Palladium-Catalyzed Phosphonylation: Synthesis of C3-, C4- and C5-Phosphonylated Pyrazoles

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1. General Experimental

All reactions were carried out under argon atmosphere unless otherwise specified. Flasks were oven-dried at 120 °C and cooled under argon prior to use. Dichloromethane was distilled over calcium hydride, THF and Et_2O were distilled over sodium/benzophenone, ethylene glycol was distilled under vacuum over $MgSO_4$, and toluene was dried over activated alumina. Triethylamine and diisopropylethylamine were distilled over calcium hydride and stored under argon. 1-SEM-1*H*-pyrazole,[1] 4-iodo-1-SEM-1*H*-pyrazole **4a**,[2] methyl(phenyl) phosphine oxide **2i**,[3] ethyl ethylphosphinate **2l**,[4] and cyclohexyl phenylphosphinate **2m**[5] were synthesized according to known literature procedures, and their spectra matched the ones previously reported. Cyclopropyl(phenyl) phosphine oxide **2j** is a *de novo* compound, synthesized according to a known literature procedure.[3] All other reagents were used as obtained from commercial sources (Sigma-Aldrich, Merck and others) without further purification unless otherwise specified.

Flash column chromatographies were carried out by using silica gel (pore size 60 Å, 230 mesh) or anionic resin (Dowex 50W8X, 200-400 mesh). TLC were performed on silica gel plate (Merck $60F_{254}$) and visualized either with a UV lamp (254 nm) or by treatment with an aqueous potassium permanganate solution ($KMnO_4/K_2CO_3$/AcOH) and subsequent heating.

^{1}H-NMR Spectra were recorded on a Bruker Avance 400 at 400 MHz. The chemical shifts δ are reported in ppm relative to tetramethylsilane. Residual $CHCl_3$ (δ_H=7.26 ppm) was used as internal reference. The multiplicity and shape of signals are designated by the following abbreviations: s singlet, d doublet, t triplet, q quartet, quin quintet, m multiplet, br broad, app apparent. Coupling constants *J* are reported in Hertz (Hz).

^{13}C-NMR Spectra were recorded on a Bruker Avance 400 at 100 MHz. The chemical shifts δ are reported in ppm relative to tetramethylsilane. $CDCl_3$ (δ_c = 77.16 ppm, triplet) was used as internal reference. The multiplicity and shape of signals are designated by the following abbreviations: d doublet, q quartet, br broad. Coupling constants *J* are reported in Hertz (Hz).

IR-Spectra were recorded on a Bruker TENSOR^{TM} 27 (IRTF). The samples were prepared as thin films or as fine powder. Only selected absorbances (ν_{max}) are reported, and wave numbers are reported in cm^{-1}.

High resolution mass spectra were performed by "Groupe de Spectrométrie de masse de l'Université Pierre et Marie Curie" (Paris).

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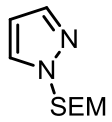
[1] Despotopoulou, C.; Klier, L.; Knochel, P. *Org. Lett.* **2009**, 11, 3326–3329.
[2] Malamas, M. S.; Erdei, J.; Gunawan, I.; Barnes, K.; Hui, Y.; Johnson, M.; Robichaud, A.; Zhou, P.; Yan, Y.; Solvibile, W.; Turner, J.; Fan, K. Y.; Chopra, R.; Bard, J.; Pangalos, M. N. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 5164–5170.
[3] Xu, Q.; Zhao, C.-Q.; Han, L.-B. *J. Am. Chem. Soc.* **2008**, *130*, 12648–12655.
[4] Pirat, J.-L.; Virieux, D.; Clarion, L.; Volle, J.-L.; Bakalara, N.; Mersel, M.; Montbrun, J.; Cristau, H.-J. Phosphorus containing heterocycles compounds, sugar analogs, and compositions having anti-cancer activity containing the same. US patent 0298272, Nov. 25, 2010.
[5] Berger, O.; Petit, C.; Deal, E.L.; Montchamp, J.-L. *Adv. Synth. Catal.* **2013**, *355*, 1361–1373.

2. Experimental Procedures and Spectroscopic Data

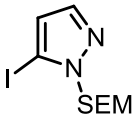
2.1. Starting materials 1a, 1b, 4a, 4c, 2i, 2j, 2l and 2m.

1-SEM-1*H*-pyrazole[1]



To a suspension of sodium hydride (2.64 g, 66 mmol, 1.5 equiv) in dry THF (30 mL) was added a solution of 1*H*-pyrazole (3 g, 44.1 mmol, 1.0 equiv) in dry THF (15 mL). The resulting orange suspension was stirred at rt for 2 h. A solution of SEM-Cl (8.07 g, 8.58 mL, 48.4 mmol, 1.1 equiv) in dry THF (15 mL) was then added dropwise at 0 °C. The solution was then allowed to warm up to rt and stirred for 2 h. Water (50 mL) was added, and the aqueous phase was extracted 4 times with EtOAc (4 x 70 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and concentrated in vacuo to give a pink oil. Distillation in vacuo using a Kugelrohr apparatus (65-70 °C, 0.02 mbar) led to 1-SEM-1*H*-pyrazole as a colorless oil (8.1 g, 40.84 mmol, 93% yield).

5-Iodo-1-SEM-1*H*-pyrazole (1a)



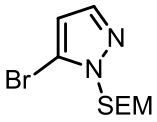
1a

To a solution of 1-SEM-1*H*-pyrazole (4 g, 20.2 mmol, 1.0 equiv) in THF (20 mL), at 0 °C, was added a 1M solution of TMP-MgCl.LiCl (22.4 mL, 22.4 mmol, 1.1 equiv) in THF/toluene dropwise. The resulting solution was allowed to slowly warm-up to rt and stirred for 3 h. A solution of iodine (5.08 g, 4.98 mL, 20 mmol, 1.0 equiv) in THF (20 mL) was then added dropwise at 0 °C. The resulting solution was stirred at this temperature for 2 h. Aqueous saturated $Na_2S_2O_3$ (50 mL) was then added, and the aqueous phase was extracted 4 times with EtOAc (4 x 70 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in vacuo to give a brown oil. Purification by flash column chromatography on silica gel (EtOAc/petroleum ether = 5:95) led to 5-iodo-1-SEM-1*H*-pyrazole **1a** as a colorless oil (5.54 g, 17.1 mmol, 85% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.53 (d, *J* = 1.8 Hz, 1H), 6.49 (d, *J* = 1.8 Hz, 1H), 5.50 (s, 2H), 3.62–3.53 (m, 2H), 0.94–0.85 (m, 2H), –0.04 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1 (CH), 116.8 (CH), 80.8 (C), 79.9 (CH_2), 66.7 (CH_2), 17.7 (CH_2), –1.4 (CH_3).
IR (neat film): υ_{max} 2952, 2895, 1488, 1449, 1366, 1287, 1247, 1101, 1075, 982, 832, 746.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_9H_{17}IN_2OSiNa$: *m/z* = 347.00470 (found: *m/z* = 347.00492).

[1] Despotopoulou, C.; Klier, L.; Knochel, P. *Org. Lett.* **2009**, 11, 3326–3329.

5-Bromo-1-SEM-1*H*-pyrazole (1b)

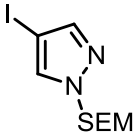


1b

To a solution of 1-SEM-1*H*-pyrazole (2 g, 10.1 mmol, 1.0 equiv) in THF (10 mL), at 0 °C, was added a 1 M solution of TMP-MgCl.LiCl (11.1 mL, 11.1 mmol, 1.1 equiv) in THF/Toluene dropwise. The resulting solution was slowly warm-up to rt and stirred for 3 h. A solution of 1,2-dibromotetrachloroethane (3.94 g, 12.1 mmol, 1.2 equiv) in THF (10 mL) was then added dropwise at 0 °C. The resulting solution was stirred at this temperature for 16 h. An aqueous saturated $NaHCO_3$ solution (30 mL) was then added, and the aqueous phase was extracted 4 times with EtOAc (4 x 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in vacuo to give a brown oil. Purification by flash column chromatography on silica gel (EtOAc/petroleum ether = 5:95) led to 5-bromo-1-SEM-1*H*-pyrazole **1b** as a colorless oil (2.24 g, 8.08 mmol, 80% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.51 (d, *J* = 1.9 Hz, 1H), 6.33 (d, *J* = 1.9 Hz, 1H), 5.47 (s, 2H), 3.67–3.50 (m, 2H), 0.93–0.86 (m, 2H), –0.04 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 141.0 (CH), 113.5 (C), 109.8 (CH), 78.3 (CH_2), 66.8 (CH_2), 17.8 (CH_2), –1.4 (CH_3).
IR (neat film): υ_{max} 2953, 2895, 1501, 1428, 1394, 1290, 1107, 1077, 988, 917, 833, 746.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_9H_{17}BrN_2OSiNa$: *m/z* = 299.01857 (found: *m/z* = 299.01907).

4-Iodo-1-SEM-1*H*-pyrazole (4a)[2]



4a

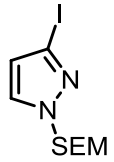
To a solution of 4-iodo-pyrazole (3 g, 15.5 mmol, 1.0 equiv) in dry THF (21mL), at 0 °C, was added sodium hydride (0.927 g, 23.2 mmol, 1.5 equiv) portionwise. The resulting white suspension was stirred at 0 °C for 2 h. SEM-Cl (3.09 g, 3.30 mL, 18.6 mmol, 1.2 equiv) was then added dropwise at 0 °C. The suspension was then allowed to warm up to rt and stirred for 2 h. The reaction was quenched with water (1 mL), and concentrated to ~5 mL. An aqueous saturated $NaHCO_3$ solution(20 mL) was then added, and the aqueous phase was extracted 4 times with EtOAc (4 x 30 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated in vacuo to give a yellow oil (7.1 g). Purification by

[2] Malamas, M. S.; Erdei, J.; Gunawan, I.; Barnes, K.; Hui, Y.; Johnson, M.; Robichaud, A.; Zhou, P.; Yan, Y.; Solvibile, W.; Turner, J.; Fan, K. Y.; Chopra, R.; Bard, J.; Pangalos, M. N. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 5164–5170.

flash column chromatography on silica gel (EtOAc/petroleum ether = 4:96) led to 4-iodo-1-SEM-1*H*-pyrazole **4a** as a pale yellow oil (4.9 g, 15.11 mmol, 98% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.62 (s, 1H), 7.54 (s, 1H), 5.40 (s, 2H), 3.64–3.47 (m, 2H), 0.92–0.87 (m, 2H), –0.04 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 145.0 (CH), 134.0 (CH), 80.5 (C), 67.1 (CH_2), 58.0 (CH_2), 17.9 (CH_2), –1.3 (CH_3).
IR (neat film): 3120, 2952, 2894, 1510, 1422, 1367, 1294, 1089, 940, 850, 747.
HRMS (ESI+): $[M+H]^+$ calcd for $C_9H_{18}IN_2OSi$: *m/z* = 325.02276 (found: *m/z* = 325.02310).

3-Iodo-1-SEM-1*H*-pyrazole (4c)

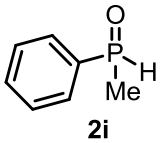


4c

The reaction was performed in an oven-dried vial. To a solution of 5-iodo-1-SEM-1*H*-pyrazole **1a** (300 mg, 0.925 mmol, 1.0 equiv) in anhydrous MeCN (0.2 mL) was added SEM-Cl (14.1 mg, 0.015 mL, 0.085 mmol, 0.1 eq). The vial was sealed with a teflon-lined cap and stirred at 95 °C for 26 h. The reaction mixture was evaporated to give a yellow oil (303 mg). Purification by flash column chromatography on silica gel (EtOAc/petroleum ether = 5:95) led to 3-iodo-1-SEM-1*H*-pyrazole **4c** as a pale yellow oil (225 mg, 0.694 mmol, 75% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.40 (d, *J* = 2.4 Hz, 1H), 6.49 (d, *J* = 2.4 Hz, 1H), 5.41 (s, 2H), 3.64–3.48 (m, 2H), 0.95–0.82 (m, 2H), –0.02 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 131.6 (CH), 116.1 (CH), 95.5 (C), 80.4 (CH_2), 67.2 (CH_2), 17.9 (CH_2), –1.3 (CH_3).
IR (neat film): 3112, 2952, 2895, 1493, 1351, 1289, 1248, 1094, 940, 832, 744.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_9H_{17}IN_2OSiNa$: *m/z* = 347.00470 (found: *m/z*=347.00480).

Methyl(phenyl) phosphine oxide (2i)[3]



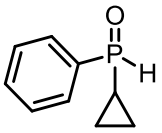
2i

To a 1.6 M of MeLi (1.6 M, 15.5 mL, 24.8 mmol, 2.1 equiv) in Et_2O, at –78 °C, was added a solution of ethyl phenylphosphinate (2 g, 11.8 mmol, 1.0 equiv) in dry THF (12 mL) dropwise. The resulting yellow solution was stirred at –78 °C for 40 min. An aqueous saturated NH_4Cl solution (6 mL) was then added, and the resulting slurry was allowed to warm up to rt. Water was then added (100 mL), the aqueous phase was washed 2 times with

[3] Xu, Q.; Zhao, C.-Q.; Han, L.-B. *J. Am. Chem. Soc.* **2008**, *130*, 12648–12655.

petroleum ether (2 x 60 mL), and then extracted 3 times with $CHCl_3$ (3 x 100 mL). The combined halogenated phases were dried over anhydrous Na_2SO_4, and concentrated in vacuo to give a colorless oil (1.2 g). Purification by column chromatography on silica gel (EtOH/$CHCl_3$ = 2.5:97.5) led to methyl(phenyl) phosphine oxide **2i** as a colorless oil (1.1 g, 7.85 mmol, 67% yield).

Cyclopropyl(phenyl) phosphine oxide (2j)

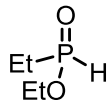


2j

To a 1.0 M solution of cyclopropylmagnesium bromide (12.5 mL, 12.5 mmol, 2.12 equiv) in 2-methyl-tetrahydrofuran, at –78 °C, was added a solution of ethyl phenylphosphinate (1 g, 5.88 mmol, 1.0 equiv) in THF (6 mL) dropwise. The resulting yellow solution was stirred at –78 °C for 40 min. An aqueous saturated NH_4Cl solution (6 mL) was then added, and the resulting slurry was allowed to warm up to rt. Water was then added (50 mL), the aqueous phase was washed 2 times with petroleum ether (2 x 30 mL), and then extracted 3 times with $CHCl_3$ (3 x 50 mL). The combined halogenated phases were dried over anhydrous Na_2SO_4, and concentrated in vacuo to give a colorless oil. Distillation in vacuo using a Kugelrohr apparatus (90 °C, 0.5 mbar) led to cyclopropyl(phenyl) phosphine oxide **2j** as a colorless oil (590 mg, 3.55 mmol, 60% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.72 (ddd, *J* = 13.2, 8.1, 1.3 Hz, 2H), 7.58–7.43 (m, 3H), 7.31 (dd, *J* = 480.0, 2.2 Hz, 1H), 1.11–0.87 (m, 5H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 132.5 (CH, d, *J* = 3 Hz), 131.7 (C, d, *J* = 101 Hz), 130.1 (CH, d, *J* = 11 Hz), 128.9 (CH, d, *J* = 13 Hz), 7.5 (CH, d, *J* = 100 Hz), 2.9 (CH_2, d, *J* = 4 Hz), 2.5 (CH_2, d, *J* = 5 Hz).
IR (neat film): 3433, 3055, 3007, 2323, 1647, 1485, 1438, 1307, 1170, 1116, 658, 893, 747, 694.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_9H_{11}OPNa$: *m/z* = 189.04397 (found: *m/z* = 189.04398).

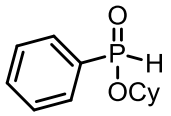
Ethyl ethylphosphinate (2l)[4]



2l

A 3 M solution of EtMgBr (9.7 mL, 29.1 mmol, 1.0 equiv) in Et_2O, at rt, was added dropwise to a solution of triethyl phosphite (4825 mg, 5 mL, 29 mmol, 1.0 equiv) in THF (20 mL). The resulting solution was then refluxed at 55 °C for 3 h, then cooled down to rt. A 6 N aqueous solution of HCl was then added until pH = 2. The medium was then evaporated in vacuo, the oily residue was diluted with CH_2Cl_2 (50 mL), and washed with water (2 x 30 mL). The organic phase was dried over anhydrous $MgSO_4$, then concentrated in vacuo to give a pale yellow oil. Distillation in vacuo using a fractional distillation apparatus (~9 mbar, Teb~54-56 °C, uncorrected) led to ethyl ethylphosphinate **2l** as a clear, colorless oil (580 mg, 4.75 mmol, 16% yield).

Cyclohexyl phenylphosphinate (2m)[5]



2m

In a flask equipped with a Dean-Stark trap was introduced phenylphosphinic acid (5.68 g, 40 mmol, 1.0 equiv), cyclohexanol (8.01 g, 8.35 mL, 80 mmol, 2 equiv) and toluene (80 mL). The resulting solution was refluxed under argon for 12 h. The reaction mixture was concentrated in vacuo, and the resulting colorless oil was dissolved in EtOAc (100 mL), and washed with an aqueous saturated $NaHCO_3$ solution (50 mL), then with brine (50 mL). The organic phase was dried over anhydrous MgSO4 and then concentrated in vacuo to give a colorless oil (8.0 g). Purification by flash chromatography (EtOAc/petroleum ether = 40:60) led to cyclohexyl phenylphosphinate **2m** as a colorless oil (7.55 g, 33.67 mmol, 84% yield).

[4] Pirat, J.-L.; Virieux, D.; Clarion, L.; Volle, J.-L.; Bakalara, N.; Mersel, M.; Montbrun, J.; Cristau, H.-J. Phosphorus containing heterocycles compounds, sugar analogs, and compositions having anti-cancer activity containing the same. US patent 0298272, Nov. 25, 2010.

[5] Berger, O.; Petit, C.; Deal, E.L.; Montchamp, J.-L. *Adv. Synth. Catal.* **2013**, *355*, 1361–1373.

2.2. Procedures for the cross-coupling

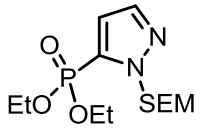
General Conditions A

$Pd(OAc)_2$ (2.5 mol %), XantPhos (5 mol %), and KOAc (10 mol %) were weighted in a microwave vial, which was then sealed and flushed with argon. THF (c = 0.25 M) and Et_3N (1.8 equiv) were then added through the septum and the resulting suspension was stirred for 20 min at 70 °C. The halo-pyrazole (1.5 equiv) and the phosphonylidene (1.0 equiv) were then added through the septum in a minimum amount of THF, and the reaction mixture was stirred at 70 °C until completion of the reaction, as determined by TLC. The reaction mixture was then diluted with EtOAc, an aqueous saturated $NaHCO_3$ solution was added, the layers were separated, and the aqueous phase was extracted 3 more times with EtOAc. The combined organic phases were then dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification by flash chromatography on silica gel led to the desired cross-coupled products.

General Conditions B

$Pd(OAc)_2$ (10 mol %), XantPhos (20 mol %), and KOAc (10 mol %) were weighted in a microwave vial, which was then sealed and flushed with argon. THF (c = 0.06 M) and Et_3N (1.8 equiv) were then added through the septum and the resulting suspension was stirred for 20 min at 70°C. The halo-pyrazole (1.5 equiv) and the phosphonylidene (1.0 equiv) were then added through the septum in a minimum amount of THF, and the reaction mixture was stirred at 70 °C until completion of the reaction, as determined by TLC. The reaction mixture was then diluted with EtOAc, an aqueous saturated $NaHCO_3$ solution was added, the layers were separated, and the aqueous phase was extracted 3 more times with EtOAc. The combined organic phases were then dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification by flash chromatography on silica gel led to the desired cross-coupled products.

Diethyl (1-SEM-1*H*-pyrazol-5-yl)phosphonate (3a)



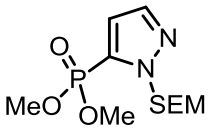
3a

According to general conditions **A**, pyrazole **1a** (565 mg, 1.74 mmol, 1.5 equiv) and diethyl phosphite **2a** (162 mg, 1.17 mmol, 1.0 equiv) were reacted together in THF (5mL). After 16 h, TLC showed total consumption of **2a**. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 30:70) led to the desired product **3a** as a pale yellow oil (315 mg, 0.942 mmol, 80% yield).

According to general conditions **B**, pyrazole **1b** (100 mg, 0.361 mmol, 1.5 equiv) and diethyl phosphite **2a** (33.5 mg, 0.242 mmol, 1.0 equiv) were reacted together in THF (4 mL). After 16 h, TLC showed total consumption of **2a**. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 30:70) led to the desired product **3a** as a pale yellow oil (60 mg, 0.181 mmol, 75% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.59 (t_{app}, *J* = 1.7 Hz, 1H), 6.81 (dd, *J* = 2.5, 1.9 Hz, 1H), 5.70 (s, 2H), 4.29–4.03 (m, 4H), 3.68–3.56 (m, 2H), 1.35 (td, *J* = 7.1, 0.6 Hz, 6H), 0.94–0.87 (m, 2H), –0.02 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 139.2 (CH, d, *J* = 17 Hz), 131.5 (C, d, *J* = 214 Hz), 116.4 (CH, d, *J* = 19 Hz), 79.5 (CH_2), 66.9 (CH_2), 63.1 (CH_2, d, *J* = 5 Hz), 17.9 (CH_2), 16.3 (CH_3, d, *J* = 7 Hz), –1.4 (CH_3).
IR (neat film): 2981, 2953, 2901, 1445, 1391, 1250, 1180, 1017, 971, 834, 747.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_{13}H_{27}N_2O_4PSiNa$: *m/z* = 357.13699 (found: *m/z* = 357.13693).

Dimethyl (1-SEM-1*H*-pyrazol-5-yl)phosphonate (3b)



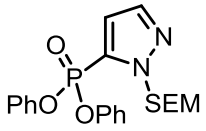
3b

<u>According to general conditions **A**</u> (*i*PrNEt$_2$ was used instead of Et$_3$N), pyrazole **1a** (243 mg, 0.75 mmol, 1.5 equiv) and dimethyl phosphite **2b** (55 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (2 mL). After 16 h, TLC showed total consumption of **2b**. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 35:65) led to the desired product **3b** as a pale yellow oil (14 mg, 0.046 mmol, 9% yield).

<u>According to general conditions **B**</u> (*i*PrNEt$_2$ was used instead of Et$_3$N), pyrazole **1b** (208 mg, 0.75 mmol, 1.5 equiv) and dimethyl phosphite **2b** (55 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (8 mL). After 6 h, TLC showed total consumption of **2b**. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 35:65) led to the desired product **3b** as a colorless oil (72 mg, 0.235 mmol, 47% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.60 (t_{app}, *J* = 1.7 Hz, 1H), 6.82 (dd, *J* = 2.5, 1.9 Hz, 1H), 5.69 (s, 2H), 3.80 (d, *J* = 11.5 Hz, 6H), 3.63–3.57 (m, 2H), 0.93–0.86 (m, 2H), –0.03 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 139.3 (CH, d, *J* = 17 Hz), 130.1 (C, d, *J* = 216 Hz), 116.8 (CH, d, *J* = 19 Hz), 79.7 (CH_2), 67.0 (CH_2), 53.4 (CH_3, d, *J* = 5 Hz), 18.0 (CH_2), –1.4 (CH_3).
IR (neat film): 2955, 2899, 2856, 160, 1381, 1251, 1185, 1087, 1025, 929, 834, 749.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_{11}H_{23}N_2O_4PSiNa$: *m/z* = 329.10569 (found: *m/z* = 329.10536).

Diphenyl (1-SEM-1*H*-pyrazol-5-yl)phosphonate (3c)



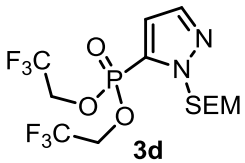
3c

According to general conditions **A**, pyrazole **1a** (243 mg, 0.75 mmol, 1.5 equiv) and diphenyl phosphite **2c** (125 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (2 mL). After 22 h, TLC showed that **2c** was not totally consumed, so the temperature was increased to 100 °C, and the reaction mixture was stirred at this temperature for 22 h. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 15:85) led to the desired product **3c** as a pale yellow oil (43 mg, 0.10 mmol, 20% yield).

According to general conditions **B**, pyrazole **1b** (208 mg, 0.75 mmol, 1.5 equiv) and diphenyl phosphite **2c** (125 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (8 mL). After 2 h, TLC did not show the presence of product **3c**, so the temperature was increased to 100 °C, and the reaction mixture was stirred at this temperature for 46 h. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 15:85) led to the desired product **3c** as a colorless oil (99 mg, 0.23 mmol, 46% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.63 (t_{app}, *J* = 1.7 Hz, 1H), 7.36–7.27 (m, 4H), 7.25–7.11 (m, 6H), 6.96 (t_{app}, *J* = 2.2 Hz, 1H), 5.80 (s, 2H), 3.66–3.50 (m, 2H), 0.88-0.84 (m, 2H), –0.06 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 150.1 (C, d, *J* = 8 Hz), 139.4 (CH, d, *J* = 18 Hz), 130.0 (C, d, *J* = 224 Hz), 130.0 (CH), 125.7 (CH), 120.7 (CH, d, *J* = 5 Hz), 117.6 (CH, d, *J* = 20 Hz), 80.0 (CH_2), 67.0 (CH_2), 17.8 (CH_2), –1.4 (CH_3).
IR (neat film): 3069, 2952, 2896, 1591, 1488, 1275, 1182, 1087, 932, 834, 754, 688.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_{21}H_{27}N_2O_4PSiNa$: *m/z* = 453,13699 (found: *m/z* = 453,13724).

Bis(2,2,2-trifluoroethyl) (1-SEM-1H-pyrazol-5-yl)phosphonate (3d)



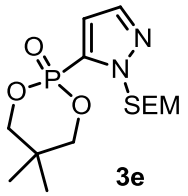
3d

According to general conditions **A**, pyrazole **1a** (243 mg, 0.75 mmol, 1.5 equiv) and bis(2,2,2-trifluoroethyl) phosphonate **2d** (technical grade, 90% purity, 137 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (2 mL). After 4 h, TLC did not show the presence of product **3d**, so the temperature was increased to 100 °C, and the reaction mixture was stirred at this temperature for 46 h. Purification by flash chromatography on silica gel (0:100 to 2:98 EtOAc/CH_2Cl_2 = 0:100 to 2:98) led to the desired product **3d** as a pale yellow oil (78 mg, 0.176 mmol, 35% yield).

According to general conditions **B**, pyrazole **1b** (208 mg, 0.75 mmol, 1.5 equiv) and bis(2,2,2-trifluoroethyl) phosphonate **2d** (technical grade, 90% purity, 137 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (8 mL). After 23 h, TLC showed that **2d** was not totally consumed, so the temperature was increased to 100 °C, and the reaction mixture was stirred at this temperature for 22 h. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 20:80) led to the desired product **3d** as a colorless oil (91 mg, 0.206 mmol, 40% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.62 (t_{app}, *J* = 1.9 Hz, 1H), 6.92 (dd, *J* = 2.6, 1.9 Hz, 1H), 5.70 (s, 2H), 4.63–4.35 (m, 4H), 3.61–3.48 (m, 2H), 0.97–0.82 (m, 2H), –0.02 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): 139.2 (CH, d, *J* = 19 Hz), 127.8 (C, d, *J* = 231 Hz), 122.5 (C, qd, *J* = 278, 9 Hz), 117.7 (CH, d, *J* = 20 Hz), 80.1 (CH_2), 67.2 (CH_2), 62.9 (CH_2, qd, *J* = 39 Hz), 17.8 (CH_2), –1.4 (CH_3).
IR (neat film): 2957, 2899, 1420, 1288, 1259, 1167, 1064, 962, 835, 751, 658.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_{13}H_{21}F_6N_2O_4PSiNa$: *m/z* = 465,08046 (found: *m/z* = 465,08042).

5,5-Dimethyl-2-(1-SEM-1H-pyrazol-5-yl)-1,3,2-dioxaphosphinane 2-oxide (3e)



3e

According to general conditions **A**, pyrazole **1a** (243 mg, 0.75 mmol, 1.5 equiv) 5,5-dimethyl-1,3,2-dioxaphosphiran-2-one **2e** (75 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (2 mL). After 8 h, TLC did not show the presence of product **3e**, so the temperature was increased to 100 °C, and the reaction mixture was stirred at this temperature for 24 h. Purification by flash chromatography on silica gel (EtOAc/toluene = 20:80) led to the desired product **3e** as a white amorphous solid (19 mg, 0.055 mmol, 11% yield).

According to general conditions **B**, pyrazole **1b** (208 mg, 0.75 mmol, 1.5 equiv) and 5,5-dimethyl-1,3,2-dioxaphosphiran-2-one **2e** (75 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (8 mL). After 23 h, TLC did not show the presence of product **3e**, so the temperature was increased to 100 °C, and the reaction mixture was stirred at this temperature for 22 h. Purification by flash chromatography on silica gel (EtOAc/toluene = 20:80) led to the desired product **3e** as a white amorphous solid (148 mg, 0.427 mmol, 86% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.63 (t_{app}, *J* = 1.8 Hz, 1H), 6.79 (dd, *J* = 2.5, 1.9 Hz, 1H), 5.68 (s, 2H), 4.13 (dd, *J* = 16.7, 11.2 Hz, 2H), 3.99 (dd, *J* = 11.2, 7.3 Hz, 2H), 3.69–3.58 (m, 2H), 1.27 (s, 3H), 0.98 (s, 3H), 0.96–0.88 (m, 2H), –0.02 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 139.6 (CH, d, *J* = 17 Hz), 130.0 (C, d, *J* = 211 Hz), 115.6 (CH, d, *J* = 19 Hz), 79.8 (CH_2), 77.4 (CH_2, d, *J* = 6 Hz), 67.1 (CH_2), 32.8 (C, d, *J* = 7 Hz), 21.9 (CH_3), 21.13 (CH_3), 18.0 (CH_2), –1.3 (CH_3).

IR (solid state): 3120, 2952, 2891, 2864, 1480, 1373, 1267, 1105, 1052, 1005, 916, 853, 787, 751, 694.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_{14}H_{27}N_2O_4PSiNa$: *m/z* = 369,13699 (found: *m/z* = 369,13697).

Diphenyl(1-SEM-1*H*-pyrazol-5-yl)phosphine oxide (3g)

3g

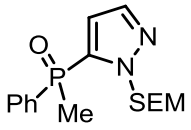
According to general conditions **A**, pyrazole **1a** (243 mg, 0.75 mmol, 1.5 equiv) and diphenylphoshine oxide **2g** (102 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (2 mL). After 22 h, TLC showed that **2g** was not totally consumed, so the temperature was increased to 100 °C, and the reaction mixture was stirred at this temperature for 5 h. Purification by flash chromatography on silica gel (EtOAc/toluene = 30:70) led to the desired product **3g** as a white amorphous solid (65 mg, 0.163 mmol, 32% yield).

According to general conditions **B**, pyrazole **1a** (100 mg, 0.308 mmol, 1.5 equiv) and diphenylphoshine oxide **2g** (47 mg, 0.208 mmol, 1.0 equiv) were reacted together in THF (3.5 mL). After 22 h, TLC showed total consumption of **2g**. Purification by flash chromatography on silica gel (EtOAc/toluene = 30:70) led to the desired product **3g** as a white amorphous solid (62 mg, 0.156 mmol, 75% yield).

According to general conditions **B**, pyrazole **1b** (209 mg, 0.75 mmol, 1.5 equiv) and diphenylphoshine oxide **2g** (102 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (8 mL). After 16 h, TLC showed total consumption of **2g**. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 20:80 to 30:70) led to the desired product **3g** as a white amorphous solid (132 mg, 0.331 mmol, 66% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.71–7.60 (m, 4H), 7.58–7.50 (m, 3H), 7.49–7.41 (m, 4H), 6.15 (t_{app}, *J* = 2.1 Hz, 1H), 5.74 (s, 2H), 3.29–3.19 (m, 2H), 0.51–0.41 (m, 2H), –0.15 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): 138.7 (CH, d, *J* = 13.8 Hz), 134.9 (C, d, *J* = 113 Hz), 132.4 (CH, d, *J* = 3 Hz), 131.9 (C, d, *J* = 111 Hz), 131.7 (CH, d, *J* = 10 Hz), 128.6 (CH, d, *J* = 13 Hz), 117.1 (CH, d, *J* = 17 Hz), 80.0 (CH_2), 66.3 (CH_2), 17.39 (CH_2), –1.5 (CH_3).
IR (solid state): 2950**,** 2928, 2869, 1439, 1368, 1289, 1250, 1199, 1121, 1090, 928, 834, 750, 694.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_{21}H_{27}N_2O_2PSiNa$: *m/z* = 421,14716 (found: *m/z* = 421,14656).

Methyl(phenyl)(1-SEM-1H-pyrazol-5-yl)phosphine oxide (3i)



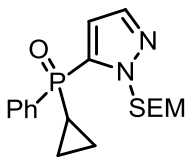
3i

<u>According to general conditions **B**,</u> pyrazole **1a** (243 mg, 0.75 mmol, 1.5 equiv) and methyl(phenyl)phosphine oxide **2i** (70 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (2 mL). After 4 h, TLC showed total consumption of **2i**. Purification by flash chromatography on silica gel ($EtOAc/CH_2Cl_2$ = 50:50) led to the desired product **3i** as an orange solid (250 mg, impure). Repurification by flash chromatography on silica gel (2.5:97.5 $EtOH/CH_2Cl_2$) led to the desired product **3i** as an amorphous, off white solid (155 mg, 0.461 mmol, 92% yield).

<u>According to general conditions **B**,</u> pyrazole **1b** (209 mg, 0.75 mmol, 1.5 equiv) and methyl(phenyl)phosphine oxide **2i** (70 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (2 mL). After 22 h, TLC showed total consumption of **2i**. Purification by flash chromatography on silica gel ($EtOAc/CH_2Cl_2$ = 50:50) led to the desired product **3i** as an orange solid (140 mg, impure). Repurified by flash chromatography on silica gel ($EtOH/CH_2Cl_2$ = 2.5:97.5) to give the desired product **3i** as an amorphous, white solid (81 mg, 0.241 mmol, 48% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.78–7.69 (m, 2H), 7.59–7.51 (m, 2H), 7.51–7.44 (m, 2H), 6.48 (t_{app}, *J* = 2.0 Hz, 1H), 5.72 (d, *J* = 10.5 Hz, 1H), 5.68 (d, *J* = 10.5 Hz, 1H), 3.39 (ddd, *J* = 11.2, 9.6, 5.8 Hz, 1H), 3.29 (ddd, *J* = 11.1, 9.6, 5.6 Hz, 1H), 2.06 (d, *J* = 14.0 Hz, 3H), 0.68 (ddd, *J* = 13.8, 11.2, 5.8 Hz, 1H), 0.56 (ddd, *J* = 13.8, 11.2, 5.6 Hz, 1H), –0.11 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 138.8 (CH, d, *J* = 13 Hz), 136.1 (C, d, *J* = 109 Hz), 133.0 (C, d, *J* = 108 Hz), 132.3 (CH, d, *J* = 2.9 Hz), 130.6 (CH, d, *J* = 10.4 Hz), 128.8 (CH, d, *J* = 13 Hz), 114.8 (CH, d, *J* = 16 Hz), 79.9 (CH_2), 66.5 (CH_2), 18.2 (CH_3, d, *J* = 78 Hz), 17.6 (CH_2), –1.4 (CH_3).
IR (solid state): 3058, 2951, 2928, 1437, 1364, 1304, 1429, 1174, 1086, 927, 861, 834, 737, 690.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_{16}H_{25}N_2O_2PSiNa$: *m/z* = 359.13151 (found: *m/z* = 359.13162).

Cyclopropyl(phenyl)(1-SEM-1H-pyrazol-5-yl)phosphine oxide (3j)



3j

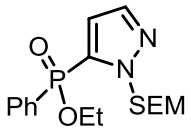
<u>According to general conditions **B**,</u> pyrazole **1a** (243 mg, 0.75 mmol, 1.5 equiv) and cyclopropyl(phenyl)phoshine oxide **2j** (83 mg, 0.5 mmol, 1.0 equiv) were reacted together in

THF (2 mL). After 4 h, TLC showed total consumption of **3j**. Purification by flash chromatography on silica gel (25:75 EtOAc/ CH_2Cl_2) led to the desired product **3j** as an orange oil (195 mg, impure). Repurification by flash chromatography on silica gel (EtOH/CH_2Cl_2 = 2.5:97.5) led to the desired product **3j** as a pale yellow oil (159 mg, 0.439 mmol, 88% yield).

According to general conditions **B**, pyrazole **1b** (209 mg, 0.75 mmol) and cyclopropyl(phenyl)phoshine oxide **2j** (83 mg, 0.5 mmol) were reacted together in 8 mL of THF. After 22 h, TLC showed that **2j** was not totally consumed, so the temperature was increased to 100 °C, and the reaction mixture was stirred at this temperature for 7 h. Purification by flash chromatography on silica gel (EtOAc/CH_2Cl_2 = 25:75) led to the desired product **3j** as an orange oil (95 mg, impure). Repurified by flash chromatography on silica gel (2.5:97.5 EtOH/CH_2Cl_2) to give the desired product **3j** as a pale yellow oil (48 mg, 0.132 mmol, 27% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.71 (dd, *J* = 11.7, 7.6 Hz, 2H), 7.61 (d, *J* = 1.2 Hz, 1H), 7.53 (m, 1H), 7.48-7.45 (m, 2H), 6.73 (s, 1H), 5.72 (d, *J* = 10.4 Hz, 1H), 5.55 (d, *J* = 10.4 Hz, 1H), 3.37 (ddd, *J* = 11.2, 9.5, 5.8 Hz, 1H), 3.27 (ddd, *J* = 11.2, 9.5, 5.6 Hz, 1H), 1.38 (br, m, 1H), 1.20–0.89 (m, 4H), 0.66 (ddd, *J* = 13.8, 11.2, 5.8 Hz, 1H), 0.52 (ddd, *J* = 13.8, 11.2, 5.6 Hz, 1H), –0.11 (s, 9H)**.**
^{13}C NMR (100 MHz, $CDCl_3$): δ 139.0 (CH, d, *J* = 12.6 Hz), 135.9 (C, d, *J* = 114 Hz), 132.3 (C, d, *J* = 183 Hz), 132.1 (CH), 130.9 (CH, d, *J* = 9.5 Hz), 128.6 (CH, d, *J* = 11.7 Hz), 115.2 (CH, d, *J* = 16 Hz), 79.7 (CH_2), 66.4 (CH_2), 17.6 (CH_2), 8.5 (CH, d, *J* = 113 Hz), 3.5 (CH_2), 3.2 (CH_2), –1.4 (CH_3).
IR (neat film): 3446, 3009, 2952, 2895, 1487, 1438, 1375, 1285, 1248, 1177, 1084, 896, 833, 750, 694.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_{18}H_{27}N_2O_2PSiNa$: *m/z* = 385.14716 (found: *m/z* = 385.14732).

Ethyl phenyl(1-SEM-1*H*-pyrazol-5-yl)phosphinate (3k)



3k

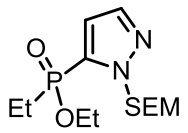
According to general conditions **A**, pyrazole **1a** (243 mg, 0.75 mmol, 1.5 equiv) and ethyl phenylphosphinate **2k** (94% pure, 91 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (2 mL). After 3 h, TLC showed total consumption of **2k**. Purification by flash chromatography on silica gel (EtOAc/CH_2Cl_2 = 10:90 to 15:85) led to the desired product **3k** as a colorless oil (160 mg, 0.437 mmol, 87% yield).

According to general conditions **B**, pyrazole **1b** (209 mg, 0.75 mmol, 1.5 equiv) and ethyl phenylphosphinate **2k** (94% pure, 91 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (8 mL). After 3 h, TLC showed total consumption of **2k**. Purification by flash

chromatography on silica gel (EtOAc/ petroleum ether = 40:60) led to the desired product **3k** as a yellow oil (170 mg, impure). Repurification by flash chromatography on silica gel (EtOAc/CH_2Cl_2 = 10:90) led to the desired product **3k** as a colorless oil (141 mg, 0.385 mmol, 77% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.89–7.77 (m, 2H), 7.59–7.49 (m, 2H), 7.50–7.40 (m, 2H), 6.73 (t_{app}, *J* = 2.0 Hz, 1H), 5.87 (d, *J* = 10.4 Hz, 1H), 5.60 (d, *J* = 10.4 Hz, 1H), 4.25–4.10 (m, 2H), 3.39 (ddd, *J* = 11.2, 9.5, 5.8 Hz, 1H), 3.28 (ddd, *J* = 11.3, 9.5, 5.5 Hz, 1H), 1.39 (t, *J* = 7.0 Hz, 3H), 0.69 (ddd, *J* = 13.8, 11.3, 5.8 Hz, 1H), 0.53 (ddd, *J* = 13.8, 11.2, 5.6 Hz, 1H), –0.11 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 139.0 (CH, d, *J* = 14 Hz), 134.2 (C, d, *J* = 153 Hz), 132.7 (CH, d, *J* = 3 Hz), 131.7 (CH, d, *J* = 11 Hz), 131.1 (C, d, *J* = 149 Hz), 128.6 (CH, d, *J* = 14 Hz), 116.0 (CH, d, *J* = 16 Hz) 79.8 (CH_2), 66.5 (CH_2), 62.0 (d, *J* = 6 Hz), 17.6 (CH_2), 16.6 (CH_3, d, *J* = 7 Hz), –1.4 (CH_3).
IR (neat film): 3058, 2952, 2898, 1489, 1438, 1389, 1234, 1189, 1086, 1025, 853, 84, 748, 693.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_{17}H_{27}N_2O_3PSiNa$: *m/z* = 389.14208 (found: *m/z* = 389.14234).

Ethyl ethyl(1-SEM-1*H*-pyrazol-5-yl)phosphinate (3l)



3l

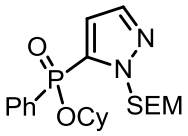
<u>According to general conditions **A**</u> (*i*PrNEt$_2$ was used instead of Et$_3$N), pyrazole **1a** (243 mg, 0.75 mmol, 1.5 equiv) and ethyl ethylphosphinate **2l** (61 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (2 mL). After 25 h, TLC showed total consumption of **2l**. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 40:60) led to the desired product **3l** as a pale yellow oil (30 mg, 0.094 mmol, 19% yield).

<u>According to general conditions **B**</u> (*i*PrNEt$_2$ was used instead of Et$_3$N), pyrazole **1b** (209 mg, 0.75 mmol, 1.5 equiv) and ethyl ethylphosphinate **2l** (61 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (8 mL). After 7 h, TLC showed total consumption of **2l**. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 40:60) led to the desired product **3l** as a pale yellow oil (92 mg, 0.289 mmol, 58% yield).

^{1}H-NMR (400MHz, $CDCl_3$): 7.58 (dd, *J* = 1.8, 1.2 Hz, 1H), 6.73 (t_{app}, *J* = 1.9 Hz, 1H), 5.88 (d, *J* = 10.5 Hz, 1H), 5.64 (d, *J* = 10.5 Hz, 1H), 4.19 (ddq, *J* = 14.2, 10.1, 7.1 Hz, 1H), 3.97 (ddq, *J* = 10.2, 8.0, 7.1 Hz, 1H), 3.66–3.49 (m, 2H), 2.05-1.95 (m, 2H), 1.13 (t, *J* = 7.1 Hz, 3H), 1.08 (t, *J* = 7.7 Hz, 3H), 0.91–0.84 (m, 2H), –0.03 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 139.0 (CH, d, *J* = 14 Hz), 133.4 (C, d, *J* = 134 Hz), 116.0 (CH, d, *J* = 15 Hz), 79.5 (CH_2), 66.8 (CH_2), 61.5 (CH_2, d, *J* = 7 Hz), 23.7 (CH_2, d, *J* = 109 Hz), 18.0 (CH_2), 16.5 (CH_3, d, *J* = 6 Hz), 5.7 (CH_3, d, *J* = 5 Hz), –1.4 (CH_3).

IR (neat film): 2954, 2900, 1460, 1381, 1287, 1246, 1219, 1083, 1029, 957, 836, 763.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_{13}H_{27}N_2O_3PSiNa$: *m/z* = 341.14208 (found: *m/z* = 341.14187).

Cyclohexyl phenyl(1-SEM-1*H*-pyrazol-5-yl)phosphinate (3m)



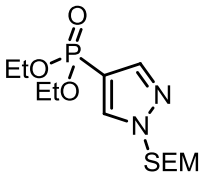
3m

According to general conditions **A**, pyrazole **1a** (243 mg, 0.75 mmol, 1.5 equiv) and cyclohexyl phenylphosphinate **2m** (112 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (2 mL). After 1.5 h, TLC showed total consumption of **2m**. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 20:80) led to the desired product **3m** as a pale yellow oil (290 mg, 0.452 mmol, 90% yield).

According to general conditions **B**, pyrazole **1b** (209 mg, 0.75 mmol, 1.5 equiv) and cyclohexyl phenylphosphinate **2m** (112 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (8 mL). After 1.5 h, TLC showed total consumption of **2m**. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 20:80) led to the desired product **3m** as a pale yellow oil (198 mg, 0.471 mmol, 94% yield).

^{1}H-NMR (400MHz, $CDCl_3$): 7.83 (ddd, *J* = 13.2, 8.2, 1.3 Hz, 2H), 7.61–7.49 (m, 2H), 7.48–7.42 (m, 2H), 6.70 (t_{app}, *J* = 1.9 Hz, 1H), 5.87 (d, *J* = 10.3 Hz, 1H), 5.63 (d, *J* = 10.3 Hz, 1H), 4.48 (m, 1H), 3.40 (ddd, *J* = 11.2, 9.6, 5.8 Hz, 1H), 3.30 (ddd, *J* = 11.2, 9.6, 5.6 Hz, 1H), 2.04–1.83 (m, 2H), 1.84–1.42 (m, 5H), 1.40–1.19 (m, 3H), 0.70 (ddd, *J* = 13.8, 11.2, 5.8 Hz, 1H), 0.57 (ddd, *J* = 13.8, 11.2, 5.6 Hz, 1H), –0.10 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 138.9 (CH, d, *J* = 14 Hz), 135.1 (C, d, *J* = 154 Hz), 132.5 (CH, d, *J* = 3 Hz), 131.9 (C, d, J = 147 Hz), 131.7 (CH, d, *J* = 11 Hz), 128.5 (CH, d, *J* = 14 Hz), 115.8 (CH, d, *J* = 16 Hz), 79.7 (CH_2), 76.1 (CH, d, *J* = 6 Hz), 66.4 (CH_2), 34.1 (CH_2, d, *J* = 4 Hz), 34.0 (CH_2, d, *J* = 4.0 Hz), 25.2 (CH_2), 23.7 (CH_2), 17.6 (CH_2), –1.4 (CH_3).
IR (neat film): 2936, 2859, 1490, 1438, 1373, 1234, 1118, 1086, 981, 833, 749, 693.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_{21}H_{33}N_2O_3PSiNa$: *m/z* = 443.18903 (found: *m/z* = 443.18953).

Diethyl (1-SEM-1*H*-pyrazol-4-yl)phosphonate (5)

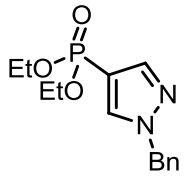


5

According to general conditions **A**, pyrazole **4a** (243 mg, 0.75 mmol, 1.5 equiv) and diethyl phosphite **2a** (69 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (2 mL). After 2.5 h, TLC showed total consumption of **2a**. Purification by flash chromatography on silica gel (EtOAc/CH_2Cl_2 = 50:50) led to the desired product **5** as a pale yellow oil (145 mg, 0.434 mmol, 87% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.93 (m, 1H), 7.75 (m, 1H), 5.44 (s, 2H), 4.19–4.00 (m, 4H), 3.62–3.51 (m, 2H), 1.31 (td, *J* = 7.1, 0.5 Hz, 6H), 0.94–0.85 (m, 2H), –0.04 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 142.6 (CH, d, *J* = 13 Hz), 135.2 (CH, d, *J* = 23 Hz), 109.3 (C, d, *J* = 220 Hz), 80.5 (CH_2), 67.4 (CH_2), 62.2 (CH_2, d, *J* = 5 Hz), 17.9 (CH_2), 16.4 (CH_3, d, *J* = 7 Hz), –1.4 (CH_3).
IR (neat film): 3106, 2981, 2953, 2900, 1531, 1376, 1246, 1095, 1022, 964, 835, 753.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_{13}H_{27}N_2O_4PSiNa$: *m/z* = 357.13699 (found: *m/z* = 357.13719).

Diethyl (1-benzyl-1H-pyrazol-4-yl)phosphonate (6)

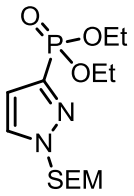


6

According to general conditions **A**, 1-benzyl-4-iodo-1H-pyrazole (213 mg, 0.75 mmol, 1.5 equiv) and diethyl phosphite **2a** (69 mg, 0.5 mmol, 1.0 equiv) were reacted together in THF (2 mL). After 2.5 h, TLC showed total consumption of **2a**. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 80:20) led to the desired product **6** as a pale yellow oil (123 mg, 0.418 mmol, 84% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.76 (dd, *J* = 1.1, 0.7 Hz, 1H), 7.74 (dd, *J* = 2.1, 0.7 Hz, 1H), 7.41–7.32 (m, 3H), 7.27–7.23 (m, 2H), 5.32 (s, 2H), 4.16-4.02 (m, 4H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 142.4 (CH, d, *J* = 13.1 Hz), 135.1 (C), 134.8 (CH, d, *J* = 24 Hz), 129.1 (CH), 128.6 (CH), 128.2 (CH), 108.1 (C, d, *J* = 221 Hz), 62.0 (CH_2, d, *J* = 5 Hz), 56.4 (CH_2), 16.3 (CH_3, d, *J* = 7 Hz).
IR (neat film): 3222, 3097, 1981, 2903, 1522 m), 1450, 1361, 1233, 1137, 1051, 1018, 951, 772, 730.
HRMS (ESI+): $[M+H]^+$ calcd for $C_{14}H_{20}N_2O_3PSi$: *m/z* = 295.12061 (found: *m/z* = 295.12055).

Diethyl (1-SEM-1*H*-pyrazol-3-yl)phosphonate (7)



7

According to general conditions **A**, 3-iodo-1-SEM-1*H*-pyrazole **4c** (280 mg, 0. 861 mmol, 1.5 equiv) and diethyl phosphite **2a** (80 mg, 0.579 mmol, 1.0 equiv) were reacted together in THF (2.5 mL). After 4 h, TLC showed total consumption of **2a**. Purification by flash chromatography on silica gel (EtOAc/ petroleum ether = 50:50) led to the desired product **7** as a pale yellow oil (161 mg, 0.481 mmol, 83% yield).

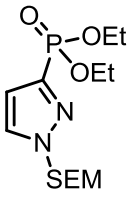
^{1}H-NMR (400MHz, $CDCl_3$): δ 7.66 (t_{app}, *J* = 2.3 Hz, 1H), 6.80 (dd, *J* = 2.4, 1.2 Hz, 1H), 5.51 (s, 2H), 4.28–4.08 (m, 4H), 3.62–3.50 (m, 2H), 1.34 (t, *J* = 7.1 Hz, 6H), 0.93–0.85 (m, 2H), –0.04 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 142.3 (C, d, *J* = 232 Hz), 130.3 (CH, d, *J* = 10 Hz), 113.0 (CH, d, *J* = 24 Hz), 80.9 (CH_2), 67.3 (CH_2), 62.7 (CH_2, d, *J* = 6 Hz), 17.9 (CH_2), 16.4 (CH_3, d, *J* = 7 Hz), –1.4 (CH_3).
IR (neat film): 3106, 2953, 2945, 1444, 1393, 1247, 1167, 1097, 1022, 967, 834, 750.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_{13}H_{27}N_2O_4PSiNa$: *m/z* = 357.13699 (found: *m/z* = 357.13715).

2.3. Procedures for the *N*-SEM group transposition

General Procedure

The reaction was performed in an oven-dried vial. Under argon, to a solution of pyrazole **3** (1.0 equiv) in anhydrous MeCN (*c* = 0.25 M) was added SEM-Cl (10 mol %). The vial was sealed with a teflon-lined cap and stirred at 95 °C for 24 h. The reaction mixture was then concentrated in vacuo, and the residue was purified by flash column chromatography on silica gel to give the desired 3-phosphonylated pyrazoles **7-10**.

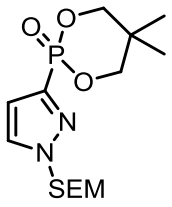
Diethyl (1-SEM-1*H*-pyrazol-3-yl)phosphonate (7) (cf. S19 for analysis)



7

Diethyl (1-SEM-1*H*-pyrazol-5-yl)phosphonate **3a** (350 mg, 1.05 mmol, 1.0 equiv) and SEM-Cl (19 μL, 0.106 mmol, 0.1 equiv) were reacted according to the general procedure. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 50:50 to 65:45) led to the desired product **7** as a colorless oil (302 mg, 0.903 mmol, 86% yield).

5,5-Dimethyl-2-(1-SEM-1*H*-pyrazol-3-yl)-1,3,2-dioxaphosphinane 2-oxide (8)

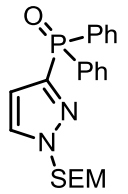


8

5,5-Dimethyl-2-(1-SEM-1*H*-pyrazol-5-yl)-1,3,2-dioxaphosphinane 2-oxide **3e** (134 mg, 0.387 mmol, 1.0 equiv) and SEM-Cl (7 μL, 0.039 mmol, 0.1 equiv) were reacted according to the general procedure. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 50:50) led to the desired product **8** as a pale yellow oil (110 mg, 0.317 mmol, 82%).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.66 (t_{app}, *J* = 2.3 Hz, 1H), 6.85 (dd, *J* = 2.4, 1.4 Hz, 1H), 5.50 (s, 2H), 4.32 (dd, *J* = 10.9, 5.3 Hz, 2H), 4.08-3.99 (m, 2H), 3.63–3.53 (m, 2H), 1.30 (s, 3H), 0.96 (s, 3H), 0.94–0.87 (m, 2H), –0.03 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 142.2 (C, d, *J* = 227 Hz), 130.4 (CH, d, *J* = 10 Hz), 112.8 (CH, d, *J* = 24 Hz), 80.8 (CH_2), 77.1 (CH_2, d, *J* = 6 Hz, cf. DEPT analysis), 67.4 (CH_2), 32.7 (C, d, *J* = 6 Hz), 22.2 (CH_3), 21.0 (CH_3), 17.9 (CH_2), –1.3 (CH_3).
IR (neat film): 3109, 2954, 2894, 1473, 1336, 1276, 1167, 1097, 1056, 1010, 916, 830, 784.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_{14}H_{27}N_2O_4PSiNa$: *m/z* = 369.13699 (found: *m/z* = 369.13691).

Diphenyl(1-SEM-1*H*-pyrazol-3-yl)phosphine oxide (9)

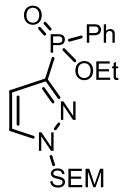


9

Diphenyl(1-SEM-1*H*-pyrazol-5-yl)phosphine oxide **3g** (67 mg, 0.168 mmol) and SEM-Cl (3 μL, 0.017 mmol) were reacted according to the general procedure. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 60:40) led to the desired product **9** as a colorless oil (55 mg, 0.138 mmol, 82% yield).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.83–7.78 (m, 4H), 7.71–7.64 (m, 1H), 7.56–7.47 (m, 2H), 7.47–7.39 (m, 4H), 6.87 (m, 1H), 5.50 (s, 2H), 3.58–3.48 (m, 2H), 0.91–0.84 (m, 2H), –0.06 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 146.4 (C, d, *J* = 135 Hz), 133.1 (C, d, *J* = 108 Hz), 131.9 (CH, d, *J* = 3 Hz), 131.8 (CH, d, *J* = 10 Hz), 130.5 (CH, d, *J* = 8 Hz), 128.5 (CH, d, *J* = 13 Hz), 113.6 (CH, d, *J* = 19 Hz), 80.8 (CH_2), 67.2 (CH_2), 17.9 (CH_2), –1.3 (CH_3).
IR (neat film): 3058, 2952, 2943, 1484, 1437, 1308, 1246, 1194, 1096, 915, 834.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_{21}H_{27}N_2O_2PSiNa$: *m/z* = 421.14716 (found: *m/z* = 421.14660).

Ethyl phenyl(1-SEM-1*H*-pyrazol-3-yl)phosphinate (10)



10

Ethyl phenyl(1-SEM-1*H*-pyrazol-5-yl)phosphinate **3k** (60 mg, 0.164 mmol, 1.0 equiv) and SEM-Cl (3 μL, 0.017 mmol, 0.1 equiv) were reacted according to the general procedure. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 65:35) led to the desired product **10** as a colorless oil (52 mg, 0.142 mmol, 87% yield).

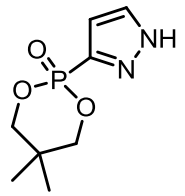
^{1}H-NMR (400MHz, $CDCl_3$): δ 7.98–7.85 (m, 2H), 7.64 (dd, *J* = 2.4, 1.7 Hz, 1H), 7.55–7.48 (m, 1H), 7.47-7.41 (m, 2H), 6.84 (dd, *J* = 2.4, 1.1 Hz, 1H), 5.49 (s, 2H), 4.21–4.09 (m, 2H), 3.58–3.42 (m, 2H), 1.37 (t, *J* = 7.1 Hz, 3H), 0.91–0.80 (m, 2H), –0.07 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 145.3 (C, d, *J* = 173 Hz), 132.3 (CH, d, *J* = 3 Hz), 131.8 (CH, d, *J* = 10 Hz), 131.5 (C, d, *J* = 145 Hz), 130.4 (CH, d, *J* = 8 Hz), 128.5 (CH, d, *J* = 14 Hz), 113.1 (CH, d, *J* = 21 Hz), 80.8 (CH_2), 67.2 (CH_2), 61.7 (CH_2, d, *J* = 6 Hz), 17.9 (CH_2), 16.7 (CH_3, d, *J* = 7 Hz), –1.4 (CH_3).

IR (neat film): 3100, 2952, 2898 w), 1493, 1439, 1333, 1225, 1163, 1030, 948, 834, 747, 694.

HRMS (ESI+): $[M+Na]^+$ calcd for $C_{17}H_{27}N_2O_3PSiNa$: *m/z* = 389.14208 (found: *m/z* = 389.14229).

2.4. Procedures for the *N*-SEM Group Cleavage.

5,5-dimethyl-2-(1H-pyrazol-3-yl)-1,3,2-dioxaphosphinane 2-oxide (11)

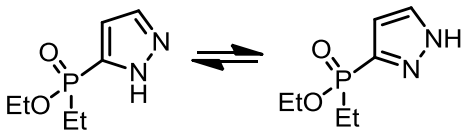


11

To a solution of 5,5-dimethyl-2-(1-SEM-1H-pyrazol-5-yl)-1,3,2-dioxaphosphinane 2-oxide **3e** (50 mg, 0.144 mmol, 1.0 equiv) in dry CH_2Cl_2 (0.5 mL) was added TFA (150 µL, 2.02 mmol, 14 equiv). The reaction mixture was stirred at rt for 4 h, then diluted in $CHCl_3$ and concentrated in vacuo to give a colorless oil, which was dissolved in EtOAc (10 mL). An aqueous saturated $NaHCO_3$ solution was added (2 mL), the layers were separated, and the aqueous phase was extracted 3 additional times with EtOAc (3 x 10 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated in vacuo to give a colorless oil. This oil was then dissolved in CH_2Cl_2 and purified by resin column chromatography on Dowex 50W8X-200-400 mesh (elution with pure CH_2Cl_2, then with pure MeOH). The desired fractions were combined and concentrated to give a white-brown solid (35 mg). The solid was then further purified by flash column chromatography on silica gel (MeOH/CH_2Cl_2 = 3:97) to give the desired product **11** as a white amorphous solid (22 mg, 0.102 mmol, 71% yield). The displacement of the aromatic carbon bearing the phosphonate moeity (δ = 140.7 ppm) suggests that, in DMSO-d_6, compound **11** exists under the C3-substituted form.

^{1}H-NMR (400MHz, DMSO-d_6): δ 13.71 (br, s, 1H), 7.98 (s, 1H), 6.70 (s, 1H), 4.20 (br, d, *J* = 8.9 Hz, 2H), 3.99 (dd, *J* = 19.9, 10.8 Hz, 2H), 1.22 (s, 3H), 0.84 (s, 3H).
^{13}C NMR (101 MHz, DMSO-d_6): δ 140.7 (C, d, *J* = 219 Hz), 129.7 (CH, br), 109.9 (CH, d, *J* = 27 Hz), 76.5 (CH_2, d, *J* = 6 Hz), 32.0 (C, d, *J* = 7 Hz), 21.3 (CH_3), 19.8 (CH_3).
IR (solid state): 3127, 3022, 2965, 2927, 1531, 1475, 1329, 1250, 1181, 1052, 1011, 972, 886, 835, 792.
HRMS (ESI+): $[M+H]^+$ calcd for $C_8H_{14}N_2O_3P$: *m/z* = 217.07366 (found: *m/z* = 217.07358).

Ethyl ethyl(1H-pyrazol-5(3)-yl)phosphinate (12)



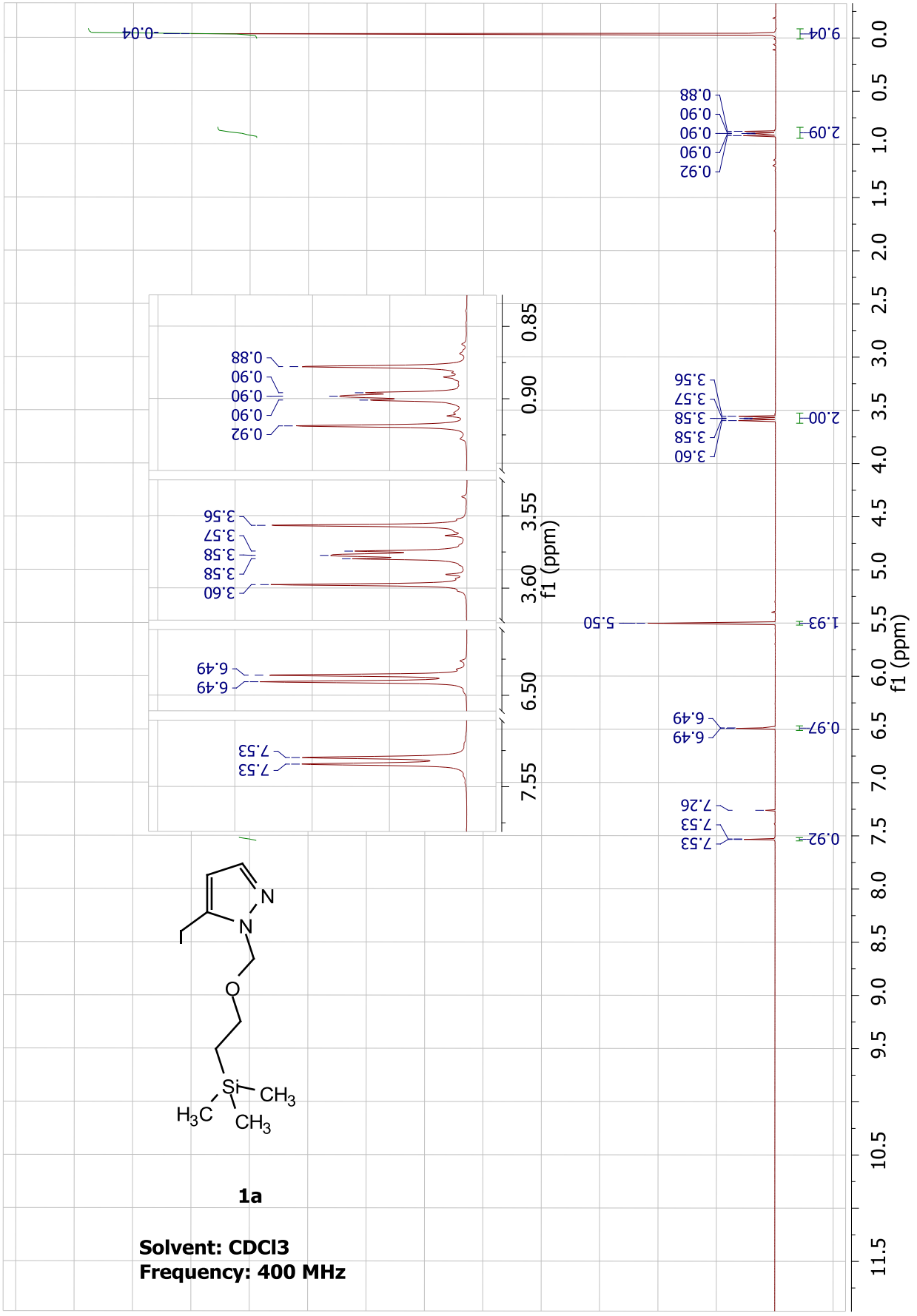
12a 25:75 **12b**

To a solution of ethyl ethyl(1-SEM-1*H*-pyrazol-5-yl)phosphinate **3l** (60 mg, 0.197 mmol, 1.0 equiv) in dry CH_2Cl_2 (0.5 mL) was added TFA (440 µL, 5.92 mmol, 30 equiv) and absolute

ethanol (23 μL, 0.394 mmol, 2.0 equiv). The reaction mixture was stirred at rt for 1 h, then diluted in $CHCl_3$ and concentrated in vacuo to give a colorless oil, to which was added Et_3N (3 mL). After concentration in vacuo to give a yellow oil, purification by flash column chromatography (4:96 MeOH/ CH_2Cl_2) led to the desired product **12** as a white amorphous solid (25 mg, 0.144 mmol, 73% yield). An equilibrium between the two tautomeric forms **12a** and **12b** was observed by ^{1}H NMR, in a ratio of 25:75. Only the major tautomer could be observed by ^{13}C NMR. The displacement of the aromatic carbon bearing the phosphinate moeity (δ = 143.6 ppm) suggests that, in DMSO-d_6, compound **12b** is the major tautomer.

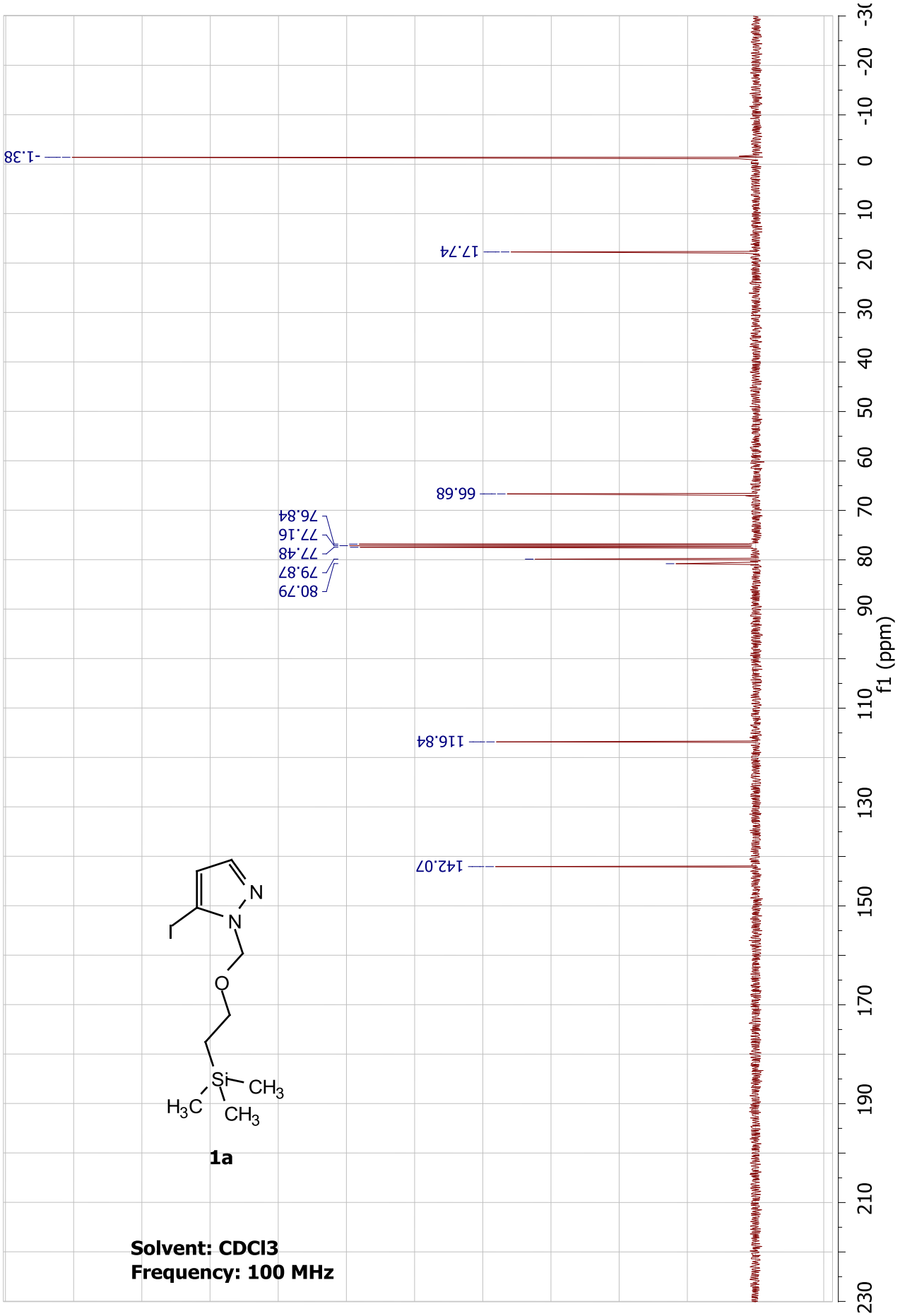
^{1}H-NMR (400MHz, DMSO-d_6): δ 13.70-13.45 (br, s, 1H (**12a**+**12b**)), 7.91 (s, 0.75H ($1H_{\mathbf{12b}}$)), 7.64 (s, 0.25H, ($1H_{\mathbf{12a}}$)), 6.75-6.62 (s, 1H, (**12a**+**12b**)), 4.02–3.89 (m, 1H, (**12a**+**12b**)), 4.08-3.98 (m, 1H, (**12a**+**12b**)), 1.88 (td, *J* = 15.0, 7.3 Hz, 2H, (**12a**+**12b**)), 1.18 (t, *J* = 7.0 Hz, 3H, (**12a**+**12b**)), 1.06–0.90 (m, 3H, (**12a**+**12b**)).
^{13}C NMR (101 MHz, DMSO-d_6): δ 143.6 (C, d, *J* = 158 Hz), 129.5 (CH), 110.0 (CH, d, *J* = 21 Hz), 60.0 (CH_2), 21.6 (CH_2, d, *J* = 104 Hz), 16.3 (CH_3, d, *J* = 6 Hz), 5.7 (CH_3).
IR (solid state): 3129 (br, m), 3100, 2983, 2907, 1501, 1444, 1395, 1329, 1244, 1189, 1023, 956, 825, 792, 742, 726.
HRMS (ESI+): $[M+Na]^+$ calcd for $C_7H_{13}N_2O_2PNa$: *m/z* = 211.06069 (found: *m/z* = 211.06086).

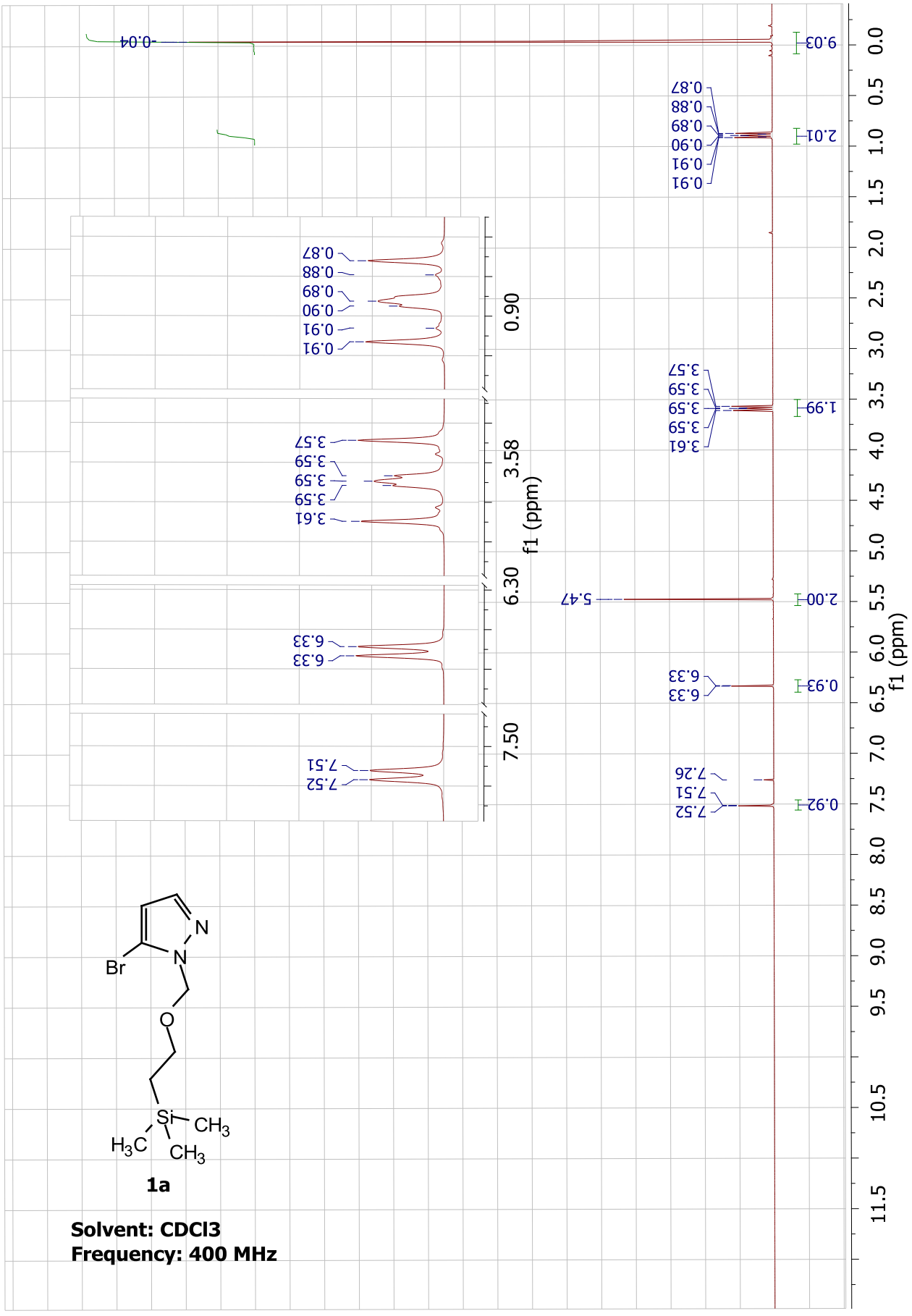
3. Experimental Spectra (^{1}H, ^{13}C)

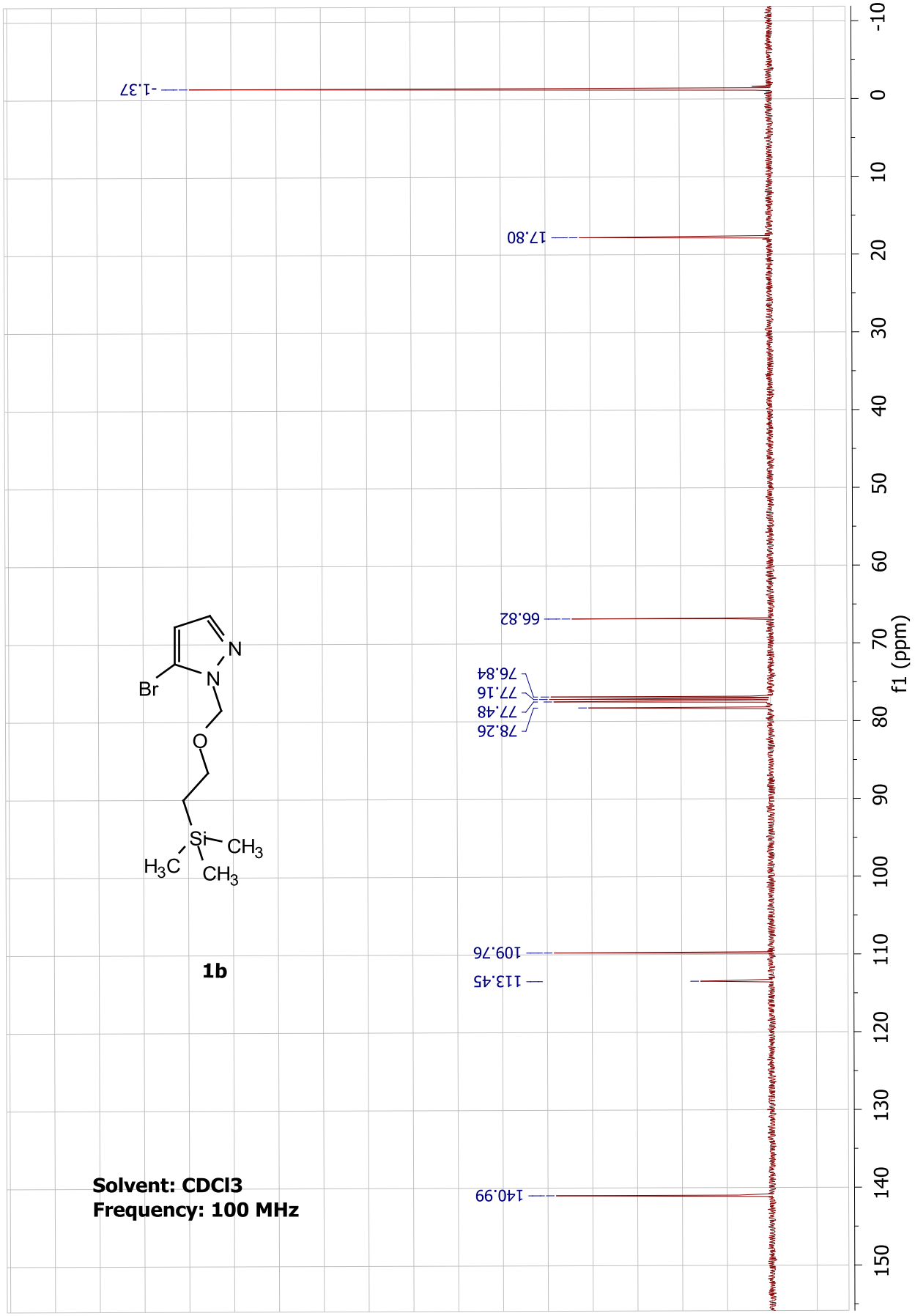


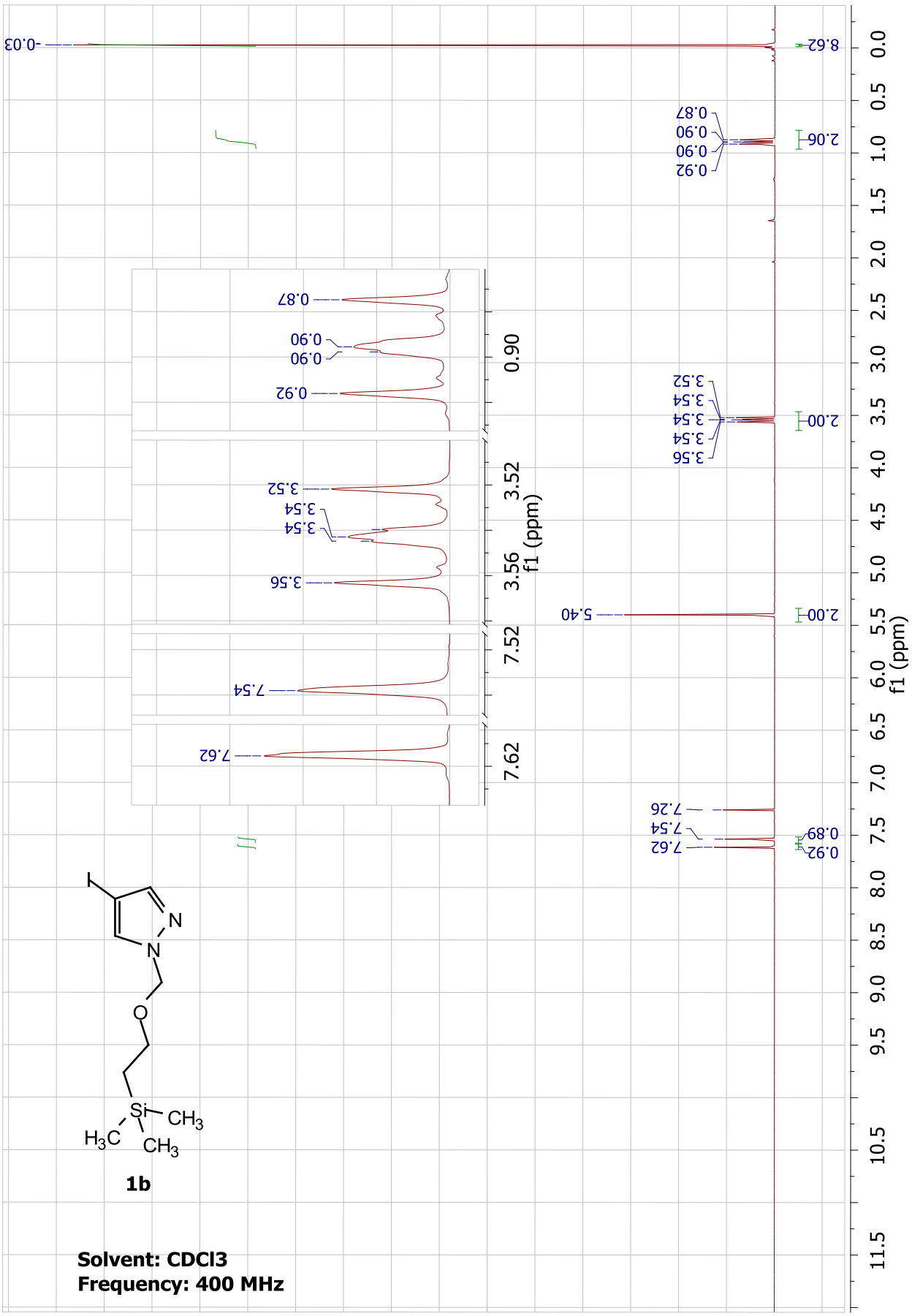
1a

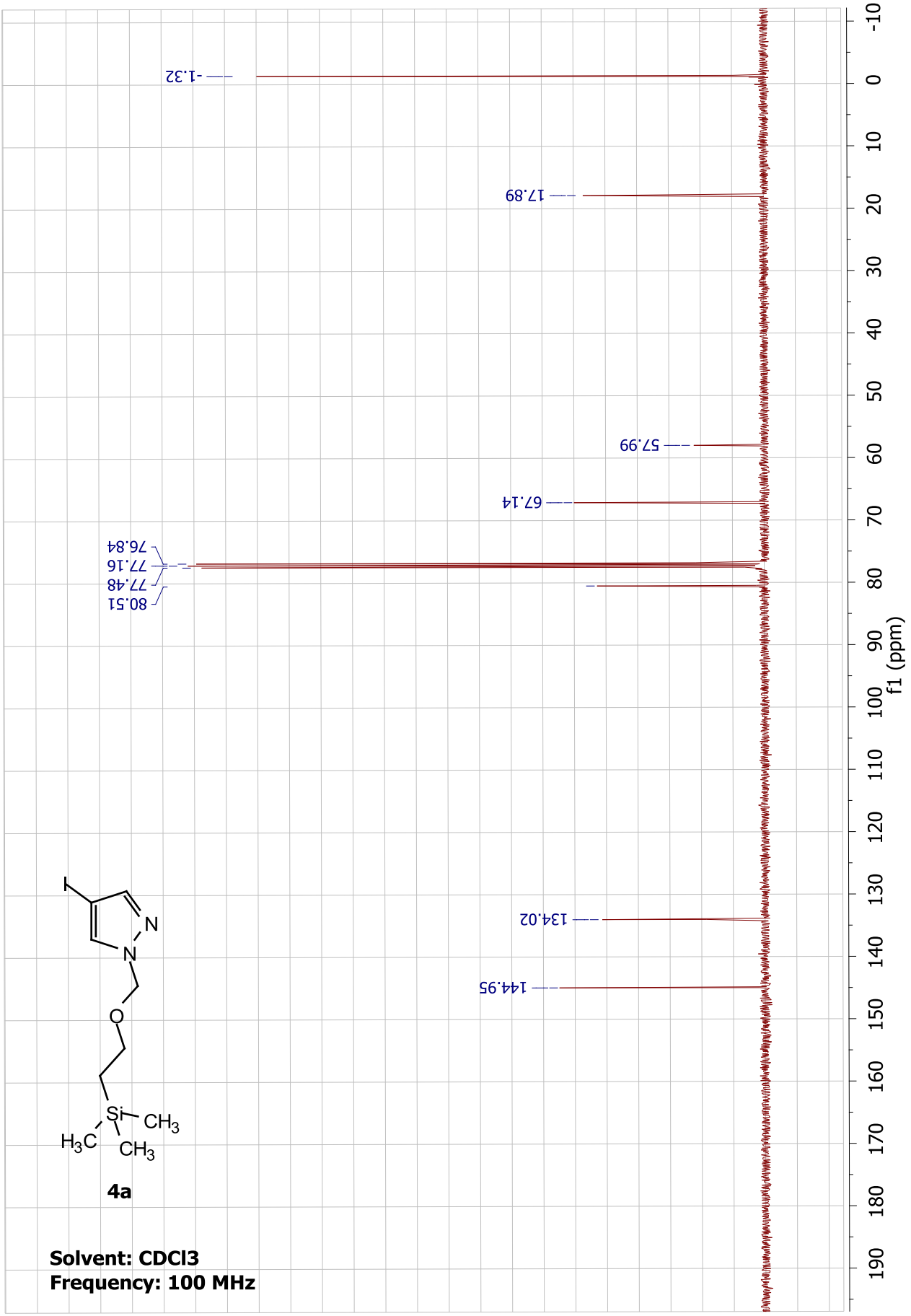
Solvent: CDCl3
Frequency: 400 MHz

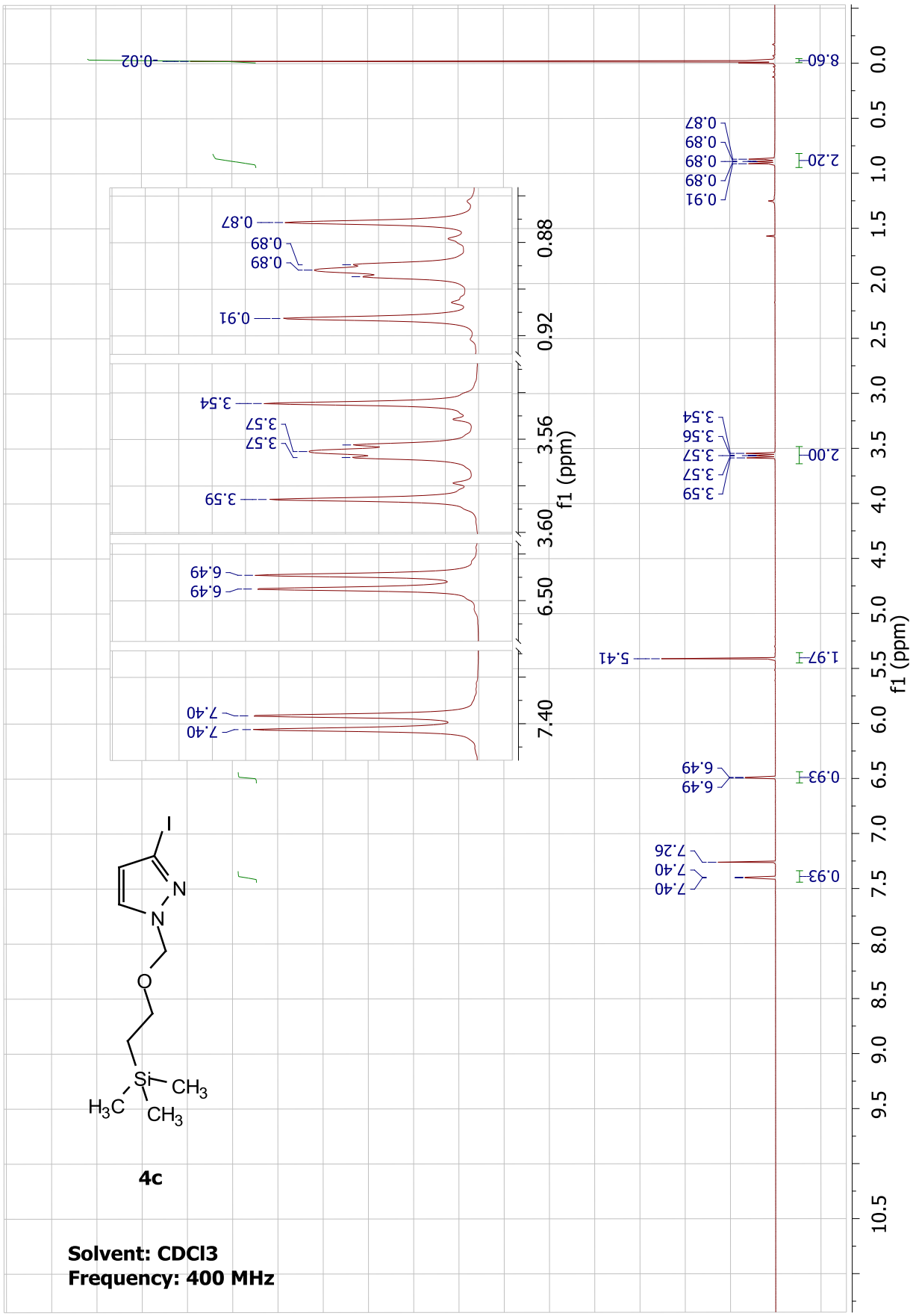

-1.38
17.74
66.68
76.84
77.16
77.48
79.87
80.79
116.84
142.07
f1 (ppm)
Solvent: CDCl3
Frequency: 100 MHz
1a


-0.04
0.87
0.88
0.89
0.90
0.91
0.91
3.57
3.59
3.59
3.59
3.61
5.47
6.33
6.33
7.26
7.51
7.52
9.03
2.01
1.99
2.00
0.93
0.92
0.90
3.58
6.30
7.50
f1 (ppm)
Br
N
N
O
Si
CH3
H3C
CH3
1a
Solvent: CDCl3
Frequency: 400 MHz

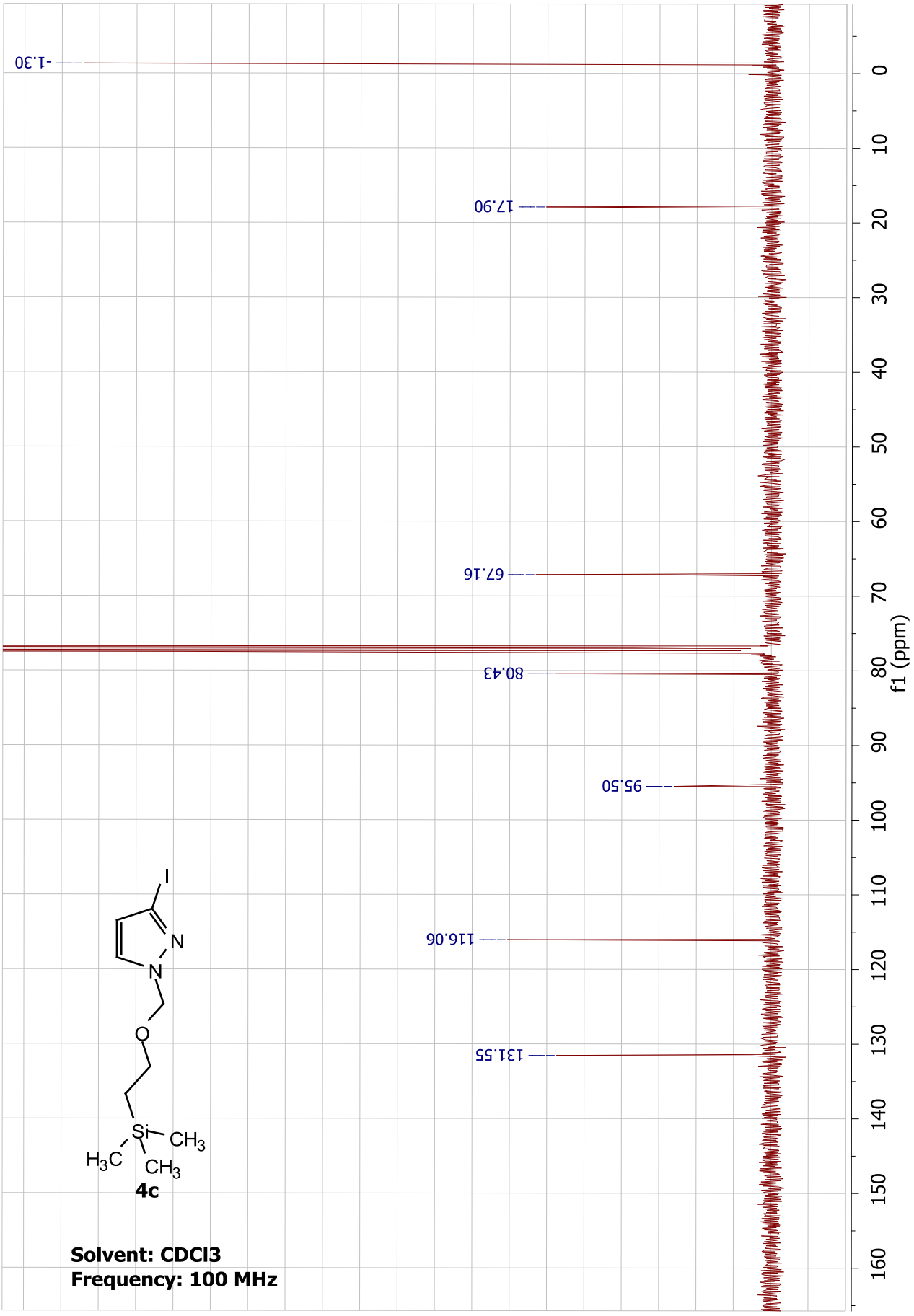

-1.37
17.80
66.82
76.84
77.16
77.48
78.26
109.76
113.45
140.99
Br
N
N
O
Si
CH3
H3C
CH3
1b
Solvent: CDCl3
Frequency: 100 MHz
f1 (ppm)

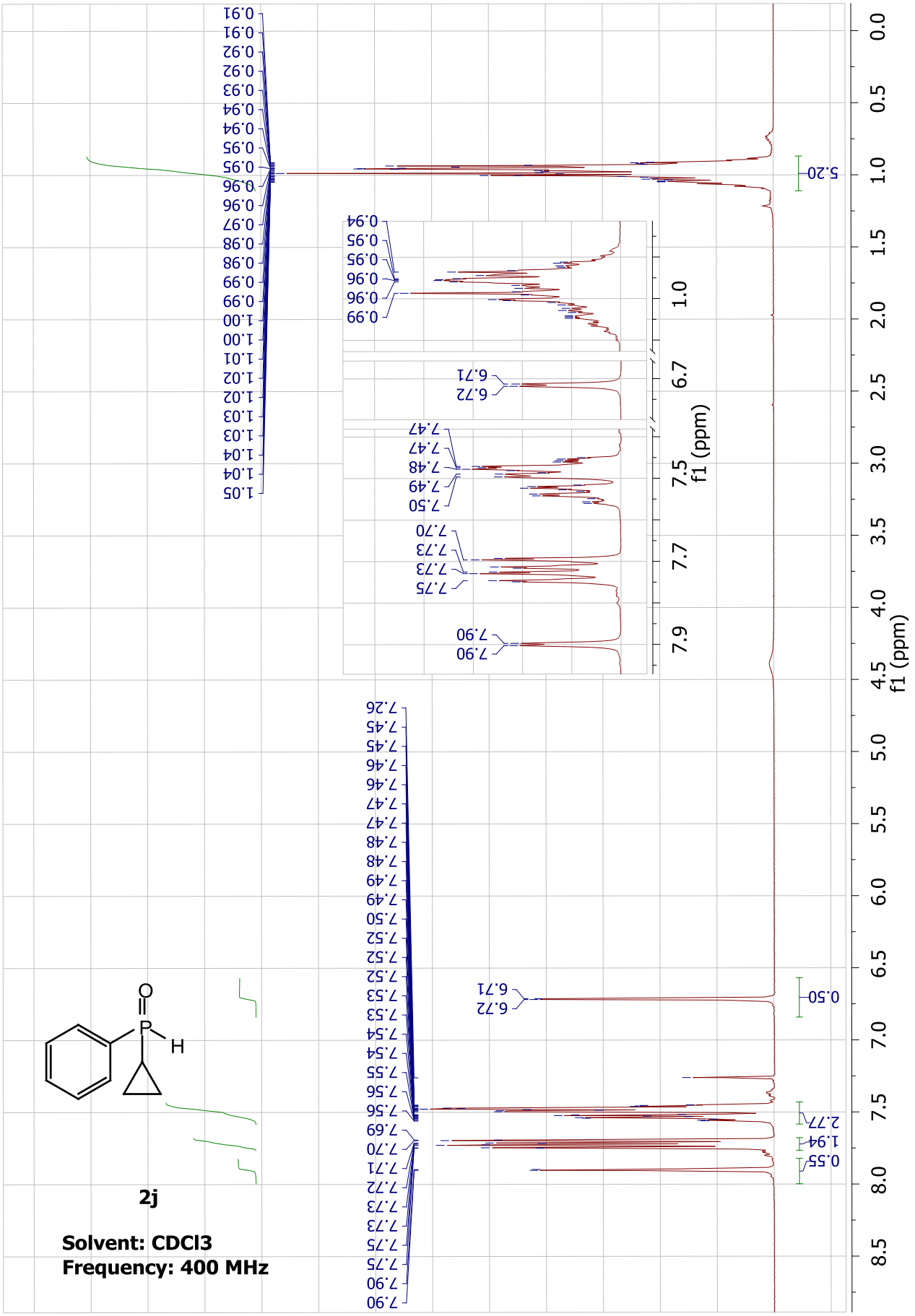

-0.03
8.62
2.06
0.92
0.90
0.90
0.87
2.00
3.56
3.54
3.54
3.54
3.52
2.00
5.40
7.62
7.54
7.26
0.89
0.92
0.87
0.90
0.90
0.92
3.52
3.54
3.54
3.56
7.54
7.62
0.90
3.52
3.56
7.52
7.62
f1 (ppm)
f1 (ppm)
N
N
O
Si
CH3
H3C
CH3
1b
Solvent: CDCl3
Frequency: 400 MHz

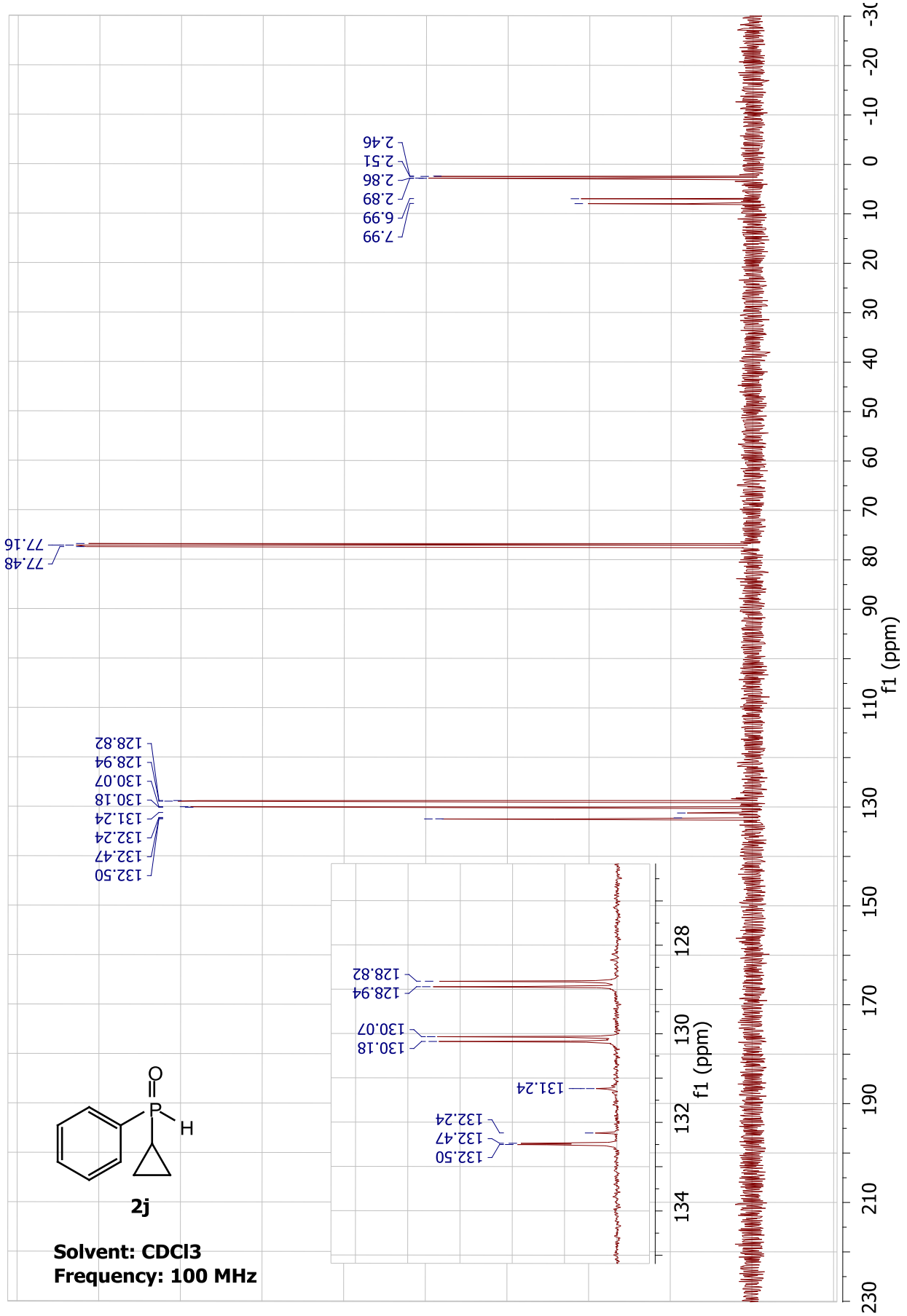

-1.32
17.89
57.99
67.14
76.84
77.16
77.48
80.51
134.02
144.95
f1 (ppm)
Solvent: CDCl3
Frequency: 100 MHz
4a

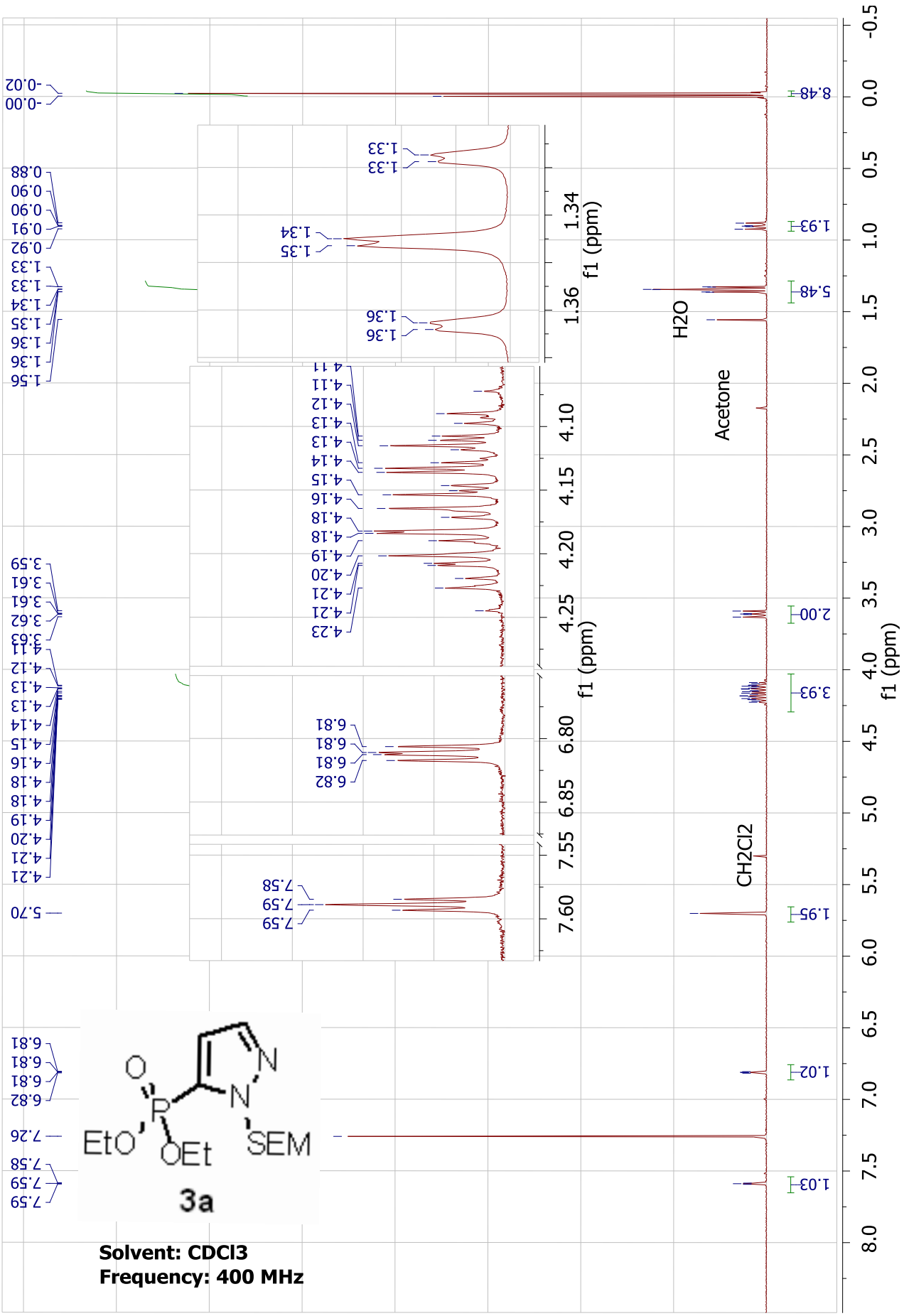


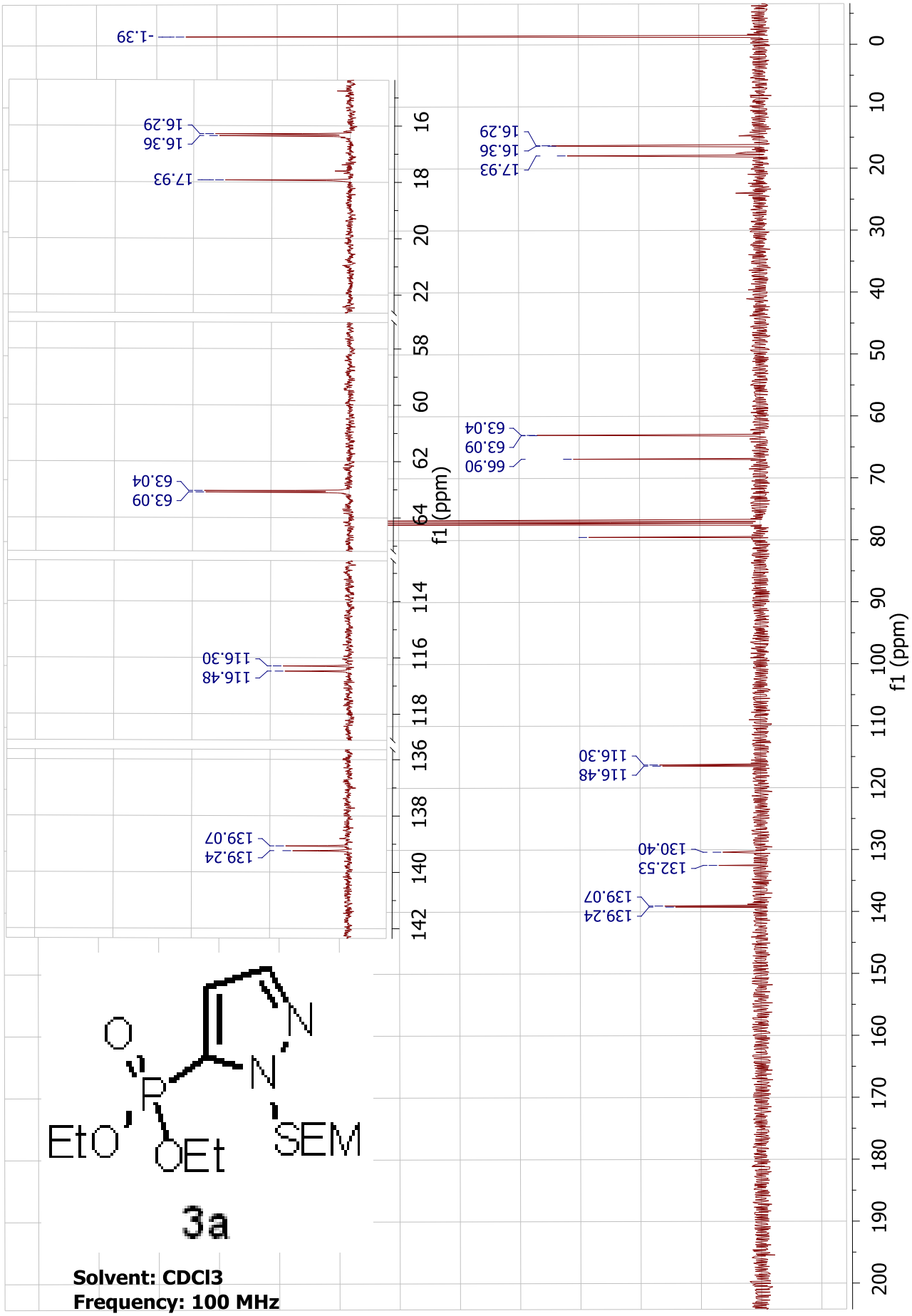
4c

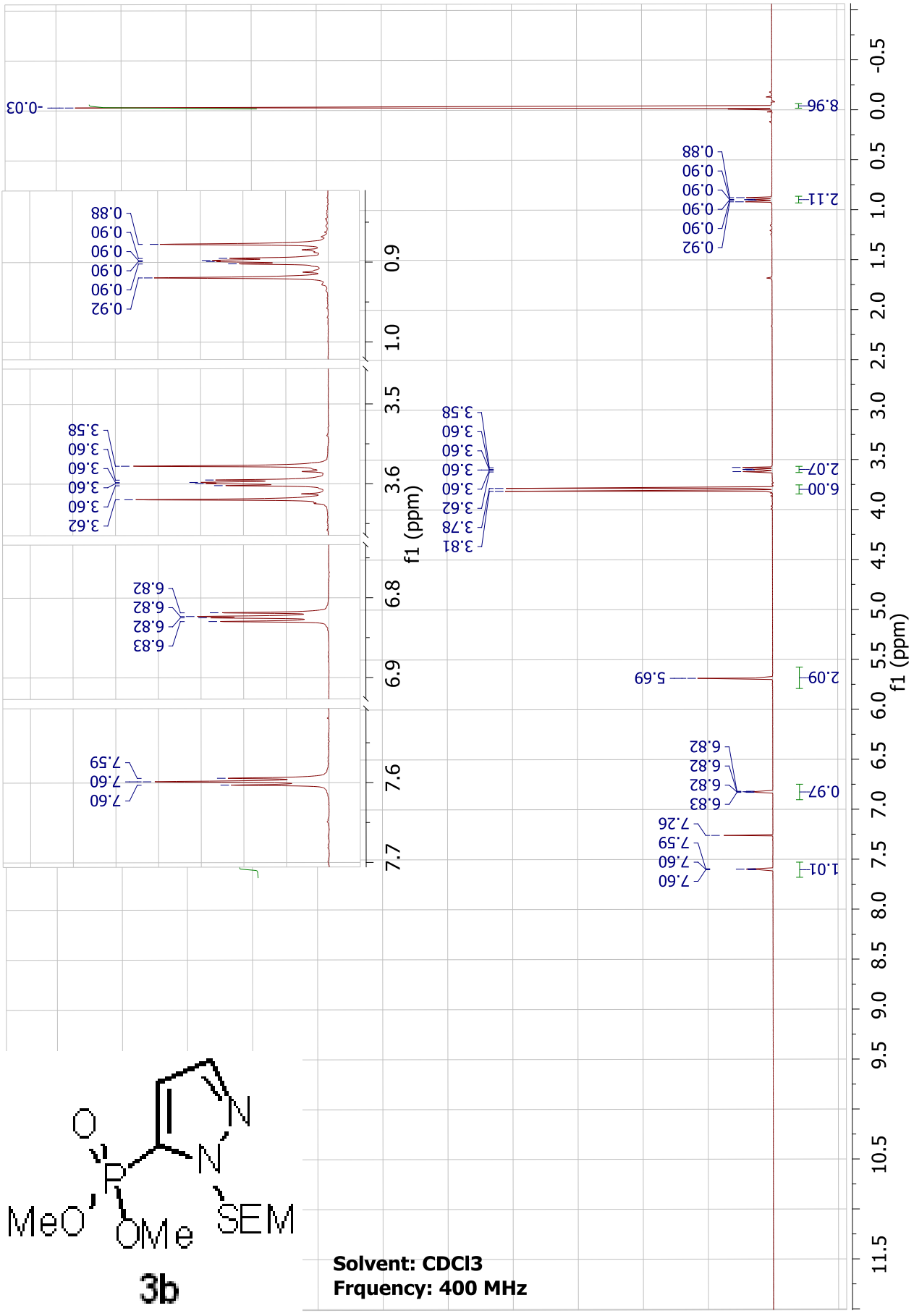

-1.30
17.90
67.16
80.43
95.50
116.06
131.55
f1 (ppm)
Solvent: CDCl3
Frequency: 100 MHz
4c


2j
Solvent: CDCl3
Frequency: 400 MHz
f1 (ppm)


2.46
2.51
2.86
2.89
6.99
7.99
77.16
77.48
128.82
128.94
130.07
130.18
131.24
132.24
132.47
132.50
f1 (ppm)
2j
Solvent: CDCl3
Frequency: 100 MHz

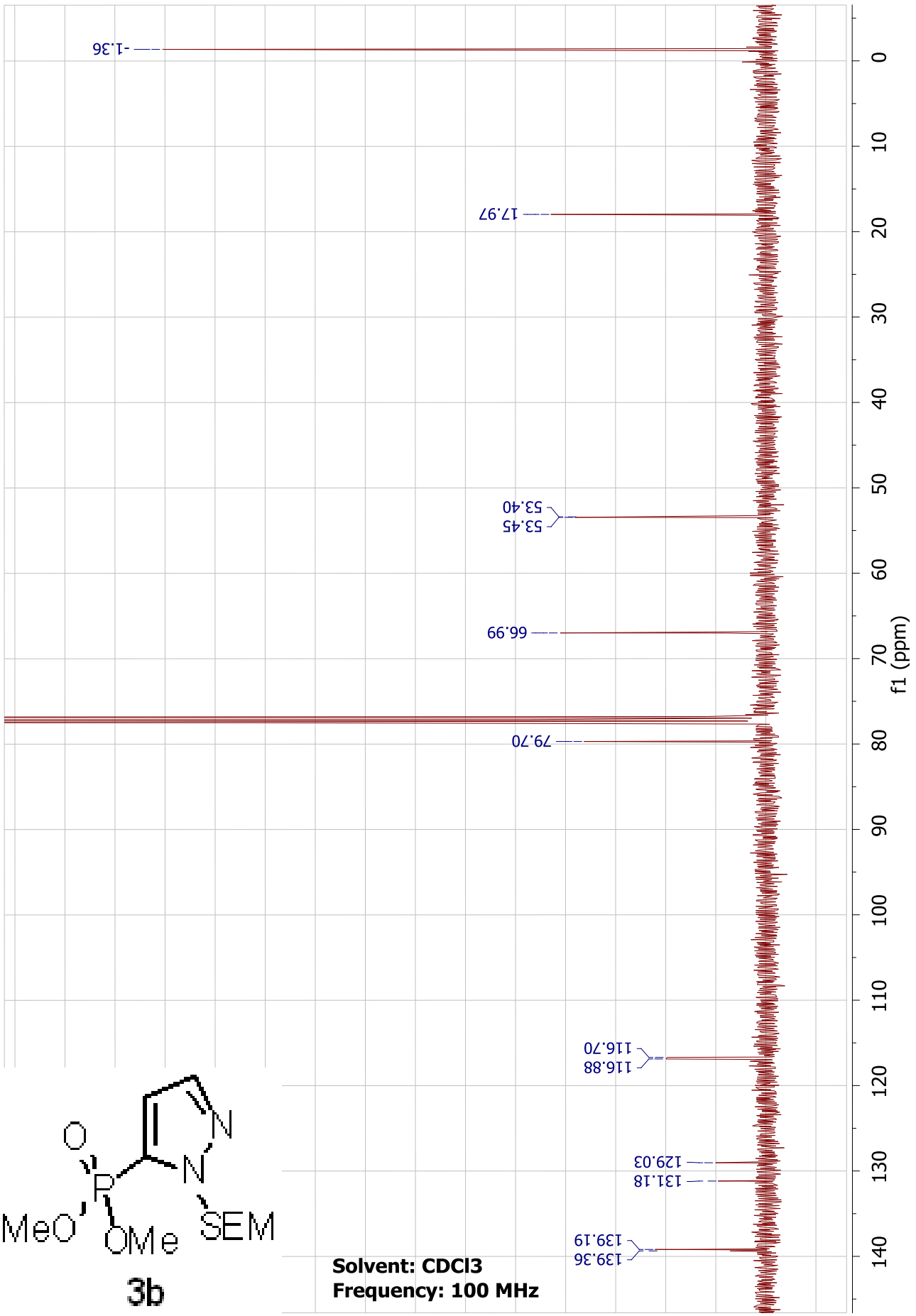

Acetone
H2O
CH2Cl2
f1 (ppm)
EtO
OEt
SEM
3a
Solvent: CDCl3
Frequency: 400 MHz


-1.39
16.29
16.36
17.93
63.04
63.09
66.90
116.30
116.48
130.40
132.53
139.07
139.24
f1 (ppm)
O
P
N
N
EtO
OEt
SEM
3a
Solvent: CDCl3
Frequency: 100 MHz


-0.03
8.96
2.11
0.88
0.90
0.90
0.90
0.90
0.92
3.58
3.60
3.60
3.60
3.60
3.62
3.78
3.81
2.07
6.00
5.69
2.09
6.82
6.82
6.82
6.83
0.97
7.26
7.59
7.60
7.60
1.01
f1 (ppm)
Solvent: CDCl3
Frquency: 400 MHz

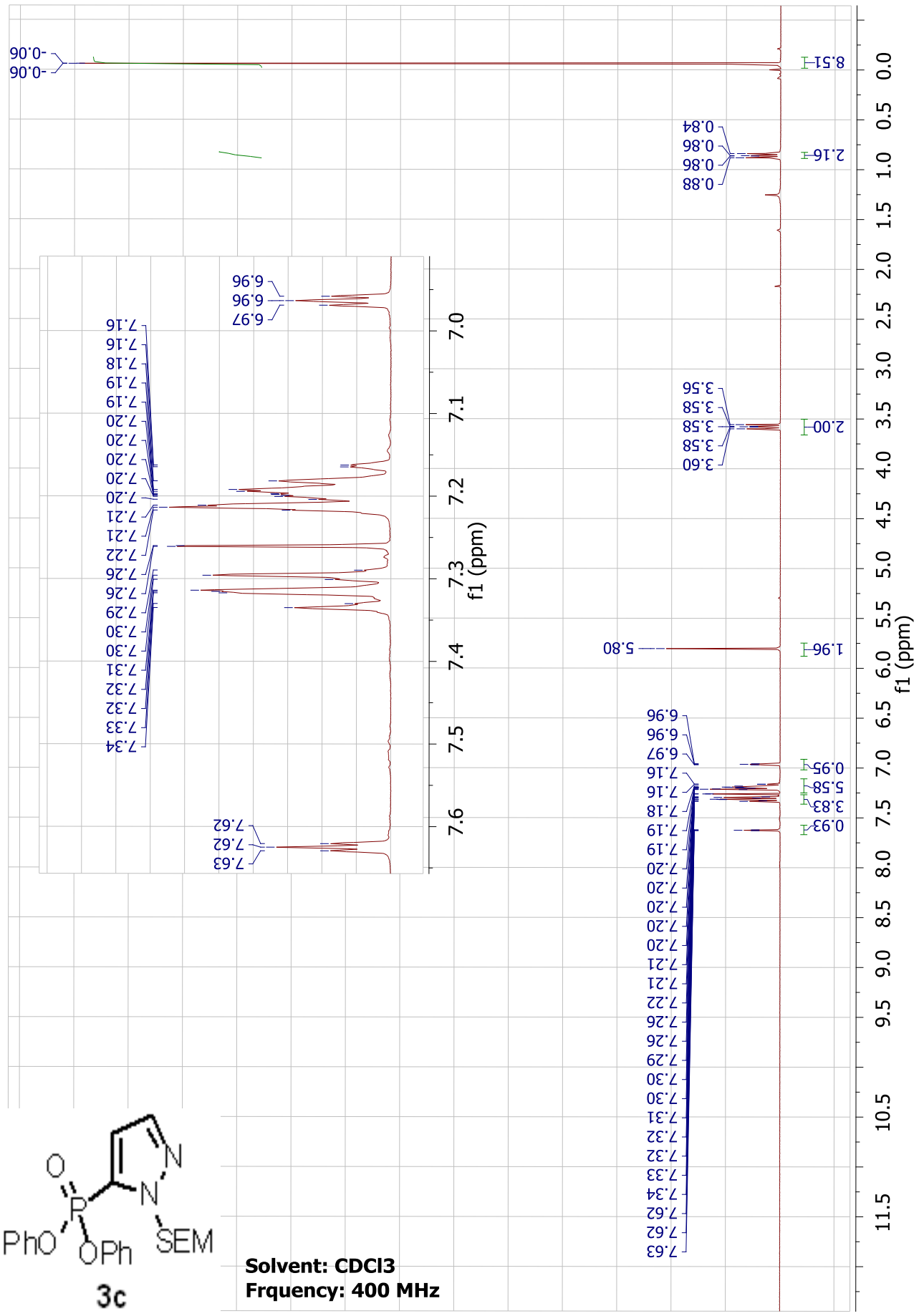
O
N
P
N
MeO
OMe
SEM

3b

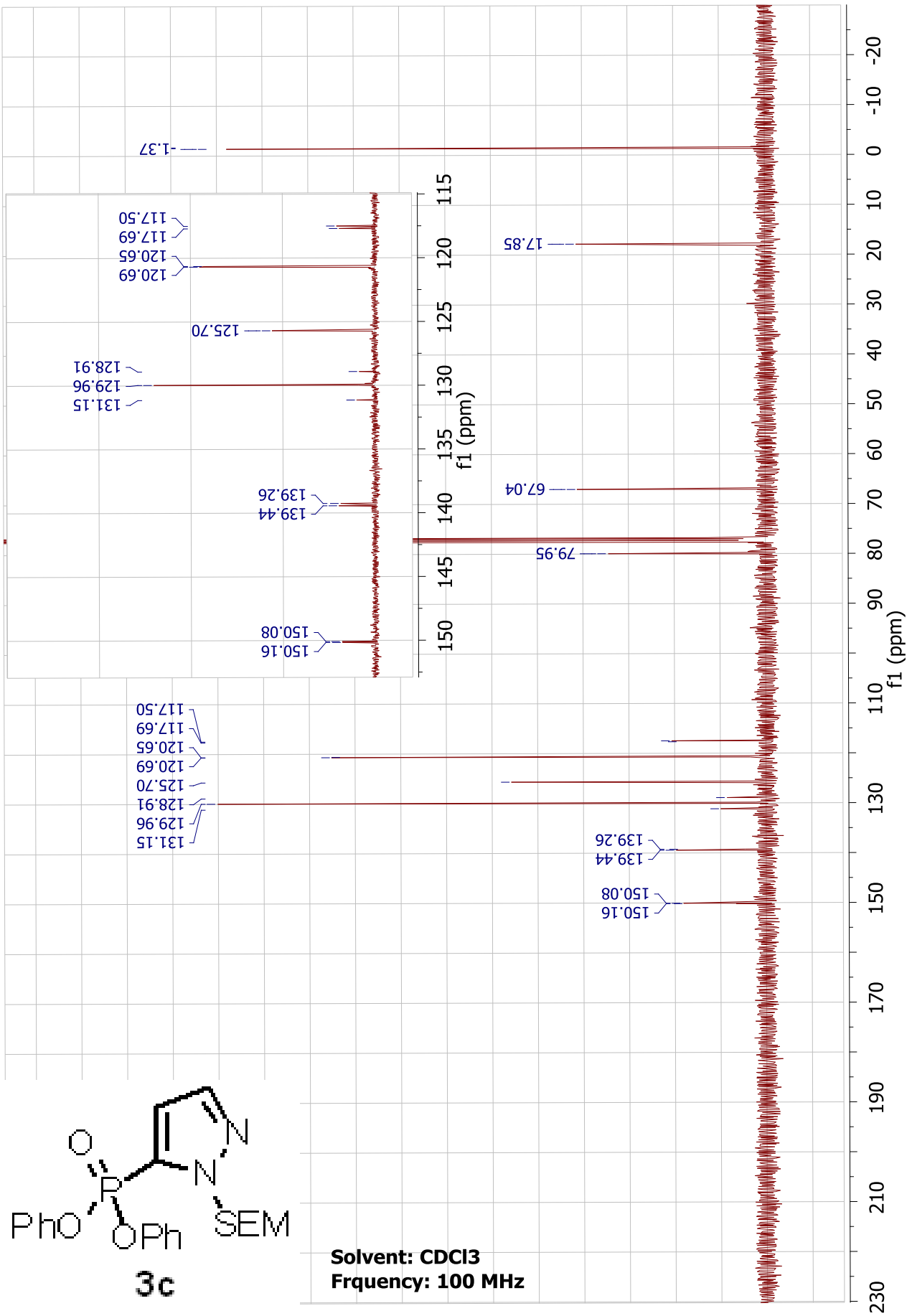

-1.36
17.97
53.40
53.45
66.99
79.70
116.70
116.88
129.03
131.18
139.19
139.36
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
f1 (ppm)
Solvent: CDCl3
Frequency: 100 MHz

O
P
N
N
MeO
OMe
SEM

3b

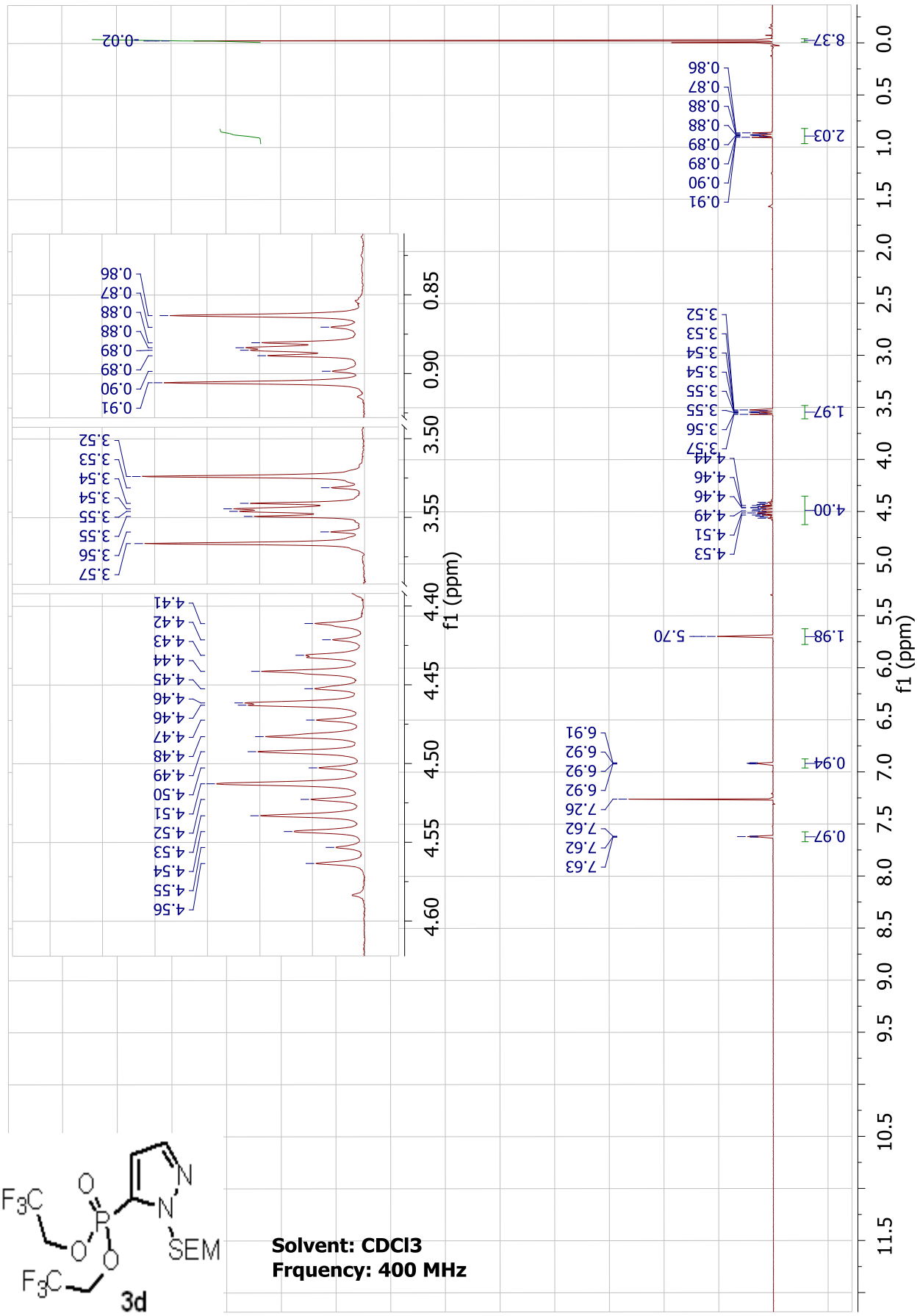


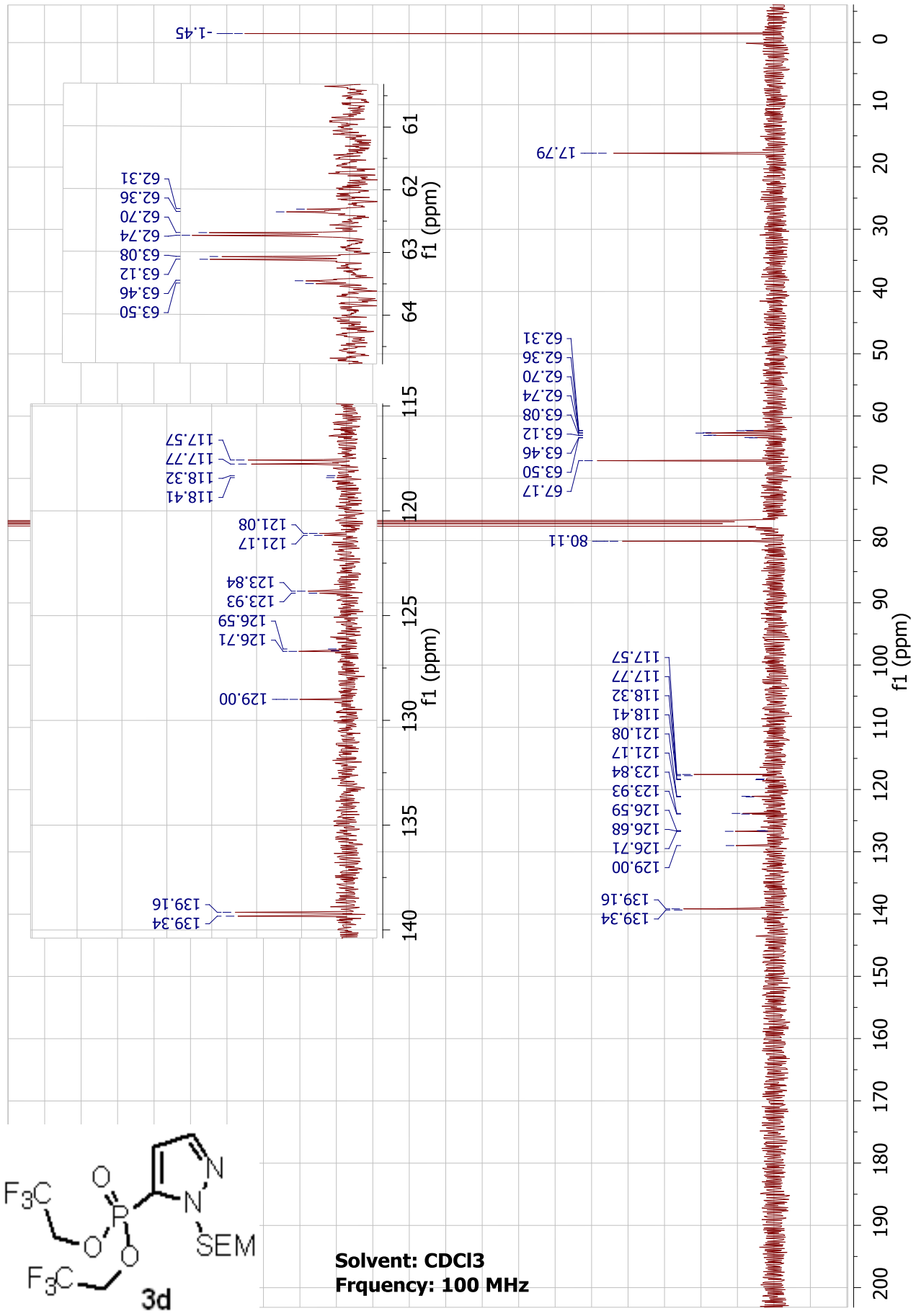
3c

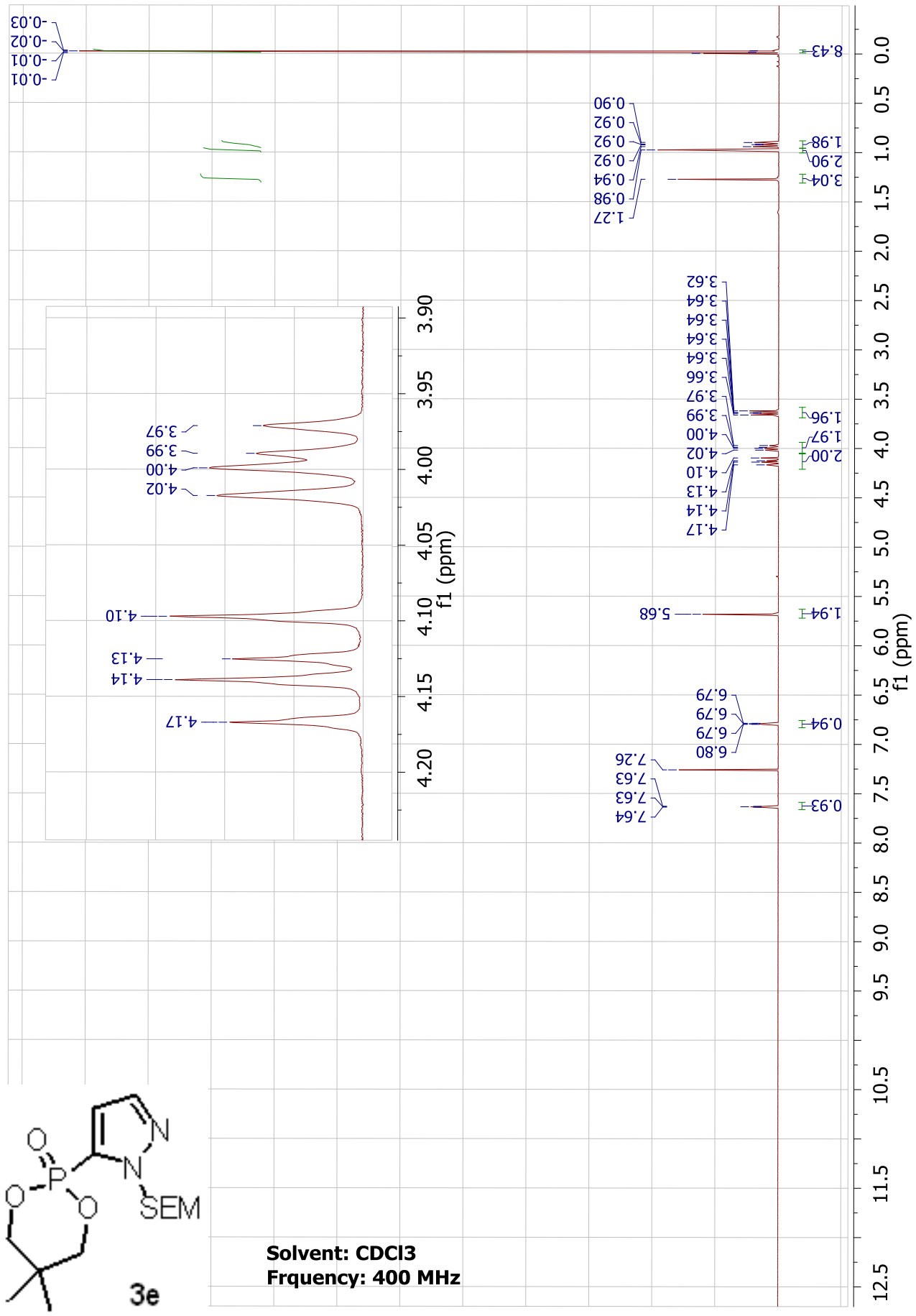

-1.37
17.85
67.04
79.95
117.50
117.69
120.65
120.69
125.70
128.91
129.96
131.15
139.26
139.44
150.08
150.16
f1 (ppm)
Solvent: CDCl3
Frquency: 100 MHz

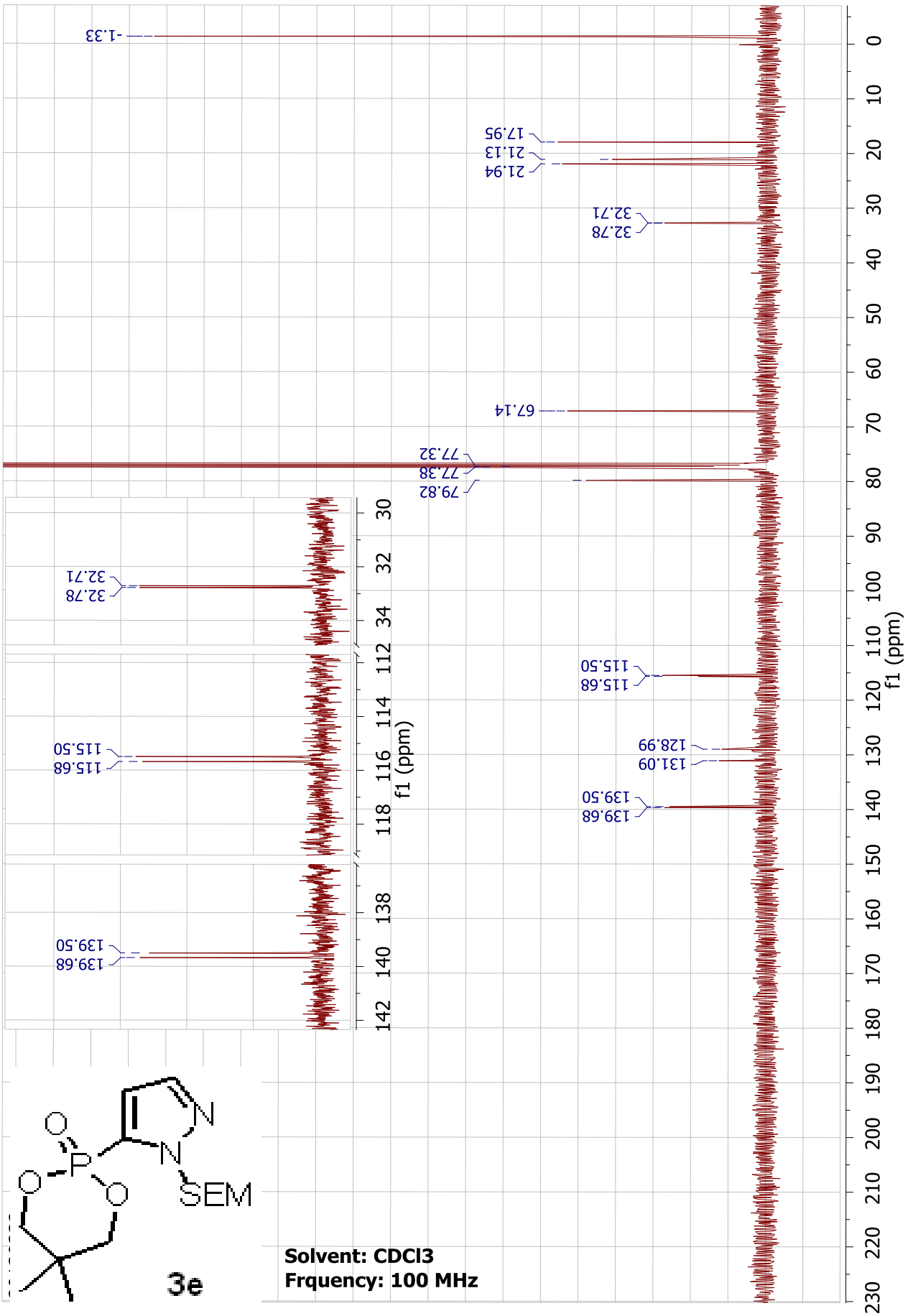
O
P
N
N
PhO
OPh
SEM

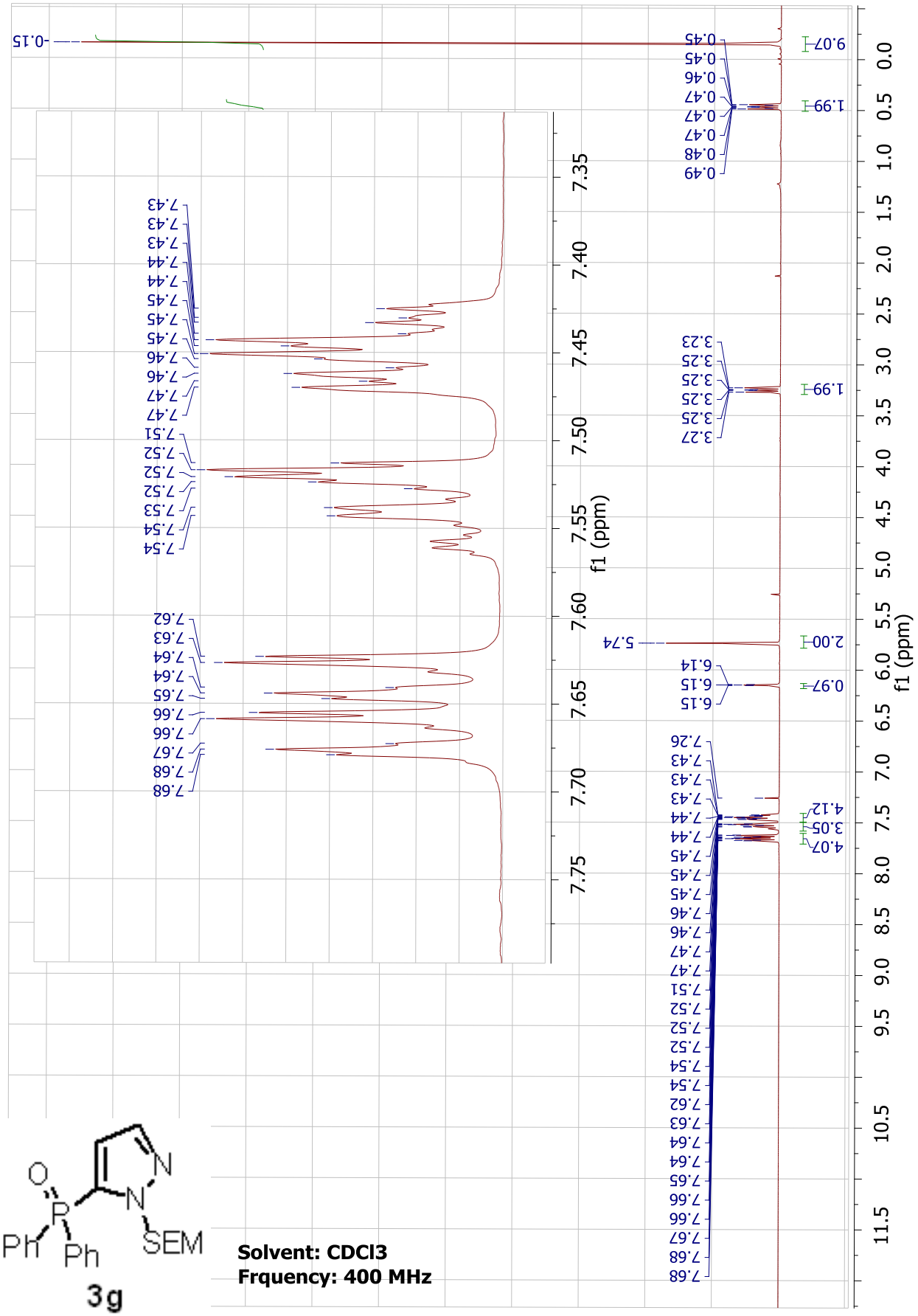
3c

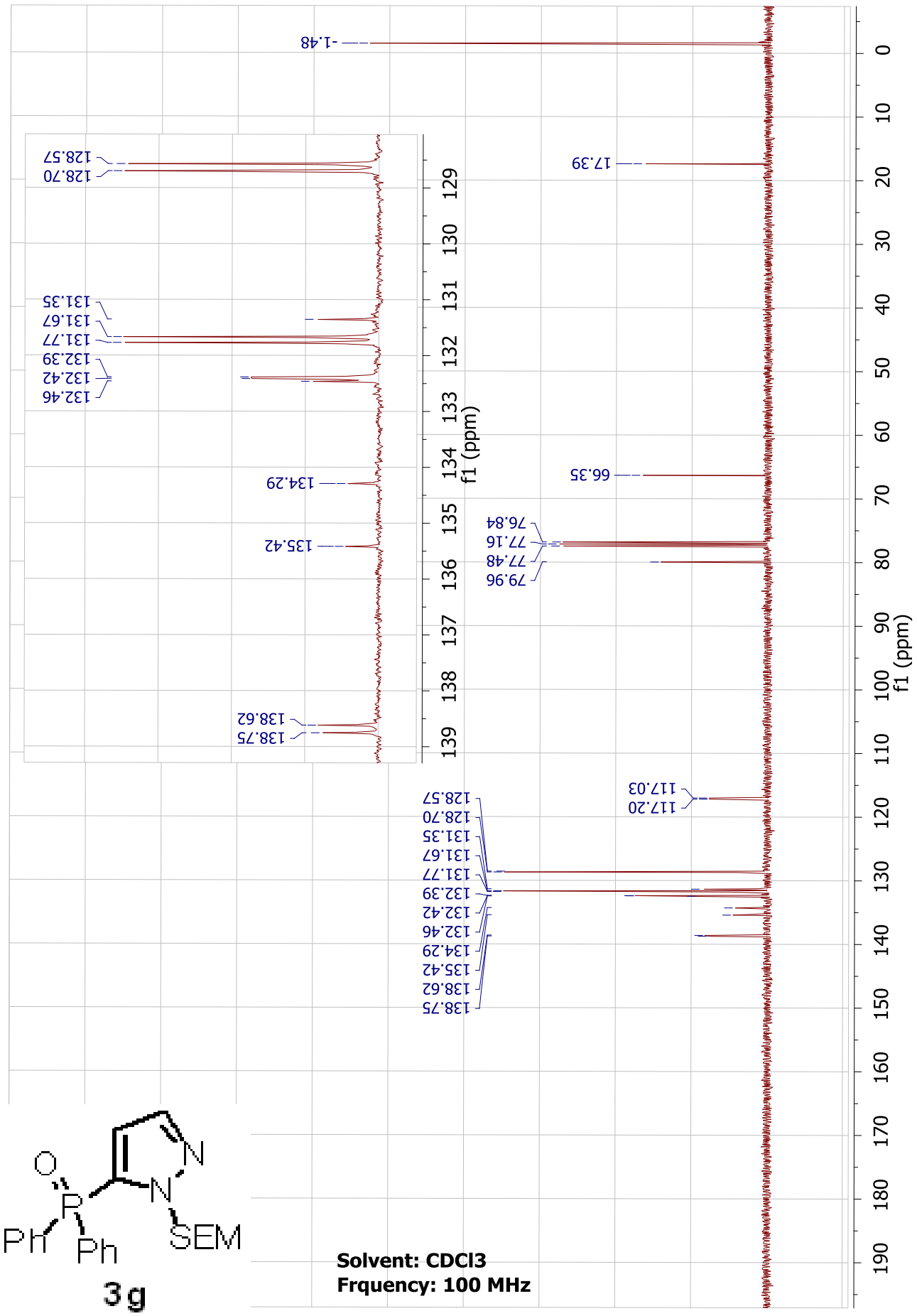

f1 (ppm)
Solvent: CDCl3
Frquency: 400 MHz
3d

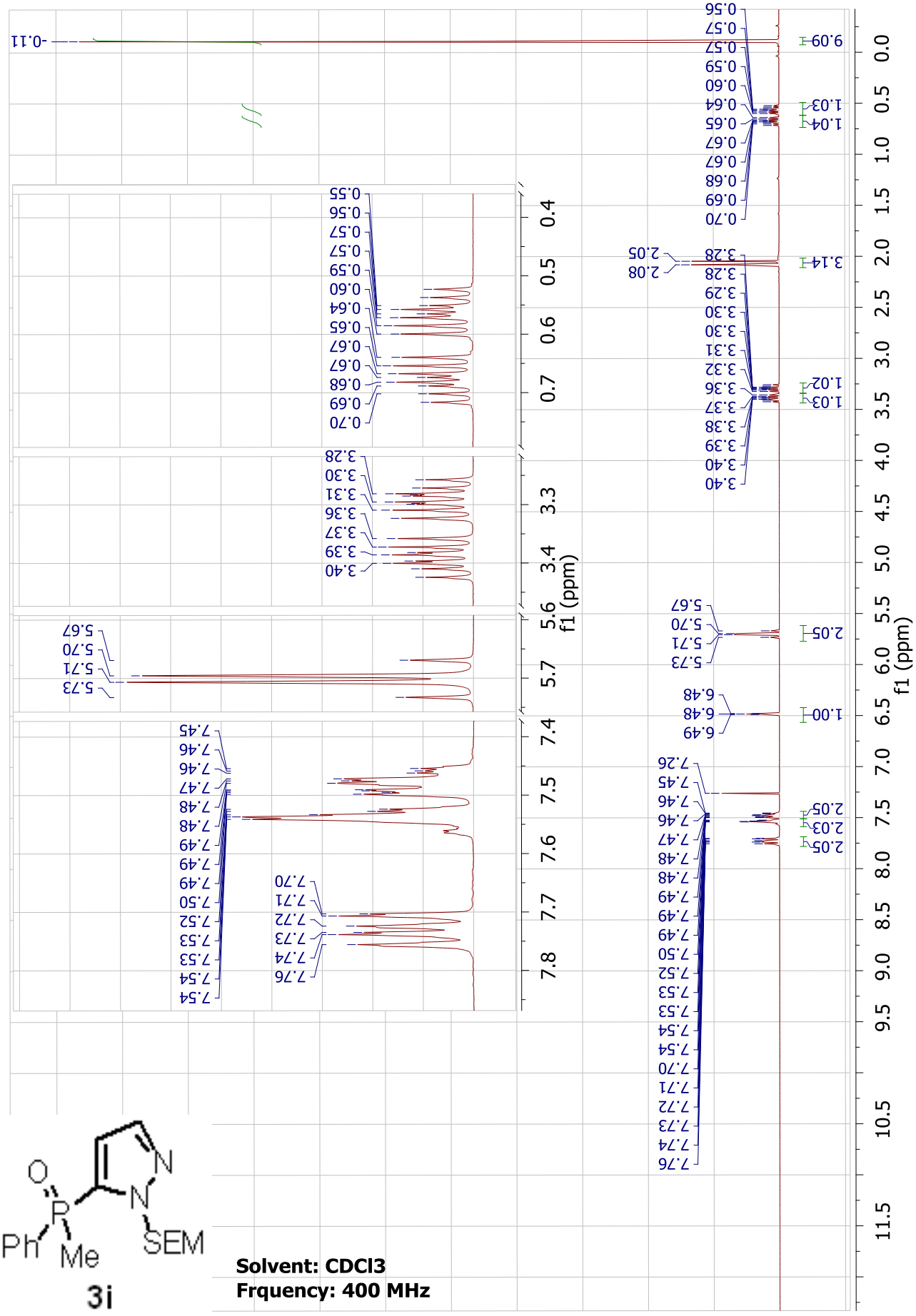

-1.45
17.79
62.31
62.36
62.70
62.74
63.08
63.12
63.46
63.50
67.17
80.11
117.57
117.77
118.32
118.41
121.08
121.17
123.84
123.93
126.59
126.68
126.71
129.00
139.16
139.34
f1 (ppm)
Solvent: CDCl3
Frquency: 100 MHz
F3C
CF3
O
P
N
N
SEM
3d


-0.03
-0.02
-0.01
-0.01
8.43
1.98
2.90
3.04
0.90
0.92
0.92
0.92
0.94
0.98
1.27
3.62
3.64
3.64
3.64
3.64
3.66
3.97
3.99
4.00
4.02
4.10
4.13
4.14
4.17
1.96
1.97
2.00
5.68
1.94
6.79
6.79
6.79
6.80
0.94
7.26
7.63
7.63
7.64
0.93
f1 (ppm)
3.90
3.95
4.00
4.05
4.10
4.15
4.20
3.97
3.99
4.00
4.02
4.10
4.13
4.14
4.17
f1 (ppm)
Solvent: CDCl3
Frquency: 400 MHz
O
P
O
O
N
N
SEM
3e


-1.33
17.95
21.13
21.94
32.78
32.71
67.14
77.32
77.38
79.82
115.50
115.68
128.99
131.09
139.50
139.68
f1 (ppm)
SEM
3e
Solvent: CDCl3
Frquency: 100 MHz

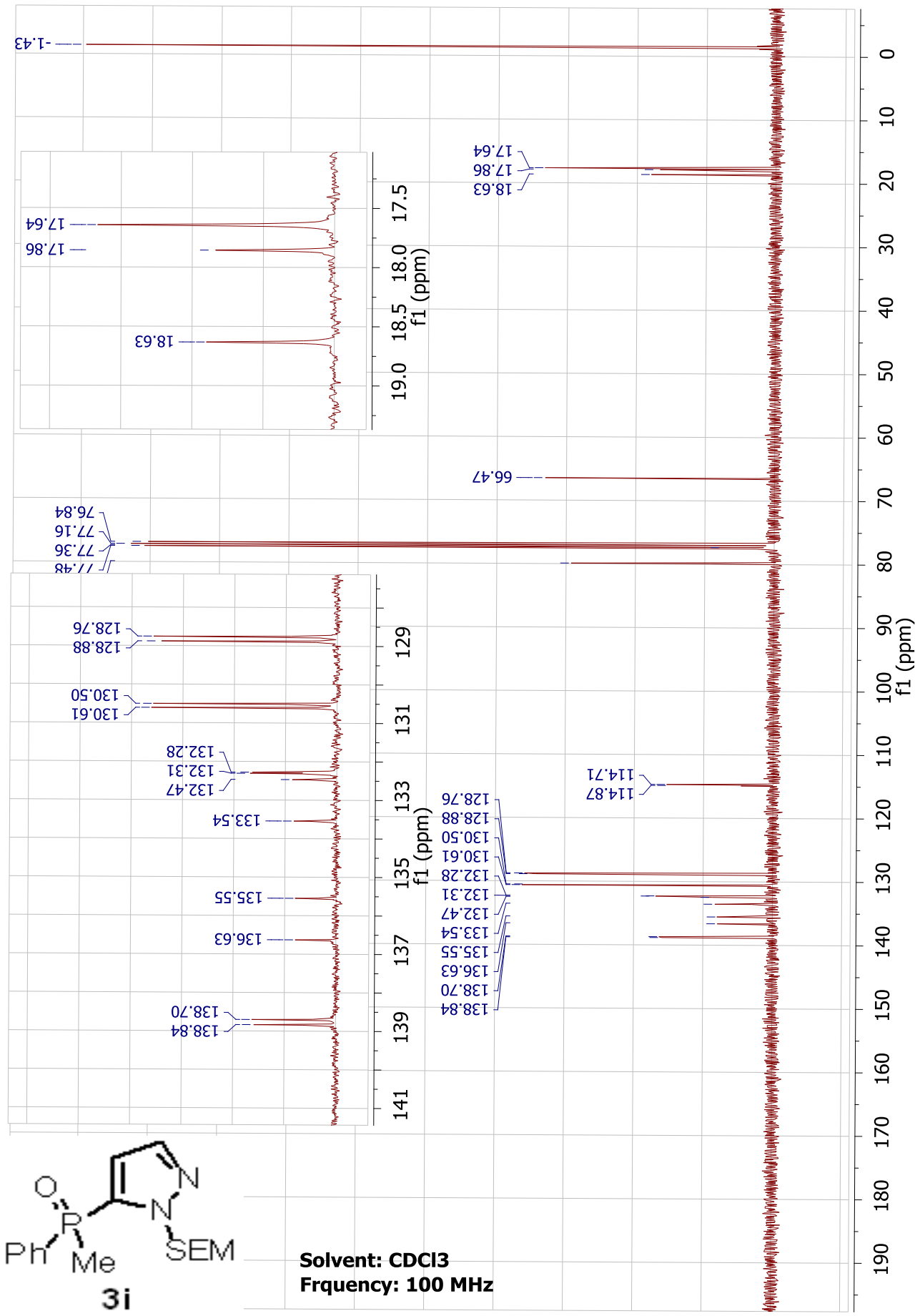

f1 (ppm)
Solvent: CDCl3
Frquency: 400 MHz
3g

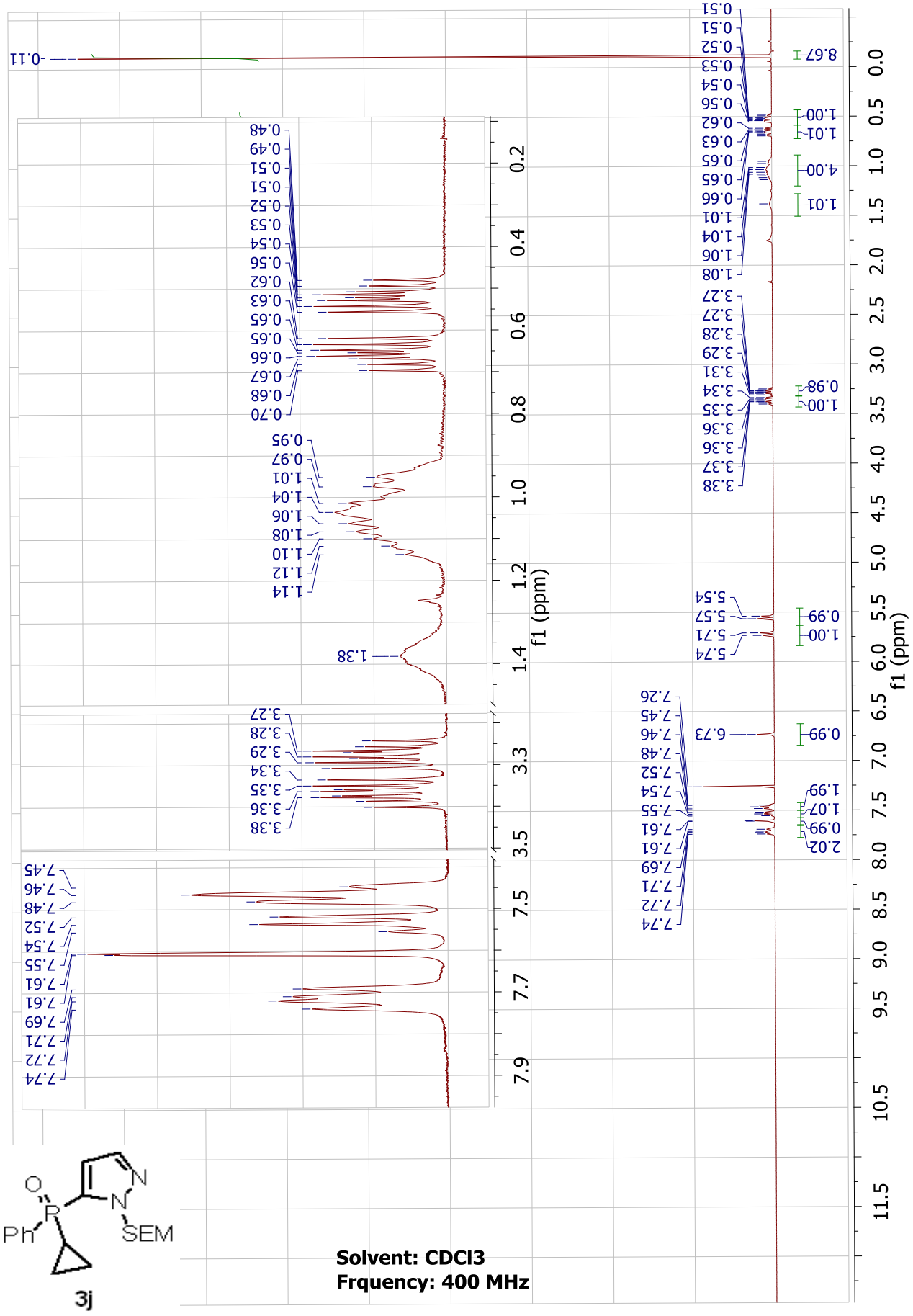

-1.48
17.39
66.35
76.84
77.16
77.48
79.96
117.03
117.20
128.57
128.70
131.35
131.67
131.77
132.39
132.42
132.46
134.29
135.42
138.62
138.75
f1 (ppm)
Ph
Ph
P
O
N
N
SEM
3g
Solvent: CDCl3
Frquency: 100 MHz



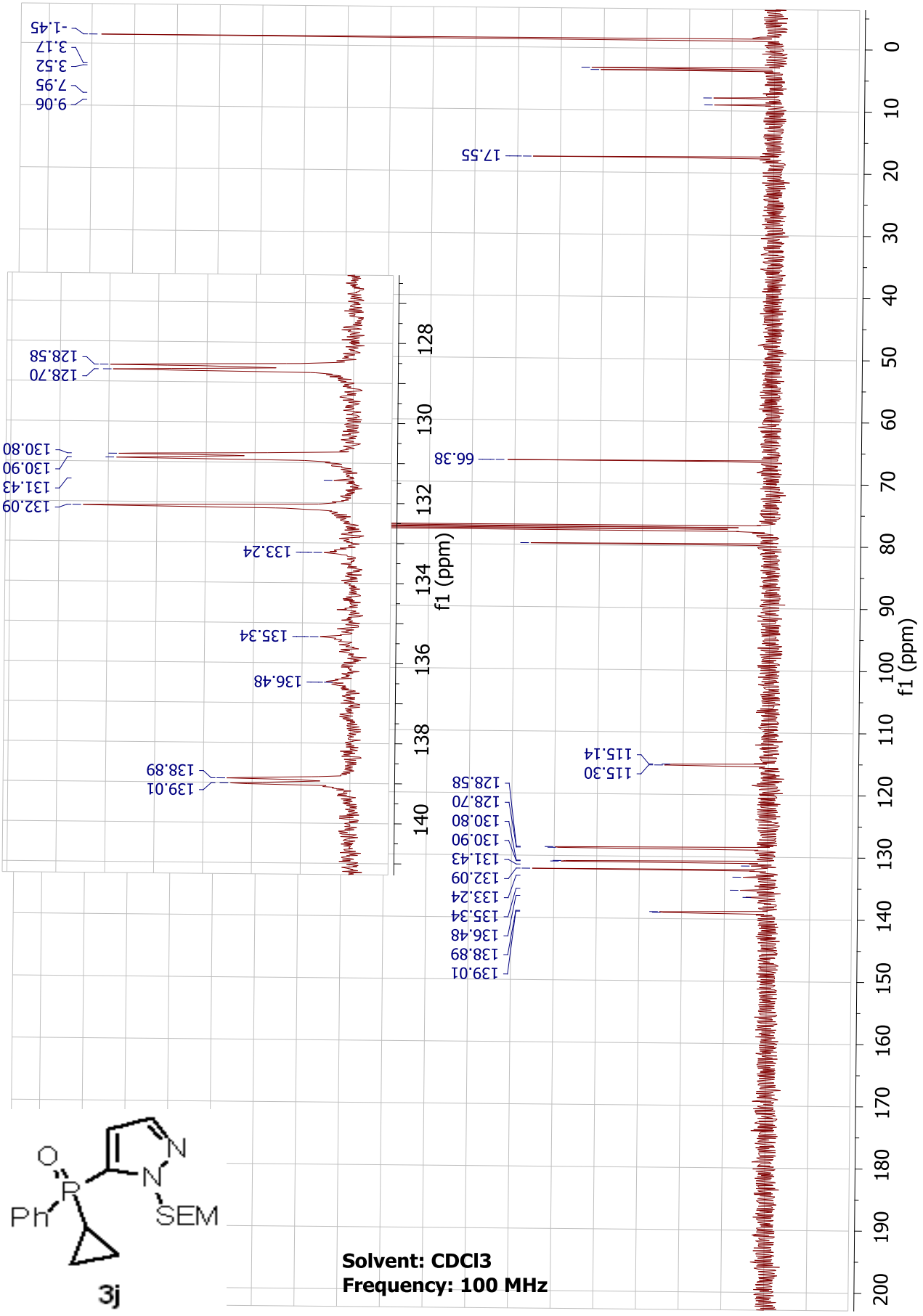
3i

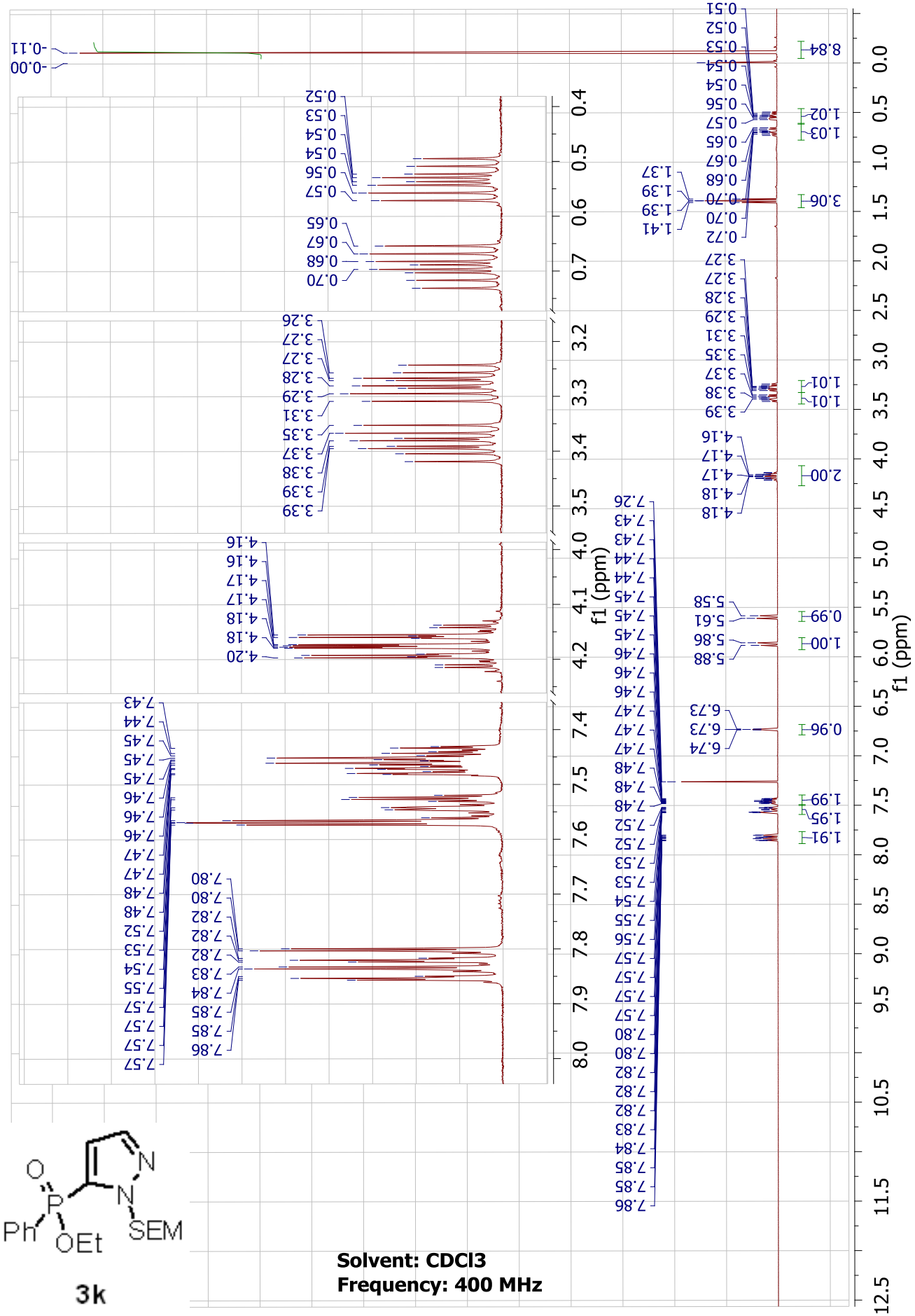
Solvent: CDCl3
Frquency: 400 MHz


-1.43
17.64
17.86
18.63
66.47
76.84
77.16
77.36
128.76
128.88
130.50
130.61
132.28
132.31
132.47
133.54
135.55
136.63
138.70
138.84
114.87
114.71
f1 (ppm)
Solvent: CDCl3
Frquency: 100 MHz
Ph
Me
SEM
3i

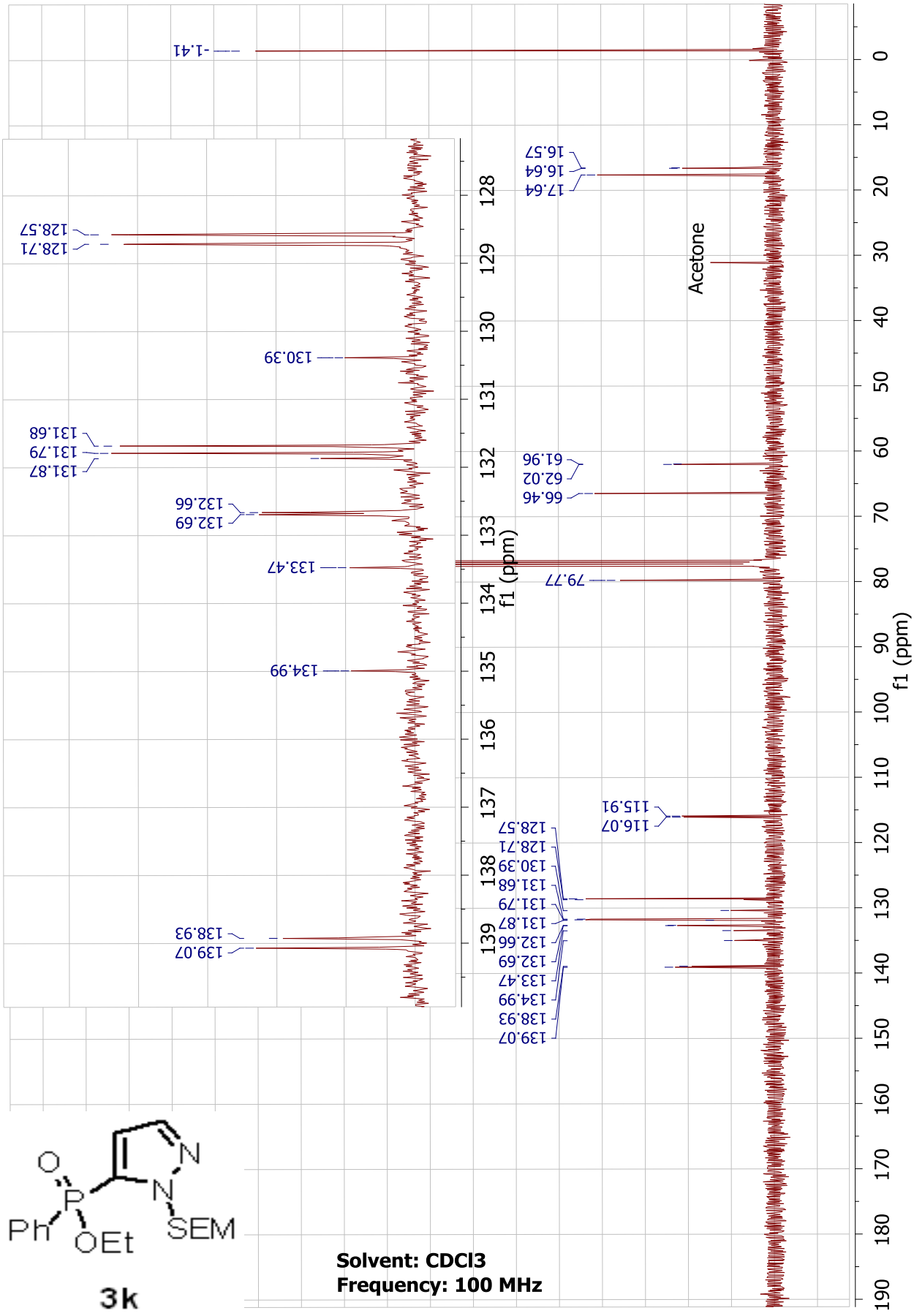


3j

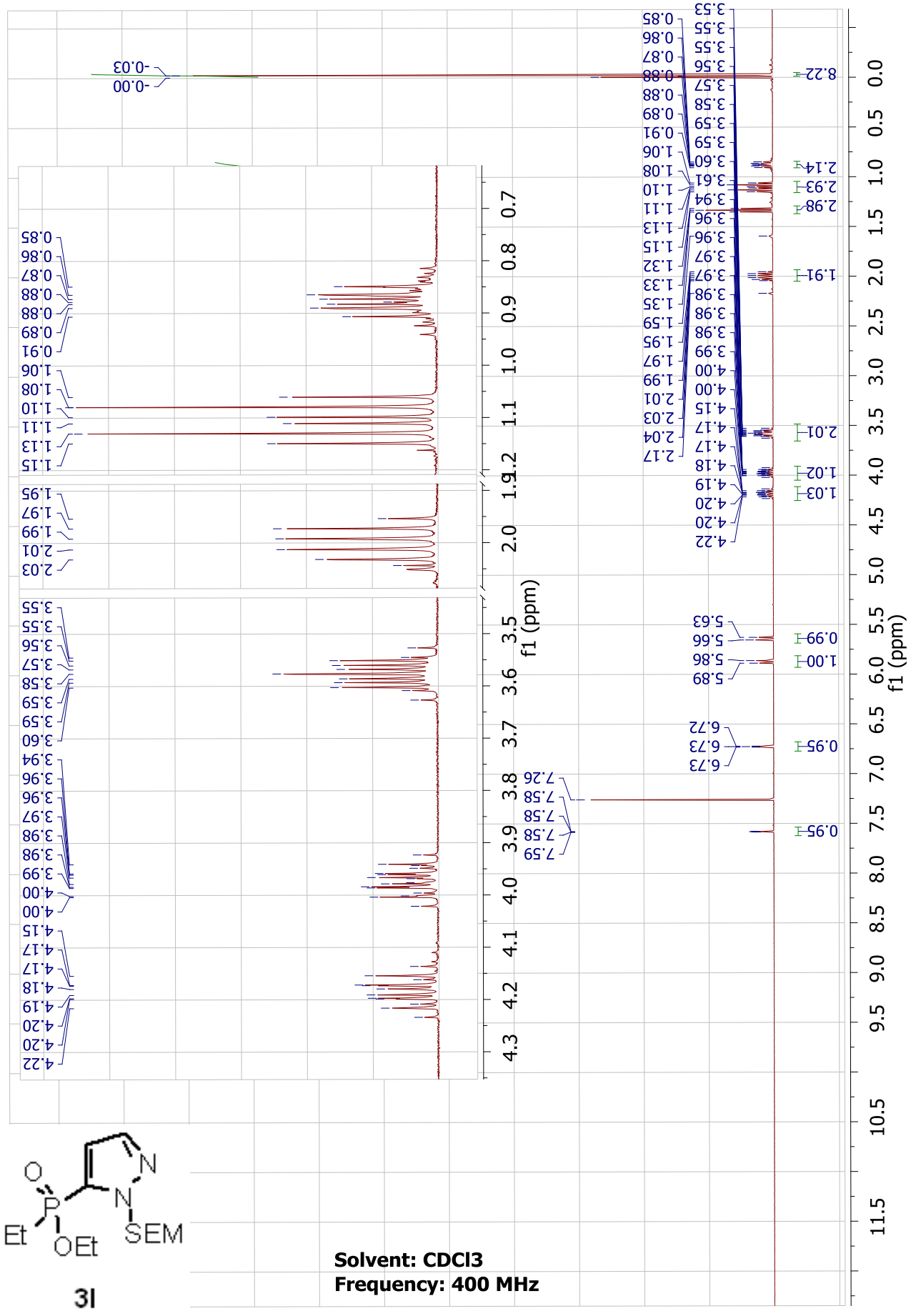

-1.45
3.17
3.52
7.95
9.06
17.55
66.38
115.14
115.30
128.58
128.70
130.80
130.90
131.43
132.09
133.24
135.34
136.48
138.89
139.01
f1 (ppm)
Ph
SEM
O
P
N
N
3j
Solvent: CDCl3
Frequency: 100 MHz



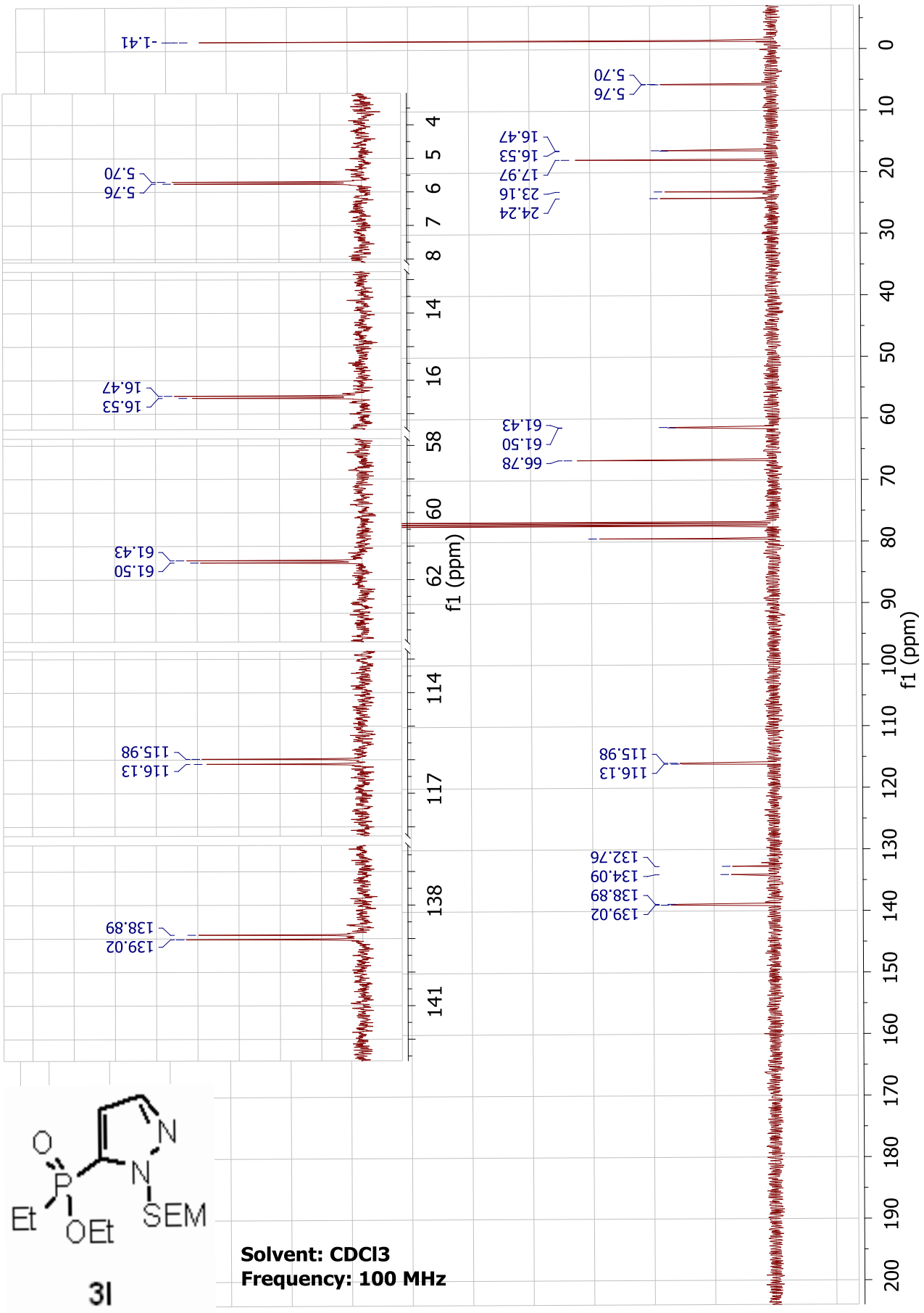
3k

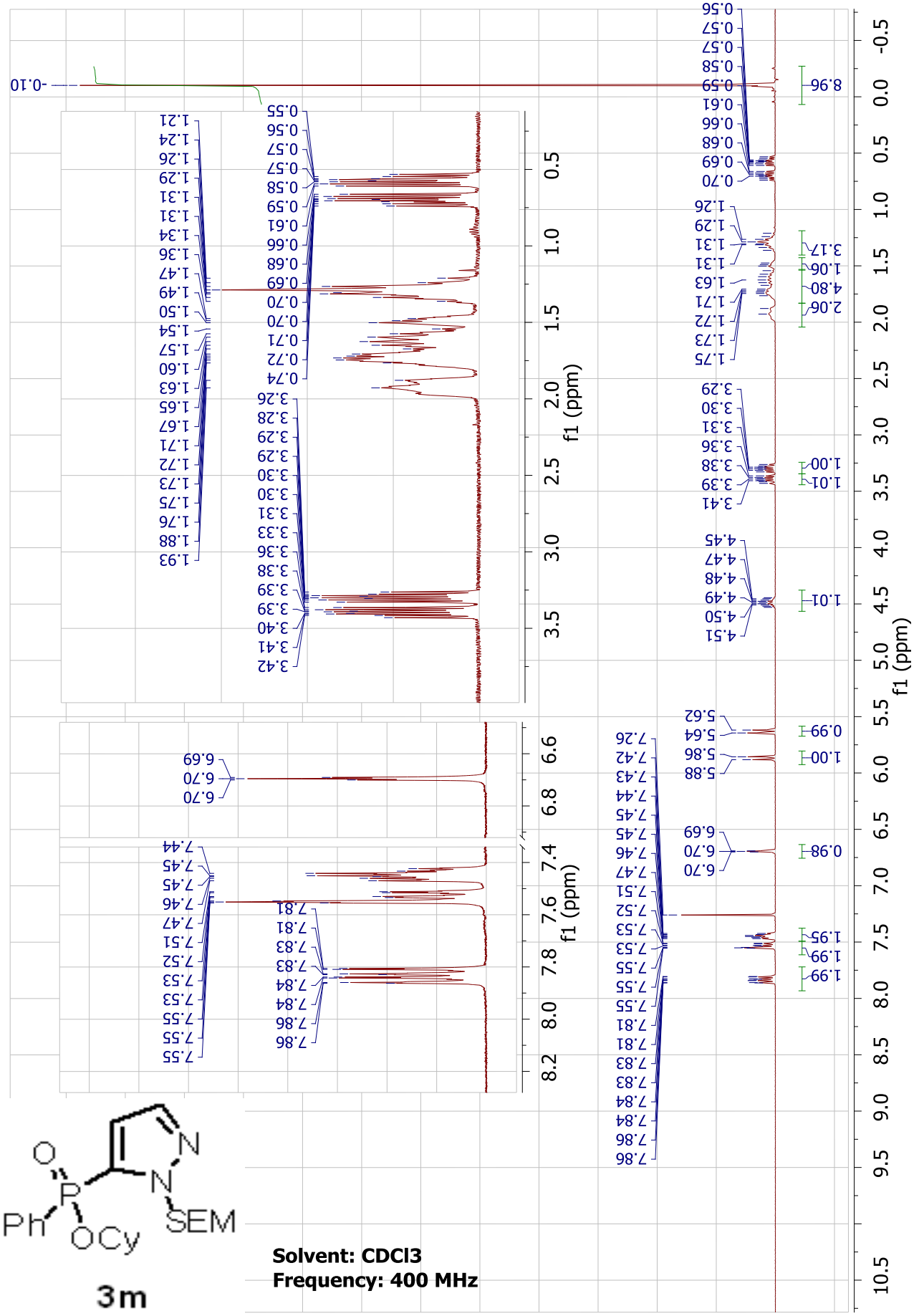

-1.41
16.57
16.64
17.64
Acetone
61.96
62.02
66.46
79.77
115.91
116.07
128.57
128.71
130.39
131.68
131.79
131.87
132.66
132.69
133.47
134.99
138.93
139.07
f1 (ppm)
Solvent: CDCl3
Frequency: 100 MHz
O
P
N
N
Ph
OEt
SEM

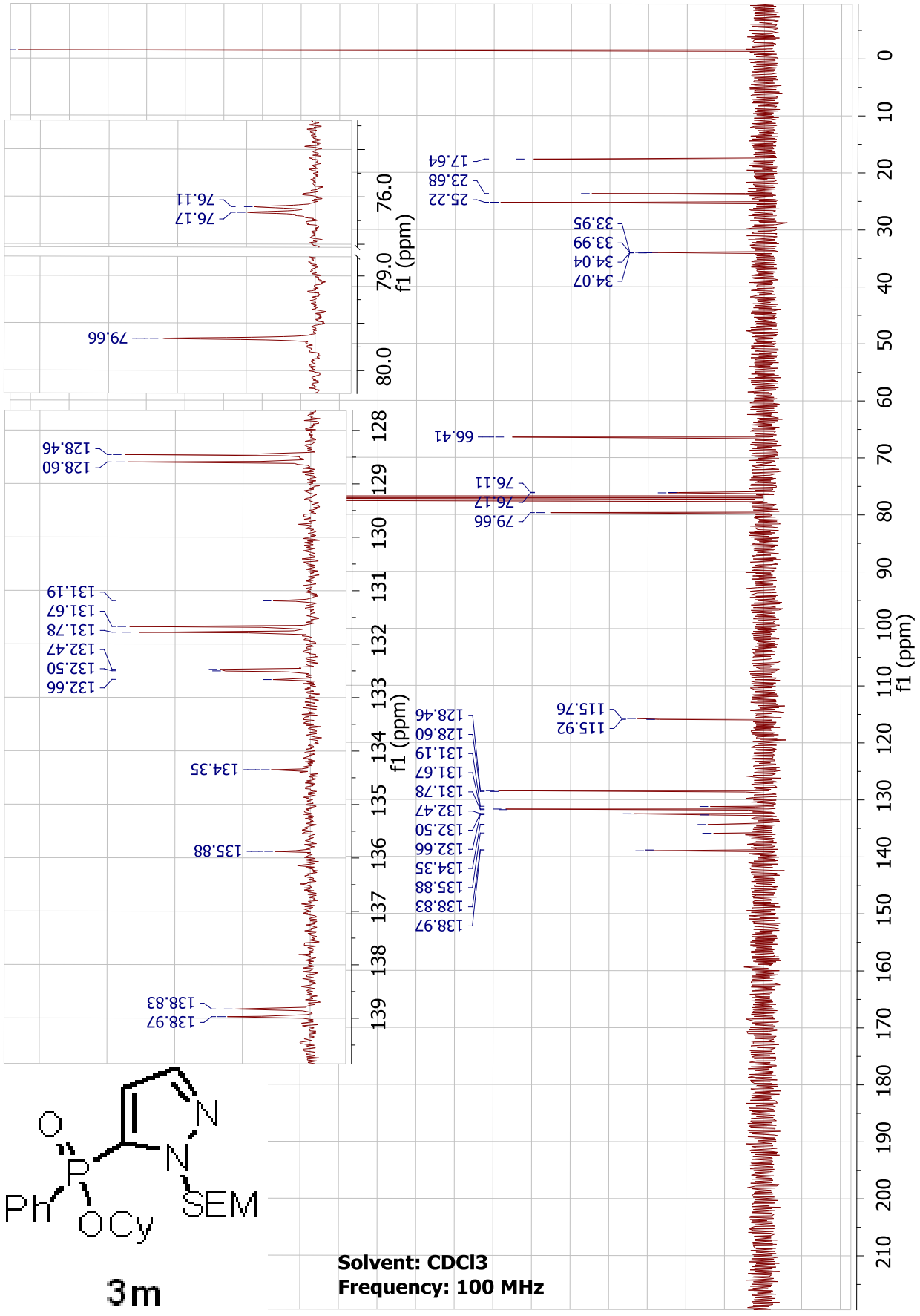
3k



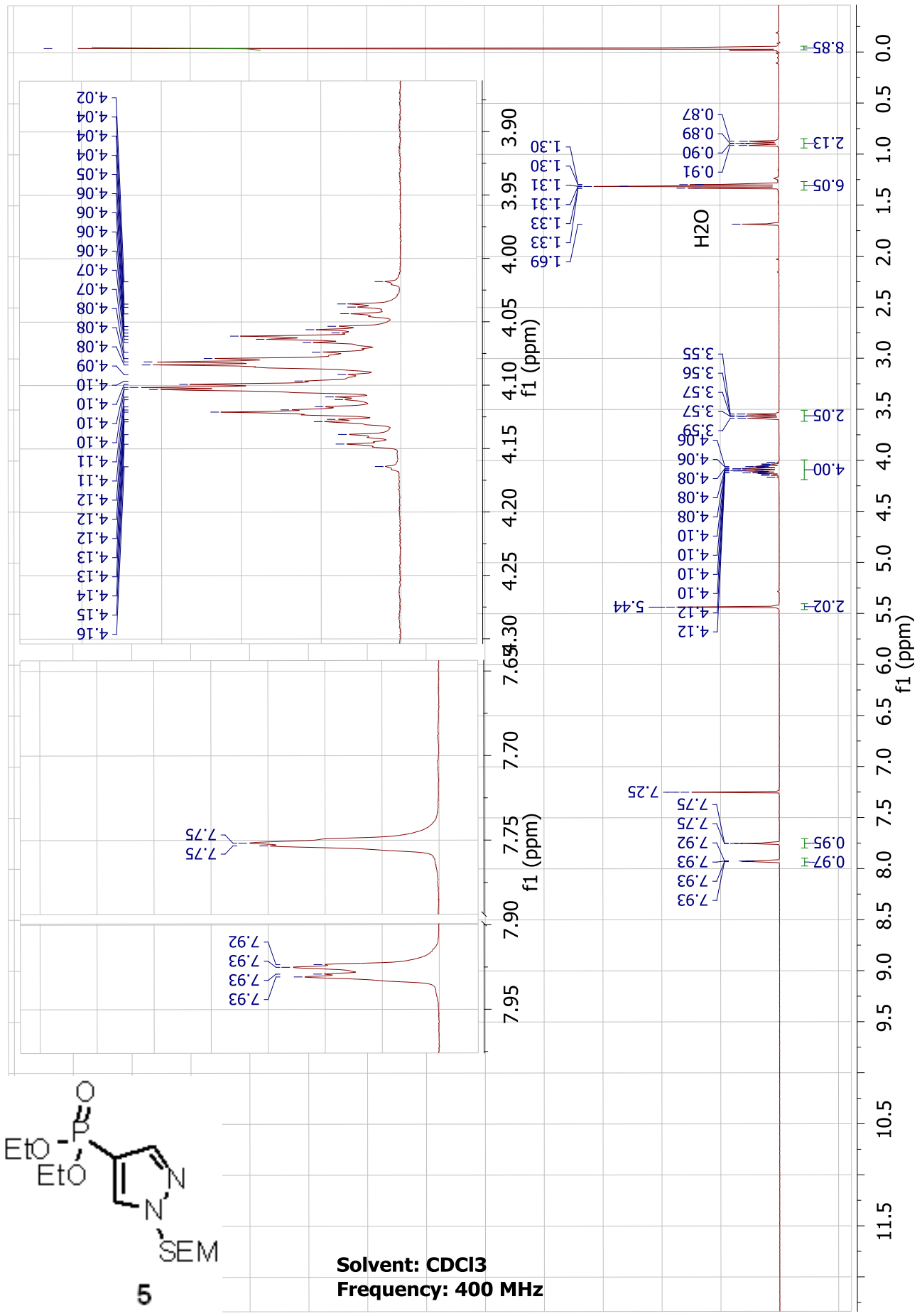
3l


-1.41
5.76
5.70
16.47
16.53
17.97
23.16
24.24
61.43
61.50
66.78
116.13
115.98
132.76
134.09
138.89
139.02
f1 (ppm)
O
P
N
N
Et
OEt
SEM
3l
Solvent: CDCl3
Frequency: 100 MHz

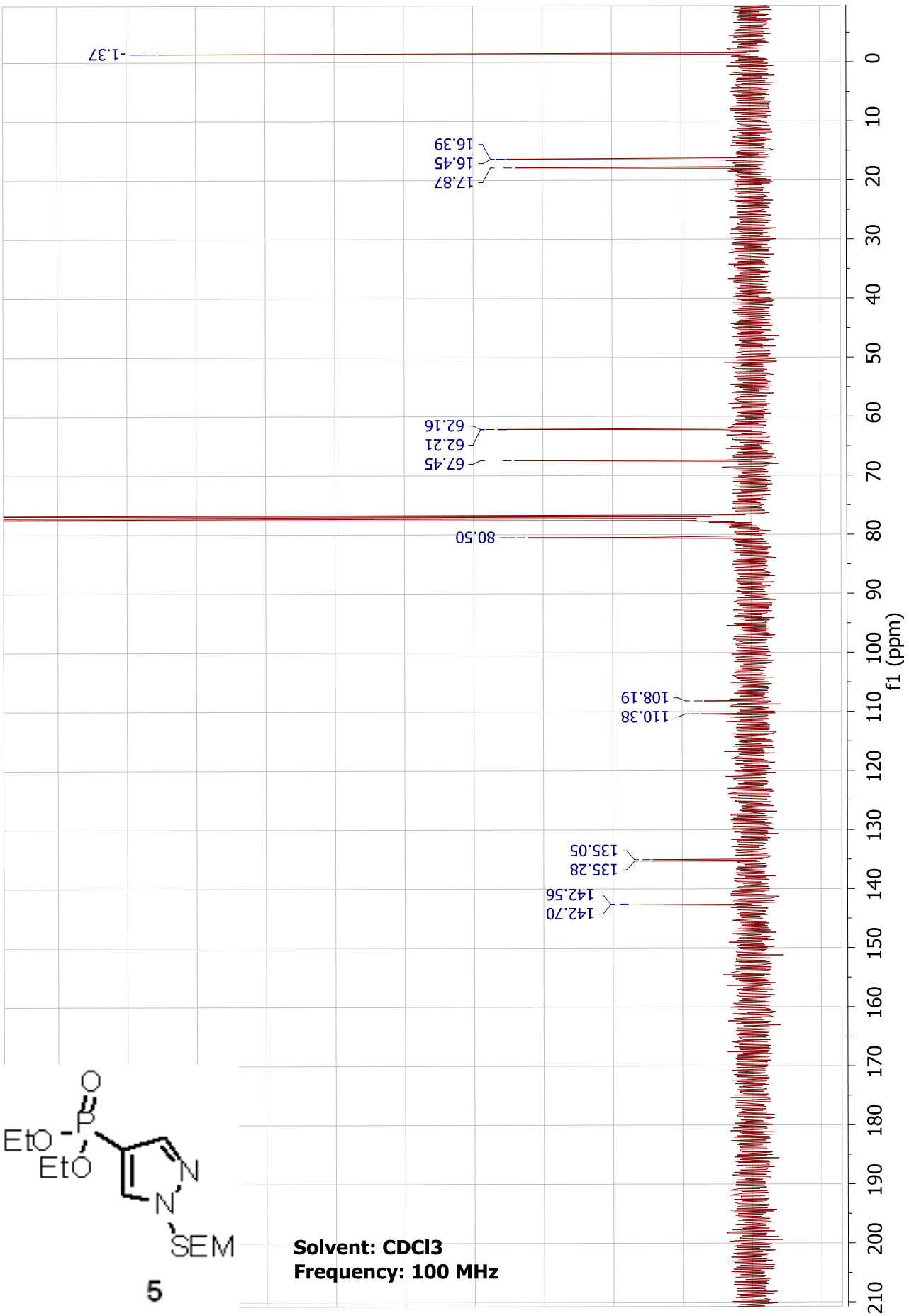

f1 (ppm)
Solvent: CDCl3
Frequency: 400 MHz
3m


17.64
23.68
25.22
33.95
33.99
34.04
34.07
66.41
76.11
76.17
79.66
115.76
115.92
128.46
128.60
131.19
131.67
131.78
132.47
132.50
132.66
134.35
135.88
138.83
138.97
76.11
76.17
79.66
128.46
128.60
131.19
131.67
131.78
132.47
132.50
132.66
134.35
135.88
138.83
138.97
O
P
N
N
Ph
OCy
SEM
Solvent: CDCl3
Frequency: 100 MHz
f1 (ppm)

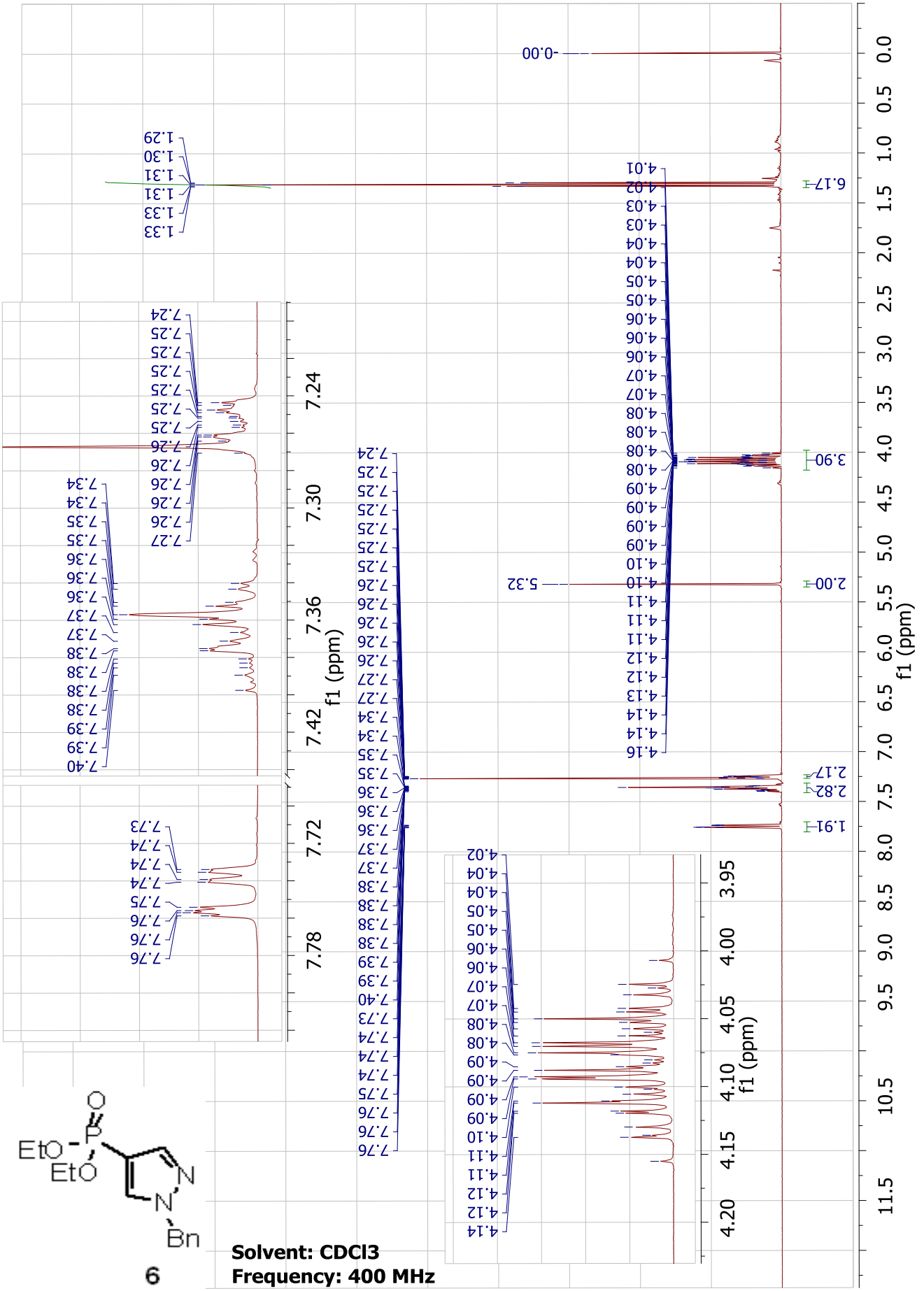
3m

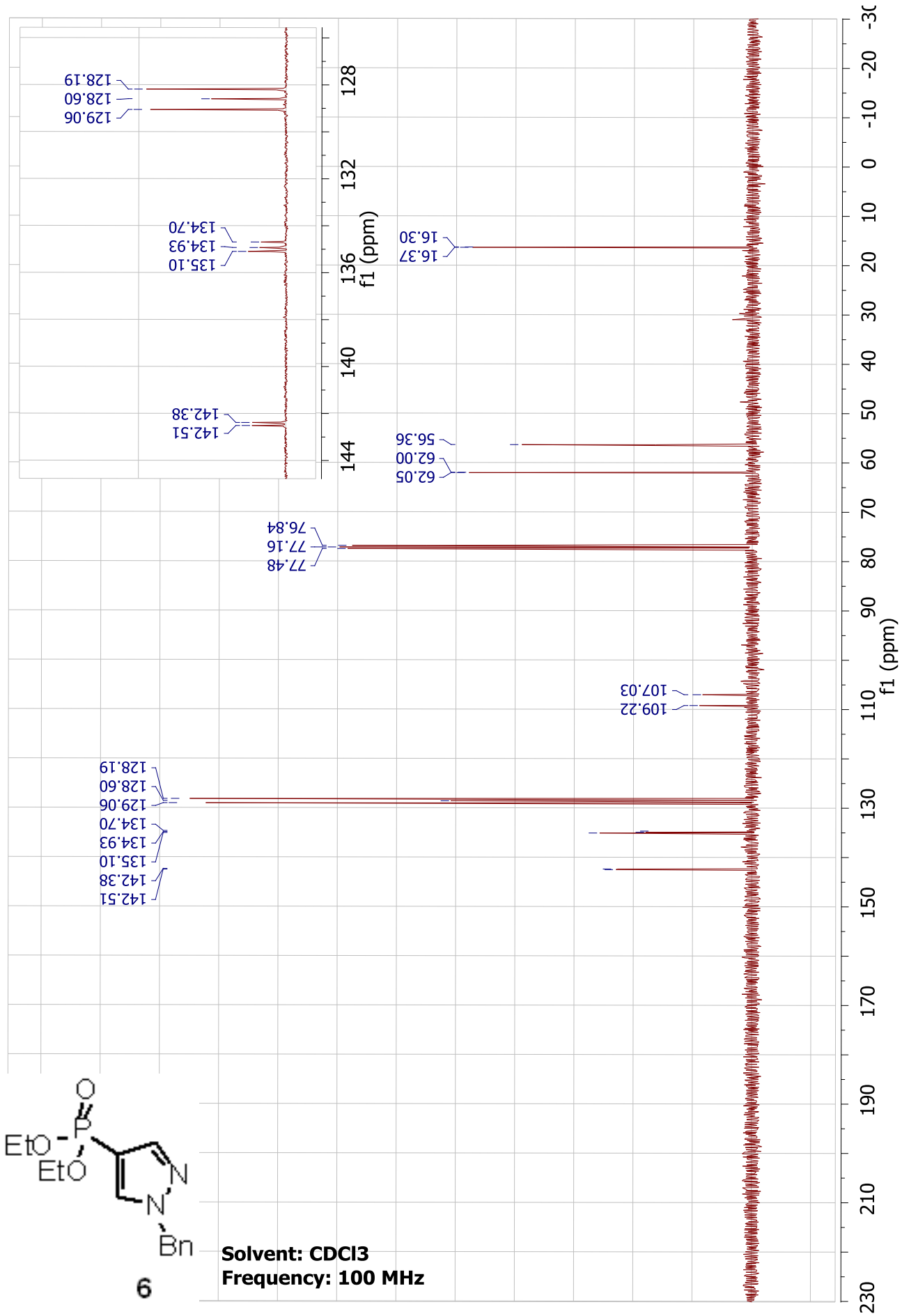


5

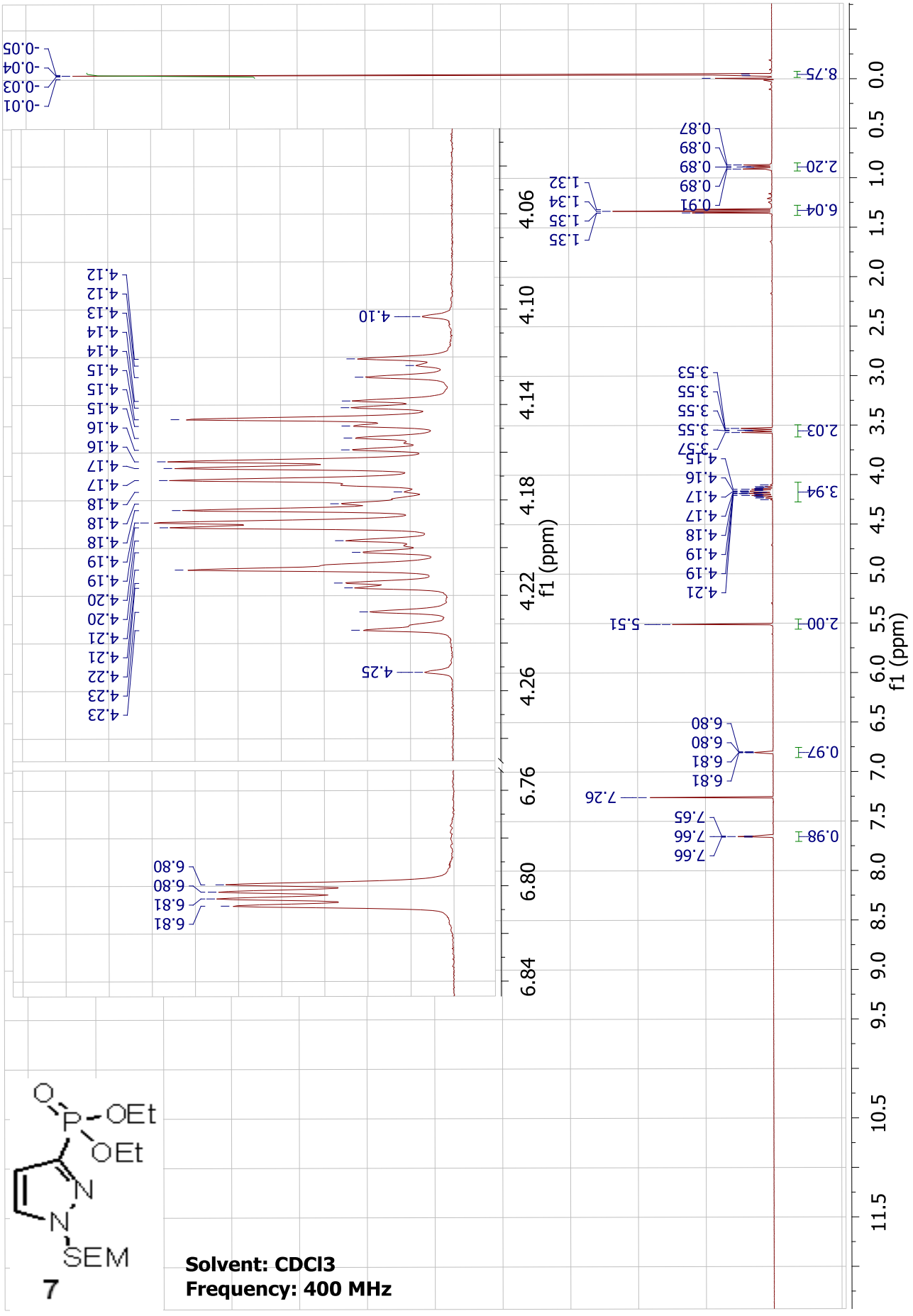

-1.37
16.39
16.45
17.87
62.16
62.21
67.45
80.50
108.19
110.38
135.05
135.28
142.56
142.70
f1 (ppm)
EtO
EtO
P
O
N
N
SEM
Solvent: CDCl3
Frequency: 100 MHz

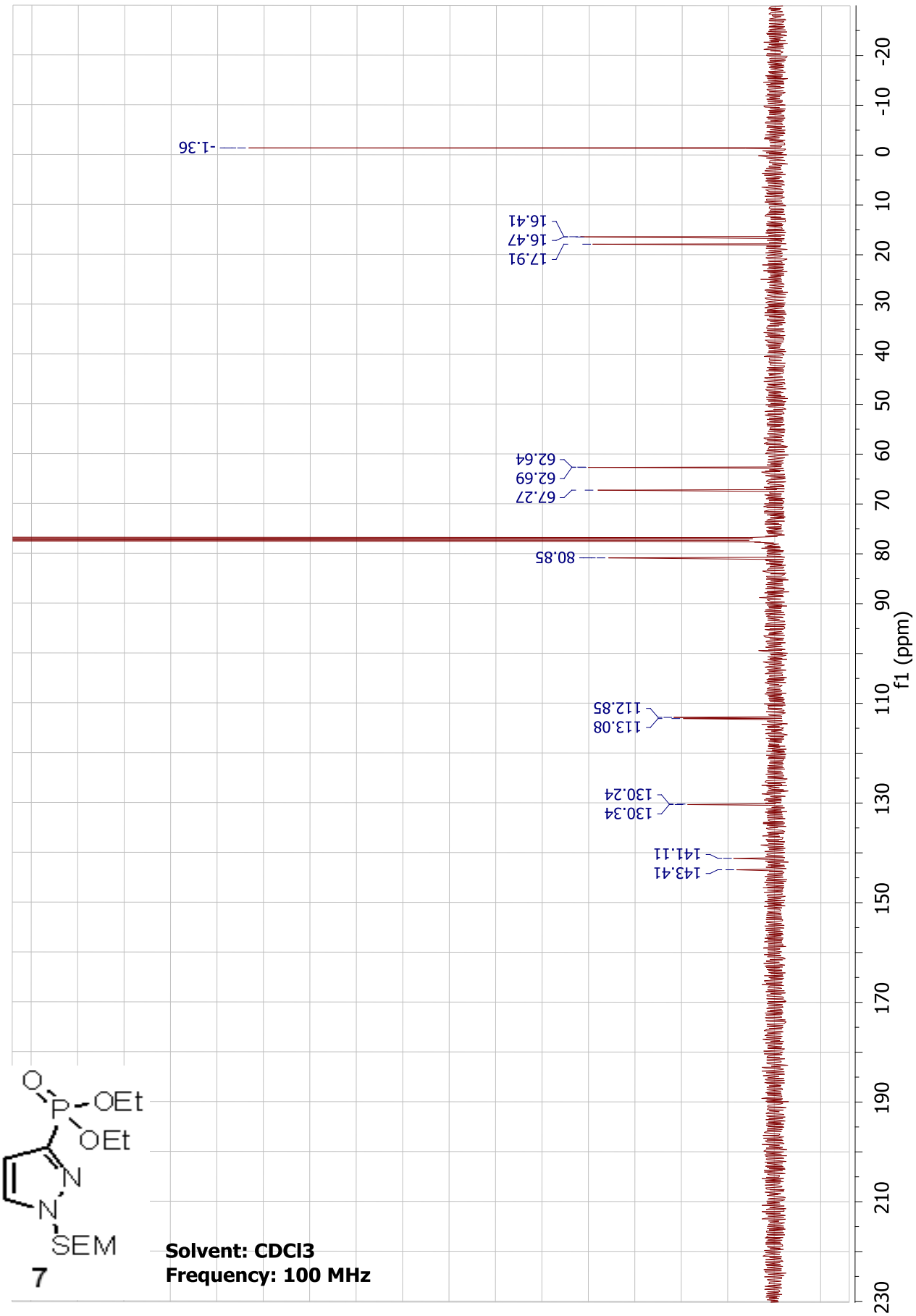
5

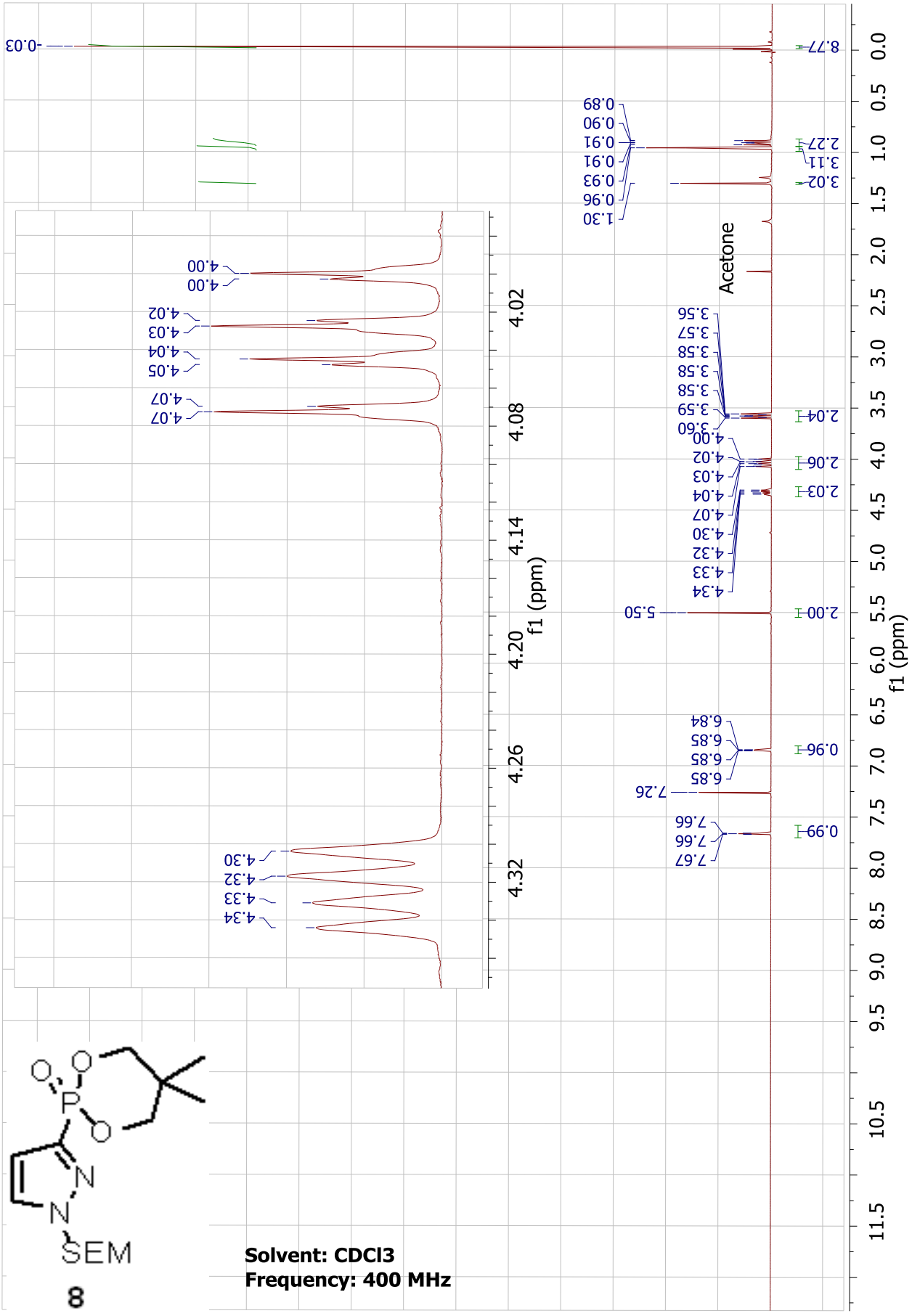

Solvent: CDCl3
Frequency: 400 MHz
f1 (ppm)
6

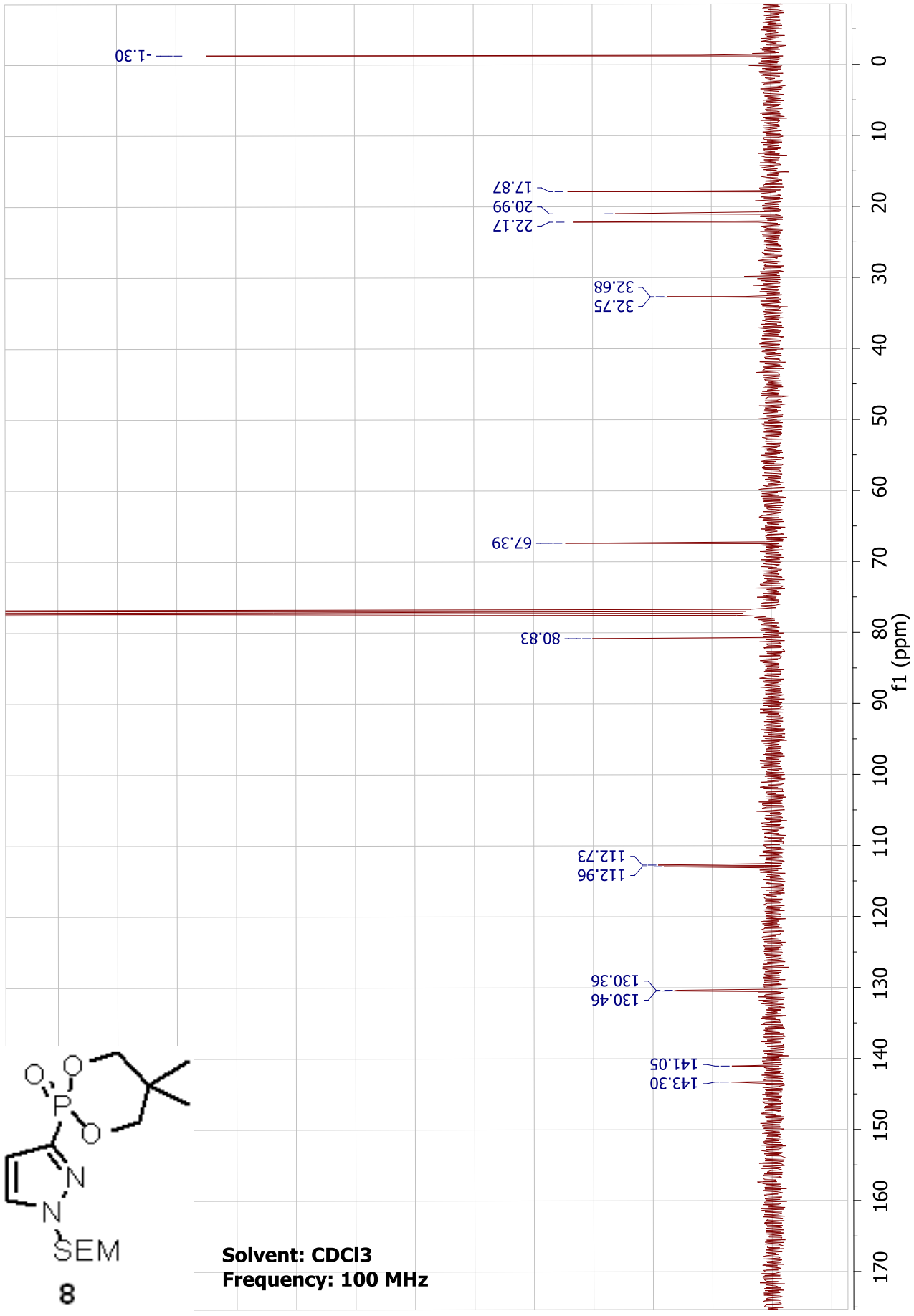

128.19
128.60
129.06
134.70
134.93
135.10
142.38
142.51
16.30
16.37
56.36
62.00
62.05
76.84
77.16
77.48
107.03
109.22
f1 (ppm)
Solvent: CDCl3
Frequency: 100 MHz
EtO
EtO
O
P
N
N
Bn

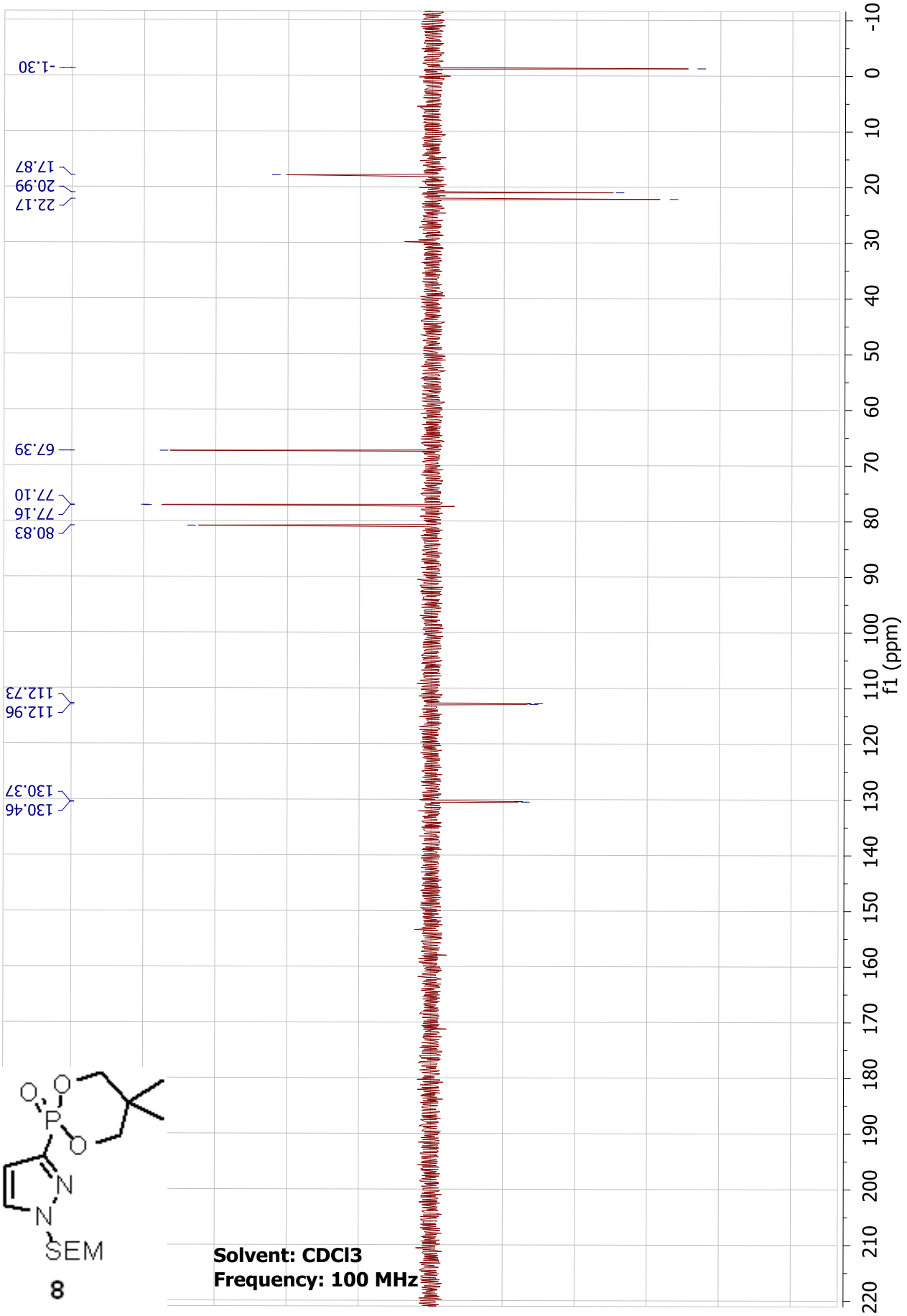
6


O
P
OEt
OEt
N
N
SEM
7
Solvent: CDCl3
Frequency: 400 MHz
f1 (ppm)

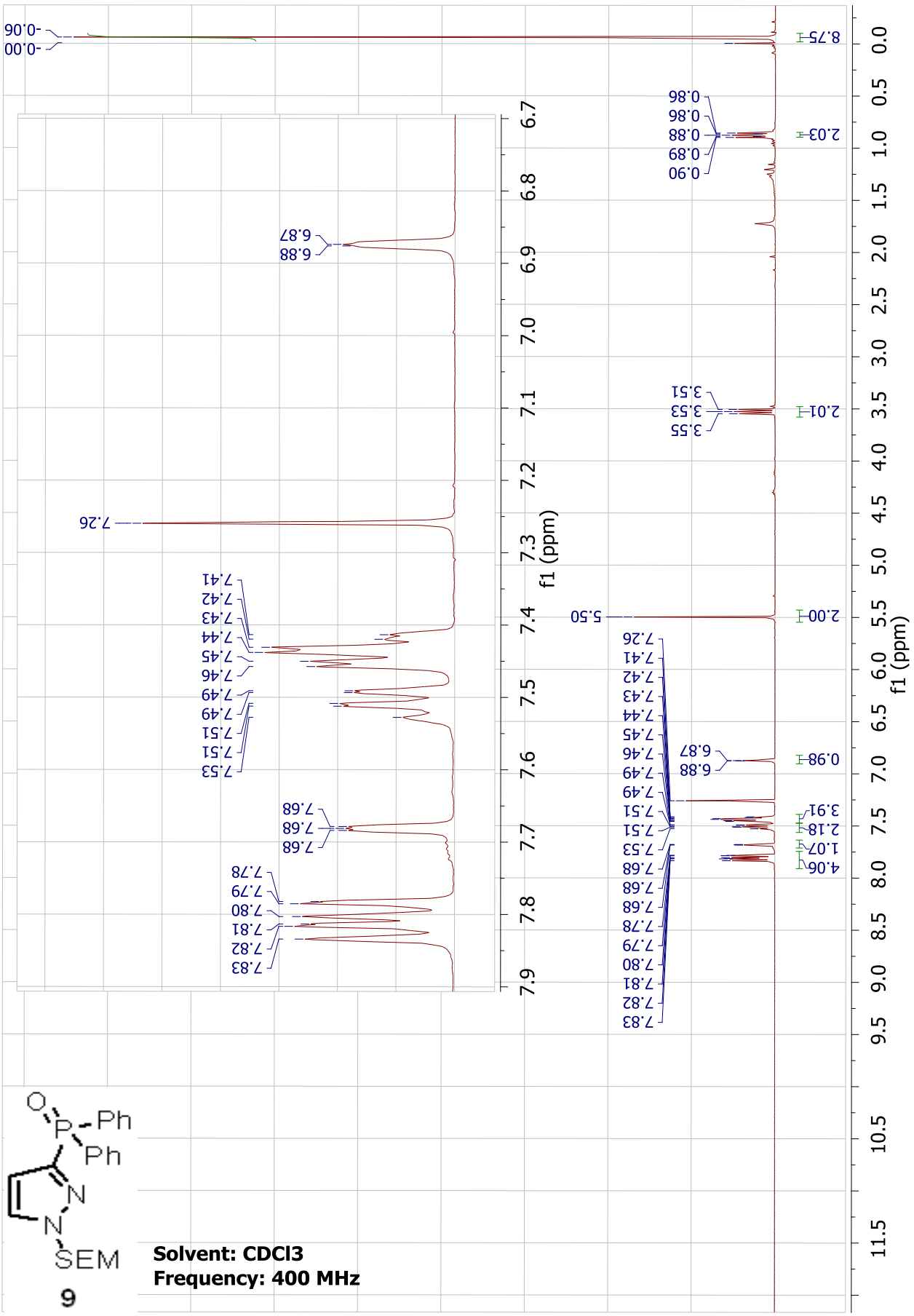

-1.36
16.41
16.47
17.91
62.64
62.69
67.27
80.85
112.85
113.08
130.24
130.34
141.11
143.41
f1 (ppm)
-20
-10
0
10
20
30
40
50
60
70
80
90
110
130
150
170
190
210
230
O
P
OEt
OEt
N
N
SEM
7
Solvent: CDCl3
Frequency: 100 MHz

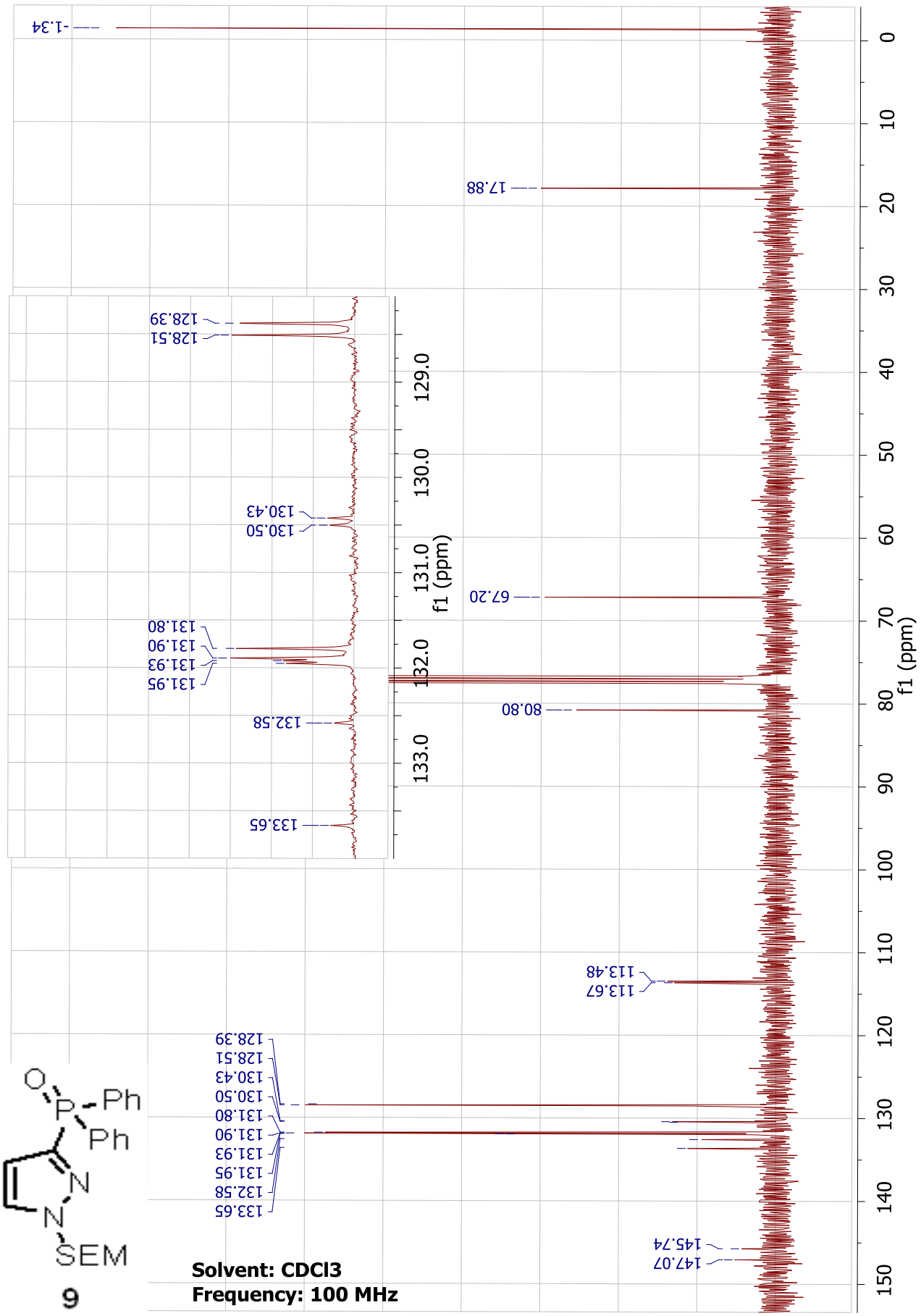

Acetone
f1 (ppm)
Solvent: CDCl3
Frequency: 400 MHz
SEM
8

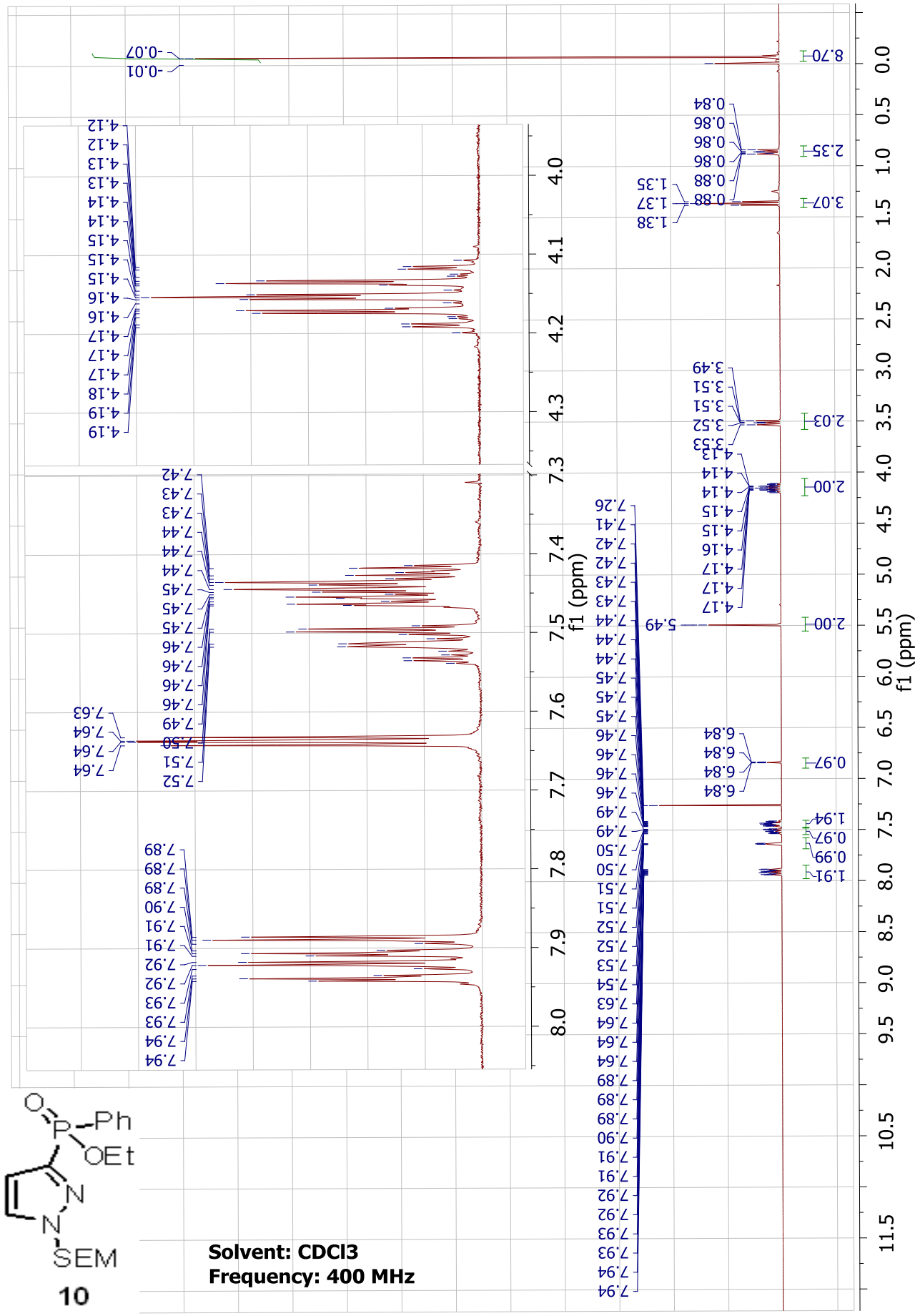

-1.30
17.87
20.99
22.17
32.68
32.75
67.39
80.83
112.73
112.96
130.36
130.46
141.05
143.30
f1 (ppm)
SEM
8
Solvent: CDCl3
Frequency: 100 MHz

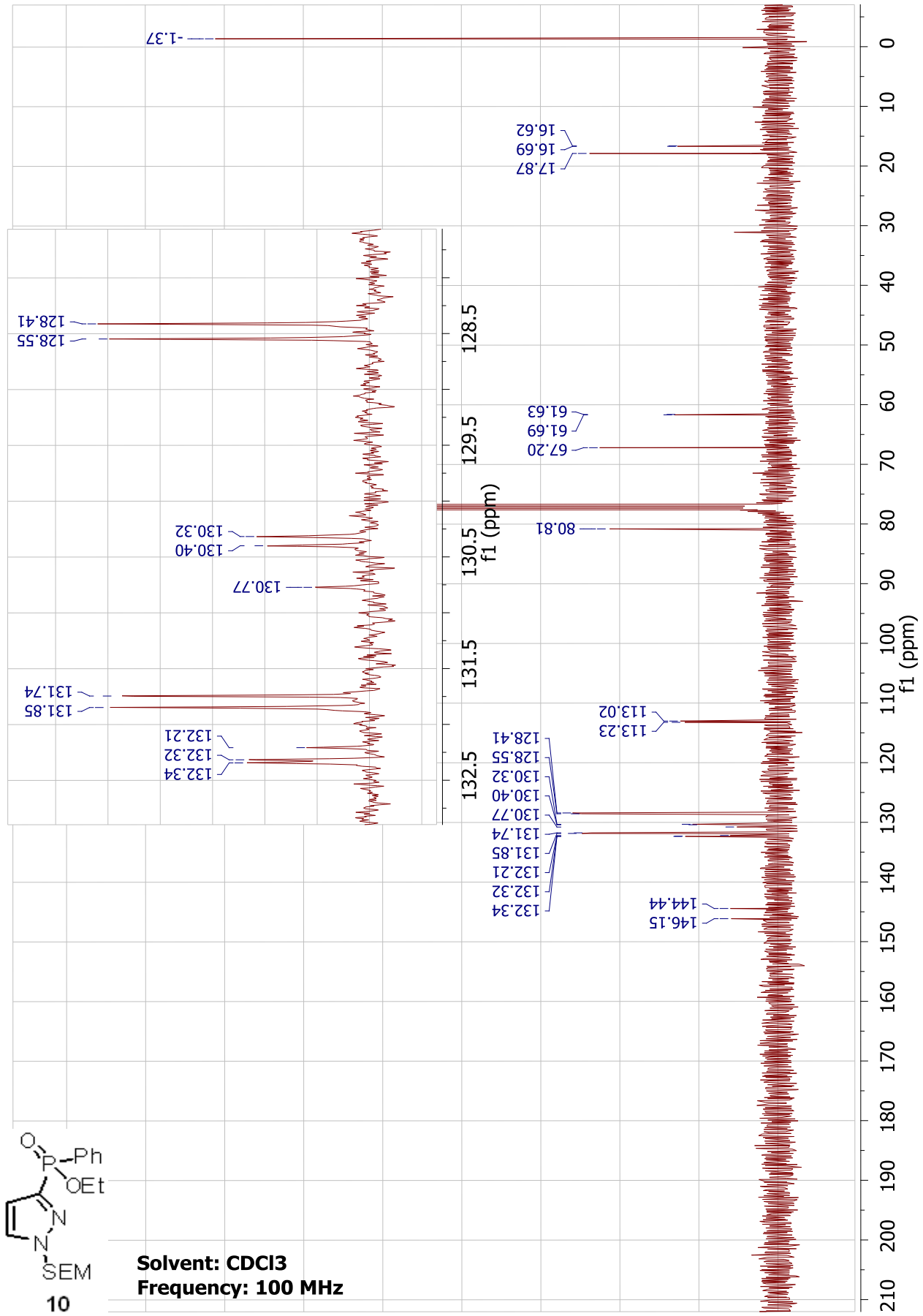

-1.30
17.87
20.99
22.17
67.39
77.10
77.16
80.83
112.73
112.96
130.37
130.46
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
f1 (ppm)
O
O
P
O
N
N
SEM
Solvent: CDCl3
Frequency: 100 MHz

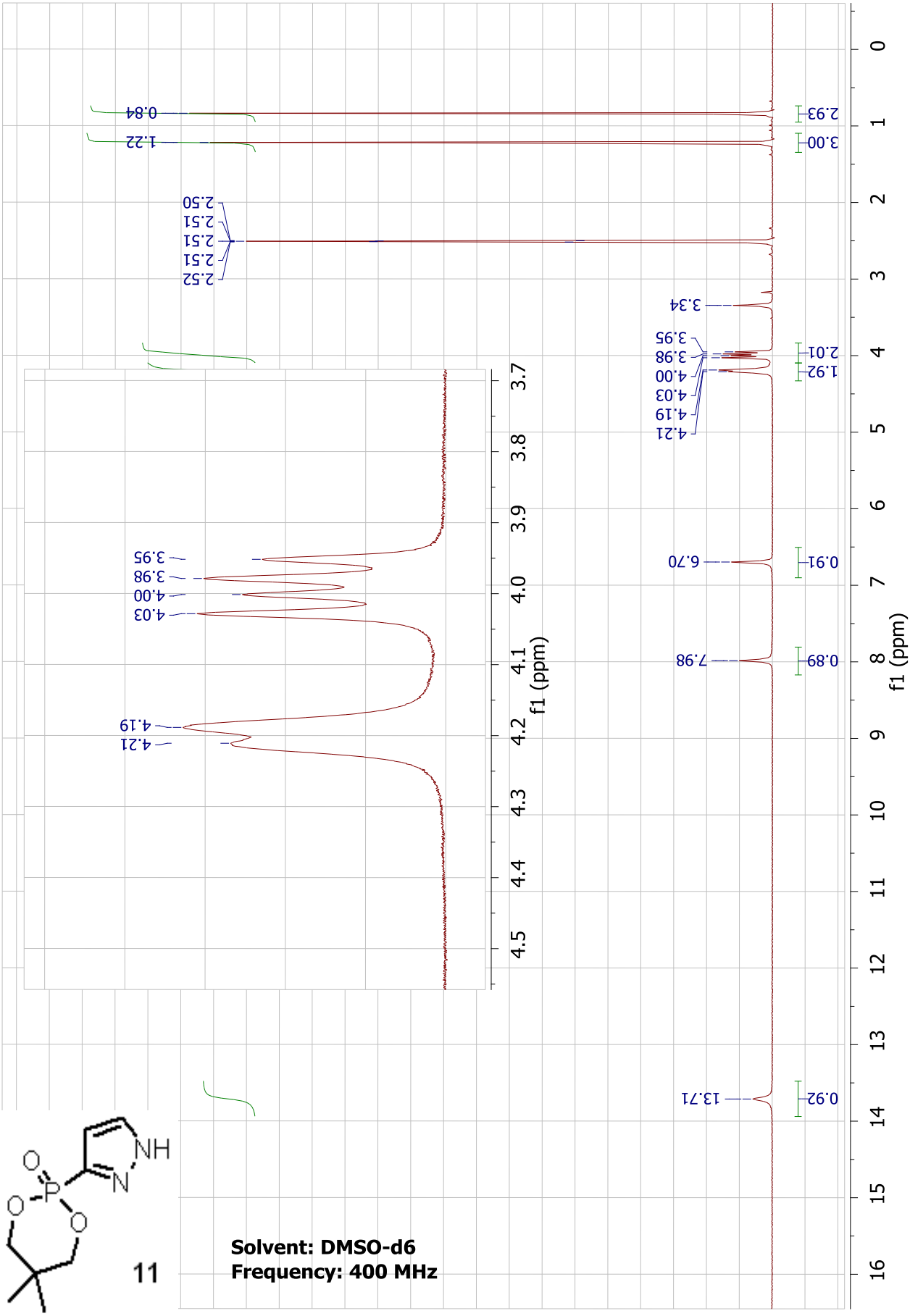
8

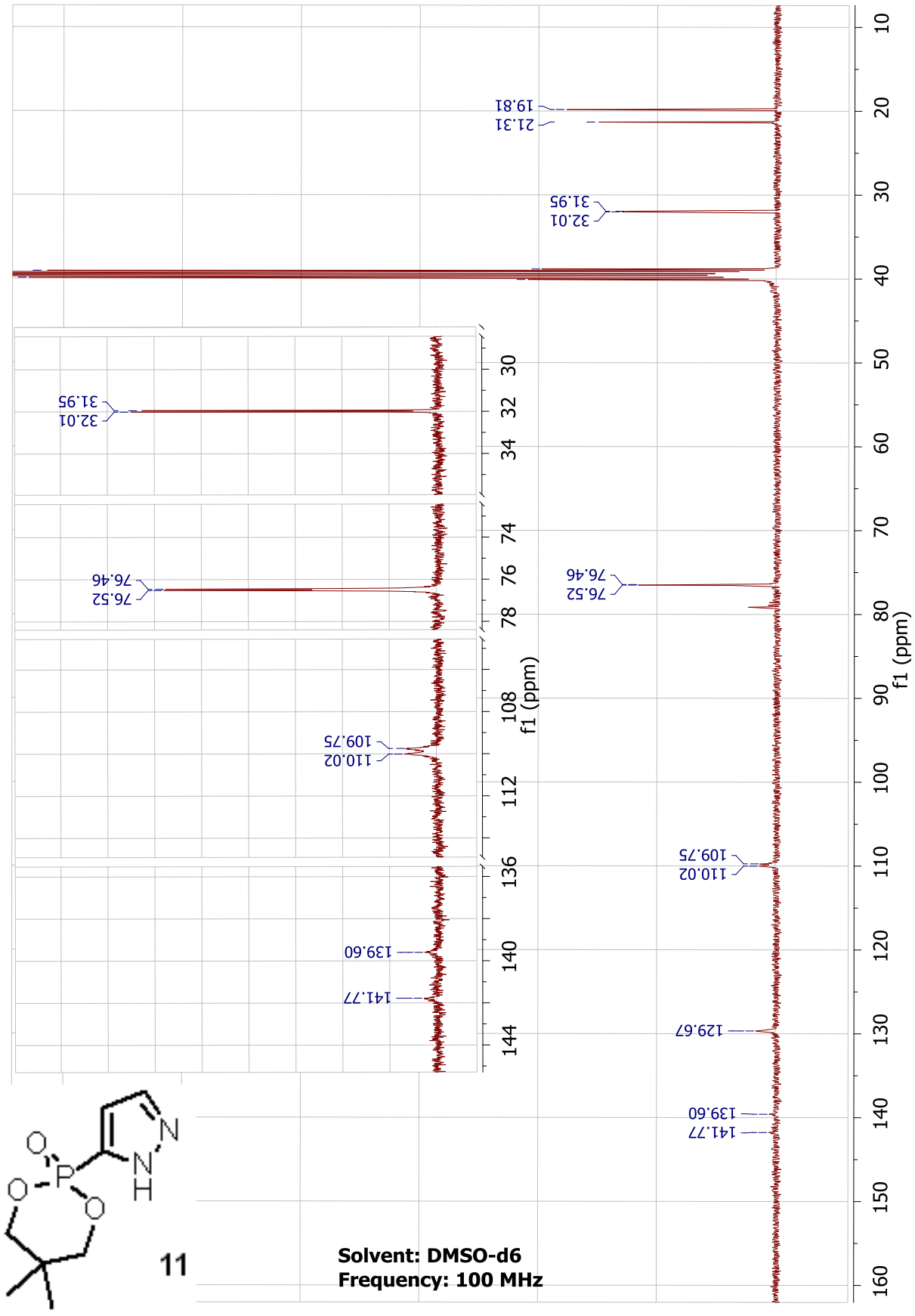

-0.06
-0.00
8.75
2.03
0.86
0.86
0.88
0.89
0.90
6.88
6.87
3.55
3.53
3.51
2.01
7.26
7.41
7.42
7.43
7.44
7.45
7.46
7.49
7.49
7.51
7.51
7.53
5.50
2.00
7.68
7.68
7.78
7.79
7.80
7.81
7.82
7.83
0.98
3.91
2.18
1.07
4.06
f1 (ppm)
f1 (ppm)
O
P
Ph
Ph
N
N
SEM
9
Solvent: CDCl3
Frequency: 400 MHz

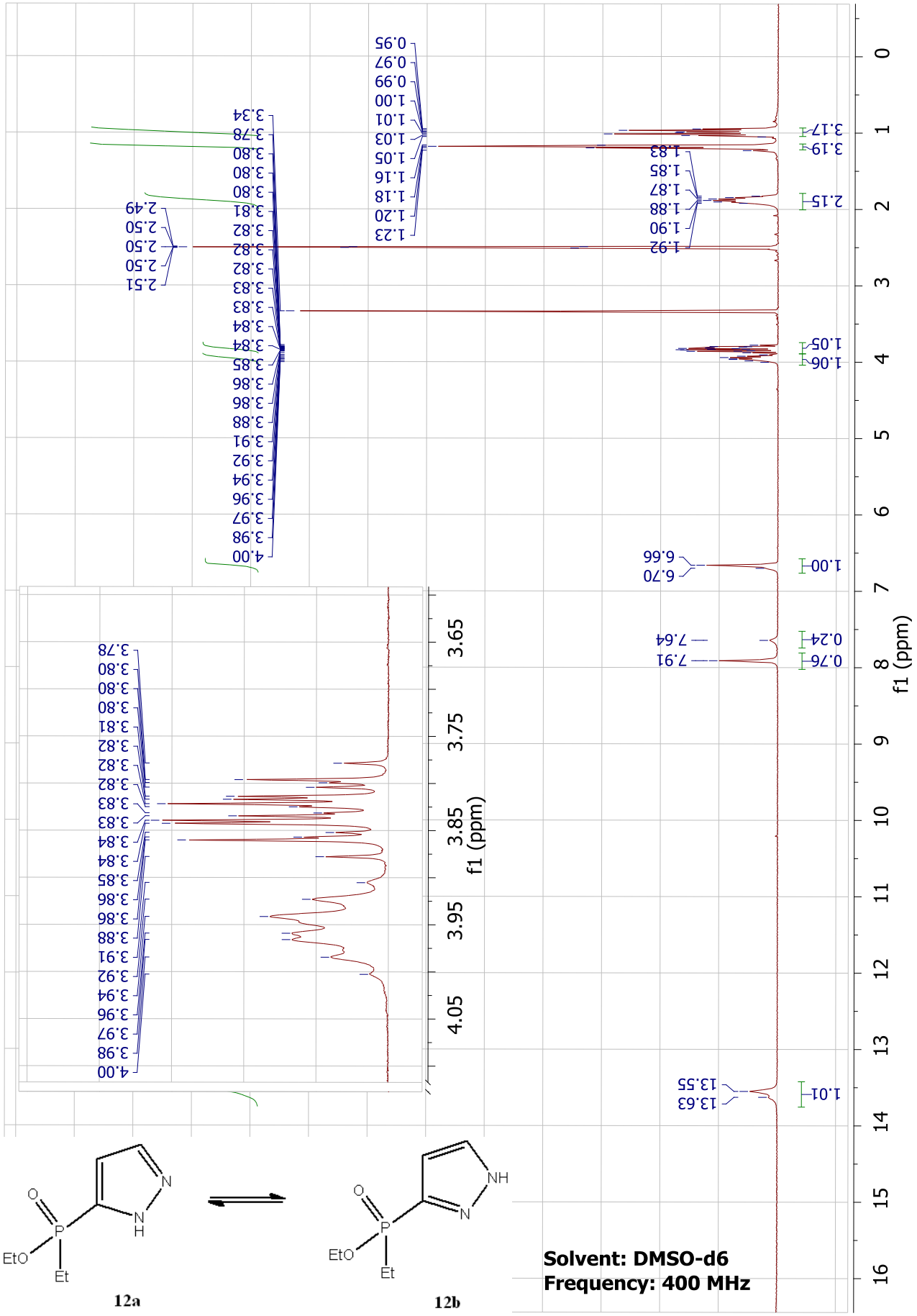

-1.34
17.88
67.20
80.80
113.67
113.48
128.39
128.51
130.43
130.50
131.80
131.90
131.93
131.95
132.58
133.65
145.74
147.07
f1 (ppm)
O
P
Ph
Ph
N
N
SEM
9
Solvent: CDCl3
Frequency: 100 MHz

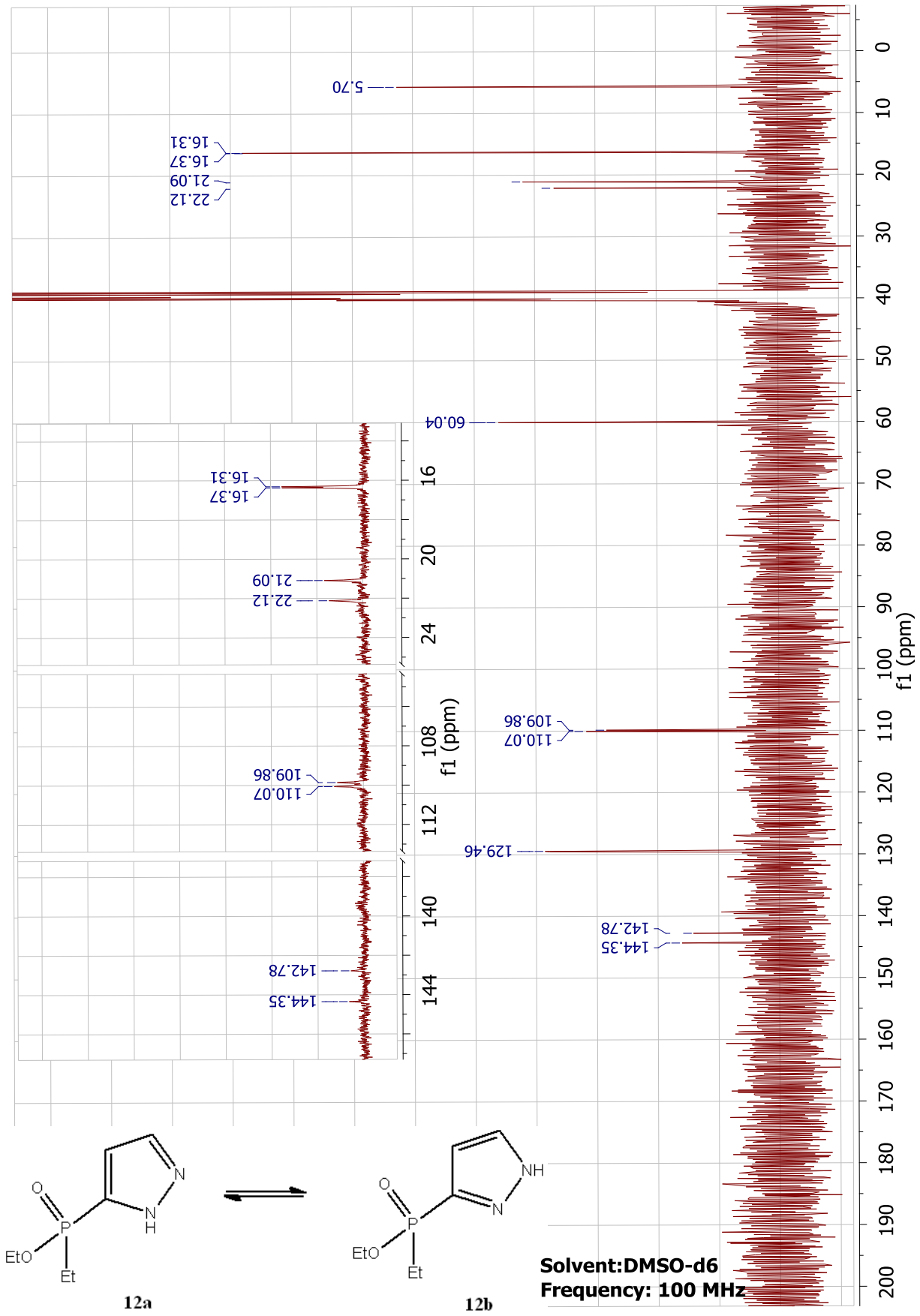

Solvent: CDCl3
Frequency: 400 MHz
10
f1 (ppm)


-1.37
16.62
16.69
17.87
61.63
61.69
67.20
80.81
113.02
113.23
128.41
128.55
130.32
130.40
130.77
131.74
131.85
132.21
132.32
132.34
144.44
146.15
f1 (ppm)
Ph
OEt
N
N
SEM
10
Solvent: CDCl3
Frequency: 100 MHz


0.84
1.22
2.50
2.51
2.51
2.51
2.52
3.34
3.95
3.98
4.00
4.03
4.19
4.21
6.70
7.98
13.71
2.93
3.00
2.01
1.92
0.91
0.89
0.92
f1 (ppm)
3.95
3.98
4.00
4.03
4.19
4.21
f1 (ppm)
NH
N
O
O
O
P
11
Solvent: DMSO-d6
Frequency: 400 MHz


19.81
21.31
31.95
32.01
76.46
76.52
109.75
110.02
129.67
139.60
141.77
f1 (ppm)
11
Solvent: DMSO-d6
Frequency: 100 MHz


Solvent: DMSO-d6
Frequency: 400 MHz
f1 (ppm)
12a
12b


5.70
16.31
16.37
21.09
22.12
60.04
109.86
110.07
129.46
142.78
144.35
f1 (ppm)
Solvent:DMSO-d6
Frequency: 100 MHz
12a
12b