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A Publication
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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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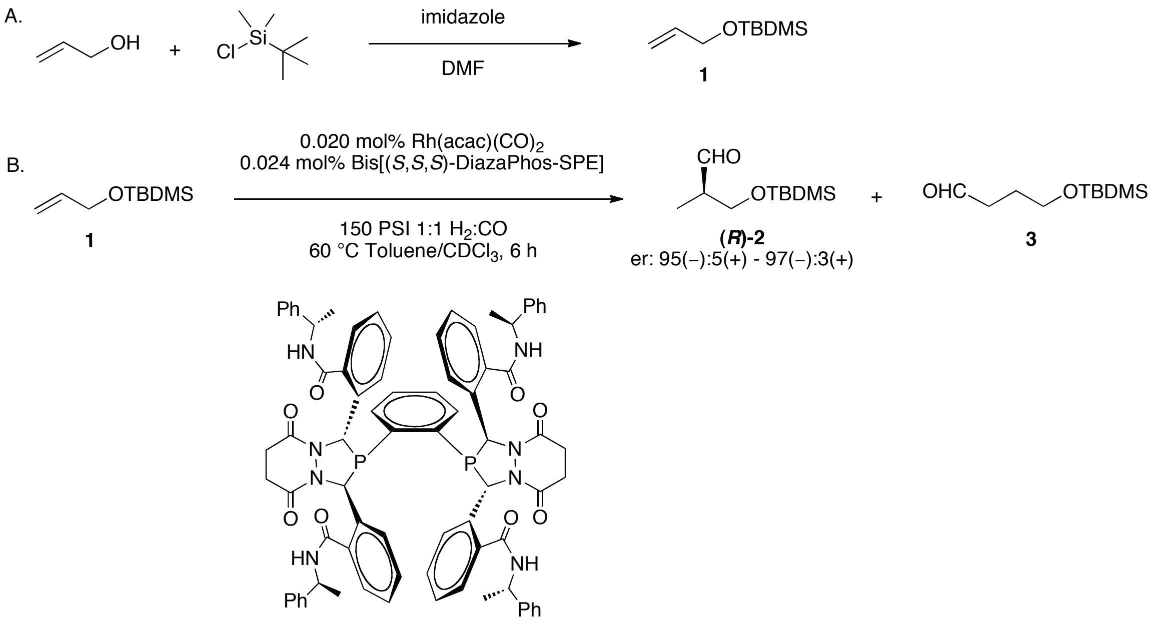
Synthesis of (2*R*)-3-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-2-methylpropanal by Rhodium-Catalyzed Asymmetric Hydroformylation



Bis[(*S*,*S*,*S*)-DiazaPhos-SPE]

Submitted by Gene W. Wong, Tyler T. Adint, Clark R. Landis.[1]
Checked by Neil Strotman, James Cuff and David Hughes.

1. Procedure

Caution! Carbon monoxide is a highly toxic gas and manipulations should be conducted in a well-ventilated fume hood in the vicinity of a carbon monoxide detector. Hydrogen gas is highly flammable and explosive gas. Precautions should be taken when using synthesis gas (H_2/CO mixtures).

*A. Allyl (t-butyldimethyl)silyl ether **1**.* An oven-dried three-necked, 500-mL round-bottomed flask equipped with a 3-cm PTFE-coated oval stir bar is charged with allyl alcohol (8.6 g, 0.15 mol, 1.0 equiv), imidazole (21.1 g, 0.31 mol, 2.1 equiv), and dimethylformamide (100 mL). (Note 1) The flask is fitted with a gas inlet adapter connected to a nitrogen line and a gas bubbler. The other two necks are capped with rubber septa; a thermocouple probe is inserted through one of the septa. (Note 2) The stirred solution is cooled to 4 °C with an ice-water bath, then *t*-butyldimethylsilyl chloride

(25.5 g, 0.17 mol, 1.1 equiv) is added in portions over 2 min. (Note 3) The water bath is removed and the hazy solution is stirred 15 h at 22–23 °C. (Note 4) The reaction mixture is transferred to a 500-mL separatory funnel along with hexanes (200 mL) and water (60 mL). After mixing and settling, the aq. layer is removed and the organic layer washed with brine (75 mL). The hazy organic layer is filtered through a bed of sodium sulfate (50 g) in a medium porosity sintered glass funnel into a 500-mL round-bottomed flask, using hexanes (2 x 50 mL) to rinse the filter cake. The filtrate is concentrated by rotary evaporation (40 °C, 20 mmHg) to an oil (22 g). Since a substantial portion of the product co-distills during concentration, the distillate from the receiver flask is re-concentrated, providing additional product (2.8 g). The combined crude product is purified by column chromatography (Note 5) to afford allyl (*t*-butyldimethyl)silyl ether **1** (18.1–18.5 g, 71–73% yield) as a colorless oil. (Note 6)

B. (2R)-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methylpropanal **2**. In a glovebox, bis[(*S,S,S*)-DiazaPhos-SPE] (9.2 mg, 0.0070 mmol, 0.024 mol%) is added to a 20 mL vial followed by 0.22 mL $CDCl_3$. To a separate 4 mL vial is added $Rh(acac)(CO)_2$ (10 mg) followed by 1.94 mL toluene to prepare a 20 mM stock solution; 0.29 mL (1.5 mg, 0.0058 mmol, 0.020 mol%) of this stock solution is transferred to the 20 mL vial containing the ligand solution (Notes 7, 8). Allyl (*t*-butyldimethyl)silyl ether **1** (5.00 g, 6.17 mL, 29 mmol, 1.0 equiv) is added to the vial. The solution is divided into 4 x 4 mL vials, each containing a 5-mm glass bead, and loaded into a Symyx Heated Orbital Shaker System (HOSS) contained within the glove box. (Note 9) The system is taken through 3 cycles of pressurization (150 psig of 1:1 H_2:CO)/depressurization (0 psig) to replace the nitrogen atmosphere with synthesis gas. The system is pressurized with 150 psig 1:1 H_2:CO and heated to 60 °C for 16 h. (Note 10) The mixture is cooled and the system depressurized, then the vials are removed from the glove box. (Note 15) The hydroformylation reaction mixture is purified immediately (Note 16) by flash column chromatography (Note 17) to afford colorless oils of branched isomer (*R*)-**2** (3.24–3.43 g, 55–58% yield, Notes 18-20) and linear isomer **3** (1.62–1.70 g, 27–29% yield, Note 21).

2. Notes

1. The following reagents and solvents in step A were used as received: allyl alcohol (Sigma-Aldrich), imidazole (Acros, 99%), *t*-butyldimethylsilyl chloride (Acros, 98%), anhydrous DMF (Sigma-Aldrich, 99.8%), hexanes (Fisher, ACS reagent, >98.5%), ethyl acetate (Fisher, ACS reagent, >99.5%) and silica gel (Fisher, 230-400 mesh, 60 Å).

2. The internal temperature is monitored using a J-Kem Gemini digital thermometer with a Teflon-coated T-Type thermocouple probe (12-inch length, 1/8 inch outer diameter, temperature range –200 to +250 °C).

3. The reaction warmed to 25 °C over 5 min after addition of TBS-Cl.

4. The reaction was monitored by TLC, 5% EtOAc/hexanes, R_f 0.6, $KMnO_4$ stain.

5. Silica gel (250 g) was slurry-packed in a 5-cm diameter column using 2.5% EtOAc/hexanes. The product was eluted with 2.5% EtOAc/hexanes, collecting 100 mL fractions. Fractions 5-13 were combined and concentrated by rotary evaporation (40 °C, 20 mmHg) to afford **1** (14.5–15.4 g) as a colorless oil. The distillate from concentration was re-concentrated to provide an additional 2.7–4.0 g (combined yield, 18.1–18.5 g, 71–73%). The distillate from the final product concentration was assayed by ^{1}H NMR using toluene as an internal standard, indicating 2.4 g (10% yield) **1** was present in the distillate.

6. *Allyl (t-butyldimethyl)silyl ether **1*** has the following physical and spectroscopic data: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.09 (s, 6 H), 0.93 (s, 9 H), 4.18–4.20 (m, 2 H), 5.07–5.11 (m, 1 H), 5.25–5.30 (m, 1 H), 5.89–5.97 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: –5.0, 18.6, 26.2, 64.3, 114.1, 137.8; GC-MS (EI) *m/z*: 172 (6 %) [M^+], 157 (6%), [M - CH_3], 116 (31%), 115 (100%) [M - *t*-Bu], 99 (21%), 85 (69%) [M – Me_2,*t*-Bu], 75 (28%), 59 (48%); GC purity: 98% (t_R = 4.4 min; conditions: Agilent DB35MS column; 30 m x 0.25 mm; initial temp 60 °C, ramp at 20 °C/min to 280 °C, hold 15 min).

7. The following reagents and solvents in step B were used as received by the checkers: dicarbonylacetylacetonato rhodium(I) (Strem), toluene (Sigma Aldrich, anhydrous, >99.9%), $CDCl_3$ (Sigma-Aldrich, 99.8% atom % D), SynGas (49% carbon monoxide/51% hydrogen, Airgas) and bis[(*S,S,S*)-DiazaPhos-SPE] ligand: 2,2′,2″,2‴-(1,2-phenylenebis[(1*S*,3*S*)-tetrahydro-5,8-dioxo-1*H*-[1,2,4]diazaphospholo[1,2-a]pyridazine-2,1,3(3*H*)-triyl])tetrakis(*N*-[(1*S*)-1-phenylethyl])benzamide (Sigma-Aldrich). The

ligand was prepared by the submitters according to their published procedure.[2] The submitters recrystallized dicarbonylacetylacetonato rhodium(I) from toluene and hexanes as fine green crystals. $CHCl_3$ may be used instead of $CDCl_3$.

8. Accurate volumes were measured and transferred using an Eppendoft® pipette.

9. Symyx HOSS equipment is described on the Symyx website. http://symyx.desantisbreindel.com/page.php?id=71

10. The submitter's equipment and experimental protocol are outlined in this Note and in Notes 11-14. A heavy wall reaction tube (Ace Glass #15 Ace-Tread®, 30 cm length x 38.1 mm O.D., 185 mL capacity) and a 0.5 x 0.125 inch magnetic stir bar are dried in a 125 °C oven overnight. In a glove box, the reaction tube is charged with stock solutions of $Rh(acac)(CO)_2$ and Bis[(*S*,*S*,*S*)-DiazaPhos-SPE] using a 1000 μL Eppendoft® pipette followed by 5 grams of substrate. The reaction tube is attached to the reactor head (Note 11). Notably, the addition of the alkene to the catalyst solution resulted in a yellow-white suspension due to partial precipitation of ligand and/or catalyst-ligand complex.

A blast shield must be used whenever the reactor is pressurized and safety procedures for using pressure tubes described in the Ace-Glass® catalog should be reviewed and followed.

The assembled reactor is removed from the glove box, placed in a fume hood, connected to the synthesis gas source and taken through 5 cycles of pressurization (150 psig of 1:1 H_2:CO)/depressurization (0 psig) to replace the nitrogen atmosphere with synthesis gas (Notes 12, 13, Figure 2). The reactor is then submerged in a heated silicon oil bath at the desired temperature. As synthesis gas is consumed, the reactor is repressurized to 150 psi to maintain approximately constant pressure (Note 14). After 2–3 hours (~30–40 psi of synthesis gas consumed) the suspension transforms to a homogeneous yellow solution. In six hours, ~90 psi of synthesis gas is consumed. At the end of the reaction time, the reactor is depressurized.

11. A custom-made reactor head used for hydroformylations is shown in Figure 1. The following parts were used to assemble the reactor head: **a**, Alltech® septum (High-temp, 3/8 in., AT79231) for aliquot-abstractions using a gas-tight syringe, **b**, Swagelok® Brass 1-Piece 40 Series Ball Valve (1.6 Cv, 1/4 in. MNPT x 1/4 in. Swagelok Tube Fitting; product #: B-43M4-

S4), **c**, Swagelok® Brass Pipe Fitting, Cross (1/4 in. Female NPT; product #: B-4-CS), **d**, Brass Pipe Fitting, Hex Nipple (1/4 in. Male NPT), **e**, Swagelok® Brass Pipe Fitting, Elbow (1/4 in. Female NPT; product #: B-4-E), **f**, Ashcroft® 0–160 psig pressure gauge (1/4 in. NPT, 3.5 in. Dial; McMaster-Carr 3846K311 0-160 psig range), **g**, Brass Pipe Fitting, Close Nipple (1/4 in. Male NPT), **h**, #15 Ace-Thred® (15 mm thread, 1/4 in. NPT PTFE Swagelok adapter; Prod. #: 5844-74), **i**, Kalrez® 6375 O-ring (9.30 mm x 2.40 mm Part #: K31016K6375), **j**, #15 Ace Glass® pressure tube (30.5 cm L, 38.1 mm OD, Prod. #: 8648-33), **k**, Swagelok® Brass 1-Piece 40 Series 3-Way Ball Valve (0.75 Cv, 1/4 in. FNPT; product #: B-43XF4), **l**, Brass Pipe Fitting (1/4 in. male NPT to 1/4 in. male Swagelok Tube Fitting), **m**, SS tubing (1/4 in OD, 2 1/2 in. length), and **n**, Swagelok® SS Instrumentation Quick-Connect Stem w/ Valve, (0.2 Cv, 1/4 in. Swagelok Tube Fitting, Part #: SS-QC4-D-400). Threads **b**, **d**, **f**, **g**, and **l** were wrapped with PTFE tape prior to assembly. A thorough pressure check of reactor should be taken before conducting an experiment. The most common source of a leak is between the brass pipe fitting **g** and the plastic #15 Ace-Thred adapter **h**. Once assembled with the 185-mL pressure tube, the reactor is rather cumbersome to transport—the use of an 11.5" (W) x 13.5" (L) x 5.25" (D) Rubbermaid® dishpan with a 3"(D) x 1" (W) rectangle cut in the tub on the width side was used to partially hold the reactor.

12. A reverse-threaded regulator is connected to a synthesis gas cylinder and Swagelok® Quick-Connects are used to attach to the reactor manifold. The synthesis gas cylinder was obtained from AirGas Inc. as a custom mixture (48.3±2% carbon monoxide balanced with hydrogen gas).

13. The reactor has two possible points of entry: Swagelok® Ball valve **b** fitted with a GC septum, for gas-tight syringe aliquots, and the Swagelok® 3-way Ball Valve **k**, for pressurizing and depressurizing the reactor. In Figure 2, **k** is opened carefully to the synthesis gas cylinder, charging the apparatus to 150 psig (it is advisable to set the regulator on the cylinder to ca. 150 psig and to have a safety shield in place). The valve on **k** is then opened to vent, releasing synthesis gas from the apparatus. After the pressure is reduced to <40 psi, the valve is turned back to the original closed position constituting one cycle. This procedure is repeated for five cycles and the reactor pressure is set at 150 psi. The glass tube of the reactor is lowered into the oil bath for hydroformylation as seen in the far-right picture.

14. Synthesis gas is added manually to maintain at least 100 psig reactor pressure. It is not advisable to maintain reactor pressure by keeping the reactor open to the regulator on the synthesis gas cylinder because, in the event of a leak on the reactor or supply lines, large amounts of H_2 and CO could be released. A carbon monoxide detector is installed near the gas cylinder. Commonly, the synthesis gas line is detached from the reactor at the Swagelok® Quick-Connect during reaction and reconnected when adding more gas. However, if the synthesis gas line is not needed for other reactions, the Swagelok® Quick-Connect system can remain assembled throughout the reaction.

15. ^{1}H NMR of the crude product mixture indicated >99% conversion of alkene and a branched: linear (**2**:**3**) ratio of 2:1.

16. Aldehyde **2** is air-sensitive and flash chromatography should be performed immediately after depressurizing the reactor and the purified product stored in a freezer.

17. Silica gel (250 g) was slurry-packed in a 5-cm diameter column using 5% EtOAc/hexanes. The product was eluted with 5% EtOAc/hexanes, collecting 50 mL fractions, monitored by TLC. (10% EtOAc/hexanes, R_f **1** = 0.7, (*R*)-**2** = 0.38, **3** = 0.31, visualized with potassium permanganate stain, prepared as follows: 3 g $KMnO_4$, 20 g potassium carbonate, 5 mL of a 5% (w/w) solution of aqueous sodium hydroxide, and 300 mL of deionized water.) Fractions 9-26 were combined and concentrated by rotary evaporation (40 °C, 20 mmHg) to afford **2** (3.24–3.43 g) as a colorless oil. Fractions 29-38 were combined and concentrated by rotary evaporation (40 °C, 20 mmHg) to afford **3** (1.62–1.70 g) as a colorless oil.

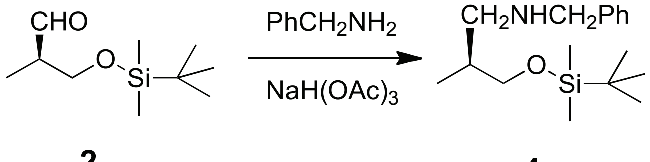
18. *(2R)-3-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-2-methylpropanal* **2** has the following physical and spectroscopic data: $[\alpha]_D^{25}$ –34 (c 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.06 (s, $-Si(CH_3)_2C(CH_3)_3$, 6 H), 0.89 (s, $-Si(CH_3)_2C(CH_3)_3$, 9 H), 1.10 (d, *J* = 6.9 Hz, $-CHCH_3$, 3 H), 2.52–2.56 (m, $-CHCH_3$, 1 H), 3.82 (dd, *J* = 6.4, 10.2 Hz, $-CH_2OSi$, 1 H), 3.86 (dd, *J* = 5.2 Hz, 10.2, $-CH_2OSi$, 1 H), 9.74 (d, *J* = 1.6 Hz, CHO-CH, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: –5.33, –5.31, 10.5, 18.4, 26.0, 49.0, 63.7, 204.9; IR (neat): 2957, 2931, 2859, 1736 (C=O), 1473, 1258, 1101, 1033, 838, 778 cm^{-1}; GC-MS *m/z* (relative intensity): 145 (100) [M – *t*-Bu], 115 (95) [$SiMe_2$*t*-Bu], 101 (31), 85 (25) [Si*t*-Bu], 75 (54), 59 (25); GC purity: 98% (t_R = 7.4 min, same conditions as in note 6); ee 94–96% determined by SFC analysis of benzylamine reductive amination derivative as described in Note 20. The aldehyde oxidizes at a rate of about 1% per week when stored in a -

20 °C freezer.

19. The (*S*)-enantiomer of **2** was prepared by the same procedure using Bis[(*R*,*R*,*S*)-DiazaPhos-SPE] as ligand; $[\alpha]_D^{25}$ +33 (c 1.0, CH_2Cl_2); ee 88%.

20. The submitters determined chiral purity by gas chromatographic analysis on a Varian Chrompack system using a β-DEX 225 capillary column from Supelco, 30 m x 0.25 mm ID x 0.25 um film thickness. The analytical method used to resolve the enantiomers as follow: 65 °C hold for 70 min, t_R(*R*)-**2**: 60.8 min, t_R(*S*)-**2**: 62.4 min. The checkers determined chiral purity by formation of the reductive amination product with benzylamine and analysis by supercritical fluid chromatography (SFC): tandem columns: 25 cm OZ : 25cm OZ, isocratic 8% 25mM *i*-butylamine in 2-propanol, 100 bar, 2.0 mL/min for 18 min. t_R (*R*)-**4** = 11.5 min, t_R (*S*)-**4** = 14 min.

Procedure for the preparation of the reductive amination product with benzylamine follows.



2 **4**

To a 20-mL vial equipped a 0.7 cm stir bar is added sequentially sodium triacetoxyborohydride (235 mg, 1.1 mmol), chloroform (2 mL), aldehyde **2** (73 mg, 0.36 mmol), and benzylamine (37 mg, 0.34 mmol). The heterogeneous mixture is stirred 16 h at ambient temperature, then quenched with 5 mL sat. $NaHCO_3$, stirring the biphasic mixture for 5 min. Dichloromethane (10 mL) is added, the layers are separated, and the organic layer dried by filtering through 2 g of sodium sulfate. The filtrate is concentrated by rotary evaporation (40 °C, 20 mmHg) to afford crude **4** (115 mg). The product is purified by silica gel chromatography using 10 g silica with an eluent of 97:2:0.5 CH_2Cl_2:MeOH:Et_3N, collecting 10 mL fractions. Fractions 7-10 were combined and concentrated by rotary evaporation to provide product **4** (68 mg, 67% yield) as a colorless oil having the following physical and spectroscopic data: TLC: R_f = 0.1 (97:2:0.5 CH_2Cl_2:MeOH:Et_3N); ^1H NMR (500 MHz, $CDCl_3$) δ: 0.04 (s, 6 H), 0.89 (s, 9 H), 0.91 (d, *J* = 6.7 Hz, 3 H), 1.68 (br s, 1 H), 1.85–1.91 (m, 1 H), 2.51 (dd, *J* = 6.0, 11.6 Hz, 1 H), 2.68 (dd, *J* = 6.8, 11.6 Hz, 1 H), 3.50–3.57 (m, 2 H), 3.77–3.82 (m, 2 H), 7.25–7.26 (m, 1 H), 7.31–7.33 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: –5.24, –5.21, 15.6, 18.5, 26.1, 36.1, 53.6, 54.5, 127.0, 128.3, 128.5, 140.9.

21. Linear product **3** has the following spectroscopic data: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.04 (s, $-Si(CH_3)_2C(CH_3)_3$, 6 H), 0.88 (s, $-Si(CH_3)_2C(CH_3)_3$, 9 H), 1.86 (tt, *J* = 6.0, 7.1 Hz $-CH_2CH_2CH_2-$, 2 H), 2.50 (dt, *J* = 7.1, 1.8 Hz, CH_2CHO, 2 H), 3.65 (t, *J* = 6.0 Hz, $-CH_2OSi$, 3 H), 9.79 (t, *J* = 1.7 Hz, CHO, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: –5.2, 18.5, 25.7, 26.1, 41.0, 62.3, 202.9; GC purity: 96% (t_R = 7.9 min, same conditions as in Note 6)

Safety and Waste Disposal Information

All hazardous materials should be handled and disposed of in accordance with "Prudent Practices in the Laboratory"; National Academies Press; Washington, DC, 2011.

3. Discussion

Protected "Roche Aldehydes" (e.g., **2**, (2R)-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methylpropanal**)** are common starting materials for the synthesis of polyketides and related molecules.[3,4] Compared with the common reduction-to-alcohol-followed-by-selective-oxidation-to-aldehyde route to **2** from "Roche Ester",[4] hydroformylation of the protected commodity monomer, allyl alcohol, provides Roche Aldehyde derivatives rapidly, at low cost, and in an easily scalable process. For comparison purposes we have collected the following approximate costs of substrates, normalized to 25 g units, from a common supplier: Roche ester ($350/25g), allyl alcohol ($1.00/25g). The only byproducts of the enantioselective hydroformylation of **1** is the corresponding linear aldehyde; although achiral the linear aldehyde is isolated cleanly and constitutes a useful synthetic material also. On larger scales, it should be possible to separate the linear and branched aldehydes by careful vacuum distillation; we have not yet optimized the distillation conditions. An advantage of hydroformylation routes to chiral aldehydes is the absence of acids or bases in the reaction solution that catalyze racemization and condensation reactions. We note that although the Roche *Ester* has been synthesized by asymmetric hydrogenation of the methyl 2-(hydroxymethyl)-prop-2-enoate,[5] there is no report of a catalytic hydrogenation route to enantiopure Roche *Aldehyde*.

Figure 1. The submitters assembled reactor with parts indicated

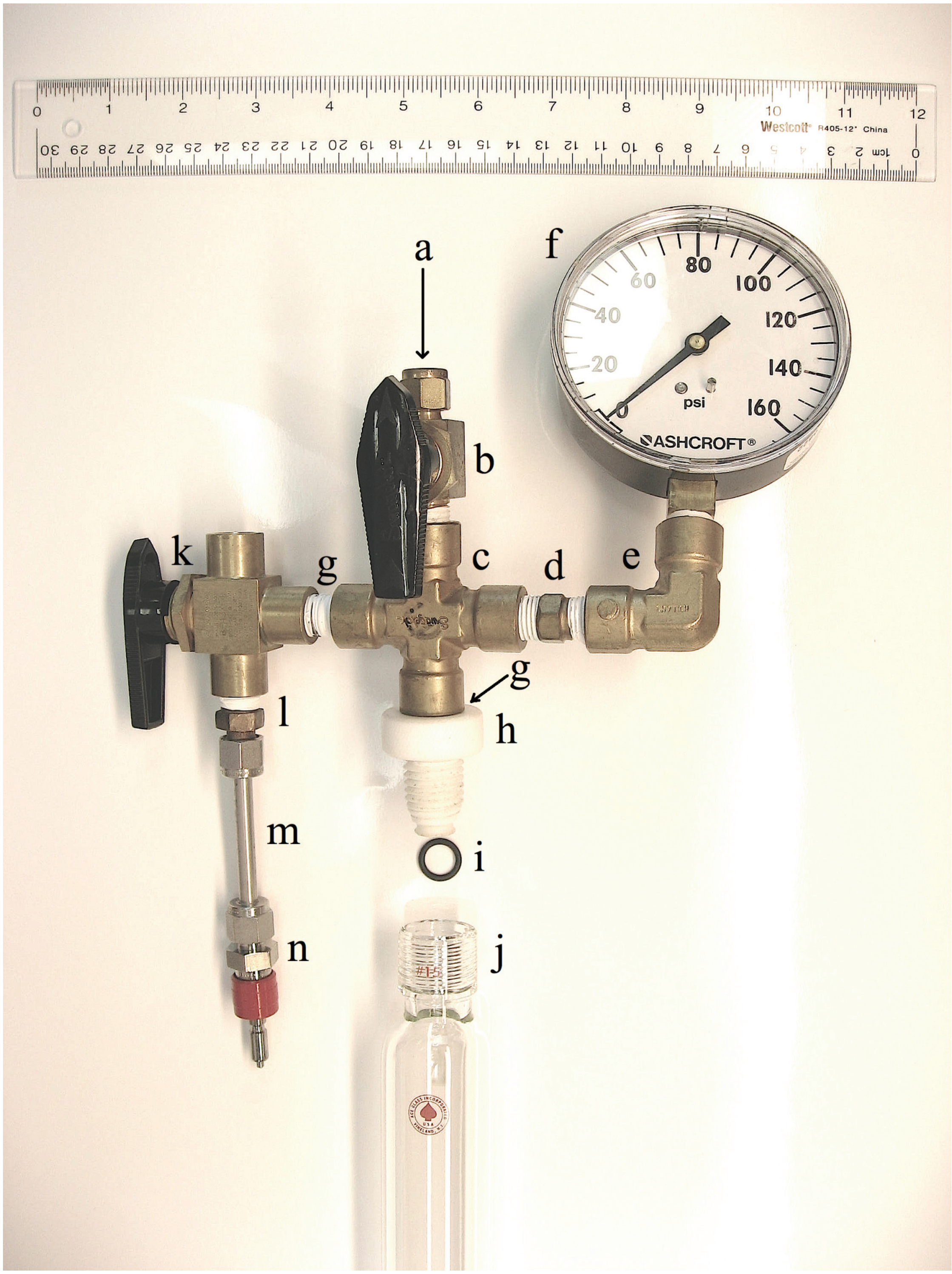


Figure 2. The submitters' reactor in-use

1. Department of Chemistry, University of Wisconsin, Madison, Wisconsin, 53706-1322. Email: Landis@chem.wisc.edu. We thank The Dow Chemical Company for their donation of Rh(acac)$(CO)_2$. Funding was provided by the National Science Foundation (CHE-0715491 and a graduate fellowship for G.W.W.).
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4. Roche Aldehyde for use in natural product syntheses see: (a) Früstner, A.; Nevado, C.; Waser, M.; Tremblay, M.; Chevrier, C.; Teplý, F.; Aïssa, C.; Moulin, E.; Müller, O. *J. Am. Chem. Soc.* **2007**, *129*, 9150–9161; (b) Canova, S.; Bellosta, V.; Bigot, A.; Mailliet, P.; Mignani, S.; Cossy, J. *Org. Lett.* **2007**, *9*, 145–148; (c) Ferrié, L.; Reymond, S.; Capdevielle, P.; Cossy, J. *Org. Lett.* **2006**, *8*, 3441–3443; (d) Ehrlich, G.; Kalesse, M. *Synlett* **2005**, 4, 655–657; (e) Smith, A. B., III, Brandt, B. M. *Org. Lett.* **2001**, *3*, 1685–1688.
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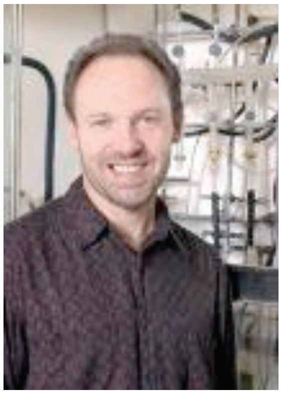
Appendix
Chemical Abstracts Nomenclature; (Registry Number)

Silane, (1,1-dimethylethyl)dimethyl(2-propen-1-yloxy)-; (85807-85-8)
Silane, chloro(1,1-dimethylethyl)dimethyl-; (18162-48-6)
Prop-2-en-1-ol; (107-18-6)
Rhodium, dicarbonyl(2,4-pentanedionato-κ-O2,κ-O4)-, (SP-4-2)-; (14874-82-9)
Benzamide, 2,2',2'',2'''-[1,2-phenylenebis[(1*S*,3*S*)-tetrahydro-5,8-dioxo-1H-[1,2,4]diazaphospholo[1,2-a]pyridazine-2,1,3(3*H*)-triyl]]tetrakis[*N*-[(1*S*)-1-phenylethyl]-; (851770-14-4)
Propanal, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-methyl-, (2*R*)-; (97826-89-6),
Butanal, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-; (87184-81-4)



Clark R. Landis was born in Aurora, IL in 1956. After completing his Ph.D. at the University of Chicago in 1983 under the direction of Jack Halpern, Professor Landis held professional positions at the Monsanto Company Corporate Research Lab, the University of Colorado-Boulder, and, since 1990, the University of Wisconsin-Madison. His research interests include bonding theory, computational methods, instrumentation development, chiral ligand synthesis, enantioselective catalysis, catalytic alkene polymerization, and the mechanisms of catalytic reactions.

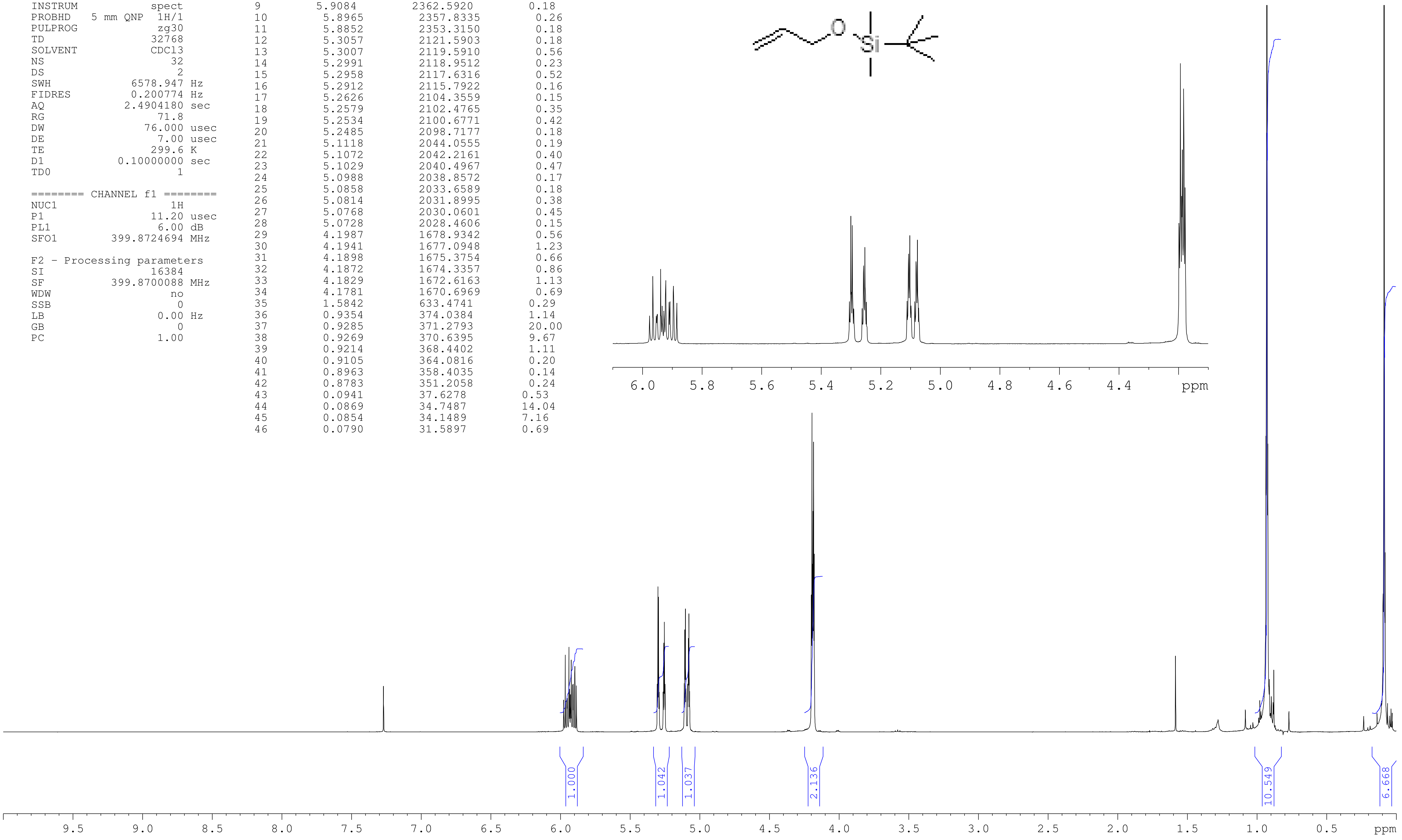
Gene W. Wong was born in Reno, Nevada in 1985. He received his undergraduate chemistry degree from University of Nevada-Reno, where he conducted research with Prof. Brian J. Frost. He then moved to University of Wisconsin-Madison, where he is currently pursuing a Ph.D. in the research group of Prof. Clark R. Landis as a NSF Predoctoral Fellow. His research focuses on the development of bisdiazaphospholane libraries and rhodium catalyzed hydroformylation.

Tyler T. Adint was born in Fairbanks, Alaska in 1984. He received his undergraduate degree in 2003 from Lewis & Clark College, where he conducted research with Prof. Louis Y. Kuo. He is now pursuing his Ph.D. at the University of Wisconsin-Madison in the research group of Prof. Clark R. Landis. His current research interests concern the synthesis of bisdiazaphospholane ligands that utilize secondary interactions to control selectivity in rhodium catalyzed hydroformylations.

32077-152
fr 5-7
nmr400b h-1

```
Current Data Parameters
NAME             32077-152
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameters
Date_             20110409
Time                 13.49
INSTRUM              spect
PROBHD   5 mm QNP   1H/1
PULPROG               zg30
TD                   32768
SOLVENT              CDCl3
NS                      32
DS                       2
SWH              6578.947 Hz
FIDRES           0.200774 Hz
AQ              2.4904180 sec
RG                    71.8
DW                  76.000 usec
DE                    7.00 usec
TE                   299.6 K
D1             0.10000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   11.20 usec
PL1                   6.00 dB
SFO1           399.8724694 MHz

F2 - Processing parameters
SI                   16384
SF             399.8700088 MHz
WDW                     no
SSB                      0
LB                    0.00 Hz
GB                       0
PC                    1.00
```

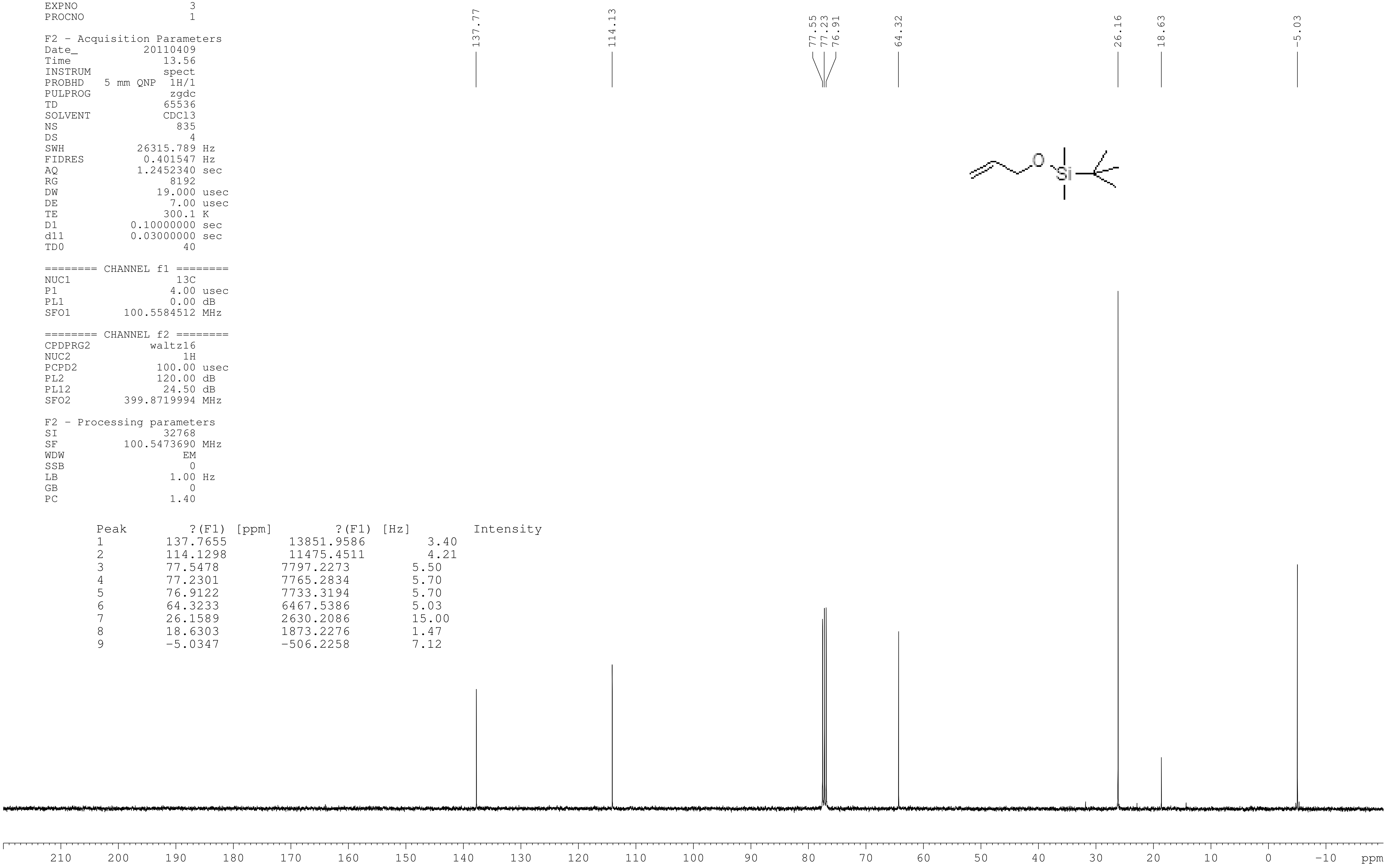
Peak	?(F1) [ppm]	?(F1) [Hz]	Intensity
1	7.2708	2907.3749	0.18
2	5.9655	2385.4245	0.29
3	5.9509	2379.5864	0.13
4	5.9394	2374.9879	0.33
5	5.9343	2372.9486	0.16
6	5.9282	2370.5094	0.14
7	5.9225	2368.2301	0.28
8	5.9113	2363.7516	0.18
9	5.9084	2362.5920	0.18
10	5.8965	2357.8335	0.26
11	5.8852	2353.3150	0.18
12	5.3057	2121.5903	0.18
13	5.3007	2119.5910	0.56
14	5.2991	2118.9512	0.23
15	5.2958	2117.6316	0.52
16	5.2912	2115.7922	0.16
17	5.2626	2104.3559	0.15
18	5.2579	2102.4765	0.35
19	5.2534	2100.6771	0.42
20	5.2485	2098.7177	0.18
21	5.1118	2044.0555	0.19
22	5.1072	2042.2161	0.40
23	5.1029	2040.4967	0.47
24	5.0988	2038.8572	0.17
25	5.0858	2033.6589	0.18
26	5.0814	2031.8995	0.38
27	5.0768	2030.0601	0.45
28	5.0728	2028.4606	0.15
29	4.1987	1678.9342	0.56
30	4.1941	1677.0948	1.23
31	4.1898	1675.3754	0.66
32	4.1872	1674.3357	0.86
33	4.1829	1672.6163	1.13
34	4.1781	1670.6969	0.69
35	1.5842	633.4741	0.29
36	0.9354	374.0384	1.14
37	0.9285	371.2793	20.00
38	0.9269	370.6395	9.67
39	0.9214	368.4402	1.11
40	0.9105	364.0816	0.20
41	0.8963	358.4035	0.14
42	0.8783	351.2058	0.24
43	0.0941	37.6278	0.53
44	0.0869	34.7487	14.04
45	0.0854	34.1489	7.16
46	0.0790	31.5897	0.69



32077-152
allylOTBS
fr 5-7
nmr400b c-13

```
Current Data Parameters
NAME          32077-152
EXPNO                 3
PROCNO                1

F2 - Acquisition Parameters
Date_          20110409
Time              13.56
INSTRUM           spect
PROBHD   5 mm QNP  1H/1
PULPROG            zgdc
TD                65536
SOLVENT           CDCl3
NS                  835
DS                    4
SWH           26315.789 Hz
FIDRES         0.401547 Hz
AQ            1.2452340 sec
RG                 8192
DW               19.000 usec
DE                 7.00 usec
TE                300.1 K
D1           0.10000000 sec
d11          0.03000000 sec
TD0                  40

======== CHANNEL f1 ========
NUC1                13C
P1                 4.00 usec
PL1                0.00 dB
SFO1        100.5584512 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                 1H
PCPD2            100.00 usec
PL2              120.00 dB
PL12              24.50 dB
SFO2        399.8719994 MHz

F2 - Processing parameters
SI                32768
SF          100.5473690 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

Peak	?(F1) [ppm]	?(F1) [Hz]	Intensity
1	137.7655	13851.9586	3.40
2	114.1298	11475.4511	4.21
3	77.5478	7797.2273	5.50
4	77.2301	7765.2834	5.70
5	76.9122	7733.3194	5.70
6	64.3233	6467.5386	5.03
7	26.1589	2630.2086	15.00
8	18.6303	1873.2276	1.47
9	-5.0347	-506.2258	7.12



Current Data Parameters

NAME	32077-169
EXPNO	8
PROCNO	1

F2 - Acquisition Parameters

Date_	20110929
Time	16.54
INSTRUM	spect
PROBHD	5 mm QNP 1H/13
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	32
DS	4
SWH	13020.833 Hz
FIDRES	0.198682 Hz
AQ	2.5166323 sec
RG	228.1
DW	38.400 usec
DE	6.50 usec
TE	300.0 K
D1	0.10000000 sec
TD0	1

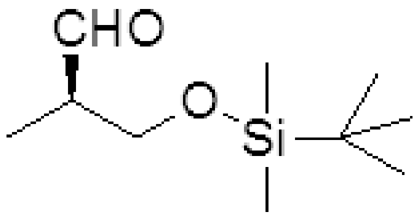
======== CHANNEL f1 ========

NUC1	1H
P1	12.00 usec
PL1	-4.00 dB
SFO1	500.1330885 MHz

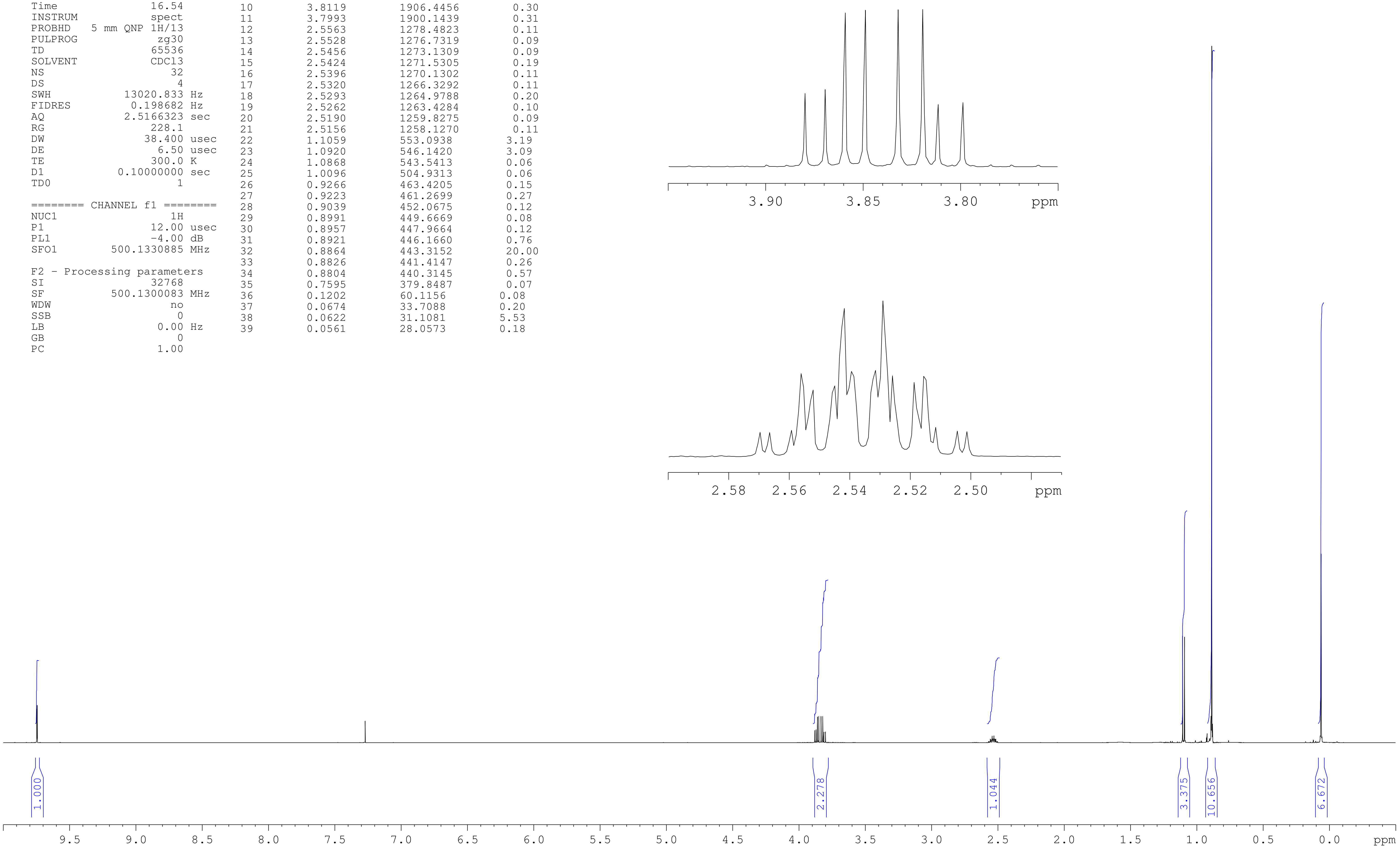
F2 - Processing parameters

SI	32768
SF	500.1300083 MHz
WDW	no
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

Peak	?(F1) [ppm]	?(F1) [Hz]	Intensity
1	9.7471	4874.8172	1.01
2	9.7439	4873.2168	1.10
3	7.2704	3636.1452	0.62
4	3.8802	1940.6045	0.35
5	3.8698	1935.4031	0.37
6	3.8597	1930.3518	0.76
7	3.8493	1925.1504	0.77
8	3.8324	1916.6982	0.75
9	3.8197	1910.3466	0.75
10	3.8119	1906.4456	0.30
11	3.7993	1900.1439	0.31
12	2.5563	1278.4823	0.11
13	2.5528	1276.7319	0.09
14	2.5456	1273.1309	0.09
15	2.5424	1271.5305	0.19
16	2.5396	1270.1302	0.11
17	2.5320	1266.3292	0.11
18	2.5293	1264.9788	0.20
19	2.5262	1263.4284	0.10
20	2.5190	1259.8275	0.09
21	2.5156	1258.1270	0.11
22	1.1059	553.0938	3.19
23	1.0920	546.1420	3.09
24	1.0868	543.5413	0.06
25	1.0096	504.9313	0.06
26	0.9266	463.4205	0.15
27	0.9223	461.2699	0.27
28	0.9039	452.0675	0.12
29	0.8991	449.6669	0.08
30	0.8957	447.9664	0.12
31	0.8921	446.1660	0.76
32	0.8864	443.3152	20.00
33	0.8826	441.4147	0.26
34	0.8804	440.3145	0.57
35	0.7595	379.8487	0.07
36	0.1202	60.1156	0.08
37	0.0674	33.7088	0.20
38	0.0622	31.1081	5.53
39	0.0561	28.0573	0.18

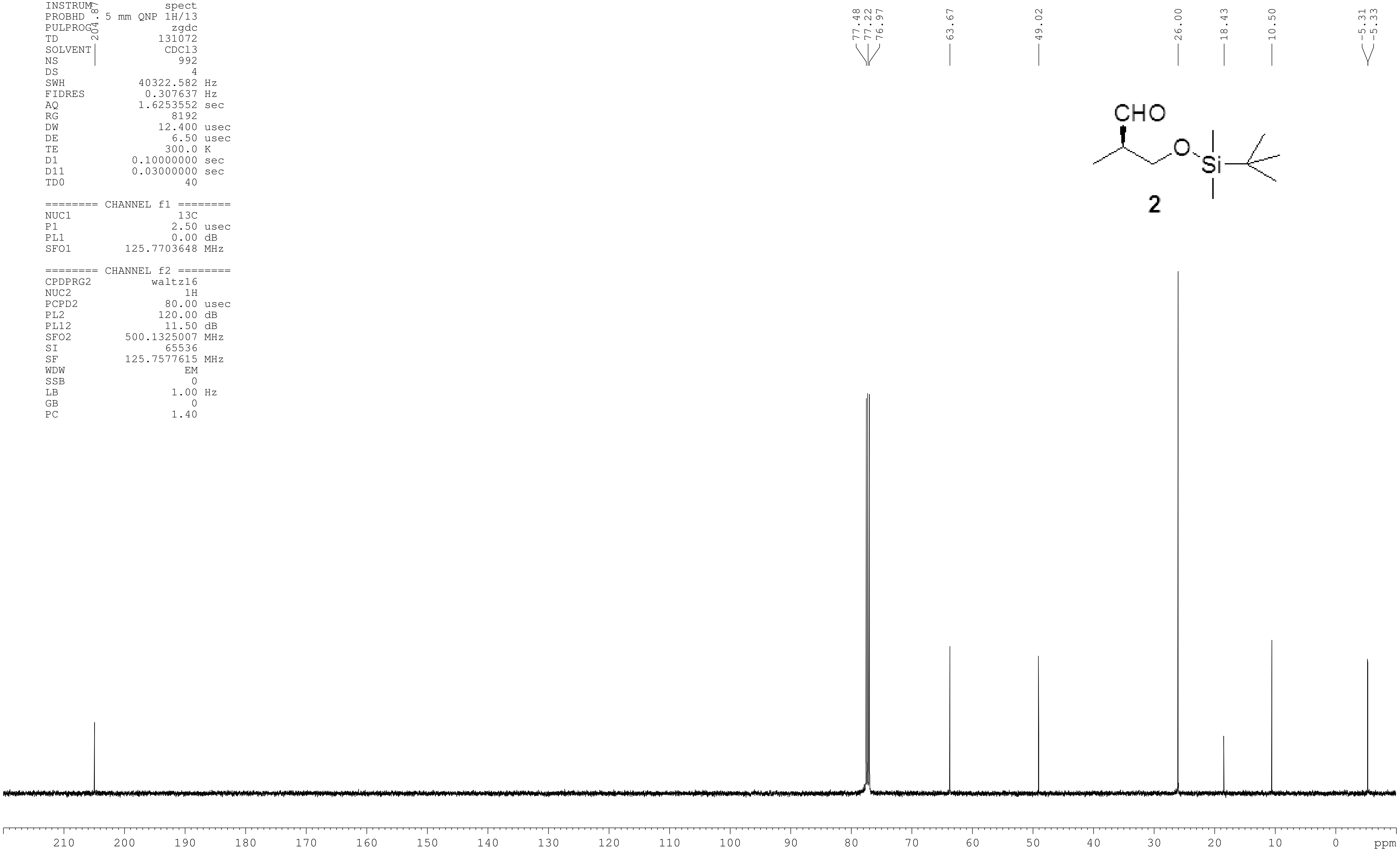


32077-169
branched
fr 16-26
nmr500c h-1



```
NAME          32077-169
EXPNO                 9
PROCNO                1
Date_          20110929
Time              17.08
INSTRUM           spect
PROBHD   5 mm QNP 1H/13
PULPROG            zgdc
TD               131072
SOLVENT           CDCl3
NS                  992
DS                    4
SWH           40322.582 Hz
FIDRES         0.307637 Hz
AQ            1.6253552 sec
RG                 8192
DW               12.400 usec
DE                 6.50 usec
TE                300.0 K
D1           0.10000000 sec
D11          0.03000000 sec
TD0                  40

======== CHANNEL f1 ========
NUC1                13C
P1                 2.50 usec
PL1                0.00 dB
SFO1        125.7703648 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                 1H
PCPD2             80.00 usec
PL2              120.00 dB
PL12              11.50 dB
SFO2        500.1325007 MHz
SI                65536
SF          125.7577615 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

32077-169
branched
fr 16-26
nmr500c c-13

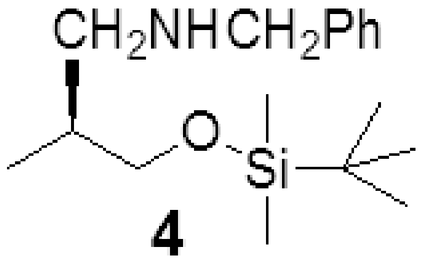


2

```
Current Data Parameters
NAME           32077-165
EXPNO                  7
PROCNO                 1

F2 - Acquisition Parameters
Date_           20110917
Time                8.13
INSTRUM            spect
PROBHD   5 mm QNP 1H/13
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    32
DS                     4
SWH            13020.833 Hz
FIDRES          0.198682 Hz
AQ             2.5166323 sec
RG                   114
DW                38.400 usec
DE                  6.50 usec
TE                 300.0 K
D1            0.10000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                -4.00 dB
SFO1         500.1330885 MHz

F2 - Processing parameters
SI                 32768
SF           500.1300082 MHz
WDW                   no
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.00
```

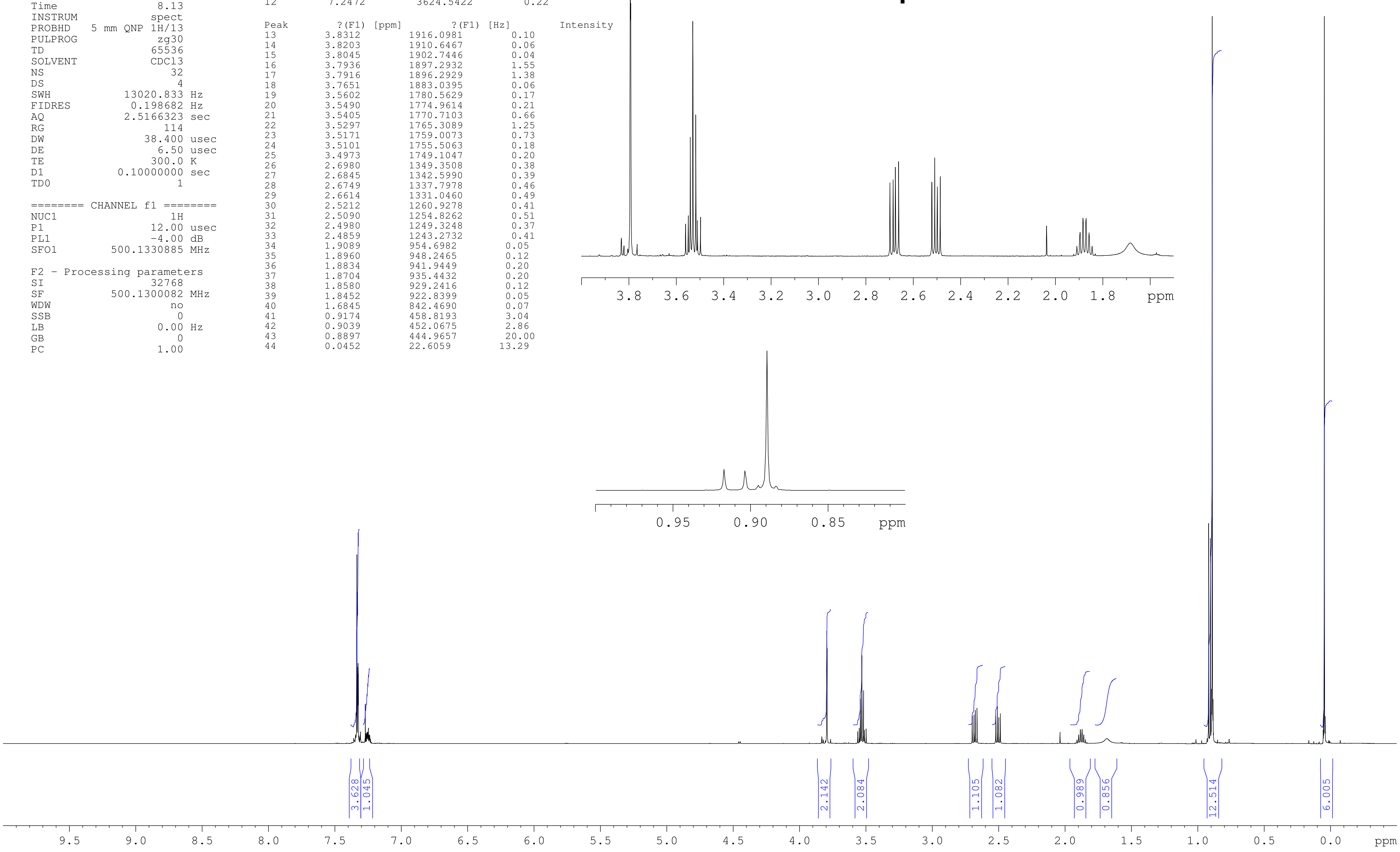
Peak	?(F1) [ppm]	?(F1) [Hz]	Intensity
1	7.3337	3667.8034	2.79
2	7.3270	3664.4526	1.06
3	7.3236	3662.7521	1.12
4	7.3225	3662.2020	1.03
5	7.3063	3654.0999	0.16
6	7.2705	3636.1952	0.54
7	7.2647	3633.2945	0.14
8	7.2590	3630.4437	0.15
9	7.2580	3629.9436	0.16
10	7.2543	3628.0931	0.16
11	7.2523	3627.0929	0.16
12	7.2472	3624.5422	0.22

Peak	?(F1) [ppm]	?(F1) [Hz]	Intensity
13	3.8312	1916.0981	0.10
14	3.8203	1910.6467	0.06
15	3.8045	1902.7446	0.04
16	3.7936	1897.2932	1.55
17	3.7916	1896.2929	1.38
18	3.7651	1883.0395	0.06
19	3.5602	1780.5629	0.17
20	3.5490	1774.9614	0.21
21	3.5405	1770.7103	0.66
22	3.5297	1765.3089	1.25
23	3.5171	1759.0073	0.73
24	3.5101	1755.5063	0.18
25	3.4973	1749.1047	0.20
26	2.6980	1349.3508	0.38
27	2.6845	1342.5990	0.39
28	2.6749	1337.7978	0.46
29	2.6614	1331.0460	0.49
30	2.5212	1260.9278	0.41
31	2.5090	1254.8262	0.51
32	2.4980	1249.3248	0.37
33	2.4859	1243.2732	0.41
34	1.9089	954.6982	0.05
35	1.8960	948.2465	0.12
36	1.8834	941.9449	0.20
37	1.8704	935.4432	0.20
38	1.8580	929.2416	0.12
39	1.8452	922.8399	0.05
40	1.6845	842.4690	0.07
41	0.9174	458.8193	3.04
42	0.9039	452.0675	2.86
43	0.8897	444.9657	20.00
44	0.0452	22.6059	13.29



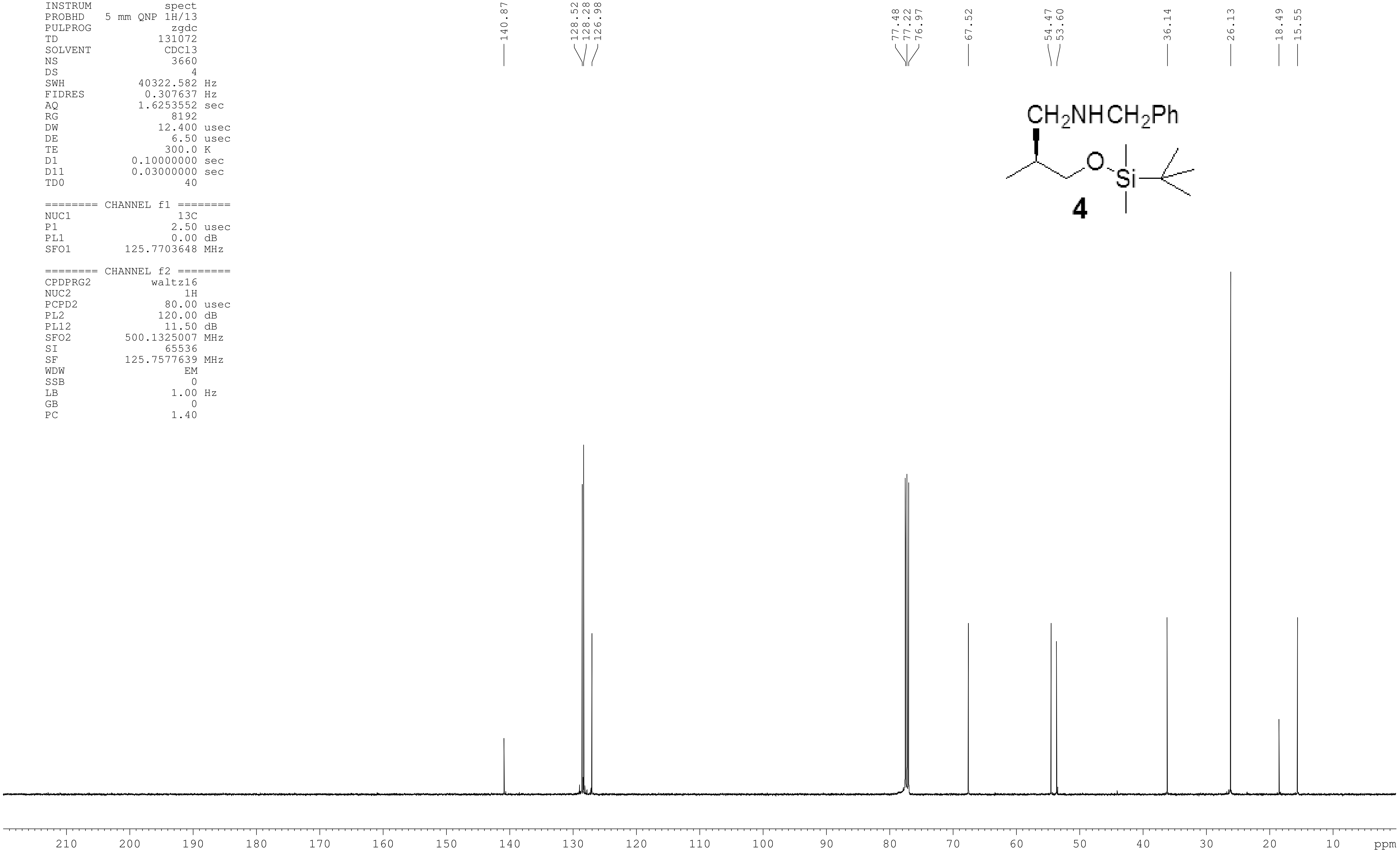
4

32077-165
(R) chromatograpy
fr 4-5
nmr500c h-1



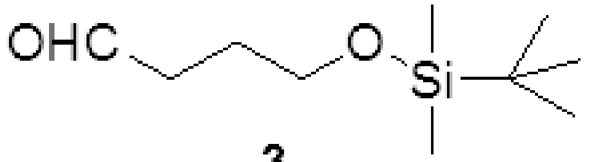
32077-165
(R) chromatography
fr 4-5
nmr500c c-13

```
NAME            32077-165
EXPNO                   8
PROCNO                  1
Date_            20110917
Time                 8.22
INSTRUM             spect
PROBHD   5 mm QNP 1H/13
PULPROG              zgdc
TD                 131072
SOLVENT             CDCl3
NS                   3660
DS                      4
SWH             40322.582 Hz
FIDRES           0.307637 Hz
AQ              1.6253552 sec
RG                   8192
DW                 12.400 usec
DE                   6.50 usec
TE                  300.0 K
D1             0.10000000 sec
D11            0.03000000 sec
TD0                    40

======== CHANNEL f1 ========
NUC1                  13C
P1                   2.50 usec
PL1                  0.00 dB
SFO1          125.7703648 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2               80.00 usec
PL2                120.00 dB
PL12                11.50 dB
SFO2          500.1325007 MHz
SI                  65536
SF            125.7577639 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```



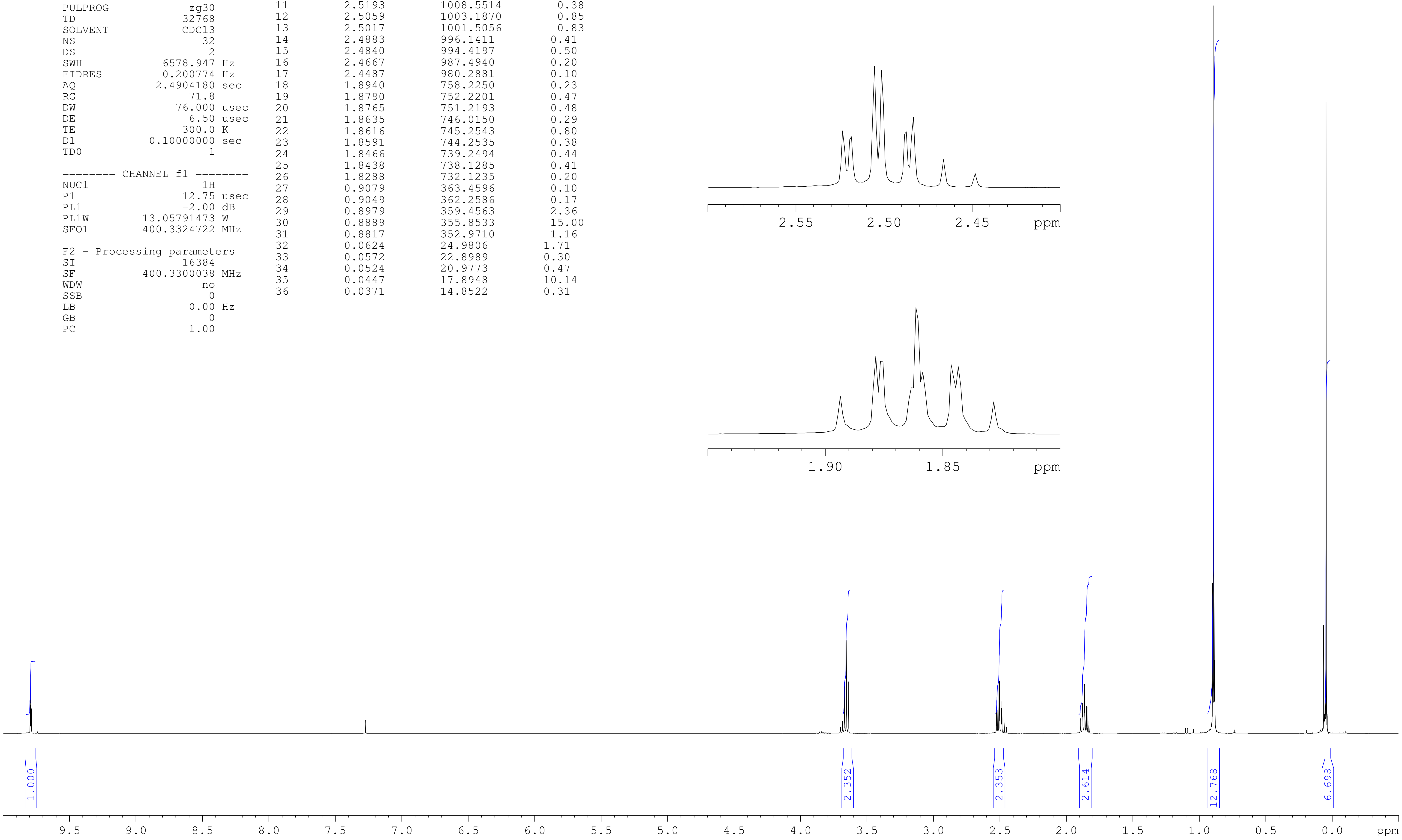
```
Current Data Parameters
NAME            32077-169
EXPNO                   5
PROCNO                  1

F2 - Acquisition Parameters
Date_            20110929
Time                12.41
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT             CDC13
NS                     32
DS                      2
SWH              6578.947 Hz
FIDRES           0.200774 Hz
AQ              2.4904180 sec
RG                   71.8
DW                 76.000 usec
DE                   6.50 usec
TE                  300.0 K
D1             0.10000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  12.75 usec
PL1                 -2.00 dB
PL1W          13.05791473 W
SFO1          400.3324722 MHz

F2 - Processing parameters
SI                  16384
SF            400.3300038 MHz
WDW                    no
SSB                     0
LB                   0.00 Hz
GB                      0
PC                   1.00
```

```
Peak        ?(F1) [ppm]       ?(F1) [Hz]          Intensity
1           9.7951        3921.2724        0.44
2           9.7909        3919.5910        0.92
3           9.7865        3917.8296        0.41
4           7.2706        2910.6393        0.21
5           3.6983        1480.5405        0.10
6           3.6834        1474.5755        0.19
7           3.6691        1468.8508        0.83
8           3.6542        1462.8859        1.46
9           3.6393        1456.9210        0.81
10           2.5238         1010.3529        0.40
11           2.5193         1008.5514        0.38
12           2.5059         1003.1870        0.85
13           2.5017         1001.5056        0.83
14           2.4883          996.1411        0.41
15           2.4840          994.4197        0.50
16           2.4667          987.4940        0.20
17           2.4487          980.2881        0.10
18           1.8940          758.2250        0.23
19           1.8790          752.2201        0.47
20           1.8765          751.2193        0.48
21           1.8635          746.0150        0.29
22           1.8616          745.2543        0.80
23           1.8591          744.2535        0.38
24           1.8466          739.2494        0.44
25           1.8438          738.1285        0.41
26           1.8288          732.1235        0.20
27           0.9079          363.4596        0.10
28           0.9049          362.2586        0.17
29           0.8979          359.4563        2.36
30           0.8889          355.8533       15.00
31           0.8817          352.9710        1.16
32           0.0624           24.9806       1.71
33           0.0572           22.8989       0.30
34           0.0524           20.9773       0.47
35           0.0447           17.8948      10.14
36           0.0371           14.8522       0.31
```



3

32077-169
linear
fr 29-38
nmr400b h-1



32077-169
linear
nmr400b c-13

```
NAME           32077-169
EXPNO                 14
PROCNO                 1
Date_           20111125
Time               10.56
INSTRUM            spect
PROBHD    5 mm PABBO BB-
PULPROG             zgdc
TD                 65536
SOLVENT            CDCl3
NS                  1308
DS                     4
SWH            26315.789 Hz
FIDRES          0.401547 Hz
AQ             1.2452340 sec
RG                  8192
DW                19.000 usec
DE                  6.50 usec
TE                 673.2 K
D1            0.10000000 sec
D11           0.03000000 sec
TD0                   40

======== CHANNEL f1 ========
NUC1                 13C
P1                  3.50 usec
PL1                 0.00 dB
PL1W         31.90095711 W
SFO1         100.6741319 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2               120.00 dB
PL12               17.00 dB
PL2W          0.00000000 W
PL12W         0.16438942 W
SFO2         400.3320017 MHz
SI                 32768
SF           100.6630386 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

```
Peak        ?(F1) [ppm]        ?(F1) [Hz]         Intensity [abs]         Annotation
1       202.8797          20422.4871         155434806.00
2       77.5507          7806.4891         303570106.00
3       77.2329          7774.4984         316153758.00
4       76.9151          7742.5077         247056616.00
5       62.2663          6267.9150         261929436.00
6       40.9890          4126.0773         274120410.00
7       26.0866          2625.9564         588206684.00
8       25.6786          2584.8859         265091424.00
9       18.4745          1859.6993         98066196.00
10       -5.2200          -525.4611         494051882.00
```