Supplementary Information (SI) for ChemComm.

Synthesis of bisenarsan; an organoarsenic metabolite from streptomycetes

Supporting information

Ihor Kholomieiev, Jeya Prathap Kaniraj‡, Rafael Tarozo, Adriaan Minnaard‡

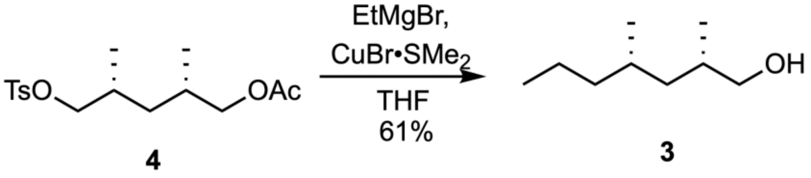
Stratingh Institute for Chemistry, University of Groningen, Nijenborgh 7, NL-9747 AG
Groningen, The Netherlands. E-mail: a.j.minnaard@rug.nl, j.p.kaniraj@rug.nl

Experimental procedures

General methods

All solvents and reagents were purchased from Sigma-Aldrich and TCI Europe and used without further purification. Flash chromatography was performed using silica gel type SiliaFlash P60 (230 – 400 mesh). The eluent composition is stated as v/v. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on an Agilent 400 NMR spectrometer at 400, 100.59 and 161.9 MHz, respectively. Chemical shifts are reported in ppm with the solvent resonance as the internal standard. Data are reported as follows: chemical shifts (δ), multiplicity, coupling constant J (Hz), and integration value. Normal phase chiral HPLC analysis was performed on a Shimadzu LC-20 series equipped with a photodiode array detector. High resolution mass spectra (HRMS) were recorded on a Thermo Scientific LTQ Orbitrap XL with electrospray ionization (ESI) in positive or negative mode using DCM as a solvent unless stated otherwise.

Synthesis of **3**



To a stirred suspension of copper(I) bromide-dimethyl sulfide complex (1.13 g, 5.50 mmol, 0.5 eq.) in 80 ml of THF at 0 °C was added 1 M ethylmagnesium bromide solution in THF (41 ml, 41 mmol, 4 eq.) dropwise. To the obtained mixture, a solution of tosylate **4**[1] (3.40 g, 10.3 mmol, 1 eq.) in 20 mL of THF was added dropwise. The mixture was allowed to warm up to room temperature overnight, cooled back to 0 °C and quenched with approximately 50 mL of a saturated NH_4Cl solution. The obtained mixture was concentrated *in vacuo* to remove THF and extracted with Et_2O (3 × 50 mL). The extracts were combined, washed with brine (~50 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to afford crude **3**. Purification by flash column chromatography (10% Et_2O in pentane, Rf ~0.3) provided **3** (913 mg, 61%) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.51 (dd, J = 10.5, 5.2 Hz, 1H), 3.36 (dd, J = 10.5, 6.8 Hz, 1H), 1.79 – 1.63 (m, 1H), 1.56 – 1.42 (m, 1H), 1.42 – 1.15 (m, 4H), 1.09 – 0.97 (m, 1H), 0.97 – 0.81 (m, 10H).

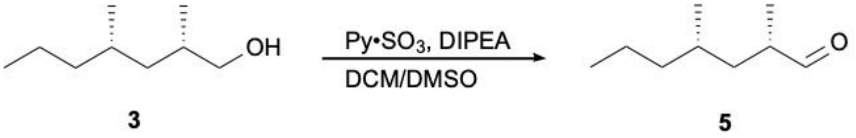
^{13}C NMR (101 MHz, $CDCl_3$) δ 77.5, 77.2, 76.8, 68.5, 41.2, 39.1, 33.2, 29.9, 20.4, 20.1, 17.4, 14.5.

$[\alpha]_{589}^{20}$ = -12.1° (c = 1.0, $CHCl_3$).

An HRMS could not be obtained due to poor ionisation of the compound.

The analytical data is in agreement with previous reports[2]

Synthesis of **5**



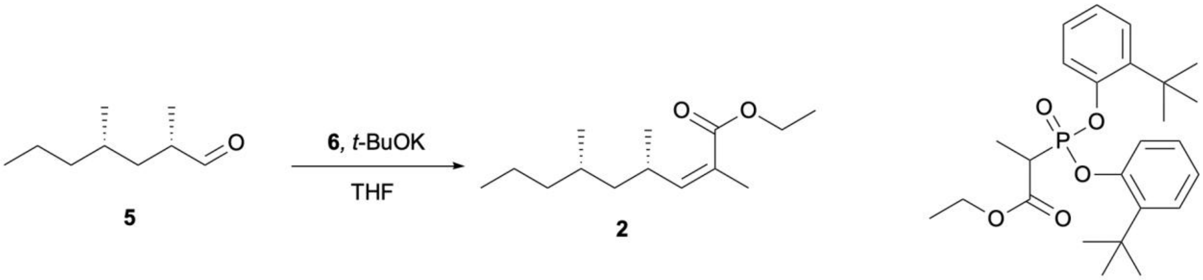
Sulfur trioxide-pyridine complex (455 mg, 2.86 mmol, 4 eq.) was dissolved in anhydrous DMSO (7 ml) and the obtained solution was stirred at rt for 15 min. In a separate flask, DIPEA (0.75 mL, 4.28 mmol, 6 eq.) was added to a solution of alcohol **3** (103 mg, 0.714 mmol, 1 eq.) in a mixture of anhydrous DCM (13 mL) and DMSO (7 mL). The Py•SO_3 solution was then added to the reaction mixture at 0 ^oC and the solution was stirred at the same temperature for 45 min. A saturated solution of NH_4Cl (20 mL) was added to the reaction mixture and the layers were separated. The aqueous solution was extracted with Et_2O (3 x 40 mL), the organic extracts were combined, washed with 1 M pH 7 phosphate buffer (2 x 30 mL), followed by brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to afford crude **3**. The crude was dissolved in 95 : 5 pentane/Et_2O mixture and passed through a column of silica (~10 g). The eluent was evaporated to yield **5** (96 mg, 94%) as a colourless oil which was used immediately in the next step.

^1H NMR (400 MHz, $CDCl_3$) δ 9.58 (d, J = 2.5 Hz, 1H), 2.43 (hd, J = 7.0, 2.5 Hz, 1H), 1.76 – 1.62 (m, 1H), 1.57 – 1.43 (m, 1H), 1.40 – 1.19 (m, 4H), 1.18 – 1.03 (m, 5H), 0.96 – 0.81 (m, 7H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 205.7, 44.3, 39.1, 38.4, 30.3, 20.0, 19.9, 14.4, 14.3.

An HRMS could not be obtained due to poor ionisation of the compound.

Synthesis of **2**

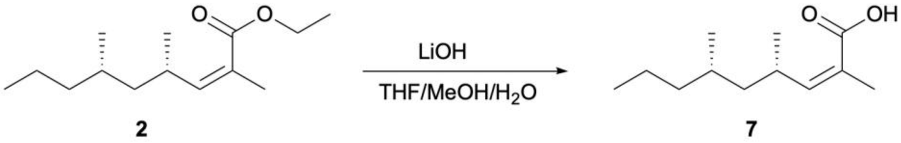


6

To a solution of the known phosphonate **6**[3] (132 mg, 0.296 mmol, 1.3 eq.) in anhydrous THF (1 mL) at 0 ^oC was added potassium *tert*-butoxide (32 mg, 0.285 mmol, 1.25 eq.) in one portion. After stirring for 15 min at this temperature, the obtained solution was added dropwise to a solution of the aldehyde **5** (32 mg, 0.228 mmol, 1 eq.) in THF (1 mL) at −78 ^oC. The stirred reaction mixture was allowed to warm up to room temperature overnight, quenched by adding saturated NH_4Cl solution (~1 mL) and concentrated *in vacuo* to remove the organic solvent. The residue was then diluted with water (~2 mL) and extracted with EtOAc (3 x 5 ml). The organic extracts were combined, washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The

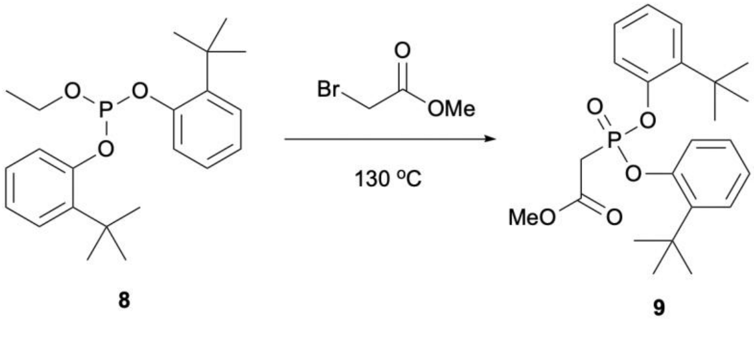
residue was purified by flash column chromatography (2% Et_2O in pentane, Rf ~0.5) to provide **2** (48 mg, 93%) as a colourless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.59 (dq, J = 10.1, 1.4 Hz, 1H), 4.19 (q, J = 7.6 Hz, 2H), 3.31 – 3.16 (m, 1H), 1.88 (d, J = 1.4 Hz, 3H), 1.38 – 1.16 (m, 8H), 1.14 – 1.02 (m, 2H), 0.95 (d, J = 6.5 Hz, 3H), 0.86 (t, J = 7.1 Hz, 3H), 0.81 (d, J = 6.5 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 148.6, 125.9, 60.2, 45.3, 40.02, 31.2, 30.6, 21.4, 21.0, 20.2, 19.7, 14.5, 14.4.
HRMS calcd. for $[C_{14}H_{26}O_2H]^+$ 227.2006, found 227.2005.

Synthesis of **7** by hydrolysis of **2**



To a solution of ester **2** (30 mg, 0.13 mmol, 1 eq.) in a mixture of THF (1 mL), methanol (1 mL) and water (1 mL) was added lithium hydroxide (32 mg, 1.33 mmol, 10 eq.) and the obtained mixture was allowed to stir at room temperature for 6 d. The solution was concentrated *in vacuo* to remove the organic solvents, acidified to pH 1 with 2 M aqueous HCl and extracted with EtOAc (3 x 5 mL). The extracts were combined, washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (10% Et_2O in pentane, Rf ~0.3) to provide **7** (19 mg, 72%) as a white waxy solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (dq, J = 10.3, 1.5 Hz, 1H), 3.51 – 3.25 (m, 1H), 1.90 (d, J = 1.5 Hz, 3H), 1.41 – 1.15 (m, 5H), 0.96 (d, J = 6.5 Hz, 3H), 0.87 (t, J = 7.1 Hz, 3H), 0.82 (d, J = 6.5 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 152.8, 124.9, 45.3, 40.0, 31.4, 30.8, 21.3, 20.8, 20.1, 19.7, 14.5.
HRMS calcd. for $[C_{12}H_{21}O_2]^-$ 197.1547, found 197.1546.

Synthesis of **9**



Ando reagent **9** was synthesised according to a modified procedure by Kwan *et al*.[4]. A mixture of the known phosphite **8**[5] (5.26 g, 14.0 mmol, 1 eq.) and methyl bromoacetate (4.30 g, 28.1 mmol, 2 eq.) was stirred at 130 °C for 3 d. The flask was then cooled down to room temperature and heptane (~20 ml) and water (~20 ml) were added. The obtained mixture was stirred vigorously for 10 min, inducing crystallization of **9**. The solid was isolated by filtration and washed with cold heptane. The organic layer of the filtrate was separated from the aqueous layer, concentrated *in vacuo* and purified by flash column chromatography (15% EtOAc in heptane, Rf ~0.3) to obtain a second crop of **9**. The crops were combined to yield **9** (5.43 g, 92%) as white crystals.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.66 (dt, J = 8.1, 1.3 Hz, 2H), 7.37 (dt, J = 7.7, 1.8 Hz, 2H), 7.15 (dd, J = 8.1, 1.8 Hz, 2H), 7.09 (td, J = 7.7, 1.3 Hz, 2H), 3.66 (s, 3H), 3.37 (d, J = 21.8 Hz, 2H), 1.37 (s, 18H).

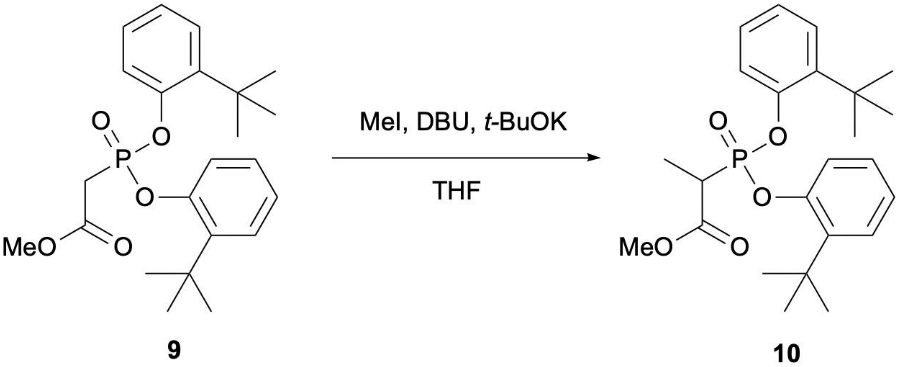
^{13}C NMR (101 MHz, CDCl$_3$) δ 165.0 (d, J = 6.3 Hz), 150.1 (d, J = 8.1 Hz), 139.3 (d, J = 8.2 Hz), 127.8, 127.5, 124.8, 119.7 (d, J = 3.0 Hz), 52.9 (d, J = 6.4 Hz), 35.4 (d, J = 138.3 Hz), 34.8, 30.1.

^{31}P NMR (162 MHz, CDCl$_3$) δ 9.64.

HRMS calcd. for $[C_{23}H_{31}O_5PH]^+$ 419.1982, found 419.1982.

The analytical data is in agreement with previous reports[2]

Synthesis of **10**

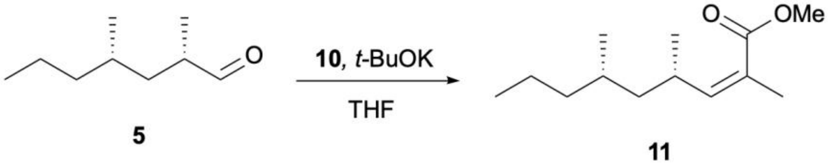


The methylation reaction was performed according to the procedure developed by Bressin *et al.*[3]. To a stirred solution of phosphonate **9** (1.50 g, 3.58 mmol, 1 eq.) in anhydrous THF (4 ml) at 0 °C was added iodomethane (0.223 mL, 3.58 mmol, 1 eq.) in one portion. Potassium tert-butoxide (400 mg, 3.58 mmol, 1 eq.) was added to the solution in small portions at the same temperature. The ice bath was removed and the reaction mixture was stirred at room temperature for 1 h. The obtained off-white slurry was cooled down to 0 °C again and DBU was added (0.535 ml, 3.58 mmol, 1 eq.), followed by iodomethane (0.223 ml, 3.58 mmol, 1 eq.), both dropwise. The mixture was allowed to stir at room temperature for 1 h, after which it was quenched by addition of saturated aqueous NH_4Cl solution (10 mL) at 0 °C. The mixture was concentrated *in vacuo* to remove THF and extracted with EtOAc (2 x 20 mL), the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The oily residue was crystallized from heptane to obtain **10** (836 mg, 54%) as white crystals.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.74 (dt, J = 8.1, 1.3 Hz, 1H), 7.65 (dt, J = 8.1, 1.3 Hz, 1H), 7.34 (dq, J = 7.8, 1.7 Hz, 2H), 7.17 – 7.01 (m, 4H), 3.62 (s, 3H), 3.50 (dq, J = 24.2, 7.3 Hz, 1H), 1.70 (dd, J = 19.6, 7.3 Hz, 3H), 1.34 (s, 9H), 1.32 (s, 9H).

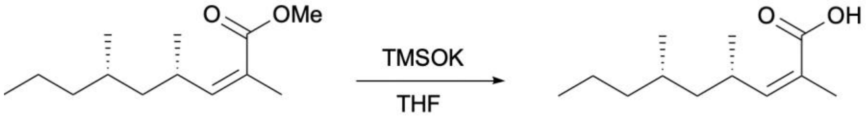
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9 (d, J = 4.7 Hz), 150.8 (dd, J = 20.9, 9.0 Hz), 139.0 (dd, J = 8.2, 4.0 Hz), 127.7, 127.4 (d, J = 2.5 Hz), 124.5, 119.7 (d, J = 11.3 Hz), 52.7 (d, J = 6.0 Hz), 40.9 (d, J = 142.2 Hz), 34.8, 30.1 (d, J = 5.9 Hz), 12.1 (d, J = 5.9 Hz).
^{31}P NMR (162 MHz, $CDCl_3$) δ 14.65.
HRMS calcd. for $[C_{24}H_{33}O_5PNa]^+$ 455.1958, found 455.1955.

Synthesis of **11**



To a solution of phosphonate **10** (206 mg, 0.430 mmol, 1.3 eq.) in anhydrous THF (1 mL) at 0 ºC was added potassium *tert*-butoxide (43 mg, 0.38 mmol, 1.2 eq.) in one portion. After stirring for 15 min at the same temperature, the obtained solution was added dropwise to a solution of aldehyde **5** (47 mg, 0.33 mmol, 1 eq.) in THF (1 mL) at -78 ºC. The stirred reaction mixture was allowed to warm up to room temperature overnight, quenched by adding saturated aqueous NH_4Cl solution (~1 mL) and concentrated *in vacuo* to remove the organic solvent. The residue was then diluted with water (~2 mL) and extracted with EtOAc (3 x 2 mL). The organic extracts were combined, washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (2% Et_2O in pentane, Rf ~0.5) to provide **11** (35 mg, 50%) as a colourless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.61 (dq, J = 10.1, 1.5 Hz, 1H), 3.73 (s, 3H), 3.32 – 3.16 (m, 1H), 1.88 (d, J = 1.5 Hz, 3H), 1.39 – 1.15 (m, 6H), 1.13 – 1.00 (m, 2H), 0.95 (d, J = 6.6 Hz, 3H), 0.86 (t, J = 7.1 Hz, 3H), 0.80 (d, J = 6.4 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 149.4, 125.5, 51.3, 45.3, 40.0, 31.2, 30.6, 21.4, 21.0, 20.1, 19.7, 14.5.
HRMS calcd. for $[C_{13}H_{24}O_2H]^+$ 213.1849, found 213.1848.

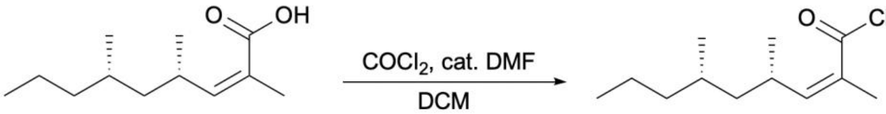
Synthesis of **7** by demethylation of **11**



11 **7**

Ester **11** (30 mg, 0.14 mmol, 1 eq.) was dissolved in anhydrous THF (1.5 mL) and 2 M potassium trimethylsilanolate solution in THF (0.425 mL, 0.848 mmol, 6 eq.) was added to the solution. The obtained mixture was brought to reflux for 4 h, after which it was allowed to cool to room temperature. The solution was acidified to pH 1 with 2 M HCl_{aq}, concentrated *in vacuo* to remove THF and extracted with Et_2O (3 x 2 ml). The extracts were combined, washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (10% Et_2O in pentane, Rf ~0.3) to obtain **7** (23 mg, 82%) as a white waxy solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (dq, J = 10.3, 1.5 Hz, 1H), 3.51 – 3.25 (m, 1H), 1.90 (d, J = 1.5 Hz, 3H), 1.41 – 1.15 (m, 5H), 0.96 (d, J = 6.5 Hz, 3H), 0.87 (t, J = 7.1 Hz, 3H), 0.82 (d, J = 6.5 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 152.8, 124.9, 45.3, 40.0, 31.4, 30.8, 21.3, 20.8, 20.1, 19.7, 14.5.
HRMS calcd. for $[C_{12}H_{21}O_2]^-$ 197.1547, found 197.1546.

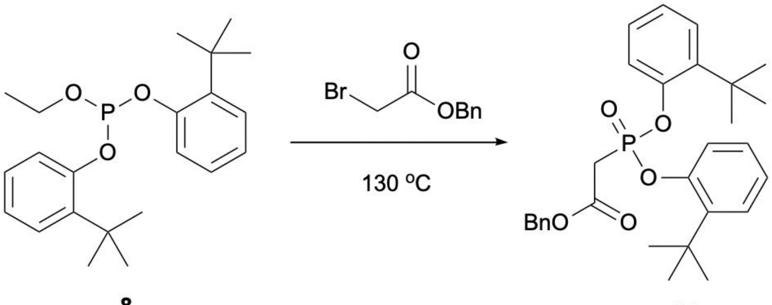
Synthesis of **12**



7 **12**

Carboxylic acid **7** (20 mg, 0.10 mmol, 1 eq) was dissolved in anhydrous DCM (2 mL) and 50 μL of a 0.1 M stock solution of DMF (5 μmol, 0.05 eq.) in DCM was added to the obtained solution. To the reaction mixture was added oxalyl chloride (18 μL, 0.21 mmol, 2 eq.) and the solution was allowed to stir for 4 h. The reaction mixture was concentrated *in vacuo* and the obtained brown residue was directly used in the next step.
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.74 (dq, J = 10.3, 1.5 Hz, 1H), 3.09 – 2.95 (m, 1H), 2.06 (d, J = 1.5 Hz, 3H), 1.38 – 1.15 (m, 6H), 1.15 – 1.02 (m, 2H), 0.97 (d, J = 6.6 Hz, 3H), 0.86 (t, J = 7.1 Hz, 3H), 0.81 (d, J = 6.4 Hz, 3H).

Synthesis of **15**



8

15

Ando reagent **15** was synthesised according to a modified procedure by Stephens *et al.*[6]. A stirred mixture of phosphite **8**[5] (10.60 g, 28.3 mmol, 1.66 eq.) and benzyl bromoacetate (2.7 mL, 17 mmol, 1 eq.) was heated to 130 °C for 3 d. The reaction mixture was allowed to cool to room temperature and purified by flash column chromatography (10% EtOAc in heptane, Rf ~0.2) to yield phosphonate **15** (5.91 g, 70%) as a colourless oil.

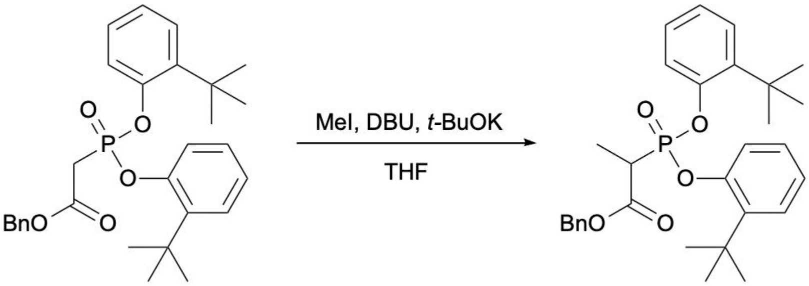
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (dt, J = 8.0, 1.4 Hz, 2H), 7.36 (dt, J = 7.7, 1.9 Hz, 2H), 7.31 – 7.27 (m, 3H), 7.25 – 7.19 (m, 2H), 7.14 (td, J = 8.0, 1.9 Hz, 2H), 7.09 (td, J = 7.7, 1.4 Hz, 2H), 5.09 (s, 2H), 3.41 (d, J = 21.7 Hz, 2H), 1.34 (s, 18H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5 (d, J = 6.0 Hz), 150.1 (d, J = 8.4 Hz), 139.3 (d, J = 8.1 Hz), 135.0, 128.6 (d, J = 2.6 Hz), 128.5, 127.8, 127.6, 124.8, 119.8 (d, J = 3.1 Hz), 67.8, 35.7 (d, J = 138.4 Hz), 34.8, 30.2.

^{31}P NMR (162 MHz, $CDCl_3$) δ 9.52.

HRMS calcd. for $[C_{29}H_{35}O_5PH^+]^+$ 495.2295, found 495.2294.

Synthesis of **16**



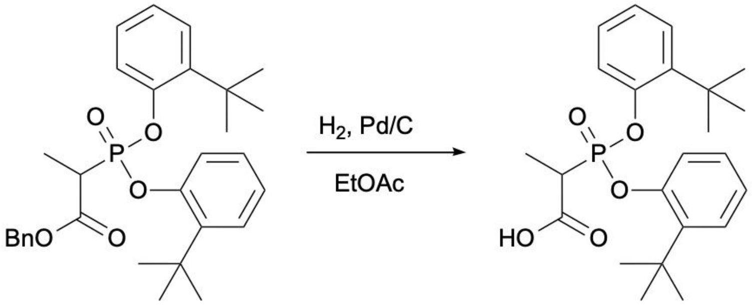
15

16

The methylation of **15** was performed according to the procedure developed by Bressin *et al.*[3]. To a stirred solution of phosphonate **15** (2.00 g, 4.04 mmol, 1 eq.) in anhydrous THF (4 mL) at 0 °C was added iodomethane (0.252 ml, 4.04 mmol, 1 eq.) in one portion. Potassium tert-butoxide (450 mg, 4.00 mmol, 1 eq.) was added to the solution in small portions at the same temperature. The ice bath was removed and the reaction mixture was stirred at room temperature for 1 h. The obtained off-white slurry was cooled down to 0 °C again and DBU was added (0.600 ml, 4.01 mmol, 1 eq.), followed by iodomethane (0.252 mL, 4.04 mmol, 1 eq.), both dropwise. The mixture was allowed to stir at room temperature for 1 h, after which it was quenched by addition of

saturated NH_4Cl solution (10 mL) at 0 °C. The mixture was concentrated *in vacuo* to remove THF and extracted with EtOAc (2 x 20 ml), the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to yield **16** (1.674 g, 81%) as a white solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (dt, J = 8.0, 1.3 Hz, 1H), 7.66 (dt, J = 8.0, 1.3 Hz, 1H), 7.33 (dt, J = 7.6, 1.9 Hz, 2H), 7.28 – 7.23 (m, 3H), 7.20 – 7.15 (m, 2H), 7.15 – 7.02 (m, 4H), 5.18 (d, J = 12.2 Hz, 1H), 4.89 (d, J = 12.2 Hz, 1H), 3.53 (dq, J = 24.1, 7.3 Hz, 1H), 1.71 (dd, J = 19.5, 7.3 Hz, 3H), 1.32 (s, 9H), 1.27 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4 (d, J = 4.1 Hz), 150.8 (dd, J = 25.2, 9.2 Hz), 139.0 (t, J = 7.9 Hz), 135.1, 128.6, 128.5, 127.7 (d, J = 2.1 Hz), 127.5 (d, J = 1.7 Hz), 124.5 (d, J = 2.2 Hz), 119.9 (d, J = 3.1 Hz), 119.6 (d, J = 2.8 Hz), 67.7, 41.2 (d, J = 138.6 Hz), 34.8, 30.1 (d, J = 9.4 Hz), 12.1 (d, J = 6.1 Hz).
^{31}P NMR (162 MHz, $CDCl_3$) δ 14.47.
HRMS calcd. for $[C_{30}H_{37}O_5PH]^+$ 509.2451, found 509.2455.

Synthesis of **17**

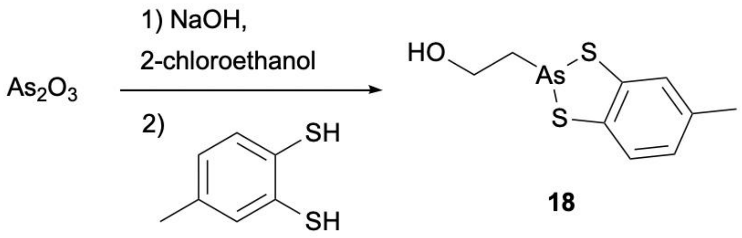


16

17

A round-bottom flask was charged with phosphonate **16** (1.21 g, 2.37 mmol) and 10% Pd/C (118 mg), after which it was evacuated and back-filled with nitrogen thrice. Dry ethyl acetate (25 mL) was added to the flask and a hydrogen balloon was attached. The flask was evacuated and back-filled with hydrogen, after which the reaction mixture was allowed to stir under a hydrogen atmosphere for 1.5 h. The reaction mixture was filtered through a pad of Celite® and the filtrate was concentrated *in vacuo* to yield **17** (984 mg, 100%) as a white solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (dt, J = 8.0, 1.3 Hz, 1H), 7.64 (dt, J = 8.0, 1.3 Hz, 1H), 7.33 (dt, J = 7.7, 1.9 Hz, 2H), 7.18 – 7.01 (m, 4H), 6.90 (br. s, 1H), 3.52 (dq, J = 24.4, 7.3 Hz, 1H), 1.67 (dd, J = 19.5, 7.3 Hz, 3H), 1.32 (s, 18H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1 (d, J = 3.8 Hz), 150.6 (dd, J = 9.2, 4.9 Hz), 139.1 (dd, J = 8.1, 5.6 Hz), 127.8 (d, J = 1.8 Hz), 127.5, 124.7 (d, J = 1.5 Hz), 119.8 (dd, J = 5.2, 3.0 Hz), 40.7 (d, J = 138.0 Hz), 34.8 (d, J = 2.1 Hz), 30.2 (d, J = 1.4 Hz), 11.9 (d, J = 6.1 Hz).
^{31}P NMR (162 MHz, $CDCl_3$) δ 14.84.
HRMS calcd. for $[C_{23}H_{31}O_5PNa^+]^+$ 441.1801, found 441.1804.

Synthesis of **18**



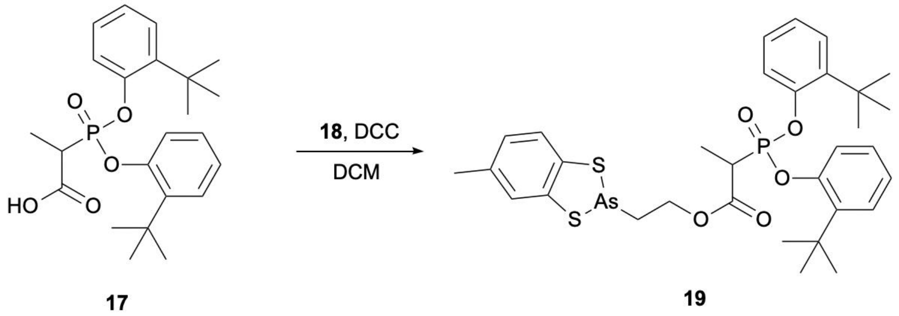
A solution of sodium hydroxide (2.40 g, 51 mmol, 10 eq.) in water (3 mL) was prepared in a 20 mL vial. Arsenic trioxide (1.00 g, 5.06 mmol, 1 eq.) was added to the solution and the mixture was stirred until no As_2O_3 was left undissolved (heating, sonication and vortexing were employed). The mixture was then cooled to 0 ^{o}C and 2-chloroethanol (1.00 mL, 15.1 mmol, 3 eq.) was added dropwise. The vial was covered with parafilm and the mixture was stirred overnight, allowing it to warm to room temperature. The obtained yellow suspension was transferred to a 50 mL round-bottom flask and concentrated hydrochloric acid (4.2 mL, 51 mmol, 10 eq.) was added to it dropwise (exotherm!). The obtained white suspension was concentrated *in vacuo* and coevaporated with ~25 mL of isopropanol to give a white solid residue. The residue was suspended in ~20 mL of methanol and filtered into a 250 mL round-bottom flask. The white solid was washed with methanol (3 x 15 mL). To the stirred filtrate containing (2-hydroxyethyl)arsonic acid was added a solution of toluene-3,4-dithiol (3.95 g, 25.3 mmol, 5 eq.) in methanol (~10 ml) under nitrogen atmosphere. The reaction mixture was allowed to stir at room temperature overnight. The obtained green suspension was filtered, the filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (20% Et_2O in pentane, Rf ~0.2) to yield **18** (1.84 g, 66%) as a green oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 8.0 Hz, 1H), 7.24 (d, J = 1.6 Hz, 1H), 6.82 (dd, J = 8.0, 1.6 Hz, 1H), 3.94 (t, J = 6.4 Hz, 2H), 2.33 (t, J = 6.4 Hz, 2H), 2.27 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.0, 136.4, 135.8, 128.0, 127.1, 126.7, 59.3, 37.7, 20.8.

HRMS calcd. for $[C_9H_{10}AsOS_2]^-$ 272.9395, found 272.9397.

Synthesis of **19**



Carboxylic acid **17** (1.29 g, 3.08 mmol, 1 eq) was dissolved in dry DCM (15 mL), and to the obtained solution were subsequently added solutions of the alcohol **18** (1.01 g, 3.70 mmol, 1.2

eq.) and DCC (763 mg, 3.70 mmol, 1.2 eq.) in DCM (4 and 7 mL, respectively). The reaction mixture was stirred overnight, the obtained suspension was filtered, the filtrate was concentrated *in vacuo* and the residue was purified by column chromatography (20% Et$_2$O in pentane, Rf ~0.2) to yield **19** (1.40 g, 67%) as an off-white solid.

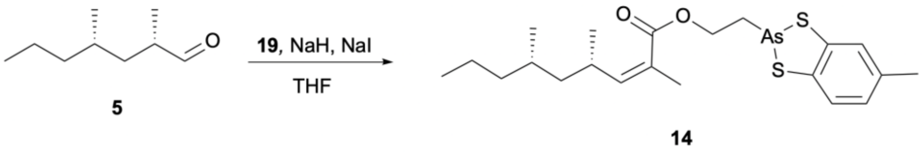
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.74 (dt, J = 8.1, 1.2 Hz, 1H), 7.66 (dt, J = 8.1, 1.2 Hz, 1H), 7.33 (tt, J = 7.5, 1.6 Hz, 2H), 7.26 (d, J = 7.9 Hz, 1H), 7.20 (s, 1H), 7.11 (tt, J = 8.2, 1.6 Hz, 2H), 7.05 (tt, J = 7.5, 1.6 Hz, 2H), 6.82 (d, J = 7.9 Hz, 1H), 4.30 (dt, J = 11.4, 6.8 Hz, 1H), 4.18 (dt, J = 11.4, 6.8 Hz, 1H), 3.48 (dq, J = 24.1, 7.3 Hz, 1H), 2.27 (s, 3H), 2.18 – 2.03 (m, 2H), 1.69 (dd, J = 19.4, 7.3 Hz, 3H), 1.34 (s, 9H), 1.30 (s, 9H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 168.5 (d, J = 4.3 Hz), 150.8 (dd, J = 25.5, 9.1 Hz), 139.8, 138.9 (dd, J = 8.1, 6.5 Hz), 136.2 (d, J = 4.4 Hz), 135.9, 127.9, 127.7, 127.5 (d, J = 3.4 Hz), 127.0, 126.8, 124.6, 119.7 (d, J = 20.3 Hz), 62.5, 41.2 (d, J = 138.6 Hz), 34.8, 33.1, 30.2 (d, J = 4.2 Hz), 20.8, 12.1 (d, J = 6.2 Hz).

^{31}P NMR (162 MHz, CDCl$_3$) δ 14.25.

HRMS calcd. for $[C_{32}H_{39}AsO_5PS_2]^-$ 673.1198, found 673.1203.

Synthesis of **14**

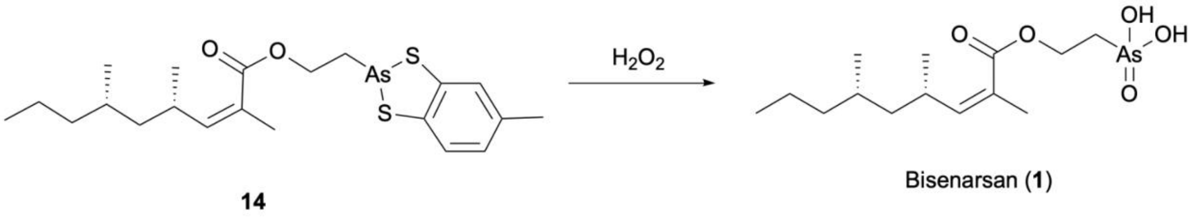


The Ando olefination reaction was performed according to a modified procedure by Pihko *et al.*[7]. To a round-bottom flask were added a 60% suspension of sodium hydride in paraffin oil (29 mg, 0.73 mmol, 1.15 eq.), sodium iodide (95 mg, 0.63 mmol, 1 eq.) and pentane (2 mL) under nitrogen atmosphere. The flask was swirled and pentane was removed with a syringe, after which the washing step was repeated with 2 mL of fresh pentane. Anhydrous THF (1 mL) was added to the flask and the mixture was cooled to −15 ^{o}C. A solution of the phosphonate **19** (512 mg, 0.759 mmol, 1.2 eq.) in anhydrous THF (1 mL) was added dropwise to the reaction flask and the mixture was allowed to stir for 15 min at that temperature. The mixture was then cooled to -78 ^{o}C and a solution of the aldehyde **5** (90 mg, 0.63 mmol, 1 eq.) in THF (0.5 mL) was added to the flask and the stirring was continued overnight, allowing the reaction mixture to warm up to room temperature. The reaction mixture was quenched by adding saturated NH$_4$Cl solution (~5 mL) and concentrated *in vacuo* to remove the organic solvent. The residue was then extracted with EtOAc (3 x 5 mL). The organic extracts were combined, washed with brine, dried over anhydrous Na$_2$SO$_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography (2% Et$_2$O in pentane, Rf ~0.5) to obtain **14** (174 mg, 61%) as a colourless oil.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.29 (d, J = 8.0 Hz, 1H), 7.24 (d, J = 1.7 Hz, 1H), 6.83 (dd, J = 8.0, 1.7 Hz, 1H), 5.66 (dq, J = 10.2, 1.4 Hz, 1H), 4.37 (t, J = 6.4 Hz, 2H), 3.34 – 3.21 (m, 1H), 2.36 (t, J = 6.4 Hz, 2H), 2.27 (s, 3H), 1.89 (d, J = 1.4 Hz, 3H), 1.39 – 1.15 (m, 6H), 1.14 – 1.01 (m, 2H), 0.96 (d, J = 6.6 Hz, 3H), 0.87 (t, J = 7.1 Hz, 3H), 0.80 (d, J = 6.4 Hz, 3H).

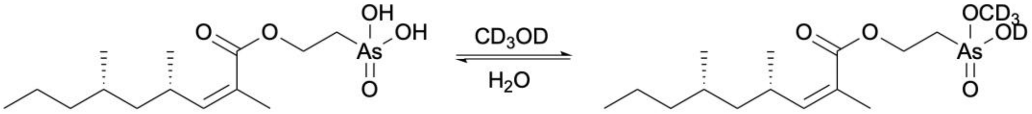
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 150.4, 139.8, 136.3, 135.8, 128.0, 127.1, 126.7, 125.2, 60.7, 45.3, 40.0, 33.8, 31.3, 30.7, 21.4, 21.0, 20.8, 20.2, 19.8, 14.5.
HRMS calcd. for $[C_{21}H_{31}AsO_2S_2Na]^+$ 477.0874, found 477.0870.

Synthesis of **1**



Ester **14** (56 mg, 0.12 mmol, 1 eq.) was dissolved in acetonitrile (2 ml) and 30% aqueous hydrogen peroxide (60 µL, 62 mmol, 5 eq.) was added to the obtained solution. The reaction mixture was allowed to stir at room temperature for 1 h, after which it was loaded directly onto a silica column. Flash column chromatography (100% CH_3CN → 10% water in CH_3CN, Rf ~0.2 in 10% water in CH_3CN) yielded a residue that was dissolved in DCM. The solution was filtered through a 0.2 µm PTFE syringe filter and the filtrate was concentrated *in vacuo* to yield Bisenarsan **1** (37 mg, 85%) as a white solid.

Analytical data is in agreement with values reported for natural bisenarsan. Similarly to natural bisenarsan, additional signals were observed in the ^{1}H and ^{13}C NMR spectra when CD_3OD was used as the solvent. When the ^{1}H NMR spectrum was recorded in CD_2Cl_2, no additional signals were observed. The additional signals are assumed to arise from the rapid esterification reaction between bisenarsan and CD_3OD[8]:



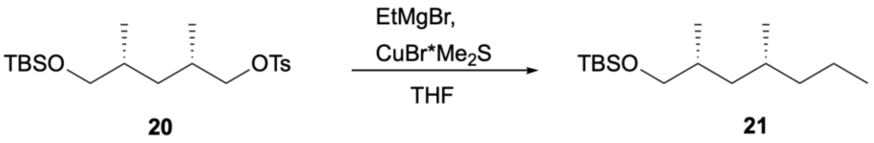
The formation of mono- and bis-(trideutero)methyl esters in CD_3OD solution is also confirmed by HRMS (see below). Since the degree of esterification is dependent on the age of the sample, the splitting pattern and the chemical shift of signals corresponding to the alkene proton and (2-hydroxyethyl)arsonic acid moiety show a certain degree of variability. Moreover, the chemical shift of the protons α- to the arsonic acid is heavily dependent on the degree of protonation of the acid. This effect has been encountered before by Hoshino *et al.*[9] during their synthesis of (2-hydroxyethyl)arsonic acid. Using CD_2Cl_2 as a solvent leads to consistent spectra, but CD_3OD was used for most of the analyses for the purpose of comparison with the natural isolate.

^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.55 (br. s, 2H), 5.68 (d, J = 10.0 Hz, 1H), 4.85 – 4.15 (m, 2H), 3.62 – 3.09 (m, 1H), 2.75 (s, 2H), 1.89 (s, 3H), 1.60 – 1.16 (m, 6H), 1.15 – 1.01 (m, 2H), 0.95 (d, J = 6.6 Hz, 3H), 0.87 (t, J = 7.1 Hz, 3H), 0.81 (d, J = 6.4 Hz, 3H).
^{1}H NMR (400 MHz, CD_3OD) δ 5.77 – 5.67 (m, 1H), 4.51 (t, J = 6.3 Hz, 2H), 3.37 (m, 1H), 2.98 (t, J = 6.6 Hz, 1H), 2.79 (t, J = 6.6 Hz, 1H), 1.92 (d, J = 1.6 Hz, 3H), 1.42 – 1.18 (m, 6H), 1.17 – 1.01 (m, 2H), 0.96 (d, J = 6.6 Hz, 3H), 0.88 (t, J = 7.1 Hz, 3H), 0.83 (d, J = 6.3 Hz, 3H).

^{13}C NMR (101 MHz, CD_3OD) δ 168.5, 168.3, 152.0, 151.6, 126.5, 126.3, 58.5, 58.2, 46.23, 46.21, 41.13, 41.11, 32.4, 32.1, 31.80, 31.78, 21.45, 21.42, 21.1, 20.89, 20.85, 20.0, 14.7.
HRMS (solution in CH_2Cl_2) calcd. for $[C_{14}H_{27}AsO_5H]^+$ 351.1147, found 351.1145.
HRMS (solution in CD_3OD) calcd. for $[C_{15}H_{25}D_4AsO_5Na^+]$ 391.1374, found 391.1377
HRMS (solution in CD_3OD) calcd. for $[C_{16}H_{25}D_6AsO_5Na^+]$ 407.1656, found 407.1651

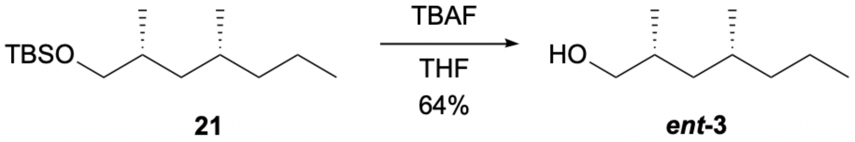
$[\alpha]_{589}^{20} = -15.8°$ (c = 0.50, CH_2Cl_2).

Synthesis of **21**



To a stirred suspension of copper(I) bromide-dimethyl sulfide complex (519 mg, 2.53 mmol, 0.5 eq.) in 10 mL of THF at 0 °C was added 1 M ethylmagnesium bromide solution in THF (20 mL, 20 mmol, 4 eq.) dropwise. To the obtained mixture was added dropwise a solution of the tosylate **20**[10] (2.00 g, 4.99 mmol, 1 eq.) in 10 ml of THF. The mixture was allowed to warm up to room temperature overnight, cooled back to 0 °C and quenched with approximately 30 mL of saturated aqueous NH_4Cl solution. The obtained mixture was concentrated *in vacuo* to remove THF and extracted with Et_2O (3 x 40 mL). The extracts were combined, washed with brine (~40 ml), dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to afford crude **21**. This was purified by flash column chromatography (pentane, Rf ~0.7) to provide **21** (1.05 g, 81%) as a colourless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45 (dd, J = 9.7, 5.3 Hz, 1H), 3.31 (dd, J = 9.7, 6.8 Hz, 1H), 1.74 – 1.61 (m, 1H), 1.53 – 1.41 (m, 1H), 1.40 – 1.17 (m, 4H), 1.09 – 0.95 (m, 1H), 0.89 (s, 9H), 0.88 – 0.82 (m, 9H), 0.03 (s, 6H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 68.5, 41.2, 39.2, 33.3, 29.9, 26.0, 20.5, 20.0, 18.4, 17.7, 14.5, -5.3.
An HRMS could not be obtained due to poor ionisation of the compound.

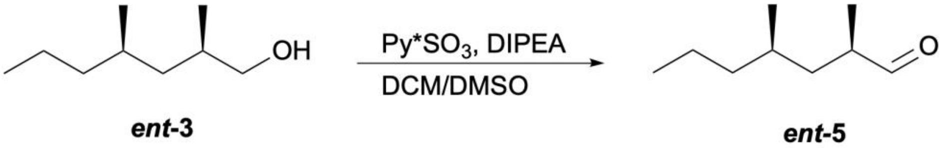
Synthesis of ***ent*-3**



To a stirred solution of **21** (798 mg, 3.09 mmol, 1 eq.) in anhydrous THF (10 mL) was added 1 M TBAF solution in THF (4.7 ml, 4.7 mmol, 1.2 eq.) and the mixture was allowed to stir overnight. Saturated aqueous $NaHCO_3$ solution (5 mL) was added to the mixture, together with sufficient water to dissolve the formed precipitate. The layers were separated and the aqueous layer was extracted with EtOAc (2 x 15 ml). The extracts were combined, washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified using flash column chromatography (10% EtOAc in heptane, Rf ~0.3) to yield ***ent*-3** (286 mg, 64%) as a colourless oil.

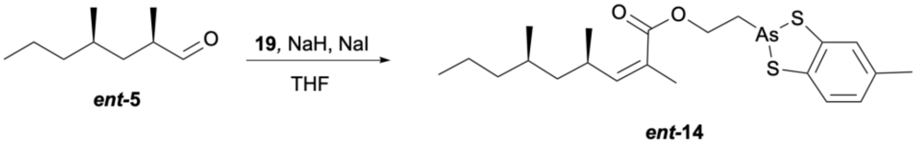
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.52 (dd, J = 10.5, 5.2 Hz, 1H), 3.38 (dd, J = 10.5, 6.8 Hz, 1H), 1.80 – 1.64 (m, 1H), 1.57 – 1.43 (m, 1H), 1.42 – 1.17 (m, 4H), 1.10 – 0.99 (m, 1H), 0.98 – 0.84 (m, 9H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 68.6, 41.2, 39.1, 33.3, 29.9, 20.5, 20.1, 17.4, 14.5.
$[\alpha]_{589}^{20}$ = +13.3° (c = 0.53, $CHCl_3$).
An HRMS could not be obtained due to poor ionisation of the compound.

Synthesis of ***ent*-5**



Sulfur trioxide-pyridine complex (221 mg, 1.39 mmol, 4 eq.) was dissolved in anhydrous DMSO (3 mL) and the obtained solution was stirred at rt for 15 min. In a separate flask, DIPEA (0.362 mL, 2.08 mmol, 6 eq.) was added to a solution of the alcohol ***ent*-3** (50 mg, 0.35 mmol, 1 eq.) in a mixture of anhydrous DCM (6 mL) and DMSO (3 mL). The Py•SO_3 solution was then added to the reaction mixture at 0 °C and the solution was stirred at the same temperature for 45 min. A saturated solution of NH_4Cl (10 mL) was added to the reaction mixture and the layers were separated. The aqueous solution was extracted with Et_2O (3 x 20 mL), the organic extracts were combined, washed with 1 M pH 7 phosphate buffer (2 x 15 ml), followed by brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to afford crude ***ent*-5**. This was dissolved in a 95 : 5 pentane/Et_2O mixture and passed through a column of silica (~10 g). The eluent was evaporated to yield ***ent*-5** (43 mg, 87%) as a colourless oil which was used immediately in the next step.
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.58 (d, J = 2.5 Hz, 1H), 2.44 (hd, J = 7.2, 2.5 Hz, 1H), 1.75 – 1.62 (m, 1H), 1.55 – 1.44 (m, 1H), 1.41 – 1.19 (m, 3H), 1.17 – 1.10 (m, 1H), 1.07 (d, J = 7.0 Hz, 3H), 0.96 – 0.82 (m, 6H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 205.7, 44.3, 39.1, 38.4, 30.3, 20.0, 20.0, 14.4, 14.3.
An HRMS could not be obtained due to poor ionisation of the compound.

Synthesis of ***ent*-14**



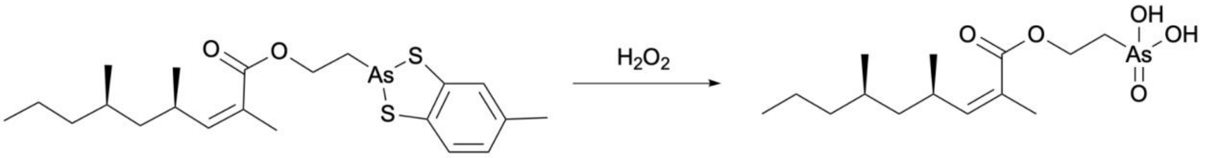
The Ando olefination reaction was performed according to a modified procedure by Pihko *et al.*[7]. To a round-bottom flask were added a 60% suspension of sodium hydride in paraffin oil (16 mg, 0.40 mmol, 1.2 eq.), sodium iodide (53 mg, 0.35 mmol, 1 eq.) and pentane (2 mL) under a nitrogen atmosphere. The flask was swirled and pentane was removed with a syringe, after which the washing step was repeated with 2 mL of fresh pentane. Anhydrous THF (1 mL) was added to the flask and the mixture was cooled to -15 °C. A solution of phosphonate **19** (308 mg, 0.457 mmol, 1.2 eq.) in anhydrous THF (1 mL) was added dropwise to the reaction flask and the mixture was allowed to stir for 15 min at the same temperature. The mixture was then cooled to -78 ^{o}C and a solution of the aldehyde ***ent*-5** (50 mg, 0.35 mmol, 1 eq.) in THF (0.5 mL) was added to the flask and the stirring was continued overnight, allowing the reaction mixture to warm up to room temperature. The reaction mixture was quenched by adding saturated NH_4Cl solution (~5 mL) and concentrated *in vacuo* to remove the organic solvent. The residue was then extracted with EtOAc (3 x 5 ml). The organic extracts were combined, washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (2% Et_2O in pentane, rf ~0.5) to provide ***ent*-14** (91 mg, 57%) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 8.0 Hz, 1H), 7.24 (d, J = 1.7 Hz, 1H), 6.83 (dd, J = 8.0, 1.7, 1H), 5.66 (dq, J = 10.2, 1.4 Hz, 1H), 4.37 (t, J = 6.4 Hz, 2H), 3.34 – 3.21 (m, 1H), 2.36 (t, J = 6.4 Hz, 2H), 2.27 (s, 3H), 1.89 (d, J = 1.4 Hz, 3H), 1.39 – 1.15 (m, 3H), 1.14 – 1.01 (m, 2H), 0.96 (d, J = 6.6 Hz, 3H), 0.87 (t, J = 7.1 Hz, 3H), 0.80 (d, J = 6.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 150.4, 139.8, 136.3, 135.8, 128.0, 127.2, 126.7, 125.2, 60.7, 45.3, 40.0, 33.8, 31.3, 30.7, 21.4, 21.1, 20.8, 20.2, 19.8, 14.5.

HRMS calcd. for $[C_{21}H_{31}O_2S_2AsH]^+$ 455.1054, found 455.1010.

Synthesis of ***ent*-1**



***ent*-14**

ent-Bisenarsan (***ent*-1**)

Ester ***ent*-14** (47 mg, 0.10 mmol, 1 eq.) was dissolved in acetonitrile (2 mL) and 30% aqueous hydrogen peroxide (50 µL, 0.51 mmol, 5 eq.) was added to the obtained solution. The reaction mixture was allowed to stir at room temperature for 1 h, after which it was loaded directly onto a silica column. Flash column chromatography (100% CH_3CN → 10% water in CH_3CN, Rf ~0.2 in 10% water in CH_3CN) yielded a residue that was dissolved in DCM. The solution was filtered through a 0.2 µm PTFE syringe filter and the filtrate was concentrated *in vacuo* to yield *ent*-bisenarsan ***ent*-1** (24 mg, 67%) as a white solid.

^{1}H NMR (400 MHz, CD_2Cl_2) δ 5.93 (br. s, 2H), 5.67 (d, J = 10.1 Hz, 1H), 4.61 – 4.36 (m, 2H), 3.37 – 3.21 (m, 1H), 2.83 – 2.58 (m, 2H), 1.88 (s, 3H), 1.39 – 1.16 (m, 7H), 1.13 – 1.00 (m, 2H), 0.94 (d, J = 6.5 Hz, 3H), 0.86 (t, J = 7.1 Hz, 3H), 0.80 (d, J = 6.4 Hz, 3H).

^{1}H NMR (400 MHz, CD_3OD) δ 5.71 (ddq, J = 20.0, 10.2, 1.4 Hz, 1H), 4.50 (dt, J = 12.5, 6.8 Hz, 2H), 3.42 – 3.33 (m, 1H), 2.98 (t, J = 6.3 Hz, 1H), 2.59 (t, J = 7.3 Hz, 1H), 1.92 (dd, J = 5.8, 1.5 Hz, 3H), 1.40 – 1.17 (m, 3H), 1.15 – 1.01 (m, 2H), 0.96 (dd, J = 6.6, 2.9 Hz, 3H), 0.88 (t, J = 7.1 Hz, 3H), 0.83 (dd, J = 6.5, 2.2 Hz, 3H).

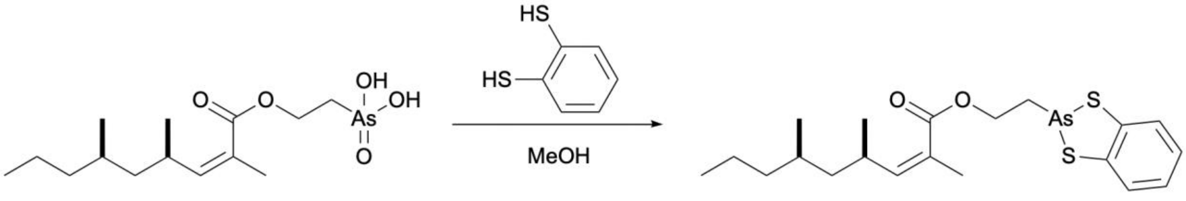
^{13}C NMR (151 MHz, CD_3OD) δ 168.8, 168.4, 152.0, 151.0, 126.8, 126.3, 59.2, 58.2, 46.3, 46.2, 41.14, 41.11, 32.5, 32.13, 32.11, 31.80, 31.78, 21.5, 21.4, 21.1, 20.91, 20.85, 20.0, 14.7.

HRMS calcd. for $[C_{14}H_{27}AsO_5H]^+$ 351.1147, found 351.1150.

$[\alpha]_{589}^{20}$ = +15.8° (c = 0.50, CH_2Cl_2).

Determination of absolute stereochemistry

Synthesis of **22** and ent-**22**

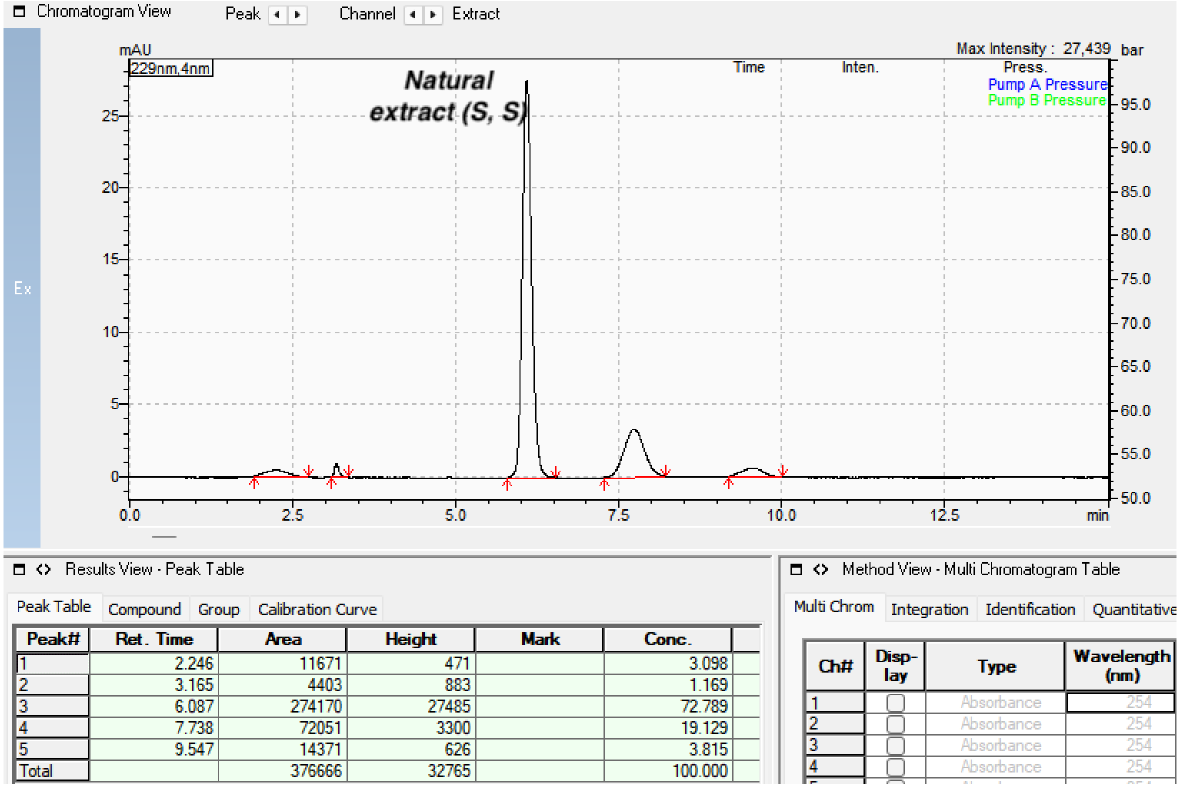


1 or ***ent*-1**

22 or ***ent*-22**

To a solution of **1** or ***ent*-1** (50 µg, 143 nmol, 1 eq.) in methanol (100 µl) was added from a stock solution benzene-1,2-dithiol (102 µg, 714 nmol, 5 eq.) in methanol (10 µl) and the mixture was stirred at room temperature for 24 h. The solution was concentrated *in vacuo*, the residue was dissolved in heptane (~ 1 mL), the obtained solution was filtered through a 0.2 µm PTFE syringe filter and used for chiral HPLC without further purification.

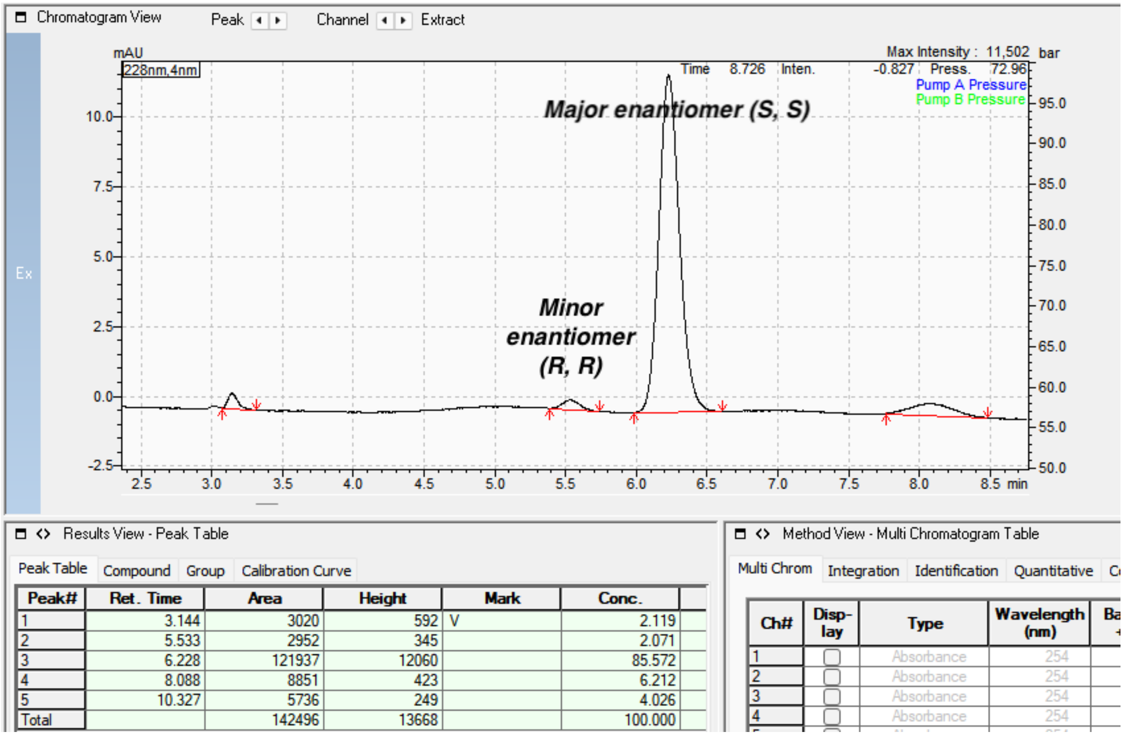
The chiral HPLC analysis of **22** and ***ent*-22** was performed using a Shimadzu LC-20 series with a photodiode array detector, Chiralpak AD-H column, n-heptane/i-PrOH: 99.5 : 0.5 as mobile phase, flow rate of 1 mL/min and UV detection at 228 nm. The results are presented in Figures S1-S4. The enantiomeric purity of the synthesized Bisenarsan enantiomers could also be determined using its functionalisation as **22** and ***ent*-22** by integrating the corresponding peaks in the chromatogram (e.r. = 98:2 for **22** and 95:5 for ***ent*-22**). The chromatograms, along with the peak tables are presented in Figures S2 and S3.



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	2.246	11671	471		3.098
2	3.165	4403	883		1.169
3	6.087	274170	27485		72.789
4	7.738	72051	3300		19.129
5	9.547	14371	626		3.815
Total		376666	32765		100.000

Ch#	Disp-lay	Type	Wavelength (nm)
1	☐	Absorbance	254
2	☐	Absorbance	254
3	☐	Absorbance	254
4	☐	Absorbance	254

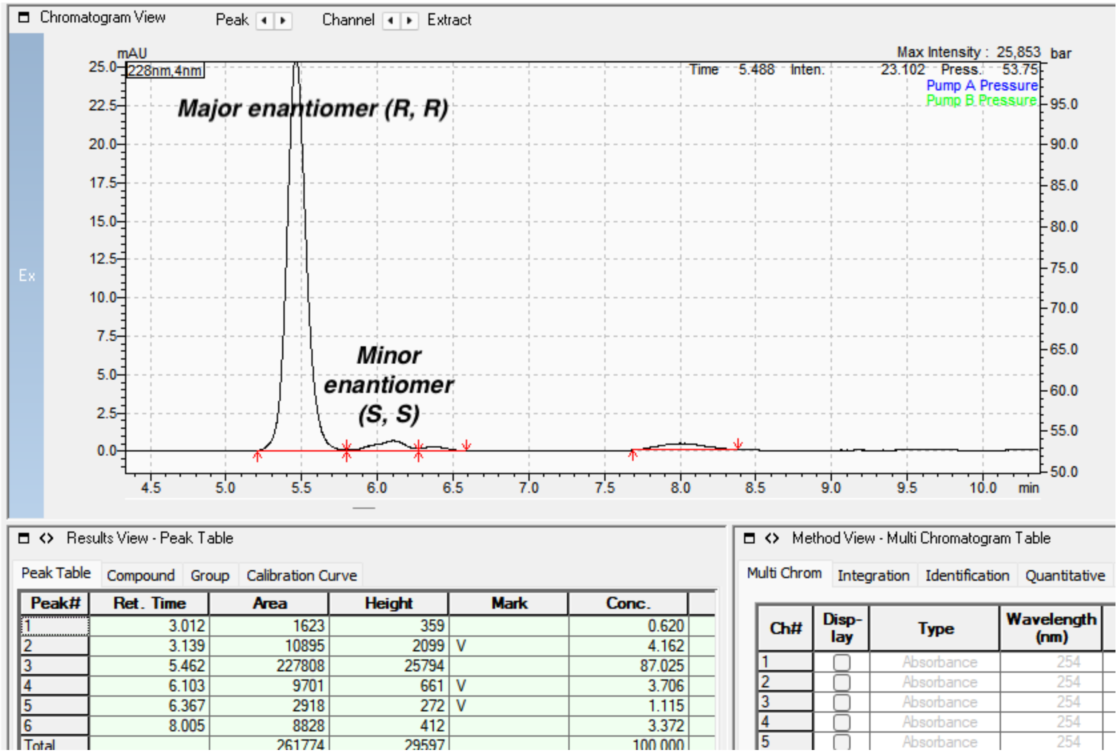
Figure S1. The chromatogram of **22** derived from natural bisenarsan



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	3.144	3020	592	V	2.119
2	5.533	2952	345		2.071
3	6.228	121937	12060		85.572
4	8.088	8851	423		6.212
5	10.327	5736	249		4.026
Total		142496	13668		100.000

Ch#	Disp-lay	Type	Wavelength (nm)
1	☐	Absorbance	254
2	☐	Absorbance	254
3	☐	Absorbance	254
4	☐	Absorbance	254

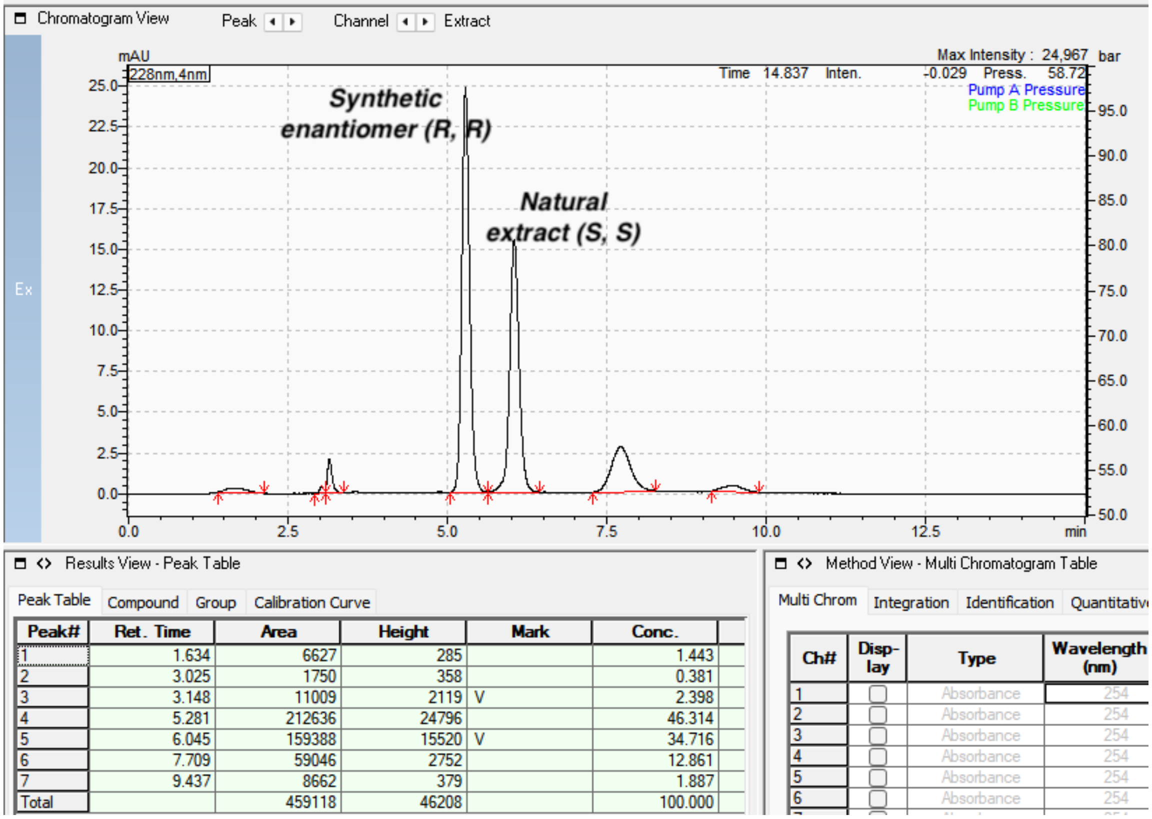
Figure S2. Determination of enantiomeric purity of synthetic **22**



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	3.012	1623	359		0.620
2	3.139	10895	2099	V	4.162
3	5.462	227808	25794		87.025
4	6.103	9701	661	V	3.706
5	6.367	2918	272	V	1.115
6	8.005	8828	412		3.372
Total		261774	29597		100.000

Ch#	Disp-lay	Type	Wavelength (nm)
1	☐	Absorbance	254
2	☐	Absorbance	254
3	☐	Absorbance	254
4	☐	Absorbance	254
5	☐	Absorbance	254

Figure S3. Determination of enantiomeric purity of synthetic ***ent*-22**

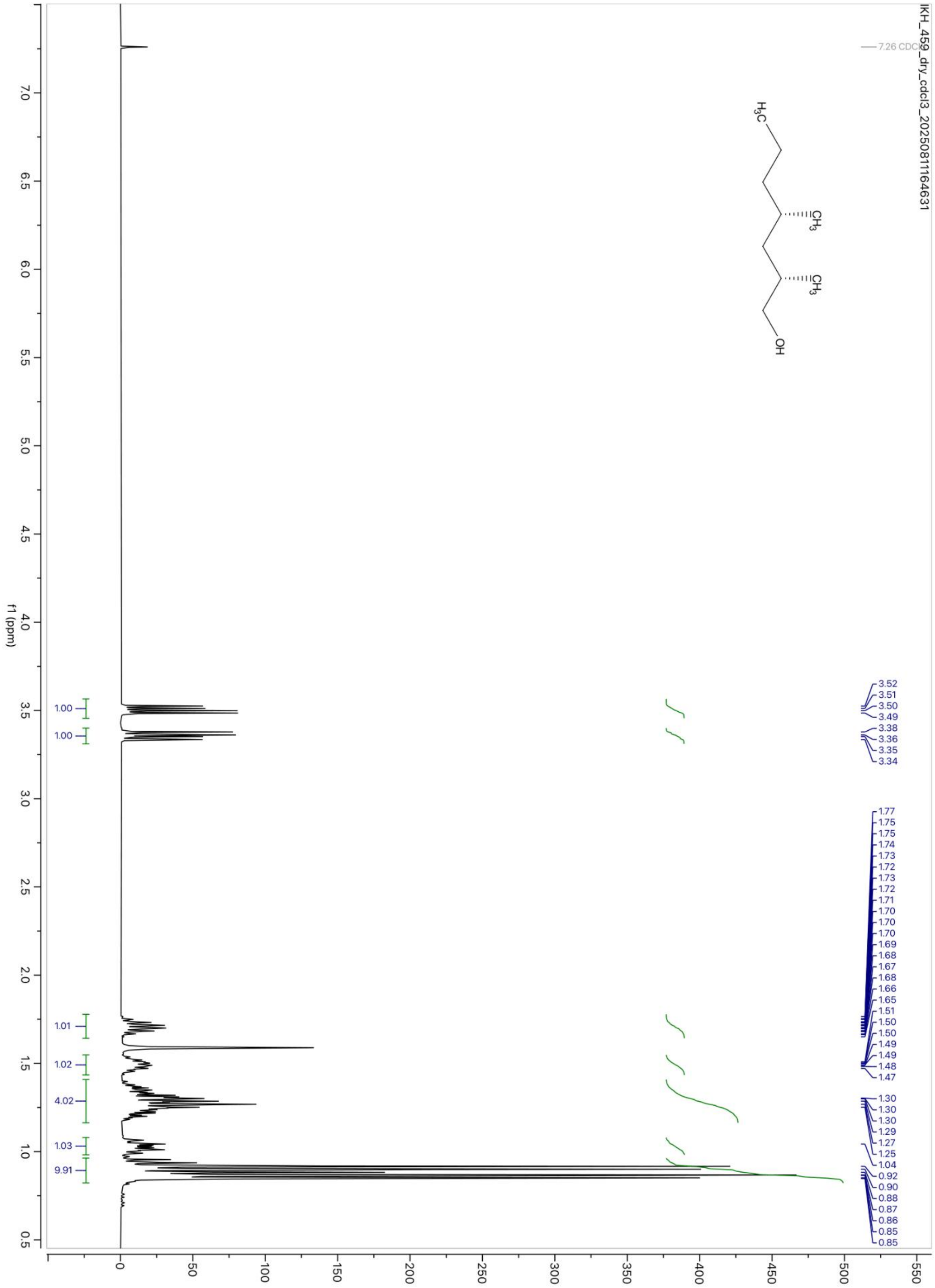


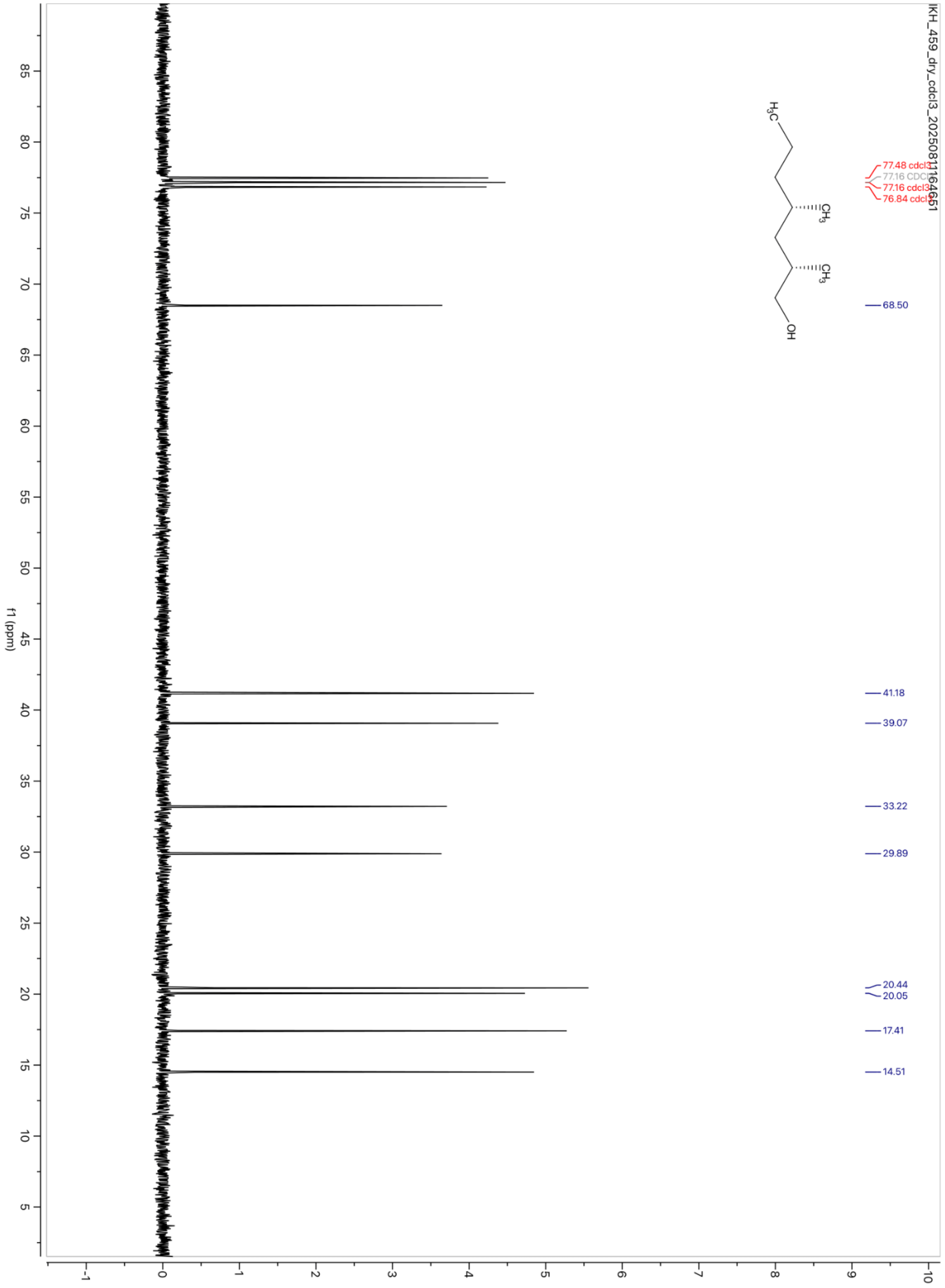
Peak#	Ret. Time	Area	Height	Mark	Conc.
1	1.634	6627	285		1.443
2	3.025	1750	358		0.381
3	3.148	11009	2119	V	2.398
4	5.281	212636	24796		46.314
5	6.045	159388	15520	V	34.716
6	7.709	59046	2752		12.861
7	9.437	8662	379		1.887
Total		459118	46208		100.000

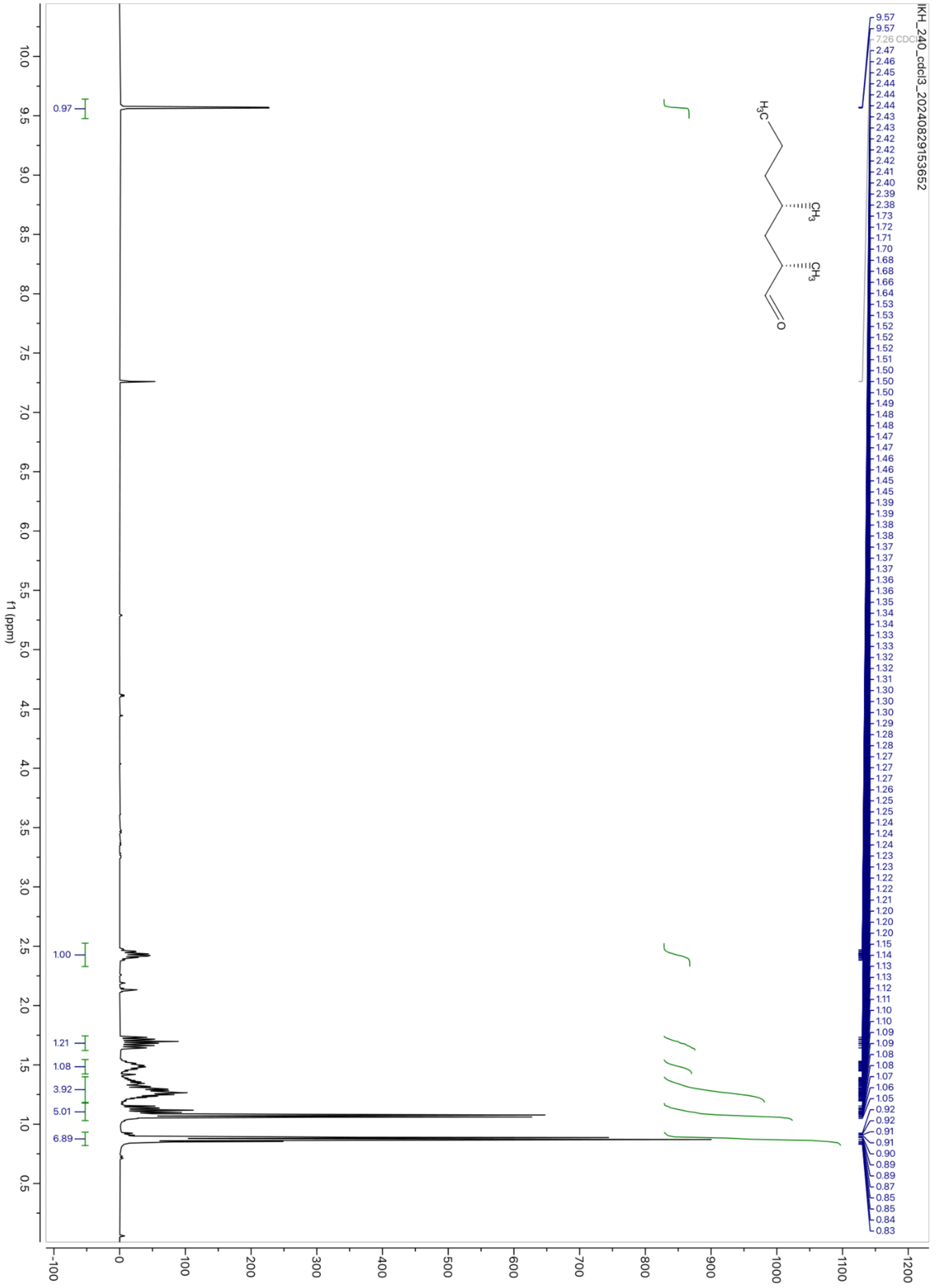
Ch#	Disp-lay	Type	Wavelength (nm)
1	☐	Absorbance	254
2	☐	Absorbance	254
3	☐	Absorbance	254
4	☐	Absorbance	254
5	☐	Absorbance	254
6	☐	Absorbance	254

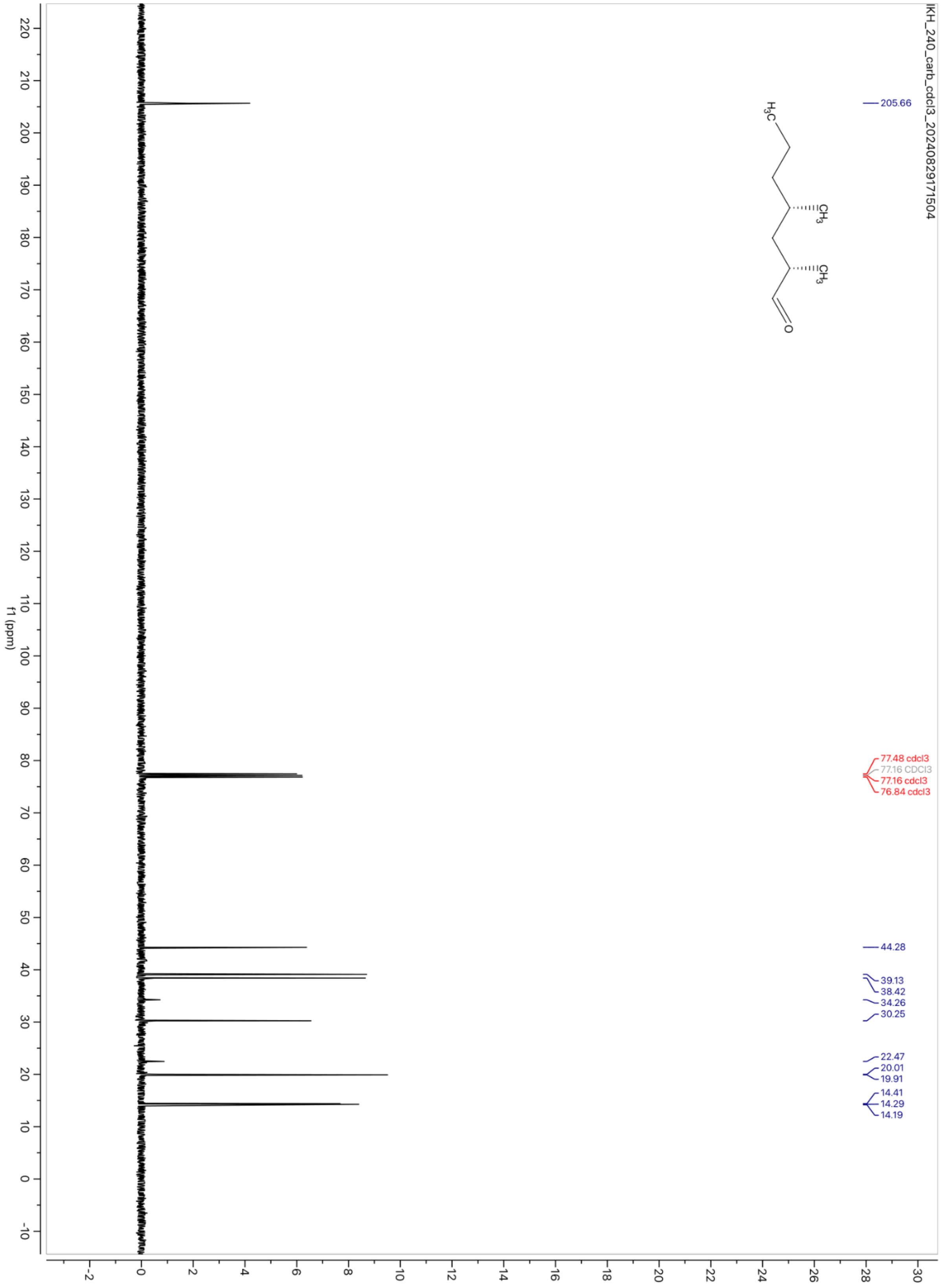
Figure S4. Comparison of **22** derived from natural bisenarsan and synthetic ***ent*-22**

NMR spectra

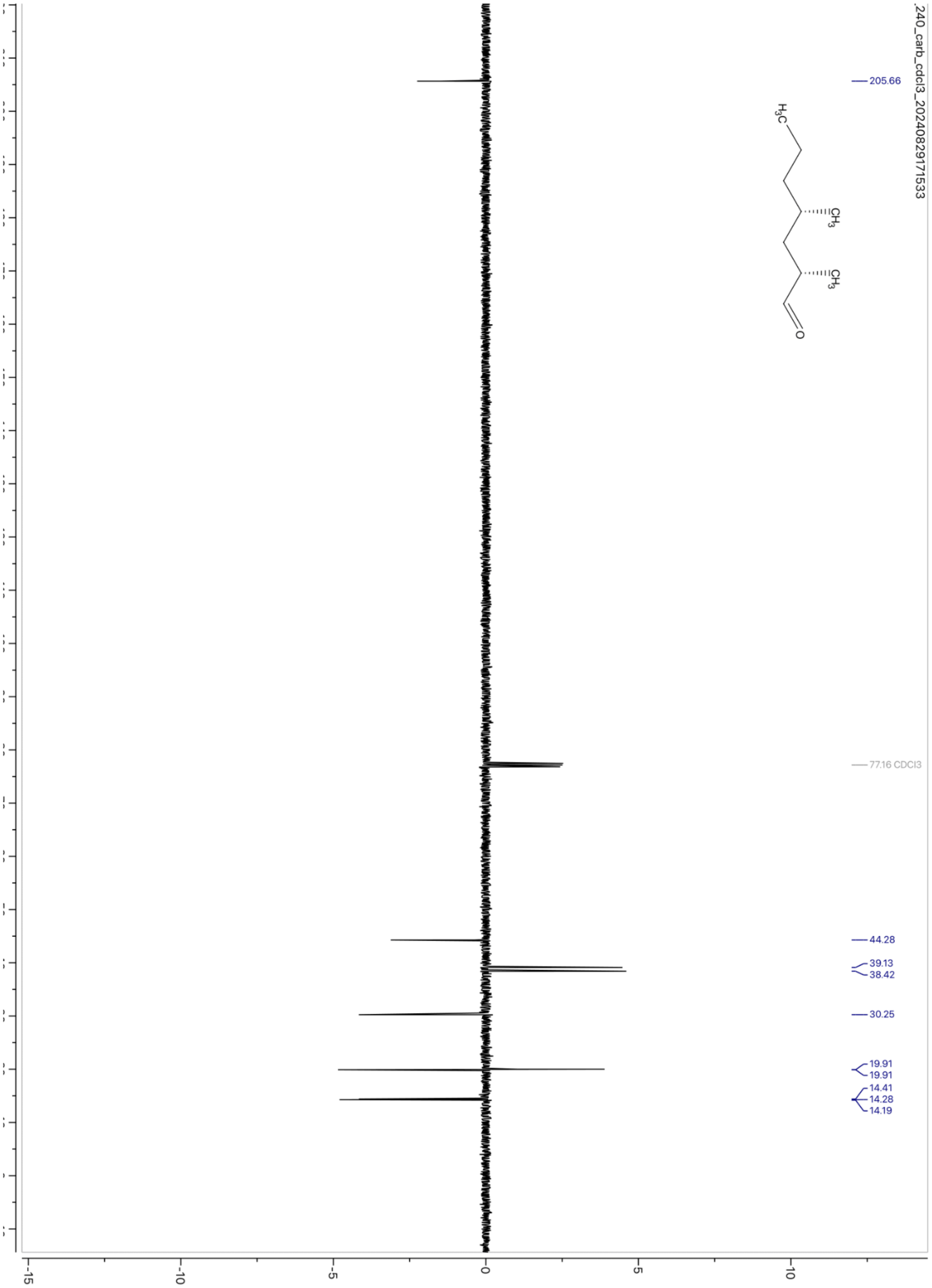

IKH_459_dry_cdcl3_20250811164631
7.26 CDCl3
H3C
CH3
CH3
OH
3.52
3.51
3.50
3.49
3.38
3.36
3.35
3.34
1.77
1.75
1.75
1.74
1.73
1.72
1.73
1.72
1.71
1.70
1.70
1.70
1.69
1.68
1.67
1.68
1.66
1.65
1.51
1.50
1.50
1.49
1.49
1.48
1.47
1.30
1.30
1.30
1.29
1.27
1.25
1.04
0.92
0.90
0.88
0.87
0.86
0.85
0.85
1.00
1.00
1.01
1.02
4.02
1.03
9.91
f1 (ppm)
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
50
100
150
200
250
300
350
400
450
500
550

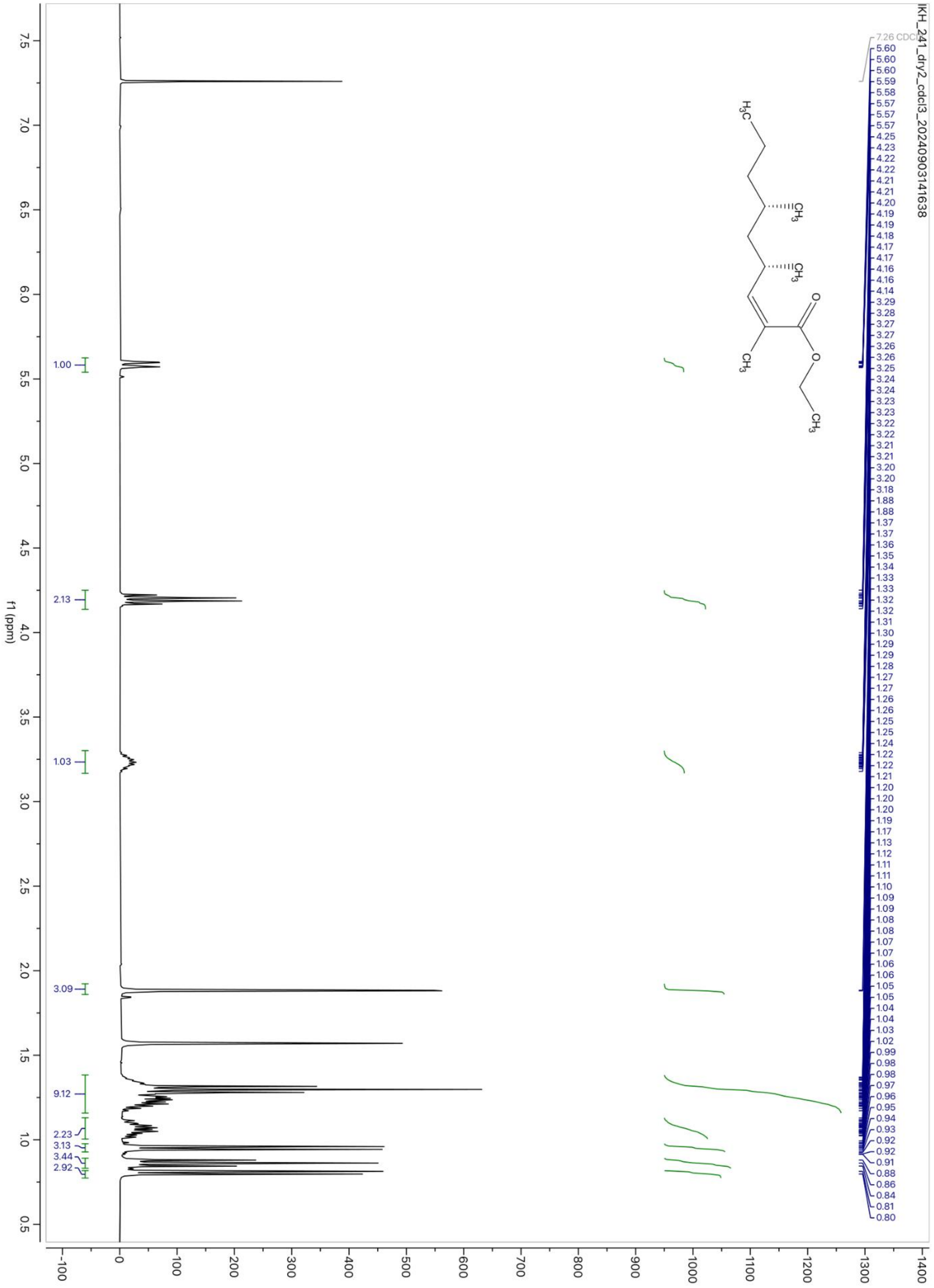

IKH_459_dry_cdcl3_20250811164651
H3C
CH3
CH3
OH
77.48 cdcl3
77.16 CDCl3
77.16 cdcl3
76.84 cdcl3
68.50
41.18
39.07
33.22
29.89
20.44
20.05
17.41
14.51
f1 (ppm)
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
-1
0
1
2
3
4
5
6
7
8
9
10

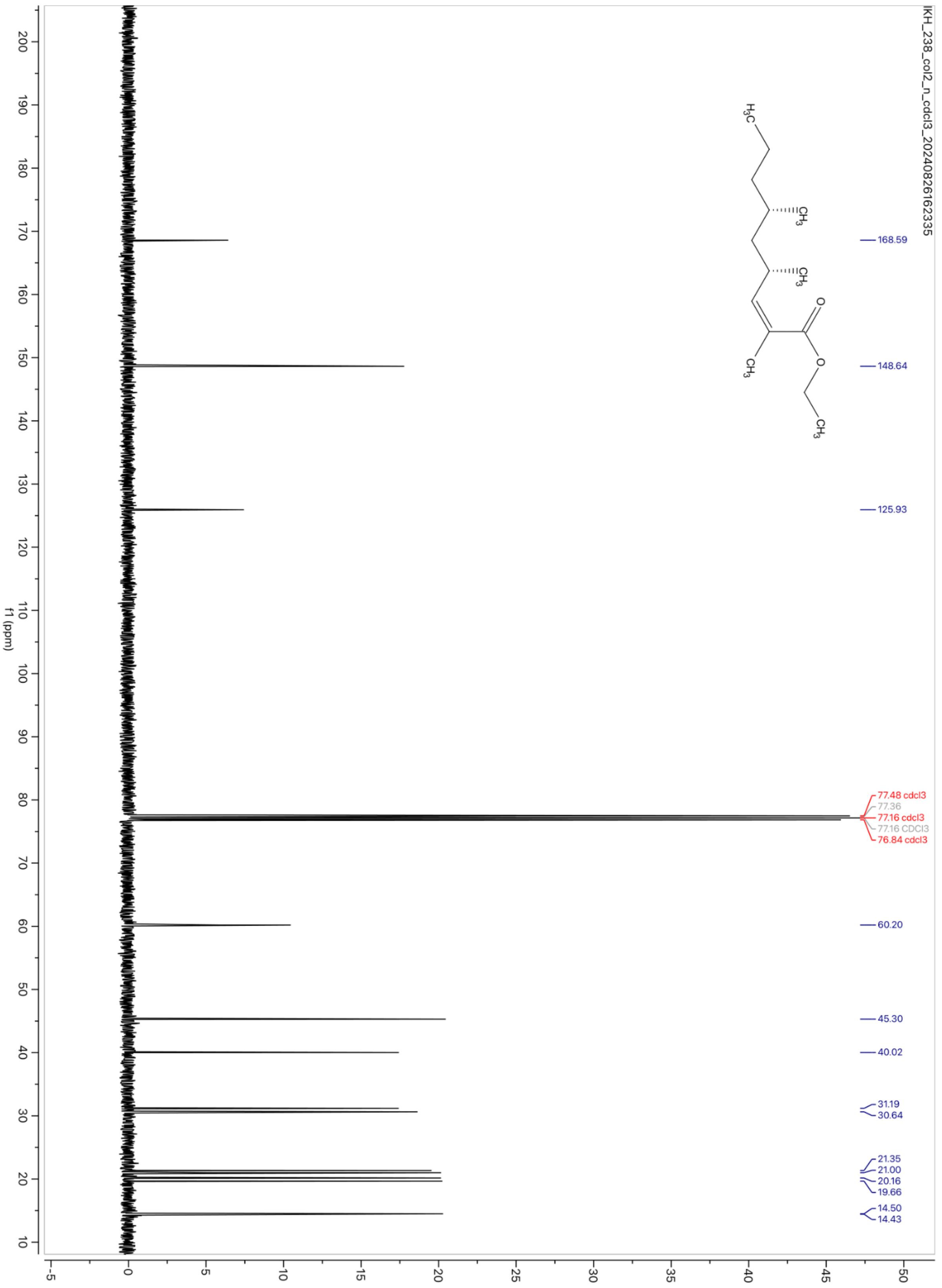

IKH_240_cdcl3_20240829153652
9.57
9.57
7.26 CDCl3
2.47
2.46
2.45
2.44
2.44
2.44
2.43
2.43
2.42
2.42
2.42
2.41
2.40
2.39
2.38
1.73
1.72
1.71
1.70
1.68
1.68
1.66
1.64
1.53
1.53
1.52
1.52
1.52
1.51
1.50
1.50
1.50
1.49
1.48
1.48
1.47
1.47
1.46
1.46
1.45
1.45
1.39
1.39
1.38
1.38
1.37
1.37
1.37
1.36
1.36
1.35
1.34
1.34
1.33
1.33
1.32
1.32
1.31
1.30
1.30
1.30
1.29
1.28
1.28
1.27
1.27
1.27
1.26
1.25
1.25
1.24
1.24
1.24
1.23
1.23
1.22
1.22
1.21
1.20
1.20
1.20
1.15
1.14
1.13
1.13
1.12
1.11
1.10
1.10
1.09
1.09
1.08
1.08
1.07
1.06
1.05
0.92
0.92
0.91
0.91
0.91
0.90
0.89
0.89
0.87
0.85
0.85
0.84
0.83
H3C
CH3
CH3
O
0.97
1.00
1.21
1.08
3.92
5.01
6.89
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
-100
0
100
200
300
400
500
600
700
800
900
1000
1100
1200


IKH_240_carb_cdcl3_20240829171504
205.66
77.48 cdcl3
77.16 CDCl3
77.16 cdcl3
76.84 cdcl3
44.28
39.13
38.42
34.26
30.25
22.47
20.01
19.91
14.41
14.29
14.19
H3C
CH3
CH3
O
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-2
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30

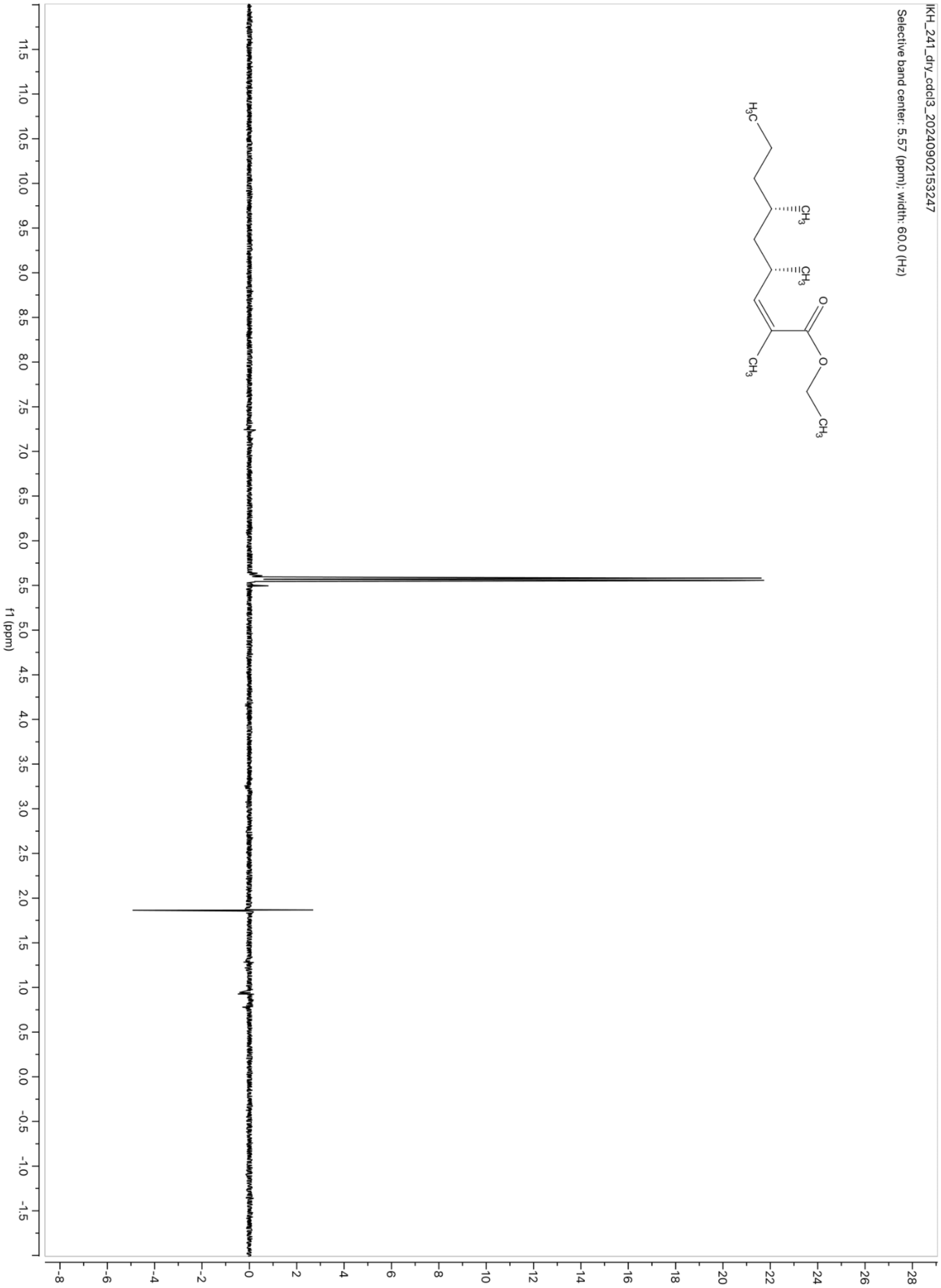
APT spectrum of ***5***



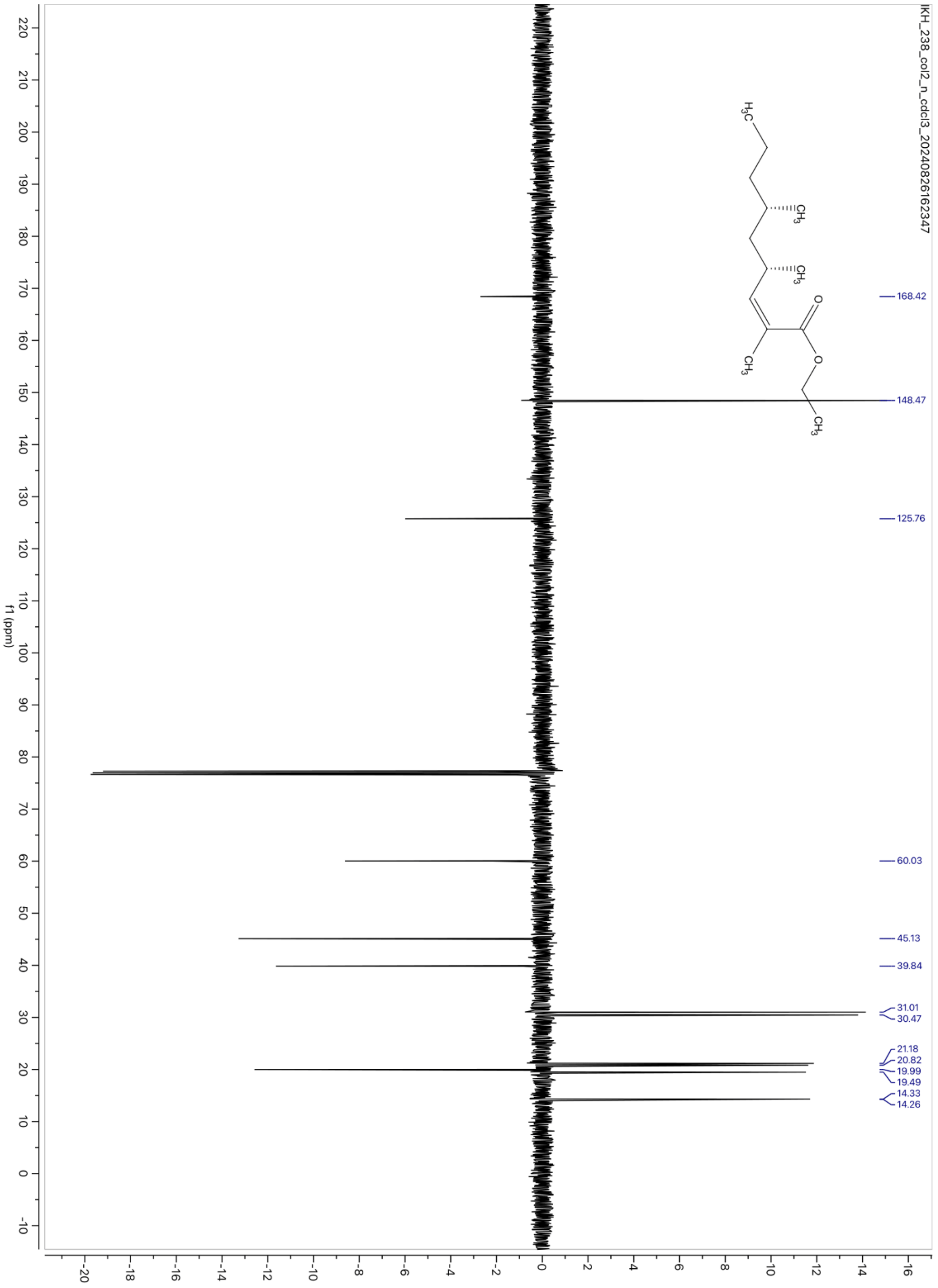

IKH_241_dry2_cdcl3_20240903141638
7.26 CDCl3
5.60
5.60
5.60
5.59
5.58
5.57
5.57
5.57
4.25
4.23
4.22
4.22
4.21
4.21
4.20
4.19
4.19
4.18
4.17
4.17
4.16
4.16
4.14
3.29
3.28
3.27
3.27
3.26
3.26
3.25
3.24
3.24
3.23
3.23
3.22
3.22
3.21
3.21
3.20
3.20
3.18
1.88
1.88
1.37
1.37
1.36
1.35
1.34
1.33
1.33
1.32
1.32
1.31
1.30
1.29
1.29
1.28
1.27
1.27
1.26
1.26
1.25
1.25
1.24
1.22
1.22
1.21
1.20
1.20
1.20
1.19
1.17
1.13
1.12
1.11
1.11
1.10
1.09
1.09
1.08
1.08
1.07
1.07
1.06
1.06
1.05
1.05
1.04
1.04
1.03
1.02
0.99
0.98
0.98
0.97
0.96
0.95
0.94
0.93
0.92
0.92
0.91
0.88
0.86
0.84
0.81
0.80
H3C
CH3
CH3
O
O
CH3
CH3
1.00
2.13
1.03
3.09
9.12
2.23
3.13
3.44
2.92
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
-100
0
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400

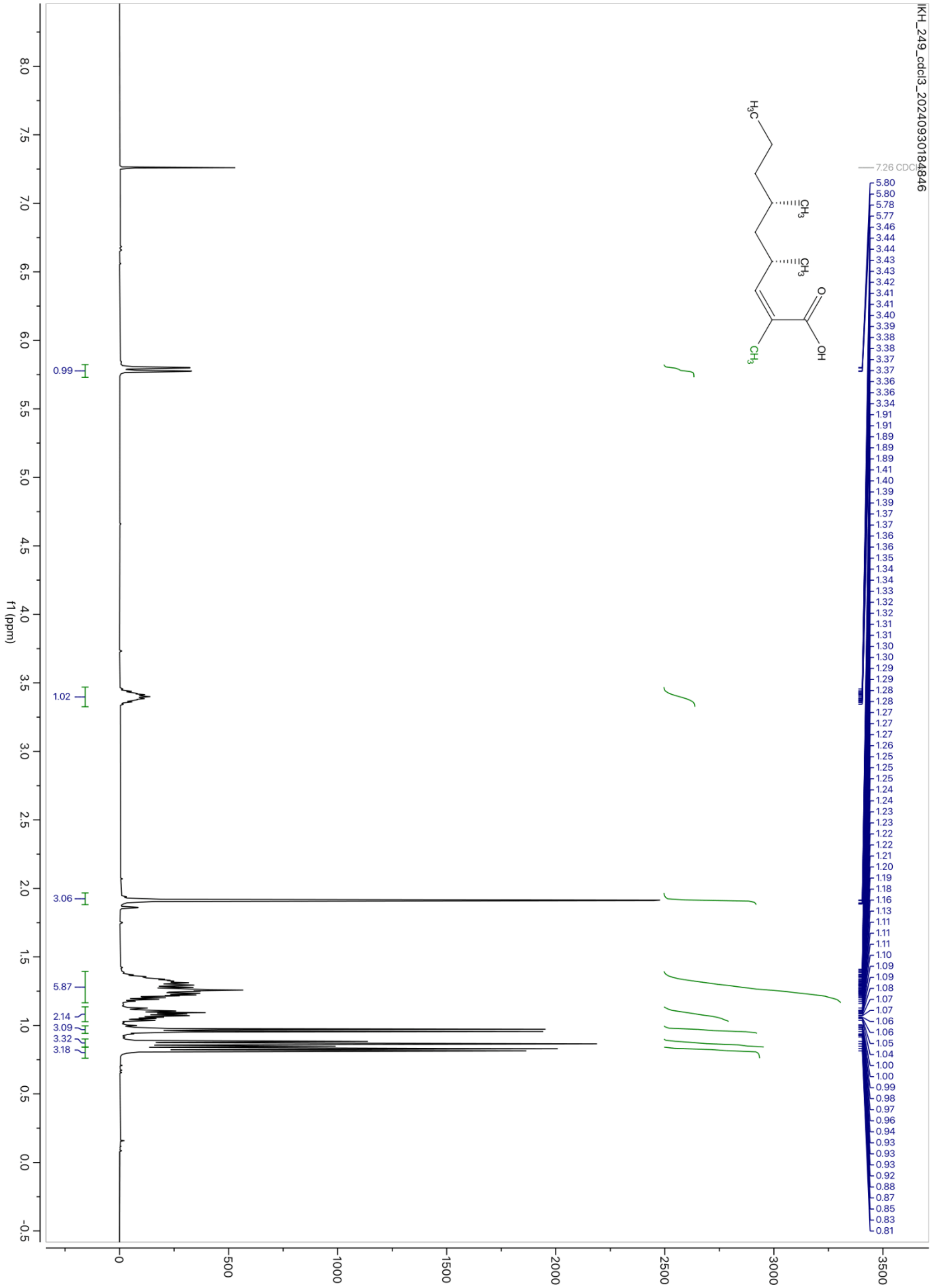

IKH_238_col2_n_cdcl3_20240826162335
168.59
148.64
125.93
77.48 cdcl3
77.36
77.16 cdcl3
77.16 CDCl3
76.84 cdcl3
60.20
45.30
40.02
31.19
30.64
21.35
21.00
20.16
19.66
14.50
14.43
H3C
CH3
CH3
O
O
CH3
CH3
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
-5
0
5
10
15
20
25
30
35
40
45
50

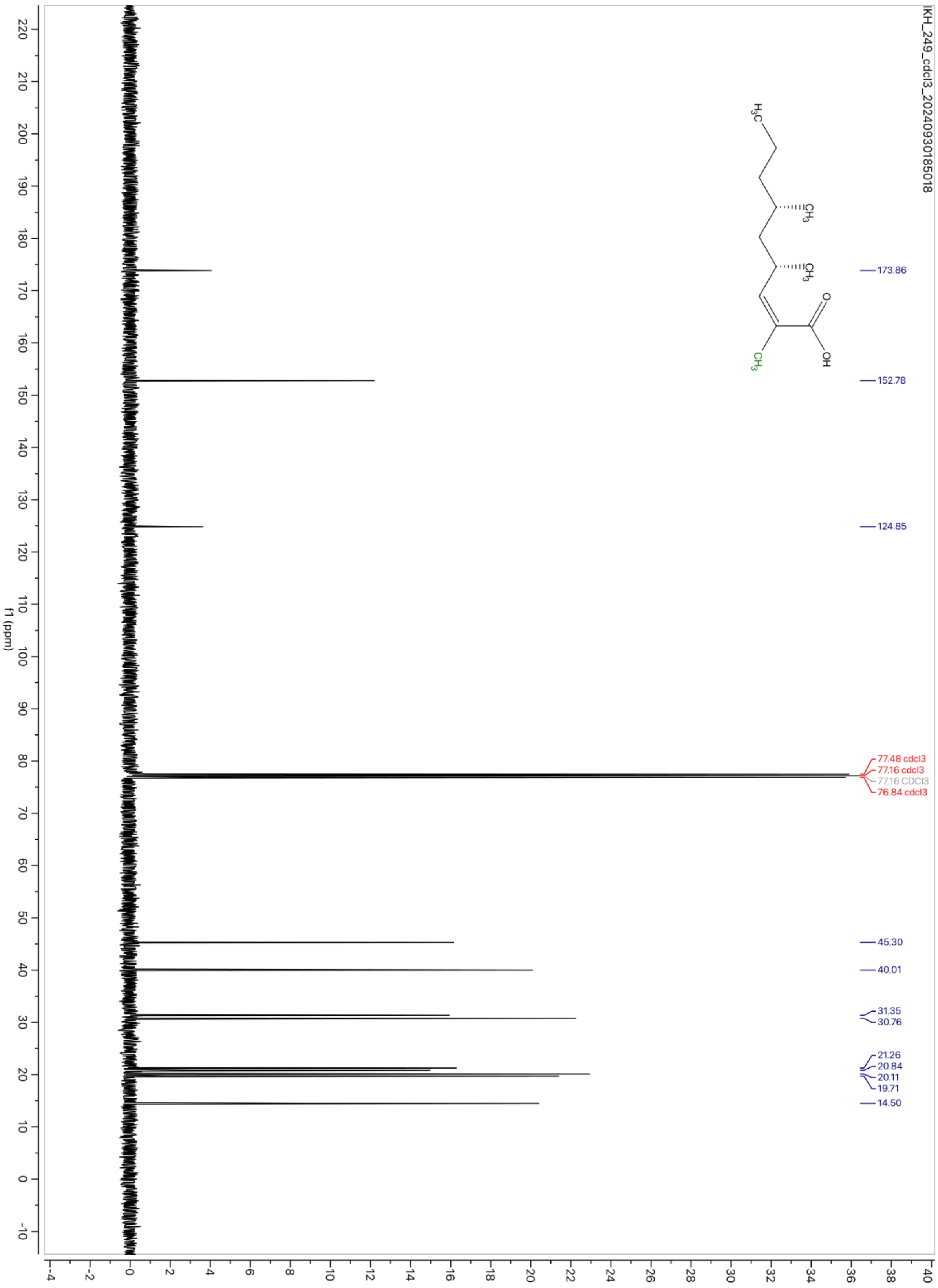
1D NOESY spectrum of ***2***



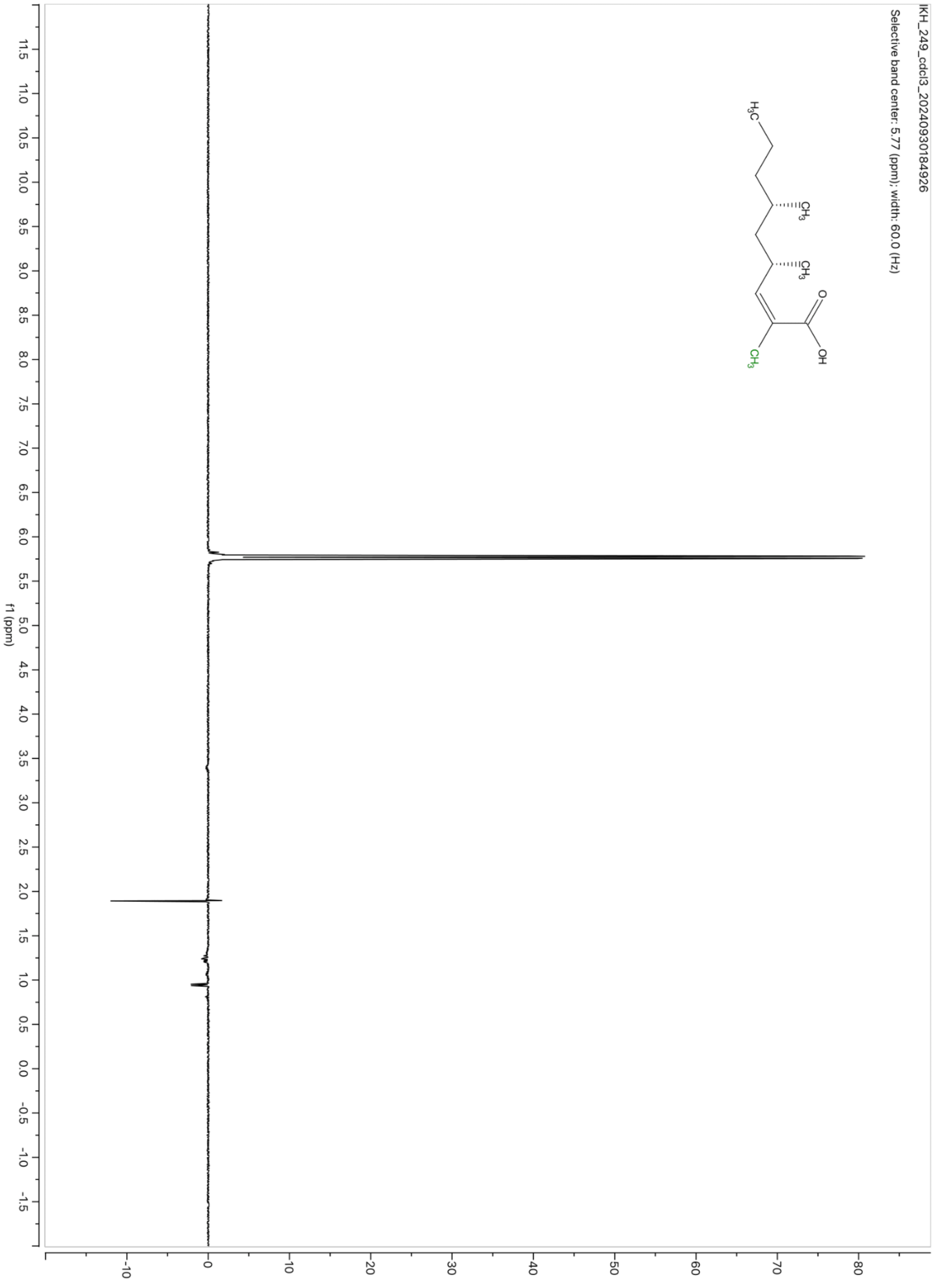
APT spectrum of ***2***

IKH_238_col2_n_cdcl3_20240826162347
H3C
CH3
CH3
O
O
CH3
CH3
168.42
148.47
125.76
60.03
45.13
39.84
31.01
30.47
21.18
20.82
19.99
19.49
14.33
14.26
f1 (ppm)

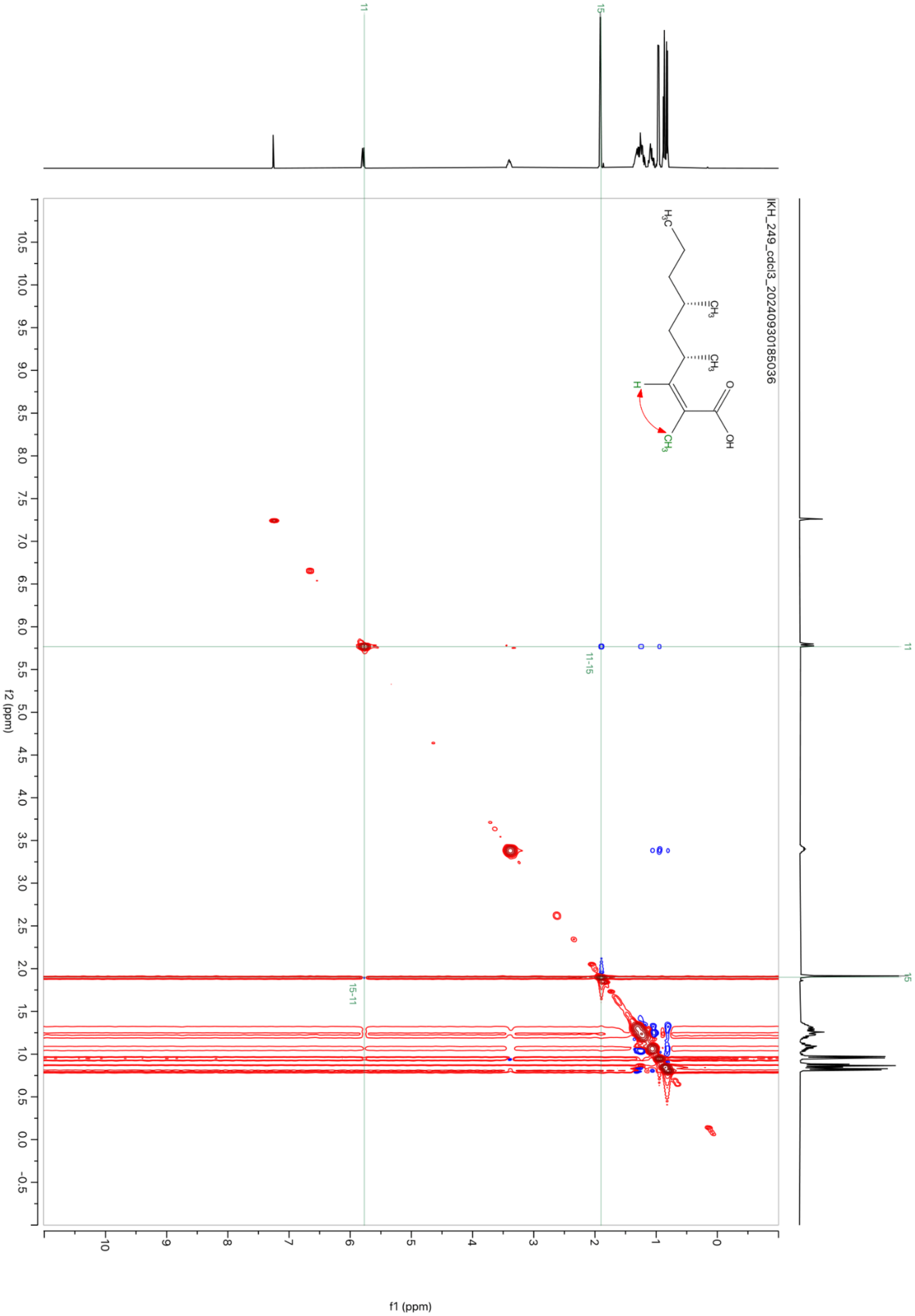

IKH_249_cdcl3_20240930184846
7.26 CDCl3
5.80
5.80
5.78
5.77
3.46
3.44
3.44
3.43
3.43
3.42
3.41
3.41
3.40
3.39
3.38
3.38
3.37
3.37
3.36
3.36
3.34
1.91
1.91
1.89
1.89
1.89
1.41
1.40
1.39
1.39
1.37
1.37
1.36
1.36
1.35
1.34
1.34
1.33
1.32
1.32
1.31
1.31
1.30
1.30
1.29
1.29
1.28
1.28
1.27
1.27
1.27
1.26
1.25
1.25
1.25
1.24
1.24
1.23
1.23
1.22
1.22
1.21
1.20
1.19
1.18
1.16
1.13
1.11
1.11
1.11
1.10
1.09
1.09
1.08
1.07
1.07
1.06
1.06
1.05
1.04
1.00
1.00
0.99
0.98
0.97
0.96
0.94
0.93
0.93
0.93
0.92
0.88
0.87
0.85
0.83
0.81
H3C
CH3
CH3
O
OH
CH3
0.99
1.02
3.06
5.87
2.14
3.09
3.32
3.18
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
0
500
1000
1500
2000
2500
3000
3500

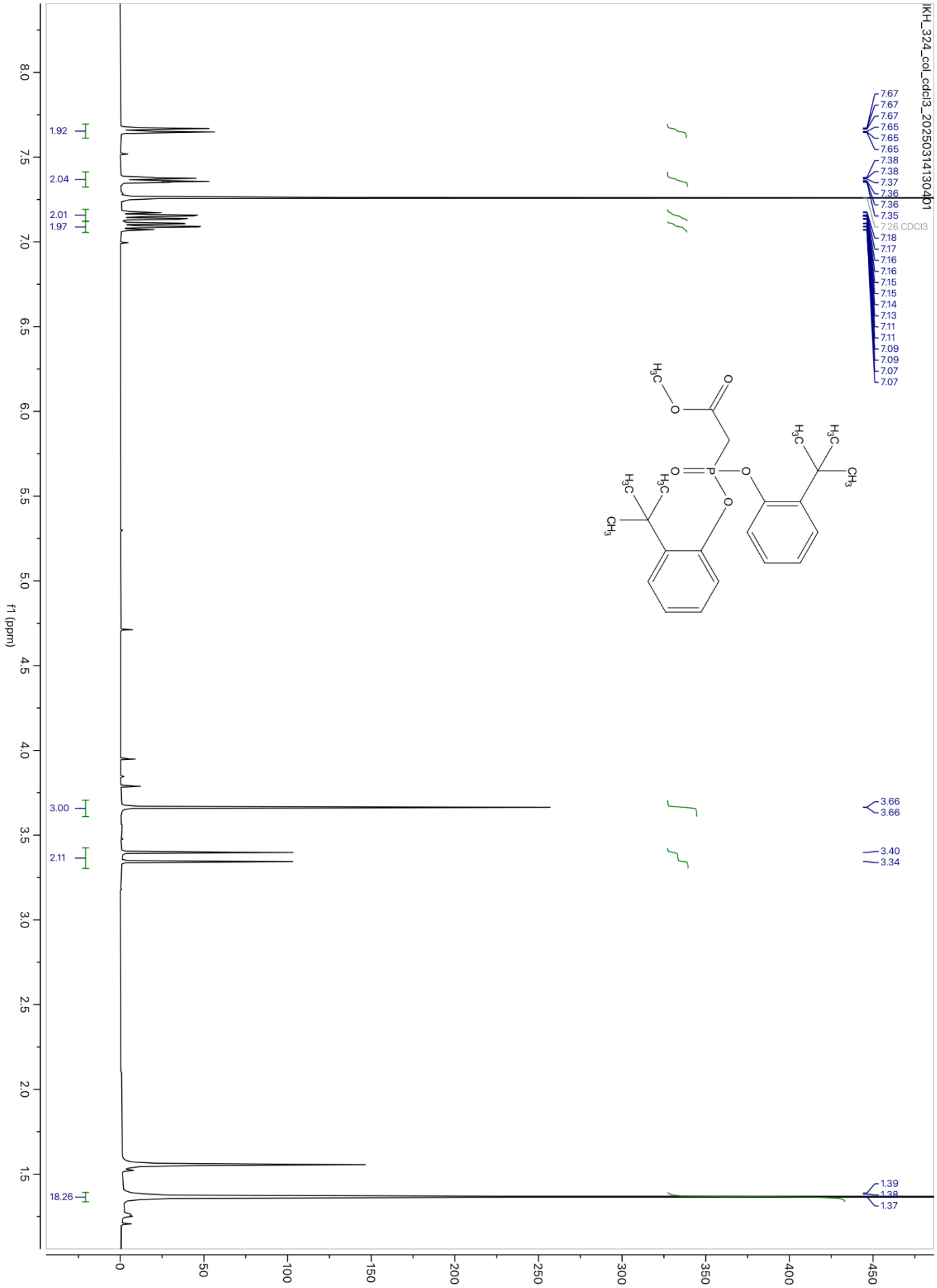

IKH_249_cdcl3_20240930185018
H_3C
CH_3
CH_3
O
OH
CH_3
173.86
152.78
124.85
77.48 cdcl3
77.16 cdcl3
77.16 CDCl3
76.84 cdcl3
45.30
40.01
31.35
30.76
21.26
20.84
20.11
19.71
14.50
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-4
-2
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
40

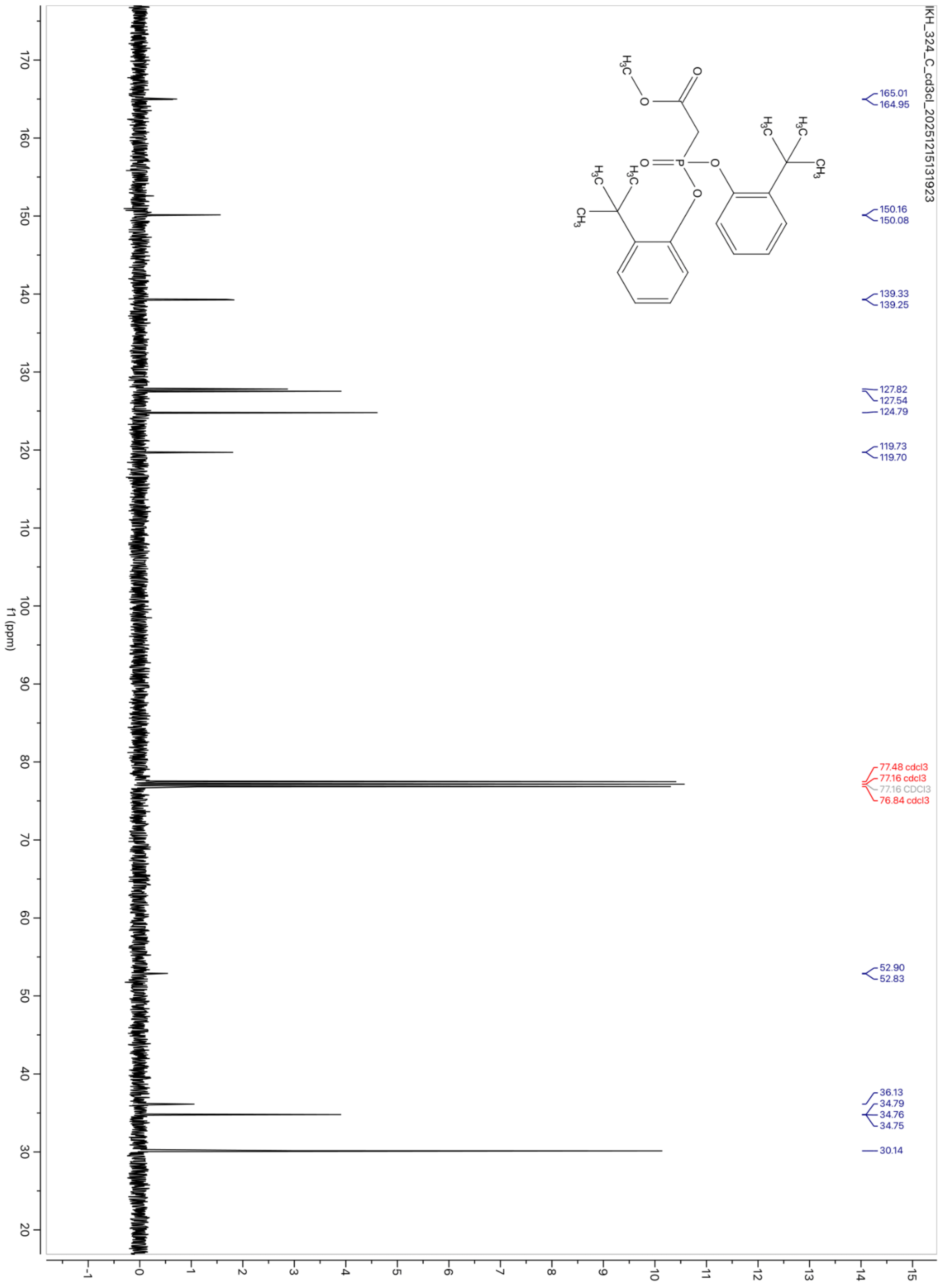
1D NOESY spectrum of ***7***

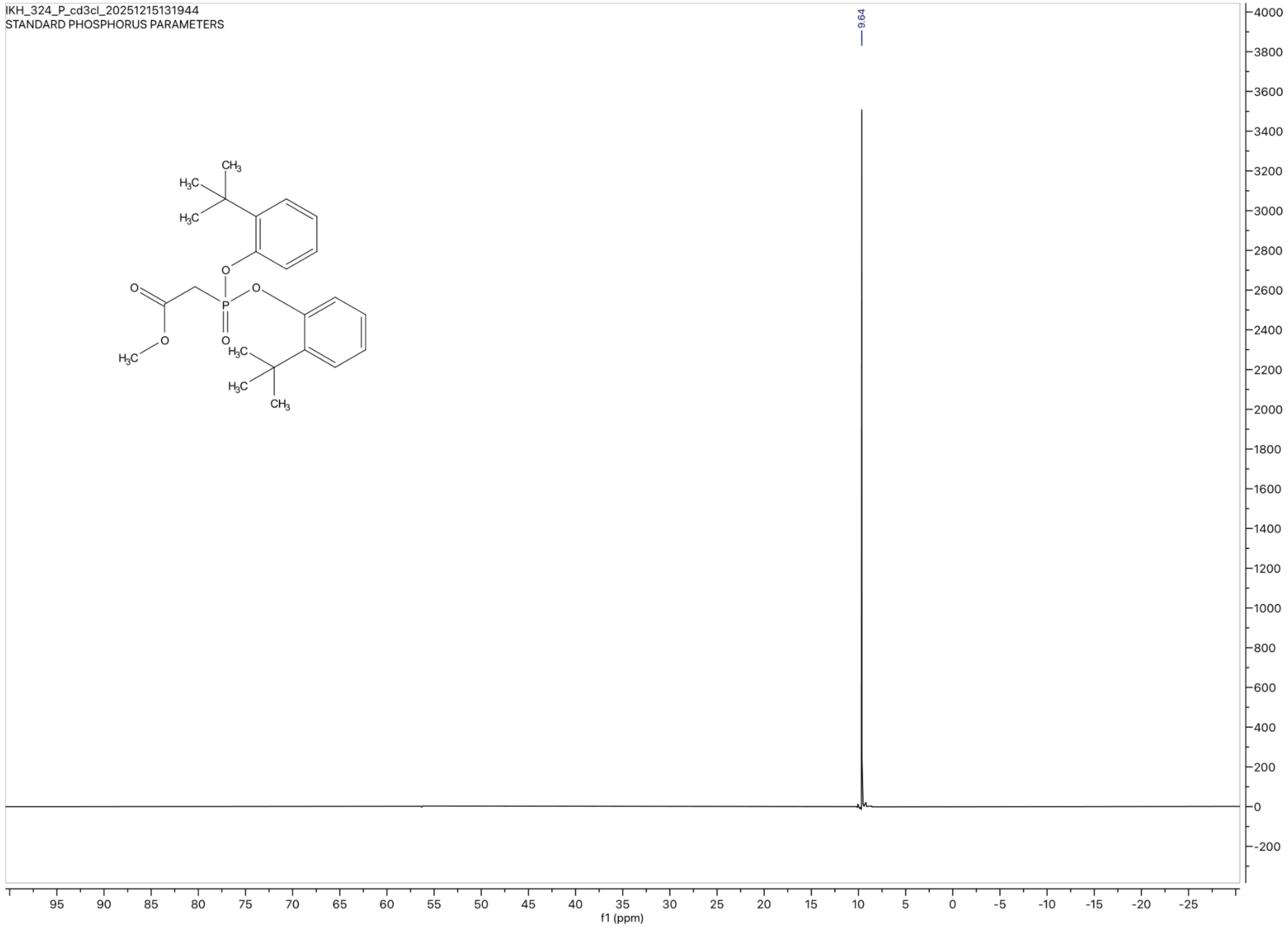


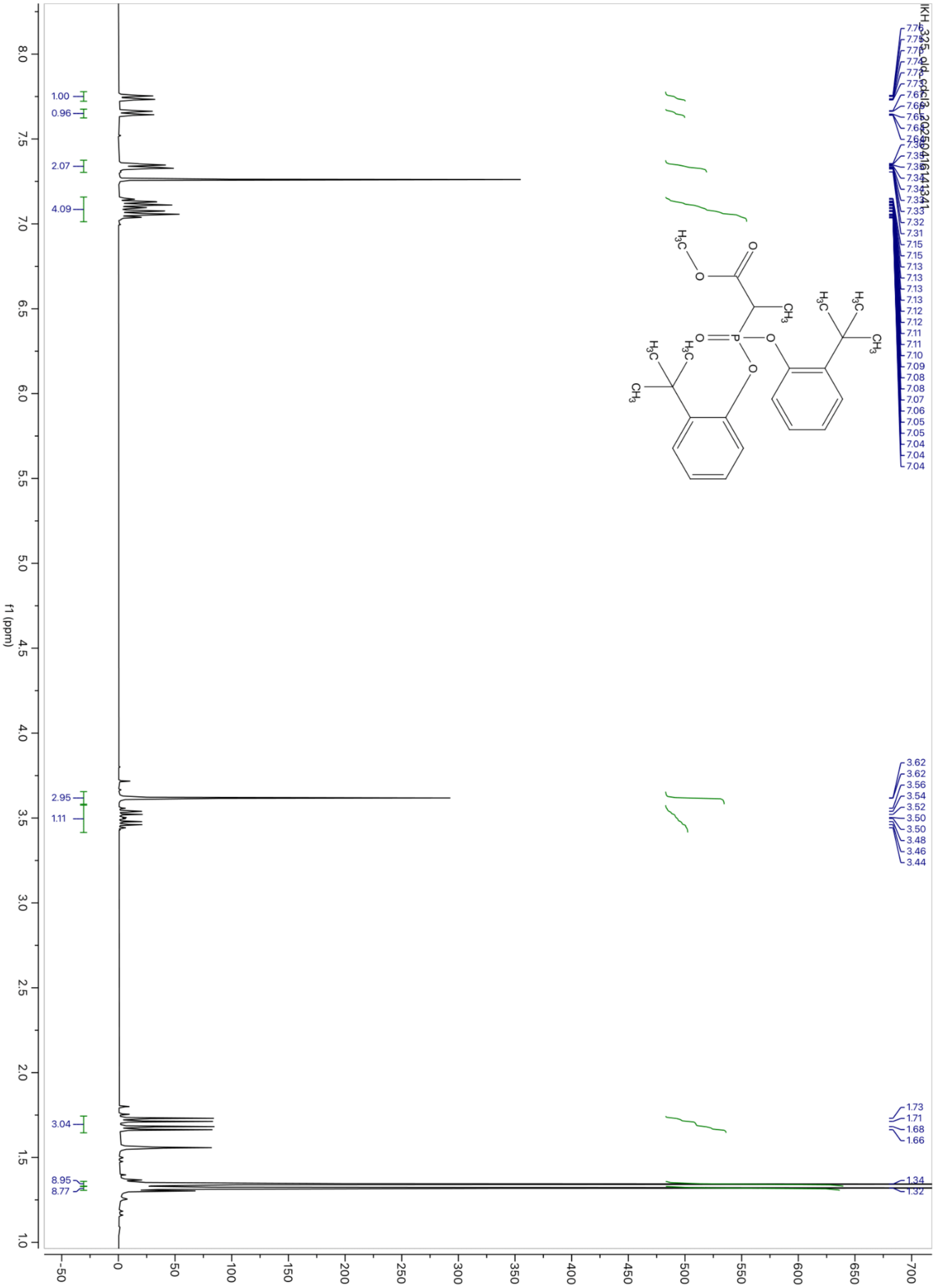
2D NOESY spectrum of ***7***

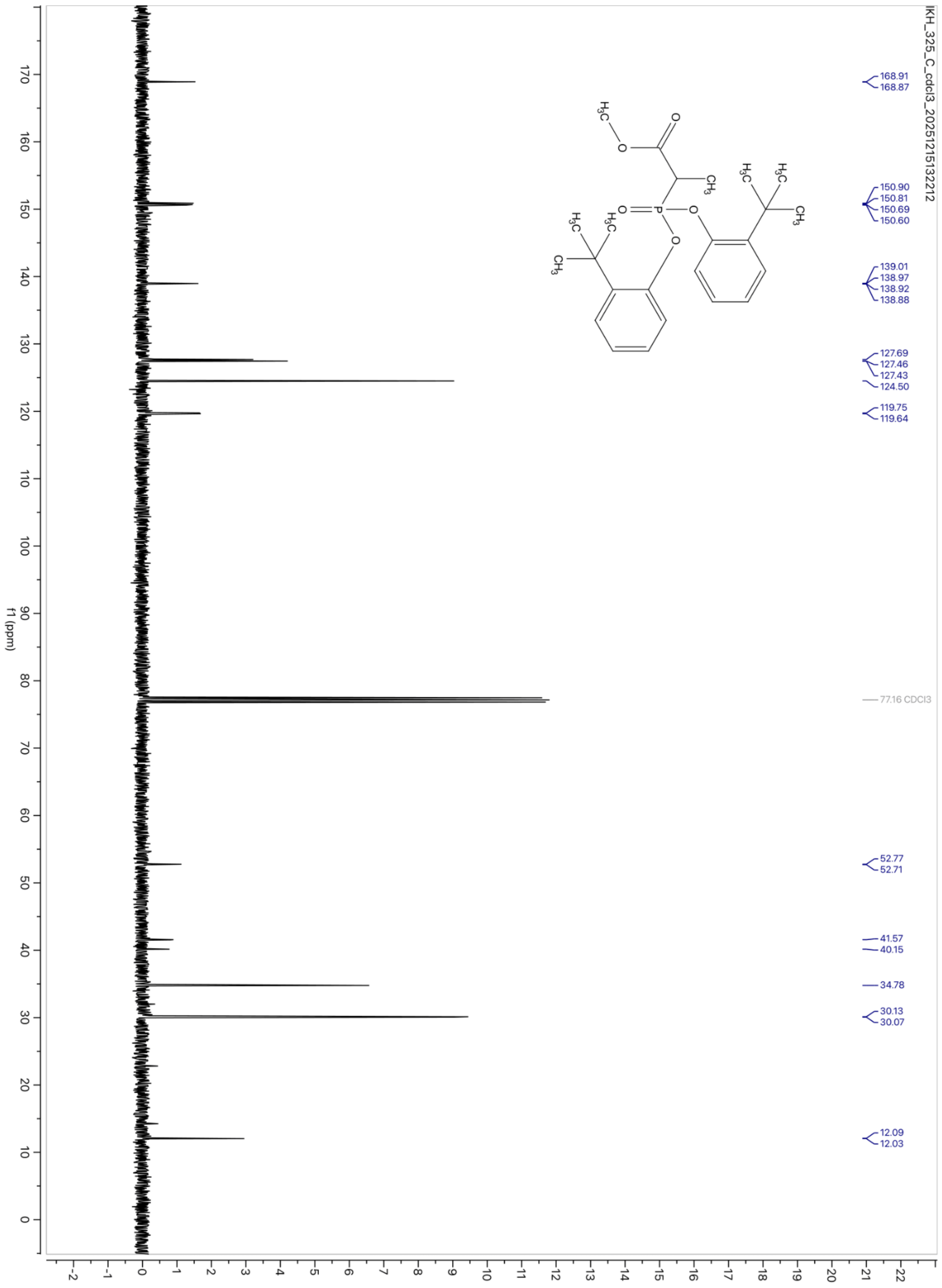



IKH_324_col_cdcl3_20250314130401
7.67
7.67
7.67
7.65
7.65
7.65
7.38
7.38
7.37
7.36
7.36
7.35
7.26 CDCl3
7.18
7.17
7.16
7.16
7.15
7.15
7.14
7.13
7.11
7.11
7.09
7.09
7.07
7.07
3.66
3.66
3.40
3.34
1.39
1.38
1.37
1.92
2.04
2.01
1.97
3.00
2.11
18.26
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
0
50
100
150
200
250
300
350
400
450
O
O
H3C
O
P
O
O
H3C
H3C
CH3
H3C
H3C
CH3

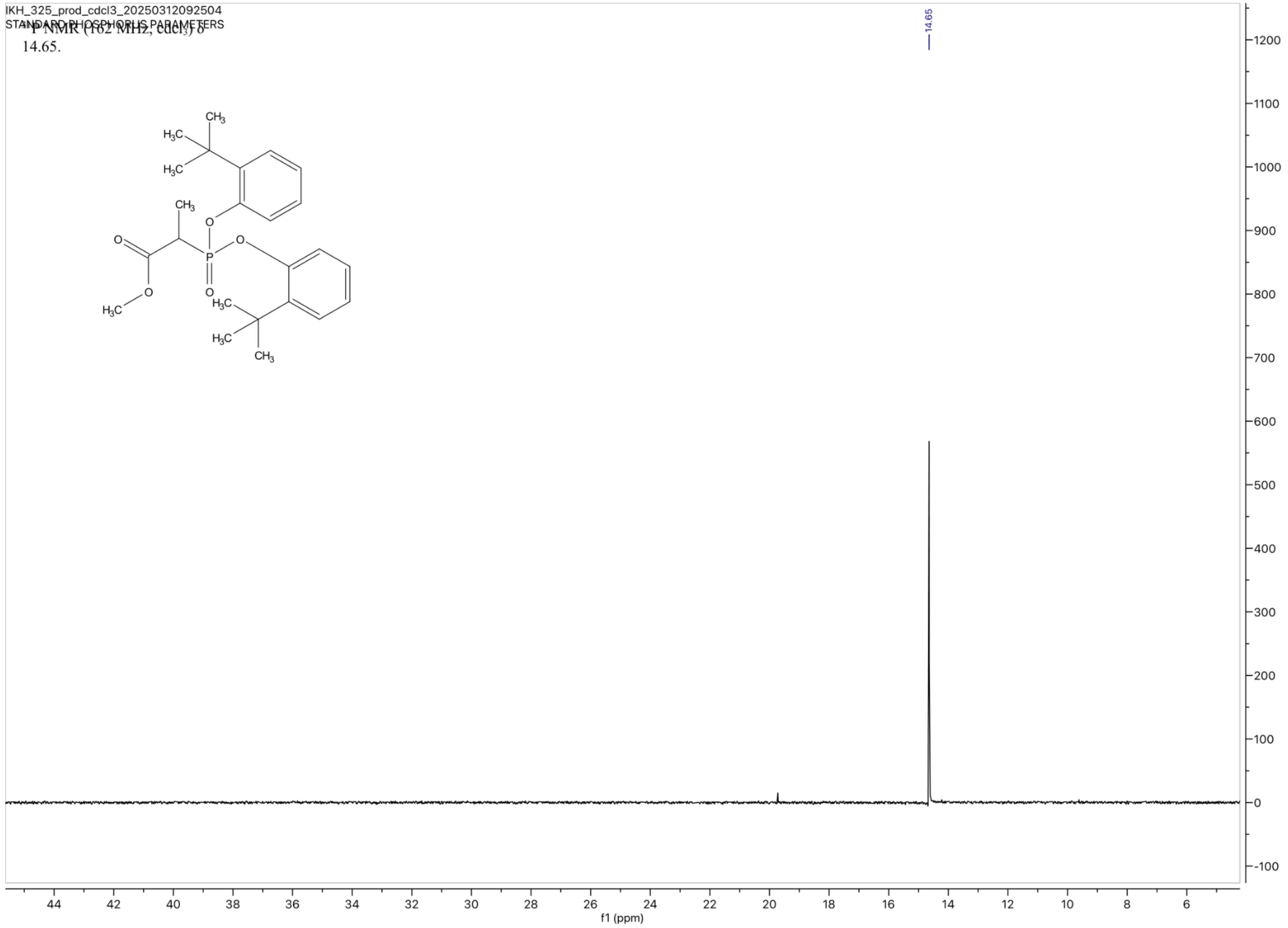

IKH_324_C_cd3cl_20251215131923
165.01
164.95
150.16
150.08
139.33
139.25
127.82
127.54
124.79
119.73
119.70
77.48 cdcl3
77.16 cdcl3
77.16 CDCl3
76.84 cdcl3
52.90
52.83
36.13
34.79
34.76
34.75
30.14
f1 (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
-1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
H_3C
O
O
P
CH_3
H_3C

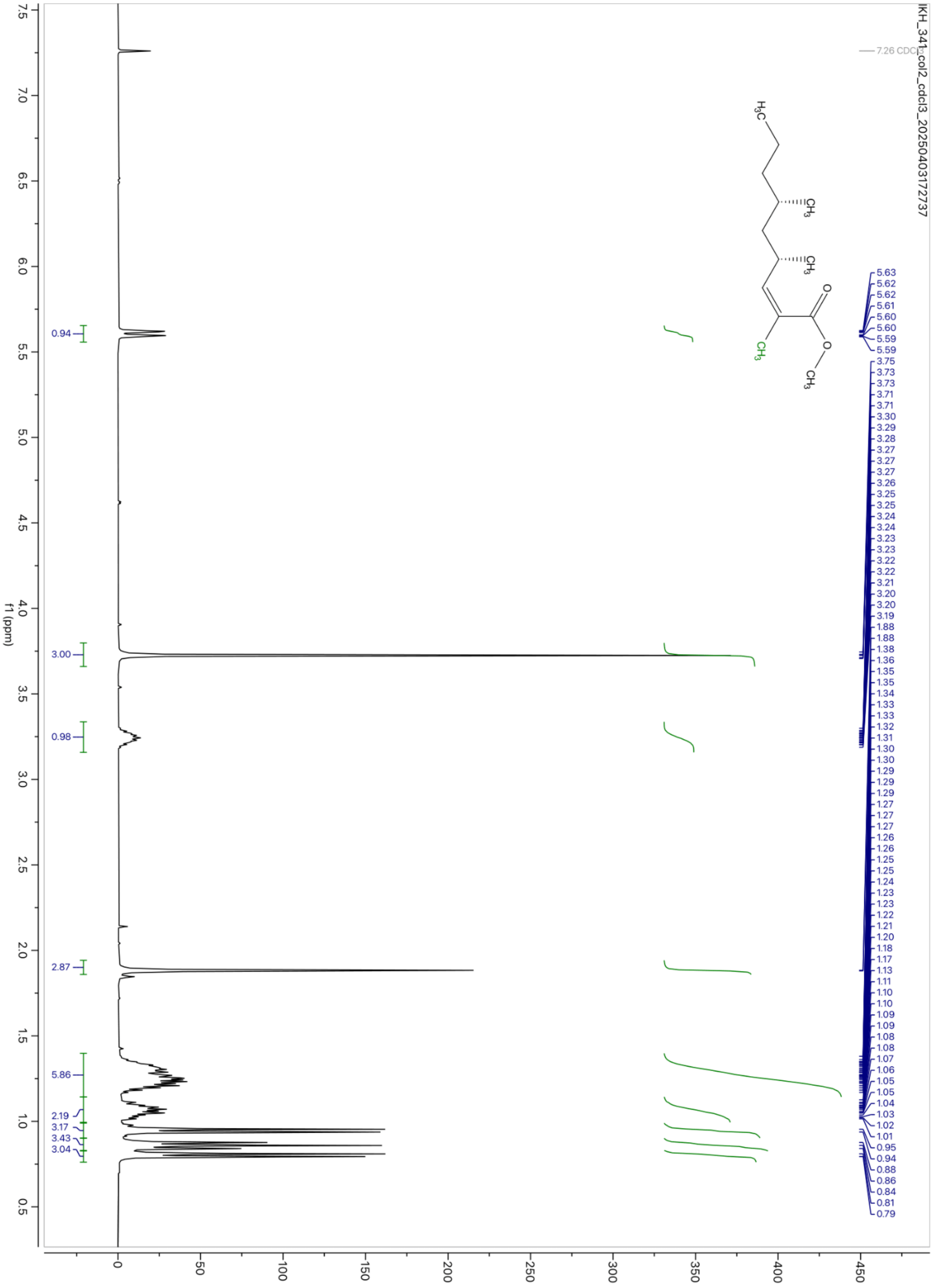

IKH_324_P_cd3cl_20251215131944
STANDARD PHOSPHORUS PARAMETERS
9.64
f1 (ppm)
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20
-25
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
CH3
H3C
H3C
O
O
P
O
O
O
H3C
H3C
H3C
CH3

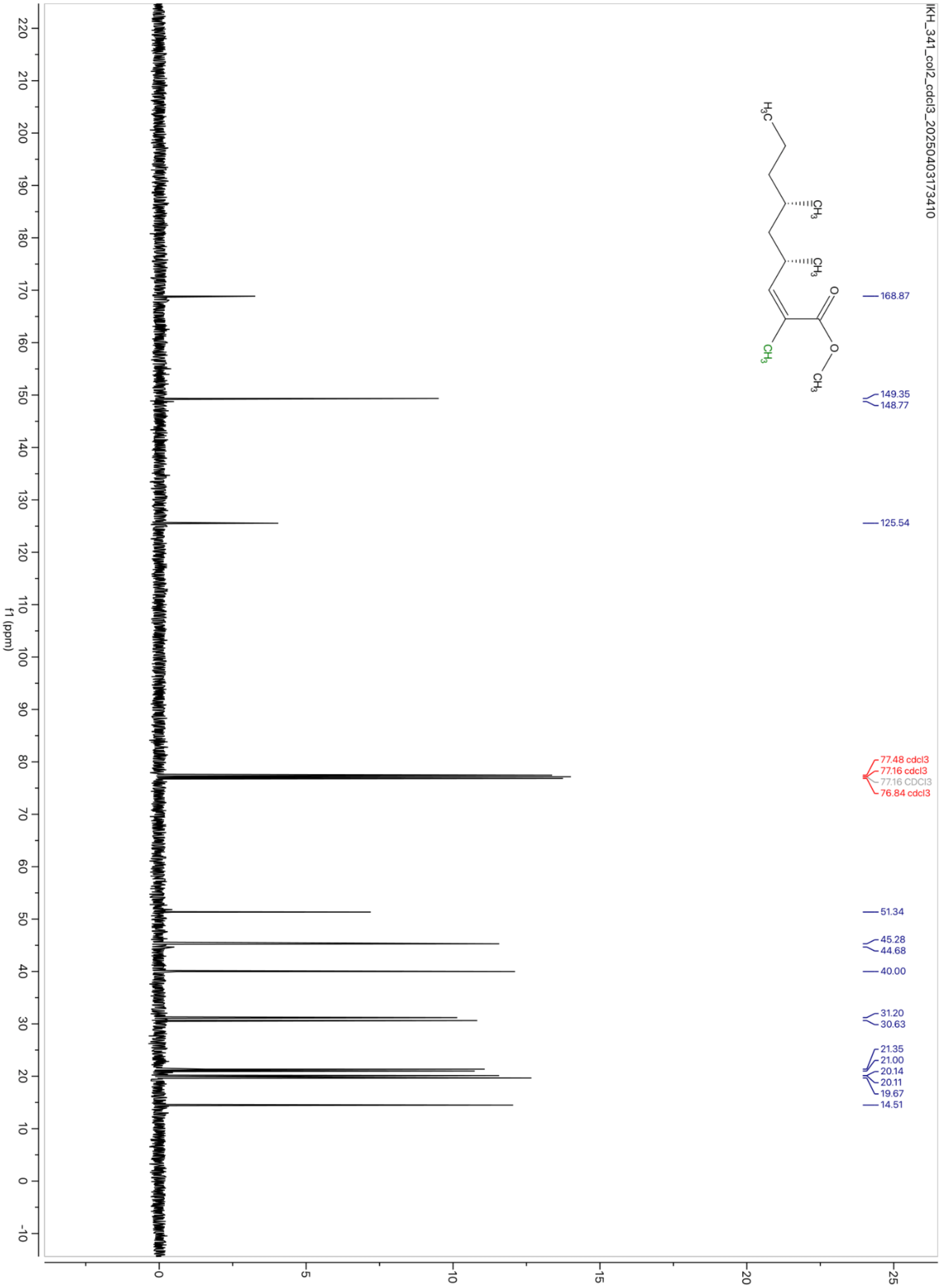

IKH_325_ald_cdcl3_20250416141341
7.76
7.75
7.75
7.74
7.73
7.73
7.67
7.66
7.65
7.64
7.64
7.36
7.35
7.35
7.34
7.34
7.33
7.33
7.32
7.31
7.15
7.15
7.13
7.13
7.13
7.13
7.12
7.12
7.11
7.11
7.10
7.09
7.08
7.08
7.07
7.06
7.05
7.05
7.04
7.04
7.04
3.62
3.62
3.56
3.54
3.52
3.50
3.50
3.48
3.46
3.44
1.73
1.71
1.68
1.66
1.34
1.32
1.00
0.96
2.07
4.09
2.95
1.11
3.04
8.95
8.77
H3C
O
O
CH3
H3C
H3C
CH3
O
P
O
O
H3C
H3C
CH3
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
-50
0
50
100
150
200
250
300
350
400
450
500
550
600
650
700



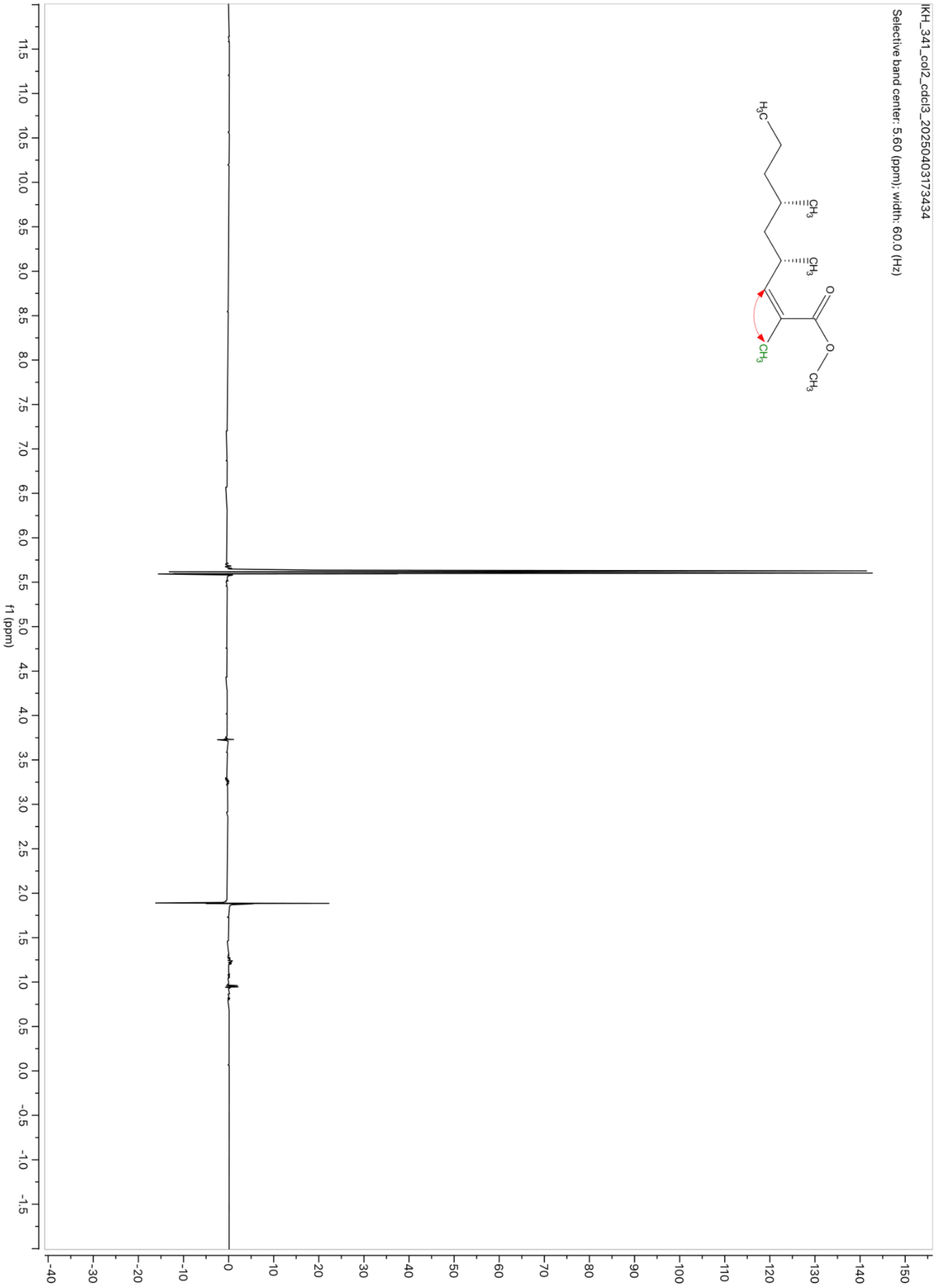
IKH_325_C_cdcl3_20251215132212
168.91
168.87
150.90
150.81
150.69
150.60
139.01
138.97
138.92
138.88
127.69
127.46
127.43
124.50
119.75
119.64
77.16 CDCl3
52.77
52.71
41.57
40.15
34.78
30.13
30.07
12.09
12.03
f1 (ppm)
H_3C
O
P
CH_3


IKH_325_prod_cdcl3_20250312092504
STANDARD PHOSPHORUS PARAMETERS
^{31}P NMR (162 MHz, cdcl$_3$) δ 14.65.
14.65
CH$_3$
H$_3$C
H$_3$C
CH$_3$
O
O
P
O
O
O
H$_3$C
H$_3$C
H$_3$C
CH$_3$
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
44
42
40
38
36
34
32
30
28
26
24
22
20
18
16
14
12
10
8
6
f1 (ppm)

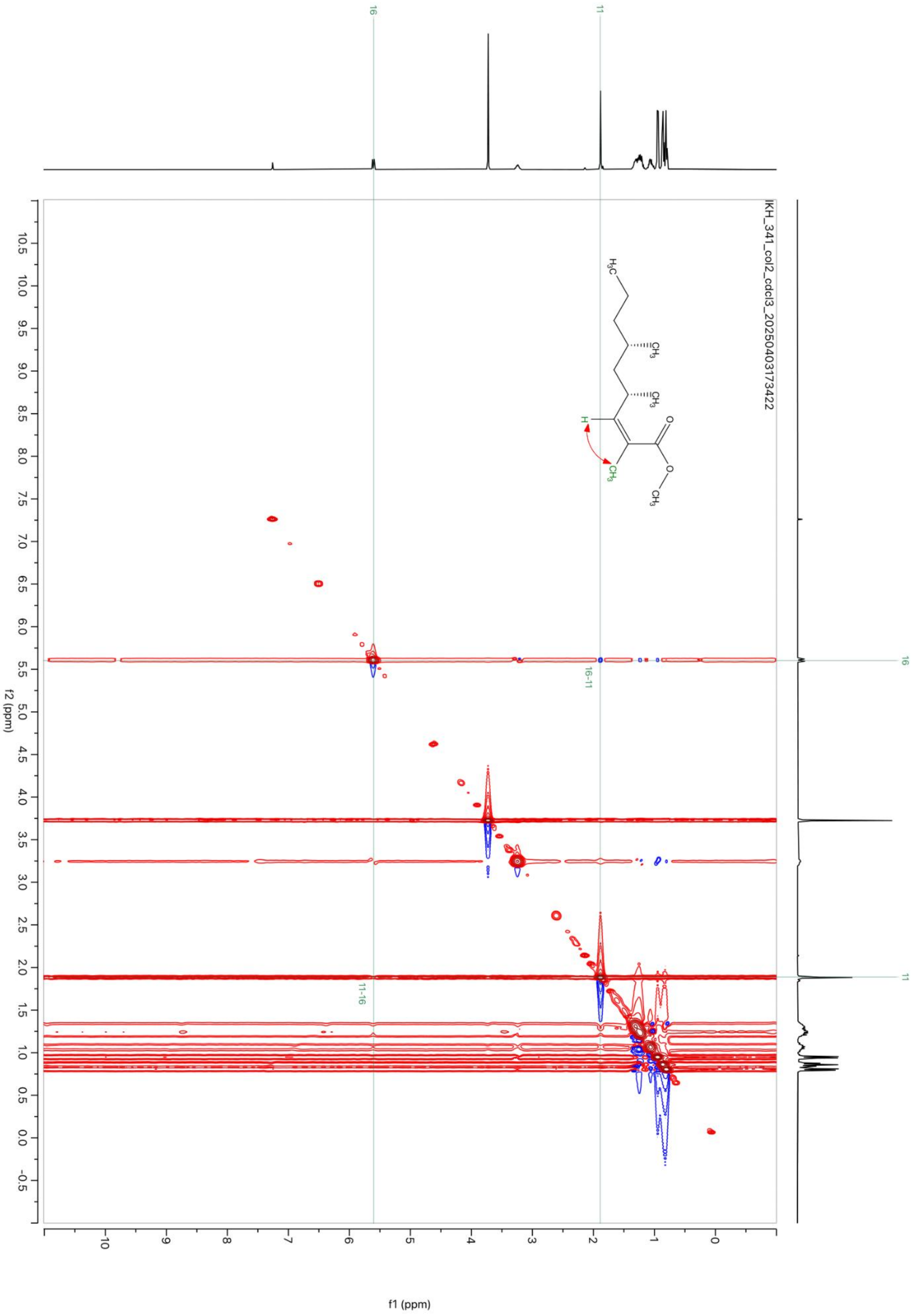

IKH_341_col2_cdcl3_20250403172737
7.26 CDCl3
H3C
CH3
CH3
O
O
CH3
CH3
5.63
5.62
5.62
5.61
5.60
5.60
5.59
5.59
3.75
3.73
3.73
3.71
3.71
3.30
3.29
3.28
3.27
3.27
3.27
3.26
3.25
3.25
3.24
3.24
3.23
3.23
3.22
3.22
3.21
3.20
3.20
3.19
1.88
1.88
1.38
1.36
1.35
1.35
1.34
1.33
1.33
1.32
1.31
1.30
1.30
1.29
1.29
1.29
1.27
1.27
1.27
1.26
1.26
1.25
1.25
1.24
1.23
1.23
1.22
1.21
1.20
1.18
1.17
1.13
1.11
1.10
1.10
1.09
1.09
1.08
1.08
1.07
1.06
1.05
1.05
1.04
1.03
1.02
1.01
0.95
0.94
0.88
0.86
0.84
0.81
0.79
0.94
3.00
0.98
2.87
5.86
2.19
3.17
3.43
3.04
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
0
50
100
150
200
250
300
350
400
450

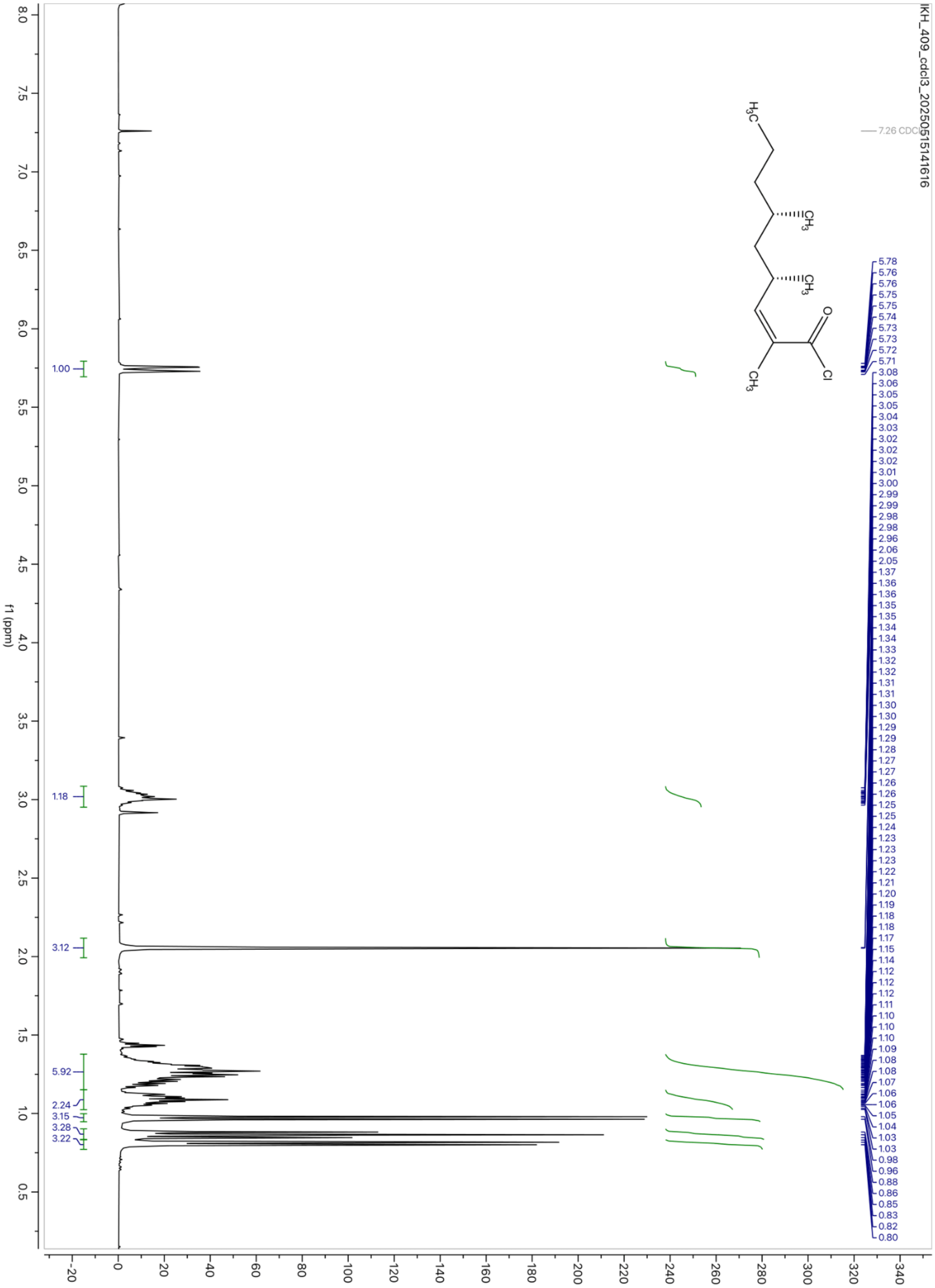

IKH_341_col2_cdcl3_20250403173410
H$_3$C
CH$_3$
CH$_3$
O
O
CH$_3$
CH$_3$
168.87
149.35
148.77
125.54
77.48 cdcl3
77.16 cdcl3
77.16 CDCl3
76.84 cdcl3
51.34
45.28
44.68
40.00
31.20
30.63
21.35
21.00
20.14
20.11
19.67
14.51
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
0
5
10
15
20
25

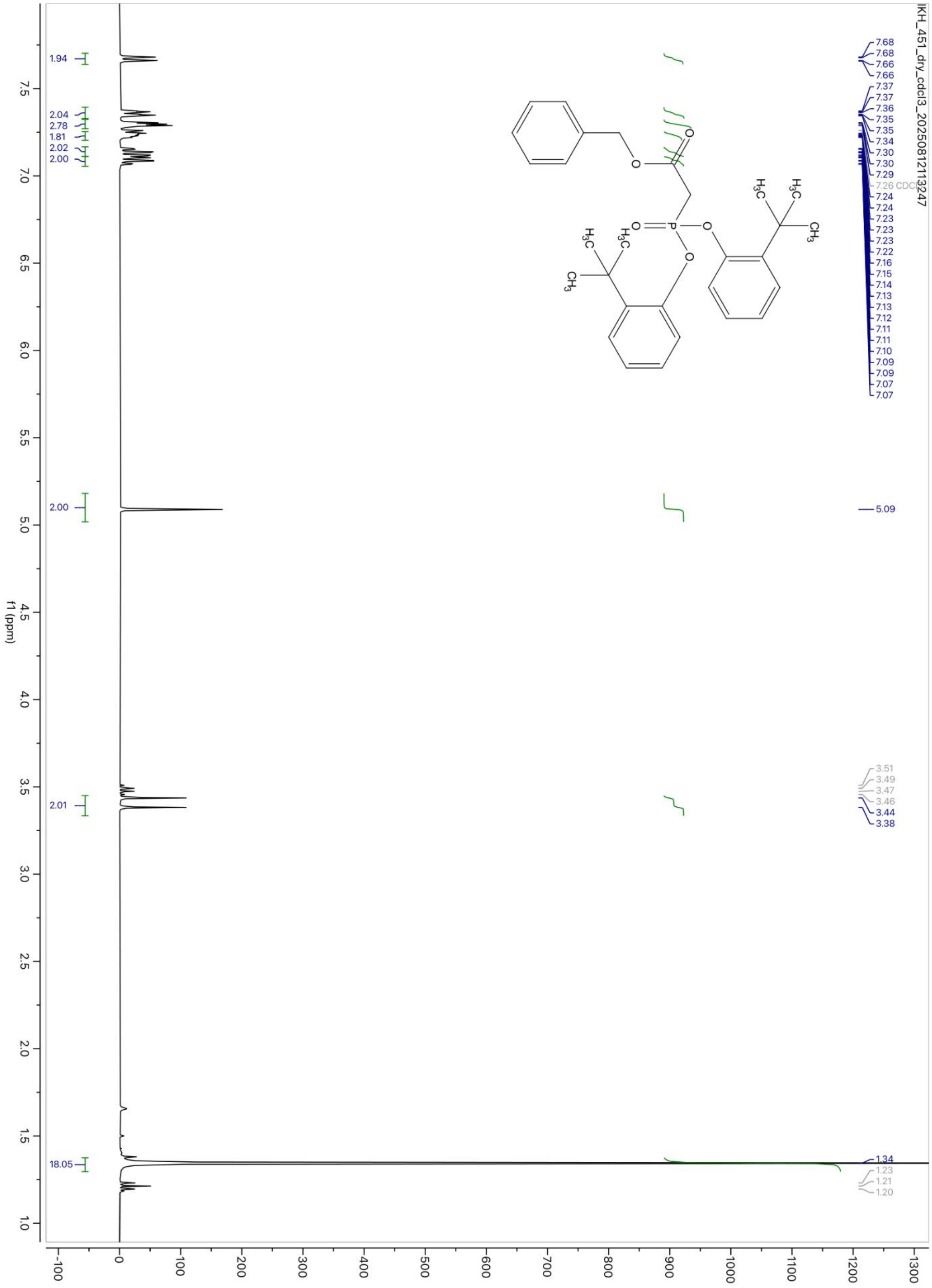
1D NOESY spectrum of ***11***

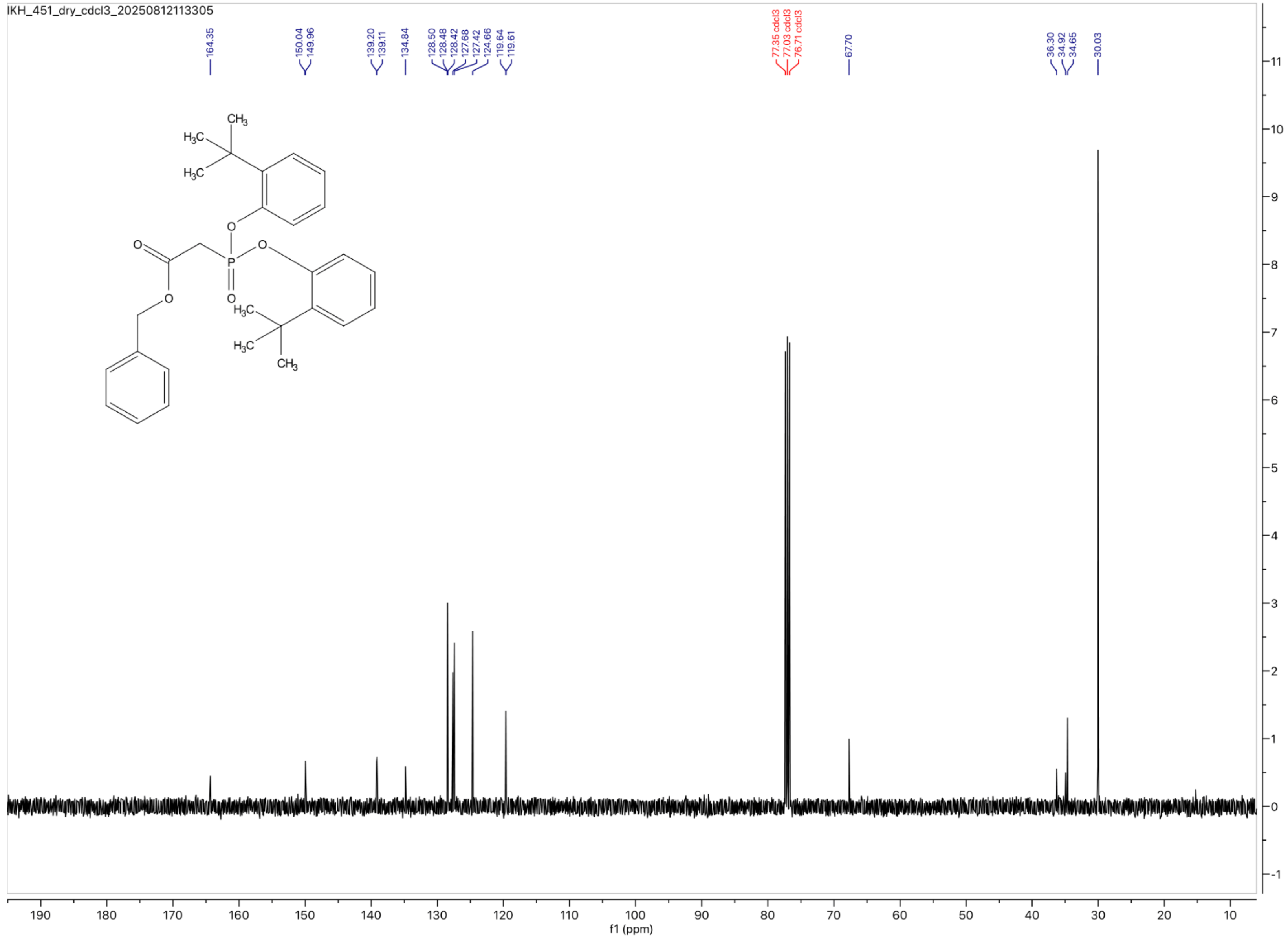


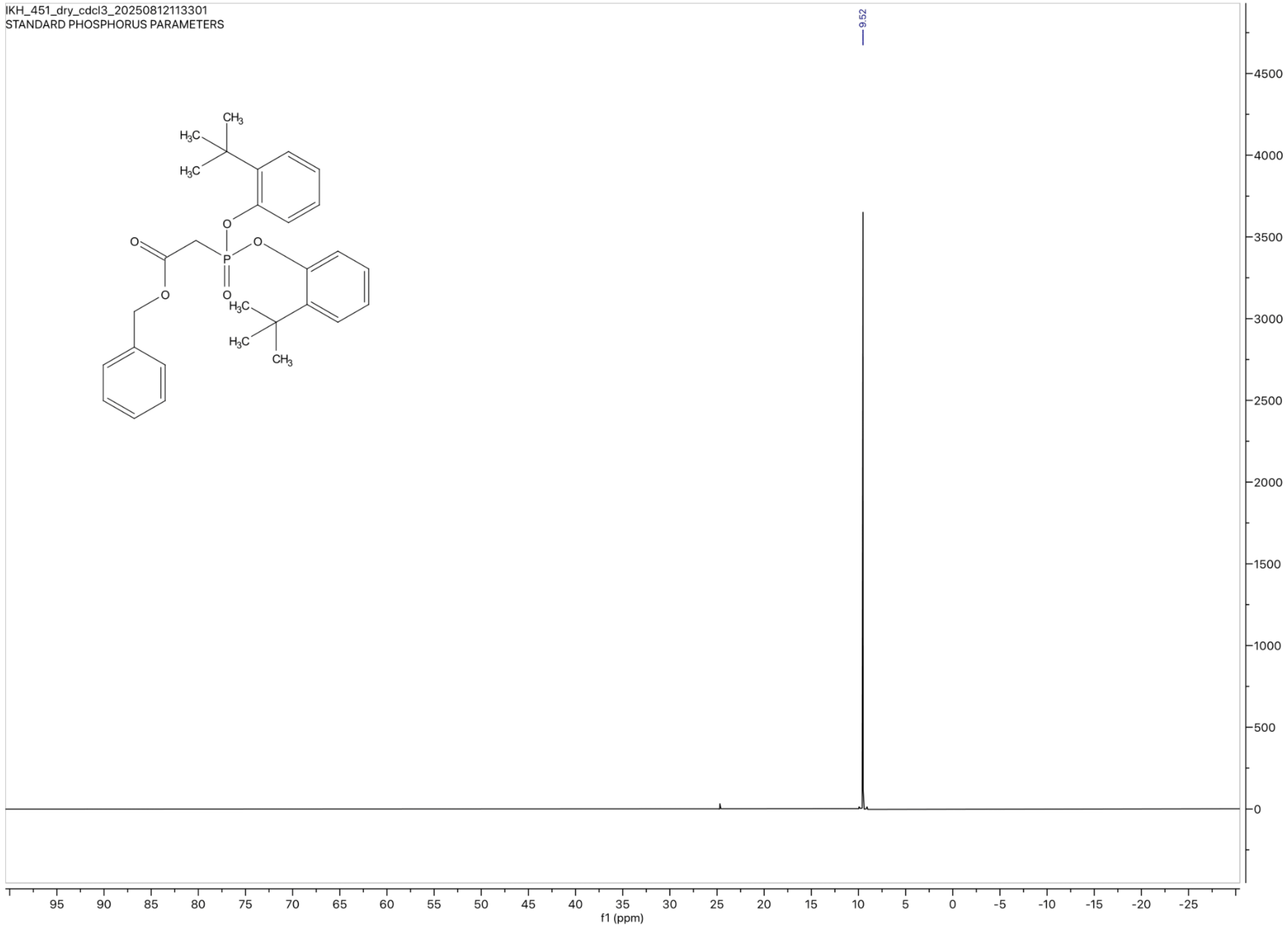
2D NOESY spectrum of ***11***



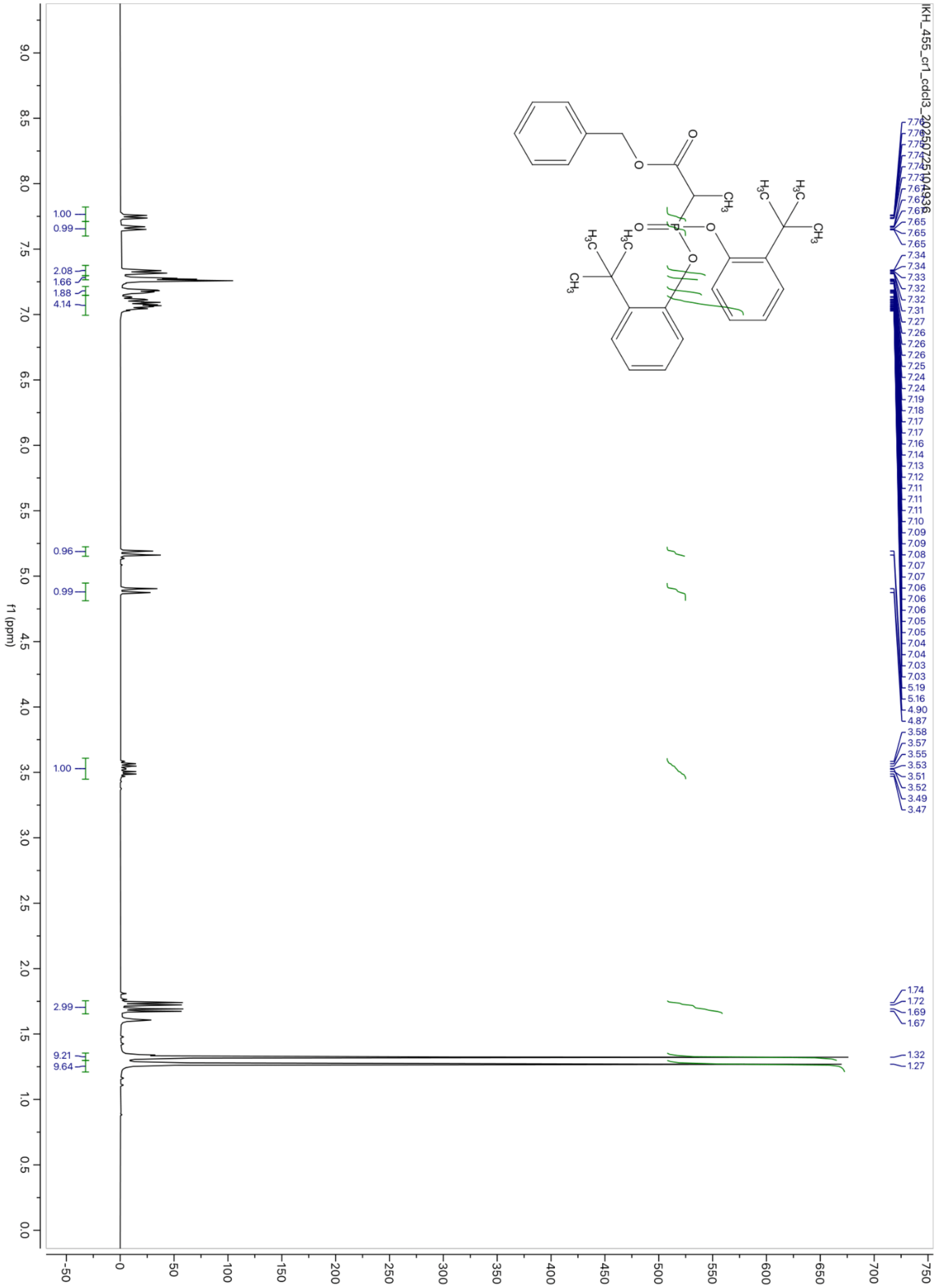

IKH_409_cdcl3_20250515141616
7.26 CDCl3
H3C
CH3
CH3
O
Cl
CH3
5.78
5.76
5.76
5.75
5.75
5.74
5.73
5.73
5.72
5.71
3.08
3.06
3.05
3.05
3.04
3.03
3.02
3.02
3.02
3.01
3.00
2.99
2.99
2.98
2.98
2.96
2.06
2.05
1.37
1.36
1.36
1.35
1.35
1.34
1.34
1.33
1.32
1.32
1.31
1.31
1.30
1.30
1.29
1.29
1.28
1.27
1.27
1.26
1.26
1.25
1.25
1.24
1.23
1.23
1.23
1.22
1.21
1.20
1.19
1.18
1.18
1.17
1.15
1.14
1.12
1.12
1.12
1.11
1.10
1.10
1.10
1.09
1.08
1.08
1.07
1.06
1.06
1.05
1.04
1.03
1.03
0.98
0.96
0.88
0.86
0.85
0.83
0.82
0.80
1.00
1.18
3.12
5.92
2.24
3.15
3.28
3.22
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
-20
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
340

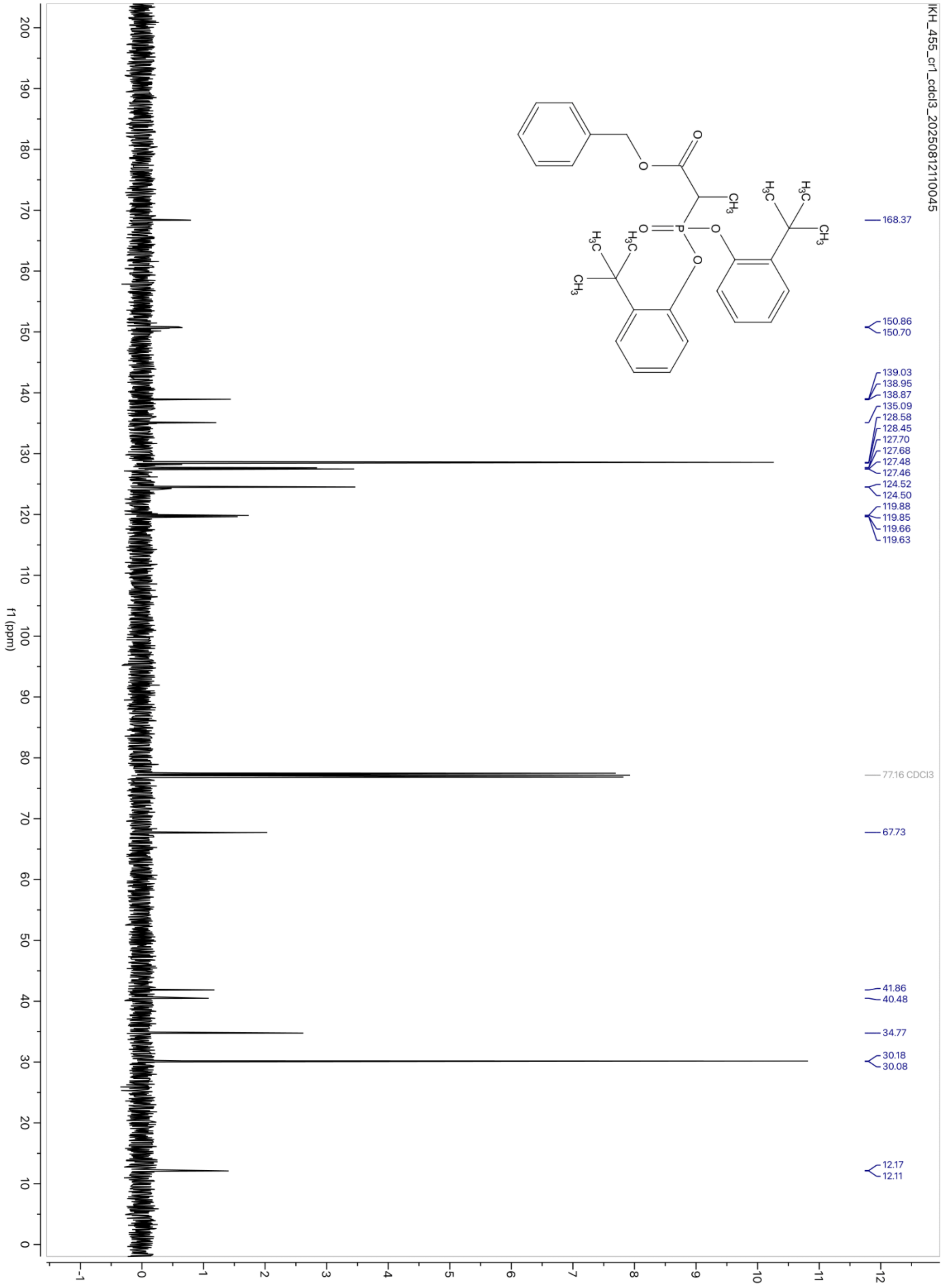

IKH_451_dry_cdcl3_20250812113247
7.68
7.68
7.66
7.66
7.37
7.37
7.36
7.35
7.35
7.34
7.30
7.30
7.29
7.26 CDCl3
7.24
7.24
7.23
7.23
7.23
7.22
7.16
7.15
7.14
7.13
7.13
7.12
7.11
7.11
7.10
7.09
7.09
7.07
7.07
5.09
3.51
3.49
3.47
3.46
3.44
3.38
1.34
1.23
1.21
1.20
1.94
2.04
2.78
1.81
2.02
2.00
2.00
2.01
18.05
O
O
P
O
O
O
H3C
H3C
CH3
H3C
H3C
CH3
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
-100
0
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300

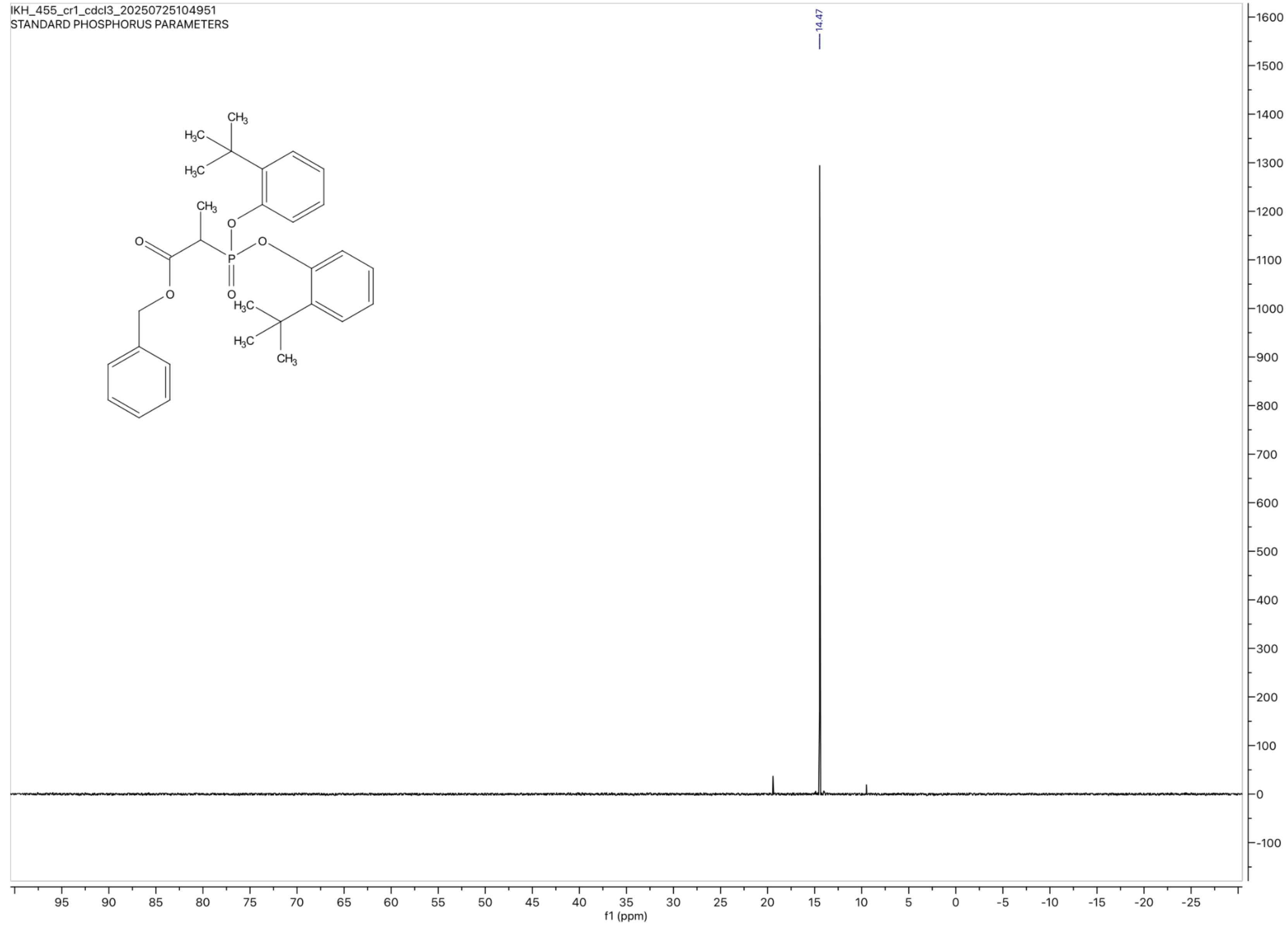

IKH_451_dry_cdcl3_20250812113305
164.35
150.04
149.96
139.20
139.11
134.84
128.50
128.48
128.42
127.68
127.42
124.66
119.64
119.61
77.35 cdcl3
77.03 cdcl3
76.71 cdcl3
67.70
36.30
34.92
34.65
30.03
CH3
H3C
H3C
O
O
P
O
O
O
H3C
H3C
CH3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)
11
10
9
8
7
6
5
4
3
2
1
0
-1

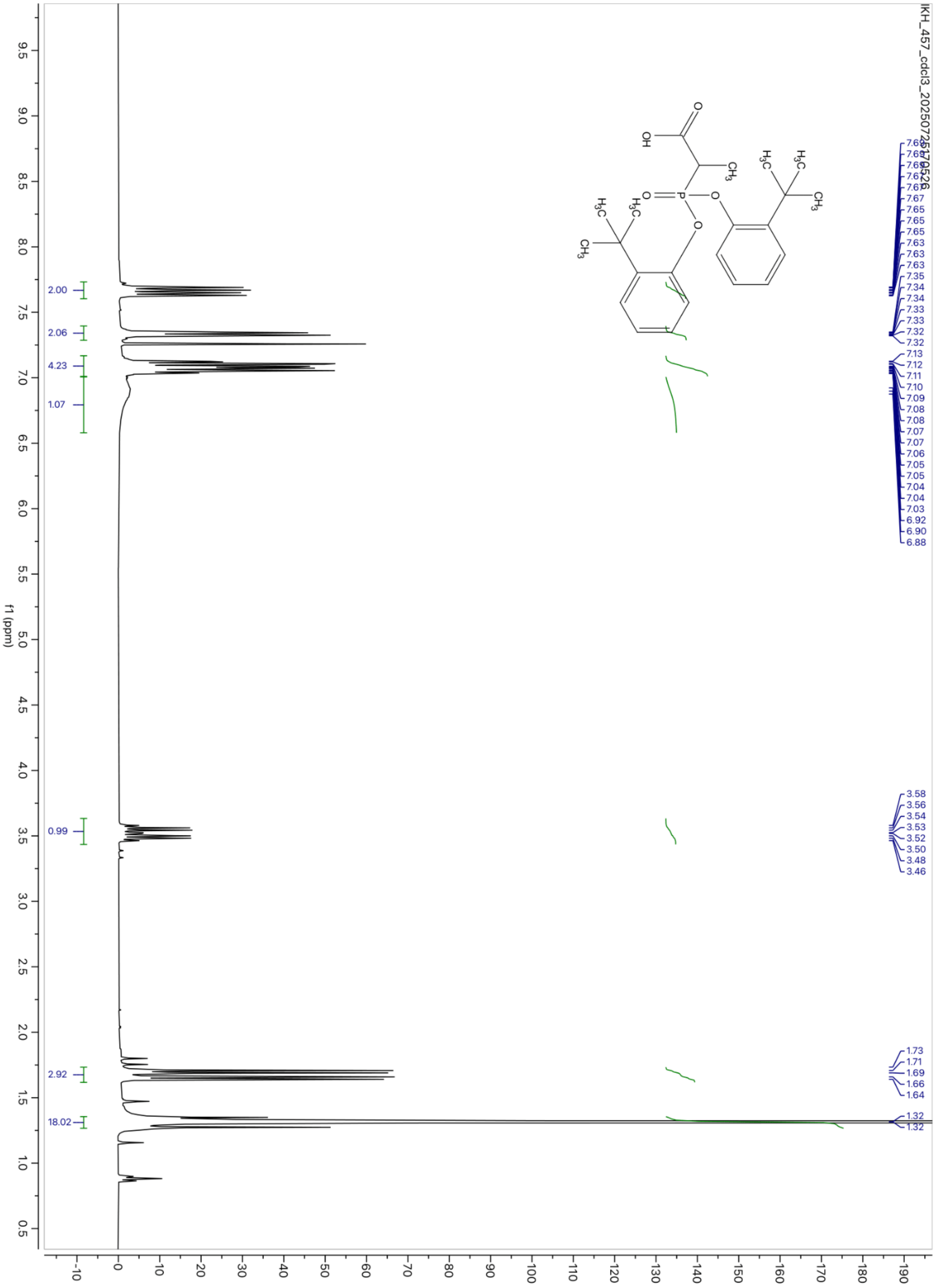


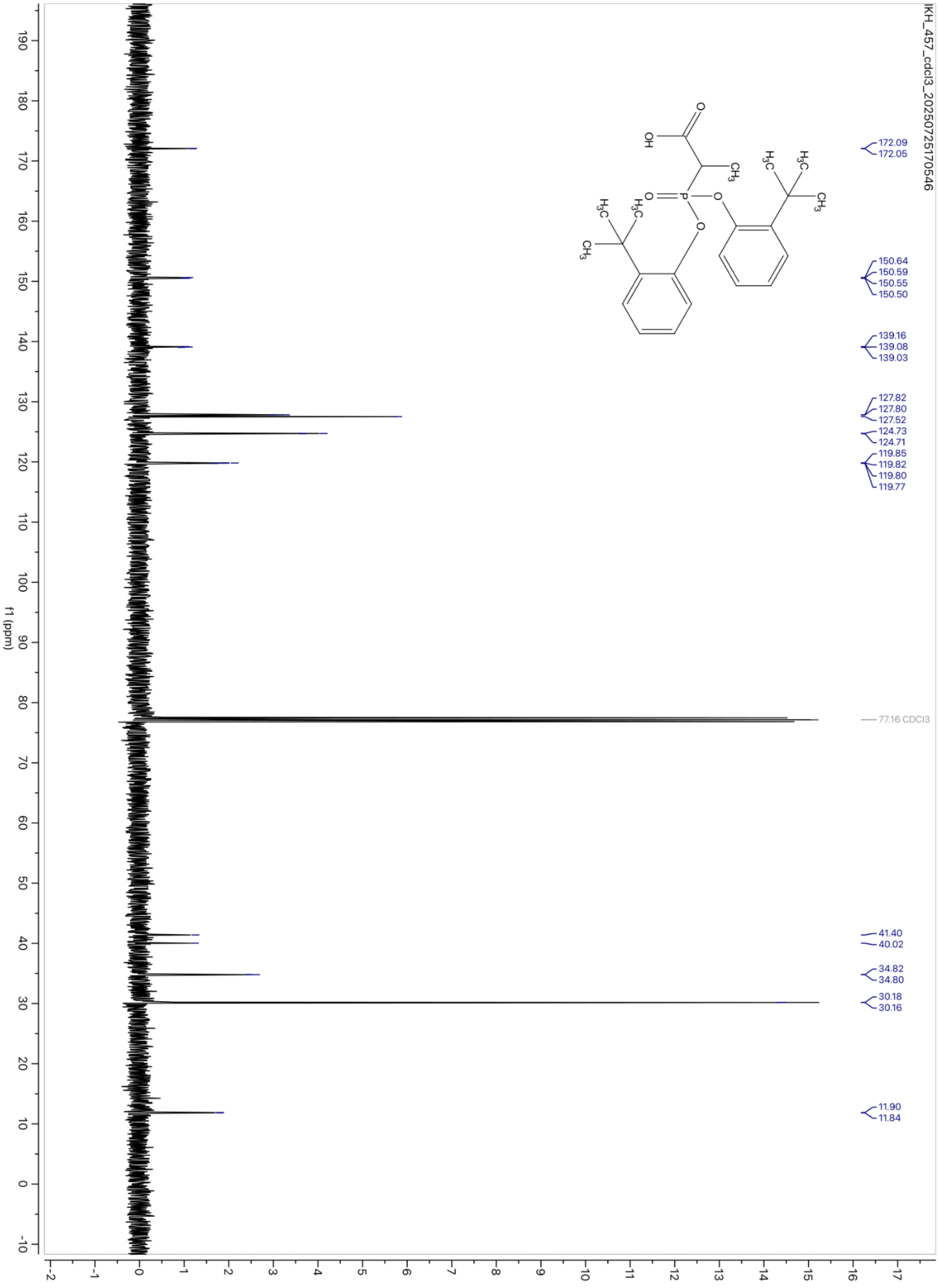
IKH_451_dry_cdcl3_20250812113301
STANDARD PHOSPHORUS PARAMETERS
9.52
CH3
H3C
H3C
O
O
P
O
O
O
H3C
H3C
CH3
4500
4000
3500
3000
2500
2000
1500
1000
500
0
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20
-25
f1 (ppm)

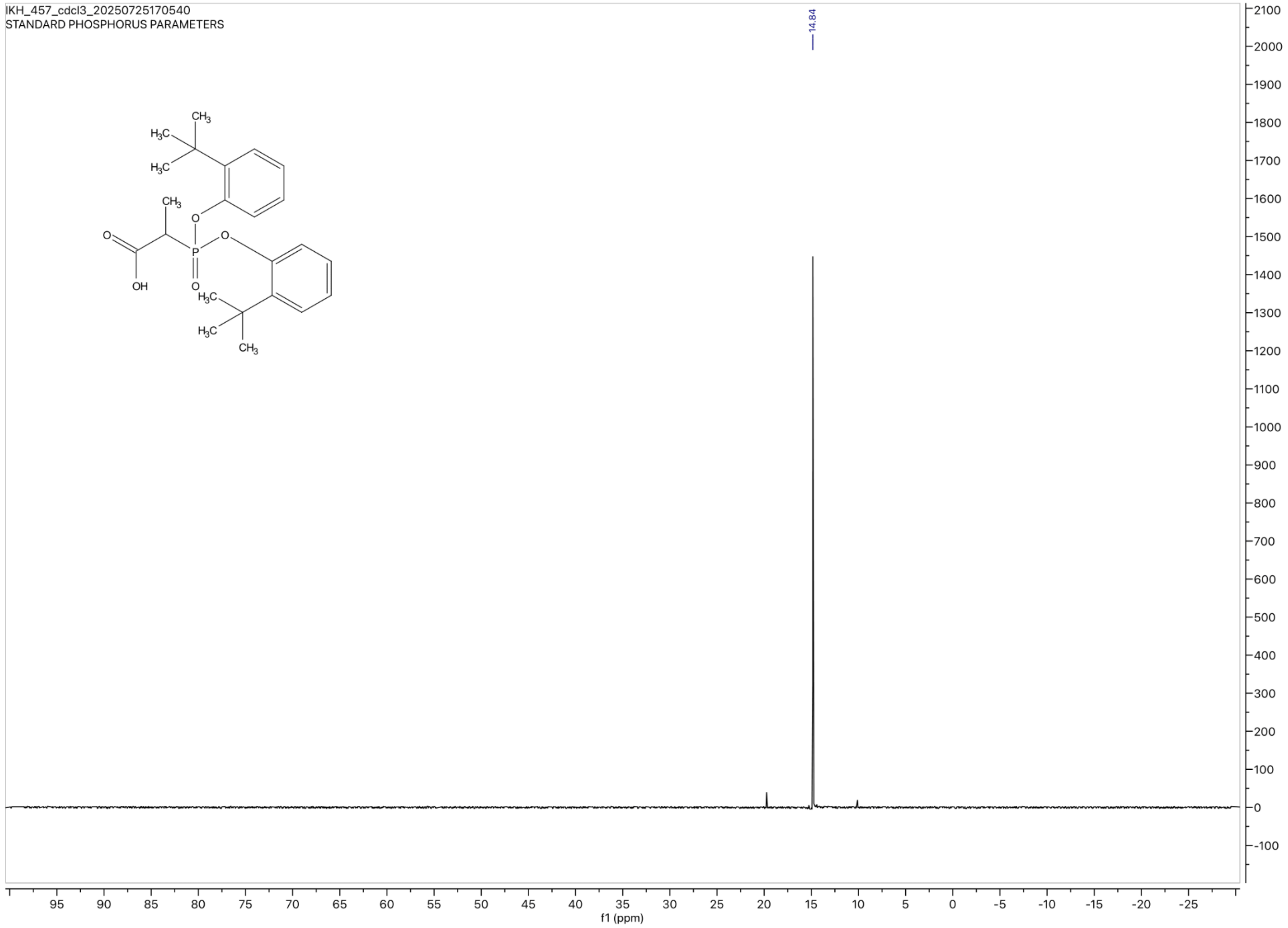

IKH_455_cr1_cdcl3_20250725104936
7.76
7.76
7.75
7.74
7.74
7.73
7.67
7.67
7.67
7.65
7.65
7.65
7.34
7.34
7.33
7.32
7.32
7.31
7.27
7.26
7.26
7.26
7.25
7.24
7.24
7.19
7.18
7.17
7.17
7.16
7.14
7.13
7.12
7.11
7.11
7.11
7.10
7.09
7.09
7.08
7.07
7.07
7.06
7.06
7.06
7.05
7.05
7.04
7.04
7.03
7.03
5.19
5.16
4.90
4.87
3.58
3.57
3.55
3.53
3.51
3.52
3.49
3.47
1.74
1.72
1.69
1.67
1.32
1.27
1.00
0.99
2.08
1.66
1.88
4.14
0.96
0.99
1.00
2.99
9.21
9.64
O
O
CH3
O
P
O
O
H3C
H3C
CH3
H3C
H3C
CH3
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
-50
0
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750

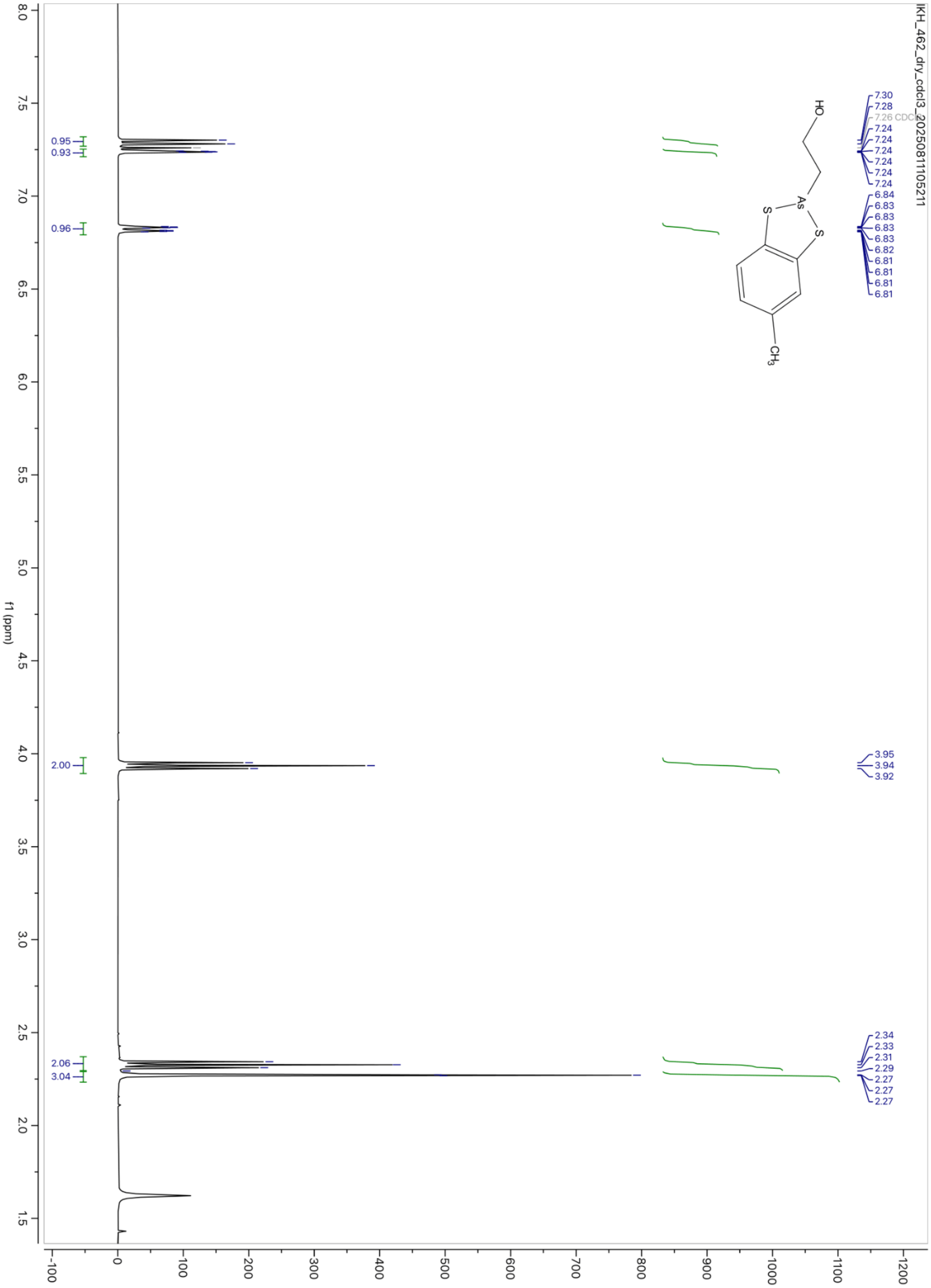

IKH_455_cr1_cdcl3_20250812110045
168.37
150.86
150.70
139.03
138.95
138.87
135.09
128.58
128.45
127.70
127.68
127.48
127.46
124.52
124.50
119.88
119.85
119.66
119.63
77.16 CDCl3
67.73
41.86
40.48
34.77
30.18
30.08
12.17
12.11
f1 (ppm)
O
P
CH3
H3C

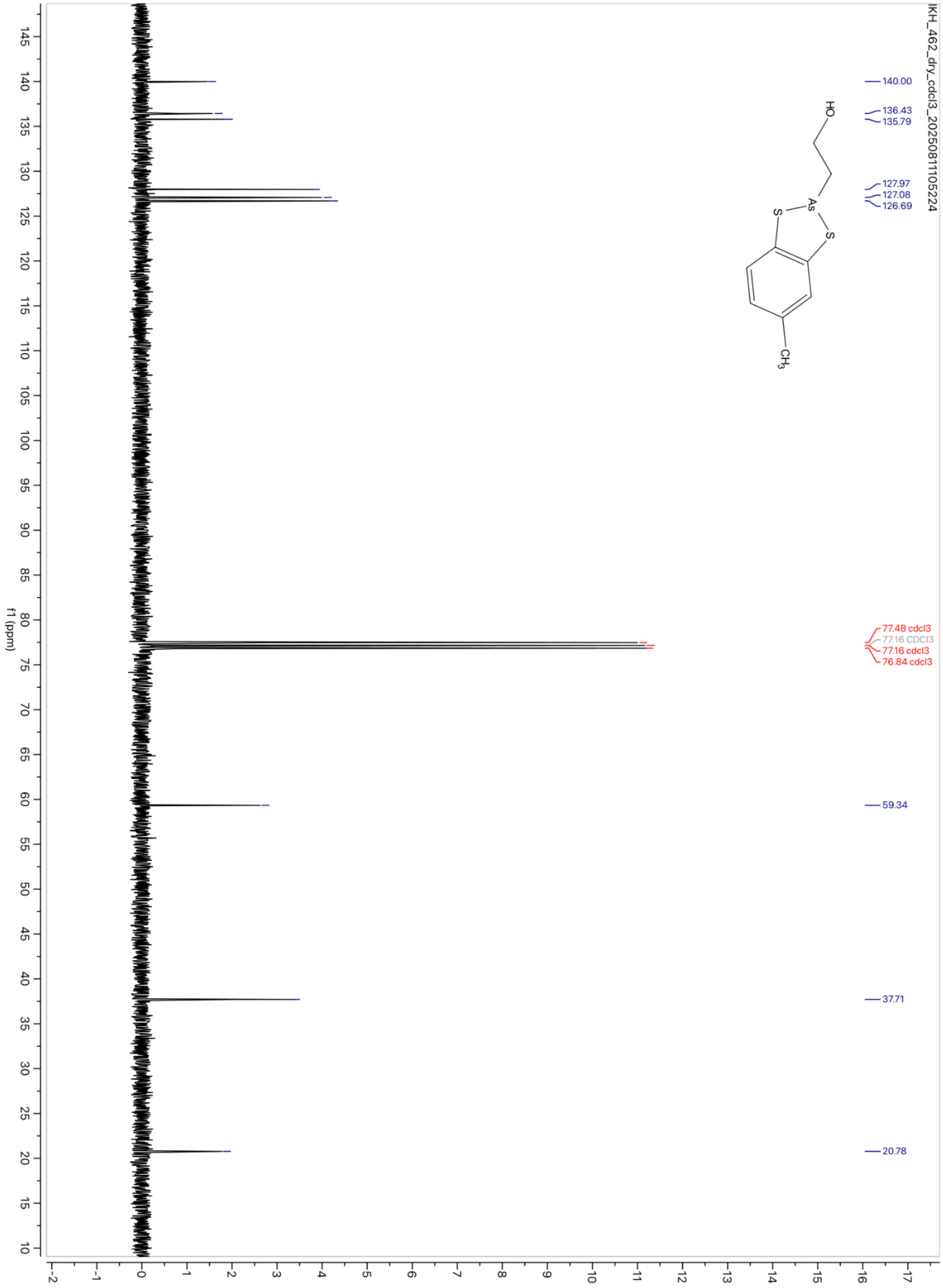

IKH_455_cr1_cdcl3_20250725104951
STANDARD PHOSPHORUS PARAMETERS
14.47
CH3
H3C
H3C
CH3
O
O
P
O
O
O
H3C
H3C
CH3
95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5 -10 -15 -20 -25
f1 (ppm)
1600 1500 1400 1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0 -100

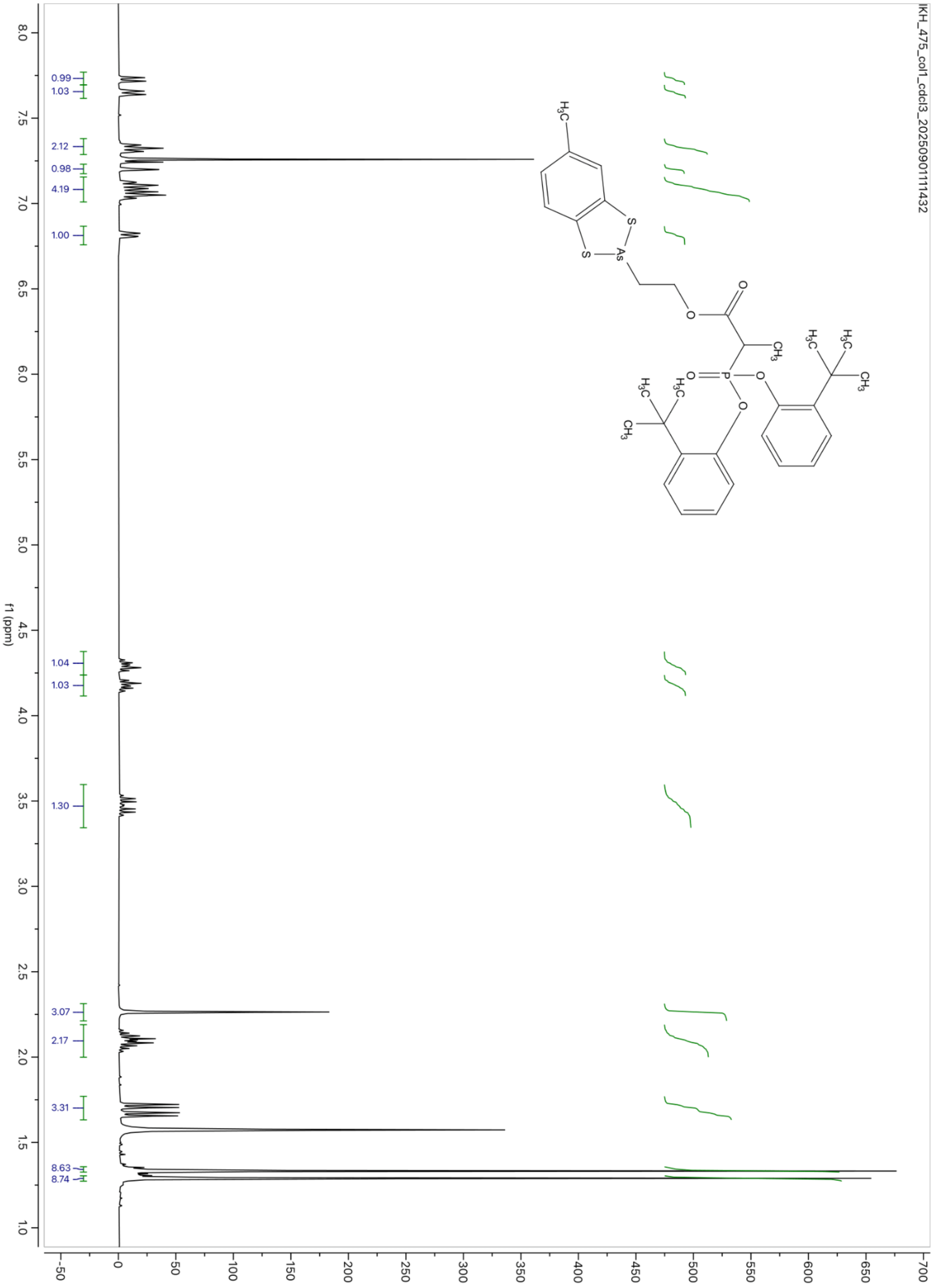

IKH_457_cdcl3_20250725170526
OH
O
CH3
O
P
O
O
H3C
H3C
CH3
H3C
H3C
CH3
7.69
7.69
7.69
7.67
7.67
7.67
7.65
7.65
7.65
7.63
7.63
7.63
7.35
7.34
7.34
7.33
7.33
7.32
7.32
7.13
7.12
7.11
7.10
7.09
7.08
7.08
7.07
7.07
7.06
7.05
7.05
7.04
7.04
7.03
6.92
6.90
6.88
3.58
3.56
3.54
3.53
3.52
3.50
3.48
3.46
1.73
1.71
1.69
1.66
1.64
1.32
1.32
2.00
2.06
4.23
1.07
0.99
2.92
18.02
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190

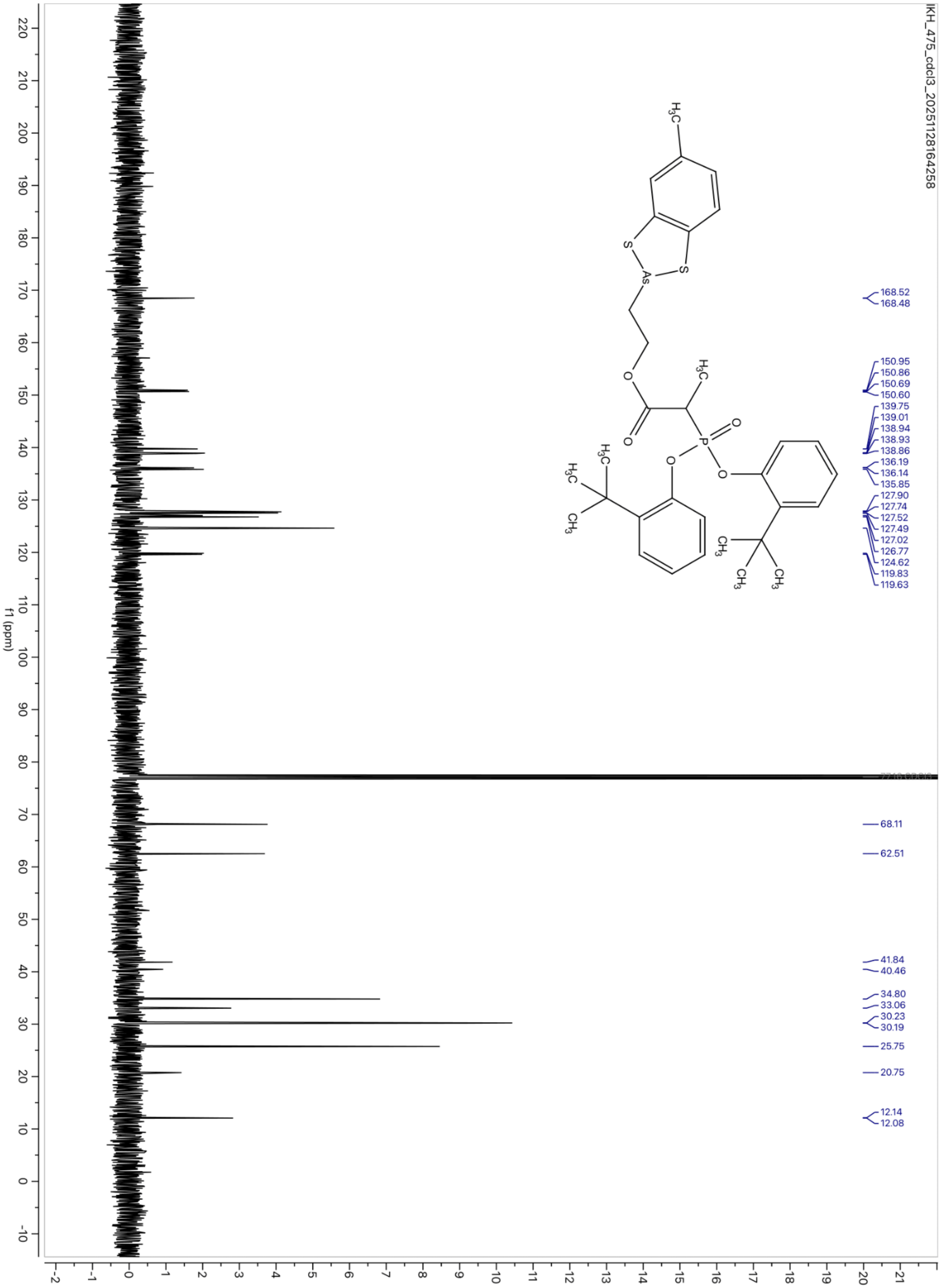

IKH_457_cdcl3_20250725170546
172.09
172.05
150.64
150.59
150.55
150.50
139.16
139.08
139.03
127.82
127.80
127.52
124.73
124.71
119.85
119.82
119.80
119.77
77.16 CDCl3
41.40
40.02
34.82
34.80
30.18
30.16
11.90
11.84
OH
O
O
P
CH3
H3C
H3C
CH3
H3C
H3C
CH3
f1 (ppm)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-2
-1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17

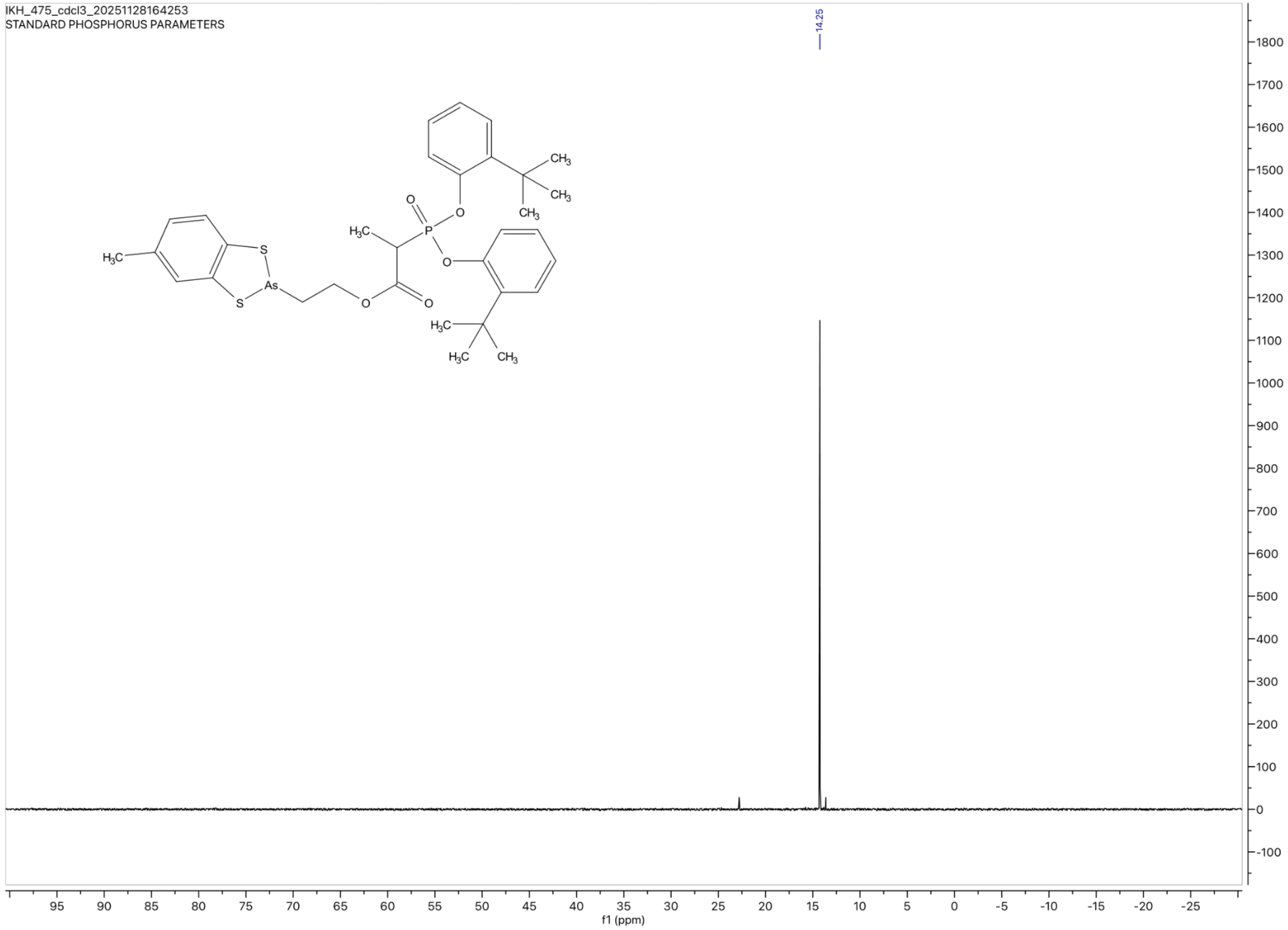

IKH_457_cdcl3_20250725170540
STANDARD PHOSPHORUS PARAMETERS
14.84
CH3
H3C
H3C
CH3
O
O
O
P
O
OH
H3C
H3C
CH3
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20
-25
f1 (ppm)
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

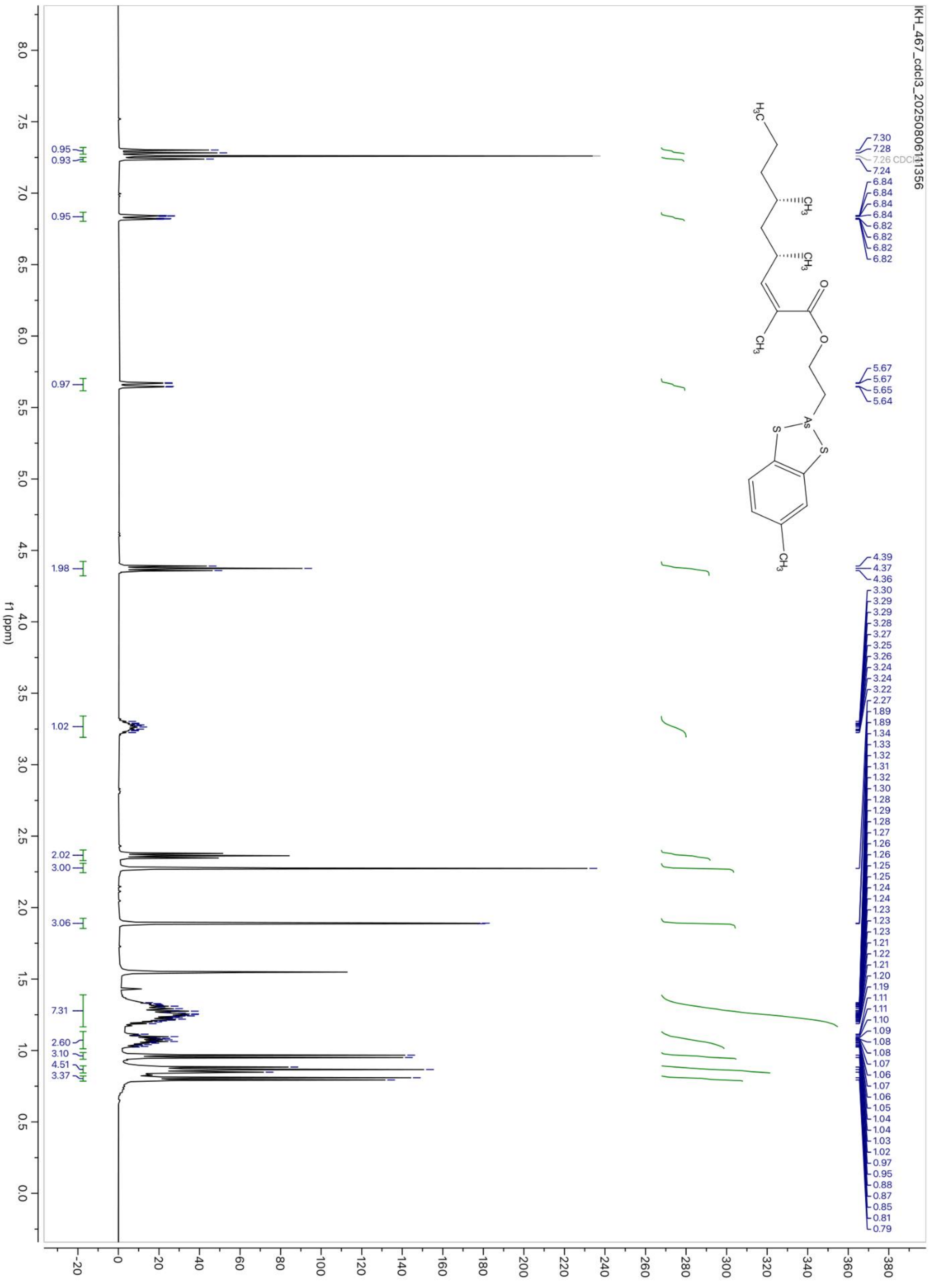

IKH_462_dry_cdcl3_20250811105211
7.30
7.28
7.26 CDCl3
7.24
7.24
7.24
7.24
7.24
7.24
6.84
6.83
6.83
6.83
6.83
6.82
6.81
6.81
6.81
6.81
3.95
3.94
3.92
2.34
2.33
2.31
2.29
2.27
2.27
2.27
HO
As
S
S
CH3
0.95
0.93
0.96
2.00
2.06
3.04
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)
-100
0
100
200
300
400
500
600
700
800
900
1000
1100
1200


IKH_462_dry_cdcl3_20250811105224
140.00
136.43
135.79
127.97
127.08
126.69
77.48 cdcl3
77.16 CDCl3
77.16 cdcl3
76.84 cdcl3
59.34
37.71
20.78
HO
As
S
S
CH3
f1 (ppm)
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
-2
-1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17

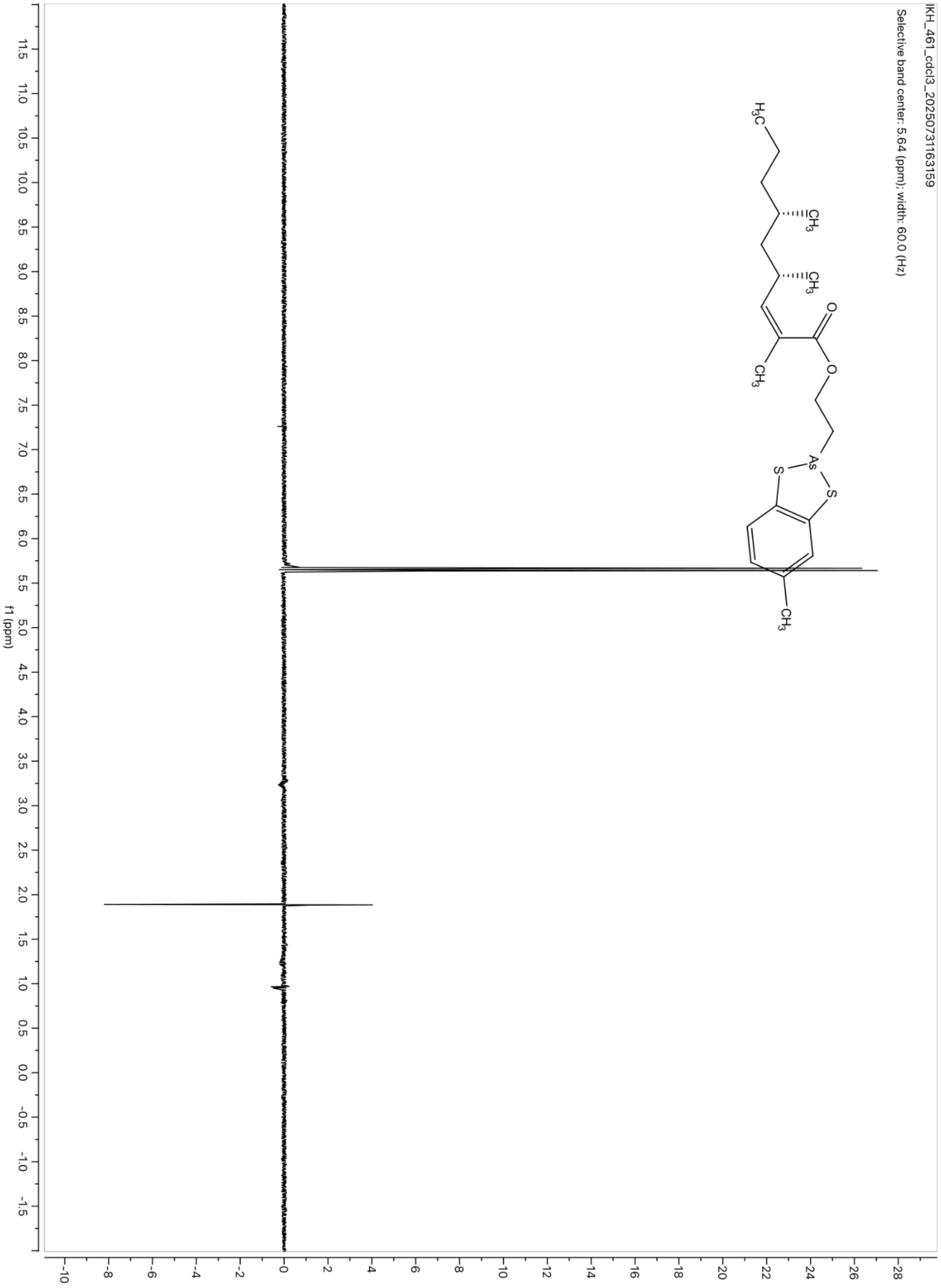

IKH_475_col1_cdcl3_20250901111432
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.99
1.03
2.12
0.98
4.19
1.00
1.04
1.03
1.30
3.07
2.17
3.31
8.63
8.74
-50
0
50
100
150
200
250
300
350
400
450
500
550
600
650
700
H3C
S
As
S
O
O
CH3
O
P
O
O
H3C
H3C
CH3
H3C
H3C
CH3


IKH_475_cdcl3_20251128164258
168.52
168.48
150.95
150.86
150.69
150.60
139.75
139.01
138.94
138.93
138.86
136.19
136.14
135.85
127.90
127.74
127.52
127.49
127.02
126.77
124.62
119.83
119.63
68.11
62.51
41.84
40.46
34.80
33.06
30.23
30.19
25.75
20.75
12.14
12.08
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-2
-1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
H3C
S
As
S
O
O
H3C
P
O
O
O
H3C
H3C
CH3
CH3
CH3
CH3

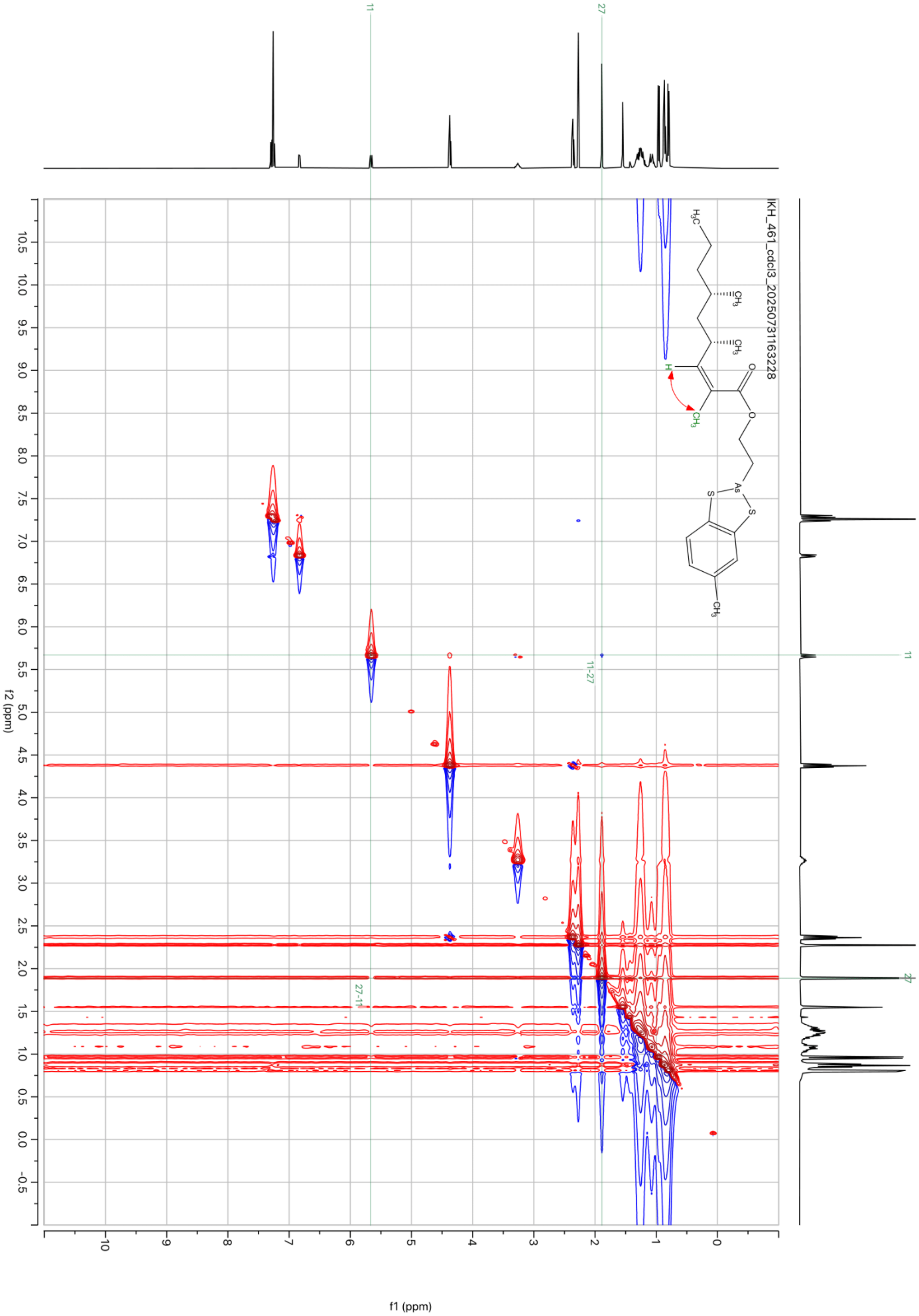

IKH_475_cdcl3_20251128164253
STANDARD PHOSPHORUS PARAMETERS
14.25
H3C
S
As
S
O
O
H3C
P
O
O
O
CH3
CH3
CH3
H3C
H3C
CH3
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20
-25
f1 (ppm)


IKH_467_cdcl3_20250806111356
7.30
7.28
7.26 CDCl3
7.24
6.84
6.84
6.84
6.84
6.82
6.82
6.82
6.82
5.67
5.67
5.65
5.64
4.39
4.37
4.36
3.30
3.29
3.29
3.28
3.27
3.25
3.26
3.24
3.24
3.22
2.27
1.89
1.89
1.34
1.33
1.32
1.31
1.32
1.30
1.28
1.29
1.28
1.27
1.26
1.26
1.25
1.25
1.24
1.24
1.23
1.23
1.23
1.21
1.22
1.21
1.20
1.19
1.11
1.11
1.10
1.09
1.08
1.08
1.07
1.06
1.07
1.06
1.05
1.04
1.04
1.03
1.02
0.97
0.95
0.88
0.87
0.85
0.81
0.79
H3C
CH3
CH3
O
O
CH3
As
S
S
CH3
0.95
0.93
0.95
0.97
1.98
1.02
2.02
3.00
3.06
7.31
2.60
3.10
4.51
3.37
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
-20
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380

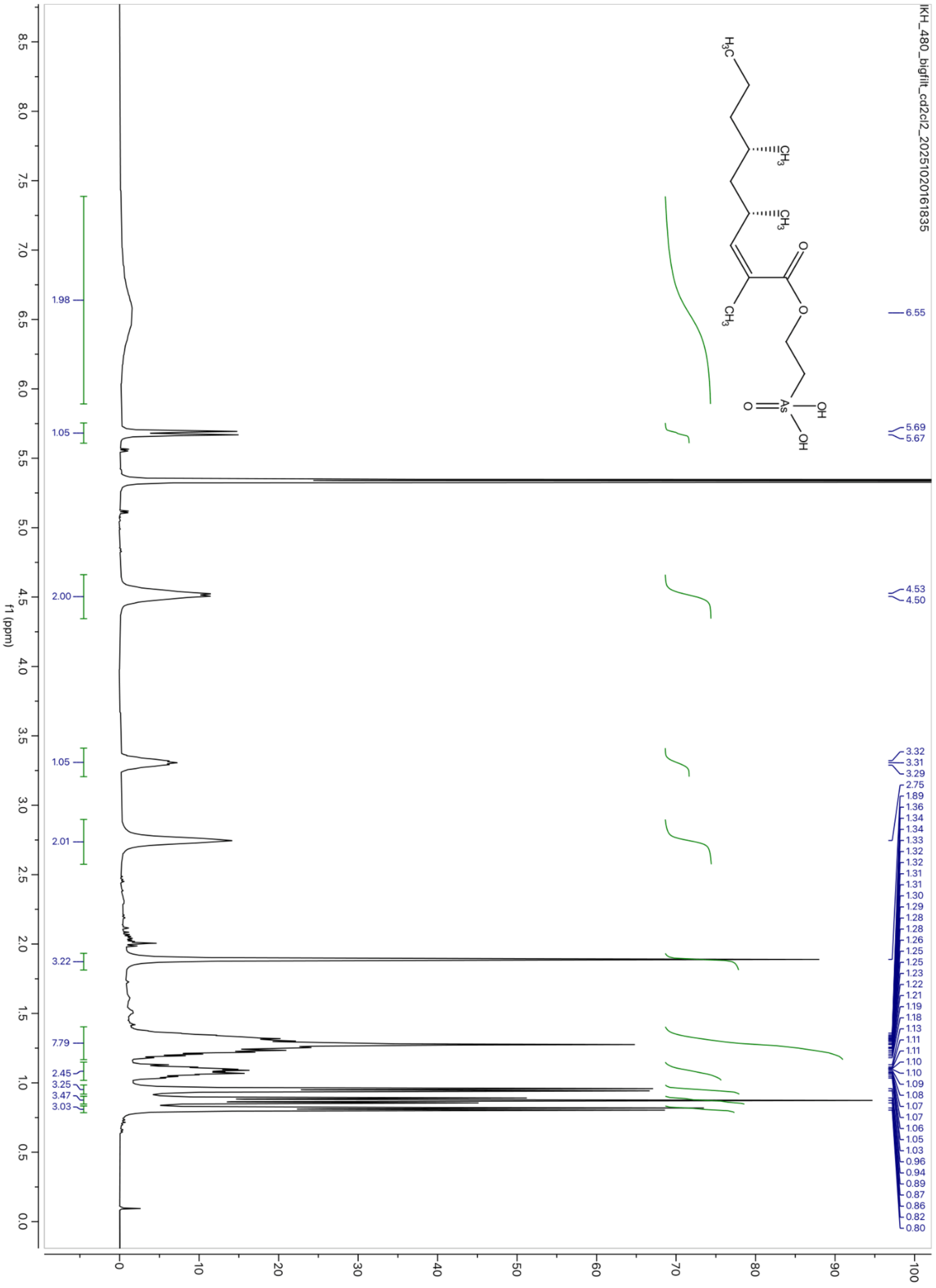
1D NOESY spectrum of ***14***



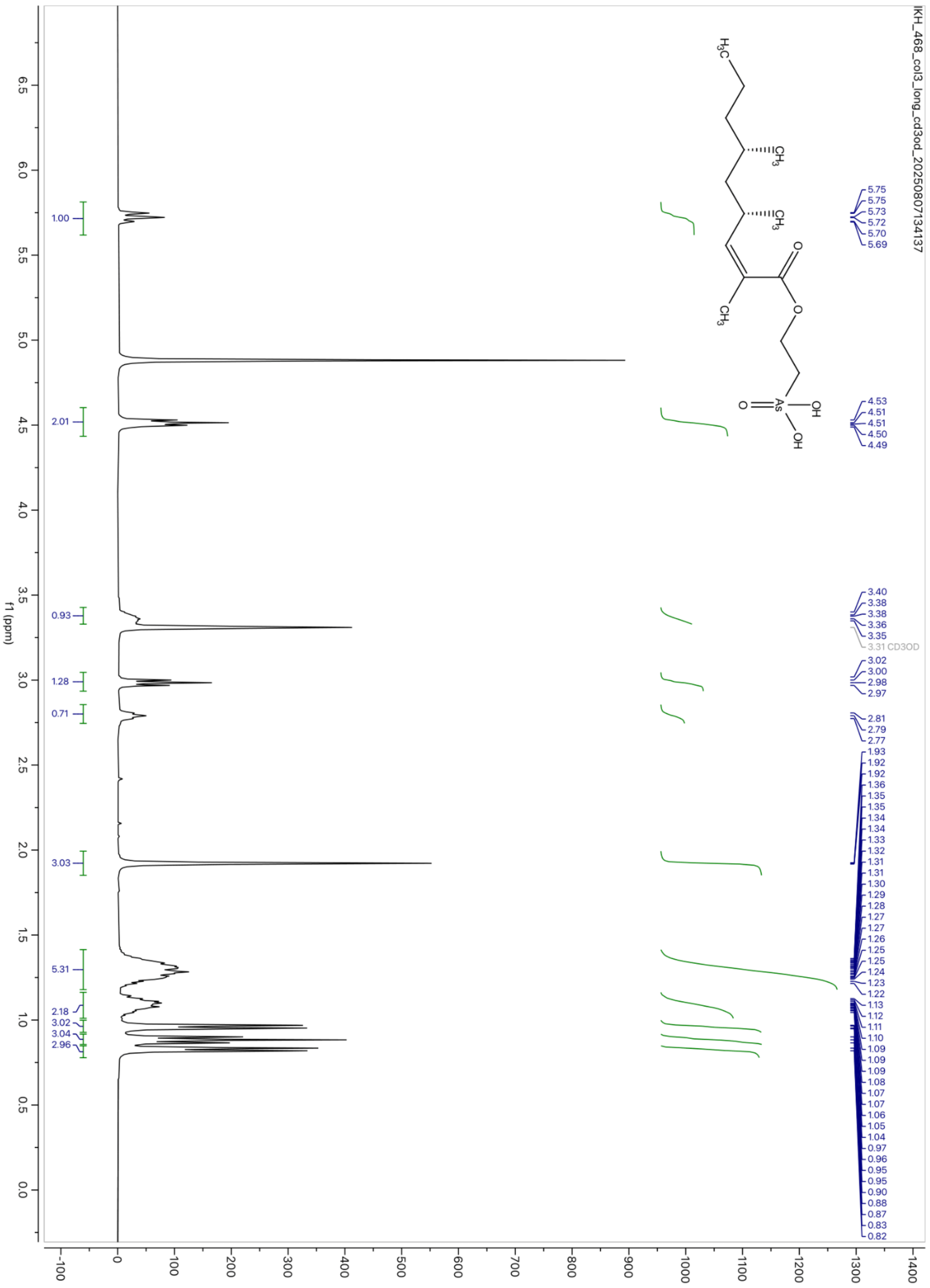
2D NOESY spectrum of ***14***



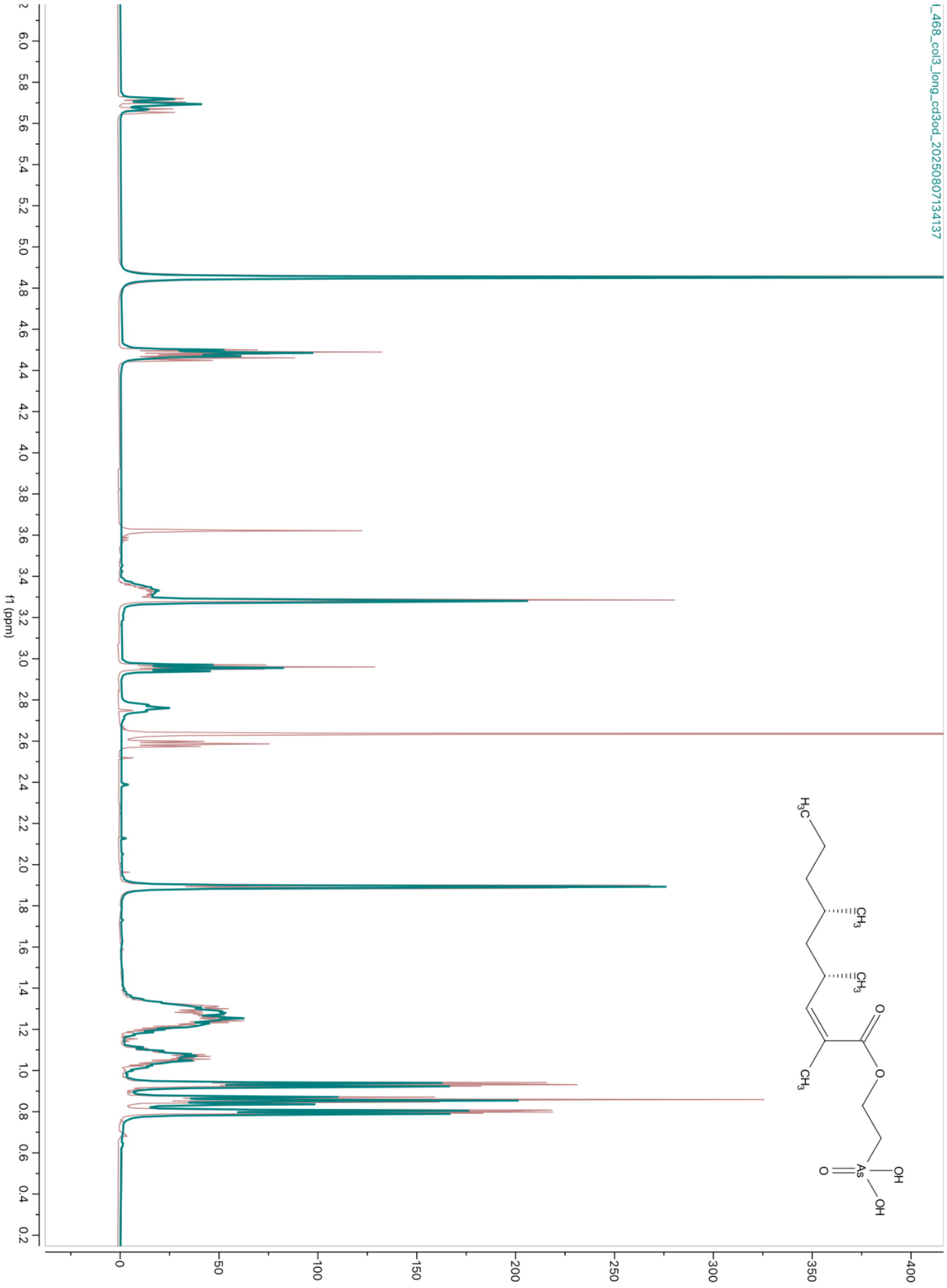
^{1}H NMR spectrum of **1** in CD_2Cl_2



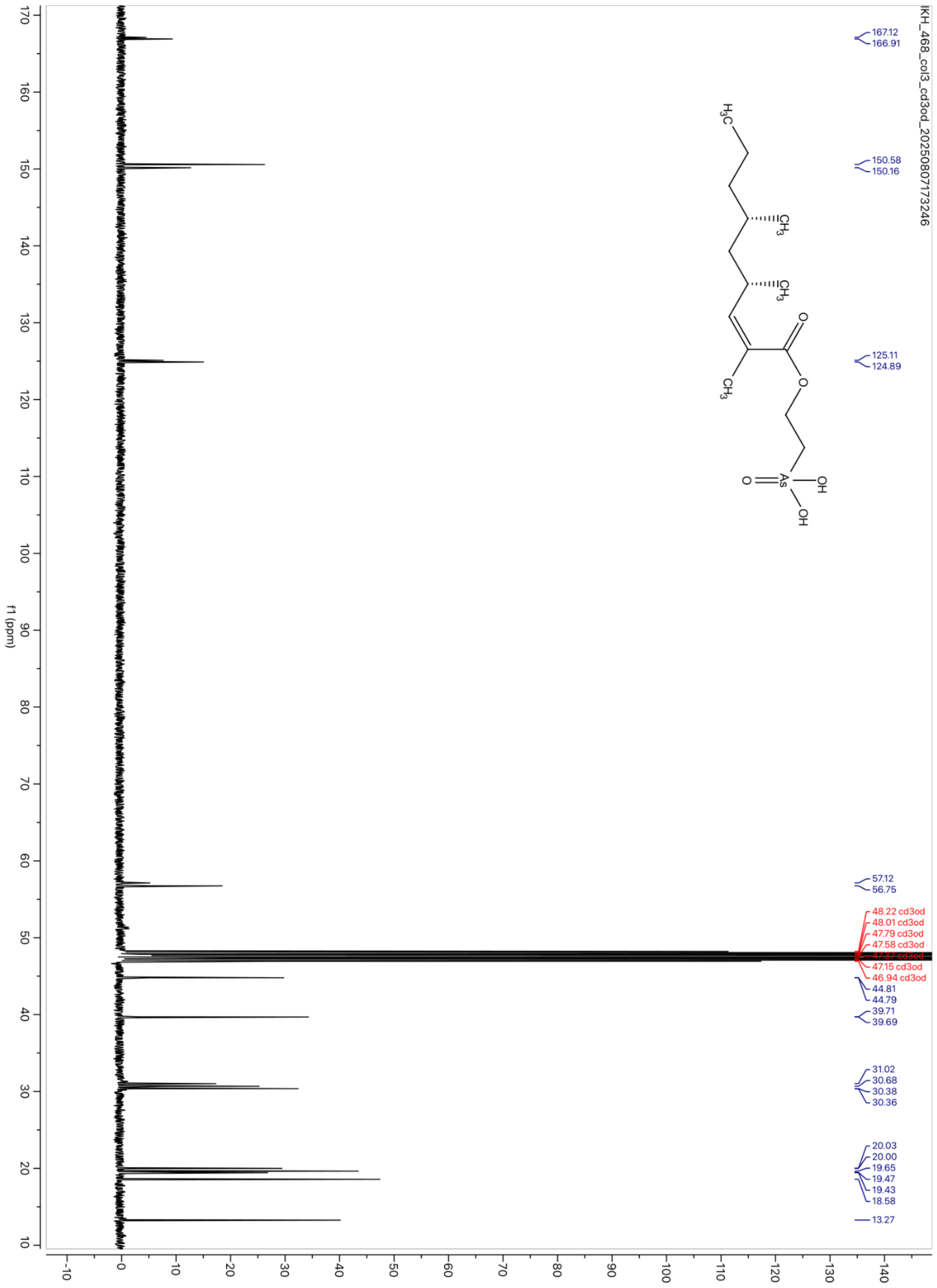
^{1}H NMR spectrum of **1** in CD_3OD



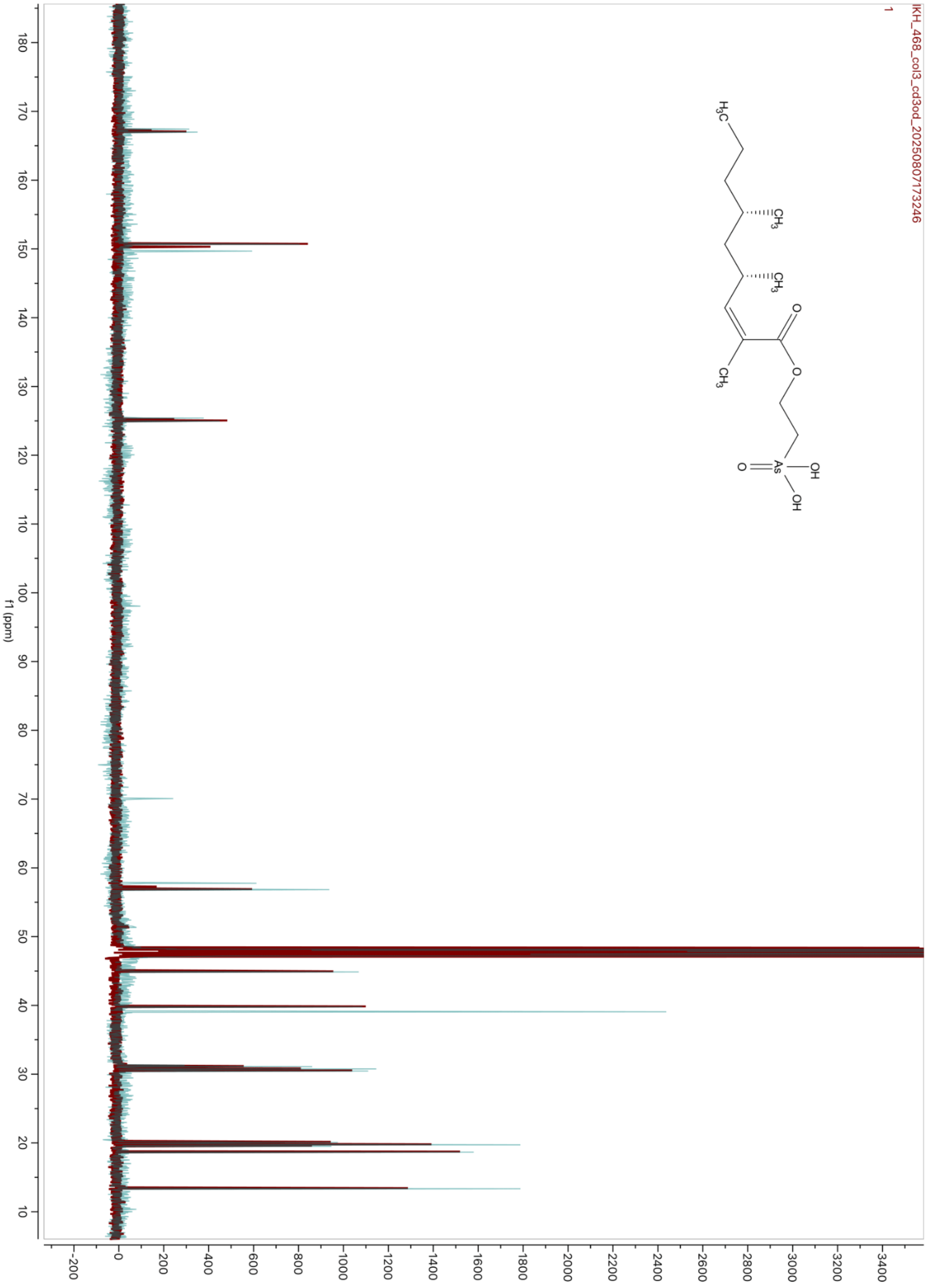
Overlayed ^1H NMR spectra of synthetic (cyan) and natural (maroon) ***1*** *in CD_3OD*



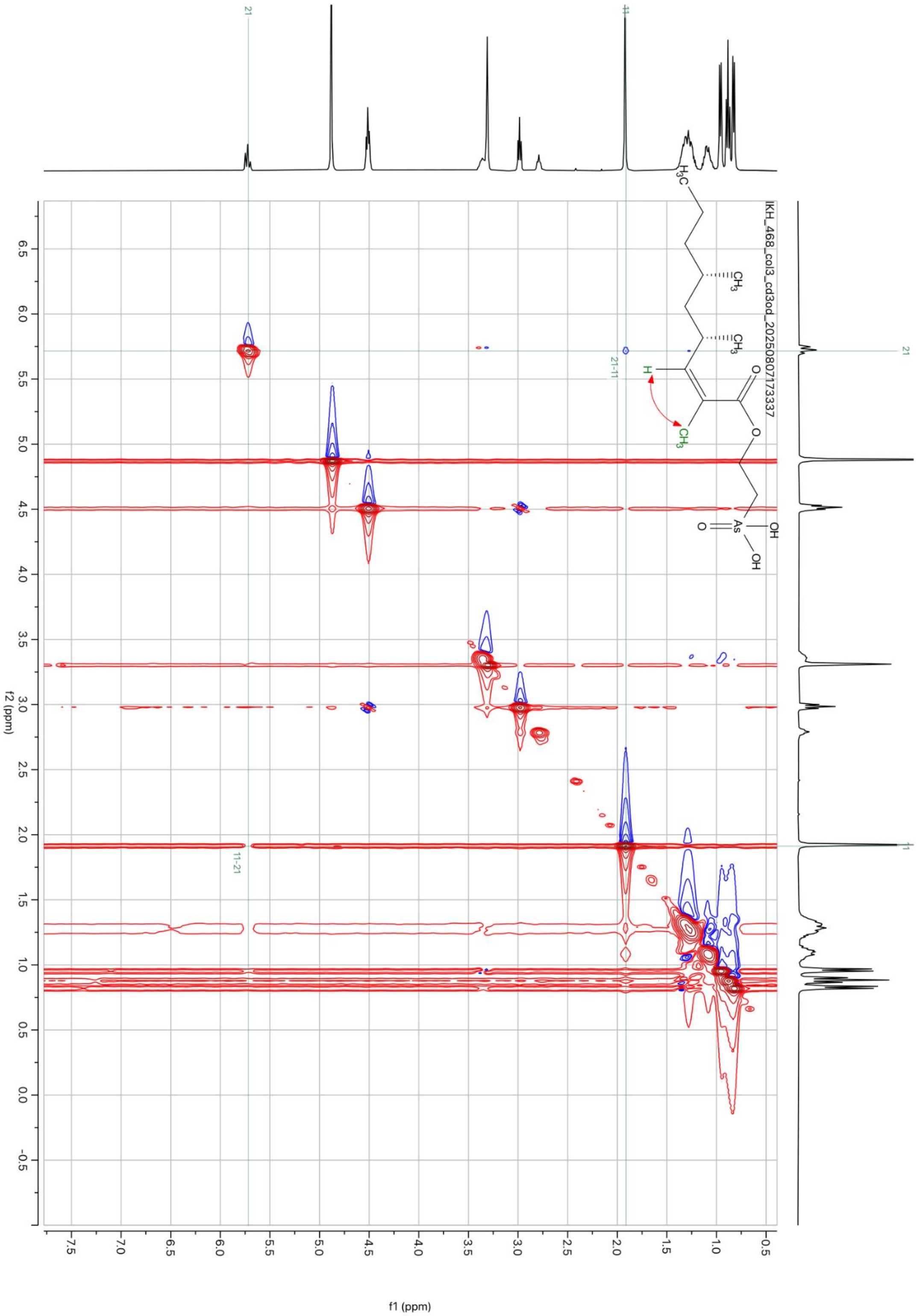
*^{13}C NMR spectrum of synthetic **1** in CD_3OD*



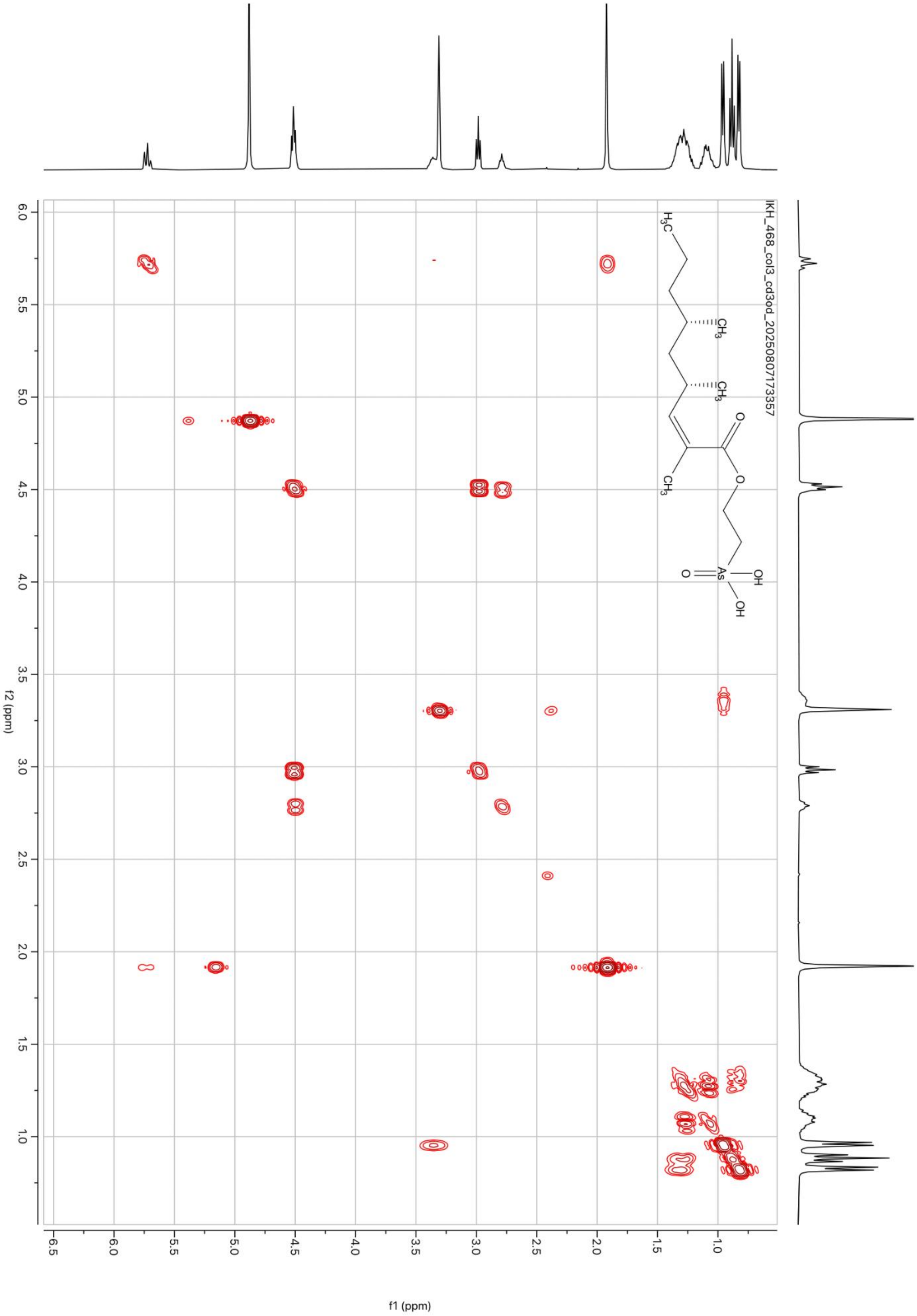
Overlayed ^{13}C NMR spectra of synthetic (maroon) and natural (cyan) ***1*** *in CD_3OD*



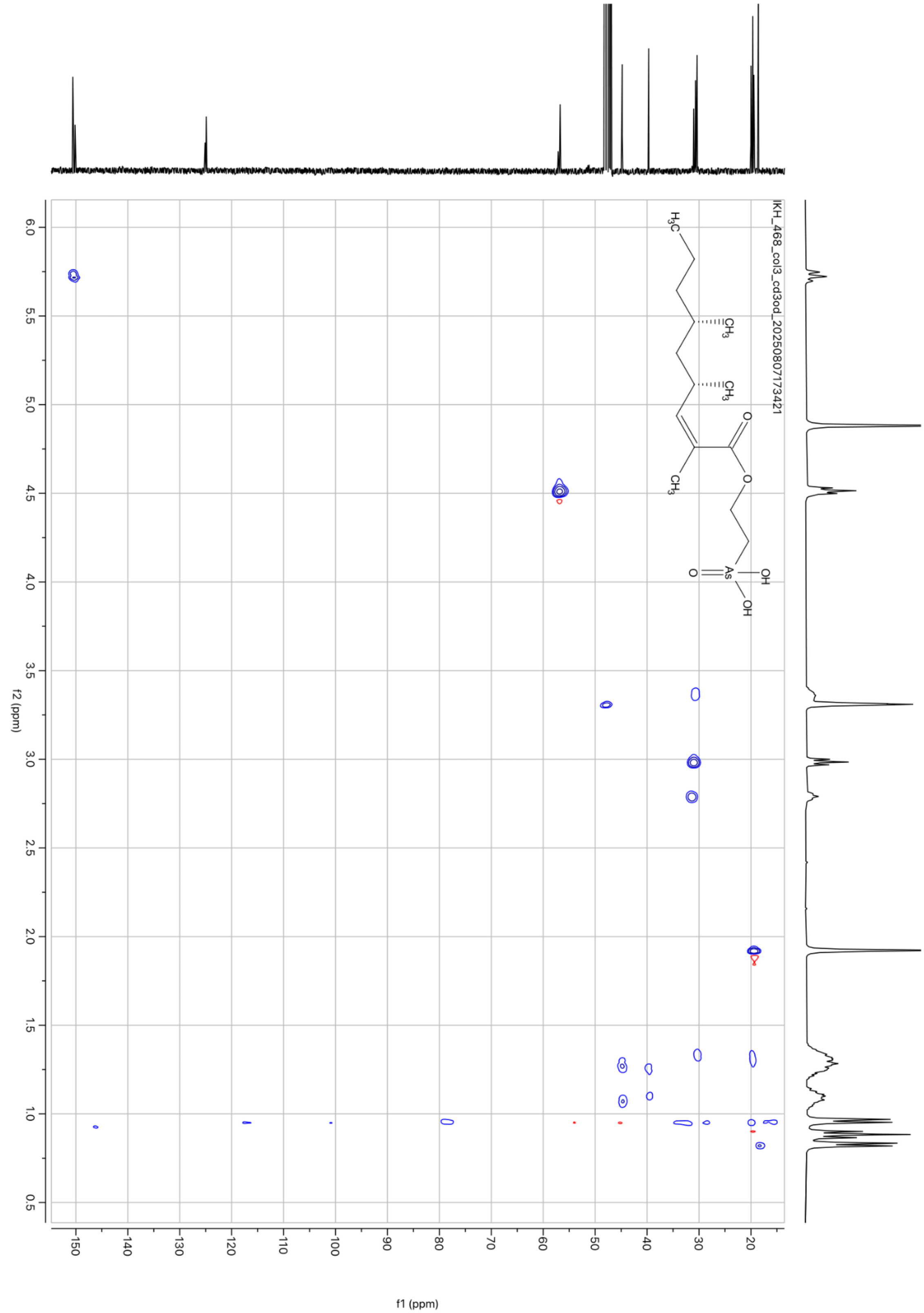
*2D NOESY spectrum of synthetic **1** in CD_3OD*

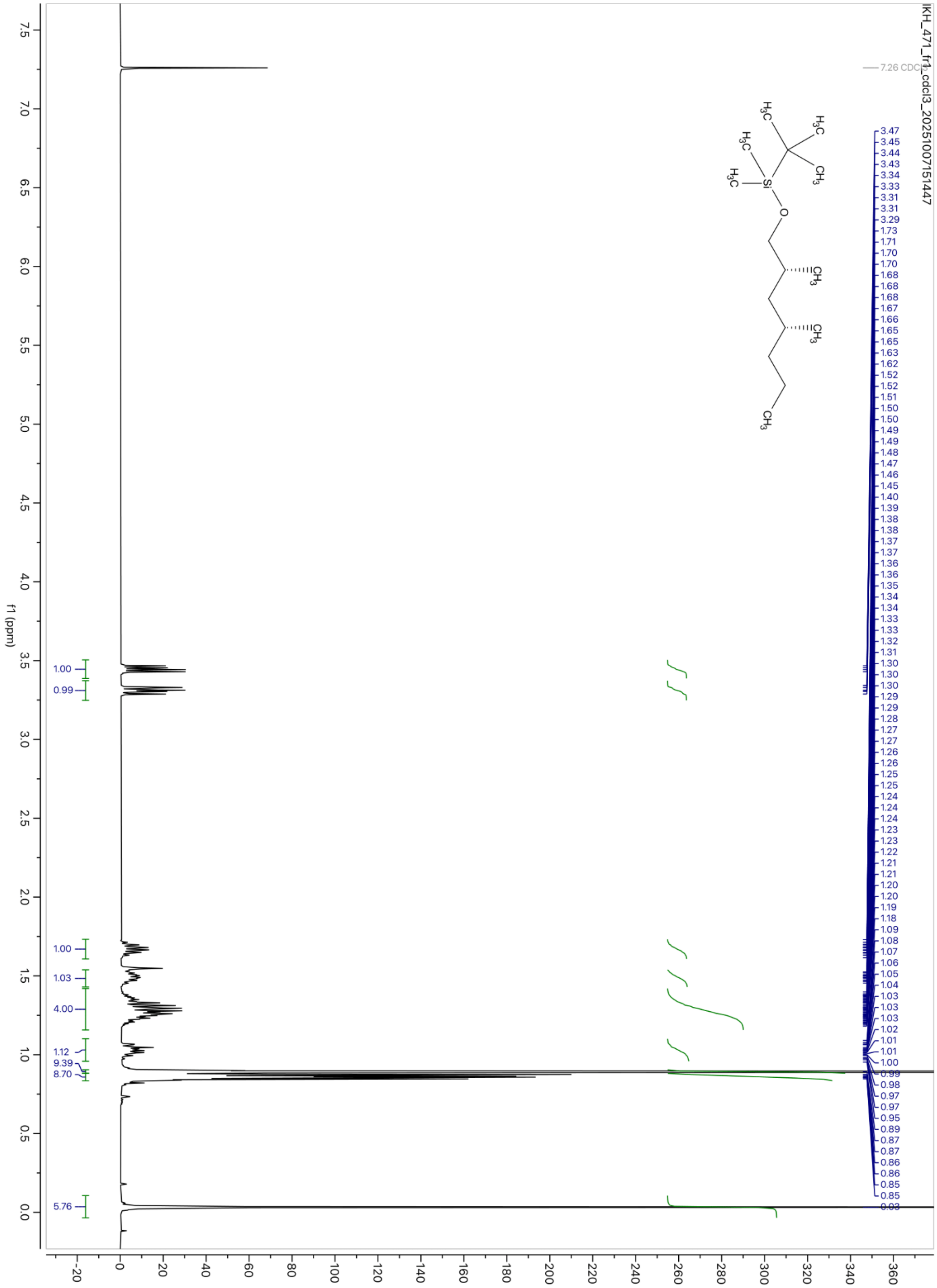


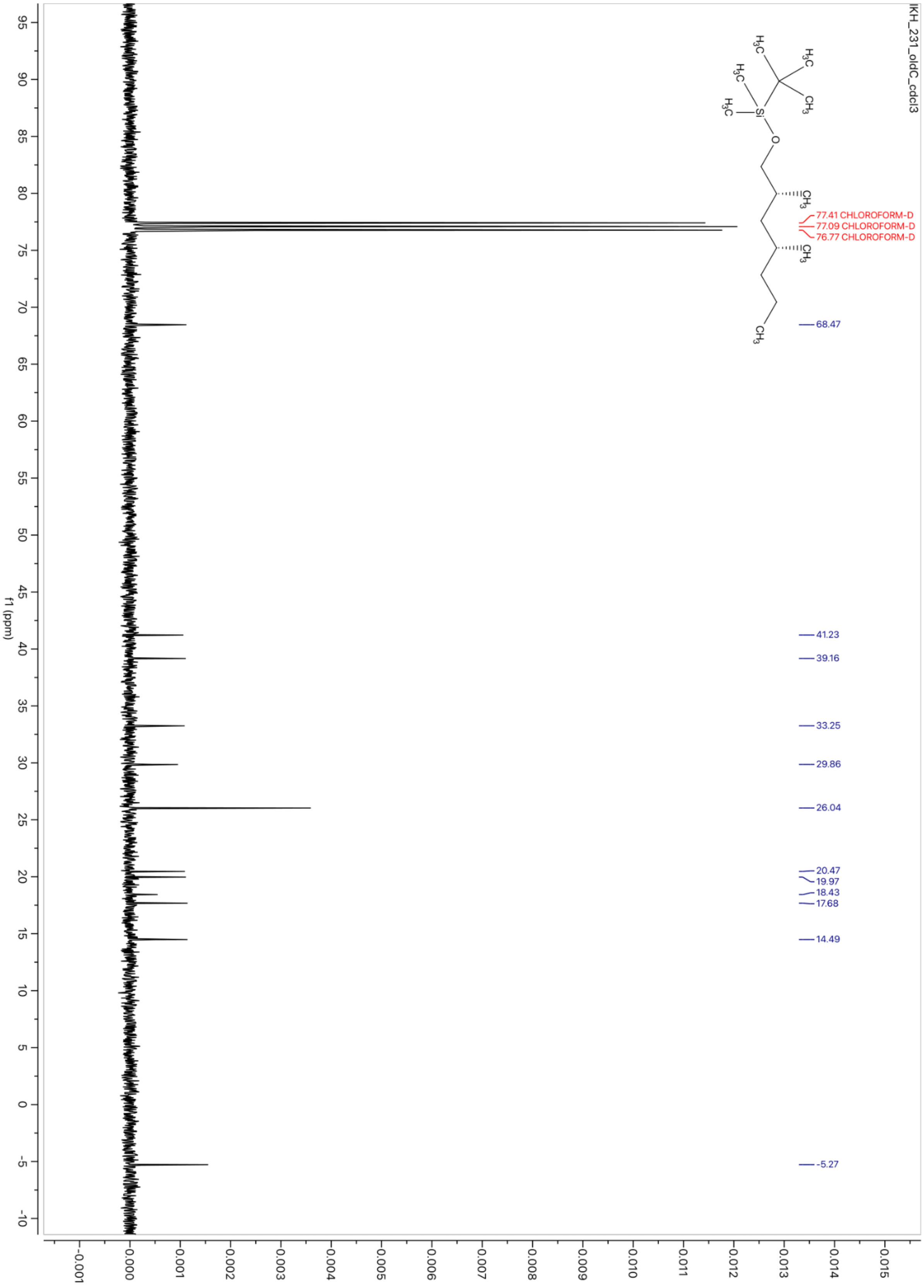
*COSY spectrum of synthetic **1** in CD_3OD*

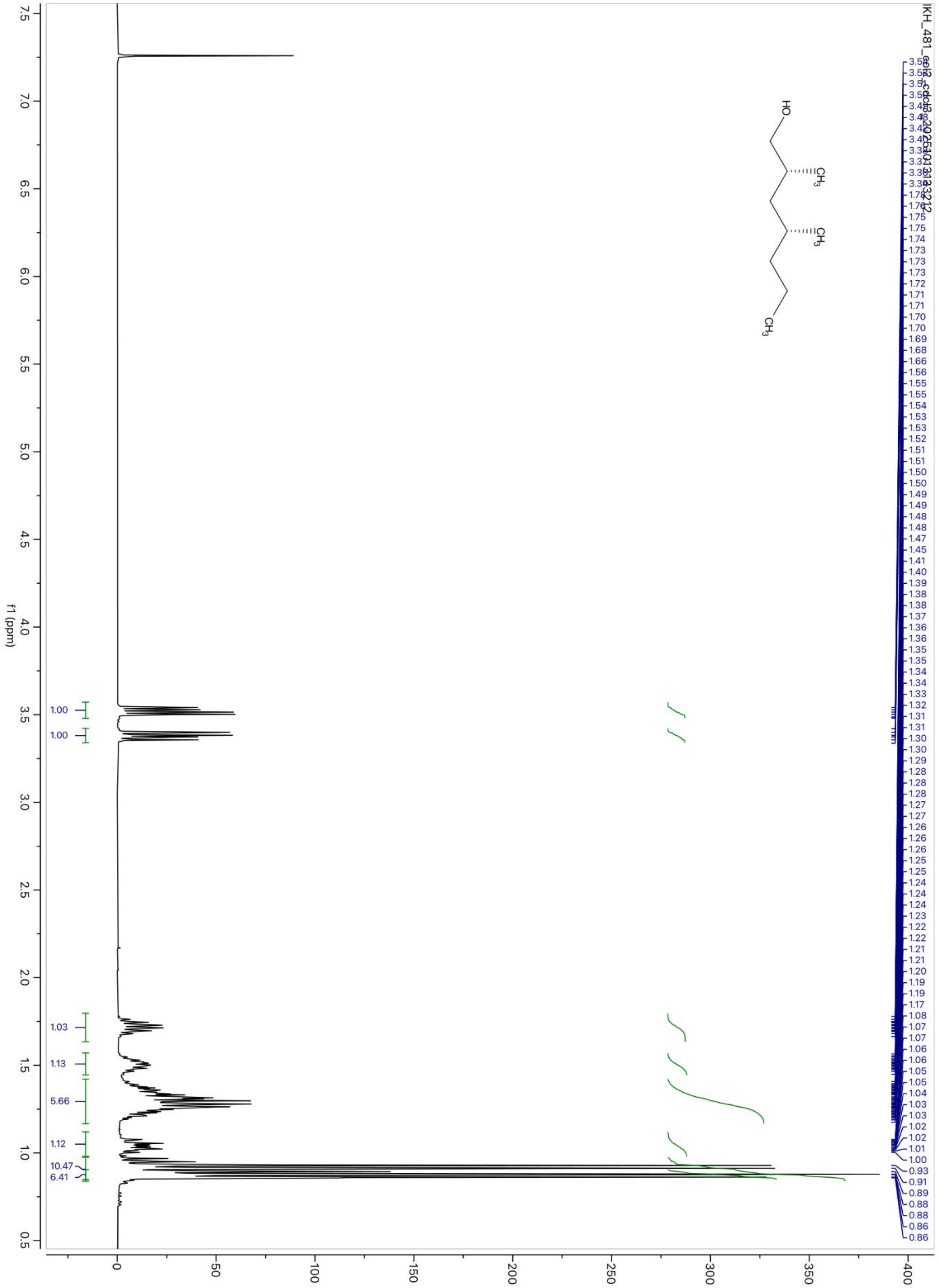


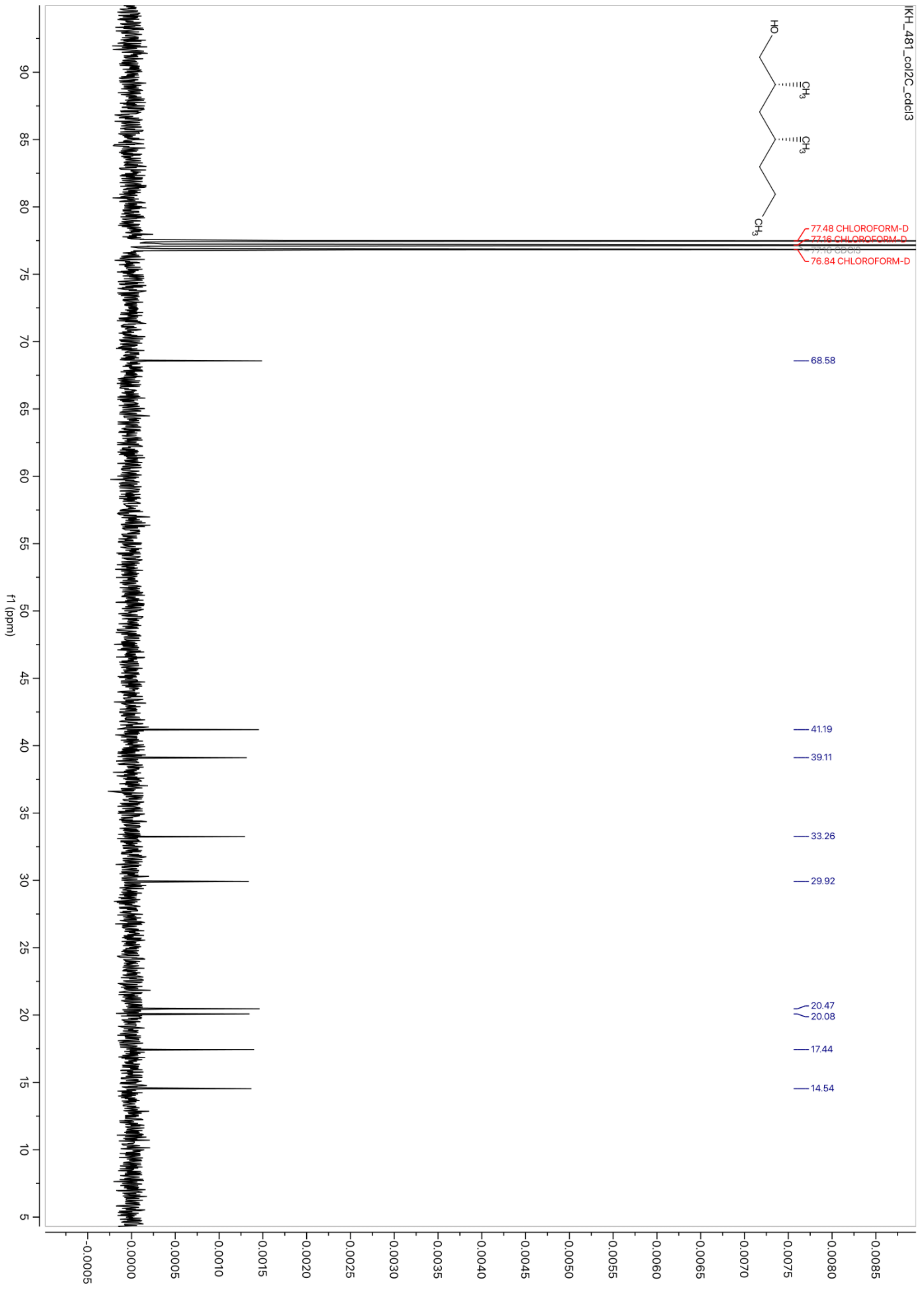
HSQC spectrum of synthetic ***1*** *in CD_3OD*

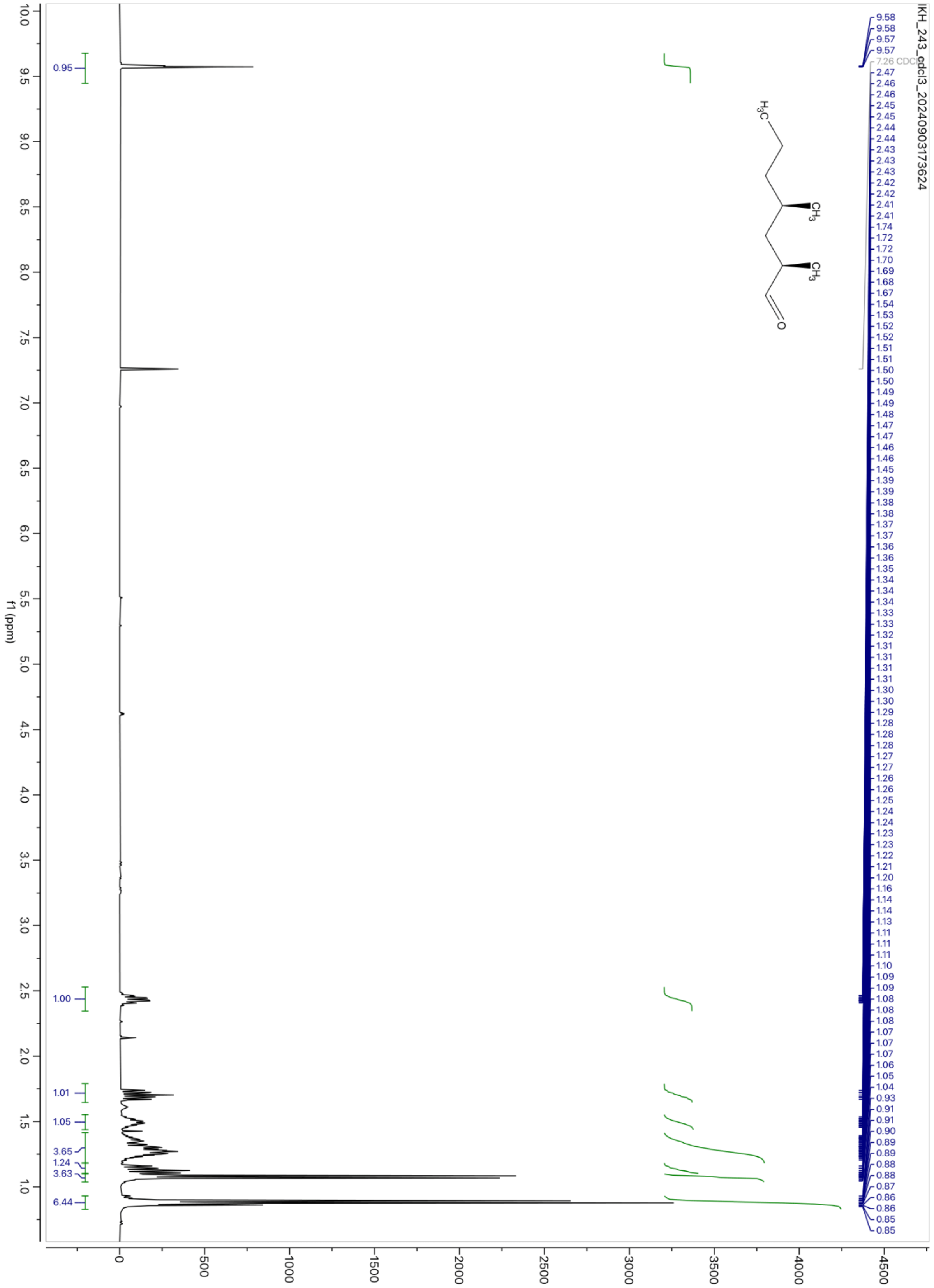


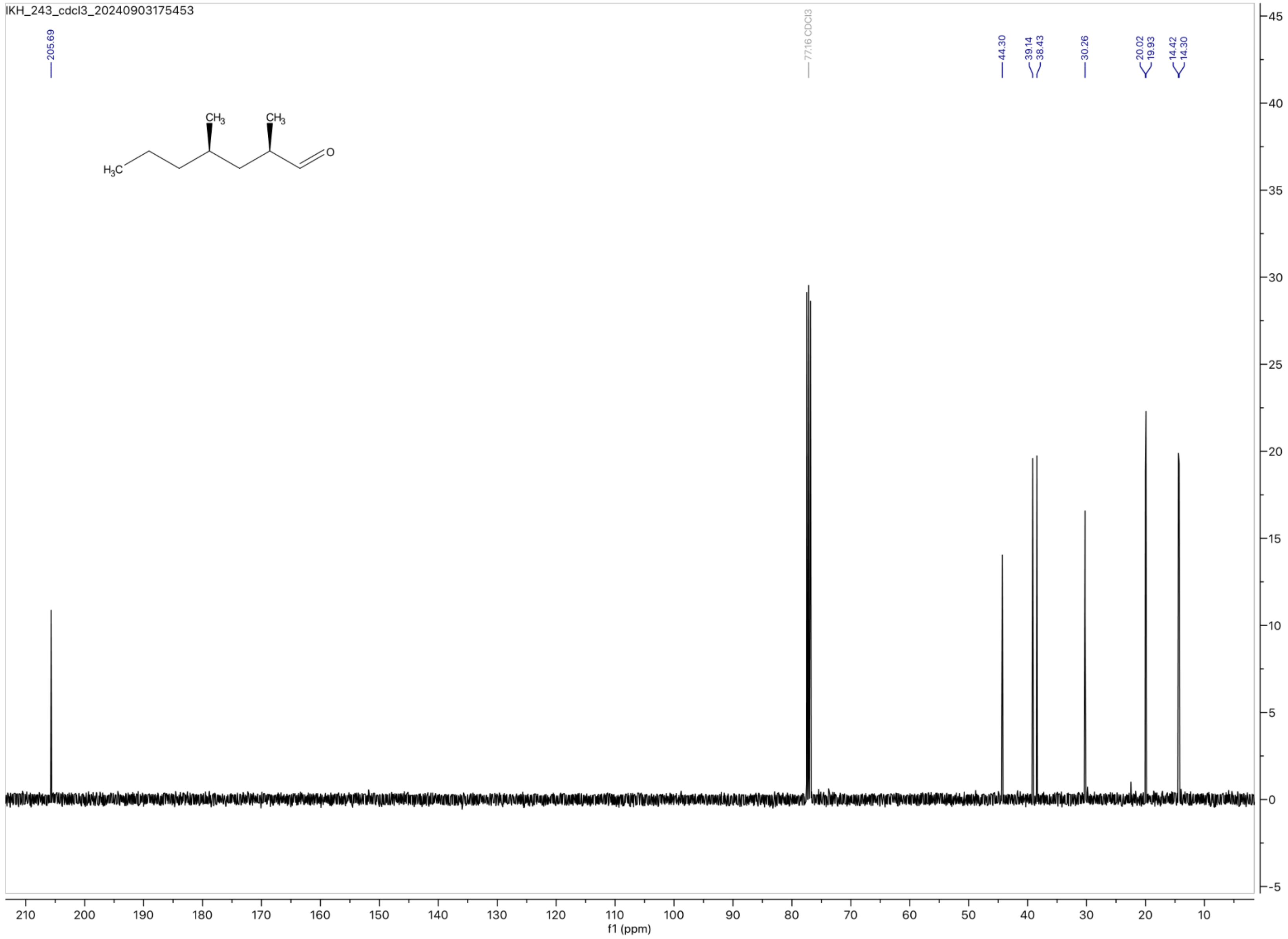

IKH_471_fr1_cdcl3_20251007151447
7.26 CDCl3
H3C
H3C
CH3
H3C
Si
H3C
O
CH3
CH3
CH3
3.47
3.45
3.44
3.43
3.34
3.33
3.31
3.31
3.29
1.73
1.71
1.70
1.70
1.68
1.68
1.68
1.67
1.66
1.65
1.65
1.63
1.62
1.52
1.52
1.51
1.50
1.50
1.49
1.49
1.48
1.47
1.46
1.45
1.40
1.39
1.38
1.38
1.37
1.37
1.36
1.36
1.35
1.34
1.34
1.33
1.33
1.32
1.31
1.30
1.30
1.30
1.29
1.29
1.28
1.27
1.27
1.26
1.26
1.25
1.25
1.24
1.24
1.24
1.23
1.23
1.22
1.21
1.21
1.20
1.20
1.19
1.18
1.09
1.08
1.07
1.06
1.05
1.04
1.03
1.03
1.03
1.02
1.01
1.01
1.00
0.99
0.98
0.97
0.97
0.95
0.89
0.87
0.87
0.86
0.86
0.85
0.85
0.03
1.00
0.99
1.00
1.03
4.00
1.12
9.39
8.70
5.76
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-20
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
340
360


IKH_231_oldC_cdcl3
H_3C
H_3C
CH_3
H_3C
H_3C
Si
O
CH_3
CH_3
CH_3
77.41 CHLOROFORM-D
77.09 CHLOROFORM-D
76.77 CHLOROFORM-D
68.47
41.23
39.16
33.25
29.86
26.04
20.47
19.97
18.43
17.68
14.49
-5.27
f1 (ppm)
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-0.001
0.000
0.001
0.002
0.003
0.004
0.005
0.006
0.007
0.008
0.009
0.010
0.011
0.012
0.013
0.014
0.015

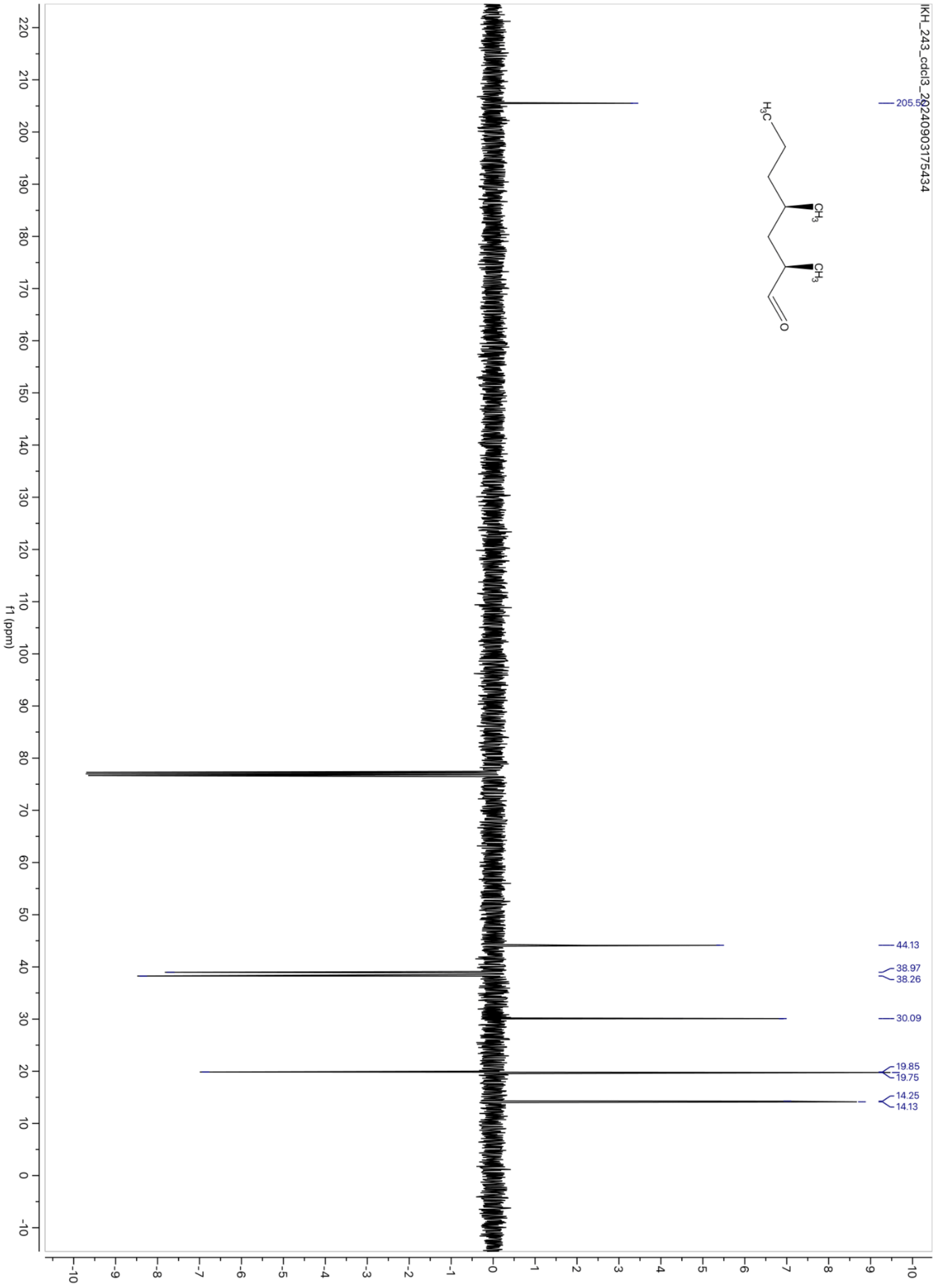

IKH_481
HO
CH3
CH3
CH3
3.53
3.52
3.51
3.50
3.48
3.48
3.40
3.40
3.38
3.37
3.36
3.34
1.78
1.76
1.75
1.75
1.74
1.73
1.73
1.73
1.72
1.71
1.71
1.70
1.70
1.69
1.68
1.66
1.56
1.55
1.55
1.54
1.53
1.53
1.52
1.51
1.51
1.50
1.50
1.49
1.49
1.48
1.48
1.47
1.45
1.41
1.40
1.39
1.38
1.38
1.37
1.36
1.36
1.35
1.35
1.34
1.34
1.33
1.32
1.31
1.31
1.30
1.30
1.29
1.28
1.28
1.28
1.27
1.27
1.26
1.26
1.26
1.25
1.25
1.24
1.24
1.24
1.23
1.22
1.22
1.21
1.21
1.20
1.19
1.19
1.17
1.08
1.07
1.07
1.06
1.06
1.05
1.05
1.04
1.03
1.03
1.02
1.02
1.01
1.00
0.93
0.91
0.89
0.88
0.88
0.86
0.86
1.00
1.00
1.03
1.13
5.66
1.12
10.47
6.41
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
0
50
100
150
200
250
300
350
400

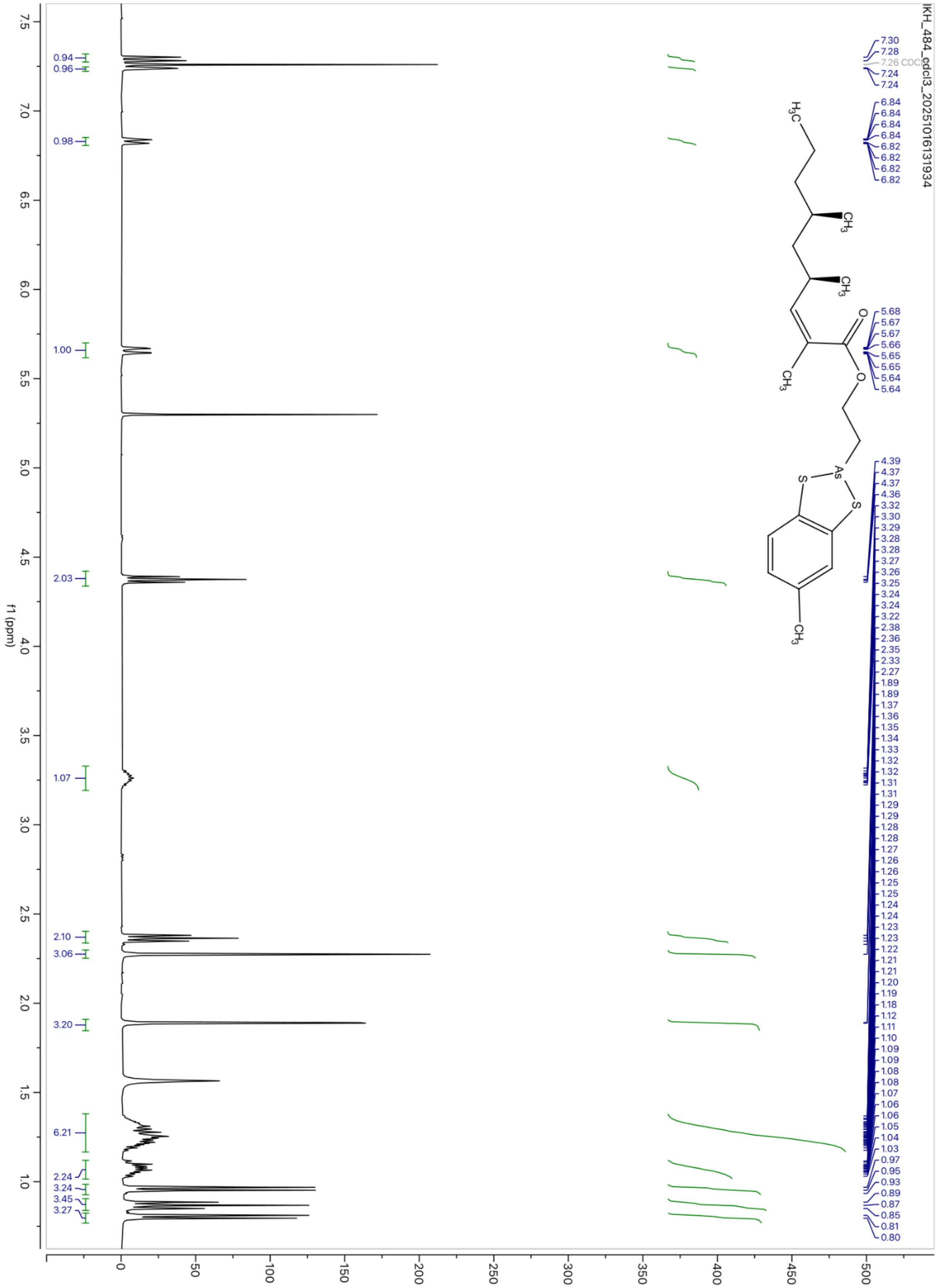

IKH_481_col2C_cdcl3
HO
CH3
CH3
CH3
77.48 CHLOROFORM-D
77.16 CHLOROFORM-D
77.16 CDCl3
76.84 CHLOROFORM-D
68.58
41.19
39.11
33.26
29.92
20.47
20.08
17.44
14.54
f1 (ppm)
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
-0.0005
0.0000
0.0005
0.0010
0.0015
0.0020
0.0025
0.0030
0.0035
0.0040
0.0045
0.0050
0.0055
0.0060
0.0065
0.0070
0.0075
0.0080
0.0085


IKH_243_cdcl3_20240903173624
9.58
9.58
9.57
9.57
7.26 CDCl3
2.47
2.46
2.46
2.45
2.45
2.44
2.44
2.43
2.43
2.43
2.42
2.42
2.41
2.41
1.74
1.72
1.72
1.70
1.69
1.68
1.67
1.54
1.53
1.52
1.52
1.51
1.51
1.50
1.50
1.49
1.49
1.48
1.47
1.47
1.46
1.46
1.45
1.39
1.39
1.38
1.38
1.37
1.37
1.36
1.36
1.35
1.34
1.34
1.34
1.33
1.33
1.32
1.31
1.31
1.31
1.31
1.30
1.30
1.29
1.28
1.28
1.28
1.27
1.27
1.26
1.26
1.25
1.24
1.24
1.23
1.23
1.22
1.21
1.20
1.16
1.14
1.14
1.13
1.11
1.11
1.11
1.10
1.09
1.09
1.08
1.08
1.08
1.08
1.07
1.07
1.07
1.06
1.05
1.04
0.93
0.91
0.91
0.90
0.89
0.89
0.88
0.88
0.87
0.86
0.86
0.85
0.85
H3C
CH3
CH3
O
0.95
1.00
1.01
1.05
3.65
1.24
3.63
6.44
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)
0
500
1000
1500
2000
2500
3000
3500
4000
4500

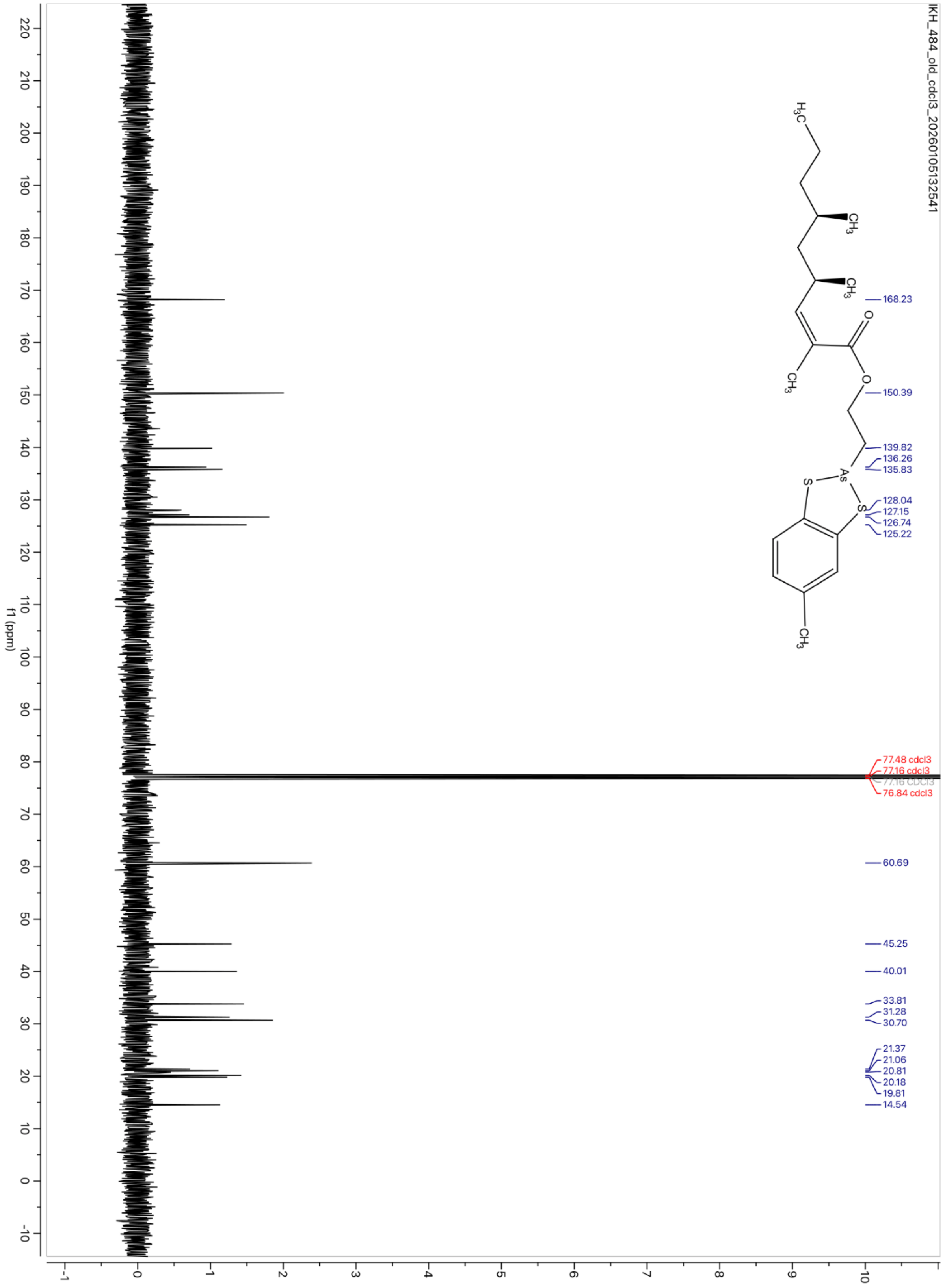

IKH_243_cdcl3_20240903175453
205.69
77.16 CDCl3
44.30
39.14
38.43
30.26
20.02
19.93
14.42
14.30
CH_3
CH_3
H_3C
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)
45
40
35
30
25
20
15
10
5
0
-5

APT spectrum of **ent-5**

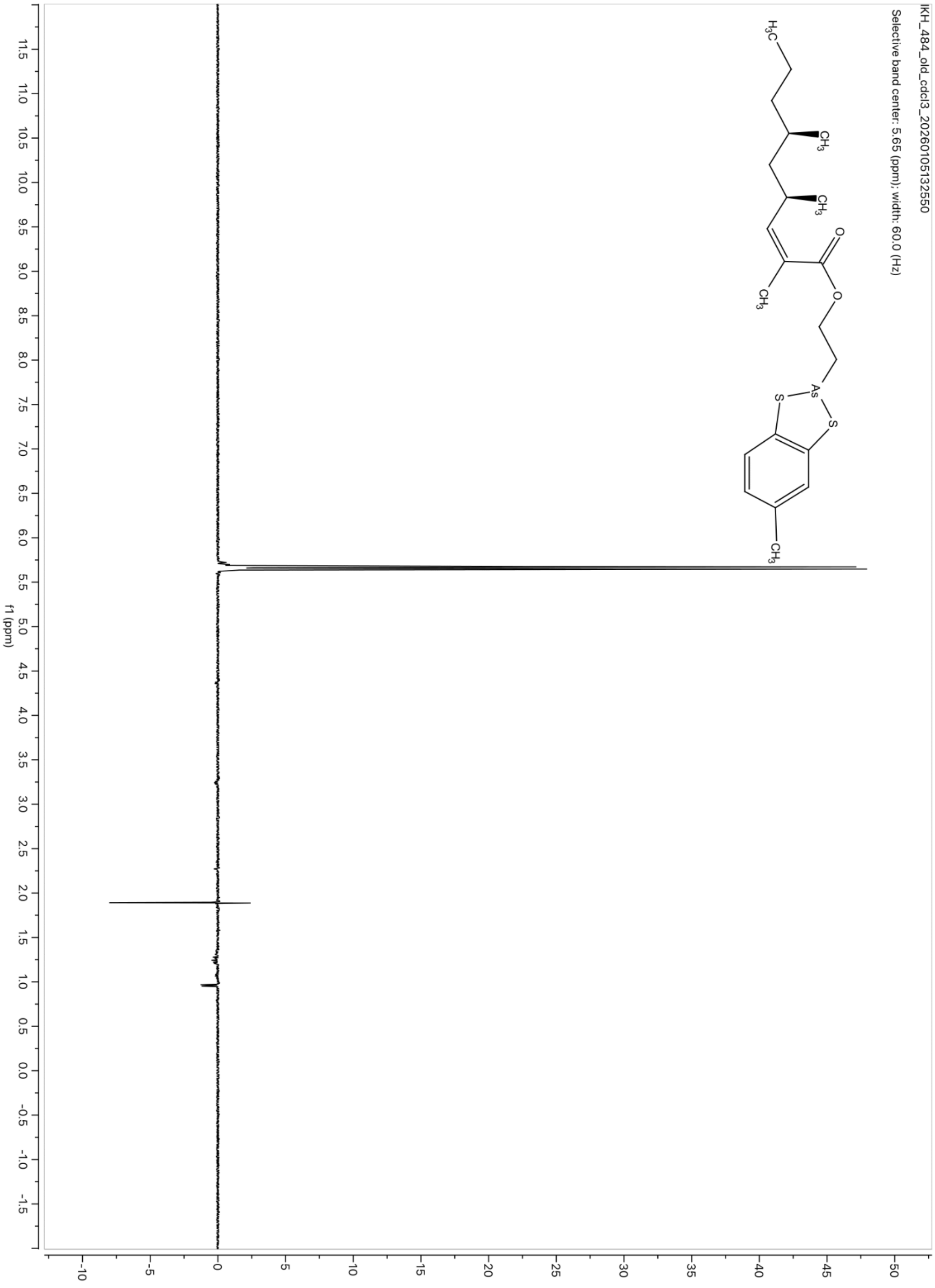




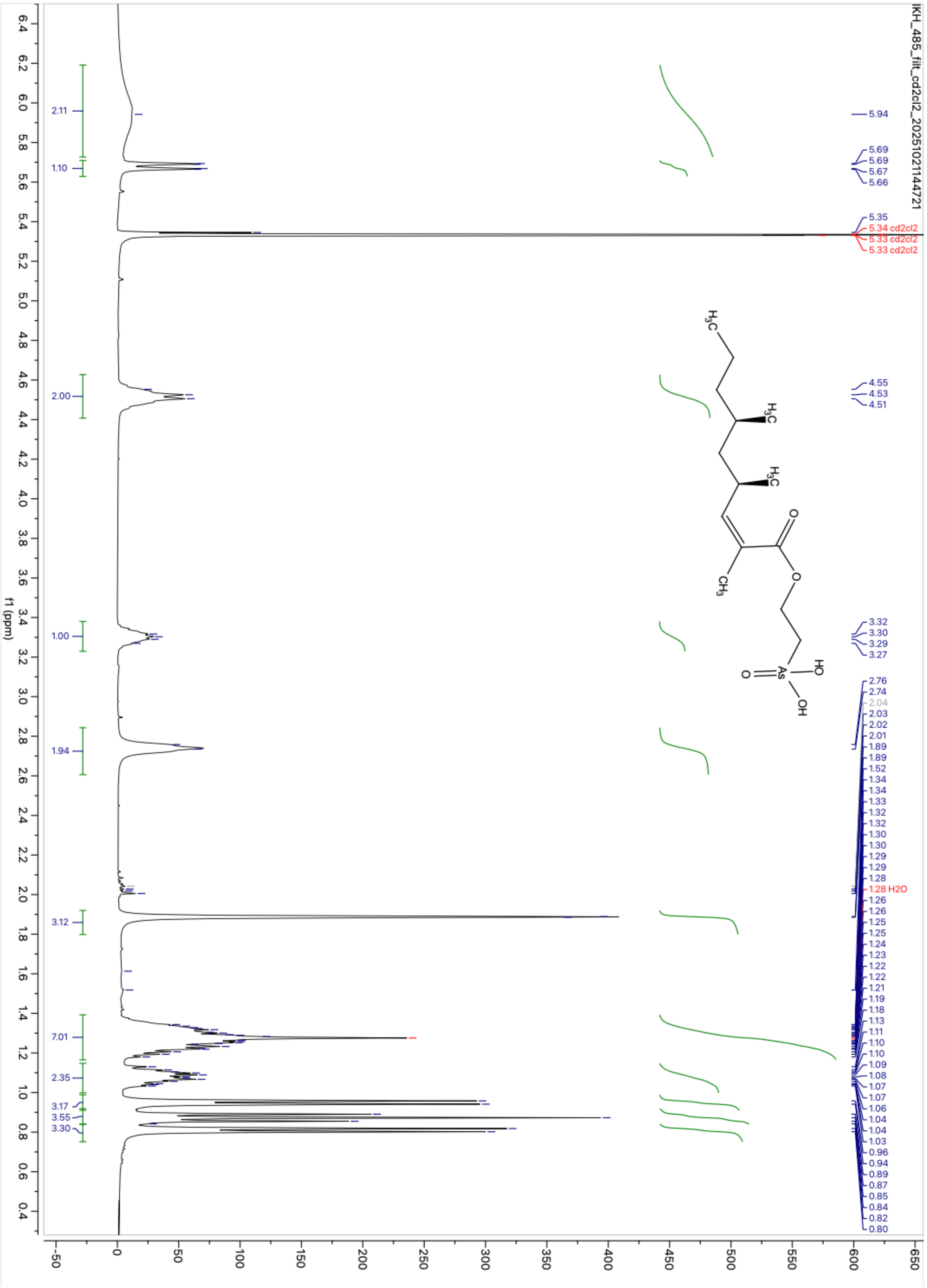
IKH_484_cdcl3_20251016131934
7.30
7.28
7.26 CDCl3
7.24
7.24
6.84
6.84
6.84
6.84
6.82
6.82
6.82
6.82
5.68
5.67
5.67
5.66
5.65
5.65
5.64
5.64
4.39
4.37
4.37
4.36
3.32
3.30
3.29
3.28
3.28
3.27
3.26
3.25
3.24
3.24
3.22
2.38
2.36
2.35
2.33
2.27
1.89
1.89
1.37
1.36
1.35
1.34
1.33
1.32
1.32
1.31
1.31
1.29
1.29
1.28
1.28
1.27
1.26
1.26
1.25
1.25
1.24
1.24
1.23
1.23
1.22
1.21
1.21
1.20
1.19
1.18
1.12
1.11
1.10
1.09
1.09
1.08
1.08
1.07
1.06
1.06
1.05
1.04
1.03
0.97
0.95
0.93
0.89
0.87
0.85
0.81
0.80
H3C
CH3
CH3
O
O
CH3
As
S
S
CH3
0.94
0.96
0.98
1.00
2.03
1.07
2.10
3.06
3.20
6.21
2.24
3.24
3.45
3.27
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)
0
50
100
150
200
250
300
350
400
450
500


KH_484_old_cdcl3_20260105132541
H3C
CH3
CH3
O
O
CH3
As
S
S
CH3
168.23
150.39
139.82
136.26
135.83
128.04
127.15
126.74
125.22
77.48 cdcl3
77.16 cdcl3
77.16 CDCl3
76.84 cdcl3
60.69
45.25
40.01
33.81
31.28
30.70
21.37
21.06
20.81
20.18
19.81
14.54
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
-1
0
1
2
3
4
5
6
7
8
9
10

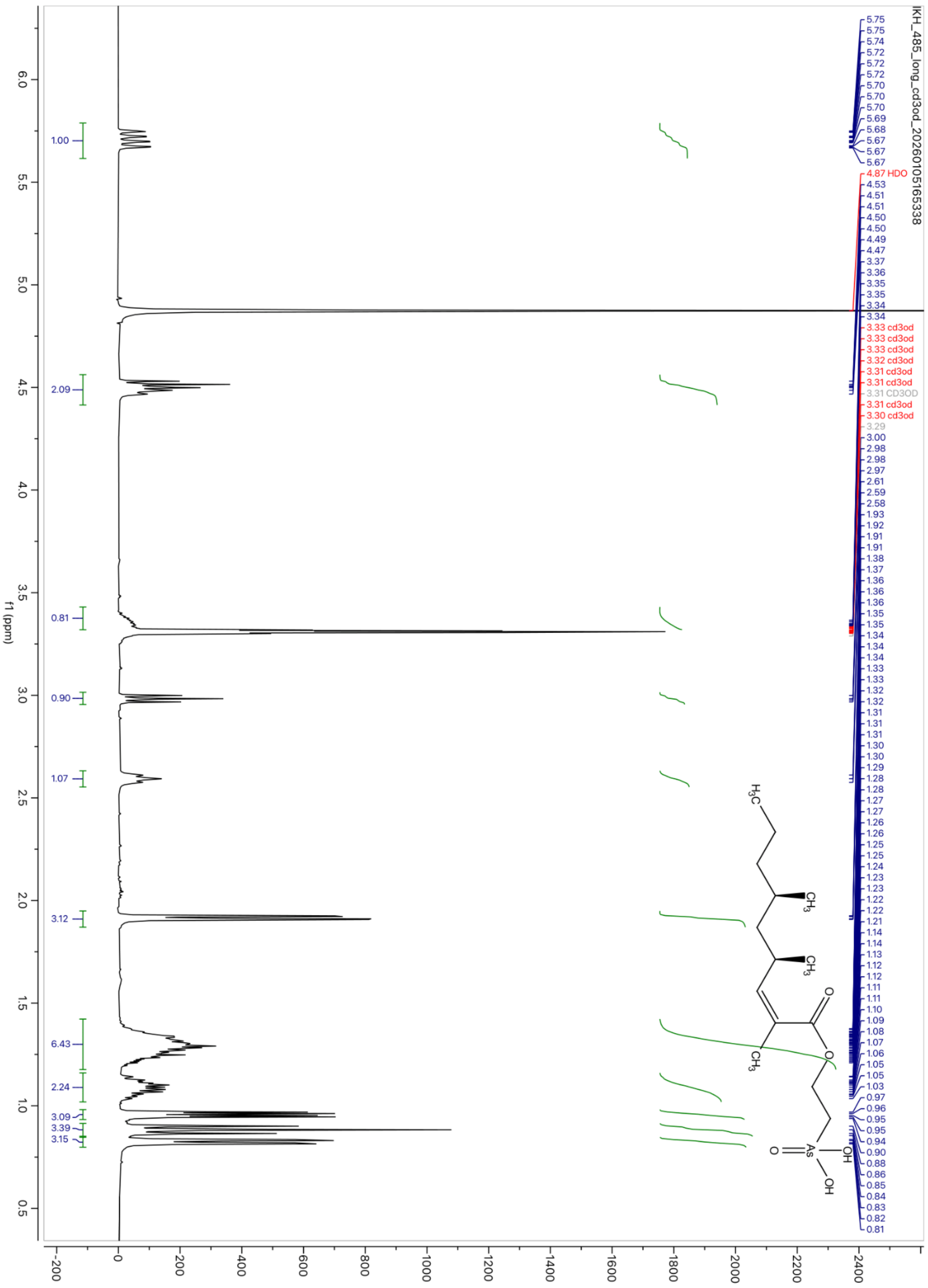
1D NOESY spectrum of ***ent-14***



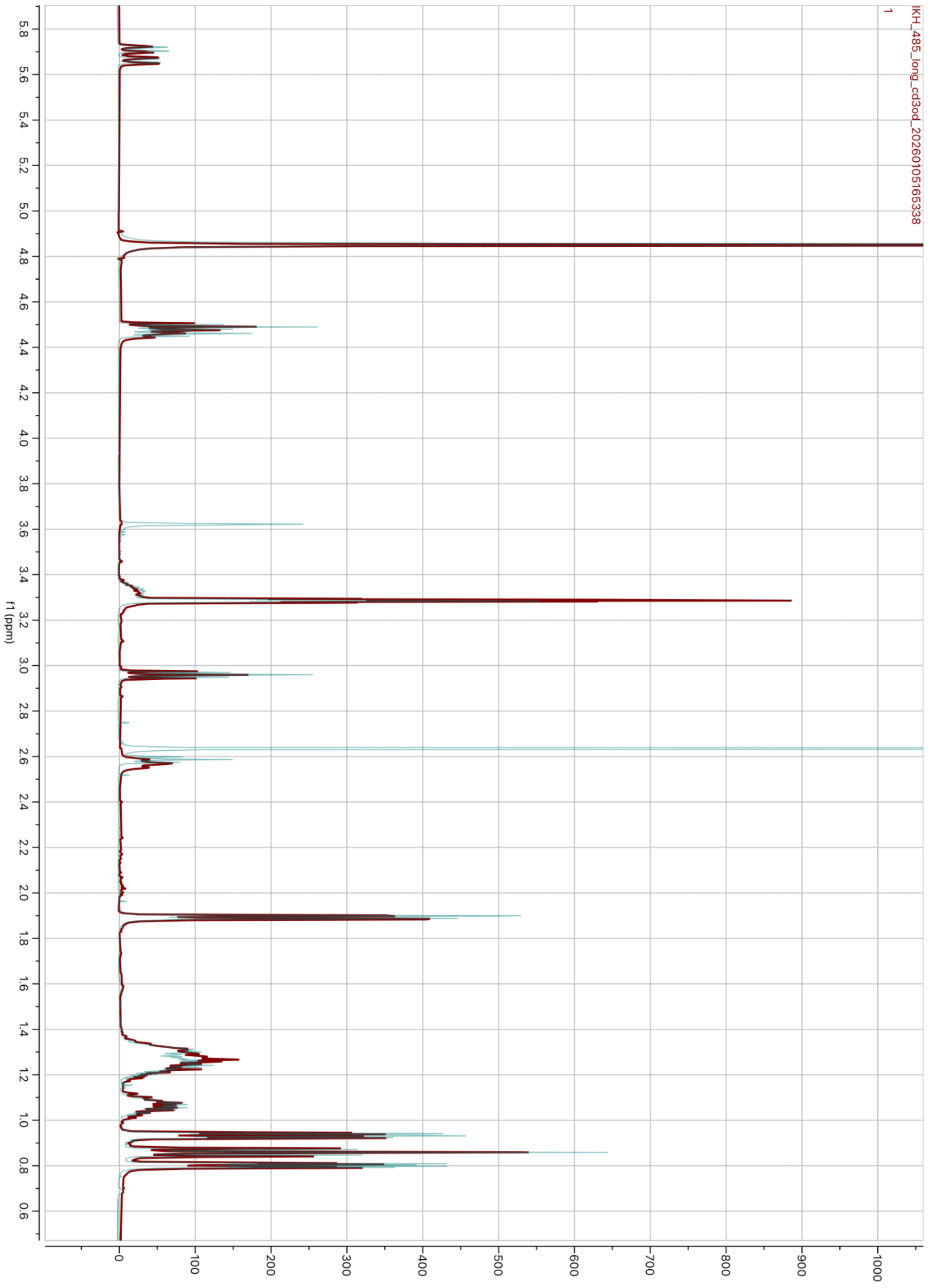
^1H *NMR spectrum of* ***ent-1*** *in* CD_2Cl_2



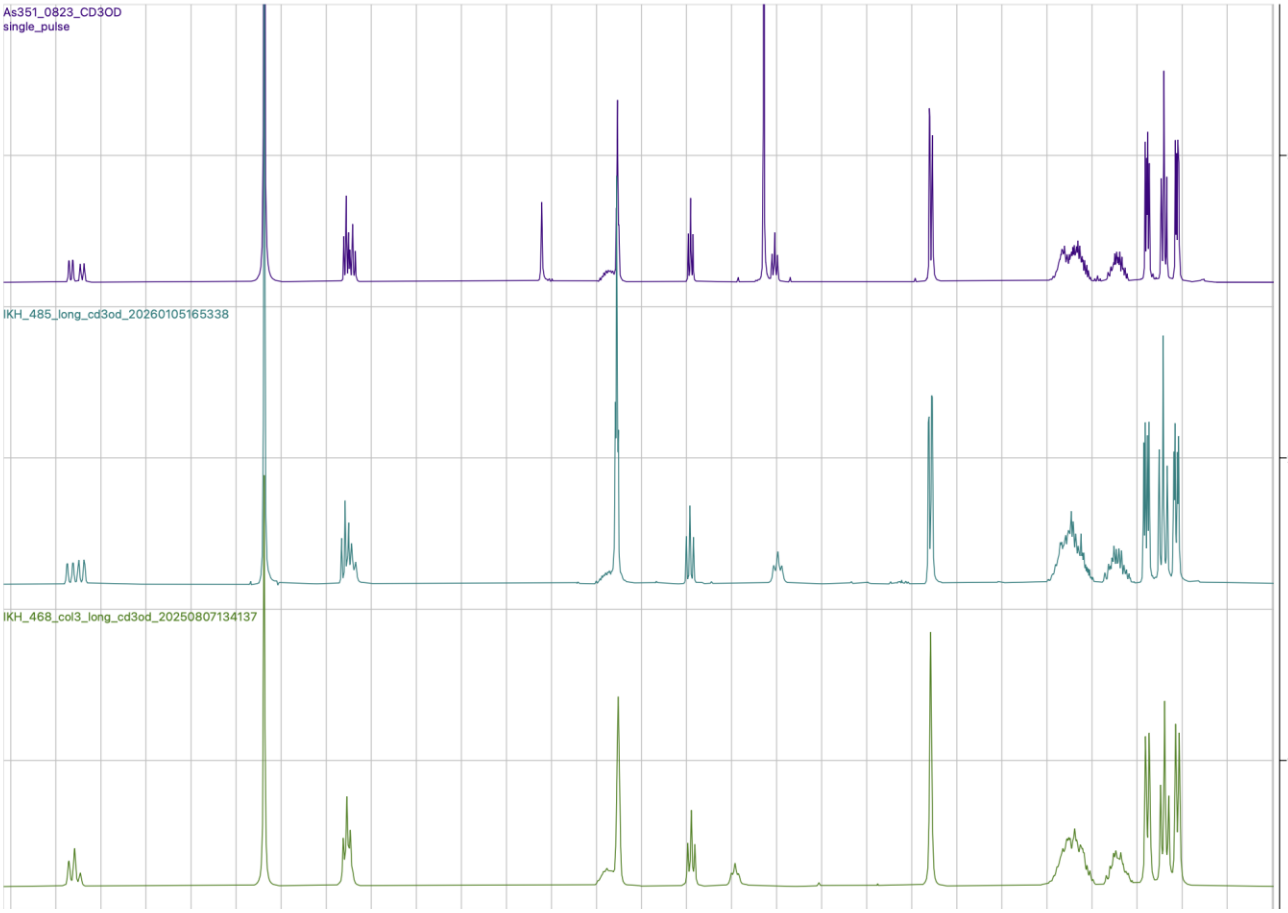
^1H *NMR spectrum of* ***ent-1*** *in* CD_3OD

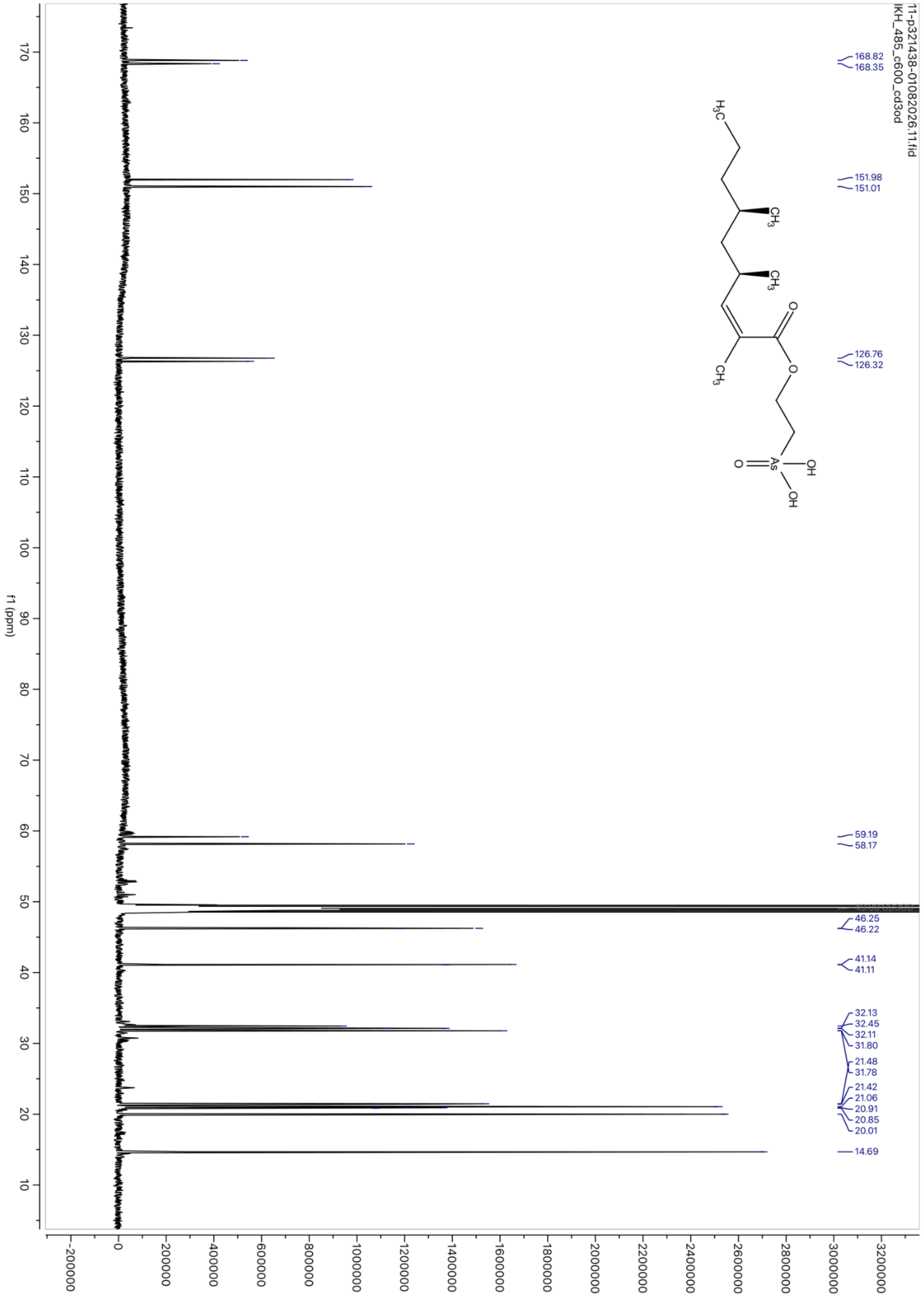

IKH_485_long_cd3od_20260105165338
5.75
5.75
5.74
5.72
5.72
5.72
5.70
5.70
5.70
5.69
5.68
5.67
5.67
5.67
4.87 HDO
4.53
4.51
4.51
4.50
4.50
4.49
4.47
3.37
3.36
3.35
3.35
3.34
3.34
3.33 cd3od
3.33 cd3od
3.33 cd3od
3.32 cd3od
3.31 cd3od
3.31 cd3od
3.31 CD3OD
3.31 cd3od
3.30 cd3od
3.29
3.00
2.98
2.98
2.97
2.61
2.59
2.58
1.93
1.92
1.91
1.91
1.38
1.37
1.36
1.36
1.36
1.35
1.35
1.34
1.34
1.34
1.33
1.33
1.32
1.32
1.31
1.31
1.31
1.30
1.30
1.29
1.28
1.28
1.27
1.27
1.26
1.26
1.25
1.25
1.24
1.23
1.23
1.22
1.22
1.21
1.14
1.14
1.13
1.12
1.12
1.11
1.11
1.10
1.09
1.08
1.07
1.06
1.05
1.05
1.03
0.97
0.96
0.95
0.95
0.94
0.90
0.88
0.86
0.85
0.84
0.83
0.82
0.81
1.00
2.09
0.81
0.90
1.07
3.12
6.43
2.24
3.09
3.39
3.15
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
-200
0
200
400
600
800
1000
1200
1400
1600
1800
2000
2200
2400
H_3C
CH_3
CH_3
CH_3
O
O
As
O
OH
OH

Overlayed ^{1}H NMR spectra of synthetic **ent-*1*** *(maroon) and natural* ***1*** *(cyan) in CD$_3$OD*

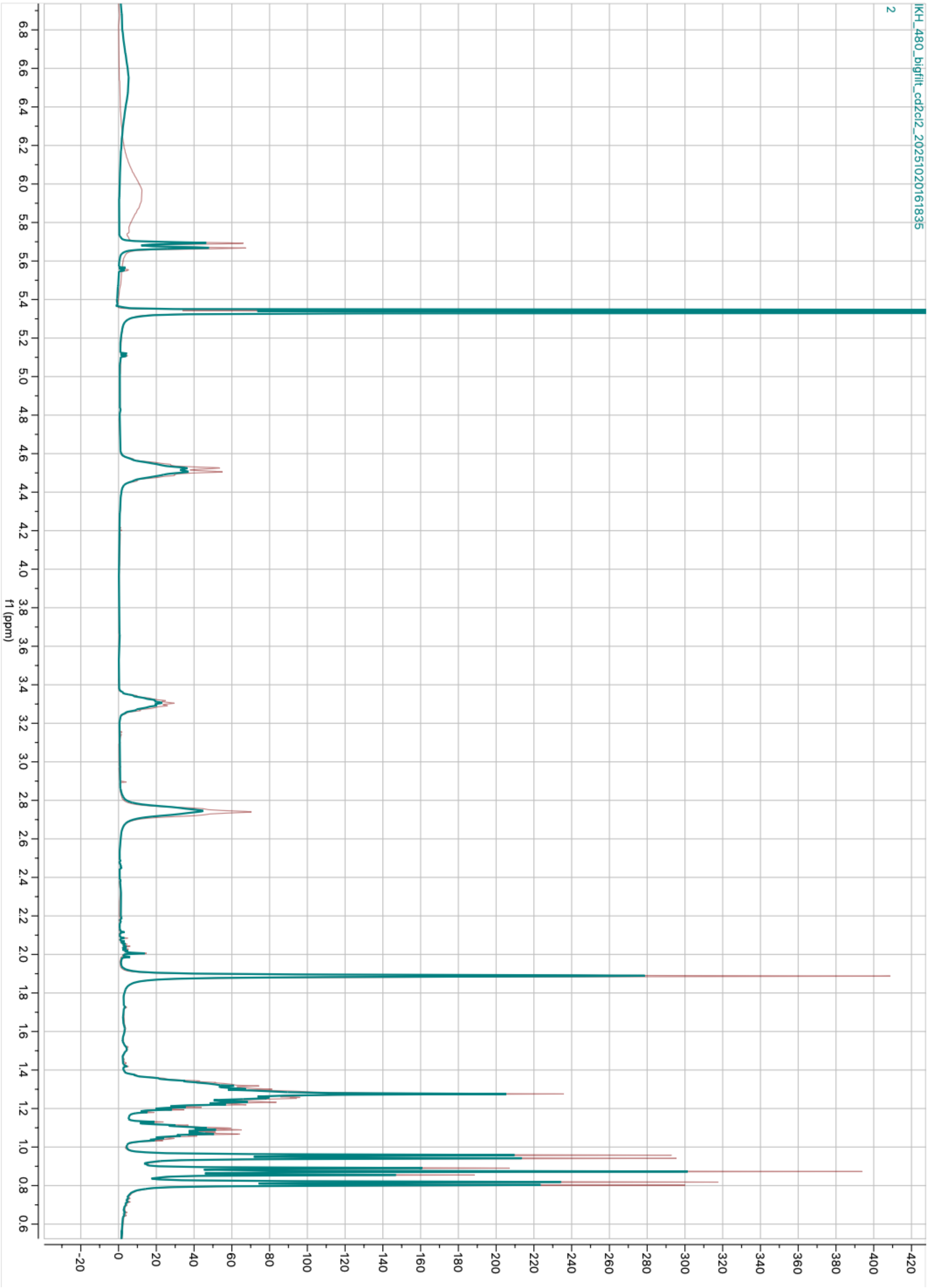


Overlayed ^{1}H NMR spectra of synthetic ***1*** *(bottom), synthetic* **ent-*1*** *(middle) and natural* ***1*** *(top) in CD_3OD*

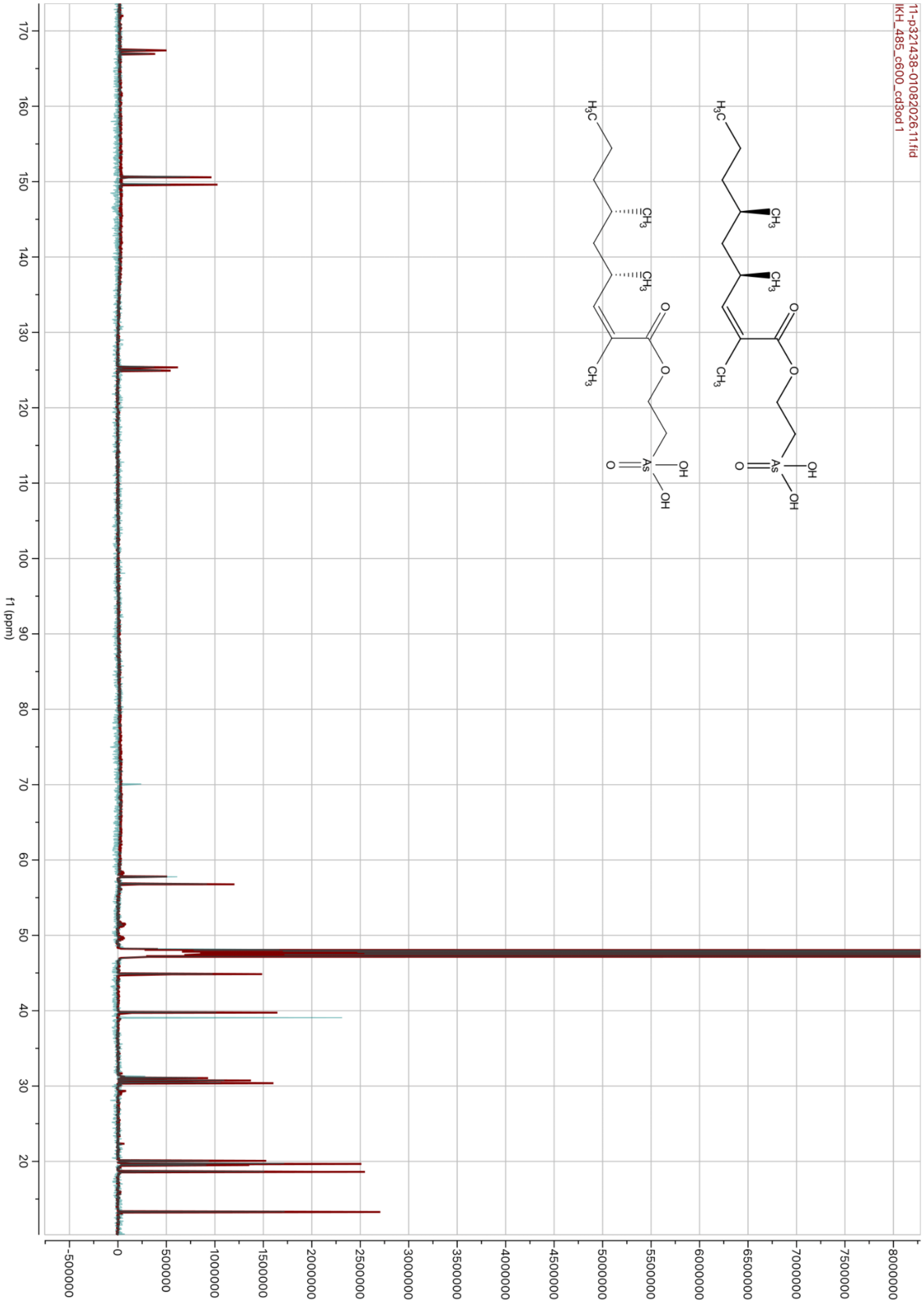



11-p321438-01082026.11.fid
KH_485_c600_cd3od
168.82
168.35
151.98
151.01
126.76
126.32
59.19
58.17
49.00 CD3OD
46.25
46.22
41.14
41.11
32.13
32.45
32.11
31.80
21.48
31.78
21.42
21.06
20.91
20.85
20.01
14.69
H3C
CH3
CH3
CH3
O
O
As
O
OH
OH
f1 (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
-200000
0
200000
400000
600000
800000
1000000
1200000
1400000
1600000
1800000
2000000
2200000
2400000
2600000
2800000
3000000
3200000

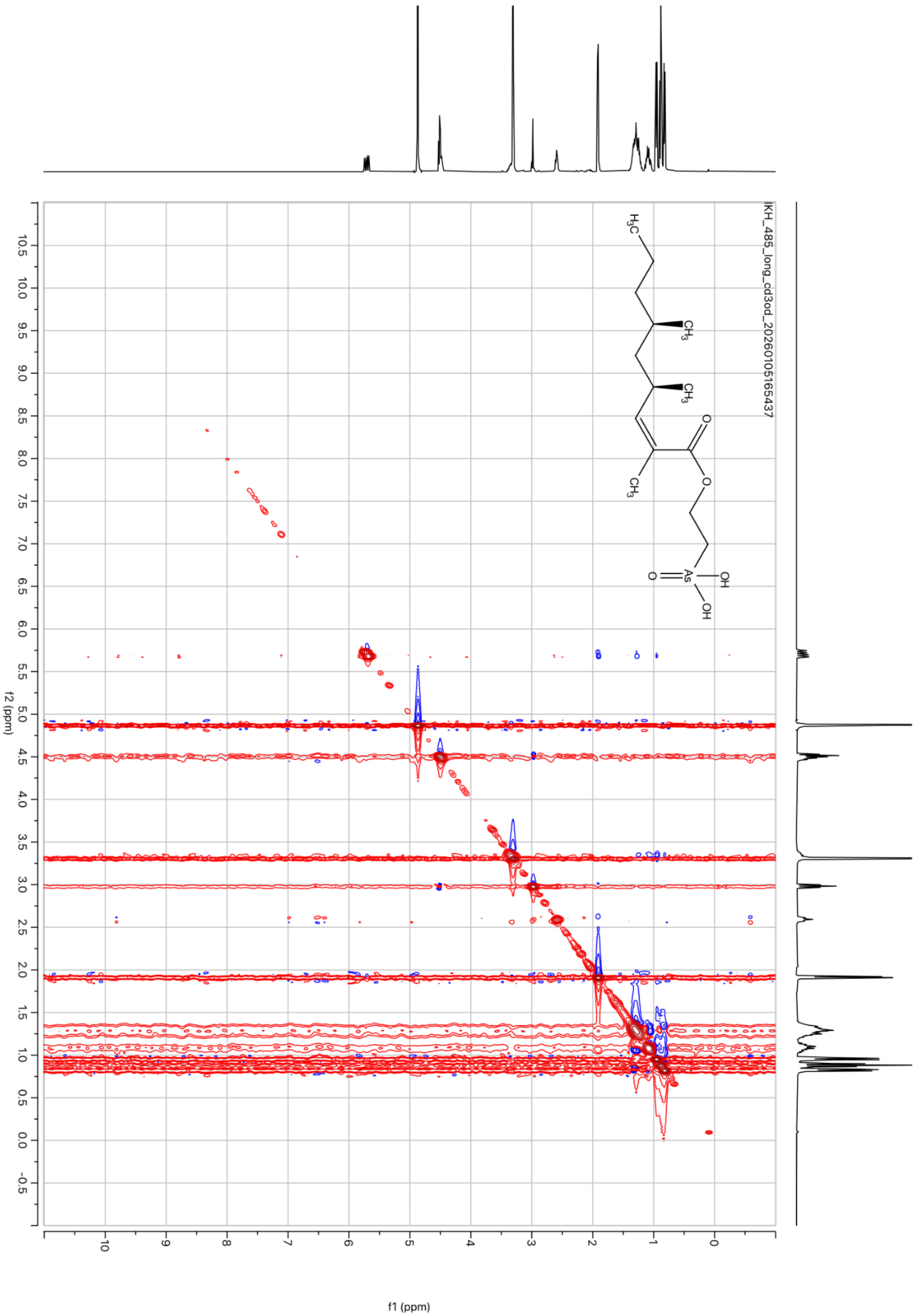
Overlayed ^{1}H NMR spectra of synthetic **ent-*1*** *(maroon) and synthetic* ***1*** *(cyan) in CD_2Cl_2*



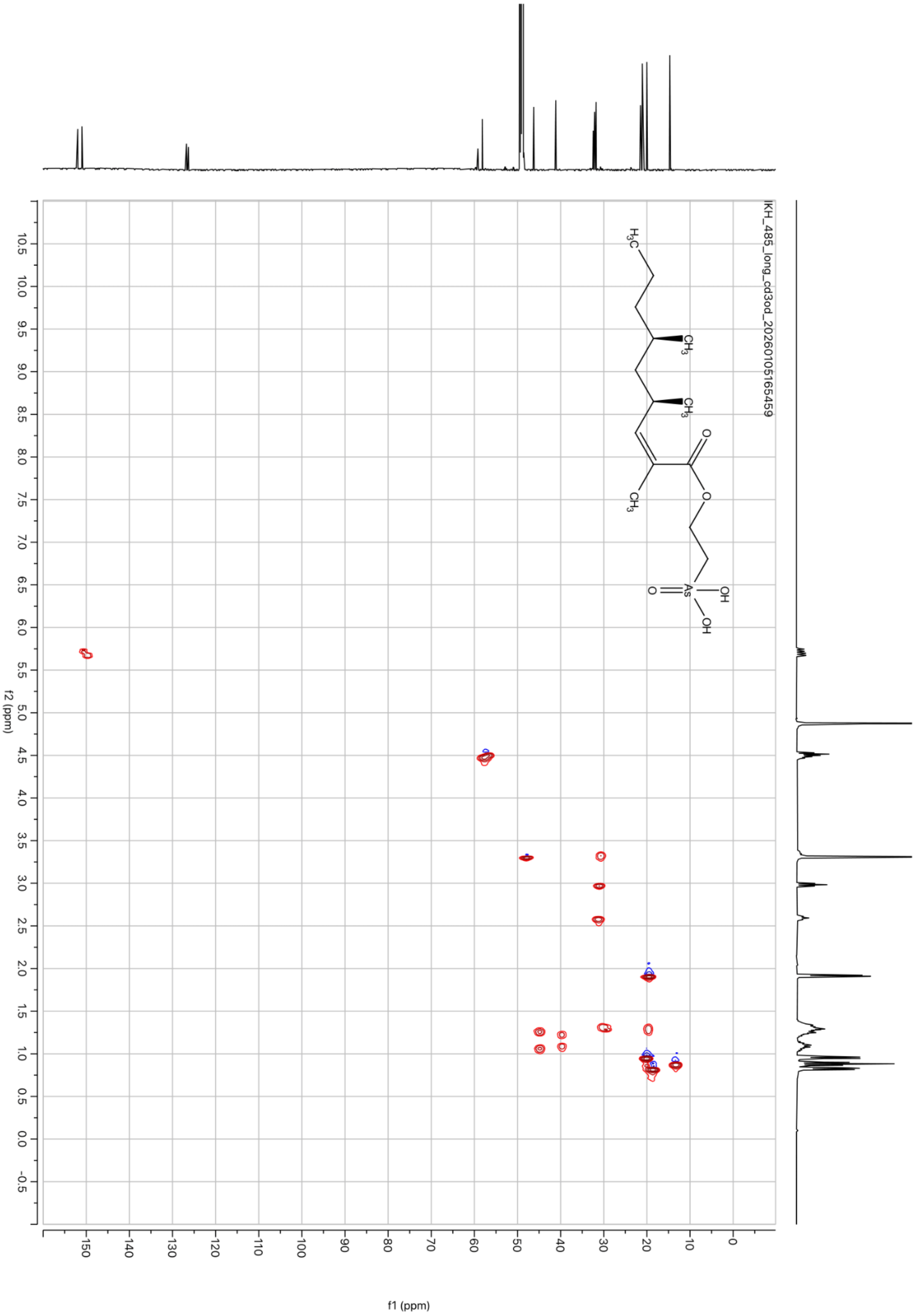
Overlayed ^{13}C NMR spectra of synthetic **ent-*1*** *(maroon) and natural* **1** *(cyan) in CD$_3$OD*



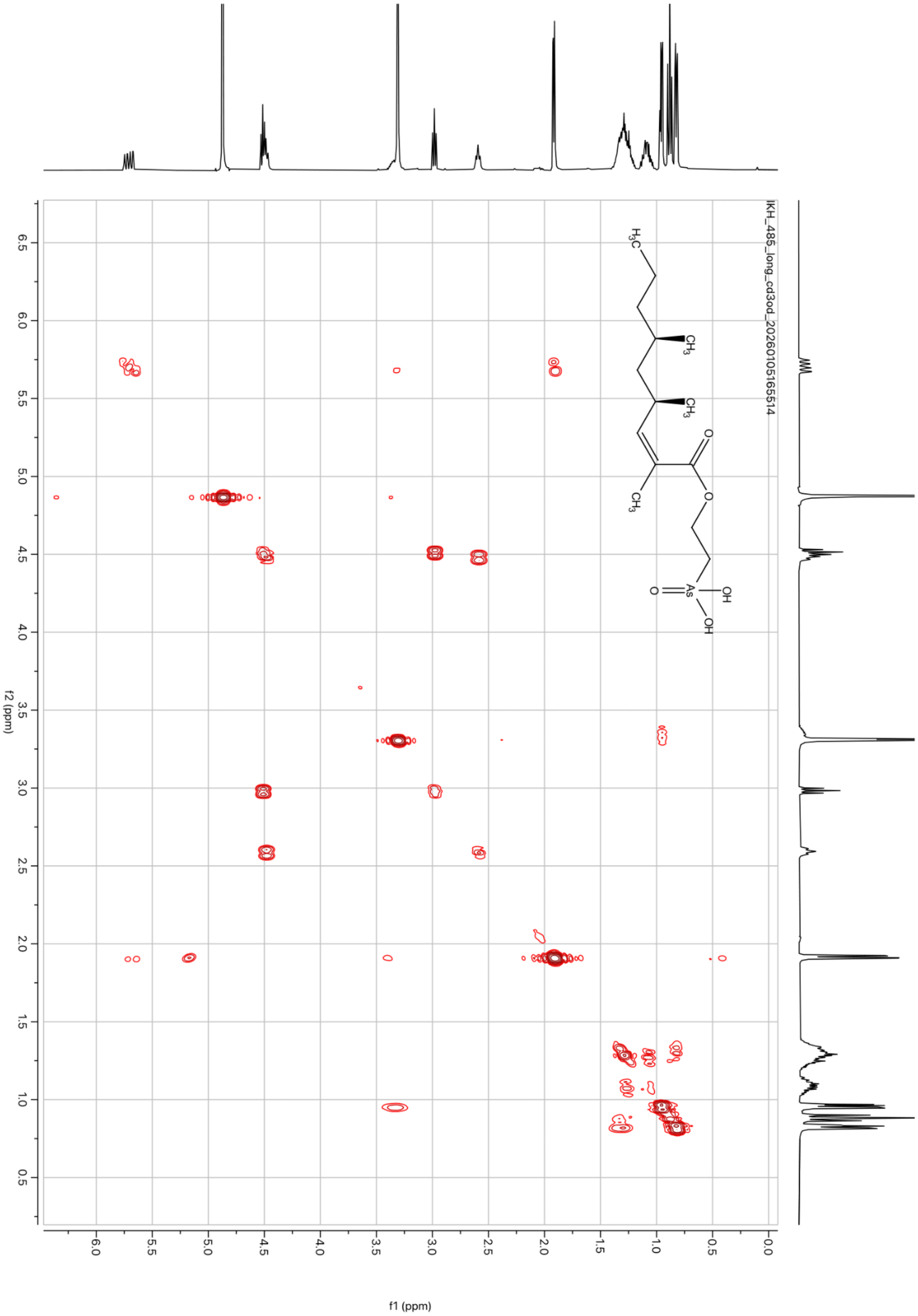
2D NOESY spectrum of ***ent-1*** *in CD_3OD*



HSQC spectrum of **ent-*1*** *in CD_3OD*



COSY spectrum of ***ent-1*** *in CD_3OD*



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