Divergent Synthesis and Chemical Reactivity of Bicyclic Lactone Fragments of Complex Rearranged Spongian Diterpenes

Martin J. Schnermann,[†] *Christopher M. Beaudry,*[†,§] *Nathan E. Genung,*[†] *Stephen M. Canham,*[†] *Nicholas L. Untiedt,*[†] *Breanne D. W. Karanikolas,*[‡] *Christine Sütterlin,*[‡] *Larry E. Overman*[†,*]

[†]Department of Chemistry, 1102 Natural Sciences II, University of California, Irvine, CA 92697-2025. [‡]Department of Developmental and Cell Biology, 2011 Biological Sciences III, University of California, Irvine, CA 92697-2300

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Chemical Materials and Methods.

Unless stated otherwise, reactions were conducted in oven- dried glassware under an atmosphere of nitrogen or argon using anhydrous solvents (either freshly distilled or passed through activated alumina columns). Titanium(IV) chloride and methylene bromide were purified by distillation. TMEDA, benzylamine, $BF_3{\cdot}OEt_2$ were purified by distillation over CaH_2. All other commercially obtained reagents were used as received. Reaction temperatures were controlled using an IKAmag temperature modulator. Thin-layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 pre-coated plates, (0.25 mm) and visualized by exposure to UV light (254 nm) or stained with anisaldehyde, ceric ammonium molybdate, potassium permanganate and iodine. Flash column chromatography was performed using normal phase silica gel (60 Å, 230-240 mesh, Merck KGA). ^{1}H NMR spectra were recorded on Bruker spectrometers (at 500 or 600 MHz) and are reported relative to deuterated solvent signals. Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz) and integration. ^{13}C NMR spectra were recorded on Bruker Spectrometers (at 125 or 150 MHz). Data for ^{13}C NMR spectra are reported in terms of chemical shift. IR spectra were recorded on a Varian 640-IR spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Optical rotations were measured with a Jasco P-1010 polarimeter. High resolution mass spectra were obtained from the UC Irvine Mass Spectrometry Facility with a Micromass LCT spectrometer. See *JOC Standard Abbreviations and Acronyms* for abbreviations (available at http://pubs.acs.org/userimages/ContentEditor/1218717864819/joceah_abbreviations.pdf).

General Information Regarding Chiral Starting Materials.

Silyl ketene acetal **28** was obtained from (5*S*,6*S*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-one.[1] (5*S*,6*S*)-5,6-Dimethoxy-5,6-dimethyl-1,4-dioxan-2-one was synthesized from (*S*)-3-chloropropane-1,2-diol via a four step procedure reported by Ley and coworkers.[2] The diol was obtained from hydrolytic kinetic resolution of epichlorohydrin.[3]

Enone **29** was obtained from Swern oxidation of (1*R*,4*S*)-4-hydroxycyclopent-2-en-1-yl acetate.[4] (1*R*,4*S*)-4-Hydroxycyclopent-2-en-1-yl acetate was obtained via two different routes, the

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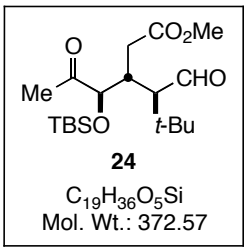
1. Ley, S.V.; Dixon, D.J.; Guy, R.T.; Rodríguez, F.; Sheppard, T. D. *Org. Biomol. Chem.* **2005**, *3*, 4095.
2. Ley, S. V.; Diez, E.; Dixon, D. J.; Guy, R. T.; Michel, P.; Nattrass, G. L.; Sheppard, T. D. *Org. Biomol. Chem.* **2004**, *2*, 3608.
3. Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307.
4. Hughes, C. C.; Miller, A. K.; Trauner, D. *Org. Lett.* **2005**, *7*, 3425.

latter of which we found to be operationally less complex. The first route involved a photochemical [3+2] cycloaddition of cyclopentadiene to give (1*R*,3*S*)-cyclopent-4-ene-1,3-diol.[5] (1*R*,3*S*)-Cyclopent-4-ene-1,3-diol was acylated to give (1*R*,3*S*)-cyclopent-4-ene-1,3-diyl diacetate which, after resolution with electric eel acetylcholine esterase, gave (1*R*,4*S*)-4-hydroxycyclopent-2-en-1-yl acetate.[6] The second route involved monoepoxidation of cyclopentadiene to give 6-oxabicyclo[3.1.0]hex-2-ene.[7] The epoxide was opened to racemic 4-hydroxycyclopent-2-en-1-yl acetate, which was further acylated to (1*R*,3*S*)-cyclopent-4-ene-1,3-diyl diacetate.[8] The (1*R*,3*S*)-cyclopent-4-ene-1,3-diyl diacetate was resolved enzymatically with Novozyme 435 to yield (1*R*,4*S*)-4-hydroxycyclopent-2-en-1-yl acetate.[5c,9]

Synthetic Experimental Procedures.

Synthesis of *t*-Bu-MacE (13). Experimental procedures and characterization data for the synthesis of **13**, **14**, **22**, **24**, **25**, **26**, **30**, **32**, **33**, **36**, **41**, **42**, **44** can be found in the *SI Appendix* of reference 10. Improved synthetic procedures follow for **24** and **22**.



24

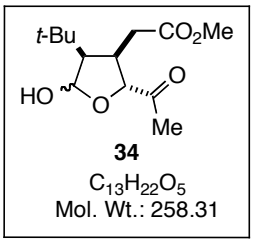
$C_{19}H_{36}O_5Si$

Mol. Wt.: 372.57

(3*R*,4*R*)-Methyl 3-((*R*)-1-(*tert*-butyldimethylsilyloxy)-2-oxopropyl)-4-formyl-5,5-dimethylhexanoate (24): To a stirred mixture of enoxy silane **25** (2.74 g, 6.23 mmol) in THF (53 mL) and H_2O (7.0 mL), 4-methylmorpholine *N*-oxide (2.66 g, 12.45 mmol) and OsO_4 (3.35 mL, 2.5 wt% in *t*BuOH, 0.31 mmol) were added. The mixture was stirred 7 h, then solid $NaHSO_3$ (2 g) was added and the resulting mixture was stirred for 1 h. The reaction mixture was diluted with H_2O (100 mL) and extracted with EtOAc (4 × 75 mL). Combined organic extracts were washed with brine (100 mL), dried over Na_2SO_4, filtered, and concentrated to afford crude α-hydroxyketone as a mixture of diastereomers, which were sufficiently pure for use in the next transformation. The crude α-hydroxyketone was dissolved in

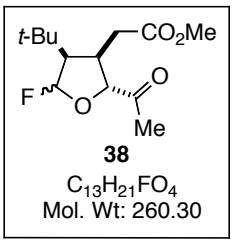
5. a) Kaneko, C.; Sugimoto, A.; Tanaka, S. *Synthesis* **1974**, 876. b) Inoue, Y.; Wada, K.; Liu, Y.; Ouchi, M.; Tai, A.; Hakushi, T. *J. Org. Chem.* **1989**, *54*, 5268. c) Tietz, L. F.; Stadler, C.; Böhnke, N.; Brasche, G.; Grube, A. *Synlett* **2007**, 485.
6. Basra, S. K.; Drew, M. G. B.; Mann, J.; Kane, P. D. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3592.
7. a) Korach, M.; Nielsen, D. R.; Rideout, W. H. *Org. Synth.* **1962**, *42*, 50. b) Crandall, J. K.; Banks, D. B.; Coyler, R. A.; Watkins, R. J.; Arrington, J. P. *J. Org. Chem.* **1968**, *33*, 423.
8. Deardorff, D. R.; Myles, D. C.; MacFerrin, K. D. *Tetrahedron Lett.* **1985**, 26, 5615.
9. Theil, F.; Schick, H.; Winter, G.; Reck, G. *Tetrahedron* **1991**, *47*, 7569. b) Khan, P. M.; Wu, R.; Bisht, K. S. *Tetrahedron* **2007**, *63*, 1116.
10. Schnermann, M. J.; Beaudry, C.; Egovora, A. V.; Polishchuk, R. S.; Sütterlin, C.; Overman. L. E. *Proc. Nat. Acad. Sci. USA* **2010**, *107,* 6158.

MeOH (30 mL) and C_6H_6 (30 mL), cooled to 0 °C, and $Pb(OAc)_4$ (3.59 g, 8.09 mmol) was added in one portion. After 15 min saturated aqueous $NaHCO_3$ (4.0 mL) was added and the mixture was diluted with EtOAc (200 mL) resulting in a orange precipitate. The resulting suspension was passed though a pad of Na_2SO_4/SiO_2 eluting with EtOAc and concentrated to give tricarbonyl **24** (2.20 g, 95%) as a clear oil that matched the previously reported analytical data.[10]



34
$C_{13}H_{22}O_5$
Mol. Wt.: 258.31

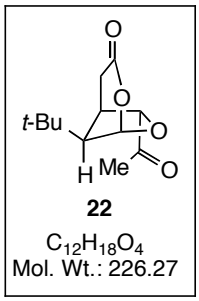
Methyl 2-((2*R*,3*R*,4*R*)-4-*tert*-butyl-2-ethanoyl-5-hydroxytetrahydrofuran-3-yl)ethanoate (34): To a solution of **24** (120 mg, 0.27 mmol) in THF (2.5 mL) at 0 ºC was added TBAF (410 mL, 1M in THF, 0.41 mmol). The solution was stirred for 10 min. Silica gel was added until the mixture became viscous, and was stirred magnetically for an additional 5 min. The mixture loaded onto a silica gel column. Purification by silica gel chromatography (30% hexanes: EtOAc) gave **34** (34 mg, 48%) as a 10:1 mixture of anomeric alcohols as a clear oil: R_f 0.32 (2:1 hexane:EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz, peaks for major isomer) δ 5.31 (s, 1H), 4.43 (s, 1H), 3.90 (br s, 1H), 3.71 (s, 3H), 2.83 (m, 1H), 2.75 (dd, *J* = 16.8, 3.8 Hz, 1H), 2.49 (dd, *J* = 12.2, 16.7 Hz, 1H), 2.31 (s, 3H), 1.75 (app t, *J* = 6.3 Hz, 1H), 1.00 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz, peaks for major isomer) δ 210.7, 173.2, 101.3, 88.0, 58.3, 52.1, 42.0, 33.9, 30.3, 29.5, 26.1; IR (thin film) 1733, 1717 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ calculated for $C_{13}H_{22}O_5Na$ 281.1365, observed: 281.1356; $[\alpha]_D^{25}$ –9.0°; $[\alpha]_{577}^{25}$ –10.3°; $[\alpha]_{546}^{25}$ –14.8°; $[\alpha]_{435}^{25}$ –58.8°; $[\alpha]_{405}^{25}$ –95.2°, (*c* = 1.0, $CHCl_3$).



38
$C_{13}H_{21}FO_4$
Mol. Wt: 260.30

Methyl 2-((2*R*,3*R*,4*R*)-4-*tert*-butyl-2-ethanoyl-5-fluorotetrahydrofuran-3-yl)ethanoate (38): A solution of **34** (19 mg, 0.070 mmol) in CH_2Cl_2 (0.7 mL) was cooled to –78 °C and DAST (17 μL, 0.11 mmol) was added. After 5 min, saturated sodium bicarbonate (1 mL) and CH_2Cl_2 (1 mL) were added to the solution and the mixture was allowed to warm to r.t.. The layers were separated and the aqueous layer was washed with additional CH_2Cl_2 (2 × 1 mL) The organic phases were combined, dried over Na_2SO_4, filtered, and concentrated to yield as **38** (18 mg, 95%) as a clean ~2:1 mixture of anomeric fluorides by NMR. Characteristic data for **38**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.90 (dd, *J* = 68.2, 3.0 Hz, 1H, major), 5.87 (d, *J* = 66.0 Hz, 1H, minor), 4.65 (s, 1H, major), 4.17 (t, *J* = 6.8 Hz, 1H, minor), 3.71 (s, 3H, minor), 3.66 (s, 3H, minor), 3.10 (m, 1H), 2.90 (d, *J* = 13.2 Hz, 1H, minor), 2.78 (m, 2H, major + m, 1H, minor), 2.63 (dd, *J* = 17.1, 7.9 Hz, 1H, minor), 2.29 (s, 3H), 2.25 (s, 3H), 2.20 (m, 1H), 1.81 (ddd, *J* = 35.2,

6.7, 3.0 Hz), 1.07 (s, 9H, major), 0.95 (s, 9H, minor); HRMS–ESI (*m/z*): $[M+Na]^+$ calculated for $C_{13}H_{21}FO_4Na$ 283.1322, observed 283.1320.



22

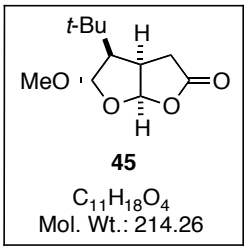
$C_{12}H_{18}O_4$
Mol. Wt.: 226.27

(1*S*,5*R*,6*R*,8*R*)-8-*tert*-butyl-6-ethanoyl-2,7-dioxabicyclo[3.2.1]octan-3-one (22)

From 34: To a solution of ester **34** (179 mg, 0.694 mmol) in MeOH (6.9 mL) at 0 °C was added 1N NaOH (1.40 mL, 1.39 mmol). The mixture was warmed to rt and stirred for 3.5 h. The reaction mixture was poured into brine (10 mL) and acidified to pH 2 with a 1M HCl solution. The aqueous layer was extracted with $CHCl_3$ until TLC indicated complete extraction of the product (15 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to give crude acid **35** as a clear oil sufficiently pure for the subsequent transformation. Crude acid **35** from above was dissolved in $CHCl_3$ (8.7 mL) and treated with CSA (48 mg, 0.21 mmol). The solution was stirred for 12 h at rt. The mixture was diluted with CH_2Cl_2 (10 mL) and poured into a saturated aqueous solution of $NaHCO_3$ (15 mL). The layers were separated and the organic phase was washed with additional $NaHCO_3$ (15 mL). The combined aqueous layers were extracted with CH_2Cl_2 (3 x 20 mL). The organic phases were combined, dried over Na_2SO_4, filtered, and concentrated. Purification by silica gel chromatography (30–50% EtOAc/hexanes) gave **22** (85 mg, 54%, 2 steps) as a clear oil that matched previously reported analytical data.[10]

From 36: To a solution of ester **36** (105 mg, 0.330 mmol) in MeOH (1.39 mL) at rt was added 1N NaOH (1.40 mL, 1.39 mmol) and the mixture was stirred for 36 h. The resulting mixture was cooled to 0 °C and 1 N HCl (5 mL) was added and the mixture was stirred for 30 min. CH_2Cl_2 (5 mL) was added and the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (10 × 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to give the crude acid **37** as a clear oil that was sufficiently pure for use in the subsequent transformation. The crude acid was dissolved in dry benzene (5 mL) and concentrated for azeotropic drying. This procedure was repeated 3 times. The crude acid **37** was dissolved in CH_2Cl_2 (2.6 mL), cooled to 0 °C, and boron-trifluoride etherate ($BF_3{\cdot}OEt_2$) (34 μL, 0.33 mmol) was added. After 1 h, saturated aqueous $NaHCO_3$ (4 mL) was added and the layers were separated and the aqueous phase was washed with additional CH_2Cl_2 (2 × 5 mL). The organic phases were combined, dried over Na_2SO_4, filtered, and concentrated. Purification of the residue by silica gel chromatography (30–50% EtOAc/hexanes) gave **22** (49 mg, 66% from **36**) as a clear oil that matched previously reported analytical data.[10]

From 38: To a solution of ester **38** (9.0 mg, 0.035 mmol) in MeOH (0.35 mL) at rt was added 1N NaOH (53 μL, 0.53 mmol) and the mixture was stirred for 2 h. To the resulting mixture, saturated aqueous ammonium chloride (4 mL) and CH_2Cl_2 (5 mL) was added and the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (10 × 10 mL).The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to give the crude acid **39** as a clear oil that was sufficiently pure for use in the subsequent transformation. The crude acid was dissolved in dry benzene (5 mL) and concentrated for azeotropic drying. This procedure was repeated 3 times. The crude acid was dissolved in dry DMF (1.7 mL) and $SnCl_2$ (13 mg, 0.070 mmol) was added and the mixture was stirred. After 18 h, saturated aqueous sodium bicarbonate (4 mL) and CH_2Cl_2 (5 mL) was added and the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel chromatography (30–50% EtOAc/hexanes) gave **22** (5.8 mg, 71% from **38**) as a clear oil that matched previously reported analytical data.[10]

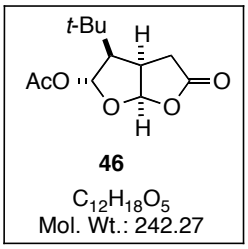


45

$C_{11}H_{18}O_4$
Mol. Wt.: 214.26

(3a*R*,4*R*,5*S*,6a*R*)-4-*tert*-butyl-5-methoxytetrahydrofuro[2,3-*b*]furan-2(6a*H*)- one (45): To a solution of ester **α-36** (160 mg, 0.50 mmol) in MeOH (2.0 mL) at rt was added 1N aqueous NaOH (2.1 mL) and the mixture was stirred for 36 h. The resulting mixture was cooled to 0 °C and 1 N HCl (3 mL) was added and the mixture was stirred for 30 min. The resulting solution was diluted with H_2O (3 mL) and extracted with CH_2Cl_2 (10 × 5 mL). Combined organic extracts were dried over Na_2SO_4, filtered, and concentrated to afford crude acid (125 mg) **α-37** as a clear oil. A solution of acid **α-37** in CH_2Cl_2 (10 mL) at 0 °C was treated with urea·H_2O_2 complex (0.686 g, 7.26 mmol) and TFAA (0.510 mL, 3.63 mmol). The mixture was stirred for 30 min and then warmed to rt and stirred for 1 h. The mixture was cooled to 0 °C and saturated aqueous $NaHCO_3$ (10 mL) was added slowly. The biphasic mixture was separated and the aqueous layer was extracted with CH_2Cl_2 (5 × 5 mL). Combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. Purification of the residue by silica gel chromatography (50% Et_2O/hexanes) gave **45** (101 mg, 82%) as a white solid: R_f 0.30 (50% Et_2O/hexanes); m.p. 104–106 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.01 (d, *J* = 4.7 Hz, 1H), 5.10 (d, *J* = 7.3 Hz, 1H), 3.49 (s, 3H), 3.05 (m, 1H), 2.70 (dd, *J* = 17.8, 9.7 Hz, 1H), 2.56 (dd, *J* = 17.8, 9.5 Hz, 1H), 2.12 (t, *J* = 7.0 Hz, 1H), 1.03 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$) δ 176.2, 106.9, 104.9, 55.6, 42.0, 31.2, 29.83, 29.81; IR (thin film) 2959, 1793, 1371, 1169, 1120, 1037, 1017 cm^{-1}; HRMS-ESI (*m/z*): $[M+Na]^+$ calculated for $C_{11}H_{18}O_4Na$ 237.1103; observed 237.1102; $[\alpha]_D^{25}$ +151.0°, $[\alpha]_{577}^{25}$ +159.7°, $[\alpha]_{546}^{25}$+180.1°, $[\alpha]_{435}^{25}$ +294.5°, $[\alpha]_{405}^{25}$ +331.7° (*c* = 1.00, CH_2Cl_2). See

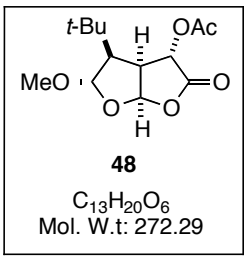
table S1 for full structural assignment.



46

$C_{12}H_{18}O_5$
Mol. Wt.: 242.27

3-*tert*-butyl-5-oxohexahydrofuro[2,3-*b*]furan-2-yl ethanoate (46). **From 45:** To a solution of **45** (5.0 mg, 0.023 mmol) in THF (0.5 mL), 1 N HCl (0.5 mL), was added. The mixture was stirred at rt for 24 h then diluted with H_2O (1 mL) and washed with CH_2Cl_2 (10 × 1 mL). Combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. The residue was dissolved in CH_2Cl_2 (0.5 mL) and treated with Ac_2O (13 μL, 0.136 mmol), pyridine (15 μL, 0.184 mmol), and DMAP (0.5 mg, 0.004 mmol). After 18 h at rt MeOH (300 μL) was added, stirred for 30 min, and concentrated. The residue was dissolved in heptane (1 mL) and concentrated; which was repeated with heptane (2 × 1 mL). Purification of the residue by silica gel chromatography (30% EtOAc/hexanes) gave **46** (3.5 mg, 61%) as a white solid: m.p. 140-142 °C; R_f 0.19 (30% ethyl acetate/ hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.38 (d, J = 7.3 Hz, 1H), 6.05 (d, J = 4.4, 1H), 3.10 (m, 1H), 2.71 (dd, J = 17.5, 10.0 Hz, 1H), 2.57 (dd, J = 17.5, 9.2 Hz, 1H), 2.41 (apt t, J = 6.8 Hz, 1H), 2.11 (s, 3H), 1.04 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.6, 170.0, 105.2, 97.0, 55.1, 42.1, 31.5, 29.6, 29.4, 21.4; IR (film) 2917, 1795, 1017 cm^{-1}; HRMS–ESI (m/z): $[M+Na]^+$ calculated for $C_{12}H_{18}O_5Na$ 265.1052, observed 265.1053; $[\alpha]_D^{18}$ +79.8°; $[\alpha]_{577}^{18}$ +75.1°; $[\alpha]_{546}^{18}$ +86.6°; $[\alpha]_{435}^{18}$ +143.6°; $[\alpha]_{405}^{18}$ +160.0° (c = 0.20, CH_2Cl_2). X-ray quality crystals were obtained via vapour diffusion by dissolving **46** in CH_2Cl_2 and exposing to hexanes vapour. See table S2 for full structural assignment.

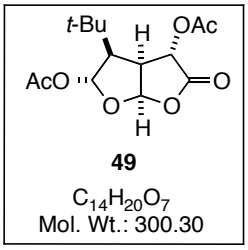


48

$C_{13}H_{20}O_6$
Mol. W.t: 272.29

(3*S*,3a*S*,4*R*,5*S*,6a*R*)-4-*tert*-butyl-5-methoxy-2-oxohexahydrofuro[2,3-*b*]furan-3-yl ethanoate (48). A solution of **45** (0.050 g, 0.234 mmol) in THF (2 mL) was cooled to 0 °C and a solution of 1 M NaHMDS in THF (490 μL, 0.490 mmol) was added. After 1 h, the solution was cooled to -78 °C and a solution of (+/-)-*trans*-2-(phenylsulfonyl)-3-phenyloxaziridine (0.098 g, 0.370 mmol) in THF (0.5 mL) was added dropwise. After 2 h, saturated aqueous $NaHCO_3$ (5 mL) and CH_2Cl_2 (5 mL) were added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (5 × 5 mL). Combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. Purification of the residue by silica gel chromatography (25% EtOAc/hexanes) afforded **47** (0.012 g, 22%) as a colorless resin. Characteristic data for **47**:^{1}H NMR (500 MHz, $CDCl_3$) δ 5.97 (d, J = 4.6 Hz, 1H), 5.08 (d, J = 7.1

Hz, 1H), 4.52 (d, J = 8.8 Hz, 1H), 3.49 (s, 3H), 2.97 (dt, J = 8.6, 5.5 Hz, 1H), 2.93 (s, 1H), 2.19 (t, J = 6.7 Hz, 1H), 1.11 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$) δ 178.0, 107.5, 102.6, 67.6, 57.1, 55.7, 50.0, 31.6, 29.2. To a solution of α-hydroxy lactone **47** (7.0 mg, 0.030 mmol) in CH_2Cl_2 (150 μL) was added Ac_2O (17 μL, 0.18 mmol), pyridine (19 μL, 0.24 mmol), and DMAP (0.5 mg, 0.004 mmol). After 18 h at rt, MeOH (100 μL) was added, stirred for 30 min, and concentrated. The residue was dissolved in heptane (1 mL) and concentrated; which was repeated with heptane (2 × 1 mL) and benzene (2 × 1 mL). Purification of the residue by silica gel chromatography (50% Et_2O/hexanes) afforded **48** (6.0 mg, 76%; 17% over two steps) as a white solid: R_f 0.38 (50% Et_2O/hexanes); m.p. 101–103 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.02 (d, J = 4.8 Hz, 1H), 5.50 (d, J = 8.8 Hz, 1H), 5.11 (d, J = 7.2 Hz, 1H), 3.49 (s, 3H), 3.26–3.22 (m, 1H), 2.20–2.16 (m, 4H), 1.03 (s, 9H); ^{13}C NMR δ (125 MHz; $CDCl_3$) δ 172.3, 169.5, 107.0, 102.3, 68.5, 57.2, 55.6, 46.7, 31.2, 29.3, 20.8; IR (thin film) 2961, 1805, 1756, 1372, 1223, 1180, 1121, 1070, 1039, 1026, 982, 948 cm^{-1}; HRMS-ESI (m/z): $[M+Na]^+$ calculated for $C_{13}H_{20}O_6Na$ 295.1158; observed 295.1148; $[\alpha]_D^{23}$ +26.6°; $[\alpha]_{577}^{23}$ +27.8°; $[\alpha]_{546}^{23}$ +31.2°; $[\alpha]_{435}^{23}$ +48.3°; $[\alpha]_{405}^{23}$ +53.1° (c = 0.57, CH_2Cl_2). See table S1 for full structural assignment.



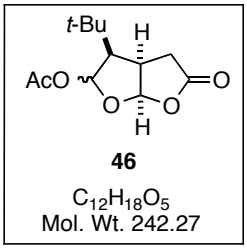
49
$C_{14}H_{20}O_7$
Mol. Wt.: 300.30

(2*R*,3*R*,3a*S*,4*S*,6a*R*)-3-*tert*-butyl-5-oxohexahydrofuro[2,3-*b*]furan-2,4-diyl diethanoate (49).

Directly From 13. To a solution of **13** (7.0 mg, 0.023 mmol) in THF (0.5 mL) was added 1 N HCl (0.5 mL), and the mixture was stirred at rt for 24 h. The mixture was extracted with CH_2Cl_2 (10 × 1 mL). Combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. The residue was dissolved in CH_2Cl_2 (0.5 mL) and treated with Ac_2O (13 μL, 0.13 mmol), pyridine (14 μL, 0.18 mmol), and DMAP (0.5 mg, 0.004 mmol). After 18 h at rt, MeOH (200 μL) was added, stirred for 30 min, and concentrated. The residue was dissolved in 1:1 THF:H_2O (0.9 mL) and treated with 2-methyl-2-butene (0.11 mL), t-BuOH (0.11 mL), NaH_2PO_4 (31 mg, 0.26 mmol), and $NaClO_2$ (11 mg, 0.12 mmol). The mixture was stirred for 16 h at rt, then diluted with saturated aqueous NH_4Cl (1.0 mL) and extracted with EtOAc (3 × 1 mL). The combined organic extracts were washed with brine (1.0 mL), dried over Na_2SO_4, filtered, and concentrated. Purification of the residue by silica gel chromatography (50% hexanes/EtOAc) gave **49** (2.5 mg, 36%) as a clear resin: R_f 0.40 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.39 (d, J = 7.1 Hz, 1H), 6.07 (d, J = 4.5 Hz, 1H), 5.47 (d, J = 8.8 Hz, 1H), 3.35–3.33 (m, 1H), 2.46 (t, J = 6.8 Hz, 1H), 2.20 (s, 3H), 2.11 (s, 3H), 1.04 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$) δ 171.7, 169.8,

169.4, 102.6, 96.9, 68.2, 54.9, 46.5, 31.4, 29.0, 21.3, 20.7; IR (thin film) 2964, 1808, 1753, 1370, 1175, 1063, 1021, 971 cm^{-1}; HRMS-ESI (*m/z*): $[M+Na]^+$ calculated for $C_{14}H_{20}O_7Na$ 323.1107, observed 323.1112; $[\alpha]_D^{23}$ −12.1°; $[\alpha]_{577}^{23}$ −12.7°, $[\alpha]_{546}^{23}$ −13.8°, $[\alpha]_{435}^{23}$ −36.9°, $[\alpha]_{405}^{23}$ −52.2° (*c* = 0.5, CH_2Cl_2). See table S3 for full structural assignment.

From 48. To a solution of **48** (3.0 mg, 0.011 mmol) in THF (0.5 mL) was added 1 N HCl (0.5 mL), and the mixture was stirred at rt for 24 h. The mixture was extracted with CH_2Cl_2 (10 × 1 mL). Combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. The residue was dissolved in CH_2Cl_2 (0.25 mL) and treated with Ac_2O (2.0 μL, 0.028 mmol), pyridine (25 μL), and DMAP (0.5 mg, 0.004 mmol). After 18 h at rt, MeOH (100 μL) was added, stirred for 30 min, and concentrated. The residue was dissolved in 1:1 THF:H_2O (0.5 mL) and treated with 2-methyl-2-butene (0.25 mL), *t*-BuOH (0.10 mL), NaH_2PO_4 (17 mg, 0.11 mmol), and $NaClO_2$ (6 mg, 0.55 mmol). The mixture was stirred for 16 h at rt, then diluted with saturated aqueous NH_4Cl (1.0 mL) and extracted with EtOAc (3 × 1 mL). The combined organic extracts were washed with brine (1.0 mL), dried over Na_2SO_4, filtered, and concentrated. Purification of the residue by silica gel chromatography (50% hexanes/EtOAc) gave **49** (1.0 mg, 24%) as a clear resin.



46
$C_{12}H_{18}O_5$
Mol. Wt. 242.27

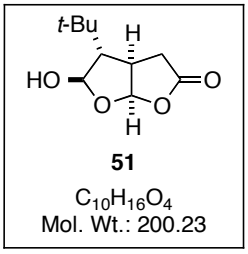
Directly From 14: A solution of **14** (4.0 mg, 0.016 mmol) and AcOH (1.9 μL, 0.033 mmol) in CH_2Cl_2 (200 μL) at 0 °C was treated with a 10% $BF_3{\cdot}OEt_2$ solution in CH_2Cl_2 (70 μL, 0.033 mmol). After 1h, saturated aqueous $NaHCO_3$ (3 mL), CH_2Cl_2 (3 mL) was added to the solution and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 3 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. Purification by silica gel chromatography (25% ethyl acetate/ hexanes) afforded **α-46** (0.8 mg, 20%) as a clear oil with analytical data identical to the material provided by the procedure described above and **β-46** (3.0 mg, 75%) as a clear oil. Data for **β-46**:[11] R_f 0.17 (30% EtOAc/ hexanes); ^1H NMR (C_6D_6, 500 MHz) δ 6.33 (d, *J* = 4.1 Hz, 1H), 5.44 (d, *J* = 5.5 Hz, 1H), 2.80 (dd, *J* = 17.1, 6.4 Hz, 1H), 1.87 (m, 2H), 1.41 (s, 3H), 1.21 (m, 1H), 0.60 (s, 9H); ^{13}C NMR (C_6D_6, 125 MHz) δ 175.1, 168.6, 107.3, 97.0, 54.0, 38.1, 31.1, 30.3, 29.5, 20.7. IR (thin film) 2956, 1788, 1753, 1225, 1066, 921 cm^{-1}; HRMS-ESI (*m/z*): $[M+Na]^+$ calculated for $C_{12}H_{18}O_5Na$

11. The chromatographic separation of **β-46** from **α-46** was challenging and a trace amount of **α-46** (~5%) remained in the final sample of **β-46.**

265.1058, observed 265.1052; $[\alpha]_D^{23}$ –80.4°, $[\alpha]_{577}^{23}$ –79.5°, $[\alpha]_{546}^{23}$ –90.3°, $[\alpha]_{435}^{23}$ –145.4°, $[\alpha]_{405}^{23}$ –165.1° (c = 0.2, CH_2Cl_2). See table S4 for full structural assignment.

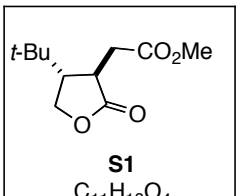
From 14 through lactol 50:

To a solution of **14** (30.0 mg, 0.124 mmol) in THF (4.0 mL), 1 N HCl (2.0 mL), was added. The mixture was stirred at 40 °C for 24 h then diluted with H_2O (2 mL) and washed with CH_2Cl_2 (10 × 2 mL). Combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. The residue was dissolved in CH_2Cl_2 (1.2 mL) and treated with Ac_2O (13 μL, 0.14 mmol), pyridine (11 μL, 0.14 mmol), and DMAP (0.5 mg, 0.004 mmol). After 18 h at rt MeOH (300 μL) was added, stirred for 30 min, and concentrated. The residue was dissolved in heptane (1 mL) and concentrated; which was repeated with heptane (2 × 1 mL) and benzene (2 × 1 mL). Purification of the residue by silica gel chromatography (30% hexanes/EtOAc) gave **46** (20 mg, 67%) as a white solid with analytical data identical to the material provided by the procedure described above.



51
$C_{10}H_{16}O_4$
Mol. Wt.: 200.23

(3a*R*,4*S*,5*R*,6a*R*)-4-*tert*-butyl-5-hydroxytetrahydrofuro[2,3-*b*]furan-2(6a*H*)- one (51). To a solution of **14** (7.0 mg, 0.029 mmol) in THF (0.60 mL), 1N aqueous NaOH (0.30 mL) was added. The mixture was stirred for 30 min at rt, then diluted with H_2O (1 mL) and washed with CH_2Cl_2 (2 × 2 mL). The aqueous layer was acidified to pH 1 with 1N aqueous HCl and extracted with CH_2Cl_2 (5 × 2 mL). Combined organic extracts were dried over Na_2SO_4, filtered, and concentrated to afford **51** as a white solid (6.0 mg, 99%): m.p. 108–109 °C; R_f 0.40 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.07 (d, J = 6.0 Hz, 1H), 5.58 (s, 1H), 2.97 (m, 1H), 2.91 (dd, J = 18.2, 11.0 Hz, 1H), 2.70 (dd, J = 18.2, 3.6 Hz, 1H), 1.98 (d, J = 1.7 Hz, 1H), 0.95 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$) δ 175.6, 109.3, 102.7, 64.5, 39.6, 36.7, 31.4, 27.4; IR (thin film) 3445, 2961, 1791, 1164, 1372, 1073, 1030, 972, 920, 895 cm^{-1}; HRMS-ESI (m/z): $[M+Na]^+$ calculated for $C_{10}H_{16}O_4Na$ 223.0946; observed 223.0946; $[\alpha]_D^{25}$ –24.5°; $[\alpha]_{577}^{25}$ –28.2°, $[\alpha]_{546}^{25}$ –34.2°, $[\alpha]_{435}^{25}$ –64.2°, $[\alpha]_{405}^{25}$ –77.3° (c = 0.43, CH_2Cl_2). See table S5 for full structural assignment.



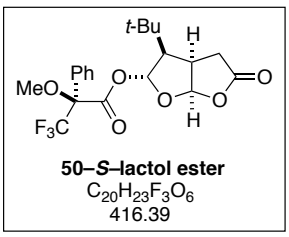
S1
$C_{11}H_{18}O_4$
Mol. Wt.: 214.26

Methyl 2-((3*R*,4*S*)-4-*tert*-butyl-2-oxotetrahydrofuran-3-yl)ethanoate (S1). To a solution of **14** (10.0 mg, 0.047 mmol) in THF (1.0 mL), 1N aqueous NaOH (1.0 mL) was added. The mixture was stirred for 72 h at rt, acidified to pH 1 with 1N aqueous HCl and extracted with CH_2Cl_2 (5 × 2

mL). Combined organic extracts were dried over Na_2SO_4, filtered, and concentrated to afford carboxylic acid **ii** as a clear oil (5.0 mg, 54%). Characteristic data for crude acid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.38 (t, *J* = 9.1 Hz, 1H), 4.11 (dd, *J* = 9.4, 7.1 Hz, 1H), 2.98 (dd, *J* = 16.9, 4.4 Hz, 1H), 2.75 (m, 2H), 2.29 (q, *J* = 8.3, 1H), 0.95 (s, 9H). The crude acid was dissolved in MeOH (1.0 mL) at room temperature and treated with a 1.0 M solution of $TMSCHN_2$ in hexanes (0.20 mL, 0.20 mmol) and stirred for 30 min. A 30% solution of AcOH in MeOH was added drop wise until effervescence ceased (~ 1 mL). Saturated aqueous $NaHCO_3$ (2 mL) and CH_2Cl_2 (2 mL) were added to the solution and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 1 mL) and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. Purification by silica gel chromatography (25% ethyl acetate/ hexanes) afforded **S1** (4.5 mg, 45% for two steps) as a clear oil:[12] R_f 0.19 (20% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.38 (t, *J* = 9.1 Hz, 1H), 4.11 (dd, *J* = 9.4, 7.1 Hz, 1H), 3.73 (s, 3H), 2.90 (dd, *J* = 18.3, 6.5 Hz, 1H), 2.75–2.71 (m, 2H), 2.25 (dt, *J* = 8.6, 7.4 Hz, 1H), 0.94 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$) δ 179.1, 171.8, 68.5, 52.3, 49.9, 38.1, 35.7, 32.3, 27.1; IR (thin film) 2957, 2875, 1772, 1737, 1370, 1177 cm^{-1}; HRMS-ESI (*m/z*): $[M+Na]^+$ calculated for $C_{11}H_{19}O_4$ 215.1283; observed 215.1280; $[\alpha]_D^{25}$ +8.6°; $[\alpha]_{577}^{25}$ +10.0°, $[\alpha]_{546}^{25}$ +14.2°, $[\alpha]_{435}^{25}$ +28.6°, $[\alpha]_{405}^{25}$ +38.5° (*c* = 0.2, CH_2Cl_2).

General procedure for preparation of MTPA-lactol esters.[13]

To a stirred solution of lactol **50** or **51** (1.0 equiv.), pyridine (3.1 equiv.), and DMAP (1.0 equiv.) in CH_2Cl_2 (0.1 M) at room temperature, *R*–(–)– or *S*–(+)–MTPA–Cl (2.0 equiv.) was added and stirred at room temperature for 18 h. MeOH (0.10 mL) was added, stirred for 30 min, and the mixture was concentrated. The residue was dissolved in heptane (1 mL) and concentrated; which was repeated with heptane (2 × 1 mL) and benzene (2 × 1 mL). Purification of the residue by silica gel chromatography (25% EtOAc/hexanes) gave the desired MTPA–lactol ester for ^{1}H NMR analysis.

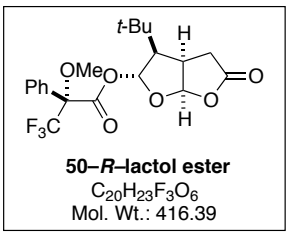


Data for *S*- and *R*-MTPA lactol-esters from lactol 50.

From **50** and *R*–(–)– MTPA–Cl. Data for **50–*S*–lactol ester**: ^{1}H NMR (600 MHz, $CDCl_3$) 7.55-7.53 (m, 2H), 7.44-7.42 (m, 3H), 6.51 (d, *J* = 6.3 Hz, 1H), 5.94 (d, *J* = 4.2 Hz, 1H), 3.55 (s, 3H), 3.11-3.06 (m, 1H), 2.73 (dd, *J* = 17.5, 10.2 Hz, 1H), 2.57 (dd, *J* = 17.5, 9.0 Hz, 1H), 2.51

12. A small amount of an inseparable impurity was obtained along with S1.
13. Hoye, T. R.; Jeffrey, C. S.; Shao, F.; *Nature Protocols* **2007**, *2*, 2451

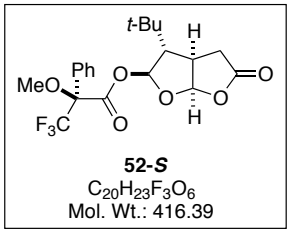
(t, *J* = 6.6 Hz, 1H), 1.04 (s, 9H).



50–*R*–lactol ester
$C_{20}H_{23}F_3O_6$
Mol. Wt.: 416.39

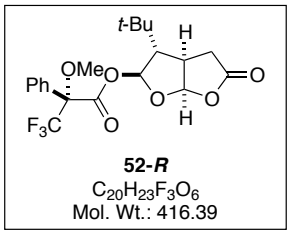
From **50** and *S*–(+)–MTPA–Cl. Data for **50–*R*–lactol ester**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55-7.53 (m, 2H), 7.42 (dd, *J* = 5.2, 1.9 Hz, 3H), 6.54 (d, *J* = 6.6 Hz, 1H), 6.07 (d, *J* = 4.2 Hz, 1H), 3.59 (s, 3H), 3.13-3.07 (m, 1H), 2.73 (dd, *J* = 17.6, 10.1 Hz, 1H), 2.58 (dd, *J* = 17.6, 9.1 Hz, 1H), 2.43 (t, *J* = 6.7 Hz, 1H), 0.92 (s, 9H).

Data for *S*- and *R*-MTPA lactol-esters 52*S* and 52*R* from lactol 51.



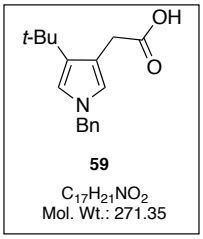
52-*S*
$C_{20}H_{23}F_3O_6$
Mol. Wt.: 416.39

From **51** and *R*–(–)– MTPA–Cl. Data for **52-*S***: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53-7.51 (m, 2H), 7.44-7.42 (m, 3H), 6.54 (d, *J* = 1.1 Hz, 1H), 6.10 (d, *J* = 6.0 Hz, 1H), 3.59 (s, 3H), 3.00-2.96 (m, 1H), 2.79 (dd, *J* = 18.5, 10.7 Hz, 1H), 2.29 (dd, *J* = 18.5, 3.9 Hz, 1H), 1.87 (d, *J* = 2.1 Hz, 1H), 0.94 (s, 9H).



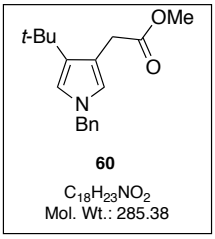
52-*R*
$C_{20}H_{23}F_3O_6$
Mol. Wt.: 416.39

From **51** and *S*–(+)–MTPA–Cl. Data for **52-*R***: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52-7.51 (m, 2H), 7.45-7.43 (m, 3H), 6.54 (s, 1H), 6.09 (d, *J* = 6.1 Hz, 1H), 3.47 (s, 3H), 3.06-3.01 (m, 1H), 2.85 (dd, *J* = 18.5, 10.8 Hz, 1H), 2.50 (dd, *J* = 18.5, 4.3 Hz, 1H), 2.08-2.07 (m, 1H), 1.00 (s, 9H).



59
$C_{17}H_{21}NO_2$
Mol. Wt.: 271.35

2-(1-benzyl-4-*tert*-butyl-pyrrol-3-yl)ethanoic acid (59): To a solution of **46** (5.0 mg, 0.021 mmol) in H_2O (0.72 mL) and DMSO (80 μL), $BnNH_2$ (9.0 μL, 0.084 mmol) was added. The solution was stirred at rt for 18 h. To the resulting solution, saturated aqueous NH_4Cl (2 mL) and CH_2Cl_2 (2 mL) were added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 2 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated. Purification of the residue by silica gel chromatography (50–100% hexanes/ EtOAc) gave **59** (5.2 mg, 93%) as a clear oil which matched the previously reported analytical data.[10]



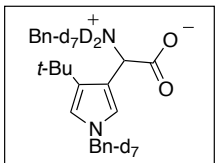
60
$C_{18}H_{23}NO_2$
Mol. Wt.: 285.38

Methyl 2-(1-benzyl-4-*tert*-butyl-1*H*-pyrrol-3-yl)acetate (60). Benzylamine (2.7 μL, 0.026 mmol) was added to a solution of **46** (3.0 mg, 0.013 mmol) in MeOH (0.25 mL). After 2 h at rt, the solution was concentrated and the residue was purified by silica gel chromatography (20% EtOAc/hexanes) to afford **60** (3.0 mg, 85%) as a clear resin, and **59** (0.4 mg, 10%). Data for **60**:

R_f 0.48 (50% Et_2O/hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.32 (m, 2H), 7.29 (m, 1H), 7.14–7.13 (m, 2H), 6.59 (d, *J* = 2.5 Hz, 1H), 6.40 (d, *J* = 2.5 Hz, 1H), 4.95 (s, 2H), 3.70 (s, 3H), 3.63 (s, 2H), 1.26 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$) δ 173.5, 138.4, 132.5, 128.9, 127.8, 127.4, 122.1, 117.7, 113.4, 53.5, 52.1, 33.1, 31.44, 31.40; IR (thin film) 2952, 2905, 1738, 1528, 1454, 1360, 1246, 1201, 1151, 1014 cm^{-1}; HRMS-ESI (*m/z*): $[M+Na]^+$ calculated for $C_{18}H_{23}O_2Na$ 308.1627, observed 308.1629. See table S6 for full structural assignment.

In situ Observation of Pyrrole formation with 13 and 14.

In situ observation of (57)

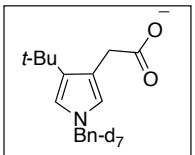


57

$C_{24}H_{14}D_{14}N_2O_2$
Mol. Wt.: 390.58

d_7-Benzylamine (5.0 μL, 0.042 mmol) was added to a solution of **13** (2.5 mg, 0.008 mmol) in d_4-methanol (500 μL, 0.02 M). This solution was placed in a NMR tube and allowed to stand at 25 ˚C for 18 h. The starting material was consumed after 24 h and the resultant pyrrole **57** was characterized *in situ*. Key spectral data for **57**: ^{1}H NMR (500 MHz, CD_3OD) δ 6.94 (d, J = 2.4 Hz, 1H), 6.47 (d, J = 2.5 Hz, 1H), 4.63 (s, 1H), 1.14 (s, 9H);^{13}C NMR (125 MHz, CD_3OD) δ 174.6, 139.5, 134.0, 133.3, 122.6, 118.6, 117.4, 59.6, 32.5, 28.5; HRMS-ESI (m/z): $[M - H]^-$ calculated for $C_{24}H_{14}D_{14}N_2O_2$ 389.2951, found 389.3957. Key spectral data for CD_3OAc: ^{1}H NMR (500 MHz, CD_3OD) δ 2.05 (s, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 173.6, 20.7. Key spectral data for AcOH: ^{1}H NMR (500 MHz, CD_3OD) δ 1.90 (s, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 180.45, 24.4, which matched precisely with authentic samples. See table S7 for full structural assignment.

In situ observation of (58)



58

$C_{17}H_{13}D_7NO_2^-$
Mol. Wt.: 277.39

d_7-Benzylamine (6.0 μL, 0.050 mmol) was added to solution of **14** (2.5 mg, 0.010 mmol) in d_4-methanol (500 μL, 0.02 M). This solution was placed in a NMR tube and allowed to stand at 25 ˚C for 18 h. The resultant pyrrole **58** was characterized *in situ*. The reaction was quenched with a saturated aqueous solution of NH_4Cl (1 mL) and extracted with CH_2Cl_2 (3 x 1 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated and purified by silica gel chromatography (50% EtOAc/hexane) to give a clear oil (1.7 mg, 61%). Key spectral data for **58**: R_f 0.18 (20% EtOAc/ hexanes), ^{1}H NMR (500 MHz, CD_3OD) δ 6.54 (d, J = 2.5 Hz, 1H), 6.36 (d, J = 2.5 Hz, 1H), 3.43 (s, 2H), 1.24 (s, 9H); ^{13}C NMR (125 MHz, CD_3OD) δ 182.0, 141.1, 133.3, 122.7, 118.2, 117.9, 38.5, 32.4, 31.8; IR (thin film) 2959, 1712, 1633, 1200 cm^{-1}; HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{17}H_{14}D_7NO_2$, 279.2090, found 279.2091. Key spectral data for CD_3OAc: ^{1}H NMR (500 MHz, CD_3OD) δ 2.05 (s, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 173.6, 20.7, which matched precisely with authentic samples. See table S8 for full structural assignment.

Lysozyme Modification.

General Procedures and Materials

Water (ddH_2O) used in biological procedures or as a reaction solvent was deionized using an Ultrapure Milli-Q™ purification system (Millipore, USA). Lysozyme (L-7001) from chicken egg white was purchased from Sigma and used without further purification. Trypsin Gold, Mass spec grade (V5280) was purchased from Promega and used without further purification.

Instrumentation and Sample Analysis Preparations

Mass Spectrometry

Mass spectra were obtained at the UCI Mass Spectrometry Facility. Electrospray LC/MS analysis was performed using a Micromass LCT time-of-flight (TOF) mass spectrometer (Waters) equipped for electrospray ionization (ESI) and connected with an Agilent 1100 series LC pump. Protein chromatography was performed using a Phenomenex Jupiter® 5μ C5 300Å reverse phase column (2.0 x 150 mm) with a gradient mobile phase MeCN:ddH_2O (2:98→ 98:2, 30 min) containing 0.01% TFA (200 μL/min). Protein mass reconstruction was performed on the charge ladder with advanced maximum entropy (MaxEnt) software (MassLynx version 4.0 SP4, Waters). Matrix assisted laser desorption-ionization time-of-flight mass spectrometry (MALDI-TOF MS) was performed on an Applied Biosystems AB SCIEX TOF/TOF 5800. All samples were co-crystallized using an α-cyano-4-hydroxycinnamic acid (CHCA) solution (10 mg/mL in 7:3 MeCN:ddH_2O with 0.1%TFA). MS/MS analyses were performed on a MALDI TOF-TOF system (AB SCIEX TOF/TOF 5800).

General procedure for protein modification. In a 1.5 mL Eppendorf tube was combined 75.0 μL of protein solution (400 μM in 200 mM phosphate buffer, pH 7.0), 220.5 μL of ddH_2O, and 4.5 μL of a 0.033M solution of the compound in DMSO. The solution was incubated at 22 °C for 20 h. The mixture was transferred to a mass spectrometry sample vial and analyzed by LCMS.

a) b)

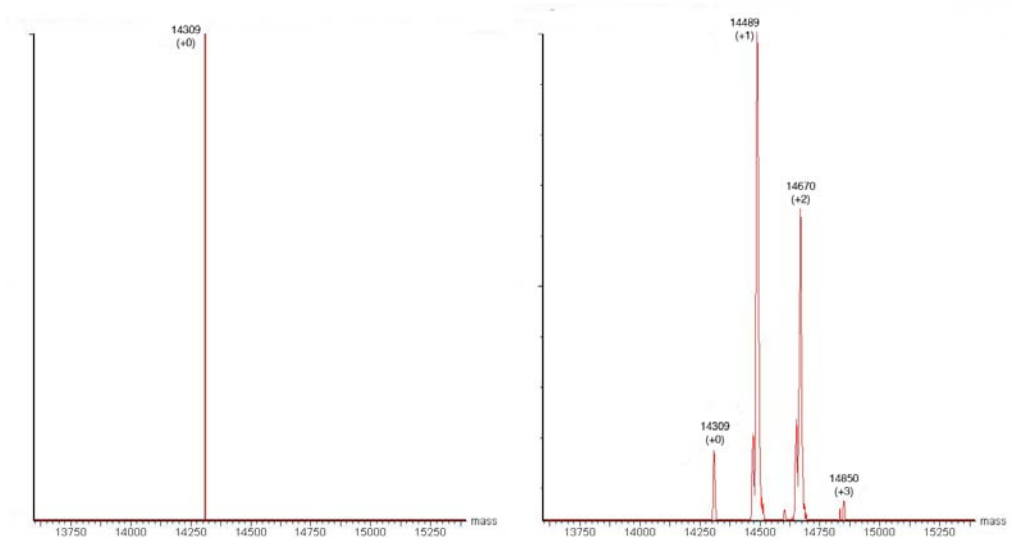
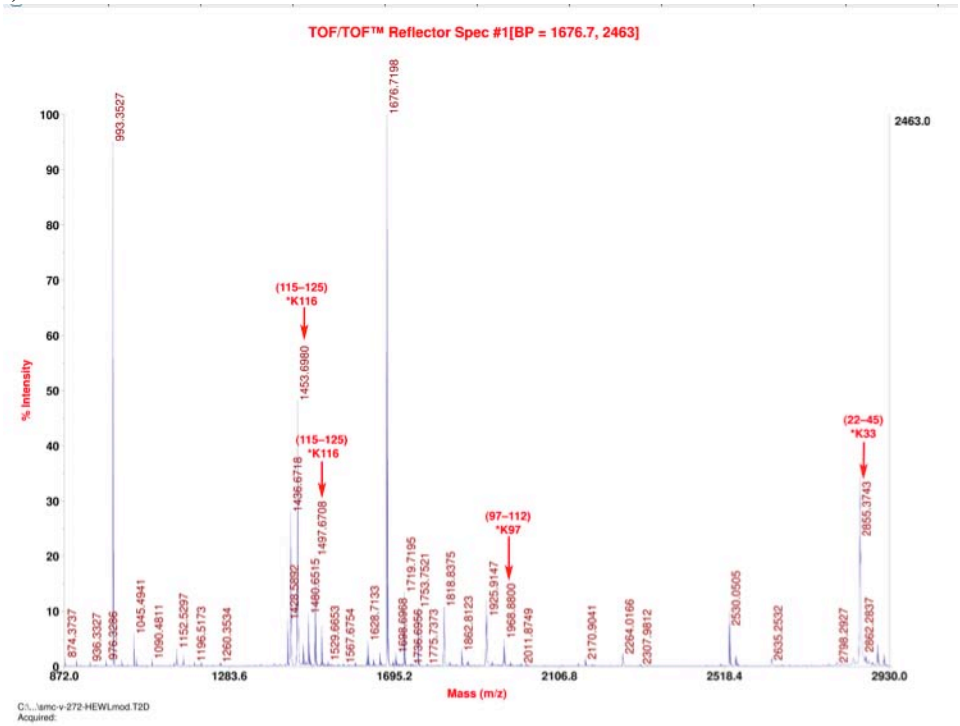


Figure S1 Lysine modification of lysozyme with *t*-BuMacE (**13**) a) A control experiment lacking *t*-BuMacE (**13**) b) A distribution of pyrrole modified products. Spectra shown are reconstructed from charge ladders obtained using ESI-MS analysis.

General procedure for trypsin digestion and peptide sequencing. Pyrrole-modified lysozyme prepared as described above was dialyzed using a Pierce slide-a-lyzer (3500 MWCO, Thermo Scientific, #PI69550) MINI dialysis unit and then lyophilized. The protein was reconstituted in 50 mM NH_4CO_3 buffer solution and treated with 3.0 mg DL-dithiothreitol and heated to 50 °C for 2 h. The solution was cooled to rt and 6.5 mg of iodoacetamide was added and maintained at rt in the dark for 1 h. 3.0 mg of DL-dithiothreitol was then added and heated to 50 °C for 1 h. The solution was dialyzed using a Pierce slide-a-lyzer (3500 MWCO) followed by lyophilization. The denatured and modified lysozyme was reconstituted in 50 mM NH_4CO_3 and treated with trypsin (Promega, 20:1 lysozyme/trypsin) and incubated for 6 h at 37 °C. The peptide solution was concentrated and purified using a ZipTip®$_{C18}$ (Millipore, USA). The peptides were eluted in 3.0 μL of MeCN:ddH_2O 70:30 containing 0.1% TFA and 10 mg/mL α-cyano-4-hydroxycinnamic acid (CHCA) directly onto the MALDI target.

a)



b)

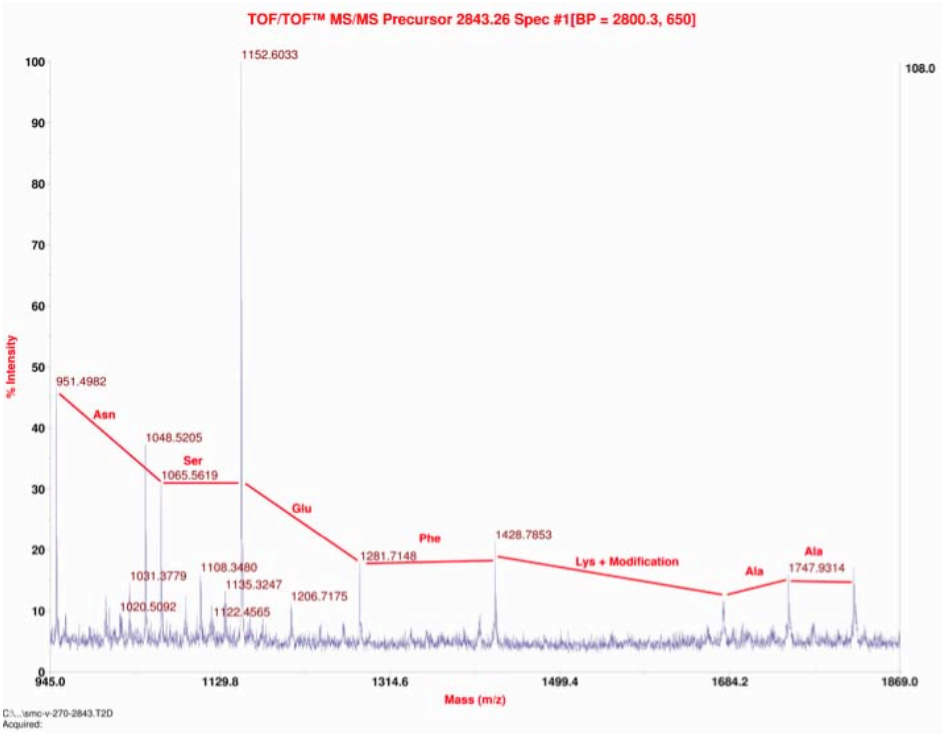
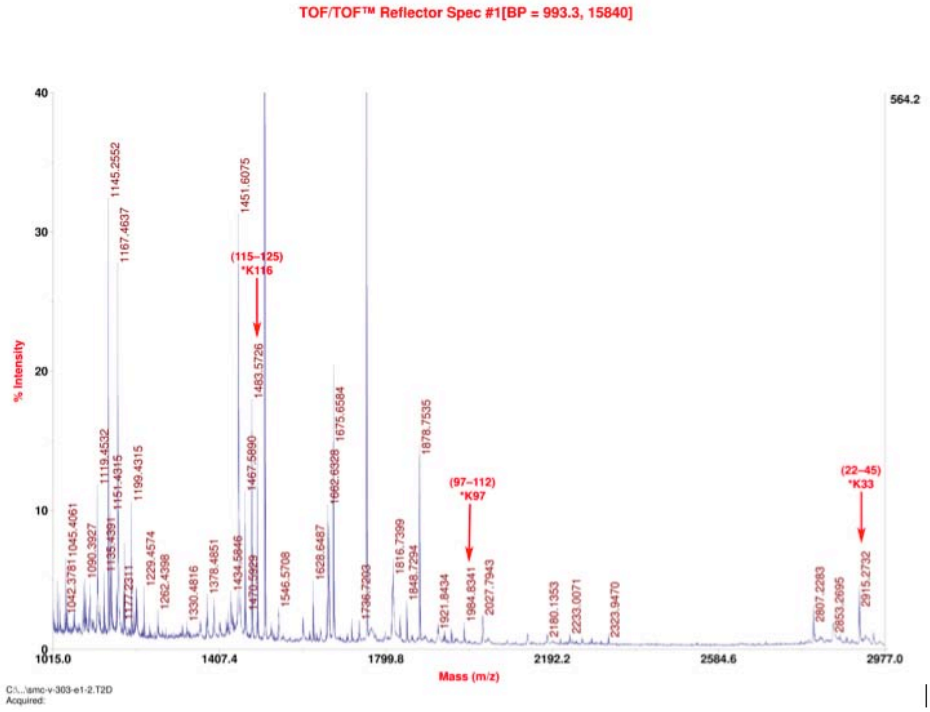


Figure S2: 14 Modification of Lysozyme a) MALDI mass-spectrum of trypsin digest of lysozyme modified with **14** (pH 8, 10 μM HEWL, 50 μM **14**, 22 °C, 20 h). Labelled peaks show modification at positions K33, K97, and K116. b) MALDI TOF/TOF mass spectrum of lysozyme peptide 22–45 with modification of *t*-BuAply (+120; **14**–CO_2) at K33; *m/z* 2843.

a)



b)

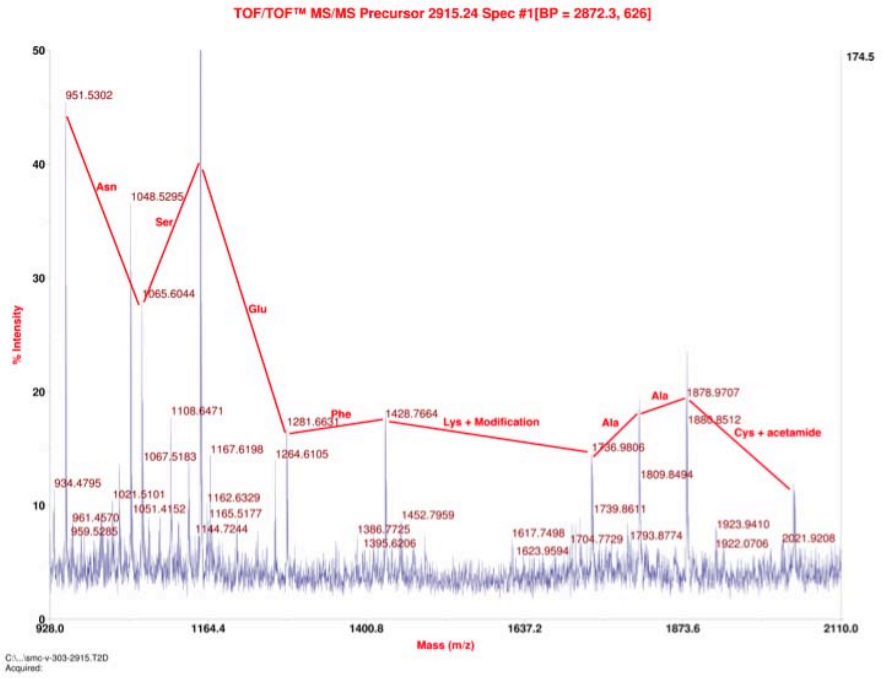


Figure S3 *t*-BuMacE (**13**) modification of Lysozyme a) MALDI mass-spectrum of trypsin digest of lysozyme modified with *t*-BuMacE (**13**) (pH 8, 10 μM HEWL, 50 μM **13**, 22 °C, 20 h). Labeled peaks show modification at positions K33, K97, and K116. b) MALDI TOF/TOF mass spectrum of lysozyme peptide 22–45 with modification of *t*-BuMacE **(13)** (+180) at K33; *m/z* 2915.

Hydrolysis Studies.

General procedure for hydrolytic rate experiments (Shown with 13):

A NMR tube containing 50 μL of a solution of **13** (0.5 mg, 0.002 mmol) in d_6-DMSO and a 50 mM sodium phosphate buffer solution of pD 8.3 in D_2O (450 μL) was added. The sample was stored in an incubator at 37 $^{\circ}$C and a ^{1}H NMR was taken of the sample at regular intervals. The percent consumption was measured via the ratio of the peak at 6.38 ppm to the DMSO peak at 2.71 ppm. The sample was run in duplicate.

Golgi Modification Procedure.

Cell Culture: Normal Rat Kidney (NRK) cells were grown in Advanced DMEM (Invitrogen), supplemented with 2% FBS and 2 mM glutaMAX-I (GIBCO) in a 5% CO_2 incubator.
Antibodies and Reagents: Antibodies to giantin and Mannosidase II were kindly provided by Vivek Malhotra (CRG Barcelona, Spain) and Kelley Moreman (University of Georgia) respectively. Fluorochrome-conjugated secondary antibodies were from Invitrogen.
Compound Treatment: NRK cells on coverslips were treated with various compounds at the indicated concentration in complete medium supplemented with 25 mM Hepes pH 7.4 at 37 °C for the indicated periods of time. Parallel control incubations were done with DMSO.
Immunofluorescence: NRK cells grown on coverslips were fixed for 10 min in 4% formaldehyde in PBS and incubated in blocking buffer (2.5% FBS, 0.1% Triton-X 100). Primary and secondary antibodies were diluted into blocking buffer. Cells were imaged with a Zeiss Axiovert 200M microscope and analyzed with linear adjustments with the Zeiss Axiovision software.

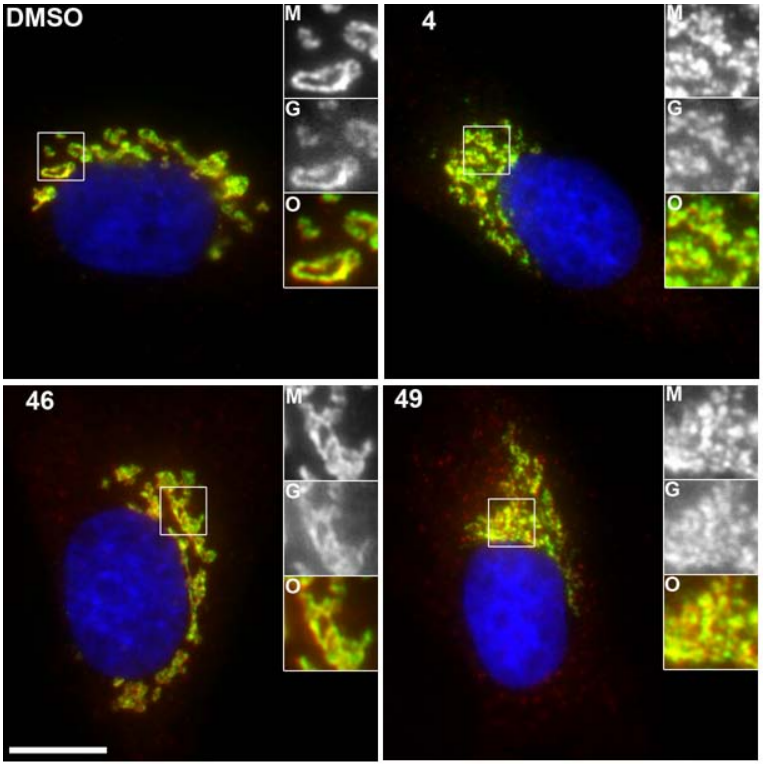
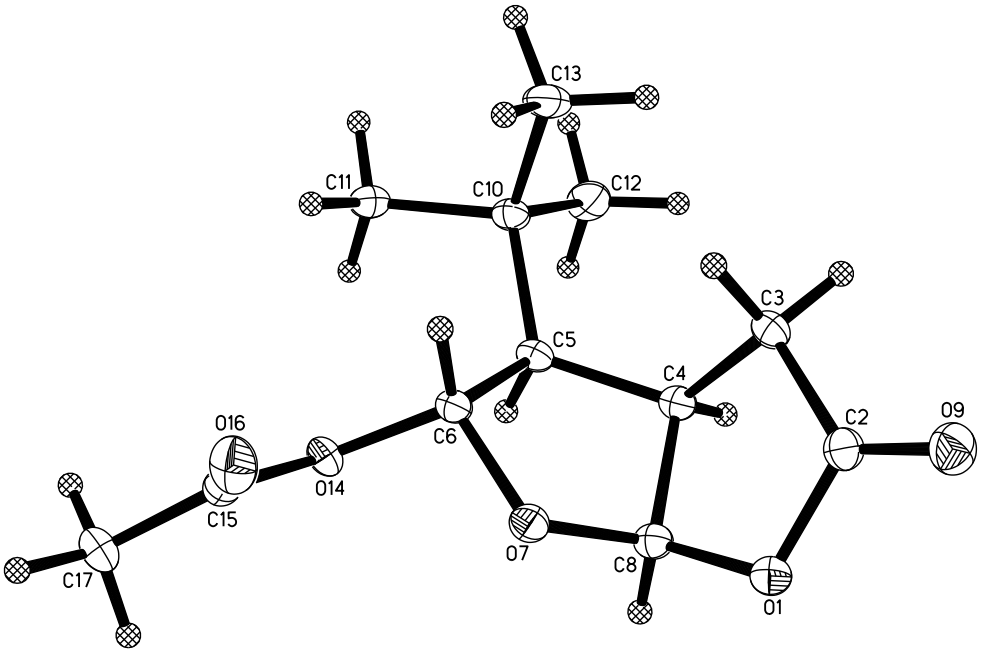
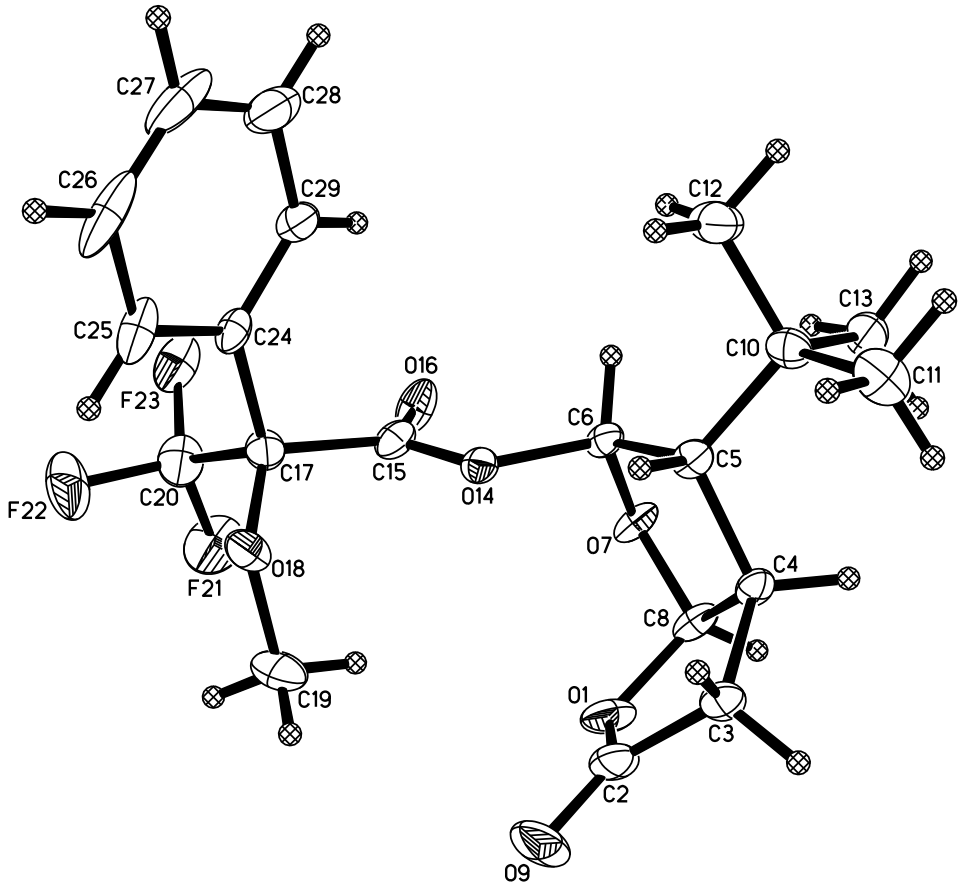


Figure S4: 4 and 49 produced similar phenotypes of fragmented, pericentriolar Golgi membranes in NRK cells**.** Normal Rat Kidney (NRK) cells were treated for one hour at 37 °C with either control (DMSO), Macfarlandin E (**4**), **46**, or **49.** Cells were fixed and stained with antibodies for the Golgi resident proteins Mannosidase II (green) and Giantin (red) and with the DNA dye Hoechst 33342. Area demarcated by the white square is enlarged in the insets to show details of Golgi reorganization induced by treatment with each of these compounds. M: Mannosidase II, G: Giantin, O: Overlay. Scale bar is 10 microns.

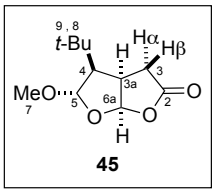
X–Ray Structure of 46.



X–Ray Structure of (*S*)–51.



NMR Tables for selected compounds.

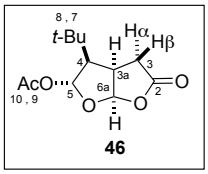


45

Table S1. ^{1}H (500 MHz), ^{13}C (125 MHz), HMBC, COSY, and NOESY NMR data for **45**, $CDCl_3$

atom	^{13}C (mult)	^{1}H mult, *J* (Hz)	HMBC[a]	COSY[b]	NOESY[b]
2	176.2 (C)				
3	29.81 (CH_2)	3-α; 2.70 (dd, 9.7, 17.8, 1H)	2, 3a, 4, 6a	3-β, 3a	3-β, 3a, 9
		3-β; 2.56 (dd, 9.5, 17.8, 1H)	2, 3a, 4, 6a	3-α, 3a	3-α, 3a, 9
3a	42.0 (CH)	3.05 (m, 1H)	2, 3, 4, 5, 6a	3-α, 3-β, 4, 6a	3-α, 3-β, 4, 9
4	55.6 (CH)	2.12 (t, 7.0, 1H)	3a, 5, 8, 9	3a, 5	3a, 5, 9
5	106.9 (CH)	5.10 (d, 7.3, 1H)	4, 6a, 7, 8	4	3-β[c], 4, 7, 9
6a	104.9 (CH)	6.01 (d, 4.7, 1H)	2, 3, 3a, 5	3a	3a
7	57.2 (CH_3)	3.49 (s, 3H)	5		
8	31.2 (C)				
9	29.83 (CH_3)	1.03, (s, 9H)	4		3-α, 3-β, 3a, 4, 5

[a]Carbons that correlate to the proton resonance. Optimized for 10 Hz coupling. [b]Protons that correlate to the proton resonance. [c]1-D NOE observed by irradiation with 2 second delay.

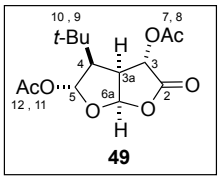


46

Table S2. ^{1}H (500 MHz), ^{13}C (125 MHz), HMBC, COSY, and NOESY NMR data for **46**, $CDCl_3$

atom	^{13}C (mult)	^{1}H mult, *J* (Hz)	HMBC[a]	COSY[b]	NOESY[b]
2	175.6 (C)				
3	29.4 (CH)	3-α; 2.57 (dd, 9.2, 17.5, 1H)	2, 3a, 4, 6	3a, 3-β	3a, 3-β, 6a, 8
		3-β; 2.71 (dd, 10.0, 17.5, 1H)	2, 3a, 4, 6	3a, 3-α	3a, 3-α, 6a, 8
3a	42.1 (CH)	3.10 (m, 1H)	3, 4, 5	3-α, 3-β, 4, 6a	3-α, 3-β, 4, 6a, 8
4	55.1 (CH)	2.41 (apt t, 6.8, 1H)	3, 3a, 5, 7, 8	3a, 5	3a, 3-β, 5, 8
5	97.0 (CH)	6.38 (d, 7.3, 1H)	4, 6a, 7, 9	4	4, 8
6a	105.2 (CH)	6.05 (d, 4.4, 1H)	2, 3a, 4, 5	3a	3a, 3-α, 3-β, 8
7	31.5 (C)				
8	29.6 (CH_3)	1.04 (s, 9H)	4, 7		3a, 3-α, 3-β, 4, 5, 6a
9	170.0 (C)				
10	21.4 (CH_3)	2.11 (s, 3H)	9		

[a]Carbons that correlate to the proton resonance; optimized 10 Hz coupling. [b]Protons that correlate to the proton resonance.

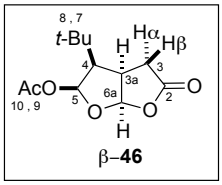


49

Table S3. ^{1}H (500 MHz), ^{13}C (125 MHz), HMBC, COSY, and NOESY NMR data for **49**, $CDCl_3$

atom	^{13}C (mult)	^{1}H mult, *J* (Hz)	HMBC[a]	COSY[b]	NOESY[b]
2	171.7 (C)				
3	68.2 (CH)	5.47 (d, 8.8, 1H)		3a	3a, 5, 10
3a	46.5 (CH)	3.34 (m, 1H)	3, 5	3, 4, 6a	3, 4, 6a, 10
4	54.9 (CH)	2.46 (t, 6.8, 1H)	3, 3a, 5, 9, 10	3a, 5	3a, 5, 6a, 10
5	96.9 (CH)	6.39 (d, 7.1, 1H)	4, 6a, 9, 11	4	3, 4, 10
6a	102.6 (CH)	6.07 (d, 4, 1H)	2, 3, 3a	3a	3a, 4
7	169.4 (C)				
8	20.7 (CH_3)	2.20 (s, 3H)	7		10
9	31.4 (C)				
10	29.0 (CH_3)	1.04 (s, 9H)	4, 9		3, 3a, 4, 5, 8, 12
11	169.8 (C)				
12	21.3 (CH_3)	2.11 (s, 3H)	11		10

[a]Carbons that correlate to the proton resonance. Optimized for 10 Hz coupling. [b]Protons that correlate to the proton resonance.

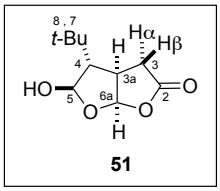


β–**46**

Table S4. ^{1}H (500 MHz), ^{13}C (125 MHz), HMBC, COSY, and NOE NMR data for **β-46**, C_6D_6

atom	^{13}C (mult)	^{1}H mult, *J* (Hz)	HMBC[a]	COSY[b]	1D-NOE[b]
2	175.1 (C)				
3	30.1 (CH_2)	3-α; 1.87 (dd, overlap, 1H)	2, 3a, 4	3-β, 3a	
		3-β; 2.80 (dd, 6.4, 17.1, 1H)	2, 3a, 4	3-α, 3a	
3a	54.0 (CH)	1.87 (overlap m, 1H)	3, 4, 5	3-α, 3-β, 6a	
4	38.1 (CH)	1.21 (t, 7.0, 1H)	5, 8, 10	3a	5, 10
5	97.0 (CH)	6.33 (d, 4.1, 1H)	4, 6a, 7	4	4, 10 (weak)
6a	107.3 (CH)	5.44 (d, 5.5, 1H)	2, 5, 4	3a	3a
7	168.6 (C)				
8	20.7 (CH_3)	1.41 (s, 3H)	4		3-β, 5, 10
9	30.3 (C)				
10	29.5 (CH_3)	0.60 (s, 9H)	5		3-β

[a]Carbons that correlate to the proton resonance. Optimized for 10 Hz coupling. [b]Protons that correlate to the proton resonance.

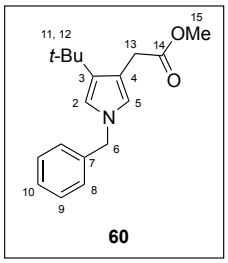


51

Table S5. ^{1}H (500 MHz), ^{13}C (125 MHz), HMBC, COSY, and NOESY NMR data for **51,** $CDCl_3$

atom	^{13}C (mult)	^{1}H mult, *J* (Hz)	HMBC[a]	COSY[b]	NOESY[b]
2	175.6 (C)				
3	36.7 (CH_2)	3-α; 2.91 (dd, 11.0, 18.2, 1H)	2, 3a, 4, 6a	3a, 3-β	3a, 3-β, 8
		3-β; 2.70 (dd, 3.6, 18.2, 1H)	2, 3a, 4, 6a	3a, 3-α	3a, 3-α, 4, 8
3a	39.6 (CH)	2.97 (m, 1H)		3-α, 3-β, 4, 6a	3-α, 3-β, 6a, 8
4	64.5 (CH)	1.98 (d, 1.7, 1H)	3, 5, 6a, 7, 8	3a, 5	3-β, 8
5	102.7 (CH)	5.58 (s, 1H)	3a, 4, 6a, 7	4	8
6a	109.3 (CH)	6.07 (d, 6.0, 1H)	2, 3a, 5	3a	3a, 8
7	31.4 (C)				
8	27.4 (CH_3)	0.95 (s, 9H)	4, 7		3a, 3-α, 3-β, 4, 5, 6a

[a]Carbons that correlate to the proton resonance. Optimized for 10 Hz coupling. [b]Protons that correlate to the proton resonance.

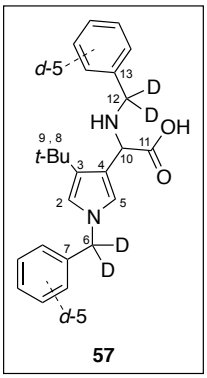


60

Table S6. ^{1}H (500 MHz), ^{13}C (125 MHz), HMBC, COSY, and NOESY NMR data for **60**, $CDCl_3$

atom	^{13}C (mult)	^{1}H mult, *J* (Hz)	HMBC[a]	COSY[b]	NOESY[b]
2	117.7 (CH)	6.4 (d, 2.5, 1H)	3, 4, 5, 6, 11	5	6, 12
3	132.5 (C)				
4	113.4 (C)				
5	122.1 (CH)	6.59 (d, 2.5, 1H)	2, 3, 4	2, 13	6, 13
6	53.5 (CH_2)	4.95, (s, 2H)	2, 5, 7, 8	8	2, 5, 8
7	138.4 (C)				
8	127.4 (CH)	7.14 (m, 2H)	9	6, 9, 10	6, 10
9	127.8 (CH)	7.29 (m, 1H)		8, 10	
10	128.9 (CH)	7.33 (m, 2H)	7	8, 9	8
11	31.44 (C)				
12	31.40 (CH_3)	1.26 (s, 9H)	3, 11		2, 13, 15
13	33.1 (CH_2)	3.63 (s, 2H)	3, 4, 5, 14	5	5, 12
14	173.5 (C)				
15	52.1 (CH_3)	3.70 (s, 3H)	14		12

[a]Carbons that correlate to the proton resonance. Optimized for 10 Hz coupling. [b]Protons that correlate to the proton resonance.

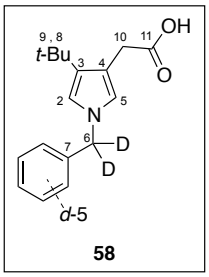


57

Table S7. ^{1}H (500 MHz), ^{13}C (125 MHz), HMBC, and COSY NMR data for **57**, CD_3OD

atom	^{13}C (mult)	^{1}H mult, *J* (Hz)	HMBC[a]	COSY[c]
2	118.6 (CH)	6.47 (d, 2.5, 1H)	3, 4[b], 5	5
3	134.0 (C)			
4	117.4 (C)			
5	122.6 (CH)	6.94 (d, 2.4, 1H)	2, 3, 4	2
7	139.5 (C)			
8	28.5 (C)			
9	32.5 (CH_3)	1.14 (s, 9H)	*2*, 3, 8	
10	59.6 (CH)	4.63 (s, 1H)	3, 4, 5, 11	
11	174.6 (C)			
13	133.3 (C)			

[a]Carbons that correlate to the proton resonance; Optimized for 2 Hz and 10 Hz coupling; correlations observed only in the 2 Hz experiment are in italics font. [b]Only observed in 10Hz experiment. [c]Protons that correlate to the proton resonance.

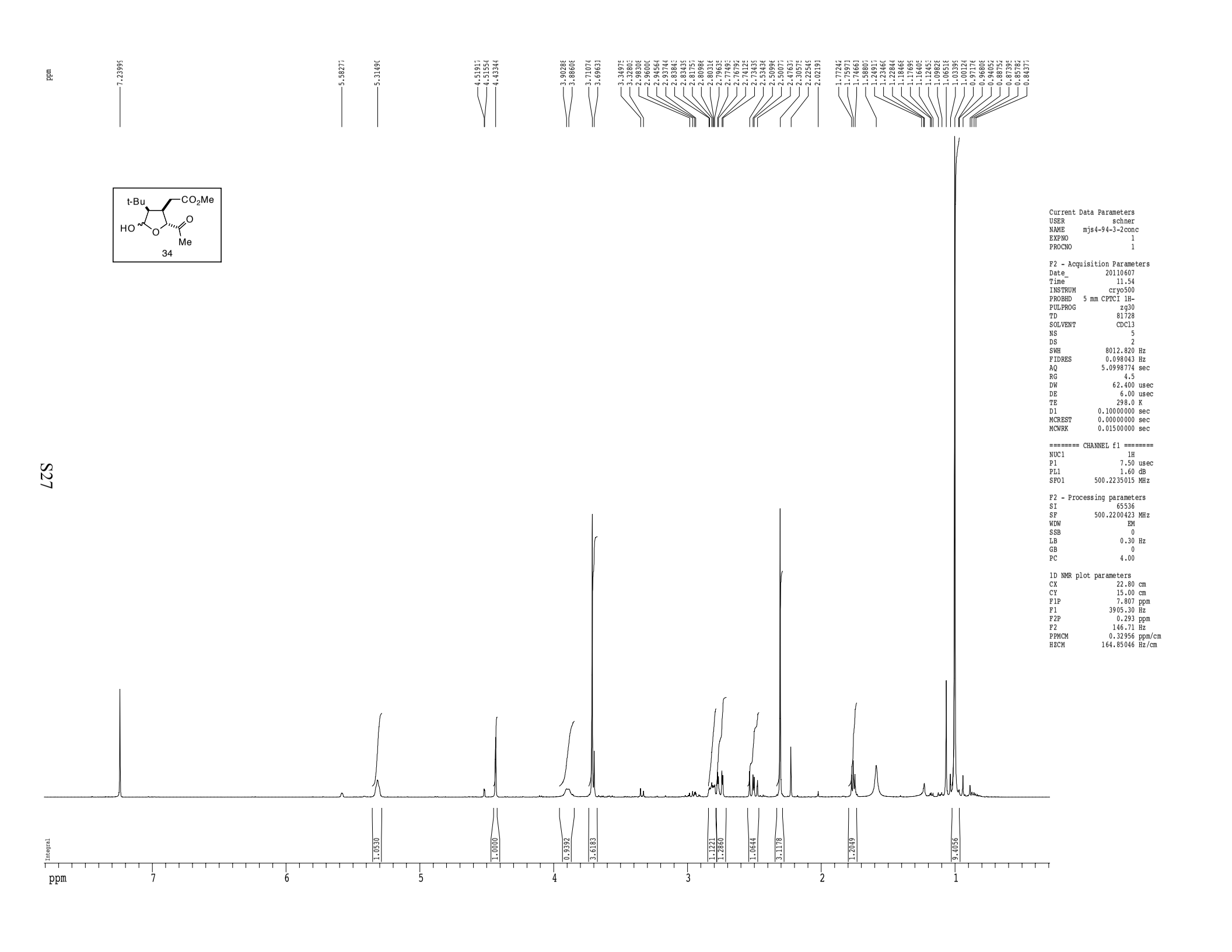


58

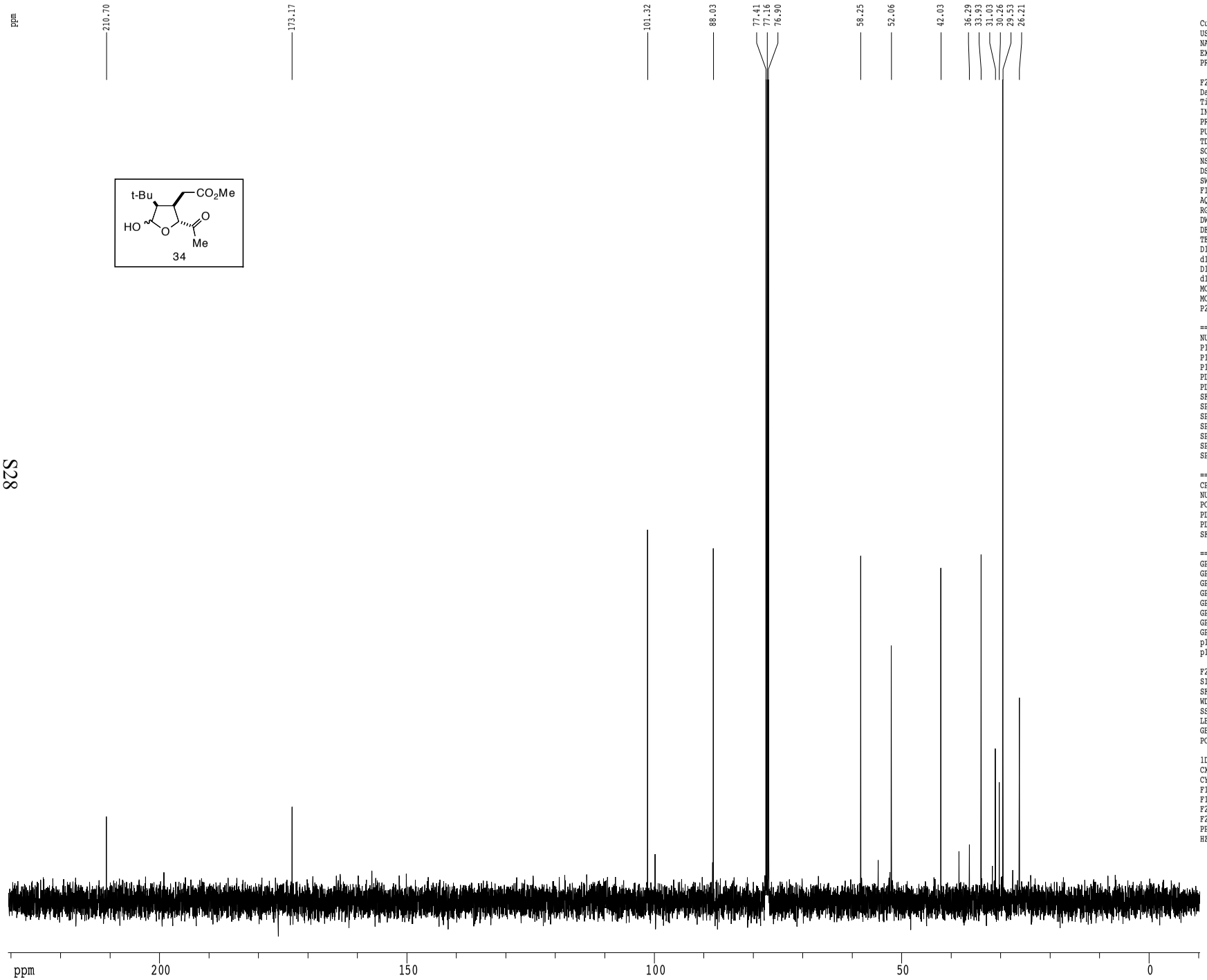
Table S8. ^{1}H (500 MHz), ^{13}C (125 MHz), HMBC, and COSY NMR data for **58**, CD_3OD

atom	^{13}C (mult)	^{1}H mult, *J* (Hz)	HMBC[a]	COSY[b]
2	117.9 (CH)	6.36 (d, 2.5, 1H)	3, 4, 5, *8*, *10*	5
3	133.3 (C)			
4	118.2 (C)			
5	122.7 (CH)	6.54 (d, 2.5, 1H)	2, 3, 4, *8*, *10*	2
7	141.1 (C)			
8	32.4 (C)			
9	31.8 (CH_3)	1.24 (s, 9H)	2, 3, 4, 8	
10	38.5 (CH_2)	3.43 (s, 2H)	3, 4, 5, *8*, 11	
11	182.0 (C)			

[a]Carbons that correlate to the proton resonance; Optimized for 2 Hz and 10 Hz coupling; correlations observed only in the 2 Hz experiment are in italics font. [b]Protons that correlate to the proton resonance.


t-Bu
CO2Me
HO
O
O
Me
34
Current Data Parameters
USER schner
NAME mjs4-94-3-2conc
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110607
Time 11.54
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 5
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 4.5
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200423 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 7.807 ppm
F1 3905.30 Hz
F2P 0.293 ppm
F2 146.71 Hz
PPMCM 0.32956 ppm/cm
HZCM 164.85046 Hz/cm
ppm
Integral
1.0530
1.0000
0.9392
3.6183
1.1221
1.2860
1.0644
3.1178
1.2049
9.4056
ppm
7
6
5
4
3
2
1

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER schner
NAME mjs4-94-3-2conc
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20110607
Time 11.55
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 139
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec

======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

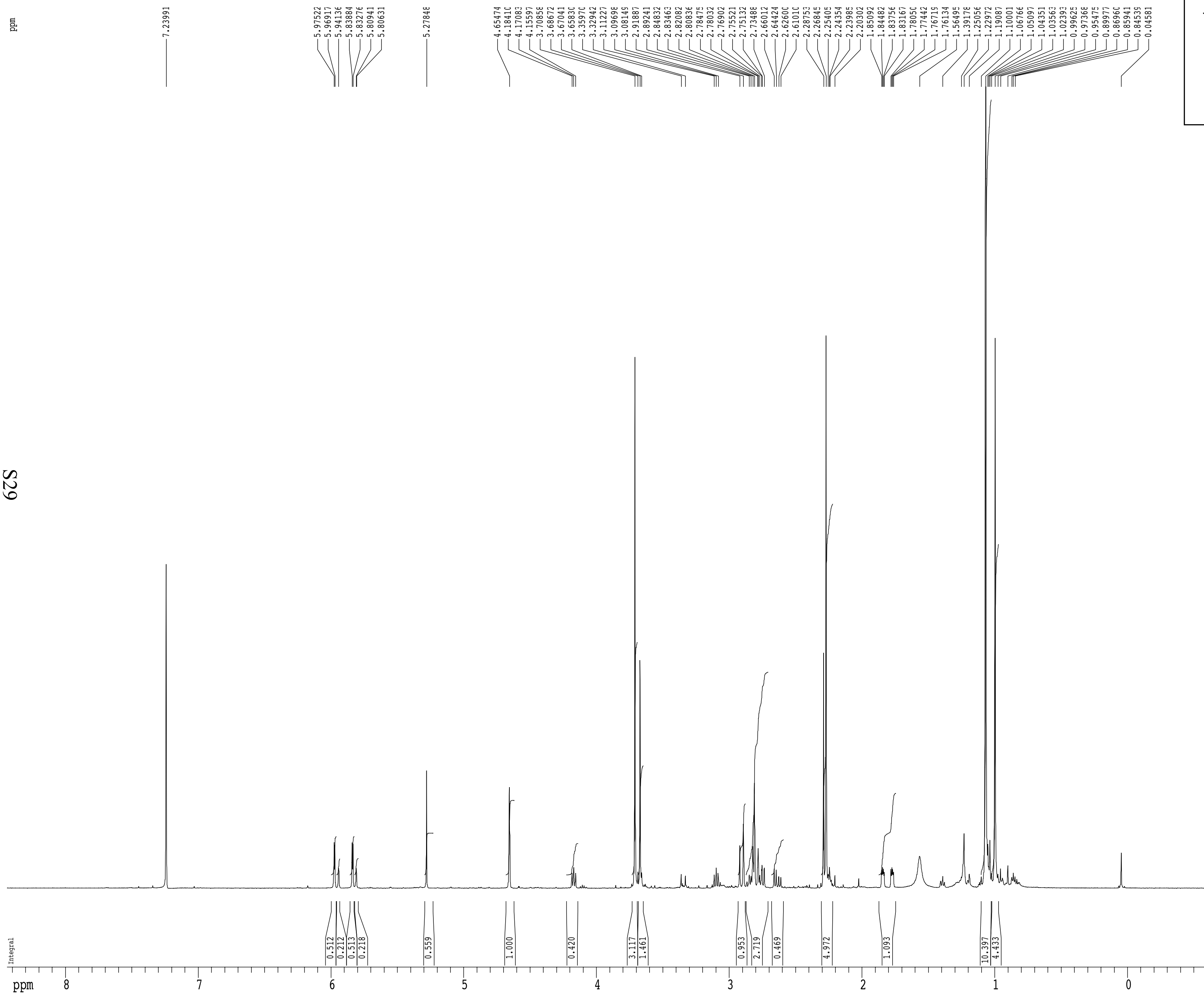
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz

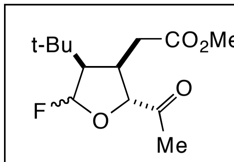
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804090 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 20.00 cm
F1P 230.637 ppm
F1 29009.68 Hz
F2P -10.287 ppm
F2 -1293.96 Hz
PPMCM 10.56688 ppm/cm
HZCM 1329.10693 Hz/cm

1H spectrum





38

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Current Data Parameters
USER              schner
NAME          mjs4-96a-2
EXPNO                  1
PROCNO                 1

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Time               15.36
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PROBHD   5 mm CPTCI 1H-
PULPROG             zg30
TD                 81728
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0998774 sec
RG                   4.5
DW                62.400 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                  7.50 usec
PL1                 1.60 dB
SFO1         500.2235015 MHz

F2 - Processing parameters
SI                 65536
SF           500.2200423 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  4.00

1D NMR plot parameters
CX                 22.80 cm
CY                 20.00 cm
F1P                8.438 ppm
F1               4220.64 Hz
F2P               -0.616 ppm
F2               -308.00 Hz
PPMCM            0.39707 ppm/cm
HZCM           198.62453 Hz/cm
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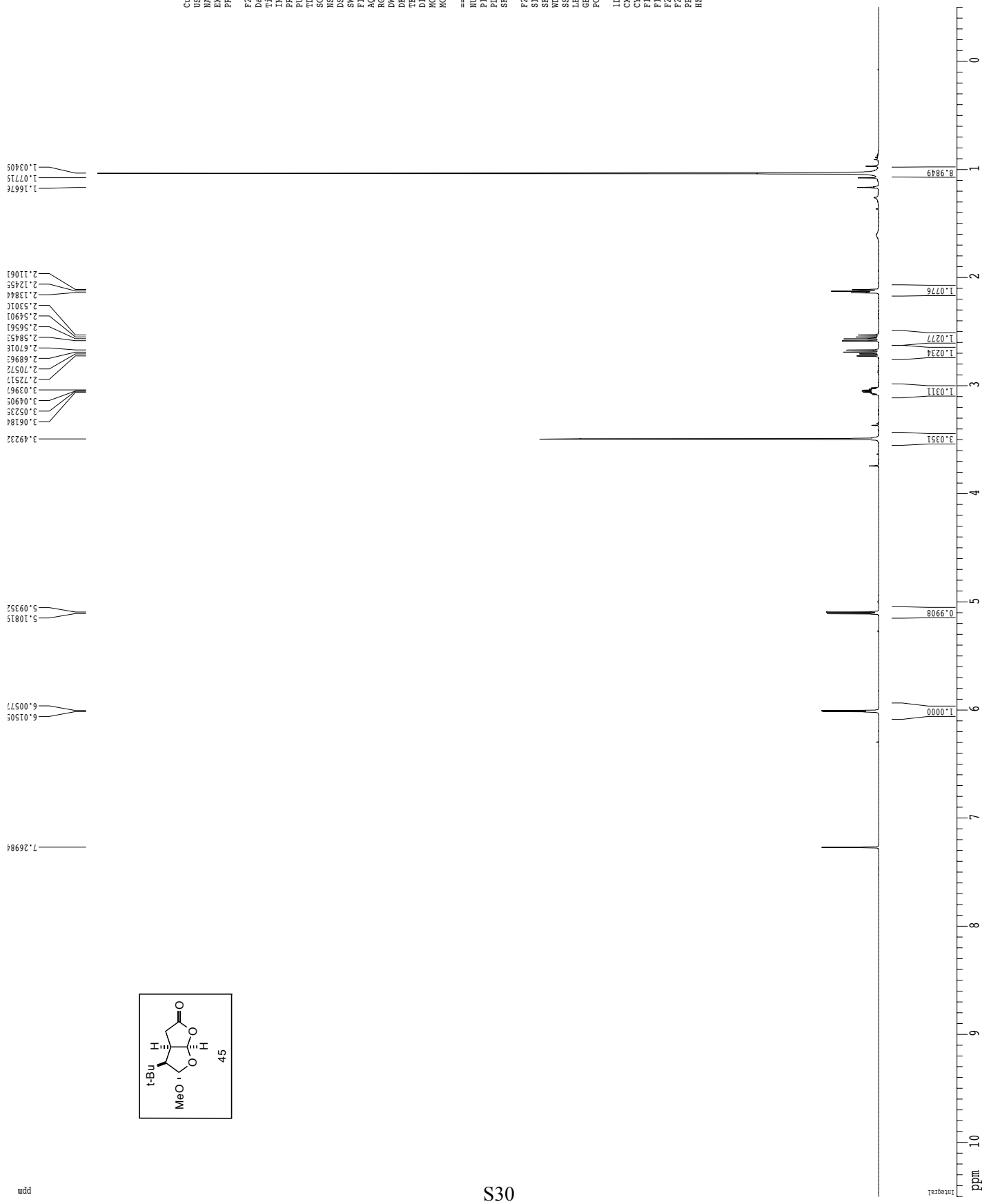
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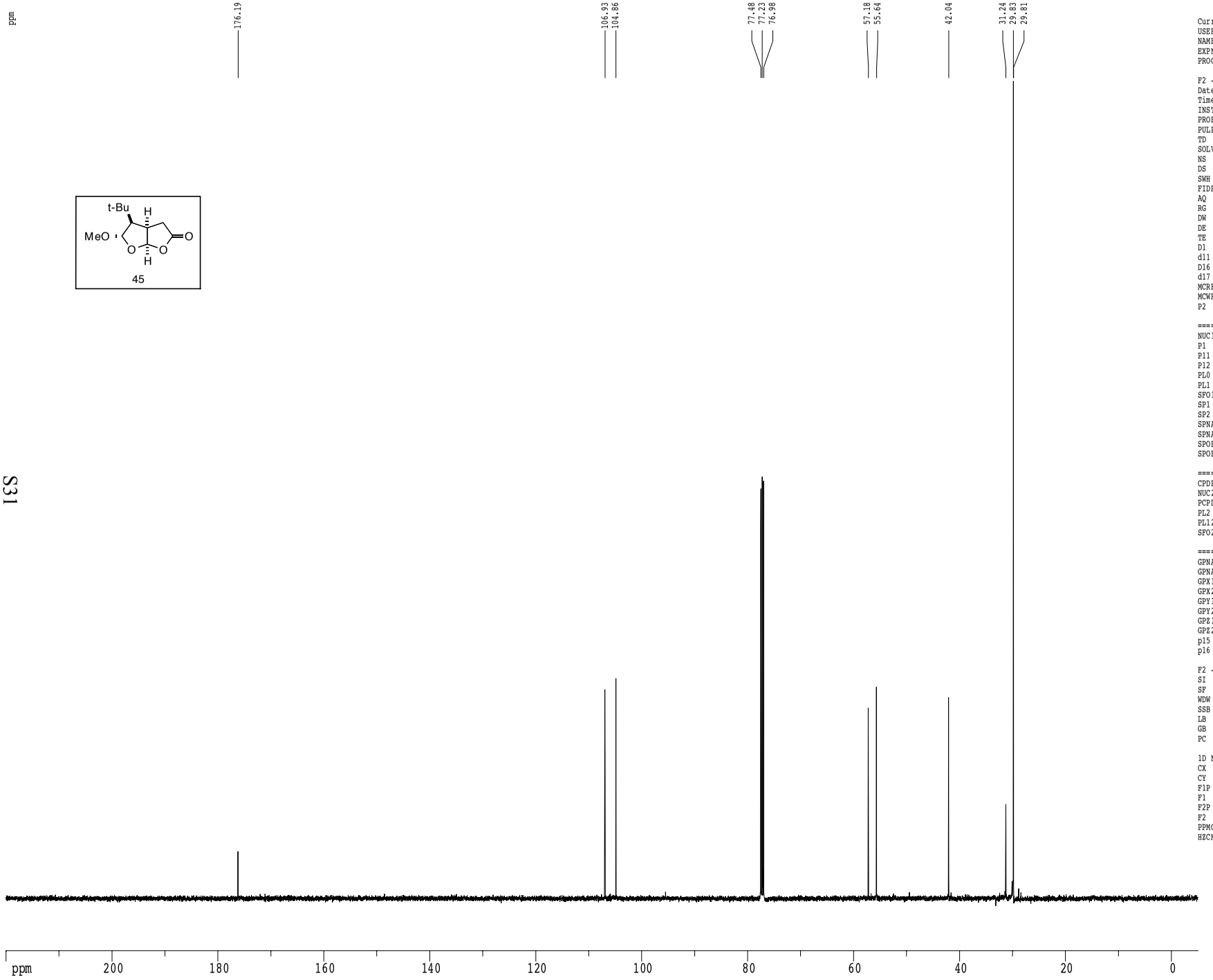
USER genung
NAME NEG-1-172
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20101105
Time 8.26
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 7.1
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200272 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.500 ppm
F1 5252.31 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.33423 Hz/cm
1.03405
1.07715
1.16676
2.11061
2.12455
2.13844
2.53010
2.54901
2.56561
2.58453
2.67018
2.68963
2.70572
2.72517
3.03967
3.04905
3.05239
3.06184
3.49232
5.10815
5.09352
6.00577
6.01505
7.26984
8.98449
1.0776
1.0277
1.0234
1.0311
3.0351
0.9908
1.0000
t-Bu
MeO
H
H
O
O
O
O
45
ppm
Integral

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Current Data Parameters
USER                genung
NAME             NEG-I-172
EXPNO                    3
PROCNO                   1

F2 - Acquisition Parameters
Date_             20101105
Time                 8.30
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                   65536
SOLVENT              CDCl3
NS                     601
DS                      16
SWH              30303.031 Hz
FIDRES           0.462388 Hz
AQ               1.0813940 sec
RG                  7298.2
DW                  16.500 usec
DE                   6.00 usec
TE                  298.0 K
D1              0.25000000 sec
d11             0.03000000 sec
D16             0.00020000 sec
d17             0.00019600 sec
MCREST          0.00000000 sec
MCWRK           0.01500000 sec
P2                  31.00 usec

======== CHANNEL f1 ========
NUC1                   13C
P1                  15.50 usec
P11                500.00 usec
P12               2000.00 usec
PL0                120.00 dB
PL1                 -1.00 dB
SFO1          125.7942548 MHz
SP1                  3.20 dB
SP2                  3.20 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2     Crp60comp.4
SPOFF1               0.00 Hz
SPOFF2               0.00 Hz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2              100.00 usec
PL2                  1.60 dB
PL12                24.60 dB
SFO2          500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPX1                 0.00 %
GPX2                 0.00 %
GPY1                 0.00 %
GPY2                 0.00 %
GPZ1                30.00 %
GPZ2                50.00 %
p15                500.00 usec
p16               1000.00 usec

F2 - Processing parameters
SI                   65536
SF            125.7804002 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00

1D NMR plot parameters
CX                  22.80 cm
CY                  15.65 cm
F1P               220.000 ppm
F1              27671.69 Hz
F2P                -5.000 ppm
F2               -628.90 Hz
PPMCM             9.86842 ppm/cm
HZCM          1241.25403 Hz/cm
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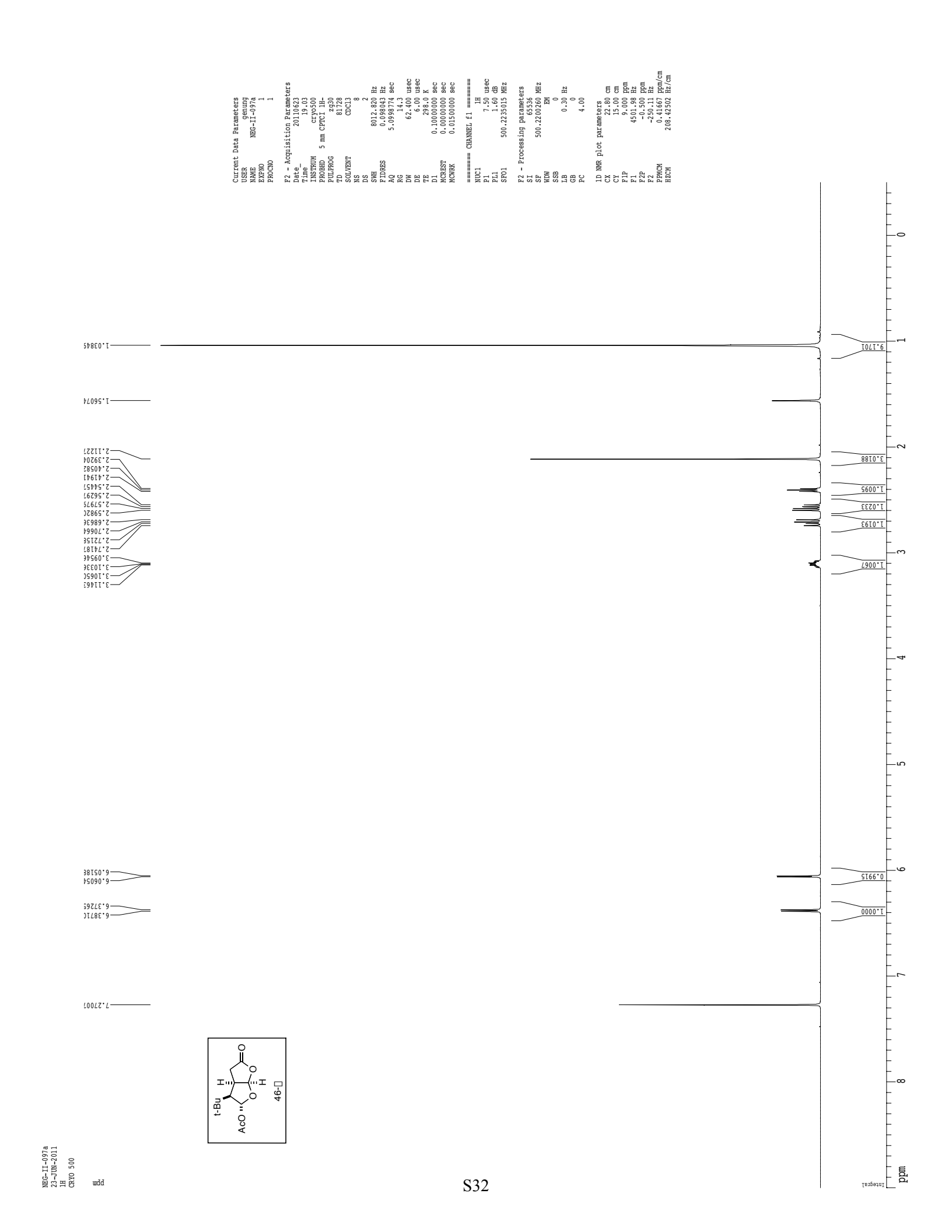
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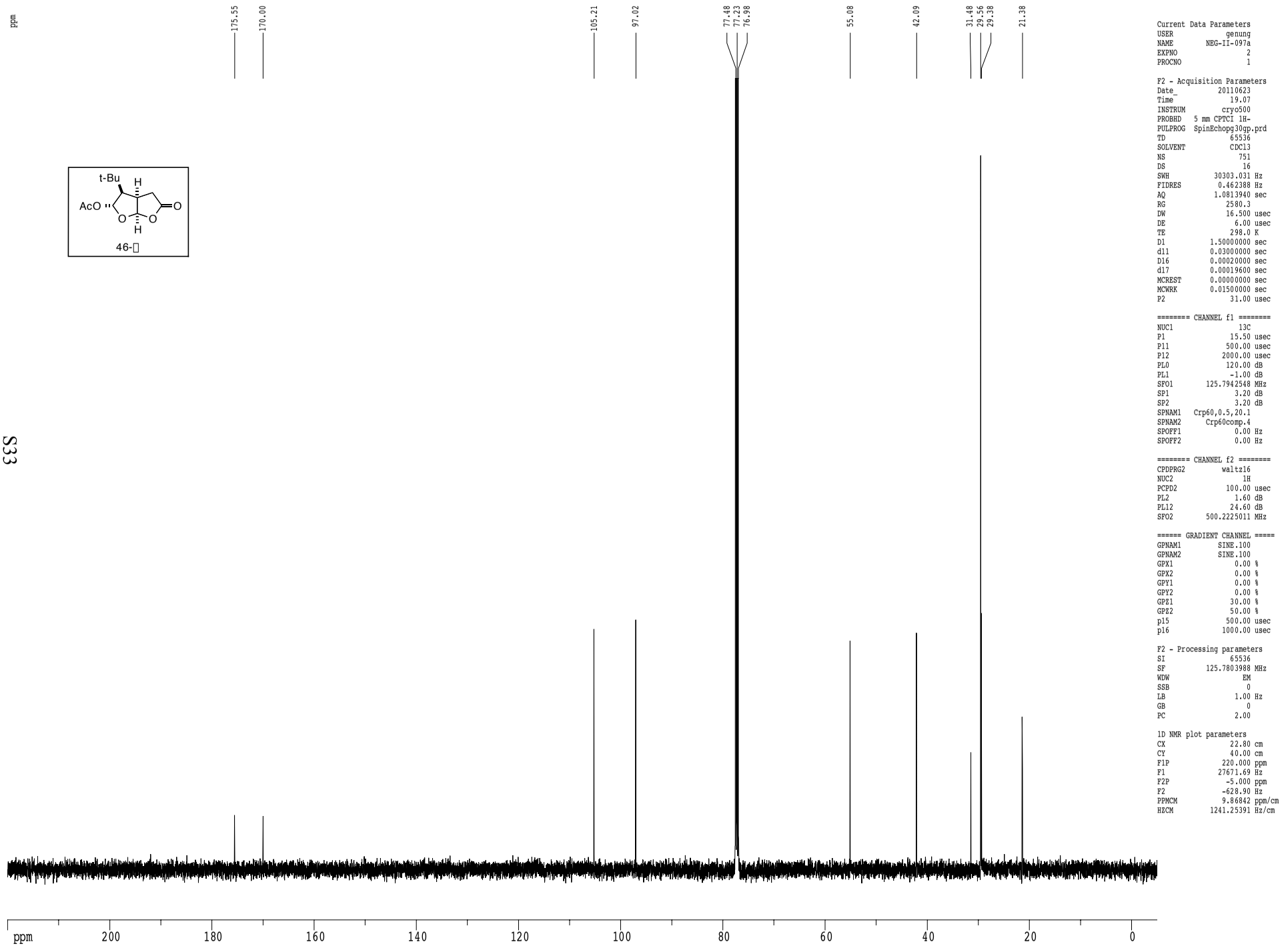
USER genung
NAME NEG-II-097a
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110623
Time 19.03
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 14.3
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200260 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
1.03845
1.56074
2.11227
2.39204
2.40582
2.41941
2.54457
2.56297
2.57975
2.59826
2.68636
2.70664
2.72156
2.74187
3.09546
3.10336
3.10656
3.11463
6.05188
6.06054
6.37261
6.38710
7.27007
9.1701
3.0188
1.0095
1.0233
1.0193
1.0067
0.9915
1.0000
t-Bu
AcO
46-□
ppm
Integral
NEG-II-097a
23-JUN-2011
1H
CRYO 500

NEG-II-097a
23-JUN-2011
13C
CRYO 500



Current Data Parameters
USER genung
NAME NEG-II-097a
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20110623
Time 19.07
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 751
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 2580.3
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 1.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec

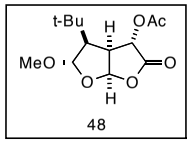
======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz

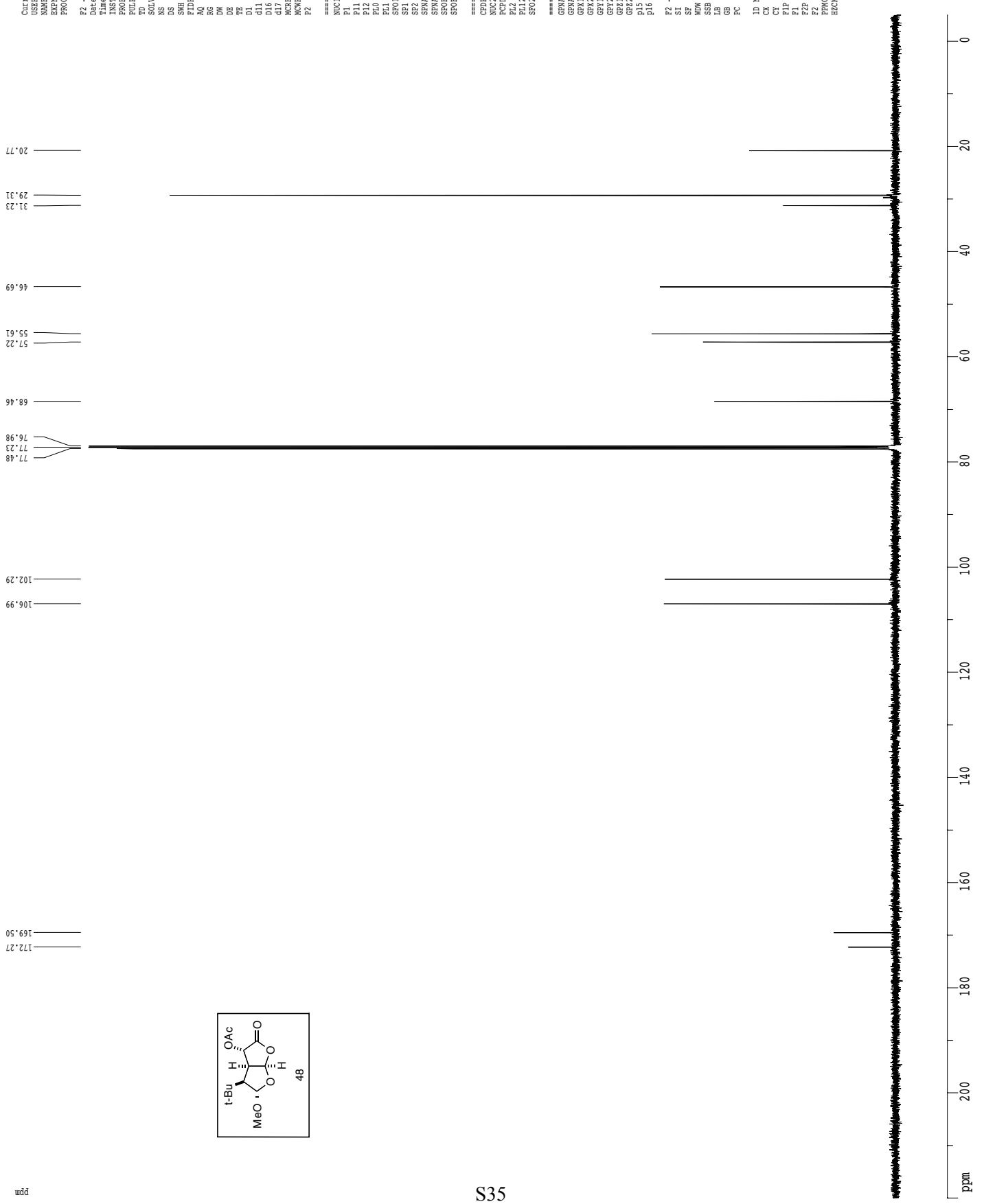
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7803988 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 40.00 cm
F1P 220.000 ppm
F1 27671.69 Hz
F2P -5.000 ppm
F2 -628.90 Hz
PPMCM 9.86842 ppm/cm
HZCM 1241.25391 Hz/cm



48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PROCNO 1
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Time_ 21.00
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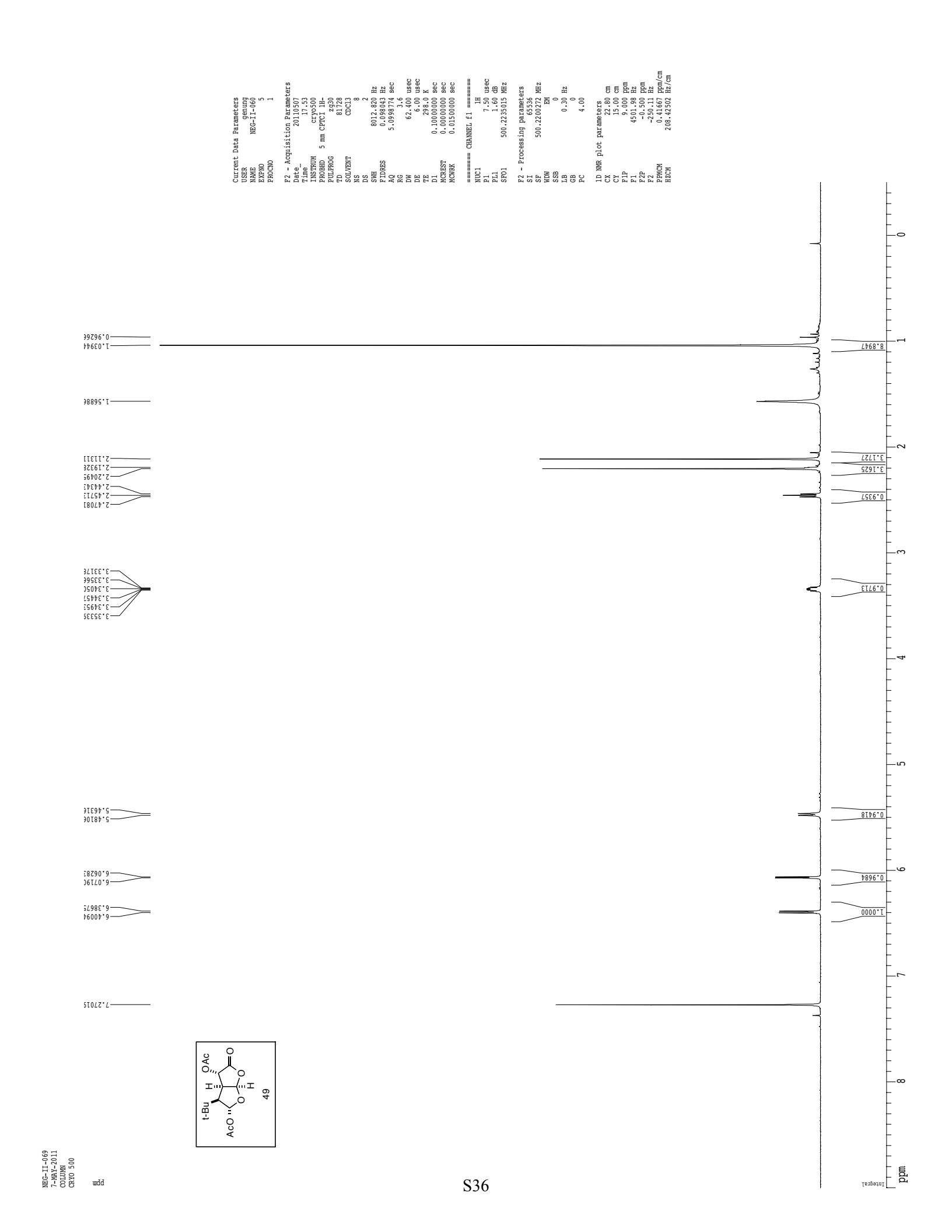
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchop230p.prd
TD 65536
SOLVENT CDCl3
NS 848
DS 16
SWH 30303.031 Hz
FIDRES 0.462398 Hz
AQ 1.0819940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7803992 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 220.000 ppm
F1 27671.69 Hz
F2P -5.000 ppm
F2 -628.90 Hz
PPMCM 9.06842 ppm/cm
HZCM 1241.25391 Hz/cm
20.77
29.31
31.23
46.69
55.61
57.22
68.46
76.98
77.23
77.48
102.29
106.99
169.50
172.27
t-Bu
OAc
MeO
48
ppm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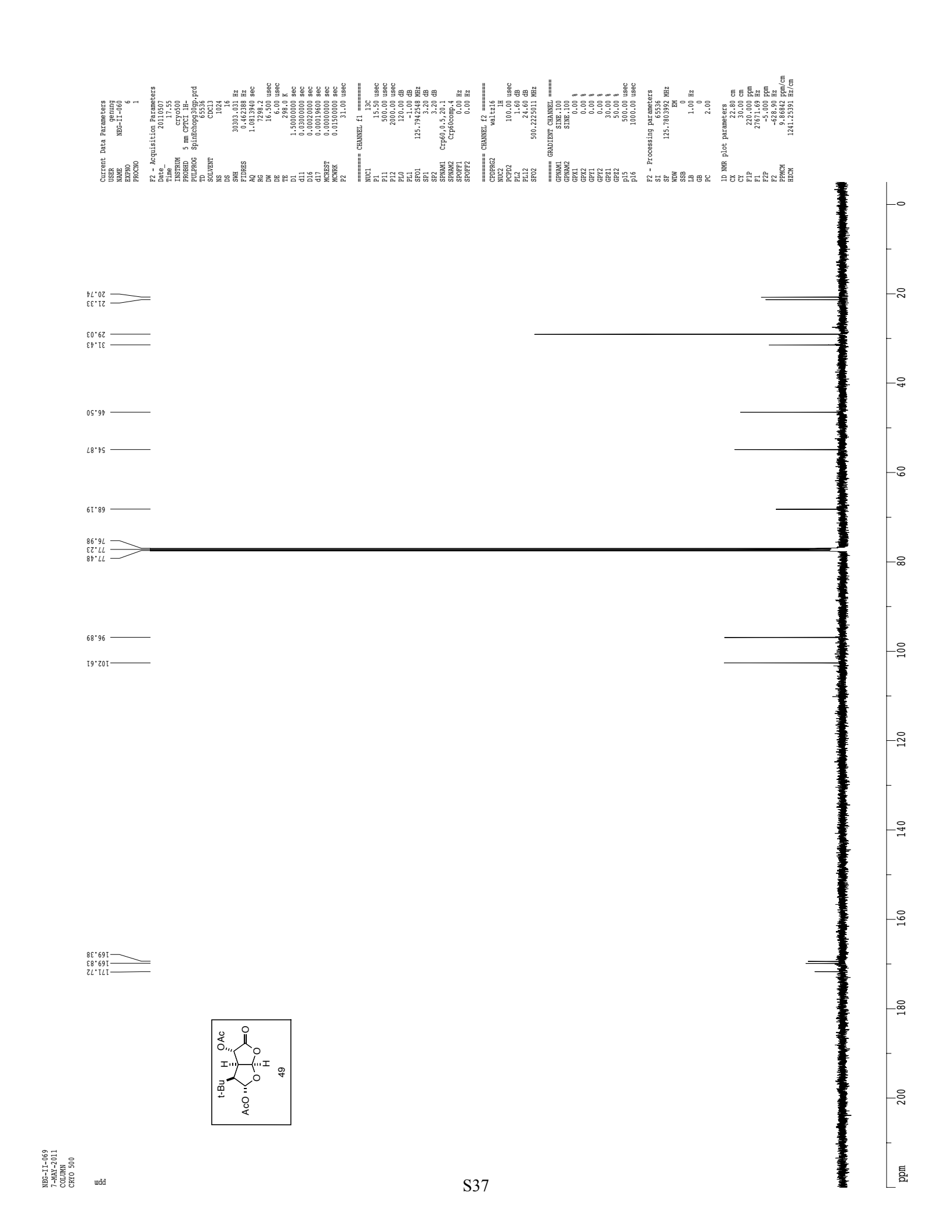
USER genung
NAME NEG-II-069
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110507
Time 17.53
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 1.6
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200272 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm
0.96266
1.03944
1.56886
2.11311
2.19328
2.20495
2.44343
2.45713
2.47083
3.33178
3.35666
3.34057
3.34457
3.34953
3.35335
5.46316
5.48106
6.06283
6.07196
6.38675
6.40094
7.27015
8.8947
3.1727
3.1625
0.9357
0.9713
0.9418
0.9684
1.0000
t-Bu
OAc
AcO
49
NEG-II-069
7-MAY-2011
COLUMN
CRYO 500
ppm
Integral
ppm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EXPNO 6
PROCNO 1
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Time_ 17.55
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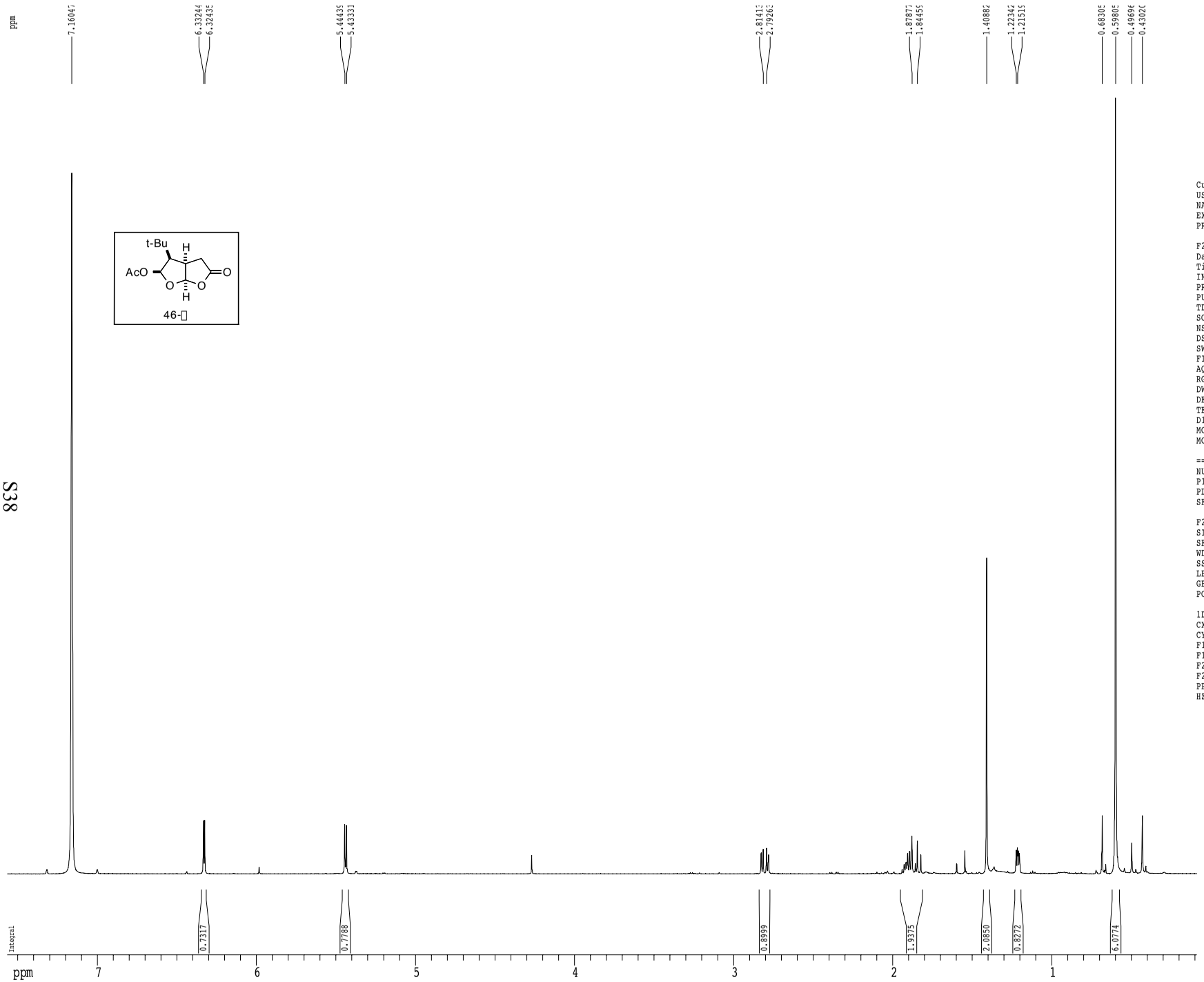
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 1024
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 1.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7803992 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 30.00 cm
F1P 220.000 ppm
F1 27671.69 Hz
F2P -5.000 ppm
F2 -628.90 Hz
PPMCM 9.86842 ppm/cm
HZCM 1241.25391 Hz/cm
20.74
21.33
29.03
31.43
46.50
54.87
68.19
76.98
77.23
77.48
96.89
102.61
169.38
169.83
171.72
t-Bu
OAc
AcO
H
O
O
H
49
ppm
0
20
40
60
80
100
120
140
160
180
200
NEG-II-069
7-MAY-2011
COLUMN
CRYO 500



Current Data Parameters
USER schner
NAME ms1-140-3-2ben
EXPNO 1
PROCNO 1

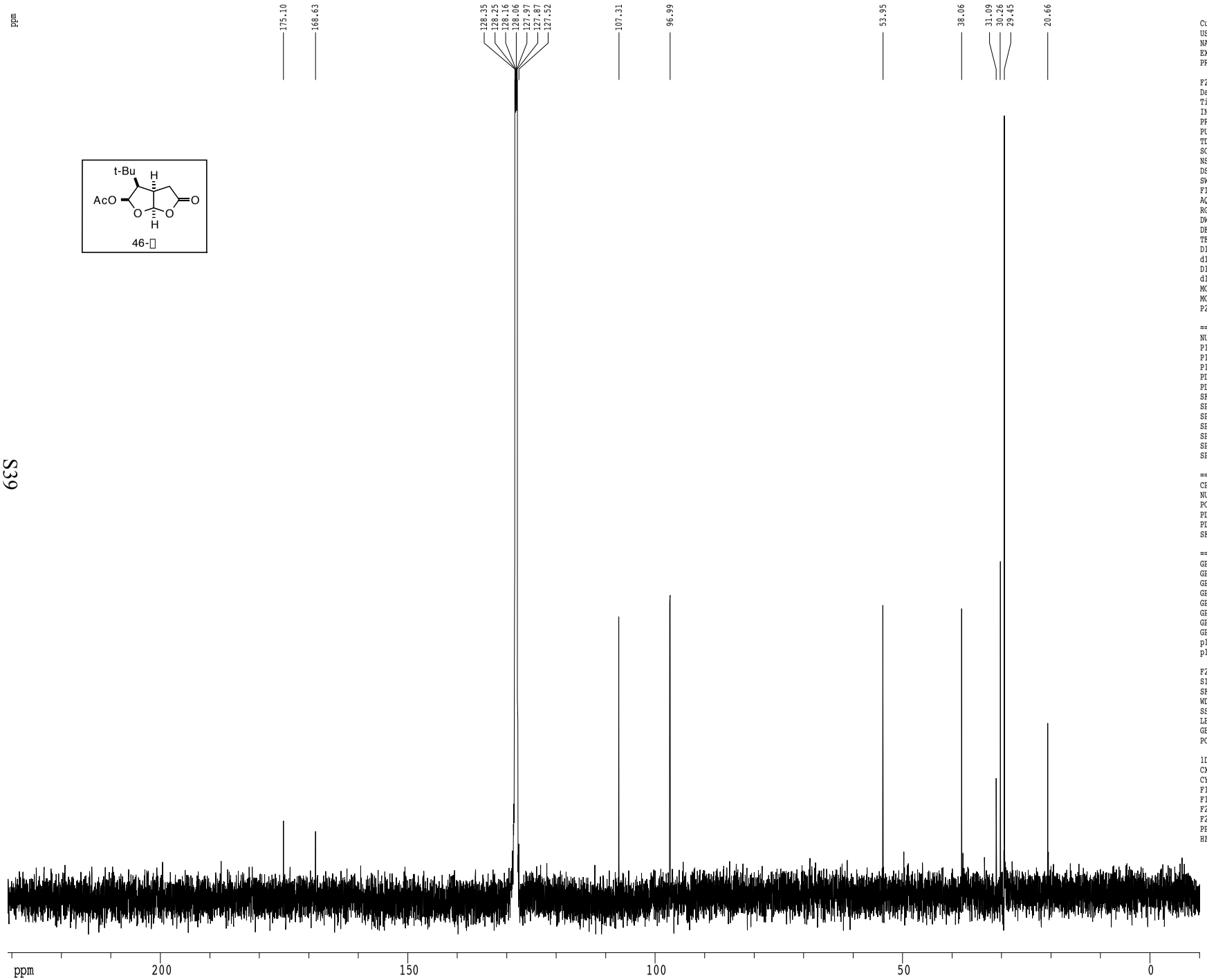
F2 - Acquisition Parameters
Date_ 20090218
Time 19.27
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT C6D6
NS 12
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 4.5
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

F2 - Processing parameters
SI 65536
SF 500.2200004 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00

1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 7.565 ppm
F1 3784.16 Hz
F2P 0.090 ppm
F2 44.85 Hz
PPMCM 0.32787 ppm/cm
HZCM 164.00510 Hz/cm

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER schner
NAME mjs4-109-32
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20110708
Time 10.46
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 734
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 4597.6
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec

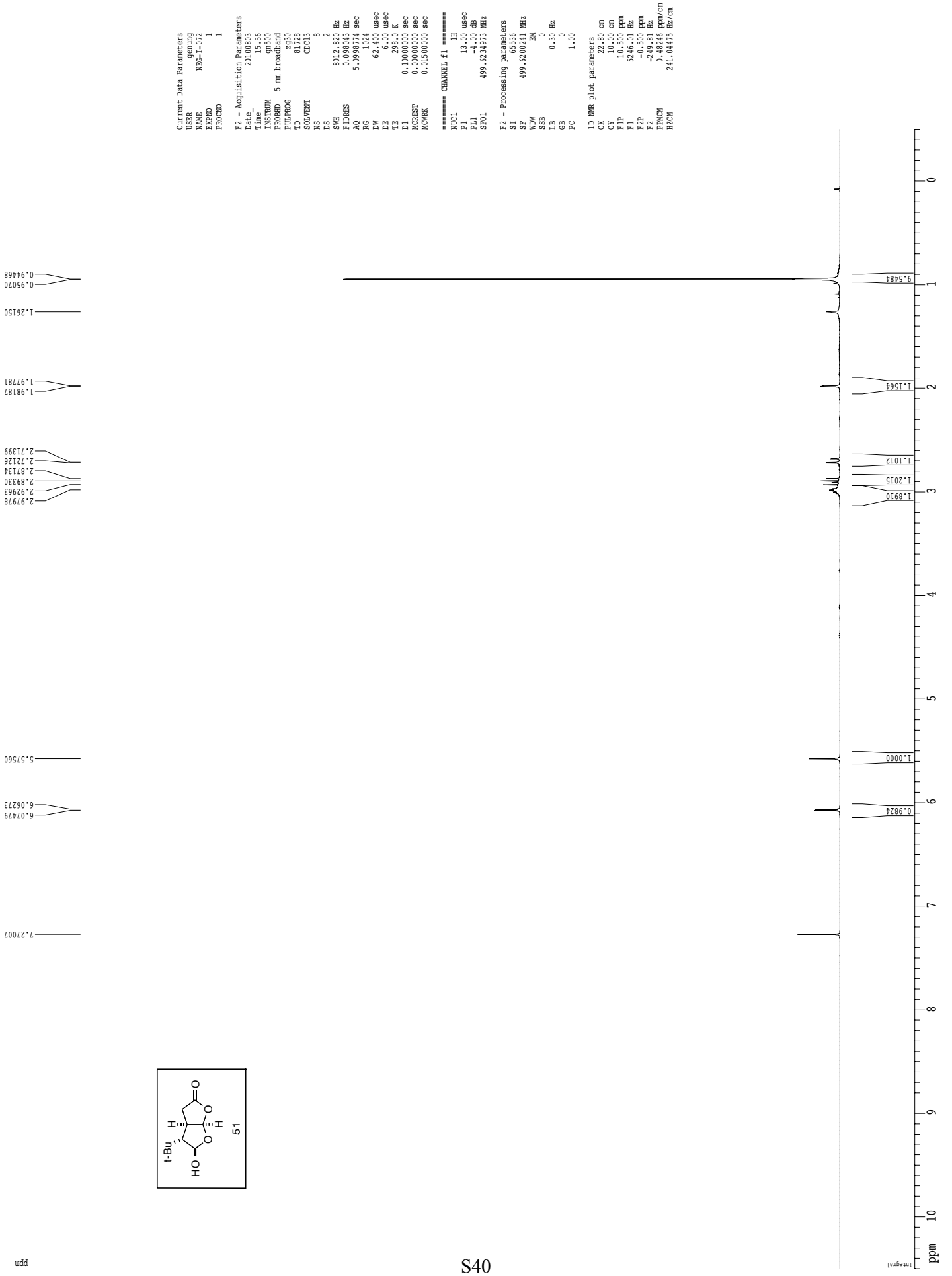
======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

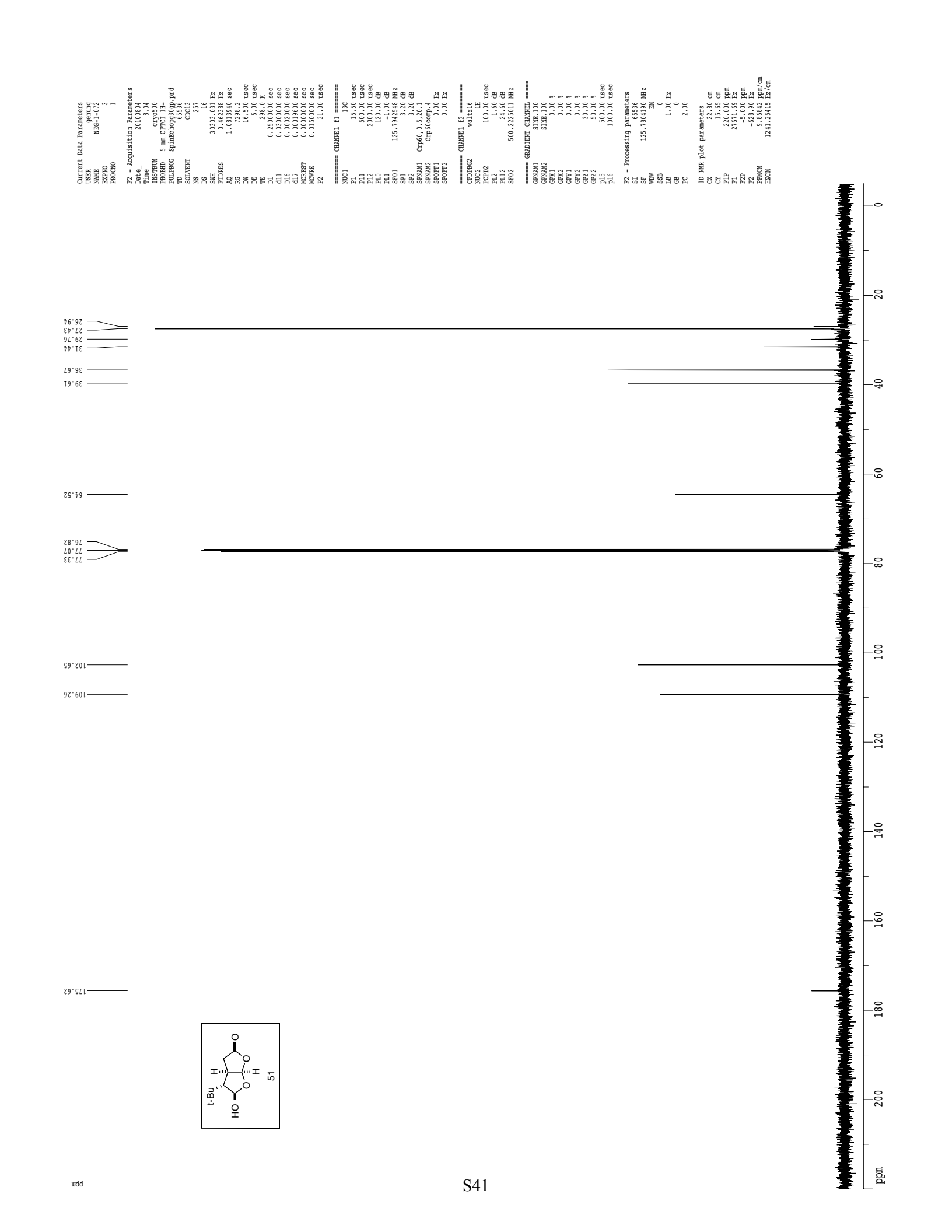
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

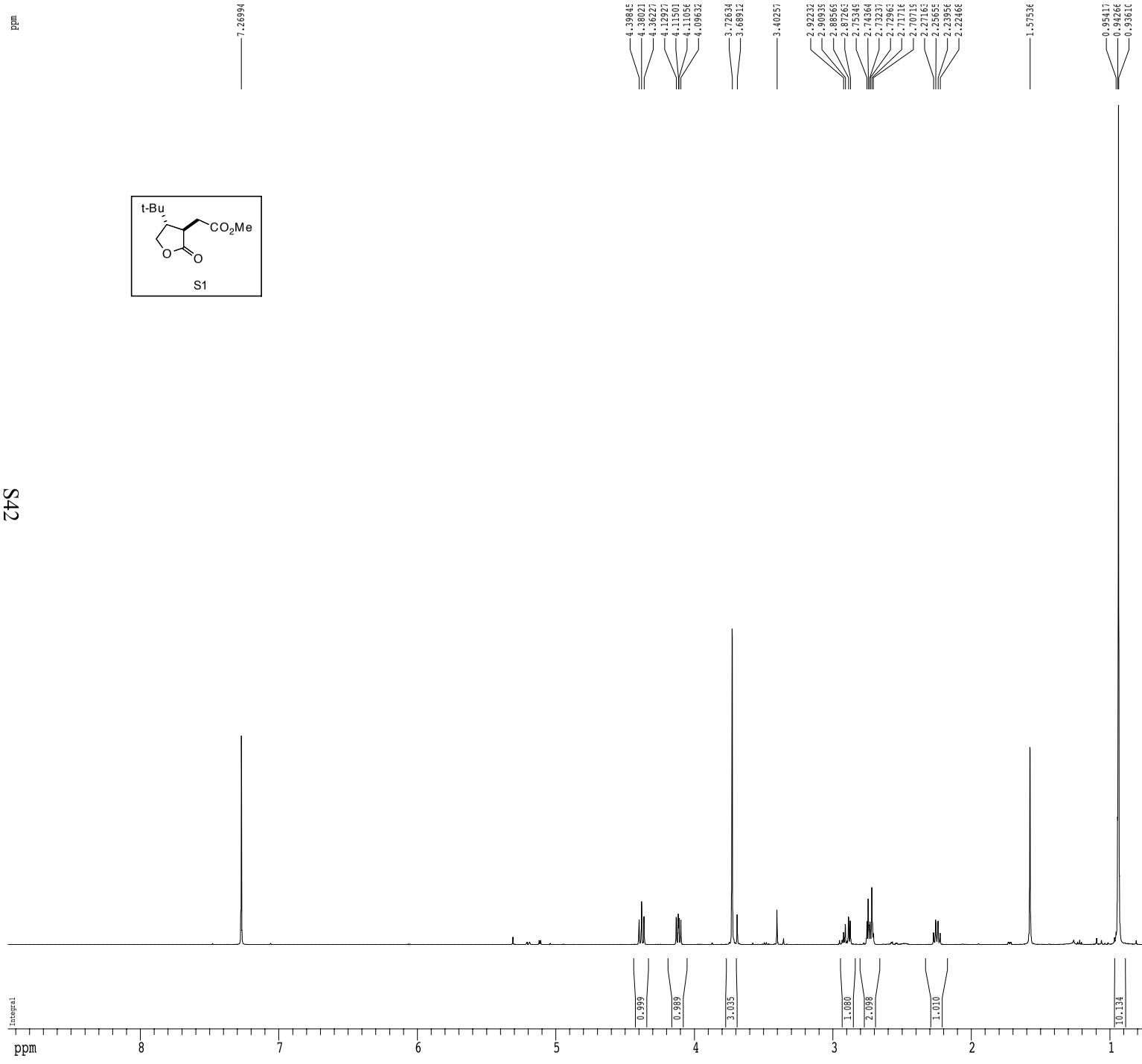
F2 - Processing parameters
SI 65536
SF 125.7803747 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.50

1D NMR plot parameters
CX 22.80 cm
CY 600.00 cm
F1P 230.812 ppm
F1 29031.63 Hz
F2P -10.108 ppm
F2 -1271.40 Hz
PPMCM 10.56668 ppm/cm
HZCM 1329.08032 Hz/cm


Current Data Parameters
USER genung
NAME NEG-I-072
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100803
Time 15.56
INSTRUM qn500
PROBHD 5 mm broadband
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 1024
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 13.00 usec
PL1 -4.00 dB
SFO1 499.6234973 MHz
F2 - Processing parameters
SI 65536
SF 499.6200241 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 10.00 cm
F1P 10.500 ppm
F1 5246.01 Hz
F2P -0.500 ppm
F2 -249.81 Hz
PPMCM 0.48246 ppm/cm
HZCM 241.04475 Hz/cm
0.94466
0.95070
1.26150
1.97781
1.98187
2.71395
2.72126
2.87134
2.89330
2.92963
2.97976
5.57560
6.06273
6.07479
7.27007
9.5484
1.1564
1.1012
1.2015
1.8910
1.0000
0.9824
t-Bu
HO
51
ppm
Integral


Current Data Parameters
USER genung
NAME NEG-I-072
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100804
Time_ 8.04
INSTRUM cryo500
PROBHD 5 mm CPCI 1H-
PULPROG SpinEchop230p.prd
TD 65536
SOLVENT CDCl3
NS 256
DS 16
SWH 30303.031 Hz
FIDRES 0.462398 Hz
AQ 1.0813940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFFS1 0.00 Hz
SPOFFS2 0.00 Hz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804190 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
F1P 220.000 ppm
F1 27671.69 Hz
F2P -5.000 ppm
F2 -628.90 Hz
PPMCM 9.06042 ppm/cm
HZCM 1241.25415 Hz/cm
26.94
27.43
29.76
31.44
36.67
39.61
64.52
76.82
77.07
77.33
102.65
109.26
175.62
t-Bu
H
O
O
H
HO
O
O
51
ppm
0
20
40
60
80
100
120
140
160
180
200
ppm

NEG-II-065a
1H
18-MAY-2011
CRYO 500



Current Data Parameters
USER genung
NAME NEG-II-065a
EXPNO 1
PROCNO 1

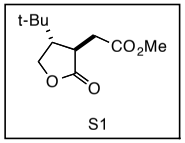
F2 - Acquisition Parameters
Date_ 20110518
Time 20.21
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 12.7
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

F2 - Processing parameters
SI 65536
SF 500.2200274 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00

1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 8.955 ppm
F1 4479.51 Hz
F2P -0.309 ppm
F2 -154.62 Hz
PPMCM 0.40632 ppm/cm
HZCM 203.25117 Hz/cm

NEG-II-065a
13C
18-MAY-2011
CRYO 500



S1

Current Data Parameters
USER genung
NAME NEG-II-065a
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20110518
Time 20.27
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 295
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 13004
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 1.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec

======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

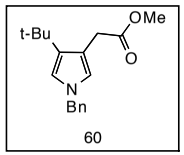
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7803997 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 40.00 cm
F1P 230.637 ppm
F1 29009.68 Hz
F2P -10.287 ppm
F2 -1293.96 Hz
PPMCM 10.56688 ppm/cm
HZCM 1329.10693 Hz/cm

NEG-II-034a
1H
5-APR-2011
CRYO 500



60

Current Data Parameters
USER genung
NAME NEG-II-034a
EXPNO 1
PROCNO 1

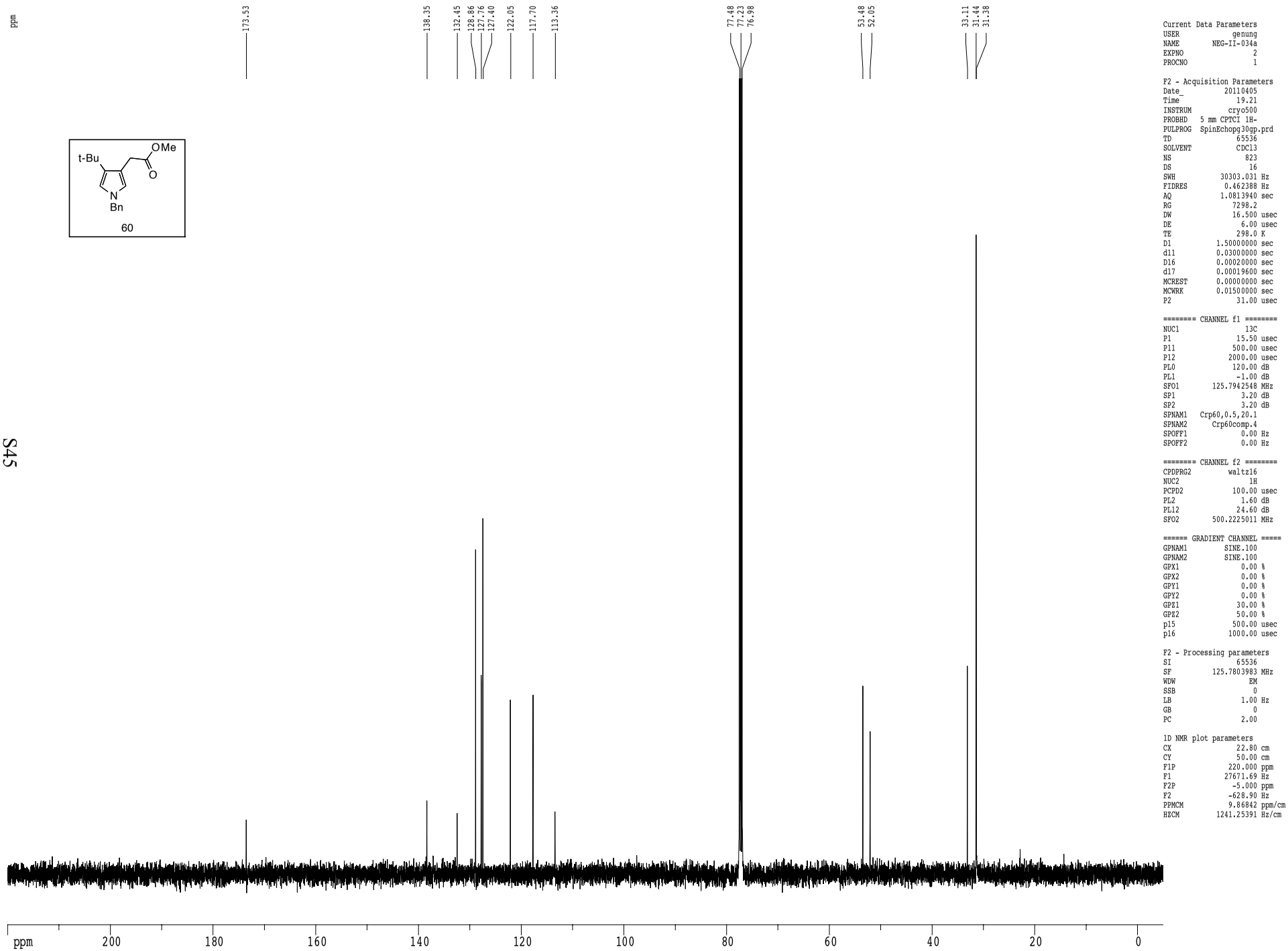
F2 - Acquisition Parameters
Date_ 20110405
Time 19.09
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

F2 - Processing parameters
SI 65536
SF 500.2200251 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00

1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42502 Hz/cm

NEG-II-034a
13C
5-APR-2011
CRYO 500



Current Data Parameters
USER genung
NAME NEG-II-034a
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20110405
Time 19.21
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 823
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 1.50000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec

======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

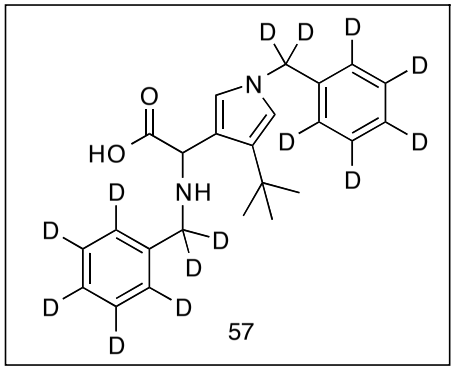
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7803983 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 50.00 cm
F1P 220.000 ppm
F1 27671.69 Hz
F2P -5.000 ppm
F2 -628.90 Hz
PPMCM 9.86842 ppm/cm
HZCM 1241.25391 Hz/cm

1H spectrum



pyrrole 57

d_3-methyl acetate

acetic acid

Current Data Parameters
USER untied
NAME NLU-02-194
EXPNO 1
PROCNO 1

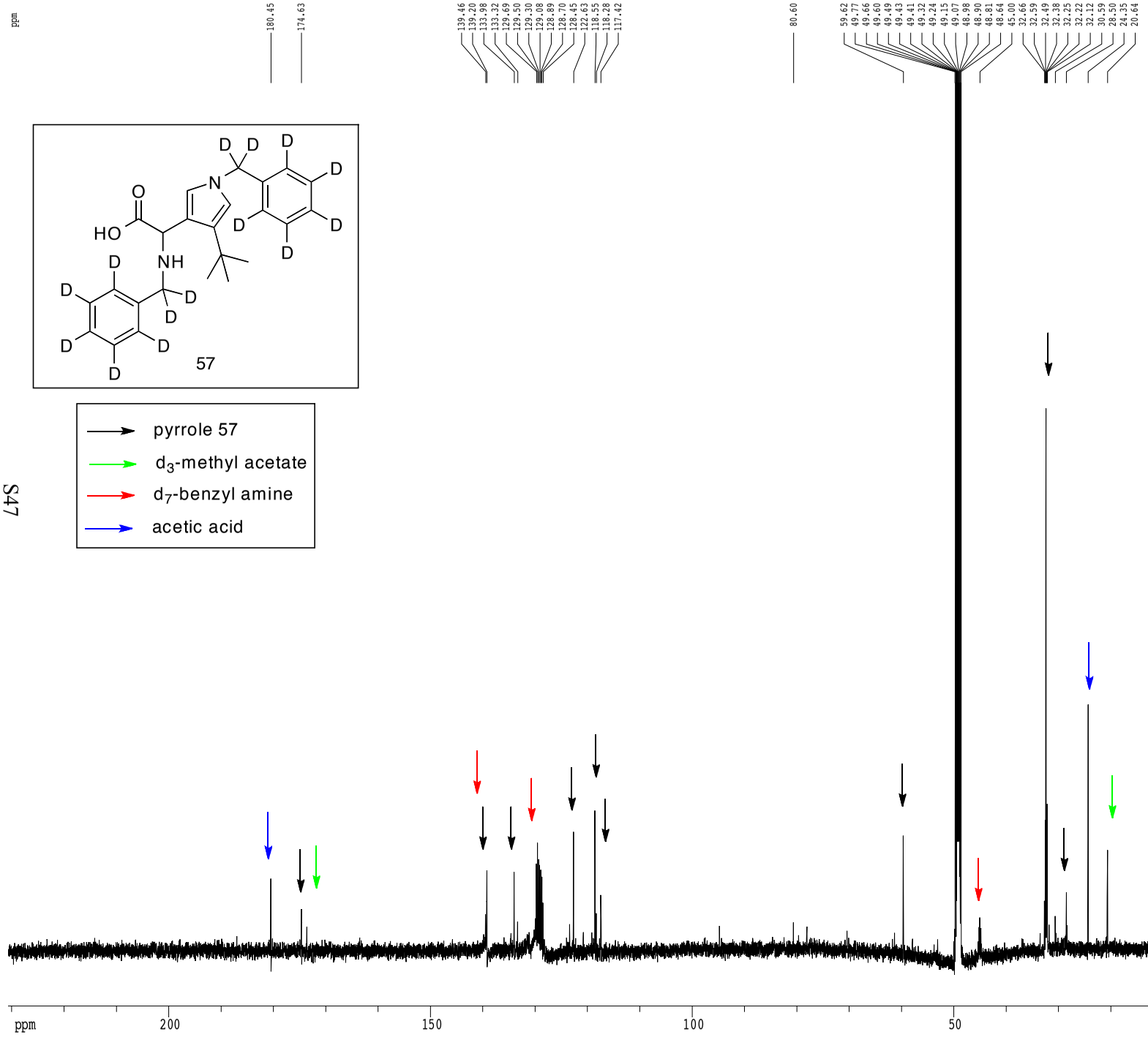
F2 - Acquisition Parameters
Date_ 20110603
Time 0.17
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT MeOH
NS 32
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 6.3
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

F2 - Processing parameters
SI 65536
SF 500.2200117 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00

1D NMR plot parameters
CX 22.80 cm
CY 50.00 cm
F1P 7.200 ppm
F1 3601.58 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.31579 ppm/cm
HZCM 157.96422 Hz/cm

Z-restored spin-echo 13C spectrum with 1H decoupling



S47

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Current Data Parameters
USER              untied
NAME          NLU-02-194
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20110603
Time              23.11
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.prd
TD                65536
SOLVENT            MeOH
NS                 4096
DS                   16
SWH           30303.031 Hz
FIDRES         0.462388 Hz
AQ             1.0813940 sec
RG                 4096
DW               16.500 usec
DE                6.00 usec
TE                298.0 K
D1            2.00000000 sec
d11           0.03000000 sec
D16           0.00020000 sec
d17           0.00019600 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec
P2               31.00 usec

======== CHANNEL f1 ========
NUC1               13C
P1               15.50 usec
P11             500.00 usec
P12            2000.00 usec
PL0             120.00 dB
PL1              -1.00 dB
SFO1        125.7942548 MHz
SP1              3.20 dB
SP2              3.20 dB
SPNAM1   Crp60,0.5,20.1
SPNAM2     Crp60comp.4
SPOFF1             0.00 Hz
SPOFF2             0.00 Hz

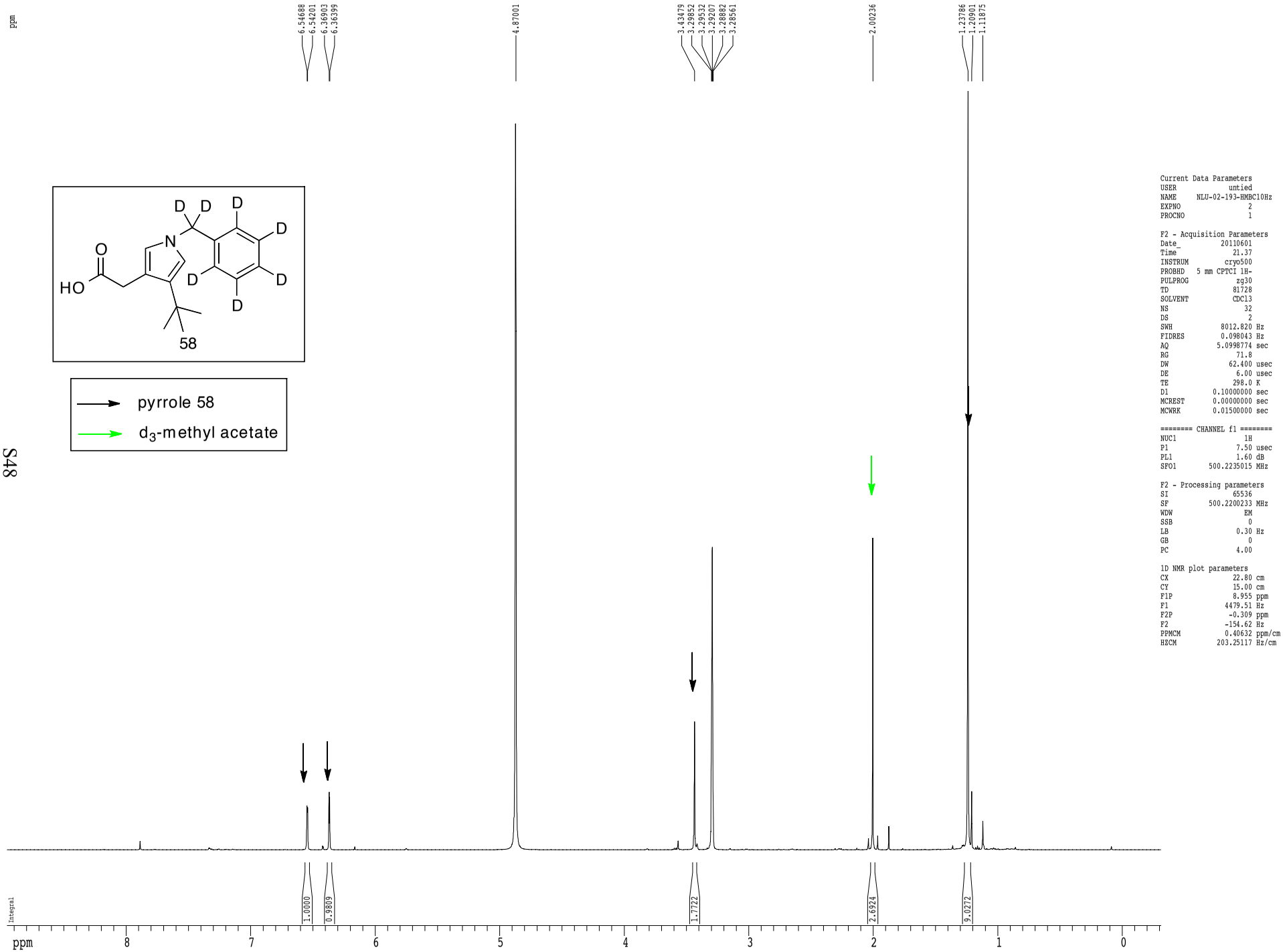
======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2               1H
PCPD2           100.00 usec
PL2              1.60 dB
PL12             24.60 dB
SFO2        500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1         SINE.100
GPNAM2         SINE.100
GPX1               0.00 %
GPX2               0.00 %
GPY1               0.00 %
GPY2               0.00 %
GPZ1              30.00 %
GPZ2              50.00 %
p15             500.00 usec
p16            1000.00 usec

F2 - Processing parameters
SI                65536
SF          125.7802260 MHz
WDW                  EM
SSB                   0
LB                1.00 Hz
GB                    0
PC                2.00

1D NMR plot parameters
CX                22.80 cm
CY                300.00 cm
F1P              230.637 ppm
F1             29009.63 Hz
F2P              -10.287 ppm
F2             -1293.96 Hz
PPMCM            10.56688 ppm/cm
HZCM          1329.10510 Hz/cm
```

1H spectrum



Current Data Parameters
USER untied
NAME NLU-02-193-HMBC10Hz
EXPNO 2
PROCNO 1

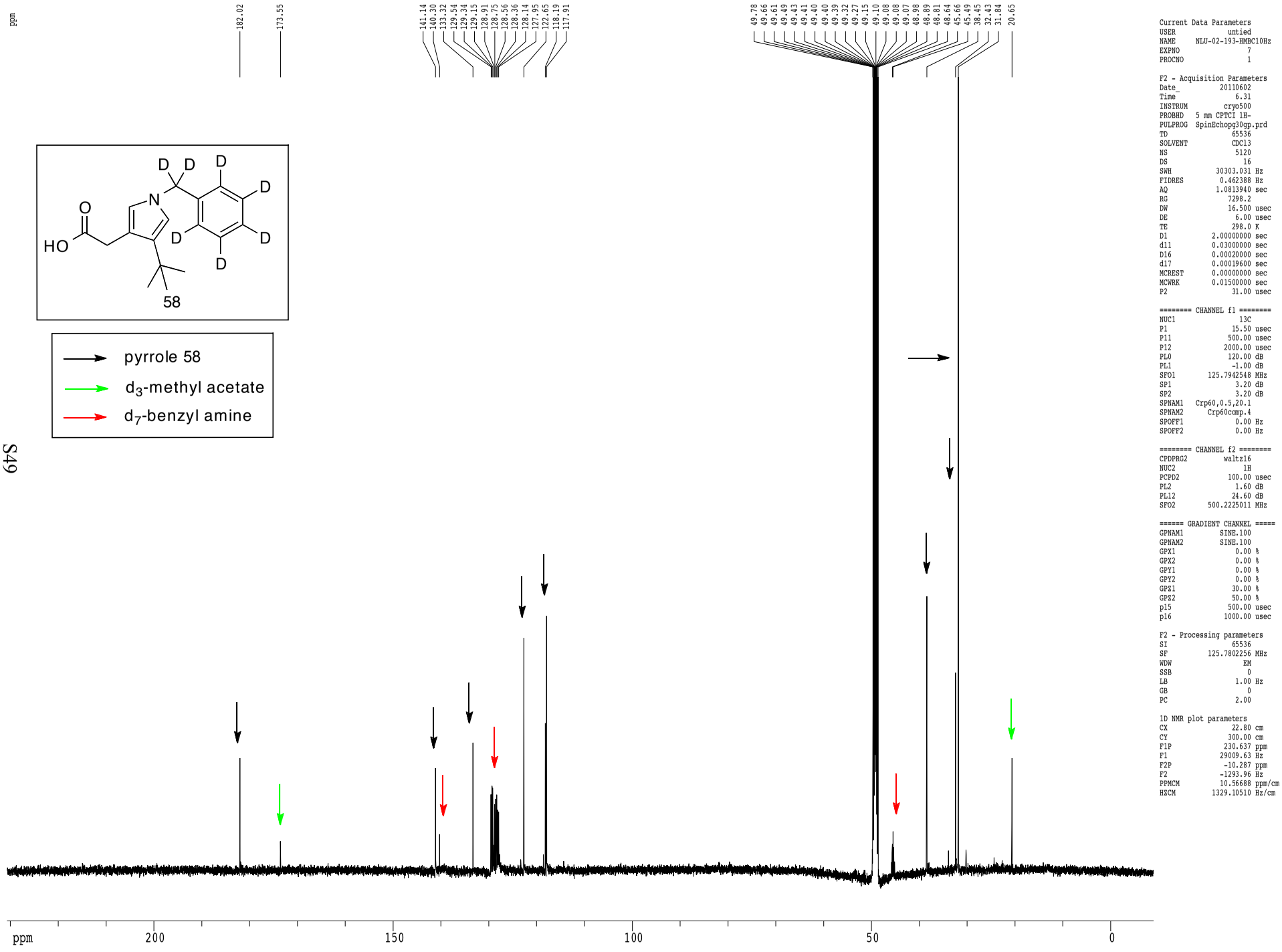
F2 - Acquisition Parameters
Date_ 20110601
Time 21.37
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 32
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 71.8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

F2 - Processing parameters
SI 65536
SF 500.2200233 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00

1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 8.955 ppm
F1 4479.51 Hz
F2P -0.309 ppm
F2 -154.62 Hz
PPMCM 0.40632 ppm/cm
HZCM 203.25117 Hz/cm

Z-restored spin-echo 13C spectrum with 1H decoupling



Current Data Parameters
USER untied
NAME NLU-02-193-HMBC10Hz
EXPNO 7
PROCNO 1

F2 - Acquisition Parameters
Date_ 20110602
Time 6.31
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.prd
TD 65536
SOLVENT CDCl3
NS 5120
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813940 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 2.00000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
P2 31.00 usec

======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM1 Crp60,0.5,20.1
SPNAM2 Crp60comp.4
SPOFF1 0.00 Hz
SPOFF2 0.00 Hz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz

====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPX1 0.00 %
GPX2 0.00 %
GPY1 0.00 %
GPY2 0.00 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7802256 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 300.00 cm
F1P 230.637 ppm
F1 29009.63 Hz
F2P -10.287 ppm
F2 -1293.96 Hz
PPMCM 10.56688 ppm/cm
HZCM 1329.10510 Hz/cm