Supplementary Material

Synthesis of nucleoside analogues using acyclic diastereoselective reactions

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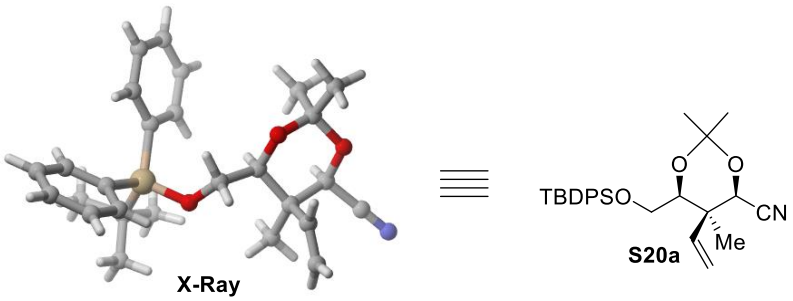
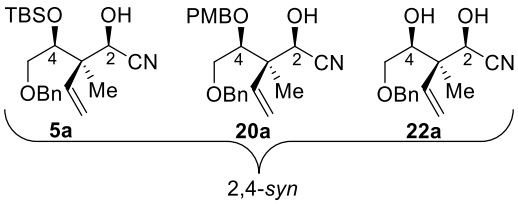
Part I. Stereochemical Proofs

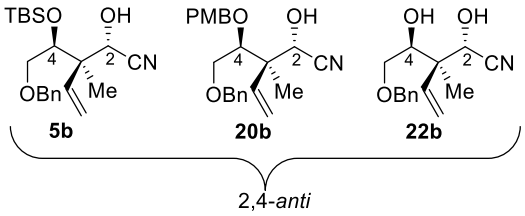
Diastereoselective Mukaiyama Aldol Reaction - The *anti*-stereochemistry of methyl ester **8a,b** obtained in the Mukaiyama aldol reaction was previously confirmed by our lab.[1]

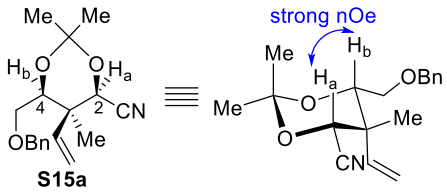
Diastereoselective Atom Transfer Cyclization - The *syn* stereochemistry of methyl ester **12** for the intramolecular vinyl transfer reaction was indirectly confirmed from the X-ray structure of acetonide **S20a**. See below for experimental procedures and full characterization of **S20a**. In addition, the stereochemistry for this transformation was confirmed in the final nucleoside analogues.



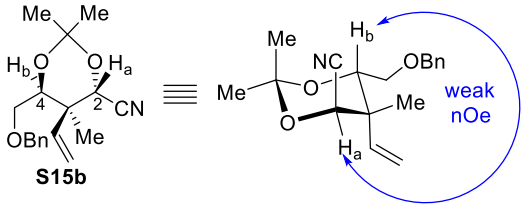
Diastereoselective Cyanation - The relative stereochemistry of the racemic cyanohydrins (Table 1) was determined by relevant nuclear Overhauser effect [nOe] enhancements and supported by ^{13}C NMR data. The two cyanohydrin diastereomers were separated, deprotected to the corresponding diols and then protected as an acetonide. See below for experimental procedures and full characterization. The relative stereochemistry of the *syn* and *anti* acetonides was determined from 1D NOESY and the ^{13}C chemical shifts of the acetal carbon and the gem-dimethyl substituents. According to Rychnovsky's study,[2] the difference in chemical shifts between the gem-dimethyl groups is an indicator of stereochemistry, with *syn* acetonides having a difference of >9 ppm (methyl shifts around 19 and 30 ppm) and *anti*-isomers showing a difference of <5 ppm (methyl shifts around 25 ppm). The chemical shift of the acetal carbon is also an indicator of the relative stereochemistry, with *syn*-acetonides having chemical shifts below 99.5 ppm and *anti*-acetals above 100.5 ppm. In Rychnovsky's study, some inconsistencies were observed in the presence of a nitrile substituent. In this study, the shift of the acetal carbon of all *syn* acetonides was around 100.5 ppm and around 102 ppm for *anti* acetonides. In addition, for substrates in which the gem-dimethyl groups of the acetonide could be clearly identified, the *syn* acetonides had a difference of 9 ppm between the methyl groups located around 19 and 30 ppm while the *anti* acetonides showed a difference of 5 ppm with methyl shifts around 25 ppm, consistent with Rychnovsky's study. Based on this and NOESY correlations, the proof of structures for cyanohydrins **5a,b**, **20a,b**, **22a,b**, **26a,b** and **28a,b** were determined.



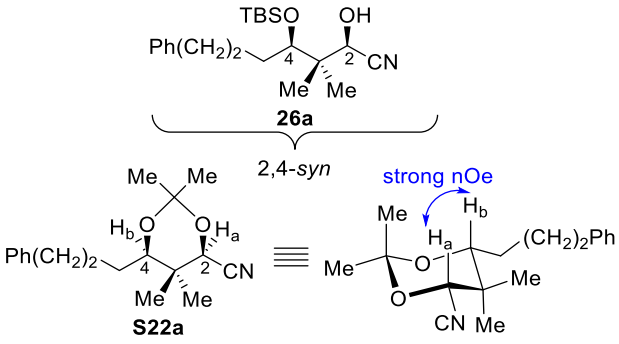




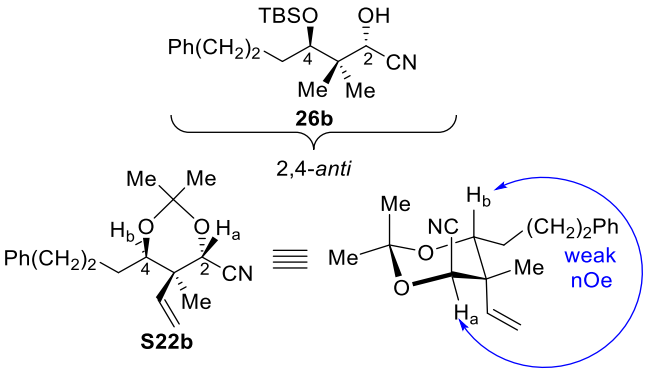
Acetal Carbon : 100.7 ppm
Gem-dimethyls: 29.5 and 18.8 ppm



Acetal Carbon : 102.4 ppm
Gem-dimethyls: 27.4 and 22.4 ppm

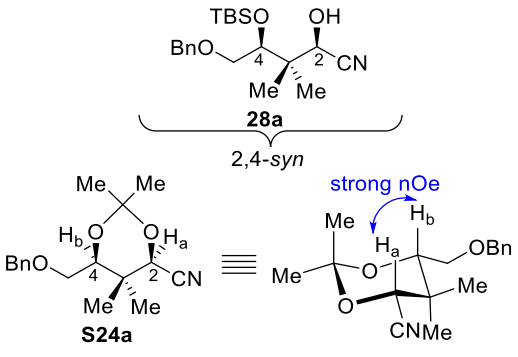


Acetal Carbon : 100.4 ppm

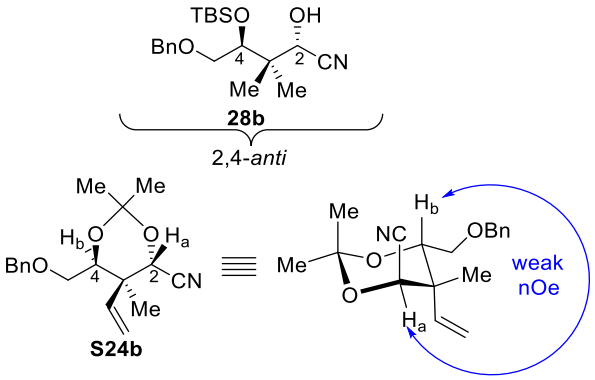


Acetal Carbon : 101.8 ppm

Chemical displacements of acetonide
gem-dimethyl substituents were difficult to identify.



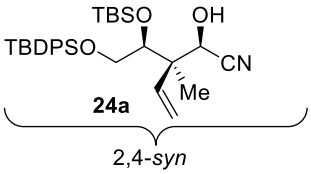
Acetal Carbon : 100.5 ppm

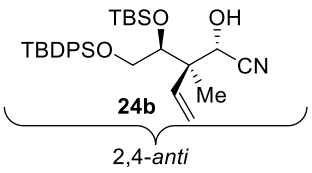


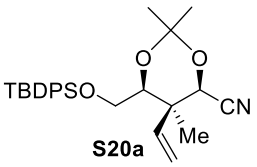
Acetal Carbon : 102.0 ppm

Chemical displacements of acetonide
gem-dimethyl substituents were difficult to identify.

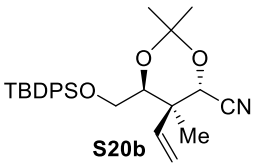
The proof of structure for cyanohydrins **24a,b** was determined through X-ray crystallography of the corresponding acetonide.



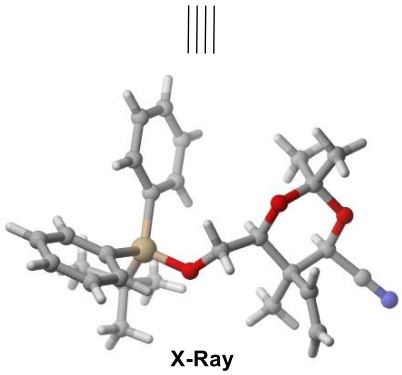




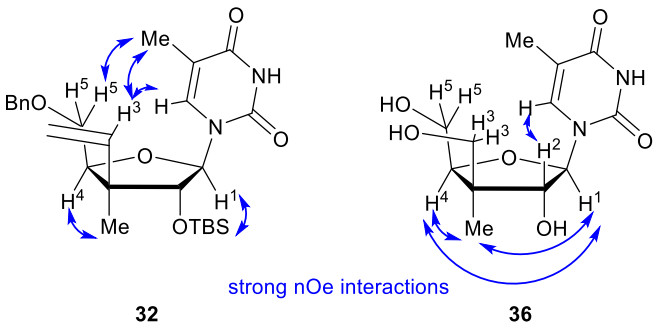
Acetal Carbon: 100.5 ppm
Gem-dimethyls: 29.4 and 18.7 ppm



Acetal Carbon: 102.4 ppm
Gem-dimethyls: 27.5 and 22.5 ppm

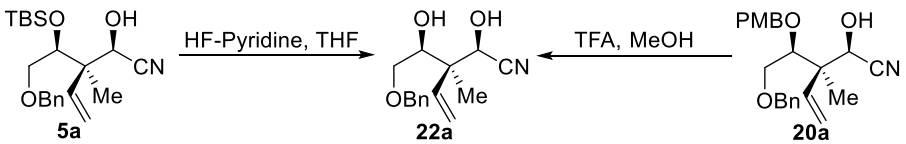


Diastereoselective Thioaminal Formation and Intramolecular Cyclization - Proof of structure for the protected nucleoside analogue **32** and the final deprotected analogue **36** was determined by 2D NOESY experiments thus confirming the 1,2-*syn* diastereoselectivity for nucleobase addition to the dithioacetal followed by O4'-C1 cyclization with inversion of configuration providing the 1',2'-*trans* nucleoside analogue.



32 **36**

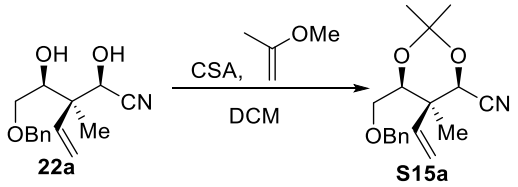
Cyanohydrins 5a,b, 20a,b and 22a,b:



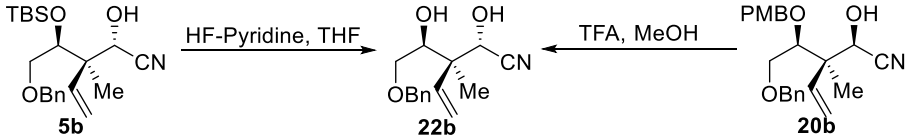
To a solution of cyanohydrin **5a** (24 mg, 0.064 mmol, 1.0 equiv.) in dry THF (0.64 mL, 0.10 M) at 0 °C, HF-pyridine (0.13 mL, 0.13 mmol, 2.0 mL/mmol) was added. The solution was warmed to room temperature and stirred overnight. An aqueous solution of $NaHCO_3$ was added and the aqueous layer extracted with Et_2O (3x). The organic layers were combined, dried with $MgSO_4$, filtered and concentrated in vacuo. Purification

by flash chromatography using 35:65 EtOAc:Hex provided **22a** (10 mg, 59% yield) as a clear oil. Characterization data for **22a** can be found in the experimental section.
Cyanohydrin **20a** was diluted in MeOH and a few drops of TFA were added. Concentration of the reaction mixture provided **22a**.

(±)-(4*R*,5*R*,6*S*)-6-(benzyloxymethyl)-2,2,5-trimethyl-5-vinyl-1,3-dioxane-4-carbonitrile (S15a):

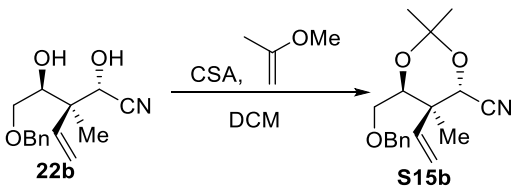


To a solution of diol **22a** (8.4 mg, 0.032 mmol, 1.0 equiv.) in dry CH_2Cl_2 (0.3 mL, 0.1 M) at 0 °C, 2-methoxypropene (12 µL, 0.13 mmol, 4.0 equiv.) and camphor sulfonic acid (1.5 mg, 0.0060 mmol, 0.20 equiv.) were added. The solution was stirred 15 minutes at 0 °C then warmed to room temperature for 45 minutes. An aqueous solution of NH_4Cl was added and the aqueous layer was extracted with Et_2O(3x). The organic layers were combined, dried with $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography using 20:80 EtOAc:Hex provided acetonide **S15a** as a clear oil (8.3 mg, 86% yield): R_f= 0.21 (20:80 EtOAc:Hex); Molecular Formula: $C_{18}H_{23}NO_3$; MW: 301.39; IR (neat) υ_{max} 2251 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H), 6.26 (dd, *J* 17.8, 11.0 Hz, 1H), 5.42 (d, *J* 11.0 Hz, 1H), 5.25 (d, *J* 17.8 Hz, 1H), 4.60 (s, 1H), 4.56 (d, *J* 12.1 Hz, 1H), 4.45 (d, *J* 12.1 Hz, 1H), 3.92 (dd, *J* 6.3, 3.6 Hz, 1H), 3.50 (dd, *J* 10.8, 3.6 Hz, 1H), 3.34 (dd, *J* 10.7, 6.3 Hz, 1H), 1.51 (s, 3H), 1.50 (s, 3H), 1.11 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.1, 134.0, 128.6, 127.9, 127.8, 118.7, 115.8, 100.7, 76.4, 73.6, 70.6, 70.4, 40.9, 29.5, 18.8, 17.0 ppm; HRMS calcd for $C_{18}H_{23}O_3NNa$ [M+Na$^+$]: 324.1570, found 324.1572 (+0.5 ppm).



To a solution of cyanohydrin **5b** (29 mg, 0.078 mmol, 1.0 equiv.) in dry THF (0.8 mL, 0.1 M) at 0 °C, HF-pyridine (0.16 mL, 0.16 mmol, 2.0 mL/mmol) was added. The solution was warmed to room temperature and stirred overnight. An aqueous solution of $NaHCO_3$ was added and the aqueous layer was extracted with Et_2O (3x). The organic layers were combined, dried with $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography using 35:65 EtOAc:Hex provided **22b** (12.7 mg, 63% yield) as a clear oil. Characterization data for **22b** can be found in the experimental section.
Cyanohydrin **20b** was diluted in MeOH and a few drops of TFA were added. Concentration of the reaction mixture provided **22b**.

(±)-(4*S*,5*R*,6*S*)-6-((benzyloxy)methyl)-2,2,5-trimethyl-5-vinyl-1,3-dioxane-4-carbonitrile (S15b):

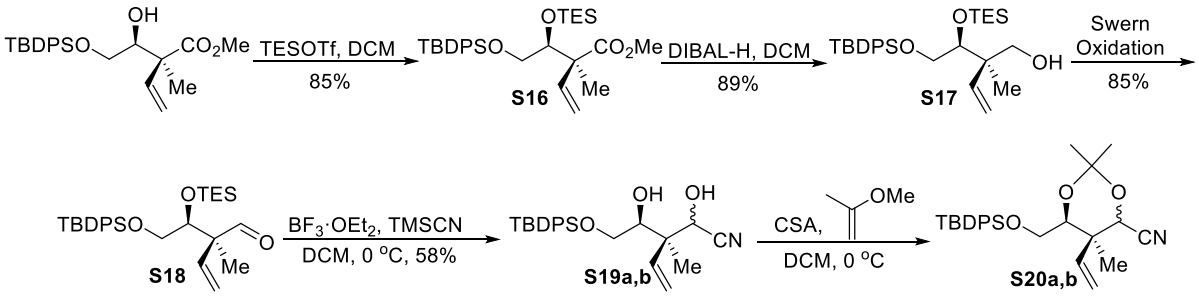


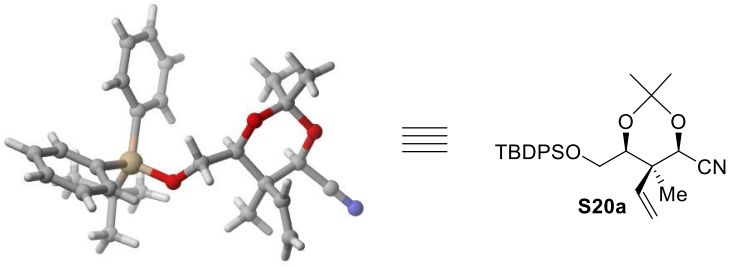
To a solution of diol **22b** (9.4 mg, 0.036 mmol, 1.0 equiv.) in dry CH_2Cl_2 (0.6 mL, 0.1 M) at 0 °C, 2-methoxypropene (14 µL, 0.14 mmol, 4.0 equiv.) and camphor sulfonic acid (1.7 mg, 0.0070 mmol, 0.20

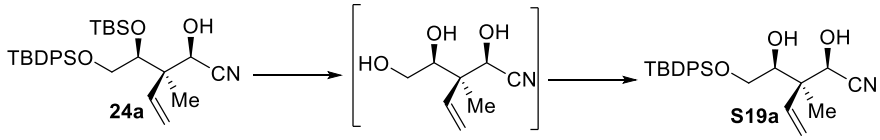
equiv.) were added. The solution was stirred for 15 minutes at 0 °C then warmed to room temperature for 45 minutes. An aqueous solution of NH_4Cl was added and the aqueous layer was extracted with Et_2O (3x). The organic layers were combined, dried with $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography using 20:80 EtOAc:Hex provided acetonide **S15b** as a clear oil (9.3 mg, 86% yield): R_f = 0.32 (20:80 EtOAc:Hex); Molecular Formula: $C_{18}H_{23}NO_3$; MW: 301.39; IR (neat) υ_{max} 2992, 2873, 1383 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 5H), 6.08 (dd, *J* 17.6, 11.0 Hz, 1H), 5.27 (d, *J* 10.9 Hz, 1H), 5.20 (d, *J* 17.6 Hz, 1H), 4.58 (d, *J* 12.1 Hz, 1H), 4.47 (d, *J* 12.1 Hz, 1H), 4.42 (s, 1H), 4.04 (dd, *J* 6.9, 3.7 Hz, 1H), 3.45 (dd, *J* 10.8, 3.7 Hz, 1H), 3.39 (dd, *J* 10.8, 7.0 Hz, 1H), 1.62 (s, 3H), 1.45 (s, 3H), 1.24 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.1, 136.6, 128.6, 127.8, 127.7, 117.29, 117.28, 102.4, 74.5, 73.5, 69.8, 68.4, 42.1, 27.4, 22.4, 17.8 ppm; HRMS calcd for $C_{18}H_{24}O_3NNa$ [M+H$^+$]: 302.17507, found 302.17510 (+0.1 ppm).

Cyanohydrins 24a,b:

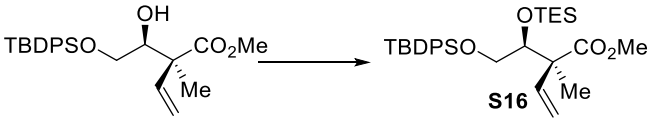
The relative stereochemistry of cyanohydrins **24a** and **24b** was determined by X-ray diffraction of *syn*-acetonide **S20a**. Acetonides **S20a,b** were obtained from the corresponding diols **S19a,b** resulting from cyanation of aldehyde **S18**. From this, the relative stereochemistry of cyanohydrin **24a** could be determined. Cleavage of the two silyl protecting groups of **24a** resulted in the corresponding triol. The primary alcohol was selectively protected providing **S19a** which corresponded to the diol with *syn* relative stereochemistry. The X-ray structure of **S20a** also confirms the relative 3,4-*syn* stereochemistry for the intramolecular vinyl transfer.





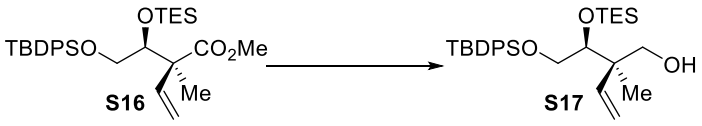


(±)-(*S*)-methyl 2-(S)-3,3-diethyl-9,9-dimethyl-8,8-diphenyl-4,7-dioxa-3,8-disiladecan-5-yl)-2-methylbut-3-enoate (S16):



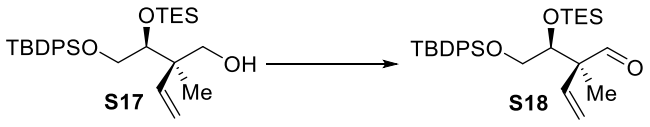
To a solution of (*S*)-methyl 2-((*S*)-2-((tert-butyldiphenylsilyl)oxy)-1-hydroxyethyl)-2-methylbut-3-enoate[3] (0.35 g, 0.84 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (28 mL, 0.10 M) at 0 °C, 2,6-lutidine (0.13 mL, 1.1 mmol, 1.3 equiv.) and TBSOTf (0.21 mL, 0.92 mmol, 1.2 equiv.) were added. The solution was stirred 4 hours at 0 °C. An aqueous solution of NH_4Cl was added to the reaction mixture and the aqueous layer was extracted with Et_2O (3x). The organic layers were combined, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography using 10:90 EtOAc:Hex provided protected ester **S16** as a clear oil (0.38 g, 85% yield): R_f = 0.5 (10:90 EtOAc:Hex); Molecular Formula: $C_{30}H_{46}O_4Si_2$; MW: 526.86; IR (neat) υ_{max} 1737 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.68 – 7.63 (m, 4H), 7.46 – 7.36 (m, 6H), 6.11 (dd, *J* 17.6, 10.8 Hz, 1H), 5.14 (dd, *J* 10.9, 1.0 Hz, 1H), 5.04 (dd, *J* 17.7, 1.0 Hz, 1H), 4.21 (t, *J* 5.6 Hz, 1H), 3.58 (s, 3H), 3.58 – 3.53 (m, 1H), 3.47 (dd, *J* 10.8, 5.6 Hz, 1H), 1.24 (s, 3H), 1.05 (s, 9H), 0.88 (t, *J* 8.0 Hz, 9H), 0.53 (q, *J* 7.8 Hz, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.1, 139.1, 135.83, 135.78, 133.44, 133.35, 129.82, 129.79, 127.80, 127.78, 114.8, 77.7, 66.5, 53.7, 52.0, 27.0, 19.3, 16.1, 7.0, 5.2 ppm; HRMS calcd for $C_{30}H_{47}O_4Si_2$ [M+H$^+$]: 527.3007, found 527.3010 (+0.4 ppm).

(±)-(*R*)-2-((S)-3,3-diethyl-9,9-dimethyl-8,8-diphenyl-4,7-dioxa-3,8-disiladecan-5-yl)-2-methylbut-3-en-1-ol (S17):



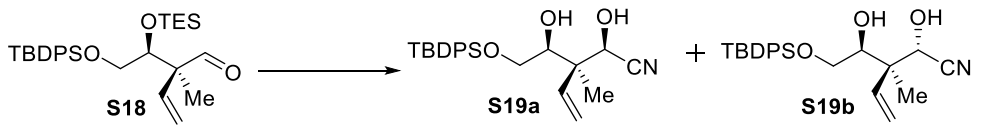
Following General Procedure A and purification by flash chromatography using 10:90 EtOAc:Hex, primary alcohol **S17** was obtained as a clear oil (0.47 g, 89% yield): R_f= 0.28 (10:90 EtOAc:Hex); Molecular Formula: $C_{29}H_{46}O_3Si_2$; MW: 498.85; IR (neat) υ_{max} 3454 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.68 – 7.64 (m, 4H), 7.47 – 7.35 (m, 6H), 5.83 (dd, *J* 17.7, 11.0 Hz, 1H), 5.04 (dd, *J* 11.0, 1.4 Hz, 1H), 4.98 (dd, *J* 17.7, 1.4 Hz, 1H), 3.76 – 3.69 (m, 2H), 3.61 (dd, *J* 10.9, 6.5 Hz, 1H), 3.54 (dd, *J* 10.0, 3.9 Hz, 1H), 3.50 (dd, *J* 10.9, 6.1 Hz, 1H), 2.72 (t, *J* 6.0 Hz, 1H), 1.06 (s, 9H), 1.04 (s, 3H), 0.89 (t, *J* 7.9 Hz, 9H), 0.56 (q, *J* 7.9 Hz, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.4, 135.9, 135.8, 133.2, 133.1, 129.92, 129.91, 127.86, 127.83, 114.5, 79.8, 68.7, 66.7, 45.8, 27.0, 19.3, 18.4, 7.0, 5.1 ppm; HRMS calcd for $C_{29}H_{47}O_3Si_2$ [M+H$^+$]: 499.3058, found 499.3057 (-0.3 ppm).

(±)-(*S*)-2-((S)-3,3-diethyl-9,9-dimethyl-8,8-diphenyl-4,7-dioxa-3,8-disiladecan-5-yl)-2-methylbut-3-enal (S18):



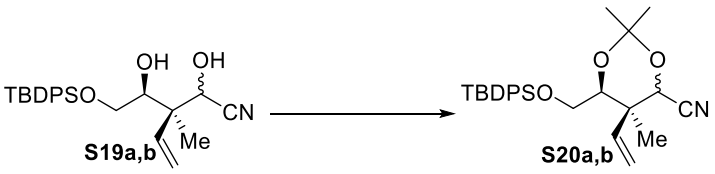
Following General Procedure B and purification by flash chromatography using 5:95 EtOAc:Hex provided aldehyde **S18** as a clear oil (0.35 g, 85 % yield): R_f = 0.28 (5:95 EtOAc:Hex); Molecular Formula: $C_{29}H_{44}O_3Si_2$; MW: 496.84; IR (neat) υ_{max} 1728 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.66 (s, 1H), 7.69 – 7.62 (m, 4H), 7.48 – 7.37 (m, 6H), 6.07 (dd, *J* 17.8, 10.9 Hz, 1H), 5.27 (dd, *J* 11.0, 0.9 Hz, 1H), 5.11 (dd, *J* 17.8, 0.9 Hz, 1H), 4.04 (dd, *J* 6.6, 4.7 Hz, 1H), 3.58 (dd, *J* 10.7, 6.6 Hz, 1H), 3.52 (dd, *J* 10.7, 4.7 Hz, 1H), 1.19 (s, 3H), 1.05 (s, 9H), 0.85 (t, *J* 7.9 Hz, 9H), 0.49 (q, *J* 7.9 Hz, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.7, 137.2, 135.82, 135.79, 133.04, 132.96, 129.9, 127.86, 127.85, one aromatic carbon missing, 117.1, 76.7, 65.6, 56.9, 26.9, 19.2, 14.3, 6.9, 5.1 ppm; HRMS calcd for $C_{29}H_{45}O_3Si_2$ [M+H$^+$]: 497.2902, found 497.2898 (-0.7 ppm).

(±)-(2*R*, 3*R*)-3-((*S*)-2-(*tert*-butyldiphenylsilyloxy)-1-hydroxyethyl)-2-hydroxy-3-methylpent-4-enenitrile (S19a) and (±)-(2*S*, 3*R*)-3-((*S*)-2-(*tert*-butyldiphenylsilyloxy)-1-hydroxyethyl)-2-hydroxy-3-methylpent-4-enenitrile (S19b):



To a solution of aldehyde **S18** (70 mg, 0.14 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (1.9 mL, 0.10 M) at 0 °C, $BF_3{\cdot}OEt_2$ (36 uL, 0.29 mmol, 1.5 equiv.) was added. The reaction mixture was stirred 5 minutes for precomplexation. TMSCN (51 µL, 0.38 mmol, 2.0 equiv.) was then added and the solution was stirred 1 hour at 0 °C. An aqueous solution of $NaHCO_3$ was poured into the reaction mixture and the aqueous layer was extracted with Et_2O (3x). The organic layers were combined, dried over $MgSO_4$, filtered and concentrated in vacuo. ^{1}H NMR spectroscopic analysis of the crude reaction indicated a ~1:2.5 mixture of 2,4-*syn* and *anti* diastereomers. Purification by flash chromatography using 25:75 EtOAc:Hex provided cyanohydrins **S19a** and **S19b** (33.1 mg, 58% yield) as clear oils. **S19a**: R_f = 0.27 (25:75 EtOAc:Hex); Molecular Formula: $C_{24}H_{31}NO_3Si$; MW: 409.60; IR (neat) υ_{max} 3436, 2248 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 – 7.60 (m, 4H), 7.50 – 7.37 (m, 6H), 6.07 (dd, *J* 17.7, 11.0 Hz, 1H), 5.35 (dd, *J* 11.0, 0.8 Hz, 1H), 5.20 (dd, *J* 17.7, 0.9 Hz, 1H), 4.65 (d, *J* 4.0 Hz, 1H), 3.84 (ddd, *J* 8.4, 3.8, 2.0 Hz, 1H), 3.67 (dd, *J* 10.5, 3.9 Hz, 1H), 3.64 (d, *J* 3.9 Hz, 1H), 3.58 (dd, *J* 10.5, 8.4 Hz, 1H), 2.98 (d, *J* 2.0 Hz, 1H), 1.07 (s, 9H), 1.01 (s, 3H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 135.62, 135.60, 135.2, 132.5, 130.3, 130.2, 128.11, 128.08, one aromatic carbon missing, 119.2, 118.1, 76.5, 68.7, 64.2, 46.7, 26.9, 19.3, 15.8 ppm; HRMS calcd for $C_{24}H_{32}O_3NSi$ [M+H$^+$]: 410.2146, found 410.2147 (+0.3 ppm). S19b: R_f = 0.23 (25:75 EtOAc:Hex); IR (neat) υ_{max} 3437, 2247 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 – 7.60 (m, 4H), 7.49 – 7.38 (m, 6H), 6.09 (dd, *J* 17.7, 11.0 Hz, 1H), 5.26 (d, *J* 11.0 Hz, 1H), 5.14 (d, *J* 17.7 Hz, 1H), 4.39 (d, *J* 9.4 Hz, 1H), 4.36 (d, *J* 9.2 Hz, 1H), 4.09 (ddd, *J* 9.1, 3.4, 1.8 Hz, 1H), 3.63 (dd, *J* 10.4, 3.3 Hz, 1H), 3.53 (dd, *J* 10.4, 9.0 Hz, 1H), 3.19 (d, *J* 1.8 Hz, 1H), 1.07 (s, 9H), 0.98 (s, 3H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 135.61, 135.58, 135.4, 132.6, 132.5, 130.3, 130.2, 128.11, 128.08, 118.7, 117.8, 76.2, 70.7, 64.2, 45.1, 27.0, 19.3, 16.6 ppm; HRMS calcd for $C_{24}H_{31}O_3NSiNa$ [M+Na$^+$]: 432.1965, found 432.1964 (-0.4 ppm).

(±)-(4*R*, 5*R*, 6*S*)-6-((*tert*-butyldiphenylsilyloxy)methyl)-2,2,5-trimethyl-5-vinyl-1,3-dioxane-4-carbonitrile (S20a) and (±)-(4*S*, 5*R*, 6*S*)-6-((*tert*-butyldiphenylsilyloxy)methyl)-2,2,5-trimethyl-5-vinyl-1,3-dioxane-4-carbonitrile (S20b):

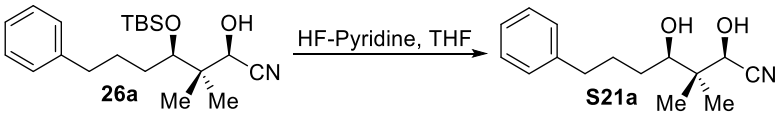


To a solution of diol **S19a,b** (33 mg, 0.081 mmol, 1.0 equiv.) in dry CH_2Cl_2 (0.8 mL, 0.1 M) at 0 °C, 2-methoxypropene (31 µL, 0.32 mmol, 4.0 equiv.) and camphor sulfonic acid (4.0 mg, 0.016 mmol, 0.20 equiv.) were added. The solution was stirred for 15 minutes at 0 °C then warmed to room temperature for 45 minutes. An aqueous solution of NH_4Cl was added and the aqueous layer was extracted with Et_2O (3x). The organic layers were combined, dried with $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography using 10:90 EtOAc:Hex provided acetonide **S20a,b** (39.5 mg, quantitative yield). **S20a**: R_f = 0.23 (10:90 EtOAc:Hex); Molecular Formula: $C_{27}H_{35}NO_3Si$; MW: 449.67; IR (neat) υ_{max} 3072, 2995, 2884, 1109 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 – 7.63 (m, 4H), 7.47 – 7.35 (m, 6H), 6.17 (dd, *J* 17.8, 11.0 Hz, 1H), 5.35

(dd, *J* 11.0, 1.0 Hz, 1H), 5.18 (dd, *J* 17.8, 1.0 Hz, 1H), 4.51 (s, 1H), 3.74 (dd, *J* 6.5, 4.0 Hz, 1H), 3.68 (dd, *J* 11.3, 4.0 Hz, 1H), 3.55 (dd, *J* 11.3, 6.5 Hz, 1H), 1.47 (s, 3H), 1.45 (s, 3H), 1.05 (s, 9H), 0.99 (s, 3H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 135.8, 135.7, 134.0, 133.6, 133.3, 129.91, 129.86, 127.80, 127.76, 118.5, 115.8, 100.5, 77.6, 70.5, 64.1, 40.7, 29.4, 26.9, 19.3, 18.7, 16.8 ppm; HRMS calcd for $C_{27}H_{36}O_3NSi$ [M+H$^+$]: 450.2459, found 450.2451 (-1.8 ppm). **S20b**: R_f = 0.30 (10:90 EtOAc:Hex); IR (neat) υ_{max} 3072, 2994, 2887, 2859, 1109 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 – 7.66 (m, 4H), 7.49 – 7.36 (m, 6H), 6.01 (ddd, *J* 17.7, 10.9, 1.1 Hz, 1H), 5.19 (d, *J* 10.9 Hz, 1H), 5.13 (d, *J* 17.6 Hz, 1H), 4.37 (s, 1H), 3.87 (ddd, *J* 5.8, 4.4, 1.2 Hz, 1H), 3.65 – 3.56 (m, 2H), 1.59 (s, 3H), 1.44 (s, 3H), 1.11 (s, 3H), 1.07 (s, 9H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 136.7, one aromatic carbon missing, 136.0, 133.7, 133.5, 130.2, 130.1, 128.1, 128.0, 117.5, 117.3, 102.4, 76.1, 68.6, 63.7, 42.0, 27.5, 27.1, 22.5, 19.5, 17.8 ppm; HRMS calcd for $C_{27}H_{36}O_3NSi$ [M+H$^+$]: 450.2459, found 450.2451 (-1.8 ppm).

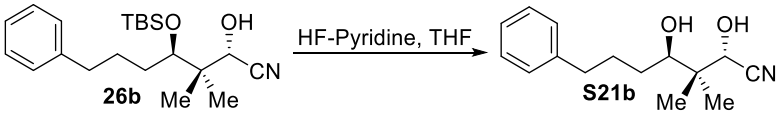
Cyanohydrins 26a,b:

(±)-(2*R*,4*R*)-2,4-dihydroxy-3,3-dimethyl-7-phenylheptanenitrile (S21a):



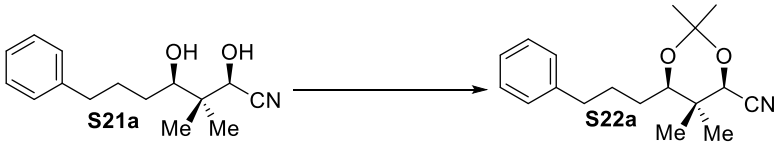
To a solution of cyanohydrin **26a** (75 mg, 0.21 mmol, 1.0 equiv.) in dry THF (2 mL, 0.1 M) at 0 °C, HF-pyridine (0.42 mL, 2.0 mL/mmol) was added. The solution was warmed to room temperature and stirred overnight. An aqueous solution of $NaHCO_3$ was added and the aqueous layer extracted with Et_2O (3x). The organic layers were combined, dried with $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography using 35:65 EtOAc:Hex provided **S21a** as a clear oil (36 mg, 70 % yield): R_f = 0.19 (35:65 EtOAc:Hex); Molecular Formula: $C_{15}H_{21}NO_2$; MW: 247.34; IR (neat) υ_{max} 3442, 2245 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 2H), 7.23 – 7.16 (m, 3H), 4.48 (d, *J* 3.2 Hz, 1H), 3.96 (s, 1H), 3.60 (ddd, *J* 10.6, 5.0, 1.8 Hz, 1H), 2.74 – 2.59 (m, 2H), 2.18 (s, 1H), 1.93 – 1.80 (m, 1H), 1.73 – 1.57 (m, 2H), 1.54 – 1.40 (m, 1H), 1.07 (s, 3H), 0.99 (s, 3H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 142.0, 128.6, 128.5, 126.1, 119.0, 78.3, 70.5, 41.7, 35.7, 31.4, 28.3, 21.6, 16.0 ppm; HRMS calcd for $C_{15}H_{22}O_2N$ [M+H$^+$]: 248.1645, found 248.1655 (+3.9 ppm).

(±)-(2*S*,4*R*)-2,4-dihydroxy-3,3-dimethyl-7-phenylheptanenitrile (S21b):



To a solution of cyanohydrin **26b** (29 mg, 0.079 mmol, 1.0 equiv.) in dry THF (0.8 mL, 0.1 M) at 0 °C, HF-pyridine (0.16 mL, 2.0 mL/mmol) was added. The solution was warmed to room temperature and stirred overnight. An aqueous solution of $NaHCO_3$ was added and the aqueous layer extracted with Et_2O (3x). The organic layers were combined, dried with $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography using 35:65 EtOAc:Hex provided **S21b** as a clear oil (14 mg, 70 % yield): R_f = 0.19 (35:65 EtOAc:Hex); Molecular Formula: $C_{15}H_{21}NO_2$; MW: 247.34; IR (neat) υ_{max} 3426, 2243 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (t, *J* 7.5 Hz, 2H), 7.23 – 7.15 (m, 3H), 4.53 (d, *J* 8.7 Hz, 1H), 4.25 (d, *J* 8.6 Hz, 1H), 3.93 (ddd, *J* 10.6, 4.5, 1.9 Hz, 1H), 2.75 – 2.60 (m, 2H), 2.15 (s, 1H), 1.92 – 1.82 (m, 1H), 1.73 – 1.61 (m, 1H), 1.60 – 1.52 (m, 1H), 1.50 – 1.39 (m, 1H), 1.04 (s, 3H), 1.00 (s, 3H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 141.8, 128.6, 128.5, 126.2, 119.3, 77.7, 71.9, 40.9, 35.7, 31.3, 28.0, 22.1, 17.8 ppm; HRMS calcd for $C_{15}H_{22}O_2N$ [M+H$^+$]: 248.1645, found 248.1650 (+2.0 ppm).

(±)-(4*R*,6*R*)-2,2,5,5-tetramethyl-6-(3-phenylpropyl)-1,3-dioxane-4-carbonitrile (S22a):



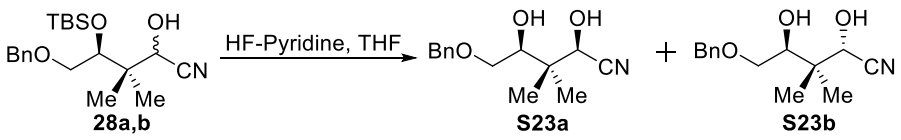
To a solution of diol **S21a** (18.7 mg, 0.0760 mmol, 1.00 equiv.) in dry CH_2Cl_2 (0.8 mL, 0.1 M) at 0 °C, 2-methoxypropene (30 µL, 0.30 mmol, 4.0 equiv.) and camphor sulfonic acid (4 mg, 0.02 mmol, 0.2 equiv.) were added. The solution was stirred for 15 minutes at 0 °C then warmed to room temperature for 45 minutes. An aqueous solution of NH_4Cl was added and the aqueous layer was extracted with Et_2O (3x). The organic layers were combined, dried with $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography using 10:90 EtOAc:Hex provided acetonide **S22a** as a clear oil (22.1 mg, quantitative yield): R_f = 0.38 (10:90 EtOAc:Hex); Molecular Formula: $C_{18}H_{25}NO_2$; MW: 287.40; IR (neat) υ_{max} 2250 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.22 – 7.15 (m, 3H), 4.41 (s, 1H), 3.47 (dd, *J* 9.6, 2.0 Hz, 1H), 2.66 – 2.55 (m, 2H), 1.89 – 1.80 (m, 1H), 1.60 – 1.45 (m, 3H), 1.44 (s, 3H), 1.41 (s, 3H), 1.14 (s, 3H), 0.91 (s, 3H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 142.4, 128.5, one aromatic carbon missing, 126.0, 116.5, 100.4, 77.0, 70.9, 36.1, 35.9, 29.7, 28.9, 28.3, 21.1, 18.8, 14.7 ppm; HRMS calcd for $C_{18}H_{26}O_2N$ [M+H$^+$]: 288.1958, found 288.1962 (+1.3 ppm).

(±)-(4*S*,6*R*)-2,2,5,5-tetramethyl-6-(3-phenylpropyl)-1,3-dioxane-4-carbonitrile (S22b):

To a solution of diol **S21b** (14 mg, 0.055 mmol, 1.0 equiv.) in dry CH_2Cl_2 (0.6 mL, 0.1 M) at 0 °C, 2-methoxypropene (21 µL, 0.22 mmol, 4.0 equiv.) and camphor sulfonic acid (3.0 mg, 0.011 mmol, 0.20 equiv.) were added. The solution was stirred for 15 minutes at 0 °C then warmed to room temperature for 45 minutes. An aqueous solution of NH_4Cl was added and the aqueous layer was extracted with Et_2O (3x). The organic layers were combined, dried with $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography using 10:90 EtOAc:Hex provided acetonide **S22b** as a clear oil (15.8 mg, quantitative yield): R_f = 0.5 (10:90 EtOAc:Hex); Molecular Formula: $C_{18}H_{25}NO_2$; MW: 287.40; IR (neat) υ_{max} 3061, 2991, 2943, 2866, 2991 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29 (t, *J* 7.6 Hz, 2H), 7.22 – 7.16 (m, 3H), 4.27 (s, 1H), 3.75 (dd, *J* 9.9, 2.5 Hz, 1H), 2.64 (t, *J* 7.9 Hz, 2H), 1.92 – 1.81 (m, 1H), 1.65 – 1.60 (m, 1H), 1.58 (s, 3H), 1.51 – 1.42 (m, 2H), 1.40 (s, 3H), 1.05 (s, 3H), 1.01 (s, 3H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 142.3, 128.53, 128.51, 126.0, 118.4, 101.8, 74.2, 70.3, 36.4, 35.9, 28.6, 28.4, 28.2, 22.2, 21.9, 19.2 ppm; HRMS calcd for $C_{18}H_{26}O_2N$ [M+H$^+$]: 288.1958, found 288.1959 (+0.4 ppm).

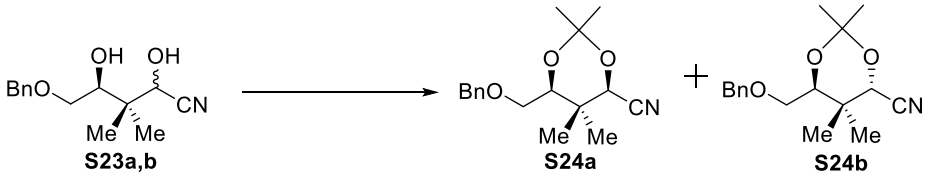
Cyanohydrins 28a,b:

(±)-(2*R*, 4*S*)- 5-(benzyloxy)-2,4-dihydroxy-3,3-dimethylpentanenitrile (S23a) and (±)-(2*S*, 4*S*)- 5-(benzyloxy)-2,4-dihydroxy-3,3-dimethylpentanenitrile (S23b):



To a solution of cyanohydrin **28a,b** (3:1 *syn*:*anti*) (54 mg, 0.15 mmol, 1.0 equiv. prepared following General Procedure C with $BF_3{\cdot}OEt_2$) in dry THF (1.5 mL, 0.1 M) at 0 °C, HF-pyridine (0.30 mL, 0.29 mmol, 2.0 mL/mmol) was added. The solution was warmed to room temperature and stirred overnight. An aqueous solution of $NaHCO_3$ was added and the aqueous layer extracted with Et_2O (3x). The organic layers were combined, dried with $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography using 40:60 EtOAc:Hex provided **S23a** and **S23b** as clear oils (23.1 mg, 63 % yield). **S23a**: R_f = 0.32 (40:60 EtOAc:Hex); Molecular Formula: $C_{14}H_{19}NO_3$; MW: 249.31; IR (neat) υ_{max} 3440, 2244 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.29 (m, 5H), 4.58 (s, 2H), 4.50 (d, *J* 4.2 Hz, 1H), 4.22 (d, *J* 4.3 Hz, 1H), 3.82 (dt, *J* 7.8, 3.1 Hz, 1H), 3.64 (dd, *J* 9.5, 3.4 Hz, 1H), 3.58 (dd, *J* 9.5, 7.9 Hz, 1H), 2.87 (d, *J* 2.8 Hz, 1H), 1.11 (s, 3H), 1.07 (s, 3H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 137.1, 128.8, 128.4, 128.0, 118.7, 76.6, 73.9, 70.3, 70.1, 40.6, 22.0, 17.3 ppm; HRMS calcd for $C_{14}H_{20}O_3N$ [M+H^+]: 250.1438, found 250.1439 (+0.5 ppm). **S23b**: R_f = 0.30 (40:60 EtOAc:Hex); IR (neat) υ_{max} 3414, 2242 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.30 (m, 5H), 4.58 (s, 2H), 4.54 (d, *J* 9.5 Hz, 1H), 4.21 (d, *J* 9.4 Hz, 1H), 4.17 (dt, *J* 8.8, 2.6 Hz, 1H), 3.60 (dd, *J* 9.3, 2.8 Hz, 1H), 3.46 (appt, *J* 9.1 Hz, 1H), 3.07 (d, *J* 2.3 Hz, 1H), 1.08 (s, 3H), 1.03 (s, 3H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 137.4, 128.8, 128.3, 127.9, 119.0, 75.5, 73.7, 72.0, 70.3, 39.5, 21.9, 18.4 ppm; HRMS calcd for $C_{14}H_{19}O_3NNa$ [M+Na^+]: 272.1257, found 272.1259 (+0.8 ppm).

(±)-(4*R*, 6*S*)- 6-(benzyloxymethyl)-2,2,5,5-tetramethyl-1,3-dioxane-4-carbonitrile (S24a) and (4*S*, 6*S*)- 6-(benzyloxymethyl)-2,2,5,5-tetramethyl-1,3-dioxane-4-carbonitrile (S24b):



To a solution of diol **S23a,b** (23 mg, 0.093 mmol, 1.0 equiv.) in dry CH_2Cl_2 (1.1 mL, 0.10 M) at 0 °C, 2-methoxypropene (41 µL, 0.43 mmol, 4.0 equiv.) and camphor sulfonic acid (5.0 mg, 0.021 mmol, 0.20 equiv.) were added. The solution was stirred for 15 minutes at 0 °C then warmed to room temperature for 45 minutes. An aqueous solution of NH_4Cl was added and the aqueous layer was extracted with Et_2O (3x). The organic layers were combined, dried with $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography using 10:90 EtOAc:Hex provided acetonide **S24a** (16.6 mg) and **S24b** (8.7 mg) as a clear oils in 94% overall yield (25.3 mg). **S24a**: R_f = 0.11 (10:90 EtOAc:Hex); Molecular Formula: $C_{17}H_{23}NO_3$; MW: 289.38; IR (neat) υ_{max} 2251 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 5H), 4.60 (d, *J* 12.1 Hz, 1H), 4.49 (d, *J* 12.1 Hz, 1H), 4.46 (s, 1H), 3.81 (dd, *J* 6.6, 3.3 Hz, 1H), 3.59 (dd, *J* 10.6, 3.3 Hz, 1H), 3.42 (dd, *J* 10.6, 6.6 Hz, 1H), 1.47 (s, 3H), 1.47 (s, 3H), 1.13 (s, 3H), 1.00 (s, 3H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 138.0, 128.6, 127.9, 127.8, 116.2, 100.5, 76.6, 73.7, 70.7, 69.9, 35.1, 29.5, 21.1, 18.8, 15.0 ppm; HRMS calcd for $C_{17}H_{23}O_3NNa$ [M+Na^+]: 312.1570, found 312.1573 (+0.8 ppm). **S24b**: R_f = 0.16 (10:90 EtOAc:Hex); IR (neat) υ_{max} 2250 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 5H), 4.61 (d, *J* 12.1 Hz, 1H), 4.51 (d, *J* 12.1 Hz, 1H), 4.25 (s, 1H), 4.02 (dd, *J* 6.9, 3.8 Hz, 1H), 3.57 (dd, *J* 10.6, 3.8 Hz, 1H), 3.47 (dd, *J* 10.6, 6.9 Hz, 1H), 1.61 (s, 3H), 1.43 (s, 3H), 1.11 (s, 3H), 1.05 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.1, 128.6, 127.9, 127.7, 117.9, 102.0, 73.9, 73.6, 70.1, 69.3, 36.0, 28.0, 22.3, 22.1, 19.3 ppm; HRMS calcd for $C_{17}H_{23}O_3NNa$ [M+Na^+]: 312.1570, found 312.1572 (+0.7 ppm).

Part II. X-ray information for acetonide S20a

Single crystals of $C_{27}H_{35}NO_3Si$ were prepared from a mixture of ethyl acetate and hexanes. A suitable crystal was selected and mounted on a diffractometer. The crystal was kept at 150 K during data collection. A mixture of enantiomers were crystallized with both enantiomers observed in the cell matrix.

All non-H atoms were refined by full-matrix least-squares with anisotropic displacement parameters. The H atoms were generated geometrically (C—H 0.95 to 1.00˚A) and were included in the refinement in the riding model approximation; their temperature factors were set to 1.5 times those of the equivalent isotropic temperature factors of the parent site (methyl) and 1.2 times for others. A final verification of possible voids was performed using the VOID routine of the PLATON program (Spek, 2000). Data collection: APEX2 (Bruker, 2004). Cell refinement: APEX2 (Bruker, 2004). Data reduction: SAINT (Bruker, 2004). Program(s) used to solve structure: SHELXS97 (Sheldrick, 1997). Program(s) used to refine structure: SHELXL97 (Sheldrick, 1997). Molecular graphics: SHELXTL (Bruker, 1997). Software used to prepare material for publication: UdMX (local program).

Empirical formula	$C_{27}H_{35}NO_3Si$
Formula weight	449.65
Temperature	150(2)K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	P21/c
Unit cell dimensions	a = 13.2363(4) Å a = 90° b = 8.5601(3) Å b = 93.899(2)° c = 22.4586(8) Å g = 90°
Volume	2538.76^4Å^3
Z	4
Density (calculated)	1.176 g/cm^3
Absorption coefficient	1.025 mm^{-1}
F(000)	968
Crystal size	0.24 x 0.22 x 0.20 mm
Theta range for data collection	3.35 to 71.66°
Index ranges	$-16 \le h \le 15$, $-10 \le k \le 10$, $-27 \le l \le 27$
Reflections collected	57950
Independent reflections	4955 [R_{int} = 0.045]
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.0000 and 0.8900
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4955 / 0 / 295
Goodness-of-fit on F^2	1.173
Final R indices [I>2sigma(I)]	R_1 = 0.0487, wR_2 = 0.1267
R indices (all data)	R_1 = 0.0495, wR_2 = 0.1276
Largest diff. peak and hole	0.365 and -0.629 e/Å^3

Bruker (1997). SHELXTL (1997). Release 5.10; The Complete Software Package for Single Crystal Structure Determination. Bruker AXS Inc., Madison, USA.

Bruker (2004). SAINT Release 7.12A. Integration Software for Single Crystal Data. Bruker AXS Inc., Madison, USA.
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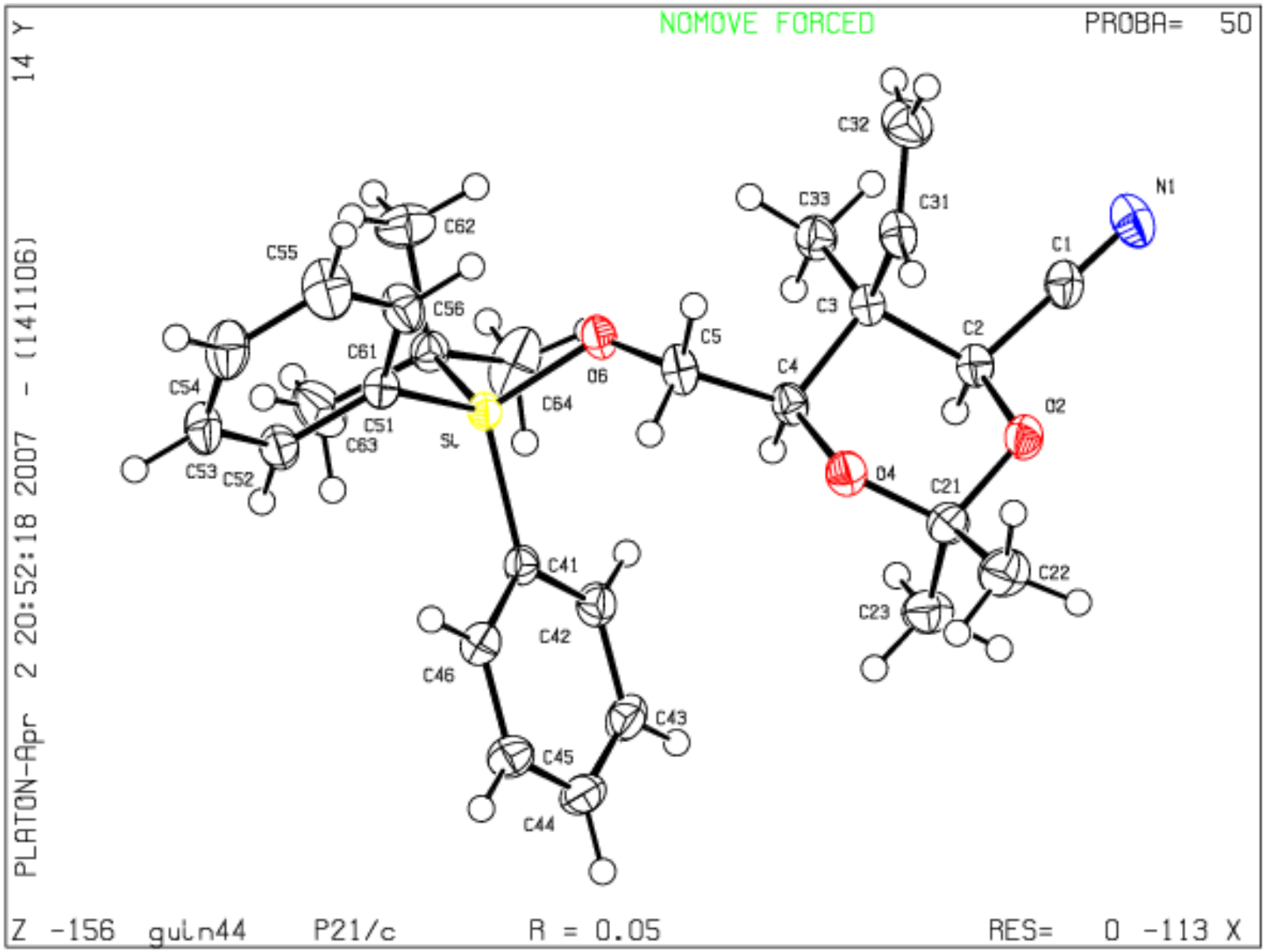
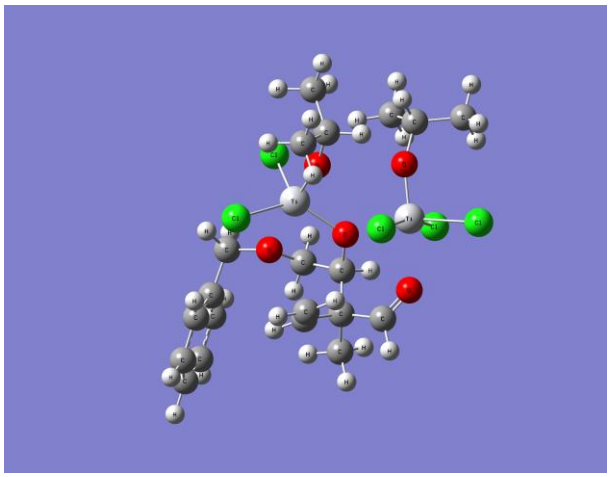
Sheldrick, G. M. (1986). SHELXS86. Program for Crystal Structure solution. University of Gottingen, Germany.
Sheldrick, G. M. (1996). SADABS, Bruker Area Detector Absorption Corrections. Bruker AXS Inc., Madison, USA.
Sheldrick, G. M. (2004). SADABS, Bruker Area Detector Absorption Corrections. Bruker AXS Inc., Madison, USA.
Sheldrick, G. M. (1997a). SHELXS97. Program for Crystal Structure solution. University of Gottingen, Germany.
Sheldrick, G. M. (1997b). SHELXL97. Program for crystal structure refinement. University of Gottingen, Germany.
Spek, A. L. (2000). PLATON, 2000 version; Molecular Geometry Program, University of Utrecht, Utrecht, Holland.



Part III. Computational Data

Density functional theory (DFT) calculations was performed in Gaussian 09 (D.01) with tight SCF convergence.[i] The different possible -OiPr and -Cl ligand coordination positions were examined, the complex with the lowest energy is presented below. The energy reported is from the fully optimized structure at the M062X[ii] /6-31G* level of theory in DCM using the polarizable continuum model (PCM).[iii]

# of imaginary frequency (vi): none
Energy (E, Ha): -5156.489258
Energy + zero-point energy (E + ZPE, Ha) at 273.15 K: -5155.989905
Energy + thermal free energies (G, Ha) at 273.15 K: -5156.052957



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C 1.37435100 -2.18340300 -0.50536200
C 0.26941700 -2.97981000 -1.15186900
O -0.92403200 -2.83035600 -0.94640900
Ti -2.23246100 -1.22018900 -0.15527700
Ti 0.22009200 1.43318800 -0.01177400
O 2.10685400 0.56809200 0.68333700
C 1.79474700 -0.58301200 1.47180500
C 2.05386300 -1.34917700 -1.57373800
C 2.38574600 -3.21989700 0.03364200
C 1.49635400 -0.96465600 -2.72021900
Cl -2.00759400 -0.44481800 -2.34877100

[i] Gaussian 09, Revision D.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, **2013**.
[ii] Zhao, Y.; Truhlar, D. G. *Acc. Chem. Res.* **2008**, *41*, 157.
[iii] Cossi, M.; Scalmani, G.; Rega, N.; Barone, V. *J. Chem. Phys.* **2002**, *117*, 43.

Cl 1.54324700 2.49125000 -1.52900200
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C 4.52196800 0.55339100 0.77133900
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C 6.77348200 -0.90853500 -0.00019800
C 6.34543700 -0.93829000 1.32422400
C 5.22193200 -0.20716100 1.70902500
H 0.30228500 -2.07575000 1.34666100
H 0.58429600 -3.76763900 -1.85253900
H 2.70183600 -1.15652400 1.67568800
H 1.35445800 -0.25311600 2.42168000
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H 3.31230400 -2.72218700 0.33370800
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H 6.42132300 -0.11212700 -1.97180100
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O -1.27235500 2.00490500 -0.55258800
C -2.36696000 2.75676100 -1.07683800
H -3.19854100 2.04511200 -1.13349100
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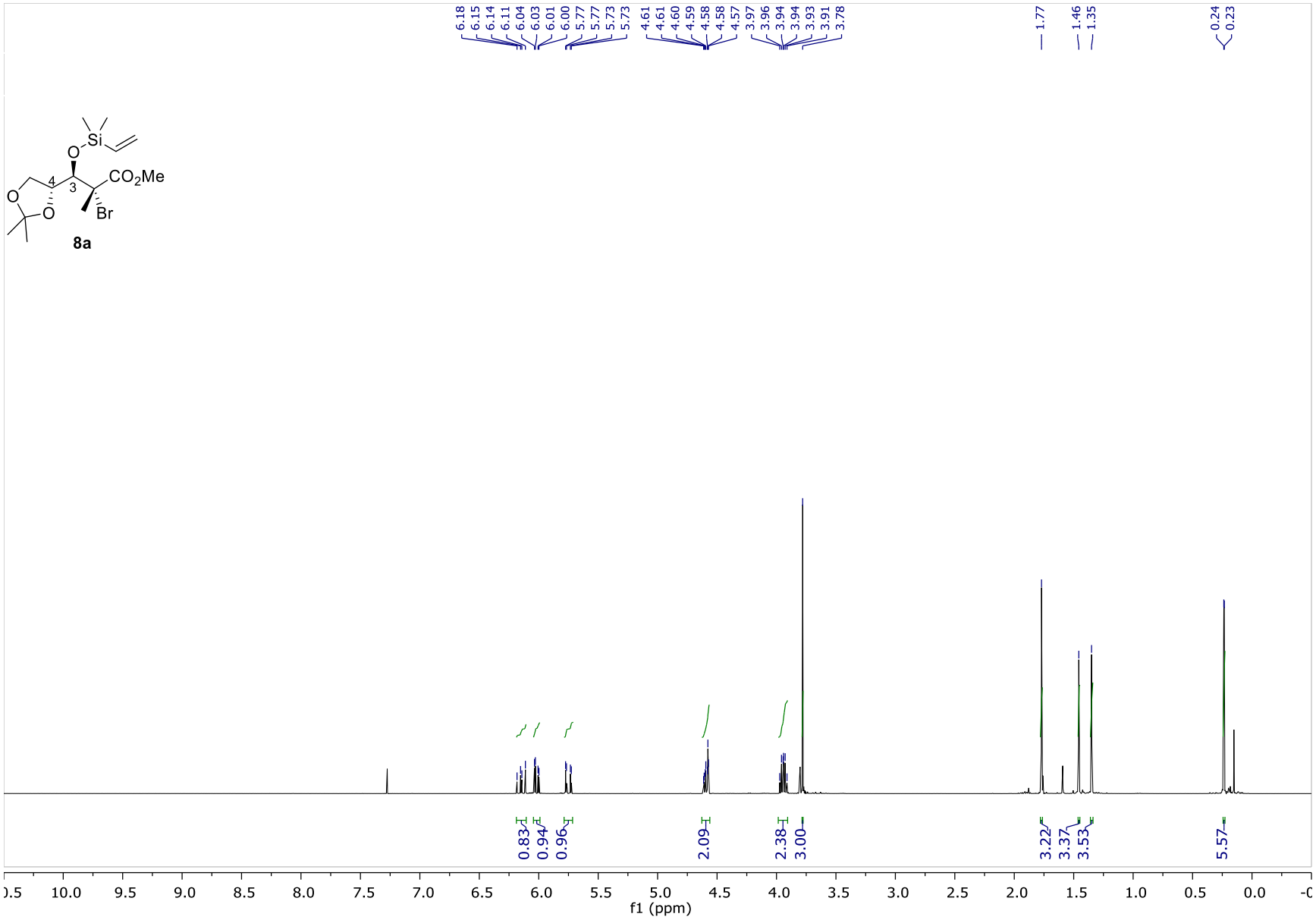
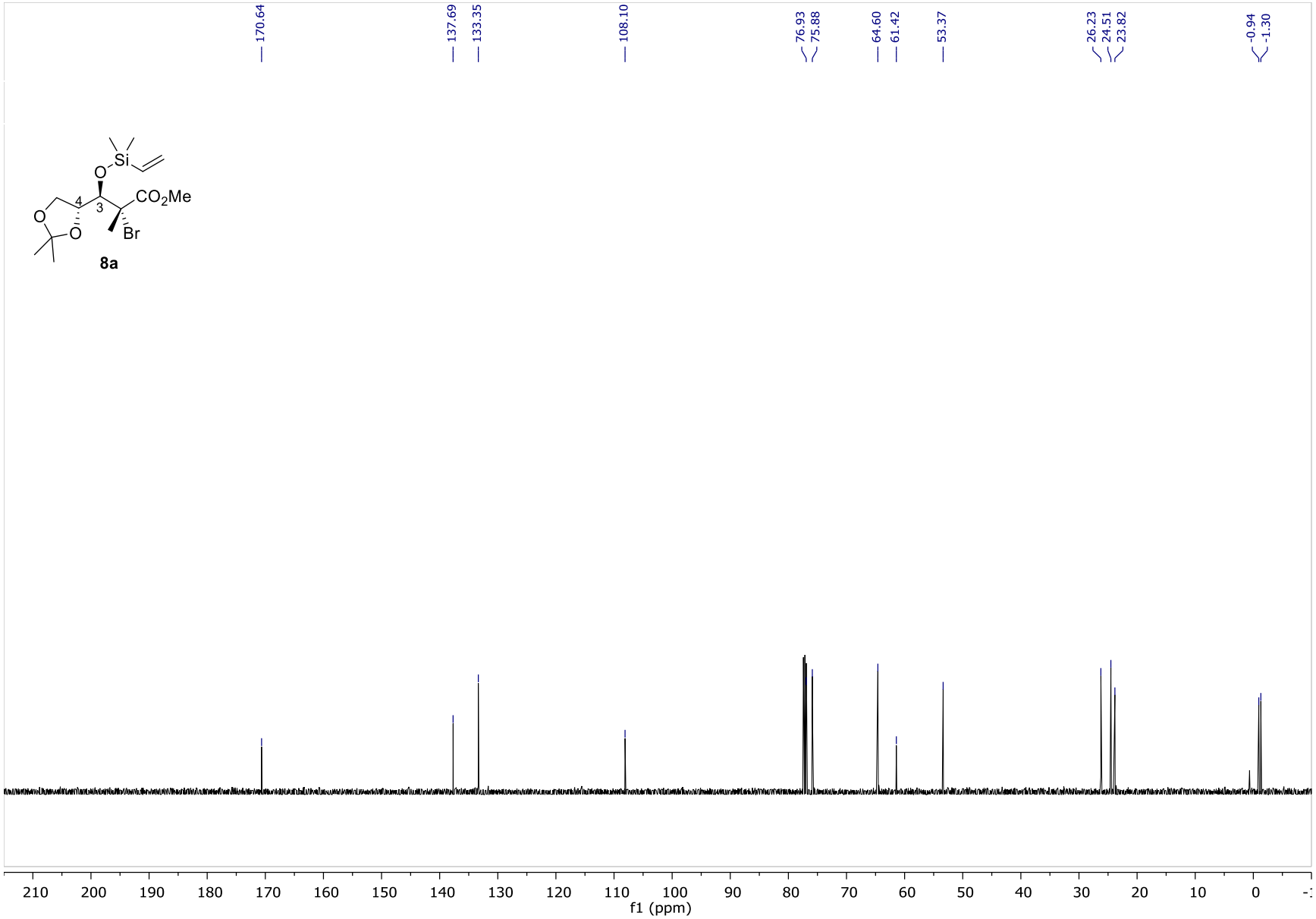
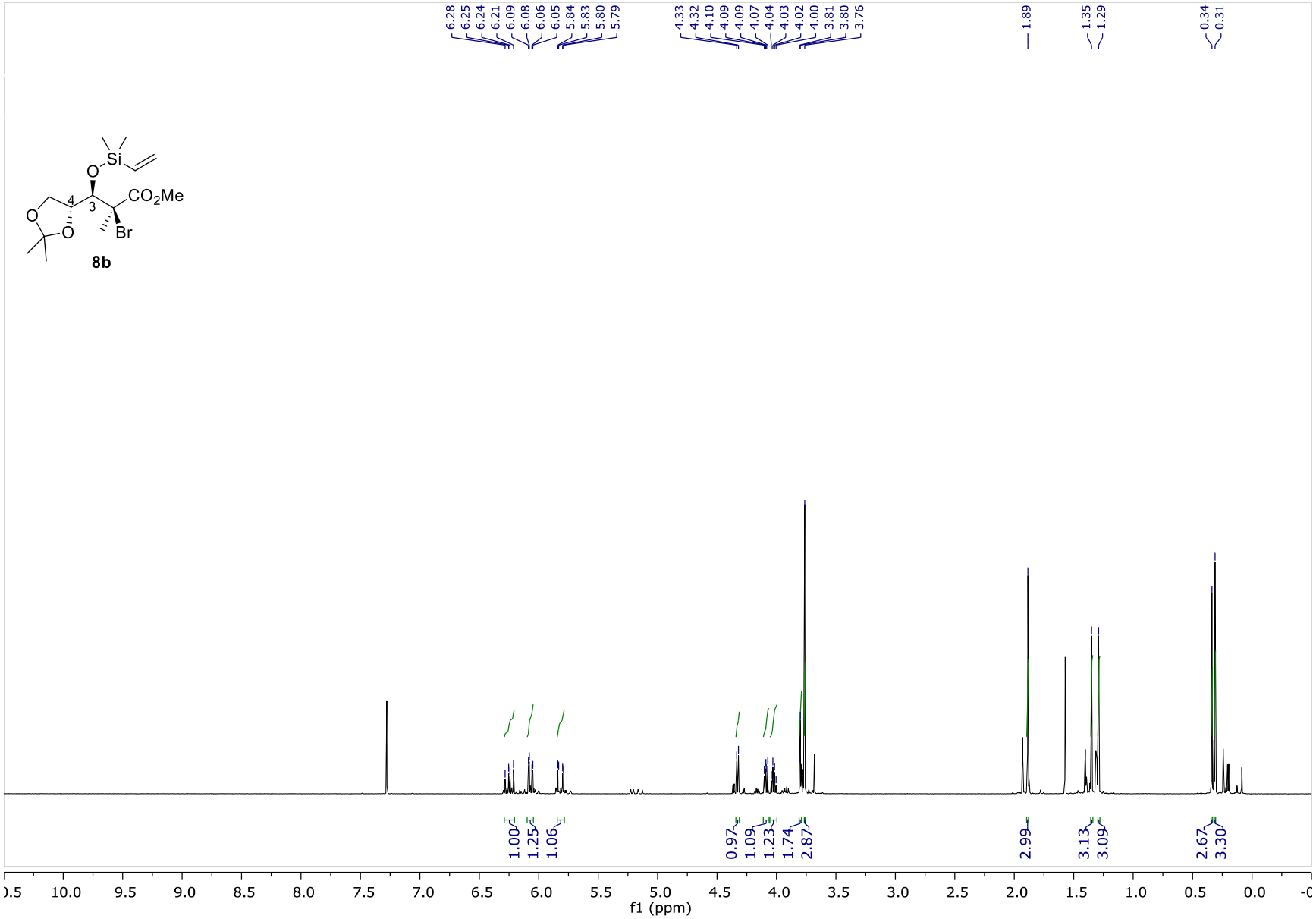
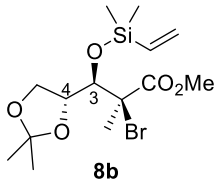
Part IV. ^{1}H and ^{13}C spectra





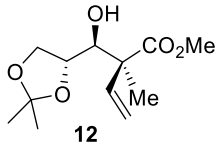


^{13}C-NMR (126 MHz, $CDCl_3$)



8b

^{1}H-NMR (500 MHz, $CDCl_3$)



12

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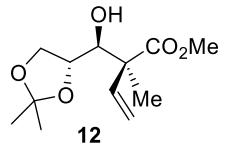

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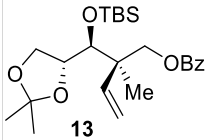

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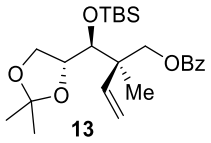

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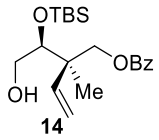

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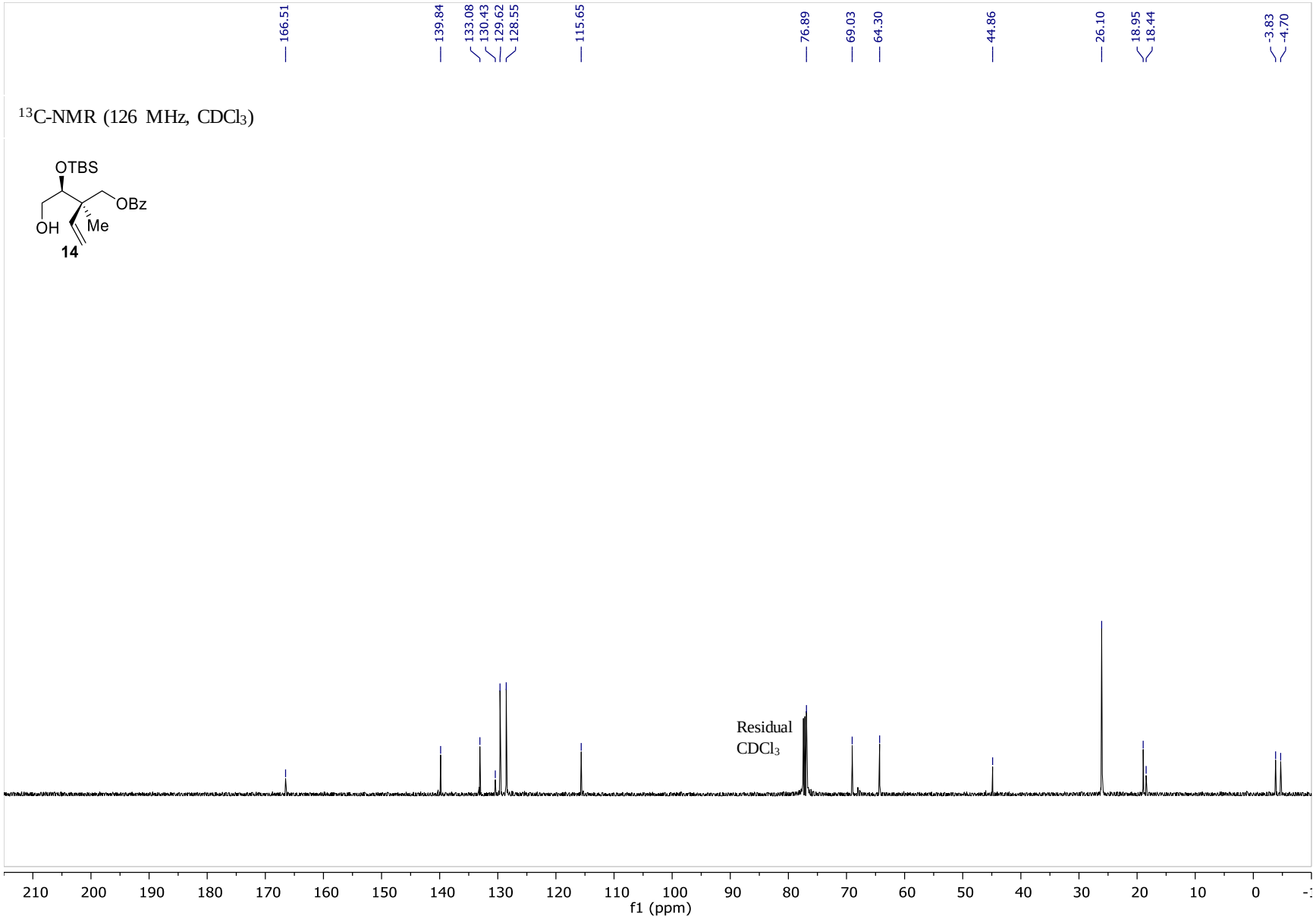

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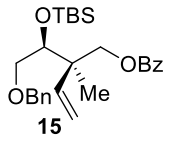

15

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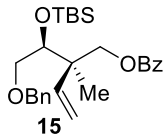

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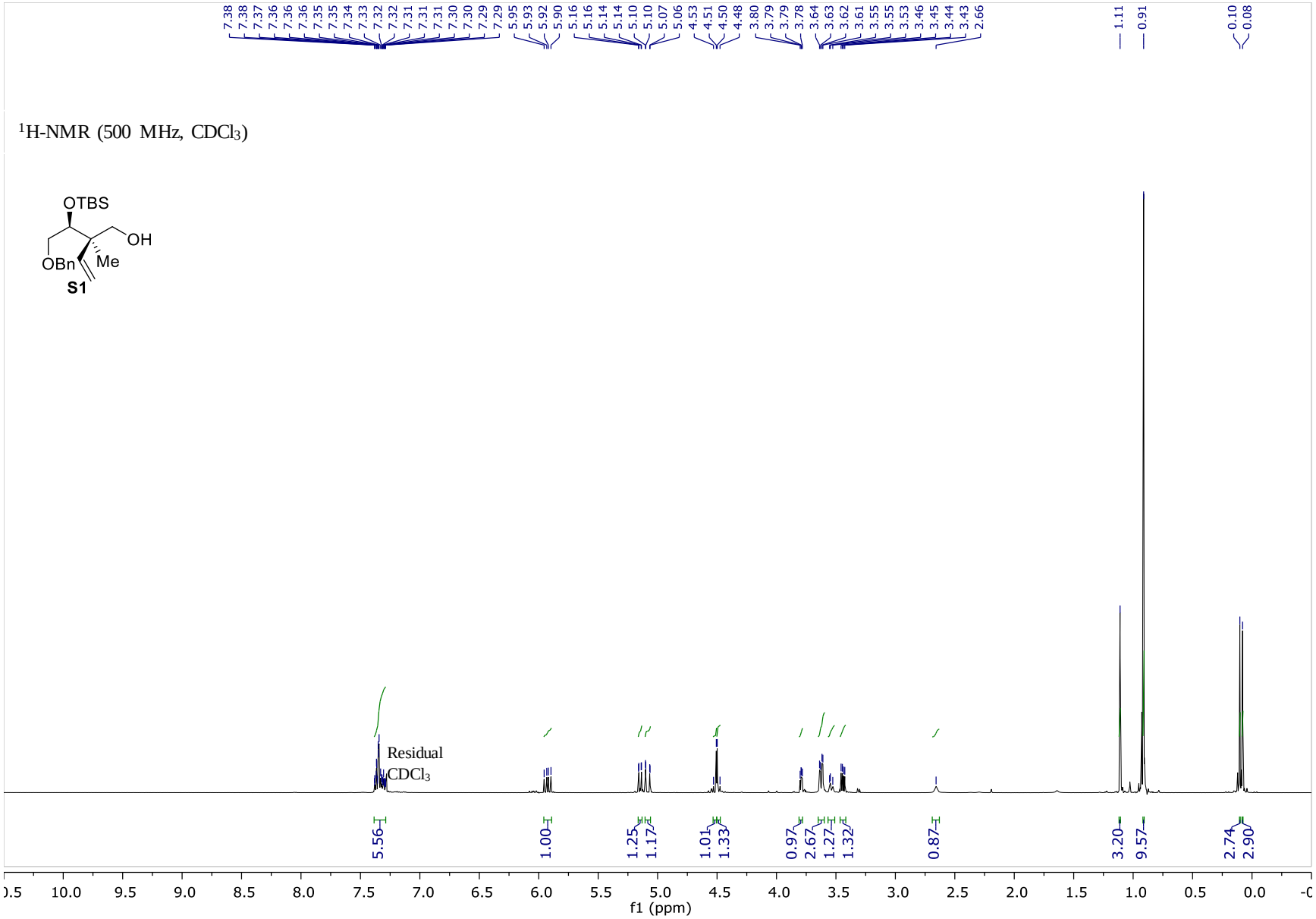

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114.75
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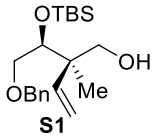
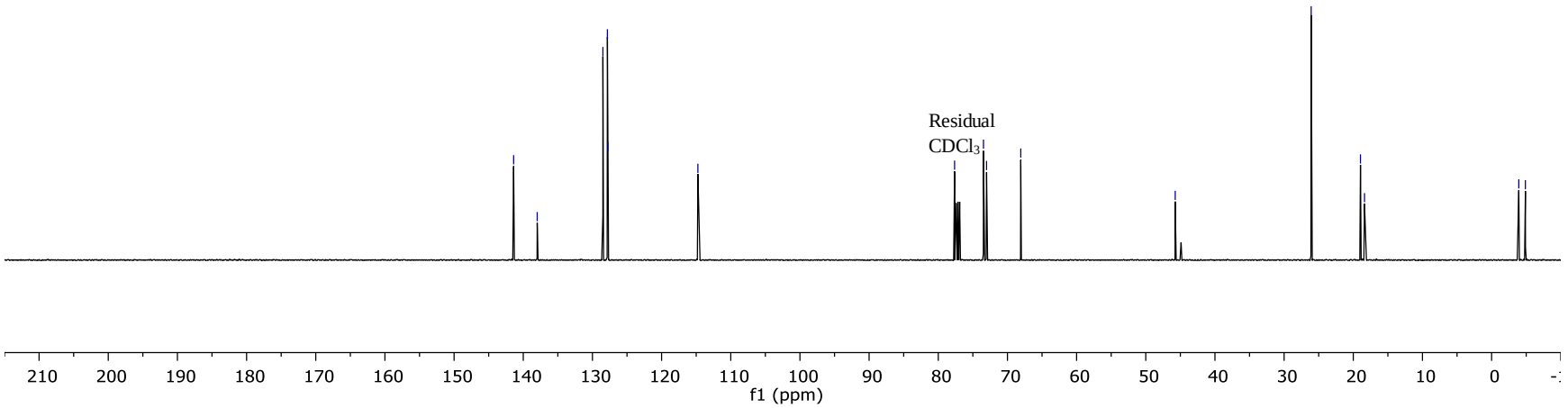
73.02
68.07
45.74
26.09
18.96
18.38
-3.93
-4.88

^{13}C-NMR (126 MHz, $CDCl_3$)





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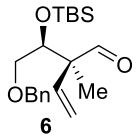

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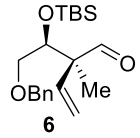

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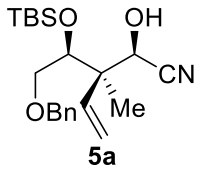
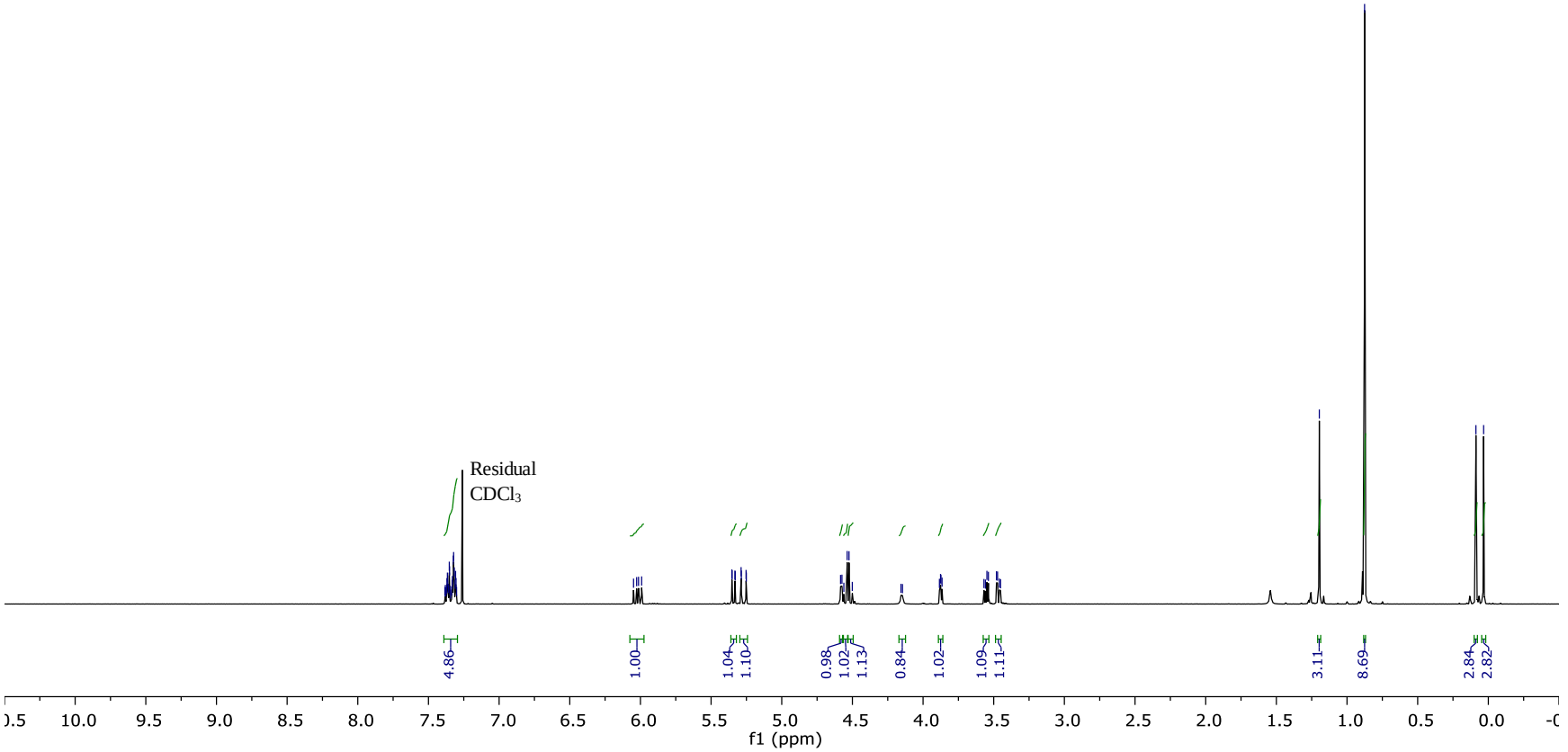


5a



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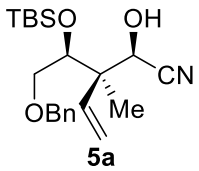

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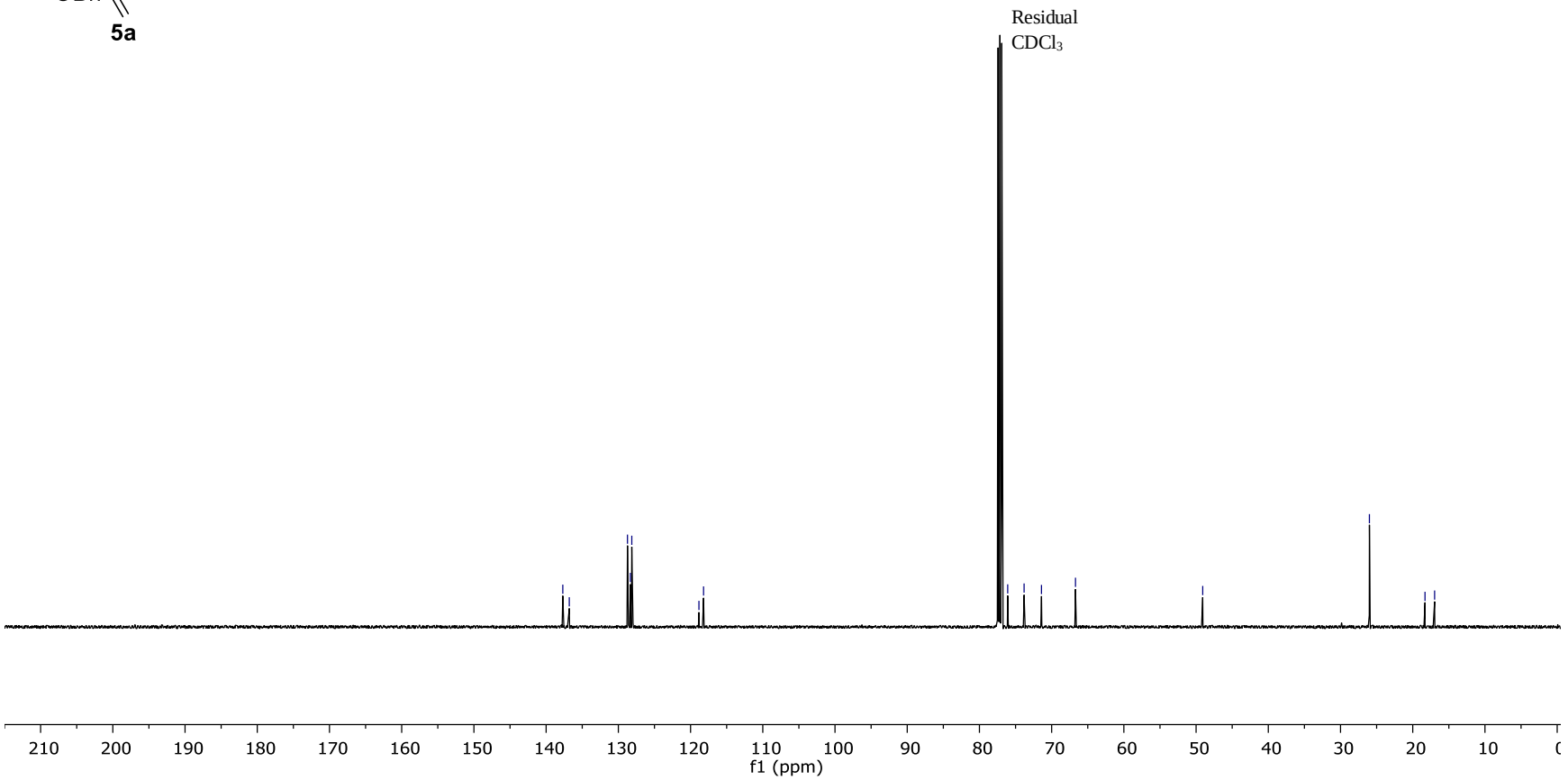

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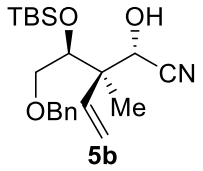

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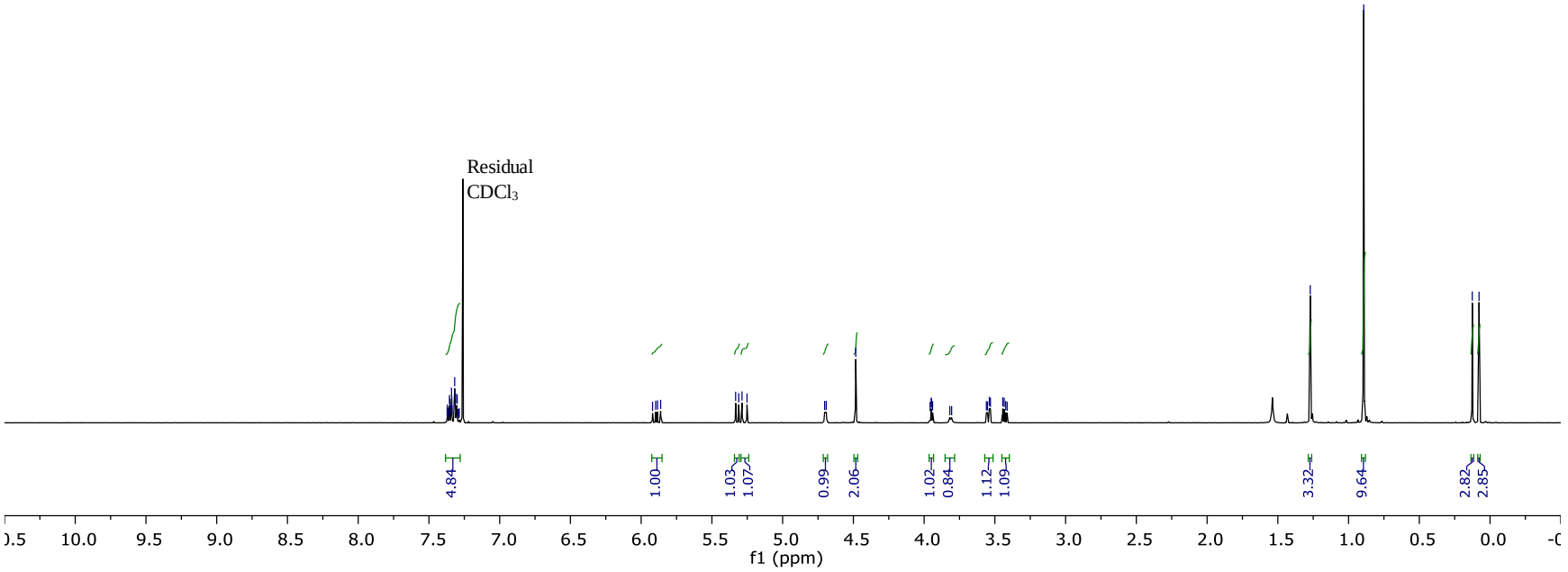
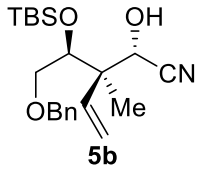


137.57
137.07
128.59
127.99
127.88
118.86
118.22
77.36
73.51
72.27
67.99
47.57
26.02
18.32
16.53
-4.07
-4.94

^{13}C-NMR (126 MHz, $CDCl_3$)



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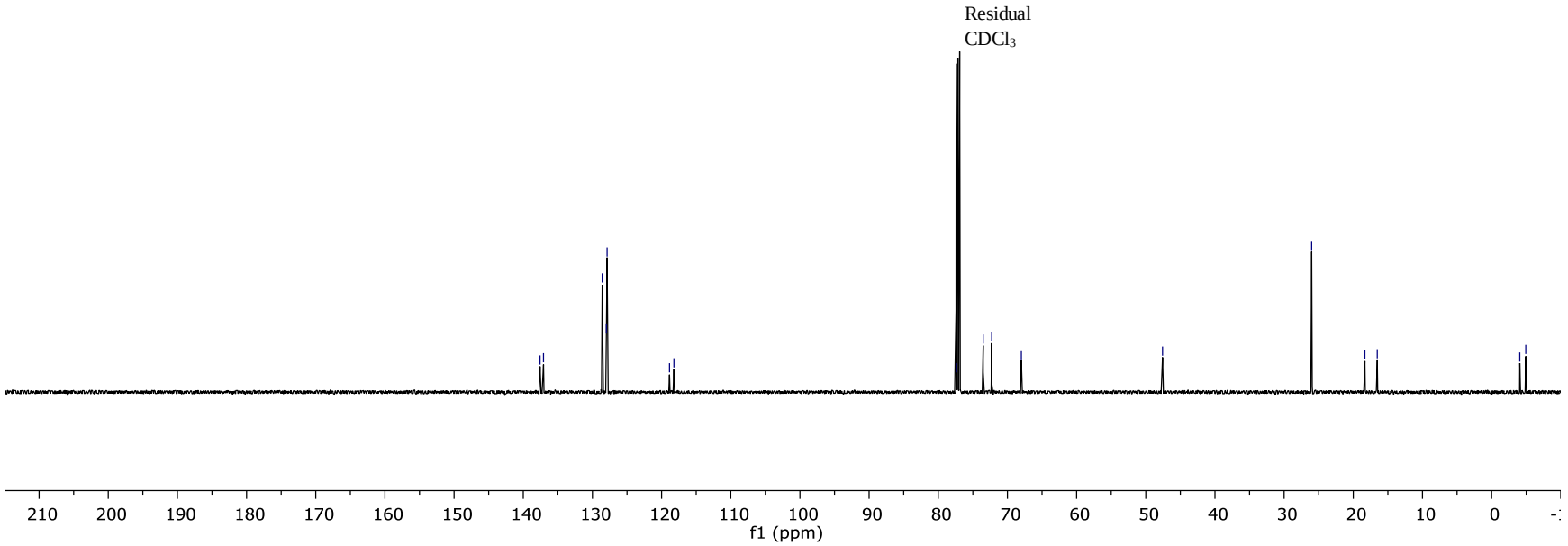
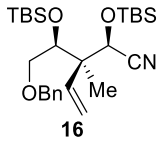
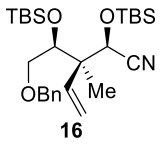


^{1}H-NMR (500 MHz, $CDCl_3$)



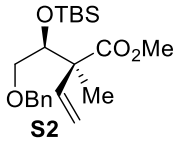
16

^{13}C-NMR (126 MHz, $CDCl_3$)



16

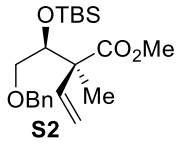
^{1}H-NMR (500 MHz, $CDCl_3$)



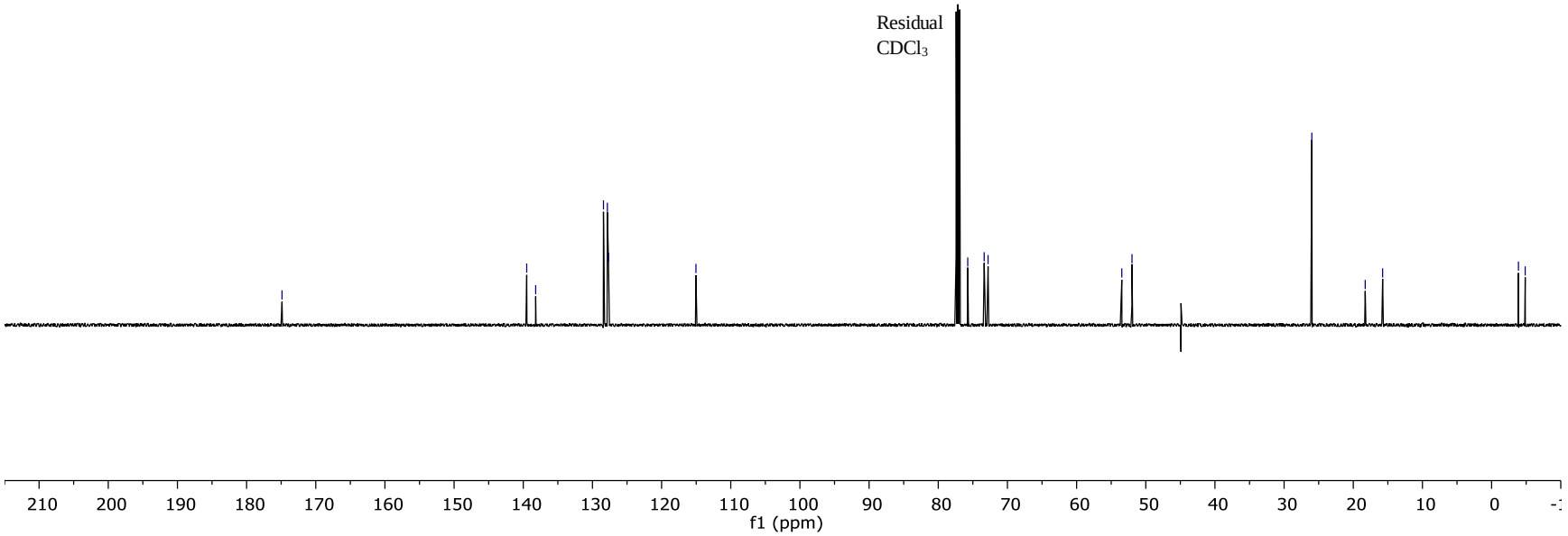
S2

174.88
139.50
138.20
128.40
127.84
127.67
115.03
75.74
73.36
72.80
53.47
51.99
25.99
18.27
15.76
-3.88
-4.86

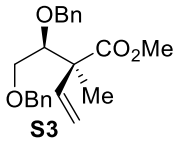
^{13}C-NMR (126 MHz, $CDCl_3$)

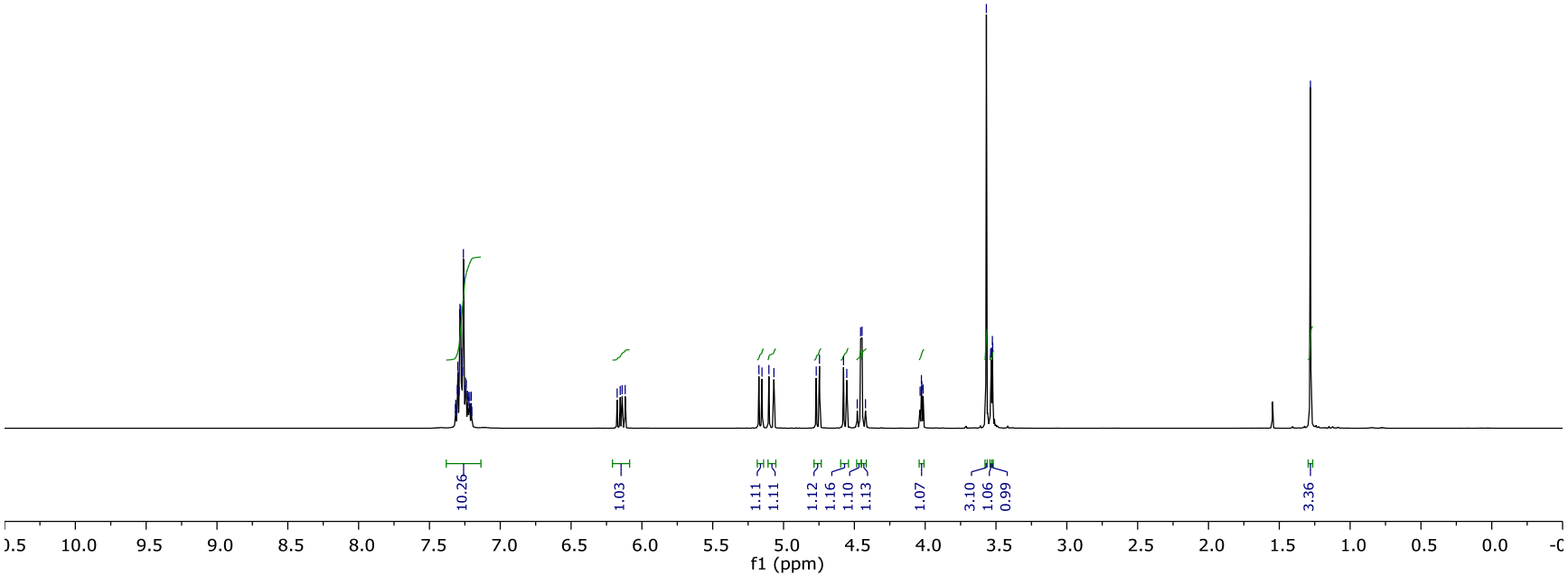


S2



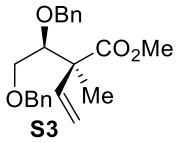
^{1}H-NMR (500 MHz, $CDCl_3$)



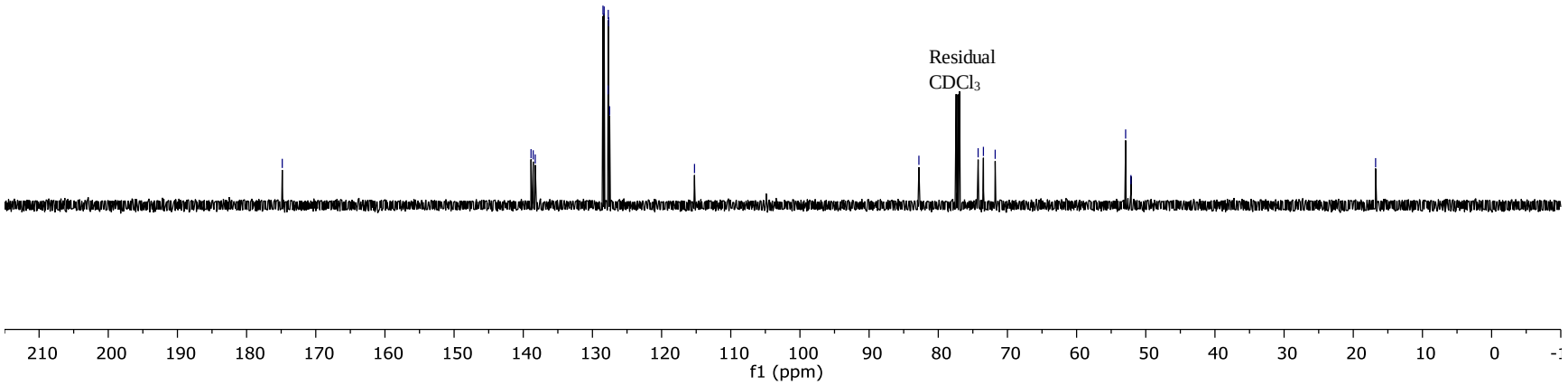


174.85
138.87
138.56
138.27
128.48
128.31
127.72
127.71
127.65
127.51
115.24
82.80
74.24
73.47
71.77
52.91
52.15
16.77

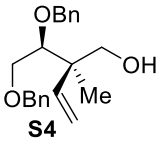
^{13}C-NMR (126 MHz, $CDCl_3$)

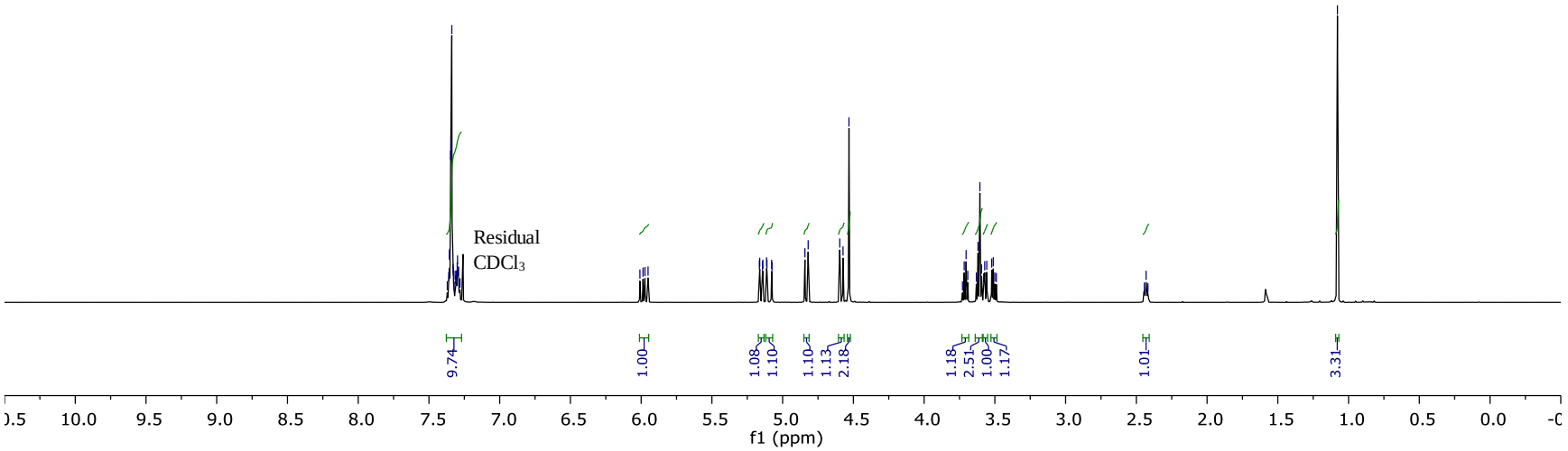


S3



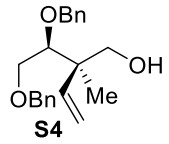
^{1}H-NMR (500 MHz, $CDCl_3$)



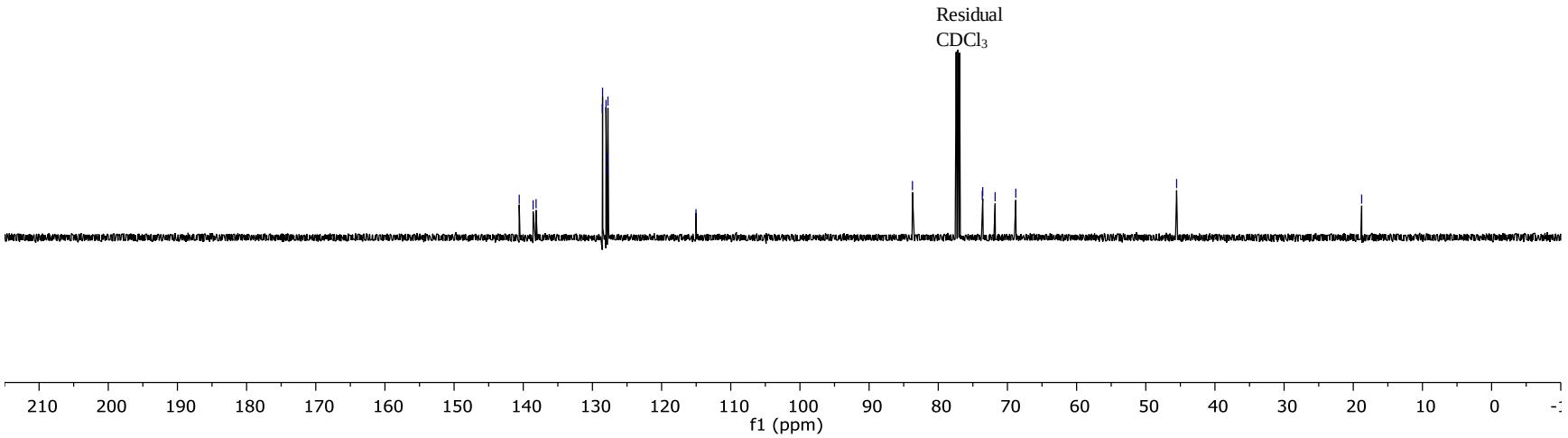


140.58
138.58
138.15
128.57
128.53
128.04
127.84
127.82
127.76
115.03
83.73
73.64
73.57
71.78
68.80
45.54
18.79

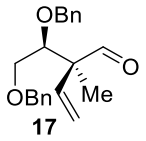
^{13}C-NMR (126 MHz, $CDCl_3$)



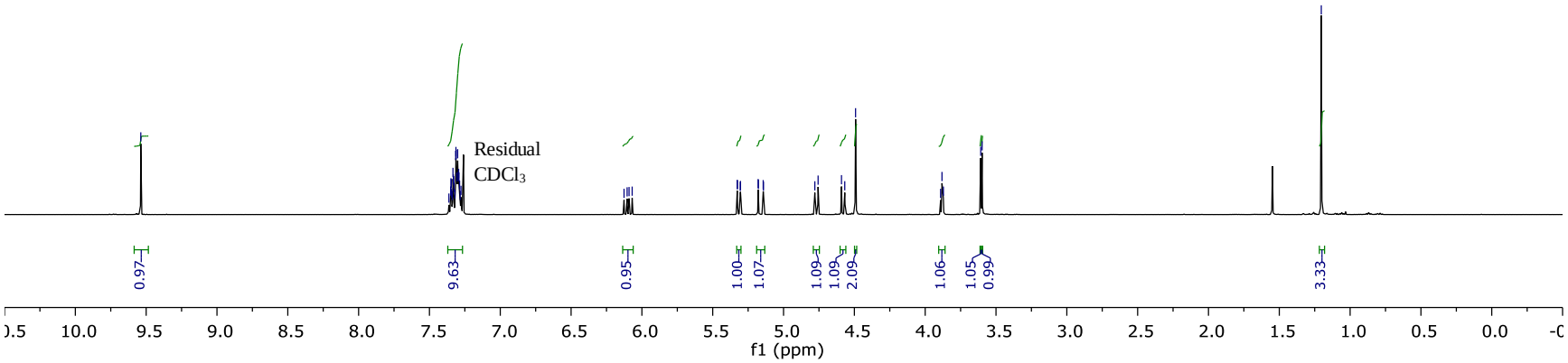
S4



^{1}H-NMR (500 MHz, $CDCl_3$)

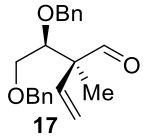


17

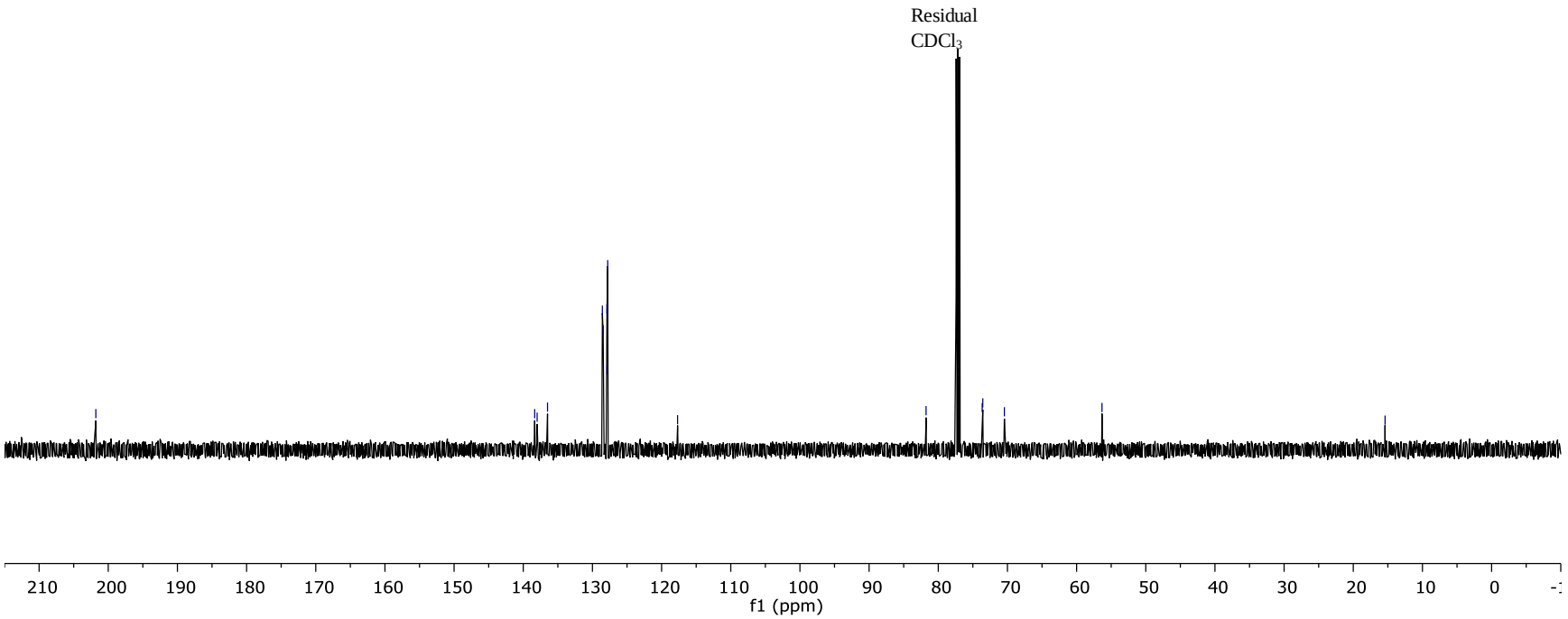


201.80
138.35
137.99
136.49
128.56
128.44
127.90
127.86
127.79
117.69
81.77
73.65
73.56
70.44
56.33
15.40

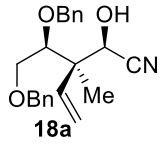
^{13}C-NMR (126 MHz, $CDCl_3$)



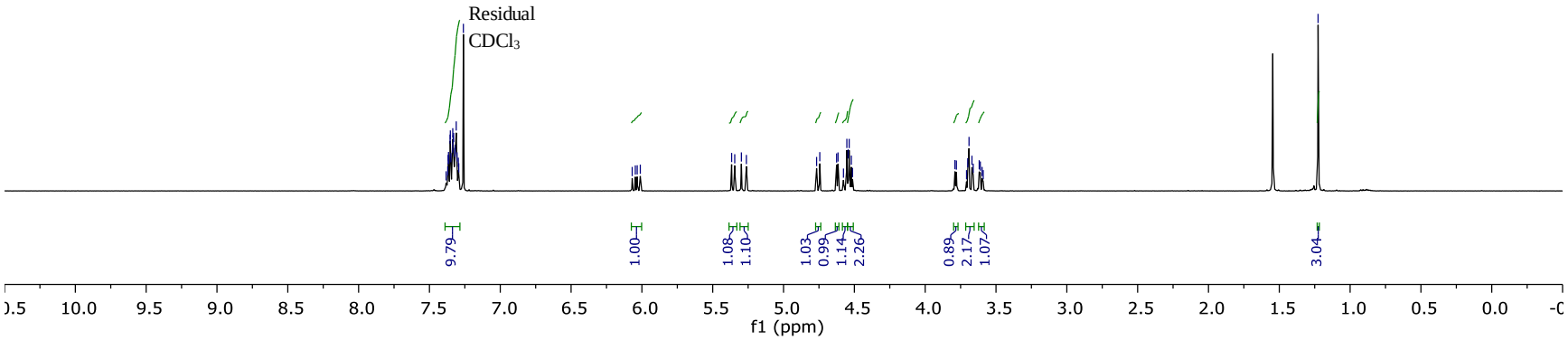
17



^{1}H-NMR (500 MHz, $CDCl_3$)

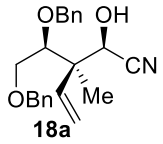


18a

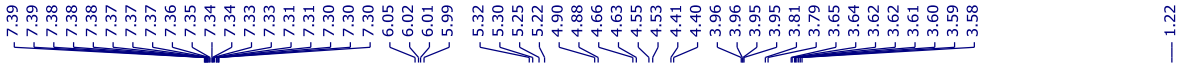


137.78
137.21
136.88
128.74
128.64
128.25
128.13
128.12
127.99
118.57
118.53
82.62
73.78
73.49
69.82
67.16
48.47
17.06

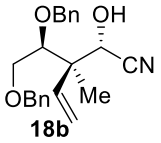
^{13}C-NMR (126 MHz, $CDCl_3$)



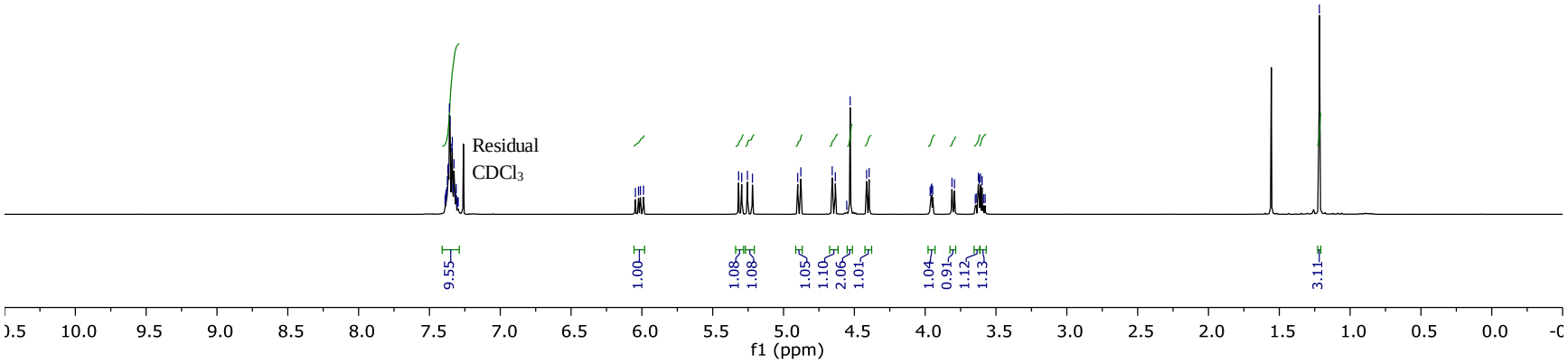
18a



^{1}H-NMR (500 MHz, $CDCl_3$)

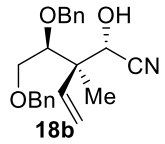


18b

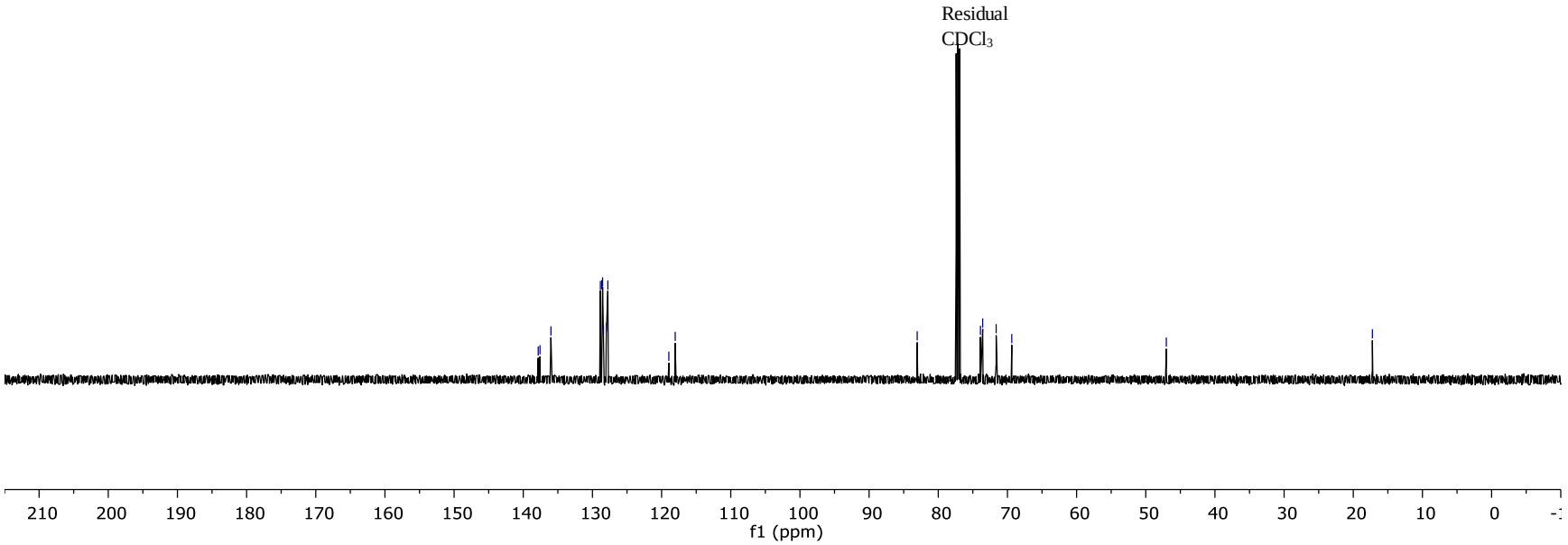


137.84
137.58
136.00
128.85
128.65
128.53
128.41
127.99
127.77
118.96
118.03
83.05
73.90
73.58
71.63
69.37
47.03
17.24

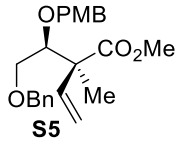
^{13}C-NMR (126 MHz, $CDCl_3$)

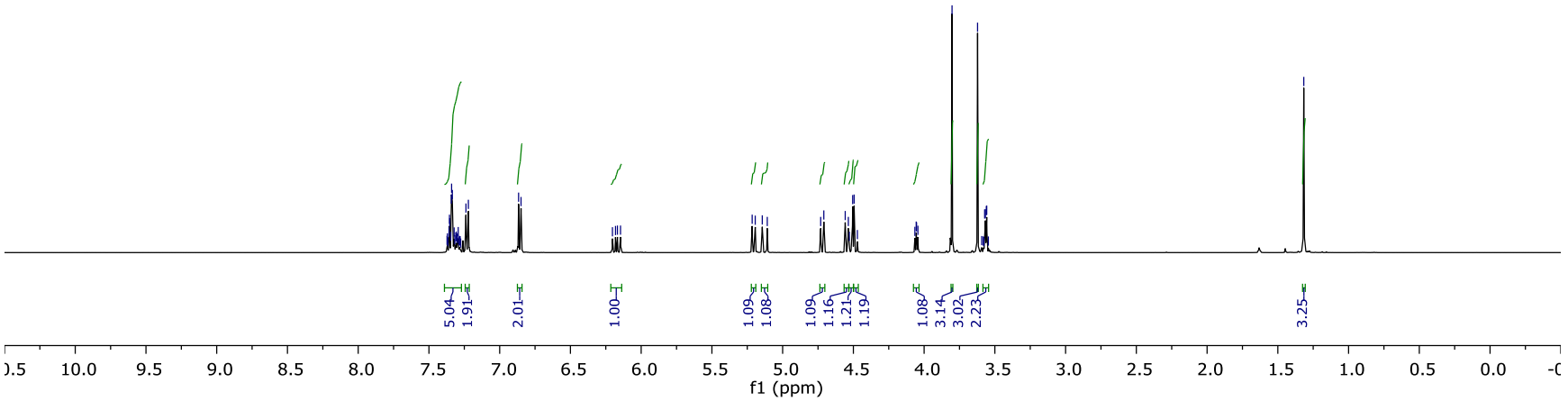


18b



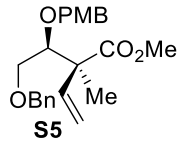
^{1}H-NMR (500 MHz, $CDCl_3$)



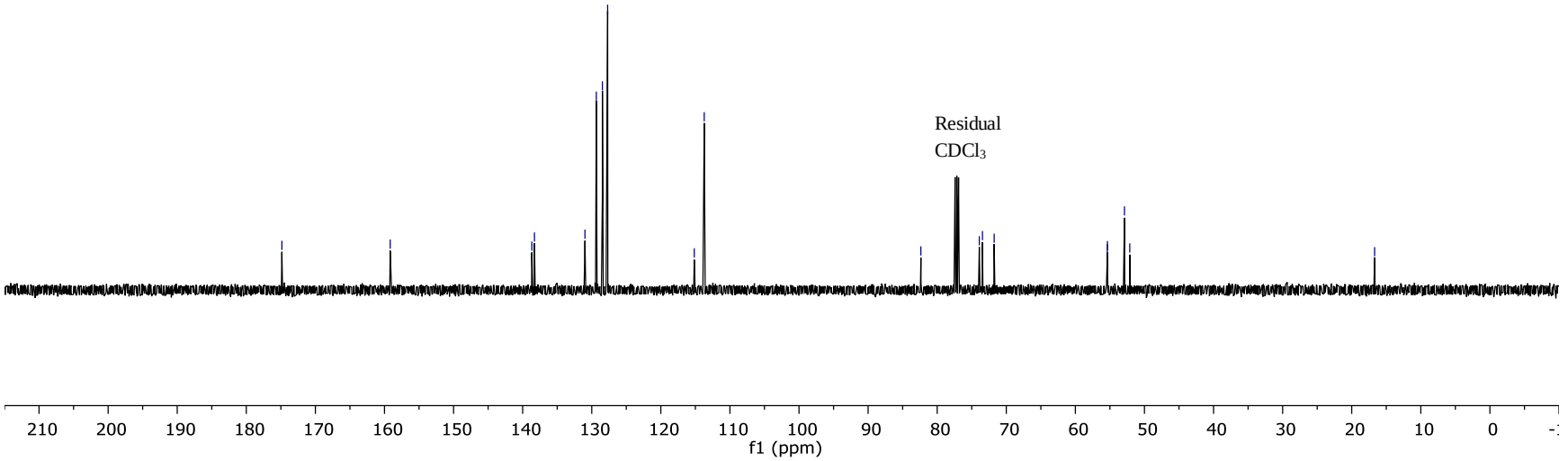


174.85
159.17
138.67
138.29
130.98
129.34
128.46
127.70
115.16
113.72
82.36
73.91
73.45
71.76
55.38
55.36
52.89
52.13
16.69

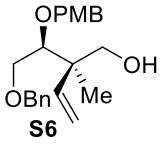
^{13}C-NMR (126 MHz, $CDCl_3$)



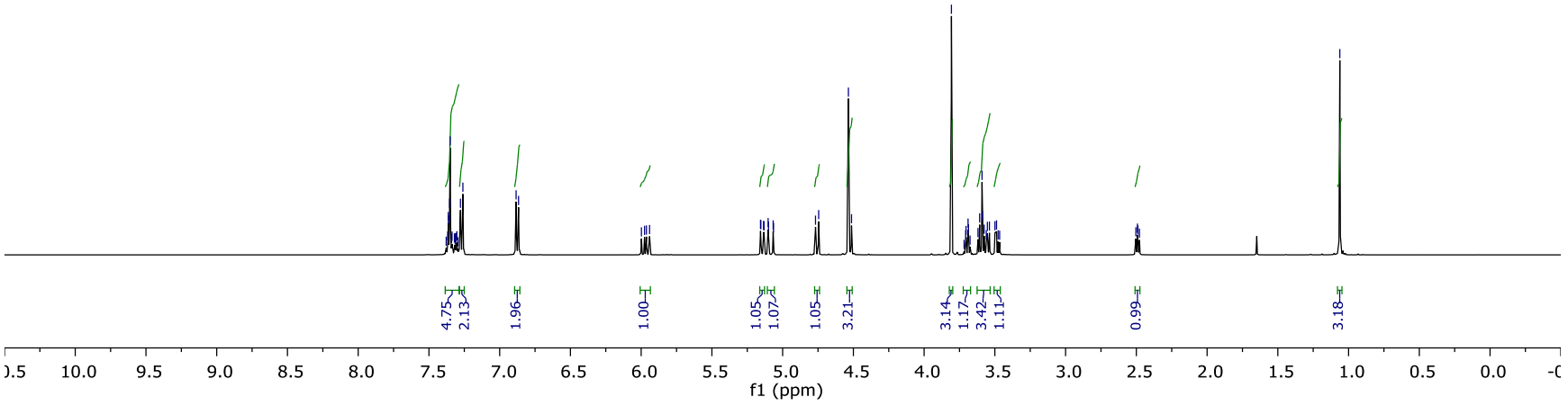
S5



^{1}H-NMR (500 MHz, $CDCl_3$)

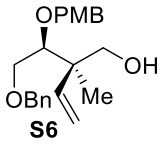


S6

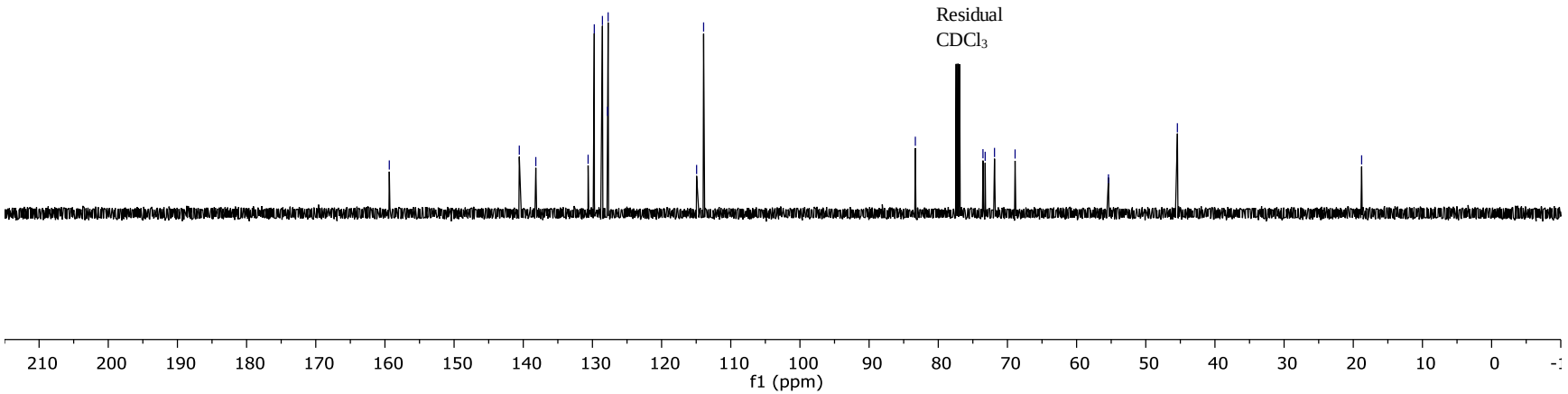


159.37
140.57
138.19
130.63
129.73
128.55
127.81
127.73
114.94
113.93
83.31
73.54
73.22
71.87
68.89
55.39
45.43
18.79

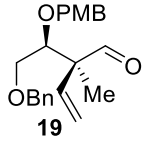
^{13}C-NMR (126 MHz, $CDCl_3$)



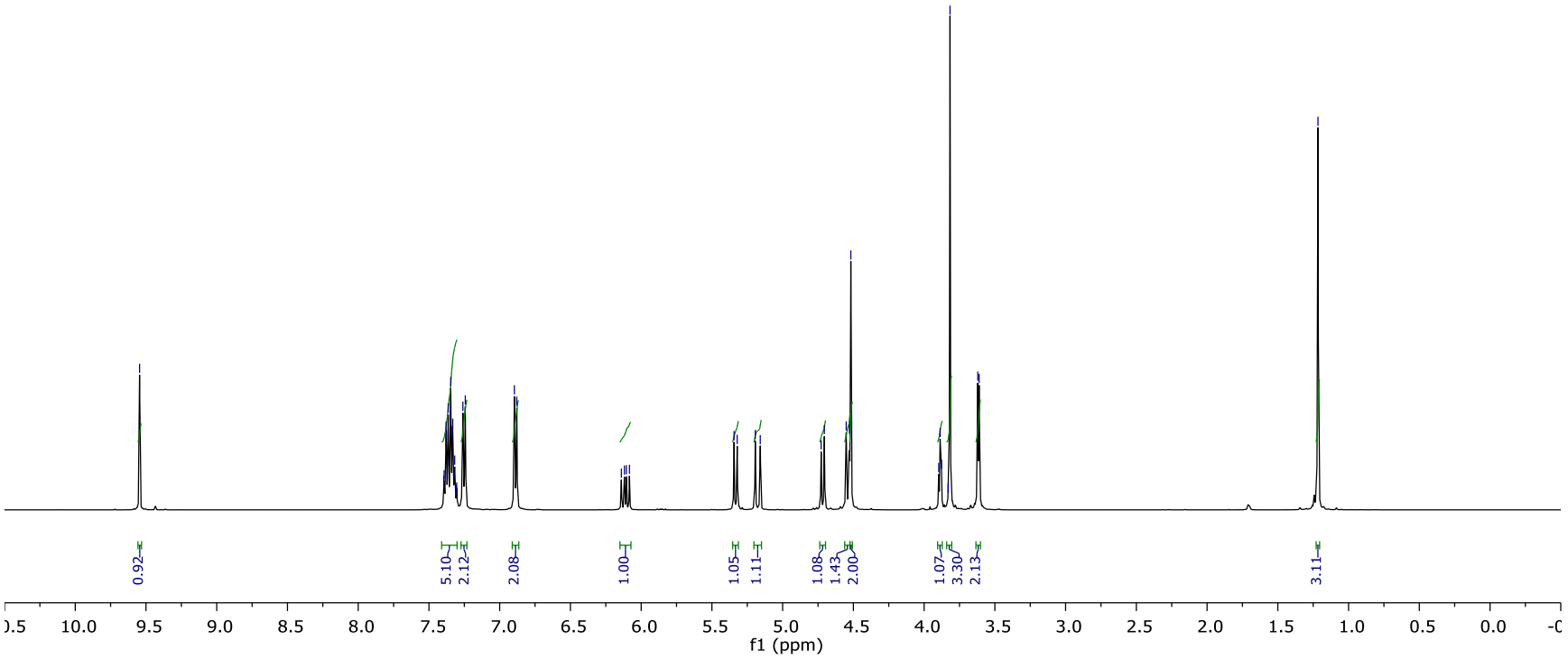
S6



^{1}H-NMR (500 MHz, $CDCl_3$)

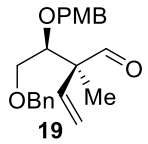


19

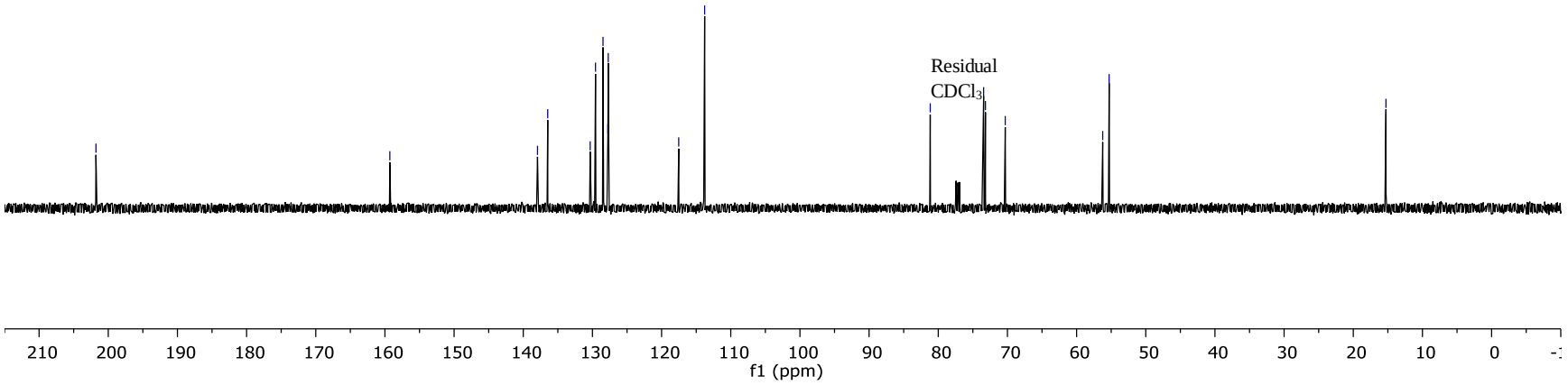


201.78
159.29
137.94
136.46
130.32
129.56
128.47
127.77
127.71
117.52
113.77
81.16
73.44
73.18
70.32
56.22
55.30
15.27

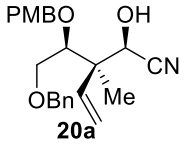
^{13}C-NMR (126 MHz, $CDCl_3$)



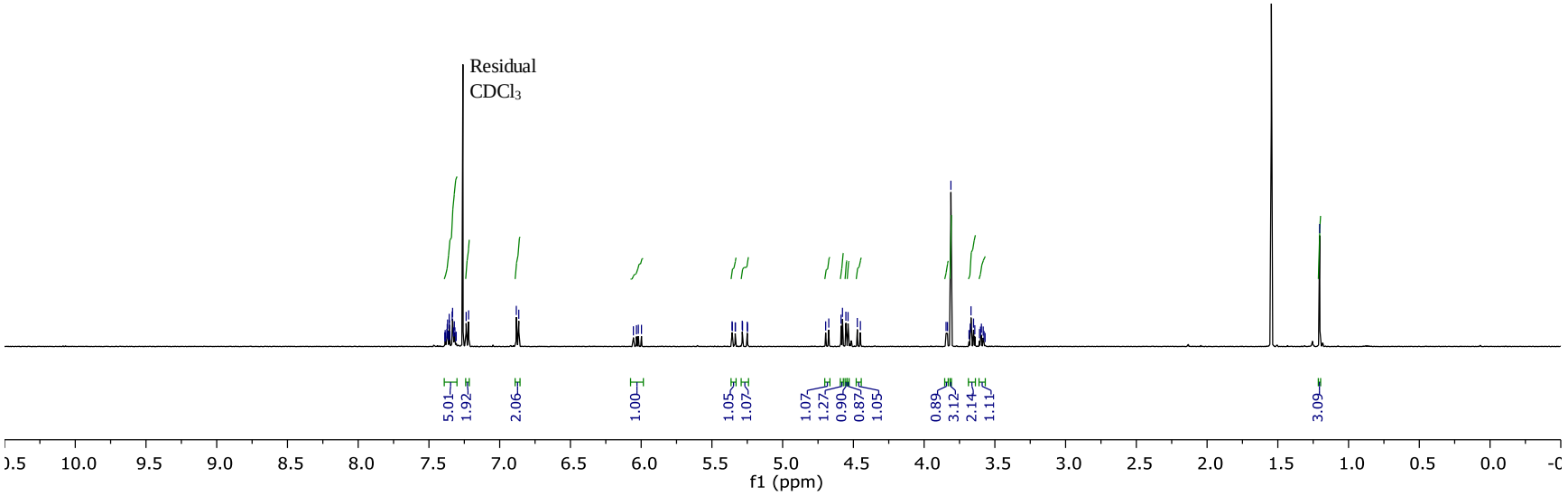
19



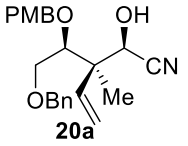
^{1}H-NMR (500 MHz, $CDCl_3$)



20a

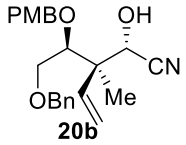


^{13}C-NMR (126 MHz, $CDCl_3$)

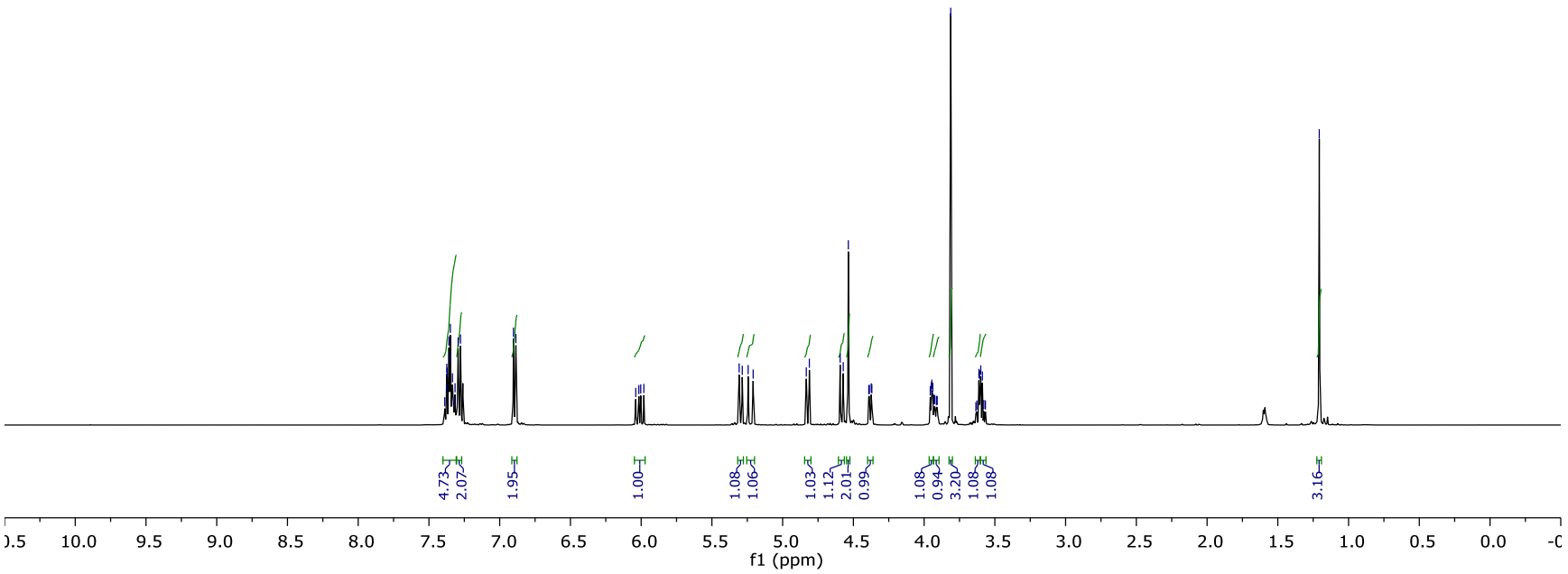


20a

^{1}H-NMR (500 MHz, $CDCl_3$)

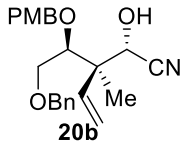


20b

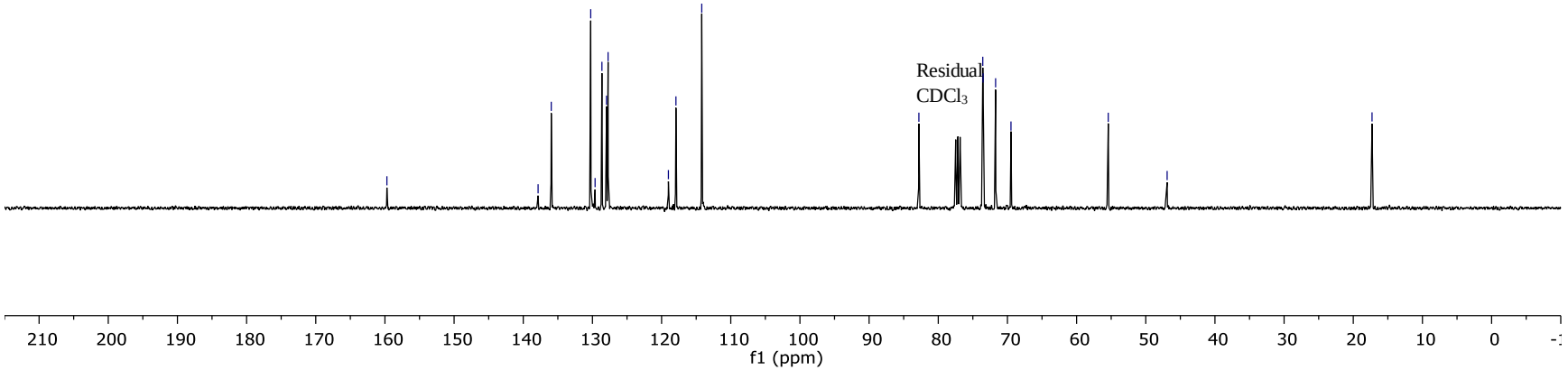


159.71
137.86
135.95
130.25
129.62
128.63
127.96
127.74
119.02
117.93
114.19
82.80
73.57
73.52
71.71
69.49
55.42
46.91
17.29

^{13}C-NMR (100.6 MHz, $CDCl_3$)

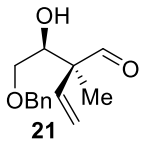


20b

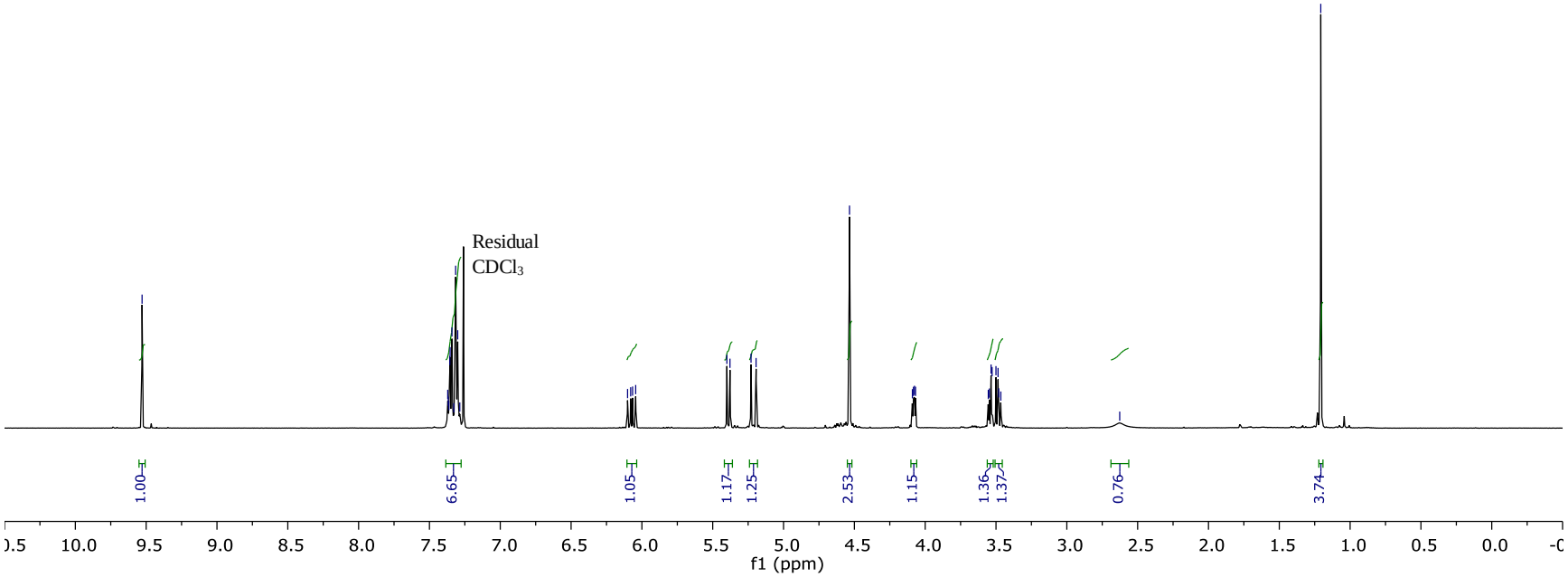


9.53
7.37 7.37 7.36 7.36 7.35 7.34 7.33 7.31 7.30 7.29
6.10 6.08 6.07 6.04
5.40 5.38 5.23 5.19
4.53
4.09 4.08 4.08 4.07
3.55 3.55 3.53 3.53 3.50 3.49 3.48 3.47
2.63
1.21

^{1}H-NMR (500 MHz, $CDCl_3$)

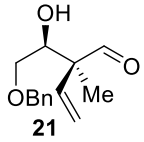


21

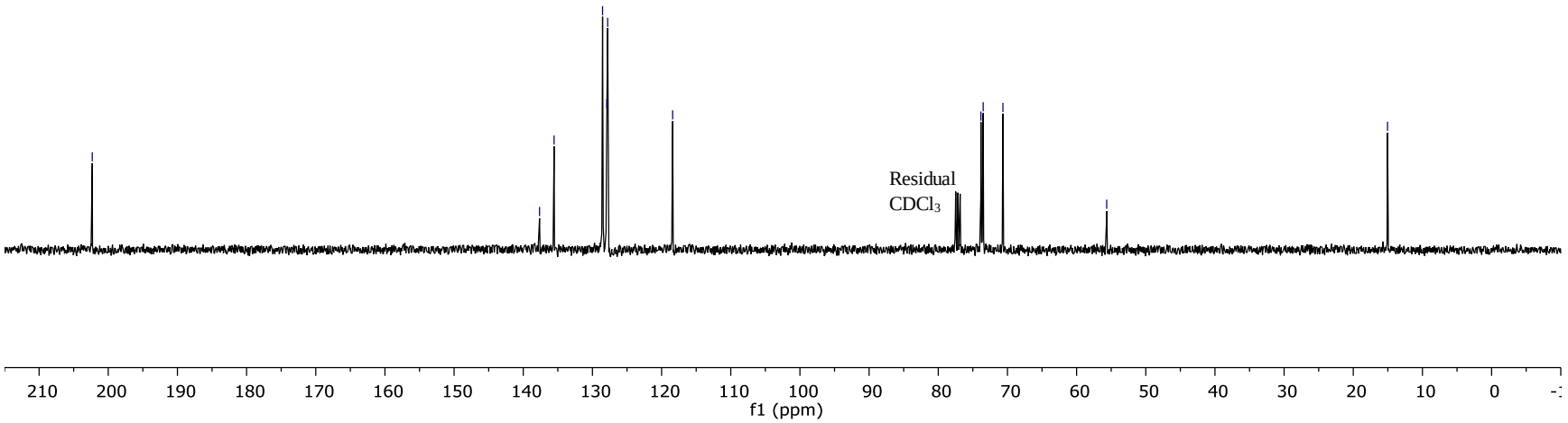


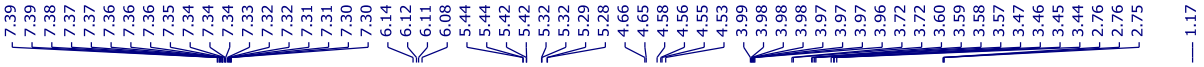
202.31
137.65
135.54
128.53
127.92
127.80
118.40
73.83
73.51
70.65
55.65
15.05

^{13}C-NMR (100.6 MHz, $CDCl_3$)

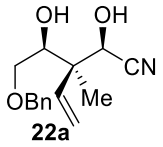


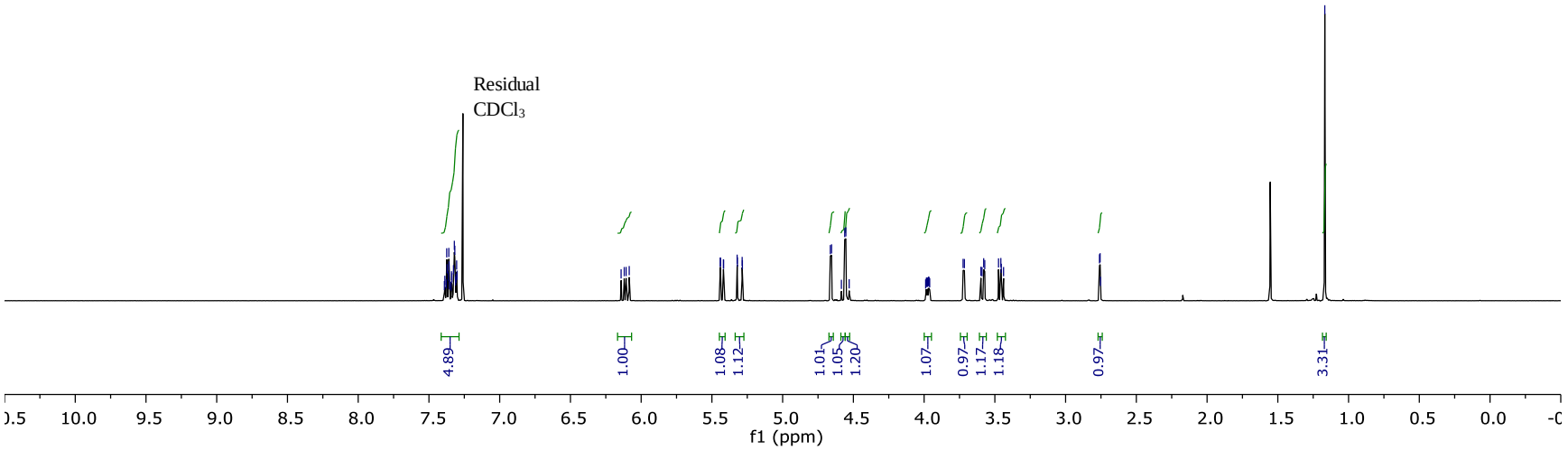
21





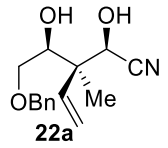
^{1}H-NMR (500 MHz, $CDCl_3$)



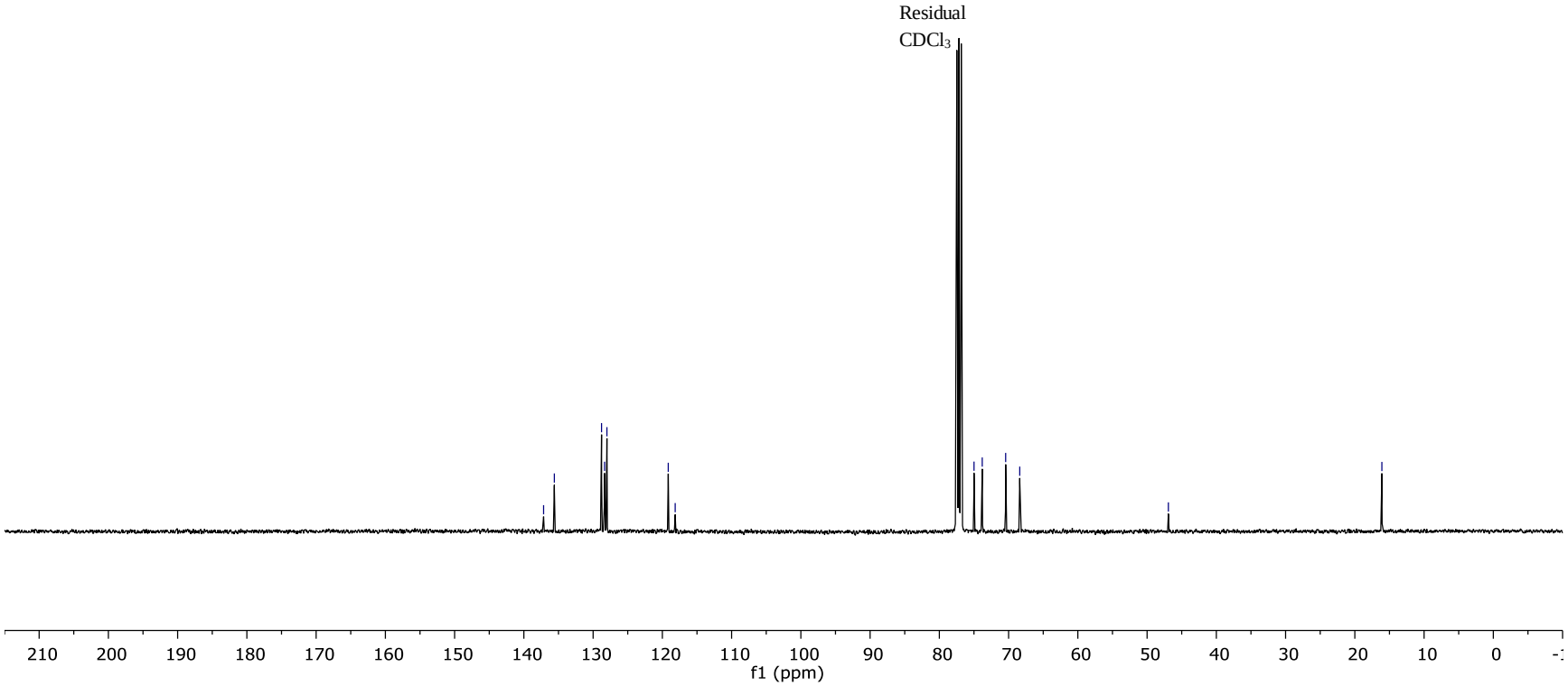


137.15
135.60
128.78
128.34
128.01
119.15
118.15
74.99
73.81
70.42
68.39
46.92
16.10

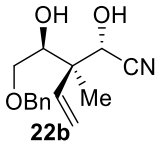
^{13}C-NMR (100.6 MHz, $CDCl_3$)



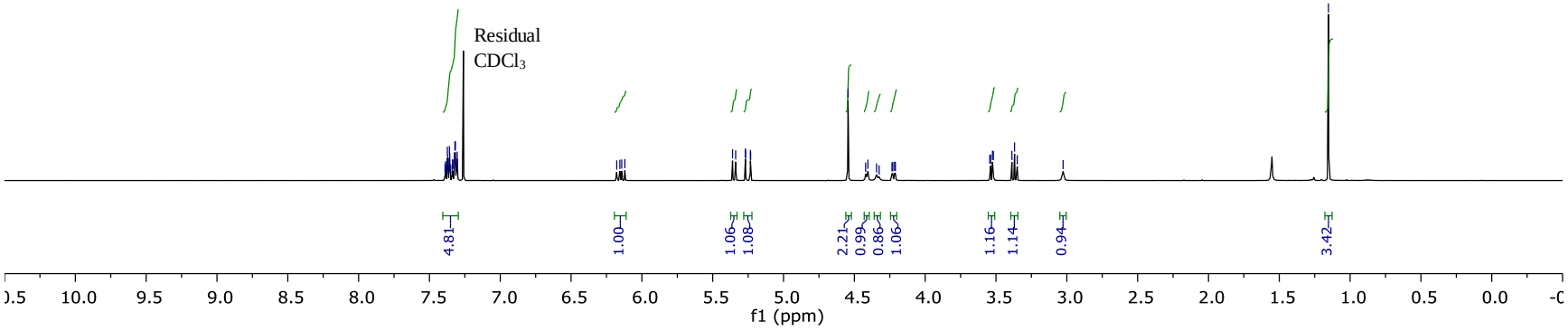
22a



^{1}H-NMR (500 MHz, $CDCl_3$)

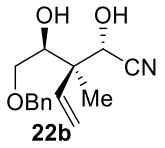


22b

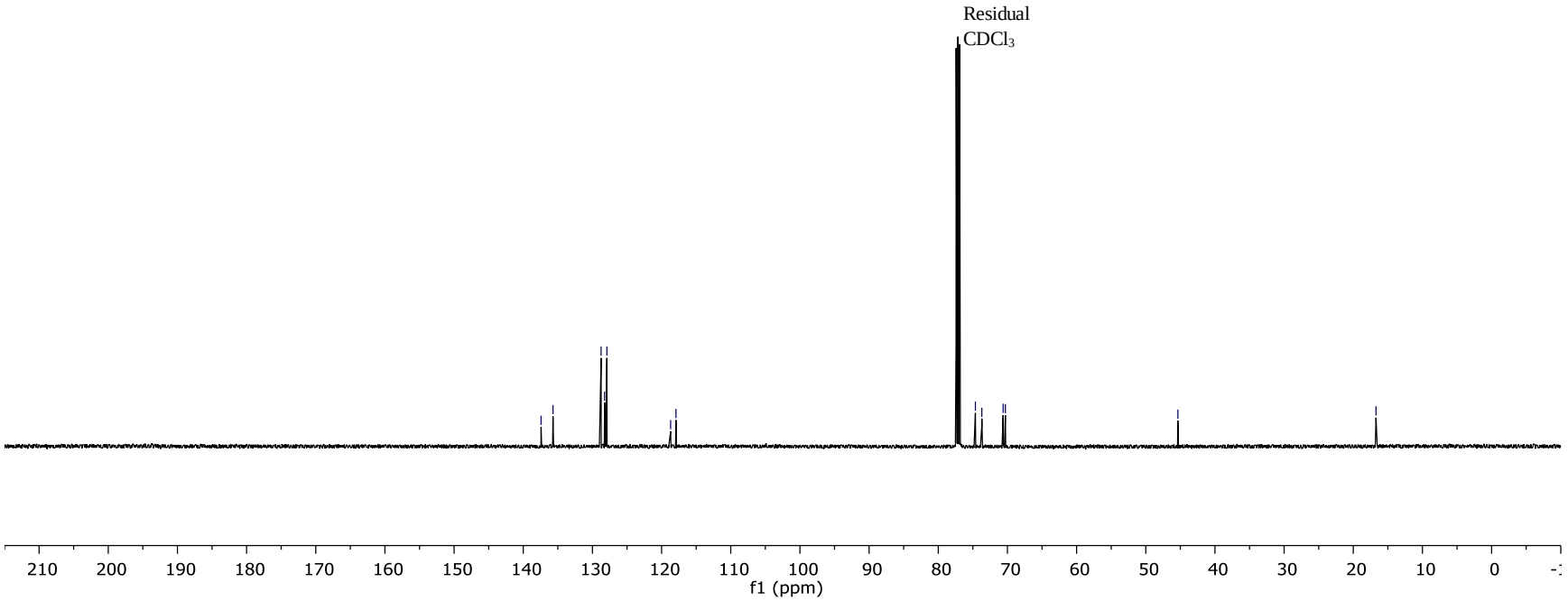


137.42
135.70
128.75
128.24
127.91
118.69
117.93
74.63
73.70
70.62
70.30
45.36
16.71

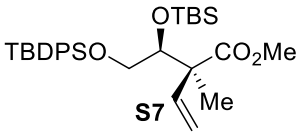
^{13}C-NMR (126 MHz, $CDCl_3$)

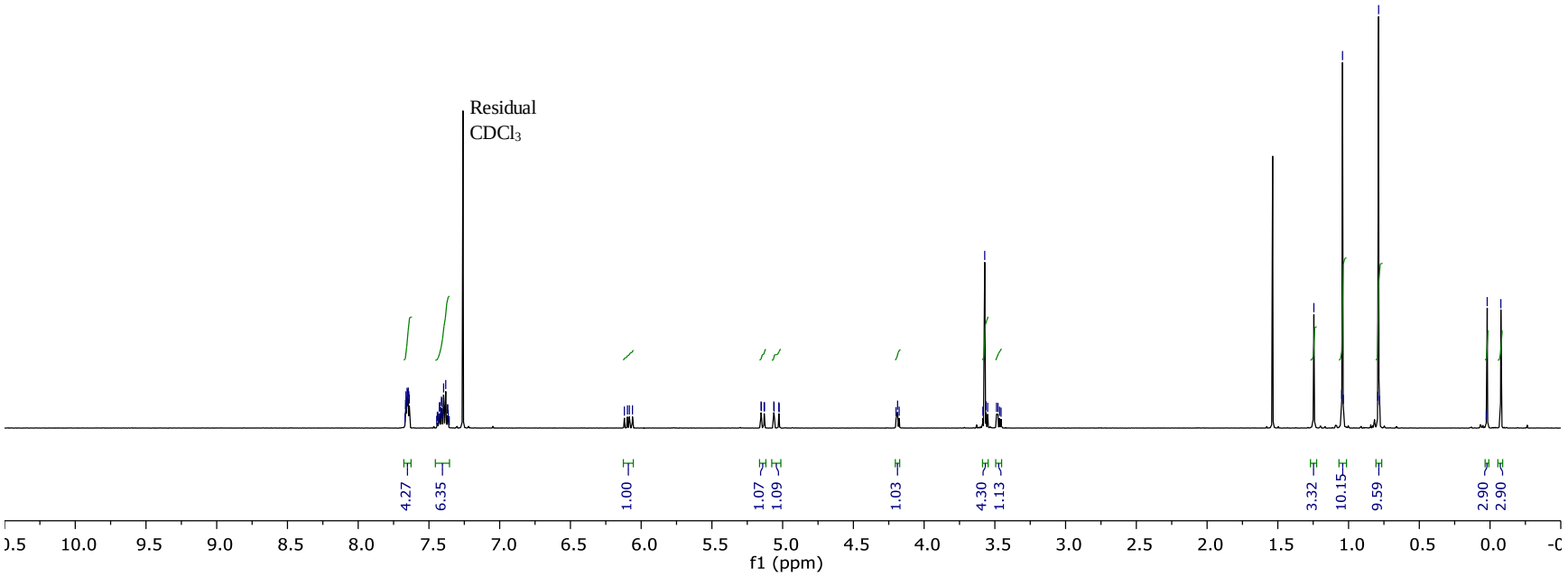


22b



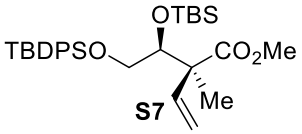
^{1}H-NMR (500 MHz, $CDCl_3$)

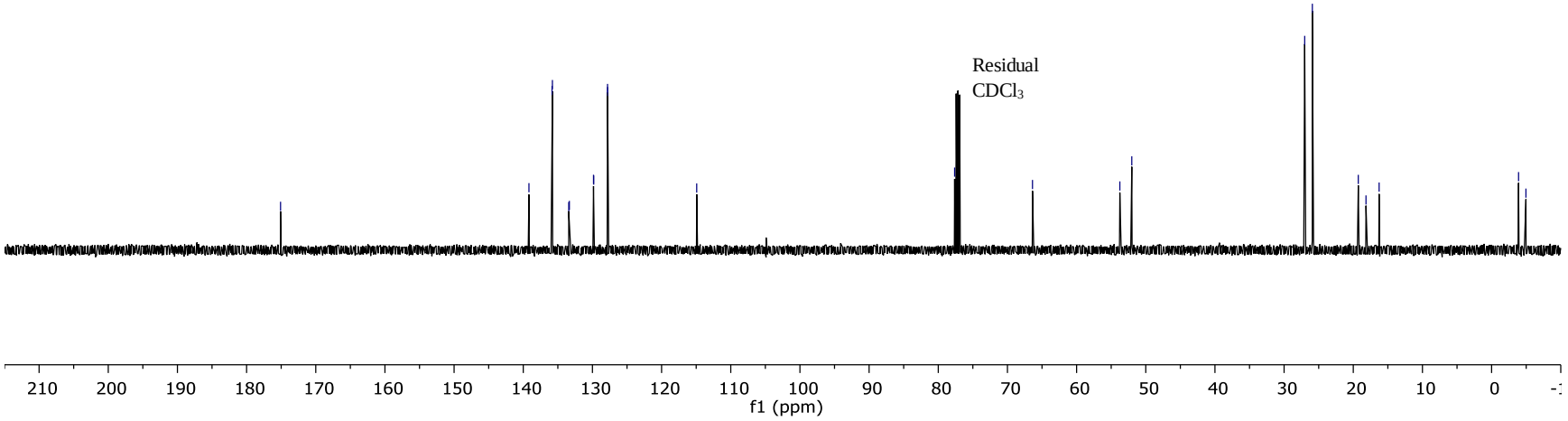




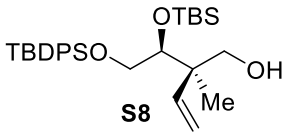
175.09
139.18
135.84
135.79
133.43
133.34
129.84
129.82
127.81
127.81
114.92
77.64
66.38
53.75
52.02
27.02
25.92
19.28
18.16
16.26
-3.90
-4.96

^{13}C-NMR (126 MHz, $CDCl_3$)



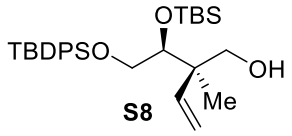


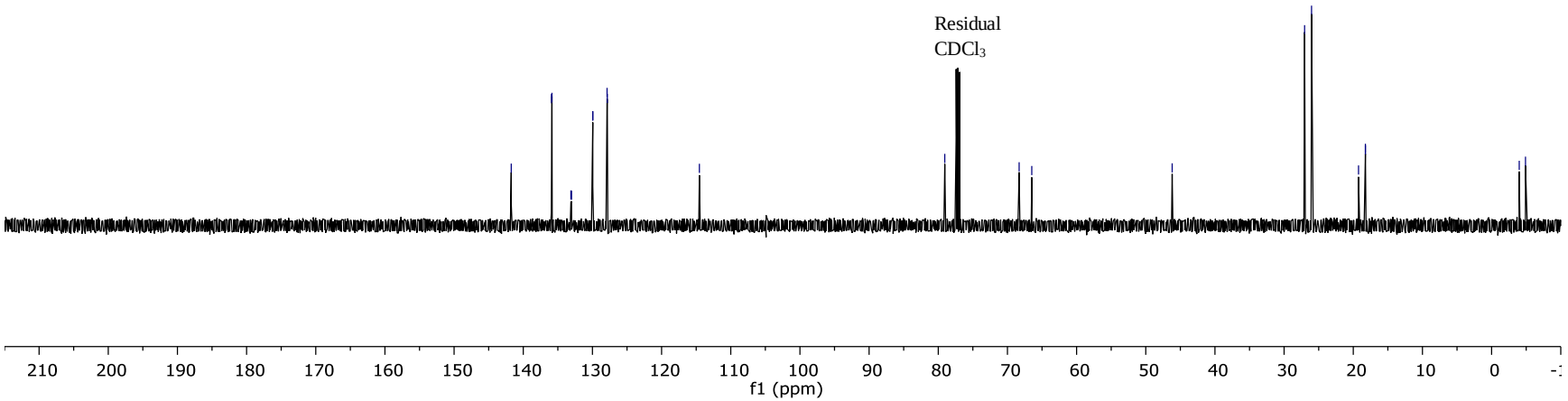
^{1}H-NMR (500 MHz, $CDCl_3$)



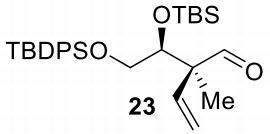
141.7392
135.9208
135.8534
133.1156
133.0201
129.9519
129.9506
127.8830
127.8515
114.5355
79.0598
68.3101
66.4805
46.1847
27.0360
26.0330
19.2384
18.2472
18.2458
-3.9940
-4.8983

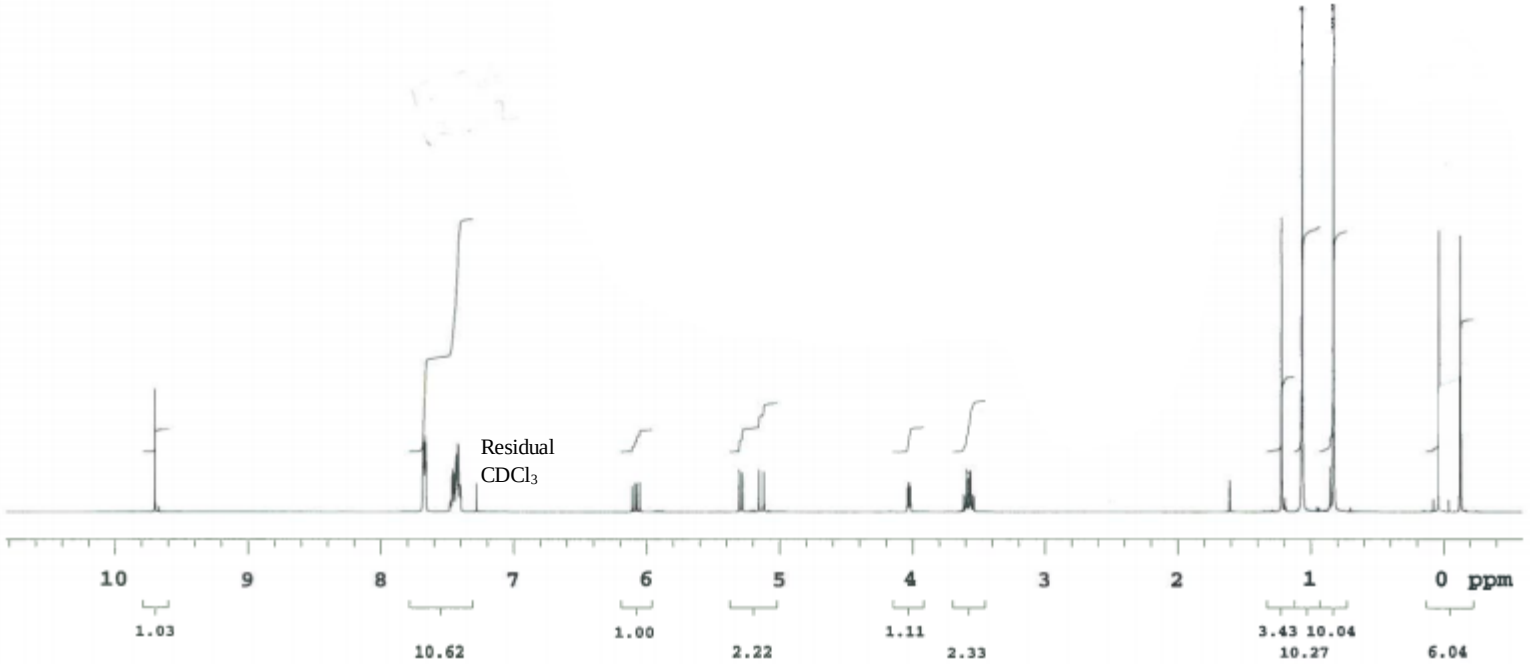
^{13}C-NMR (126 MHz, $CDCl_3$)





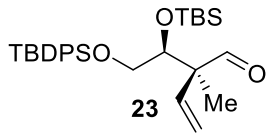
^{1}H-NMR (500 MHz, $CDCl_3$)

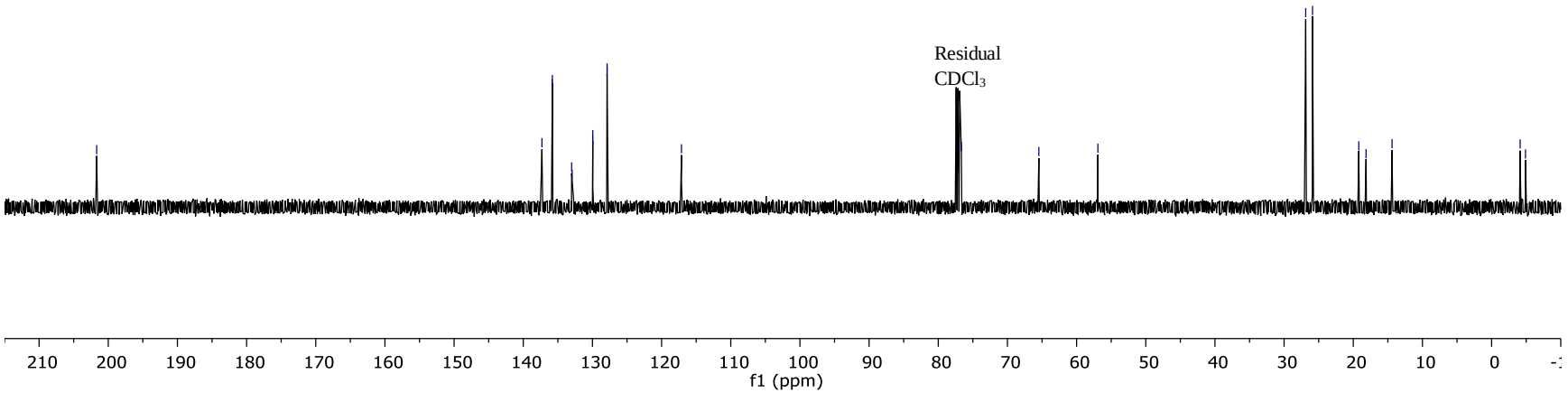




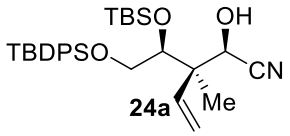
201.68
137.30
135.83
135.79
133.01
132.93
129.96
129.95
127.89
127.87
117.13
76.66
65.46
56.92
26.88
25.89
19.20
18.15
14.40
-4.12
-4.90

^{13}C-NMR (126 MHz, $CDCl_3$)

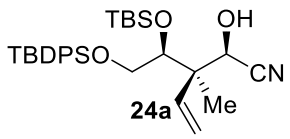




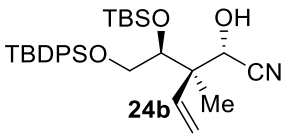
^{1}H-NMR (500 MHz, $CDCl_3$)

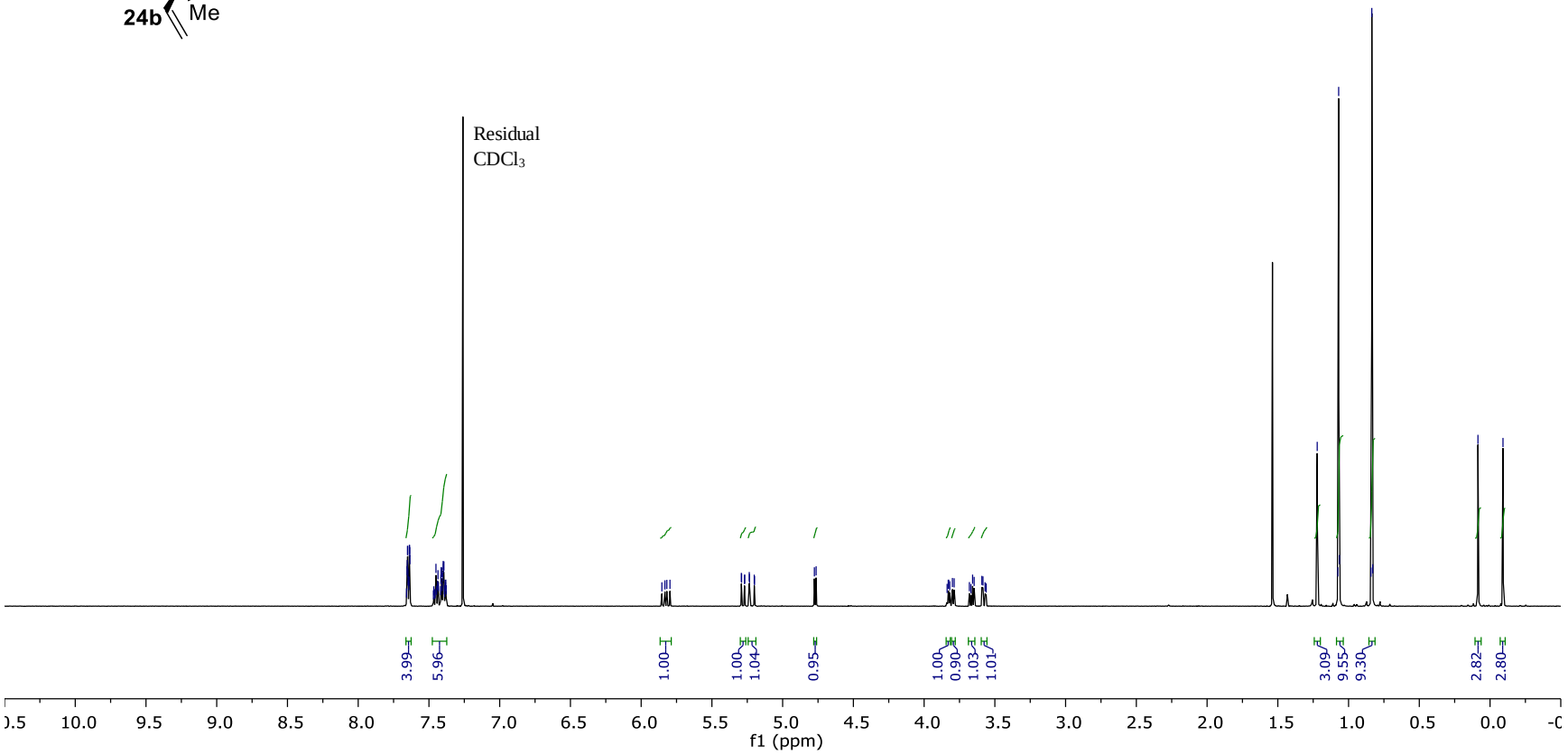


^{13}C-NMR (126 MHz, $CDCl_3$)



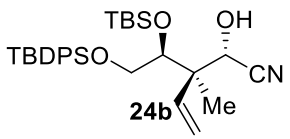
^{1}H-NMR (500 MHz, $CDCl_3$)

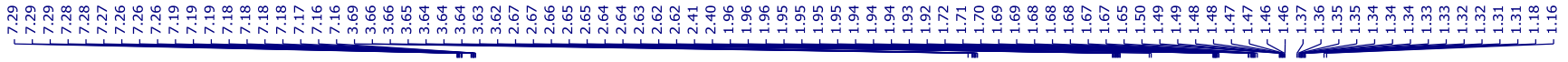




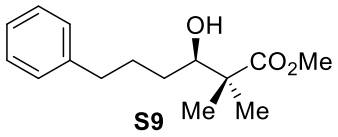
137.03
135.93
135.85
132.79
132.69
130.13
130.12
128.00
127.95
118.88
118.36
78.43
68.17
65.95
47.93
27.03
25.95
19.23
18.17
16.22
-4.16
-4.98

^{13}C-NMR (126 MHz, $CDCl_3$)

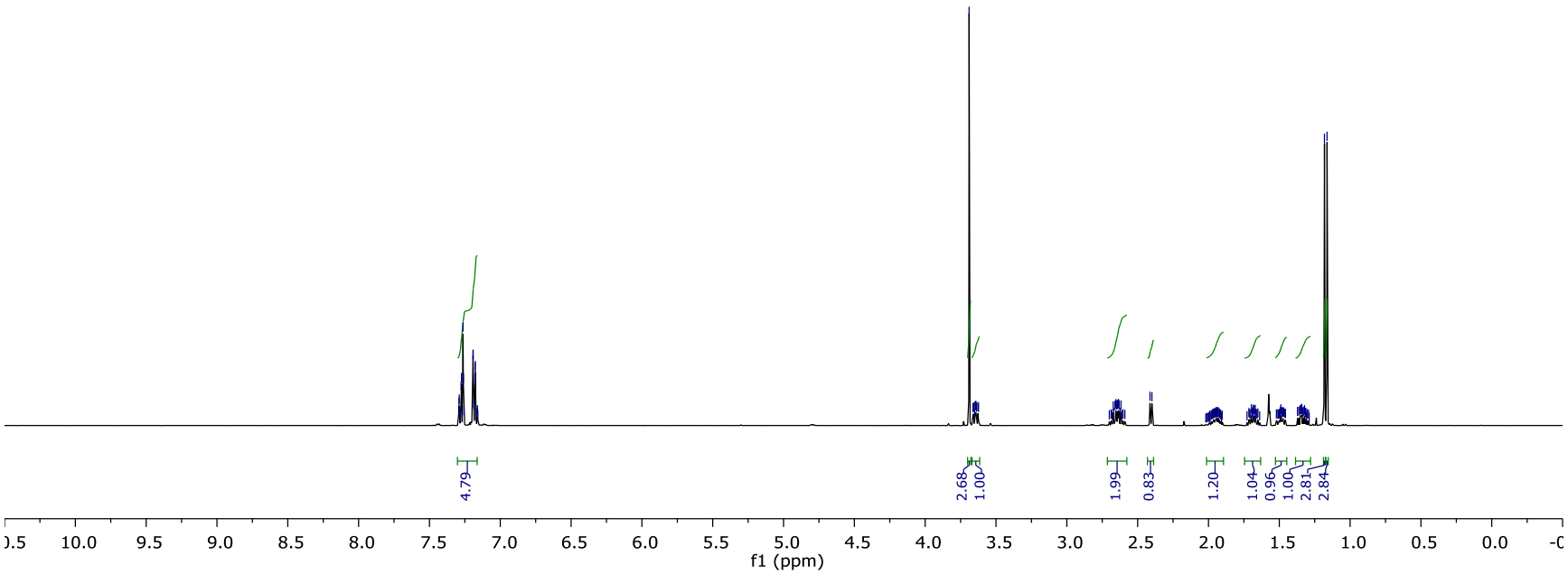




^{1}H-NMR (500 MHz, $CDCl_3$)

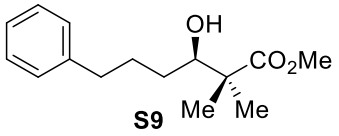


S9

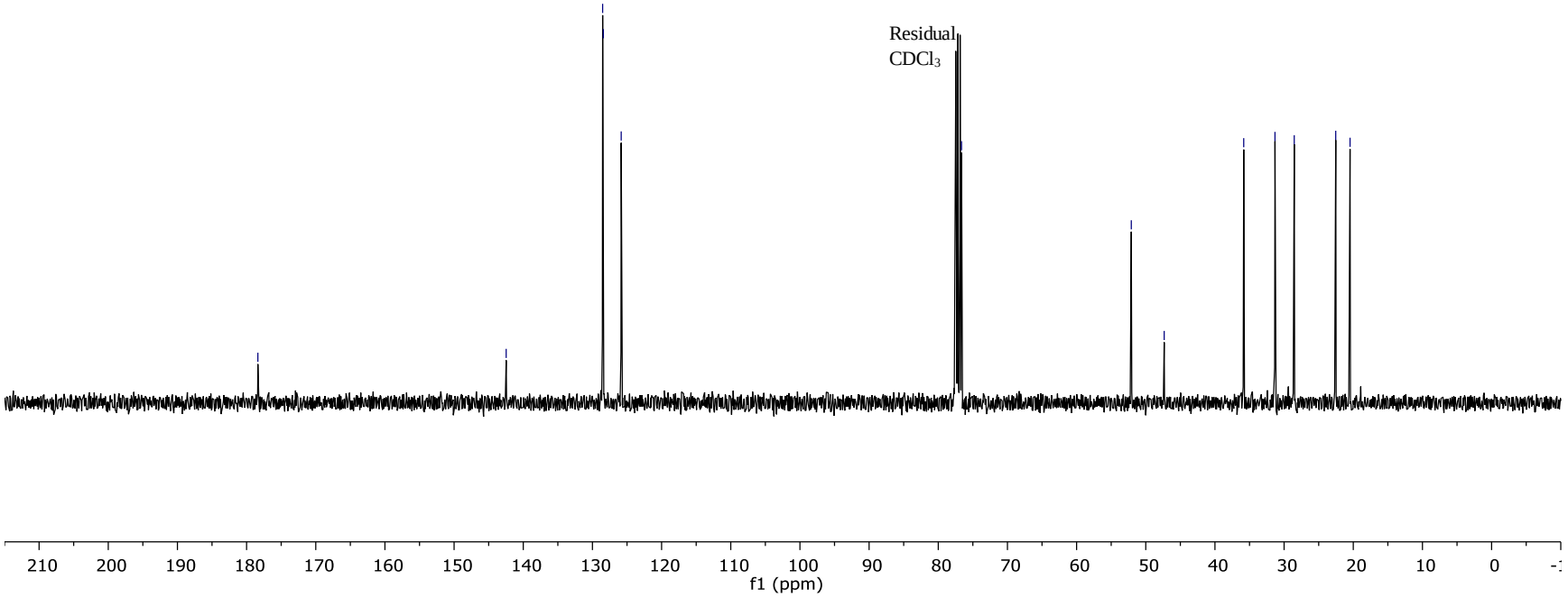


178.37 142.47 128.52 128.42 125.84 76.64 52.09 47.34 35.84 31.32 28.53 22.54 20.47

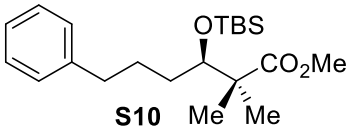
^{13}C-NMR (100.6 MHz, $CDCl_3$)

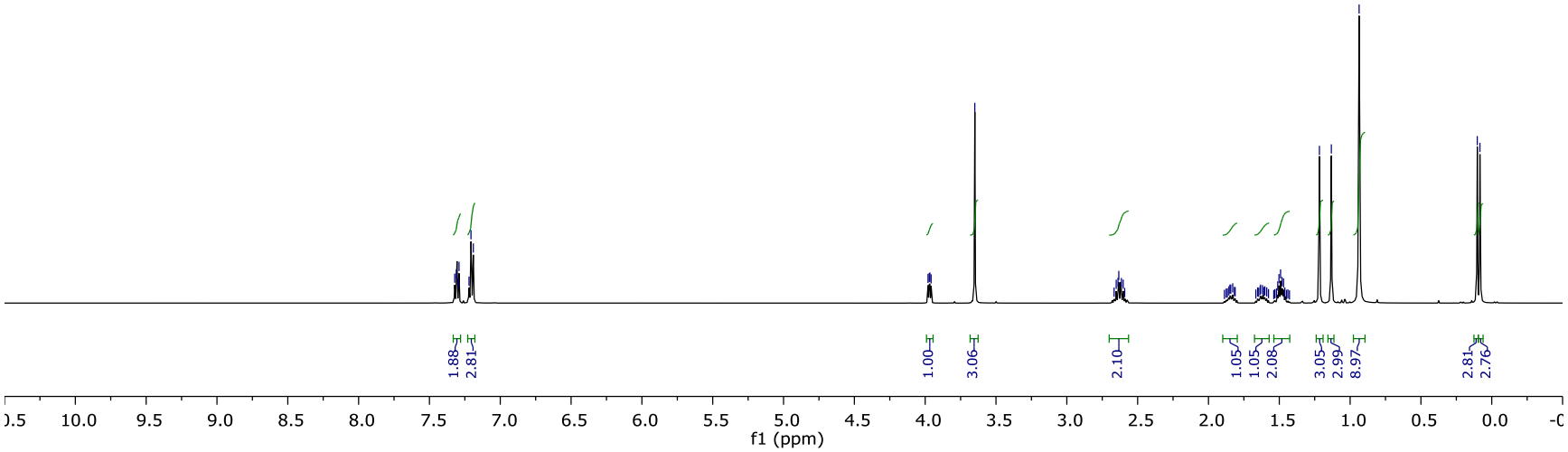


S9



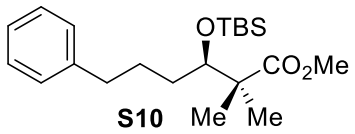
^{1}H-NMR (500 MHz, $CDCl_3$)



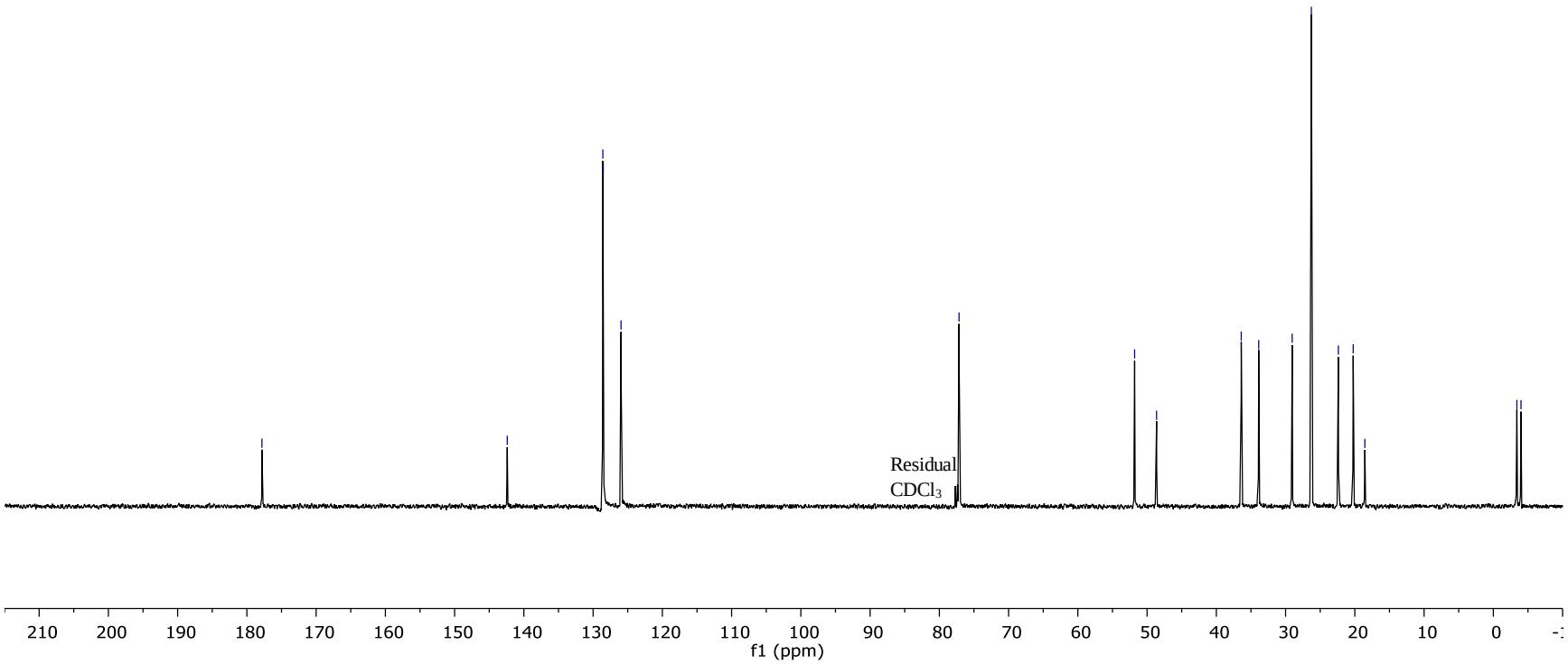


177.82 142.40 128.60 128.53 125.97 77.16 51.80 48.63 36.40 33.88 29.05 26.28 22.38 20.24 18.55 -3.40 -4.00

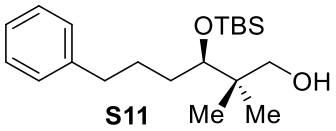
^{13}C-NMR (100.6 MHz, $CDCl_3$)



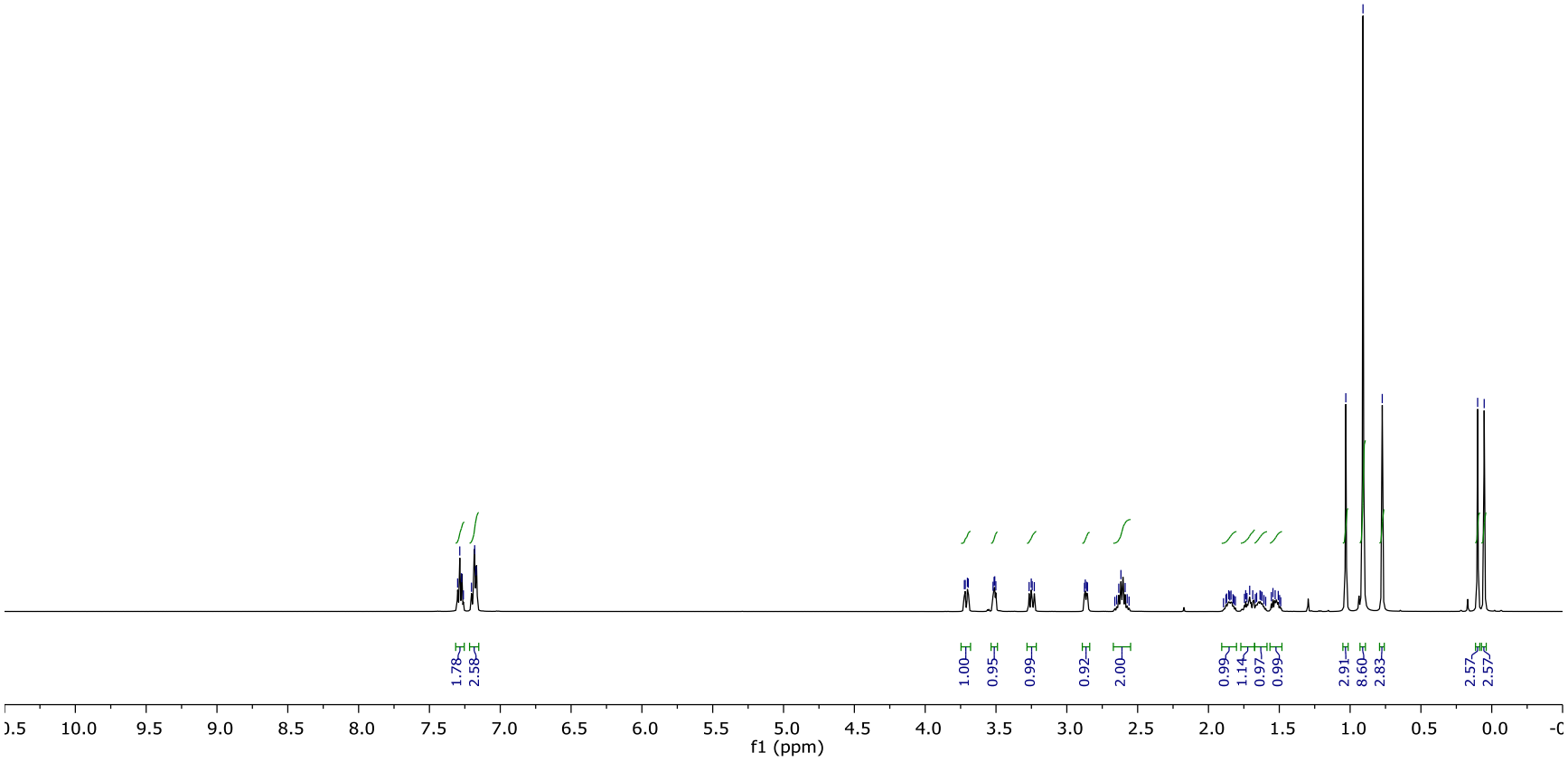
S10



^{1}H-NMR (500 MHz, $CDCl_3$)

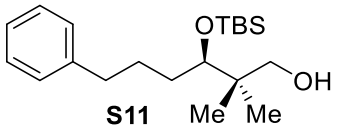


S11

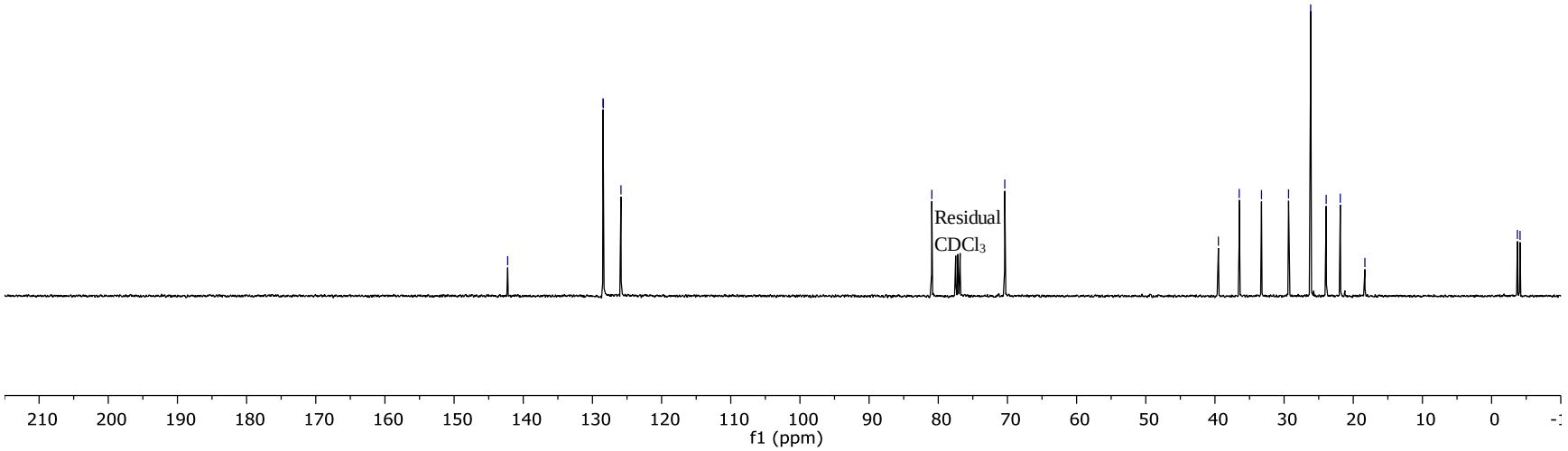


142.25
128.47
128.42
125.87
80.93
70.39
39.50
36.49
33.27
29.35
26.16
23.92
21.88
18.32
-3.73
-4.11

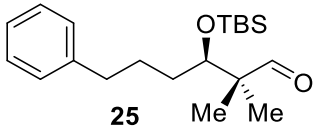
^{13}C-NMR (100.6 MHz, $CDCl_3$)



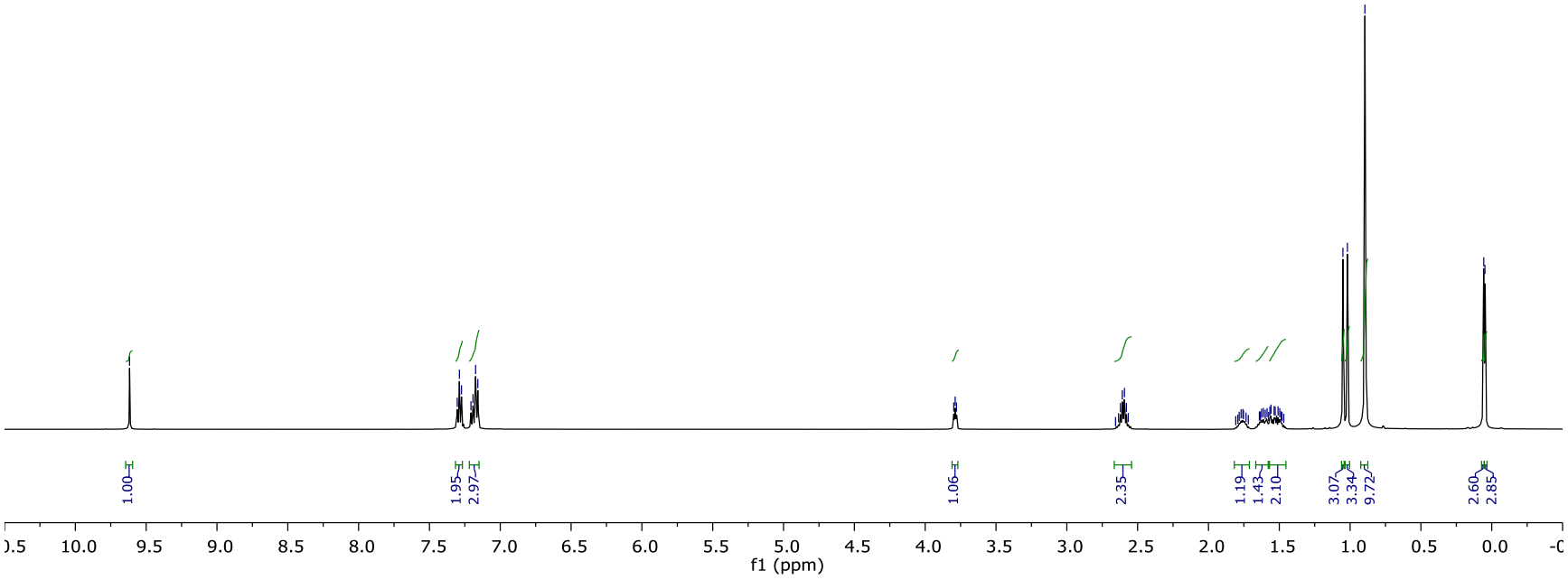
S11



^{1}H-NMR (500 MHz, $CDCl_3$)

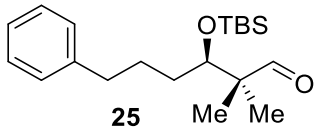


25

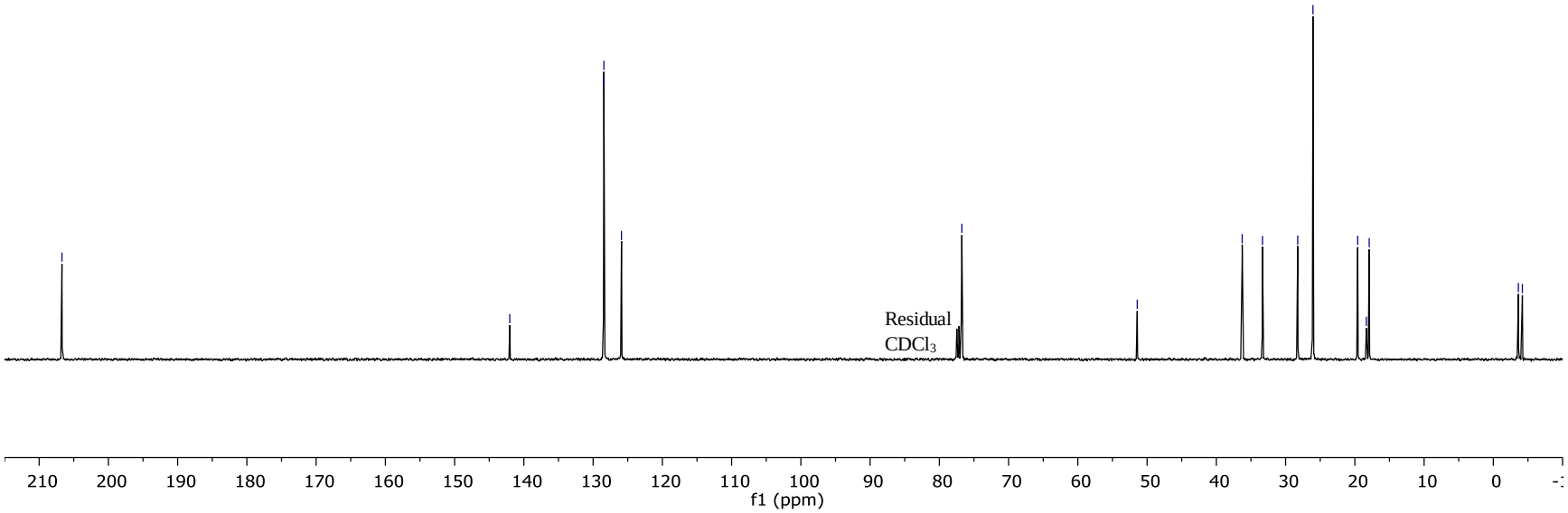


206.70
142.04
128.44
128.43
125.90
76.75
51.42
36.27
33.34
28.25
26.04
19.59
18.34
17.92
-3.62
-4.20

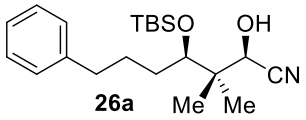
^{13}C-NMR (100.6 MHz, $CDCl_3$)



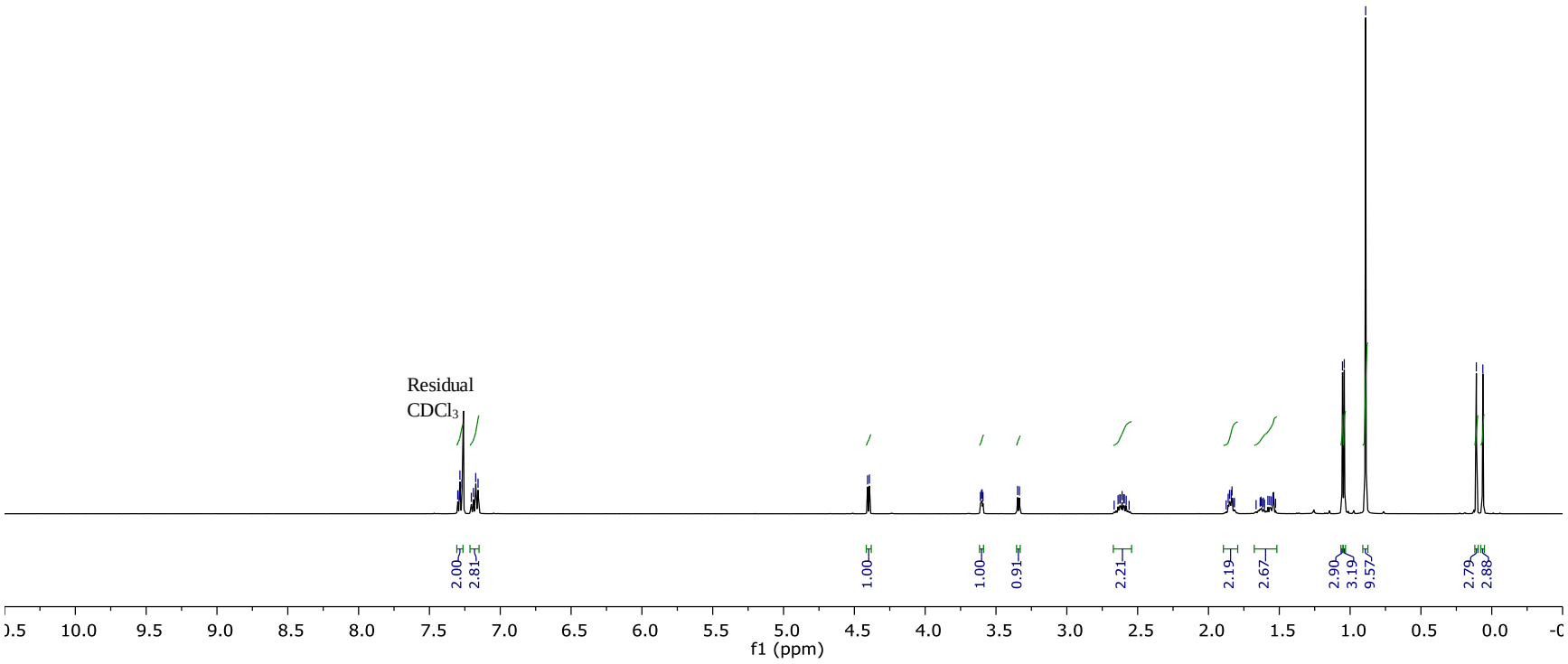
25



^{1}H-NMR (500 MHz, $CDCl_3$)

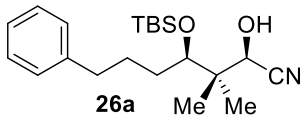


26a

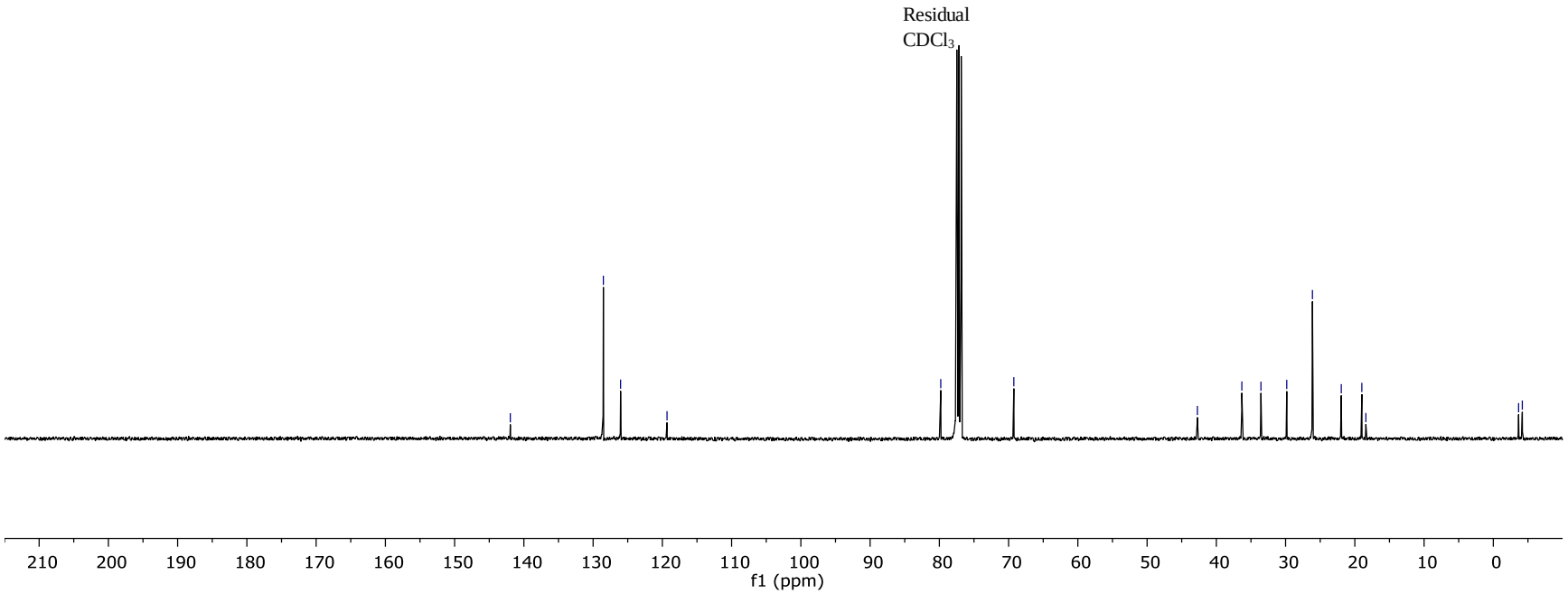


141.96
128.52
126.03
119.33
79.80
69.24
42.73
36.32
33.56
29.83
26.12
21.96
18.99
18.41
-3.65
-4.19

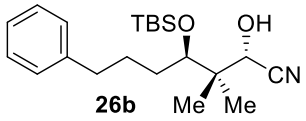
^{13}C-NMR (100.6 MHz, $CDCl_3$)



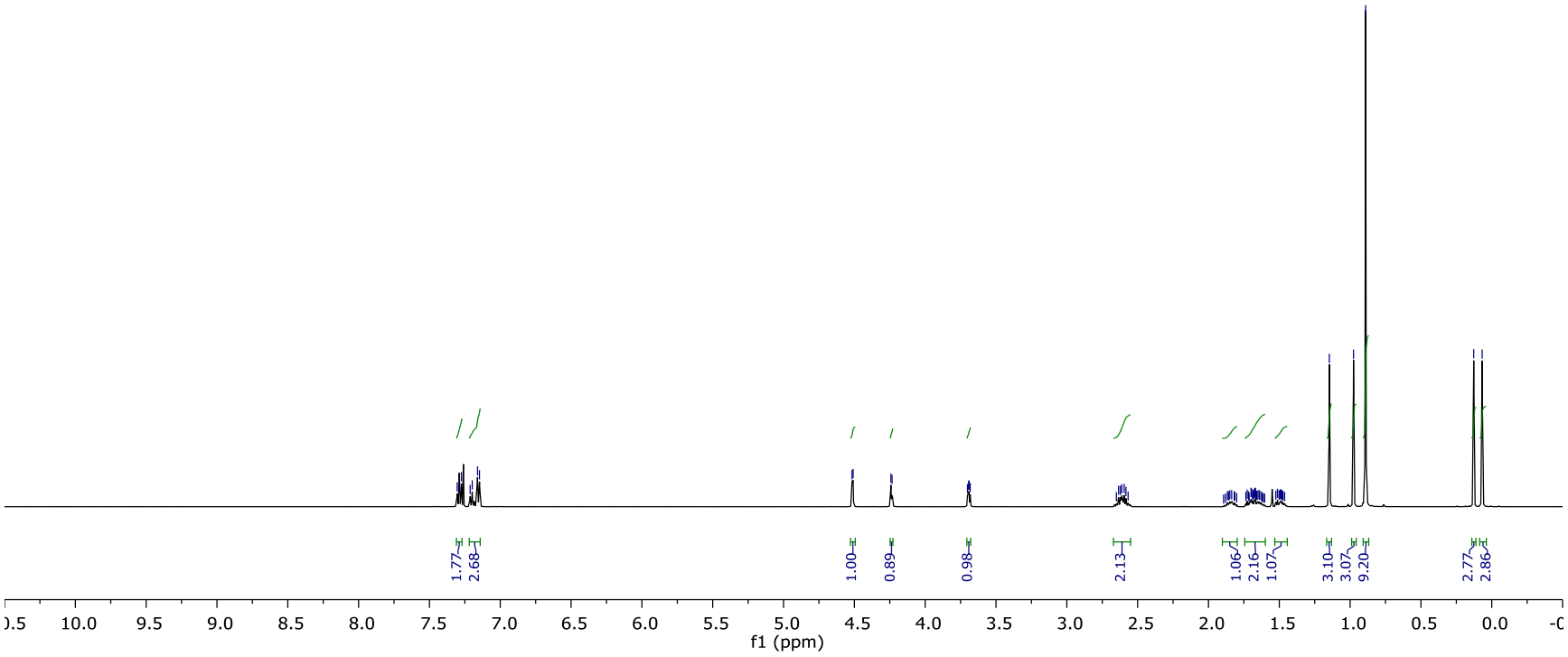
26a



^{1}H-NMR (500 MHz, $CDCl_3$)

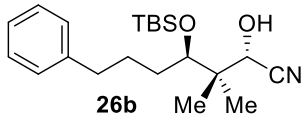


26b

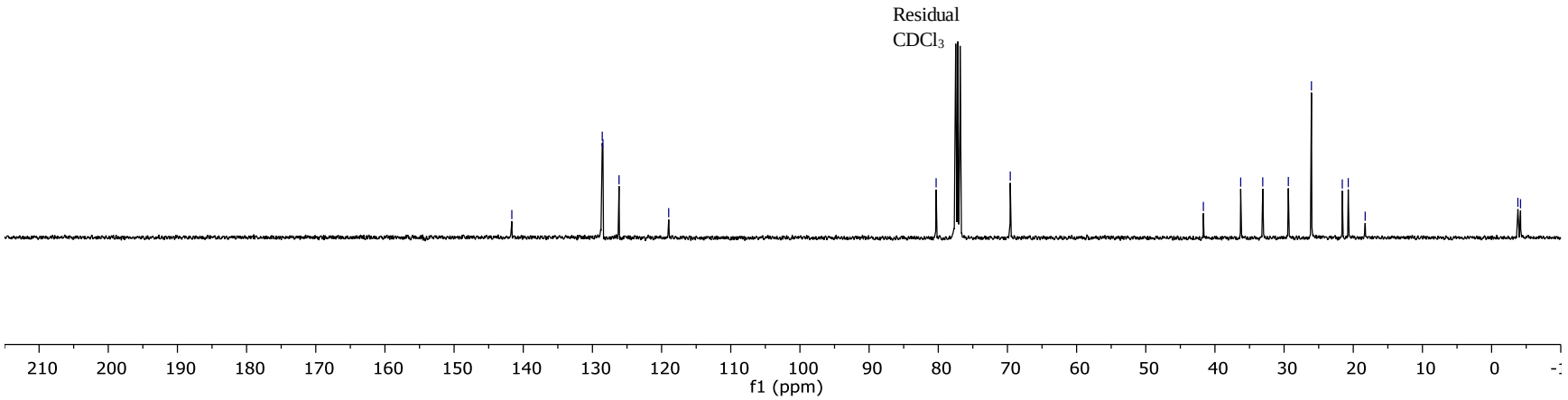


141.66
128.58
128.48
126.15
118.97
80.31
69.59
41.67
36.28
33.09
29.39
26.05
21.59
20.73
18.28
-3.80
-4.18

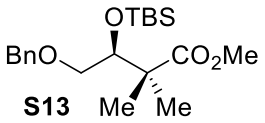
^{13}C-NMR (100.6 MHz, $CDCl_3$)



26b

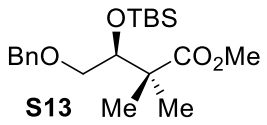


^{1}H-NMR (500 MHz, $CDCl_3$)

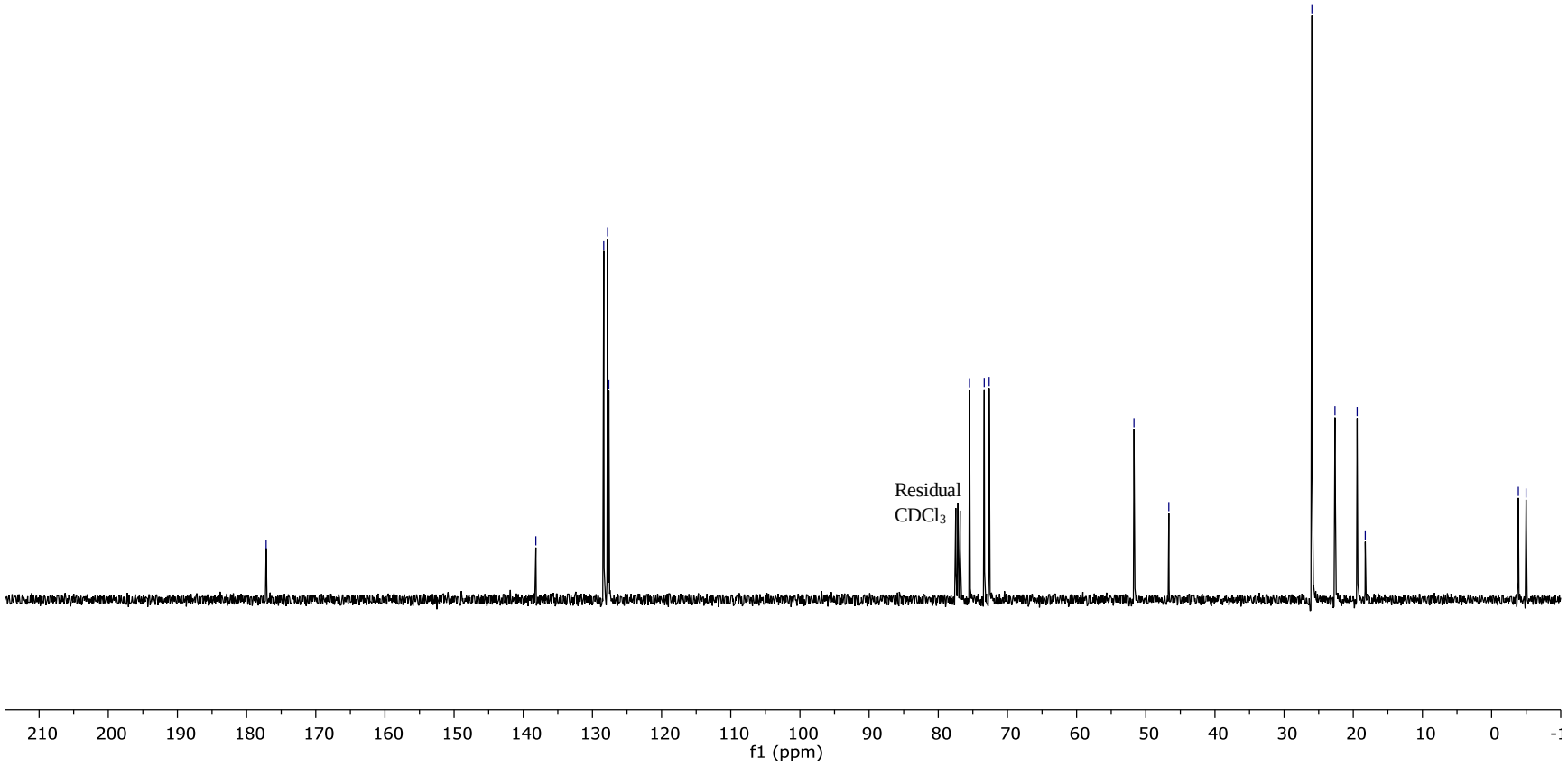


177.18
138.18
128.36
127.80
127.63
75.48
73.35
72.64
51.71
46.67
25.98
22.65
19.44
18.27
-3.87
-4.99

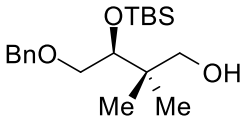
^{13}C-NMR (100.6 MHz, $CDCl_3$)



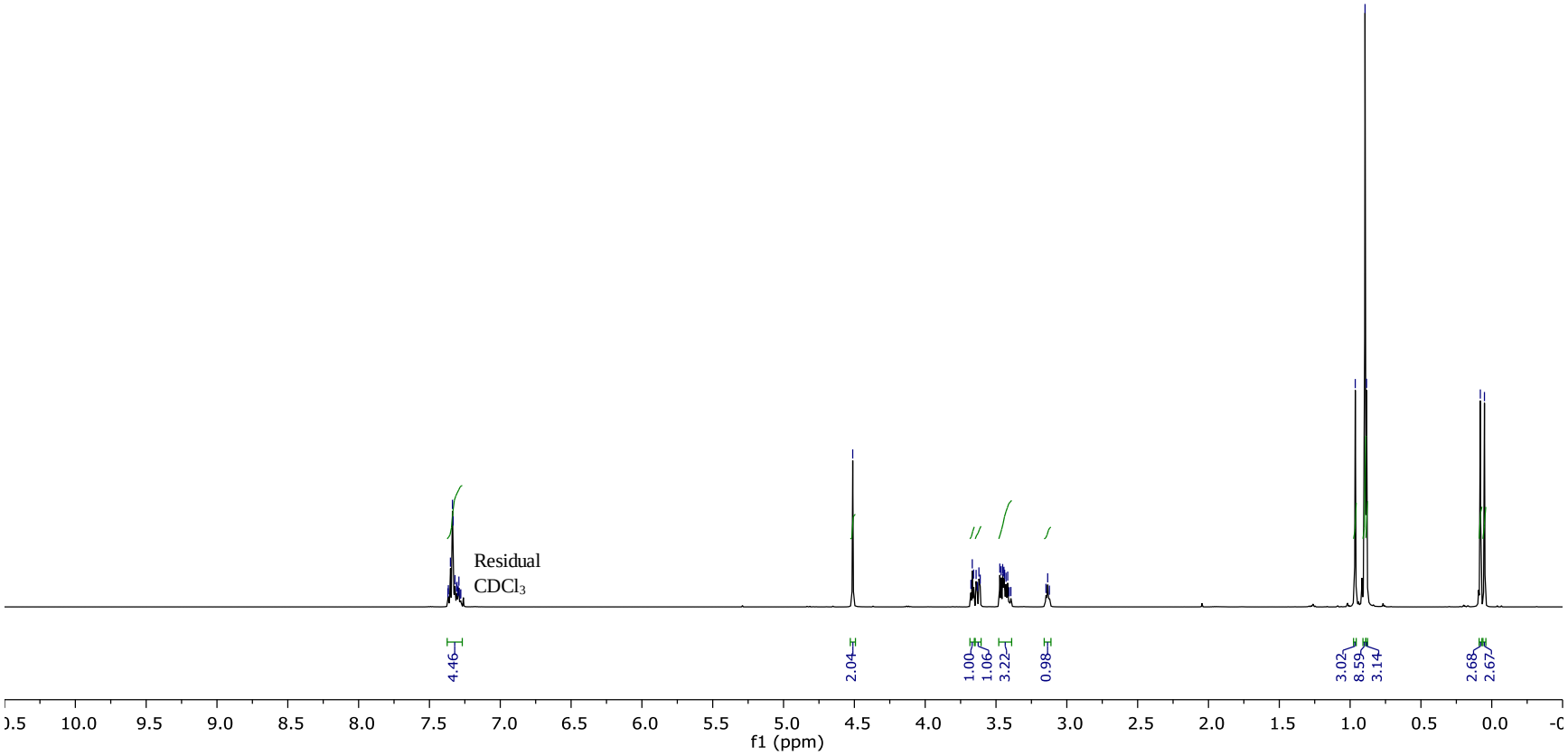
S13



^{1}H-NMR (500 MHz, $CDCl_3$)

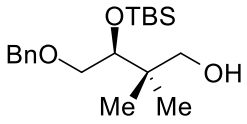


S14

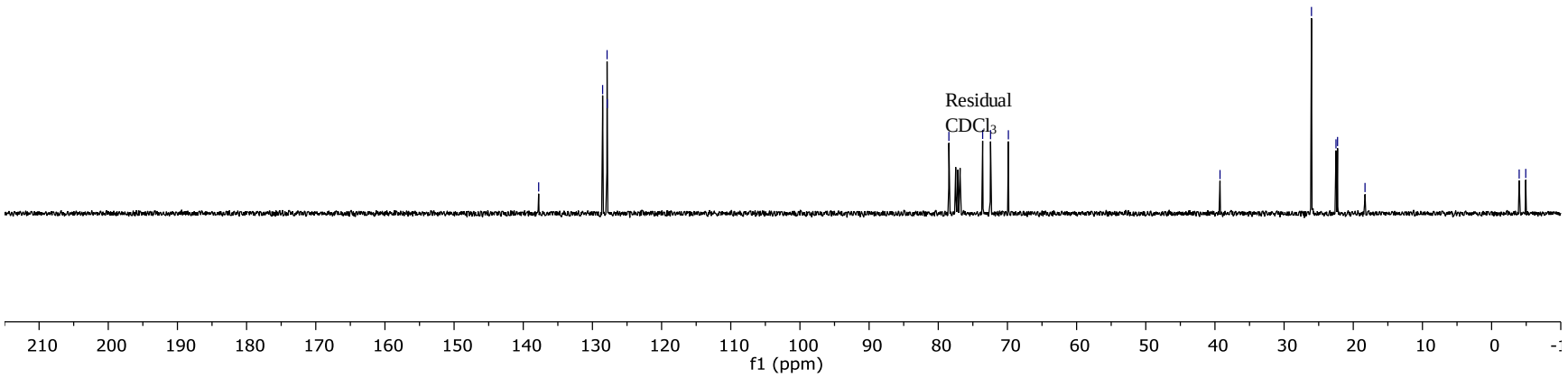


137.77
128.53
127.88
127.86
78.46
73.58
72.44
69.86
39.27
26.05
22.50
22.27
18.30
-3.99
-4.93

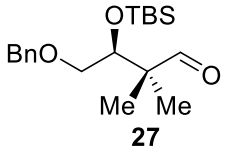
^{13}C-NMR (100.6 MHz, $CDCl_3$)



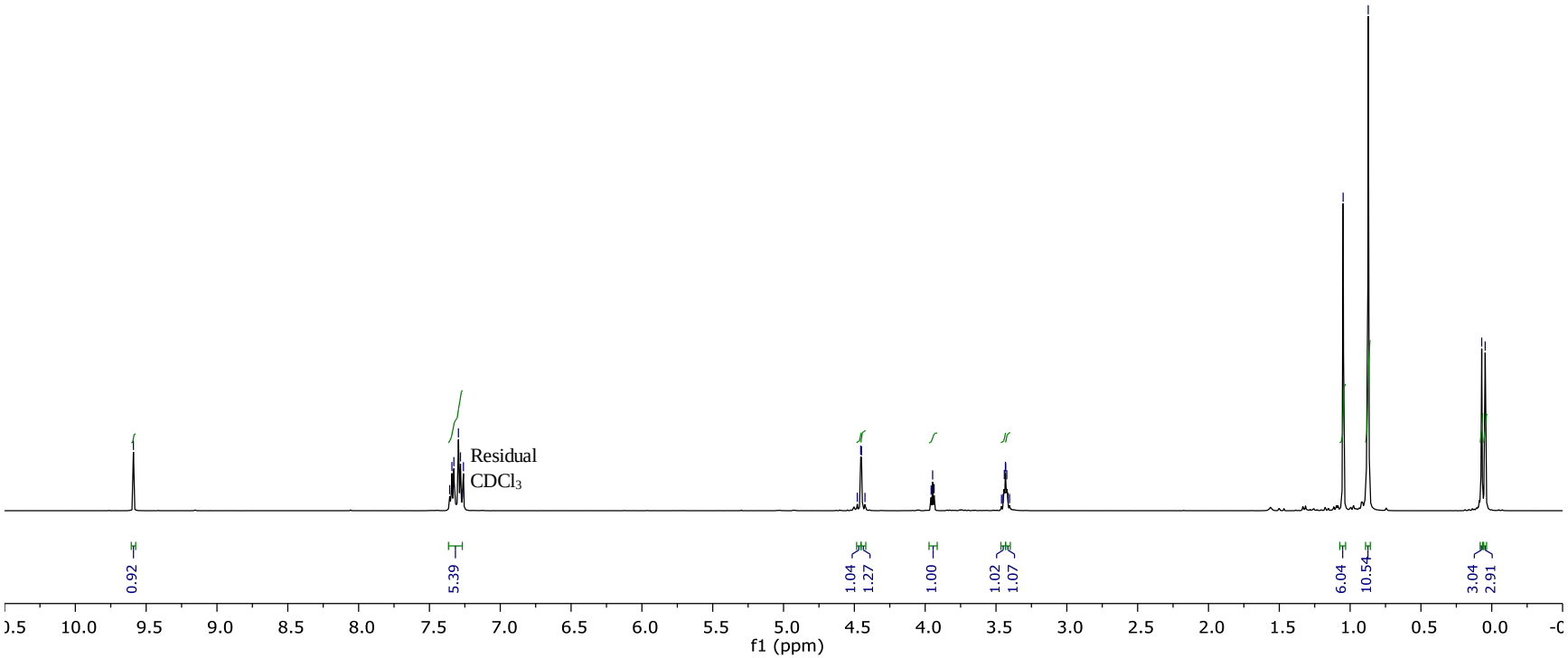
S14



^{1}H-NMR (500 MHz, $CDCl_3$)

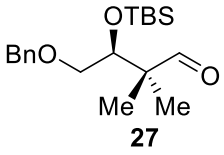


27



204.99 137.91 128.50 127.82 127.79 75.48 73.50 71.83 50.12 25.96 19.10 18.28 17.92 -3.95 -4.89

^{13}C-NMR (126 MHz, $CDCl_3$)



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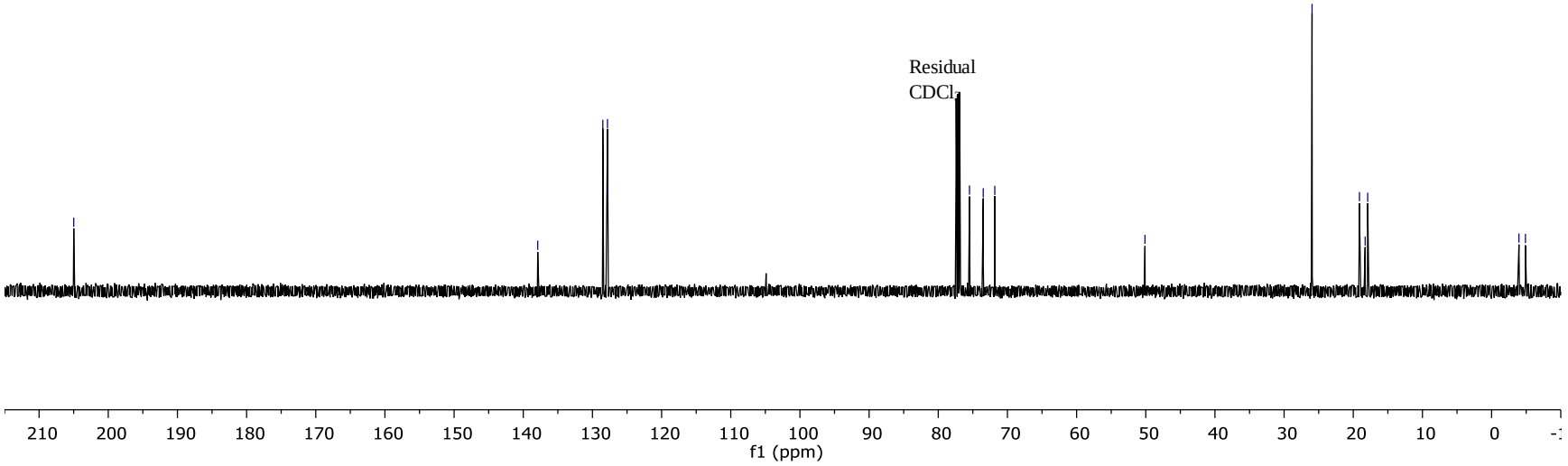
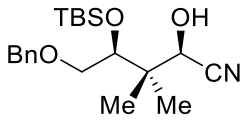
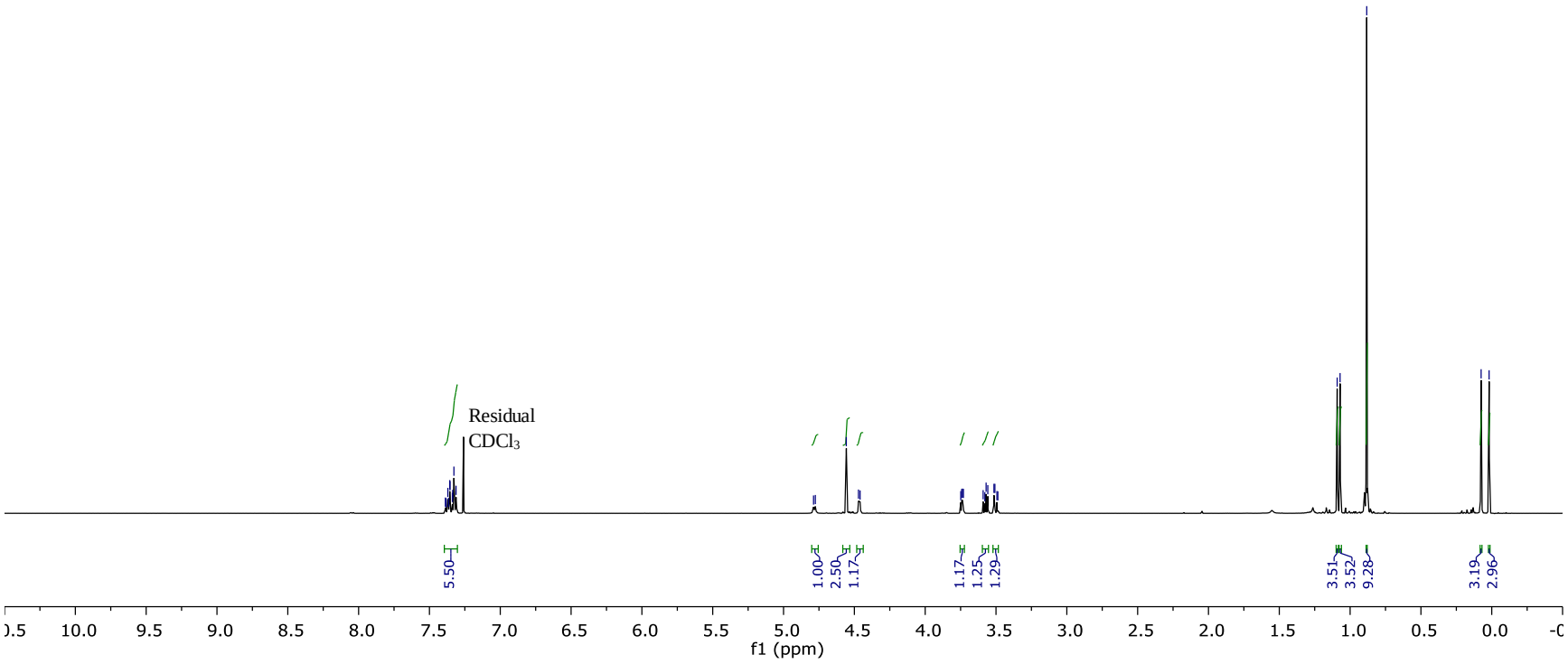


^{1}H-NMR (500 MHz, $CDCl_3$)

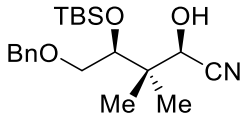


28a



136.47
128.79
128.47
128.24
119.39
76.18
73.95
70.70
67.73
42.87
25.94
21.51
20.87
18.23
-4.12
-4.90

^{13}C-NMR (100.6 MHz, $CDCl_3$)



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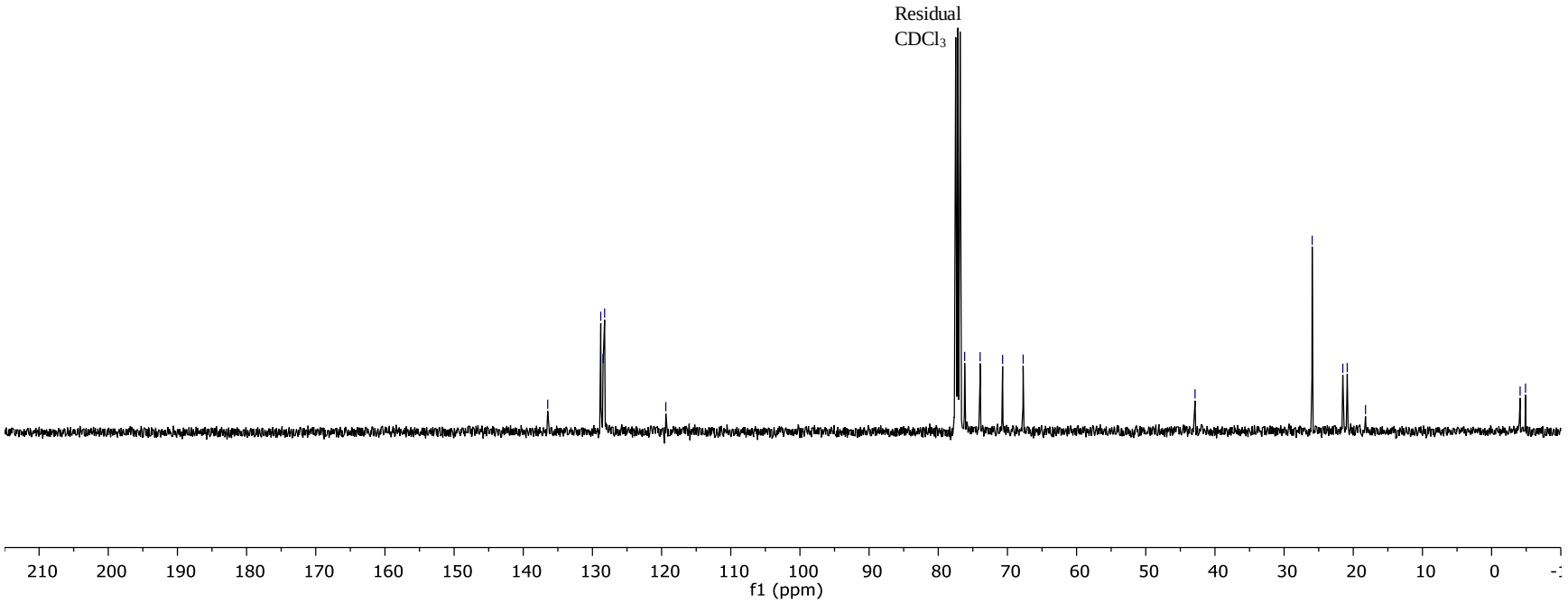
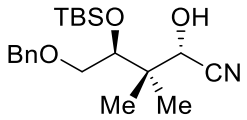
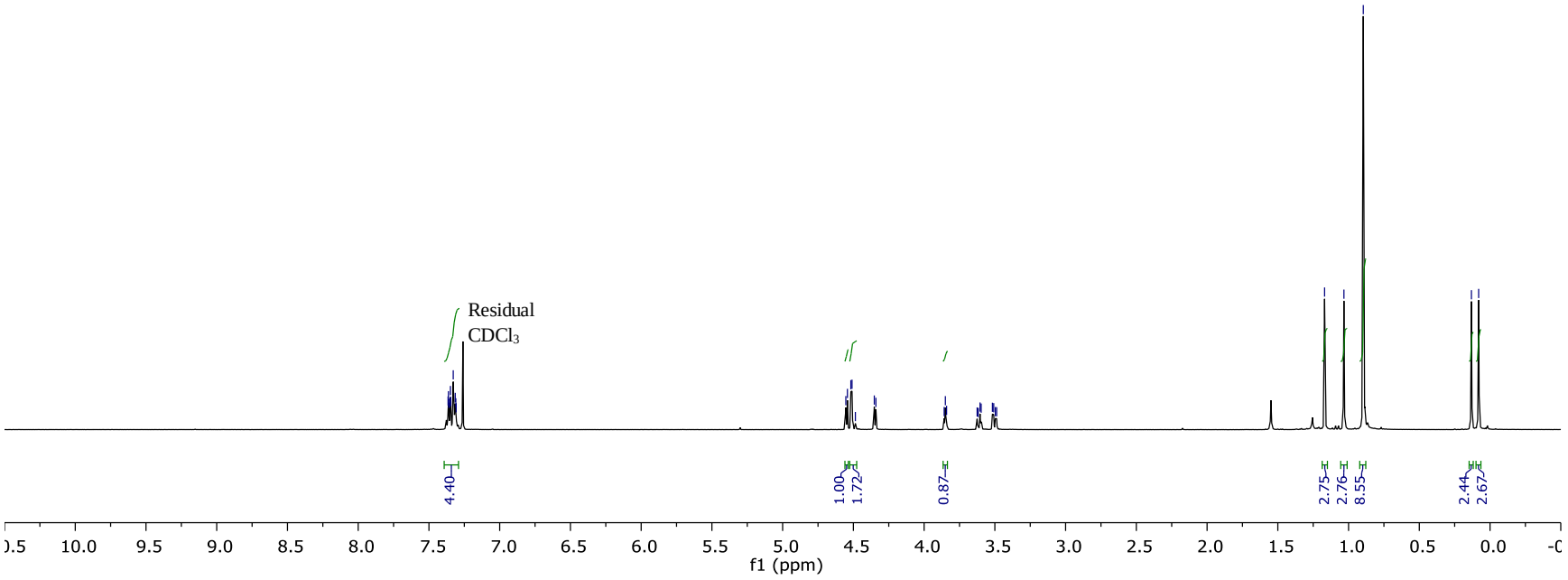


^{1}H-NMR (500 MHz, $CDCl_3$)

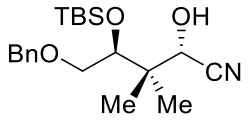


28b

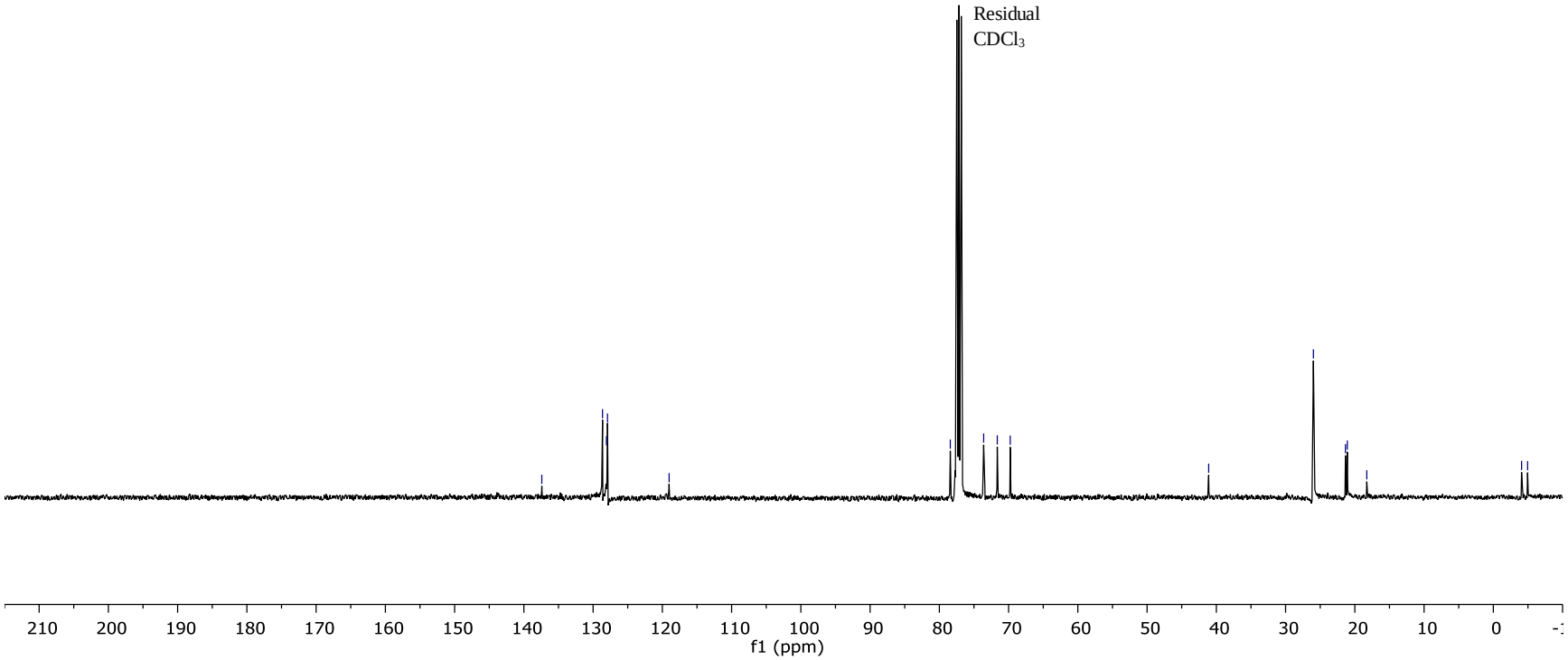


137.41
128.64
128.07
127.92
119.02
78.42
73.60
71.63
69.76
41.10
25.98
21.36
21.08
18.27
-4.08
-4.95

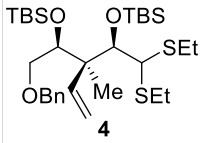
^{13}C-NMR (100.6 MHz, $CDCl_3$)



28b



^{1}H-NMR (500 MHz, $CDCl_3$)



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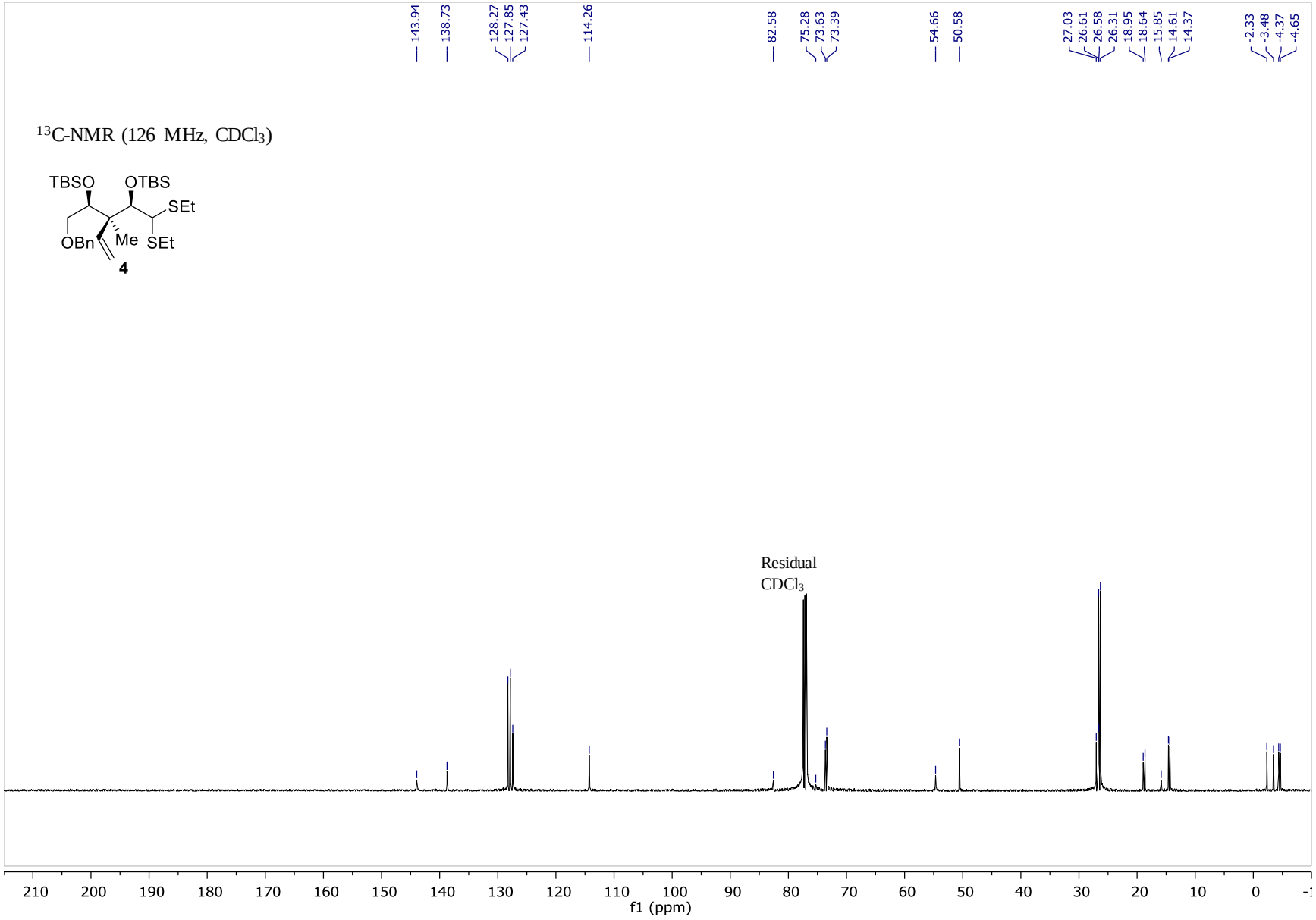
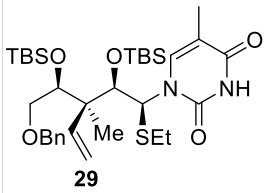


^{13}C-NMR (126 MHz, $CDCl_3$)

4

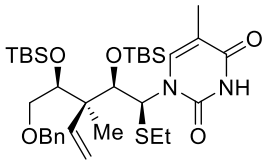
^{1}H-NMR (500 MHz, $CDCl_3$)



29

163.56 150.53 141.00 138.30 138.09 128.39 128.04 127.70 116.07 111.24 79.46 73.51 73.38 72.99 64.90 50.49 26.62 26.10 24.26 19.30 18.50 14.32 13.88 12.45 -1.81 -3.53 -3.57 -4.53

^{13}C-NMR (126 MHz, $CDCl_3$)



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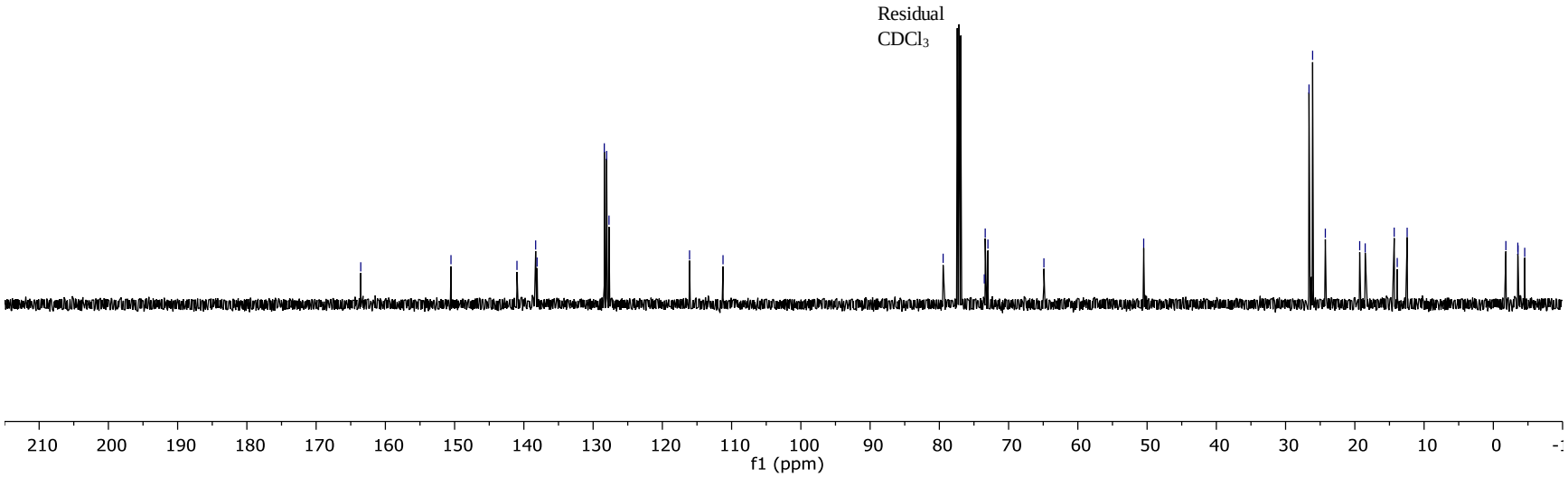
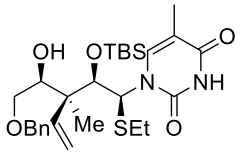


^{1}H-NMR (500 MHz, $CDCl_3$)



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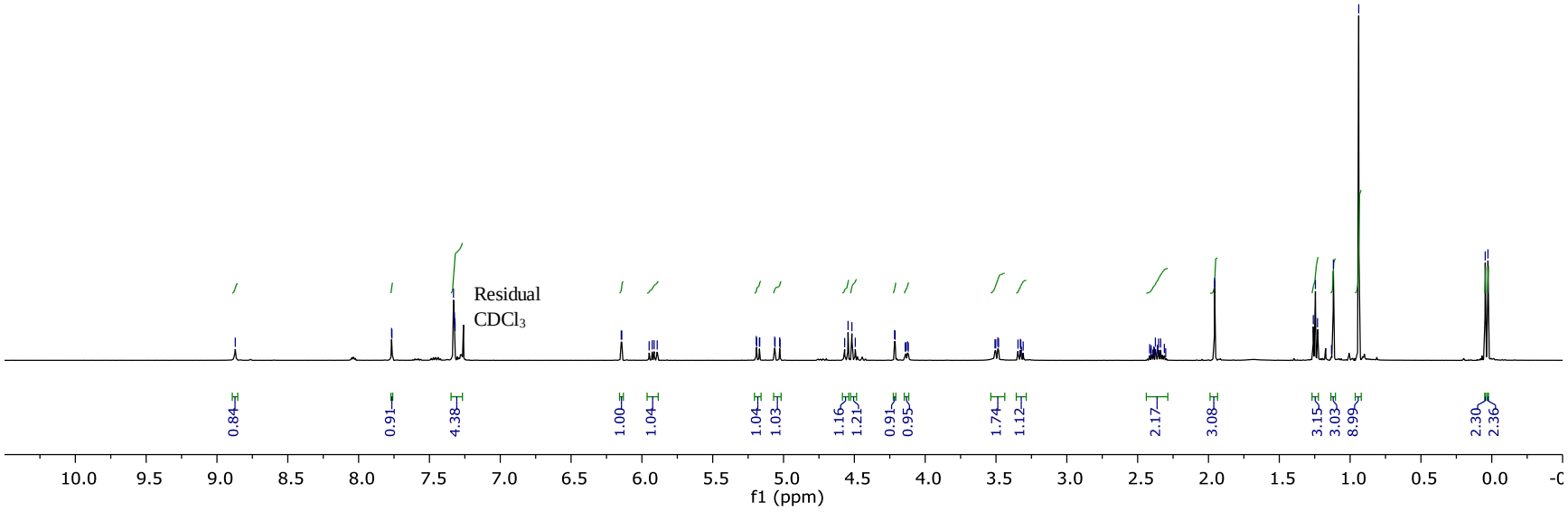
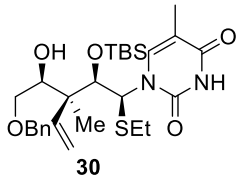


163.58 151.48 140.51 138.29 138.07 128.47 127.87 127.72 116.98 111.36 79.33 73.77 73.38 72.47 64.39 49.14 26.52 24.34 19.12 14.45 14.37 12.57 -1.41 -3.13

^{13}C-NMR (126 MHz, $CDCl_3$)



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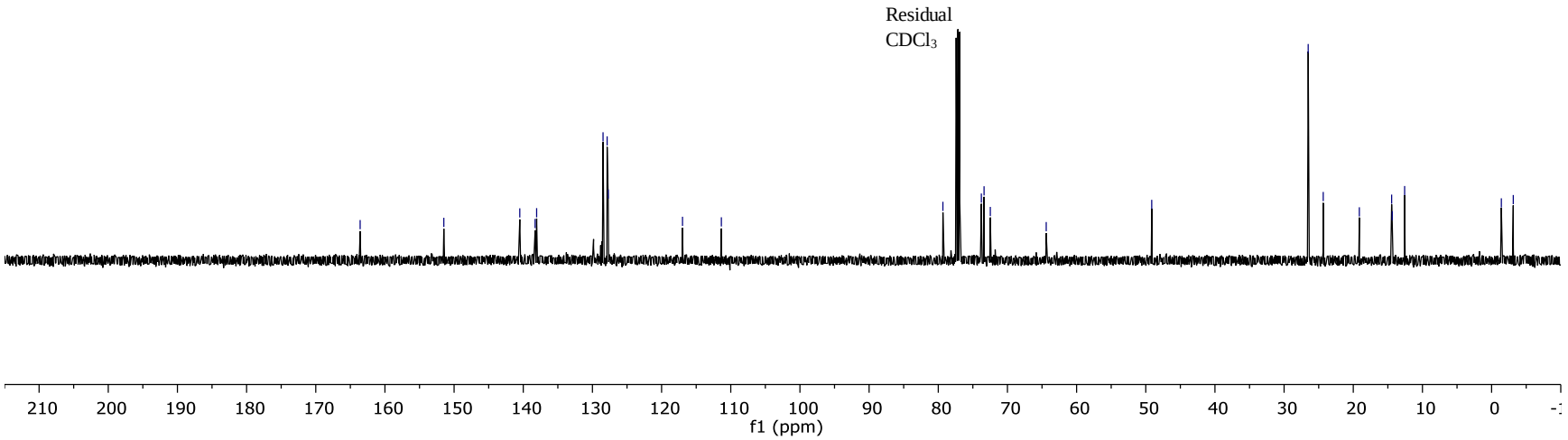
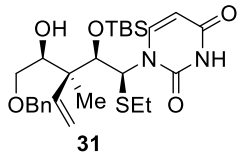


^{1}H-NMR (500 MHz, $CDCl_3$)



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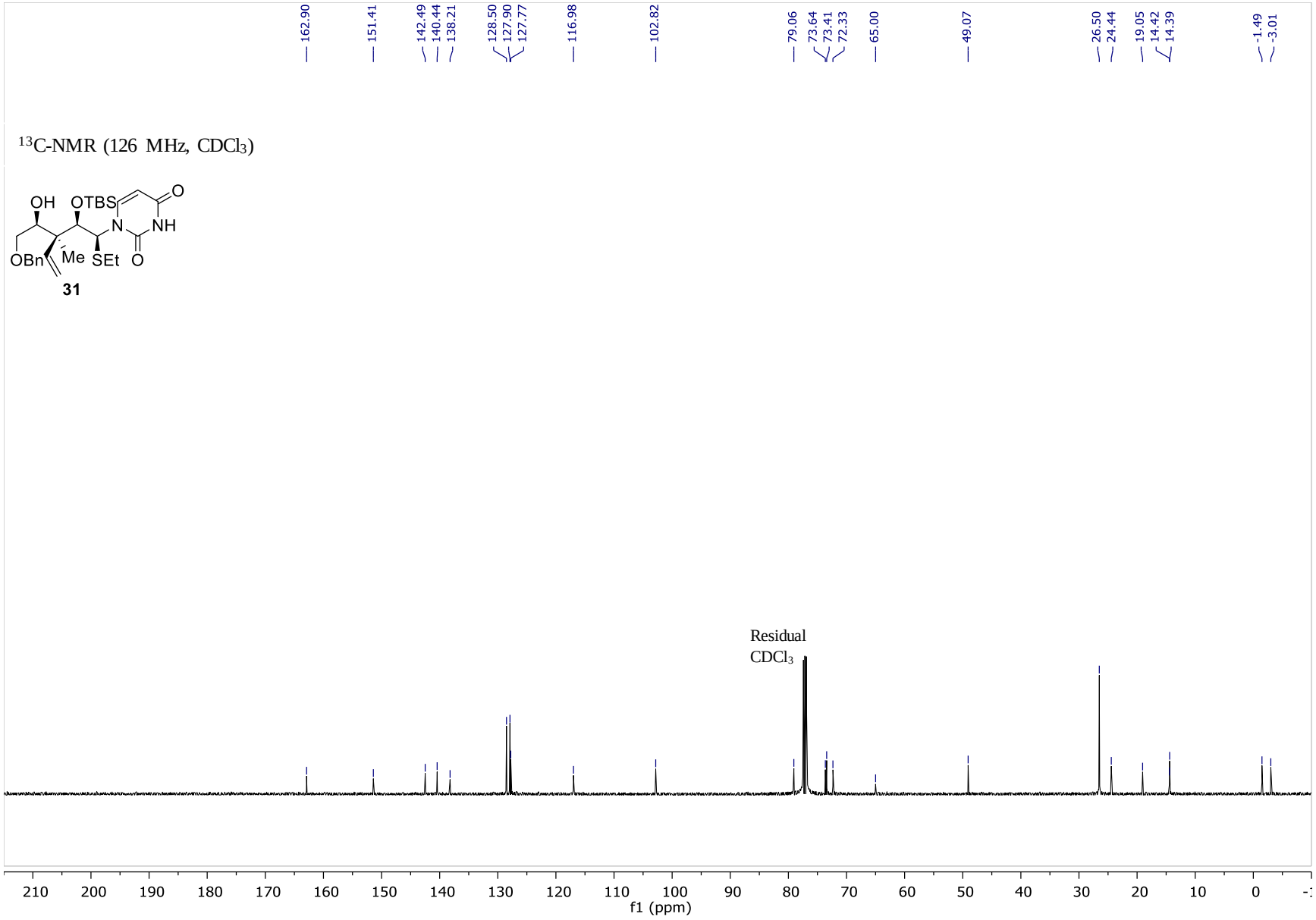
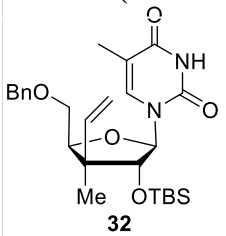


^{13}C-NMR (126 MHz, $CDCl_3$)

31

^{1}H-NMR (500 MHz, $CDCl_3$)



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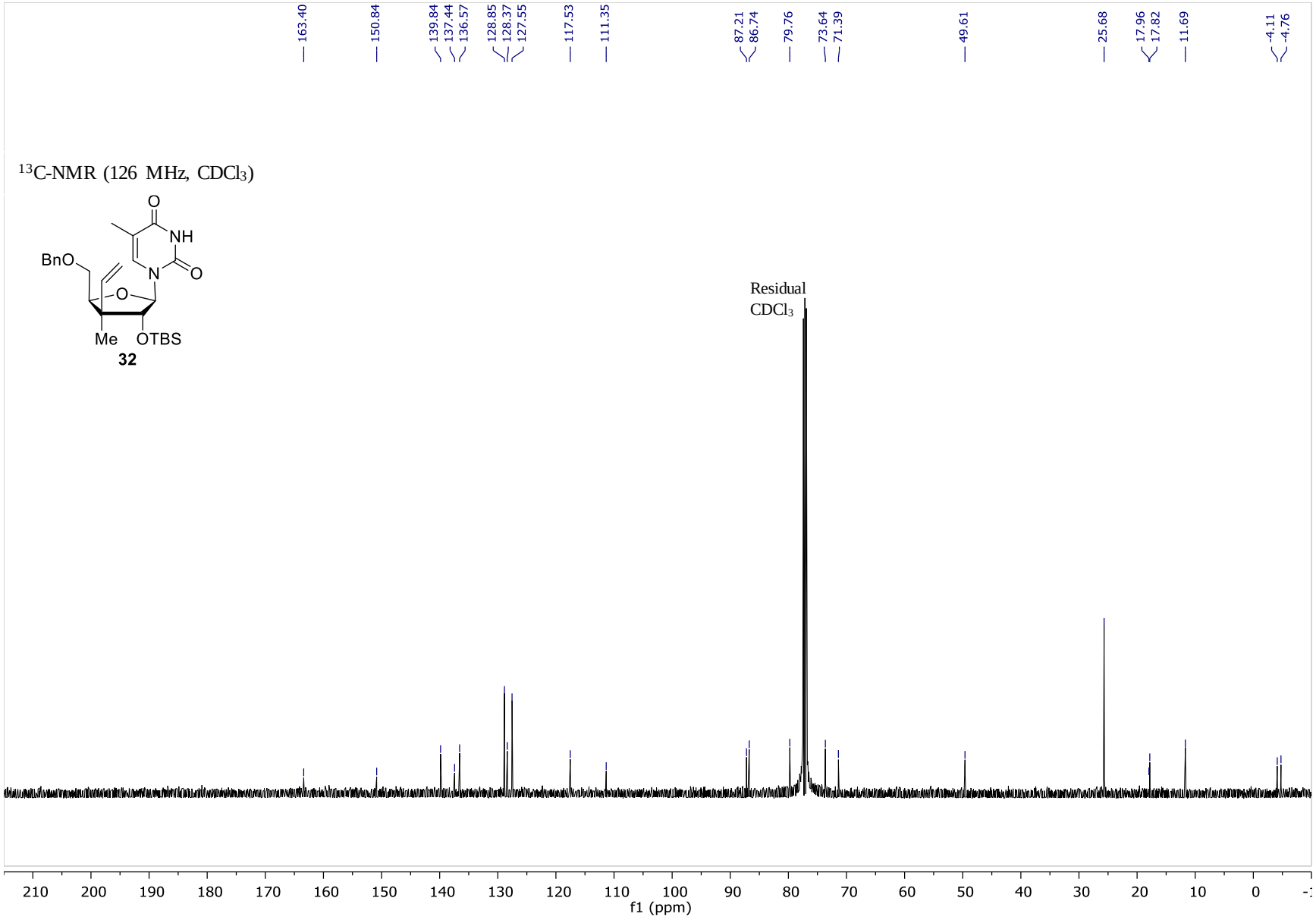
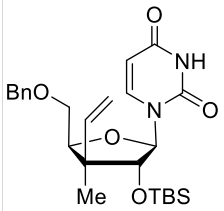


^{13}C-NMR (126 MHz, $CDCl_3$)

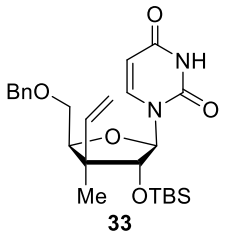
32

^{1}H-NMR (500 MHz, $CDCl_3$)



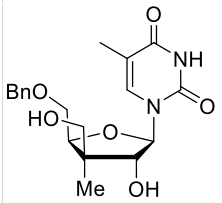
33

^{13}C-NMR (126 MHz, $CDCl_3$)



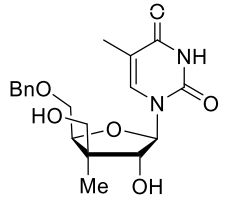
33

^{1}H-NMR (500 MHz, $CDCl_3$)



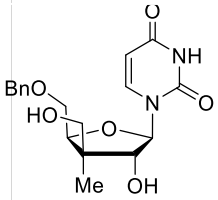
34

^{13}C-NMR (126 MHz, $CDCl_3$)



34

^{1}H-NMR (500 MHz, CD_3OD)



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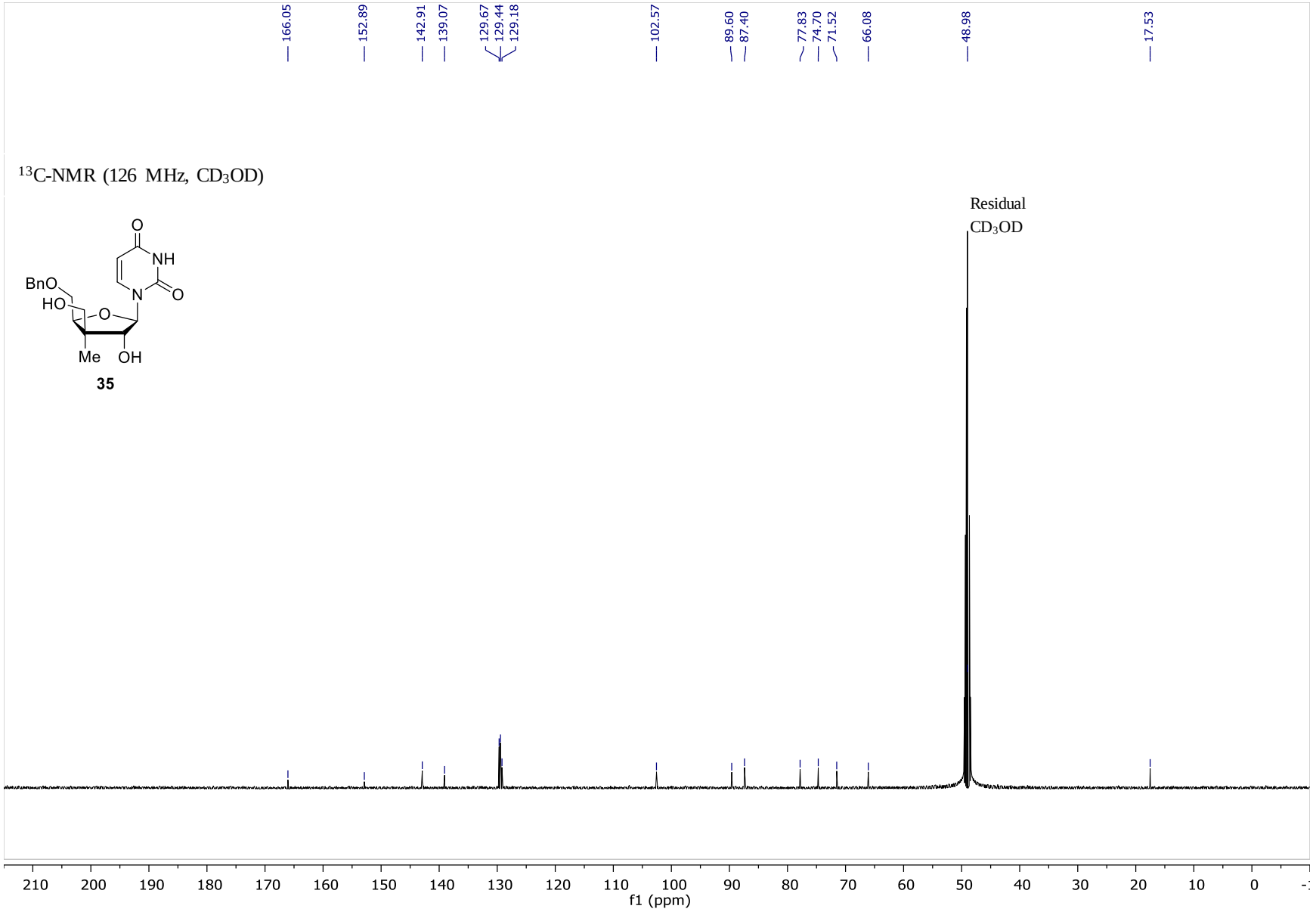
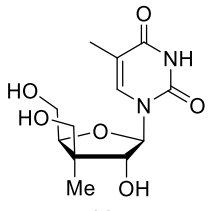


^{13}C-NMR (126 MHz, CD_3OD)

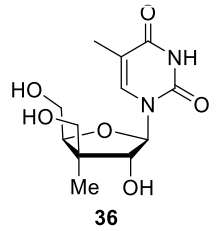
35

^{1}H-NMR (500 MHz, CD_3OD)



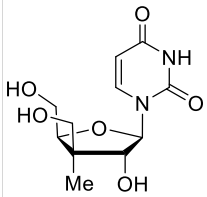
36

^{13}C-NMR (126 MHz, CD_3OD)



36

^{1}H-NMR (500 MHz, CD_3OD)



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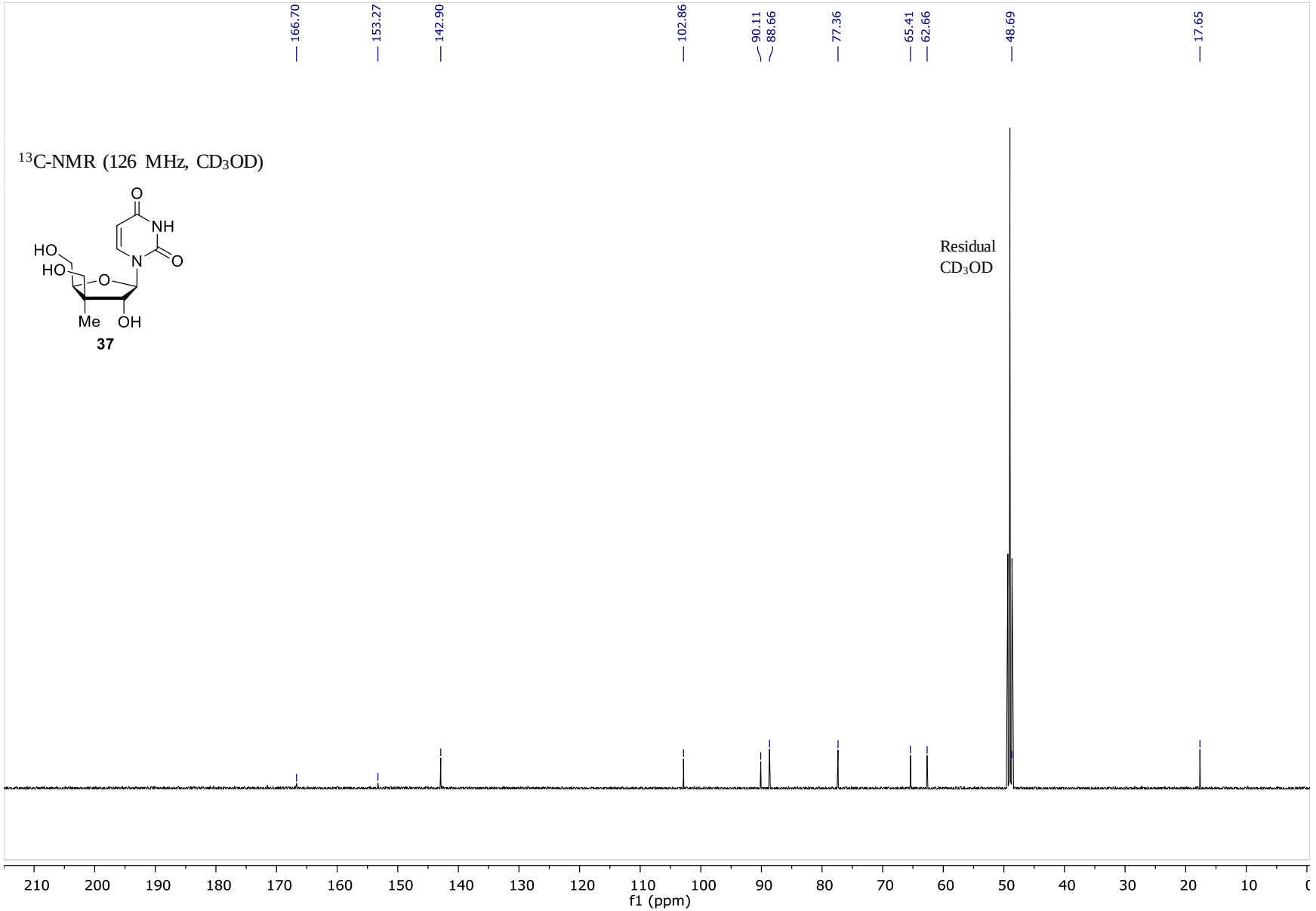
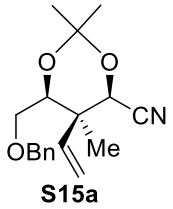
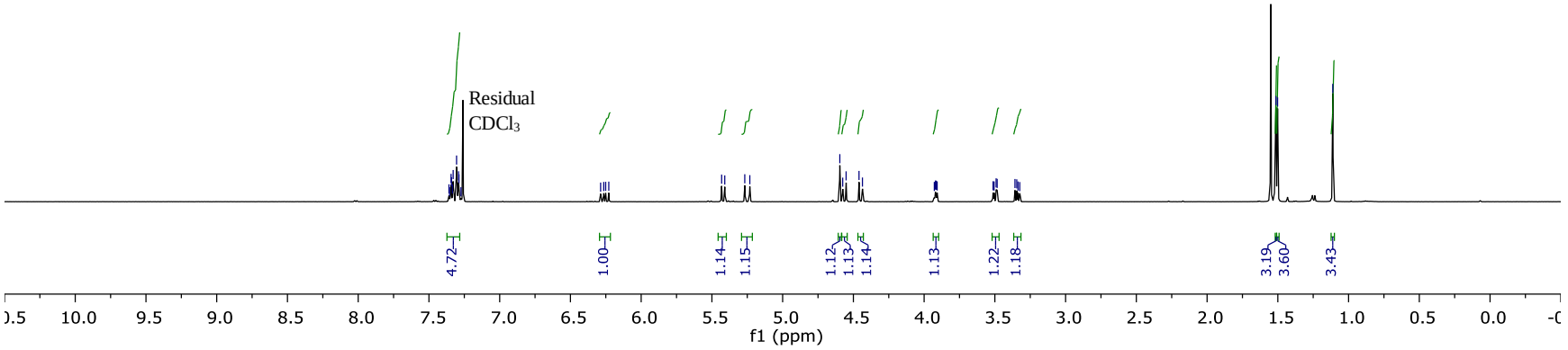


37

^{1}H-NMR (500 MHz, $CDCl_3$)

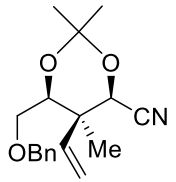


S15a

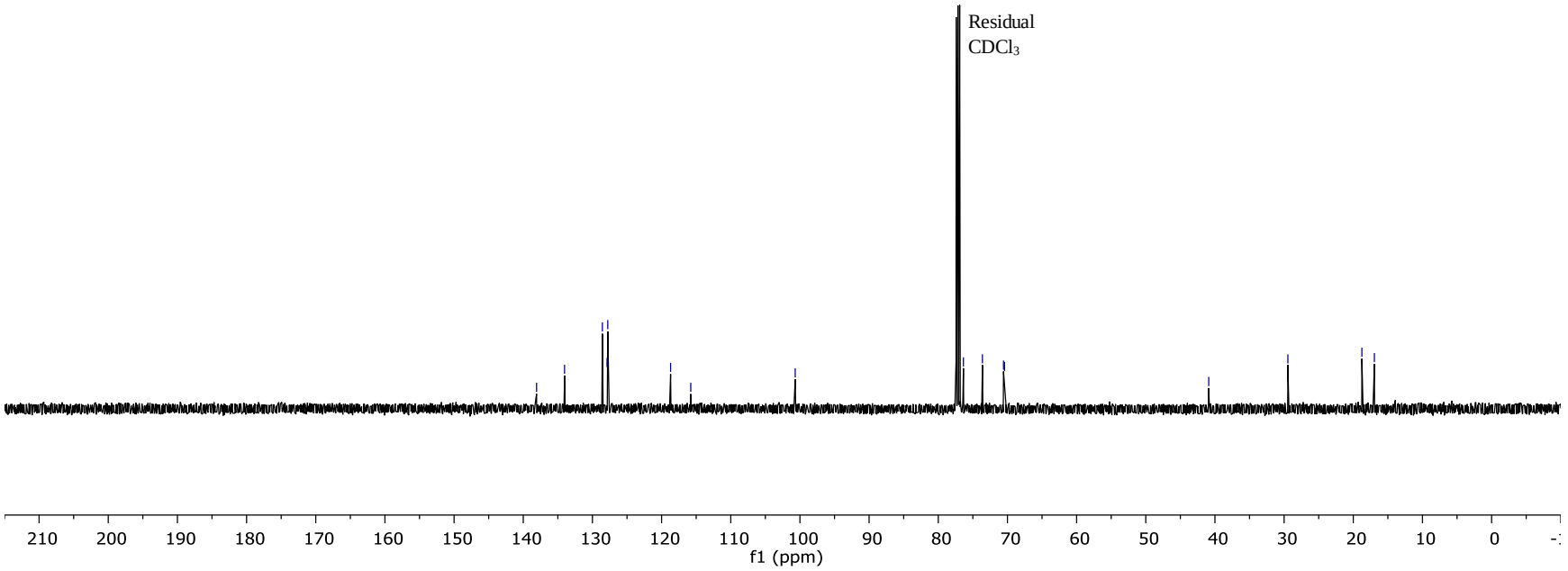


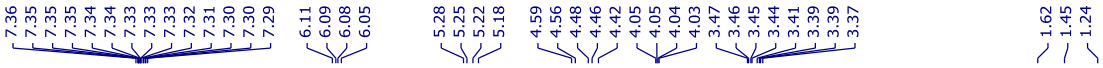
138.08
134.03
128.56
127.89
127.78
118.70
115.78
100.69
76.36
73.61
70.57
70.42
40.90
29.45
18.76
16.95

^{13}C-NMR (126 MHz, $CDCl_3$)

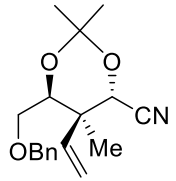


S15a

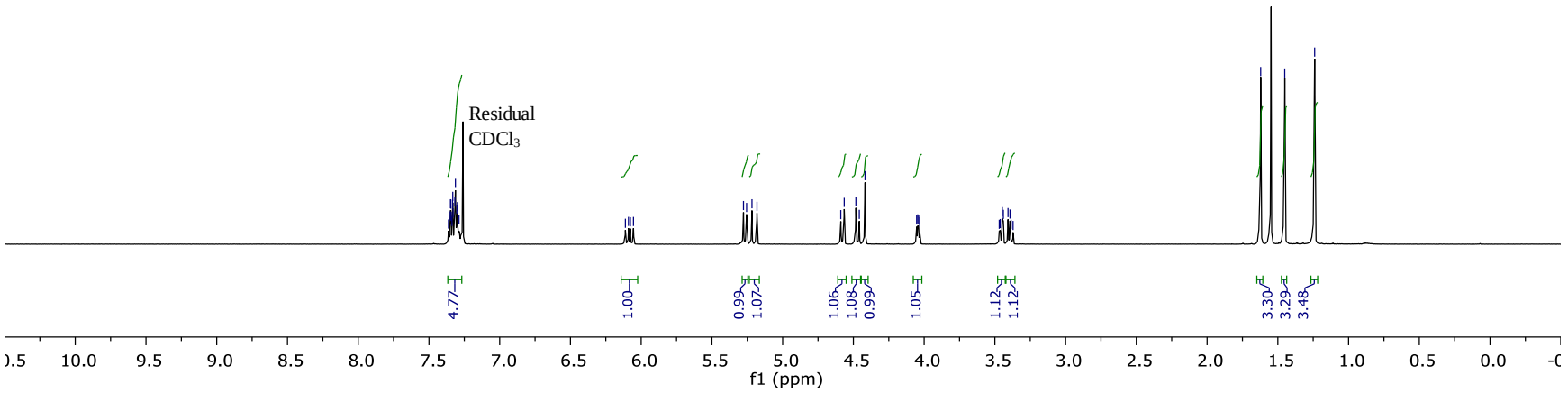




^{1}H-NMR (500 MHz, $CDCl_3$)

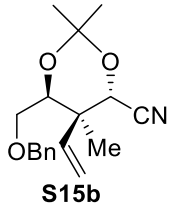


S15b

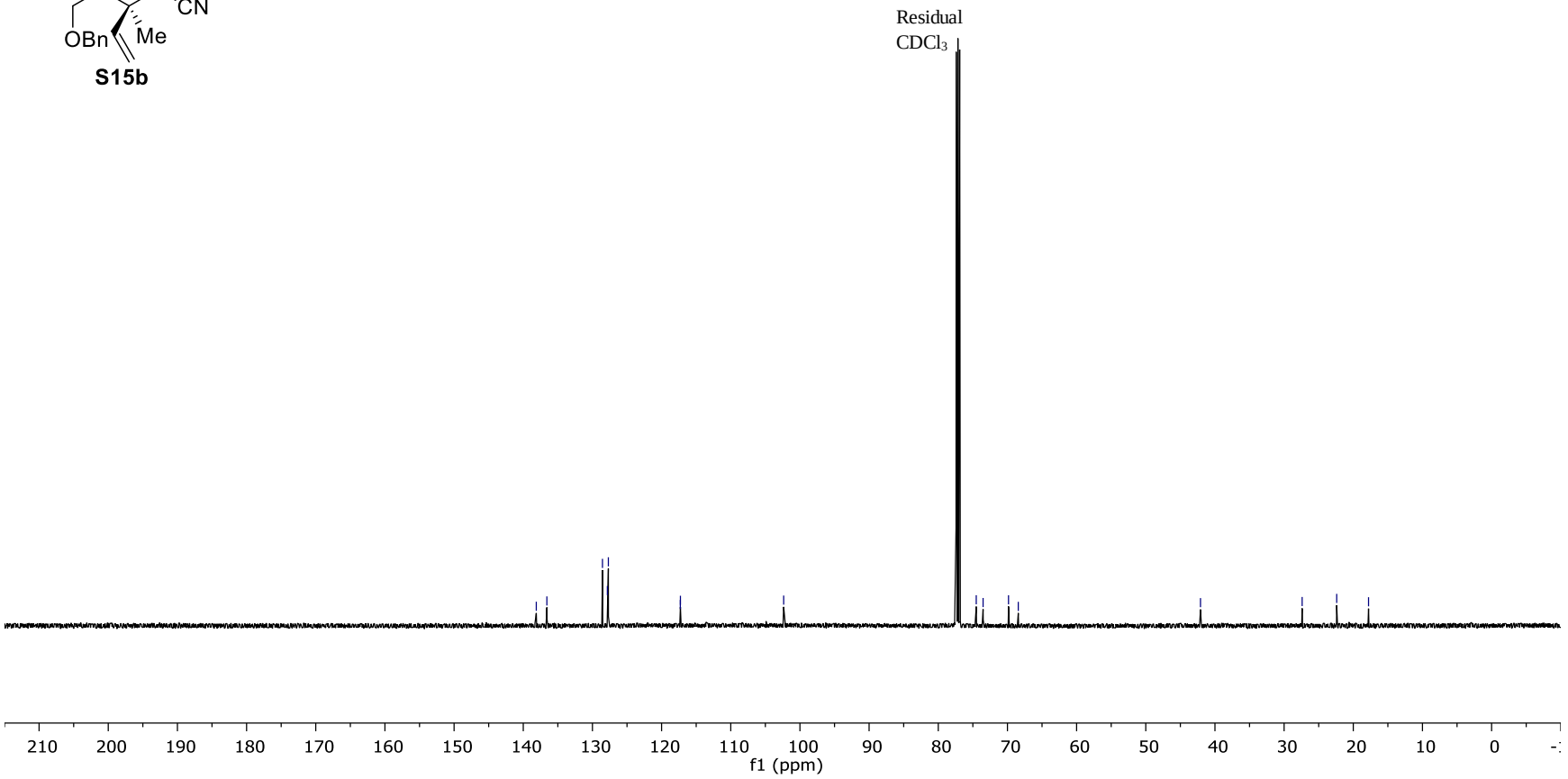


138.12
136.59
128.55
127.84
127.70
117.29
117.28
102.35
74.51
73.52
69.84
68.43
42.09
27.39
22.40
17.79

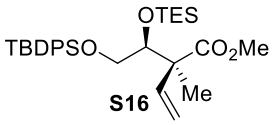
^{13}C-NMR (126 MHz, $CDCl_3$)

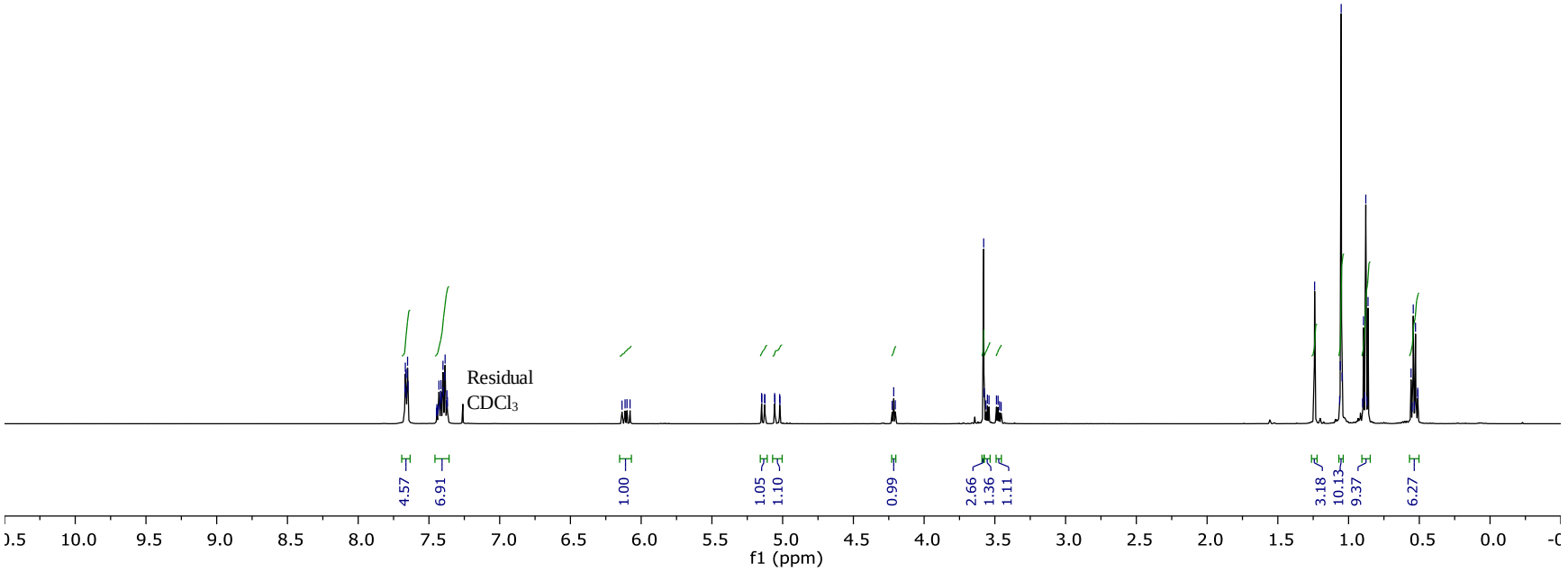


S15b



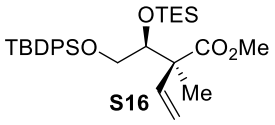
^{1}H-NMR (500 MHz, $CDCl_3$)



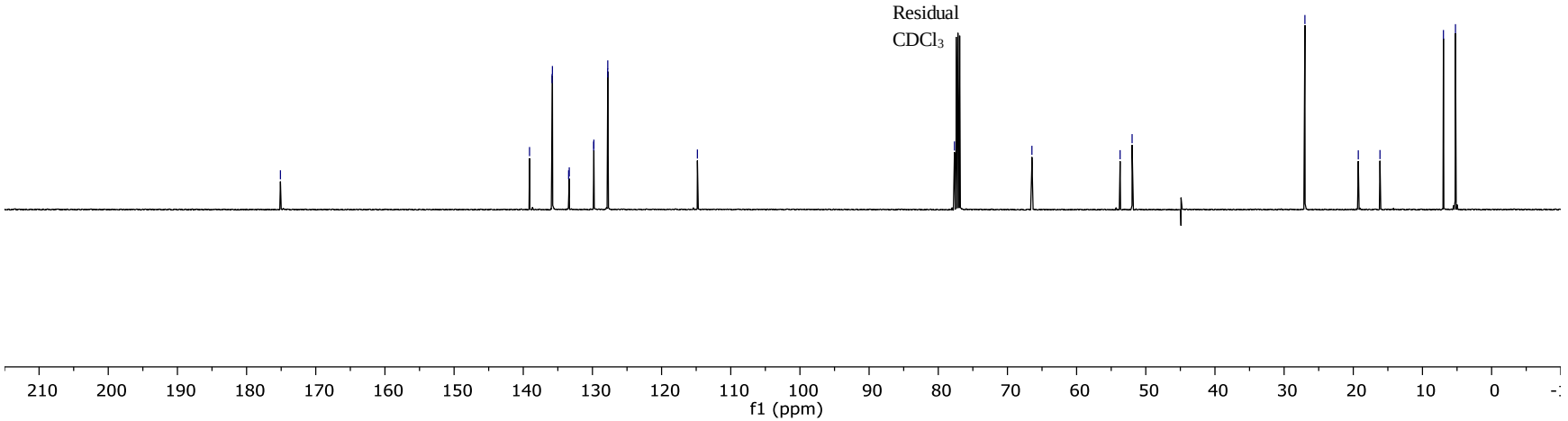


175.11
139.09
135.83
135.78
133.44
133.35
129.82
129.79
127.80
127.78
114.82
77.66
66.46
53.71
51.98
26.99
19.28
16.14
6.97
5.23

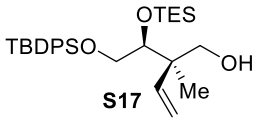
^{13}C-NMR (126 MHz, $CDCl_3$)

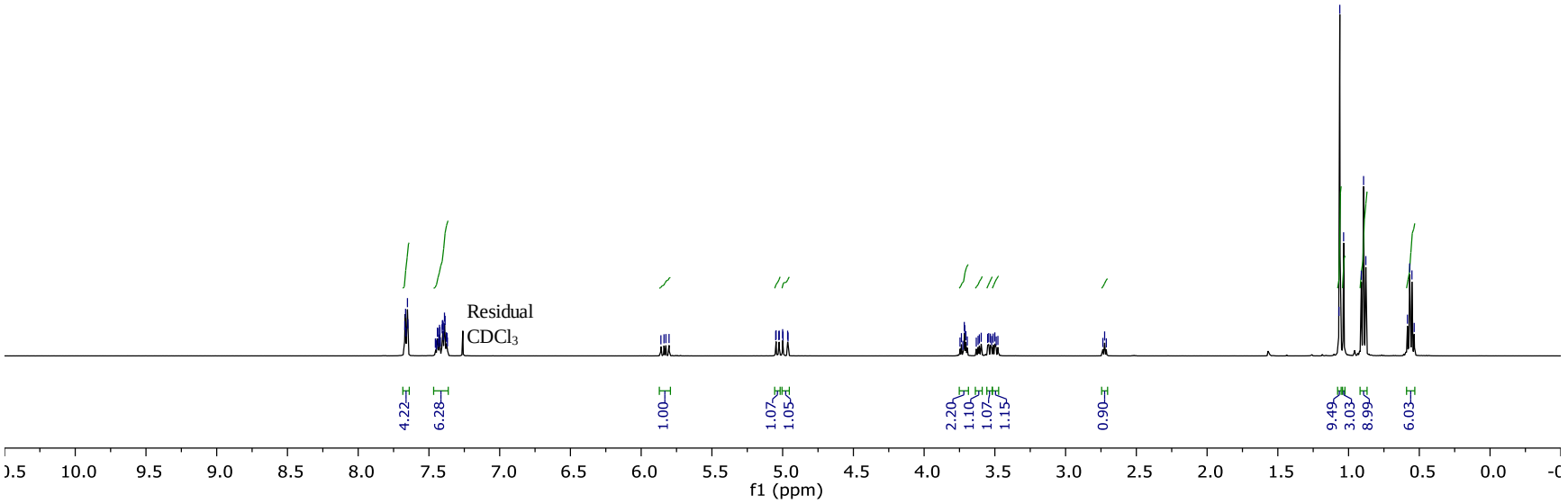


S16



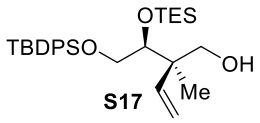
^{1}H-NMR (500 MHz, $CDCl_3$)

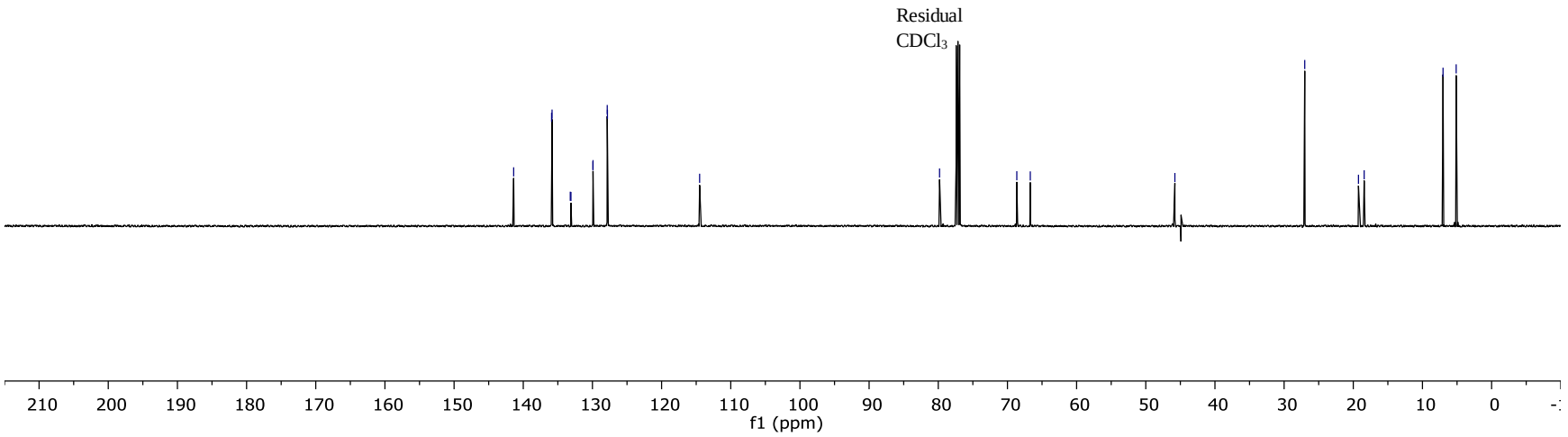




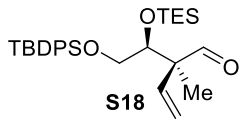
141.39
135.90
135.84
133.20
133.11
129.92
129.91
127.86
127.83
114.50
79.81
68.65
66.70
45.79
27.02
19.25
18.42
7.02
5.12

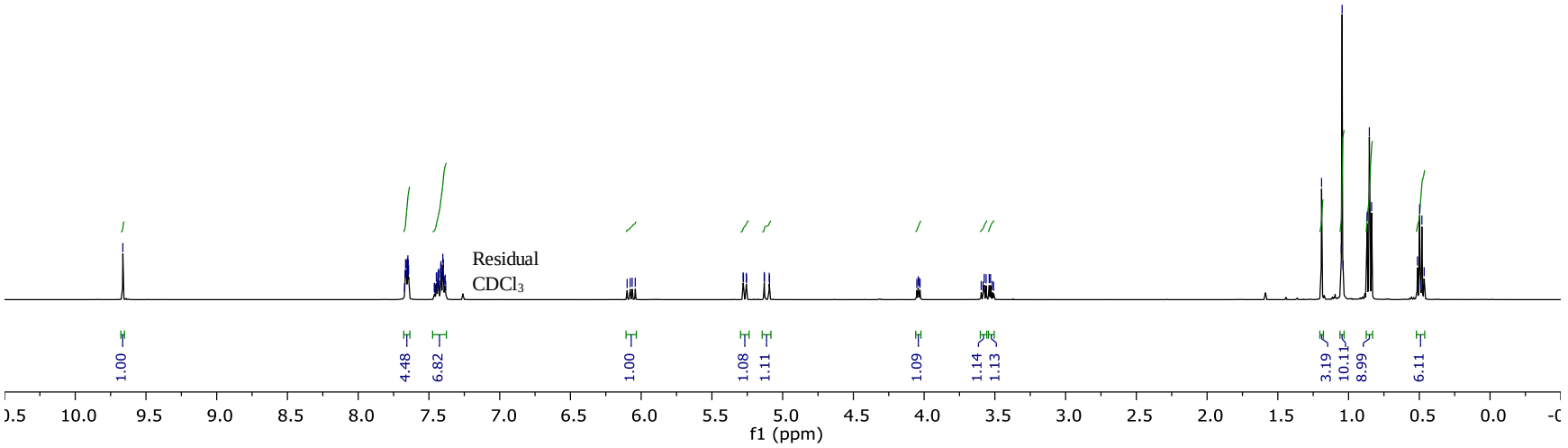
^{13}C-NMR (126 MHz, $CDCl_3$)





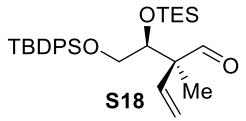
^{1}H-NMR (500 MHz, $CDCl_3$)

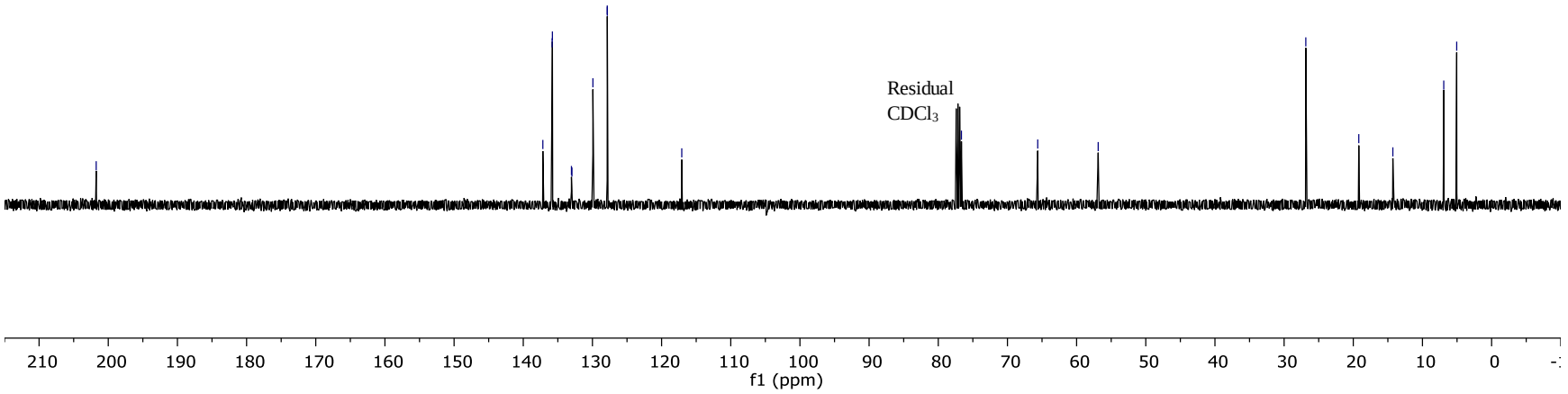




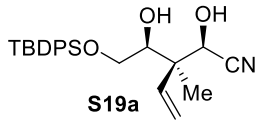
201.74
137.17
135.82
135.79
133.04
132.96
129.93
127.86
127.85
117.08
76.65
65.62
56.88
26.86
19.20
14.28
6.92
5.05

^{13}C-NMR (126 MHz, $CDCl_3$)

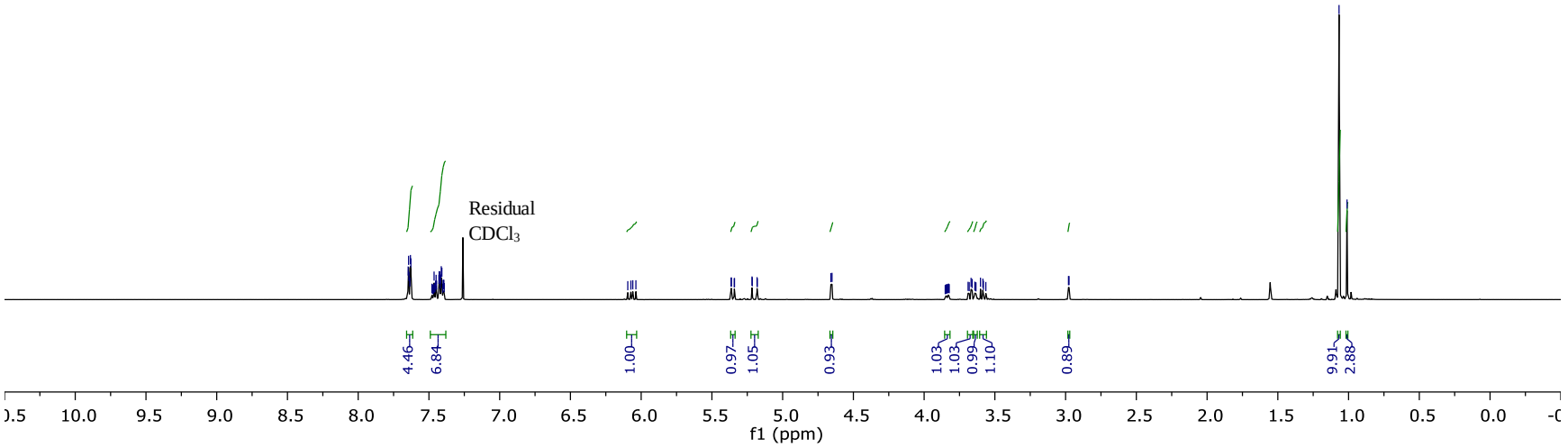




^{1}H-NMR (500 MHz, $CDCl_3$)

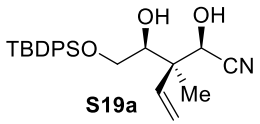


S19a

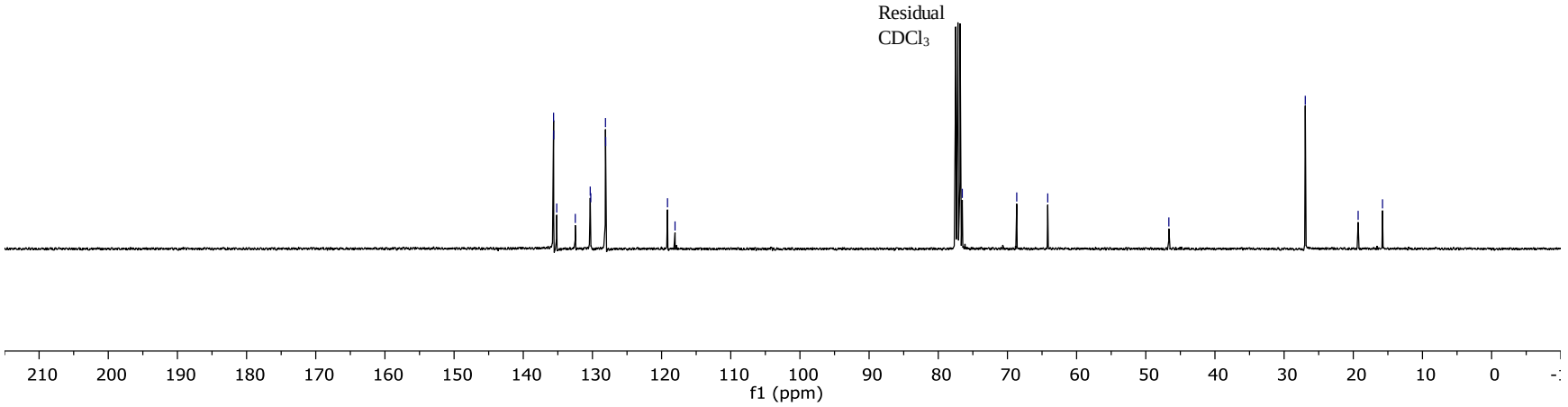


135.62
135.60
135.16
132.48
130.32
130.24
128.11
128.08
119.15
118.06
76.53
68.66
64.17
46.66
26.94
19.30
15.77

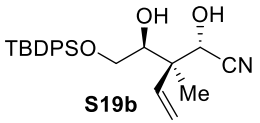
^{13}C-NMR (100.6 MHz, $CDCl_3$)



S19a



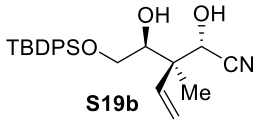
^{1}H-NMR (500 MHz, $CDCl_3$)



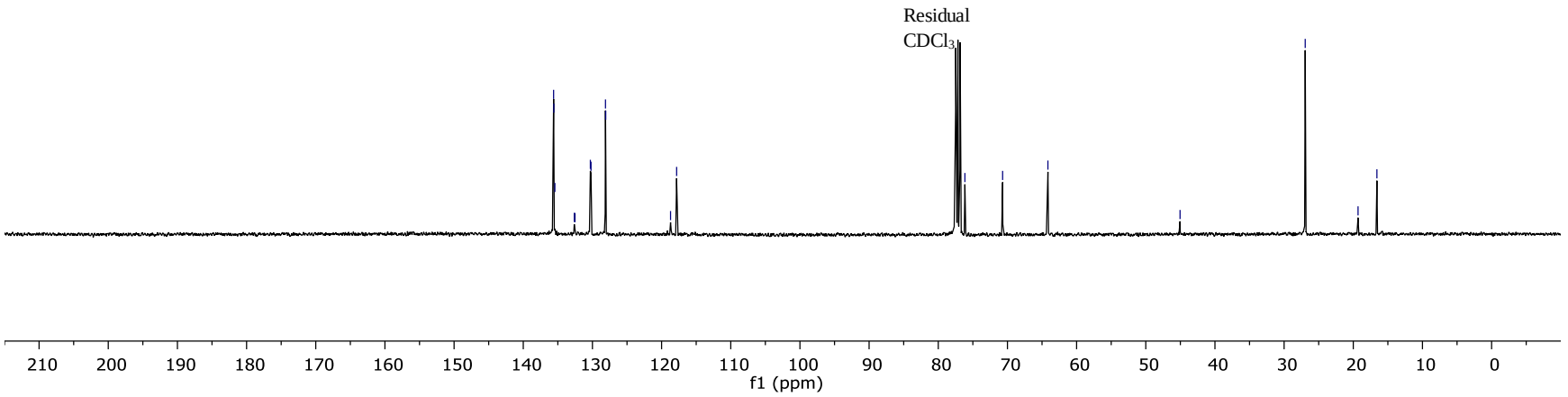
S19b

135.61
135.58
135.43
132.63
132.52
130.30
130.21
128.11
128.08
118.70
117.82
76.15
70.70
64.15
45.05
26.95
19.31
16.58

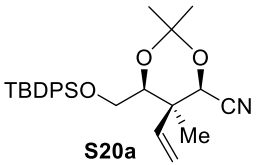
^{13}C-NMR (100.6 MHz, $CDCl_3$)



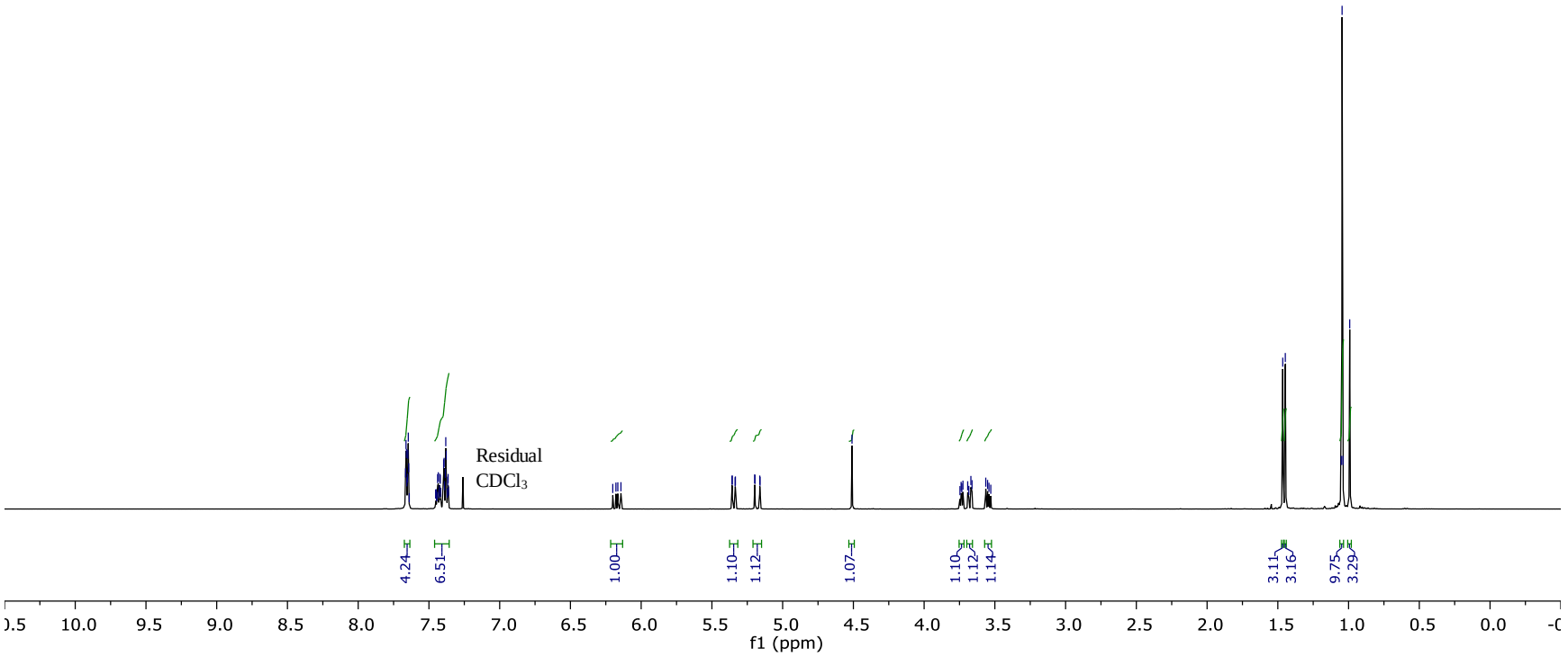
S19b



^{1}H-NMR (500 MHz, $CDCl_3$)

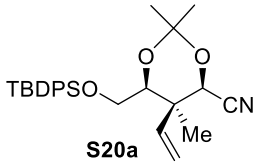


S20a

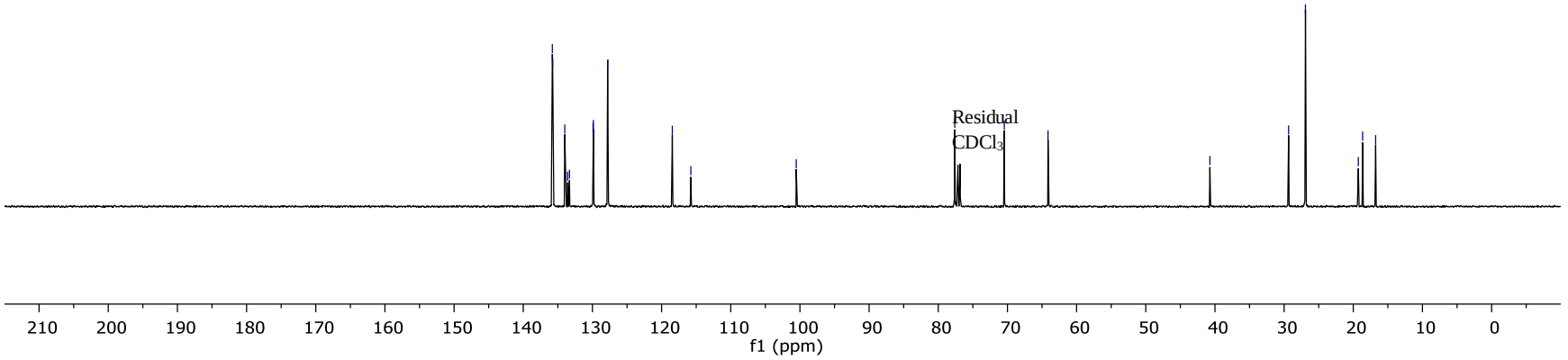


135.79
135.74
134.00
133.58
133.32
129.91
129.86
127.80
127.76
118.45
115.77
100.53
77.62
70.45
64.13
40.73
29.35
26.92
19.27
18.65
16.77

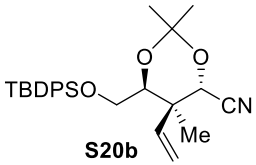
^{13}C-NMR (100.6 MHz, $CDCl_3$)



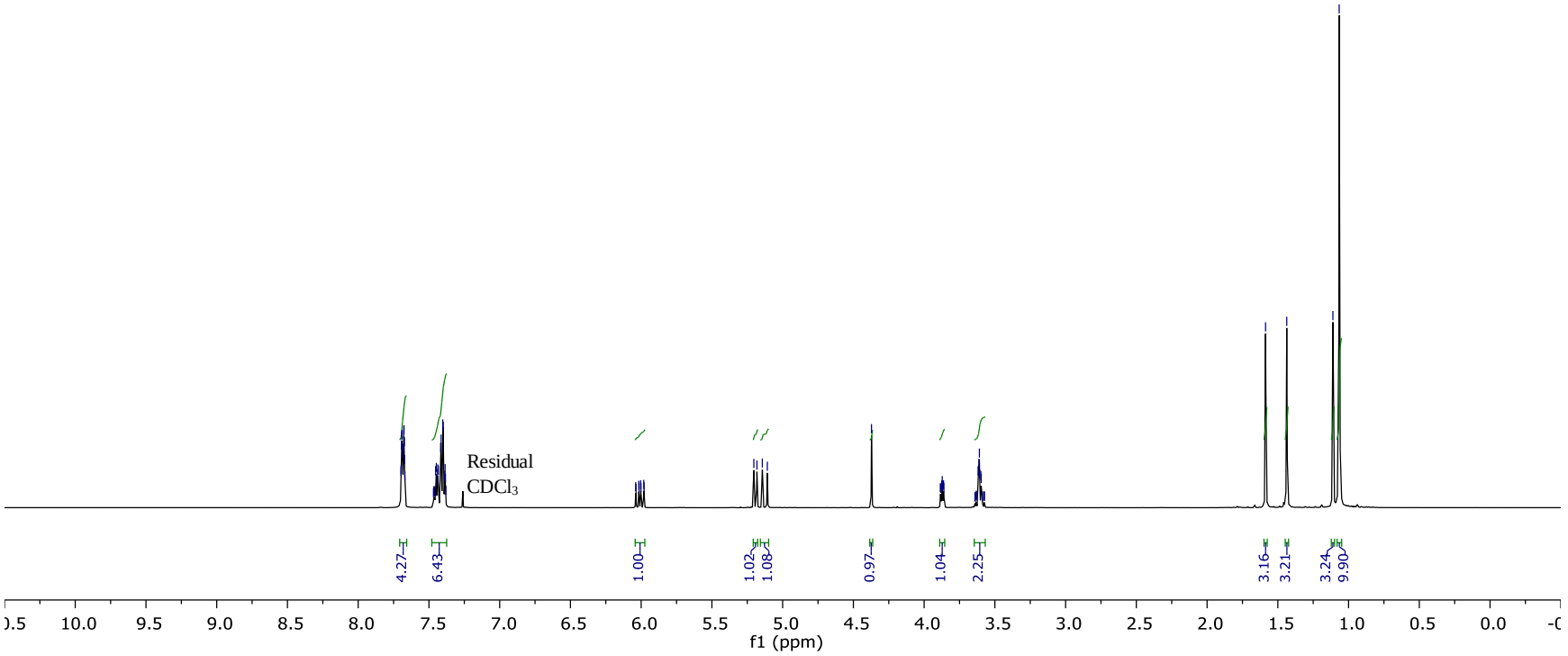
S20a



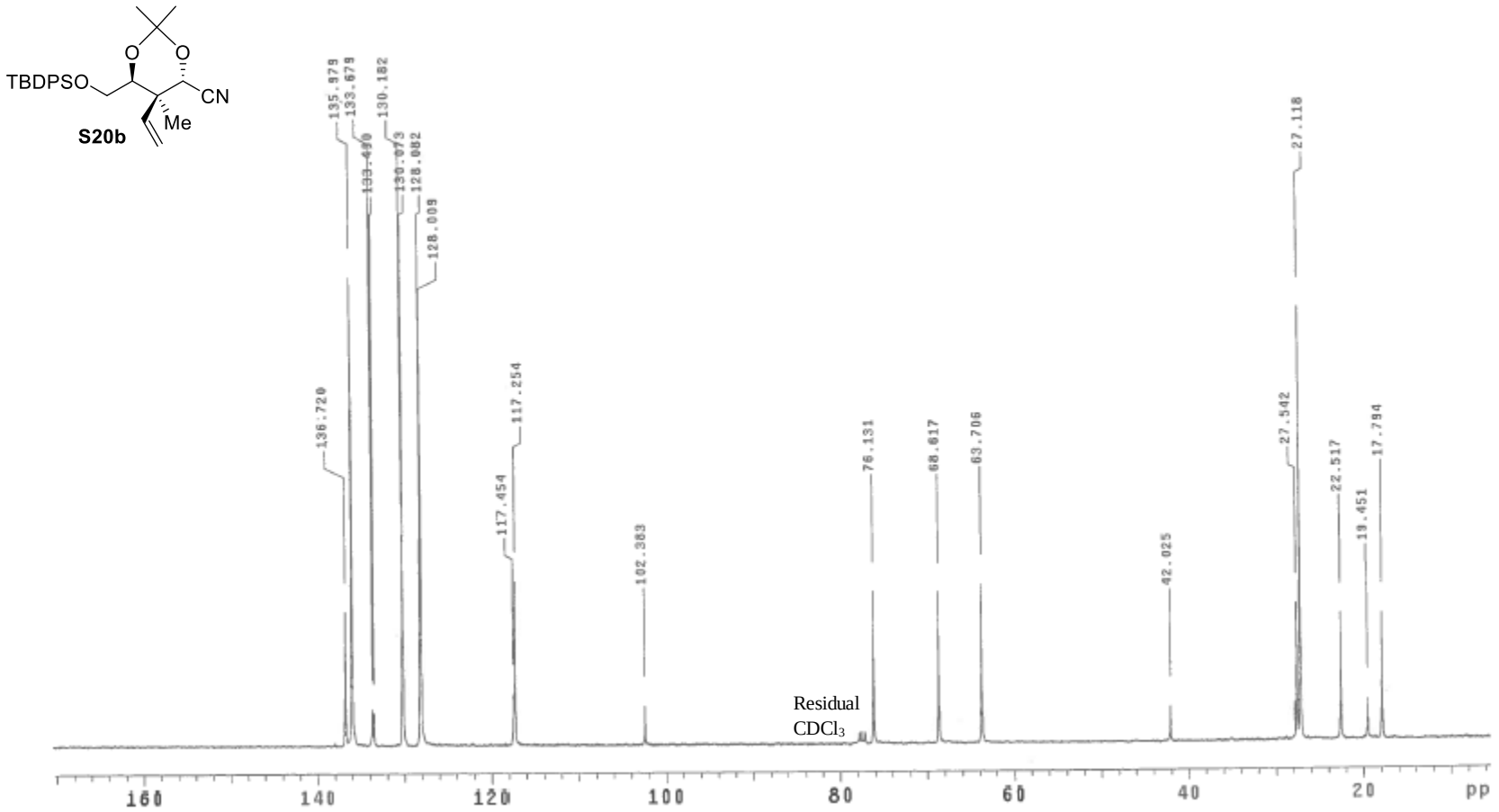
^{1}H-NMR (500 MHz, $CDCl_3$)

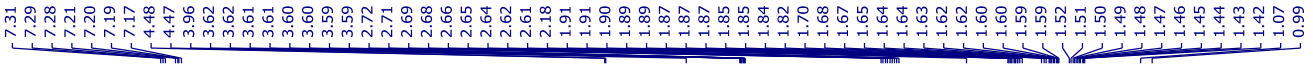


S20b

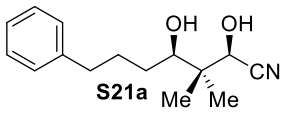


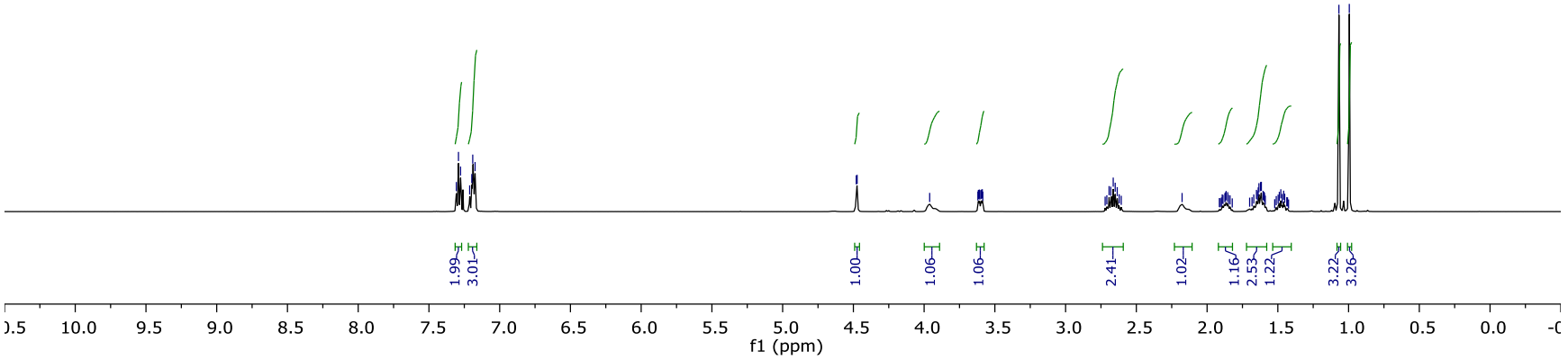
^{13}C-NMR (100.6 MHz, $CDCl_3$)





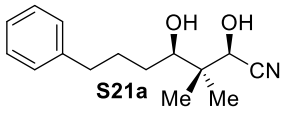
^{1}H-NMR (500 MHz, $CDCl_3$)



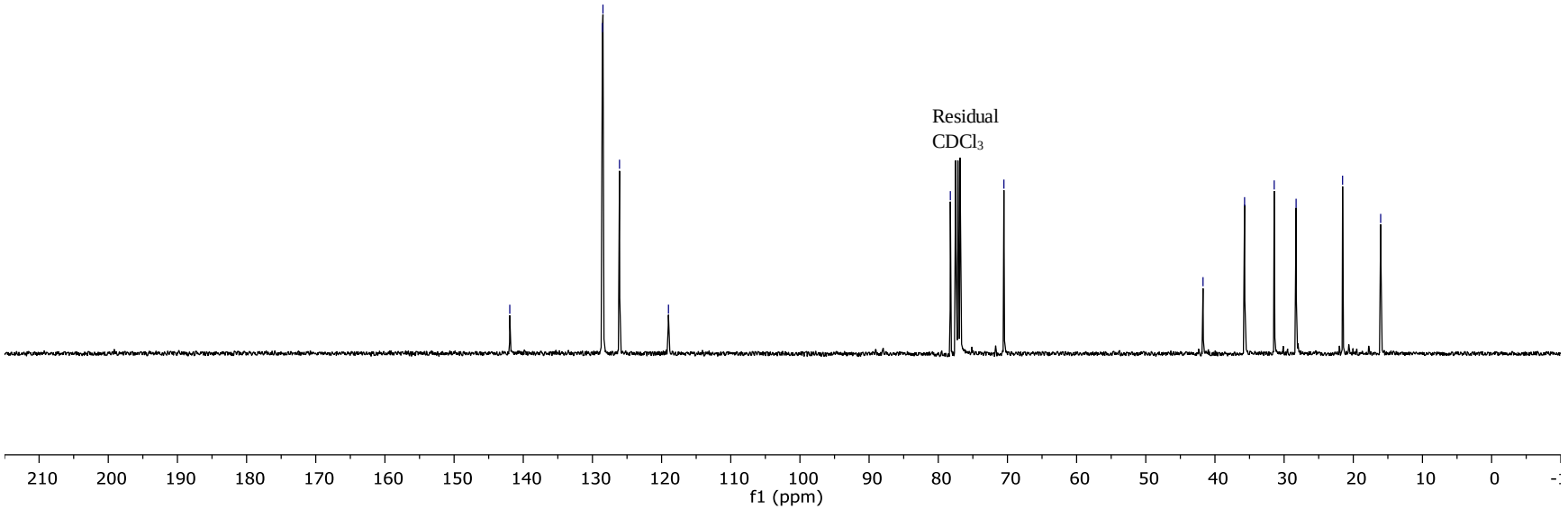


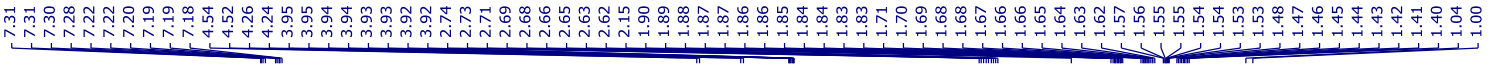
141.95
128.56
128.48
126.09
119.00
78.25
70.51
41.72
35.72
31.43
28.27
21.55
16.04

^{13}C-NMR (100.6 MHz, $CDCl_3$)

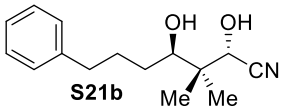


S21a

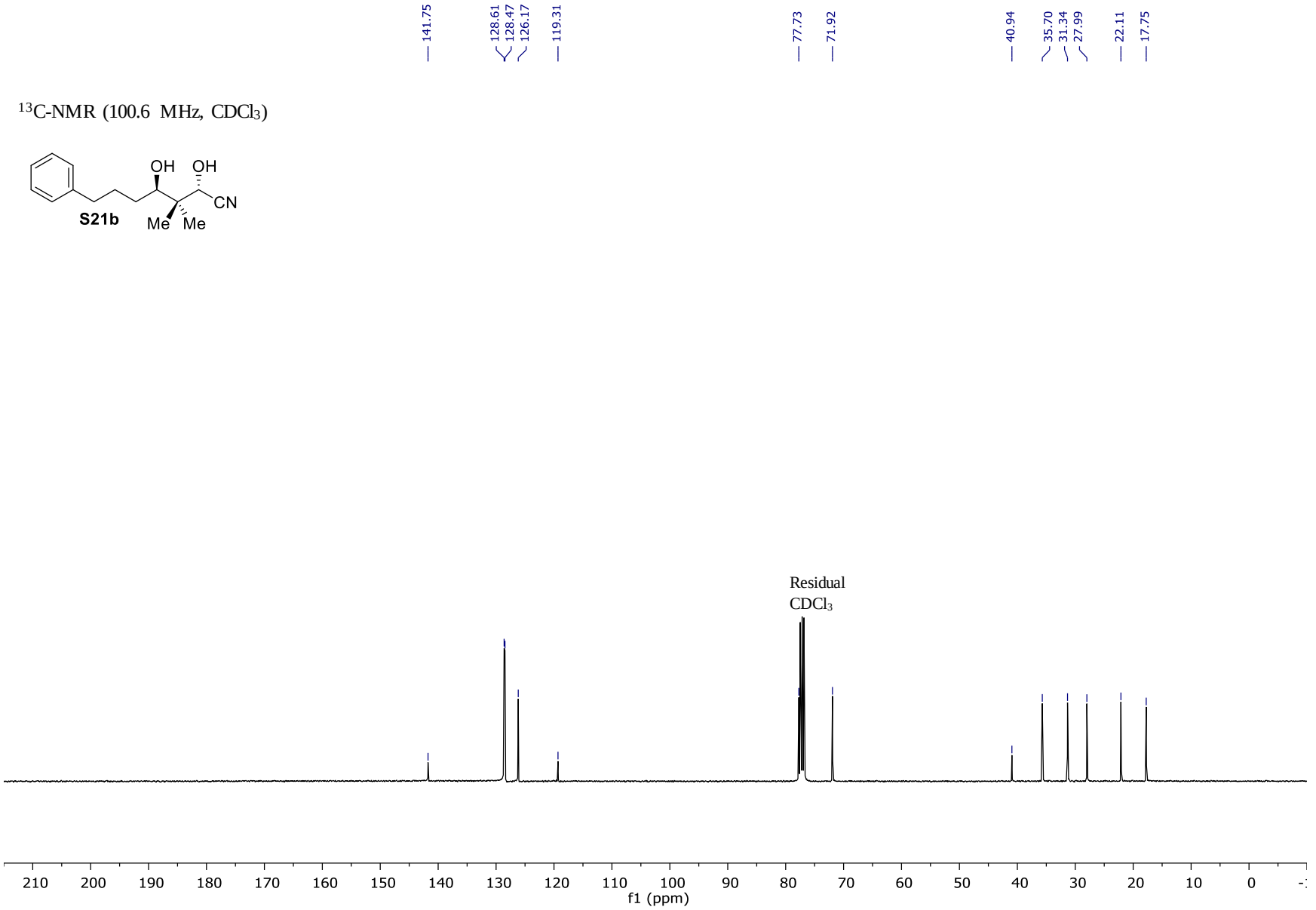




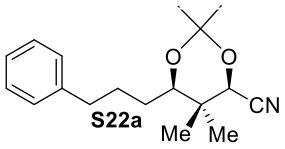
^{1}H-NMR (500 MHz, $CDCl_3$)

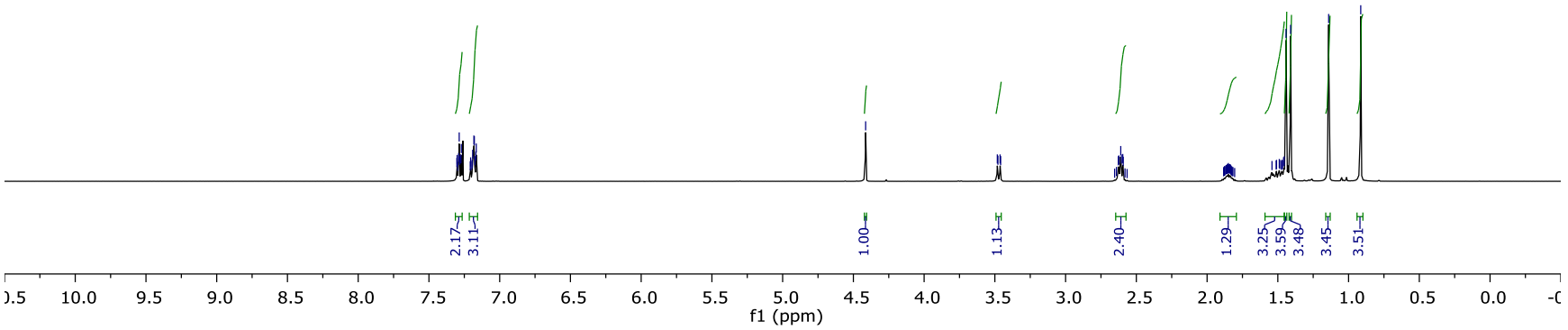


S21b



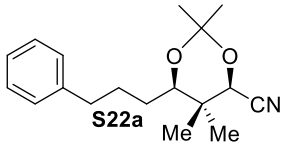
^{1}H-NMR (500 MHz, $CDCl_3$)



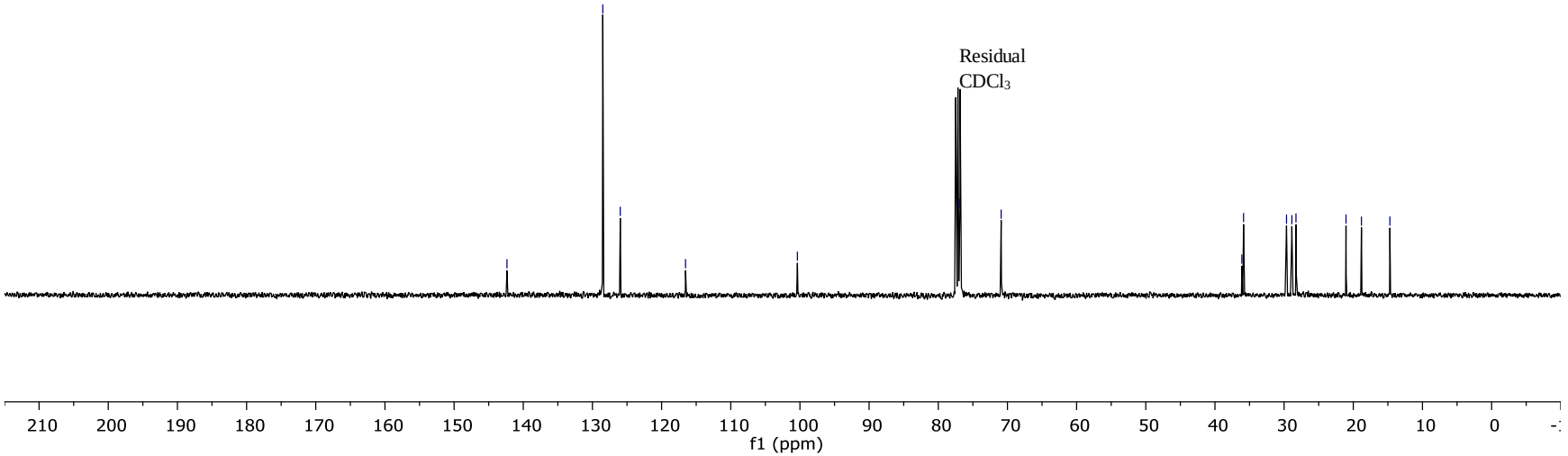


142.36
128.50
125.98
116.54
100.37
76.97
70.91
36.11
35.86
29.65
28.88
28.29
21.05
18.82
14.70

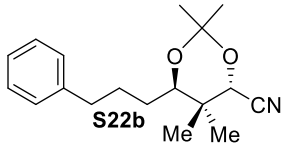
^{13}C-NMR (100.6 MHz, $CDCl_3$)

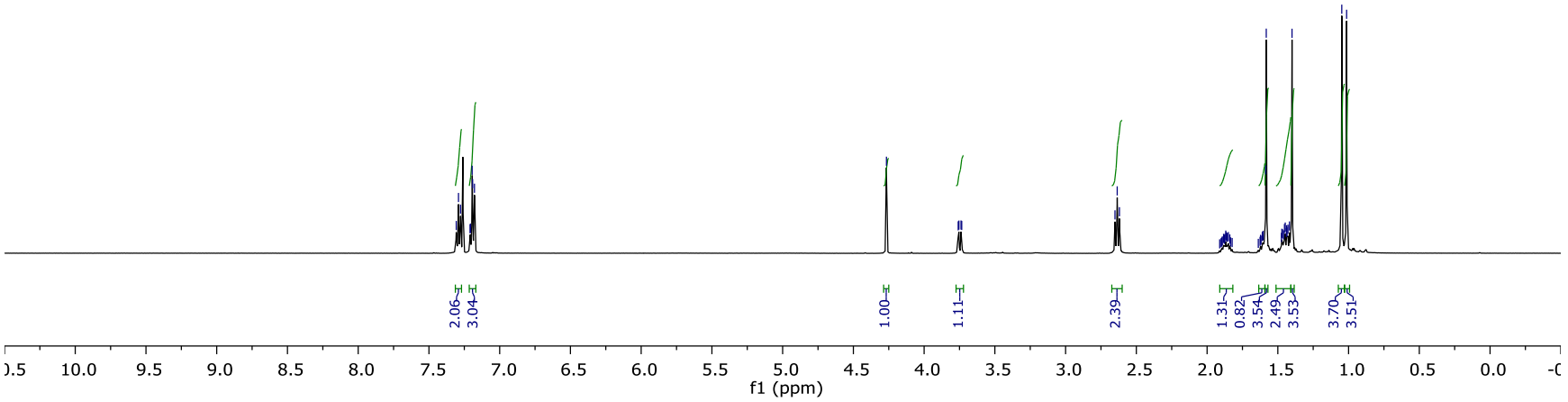


S22a



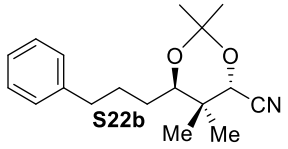
^{1}H-NMR (500 MHz, $CDCl_3$)

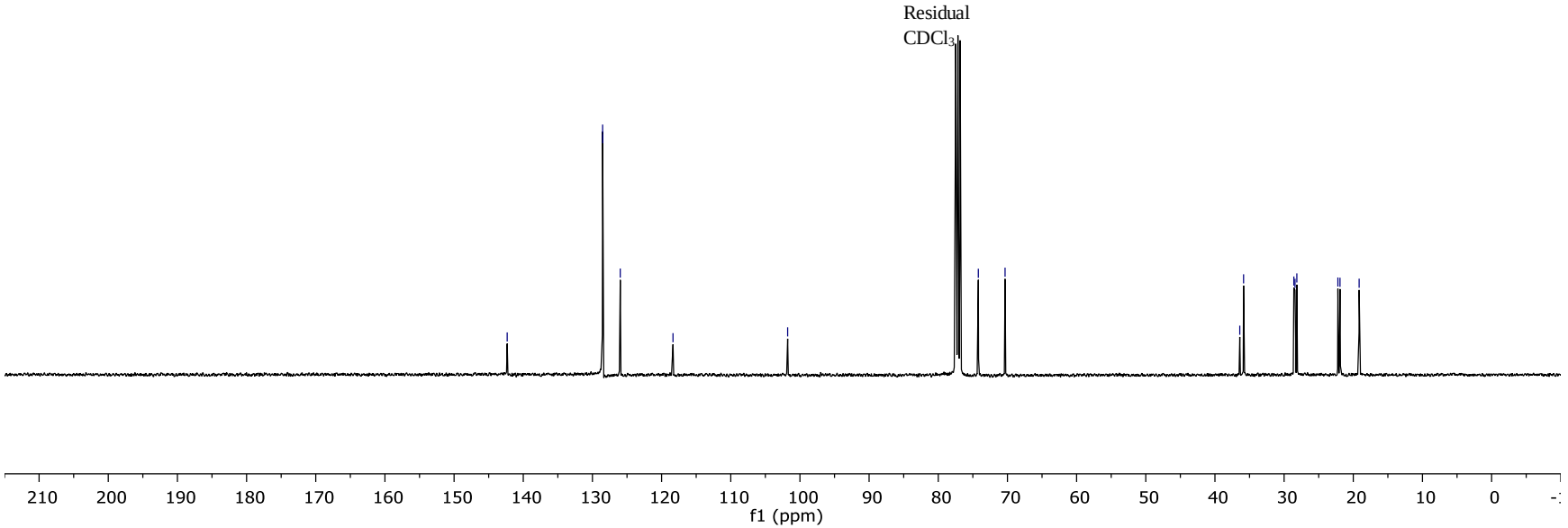




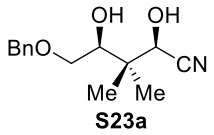
142.32
128.53
128.51
125.98
118.35
101.78
74.21
70.34
36.41
35.86
28.59
28.42
28.16
22.23
21.92
19.15

^{13}C-NMR (100.6 MHz, $CDCl_3$)

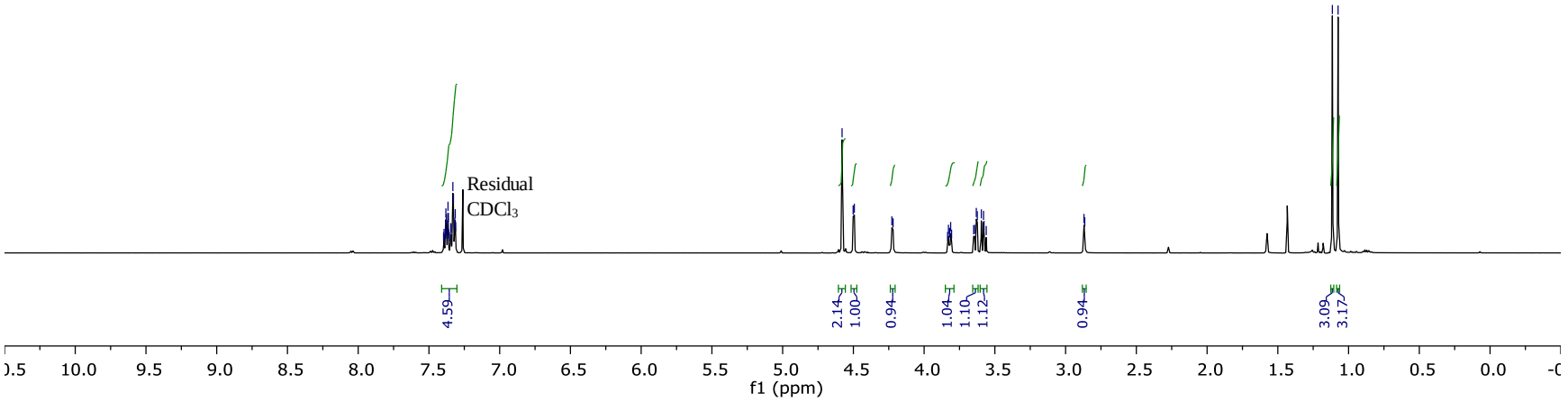




^{1}H-NMR (500 MHz, $CDCl_3$)

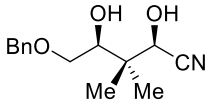


S23a

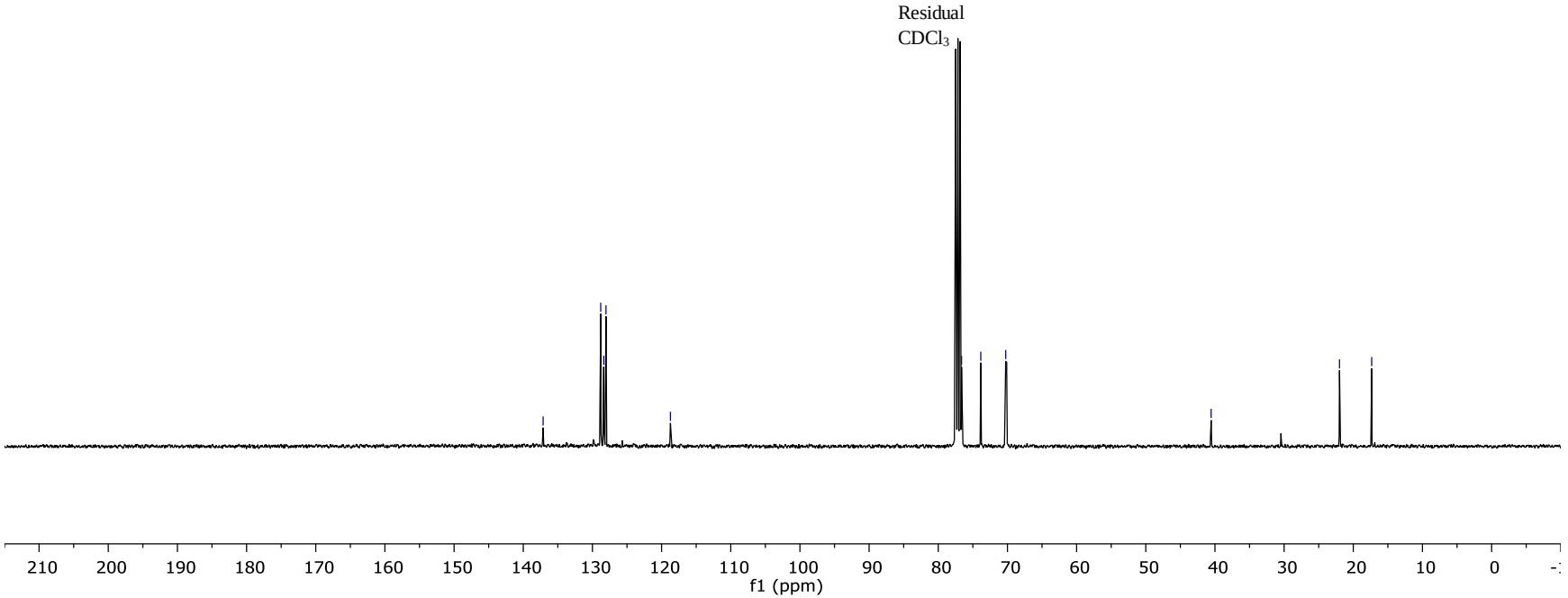


137.13
128.80
128.37
128.04
118.72
76.64
73.85
70.25
70.10
40.55
21.99
17.34

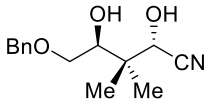
^{13}C-NMR (100.6 MHz, $CDCl_3$)



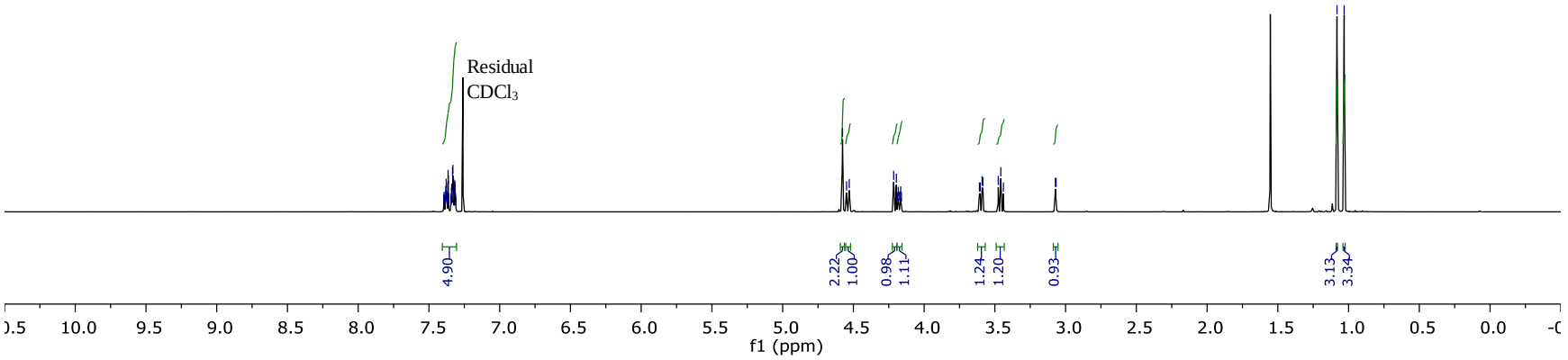
S23a



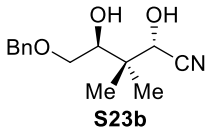
^{1}H-NMR (500 MHz, $CDCl_3$)



S23b

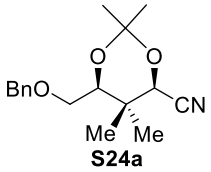


^{13}C-NMR (100.6 MHz, $CDCl_3$)

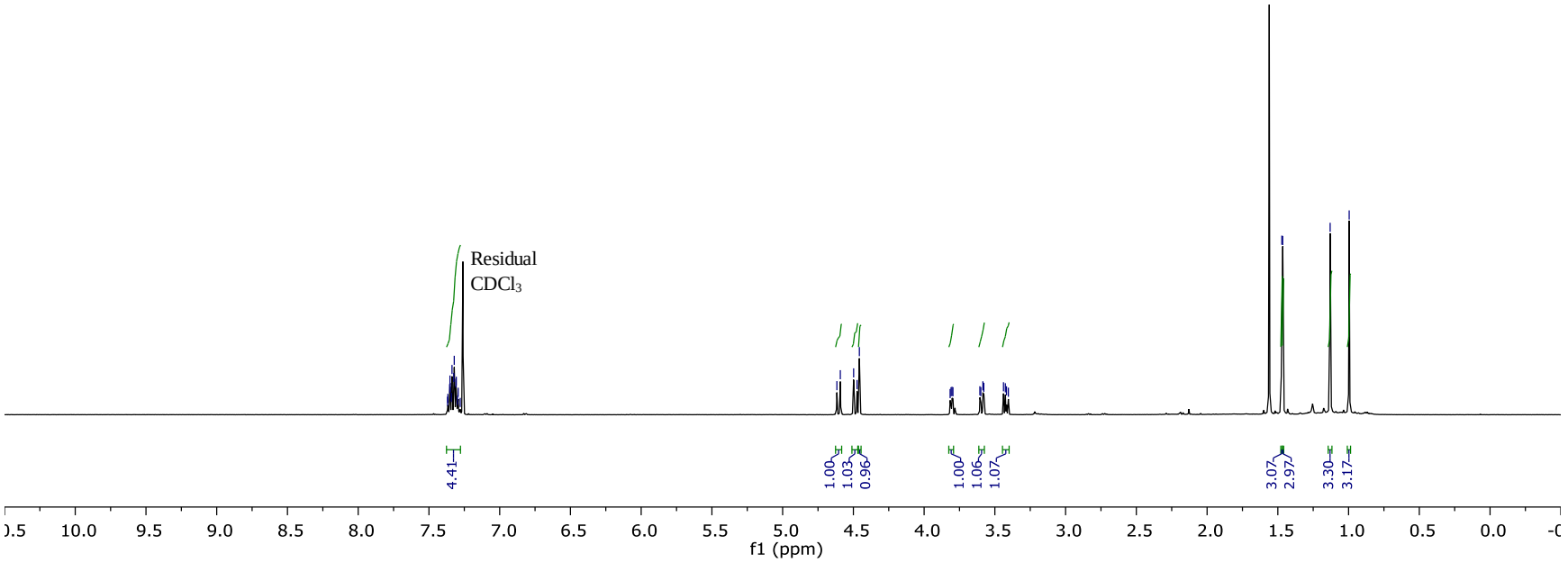


S23b

^{1}H-NMR (500 MHz, $CDCl_3$)

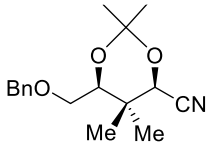


S24a

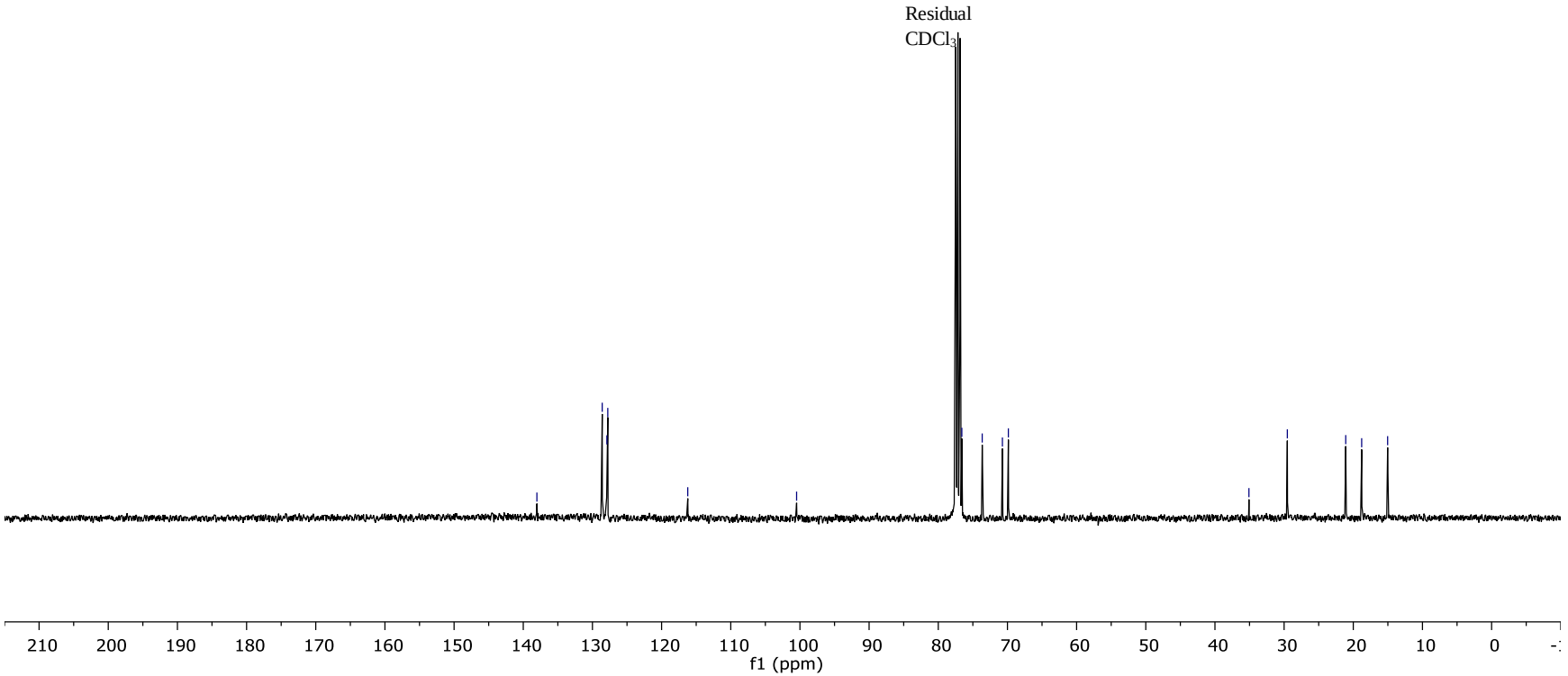


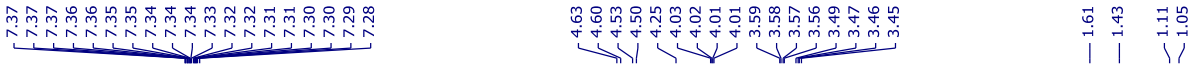
138.03
128.59
127.91
127.78
116.22
100.48
76.60
73.65
70.73
69.87
35.09
29.54
21.09
18.79
15.04

^{13}C-NMR (100.6 MHz, $CDCl_3$)

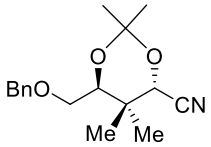


S24a

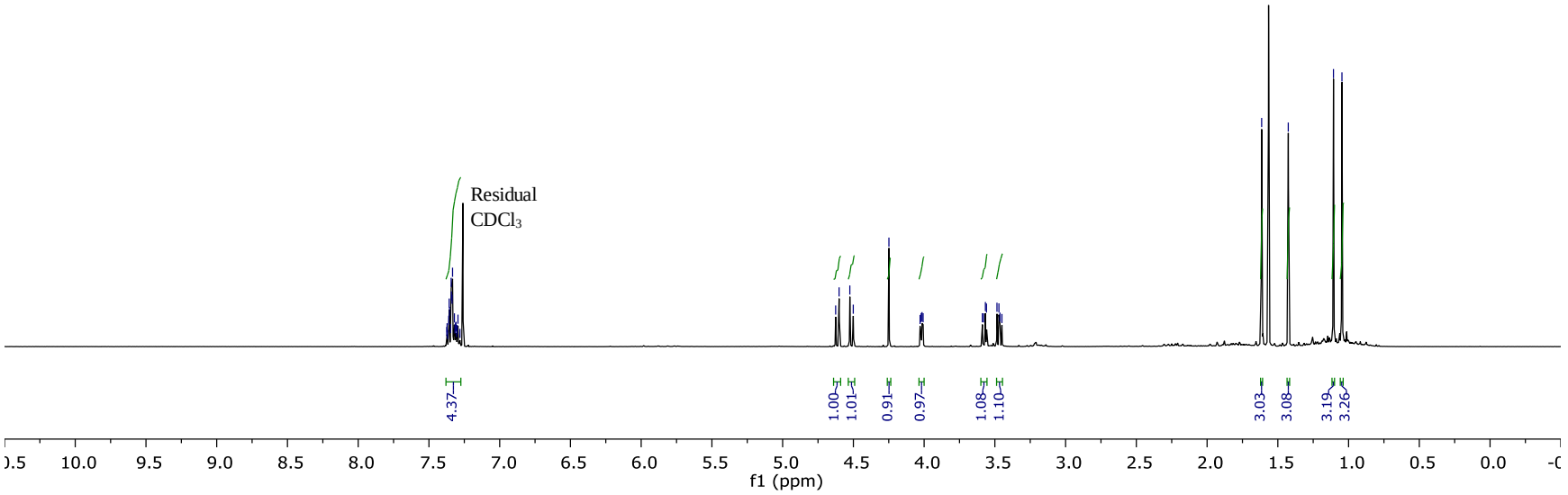




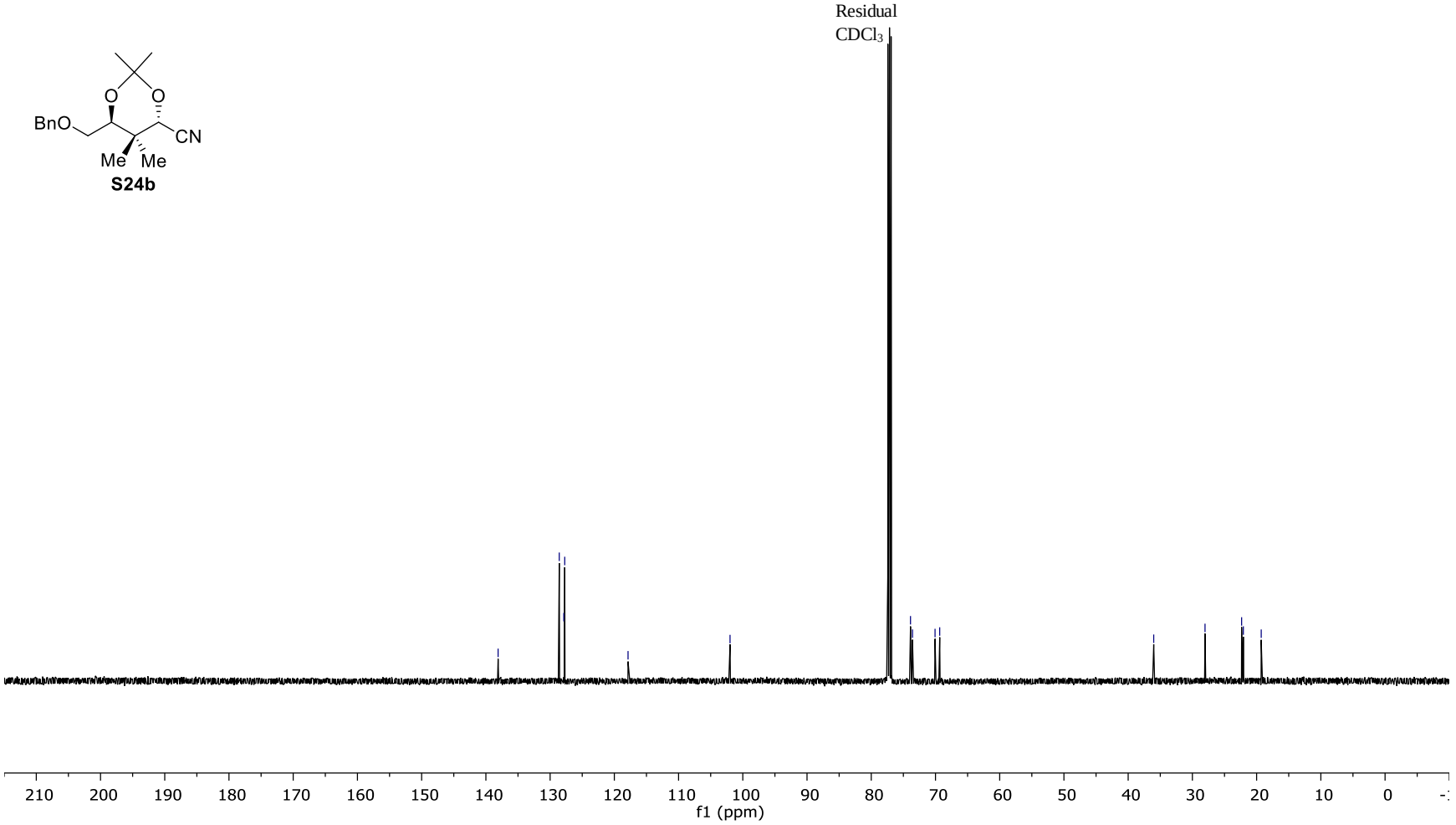
^{1}H-NMR (500 MHz, $CDCl_3$)



S24b



^{13}C-NMR (126 MHz, $CDCl_3$)



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