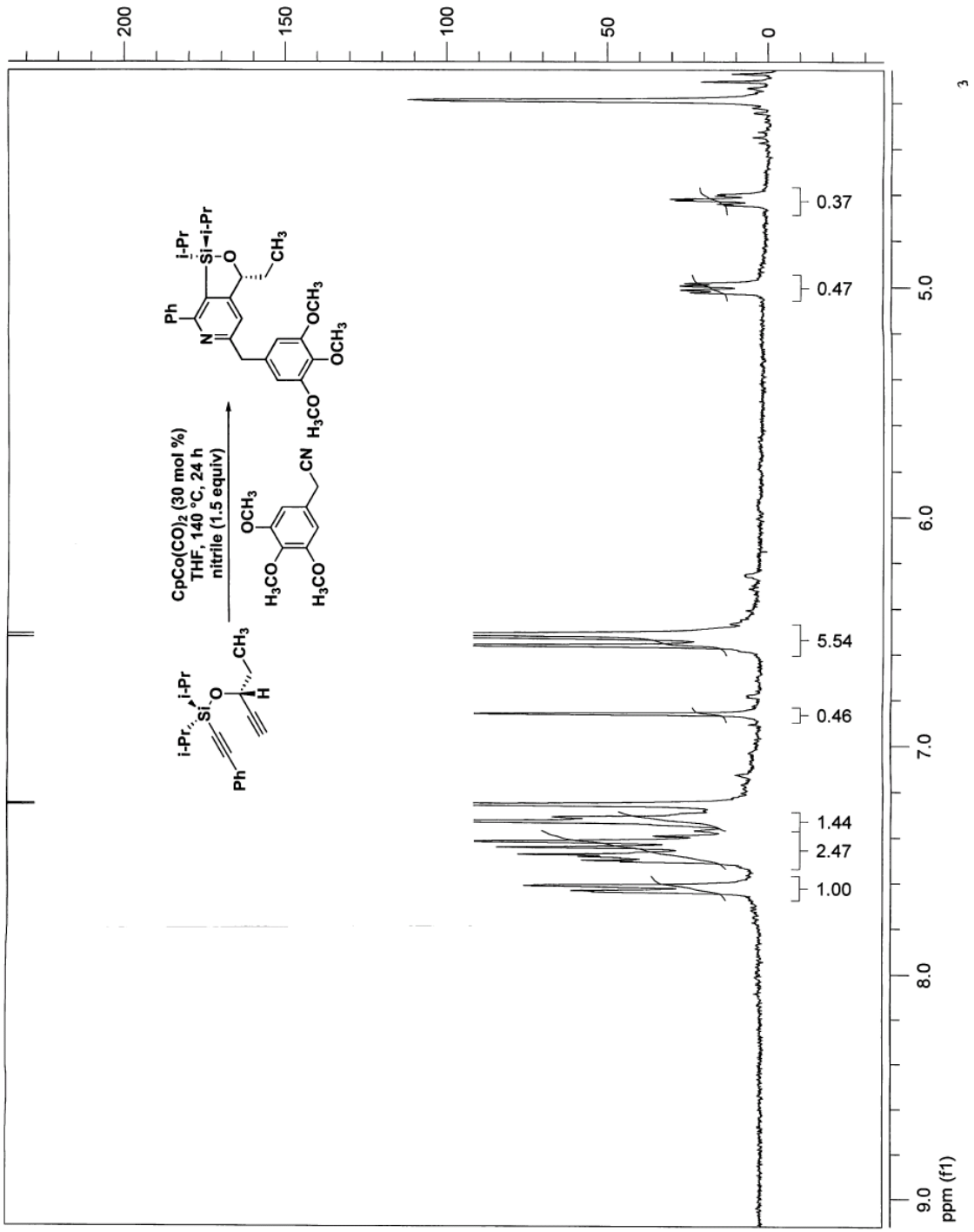
Diisopropyl(pent-1-yn-3-yloxy)(phenylethynyl)silane **1** (10.0 mg, 0.033 mmol) was placed into an oven-dried sealed tube equipped with magnetic stirrer and dissolved in degassed THF (0.67 ml). Nitriles **7-18** (0.05 mmol, 1.5 equiv) were added either as solids or as solutions in degassed THF (0.1 – 0.2 ml) to the stirring solution. After complete dissolution, a solution of cyclopentadienylcobalt(I) dicarbonyl (1.8 mg, 0.010 mmol, 30 mol %) in degassed xylenes (50 μl) was introduced by syringe, giving a pale yellow solution. The sealed tube was immediately submerged into an oil bath preheated to 140 °C. After 24 h, the dark brown solution was cooled to ambient temperature and loaded onto a 4 g silica plug. Filtration was performed using an *Isco Combiflash* system using a gradient solvent commencing with hexanes and ending with 1/1 hexanes/ethyl acetate (total volume of approximately 40 ml), which effectively removed insoluble cobalt byproducts. Pooled fractions were concentrated *in vacuo* and assayed for conversion by ^{1}H NMR. Purification was performed by silica gel chromatography using an *Isco Combiflash* 12 g column with 20:1 hexanes:EtOAc as eluant, providing the corresponding pyridines **19-26**.

Representative spectral data for nitrile screening experiments (Table II):
1H NMR spectra for selected entries:

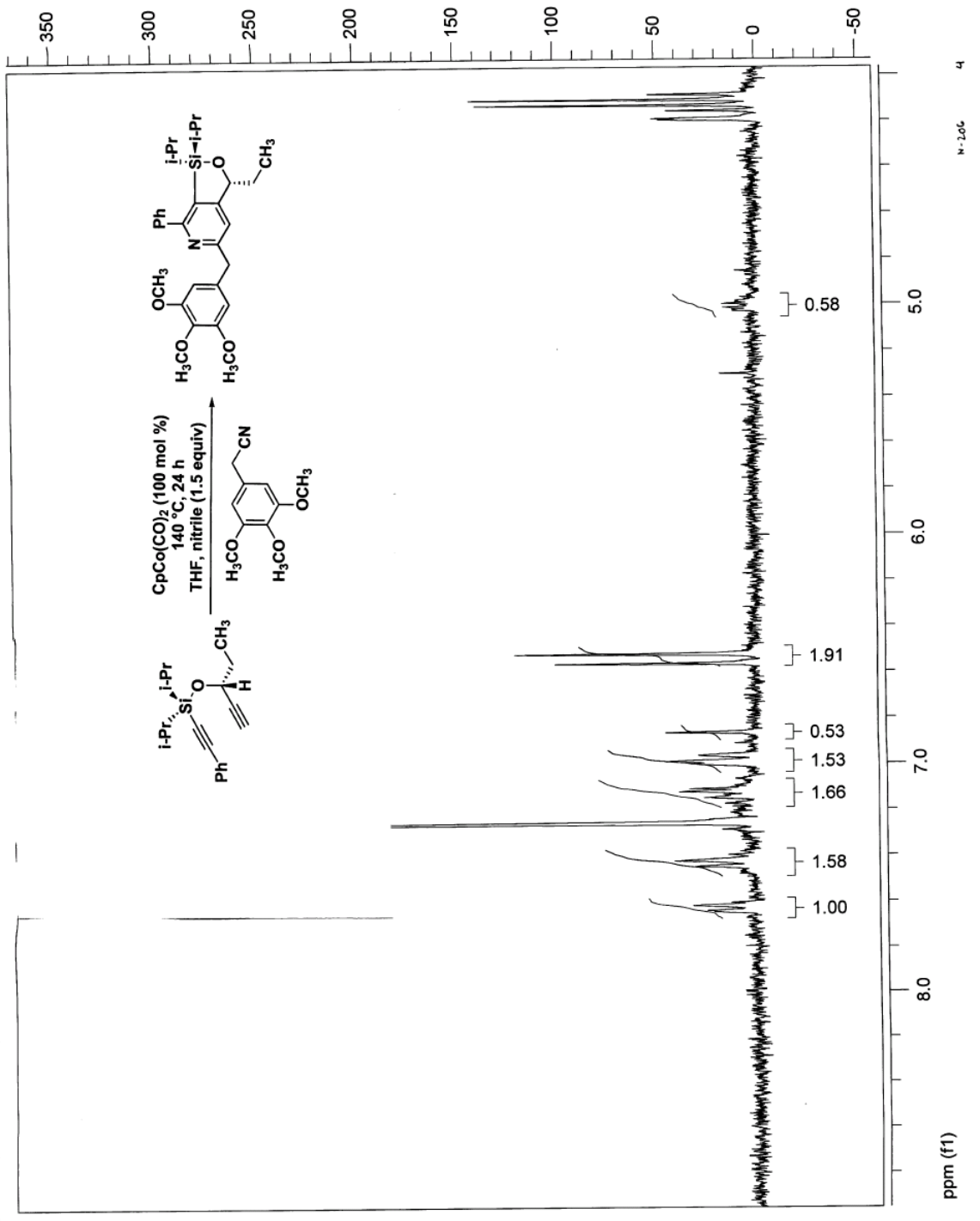
page	*table 2 entry*	*nitrile*	*δ subst (ppm)*	*δ product (ppm)*	*conversion*
S-34	3	**8**	4.6 ppm	5.0 ppm	56%
S-35	4	**8**	4.6 ppm	5.0 ppm	>95%
S-36	5	**9**	4.6 ppm	5.1 ppm	74%
S-37	6	**9**	4.6 ppm	5.1 ppm	>95%
S-38	10	**13**	4.6 ppm	5.2 ppm	46%
S-39	11	**13**	4.6 ppm	5.2 ppm	>95%
S-40	12	**14**	4.6 ppm	5.0 ppm	67%

Conversions were determined on the basis of integration between the methine proton H(A) at 4.6 ppm in diisopropyl(pent-1-yn-3-yloxy)(phenylethynyl)silane **1** and the equivalent methine proton H(A) in pyridine adducts **19-26**. See above table for specific chemical shifts for each reaction.

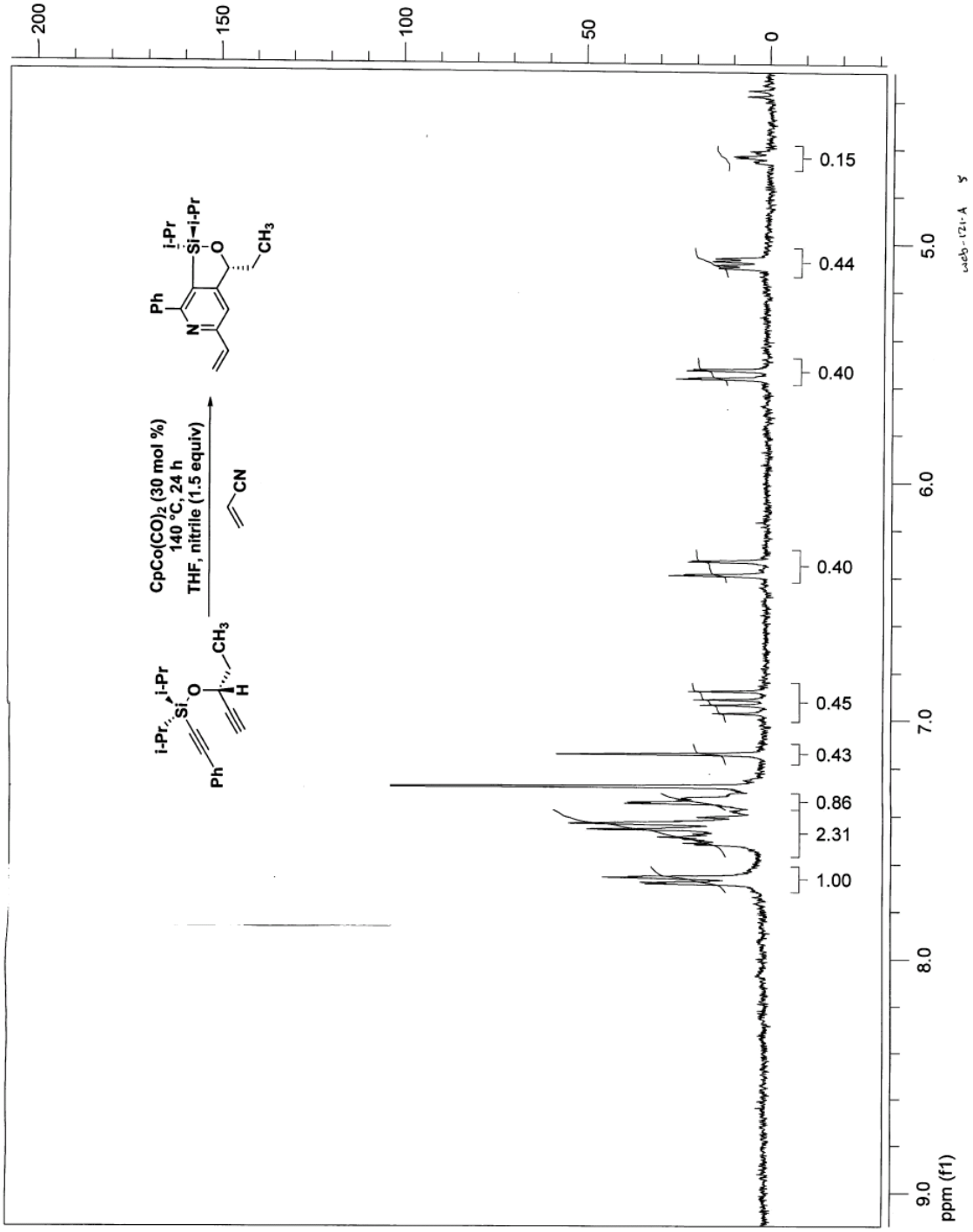
Solvent: $CDCl_3$ – Frequency: 300 MHz



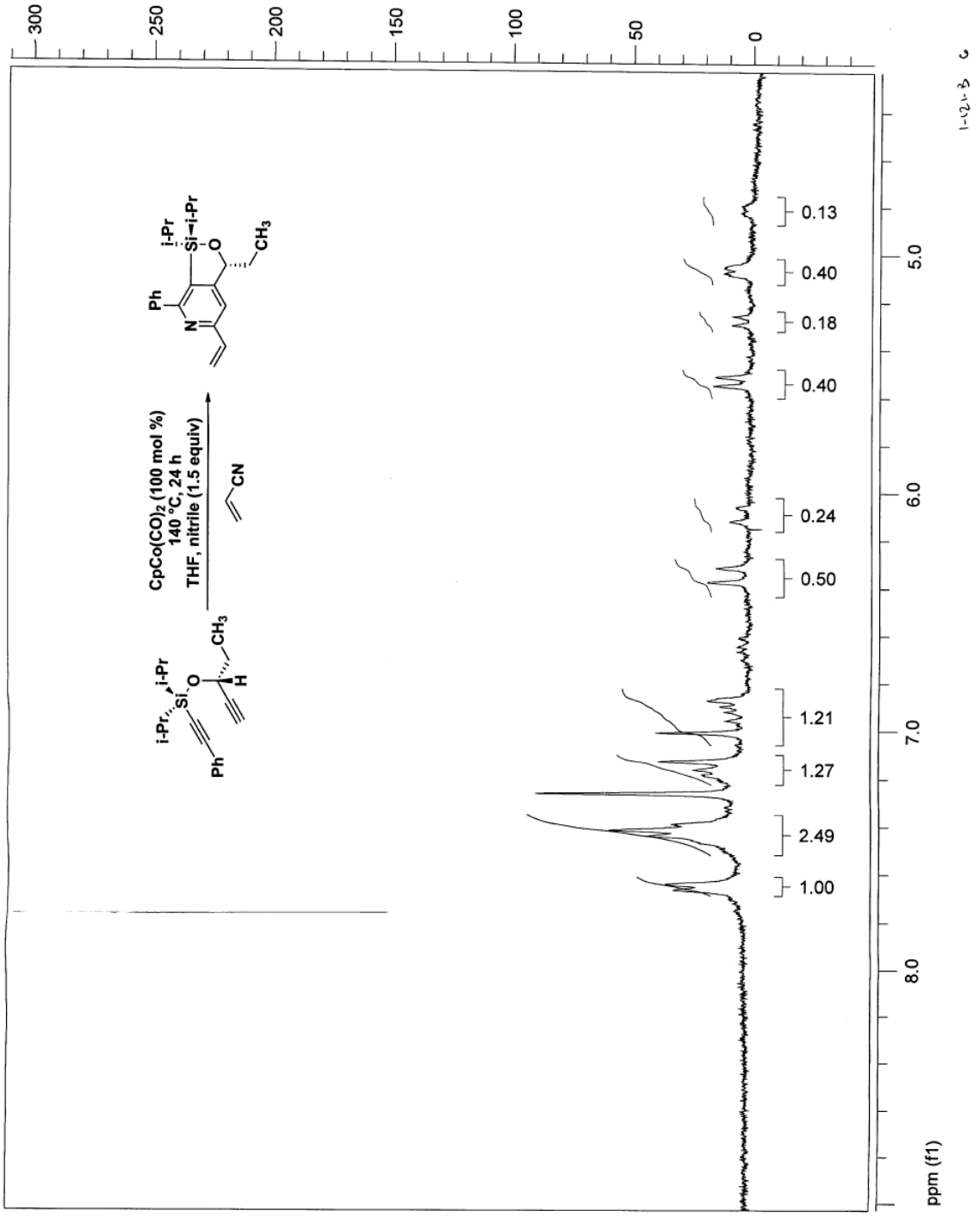
Solvent: $CDCl_3$ – Frequency: 300 MHz



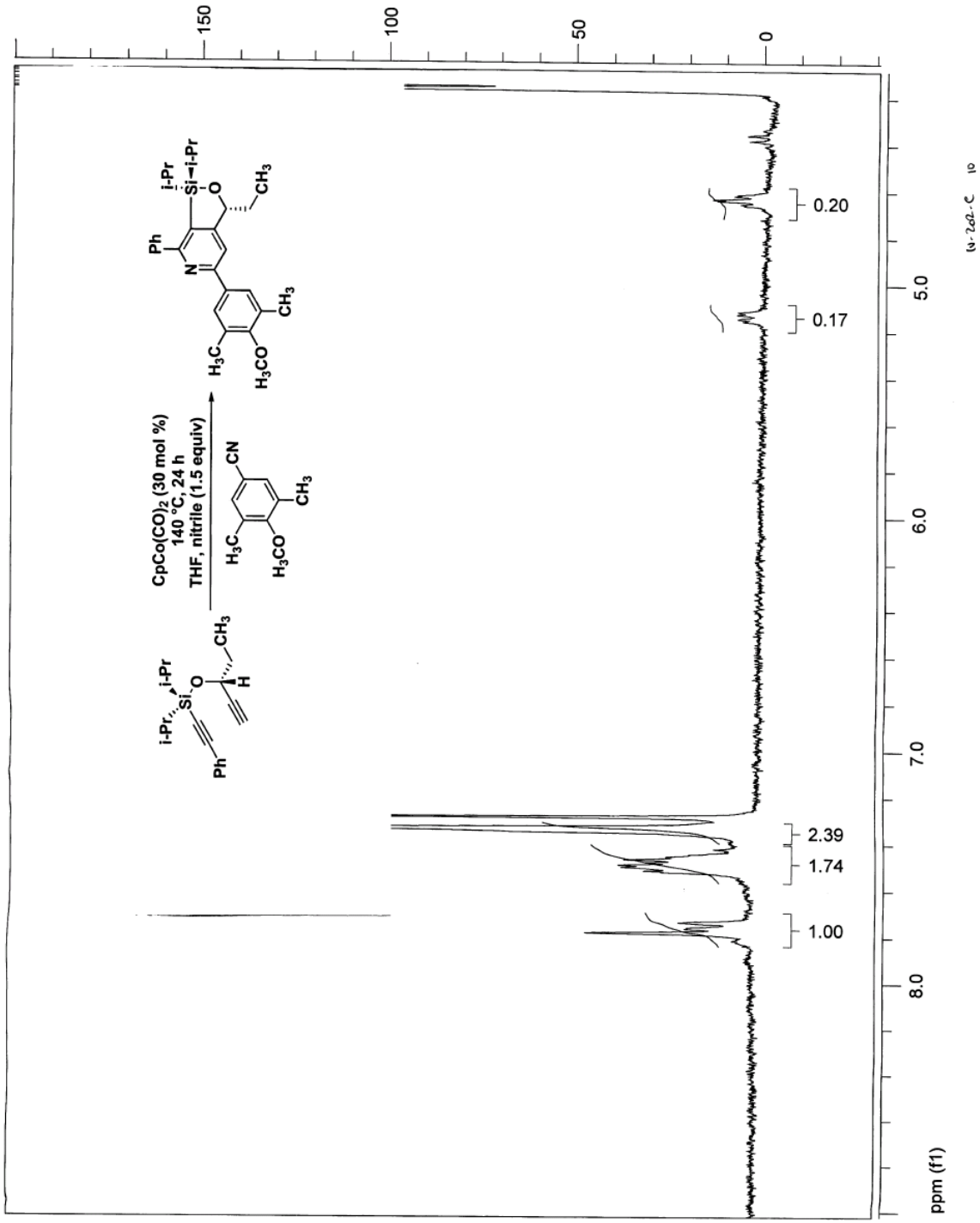
Solvent: $CDCl_3$ – Frequency: 300 MHz



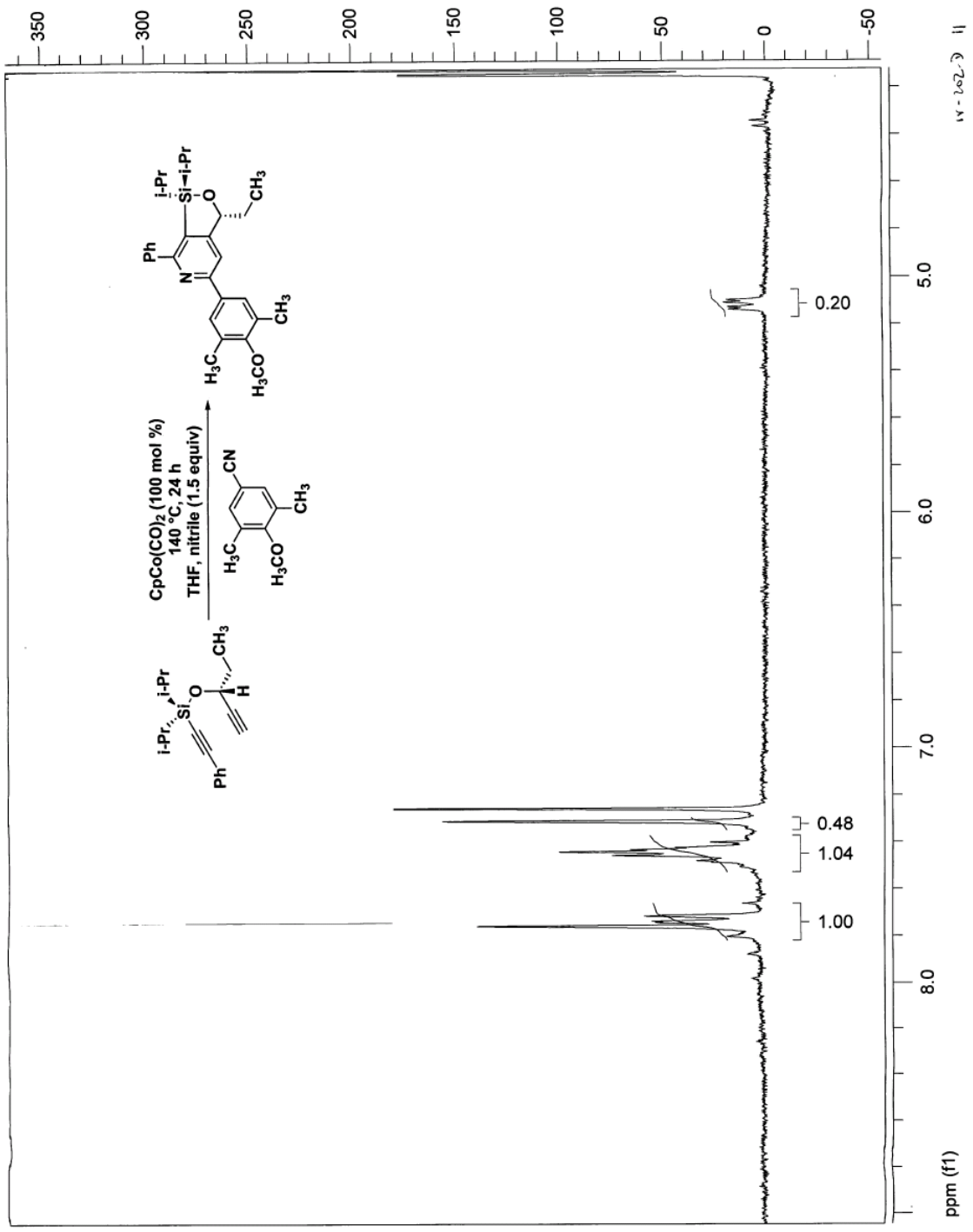
Solvent: $CDCl_3$ – Frequency: 300 MHz



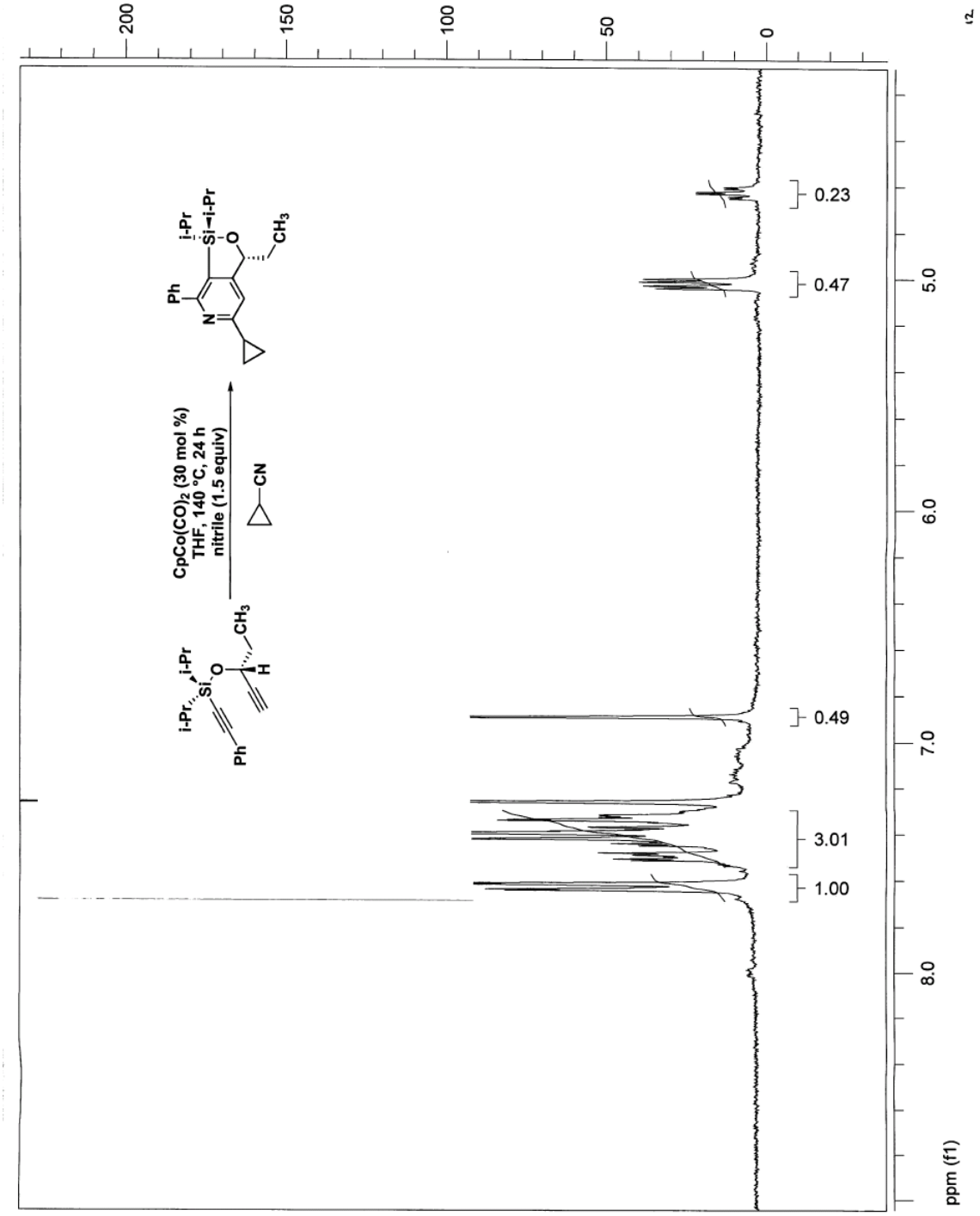
Solvent: $CDCl_3$ – Frequency: 300 MHz



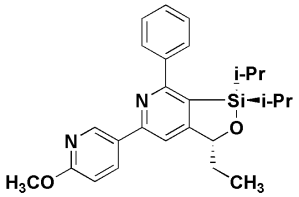
Solvent: $CDCl_3$ – Frequency: 300 MHz



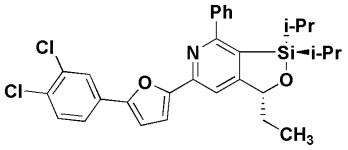
Solvent: $CDCl_3$ – Frequency: 300 MHz



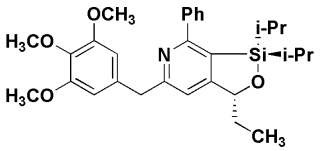
Characterization data for pyridines (Table II):



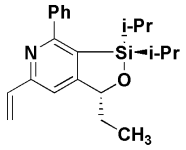
3-ethyl-1,1-diisopropyl-5-(6-methoxypyridin-3-yl)-7-phenyl-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridine (5). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.88 (d, *J* = 2.20, 1 H); 8.43-8.42 (m, 1 H); 7.75-7.74 (m, 2 H); 7.49-7.44 (m, 4 H); 6.87 (d, *J* = 8.79, 1 H); 5.15 (dd, *J* = 8.60, 3.66, 1 H); 4.02 (s, 3 H); 2.21-2.04 (m, 2 H); 1.26-1.21 (m, 2 H); 1.14 (t, *J* = 6.96, 3 H); 1.02 (d, *J* = 7.32, 3 H); 0.91 (d, *J* = 7.32, 3 H); 0.86 (d, *J* = 7.32, 3 H); 0.69 (d, *J* = 7.32, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 164.8, 163.1, 155.1, 145.9, 143.2, 137.7, 128.7, 128.6, 128.5, 127.9, 125.0, 111.5, 110.7, 82.1, 53.6, 31.5, 17.5, 17.3, 17.2, 16.9, 14.4, 13.7, 10.1; IR (film): 2944, 2860, 1602, 1567, 1525, 1490, 1456, 1386, 1344, 1281, 1253, 1106, 1085, 1057, 1022, 987, 889, 833, 770, 708, 659 cm^{-1}; HRMS calcd for $C_{26}H_{32}N_2O_2Si$ (M^+ + H), 433.2311; found, 433.2330



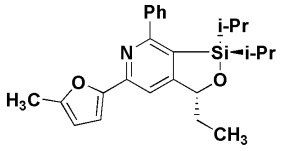
5-(5-(3,4-dichlorophenyl)furan-2-yl)-3-ethyl-1,1-diisopropyl-7-phenyl-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridine (19) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, *J* = 1.80, 1 H); 7.74-7.71 (m, 2 H); 7.59 (dd, *J* = 8.40, 1.80, 1 H); 7.56 (br s, 1 H); 7.50-7.43 (m, 4 H); 7.31 (d, *J* = 3.6, 1 H); 6.84 (d, *J* = 3.30, 1 H); 5.16 (dd, *J* = 8.7, 3.3, 1 H); 2.21-2.08 (m, 1 H); 1.74-1.64 (m, 1 H); 1.27-1.21 (m, 2 H); 1.16 (t, *J* = 7.20, 3 H); 1.03 (d, *J* = 7.20, 3 H); 0.87 (app t, *J* = 6.90, 6 H); 0.65 (d, *J* = 7.50, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 163.3, 154.4, 152.1, 149.1, 143.1, 133.1, 131.4, 130.8, 130.4, 128.8, 128.5, 128.0, 125.6, 123.1, 111.8, 110.4, 109.1, 82.2, 31.5, 17.4, 17.3, 17.1, 16.8, 14.4, 13.7, 10.2; IR (film): 2952, 2891, 2865, 1783, 1622, 1591, 1578, 1539, 1483, 1461, 1391, 1352, 1243, 1104, 1070, 991, 939, 883, 822, 748, 700, 678 cm^{-1}; HRMS calcd for $C_{30}H_{31}Cl_2NO_2Si$ (M^+ + H), 536.1579; found, 536.1567



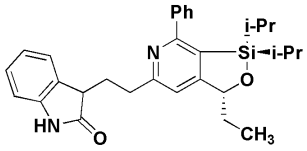
3-ethyl-1,1-diisopropyl-7-phenyl-5-(3,4,5-trimethoxybenzyl)-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridine (20) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64-7.63 (m, 2 H); 7.45 (t, *J* = 6.96, 2 H); 7.41 (d, *J* = 6.96, 1 H); 6.87 (s, 1 H); 6.57 (s, 2 H); 5.01 (dd, *J* = 8.60, 3.29, 1 H); 4.21-4.18 (m, 2 H); 3.85 (s, 3 H); 3.84 (s, 6 H); 1.94-1.89 (m, 2 H); 1.22-1.13 (m, 2 H); 1.06 (t, *J* = 7.32, 3 H); 0.98 (d, *J* = 7.32, 3 H); 0.85 (d, *J* = 7.32, 3 H); 0.82 (d, *J* = 7.69, 3 H); 0.63 (d, *J* = 7.69, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 162.9, 161.3, 153.7, 153.2, 143.3, 137.9, 136.7, 135.0, 128.9, 127.9, 125.4, 124.4, 117.8, 115.1, 107.3, 105.2, 82.0, 60.4, 56.2, 44.8, 36.6, 31.6, 24.7, 21.0, 17.7, 17.5, 17.4, 17.2, 17.1, 16.7, 14.6, 14.2, 13.5; IR (film): 2943, 2865, 2839, 1743, 1587, 1570, 1539, 1509, 1465, 1417, 1374, 1326, 1235, 1191, 1126, 1061, 991, 883, 830, 704, 674 cm^{-1}; HRMS calcd for $C_{30}H_{39}NO_4Si$ (M^+ + H), 506.2726; found, 506.2709



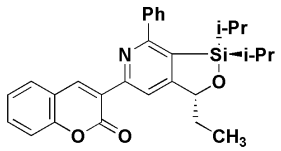
3-ethyl-1,1-diisopropyl-7-phenyl-5-vinyl-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridine (21) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68-7.65 (m, 2 H); 7.48-7.40 (m, 3 H); 7.13 (br s, 1 H); 6.92 (dd, *J* = 17.40, 10.80, 1 H); 6.35 (dd, *J* = 17.55, 1.50, 1 H); 5.54 (dd, *J* = 10.80, 1.20, 1 H); 5.07 (dd, *J* = 8.55, 3.30, 1 H); 2.06-1.96 (m, 1 H); 1.68-1.60 (m, 1 H); 1.25-1.16 (m, 2 H); 1.101 (t, *J* = 7.20, 3 H); 0.99 (d, *J* = 7.20, 3 H); 0.86 (d, *J* = 7.50, 3 H); 0.82 (d, *J* = 7.50, 3 H); 0.64 (d, *J* = 7.50, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 163.1, 156.1, 143.4, 137.3, 128.6, 128.5, 128.0, 126.0, 118.8, 113.2, 82.0, 31.4, 17.4, 17.2, 17.1, 16.8, 14.3, 13.6, 10.1; IR (film): 2948, 2896, 2861, 1574, 1513, 1465, 1370, 1109, 1065, 1039, 987, 926, 883, 822, 761, 704, 674, 578 cm^{-1}; HRMS calcd for $C_{22}H_{29}NOSi$ (M^+ + H), 352.2096; found, 352.2102



3-ethyl-1,1-diisopropyl-5-(5-methylfuran-2-yl)-7-phenyl-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridine (22) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71-7.68 (m, 2 H); 7.48-7.40 (m, 4 H); 7.09 (d, *J* = 3.00, 1 H); 6.14 (d, *J* = 3.00, 1 H); 5.10 (dd, *J* = 8.40, 3.30, 1 H); 2.41 (s, 3 H); 2.12-2.03 (m, 1 H); 1.78-1.60 (m, 1 H); 1.26-1.16 (m, 2 H); 1.11 (t, *J* = 7.20, 3 H); 1.01 (d, *J* = 7.20, 3 H); 0.85 (app t, *J* = 7.80, 6 H); 0.64 (d, *J* = 7.50, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 163.2, 153.5, 152.5, 149.9, 143.4, 128.7, 128.6, 128.4, 128.0, 124.4, 110.6, 109.8, 108.4, 82.1, 31.3, 17.4, 17.3, 17.1, 16.8, 14.4, 13.9, 13.6, 10.1; IR (film): 2943, 2891, 2861, 1604, 1578, 1513, 1461, 1378, 1339, 1226, 1113, 1056, 1022, 996, 878, 830, 796, 752, 696, 665, 635 cm^{-1}

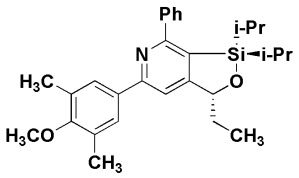


3-(2-(3-ethyl-1,1-diisopropyl-7-phenyl-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridin-5-yl)ethyl)indolin-2-one (23) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60-7.57 (m, 2 H); 7.50-7.42 (m, 3 H); 7.13-7.11 (m, 1 H); 7.01-6.90 (m, 2 H); 6.84 (br s, 1 H); 6.66-6.63 (m, 1 H); 4.92 (dd, *J* = 8.70, 3.30, 1 H); 4.40-4.25 (m, 2 H); 3.33 (t, *J* = 6.60, 2 H); 1.83-1.74 (m, 1 H); 1.43-1.33 (m, 1 H); 1.25 (m, 2 H); 1.18-1.07 (m, 2 H); 0.97-0.92 (m, 6 H); 0.82 (d, *J* = 7.50, 3 H); 0.76 (d, *J* = 7.50, 3 H); 0.59 (d, *J* = 7.50, 3 H); 13-C NMR (75 MHz, $CDCl_3$) δ 165.5, 163.3, 158.1, 154.5, 143.2, 142.5, 131.4, 128.7, 128.6, 127.8, 125.1, 123.6, 122.0, 116.0, 109.8, 108.4, 81.8, 42.2, 36.4, 31.1, 17.3, 17.2, 17.1, 16.7, 14.2, 13.5, 9.9; IR (film): 2939, 2891, 2861, 1774, 1613, 1587, 1570, 1535, 1487, 1461, 1387, 1361, 1248, 1100, 1070, 983, 948, 874, 826, 752, 709, 665, 639 cm^{-1}



3-(3-ethyl-1,1-diisopropyl-7-phenyl-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridin-5-yl)-2H-chromen-2-one (24) ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 (s, 1 H); 8.30 (s, 1 H); 7.72 (dd, *J* = 8.24, 1.46, 2 H); 7.67 (dd, *J* =

7.69, 1.10, 1 H); 7.59-7.56 (m, 1 H); 7.52-7.49 (m, 2 H); 7.47-7.44 (m, 1 H); 7.40 (d, *J* = 8.42, 1 H); 7.32 (dt, *J* = 7.50, 1.10, 1 H); 5.17 (dd, *J* = 8.79, 2.93, 1 H); 2.14-2.08 (m, 1 H); 1.69-1.63 (m, 1 H); 1.26-1.18 (m, 2 H); 1.13 (m, 4 H); 1.02 (d, *J* = 7.32, 3 H); 0.90 (d, *J* = 7.32, 3 H); 0.85 (d, *J* = 7.69, 3 H); 0.68 (d, *J* = 7.32, 3 H); 13-C NMR (75 MHz, $CDCl_3$) δ 165.9, 162.7, 160.4, 154.0, 151.3, 143.4, 143.0, 132.1, 129.0, 128.8, 128.7, 128.0, 127.2, 125.3, 124.6, 119.6, 116.4, 116.0, 82.4, 36.6, 31.4, 24.7, 23.3, 17.4, 17.2, 17.1, 16.8, 14.3, 13.6, 10.2; IR (film): 2944, 2860, 1721, 1604, 1574, 1526, 1456, 1378, 1348, 1248, 1213, 1156, 1096, 1056, 1009, 991, 917, 883, 822, 822, 761, 709, 670, 630 cm^{-1}; HRMS calcd for $C_{29}H_{31}NO_3Si$ (M^+ + H), 470.2151; found, 470.2158

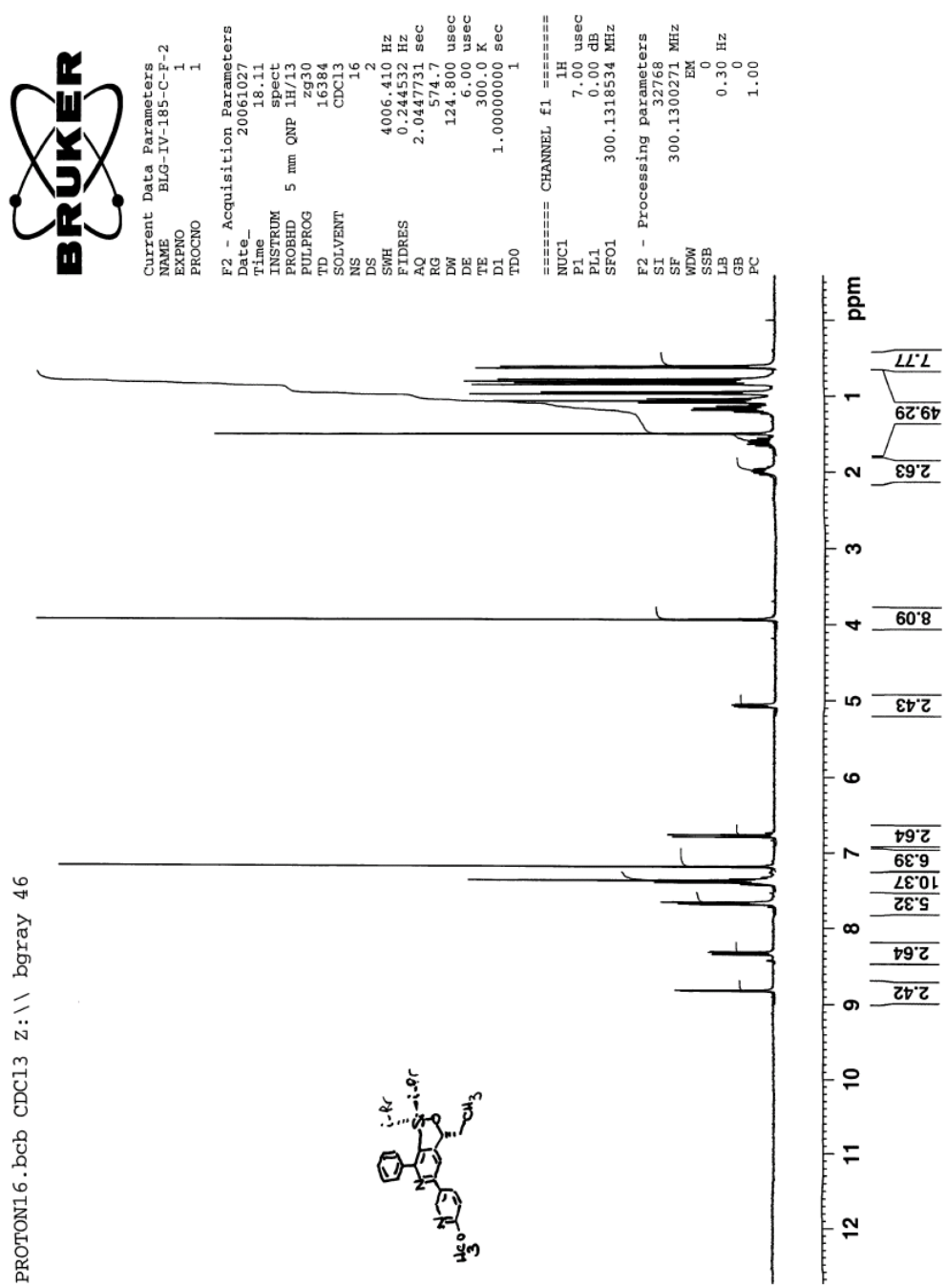


3-ethyl-1,1-diisopropyl-5-(4-methoxy-3,5-dimethylphenyl)-7-phenyl-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridine (25) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77-7.73 (m, 4 H); 7.49-7.41 (m, 4 H); 5.13 (dd, *J* = 8.40, 3.30, 1 H); 3.76 (s, 3 H); 2.37 (s, 6 H); 2.13-2.02 (m, 1 H); 1.72-1.62 (m, 1 H); 1.26-1.19 (m, 2 H); 1.12 (t, *J* = 7.50, 3 H); 1.01 (d, *J* = 7.20, 3 H); 0.90-0.84 (m, 6 H); 0.67 (d, *J* = 7.50, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 163.0, 158.2, 157.6, 143.6, 135.0, 132.8, 131.1, 128.6, 128.5, 128.0, 127.8, 124.6, 112.2, 82.1, 59.7, 31.5, 30.9, 17.4, 17.3, 17.2, 16.8, 16.3, 16.0, 14.4, 13.6, 10.1; IR (film): 2943, 2865, 1591, 1574, 1526, 1491, 1465, 1409, 1357, 1230, 1152, 1104, 1061, 1013, 983, 922, 878, 826, 765, 700, 630 cm^{-1}; HRMS calcd for $C_{29}H_{37}NO_2Si$ (M^+ + H), 460.2672; found, 460.2685

Representative 1-H & 13-C NMR Spectra for Pyridines synthesized in Table II:
*Spectra for compounds **5, 22-23, & 25**:*

^{1}H and ^{13}C NMR spectra for pyridine products:

Page	subst	spectrum	Page	subst	spectrum
S-44	**5**	1H	S-48	**23**	1H
S-45	**5**	13C	S-49	**23**	13C
S-46	**25**	1H	S-50	**22**	1H
S-47	**25**	13C	S-51	**22**	13C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Time 18.11
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PULPROG zg30
TD 16384
SOLVENT CDC13
NS 16
DS 2
SWH 4006.410 Hz
FIDRES 0.244532 Hz
AQ 2.0447731 sec
RG 574.7
DW 124.800 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 7.00 usec
PL1 0.00 dB
SFO1 300.1318534 MHz
F2 - Processing parameters
SI 32768
SF 300.1300271 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
12
11
10
9
8
7
6
5
4
3
2
1
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2.64
5.32
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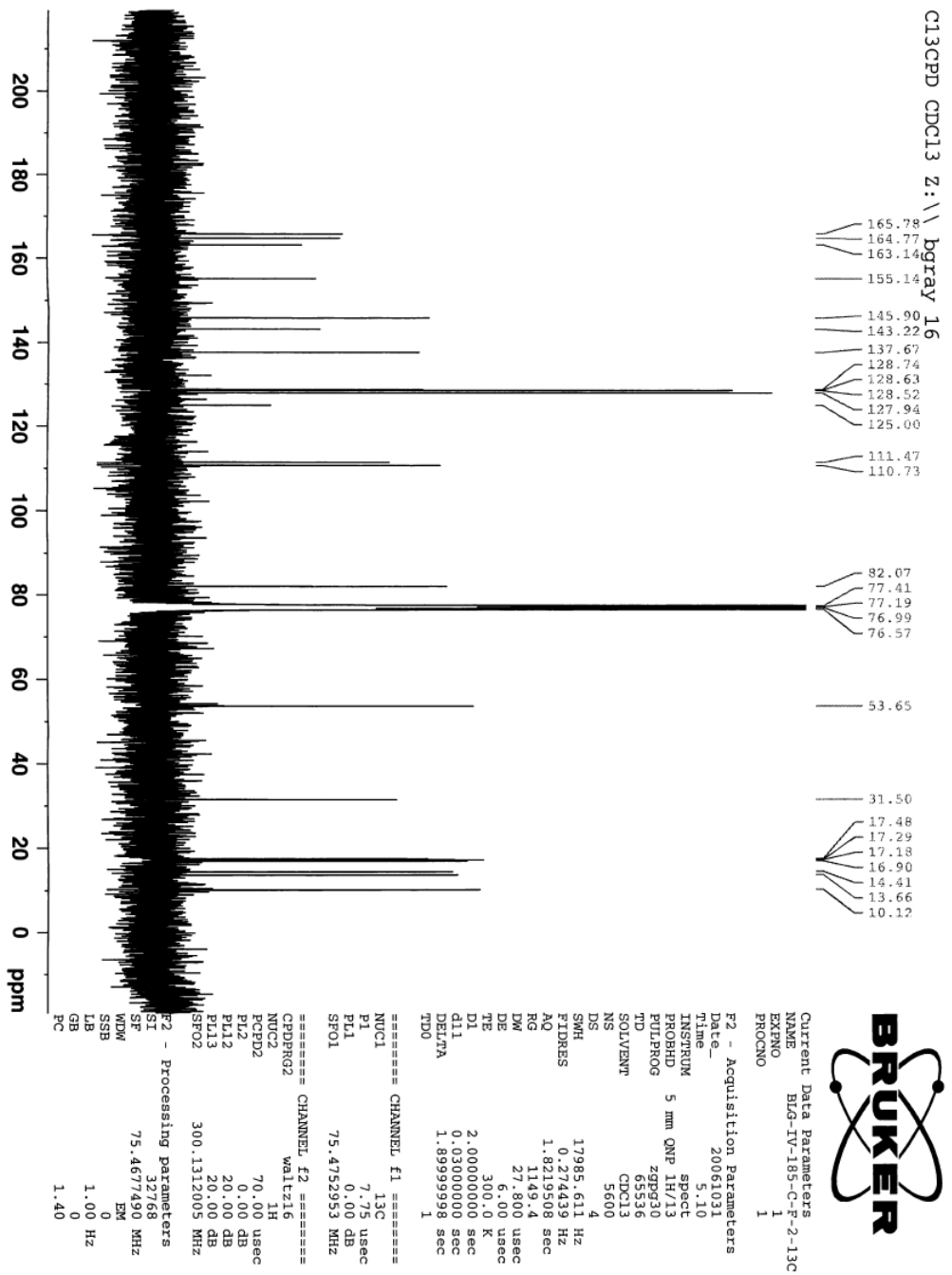
2.64
8.09
2.43
2.63
49.29
7.77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155.14
145.90
143.22
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128.63
128.52
127.94
125.00
111.47
110.73
82.07
77.41
77.19
76.99
76.57
53.65
31.50
17.48
17.29
17.18
16.90
14.41
13.66
10.12
200
180
160
140
120
100
80
60
40
20
0
ppm
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EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
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Time_ 5.10
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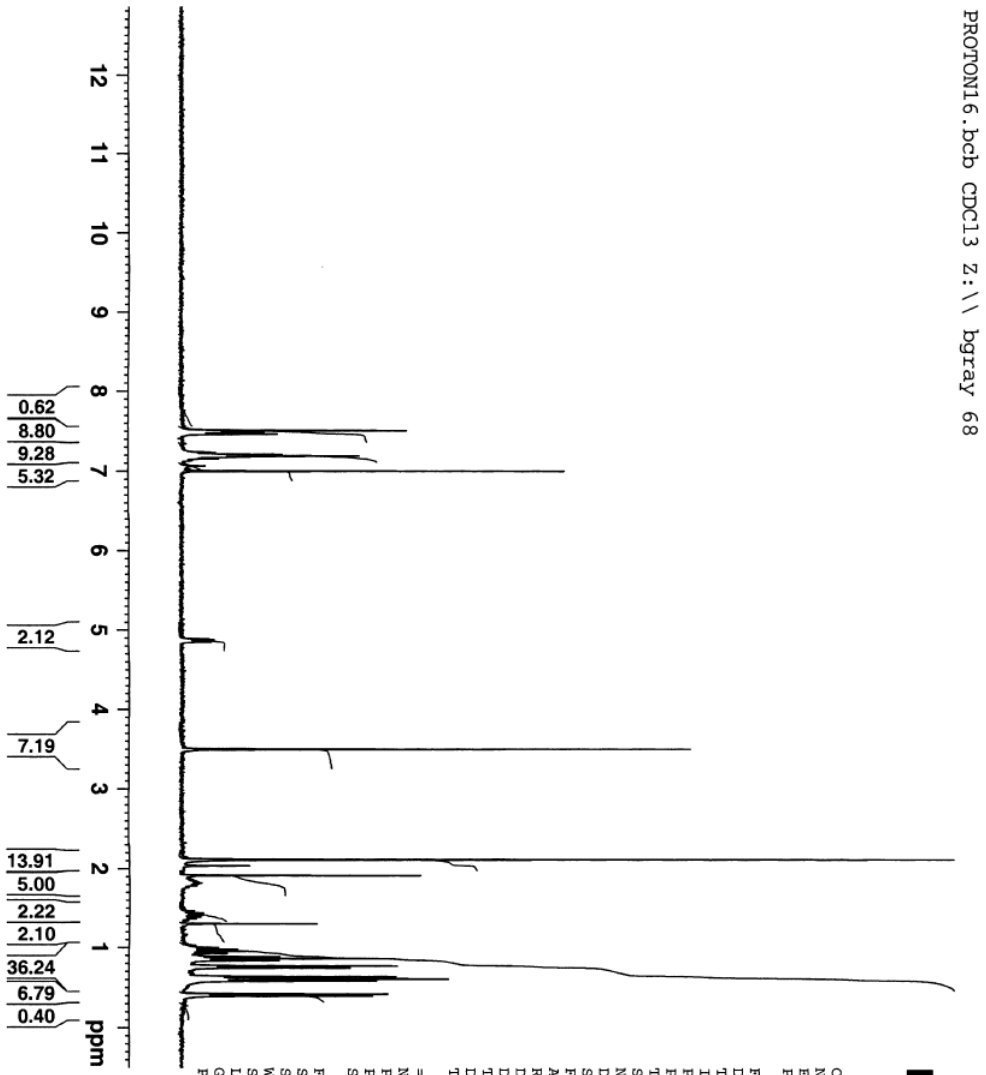
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 560
DS 4
SWH 17985.611 Hz
FIDRES 0.274439 Hz
AQ 1.8219508 sec
RG 1149.4
DW 27.800 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.75 usec
PL1 0.00 dB
SFO1 75.4752953 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 70.00 usec
PL2 0.00 dB
PL12 20.00 dB
PL13 20.00 dB
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40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EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
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Time 18.29
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PULPROG zg30
TD 16384
SOLVENT CDC13
NS 16
DS 2
SWH 4006.410 Hz
FIDRES 0.244532 Hz
AQ 2.0447731 sec
RG 1824.6
DW 124.800 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
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P1 7.00 usec
PL1 0.00 dB
SFO1 300.1318534 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
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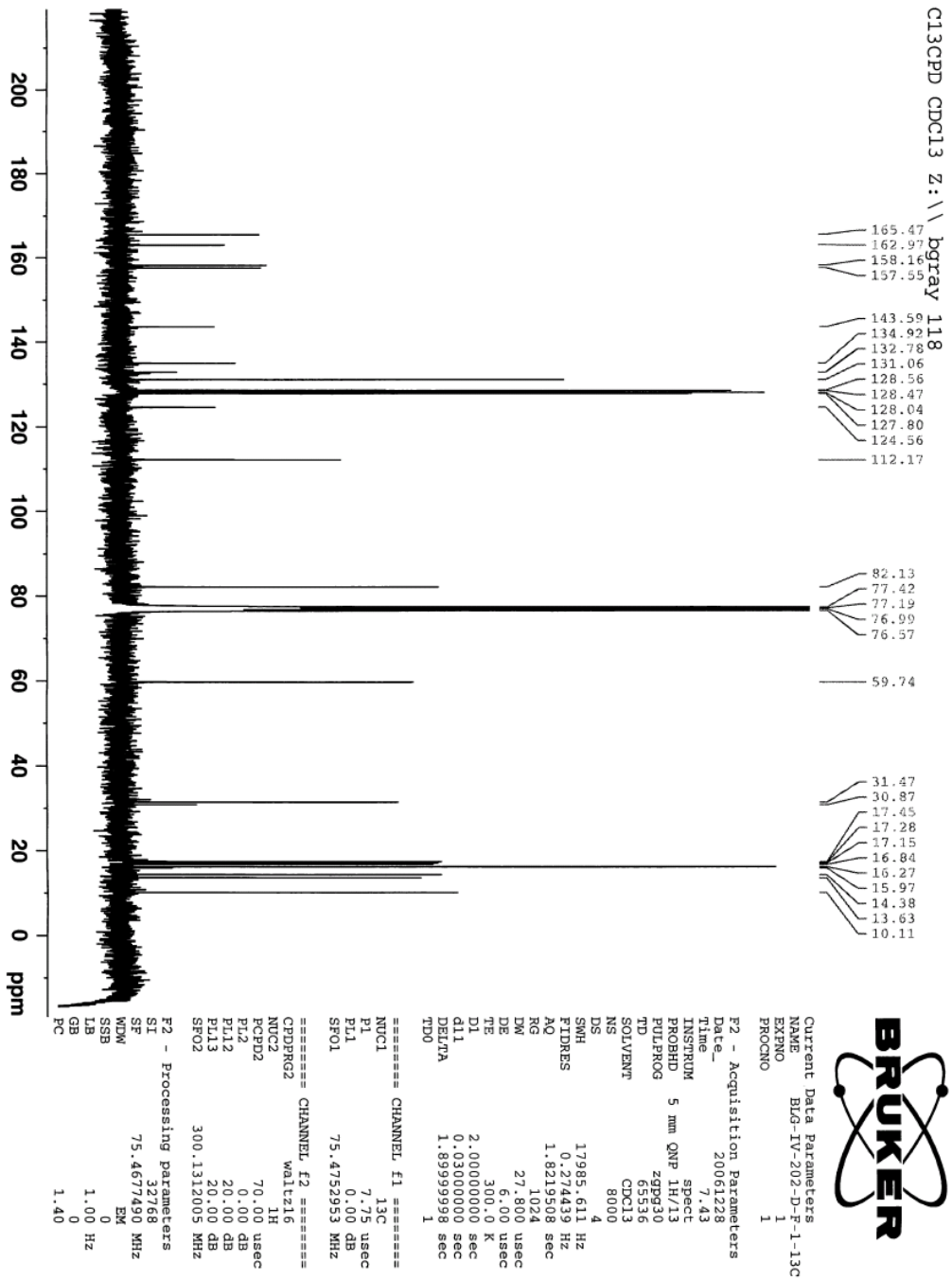
8.80
9.28
5.32
2.12
7.19
13.91
5.00
2.22
2.10
36.24
6.79
0.40
12
11
10
9
8
7
6
5
4
3
2
1
ppm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158.16
157.55
143.59
134.92
132.78
131.06
128.56
128.47
128.04
127.80
124.56
112.17
82.13
77.42
77.19
76.99
76.57
59.74
31.47
30.87
17.45
17.28
17.15
16.84
16.27
15.97
14.38
13.63
10.11
200
180
160
140
120
100
80
60
40
20
0
ppm
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EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20061228
Time 7.43
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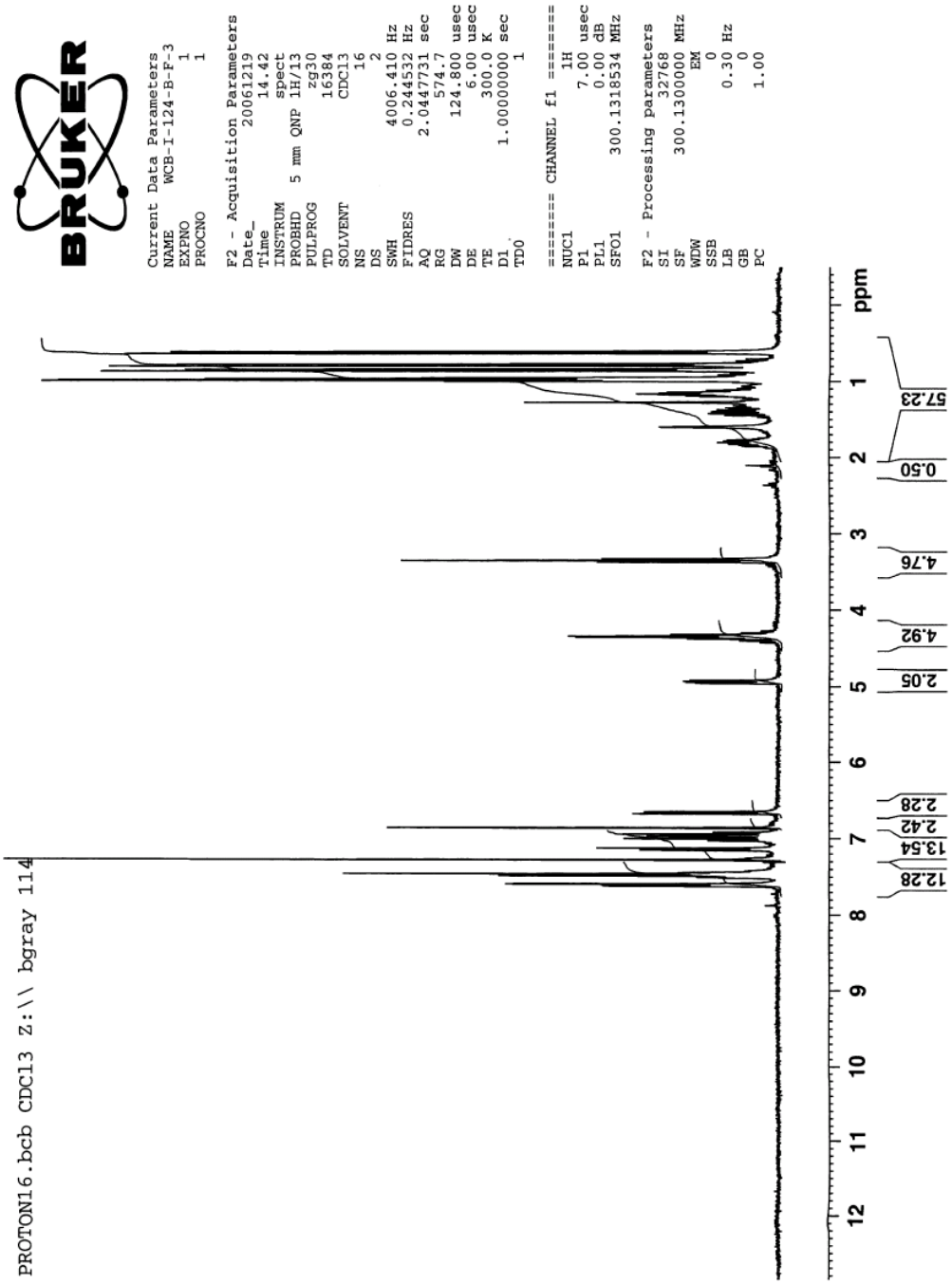
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 8000
DS 4
SWH 17985.611 Hz
FIDRES 0.274439 Hz
AQ 1.8219508 sec
RG 1024
DW 27.800 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.75 usec
PL1 0.00 dB
SFO1 75.4752953 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 70.00 usec
PL2 0.00 dB
PL12 20.00 dB
PL13 20.00 dB
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40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PROCNO 1
F2 - Acquisition Parameters
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Time 14.42
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PULPROG zg30
TD 16384
SOLVENT CDCl3
NS 16
DS 2
SWH 4006.410 Hz
FIDRES 0.244532 Hz
AQ 2.0447731 sec
RG 574.7
DW 124.800 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 7.00 usec
PL1 0.00 dB
SFO1 300.1318534 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
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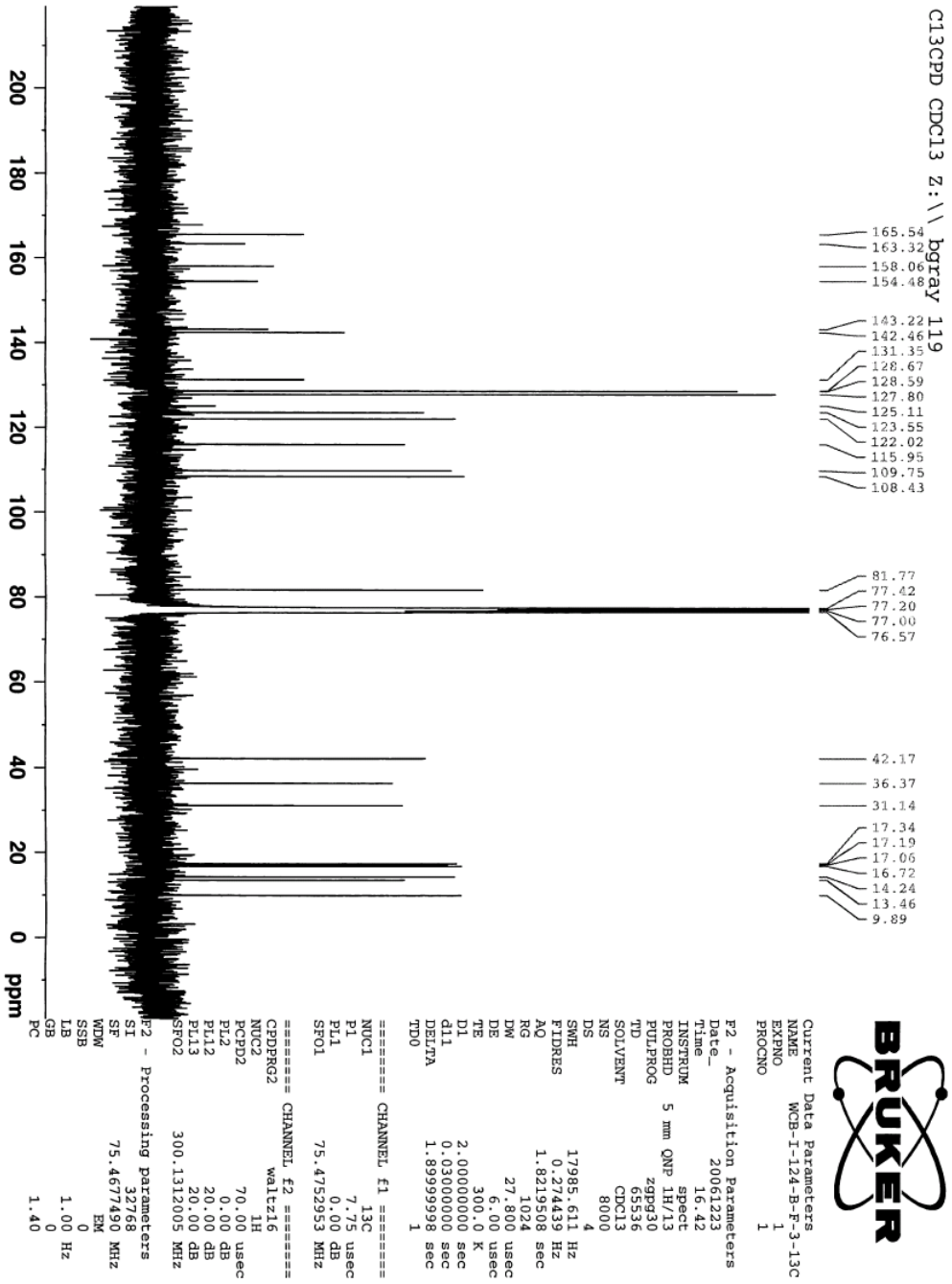
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158.06
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128.59
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109.75
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77.20
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17.19
17.06
16.72
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13.46
9.89
200
180
160
140
120
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80
60
40
20
0
ppm
BRUKER
Current Data Parameters
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EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
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Time 16.42
INSTRUM spect
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PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 8000
DS 4
SWH 17985.611 Hz
FIDRES 0.2744439 Hz
AQ 1.8219508 sec
RG 1024
DW 27.800 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
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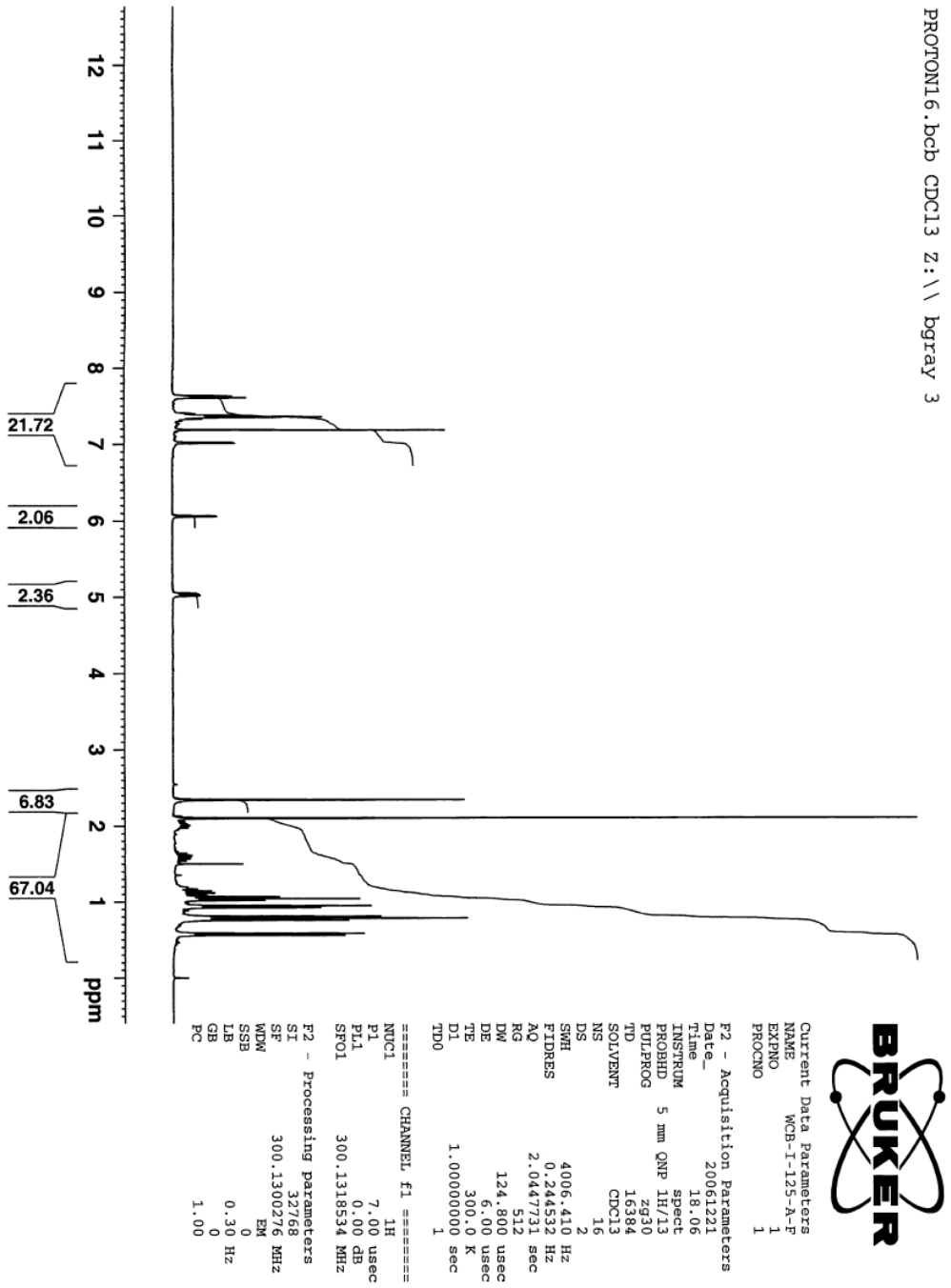
NUC1 13C
P1 7.75 usec
PL1 0.00 dB
SFO1 75.4752953 MHz
========== CHANNEL f2 ==========
CPDPRG2 waltz16
NUC2 1H
PCPD2 70.00 usec
PL2 0.00 dB
PL12 20.00 dB
PL13 20.00 dB
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40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PROCNO 1
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Time_ 18.06
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PULPROG zg30
TD 16384
SOLVENT CDC13
NS 16
DS 2
SWH 4006.410 Hz
FIDRES 0.244532 Hz
AQ 2.0447731 sec
RG 512
DW 124.800 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 7.00 usec
PL1 0.00 dB
SFO1 300.1318534 MHz
F2 - Processing parameters
SI 32768
SF 300.1300276 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
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7
6
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4
3
2
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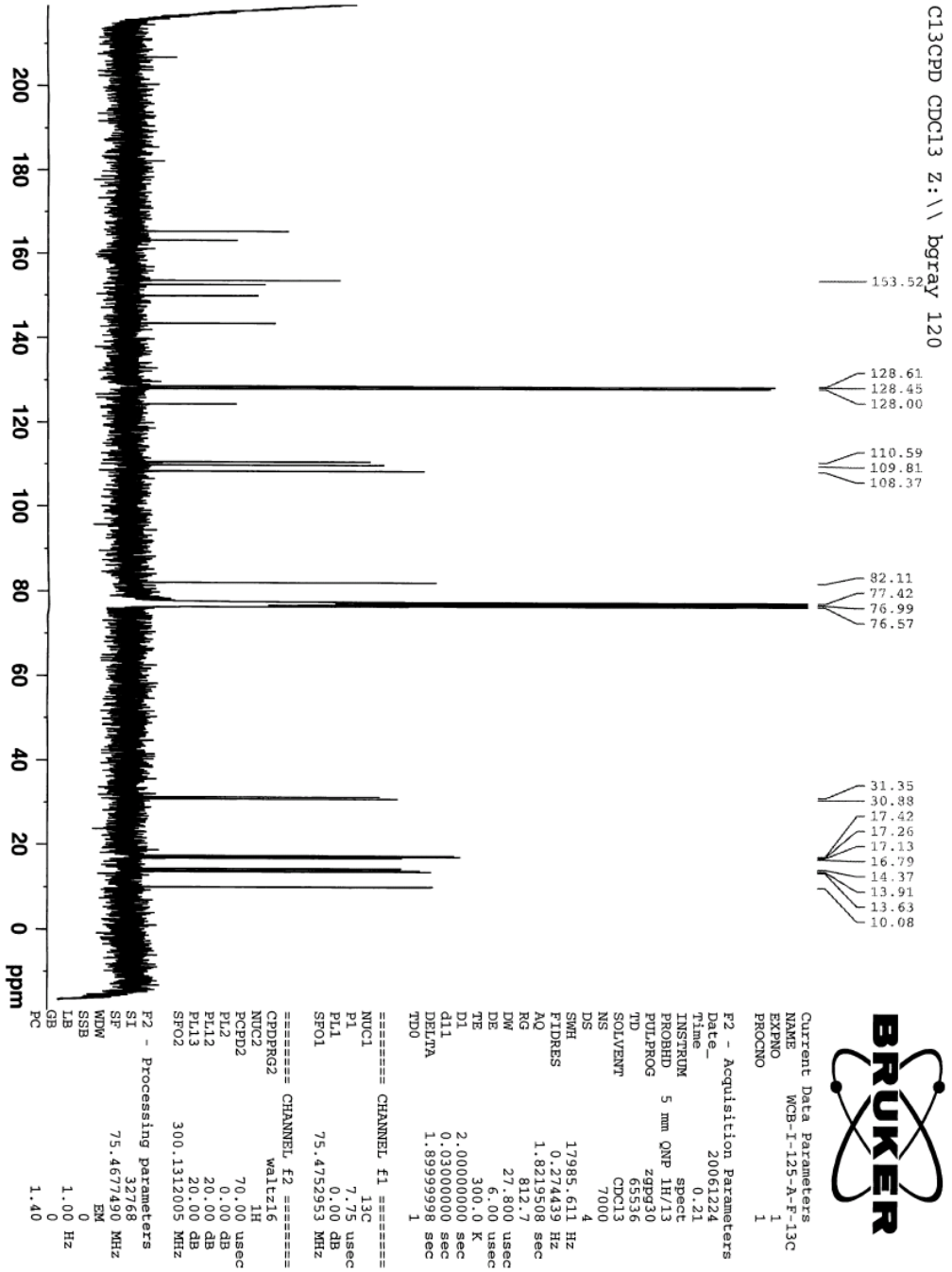
ppm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17.26
17.13
16.79
14.37
13.91
13.63
10.08
200
180
160
140
120
100
80
60
40
20
0
ppm
Current Data Parameters
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EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20061224
Time_ 0.21
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PULPROG zgpg30
TD 65536
SOLVENT CDC13
NS 7000
DS 4
SWH 17985.611 Hz
FIDRES 0.274439 Hz
AQ 1.8219508 sec
RG 812.7
DW 27.800 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.75 usec
PL1 0.00 dB
SFO1 75.4752953 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 70.00 usec
PL2 0.00 dB
PL12 20.00 dB
PL13 20.00 dB
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

Representative procedure for diyne screening (Table III):

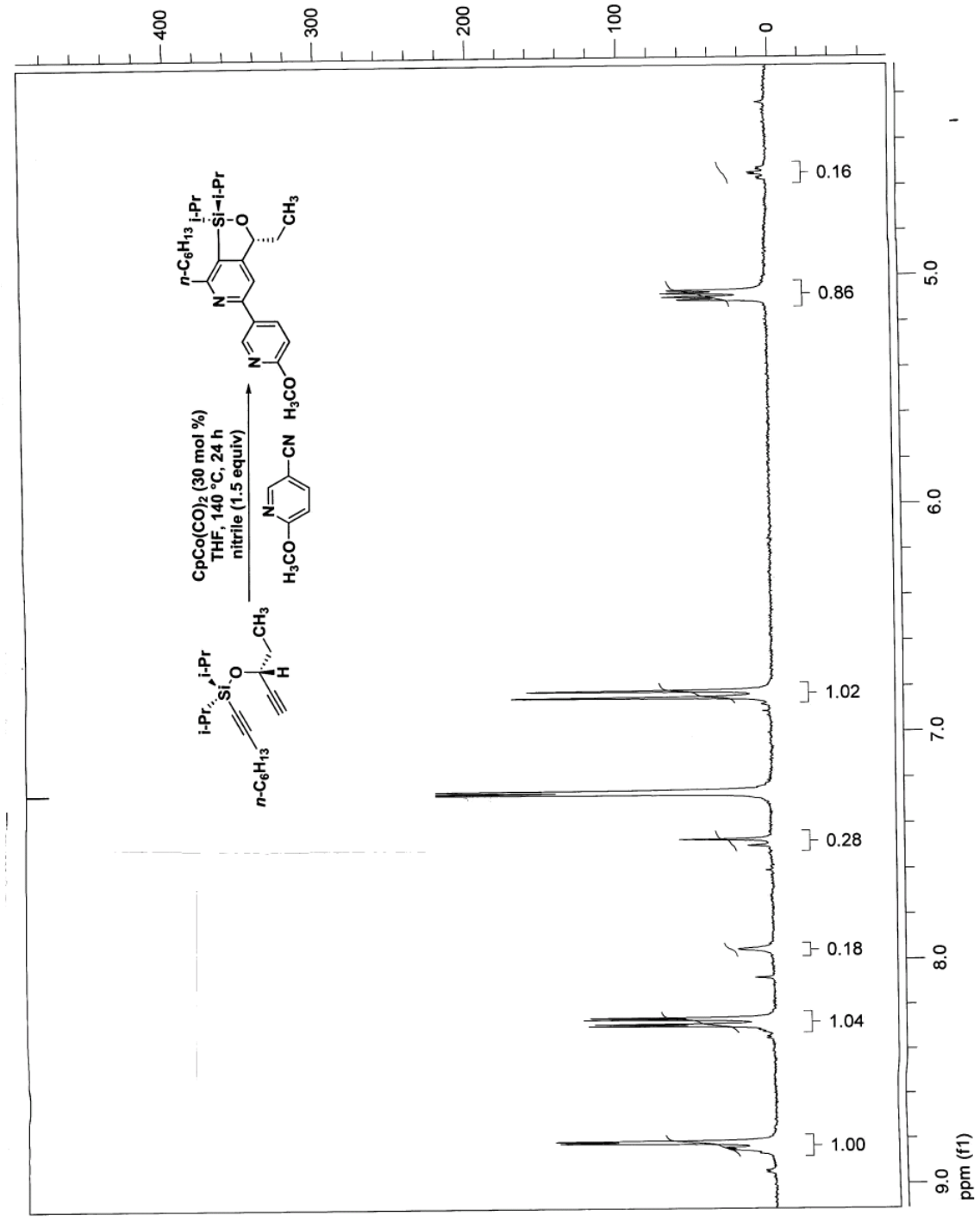
Diynes **36-41** (0.033 mmol, 1 equiv) were placed into an oven-dried sealed tube equipped with magnetic stirrer and dissolved in degassed THF (0.67 ml). 5-methoxy-2-pyridinecarbonitrile (6.7 mg, 0.050 mmol) was added as a solid to the stirring solution. After complete dissolution, a solution of cyclopentadienylcobalt(I) dicarbonyl (1.8 mg, 0.010 mmol, 30 mol %) in degassed xylenes (50 μl) was introduced by syringe, giving a pale yellow solution. The sealed tube was immediately submerged into an oil bath preheated to 140 °C. After 24 h, the dark brown solution was cooled to ambient temperature and loaded onto a 4 g silica plug. Filtration was performed using an *Isco Combiflash* system using a gradient solvent commencing with hexanes and ending with 1/1 hexanes/ethyl acetate (total volume of approximately 40 ml), which effectively removed insoluble cobalt byproducts. Pooled fractions were concentrated *in vacuo* and assayed for conversion by ^{1}H NMR. Purification was performed by silica gel chromatography using an *Isco Combiflash* 12 g column with 20:1 hexanes:EtOAc as eluant, providing pyridines **42-48**.

Representative spectral data for diyne screening experiments (Table III):
1H NMR spectra for selected entries:

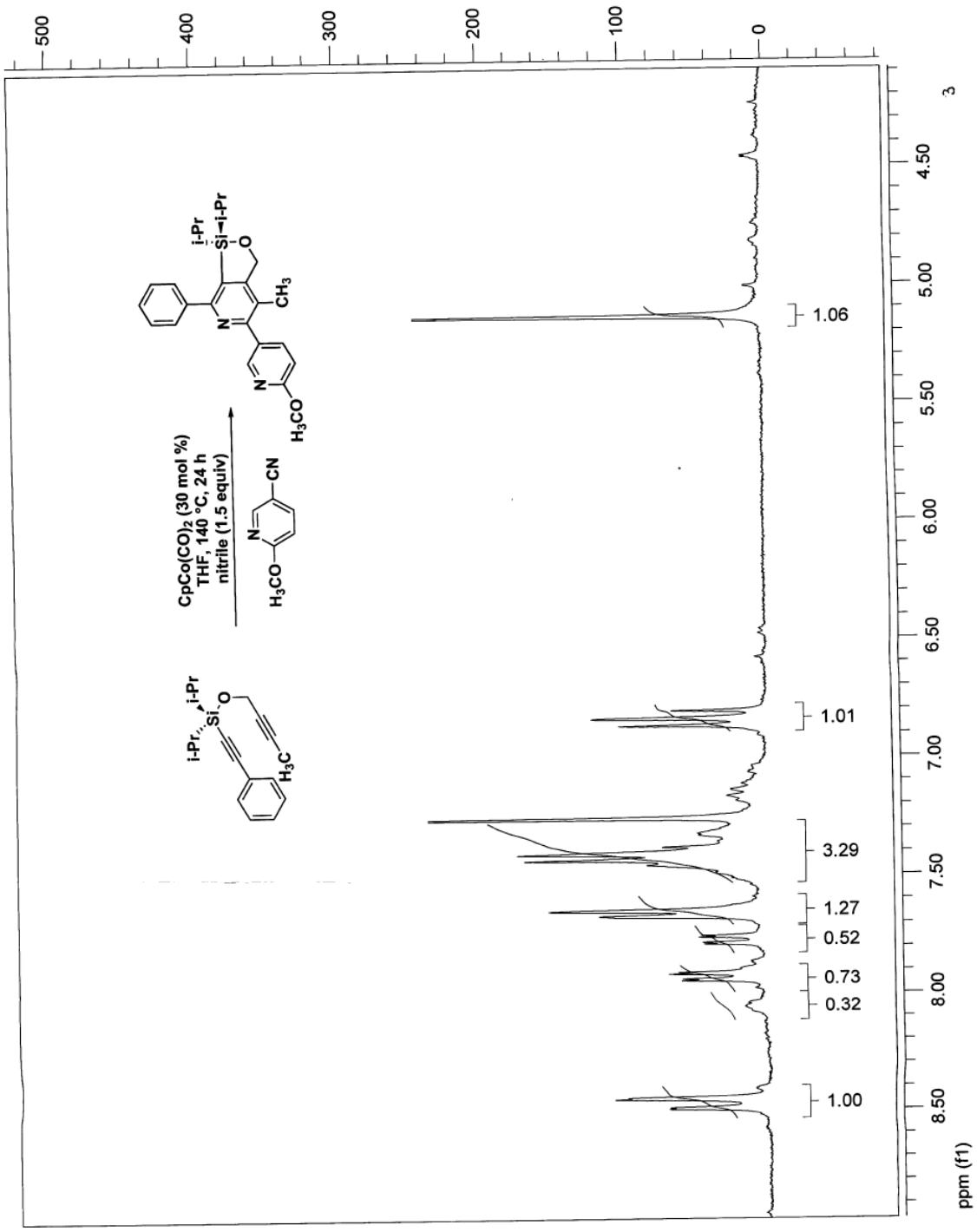
page	*table 3 entry*	*pyridine*	*δ subst (ppm)*	*δ product (ppm)*	*conversion*
S-53	1	**42**	4.6 ppm	5.0 ppm	84%
S-54	3	**43/44**	4.5 ppm	5.2 ppm	>95%
S-55	5	**45**	4.6 ppm	5.1 ppm	57%
S-56	7	**46**	5.0 ppm	5.6 ppm	68%

Conversions were determined on the basis of integration between the methine proton H(A) in the substrate and the equivalent methine proton H(A) in pyridine adducts. See above table for specific chemical shifts for each reaction.

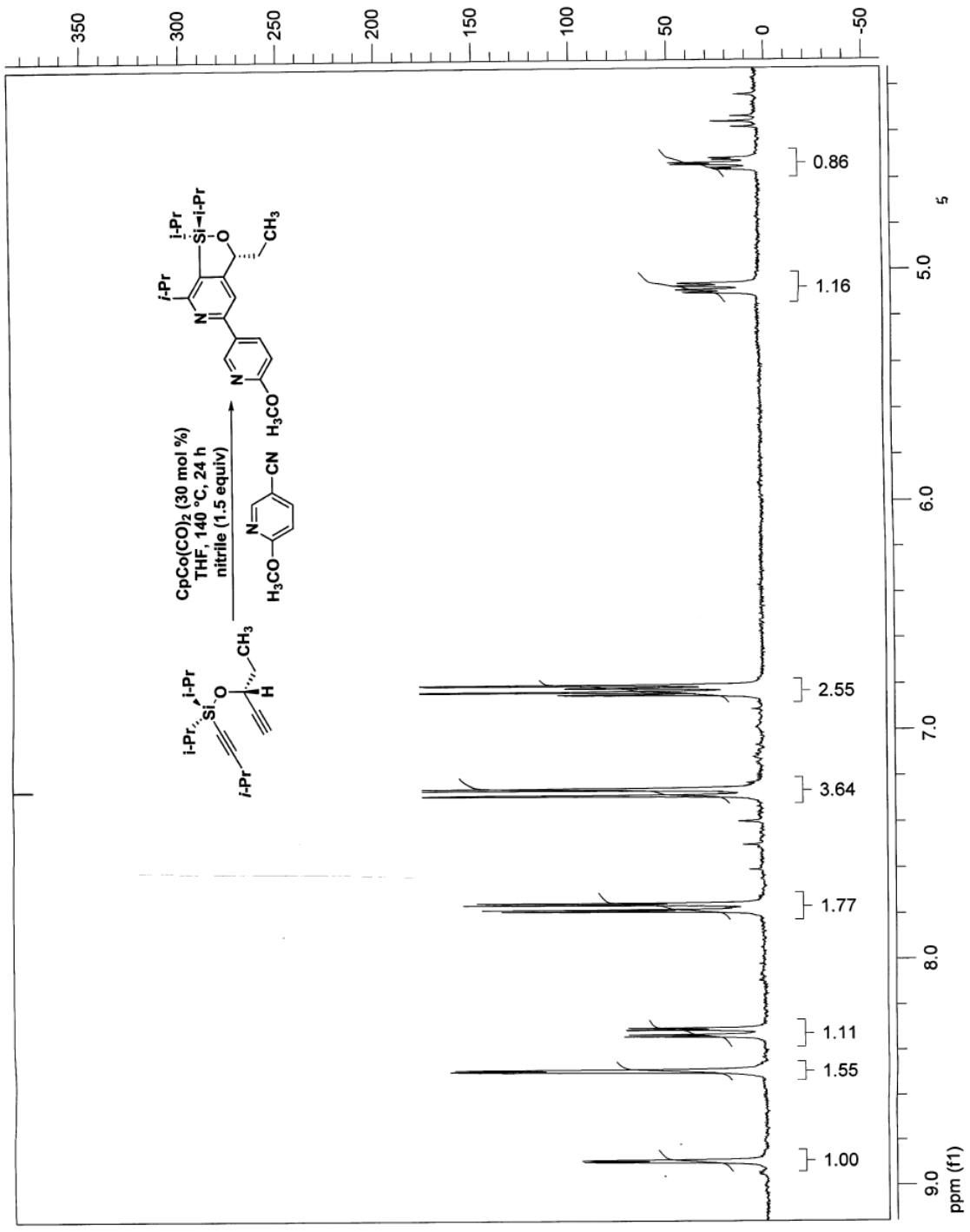
Solvent: $CDCl_3$ – Frequency: 300 MHz



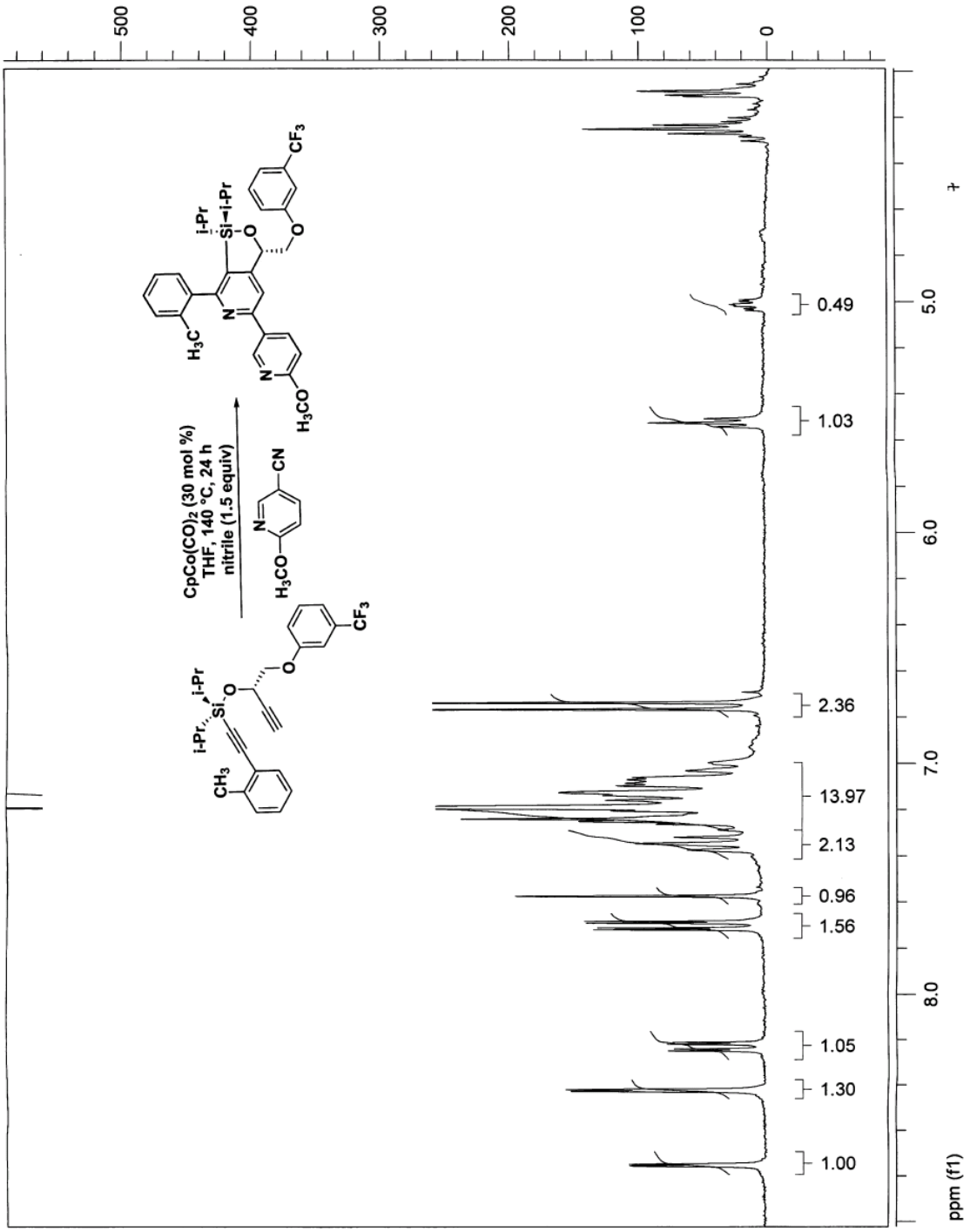
Solvent: $CDCl_3$ – Frequency: 300 MHz



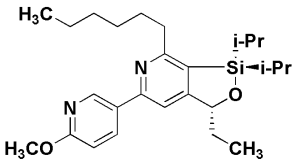
Solvent: $CDCl_3$ – Frequency: 300 MHz



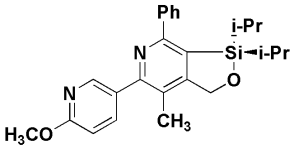
Solvent: $CDCl_3$ – Frequency: 300 MHz



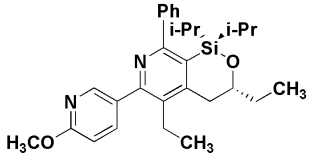
Characterization data for pyridines (Table III):



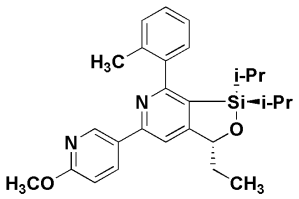
3-ethyl-7-hexyl-1,1-diisopropyl-5-(6-methoxypyridin-3-yl)-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridine (42) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (d, *J* = 2.20, 1 H); 8.28 (dd, *J* = 8.42, 2.56, 1 H); 7.27 (s, 1 H); 6.83 (d, *J* = 8.42, 1 H); 5.08 (dd, *J* = 8.60, 3.66, 1 H); 4.00 (s, 3 H); 2.80 (t, *J* = 8.05, 2 H); 2.02-1.97 (m, 1 H); 1.87 (app quint, *J* = 7.69, 2 H); 1.64-1.58 (m, 1 H); 1.45-1.40 (m, 2 H); 1.36-1.33 (m, 4 H); 1.31-1.26 (m, 2 H); 1.14 (d, *J* = 7.32, 3 H); 1.08 (t, *J* = 7.32, 3 H); 1.03-0.98 (m, 9 H); 0.90 (t, *J* = 6.96, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.7, 162.8, 156.5, 147.6, 140.0, 130.0, 121.8, 110.3, 82.7, 53.6, 41.0, 31.8, 30.4, 30.0, 29.6, 22.6, 18.1, 17.5, 17.4, 17.2, 16.6, 14.0, 13.8, 13.3, 10.8; IR (film): 2937, 2860, 1609, 1574, 1532, 1490, 1456, 1393, 1351, 1281, 1106, 1064, 1029, 987, 878, 826, 761, 661 cm^{-1}; HRMS calcd for $C_{26}H_{40}N_2O_2Si$ (M^+ + H), 441.2937; found, 441.2955



1,1-diisopropyl-5-(6-methoxypyridin-3-yl)-4-methyl-7-phenyl-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridine (43) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48-8.45 (m, 1 H); 7.92 (dt, *J* = 7.50, 2.40, 1 H); 7.68-7.62 (m, 2 H); 7.49-7.38 (m, 3 H); 6.86 (d, *J* = 8.70, 1 H); 5.14 (s, 2 H); 4.00 (s, 3 H); 2.50 (s, 3 H); 1.30-1.19 (m, 2 H); 0.98 (d, *J* = 7.20, 3 H); 0.92 (t, *J* = 7.80, 3 H); 0.77 (d, *J* = 7.50, 3 H); 0.67 (d, *J* = 7.50, 3 H); IR (film): 2958, 2868, 1749, 1616, 1560, 1511, 1461, 1404, 1374, 1352, 1283, 1252, 1122, 1065, 1026, 926, 870, 835, 774, 704, 656 cm^{-1}; HRMS calcd for $C_{25}H_{30}N_2O_2Si$ (M^+ + H), 419.2155; found, 419.2151



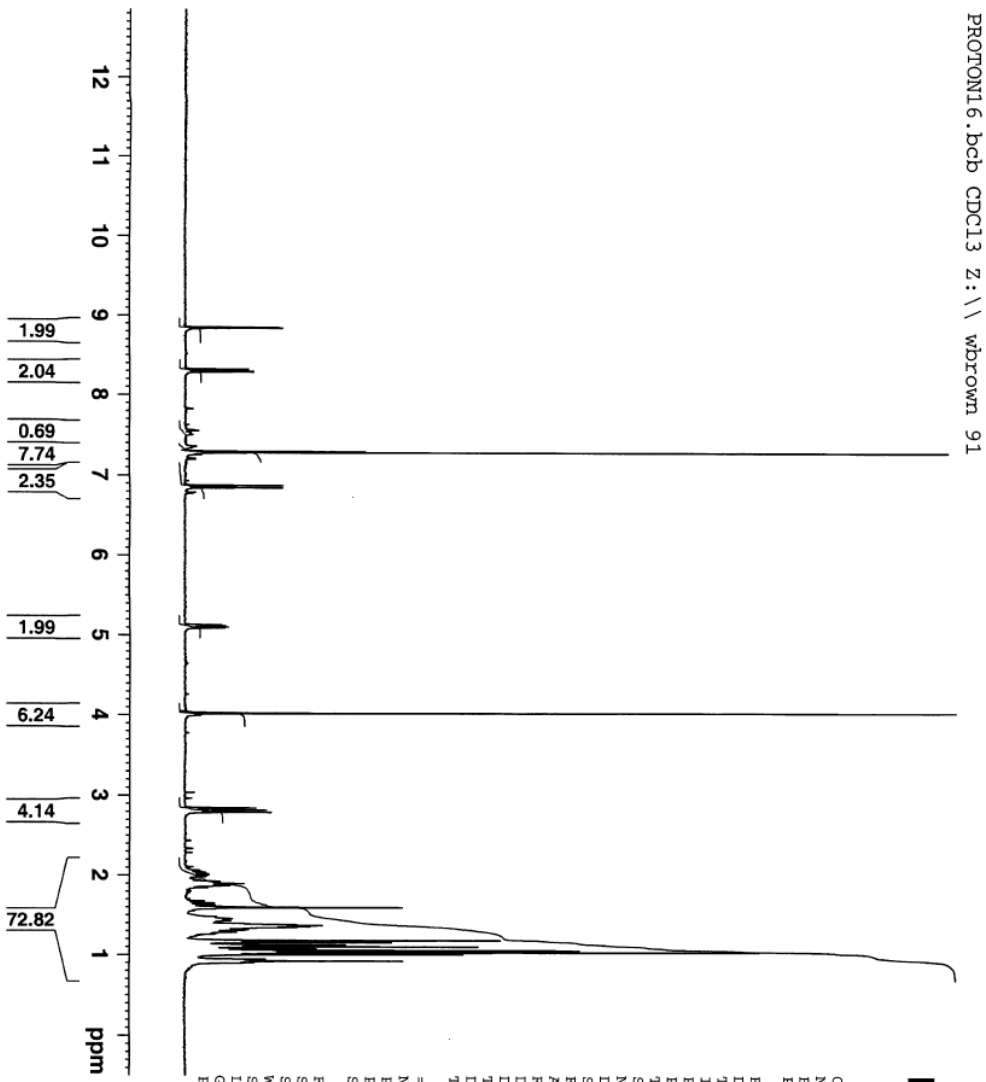
3,5-diethyl-1,1-diisopropyl-6-(6-methoxypyridin-3-yl)-8-phenyl-3,4-dihydro-1H-[1,2]oxasilino[3,4-c]pyridine (47) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, *J* = 2.56, 1 H); 7.74 (dd, *J* = 8.42, 2.56, 1 H); 7.44-7.42 (m, 2 H); 7.38-7.36 (m, 3 H); 6.80 (d, *J* = 8.42, 1 H); 3.97 (s, 3 H); 3.89-3.84 (m, 1 H); 3.04 (dd, *J* = 16.11, 1.83, 1 H); 2.71 (q, *J* = 7.32, 2 H); 2.64 (dd, *J* = 15.74, 9.88, 1 H); 1.62 (quint, *J* = 6.96, 2 H); 1.56-1.51 (m, 2 H); 1.12 (t, *J* = 7.32, 3 H); 1.05-1.02 (m, 5 H); 0.90 (m, 4 H); 0.85 (d, *J* = 7.69, 3 H); 0.71 (d, *J* = 7.32, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.6, 161.8, 155.9, 155.8, 146.7, 143.6, 139.6, 132.9, 130.8, 128.9, 128.2, 128.0, 126.4, 110.3, 73.3, 53.5, 36.7, 31.4, 22.3, 18.6, 18.0, 17.7, 17.4, 15.1, 15.0, 14.8, 10.0; IR (film): 2951, 2868, 1602, 1567, 1532, 1490, 1462, 1386, 1288, 1127, 1071, 1029, 917, 882, 833, 770, 742, 700, 631 cm^{-1}; HRMS calcd for $C_{29}H_{38}N_2O_2Si$ (M^+ + H), 475.2781; found, 475.2787



(3)-3-ethyl-1,1-diisopropyl-5-(6-methoxypyridin-3-yl)-7-o-tolyl-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridine (48) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.82 (d, *J* = 2.40, 1 H); 8.30 (dd, *J* = 8.70, 2.70, 1 H); 7.43 (br s, 1 H); 7.31-7.23 (m, 4 H); 6.82 (d, *J* = 8.70, 1 H); 5.15 (dd, *J* = 8.70, 2.70, 1 H); 3.99 (s, 3 H); 2.31 (s, 3 H); 2.11-1.98 (m, 1 H); 1.73-1.63 (m, 1 H); 1.16-1.09 (m, 5 H); 0.93-0.85 (m, 6 H); 0.74 (d, *J* = 7.20, 3 H); 0.61 (d, *J* = 7.50, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 164.7, 164.3, 154.6, 146.1, 145.9, 142.7, 137.8, 136.3, 130.7, 128.8, 128.4, 128.2, 126.6, 125.7, 125.6, 111.4, 110.7, 82.3, 53.6, 31.4, 20.1, 17.0, 17.0, 16.8, 16.2, 13.7, 13.4, 13.0, 10.2; IR (film): 2948, 2870, 1604, 1570, 1526, 1500, 1461, 1387, 1343, 1287, 1261, 1104, 1083, 1061, 1030, 987, 887, 865, 822, 756, 665 cm^{-1}; HRMS calcd for $C_{27}H_{34}N_2O_2Si$ (M^+ + H), 447.2468; found, 447.2452

Representative Spectra for Pyridines synthesized in Table III:
*Spectra for compounds **42-44 & 46-48**:*

page	Pyridine	spectrum	page	pyridine	spectrum
59	**42**	1H	61	**46**	1H
60	**43/44**	1H	62	**47**	1H
			63	**48**	1H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PROCNO 1
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Time 11.08
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PULPROG zg30
TD 16384
SOLVENT CDC13
NS 16
DS 2
SWH 4006.410 Hz
FIDRES 0.244532 Hz
AQ 2.0447731 sec
RG 574.7
DW 124.800 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
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P1 7.00 usec
PL1 0.00 dB
SFO1 300.1318534 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1.99
2.04
0.69
7.74
2.35
1.99
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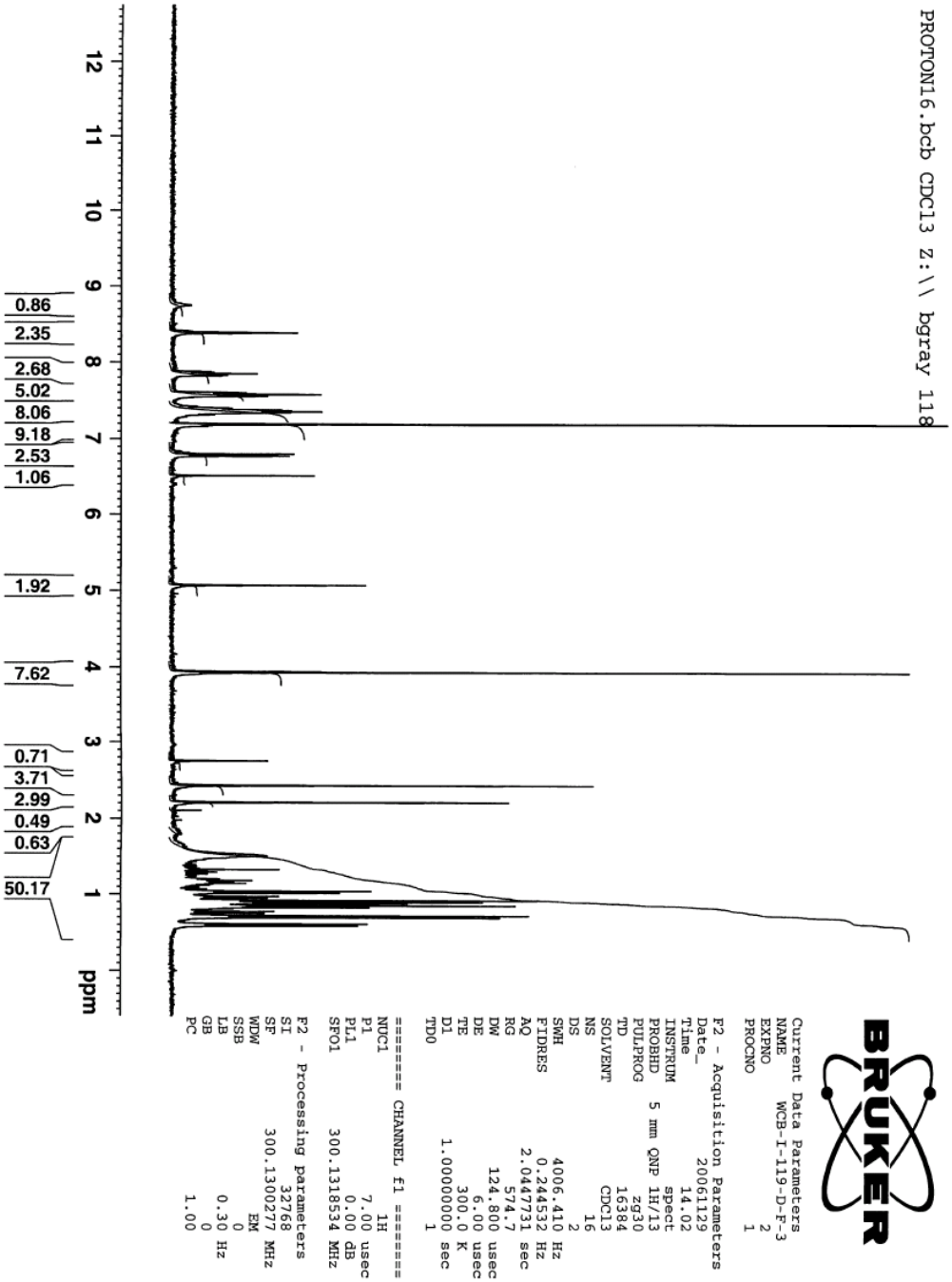
4.14
72.82
12
11
10
9
8
7
6
5
4
3
2
1
ppm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PROCNO 1
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FIDRES 0.244532 Hz
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RG 574.7
DW 124.800 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
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PL1 0.00 dB
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F2 - Processing parameters
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SF 300.1300277 MHz
WDW EM
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LB 0.30 Hz
GB 0
PC 1.00
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2.68
5.02
8.06
9.18
2.53
1.06
1.92
7.62
0.71
3.71
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0.63
50.17
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8
7
6
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3
2
1
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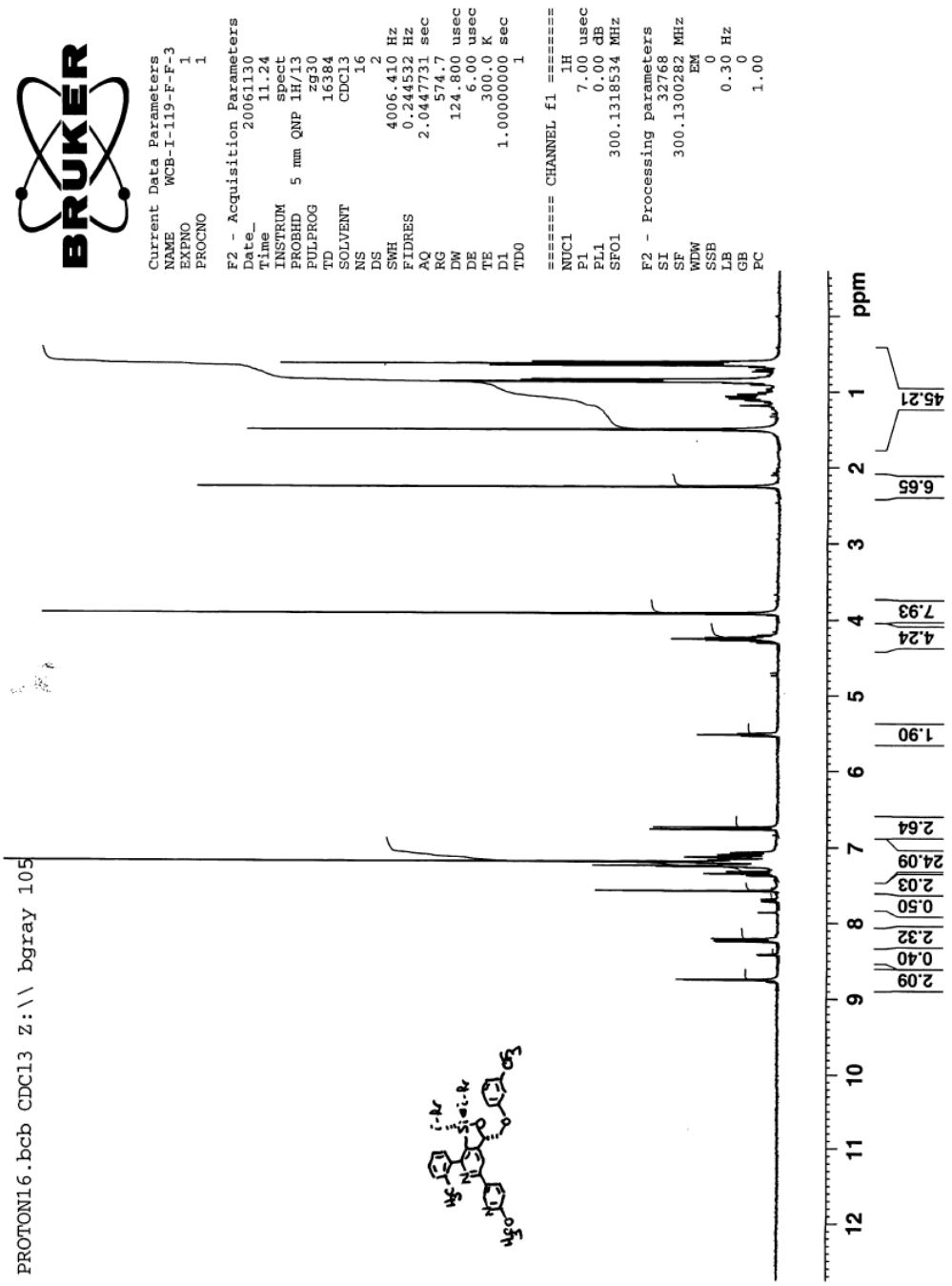
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PROCNO 1
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PULPROG zg30
TD 16384
SOLVENT CDC13
NS 16
DS 2
SWH 4006.410 Hz
FIDRES 0.244532 Hz
AQ 2.0447731 sec
RG 574.7
DW 124.800 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
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NUC1 1H
P1 7.00 usec
PL1 0.00 dB
SFO1 300.1318534 MHz
F2 - Processing parameters
SI 32768
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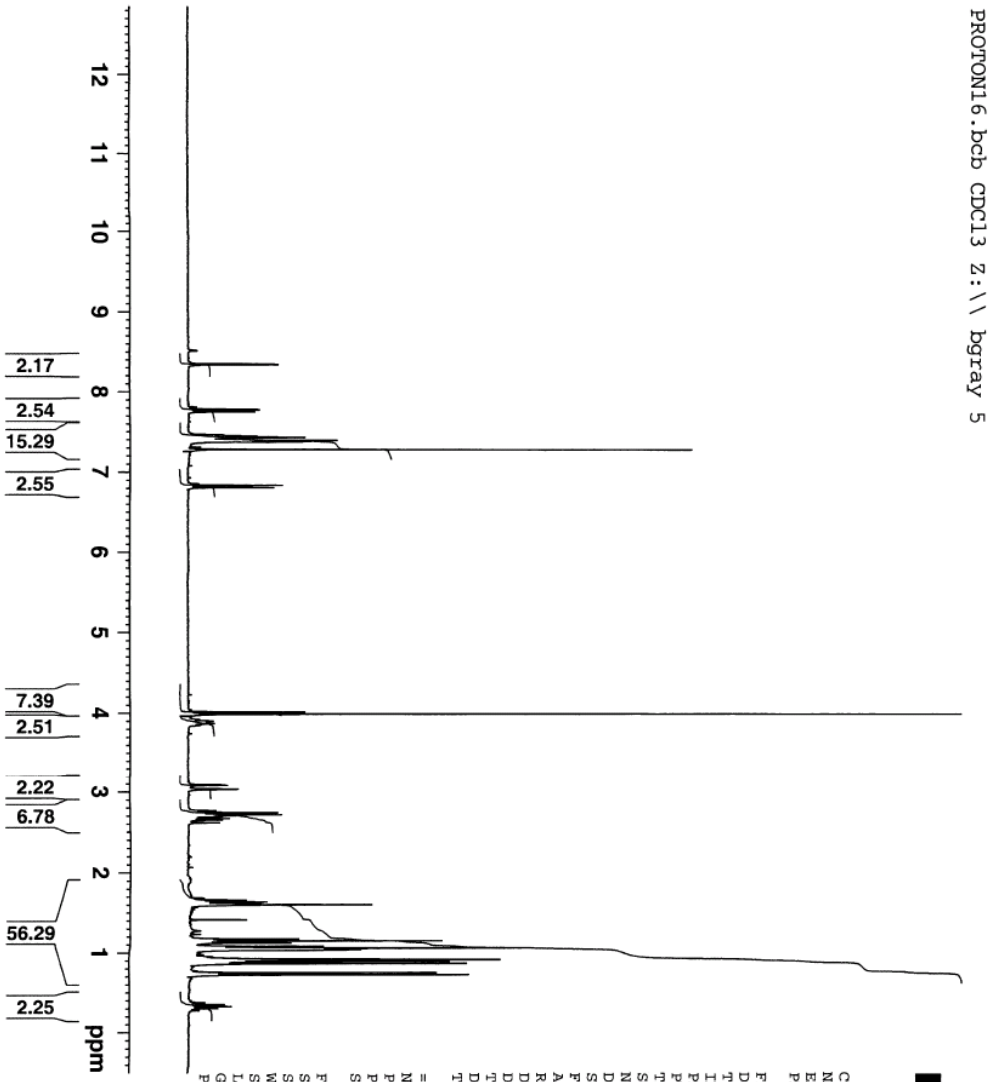
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PROCNO 1
F2 - Acquisition Parameters
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INSTRUM spect
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PULPROG zg30
TD 16384
SOLVENT CDC13
NS 16
DS 2
SWH 4006.410 Hz
FIDRES 0.244532 Hz
AQ 2.0447731 sec
RG 512
DW 124.800 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
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P1 7.00 usec
PL1 0.00 dB
SFO1 300.1318534 MHz
F2 - Processing parameters
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SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
12
11
10
9
8
7
6
5
4
3
2
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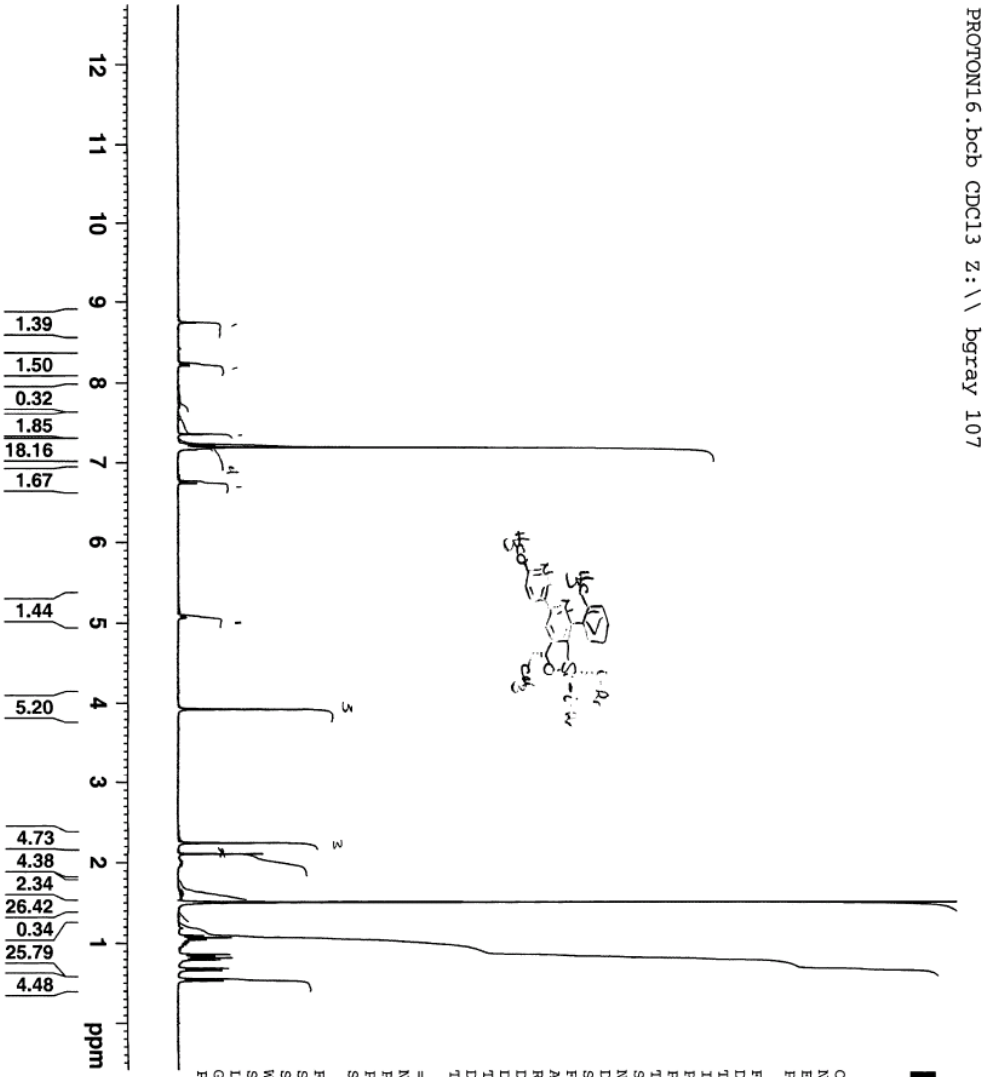
7.39
2.51
2.22
6.78
56.29
2.25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PULPROG zg30
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SOLVENT CDC13
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DS 2
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FIDRES 0.244532 Hz
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P1 7.00 usec
PL1 0.00 dB
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F2 - Processing parameters
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SF 300.1300265 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
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1.50
0.32
1.85
18.16
1.67
1.44
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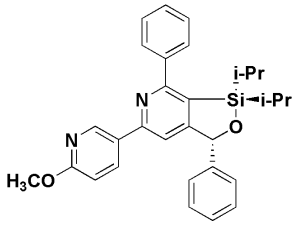
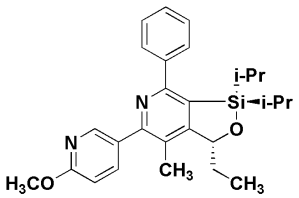
2.34
26.42
0.34
25.79
4.48
ppm

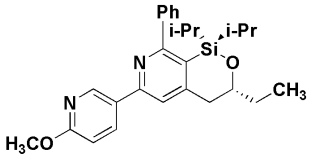
Representative 1H NMR & HRMS data for compounds screened (Figure 2):



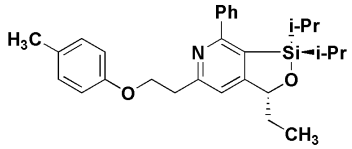
(R)-1,1-diisopropyl-5-(6-methoxypyridin-3-yl)-3,7-diphenyl-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridine (BLG-IV-198-C) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.76 (d, *J* = 2.40, 1 H); 8.30 (dd, *J* = 8.70, 2.40, 1 H); 7.81-7.78 (m, 2 H); 7.51-7.48 (m, 3 H); 7.38 (m, 5 H); 7.20 (s, 1 H); 6.79 (d, *J* = 8.70, 1 H); 6.15 (s, 1 H); 3.96 (s, 3 H); 1.44-1.34 (m, 1 H); 1.31-1.24 (m, 1 H); 1.08 (d, *J* = 7.20, 3 H); 0.98 (d, *J* = 7.20, 3 H); 0.89 (d, *J* = 7.80, 3 H); 0.83 (d, *J* = 7.50, 3 H); HRMS calcd for $C_{30}H_{32}N_2O_2Si$ (M^+ + H), 481.2311; found, 481.2317



3-ethyl-1,1-diisopropyl-5-(6-methoxypyridin-3-yl)-4-methyl-7-phenyl-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridine (BLG-IV-198-D) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (d, *J* = 2.40, 1 H); 7.92 (dd, *J* = 8.55, 2.40, 1 H); 7.66-7.63 (m, 2 H); 7.46-7.38 (m, 3 H); 6.85 (d, *J* = 8.40, 1 H); 5.14-5.10 (m, 1 H); 4.00 (s, 3 H); 2.33 (s, 3 H); 2.17-2.07 (m, 1 H); 1.22 (t, *J* = 7.20, 3 H); 1.16 (d, *J* = 6.90, 3 H); 1.08 (d, *J* = 7.20, 3 H); 0.70 (d, *J* = 7.20, 3 H); 0.45 (d, *J* = 7.50, 3 H); HRMS calcd for $C_{27}H_{34}N_2O_2Si$ (M^+ + H), 447.2468; found, 447.2454



3-ethyl-1,1-diisopropyl-6-(6-methoxypyridin-3-yl)-8-phenyl-3,4-dihydro-1H-[1,2]oxasilino[3,4-c]pyridine (WCB-I-118-C) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.81 (d, *J* = 2.20, 1 H); 8.34 (dd, *J* = 8.79, 2.20, 1 H);7.52-7.50 (m, 2 H); 7.43-7.42 (m, 3 H); 7.39 (s, 1 H); 6.81 (d, *J* = 8.42, 1 H); 3.99 (s, 3 H); 3.92-3.90 (m, 1 H); 2.85-2.84 (m, 2 H); 1.60-1.55 (m, 2 H); 1.04-1.00 (m, 6 H); 0.96-0.92 (m, 2 H); 0.90-0.89 (m, 3 H); 0.86 (d, *J* = 7.32, 3 H); 0.65 (d, *J* = 7.69, 3 H); HRMS calcd for $C_{27}H_{34}N_2O_2Si$ (M^+ + H), 447.2468; found, 447.2451

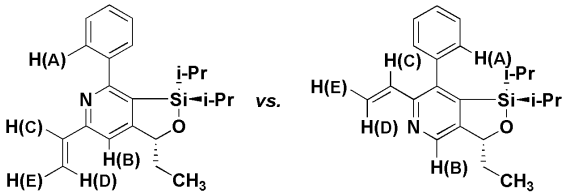


3-ethyl-1,1-diisopropyl-7-phenyl-5-(2-(p-tolyloxy)ethyl)-1,3-dihydro-[1,2]oxasilolo[3,4-c]pyridine (BLG-IV-196-B) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61-7.59 (m, 2 H); 7.46-7.36 (m, 3 H); 7.08-7.05 (m, 3 H); 6.82 (d, 8.40, 2 H); 5.06 (dd, *J* = 8.55, 3.30, 1 H); 4.41 (dt, *J* = 6.60, 1.80, 2 H); 3.33 (t, *J* = 6.60, 2 H); 2.27 (s, 3 H); 2.03-1.95 (m, 1 H); 1.66-1.58 (m, 1 H); 1.21-1.14 (m, 2 H); 1.08 (t, *J* = 7.20, 2 H); 0.98 (d, *J* = 7.20, 3 H); 0.85-0.81 (m, 7 H); 0.63 (d, *J* = 7.50, 3 H); IR (film): 2952, 2865, 1617, 1587, 1570, 1504,

1461, 1383, 1287, 1243, 1178, 1104, 1065, 1035, 987, 878, 817, 761, 700, 665, 513, 465 cm^{-1}; HRMS calcd for $C_{29}H_{37}NO_2Si$ ($M^+ + H$), 460.2672; found, 460.2651

Regiochemistry of nitrile addition to silyl-tethered diynes

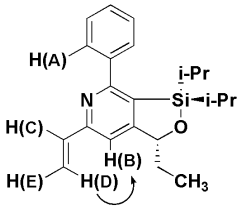
*1D nOe studies performed on compound **21**:*



21 **21-*B***

entry	H irradiated	observed nOe
1	H(A)	*None*
2	H(B)	*None*
3	H(C)	H(E)
4	H(D)	H(E)
5	***H(D)***	***H(B)***
6	H(E)	H(D)

*The structure of this compound is therefore designated as **21**:*



21

Experimental Procedures for Screening Experiments:

Materials, cell culturing methods, and imaging procedures:

Materials: The EGF domain of Neuregulin 1β1 (corresponding to amino acid residues 176 – 246 of Heregulin-1β1), was expressed and purified from *E. coli* (R&D Systems; #396-HB) and reconstituted in phosphate-buffered saline (PBS) with 0.1% bovine serum albumin as a non-specific carrier and frozen in aliquots at -20 °C.

Cell culturing: PC12-ErbB4-GFP and PC12-GFP cells were maintained in RPMI 1640 media (Gibco; 22400) containing 10% heat inactivated horse serum (Gibco; 26050), 5% heat inactivated fetal bovine serum (Gibco; 16140) and 750 μg/ml gentamicin (Gibco; 15750) referred to here as RPMI+. Cells were passaged at 80-90% confluency and incubated at 37 °C in 5% CO_2. Media was changed every 3 days.

Compound screen, cell imaging, and neurite measurements: Cells (300 cells per well) were seeded in black, clear bottom, tissue culture-treated 384-well (Corning; 3712) plates in 40 μL of RPMI+ media. Even distribution was achieved by a quick centrifuge at 500 r.p.m. using a tabletop centrifuge (Sorvall, LegendRT) and multiwell plate adaptors shortly after seeding. Cells were then incubated for 12 h before use. 5.0 μL of compound solution in RPMI+ media were transferred into wells of 384-well plates containing PC12-ErbB4-GFP cells 30 minutes prior to treatment of 5.0 μL of Neuregulin solution (200 ng/mL in RPMI+ media). After 48 hours, images were taken using an ImageXpress Micro automated microscopy (Molecular Devices) laser-based autofocus with a Nikon 4X objective (ELWD S Fluor/0.20 NA), and an image acquisition time of 150 ms using a Xenon light source and 483/536 nm filter sets for measuring GFP fluorescence. Neurite detection and analysis were performed with MetaXpress (Molecular Devices) using the "Neurite Detection" analysis module. Cell bodies were specified as pixel blocks of

minimum width 8 μm, maximum area of 150 μm^2 and pixel intensities 1,000 units above local background. Neurites were specified as linear objects with maximum width 3 μm and pixel intensities 500 units above the local background of the object being measured. Fluorescent images shown were imported as Tagged Image File Format (TIFF) files into Adobe Photoshop (San Jose, CA). Screening data were visualized in Microsoft Excel (Seattle, WA).

Screening Data of 25 Pyridines against PC12 Cells Expressing Exogenous ErbB4

A live-cell high-content screening system (LC-HCS) was used; all experiments were run in duplicate:

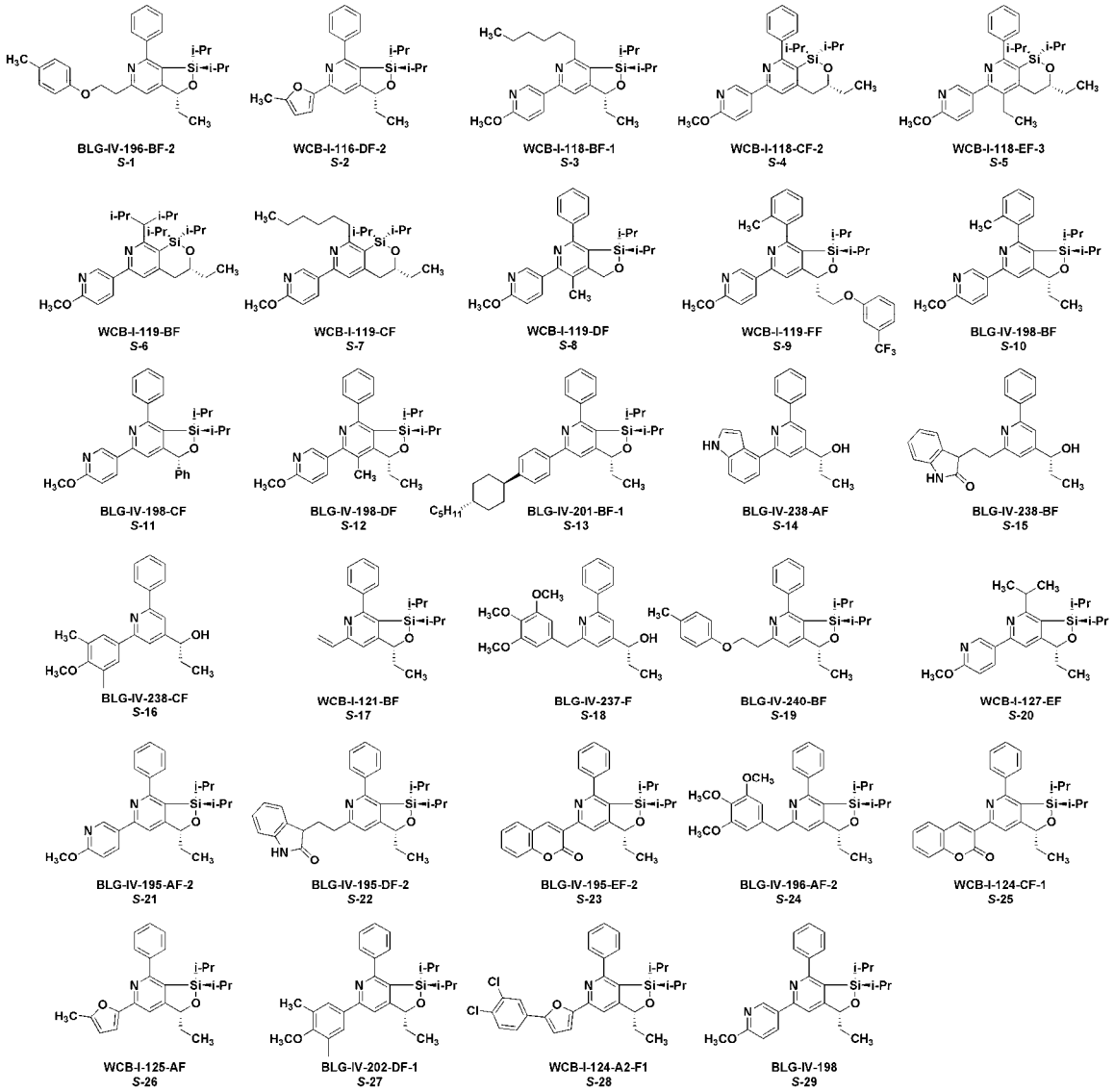
				mean outgrowth/cell	
entry	compound ID	conc (uM)	Hormone	Expt #1	Expt #2
1	BLG-IV-196-BF2	4		6.0	5.2
2	BLG-IV-196-BF2	4	*Neuregulin*	26.4	25.3
3	WCB-I-116-DF2	4		5.6	5.5
4	WCB-I-116-DF2	4	*Neuregulin*	32.6	25.1
5	WCB-I-118-BF1	4		5.4	4.1
6	WCB-I-118-BF1	4	*Neuregulin*	28.4	25.4
7	WCB-I-118-CF2	4		5.1	6.4
8	WCB-I-118-CF2	4	*Neuregulin*	27.7	26.8
9	WCB-I-118-EF3	4		4.2	5.6
10	WCB-I-118-EF3	4	*Neuregulin*	23.5	29.7
11	WCB-I-119-BF	4		5.9	5.7
12	WCB-I-119-BF	4	*Neuregulin*	29.5	30.3
13	WCB-I-119-CF	4		4.6	3.8
14	WCB-I-119-CF	4	*Neuregulin*	24.7	22.4
15	WCB-I-119-DF	4		5.0	4.6
16	WCB-I-119-DF	4	*Neuregulin*	27.1	25.6
17	WCB-I-119-FF	4		5.0	5.3
18	WCB-I-119-FF	4	*Neuregulin*	27.5	27.3
19	BLG-IV-198-BF	4		5.3	6.6
20	BLG-IV-198-BF	4	*Neuregulin*	27.6	30.4
21	BLG-IV-198-CF	4		6.6	5.4
22	BLG-IV-198-CF	4	*Neuregulin*	26.7	22.9
23	BLG-IV-198-DF	4		6.1	6.9
24	BLG-IV-198-DF	4	*Neuregulin*	26.3	34.5
25	BLG-IV-201-BF1	4		5.7	4.5
26	BLG-IV-201-BF1	4	*Neuregulin*	24.9	31.8
27	BLG-IV-238-AF	4		6.6	6.0
28	BLG-IV-238-AF	4	*Neuregulin*	34.9	28.4
29	BLG-IV-238-BF	4		4.3	4.8
30	BLG-IV-238-BF	4	*Neuregulin*	30.0	31.8
31	BLG-IV-238-CF	4		4.4	4.7
32	BLG-IV-238-CF	4	*Neuregulin*	31.8	29.6
33	WCB-I-121-BF	4		4.8	4.1
34	WCB-I-121-BF	4	*Neuregulin*	27.3	30.7
35	BLG-IV-237-F	4		3.4	2.6
36	BLG-IV-237-F	4	*Neuregulin*	7.3	6.6
37	BLG-IV-240-BF	4		3.9	3.2
38	BLG-IV-240-BF	4	*Neuregulin*	11.9	25.8
39	WCB-I-127-EF	4		3.7	4.1
40	WCB-I-127-EF	4	*Neuregulin*	35.3	27.6
41	BLG-IV-195-AF2	4		3.9	4.4
42	BLG-IV-195-AF2	4	*Neuregulin*	28.0	29.6
43	BLG-IV-195-DF2	4		4.8	4.7

44	BLG-IV-195-DF2	4	*Neuregulin*	31.2	21.4
45	BLG-IV-195-EF2	4		4.8	5.3
46	BLG-IV-195-EF2	4	*Neuregulin*	24.0	34.7
47	BLG-IV-196-AF2	4		4.5	6.7
48	BLG-IV-196-AF2	4	*Neuregulin*	27.6	35.2
49	BLG-IV-196-BF2	20		5.2	5.7
50	BLG-IV-196-BF2	20	*Neuregulin*	27.3	32.6
51	WCB-I-116-DF2	20		6.4	4.0
52	WCB-I-116-DF2	20	*Neuregulin*	25.7	24.4
53	WCB-I-118-BF1	20		3.4	3.7
54	WCB-I-118-BF1	20	*Neuregulin*	26.3	26.1
55	WCB-I-118-CF2	20		4.1	2.4
56	WCB-I-118-CF2	20	*Neuregulin*	34.9	22.8
57	WCB-I-118-EF3	20		3.7	3.1
58	WCB-I-118-EF3	20	*Neuregulin*	27.6	27.8
59	WCB-I-119-BF	20		3.3	4.6
60	WCB-I-119-BF	20	*Neuregulin*	28.2	26.0
61	WCB-I-119-CF	20		52.2	4.8
62	WCB-I-119-CF	20	*Neuregulin*	29.6	33.6
63	WCB-I-119-DF	20		3.6	3.2
64	WCB-I-119-DF	20	*Neuregulin*	25.2	24.0
65	WCB-I-119-FF	20		5.1	3.6
66	WCB-I-119-FF	20	*Neuregulin*	28.4	27.1
67	BLG-IV-198-BF	20		3.2	4.5
68	BLG-IV-198-BF	20	*Neuregulin*	25.4	25.0
69	BLG-IV-198-CF	20		5.3	4.6
70	BLG-IV-198-CF	20	*Neuregulin*	27.9	37.0
71	BLG-IV-198-DF	20		3.4	4.3
72	BLG-IV-198-DF	20	*Neuregulin*	16.3	42.8
73	BLG-IV-201-BF1	20		5.3	5.9
74	BLG-IV-201-BF1	20	*Neuregulin*	30.0	46.3
75	BLG-IV-238-AF	20		4.7	4.3
76	BLG-IV-238-AF	20	*Neuregulin*	29.5	57.2
77	BLG-IV-238-BF	20		4.4	4.2
78	BLG-IV-238-BF	20	*Neuregulin*	36.1	54.9
79	BLG-IV-238-CF	20		4.0	4.9
80	BLG-IV-238-CF	20	*Neuregulin*	26.2	50.3
81	WCB-I-121-BF	20		4.0	3.6
82	WCB-I-121-BF	20	*Neuregulin*	27.4	55.8
83	BLG-IV-237-F	20		4.2	3.2
84	BLG-IV-237-F	20	*Neuregulin*	7.9	9.2
85	BLG-IV-240-BF	20		4.3	4.4
86	BLG-IV-240-BF	20	*Neuregulin*	24.9	49.0
87	WCB-I-127-EF	20		3.3	4.6
88	WCB-I-127-EF	20	*Neuregulin*	30.2	45.7
89	BLG-IV-195-AF2	20		4.6	3.3
90	BLG-IV-195-AF2	20	*Neuregulin*	28.4	53.0
91	BLG-IV-195-DF2	20		2.3	5.4
92	BLG-IV-195-DF2	20	*Neuregulin*	24.6	43.9
93	BLG-IV-195-EF2	20		4.6	4.6
94	BLG-IV-195-EF2	20	*Neuregulin*	29.9	59.5
95	BLG-IV-196-AF2	20		3.4	4.3
96	BLG-IV-196-AF2	20	*Neuregulin*	16.3	42.8

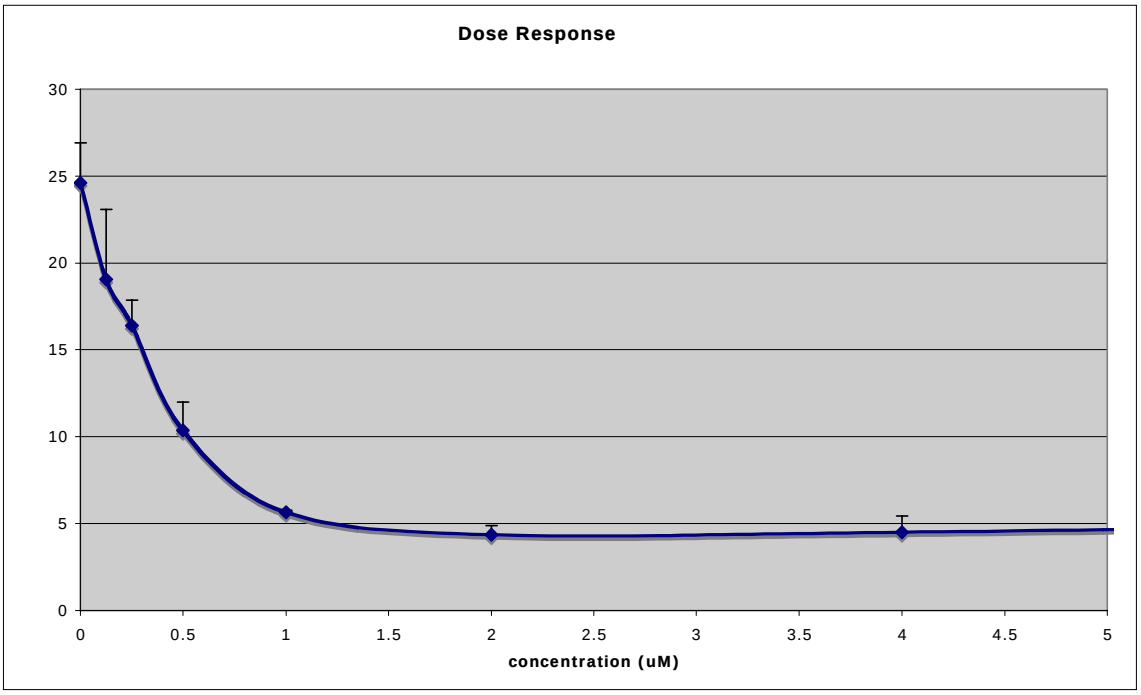
97	WCB-I-124-CF1	4		4.7	4.4
98	WCB-I-124-CF1	4	*Neuregulin*	32.2	39.3
99	WCB-I-125-AF	4		6.4	5.9
100	WCB-I-125-AF	4	*Neuregulin*	30.3	27.1
101	BLG-IV-202-DF1	4		5.8	5.4
102	BLG-IV-202-DF1	4	*Neuregulin*	30.6	35.3
103	WCB-I-124-A2F1	4		4.1	5.8
104	WCB-I-124-A2F1	4	*Neuregulin*	22.1	20.2
105	BLG-IV-198-AF	4		4.6	3.7
106	BLG-IV-198-AF	4	*Neuregulin*	27.7	19.8
107	WCB-I-124-CF1	20		3.9	6.9
108	WCB-I-124-CF1	20	*Neuregulin*	29.7	26.2
109	WCB-I-125-AF	20		4.8	4.1
110	WCB-I-125-AF	20	*Neuregulin*	29.2	34.1
111	BLG-IV-202-DF1	20		4.1	4.0
112	BLG-IV-202-DF1	20	*Neuregulin*	34.8	18.6
113	WCB-I-124-A2F1	20		15.4	6.0
114	WCB-I-124-A2F1	20	*Neuregulin*	26.5	21.9
115	BLG-IV-198-AF	20		4.1	4.0
116	BLG-IV-198-AF	20	*Neuregulin*	23.2	26.0

Structures of compounds screened against PC12 Cells Expressing Exogenous ErbB4

A live-cell high-content screening system (LC-HCS) was used; all experiments were run in duplicate:



Dose response curve for the compound with the highest inhibitory activity
*Pyridine **52** (manuscript); compound **BLG-IV-237F (S-18)** in supporting information:*



Additional References:

[3] (e) Tekavee, T. N.; Zuo, G.; Simon, K.; Louie, J. *J. Org. Chem.* **2006**, *71*, 5834. (f) Tenaka, K.; Suzuki, N.; Nishida, G. *Eur. J. Org. Chem.* **2006**, 3917. (g) McCornick, M. M.; Duong, H. A.; Zuo. G.; Louie, J. *J. Am. Chem. Soc.* **2005**, *127*, 5030. (h) Bonaga, L. V. R.; Zhang, H-C.; Moretto, A. F.; Ye, H.; Gauthier, J.; Li, J.; Leo, G. C.; Maryanoff, B. E. *J. Am. Chem. Soc.* **2005**, *127*, 3473-3485. (i) Petit, M.; Aubert, C.; Malacria, M. *Org. Lett.* **2004**, *6*, 3937-3940. (j) Hoshi, T.; Katano, M.; Nozawa, E.; Suzuki, T.; Hagiwara, H. *Tetrahedron Lett.* **2004**, *45*, 3489-3491. (k) Chouraqui, G.; Petit, M.; Aubert, C.; Malacria, M. *Org. Lett.* **2004**, *6*, 1519-1521.