Supporting Information

For

Enantioselective Iodolactonization of Disubstituted Olefinic Acids Using a Bifunctional Catalyst

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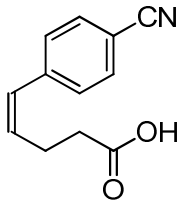
General

Solvents were purified before use as follows unless otherwise noted. Dichloromethane and benzene were distilled from calcium hydride immediately prior to use. Tetrahydrofuran and diethyl ether were dried by filtration through two columns of activated, neutral alumina according to the procedure described by Grubbs.[1] Methanol (MeOH), acetonitrile (MeCN), and dimethylformamide (DMF) were dried by filtration through two columns of activated molecular sieves, and toluene was dried by filtration through one column of activated, neutral alumina followed by one column of Q5 reactant. These solvents were determined to have less than 50 ppm H_2O by Karl Fischer coulometric moisture analysis. Reagents were reagent grade and used without purification unless otherwise noted. *N*-iodosuccinimide (NIS) was freshly prepared from NCS and NaI,[2] and triturated from dioxane/CCl_4 (1:2). All reactions were performed in flame-dried glassware under nitrogen or argon; reaction temperatures refer to the temperature of the cooling/heating bath.

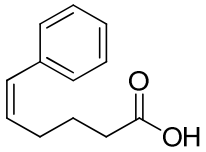
Analytical HPLC separations were performed using a Pirkle Covalent (S,S) Whelk-O1 (Regis Technologies, Inc.), or a Chiralcel OD-H (Daicel Chemical Industries, Ltd.) column, as indicated. Infrared (IR) spectra were obtained neat on sodium chloride and reported as wavenumbers (cm^{-1}). Proton nuclear magnetic resonance (^1H NMR) and carbon nuclear magnetic resonance (^{13}C NMR) spectra were obtained at the indicated field as solutions in $CDCl_3$ unless otherwise indicated. Chemical shifts are referenced to the deuterated solvent (*e.g.,* for $CDCl_3$, δ = 7.26 ppm and 77.0 ppm for ^1H and ^{13}C NMR, respectively) and are reported in parts per million (ppm, δ) relative to tetramethylsilane (TMS, δ = 0.00 ppm). Coupling constants (*J*) are reported in Hz and the splitting abbreviations used are: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; comp, overlapping multiplets of magnetically nonequivalent protons; br, broad; app, apparent.

Synthesis of Olefinic Acids

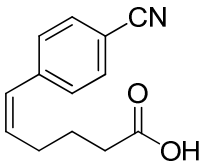
Catalyst **4** was prepared according to our previously reported method.[3] All olefinic acids were made by literature procedures as follows: 5-Substituted-4(*Z*)-pentenoic acids **5a-h** and 6-Substituted-5(*Z*)-hexanoic acids **7a-d** were made by the method of Yeung, et al.;[4] (*E*)-6-methylhept-4-enoic acid (**9a**) was made by the method of Kaga, et al.;[5] 5-Aryl-4(*E*)-pentenoic acid (**9b-d**) were made of the method of Yeung, et al.[4] Characterization data is reported below for new compounds.



(*Z*)-5-(4-Cyanophenyl)pent-4-enoic acid (5f): white solid; > 20:1 *Z/E* ratio; mp 62–64 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.0 (br s, 1 H), 7.63 (d, *J* = 8.4 Hz, 2 H), 7.36 (d, *J* = 8.0 Hz, 1 H), 6.49 (d, *J* = 12.0 Hz, 1 H), 5.78 (dt, *J* = 11.6, 7.2 Hz, 1 H), 2.67–2.62 (m, 2 H), 2.52 (t, *J* = 7.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 179.0, 141.2, 133.0, 132.0, 129.2, 128.9, 118.8, 110.2, 33.7, 23.6; IR (neat) 3020, 2919, 2228, 1711, 1605, 1416, 1287, 1213, 855 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{12}H_{11}NNaO_2]^+$ (M+Na), 224.0682; found 224.0681.

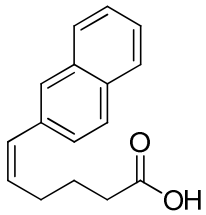


(*Z*)-6-Phenylhex-5-enoic acid (7a): clear, colorless oil: 14:1 *Z/E* ratio; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 10.2 (br s, 1 H), 7.36–7.19 (comp, 5 H), 6.47 (d, *J* = 11.7 Hz, 1 H), 5.63 (dt, *J* = 11.7, 7.2 Hz, 1 H), 2.44–3.25 (comp, 4 H), 1.85–1.74 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 179.8, 137.7, 131.3, 129.9, 128.7, 128.1, 126.6, 33.4, 27.8, 24.8; IR (neat) 3012, 2938, 1709, 1412, 1240, 768, 700 cm^{-1}; HRMS (CI) *m/z* calcd for $[C_{12}H_{13}O_2]^-$ (M–H), 189.0921; found 189.0918.



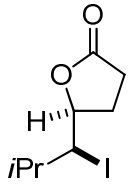
(*Z*)-6-(4-Cyanophenyl)hex-5-enoic acid (7b): white solid; 20:1 *Z/E* ratio; mp 86–88 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 10.8 (br s, 1 H), 7.61 (d, *J* = 6.6 Hz, 2 H), 7.35 (d, *J* = 8.1 Hz, 2 H), 6.47 (d, *J* = 11.7 Hz, 1 H), 5.80 (dt, *J* = 11.7, 7.5 Hz, 1 H), 2.42–2.33 (comp, 4 H), 1.86–1.76 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 179.6, 142.0, 134.5, 132.0, 129.3, 128.5, 119.0, 110.1, 33.2, 27.8, 24.4; IR (neat) 3019, 2935, 2908, 2223, 1699, 1604,

1411, 1319, 1242, 1205, 946, 849 cm^{-1}; HRMS (CI) *m/z* calcd for $[C_{13}H_{12}NO_2]^-$ (M–H), 214.0874; found 214.0871.



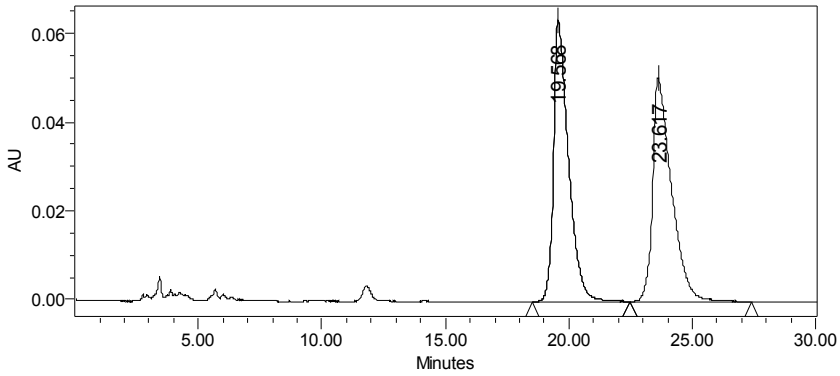
(*Z*)-6-(Naphthalen-2-yl)hex-5-enoic acid (7c) white solid; 72–73 °C; > 20:1 *Z/E* ratio; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 11.1 (br s, 1 H), 7.80–7.76 (comp, 3 H), 7.69 (s, 1 H), 7.47–7.37 (comp, 3 H), 6.59 (d, *J* = 11.7 Hz, 1 H), 5.69 (dt, *J* = 11.7, 7.2 Hz, 1 H), 2.49–2.34 (m, 2 H), 2.36 (t, *J* = 7.5 Hz, 2 H), 1.85–1.78 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 180.0, 134.9, 133.3, 132.2, 131.8, 130.0, 127.9, 127.6, 127.5, 127.4, 127.1, 126.0, 125.7, 33.5, 27.9, 24.7; IR (neat) 3050, 2945, 1704, 1330, 1242, 950, 897, 860, 821, 716 cm^{-1}; HRMS (CI) *m/z* calcd for $[C_{16}H_{15}O_2]^-$ (M–H), 239.1078; found 239.1076.

General Procedure for Enantioselective Iodolactonizations



(*S*)-5-[(*S*)-1-Iodo-2-methylpropyl]dihydrofuran-2(*3H*)-one (6a). NIS (0.135 g, 0.600 mmol) was added to a solution of **5a** (0.071 g, 0.500 mmol) and catalyst **4** (0.026 g, 0.050 mmol) in toluene (10 mL) and CH_2Cl_2 (5 mL) at –20 °C. The solution was stirred for 14 h, whereupon saturated aqueous $Na_2S_2O_3$ (5 mL) was added, and the mixture was warmed to room temperature with vigorous stirring. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography, eluting with hexanes/EtOAc (5:1, v/v) to give 0.127 g (95%) of **6a** as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.36–4.25 (m, 1 H), 4.08 (dd, *J* = 5.1, 4.6 Hz, 1 H), 2.80–2.66 (m, 1 H), 2.64–2.49 (m, 1 H), 2.48–2.34 (m, 1 H), 2.14–2.00 (m, 1 H), 1.70–1.58 (m, 1 H), 1.07 (app dd, *J* = 6.5, 1.0 Hz, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.0, 81.0, 51.5, 33.6, 28.6, 28.5, 22.9, 22.1; IR (neat) 1775 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_8H_{13}INaO_2]^+$ (M+Na), 290.9852; found 290.9851; $[\alpha]^{25}_D$ +84.6 (c = 1.0, $CHCl_3$); HPLC (259 nm): Whelk-O1 (20% *i*-PrOH / hexanes, 1.2 mL/min) 20.1 min (minor), 23.5 min (major); 97.5:2.5 er.

Racemic:



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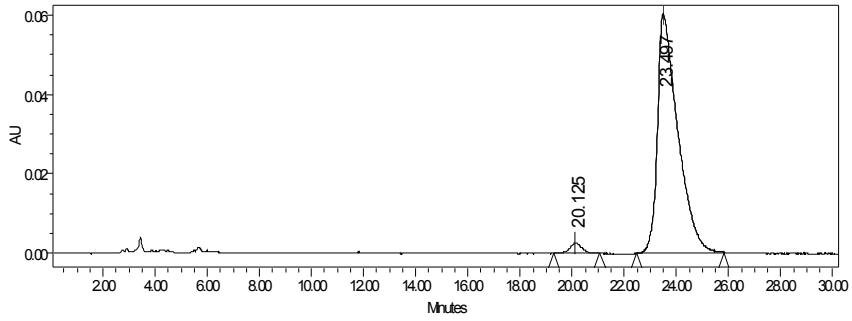

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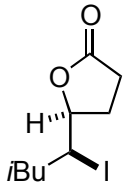

(*S*)-5-[(*S*)-1-Iodo-3-methylbutyl]dihydrofuran-2(*3H*)-one (6b). Isolated 0.027 g (94%) of **6b** as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.38–4.32 (m, 1 H), 4.25–4.18 (m, 1 H), 2.78–2.64 (m, 1 H), 2.62–2.51 (m, 1 H), 2.49–2.37 (m, 1 H), 2.18–2.07 (m, 1 H), 2.00–1.82 (comp, 2 H), 1.46–1.38 (m, 1 H), 0.98 (d, J = 6.8 Hz, 3 H), 0.88 (d, J = 6.8 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.4, 82.0, 43.9, 37.6, 28.6, 27.9, 26.8, 22.9, 20.6; IR (neat) 1780 cm^{-1}; HRMS (CI) *m/z* calcd for $[C_9H_{16}IO_2]^+$ (M+H), 283.0195; found 283.0192; $[\alpha]^{26}_D$ –16.5 (c = 0.6, $CHCl_3$); HPLC (258 nm): Whelk-O1 (20% *i*-PrOH / hexanes, 1.2 mL/min) 13.0 min (minor), 18.8 min (major); 98:2 er

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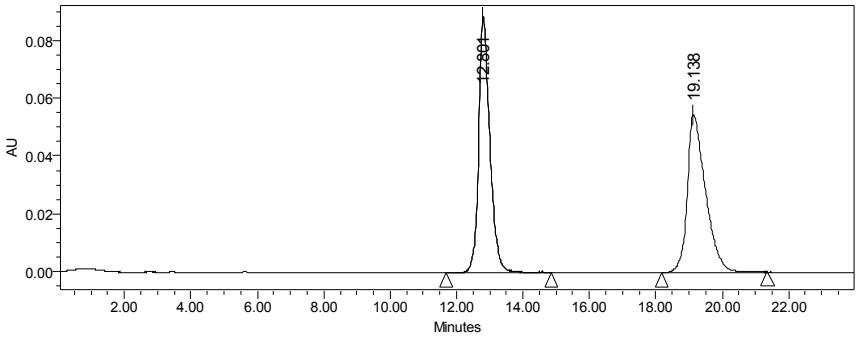

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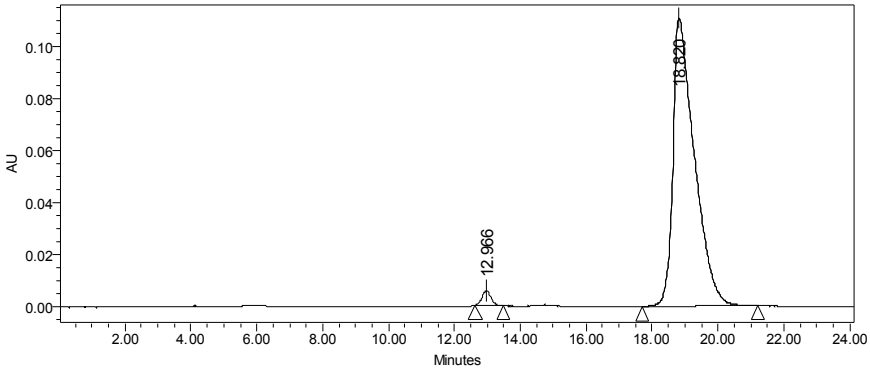

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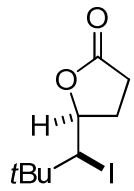

(*S*)-5-[(*S*)-1-Iodo-2,2-dimethylpropyl]dihydrofuran-2(*3H*)-one (6c). Isolated 0.028 g (99%) of **6c** as a white solid: mp 99-100 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.21 (t, J = 7.5 Hz, 1 H), 4.06 (s, 1 H), 2.75–2.65 (m, 1 H), 2.56–2.31 (comp, 2 H), 2.13–2.01 (m, 1 H), 1.18 (s, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.6, 77.7, 60.0, 36.6, 29.6, 29.5, 27.8; IR (neat) 2960, 1768, 1463, 1352, 1176, 914 cm^{-1}; HRMS (CI) *m/z* calcd for $[C_9H_{16}O_2I]^+$ (M+H), 283.0195; found 283.0196; $[\alpha]^{25}_D$ +41.7 (c = 1.0, $CHCl_3$); HPLC (259 nm): Whelk-O1 (20% *i*-PrOH / hexanes, 1.2 mL/min) 11.1 min (minor), 15.4 min (major); 97:3 er.

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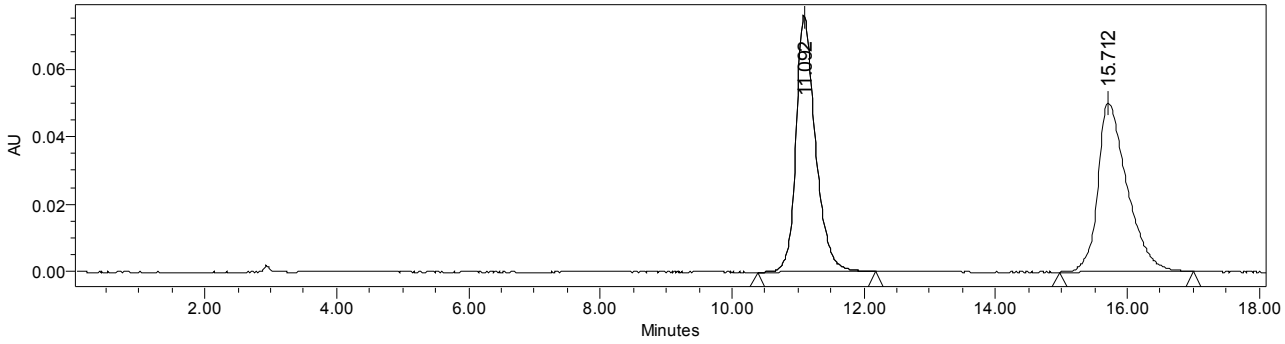

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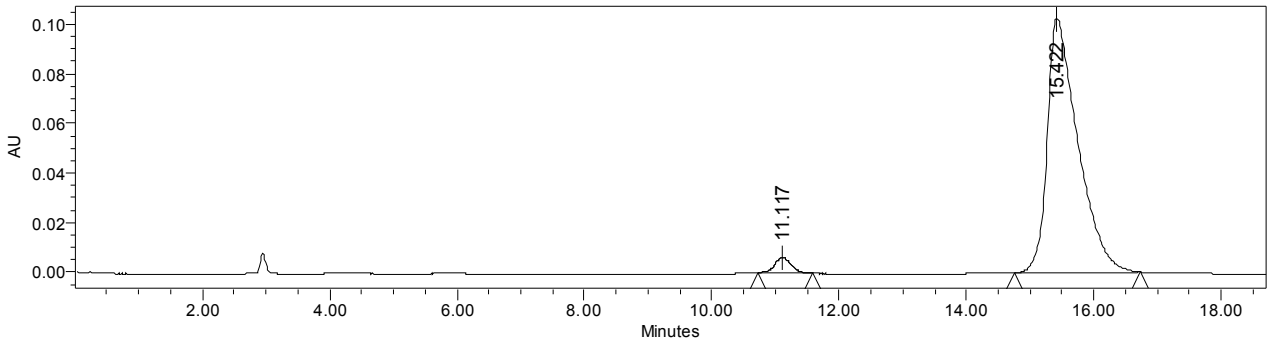

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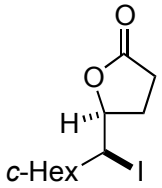

(*S*)-5-[(*S*)-Iodo(cyclohexyl)methyl]dihydrofuran-2(*3H*)-one (6d). Isolated 0.030 g (97%) of **6d** as a white solid: mp: 111-112 ºC; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.31 (ddd, *J* = 7.2, 7.2, 3.2 Hz, 1 H), 4.05 (dd, *J* = 6.0, 3.6 Hz, 1 H), 2.76–2.68 (m, 1 H), 2.58–2.50 (m, 1 H), 2.43–2.34 (m, 1 H), 2.13–2.03 (m, 1 H), 1.99–1.96 (m, 1 H), 1.86–1.83 (m, 1 H), 1.79–1.73 (comp, 2 H), 1.68–1.63 (m, 1 H), 1.44–1.38 (m, 1 H), 1.36–1.24 (comp, 4 H), 1.21–1.07 (comp, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.2, 79.8, 50.8, 43.3, 33.3, 32.7, 28.7, 28.4, 26.1, 26.0; IR (neat) 2924, 1768, 1453, 1178 cm^{-1}; HRMS (CI) *m/z* calcd for $[C_{11}H_{18}IO_2]^+$ (M+H), 309.0352; found 309.0353; $[\alpha]^{25}_D$ +38.0 (c = 1.0, $CHCl_3$); HPLC (259 nm): Whelk-O1 (20% *i*-PrOH / hexanes, 1.2 mL/min) 19.5 min (minor), 27.7 min (major); 98:2 er.

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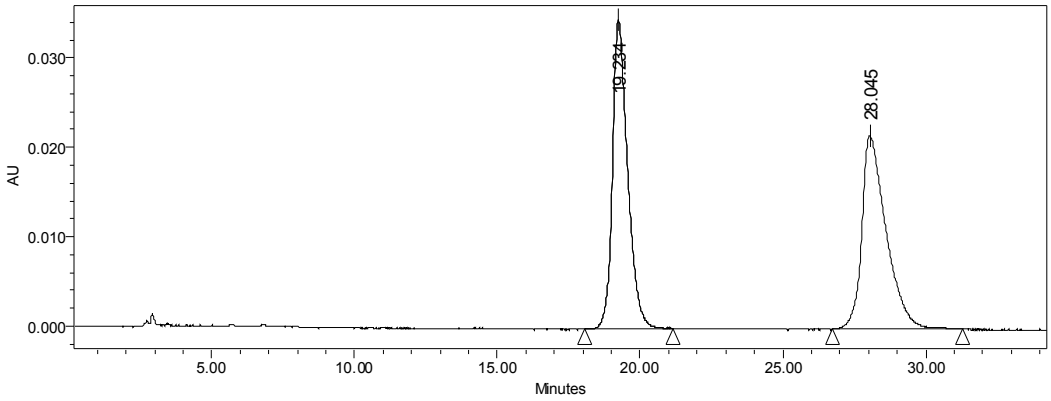

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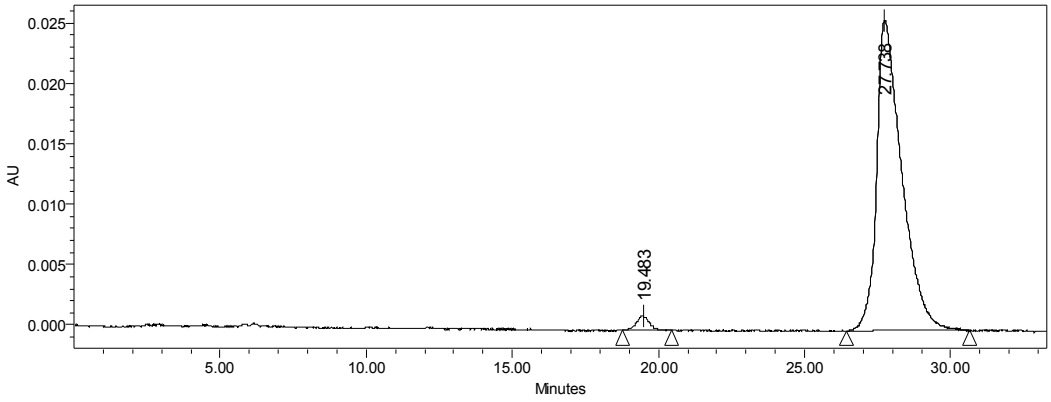

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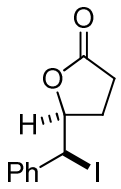

(*S*)-5-[(*S*)-Iodo(phenyl)methyl]dihydrofuran-2(*3H*)-one (6e). Isolated 0.028 g (93%) of **6e** as white solid: mp 95 °C (decomposition); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.47–7.44 (comp, 2 H), 7.33–7.30 (comp, 3 H), 5.13 (d, *J* = 6.0 Hz, 1 H), 4.70–4.64 (m, 1 H), 2.55–2.49 (comp, 2 H), 2.35–2.23 (m, 1 H), 2.04–1.91 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.7, 139.1, 128.9, 128.7, 128.5, 82.8, 34.1, 28.7, 26.9; IR (neat) 2938, 1780, 1455, 1177, 701 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{11}H_{11}INaO_2]^+$ (M+Na), 324.9696; found 324.9698; $[\alpha]^{25}_D$ +123 (c = 1.0, $CHCl_3$); HPLC (214 nm): Whelk-O1 (3% CH_3CN, 20% *i*-PrOH / hexanes, 1.2 mL/min) 12.0 min (minor), 13.5 min (major); 98:2 er.

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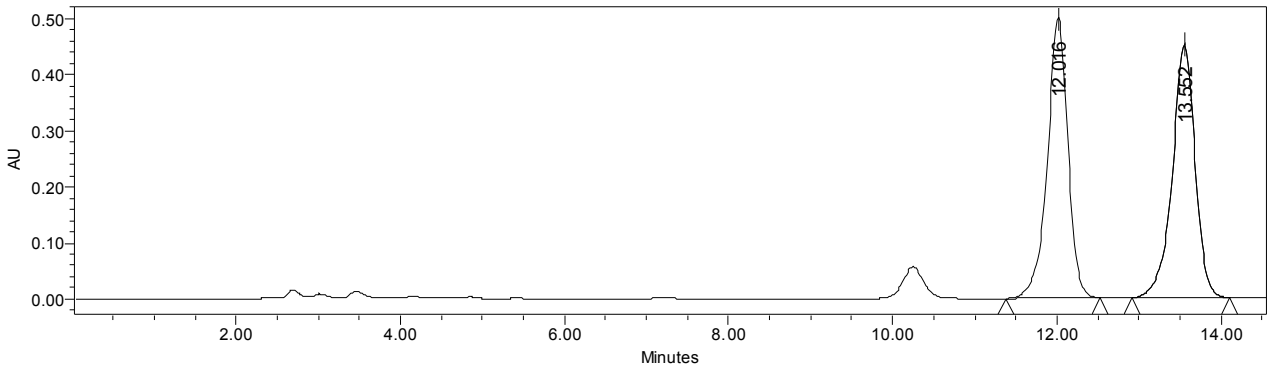

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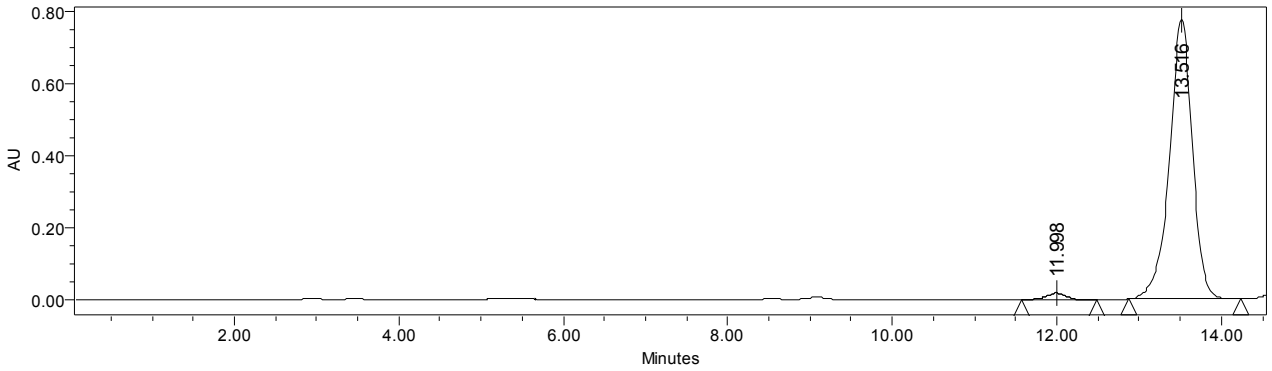

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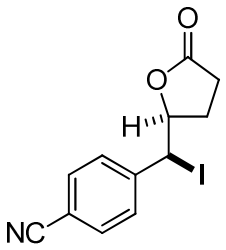

4-{(*S*)-Iodo[(*S*)-5-oxotetrahydrofuran-2-yl]methyl}benzonitrile (6f). Isolated 0.031 g (95%) of **6f** as white solid: mp 159 °C (decomposition); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.64–7.59 (comp, 4 H), 5.15 (d, J = 4.4 Hz, 1 H), 4.45 (dt, J = 7.6, 4.8 Hz, 1 H), 2.69–2.54 (comp, 2 H), 2.44–2.35 (m, 1 H), 2.06–1.96 (m, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.3, 144.8, 132.6, 129.3, 118.1, 112.4, 81.3, 33.0, 28.4, 27.5; IR (neat) 2956, 2230, 1775, 1606, 1182, 1025, 916 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{12}H_{10}INNaO_2]^+$ (M+Na), 349.9648; found 349.9645; $[\alpha]^{25}_D$ +180 (c = 1.0, $CHCl_3$); HPLC (239 nm): Whelk-O1 (3% CH_3CN, 20% *i*-PrOH / hexanes, 1.2 mL/min) 22.8 min (minor), 26.2 min (major); 99:1 er.

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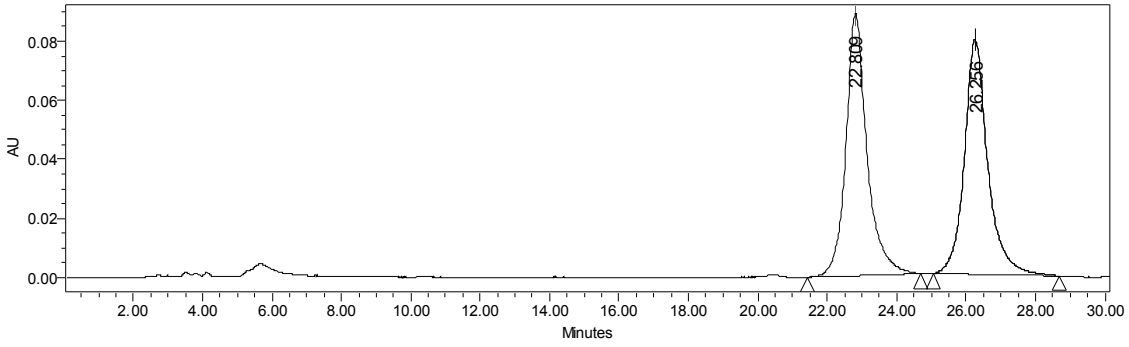

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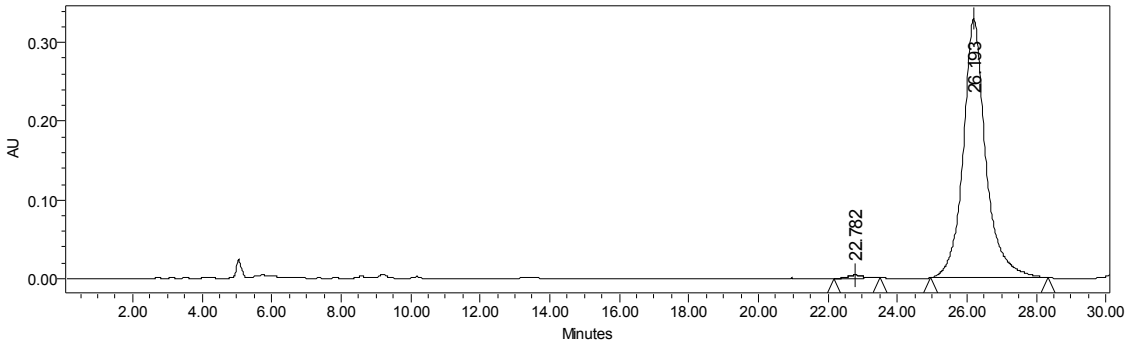

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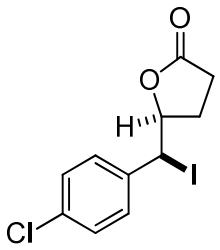
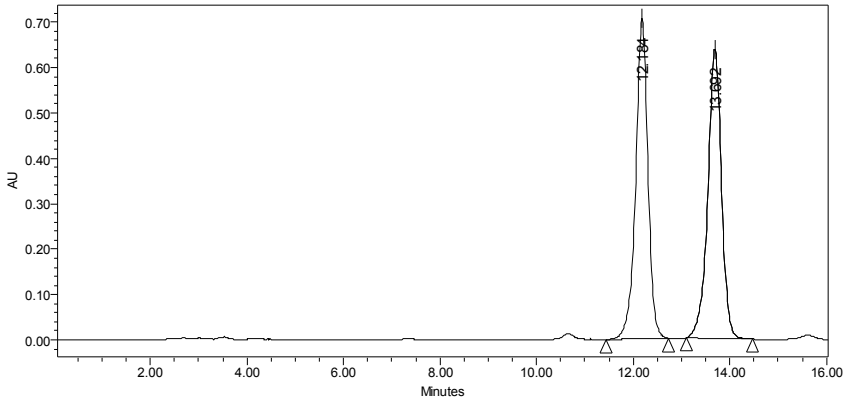
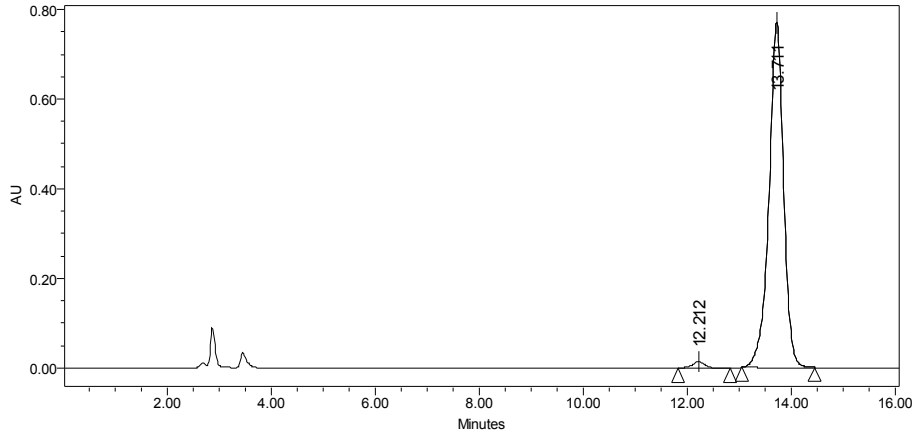


4-{(*S*)-Iodo[(*S*)-5-oxotetrahydrofuran-2-yl]methyl}benzonitrile (6g). Isolated 0.030 g (89%) of **6g** as semi-solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.42–7.40 (comp, 2 H), 7.31–7.29 (comp, 2 H), 5.10 (d, *J* = 6.0 Hz, 1 H), 4.54 (ddd, *J* = 7.6, 7.6, 5.2 Hz, 1 H), 2.58–2.54 (comp, 2 H), 2.38–2.29 (m, 1 H), 2.03–1.93 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.5, 137.9, 134.5, 129.8, 129.1, 82.3, 33.3, 28.6, 27.1; IR (neat) 1779, 1491, 1178, 1154, 1015 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{11}H_{10}ClINaO_2]^+$ (M+Na), 358.9306; found 358.9307; $[\alpha]^{25}_D$ +141 (c = 1.0, $CHCl_3$); HPLC (236 nm): Whelk-O1 (3% CH_3CN, 20% *i*-PrOH / hexanes, 1.2 mL/min) 12.2 min (minor), 13.7 min (major); 98:2 er.

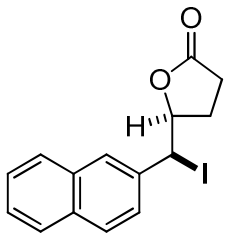
Racemic:



Enantiomeric:

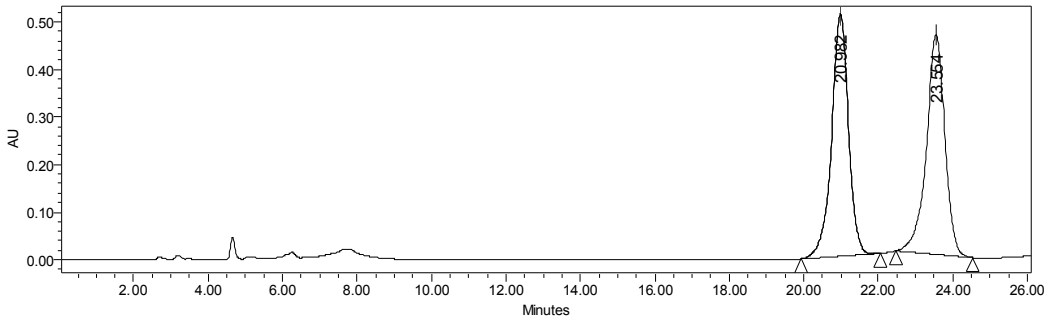


	Name	Retention Time	Area	% Area	Height	Int Type
1		12.212	244891	1.59	14675	bb
2		13.711	15165503	98.41	771260	bb

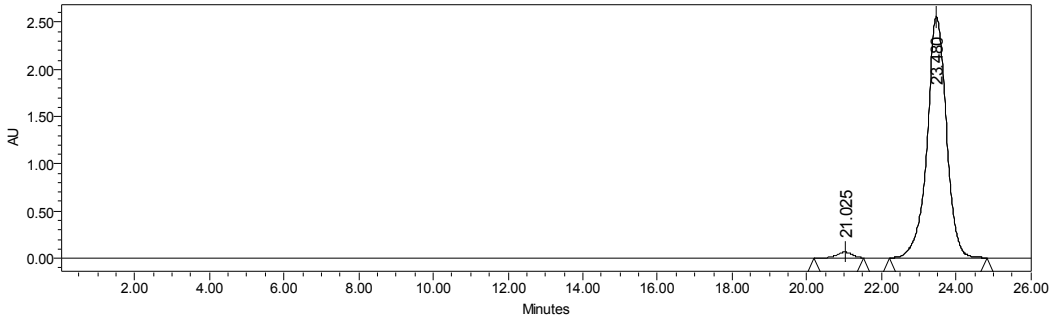


(*S*)-5-[(*S*)-Iodo(naphthalene-2-yl)methyl]dihydrofuran-2(*3H*)-one (6h). Isolated 0.033 g (94%) of **6h** as white solid: mp 87 °C (decomposition); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.87 (d, *J* = 1.6 Hz, 1 H), 7.83–7.81 (comp, 3 H), 7.57 (dd, *J* = 8.8, 2.0 Hz, 1 H), 7.52–7.50 (comp, 2 H), 5.29 (d, *J* = 6.0 Hz, 1 H), 4.75 (dt, *J* = 7.2, 5.6 Hz, 1 H), 2.59–2.54 (comp, 2 H), 2.34–2.25 (m, 1 H), 2.05–1.95 (m, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.7, 136.6, 133.1, 132.9, 129.0, 128.0, 127.7, 126.9, 126.8, 126.1, 82.8, 34.8, 28.8, 27.1; IR (neat) 3054, 2920, 1779, 1174, 917, 752 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{15}H_{13}INaO_2]^+$ (M+Na), 374.9852; found 374.9851; $[\alpha]^{24}_D$ +151 (c = 1.0, $CHCl_3$); HPLC (226 nm): Whelk-O1 (3% CH_3CN, 20% *i*-PrOH / hexanes, 1.2 mL/min) 21.0 min (minor), 23.5min (major); 98:2 er.

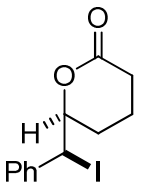
Racemic:



Enantiomeric:

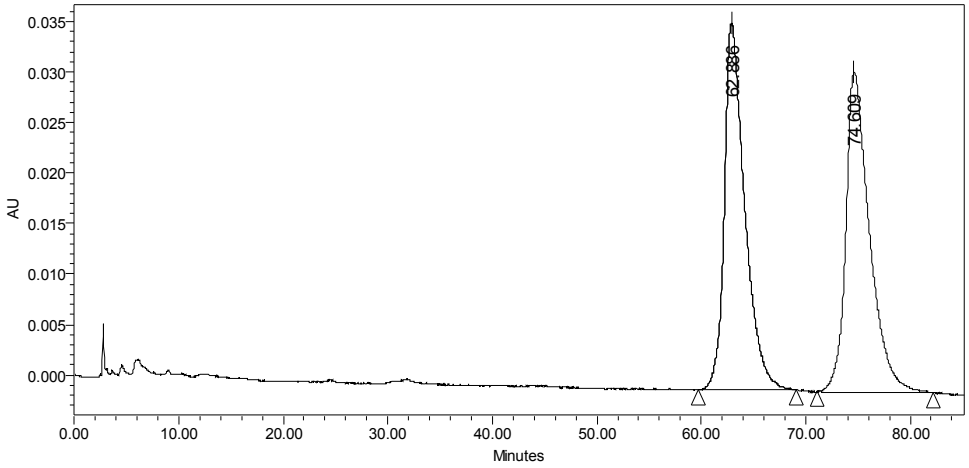


	Name	Retention Time	Area	% Area	Height	Int Type
1		21.025	1891443	2.02	64208	bb
2		23.480	91780163	97.98	2552433	bb

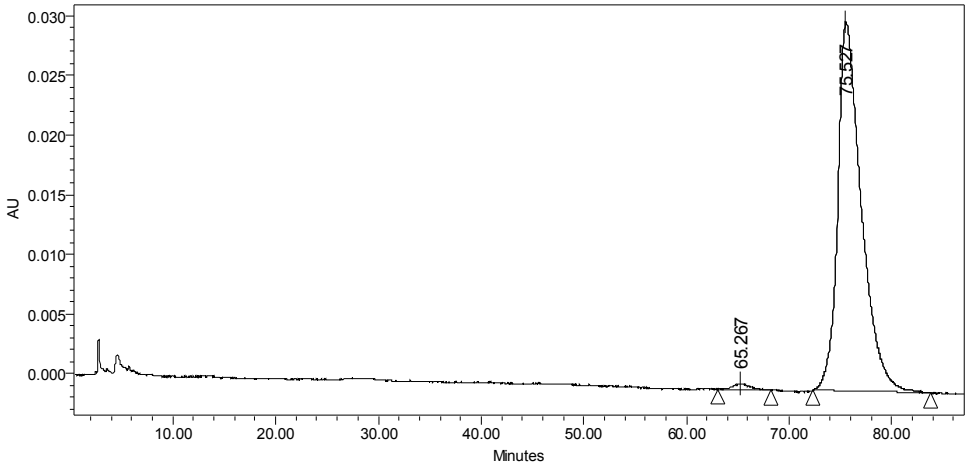


(*S*)-6-[(*S*)-Iodo(phenyl)methyl]tetrahydro-*2H*-pyran-2-one (8a). Isolated 0.028 g (89%) of **8a** as white solid: mp 97 °C (decomposition); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.47–7.44 (comp, 2 H), 7.35–7.26 (comp, 3 H), 5.07 (d, *J* = 6.3 Hz, 1 H), 4.40 (ddd, *J* = 9.3, 6.0, 2.7 Hz, 1 H), 2.66–2.56 (m, 1 H), 2.50–2.39 (m, 1 H), 1.98–1.80 (m, 3 H), 1.61–1.48 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.4, 139.7, 128.8, 128.5, 128.5, 82.9, 34.4, 29.4, 26.9, 18.1; IR (neat) 2955, 1735, 1234, 1052 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{12}H_{13}INaO_2]^+$ (M+Na), 338.9852; found 338.9850; $[\alpha]^{24}_D$ +203 (c = 1.0, $CHCl_3$); HPLC (230 nm): Whelk-O1 (20% *i*-PrOH / hexanes, 1.2 mL/min) 65.3 min (minor), 75.5 min (major); 99:1 er.

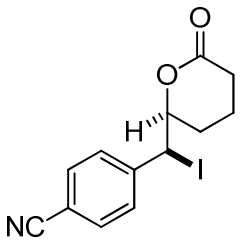
Racemic:



Enantiomeric:

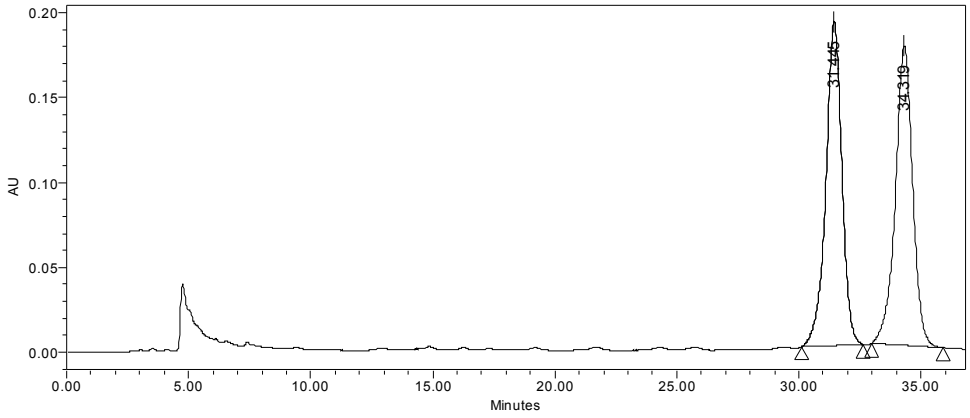


	Retention Time	Area	% Area	Height	Int Type
1	65.267	53655	1.08	474	bb
2	75.527	4927341	98.92	30903	bb

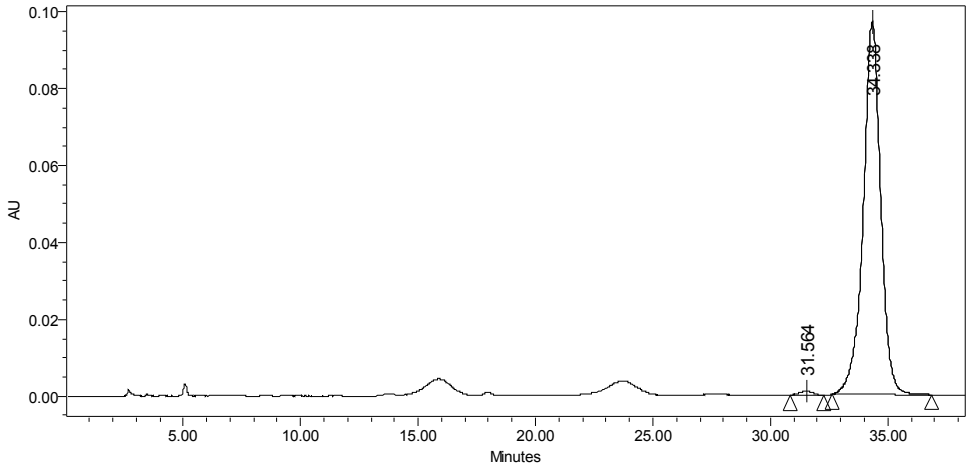


4-{(*S*)-Iodo[(*S*)-6-oxotetrahydro-*2H*-pyran-2-yl]methyl}benzonitrile (8b). Isolated 0.030 g (88%) of **8b** as semi-solid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.62 (m, 4 H), 5.07 (d, *J* = 4.8 Hz, 1 H), 4.40 (ddd, *J* = 7.8, 4.8, 3.0 Hz, 1 H), 2.69–2.59 (m, 1 H), 2.53–2.42 (m, 1 H), 2.05–1.86 (m, 3 H), 1.72–1.58 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.0, 145.0, 132.5, 129.5, 118.2, 112.3, 81.8, 32.6, 29.4, 27.6, 18.1; IR (neat) 2958, 2228, 1740, 1236, 1056 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{13}H_{12}INNaO_2]^+$ (M+Na), 363.9805; found 363.9808; $[\alpha]^{24}_D$ +123 (c = 1.0, $CHCl_3$); HPLC (239 nm): Whelk-O1 (3% CH_3CN, 20% *i*-PrOH / hexanes, 1.2 mL/min) 31.6 min (minor), 34.3 min (major); 99:1 er.

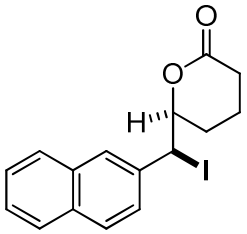
Racemic:



Enantiomeric:

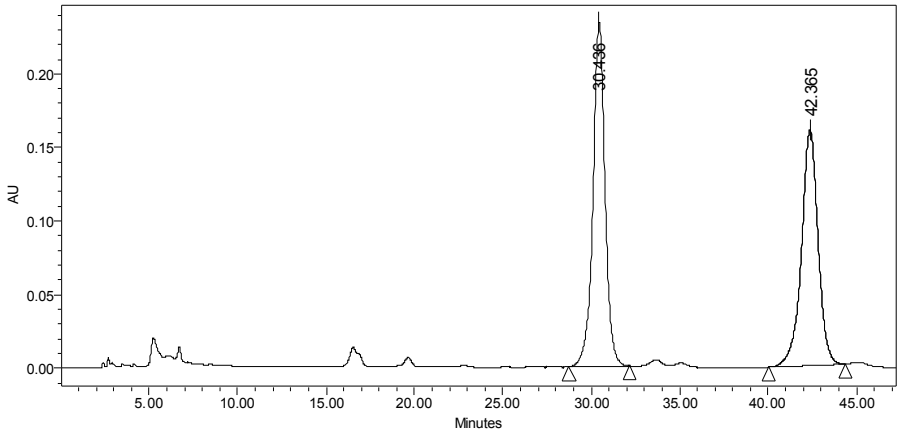


	Retention Time	Area	% Area	Height	Int Type
1	31.564	36009	0.71	917	bb
2	34.338	5037000	99.29	96940	bb

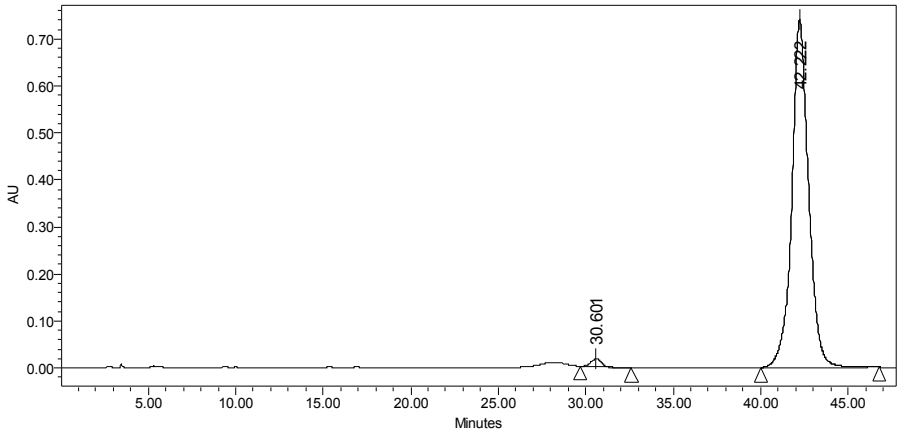


(*S*)-6-[(*S*)-Iodo(naphthalene-2-yl)methyl]tetrahydro-*2H*-pyran-2-one (8c). Isolated 0.034 g (93%) of **8c** as white solid: mp 85 °C (decomposition); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.84–7.80 (comp, 4 H), 7.59 (dd, *J* = 8.4, 1.8 Hz, 1 H), 7.52–7.48 (comp, 2 H), 5.25 (d, *J* = 6.3 Hz, 1 H), 4.53 (ddd, *J* = 9.6, 6.6, 3.0 Hz, 1 H), 2.67–2.57 (m, 1 H), 2.51–2.40 (m, 1 H), 1.97–1.80 (m, 3 H), 1.64–1.51 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.4, 137.0, 133.1, 132.9, 128.9, 128.0, 127.7, 126.8, 126.7, 126.7, 126.3, 82.9, 34.9, 29.4, 27.0, 18.1; IR (neat) 2958, 1740, 1234, 1055, 751 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{16}H_{15}INaO_2]^+$ (M+Na), 389.0009; found 389.0011; $[\alpha]^{23}_D$ +155 (c = 1.0, $CHCl_3$); HPLC (226 nm): Whelk-O1 (3% CH_3CN, 20% *i*-PrOH / hexanes, 1.2 mL/min) 30.6 min (minor), 42.2 min (major); 98.5:1.5 er.

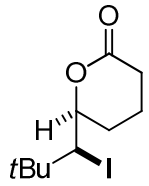
Racemic:



Enantiomeric:

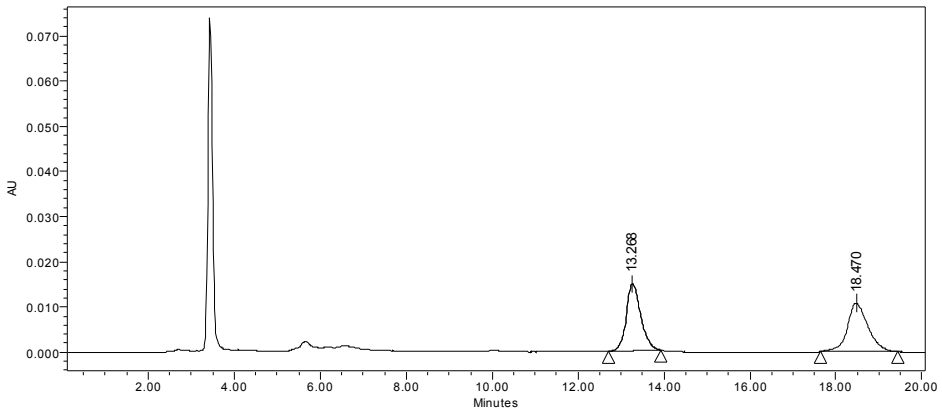


	Name	Retention Time	Area	% Area	Height	Int Type
1		30.601	728584	1.45	16994	bb
2		42.222	49463828	98.55	739456	bb

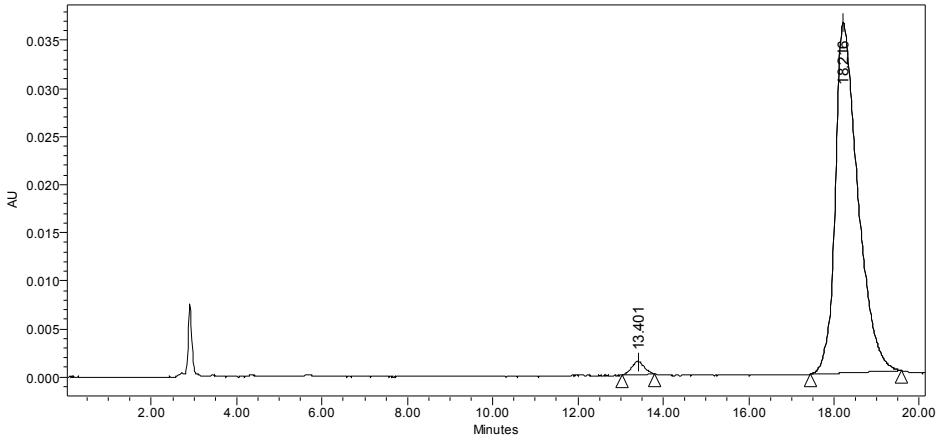


(*R*)-6-[(*R*)-1-Iodo-2,2-dimethylpropyl]tetrahydro-2*H*-pyran-2-one (8d). Isolated 0.029 (98%) of **8d** as a clear, colorless oil. ^{1}H NMR (300 MHz; $CDCl_3$): δ 4.03 (d, *J* = 1.0 Hz, 1 H), 3.96 (dd, *J* = 10.2, 3.4 Hz, 1 H), 2.67–2.58 (m, 1 H), 2.53–2.41 (m, 1 H), 2.09–1.78 (comp, 4 H), 1.21 (s, 9 H); ^{13}C NMR (75 MHz; $CDCl_3$): δ 170.5, 78.5, 58.2, 36.6, 31.1, 29.96, 29.91, 18.5; IR (neat) 2959, 1737, 1240, 1177 cm^{-1}; HRMS (CI) *m/z* calcd for $[C_{10}H_{18}O_2I]^+$ (M+H), 297.0352; found 297.0354; $[\alpha]^{23}_D$ –17 (c = 1.0, $CHCl_3$); HPLC (254 nm): Whelk-O1 (20% *i*-PrOH / hexanes, 1.2 mL/min) 13.4 min (minor), 18.2 min (major); 98:2 er.

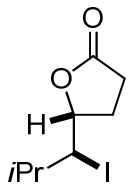
Racemic:



Enantiomeric:

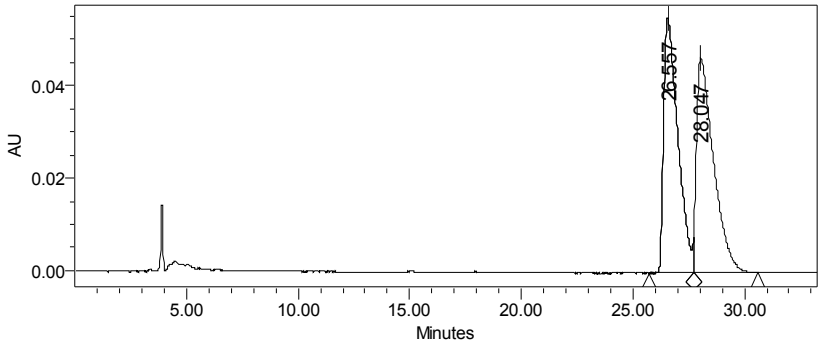


	Retention Time	Area	% Area	Height	Int Type
1	13.401	28276	2.07	1352	bb
2	18.216	1339975	97.93	36429	bb

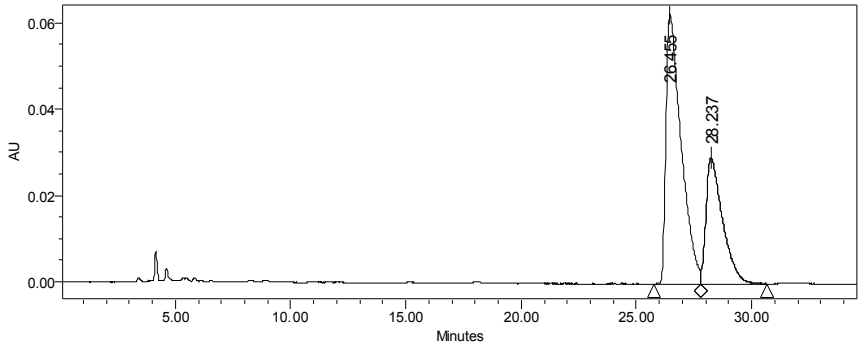


(*R*)-5-[(*S*)-1-Iodo-2-methylpropyl]dihydrofuran-2(*3H*)-one (10a). Isolated 0.021 g (78%) of **10a** as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.66–4.58 (m, 1 H), 4.08 (dd, *J* = 10.0, 2.8 Hz, 1 H), 2.64–2.45 (comp, 3 H), 2.23–2.16 (m, 1 H), 1.57–1.45 (m, 1 H), 0.97 (d, *J* = 6.4 Hz, 3 H), 0.92 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.6, 80.6, 51.4, 30.1, 29.9, 29.1, 23.6, 19.0; IR (neat) 1783 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_8H_{13}INaO_2]^+$ (M+Na), 290.9852; found 290.9851; $[\alpha]^{23}_D$ +14.0 (c = 0.5, $CHCl_3$); HPLC (259 nm): OD-H (0.75% *i*-PrOH / hexanes, 1.0 mL/min) 26.5 min (major), 28.2 min (minor); 67:33 er.

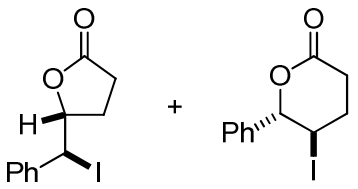
Racemic:



Enantiomeric:

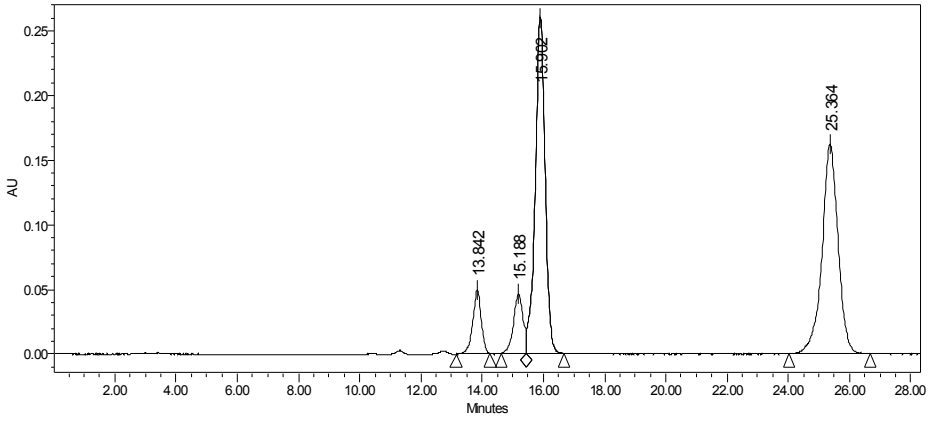


	Name	Retention Time	Area	% Area	Height	Int Type
1		26.455	2875482	66.36	62425	bv
2		28.237	1457571	33.64	29208	vb

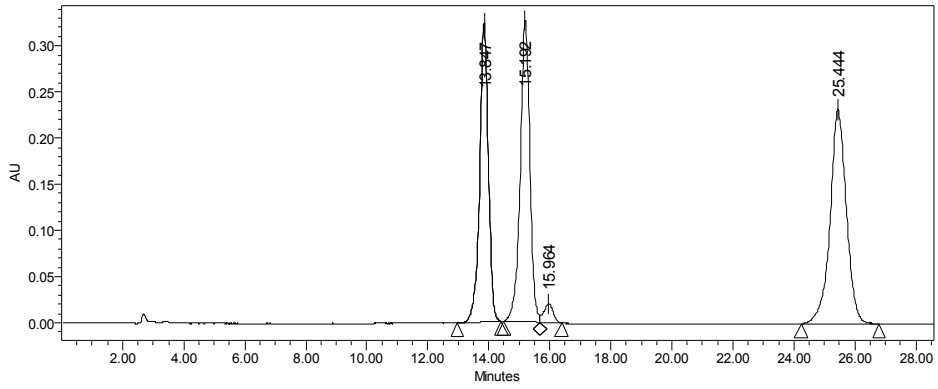


(*R*)-5-[(*S*)-Iodo(phenyl)methyl]dihydrofuran-2(*3H*)-one (10b) and **(5*R*, 6*S*)-5-Iodo-6-phenyltetrahydro-2*H*-pyran-2-one (11b).** Isolated 0.027 g (89%) of **10b** and **11b** as a white solid, and the yields of **10b** and **11b** were based on NMR integrals: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.43–7.39 (comp, 2.4 H), 7.34–7.26 (comp, 2.6 H), 5.56 (d, *J* = 8.0 Hz, 0.4 H), 5.12 (d, *J* = 8.0 Hz, 0.6 H), 4.92–4.87 (m, 0.6 H), 4.42 (ddd, *J* = 8.0, 8.0, 4.4 Hz, 0.4 H), 2.90–2.82 (m, 0.4 H), 2.76–2.65 (m, 0.4 H), 2.65–2.62 (m, 0.4 H), 2.62–2.53 (comp, 1.2 H), 2.50–2.39 (comp, 1.2 H), 2.20–2.10 (m, 0.4 H); HPLC (214 nm): Whelk-O1 (3% CH_3CN, 20% *i*-PrOH / hexanes, 1.2 mL/min) **10b**: 13.8 min (minor), 15.2 (major); 52:48 er; **11b**: 16.0 min (minor), 25.4 min (major); 95:5 er.

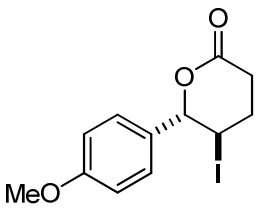
Racemic:



Enantiomeric:

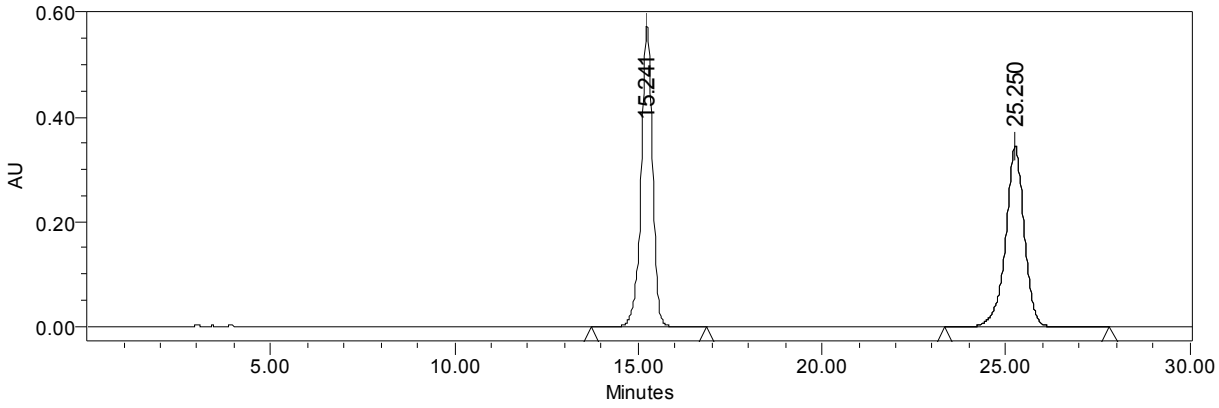


	Retention Time	Area	% Area	Height	Int Type
1	13.847	6430258	28.51	324294	bb
2	15.192	7087469	31.43	326686	bv
3	15.964	429636	1.91	20161	vb
4	25.444	8603098	38.15	231936	bb

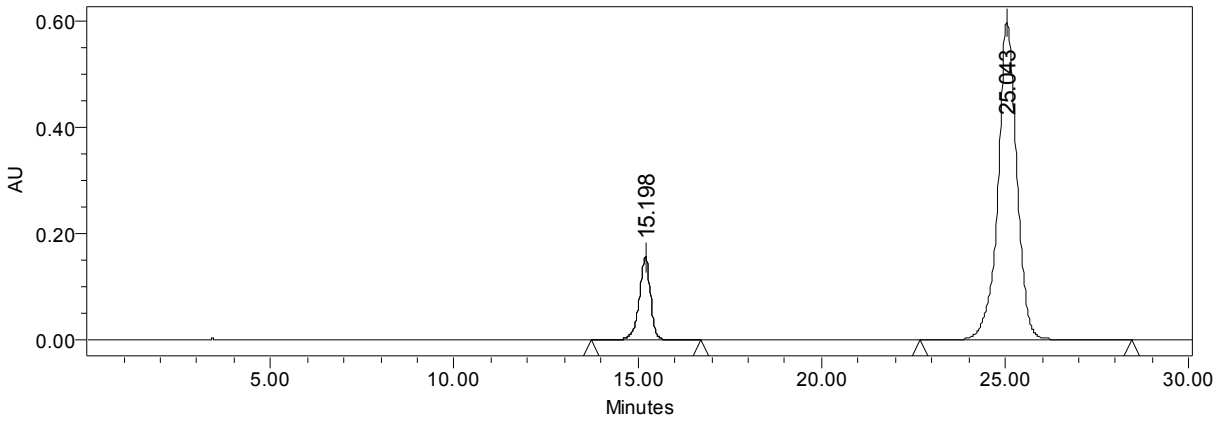


(5*R*,6*S*)-5-Iodo-6-(4-methoxyphenyl)tetrahydro-*2H*-pyran-2-one (11c). Isolated 0.030 g (89%) of **11c** as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28–7.22 (m, 2 H), 6.94–6.88 (m, 2 H), 5.48 (d, *J* = 8.2 Hz, 1 H), 4.39 (app dt, *J* = 8.2, 4.8 Hz, 1 H), 3.82 (s, 3 H), 2.87–2.78 (m, 1 H), 2.74–2.65 (m, 1 H), 2.55–2.35 (comp, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.4, 160.1, 129.8, 128.2, 114.0, 86.8, 55.3, 31.0, 30.7, 24.8; IR (neat) 1738 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{12}H_{14}O_3I]^+$ (M+H), 332.9988; found 332.9982; HPLC (229 nm): Whelk-O1 (6% CH_3CN, 20% *i*-PrOH / hexanes, 1.2 mL/min) 15.2 min (minor), 25.0 min (major); 86.5:13.5 er.

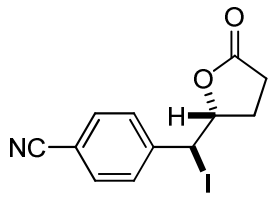
Racemic:



Enantiomeric:

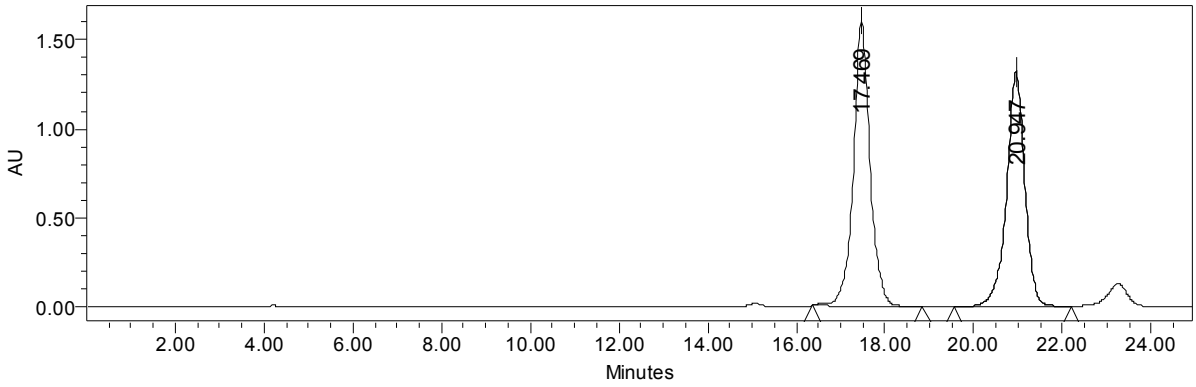


	Retention Time	Area	% Area	Height	Int Type
1	15.198	3298979	13.50	155763	bb
2	25.043	21129997	86.50	596482	bb

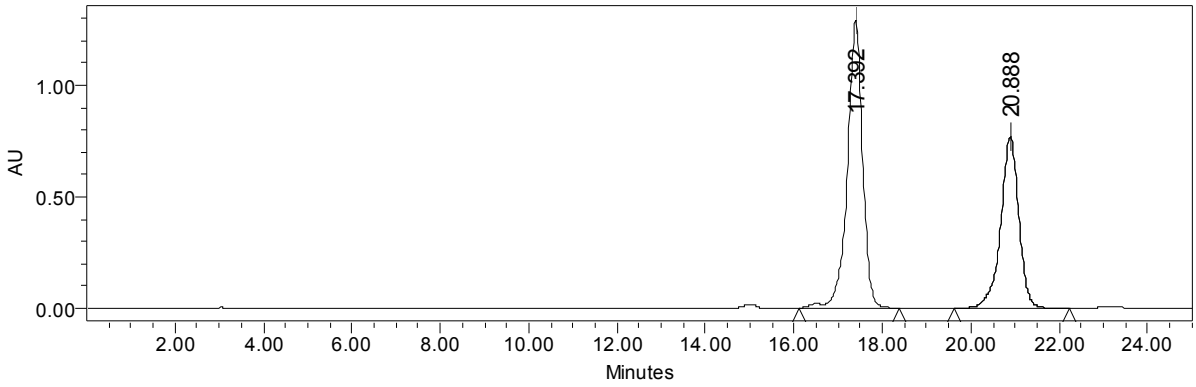


4-{(*S*)-Iodo[(*R*)-5-oxotetrahydrofuran-2-yl]methyl}benzonitrile (10d). Reaction run in 1:1 CH_2Cl_2/tol for 14 h at –20 °C and 48 h at –10 °C on a 0.1 mmol scale, to give 0.031 g (94%) of **10d** as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.64–7.60 (m, 2 H), 7.54–7.49 (m, 2 H), 5.02 (d, J = 9.2 Hz, 1 H), 5.02–4.92 (m, 1 H), 2.77–2.67 (m, 1 H), 2.65–2.58 (comp, 2 H), 2.18–2.06 (m, 1 H); ^{13}C NMR ($CDCl_3$, 10 MHz) δ 175.6, 144.7, 132.7, 128.8, 118.2, 112.3, 81.9, 31.1, 29.3, 29.2; IR (neat) 2229, 1778 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{12}H_{11}NO_2I]^+$ (M+H), 327.9835; found 327.9836; $[\alpha]^{25}_D$ +3.0 (c = 0.1, $CHCl_3$); HPLC (239 nm): Whelk-O1 (6% CH_3CN, 20% *i*-PrOH / hexanes, 1.2 mL/min) 17.4 min (major), 20.9 min (minor); 58:42 er.

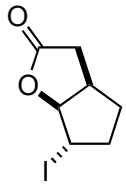
Racemic:



Enantiomeric:

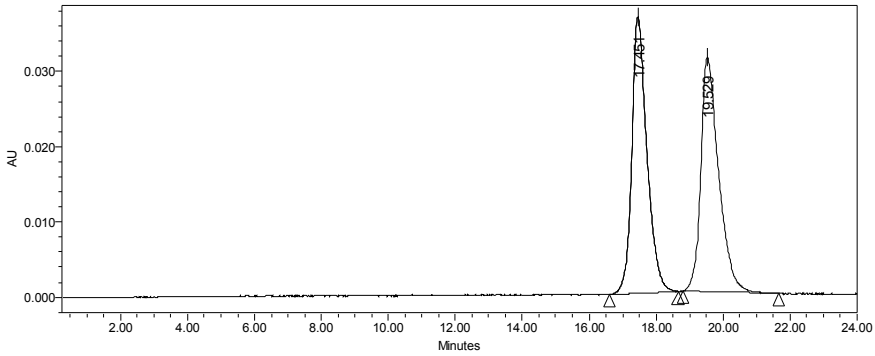


	Retention Time	Area	% Area	Height	Int Type
1	17.392	29957461	57.96	1284830	bb
2	20.888	21728455	42.04	768032	bb

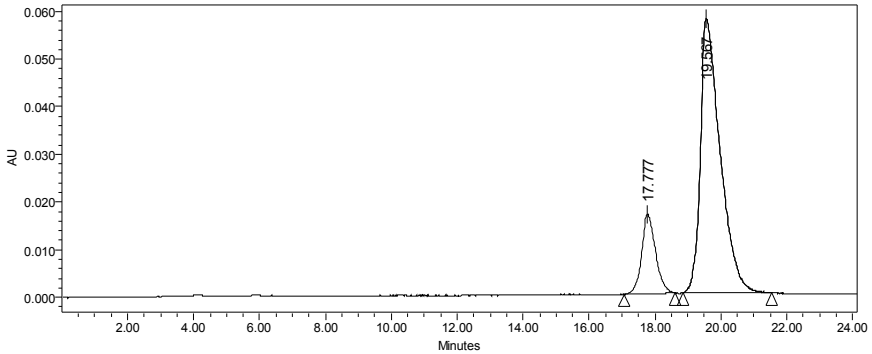


(3a*R*, 6*S*, 6a*S*)-6-Iodohexahydro-2*H*-cyclopenta[*b*]furan-2-one (13). Isolated 0.011 (44%) of **13** as a colorless oil. ^{1}H NMR (400 MHz; $CDCl_3$): δ 5.21 (d, J = 5.6 Hz, 1 H), 4.48 (d, J = 4.4 Hz, 1 H), 3.20–3.14 (m, 1 H), 2.90 (dd, J = 18.4, 10.4 Hz, 1 H), 2.51–2.43 (m, 1 H), 2.38 (dd, J = 18.4, 2.0 Hz, 1 H), 2.20–2.11 (m, 1 H), 2.08–2.03 (m, 1 H), 1.63–1.58 (m, 1 H); ^{13}C NMR (100 MHz; $CDCl_3$): δ 176.6, 92.4, 36.1, 34.6, 32.1, 29.4; IR (neat) 2960, 1778, 1159, 1002 cm^{-1}; HRMS (CI) *m/z* calcd for $[C_7H_{10}O_2I]^+$ $(M+H)^+$, 252.9726; found 252.9728; $[\alpha]^{21}_D$ +25.2 (c = 1.31, CH_2Cl_2); HPLC (260 nm): Whelk-O1 (20% *i*-PrOH / hexanes, 1.2 mL/min) 17.8 min (minor), 19.6 min (major); 83:17 er.

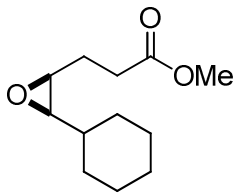
Racemic:



Enantiomeric:

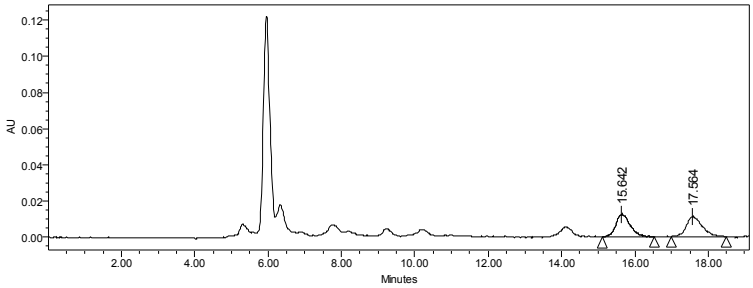


	Retention Time	Area	% Area	Height	Int Type
1	17.777	489414	16.94	16688	bb
2	19.567	2400492	83.06	57485	bb

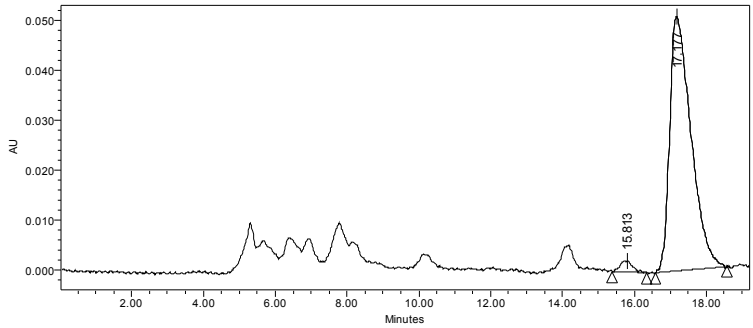


Methyl 3-((2*S*, 3*R*)-3-cyclohexyloxiran-2-yl)propanoate (14). To a stirred solution of **6d** (0.025 g, 0.081 mmol) in MeOH (1.6 mL) at room temperature was added Cs_2CO_3 (0.053 g, 0.162 mmol), and the resulting solution was stirred for 38 h before saturated NH_4Cl solution (2 mL) was added. The mixture was extracted with EtOAc (3 × 5mL), and the combined organic layers were washed with brine (5 mL), dried (Na_2SO_4), filtered, and concentrated. The crude residue was purified by column chromatography, eluting with hexanes/EtOAc (10:1, v/v) to give 0.015 g (87%) of **14** as a clear, colorless oil: ^{1}H NMR (300 MHz; $CDCl_3$): δ 3.70 (s, 3 H), 3.00–2.94 (m, 1 H), 2.68–2.64 (m, 1 H), 2.56–2.49 (comp, 2 H), 2.03–1.92 (comp, 2 H), 1.80–1.68 (comp, 4 H), 1.60–1.59 (m, 1 H), 1.26–1.07 (comp, 6 H); ^{13}C NMR (75 MHz; $CDCl_3$): δ 173.4, 61.9, 56.1, 51.7, 36.5, 31.2, 30.7, 28.9, 26.2, 25.5, 25.4, 23.5; IR (neat) 2927, 2852, 1741, 1449, 1174 cm^{-1}; HRMS (ESI) *m/z* calcd for $[C_{12}H_{20}NaO_3]^+$ $(M+Na)^+$, 235.1305; found 235.1304; $[\alpha]^{25}_D$ –28.7 (c = 0.5, $CHCl_3$); HPLC (214 nm): Whelk-O1 (10% *i*-PrOH / hexanes, 1.2 mL/min) 15.8 min (minor), 17.2 min (major); 97.5:2.5 er.

Racemic:



Enantiomeric:



	Retention Time	Area	% Area	Height	Int Type
1	15.813	55000	2.55	2320	bb
2	17.177	2105995	97.45	51108	bb

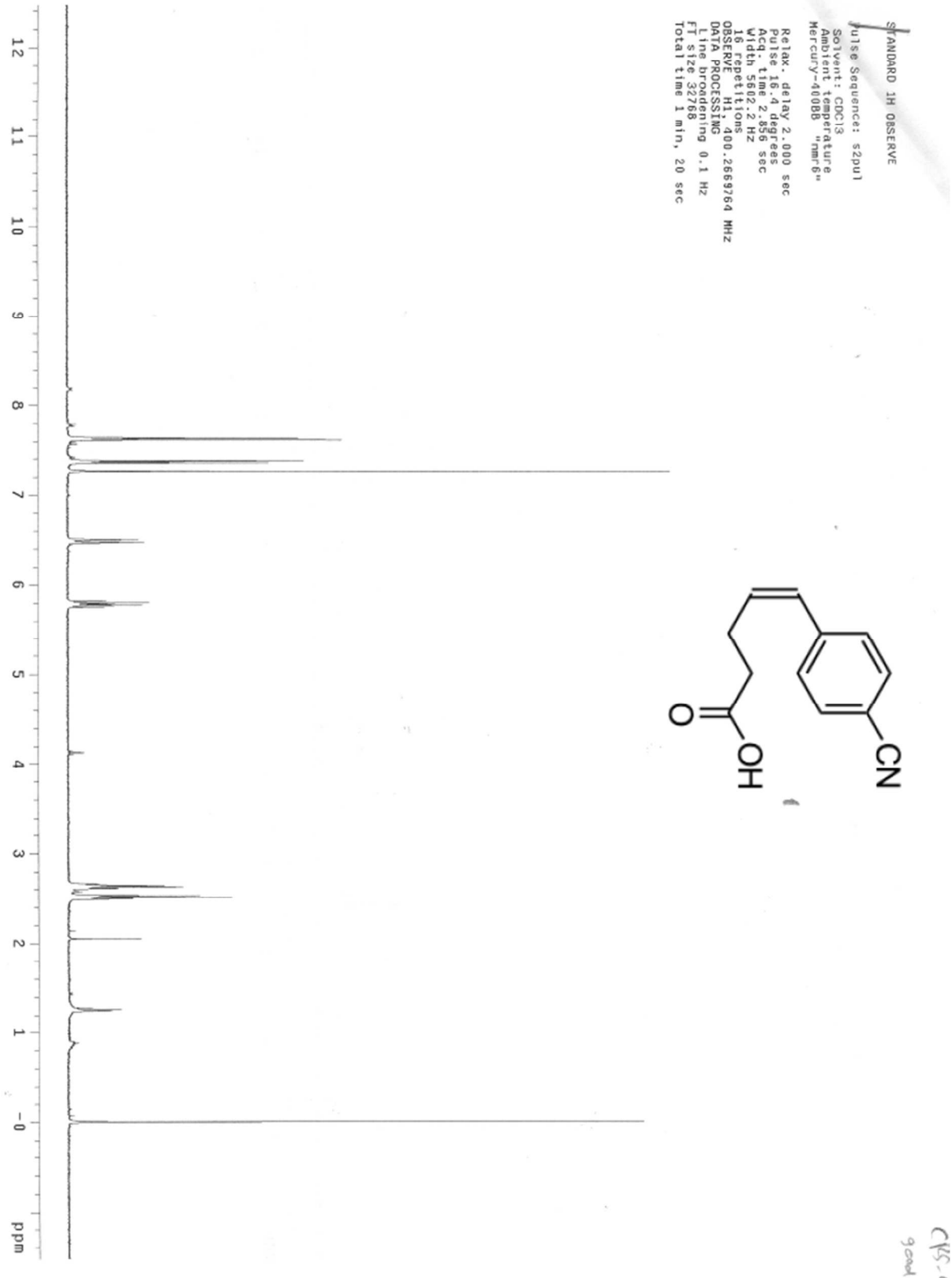


Figure S-1 ^{1}H NMR of Compound 5f

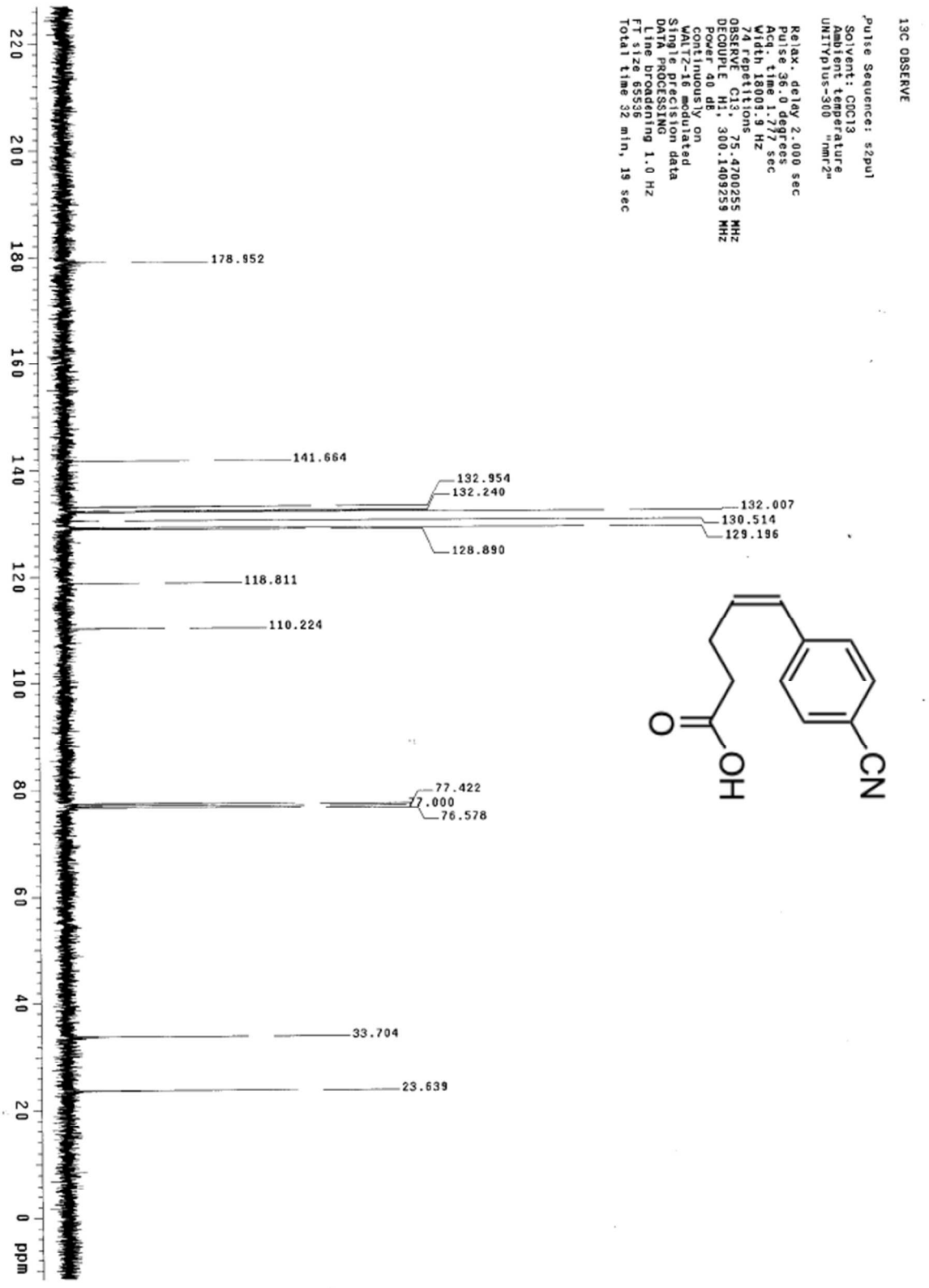


Figure S-2 ^{13}C NMR of Compound 5f

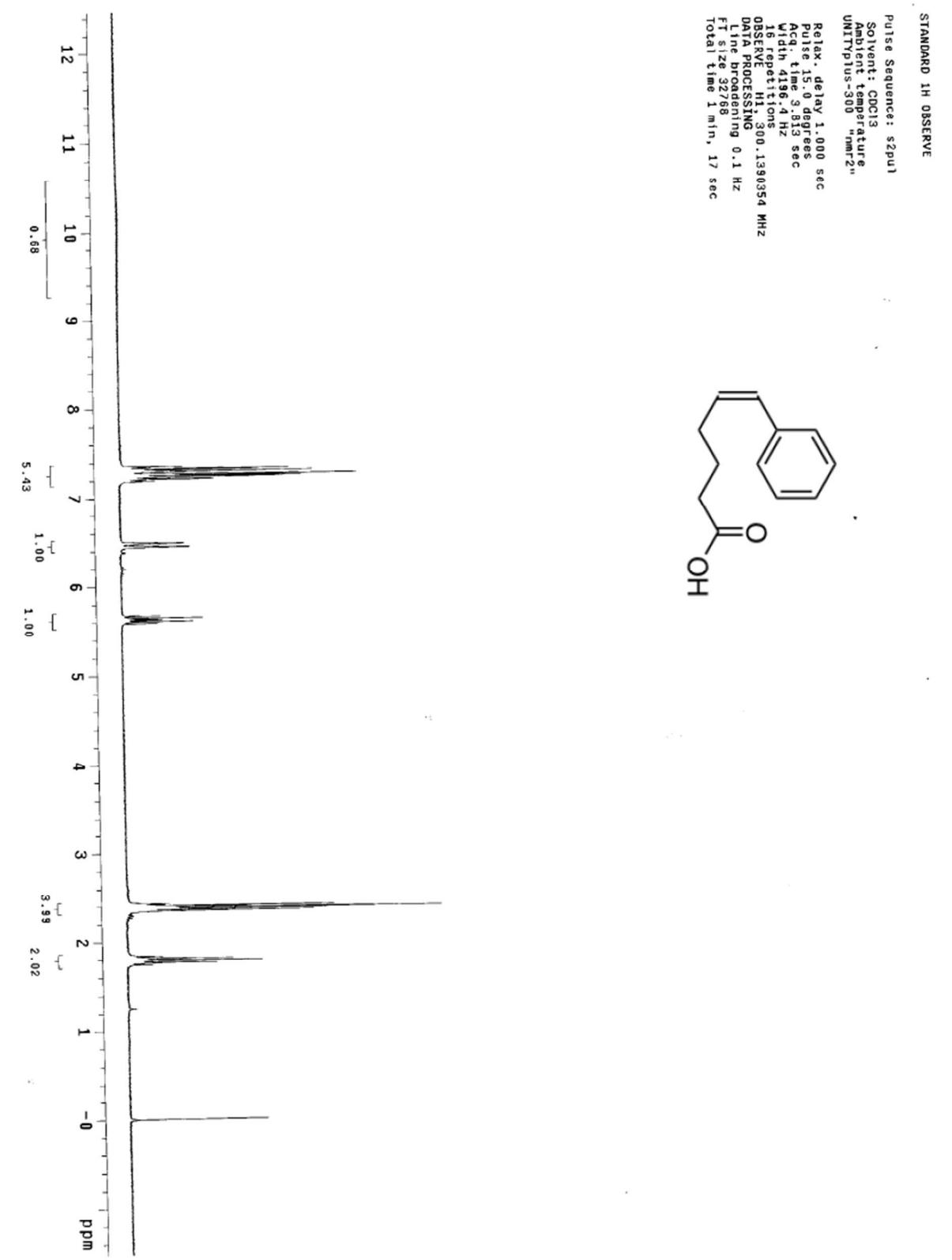


Figure S-3 ^{1}H NMR of Compound 7a

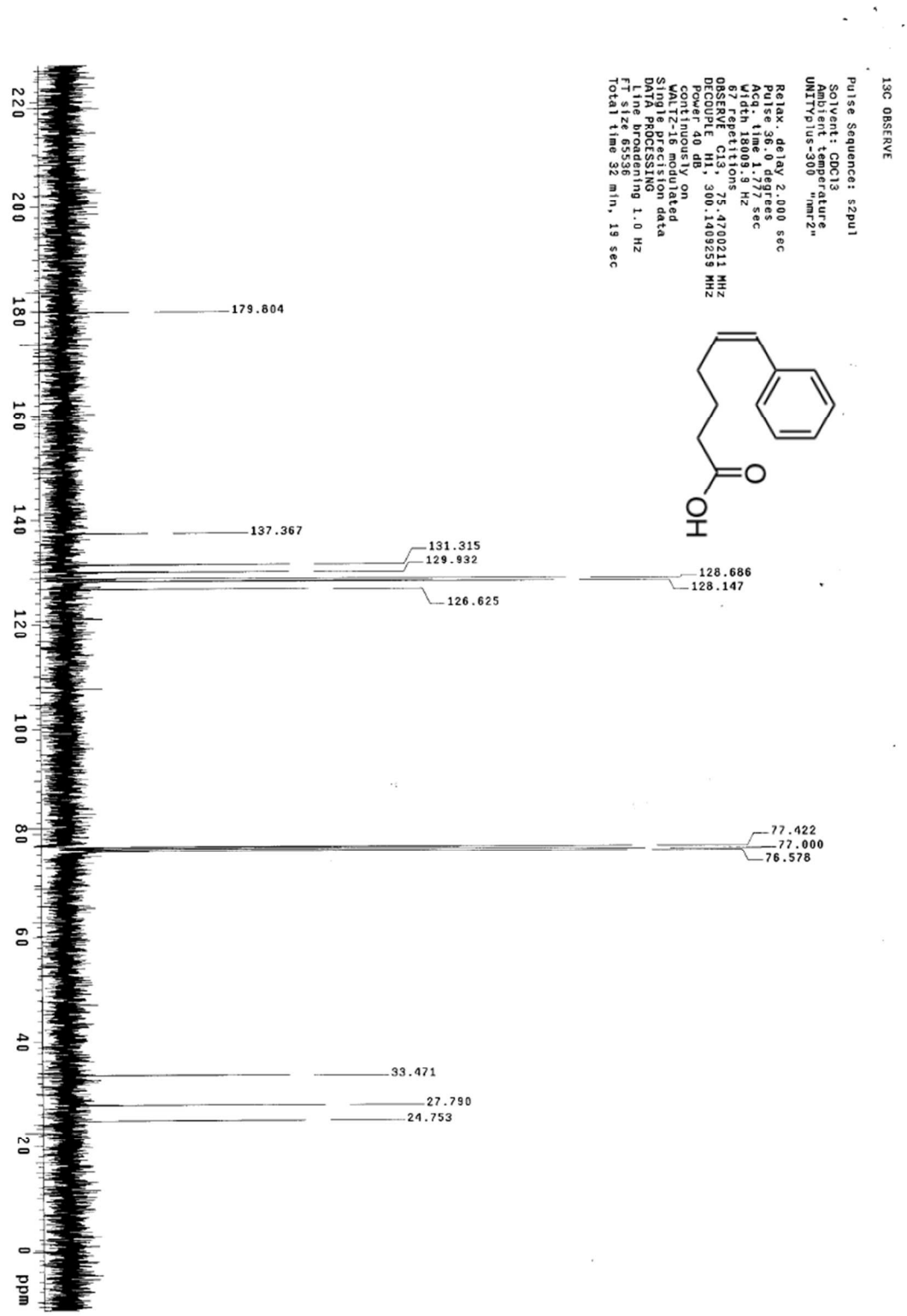


Figure S-4 ^{13}C NMR of Compound 7a

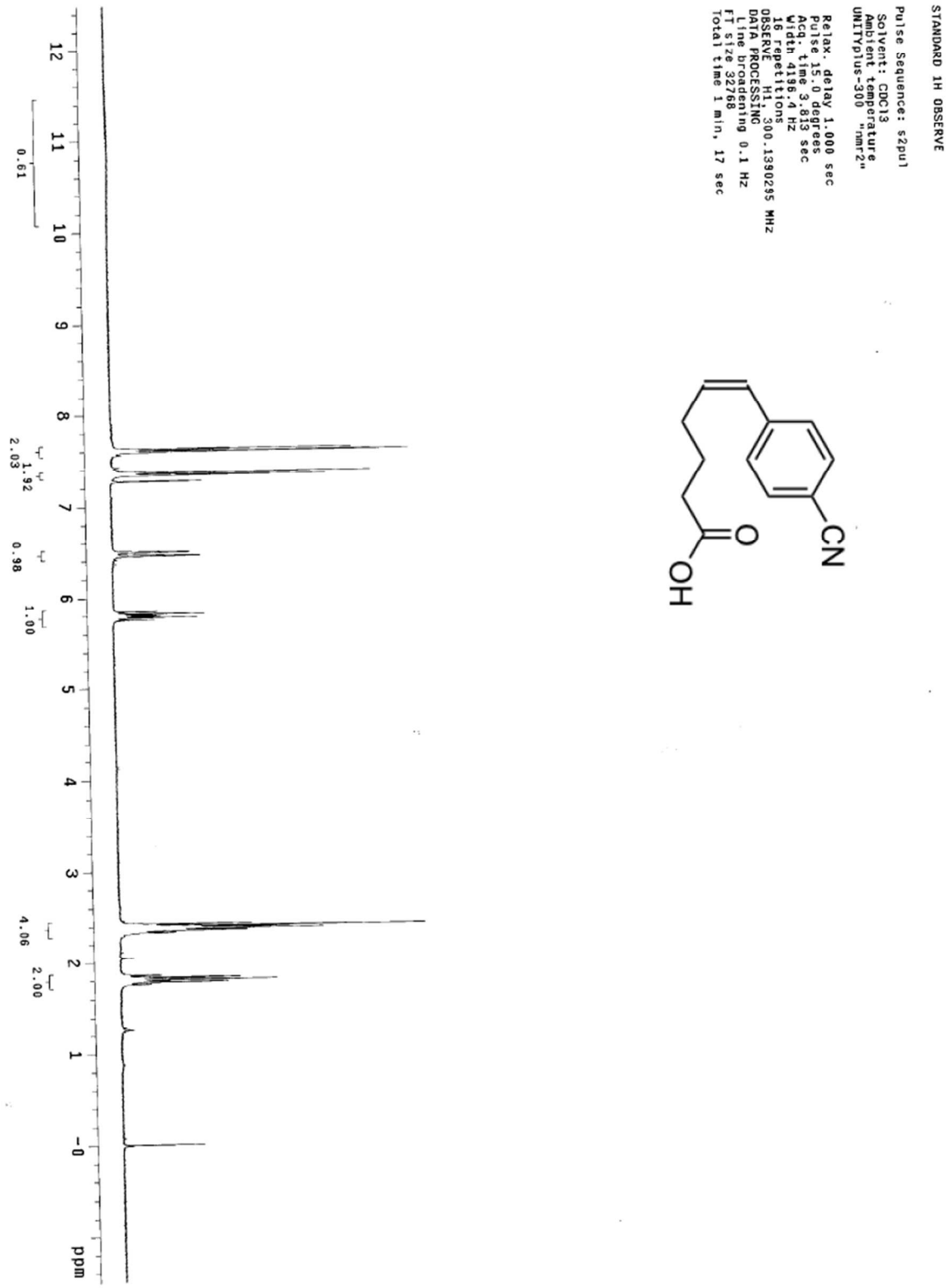


Figure S-5 ^{1}H NMR of Compound 7b

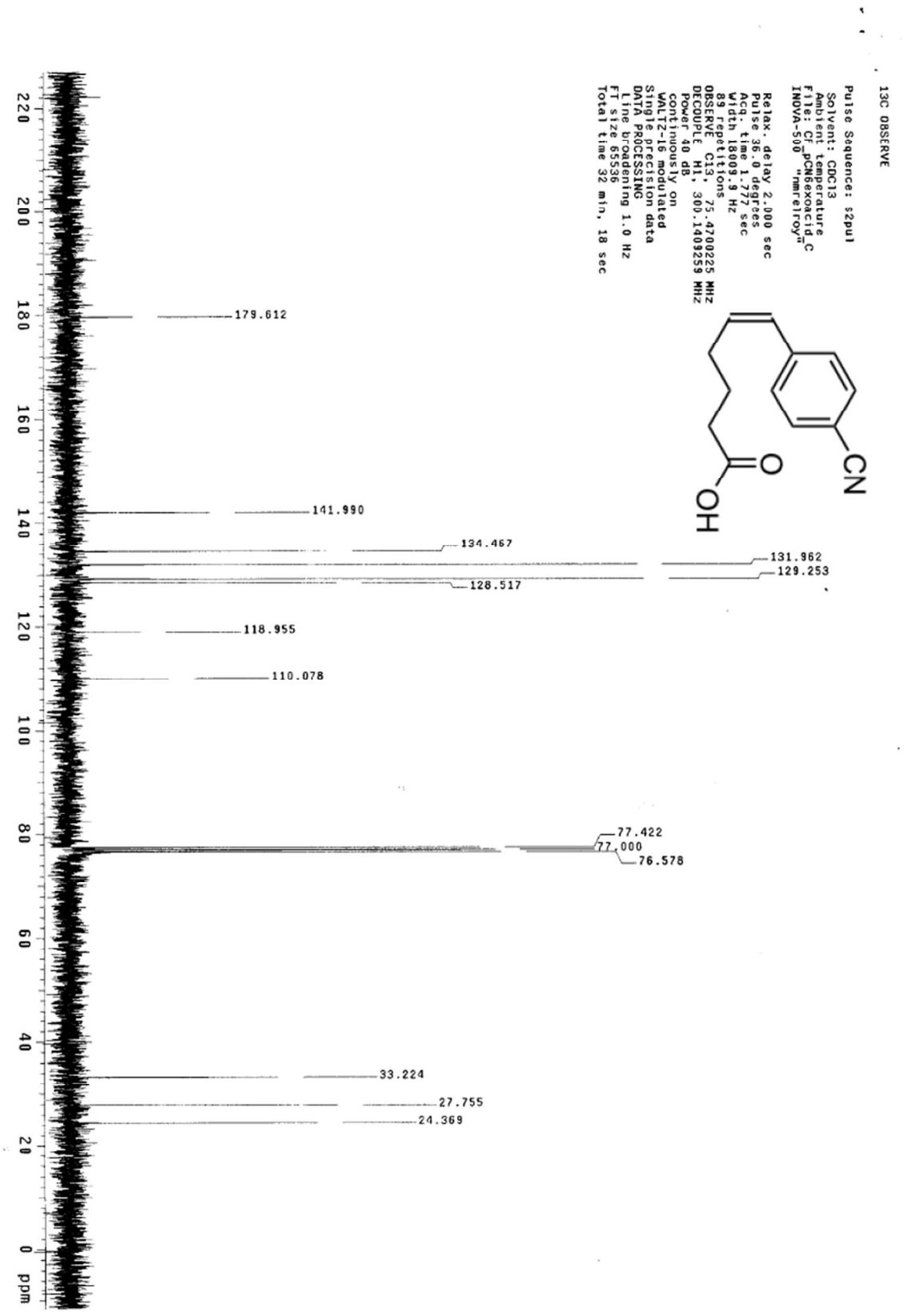


Figure S-6 ^{13}C NMR of Compound 7b

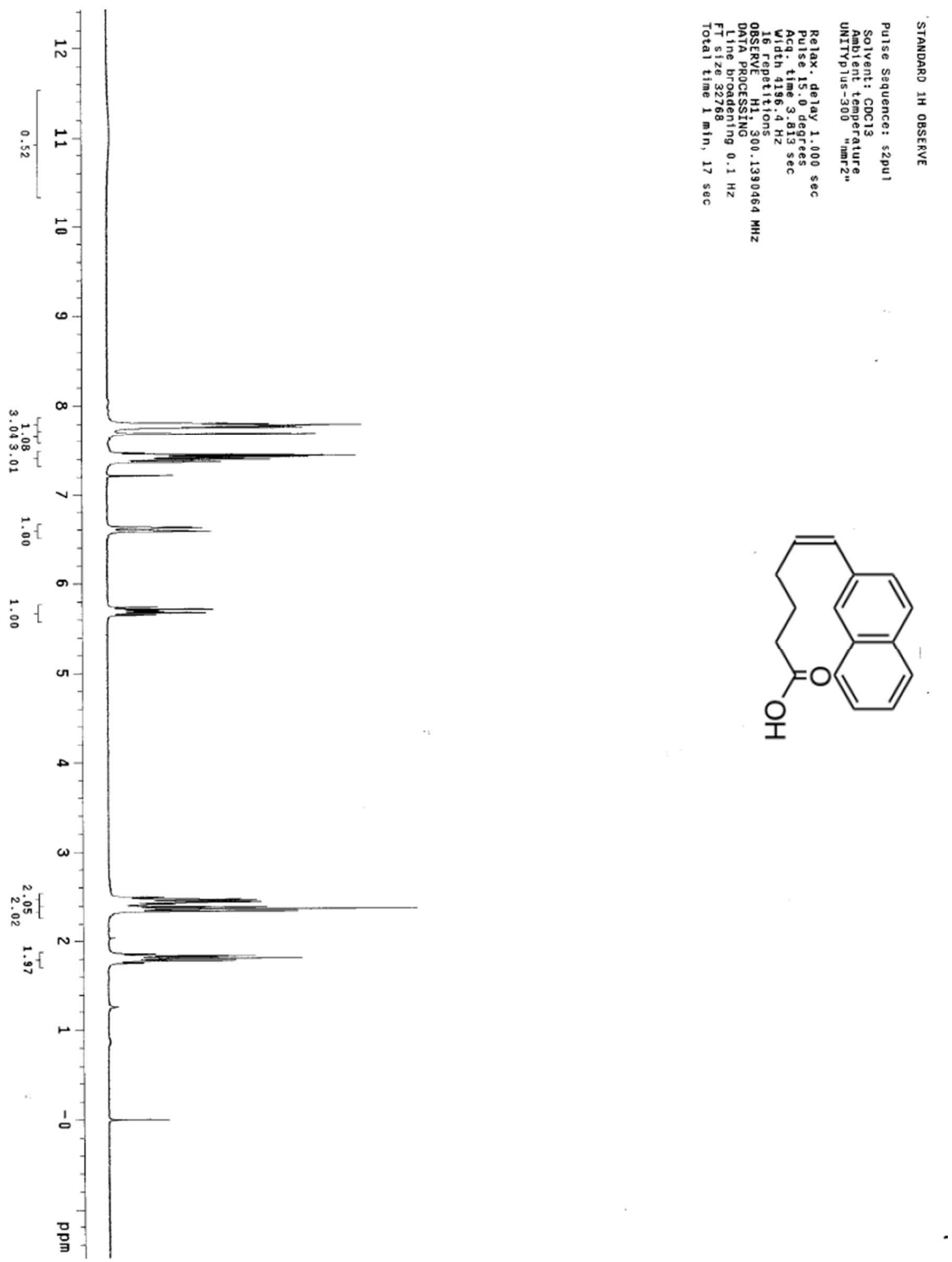


Figure S-7 ^{1}H NMR of Compound 7c

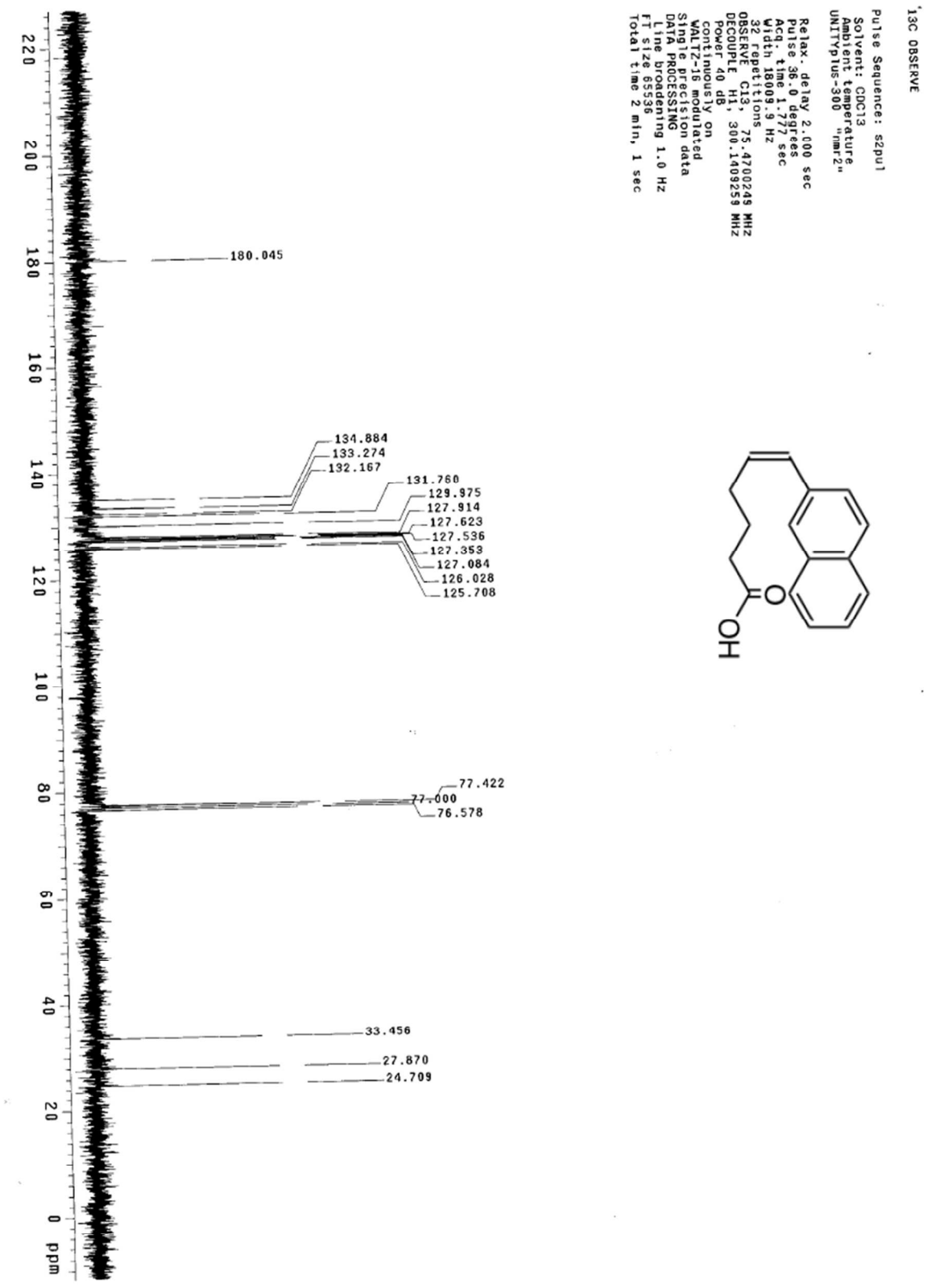


Figure S-8 ^{13}C NMR of Compound 7c

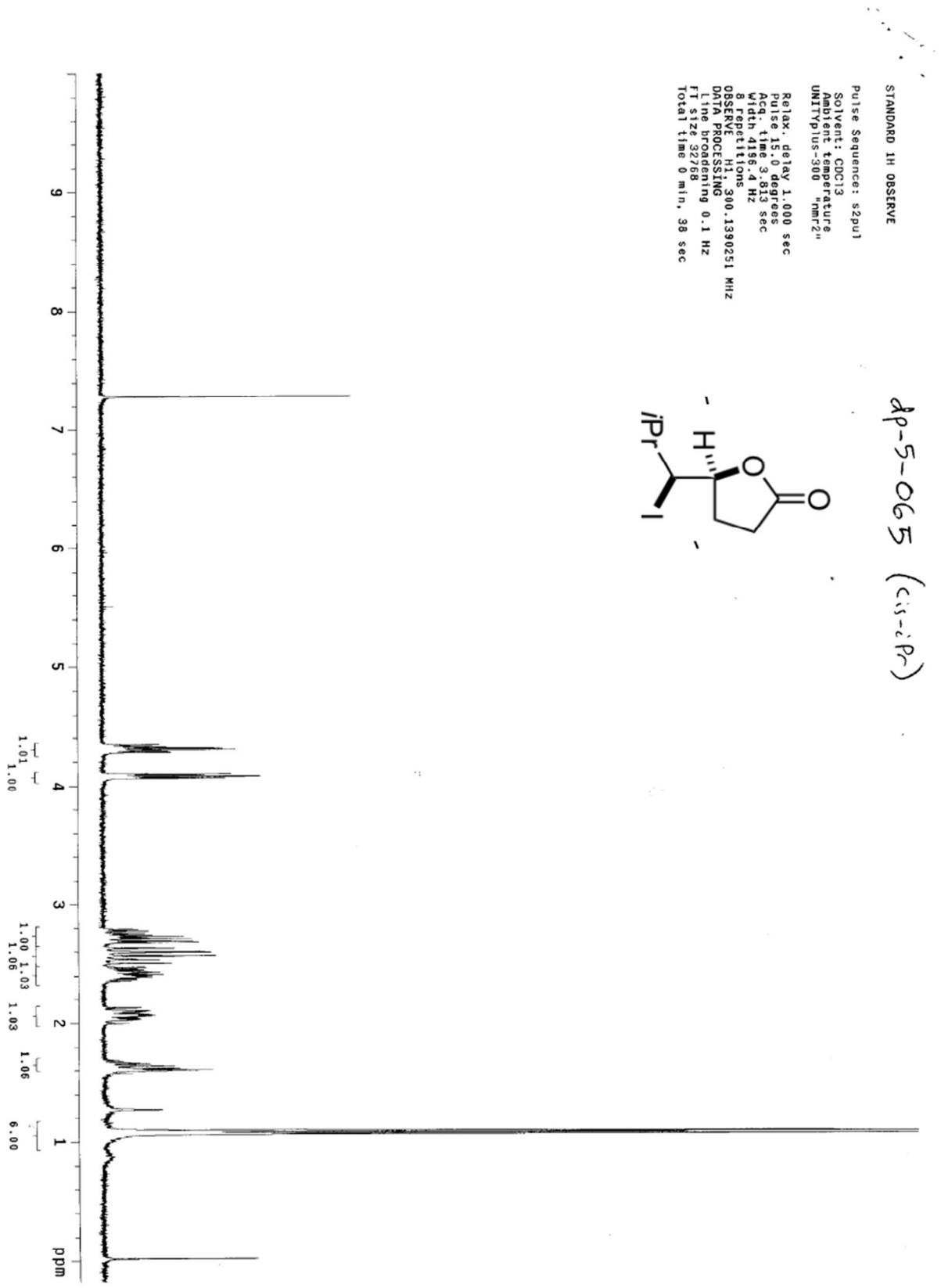


Figure S-9 ^{1}H NMR of Compound 6a

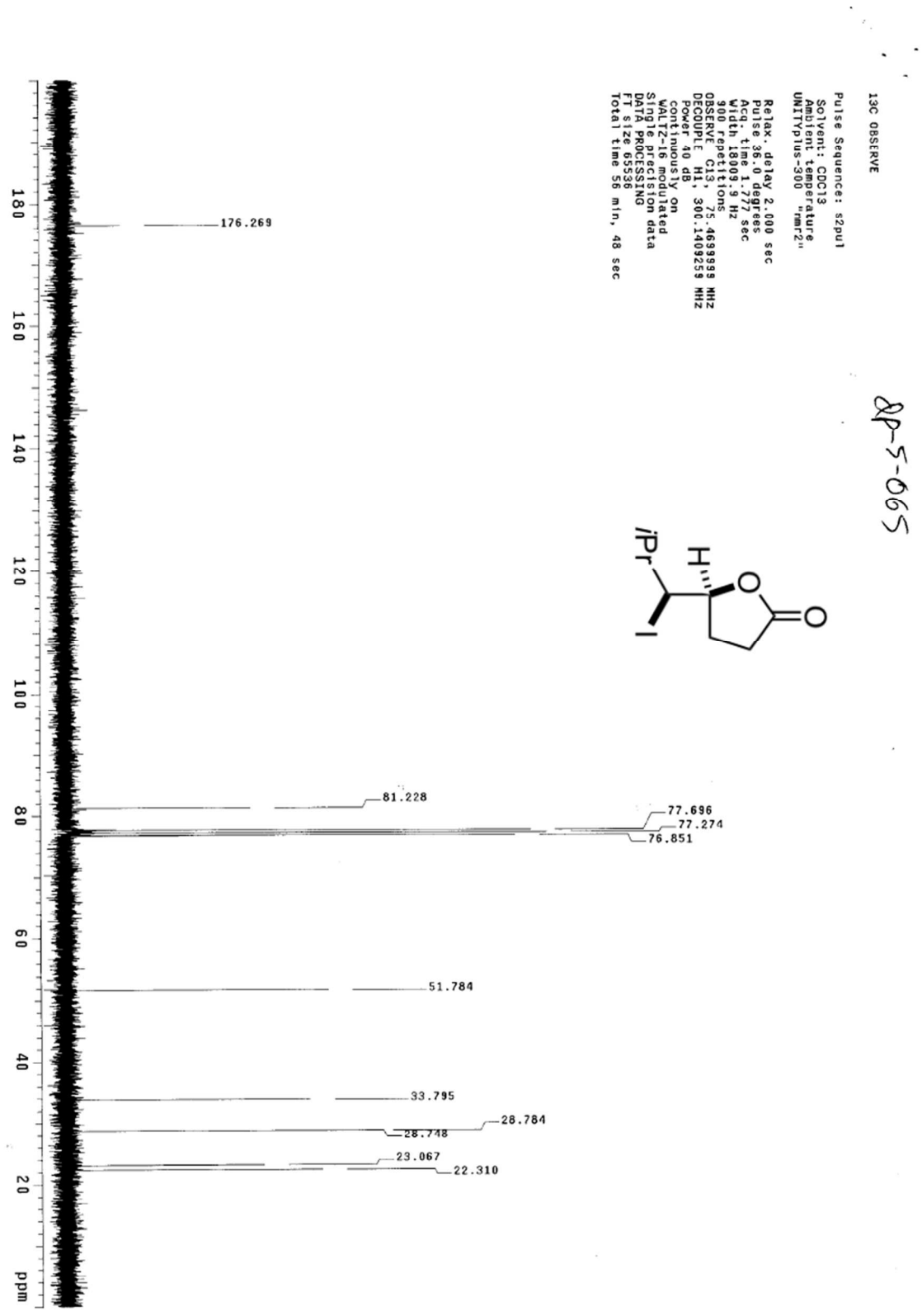


Figure S-10 ^{13}C NMR of Compound 6a

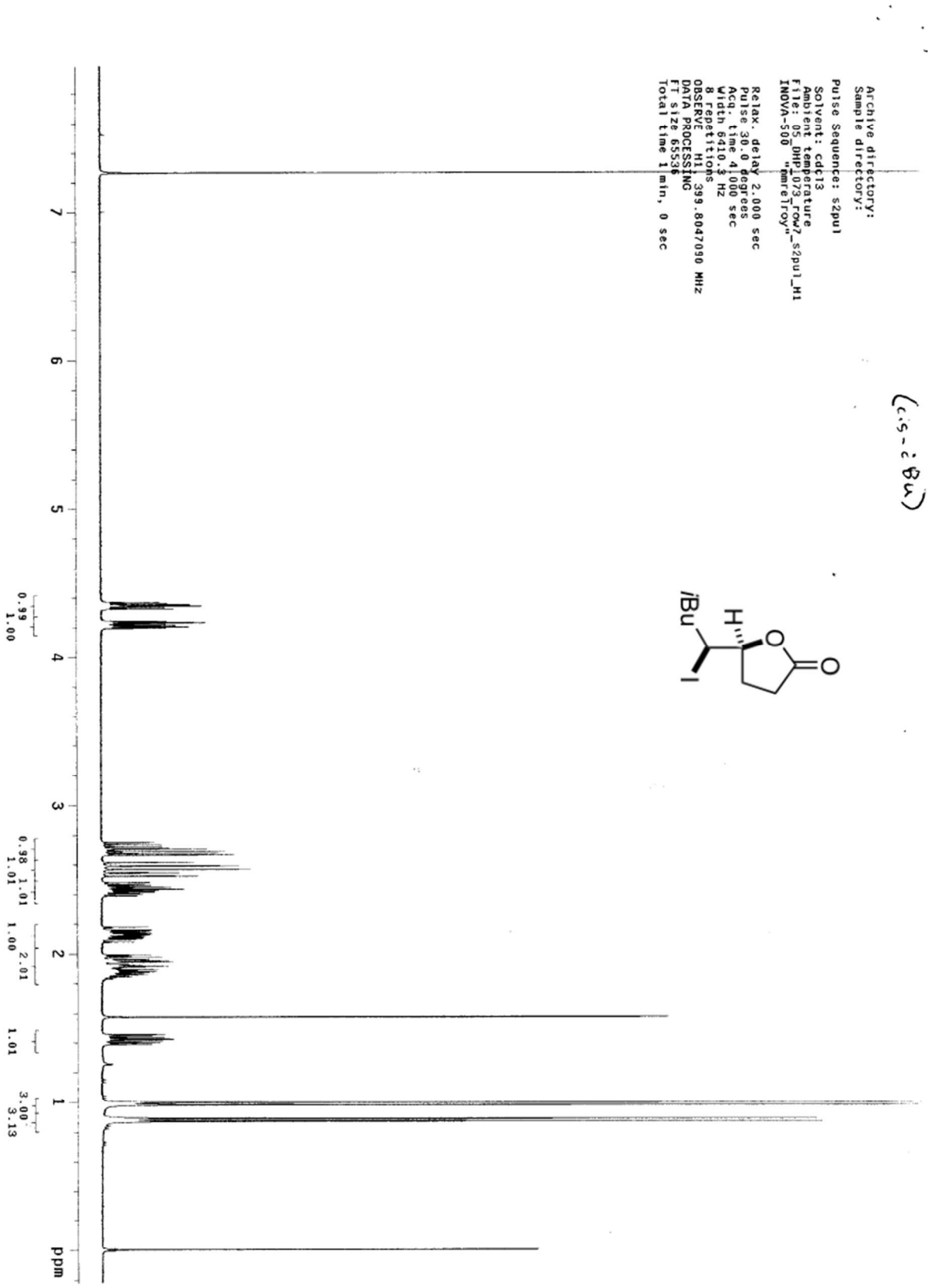


Figure S-11 ^{1}H NMR of Compound 6b

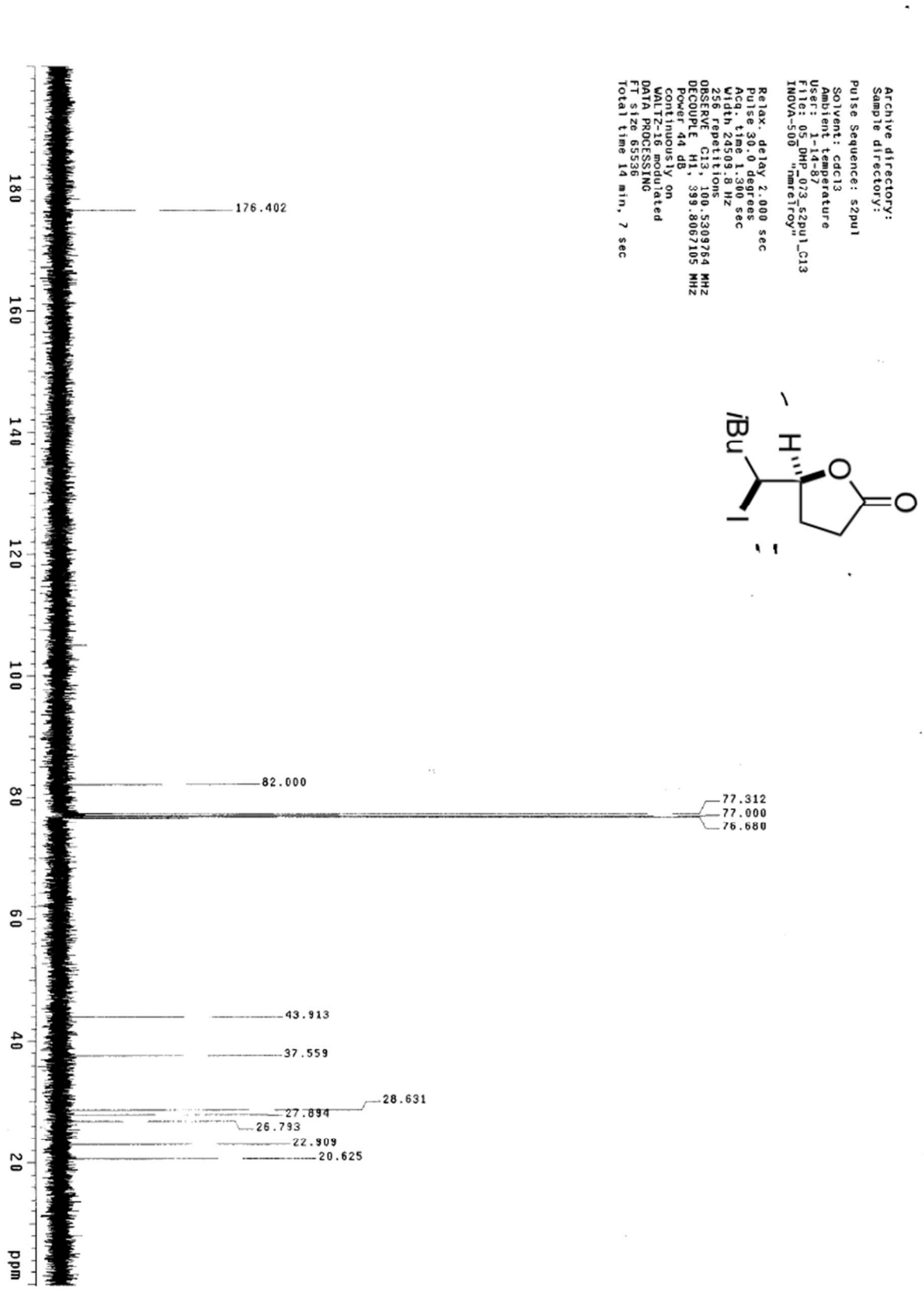


Figure S-12 ^{13}C NMR of Compound 6b

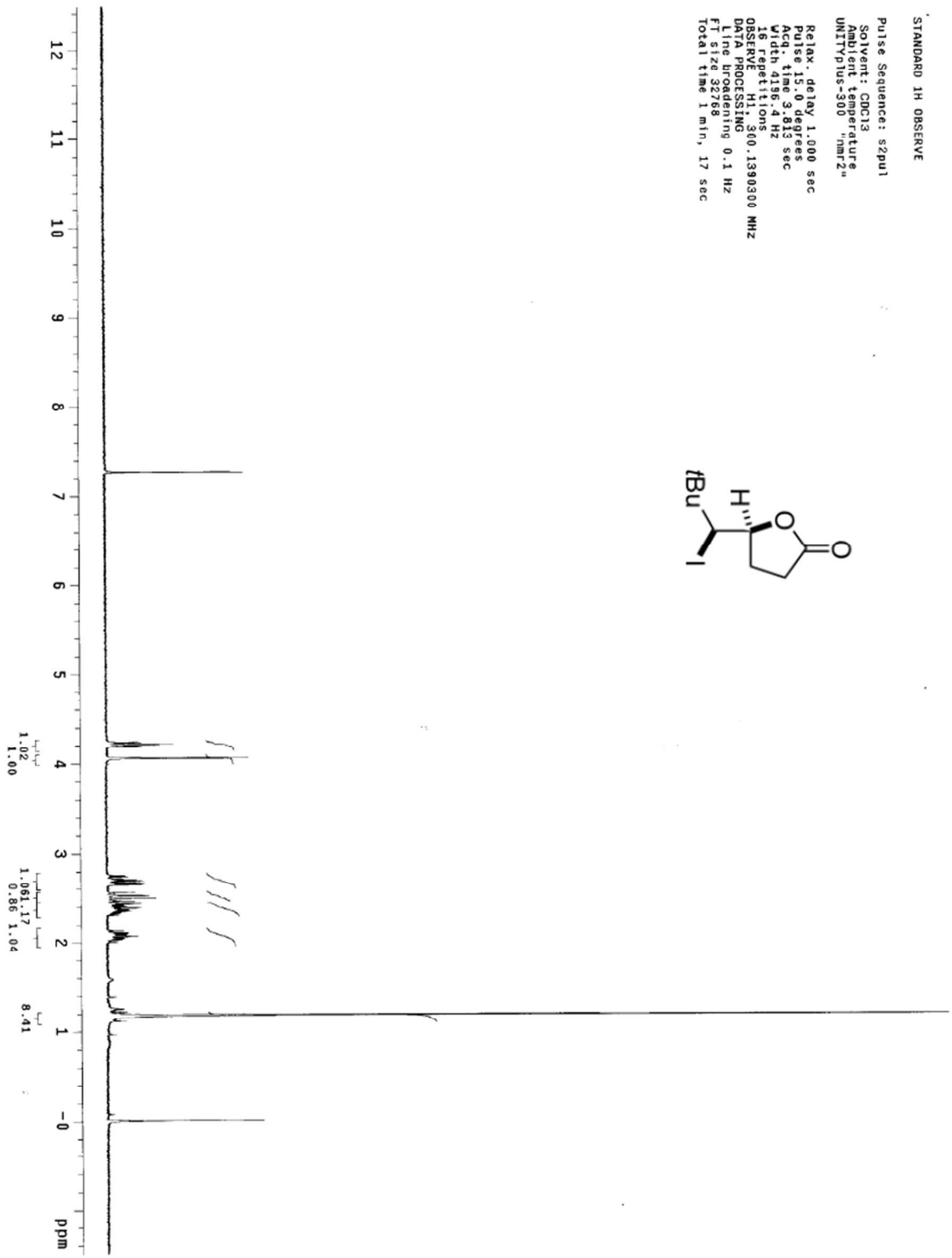


Figure S-13 ^{1}H NMR of Compound 6c

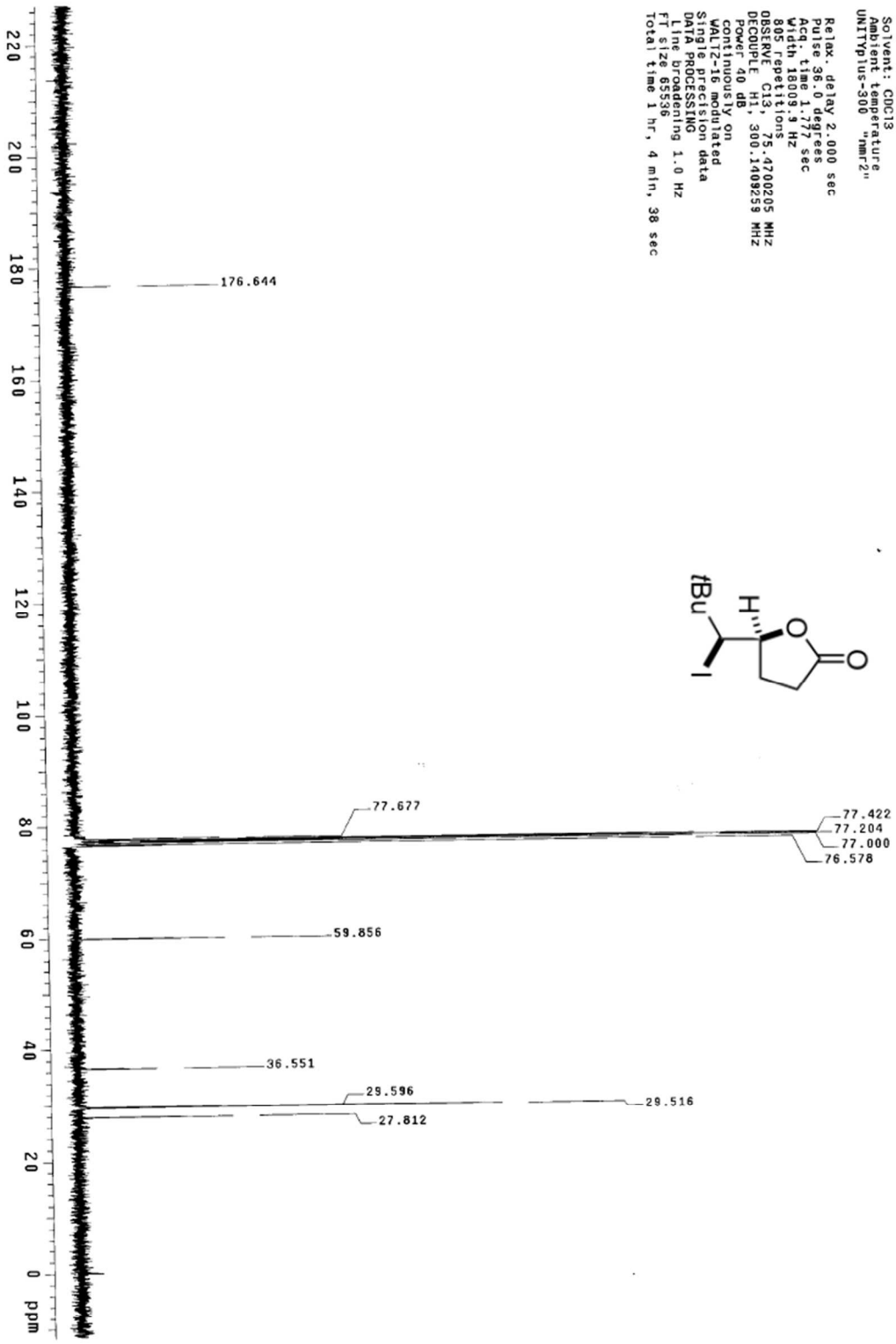


Figure S-14 ^{13}C NMR of Compound 6c

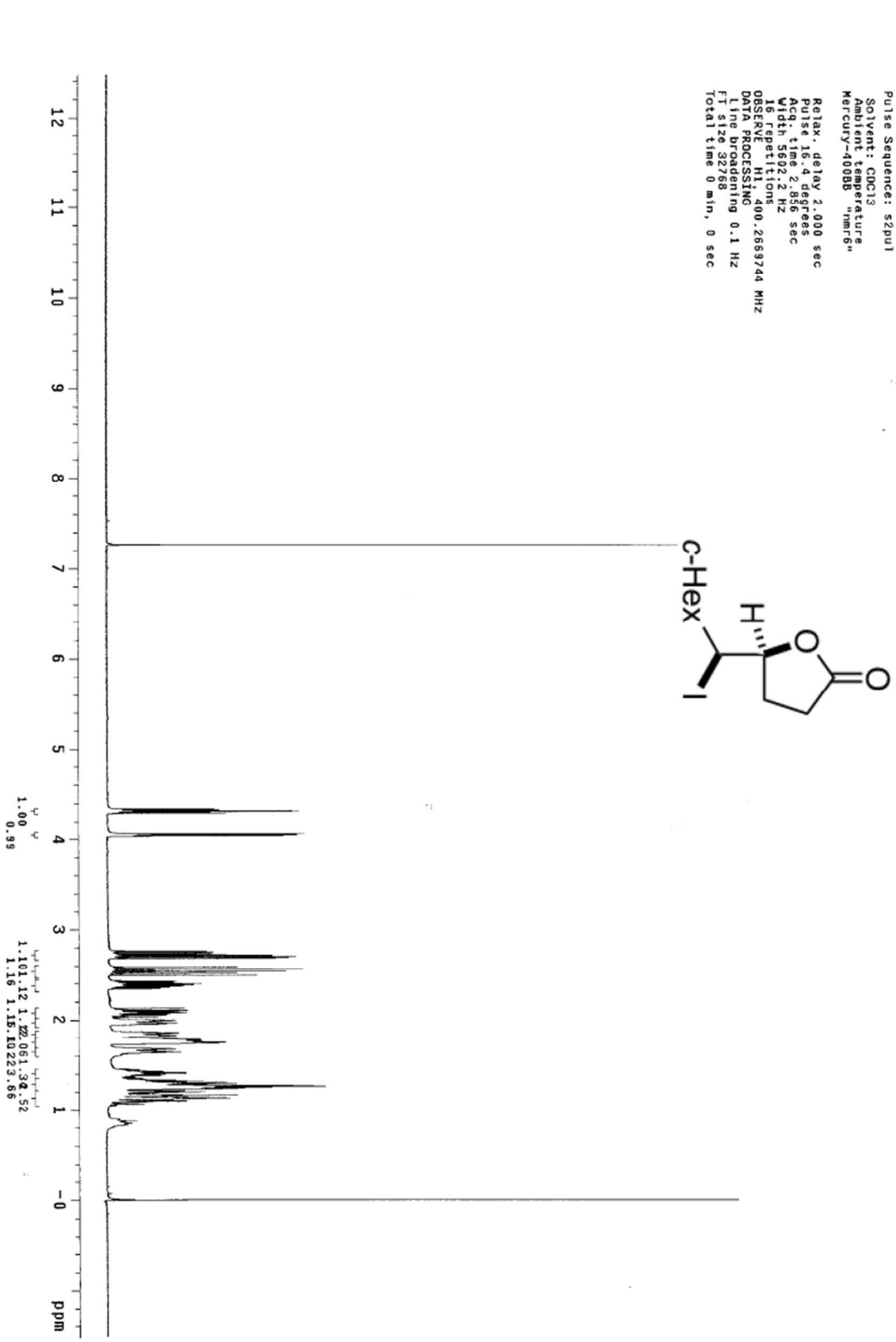


Figure S-15 ^{1}H NMR of Compound 6d

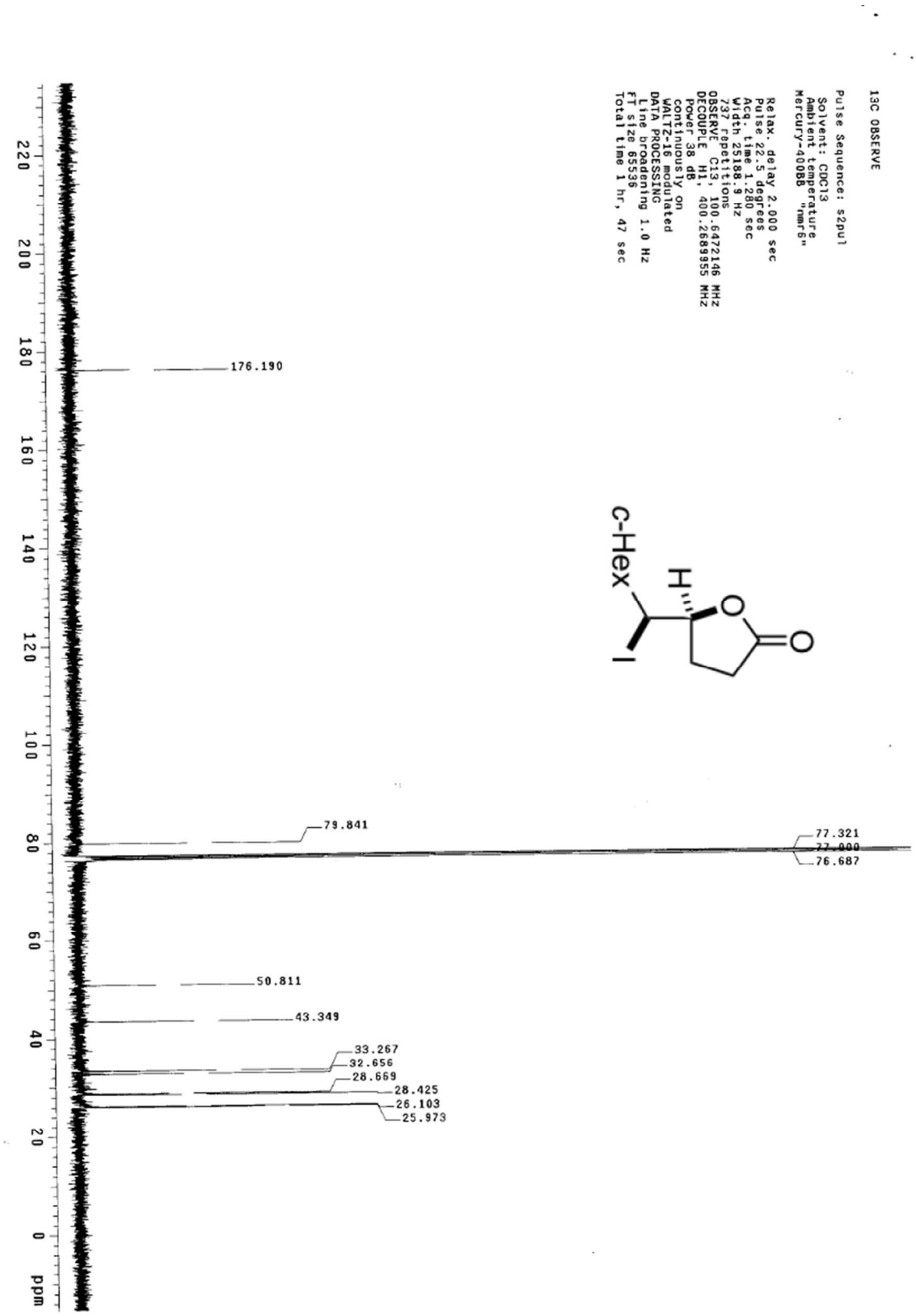


Figure S-16 ^{13}C NMR of Compound 6d

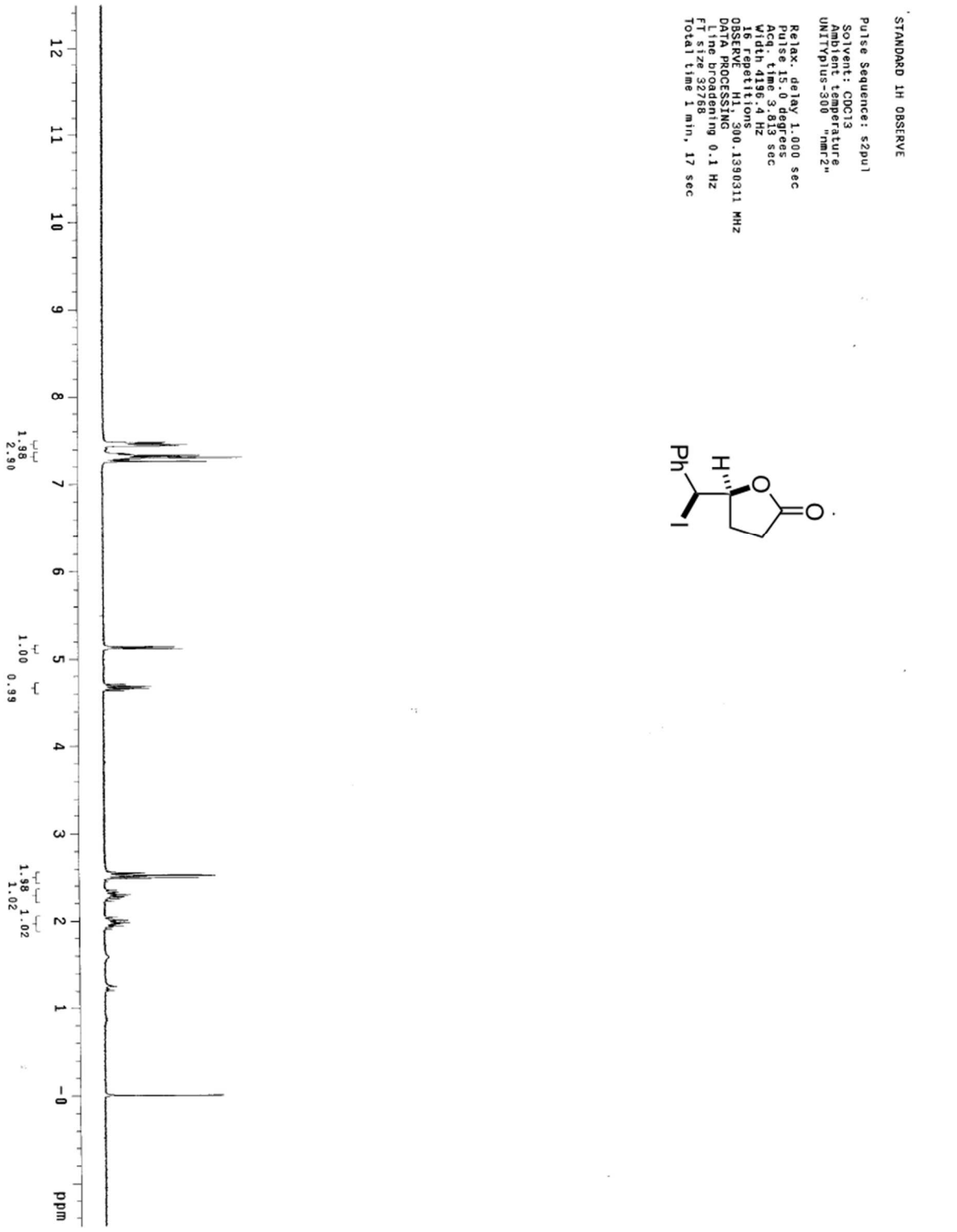


Figure S-17 ^{1}H NMR of Compound 6e

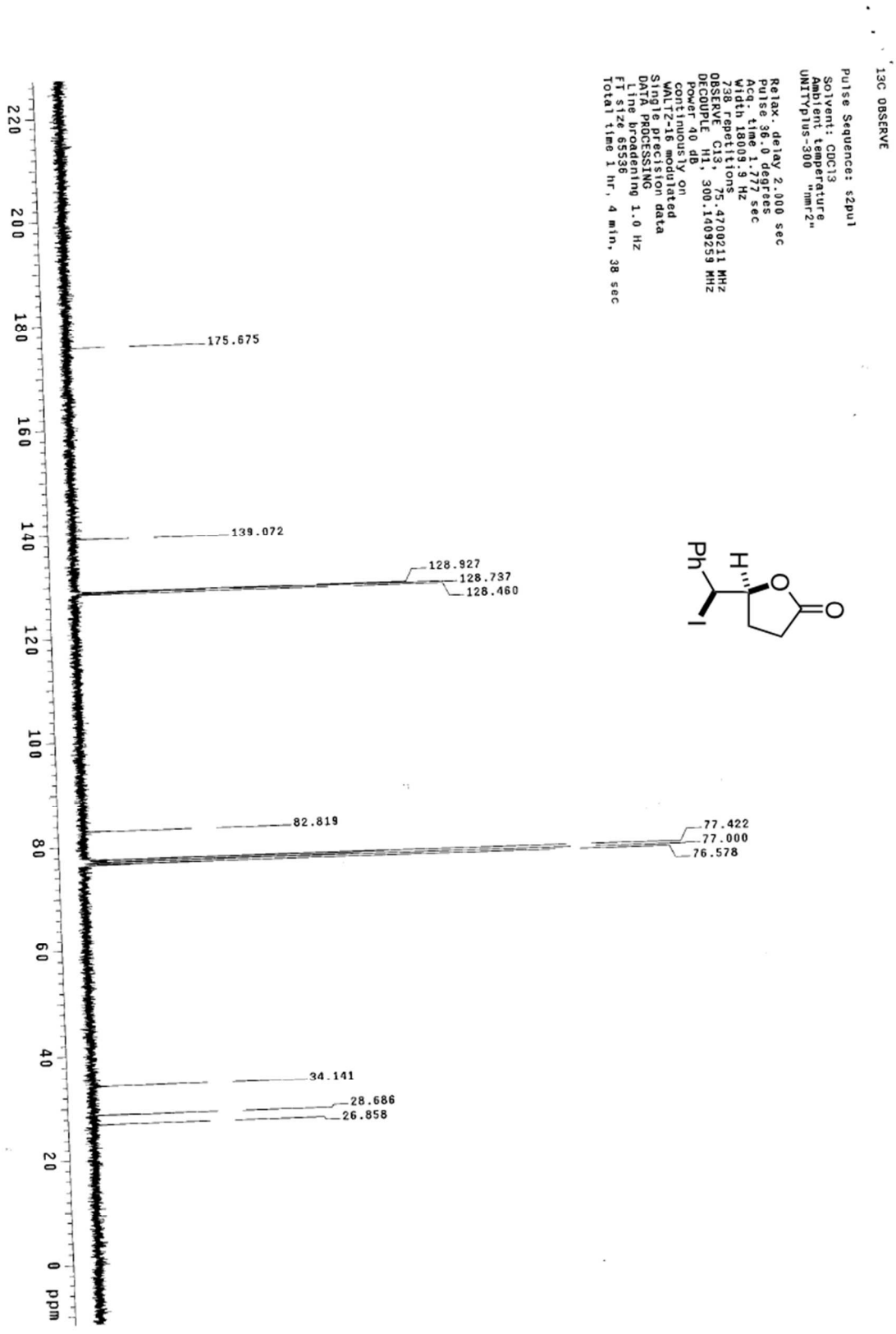


Figure S-18 ^{13}C NMR of Compound 6e

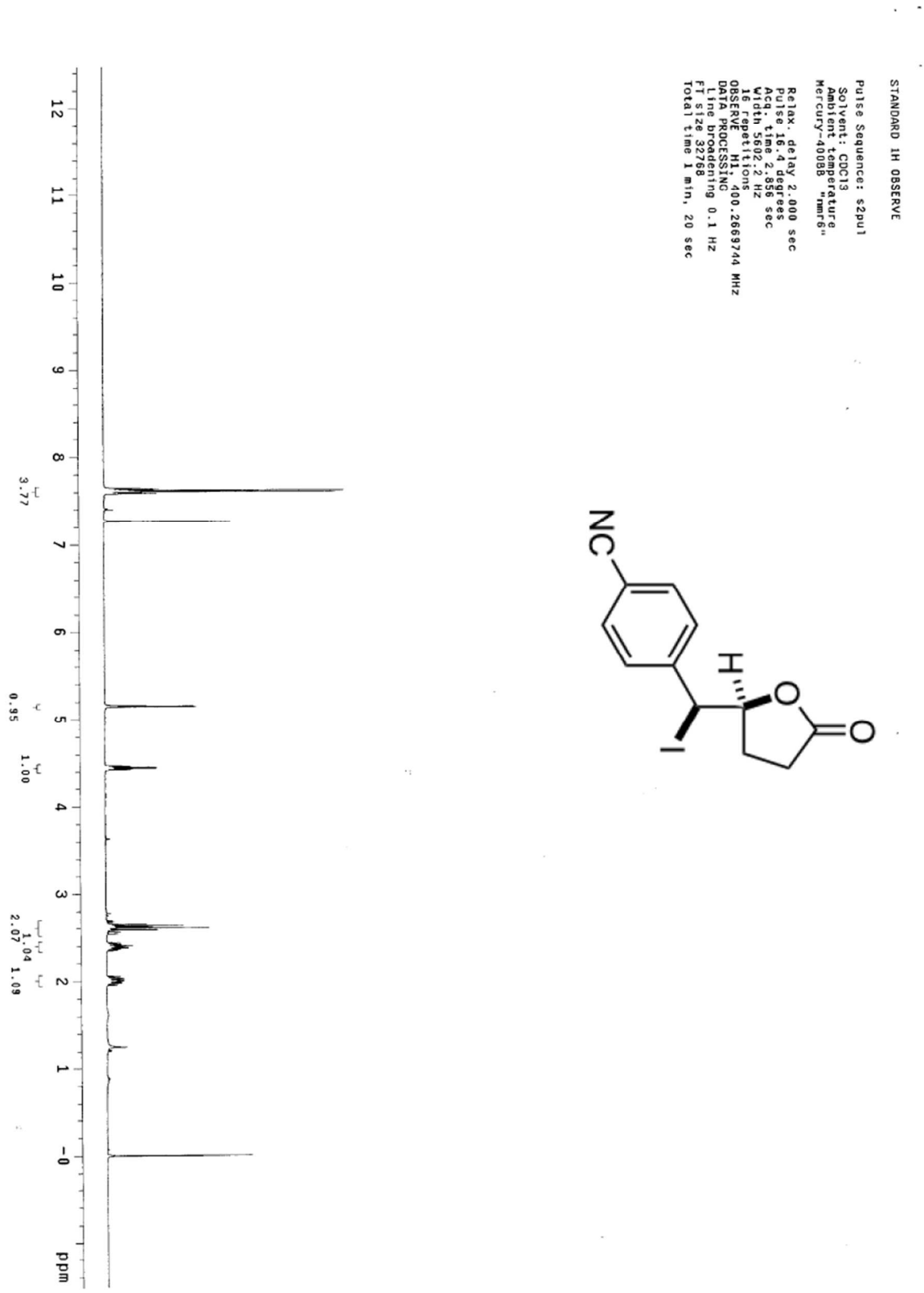


Figure S-19 ^{1}H NMR of Compound 6f

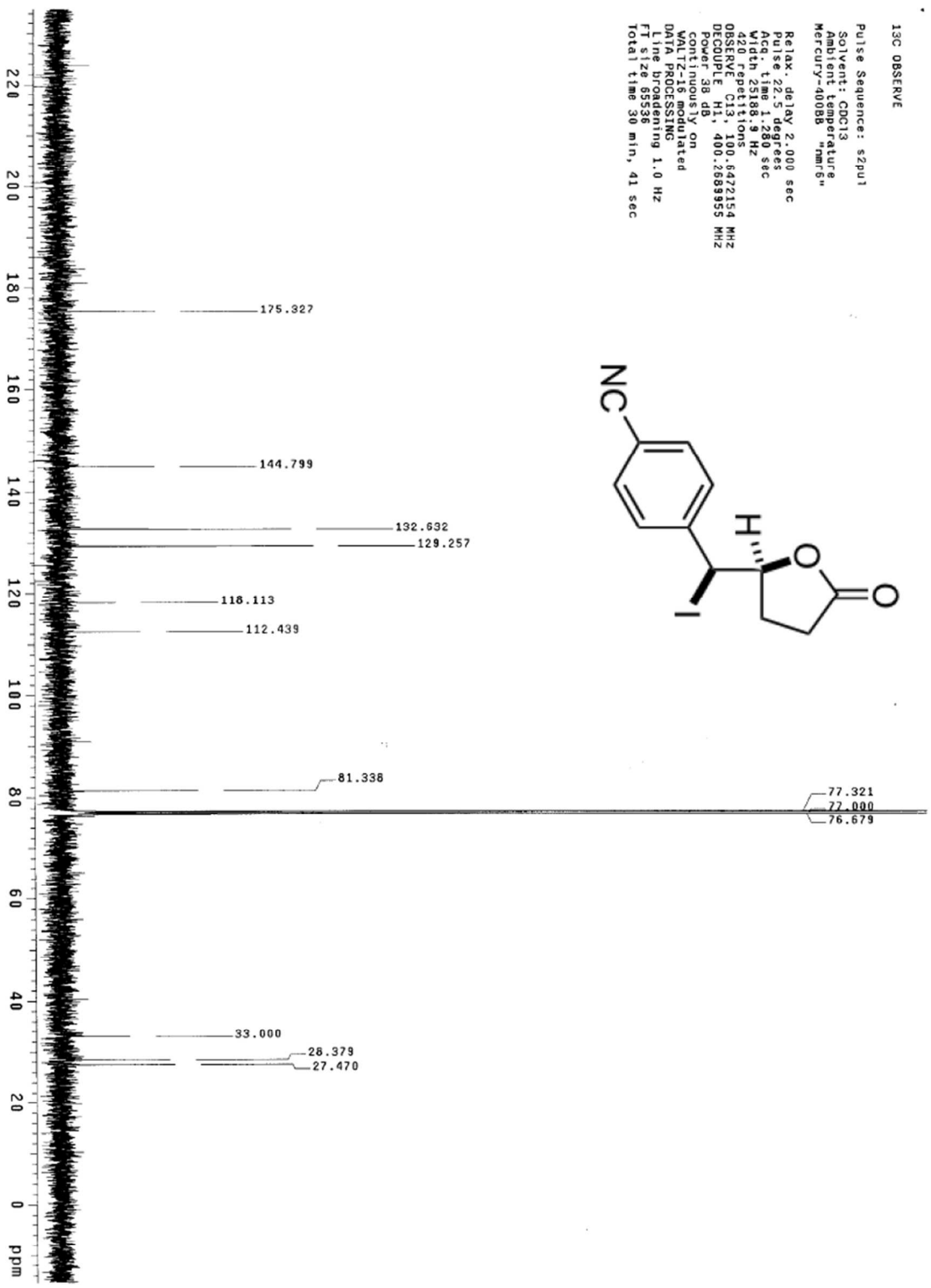


Figure S-20 ^{13}C NMR of Compound 6f

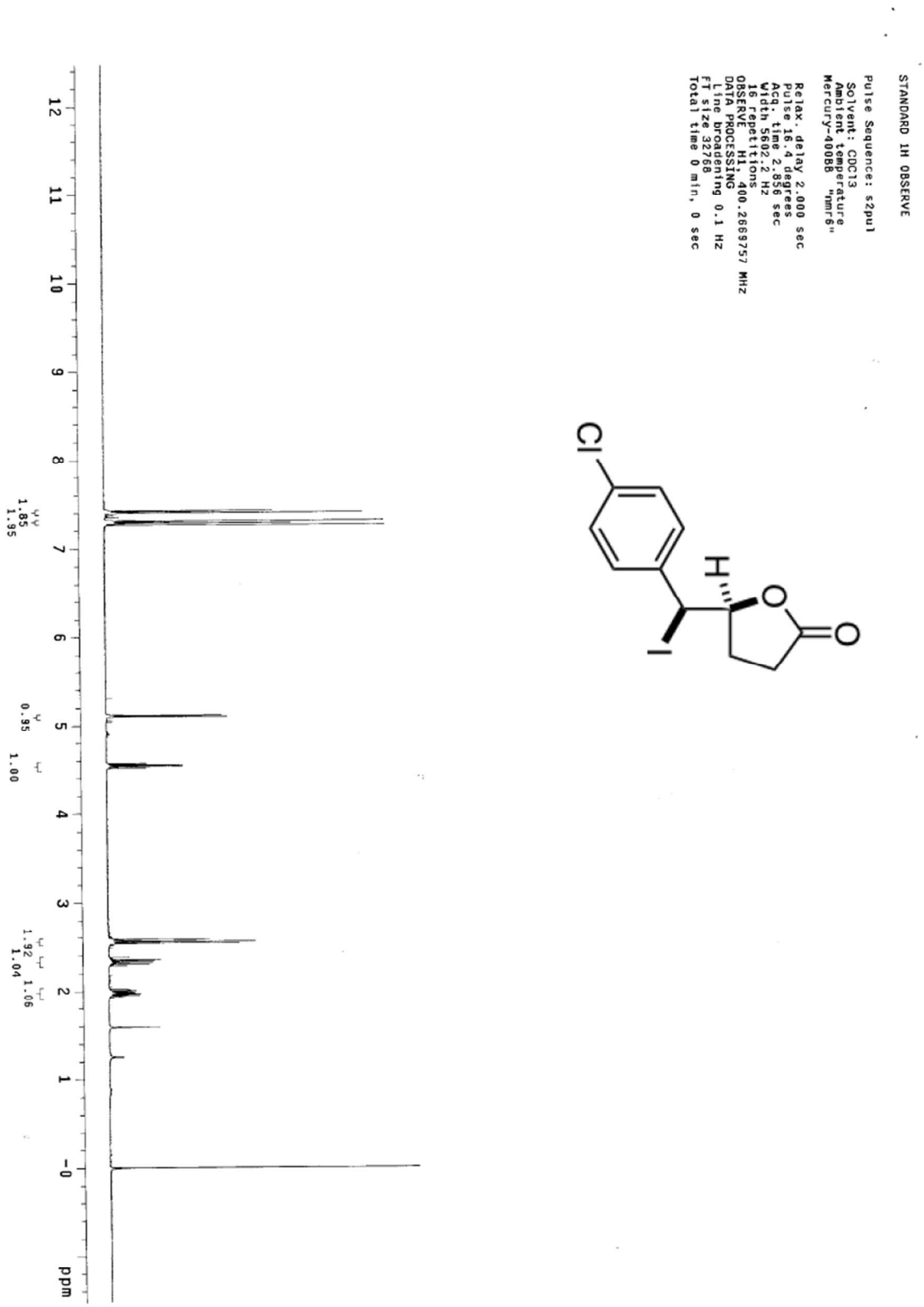


Figure S-21 ^{1}H NMR of Compound 6g

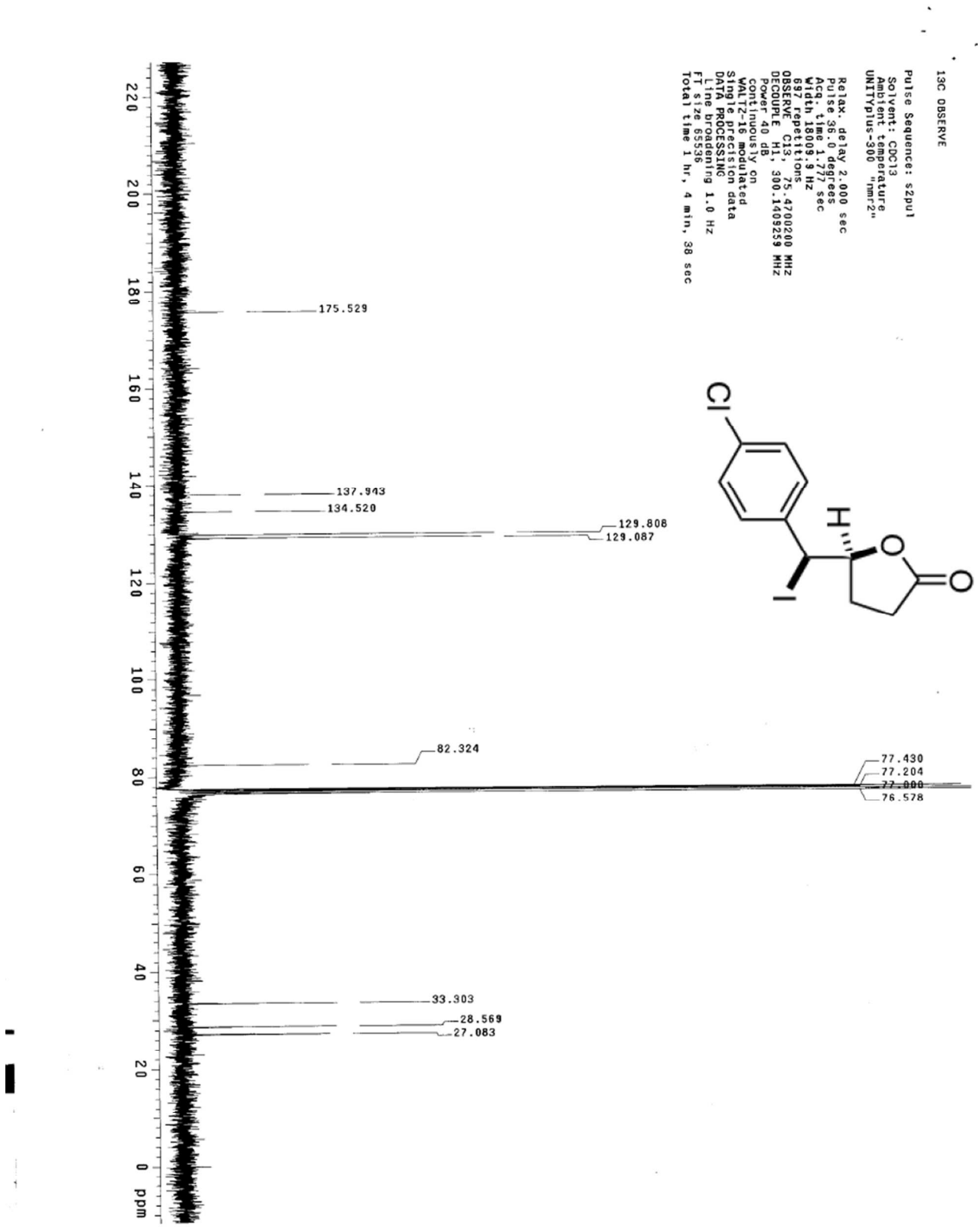


Figure S-22 ^{13}C NMR of Compound 6g

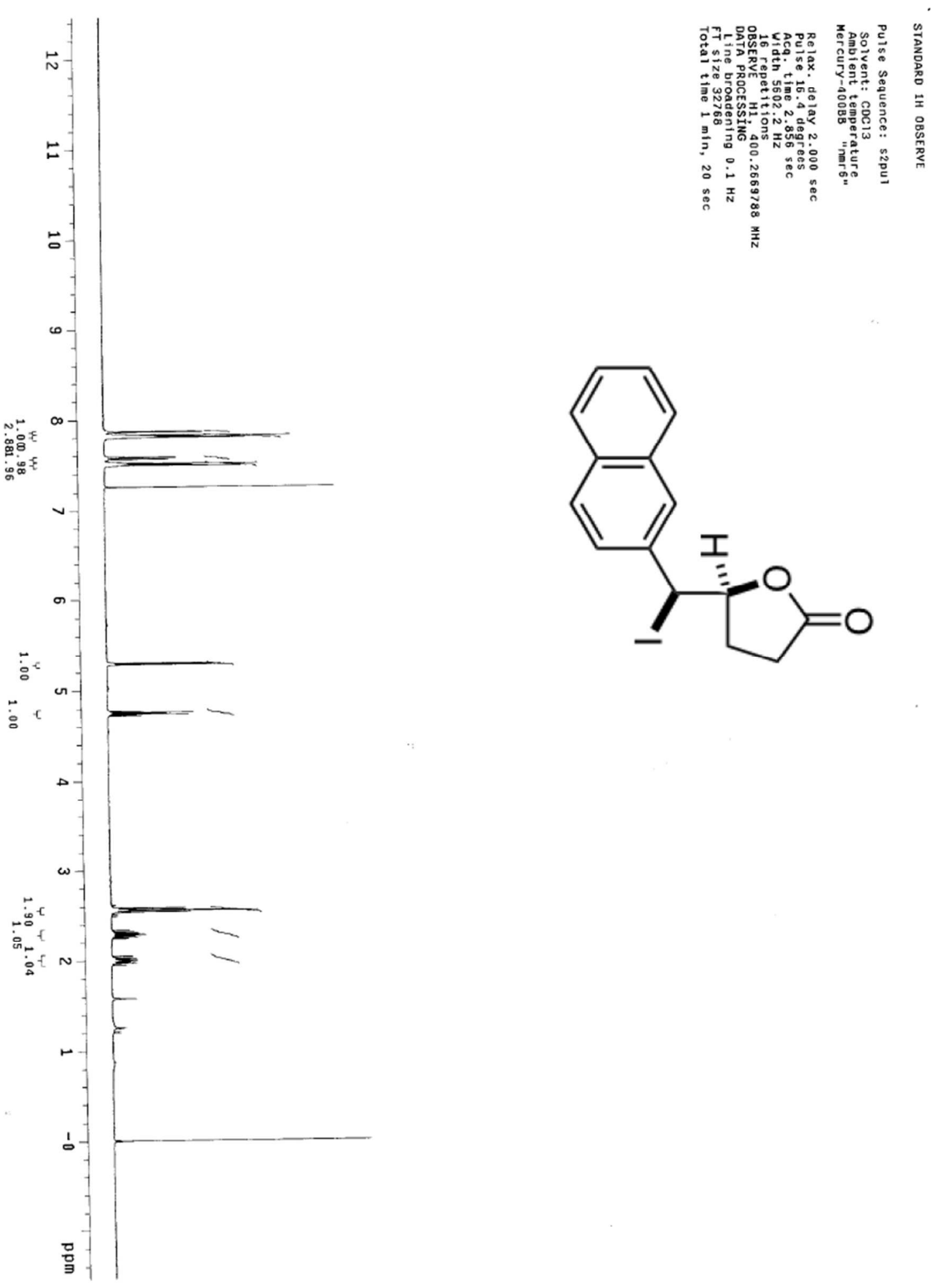


Figure S-23 ^{1}H NMR of Compound 6h

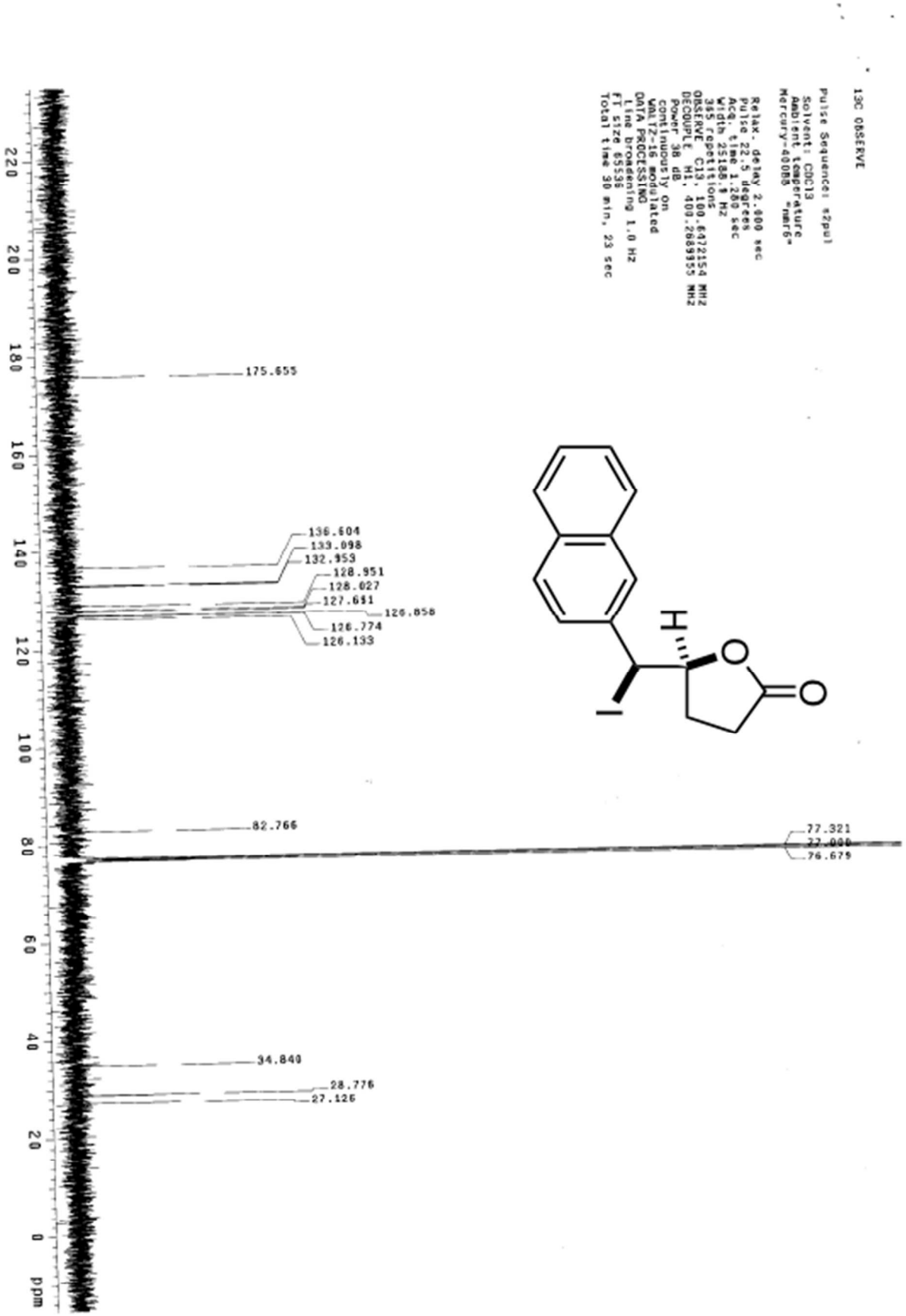


Figure S-24 ^{13}C NMR of Compound 6h

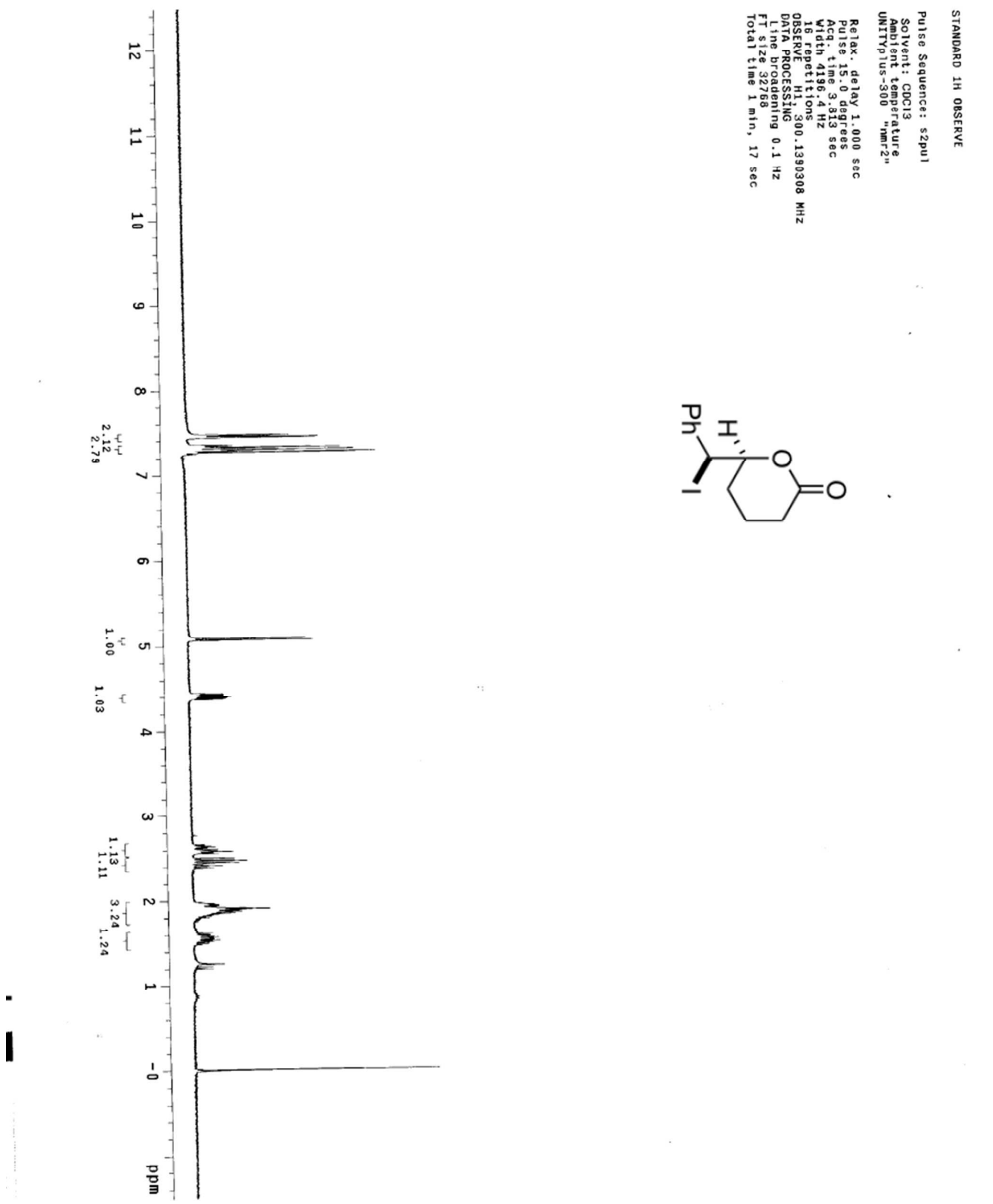


Figure S-25 ^{1}H NMR of Compound 8a

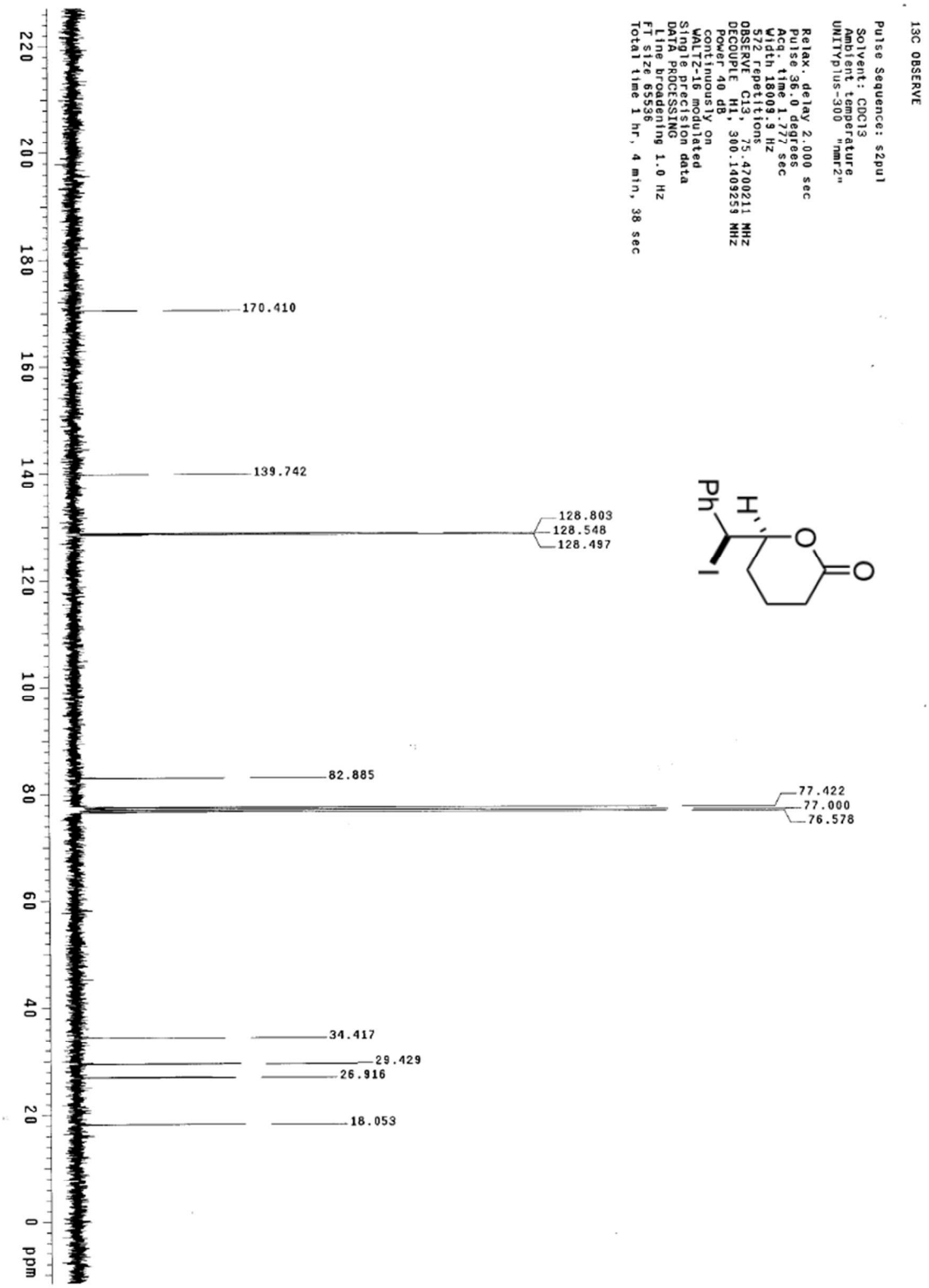


Figure S-26 ^{13}C NMR of Compound 8a

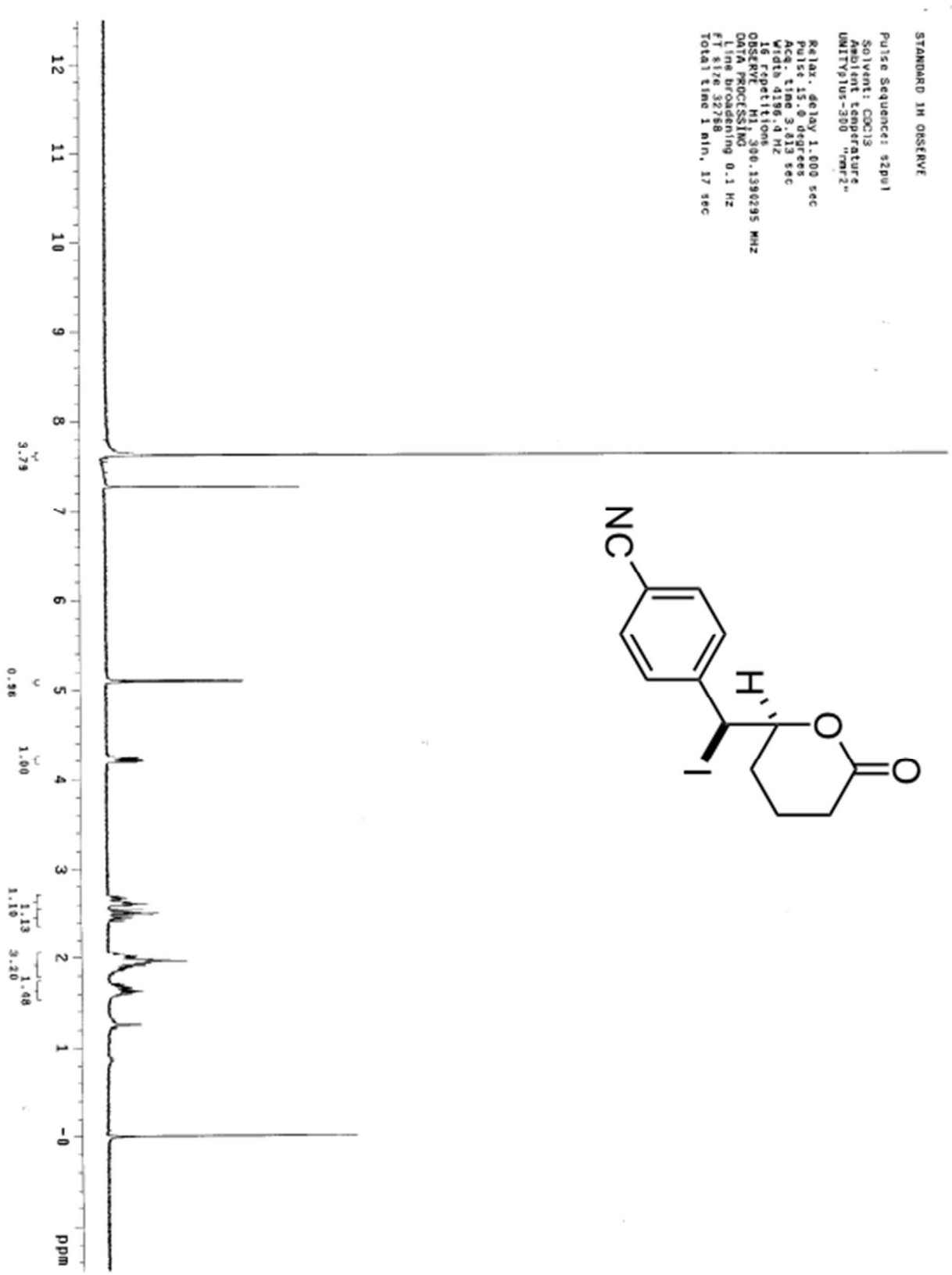


Figure S-27 ^{1}H NMR of Compound 8b

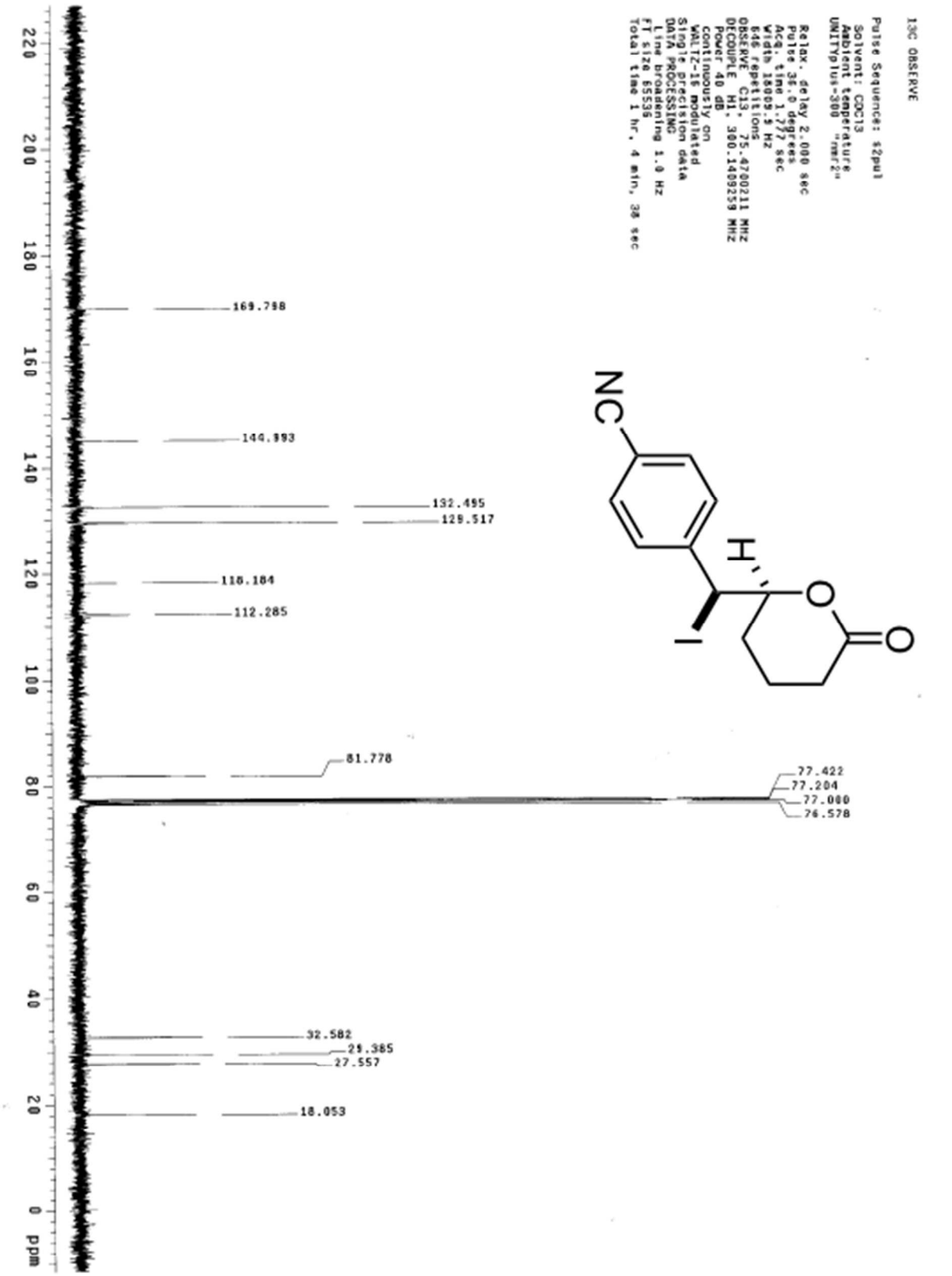


Figure S-28 ^{13}C NMR of Compound 8b

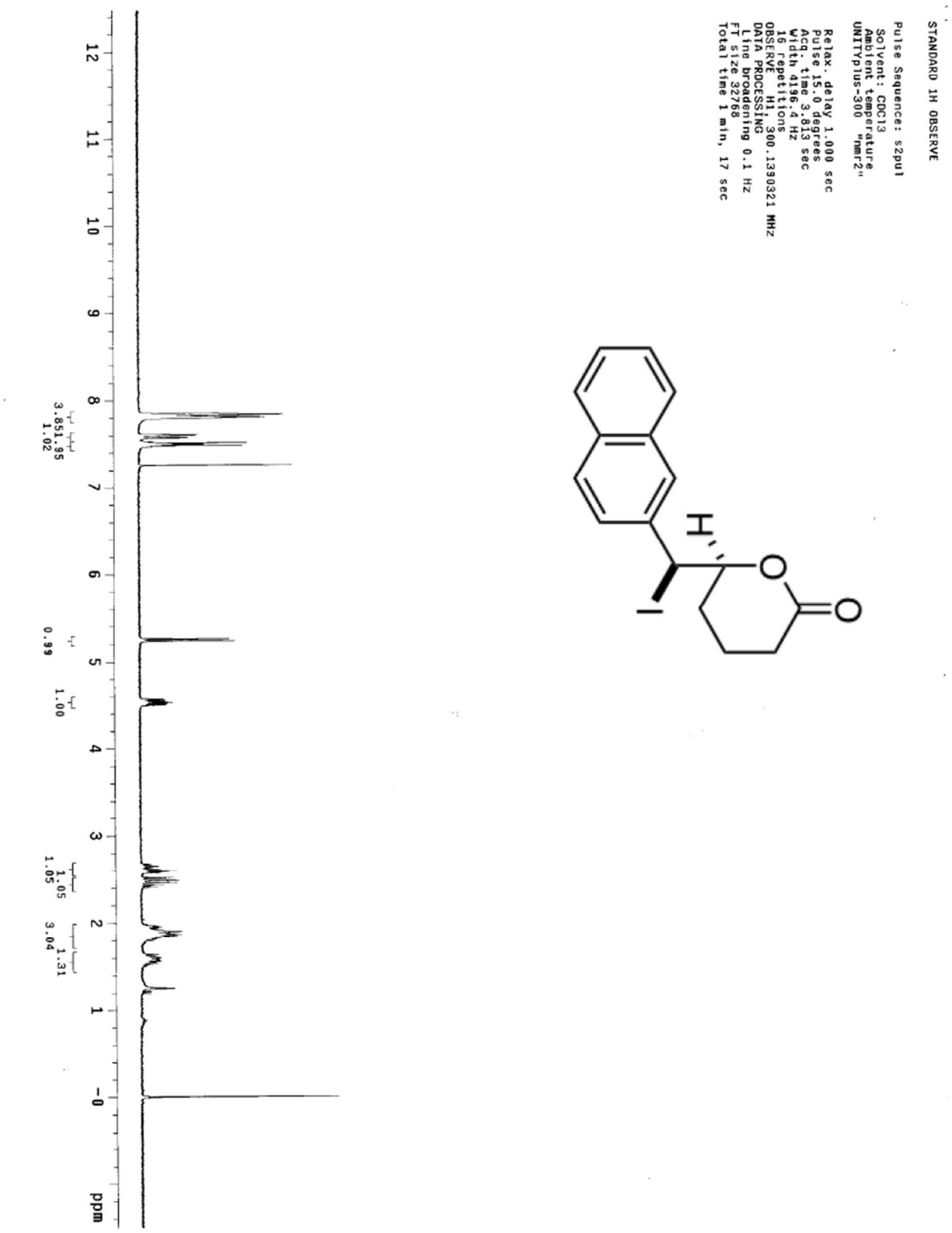


Figure S-29 ^{1}H NMR of Compound 8c

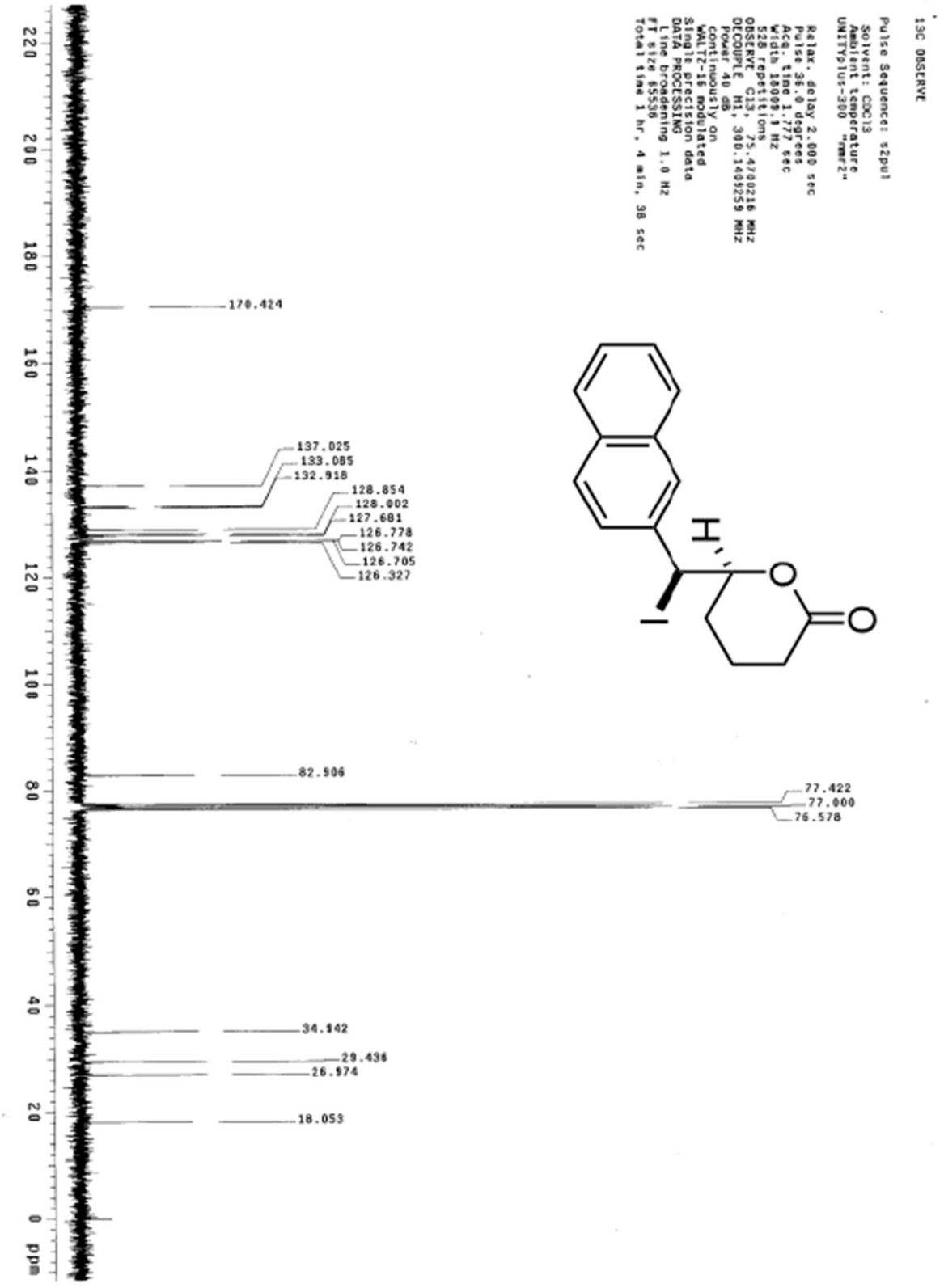


Figure S-30 ^{1}C NMR of Compound 8c

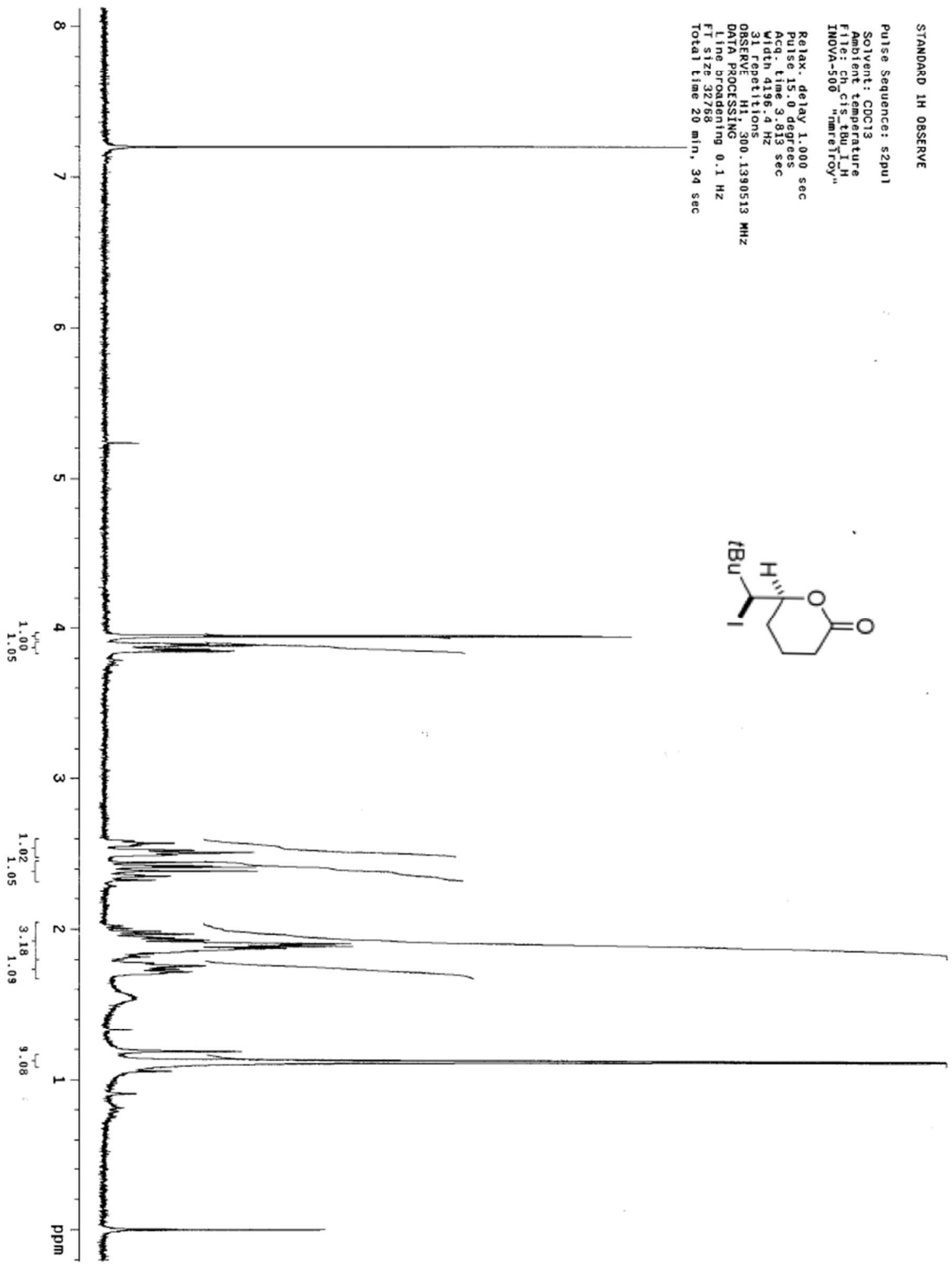


Figure S-31 ^{1}H NMR of Compound 8d

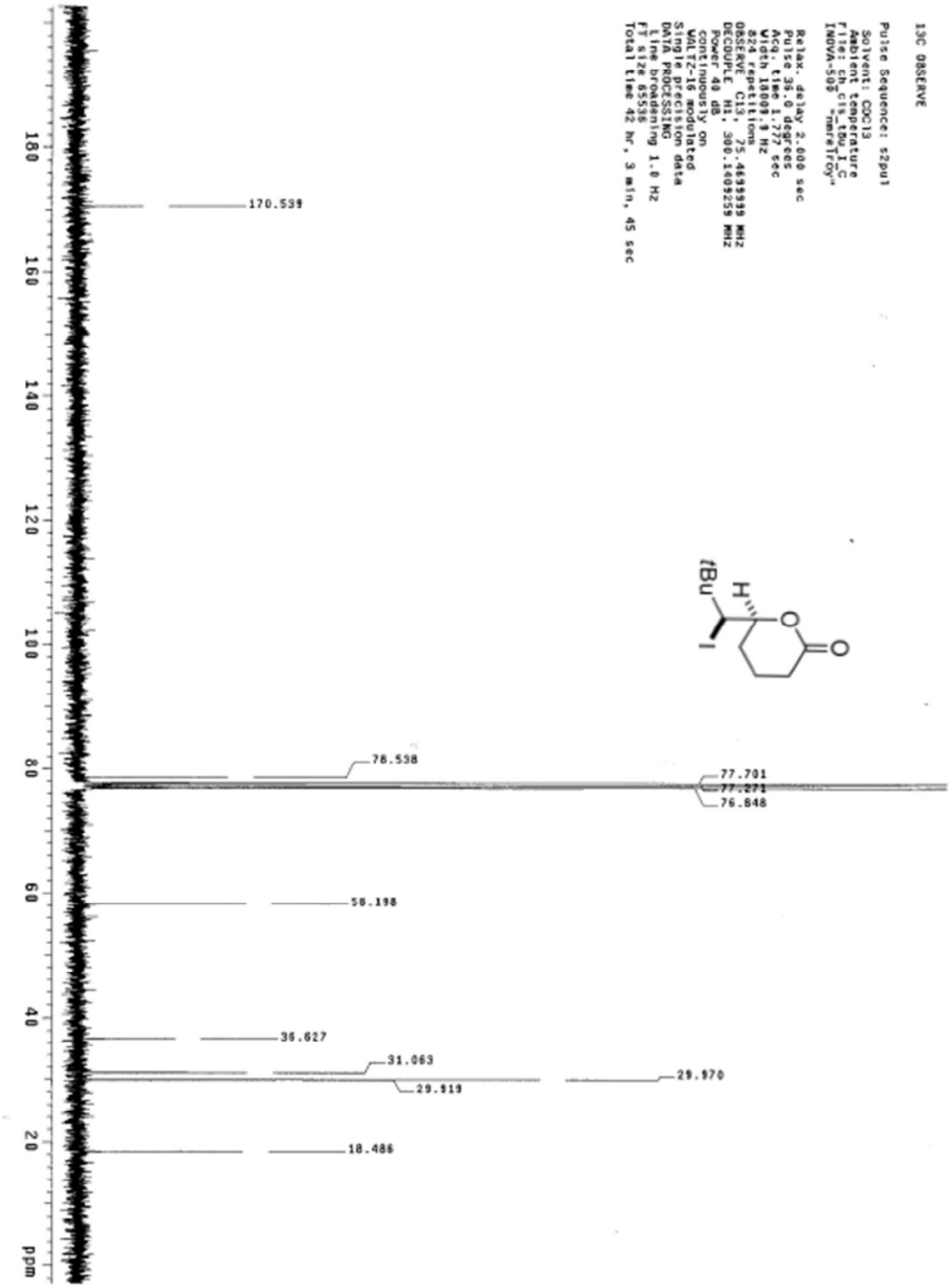


Figure S-32 ^{13}C NMR of Compound 8d

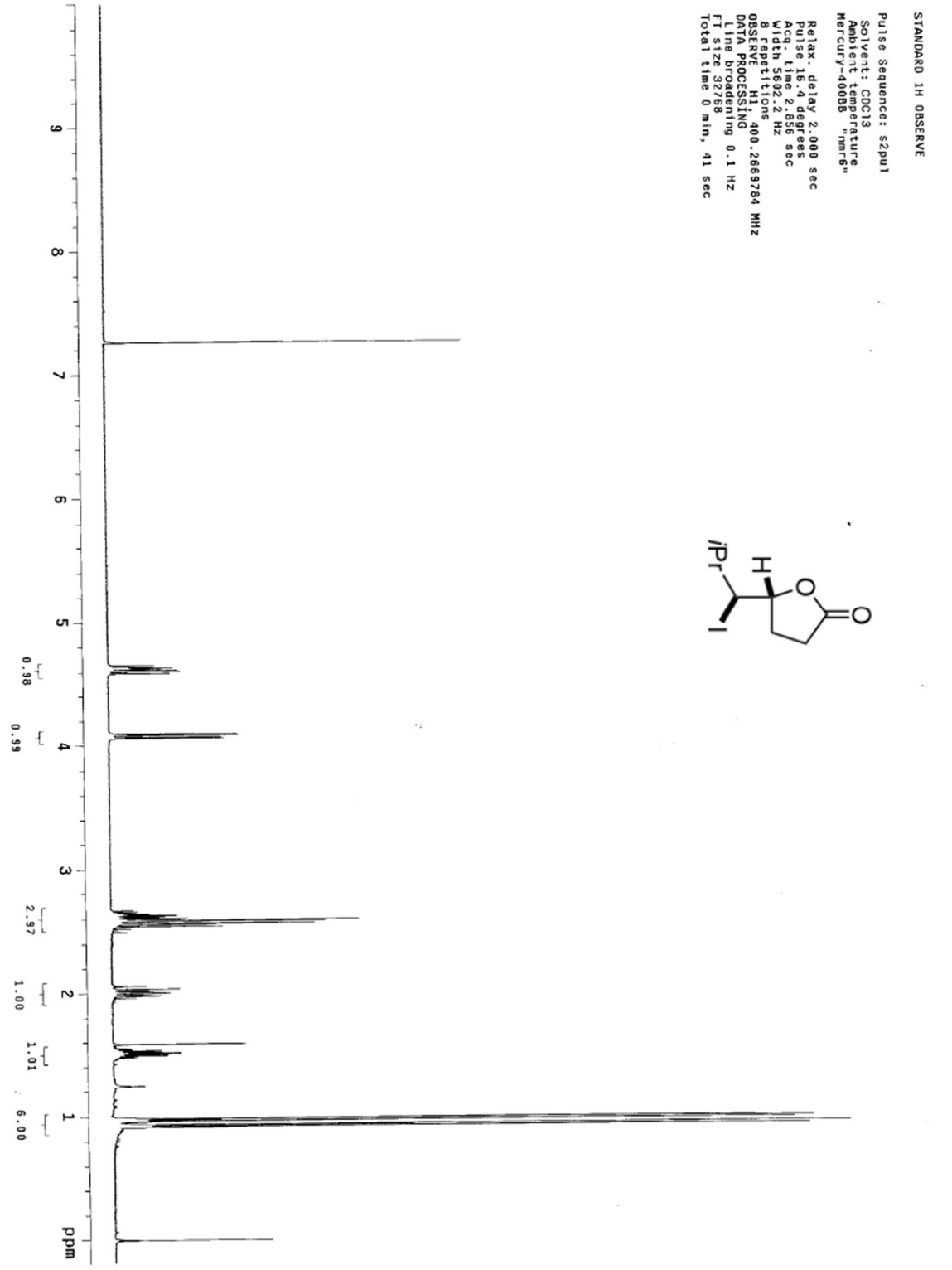


Figure S-33 ^{1}H NMR of Compound 10a

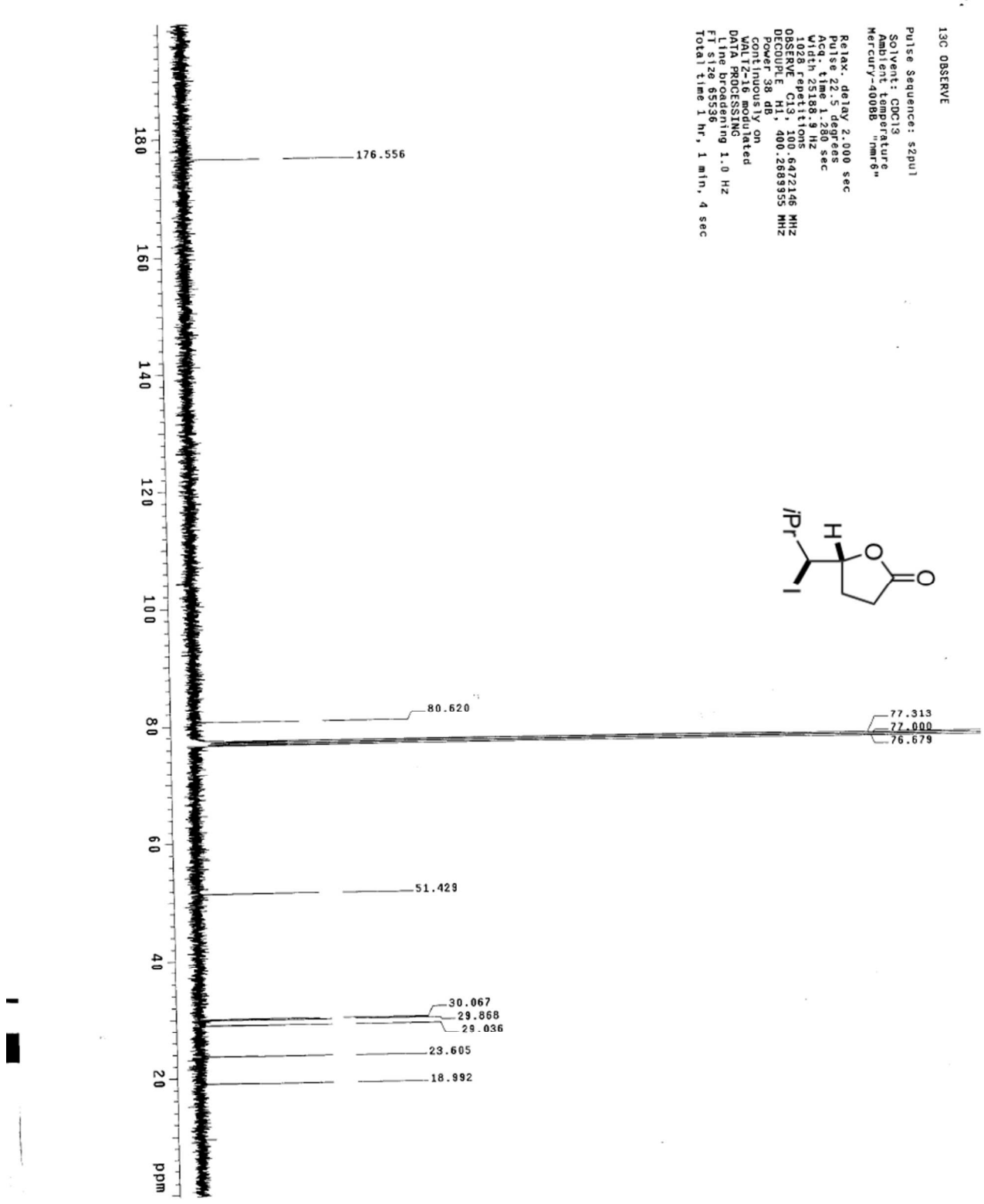


Figure S-34 ^{13}C NMR of Compound 10a

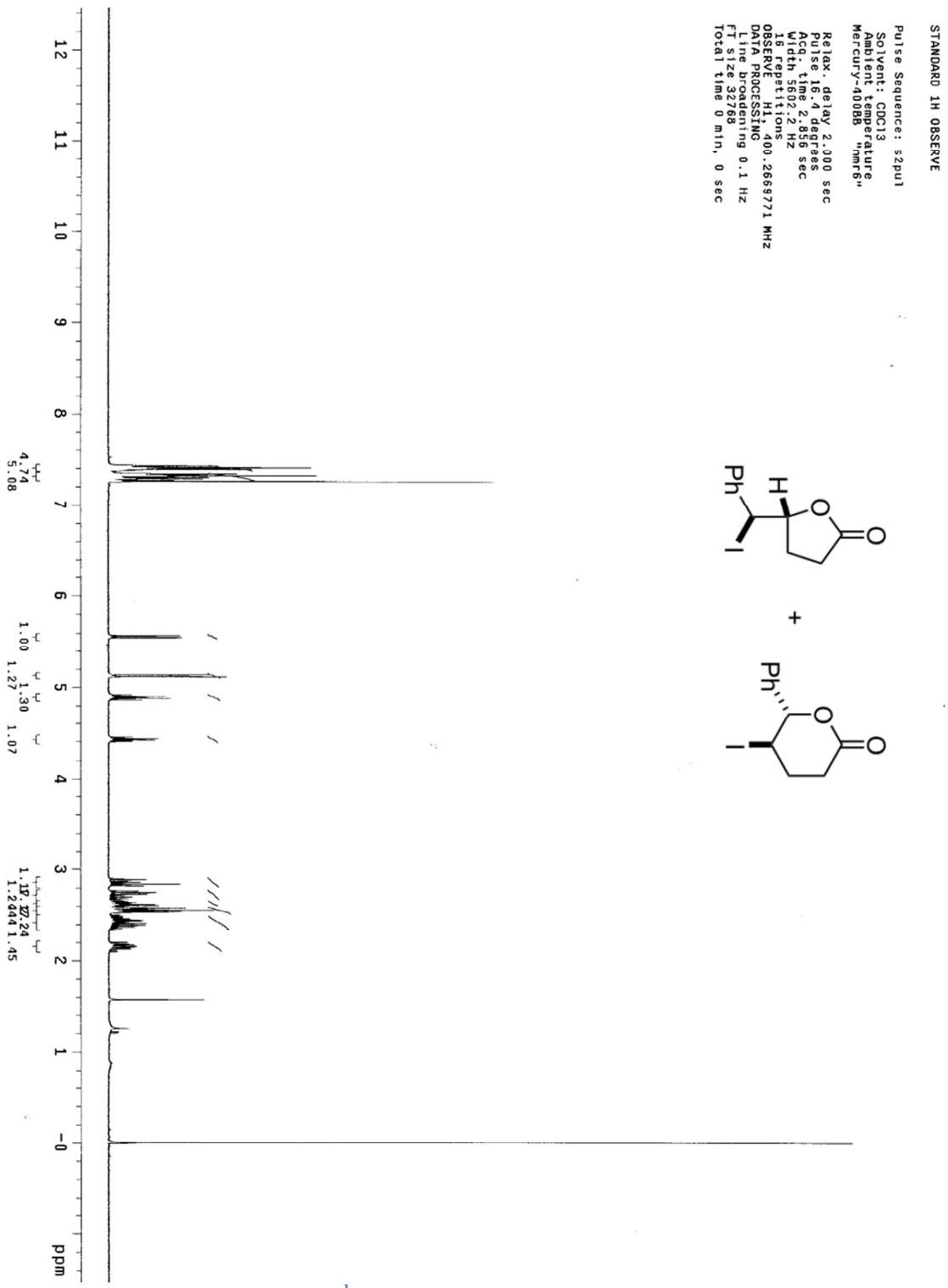


Figure S-35 ^{1}H NMR of Compound 10b and 11b

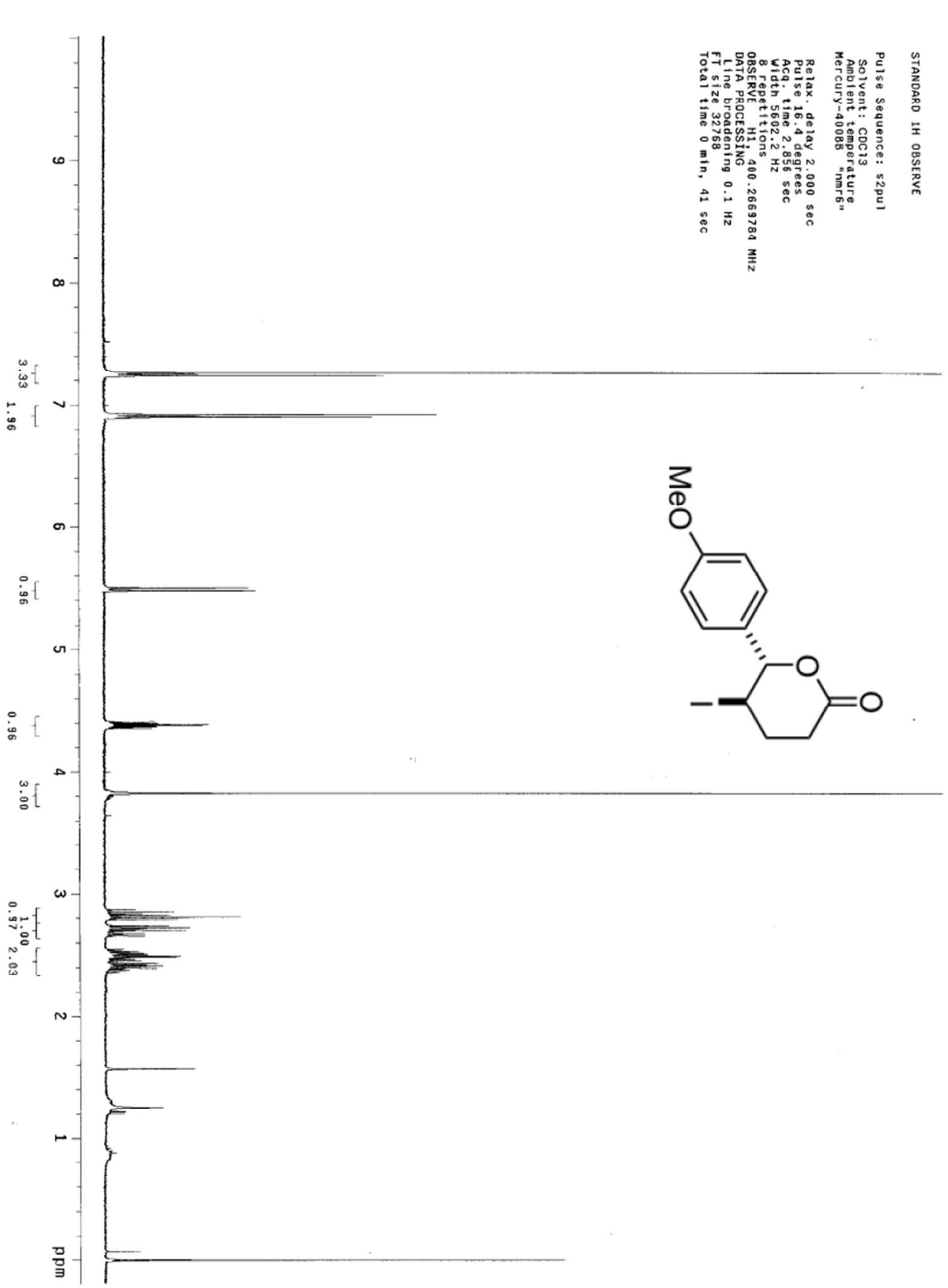


Figure S-36 ^{1}H NMR of Compound 11c

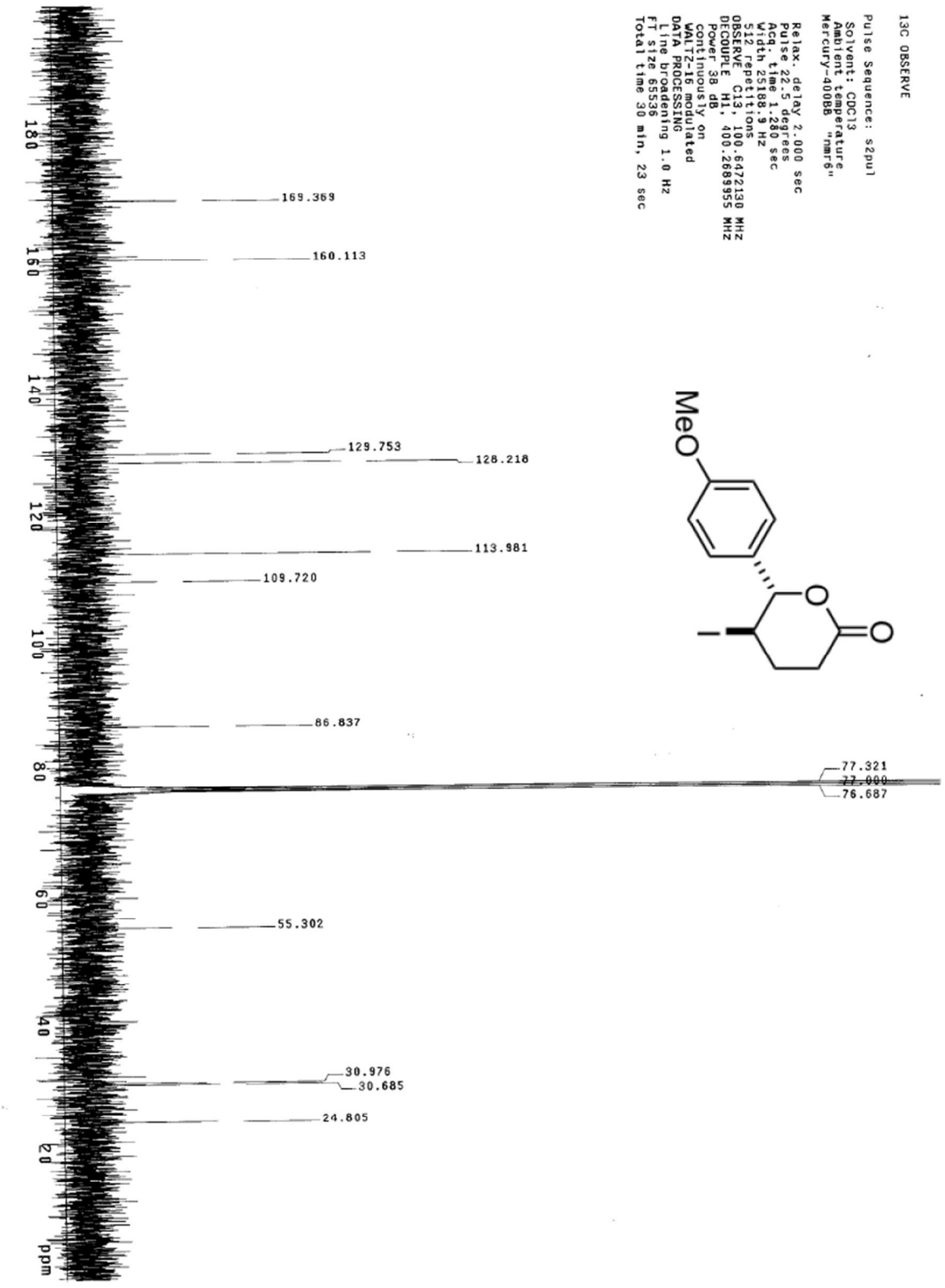


Figure S-37 ^{13}C NMR of Compound 11c

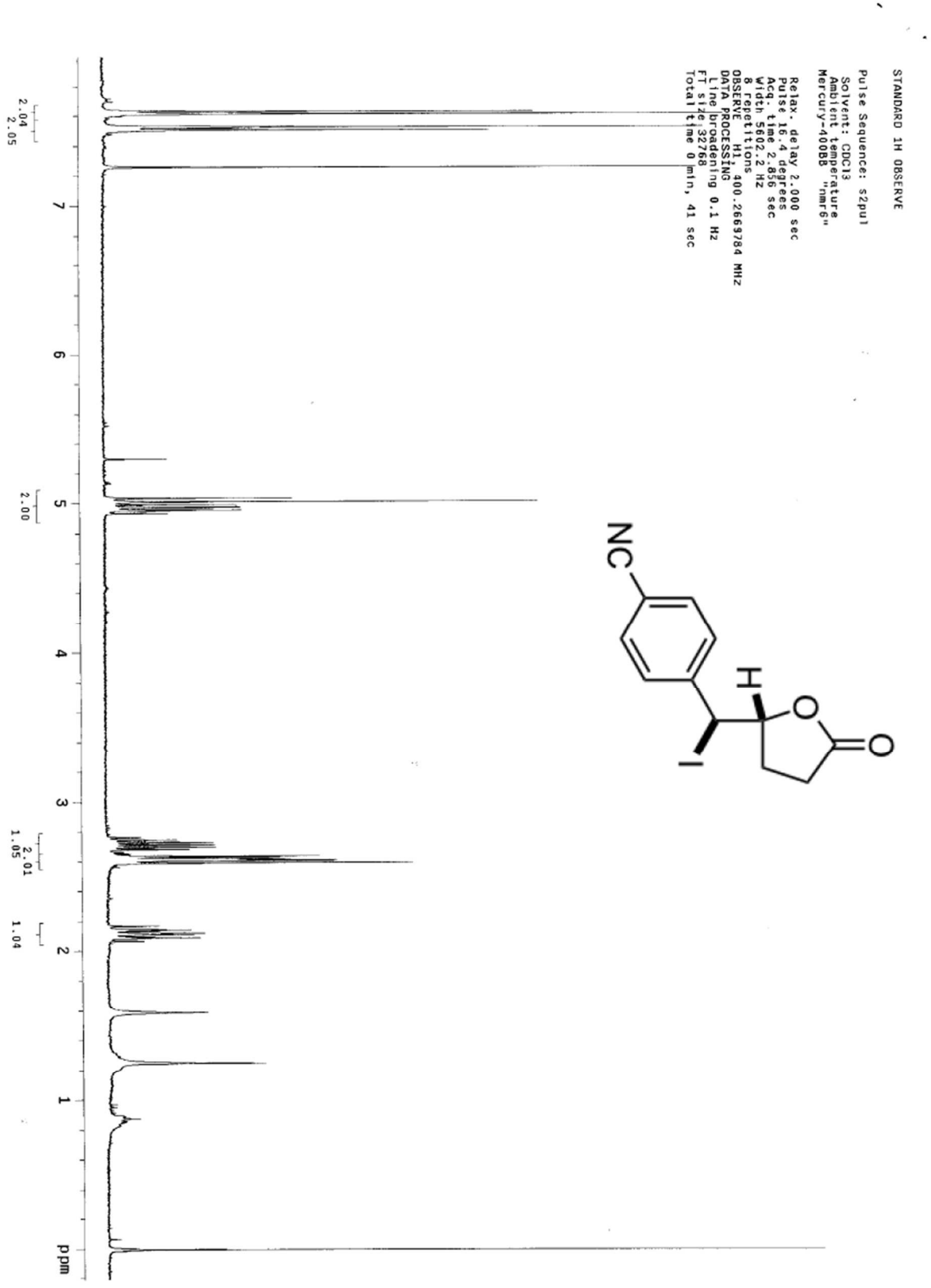


Figure S-38 ^{1}H NMR of Compound 10d

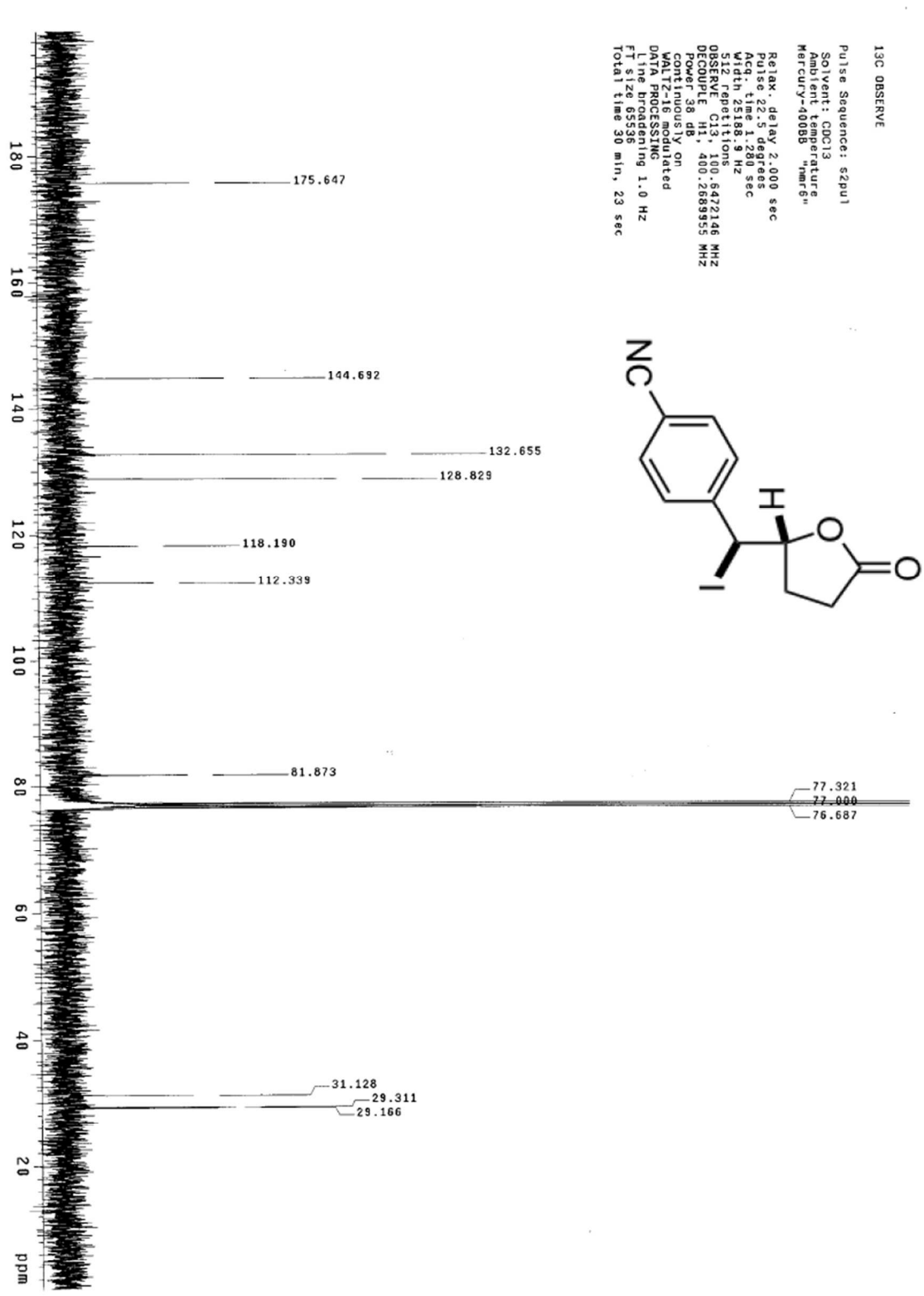


Figure S-39 ^{13}C NMR of Compound 10d

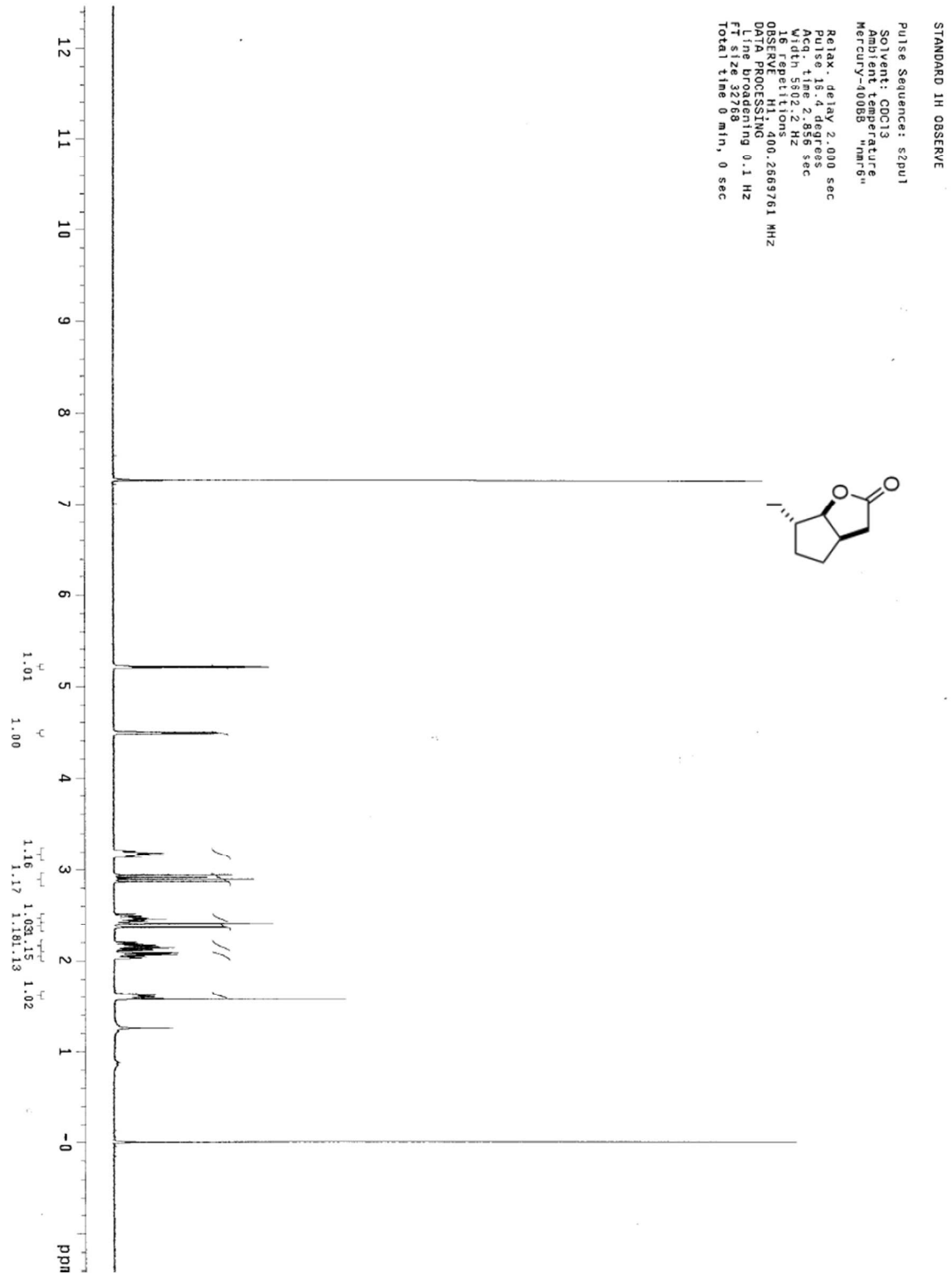


Figure S-40 ^{1}H NMR of Compound 13

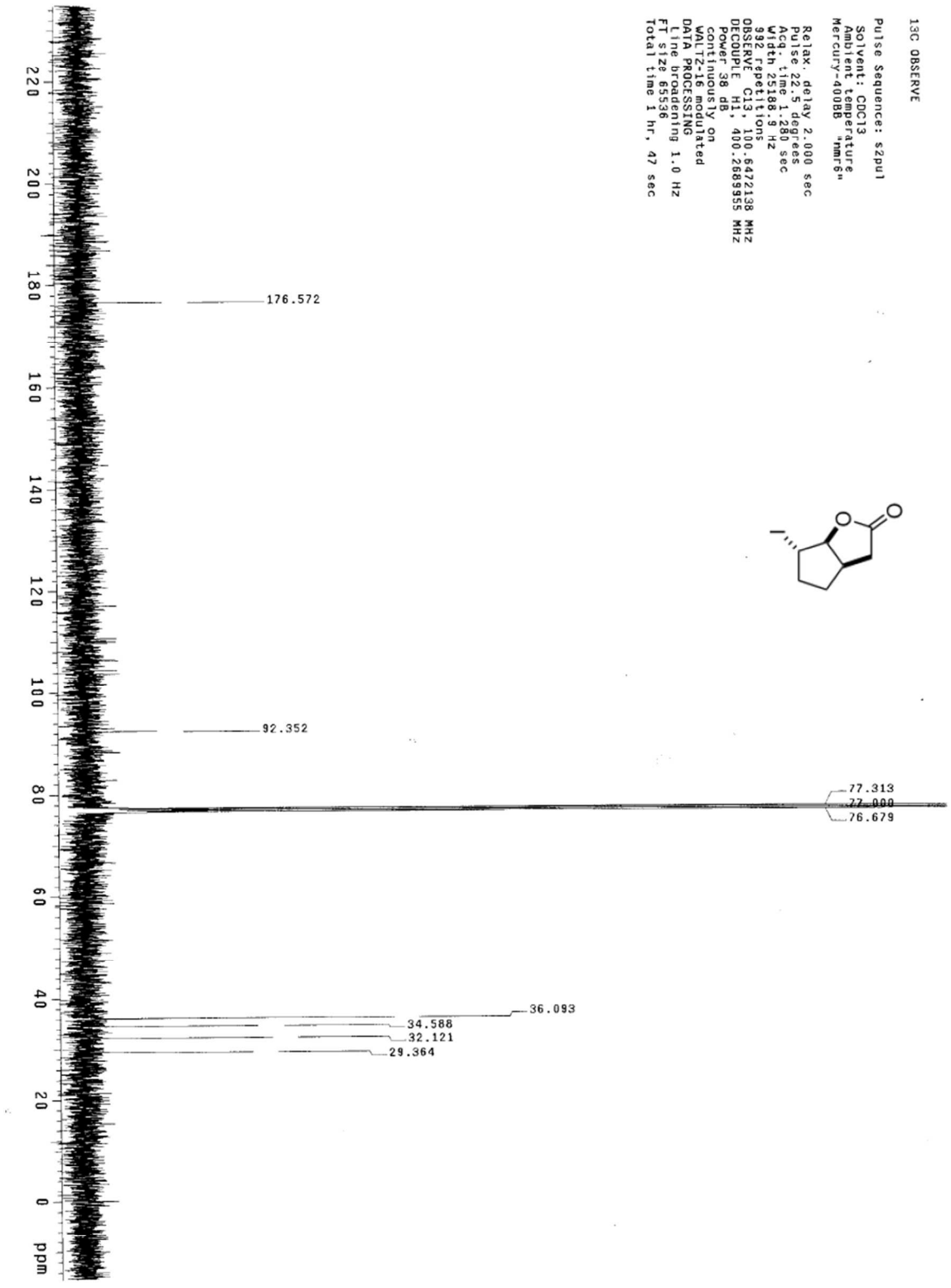


Figure S-41 ^{13}C NMR of Compound 13

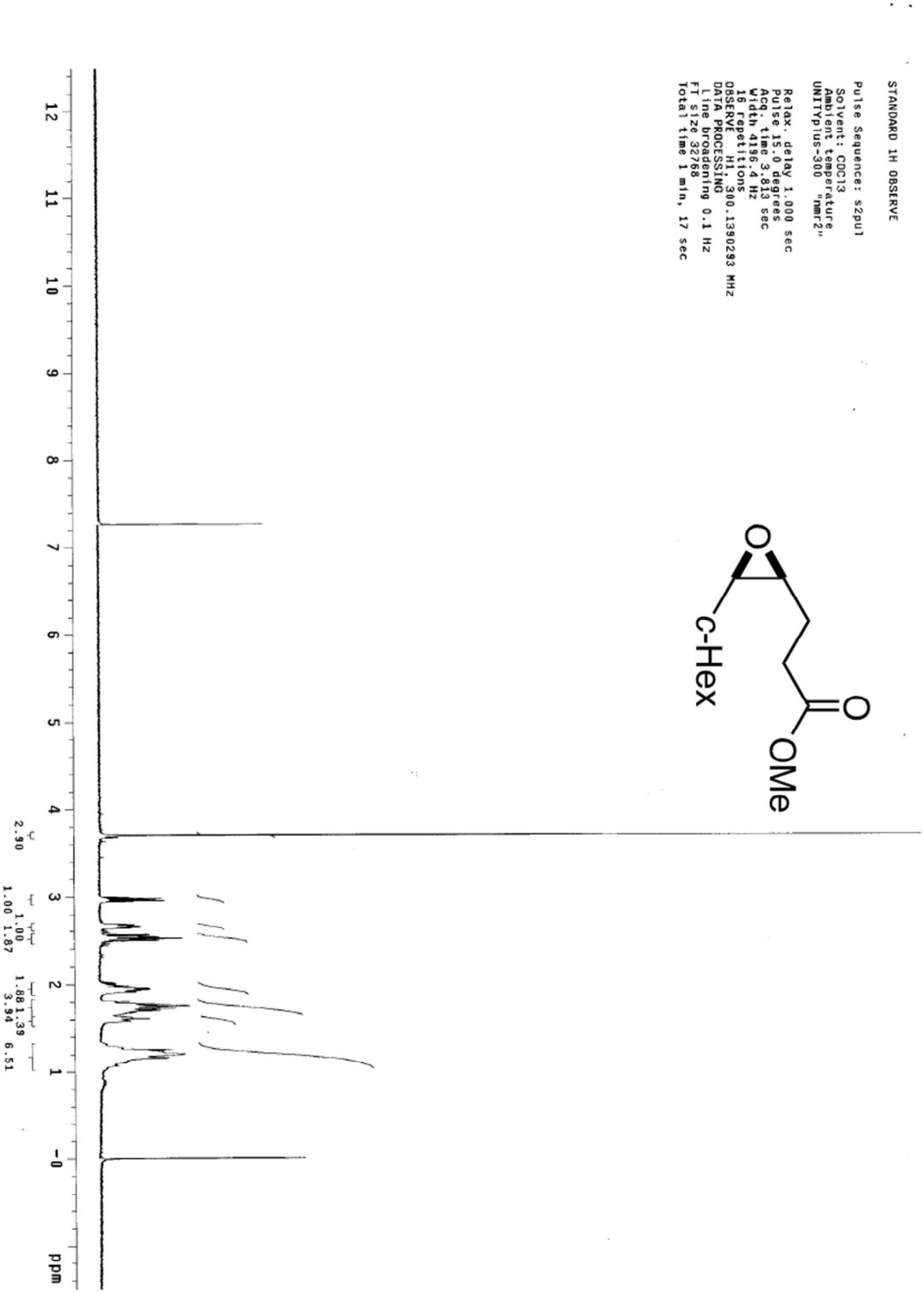


Figure S-42 ^{1}H NMR of Compound 14

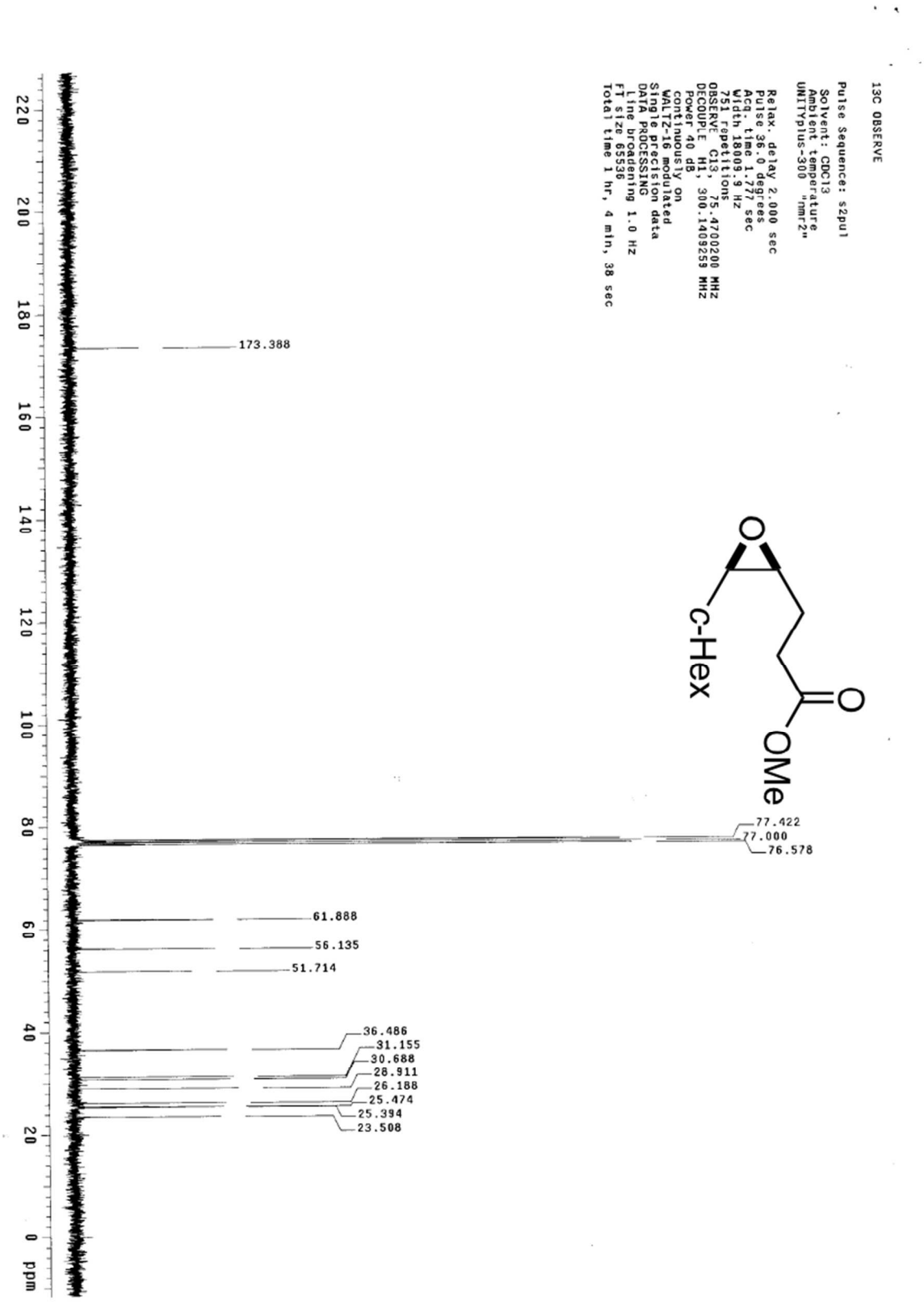


Figure S-43 ^{13}C NMR of Compound 14

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