Tertiary Aminourea-Catalyzed Enantioselective Iodolactonization

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Contents

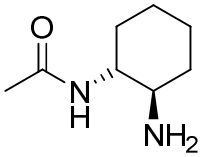
A. General Information

All reactions were carried out under a nitrogen atmosphere. Optimization reactions were performed in flame-dried 2-dram vials; other reactions were performed in flame-dried 20 mL scintillation vials. Stainless steel syringes were used to transfer air- and moisture-sensitive liquids. Flash chromatography was performed using silica gel 60 (230-400mesh) from EM Science. Commercial reagents were purchased from Sigma Aldrich, Alfa Aesar, Lancaster, Otava or TCI, and used as received with the following exceptions: dichloromethane, tetrahydrofuran, and methanol were dried by passing through columns of activated alumina, *N*-iodosuccinimide was recrystallized from a mixture of dioxane and carbon tetrachloride
Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on Inova-500 (500 MHz) and Inova-600 (600 MHz) spectrometers. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent (CHCl3 = δ 7.27). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent (CDCl3 = δ 77.0). Data are represented as follows: chemical shift, multiplicity (br. s = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz), integration. Infrared (IR) spectra were obtained using a Bruker Optics Tensor 27 FTIR spectrometer. Optical rotations were measured using a 1 mL cell with a 0.5 dm path length on a Jasco DIP 370 digital polarimeter. The mass spectral data were obtained on an Agilent Technologies 6120 quadrupole LC/MS spectrometer. Gas chromatography (GC) analysis was performed on an Agilent Technologies 7890A gas chromatograph using an HP-5 (30 m x 0.32 mm x 0.25 μm) column, chiral HPLC analysis was performed using a Shimadzu VP-series instrument.

B. Experimental Procedures and Characterisation

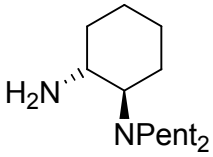
Preparation of Catalyst 1

_N_-((1_R_, 2_R_)-2-aminocyclohexyl)acetamide



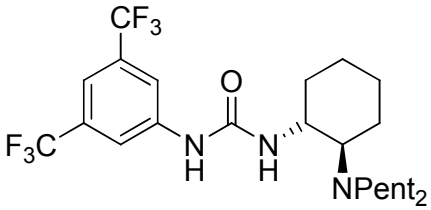
_N_-((1_R_, 2_R_)-2-aminocyclohexyl)acetamide was prepared according to the procedure of Mitchell.[1]

(1_R_, 2_R_)-N^1, N^1-dipentylcyclohexane-1,2-diamine



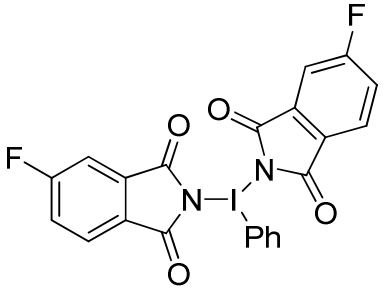
Prepared from _N_-((1_R_, 2_R_)-2-aminocyclohexyl)acetamide *via* reductive amination with valeraldehyde and subsequent acetamide hydrolysis according to the procedure of Fuerst.[2]

1-(3,5-bis(trifluoromethyl)phenyl)-3-((1_R_, 2_R_)-20(dipentylamino)cyclohexyl)urea 1



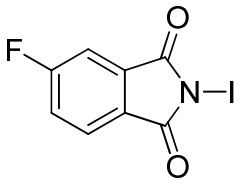
To a solution of (1_R_, 2_R_)-N^1, N^1-dipentylcyclohexane-1,2-diamine (2.00 g, 7.87 mmol) in CH_2Cl_2 (20 mL) was added bistrifluoromethylphenyl isocyanate (1.27 mL, 7.50 mmol) over 5 min. After 4 h the reaction mixture was concentrated in vacuo and purified via column chromatography on silica gel (0-20% MeOH in CH_2Cl_2) to afford **1** as a white solid (2.65 g, 69%); $[\alpha]_D^{23}$ = -46.6 (_c_ = 1.0, $CHCl_3$); IR (Film) 2980, 2932, 1681, 1665, 1574, 1491, 1474, 1387, 1277, 1130, 879, 681 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): 7.89 (s, 2 H), 7.50 (s, 1 H), 6.79 (s, 1 H), 5.75 (s, 1 H), 3.33 (t, _J_ = 9.0 Hz, 1 H), 2.60 (d, _J_ = 12 Hz, 1 H), 2.53-2.47 (m, 2 H), 2.34-2.27 (m, 3 H), 1.90-1.83 (m, 2 H), 1.71 (d, _J_ = 13 Hz, 1 H), 1.47-1.43 (m, 2 H), 1.37-1.20 (m, 13 H), 1.11 (q, _J_ = 13.5 Hz, 1 H), 0.87 (t, _J_ = 6.5 Hz, 6 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 155.8, 141.0, 132.4 (q, _J_ = 33.6 Hz), 123.4 (q, _J_ = 271.3 Hz), 118.9, 115.9, 63.6, 52.3, 50.0, 33.5, 30.0, 29.0, 25.9, 24.7, 23.5, 22.8, 14.3; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{25}H_{37}F_6N_3O$) requires *m/z* 510.3, found *m/z* 510.3.

Phenyliodine(III) Bis(4-fluorophthalimidate)[3]



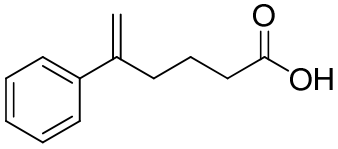
To potassium 4-fluorophthalimide[4] (3.88 g, 19.11 mmol) in MeCN (105 mL) was added bis-(trifluoroacetoxy)-iodobenzene (4.10 g, 9.56 mmol). The reaction mixture was stirred at ambient temperature for 24 h and then filtered, washing with MeCN and dried *in vacuo* to afford an off-white solid (4.47 g, 88%). This product was used immediately in the subsequent step.

4-Fluoro-*N*-iodophthalimide 5



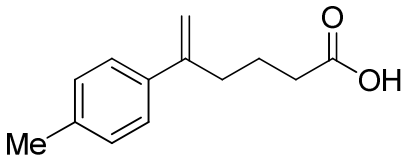
To phenyliodine(III) bis(4-fluorophthalimidate) (4.47 g, 8.42 mmol) in CCl_4 (170 mL) was added iodine (2.14 g, 8.42 mmol). The reaction mixture was stirred for 24 h and then filtered, washing with CCl_4, to afford the desired product as an off-white solid (3.20 g, 65%). The reagent was stored under an inert atmosphere at 0 °C for > 6 months without observable decomposition: IR (Film) 3070, 1690, 1610, 1477, 1355, 1295, 1075, 915, 836, 730 cm^{-1}; ^1H NMR (*d*6 benzene, 500 MHz): 6.98 (dd, *J* = 8.5 Hz, 4.0 Hz, 1 H), 6.82 (dd, *J* = 7.0, 2.0 Hz, 1 H), 6.28 (td, *J* = 9.0, 2.0 Hz, 1 H); ^{13}C NMR (*d*6 benzene, 125 MHz): 167.0, 166.9 (d, *J* = 123.9 Hz), 164.4, 135.3 (d, *J* = 9.1 Hz), 128.7 (d obs.), 125.4 (d, *J* = 9.1 Hz), 119.7 (d, *J* = 23.6 Hz), 110.9 (d, *J* = 26.9 Hz).

5-Phenylhex-5-enoic acid 2a



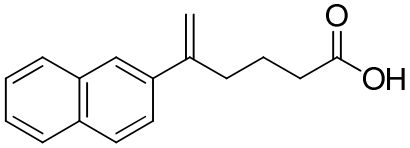
Prepared *via* Wittig reaction from the commercially available keto-acid according to the procedure of Hartwig.[5] IR (film) 2956, 1707, 1419, 1406, 1282, 1197, 887 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): 7.43 (d, *J* = 7.5 Hz, 2 H), 7.36 (t, *J* = 7.5 Hz, 2 H), 7.30 (t, *J* = 7.5 Hz, 1 H), 5.34 (s, 1 H), 5.11 (s, 1 H), 2.60 (t, *J* = 7 Hz, 2 H), 2.41 (t, *J* = 7.5 Hz, 2 H), 1.85-1.81 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 180.1, 147.6, 141.0, 128.6, 127.8, 126.4, 113.3, 34.7, 33.5, 23.3. MS (ESI-APCI) exact mass calculated for [M+H] ($C_{12}H_{14}O_2$) requires *m/z* 191.1, found *m/z* 191.1.

5-*p*-tolylhex-5-enoic acid 2b



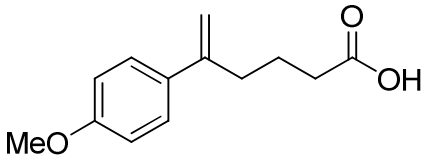
Prepared *via* Wittig reaction from the commercial keto-acid according to the procedure of Hartwig.[5] IR (Film) 1699, 1626, 1511, 1415, 1248, 953 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): 7.33 (d, *J* = 8 Hz, 2 H), 7.16 (d, *J* = 8 Hz, 2 H), 5.31 (s, 1H), 5.06 (s, 1 H), 2.59 (t, *J* = 7.5 Hz, 2 H), 2.40 (t, *J* = 7.5 Hz, 2 H), 2.37 (s, 3 H), 1.82 (quin., *J* = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): 180.2, 147.3, 138.0, 137.5, 129.3, 126.2, 112.6, 34.7, 33.5, 23.3, 21.3; MS (ESI-APCI) exact mass calculated for [M-H] ($C_{13}H_{15}O_2$) requires *m/z* 203.1, found *m/z* 203.1.

5-(naphthalen-2-yl)hex-5-enoic acid 2c



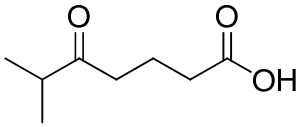
Prepared *via* Wittig reaction from the known keto-acid[6] according to the procedure of Hartwig.[5] IR (Film) 2973, 1693, 1412, 1300, 1198, 1152, 931, 754 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): 7.86-7.82 (m, 3 H), 7.60 (d, *J* = 5.5 Hz, 1 H), 7.51-7.46 (m, 2 H), 5.50 (s, 1 H), 5.22 (s, 1 H), 2.73 (t, *J* = 8.0 Hz, 2 H), 2.45 (t, *J* = 7.5 Hz, 2 H), 1.89 (quin., *J* = 7.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 180.1, 147.4, 138.2, 133.6, 133.1, 128.4, 128.2, 127.8, 126.4, 126.1, 125.0, 124.8, 113.9, 34.7, 33.5, 23.4; MS (ESI-APCI) exact mass calculated for [M-H] ($C_{16}H_{15}O_2$) requires *m/z* 239.1, found *m/z* 239.1.

5-(4-methoxyphenyl)hex-5-enoic acid 2d



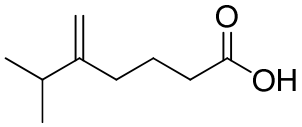
Prepared *via* Wittig reaction from the known keto-acid[7] according to the procedure of Hartwig.[5] IR (Film) 1704, 1602, 1516, 1439, 1307, 1261, 1031, 889 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): 7.37 (d, *J* = 8.5 Hz, 2 H), 6.89 (d, *J* = 8.5 Hz, 2 H), 5.26 (s, 1 H), 5.02 (s, 1 H), 3.84 (s, 3 H), 2.57 (t, *J* = 7.5 Hz, 2 H), 2.40 (t, *J* = 7.5 Hz, 2 H), 1.82 (quin., *J* = 7.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 180.0, 159.4, 146.8, 133.3, 127.4, 114.0, 111.8, 55.5, 34.7, 33.5, 23.3; MS (ESI-APCI) exact mass calculated for [M-H] ($C_{13}H_{15}O_3$) requires *m/z* 219.1, found *m/z* 219.1.

6-methyl-5-oxoheptanoic acid



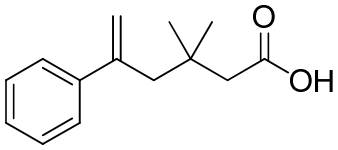
To a solution of glutaric anhydride (5 g, 43.9 mmol) in THF (20 mL) at 0 C was added isopropylmagnesium bromide (2.0 M in THF, 43.9 mmol, 21.9 mL) dropwise. The reaction mixture was then heated to relux for 4 h and allowed to cool in ice before quenching with saturated aqueous NH_4Cl solution (10 mL). Following removal of THF *in vacuo* the reaction mixture was partitioned between CH_2Cl_2 (50 mL) and 1 M HCl (50 mL). The organic layer was then separated, dried ($MgSO_4$) and concentrated to afford a yellow oil. Purification by column chromatography on silica gel (10-50% ethyl acetate in hexanes) afforded 6-methyl-5-oxoheptanoic acid (2.90 g, 42%) as a colourless oil; IR (film) 2971, 1703, 1457, 1408, 1385, 1239; ^{1}H NMR ($CDCl_3$, 500 MHz): 2.57 (sept., J = 7 Hz, 1 H), 2.53 (t, J = 7.5 Hz, 2 H), 2.36 (t, J = 7 Hz, 2 H), 1.88 (quin., J = 7.5 Hz, 2 H), 1.07 (d, J = 7 Hz, 6 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 214.5, 179.5, 41.1, 39.1, 33.3, 18.8, 18.4.

6-methyl-5-methyleneheptanoic acid 2e[8]



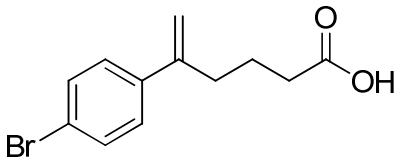
Prepared *via* Wittig reaction from the 6-methyl-5-oxoheptanoic acid according to the procedure of Hartwig.[5] Data consistent with literature values.[8]

3,3-dimethyl-5-phenylhex-5-enoic acid 2f



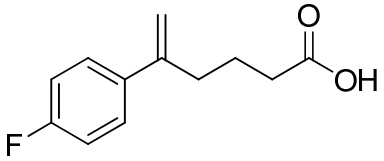
Prepared *via* Wittig reaction from the known keto-acid[9] according to the procedure of Hartwig.[5] IR (Film) 2967, 1700, 1405, 1264, 1237, 896, 779 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): 7.42 (d, J = 7.5 Hz, 2 H), 7.35 (t, J = 7.5 Hz, 2 H), 5.35 (s, 1 H), 5.15 (s, 1 H), 2.71 (s, 3 H), 2.24 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 179.4, 146.8, 143.6, 128.5, 127.5, 126.8, 117.9, 47.1, 46.1, 34.4, 28.1; MS (ESI-APCI) exact mass calculated for [M-H] ($C_{14}H_{17}O_2$) requires *m/z* 217.1, found *m/z* 217.1.

5-(4-bromophenyl)hex-5-enoic acid 2g



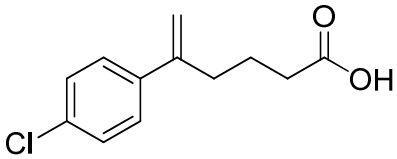
Prepared *via* Wittig reaction from the commercial keto-acid according to the procedure of Hartwig.[5] IR (film) 3080, 2957, 2917, 1703, 1488, 1438, 1250, 1168, 902, 836 cm $^{-1}$; ^{1}H NMR ($CDCl_3$, 500 MHz): 7.47 (d, *J* = 7 Hz, 2 H), 7.29 (d, *J* = 7 Hz, 2 H), 5.33 (s, 1 H), 5.12 (s, 1 H), 2.56 (t, *J* = 7.5 Hz, 2 H), 2.40 (t, *J* = 7.5 Hz, 2 H), 1.80 (t, *J* = 7.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 179.9, 146.5, 139.9, 131.7, 128.0, 121.7, 113.9, 34.5, 33.4, 23.2. MS (ESI-APCI) exact mass calculated for [M-H] ($C_{12}H_{12}BrO_2$) requires *m/z* 267.0, found *m/z* 267.0.

5-(4-fluorophenyl)hex-5-enoic acid 2h



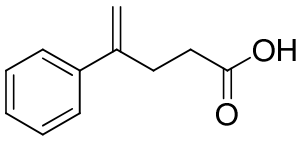
Prepared *via* Wittig reaction from the commercial keto-acid according to the procedure of Hartwig.[5] IR (Film) 1704, 1601, 1509, 1405, 1298, 1204 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): 7.38 (dd, *J* = 9, 5.5 Hz, 2 H), 7.03 (t, *J* = 8.5 Hz, 2 H), 5.28 (s, 1 H), 5.09 (s, 1 H), 2.56 (t, *J* = 8.0 Hz, 2 H), 2.40 (t, *J* = 7.5 Hz, 2 H), 1.80 (quin., *J* = 7 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 180.0, 163.6, 161.6, 146.6, 137.0, 128.0, 127.9, 115.5, 115.3, 113.3, 34.8, 33.5, 23.2; MS (ESI-APCI) exact mass calculated for [M-H] ($C_{12}H_{12}FO_2$) requires *m/z* 207.1, found *m/z* 207.1.

5-(4-chlorophenyl)hex-5-enoic acid 2i



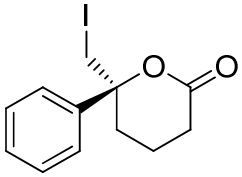
Prepared *via* Wittig reaction from the commercial keto-acid according to the procedure of Hartwig.[5] IR (Film) 1702, 1297, 1206, 922, 891, 832 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): 7.36-7.30 (m, 5 H), 5.32 (s, 1 H), 5.11 (s, 1 H), 2.56 (t *J* = 8 Hz, 2 H), 2.40 (t *J* = 7.5 Hz, 2 H), 1.80 (quin. *J* = 7.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 180.0, 146.5, 139.4, 133.6, 128.8, 127.7, 113.9, 34.6, 33.5, 23.2; MS (ESI-APCI) exact mass calculated for [M-H] ($C_{12}H_{12}ClO_2$) requires *m/z* 223.0, found *m/z* 222.9.

4-Phenylpent-4-enoic acid 9a



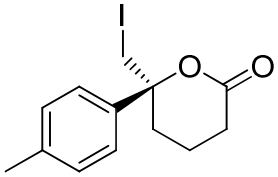
Prepared according to the procedure of Hartwig; data consistent with literature values.[5]

6-(iodomethyl)-6-phenyltetrahydro-2*H*-one 3a



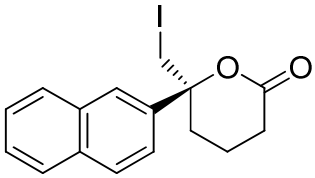
The reaction was run on 0.20 mmol scale. The crude material was purified by silica gel chromatography (5-40% ethyl acetate in hexanes) to give **3a** as a colorless oil (54.5 mg, 87%). The enantiomeric excess was determined to be 94% by chiral HPLC analysis (CHIRALPAK AD-H, 1 mL/min, 2% IPA in Hexanes, λ = 254 nm): t_R(major) = 27.5 min, t_R(minor) = 30.7 min; $[\alpha]_D^{24}$ = +29.1 (*c* = 1.2, $CHCl_3$); IR (film) 2956, 2933, 2863, 1734, 1682, 1575, 1388, 1276, 1130, 879 cm; ^{1}H NMR ($CDCl_3$, 500 MHz): 7.41-7.36 (m, 5 H), 3.59 (m, 2 H), 2.56-2.37 (m, 4 H), 2.85-2.81 (m, 1H), 1.62-1.58 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): 170.7, 140.5, 129.3, 128.7, 125.5, 84.7, 32.3, 29.2, 17.9, 16.8; MS (ESI-APCI) exact mass calculated for [M+Na] ($C_{12}H_{13}INaO_2$) requires *m/z* 339.0, found *m/z* 339.0.

6-(iodomethyl)-6-*p*-tolyltetrahydro-2*H*-pyran-2-one 3b



The reaction was run on 0.20 mmol scale. The crude material was purified by silica gel chromatography (5-40% ethyl acetate in hexanes) to give **3b** as a colorless oil (63.5 mg, 96%). The enantiomeric excess was determined to be 88% by chiral HPLC analysis (CHIRALPAK AD-H, 1 mL/min, 2% IPA in Hexanes, λ = 254 nm): t_R(major) = 26.7 min, t_R(minor) = 34.7 min; $[\alpha]_D^{24}$ = + 34.1 (*c* = 1.1, $CHCl_3$); IR (film) 1724, 1510, 1443, 1259, 1231, 1038, 937, 812, 634 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): 7.26 (d, *J* = 8 Hz, 2 H), 7.21 (d, *J* = 8.5 Hz, 2 H), 3.57 (d, *J* = 12.5 Hz, 1 H), 3.55 (d, *J* = 12.5 Hz, 1 H), 2.50-2.32 (m, 7 H), 1.85-1.83 (m, 1 H), 1.62-1.58 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 170.8, 138.5, 137.4, 129.9, 125.4, 84.7, 32.2, 29.2, 21.3, 18.2, 16.8; MS (ESI-APCI) exact mass calculated for [M+Na] ($C_{13}H_{15}INaO_2$) requires *m/z* 353.0, found *m/z* 353.0.

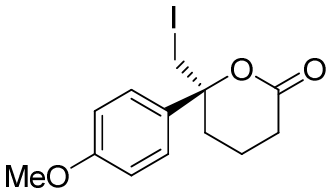
6-(iodomethyl)-6-(naphthalen-2-yl)tetrahydro-2*H*-pyran-2-one 3c



The reaction was run on 0.20 mmol scale. The crude material was purified by silica gel chromatography (5-40% ethyl acetate in hexanes) to give **3c** as a colorless oil (67.5 mg, 92%). The enantiomeric excess was determined to be 94% by chiral HPLC analysis (CHIRALPAK OD-H, 1 mL/min, 10% IPA in Hexanes, λ = 254 nm): t_R(major) = 25.6 min, t_R(minor) = 31.8 min; $[\alpha]_D^{24}$ = +25.8 (*c* = 2.0, $CHCl_3$); IR (film) 3018, 1736, 1263, 1215, 1180, 1037, 817, 745 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): 7.91-7.86 (m, 4 H), 7.56-7.54 (m, 2 H), 7.42 (d, *J* = 8 Hz, 1 H), 3.70 (d, *J* = 11 Hz, 1 H), 3.67 (d, *J* = 11 Hz, 1 H), 2.56-2.42 (m, 4 H), 1.88-1.85 (m, 1

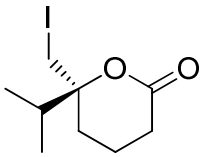
H), 1.64-1.61 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 170.7, 137.7, 133.3, 133.1, 129.3, 128.6, 127.8, 127.1, 125.3, 122.6, 84.8, 32.3, 29.3, 17.6, 16.9; MS (ESI-APCI) exact mass calculated for [M+Na] ($C_{16}H_{16}IO_2$) requires *m/z* 367.0, found *m/z* 367.0.

6-(iodomethyl)-6-(4-methoxyphenyl)tetrahydro-2*H*-pyran-2-one 3d



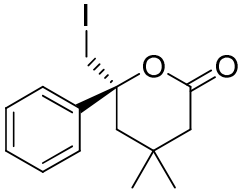
The reaction was run on 0.20 mmol scale. The crude material was purified by silica gel chromatography (5-40% ethyl acetate in hexanes) to give **3d** as a colorless oil (62.7 mg, 91%). The enantiomeric excess was determined to be 48% by chiral HPLC analysis (CHIRALPAK AD-H, 1 mL/min, 2% IPA in Hexanes, λ = 254 nm): t_R(major) = 41.8 min, t_R(minor) = 52.4 min; $[\alpha]_D^{24}$ = +11.8 (*c* = 1.0, $CHCl_3$); IR (film) 3031, 1722, 1508, 1443, 1231, 1038, 812 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): 7.29 (d, *J* = 9 Hz, 2 H), 6.93 (d, *J* = 9 Hz, 2 H), 3.84 (s, 3 H), 3.58 (d, *J* = 11 Hz, 1 H), 3.54 (d, *J* = 11 Hz, 1 H), 2.49-2.35 (m, 4 H), 1.84-1.81 (m, 1 H), 1.64-1.61 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 170.8, 159.7, 132.2, 126.8, 114.5, 84.5, 55.6, 32.0, 29.2, 18.3, 16.8; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{13}H_{16}IO_3$) requires *m/z* 347.0, found *m/z* 347.1.

6-(iodomethyl)-6-isopropyltetrahydro-2*H*-pyran-2-one 3e



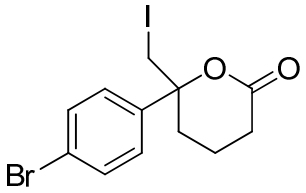
The reaction was run on 0.20 mmol scale. The crude material was purified by silica gel chromatography (5-40% ethyl acetate in hexanes) to give **3e** as a colorless oil (48 mg, 85%). The enantiomeric excess was determined to be 94% by chiral GC analysis (γ-TA, 150 °C isothermal, t_R(major) = 30.7 min, t_R(minor) = 50.7 min; $[\alpha]_D^{24}$ = +8.6 (*c* = 2.0, $CHCl_3$); IR (film) 2956, 2882, 1733, 1472, 1457, 1207, 1228, 1029 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): 3.46 (s, 2 H), 2.55 (dt, *J* = 18.5, 6.5 Hz, 1 H), 2.44 (dt, *J* = 18, 7 Hz, 1 H), 2.23 (sept., *J* = 7 Hz, 1 H), 2.08-2.04 (m, 1 H), 1.96-1.89 (m, 3 H), 1.02 (d, *J* = 7 Hz, 6 H), ^{13}C NMR ($CDCl_3$, 125 MHz): 170.8, 85.2, 35.6, 29.9, 27.2, 17.1, 16.8, 13.1; MS (ESI-APCI) exact mass calculated for [M+Na] ($C_9H_{15}NaIO_2$) requires *m/z* 305.0, found *m/z* 305.0.

6-(iodomethyl)-4,4-dimethyl-6-phenyltetrahydro-2*H*-pyran-2-one 3f



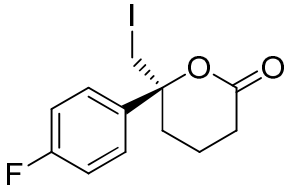
The reaction was run on 0.20 mmol scale. The crude material was purified by silica gel chromatography (5-40% ethyl acetate in hexanes) to give **3f** as a colorless oil (62 mg, 90%). The enantiomeric excess was determined to be 87% by chiral HPLC analysis (CHIRALPAK AD-H, 1 mL/min, 2% IPA in Hexanes, λ = 254 nm): t_R(major) = 16.6 min, t_R(minor) = 19.5 min; $[\alpha]_D^{24}$ = + 26.7 (*c* = 1.1, $CHCl_3$); IR (film) 2962, 1732, 1444, 1259, 1187, 1037, 812, 702 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): 7.46 (d, *J* = 8 Hz, 2 H), 7.40 (t, *J* = 8 Hz, 2 H), 7.34 (t, *J* = 8 Hz, 1 H), 3.55 (d, *J* = 11 Hz, 1 H), 3.49 (d, *J* = 11 Hz, 1 H), 2.49 (d, *J* = 14.5 Hz, 1 H), 2.33 (d, *J* = 14.5 Hz, 1 H), 2.30 (d, *J* = 16 Hz, 1 H), 2.21 (d, *J* = 16 Hz, 1 H), 1.12 (s, 3 H), 0.77 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 171.1, 141.3, 129.1, 128.5, 125.3, 83.5, 44.6, 43.8, 32.0, 30.8, 28.8, 20.7; MS (ESI-APCI) exact mass calculated for [M+Na] ($C_{14}H_{17}INaO_2$) requires *m/z* 367.0, found *m/z* 367.0.

6-(4-bromophenyl)-6-(iodomethyl)tetrahydro-2*H*-pyran-2-one 3g



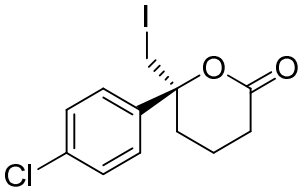
The reaction was run on 0.20 mmol scale. The crude material was purified by silica gel chromatography (5-40% ethyl acetate in hexanes) to give **3g** as a crystalline solid (56 mg, 71%). The enantiomeric excess was determined to be 96% by chiral HPLC analysis (CHIRALPAK AD-H, 1 mL/min, 2% IPA in Hexanes, λ = 254 nm): t_R(major) = 35.6 min, t_R(minor) = 49.6 min; $[\alpha]_D^{24}$ = +28.7 (*c* = 1.4, $CHCl_3$); IR (film) 2957, 2929, 1740, 1489, 1238, 1180, 1132, 1039 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): 7.55 (d, *J* = 8 Hz, 2 H), 7.27 (d, *J* = 8 Hz, 2 H), 3.55 (s, 2 H), 2.55-2.31 (m, 4 H), 1.84 (m, 1 H), 1.59 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 170.2, 139.7, 132.4, 127.3, 122.9, 84.3, 32.2, 29.2, 17.1, 16.8; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{12}H_{13}{}^{79}BrIO_2$) requires *m/z* 394.9, found *m/z* 394.9.

6-(4-fluorophenyl)-6-(iodomethyl)tetrahydro-2*H*-pyran-2-one 3h



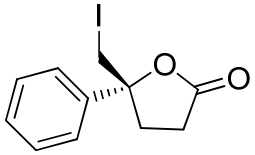
The reaction was run on 0.20 mmol scale. The crude material was purified by silica gel chromatography (5-40% ethyl acetate in hexanes) to give **3h** as a colorless oil (61 mg, 91%). The enantiomeric excess was determined to be 96% by chiral HPLC analysis (CHIRALPAK AD-H, 1 mL/min, 2% IPA in Hexanes, λ = 254 nm): t_R(major) = 32.8 min, t_R(minor) = 38.5 min; $[\alpha]_D^{24}$ = + 22.7 (*c* = 1.3, $CHCl_3$); IR (film) 2962.2, 2872, 1733, 1603, 1509, 1443, 1411, 1231, 1186, 1038, 936, 841 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): 7.29 (dd, *J* = 8, 5.5 Hz, 2 H), 7.02 (t, *J* = 8 Hz, 2 H), 3.47 (m, 2 H), 2.46-2.25 (m, 4 H), 1.79 (m, 1 H), 1.52 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 170.4, 163.7, 161.8, 136.3, 127.5, 127.4, 116.3, 116.1, 84.3, 32.2, 29.2, 17.7, 16.8; MS (ESI-APCI) exact mass calculated for [M+Na] ($C_{12}H_{12}FINaO_2$) requires *m/z* 357.0, found *m/z* 357.0.

6-(4-chlorophenyl)-6-(iodomethyl)tetrahydro-2*H*-pyran-2-one 3i



The reaction was run on 0.20 mmol scale. The crude material was purified by silica gel chromatography (5-40% ethyl acetate in hexanes) to give **3i** as a colorless oil (56 mg, 80%). The enantiomeric excess was determined to be 96% by chiral HPLC analysis (CHIRALPAK AD-H, 1 mL/min, 2% IPA in Hexanes, λ = 254 nm): t_R(major) = 32.9 min, t_R(minor) = 44.3 min; $[\alpha]_D^{24}$ = +27.8 (*c* = 1.0, $CHCl_3$); IR (film) 2957, 1738, 1492, 1278, 1179, 1094, 1039, 822, 752 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): 7.31 (d, *J* = 8.5 Hz, 2 H), 7.22 (d, *J* = 8.5 Hz, 2 H), 3.47 (s, 2 H), 2.43-2.26 (m, 4 H), 1.78 (m, 1 H), 1.50 (m, 1 H), ^{13}C NMR ($CDCl_3$, 125 MHz): 170.3, 139.1, 134.8, 129.4, 127.0, 84.3, 32.2, 29.2, 17.3, 16.8; MS (ESI-APCI) exact mass calculated for [M+Na] ($C_{12}H_{12}{}^{35}ClINaO_2$) requires *m/z* 372.9, found *m/z* 372.9.

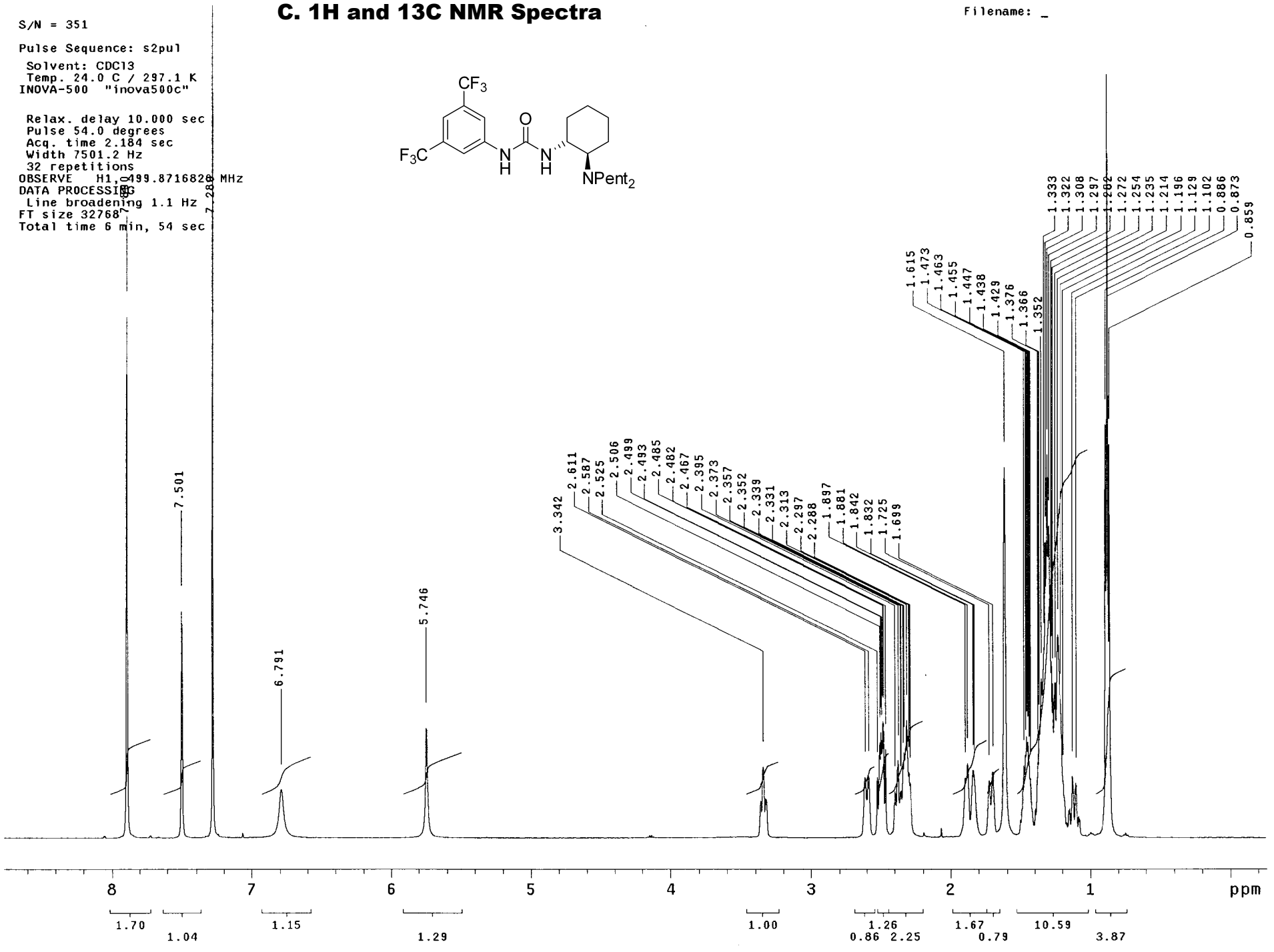
5-(iodomethyl)-5-phenyldihydrofuran-2(3*H*)-one 10a

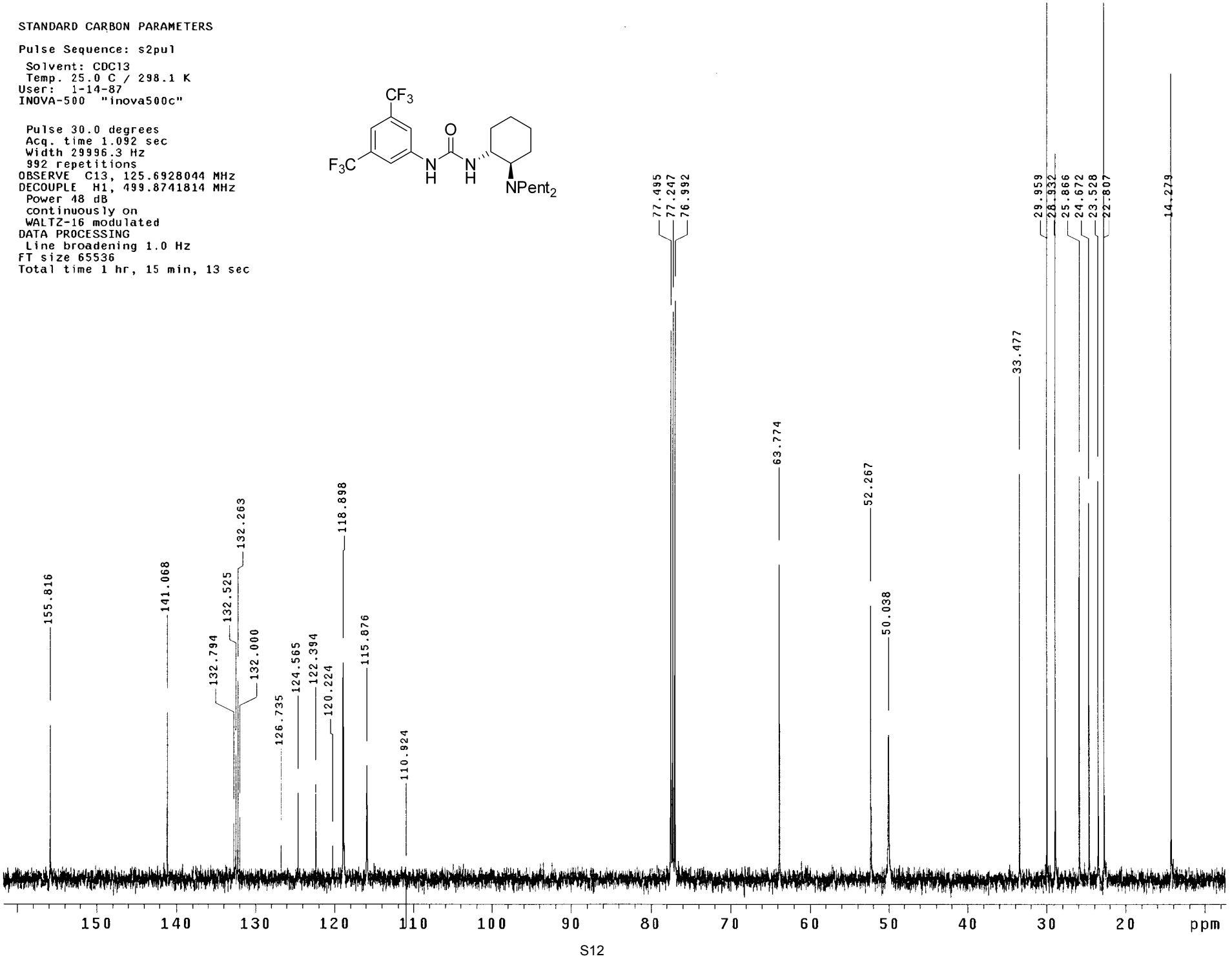


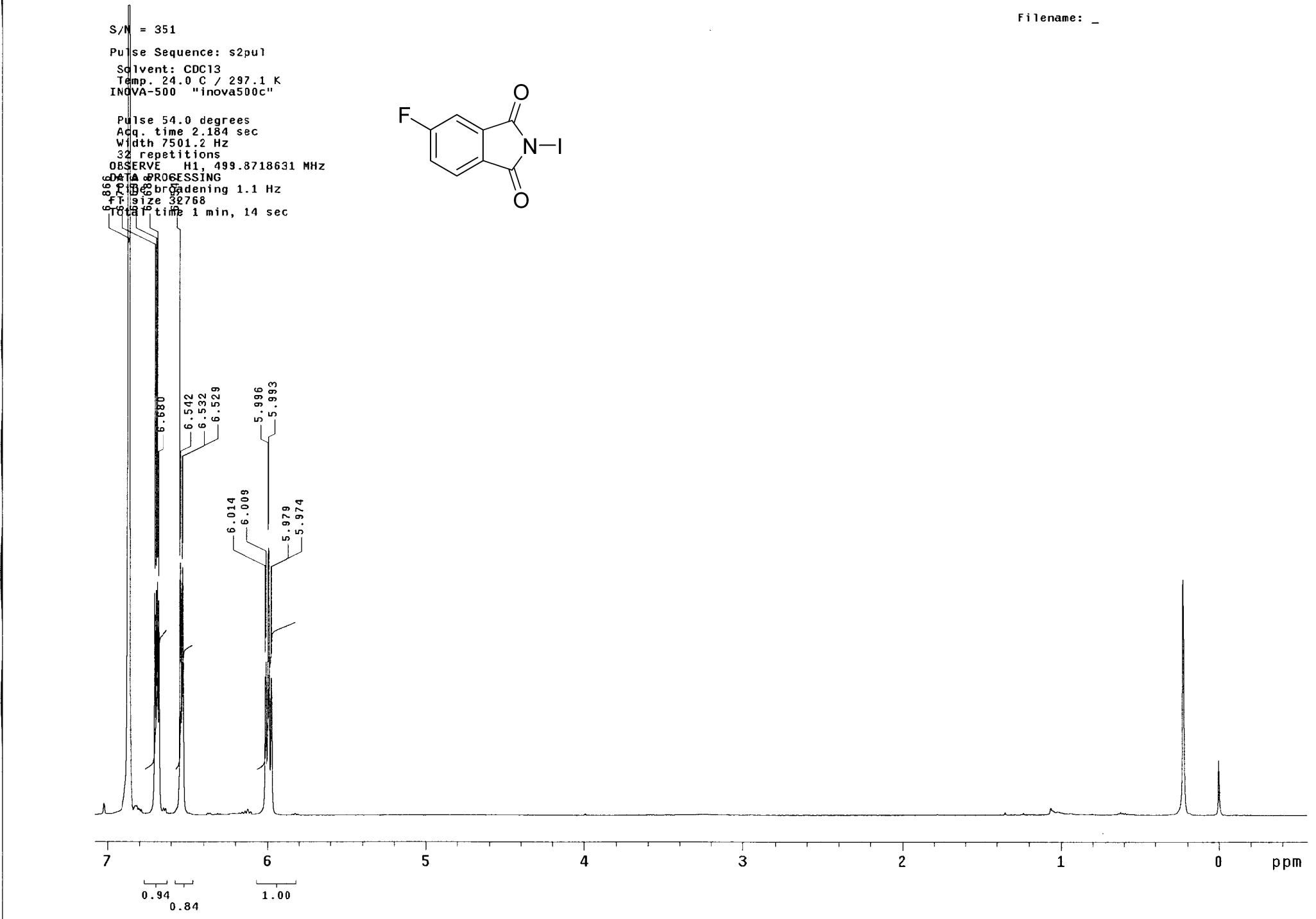
The reaction was run on 0.20 mmol scale. The crude material was purified by silica gel chromatography (5-40% ethyl acetate in hexanes) to give **10a** as a colorless oil (52.5 mg, 87%). The enantiomeric excess was determined to be 89% by chiral HPLC analysis (CHIRALPAK AD-H, 1 mL/min, 2% IPA in Hexanes, λ = 254 nm): t_R(major) = 24.1 min, t_R(minor) = 27.8 min; $[\alpha]_D^{24}$ +14.2 (*c* = 1.3, $CHCl_3$); IR (film) 3030, 2958, 1779, 1541, 1449, 1154, 1025, 929, 766 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): 7.43-7.27 (m, 5 H), 3.66 (d, *J* = 11 Hz, 1 H), 3.64 (d, *J* = 11 Hz, 1 H), 2.77-2.50 (m, 4 H); ^{13}C NMR ($CDCl_3$, 125 MHz): 175.5, 140.9, 129.1, 128.8, 125.1, 86.3, 34.2, 29.4, 16.5; MS (ESI-APCI) exact mass calculated for [M+H] ($C_{11}H_{12}IO_2$) requires *m/z* 303.1, found *m/z* 303.1; Data consistent with literature values.[10]

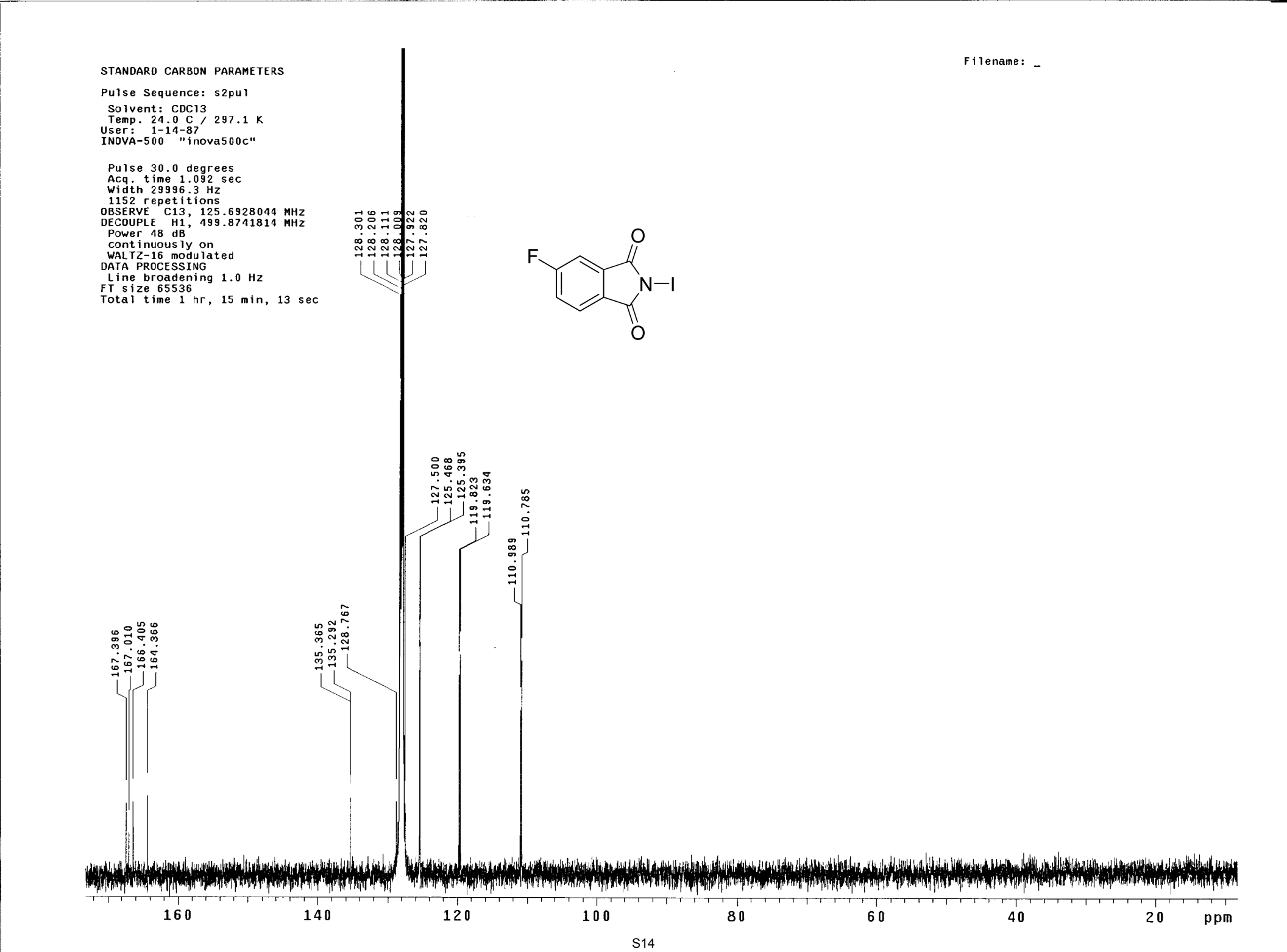
All of the iodolactone products were treated as light-sensitive and were stored at -30 °C under argon. These products should not be subjected to high-vacuum for >10 min.

C. 1H and 13C NMR Spectra




STANDARD CARBON PARAMETERS
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
INOVA-500 "inova500c"
Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
992 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 15 min, 13 sec
CF3
F3C
N
H
O
N
H
NPent2
155.816
141.068
132.794
132.525
132.263
132.000
126.735
124.565
122.394
120.224
118.898
115.876
110.924
77.495
77.247
76.992
63.774
52.267
50.038
33.477
29.959
28.932
25.866
24.672
23.528
22.807
14.279
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


S/N = 351
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
INOVA-500 "inova500c"
Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
32 repetitions
OBSERVE H1, 499.8718631 MHz
DATA PROCESSING
FT broadening 1.1 Hz
FT size 32768
Total time 1 min, 14 sec
Filename: _
F
O
N—I
O
6.680
6.542
6.532
6.529
5.996
5.993
6.014
6.009
5.979
5.974
7
6
5
4
3
2
1
0
ppm
0.94
0.84
1.00

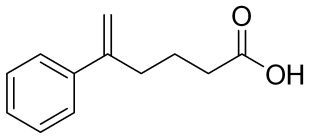

STANDARD CARBON PARAMETERS
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
User: 1-14-87
INOVA-500 "inova500c"
Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
1152 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 15 min, 13 sec
Filename: _
128.301
128.206
128.111
128.009
127.922
127.820
127.500
125.468
125.395
119.823
119.634
110.989
110.785
167.396
167.010
166.405
164.366
135.365
135.292
128.767
F
O
N—I
O
160
140
120
100
80
60
40
20
ppm

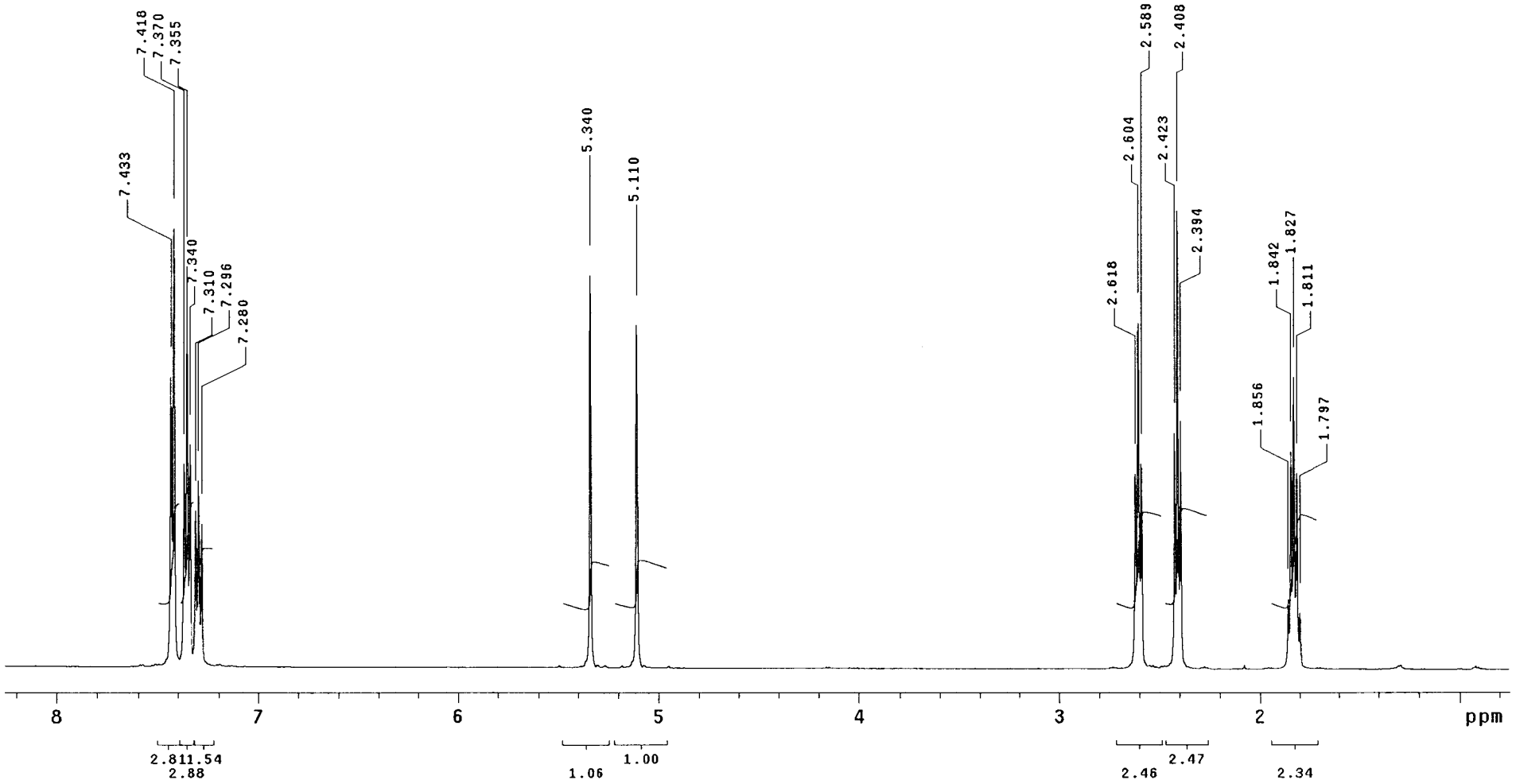
Filename: _

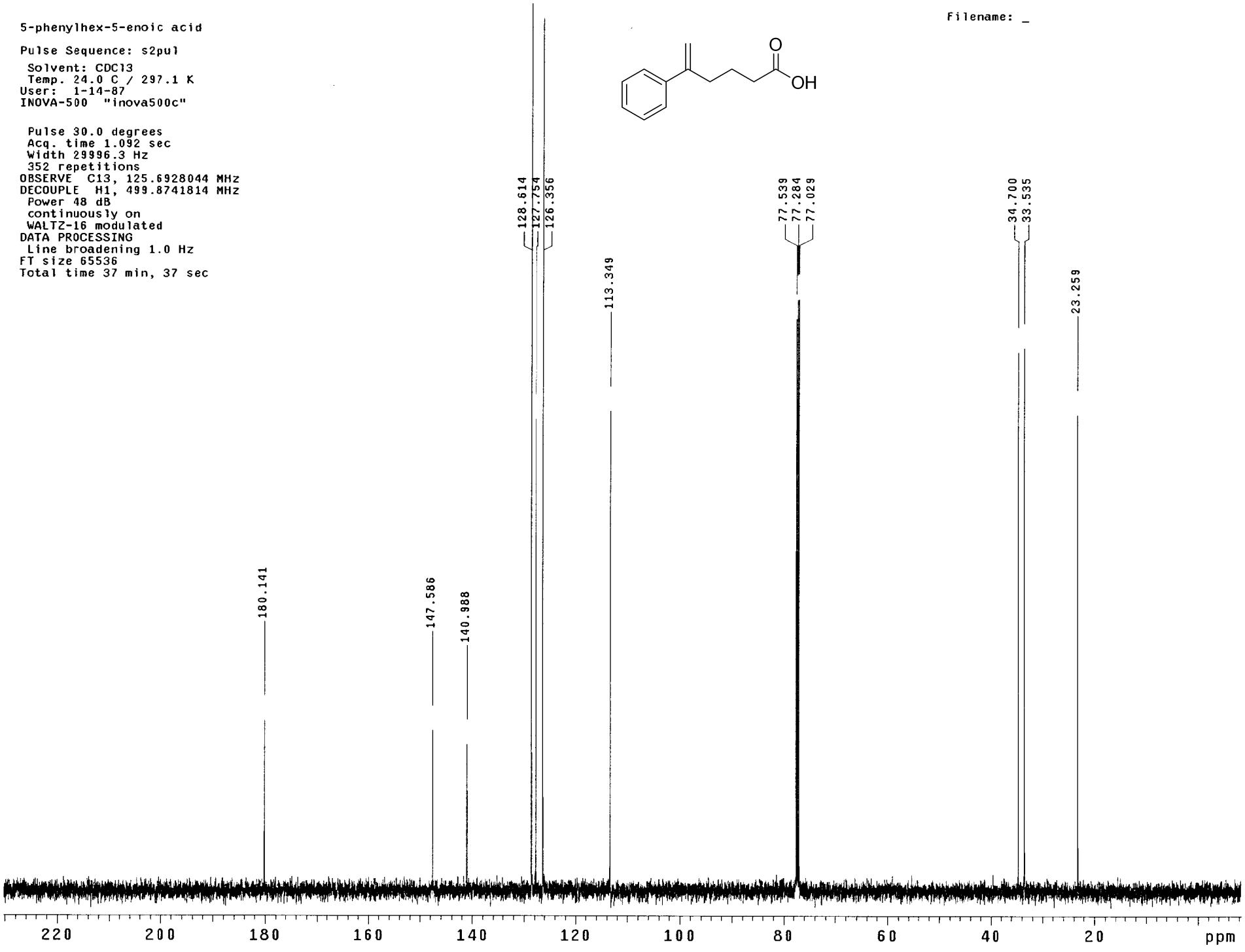
5-phenylhex-5-enoic acid

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
INOVA-500 "inova500c"

Relax. delay 10.000 sec
Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
16 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 32768
Total time 6 min, 54 sec





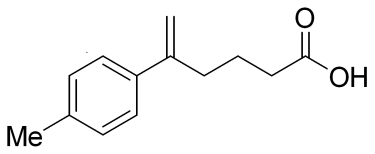

5-phenylhex-5-enoic acid
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
User: 1-14-87
INOVA-500 "inova500c"
Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
352 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 37 min, 37 sec
Filename: _
O
OH
180.141
147.586
140.988
128.614
127.754
126.356
113.349
77.539
77.284
77.029
34.700
33.535
23.259
220
200
180
160
140
120
100
80
60
40
20
ppm

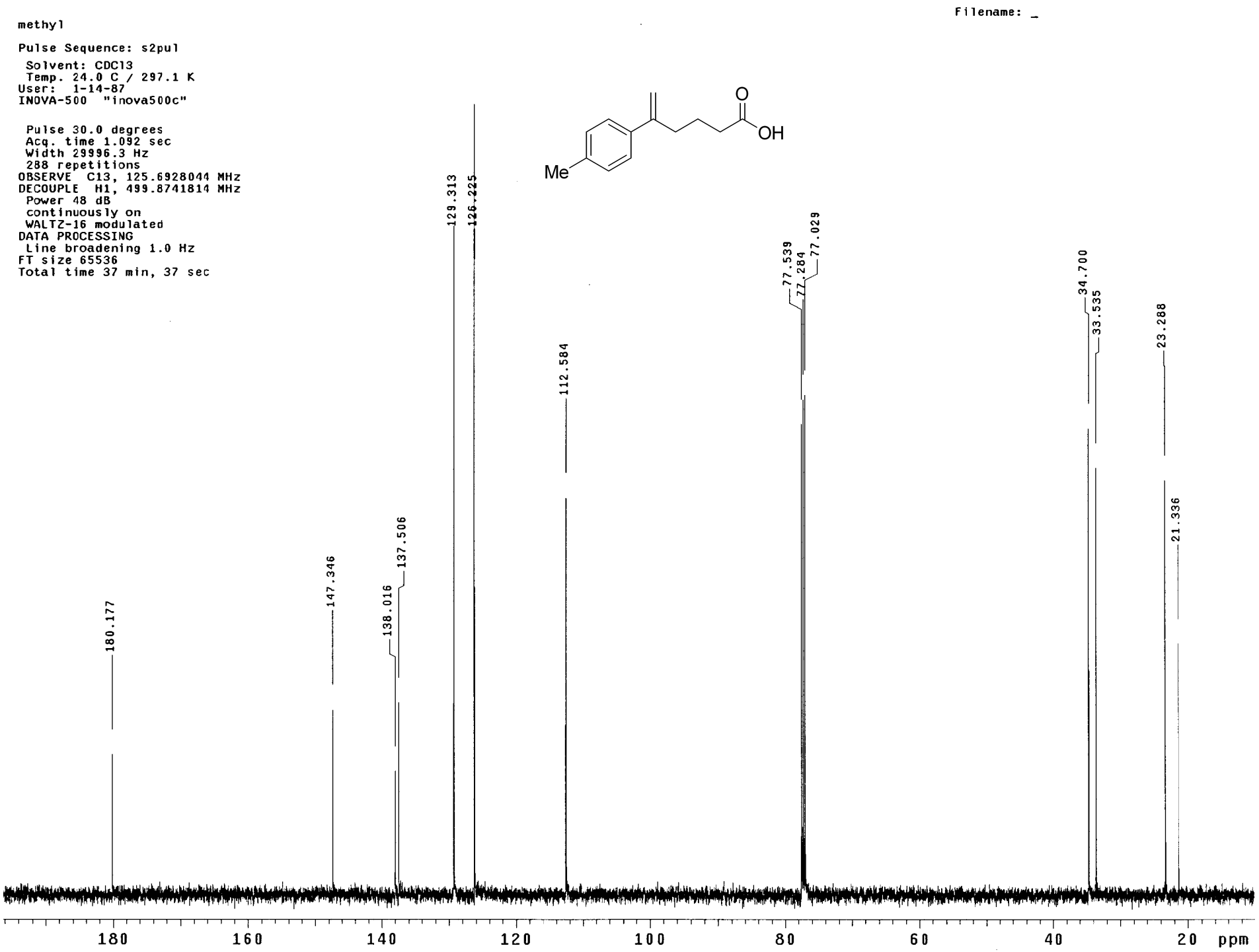
Filename: _

methyl

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
INOVA-500 "inova500c"

Relax. delay 10.000 sec
Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
4 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 32768
Total time 1 min, 13 sec



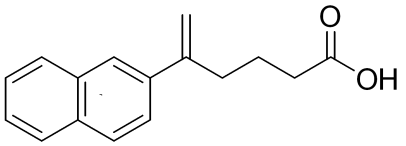

Filename: _
methyl
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
User: 1-14-87
INOVA-500 "inova500c"
Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
288 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 37 min, 37 sec
O
OH
Me
180.177
147.346
138.016
137.506
129.313
126.225
112.584
77.539
77.284
77.029
34.700
33.535
23.288
21.336
180
160
140
120
100
80
60
40
20
ppm

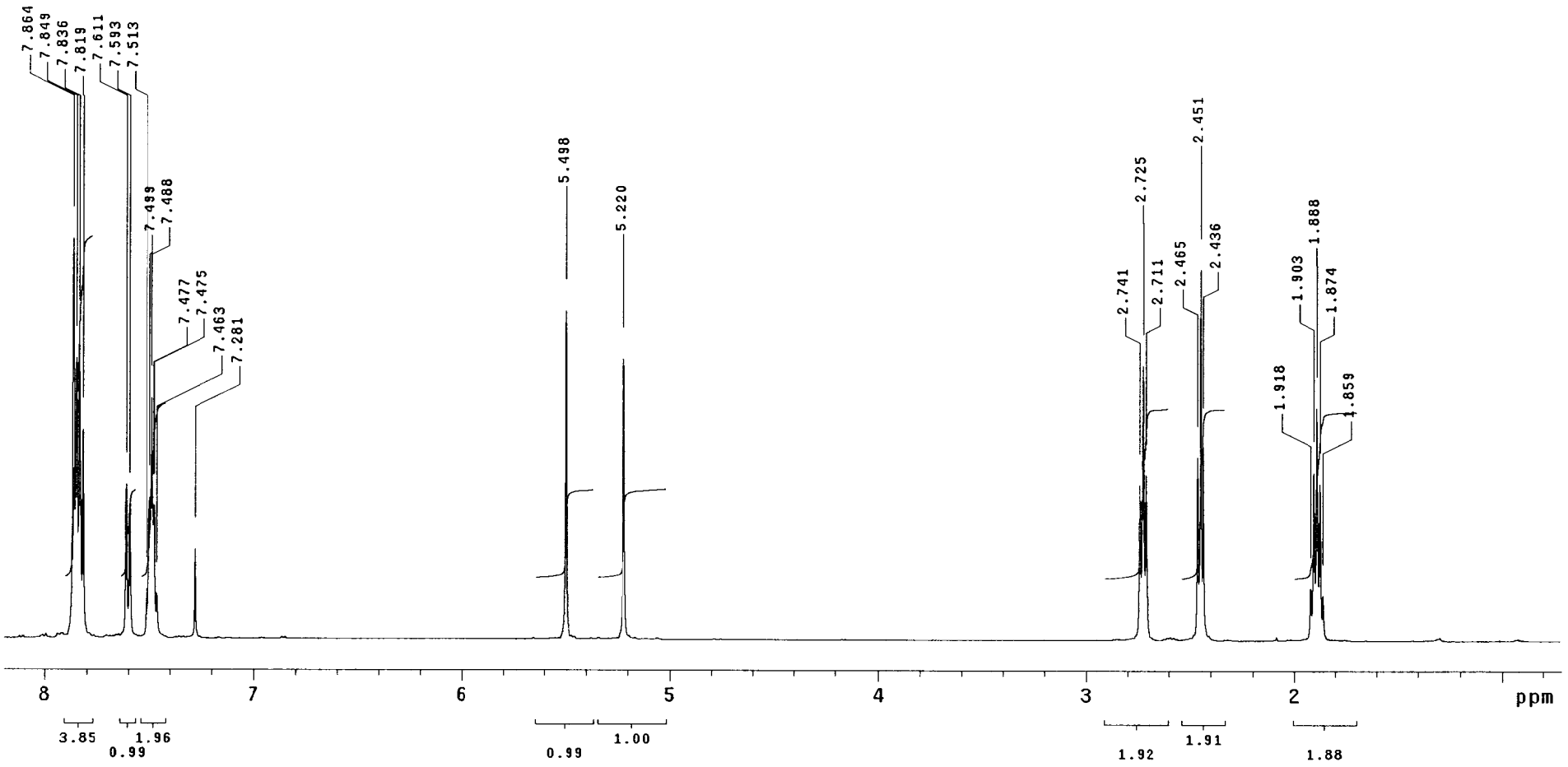
Filename: _

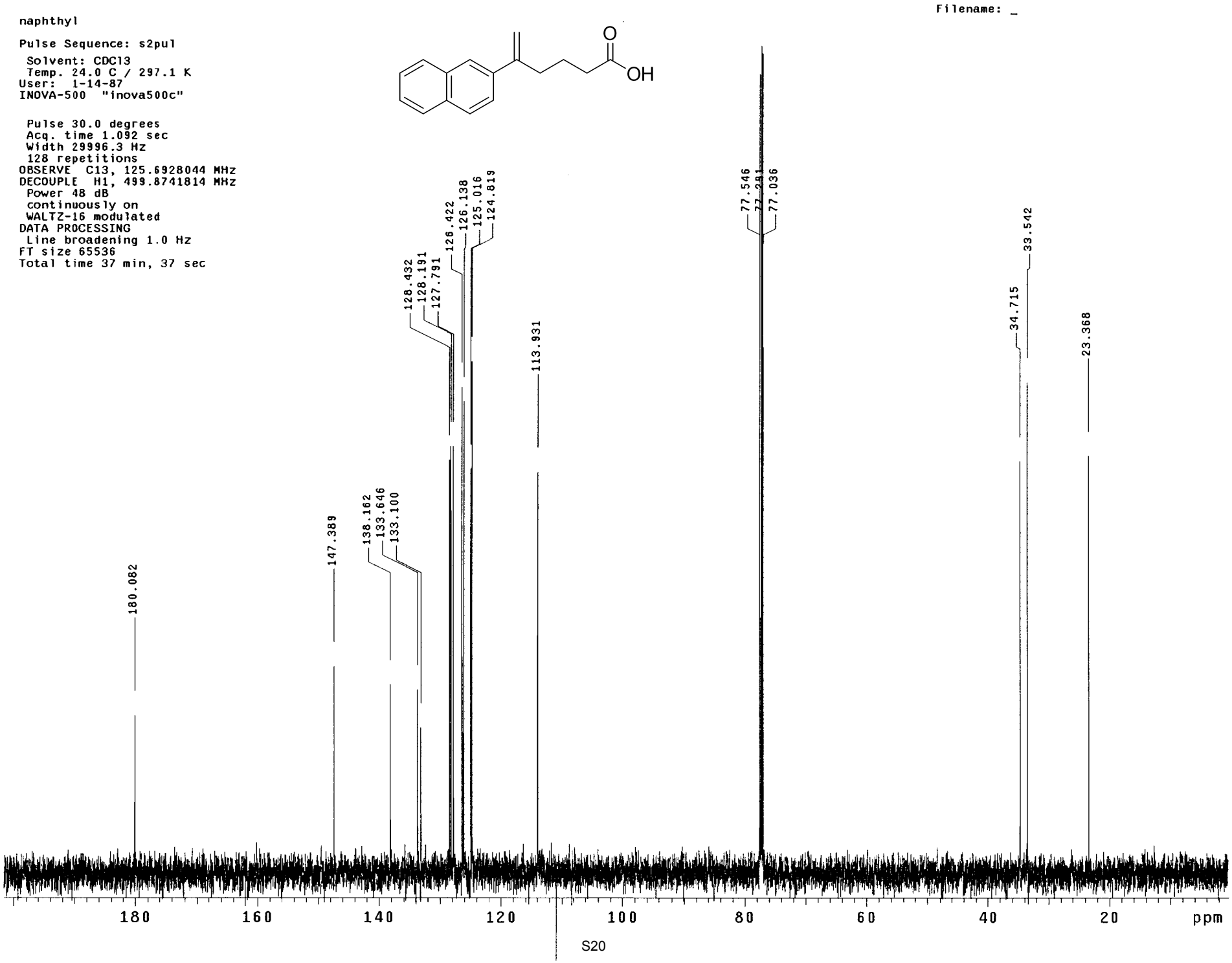
2naphthyl

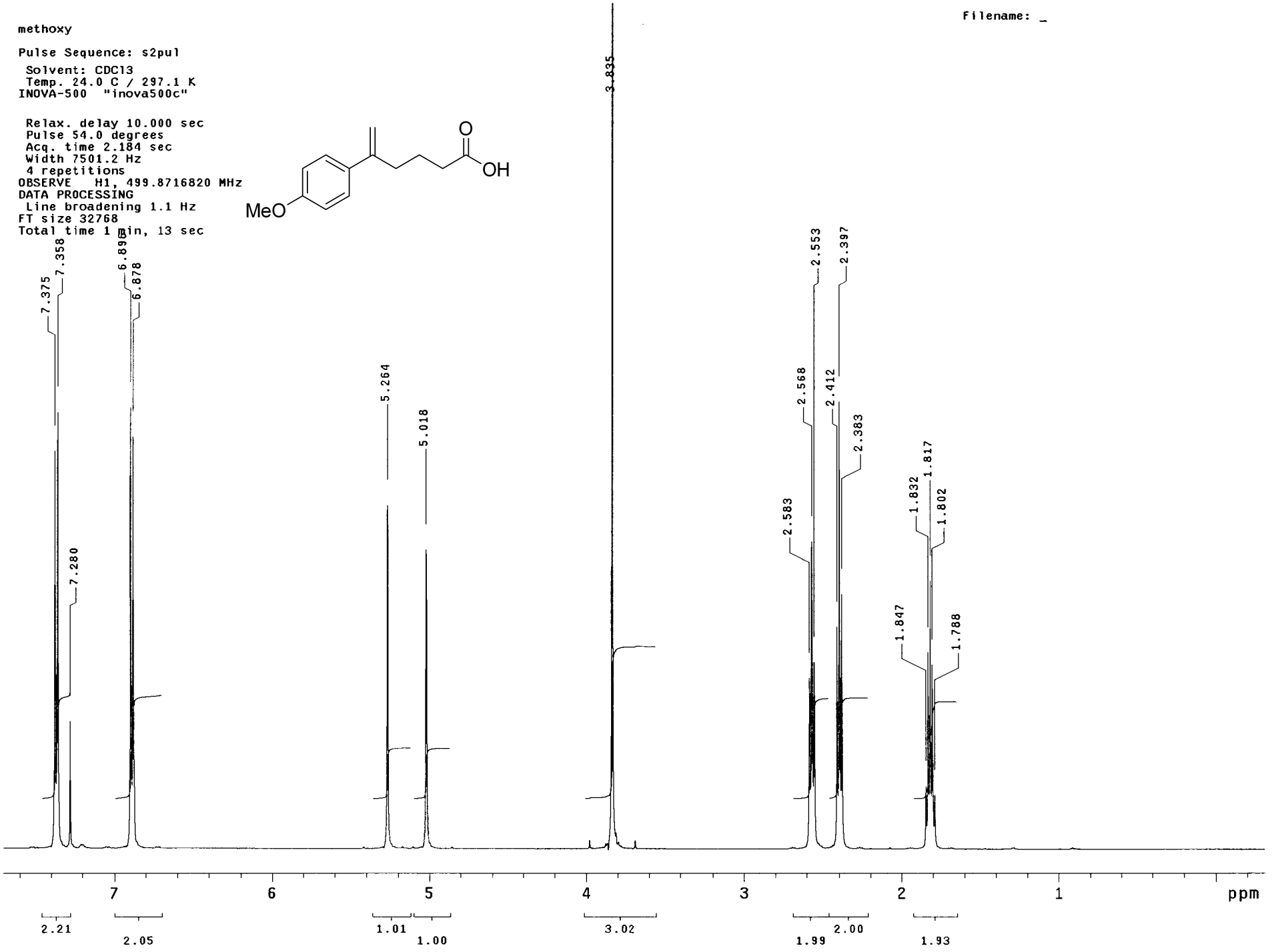
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
INOVA-500 "inova500c"

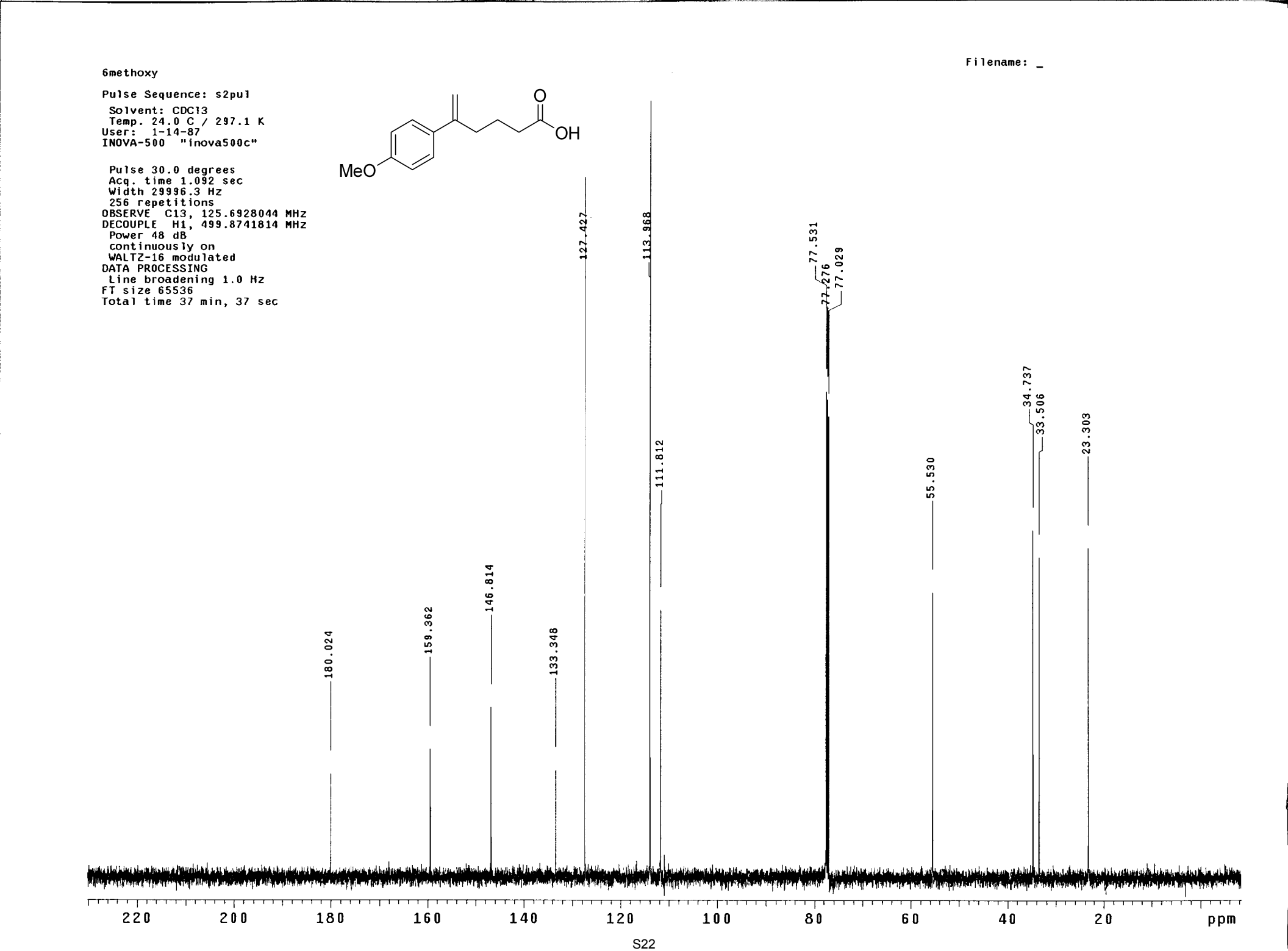
Relax. delay 10.000 sec
Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
4 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 32768
Total time 1 min, 13 sec






naphthyl
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
User: 1-14-87
INOVA-500 "inova500c"
Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
128 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 37 min, 37 sec
Filename: _
O
OH
180.082
147.389
138.162
133.646
133.100
128.432
128.191
127.791
126.422
126.138
125.016
124.819
113.931
77.546
77.281
77.036
34.715
33.542
23.368
180
160
140
120
100
80
60
40
20
ppm

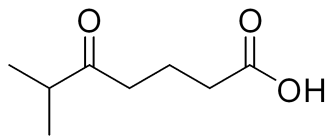

methoxy
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
INOVA-500 "inova500c"
Relax. delay 10.000 sec
Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
4 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 32768
Total time 1 min, 13 sec
Filename: _
MeO
OH
7.375
7.358
7.280
6.898
6.878
5.264
5.018
3.835
2.583
2.568
2.553
2.412
2.397
2.383
1.847
1.832
1.817
1.802
1.788
7
6
5
4
3
2
1
ppm
2.21
2.05
1.01
1.00
3.02
1.99
2.00
1.93


6methoxy
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
User: 1-14-87
INOVA-500 "inova500c"
Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
256 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 37 min, 37 sec
Filename: _
MeO
O
OH
180.024
159.362
146.814
133.348
127.427
113.968
111.812
77.531
77.276
77.029
55.530
34.737
33.506
23.303
220
200
180
160
140
120
100
80
60
40
20
ppm

isopropyl ketone

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
INOVA-500 "inova500c"

Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
4 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 32768
Total time 0 min, 13 sec

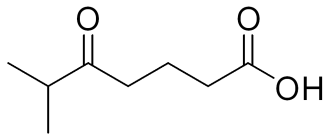


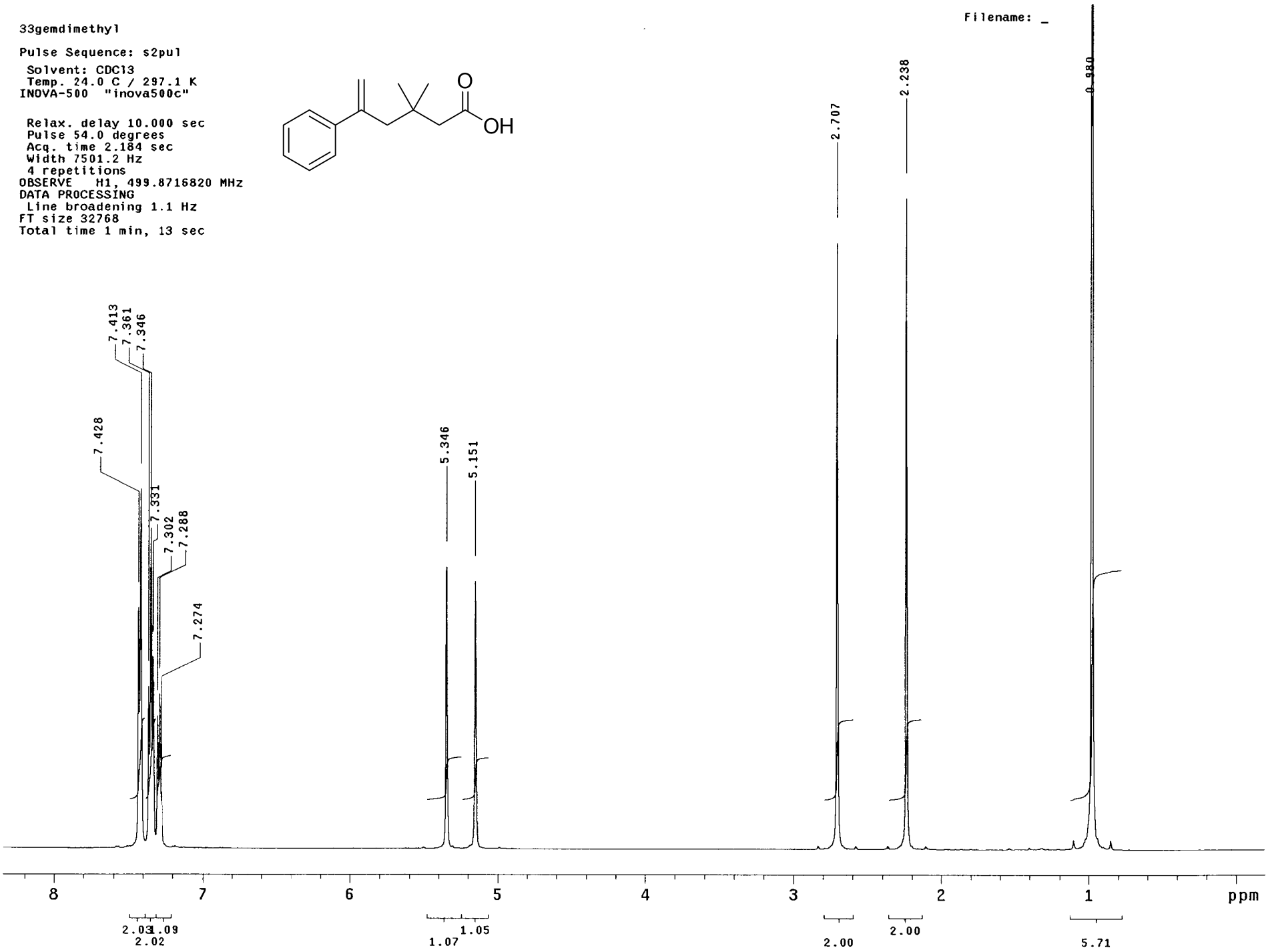
Filename: _

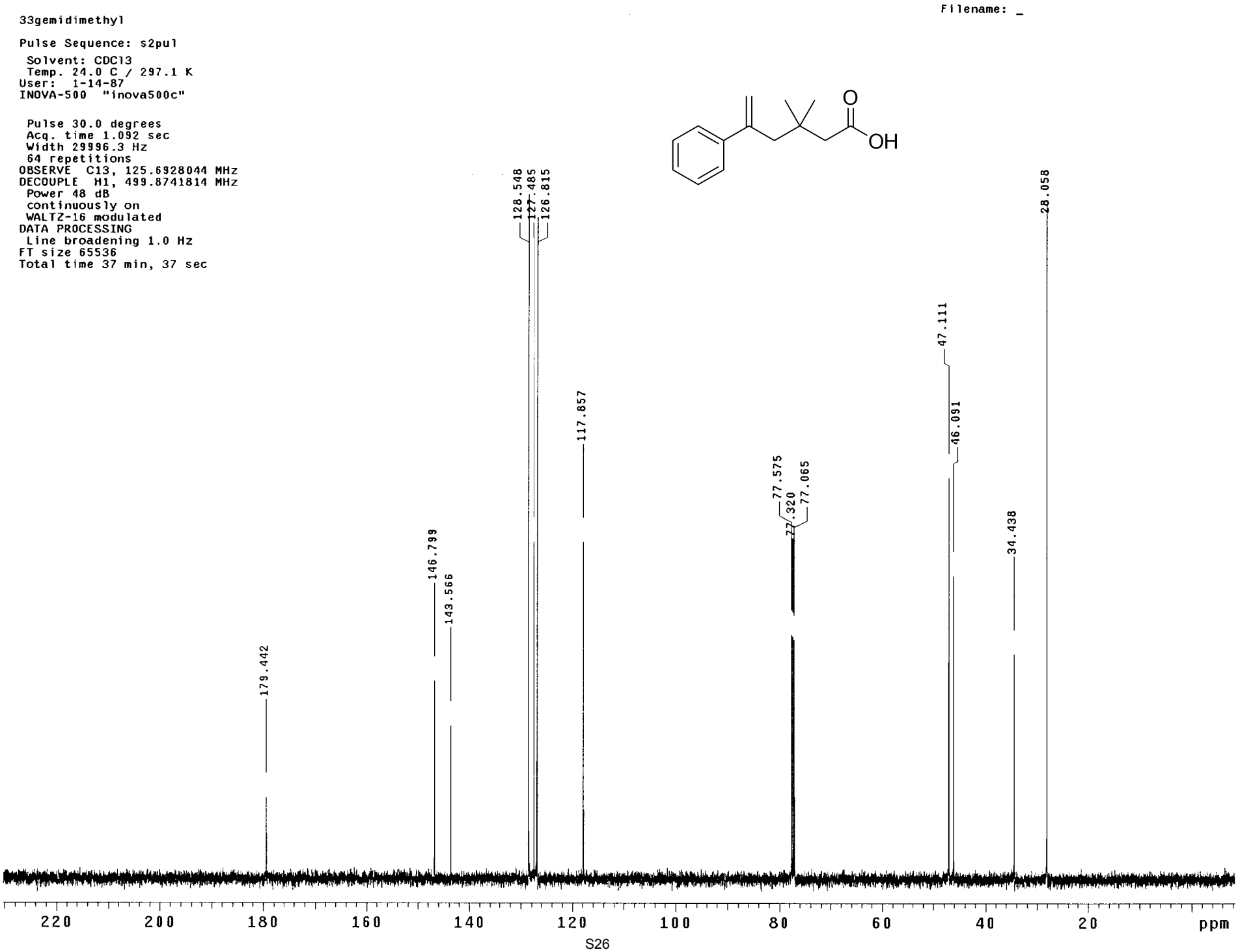
isopropyl ketone

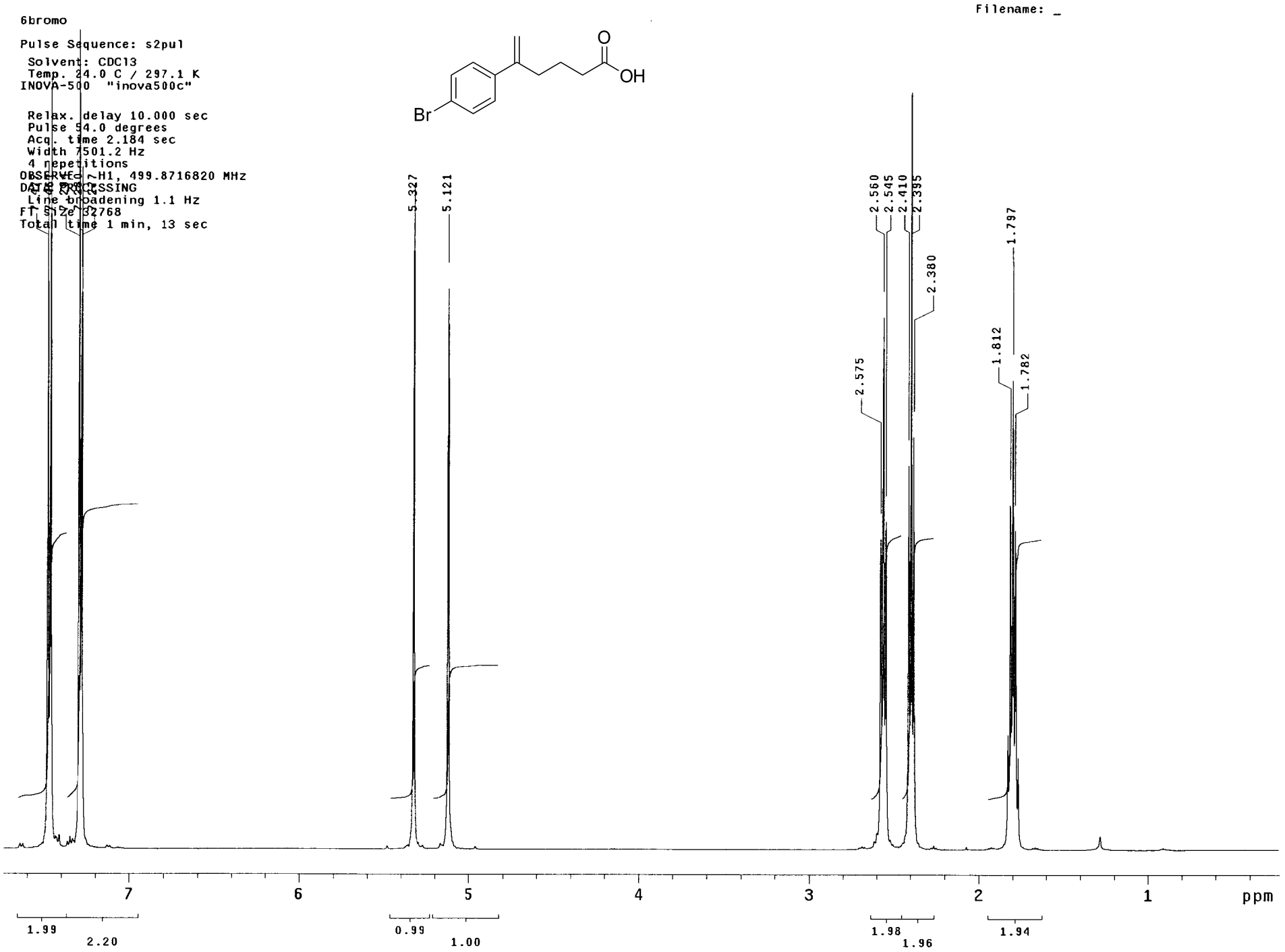
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
User: 1-14-87
INOVA-500 "inova500c"

Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
128 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 37 min, 37 sec




33gemdimethyl
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
INOVA-500 "inova500c"
Relax. delay 10.000 sec
Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
4 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 32768
Total time 1 min, 13 sec
Filename: _
O
OH
7.413
7.361
7.346
7.428
7.331
7.302
7.288
7.274
5.346
5.151
2.707
2.238
0.980
8
7
6
5
4
3
2
1
ppm
2.03
1.09
2.02
1.07
1.05
2.00
2.00
5.71


Filename: _
33gemidimethyl
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
User: 1-14-87
INOVA-500 "inova500c"
Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
64 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 37 min, 37 sec
O
OH
179.442
146.799
143.566
128.548
127.485
126.815
117.857
77.575
77.320
77.065
47.111
46.091
34.438
28.058
220
200
180
160
140
120
100
80
60
40
20
ppm

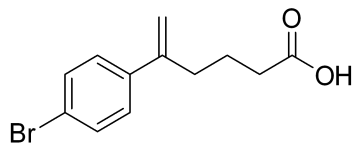

6bromo
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
INOVA-500 "inova500c"
Relax. delay 10.000 sec
Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
4 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT Size 32768
Total time 1 min, 13 sec
Filename: _
Br
O
OH
5.327
5.121
2.560
2.545
2.410
2.395
2.380
2.575
1.812
1.797
1.782
7
6
5
4
3
2
1
ppm
1.99
2.20
0.99
1.00
1.98
1.96
1.94

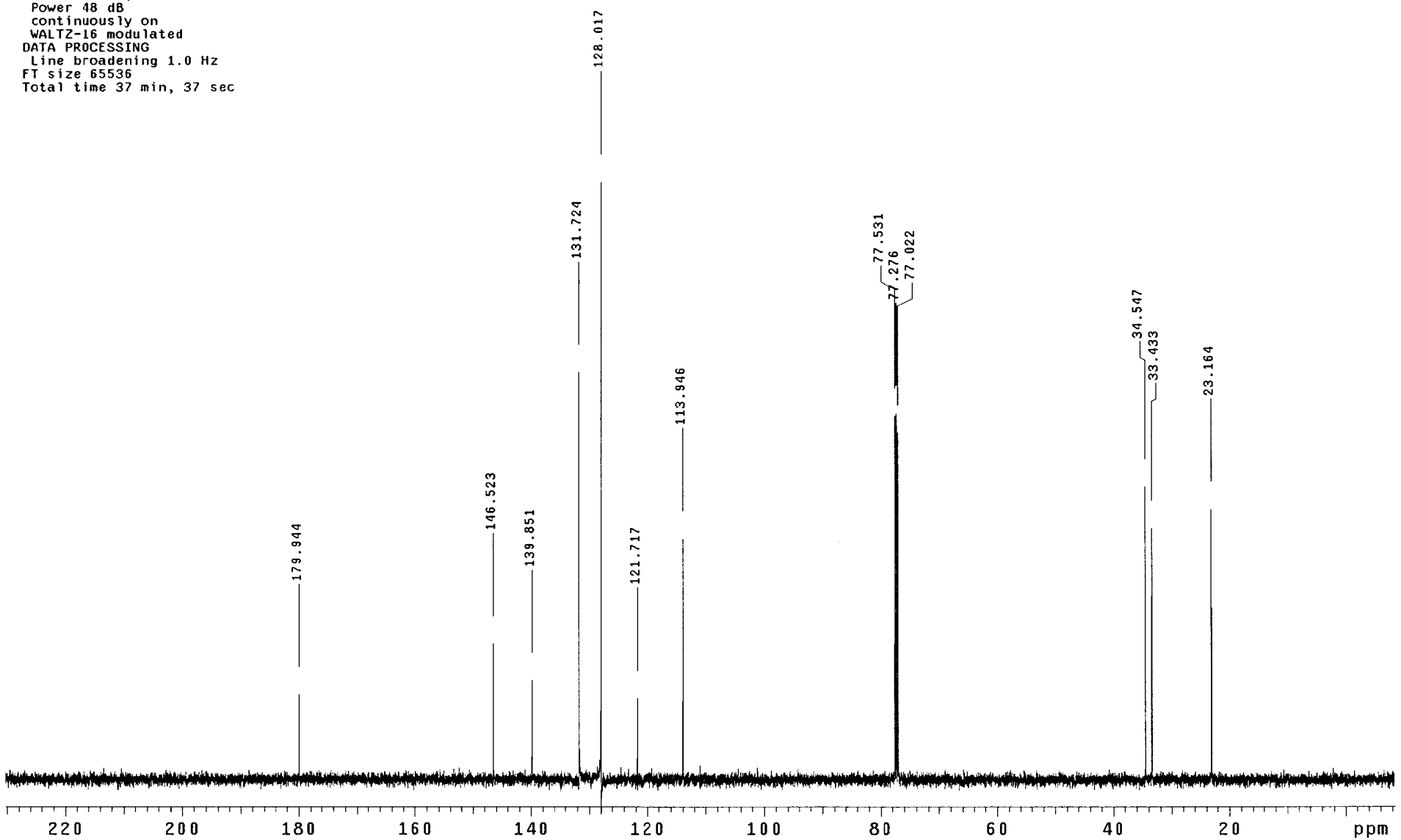
Filename: _

6bromo

Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp. 24.0 C / 297.1 K
User: 1-14-87
INOVA-500 "inova500c"

 Pulse 30.0 degrees
 Acq. time 1.092 sec
 Width 29996.3 Hz
 224 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
 Power 48 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 37 min, 37 sec



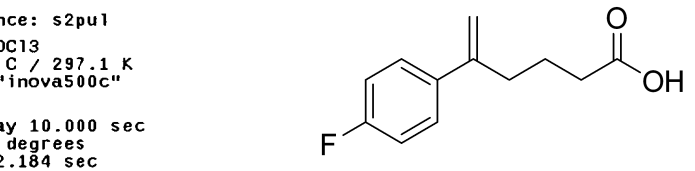


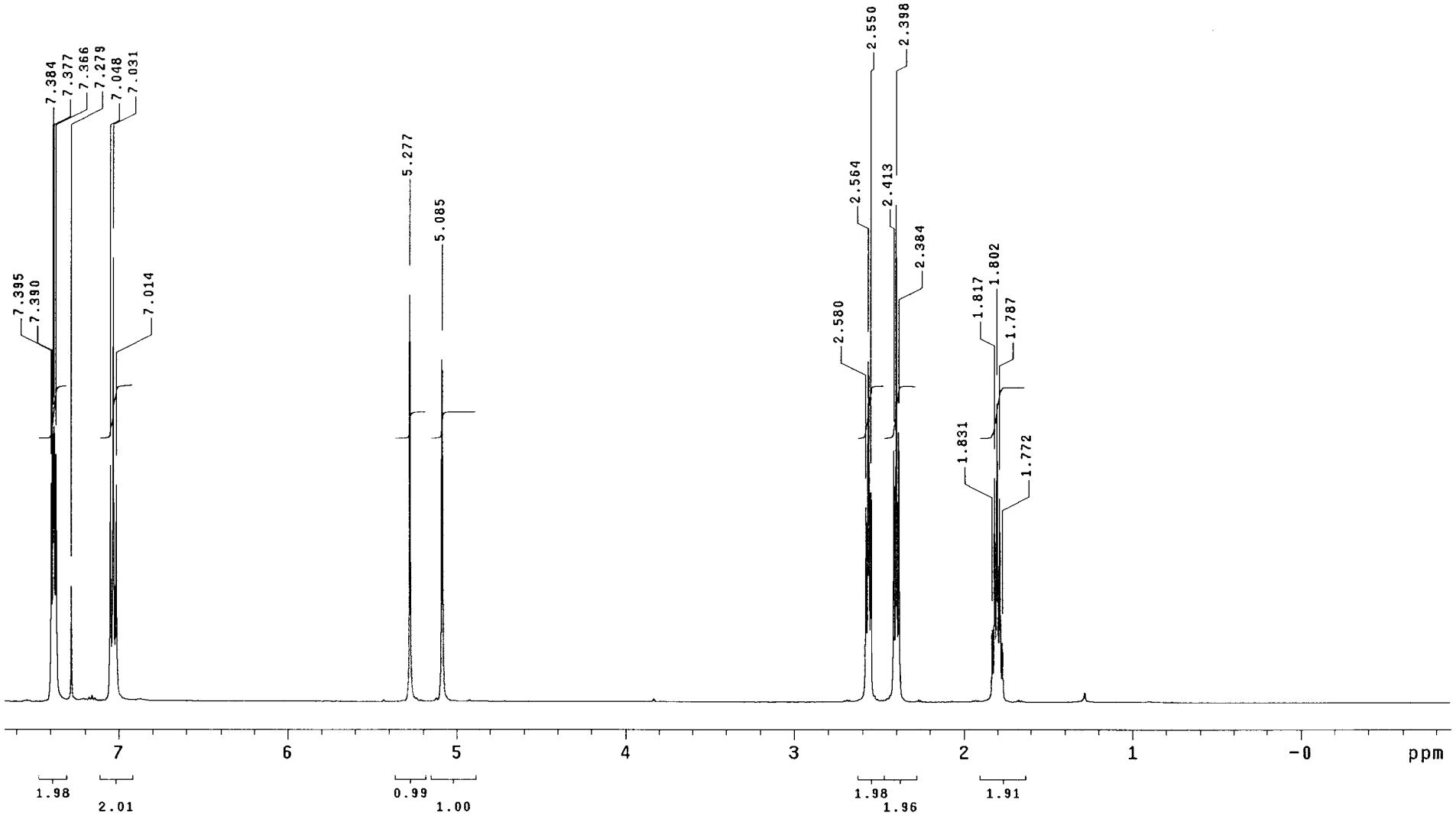
Filename: _

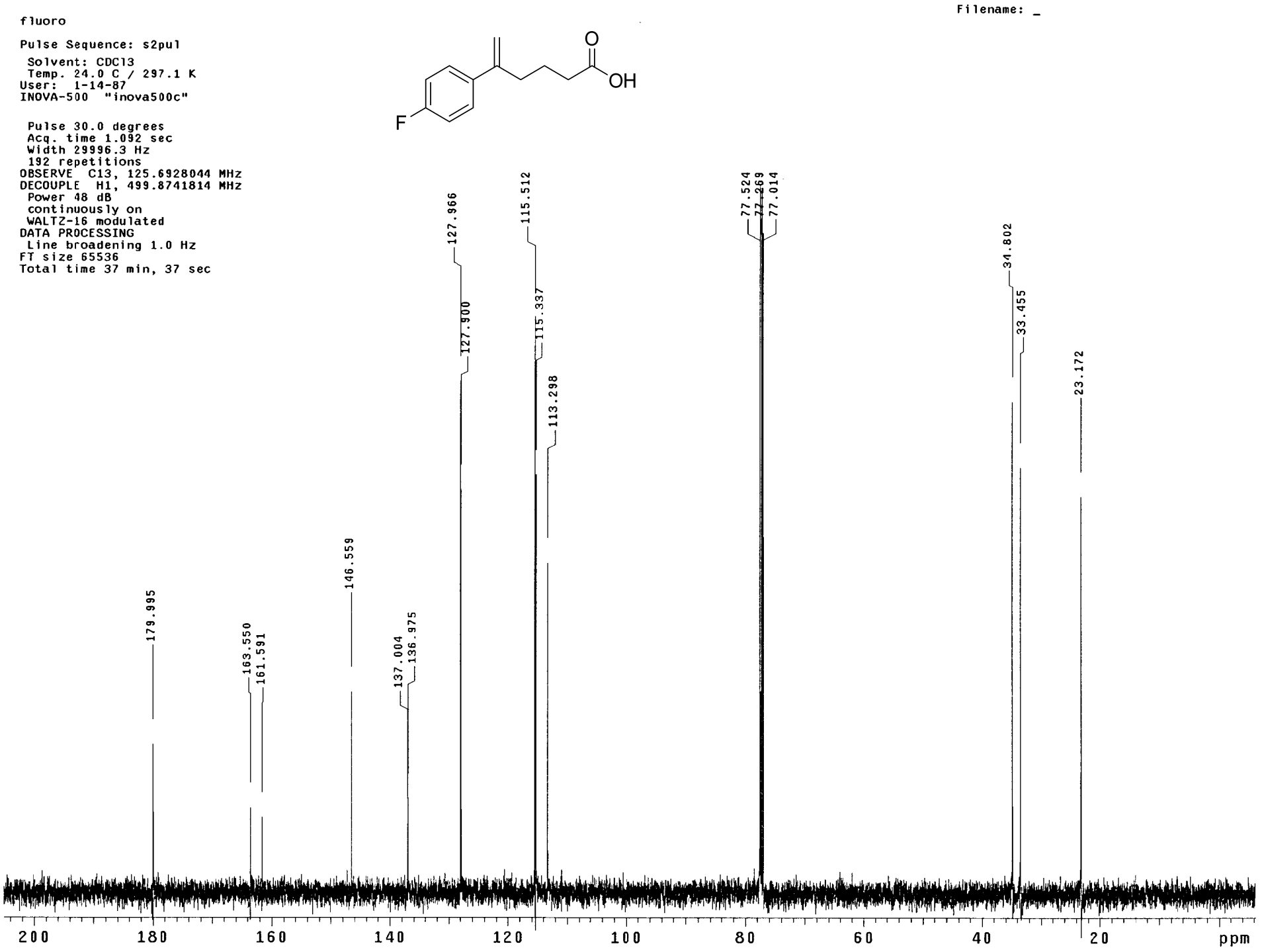
fluoro

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
INOVA-500 "inova500c"

Relax. delay 10.000 sec
Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
4 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 32768
Total time 1 min, 13 sec





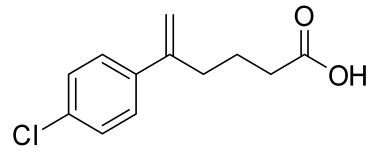

fluoro
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
User: 1-14-87
INOVA-500 "inova500c"
Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
192 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 37 min, 37 sec
Filename: _
O
OH
F
179.995
163.550
161.591
146.559
137.004
136.975
127.966
127.900
115.512
115.337
113.298
77.524
77.269
77.014
34.802
33.455
23.172
200
180
160
140
120
100
80
60
40
20
ppm

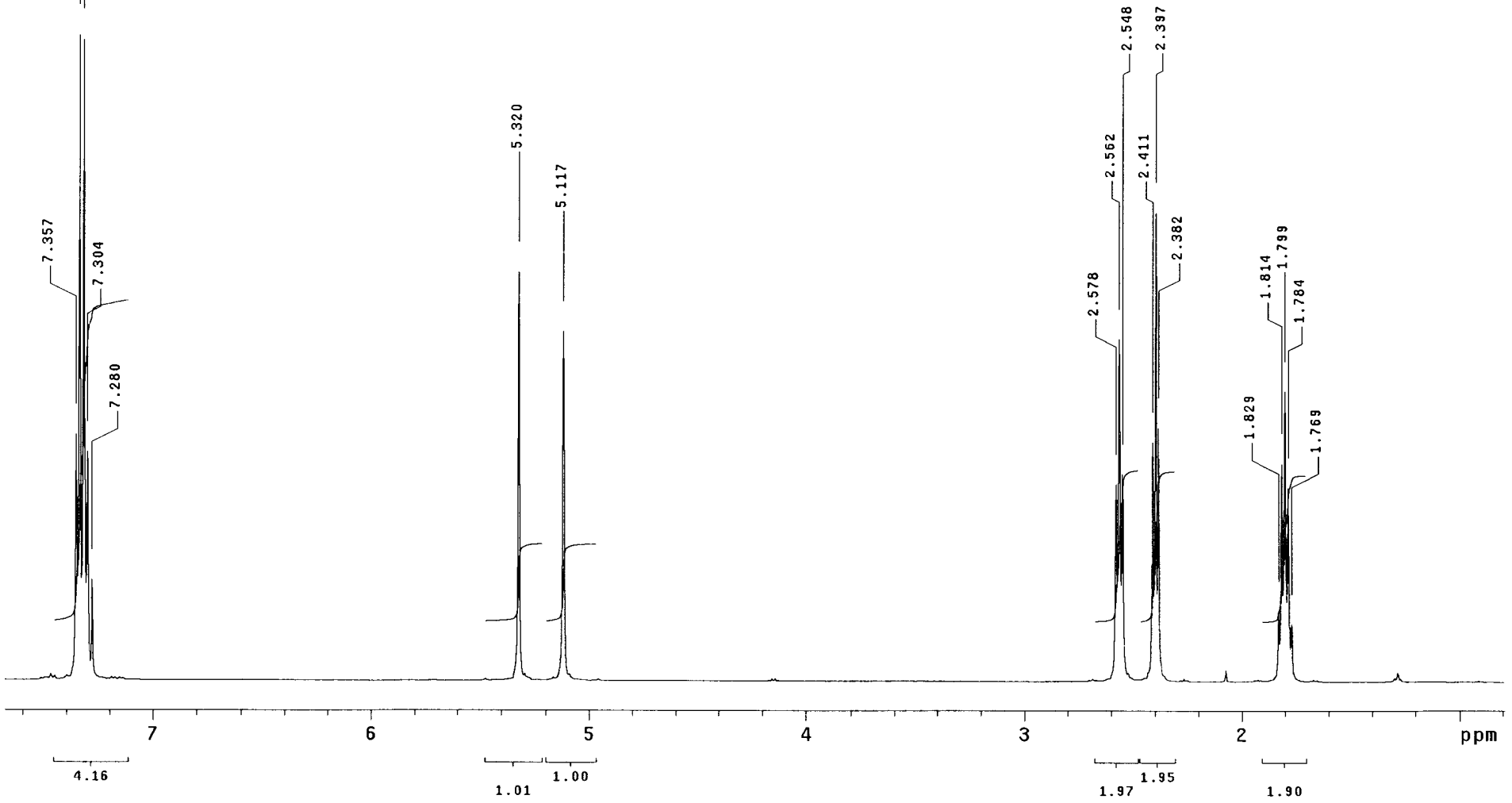
chloro

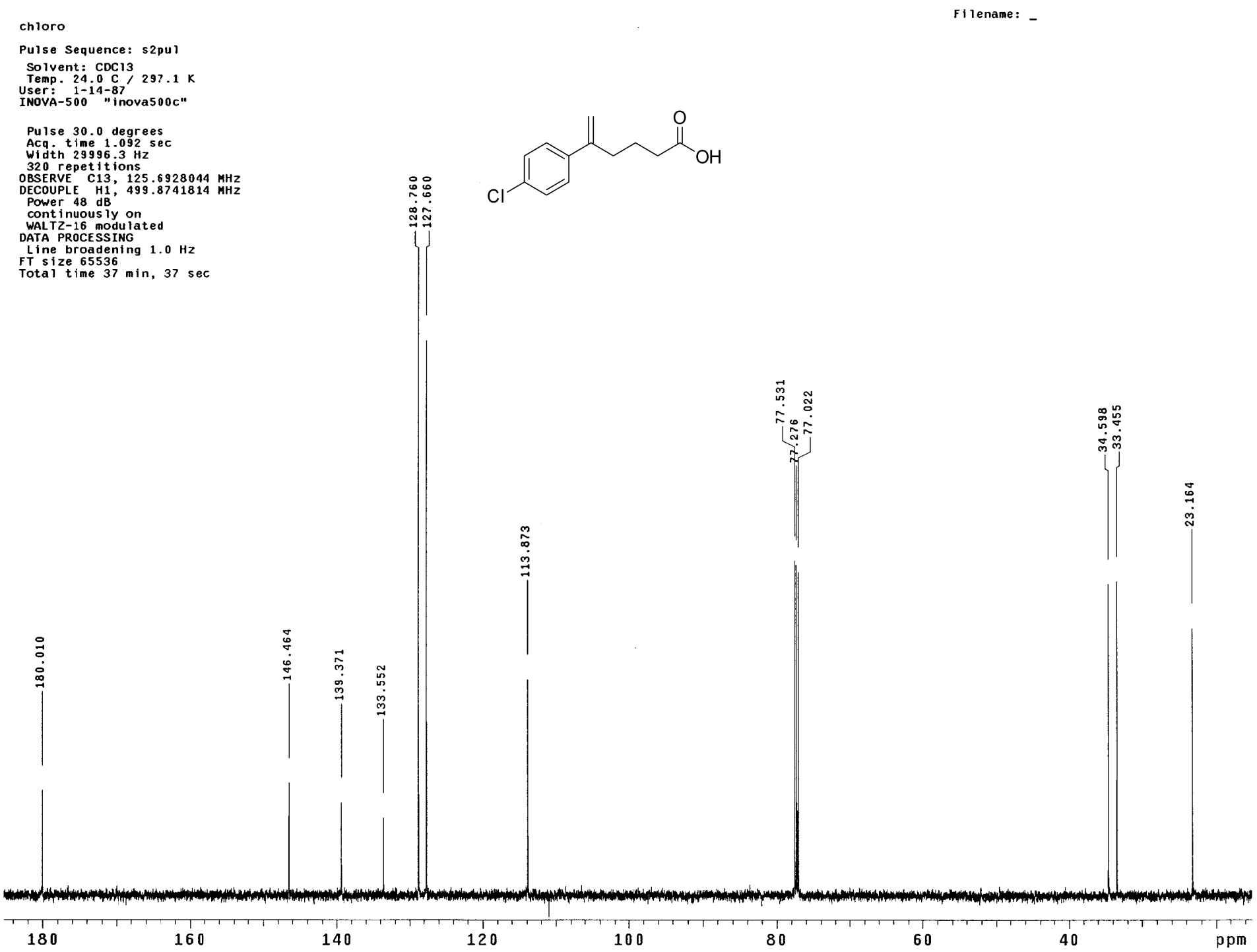
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
INOVA-500 "inova500c"

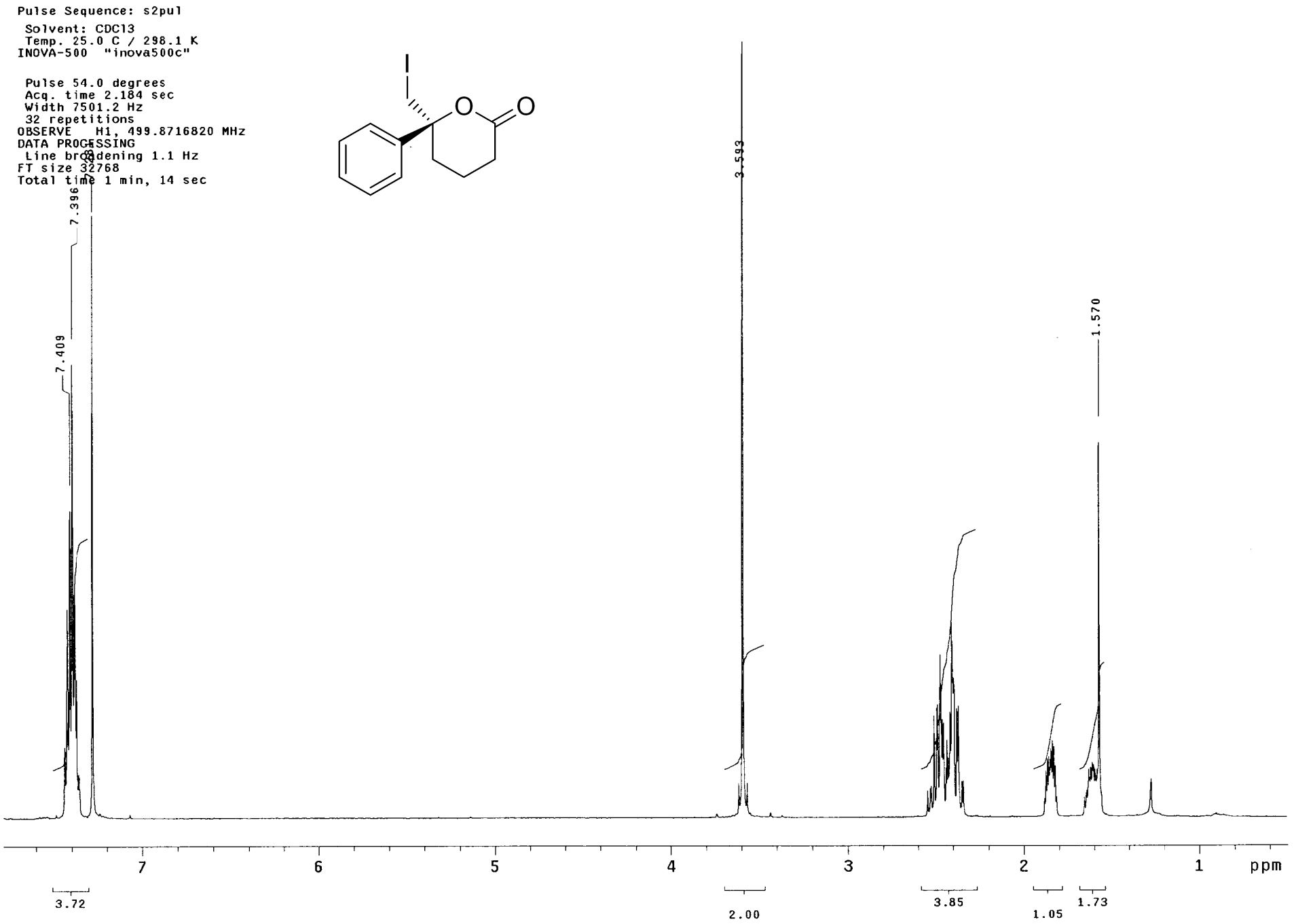
Relax. delay 10.000 sec
Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
4 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 32768
Total time 1 min, 13 sec

Filename: _





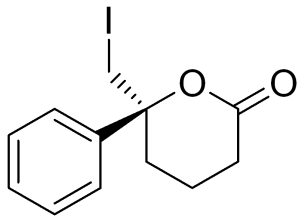

chloro
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
User: 1-14-87
INOVA-500 "inova500c"
Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
320 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 37 min, 37 sec
Filename: _
O
OH
Cl
180.010
146.464
139.371
133.552
128.760
127.660
113.873
77.531
77.276
77.022
34.598
33.455
23.164
180
160
140
120
100
80
60
40
ppm


Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inova500c"
Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
32 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 32768
Total time 1 min, 14 sec
I
O
O
7.396
7.409
3.593
1.570
7
6
5
4
3
2
1
ppm
3.72
2.00
3.85
1.05
1.73

STANDARD CARBON PARAMETERS

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
INOVA-500 "inova500c"

Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
1952 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 15 min, 13 sec



methyl

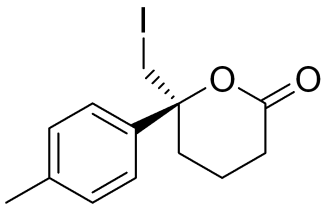
Data Collected on:
nmrsun2-inova500
Archive directory:
/export/home/ds2/vnmrsys/data
Sample directory:

File: Gev398-2protonmethylproduct

Pulse Sequence: s2pul
Solvent: CDCl3

Temp. 24.0 C / 297.1 K

Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
32 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 32768
Total time 1 min

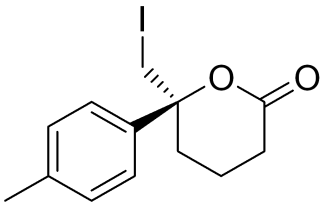


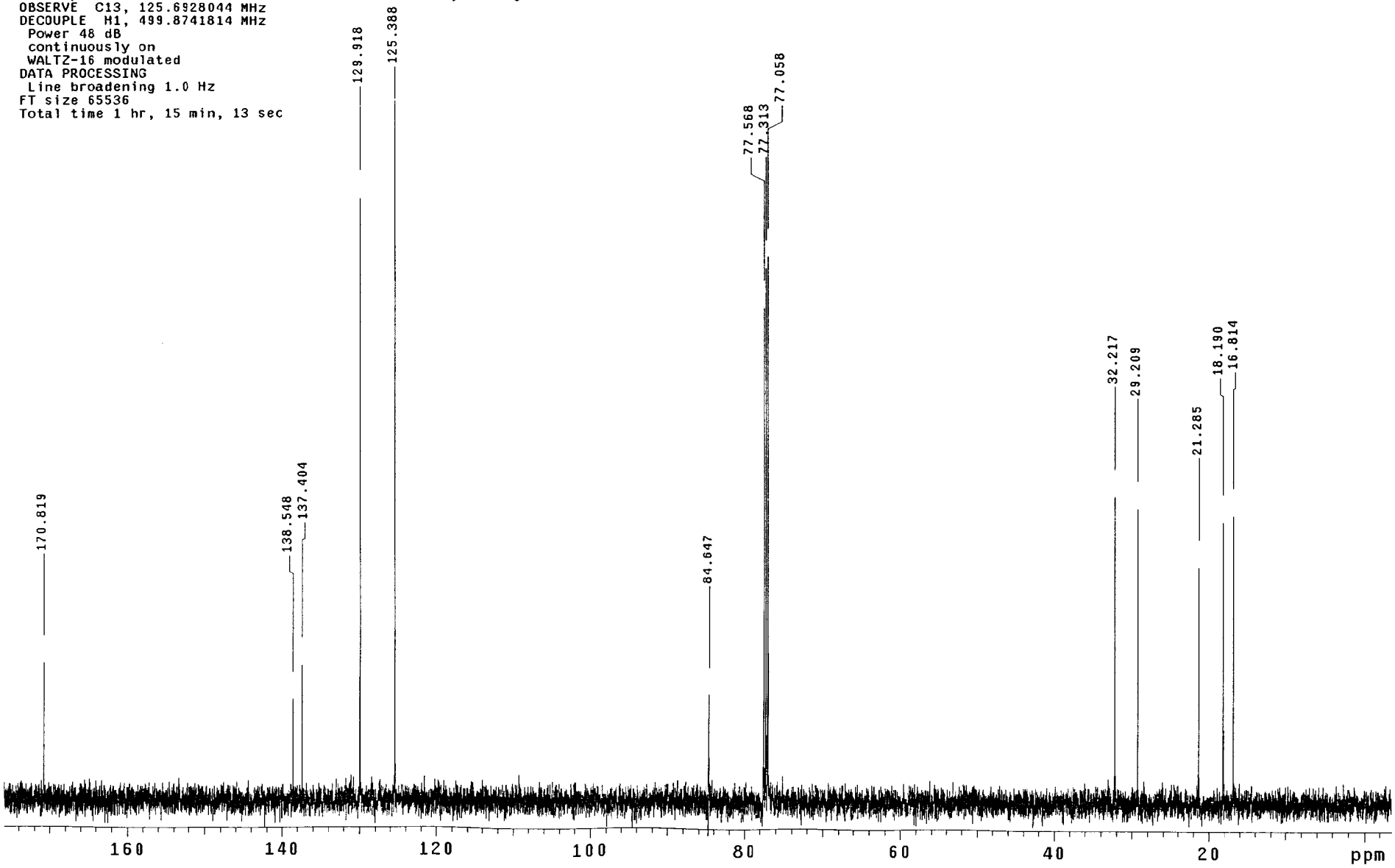
Filename: _

methyl

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
User: 1-14-87
INOVA-500 "inova500c"

Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
64 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 15 min, 13 sec





naphthyl

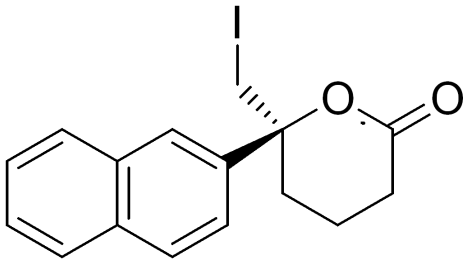
Data Collected on:
nmrsun2-inova500
Archive directory:
/export/home/ds2/vnmrsys/data
Sample directory:

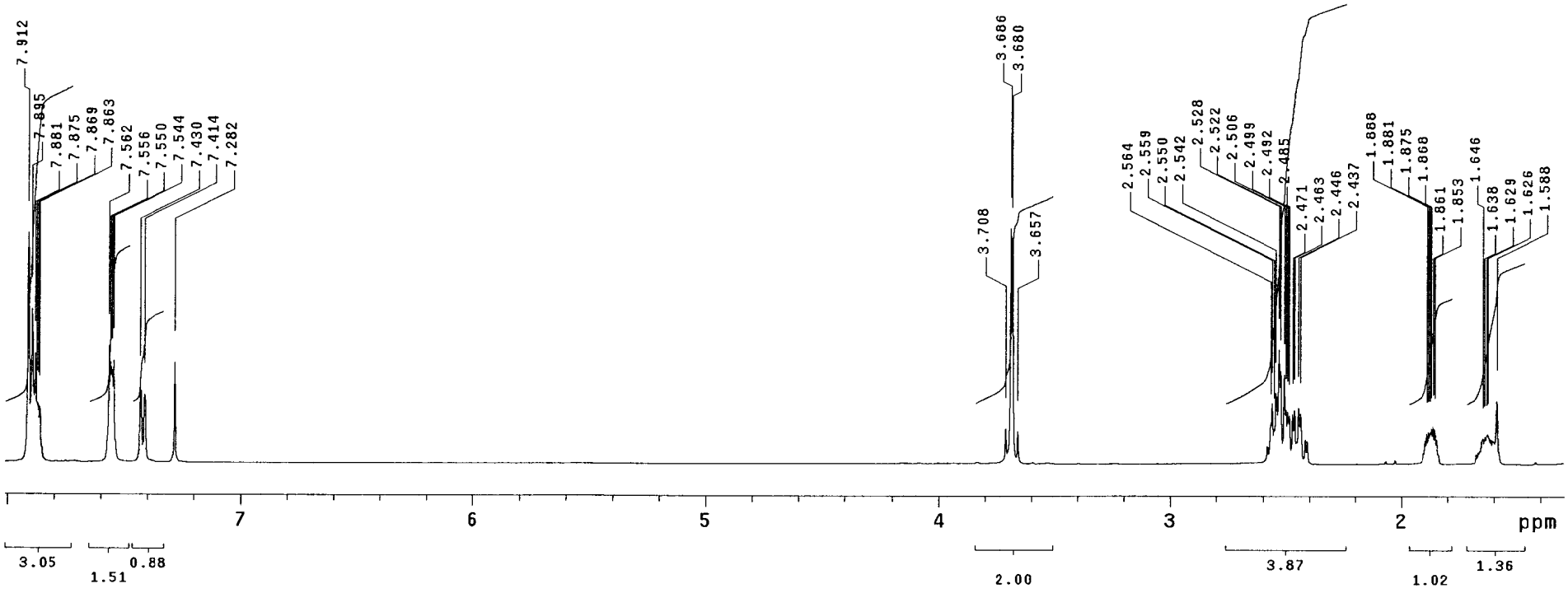
File: Gev388-2proton

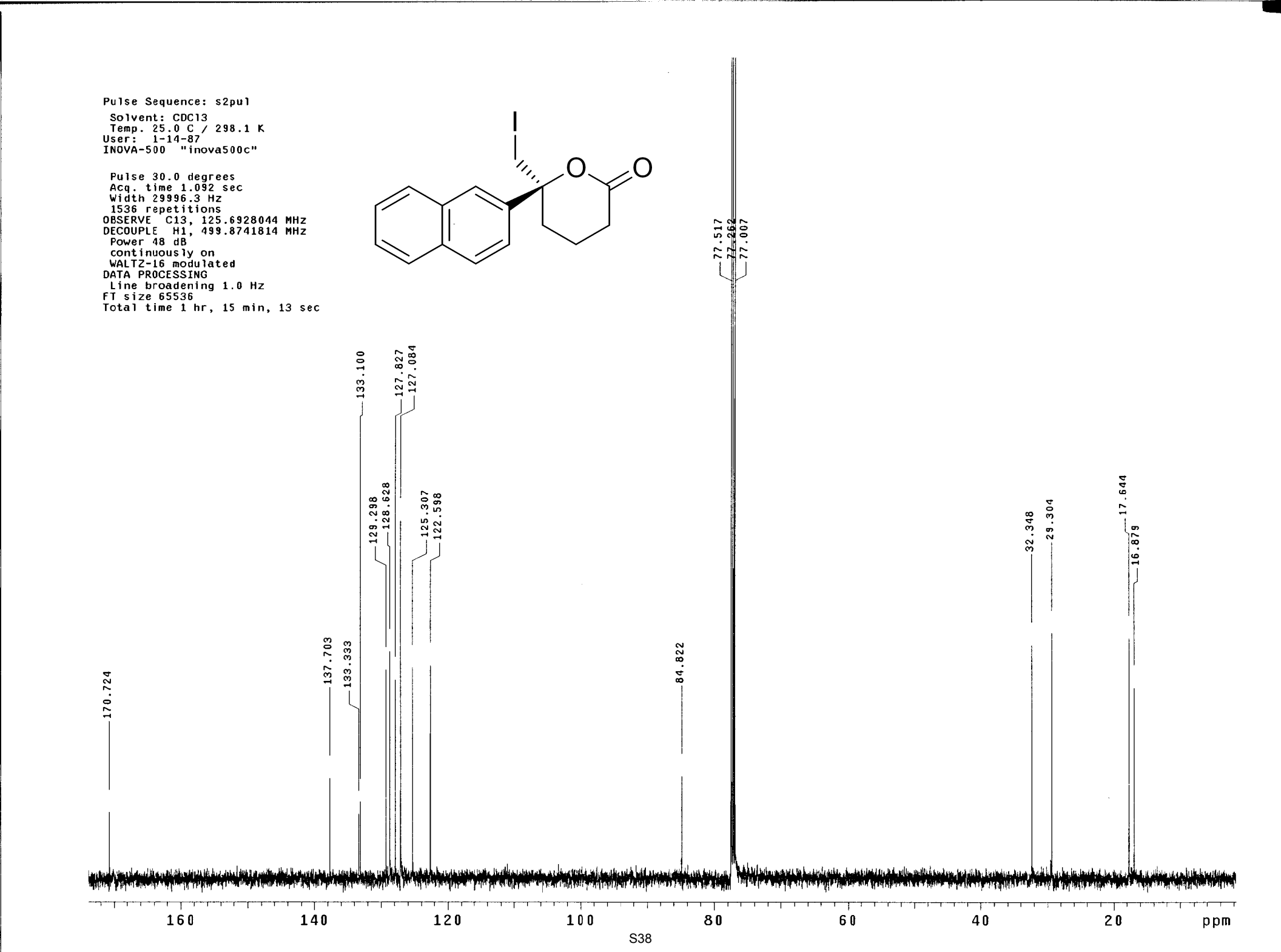
Pulse Sequence: s2pul
Solvent: CDCl3

Temp. 25.0 C / 298.1 K

Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
32 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 32768
Total time 1 min



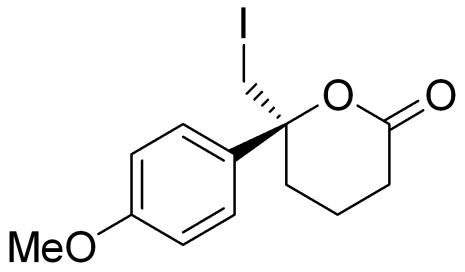


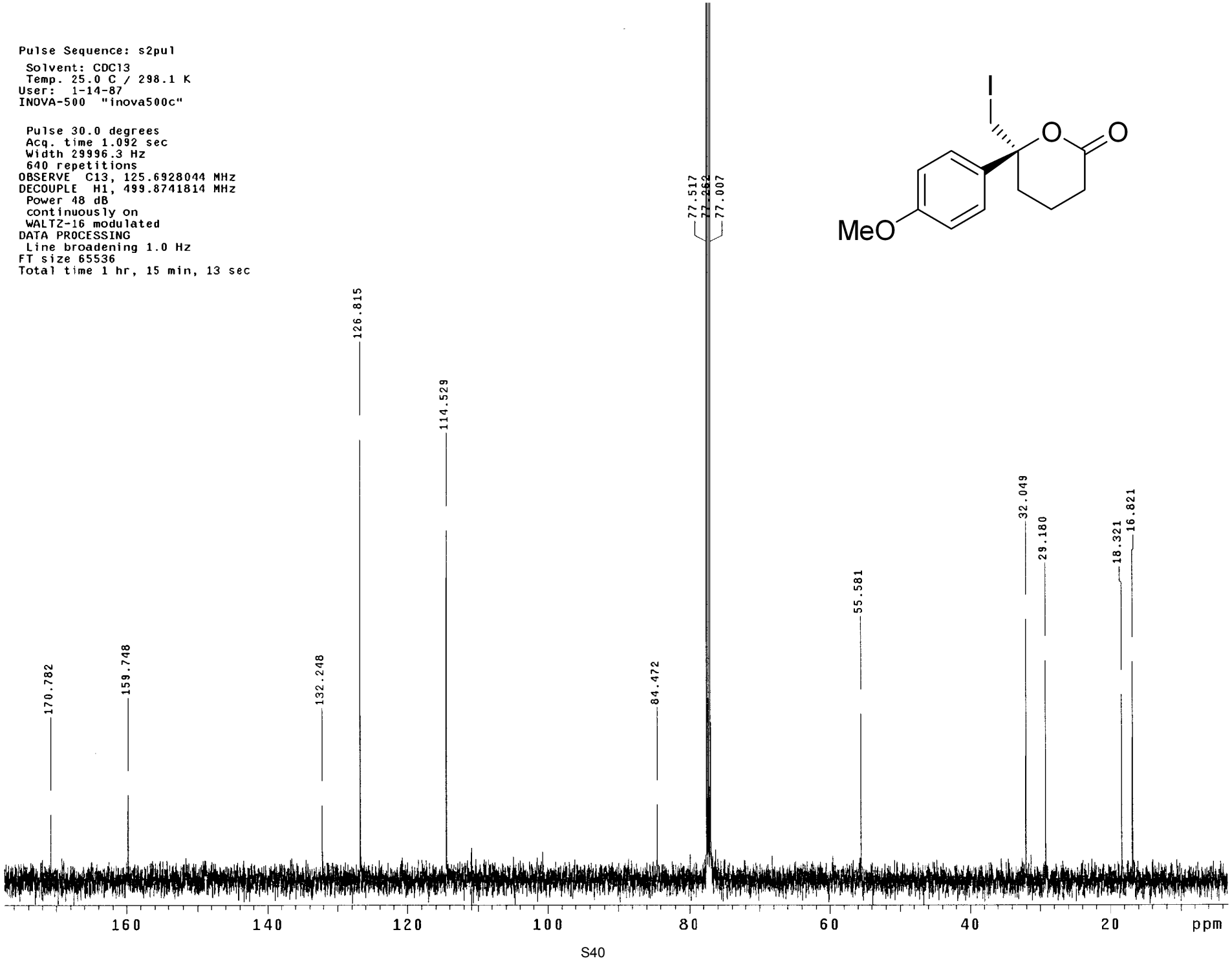

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
INOVA-500 "inova500c"
Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
1536 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 15 min, 13 sec
I
O
O
77.517
77.262
77.007
133.100
127.827
127.084
129.298
128.628
125.307
122.598
137.703
133.333
84.822
32.348
29.304
17.644
16.879
170.724
160
140
120
100
80
60
40
20
ppm

STANDARD PROTON PARAMETERS

exp1 PROTON

SAMPLE		SPECIAL	
date	Jun 11 2010	temp	22.0
solvent	CDCl3	gain	12
file	exp	spin	not used
ACQUISITION		hst	0.008
sw	9596.9	pw90	6.300
at	3.414	alfa	0
np	65536	FLAGS	
fb	5000	il	n
bs	4	in	n
ss	2	dp	y
d1	1.000	hs	nn
nt	32	PROCESSING	
ct	0	lb	0.10
TRANSMITTER		fn	131072
tn	H1	DISPLAY	
sfrq	599.790	sp	-141.6
tof	576.6	wp	4867.1
tpwr	60	rfl	1199.7
pw	4.200	rfp	0
DECOUPLER		rp	118.6
dn	C13	lp	-16.8
dof	0	PLOT	
dm	nnn	wc	250
decwave	waltz	sc	0
dpwr	49	vs	129
dmf	14500	th	7
		nm cdc ph	




Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
INOVA-500 "inova500c"
Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
640 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 15 min, 13 sec
I
O
O
MeO
170.782
159.748
132.248
126.815
114.529
84.472
77.517
77.262
77.007
55.581
32.049
29.180
18.321
16.821
160
140
120
100
80
60
40
20
ppm

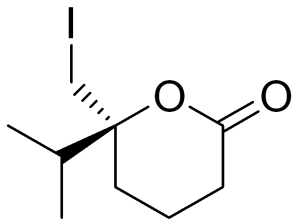
Data Collected on:
nmrsun2-inova500
Archive directory:
/export/home/ds2/vnmrsys/data
Sample directory:

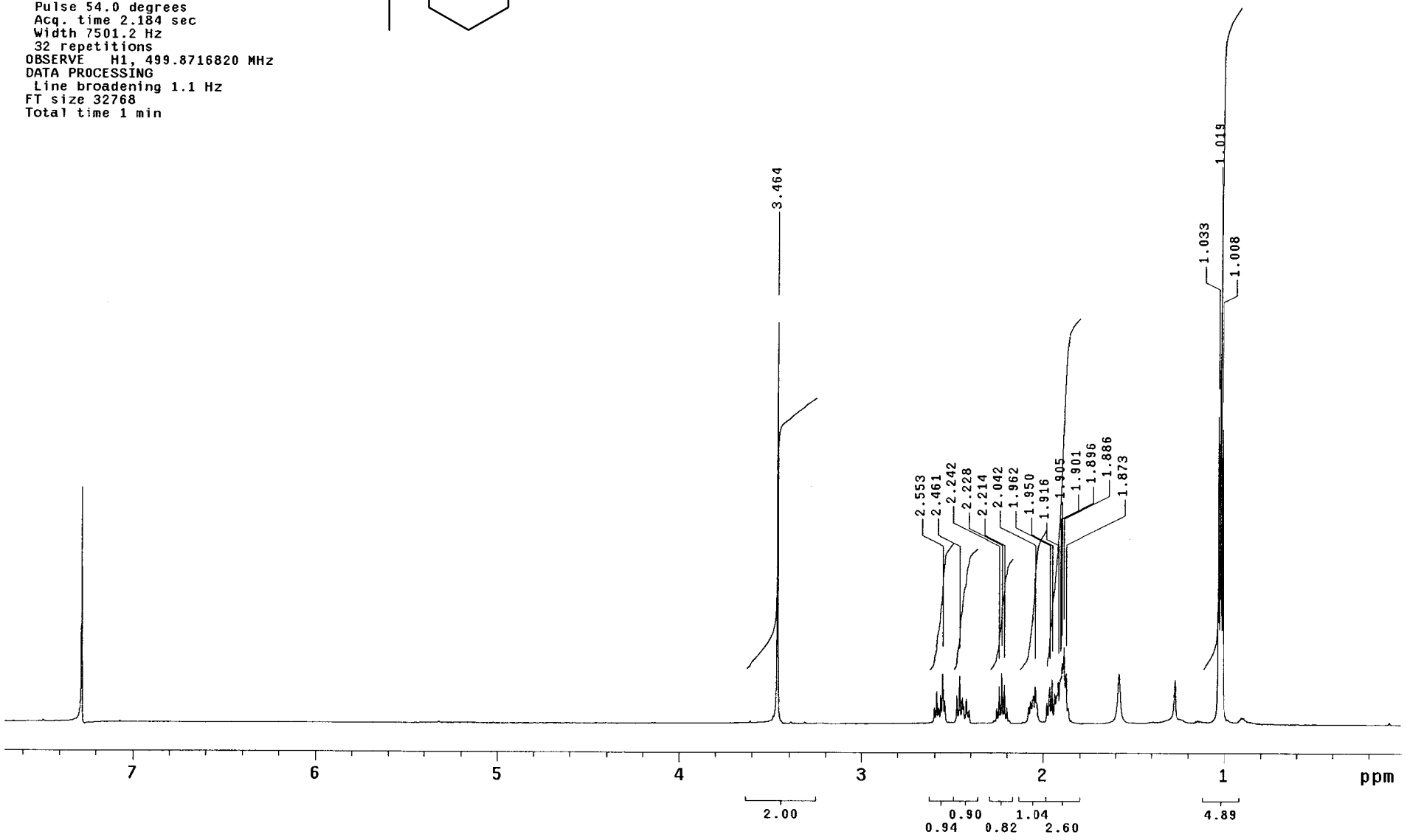
File: Gev392-4proton

Pulse Sequence: s2pul
Solvent: CDCl3

Temp. 24.0 C / 297.1 K

Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
32 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 32768
Total time 1 min

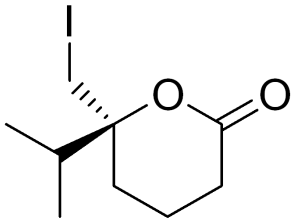




Filename: _

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
User: 1-14-87
INOVA-500 "inova500c"

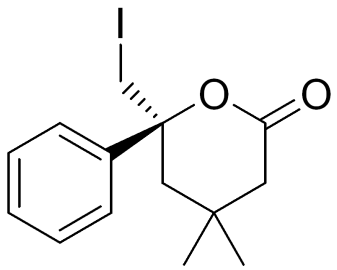
Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
1344 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 15 min, 13 sec

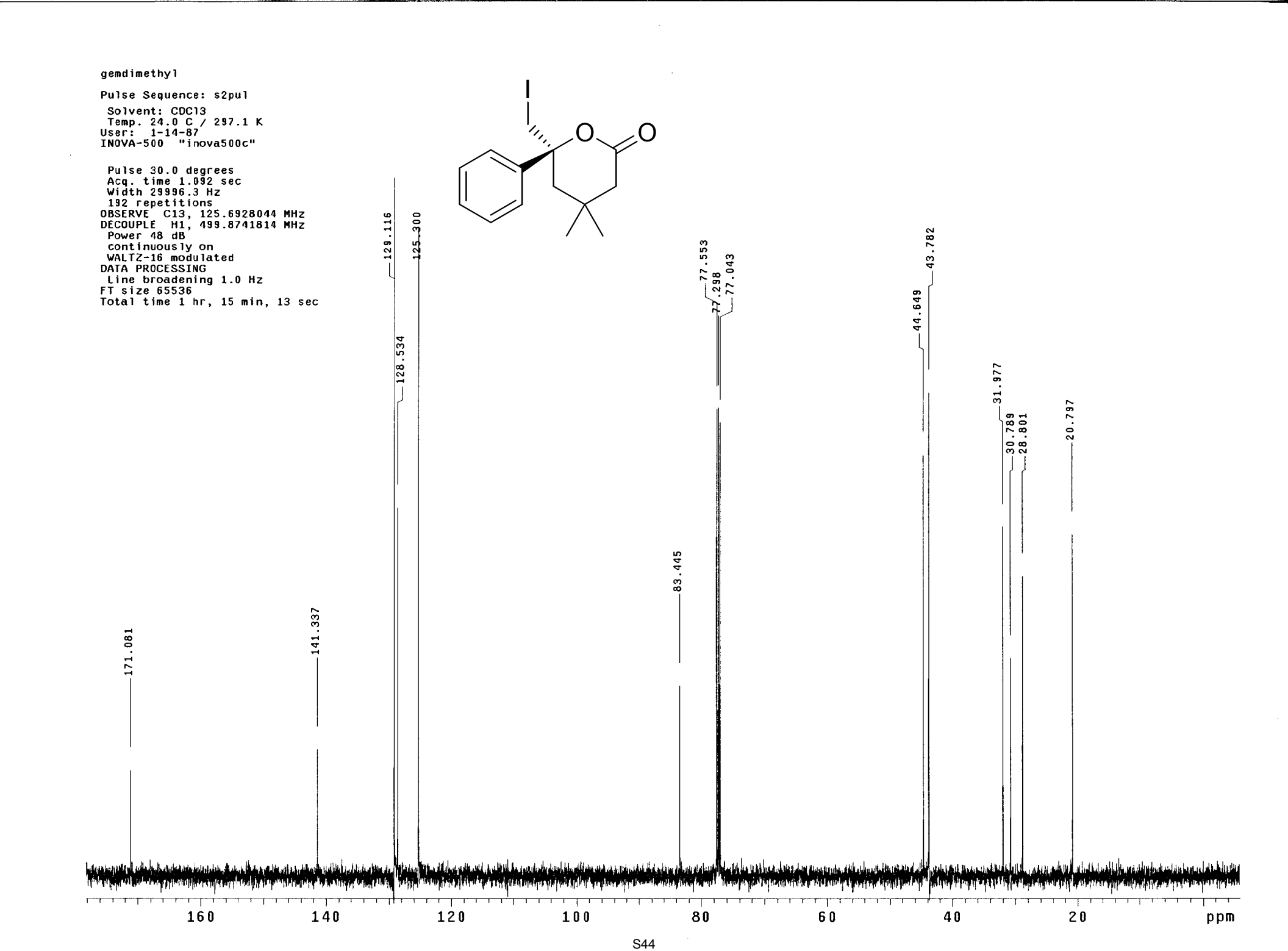


gemdimethyl

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
INOVA-500 "inova500c"

Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
32 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 32768
Total time 1 min, 14 sec




gemdimethyl
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
User: 1-14-87
INOVA-500 "inova500c"
Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
192 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 15 min, 13 sec
I
O
O
171.081
141.337
129.116
128.534
125.300
83.445
77.553
77.298
77.043
44.649
43.782
31.977
30.789
28.801
20.797
160
140
120
100
80
60
40
20
ppm

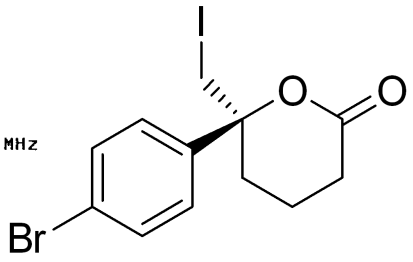
bromo

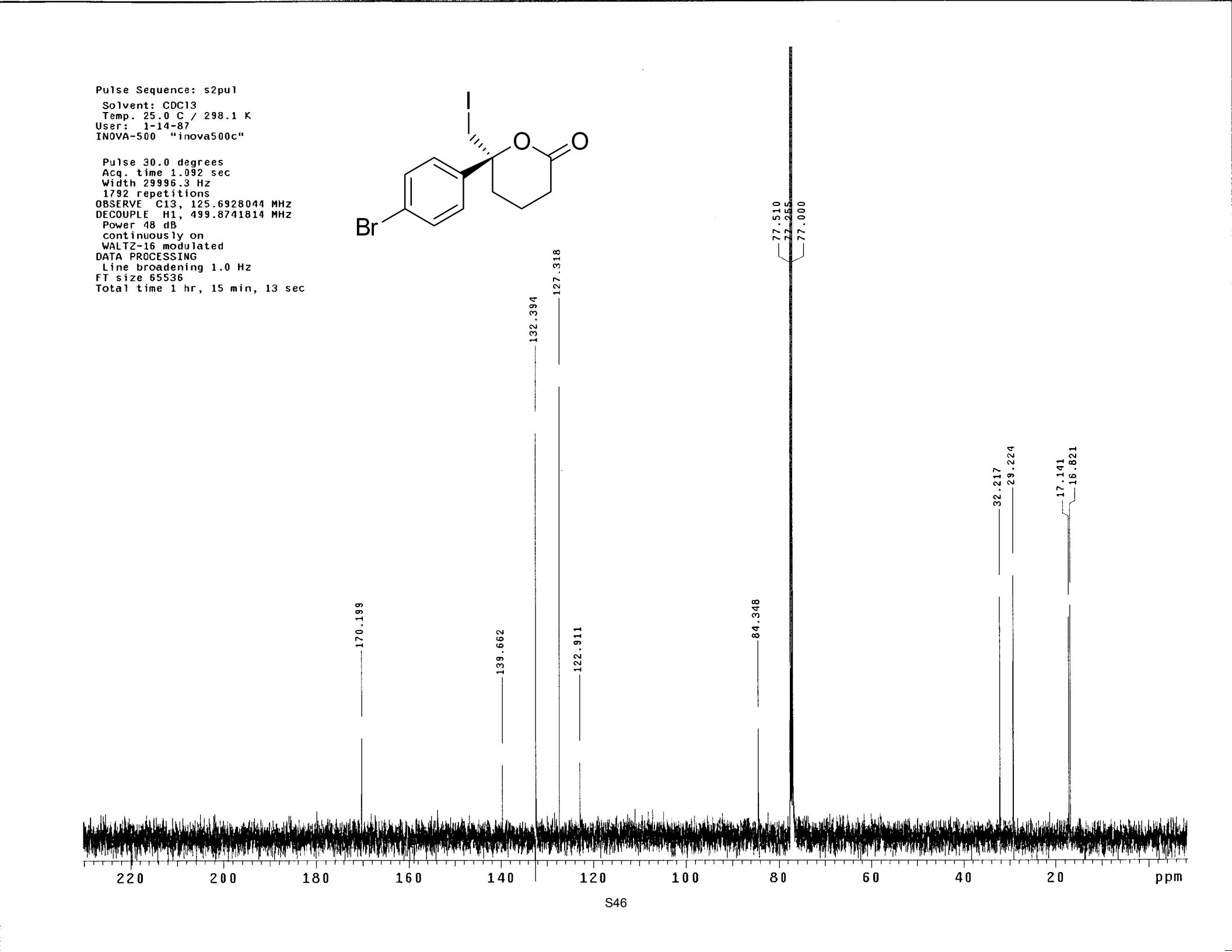
Pulse Sequence: s2pul

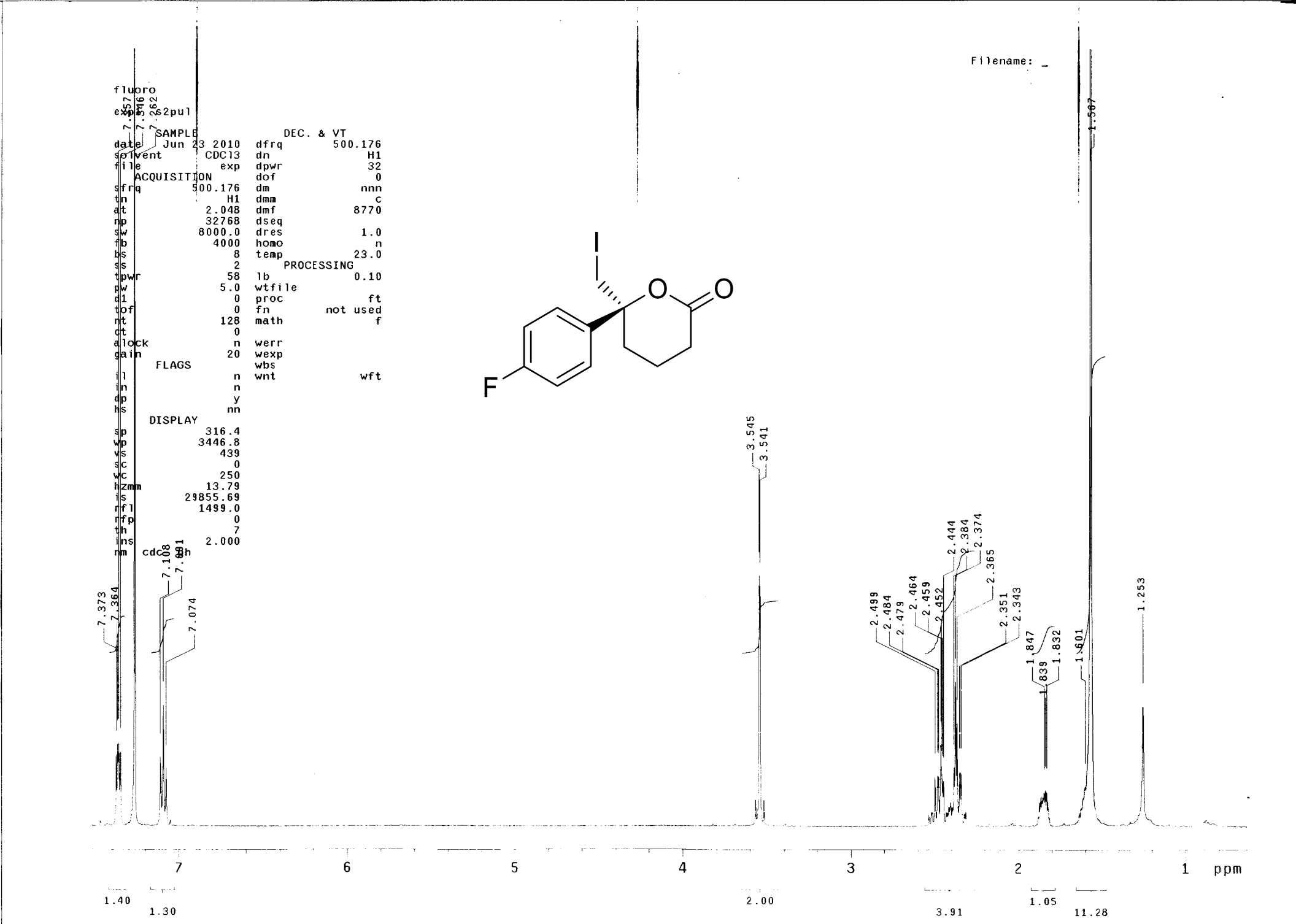
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inova500c"

Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
64 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line Broadening 1.1 Hz
FT size 32768
Total time 2 min, 24 sec

Filename: _



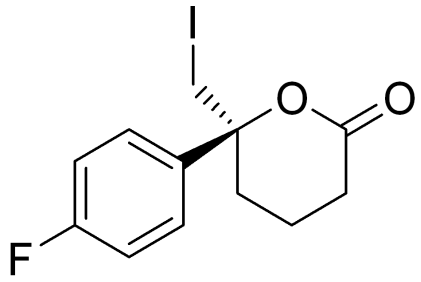

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
INOVA-500 "inova500c"
Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
1792 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 15 min, 13 sec
I
O
O
Br
170.199
139.662
132.394
127.318
122.911
84.348
77.510
77.255
77.000
32.217
29.224
17.141
16.821
220
200
180
160
140
120
100
80
60
40
20
ppm


fluoro
exp3 s2pul
SAMPLE
date Jun 23 2010
solvent CDCl3
file exp
ACQUISITION
sfrq 500.176
tn H1
at 2.048
np 32768
sw 8000.0
fb 4000
bs 8
ss 2
tpwr 58
pw 5.0
d1 0
tof 0
nt 128
ct 0
alock n
gain 20
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp 316.4
wp 3446.8
vs 439
sc 0
wc 250
hzmm 13.79
is 29855.69
rfl 1499.0
rfp 0
th 7
ins 2.000
nm cdcl3h
DEC. & VT
dfrq 500.176
dn H1
dpwr 32
dof 0
dm nnn
dmm c
dmf 8770
dseq
dres 1.0
homo n
temp 23.0
PROCESSING
lb 0.10
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt wft
Filename:
I
O
O
F
7.373
7.364
7.108
7.091
7.074
3.545
3.541
2.499
2.484
2.479
2.464
2.459
2.452
2.444
2.384
2.374
2.365
2.351
2.343
1.847
1.839
1.832
1.601
1.567
1.253
7
6
5
4
3
2
1
ppm
1.40
1.30
2.00
3.91
1.05
11.28

Filename: _

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
User: 1-14-87
INOVA-500 "inova500c"

Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
7744 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 3 hr, 45 min, 35 sec

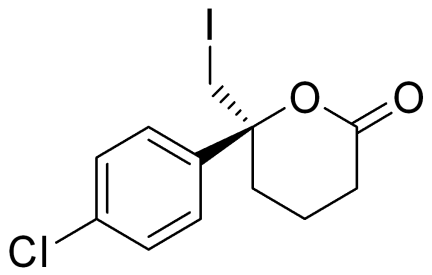


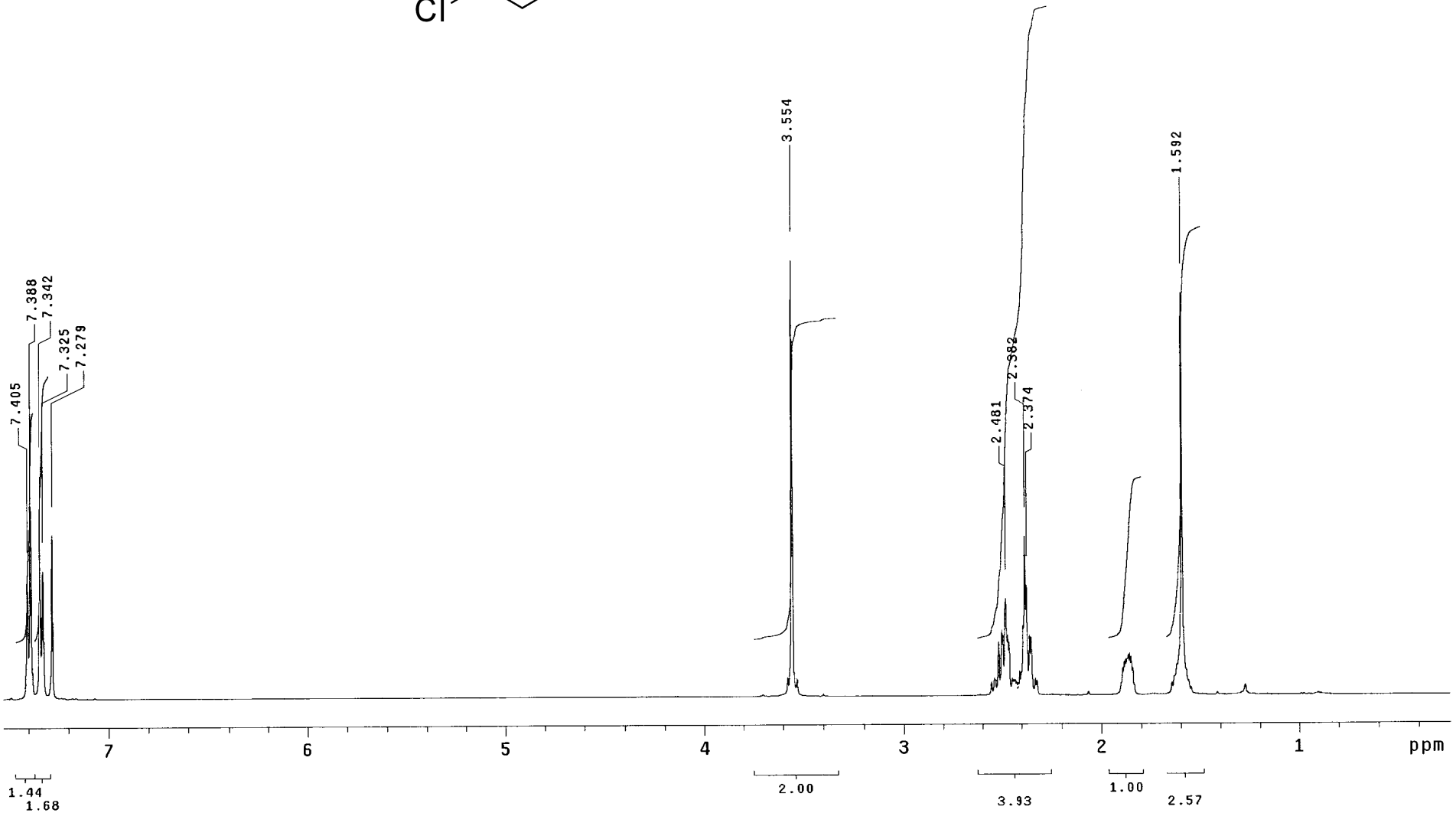
Filename: _

chloro

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inova500c"

Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
32 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 32768
Total time 1 min, 14 sec





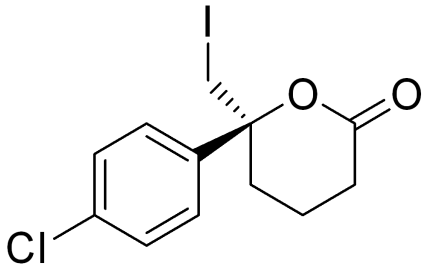
STANDARD CARBON PARAMETERS

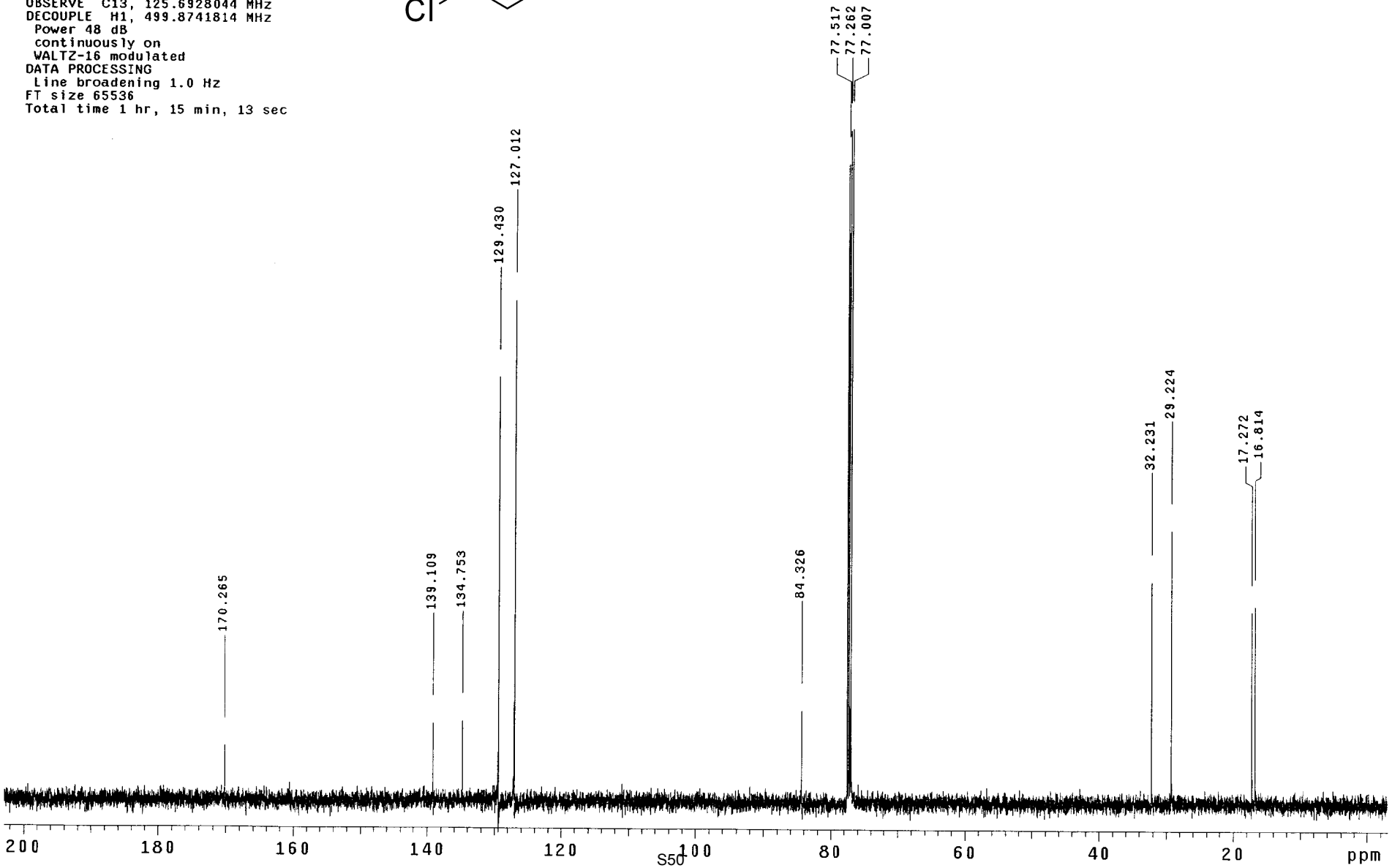
Pulse Sequence: s2pul

Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
INOVA-500 "inova500c"

Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
640 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 15 min, 13 sec

Filename: _



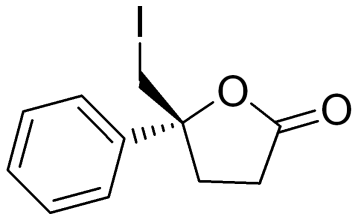


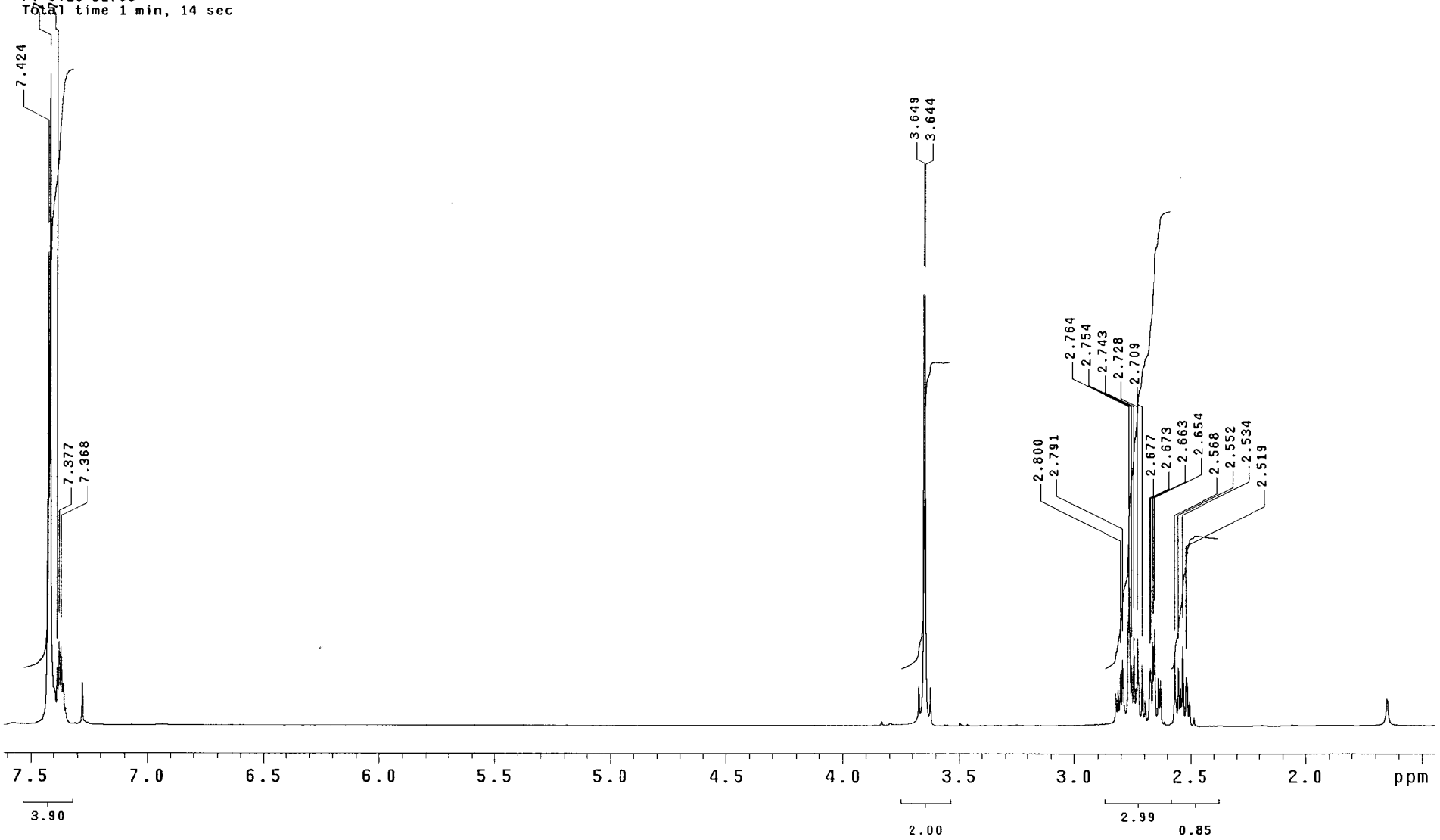
Filename: _

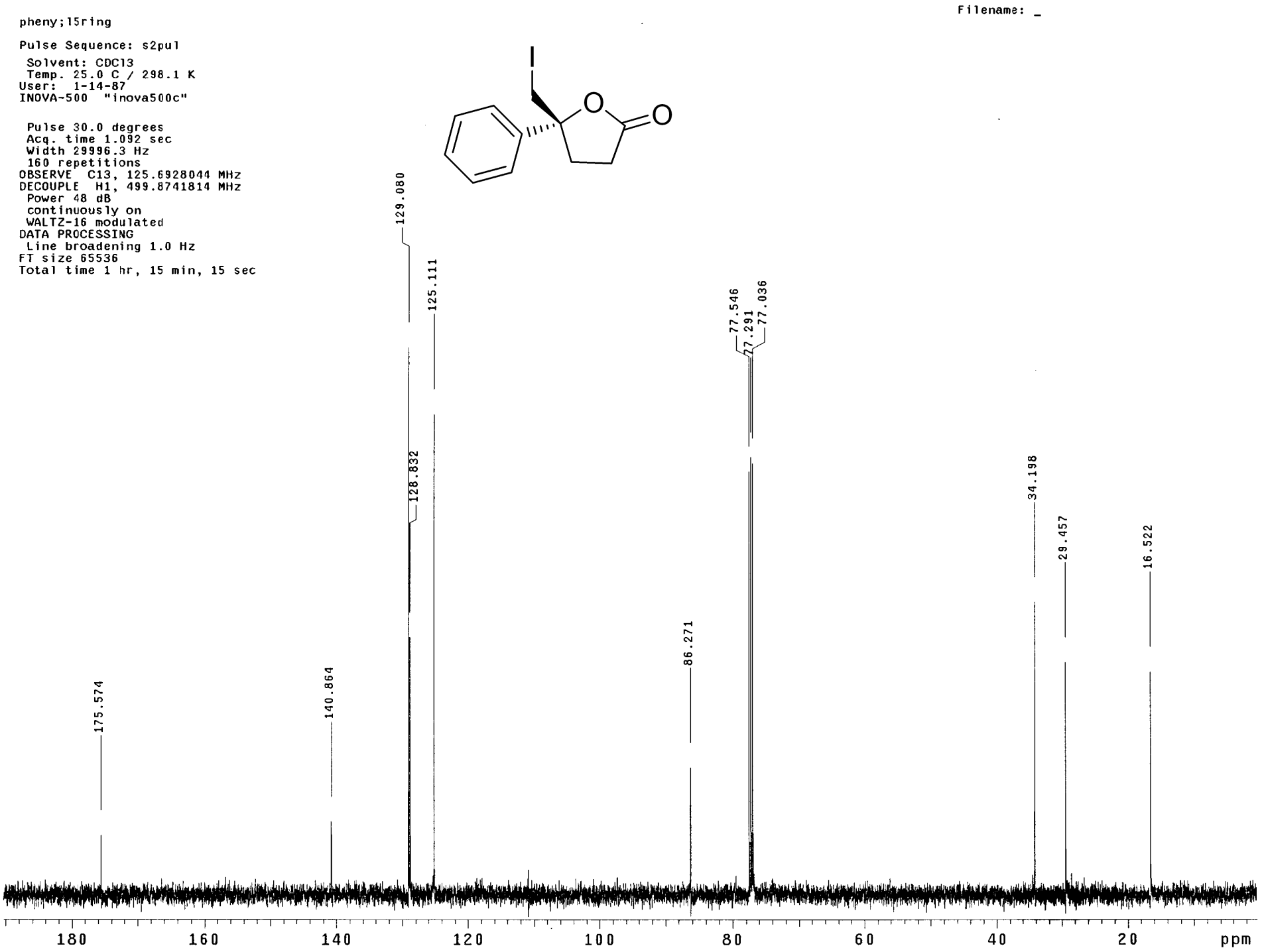
phenyl5ring

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inova500c"

Pulse 54.0 degrees
Acq. time 2.184 sec
Width 7501.2 Hz
32 repetitions
OBSERVE H1, 499.8716820 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 32768
Total time 1 min, 14 sec






Filename: _
pheny;15ring
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
INOVA-500 "inova500c"
Pulse 30.0 degrees
Acq. time 1.092 sec
Width 29996.3 Hz
160 repetitions
OBSERVE C13, 125.6928044 MHz
DECOUPLE H1, 499.8741814 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 15 min, 15 sec
I
O
O
129.080
125.111
128.832
77.546
77.291
77.036
175.574
140.864
86.271
34.198
29.457
16.522
180
160
140
120
100
80
60
40
20
ppm

D. Chiral HPLC and GC traces for enantioenriched iodolactone products

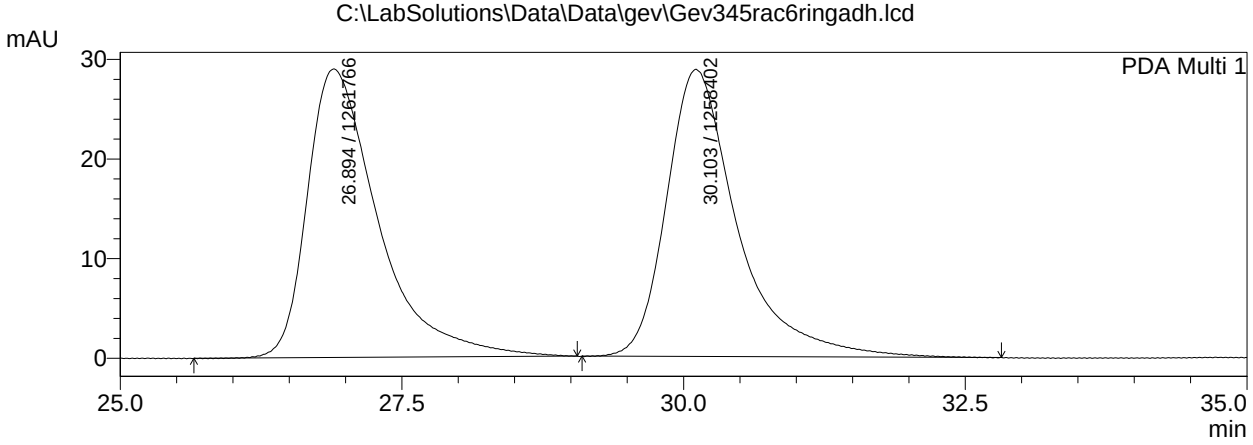
Racemic 3a

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev345rac6ringadh.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev345rac6ringadh.lcd
Method File Name	: Col2_60min_02%C_1ml_min.lcm
Batch File Name	: Gev345rac6ringo.lcb
Data Acquired	: 3/14/2010 7:11:22 PM

C:\LabSolutions\Data\Data\gev\Gev345rac6ringadh.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.894	1261766	28995	50.067	50.144
2	30.103	1258402	28829	49.933	49.856
Total		2520168	57823	100.000	100.000

PeakTable

PDA Ch2

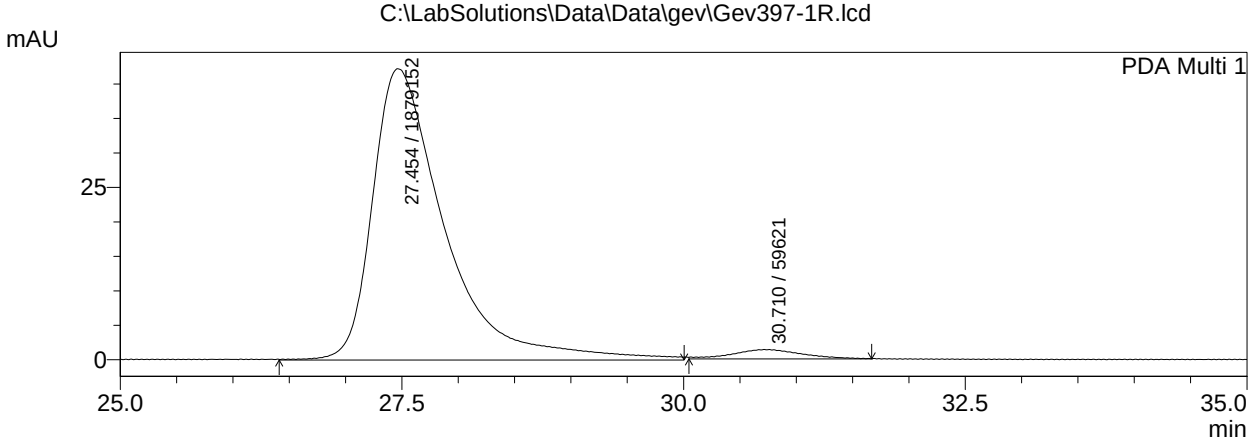
Enantioenriched 3a

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev397-1R.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev397-1R.lcd
Method File Name	: Col2_60min_02%C_1ml_min.lcm
Batch File Name	: gev397and398.lcb
Data Acquired	: 5/26/2010 1:20:01 PM

C:\LabSolutions\Data\Data\gev\Gev397-1R.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.454	1879152	42279	96.925	96.869
2	30.710	59621	1367	3.075	3.131
Total		1938774	43646	100.000	100.000

PeakTable

PDA Ch2

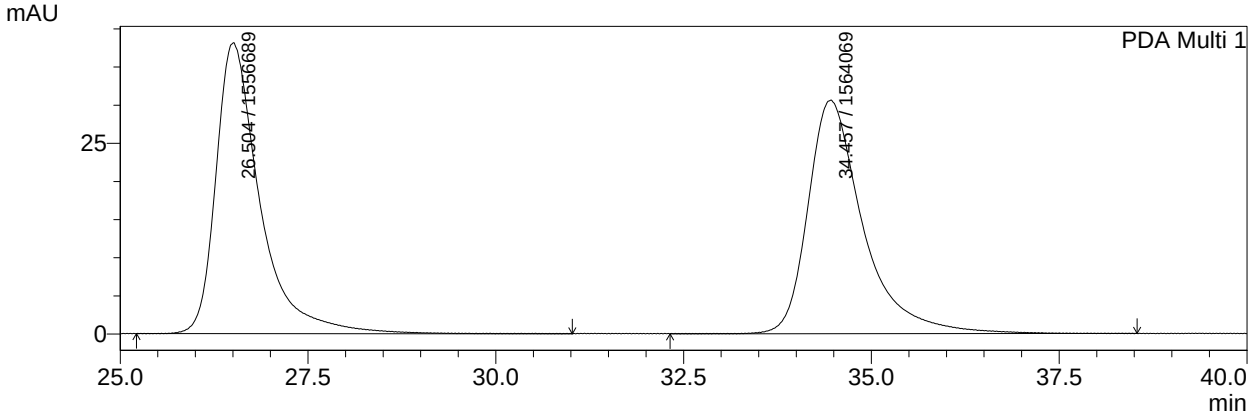
Racemic 3b

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev376-2.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev376-2.lcd
Method File Name	: Col2_60min_02%C_1ml_min.lcm
Batch File Name	: Gev376.lcb
Data Acquired	: 4/27/2010 4:48:50 PM

C:\LabSolutions\Data\Data\gev\Gev376-2.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.504	1556689	38123	49.882	55.442
2	34.457	1564069	30639	50.118	44.558
Total		3120757	68762	100.000	100.000

PeakTable

PDA Ch2

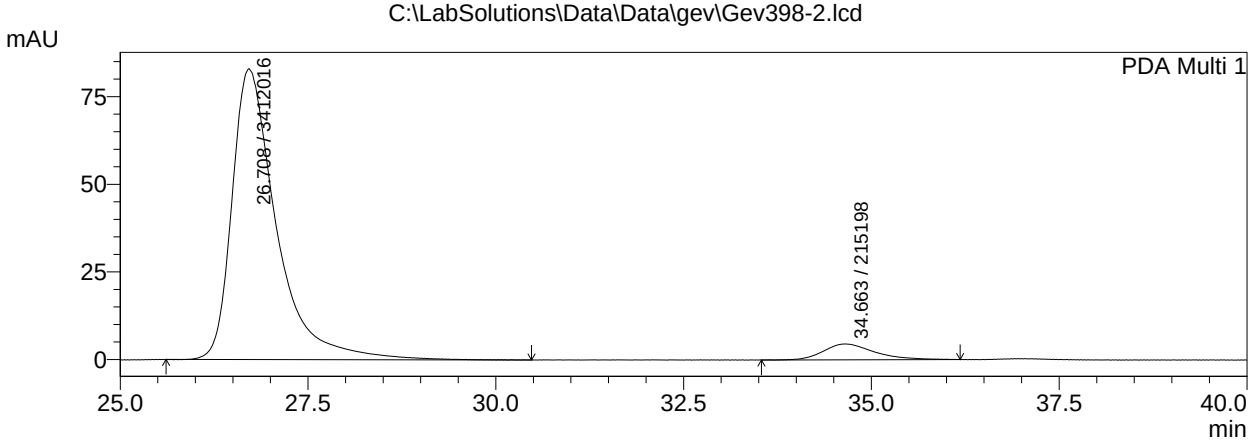
Enantioenriched 3b

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev398-2.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev398-2.lcd
Method File Name	: Col2_60min_02%C_1ml_min.lcm
Batch File Name	: gev397and398.lcb
Data Acquired	: 5/26/2010 11:15:51 AM

C:\LabSolutions\Data\Data\gev\Gev398-2.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.708	3412016	83011	94.067	94.799
2	34.663	215198	4554	5.933	5.201
Total		3627214	87565	100.000	100.000

PeakTable

PDA Ch2

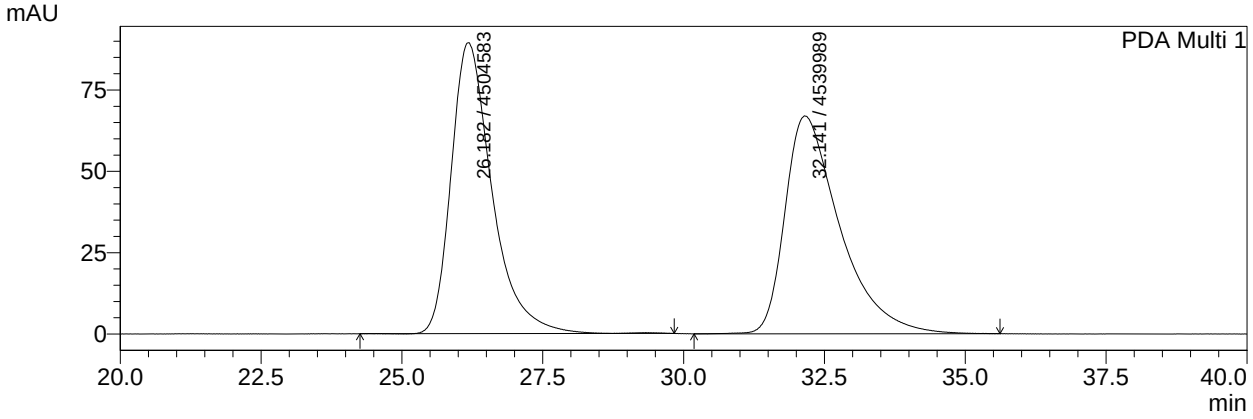
Racemic 3c

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev388-2odh.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev388-2odh.lcd
Method File Name	: Col3_60min_10%C_1ml_min.lcm
Batch File Name	: Gev388odh.lcb
Data Acquired	: 5/9/2010 11:06:20 PM

C:\LabSolutions\Data\Data\gev\Gev388-2odh.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.182	4504583	89417	49.804	57.167
2	32.141	4539989	66997	50.196	42.833
Total		9044572	156414	100.000	100.000

PeakTable

PDA Ch2

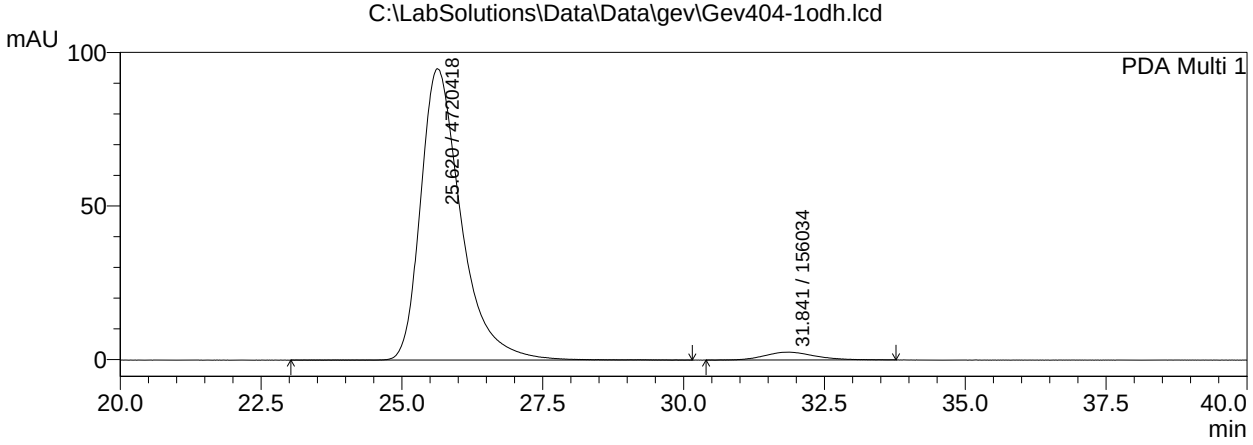
Enantioenriched 3c

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev404-1odh.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev404-1odh.lcd
Method File Name	: Col3_60min_10%C_1ml_min.lcm
Batch File Name	: Gev404-1odh.lcb
Data Acquired	: 6/2/2010 12:20:16 PM

C:\LabSolutions\Data\Data\gev\Gev404-1odh.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.620	4720418	94946	96.800	97.375
2	31.841	156034	2559	3.200	2.625
Total		4876452	97505	100.000	100.000

PeakTable

PDA Ch2

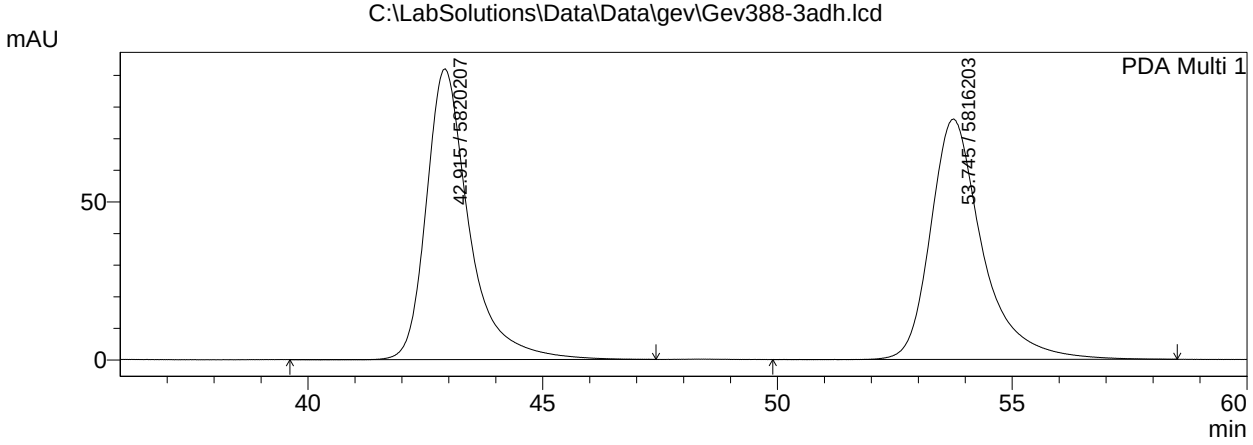
Racemic 3d

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev388-3adh.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev388-3adh.lcd
Method File Name	: Col2_60min_02%C_1ml_min.lcm
Batch File Name	: Gev388adh.lcb
Data Acquired	: 5/9/2010 8:01:43 PM

C:\LabSolutions\Data\Data\gev\Gev388-3adh.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	42.915	5820207	92013	50.017	54.743
2	53.745	5816203	76070	49.983	45.257
Total		11636410	168084	100.000	100.000

PeakTable

PDA Ch2

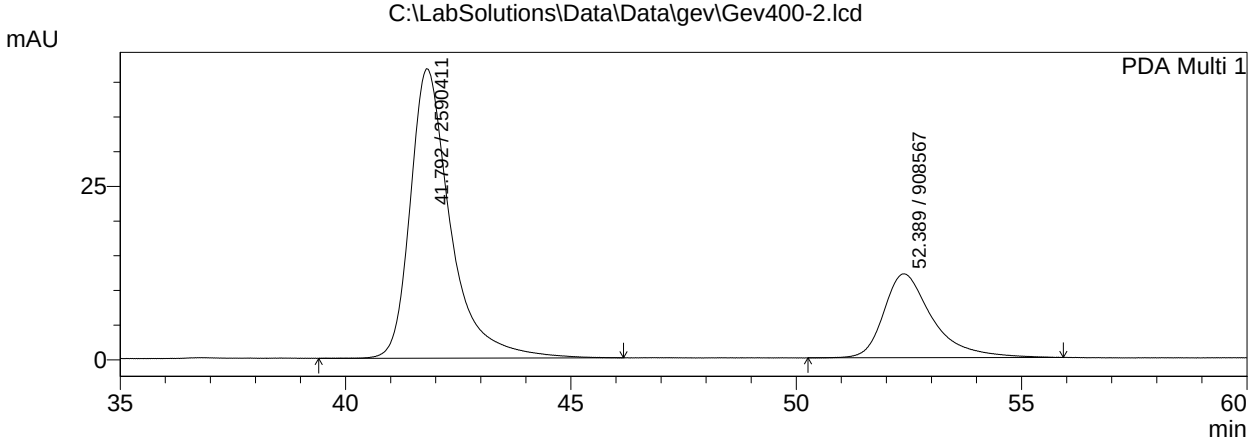
Enantioenriched 3d

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev400-2.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev400-2.lcd
Method File Name	: Col2_60min_02%C_1ml_min.lcm
Batch File Name	: Gev400.lcb
Data Acquired	: 6/1/2010 3:12:33 PM

C:\LabSolutions\Data\Data\gev\Gev400-2.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

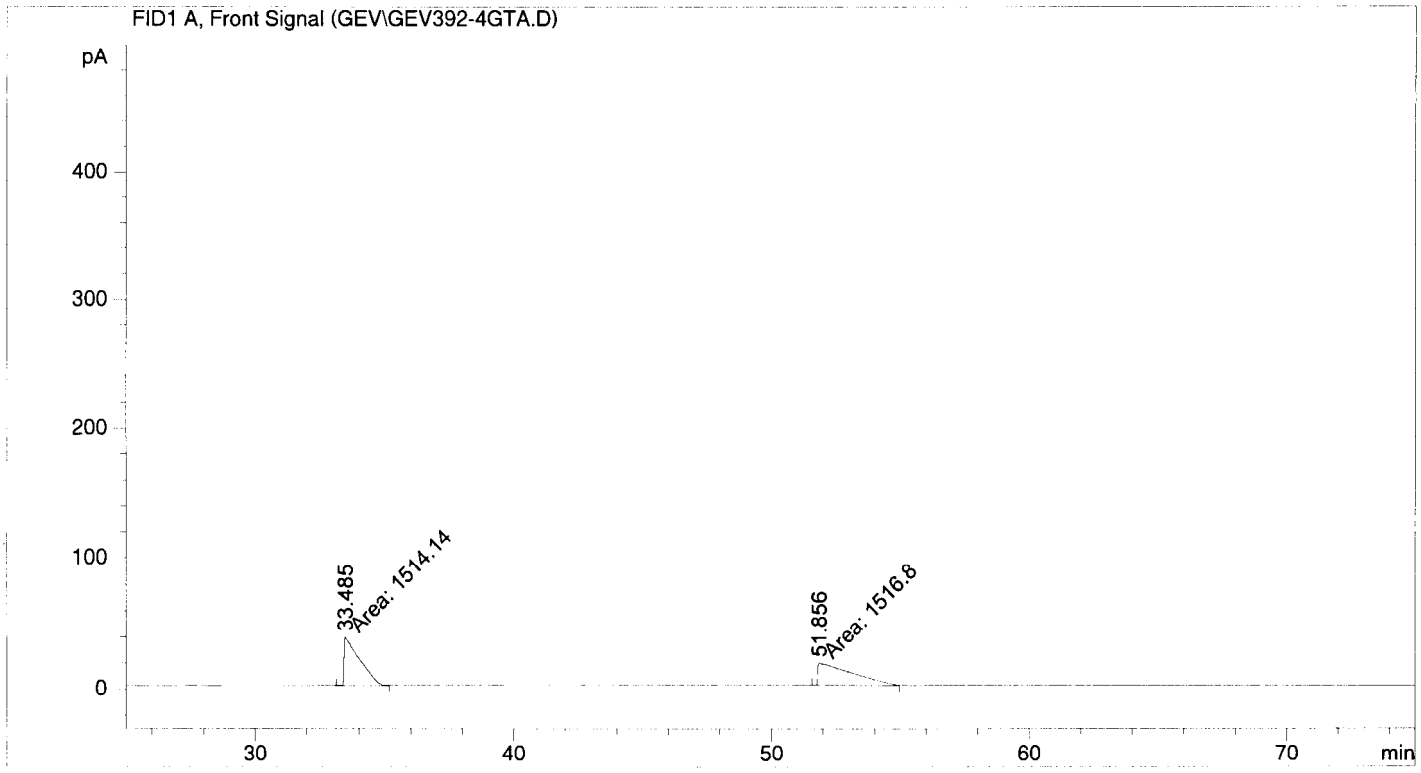
Peak#	Ret. Time	Area	Height	Area %	Height %
1	41.792	2590411	41736	74.033	77.528
2	52.389	908567	12097	25.967	22.472
Total		3498979	53834	100.000	100.000

PeakTable

PDA Ch2

Racemic 3e

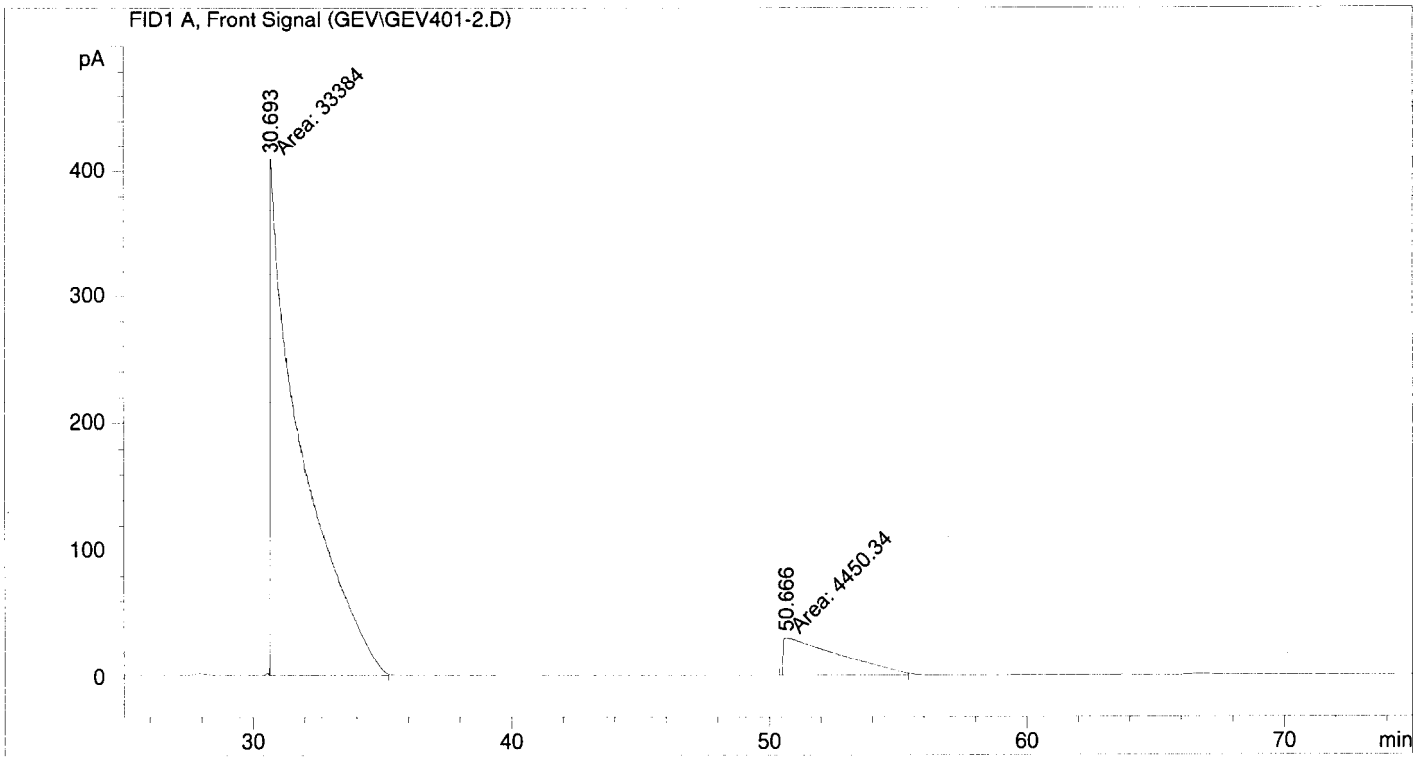
```
==========================================================================
Acq. Operator   : gev                              Seq. Line :   2
Acq. Instrument : Instrument 2                      Location : Vial 1
Injection Date  : 5/15/2010 7:11:07 PM                  Inj :   1
                                                  Inj Volume : 1 µl
Acq. Method     : C:\CHEM32\2\METHODS\GEV-DUAL150ISO120_7PSI.M
Last changed    : 5/15/2010 6:34:38 PM by ARB
Analysis Method : C:\CHEM32\2\METHODS\ARB-DUAL040ISO_7PSI.M
Last changed    : 6/5/2010 3:34:25 PM by CU
                  (modified after loading)
Method Info     : standard FID test at  install DUAL INJECTION
```




```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: FID1 A, Front Signal

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  33.485 MM    0.6808 1514.13623   37.06898 49.95603
   2  51.856 MM    1.5141 1516.80176   16.69694 50.04397

Totals :                  3030.93799   53.76592

==========================================================================
```

Enantioenriched 3e

```
==========================================================================
Acq. Operator    : GEV                                Seq. Line :   2
Acq. Instrument : Instrument 2                         Location : Vial 10
Injection Date   : 6/2/2010 3:01:00 PM                     Inj :   1
                                                     Inj Volume : 1 µl
Acq. Method      : C:\CHEM32\2\METHODS\GEV-DUAL150ISO120_7PSI.M
Last changed     : 5/15/2010 6:34:38 PM by ARB
Analysis Method : C:\CHEM32\2\METHODS\ARB-DUAL040ISO_7PSI.M
Last changed     : 6/5/2010 3:33:46 PM by CU
                   (modified after loading)
Method Info      : standard FID test at  install DUAL INJECTION
```




```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: FID1 A, Front Signal

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  30.693 MM    1.3638 3.33840e4   407.97794 88.23732
   2  50.666 MM    2.5022 4450.33691   29.64328 11.76268

Totals :                  3.78344e4   437.62121


==========================================================================
```

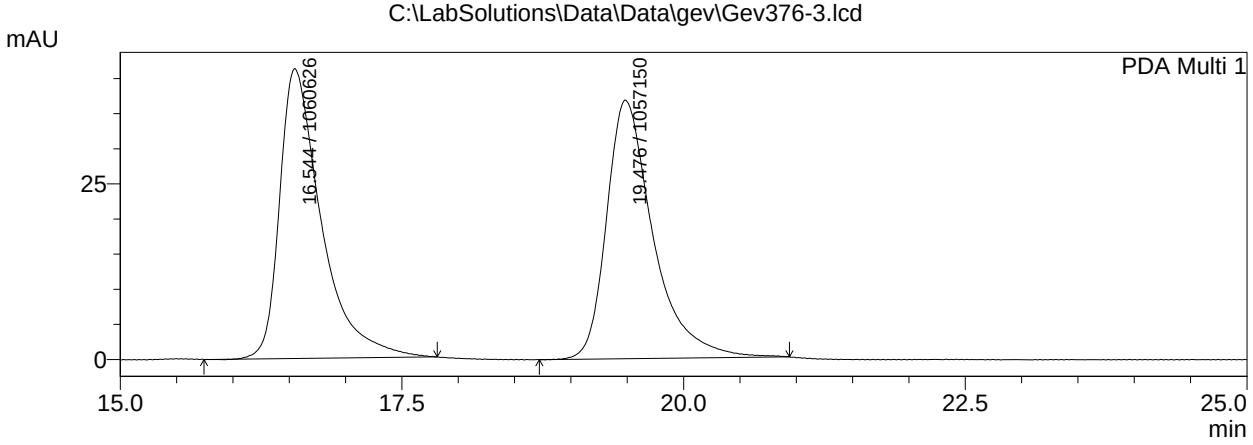
Racemic 3f

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev376-3.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev376-3.lcd
Method File Name	: Col2_60min_02%C_1ml_min.lcm
Batch File Name	: Gev376.lcb
Data Acquired	: 4/27/2010 5:51:14 PM

C:\LabSolutions\Data\Data\gev\Gev376-3.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.544	1060626	41261	50.082	52.833
2	19.476	1057150	36836	49.918	47.167
Total		2117776	78097	100.000	100.000

PeakTable

PDA Ch2

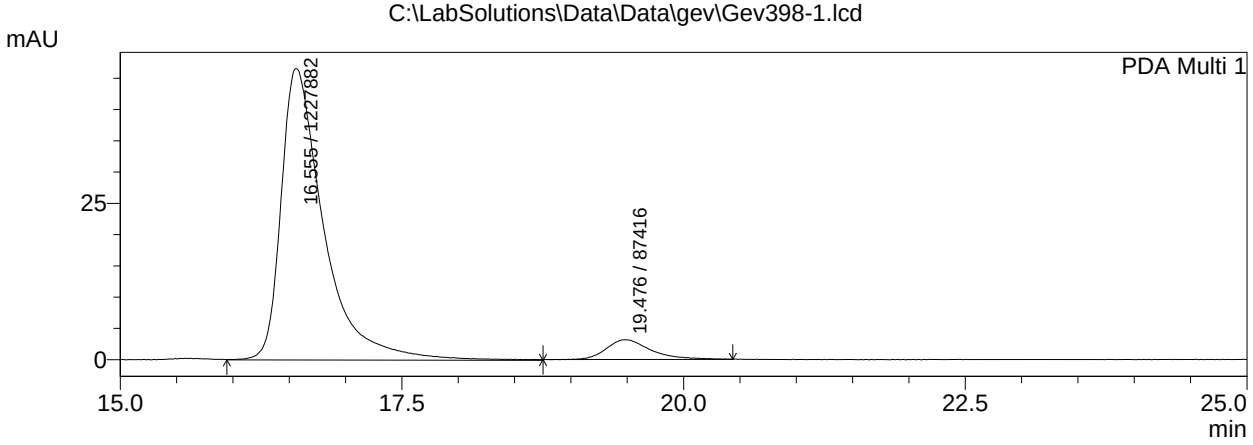
Enantioenriched 3f

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev398-1.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev398-1.lcd
Method File Name	: Col2_60min_02%C_1ml_min.lcm
Batch File Name	: gev397and398.lcb
Data Acquired	: 5/26/2010 12:17:37 PM

C:\LabSolutions\Data\Data\gev\Gev398-1.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.555	1227882	46575	93.354	93.590
2	19.476	87416	3190	6.646	6.410
Total		1315297	49765	100.000	100.000

PeakTable

PDA Ch2

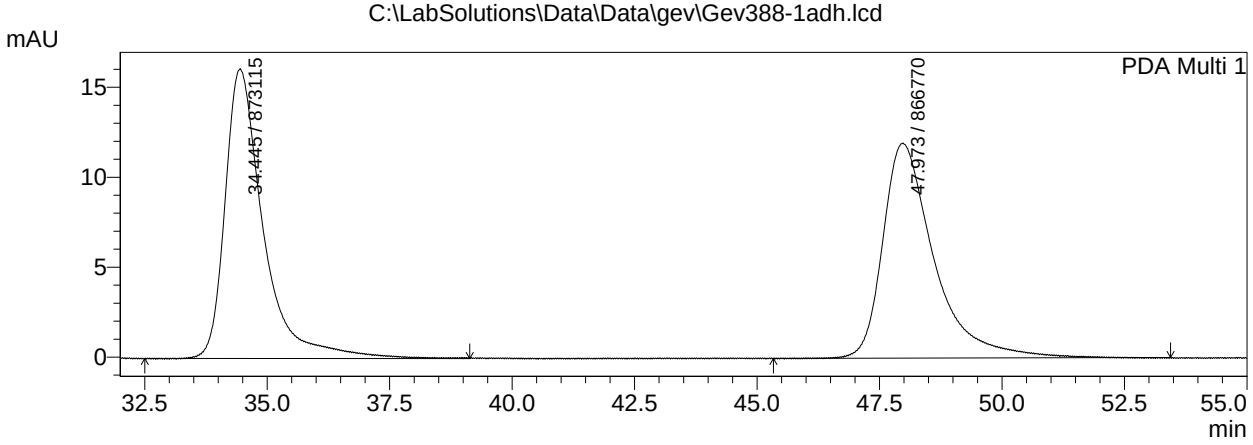
Racemic 3g

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev388-1adh.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev388-1adh.lcd
Method File Name	: Col2_60min_02%C_1ml_min.lcm
Batch File Name	: Gev388adh.lcb
Data Acquired	: 5/9/2010 5:58:14 PM

C:\LabSolutions\Data\Data\gev\Gev388-1adh.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.445	873115	16113	50.182	57.389
2	47.973	866770	11964	49.818	42.611
Total		1739886	28076	100.000	100.000

PeakTable

PDA Ch2

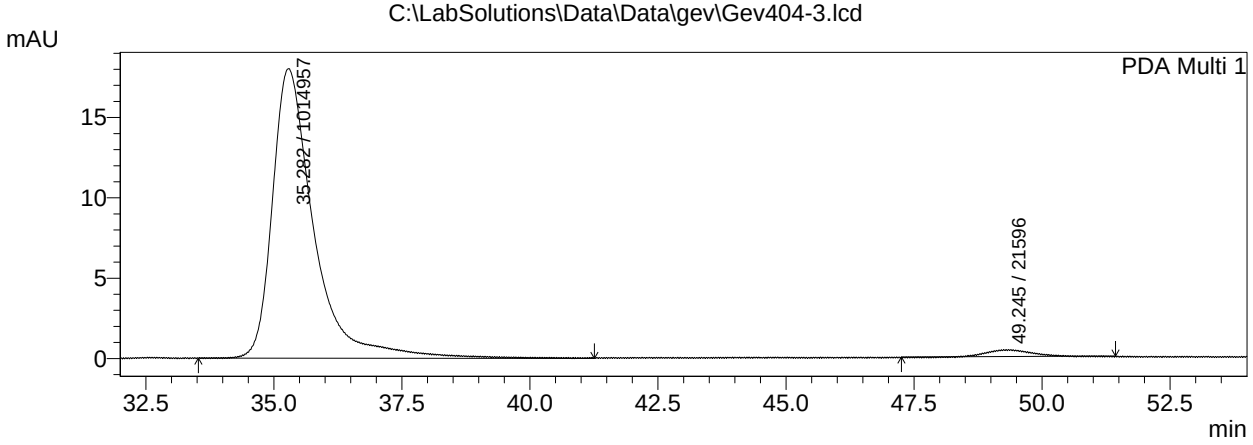
Enantioenriched 3g

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev404-3.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev404-3.lcd
Method File Name	: Col2_60min_02%C_1ml_min.lcm
Batch File Name	: Gev407efg.lcb
Data Acquired	: 6/9/2010 7:44:33 AM

C:\LabSolutions\Data\Data\gev\Gev404-3.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	35.282	1014957	18023	97.917	97.642
2	49.245	21596	435	2.083	2.358
Total		1036553	18458	100.000	100.000

PeakTable

PDA Ch2

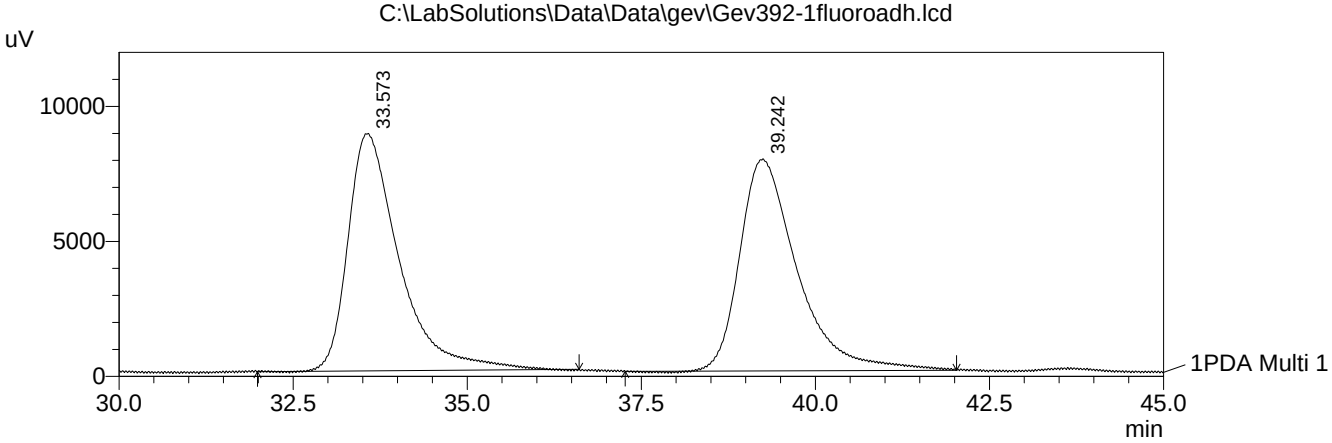
Racemic 3h

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev392-1fluoroadh.lcd

Acquired by : Admin
Sample Name : run
Sample ID :
Data File Name : Gev392-1fluoroadh.lcd
Method File Name : Col2_60min_02%C_1ml_min.lcm
Batch File Name : Gev390.lcb
Data Acquired : 5/12/2010 11:51:21 PM

C:\LabSolutions\Data\Data\gev\Gev392-1fluoroadh.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.573	449295	8802	49.947	52.850
2	39.242	450245	7852	50.053	47.150
Total		899539	16654	100.000	100.000

PeakTable

PDA Ch2

PeakTable

PDA Ch3

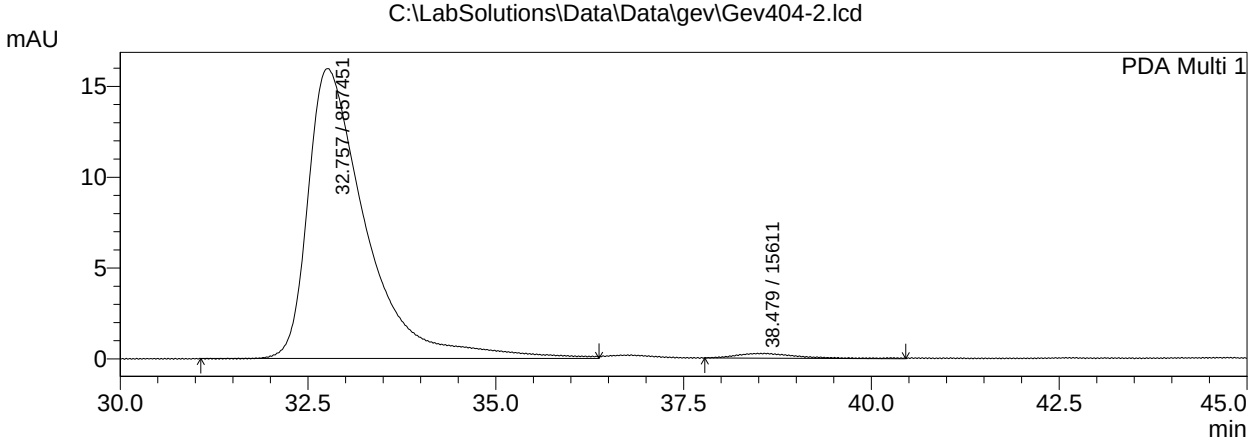
Enantioenriched 3h

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev404-2.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev404-2.lcd
Method File Name	: Col2_60min_02%C_1ml_min.lcm
Batch File Name	: 4041and2.lcb
Data Acquired	: 6/2/2010 2:10:09 AM

C:\LabSolutions\Data\Data\gev\Gev404-2.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	32.757	857451	15955	98.212	98.290
2	38.479	15611	278	1.788	1.710
Total		873063	16232	100.000	100.000

PeakTable

PDA Ch2

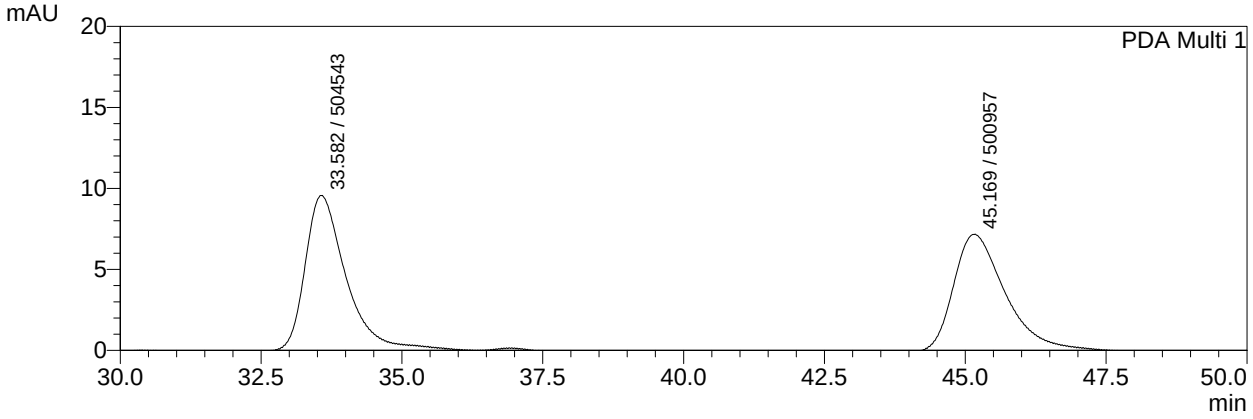
Racemic 3i

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev376-1.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev376-1.lcd
Method File Name	: Col2_60min_02%C_1ml_min.lcm
Batch File Name	: Gev376.lcb
Data Acquired	: 4/27/2010 3:47:05 PM

C:\LabSolutions\Data\Data\gev\Gev376-1.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.582	504543	9694	50.178	56.821
2	45.169	500957	7367	49.822	43.179
Total		1005500	17061	100.000	100.000

PeakTable

PDA Ch2

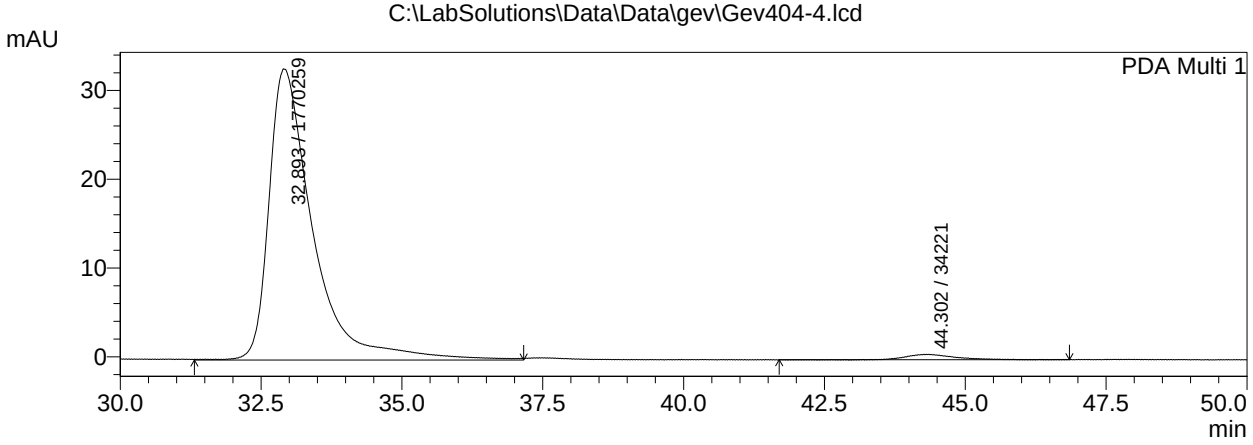
Enantioenriched 3i

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev404-4.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev404-4.lcd
Method File Name	: Col2_60min_02%C_1ml_min.lcm
Batch File Name	: 4044.lcb
Data Acquired	: 6/2/2010 10:57:44 AM

C:\LabSolutions\Data\Data\gev\Gev404-4.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	32.893	1770259	32818	98.104	98.175
2	44.302	34221	610	1.896	1.825
Total		1804480	33428	100.000	100.000

PeakTable

PDA Ch2

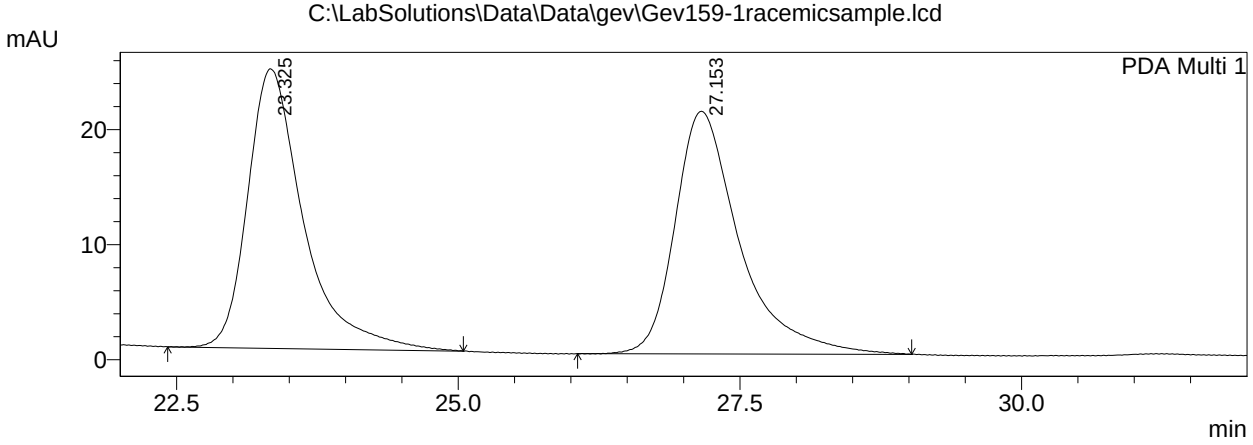
Racemic 10a

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev159-1racemicsample.lcd

Acquired by : Admin
Sample Name : run
Sample ID :
Data File Name : Gev159-1racemicsample.lcd
Method File Name : Col2_60min_02%C_1ml_min.lcm
Batch File Name : Gev159-1racemic.lcb
Data Acquired : 8/7/2009 5:06:05 PM

C:\LabSolutions\Data\Data\gev\Gev159-1racemicsample.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.325	837126	24311	49.922	53.519
2	27.153	839743	21114	50.078	46.481
Total		1676870	45425	100.000	100.000

PeakTable

PDA Ch2

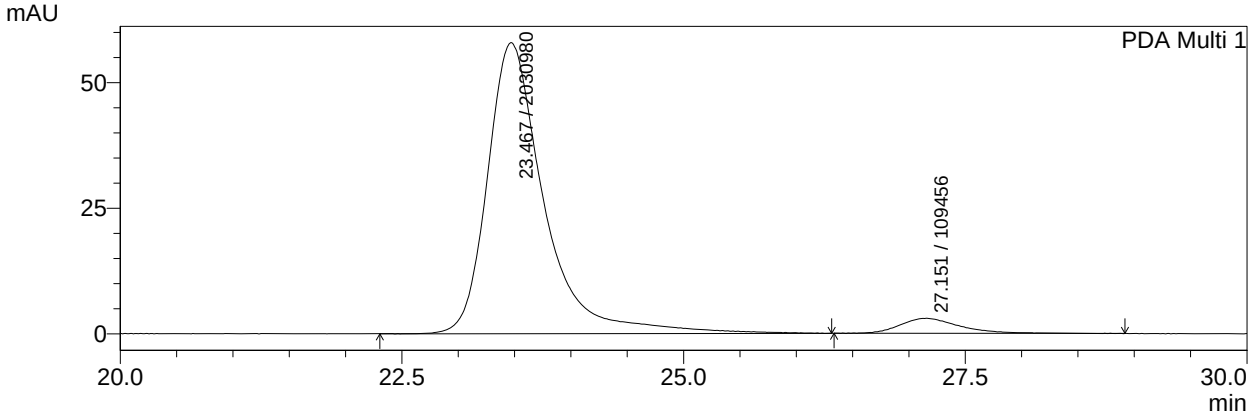
Enantioenriched 10 a

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Data\gev\Gev401-2.lcd

Acquired by	: Admin
Sample Name	: run
Sample ID	:
Data File Name	: Gev401-2.lcd
Method File Name	: Col2_60min_02%C_1ml_min.lcm
Batch File Name	: Gev407efg.lcb
Data Acquired	: 6/9/2010 6:42:48 AM

C:\LabSolutions\Data\Data\gev\Gev401-2.lcd



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.467	2030980	57942	94.886	95.079
2	27.151	109456	2999	5.114	4.921
Total		2140436	60941	100.000	100.000

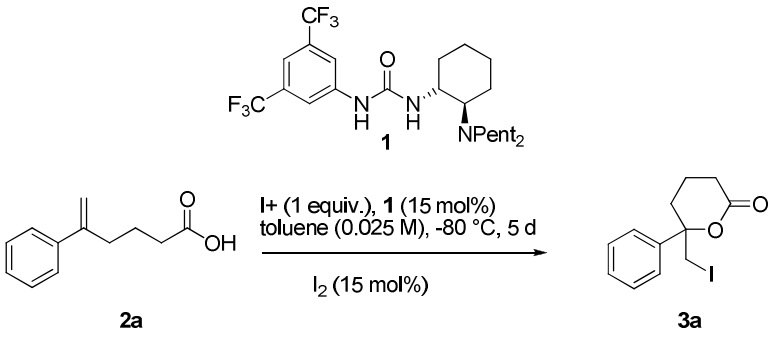
PeakTable

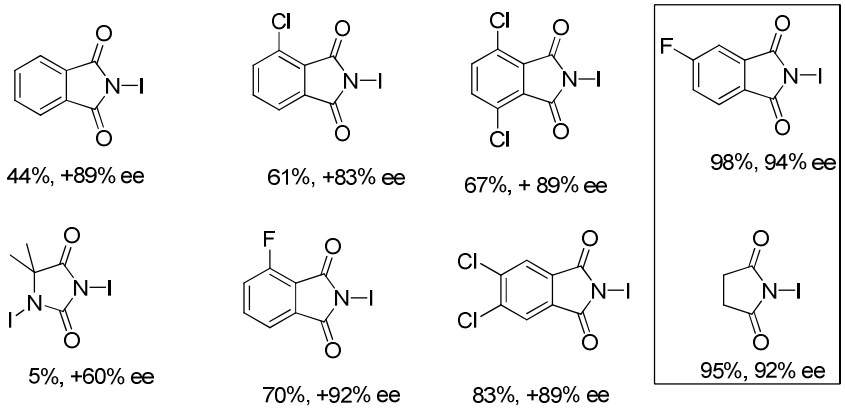
PDA Ch2

E. Optimization of Catalyst and Iodinating Agent

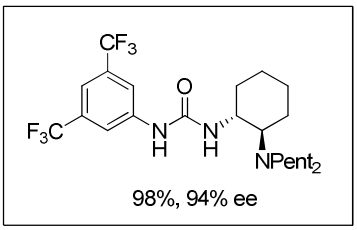
Optimization of the Iodinating Agent

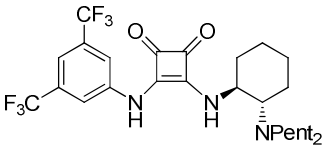
All substituted phthalimides were prepared according to the procedure used for **5** (*N*-iodo-4-fluorophthalimide) from the corresponding substituted anhydride.



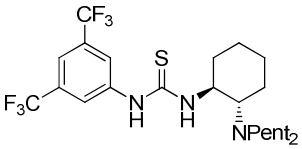


Catalyst Optimization

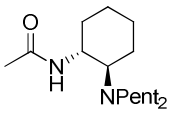




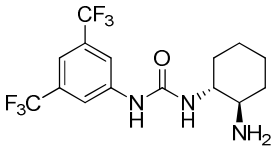
27%, -12% ee



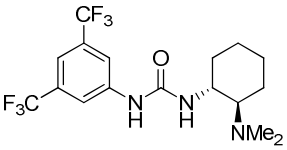
3%, +7% ee



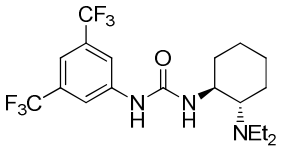
66%, +5% ee



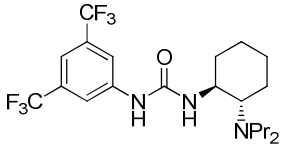
10%, +73% ee



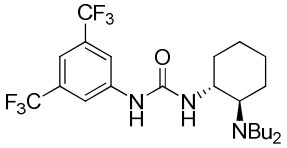
6%, +49% ee



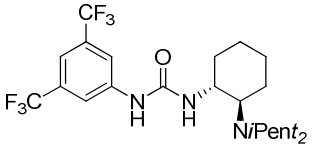
46%, -76% ee



50%, -81% ee



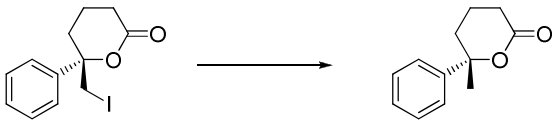
70%, +91% ee



27%, + 91% ee

F. Determination of the Absolute Configuration of the Iodolactone Products

(3a)



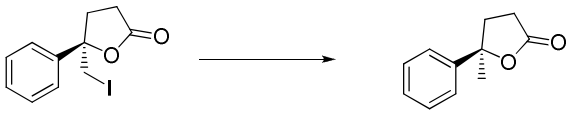
3a

Radical-mediated deiodination[11] of **3a** (90% ee) provided the known methyl lactone[12]: $[\alpha]_D^{24}$ = -34 (*c* = 1.6), literature reports the (*R*) enantiomer with 90% ee to have $[\alpha]_D^{12}$ = +39.8 (*c* = 1.0, $CHCl_3$); **3a** is therefore (*S*).

(3g)

X-ray crystallographic analysis confirmed the (*S*) stereochemistry for **3g**.

(10a)

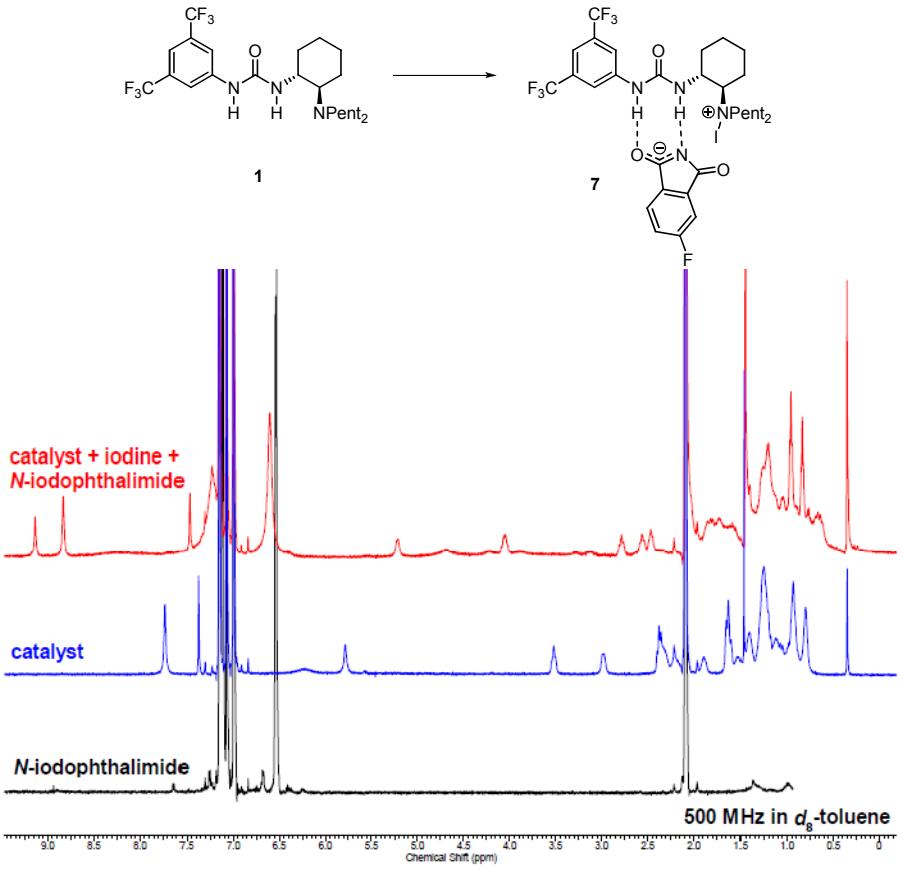


10a

Radical-mediated deiodination[11] of **10a** (85% ee) provided the known methyl lactone[13]: $[\alpha]_D^{24}$ = +51 (*c* = 1.6, $CHCl_3$), literature reports the (*R*) enantiomer to have $[\alpha]_D^{15}$ = +72.4 (*c* = 1.0, $CHCl_3$); **10a** is therefore (*R*).

G. Experimental Support for the Intermediacy of 7

Premixing of 4-fluoro-*N*-iodophthalimide (0.1 mmol) with I_2 (0.1 mol%) and catalyst **1** (15 mol%) in toluene afforded immediate changes in the ^{1}H NMR spectrum of the catalyst **1**. Most notably, the bis-trifluoromethylphenyl protons were shifted significantly downfield.
The direct quenching of this reaction with saturated aqueous sodium thiosulfate solution afforded peaks in the mass spectrum consistent with the starting catalyst **1** and also the secondary amine (which is not seen as a fragmentation product from **1**). The dealkylation of **1** is consistent with the *N*-iodo species **7** which could undergo elimination of HI to form an iminium ion, followed by hydrolysis, upon aqueous quenching.



References

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[3] For the preparation of *N*-iodophthalimide from potassium phthalimide, see:, L. Hadjiarapoglou, S. Spyroudis, A. Varvoglis, *Synthesis* **1983**, 207.
[4] For the preparation of potassium 4-fluorophthalimide see:, T. J. Watson, T. A. Ayers, N. Shah, D. Wenstrup, M. Webster, D. Freund, S. Horgan, J. P. Carey, *Org. Proc. Res. Dev.* **2003**, *7*, 521.
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[11] For the procedure used for deiodination see: D. C Whitehead, R. Yousefi, A. Jaganathan, B. Borhan, *J. Am. Chem. Soc.,* **2010**, *132*, 3298.
[12] M. Date, Y. Tamai, T. Hattori, H. Takayama, Y. Kamikubo, S. Miyano, *J. Chem. Soc., Perkin Trans. 1* **2001**, *2001*, 645.
[13] A. Albinati, P. Bravo, F. Ganazzoli, G. Resnati, F. Viani, *J. Chem. Soc., Perkin Trans. 1* **1986**, 1405.