Total Synthesis of (–)-Sarain A

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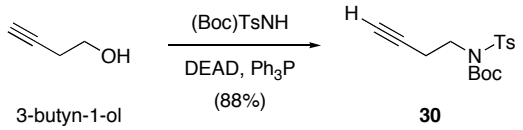
Supporting Information – Table of Contents

Materials and Methods. Unless stated otherwise, reactions were conducted in flame-dried glassware under an atmosphere of nitrogen using anhydrous solvents (either freshly distilled or passed through activated alumina columns). All commercially obtained reagents were used as received. Reaction temperatures were controlled using an IKAmag temperature modulator, and unless stated otherwise, reactions were performed at room temperature (rt, approximately 23 °C). Thin-layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 pre-coated plates, (0.25 mm) and visualized using a combination of UV, anisaldehyde, ceric ammonium molybdate, and potassium permanganate staining. ICN silica gel (particle size 0.032–0.063 mm) was used for flash column chromatography. ^{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 an Applied Systems REACT-IR 1000 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. Elemental analyses were performed at Atlantic Microlab, Inc., P.O. Box 2288, Norcross, Georgia 30091. CD spectra were recorded on a Jasco 810 spectrometer at the UC Irvine Laser Spectroscopy Facility.

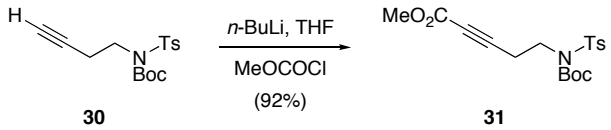
Experimental Procedures.

Supporting information for compounds **35**, **36**, **37**, **38**, **41**–**50** has previously been reported in an earlier publication from our laboratory.[1]



3-butyn-1-ol **30**

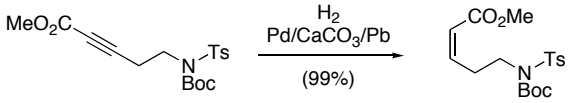
Sulfonamide 30. A solution of 3-butynol-1-ol (6.9 mL, 88.0 mmol), triphenylphosphine (38.5 g, 146 mmol), *N-tert*-butoxycarbonyl-*p*-toluenesulfonamide (19.9 g, 73.3 mmol) and THF (400 mL) was cooled in an ice bath under an N_2 atmosphere. After the dropwise addition of diethylazidodicarboxylate (20.8 mL, 131.9 mmol), the ice bath was removed and the solution was allowed to stir for 24 h. The mixture was then concentrated under reduced pressure, absorbed onto silica gel and purified by flash chromatography (1:7 EtOAc:hexanes, then 1:6 EtOAc:hexanes) to yield sulfonamide **30** (20.9 g, 88%) as a colorless oil. R_f 0.57 (20% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79 (d, J = 8.3, 2H), 7.31 (d, J = 8.3, 2H), 4.00 (m, 2H), 2.65 (m, 2H), 2.43 (s, 3H), 2.03 (t, J = 2.7, 1H), 1.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.6, 144.2, 137.0, 129.1, 127.7, 84.4, 80.3, 70.4, 45.1, 27.7, 21.4, 19.8; IR (film): 3289, 2982, 1732, 1359, 1157 cm^{-1}; HRMS-CI (*m/z*): [M + H]$^+$ calcd for $C_{16}H_{22}NO_4S$, 32.1269; found, 324.1279; Anal. Calcd for $C_{16}H_{21}NO_4S$: C, 59.42; H, 6.55; N, 4.33; found: C, 59.33; H, 6.56; N, 4.33.



30 **31**

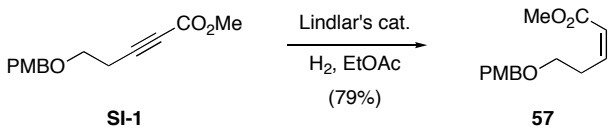
Ynoate 31. A solution of alkyne **30** (21.46 g, 66.5 mmol) in THF (200 mL) was cooled to –78 °C under N_2 atmosphere. *n*-BuLi (2.5 M, 28.4 mL, 71.1 mmol) was added dropwise down the side of the flask at a rate that does not cause the internal temperature of the reaction to go above –60 °C as monitored by a thermocouple probe. The reaction was slowly warmed to –30 °C and then re-cooled to –78 °C. Another flask was charged with THF (200 mL) and methyl chloroformate (18.4 mL, 199.4 mmol) and was cooled to –78 °C under N_2 atmosphere. The anion was added to the chloroformate via cannula, again in a manner such that the solution of the anion

travels down the side of the cooled flask. After the addition was complete, the mixture was allowed to warm to rt, quenched with saturated NH_4Cl (50 mL), and concentrated under reduced pressure. The resulting solution was extracted with Et_2O (3 × 100 mL) and the organic phases were collected, washed with 10% HCl (50 mL) and saturated $NaHCO_3$(2 × 50 mL), dried with Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography (gradient: 1:7 EtOAc:hexanes to 1:2 EtOAc:hexanes) to give ynoate **31** (23.25 g, 92%) as a viscous oil which solidified upon standing to give a white amorphous solid. R_f 0.38, 20% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, J = 8.1, 2H), 7.79 (d, J = 8.1, 2H), 4.04 (t, J = 7.4, 2H), 3.76 (s, 3H), 2.82 (t, J = 7.4, 2H), 2.45 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.8, 150.5, 144.4, 136.9, 129.3, 127.8, 85.2, 84.8, 74.4, 52.6, 44.1, 27.8, 21.6, 20.2; IR (film): 2981, 2242, 1720, 1356, 1259 cm^{-1}; HRMS-FAB (m/z): [M + Na]$^+$ calcd for $C_{18}H_{23}NO_6SNa$, 404.1144; found, 404.1150; Anal. Calcd for $C_{18}H_{23}NO_6S$: C, 56.68; H, 6.08; N, 3.67; found: C, 56.75; H, 6.09; N, 3.65.



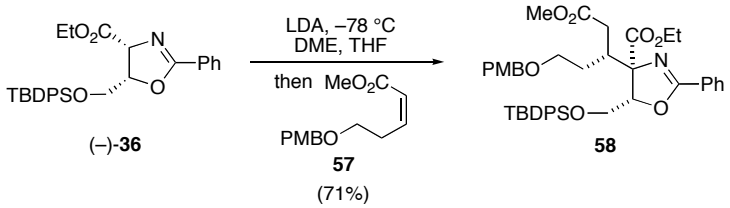
31 **32**

(*Z*)-Enoate 32. A three–neck flask containing ynoate **31** (4.74 g, 12.4 mmol), Lindlar catalyst (5% Pd/$CaCO_3$ with 3.5% Pb, 185 mg, 0.04 wt% catalyst loading) and toluene (100 mL) was fitted with 2 septa and a balloon of hydrogen gas. The reaction vessel was evacuated and backfilled with hydrogen 5 times. The reaction mixtures was stirred at rt for 3 h, filtered through celite, and concentrated at ambient temperature to give enoate **32** (4.7 g, 99%) as a near colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, J = 8.2, 2H), 7.31 (d, J = 8.2, 2H), 6.31 (dt, J = 11.5, 7.5, 1H), 5.92 (dt, J = 11.5, 1.7, 1H), 3.97 (m, 2H), 3.73 (s, 3H), 3.12 (m, 2H), 2.43 (s, 3H), 1.32 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.4, 150.8, 145.2, 144.1, 137.3, 129.2, 127.8, 121.5, 84.3, 51.1, 45.7, 29.5, 27.8, 21.5; IR (film): 2981, 1725, 1649, 1598, 1439, 1357, 1291, 1257, 1157, 1088, 816, 721, 674 cm^{-1}; HRMS-CI(m/z): [M + H]$^+$ calcd for $C_{18}H_{26}NO_6S$, 384.1480; found, 384.1469.



SI-1 **57**

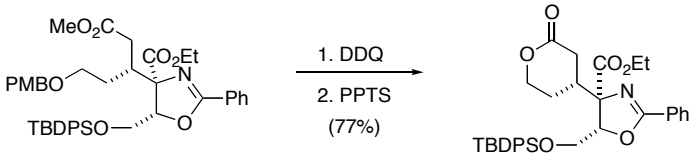
(*Z*)-Enoate 57. Lindlar's catalyst was added to a suspension of polyvinylpyridine, ynoate **SI–1**[2] (39.0 g, 157.1 mmol) and EtOAc (300 mL) at rt under nitrogen. The reaction vessel was evacuated and backfilled with hydrogen 3 times, then allowed to stir under an atmosphere of H_2 for 2 d. The reaction mixture was filtered through celite, concentrated under reduced pressure, diluted with Et_2O, absorbed on silica gel, then purified by flash chromatography (3% EtOAc-hexanes; then 5% EtOAc-hexanes; then 10% EtOAc-hexanes; then 15% EtOAc-hexanes) to give enoate **57** (31.0 g, 123.9 mmol, 79% yield). Enoate **57** was used directly in the subsequent transformation.



(–)-**36** **57** (71%) **58**

Michael adduct 58. Oxazoline (–)-**36** was prepared following the procedure previously used to synthesize (+)-**36**.[1] Both enoate **57** and oxazoline (–)-**36** were separately dried by azeotroping with PhMe, and then further dried under vacuum for 2 h. A solution of oxazoline (–)-**36** (10.3 g, 21.1 mmol, 1.00 equiv) and DME (20 mL) was added dropwise by syringe pump to a solution of freshly prepared LDA (28.6 mmol, 1.4 equiv) at –78 °C. The reaction was maintained at –78 °C for 30 min. A solution of enoate **57** (14.0 g, 55.9 mmol, 2.7 equiv) and DME (10 mL) was added dropwise by syringe pump to the newly generated oxazoline enolate solution. After addition, the reaction mixture was stirred at –78 °C for 2 h and then placed in a cryocool bath maintained at –65 °C for 19 h. The reaction mixture was poured into sat. aqueous NH_4Cl and extracted with Et_2O (3 x 100 mL). The combined organic extracts was dried over $MgSO_4$ and concentrated under reduced pressure to give a residue that was purified by flash chromatography (3% EtOAc-hexanes, 5% EtOAc-hexanes, 10% EtOAc-hexanes, 15% EtOAc-hexanes, 20% EtOAc-hexanes), affording Michael adduct **58** (11.1 g, 15.0 mmol, 71% yield) as a pale yellow viscous oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.05 (d, J =7.1, 2H), 7.66 (td, J = 6.6, 1.4, 3H), 7.52–7.49 (m, 1H), 7.44–7.35 (m, 9H), 7.27 (d, J = 8.4, 2H), 6.88 (d, J = 8.6, 2H), 4.76

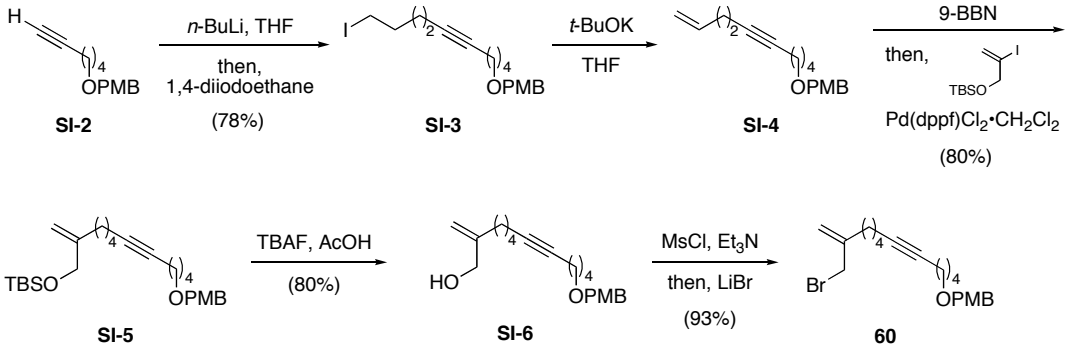
(dd, *J* = 2.7, 2.8, 1H), 4.42 (q, *J* = 16.9, 5.3, 2H), 4.21–4.11 (m, 3H), 3.97 (dd, *J* = 11.5, 2.6, 1H), 3.77 (s, 3H), 3.58 (s, 3H), 3.63–3.50 (m, 2H), 2.74–2.67 (m, 2H), 2.33 (dd, *J* = 15.7, 7.1, 1H), 2.05–1.99 (m, 1H), 1.87–1.81 (m, 1H), 1.18 (t, *J* = 7.1, 3H), 0.99 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.6, 135.3, 133.1, 132.6, 131.4, 130.4, 129.54, 129.51, 128.9, 128.5, 128.0, 127.5, 127.4, 127.2, 113.5, 85.4, 81.2, 72.3, 68.0, 63.4, 61.2, 55.0, 51.4, 41.8, 34.6, 31.1, 26.5, 18.9, 13.8; IR (film): 1731, 1656 cm^{-1}; HRMS-FAB (*m/z*): $[M + H]^+$ calcd for $C_{43}H_{52}NO_8Si$, 738.3462; found, 738.3443; Anal. Calcd for $C_{43}H_{51}NO_8Si$: C, 69.99; H, 6.97; N, 1.90; found: C, 70.26; H, 7.19; N, 1.96; $[\alpha]^{26}_{405}$ +111.8, $[\alpha]^{26}_{435}$ +94.6, $[\alpha]^{26}_{546}$ +54.4, $[\alpha]^{26}_{577}$ +44.6, $[\alpha]^{26}_{D}$ +48.5, (*c* 0.75, $CHCl_3$).



58 **59**

Lactone 59. DDQ (14.0 g, 61.7 mmol, 1.91 equiv) was added to a solution of Michael adduct **58** (23.8 g, 32.3 mmol, 1.00 equiv), CH_2Cl_2 (200 mL) and H_2O (10 mL). The reaction mixture was vigorously stirred at rt for 1.5 h, then poured into chilled 1 N aqueous NaOH and extracted with CH_2Cl_2 (3 x 200 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and evaporated under reduced pressure to give the crude product. Purification by flash chromatography (10% EtOAc-hexanes, 30% EtOAc-hexanes, 50% EtOAc-hexanes) furnished a mixture of alcohol and lactone products. The mixture of crude products was dissolved in CH_2Cl_2 (300 mL) and treated with PPTS (2.0 g, 7.96 mmol). After stirring at rt for 1.5 h, the reaction mixture was poured into chilled 1 N aqueous HCl, and extracted with CH_2Cl_2 (3 x 200 mL). The combined organic layers were dried over $MgSO_4$, then concentrated under reduced pressure to give a residue the crude product. Purification by flash chromatography (SiO_2, 25% EtOAc-hexanes, 30% EtOAc-hexanes, 50% EtOAc-hexanes) afforded lactone **59** (16.5 g, 28.2 mmol, 77% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (d, *J* = 8.1, 2H), 7.60 (t, *J* = 7.0, 4H), 7.54–7.51 (m, 1H), 7.44–7.39 (m, 4H), 7.37–7.32 (m, 4H), 4.53 (t, *J* = 3.1, 1H), 4.42 (ddd, *J* = 11.4, 10.7, 5.0, 1H), 4.25–4.20 (m, 1H), 4.19–4.10 (m, 2H), 4.01 (dd, *J* = 11.7, 4.2, 1H), 3.89 (dd, *J* = 11.7, 2.8, 1H), 2.62–2.58 (m, 2H), 2.26 (dd, *J* = 18.2, 12.2, 1H), 2.07–2.03 (m, 1H), 1.92–1.89 (m, 1H), 1.16 (t, *J* = 7.1, 3H), 0.97 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.9, 170.5, 165.2,

135.6, 135.4, 132.9, 132.5, 131.9, 129.73, 129.69, 128.6, 128.2, 127.60, 127.56, 84.4, 80.5, 67.7, 63.1, 61.6, 39.4, 30.3, 26.5, 24.3, 18.9, 13.9; IR (film): 1749, 1643 cm^{-1}; HRMS-FAB (*m/z*): [M + H]$^+$ calcd for $C_{34}H_{40}NO_6Si$, 586.2625; found, 586.2630; Anal. Calcd for $C_{34}H_{39}NO_6Si$: C, 69.71; H 6.71; N, 2.39; found: C, 69.45; H, 6.62; N, 2.25; $[\alpha]^{26}_{405}$ +147.4, $[\alpha]^{26}_{435}$ +122.8, $[\alpha]^{26}_{546}$ +69.5, $[\alpha]^{26}_{577}$ +59.8 $[\alpha]^{26}_{D}$ +64.8 (*c* 0.95, $CHCl_3$).



Allylic bromide 60. Alkyne **SI-2**[3] (10.0 g, 45.8 mmol, 1.00 equiv) was added dropwise to a solution of *n*-BuLi (62.1 mmol, 1.36 equiv) in THF (60 mL) at –78 °C. The reaction mixture was stirred at –78 °C for 1.5 h, then neat 1,4-diiodobutane (12 mL, 91.0 mmol, 2.00 equiv) was added. The solution was allowed to warm to rt, heated at 60 °C for 18 h, cooled to rt, then poured into sat. aqueous NH_4Cl. The mixture was extracted with Et_2O (2 x 150 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (5% EtOAc-hexanes, 10% EtOAc-hexanes, 15% EtOAc-hexanes) provided iodide **SI-3** (14.2 g, 35.5 mmol, 78% yield) as an oil. This intermediate was typically used directly in subsequent transformations.

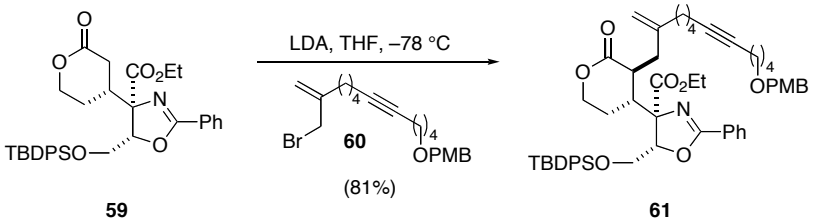
A solution of *t*-BuOK (1.0 M in THF, 14.0 mL, 14.0 mmol, 1.30 equiv) was added dropwise to a solution of iodide **SI-3** (4.30 g, 10.74 mmol, 1.00 equiv) in THF (15 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min, poured into ice-cold H_2O, and extracted with Et_2O (2 x 50 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure to give alkene **SI-4**. This intermediate was typically used directly in the subsequent transformation.

A solution of alkene **SI-4** (3.72 g, 13.66 mmol) in THF (5.0 mL) was added dropwise to a solution of 9-BBN dimer (1.60 g, 6.56 mmol) in THF (30 mL) at 0 °C. The reaction mixture was allowed to warm to rt. After 3 h at rt, the mixture was cooled to 0 °C and 3 N aqueous NaOH

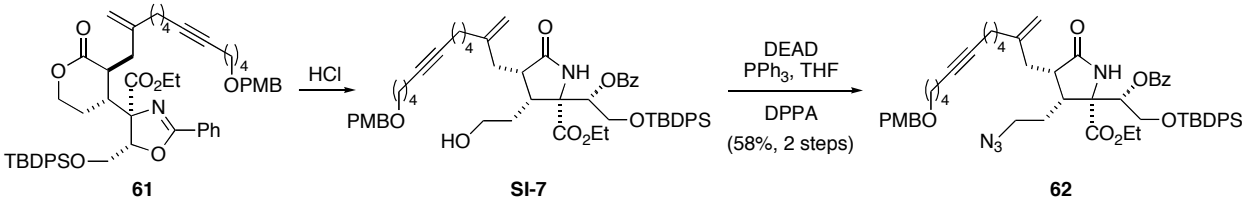
(7.5 mL) was added. After stirring vigorously for 45 min, this mixture was added to a suspension of (2-iodoallyloxy)(*t*-butyl)dimethylsilane[4] (4.04 g, 13.55 mmol) and $PdCl_2(pddf)_2 \bullet CH_2Cl_2$ (720 mg, 0.88 mmol) in THF (15 mL). The reaction mixture was stirred at rt for 16 h, poured into brine, and extracted with Et_2O (3 x 30 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The crude residue was purified by flash chromatography (100% hexanes, 3% EtOAc-hexanes, 5% EtOAc-hexanes, 10% EtOAc-hexanes) to furnish product **SI-5** (4.80 g, 80%) as an oil.

A solution of glacial acetic acid (1.8 mL) and TBAF (30 mL, 30.0 mmol, 1 M in THF) was added to a solution of **SI-5** (4.8 g, 10.8 mmol, 1.00 equiv) and THF (30 mL) at 0 °C. The reaction mixture was allowed to warm to rt. After stirring at rt for 24 h, the mixture was poured into sat. aqueous $NaHCO_3$ (50 mL) and extracted with Et_2O (3 x 40 mL). The combined organic extracts were dried over $MgSO_4$, then concentrated under reduced pressure. Purification by flash chromatography (5% EtOAc-hexanes, 30% EtOAc-hexanes) gave allylic alcohol **SI-6** (2.86 g, 80% yield) as a pale yellow oil.

MsCl (2.6 mL, 33.6 mmol) was added dropwise to a solution of **SI-6** (4.40 g, 13.3 mmol) and Et_3N (9.3 mL, 66.7 mmol) in (120 mL) at –78 °C. After 2 h and 15 min, the reaction mixture was poured into sat. aqueous $NaHCO_3$ and extracted with CH_2Cl_2 (3x). The combined organic extracts were dried over $MgSO_4$, and concentrated under reduced pressure. The crude mesylate was added to LiBr (10 g) in THF (100 mL) at 0 °C. The reaction mixture was allowed to warm to rt, then stirred for ~12 h. The resulting mixture was poured into brine and extracted with Et_2O (3x). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Filtration through basic alumina afforded allylic bromide **60** (4.9 g, 93%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 (d, *J* = 8.6, 2H), 6.88 (d, J = 8.6, 2H), 5.16 (s, 1H), 4.97 (s, 1H), 4.43 (s, 2H), 3.97 (s, 2H), 3.80 (s, 3H), 3.46 (t, *J* = 6.4, 2H), 2.23 (t, *J* = 7.3, 2H), 2.21–2.16 (m, 4H), 1.73–1.71 (m, 2H), 1.67–1.51 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.1, 145.3, 130.7, 129.2, 115.0, 113.7, 80.2, 80.0, 72.5, 69.6, 55.2, 36.7, 32.8, 28.9, 28.5, 26.4, 25.8, 18.56, 18.54; IR (film): 1607, 1507 cm^{-1}; HRMS-EI (*m/z*): $[M - H]^+$ calcd for $C_{20}H_{29}BrO_2$, 391.1273, 393.1255; found, 391.1286, 393.1262.

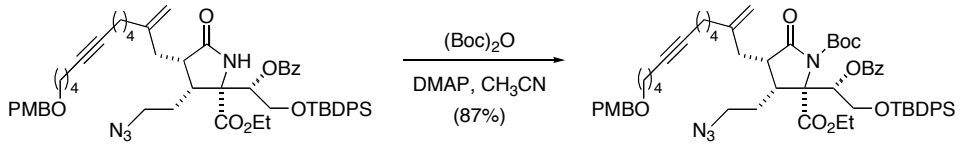


Lactone 61. A solution of lactone **59** (690 mg, 1.18 mmol) in THF (10 mL) was added dropwise via syringe pump to a solution of LDA (2.3 mL, 1.79 mmol, 0.78 M in THF) –78 °C. The reaction was stirred at –78 °C for 1.3 h, then a solution of bromide **60** (700 mg, 1.78 mmol) and HMPA (1 mL) was added dropwise via syringe pump to the newly generated enolate. The reaction mixture was stirred at –78 °C for 30 min, then placed in a cryocool bath maintained at –55 °C for 14 h. The reaction mixture was poured into sat. aqueous NH_4Cl (5 mL) and extracted with EtOAc (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash chromatography (5% EtOAc-hexanes, 10% EtOAc-hexanes, 30% EtOAc-hexanes, 40% EtOAc-hexanes) provided alkyne **61** (862 mg, 81%) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (d, *J* = 7.5, 2H), 7.62 (d, *J* = 6.8, 4H), 7.49 (t, *J* = 7.2, 1H), 7.43–7.34 (m, 8H), 7.25 (d, *J* = 8.5, 2H), 6.87 (d, *J* = 8.5, 2H), 4.90 (s, 1H), 4.85–4.82 (m, 2H), 4.42 (s, 2H), 4.41–4.40 (m, 1H), 4.34 (q, *J* = 5.8, 1H), 4.22–4.16 (m, 1H), 4.12–4.07 (m, 2H), 3.94 (dd, *J* = 11.7, 2.4, 1H), 3.79 (s, 3H), 3.45 (t, *J* = 6.4, 2H), 2.65–2.60 (m, 1H), 2.50 (dd, *J* = 13.6, 5.3, 1H), 2.45 (t, *J* = 5.7, 1H), 2.33 (dd, *J* = 13.5, 10.0, 1H), 2.15–2.03 (m, 7H), 1.96–1.91 (m, 1H), 1.74–1.65 (m, 2H), 1.57–1.46 (m, 6H), 1.16 (t, *J* = 7.1, 3H), 0.96 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.4, 170.8, 165.4, 159.1, 145.3, 135.7, 135.4, 133.2, 132.6, 131.8, 130.7, 129.8, 129.7, 129.1, 128.7, 128.2, 127.63, 127.61, 126.6, 113.9, 113.7, 86.2, 80.9, 80.0, 72.4, 69,6, 66.6, 63.1, 61.5, 55.2, 44.1, 40.5, 39.8, 34.3, 28.8, 28.6, 26.7, 26.6, 25.8, 22.5, 19.0, 18.52, 18.48, 13.9; IR (film): 1745, 1654 cm^{-1}; HRMS-FAB (*m/z*): $[M + H]^+$ calcd for $C_{55}H_{68}NO_8Si$, 898.4714; found, 898.4727; $[\alpha]^{26}_{405}$ –18.2, $[\alpha]^{26}_{435}$ –13.5, $[\alpha]^{26}_{546}$ –5.9, $[\alpha]^{26}_{577}$ –3.9, $[\alpha]^{26}_{D}$ –3.2 (*c* 0.90, $CHCl_3$).

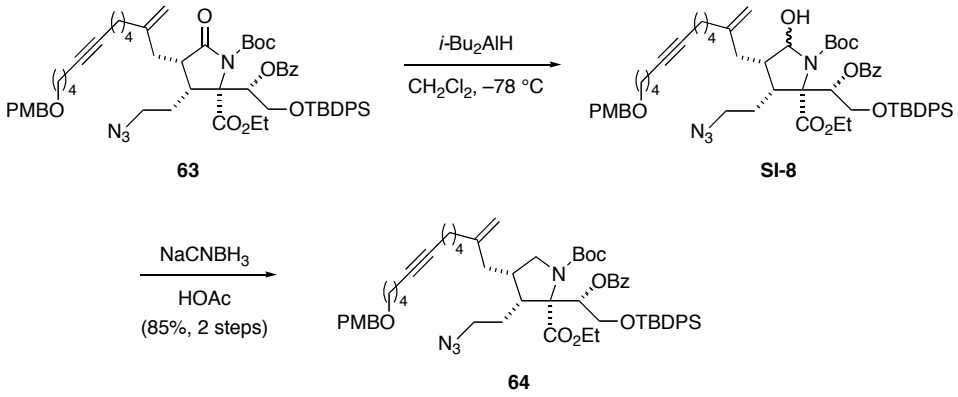


Azide 62. A homogeneous solution of alkyne **61** (2.05 g, 2.28 mmol), THF (10 mL) and 1.0 N aqueous HCl (14 mL) was stirred at rt for 12 h, then extracted with EtOAc (3 × 100 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash chromatography (5% EtOAc-hexanes, 10% EtOAc-hexanes, 30% EtOAc-hexanes, 50% EtOAc-hexanes) provides starting material alkyne **61** (0.37 g, 0.41 mmol, 18%) and pyrrolidinone **SI-7** (1.35 g, 1.47 mmol, 64%) as a white foam. Pyrrolidinone **SI-7** was typically used directly in subsequent transformations.

A solution of pyrrolidinone-alcohol **SI-7** (920 mg 1.00 mmol, 1.00 equiv) in THF (12 mL) was cooled to 0 °C. Reagents were added in the following order: solid PPh_3 (340 mg, 1.30 mmol, 1.30 equiv), dropwise addition of DEAD (210 μL, 1.33 mmol, 1.33 equiv), and then dropwise addition of DPPA (300 μL, 1.40 mmol, 1.40 equiv). The reaction mixture was stirred at 0 °C for 2.3 h, then concentrated under reduced pressure. Purification of the residue by flash chromatography (5% EtOAc-hexanes, 10% EtOAc-hexanes, 30% EtOAc-hexanes, 50% EtOAc-hexanes) furnished azide **62** (850 mg, 0.903 mmol, 90%) as a viscous oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10 (dd, *J* = 7.2, 1.1, 2H), 7.65 (tt, *J* = 7.5, 1.2, 1H), 7.58–7.54 (m, 4H), 7.51 (t, *J* = 7.6, 2H), 7.41 (tt, *J* = 7.3, 1.3, 1H), 7.34–7.30 (m, 3H), 7.25 (d, *J* = 8.6, 2H), 7.13 (t, *J* = 7.7, 2H), 6.87 (d, *J* = 8.7, 2H), 6.83 (s, 1H), 5.59 (t, *J* = 2.7, 1H), 4.83 (s, 1H), 4.78 (s, 1H), 4.43 (s, 2H), 4.30–4.27 (m, 2H), 3.98 (dd, *J* = 12.2, 3.0, 1H), 3.87 (dd, *J* = 12.3, 2.4, 1H), 3.80 (s, 3H), 3.46 (t, *J* = 6.5, 2H), 3.31–3.27 (m, 1H), 3.22–3.19 (m, 1H), 2.70–2.67 (m, 2H), 2.39 (dd, *J* = 14.9, 4.8, 1H), 2.19–2.13 (m, 5H), 2.06–2.04 (m, 2H), 1.88–1.83 (m, 1H), 1.75–1.66 (m, 3H), 1.57–1.44 (m, 6H), 1.34 (t, *J* = 7.2, 3H), 1.07 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 177.6, 171.2, 165.4, 159.1, 146.5, 135.4, 135.3, 133.7, 131.8, 131.6, 130.7, 130.1, 111.4, 80.1, 80.0, 72.45, 72.40, 69.6, 64.4, 62.3, 55.2, 49.7, 41.5, 40.3, 34.8, 33.6, 28.9, 28.7, 26.7, 26.6, 25.8, 25.4, 19.0, 18.6, 18.5, 4.1; IR (film): 3428, 3200, 2098, 1740, 1721, 1697 cm^{-1}; HRMS-FAB (*m*/*z*): $[M + H]^+$ calcd for $C_{55}H_{69}N_4O_8Si$, 941.4885; found, 941.4916; $[\alpha]^{26}_{405}$ –6.2, $[\alpha]^{26}_{435}$ –4.6, $[\alpha]^{26}_{546}$ –3.2, $[\alpha]^{26}_{577}$ –3.1, $[\alpha]^{26}_{D}$ –4.2 (*c* 0.90, $CHCl_3$).



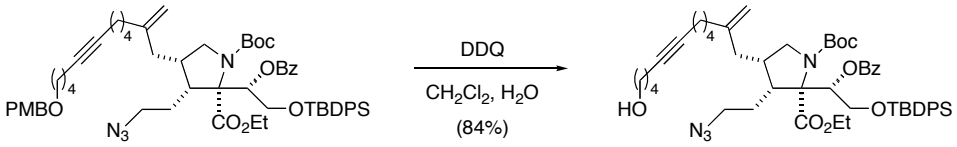
Imide 63. Di-*tert*-butyl dicarbonate (800 mg, 3.67 mmol, 2.19 equiv) and DMAP (50 mg, 0.41 mmol) were added sequentially to a solution of pyrrolidinone **62** (1.58 g, 1.67 mmol, 1.00 equiv) and CH_3CN (20 mL) at rt. The reaction mixture was stirred at rt for 3 h, quenched with saturated aqueous $NaHCO_3$ (25 mL), then extracted with Et_2O (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude product by flash chromatography (5% EtOAc-hexanes, 10% EtOAc-hexanes, 25% EtOAc-hexanes) afforded imide **63** (151 g, 1.45 mmol, 87% yield) as a thick oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18 (d, *J* = 8.2, 2H), 7.67–7.63 (m, 3H), 7.59 (d, *J* = 7.8, 2H), 7.54 (t, *J* = 7.3, 2H), 7.40–7.37 (m, 1H), 7.32 (t, *J* = 6.9, 2H), 7.29–7.25 (m, 3H), 7.09 (t, *J* = 7.4, 2H), 6.87 (d, *J* = 8.5, 2H), 6.21 (br s, 1H), 4.92 (s, 1H), 4.87 (s, 1H), 4.43 (s, 2H), 4.17 (q, *J* = 7.2, 2H), 3.92–3.88 (m, 2H), 3.83–3.80 (m, 1H), 3.79 (s, 3H), 3.51–3.45 (m, 3H), 3.40–3.34 (m, 1H), 2.90 (dd, *J* = 15.2, 8.5, 1H), 2.59 (dd, *J* = 15.0, 8.5, 1H), 2.39 (dd, *J* = 15.0, 6.2, 1H), 2.19–2.09 (m, 7H), 1.72–1.51 (m, 9H), 1.46 (s, 9H), 1.19 (t, *J* = 7.1, 3H), 1.01 (s, 9H);); ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.3, 170.3, 164.8, 159.1, 149.7, 145.9, 135.4, 135.3, 133.2, 132.0, 131.9, 130.7, 130.0, 129.8, 129.7, 129.1, 128.6, 127.8, 127.6, 113.7, 112.3, 84.0, 80.1, 80.0, 73.4, 72.4, 69.9, 69.6, 63.5, 61.8, 55.2, 50.4, 41.8, 35.1, 34.7, 34.3, 29.0, 28.9, 28.8, 27.8, 26.7, 26.5, 26.1, 25.8, 18.8, 18.6, 18.5, 13.9; IR (film): 2099, 1796, 1750, 1721 cm^{-1}; MS-FAB (*m*/*z*): [M + Na]$^+$ calcd for $C_{60}H_{76}N_4O_{10}SiNa$, 1063; found, 1063; $[\alpha]^{26}_{405}$ +98.9, $[\alpha]^{26}_{435}$ +79.5, $[\alpha]^{26}_{546}$ +39.8, $[\alpha]^{26}_{577}$ +32.4, $[\alpha]^{26}_{D}$ +38.6 (*c* 1.35, $CHCl_3$).



Pyrrolidine 64. *i*-BuAl_2H (1.5 M in PhMe, 300 μL, 0.45 mmol, 1.47 equiv) was added dropwise to a solution of imide **63** (320 mg, 0.31 mmol, 1.00 equiv) in CH_2Cl_2 (4.0 mL) at –78 °C. The reaction mixture was held at –78 °C for 30 min, quenched with EtOAc (0.7 mL), then slowly warmed to 0 °C. 1 N aqueous HCl (5.0 mL) was added, and the resulting mixture was vigorously stirred until two clear layers were present. The mixture was partitioned, and the aqueous phase was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated to give a 3:2 mixture of hemiaminals **SI-8** as an oil. The crude hemiaminal product was used directly in the next step without further purification.

Hemiaminal **SI-8** was dissolved in glacial acetic acid (10 mL), then $NaCNBH_3$ (100 mg, 1.59 mmol, 5.1 equiv) was added in three portions over a period of 4 h. The reaction mixture was poured into chilled 1 N aqueous NaOH, then extracted with EtOAc (3 x 25 mL). The combined organic extracts were washed with brine (1 x 50 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude product by flash chromatography (5% EtOAc-hexanes, 10% EtOAc-hexanes, 25% EtOAc-hexanes) gave pyrrolidine **64** (268 mg, 0.261 mmol, 85% yield, 2 steps), which was characterized as a mixture of rotamers. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19–8.11 (m, 2H), 7.73–7.48 (m, 4H), 7.42–7.37 (m, 4H), 7.34–7.27 (m, 5H), 7.23–7.08 (m, 2H), 6.88 (d, *J* = 8.6, 2H), 6.16 & 6.12 (minor rotamer: *J* = 2.9, major rotamer: *J* = 3.1, 1H), 4.89 & 4.87 (minor and major rotamer: s, 1H), 4.77 & 4.75 (major and minor rotamer: s, 1H), 4.43 (s, 2H), 4.14–4.08 (m, 2H), 3.99–3.88 (m, 3H), 3.80 (s, 3H), 3.77–3.65 (m, 1H), 3.57–3.22 (m, 5H), 2.49–2.33 (m, 2H), 2.19–1.95 (m, 9H), 1.74–1.68 (m, 2H), 1.59–1.42 (m, 6H), 1.41 & 1.34 (minor and major rotamer: s, 9H), 1.18 & 1.15 (major rotamer: t, *J* = 7.1, minor rotamer: t, *J* = 7.1, 3H), 1.01 & 0.99 (minor and major rotamer: s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.0, 170.6, 165.1, 164.9, 159.1, 153.8, 152.6, 147.7, 147.1, 135.6, 135.5, 135.5,

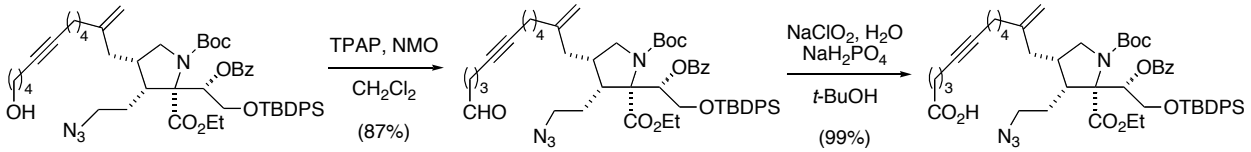
135.4, 133.1, 133.0, 132.8, 132.7, 132.4, 130.7, 130.3, 129.8, 129.7, 129.1, 128.5, 127.7, 127.6, 127.6, 127.5, 113.7, 111.4, 111.3, 80.9, 80.1, 80.0, 74.8, 74.5, 70.5, 70.3, 69.6, 63.7, 63.4, 61.2, 61.1, 55.2, 51.3, 51.1, 50.4, 50.3, 50.0, 45.4, 44.3, 36.5, 35.6, 35.5, 35.4, 33.3, 33.1, 28.9, 28.7, 28.3, 28.1, 26.6, 26.5, 25.8, 19.2, 18.9, 18.6, 18.5, 14.0, 13.9; IR (film): 2097, 1738, 1714, 1696 cm-1; MS-FAB (*m/z*): $[M + Na]^+$ calcd for $C_{60}H_{78}N_4O_9SiNa$, 1049; found, 1049; $[\alpha]^{26}_{405}$ +35.4, $[\alpha]^{26}_{435}$ +27.8, $[\alpha]^{26}_{546}$ +15.2, $[\alpha]^{26}_{577}$ +11.6, $[\alpha]^{26}_{D}$ +11.9 (*c* 1.00, $CHCl_3$).



64 **65**

Alcohol 65. DDQ (240 mg, 1.057 mmol, 2.01 equiv) was added to a mixture of pyrrolidine **64** (540 mg, 0.525 mmol, 1.00 equiv) in CH_2Cl_2 (15 mL) and H_2O (2 mL) at rt. After stirring for 30 min, the mixture was poured into chilled 3 N aqueous NaOH and extracted with CH_2Cl_2 (3 x 25 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude product by flash chromatography (5% EtOAc-hexanes, 25% EtOAc-hexanes, 40% EtOAc-hexanes, 50% EtOAc-hexanes) gave alcohol **65** (400 mg, 0.441 mmol, 84% yield), which was characterized as a mixture of rotamers. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.16 (t, *J* = 8.1, 2H), 7.70 (t, *J* = 8.1, 1H), 7.63–7.56 (m, 4H), 7.53–7.50 (m, 2H), 7.41–7.37 (m, 2H), 7.32–7.27 (m, 2H), 7.12 & 7.08 (major rotamer: t, *J* = 7.5; minor rotamer: t, *J* = 7.6, 2H), 6.13 & 6.09 (minor rotamer: t, *J* = 3.0; major rotamer: t, *J* = 3.3, 1H), 4.86 (s, 1H), 4.76 & 4.71 (major and minor rotamer: s, 1H), 4.23–4.08 (m, 2H), 3.91–3.89 (m, 2H), 3.67–3.64 (m, 2H), 3.51–3.21 (m, 2H), 2.50–2.26 (m, 2H), 2.20–2.16 (m, 6H), 2.10–1.93 (m, 4H), 1.69–1.64 (m, 4H), 1.59–1.45 (m, 6H), 1.40 & 1.33 (minor and major rotamer: s, 9H), 1.19 & 1.13 (major rotamer: t, *J* = 7.1; minor rotamer: t, *J* = 7.1, 3H), 1.00 & 0.98 (minor and major rotamer: s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.0, 170.7, 165.1, 164.9, 153.8, 152.7, 147.8, 147.2, 135.7, 135.6, 135.5, 135.4, 133.0, 133.0, 133.0, 132.6, 132.3, 132.2, 130.5, 130.3, 129.8, 129.7, 128.5, 128.5, 127.8, 127.7, 127.6, 127.6, 111.3, 81.0, 80.3, 80.3, 80.0, 80.0, 74.8, 74.1, 73.7, 70.4, 70.3, 64.4, 63.7, 63.4, 62.4, 61.3, 61.2, 61.15, 51.3, 51.1, 50.4, 50.3, 50.2, 50.0, 45.4, 44.3, 36.5, 35.5, 35.4, 33.3, 33.1, 31.9, 28.7, 28.3, 28.1, 26.8, 26.6, 26.5, 25.3, 19.2, 19.0, 18.6, 14.0, 13.9; IR (film): 3498, 2089, 1731, 1711, 1692 cm^{-1}; HRMS-FAB (*m/z*): $[M + Na]^+$

calcd for $C_{52}H_{70}N_4O_8SiNa$, 929.4861; found, 929.4878; $[\alpha]^{26}_{405}$ +51.5, $[\alpha]^{26}_{435}$ +41.7, $[\alpha]^{26}_{546}$ +21.9, $[\alpha]^{26}_{577}$ +17.8, $[\alpha]^{26}_{D}$ +20.5 (*c* 1.00, $CHCl_3$).

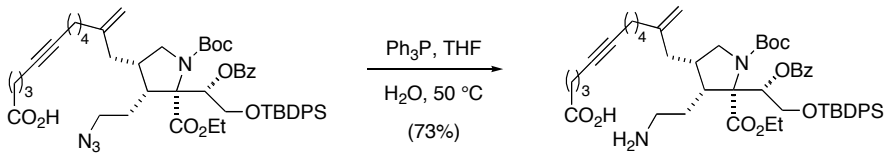


65 **SI-9** **66**

Acid 66. TPAP (25 mg, 0.071 mmol) was added to a suspension of powdered 4Å molecular sieves (200 mg), NMO (90 mg, 0.768 mmol, 1.83 equiv), and alcohol **65** (380 mg, 0.419 mmol, 1.00 equiv) in CH_2Cl_2 at 0 °C. The reaction mixture was allowed to warm to rt. After stirring at rt for 20 min, the reaction mixture was directly purified by flash chromatography (100% hexanes, then 50% EtOAc-hexanes) to furnish aldehyde **SI-9** (330 mg, 0.365 mmol, 87% yield) as a yellow oil. Aldehyde **SI-9** was typically used directly in subsequent transformations.

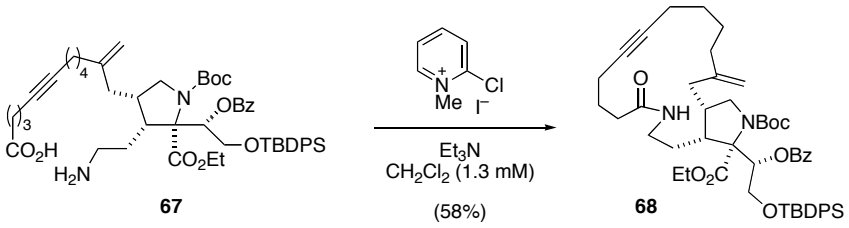
A premixed solution of sodium chlorite (60 mg, 0.664 mmol, 4.15 equiv) and sodium phosphate monobasic (120 mg, 0.870 mmol, 5.43 equiv) in H_2O (3.0 mL) was added to a solution of aldehyde **SI-9** (145 mg, 0.160 mmol, 1.00 equiv) and 2-methyl-2-butene (3 mL) in *t*-BuOH (3.0 mL) at rt. The reaction mixture was vigorously stirred for 45 min, poured into brine (10 mL), and extracted with EtOAc (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated to give carboxylic acid **66** (150 mg, 0.163 mmol, near quantitative yield) as an oily residue that was taken to the next step. Carboxylic acid **66** was characterized as a mixture of rotamers. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17–8.11 (m, 2H), 7.71–7.56 (m, 5H), 7.54–7.51 (m, 2H), 7.38 (g, *J* = 8.2, 2H), 7.33–7.27 (m, 2H), 7.24–7.10 (m, 2H), 6.13 & 6.09 (minor rotamer: t, *J* = 3.2; major rotamer: t, *J* = 3.1, 1H), 4.86 (br s, 1H), 4.74 (br s, 1H), 4.19–4.05 (m, 2H), 3.93–3.76 (m, 2H), 3.69–3.67 (m, 1H), 3.56–3.50 (m, 2H), 3.47–3.38 (m, 1H), 2.52–2.49 (m, 2H), 2.46–2.34 (m, 1H), 2.25 (app. t, *J* = 6.8, 2H), 2.18–2.17 (m, 2H), 2.10–1.93 (m, 3H), 1.82 (ap t, *J* = 6.9, 2H), 1.54–1.42 (m, 8H), 1.40 & 1.33 (minor and major rotamers: s, 9H), 1.17 & 1.13 (major rotamer: t, *J* = 7.2; minor rotamer: t, *J* = 7.2, 3H), 1.00 & 0.98 (minor and major rotamers: s, 9H) ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.2, 177.7, 171.0, 170.7, 165.1, 164.9, 153.8, 152.8, 147.8, 147.2, 135.5, 135.4, 134.4, 134.2, 133.5, 133.2, 130.8, 130.5, 129.8, 129.7, 128.5, 127.8, 127.6, 111.4, 111.3, 81.2, 81.2, 80.1, 78.9, 78.8, 74.8, 70.5, 70.3, 63.7, 63.4, 61.3, 61.2, 51.4, 51.2, 50.4, 50.3, 45.5, 44.3, 36.5, 35.6, 35.5, 32.6, 32.4, 33.2, 32.6, 32.5, 28.6,

28.4, 28.1, 26.8, 26.6, 26.5, 24.0, 24.0, 19.0, 18.6, 18.12, 18.10, 13.9; IR (film): br 3500–3100, 2100, 1704 cm^{-1}; HRMS-FAB (*m/z*): $[M + Na]^+$ calcd for $C_{52}H_{68}N_4O_9SiNa$, 943.4653; found, 943.4627; $[\alpha]^{26}_{405}$ +47.6, $[\alpha]^{26}_{435}$ +39.3, $[\alpha]^{26}_{546}$ +21.7, $[\alpha]^{26}_{577}$ +20.0, $[\alpha]^{26}_{D}$ +16.8 (*c* 1.40, $CHCl_3$).

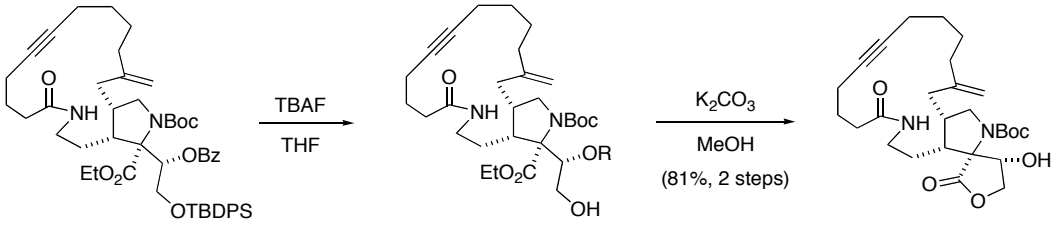


66 **67**

Amino acid 67. Solid triphenylphospine (150 mg, 0.570 mmol, 3.57 equiv) was added to a solution of azide **66** (150 mg, 0.16 mmol, 1.00 equiv) in THF (4.0 mL) at rt. After stirring for 1.5 h, H_2O (0.5 mL) was added, and the reaction vessel was heated at 50 °C for 3 days. The organic solvent was removed under reduced pressure and the residue was purified by flash chromatography (50% EtOAc-hexanes, 100% EtOAc, 5% MeOH-CH_2Cl_2, 10% MeOH-CH_2Cl_2), providing amino acid **67** (105 mg, 0.117 mmol, 73% yield over 2 steps) as a mixture of rotamers. ^1H NMR (500 MHz, $CDCl_3$): δ 8.04 (dd, *J* = 13.4, 7.2, 2H), 7.60–7.55 (m, 6H), 6.05 & 6.00 (minor rotamer: t, *J* = 3.0; major rotamer: t, *J* = 3.0, 1H), 4.87 (s, 1H), 4.68 (s, 1H), 4.18–4.10 (m, 2H), 3.98–3.87 (m, 2H), 3.85–3.78 (m, 1H), 3.75–3.68 (m, 1H), 3.53–3.47 (m, 1H), 2.50–2.43 (m, 2H), 2.39–2.33 (m, 1H), 2.27–2.22 (m, 2H), 2.18–2.12 (m, 2H), 2.02–1.91 (m, 4H), 1.86 (t, *J* = 7.0, 2H), 1.64–1.54 (m, 8H), 1.25 (s, 9H), 1.18 (t, *J* = 7.2, 3H), 0.98 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 169.7, 166.2, 166.0, 153.7, 152.8, 147.4, 135.4, 135.4, 135.3, 133.2, 133.1, 132.9, 132.7, 132.6, 129.8, 129.7, 129.5, 128.7, 128.6, 127.7, 127.6, 127.5, 111.7, 111.5, 81.0, 80.8, 79.9, 79.4, 70.5, 64.2, 64.1, 61.5, 61.3, 51.4, 38.5, 37.4, 36.3, 36.0, 35.8, 33.3, 32.5, 31.9, 29.6, 28.3, 28.2, 27.9, 27.9, 27.1, 27.0, 26.7, 26.6, 26.5, 24.2, 18.9, 18.4, 13.9; IR (film): 3389, 3041, 1725 cm^{-1}; HRMS-FAB (*m/z*): $[M + H]^+$ calcd for $C_{52}H_{71}N_2O_9Si$, 895.4929; found, 895.4931.



Lactam 68. A solution of amino acid **67** (105 mg, 0.117 mmol, 1.00 equiv) and triethylamine (50 μL, 0.359 mmol, 3.07 equiv) in CH_2Cl_2 (10 mL) was added using a syringe pump (0.49 mL/h) to a solution of Mukaiyama's salt (60 mg, 0.235 mmol, 2.01 equiv) and triethylamine (50 μL, 0.359 mmol, 3.07 equiv) in CH_2Cl_2 (80 mL) at rt. The addition was complete after 18 h, and the resulting solution was stirred for 1 h. The reaction mixture was poured into H_2O (40 mL) and extracted with CH_2Cl_2 (2 x 30 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (10% EtOAc-hexanes, 40% EtOAc-hexanes, 50% EtOAc-hexanes) provided macrolactam **68** (60 mg, 0.068 mmol, 58% yield), which was characterized as a mixture of rotamers. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10–8.05 (m, 2H), 7.63–7.51 (m, 7H), 7.37–7.35 (m, 1H), 7.32–7.28 (m, 3H), 7.22–7.10 (m, 2H), 6.12 & 6.08 (minor rotamer: dd, *J* = 4.6, 2.6; major rotamer: dd, *J* = 5.0, 2.8, 1H), 5.86 & 5.81 (minor rotamer: br t, *J* = 5.0; major rotamer: br t, *J* = 5.0, 1H), 4.87 & 4.85 (minor and major rotamer: s, 1H), 4.75 & 4.73 (major and minor rotamer: s, 1H), 4.16–4.03 (m, 2H), 3.97 (dd, *J* = 11.7, 2.6, 1H), 3.90–3.85 (m, 1H), 3.82–3.75 (m, 1H), 3.53–3.41 (m, 2H), 3.17–2.97 (m, 1H), 2.47–2.42 (m, 1H), 2.39–2.32 (m, 2H), 2.30–2.25 (m, 2H), 2.24–2.15 (m, 4H), 2.13–2.08 (m, 2H), 2.03–1.97 (m, 1H), 1.79 (t, *J* = 6.4, 2H), 1.65–1.61 (m, 1H), 1.51–1.43 (m, 4H), 1.40 & 1.30 (minor and major rotamer: s, 9H), 1.22–1.13 (m, 3H), 0.96 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.1, 172.5, 172.4, 170.8, 170.4, 165.5, 165.4, 153.8, 152.7, 148.0, 147.4, 146.6, 135.5, 135.4, 135.4, 133.1, 133.0, 132.7, 132.5, 132.4, 130.3, 130.1, 129.7, 129.7, 129.6, 129.5, 129.4, 128.6, 128.5, 128.4, 127.7, 127.6, 127.5, 127.4, 112.4, 112.2, 81.6, 81.3, 81.0, 80.0, 79.5, 75.9, 75.3, 70.7, 70.5, 63.8, 63.5, 61.3, 61.2, 61.1, 51.6, 51.3, 47.2, 45.8, 38.6, 36.9, 35.8, 35.6, 35.2, 35.2, 35.0, 34.9, 33.0, 28.3, 28.1, 28.0, 28.0, 27.9, 27.9, 27.8, 27.45, 27.36, 26.8, 26.7, 26.6, 26.5, 26.4, 24.1, 23.9, 22.9, 19.0, 18.4, 18.3, 17.6, 13.9; IR (film): 3378, 3312, 1731, 1698, 1655 cm^{-1}; HRMS-FAB (*m*/*z*): [M + Na]$^+$ calcd for $C_{52}H_{68}N_2O_8SiNa$, 899.4643; found, 899.4646; $[\alpha]^{26}_{405}$ +53.1, $[\alpha]^{26}_{435}$ +50.1, $[\alpha]^{26}_{546}$ +28.8, $[\alpha]^{26}_{577}$ +26.1, $[\alpha]^{26}_{D}$ +26.0 (*c* 1.00, $CHCl_3$).

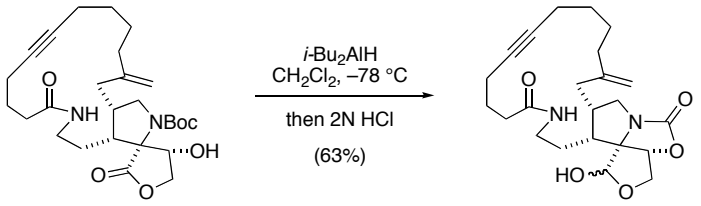


68 **SI-10**, R = Bz **SI-11**, R = H **69**

Spirolactone 69. TBAF (1.0 M in THF, 0.20 mL, 0.20 mmol, 2.94 equiv) was added to a solution of macrolactam **68** (60 mg, 0.068 mmol, 1.00 equiv) in THF (3.0 mL) at 0 °C. The resulting solution was allowed to warm to rt and stirring was continued for 1.5 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and extracted with EtOAc (3 x 5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The crude mixture of products **SI-10** and **SI-11** was used directly in the next step.

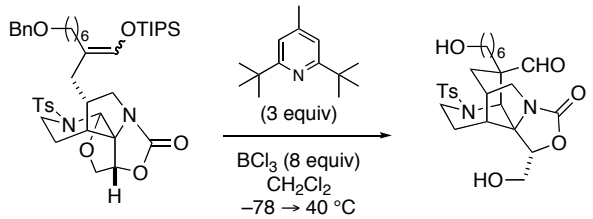
The crude mixture of products was dissolved in MeOH (10.0 mL) and solid anhydrous potassium carbonate (20 mg, 0.145 mmol, 2.14 equiv) was added. The mixture was stirred at rt for 20 h and quenched with saturated aqueous NH_4Cl (5 mL). The methanol was removed under reduced pressure and the residue was extracted with EtOAc (4 × 5 mL). The organic extracts were combined, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (25% EtOAc-hexanes, 50% EtOAc-hexanes, 100% EtOAc) afforded spirolactone **69** (27 mg, 0.055 mmol, 81% yield over the two steps), which was characterized as a mixture of rotamers. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.25 (br d, *J* = 6.8, 1H, N*H*), 5.06 (d, *J* = 11.2, 1H), 4.94 (s, 1H), 4.83 (s, 1H), 4.81 (dd, *J* = 10.7, 4.3, 1H), 4.39 & 4.32 (major rotamer: d, *J* = 10.7; minor rotamer: d, *J* = 10.6, 1H), 4.02 & 3.97 (major rotamer: dd, *J* = 11.0, 4.1; minor rotamer: dd, *J* = 10.5, 4.6, 1H), 3.61 & 3.57 (minor rotamer: dd, *J* = 10.1, 7.5; major rotamer: dd, *J* = 10.1, 7.0, 1H), 3.45 (ddd, *J* = 12.0, 9.7, 2.2, 1H), 3.24 & 3.16 (minor rotamer: t, *J* = 10.8; major rotamer: t, *J* = 10.8, 1H), 2.42 (ddd, *J* = 12.8, 7.5, 7.5, 1H), 2.30 (ddd, *J* = 14.1, 7.5, 6.7, 1H), 2.26–2.22 (m, 5H), 2.19–2.10 (m, 2H), 2.07 (dd, *J* = 9.5, 6.0, 1H), 2.00–1.94 (m, 2H), 1.91–1.82 (m, 1H), 1.79–1.68 (m, 2H), 1.66–1.60 (m, 1H), 1.59–1.53 (m, 1H), 1.56 & 1.47 (minor and major rotamer: s, 9H), 1.44–1.38 (m, 2H), 1.56 & 1.47 (minor and major rotamer: s, 9H), 1.44–1.38 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.3, 172.6, 157.1, 147.0, 111.3, 82.1, 80.9, 80.1, 78.3, 74.7, 71.2, 51.4, 45.0, 37.8, 36.9, 34.4, 34.3, 34.1, 28.2, 27.4, 26.0, 24.2, 22.9, 18.1, 17.6;

IR (film): 3342, 1772, 1654 cm^{-1}; HRMS-FAB (*m/z*): $[M + H]^+$ calcd for $C_{27}H_{41}N_2O_6$, 489.2965; found, 489.2967; $[\alpha]^{26}_{405}$ –59.4, $[\alpha]^{26}_{435}$ –46.0, $[\alpha]^{26}_{546}$ –26.0, $[\alpha]^{26}_{577}$ –21.9, $[\alpha]^{26}_{D}$ –27.8 (*c* 1.00, $CHCl_3$).



69 **70**

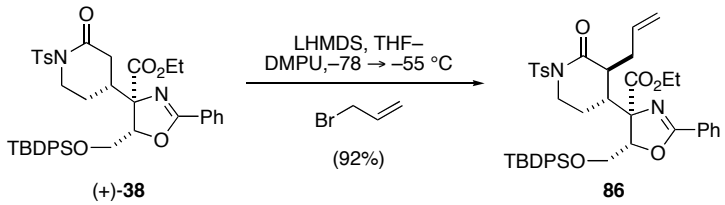
Lactol 70. *i*-$BuAl_2H$ (50 μL, 0.075 mmol, 3.33 equiv) was added to a solution of spirolactone **69** (11 mg, 0.023 mmol, 1.00 equiv) in CH_2Cl_2 (1.0 mL) at –78 °C. The reaction mixture was stirred at –78 °C for 1.2 h, quenched with EtOAc, and slowly warmed to 0 °C. 1 N aqueous HCl was added and the mixture was vigorously stirred, then extracted with EtOAc (4 x 5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (50% EtOAc-hexanes, 100% EtOAc) furnished oxazolidinone-lactol **70** (7 mg, 0.0168 mmol, 63% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.83 (s, 1H), 5.68 (br t, *J* = 5.6, 1H, NH), 4.94 (s, 1H), 4.83 (s, 1H), 4.14 (dd, *J* = 9.3, 6.9, 1H), 4.06–4.01 (m, 1H), 3.68 (dd, *J* = 11.6, 3.1, 1H), 3.55–3.46 (m, 2H), 3.26–3.19 (m, 1H), 3.16 (dd, *J* = 11.5, 5.6, 1H), 2.63–2.60 (m, 1H), 2.44–3.37 (m, 3H), 2.27–2.22 (m, 6H), 2.17–2.12 (m, 1H), 2.07–2.00 (m, 1H), 1.90 (d, *J* = 11.9, 1H), 1.84–1.80 (m, 2H), 1.72–1.69 (m 2H), 1.62–1.58 (m, 1H), 1.48–1.40 (m, 2H), 1.31–1.07 (m, 1H); IR (film): 3335, 1752, 1730, 1649 cm^{-1}; MS-FAB (*m/z*): $[M + Na]^+$ calcd for $C_{23}H_{32}N_2O_5Na$, 439.23; found, 439.18.



74 **75**

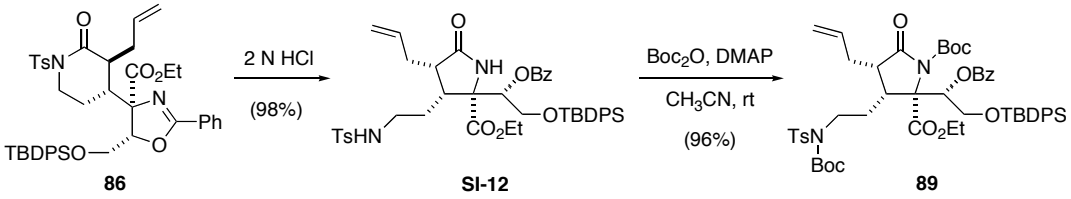
Aldehyde 75. Enoxysilane **74** was prepared by the general strategy used to synthesize enoxysilanes **48** and **103**. A round bottom flask containing a mixture of enoxysilane isomers **74** (450 mg, 0.586 mmol) and 2,6-di-*tert*-butyl-4-methyl-pyridine (360 mg, 1.76 mmol) was purged

with N_2, charged with CH_2Cl_2 (18 mL) and cooled to –78 °C. BCl_3 (1.0 M heptane, 4.7 mL, 4.69 mmol) was added dropwise. The flask was then sealed and placed to stir in a cryocool maintained at –78°C. Every hour, the temperature was increased by approximately 5 °C until a temperature of –40 °C was attained. Stirring was continued for another 6 h, then the reaction was cooled to –78 °C and quenched by rapid transfer via cannula into a solution of saturated aqueous $NaHCO_3$ (20 mL) with rapid stirring. The mixture was extracted with EtOAc (5 × 30 mL) and the combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure. Purification by preparative TLC (1 mm thickness, 20 cm × 20 cm EM Science plates, ~100 mg crude per plate, eluting 3 × with 100% EtOAc) afforded aldehyde **75** (253 mg, 0.49 mmol, 83%) as a colorless oil. R_f 0.48 (19:1 EtOAc:MeOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.33 (d, *J* = 1.3, 1H), 7.71 (d, *J* = 8.4, 2H), 7.33 (d, *J* = 8.4, 2H), 5.13 (s, 1H), 4.45 (t, *J* = 4.1, 1H), 4.34 (dd, *J* = 12.9, 3.8, 1H), 4.27 (dd, *J* = 13.0, 4.1, 1H), 3.68 (dd, *J* = 12.9, 8.5, 1H), 3.58 (t, *J* = 6.6, 2H), 3.22 (ddd, *J* = 9.5, 3.6, 1.3, 1H), 3.15 (dt, *J* = 12.9, 5.0, 1H), 3.03 (d, *J* = 9.9, 1H), 2.70–2.55 (m, 2H), 2.44 (s, 3H), 2.41 (s, 1H), 2.24–2.16 (m, 1H), 2.03–1.98 (m, 2H), 1.73–0.70 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.6, 160.7, 144.2, 136.2, 129.9, 127.8, 82.7, 66.9, 62.7, 60.0, 56.8, 53.3, 53.2, 42.1, 41.5, 39.6, 34.0, 21.5, 29.7, 29.5, 29.4, 25.4, 22.0, 21.5; IR (film): 3444, 2932, 2857, 1748, 1325 cm^{-1}; HRMS-FAB (*m/z*): $[M + H]^+$ calcd for $C_{26}H_{36}N_2O_7S$, 521.2321; found, 521.2320; $[\alpha]^{28}_{405}$ –100.2, $[\alpha]^{28}_{435}$ –71.7, $[\alpha]^{28}_{546}$ –32.8, $[\alpha]^{28}_{577}$ –25.4, $[\alpha]^{28}_{D}$ –25.8 (*c* 1.45, $CHCl_3$).



Allylated lactam 86. Lactam (+)-**38** was prepared following the procedure previously used to synthesize (–)-**38**.[1] A solution of lactam (+)-**38** (16.5 g, 22.3 mmol), THF (150 mL) and DMPU (50.0 mL) in a flask equipped with a sealable top was cooled at –78 °C under an Ar atmosphere for 15 min and LHMDS (1.0 M in THF, 7.80 mL, 7.80 mmol) was added dropwise. After 30 min, allyl bromide (5.80 mL, 66.9 mmol) was added dropwise and the flask was sealed. The reaction flask was placed in a cryocool bath and maintained at –55 °C for 24 h. The reaction mixture was quenched with saturated aqueous NH_4Cl (50 mL) and allowed to warm to room

temperature. Hexanes (20 mL) and EtOAc (150 mL) were added to the resulting mixture and the aqueous layer was extracted with EtOAc (3 × 100 mL). The combined organic extracts were washed with brine (1 × 100 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the crude product by flash chromatography (25% EtOAc-hexanes) afforded lactam **86** (15.4 g, 20.4 mmol, 92%) as a colorless foam. R_f 0.31, (25% EtOAc-hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.3, 2H), 7.63–7.61 (d, *J* = 8.3, 2H), 7.58–7.55 (m, 4H), 7.44–7.21 (m, 11H), 5.63–5.55 (m, 1H), 5.03–4.98 (m, 2H), 4.35–4.27 (m, 2H), 4.21–4.13 (m, 1H), 4.10–4.00 (m, 3H), 3.90 (dd, *J* = 11.7, 2.4, 1H), 2.47–2.43 (m, 3H), 2.37–2.24 (m, 3H), 2.11–2.04 (m, 1H), 1.95–1.92 (m, 1H), 1.15 (t, *J* = 7.1, 3H), 0.89 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.5, 170.8, 165.3, 144.1, 136.4, 135.7, 135.4, 134.3, 133.2, 132.6, 131.4, 129.8, 129.7, 129.2, 128.72, 128.70, 127.9, 127.64, 127.57, 126.5, 118.8, 86.1, 81.0, 62.9, 61.5, 44.7, 44.6, 44.0, 38.3, 26.6, 23.5, 21.7, 19.0, 13.9; IR (film): 3073, 2934, 2860, 1752, 1714, 1652, 1351, 1274, 1170, 1112, 1089 cm^{-1}; HRMS-ESI (*m/z*) [M + H]$^+$ calcd for $C_{44}H_{51}N_2O_7SSi$, 779.3187; found, 779.3203; Anal. Calcd for $C_{44}H_{50}N_2O_7SSi$: C, 67.84; H, 6.47; N, 3.60; found: C, 67.88, H, 6.53; N, 3.66; $[\alpha]^{27}_D$ +94.6, $[\alpha]^{27}_{577}$ +97.1, $[\alpha]^{27}_{546}$ +112.0, $[\alpha]^{27}_{435}$ +206.7, $[\alpha]^{27}_{405}$ +257.5 (*c* 1.00, $CHCl_3$).

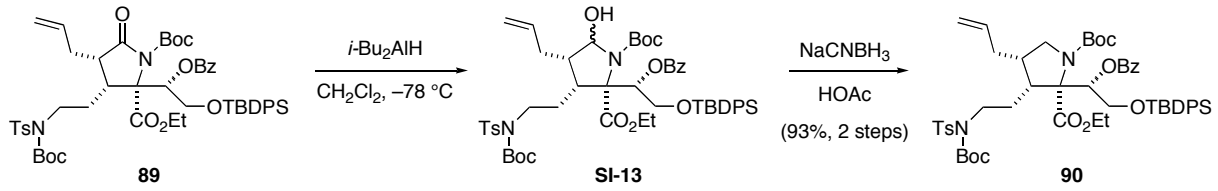


86 **SI-12** **89**

Imide 89. A solution of alkene **86** (6.78 g, 8.71 mmol), THF (60 mL) and 2.0 N HCl (15 mL) was maintained at rt for 2 days. The reaction was quenched with saturated aqueous $NaHCO_3$ (70 mL), concentrated, and extracted with EtOAc (4 × 100 mL). The combined organic extracts were washed with brine (1 × 200 ml), dried over $MgSO_4$, and concentrated to give pyrrolidinone **SI-12** (6.77 g, 8.49 mmol, 98%) as a colorless foam, which was typically used directly in the subsequent transformation.

Di-*tert*-butyl dicarbonate (9.91 g, 45.5 mmol) and DMAP (2.22 g, 18.2 mmol) were added sequentially to a solution of pyrrolidinone **SI-12** (14.5 g, 18.2 mmol) and CH_3CN (180 mL) at rt. The mixture was stirred for 15 h, then quenched with water (150 ml) and saturated aqueous $NHCl_4$ (100 mL). Hexanes (50 mL) was added and the aqueous layer was extracted with

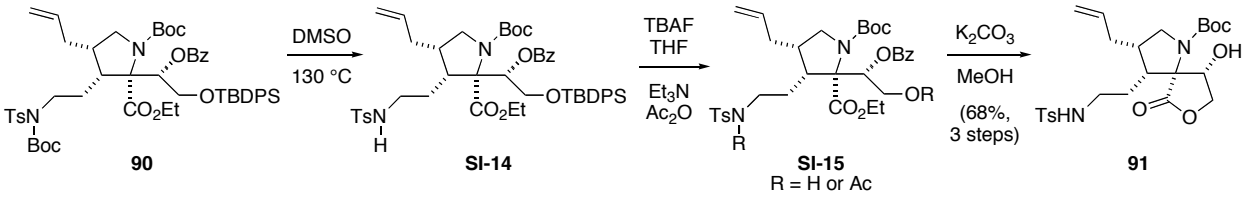
EtOAc (3 × 70 mL). The organic extracts were combined, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the residue by flash chromatography (33% EtOAc-hexanes) provided imide **89** (17.4 g, 17.5 mmol, 96%) as a colorless foam. R_f 0.35 (25% EtOAc-hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (dd, *J* = 8.0, 1.5, 2H), 7.66 (d, *J* = 7.0, 2H), 7.61 (dd, *J* = 8.0, 1.5, 2H) 7.57–7.50 (m, 5H), 7.38–7.21 (m, 6H), 7.01 (t, *J* = 7.6, 2H), 6.23 (t, *J* = 2.8, 1H), 6.10 (dddd, *J* = 19.8, 10.3, 6.4, 6.3, 1H), 5.19 (dd, *J* = 17.1, 1.6, 1H), 5.09 (d, *J* = 10.1, 1H), 4.20–4.14 (m, 2H), 4.04 (ddd, *J* = 14.1, 11.6, 5.2, 1H), 3.88–3.74 (m, 4H), 2.85–2.81 (m, 1H), 2.71–2.66 (m, 1H), 2.62–2.55 (m, 1H), 2.42 (s, 3H), 2.39–2.33 (m, 1H), 1.82 (ddd, *J* = 24.0, 11.9, 4.0, 1H), 1.45 (s, 9H), 1.28 (s, 9H), 1.17 (t, *J* = 7.1, 3H), 0.98 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.6, 170.0, 165.4, 150.7, 149.6, 144.2, 137.4, 136.1, 135.5, 135.4, 133.0, 132.0, 131.9, 130.1, 129.8, 129.69, 129.68, 129.2, 128.8, 127.8, 127.6, 127.6, 116.4, 84.6, 84.0, 73.1, 70.0, 63.5, 61.7, 45.5, 44.6, 35.7, 30.8, 27.83, 27.79, 26.6, 21.5, 18.9, 13.8; IR (film): 2980, 2934, 2860, 1795, 1722, 1359, 1285, 1258, 1150, 1112, 1089 cm^{-1}; HRMS-ESI (*m/z*) [M + Na]$^+$ calcd for $C_{54}H_{68}N_2O_{12}SSiNa$, 1019.4160; found, 1019.4149; Anal. Calcd for $C_{54}H_{68}N_2O_{12}SSi$: C, 65.03; H, 6.87; N, 2.81; found: C, 64.89; H, 6.92; N, 2.83; $[\alpha]^{27}_D$ +21.7, $[\alpha]^{27}_{577}$ +22.6, $[\alpha]^{27}_{546}$ +25.5, $[\alpha]^{27}_{435}$ +50.4, $[\alpha]^{27}_{405}$ +64.2 (*c* 1.00, $CHCl_3$).



Pyrrolidine 90. DIBAL-H (1.5 M in PhMe, 17.3 mL, 25.9 mmol) was added dropwise over 35 min to a solution of pyrrolidinone **89** (17.2 g, 17.3 mmol) in CH_2Cl_2 (330 mL). The reaction was maintained at –78 °C for 25 min, then quenched with EtOAc (25 mL). The mixture was warmed to 0 °C, diluted with 1.0 M NaOH (300 mL), and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were dried over $MgSO_4$, filtered through Celite®, and concentrated under reduced pressure to give a mixture of hemiaminals **SI-13** as an oily residue, which was immediately subjected to further reduction.

This crude mixture of hemiaminals **SI-13** was combined with glacial acetic acid (90 mL). Sodium cyanoborohydride (7.05 g, 112 mmol) was added to this mixture in three portions over a period of 5 h. After stirring at rt for 12 h, the reaction mixture was quenched slowly with 1 M

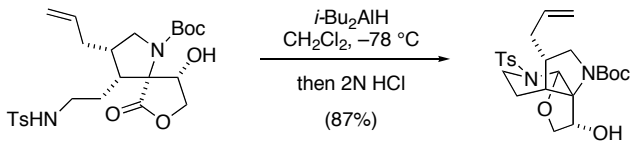
NaOH (700 mL), such that pH = 9, then CH_2Cl_2 (200 mL) was added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic extracts were dried over Mg_2SO_4, filtered through Celite®, and concentrated under reduced pressure. Purification of the residue by flash chromatography (50% Et_2O-pentane) provided pyrrolidine **90** (15.9 g, 16.1 mmol, 93% over two steps) as a colorless foam. R_f 0.40 (25% EtOAc-hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19 (d, *J* = 7.7, 2H), 7.70–7.67 (m, 2H), 7.64–7.47 (m, 6H), 7.39–7.36 (m, 1H), 7.33–7.21 (m, 5H), 7.09–7.02 (m, 2H), 6.17 & 6.12 (minor rotamer: t, *J* = 3.2; major rotamer: t, *J* = 3.6, 1H), 5.83–5.75 (m, 1H), 5.15–5.04 (m, 2H), 4.16–3.87 (m, 6H), 3.84–3.77 (m, 2H), 3.64 (m, 1H), 3.55–3.47 (m, 1H), 2.46–2.35 (m, 2H), 2.41 & 2.40 (major and minor rotamers, s, 3H), 2.28–2.24 (m, 1H), 2.16 (m, 1H), 1.83–1.77 (m, 1H), 1.40 & 1.34 (minor and major rotamers, s, 9H), 1.30 & 1.29 (major and minor rotamers, s, 9H), 1.14 & 1.12 (major rotamer, t, *J* = 7.1; minor rotamers, t, *J* = 7.1, 3H), 1.00 & 0.99 (minor and major rotamers, s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7, 170.4, 165.6, 165.3, 153.8, 152.8, 150.7, 144.0, 144.0, 138.0, 137.6, 137.5, 137.5, 135.6, 135.5, 135.4, 133.2, 132.8, 132.7, 132.6, 132.3, 132.2, 130.3, 130.1, 130.1, 130.1, 129.7, 129.7, 129.6, 129.6, 129.2, 128.7, 128.6, 128.4, 128.0, 128.0, 127.8, 127.7, 127.6, 116.5, 116.4, 84.4, 84.3, 81.0, 80.0, 74.3, 74.2, 70.5, 70.3, 63.6, 63.3, 61.1, 61.0, 51.0, 46.1, 45.7, 45.6, 45.0, 38.9, 38.4, 31.1, 31.0, 28.4, 28.13, 28.09, 28.0, 27.8, 26.7, 26.7, 21.5, 19.0, 13.8; IR (film): 2980, 2934, 2860, 1725, 1702, 1393, 1363, 1266, 1154, 1112 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calcd for $C_{54}H_{70}N_2O_{11}SSiNa$, 1005.4367; found, 1005.4373; $C_{54}H_{70}N_2O_{11}SSi$: C, 65.96; H, 7.18; N, 2.85; found: C, 65.96; H, 7.26; N, 2.79; $[\alpha]^{26}_D$ +1.37, $[\alpha]^{26}_{577}$ +0.98, $[\alpha]^{26}_{546}$ +1.74, $[\alpha]^{26}_{435}$ +4.11, $[\alpha]^{26}_{405}$ +5.30 (*c* 1.00, $CHCl_3$).



Spirolactone 91. A solution of pyrrolidine **90** (15.3 g, 15.6 mmol) in DMSO (50 mL) was sparged with Ar for 20 min, then heated to 130 °C for 4.5 h. The solution was cooled to rt and purified by flash chromatography (50% Et_2O/pentane, R_f = 0.36, 50% Et_2O/pentane) to yield pyrrolidine **SI-14** (10.7 g, 12.1 mmol, 78%) as a colorless foam, which was used directly in the subsequent transformation.

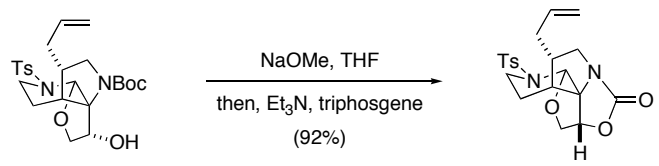
TBAF (1.0 M in THF, 60.3 mL, 60.3 mmol) was added to a solution containing pyrrolidine **SI-14**, Et_3N (25.0 mL, 181 mmol), and acetic anhydride (11.0 mL, 121 mmol) in THF (150 mL). The resulting solution was heated to 70 °C under a N_2 atmosphere. After 13 h, the mixture was quenched with water (300 mL) and extracted with 66% EtOAc-hexanes (1 × 150 mL), then EtOAc (3 × 100 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was filtered through silica gel (33–50% EtOAc-hexanes) to give the crude desilylated pyrrolidine **SI-15** as a colorless foam.

The crude mixture was dissolved in MeOH (60 mL), and solid anhydrous potassium carbonate (10.1 g, 73.2 mmol) was added. The mixture was stirred for 12 h, then quenched with water (100 mL). EtOAc (150 mL) and hexanes (50 mL) were added and the pH was adjusted to pH 8 by the addition of 2 M HCl. The layers were separated and the aqueous phase was extracted with EtOAc (3 × 100 mL). The combined organic extracts were washed with brine (1 × 150 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the residue by flash chromatography (33 to 50% EtOAc-hexanes) afforded spirolactone **91** (5.76 g, 10.6 mmol, 68% over three steps) as a colorless solid, which can be crystallized from Et_2O/pentane. R_f 0.33 (50% EtOAc-hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 (d, *J* = 8.2, 2H), 7.30 (d, *J* = 8.3, 2H), 5.77–5.69 (m, 1H), 5.11–5.08 (m, 2H), 4.83 (d, *J* = 11.3, 1H), 4.73 & 4.65 (minor rotamer: dd, *J* = 11.2, 5.5; major rotamer: dd, *J* = 10.7, 4.7, 1H), 4.36 (d, *J* = 10.7, 1H), 4.31–4.28 (m, 1H), 4.09 (dd, *J* = 11.2, 4.4, 1H), 3.55 (dd, *J* = 10.4, 6.9, 1H), 3.30 & 3.19 (minor rotamer: t, *J* = 9.9; major rotamer: t, *J* = 10.3, 1H), 2.87–2.78 (m, 2H), 2.50–2.44 (m, 1H), 2.42 (s, 3H), 2.39–2.36 (m, 1H), 2.24–2.10 (m, 2H), 1.80–1.73 (m, 1H), 1.57–1.48 (m, 1H), 1.45 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.7, 157.1, 143.6, 136.5, 135.5, 129.8, 127.0, 117.1, 83.3, 82.1, 77.6, 75.8, 74.7, 74.0, 71.0, 51.2, 51.1, 47.8, 45.7, 41.5, 41.4, 40.2, 39.2, 31.8, 29.6, 28.2, 28.0, 23.4, 21.5; IR (film): 3482, 3277, 2980, 2930, 1772, 1668, 1409, 1370, 1328, 1158, 1092 cm^{-1}; HRMS-FAB (*m*/*z*) $[M + Na]^+$ calcd for $C_{24}H_{34}N_2O_7SNa$, 517.1985; found, 517.1993; Anal. Calcd for $C_{24}H_{34}N_2O_7S$: C, 58.28; H, 6.93; N, 5.66; found: C, 58.41; H, 6.90; N, 5.50; $[\alpha]^{27}_D$ –52.5, $[\alpha]^{27}_{577}$ –54.9, $[\alpha]^{27}_{546}$ –63.1, $[\alpha]^{27}_{435}$ –116, $[\alpha]^{27}_{405}$ –144 (*c* 1.00, $CHCl_3$).



91 **92**

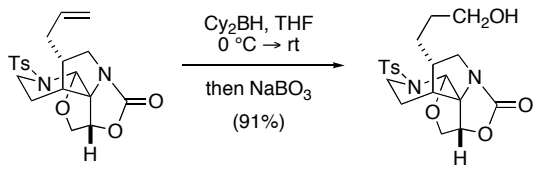
Aminal 92. A solution of spirolactone **91** (5.12 g, 10.4 mmol) in CH_2Cl_2 (65.0 mL) was cooled to –78 °C under a N_2 atmosphere. DIBAL-H (1.5 M in PhMe, 41.5 mL, 62.2 mmol) was added dropwise over 75 min. The resulting mixture was maintained at –78 °C for 5 h, then quenched with EtOAc (25.0 ml) at –78 °C. The reaction mixture was slowly warmed to 0 °C and 2 N HCl (100 mL) and THF (10.0 mL) were added. The reaction mixture was stirred vigorously for 40 h, then extracted with EtOAc (3 × 100 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (1 × 100 mL) and brine (1 × 100 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the residue by flash chromatography (33% EtOAc-hexanes) gave aminal **92** (3.22 g, 6.73 mmol, 65%) and a mixture of lactone **91** and the corresponding lactol (1.30 g, 2.63 mmol, 25%). The mixture of lactone **91** and the corresponding lactol was resubjected to the reaction conditions and purified as described above, affording aminal **92** (1.10 g, 2.31 mmol, 88%) as a colorless foam (4.32 g, 9.03 mmol, 87% combined yield for both reactions). R_f 0.67 (50% EtOAc-hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.2, 2H), 7.25 (d, *J* = 7.8, 2H), 6.68 & 6.49 (major and minor isomers, s, 1H), 5.73–5.65 (m, 1H), 5.07–5.00 (m, 2H), 4.63 (d, *J* = 10.6, 1H), 4.16 (dd, *J* = 9.5, 6.2, 1H), 3.75–3.68 (m, 2H), 3.60–3.56 (m, 2H), 3.08 (t, *J* = 11.0, 1H), 2.78 (t, *J* = 12.0, 1H), 2.39 (s, 4H), 2.07 (t, *J* = 6.9, 2H), 1.77–1.72 (m, 1H), 1.59–1.35 (m, 2H), 1.48 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.3, 143.2, 136.7, 135.5, 129.4, 127.7, 116.6, 81.5, 80.3, 78.5, 73.8, 69.2, 51.1, 42.7, 37.6, 37.2, 31.3, 28.3, 21.6, 21.5; IR (film): 3435, 2976, 2034, 2883, 1660 cm, 1393, 1370, 1343, 1162, 961 cm^{-1}; HRMS-FAB (*m/z*) $[M + H]^+$ calcd for $C_{24}H_{35}N_2O_6S$, 479.2216; found, 479.2221; Anal. Calcd for $C_{24}H_{34}N_2O_6S$: C, 60.23; H, 7.18; N, 5.85; found: C, 59.98; H, 7.16; N, 5.70; $[\alpha]^{27}_D$ –26.8, $[\alpha]^{27}_{577}$ –29.0, $[\alpha]^{27}_{546}$ –34.8, $[\alpha]^{27}_{435}$ –57.1, $[\alpha]^{27}_{405}$ –69.9 (*c* 0.470, $CHCl_3$).



92 **87**

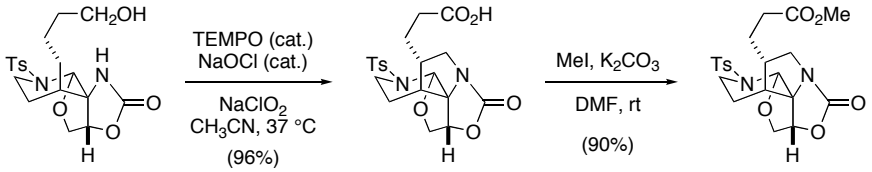
Tetracycle 87. A solution of tricyclic aminal **92** (1.99 g, 4.16 mmol) in THF (40.0 mL) was cooled to 0 °C under an N_2 atmosphere, and sodium methoxide (270 mg, 5.00 mmol) was added. The reaction mixture was allowed to warm to rt, then stirred for 4 h. H_2O (100 ml), EtOAc (40 ml) and hexanes (10 ml) were added. The reaction was neutralized by the dropwise addition of 2 M HCl. The phases were separated and the aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed with brine (1 × 500 mL), dried over Na_2SO_4, and concentrated under reduced pressure to give a mixture of tetracycle **87** and Boc-deprotected amino alcohol.

This crude mixture was dissolved in CH_2Cl_2 (42.0 ml) and cooled to 0 °C in an ice bath. Triethylamine (1.50 ml, 10.4 mmol) and triphosgene (3.85 g, 13.0 mmol) were added, and the reaction mixture was maintained at 0 °C for 45 min. The reaction mixture was poured into saturated aqueous $NaHCO_3$ (50 mL) and water (50 ml). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by flash chromatography (33 to 50 % EtOAc-hexanes) afforded tetracycle **87** (1.55 g, 3.82 mmol, 92%) as a colorless foam. R_f 0.36 (50% EtOAc-hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.3, 2H), 7.28 (d, *J* = 8.5, 2H), 5.69 (dddd, *J* = 21.1, 10.2, 6.8, 6.8, 1H), 5.50 (s, 1H), 5.07–5.02 (m, 2H), 4.49 (dd, *J* = 6.3, 3.3, 1H), 4.21 (dd, *J* = 11.2, 6.3, 1H), 3.92 (dd, *J* = 11.2, 3.2, 1H), 3.72 (dd, *J* = 11.8, 6.4, 1H), 3.64 (dt, *J* = 12.5, 3.6, 1H), 2.86 (t, *J* = 11.5, 1H), 2.77 (dt, *J* = 12.6, 2.0, 1H), 2.42 (s, 3H), 2.23–2.14 (m, 2H), 2.11–2.07 (m, 2H), 1.47 (ddd, *J* = 13.3, 9.1, 4.1, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.2, 143.7, 136.1, 135.0, 129.4, 127.7, 116.7, 87.5, 85.2, 72.5, 68.8, 51.9, 43.3, 40.1, 38.2, 30.5, 21.9, 21.4; IR (film): 2934 2887, 1760, 1343, 1305, 1162 cm^{-1}; HRMS-FAB (*m/z*) $[M + H]^+$ calcd for $C_{20}H_{25}N_2O_5S$, 405.1484; found, 405.1484; Anal. Calcd for $C_{20}H_{24}N_2O_5S$: C, 59.39; H, 5.98; N, 6.93; found: C, 59.38; H, 6.00; N, 6.98; $[\alpha]^{27}_D$ +8.8, $[\alpha]^{27}_{577}$ +8.8, $[\alpha]^{27}_{546}$ +10.9, $[\alpha]^{27}_{435}$ +19.7, $[\alpha]^{27}_{405}$ +24.6 (*c* 1.00, $CHCl_3$).



87 **93**

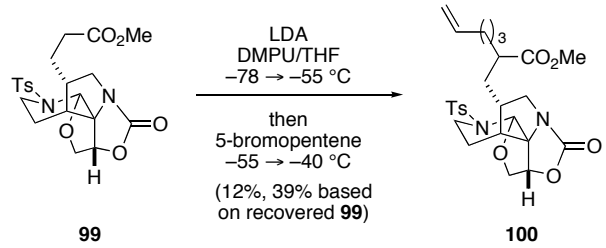
Alcohol 93. Borane-THF complex (1.0 M in THF, 5.06 mL, 5.06 mmol) was added dropwise over 5 min to cyclohexene (1.03 ml, 10.1 mmol) under an N_2 atmosphere at 0 °C (ice bath). The mixture was allowed to warm to rt with stirring, and a colorless precipitate formed. After 2.5 h the mixture was cooled to 0 °C (ice bath) and a solution of oxazolidinone **87** (1.02 g, 2.53 mmol) in THF (6 .00 ml) was added dropwise. The resulting mixture was allowed to warm to rt. After 16 h at rt, the colorless solution was cooled to 0 °C (ice bath), and a suspension of $NaBO_3 \cdot 4H_2O$ (2.31 g, 15.0 mmol) in H_2O (10 mL) was added slowly. The reaction mixture was allowed to warm to rt. After 8 h, the reaction was neutralized with 2 M HCl, diluted with water (50 mL) and extracted with EtOAc (5 × 40 mL). The combined organic extracts were washed with brine (1 × 100 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the residue by flash chromatography (100% EtOAc) gave alcohol **93** (972 mg, 2.30 mmol, 91%) as a colorless foam. R_f 0.35 (100% EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.3, 2H), 7.27 (d, *J* = 8.6, 2H), 4.50 (dd, *J* = 6.2, 3.1, 1H), 4.19 (dd, *J* = 11.2, 6.3, 1H), 3.90 (dd, *J* = 11.2, 3.1, 1H), 3.69 (dd, *J* = 11.7, 6.5, 1H), 3.61–3.59 (m, 3H), 2.82 (t, *J* = 11.6, 1H), 2.75 (dt, *J* = 12.6, 1.8, 1H), 2.40 (s, 3H), 2.22–2.17 (m, 1H), 2.14–2.07 (m, 1H), 1.79–1.77 (m, 1H), 1.69–1.65 (m, 1H), 1.53–1.45 (m, 2H), 1.44–1.37 (m, 2H), 1.34–1.31 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.5, 143.8, 136.1, 129.5, 127.8, 87.6, 85.4, 72.5, 68.9, 62.2, 52.2, 43.9, 40.5, 38.3, 31.0, 22.6, 22.1, 21.5; IR (film): 3505, 2937, 2880, 1756, 1343, 1309, 1158, 1073, 1042, 972 cm^{-1}; HRMS-FAB (*m/z*) $[M + H]^+$ calcd for $C_{20}H_{27}N_2O_6S$, 423.5190; found, 423.1590; Anal. Calcd for $C_{20}H_{26}N_2O_6S$: C, 56.86; H, 6.20; N, 6.63; found: C, 56.63; H, 6.35; N, 6.44; $[\alpha]^{27}_D$ +6.75, $[\alpha]^{27}_{577}$ +6.17, $[\alpha]^{27}_{546}$ +7.53, $[\alpha]^{27}_{435}$ +14.6, $[\alpha]^{27}_{405}$ +18.3 (*c* 1.00, $CHCl_3$).



Ester 99. A mixture of alcohol **93** (1.12 g, 2.65 g), sodium chlorite (630 mg, 5.57 mmol), MeCN (20.0 mL), sodium phosphate buffer (20 mL, 0.67 M NaH_2PO_4/Na_2HPO_4, pH 6.7) and TEMPO (41.4 mg, 0.265 mmol) was heated to 37 °C. Then, 3 × 200 μL of dilute bleach (1.06 mL 5.25 % NaOCl diluted into 20 mL water) was added dropwise over a period of 45 min. After stirring the mixture for another 4.5 h, sodium chlorite (370 mg, 3.27 mmol) and another 500 μL of dilute bleach were added. After 24 h, the mixture was cooled to rt and diluted with water (30 mL). The pH of the mixture was adjusted to pH 8 with 2 M NaOH. The mixture was poured into a cold (~0 °C) solution of 0.5 M Na_2SO_3 and maintained <20 °C (pH of the aqueous layer 8.5–9.0). After stirring 0.5 h at rt, MTBE (30 mL) was added. The organic layer was separated and discarded. EtOAc (30 mL) was added and the aqueous layer was acidified with 2 M HCl to pH 3–4. The layers were separated and the aqueous phase was extracted with EtOAc (2 × 30 mL). The combined organic extracts were washed with water (2 × 30 mL) and brine (1 × 50 mL), dried over Na_2SO_4, and concentrated under reduced pressure to give the crude acid **98** (1.11 g, 2.53 mmol, 96%) as a colorless foam, which was used without further purification.

Methyl iodide (0.500 mL, 8.00 mmol) was added dropwise to a mixture of the crude acid **98** (436 mg, 1.00 mmol), potassium carbonate (691 mg, 5.00 mmol) and DMF (10.0 mL). After 0.5 h at rt, the reaction mixture was cooled to 0 °C, then diluted with water (30 mL), saturated aqueous $Na_2S_2O_3$ (10 mL), and EtOAc (30 mL). The pH was adjusted to pH 8 with 2 M HCl. The layers were separated and the aqueous phase was extracted with EtOAc (3 × 40 mL). The combined organic extracts were washed with brine (1 × 100 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the residue by flash chromatography (5 to 10% Et_2O-CH_2Cl_2) gave methyl ester **99** (407 mg, 0.903 mmol, 90%) as a colorless foam, which can be crystallized from EtOAc. R_f 0.57 (10% Et_2O-CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.3, 2H), 7.28 (d, *J* = 8.3, 2H), 5.50 (s, 1H), 4.48 (dd, *J* = 6.3, 3.2, 1H), 4.22 (dd, *J* = 11.2, 6.3, 1H), 3.92 (dd, *J* = 11.2, 3.3, 1H), 3.71 (dd, *J* = 11.7, 6.5, 1H), 3.67 (s, 3H), 3.65–3.62 (m, 1H), 2.82 (m, 1H), 2.78 (dt, *J* = 12.6, 1.9, 1H), 2.42 (s, 3H), 2.30 (t, *J* = 7.0, 2H), 2.24–2.19 (m, 1H), 2.11–2.06 (m, 1H), 1.76–1.57 (m, 3H), 1.46 (ddd, *J* = 13.3, 9.1, 4.1, 1H); ^{13}C NMR

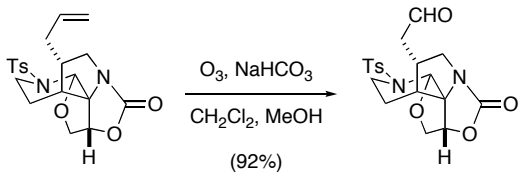
(125 MHz, $CDCl_3$): δ 172.9, 162.3, 143.8, 136.2, 129.5, 127.8, 87.6, 85.3, 72.3, 68.9, 51.81, 51.78, 43.3, 40.6, 38.2, 32.3, 22.2, 21.5; IR (film): 2935, 2883, 1764, 1343, 1309, 1162, 1092, 1038, 972 cm^{-1}; HRMS-FAB (*m/z*) $[M + H]^+$ calcd for $C_{20}H_{27}N_2O_6S$, 451.1539; found, 451.1548; Anal. Calcd for $C_{21}H_{26}N_2O_7S$: C, 55.99; H, 5.82; N, 6.22; found: C, 56.26; H, 5.88; N, 6.15; $[\alpha]^{27}_D$ +8.8, $[\alpha]^{27}_{577}$ +8.6, $[\alpha]^{27}_{546}$ +10.4, $[\alpha]^{27}_{435}$ +19.0, $[\alpha]^{27}_{405}$ +23.76 (*c* 1.00, $CHCl_3$).



99 **100**

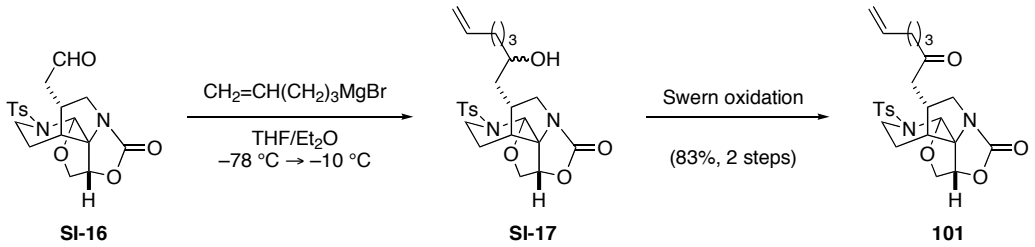
Alkene 100. LDA (0.3 M in THF-hexanes, 1.50 mL, 0.458 mmol) was added dropwise over 5 min to a solution of ester **99** (712 mg, 0.330 mmol) in THF (1.40 mL) and DMPU (0.950 mL) at –78 °C (acetone/dry ice). The solution was maintained at –78 °C for 10 min, then allowed to warm up to –55 °C over 20 min. 5-bromo-1-pentene (45.0 μL, 0.382 mmol) was added to the resulting deep yellow solution. After 15 min at –55 °C, another equivalent of 5-bromo-1-pentene (45.0 μL, 0.382 mmol) was added and the solution was allowed to warm up –40 °C over 0.5 h. The pale yellow solution was quenched with saturated aqueous NH_4Cl (3.00 ml), then allowed to warm up to rt. Water (100 mL) was added and the mixture was extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed brine (1 × 50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the residue by flash chromatography (60 to 75% EtOAc-hexanes) furnished recovered starting material **99** (100 mg, 0.222 mmol, 58%) and alkylated ester **100** (24.2 mg, 0.0467 mmol, 12%) as a colorless foam, which could be crystallized from EtOAc-hexanes. R_f 0.44 (50% EtOAc-hexanes); ^1H NMR (500 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.2, 2H), 7.27 (d, *J* = 8.1, 2H), 5.77–5.68 (m, 1H), 5.47 (s, 1H), 4.99–4.92 (m, 2H), 4.46 & 4.44 (minor diastereomer: dd, *J* = 6.3, 3.2; major diastereomer: dd, *J* = 6.3, 3.2, 1H), 4.21 & 4.18 (major diastereomer: dd, *J* = 11.2, 6.3; minor diastereomer: dd, *J* = 11.2, 6.2, 1H), 3.90 & 3.89 (major diastereomer: dd, *J* = 11.2, 3.2; minor diastereomer: dd, *J* = 11.2, 3.3, 1H), 3.74 & 3.59 (minor diastereomer: dd, *J* = 11.6, 6.6; minor diastereomer: dd, *J* = 11.8, 6.5, 1H), 3.66 & 3.65 (major and minor diastereomer, s, 3H), 3.63–3.59 (m, 1H), 2.84–2.71 (m, 2H), 2.41 (s, 3H), 2.27–2.13 (m, 2H), 2.01–1.96 (m, 3H), 1.77–1.54 (m, 4H), 1.47–1.38 (m, 3H), 1.37–1.27 (m,

2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.9, 175.6, 162.3, 162.2, 143.8, 143.8, 138.0, 138.0, 136.2, 129.5, 129.5, 127.8, 127.8, 115.0, 87.7, 87.6, 85.3, 85.2, 72.4, 72.1, 68.9, 68.9, 61.0, 51.9, 51.8, 51.7, 44.3, 44.0, 42.3, 42.1, 41.0, 40.3, 38.2, 38.0, 33.3, 32.5, 32.3, 29.1, 28.7, 26.4, 26.3, 22.3, 22.1, 21.5; IR (film): 2937, 2887, 1764, 1733, 1459, 1440, 1343, 1162, 973 cm^{-1}; HRMS-CI (*m/z*) $[M]^+$ calcd for $C_{26}H_{34}N_2O_7S$, 518.2087; found, 518.2094; Anal. Calcd for $C_{26}H_{34}N_2O_7S$: C, 60.21; H, 6.61; N, 5.40; found: C, 60.48; H, 6.80; N, 5.35; $[\alpha]^{27}_D$ +13.4, $[\alpha]^{27}_{577}$ +13.1, $[\alpha]^{27}_{546}$ +15.6, $[\alpha]^{27}_{435}$ +28.1, $[\alpha]^{27}_{405}$ +34.9 (*c* 0.640, $CHCl_3$).



87 **SI-16**

Aldehyde SI-16. Sodium bicarbonate (620 mg, 7.4 mmol) was added to a solution of alkene **87** (3.0 g, 7.4 mmol) in CH_2Cl_2:CH_3OH (8:1, 70 mL). The suspension was stirred vigorously and cooled to –78 ºC. Ozone was bubbled through the reaction mixture until the suspension remained a dark blue color. Oxygen was bubbled through the reaction mixture until the suspension became colorless. Dimethyl sulfide (1.2 mL, 16.3 mmol) was added to the reaction mixture dropwise over 2 min and the suspension was warmed to rt and stirred for 12 h. The mixture was washed with water (1 x 15 mL) and the aqueous portion was back extracted with CH_2Cl_2 (3 x 25 mL). The combined organic extracts were washed with brine (1 x 15 mL), dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the residue by flash chromatography (1:1 EtOAc:hex, then 3:1 EtOAc:hex) provided aldehyde **SI-16** as a colorless foam (2.75 g, 92%). R_f 0.23 (3:1 EtOAc:hex); ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.78 (s, 1H), 7.76 (d, *J* = 8.3, 2H), 7.29 (d, *J* = 8.0, 2H), 5.53 (s, 1H), 4.58 (dd, *J* = 6.3, 3.3, 1H), 4.23 (dd, *J* = 11.2, 6.3, 1H), 3.93 (dd, *J* = 11.2, 3.3, 1H), 3.79 (m, 1H), 3.64 (dt, *J* = 12.6, 3.6, 1H), 2.88 (m, 1H), 2.75 (td, *J* = 12.5, 2.0, 1H), 2.65–2.55 (m, 3H), 2.49–2.43 (m, 4H), 1.58–1.54 (m, 1H), 1.40 (qd, 12.8, 4.1, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.2, 162.1, 143.9, 136.0, 129.6, 127.8, 87.6, 85.3, 72.2, 70.0, 51.6, 40.5, 39.6, 38.0, 37.4, 22.4, 21.6; IR (film): 2934, 2887, 2841, 2737, 1760, 1722, 1598, 1343, 1162 cm^{-1}; HRMS-ESI (*m/z*) $[M + CH_3OH]^+$ calcd for $C_{20}H_{26}N_2O_7S$, 461.1358; found, 461.1367; $[\alpha]^{23}_D$ +6.6, $[\alpha]^{23}_{577}$ +7.2, $[\alpha]^{23}_{435}$ +12.5, $[\alpha]^{23}_{546}$ +8.0, $[\alpha]^{23}_{405}$ +14.8 (*c* 0.17, CH_2Cl_2).

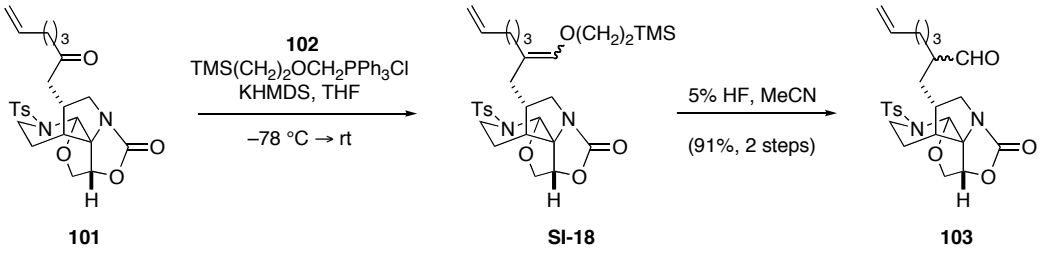


Ketone 101. A 100 mL 3-neck flask equipped with a glass stopper, reflux condenser, and a rubber septa was charged with Mg (1.26 g, 52.0 mmol). The Mg was activated by flame drying under a flow of N_2 and suspended in Et_2O (30 mL). The suspension was stirred and a small crystal of I_2 (~10 mg) was added, generating a brown suspension. This suspension was heated to reflux and the brown color dissipated. A solution of 5-bromo-1-pentene (6.0 mL, 40 mmol) in Et_2O (10 mL) was added to the suspension via cannula and the suspension was brought to reflux. At the beginning of the addition, the suspension turned yellow and then slowly turned gray. Upon completion of the addition of bromide, the external heat source was removed and the suspension was allowed to cool to rt with stirring over a period of 3.5 h. The suspension was filtered into a sealable tube under argon atmosphere using a Shlenk filter to provide a brown solution of 4-pentenyl-1-magnesium bromide (0.75 M). This solution could be stored under argon at rt indefinitely.

A solution of 4-pentenyl-1-magnesium bromide (13.6 mL, 10 mmol, 0.75 M in Et_2O) was added dropwise over 20 min to a solution of aldehyde **SI-16** (3.70 g, 9.14 mmol) in THF (91 mL) at –78 °C. The mixture was warmed to –10 °C and maintained at this temperature for 1 h. A saturated aqueous solution of NH_4Cl (100 mL) was added to the mixture in one portion. The mixture was diluted with water (50 mL) and the pH of the aqueous portion was adjusted to ~3.0 by dropwise addition of 1 M HCl. The mixture was extracted with EtOAc (2 x 100 mL) and the combined organic extracts were washed with saturated aqueous $NaHCO_3$ (1 x 100 mL), dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the residue by flash chromatography (4:1 EtOAc:hex) gave alcohol **SI-17** a colorless foam (3.96 g, 8.32 mmol, 91%), which was typically used directly in subsequent transformations. Eluting the column with EtOAc gave recovered starting material **SI-16** (300 mg, 0.74 mmol, 8%).

A solution of DMSO (10.7 mL, 150 mmol) in CH_2Cl_2 (90 mL) was added dropwise to a solution of oxalyl chloride (7.8 mL, 90 mmol) in CH_2Cl_2 (120 mL) at –78 ºC. The resulting suspension was stirred for 15 min and a solution of alcohol **SI-17** from above (8.43 g, 17.8

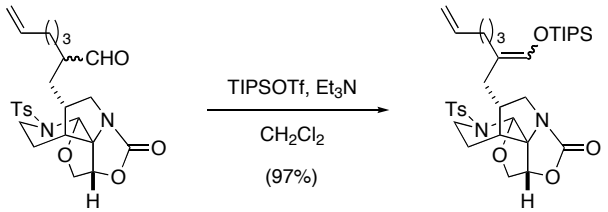
mmol) in CH_2Cl_2 (120 mL) was added via cannula to the reaction mixture. The suspension was stirred at –78 ºC for 15 min and then Et_3N (26 mL, 250 mmol) was added in one portion. The suspension was allowed to warm to rt and diluted with CH_2Cl_2 (100 mL) and water (1×150 mL). The layers were separated and the aqueous portion was extracted with EtOAc (2×150 mL). The combined organic portions were washed with brine (1×150 mL), dried over $MgSO_4$, and concentrated under reduced pressure to give a yellow residue. Purification of this residue by flash chromatography (1:1 EtOAc:hex) gave **101** as a colorless oil which crystallized on standing (7.70 g, 16.2 mmol, 91%, 83% over the 2 steps). mp 138–140 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.3, 2H), 7.27 (d, *J* = 8.3, 2H), 5.72 (ddt, *J* = 17.0, 10.3, 6.7, 1H), 5.50 (s, 1H), 5.00–4.95 (m, 2H), 4.56 (dd, *J* = 6.2, 3.2, 1H), 4.18 (dd, *J* = 11.2, 6.3, 1H), 3.90 (dd, *J* = 11.2, 3.1, 1H), 3.73 (dd, *J* = 11.6, 6.2, 1H), 3.61 (dt, *J* = 12.6, 3.6, 3.6, 1H), 2.82 (t, *J* = 11.1, 1H), 2.73 (td, *J* = 12.5, 2.0, 1H), 2.51–2.35 (m, 9H), 2.02 (q, *J* = 7.1, 2H), 1.67–1.61 (m, 2H), 1.53–1.49 (m, 1H), 1.37 (qd, *J* = 12.6, 4.1, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 208.2, 162.1, 143.8, 137.6, 136.3, 129.5, 127.8, 115.5, 87.7, 85.3, 72.4, 69.0, 51.7, 42.0, 39.7, 39.0, 38.7, 38.2, 32.9, 22.7, 22.4, 21.5; IR (film): 2934, 2891, 1764, 1710, 1640, 1598, 1343, 1162 cm^{-1}; Anal. Calcd for $C_{24}H_{30}N_2O_6S$: C, 60.74; H, 6.37; N, 5.90; found: C, 60.68; H, 6.33; N, 5.74; $[\alpha]^{23}_D$ +6.5, $[\alpha]^{23}_{577}$ +7.3, $[\alpha]^{23}_{546}$ +8.4, $[\alpha]^{23}_{435}$ +13.5, $[\alpha]^{23}_{405}$ +17.6 (*c* 0.17, CH_2Cl_2).



Aldehyde 103. Phosphonium salt **102**[5] (61.2 g, 154 mmol) was suspended in THF (1.1 L) and cooled to –78 °C. *N*-potassiumhexamethyldisilazane (24.0 g, 120 mmol) was added in one portion and the suspension was vigorously stirred for 15 min. The colorless reaction mixture became red. A solution of ketone **101** (8.14 g, 17.2 mmol) in THF (100 mL) was added to the reaction mixture by cannula. The reaction was allowed to warm to rt over 30 min at which point TLC analysis indicated the complete consumption of ketone **101**. Saturated aqueous $NaHCO_3$ (400 mL) was added and the mixture was extracted (3 x 500 mL) with EtOAc. The combined organic extracts were washed with brine (1 x 500 mL), dried over Na_2SO_4, and concentrated onto

Celite (200 g) under reduced pressure. Purified by flash chromatography using a gradient solvent system (1:4 EtOAc:hex, then 2:3 EtOAc:hex) afforded **SI-18** as a mixture of *E* and *Z* isomers (2:5, unassigned). The crude product was used directly in the subsequent transformation.

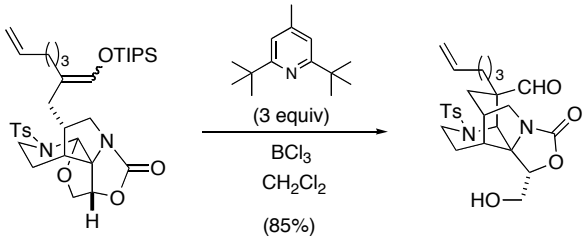
A solution of HF (10 mL, 49% aq) was added dropwise over 2 min to a solution of enol ether **SI-18** in MeCN (100 mL) in a polyethylene reaction vessel. The resulting solution was maintained at rt for 18 h. A solution of saturated aqueous $NaHCO_3$ was added dropwise (CAUTION! Gas evolution) until pH = 8. The mixture was extracted with EtOAc (3 x 150 mL) and the combined organic extracts were washed with brine (1 x 150 mL), dried over Na_2SO_4, and concentrated onto Celite (30 g). Purification by flash chromatography on silica gel (2:3 EtOAc:hex, then 1:1 EtOAc:hex) provided a mixture of aldehydes **103** (7.69 g, 15.7 mmol, 91% over 2 steps) as a colorless foam. This mixture of diastereomers was not separated and was characterized as a mixture. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.58 (d, *J* = 1.9, 1.7H), 9.53 (d, *J* = 2.8, 1H), 7.76 (d, *J* = 8.1, 5.4H), 7.29 (d, *J* = 8.0, 5.4 H), 5.73 (m, 2.7H), 5.50 (s, 2.7H), 5.03–4.96 (m, 5.4H), 4.49–4.46 (m, 2.7H), 4.23–4.19 (m, 2.7H), 3.92–3.90 (m, 2.7H), 3.71 (dd, *J* = 11.6, 6.5, 2H), 3.65–3.61 (m, 4.4H), 2.87–2.73 (m 5.4H), 2.42 (s, 8.1H), 2.23–2.17 (m, 5.4H), 2.08–2.04 (m, 8.1), 1.82–1.25 (m, 26H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 203.7, 203.5, 162.3, 162.2, 143.9, 143.86, 137.6, 136.1, 129.6, 129.5, 127.9, 127.8, 115.4, 115.38, 87.6, 87.5, 85.3, 72.3, 72.1, 68.9, 52.12, 52.0, 41.8, 41.78, 40.8, 40.2, 38.1, 38.0, 33.5, 28.9, 28.8, 26.0, 25.96, 25.0, 24.8, 22.3, 22.2, 21.6 (not all peaks for the two diastereomers are resolved); IR (film), 3068, 2930, 2883, 2860, 2722, 1763, 1719, 1640, 1597 cm^{-1}; HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{25}H_{33}N_2O_6S$, 489.2059; found, 489.2039; $[\alpha]^{23}_D$ +20.0, $[\alpha]^{23}_{577}$ +20.1, $[\alpha]^{23}_{546}$ +22.7, $[\alpha]^{23}_{435}$ +46.4, $[\alpha]^{23}_{405}$ +65.5 (*c* 0.19, CH_2Cl_2).



103 **104**

Enoxysilanes 104. Tri-*iso*-propylsilyltriflate (TIPSOTf, 14.7 mL, 54.6 mmol) was added dropwise to a solution of diastereomeric aldehydes **103** (7.62 g, 15.60 mmol) and Et_3N (15.2 mL, 109.2 mmol) in CH_2Cl_2 (150 mL) at –78 °C. The reaction was allowed to warm to rt, then stirred

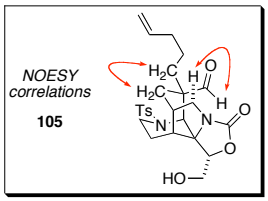
for 12 h. A saturated aqueous solution of $NaHCO_3$ (50 mL) was added and the mixture was extracted with EtOAc (3 x 150 mL). The combined organic extracts were washed with brine (1 x 100 mL), dried over Na_2SO_4, and concentrated onto Celite (20 g). Purification by flash chromatography on silica gel (1:10:39 Et_3N:EtOAc:hex) furnished a ~3:2 mixture of enoxysilanes **104** (9.75 g, 15.1 mmol, 97%) as a pale yellow foam. This mixture of isomers was not separated and was characterized as a mixture. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (d, J = 8.2, 5H), 7.29 (d, J = 8.5, 1H), 6.15 (s, 2.5H), 5.82–5.76 (m, 2.5 H), 5.49 (s, 1.5H), 5.48 (s, 1H), 5.00–4.91 (m, 5H), 4.50–4.47 (m, 1.5H), 4.21–4.71 (m, 2.5H), 3.92–3.90 (m, 2.5H), 3.66–3.62 (m, 5H), 2.90–2.74 (m, 5H), 2.24 (s, 7.5H), 2.30–2.19 (m, 2.5H), 2.13–1.71 (m, 19.5H), 1.48–1.40 (m, 8.0), 1.14–1.03 (m, 56H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.0, 162.8, 144.3, 144.2, 139.2, 138.9, 136.8, 136.76, 130.0, 129.95, 128.3, 116.9, 116.5, 115.2, 114.9, 88.2, 88.17, 85.8, 85.77, 73.2, 73.1, 69.42, 69.4, 52.9, 52.8, 42.7, 42.6, 41.3, 41.1, 38.9, 38.7, 34.1, 33.5, 31.0, 27.8, 27.5, 26.3, 23.3, 22.7, 22.0, 18.2, 18.18, 12.34, 12.3 (not all peaks for the two isomers are resolved); IR (film): 2943, 1772, 1653, 1458 cm^{-1}; HRMS-ESI (m/z) [M + Na]$^+$ calcd for $C_{34}H_{52}N_2NaO_6SSi$, 667.3213; found, 667.3228; $[\alpha]^{23}_D$ +1.7, $[\alpha]^{23}_{577}$ +1.9, $[\alpha]^{23}_{546}$ +2.6, $[\alpha]^{23}_{435}$ +4.8, $[\alpha]^{23}_{405}$ +6.5 (*c* 0.79, CH_2Cl_2).

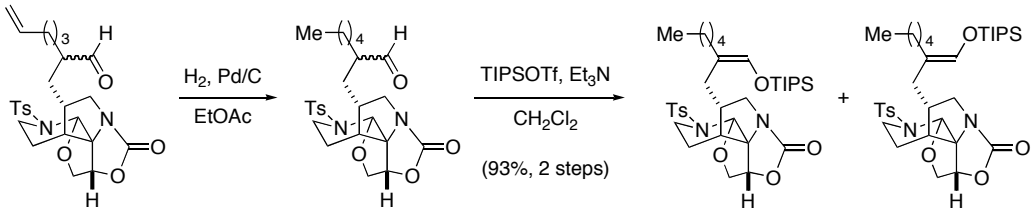


104 105

Aldehyde 105. A flask was charged enol ethers **104** (2.0 g, 3.1 mmol) and 2,6-di-*tert*-butyl-4-methylpyridine (1.9 g, 9.32 mmol). The mixture was dried by azeotropic distillation with benzene (3x). The flask was equipped with a sealable top and placed under an argon atmosphere. Methylene chloride (111 mL) was added via syringe and the solution was cooled to 0 °C. A solution of BCl_3 (12.4 mL, 12.4 mmol, 1.0 M in heptane) was added in one portion via an oven-dried glass syringe and the solution was allowed to warm to rt. The vessel was sealed under an argon atmosphere. The colorless solution turned slightly pink and cloudy precipitate slowly formed. The suspension was gently stirred for 15 h at rt. The seal was opened to an N_2 atmosphere and methylene chloride (200 mL) was added to the reaction mixture. The suspension

was transferred by rapid cannulation into a solution of saturated aqueous $NaHCO_3$ (250 mL). The two homogeneous phases were separated and the aqueous portion was extracted with EtOAc (5 x 100 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of this foam by flash chromatography (1:1 EtOAc:hex, then 2:1 EtOAc:hex, then 3:1 EtOAc:hex) gave **105** as a colorless powder (1.29 g, 85%). R_f 0.23 (1:3 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.34 (d, *J* = 1.7, 1H), 7.71 (d, *J* = 8.4, 2H), 7.33 (d, *J* = 8.0, 2H), 5.56 (ddt, *J* = 17.9, 10.4, 6.5, 1H), 5.13 (s, 1H), 4.88–4.84 (m, 2H), 4.45 (t, *J* = 4.1, 1H), 4.34–4.32 (m, 1H), 4.27–4.24 (m, 1H), 3.67 (dd, *J* = 13.0, 8.4, 1H), 3.23–3.20 (m, 1H), 3.13 (td, *J* = 12.9, 5.0, 1H), 3.03 (d, *J* = 9.9, 1H), 2.64–2.60 (m, 2H), 2.44–2.41 (m, 4H), 2.22–2.19 (m, 1H), 2.02–2.00 (m, 2H), 1.72–1.69 (m, 1H), 1.57–1.48 (m, 2H), 1.28–1.01 (m, 1H) 0.91–0.84 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.5, 160.7, 144.3, 137.6, 136.4, 129.9, 127.8, 114.9, 82.7, 60.1, 56.8, 53.3, 53.2, 42.1, 41.6, 39.7, 33.6, 33.4, 29.7, 21.6, 21.5, 21.46; IR (film): 3466, 2934, 2717, 1756, 1640, 1598, 1324, 1158 cm^{-1}; LRMS-ESI (*m*/*z*) $[M + H]^+$ calcd for $C_{25}H_{32}N_2O_6S$, 489; found, 489; Anal. Calcd for $C_{25}H_{32}N_2O_6S$: C, 61.46; H, 6.60; N, 5.73; found: C, 61.22; H, 6.62; N, 5.61; $[\alpha]^{23}_D$ –21.3, $[\alpha]^{23}_{577}$ –21.5, $[\alpha]^{23}_{546}$ –26.4, $[\alpha]^{23}_{435}$ –53.3, $[\alpha]^{23}_{405}$ –79.1 (*c* 0.3, CH_2Cl_2); The structure of aldehyde **105** was confirmed by COSY, HMQC, and NOESY experiments.

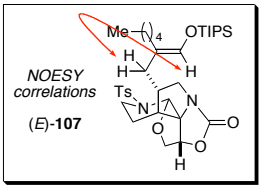


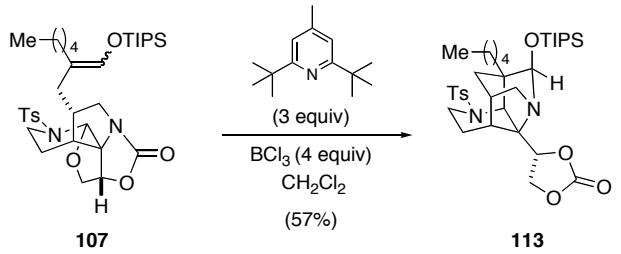


Enoxysilanes 107. A reaction vessel containing alkene **103** (55 mg, 0.113 mmol) and Pd/C (10 mg, 10% Degüssa Type) in EtOAc (4 mL) was stirred under H_2 gas (1 atm). After 15 min, the mixture was filtered over a plug of SiO_2 topped with Celite (EtOAc eluent). Removal of solvent under reduced pressure afforded aldehydes **SI-19**, which were used directly in the subsequent transformation.

TIPSOTf (110 μL, 0.407 mmol) was added dropwise to a solution of diastereomeric aldehydes **SI-19** prepared above, Et_3N (113 μL, 0.814 mmol), and CH_2Cl_2 (1.2 mL) at –78 °C.

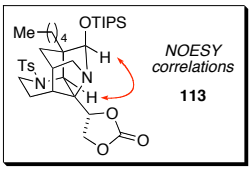
The reaction mixture was allowed to warm to rt over 30 min. After 4 h at rt, a saturated aqueous solution of $NaHCO_3$ (2 mL) was added and the mixture was extracted with EtOAc (5 x 1.5 mL). The combined organic extracts were washed with brine (1 x 1 mL), dried by passage over a short plug of SiO_2 (EtOAc eluent), and evaporated under reduced pressure. The resulting material was purified by flash chromatography on silica gel (4:1 hexanes: EtOAc containing 2% Et_3N; then, 3:1 hexanes: EtOAc containing 2% Et_3N) to give a ~3:2 mixture of enoxysilanes **107** (68 mg, 93% over 2 steps). The enoxysilane isomers could be separated by preparative HPLC (2 x 15 mg injections, Alltech Alltima 5 μ silica column (250 × 10 mm), 10.0 mL/min, 12% EtOAc in hexanes, λ = 254 nm, T_R = 19.9 min, minor isomer, T_R = 22.7 min, major isomer) to provide 12.0 mg of minor isomer (*Z*)-**107** and 17.1 mg of major isomer (*E*)-**107**. For (*Z*)-**107**: R_f 0.69 (1:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.3, 2H), 7.29 (d, *J* = 8.1, 2H), 6.15 (s, 1H), 5.50 (s, 1H), 4.47 (app. q, *J* = 3.1, 1H), 4.22 (dd, *J* = 11.2, 6.3, 1H), 3.93 (dd, *J* = 11.2, 3.1), 3.70–3.59 (m, 2H), 2.91 (app. t, *J* = 11.7, 1H), 2.80 (app. t, *J* = 11.7, 1H), 2.43 (s, 3H), 2.32–2.24 (m, 1H), 2.19–2.05 (m, 3H), 1.85–1.78 (m, 3H), 1.50–1.36 (m, 1H), 1.33–1.24 (m, 4H), 1.24–0.98 (m, 23H), 0.88 (t, *J* = 7.2, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.8, 143.9, 136.6, 136.3, 129.7, 129.1, 116.6, 87.9, 85.6, 72.8, 69.2, 52.8, 42.5, 41.1, 38.7, 31.5, 31.3, 28.0, 23.1, 22.7, 22.4, 21.8, 18.0, 14.3, 12.0; IR (film): 2929, 2867, 1767, 1465, 1347, 1204, 1162, 1142, 812 cm^{-1}; HRMS-ESI (*m*/*z*) [M + Na]$^+$ calcd for $C_{34}H_{54}N_2NaO_6SSi$, 669.3370; found, 669.3379; $[\alpha]^{26}_D$ –7.9, $[\alpha]^{26}_{577}$ –8.4, $[\alpha]^{26}_{546}$ –8.9, $[\alpha]^{26}_{435}$ –14.1, $[\alpha]^{26}_{405}$ –16.6 (*c* 1, CH_2Cl_2). For (*E*)-**107**: R_f 0.69 (1:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.3, 2H), 7.30 (d, *J* = 8.1, 2H), 6.14 (s, 1H), 5.51 (s, 1H), 4.50 (app. q, *J* = 3.1, 1H), 4.21 (dd, *J* = 11.2, 6.3, 1H), 3.93 (dd, *J* = 11.2, 3.2, 1H), 3.71–3.61 (m, 2H), 2.84 (app. t, *J* = 11.7, 1H), 2.75 (td, *J* = 11.7, 1.6, 1H), 2.43 (s, 3H), 2.30–2.20 (m, 1H), 2.19–1.96 (m, 3H), 1.95–1.82 (m, 2H), 1.77–1.70 (m, 1H), 1.54–1.45 (m, 1H), 1.37–1.20 (m, 6H), 1.17–1.01 (m, 21H), 0.87 (t, *J* = 7.2, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.6, 144.0, 136.5, 136.3, 129.7, 128.1, 117.0, 88.0, 85.5, 73.0, 69.2, 52.6, 42.4, 40.8, 38.5, 32.0, 28.3, 27.5, 26.4, 22.7, 22.4, 21.8, 17.9, 14.3, 12.1; IR (film): 2944, 2929, 2867, 1767, 1663, 1465, 1347, 1162, 816 cm^{-1}; HRMS-ESI (*m*/*z*) [M + Na]$^+$ calcd for $C_{34}H_{54}N_2NaO_6SSi$, 669.3370; found, 669.3690; $[\alpha]^{26}_D$ +5.3, $[\alpha]^{26}_{577}$ +5.5, $[\alpha]^{26}_{546}$ +6.4, $[\alpha]^{26}_{435}$ +12.2, $[\alpha]^{26}_{405}$ +15.8 (*c* 1.00, CH_2Cl_2). The olefin geometry of (*E*)-**107** was determined from NOESY experiments, as depicted.

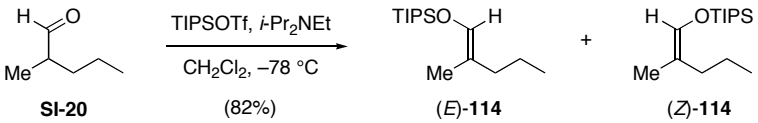




107 **113**

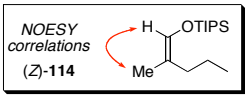
***N,O*-acetal 113.** *N,O*-acetal **113** was routinely observed in cyclization experiments that were carried out at low temperatures for short reaction times. An analytical sample of **113** was prepared as follows: A solution of BCl_3 (75 μL, 0.0745 mmol, 1 M solution in heptane) was added dropwise over 15 sec to a stirred solution of enoxysilanes **107** (12 mg, 0.186 mmol) and 2,6-di-*t*-butyl-4-methylpyridine (11.5 mg, 0.0559 mmol) in CH_2Cl_2 (745 μl) at 0 °C. After an additional 30 sec, the reaction mixture was quenched by the addition of saturated aq. $NaHCO_3$ (1 mL). After warming to rt, the layers were separated and the aqueous layer was extracted with EtOAc (4 x 1 mL) The combined organic layers were washed with brine (1 mL), dried by passage over a plug of silica gel (EtOAc eluent), and evaporated under reduced pressure. Purification of the residue by flash chromatography (CH_2Cl_2; then 4:1 hexanes:EtOAc eluent) afforded *N,O*-acetal **113** (6.9 mg, 57%) as a white foam. R_f 0.26 (4:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$): 7.65 (d, J = 8.1, 2H), 7.30, (d, J = 8.1, 2H), 4.86 (dd, J = 8.2, 5.7, 1H), 4.57 (app. t, J = 8.2, 1H), 4.37 (dd, J = 8.1, 5.8, 1H), 4.43 (s, 1H), 3.80–3.74 (m, 2H), 3.62 (d, J = 11.4, 1H), 3.39 (td, J =13.8, 4, 1H), 2.49 (br s, 1H), 2.45–2.39 (m, 4H), 2.16–2.05 (m, 2H), 2.03–1.97 (m, 1H), 1.90–1.80 (m, 2H), 1.20–0.93 (m, 29H), 0.83 (t, J = 7.3, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.4, 143.9, 138.2, 130.0, 126.9, 90.4, 74.9, 66.5, 65.3, 57.2, 52.6, 47.6, 40.2, 39.9, 39.7, 34.0, 33.0, 30.4, 23.5, 22.8, 22.4, 21.7, 18.0, 14.4, 12.6; IR (film): 2943, 2933, 2869, 1810, 1468, 1331, 1158, 1086 cm^{-1}; HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{34}H_{55}N_2O_6SSi$, 647.3550; found, 647.3558; $[\alpha]^{25}_D$ +30.3, $[\alpha]^{25}_{577}$ +30.0, $[\alpha]^{25}_{546}$ +31.8, $[\alpha]^{25}_{435}$ +60.2, $[\alpha]^{25}_{405}$ +69.3 (*c* 1.00, CH_2Cl_2). The relative stereochemistry of *N,O*-acetal **113** was determined from NOE experiments, as depicted.

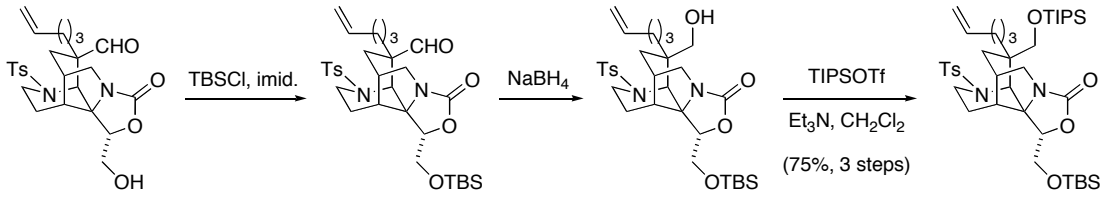




SI-20 (*E*)-**114** (*Z*)-**114**

Enoxysilanes 114. TIPSOTf (1.9 mL, 7.07 mmol) was added dropwise to a solution of 2-methylpentanal (**SI-20**) (250 μL, 2.02 mmol), *i*-Pr_2NEt (2.46 mL, 14.14 mmol), and CH_2Cl_2 (20 mL) at –78 °C. The reaction mixture was allowed to warm to rt over 30 min. After 12 h at rt, the reaction mixture was poured into a saturated aqueous solution of $NaHCO_3$ (30 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic extracts were dried over Na_2SO_4 and evaporated under reduced pressure. The resulting material was purified by flash chromatography on SiO_2 (hexanes eluent) to give a 2.3:1 mixture of enoxysilanes **114** (610 mg, 82%). (*Z*)-**114** (higher R_f) could be isolated as a single stereoisomer by careful flash chromatography (hexanes eluent) using copious quantities of SiO_2 (i.e., 100 mg of enoxysilanes **114** chromatographed using a 2 x 20 cm column). R_f 0.71 (hexanes); ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.16 (s, 1H), 2.09 (d, *J* = 7.58, 2H), 1.51 (d, *J* = 1.3, 3H), 1.41 (app. sextet, *J* = 7.4, 2H), 1.20–1.06 (m, 21H), 0.90, (t, *J* = 7.4, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 134.4, 116.1, 30.9, 20.7, 18.0, 17.3, 14.3, 12.2; IR (film): 2958, 2944, 2867, 1677, 1465, 1169, 996 cm^{-1}; HRMS-APCI (*m*/*z*) $[M + H]^+$ calcd for $C_{15}H_{33}NOSi$, 257.2301; found, 257.2308. The olefin geometry of (*Z*)-**114** was determined from NOESY experiments, as depicted.





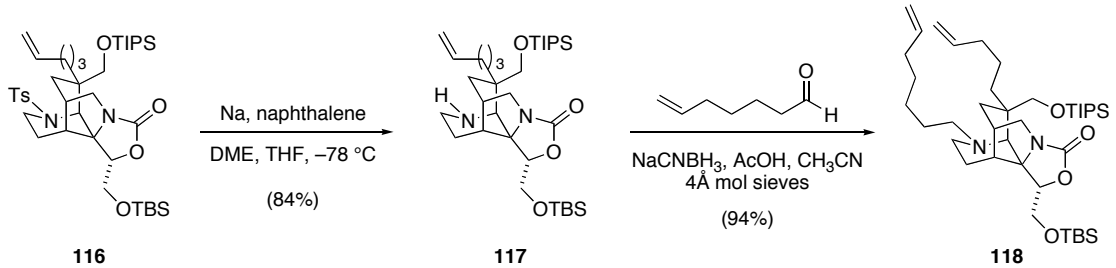
104 **SI-21** **SI-22** **116**

TIPS ether 116. In one portion, TBSCl (2.16 g, 14.40, mmol) was added to a solution of alcohol **104** (4.69 g, 9.62, mmol) and imidazole (1.96 g, 28.84 mmol) in MeCN (96 mL). After 2 h, the mixture was poured into water (200 mL) and extracted with EtOAc (3 x 100 mL). The combined organic extracts were dried over Na_2SO_4, and concentrated onto Celite (20 g). Purification by filtration through silica gel (1:1 EtOAc:hex) provided silyl ether **SI-21** as a slightly yellow foam (5.34 g) which was carried on immediately.

SI-21 (5.34 g) was dissolved in MeOH (88 mL) and the resulting solution was cooled to 0 °C. Sodium borohydride (1.68 g, 44.4 mmol) was added in one portion and the resulting suspension was stirred at 0 °C for 2 h. The reaction mixture was slowly poured into a saturated

aqueous solution of NH_4Cl (150 mL) and the resulting mixture was extracted with EtOAc (3 x 200 mL). The combined organic extracts were washed with brine (1 x 100 mL), dried over $MgSO_4$, and concentrated onto Celite (20 g). Purification by filtration through silica gel (3:1 EtOAc:hex) furnished alcohol **SI-22** as a slightly yellow foam (5.31 g) which was carried on immediately.

Tri-*iso*-propylsilyltriflate (5.9 mL, 21.9 mmol) was added to a solution of crude **SI-22** (5.31 g) and Et_3N (4.88 mL, 35.1 mmol) in CH_2Cl_2 (87 mL). The solution was maintained at rt for 2 d and then quenched by the addition of saturated aqueous $NaHCO_3$ (50 mL). The phases were separated and the aqueous portion was extracted with EtOAc (3 x 100 mL). The combined organic portions were dried over $MgSO_4$ and concentrated onto Celite (20 g). Purification by flash chromatography on silica gel (2:5 EtOAc:hex) provided **116** as a colorless foam (5.60 g, 7.37 mmol, 75% over the three steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 8.3, 2H), 7.27 (d, *J* = 8.2, 2H), 5.72 (ddt, *J* = 17.0, 10.3, 6.7, 1H), 4.94–4.89 (m, 2H), 4.55 (dd, *J* = 11.8, 1.7, 1H), 4.49 (s, 1H), 4.43 (dd, *J* = 7.7, 1.7, 1H), 4.05–3.97 (m, 2H), 3.66 (d, *J* = 9.8, 1H), 3.53 (dd, *J* = 10.4, 5.6, 1H), 3.38 (dd, *J* = 12.8, 8.5, 1H), 3.18 (td, *J* = 12.8, 5.2, 1H), 2.98 (d, *J* = 10.7, 1H), 2.55–2.49 (m, 1H), 2.41 (s, 3H), 2.04–1.60 (m, 8H), 1.57–1.42 (m, 1H), 1.21–1.04 (m, 24H), 1.00–0.89 (m, 10H), 0.12 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.7, 143.5, 138.7, 137.0, 129.6, 127.7, 114.2, 80.8, 68.3, 66.0, 62.8, 56.2, 55.0, 42.9, 40.2, 40.0, 39.7, 37.1, 34.2, 25.8, 22.6, 21.4, 21.2, 18.3, 18.1, 18.05, 12.3, –5.4, –5.5; IR (film): 2930, 2866, 1760, 1641, 1598, 1463, 1331 cm^{-1}; LRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{40}H_{69}N_2O_6SSi_2$, 761; found, 761; Anal. Calcd for $C_{40}H_{68}N_2O_6SSi_2$: C, 63.11; H, 9.00; N, 3.68; found: C, 63.06; H, 9.04; N, 3.67; $[\alpha]^{23}_D$ –21.3, $[\alpha]^{23}_{577}$ –21.5, $[\alpha]^{23}_{546}$ –26.4, $[\alpha]^{23}_{435}$ –53.3, $[\alpha]^{23}_{405}$ –79.1 (*c* 0.3, CH_2Cl_2).

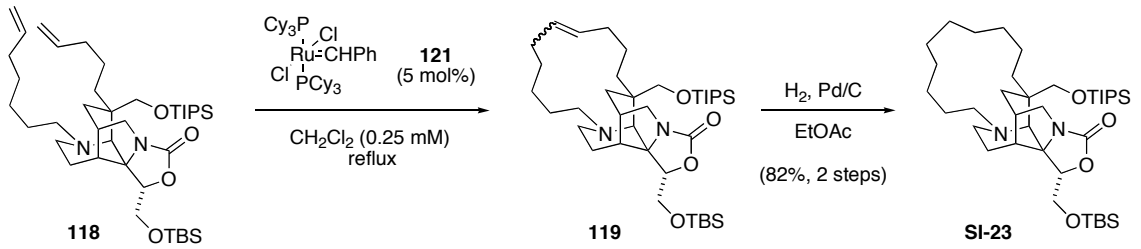


116 **117** **118**

Diene 118. Freshly cut sodium (1.15 g, 50.0 mmol) was added to a solution of naphthalene (6.20 g, 50.0 mmol) in DME (100 mL). The mixture was stirred for 1 h and the clear, colorless mixture became a dark green solution. Sulfonamide **116** (5.60 g, 7.40 mmol) was

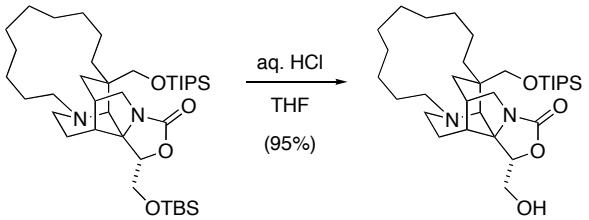
dried by azeotropic distillation of benzene (3 x 14 mL). The resulting residue was dissolved in THF (75 mL) and cooled to –78 ºC. The solution of sodium naphthalide was added dropwise to the sulfonamide solution until the dark green color persisted and TLC analysis indicated complete consumption of the sulfonamide. Saturated aqueous $NaHCO_3$ (50 mL) was added rapidly and the resulting cloudy colorless suspension was allowed to warm to rt. Water (50 mL) was added and the mixture was extracted with EtOAc (3 x 100 mL). The combined organic extracts were washed with brine (1 x 50 mL), dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography (1:10 EtOAc:hex then, 1:5 EtOAc:hex) to gave amine **117** as a viscous, colorless oil (3.77 g, 6.20 mmol, 84%) that yellowed upon exposure to air. The product was carried on immediately.

In one portion, $NaBH_3CN$ (3.10 g, 49.6 mmol) was added to a stirred suspension of amine **117** (3.77 g, 6.2 mmol), 6-hepten-1-al (1.7 mL, 12.4 mmol), powdered 4 Å mol sieves (3.10 g) and acetic acid (0.73 mL, 12.4 mmol) in MeCN (62 mL). The suspension was stirred for 10 min and a second portion of 6-hepten-1-al (1.7 mL, 12.4 mmol) was added. The suspension was stirred for an additional 15 min. The reaction mixture was poured into saturated aqueous $NaHCO_3$ (100 mL) and extracted with EtOAc (3 x 100 mL). The combined organic extracts were washed with brine (1 x 50 mL), dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography (EtOAc:hex, 1:10) gave a mixture of diene **118** and an unidentified byproduct. The residue was further purified by flash chromatography (1:9 EtOAc:benzene) to give diene **118** as a colorless oil (4.08 g, 5.81 mmol, 94%). R_f 0.55 (3:7 EtOAc:hex); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.79 (m, 2H), 5.01–4.93 (m, 4H), 4.51 (d, *J* = 5.9, 1H), 4.14 (dd, *J* = 10.7, 2.0, 1H), 3.90–3.81 (m, 2H), 3.53 (d, *J* = 9.7, 1H), 3.47–3.43 (m, 1H), 3.10–2.97 (m, 2H), 2.90–2.83 (m, 2H), 2.64 (br t, *J* = 10.2, 1H), 2.48–2.46 (m, 2H), 2.07–2.02 (m, 5H), 1.89 (dd, *J* = 14.1, 4.5, 1H), 1.81–1.75 (m, 3H), 1.53–1.50 (m, 1H), 1.41–1.20 (m, 9H), 1.11–1.07 (m, 20H), 0.08 (d, *J* = 3.8, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.9, 138.8, 138.79, 114.5, 114.4, 82.1, 68.8, 66.1, 63.0, 61.0, 58.6, 55.6, 45.7, 41.2, 40.5, 36.4, 35.1, 34.8, 33.7, 29.5, 28.8, 26.7, 25.6, 22.4, 22.3, 18.4, 18.1, 12.1, –5.2, –5.6; IR (film): 3076, 2930, 2864, 1760, 1640, 1463 cm^{-1}; LRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{40}H_{75}N_2O_4Si_2$, 703; found, 703; Anal. Calcd for $C_{40}H_{74}N_2O_4Si_2$: C, 68.32; H, 10.61; N, 3.98; found: C, 68.45; H, 10.81; N, 4.02; $[\alpha]^{23}_D$ –3.2, $[\alpha]^{23}_{577}$ –3.2, $[\alpha]^{23}_{546}$ –4.2, $[\alpha]^{23}_{435}$ –6.1, $[\alpha]^{23}_{405}$ –9.8 (*c* 0.3, CH_2Cl_2).



Macrocycle SI-23. A 5-L 3-neck flask was equipped with a magnetic stir bar, a reflux condenser, a gas dispersion tube, and a straight tube adaptor with an in-line Teflon screw seal. A septum was fitted to the straight tube adaptor and a gas flow adaptor, fitted with an argon inlet and an oil bubbler outlet, was placed atop the reflux condenser. The flask was charged with CH_2Cl_2 (2.4 L) and diene **118** (416 mg, 0.59 mmol), and the solution was sparged for 1 h with a flow of argon through the gas dispersion tube. The solution was heated to reflux and a solution of catalyst **121** (24.3 mg, 0.030 mmol) in CH_2Cl_2 (11 mL) was added in one portion through the septum and the Teflon screw was firmly sealed to avoid contact of the solvent vapor with the rubber septum. The solution was refluxed for 8 h under a flow of argon and DMSO (400 μL) was added. The solution was allowed to cool to rt over 12 h, then the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography on silica using a gradient solvent system (1:99 EtOAc:benzene; then 5:95 EtOAc:benzene) to provide macrocycles **119** as a slightly yellow (2:1 mixture of *E* and *Z* isomers). **119** was used directly in the subsequent transformation. As separation of the alkene stereoisomers proved difficult, **119** was characterized as a mixture. R_f 0.55 (1:9 EtOAc:benzene); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.40–5.34 (overlapping, m, 1H), 5.30–5.23 (overlapping, m, 1H), 4.34 (dd, *J* = 8.4, 2.0, 0.33H), 4.41 (dd, *J* = 6.9, 2.1, 0.67H), 3.97 (overlapping, m, 1H), 3.87 (d, *J* = 9.5, 0.33H), 3.80–3.75 (overlapping m, 1.67H), 3.61 (d, *J* = 9.7, 0.67H), 3.51 (d, *J* = 9.5, 0.33H), 3.41 (overlapping apt dd, *J* = 10.3, 5.2, 1H), 3.03–2.92 (overlapping m, 3.66H), 2.42–2.39 (overlapping m, 3.66H), 2.35–2.13 (overlapping m, 1.33H), 2.03–1.95 (overlapping m, 3H), 1.66–1.10 (overlapping m, 13H), 1.09–1.02 (overlapping peaks, 18H), 0.90 (s, 9H), 0.75 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.1, 130.4, 98.2, 83.6, 83.4, 69.3, 69.2, 66.2, 63.2, 62.8, 62.4, 62.0, 59.1, 59.0, 54.5, 54.8, 43.5, 43.4, 43.0, 41.9, 41.4, 41.3, 40.4, 38.2, 37.7, 32.9, 29.7, 28.2, 26.9, 26.8, 25.9, 25.9, 24.6, 22.6, 21.9, 21.8, 21.5, 18.4, 18.3, 18.2, 13.7, 12.2, –5.2, –5.3, –5.4 (not all peaks for the two isomers are resolved).

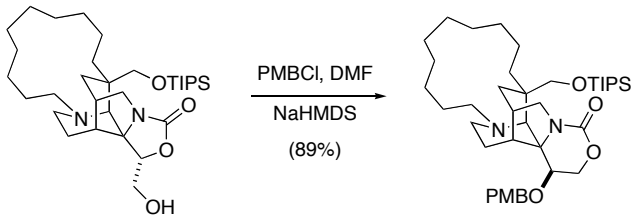
Palladium on carbon (155 mg, 10% Degüssa Type) was added to a degassed solution of alkenes **119** in EtOAc (4.5 mL). The reactor was purged with H_2 and the suspension was stirred under H_2 (1 atm) for 6 h. The reaction mixture was filtered through a plug of SiO_2 topped with Celite (EtOAc eluent). Evaporation under reduced pressure afforded macrocycle **SI-23** (330 mg, 82%, 2 steps) as a colorless foam. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.40 (t, *J* = 2.7, 1H), 4.01 (dd, *J* = 11.5, 3.0, 1H), 3.92 (dd, *J* = 11.4, 2.5, 1H), 3.88 (d, *J* = 10.3, 1H), 3.50 (d, *J* = 10.3, 1H), 3.40 (dd, *J* = 9.6, 5.2, 1H), 3.13 (d, *J* = 10.3, 1H), 3.07–2.95 (m, 3H), 2.60–2.51 (m, 2H), 2.46–2.42 (m, 1H), 2.05–1.99 (m, 1H), 1.95–1.88 (m, 2H), 1.80–1.75 (m, 1H), 1.62–1.56 (m, 3H), 1.46–1.41 (m, 8H), 1.27–1.21 (m, 9H), 1.09–1.05 (m, 22H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.0, 81.8, 68.9, 64.8, 61.8, 61.5, 59.1, 54.9, 45.1, 41.5, 41.1, 40.9, 36.7, 33.7, 28.0, 27.1, 26.4, 25.9, 25.5, 24.7, 24.4, 23.6, 22.2, 20.4, 18.3, 18.2, 12.3, –5.4, –5.6; IR (film): 2935, 2866, 1753, cm^{-1} LRMS-ESI (*m*/*z*) $[M + H]^+$ calcd for $C_{38}H_{73}N_2O_4Si_2$, 677; found, 677; Anal. Calcd for $C_{38}H_{72}N_2O_4Si_2$: C, 67.40; H, 10.72; N, 4.14; found: C, 67.49; H, 10.81; N, 4.16. $[\alpha]^{23}_D$ +9.9, $[\alpha]^{23}_{577}$ +9.9, $[\alpha]^{23}_{546}$ +11.2, $[\alpha]^{23}_{435}$ +14.5, $[\alpha]^{23}_{405}$ +15.6 (*c* 0.21, CH_2Cl_2).



SI-23 **122**

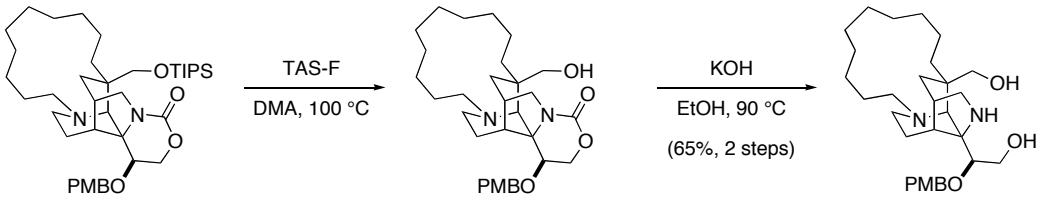
One molar aqueous HCl (975 μL) was added to a solution of TBS ether **SI-23** (330 mg, 0.487 mmol) in THF (4.13 mL). The solution was maintained at rt for 6 h. The reaction mixture was poured into 10 mL saturated aqueous $NaHCO_3$ (CAUTION! Gas evolution) and then extracted with EtOAc (4 x 15 mL). The combined organic extracts were washed with brine (1 x 15 mL), dried over $MgSO_4$, and evaporated under reduced pressure. Purification of the resulting residue by flash chromatography (4:1 benzene: EtOAc; then 3:1 benzene: EtOAc) gave **122** as a colorless foam (260 mg, 95%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.51 (t, *J* = 6.4, 1H), 3.92–3.89 (m, 2H), 3.82 (dd, *J* = 11.3, 6.8, 1H), 3.73 (d, *J* = 10.0, 1H), 3.66 (d, *J* = 10.0, 1H), 3.42 (dd, *J* = 10.0, 5.3, 1H), 3.07–3.04 (m, 3H), 3.01–2.94 (m, 1H), 2.72–2.67 (m, 2H), 2.58–2.53 (m, 1H), 2.15–2.07 (m, 1H), 1.93–1.78 (m, 4H), 1.62–1.07 (m, 39H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.6, 84.0, 69.1, 65.5, 60.6, 60.5, 57.8, 53.5, 45.3, 43.0, 41.9, 41.4, 36.8, 35.0, 27.3, 26.2, 26.0,

25.2, 24.7, 24.2, 22.0, 20.7, 18.14, 18.1, 12.2; IR (film): 3412, 2926, 2864, 1733, 1463 cm^{-1}; LRMS-ESI (*m*/*z*) $[M + H]^+$ calcd for $C_{32}H_{59}N_2O_4Si$, 563; found, 563; Anal. Calcd for $C_{32}H_{58}N_2O_4Si$: C, 68.28; H, 10.39; N, 4.98; found: C, 68.24; H, 10.54; N, 4.81; $[\alpha]^{24}_D$ –12.4, $[\alpha]^{24}_{577}$ –13.0, $[\alpha]^{24}_{546}$ –15.1, $[\alpha]^{24}_{435}$ –28.0 (*c* 0.77, CH_2Cl_2).



122 **123**

PMB ether 123. A solution of NaHMDS (0.85 mL, 1.0 M in THF) was added to a stirred solution of alcohol **122** (435 mg, 0.77 mmol), *para*-methoxybenzyl chloride (PMBCl, 0.16 mL, 0.85 mmol), and DMF (7.7 mL). A flocculent colorless precipitate formed and the suspension was stirred for 30 min while the precipitate slowly dissolved. The reaction mixture was poured into water (50 mL) and extracted with EtOAc (3 x 50 mL). The combined organic extracts were washed with brine (1 x 50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification by flash chromatography (3:7 EtOAc:hex) provided **123** as a white foam (467 mg, 0.69 mmol, 89%) which yellowed upon exposure to air. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.40 (t, *J* = 2.7, 1H), 4.01 (dd, *J* = 11.5, 3.0, 1H), 3.92 (dd, *J* = 11.4, 2.5, 1H), 3.88 (d, *J* = 10.3, 1H), 3.50 (d, *J* = 10.3, 1H), 3.40 (dd, *J* = 9.6, 5.2, 1H), 3.13 (d, *J* = 10.3, 1H), 3.07–2.95 (m, 3H), 2.60–2.51 (m, 2H), 2.46–2.42 (m, 1H), 2.05–1.99 (m, 1H), 1.95–1.88 (m, 2H), 1.80–1.75 (m, 1H), 1.62–1.56 (m, 3H), 1.46–1.41 (m, 8H), 1.27–1.21 (m, 9H), 1.09–1.05 (m, 22H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.4, 152.7, 129.6, 113.9, 70.3, 69.2, 66.6, 66.5, 64.8, 62.9, 59.8, 55.3, 53.9, 43.1, 42.9, 36.8, 36.2, 35.8, 33.6, 27.8, 26.6, 25.8, 25.3, 24.9, 24.3, 24.1, 22.0, 21.8, 18.2, 18.16, 12.1; IR (film): 2937, 2864, 1695, 1613, 1513 cm^{-1}; LRMS-ESI (*m*/*z*) $[M + H]^+$ calcd for $C_{40}H_{66}N_2O_5Si$, 684; found, 684; $[\alpha]^{23}_{405}$ –9.8, $[\alpha]^{23}_{435}$ –6.1, $[\alpha]^{23}_{546}$ –4.2, $[\alpha]^{23}_{577}$ –3.2, $[\alpha]^{23}_D$ –3.2 (*c* 0.3, CH_2Cl_2); This structure was further confirmed by COSY, HMQC, and HMBC.

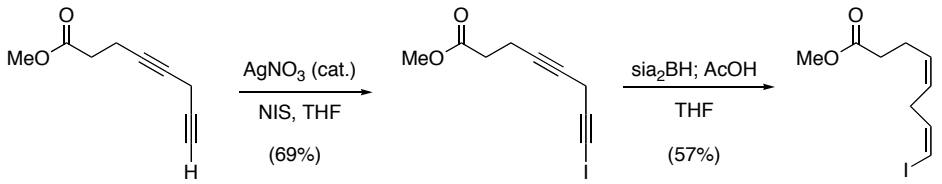


123 **SI-24** **124**

Diamine diol 124. In a glove box with an N_2 atmosphere, a mixture of **123** (340 mg, 0.498 mmol) and tris(dimethylamino)sulfur (trimethylsilyl)difluoride (TAS-F, 642 mg, 2.49 mmol) was dissolved in *N*,*N*-dimethylacetamide (DMA, 5.0 mL). The resulting yellow solution was heated to 100 °C for 1 h. The reaction vessel was allowed to cool to rt, then removed from the glove box. The reaction mixture was poured into water (30 mL) and the resulting mixture was extracted with EtOAc (3 x 30 mL). The combined organic extracts were washed with brine (1 x 30 mL), dried over Na_2SO_4, and concentrated onto Celite (2 g). Purification by flash chromatography (1:1 EtOAc:hex; then, 3:1 EtOAc:hex eluent) provided alcohol **SI-24** as a yellow foam that was used directly in the subsequent transformation.

A Teflon screw cap sealable tube with a ground glass adaptor was charged with a magnetic stir bar and freshly pulverized KOH (800 mg, 14.26 mmol) then placed under an atmosphere of argon. A solution of crude oxazinanone **SI-24** (prepared above) in EtOH (4 mL) was added by syringe and the resulting suspension was stirred until homogeneous. The solution was degassed by 5 cycles of freeze-pump-thaw, sealed under an atmosphere of argon, and heated in a 90 °C oil bath and maintained for 12 h. The mixture was allowed to cool to rt and the reaction mixture was poured into 30 mL brine with the aid of 60 mL CH_2Cl_2 and 15 mL brine. The cloudy phases were separated and the organic portion was washed with brine (1 x 40 mL). The combined aqueous portions were extracted with CH_2Cl_2 (5 x 50 mL). The combined organic portions were dried over $MgSO_4$ and then filtered through a plug of basic alumina (Brockman I, 4 × 2 cm). The filter cake was washed with CH_2Cl_2:MeOH (9:1, 3 x 75 mL). The filtrate was concentrated and the resulting residue dissolved in CH_2Cl_2 (10 mL), filtered through cotton, and then concentrated to give **124** as slightly yellow flakes (161 mg, 65% over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.40 (t, *J* = 2.7, 1H), 4.01 (dd, *J* = 11.5, 3.0, 1H), 3.92 (dd, *J* = 11.4, 2.5, 1H), 3.88 (d, *J* = 10.3, 1H), 3.50 (d, *J* = 10.3, 1H), 3.40 (dd, *J* = 9.6, 5.2, 1H), 3.13 (d, *J* = 10.3, 1H), 3.07–2.95 (m, 3H), 2.60–2.51 (m, 2H), 2.46–2.42 (m, 1H), 2.05–1.99 (m, 1H), 1.95–1.88 (m, 2H), 1.80–1.75 (m, 1H), 1.62–1.56 (m, 3H), 1.46–1.41 (m, 8H), 1.27–1.21 (m, 9H), 1.09–

1.05 (m, 22H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2): δ 160.1, 130.9, 130.2, 114.4, 79.0, 73.1, 72.2, 67.3, 66.1, 60.7, 60.4, 55.8, 52.1, 43.24, 43.2, 42.5, 40.0, 38.1, 37.2, 28.1, 27.7, 26.7, 25.9, 25.0, 24.5, 23.9, 22.8, 22.1; IR (film): 3351, 2933, 2860, 1614, 1514 cm^{-1}; LRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{30}H_{49}N_2O_4$, 501; found, 501; Anal. Calcd for $C_{30}H_{48}N_2O_4$: C, 71.96; H, 9.66; N, 5.59; found: C, 71.71; H, 9.67; N, 5.61; $[\alpha]^{24}_D$ –1.3, $[\alpha]^{24}_{577}$ –1.1, $[\alpha]^{24}_{546}$ – 0.3, $[\alpha]^{24}_{435}$ +2.0, $[\alpha]^{24}_{405}$ +5.5 (*c* 0.9, CH_2Cl_2).

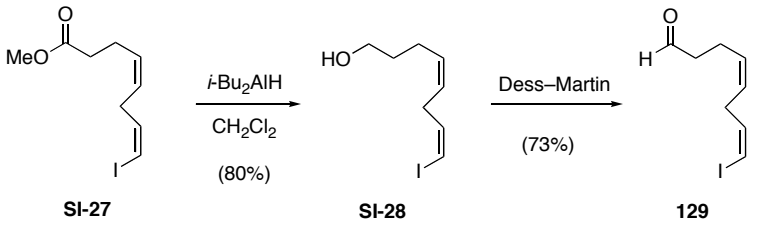


SI-25 **SI-26** **SI-27**

Ester SI-27. Silver nitrate (0.74 g, 4.40 mmol) was added to a solution of **SI-25**[6] (6.77 g, 44.0 mmol) in THF (45 mL). The suspension was shielded from light and stirred at rt for 5 min. *N*-iodosuccinimide (10.1 g, 44.0 mmol) was added to the reaction mixture in one portion and stirring was maintained for 2 h. The reaction mixture was poured into 100 mL water and extracted with Et_2O (3 x 100 mL). The combined extracts were dried over Na_2SO_4 and concentrated onto Celite. Purification by flash chromatography (1:10 Et_2O:pentane) gave **SI-26** as a light and air sensitive colorless powder (8.52 g, 30.4 mmol, 69%) that was used directly in subsequent reactions.

A reaction vessel equipped with a Teflon screw-cap top was charged with 2-methyl-2-butene (3.7 mL, 34.8 mmol) and cooled to 0 °C. BH_3•DMS (1.74 mL, 17.4 mmol) was added dropwise by syringe pump over 30 min. The reaction vessel was sealed and the reaction was allowed to warm to rt over 2 h. The reaction was cooled to 0 °C and a solution of diyne **SI-26** (1.20 g, 4.34 mmol) in THF (4.2 mL) was added dropwise by syringe pump over 30 min. The reaction vessel was sealed and allowed to warm to rt over 8 h. Acetic acid (8.0 mL, 139 mmol) was added to the reaction mixture dropwise (CAUTION! Gas evolution) over 10 min and the solution was maintained for 14 h. The reaction was diluted with CH_2Cl_2 (50 mL) and poured into a stirred saturated aqueous solution of $NaHCO_3$ (300 mL, CAUTION! gas evolution). The aqueous phase was adjusted to pH = 8 by the addition of a solution of 3M aqueous NaOH (10 mL) and the mixture was extracted with CH_2Cl_2 (2 x 100 mL). The combined organic portions

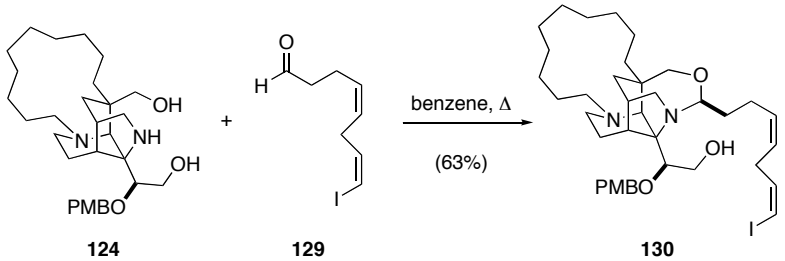
were dried over Na_2SO_4 and concentrated onto Celite (50 g). Purification by flash chromatography (1:20 Et_2O:pentane) gave diene **SI-27** (694 mg, 2.58 mmol, 57%) as a light sensitive colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.24 (d, *J* = 7.3, 1H), 6.15 (app. q, *J* = 7.0), 5.47–5.39 (m, 2H), 3.68 (s, 3H), 2.91 (t, *J* = 5.8, 2H), 2.47–2.35 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.42, 139.2, 129.4, 126.4, 82.7, 51.6, 33.9, 33.3, 23.0; IR (film): 3014, 2952, 1736, 1605, 1435 cm^{-1}; LRMS-CI (*m*/*z*) $[M + NH_4]^+$ calcd for $C_9H_{17}INO_2$, 298; found, 298.



SI-27 **SI-28** **129**

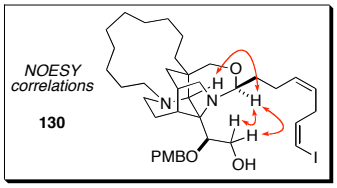
Aldehyde 129. *i*-Bu_2AlH (1.7 mL, 1.5 M in toluene) was added dropwise to a solution of ester **SI-27** (334 mg, 1.2 mmol) in CH_2Cl_2 (4.8 mL) at –78 °C. The solution was allowed to warm to rt over 1 h, then quenched by the addition of saturated aqueous sodium potassium tartrate (5 mL). The resulting mixture was stirred for 1 h, diluted with water (20 mL), and extracted with CH_2Cl_2 (2 x 40 mL). The combined organic extracts were washed with brine (1 x 40 mL), dried over Na_2SO_4, and concentrated to provide alcohol **SI-28** (242 mg, 0.96 mmol, 80%) as a colorless, light-sensitive oil.

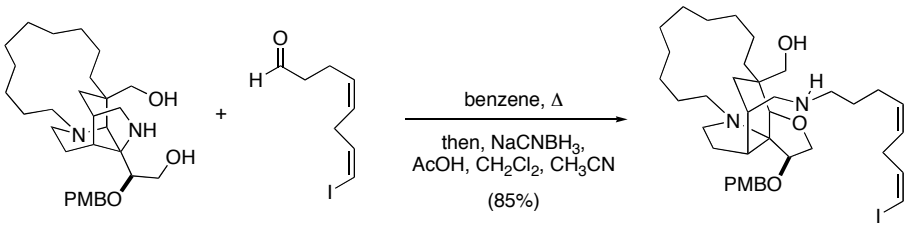
A portion of freshly prepared alcohol **SI-28** from above (86 mg) was dissolved in CH_2Cl_2 (3.4 mL) and Dess–Martin Periodinane (160 mg, 0.376) was added in one portion. The cloudy mixture was stirred at rt for 30 min, then concentrated onto Celite (400 mg). Purification by flash chromatography on silica gel (1:7 Et_2O:pentane) gave aldehyde **129** as a colorless oil (62 mg, 73%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.79 (t, *J* = 1.4, 1H), 6.25 (dt, *J* = 7.3, 1.4, 1H), 6.15 (app. q, *J* = 7.0, 1H), 5.47–5.41 (m, 2H), 2.92 (t, *J* = 5.5, 2H), 2.55–2.51 (m, 2H), 2.47–2.42 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 201.8, 139.1, 129.2, 126.5, 82.8, 43.6, 33.4, 20.4; IR (film): 3014, 2917, 2823, 2722, 1724, 1654, 1606, 1408 cm^{-1}; HRMS-ESI (*m*/*z*) $[M + H]^+$ calcd for $C_8H_{12}IO$, 250.9933; found, 250.9925.



124 **129** **130**

***N,O*-acetal 130.** Diamine diol **124** (55 mg, 0.11 mmol) and aldehyde **129** (68 mg, 0.27 mmol) were dissolved in benzene (2.5 mL) and heated to reflux using a Dean–Stark trap. After 18 h, the reaction mixture was allowed to cool to rt and the solution was placed directly on a silica gel column. Flash chromatography (1:4, EtOAc:hex) gave *N,O*-acetal **130** (50 mg, 63%) as a white foam. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (d, *J* = 8.4, 2H), 6.88 (d, *J* = 8.4, 2H), 6.21 (dt, *J* = 7.3, 1.3, 1H), 6.13 (dt, *J* = 7.1, 6.7, 1H), 5.50–5.41 (m, 1H), 5.38–5.31 (m, 1H), 4.71 (d, *J* = 11.2, 1H), 4.45 (d, *J* = 11.2, 1H), 4.14 (dd, *J* = 7.8, 4.9, 1H), 3.92 (dd, *J* = 11.6, 2.9, 1H), 3.81 (s, 3H), 3.68–3.64 (m, 2H), 3.33 (d, *J* = 11.8, 1H), 3.28 (d, *J* = 11.8, 1H), 3.14 (d, *J* = 9.3, 1H), 3.09 (s, 1H), 3.06–3.02 (m, 1H), 2.86 (t, *J* = 6.8, 2H), 2.79–2.62 (m, 3H), 2.60–2.57 (m, 1H), 2.20–1.97 (m, 4H), 1.95–1.94 (m, 1H), 1.77–1.12 (m, 23H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0, 139.8, 131.5, 131.2, 129.2, 125.0, 113.8, 87.3, 85.1, 82.4, 80.2, 70.7, 68.5, 65.5, 59.4, 59.1, 55.3, 50.1, 43.8, 42.6, 41.0, 39.2, 38.4, 38.3, 36.6, 33.4, 27.7, 26.9, 25.7, 25.4, 25.0, 24.2, 23.8, 22.3, 21.7; LRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{38}H_{57}IN_2O_4$, 733; found, 733. This structural assignment was confirmed by COSY, HMQC, and HMBC. The relative stereochemistry of *N,O*-acetal **130** was determined from NOESY experiments, as depicted.

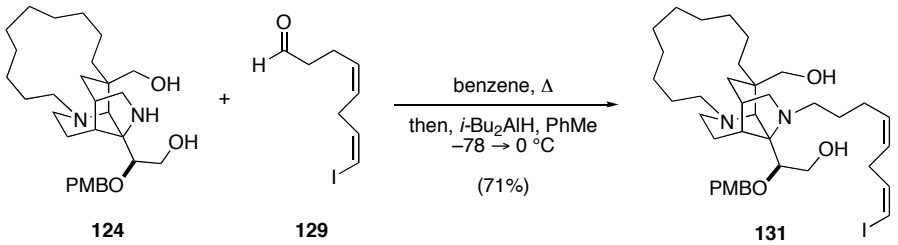




124 **129** **132**

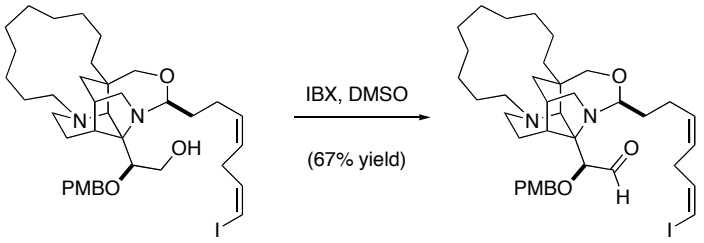
Tetracycle 132. Benzene (1.8 mL) was added to a mixture of aldehyde **129** (47 mg, 0.19 mmol) and diamine diol **124** (37 mg, 0.075 mmol). The solution was maintained at reflux for 14 h with a Dean–Stark apparatus topped with a $CaCl_2$ drying tube, shielded from light. The reaction mixture was concentrated, and the resulting residue suspended in MeCN (1.0 mL).

Sodium cyanoborohydride (70 mg, 1.13 mmol) was added and the reaction mixture was vigorously stirred until consumption of aldehyde **129** was complete, as judged by TLC analysis. Methylene chloride (1.0 mL) and AcOH (0.04 mL) were added, followed by a second charge of $NaBH_3CN$ (70 mg, 1.13 mmol). The suspension was vigorously stirred for 12 h, then diluted with CH_2Cl_2 (25 mL) and washed with aqueous phosphate buffer (pH = 8). The aqueous portion was back extracted with CH_2Cl_2 (4 x 10 mL). The combined organic portions were washed with brine (2 x 20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the resulting residue by column chromatography on silica using a gradient solvent system (10:36:1 EtOAc:hex:Et_3N, then 40:9:1 EtOAc:hex:Et_3N) gave tetracycle **132** as a viscous oil (47 mg, 0.064 mmol, 85%). ^{1}H NMR (500 MHz, $CDCl_3$, 318 K): δ 7.18 (d, *J* = 8.6, 2H), 6.86 (d, *J* = 8.6, 2H), 6.21 (d, *J* = 7.3, 1H), 6.14 (dd, *J* = 13.9, 6.9 1H), 5.49–5.45 (m, 1H), 5.41–5.36 (m, 1H), 4.42 (app. s, 2H), 4.24–4.20 (m, 1H), 3.84–3.77 (m, 6H), 3.75 (m, 1H), 3.45 (d, *J* = 11.4, 1H), 3.34 (m, 1H), 3.11 (m, 1H), 3.04–2.29 (m, 5H), 2.60–2.50 (m, 2H), 2.34–2.25 (m, 4H), 2.16–2.08 (m, 1H), 2.06–1.98 (m, 1H), 1.97–1.91 (m, 3H), 1.90 (t, *J* = 9.6, 1H), 1.52–1.33 (m, 18H), 1.24–1.19 (m, 1H), 1.18–1.09 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, 318 K): δ 159.2, 139.5, 131.4, 130.2, 129.2, 125.1, 113.7, 82.4, 79.2, 77.1, 73.5, 72.0, 70.3, 69.5, 55.3, 54.9, 51.2, 48.9, 39.4, 39.0, 35.7, 33.4, 32.8, 31.7, 27.7, 26.5, 26.2, 25.9, 25.89, 25.3, 24.7, 24.4, 23.1, 22.7, 21.4 (two carbons observed at 49.8 are not resolved); IR (film): 3512, 2929, 2860, 1611, 1586 cm^{-1}; HRMS-ESI (*m*/*z*) $[M + H]^+$ calcd for $C_{38}H_{59}IN_2O_4$, 735.3598; found, 735.3615; $[\alpha]^{27}_D$ +15.1, $[\alpha]^{27}_{577}$ +15.6, $[\alpha]^{27}_{546}$ +17.6, $[\alpha]^{27}_{435}$ +29.0, $[\alpha]^{27}_{405}$ +35.6 (*c* 2.0, $CHCl_3$); This structure was confirmed by COSY, HMQC, and HMBC.



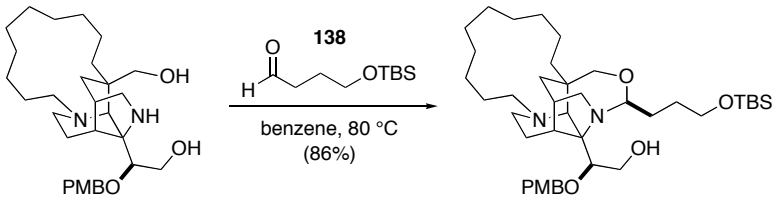
Diol 131. Diamine diol **124** (40 mg, 0.08 mmol) and aldehyde **129** (50 mg, 0.20 mmol) were dissolved in benzene (2.5 mL) and heated to reflux using a Dean–Stark trap. After 18 h, the reaction mixture was allowed to cool to rt and the solvent was removed under reduced pressure. The crude residue was dissolved in toluene (2.0 mL), cooled to –78 °C, and *i*-Bu_2AlH (264 μl,

1.5 M in toluene, 0.40 mmol) was added. The reaction was maintained at –78 °C for 30 min. and then quenched by addition of saturated aqueous sodium potassium tartrate (2 mL) and EtOAc (2 mL). After warming to rt and stirring for 2 h, the layers were separated and the aqueous layer was extracted with EtOAc (3 x 5 mL) and CH_2Cl_2 (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by flash chromatography (EtOAc:hex, 1:1) to give diol **131** (41 mg, 71%) as an oil. ^{1}H NMR (500 MHz, $CDCl_3$, 318K): δ 7.29 (d, *J* = 8.5, 2H), 6.89 (d, *J* = 8.5, 2H), 6.20 (d, *J* = 7.3, 1H), 6.13–6.09 (m, 1H), 5.42–5.37 (m, 1H), 5.34–5.29 (m, 1H), 4.79 (d, *J* = 11.1, 1H), 4.40 (d, *J* = 11.1, 1H), 4.12–4.10 (m, 1H), 3.90–3.88 (m, 1H), 3.82 (s, 3H), 3.76–3.74 (m, 1H), 3.56 (d, *J* = 11.1, 1H), 3.49 (d, *J* = 11.2, 1H), 3.17–3.15 (m, 2H), 2.89–2.60 (m, 11H), 2.18–2.14 (m, 2H), 2.05–1.99 (m, 3H), 1.74–1.15 (m 23H); ^{13}C NMR (125 MHz, $CDCl_3$, 318K): δ 159.1, 139.6, 131.5, 131.2, 128.8, 128.3, 125.1, 113.8, 82.2, 81.8, 71.1, 70.3, 69.7, 60.8, 60.7, 59.2, 58.6, 55.3, 51.8, 43.9, 42.7, 41.0, 39.9, 38.6, 37.6, 33.5, 29.3, 27.9, 26.7, 25.9, 25.8, 25.6, 25.5, 24.4, 24.3, 22.8, 22.3; IR (film): 3374, 2922, 2857, 1613, 1514, 1246, 1035 cm^{-1}; HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{38}H_{60}IN_2O_4$, 735.3598; found, 735.3583; $[\alpha]^{23}_{405}$ –102.1, $[\alpha]^{23}_{435}$ –84.9, $[\alpha]^{23}_{546}$ –50.0, $[\alpha]^{23}_{577}$ –39.5, $[\alpha]^{23}_{D}$ –39.7 (*c* 0.3, CH_2Cl_2); This structure was further confirmed by COSY, HMQC, and HMBC.



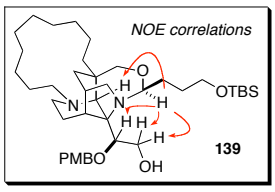
Aldehyde SI-29. IBX (69 mg, 0.25 mmol) was added to alcohol **130** (90 mg, 0.12 mmol) in DMSO (1.2 mL) at rt. After 60 min, the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (3 mL). NaCl was added to the aqueous layer until it was saturated, and the mixture was extracted with CH_2Cl_2 (5 x 5 mL). The combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure. Purification by flash chromatography (EtOAc:hex:Et_3N, 10:90:2 to 20:80:2) gave aldehyde **SI-29** (60 mg, 67%) as an oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.20 (d, *J* = 2.7, 1H), 7.28 (d, *J* = 8.4, 2H), 6.88 (d, *J* = 8.6, 2H), 6.20 (d, *J* = 7.4, 1H), 6.12 (dt, *J* = 7.3, 6.8, 1H), 5.32 (m, 2H), 4.53 (d, *J* = 11.1, 1H), 4.46 (d, *J* = 11.4,

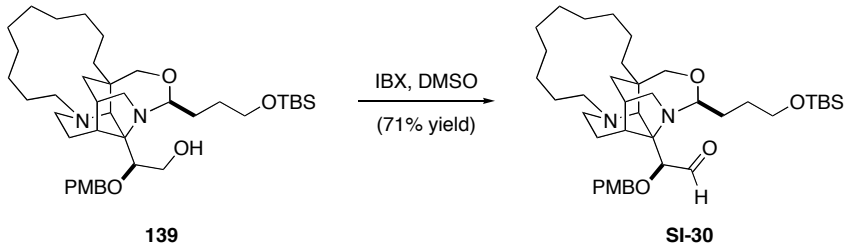
1H), 4.34 (m, 1H), 3.81 (s, 3H), 3.56 (d, *J* = 2.9, 1H), 3.31 (d, *J* = 11.7, 1H), 3.26 (d, *J* = 11.9, 1H), 3.21 (d, *J* = 9.4, 1H), 3.08 (s, 1H), 2.99–2.74 (m, 5H), 2.58 (m, 2H), 2.22–1.90 (m, 4H), 1.73–1.10 (m, 22H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.3, 159.3, 139.8, 131.5, 130.0, 129.5, 124.8, 113.8, 91.3, 87.8, 82.3, 80.0, 72.4, 71.0, 64.5, 59.2, 55.3, 50.0, 42.8, 41.3, 40.5, 40.1, 39.6, 38.7, 36.3, 33.3, 27.6, 26.4, 26.0, 25.9, 25.0, 24.2, 24.2, 23.5, 20.9, 20.7; IR (film): 2927, 2854, 1702, 1612, 1514, 1454, 1303, 1248, 1171, 1116, 1034, 821, 736 cm^{-1}; HRMS-ESI (*m/z*) [M + Na]$^+$ calcd for $C_{38}H_{55}IN_2O_4Na$, 753.3104; found, 753.3124.



124 **139**

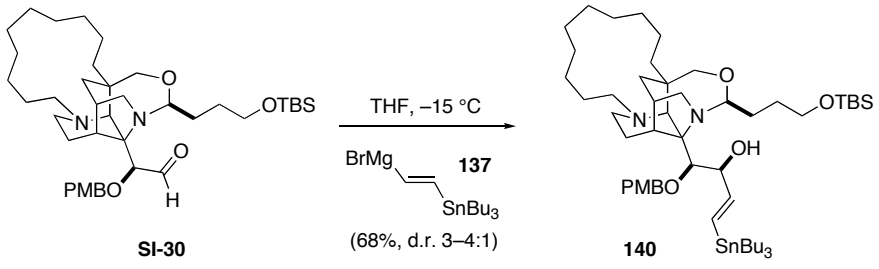
***N,O*-acetal 139.** A mixture of diamine diol **124** (54.0 mg, 0.108 mmol) and aldehyde **138**[7] (70.0 mg, 0.346 mmol) in dry benzene (6.0 mL) was heated in a sealed vial at 80 °C for 2 h 45 min, then cooled to rt. After evaporation of solvent under reduced pressure, the crude residue was purified by flash chromatography (9:1 hexanes:EtOAc containing 2% Et_3N, then 4:1 hexanes:EtOAc containing 2% Et_3N) to afford *N,O*-acetal **139** (63.5 mg, 0.093 mmol, 86% yield) as a yellow oil. R_f 0.24 (4:1 hexanes:EtOAc containing 2% Et_3N); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (d, *J* = 8.6, 2H), 6.87 (d, *J* = 8.6, 2H), 4.70 (d, *J* = 11.1, 1H), 4.41 (d, *J* = 11.1, 1H), 4.19–4.15 (m, 1H), 3.92 (dd, *J* = 11.9, 3.3, 1H), 3.81 (s, 3H), 3.69–3.62 (m, 2H), 3.62–3.54 (m, 2H), 3.28 (s, 2H), 3.13 (d, *J* = 9.2, 1H), 3.10 (s, 1H), 3.08–3.02 (m, 1H), 2.76–2.66 (m, 3H), 2.64–2.58 (m, 1H), 2.13–2.08 (m, 1H), 2.08–2.00 (m, 1H), 1.96–1.92 (m, 1H), 1.75–1.66 (m, 3H), 1.60–1.10 (m, 23H), 0.88 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.9, 131.2, 129.2, 113.7, 87.8, 85.8, 80.1, 70.5, 68.5, 65.5, 63.2, 59.1, 59.0, 55.2, 49.9, 43.8, 42.5, 41.0, 39.3, 38.6, 38.4, 33.2, 29.6, 27.7, 26.8, 26.0, 25.7, 25.2, 25.1, 24.2, 23.7, 22.4, 21.6, 18.3, –5.3; IR (film): 3400 (br), 2928, 2854, 1613, 1514, 1471, 1388, 1361, 1302, 1248, 1097, 906 cm^{-1}; HRMS-ESI (*m/z*) [M + H]$^+$ calcd for $C_{40}H_{69}N_2O_5Si$, 685.4976; found, 685.4988; $[\alpha]^{25}_{405}$ –46.3, $[\alpha]^{25}_{435}$ –38.6, $[\alpha]^{25}_{546}$ –22.6, $[\alpha]^{25}_{577}$ –19.9, $[\alpha]^{25}_{D}$ –18.4 (*c* 1, $CHCl_3$). The relative stereochemistry of *N,O*-acetal **139** was determined from NOE experiments, as depicted.





139 **SI-30**

Aldehyde SI-30. IBX (75.0 mg, 0.268 mmol) was added to a solution of alcohol **139** (80.0 mg, 0.117 mmol) in DMSO (2 mL) at rt. After 1 h, an additional portion of IBX (8.0 mg, 0.028 mmol) was added. After an additional 45 min of stirring at rt, the reaction mixture was loaded directly onto silica gel and rapidly purified by flash chromatography (14 x 1.5 cm column, 4:1 hexanes: EtOAc containing 2% Et_3N) to afford aldehyde **SI-30** (57.0 mg, 71% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.19 (d, *J* = 2.9, 1H), 7.29 (d, *J* = 8.6, 2H), 6.88 (d, *J* = 8.6, 2H), 4.47 (s, 2H), 4.33 (m, 1H), 3.81 (s, 3H), 3.55 (d, *J* = 3.0, 1H), 3.55 (m, 2H), 3.30 (d, *J* = 11.9, 1H), 3.22 (m, 2H), 3.08 (s, 1H), 2.95 (m, 1H), 2.88 (m, 1H), 2.75 (d, *J* = 7.9, 1H), 2.62 (m, 1H), 2.57 (m, 1H), 2.17 (m, 1H), 2.03 (m, 1H), 1.92 (m, 1H), 1.75–1.10 (m, 25H), 0.88 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.4, 159.3, 130.0, 129.7, 113.7, 91.4, 88.5, 79.9, 72.4, 71.0, 64.4, 63.3, 59.1, 55.2, 49.8, 42.8, 41.3, 40.4, 40.1, 39.6, 38.7, 33.1, 29.6, 27.6, 26.4, 26.0, 25.9, 25.0, 24.2, 23.5, 20.8, 20.7, 18.3, –5.3; IR (film): 2927, 2855, 1702, 1613, 1515, 1462, 1249, 1173, 1095, 1088, 1035, 909, 834, 776, 731 cm^{-1}; HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{40}H_{67}N_2O_5Si$, 683.4819; found, 683.4839; $[\alpha]^{25}_{405}$ –46.5, $[\alpha]^{25}_{435}$ –35.3, $[\alpha]^{25}_{546}$ –17.4, $[\alpha]^{25}_{577}$ –14.0, $[\alpha]^{25}_{D}$ –13.7 (*c* 1, CH_2Cl_2); This structure was further confirmed by COSY, HMQC and HMBC.

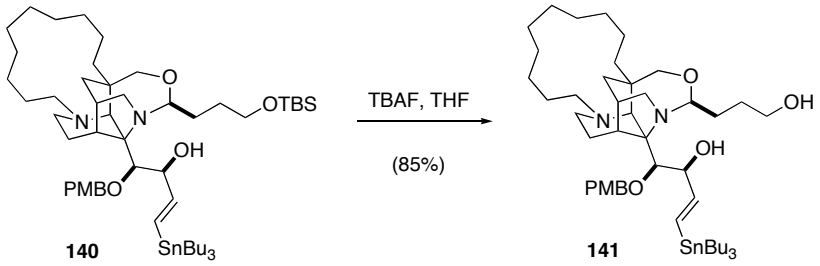


SI-30 **140**

Stannane 140. *n*-BuLi (760 μL of a 2.3 M solution in hexanes, 1.75 mmol) was added dropwise to a solution of (*E*)-1,2-bis(tributylstannyl)ethene[8] (1 mL, 1.94 mmol) in THF (4 mL) at –78 °C. After 10 min at –78 °C, the solution was warmed to –40 °C for 1 h. The reaction mixture was cooled to –78 °C and transferred *via* cannula to a flask cooled to –78 °C containing

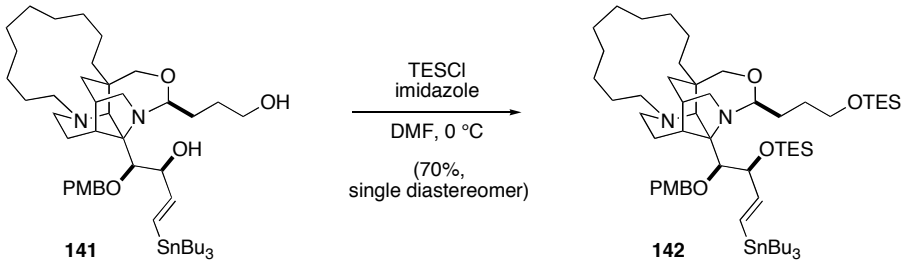
$MgBr_2$ (715 mg, 3.88 mmol). The resulting heterogeneous mixture was stirred while being warmed to 0 °C over 45 min. After 10 min at 0 °C, the suspension of Grignard **137** was cooled to –5 °C and used in the subsequent transformation.

Grignard **137** (500 μL, of a 0.5 M solution in THF, 0.25 mmol) was added to aldehyde **SI-30** (19.5 mg, 0.031 mmol) in THF (500 μL) at –20 °C. Additional Grignard reagent **137** was added after 30 min (500 μL), then again at 1 h (500 μL) after the start of the reaction. 30 min after the final addition of Grignard reagent, the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ solution (1.5 mL) and H_2O (5 mL). The resulting mixture was extracted with EtOAc (4 x 1.5 mL) and the combined organics were washed with brine (1 mL) and dried by passage over a plug of SiO_2 (EtOAc eluent). Evaporation under reduced pressure afforded the crude product, which was purified by flash chromatography (hexanes containing 2% Et_3N; then 9:1 hexanes:EtOAc containing 2% Et_3N) to provide vinyl stannane **140** (21.0 mg, 68%) as a ~3–4:1 ratio of isomers. Spectral data are reported for the major isomer. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 (d, 2H), 6.85 (d, *J* = 8.6, 2H), 6.39 (d, *J* = 19.3, 1H), 6.28 (dd, *J* = 4.3, 19.1, 1H), 4.80 (d, *J* = 11.1, 1H), 4.46 (d, *J* = 11.1, 1H), 4.39 (d, *J* = 4.4, 1H), 4.10 (m, 1H), 3.85 (s, 1H), 3.80 (s, 3H), 3.58 (m, 2H), 3.29 (m, 2H), 3.15 (d, *J* = 9.3, 1H), 3.11 (s, 1H), 3.02 (m, 1H), 2.82–2.55 (m, 4H), 2.2–1.2 (m, 41H), 0.92–0.8 (m, 24H), 0.02 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.9, 151.5, 131.2, 128.8, 126.8, 113.6, 88.2, 85.7, 80.1, 74.4, 72.7, 68.7, 66.2, 63.4, 59.4, 55.2, 50.4, 43.9, 42.4, 40.9, 38.9, 38.6, 38.4, 33.9, 29.7, 29.1, 27.7, 27.3, 25.9, 25.7, 25.3, 25.1, 24.3, 23.5, 22.3, 21.5, 18.3, 13.7, 9.4, –5.3; LRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{52}H_{88}IN_2O_4Sn$, 1001; found, 1001.



Diol 141. TBAF (100 μL of a 1.0 M solution in THF, 0.10 mmol) was added to silyl ether **140** (20.0 mg, 0.020 mmol) in THF (1 mL) at rt. The reaction was stirred for 1 h 45 min, diluted with H_2O (500 μL) and brine (1.5 mL). The aqueous layer was extracted with EtOAc (5 x 1 mL) and the combined organic layers were dried by passage over a plug of SiO_2 (EtOAc

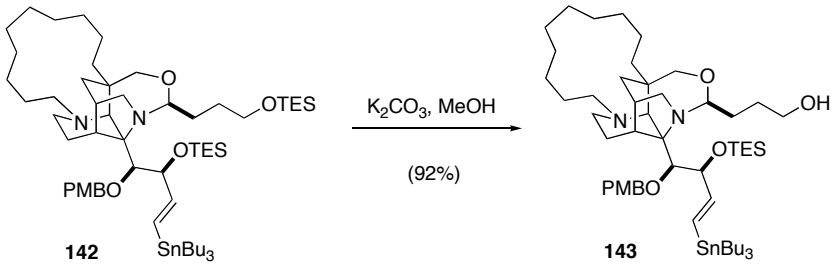
eluent). Evaporation under reduced pressure afforded the crude product which was purified by flash chromatography (3:1 hexanes:EtOAc containing 2% Et_3N) to afford diol **141** (15.1 mg, 85%) as a ~3–4:1 mixture of diastereomers. Spectral data are reported for the major isomer. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25 (d, 2H), 6.85 (d, *J* = 8.6, 2H), 6.41 (d, *J* = 19.1, 1H), 6.23 (dd, *J* = 4.1, 19.1, 1H), 4.76 (d, *J* = 11.0, 1H), 4.49 (d, *J* = 11.0, 1H), 4.45 (m, 1H), 4.08 (m, 1H), 3.89 (s, 1H), 3.80 (s, 3H), 3.61 (m, 2H), 3.36 (d, *J* = 11.8, 1H), 3.27 (d, *J* = 11.9, 1H), 3.15 (d, *J* = 9.4, 1H), 3.01 (m, 1H), 2.99 (s, 1H), 2.81 (m, 1H), 2.69 (m, 1H), 2.60 (m, 1H), 2.49 (m, 1H), 2.21 (m, 1H), 1.89 (m, 2H), 1.80–1.10 (m, 39H), 0.92–0.82 (m, 15H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.1, 151.2, 130.6, 129.2, 127.2, 113.7, 87.6, 81.5, 80.1, 74.5, 71.6, 68.0, 67.3, 62.0, 60.0, 55.3, 50.9, 43.6, 42.5, 40.9, 38.2, 38.1, 38.0, 34.0, 29.2, 28.4, 28.0, 27.5, 27.3, 25.7, 25.6, 24.4, 24.3, 23.1, 21.9, 21.7, 13.7, 9.4; IR (film): 3400 (br), 2918, 2850, 1613, 1514, 1464, 1248, 1172, 1120, 1072, 1039, 821, 805 cm^{-1}; HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{48}H_{83}N_2O_5Sn$, 887.5336; found, 887.5345.



141 142

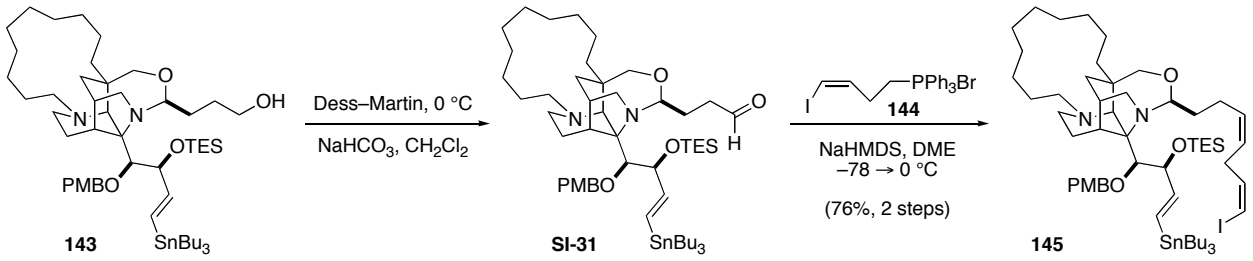
Bis(TES) ether 142. TESCl (14.2 μL, 0.0847 mmol) was added to a solution of diol **141** (15.0 mg, 0.0169 mmol) and imidazole (11.5 mg, 0.169 mmol) in dry DMF (600 μL) at 0 °C. After 15 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (1 mL), then diluted with H_2O (500 μL) and brine (500 μL). EtOAc (500 μL) was added and the resulting mixture was warmed to rt. The layers were separated and the aqueous layer was extracted with EtOAc (5 x 1 mL). The combined organic layers were washed with brine (1 x 1 mL), dried by passage over a plug of silica gel (EtOAc eluent), and evaporated under reduced pressure with gentle heating (approximately 30 °C). The residue was first purified by passage over a second plug of silica gel (4:1 hexanes:EtOAc containing 2% Et_3N), then by flash chromatography (40:1 hexanes:EtOAc; then 19:1 hexanes:EtOAc; then 9:1 hexanes:EtOAc) to separate the diastereomers. The major (desired) isomer of **142** (13.3 mg, 70%), which eluted after its epimer, was isolated as a colorless oil. R_f 0.62 (4:1 hexanes:EtOAc containing 2% Et_3N); ^{1}H NMR (500

MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.7, 2H), 6.85 (d, *J* = 8.7, 2H), 6.31–6.14 (m, 2H), 4.99 (d, *J* = 11.5, 1H), 4.54 (d, *J* = 11.5, 1H), 4.30 (t, *J* = 6.8, 1H), 4.16–4.09 (m, 1H), 3.81 (s, 3H), 3.72 (d, *J* = 8.0, 1H), 3.68–3.58 (m, 2H), 3.28 (d, *J* = 11.7, 1H), 3.17–3.03 (m, 3H), 2.97–2.88 (m, 1H), 2.87–2.76 (m, 1H), 2.75–2.68 (m, 1H), 2.68–2.55 (m, 2H), 2.49–2.42 (m, 1H), 2.11–1.99 (m, 2H), 1.86–1.76 (m, 2H), 1.75–1.16 (m, 32H), 1.05–0.85 (m, 36H), 0.66–0.53 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.6, 151.3, 132.7, 131.9, 128.4, 113.6, 88.4, 83.8, 80.7, 79.7, 74.5, 69.4, 68.9, 63.5, 60.5, 55.4, 50.8, 44.5, 42.2, 41.1, 38.8, 38.1, 37.5, 33.8, 30.5, 29.9, 29.5, 27.7, 25.3, 25.1, 24.9, 24.4, 23.3, 23.1, 21.6, 13.9, 9.4, 7.2, 7.1, 5.5, 4.6; IR (film): 2956, 2929, 2875, 1615, 1528, 1463, 1254, 1094, 1032 cm^{-1}; LRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{60}H_{111}N_2O_5Si_2Sn$, 1115.7; found, 1115.8; $[\alpha]^{26}_{405}$ –6.5, $[\alpha]^{26}_{435}$ –6.1, $[\alpha]^{26}_{546}$ –4.6, $[\alpha]^{26}_{577}$ –3.5, $[\alpha]^{26}_{D}$ –3.8 (*c* 1.00, CH_2Cl_2).



Alcohol 143. A mixture of bis(TES) ether **142** (34.6 mg, 0.031 mmol) and K_2CO_3 (130 mg, 0.94 mmol) in methanol (5 mL) was stirred at 0 °C. The reaction mixture was allowed to warm to rt over 3 h. After 10 h at rt, additional K_2CO_3 (35 mg, 0.25 mmol) was added and stirring was continued for 1.5 h. The reaction mixture was diluted with H_2O (2 mL) and brine (6 mL), then extracted with EtOAc (4 x 2.5 mL). The combined organic layers were dried by passage over a plug of silica gel (EtOAc eluent) and evaporated under reduced pressure. Purification of the resulting residue by flash chromatography (19:1 hexanes:EtOAc containing 2% Et_3N; then 4:1 hexanes:EtOAc containing 2% Et_3N) afforded alcohol **143** (28.6 mg, 92%) as a yellow oil. R_f 0.13 (4:1 hexanes:EtOAc containing 2% Et_3N); ^1H NMR (500 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.5, 2H), 6.86 (d, *J* = 8.4, 2H), 6.32–6.16 (m, 2H), 4.94 (d, *J* = 11.4, 1H), 4.54 (d, *J* = 11.4, 1H), 4.33 (app. t, *J* = 6.7, 1H), 4.24–4.20 (m, 1H), 3.81 (s, 3H), 3.73 (d, *J* = 7.3, 1H), 2.25 (app. t, *J* = 5.5, 2H), 3.29 (d, *J* = 11.6, 1H), 3.15–3.10 (m, 2H), 3.06 (s, 1H), 2.97–2.89 (m, 1H), 2.84–2.76 (m, 1H), 2.76–2.63 (m, 2H), 2.63–2.55 (m, 1H), 2.41–2.36 (m, 1H), 1.84–0.88 (m, 64H), 0.64–0.57 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.7, 151.4, 132.4, 131.7, 128.6,

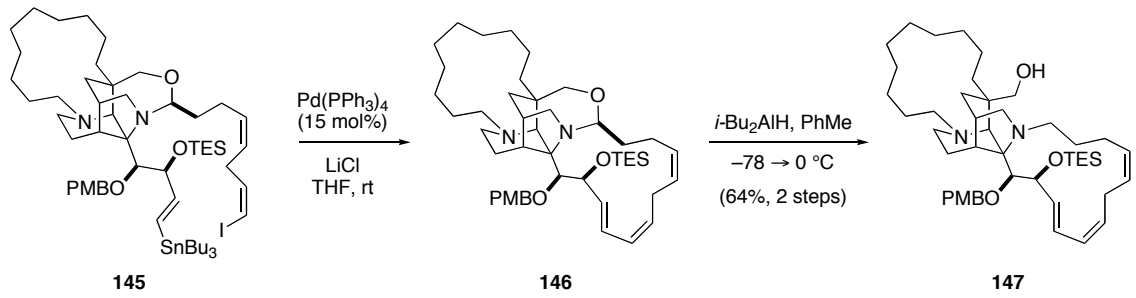
113.6, 88.5, 83.9, 80.5, 79.6, 74.7, 69.3, 68.9, 63.5, 60.4, 55.5, 50.9, 44.4, 42.2, 41.1, 38.7, 38.3, 37.6, 34.1, 29.6, 29.5, 27.9, 27.7, 25.3, 25.2, 25.0, 24.4, 23.3, 23.1, 21.6, 13.9, 9.5, 7.2, 5.6; IR (film): 3440 (br), 2952, 2926, 2872, 2852, 1514, 1458, 1247, 1172, 1120, 1099, 1041, 1002 cm^{-1}; LRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{54}H_{97}N_2O_5SiSn$, 1001.6; found, 1001.5; $[\alpha]^{25}_{405}$ –9.6, $[\alpha]^{25}_{435}$ –7.9, $[\alpha]^{25}_{546}$ –5.6, $[\alpha]^{25}_{577}$ –4.6, $[\alpha]^{25}_{D}$ –4.6 (*c* 1.00, CH_2Cl_2).



Stille substrate 145. Dess–Martin Periodinane (35.6 mg, 0.084 mmol) was added to a mixture of alcohol **143** (28 mg, 0.028 mmol) and $NaHCO_3$ (73 mg, 0.869 mmol) in CH_2Cl_2 (2 mL) at 0 °C. After 1 h, additional Dess–Martin Periodinane was added (5.0 mg, 0.012 mmol). After 30 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (1 mL) and saturated aqueous sodium metabisulfite (1 mL). The resulting cloudy mixture was stirred vigorously for 5 min at 0 °C, then for 30 min at rt. The layers were separated and the aqueous layer was extracted with EtOAc (5 x 1 mL). The combined organic layers were washed with brine (1 x 1 mL), dried by passage over a plug of silica gel (EtOAc eluent), and evaporated under reduced pressure. The residue was purified by flash chromatography (19:1 hexanes:EtOAc containing 2% Et_3N; then 9:1 hexanes:EtOAc containing 2% Et_3N) to afford aldehyde **SI-31** (24.0 mg, 86%) as a colorless foam which was used directly in the subsequent transformation.

NaHMDS (288 μL, 0.288 mmol, 1 M in THF) was added dropwise over 1 min to a mixture of phosphonium salt **144**[9] (251.5 mg, 0.481 mmol) in DME (4.3 mL) at –78 °C. After stirring 1 h 10 min, aldehyde **SI-31** (24.0 mg, 0.0.024 mmol, dried under vacuum over $CaSO_4$) in DME (1 mL) was added. The mixture was maintained at –78 °C for 25 min, then placed in a 0 °C bath for 15 min. The reaction mixture was diluted with H_2O (2 mL), brine (2 mL), and EtOAc (2 mL). The mixture was warmed to rt and the layers were separated. The aqueous layer was further extracted with EtOAc (4 x 2 mL). The combined organic layers were dried by passage over a plug of silica gel (EtOAc eluent) and evaporated under reduced pressure. The residue was first purified by passage over a second plug of silica gel (4:1 hexanes:EtOAc containing 2%

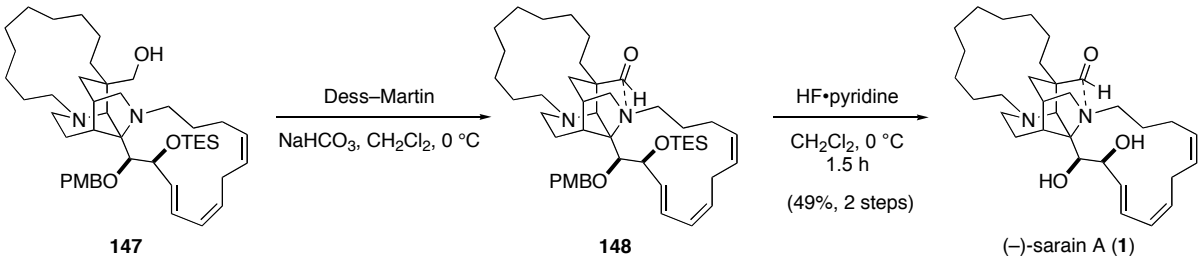
Et_3N) then by flash chromatography (40:1 hexanes: EtOAc; then 19:1 hexanes: EtOAc containing 2% Et_3N) to afford Stille substrate **145** (24.5 mg, 88% yield). R_f 0.41 (9:1 hexanes:EtOAc containing 2% Et_3N); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.5, 2H), 6.85 (d, *J* = 8.5, 2H), 6.41–6.11 (m, 4H), 5.58–5.49 (m, 1H), 5.42–5.33 (m, 1H), 4.99 (d, *J* = 11.5, 1H), 4.54 (d, *J* = 11.5, 1H), 4.29 (t, *J* = 8.0, 1H), 4.17–4.10 (m, 1H), 3.81 (s, 3H), 3.73 (d, *J* = 8.0, 1H), 3.31 (d, *J* = 11.7, 1H), 3.16–3.01 (m, 3H), 3.00–2.85 (m, 3H), 2.84–2.71 (m, 2H), 2.68–2.54 (m, 2H), 2.50–2.43 (m, 1H), 2.33–2.13 (m, 2H), 1.86–1.78 (m, 2H), 1.77–0.80 (m, 59H), 0.66–0.49 (q, *J* = 7.9, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.6, 151.4, 139.9, 132.7, 132.1, 131.8, 128.4, 125.1, 113.6, 87.7, 83.4, 82.6, 79.8, 74.6, 69.3, 68.9, 60.4, 55.5, 51.0, 44.5, 42.2, 41.1, 38.8, 38.2, 37.6, 37.0, 33.5, 29.5, 27.7, 25.3, 25.1, 25.0, 24.8, 24.4, 23.4, 23.2, 21.6, 14.0, 9.5, 7.3, 5.6; IR (film): 2931, 2875, 1615, 1515, 1463, 1248, 1175, 1119, 1102, 1077, 1044, 1007 cm^{-1}; LRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{58}H_{100}IN_2O_4SiSn$, 1163.6; found, 1163.6; $[\alpha]^{23}_{405}$ +11.0, $[\alpha]^{23}_{435}$ +9.6, $[\alpha]^{23}_{546}$ +4.7, $[\alpha]^{23}_{577}$ +4.4, $[\alpha]^{23}_{D}$ +3.8 (*c* 1.00, CH_2Cl_2).



Alcohol 147. In a glove box, a solution of $Pd(PPh_3)_4$ (3.0 mg, 0.00258 mmol) in THF (200 μL) was added to vinyl iodide **145** (20.0 mg, 0.0172 mmol) and LiCl (10.9 mg, 0.258 mmol) in THF (11.5 mL) at rt. After 7 d, the reaction vessel was removed from the glove box and the solvent was evaporated under reduced pressure. The residue was passed over a plug of silica gel (4:1 hexanes:EtOAc containing 2% Et_3N), and the solvent was evaporated. Purification by flash chromatography (40:1 hexanes: EtOAc, then 19:1 hexanes: EtOAc, then 9:1 hexanes: EtOAc) afforded Stille product **146** (11.2 mg), which was contaminated with a byproduct believed to be the *des*-iodo derivative of **145**. Nonetheless, this mixture was used directly in the subsequent transformation. From a different batch of material, an analytically pure sample of Stille product **147** was obtained by slow column chromatography using the conditions described above. R_f 0.55 (4:1 hexanes:EtOAc containing 2% Et_3N); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30

(d, J = 8.6, 2H), 6.88 (d, J = 8.6, 2H), 6.65 (app. t, J = 13, 1H), 6.18–6.14 (m, 1H), 5.97 (app. t, J = 10.8, 1H), 5.60–5.42 (m, 3H), 4.83 (br s, 1H), 4.67 (d, J = 10.8, 1H), 4.54 (d, J = 11.0, 1H), 4.38–4.35 (m, 1H), 4.19 (br s, 1H), 3.81 (s, 3H), 3.30 (d, J = 11.7, 1H), 3.22–3.11 (m, 2H), 3.05–2.97 (m, 2H), 2.83–2.77 (m, 2H), 2.66–2.60 (m, 1H), 2.59–2.53 (m, 2H), 2.52–2.39 (m, 2H), 2.30–2.23 (m, 1H), 2.08–1.91 (m, 2H), 1.88–1.80 (m, 2H), 1.70–0.65 (m, 38H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 159.4, 134.5, 131.2, 130.9, 129.7, 128.1, 127.6, 113.9, 89.1, 79.5, 76.9, 73.8, 70.3, 69.8, 60.8, 55.5, 51.3, 43.6, 42.2, 41.4, 38.9, 38.7, 38.0, 36.3, 29.9, 28.6, 27.5, 26.4, 26.0, 25.8, 25.4, 24.7, 24.4, 23.3, 22.9, 21.4, 7.4, 5.5; IR (film): 2928, 2874, 2854, 1514, 1463, 1250, 1117, 1066, 1044, 1012 cm^{-1}; HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{46}H_{73}N_2O_4Si$, 745.5339; found, 745.5336; $[\alpha]^{26}_{405}$ –8.3, $[\alpha]^{26}_{435}$ –4.1, $[\alpha]^{26}_{546}$ +10.0, $[\alpha]^{26}_{577}$ +11.4, $[\alpha]^{26}_{D}$ +15.9 (*c* 1.00, CH_2Cl_2).

i-Bu_2AlH (120 μL, 0.12 mmol, 1 M in hexanes) was added to a solution of crude Stille product **145** in toluene (1.5 mL) at –78 °C. After 10 min, the reaction mixture was warmed to 0 °C, held at this temperature for 15 min, then quenched with saturated Na-K tartrate solution (1.5 mL) and EtOAc (1 mL). The resulting biphasic mixture was stirred at rt for 1 h and the layers were separated. The aqueous layer was extracted with EtOAc (5 x 1 mL). The combined organic layers were washed with brine (1 x 1 mL), dried by passage over a plug of silica gel (EtOAc eluent) and evaporated under reduced pressure. The residue was purified by flash chromatography (9:1 hexanes:EtOAc containing 2% Et_3N, then 6:1 hexanes:EtOAc containing 2% Et_3N) to afford neopentyl alcohol **147** (8.2 mg, 64%). R_f 0.43 (3:1 hexanes:EtOAc containing 2% Et_3N); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (d, *J* = 8.6, 2H), 6.91 (d, *J* = 8.6, 2H), 6.80–6.68 (m, 1H), 6.16–6.06 (m, 2H), 5.65–5.48 (m, 3H), 4.94 (d, *J* = 11.5, 1H), 4.87 (d, *J* = 9.7, 1H), 4.64 (s, 1H), 4.52 (d, *J* = 11.5, 1H), 4.23–4.15 (m, 1H), 3.83 (s, 3H), 3.59–3.45 (m, 3H), 3.25–2.98 (m, 5H), 2.82–2.71 (m, 1H), 2.58–2.48 (m, 1H), 2.46–2.30 (m, 4H), 2.22–2.11 (m, 2H), 1.84–0.79 (m, 34H), 0.63 (q, *J* = 7.7, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.1, 133.5, 131.9, 131.8, 128.9, 128.8, 126.6, 126.5, 113.8, 88.5, 84.4, 73.0, 72.0, 71.5, 64.5, 63.6, 61.3, 59.7, 55.5, 43.3, 43.2, 42.8, 39.5, 38.9, 29.9, 28.3, 27.1, 26.7, 26.5, 25.8, 24.4, 23.7, 23.1, 22.8, 21.8, 7.3, 5.6; IR (film): 3250 (br), 2931, 2875, 1615, 1517, 1465, 1250, 1042 cm^{-1}; HRMS-ESI (*m/z*) $[M + H]^+$ calcd for $C_{46}H_{75}N_2O_4Si$, 747.5496; found, 747.5492; $[\alpha]^{24}_{405}$ –83.3, $[\alpha]^{24}_{435}$ –77.6, $[\alpha]^{24}_{546}$ –50.1, $[\alpha]^{24}_{577}$ –44.4, $[\alpha]^{24}_{D}$ –42.9 (*c* 1.00, CH_2Cl_2).

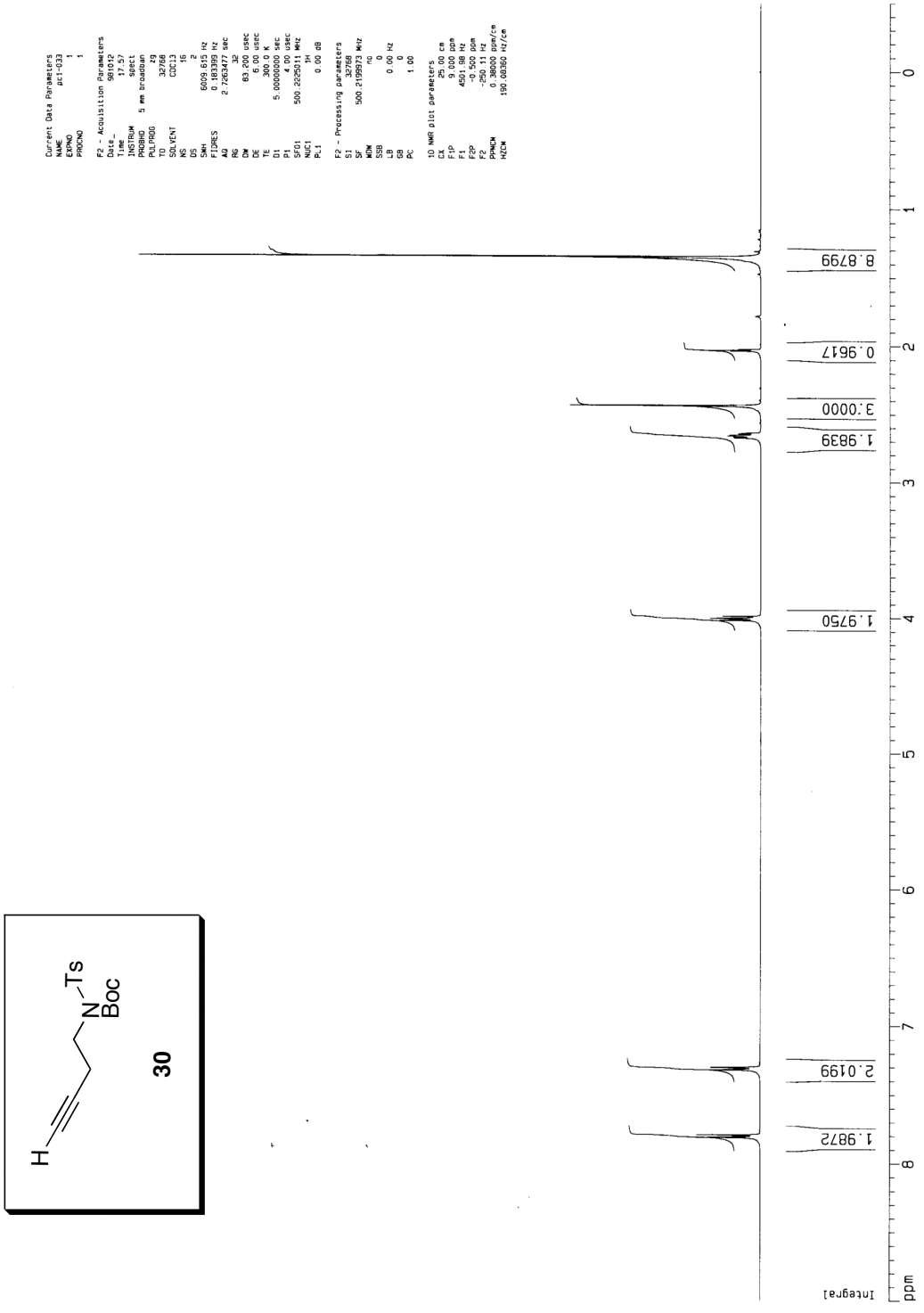


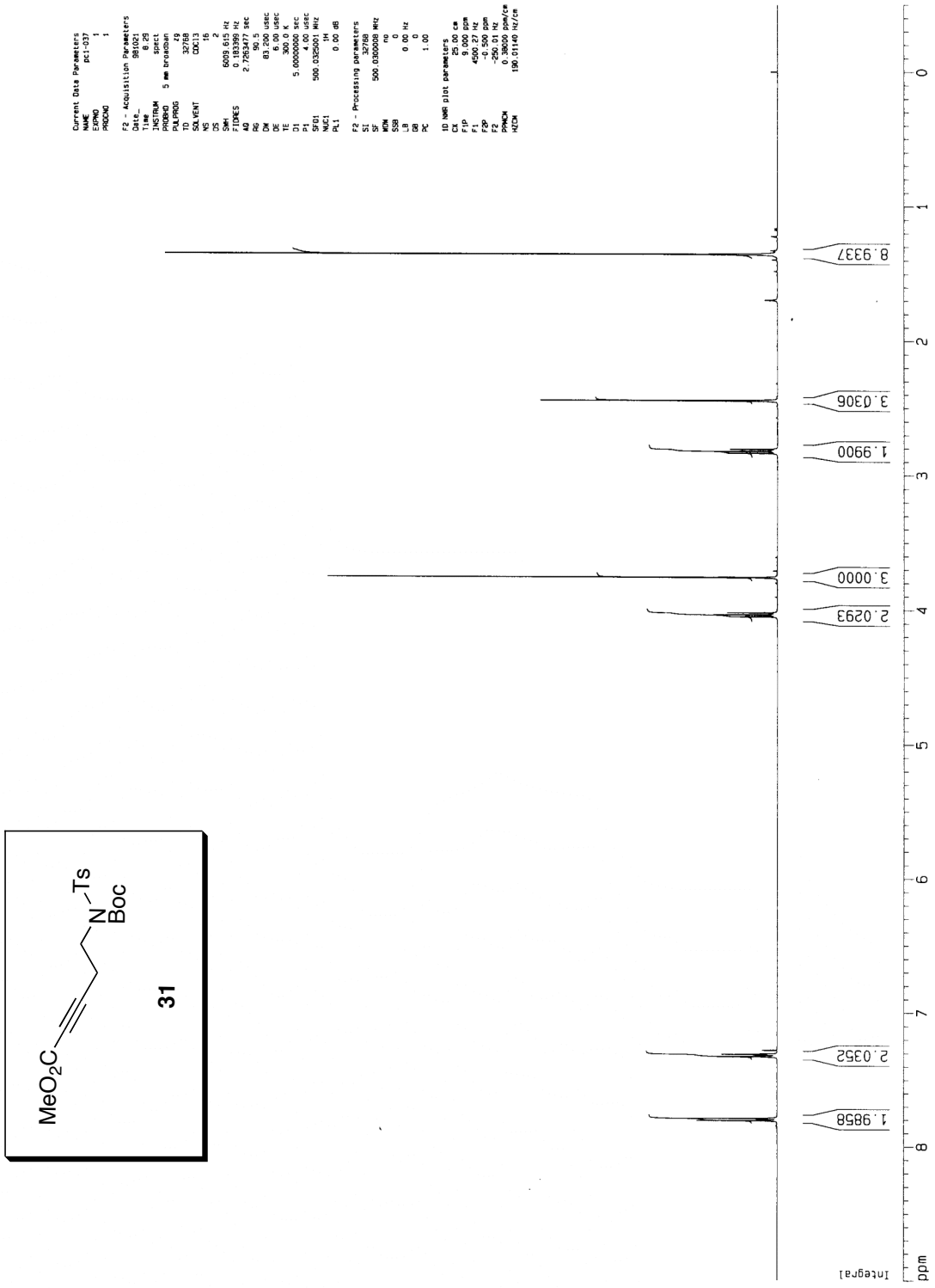
(–)-Sarain A. Freshly prepared Dess–Martin Periodinane[10] (1.5 mg, 0.00335 mmol) was added to a mixture of alcohol **147** (2.7 mg, 0.0036 mmol) and $NaHCO_3$ (10 mg, 0.119 mmol) in CH_2Cl_2 (1 mL) at 0 °C. After 15 min, additional Dess–Martin Periodinane was added (1.5 mg, 0.00335 mmol). After an additional 5 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (750 μL) and saturated aqueous sodium metabisulfite (750 μL). The resulting cloudy mixture was stirred vigorously for 15 min at 0 °C, then allowed to warm to rt. The layers were separated and the aqueous layer was extracted with EtOAc (5 x 500 μL) and CH_2Cl_2 (1 x 500 μL). The combined organic layers were washed with brine (1 x 500 μL), loaded onto a plug of silica gel with EtOAc (pipette column). The silica gel column was eluted with EtOAc, then 30:1 CH_2Cl_2:MeOH to remove impurities. Next, the column was eluted with 6:1 CH_2Cl_2:MeOH to collect aldehyde **148**. This material was used directly in the subsequent transformation.

HF•pyridine (30 μL, 1.15 mmol) was added to crude aldehyde **148** in CH_2Cl_2 (1.1 mL) in a polyethylene vial at 0 °C. After approximately 1.5 h, the reaction mixture was cooled to –10 °C, carefully quenched by the dropwise addition of saturated aqueous $NaHCO_3$ (2.5 mL), then warmed to rt. The layers were separated and the aqueous layer was extracted with EtOAc (4 x 500 μL) and CH_2Cl_2 (4 x 500 μL). The combined organic layers were loaded onto a plug of silica gel with EtOAc (pipette column). The silica gel column was eluted with EtOAc, then 30:1 CH_2Cl_2:MeOH, and then 9:1 CH_2Cl_2:MeOH to remove impurities. Next, the column was eluted with 6:1 CH_2Cl_2:MeOH to collect (–)-sarain A (**1**) (0.9 mg, 49%, 2 steps). *NOTE: (a) Omnisolve CH_2Cl_2 from EMD Chemicals was used for chromatography; (b) prior to equilibrating the silica gel column with EtOAc for loading, the silica gel was washed with 6:1 CH_2Cl_2:MeOH; (c) fractions collected during chromatography of aldehyde **SI-31** and sarain A (**1**) were routinely analyzed by both TLC (R_f 0.38 CH_2Cl_2:MeOH; I_2 and anisaldehyde staining) and LRMS-ESI.* Characterization data for synthetic sarain A (^{1}H NMR, ^{13}C NMR, IR, HRMS) was indistinguishable from that reported for the naturally occurring material.[11] In addition, a sample of natural sarain A was chromatographed following the exact same method used to purify our

synthetic material. ^{1}H NMR and circular dichroism spectral comparisons confirmed that the natural and synthetic samples were identical (see comparison spectra).

^{1}H NMR Spectra (in order of appearance in manuscript and SI):

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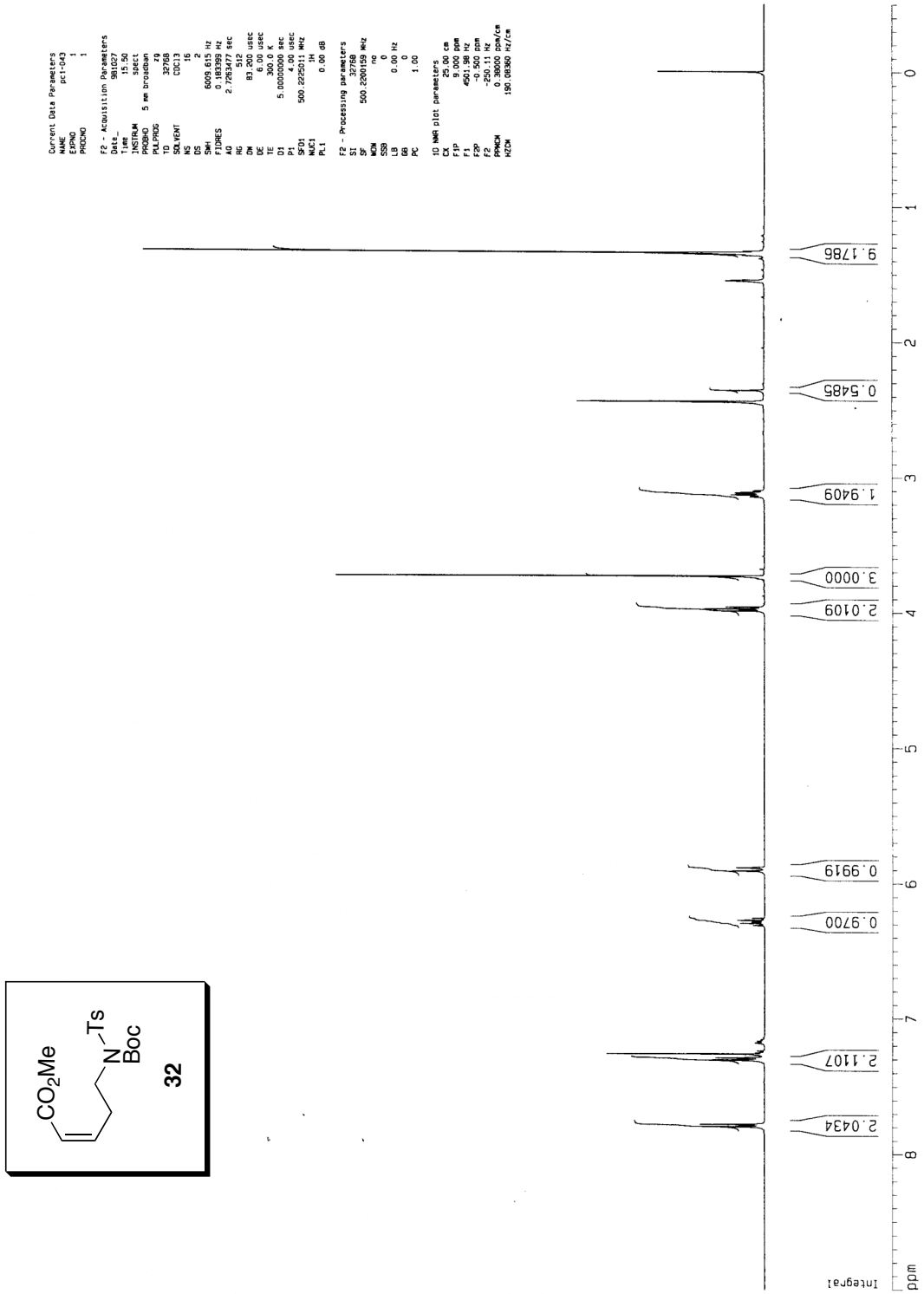
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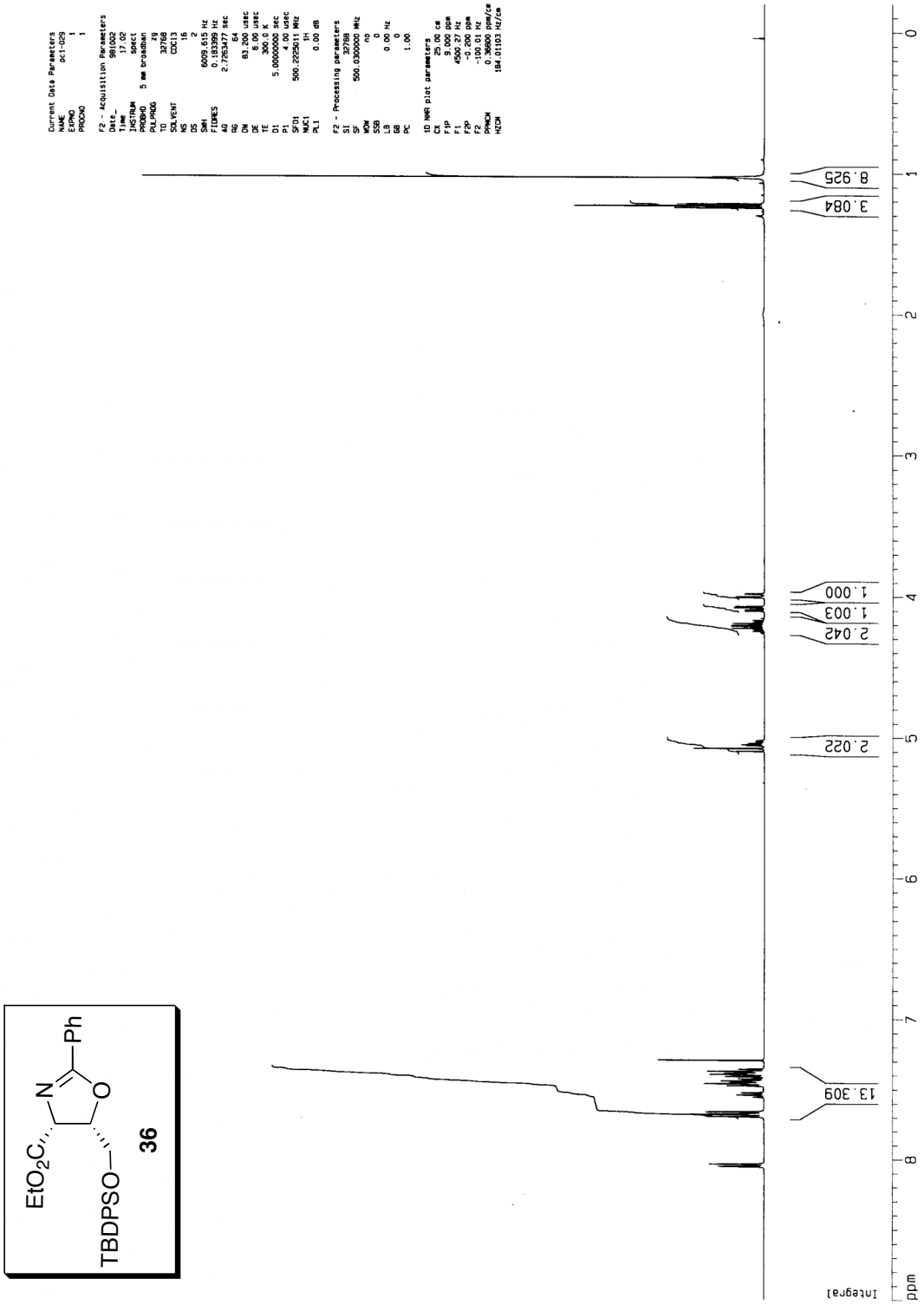
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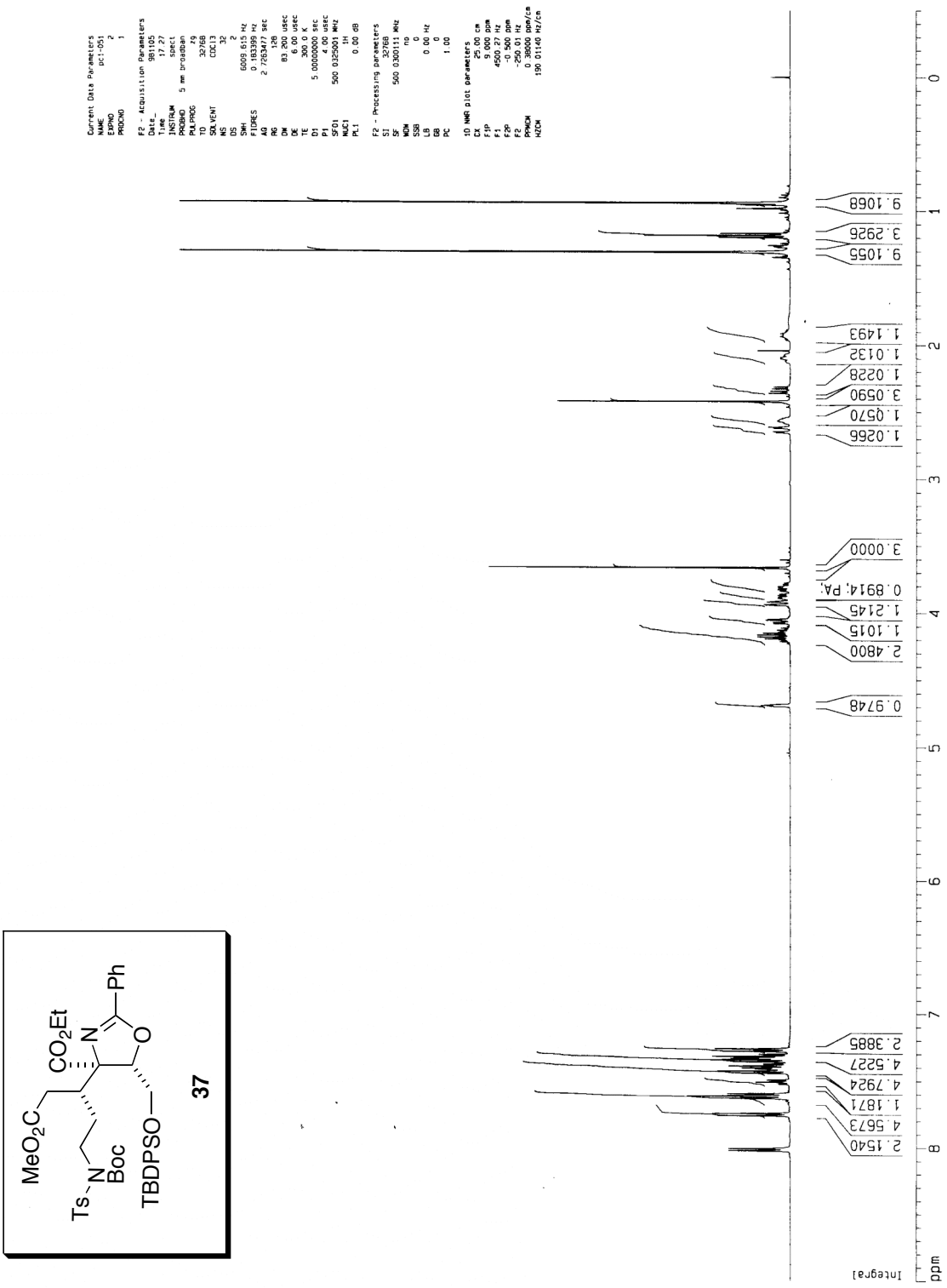
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9.1055
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1.0132
1.0228
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1.0570
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3.0000
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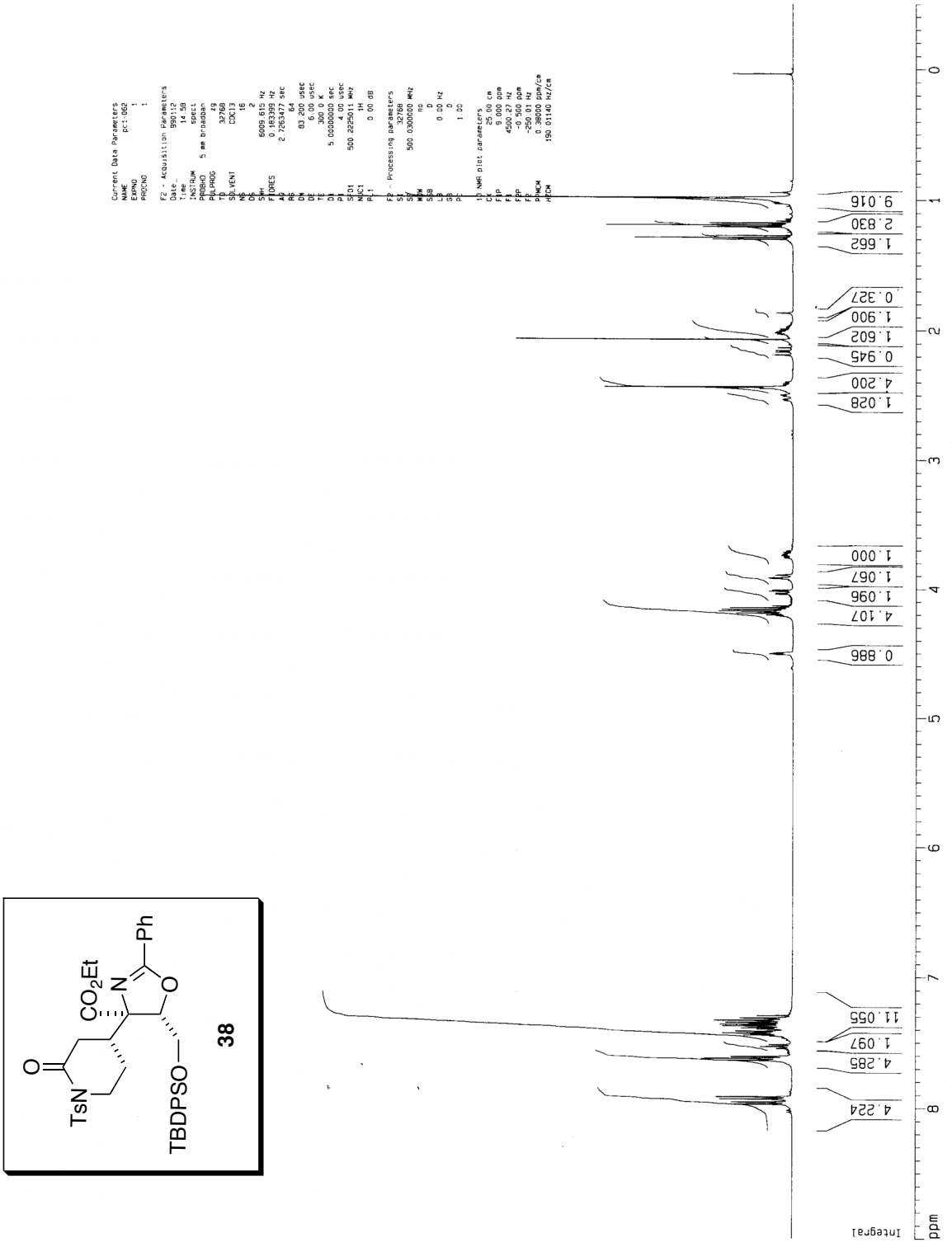
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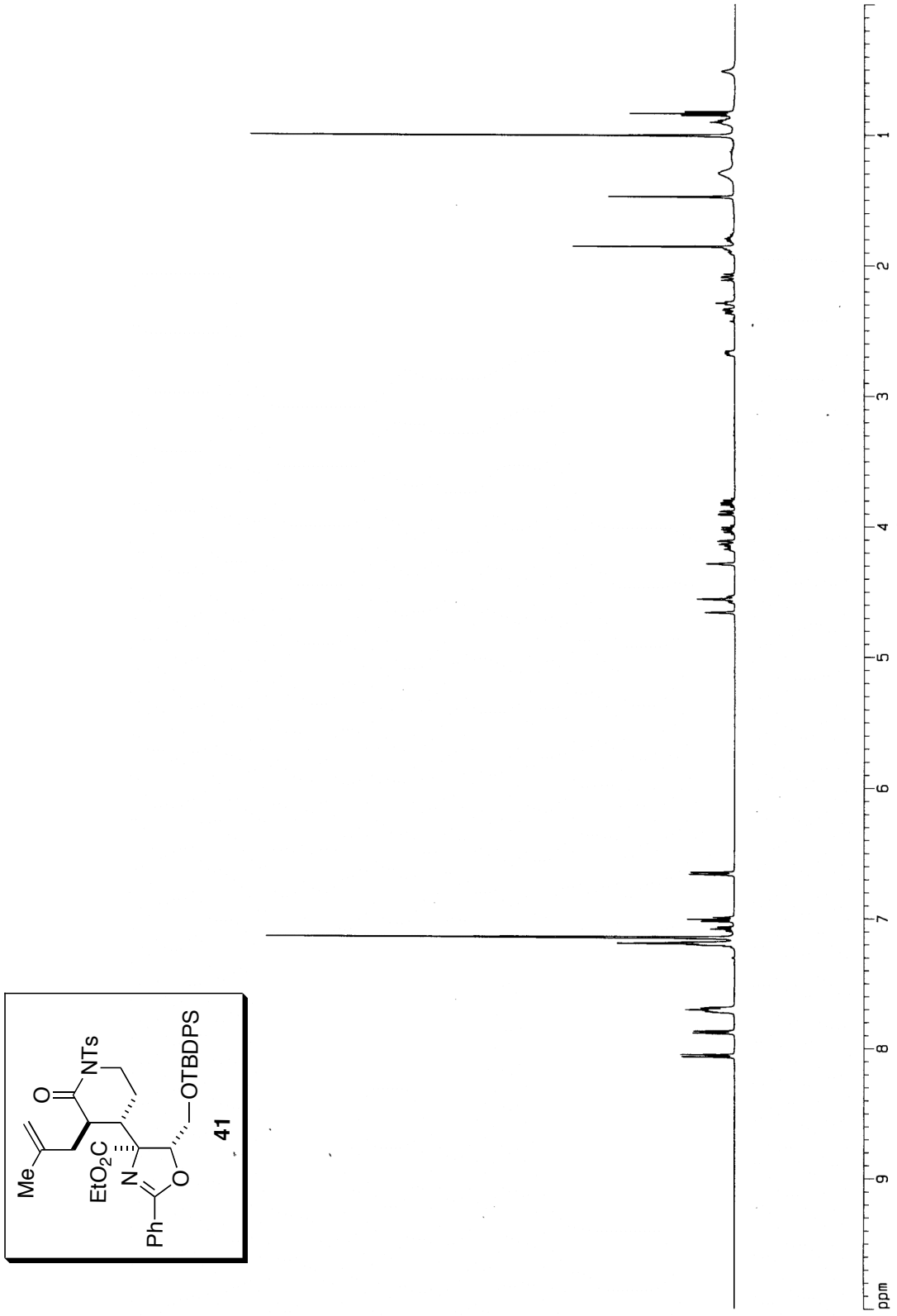
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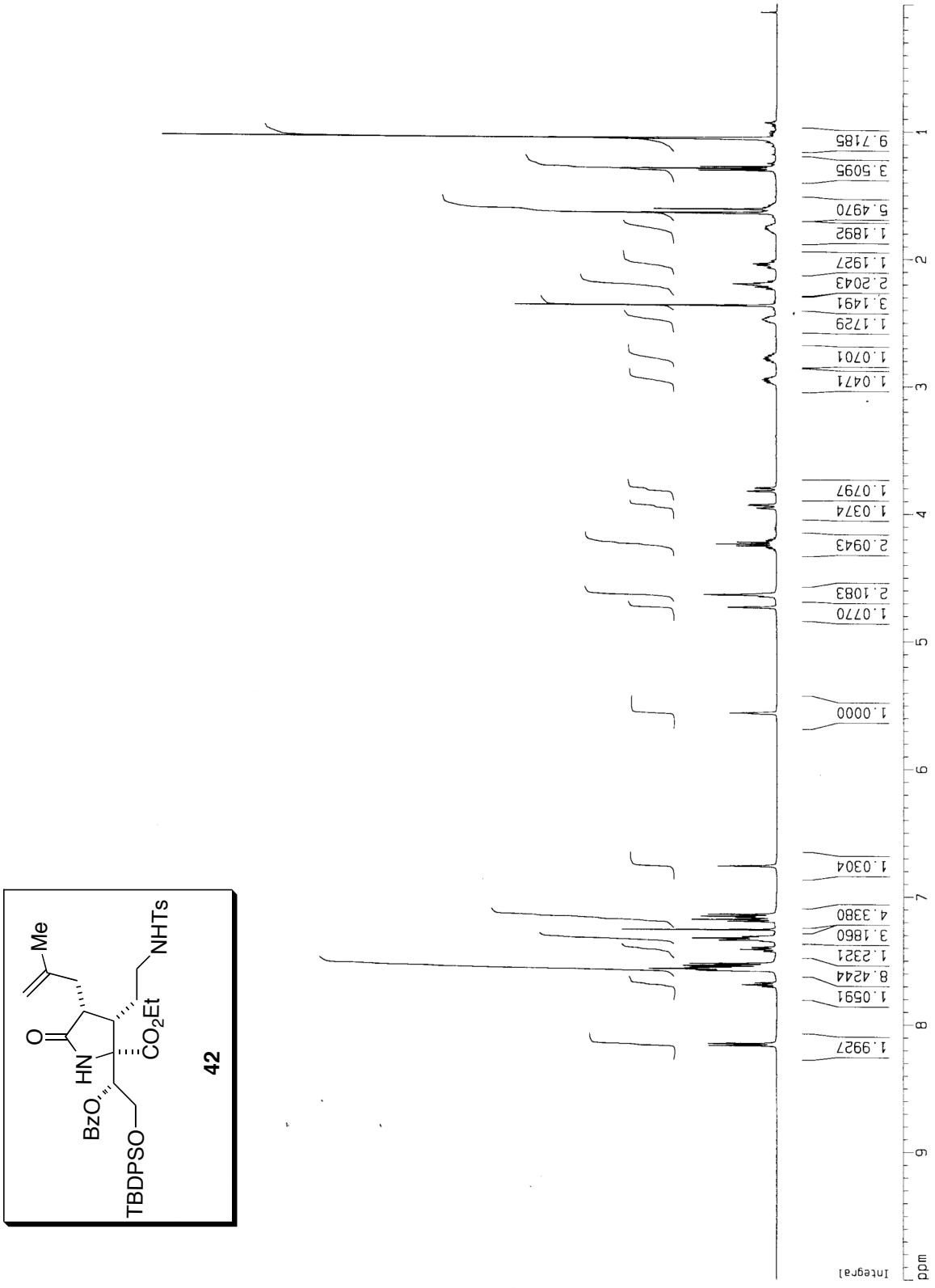
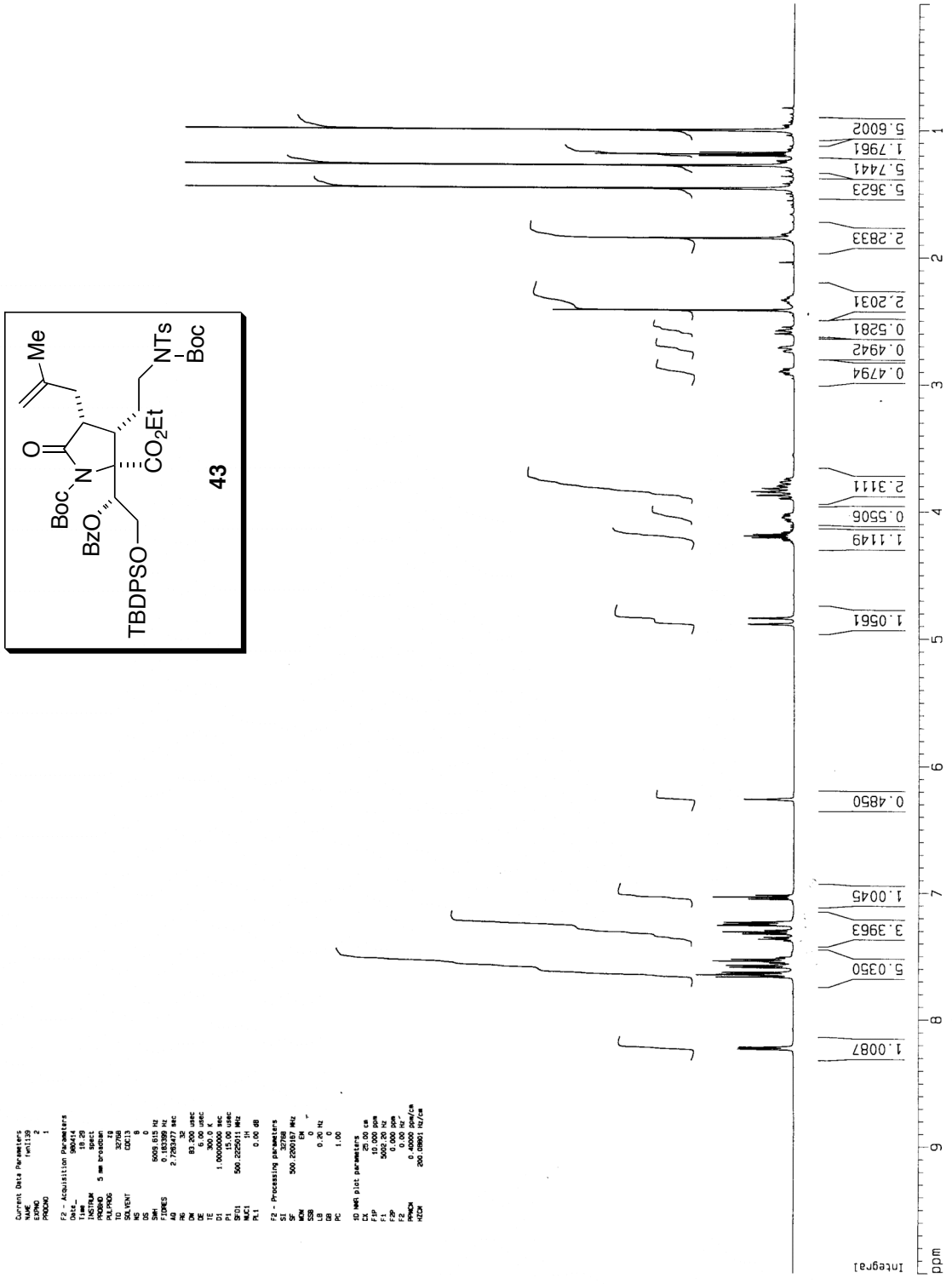
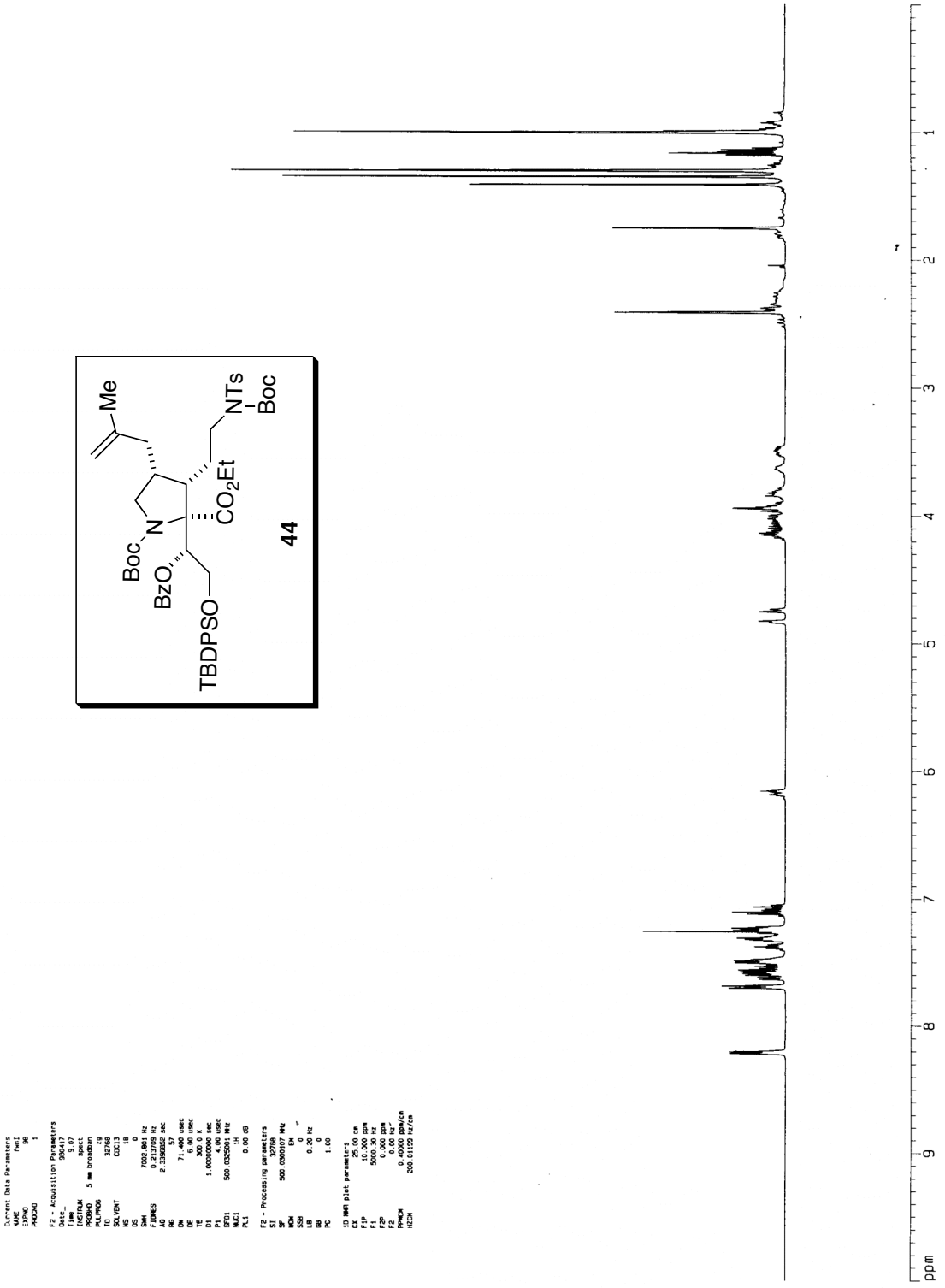
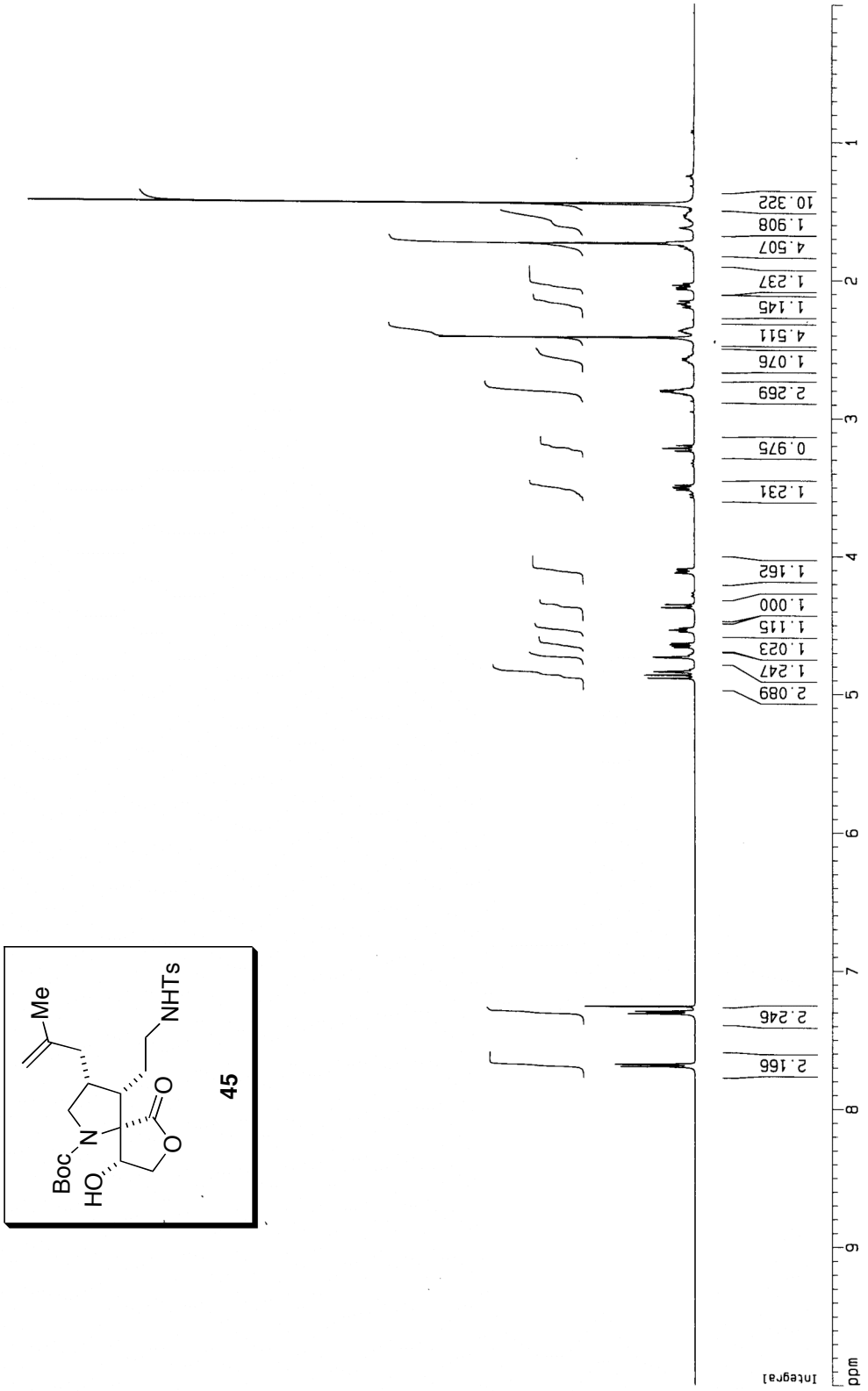
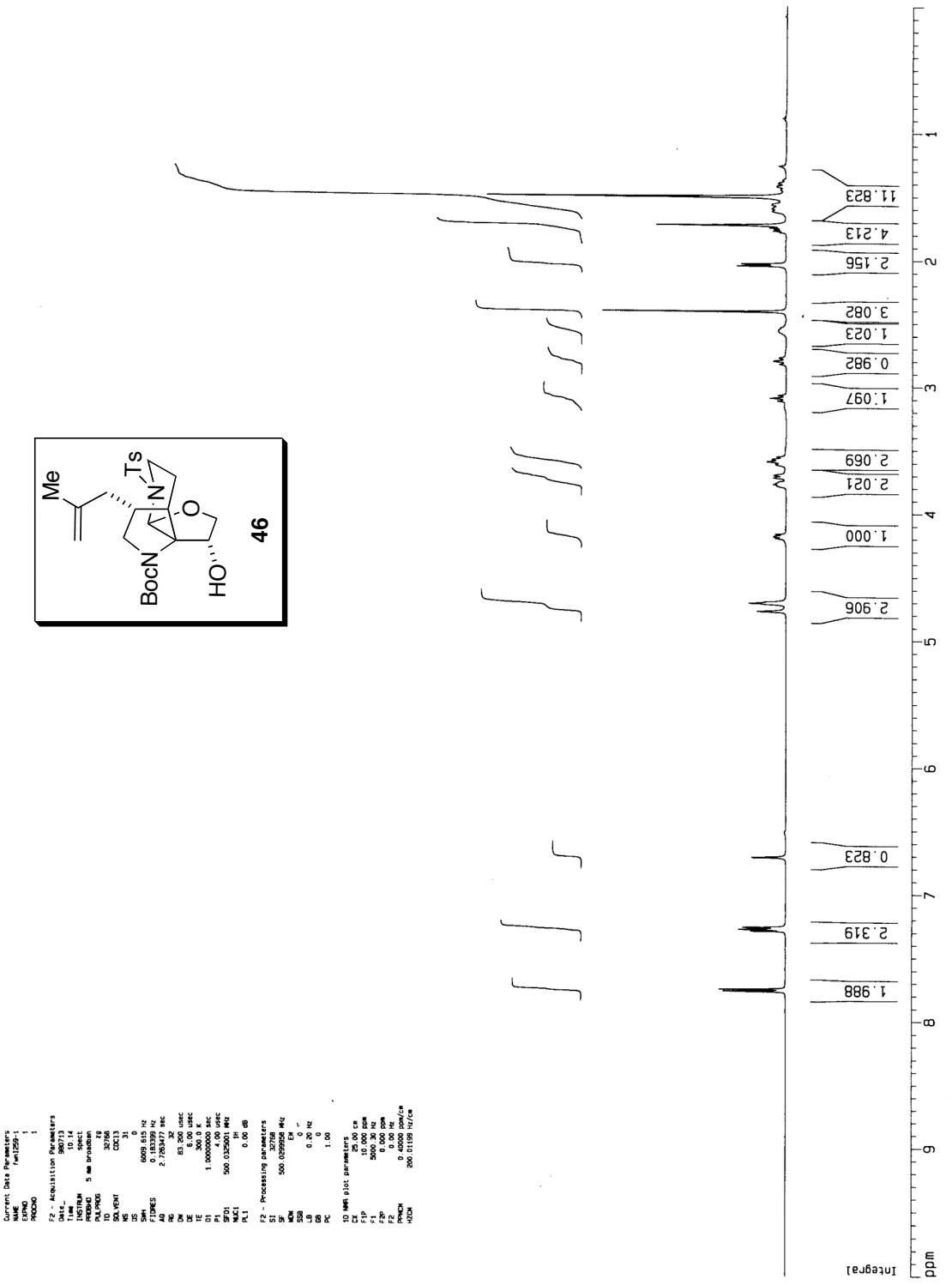
8
9

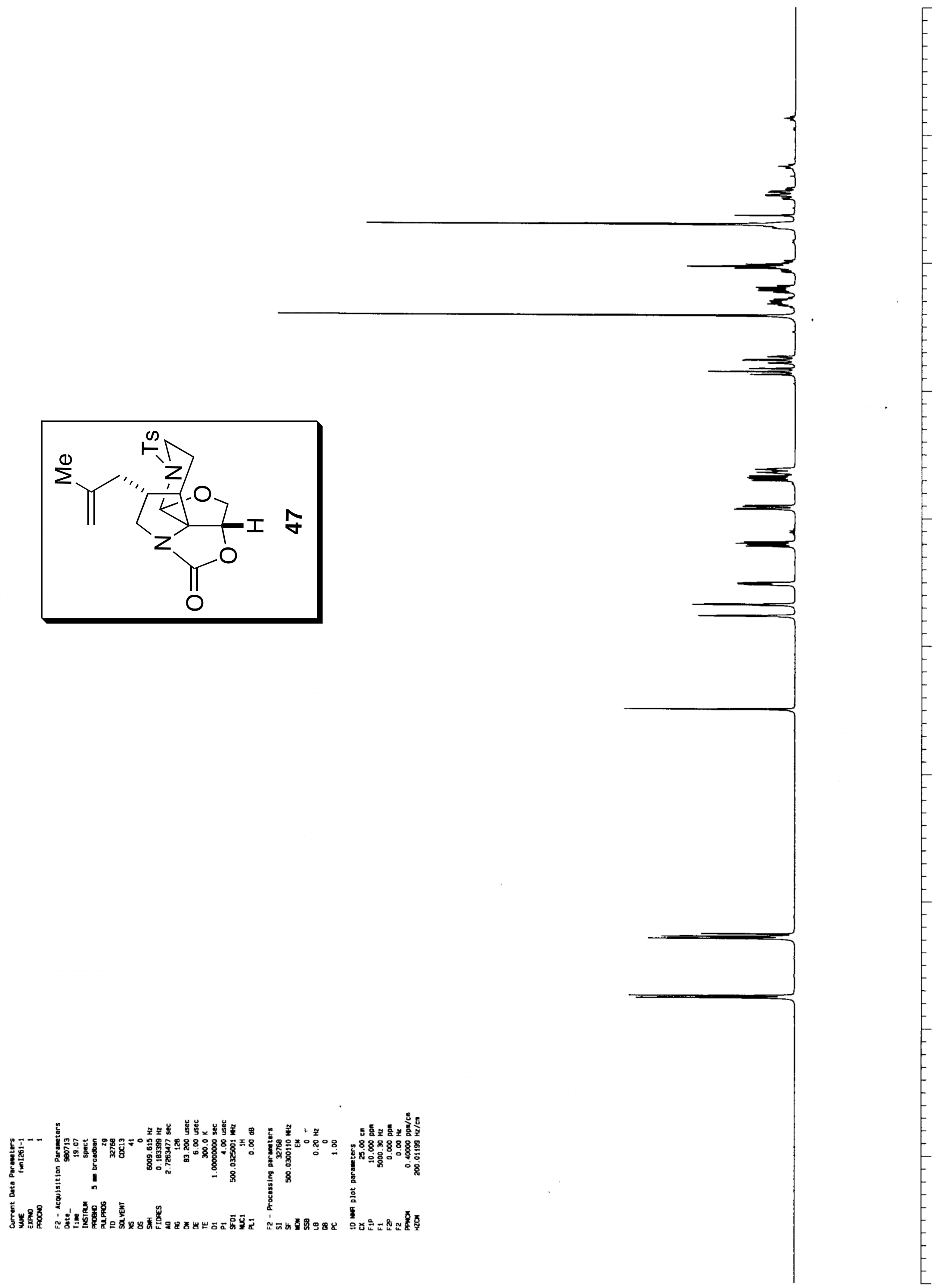

Me
O
HN
BzO
TBDPSO
CO2Et
NHTs
42
Integral
ppm
9.7185
3.5095
5.4970
1.1892
1.1927
2.2043
3.1491
1.1729
1.0701
1.0471
1.0797
1.0374
2.0943
2.1083
1.0770
1.0000
1.0304
4.3380
3.1860
1.2321
8.4244
1.0591
1.9927


Me
O
Boc
N
BzO
CO2Et
NTs
Boc
TBDPSO
43
1.0087
5.0350
3.3963
1.0045
0.4850
1.0561
1.1149
0.5506
2.3111
0.4794
0.4942
0.5281
2.2031
2.2833
5.3623
5.7441
1.7961
5.6002
Integral
ppm

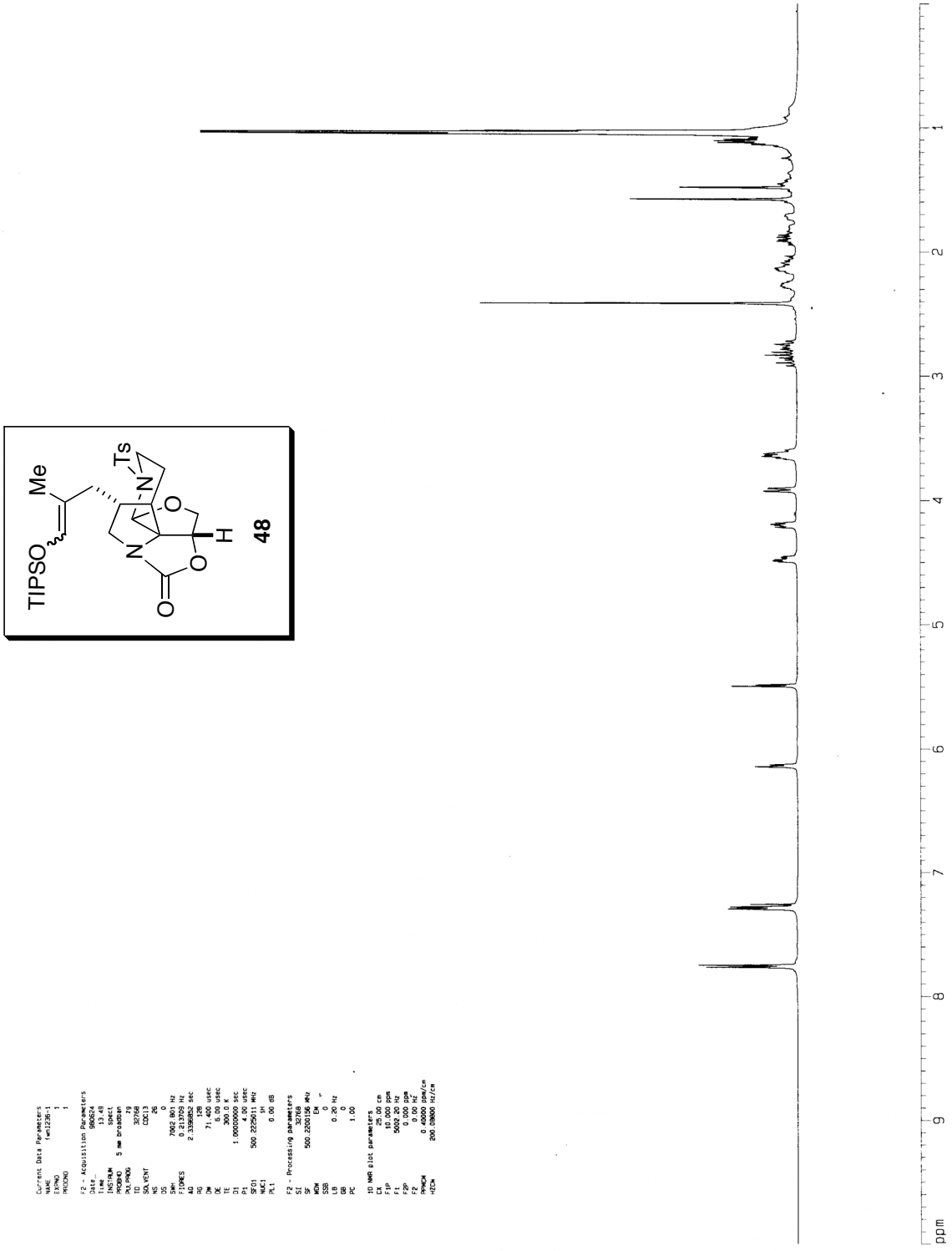

Me
Boc
N
BzO
CO2Et
NTs
Boc
TBDPSO
44
ppm

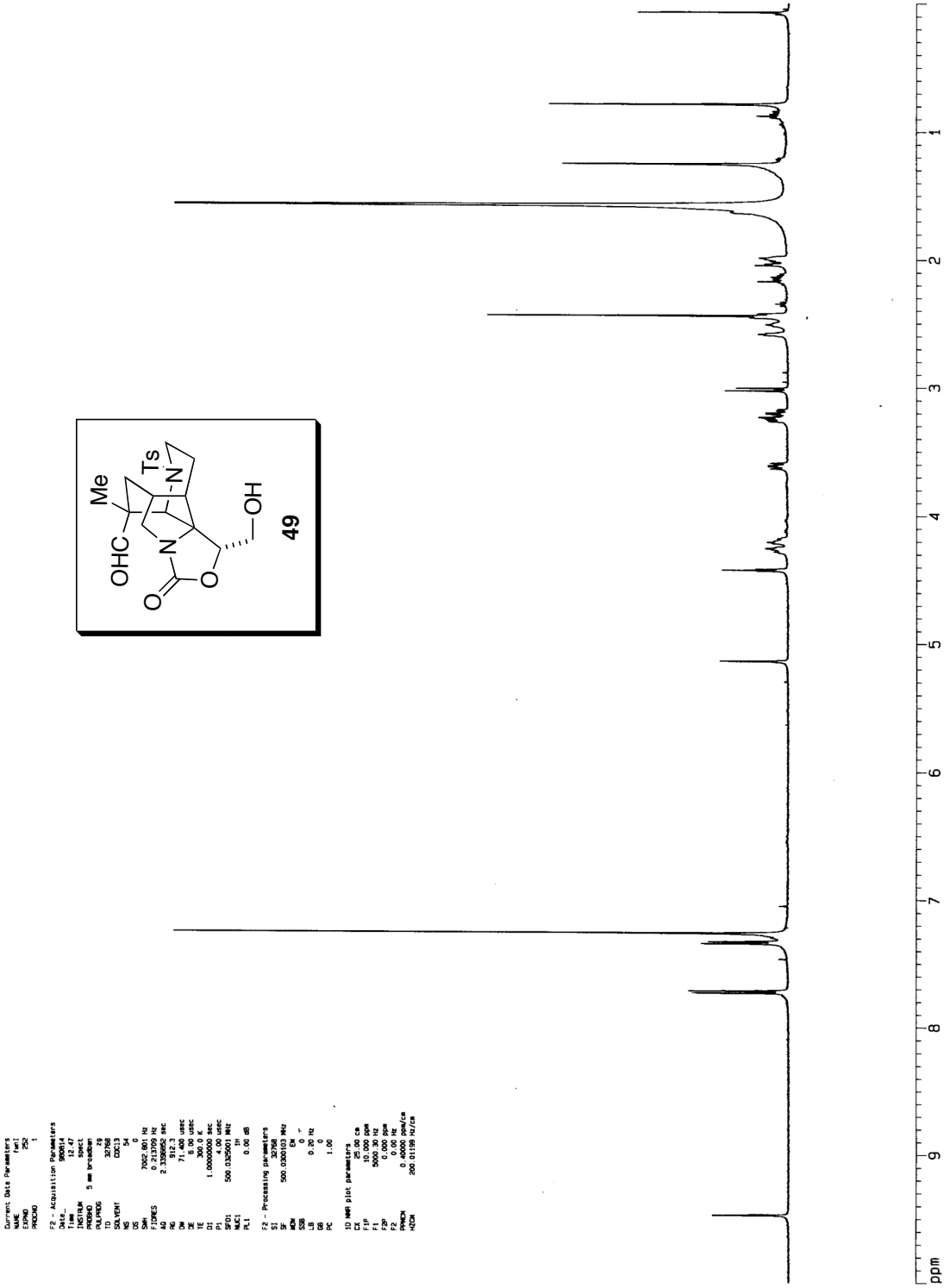

Me
NHTs
Boc
N
HO
O
O
45
2.166
2.246
2.089
1.247
1.023
1.115
1.000
1.162
1.231
0.975
2.269
1.076
4.511
1.145
1.237
4.507
1.908
10.322
Integral
ppm

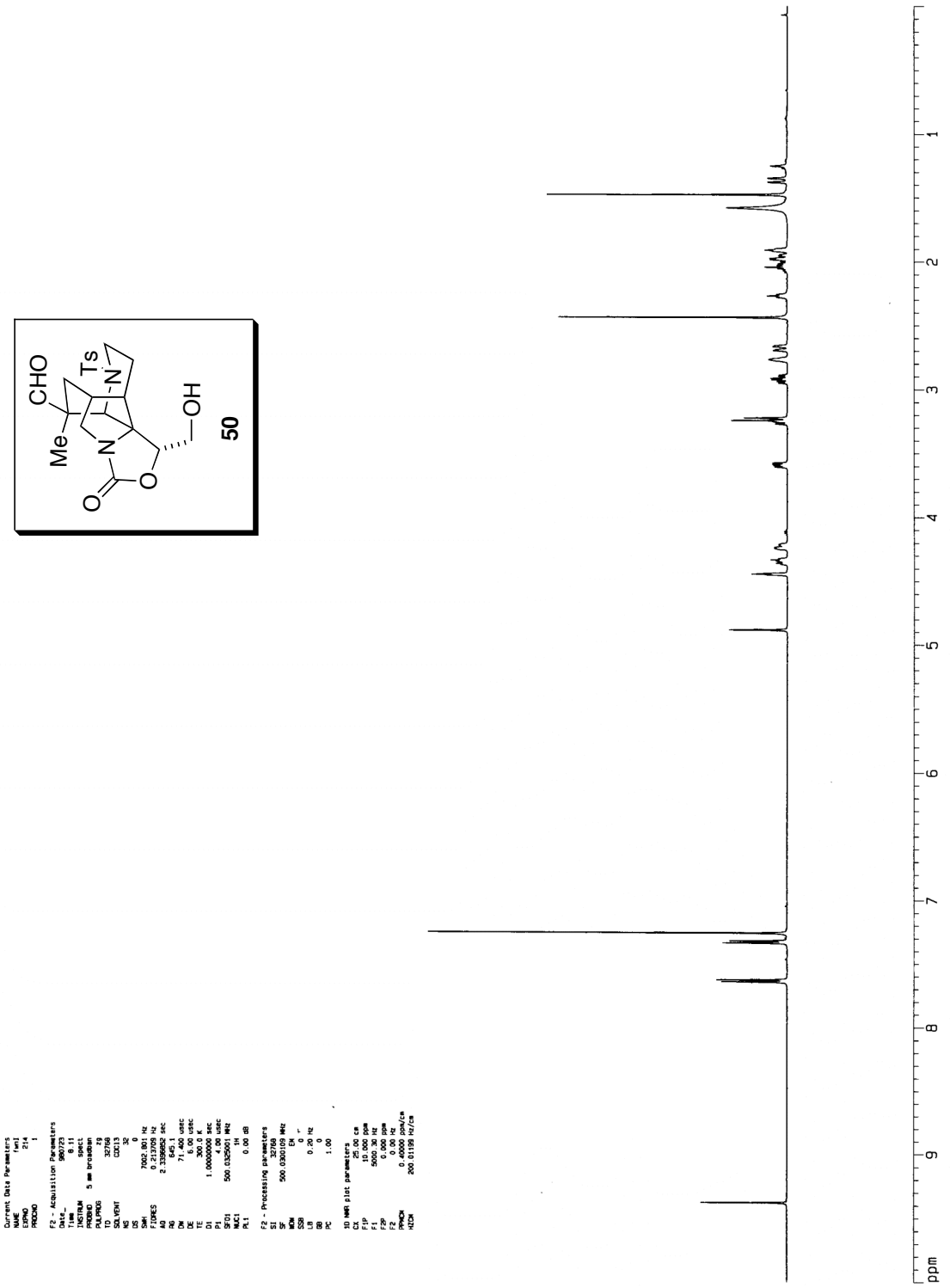

Me
Ts
N
O
BocN
HO
46
1.988
2.319
0.823
2.906
1.000
2.021
2.069
1.097
0.982
1.023
3.082
2.156
4.213
11.823
Integral
ppm

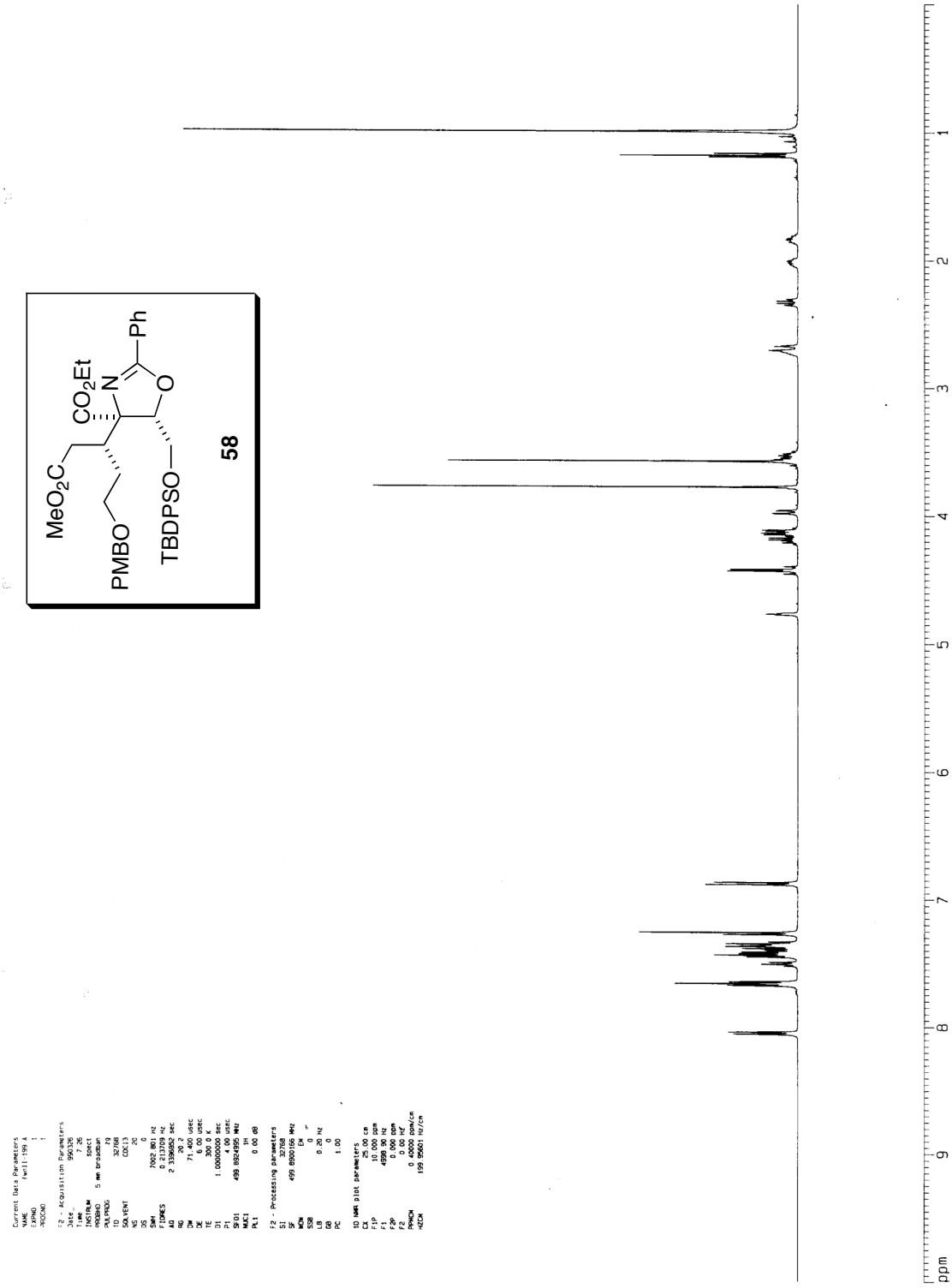


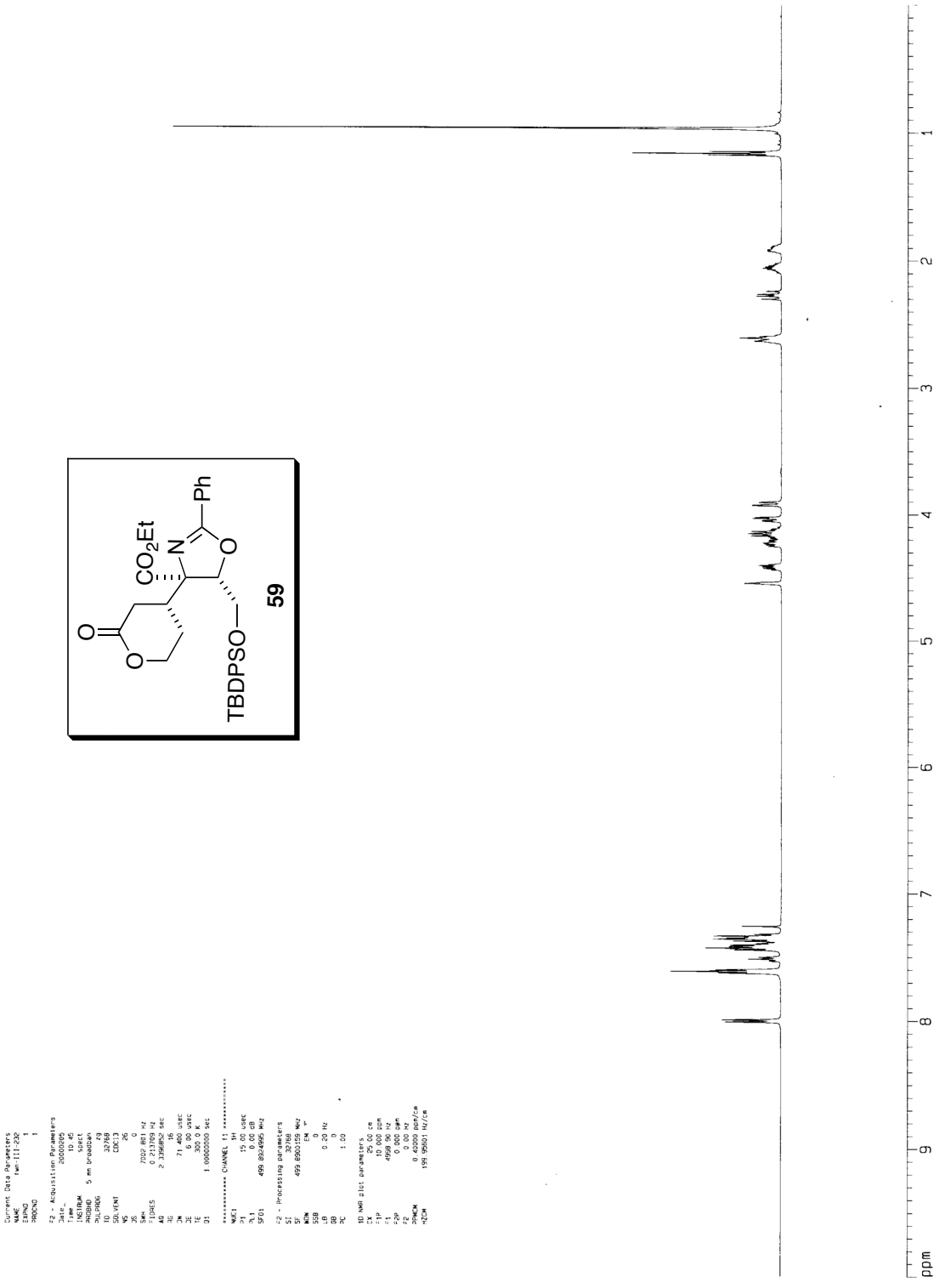
47

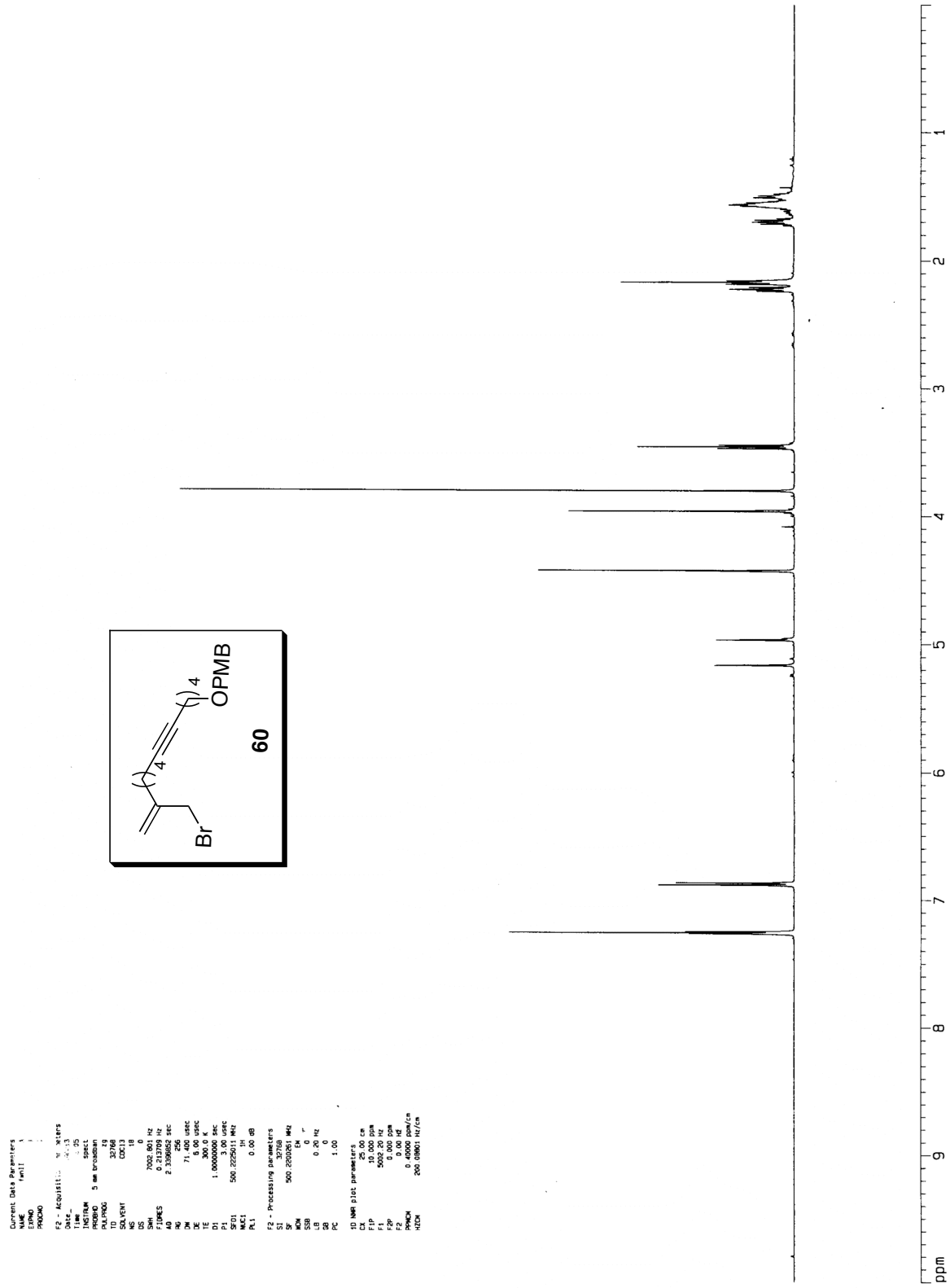

TIPSO
Me
Ts
N
O
O
H
O
N
48
Current Data Parameters
NAME tam1236-1
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 990504
Time 13.48
INSTRUM spect
PROBHD 5 mm broadban
PULPROG zg
TD 32768
SOLVENT CDCl3
NS 26
DS 4
SWH 7002.801 Hz
FIDRES 0.213720 Hz
AQ 2.3398852 sec
RG 128
DW 71.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
P1 8.00 usec
SFO1 500.2325611 MHz
NUC1 1H
PL1 0.00 dB
F2 - Processing parameters
SI 32768
SF 500.2200156 MHz
WDW EM
SSB 0
LB 0.20 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 25.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.40000 ppm/cm
HZCM 200.08800 Hz/cm
ppm
9
8
7
6
5
4
3
2
1

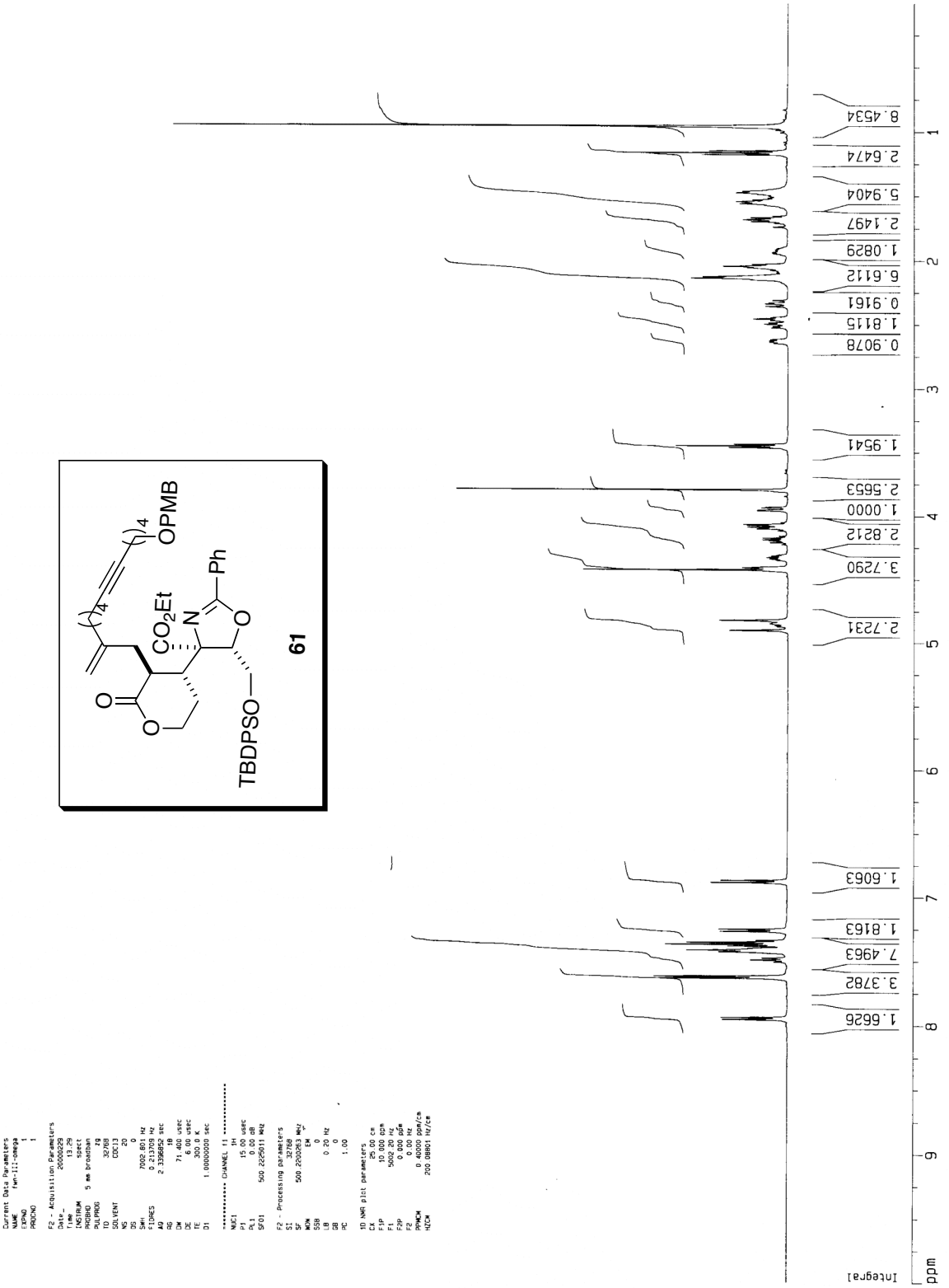

Me
OHC
Ts
N
N
O
O
OH
49
ppm


CHO
Ts
Me
OH
50
ppm

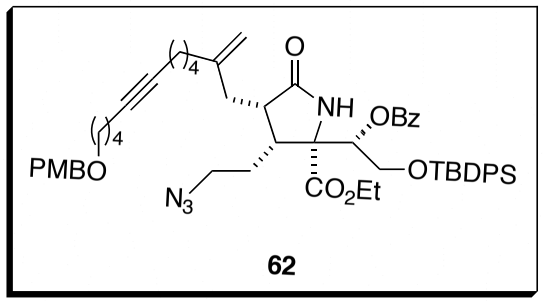

MeO2C
CO2Et
N
Ph
O
PMBO
TBDPSO
58
ppm


Current Data Parameters
NAME fam111-232
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200205
Time 10.45
INSTRUM spect
PROBHD 5 mm broadban
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 26
DS 0
SWH 7002.801 Hz
FIDRES 0.213799 Hz
AQ 2.3364852 sec
RG 71.489
DW 6.00 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 15.05 usec
PL1 0.00 dB
SFO1 499.8924995 MHz
F2 - Processing parameters
SI 32768
SF 499.8900155 MHz
WDW EM
SSB 0
LB 0.20 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 25.00 cm
F1P 10.000 ppm
F1 4998.90 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.42000 ppm/cm
HZCM 199.95601 Hz/cm
CO2Et
N
Ph
O
O
O
TBDPSO
59
ppm
9
8
7
6
5
4
3
2
1

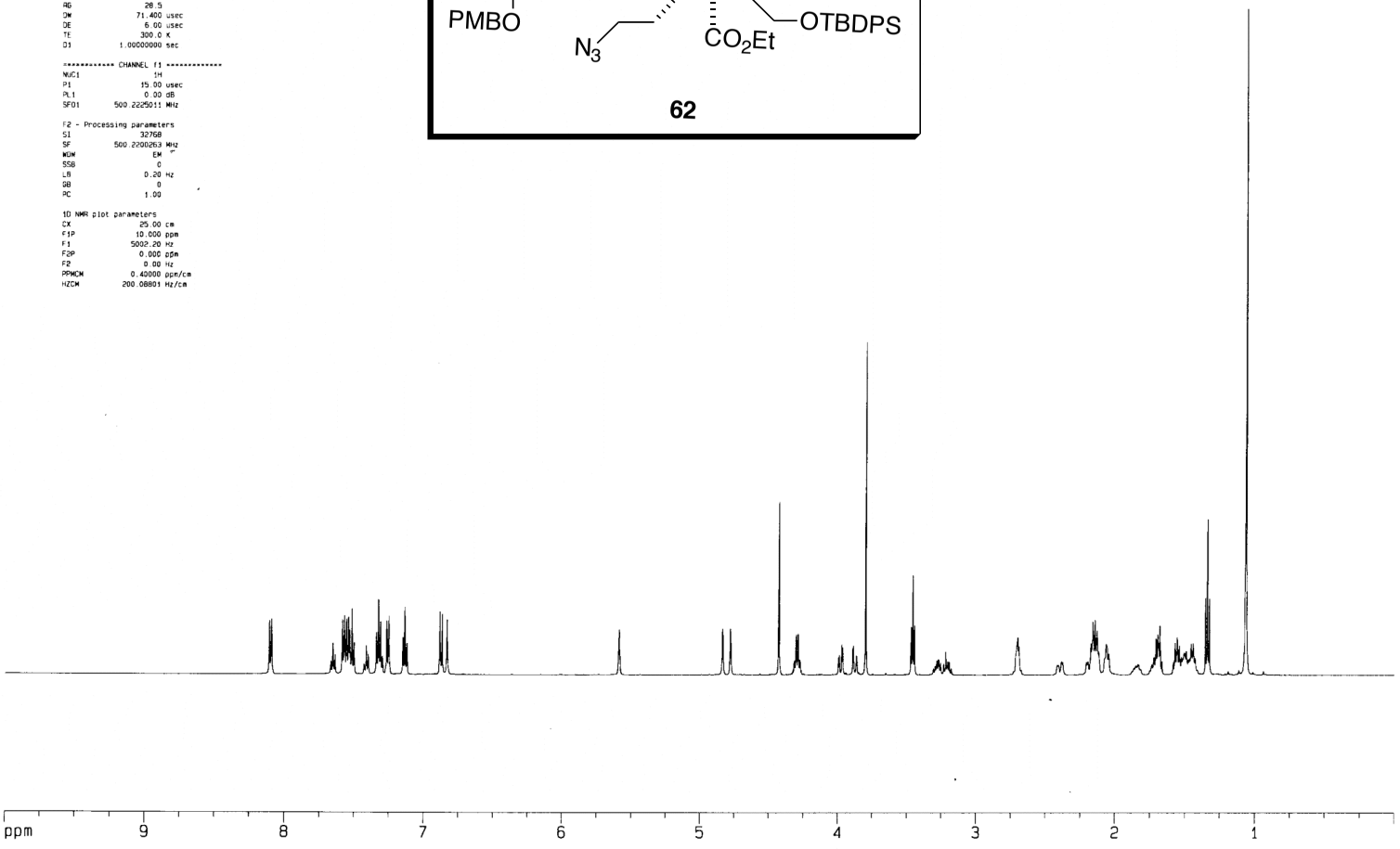

Br
4
4
OPMB
60
ppm
1
2
3
4
5
6
7
8
9

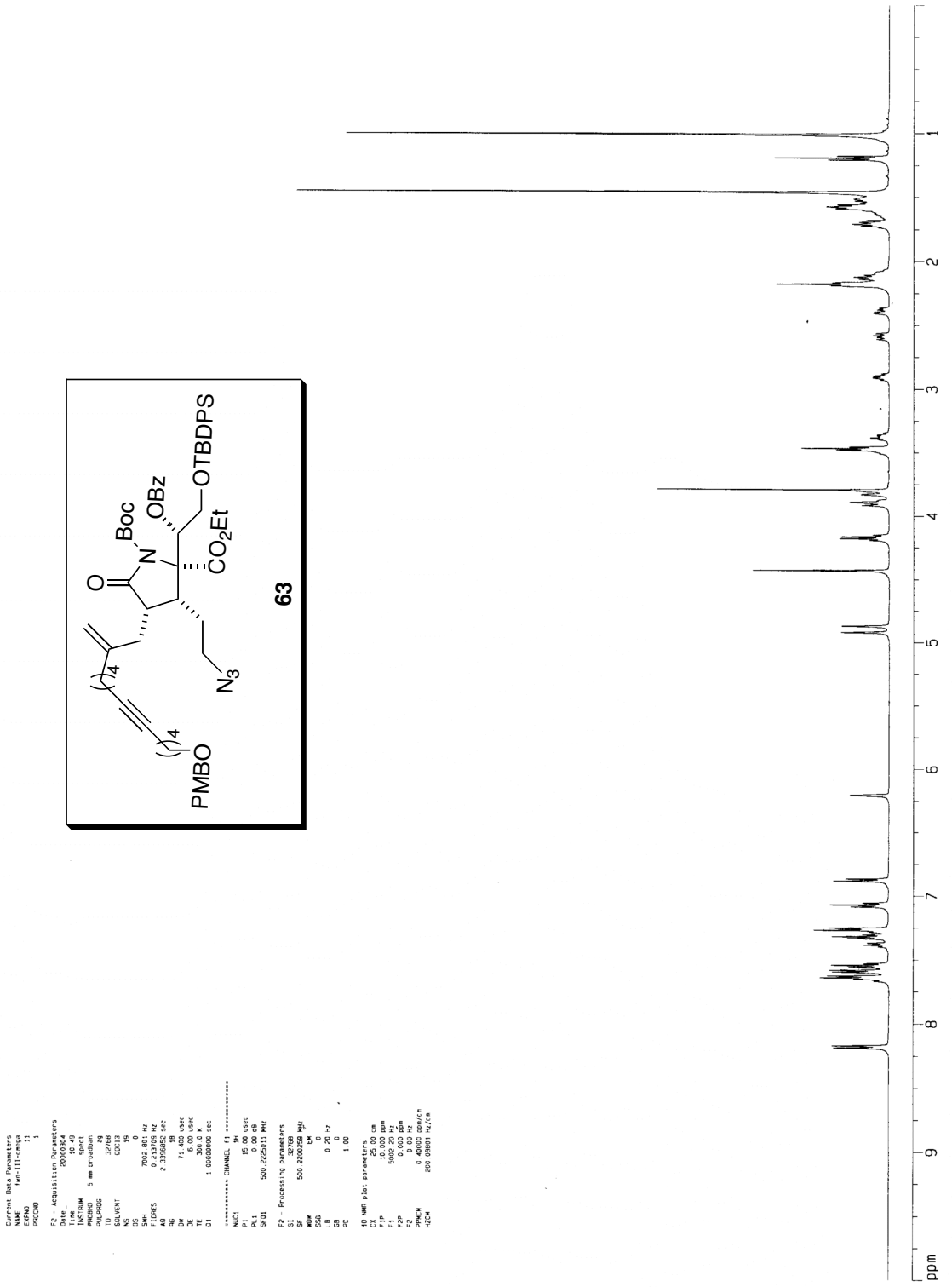

61
TBDPSO
CO2Et
OPMB
Ph
8.4534
2.6474
5.9404
2.1497
1.0829
6.6112
0.9161
1.8115
0.9078
1.9541
2.5553
1.0000
2.8212
3.7290
2.7231
1.6063
1.8163
7.4963
3.3782
1.6626
Integral
ppm

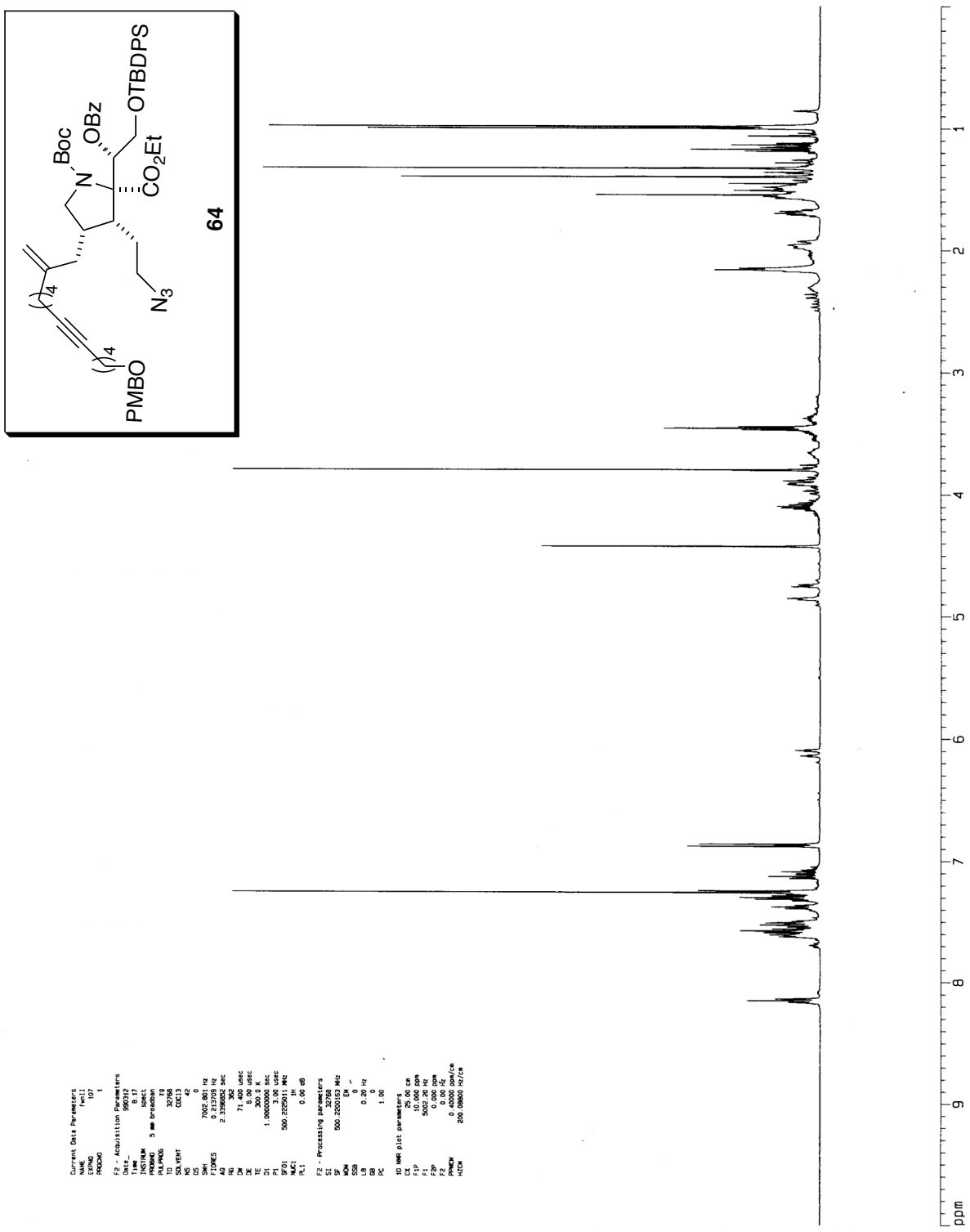
```
Current Data Parameters
NAME        fwn-III-omega
EXPNO                   7
PROCNO                  1

F2 - Acquisition Parameters
Date_            20000302
Time                13.45
INSTRUM             spect
PROBHD    5 mm broadban
PULPROG                zg
TD                  32768
SOLVENT             CDCl3
NS                     25
DS                      0
SWH              7002.801 Hz
FIDRES           0.213709 Hz
AQ               2.3396852 sec
RG                    28.5
DW                71.400 usec
DE                 6.00 usec
TE                300.0 K
D1             1.00000000 sec

========== CHANNEL f1 ============
NUC1                   1H
P1                 15.00 usec
PL1                 0.00 dB
SFO1         500.2225011 MHz

F2 - Processing parameters
SI                  32768
SF           500.2200263 MHz
WDW                    EM
SSB                     0
LB                 0.20 Hz
GB                      0
PC                   1.00

1D NMR plot parameters
CX                 25.00 cm
F1P               10.000 ppm
F1                5002.20 Hz
F2P                0.000 ppm
F2                   0.00 Hz
PPMCM            0.40000 ppm/cm
HZCM           200.08801 Hz/cm
```

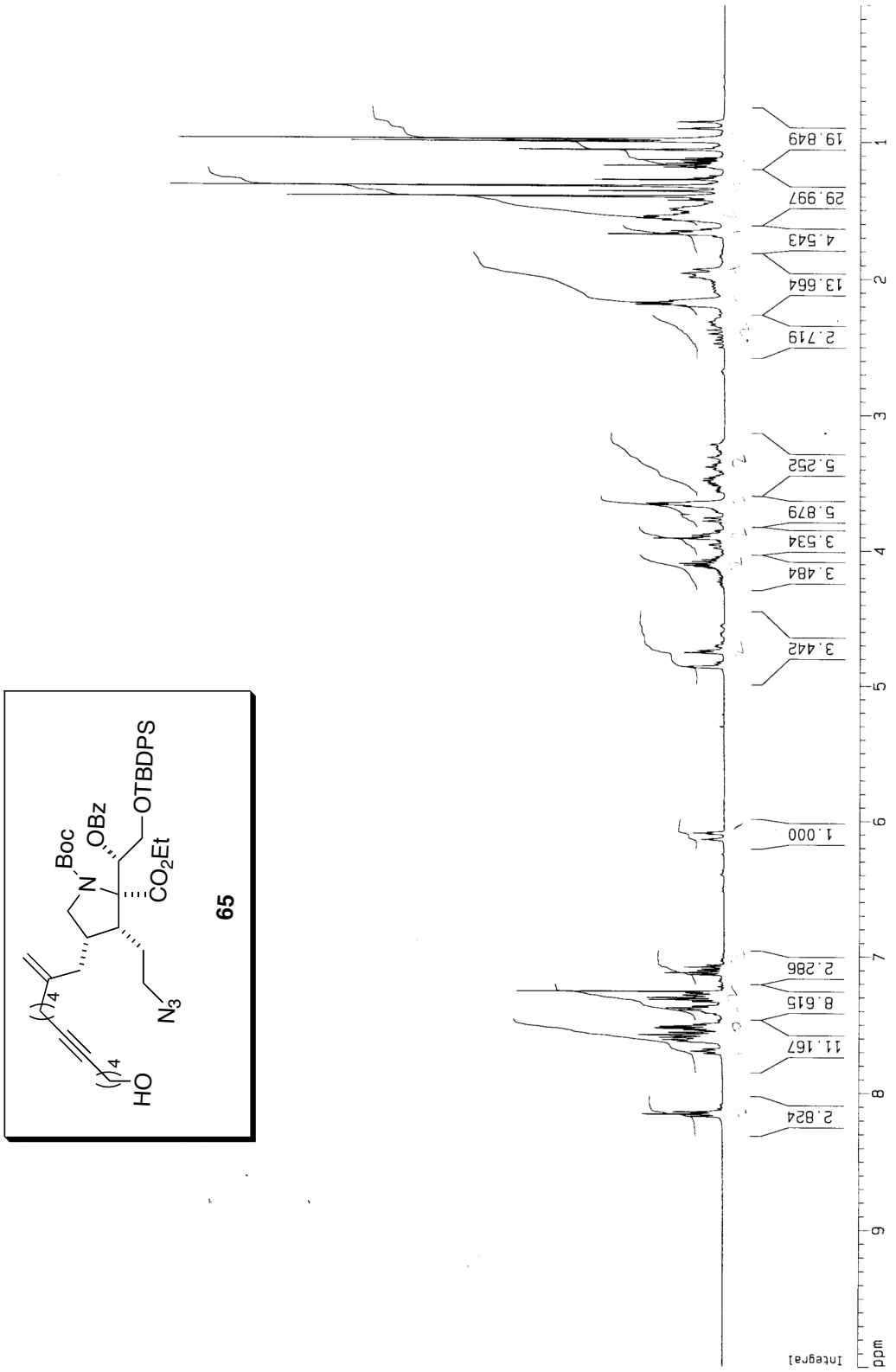


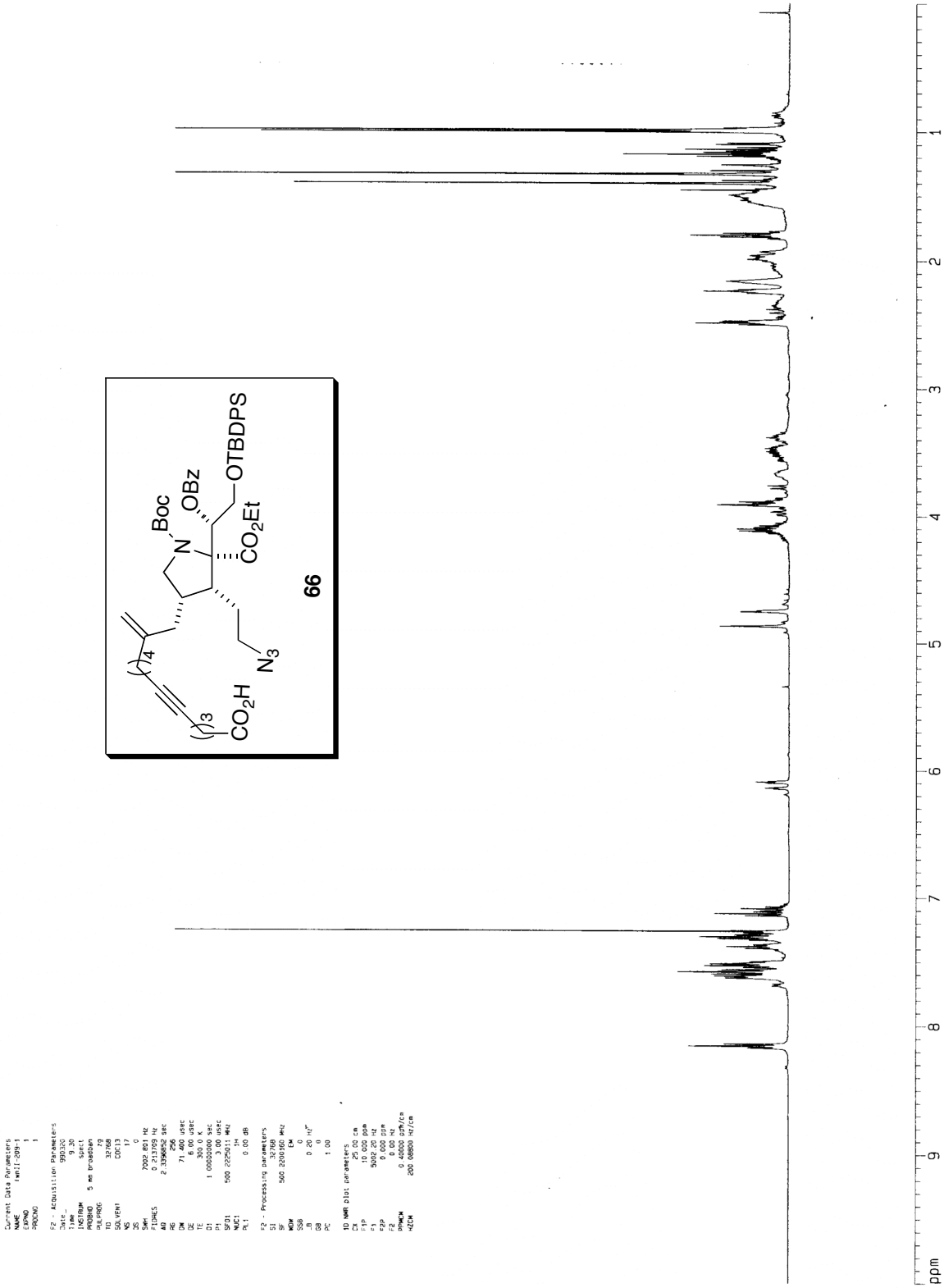
62

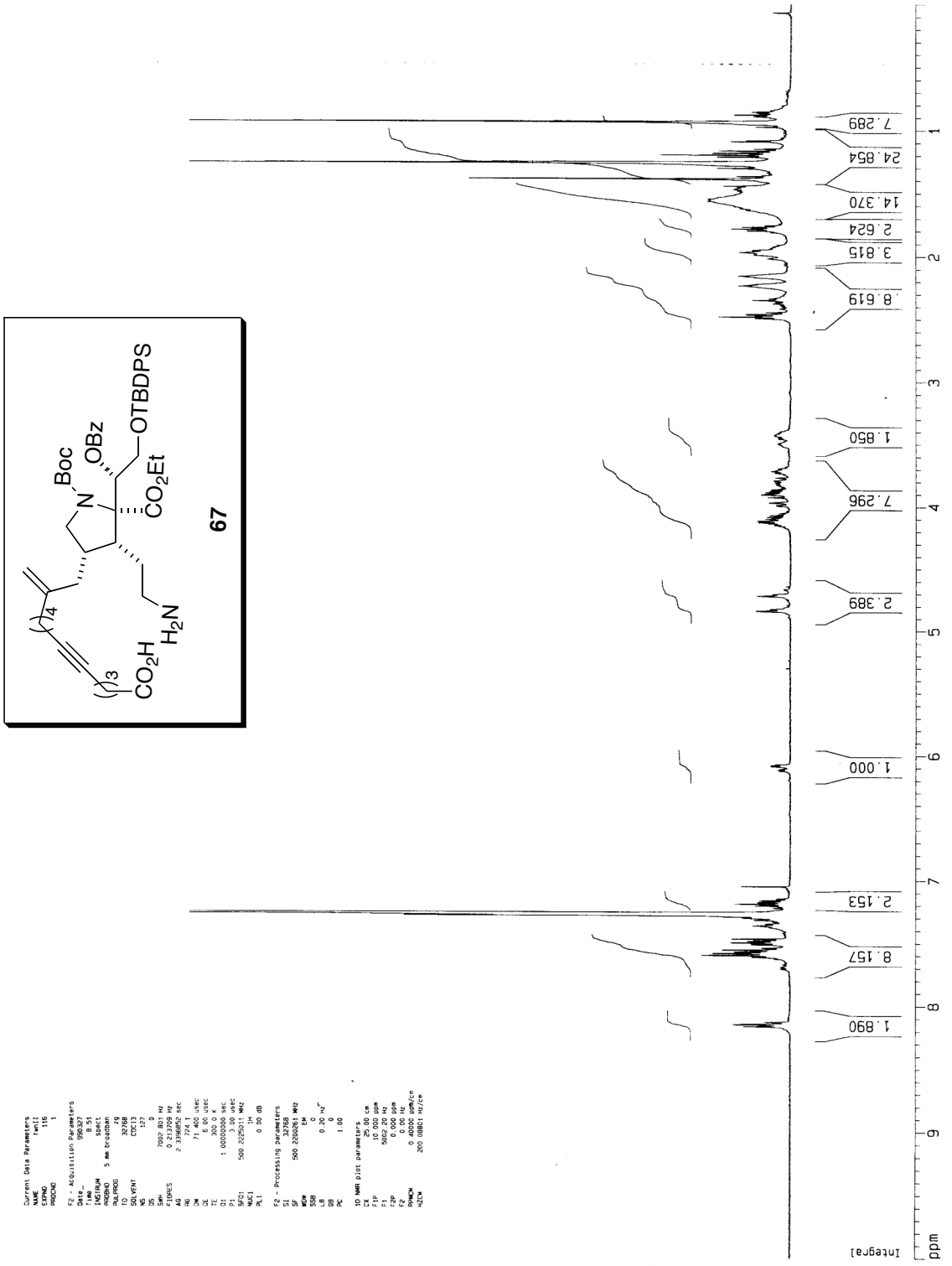


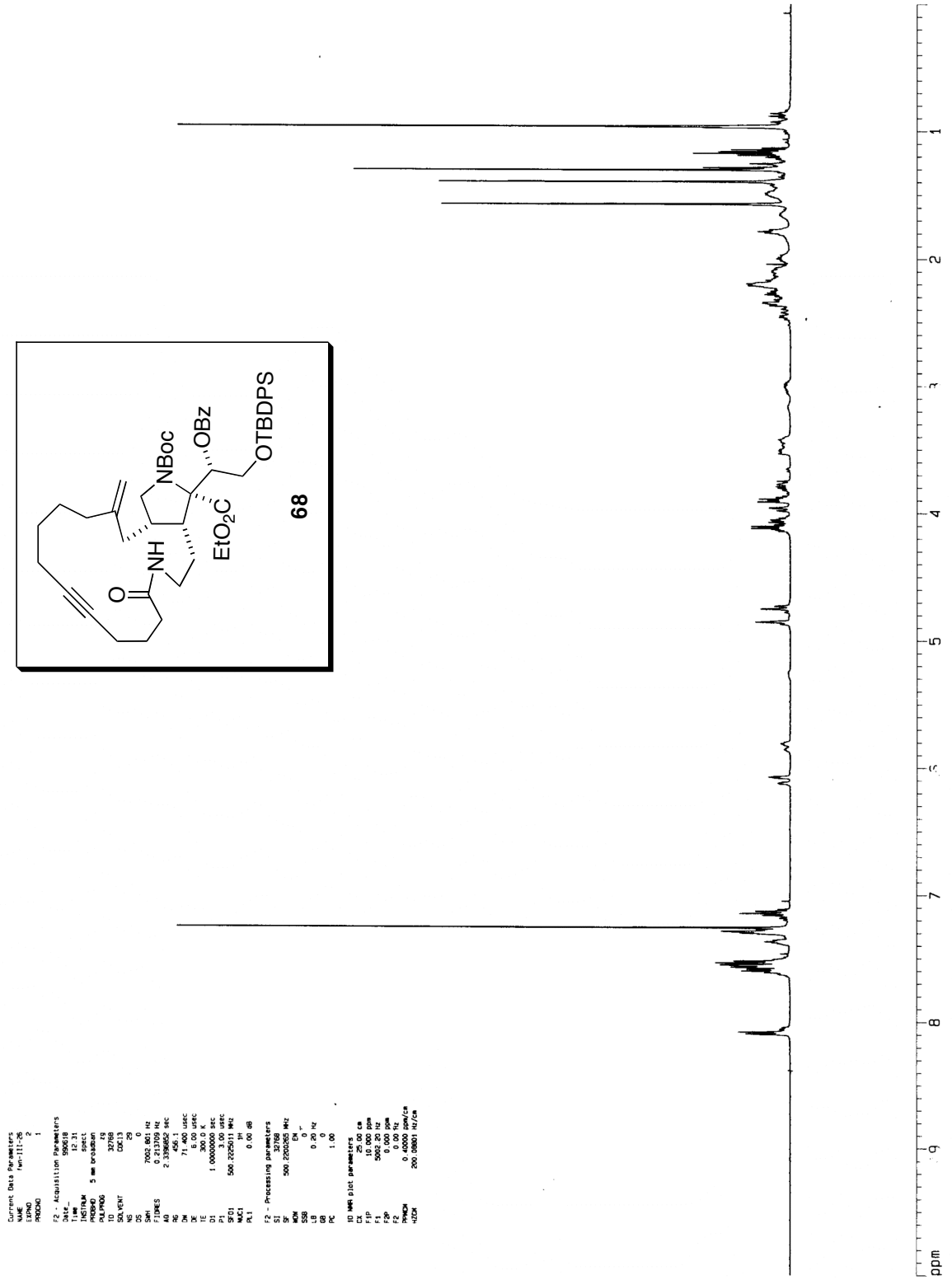

Boc
OBz
OTBDPS
CO2Et
PMBO
N3
63
ppm

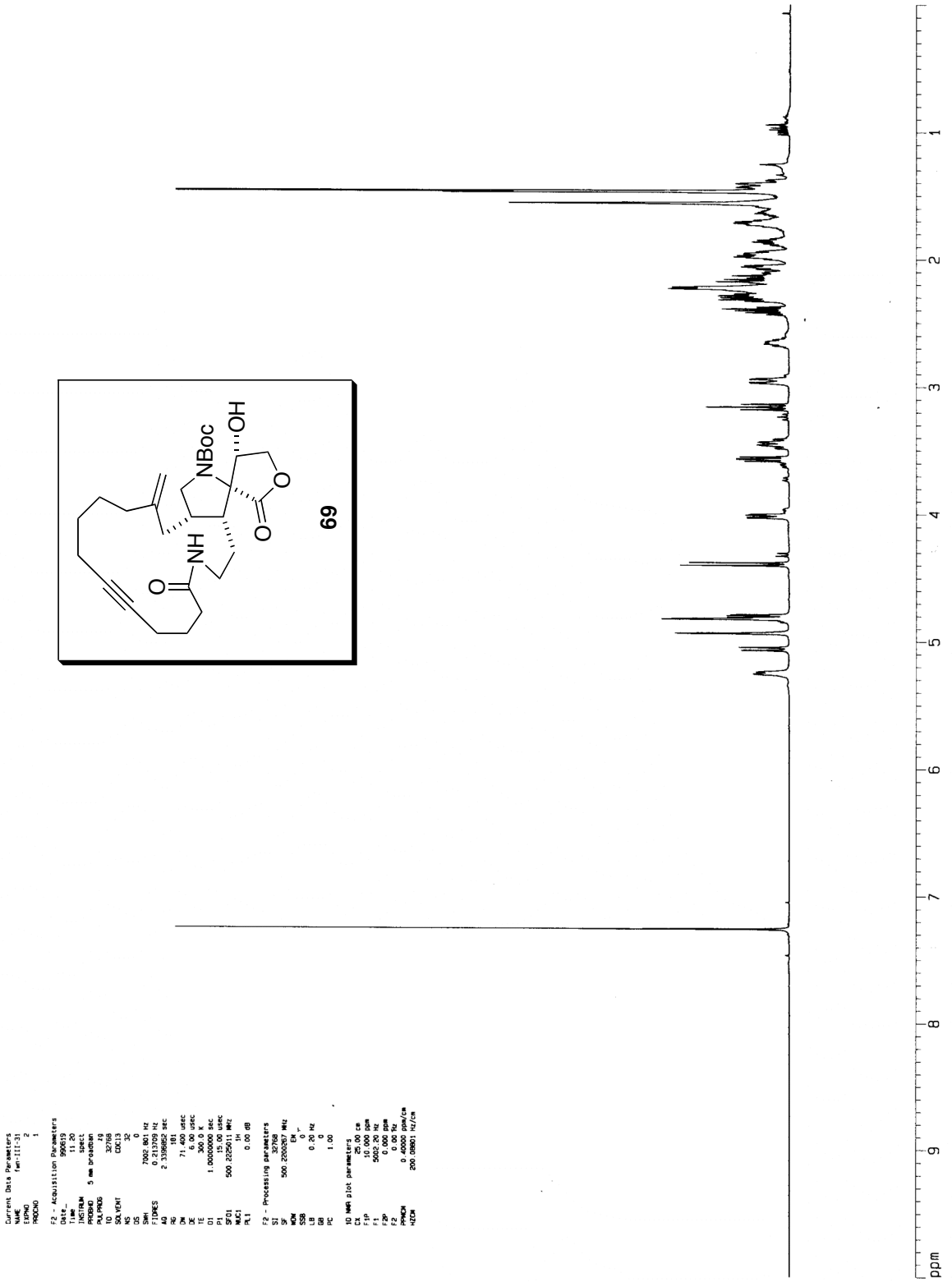

Boc
OBz
OTBDPS
N
CO2Et
N3
PMBO
4
4
64
ppm
1
2
3
4
5
6
7
8
9


Boc
N
OBz
OTBDPS
CO2Et
N3
HO
4
4
65
19.849
29.997
4.543
13.664
2.719
5.252
5.879
3.534
3.484
3.442
1.000
2.286
8.615
11.167
2.824
Integral
ppm

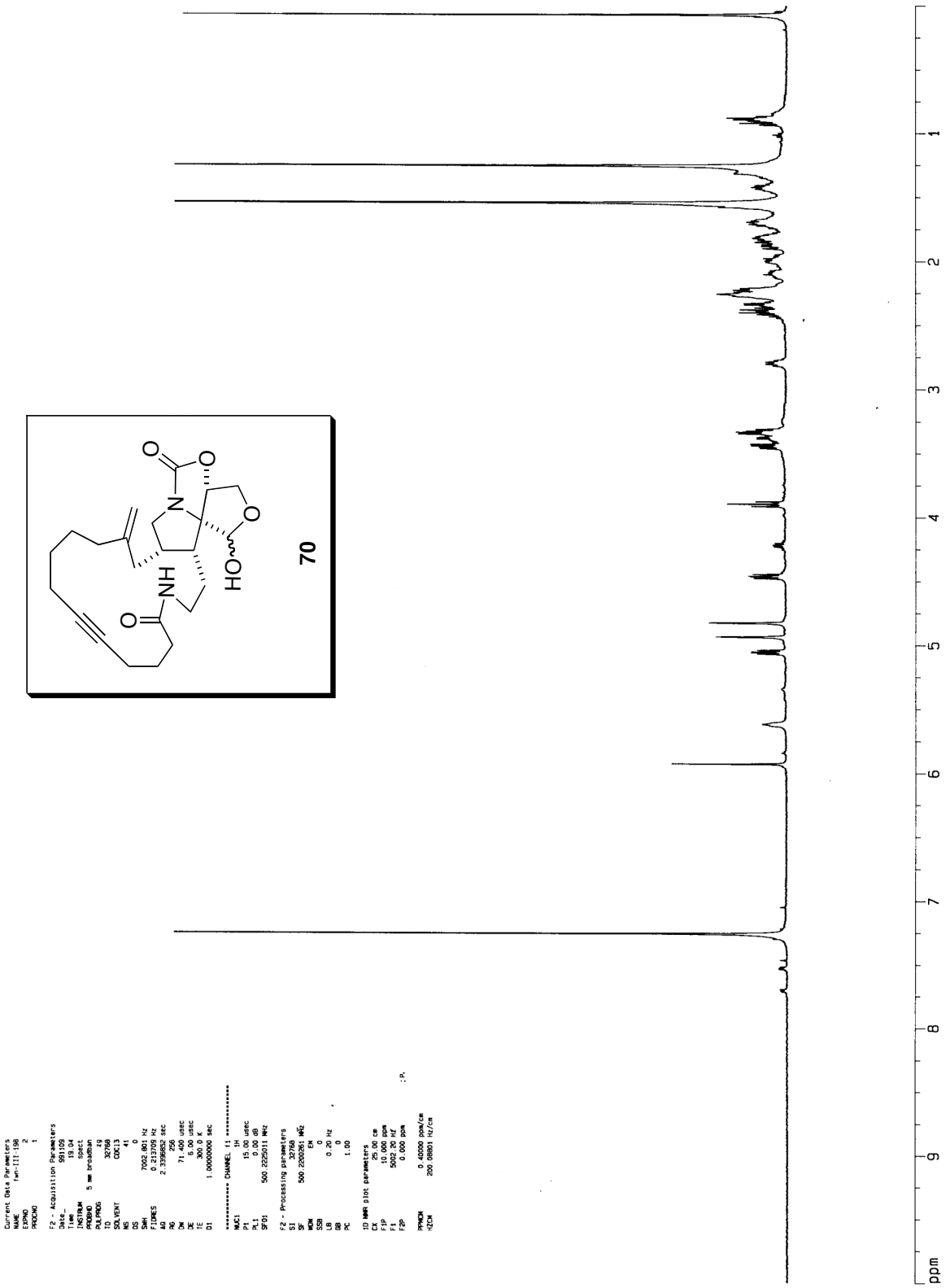

Boc
OBz
OTBDPS
CO2Et
N3
CO2H
66
ppm


Boc
OBz
OTBDPS
CO2Et
CO2H
H2N
67
1.890
8.157
2.153
1.000
2.389
7.296
1.850
8.619
3.815
2.624
14.370
24.854
7.289
Integral
ppm


NBoc
OBz
OTBDPS
NH
O
EtO_2C
68
ppm




```
Current Data Parameters
NAME          fam-III-31
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_          990619
Time           11.20
INSTRUM        spect
PROBHD     5 mm broadban
PULPROG            zg
TD                32768
SOLVENT           CDCl3
NS                   32
DS                    2
SWH           7002.801 Hz
FIDRES        0.213709 Hz
AQ            2.3396952 sec
RG                  181
DW              71.400 usec
DE               6.00 usec
TE              300.0 K
D1              1.00000000 sec
P1                10.00 usec
SFO1         500.2225611 MHz
NUC1               1H
PL1              0.00 dB

F2 - Processing parameters
SI                32768
SF           500.2200267 MHz
WDW                  EM
SSB                   0
LB                 0.20 Hz
GB                    0
PC                 1.00

1D NMR plot parameters
CX              20.00 cm
F1P             10.000 ppm
F1              5002.20 Hz
F2P              0.000 ppm
F2               0.00 Hz
PPMCM          0.40000 ppm/cm
HZCM          200.08801 Hz/cm
```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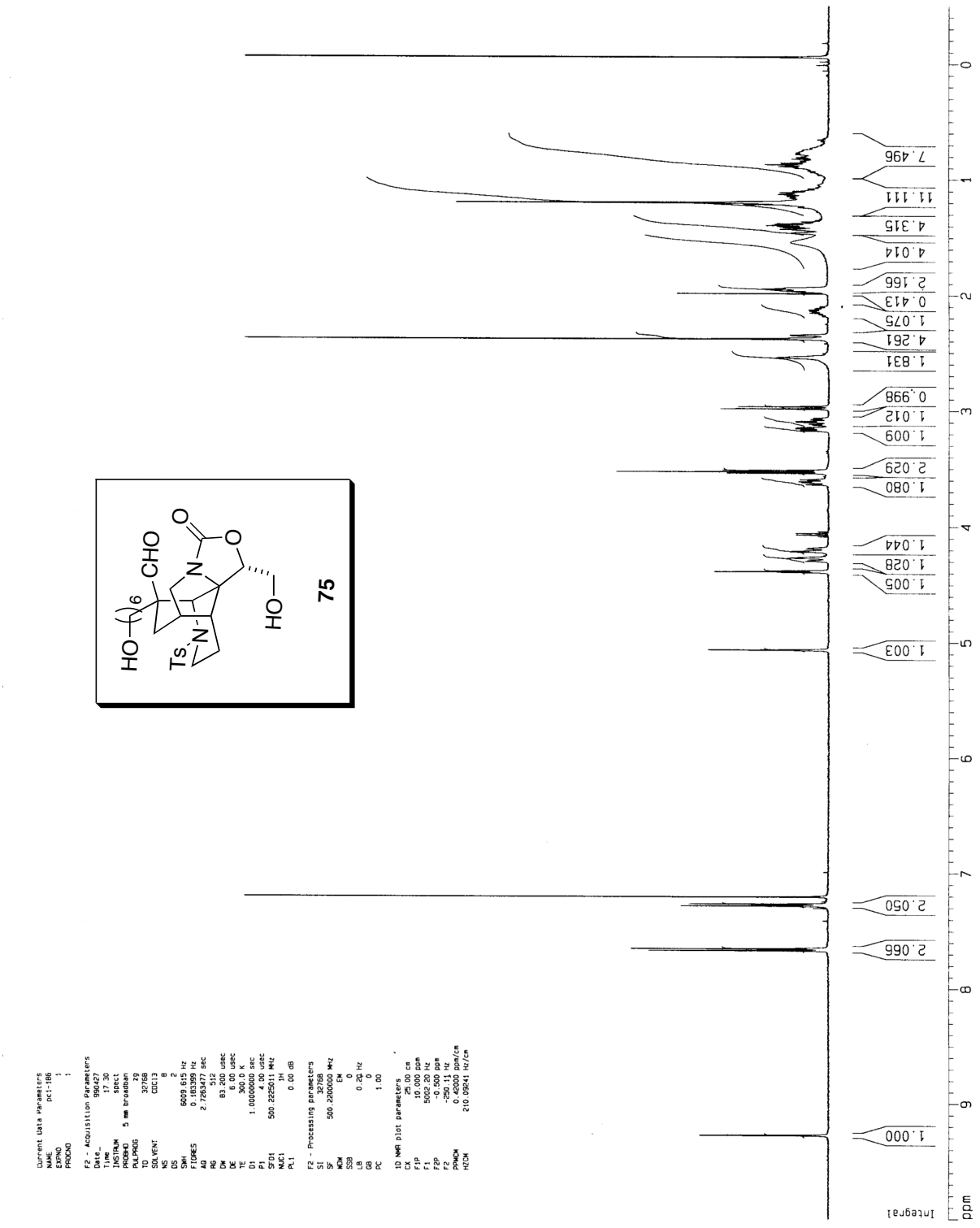
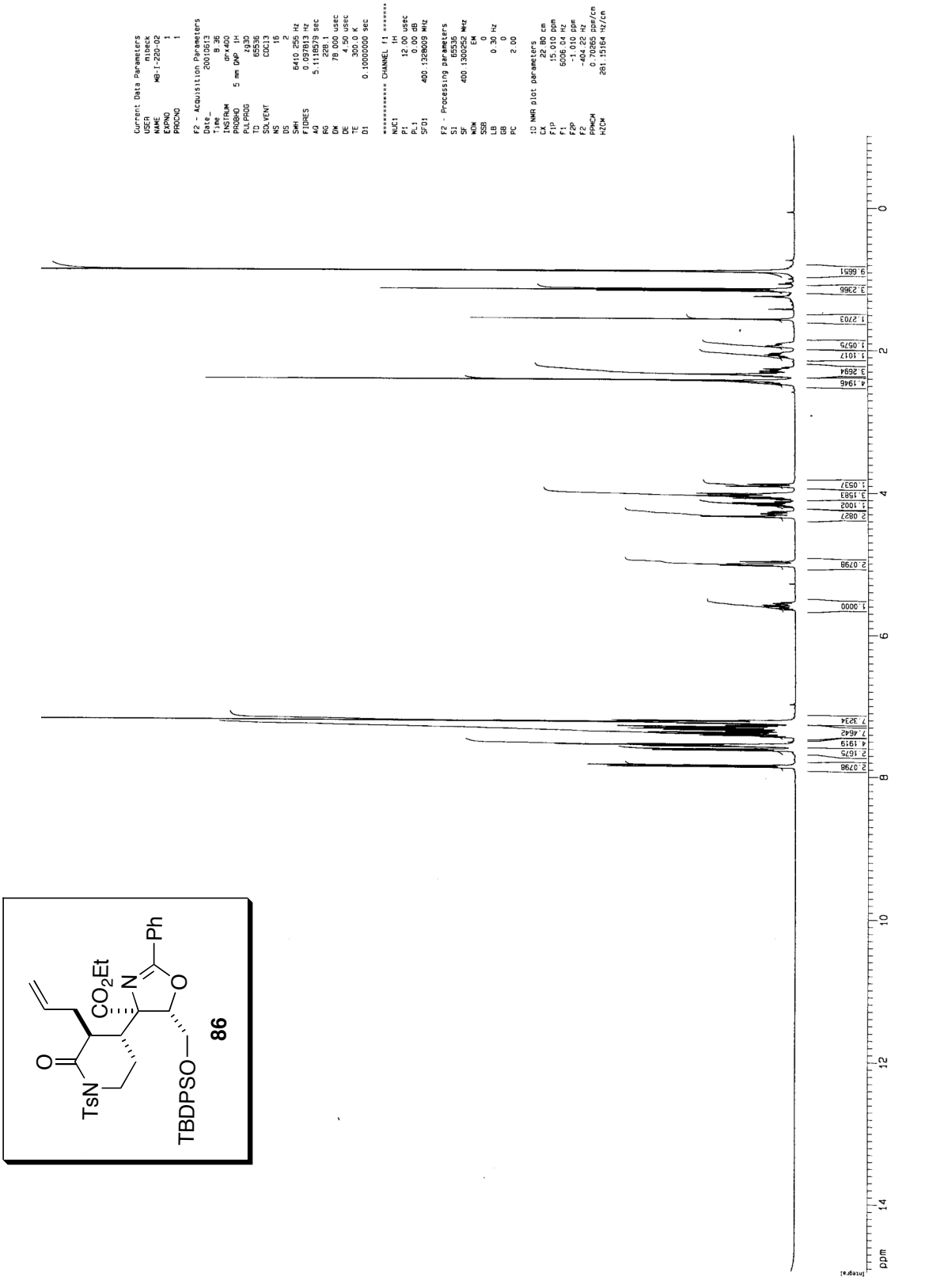
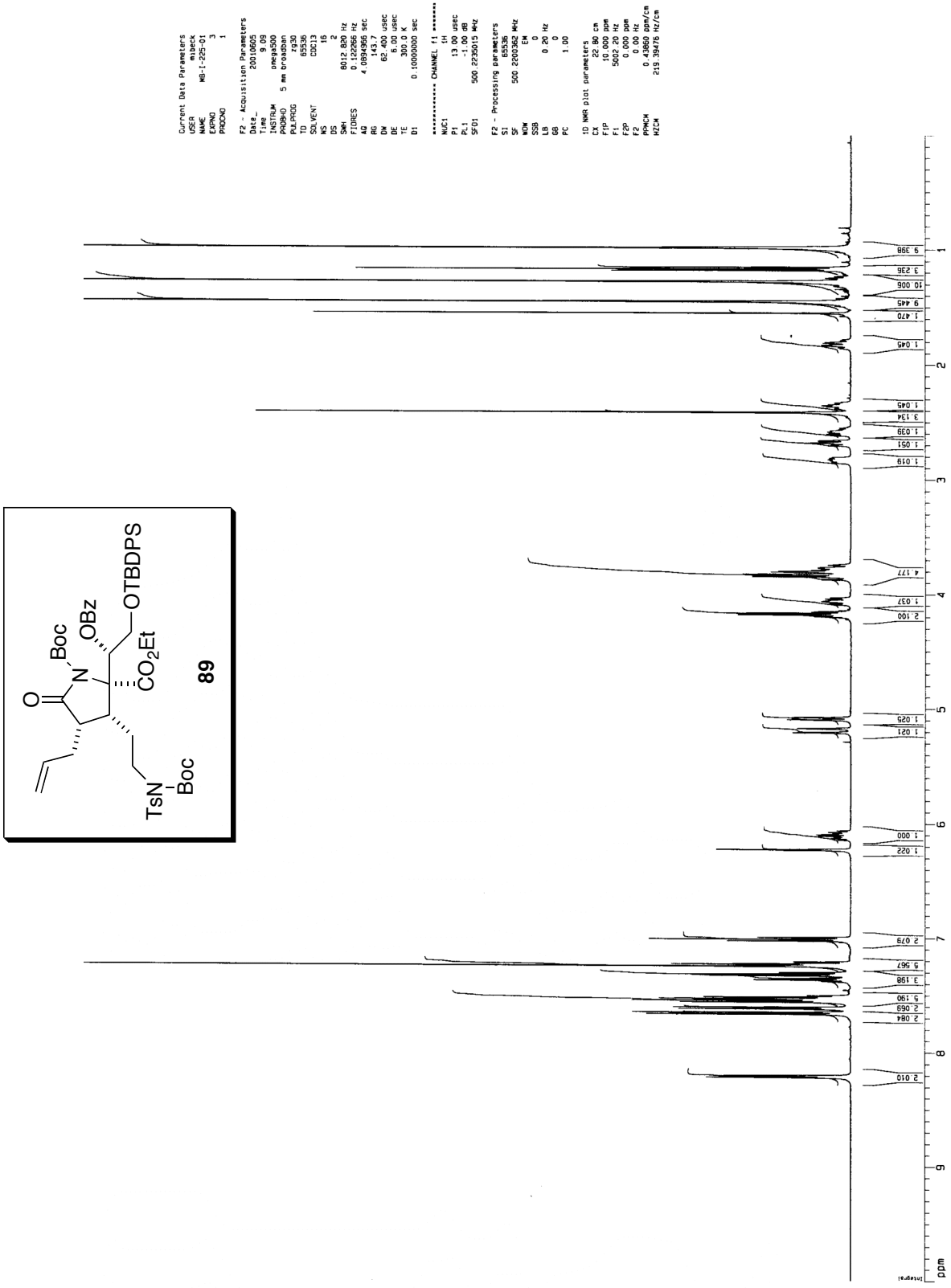
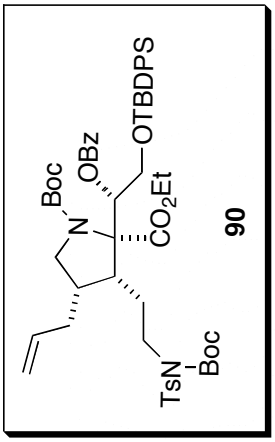
NAME rwn-III-198
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 991109
Time 19.04
INSTRUM spect
PROBHD 5 mm broadban
PULPROG zg
TD 32768
SOLVENT CDCl3
NS 41
DS 0
SWH 7002.801 Hz
FIDRES 0.213709 Hz
AQ 2.3396852 sec
RG 256
DW 71.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 15.00 usec
PL1 0.00 dB
SFO1 500.2225011 MHz
F2 - Processing parameters
SI 32768
SF 500.2200261 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 20.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P 0.000 ppm
PPMCM 0.40000 ppm/cm
HZCM 200.08801 Hz/cm
70
ppm

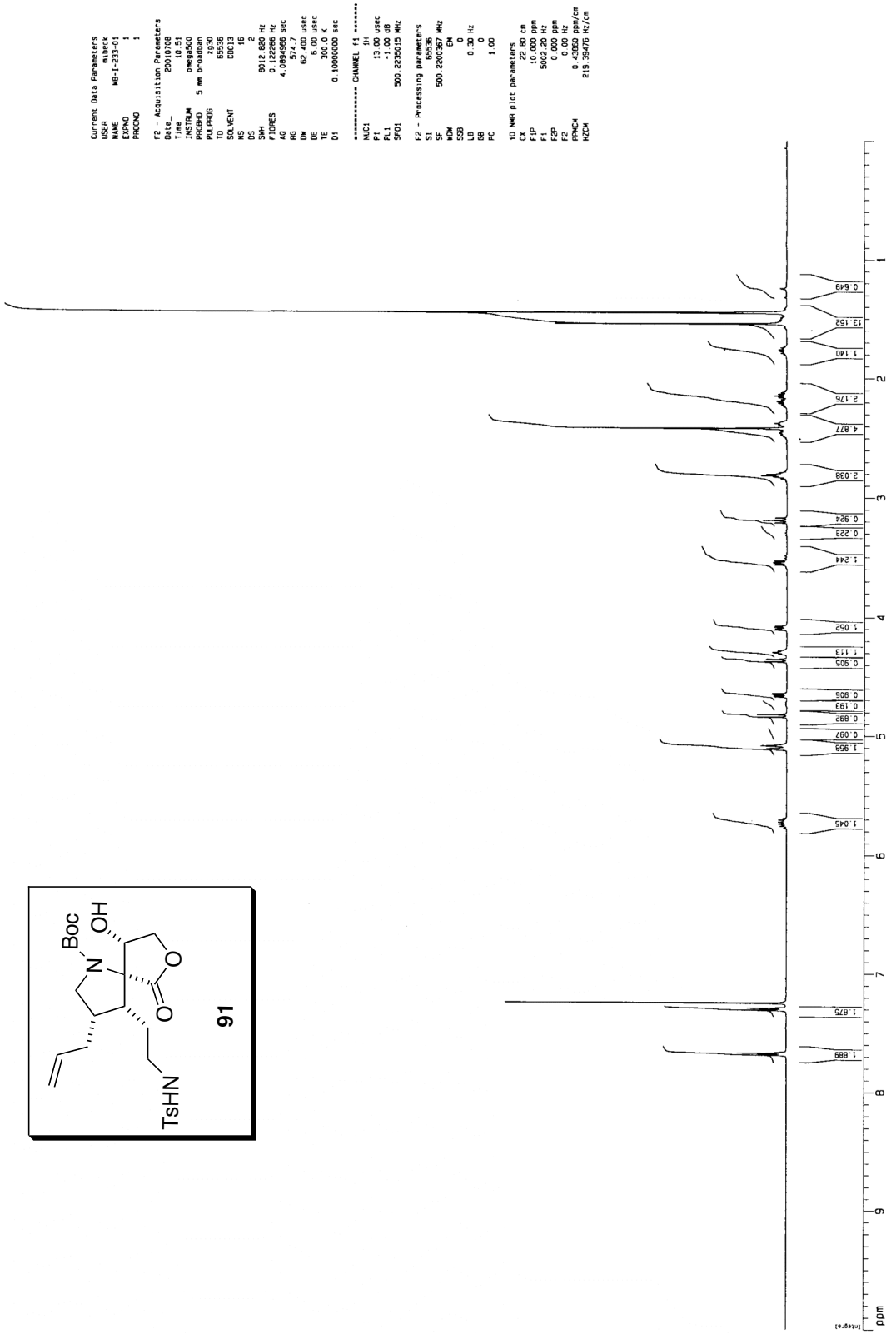

HO
CHO
6
Ts
N
O
O
N
HO
75
Integral
ppm
1.000
2.066
2.050
1.003
1.005
1.028
1.044
1.080
2.029
1.009
1.012
0.998
1.831
4.261
1.075
0.413
2.166
4.014
4.315
11.111
7.496
0
1
2
3
4
5
6
7
8
9


Current Data Parameters
USER nideck
NAME MB-I-220-02
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20010613
Time 8.36
INSTRUM drx400
PROBHD 5 mm QNP 1H
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 228.1
DW 78.000 usec
DE 4.50 usec
TE 300.0 K
D1 0.10000000 sec
========== CHANNEL f1 ======
NUC1 1H
P1 12.00 usec
PL1 0.00 dB
SFO1 400.1328009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300252 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
F1P 15.010 ppm
F1 6006.04 Hz
F2P -1.010 ppm
F2 -404.22 Hz
PPMCM 0.70265 ppm/cm
HZCM 281.15164 Hz/cm
9.6651
3.2366
1.2703
1.0575
1.1017
3.2694
4.1946
1.0537
3.1593
1.1002
2.0827
2.0798
1.0000
7.3234
7.4642
4.1919
2.1675
2.0798
ppm
integral
TsN
O
CO2Et
N
Ph
O
TBDPSO
86


Boc
OBz
OTBDPS
CO_2Et
TsN
Boc
89
ppm


Boc
N
OBz
OTBDPS
CO2Et
TsN
Boc
90

ppm
0
2
4
6
8
10
12
14


Boc
N
OH
O
O
TsHN
91
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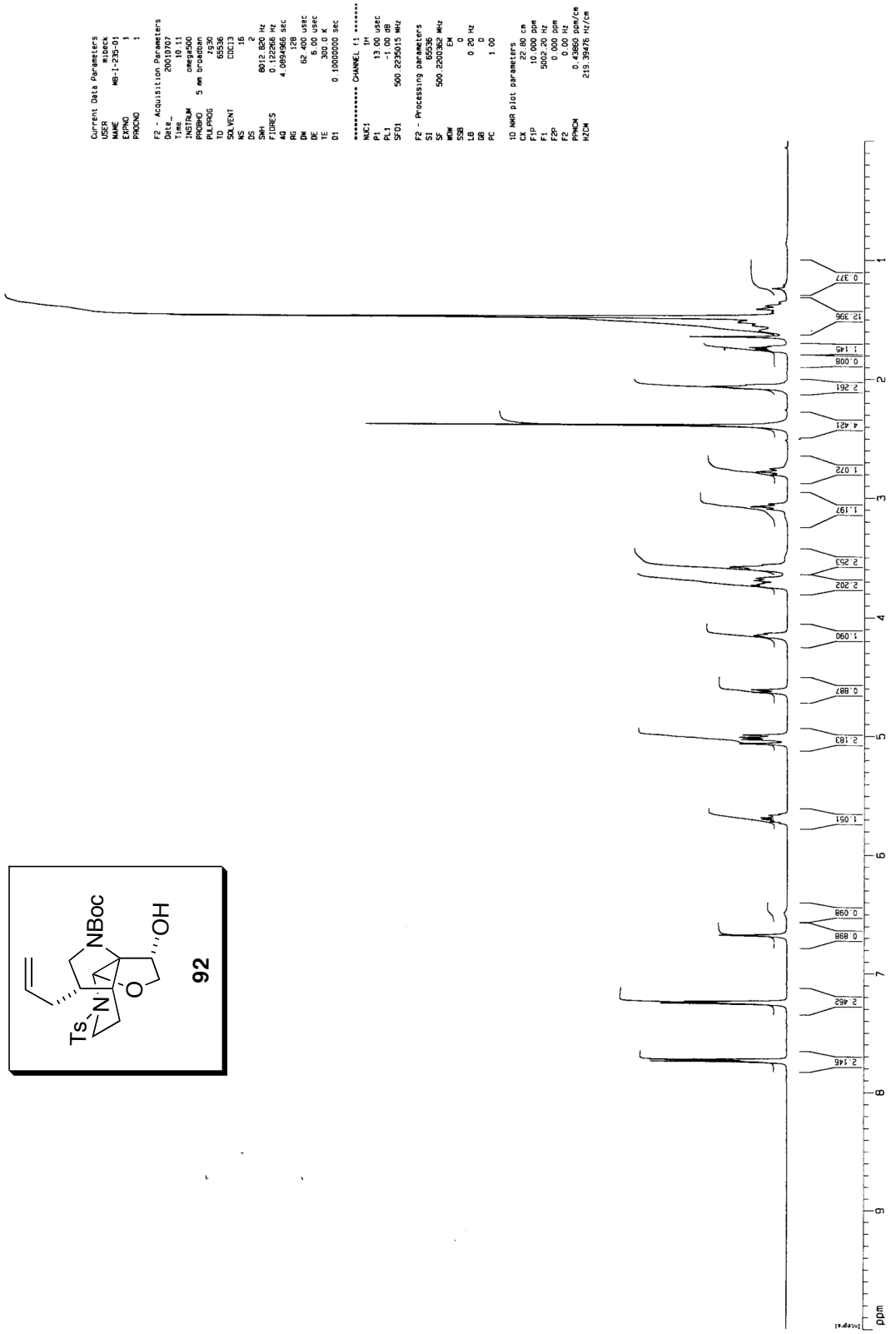
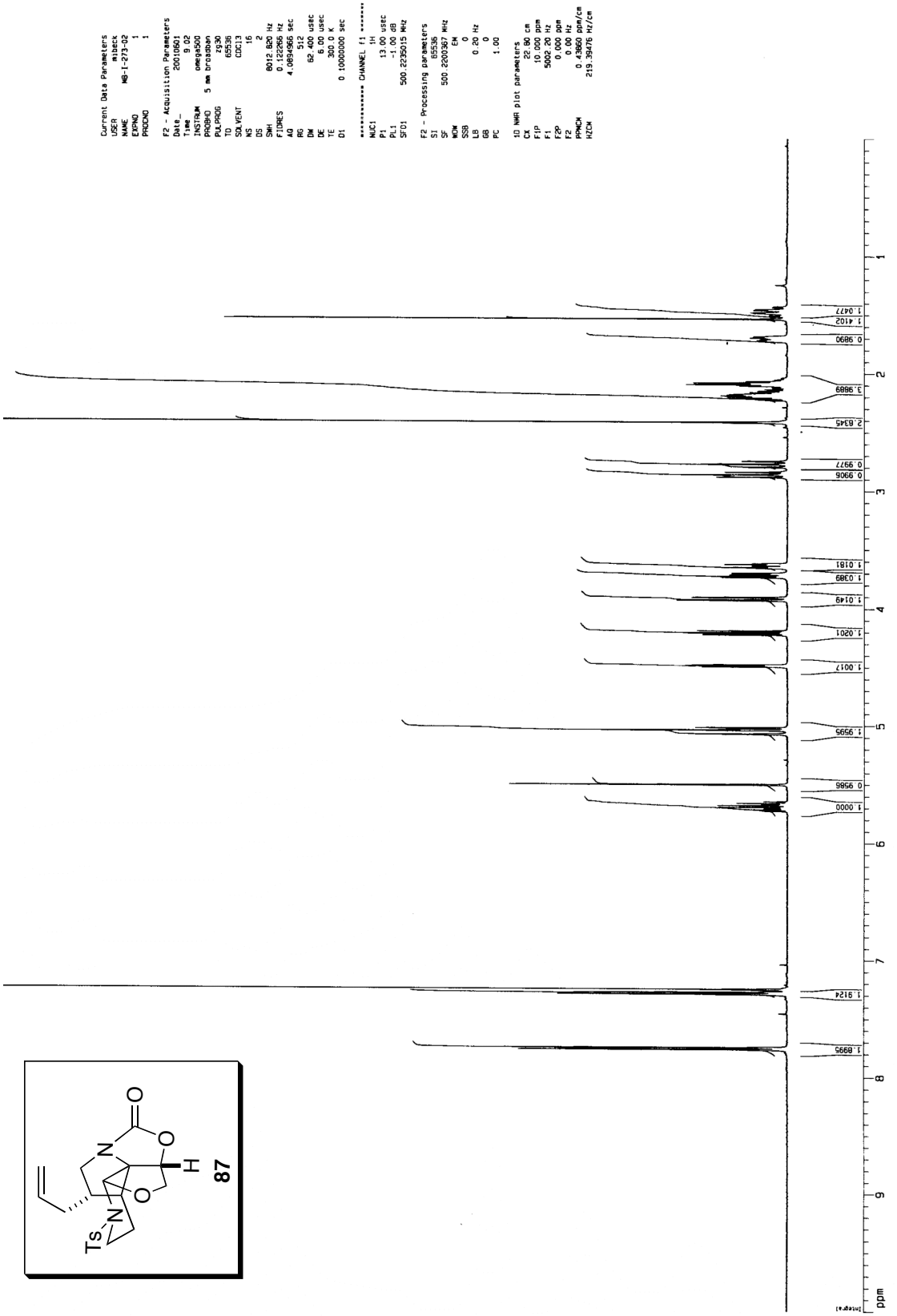
USER mlbeck
NAME MB-I-233-01
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141008
Time 10.51
INSTRUM omega500
PROBHD 5 mm broadban
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122265 Hz
AQ 4.0894966 sec
RG 574.7
DW 62.400 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
========== CHANNEL f1 ========
NUC1 1H
P1 13.00 usec
PL1 -1.00 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200367 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.43860 ppm/cm
HZCM 219.39476 Hz/cm
0.649
13.152
1.140
2.176
4.877
2.038
0.924
0.223
1.244
1.050
1.113
0.905
0.906
0.193
0.892
0.097
1.956
1.045
1.875
1.889
ppm


Current Data Parameters
USER mlbeck
NAME MB-I-235-01
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20010707
Time 10.11
INSTRUM omega500
PROBHD 5 mm broadban
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.8206 Hz
FIDRES 0.122265 Hz
AQ 4.0894966 sec
RG 128
DW 62.400 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
********** CHANNEL f1 **********
NUC1 1H
P1 13.00 usec
PL1 -1.00 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200362 MHz
WDW EM
SSB 0
LB 0.20 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.43860 ppm/cm
HZCM 219.39476 Hz/cm
0.377
12.396
1.145
0.008
2.261
4.421
1.072
1.197
2.252
2.202
1.090
0.887
2.183
1.051
0.860
0.898
2.462
2.145
ppm
1
2
3
4
5
6
7
8
9
NBoc
OH
Ts
N
O
92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USER mlbeck
NAME MB-I-273-02
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
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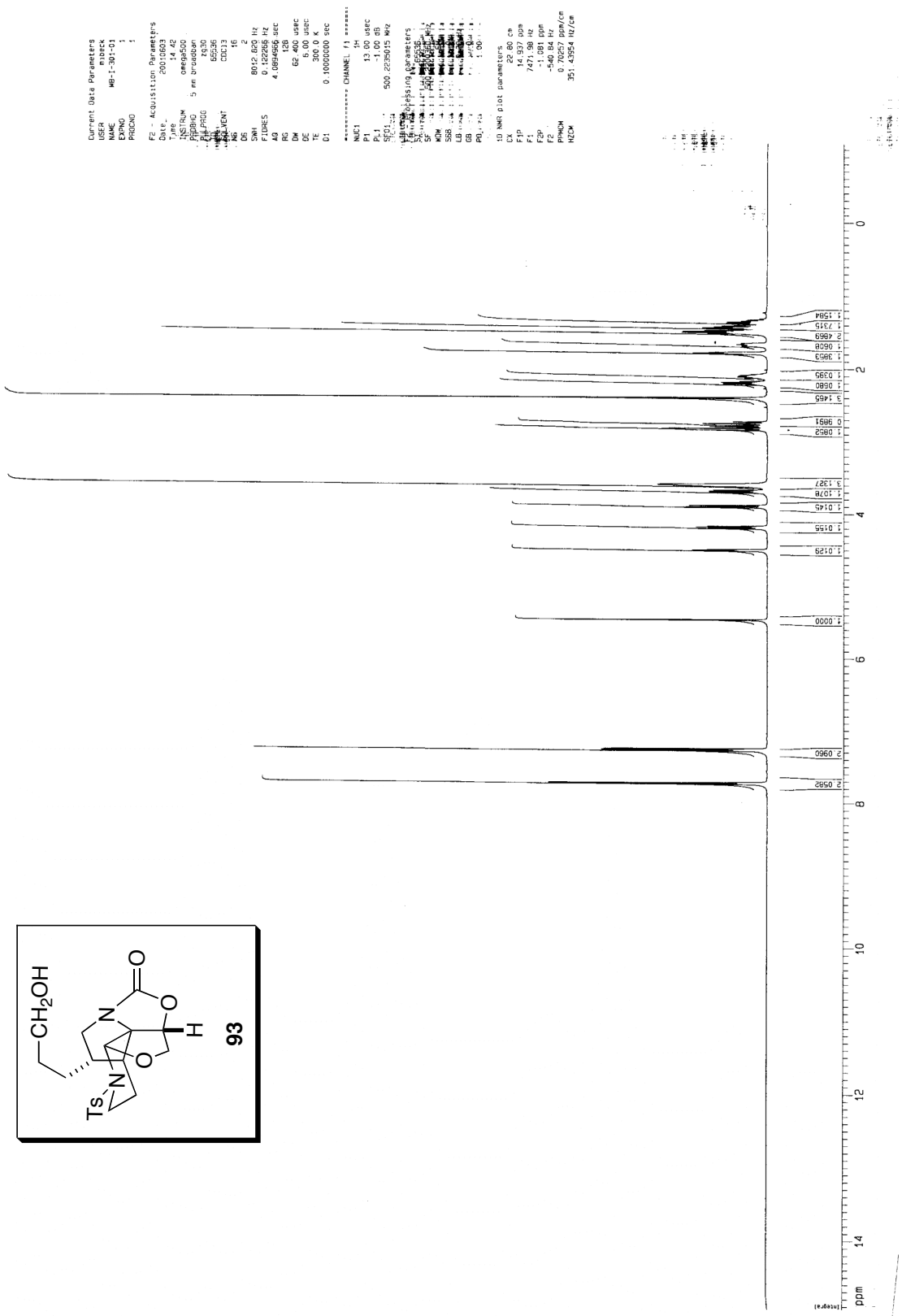
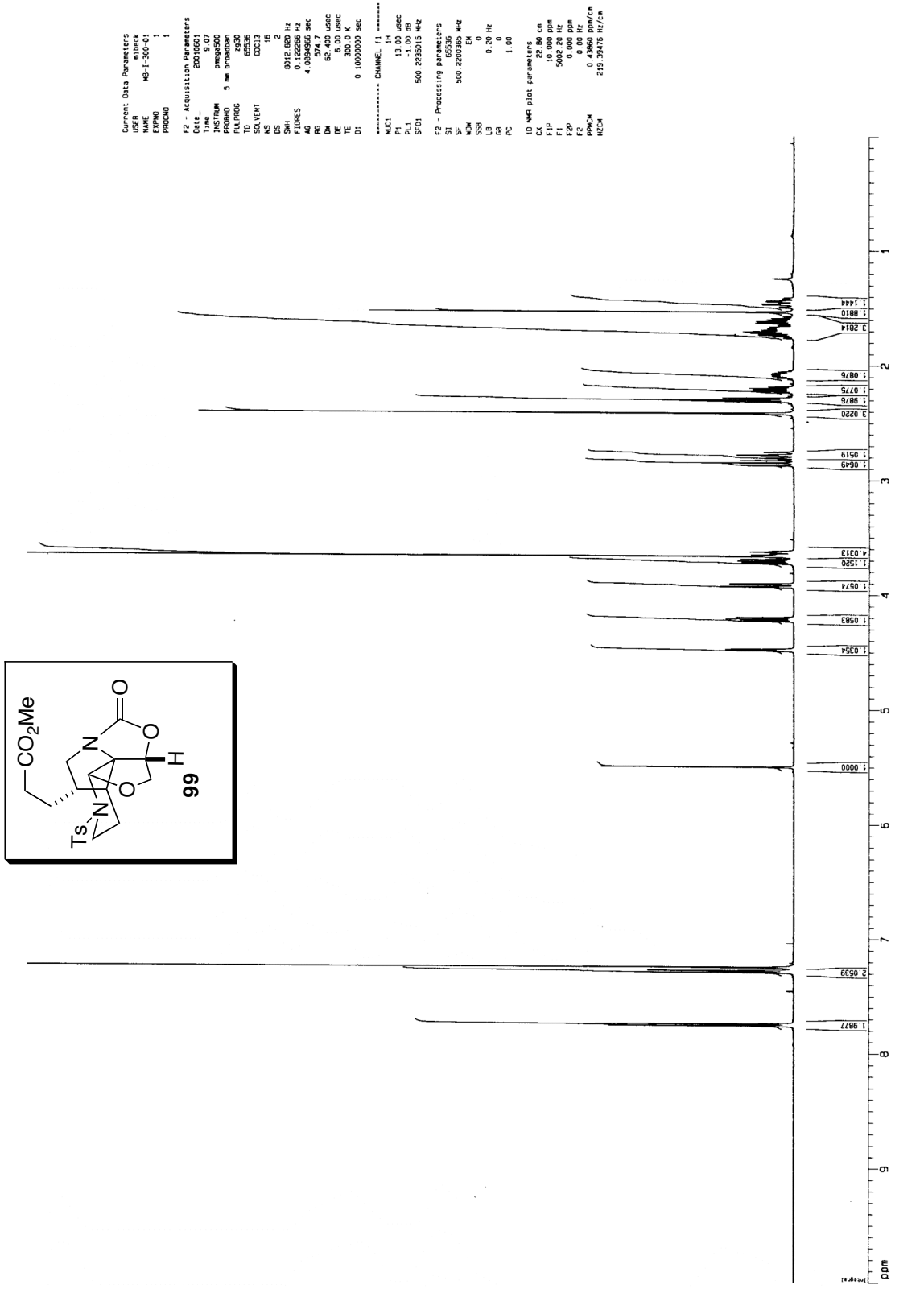
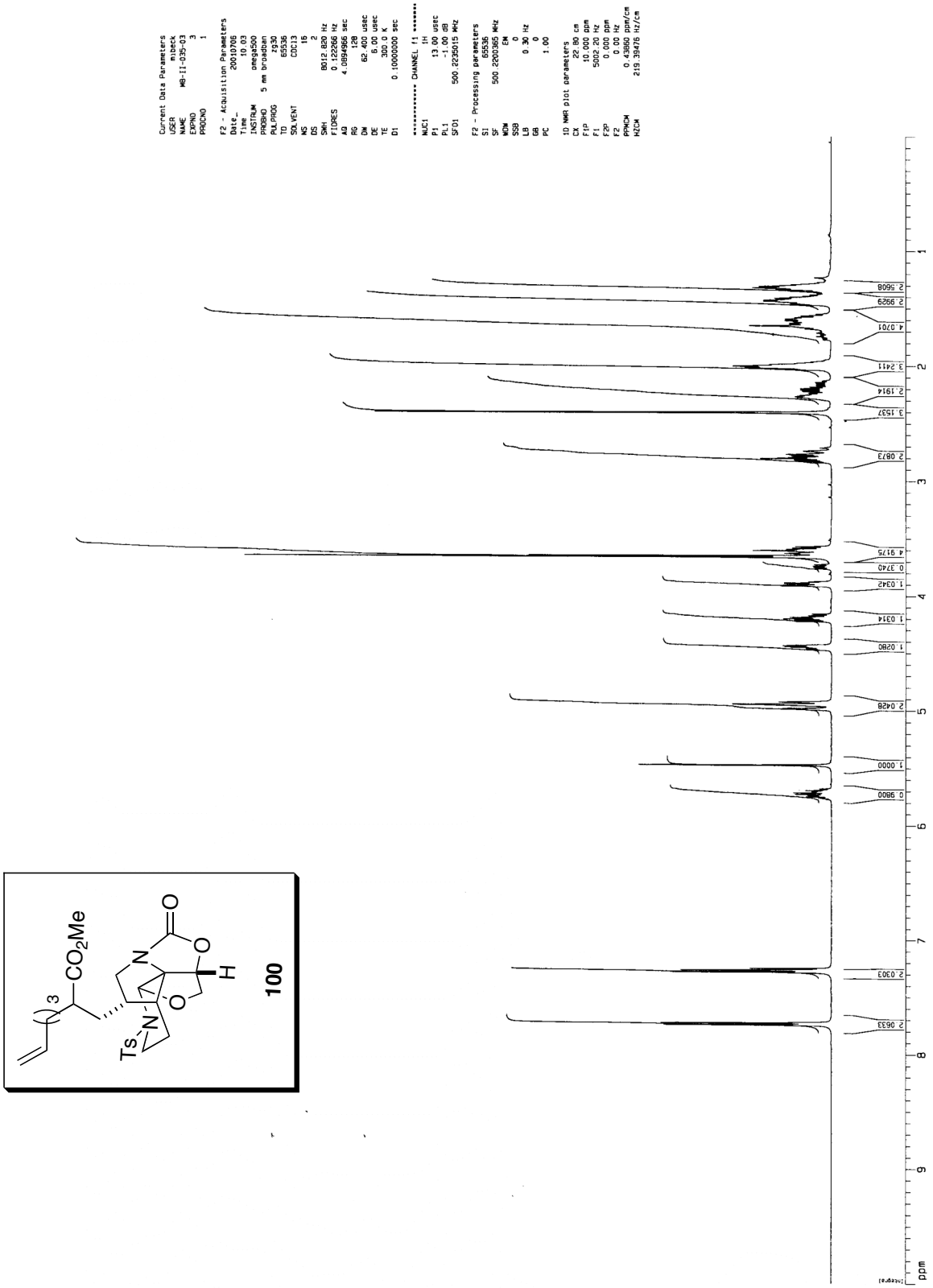
Time 9.02
INSTRUM omega500
PROBHD 5 mm broadban
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894966 sec
RG 512
DW 62.400 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 13.00 usec
PL1 -1.00 dB
SF01 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200387 MHz
WDW EM
SSB 0
LB 0.20 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.43860 ppm/cm
HZCM 219.39476 Hz/cm
1.0477
1.4102
0.9890
3.9869
2.8345
0.9927
0.9906
1.0181
1.0389
1.0149
1.0201
1.0017
1.9959
0.9586
1.0000
1.9124
1.8999
integral
ppm
1
2
3
4
5
6
7
8
9
Ts
N
O
O
O
N
H
87


93
Ts
N
O
H
CH2OH
ppm


CO2Me
Ts
N
O
H
99
Current Data Parameters
USER mlbeck
NAME MG-I-300-01
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20010601
Time 9.07
INSTRUM omega500
PROBHD 5 mm broadban
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894966 sec
RG 574.7
DW 62.400 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
CHANNEL f1
NUC1 1H
P1 13.00 usec
PL1 -1.00 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200365 MHz
WDW EM
SSB 0
LB 0.20 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.43860 ppm/cm
HZCM 219.39476 Hz/cm
1.1444
1.8810
3.2814
1.0876
1.0775
1.9876
3.0220
1.0619
1.0649
4.0313
1.1520
1.0574
1.0583
1.0354
1.0000
2.0539
1.9877
integral
ppm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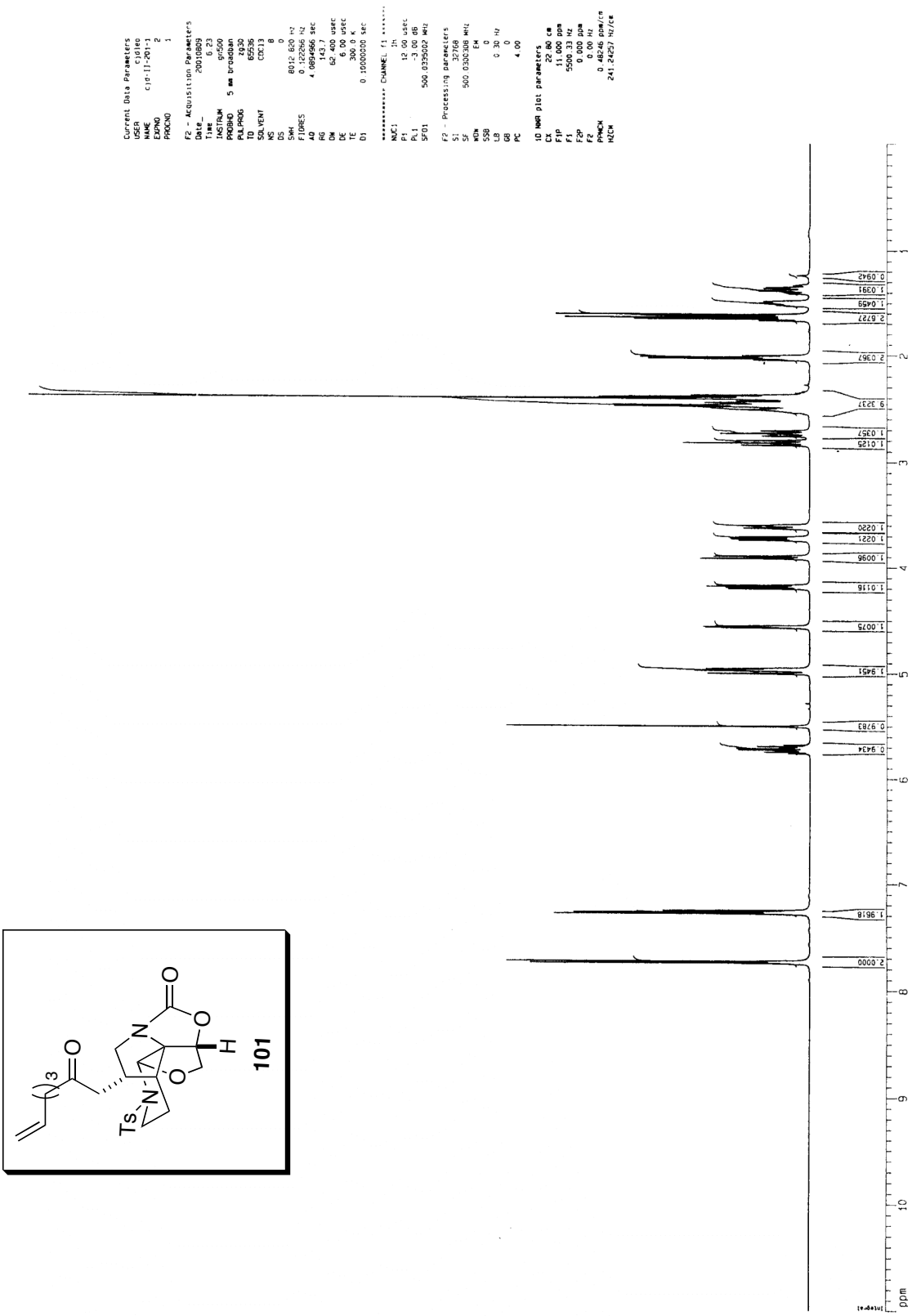
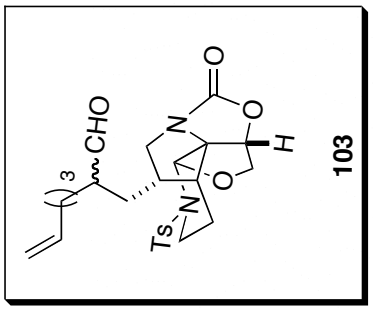
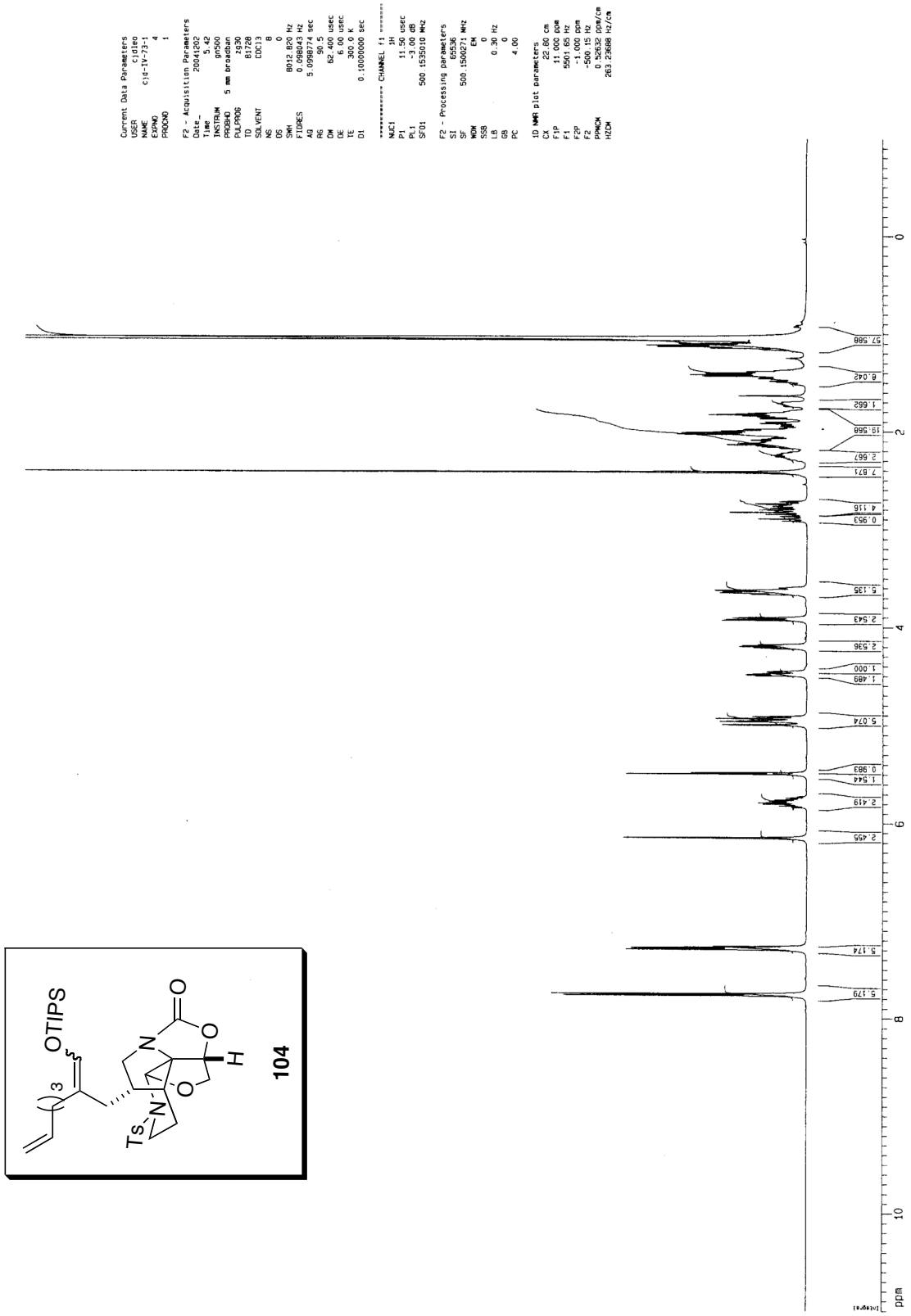
USER mbeck
NAME MB-II-035-03
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20010706
Time 10.03
INSTRUM omega500
PROBHD 5 mm broadban
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894966 sec
RG 128
DW 62.400 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
========== CHANNEL f1 ========
NUC1 1H
P1 13.00 usec
PL1 -1.00 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200365 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.43860 ppm/cm
HZCM 219.39476 Hz/cm
2.0633
2.0303
1.0000
0.9800
2.0428
1.0280
1.0314
1.0342
0.3740
4.9175
2.0873
3.1537
2.1914
3.2411
4.0701
2.9929
2.5608
ppm
Integral

CO2Me
3
Ts
N
O
O
H
100


101
Ts
N
O
H
ppm


CHO
3
N
O
O
H
Ts
N
O
103

Current Data Parameters
USER cidlab
NAME cid-1V-eb-1
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20041203
Time 23.14
INSTRUM omega500
PROBHD 5 mm broadban
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 0
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 128
DW 62.400 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
========== CHANNEL f1 =======
NUC1 1H
P1 13.00 usec
PL1 -1.00 dB
SFO1 500.2335015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200311 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
F1P 11.000 ppm
F1 5502.42 Hz
F2P -1.000 ppm
F2 -500.22 Hz
PPMCM 0.52632 ppm/cm
HZCM 263.27371 Hz/cm
2.158
14.173
8.256
2.065
9.307
6.171
9.505
2.983
3.221
4.151
1.944
3.003
3.034
2.861
5.925
2.877
2.898
5.951
6.044
1.799
1.000
integral
ppm
0
2
4
6
8
10


OTIPS
3
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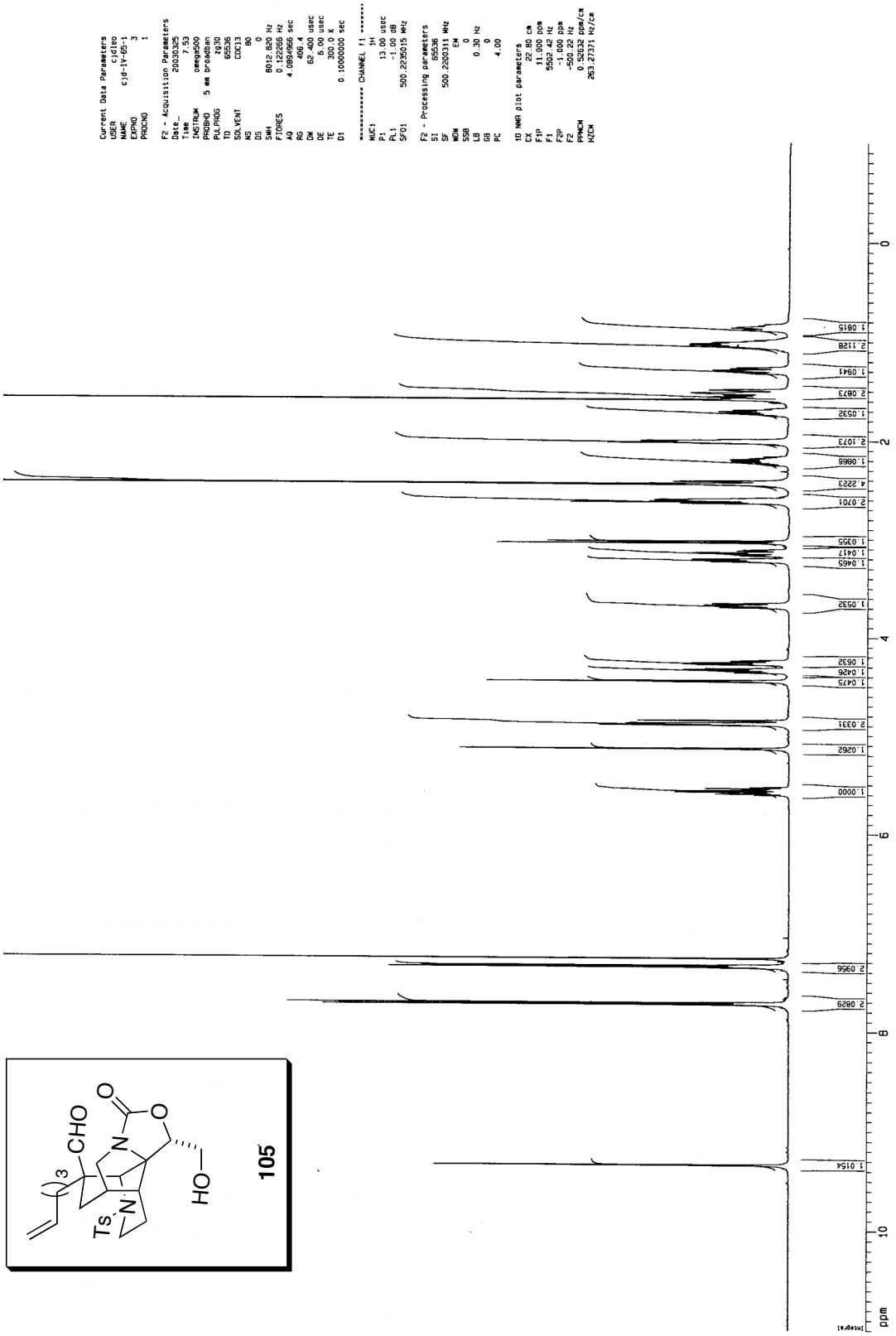
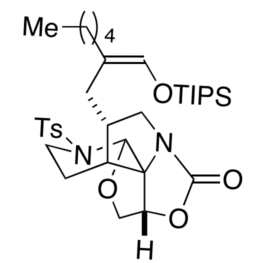
O
O
H
Ts
N
O
104
Current Data Parameters
USER cjdieo
NAME cjd-IV-73-1
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20041202
Time 5.42
INSTRUM gn500
PROBHD 5 mm broadban
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 0
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 90.5
DW 62.400 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -3.00 dB
SFO1 500.1535010 MHz
F2 - Processing parameters
SI 65536
SF 500.1500271 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 11.000 cm
F1P 5501.65 Hz
F1 -1.000 ppm
F2P -500.15 Hz
F2 0.52632 ppm/cm
PPMCM
HZCM 263.23688 Hz/cm
7.580
8.042
1.662
19.566
2.667
7.871
4.116
0.953
5.135
2.543
2.536
1.000
1.489
5.074
0.983
1.544
2.419
2.455
5.174
5.179
ppm


105
Ts
CHO
HO
ppm



(*Z*)-107

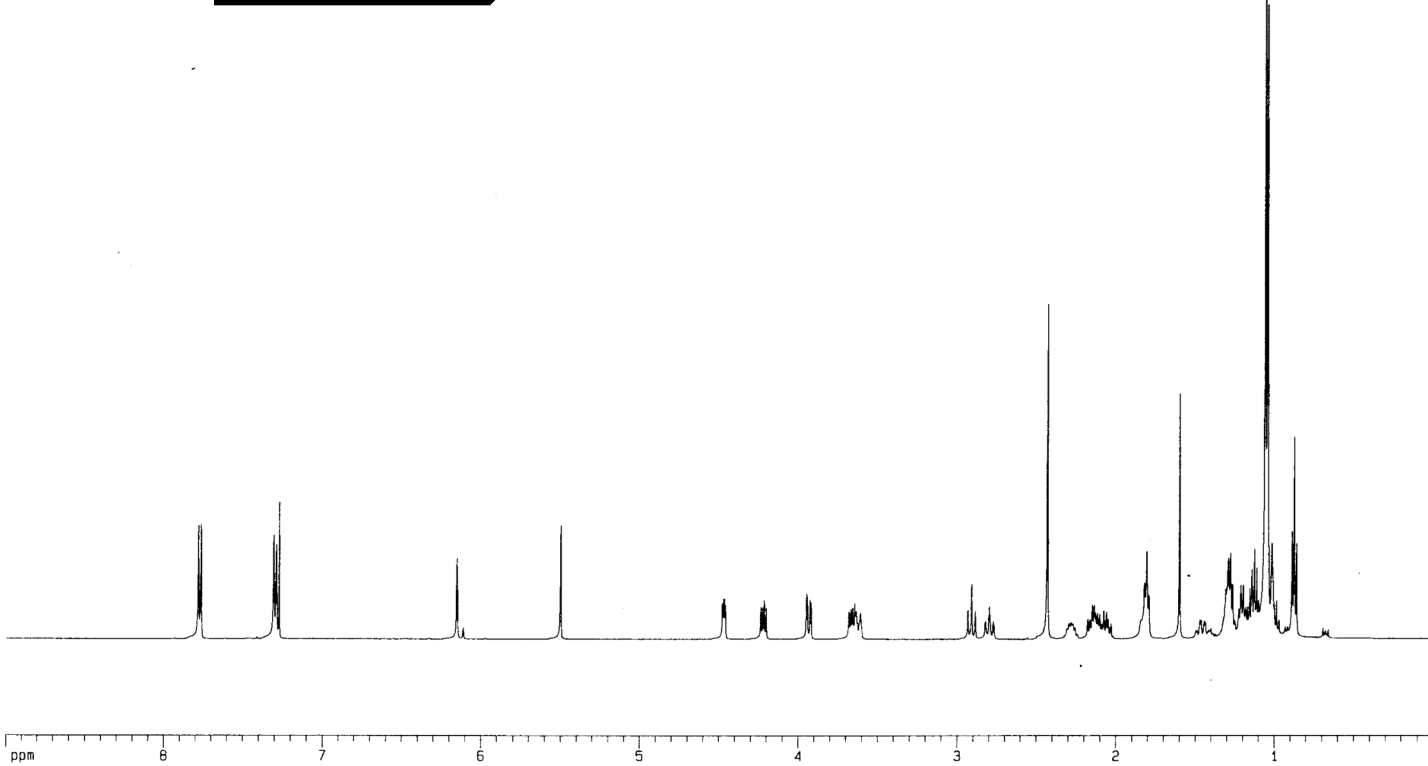
Current Data Parameters
USER nkgarg
NAME nkg-ii-102-a
EXPNO 2
PROCNO 1

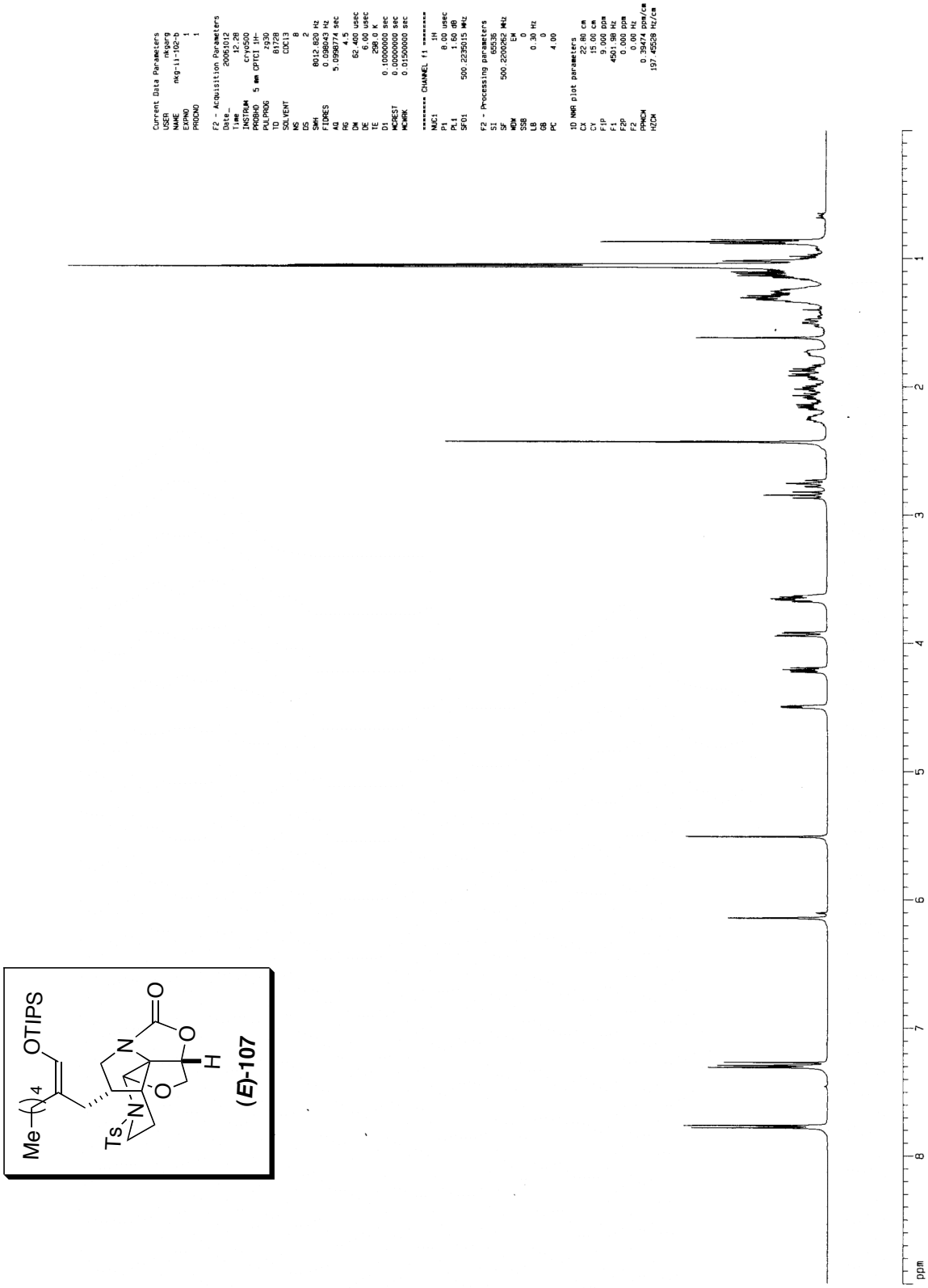
F2 - Acquisition Parameters
Date_ 20061012
Time 11.32
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 7
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 5
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

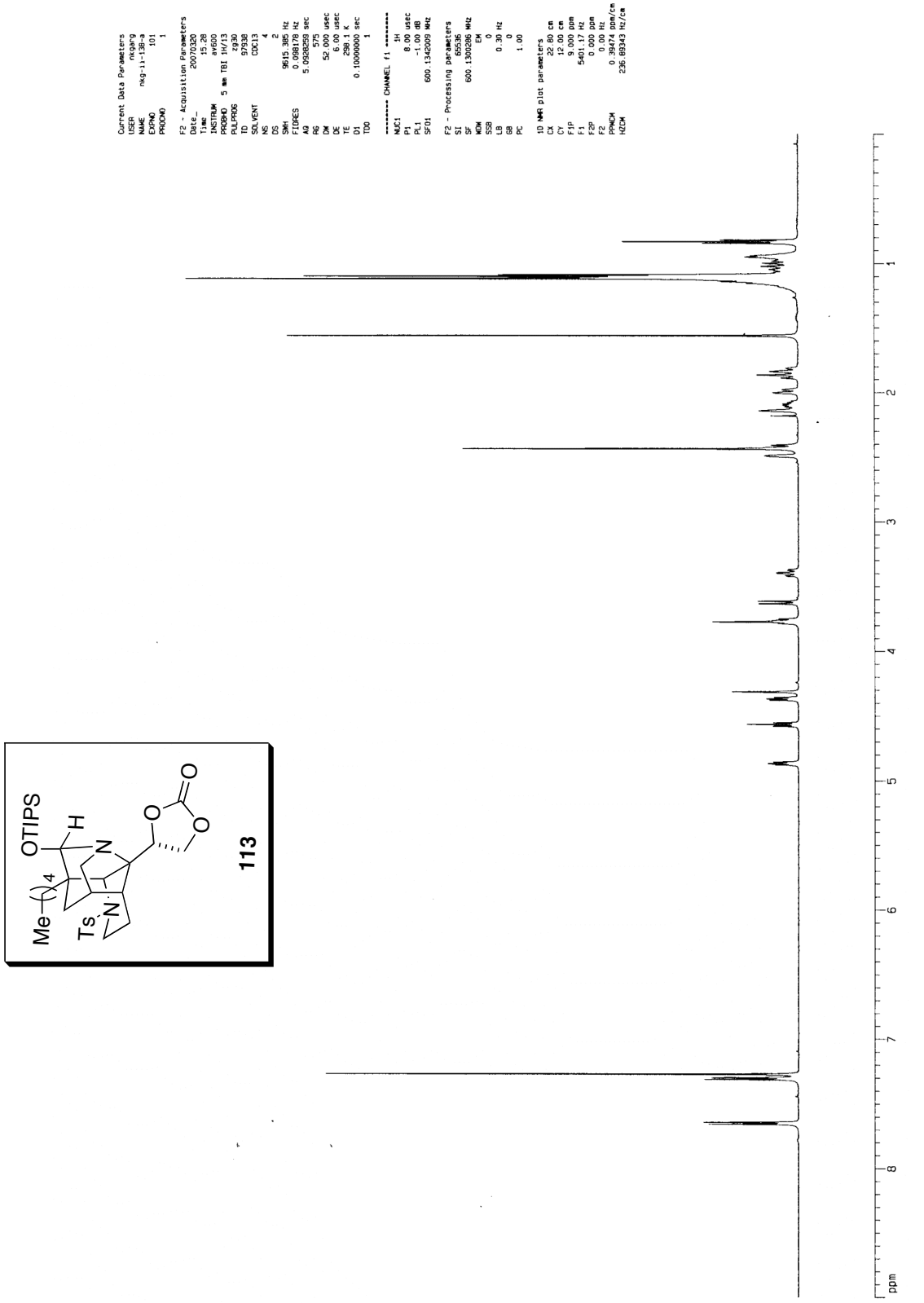
======== CHANNEL f1 ========
NUC1 1H
P1 8.00 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

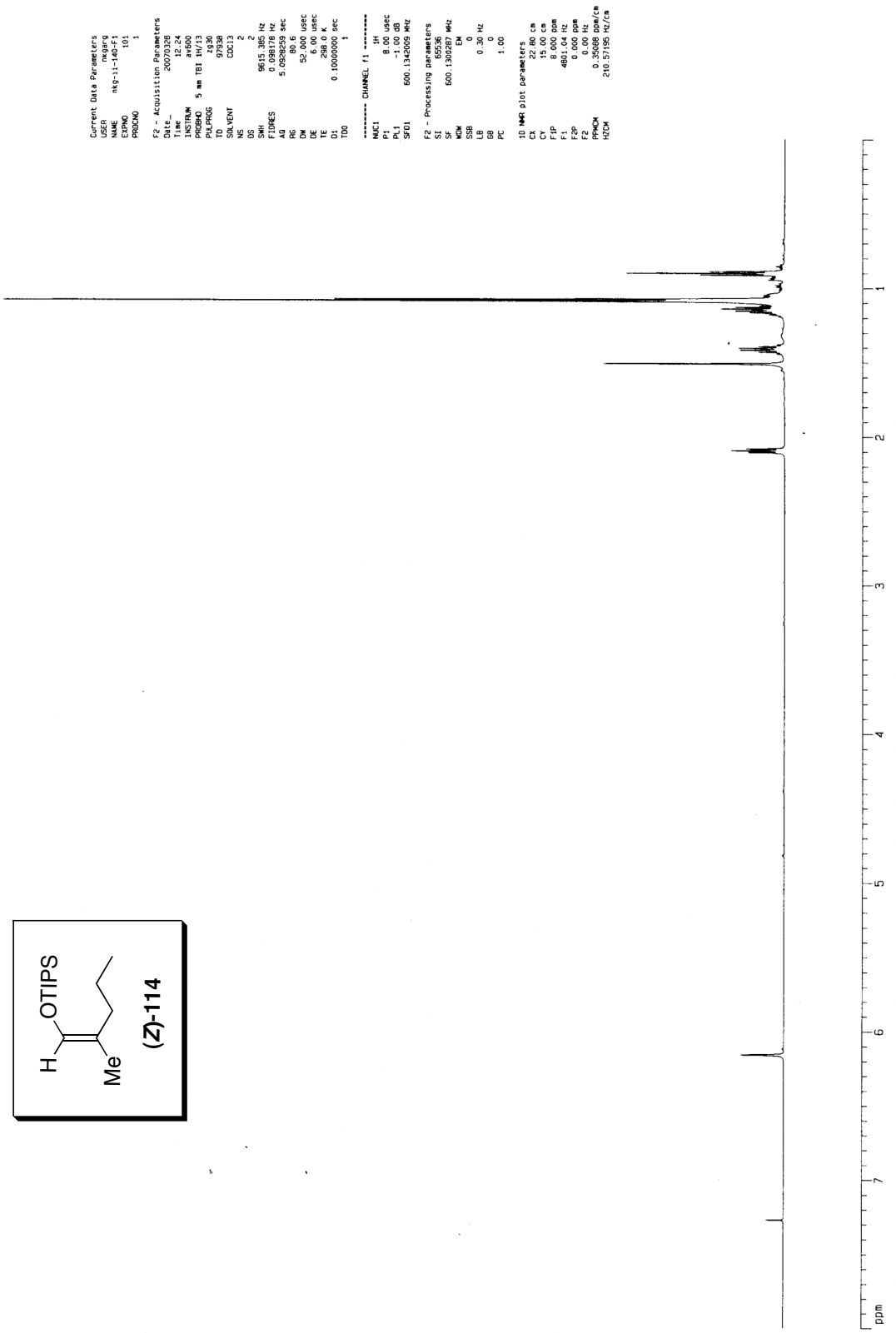
F2 - Processing parameters
SI 65536
SF 500.2200262 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00

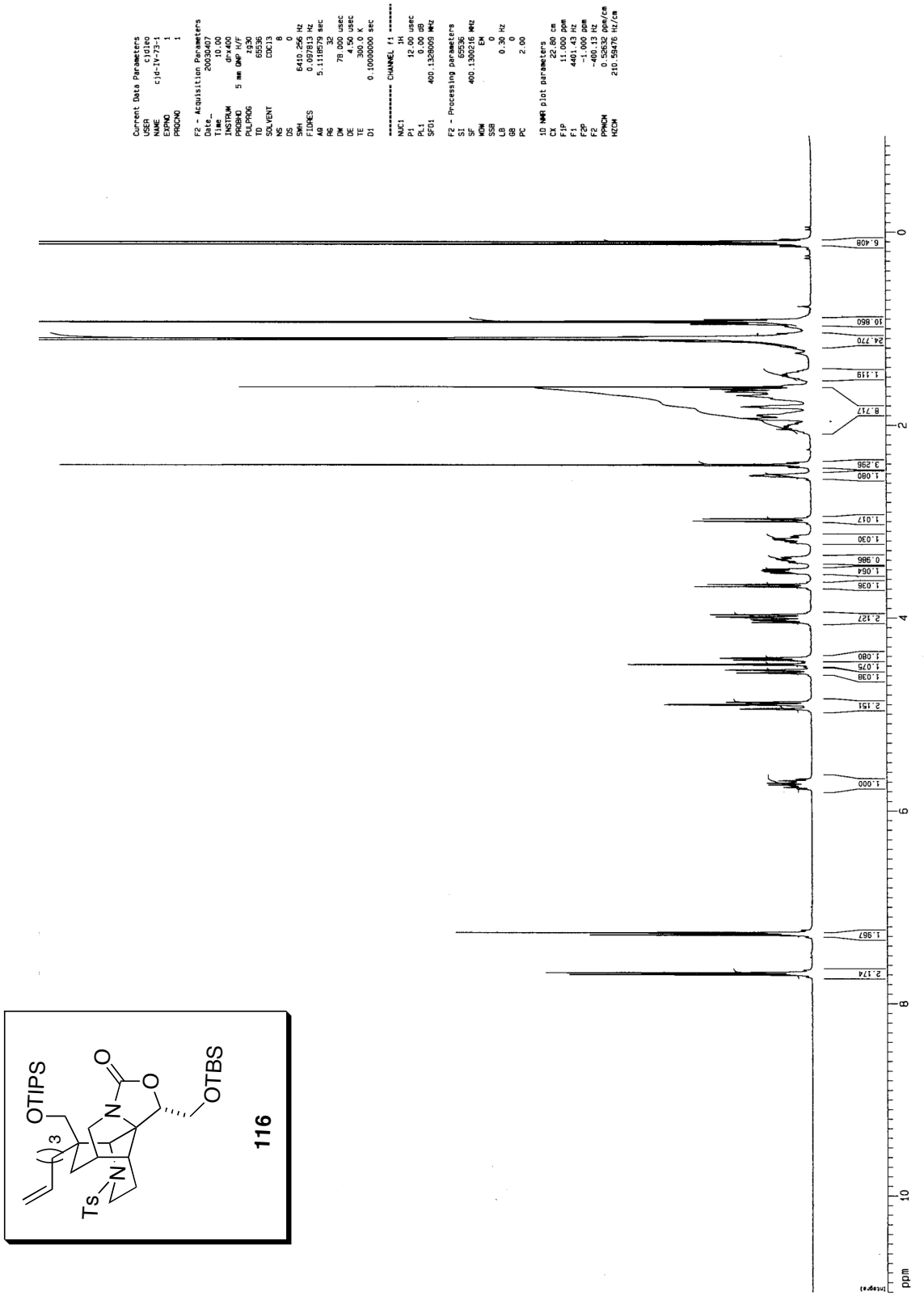
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 4501.98 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.39474 ppm/cm
HZCM 197.45528 Hz/cm

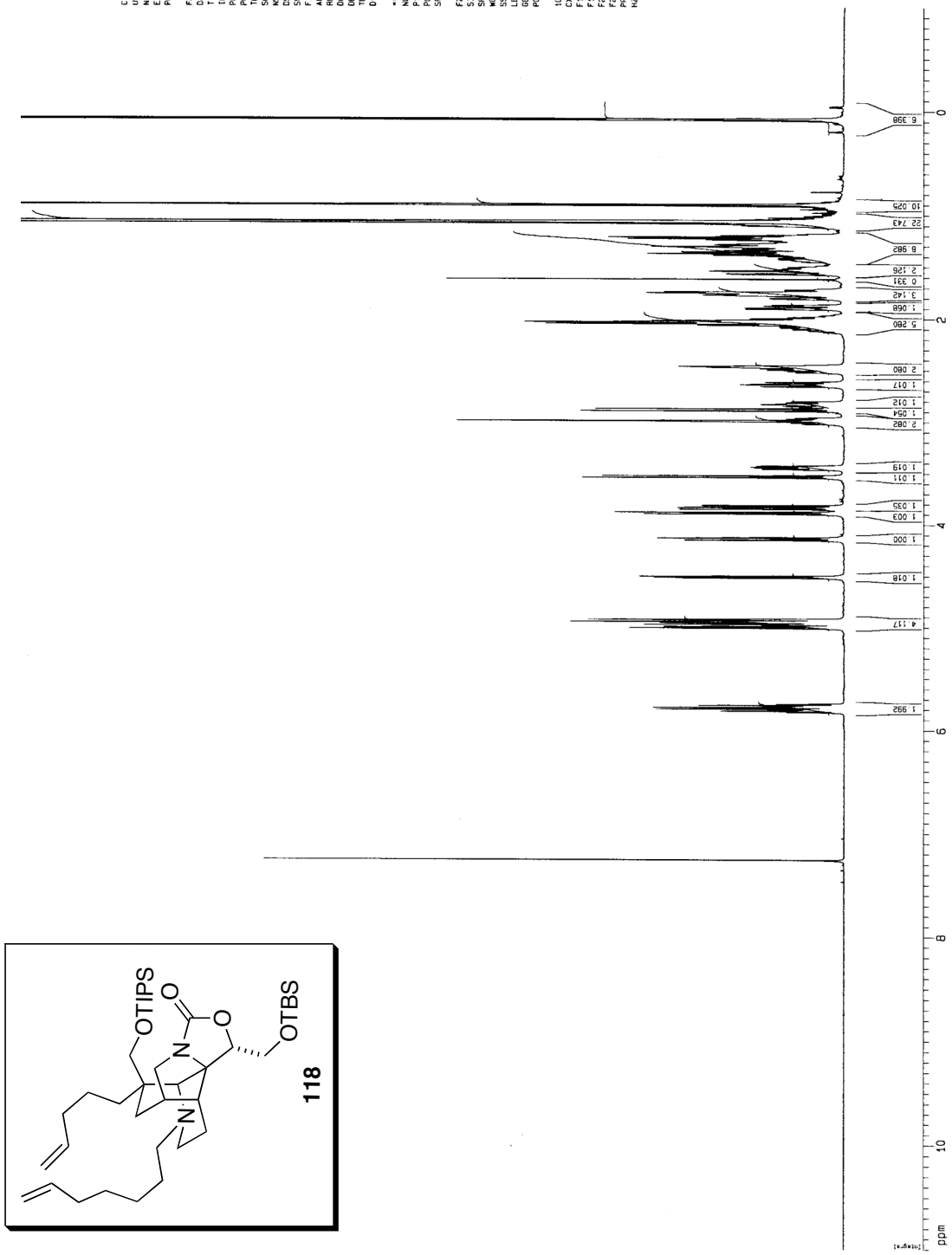


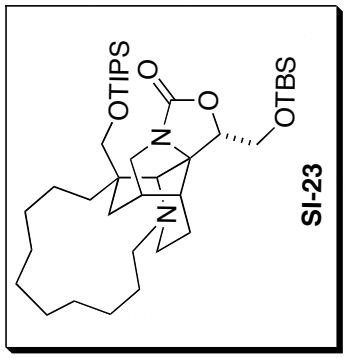

Me
4
OTIPS
Ts
N
O
O
H
(E)-107
ppm
1
2
3
4
5
6
7
8


OTIPS
H
N
O
O
O
Me
4
Ts
N
113
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm


H
OTIPS
Me
(Z)-114
ppm

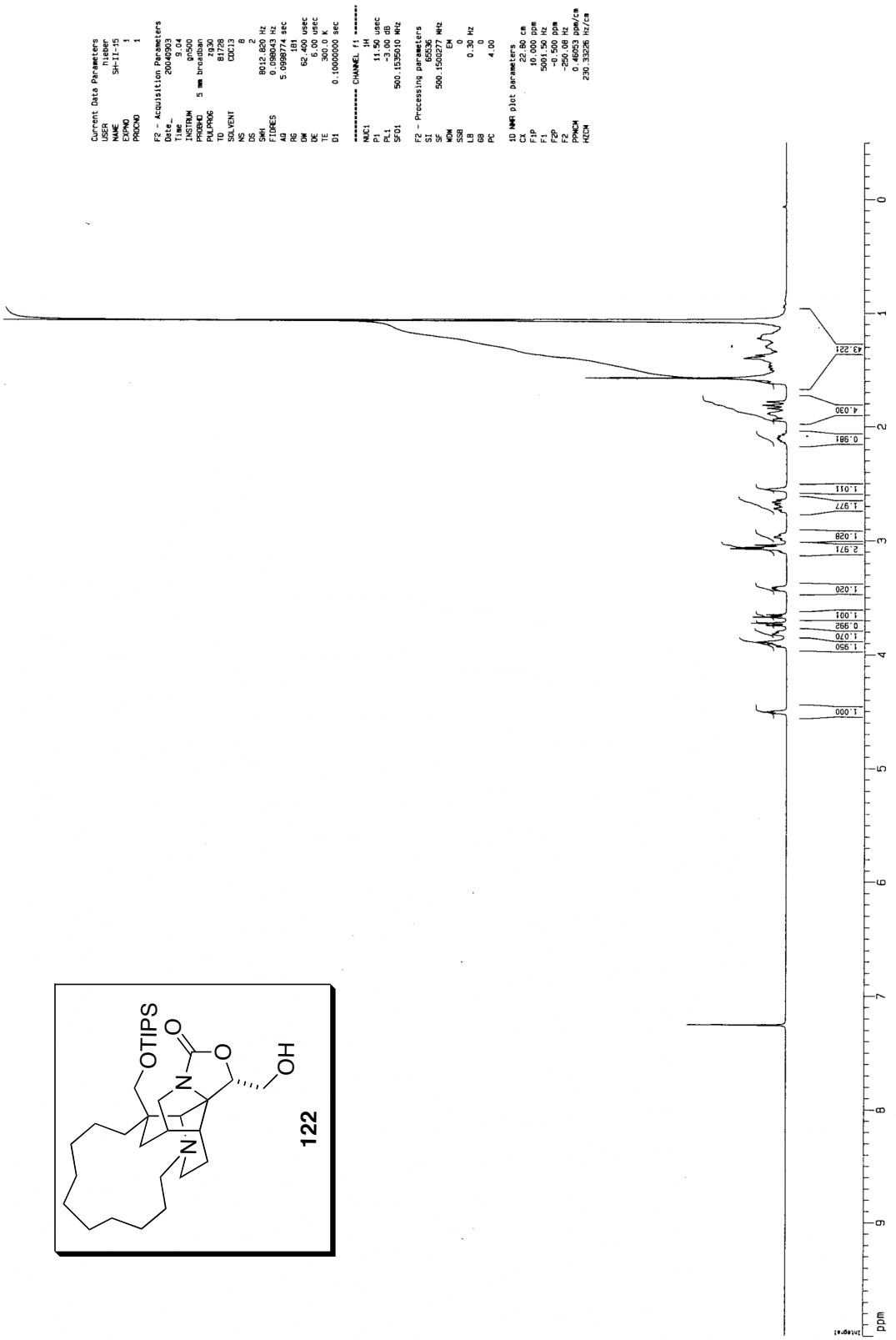

OTIPS
OTBS
Ts
116
ppm


OTIPS
OTBS
118
ppm


OTIPS
O
O
N
N
OTBS

SI-23

Current Data Parameters
USER cjdieo
NAME cjd-IV-83-1
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20030421
Time 21.43
INSTRUM gn500
PROBHD 5 mm broadban
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 0
SWH 8012.820 Hz
FIDRES 0.122256 Hz
AQ 4.0894965 sec
RG 181
DW 62.400 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
========== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -3.00 dB
SFO1 499.9334995 MHz
F2 - Processing parameters
SI 65536
SF 499.9300295 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
F1P 11.000 ppm
F1 5499.23 Hz
F2P -1.000 ppm
F2 -499.93 Hz
PPMCM 0.52632 ppm/cm
HZCM 263.12105 Hz/cm
6.378
10.015
23.902
20.632
1.100
2.119
1.132
1.042
2.058
3.106
1.048
1.047
1.033
1.015
1.038
1.025
1.000
ppm


OTIPS
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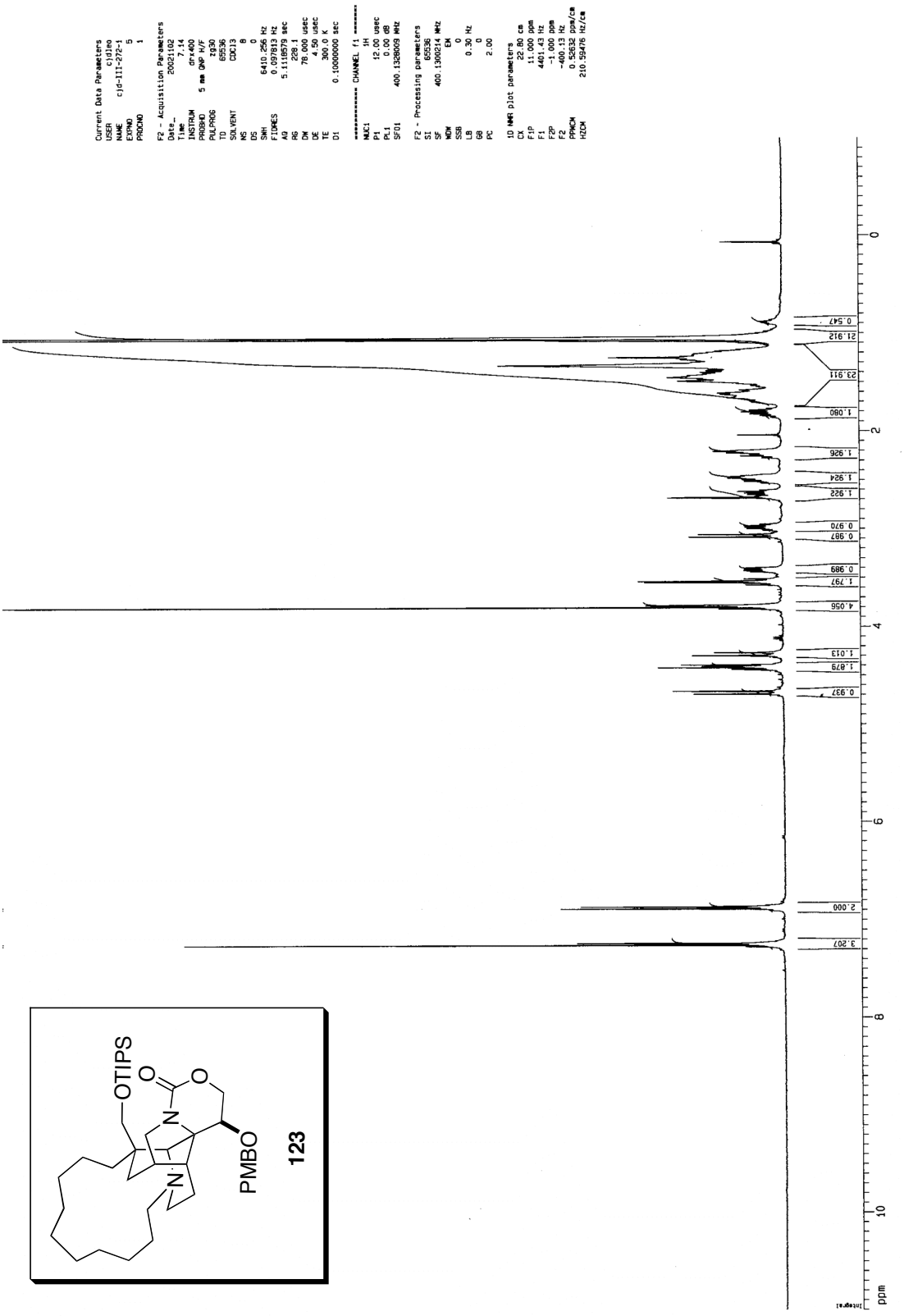
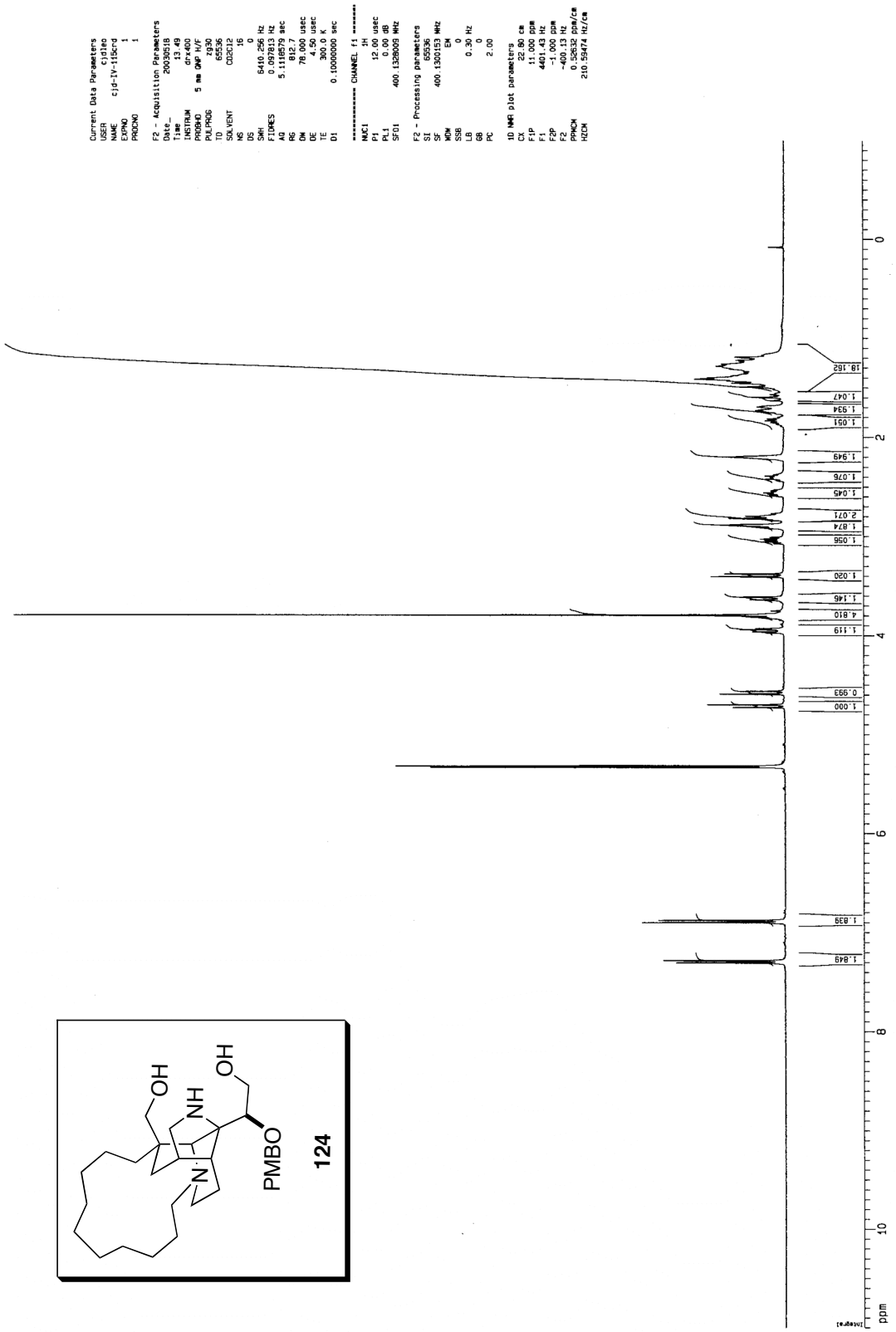
O
N
N
OH
122
Current Data Parameters
USER Tieber
NAME SH-II-15
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20040903
Time 9.04
INSTRUM gn500
PROBHD 5 mm broadban
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 181
DW 62.400 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
------------ CHANNEL f1 -------
NUC1 1H
P1 11.50 usec
PL1 -3.00 dB
SFO1 500.1335010 MHz
F2 - Processing parameters
SI 65536
SF 500.1500277 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
F1P 10.000 ppm
F1 5001.50 Hz
F2P -0.500 ppm
F2 -250.08 Hz
PPMCM 0.46053 ppm/cm
HZCM 230.33226 Hz/cm
43.221
4.030
0.981
1.011
1.977
1.028
2.971
1.020
0.992
1.001
1.070
1.950
1.000
ppm


OTIPS
O
O
N
N
PMBO
123
Current Data Parameters
USER cjdieo
NAME cjd-III-27Z-1
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20021102
Time 7.14
INSTRUM drx400
PROBHD 5 mm QNP H/F
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 0
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118579 sec
RG 228.1
DW 78.000 usec
DE 4.50 usec
TE 300.0 K
D1 0.10000000 sec
---------- CHANNEL f1 ----------
NUC1 1H
P1 12.00 usec
PL1 0.00 dB
SFO1 400.1308009 MHz
F2 - Processing parameters
SI 65536
SF 400.1300214 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.86 cm
F1P 11.000 ppm
F1 4401.43 Hz
F2P -1.000 ppm
F2 -400.13 Hz
PPMCM 0.52632 ppm/cm
HZCM 210.59476 Hz/cm
0.547
21.912
23.911
1.080
1.926
1.924
1.922
0.970
0.987
0.989
1.797
4.056
1.013
1.079
0.937
2.000
3.207
ppm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USER cjdleo
NAME cjd-IV-115crd
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20030518
Time 13.49
INSTRUM dpx400
PROBHD 5 mm CMP H/F
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 0
SWH 6410.256 Hz
FIDRES 0.097813 Hz
AQ 5.1118079 sec
RG 812.7
DW 78.000 usec
DE 4.50 usec
TE 300.0 K
D1 0.10000000 sec
========== CHANNEL f1 ======
NUC1 1H
P1 12.00 usec
PL1 0.00 dB
SFO1 400.1328005 MHz
F2 - Processing parameters
SI 65536
SF 400.1300153 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
F1P 11.000 ppm
F1 4401.43 Hz
F2P -1.000 ppm
F2 -400.13 Hz
PPMCM 0.58632 ppm/cm
HZCM 210.59474 Hz/cm
18.162
1.047
1.934
1.051
1.949
1.076
1.045
2.071
1.874
1.056
1.020
1.146
4.810
1.119
0.993
1.000
1.839
1.849
integral
ppm
0
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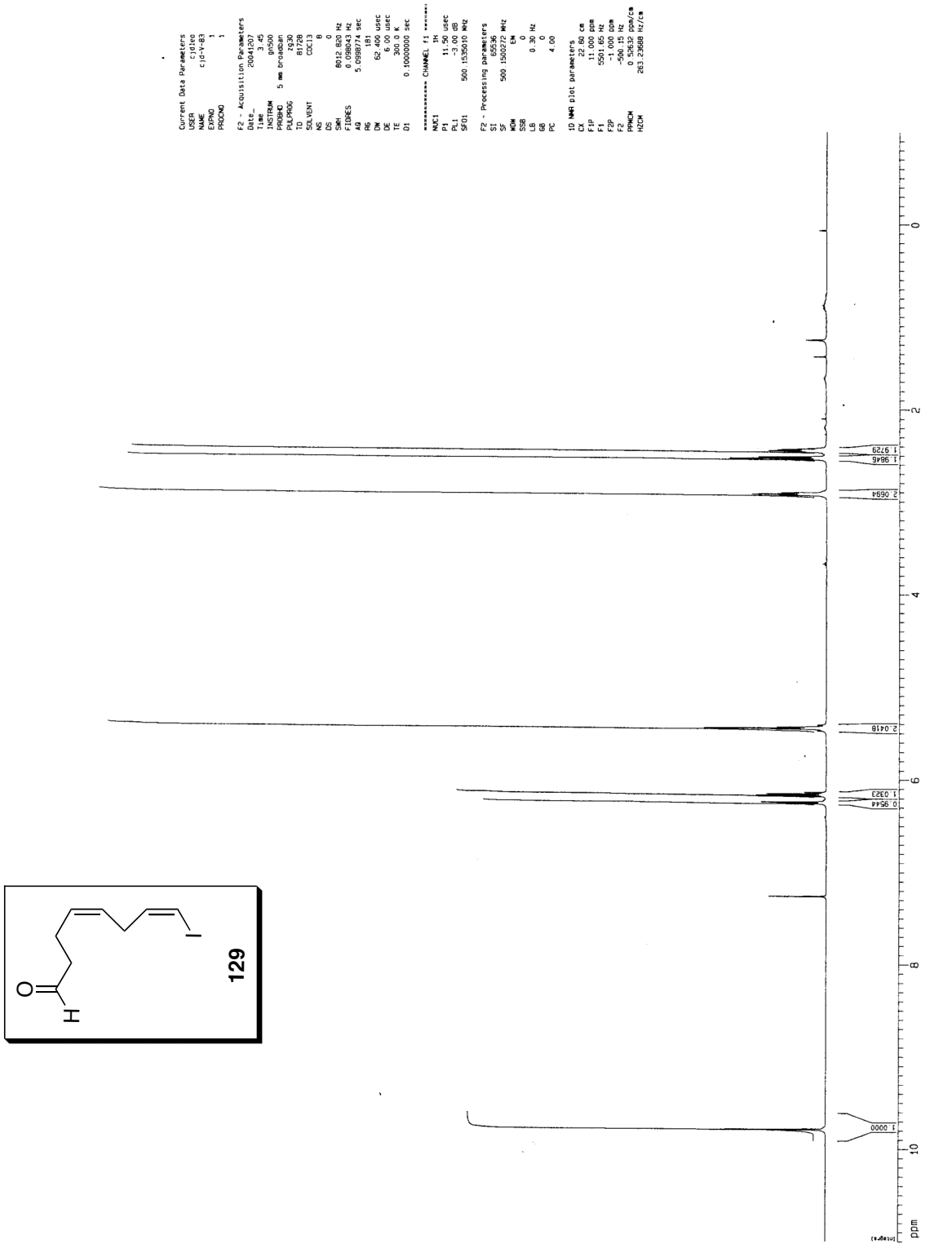
4
6
8
10
OH
NH
OH
N
PMBO
124


129
Current Data Parameters
USER cidiwo
NAME cid-V-83
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20041207
Time 3.45
INSTRUM gn500
PROBHD 5 mm broadban
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 0
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 181
DW 62.400 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
========== CHANNEL f1 ==========
NUC1 1H
P1 11.50 usec
PL1 -3.00 dB
SFO1 500.1535010 MHz
F2 - Processing parameters
SI 65536
SF 500.1500222 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
F1P 11.000 ppm
F1 5501.65 Hz
F2P -1.000 ppm
F2 -500.15 Hz
PPMCM 0.95625 ppm/cm
HZCM 263.23688 Hz/cm
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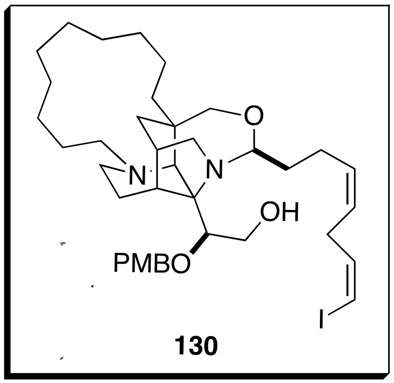
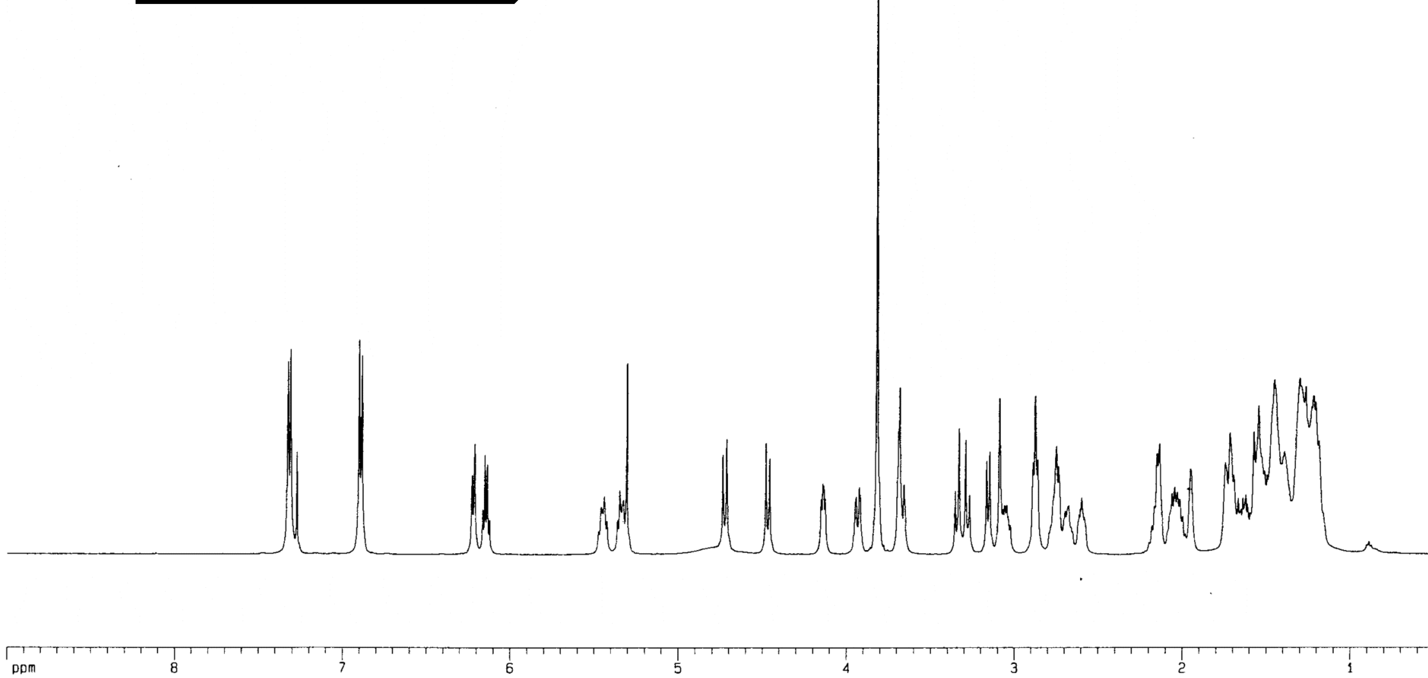
1.9846
2.0694
2.0418
1.0323
0.9544
1.0000
ppm





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NAME SH-I-214
EXPNO 6
PROCNO 1

F2 - Acquisition Parameters
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Time 17.27
INSTRUM gn500
PROBHD 5 mm broadban
PULPROG zg30
TD 81728
SOLVENT CDC13T
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 90.5
DW 62.400 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec

============ CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -3.00 dB
SFO1 500.1535010 MHz

F2 - Processing parameters
SI 65536
SF 500.1500222 MHz
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SSB 0
LB 0.30 Hz
GB 0
PC 4.00

1D NMR plot parameters
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CY 12.00 cm
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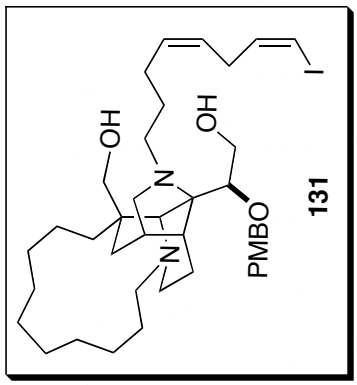
F2P 0.500 ppm
F2 250.08 Hz
PPMCM 0.37281 ppm/cm
HZCM 186.45944 Hz/cm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N
OH
PMBO
I
131

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NAME SH-I-295
EXPNO 3
PROCNO 1
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Time 19.51
INSTRUM omega500
PROBHD 5 mm broadban
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 128
DW 62.400 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
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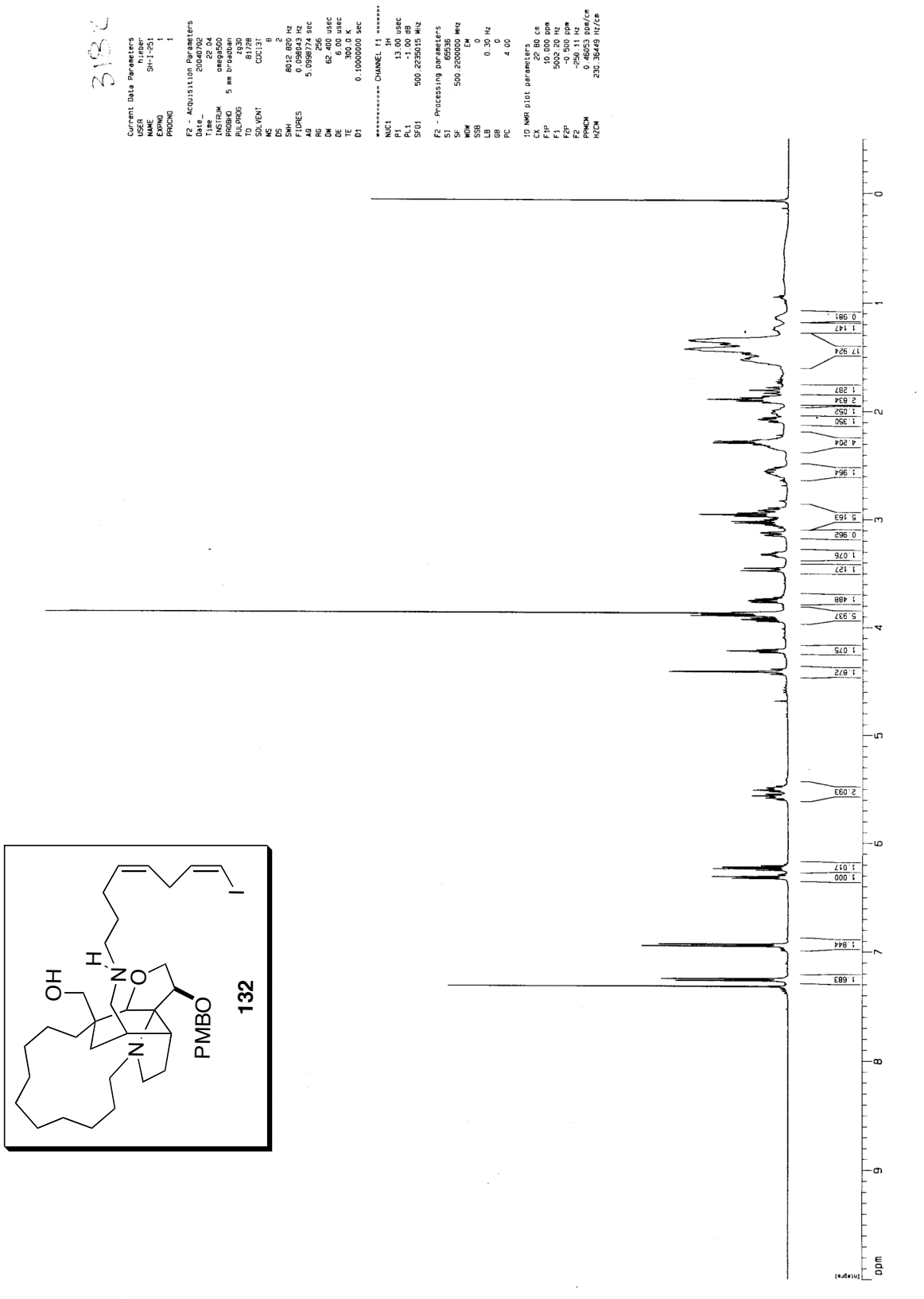
NUC1 1H
P1 13.00 usec
PL1 -1.00 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.46053 ppm/cm
HZCM 230.36449 Hz/cm
23.666
3.250
3.283
2.074
4.472
5.175
2.124
1.063
1.026
4.262
0.947
1.018
1.000
1.129
2.090
0.990
0.990
2.103
2.824
ppm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H
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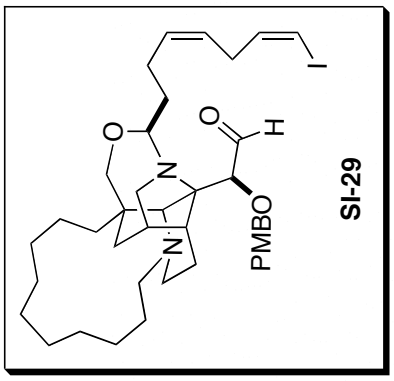
O
N
PMBO
I
132
ppm


PMBO
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N
O
H
I

SI-29

Current Data Parameters
USER megang
NAME SH-II-216
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20050527
Time 15.57.08
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098641 Hz
AQ 5.0998774 sec
RG 32
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00500000 sec
MCWRK 0.01500000 sec
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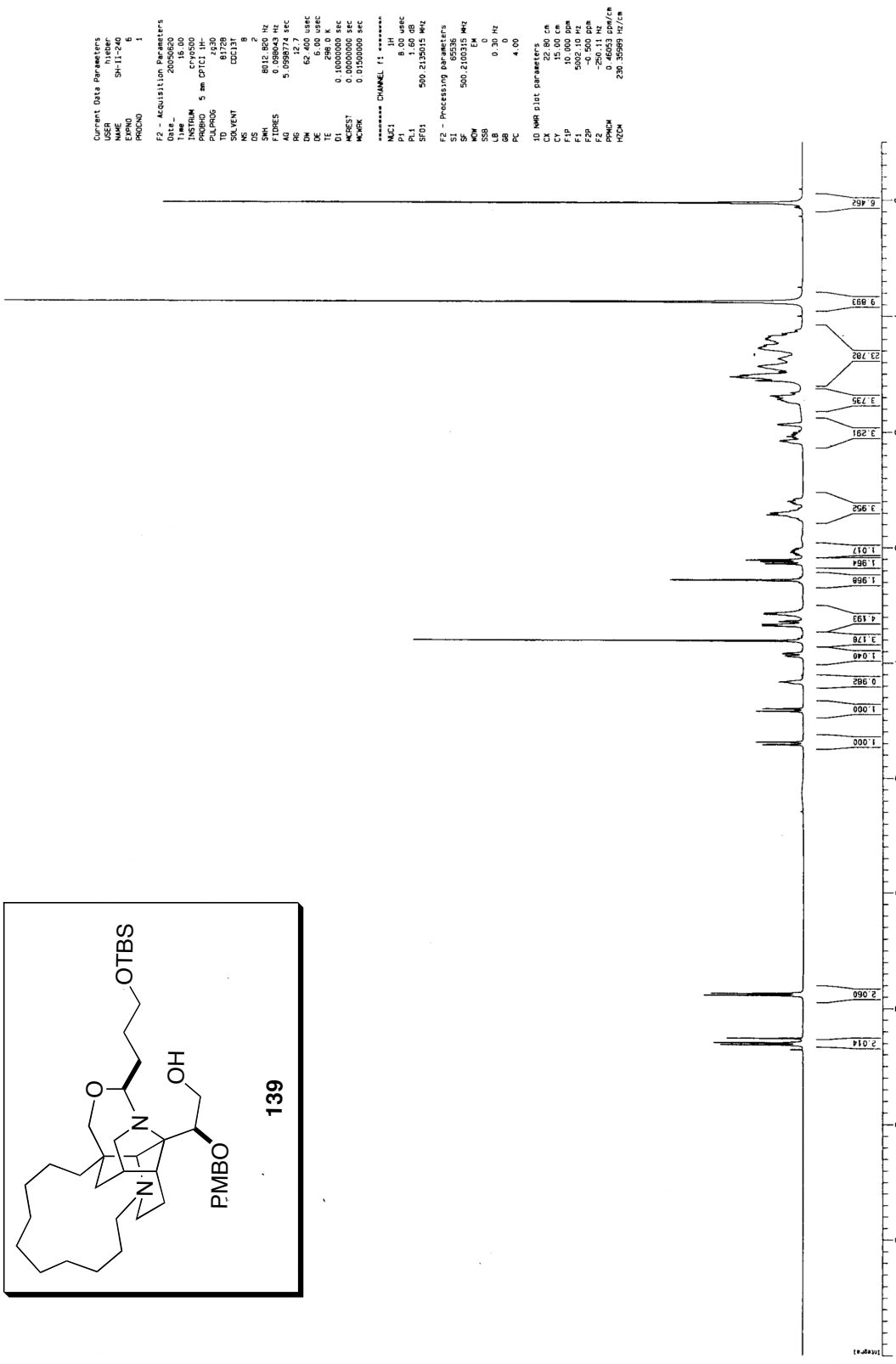
NUC1 1H
P1 8.00 usec
PL1 1.60 dB
SFO1 500.2135015 MHz
F2 - Processing parameters
SI 65536
SF 500.2100269 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 8.00 cm
F1P 10.000 ppm
F1 5002.10 Hz
F2P 0.500 ppm
F2 250.11 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.42665 Hz/cm
ppm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PMBO
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N
O
139
Current Data Parameters
USER hieber
NAME SH-II-240
EXPNO 6
PROCNO 1
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Date_ 20050620
Time 16.00
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 6.50 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 8.00 usec
PL1 1.00 dB
SFO1 500.2135015 MHz
F2 - Processing parameters
SI 65536
SF 500.2100315 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 10.000 ppm
F1 5002.14 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.46053 ppm/cm
HZCM 230.35989 Hz/cm
6.462
9.883
23.782
3.735
3.291
3.952
1.017
1.964
1.966
4.193
3.178
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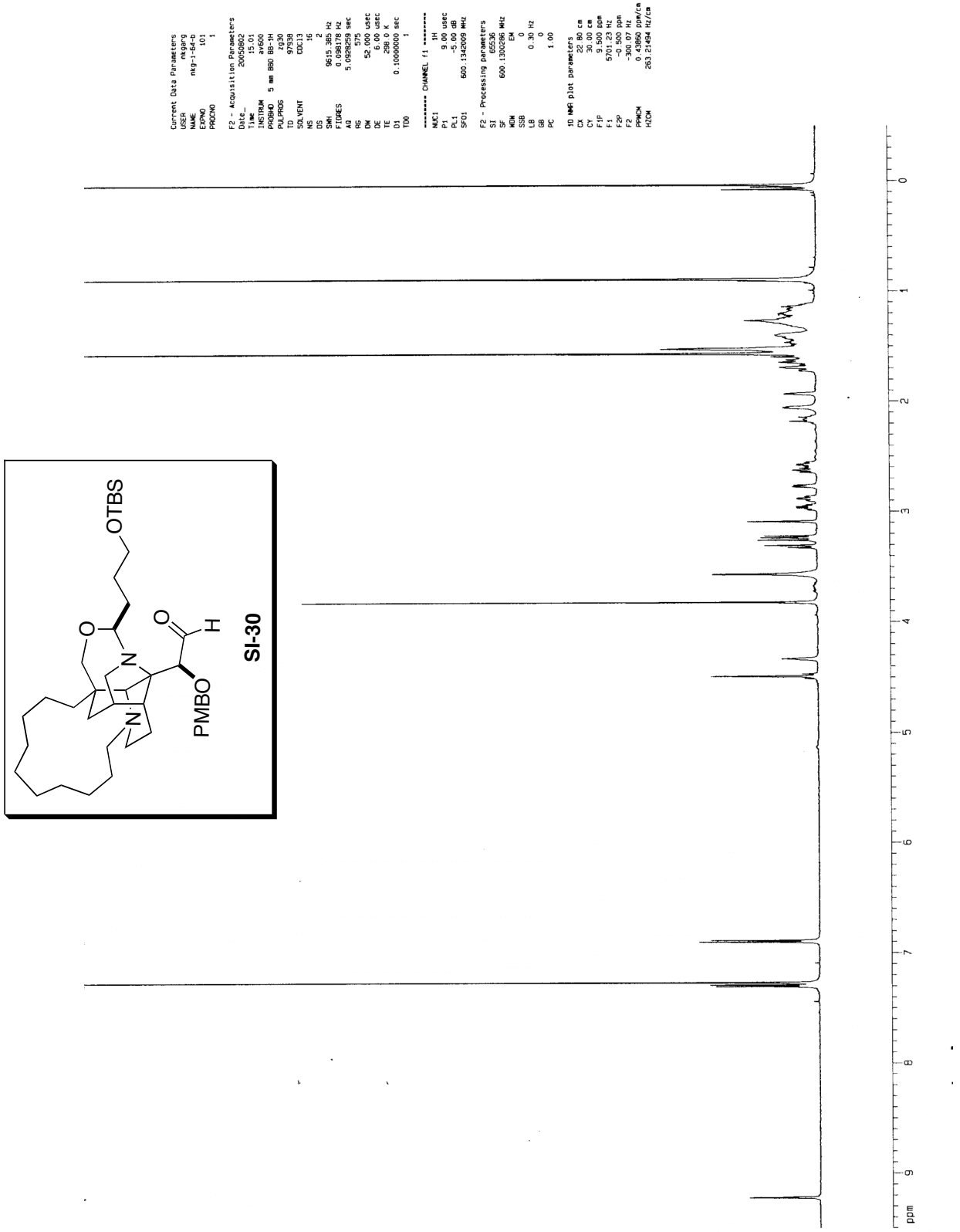
0.982
1.000
1.000
2.060
2.014
ppm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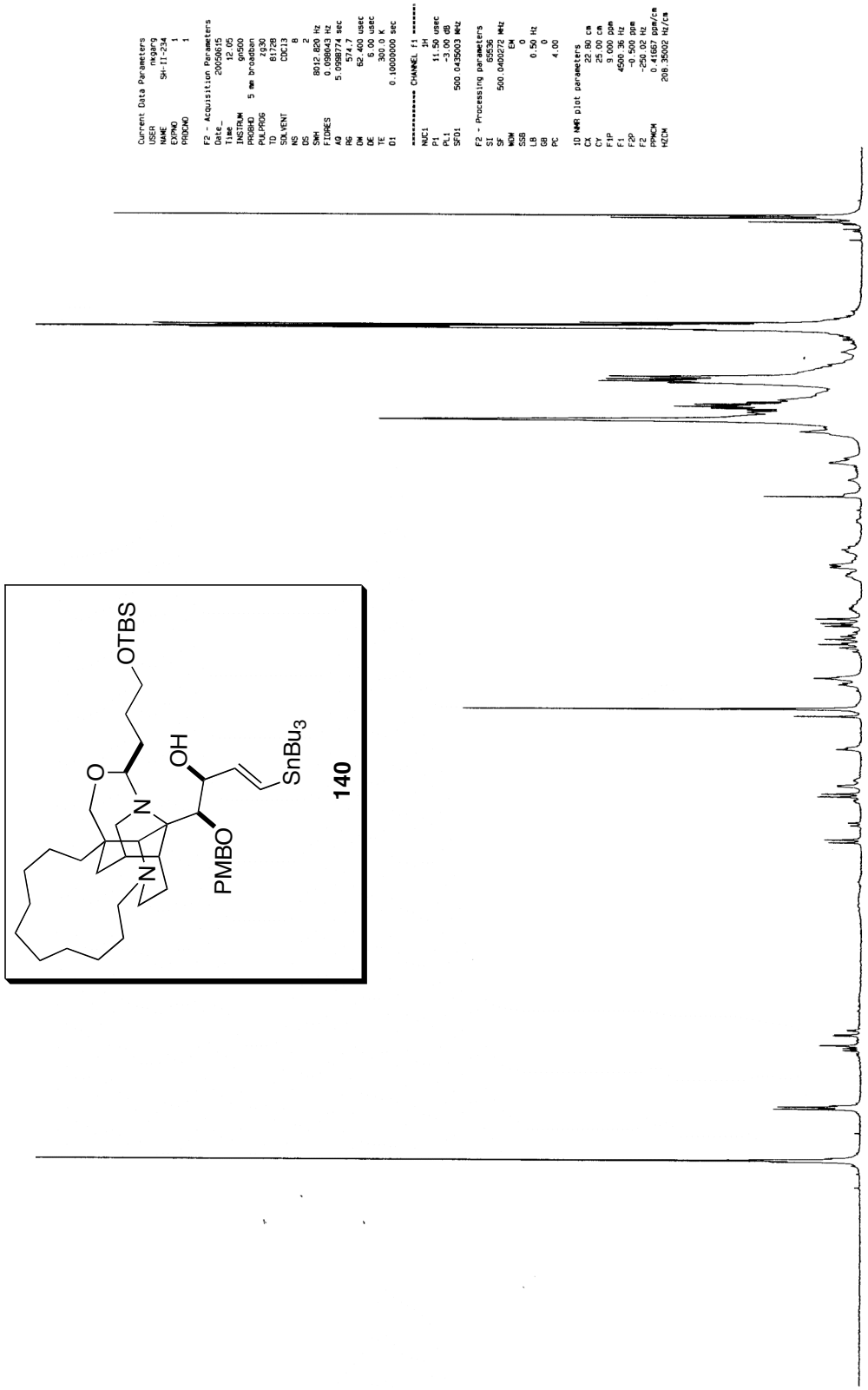
N
N
O
H
PMBO
SI-30
Current Data Parameters
USER nkgarg
NAME nkg-1-64-b
EXPNO 101
PROCNO 1
F2 - Acquisition Parameters
Date_ 20050602
Time 15.01
INSTRUM av600
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 97938
SOLVENT CDCl3
NS 16
DS 2
SWH 9615.385 Hz
FIDRES 0.098178 Hz
AQ 5.0928259 sec
RG 575
DW 52.000 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -5.00 dB
SFO1 600.1342009 MHz
F2 - Processing parameters
SI 65536
SF 600.1300298 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 30.00 cm
F1P 9.500 ppm
F1 5701.23 Hz
F2P -0.500 ppm
F2 -300.07 Hz
PPMCM 0.43860 ppm/cm
HZCM 263.21494 Hz/cm
ppm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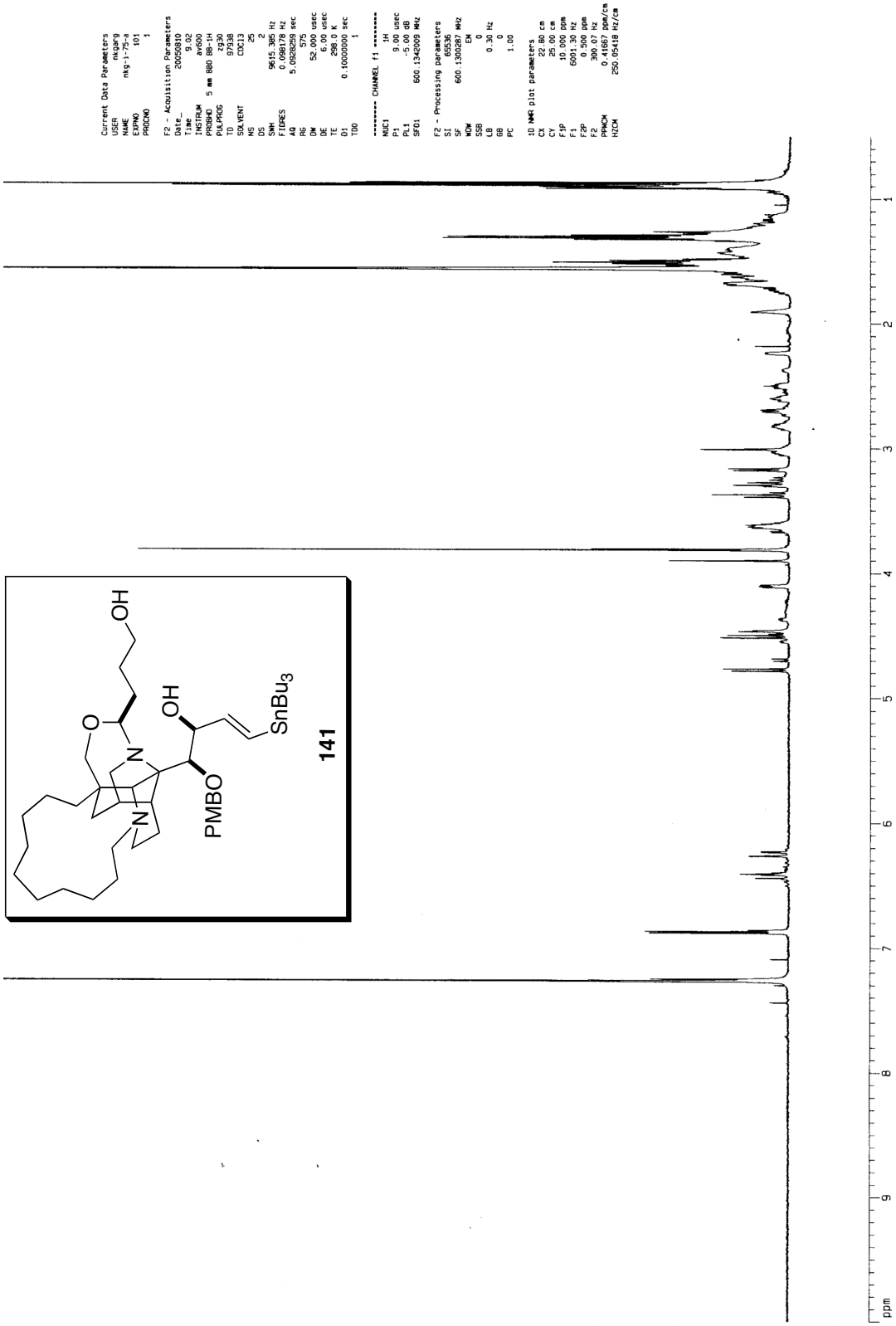
O
N
N
OH
SnBu3
PMBO
140
Current Data Parameters
USER mgarg
NAME SH-II-234
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20050615
Time 12.05
INSTRUM gn500
PROBHD 5 mm broadban
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0988774 sec
RG 574.7
DW 62.400 usec
DE 6.00 usec
TE 300.1 K
D1 0.10000000 sec
---------- CHANNEL f1 ----------
NUC1 1H
P1 11.50 usec
PL1 -3.00 dB
SFO1 500.0435003 MHz
F2 - Processing parameters
SI 65536
SF 500.0400272 MHz
WDW EM
SSB 0
LB 0.50 Hz
GB 0
PC 4.00
1D NMR plot parameters
CX 22.80 cm
CY 25.00 cm
F1P 9.000 ppm
F1 4500.36 Hz
F2P -0.500 ppm
F2 -250.02 Hz
PPMCM 0.41667 ppm/cm
HZCM 208.35002 Hz/cm
ppm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NAME ntg-1-175
EXPNO 101
PROCNO 1
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Time 9.02
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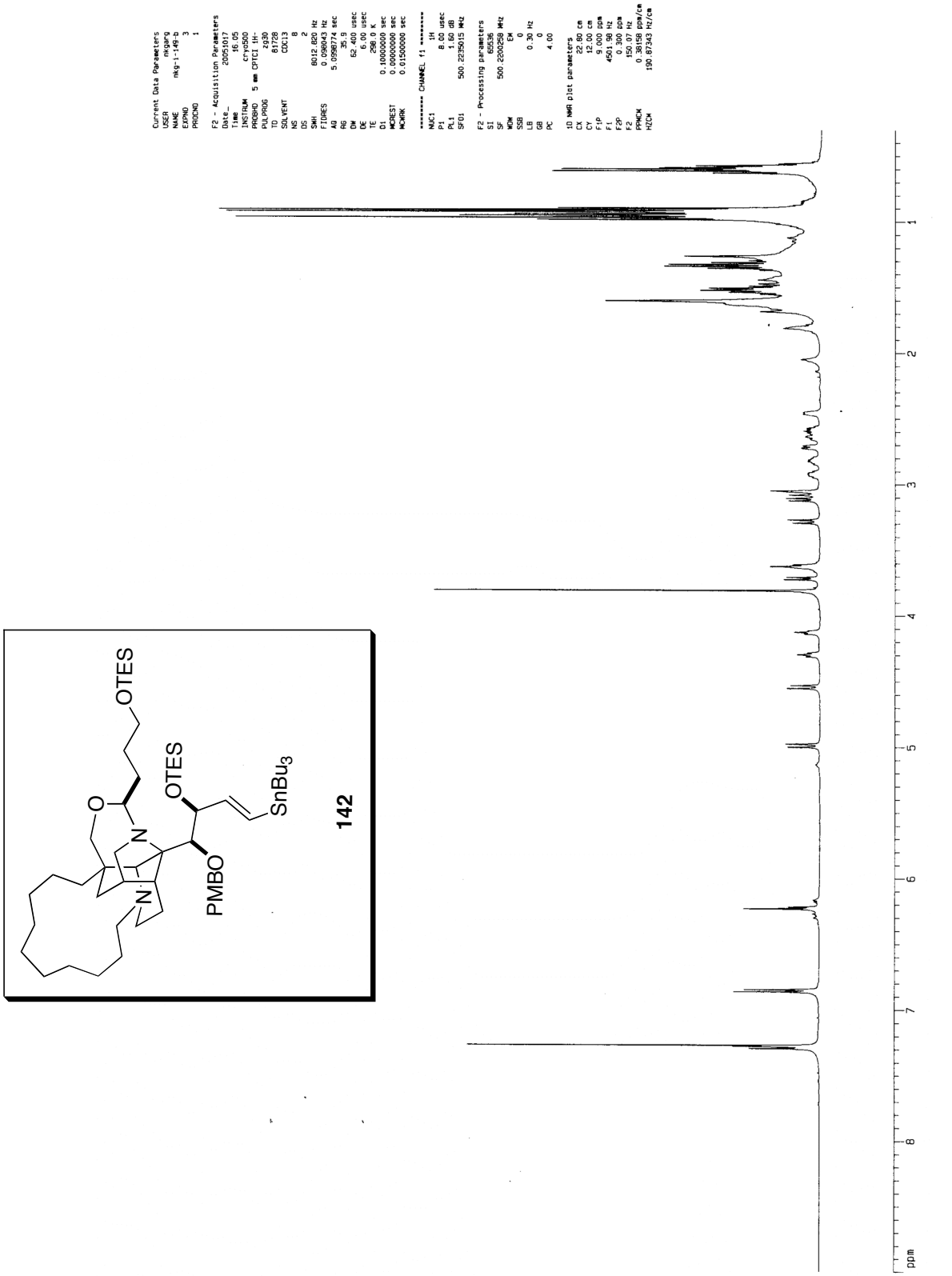
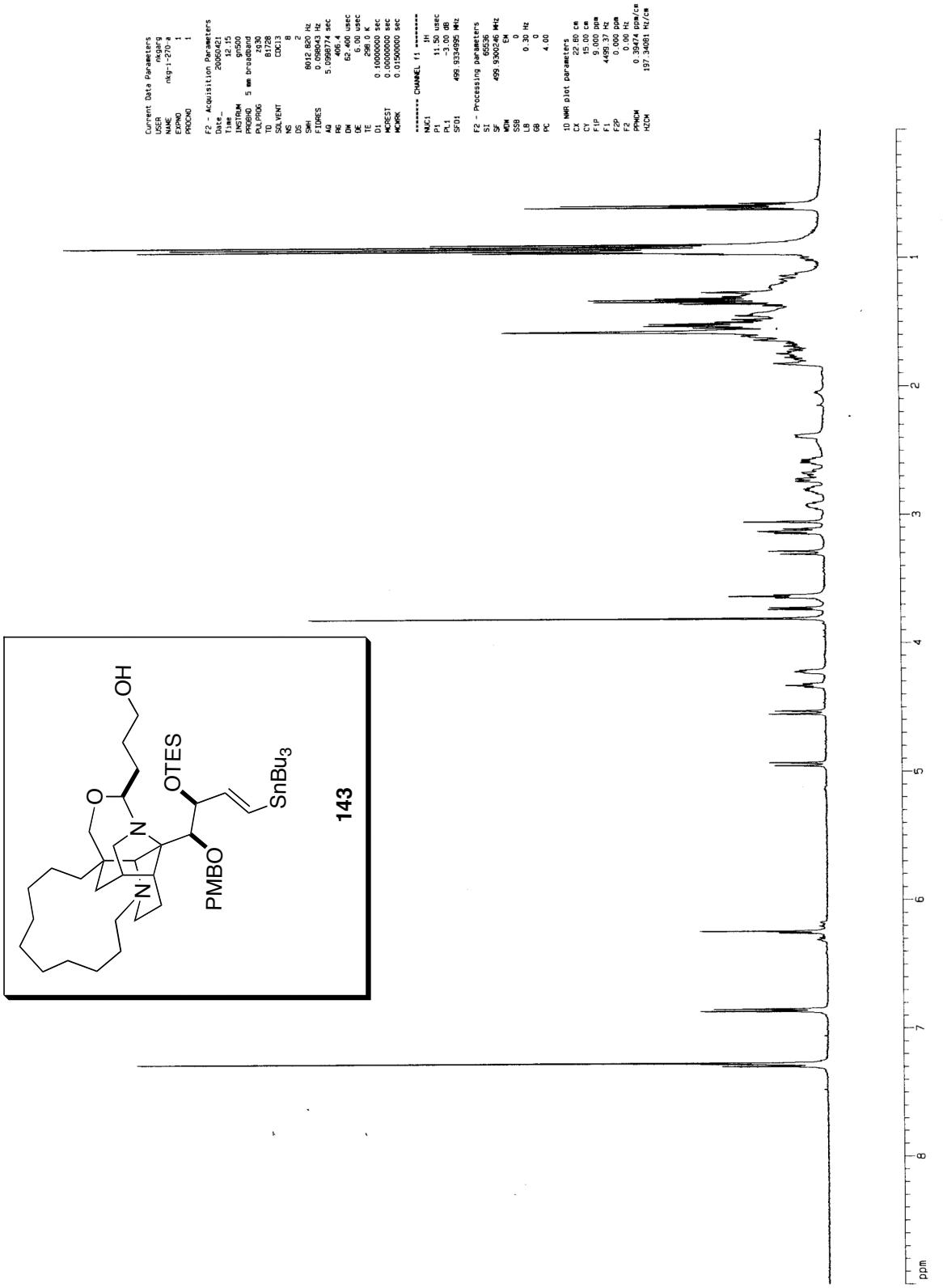
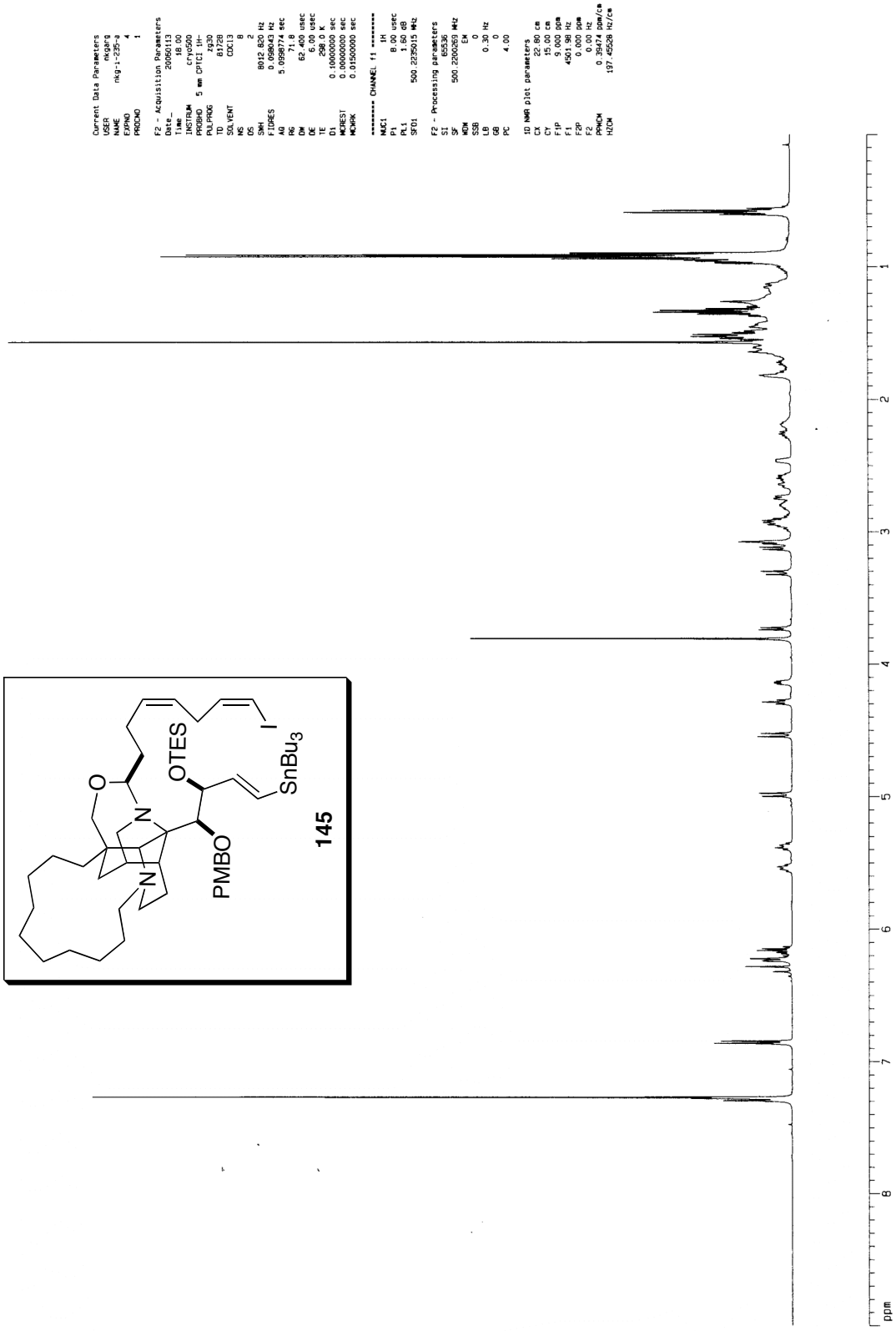
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 25
DS 2
SWH 9615.385 Hz
FIDRES 0.098178 Hz
AQ 5.0928259 sec
RG 575
DW 52.000 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -5.00 dB
SFO1 600.1342009 MHz
F2 - Processing parameters
SI 65536
SF 600.1300287 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 25.00 cm
F1P 10.000 ppm
F1 6001.30 Hz
F2P 0.500 ppa
F2 300.07 Hz
PPMCM 0.41667 ppm/cm
HZCM 250.05418 Hz/cm
OH
O
N
N
OH
PMBO
SnBu3
141
ppm


OTES
OTES
SnBu3
PMBO
142
Current Data Parameters
F2 - Acquisition Parameters
F2 - Processing parameters
1D NMR plot parameters
ppm


OH
O
N
N
OTES
SnBu3
PMBO
143
ppm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NAME mcg-1-235-a
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20050113
Time 18.00
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 65728
SOLVENT CDCl3
NS 8
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 8.00 usec
PL1 1.60 dB
SFO1 500.2325015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200269 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 4501.84 Hz
F2P 0.000 ppm
F2 0.00 Hz
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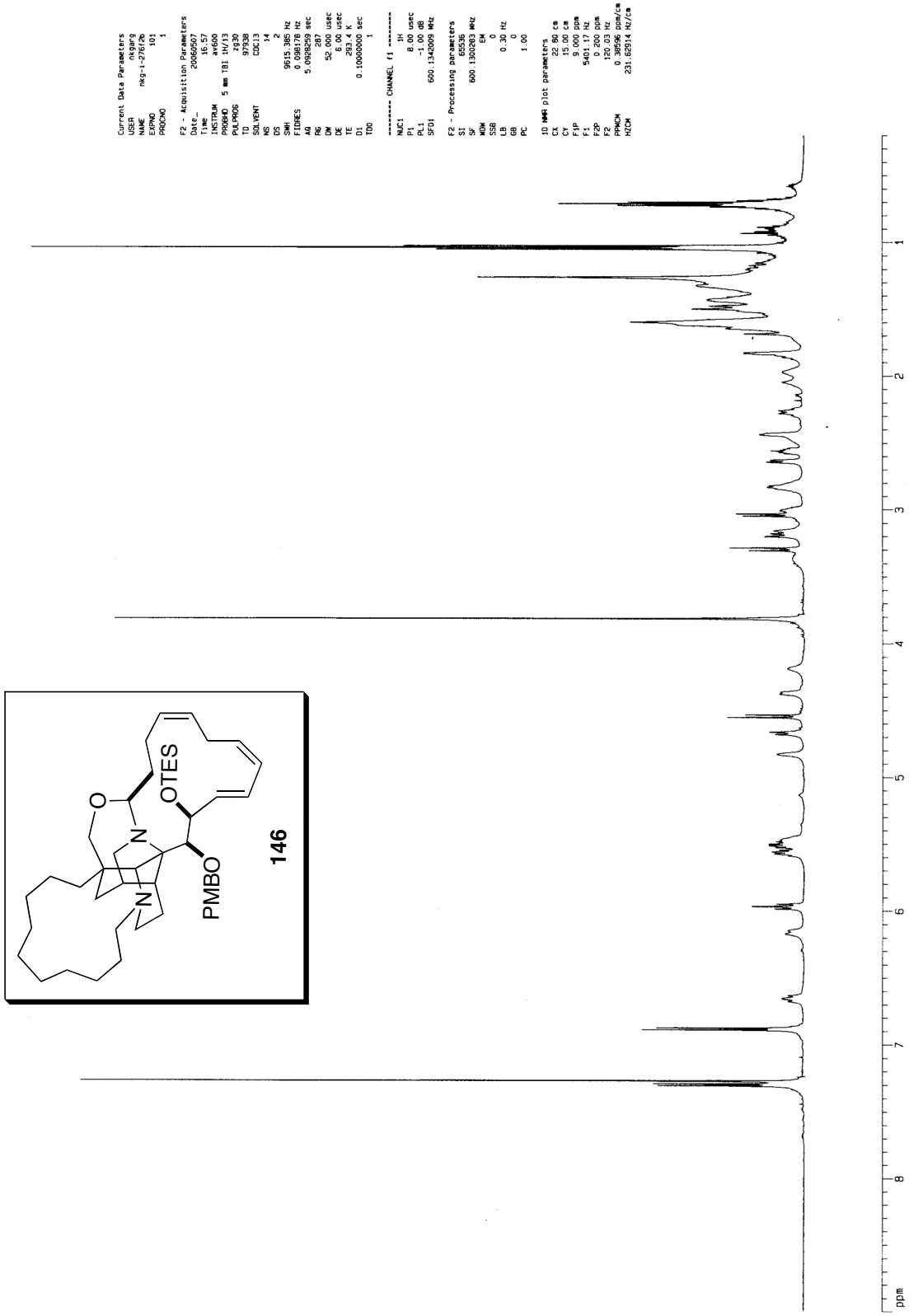
HZCM 197.45528 Hz/cm
O
N
N
OTES
PMBO
SnBu3
I
145
ppm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NAME nkg-i-276f2a
EXPNO 101
PROCNO 1
F2 - Acquisition Parameters
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Time 16.57
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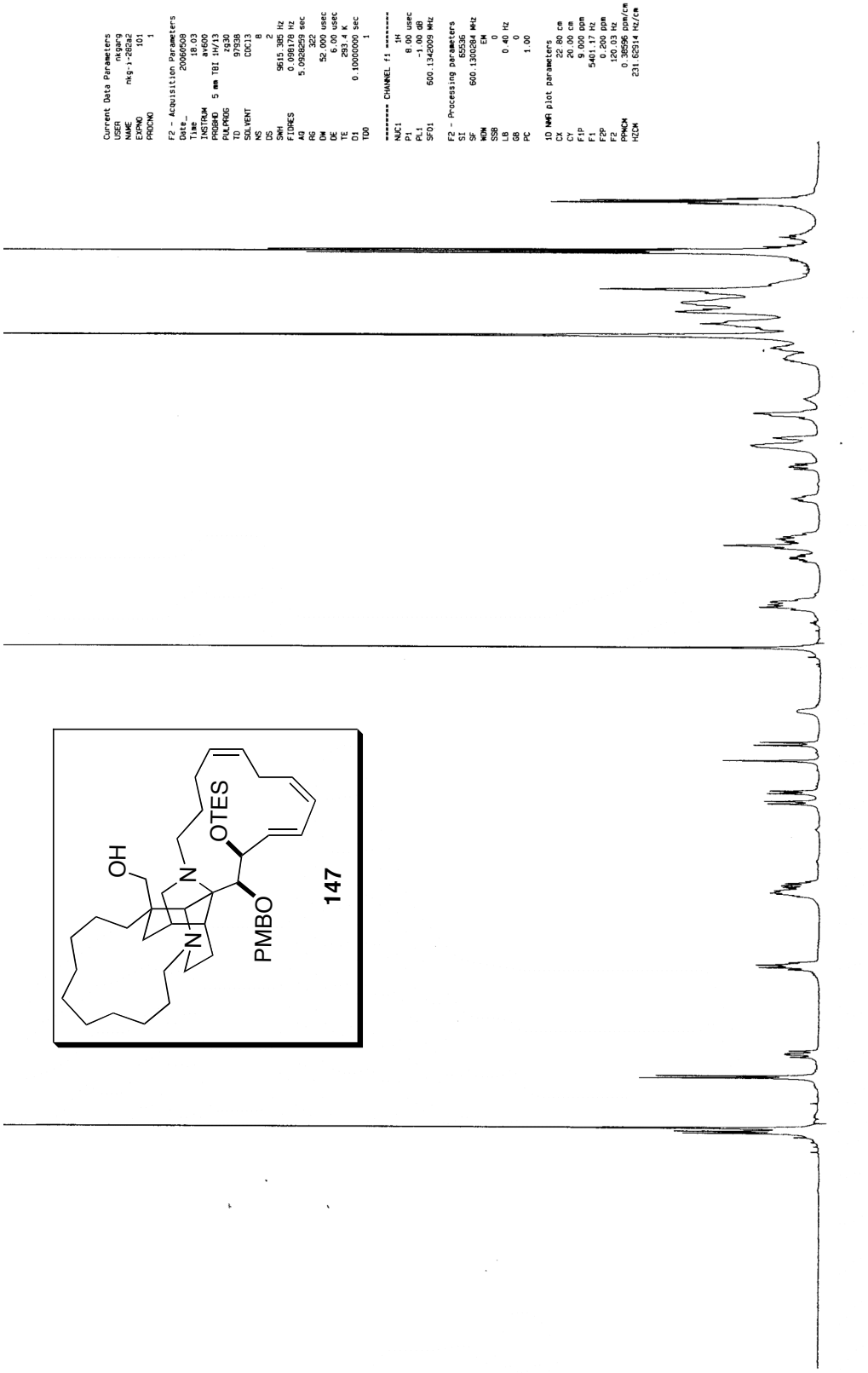
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 97938
SOLVENT CDCl3
NS 14
DS 2
SWH 9615.385 Hz
FIDRES 0.098178 Hz
AQ 5.0928259 sec
RG 203
DW 52.000 usec
DE 6.00 usec
TE 293.4 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 8.00 usec
PL1 -1.00 dB
SFO1 600.1342009 MHz
F2 - Processing parameters
SI 65536
SF 600.1300283 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 9.000 ppm
F1 5401.17 Hz
F2P 0.200 ppm
F2 120.03 Hz
PPMCM 0.38956 ppm/cm
HZCM 231.02914 Hz/cm
O
N
N
OTES
PMBO
146
ppm
1
2
3
4
5
6
7
8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PROCNO 1
F2 - Acquisition Parameters
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Time 18.03
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 97938
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098179 Hz
AQ 5.0628295 sec
RG 322
DW 52.000 usec
DE 6.00 usec
TE 293.4 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 8.00 usec
PL1 -1.00 dB
SFO1 600.1342009 MHz
F2 - Processing parameters
SI 65536
SF 600.1300284 MHz
WDW EM
SSB 0
LB 0.40 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.80 cm
CY 20.00 cm
F1P 9.600 ppm
F1 5401.17 Hz
F2P 0.200 ppm
F2 120.03 Hz
PPMCM 0.38596 ppm/cm
HZCM 231.62514 Hz/cm
OH
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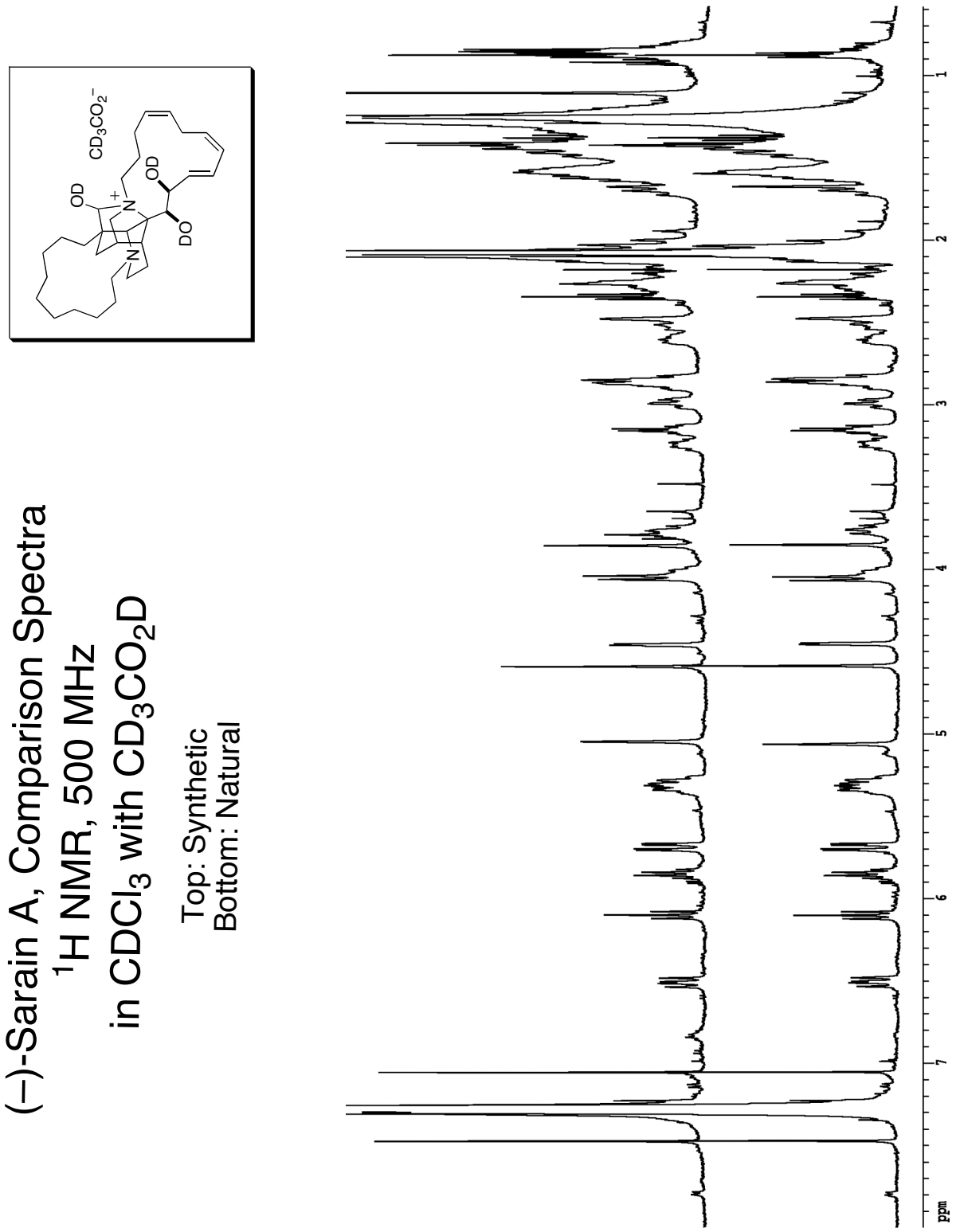
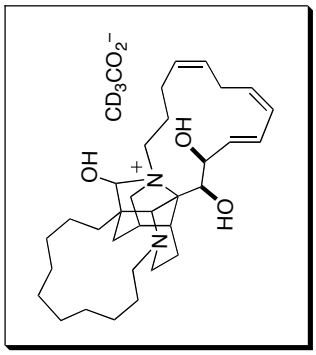
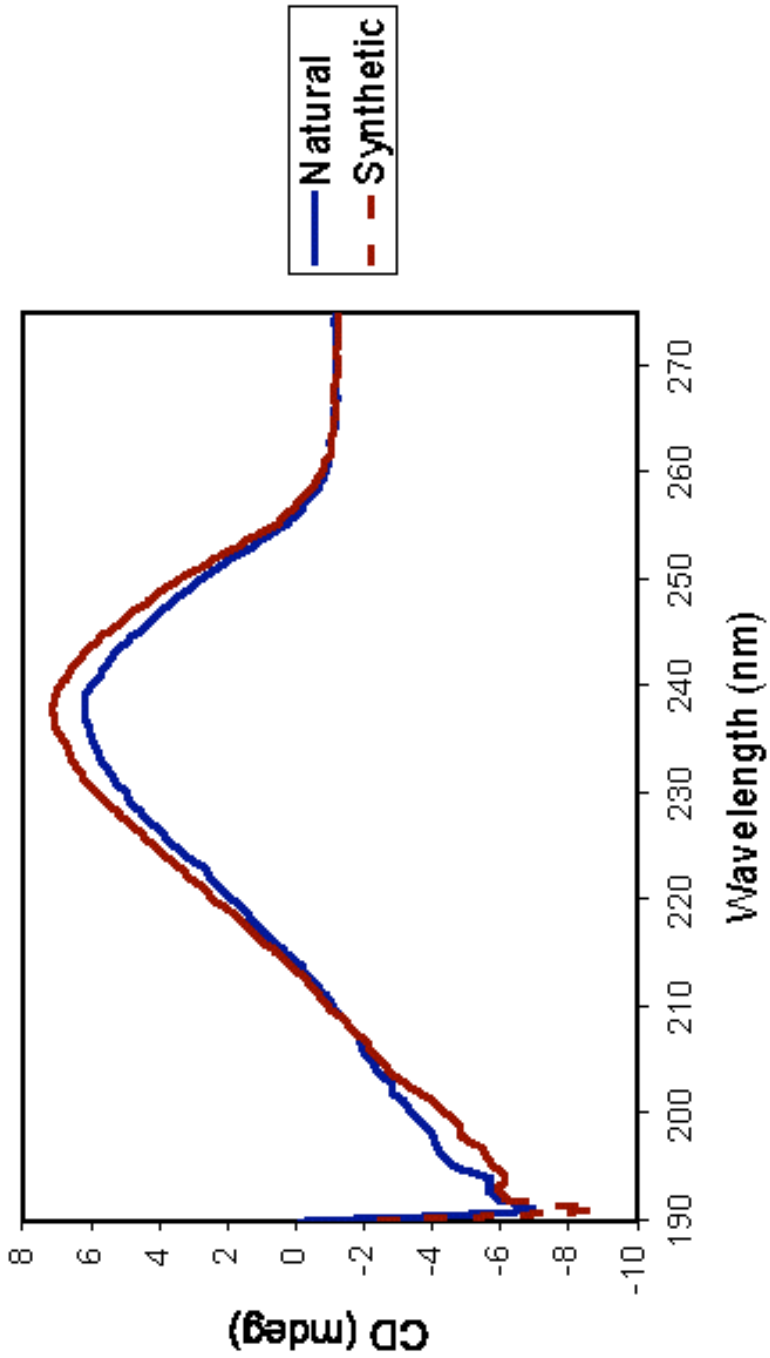
N
OTES
PMBO
147
ppm
1
2
3
4
5
6
7
8

Comparison Spectra for (–)-Sarain A (1):



(–)-Sarain A, Comparison Spectra
Circular Dichroism in Methanol





References:

[1] Downham, R.; Ng, F. W.; Overman, L. E. *J. Org. Chem.* **1998**, *63*, 8096–8097.

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[11] (a) Cimino, G.; Scognamiglio, G.; Spinella, A.; Trivellone, E. *J. Nat. Prod.* **1990**, *53*, 1519–1525. (b) Guo, Y.; Madaio, A.; Trivellone, E.; Scognamiglio, G.; Cimino, G. *Tetrahedron* **1996**, *52*, 8341–8348.