Supporting Information

Mild, Redox-Neutral Formylation of Aryl Chlorides via Photocatalytic Generation of Chlorine Radicals

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I. General Information

Materials. 1,3-Dioxolane (99.5% with 75 ppm BHT stabilizer) was purchased from Alfa Aesar. 4,4'-Di-*tert*-butyl-2,2'-bipyridine (dtbbpy) was purchased from Aldrich, Astatech, and Alfa Aesar. Nickel(II) chloride, dimethoxyethane adduct ($NiCl_2$·glyme) and (4,4'-Di-t-butyl-2,2'-bipyridine)bis[3,5-difluoro-2-[5-trifluoromethyl-2-pyridinyl-κ*N*)phenyl-κ*C*]iridium(III) hexafluorophosphate ($Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$) were purchased from Strem. Anhydrous potassium phosphate tribasic (K_3PO_4) was purchased from Aldrich.

Methods. Unless otherwise noted, reactions were performed with rigorous exclusion of air and moisture. Solvent was freshly distilled/degassed prior to use unless otherwise noted. Reactions were monitored by thin-layer chromatography (TLC) on EMD Silica Gel 60 F254 plates, visualizing with UV-light (254 nm) fluorescence quenching. Organic solutions were concentrated under reduced pressure using a rotary evaporator (23 °C, <50 torr). Automated column chromatography was performed using silica gel cartridges on a Biotage Isolera 4 (40-53 μm, 60 Å).

Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker 500 AVANCE equipped with a cryoprobe (500 and 125 MHz, respectively). Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$ = δ 7.26 ppm, $CHDCl_2$ = δ 5.32 ppm, C_6H_5D = δ 7.16 ppm, DMSO-d_5 = δ 2.50 ppm, acetone-d_5 = 2.05 ppm). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent peak ($CDCl_3$ = δ 77.16 ppm, CD_2Cl_2 = δ 53.84 ppm, C_6D_6 = δ 128.06 ppm, DMSO-d_6 = δ 39.52 ppm, acetone-d_6 ($\underline{C}D_3$) = 29.84 ppm. ^{19}F fluorine spectra were recorded on a Bruker 300 AVANCE (282 MHz); chemical shifts are reported in parts per million and are referenced to $CFCl_3$ (δ 0 ppm). NMR data are represented as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, hept = heptet, m = multiplet), coupling constant in Hertz (Hz), integration. All NMR spectra were taken at 25 °C. High-resolution mass spectra were obtained on an Agilent 6220 LC/MS with an electrospray ionization time-of-flight (ESI-TOF) detector. FTIR and FT-ATR spectra were recorded on a Perkin-Elmer Spectrum 100 and are reported in terms of frequency of absorption (cm^{-1}) and intensity (s = strong, m = moderate, w = weak, br = broad). Gas chromatography (GC) was performed on an Agilent 7890A series instrument equipped with a split-mode capillary injection system and flame ionization detectors. Liquid chromatograpy/mass spectrometry (LCMS) data was obtained on an Agilent 1260 Infinity instrument with a binary pump, a diode array detector, and an Agilent 6120 quadrupole detector.

Light Sources. Reactions were carried out using 25W blue LED arrays (12-inch Sapphire Flex LED Strips 5050, High Density, 12V DC Power Leads, Waterproof, Black backing) purchased from Creative Lightings (λ_{max} = 467 nm) or 34W blue LED lamps (Kessil H150 LED Grow Lights) purchased from Kessil (λ_{max} = 450 nm flanked by a second peak at λ = 422 nm). Blue LED arrays were assembled in 4×4 plastic blocks, holding 12×35mm ½ dram vials, with 2×3 side lighting strips and 1×2 bottom lighting strip (Figure S1).

II. Reaction Optimization and Control Experiments

General procedure for reaction optimization:

Reagent handling: $NiCl_2$·glyme, dtbbpy, $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$, and K_3PO_4 were stored in an N_2-filled glovebox. 1,3-Dioxolane (with up to 75 ppm BHT stabilizer) was degassed with argon or nitrogen, brought into the glovebox, and stored on activated 4Å molecular sieves. *Note: Distillation of commercial 1,3-dioxolane to remove BHT inhibitor is unnecessary and does not lead to any significant improvement in yield.*

Reaction setup (0.05 mmol scale): A ½-dram vial (Fisher part number: 03-338AA) equipped with a PTFE-coated stir bar was brought into a N_2-filled glove box and charged with K_3PO_4 (21.2 mg, 0.1 mmol, 2 equiv.). To the reaction vial the following were added successively: 1,3-dioxolane (0.500 mL), a clear solution of 4-chlorobenzonitrile (6.9 mg, 0.05 mmol, 1 equiv.) in 1,3-dioxolane (0.050 mL), a yellow solution of $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (0.6 mg, 0.5 µmol, 0.01 equiv.) in 1,3-dioxolane (0.150 mL) and a light green solution of $NiCl_2$·glyme (1.1 mg, 5 µmol, 0.1 equiv.) and 4,4´-di-*tert*-butyl-2,2´-bipyridine (2.0 mg, 7.5 µmol, 0.15 equiv.) in 1,3-dioxolane (0.300 mL). The vial was capped with a Teflon septum cap and sealed with electrical tape. The reaction vial was removed from the glove box, set to stir (800 rpm) and irradiated with a blue LED array (Figure S1, cooled with both a fan above and pressurized air that was directed through tygon tubing mounted next to the reaction array) for 72 hours. The crude reaction was analyzed by GC-FID relative to 1-fluoronaphthalene as an external standard.

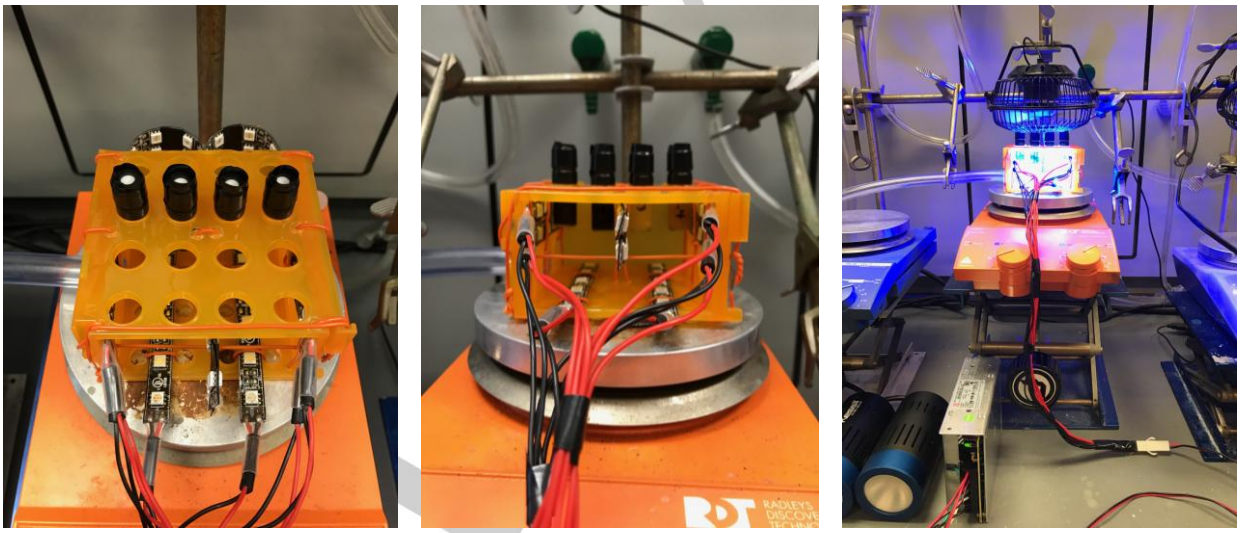
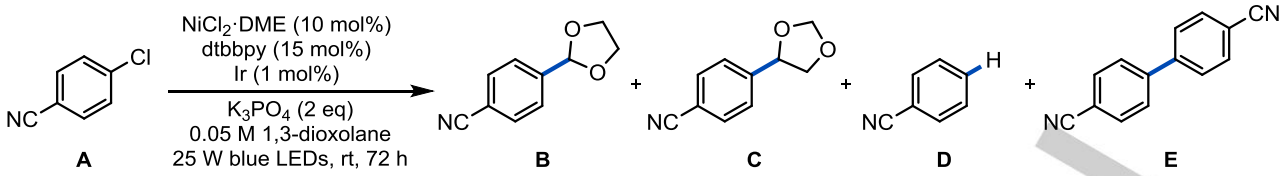


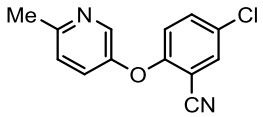
Figure S1. Example of a blue LED array used for small scale screening.



Entry	Conditions	Conversion **A**	Yield **B**	Yield **C**	Yield **D**	Yield **E**
1	34 W Blue LEDs[a]	NA	**82%**	7%	NA	NA
2	25 W Blue LEDs	100%	**73%**	10%	0%	0%
3	no light	4%	**0%**	0%	0%	0%
4	no Ir[dF(CF_3)-ppy]$_2$(dtbbpy)PF_6	2%	**0%**	0%	0%	0%
5	no $NiCl_2$·DME/dtbbpy	9%	**0%**	0%	0%	0%
6	no K_3PO_4	52%	**11%**	5%	3%	0%
7	1:1 (v:v) 1,3-dioxolane:benzene	100%	**71%**	11%	0%	0%
8	[Ni] (5 mol%), [Ir] (0.5 mol%)	73%	**55%**	8%	0%	0%
9	$Ni(cod)_2$ (10 mol%)	100%	**66%**	8%	0%	7%

Table S1. Controls and optimization for 1,3-dioxolane arylation reaction. Yields and conversion determined by GC-FID using 1-fluoronaphthalene as an external standard. Reactions were carried out on 0.05 mmol scale. [a]Yield was determined by ^{1}H NMR using 1-fluoronaphthalene as an external standard. Reaction was carried out on 0.25 mmol scale. Note that the reactions carried out in the 25 W LED arrays generally performed worse that those carried out with 34 W LED lamps.

III. Substrate Synthesis



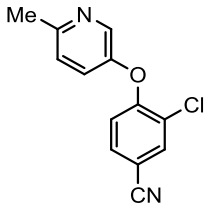
5-chloro-2-((6-methylpyridin-3-yl)oxy)benzonitrile: A 25 mL round bottom flask with a magnetic stir bar was charged with 6-methylpyridin-3-ol (1.26 g of 95% solid, 11.0 mmol) and 5-chloro-2-fluorobenzonitrile (1.55 g, 10.0 mmol), followed by DMAc (6 mL) and DBU (1.64 mL, 11.0 mmol). The resulting solution was heated to T_i = 50 °C for 3 h, after which HPLC assay showed complete consumption of the nitrile. After cooling to T_i = 20 °C, H_2O (4 mL) was added, followed by seed. The resulting slurry was aged 1 h to allow seed bed formation. H_2O (8 mL) was added over 1 h via syringe pump. The resulting slurry was aged 2 h, then filtered. The beige solid was displacement washed with 2:1 H_2O:DMAc (3 mL), then H_2O (3 mL). Drying with vacuum/N_2 sweep afforded a beige solid that was subjected to further purification by silica gel chromatography (gradient elution 0 to 40% EtOAc/heptane) to afford, after concentration, a white solid. The solid was suspended in heptane (12 mL) with magnetic stirring for 1 h. The slurry was filtered and displacement washed with heptanes (3 mL). Drying with vacuum/N_2 sweep afforded the title compound (2.07 g, 85% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.34 (dd, *J* = 2.8, 0.7 Hz, 1H), 7.63 (d, *J* = 2.6 Hz, 1H), 7.44 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.31 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 6.78 (d, *J* = 9.0 Hz, 1H), 2.58 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 158.14, 155.81, 149.36, 141.52, 134.57, 133.43, 128.51, 127.93, 124.27, 117.75, 114.47, 105.17, 23.93.

IR (ATR, cm^{-1}): 3055 (w), 3026 (w), 2229 (m). 1598 (w), 1569 (w), 1478 (s), 1464 (w), 1399 (m), 1382 (w), 1374 (w), 1282 (w), 1270 (m), 1247 (s), 1229 (s), 1206 (m), 1182 (w), 1130 (m), 1091 (w), 1039 (w), 1024 (m), 914 (w), 880 (m), 843 (m), 824 (s), 786 (w), 718 (w), 660 (w).

HRMS (ESI+): Calculated for $C_{13}H_{10}ClN_2O^+$ $[M + H]^+$: 245.0476; found: 245.0487.



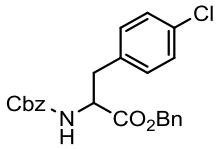
3-chloro-4-((6-methylpyridin-3-yl)oxy)benzonitrile: A 25 mL round bottom flask with a magnetic stir bar was charged with 6-methylpyridin-3-ol (1.34 g of 95% solid, 11.6 mmol) and 3-chloro-4-fluorobenzonitrile (1.55 g, 10.0 mmol), followed by DMAc (6 mL) and DBU (1.64 mL, 11.0 mmol). The resulting solution was heated to T_i = 50 °C for 3 h, after which HPLC assay showed complete consumption of the nitrile. After cooling to T_i = 20 °C, H_2O (12 mL) was added, followed by EtOAc (10 mL). The resulting mixture was transferred to a separatory funnel and the phases were separated. The aqueous phase was extracted with EtOAc (4 mL), and the aqueous phase was discarded. The combined organic phases were washed with 10% aq. LiCl (3 × 4 mL), then dried over $MgSO_4$, filtered, and concentrated. The oil was purified by silica gel chromatography (gradient elution 0 to 40% EtOAc/heptane) to afford, after concentration, a white solid. The solid was suspended in heptane (12 mL) with magnetic stirring, for 1 h. The slurry was filtered and displacement washed with heptanes (3 mL). Drying with vacuum/N_2 sweep afforded the title compound (1.79 g, 73% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.32 (d, *J* = 2.6 Hz, 1H), 7.77 (d, *J* = 2.0 Hz, 1H), 7.48 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.28 (dd, *J* = 8.6, 2.8 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 6.86 (d, *J* = 8.6 Hz, 1H), 2.58 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 157.13, 155.71, 149.29, 141.43, 134.61, 132.23, 127.70, 125.45, 124.25, 117.92, 117.35, 107.78, 23.91.

IR (ATR, cm^{-1}): 3065 (w), 2234 (m), 1602 (w), 1572 (w), 1474 (s), 1387 (m), 1285 (w), 1273 (s), 1261 (w), 1239 (m), 1197 (s), 1135 (w), 1121 (m), 1064 (m), 1018 (m), 902 (s), 857 (s), 842 (m), 820 (s), 792 (m), 749 (w), 717 (w), 673 (w).

HRMS (ESI+): Calculated for $C_{13}H_{10}ClN_2O^+$ $[M + H]^+$: 245.0476; found: 245.0485.



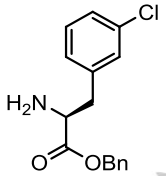
***N*-Cbz-DL-4-chlorophenylalanine benzyl ester:** *N*-Cbz-DL-4-chlorophenylalanine (501 mg, 1.5 mmol, Combi-Blocks) and di-*tert*-butyl dicarbonate (360 mg, 1.1 equiv, Aldrich) were dissolved in dichloromethane (10 mL) followed by addition of *N*-Boc-1-*tert*-butoxy-1,2-dihydroisoquinoline (45.5 mg, 0.1 equiv, Aldrich). The suspension was stirred for 30 minutes and then charged with benzyl alcohol (180 μL, 1.1 equiv). After stirring for 24 hours, the reaction was concentrated, dissolved in 50 mL ethyl acetate and rinsed twice with 50 mL 1M HCl. The organic layer was dried with sodium sulfate, concentrated, and purified by automated column chromatography (100 g triethylamine pre-treated silica, 0 → 20% ethyl acetate in hexanes) and pure fractions were combined to afford 256 mg product as a white crystalline solid (40% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 – 7.26 (m, 10H), 7.14 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 8.0 Hz, 2H), 5.25 (d, *J* = 8.2 Hz, 1H), 5.19 – 5.06 (m, 4H), 4.68 (dt, *J* = 8.2, 5.9 Hz, 1H), 3.07 (qd, *J* = 13.9, 5.8 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.18, 155.64, 136.27, 135.01, 134.13, 133.10, 130.80, 128.83, 128.80, 128.80, 128.80, 128.68, 128.40, 128.27, 67.52, 67.18, 54.80, 37.72.

IR (ATR, cm^{-1}): 3423 (m), 3088 (w), 3067 (w), 3036 (w), 2967 (w), 2934 (w), 1739 (w), 1715 (s), 1506 (m), 1494 (m), 1454 (m), 1386 (m), 1350 (m), 1310 (w), 1227 (w), 1212 (w), 1176 (s), 1104 (w), 1087 (w), 1059 (m), 1010 (m), 981 (w), 934 (w), 912 (w), 867 (w), 836 (m), 790 (w), 775 (w), 754 (m), 739 (m), 696 (s).

HRMS (ESI+): Calculated for $C_{24}H_{23}ClNO_4^+$ $[M + H]^+$: 424.1310; found: 424.1308.



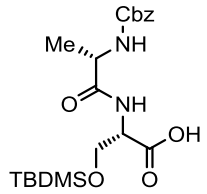
L-3-chlorophenylalanine benzyl ester: A mixture of L-3-chlorophenylalanine (1.00 g, 5.01 mmol, Ark Pharm), benzyl alcohol (5.2 mL, 10 equiv), and *p*-toluenesulfonic acid monohydrate (1.14 g, 1.2 equiv) in benzene (50 mL) was heated to reflux for 5 hours while removing water *via* a Dean-Stark apparatus. Benzene was removed under reduced pressure, and the resulting solid was added to 100 mL saturated aqueous sodium bicarbonate and extracted with 100 mL dichloromethane. The organic layers were dried with sodium sulfate and concentrated without further purification to afford 901 mg product as a colorless oil (62% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 – 7.33 (m, 3H), 7.34 – 7.28 (m, 2H), 7.24 – 7.15 (m, 3H), 7.02 (d, *J* = 6.9 Hz, 1H), 5.14 (d, *J* = 2.6 Hz, 2H), 3.76 (dd, *J* = 7.6, 5.5 Hz, 1H), 3.05 (dd, *J* = 13.6, 5.6 Hz, 1H), 2.86 (dd, *J* = 13.6, 7.6 Hz, 1H), 1.50 (s, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 174.76, 139.34, 135.49, 134.39, 129.85, 129.51, 128.75, 128.59, 128.57, 127.61, 127.13, 67.00, 55.79, 40.74.

IR (film, cm^{-1}): 3384 (w), 3064 (w), 3034 (w), 2947 (w), 1732 (s), 1598 (m), 1573 (m), 1497 (w), 1476 (w), 1456 (w), 1373 (w), 1259 (w), 1211 (w), 1168 (s), 1079 (m), 999 (m), 908 (m), 781 (m), 730 (s), 696 (s), 683 (w).

HRMS (ESI+): Calculated for $C_{16}H_{17}ClNO_2^+$ $[M + H]^+$: 290.0942; found: 290.0942.



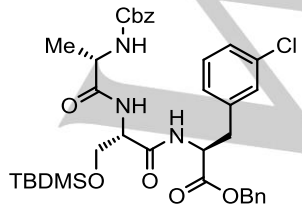
***N*-Cbz-L-alanyl-*O*-(tert-butyldimethylsilyl)-L-serine:** *N*-Cbz-L-alanyl-L-serine methyl ester (1.00 g, 3.08 mmol, Aldrich) and imidazole (630 mg, 3 equiv, Aldrich) were dissolved in dry DMF (6 mL). The mixture was cooled to 0 °C, and TBDMS chloride (581 mg, 1.25 equiv, Aldrich) was added in one portion. The reaction was allowed to warm to room temperature while stirring. After 12 hours, the reaction mixture was diluted with 50 mL saturated aqueous ammonium chloride and extracted with 75 mL ethyl acetate. The organic layer was rinsed with saturated aqueous sodium chloride (3 × 50 mL), dried with sodium sulfate, and concentrated to afford a colorless oil consisting primarily of *N*-Cbz-L-alanyl-*O*-(tert-butyldimethylsilyl)-L-serine methyl ester as determined by LCMS. This material was dissolved in THF (20 mL) and cooled to 0 °C. A solution of lithium hydroxide (90 mg, 1.2 equiv) in 5 mL water was added dropwise and the solution was allowed to warm to room temperature for one hour. The reaction was diluted with 50 mL water and extracted with ethyl acetate (3 × 50 mL). The organic layers were dried with sodium sulfate and concentrated without further purification to afford the 1.24 g of the title compound as a viscous colorless oil (95% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.71 (br s, 1H), 7.40 – 7.27 (m, 5H), 6.78 (d, *J* = 7.9 Hz, 1H), 5.53 (d, *J* = 7.7 Hz, 1H), 5.12 (t, *J* = 12.6 Hz, 2H), 4.62 (dt, *J* = 7.4, 3.3 Hz, 1H), 4.33 (p, *J* = 7.3 Hz, 1H), 4.17 – 4.06 (m, 1H), 3.83 (dd, *J* = 10.6, 3.7 Hz, 1H), 1.41 (d, *J* = 7.0 Hz, 3H), 0.86 (s, 9H), 0.04 (d, *J* = 3.7 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 173.89, 172.63, 156.06, 136.25, 128.67, 128.36, 128.23, 67.22, 63.04, 54.22, 50.63, 25.85, 18.92, 18.31, −5.39, −5.48.

IR (film, cm^{-1}): 3309 (br, m), 3034 (w), 2931 (w), 2885 (w), 2857 (w), 1715 (s), 1657 (s), 1522 (s), 1454 (m), 1410 (w), 1327 (w), 1250 (s), 1109 (s), 1071 (w), 1045 (w), 938 (w), 907 (w), 833 (s), 776 (s), 733 (m), 696 (s), 665 (w).

HRMS (ESI+): Calculated for $C_{20}H_{33}N_2O_6Si^+$ $[M + H]^+$: 425.2102; found: 425.2098.



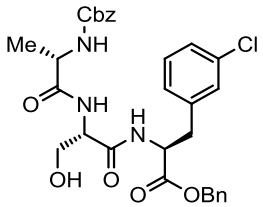
***N*-Cbz-L-alanyl-*O*-(tert-butyldimethylsilyl)-L-seryl-L-3-chlorophenylalanine benzyl ester:** A 250 mL round bottom flask was charged with *N*-Cbz-L-alanyl-*O*-(tert-butyldimethylsilyl)-L-serine (1.239 g, 2.92 mmol), L-3-chlorophenylalanine benzyl ester (888 mg, 1.05 equiv), 1-hydroxybenzotriazole (≥20 wt. % water, 600 mg, 1.2 equiv, Chem-Impex), 4-dimethylaminopyridine (DMAP, 71 mg, 0.2 equiv, Aldrich), dry dichloromethane (100 mL), and triethylamine (1.22 mL, 3 equiv). The mixture was cooled to 0 °C, and a solution of *N*-(3-dimethylaminopropyl)-*N′*-ethylcarbodiimide hydrochloride (EDCI, 1.12 g, 2 equiv, Chem-Impex) in 40 mL dichloromethane was added dropwise over 10 minutes while stirring, after which the reaction was allowed to warm to room temperature. At 12 hours, the reaction was quenched with 100 mL saturated aqueous ammonium chloride and extracted with ethyl acetate (2 × 100 mL). The organic extracts were dried with sodium sulfate, concentrated, and purified by automated column chromatography (50 g silica, 10 → 40% ethyl acetate in hexanes). Pure fractions were concentrated to afford 907 mg of the title compound as a white solid (45% yield).

^{1}H NMR (500 MHz, CD_2Cl_2): δ 7.38 – 7.30 (m, 8H), 7.28 (d, *J* = 7.2 Hz, 2H), 7.25 – 7.14 (m, 3H), 7.11 (s, 1H), 6.98 (d, *J* = 7.2 Hz, 1H), 6.84 (d, *J* = 6.7 Hz, 1H), 5.39 (d, *J* = 6.8 Hz, 1H), 5.16 – 5.08 (m, 3H), 5.03 (d, *J* = 12.5 Hz, 1H), 4.83 (q, *J* = 6.3 Hz, 1H), 4.35 (q, *J* = 5.5 Hz, 1H), 4.18 (dt, *J* = 15.6, 7.2 Hz, 1H), 4.03 (dd, *J* = 10.2, 3.8 Hz, 1H), 3.62 (t, *J* = 8.2 Hz, 1H), 3.11 (dd, *J* = 14.0, 6.2 Hz, 1H), 3.04 (dd, *J* = 14.4, 6.3 Hz, 1H), 1.36 (d, *J* = 7.0 Hz, 3H), 0.87 (s, 9H), 0.06 (s, 6H).

^{13}C NMR (125 MHz, CD_2Cl_2): δ 172.36, 170.99, 170.13, 156.47, 138.75, 136.77, 135.65, 134.44, 130.21, 129.69, 128.93, 128.87, 128.80, 128.79, 128.53, 128.34, 127.90, 127.51, 67.55, 67.37, 62.88, 54.63, 53.89, 51.44, 37.90, 25.95, 18.66, 18.43, −5.43, −5.46.

IR (ATR, cm^{-1}): 3287 (br, m), 3066 (w), 3036 (w), 2930 (w), 2856 (w), 1734 (m), 1693 (m), 1640 (s), 1526 (s), 1450 (w), 1398 (w), 1336 (w), 1250 (s), 1217 (m), 1193 (m), 1114 (s), 1081 (w), 1049 (w), 1029 (w), 1004 (w), 940 (w), 910 (w), 887 (w), 837 (s), 776 (s), 749 (m), 695 (s).

HRMS (ESI+): Calculated for $C_{36}H_{47}ClN_3O_7Si^+$ $[M + H]^+$: 696.2866; found: 696.2857.



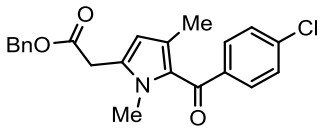
***N*-Cbz-L-alanyl-L-seryl-L-3-chlorophenylalanine benzyl ester:** *N*-Cbz-L-alanyl-*O*-(tert-butyldimethylsilyl)-L-seryl-L-3-chlorophenylalanine benzyl ester (877 mg, 1.26 mmol) was dissolved in 10 mL dry THF and cooled to 0 °C. Tetrabutylammonium fluoride (TBAF, 1.0 M in THF, 1.5 mL, 1.2 equiv, Aldrich) was added dropwise, and the reaction was stirred at 0 °C for 20 minutes while monitoring by TLC. The mixture was immediately diluted with 50 mL saturated aqueous ammonium chloride and extracted with ethyl acetate (3 × 50 mL). The organic extracts were concentrated and purified by automated column chromatography (50 g silica, 0 → 3% methanol in dichloromethane) to afford 654 mg product as a white solid (89% yield).

^{1}H NMR (500 MHz, DMSO-d_6): δ 8.31 (d, *J* = 7.5 Hz, 1H), 7.86 (d, *J* = 7.9 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.40 – 7.23 (m, 13H), 7.15 (ddt, *J* = 6.4, 4.7, 2.2 Hz, 1H), 5.06 (d, *J* = 2.0 Hz, 2H), 5.02 (d, *J* = 4.6 Hz, 2H), 4.86 (t, *J* = 5.5 Hz, 1H), 4.56 (td, *J* = 7.9, 6.3 Hz, 1H), 4.32 (dt, *J* = 8.0, 5.6 Hz, 1H), 4.12 (dt, *J* = 16.8, 7.2 Hz, 1H), 3.53 (dt, *J* = 5.9, 3.6 Hz, 2H), 3.06 (dd, *J* = 13.9, 6.2 Hz, 1H), 2.98 (dd, *J* = 13.8, 8.3 Hz, 1H), 1.19 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 172.37, 170.81, 170.01, 155.72, 139.48, 136.98, 135.62, 132.86, 130.03, 129.07, 128.39, 128.36, 128.05, 127.93, 127.84, 127.80, 127.73, 126.61, 66.13, 65.42, 61.67, 54.92, 53.40, 50.06, 36.15, 18.23.

IR (ATR, cm^{-1}): 3287 (br, s), 3065 (w), 3035 (w), 2940 (w), 1736 (m), 1689 (m), 1639 (s), 1529 (s), 1449 (m), 1399 (w), 1340 (w), 1253 (m), 1217 (m), 1125 (w), 1047 (m), 909 (w), 777 (w), 746 (m), 695 (s).

HRMS (ESI+): Calculated for $C_{30}H_{33}ClN_3O_7^+$ $[M + H]^+$: 582.2002; found: 582.1996.



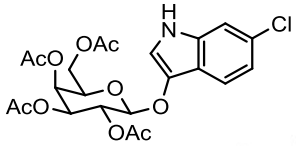
benzyl 2-(5-(4-chlorobenzoyl)-1,4-dimethyl-1*H*-pyrrol-2-yl)acetate: Synthesized by Steglich esterification of zomepirac sodium salt. A 50-mL round-bottom flask was charged with a stirbar, sodium 2-(5-(4-chlorobenzoyl)-1,4-dimethyl-1*H*-pyrrol-2-yl)acetate (zomepirac, 250 mg, 0.80 mmol, Aldrich), benzyl alcohol (95 mg, 1.1 equiv, Aldrich), 4-(dimethylamino)pyridine (DMAP, 30 mg, 0.3 equiv, Aldrich), and dichloromethane (16 mL, 0.05 M). The suspension was cooled to 0 °C. *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDCI, 240 mg, 1.6 equiv, TCI) was dissolved in 20 mL DCM and added dropwise to the reaction mixture over 10 minutes while stirring. The reaction allowed to warm to room temperature and was stirred for 12 hours. The reaction mixture was then poured on 50 mL saturated ammonium chloride and extracted twice with 50 mL dichloromethane. The organic extracts were dried with sodium sulfate, concentrated, and purified by automated column chromatography (50 g silica, 0 → 12% ethyl acetate in hexanes) to afford 224 mg product as a white solid (74% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.39 – 7.31 (m, 5H), 5.94 (s, 1H), 5.18 (s, 2H), 3.70 (s, 3H), 3.70 (s, 2H), 1.75 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 186.59, 169.41, 139.39, 138.05, 135.53, 133.04, 130.68, 129.89, 129.15, 128.78, 128.77, 128.64, 128.48, 112.68, 67.29, 33.22, 32.92, 14.59.

IR (ATR, cm^{-1}): 3070 (w), 3037 (w), 2959 (w), 2922 (w), 1720 (s), 1614 (s), 1588 (w), 1566 (w), 1481 (w), 1456 (m), 1425 (w), 1399 (w), 1385 (m), 1377 (w), 1321 (m), 1272 (m), 1231 (w), 1220 (w), 1190 (s), 1170 (s), 1101 (w), 1085 (m), 1015 (w), 951 (s), 930 (w), 913 (w), 855 (w), 835 (w), 821 (w), 803 (m), 759 (m), 745 (s), 698 (s), 674 (w).

HRMS (ESI+): Calculated for $C_{22}H_{21}ClNO_3^+$ $[M + H]^+$: 382.1204; found: 382.1199.



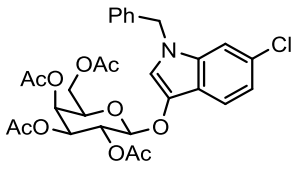
6-chloro-3-indolyl-β-D-galactopyranoside tetraacetate: To a suspension of 6-chloro-3-indolyl-β-D-galactopyranoside (salmon-gal, 1.00 g, 3.0 mmol, Chem-Impex) in 15 mL dichloromethane was added pyridine (1.7 mL, 7 equiv, Aldrich), acetic anhydride (2.0 mL, 7 equiv, Aldrich), and 4-dimethylaminopyridine (DMAP, 37 mg, 0.1 equiv). After stirring at room temperature for 4 hours, the reaction was concentrated and the residue was purified by automated column chromatography (50 g silica, 20 → 70% ethyl acetate in hexanes) to afford 1.38 g product as a white solid (91% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.46 (d, *J* = 8.5 Hz, 1H), 7.30 (d, *J* = 1.7 Hz, 1H), 7.06 (dd, *J* = 8.5, 1.7 Hz, 1H), 6.95 (d, *J* = 2.2 Hz, 1H), 5.52 (dd, *J* = 10.5, 8.0 Hz, 1H), 5.44 (dd, *J* = 3.4, 1.1 Hz, 1H), 5.09 (dd, *J* = 10.5, 3.4 Hz, 1H), 4.87 (d, *J* = 8.0 Hz, 1H), 4.27 – 4.15 (m, 2H), 3.97 (td, *J* = 6.6, 1.2 Hz, 1H), 2.18 (s, 3H), 2.14 (s, 3H), 2.04 (s, 3H), 2.02 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.52, 170.41, 170.31, 169.61, 137.79, 133.98, 128.93, 120.61, 118.94, 118.65, 111.80, 111.42, 102.76, 71.21, 70.94, 68.93, 67.08, 61.54, 21.00, 20.83, 20.81, 20.75.

IR (ATR, cm^{-1}): 3393 (br, w), 2976 (w), 1741 (s), 1620 (w), 1581 (w), 1552 (w), 1456 (w), 1431 (w), 1368 (m), 1333 (w), 1215 (s), 1138 (w), 1052 (s), 953 (w), 904 (m), 848 (w), 800 (w), 773 (w), 730 (m), 685 (w).

HRMS (ESI+): Calculated for $C_{22}H_{24}ClNNaO_{10}^{+}$ $[M + Na]^+$: 520.0981; found: 520.0986.



***N*-benzyl-6-chloro-3-indolyl-β-D-galactopyranoside tetraacetate:** Sodium hydride (60% dispersion in mineral oil, 120 mg, 1.1 equiv, Aldrich) was dissolved in 3 mL DMF under nitrogen and cooled to 0 °C. A solution of 6-chloro-3-indolyl-β-D-galactopyranoside tetraacetate (1.36 g, 2.73 mmol) in 7 mL DMF was added dropwise over ~10 minutes. The mixture was allowed to warm to room temperature and benzyl bromide (325 μL, 1 equiv) was added dropwise. After stirring for four hours, the reaction was diluted with 25 mL ethyl acetate and rinsed three times with 25 mL saturated sodium chloride. The organic layer was dried with sodium sulfate, concentrated, and purified by automated column chromatography (50 g silica, 10 → 40% ethyl acetate in hexanes) to afford 519 mg product as a white solid (32% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.5 Hz, 1H), 7.34 – 7.26 (m, 3H), 7.23 (d, *J* = 1.6 Hz, 1H), 7.08 (d, *J* = 6.4 Hz, 2H), 7.05 (dd, *J* = 8.5, 1.7 Hz, 1H), 6.88 (s, 1H), 5.52 (dd, *J* = 10.5, 8.0 Hz, 1H), 5.44 (dd, *J* = 3.5, 1.1 Hz, 1H), 5.19 (s, 2H), 5.09 (dd, *J* = 10.5, 3.4 Hz, 1H), 4.87 (d, *J* = 8.0 Hz, 1H), 4.19 (qd, *J* = 11.4, 6.6 Hz, 2H), 3.98 (t, *J* = 6.6 Hz, 1H), 2.18 (s, 3H), 2.13 (s, 3H), 2.02 (s, 3H), 1.96 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.44, 170.36, 170.26, 169.53, 137.08, 136.89, 134.30, 129.03, 128.92, 128.03, 126.70, 120.28, 119.26, 118.94, 115.71, 109.72, 102.74, 71.20, 70.92, 68.88, 67.06, 61.60, 50.15, 20.99, 20.80, 20.74, 20.72.

IR (ATR, cm^{-1}): 3132 (w), 3094 (w), 2974 (w), 2922 (w), 1741 (s), 1611 (w), 1573 (w), 1552 (w), 1497 (w), 1468 (m), 1455 (w), 1435 (w), 1367 (m), 1329 (m), 1262 (w), 1222 (s), 1160 (m), 1134 (w), 1116 (w), 1083 (w), 1045 (s), 964 (w), 938 (w), 904 (m), 871 (w), 853 (w), 841 (w), 818 (m), 807 (w), 784 (m), 749 (w), 732 (m), 696 (m), 681 (w), 652 (w).

HRMS (ESI+): Calculated for $C_{29}H_{30}ClNNaO_{10}^{+}$ $[M + Na]^+$: 610.1450; found: 610.1460.

IV. Isolated Yields and Characterization of Products

General procedure for formylation:

Reagent handling: $NiCl_2$·glyme, dtbbpy, $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$, and K_3PO_4 were stored in an N_2-filled glovebox. 1,3-Dioxolane (with up to 75 ppm BHT stabilizer) was degassed with argon, brought into the glovebox, and stored on activated 4Å molecular sieves. *Note: Distillation of commercial 1,3-dioxolane to remove BHT inhibitor is unnecessary and does not lead to any significant improvement in yield.* Liquid aryl chlorides were degassed and solid aryl chlorides were purged under vacuum and brought into the glovebox during reaction setup.

Reaction setup (0.25 mmol scale): In the glovebox, a 1-dram vial with a teflon stirbar is charged with $NiCl_2$·glyme (5.5 mg, 10 mol%), dtbbpy (10.1 mg, 15 mol%), and 1,3-dioxolane (2 mL). This nickel catalyst solution is stirred for a minimum of 10 minutes prior to addition to the reaction mixture and should form a light green homogeneous solution.

Meanwhile, a threaded 16 × 125 mm borosilicate reaction tube with a teflon stirbar is charged with substrate (0.25 mmol), K_3PO_4 (106 mg, 2 equiv), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ photocatalyst (2.8 mg, 1 mol%), and 1,3-dioxolane (3 mL). Finally, the nickel catalyst solution is added (total reaction volume: 5 mL, 0.05 M.) The reaction tube is capped with a septum cap, sealed with electrical tape, and removed from the glovebox.

The reaction is stirred at 500 rpm for 72 hours while illuminating with a 34 W blue LED lamp (Kessil KSH150B) placed horizontally at 2 cm distance from the reaction tube (Figure S2). Two or three reactions can be placed side by side in front of a single lamp. Owing to the significant heat output of the lamp, a fan is used to cool the reaction tube to nominally room temperature; however, the actual reaction temperature is typically around 30 °C.

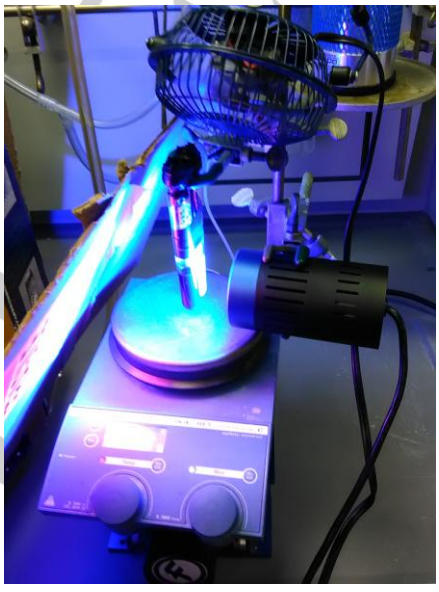
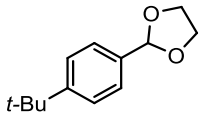


Figure S2. Typical setup for 0.25 mmol scale reaction.

Upon completion, the reaction mixture is concentrated on a rotary evaporator and transferred to a 20 mL scintillation vial in 5 mL acetone followed by addition of 5 mL aqueous 1 M HCl. The mixture is stirred for 1 hour to hydrolyze the acetal to the desired aldehyde. The solution is then diluted with 25 mL saturated sodium bicarbonate and extracted with 3 × 25 mL ethyl acetate. The organic extracts are dried with anhydrous sodium sulfate, concentrated, and purified by automated column chromatography.

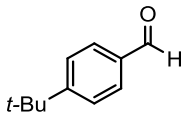
Notes on purification: 1,3-Dioxolane was selected as a formyl precursor because it is an inexpensive, frequently used solvent, that allows for a simple procedure. However, C–H functionalization at the 4-position of 1,3-dioxolane results in the 1,3-dioxolan-4-yl acetal isomer, which was formed in a 1:9 ratio on average to the desired product. This acetal isomer does not deprotect under the standard hydrolysis conditions. For most of the examples in this manuscript, a single silica gel flash column using hexanes:ethyl acetate as eluant was sufficient to obtain the desired product in good to high purity (out of 25 substrates, 20 compounds were isolated in purity ≥ 10:1 and 15 compounds isolated in purity ≥ 20:1). Note that some of these separations were challenging and small changes in fraction collection could lead to differences in purity from run to run. The poorest mixtures were isolated mainly for the most complex substrates for which formylation only induces a small change in substrate polarity. In some of these cases, pure samples could be obtained with additional chromatography (eg. **17**), however for others, more sophisticated separations, such as preparatory HPLC, would likely be necessary. In cases where the acetal isomer and product were not separated by a silica gel flash column, the identifable NMR shifts of the side product are reported separately below those of the desired product. The acetal isomer can be easily identified by ^{13}C NMR—the 1,3-dioxolan-4-yl moiety gives rise to a methylene peak at 96 ppm, a methine peak at 77 ppm, and a methylene peak at 72 ppm in $CDCl_3$. A pure sample of the 4-functionalization isomer 4-(1,3-dioxolan-4-yl)benzonitrile was isolated and fully characterized.



2-(4-(*tert*-butyl)phenyl)-1,3-dioxolane (10): Synthesized from 1-(*tert*-butyl)-4-chlorobenzene (42.2 mg, 0.25 mmol, Accela ChemBio) following the general procedure but omitting the final acid hydrolysis step. Purified by automated column chromatography (50 g basic alumina, 0 → 10% ethyl acetate in hexanes) to afford 39.2 mg product (76% yield) as a white crystalline solid. A second run provided a mixture of 39.2 mg product (76% yield) and 4.5 mg of the acetal isomer side product 4-(4-(*tert*-butyl)phenyl)-1,3-dioxolane (9% yield, 8.8:1 ratio). Compound was previously reported.[1]

^{1}H NMR (500 MHz, C_6D_6): δ 7.57 (d, *J* = 8.2 Hz, 2H), 7.29 (dd, *J* = 8.2 Hz, 2H), 5.82 (s, 1H), 3.68 – 3.62 (m, 2H), 3.52 – 3.47 (m, 2H), 1.19 (s, 9H).

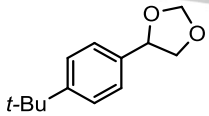
^{13}C NMR (125 MHz, C_6D_6): δ 151.92, 136.30, 126.85, 125.45, 104.11, 65.14, 34.62, 31.41.



4-(*tert*-butyl)benzaldehyde (11): Synthesized from 1-(*tert*-butyl)-4-chlorobenzene (42.2 mg, 0.25 mmol, Accela ChemBio) following the general procedure. Purified by automated column chromatography (50 g silica, 0 → 15% ethyl acetate in hexanes) to afford 30.0 mg product (74% yield) as a colorless oil. A second run provided a mixture of 30.2 mg product (74% yield) and 4.8 mg of the acetal isomer side product 4-(4-(*tert*-butyl)phenyl)-1,3-dioxolane (9% yield, 8.0:1 ratio). Compound has been characterized previously.[2]

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.98 (s, 1H), 7.82 (d, *J* = 8.5 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 1.35 (s, 9H).

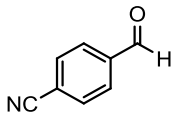
^{13}C NMR (125 MHz, $CDCl_3$): δ 192.19, 158.57, 134.20, 129.83, 126.12, 35.49, 31.21.



4-(4-(*tert*-butyl)phenyl)-1,3-dioxolane (side product):

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 5.26 (s, 1H), 5.08 (s, 1H), 4.97 (t, *J* = 6.8 Hz, 1H), 4.24 (t, *J* = 7.4 Hz, 1H), 3.72 (t, *J* = 7.5 Hz, 1H), 1.31 (s, 9H).

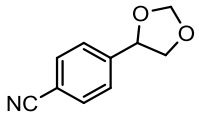
^{13}C NMR (125 MHz, $CDCl_3$): δ 151.31, 136.29, 126.10, 125.67, 96.09, 77.67, 71.84, 34.71, 31.45.



4-formylbenzonitrile (12): Synthesized following the general procedure from 4-chlorobenzonitrile (34.4 mg, 0.25 mmol, Aldrich). Purified by automated column chromatography (25 g silica, 0 → 18% ethyl acetate in hexanes) to afford 27.6 mg product (84% yield) as a white crystalline solid. A second run provided 27.0 mg (82% yield). NMR spectra were previously reported.[3]

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.10 (s, 1H), 8.00 (d, *J* = 8.2 Hz, 2H), 7.85 (d, *J* = 8.2 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 190.73, 138.85, 133.04, 130.03, 117.84, 117.75.



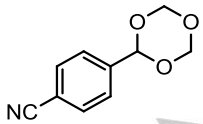
4-(1,3-dioxolan-4-yl)benzonitrile (37–CN): Synthesized following the general procedure (2 × scale up) from 4-chlorobenzonitrile (68.8 mg, 0.5 mmol, Aldrich). The regioisomers were collected via automated column chromatography (100 g silica, gradient 100:0 → 80:20 hexanes:ethyl acetate), which failed to separate the mixture, and subjected to selective hydrolysis of 4-(1,3-dioxolan-2-yl)benzonitrile by stirring in 1:1 (v:v) acetone:1M aqueous HCl for 1.5 hrs. The mixture was diluted with saturated K_2CO_3 until pH = 11 and extracted with DCM (3 × 30 mL). The organic extracts were dried over anhydrous $MgSO_4$, concentrated, and purified by automated column chromatography (100 g silica, 90:10 hexanes:ethyl acetate). A pure sample of the title compound was obtained by selecting a fraction from the right tail of the overlapping chromatogram peaks.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 2H), 5.28 (s, 1H), 5.09 (s, 1H), 5.06 (t, *J* = 6.5 Hz, 1H), 4.28 (dd, *J* = 8.6, 7.0 Hz, 1H), 3.68 (dd, *J* = 8.2, 6.3 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 145.36, 132.61, 126.73, 118.76, 112.08, 96.45, 76.76, 71.90.

IR (ATR, cm^{-1}): 2923 (m), 2854 (m), 2229 (m), 1611 (w), 1505 (w), 1466 (w), 1414 (w), 1365 (w), 1305 (w), 1284 (w), 1211 (w), 1153 (m), 1084 (s), 1017 (m), 948 (s), 924 (s), 836 (s), 780 (w), 730 (w).

HRMS (ESI+): Calculated for $C_{10}H_{10}NO_2^+$ $[M + H]^+$: 176.0706; found: 176.0706



4-(1,3,5-trioxan-2-yl)benzonitrile: The purpose of this experiment was to evaluate 1,3,5-trioxane as a formyl precursor and alternative to 1,3-dioxolane that would afford a single regioisomer. The principal challenge is that trioxane is a solid with a melting point of 64 °C. This reaction was performed general procedure from 4-chlorobenzonitrile (34.4 mg, 0.25 mmol, Aldrich) with a reaction time of 120 hours *and with the following modifications*: **(1)** Benzene was used in place of 1,3-dioxolane as solvent, including for the Ni/ligand prestir. **(2)** The reaction was also charged with 1,3,5-trioxane (1.13 g, 50 equiv, Aldrich). Following acid hydrolysis, the residue was analyzed by NMR and found to contain 2% yield of the aldehyde 4-formylbenzonitrile and 55% yield of the title compound, acetal adduct 4-(1,3,5-

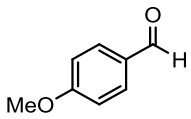
trioxan-2-yl)benzonitrile. This represents a combined effective yield of 57% and indicates that more forcing hydrolysis conditions may be necessary to quantitatively obtain the aldehyde. The acetal adduct can be purified by automated chromatography (25 g silica, 0 → 30% ethyl acetate in hexanes) and isolated as a white crystalline solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, *J* = 8.5 Hz, 2H), 7.62 (d, *J* = 8.3 Hz, 2H), 5.90 (s, 1H), 5.38 (d, *J* = 6.6 Hz, 2H), 5.32 (d, *J* = 6.7 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 141.39, 132.37, 127.00, 118.58, 113.38, 99.99, 93.67.

IR (ATR, cm^{-1}): 2878 (w), 2231 (m), 1398 (m), 1190 (m), 1165 (s), 1084 (m), 1067 (s), 1025 (m), 987 (m), 973 (w), 960 (s), 945 (s), 891 (m), 826 (s), 775 (w), 734 (w), 708 (w).

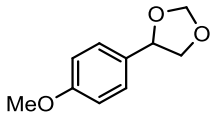
HRMS (ESI+): Calculated for $C_{10}H_{10}NO_3^+$ $[M + H]^+$: 192.0655; found: 192.0653.



***p*-anisaldehyde (13):** Synthesized following the general procedure from 4-chloroanisole (35.6 mg, 0.25 mmol, Oakwood). Purified by automated column chromatography (25 g silica, 0 → 12% ethyl acetate in hexanes) to afford 19.8 mg product (58% yield) as a colorless oil. A repeat experiment generated a mixture of 19.8 mg product (58% yield) and 3.6 mg of the acetal isomer side product 4-(4-methoxyphenyl)-1,3-dioxolane (8% yield, 7.2:1 ratio). Spectra are in accordance with the literature.[4]

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.89 (s, 1H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 3.89 (s, 3H).

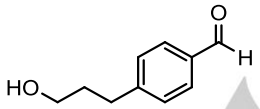
^{13}C NMR (125 MHz, $CDCl_3$): δ 191.00, 164.72, 132.14, 130.06, 114.44, 55.74.



4-(4-methoxyphenyl)-1,3-dioxolane (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 5.26 (s, 1H), 5.06 (s, 1H), 4.94 (t, *J* = 6.8 Hz, 1H), 4.21 (dd, *J* = 8.0, 6.6 Hz, 1H), 3.86 (s, 3H), 3.68 (dd, *J* = 8.1, 7.0 Hz, 1H).

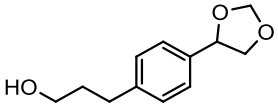
^{13}C NMR (125 MHz, $CDCl_3$): δ 159.68, 131.26, 127.74, 114.15, 96.04, 77.63, 71.88, 55.44.



4-(3-hydroxypropyl)benzaldehyde (14): Synthesized according to the general procedure from 3-(4-chlorophenyl)propan-1-ol (42.7 mg, 0.25 mmol, Matrix). Purified by automated column chromatography (25 g silica, 0 → 45% ethyl acetate in hexanes) to afford 29.5 mg of a colorless oil. By NMR, this was found to be a partially resolved mixture containing 28.0 mg product (69% yield) and 1.5 mg of the acetal isomer 3-(4-(1,3-dioxolan-4-yl)phenyl)propan-1-ol (2% yield, 33:1 ratio). A second run afforded a combined 24.2 mg product (59% yield) and 3.2 mg acetal isomer (6% yield, 9.8:1 ratio). Product was previously characterized.[5]

^{1}H NMR (500 MHz, $CDCl_3$): [33:1 mixture of product:acetal isomer] δ 9.97 (s, 1H), 7.80 (d, *J* = 8.1 Hz, 2H), 7.36 (d, *J* = 7.9 Hz, 2H), 3.69 (t, *J* = 6.4 Hz, 2H), 2.80 (t, *J* = 7.8 Hz, 2H), 1.92 (dt, *J* = 14.0, 6.4 Hz, 2H), 1.52 (s, 1H).

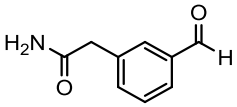
^{13}C NMR (125 MHz, $CDCl_3$): [33:1 mixture of product:acetal isomer] δ 192.17, 149.56, 134.67, 130.14, 129.26, 62.04, 33.87, 32.44.



3-(4-(1,3-dioxolan-4-yl)phenyl)propan-1-ol (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [1:33 mixture with desired product, some peaks are not identified] δ 7.27 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 8.2 Hz, 2H), 5.26 (s, 1H), 5.07 (s, 1H), 4.96 (t, *J* = 6.8 Hz, 1H), 4.23 (dd, *J* = 8.1, 6.7 Hz, 1H), 2.70 (t, *J* = 7.7 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): [1:33 mixture with desired product, some peaks are not identified] 128.81, 126.42, 96.10, 77.69, 71.92, 62.30, 34.28, 31.86.



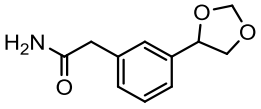
2-(3-formylphenyl)acetamide (15): Synthesized according to the general procedure from 2-(3-chlorophenyl)acetamide (42.4 mg, 0.25 mmol, Aldrich). Purified by automated column chromatography (50 g silica, 0 → 5% methanol in dichloromethane) to afford 32.4 mg of a white solid. NMR indicated a mixture of 28.8 mg product (71% yield) and 3.6 mg of the acetal isomer 2-(3-(1,3-dioxolan-4-yl)phenyl)acetamide (6% yield, 11.1:1 ratio). A second run provided 28.5 mg product (70% yield) and 5.1 mg acetal isomer side product (10% yield, 7.1:1 ratio).

^{1}H NMR (500 MHz, acetone-d_6): [11.1:1 mixture of product:acetal isomer] δ 10.03 (s, 1H), 7.86 (s, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.01 (s, 1H), 6.41 (s, 1H), 3.63 (s, 2H).

^{13}C NMR (125 MHz, acetone-d_6): [11.1:1 mixture of product:acetal isomer] δ 192.99, 172.60, 138.56, 137.73, 136.15, 130.86, 129.82, 128.68, 42.75.

IR (ATR, cm^{-1}): 3362 (br, m), 3170 (br, m), 2929 (w), 2826 (w), 2742 (w), 1692 (m), 1642 (s), 1604 (m), 1483 (w), 1415 (m), 1391 (m), 1303 (m), 1235 (s), 1191 (w), 1140 (m), 1089 (w), 1002 (w), 915 (m), 885 (w), 813 (w), 777 (s).

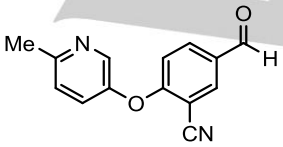
HRMS (ESI+): Calculated for $C_9H_{10}NO_2^+$ $[M + H]^+$: 164.0706; found: 164.0705.



2-(3-(1,3-dioxolan-4-yl)phenyl)acetamide (side product)**:**

^{1}H NMR (500 MHz, acetone-d_6): [1:11.1 mixture with desired product] δ 7.34 (s, 1H), 7.32 – 7.22 (m, 3H), 6.86 (s, 1H), 6.29 (s, 1H), 5.19 (s, 1H), 5.00 (s, 1H), 4.99 (t, *J* = 6.7 Hz, 1H), 4.25 (dd, *J* = 8.0, 6.8 Hz, 1H), 3.59 (dd, *J* = 8.0, 6.8 Hz, 1H), 3.51 (s, 2H).

^{13}C NMR (125 MHz, acetone-d_6): [1:11.1 mixture with desired product, some peaks are not identified] δ 141.17, 137.58, 129.55, 129.21, 127.77, 125.08, 96.38, 78.06, 72.45.



5-formyl-2-((6-methylpyridin-3-yl)oxy)benzonitrile (16): A threaded 16 × 125 mm borosilicate reaction tube with a Teflon-coated re-sealable septum was charged (in open air) with a teflon-coated stirbar, K_3PO_4 (106 mg, 0.5 mmol), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.8 mg, 0.0025 mmol), $NiCl_2$·glyme (5.5 mg, 0.025 mmol), and dtbbpy (10.1 mg, 0.0375 mmol). The atmosphere of the reaction tube was sparged with Ar for 30 minutes. Separately, a 1-dram vial with a Teflon-coated re-sealable septum was charged (in open air) with 5-chloro-2-((6-methylpyridin-3-yl)oxy)benzonitrile (61 mg, 0.25 mmol) and 1,3-dioxolane (5 mL). The resulting homogeneous solution was sparged (sub-surface) with N_2 for 30 minutes. The chloride/dioxolane solution was then charged via syringe (sparged using standard Schlenk techniques) to the reaction tube, and the resulting solution was sparged (sub-surface) with Ar for an additional 20 minutes. The resulting solution was sealed under Ar and irradiated for 3 days. The reaction was concentrated to remove dioxolane, followed by the addition of H_2O (2 mL) and MeTHF (4 mL). The resulting mixture was transferred to a separatory funnel and the phases were separated. The aqueous phase was extracted with MeTHF (1 mL), and the aqueous phase was discarded. The combined organic phases were washed with saturated aq. NaCl (4 mL), then dried over $MgSO_4$, filtered, and concentrated. The oil was purified by silica gel chromatography (gradient elution 0 to 40% EtOAc/heptane) to afford, after concentration, the intermediate acetal (58 mg). The oil was dissolved in acetone (2 mL), to which was added 1N HCl (1 mL) and the resulting mixture was stirred overnight (16 h). The solution was concentrated to remove acetone, and the crude oil was diluted with EtOAc (4 mL) and treated with saturated aq. $NaHCO_3$ (1 mL), resulting in aqueous pH = 7. The resulting mixture was transferred to a separatory funnel and the phases were separated. The aqueous phase was extracted with EtOAc (1 mL), and the aqueous phase was discarded. The combined organic phases were washed with saturated aq. NaCl (2 mL), then dried over $MgSO_4$, filtered, and concentrated. The oil was purified by silica gel chromatography (gradient elution 0 to 40% EtOAc/heptane) to afford, after concentration, the title compound (45 mg, 75% yield).

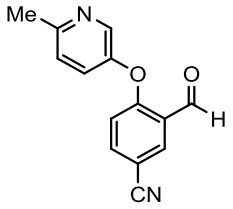
4.09 mmol scale-up. A 500 mL graduated cylinder with a flat bottom and a 24/40 ground glass neck (CG 1223-07, 370 mm height x 41 mm ID) was, in open air, charged with a Teflon-coated octagon stir bar with pivot ring (8 mm x 38 mm), 5-chloro-2-((6-methylpyridin-3-yl)oxy)benzonitrile (1.00 g, 4.09 mmol), 4,4'-di-tert-butyl-2,2'-bipyridine (0.165 g, 0.613 mmol), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (0.046 g, 0.041 mmol), K_3PO_4 (1.735 g, 8.17 mmol) and $NiCl_2$-DME (0.090 g, 0.409 mmol) as solids, followed by 1,3-dioxolane (82 mL). The resulting stirred solution was sparged (sub-surface) with N_2 for 30 minutes, then placed under a light static N_2 atmosphere. While stirring at 1000 rpm, the solution was irradiated for 3 days with two lamps placed 180° from each other. The crude solution was filtered to remove K_3PO_4, then concentrated and subjected to silica gel chromatography, then concentrated to an oil. The oil was purified by silica gel chromatography (gradient elution 0 to 40% EtOAc/heptane) to afford, after concentration, a mixture of the intermediate acetals. The mixture was dissolved in acetone (20 mL), to which was added 1N HCl (10 mL) and the resulting mixture was stirred overnight (15 h). The solution was with saturated aq. $NaHCO_3$ (10 mL), resulting in aqueous pH = 6. The resulting mixture was transferred to a separatory funnel and the phases were separated. The aqueous phase was extracted with EtOAc (5 mL), and the aqueous phase was discarded. The combined organic phases were washed with saturated aq. NaCl (10 mL), then dried over $MgSO_4$, filtered, and concentrated. Silica gel column purification as above afforded an inseparable mixture of the desired aldehyde and the unreacted acetal regioisomer (676 mg). Calculations based on ^1H NMR integration showed 610 mg of desired aldehyde (64% yield). An analytically pure sample of the aldehyde was obtained by recrystallization from EtOAc/*n*-heptane as follows: the solid mixture was slurried in EtOAc (2 mL) and heated to 60 °C, resulting in a homogeneous solution. Upon cooling to 25 °C, the solution was seeded with pure aldehyde, followed by 30 minute age to form a seed bed. *n*-Heptane (8 mL) was added via syringe pump over 2 h. The resulting slurry was stirred for an additional 2 h, then filtered and displacement-washed with 1:4 EtOAc:*n*-heptane. The resulting cake was dried to afford pure **16**.

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.92 (s, 1H), 8.39 (d, *J* = 2.7 Hz, 1H), 8.19 (d, *J* = 2.0 Hz, 1H), 7.98 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.39 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.27 (d, *J* = 8.5 Hz, 1H), 6.89 (d, *J* = 8.7 Hz, 1H), 2.61 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 188.61, 163.85, 156.86, 148.31, 142.15, 136.23, 135.26, 131.46, 128.80, 124.53, 115.64, 114.63, 104.26, 24.06.

IR (ATR, cm^{-1}): 3042 (w), 2859 (w), 2835 (w), 2231 (m), 1688 (s), 1604 (s), 1573 (m), 1483 (s), 1425 (m), 1378 (m), 1267 (s), 1237 (w), 1199 (m), 1157 (w), 1101 (m), 1026 (m), 928 (m), 828 (s), 766 (m), 732 (w), 715 (w).

HRMS (ESI+): Calculated for $C_{14}H_{10}N_2O_2^+$ $[M + H]^+$: 239.0815; found: 239.0827.



3-formyl-4-((6-methylpyridin-3-yl)oxy)benzonitrile (17): A threaded 16 × 125 mm borosilicate reaction tube with a Teflon-coated re-sealable septum was charged (in open air) with a teflon-coated stirbar, K_3PO_4 (106 mg, 0.5 mmol), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.8 mg, 0.0025 mmol), $NiCl_2$·glyme (5.5 mg, 0.025 mmol), and dtbbpy (10.1 mg, 0.0375 mmol). The atmosphere of the reaction tube was sparged with Ar for 30 minutes. Separately, a 1-dram vial with a Teflon-coated re-sealable septum was charged (in open air) with 3-chloro-4-((6-methylpyridin-3-yl)oxy)benzonitrile (61 mg, 0.25 mmol) and 1,3-dioxolane (5 mL). The resulting homogeneous solution was sparged (sub-surface) with N_2 for 30 minutes. The chloride/dioxolane solution was then charged via syringe (sparged using standard Schlenk techniques) to the reaction tube, and the resulting solution was sparged (sub-surface) with Ar for an additional 20 minutes. The resulting solution was sealed under Ar and irradiated for 3 days. The reaction was concentrated to remove dioxolane, followed by the addition of H_2O (2 mL) and MeTHF (4 mL). The resulting mixture was transferred to a separatory funnel and the phases were separated. The aqueous phase was extracted with MeTHF (1 mL), and the aqueous phase was discarded. The combined organic phases were washed with saturated aq. NaCl (4 mL), then dried over $MgSO_4$, filtered, and concentrated. The oil was purified by silica gel chromatography (gradient elution 0 to 40% EtOAc/heptane) to afford, after concentration, the intermediate acetal (42 mg). The oil was dissolved in acetone (2 mL), to which was added 1N HCl (1 mL) and the resulting mixture was stirred overnight (16 h). The solution was concentrated to remove acetone, and the crude oil was diluted with EtOAc (4 mL) and treated with saturated aq. $NaHCO_3$ (1 mL), resulting in aqueous pH = 7. The resulting mixture was transferred to a separatory funnel and the phases were separated. The aqueous phase was extracted with EtOAc (1 mL), and the aqueous phase was discarded. The combined organic phases were washed with saturated aq. NaCl (2 mL), then dried over $MgSO_4$, filtered, and concentrated. The oil was purified by silica gel chromatography (gradient elution 0 to 40% EtOAc/heptane) to afford, after concentration, the title compound (34 mg, 59% yield).

4.09 mmol scale-up. A 500 mL graduated cylinder with a flat bottom and a 24/40 ground glass neck (CG 1223-07, 370 mm height x 41 mm ID) was, in open air, charged with a Teflon-coated octagon stir bar with pivot ring (8 mm x 38 mm), 3-(1,3-dioxolan-2-yl)-4-((6-methylpyridin-3-yl)oxy)benzonitrile (1.00 g, 4.09 mmol), 4,4'-di-tert-butyl-2,2'-bipyridine (0.165 g, 0.613 mmol), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (0.046 g, 0.041 mmol), K_3PO_4 (1.735 g, 8.17 mmol) and $NiCl_2$-DME (0.090 g, 0.409 mmol) as solids, followed by 1,3-dioxolane (82 mL). The resulting stirred solution was sparged (sub-surface) with N_2 for 30 minutes, then placed under a light static N_2 atmosphere. While stirring at 1000 rpm, the solution was irradiated for 3 days with two lamps placed 180° from each other.

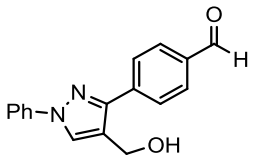
The crude solution was filtered to remove K_3PO_4, then concentrated and subjected to silica gel chromatography, then concentrated to an oil. The oil was purified by silica gel chromatography (gradient elution 0 to 40% EtOAc/heptane) to afford, after concentration, the pure intermediate acetal (807 mg). The acetal was dissolved in acetone (20 mL), to which was added 1N HCl (20 mL) and the resulting mixture was stirred overnight (15 h). The solution was with saturated aq. $NaHCO_3$ (25 mL), resulting in aqueous pH = 7. The resulting mixture was transferred to a separatory funnel and the phases were separated. The aqueous phase was extracted with EtOAc (5 mL), and the aqueous phase was discarded. The combined organic phases were washed saturated aq. NaCl (10 mL), then dried over $MgSO_4$, filtered, and concentrated. Silica gel purification as above afforded the desired aldehyde **17** as a solid (681 mg, 2.86 mmol, 70% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.55 (s, 1H), 8.40 (d, *J* = 2.8 Hz, 1H), 8.22 (d, *J* = 2.2 Hz, 1H), 7.73 (dd, *J* = 8.7, 2.2 Hz, 1H), 7.39 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 1H), 6.87 (d, *J* = 8.7 Hz, 1H), 2.62 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 186.88, 162.81, 156.63, 148.58, 142.13, 138.75, 133.51, 128.66, 126.27, 124.56, 117.53, 116.93, 107.30, 24.02.

IR (ATR, cm^{-1}): 3072 (w), 2922 (w), 2232 (m), 1681 (s), 1607 (w), 1595 (m), 1575 (w), 1476 (s), 1398 (w), 1381 (w), 1276 (w), 1246 (s), 1230 (w), 1199 (w), 1153 (w), 1101 (m), 1025 (m), 945 (m), 913 (m), 869 (w), 838 (m), 811 (w), 755 (w), 722 (w) 692 (w).

HRMS (ESI+): Calculated for $C_{14}H_{10}N_2O_2^+$ $[M + H]^+$: 239.0815; found: 239.0827.



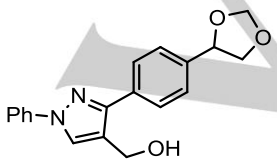
4-(4-(hydroxymethyl)-1-phenyl-1*H*-pyrazol-3-yl)benzaldehyde (18): Synthesized following the general procedure from (3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)methanol (71.0 mg, 0.25 mmol, Chem-Impex). Purified by automated column chromatography (25 g silica, 0 → 40% ethyl acetate in hexanes) to afford 49.6 mg of a white solid. NMR analysis indicated this to be a mixture of 43.5 mg product (63% yield) and 6.1 mg of the acetal isomer (3-(4-(1,3-dioxolan-4-yl)phenyl)-1-phenyl-1*H*-pyrazol-4-yl)methanol (8% yield, 8.3:1 ratio). A second run yielded 38.2 mg product (55% yield) and 5.3 mg isomer (7% yield, 8.3:1 ratio).

^{1}H NMR (500 MHz, $CDCl_3$): [8.3:1 mixture of product:acetal isomer] δ 10.04 (s, 1H), 8.08 (d, *J* = 7.9 Hz, 2H), 8.01 (s, 1H), 7.94 (d, *J* = 7.9 Hz, 2H), 7.74 (d, *J* = 8.5 Hz, 2H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.32 (t, *J* = 8.7 Hz, 1H), 4.78 (s, 2H), 2.09 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): [8.3:1 mixture of product:acetal isomer] δ 192.21, 150.11, 139.77, 139.04, 135.68, 130.24, 129.66, 128.38, 128.20, 127.02, 121.51, 119.20, 55.97.

IR (ATR, cm^{-1}): 3315 (br, w), 3138 (w), 2922 (w), 2851 (w), 2736 (w), 1693 (s), 1598 (s), 1576 (m), 1552 (m), 1504 (s), 1465 (m), 1423 (m), 1393 (m), 1336 (m), 1306 (m), 1293 (m), 1244 (m), 1212 (s), 1167 (m), 1112 (w), 1038 (m), 1011 (m), 986 (m), 959 (m), 902 (w), 838 (s), 749 (s), 729 (m), 706 (w).

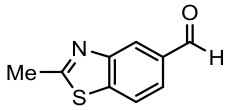
HRMS (ESI+): Calculated for $C_{17}H_{15}N_2O_2^+$ $[M + H]^+$: 279.1128; found: 279.1125.



(3-(4-(1,3-dioxolan-4-yl)phenyl)-1-phenyl-1*H*-pyrazol-4-yl)methanol (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [1:8.3 mixture with desired product, some peaks are not identified] δ 7.98 (s, 1H), 7.86 (d, *J* = 7.9 Hz, 2H), 7.71 (d, 2H, *J* = 8.5 Hz), 7.43 (t, *J* = 7.6 Hz, 2H), 7.29 (t, *J* = 8.7 Hz, 1H), 5.29 (s, 1H), 5.11 (s, 1H), 5.04 (t, *J* = 6.8 Hz, 1H), 4.75 (s, 2H), 4.28 (dd, *J* = 8.1, 6.7 Hz, 1H), 3.72 (dd, *J* = 8.1, 6.8 Hz, 1H), 1.96 (s, 1H).

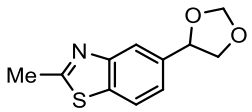
^{13}C NMR (125 MHz, $CDCl_3$): [1:8.3 mixture with desired product, some peaks are not identified] δ 151.18, 139.93, 139.30, 132.90, 129.58, 128.12, 126.67, 126.53, 120.94, 119.10, 96.20, 77.57, 71.98, 56.07.



2-methylbenzo[*d*]thiazole-5-carbaldehyde (19): Synthesized following the general procedure from 5-chloro-2-methylbenzothiazole (45.9 mg, 0.25 mmol, TCI). Purified by automated column chromatography (50 g silica, 0 → 19% ethyl acetate in hexanes to afford 31.5 mg product (71% yield) as a white crystalline solid. A repeat experiment afforded an unresolved mixture of 30.0 mg product (68% yield) and 4.0 mg of the acetal isomer 5-(1,3-dioxolan-4-yl)-2-methylbenzo[*d*]thiazole (7% yield, 9.3:1 ratio). Compound was previously reported.[6]

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.11 (s, 1H), 8.38 (d, *J* = 1.5 Hz, 1H), 7.95 (d, *J* = 8.2 Hz, 1H), 7.88 (dd, *J* = 8.3, 1.5 Hz, 1H), 2.87 (s, 3H).

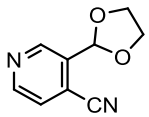
^{13}C NMR (125 MHz, $CDCl_3$): δ 191.84, 169.10, 153.60, 142.35, 134.94, 125.20, 124.26, 122.21, 20.47.



5-(1,3-dioxolan-4-yl)-2-methylbenzo[*d*]thiazole (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (s, 1H), 7.74 (d, *J* = 8.3 Hz, 1H), 7.29 (d, *J* = 8.3 Hz, 1H), 5.24 (s, 1H), 5.07 (t, *J* = 6.7 Hz, 1H), 5.06 (s, 1H), 4.24 (t, *J* = 7.4 Hz, 1H), 3.68 (t, *J* = 7.4 Hz, 1H), 2.77 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): [some peaks are not identified] δ 122.66, 121.65, 120.03, 96.17, 77.47, 72.13, 20.22.



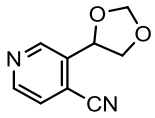
3-(1,3-dioxolan-2-yl)isonicotinonitrile (20): Synthesized according to the general procedure from 3-chloro-4-cyanopyridine (34.6 mg, 0.25 mmol, Matrix). Aldehyde formation was not observed under the standard hydrolysis conditions. The residue was by automated column chromatography (25 g silica, 0 → 40% ethyl acetate in hexanes with 5% triethylamine) to afford 33.6 mg of a white crystalline solid. NMR analysis indicated that this consisted of 30.4 mg desired acetal product (69% yield) and 3.2 mg of the acetal isomer 3-(1,3-dioxolan-4-yl)isonicotinonitrile (7% yield, 9.5:1 ratio). A replicate experiment provided 32.0 mg product (73% yield) and 3.8 mg of the acetal isomer (9% yield, 8.4:1 ratio).

^{1}H NMR (500 MHz, $CDCl_3$): [9.5:1 mixture of product:acetal isomer] δ 8.88 (s, 1H), 8.80 (d, *J* = 5.0 Hz, 1H), 7.58 (dd, *J* = 5.0, 0.8 Hz, 1H), 5.98 (s, 1H), 4.34 – 4.23 (m, 2H), 4.18 – 4.05 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): [9.5:1 mixture of product:acetal isomer]: δ 151.53, 149.87, 134.71, 126.53, 119.67, 115.07, 100.80, 66.35.

IR (ATR, cm^{-1}): 2970 (w), 2899 (m), 2234 (w), 1593 (m), 1559 (w), 1482 (w), 1386 (s), 1291 (w), 1241 (m), 1091 (s), 1047 (w), 1020 (w), 966 (m), 941 (m), 912 (s), 831 (s), 743 (w), 725 (w), 689 (w).

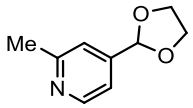
HRMS (ESI+): Calculated for $C_9H_9N_2O_2^+$ $[M + H]^+$: 177.0659; found: 177.0657.



3-(1,3-dioxolan-4-yl)isonicotinonitrile (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [1:9.5 mixture with desired product] δ 8.91 (s, 1H), 8.74 (d, *J* = 4.9 Hz, 1H), 7.52 (dd, *J* = 5.0, 0.9 Hz, 1H), 5.38 (s, 1H), 5.34 (t, *J* = 6.3 Hz, 1H), 5.12 (s, 1H), 4.41 (dd, *J* = 8.6, 6.8 Hz, 1H), 3.83 (dd, *J* = 8.6, 5.7 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): [1:9.5 mixture with desired product] δ 150.07, 149.06, 137.44, 125.51, 118.29, 115.13, 96.73, 73.94, 71.40.



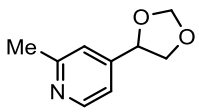
4-(1,3-dioxolan-2-yl)-2-methylpyridine (21): Synthesized following the general procedure from 4-chloro-2-methylpyridine (31.9 mg, 0.25 mmol, Alfa Aesar). Purified by automated column chromatography (25 g silica, 0 → 50% ethyl acetate in hexanes) to afford 32.8 mg of a light yellow liquid. NMR analysis indicated this to be a mixture of 30.4 mg product (74% yield) and 2.4 mg of the acetal isomer 4-(1,3-dioxolan-4-yl)-2-methylpyridine (6% yield, 12.5:1 ratio). A second run yielded 29.6 mg product (72% yield) and 1.2 mg isomer (3% yield, 25:1 ratio).

^{1}H NMR (500 MHz, $CDCl_3$): [12.5:1 mixture product:acetal isomer] δ 8.50 (d, *J* = 5.0 Hz, 1H), 7.25 (s, 1H), 7.18 (d, *J* = 5.1 Hz, 1H), 5.77 (s, 1H), 4.10 – 4.02 (m, 4H), 2.57 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): [12.5:1 mixture product:acetal isomer] δ 158.90, 149.48, 147.00, 120.63, 118.29, 102.19, 65.48, 24.59.

IR (film, cm^{-1}): 3093 (w), 2960 (w), 2906 (m), 2854 (w), 1728 (m), 1614 (m), 1567 (w), 1476 (w), 1449 (m), 1400 (s), 1305 (s), 1210 (s), 1101 (s), 1026 (s), 1010 (s), 955 (m), 890 (w), 838 (m), 764 (w), 717 (w), 689 (w).

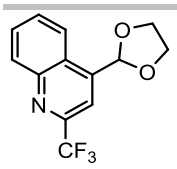
HRMS (ESI+): Calculated for $C_9H_{12}NO_2^+$ $[M + H]^+$: 166.0863; found: 166.0863.



4-(1,3-dioxolan-4-yl)-2-methylpyridine (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [1:12.5 mixture with desired product] δ 8.46 (d, *J* = 5.2 Hz, 1H), 7.12 (s, 1H), 7.04 (d, *J* = 5.3 Hz, 1H), 5.24 (s, 1H), 5.08 (s, 1H), 4.96 (t, *J* = 6.6 Hz, 1H), 4.26 (t, *J* = 7.5 Hz, 1H), 3.67 (dd, *J* = 8.2, 6.4 Hz, 1H), 2.55 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): [1:12.5 mixture with desired product, some peaks are not identified] δ 158.98, 149.52, 120.22, 117.93, 96.36, 76.12, 71.61.



4-(1,3-dioxolan-2-yl)-2-(trifluoromethyl)quinoline (22): Synthesized following the general procedure from 4-chloro-2-(trifluoromethyl)quinoline (57.9 mg, 0.25 mmol, Aldrich). Purified by automated column chromatography (25 g silica, 0 → 20% ethyl acetate in hexanes) to afford 63.3 mg of a white crystalline solid. NMR analysis indicated this to be a mixture of 55.0 mg product (82% yield) and 8.3 mg of the acetal isomer 4-(1,3-dioxolan-4-yl)-2-(trifluoromethyl)quinoline (12% yield, 6.7:1 ratio). A second run (46.3 mg, 0.2 mmol) yielded 40.0 mg product (74% yield) and 2.0 mg isomer (4% yield, 20:1 ratio).

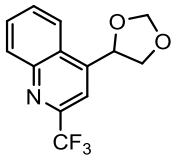
^{1}H NMR (500 MHz, $CDCl_3$): [20:1 mixture product:acetal isomer] δ 8.26 (d, *J* = 8.7 Hz, 2H), 7.98 (s, 1H), 7.82 (t, *J* = 7.7 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 6.49 (s, 1H), 4.19 (s, 4H).

^{13}C NMR (125 MHz, $CDCl_3$): [20:1 mixture product:acetal isomer] δ 147.92 (q, *J* = 34.7 Hz), 147.65, 145.49, 130.79, 130.67, 128.95, 126.70, 124.38, 121.66 (q, *J* = 275.3 Hz), 113.38, 100.30, 65.78.

^{19}F NMR (282 MHz, $CDCl_3$): [20:1 mixture product:acetal isomer] δ −67.53.

IR (ATR, cm^{-1}): 2890 (w), 1514 (w), 1468 (m), 1361 (m), 1345 (w), 1312 (w), 1271 (m), 1254 (m), 1215 (m), 1185 (s), 1117 (s), 1093 (s), 1034 (m), 1019 (m), 970 (m), 942 (m), 890 (s), 863 (w), 798 (w), 781 (w), 761 (s), 739 (w), 710 (w), 660 (m).

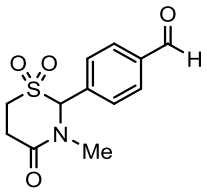
HRMS (ESI+): Calculated for $C_{13}H_{11}F_3NO_2^+$ $[M + H]^+$: 270.0736; found: 270.0734.



4-(1,3-dioxolan-4-yl)-2-(trifluoromethyl)quinoline (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [1:20 mixture with desired product, some peaks are not identified] δ 5.39 (s, 1H), 5.20 (s, 1H), 4.58 (t, *J* = 7.8 Hz, 1H), 3.77 (t, *J* = 7.8 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): [1:20 mixture with desired product, some peaks are not identified] δ 96.25, 73.79, 71.16.



4-(3-methyl-1,1-dioxido-4-oxo-1,3-thiazinan-2-yl)benzaldehyde (23): Synthesized according to the general procedure from 2-(4-chlorophenyl)-3-methyl-1,3-thiazinan-4-one 1,1-dioxide (chlormezanone, 68.4 mg, 0.25 mmol, Enamine). Purified by automated column chromatography (50 g silica, 0 → 4% methanol in dichloromethane) affording 66.1 mg of a pale orange solid. By NMR, this consisted of 59.7 mg desired product (89% yield) and 6.4 mg of the acetal isomer 2-(4-(1,3-dioxolan-4-yl)phenyl)-3-methyl-1,3-thiazinan-4-one 1,1-dioxide (8% yield, 10.8:1 ratio). A second run provided a mixture of 59.3 mg product (89% yield) and 7.6 mg acetal isomer side product (10% yield, 9.1:1 ratio).

Benchtop procedure: The above reaction was performed on the benchtop on the same scale using Schlenk technique. All reagents were stored in a dessicator and weighed on the benchtop. Nickel(II)

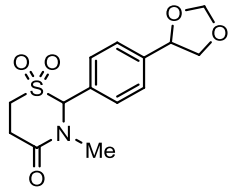
chloride glyme and dtbbpy ligand were added to a 1 dram vial with a septum cap, purged with nitrogen, and prestirred for 10 minutes in 2 mL degassed dioxolane. Substrate, K_3PO_4, and Ir photocatalyst were added to a reaction tube with a septum cap, purged with nitrogen, and suspended in 3 mL degassed dioxolane. The nickel/ligand solution was transferred to the reaction tube *via* syringe, and the entire solution was degassed vigorously with argon for 60 seconds. The degassing needles were removed and the cap and septum were thoroughly sealed with electrical tape. At this point the reaction was illuminated and proceeded as usual for 72 hours. Isolation afforded a mixture of 54.1 mg product (81% yield) and 6.5 mg of the acetal isomer side product (8% yield, 9.8:1 ratio).

^{1}H NMR (500 MHz, $CDCl_3$): [10.8:1 mixture of product:acetal isomer] δ 10.07 (s, 1H), 8.00 (d, *J* = 8.3 Hz, 2H), 7.58 (d, *J* = 8.1 Hz, 2H), 5.40 (d, *J* = 2.1 Hz, 1H), 3.35 – 3.10 (m, 4H), 2.96 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): [10.8:1 mixture of product:acetal isomer] δ 191.23, 166.12, 137.79, 136.36, 130.42, 129.02, 80.57, 44.07, 36.41, 30.63.

IR (ATR, cm^{-1}): 2930 (w), 2854 (w), 2746 (w), 1698 (m), 1646 (s), 1607 (m), 1580 (w), 1453 (w), 1420 (w), 1385 (m), 1319 (s), 1294 (w), 1238 (w), 1208 (m), 1170 (w), 1127 (s), 1034 (w), 1015 (w), 996 (w), 959 (w), 918 (w), 881 (m), 861 (w), 811 (w), 796 (w), 727 (m).

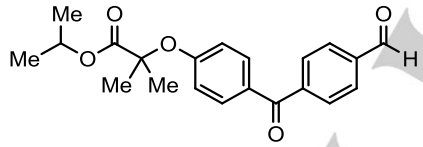
HRMS (ESI+): Calculated for $C_{12}H_{14}NO_4S^+$ $[M + H]^+$: 268.0638; found: 268.0643.



2-(4-(1,3-dioxolan-4-yl)phenyl)-3-methyl-1,3-thiazinan-4-one 1,1-dioxide (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [1:10.8 mixture with desired product] δ 7.46 (d, *J* = 8.1 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 5.29 (s, 1H), 5.27 (d, *J* = 2.7 Hz, 1H), 5.08 (d, *J* = 2.0 Hz, 1H), 5.04 (t, *J* = 6.6 Hz, 1H), 4.26 (ddd, *J* = 8.5, 6.7, 2.1 Hz, 1H), 3.71 (ddd, *J* = 7.7, 6.5, 0.9 Hz, 1H), 3.35 – 3.09 (m, 4H), 2.94 (d, *J* = 1.5 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): [1:10.8 mixture with desired product] δ 166.24, 142.50, 129.93, 128.53, 127.08, 96.29, 80.42, 77.05, 71.85, 43.46, 36.34, 30.66.



isopropyl 2-(4-(4-formylbenzoyl)phenoxy)-2-methylpropanoate (24): Synthesized following the general procedure from isopropyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (fenofibrate, 90.2 mg, 0.25 mmol, Aldrich). Purified by automated column chromatography (25 g silica, 0 → 17% ethyl acetate in hexanes) to afford 72.3 mg product (82% yield) as a colorless oil. A second run provided 70.5 mg (80% yield).

5 mmol scale-up: In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with $NiCl_2$·glyme (110 mg, 10 mol%), dtbbpy (201 mg, 15 mol%), and 1,3-dioxolane (20 mL). This nickel/ligand solution was stirred for 10 minutes prior to addition to the reaction mixture. Meanwhile, a Chemglass threaded 250 mL cylindrical pressure vessel (50 mm × 245 mm) with a teflon stirbar was charged with fenofibrate (1.804 g, 5 mmol), K_3PO_4 (2.123 g, 2 equiv), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ photocatalyst (56.1 mg, 1 mol%), and 1,3-dioxolane (80 mL). The prestirred nickel catalyst solution was added and the flask was closed with a teflon cap/rubber O-ring and sealed with electrical tape. The reaction was stirred at 800 rpm for 120 hours while illuminating with four 34 W blue LED lamps

(Kessil KSH150B) placed at horizontally at 2 cm distance with 90° spacing (Figure S3). The reaction was cooled with both a fan and pressurized air that was directed through tygon tubing mounted next to the reaction vessel. At completion, the reaction had an internal temperature of 35 °C. The reaction mixture was concentrated and the residue was stirred for 1 hour in 100 mL of 1:1 (v:v) acetone:1 M HCl. The mixture was diluted with 200 mL saturated sodium bicarbonate and extracted three times with 150 mL ethyl acetate. The organic extracts were dried with sodium sulfate, concentrated, and the residue purified by automated column chromatography (100 g silica, 0 → 20% ethyl acetate in hexanes) to afford 1.655 g of a pale yellow solid. By NMR, this consisted of 1.467 g product (83% yield) and 0.188 g of the acetal isomer isopropyl 2-(4-(4-(1,3-dioxolan-4-yl)benzoyl)phenoxy)-2-methylpropanoate (9% yield, 8.8:1 ratio).

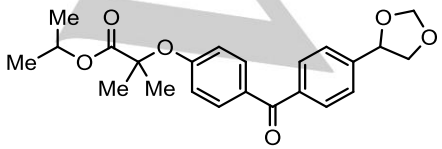
Figure S3. Setup for 5 mmol scale reaction.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.11 (s, 1H), 7.97 (d, *J* = 8.3 Hz, 2H), 7.85 (d, *J* = 8.1 Hz, 2H), 7.75 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 5.07 (hept, *J* = 6.3 Hz, 1H), 1.65 (s, 6H), 1.19 (d, *J* = 6.3 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 194.59, 191.77, 173.10, 160.23, 143.39, 138.26, 132.24, 130.08, 129.80, 129.57, 117.36, 79.58, 69.49, 25.47, 21.63.

IR (film, cm^{-1}): 2984 (w), 2939 (w), 1728 (m), 1705 (m), 1655 (m), 1596 (s), 1500 (w), 1467 (w), 1419 (w), 1385 (w), 1278 (m), 1249 (s), 1204 (w), 1178 (m), 1142 (s), 1100 (s), 1011 (w), 973 (w), 929 (s), 852 (m), 830 (m), 790 (w), 763 (m), 692 (w).

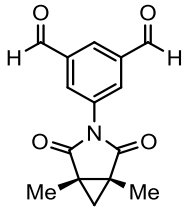
HRMS (ESI+): Calculated for $C_{21}H_{23}O_5^+$ $[M + H]^+$: 355.1540; found: 355.1535.



isopropyl 2-(4-(4-(1,3-dioxolan-4-yl)benzoyl)phenoxy)-2-methylpropanoate (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [some peaks are not identified] δ 7.43 (d, *J* = 8.0 Hz, 2H), 5.26 (s, 1H), 4.27 (dd, *J* = 8.1, 6.8 Hz, 1H), 3.70 (dd, *J* = 8.1, 6.6 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): [some peaks are not identified] δ 173.14, 159.64, 143.79, 137.90, 132.06, 130.13, 125.81, 117.20, 96.23, 79.41, 77.11, 71.87, 69.35.



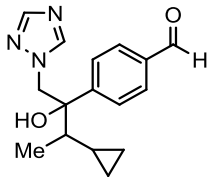
5-(1,5-dimethyl-2,4-dioxo-3-azabicyclo[3.1.0]hexan-3-yl)isophthalaldehyde (25): Synthesized according to the general procedure from 3-(3,5-dichlorophenyl)-1,5-dimethyl-3-azabicyclo[3.1.0]hexane-2,4-dione (procymidone, 35.5 mg, 0.125 mmol, Aldrich). Note that only 0.5 equiv of the aryl dichloride substrate is used so as to maintain 1.0 equiv reactive chloride relative to the catalyst. Purified by automated column chromatography (50 g silica, 10 → 40% ethyl acetate in hexanes) affording 18.3 mg product as a white solid (54% yield). A second run provided 15.8 mg (47% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.09 (s, 2H), 8.34 (s, 1H), 8.09 (d, *J* = 1.5 Hz, 2H), 1.83 (d, *J* = 4.8 Hz, 1H), 1.54 (s, 6H), 1.27 (d, *J* = 4.7 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 190.07, 176.08, 137.84, 134.06, 132.01, 129.43, 33.07, 30.47, 10.09.

IR (ATR, cm^{-1}): 3078 (w), 2981 (w), 2936 (w), 2853 (w), 2752 (w), 1776 (w), 1691 (s), 1597 (m), 1464 (m), 1392 (m), 1371 (s), 1344 (w), 1257 (w), 1153 (w), 1139 (m), 1118 (s), 1087 (m), 1048 (w), 1011 (w), 967 (m), 920 (w), 880 (w), 809 (m), 764 (w), 733 (s), 677 (s).

HRMS (ESI+): Calculated for $C_{15}H_{14}NO_4^+$ $[M + H]^+$: 272.0917; found: 272.0919.



(±)-4-(3-cyclopropyl-2-hydroxy-1-(1*H*-1,2,4-triazol-1-yl)butan-2-yl)benzaldehyde (26): Synthesized following the general procedure from (±)-2-(4-chlorophenyl)-3-cyclopropyl-1-(1*H*-1,2,4-triazol-1-yl)butan-2-ol (cyproconazole, 72.9 mg, 0.25 mmol, 2.3:1 dr, Alfa Aesar). Purified by automated column chromatography (50 g silica, 0 → 3% methanol in dichloromethane, slow gradient) to afford 48.9 mg of a white solid. By NMR, this was found to be a mixture of 44.0 mg product (62% yield, 2.5:1 dr) and 4.9 mg of the acetal isomer (±)-2-(4-(1,3-dioxolan-4-yl)phenyl)-3-cyclopropyl-1-(1*H*-1,2,4-triazol-1-yl)butan-2-ol (6% yield, 10.2:1 ratio, dr not determined). A second run provided a mixture of 49.1 mg product (69% yield, 2.0:1 dr) and 5.6 mg of the acetal isomer (7% yield, 10.2:1 ratio).

Major diastereomer:

^{1}H NMR (500 MHz, $CDCl_3$): [2.5:1 ratio of diastereomers, 10.2:1 ratio of product:acetal isomer] δ 9.94 (s, 1H), 7.84 (s, 1H), 7.77 (s, 1H), 7.74 (d, *J* = 7.5 Hz, 2H), 7.55 (d, *J* = 8.3 Hz, 2H), 4.95 (d, *J* = 14.0 Hz, 1H), 4.73 (s, 1H), 4.54 (d, *J* = 14.1 Hz, 1H), 1.31 (dq, *J* = 9.8, 6.8 Hz, 1H), 1.07 (d, *J* = 6.8 Hz,

3H), 0.66 – 0.55 (m, 1H), 0.46 – 0.39 (m, 1H), 0.39 – 0.31 (m, 1H), 0.02 (dq, *J* = 9.6, 5.0 Hz, 1H), −0.09 (dq, *J* = 9.8, 5.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): [2.5:1 ratio of diastereomers, 10.2:1 ratio of product:acetal isomer] δ 191.93, 151.88, 148.99, 144.26, 135.35, 129.32, 126.97, 79.87, 57.04, 47.43, 14.68, 13.45, 6.52, 3.08.

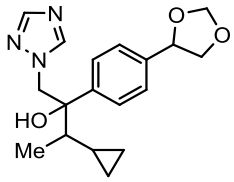
Minor diastereomer (inidcated on spectra by *):

^{1}H NMR (500 MHz, $CDCl_3$): [2.5:1 ratio of diastereomers, 10.2:1 ratio of product:acetal isomer] δ 9.93* (s, 1H), 7.77* (s, 1H), 7.74* (d, *J* = 7.5 Hz, 2H), 7.64* (s, 1H), 7.42* (d, *J* = 8.3 Hz, 2H), 5.03* (d, *J* = 14.2 Hz, 1H), 4.73* (s, 1H), 4.58* (d, *J* = 13.6 Hz, 1H), 1.21* (dt, *J* = 9.7, 6.8 Hz, 1H), 1.16 – 1.09* (m, 1H), 0.83* (d, *J* = 6.8 Hz, 3H), 0.77 – 0.69* (m, 1H), 0.66 – 0.55* (m, 1H), 0.39 – 0.31* (m, 1H), 0.14* (dq, *J* = 10.0, 5.1 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): [2.5:1 ratio of diastereomers, 10.2:1 ratio of product:acetal isomer] δ 191.81*, 151.90*, 150.25*, 144.23*, 135.37*, 129.75*, 126.00*, 80.32*, 57.99*, 47.91*, 15.05*, 12.97*, 7.73*, 2.99*.

IR (film, cm^{-1}): 3389 (br, m), 3126 (w), 3078 (w), 2997 (w), 2969 (w), 2879 (w), 2739 (w), 1698 (s), 1607 (s), 1574 (w), 1509 (m), 1389 (w), 1309 (w), 1276 (m), 1213 (s), 1173 (w), 1138 (m), 1064 (w), 1017 (m), 967 (w), 924 (w), 888 (w), 829 (s), 733 (s), 679 (s), 658 (m).

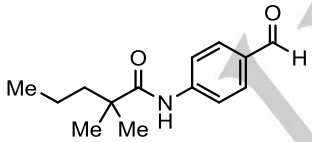
HRMS (ESI+): Calculated for $C_{16}H_{20}N_3O_2^+$ $[M + H]^+$: 286.1550; found: 286.1548.



2-(4-(1,3-dioxolan-4-yl)phenyl)-3-cyclopropyl-1-(1*H*-1,2,4-triazol-1-yl)butan-2-ol (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [1:10.2 mixture with desired product, some peaks are not identified, peaks associated with the minor diastereomer are identified with *, peaks arising from acetal diastereoisomerism are not indicated]: δ 7.67* (s, 1H), 7.60* (d, *J* = 7.2 Hz, 2H), 7.47* (d, *J* = 9.5 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.2 Hz, 2H), 7.21 (s, 1H), 5.23 (d, *J* = 4.1 Hz, 1H), 5.05 (s, 1H), 4.23 – 4.17 (m, 1H), 3.62 (dd, *J* = 8.9, 5.9 Hz, 1H), 1.00 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): [1:10.2 mixture with desired product, some peaks are not identified, peaks associated with the minor diastereomer are identified with *, peaks arising from acetal diastereoisomerism are not indicated] δ 126.61, 126.12*, 125.74, 125.53*, 96.11, 77.33, 71.86, 58.20*, 57.16, 47.81*, 47.35, 15.10*, 14.51, 13.38, 12.94*, 7.65*, 6.32, 2.91*.



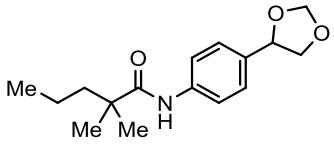
***N*-(4-formylphenyl)-2,2-dimethylpentanamide (27):** Synthesized according to the general procedure from *N*-(4-chlorophenyl)-2,2-dimethylpentanamide (monalide, 59.9 mg, 0.25 mmol, Aldrich). Purified by automated column chromatography (50 g silica, 0 → 20% ethyl acetate in hexanes) to afford 44.4 mg of a colorless oil. NMR analysis indicated a mixture of 38.6 mg product (66% yield) and 5.8 mg of the acetal isomer *N*-(4-(1,3-dioxolan-4-yl)phenyl)-2,2-dimethylpentanamide (8% yield, 7.7:1 ratio). A second run provided 37.8 mg product (65% yield) and 6.2 mg acetal isomer side product (9% yield, 7.2:1 ratio).

^{1}H NMR (500 MHz, $CDCl_3$): [7.7:1 mixture of product:acetal isomer] δ 9.92 (s, 1H), 7.85 (d, *J* = 8.4 Hz, 2H), 7.72 (d, *J* = 8.6 Hz, 2H), 7.50 (s, 1H), 1.60 (t, *J* = 4.3 Hz, 2H), 1.37 – 1.31 (m, 2H), 1.30 (s, 6H), 0.92 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): [7.7:1 mixture of product:acetal isomer] δ 191.12, 176.56, 143.65, 132.37, 131.27, 119.52, 43.91, 43.56, 25.56, 18.29, 14.71.

IR (film, cm^{-1}): 3355 (br, m), 2960 (w), 2931 (w), 2872 (w), 2737 (w), 1682 (s), 1587 (s), 1513 (s), 1474 (w), 1411 (w), 1390 (w), 1306 (m), 1243 (m), 1216 (w), 1163 (s), 1146 (w), 1112 (w), 1011 (w), 927 (w), 830 (m), 790 (m), 769 (w), 732 (m).

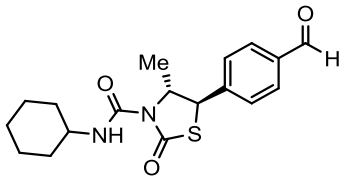
HRMS (ESI+): Calculated for $C_{14}H_{20}NO_2^+$ $[M + H]^+$: 234.1489; found: 234.1487.



***N*-(4-(1,3-dioxolan-4-yl)phenyl)-2,2-dimethylpentanamide** (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [1:7.7 mixture with desired product, some peaks are not identified] δ 7.53 (d, *J* = 8.6 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 5.26 (s, 1H), 5.07 (s, 1H), 4.96 (t, *J* = 6.8 Hz, 1H), 4.22 (t, *J* = 7.4 Hz, 1H), 3.65 (t, *J* = 7.5 Hz, 1H), 1.28 (s, 6H), 0.91 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): [1:7.7 mixture with desired product, some peaks are not identified] δ 176.23, 137.98, 135.16, 126.95, 120.23, 96.13, 77.41, 71.97, 44.01, 43.22, 25.63, 14.74.



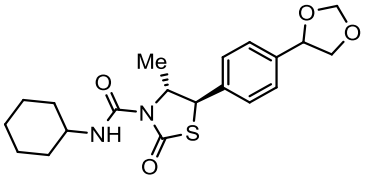
(±)-(4*R*,5*R*)-*N*-cyclohexyl-5-(4-formylphenyl)-4-methyl-2-oxothiazolidine-3-carboxamide (28): Synthesized following the general procedure from (±)-(4*R*,5*R*)-5-(4-chlorophenyl)-*N*-cyclohexyl-4-methyl-2-oxothiazolidine-3-carboxamide (hexythiazox, 88.2 mg, 0.25 mmol, Aldrich). Purified by automated column chromatography (25 g silica, 0 → 30% ethyl acetate in hexanes) to afford 58.1 mg of a colorless oil. NMR analysis indicated that this was a partially resolved mixture of 55.8 mg product (64% yield) and 2.3 mg of the acetal isomer (±)-(4*R*,5*R*)-5-(4-(1,3-dioxolan-4-yl)phenyl)-*N*-cyclohexyl-4-methyl-2-oxothiazolidine-3-carboxamide (2% yield, 27:1 ratio). A second run provided 60.3 mg product (70% yield) and 6.9 mg acetal isomer side product (7% yield, 9.8:1 ratio).

^{1}H NMR (500 MHz, $CDCl_3$): [27:1 mixture of product:acetal isomer] δ 10.01 (s, 1H), 8.05 (d, *J* = 7.8 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 2H), 7.50 (d, *J* = 8.3 Hz, 2H), 4.90 (qd, *J* = 6.3, 1.1 Hz, 1H), 4.27 (d, *J* = 1.0 Hz, 1H), 3.75 – 3.63 (m, 1H), 1.98 – 1.88 (m, 2H), 1.75 – 1.67 (m, 2H), 1.63 (d, *J* = 6.3 Hz, 3H), 1.62 – 1.55 (m, 1H), 1.42 – 1.31 (m, 2H), 1.30 – 1.18 (m, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): [27:1 mixture of product:acetal isomer] δ 191.49, 172.46, 150.16, 147.42, 136.38, 130.70, 127.42, 61.62, 50.62, 49.28, 33.05, 33.00, 25.60, 24.77, 24.77, 20.55.

IR (film, cm^{-1}): 3324 (w), 2930 (m), 2854 (w), 1696 (s), 1660 (m), 1607 (m), 1525 (s), 1451 (w), 1364 (m), 1310 (w), 1209 (m), 1167 (s), 1103 (m), 1064 (w), 1006 (w), 913 (w), 891 (w), 828 (m), 754 (w), 729 (s), 672 (m).

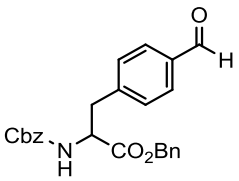
HRMS (ESI+): Calculated for $C_{18}H_{23}N_2O_3S^+$ $[M + H]^+$: 347.1424; found: 347.1418.



(±)-(4*R*,5*R*)-5-(4-(1,3-dioxolan-4-yl)phenyl)-*N*-cyclohexyl-4-methyl-2-oxothiazolidine-3-carboxamide (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [1:27 mixture with desired product, some peaks are not identified] δ 7.33 (d, *J* = 2.6 Hz, 2H), 5.25 (s, 1H), 5.07 (s, 1H), 4.99 (t, *J* = 6.7 Hz, 1H), 4.24 (t, *J* = 6.7 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): [1:27 mixture with desired product, some peaks are not identified] δ 126.99, 126.95, 96.21, 77.23, 71.92.



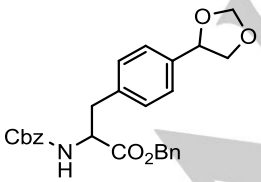
***N*-Cbz-DL-4-formylphenylalanine benzyl ester (29):** Synthesized according to the general procedure from *N*-Cbz-DL-4-chlorophenylalanine benzyl ester (106.0 mg, 0.25 mmol). The acetal was only stirred in HCl for 10 minutes as significant benzyl ester hydrolysis was observed at 1 hour. Purified by automated column chromatography (25 g silica, 0 → 40% ethyl acetate in hexanes) to afford 75.1 mg of a white solid. By NMR, this was found to be a mixture of 66.5 mg product (64% yield) and 8.6 mg of the acetal isomer *N*-Cbz-DL-4-(1,3-dioxolan-4-yl)phenylalanine benzyl ester (7% yield, 8.5:1 ratio). A second run yielded 67.6 mg product (65% yield) and 9.0 mg of the of the 1,3-dioxolan-4-yl acetal isomer (8% yield, 8.3:1 ratio).

^{1}H NMR (500 MHz, $CDCl_3$): [8.5:1 mixture of product:acetal isomer] δ 9.94 (s, 1H), 7.68 (d, *J* = 7.7 Hz, 2H), 7.39 – 7.27 (m, 10H), 7.14 (d, *J* = 7.7 Hz, 2H), 5.31 (d, *J* = 8.1 Hz, 1H), 5.22 – 5.02 (m, 4H), 4.74 (q, *J* = 6.6 Hz, 1H), 3.18 (ddd, *J* = 44.1, 13.9, 6.1 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): [8.5:1 mixture of product:acetal isomer] δ 191.92, 170.98, 155.60, 142.95, 136.20, 135.36, 134.91, 130.17, 130.00, 128.87, 128.87, 128.81, 128.69, 128.43, 128.27, 67.62, 67.22, 54.67, 38.56.

IR (film, cm^{-1}): 3339 (m br), 3034 (w), 2953 (w), 1696 (s), 1607 (m), 1578 (w), 1515 (m), 1499 (m), 1455 (w), 1387 (w), 1343 (w), 1307 (w), 1254 (w), 1211 (s), 1170 (s), 1107 (w), 1054 (m), 1027 (w), 911 (w), 843 (w), 823 (w), 777 (w), 739 (m), 697 (s).

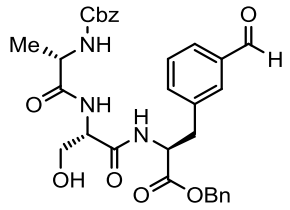
HRMS (ESI+): Calculated for $C_{25}H_{24}NO_5^+$ $[M + H]^+$: 418.1649; found: 418.1644.



***N*-Cbz-DL-4-(1,3-dioxolan-4-yl)phenylalanine benzyl ester** (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [1:8.5 mixture with desired product, some peaks are not identified] δ 7.19 (d, *J* = 7.8 Hz, 2H), 7.00 (d, *J* = 7.4 Hz, 2H), 5.25 (s, 1H), 4.94 (t, *J* = 6.9 Hz, 1H), 4.65 – 4.55 (m, 2H), 4.22 (t, *J* = 7.4 Hz, 1H), 3.64 (t, *J* = 7.5 Hz, 1H), 3.14 – 3.00 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): [1:8.5 mixture with desired product, some peaks are not identified] δ 129.72, 128.75, 128.74, 128.66, 128.34, 128.24, 126.50, 96.13, 77.47, 71.88, 67.44, 67.13, 54.87, 37.90.



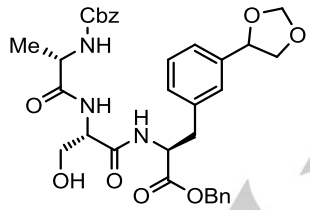
***N*-Cbz-L-alanyl-L-seryl-L-3-formylphenylalanine benzyl ester (30):** Synthesized according to the general procedure from *N*-Cbz-L-alanyl-L-seryl-L-3-chlorophenylalanine benzyl ester (145.5 mg, 0.25 mmol). The acetal was stirred in HCl for only 10 minutes to limit ester hydrolysis. Purified by automated column chromatography (50 g silica, 0 → 4% methanol in dichloromethane) and isolated 99.3 mg of a pale yellow solid. NMR analysis indicated that this consisted of a mixture of 79.3 mg product (55% yield), 10.1 mg of unreacted starting material (7% of mass balance, some material not isolated), and 9.9 mg of the acetal isomer *N*-Cbz-L-alanyl-L-seryl-L-3-(1,3-dioxolan-4-yl)phenylalanine benzyl ester (6% yield, 8.6:1 ratio). A second run afforded 79.9 mg product (56% yield), 31.7 mg unreacted substrate (22% of mass balance), and 11.5 mg acetal isomer side product (7% yield, 7.5:1 ratio).

^{1}H NMR (500 MHz, DMSO-d_6): [8.6:1.1:1 mixture of product:substrate:acetal isomer] δ 9.95 (s, 1H), 8.33 (d, *J* = 7.6 Hz, 1H), 7.86 (d, *J* = 7.9 Hz, 1H), 7.78 – 7.71 (m, 2H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.47 (t, *J* = 8.1 Hz, 2H), 7.38 – 7.22 (m, 10H), 5.07 (s, 2H), 5.02 (d, *J* = 4.9 Hz, 2H), 4.88 (t, *J* = 5.5 Hz, 1H), 4.61 (q, *J* = 7.4 Hz, 1H), 4.32 (q, *J* = 6.4 Hz, 1H), 4.10 (t, *J* = 7.2 Hz, 1H), 3.54 (t, *J* = 5.8 Hz, 2H), 3.16 (dd, *J* = 13.8, 6.1 Hz, 1H), 3.08 (dd, *J* = 13.8, 8.4 Hz, 1H), 1.17 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6): [8.6:1.1:1 mixture of product:substrate:acetal isomer] δ 193.13, 172.39, 170.82, 170.04, 155.74, 138.12, 136.98, 136.25, 135.63, 135.45, 130.71, 129.10, 128.39, 128.37, 128.06, 127.89, 127.81, 127.74, 127.49, 66.17, 65.43, 61.64, 54.93, 53.44, 50.06, 36.25, 18.21.

IR (ATR, cm^{-1}): 3286 (br, s), 3065 (w), 3034 (w), 2935 (w), 1720 (w), 1689 (m), 1639 (s), 1530 (s), 1452 (m), 1388 (w), 1344 (w), 1241 (s), 1125 (w), 1051 (m), 1027 (m), 952 (w), 907 (w), 843 (w), 746 (m), 694 (s).

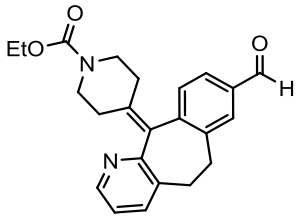
HRMS (ESI+): Calculated for $C_{31}H_{34}N_3O_8^+$ $[M + H]^+$: 576.2340; found: 576.2341.



***N*-Cbz-L-alanyl-L-seryl-L-3-(1,3-dioxolan-4-yl)phenylalanine benzyl ester** (side product)**:**

^{1}H NMR (500 MHz, DMSO-d_6): [1:1.1:8.6 acetal isomer:substrate:aldehyde, most peaks are not identified] δ 5.15 (s, 1H), 4.99 (t, *J* = 8.4 Hz, 1H), 4.20 (t, *J* = 7.4 Hz, 1H).

^{13}C NMR (125 MHz, DMSO-d_6): [1:1.1:8.6 acetal isomer:substrate:aldehyde, most peaks are not identified] δ 130.94, 129.16, 95.17, 76.48, 71.20.



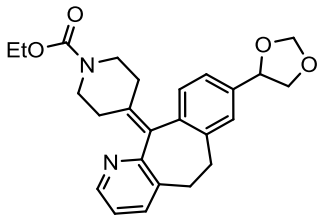
ethyl 4-(8-formyl-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene) piperidine-1-carboxylate (31): Synthesized following the general procedure from ethyl 4-(8-chloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (loratadine/Claritin®, 95.7 mg, 0.25 mmol, TCI). Purified by automated column chromatography (25 g silica, 20 → 60% ethyl acetate in hexanes with 5% triethylamine additive) to afford 78.0 mg of a colorless oil. NMR analysis indicated this to be a mixture of 69.8 mg product (74% yield) and 8.2 mg of the acetal isomer ethyl 4-(8-(1,3-dioxolan-4-yl)-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (8% yield, 9.2:1 ratio). A second run yielded 73.2 mg product (78% yield) and 7.3 mg of the of the 1,3-dioxolan-4-yl acetal isomer (7% yield, 11.4:1 ratio).

^{1}H NMR (500 MHz, $CDCl_3$): [11.4:1 mixture of product:acetal isomer] δ 9.94 (s, 1H), 8.41 (d, *J* = 4.4 Hz, 1H), 7.71 (s, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 7.7 Hz, 1H), 7.11 (dd, *J* = 7.7, 4.8 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.89 – 3.74 (m, 2H), 3.48 (ddd, *J* = 16.3, 10.6, 4.7 Hz, 2H), 3.15 (ddt, *J* = 13.4, 8.7, 4.1 Hz, 2H), 2.97 – 2.81 (m, 2H), 2.50 (ddd, *J* = 14.2, 9.4, 4.6 Hz, 1H), 2.33 (dtt, *J* = 23.7, 13.8, 4.5 Hz, 3H), 1.23 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): [11.4:1 mixture of product:acetal isomer] δ 192.01, 156.17, 155.56, 146.85, 146.09, 138.96, 138.45, 137.98, 135.70, 134.49, 133.54, 130.00, 129.91, 128.24, 122.61, 61.48, 44.86, 44.86, 31.70, 31.68, 30.97, 30.67, 14.79.

IR (film, cm^{-1}): 2979 (w), 2913 (w), 2858 (w), 2730 (w), 1689 (s), 1601 (w), 1566 (w), 1428 (m), 1384 (w), 1300 (w), 1277 (w), 1221 (s), 1171 (w), 1113 (m), 1061 (w), 1026 (w), 996 (m), 898 (m), 859 (w), 831 (w), 800 (w), 766 (w), 728 (m), 675 (w).

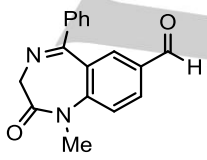
HRMS (ESI+): Calculated for $C_{23}H_{25}N_2O_3^+$ $[M + H]^+$: 377.1860; found: 377.1854.



ethyl 4-(8-(1,3-dioxolan-4-yl)-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [1:11.4 mixture with desired product, some peaks are not identified] δ 8.38 (d, *J* = 4.8 Hz, 1H), 7.19 – 7.14 (m, 2H), 5.24 (s, 1H), 5.04 (d, *J* = 1.7 Hz, 1H), 4.92 (td, *J* = 6.7, 3.8 Hz, 1H), 4.20 (ddd, *J* = 8.5, 6.8, 2.2 Hz, 1H), 3.68 (ddd, *J* = 8.2, 6.7, 1.7 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): [1:11.4 mixture with desired product, some peaks are not identified] δ 135.70, 129.72, 129.59, 127.00, 126.80, 124.23, 122.33, 96.10, 77.52, 71.80, 61.40, 44.93, 31.95, 31.78, 29.79.



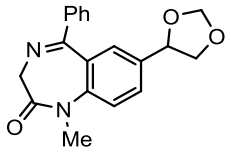
1-methyl-2-oxo-5-phenyl-2,3-dihydro-1*H*-benzo[*e*][1,4]diazepine-7-carbaldehyde (32): Synthesized according to the general procedure from 7-chloro-1-methyl-5-phenyl-1,3-dihydro-2*H*-benzo[*e*][1,4]diazepin-2-one [7] (diazepam, 71.2 mg, 0.25 mmol). Purified by automated column chromatography (50 g silica, 0 → 60% ethyl acetate in hexanes) to afford 50.2 mg product (72% yield) as a pale yellow solid. A second run provided a mixture of 51.4 mg product (74% yield) and 6.3 mg of the acetal isomer side product 7-(1,3-dioxolan-4-yl)-1-methyl-5-phenyl-1,3-dihydro-2*H*-benzo[*e*][1,4]diazepin-2-one (8% yield, 9.5:1 ratio).

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.93 (s, 1H), 8.08 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.83 (d, *J* = 1.9 Hz, 1H), 7.58 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.49 (dd, *J* = 10.5, 8.0 Hz, 2H), 7.42 (dd, *J* = 8.2, 6.8 Hz, 2H), 4.88 (d, *J* = 10.9 Hz, 1H), 3.78 (d, *J* = 10.9 Hz, 1H), 3.46 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 190.19, 169.88, 169.75, 148.65, 138.35, 133.36, 131.72, 131.34, 131.00, 129.62, 129.17, 128.63, 121.80, 57.10, 35.08.

IR (ATR, cm^{-1}): 3057 (w), 2922 (w), 2852 (w), 1733 (w), 1676 (s), 1608 (s), 1596 (w), 1570 (w), 1489 (w), 1474 (w), 1446 (m), 1420 (m), 1374 (m), 1330 (s), 1275 (m), 1243 (w), 1208 (m), 1195 (w), 1123 (s), 1071 (s), 1025 (w), 985 (m), 913 (w), 871 (w), 831 (m), 783 (m), 757 (w), 746 (s), 721 (m), 698 (s), 672 (w).

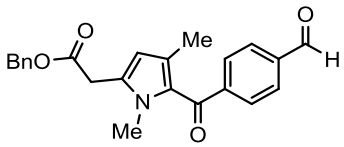
HRMS (ESI+): Calculated for $C_{17}H_{15}N_2O_2^+$ $[M + H]^+$: 279.1128; found: 279.1128.



7-(1,3-dioxolan-4-yl)-1-methyl-5-phenyl-1,3-dihydro-2*H*-benzo[*e*][1,4]diazepin-2-one (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [some peaks are not identified] δ 7.68 (dd, *J* = 8.5, 2.1 Hz, 1H), 5.20 (d, *J* = 8.2 Hz, 1H), 5.01 (d, *J* = 7.7 Hz, 1H), 4.96 (q, *J* = 6.5 Hz, 1H), 4.81 (d, *J* = 10.7 Hz, 1H), 4.20 (ddd, *J* = 14.7, 8.2, 6.7 Hz, 1H), 3.77 (d, *J* = 10.4 Hz, 1H), 3.68 (ddd, *J* = 23.3, 8.1, 6.4 Hz, 1H), 3.40 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): [some peaks are not identified] δ 96.20, 76.69, 71.84.



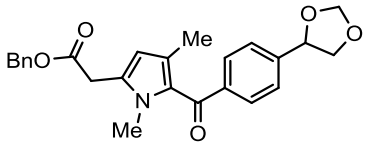
benzyl 2-(5-(4-formylbenzoyl)-1,4-dimethyl-1*H*-pyrrol-2-yl)acetate (33): Synthesized according to the general procedure from benzyl 2-(5-(4-chlorobenzoyl)-1,4-dimethyl-1*H*-pyrrol-2-yl)acetate (95.5 mg, 0.25 mmol). Purified by automated column chromatography (50 g silica, 0 → 25% ethyl acetate in hexanes) to afford 69.9 mg product (74% yield) as a yellow solid. A second run afforded a mixture of 68.4 mg product (73% yield) and 9.5 mg of the acetal isomer side product benzyl 2-(5-(4-(1,3-dioxolan-4-yl)benzoyl)-1,4-dimethyl-1*H*-pyrrol-2-yl)acetate (9% yield, 8.0:1 ratio).

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.10 (s, 1H), 7.96 (d, *J* = 8.1 Hz, 2H), 7.80 (d, *J* = 7.9 Hz, 2H), 7.41 – 7.31 (m, 5H), 5.95 (s, 1H), 5.19 (s, 2H), 3.76 (s, 3H), 3.71 (s, 2H), 1.68 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 191.93, 186.52, 169.27, 146.42, 138.03, 135.48, 133.84, 130.21, 129.85, 129.65, 129.39, 128.79, 128.67, 128.49, 113.10, 67.34, 33.45, 32.90, 14.69.

IR (ATR, cm^{-1}): 3032 (w), 2921 (w), 2851 (w), 1721 (s), 1700 (s), 1615 (s), 1567 (w), 1501 (w), 1485 (w), 1455 (m), 1425 (w), 1385 (s), 1376 (s), 1323 (m), 1301 (w), 1271 (m), 1220 (w), 1183 (s), 953 (m), 859 (w), 840 (m), 804 (m), 759 (m), 744 (s), 697 (s).

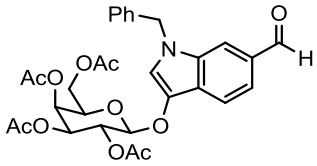
HRMS (ESI+): Calculated for $C_{21}H_{22}O_5^+$ $[M + H]^+$: 376.1543; found: 376.1547.



benzyl 2-(5-(4-(1,3-dioxolan-4-yl)benzoyl)-1,4-dimethyl-1*H*-pyrrol-2-yl)acetate (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [some peaks are not identified] δ 7.70 (d, *J* = 7.9 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 5.93 (s, 1H), 5.29 (s, 1H), 5.11 (s, 1H), 5.06 (t, *J* = 6.8 Hz, 1H), 4.30 (t, *J* = 7.5 Hz, 1H), 1.73 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): [some peaks are not identified] δ 187.44, 169.46, 143.41, 140.83, 135.55, 134.06, 132.76, 129.59, 128.79, 128.61, 128.45, 126.01, 112.54, 96.31, 77.32, 72.03, 67.24, 33.22, 32.92, 14.51.



***N*-benzyl-6-formyl-3-indolyl-β-D-galactopyranoside tetraacetate (34):** Synthesized according to the general procedure from *N*-benzyl-6-chloro-3-indolyl-β-D-galactopyranoside tetraacetate (147.0 mg, 0.25 mmol). Purified by automated column chromatography (50 g silica, 10 → 45% ethyl acetate in hexanes) and obtained 59.5 mg of a pale orange solid. NMR analysis indicated that this consisted of 53.9 mg desired product (37% yield) and 5.6 mg of the acetal isomer *N*-benzyl-6-(1,3-dioxolan-4-yl)-3-indolyl-β-D-galactopyranoside tetraacetate (4% yield, 10.3:1 ratio). A second run afforded 55.7 mg product (38% yield) and 7.2 mg acetal isomer side product (5% yield, 8.1:1 ratio). The product fluoresces blue when irradiated at 365 nm (Figure S4)

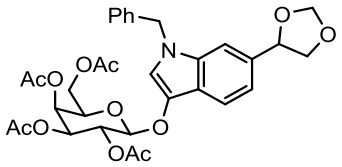
Figure S4. Fluorescence of product **34** upon excitation at 365 nm (1 mg/mL in 40% ethyl acetate:hexanes).

^{1}H NMR (500 MHz, $CDCl_3$): [10.3:1 mixture of product:acetal isomer] δ 10.00 (s, 1H), 7.82 (s, 1H), 7.68 (d, *J* = 8.2 Hz, 1H), 7.62 (d, *J* = 8.3 Hz, 1H), 7.36 – 7.28 (m, 3H), 7.13 (s, 1H), 7.10 (d, *J* = 6.3 Hz, 2H), 5.53 (dd, *J* = 10.5, 8.0 Hz, 1H), 5.45 (d, *J* = 3.1 Hz, 1H), 5.34 (s, 2H), 5.10 (dd, *J* = 10.5, 3.4 Hz, 1H), 4.90 (d, *J* = 8.0 Hz, 1H), 4.19 (qd, *J* = 11.3, 6.6 Hz, 2H), 3.98 (t, *J* = 6.6 Hz, 1H), 2.18 (s, 3H), 2.15 (s, 3H), 2.02 (s, 3H), 1.97 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): [10.3:1 mixture of product:acetal isomer] δ 192.32, 170.31, 170.22, 170.14, 169.41, 136.90, 136.50, 133.41, 131.58, 129.01, 128.12, 126.65, 124.88, 120.42, 119.95, 118.28, 112.70, 102.60, 71.17, 70.78, 68.74, 66.92, 61.45, 50.23, 20.88, 20.69, 20.61, 20.61.

IR (ATR, cm^{-1}): 2927 (w), 2855 (w), 1743 (s), 1686 (m), 1612 (w), 1545 (m), 1469 (w), 1454 (w), 1367 (m), 1214 (s), 1162 (m), 1048 (s), 953 (w), 903 (w), 812 (w), 772 (w), 741 (w), 704 (m).

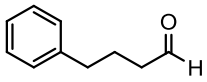
HRMS (ESI+): Calculated for $C_{30}H_{32}NO_{11}^+$ $[M + H]^+$: 582.1970; found: 582.1976.



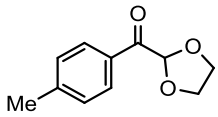
***N*-benzyl-6-(1,3-dioxolan-4-yl)-3-indolyl-β-D-galactopyranoside tetraacetate** (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [1:10.3 mixture with desired product, some peaks are not identified] δ 7.57 (dd, *J* = 8.3, 1.7 Hz, 1H), 5.26 (s, 1H), 5.25 (d, *J* = 2.7 Hz, 1H), 5.07 – 5.04 (m, 1H), 4.87 (s, 1H), 3.70 (td, *J* = 8.2, 7.6, 1.9 Hz, 1H), 2.17 (s, 3H), 2.13 (s, 3H), 2.04 (s, 3H), 1.96 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): [1:10.3 mixture with desired product, some peaks are not identified] δ 170.33, 170.17, 169.44, 128.85, 127.79, 126.68, 124.88, 117.64, 107.34, 102.75, 95.97, 78.27, 72.10, 71.05, 70.87, 68.85, 66.98, 49.85.



4-phenylbutanal: Synthesized according to the general procedure from 1-bromo-3-phenylpropane (49.8 mg, 0.25 mmol, Aldrich). A yield of 6% was determined by GC using 1-fluoronaphthalene as an external standard and commercial 4-phenylbutanal (J&W PharmaLab) to confirm product identity. The reaction was repeated with omission of the acid rinse, and the acetal 2-(3-phenylpropyl)-1,3-dioxolane was likewise obtained in 6% GC yield, indicating that no product is lost during hydrolysis.



(1,3-dioxolane-2-yl)(*p*-tolyl)methanone:

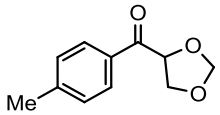
Synthesized following the general procedure from *p*-toluoyl chloride (38.6 mg, 0.25 mmol, Aldrich). Purified by automated column chromatography (50 g basic alumina, 0 → 20% ethyl acetate in hexanes) to afford 20.7 mg of a white solid. NMR analysis indicated this to be a mixture of 18.5 mg product (39% yield) and 2.2 mg of the acetal isomer (1,3-dioxolan-4-yl)(*p*-tolyl)methanone (5% yield, 8.3:1 ratio).

^{1}H NMR (500 MHz, acetone-d_6): [8.3:1 mixture of product:acetal isomer] δ 7.95 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 5.98 (s, 1H), 4.08 – 4.02 (m, 4H), 2.41 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): [8.3:1 mixture of product:acetal isomer] δ 192.96, 144.92, 131.63, 129.48, 129.46, 100.31, 65.68, 21.93.

IR (ATR, cm^{-1}): 2925 (w), 1804 (s), 1775 (m), 1723 (m), 1672 (s), 1605 (s), 1573 (w), 1513 (w), 1480 (w), 1448 (w), 1418 (m), 1389 (w), 1282 (s), 1221 (m), 1205 (m), 1173 (s), 1117 (m), 970 (m), 948 (m), 886 (m), 834 (m), 774 (m), 753 (s), 717 (m), 688 (m).

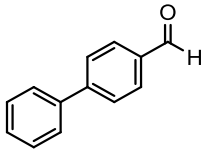
HRMS (ESI+): Calculated for $C_{11}H_{13}O_3^+$ $[M + H]^+$: 193.0859; found: 193.0861.



(1,3-dioxolane-4-yl)(*p*-tolyl)methanone (side product)**:**

^{1}H NMR (500 MHz, acetone-d_6): [1:8.3 mixture with desired product, some peaks are not identified] ^{1}H NMR (500 MHz, Acetone-d_6) δ 5.41 (dd, *J* = 7.6, 5.1 Hz, 1H), 5.02 (s, 1H), 4.96 (s, 1H), 4.23 (t, *J* = 7.9 Hz, 1H).

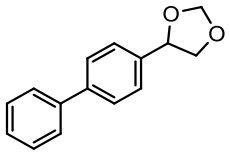
^{13}C NMR (125 MHz, $CDCl_3$): [1:8.3 mixture with desired product, some peaks are not identified] δ 96.42, 78.79, 67.08.



[1,1'-biphenyl]-4-carbaldehyde (38): Synthesized according to the general procedure from benzyl 4-chloro-1,1'-biphenyl (47.2 mg, 0.25 mmol). After hydrolysis the mixture was extracted with DCM (3 × 30 mL) and dried over $MgSO_4$. Procedure was otherwise the same. Purified by automated column chromatography (50 g silica, gradient 100:0 → 90:10 hexanes:ethyl acetate) to afford the title compound (34.0 mg, 75% yield) as a white solid as a mixture with acetal isomer side product 4-[1,1'-biphenyl-4-yl]-1,3-dioxolane (3.4 mg, 6% yield, 12.5:1 ratio). This compound was previously reported.[8]

^{1}H NMR (500 MHz, $CDCl_3$): [12.5:1 mixture of product:acetal isomer] δ 10.07 (s, 1H), 7.96 (d, *J* = 7.4 Hz, 2H), 7.76 (d, *J* = 7.5 Hz, 2H), 7.65 (d, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.3 Hz, 2H), 7.43 (d, *J* = 7.2 Hz, 1H).

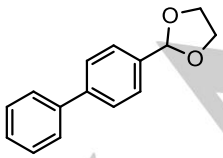
^{13}C NMR (125 MHz, $CDCl_3$): [12.5:1 mixture of product:acetal isomer] δ 192.08, 147.35, 139.87, 135.33, 130.42, 129.16, 128.62, 127.84, 127.52.



4-[1,1'-biphenyl-4-yl]-1,3-dioxolane (37–Ph) (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): [1:12.5 mixture with desired product, some peaks are not identified] δ 7.59 (t, *J* = 6.4 Hz, 4H), 7.41 (s, 2H), 7.35 (t, *J* = 7.4 Hz, 1H), 5.31 (s, 1H), 5.12 (s, 1H), 5.05 (t, *J* = 6.8 Hz, 1H), 4.29 (t, *J* = 7.3 Hz, 1H), 3.75 (t, *J* = 7.5 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ [1:12.5 mixture with desired product, some peaks are not identified] 128.94, 127.25, 126.72, 96.24, 77.58, 72.01.



2-([1,1'-biphenyl]-4-yl)-1,3-dioxolane (36–Ph): Synthesized as an analytical standard for GC selectivity determination. To a 100 mL flask with a stirbar was added [1,1'-biphenyl]-4-carbaldehyde (1 g, 5.5 mmol, Aldrich), *p*-toluenesulfonic acid monohydrate (20 mg, 0.02 equiv, Aldrich), ethylene glycol (1 mL, 3 equiv, Baker), and dry toluene (50 mL). The reaction was refluxed for one hour while removing water with a Dean Stark apparatus. The reaction was diluted with an additional 50 mL

toluene, rinsed with 50 mL saturated sodium bicarbonate and then 3 × 50 mL saturated sodium chloride, and concentrated. The resulting oil was cooled on ice at which point a white solid precipitated. The solid was triturated twice with 50 mL pentane and dried to afford 851 mg product (69% yield). Compound was previously characterized.[9]

^{1}H NMR (500 MHz, C_6D_6): δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.47 (d, *J* = 7.9 Hz, 2H), 7.43 (d, *J* = 7.0 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 5.82 (s, 1H), 3.69 – 3.60 (m, 2H), 3.55 – 3.46 (m, 2H).

^{13}C NMR (125 MHz, C_6D_6): δ 142.32, 141.32, 138.11, 129.04, 127.57, 127.57, 127.48, 127.38, 103.92, 65.18.

V. Time Point Experiments

General procedure for time point experiments:

Reagent handling: $NiCl_2$·glyme, dtbbpy, $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$, and K_3PO_4 were stored in an N_2-filled glovebox. 1,3-Dioxolane (with up to 75 ppm BHT stabilizer) was degassed with argon or nitrogen, brought into the glovebox, and stored on activated 4Å molecular sieves. *Note: Distillation of commercial 1,3-dioxolane to remove BHT inhibitor is unnecessary and does not lead to any significant improvement in yield.*

Reaction setup (0.05 mmol scale): A ½-dram vials (Fisher part number: 03-338AA) equipped with a PTFE-coated stir bar was brought into a N_2-filled glove box and charged with K_3PO_4 (21.2 mg, 0.1 mmol, 2 equiv). To the reaction vial the following were added successively: a yellow solution of $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (0.6 mg, 0.5 µmol, 0.01 equiv.) in 1,3-dioxolane (0.250 mL) a clear solution of 4-chlorobenzonitrile (6.9 mg, 0.05 mmol, 1 equiv.) in 1,3-dioxolane (0.250 mL), and a light green solution of $NiCl_2$·glyme (1.1 mg, 5 µmol, 0.1 equiv.) and 4,4′-di-*tert*-butyl-2,2′-bipyridine (2.0 mg, 7.5 µmol, 0.15 equiv.) in 1,3-dioxolane (0.500 mL). The vial was capped with a Teflon septum cap and sealed with electrical tape. The reaction vial was removed from the glove box, set to stir (800 rpm) and irradiated with a blue LED array (Figure S1, cooled with both a fan above and pressurized air that was directed through tygon tubing mounted next to the reaction array) for the indicated time. The crude reaction was then analyzed by GC-FID relative to 1-fluoronaphthalene as an external standard.

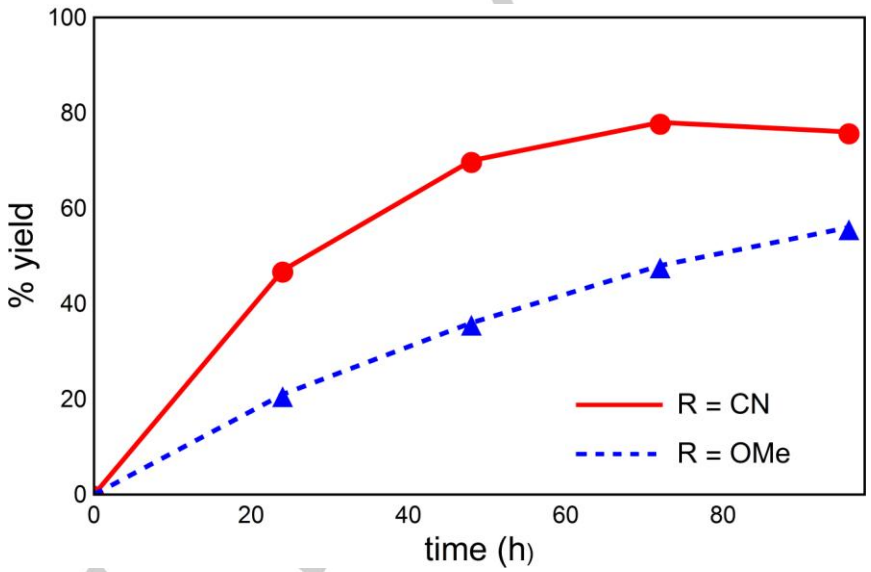


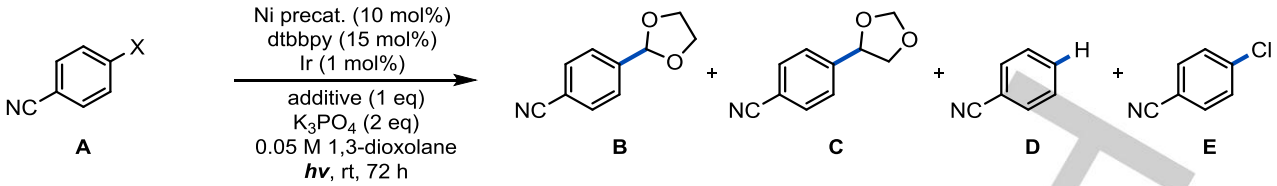
Figure S5. Time point experiments for the production of 4-(1,3-dioxolan-2-yl)benzonitrile and 4-(1,3-dioxolan-2-yl)anisole to 96 hours with 25W blue LED array. Yields and conversion determined by ^1H NMR using 1-fluoronaphthalene as an external standard. Reactions were carried out on 0.05 mmol scale. Notice that the relative reaction rate trends with aryl chloride electronics; the reaction of 4-chlorobenzonitrile reached near completion after 48 hours while 4-chloroanisole did not plateau even within the 96 hour monitoring period.

VI. Halide Selectivity Studies

General procedure for halide additive experiments:

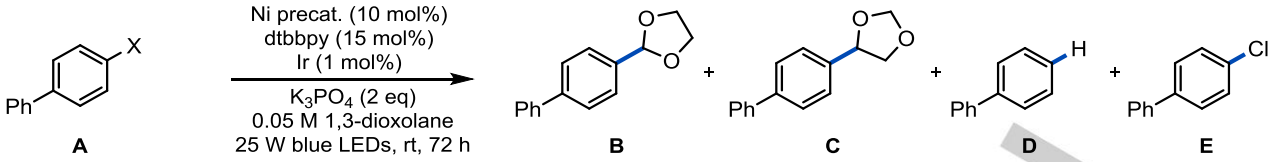
Reagent handling: $NiCl_2$·glyme, dtbbpy, $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$, and K_3PO_4 were stored in an N_2-filled glovebox. 1,3-Dioxolane (with up to 75 ppm BHT stabilizer) was degassed with argon or nitrogen, brought into the glovebox, and stored on activated 4Å molecular sieves. *Note: Distillation of commercial 1,3-dioxolane to remove BHT inhibitor is unnecessary and does not lead to any significant improvement in yield.*

Reaction setup (0.05 mmol scale): Reactions irradiated with 25 W arrays were carried out in ½-dram vials (Fisher part number: 03-338AA) and reactions irradiated with 34 W lamps were carried out in 16 × 125 mm borosilicate reaction tubes. A reaction vessel equipped with a PTFE-coated stir bar was brought into a N_2-filled glove box and charged with K_3PO_4 (21.2 mg, 0.1 mmol, 2 equiv.) followed by TBACl (13.9 mg, 0.05 mmol, 1 equiv.). To the reaction vessel the following were added successively: 1,3-dioxolane (0.500 mL), a clear solution of aryl halide (0.05 mmol, 1 equiv.) in 1,3-dioxolane (0.050 mL), a yellow solution of $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (0.6 mg, 0.5 μmol, 0.01 equiv.) in 1,3-dioxolane (0.150 mL) and a solution of the indicated Ni precatalyst (5 μmol, 0.1 equiv.) and 4,4′-di-*tert*-butyl-2,2′-bipyridine (2.0 mg, 7.5 μmol, 0.15 equiv.) in 1,3-dioxolane (0.300 mL). The reaction vessel was capped with a Teflon septum cap and sealed with electrical tape. The reaction vessel was removed from the glove box, set to stir (800 rpm) and irradiated with the indicated light source. 25 W arrays were cooled with a fan above and pressurized air that was directed through tygon tubing mounted next to the array (Figure S1) and 34 W lamps (Kessil KSH150B) were placed horizontally at 2 cm distance from the reaction tube with a fan to cool the reaction (Figure S2). The crude reaction was analyzed by GC-FID relative to 1-fluoronaphthalene as an external standard.



Entry	X	Additive	Ni precat.	*hv*	Conversion **A**	Yield **B**	Yield **C**	Yield **D**	Yield **E**	Selectivity (**B**:**C**)
1	Cl	none	$NiCl_2$·DME	25 W Array	100.0%	**73.1%**	**10.3%**	0%	NA	**7.1:1**
2	Br	none	$NiCl_2$·DME	25 W Array	100.0%	**51.8%**	**3.3%**	0%	0%	**15.8:1**
3	I	none	$NiCl_2$·DME	25 W Array	14.4%	**0%**	**0%**	0%	9%	**NA**
4	I	none	$NiCl_2$·DME	34 W Lamp	4.4%	**0%**	**0%**	8.3%	0%	**NA**
5	Cl	TBACl	$NiCl_2$·DME	25 W Array	100.0%	**79.5%**	**11.0%**	0%	NA	**7.2:1**
6	Br	TBACl	$NiCl_2$·DME	25 W Array	100.0%	**45.9%**	**4.0%**	0%	0%	**13.6:1**
7	I	TBACl	$NiCl_2$·DME	25 W Array	100.0%	**0%**	**0%**	0%	98.2%	**NA**
8[a]	I	TBACl	$NiCl_2$·DME	34 W Lamp	96.6%	**10.0%**	**2.8%**	0%	64.6%	**3.5:1**
9	Cl	none	$Ni(cod)_2$	25 W Array	100.0%	**66.0%**	**7.6%**	0%	NA	**8.7:1**
10	Br	none	$Ni(cod)_2$	25 W Array	100.0%	**52.9%**	**2.6%**	0%	0%	**20.1:1**
11	I	none	$Ni(cod)_2$	25 W Array	14.1%	**0%**	**0%**	0%	0%	**NA**
12	I	none	$Ni(cod)_2$	34 W Lamp	22.6%	**1.7%**	**0%**	8.9%	0%	**NA**
13	Cl	TBACl	$Ni(cod)_2$	25 W Array	94.5%	**51.3%**	**5.4%**	0%	NA	**9.6:1**
14	Br	TBACl	$Ni(cod)_2$	25 W Array	100.0%	**43.5%**	**3.6%**	0%	0%	**12.2:1**
15	I	TBACl	$Ni(cod)_2$	25 W Array	100.0%	**0%**	**0%**	0%	72.4%	**NA**
16[a]	I	TBACl	$Ni(cod)_2$	34 W Lamp	100.0%	**18.1%**	**3.6%**	0%	37.8%	**5.0:1**

Table S2. Investigation of the effect halide, precatalyst and light source on reaction yield and selectivity. Yields and conversion determined by GC-FID using 1-fluoronaphthalene as an external standard. Reactions were carried out on 0.05 mmol scale. Note that 4-iodobenzonitrile with TBACl as an additive only gave **B** when 34 W lamps were used and in contrast to all other reactions $Ni(cod)_2$ outperformed $NiCl_2$·DME (entries 8 and 16). The observed selectivity for **B** over **C** was greatest for 4-bormobenzonitrile using $Ni(cod)_2$ as a precatalyst. Notice that in all reactions with 4-iodobenzonitirle and TBACl the mass balance is accounted for by 4-chlorobenzonitirle and in some cases the yield of halogen exchange product was excellent (entry 7). Together with the lack of product observed with 25 W LEDs this indicates that the halogen exchange catalyst and photoelimination catalyst are different species in this system. [a]Reaction was carried out for 74 h.



Entry	X	Additive	Ni precat.	*hv*	Conversion **A**	Yield **B**	Yield **C**	Yield **D**	Yield **E**	Selectivity (**B**:**C**)
1[a]	Cl	none	$NiCl_2$·DME	25 W Array	100.0%	**65.0%**	**7.2%**	0%	NA	**9.1:1**
2	Cl	none	$NiCl_2$·DME	34 W Lamp	100.0%	**68.8%**	**7.5%**	12.9%	NA	**9.1:1**
3[a]	Cl	none	$Ni(cod)_2$	25 W Array	83.9%	**50.8%**	**4.6%**	0%	NA	**11.0:1**
4	Cl	none	$Ni(cod)_2$	34 W Lamp	100.0%	**67.6%**	**8.7%**	4.0%	NA	**7.8:1**
5[a]	Cl	TBACl	$NiCl_2$·DME	25 W Array	100.0%	**60.7%**	**6.5%**	0%	NA	**9.4:1**
6	Cl	TBACl	$NiCl_2$·DME	34 W Lamp	100.0%	**63.0%**	**7.5%**	9.2%	NA	**8.5:1**
7[a]	Cl	TBACl	$Ni(cod)_2$	25 W Array	50.7%	**16.4%**	**1.4%**	0%	NA	**11:5:1**
8	Cl	TBACl	$Ni(cod)_2$	34 W Lamp	100.0%	**59.8%**	**5.5%**	2.7%	NA	**10.9:1**
9[a]	Br	none	$NiCl_2$·DME	25 W Array	100.0%	**36.4%**	**2.0%**	4.0%	0%	**18.1:1**
10	Br	none	$NiCl_2$·DME	34 W Lamp	100.0%	**16.3%**	**4.4%**	35.0%	7.9%	**3.7:1**
11[a]	Br	none	$Ni(cod)_2$	25 W Array	100.0%	**37.4%**	**1.9%**	2.9%	0%	**19:6:1**
12	Br	none	$Ni(cod)_2$	34 W Lamp	100.0%	**22.2%**	**3.5%**	22.3%	0%	**6.4:1**
13[a]	Br	TBACl	$NiCl_2$·DME	25 W Array	100.0%	**38.2%**	**3.3%**	3.3%	0%	**11.8:1**
14	Br	TBACl	$NiCl_2$·DME	34 W Lamp	100.0%	**29.4%**	**6.6%**	21.2%	1.6%	**4.5:1**
15[a]	Br	TBACl	$Ni(cod)_2$	25 W Array	62.9%	**22.7%**	**2.1%**	3.5%	1.9%	**10.6:1**
16	Br	TBACl	$Ni(cod)_2$	34 W Lamp	100.0%	**34.6%**	**4.9%**	17.3%	0%	**7.1:1**
17[a]	I	none	$NiCl_2$·DME	25 W Array	22.0%	**0%**	**0%**	6.2%	6.0%	**NA**
18	I	none	$NiCl_2$·DME	34 W Lamp	47.3%	**0%**	**0%**	37.8%	8.6%	**NA**
19[a]	I	none	$Ni(cod)_2$	25 W Array	25.1%	**0%**	**0%**	4.1%	0%	**NA**
20	I	none	$Ni(cod)_2$	34 W Lamp	57.0%	**2.8%**	**1.1%**	38.5%	0%	**2.5:1**
21[a]	I	TBACl	$NiCl_2$·DME	25 W Array	100.0%	**0%**	**0%**	0%	83.5%	**NA**
22	I	TBACl	$NiCl_2$·DME	34 W Lamp	100.0%	**28.5%**	**4.1%**	3.1%	42.0%	**6.9:1**
23[a]	I	TBACl	$Ni(cod)_2$	25 W Array	100.0%	**4.6%**	**1.0%**	2.1%	59.5%	**4.5:1**
24	I	TBACl	$Ni(cod)_2$	34 W Lamp	100.0%	**24.6%**	**3.2%**	2.7%	34.2%	**7.7:1**

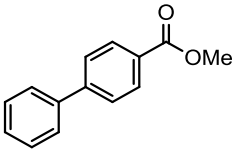
Table S3. Investigation of the effect halide, precatalyst and light source on reaction yield and selectivity. Yields and conversion determined by GC-FID using 1-fluoronaphthalene as an external standard. Reactions were carried out on 0.05 mmol scale. Note that 4-iodobiphenyl with TBACl as an additive only gave significant amounts of **B** when 34 W lamps were used (entries 22 and 24). The observed selectivity for **B** over **C** was greatest for 4-bromobiphenyl using $Ni(cod)_2$ as a precatalyst with 25 W LEDs (entry 11). Notice that in all reactions with 4-iodobiphenyl and TBACl the mass balance is accounted for by 4-chlorobiphenyl and in some cases the yield of halogen exchange product was good (entry 21). Together with the lack of product observed with 25 W LEDs this indicates that the halogen exchange catalyst and photoelimination catalyst are different species in this system. [a]Reaction was carried out for 70 h.

VII. Ester and Benzyl Alcohol Synthesis

General procedure for ester and benzyl alcohol synthesis:

Reagent handling: $NiCl_2$·glyme, dtbbpy, $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$, and K_3PO_4 were stored in an N_2-filled glovebox. trimethyl orthoformate (Sigma Aldrich) and trimethyl orthoacetate (Alpha Aesar) were degassed with nitrogen and brought into the glovebox.

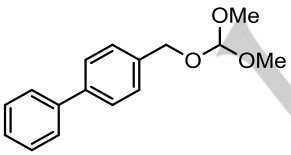
Reaction setup (0.25 mmol scale): In the glovebox, a threaded 16 × 125 mm borosilicate reaction tube equipped with a teflon coated stirbar was charged with $NiCl_2$·glyme (5.5 mg, 0.025 mmol, 0.1 eq), dtbbpy (10.1 mg, 0.038 mmol, 0.15 eq), benzene (1.500 mL) and C–H coupling partner (1.500 mL) and stirred for 20 min to give a light green solution. To the reaction tube 4-chloro-1,1'-biphenyl (47.2 mg, 0.25 mmol, 1 eq), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.8 mg, 0.0025 mmol, 0.01 eq), K_3PO_4 (106.0 mg, 0.50 mmol, 2 eq), benzene (1.000 mL) and C–H coupling partner (1.000 mL) were added successively. The reaction tube was capped with a septum cap, sealed with electrical tape, and removed from the glovebox. The reaction was stirred at 800 rpm for 72 hours while illuminating with a 34 W blue LED lamp (Kessil KSH150B) placed horizontally at 2 cm distance from the reaction tube (Figure S2). A fan was used to cool the reaction tube to nominally room temperature; however, the actual reaction temperature was typically around 30 °C. Upon completion, the reaction mixture was concentrated on a rotary evaporator and purified by under the specified method.



methyl [1,1'-biphenyl]-4-carboxylate (39): Synthesized following the general procedure from 4-chloro-1,1'-biphenyl (42.7 mg, 0.25 mmol) and trimethylorthoformate. Purified by automated column chromatography (100 g silica, Gradient, 100:0 → 90:10 hexanes:ethyl acetate, 3rd peak off the column) to afford methyl [1,1'-biphenyl]-4-carboxylate (7.5 mg, 14% yield) as a white crystalline solid. Compound was previously reported.[10] A second fraction (4th peak off the column) was collected to give the methoxy functionalization product 4-((dimethoxymethoxy)methyl)-1,1'-biphenyl (9.9 mg, 15% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): 8.11 (d, *J* = 8.3 Hz, 2H), 7.67 (d, *J* = 8.3 Hz, 2H), 7.63 (d, *J* = 7.3 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 1H), 3.95 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): 167.14, 145.77, 140.14, 130.24, 129.06, 129.02, 128.28, 127.42, 127.19, 52.28.



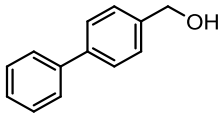
4-((dimethoxymethoxy)methyl)-1,1'-biphenyl (side product)**:**

^{1}H NMR (500 MHz, $CDCl_3$): 7.49 (m, 4H), 7.34 (at, *J* = 7.7 Hz, 4H), 7.25 (t, *J* = 7.4 Hz, 1H), 5.08 (s, 1H), 4.57 (s, 2H), 3.29 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): 140.98, 140.81, 136.63, 128.90, 128.36, 127.44, 127.33, 127.24, 113.53, 65.70, 51.68.

IR (ATR, cm^{-1}): 3030 (w), 2926 (w), 2851 (w), 1725 (w), 1682 (w), 1602 (w), 1566 (w), 1521 (w), 1488 (w), 1448 (w), 1409 (w), 1370 (w), 1346 (w), 1312 (w), 1266 (w), 1214 (w), 1195 (w), 1095 (s), 1064 (s), 1007 (s), 995 (m), 910 (m), 845 (w), 823 (m), 760 (s), 733 (s), 696 (s).

HRMS (ESI+): Calculated for $C_{16}H_{18}O_3Na^+$ $[M + Na]^+$: 281.1148 ; found: 281.1149



[1,1'-biphenyl]-4-ylmethanol (40): Synthesized following the general procedure from 4-chloro-1,1'-biphenyl (42.7 mg, 0.25 mmol) and trimethylorthoacetate. The concentrated reaction mixture was transferred to a 20 mL scintillation vial in 5 mL acetone followed by addition of 5 mL aqueous 1 M HCl. The mixture was stirred for 1.5 hours and diluted with saturated K_2CO_3 until pH = 12 and extracted with DCM (3 × 20 mL). The organic extracts were dried over anhydrous $MgSO_4$, concentrated, and purified by automated column chromatography (100 g silica, Gradient, 100:0 → 90:10 hexanes:ethyl acetate, 5th peak off the column) to afford the title compound (10.9 mg, 24% yield) as a white solid. A second fraction (4th peak off the column) gave crude [1,1'-biphenyl]-4-ylmethyl acetate which was saponified by stirring in 10 mL of 1 M sodium methoxide in methanol for 2 hours. The resulting solution was diluted with 10 mL of water, acidified with 3 M aqueous hydrochloric acid to pH = 8, and extracted with ethyl ether (3 × 30 mL). The combined organic extracts where then dried over anhydrous $MgSO_4$ and concentrated to give a second portion of the title compound (8.8 mg, 18% yield after correction) with 3% [1,1'-biphenyl]-4-carbaldehyde as an impurity and a combined yield of 42% for both portions. ^{1}H NMR spectrum in acetone–d_6 matched that of an authentic product purchased from Oakwood.

^{1}H NMR (500 MHz, acetone-d_6): 7.65 (d, J = 7.6 Hz, 2H), 7.62 (d, J = 8.1 Hz, 2H), 7.50 – 7.41 (m, 4H), 7.34 (t, J = 7.4 Hz, 1H), 4.68 (d, J = 5.7 Hz, 2H), 4.23 (t, J = 5.7 Hz, 1H).

^{13}C NMR (125 MHz, acetone-d_6): 142.65, 141.78, 140.37, 129.68, 128.01, 127.94, 127.63, 127.50, 64.38.

VIII. Cyclic Voltammetry

Cyclic Voltammetry was performed on a CH Instruments Electrochemical Analyzer (CH1600E). A solution of 1 mM 1,3-dioxolane, 1 mM ferrocene and 0.1 M tetrabutylammonium hexafluorophosphate as a supporting electrolyte in MeCN was prepared on the bench and sparged with nitrogen. A cyclic voltammogram was obtained under nitrogen atmosphere using a glassy carbon working electrode, a platinum mesh counter electrode, and a saturated calomel reference electrode. Scan rate = 0.1 Vs^{-1}.

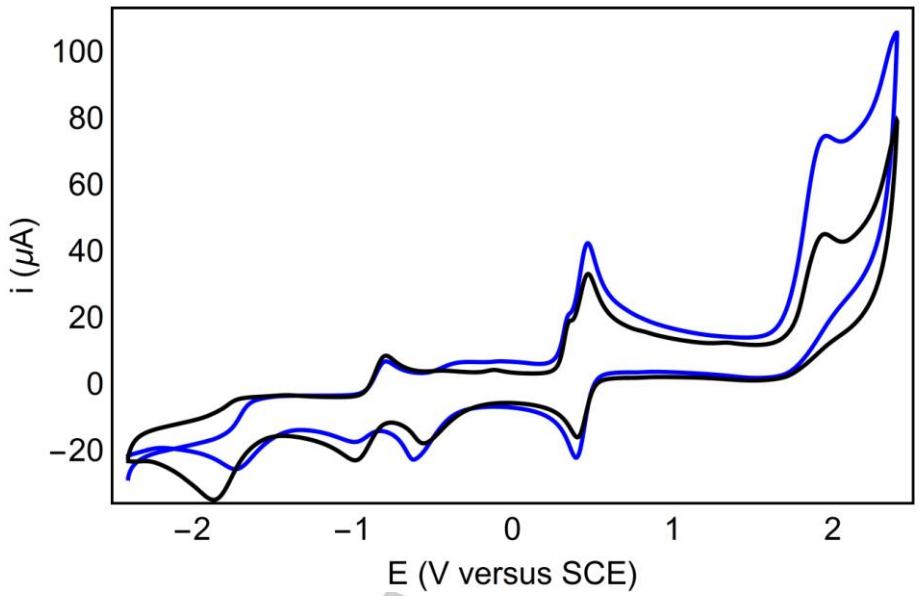


Figure S6. Cyclic voltammograms of 1,3-dioxolane (1 mM) with ferrocene (1 mM) as in internal standard in black and ferrocene (1 mM) standard in blue. No wave corresponding to the oxidation of 1,3-dioxolane was observed prior to solvent oxidation. These data show that photocatalytic oxidation of 1,3-dioxolane is not feasible in this system.

IX. Computational Studies

Calculations were performed on Gaussian 09 D.01 software suite.[11] For all BDE and BDFE calculations the Complete Basis Set extrapolation method was used. Gas-phase composite calculations were carried out using CBS-QB3. Solution-phase composite calculations were carried out using CBS-QB3 and SMD (benzene or 1,3-dioxolane) solvation model. Electronic absorption spectra were computed with time-dependent density functional theroy (TDDFT) from the gas-phase optimized geometry using the B3LYP hybrid exchange-correlation functional and TZVP basis set. All frequency calculations gave no imaginary frequencies. 1,3-Dioxolane is not defined as a solvent in Gaussian 09 D.01. In the SMD model solvents are defined by their static dielectric constant (ε) and dynamic (optical) dielectric constant (ε_{inf}). Maxwell's relation,

$$n = (k_m \varepsilon_{inf})^{1/2}$$

where n = 1.401 is the refractive index and $k_m \approx 1$ is the relative permeability, was used to approximate $\varepsilon_{inf} \approx 1.963$. The following is an example input file for 1,3-dioxolane with solvation:

```
%chk=1,3-dioxolane1_solv.chk
# cbs-qb3 scrf=(smd,solvent=generic,read)

1,3-dioxolane

0 1
 C              0.01980335   -0.19318933    0.00531830
 O              1.34378935    0.20591567    0.35890530
 C              0.01985335   -1.66893533    0.38171230
 H             -0.68394865    0.41547767    0.57405030
 H             -0.15962465   -0.05610933   -1.06953270
 H             -0.68389765   -2.27764133   -0.18697870
 H             -0.15950065   -1.80602633    1.45657430
 O              1.34383735   -2.06796133    0.02803930
 C              2.17715635   -0.93101733    0.19352930
 H              2.80484735   -0.84307233   -0.70219770
 H              2.80473035   -1.01894833    1.08934230

stoichiometry=C3H6O2
solventname=1,3-dioxolane
eps=7.13
epsinf=1.963
```

	BDEs			BDFEs		
	gas phase	1,3-dioxolane	benzene	gas phase	1,3-dioxolane	benzene
	94.6	94.8	95.4	85.3	86.8	87.4
	96.0	96.3	96.5	86.6	88.2	88.3

Table S4. Computed bond dissociation energies. Energies are in kcal mol^{-1}.

Entry		CBS-QB3 Enthalpies			CBS-QB3 Free Energies		
		gas phase	1,3-dioxolane	benzene	gas phase	1,3-dioxolane	benzene
a		-267.928198	-267.937269	-267.932974	-267.959906	-267.971036	-267.966652
b		-267.27997	-267.288449	-267.283821	-267.31354	-267.322037	-267.317277
c		-267.277786	-267.286052	-267.282108	-267.311499	-267.319713	-267.315831
d	H·	-0.497457	-0.497705	-0.497103	-0.510472	-0.510719	-0.510118

Table S5. Computed enthalpies and free energies. Energies are in hartrees.

Table S6. Cartesian coordinates for gas phase geometry-optimized 1,3-dioxolane (**a**).

Atom Type	x	y	z
C	-0.948309	0.737849	-0.188186
O	0.375677	1.136954	0.165401
C	-0.948259	-0.737897	0.188208
H	-1.652061	1.346516	0.380546
H	-1.127737	0.874929	-1.263037
H	-1.65201	-1.346603	-0.380483
H	-1.127613	-0.874988	1.26307
O	0.375725	-1.136923	-0.165465
C	1.209044	0.000021	0.000025
H	1.836735	0.087966	-0.895702
H	1.836618	-0.08791	0.895838

Table S7. Cartesian coordinates for gas phase geometry-optimized 1,3-dioxolanyl radical **b**.

Atom Type	x	y	z
C	0.93229	0.73461	0.143127
O	-0.427481	1.140663	-0.089515
C	-1.202161	-0.000458	-0.150226
C	0.899116	-0.766442	-0.148354
H	1.590478	1.29533	-0.521273
H	1.193957	0.946851	1.185145
H	-2.157729	0.054041	0.368197
H	1.559847	-1.359309	0.482352
H	1.099612	-0.979552	-1.204417
O	-0.455223	-1.111115	0.167354

Table S8. Cartesian coordinates for gas phase geometry-optimized 1,3-dioxolanyl radical **c**.

Atom Type	x	y	z
C	-1.182043	-0.330926	-0.088411
O	-0.048626	-1.157139	0.222602
C	1.078449	-0.406569	-0.138739
C	-0.603362	1.058558	-0.087438
H	-1.605526	-0.615397	-1.063896
H	-1.945922	-0.497414	0.677807
H	1.922289	-0.686581	0.490673
H	1.321233	-0.522611	-1.206314
H	-1.062602	1.942314	0.333364
O	0.750159	0.963802	0.109384

Table S9. Cartesian coordinates for gas phase geometry-optimized $[Ni(III)(dtbbpy)(Ph)Cl]^+$.

Atom Type	x	y	z
Ni	1.381823	-1.42442	-0.08078
C	-0.39976	0.799212	-0.03671
C	1.801695	1.533037	-0.12994
C	-0.84506	2.110452	-0.03012
C	1.405172	2.858967	-0.1278
H	2.847174	1.26396	-0.16522
C	0.049842	3.187444	-0.0773
H	-1.90647	2.301062	0.012698
H	2.16939	3.620308	-0.16399
C	-1.29642	-0.37691	0.008083
C	-2.6796	-0.30988	0.050799
C	-3.45546	-1.47726	0.095452
H	-3.16739	0.653042	0.048768
C	-1.37165	-2.68952	0.033759
C	-2.75778	-2.68512	0.085749
H	-0.80751	-3.6129	0.005112
H	-3.27342	-3.63272	0.11425
C	3.291619	-1.19851	0.072621
C	4.107354	-0.93181	-1.01359
C	3.756102	-1.19532	1.377578
C	5.434317	-0.57378	-0.76851
C	5.086502	-0.83135	1.604527
C	5.919057	-0.5208	0.5353
H	6.087919	-0.35719	-1.60449
H	5.465185	-0.81289	2.61897
Cl	1.81649	-3.42616	-0.69471
N	0.93034	0.51689	-0.08895
N	-0.65492	-1.56559	0.002336
H	3.12678	-1.46948	2.216961
H	6.953376	-0.25768	0.716344
H	3.743676	-1.00506	-2.03047
C	-0.46674	4.62655	-0.07283
C	-4.9829	-1.39046	0.143969
C	-1.3602	4.839871	-1.31643
H	-0.80152	4.673876	-2.23949
H	-2.22806	4.178155	-1.32142
H	-1.73036	5.86628	-1.32758
C	-1.29726	4.859164	1.210057
H	-2.1658	4.201082	1.266822
H	-0.69413	4.704112	2.106736
H	-1.66402	5.886692	1.22551

C	0.678006	5.65046	-0.10876
H	1.333072	5.564609	0.760684
H	1.283323	5.557643	-1.01273
H	0.260573	6.657726	-0.10135
C	-5.48361	-0.6774	-1.13276
H	-5.09561	0.339169	-1.21675
H	-5.19563	-1.22596	-2.03157
H	-6.57273	-0.61261	-1.1129
C	-5.40235	-0.57902	1.390728
H	-5.05075	-1.05304	2.309199
H	-5.01902	0.442645	1.367751
H	-6.49072	-0.51886	1.438923
C	-5.63767	-2.77857	0.219478
H	-5.40722	-3.38988	-0.65541
H	-5.33726	-3.32544	1.115629
H	-6.72146	-2.66401	0.257085

Table S10. Cartesian coordinates for gas phase geometry-optimized Ni(II)(dtbbpy)(*o*-tolyl)Cl.

Atom Type	x	y	z
Ni	-0.62438	0.153617	0
C	1.203694	2.304729	0.047731
C	-0.96717	3.08463	-0.00289
C	1.687488	3.605215	0.086685
C	-0.53829	4.402881	0.0344
H	-2.01837	2.840206	-0.04295
C	0.822091	4.701776	0.082809
H	2.755168	3.763292	0.123753
H	-1.28862	5.179311	0.026443
C	2.066044	1.107966	0.054137
C	3.45489	1.135727	0.061677
C	4.193095	-0.05165	0.071197
H	3.966748	2.086824	0.05899
C	2.069123	-1.19768	0.060359
C	3.456945	-1.23585	0.071015
H	1.462045	-2.09518	0.058361
H	3.941031	-2.20082	0.077902
C	-2.49715	0.489003	-0.109
C	-3.30271	0.635455	1.033907
C	-3.07745	0.660913	-1.36772
C	-4.65067	0.976257	0.879856
C	-4.42397	0.997228	-1.51038
C	-5.21388	1.162994	-0.37939
H	-5.27139	1.087324	1.763637
H	-4.85045	1.120961	-2.49984
Cl	-1.03994	-2.00009	0.042886
N	-0.12838	2.040521	0.004669
N	1.382405	-0.05496	0.051796
H	-2.47887	0.519992	-2.26182
H	-6.26216	1.421879	-0.47307
C	1.373847	6.130495	0.134352
C	5.726197	-0.0126	0.079017
C	2.193587	6.311537	1.430889
H	1.574169	6.141487	2.313832
H	3.041509	5.626277	1.479236
H	2.586982	7.329118	1.483884
C	2.284764	6.370314	-1.08951
H	3.133808	5.684938	-1.10957
H	1.730649	6.245676	-2.02204
H	2.681668	7.387624	-1.06483
C	0.253535	7.182044	0.118285

H	-0.34844	7.122387	-0.79067
H	-0.4112	7.08287	0.978742
H	0.691834	8.180841	0.156153
C	6.209668	0.740803	1.337481
H	5.84997	1.770755	1.360846
H	5.867046	0.244827	2.247844
H	7.301306	0.770978	1.358322
C	6.22246	0.722823	-1.18511
H	5.889856	0.213209	-2.09163
H	5.86212	1.751904	-1.22742
H	7.314259	0.75356	-1.19484
C	6.340447	-1.42148	0.092185
H	6.047446	-1.98594	0.979697
H	6.058029	-1.99808	-0.79093
H	7.428939	-1.34218	0.097993
C	-2.73828	0.410542	2.416182
H	-2.33917	-0.60234	2.504301
H	-1.91357	1.097064	2.631701
H	-3.50045	0.551322	3.185342

X. Spectral Overlap of LEDs and Photocatalysts

Emission spectra were measured on a digital spectrometer with optical fiber (Ocean Optics USB4000). Linear absorption spectra were collected on an Agilent 8453 Spectrophotometer using a 1.0 cm quartz cuvette. All reagents were dispensed in stock solutions prepared volumetrically inside a nitrogen filled glove box. Computed absorption spectra were obtained via TDDFT by computing the first 50 to 100 states, see section IX for details. All spectra were normalized to 1.0 at the emission/absorption maximum. Ni(II)(dtbbpy)(*o*-tolyl)Cl was prepared according the previously reported procedure.[12]

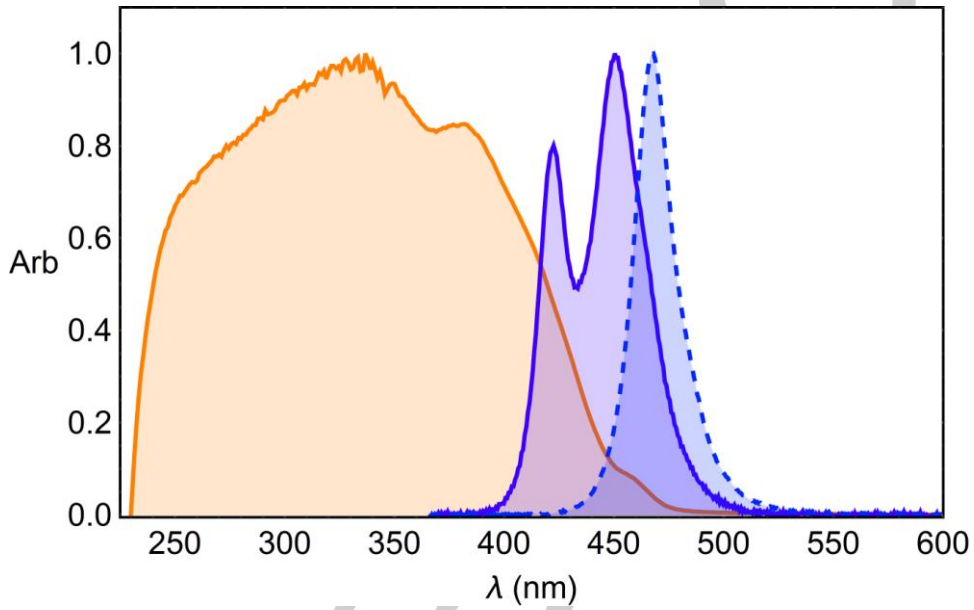


Fig. S7. Normalized photocatalyst absorption and lamp emission data. Experimental absorption spectrum of Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (solid orange) displayed with emission spectrum for 34W blue LED lamp (solid blue) and 25W blue LED array (dashed blue).

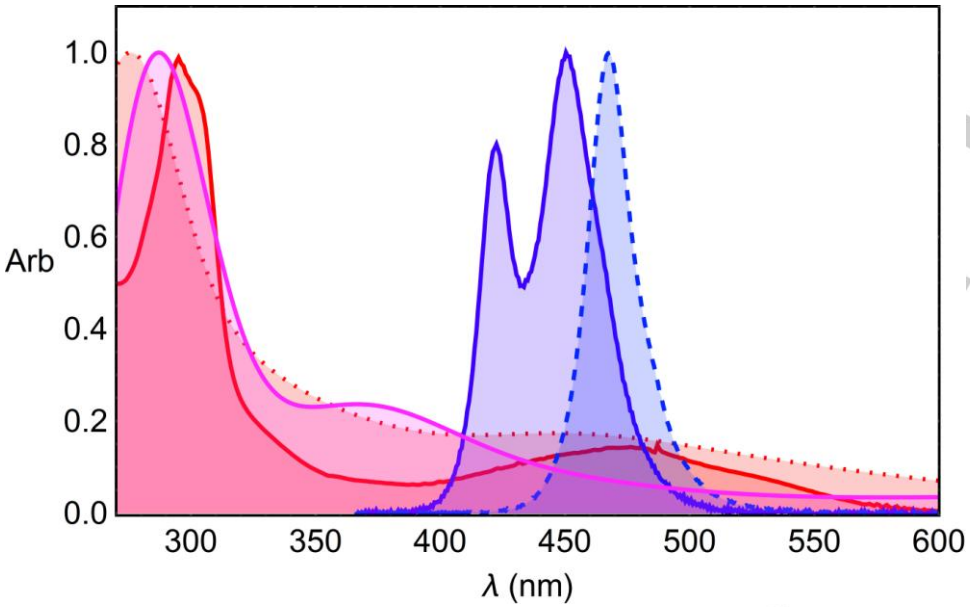


Fig. S8. Normalized catalyst absorption and lamp emission data. Computed absorption spectrum of hypothetical distorted square planer $[Ni(III)(dtbbpy)(Ph)Cl]^+$ (solid magenta) displayed with experimental absorption spectrum of Ni(II)(dtbbpy)(*o*-tolyl)Cl (solid red), computed absorption spectrum of square planar Ni(II)(dtbbpy)(*o*-tolyl)Cl (dotted red), and emission spectra for 34W blue LED lamp (solid blue) and 25W blue LED array (dashed blue). The structure of the photoactive Ni(III) species is currently unknown so the hypothetical species $[Ni(III)(dtbbpy)(Ph)Cl]^+$, presumed to be the successor complex after single electron oxidation by the iridium photocatalyst, was used for an initial investigation of spectral overlap. The computed Ni(II)(dtbbpy)(*o*-tolyl)Cl absorption spectrum was included as a benchmark of the computational method.

XI. References

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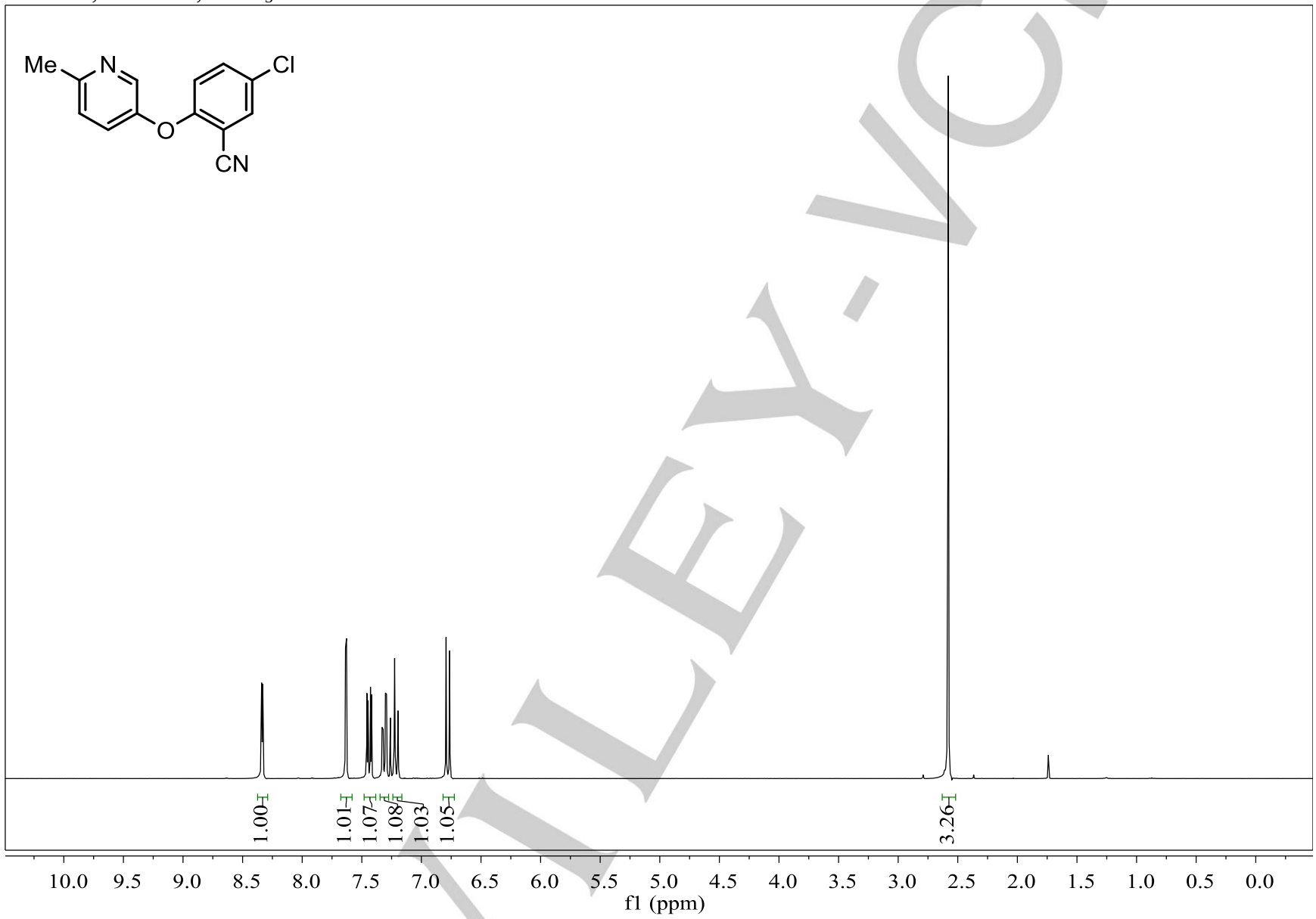
^{1}H NMR, 300 MHz, $CDCl_3$



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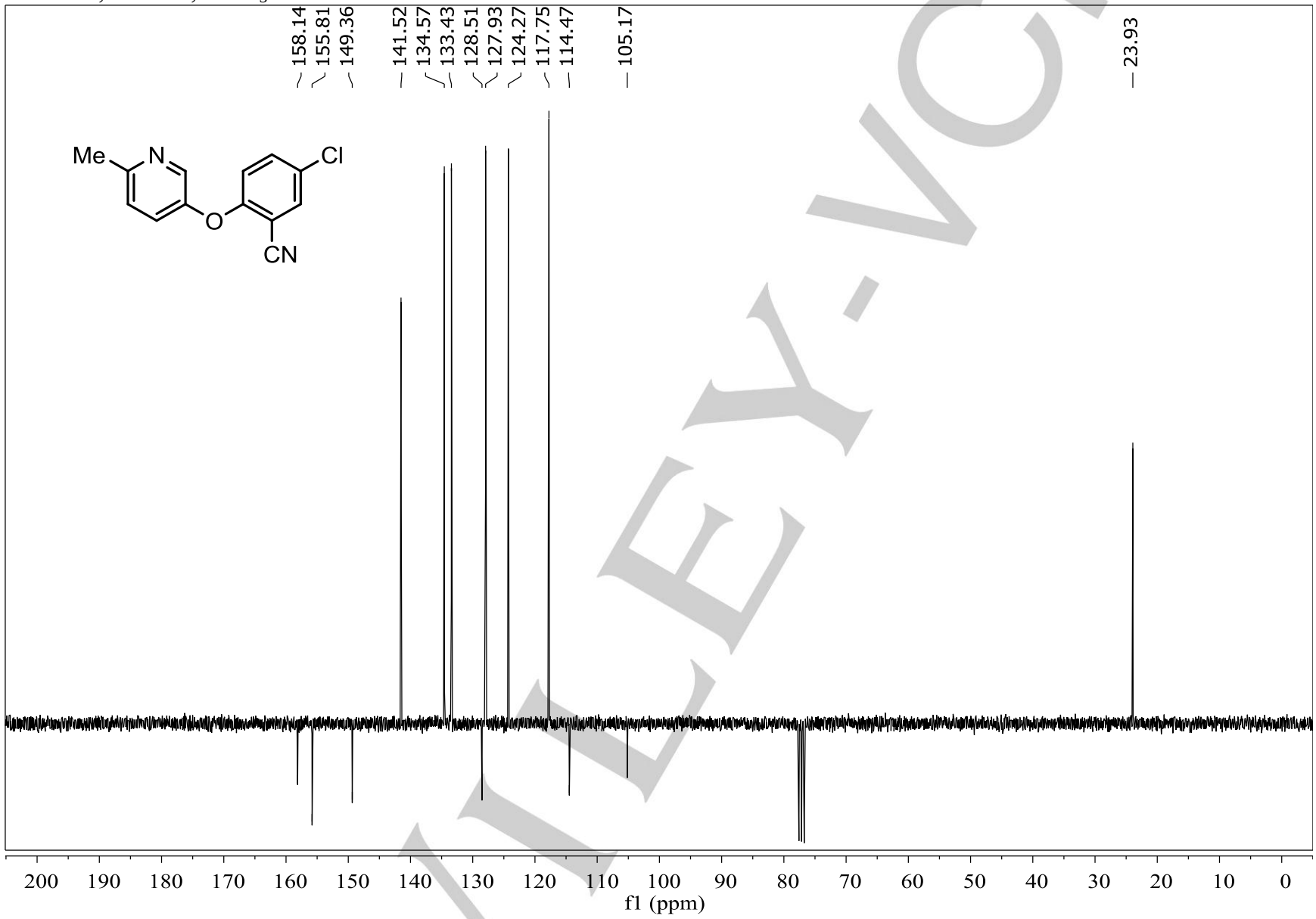

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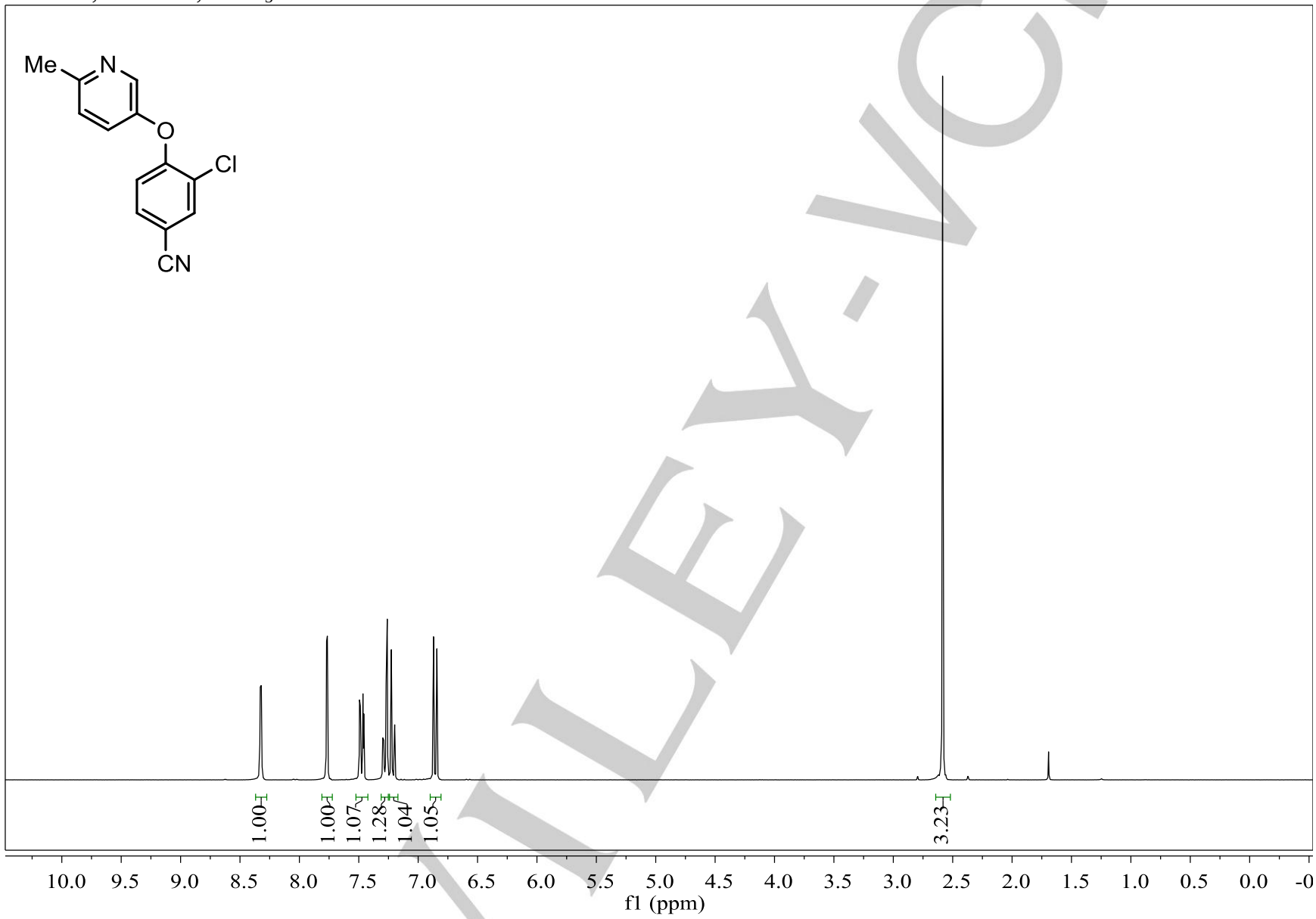

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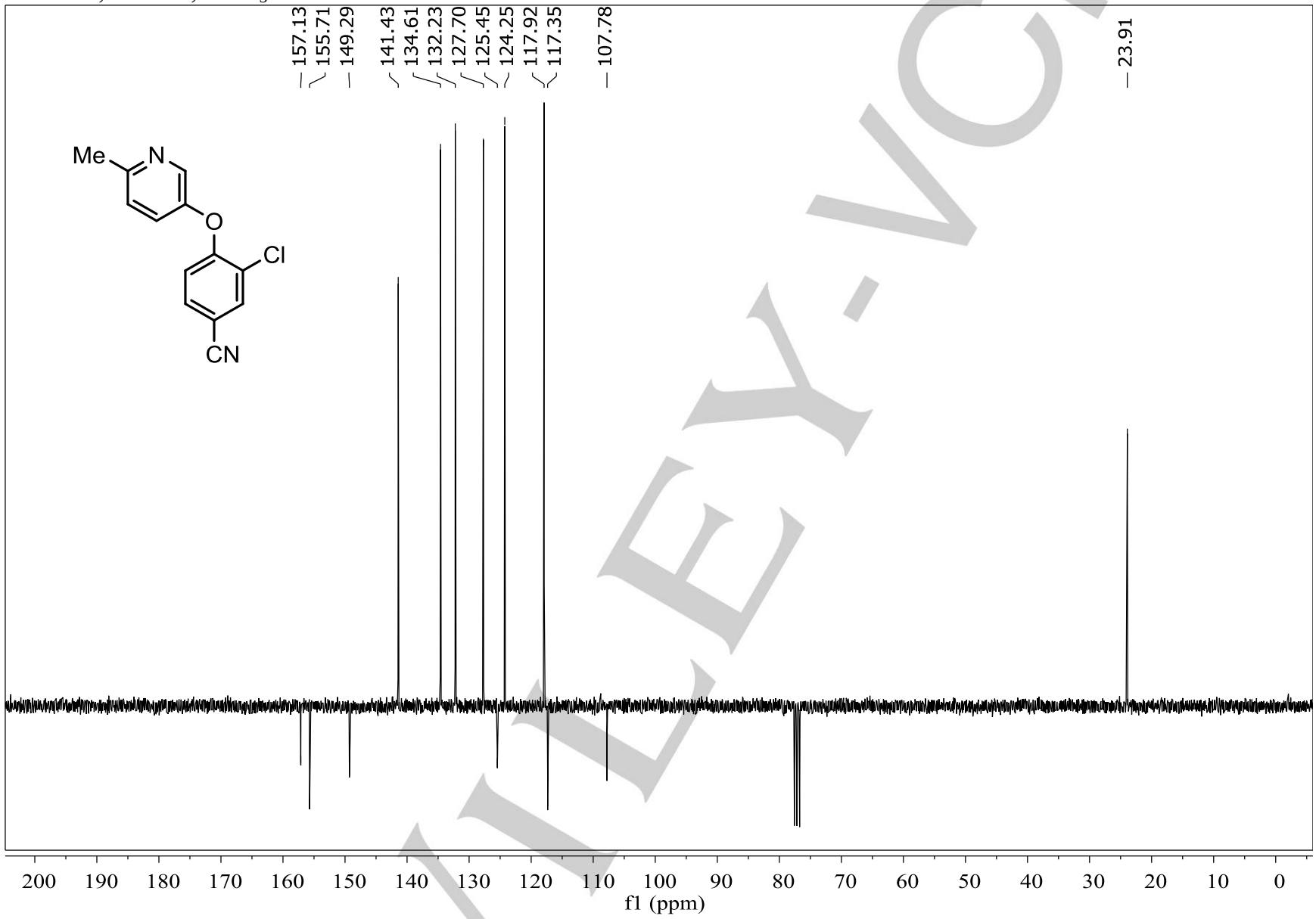
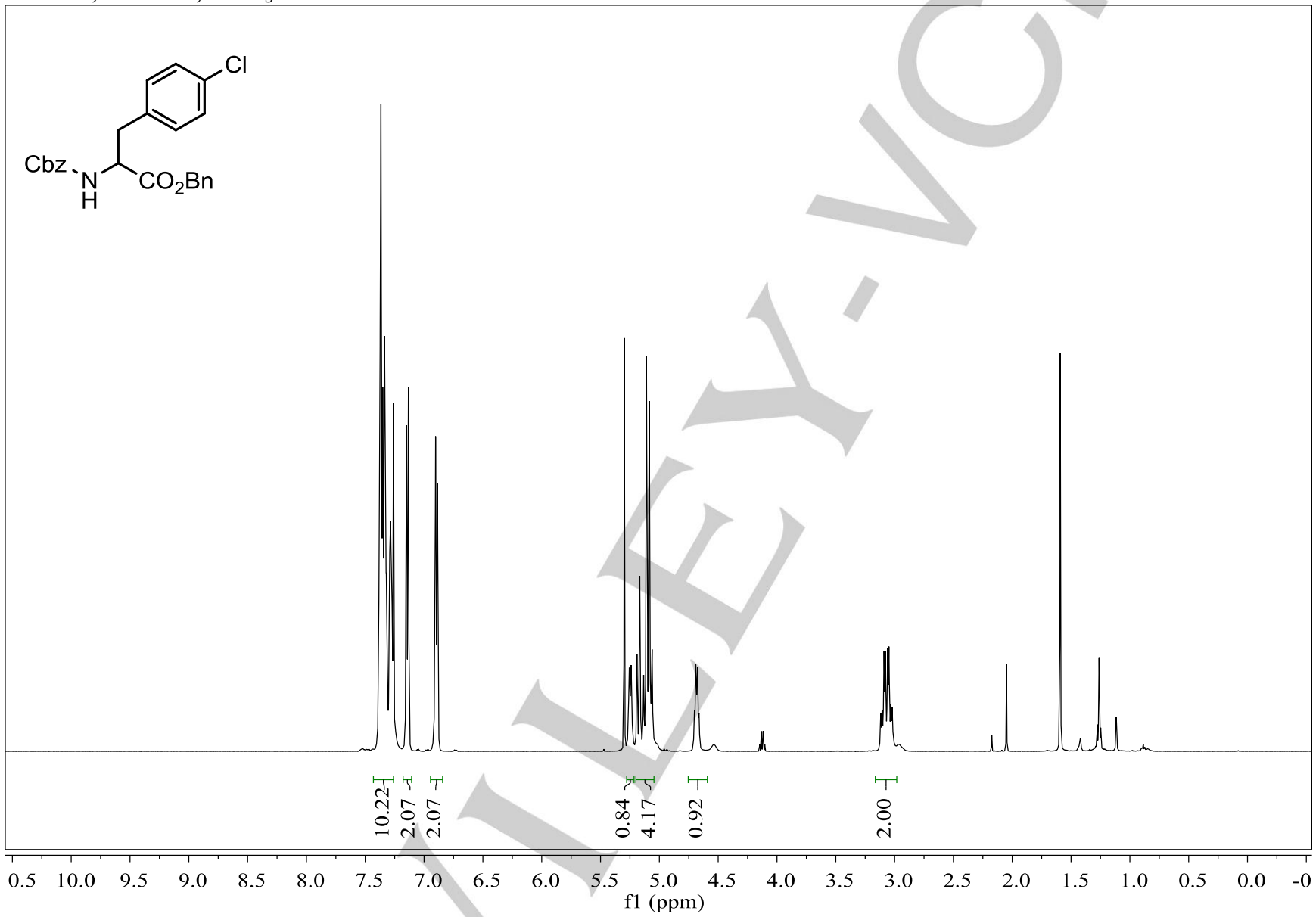


^{1}H NMR, 500 MHz, $CDCl_3$



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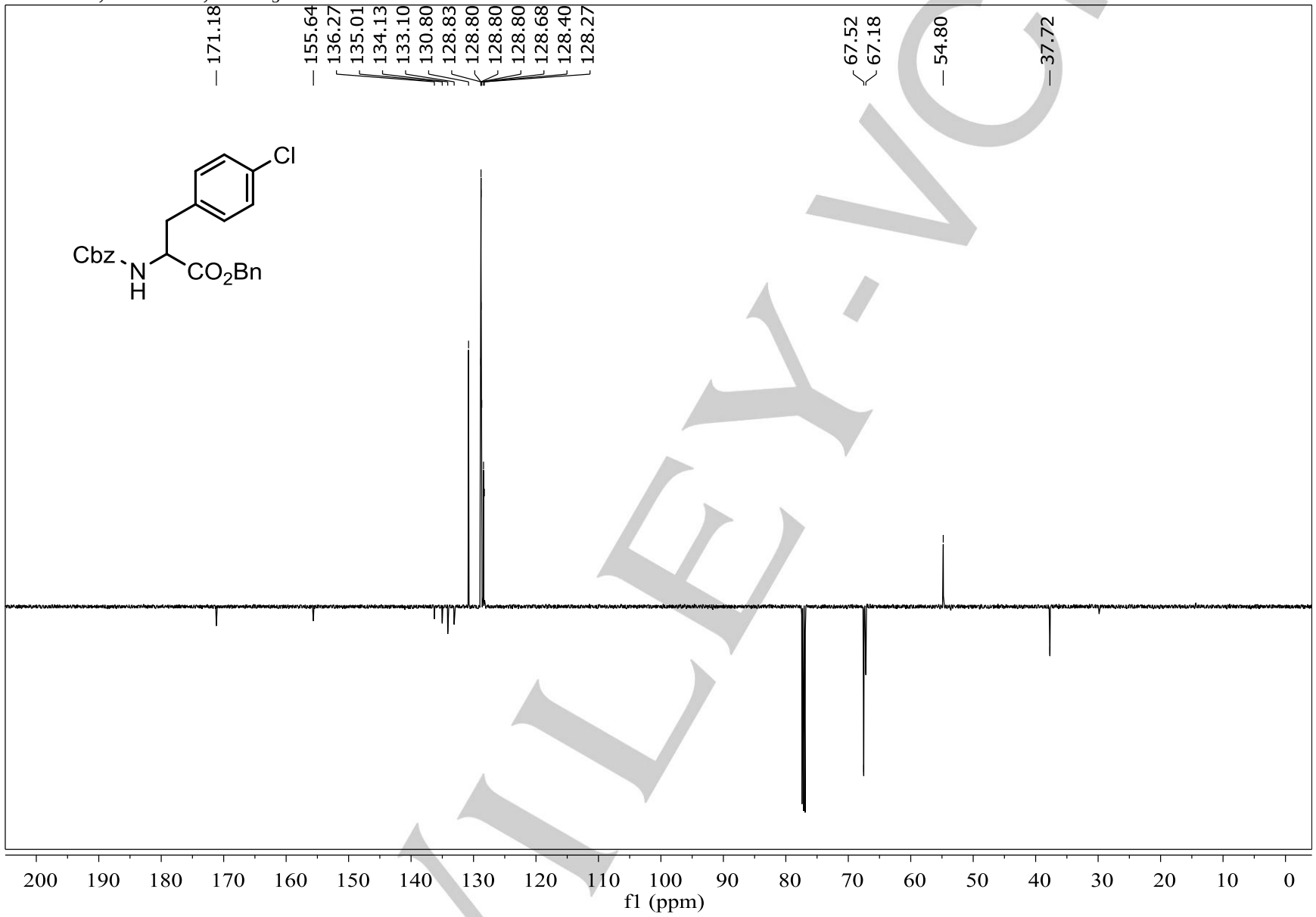

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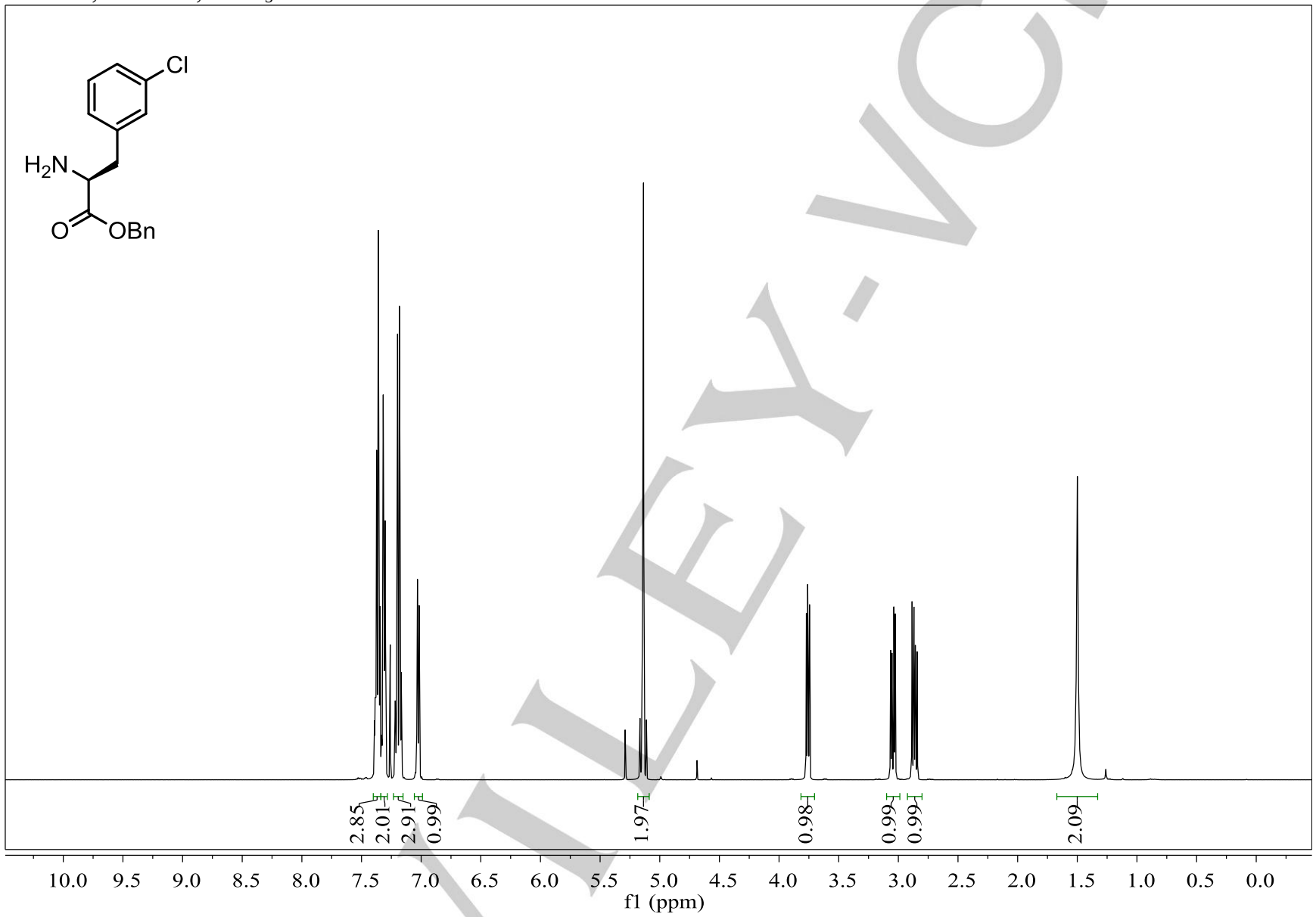

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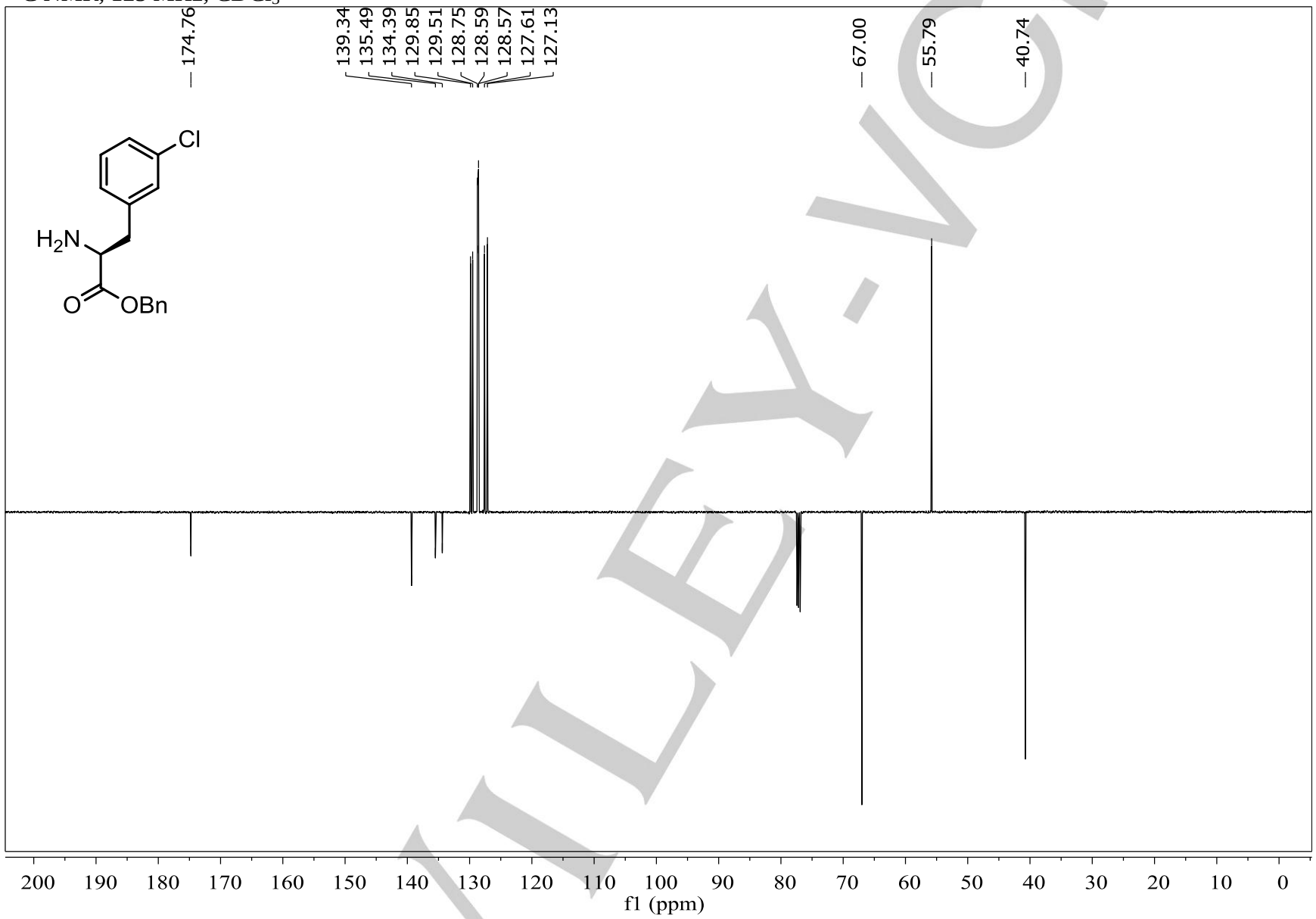

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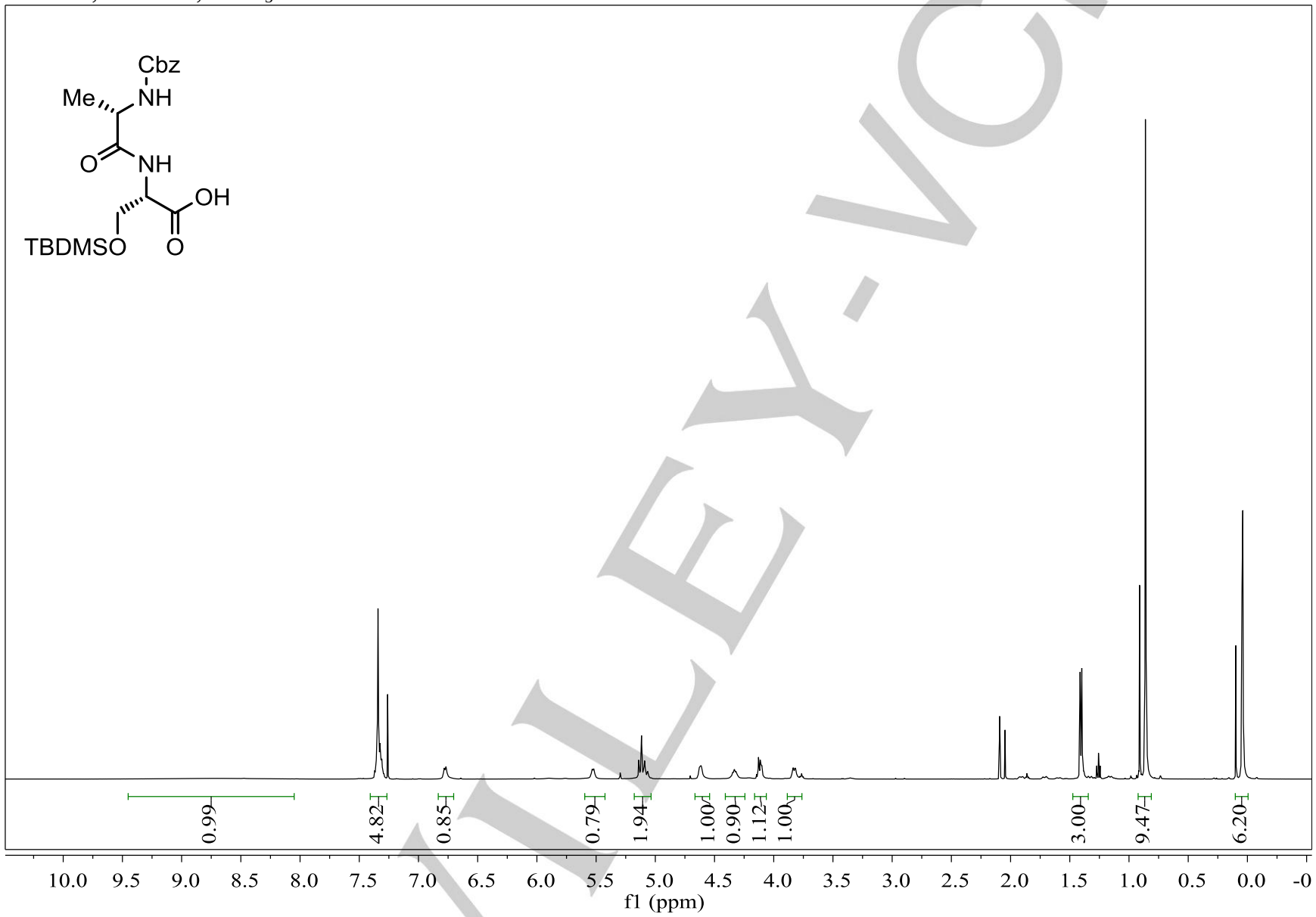

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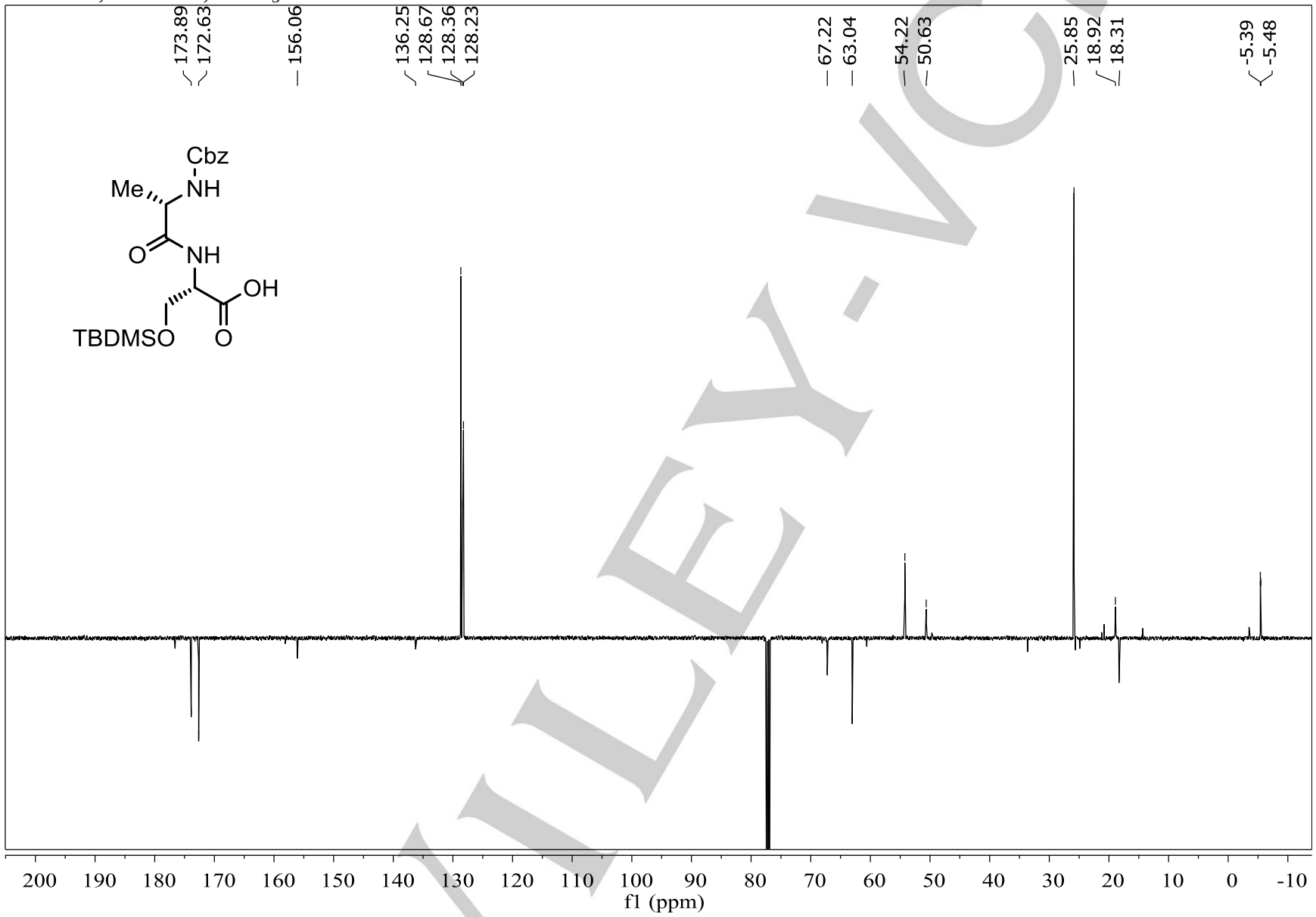

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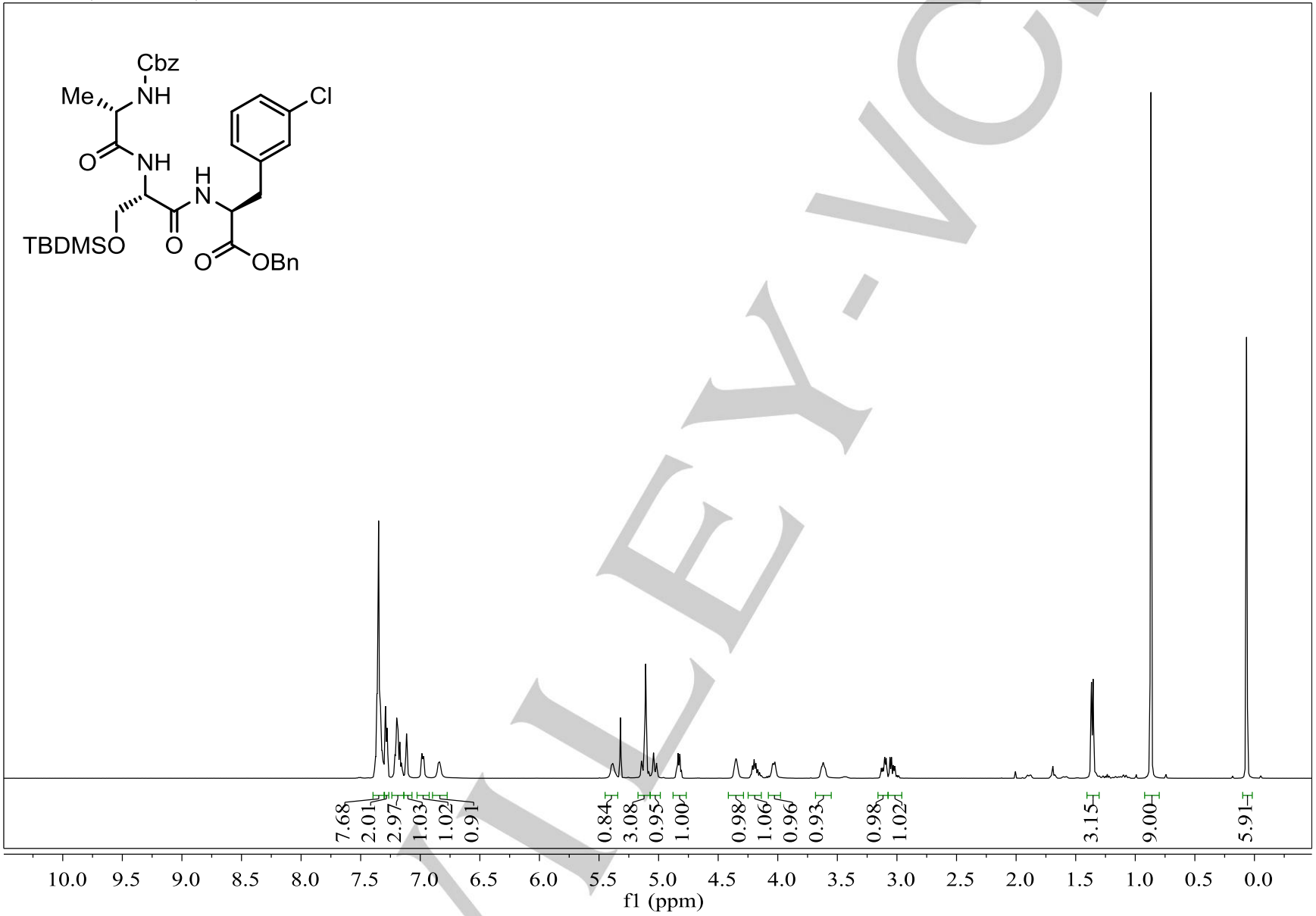

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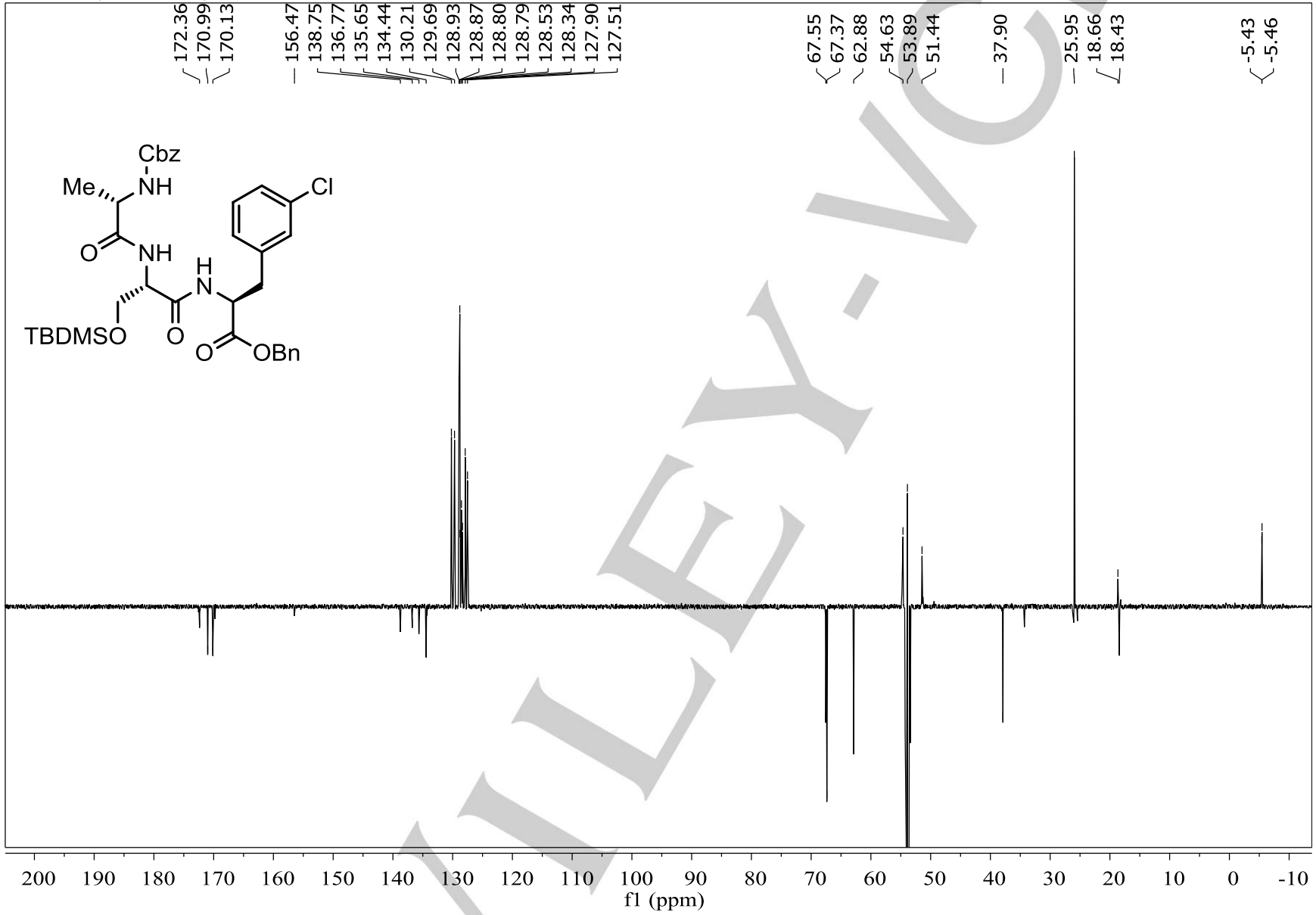

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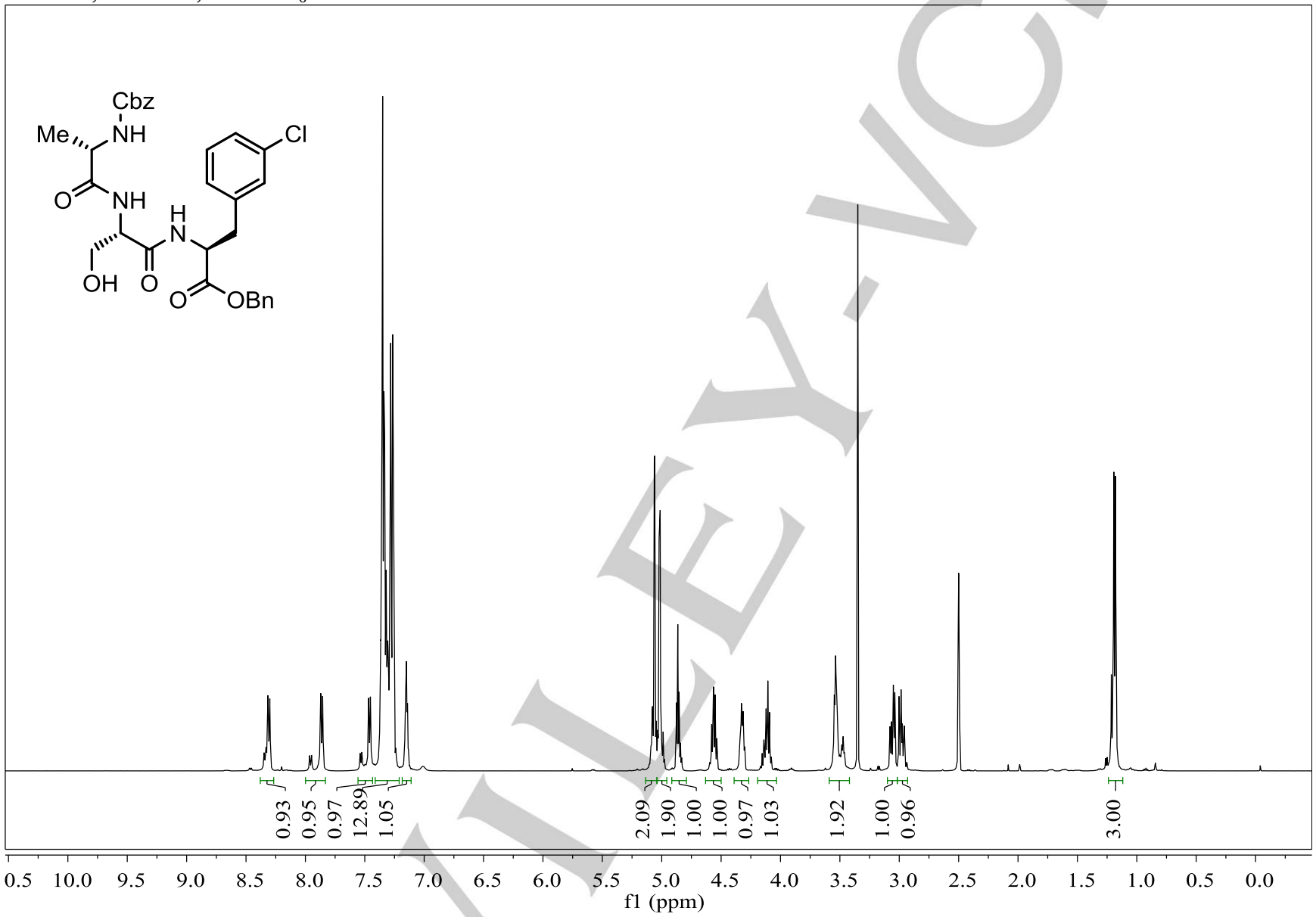

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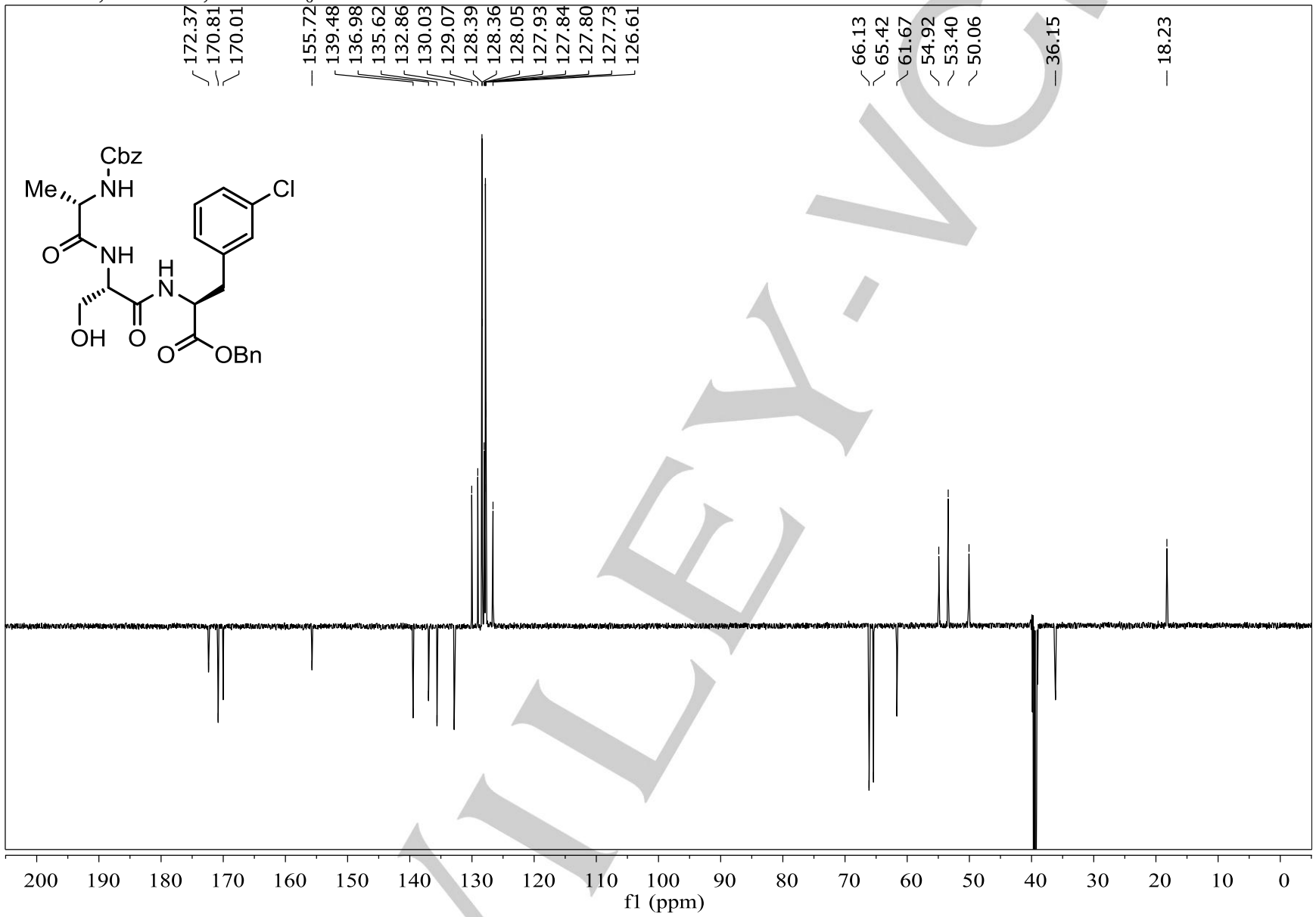

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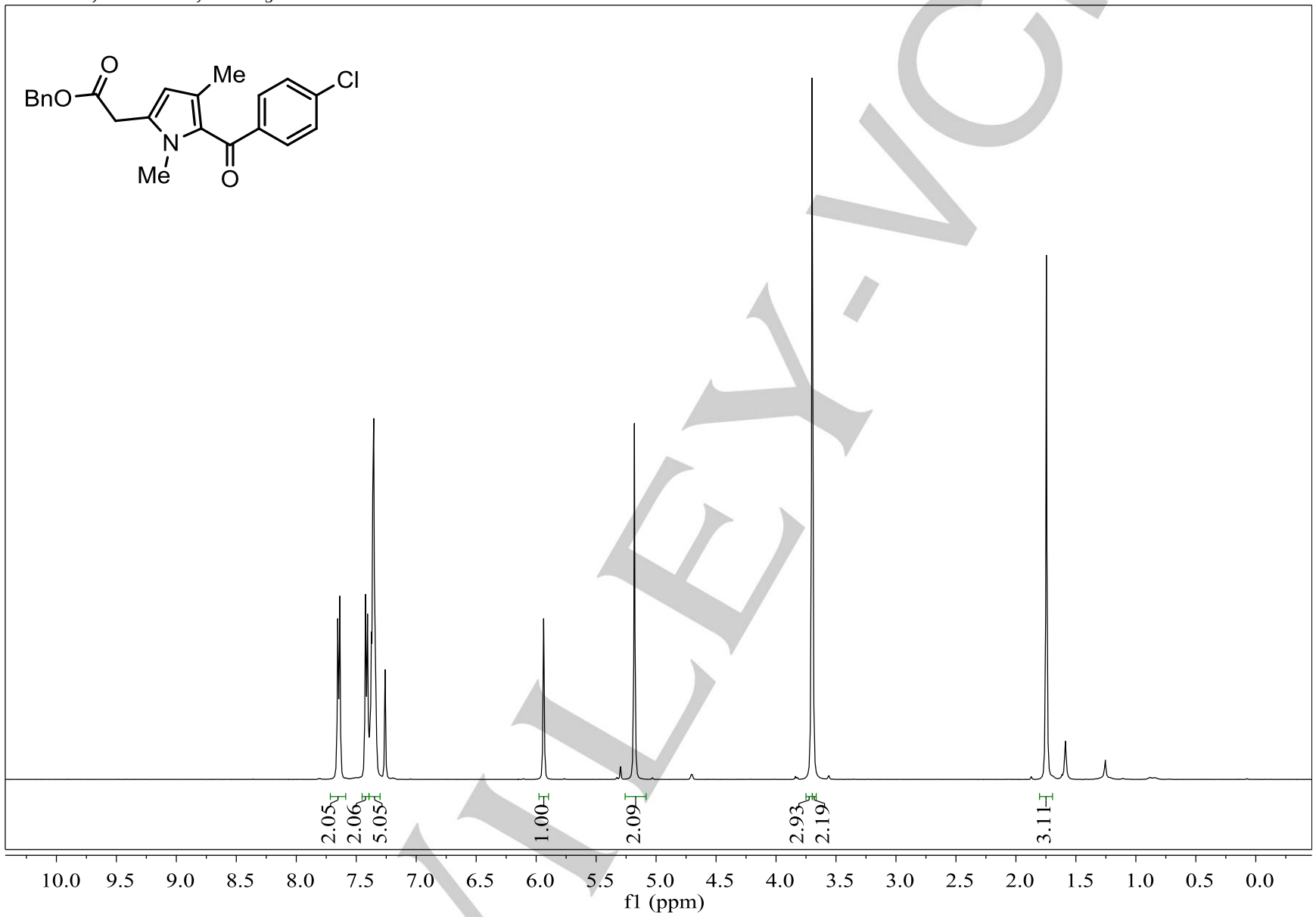

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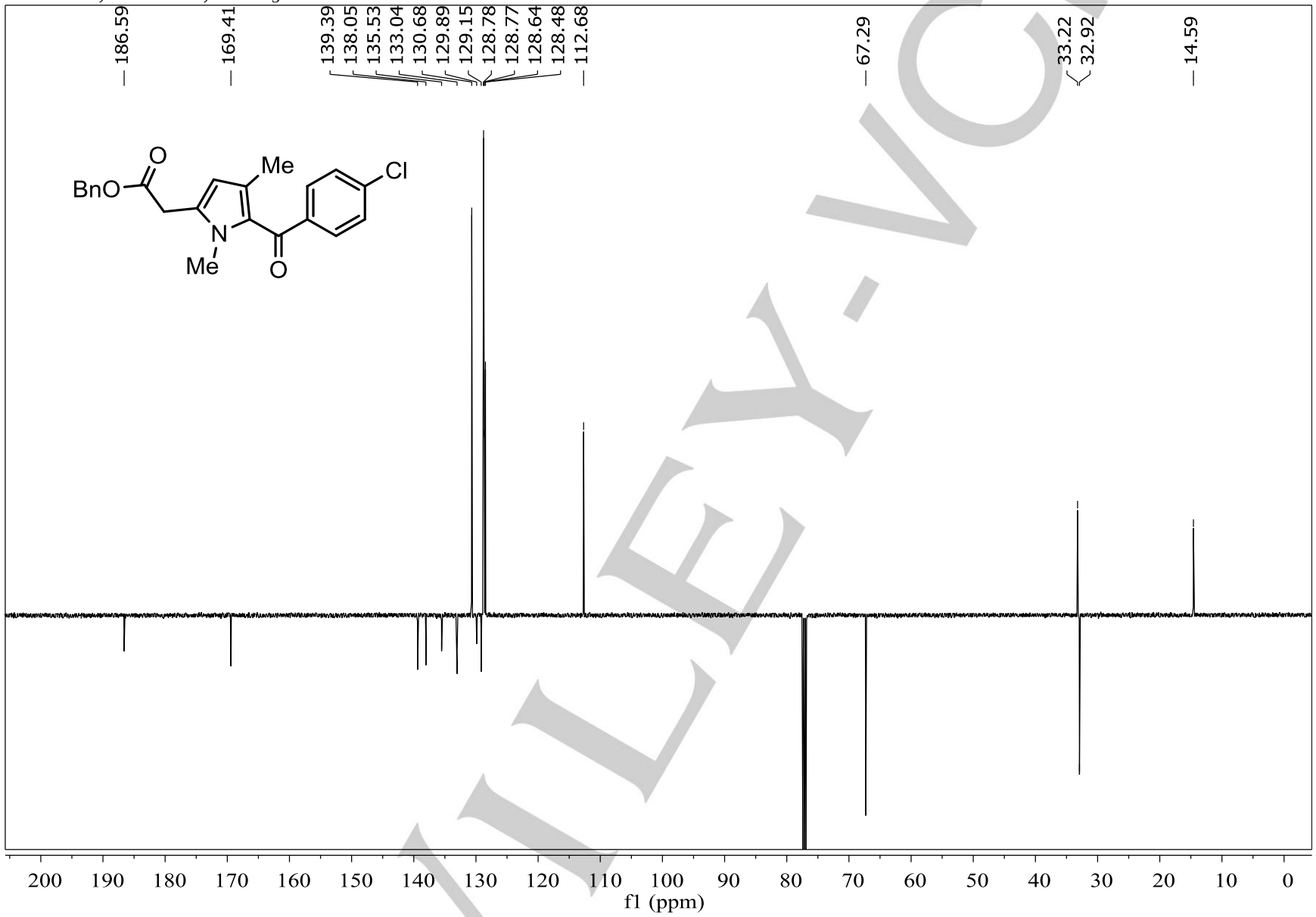

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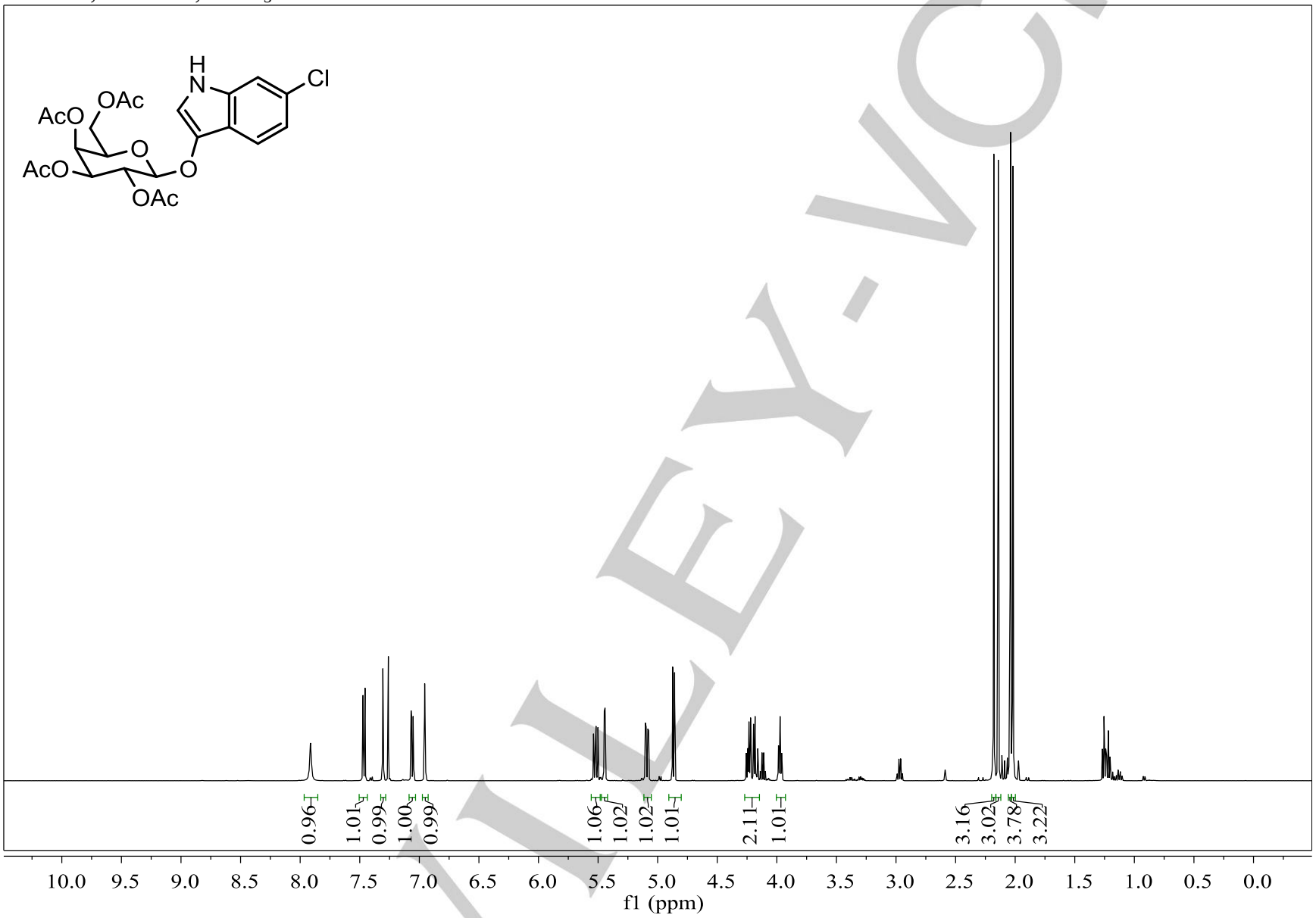

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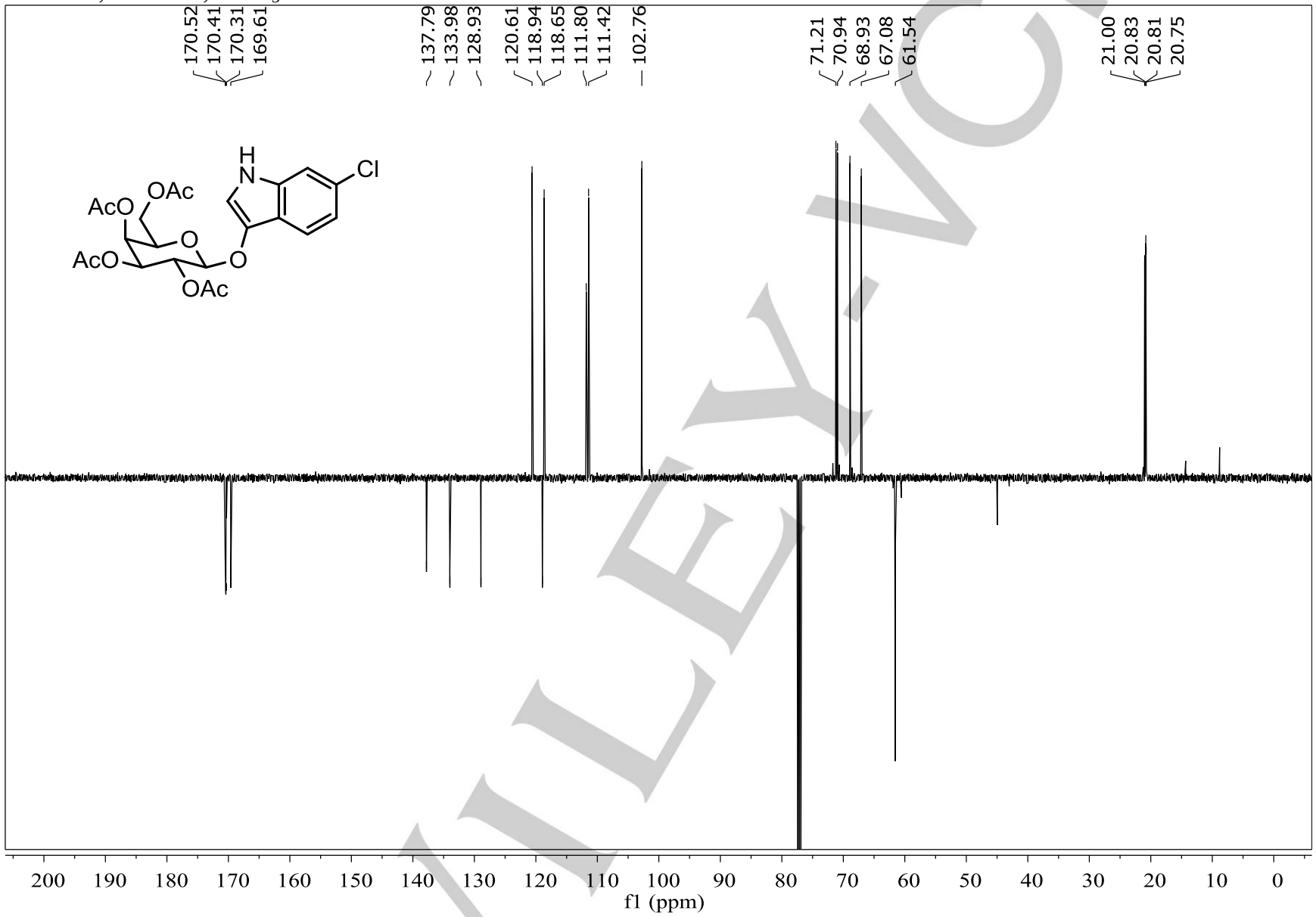

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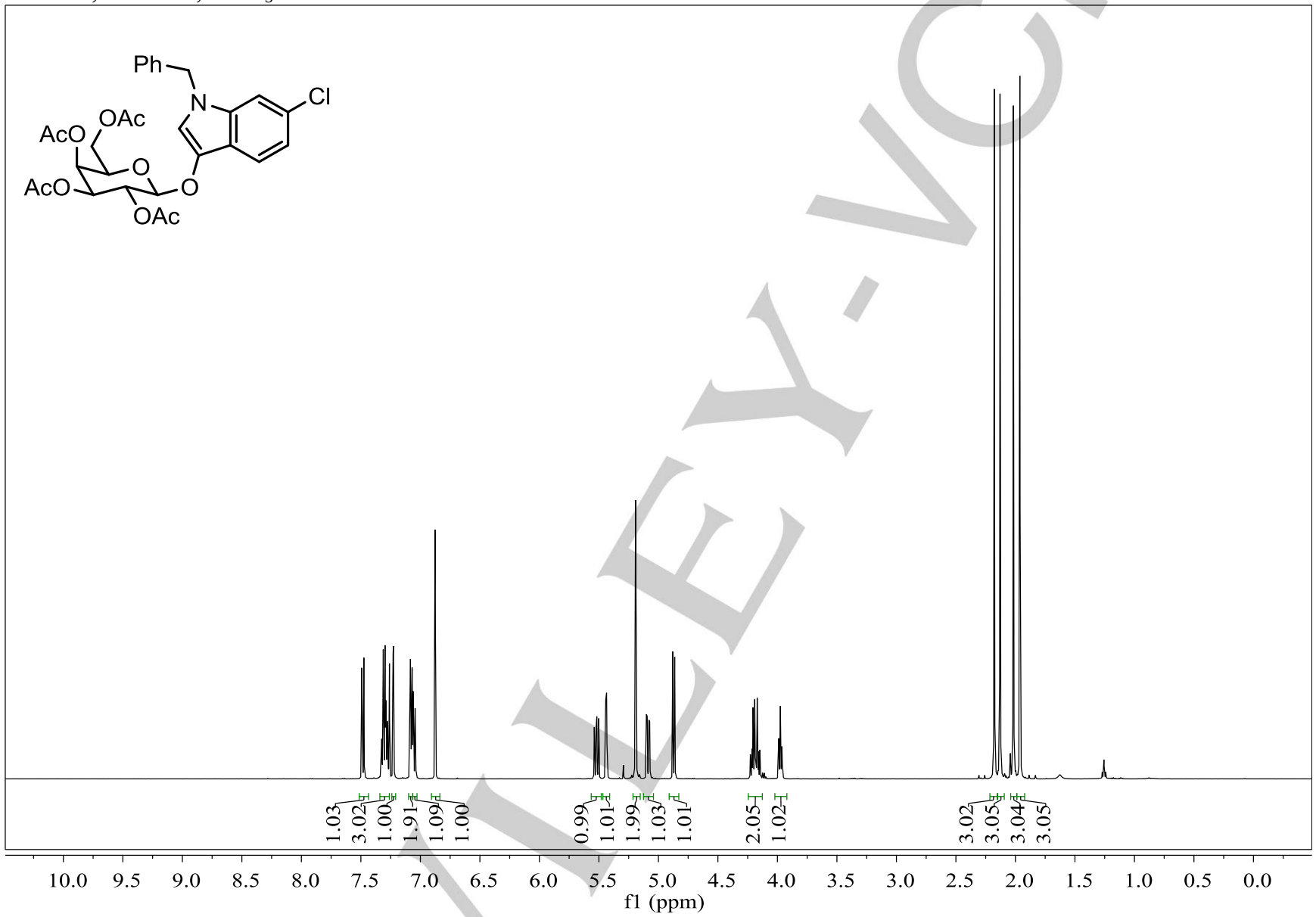

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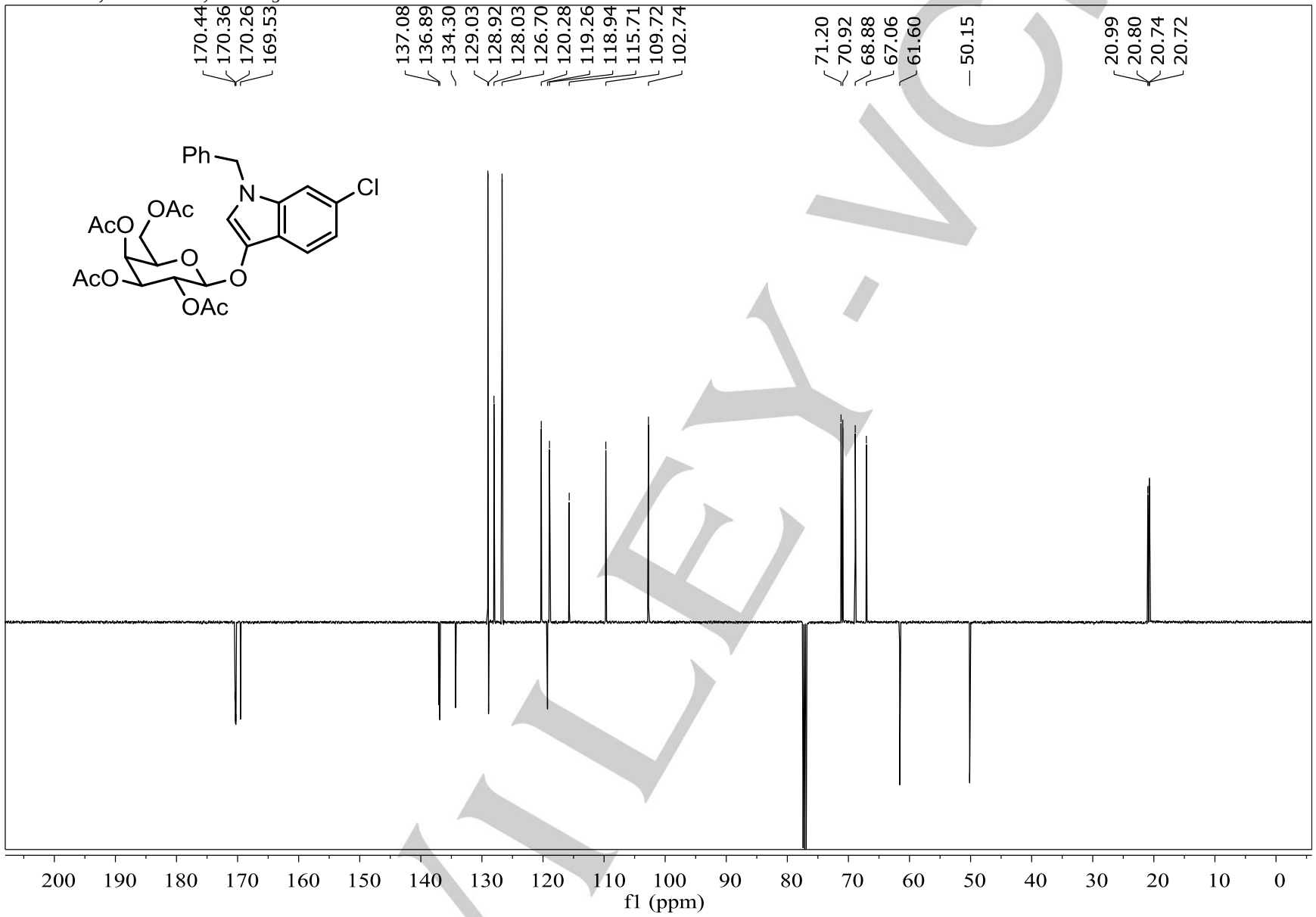
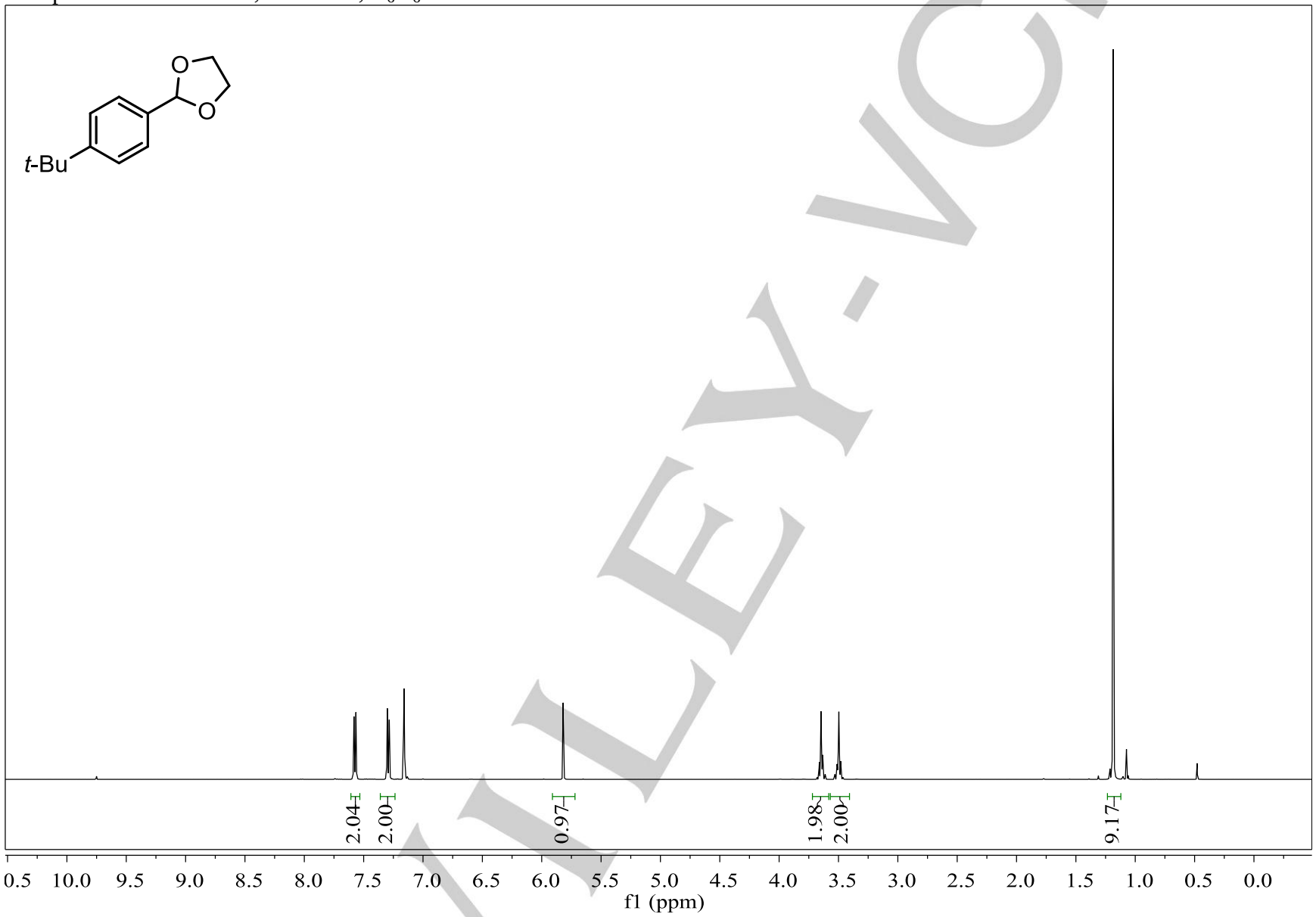
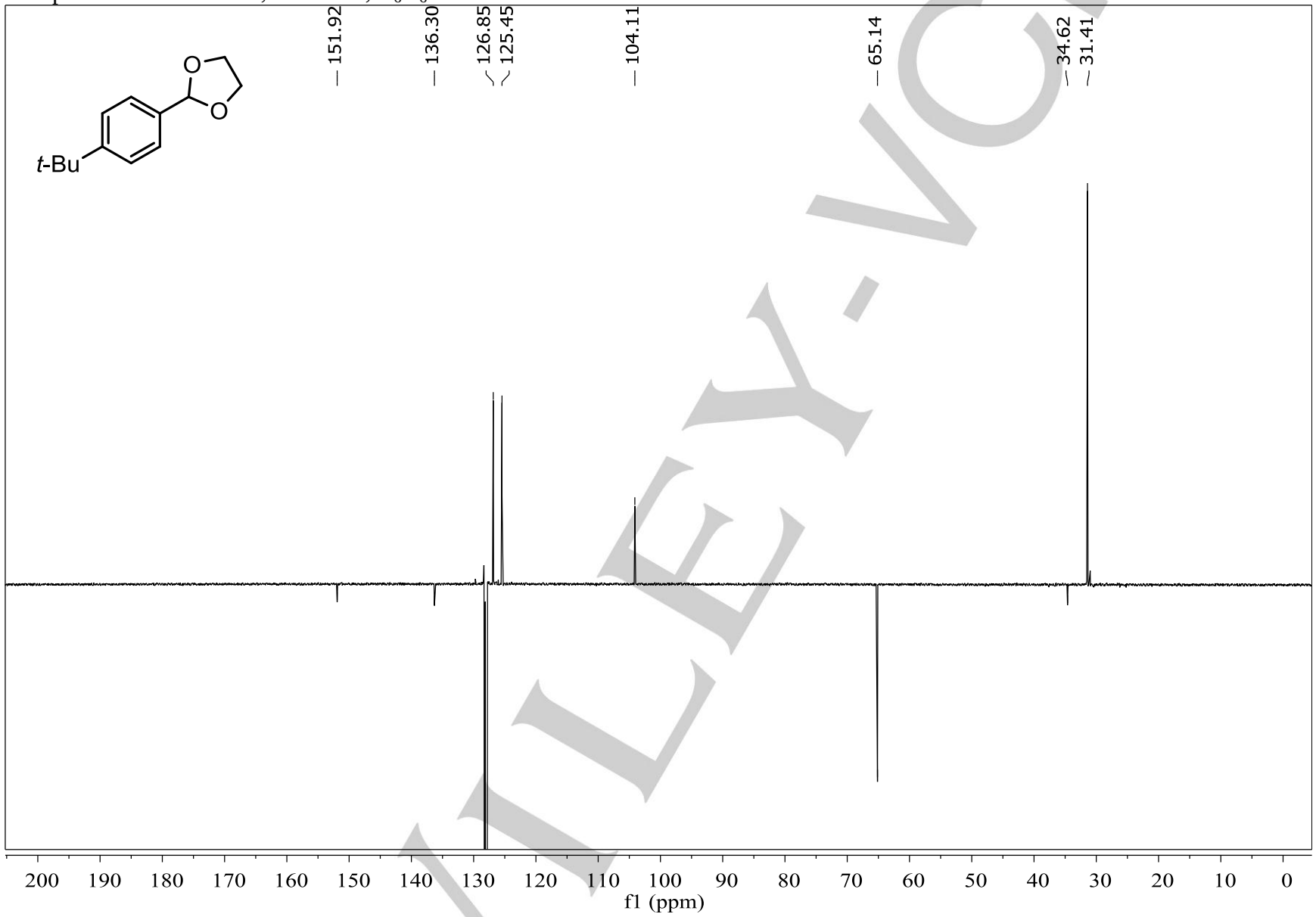


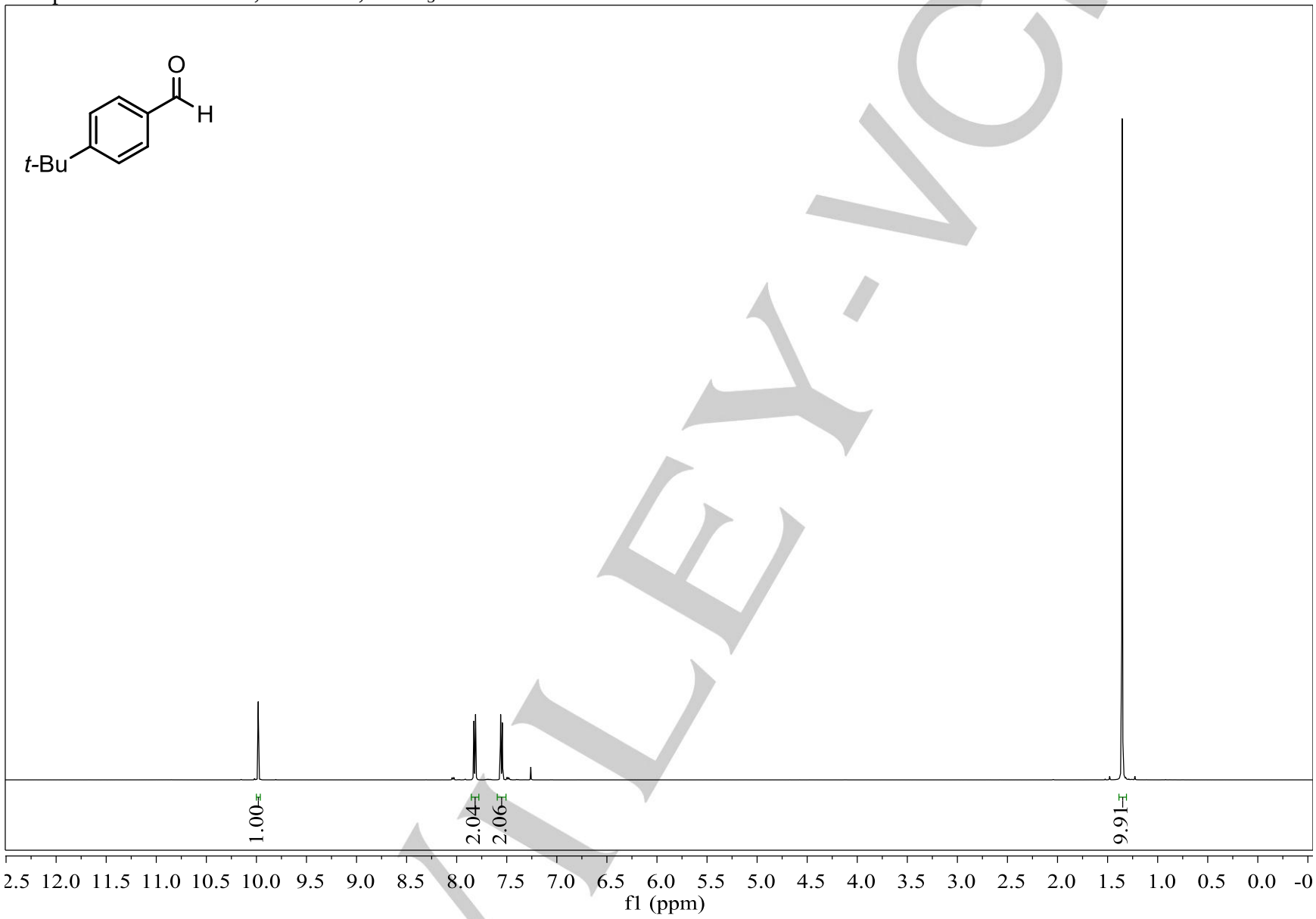
Compound **10** – ^{1}H NMR, 500 MHz, C_6D_6



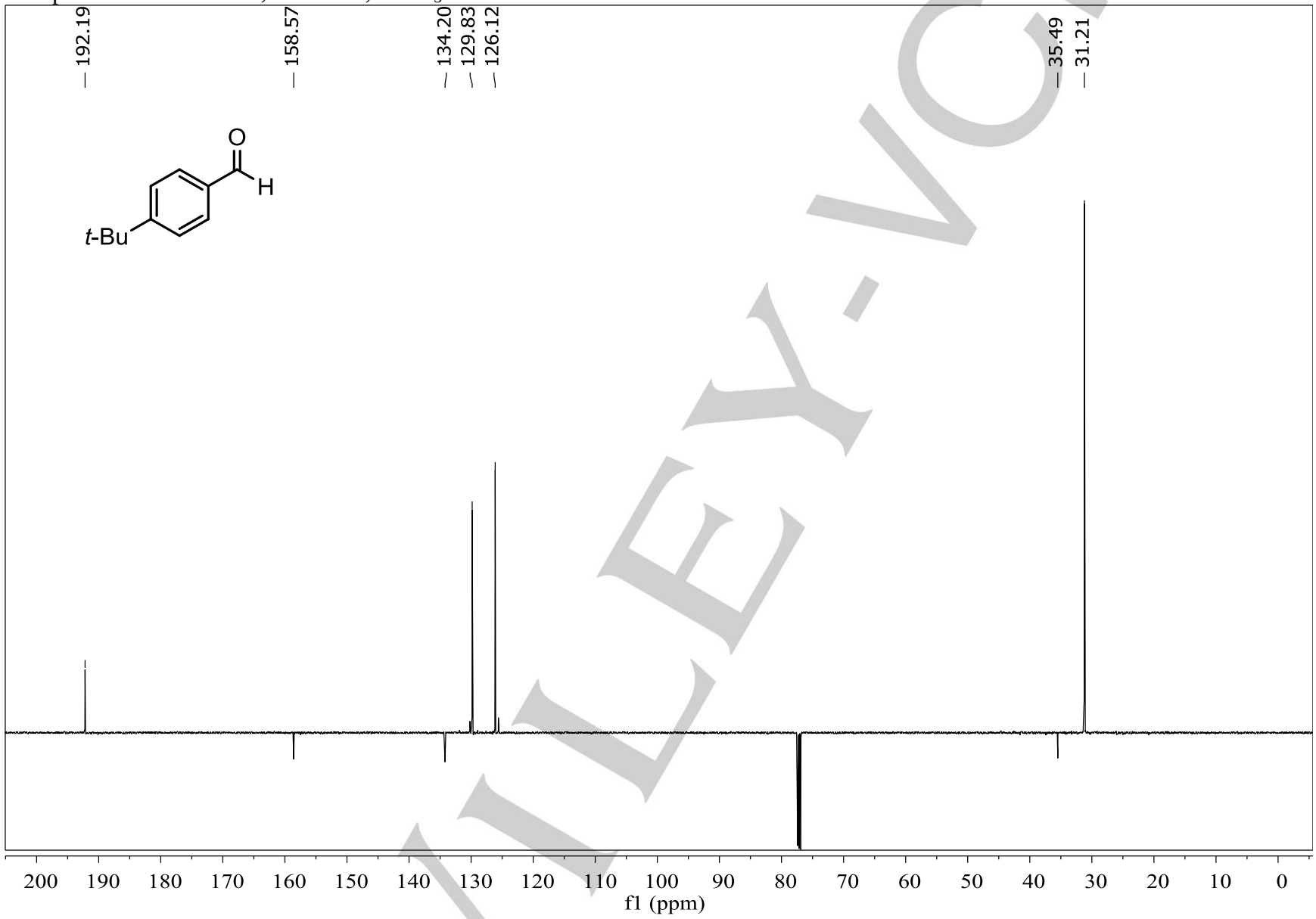
Compound **10** – ^{13}C NMR, 125 MHz, C_6D_6



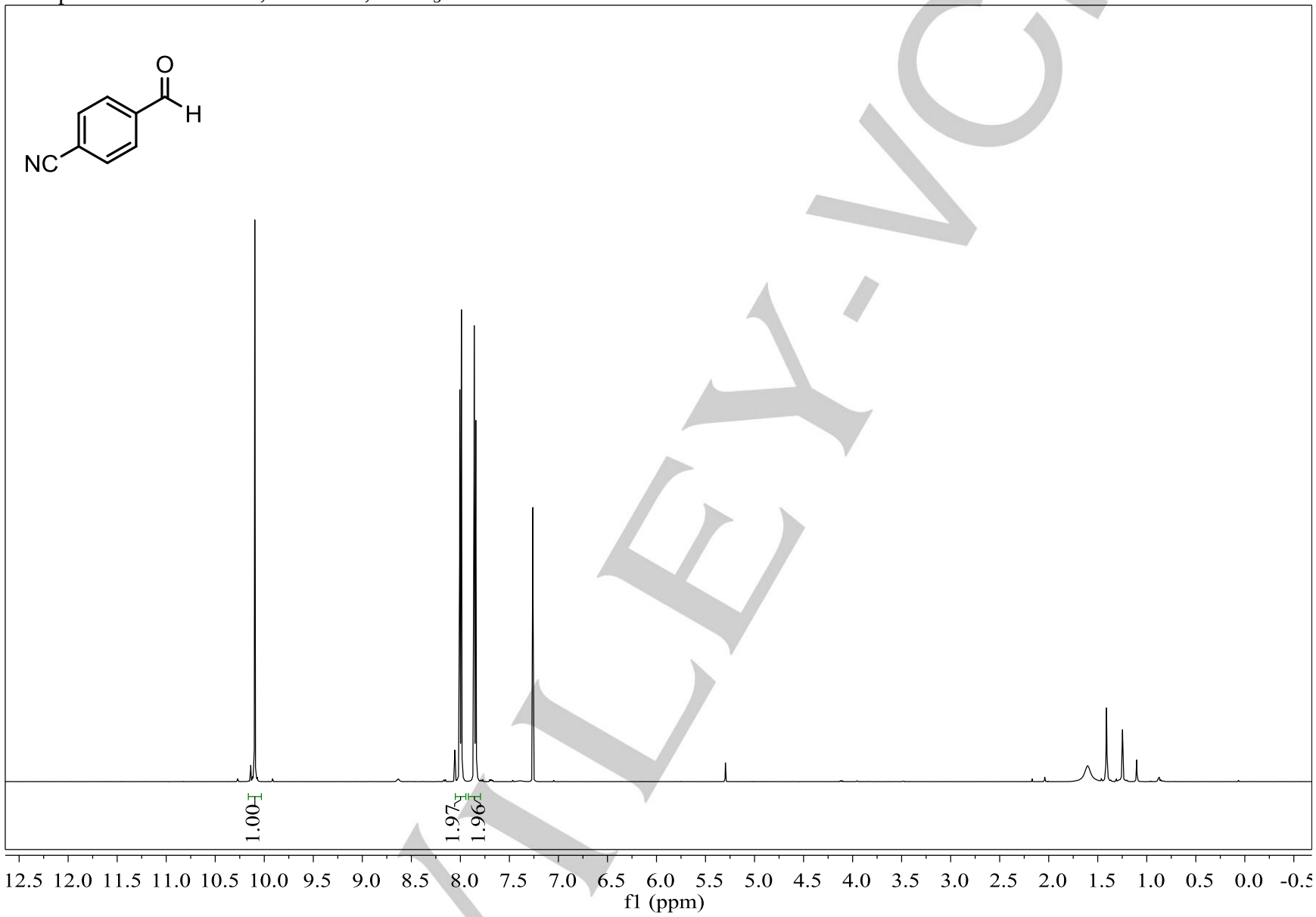
Compound **11** – ^{1}H NMR, 500 MHz, $CDCl_3$



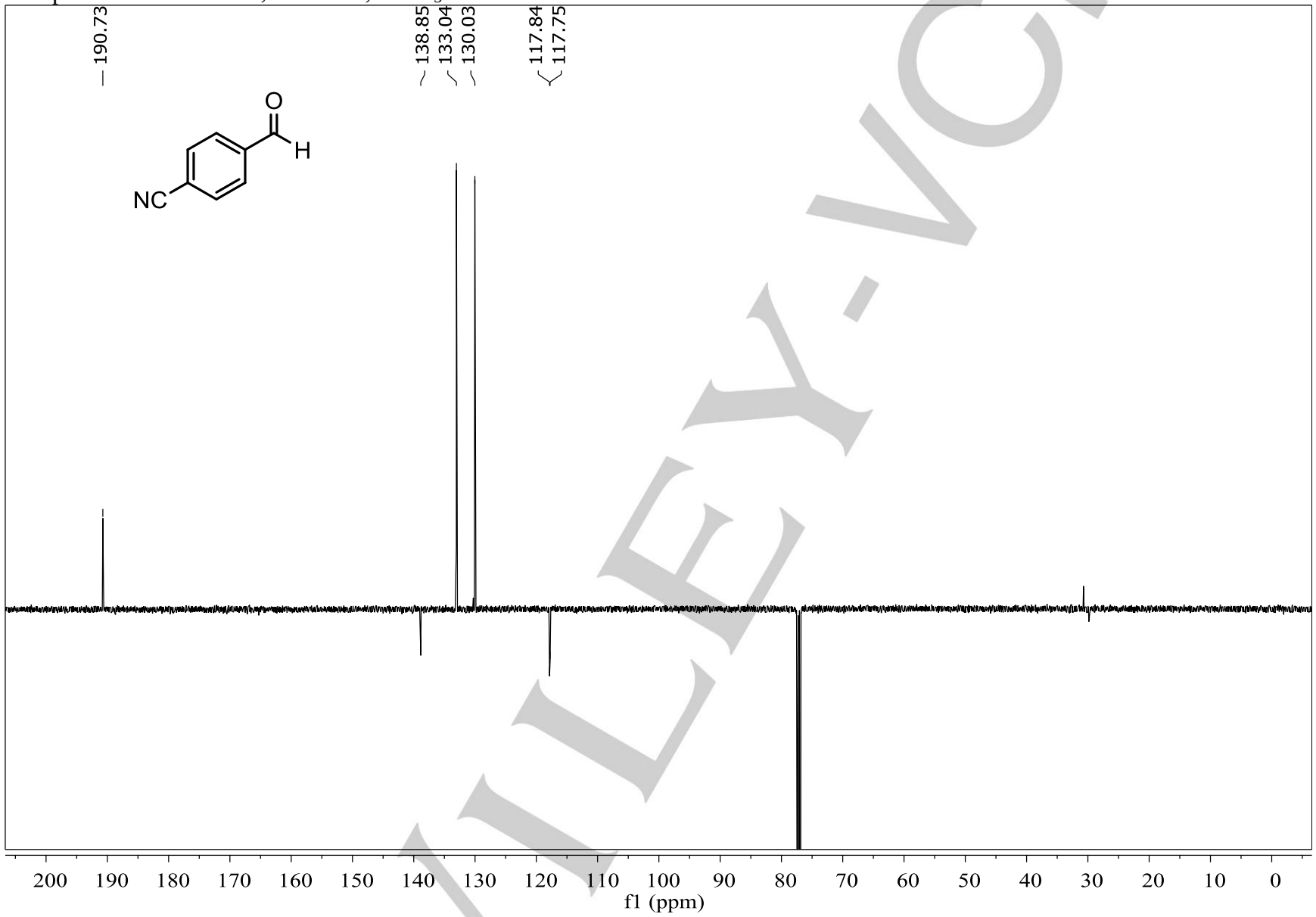
Compound **11** – ^{13}C NMR, 125 MHz, $CDCl_3$



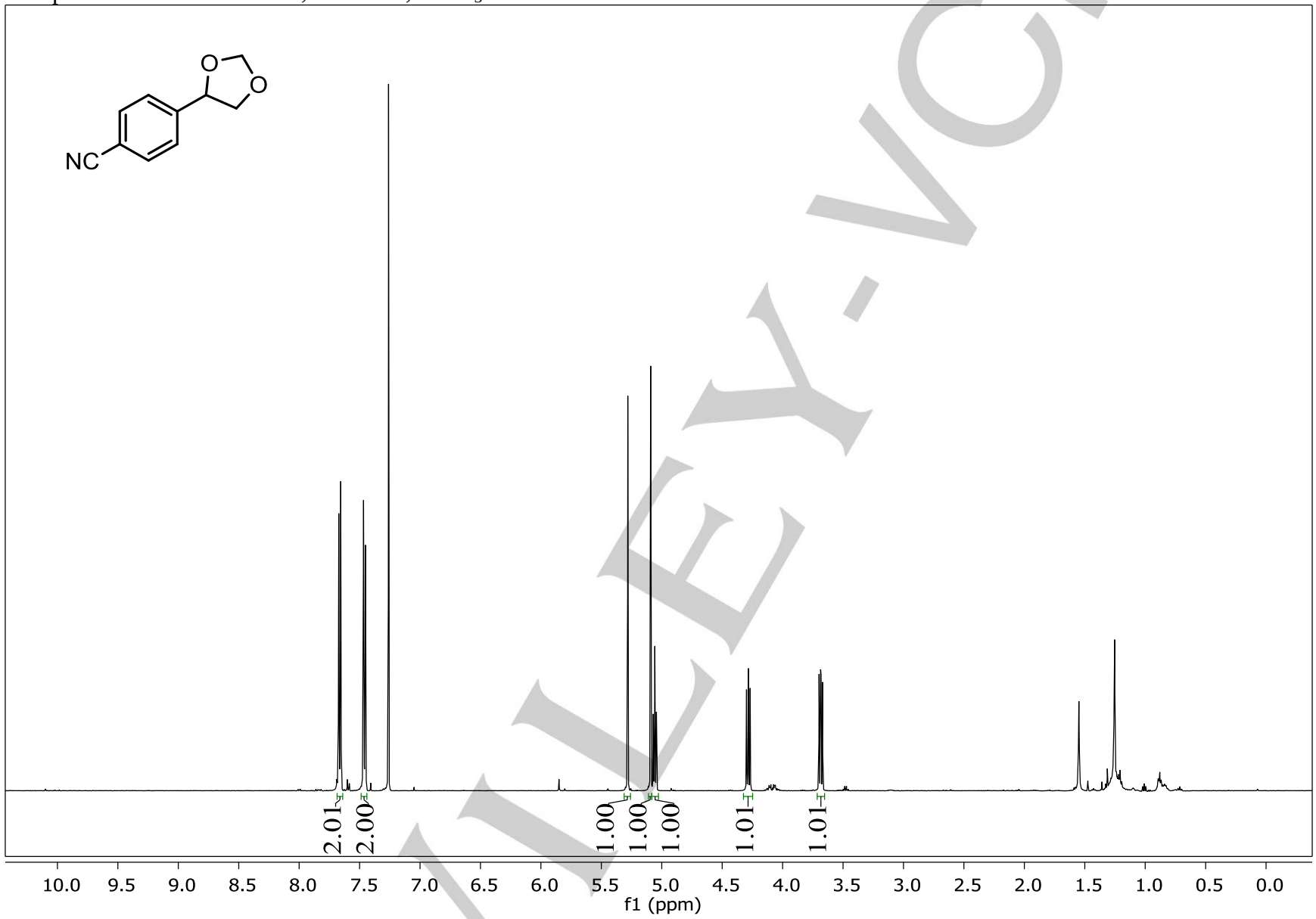
Compound **12** – ^{1}H NMR, 500 MHz, $CDCl_3$



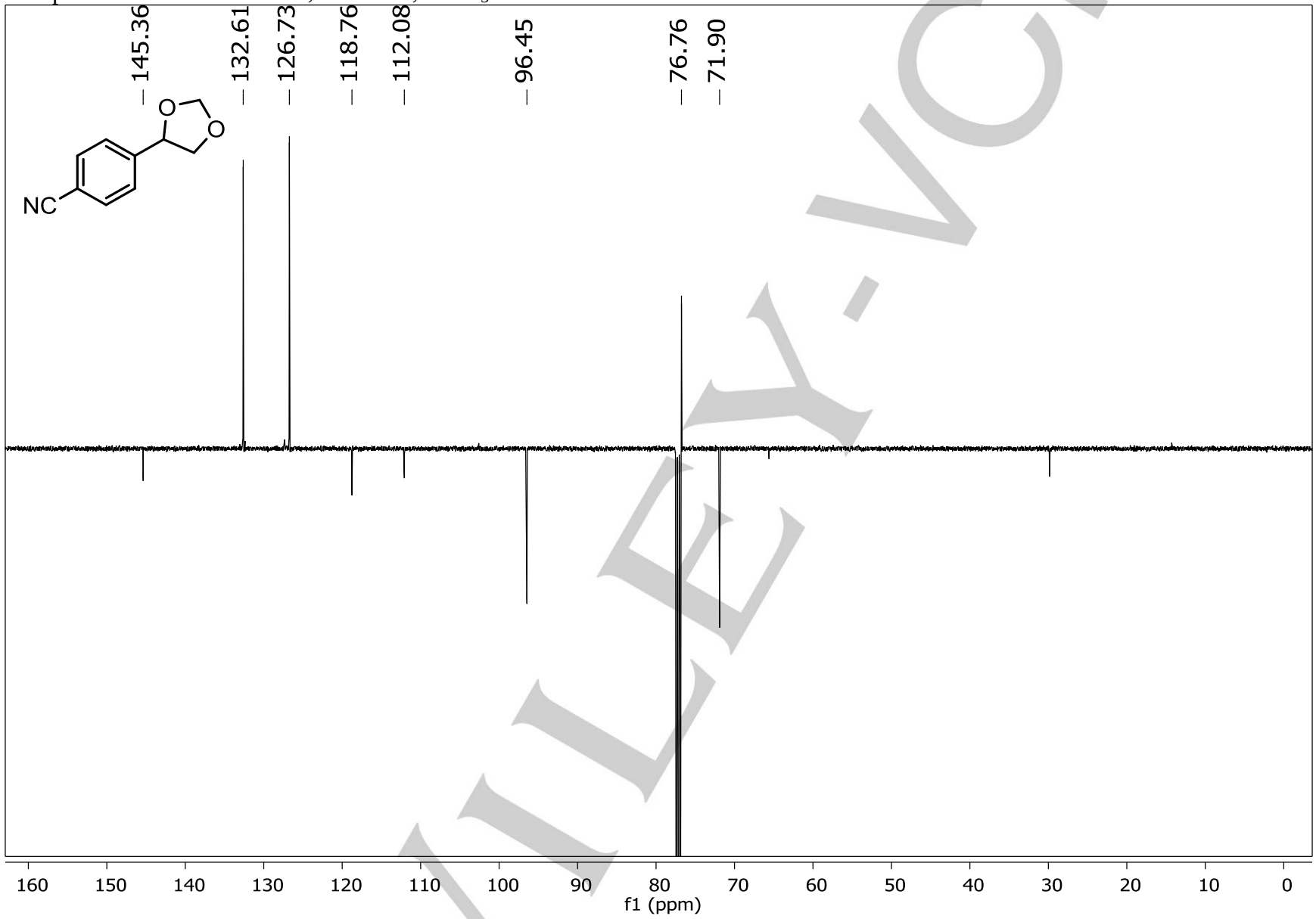
Compound **12** – ^{13}C NMR, 125 MHz, $CDCl_3$



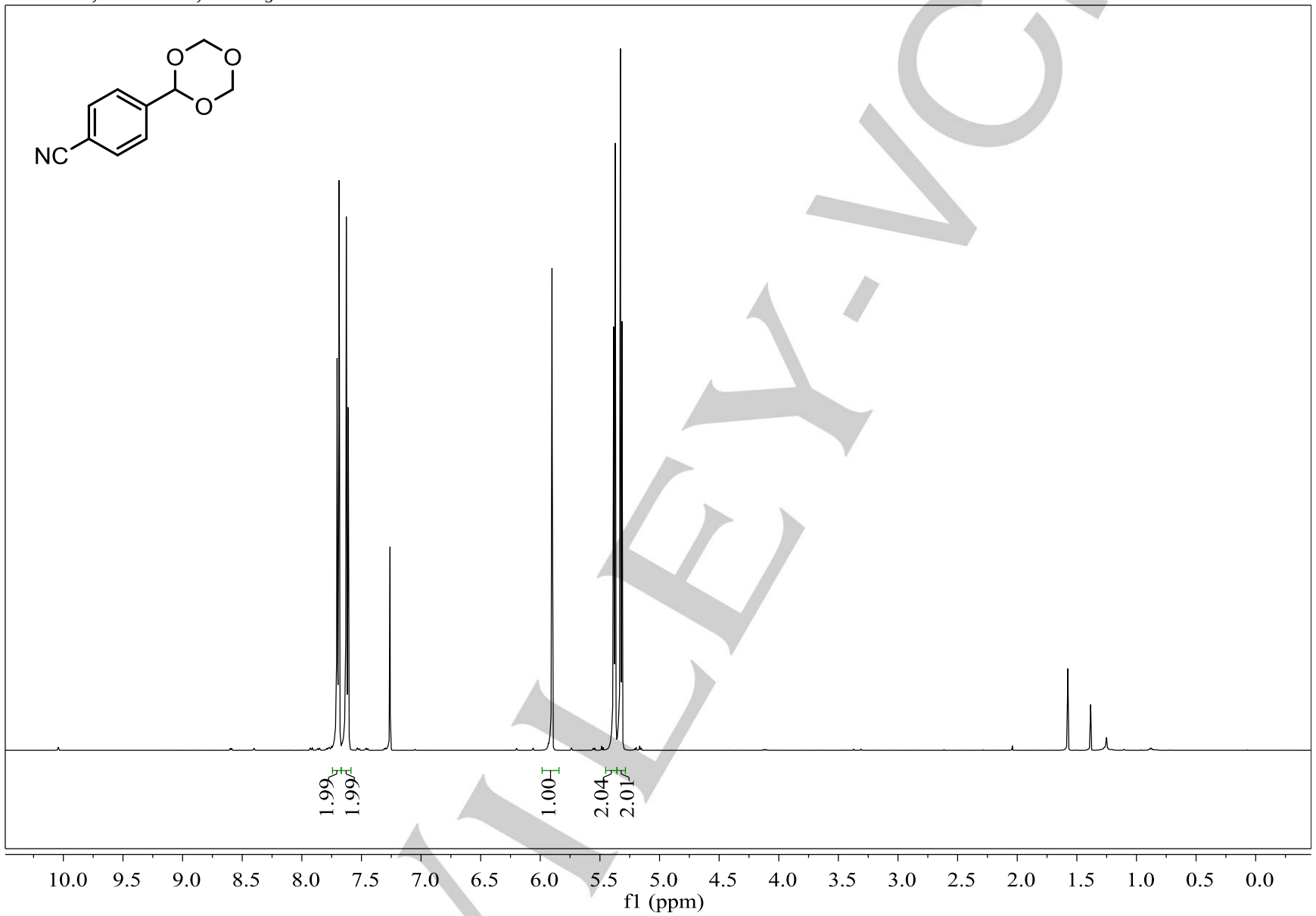
Compound **37–CN** – ^{1}H NMR, 500 MHz, $CDCl_3$



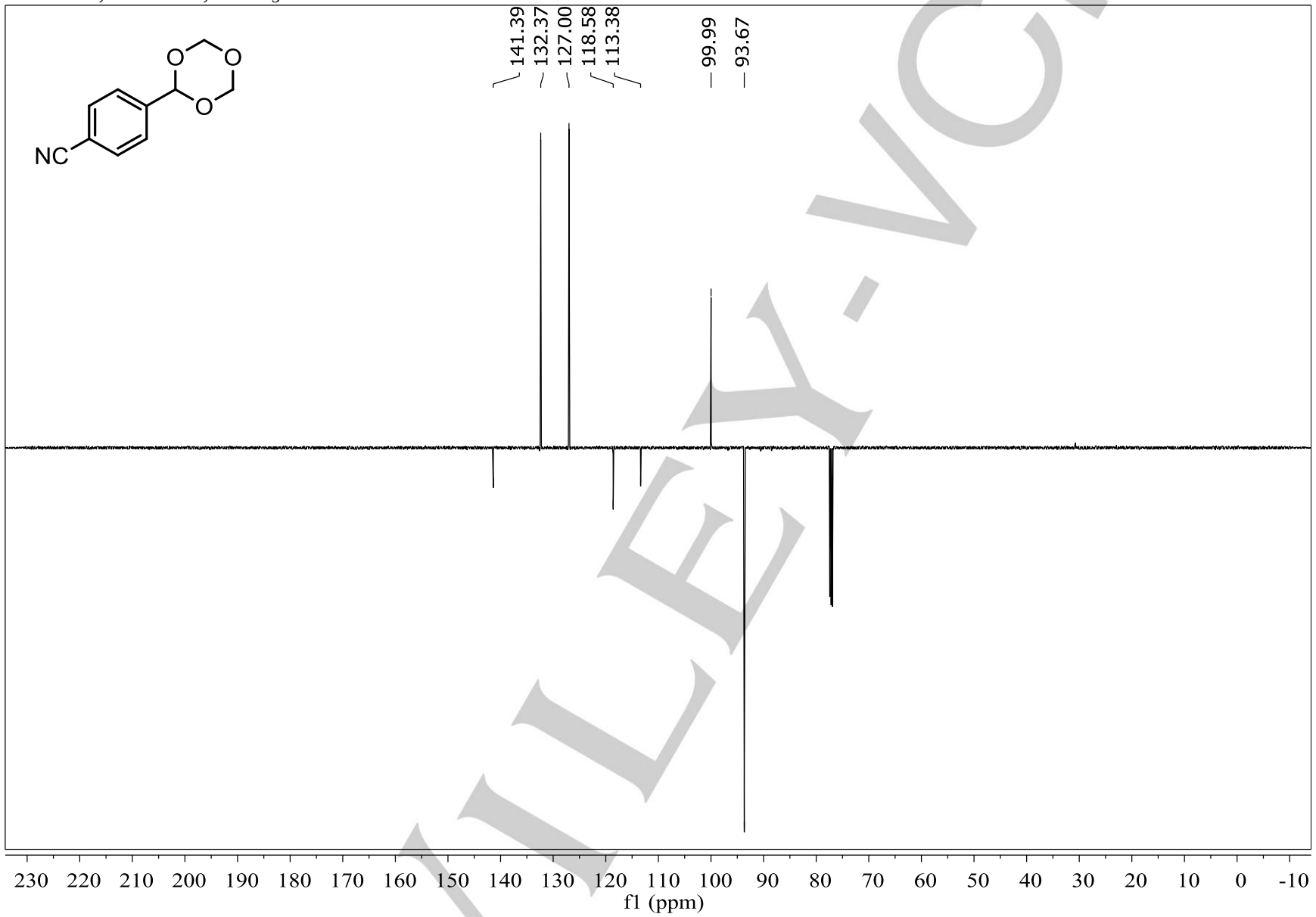
Compound **37–CN** – ^{13}C NMR, 125 MHz, $CDCl_3$



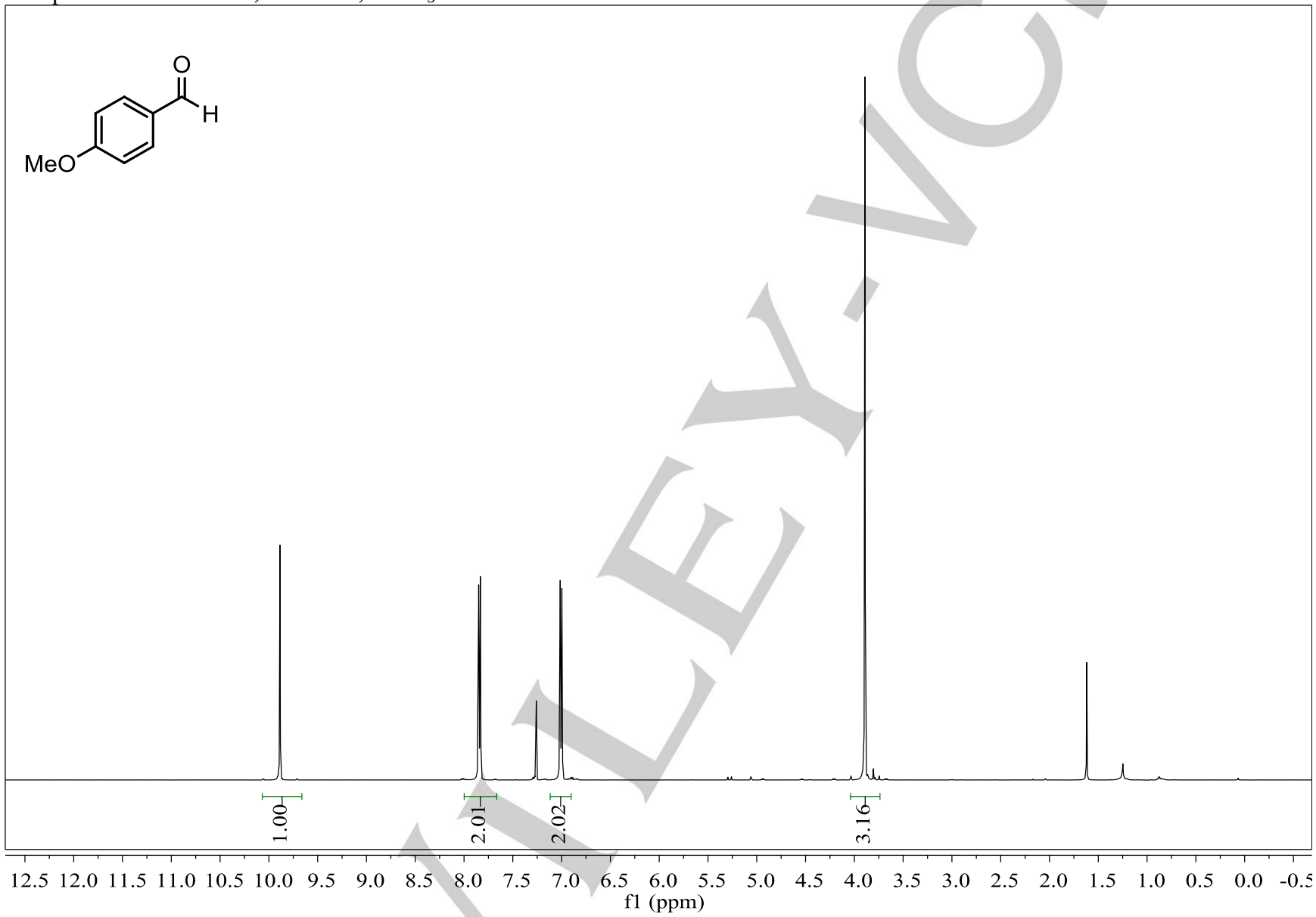
^{1}H NMR, 500 MHz, $CDCl_3$



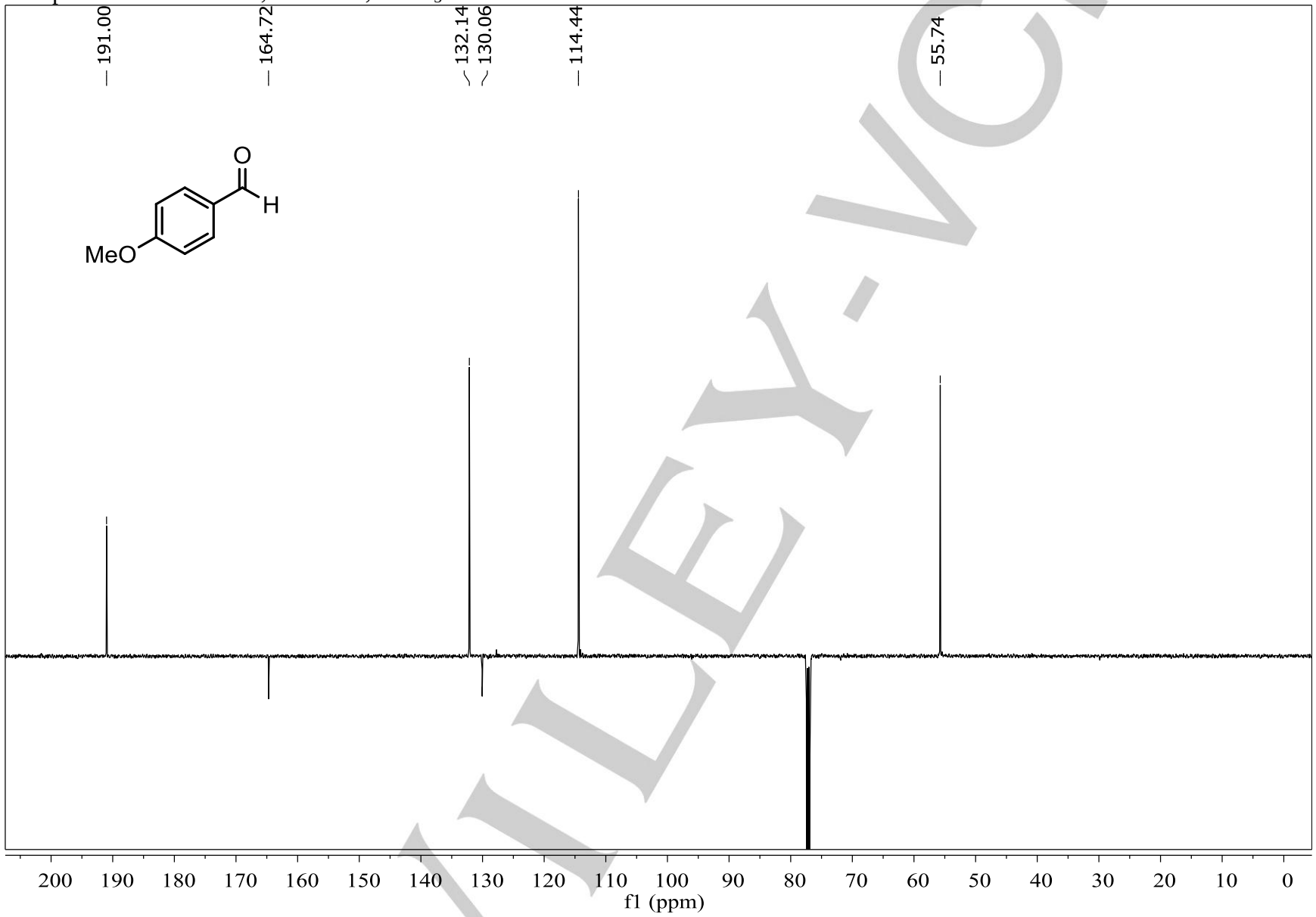
^{13}C NMR, 125 MHz, $CDCl_3$



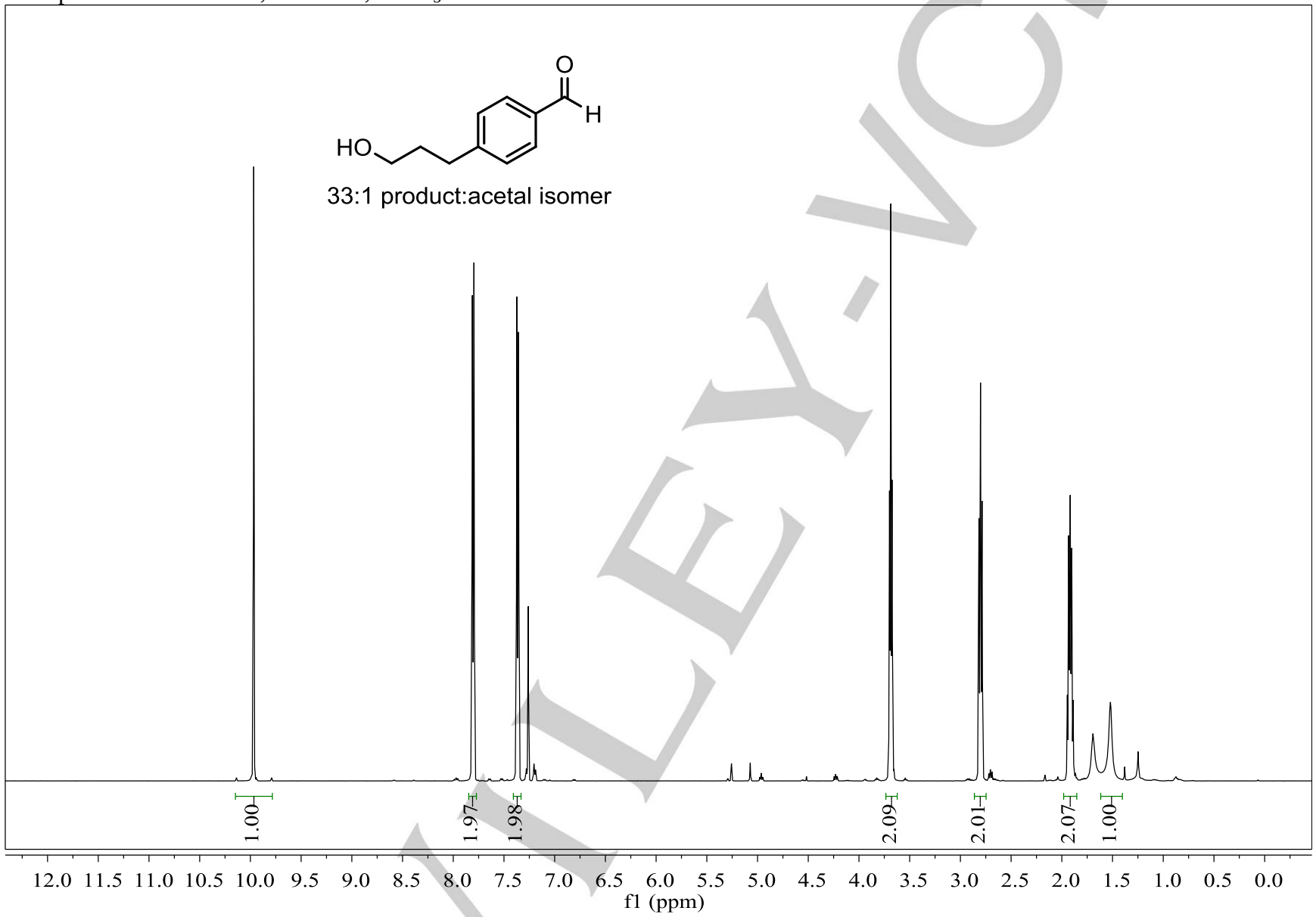
Compound **13** – ^{1}H NMR, 500 MHz, $CDCl_3$



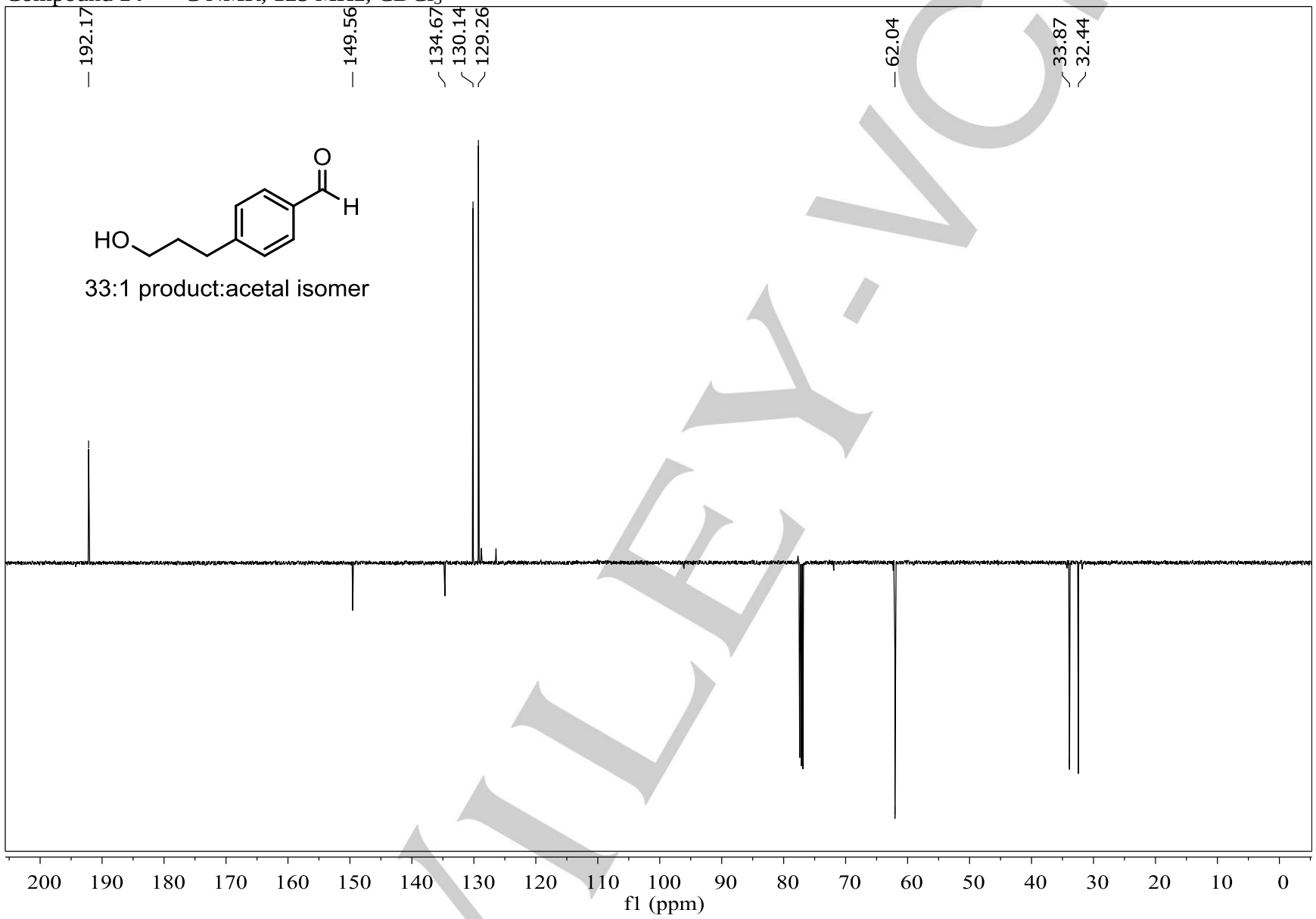
Compound **13** – ^{13}C NMR, 125 MHz, $CDCl_3$



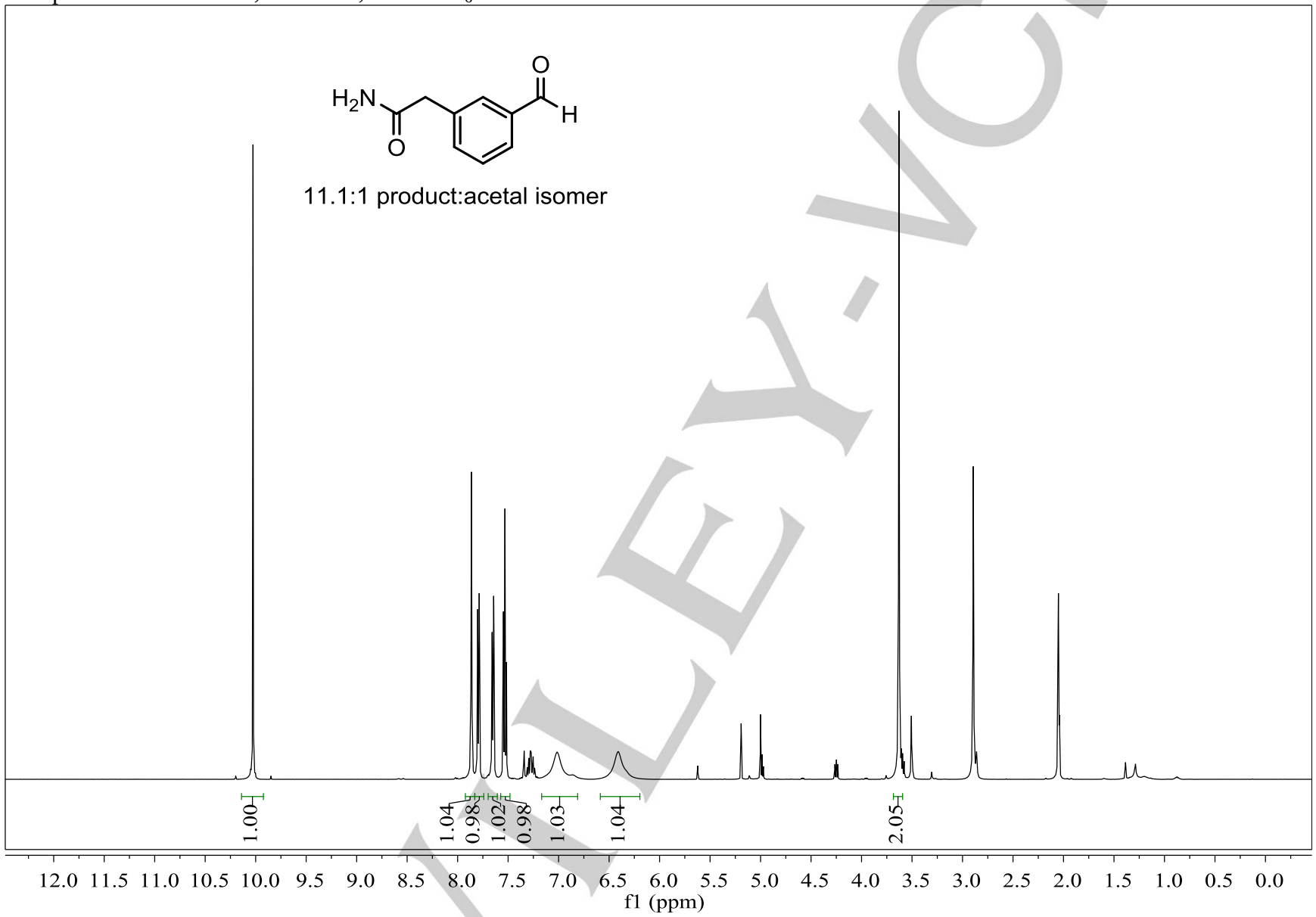
Compound **14** – ^{1}H NMR, 500 MHz, $CDCl_3$



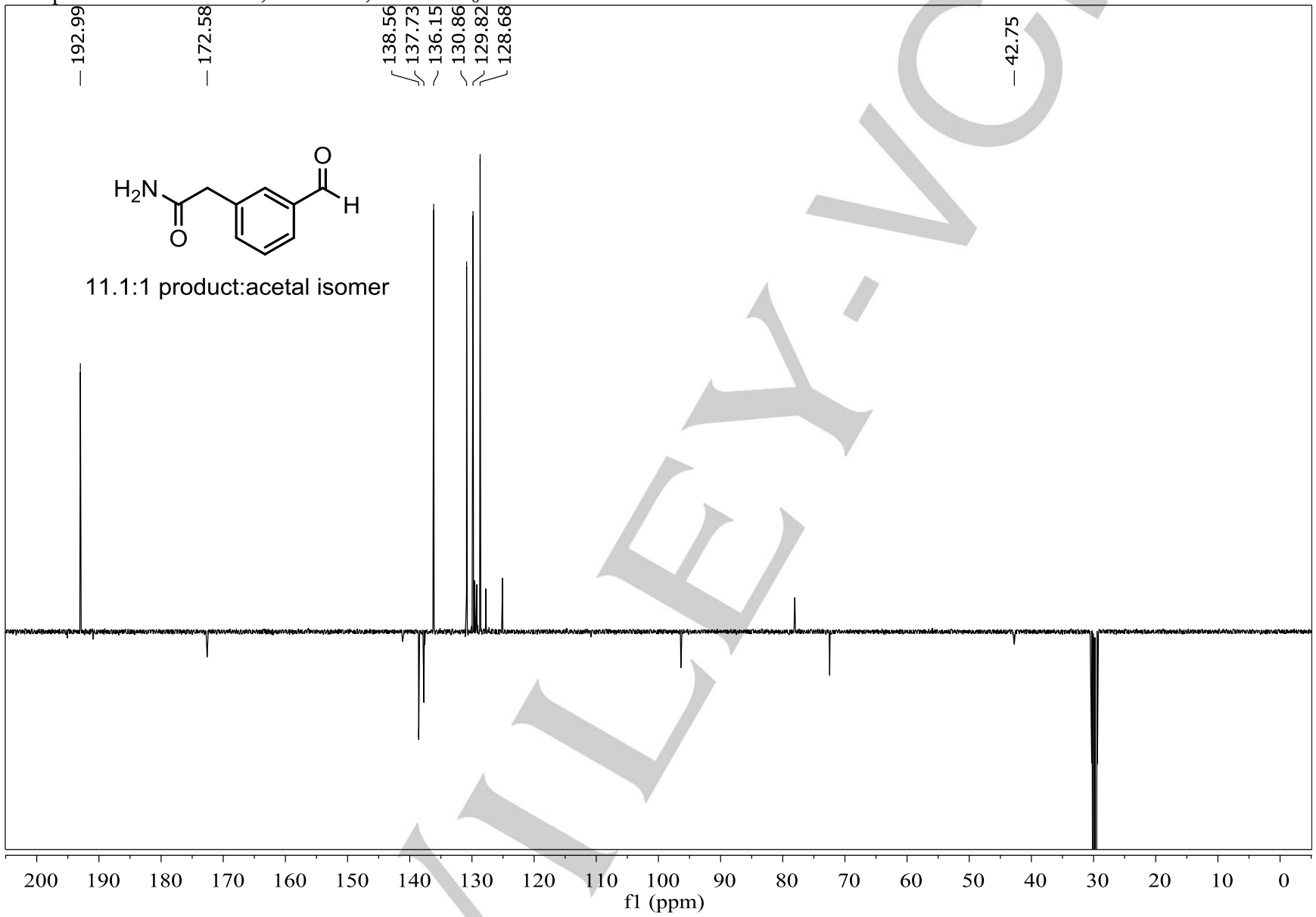
Compound **14** – ^{13}C NMR, 125 MHz, $CDCl_3$



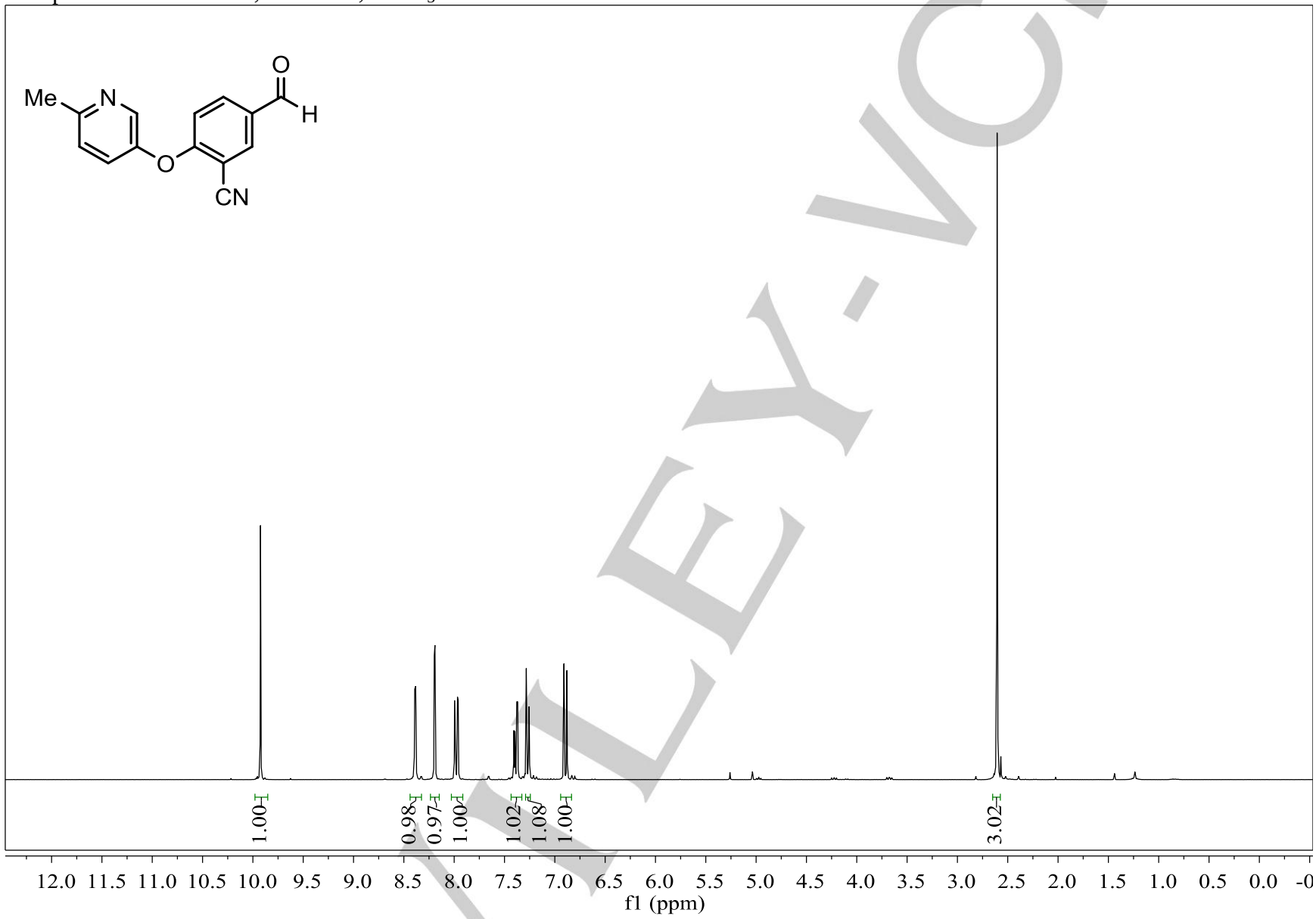
Compound **15** – ^{1}H NMR, 500 MHz, acetone-d_6



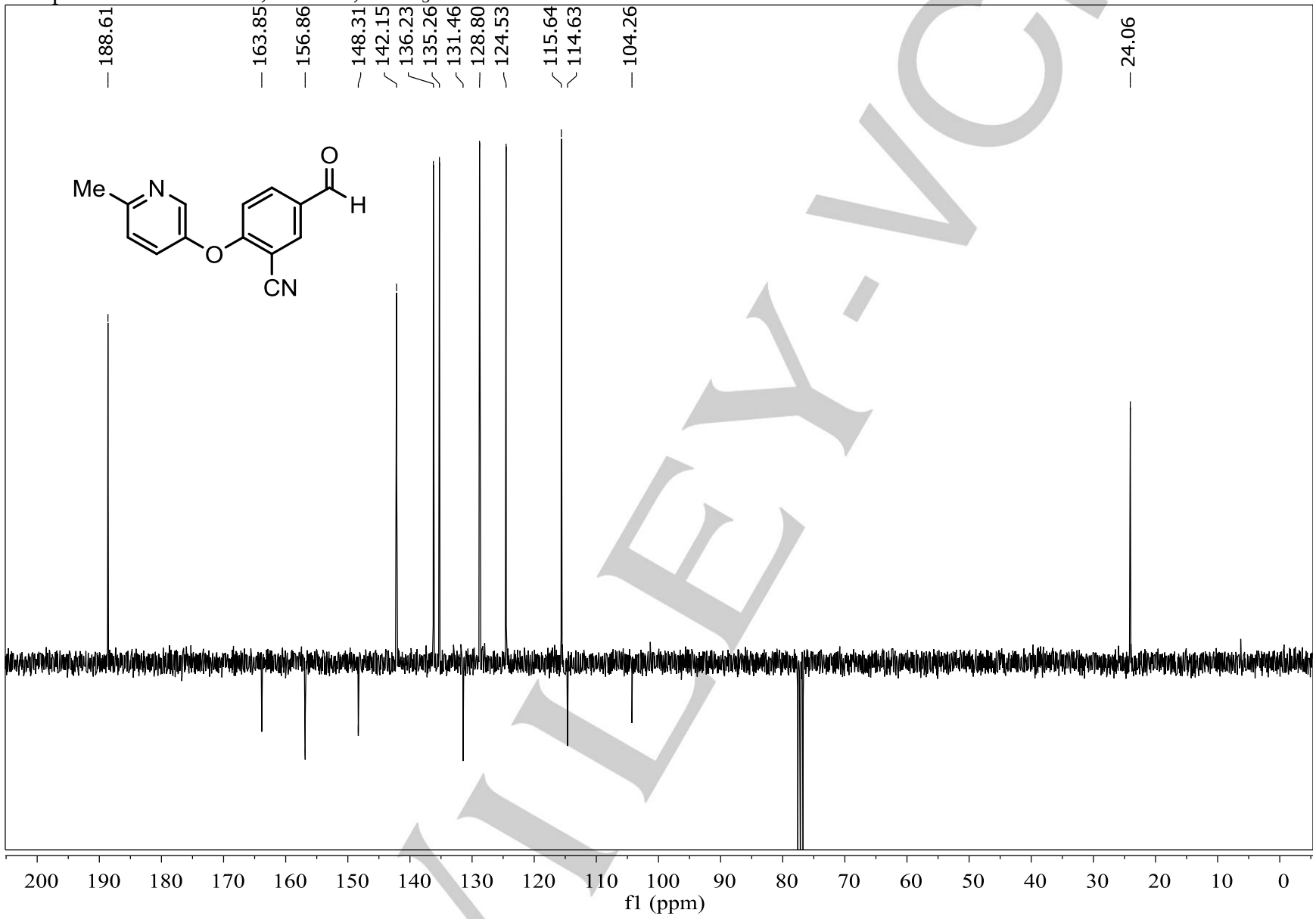
Compound **15** – ^{13}C NMR, 125 MHz, acetone-d_6



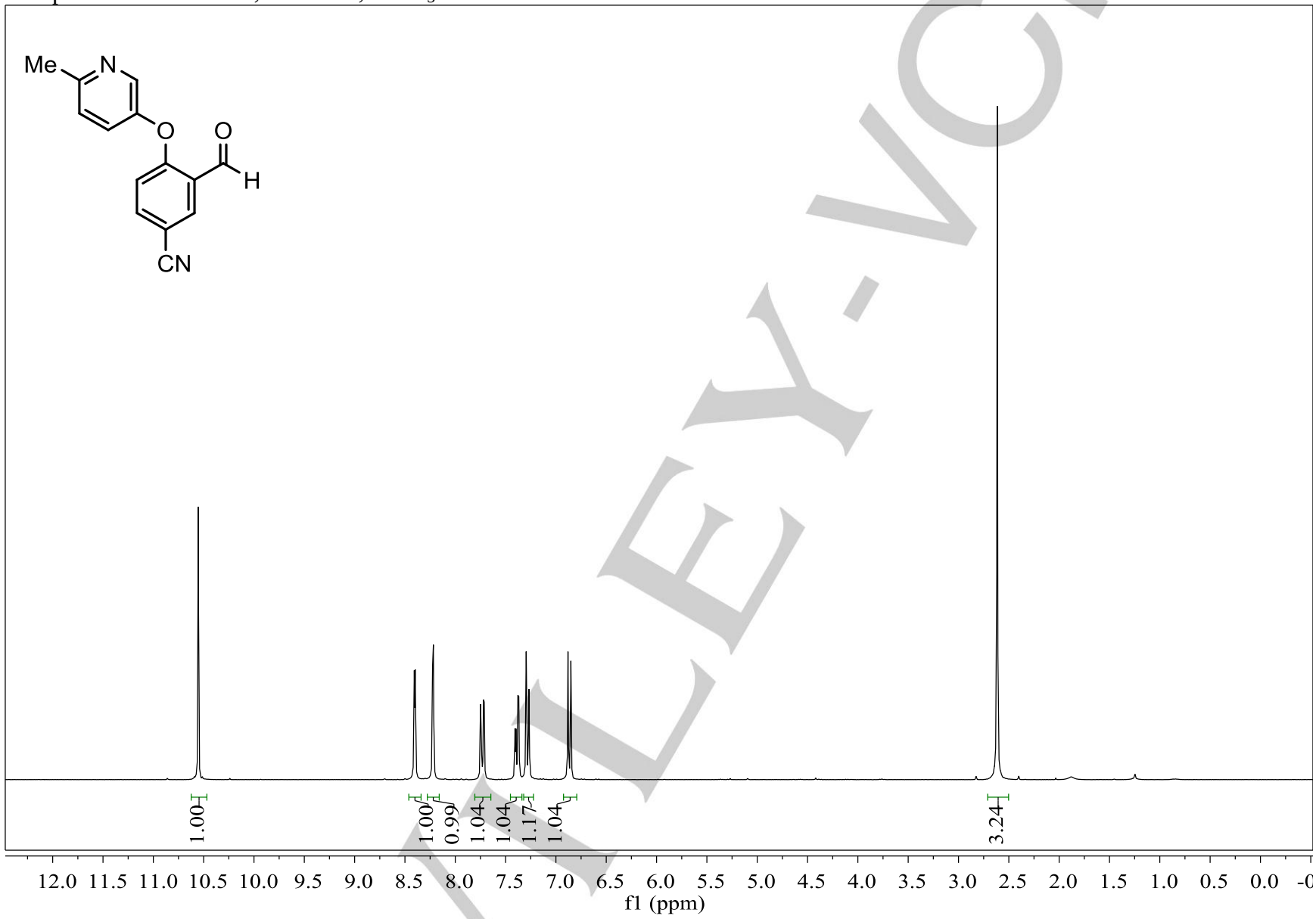
Compound **16** – ^{1}H NMR, 300 MHz, $CDCl_3$



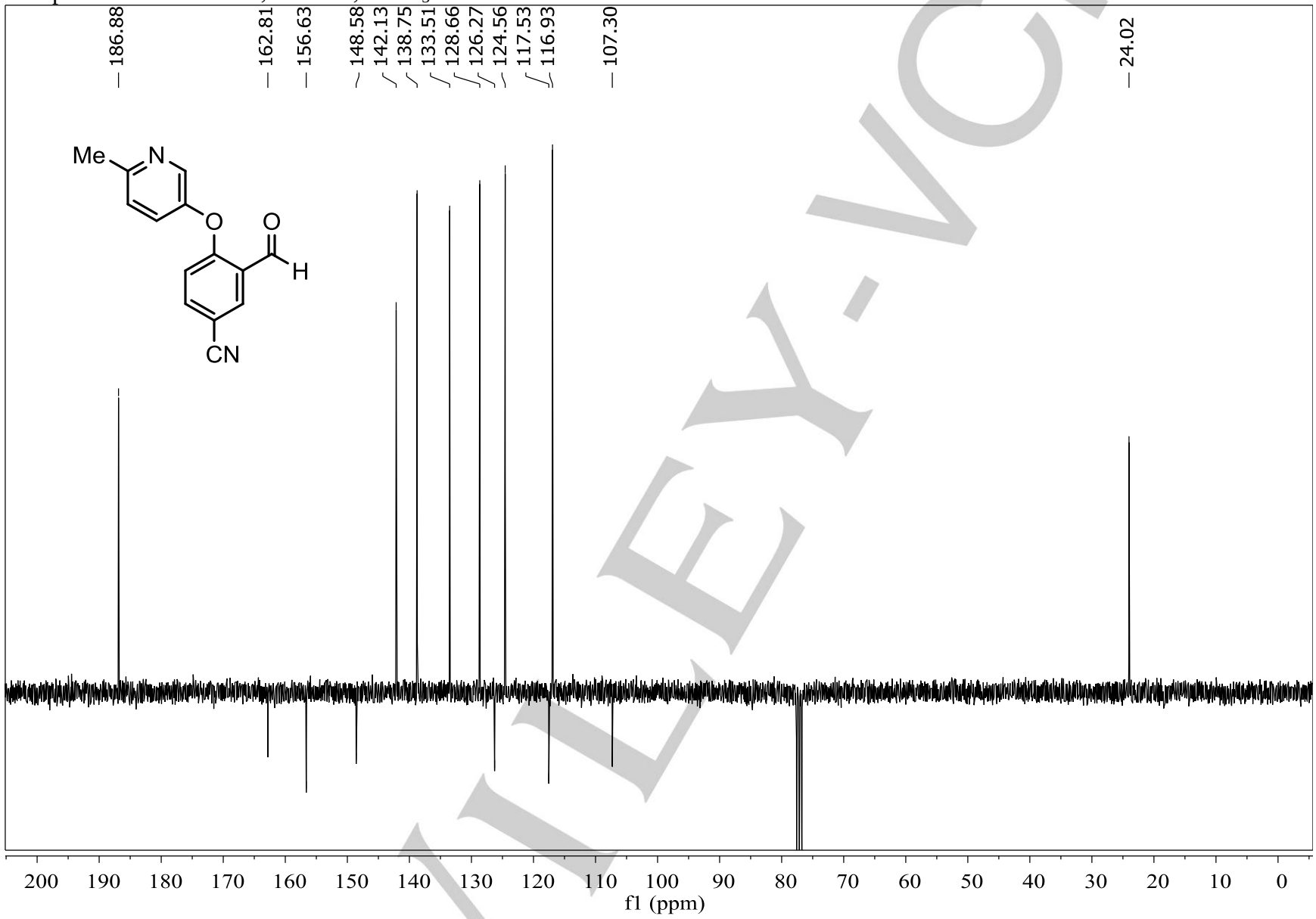
Compound **16** – ^{13}C NMR, 75 MHz, $CDCl_3$



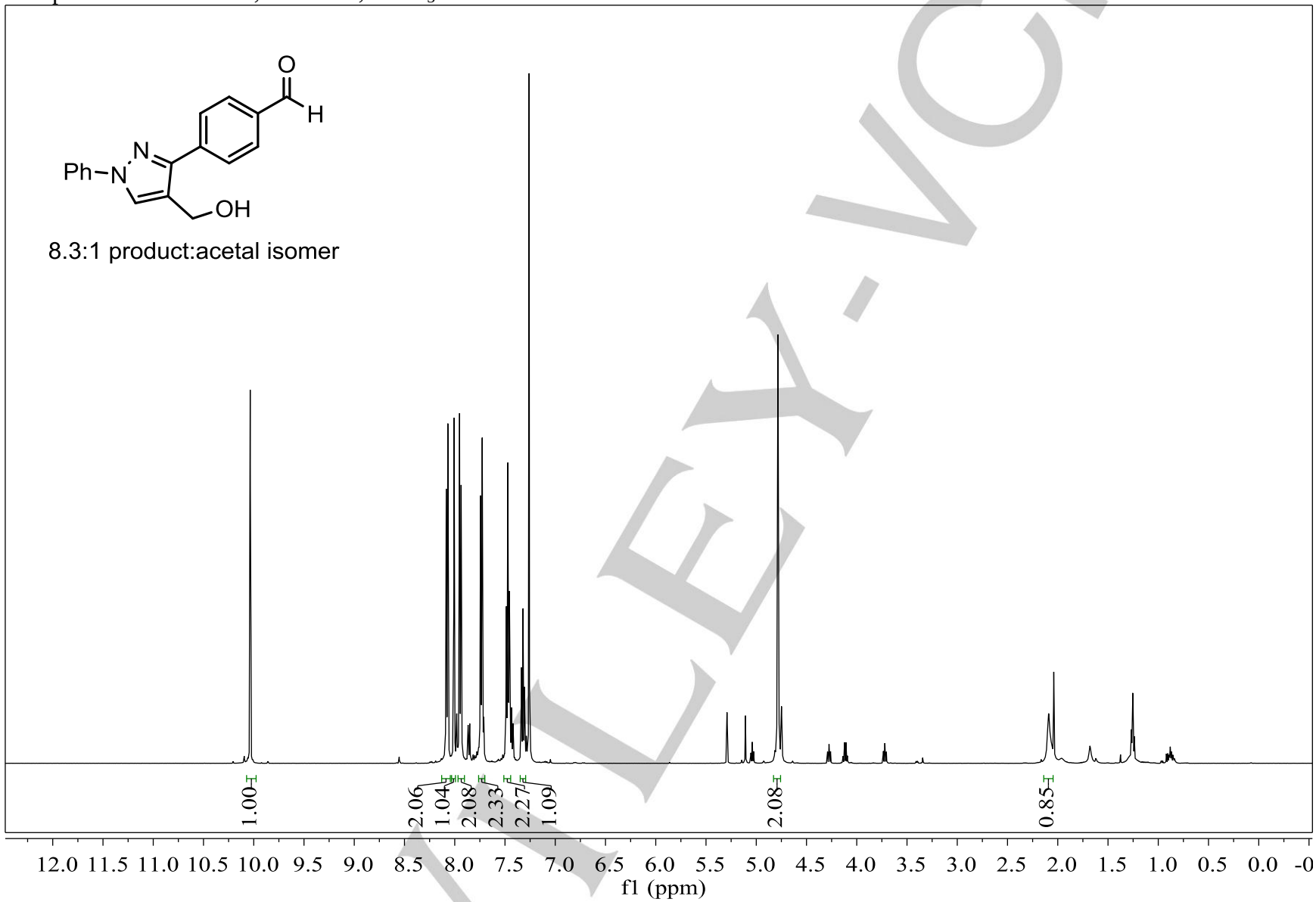
Compound **17** – ^{1}H NMR, 300 MHz, $CDCl_3$



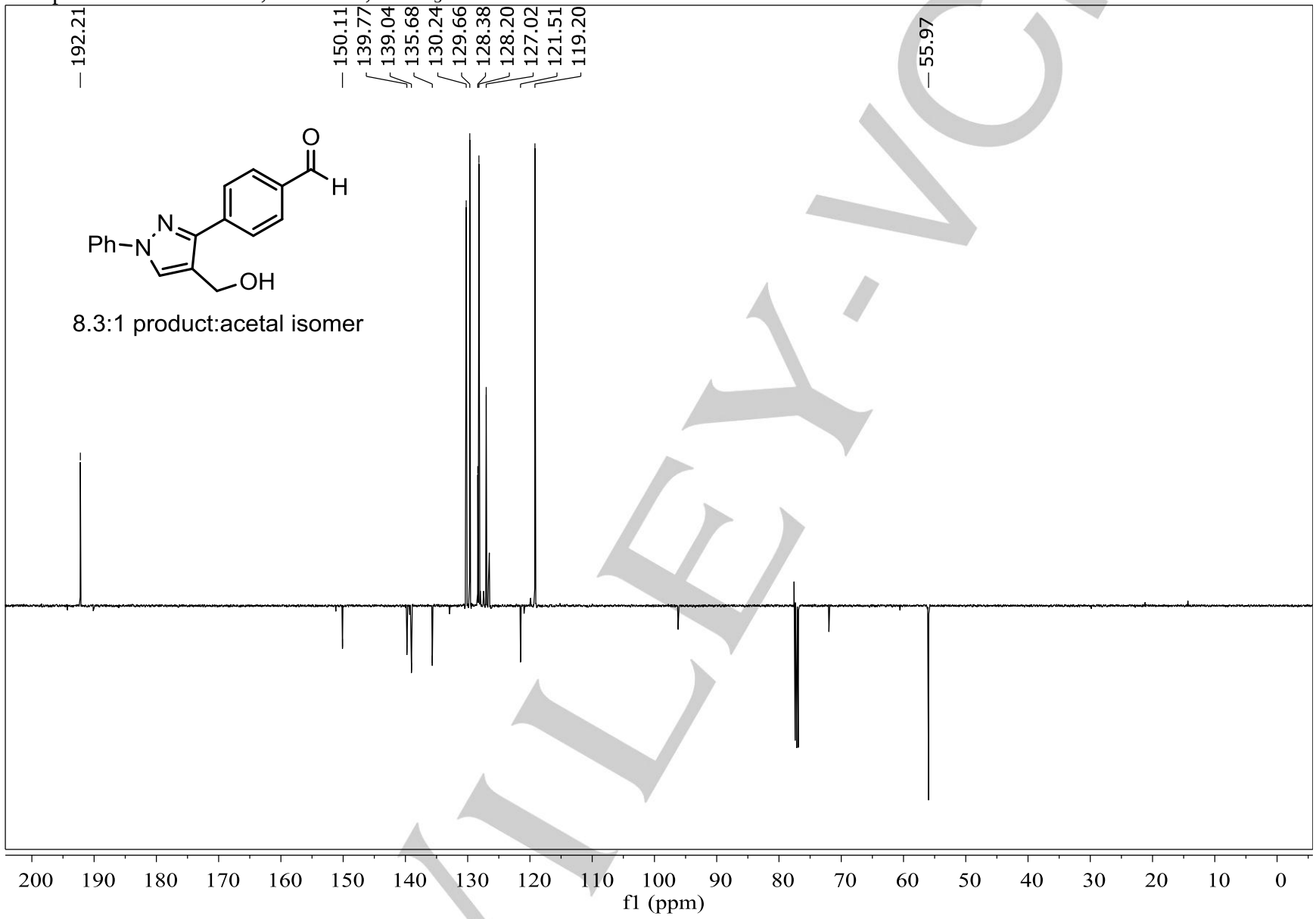
Compound **17** – ^{13}C NMR, 75 MHz, $CDCl_3$



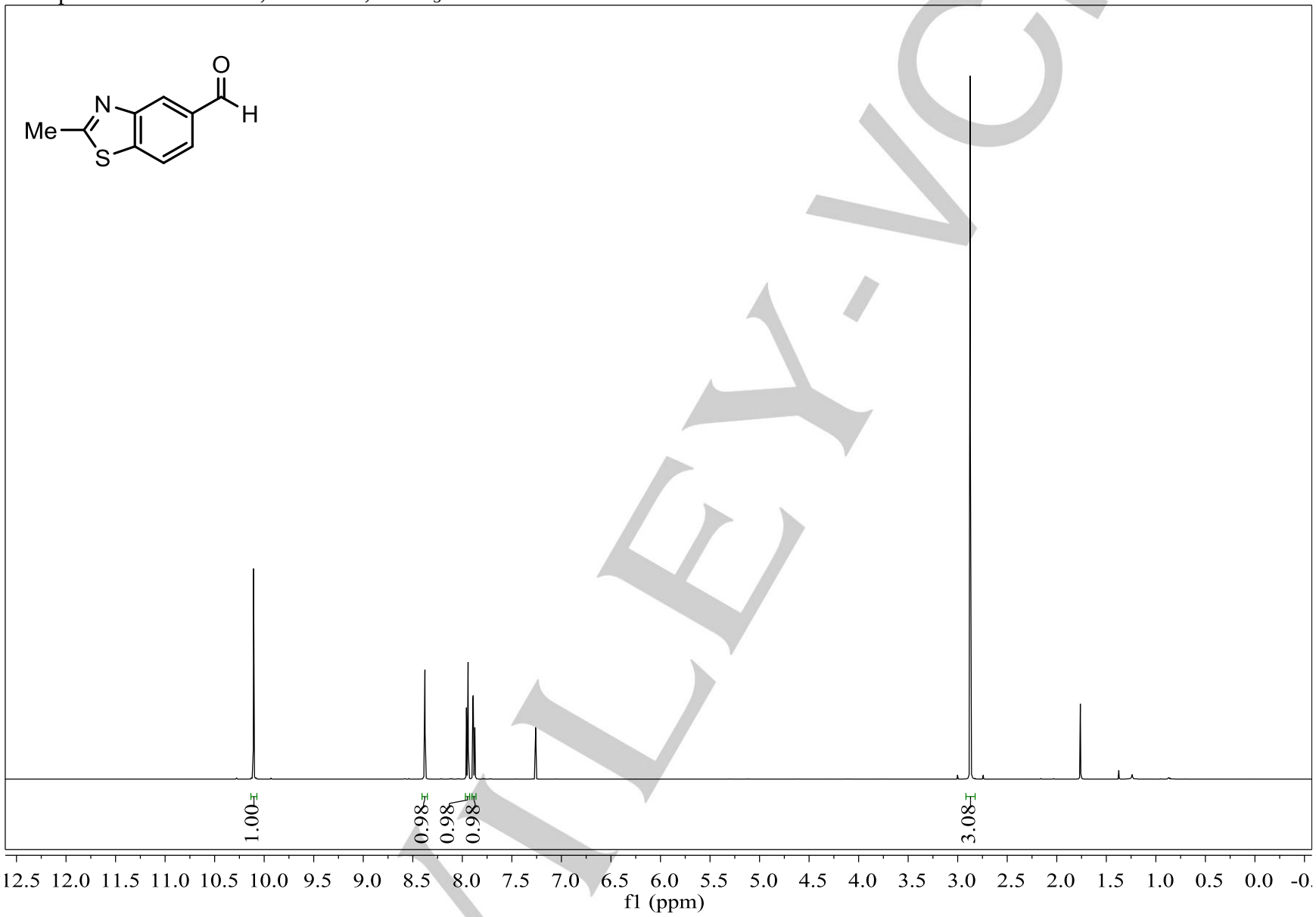
Compound **18** – ^{1}H NMR, 500 MHz, $CDCl_3$



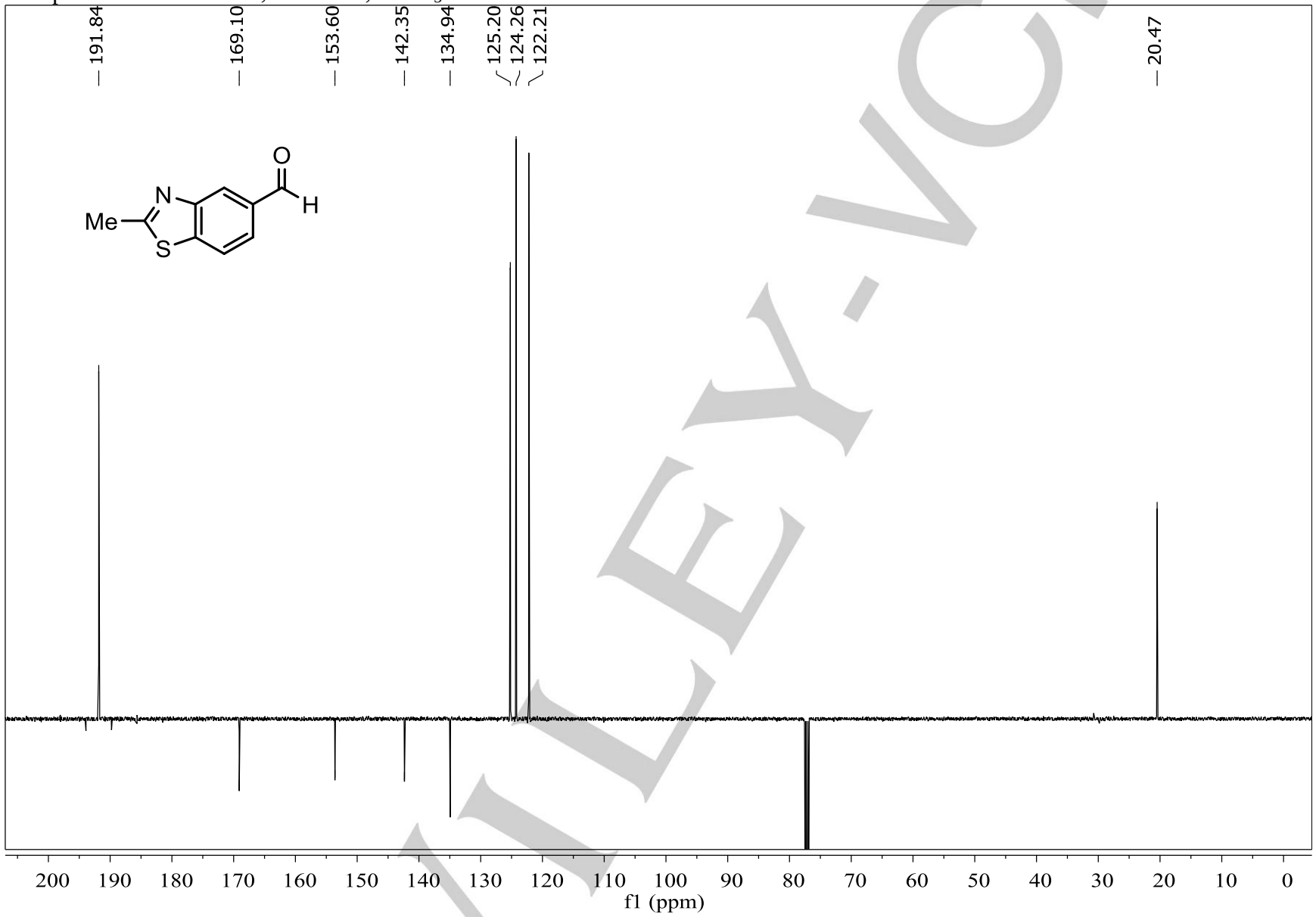
Compound **18** – ^{13}C NMR, 125 MHz, $CDCl_3$



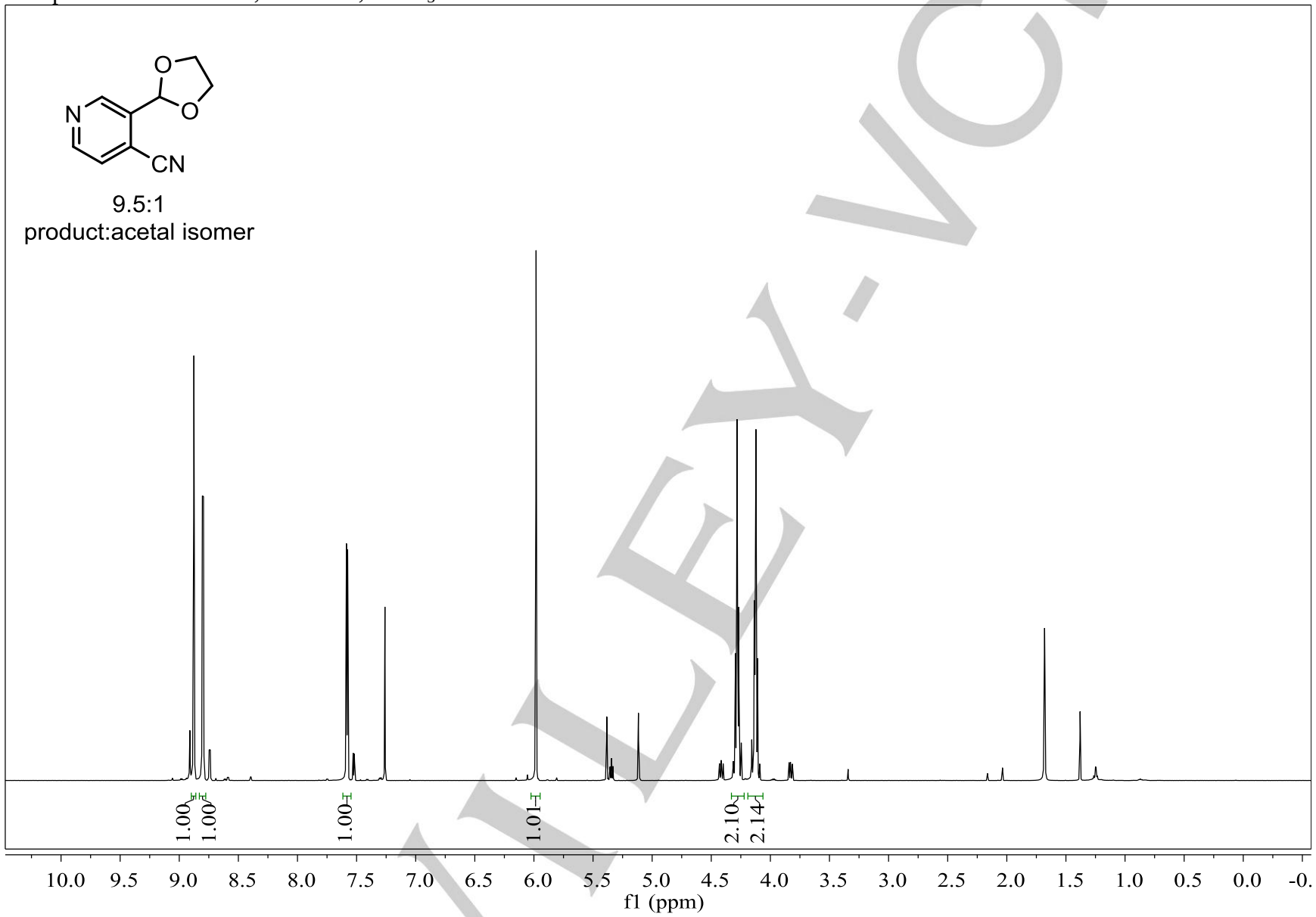
Compound **19** – ^{1}H NMR, 500 MHz, $CDCl_3$



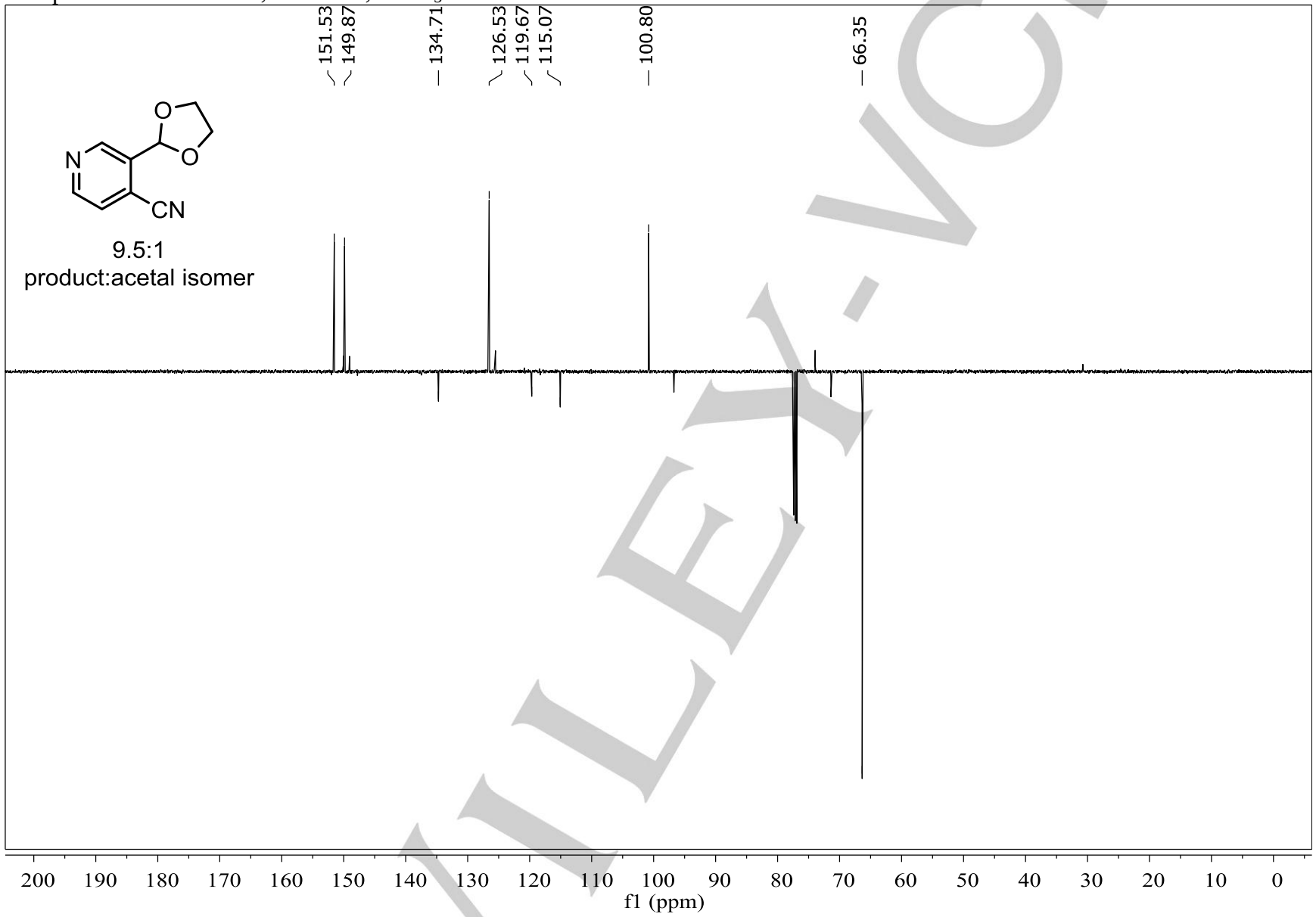
Compound **19** – ^{13}C NMR, 125 MHz, $CDCl_3$



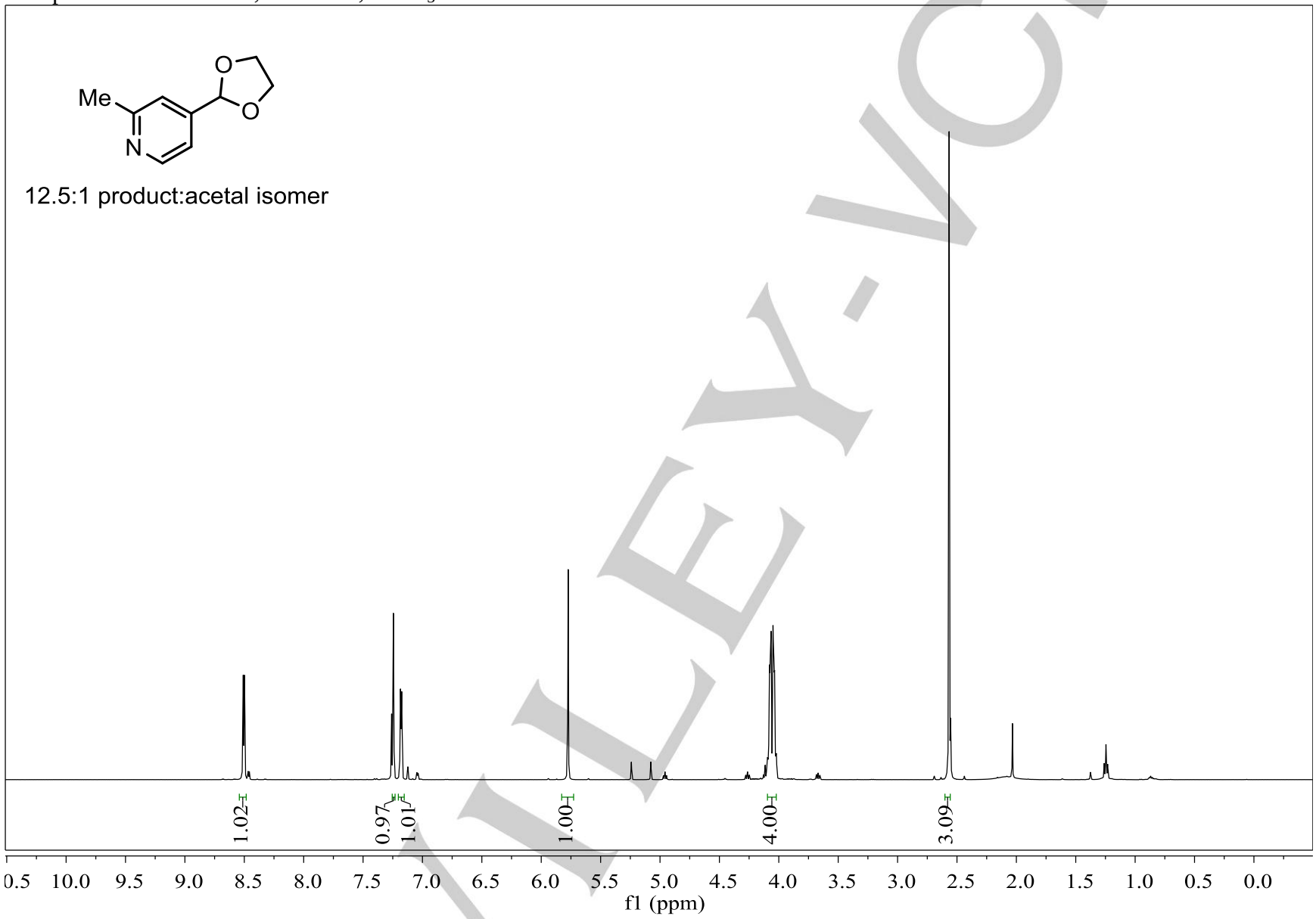
Compound **20** – ^{1}H NMR, 500 MHz, $CDCl_3$



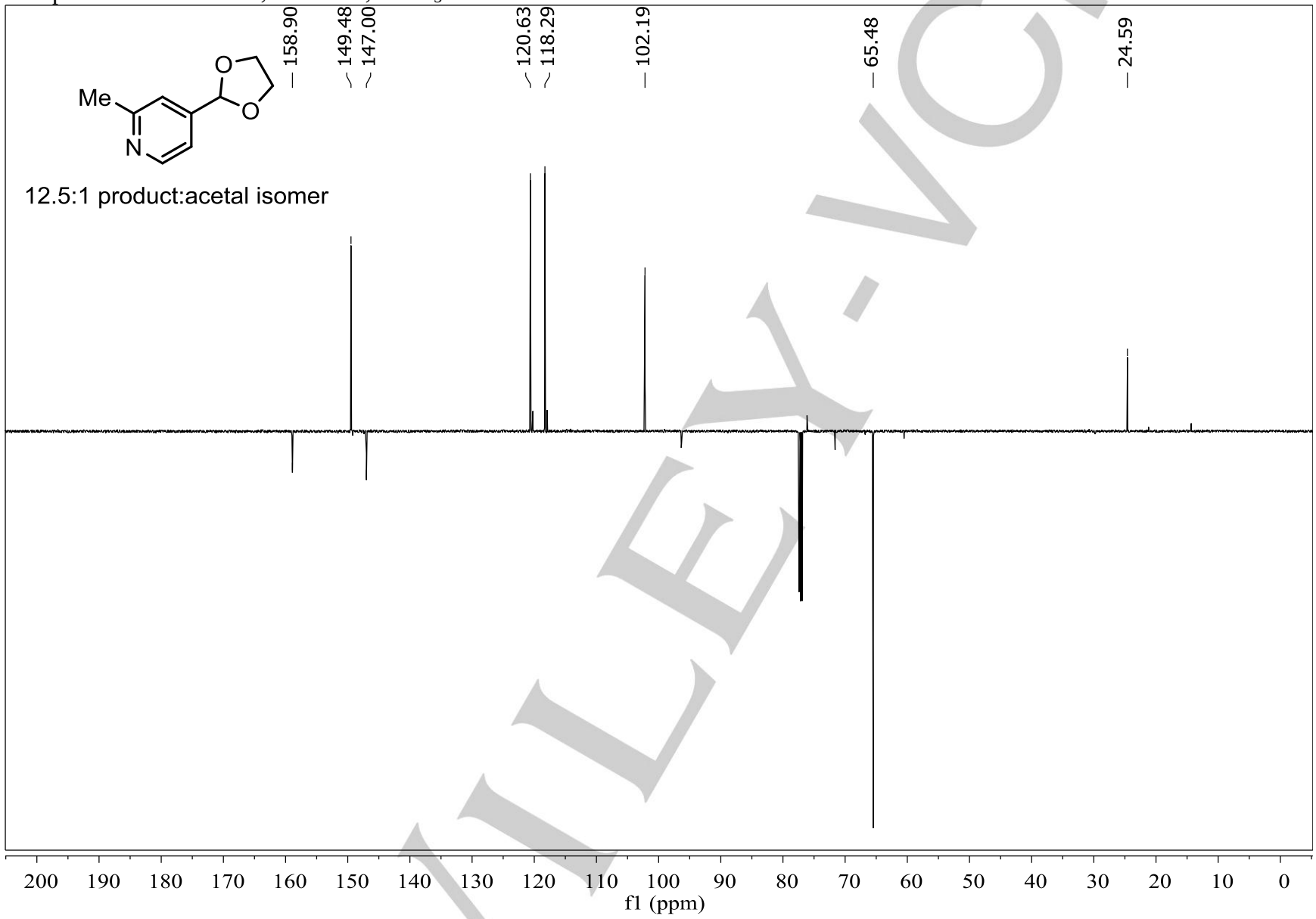
Compound **20** – ^{13}C NMR, 125 MHz, $CDCl_3$



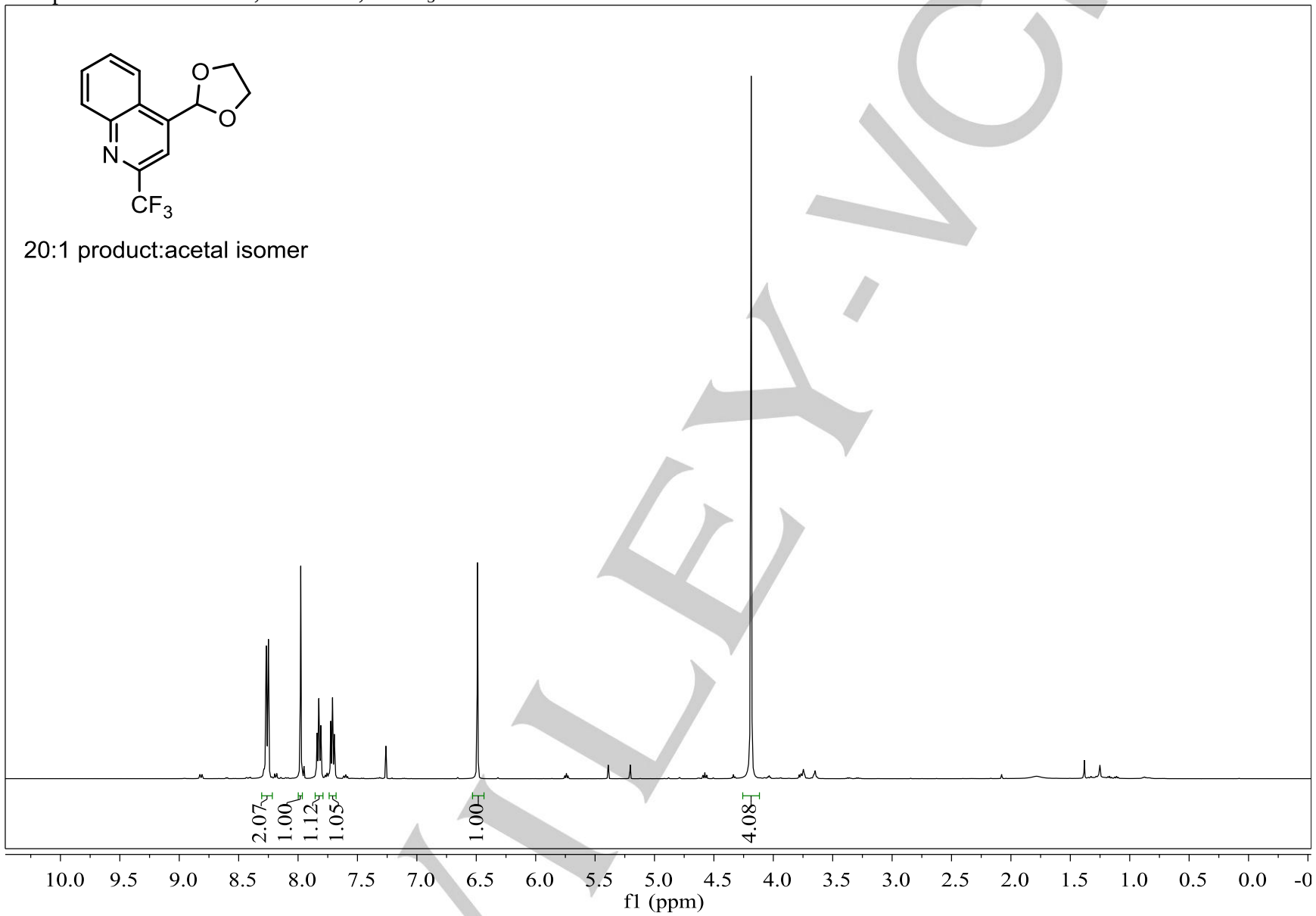
Compound **21** – ^{1}H NMR, 500 MHz, $CDCl_3$



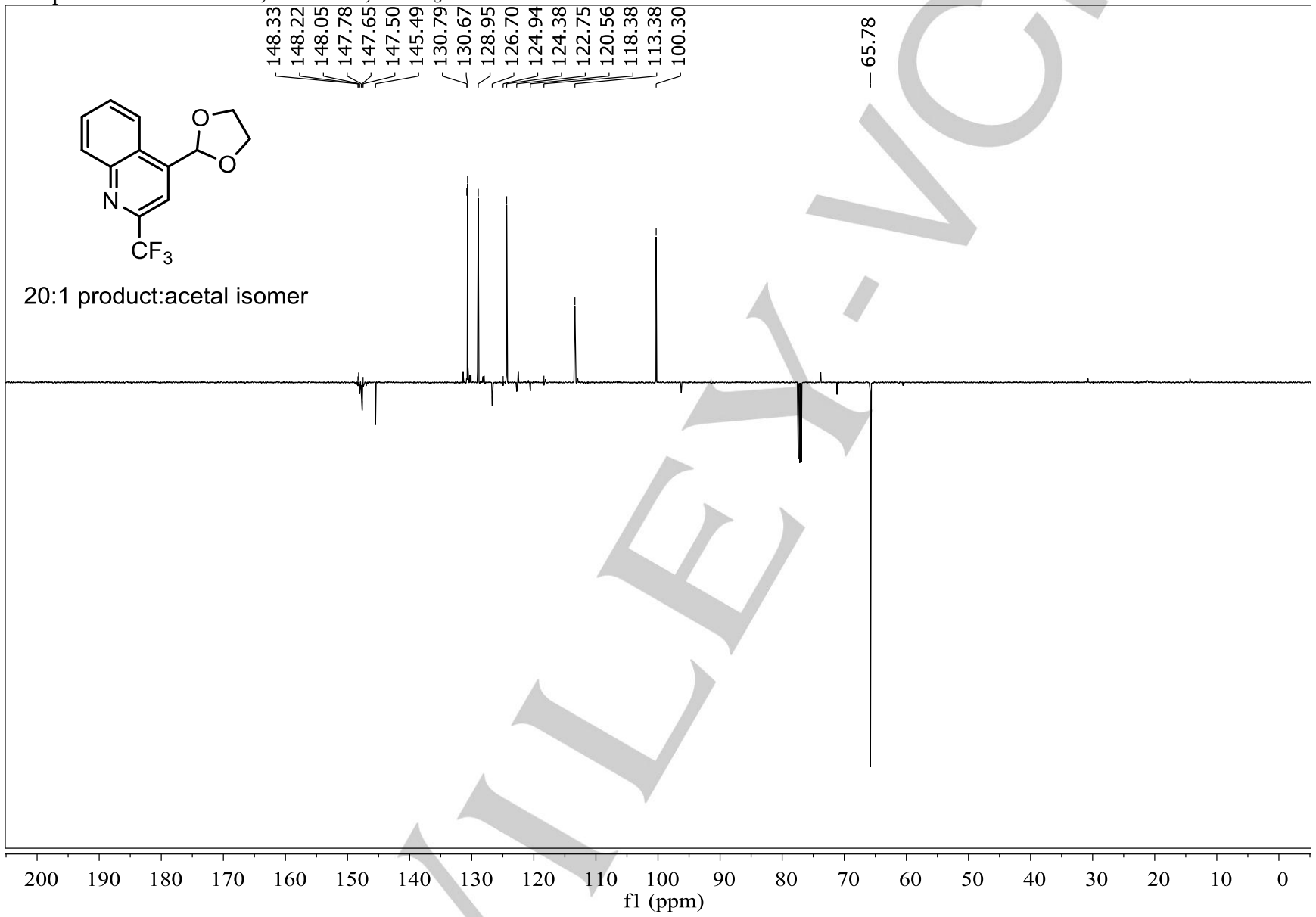
Compound **21** – ^{13}C NMR, 125 MHz, $CDCl_3$



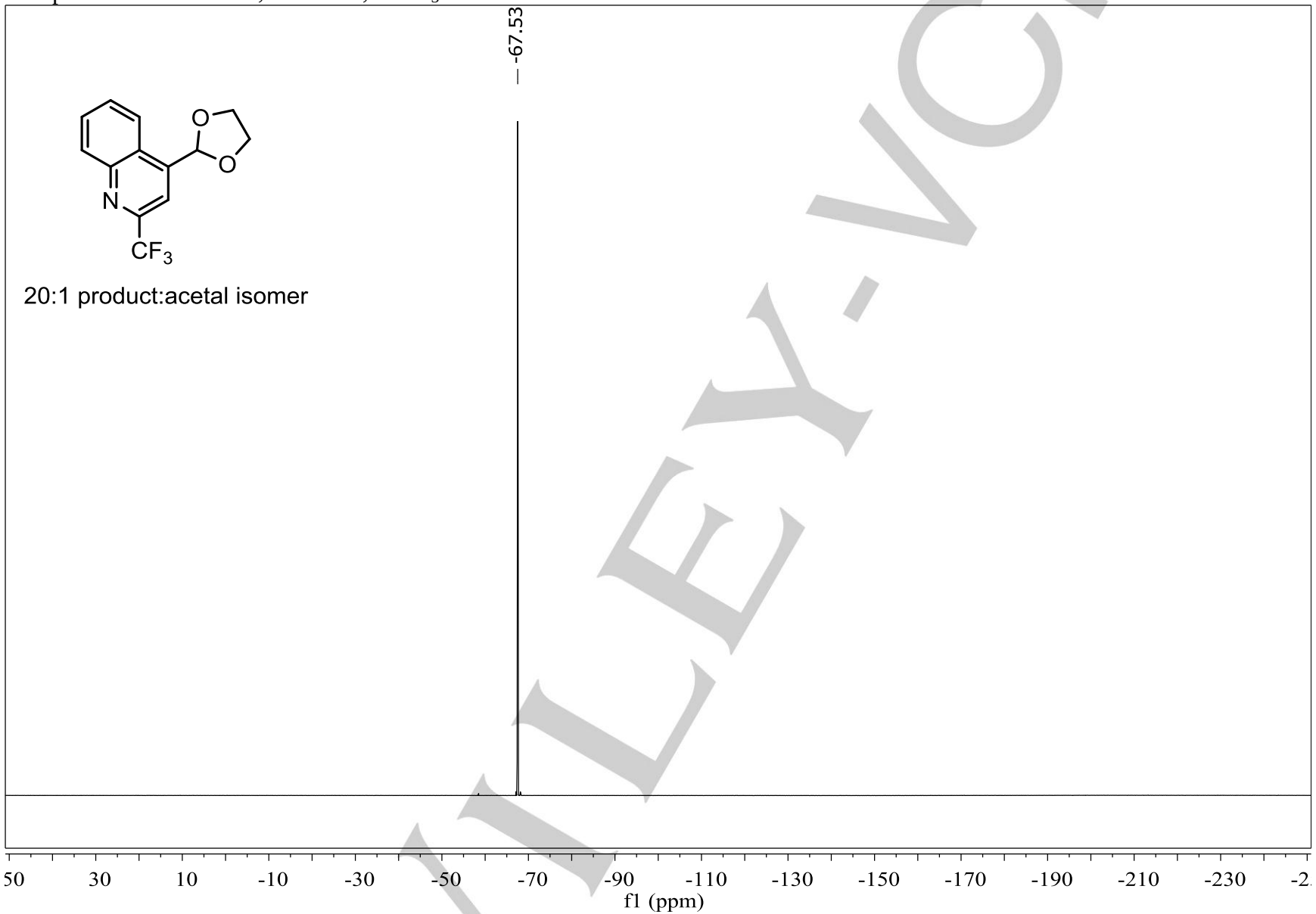
Compound **22** – ^{1}H NMR, 500 MHz, $CDCl_3$



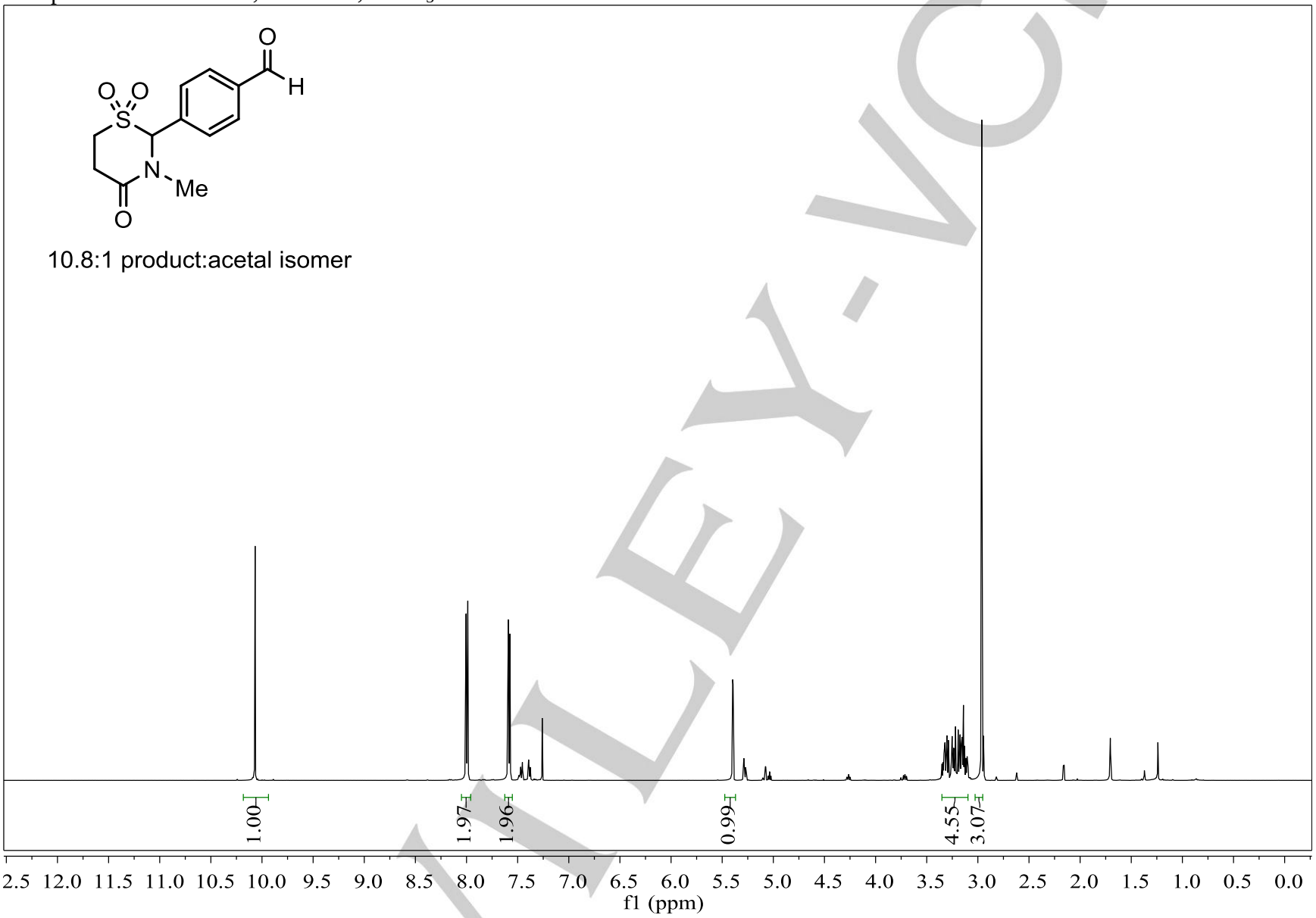
Compound **22** – ^{13}C NMR, 125 MHz, $CDCl_3$



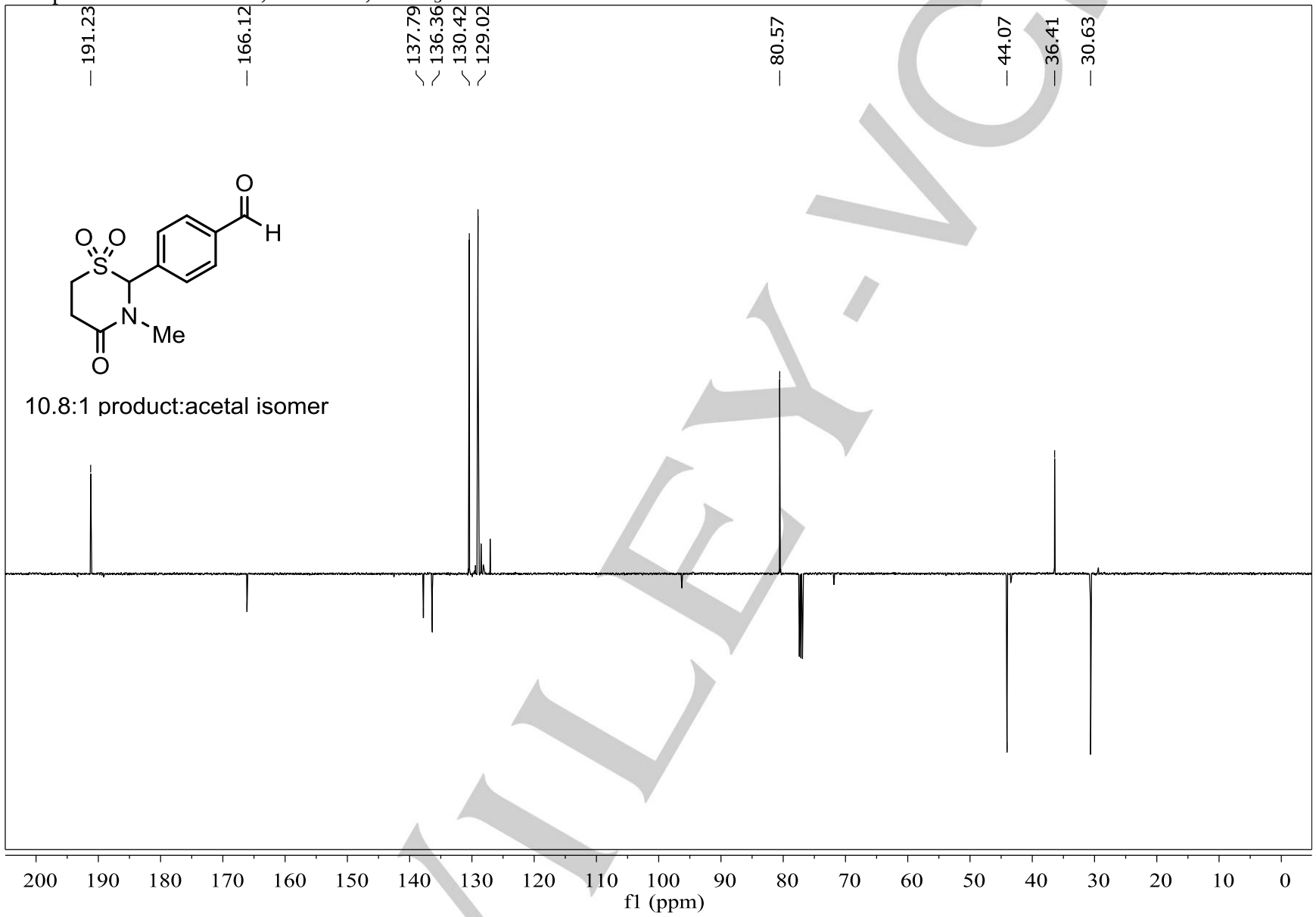
Compound **22** – ^{19}F NMR, 282 MHz, $CDCl_3$



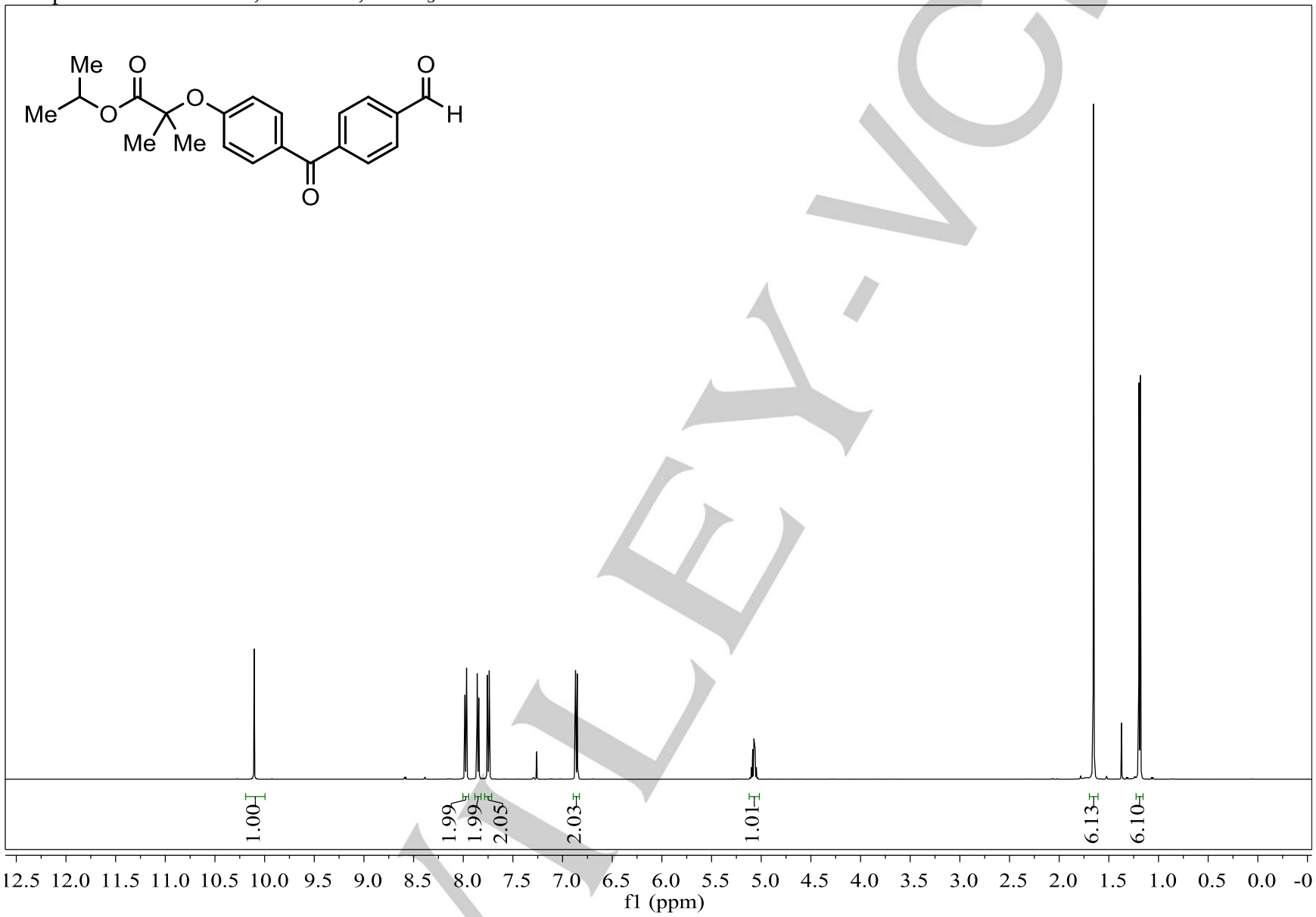
Compound **23** – ^{1}H NMR, 500 MHz, $CDCl_3$



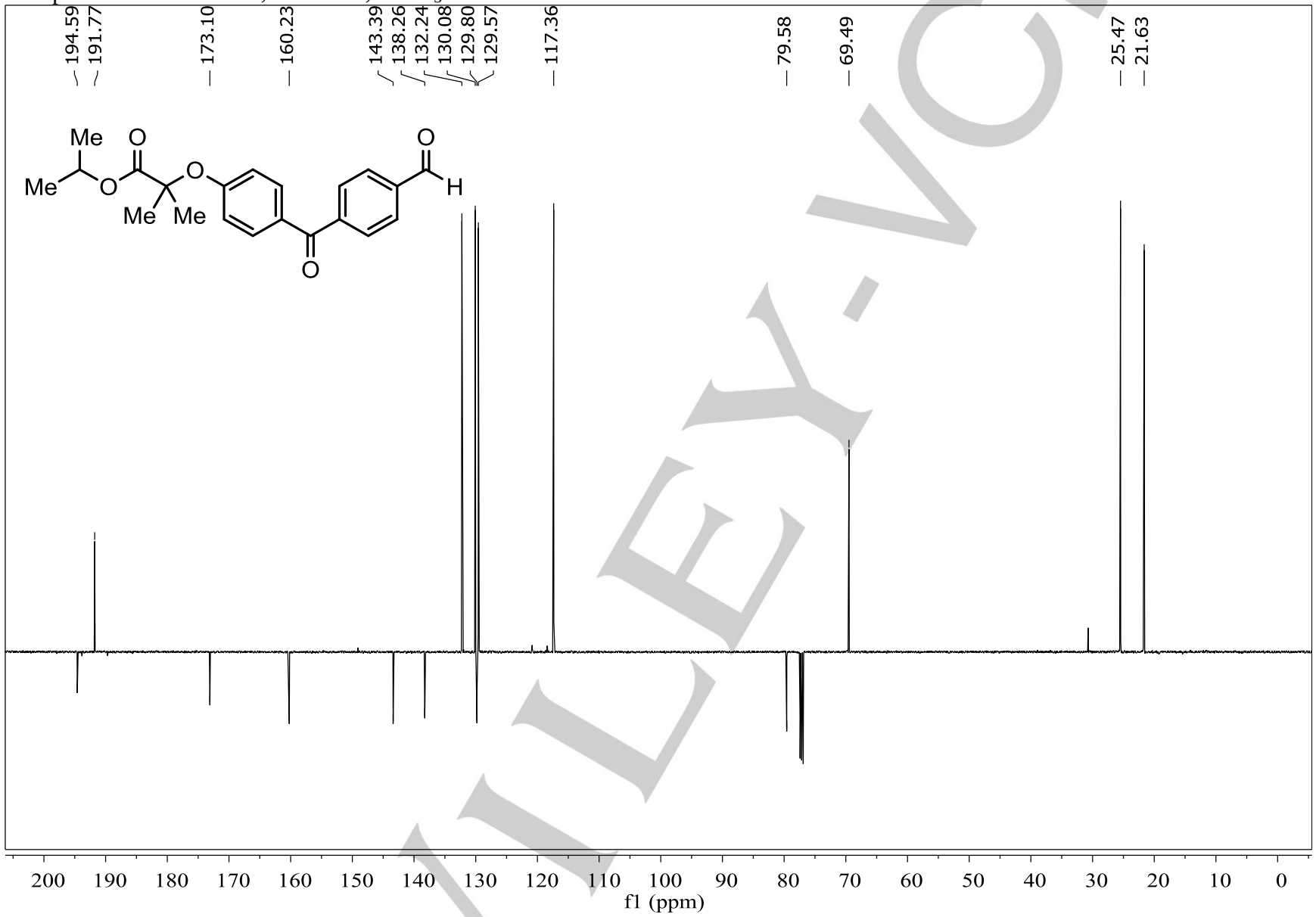
Compound **23** – ^{13}C NMR, 125 MHz, $CDCl_3$



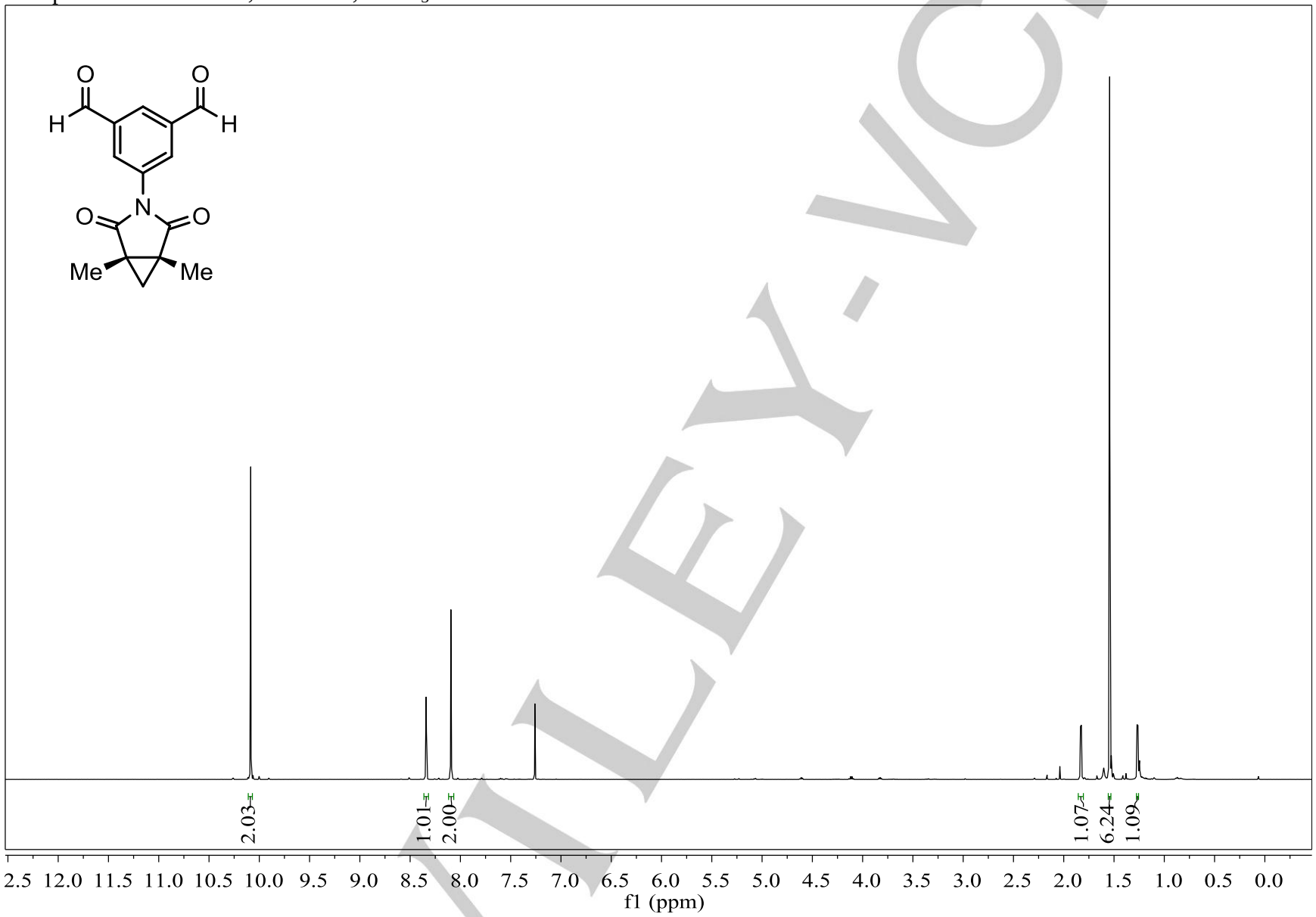
Compound **24** – ^{1}H NMR, 500 MHz, $CDCl_3$



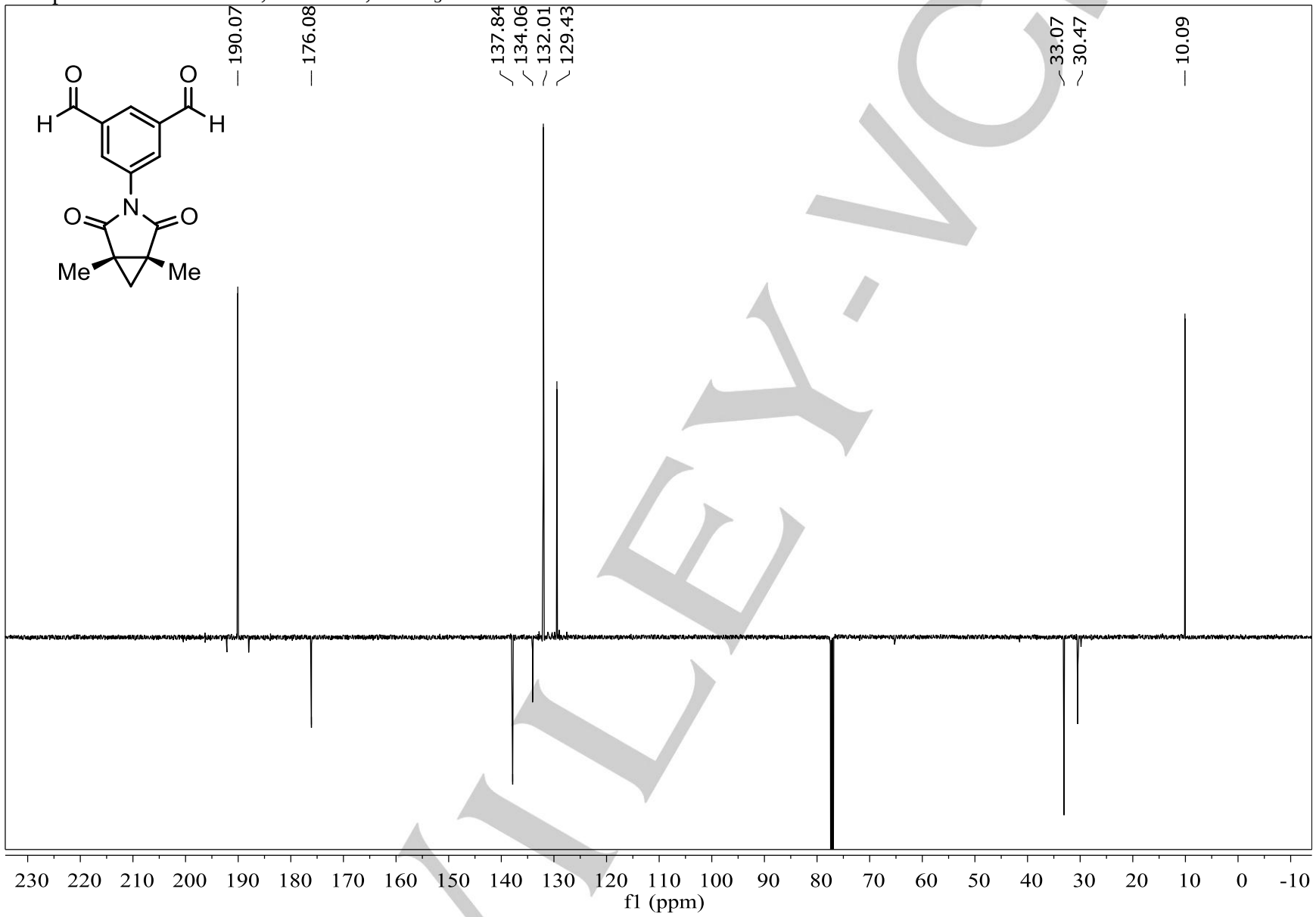
Compound **24** – ^{13}C NMR, 125 MHz, $CDCl_3$



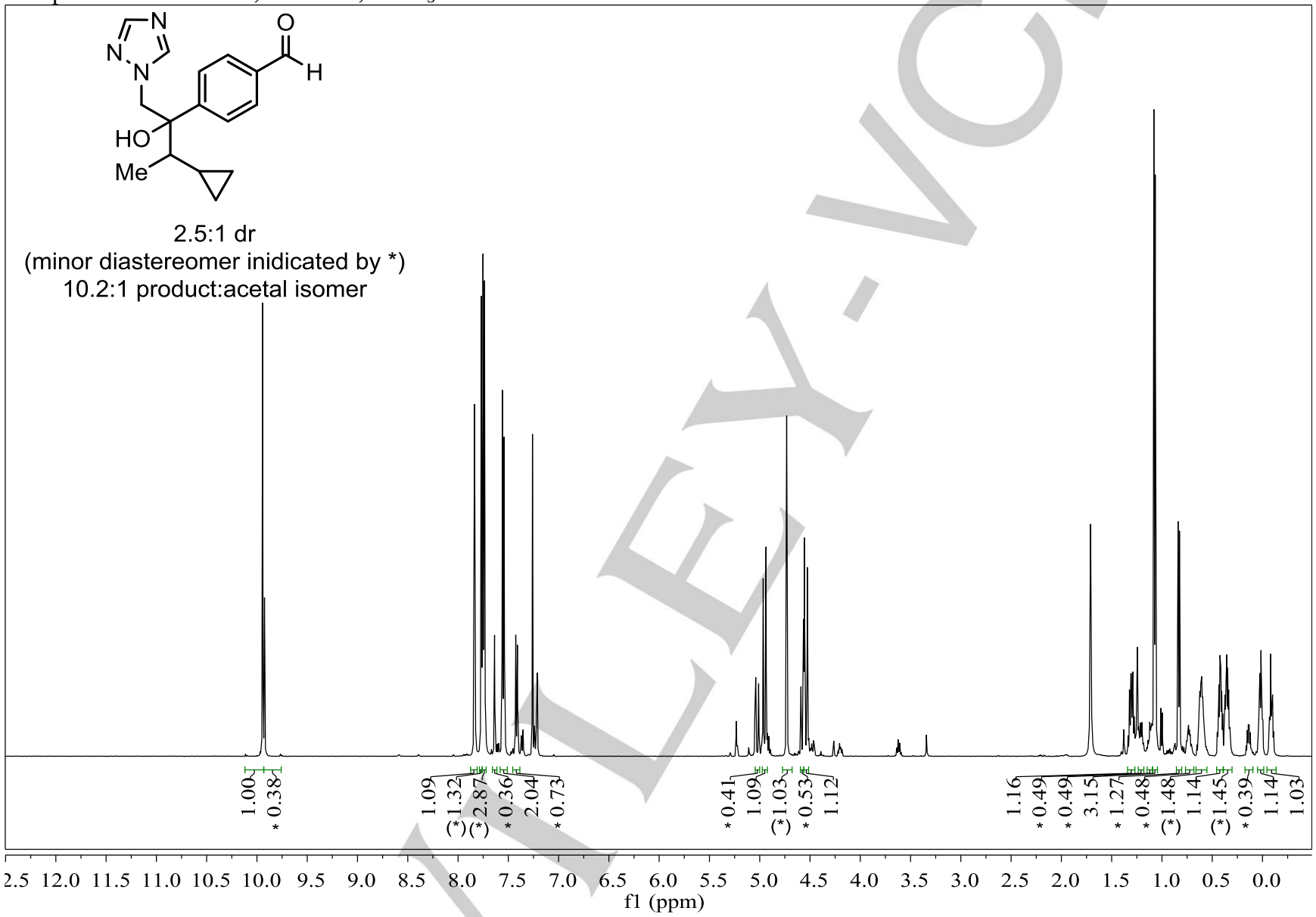
Compound **25** – ^{1}H NMR, 500 MHz, $CDCl_3$



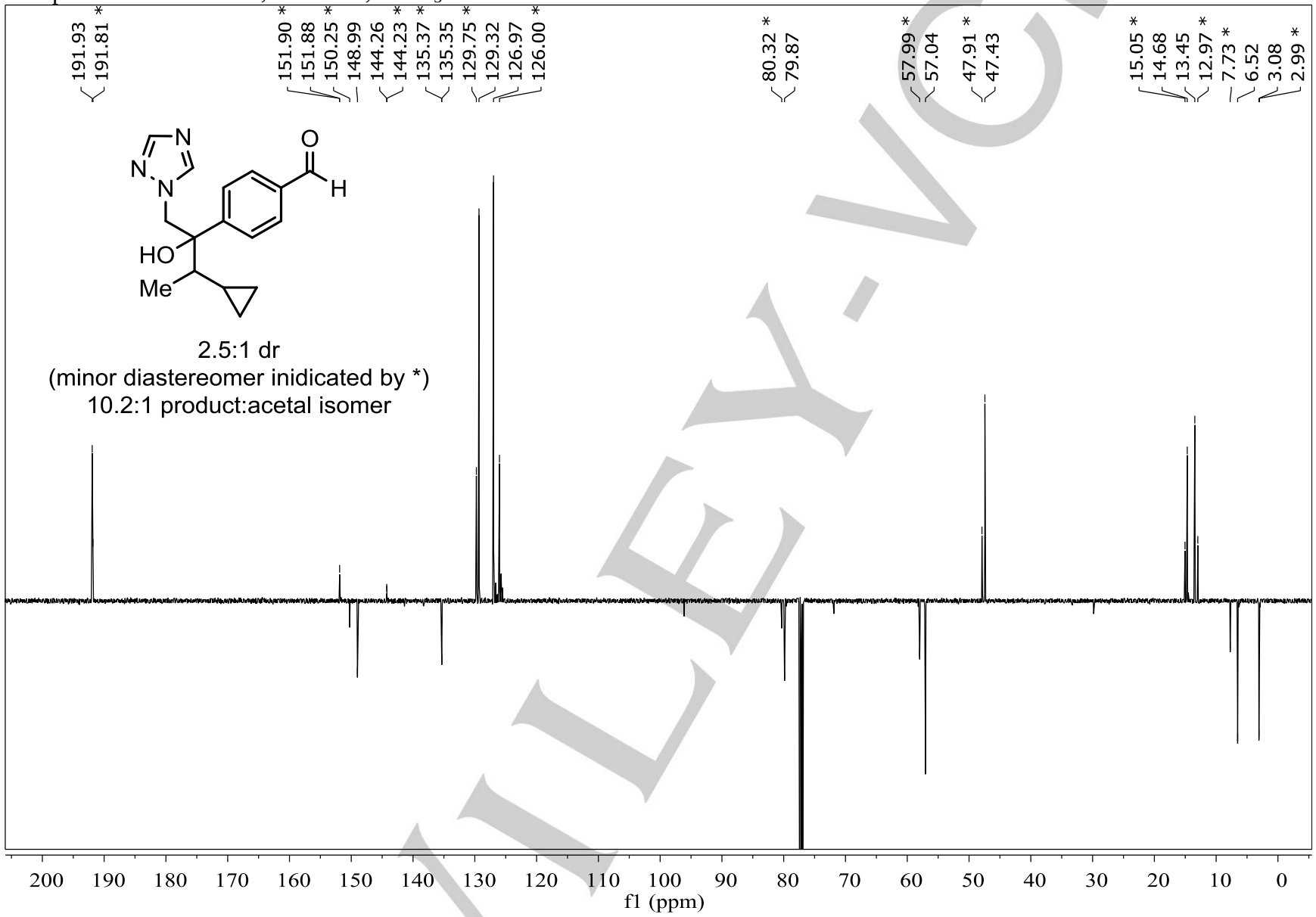
Compound **25** – ^{13}C NMR, 125 MHz, $CDCl_3$



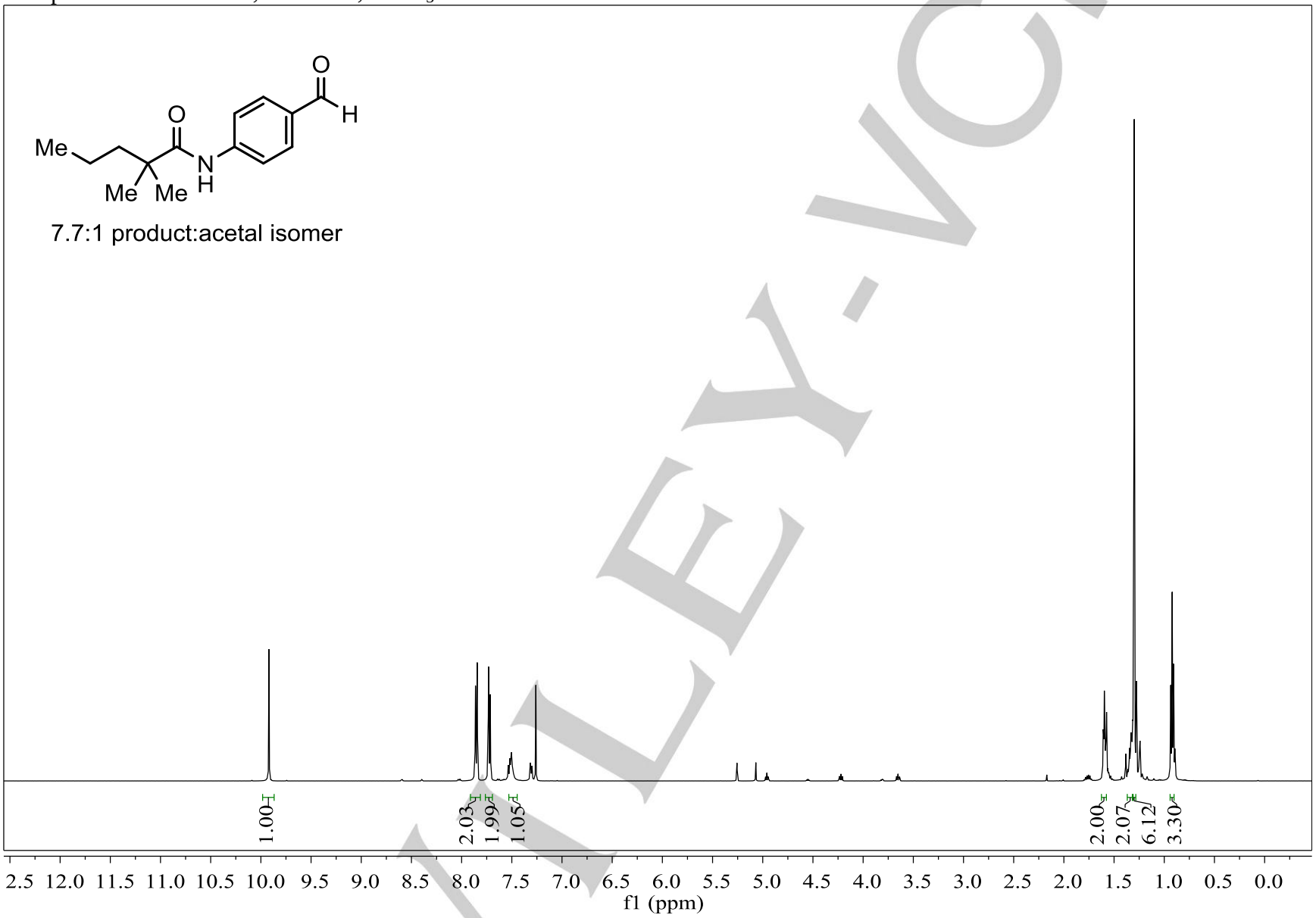
Compound **26** – ^{1}H NMR, 500 MHz, $CDCl_3$



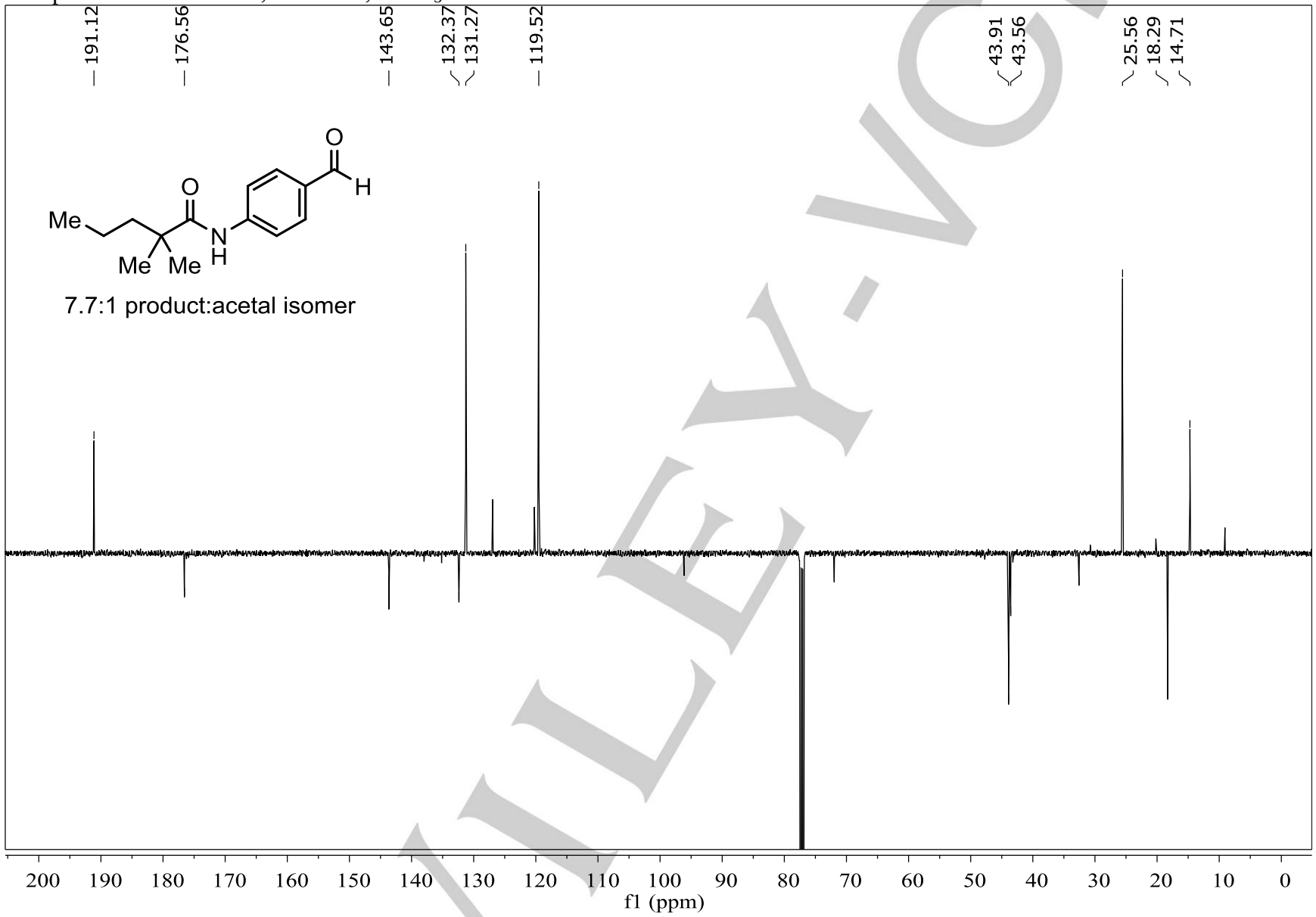
Compound **26** – ^{13}C NMR, 125 MHz, $CDCl_3$



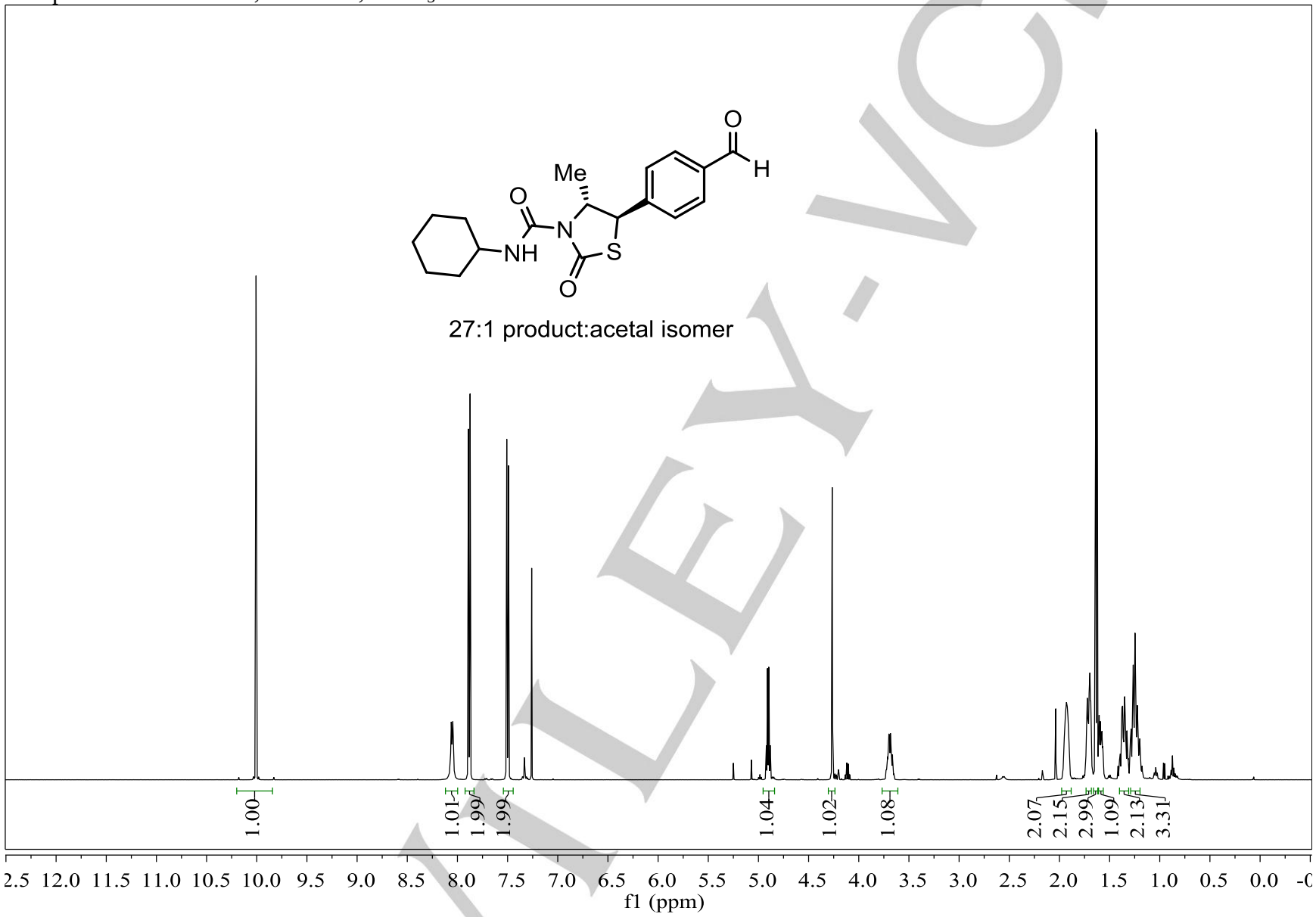
Compound **27** – ^{1}H NMR, 500 MHz, $CDCl_3$



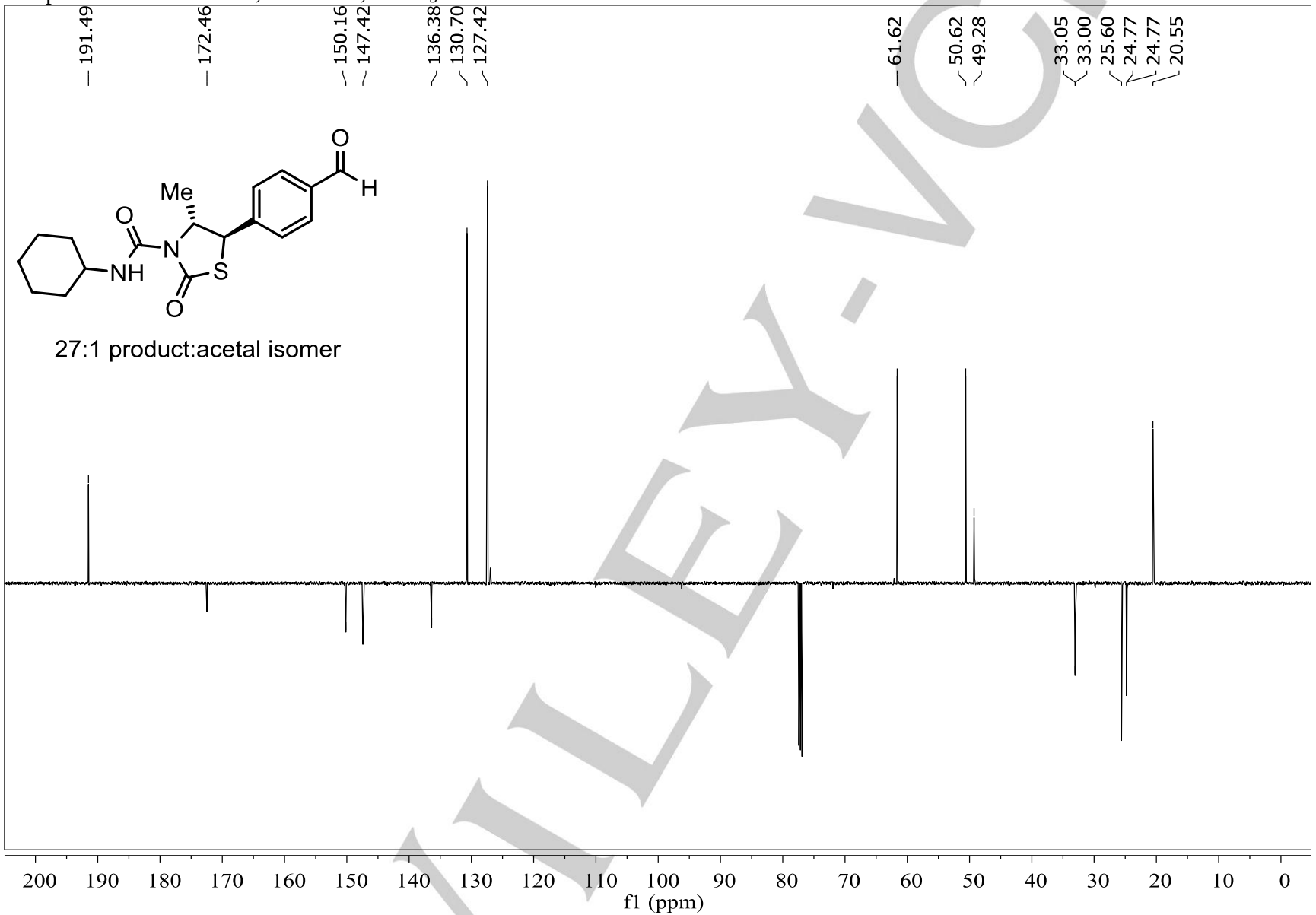
Compound **27** – ^{13}C NMR, 125 MHz, $CDCl_3$



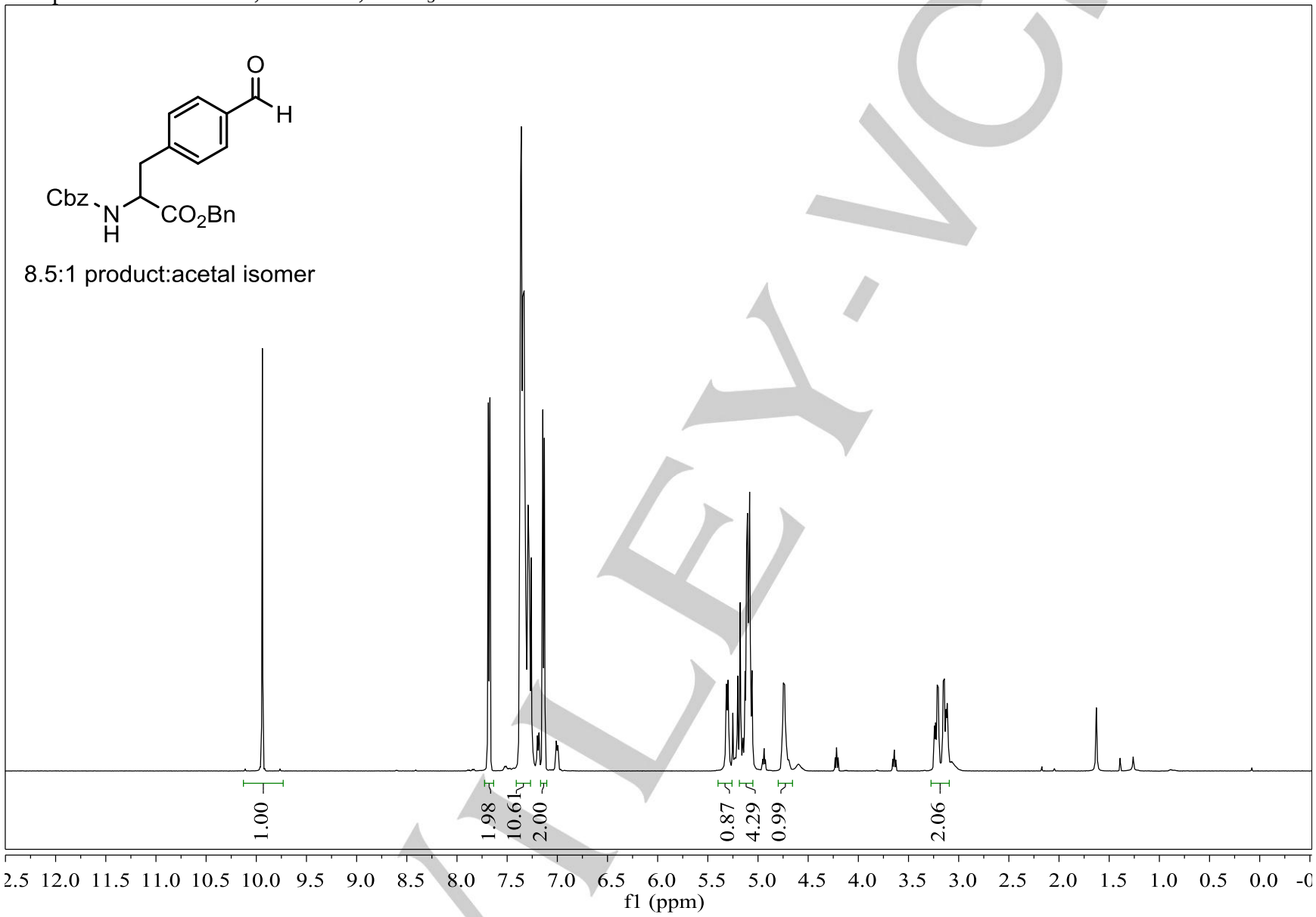
Compound **28** – ^{1}H NMR, 500 MHz, $CDCl_3$



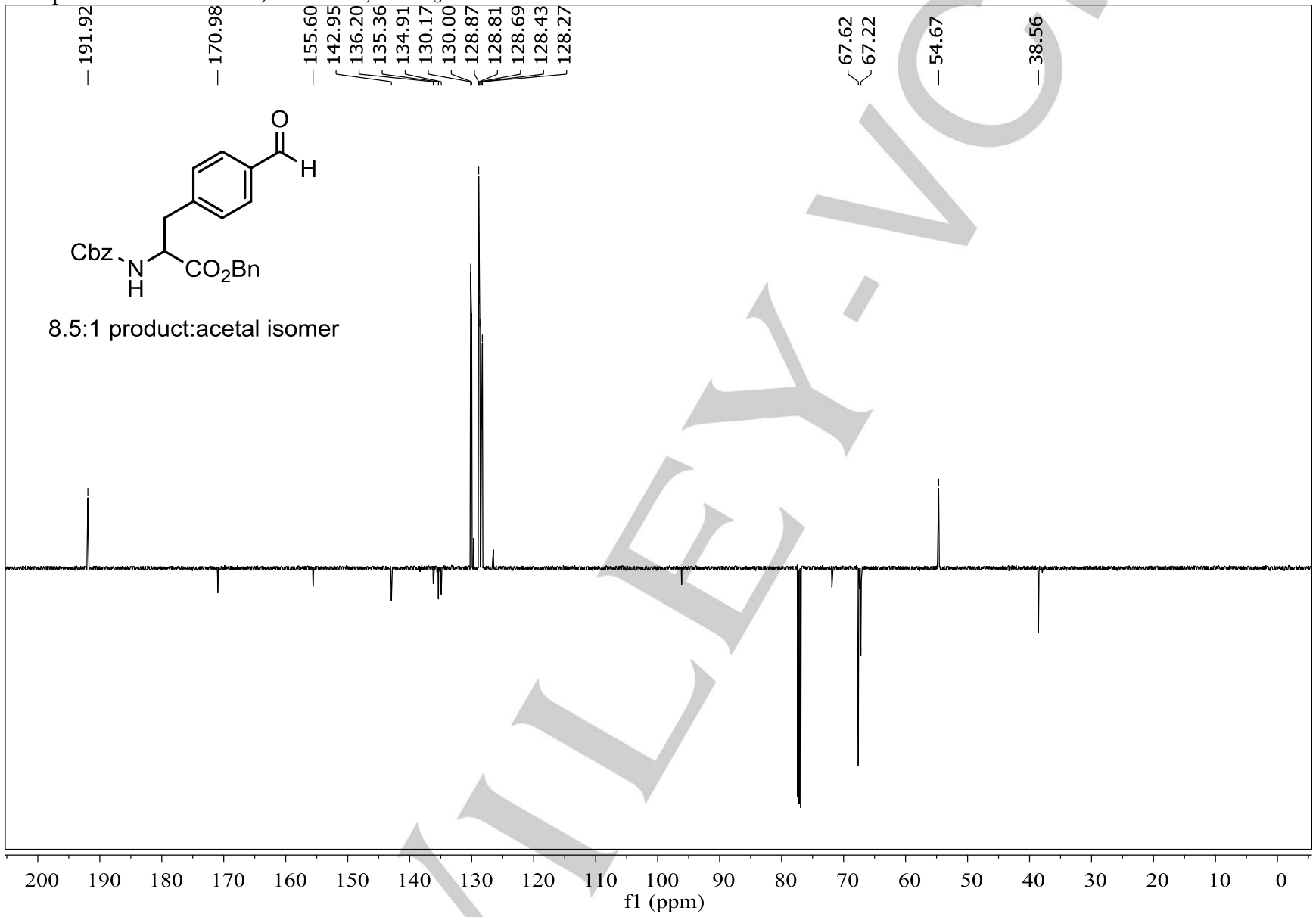
Compound **28** – ^{13}C NMR, 125 MHz, $CDCl_3$



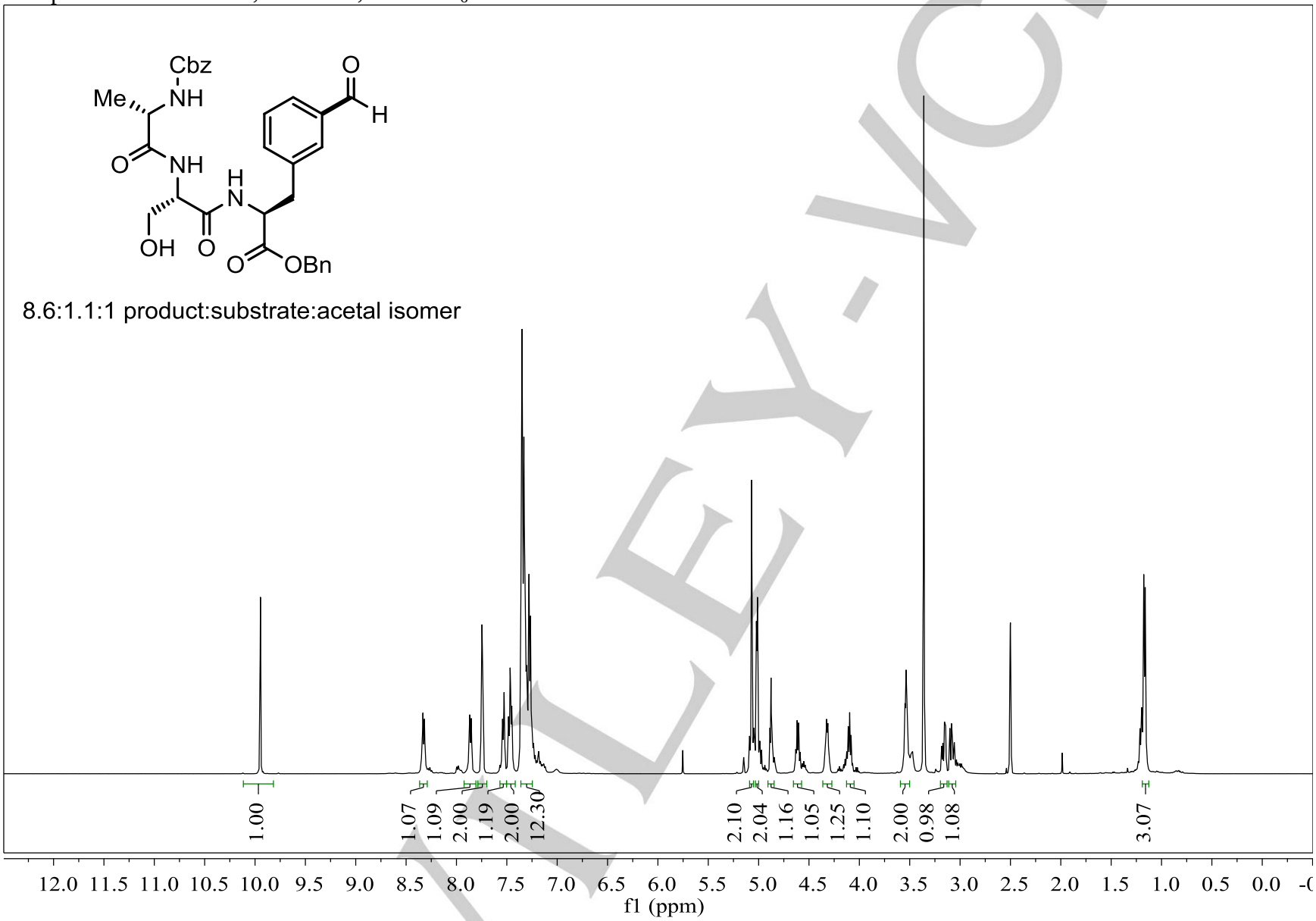
Compound **29** – ^{1}H NMR, 500 MHz, $CDCl_3$



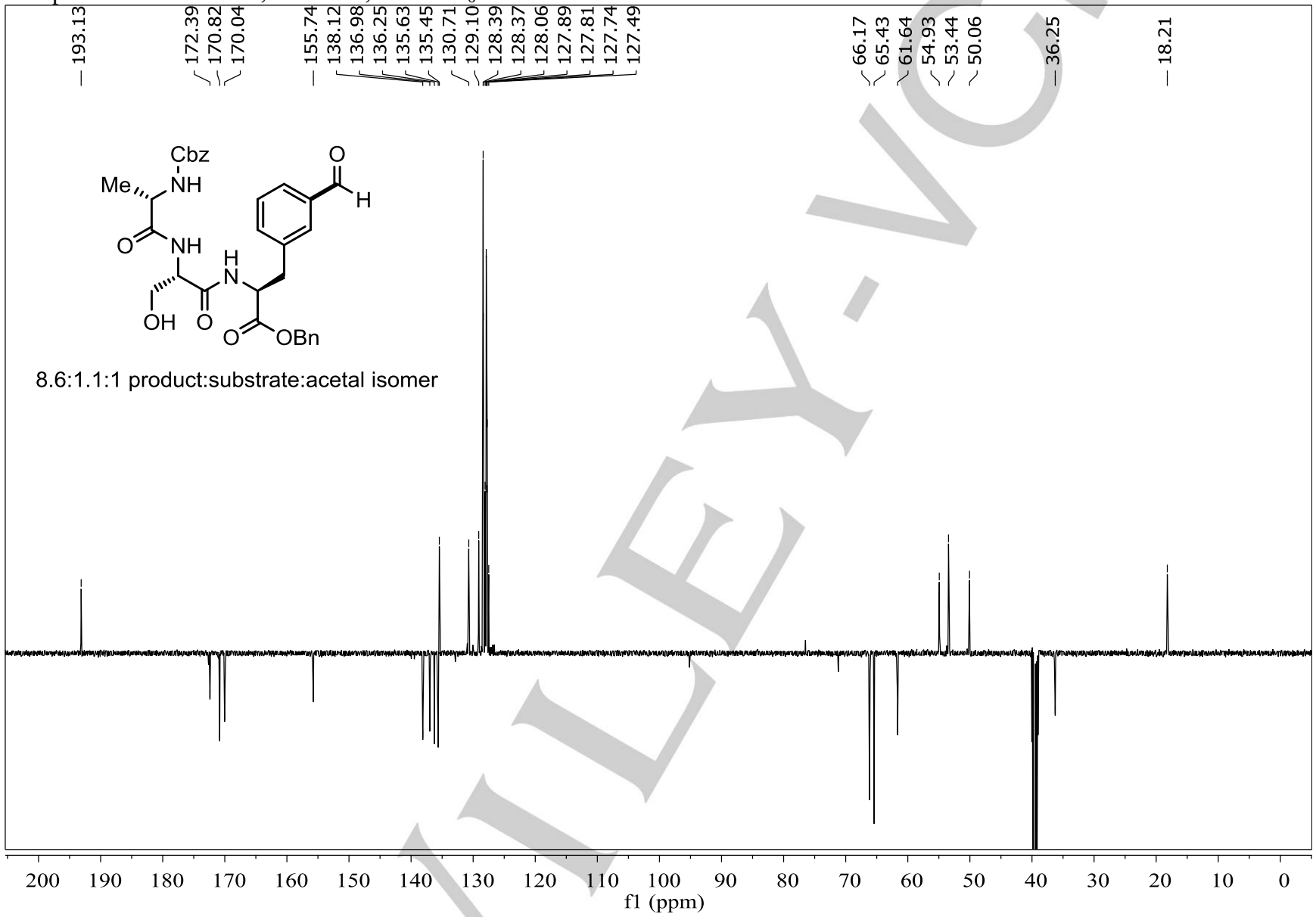
Compound **29** – ^{13}C NMR, 125 MHz, $CDCl_3$



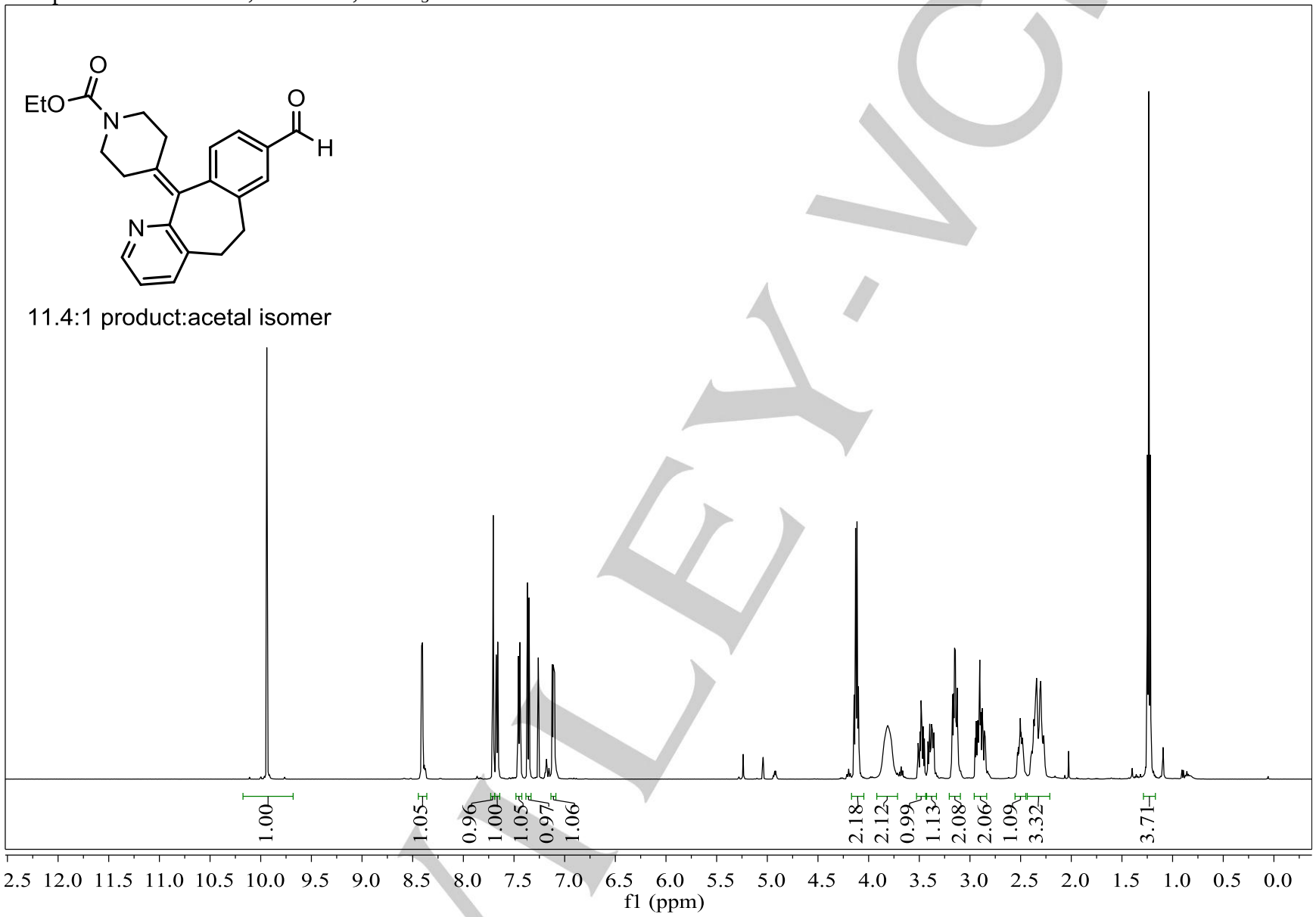
Compound **30** – ^{1}H NMR, 500 MHz, DMSO-d_6



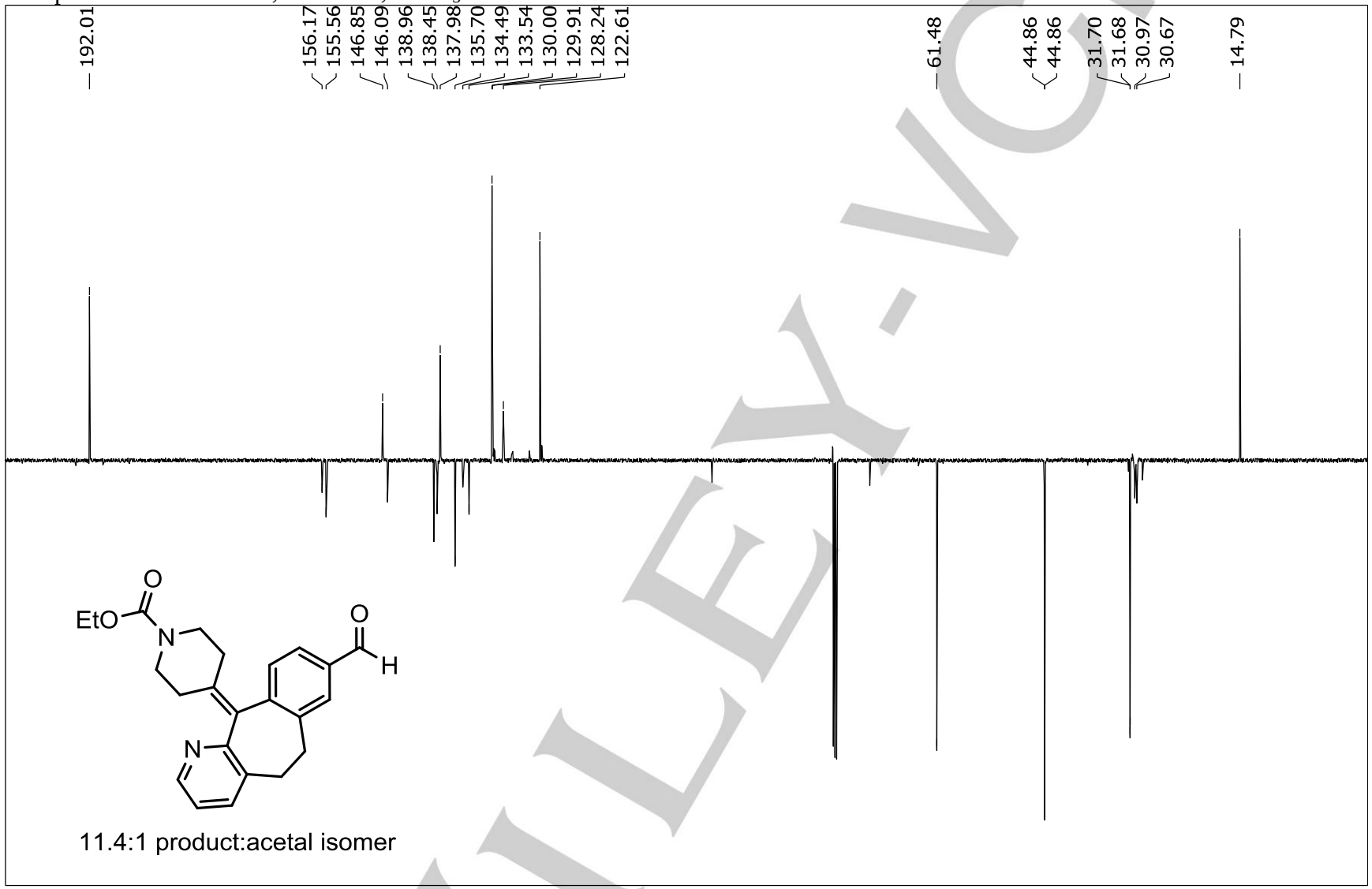
Compound **30** – ^{13}C NMR, 125 MHz, DMSO-d_6



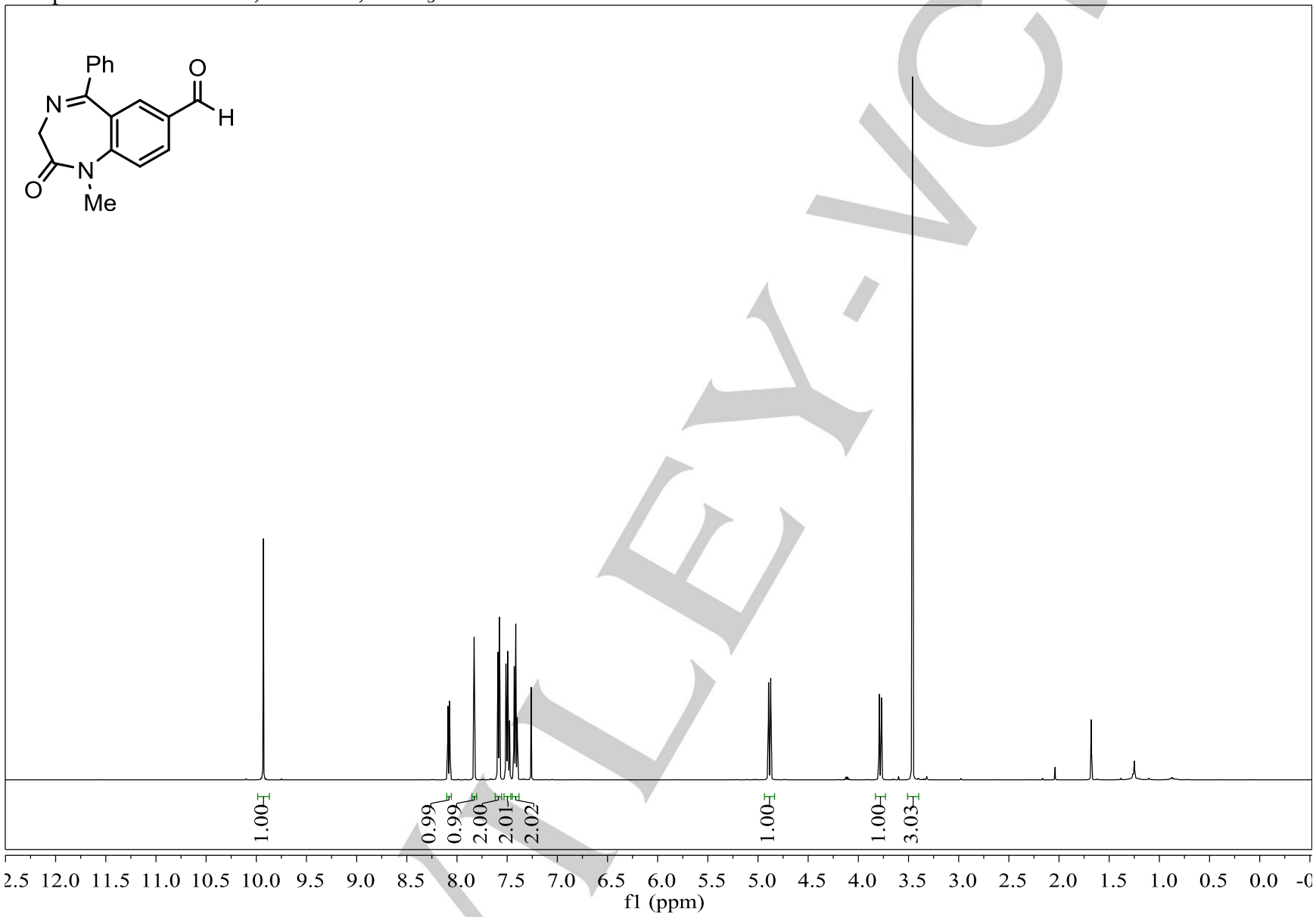
Compound **31** – ^{1}H NMR, 500 MHz, $CDCl_3$



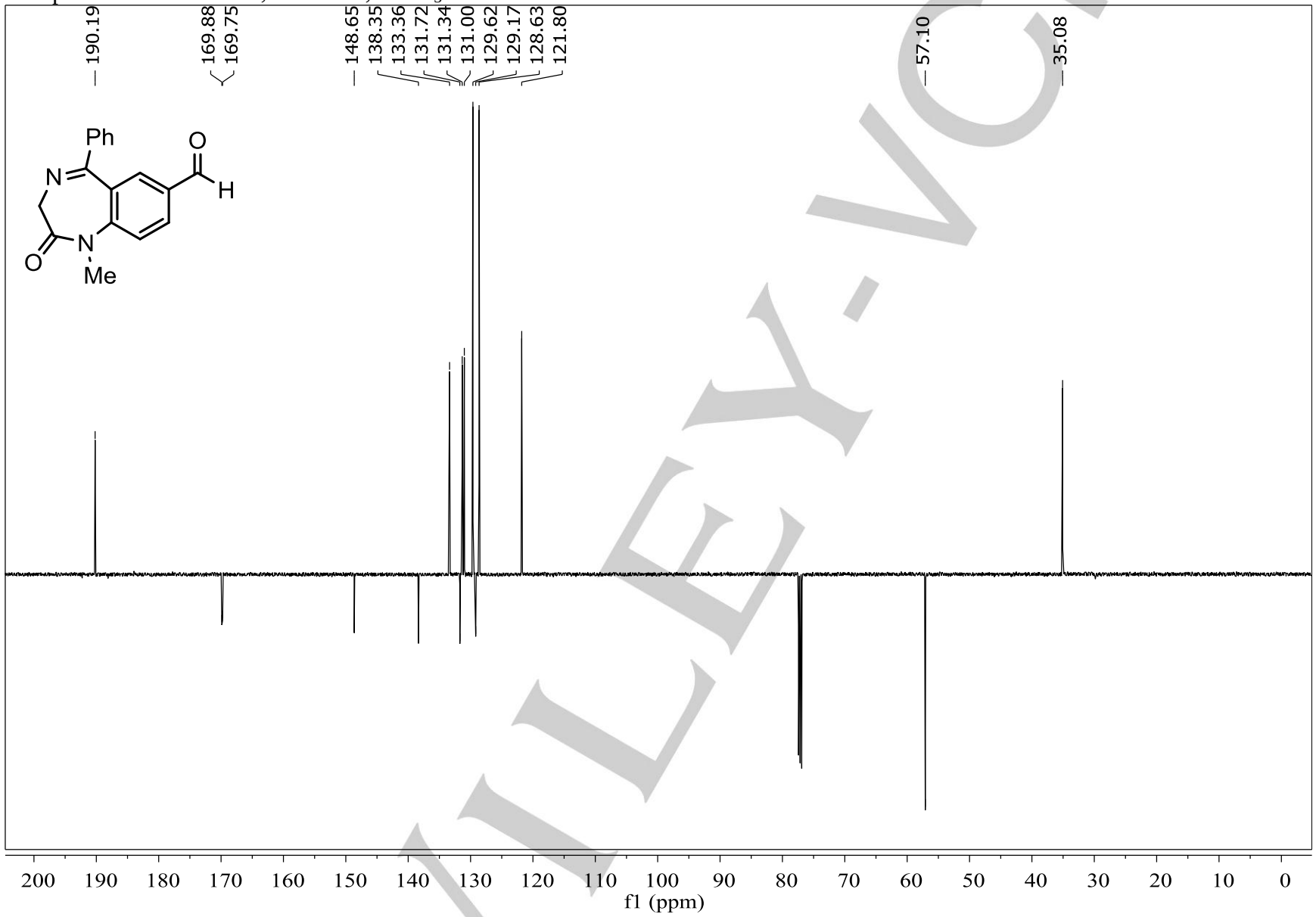
Compound **31** – ^{13}C NMR, 125 MHz, $CDCl_3$



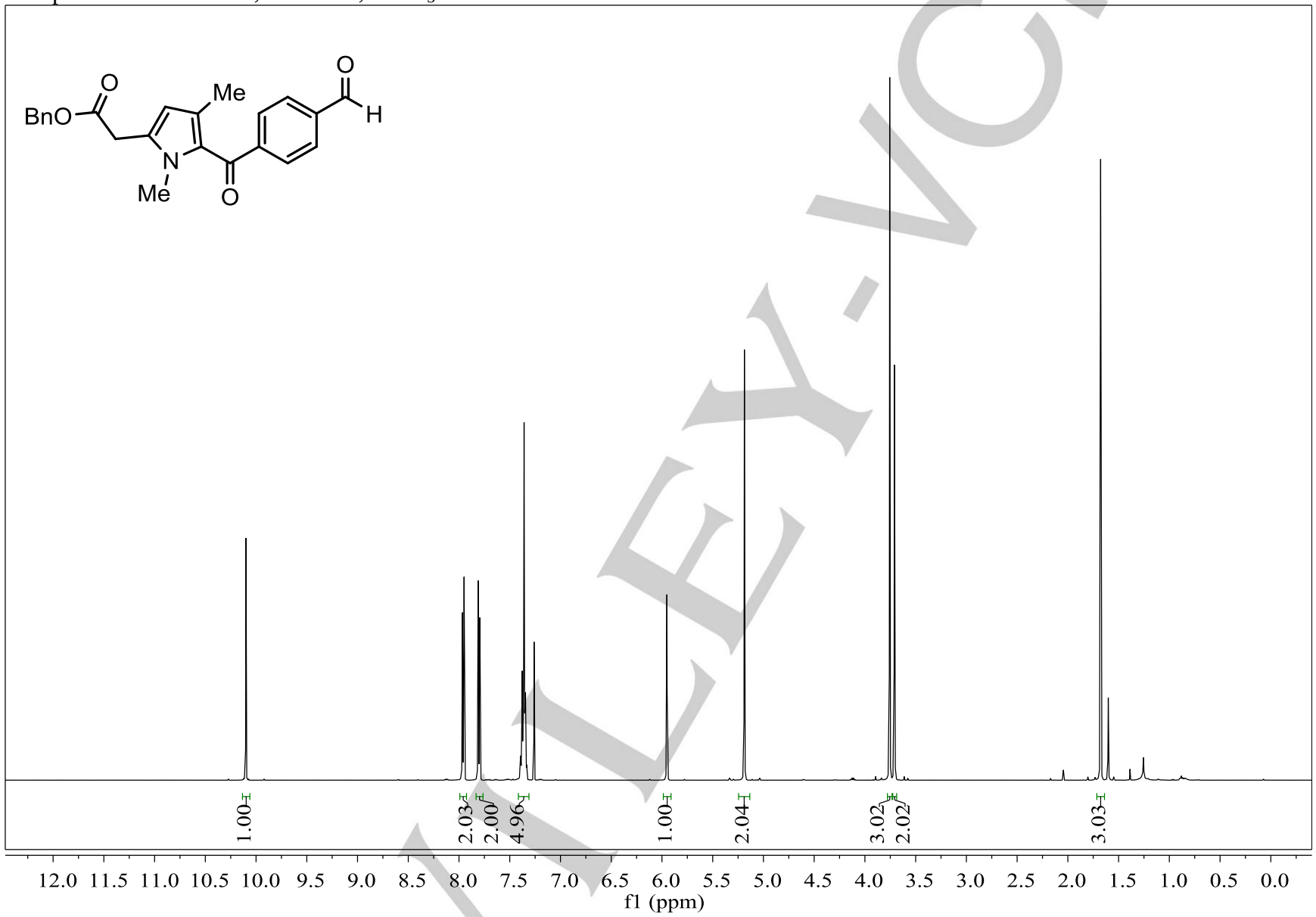
Compound **32** – ^{1}H NMR, 500 MHz, $CDCl_3$



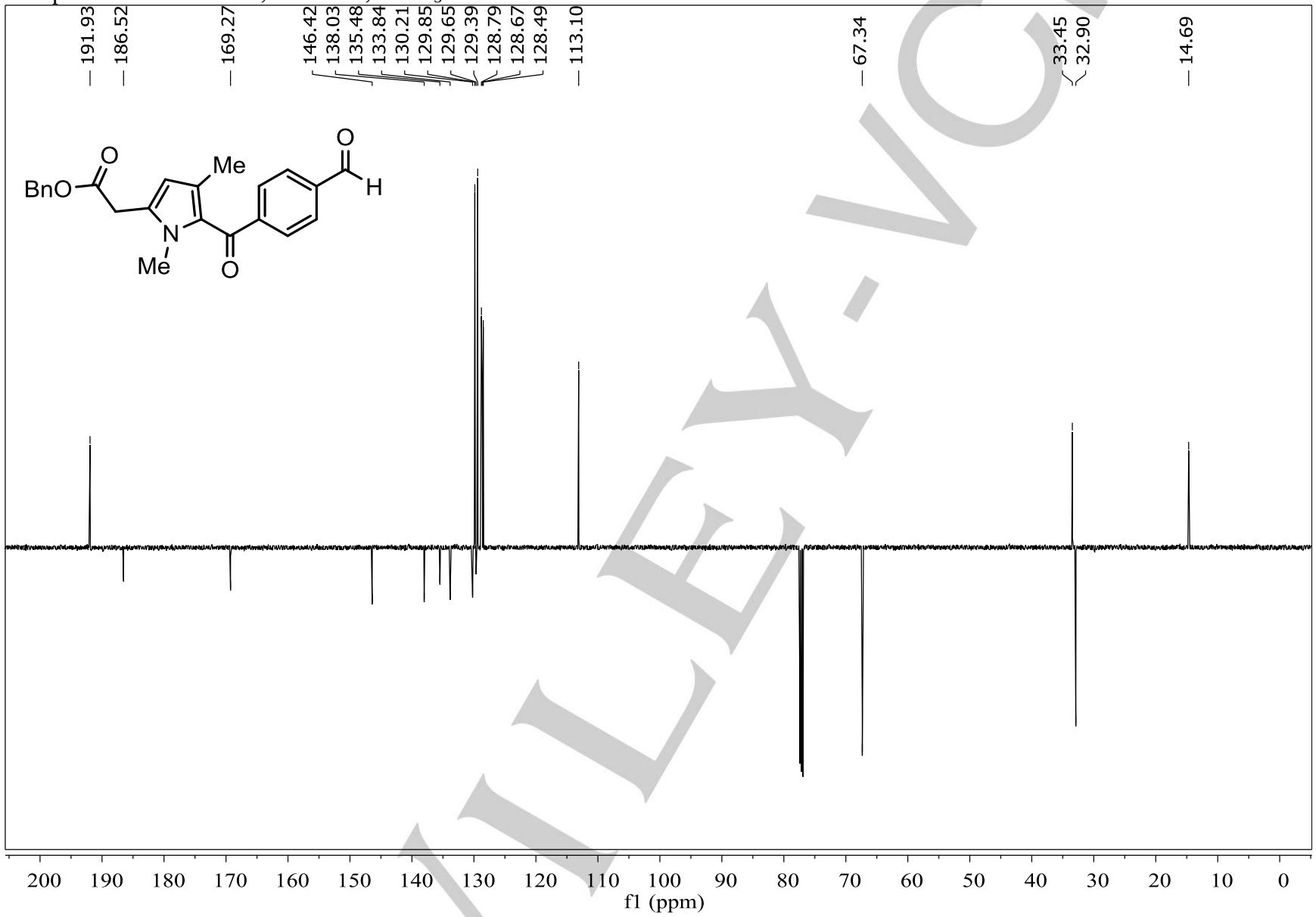
Compound **32** – ^{13}C NMR, 125 MHz, $CDCl_3$



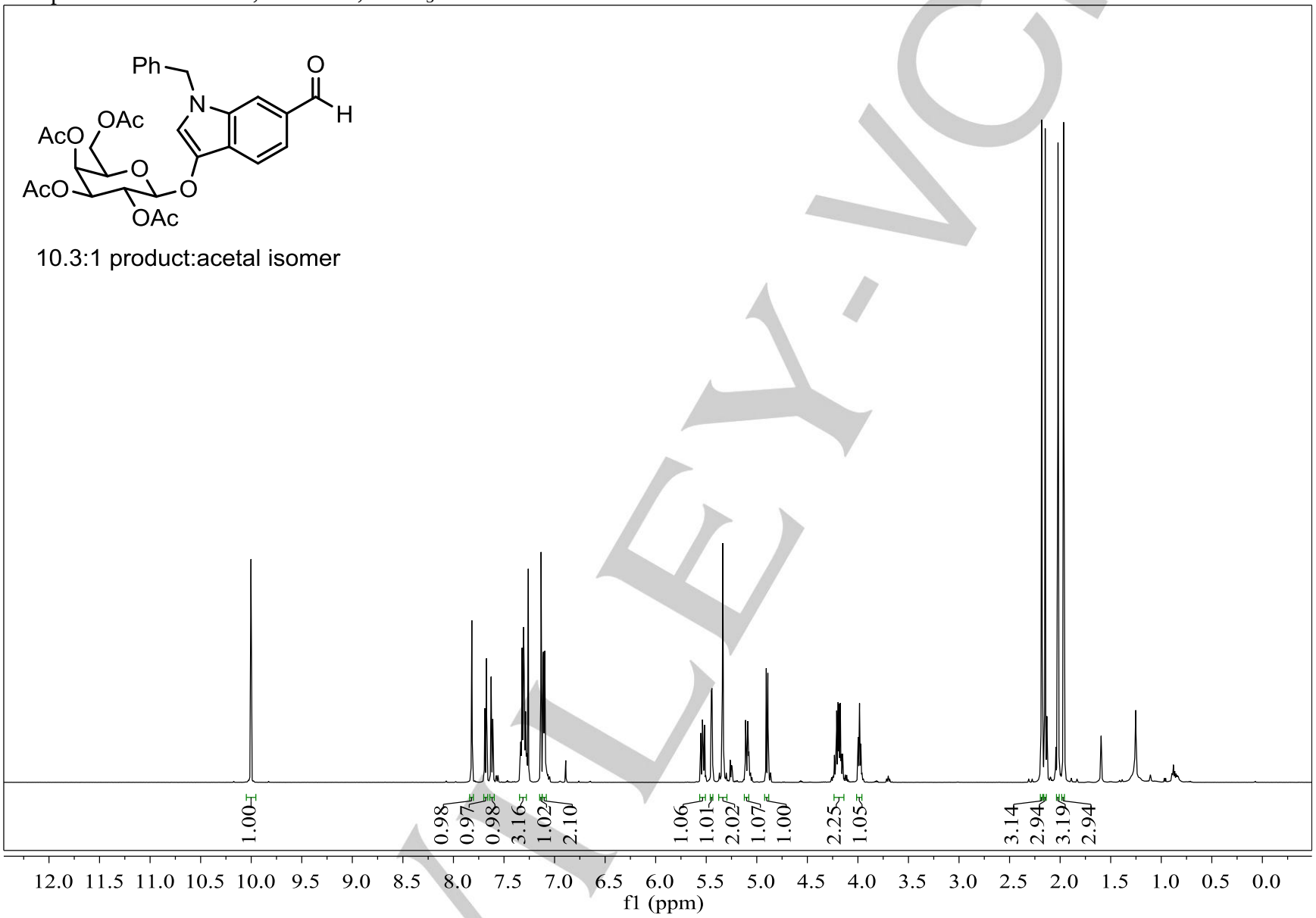
Compound **33** – ^{1}H NMR, 500 MHz, $CDCl_3$



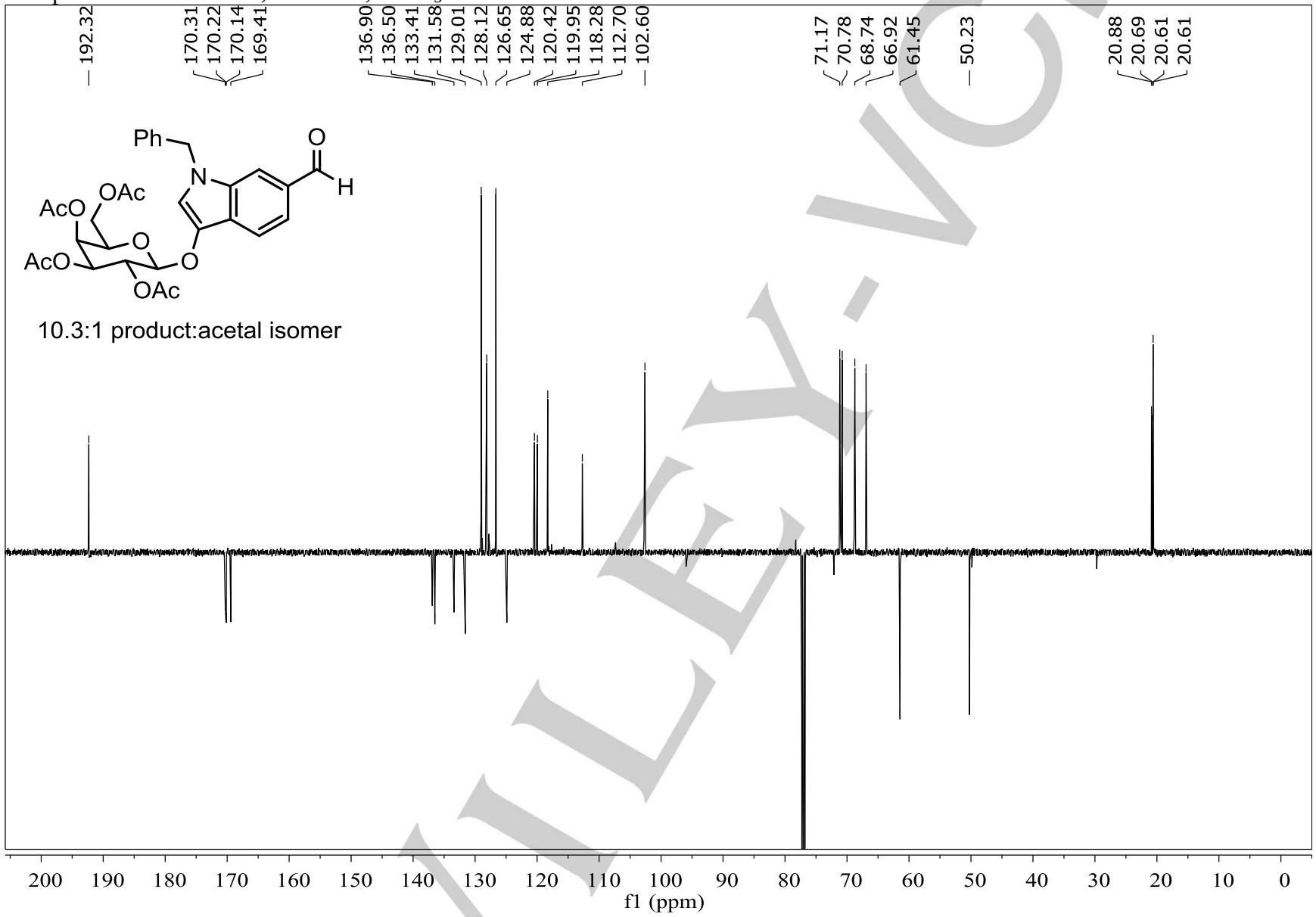
Compound **33** – ^{13}C NMR, 125 MHz, $CDCl_3$



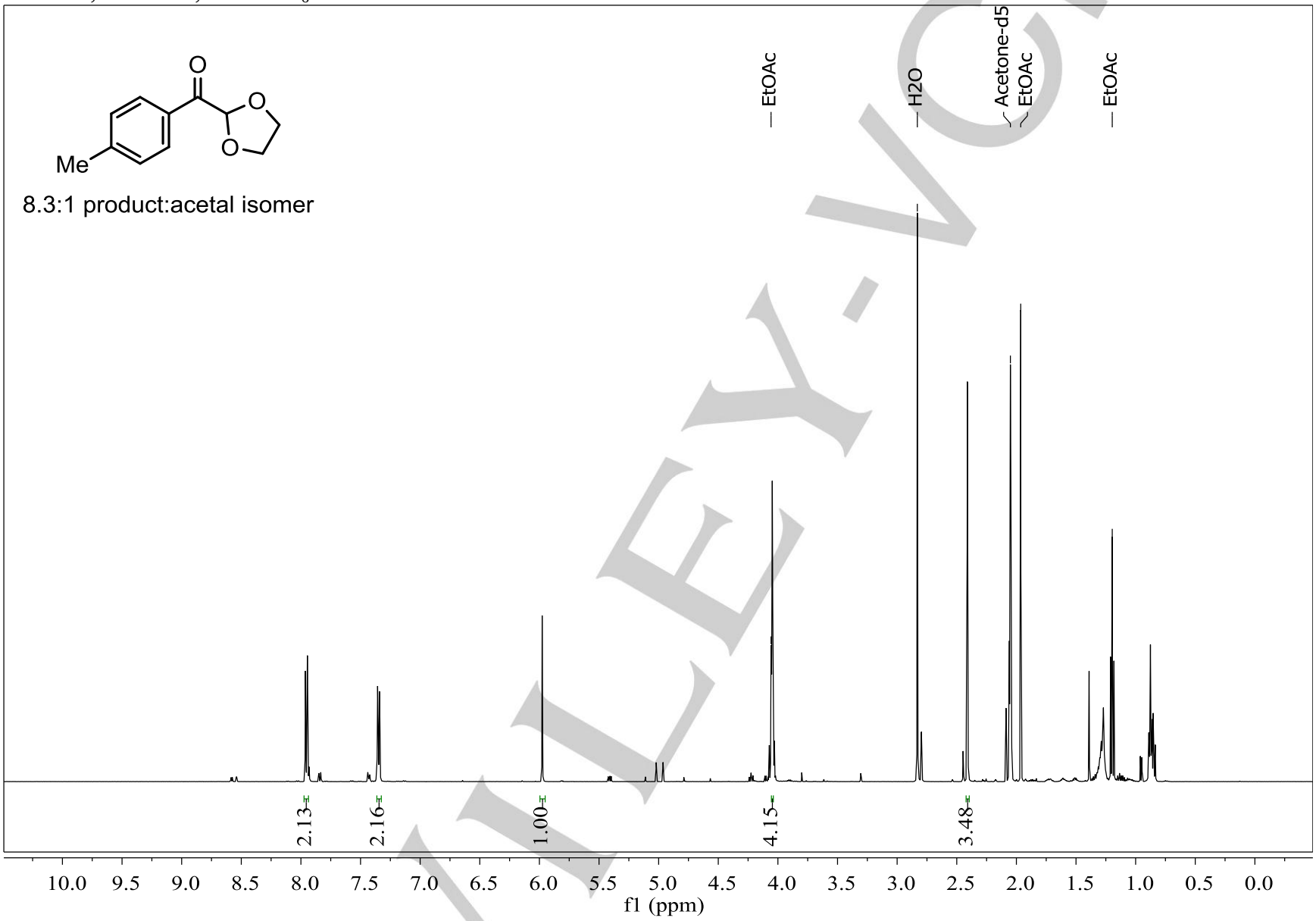
Compound **34** – ^{1}H NMR, 500 MHz, $CDCl_3$



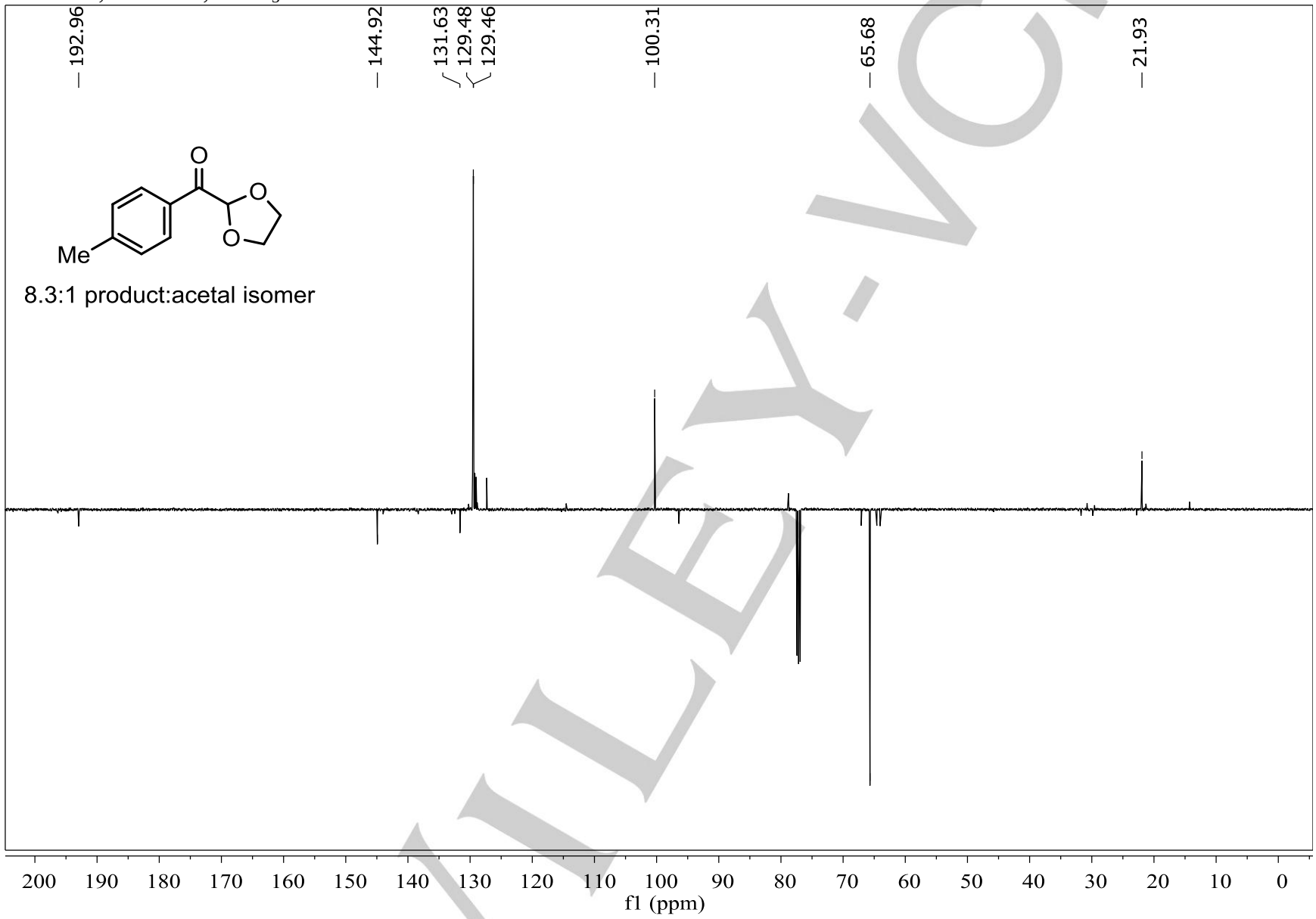
Compound **34** – ^{13}C NMR, 125 MHz, $CDCl_3$



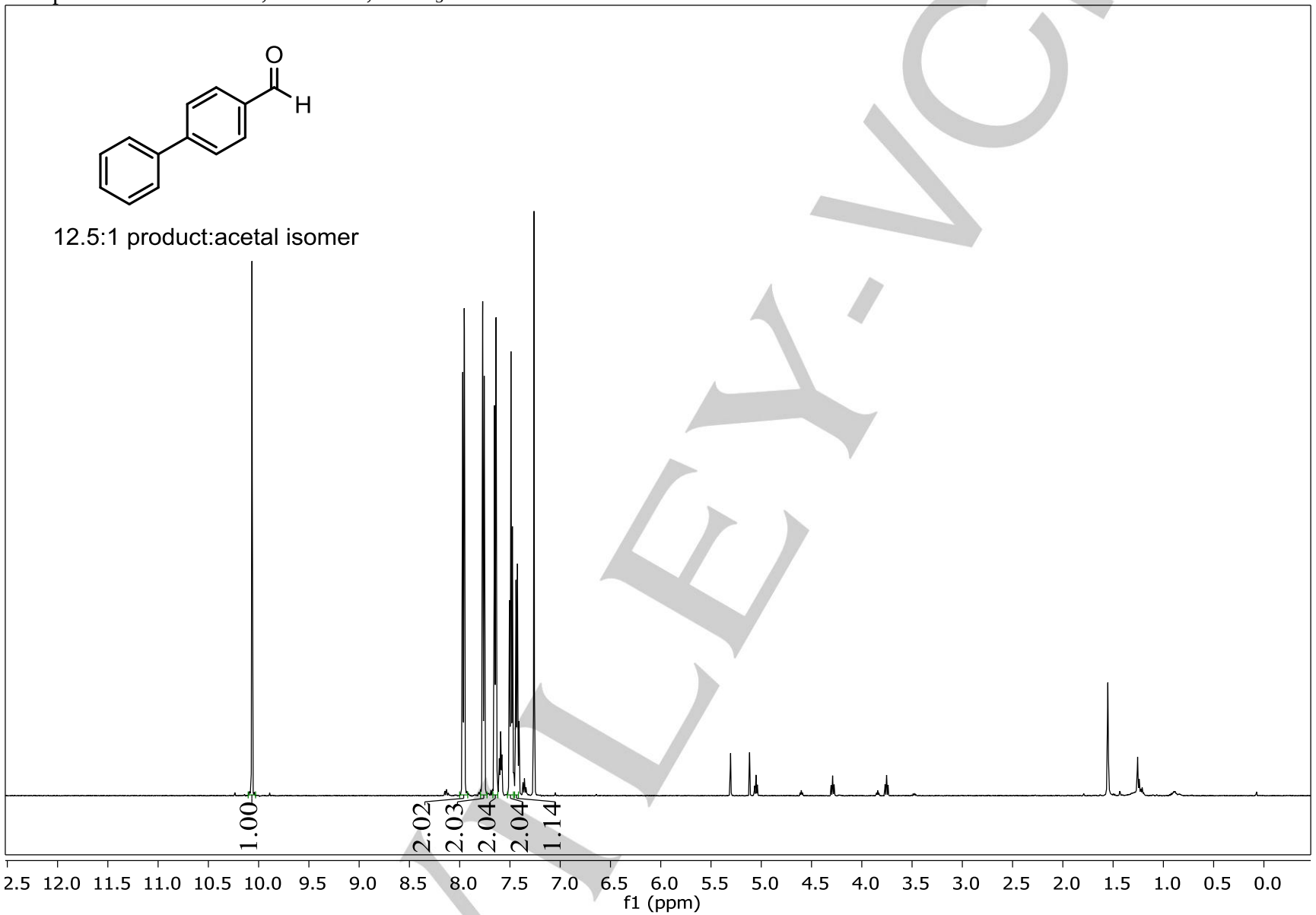
^{1}H NMR, 500 MHz, acetone-d_6



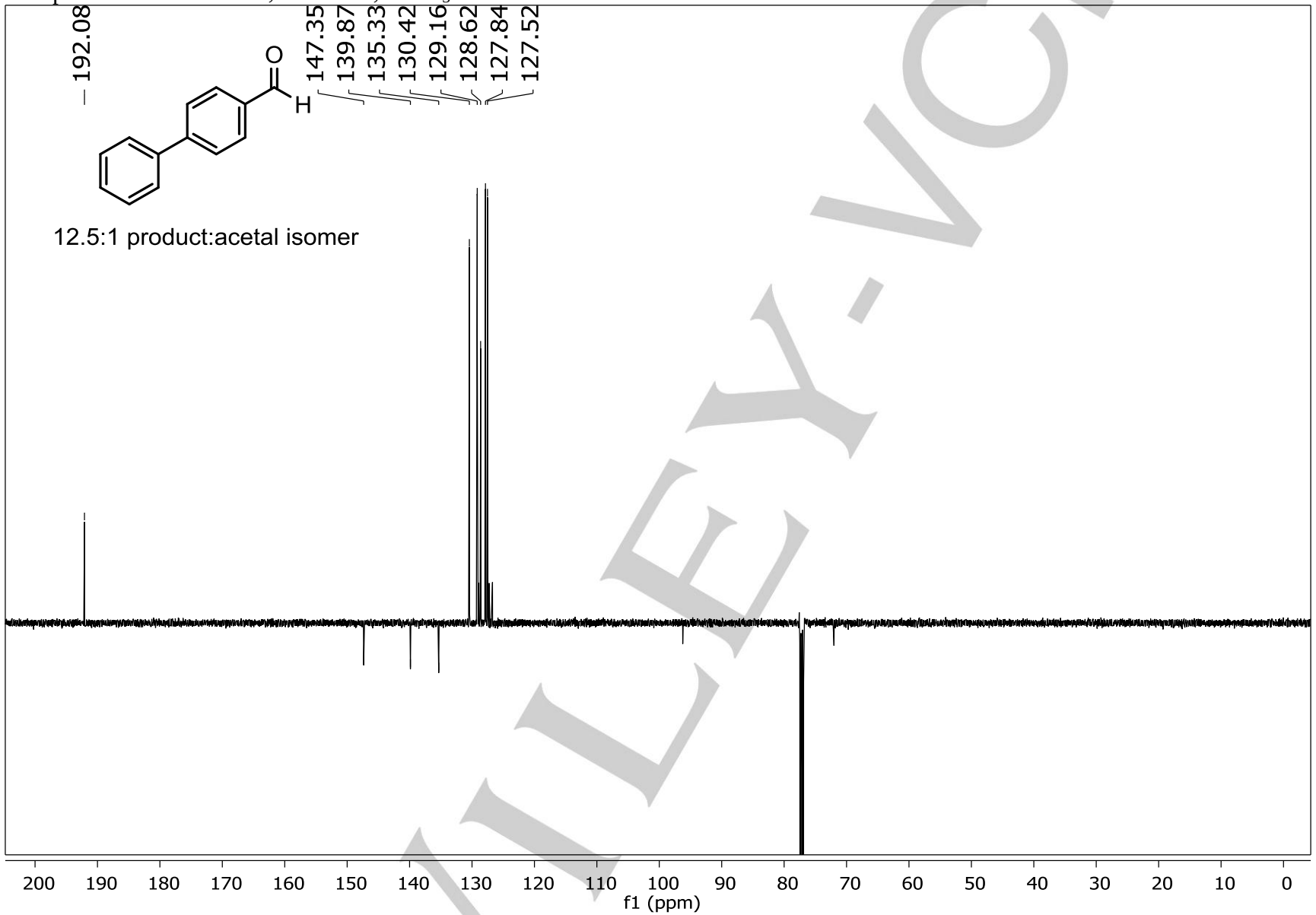
^{13}C NMR, 125 MHz, $CDCl_3$



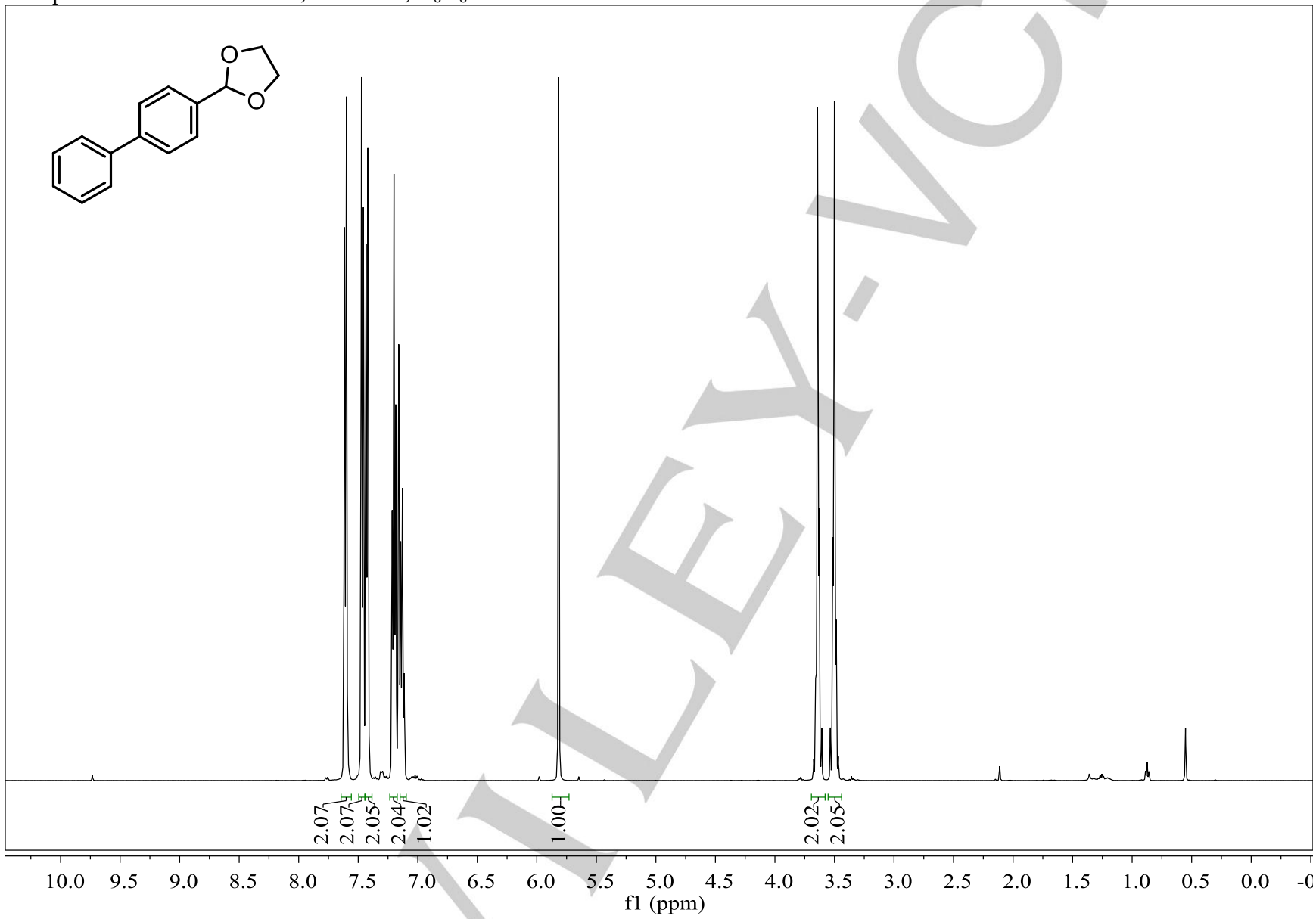
Compound **38** – ^{1}H NMR, 500 MHz, $CDCl_3$



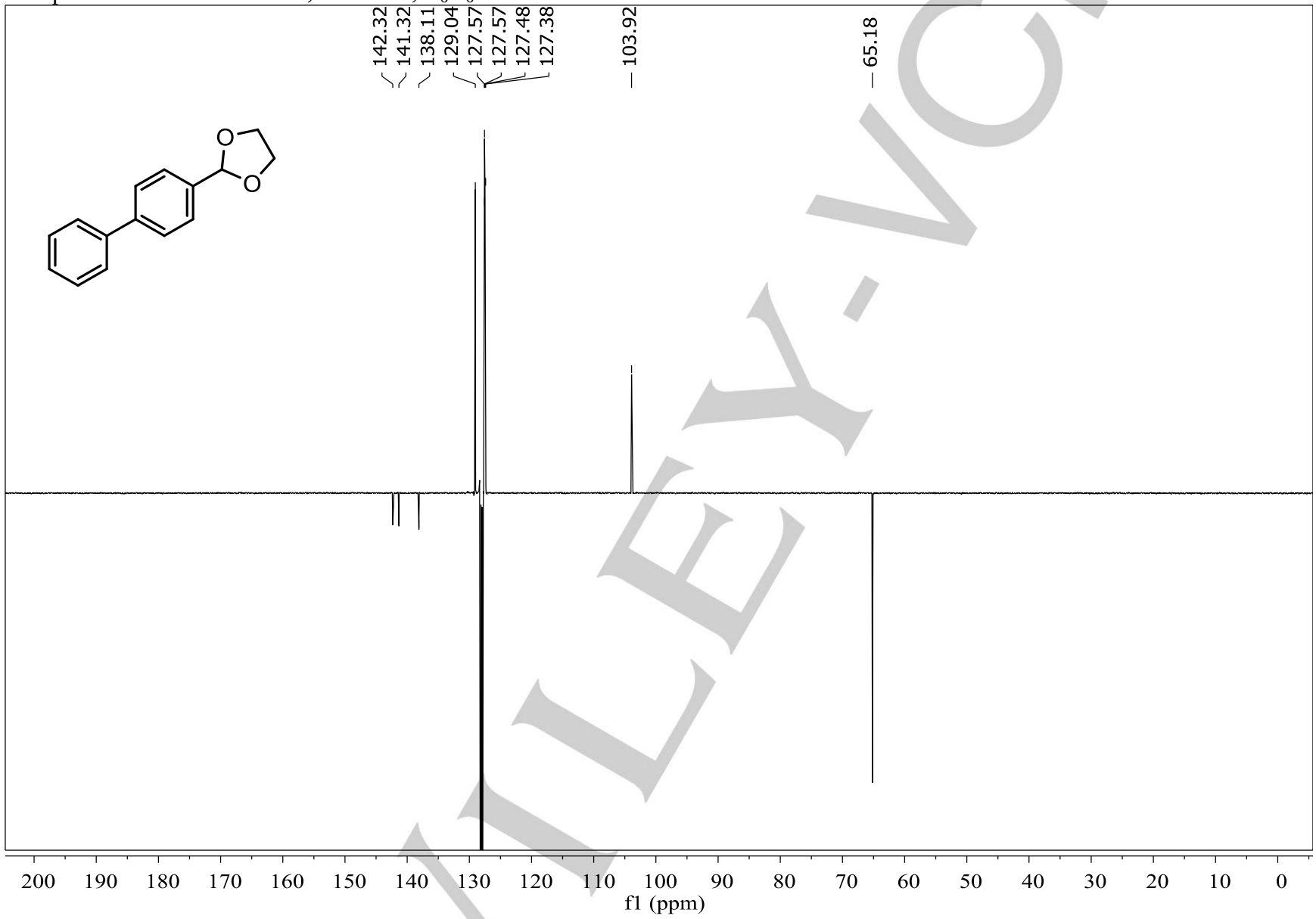
Compound **38** – ^{13}C NMR, 125 MHz, $CDCl_3$



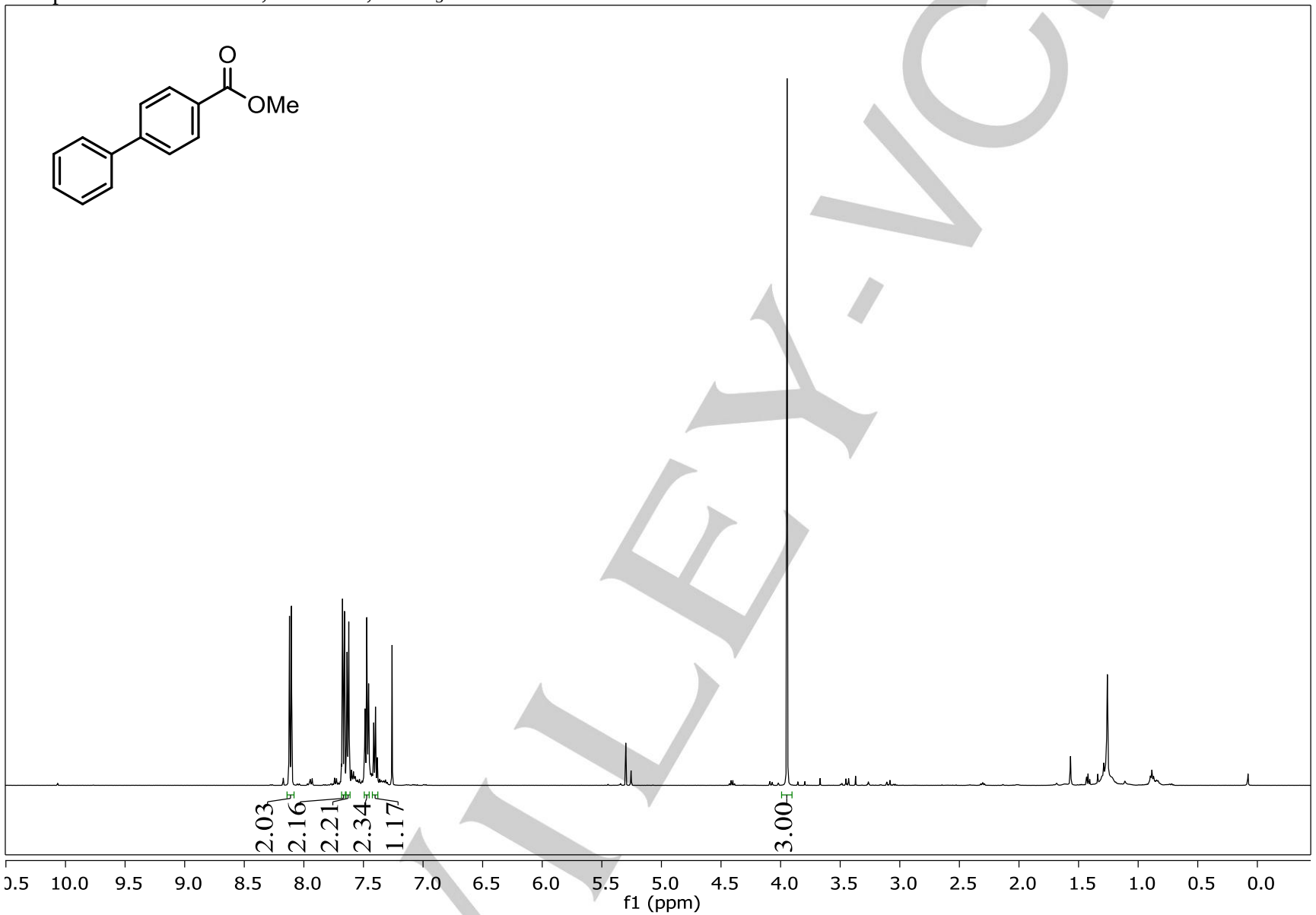
Compound **36–Ph –** ^{1}H NMR, 500 MHz, C_6D_6



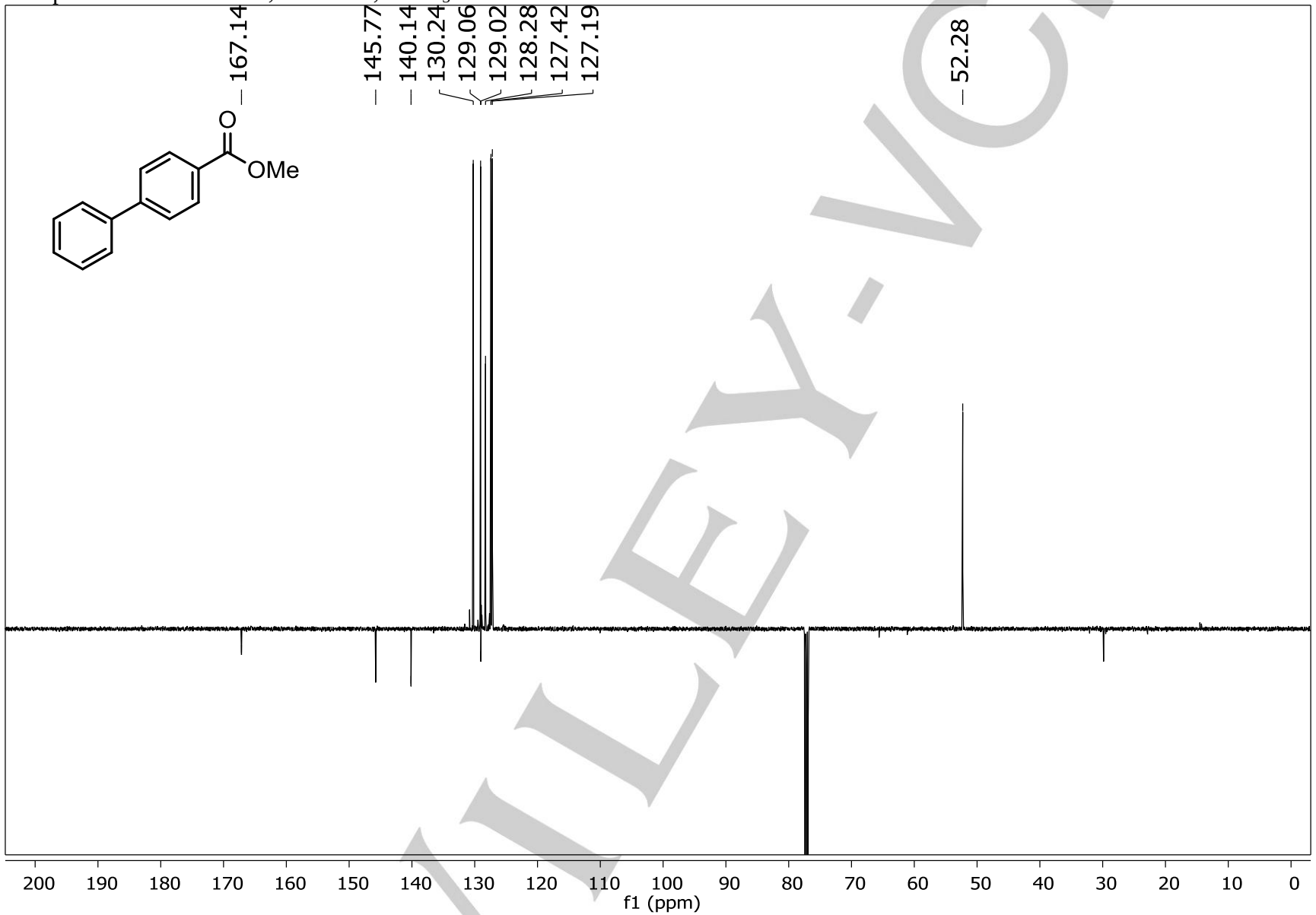
Compound **36–Ph** – ^{13}C NMR, 125 MHz, C_6D_6



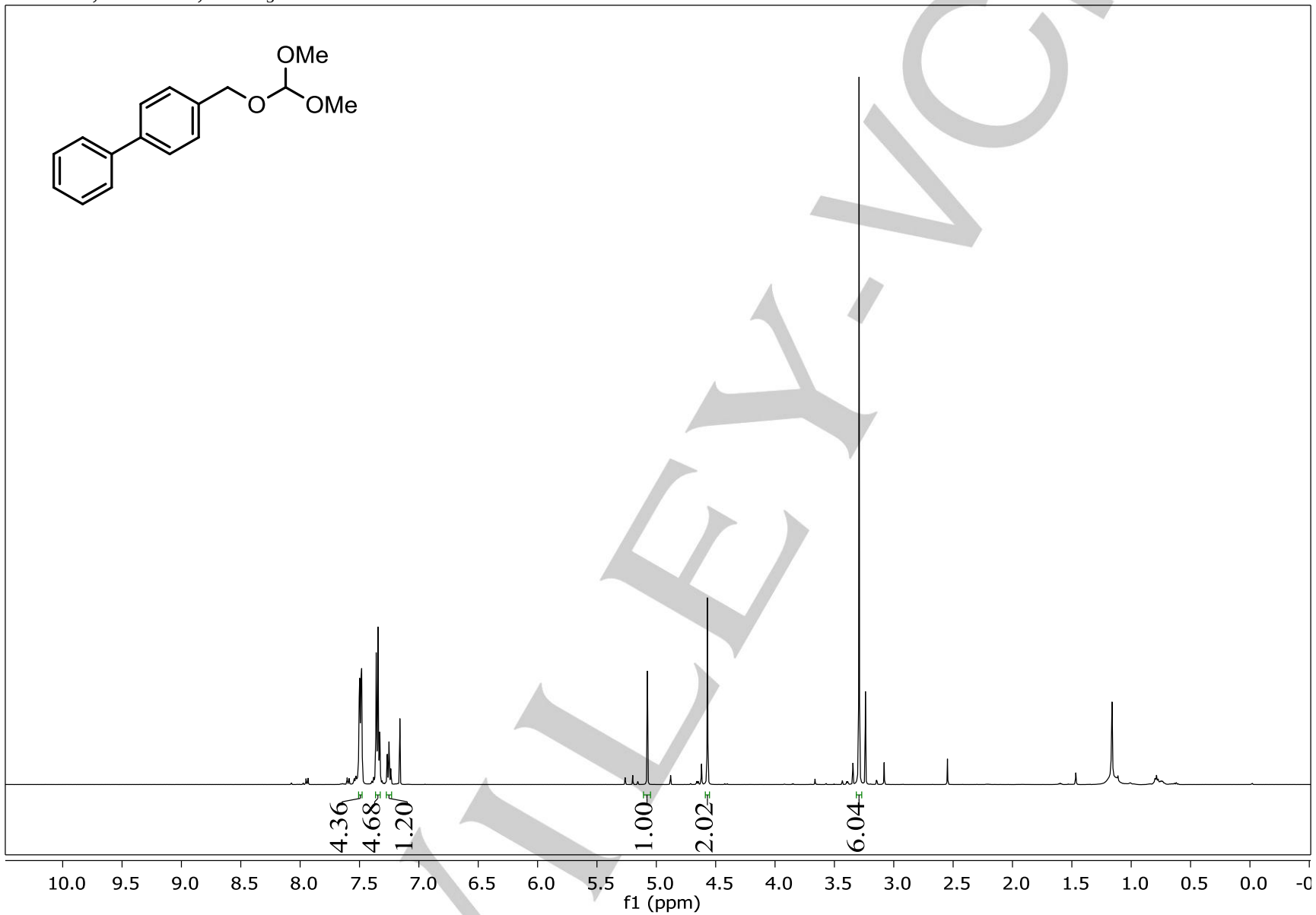
Compound **39** – ^{1}H NMR, 500 MHz, $CDCl_3$



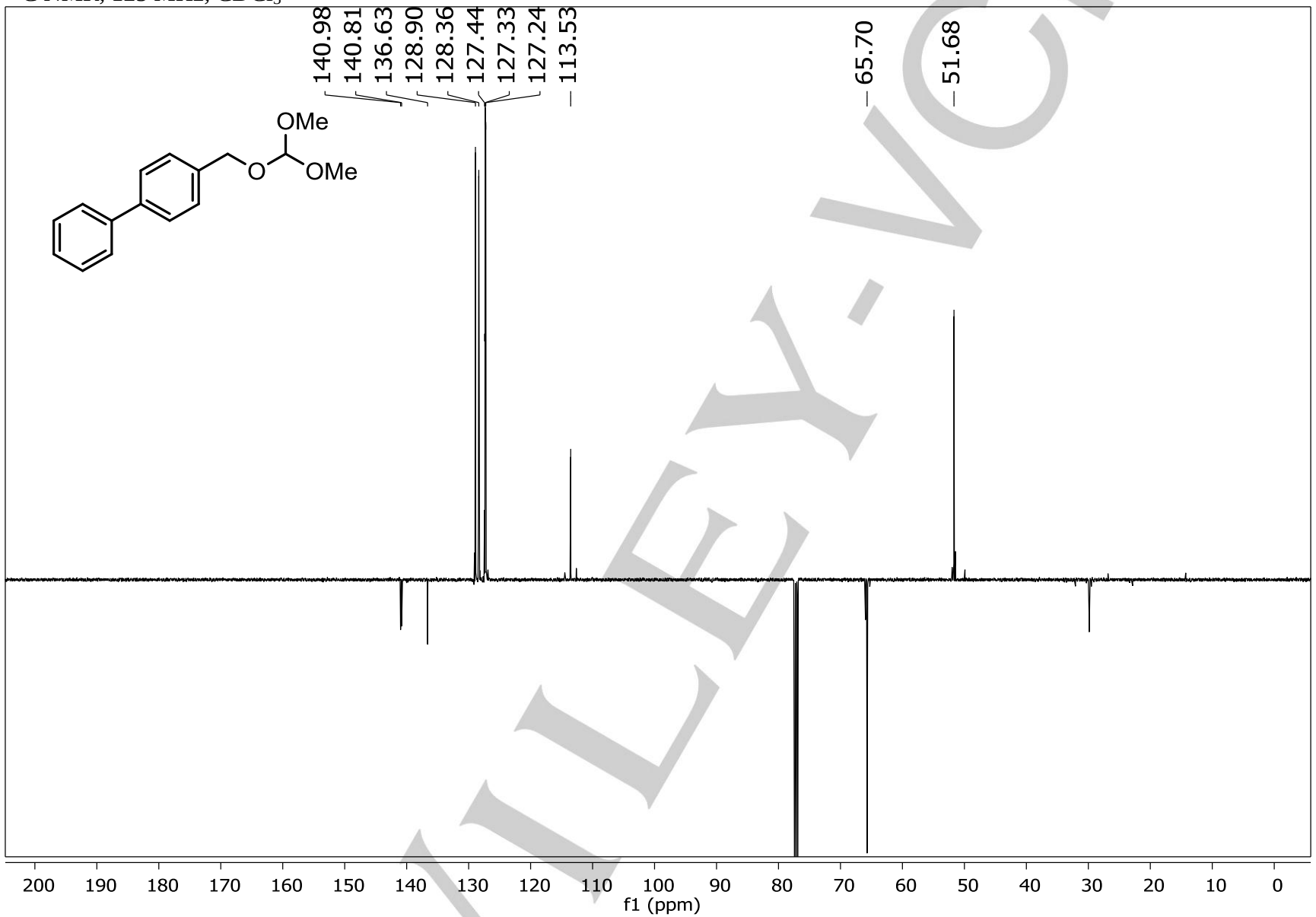
Compound **39** – ^{13}C NMR, 125 MHz, $CDCl_3$



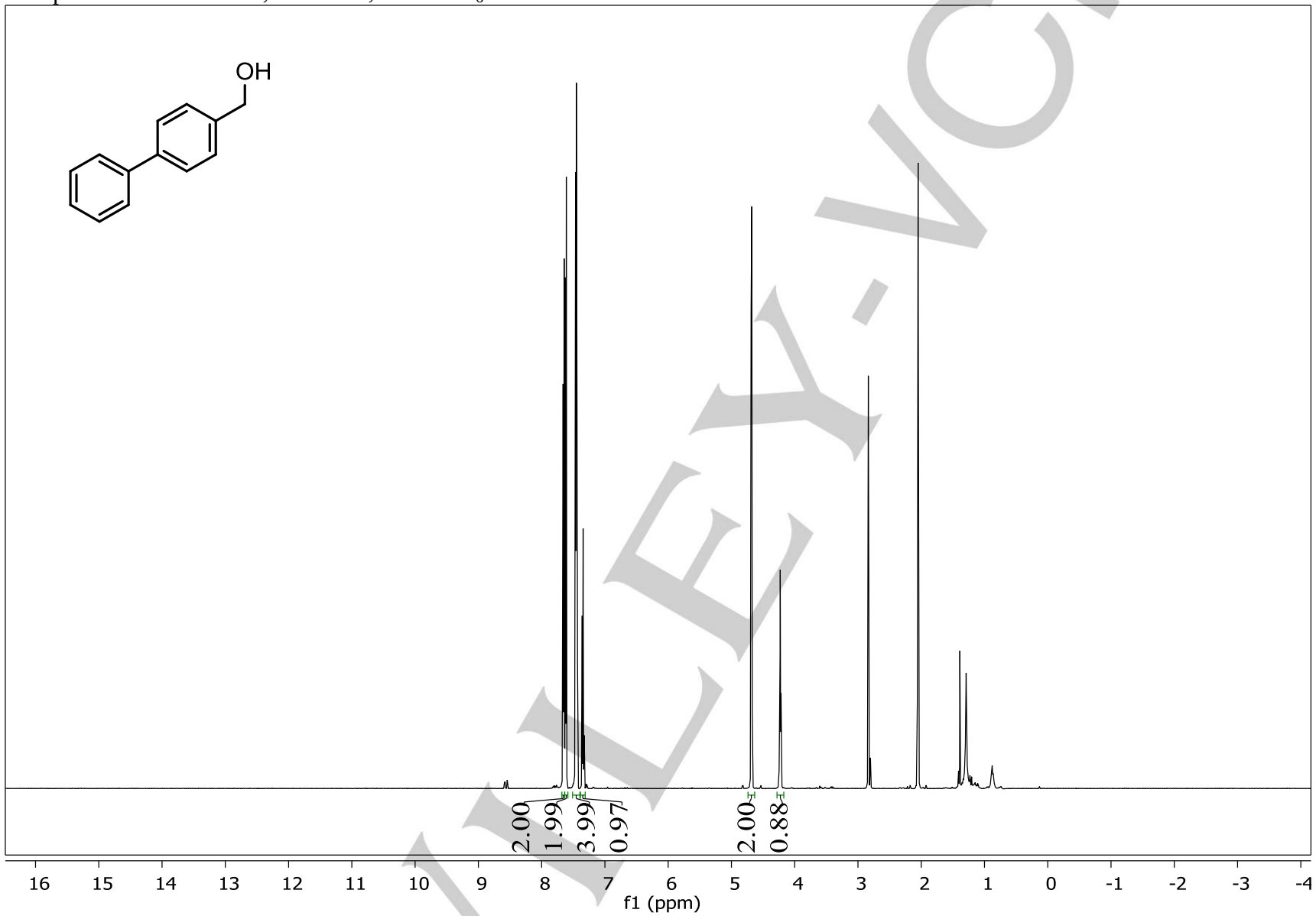
^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$



Compound **40** – ^{1}H NMR, 500 MHz, acetone-d_6



Compound **40** – ^{13}C NMR, 125 MHz, acetone-d_6