Total syntheses of indolactam alkaloids (–)-indolactam V, (–)-pendolmycin, (–)-lyngbyatoxin A, and (–)-teleocidin A-2

Noah F. Fine Nathel,† Tejas K. Shah,† Sarah M. Bronner, and Neil K. Garg*

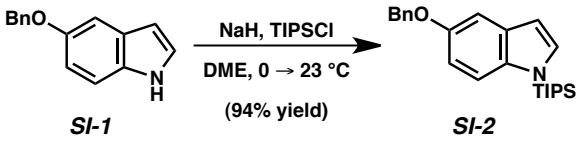
Department of Chemistry and Biochemistry, University of California
Los Angeles, California 90095

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 unless otherwise specified. 6-Benzyloxyindole was obtained from Combi-Blocks, Inc. Cesium fluoride (CsF), di-μ-bromobis(tri-*tert*-butylphosphino)dipalladium(I) ($[P(t\text{-}Bu)_3PdBr]_2$), tris(dibenzylideneacetone)dipalladium ($Pd(dba)_2$), and bis(cyclopentadienyl)zirconium(IV) chloride hydride (Schwartz's reagent) were purchased from Strem Chemicals. Tri-*tert*-butylphosphine and methyl trimethyl dimethylketene acetal was purchased from Sigma-Aldrich. The following reagents were distilled prior to use: chlorotrimethylsilane (TMSCl), *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf), and tetramethylethylenediamine (TMEDA); 1,2-dibromoethane was passed over basic Brockman Grade I 58 Å activated alumina and then stirred over 4 Å molecular sieves for 7 h before distillation. Diethylamine (Et_2NH) was stirred over KOH for 1 h and then passed over basic Brockman Grade I 58 Å activated alumina prior to use. DBU was stirred over 4 Å molecular sieves for 3 h and then passed over basic Brockman Grade I 58 Å. *N*-pentane was dried over $MgSO_4$. *N*-bromosuccinamide (NBS) was purified by recrystallization from deionized water. Reaction temperatures were controlled using an IKAmag temperature modulator, and unless stated otherwise, reactions were performed at room temperature (rt, approximately 23 °C). Melting points were determined using a MEL TEMP II melting point apparatus. Thin-layer chromatography (TLC) was conducted with EMD gel 60 F254 pre-coated plates (0.25 mm) and visualized using a combination of UV, anisaldehyde, iodine, vanillin, ninhydrin, and potassium permanganate staining. Silicycle Siliaflash P60 (particle size 0.040–0.063 mm) was used for flash column chromatography. ^{1}H NMR spectra were recorded on Bruker spectrometers (at 500 MHz or 600 MHz) and are reported relative to deuterated solvent signals. Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz) and integration. ^{13}C NMR spectra were recorded on Bruker Spectrometers (at 125 or 150 MHz). Data for ^{13}C NMR spectra are reported in terms of chemical shift. IR spectra were recorded on a Perkin-Elmer 100 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Optical rotations were measured with a Rudolf Autopol III Automatic Polarimeter. High-resolution mass spectra were obtained from the UC Irvine Mass Spectrometry Facility and the UCLA Molecular Instrumentation Center.

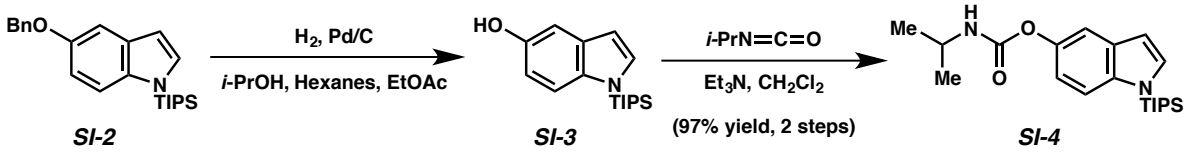
Experimental Procedures

A. Optimization of the total synthesis of indolactam V (1)



SI-1 *SI-2*

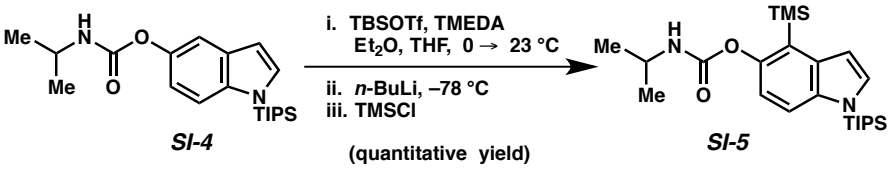
***N*-TIPS benzyloxyindole SI-2.** To a flask containing NaH (60% dispersion in mineral oil, 0.700 g, 17.5 mmol, 1.3 equiv) at 0 °C was added a solution of 5-benzyloxyindole **SI-1** (3.00 g, 13.5 mmol) in 1,2-dimethoxyethane (40 mL). The resulting solution was stirred at 0 °C for 20 min, then TIPSCl (4.34 mL, 20.3 mmol, 1.5 equiv) was added dropwise over 5 min. The resulting mixture was removed from the 0 °C bath and allowed to warm to 23 °C. After stirring for an additional 90 min, the reaction was quenched with H_2O (2 mL). The biphasic mixture was concentrated under reduced pressure, then further diluted with Et_2O (50 mL) and H_2O (10 mL). The layers were separated, and then the aqueous layer was extracted with Et_2O (2 × 50 mL). The combined organic layers were dried over $MgSO_4$. Evaporation of the solvent under reduced pressure afforded the crude product, which was further purified by flash chromatography (3:1 Hexanes:CH_2Cl_2) to afford known **SI-2**[1] (4.82 g, 94% yield) as a white solid.



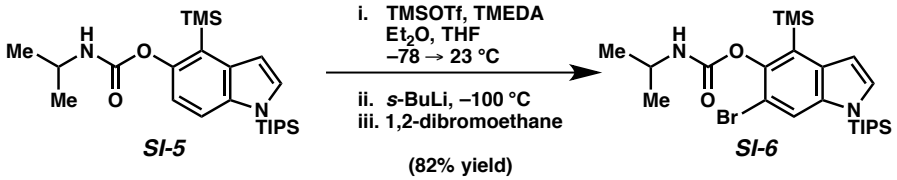
SI-2 *SI-3* *SI-4*

***N*-TIPS carbamate SI-4.** Carbamate **SI-4** was prepared following the general procedure described by Igarashi.[2] To a solution of *N*-TIPS benzyloxyindole (4.72 g, 12.4 mmol) in 1:1:1 *i*-PrOH:Hexanes:EtOAc (108 mL) was added 5% Pd/C (0.67 g, 0.32 mmol, 2.6 mol% Pd). The mixture was placed under an atmosphere of hydrogen (double-balloon), stirred for 2.5 h at 23 °C, and then filtered over celite (EtOAc eluent). Evaporation of the solvent under reduced pressure afforded crude **SI-3** as a pink solid, which was used in the subsequent step without further purification.

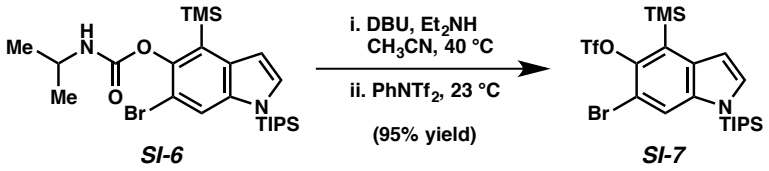
To a solution of crude **SI-3** in CH_2Cl_2 (60.0 mL) and Et_3N (0.518 mL, 3.72 mmol, 0.3 equiv), was added *i*-PrNCO (3.64 mL, 37.2 mmol, 3 equiv. The solution was stirred at 23 °C for 24 h, then concentrated to dryness under reduced pressure. Purification by flash chromatography (2:1 Hexanes:Et_2O) provided known *N*-TIPS carbamate **SI-4**[1] (4.48 g, 97% yield, 2 steps) as a white solid.



***N*-TIPS silylcarbamate SI-5.** Silyl carbamate **SI-5** was prepared following the general procedure described by Hoppe and Snieckus for *o*-lithiation of isopropyl carbamates, with minor modifications.[3,4] To a solution of *N*-TIPS carbamate **SI-4** (4.48 g, 11.98 mmol) and TMEDA (2.51 mL, 16.8 mmol, 1.4 equiv) in 3:1 Et_2O:THF (120 mL) at 0 °C was added a solution of TBSOTf in *n*-pentane (1.30 M, 17.3 mL, 14.4 mmol, 1.2 equiv). After stirring for 5 min, the white suspension was allowed to warm to 23 °C over 30 min. TMEDA (6.28 mL, 41.9 mmol, 3.5 equiv) was added, and the mixture was cooled to –78 °C. A solution of *n*-BuLi in hexanes (1.43 M, 29.3 mL, 41.9 mmol, 3.5 equiv) was added dropwise over 55 min. The mixture was stirred at –78 °C for 3 h, then neat TMSCl (10.6 mL, 83.9 mmol, 7 equiv) was added dropwise over 1 h. The resulting mixture was stirred at –78 °C for 1 h, quenched with 1 M $NaHSO_4$ (50 mL), and allowed to warm to 23 °C over 45 min with vigorous stirring. The biphasic mixture was further diluted with Et_2O (50 mL), the layers were separated, and then the aqueous layer was extracted with Et_2O (2 × 50 mL). The combined organic layers were dried over $MgSO_4$. Evaporation of the solvent under reduced pressure afforded the crude product, which was further purified by flash chromatography (2:1 Hexanes:Et_2O) to afford known silylcarbamate **SI-5**[1] (5.33 g, quantitative yield) as a white solid.

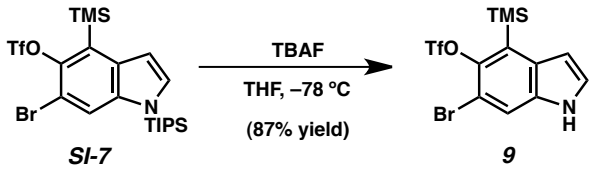


6-Bromo silylcarbamate SI-6. 6-Bromo silylcarbamate **SI-6** was prepared following the general procedure described by Snieckus for *o*-lithiation, with modifications.[5] To a solution of silylcarbamate **SI-5** (2.19 g, 4.90 mmol) in 3:1 Et_2O:THF (69.6 mL) at –78 °C was added TMEDA (1.02 mL, 6.86 mmol, 1.4 equiv), followed by a solution of TMSOTf in *n*-pentane (1.30 M, 3.91 mL, 5.90 mmol, 1.2 equiv). After stirring for 5 min, the white suspension was allowed to warm to 23 °C over 28 min, by which time TMEDA·TfOH had formed as an oil on the bottom of the flask. The mixture was placed in a hexanes and liquid nitrogen bath at –100 °C and TMEDA (2.56 mL, 17.2 mmol, 3.5 equiv) was added. A solution of *sec*-BuLi in cyclohexane (1.18 M, 37.4 mL, 44.1 mmol, 9 equiv) was added dropwise over 1.2 h. The mixture was stirred at –100 °C for 4.5 h, then neat 1,2-dibromoethane (5.09 mL, 58.8 mmol, 12.0 equiv) was added dropwise over 10 min. The resulting mixture was stirred at –100 °C for 3 h, quenched with 0.5 M aqueous $NaHSO_4$ (50 mL), and warmed to 23 °C over 40 min with vigorous stirring. The layers were separated, and the organic layer was washed successively with 1 M aqueous $NaHSO_4$ (50 mL) and brine (50 mL), then dried over $MgSO_4$. Evaporation under reduced pressure afforded the crude product, which was purified by flash chromatography (5:1 Benzene:CH_2Cl_2) to afford known 6-bromo silylcarbamate **SI-6**[6] (2.12 g, 82% yield) as a white solid.



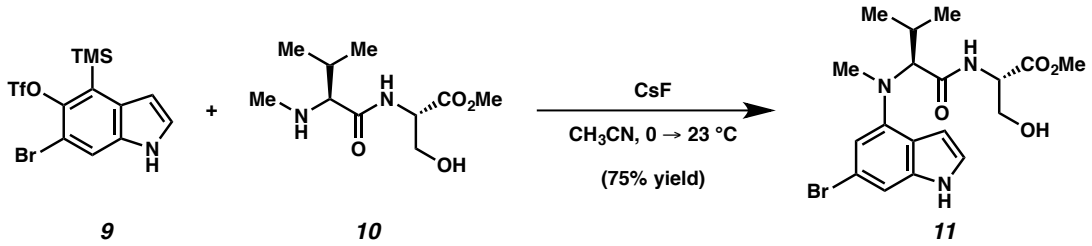
***N*-TIPS 6-bromo silyltriflate SI-7.** To a solution of 6-bromo silylcarbamate **SI-6** (0.636 g, 1.21 mmol) in MeCN (24 mL) were added DBU (0.427 mL, 3.03 mmol, 2.5 equiv) and Et_2NH (0.187 μL, 1.82 mmol, 1.5 equiv). The resulting mixture was placed in a heating bath maintained at 40 °C for 15 min, then allowed to cool to 23 °C. Next, a solution of $PhNTf_2$ (0.650 g, 1.82 mmol, 1.5 equiv) in MeCN (2.1 mL) was added. After stirring for 25 min, the reaction mixture was

passed over a plug of silica gel (EtOAc eluent). Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (30:1 Hexanes:Et_2O) to provide known *N*-TIPS 6-bromo silyltriflate **SI-7**[6] (0.654 g, 95% yield) as a white solid.



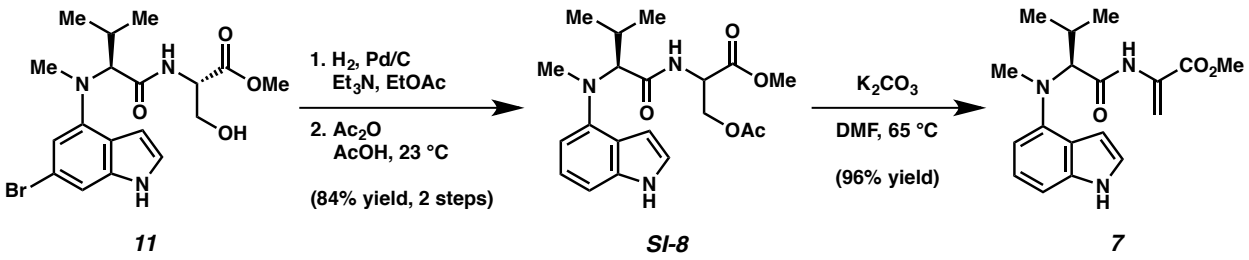
SI-7 *9*

***N*-H 6-bromo silyltriflate 9.** To a solution of *N*-TIPS 6-bromo silyltriflate **SI-7** (0.143 g, 0.250 mmol) in THF (9.4 mL) at –78 °C was added a solution of TBAF in THF (1.0 M, 250 μL, 0.250 mmol, 1 equiv) dropwise over 3 min. The solution was stirred for 15 min, then quenched with H_2O (12 mL). The biphasic mixture was further diluted with EtOAc (12 mL). The layers were separated, and then the aqueous layer was extracted with EtOAc (2 × 12 mL). The combined organic layers were dried over $MgSO_4$. Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (2.5:1 Hexanes:CH_2Cl_2) to provide known bromo silyltriflate **9**[6] (90.9 mg, 87% yield) as a white solid.

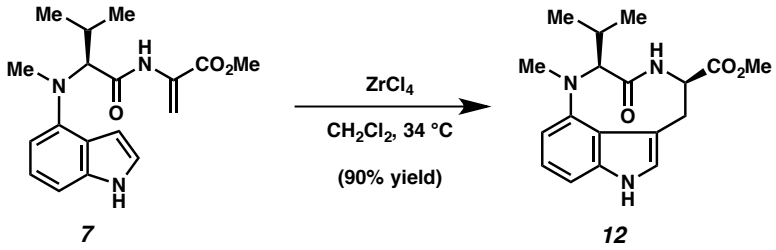


9 *10* *11*

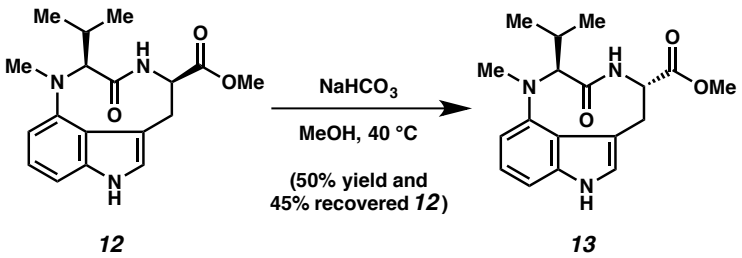
Indolyne adduct 11. To a stirred solution of *N*-H 6-bromo silyltriflate **9** (52.1 mg, 0.125 mmol) and peptide **10**[6] (87.1 mg, 0.375 mmol, 3 equiv) in MeCN (1.25 mL) was placed in a 0 °C bath and added CsF (38.0 mg, 0.250 mmol, 2 equiv). The reaction mixture was stirred at 0 °C for 12 h, and was then allowed to warm to 23 °C. After stirring for an additional 12 h, the reaction mixture was filtered over silica gel (EtOAc eluent). Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (1:0.7:0.7 Hexanes:CH_2Cl_2:Et_2O) to provide known indolyne adduct **11**[6] (40.0 mg, 75% yield) as a clear oil.



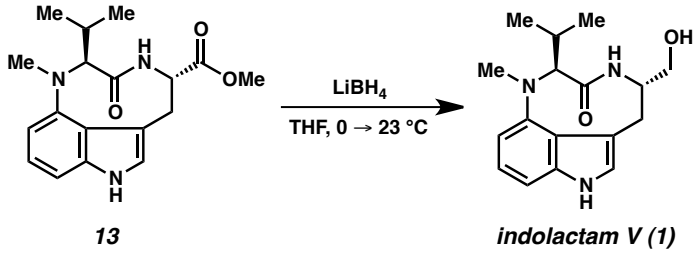
Unsaturated ester 7. Indolyne adduct **11** was converted to **SI-8** in 84% yield using our previously reported two-step procedure.[6] To a solution of **SI-8** (98.2 mg, 0.252 mmol) in DMF (2.5 mL) was added K_2CO_3 (69.7 mg, 0.504 mmol, 2 equiv). The resulting mixture was placed in a heating bath maintained at 65 °C for 10 h, then allowed to cool to 23 °C. The reaction mixture was passed over a plug of cotton (EtOAc eluent). Evaporation at 60 °C under reduced pressure afforded the crude product, which was further purified by flash chromatography (5:1 Hexanes:EtOAc) to provide known ester **7**[6] (79.7 mg, 96% yield) as a white solid.



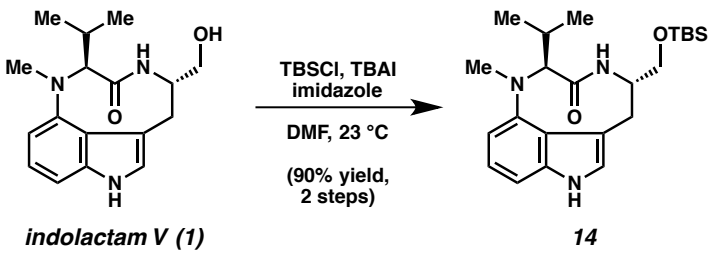
Tricycle 12. A modification of Piersanti's procedure for alkylation of indoles was employed to construct the desired 9-membered ring.[7] Inside a glove box, $ZrCl_4$ (336.5 mg, 1.45 mmol, 15 equiv) and then CH_2Cl_2 (0.96 mL) were added to a vial containing **7** (31.7 mg, 0.096 mmol). The reaction vessel was placed into an aluminum block maintained at 34 °C. After 16 h, the vial was transferred out of the glove box and the reaction mixture was added dropwise to saturated aqueous $NaHCO_3$ (15 mL) at 0 °C. The resulting solids were removed by filtration over celite (EtOAc eluent). The layers were separated and the aqueous layer was extracted with EtOAc (15 mL). The combined organic layers were dried over Na_2SO_4. Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (5:1 → 2:1 Hexanes:EtOAc) to afford known tricycle **12**[6] (28.5 mg, 90% yield) as a white solid.



Ester 13. Tricycle **12** was epimerized following the protocol described by Nakatsuka, with modifications.[8] To a solution of **12** (42.1 mg, 0.128 mmol) in MeOH (8.5 mL) was added $NaHCO_3$ (294.4 mg, 3.5 mmol, 27.4 equiv). The resulting mixture was placed in a heating bath maintained at 40 °C for 3 d, then allowed to cool to 23 °C. The reaction mixture was concentrated and diluted with EtOAc (50 mL) and H_2O (50 mL). The organic layer was separated, and then the organic layer was washed with brine (50 mL), and dried over $MgSO_4$. Evaporation under reduced pressure afforded the crude mixture, which was purified by flash chromatography (95:5 → 90:10 Benzene:CH_3CN) to afford known ester **13**[8] (21.0 mg, 50% yield) and recovered epimer **12**[8] (19.0 mg, 45% yield) as a white solid.



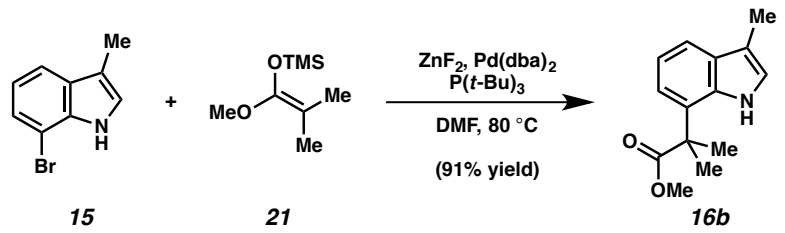
Indolactam V (1). Ester **13** was reduced following the protocol described by Nakatsuka, with modifications.[8] Inside a glove box, a vial was charged with **13** (125.4 mg, 0.381 mmol), $LiBH_4$ (54.8 mg, 2.515 mmol, 6.6 equiv) and THF (0.381 mL). The vial was removed from the glove box and allowed to stir for 2 h at 23 °C. After 2 h, the reaction mixture was poured into ice water (5 mL). The mixture was then extracted with CH_2Cl_2 (50 mL). The organic layers were combined, washed with brine (15 mL), and dried over $MgSO_4$. Evaporation of the solvent under reduced pressure afforded crude indolactam V (**1**), which was used in the subsequent step without further purification. Spectral data match those previously reported.[8]



indolactam V (1) ***14***

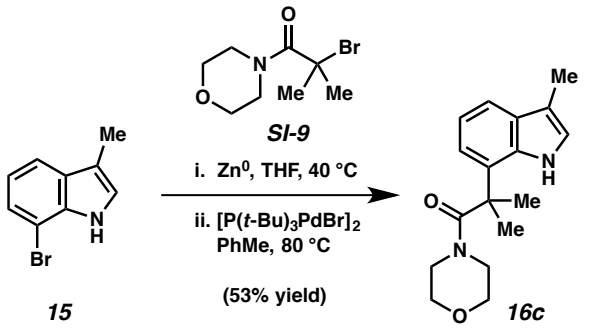
Silylether 14. Indolactam V (**1**) was silyl protected following the protocol described by Kishi.[9] To a stirred solution of indolactam V (**1**) (41.7 mg, 0.317 mmol) in DMF (1.4 mL) was added TBSCl (20.6 mg, 0.137 mmol, 1.0 equiv), imidazole (46.5 mg, 0.684 mmol, 5.0 equiv), and TBAI (5.0 mg, 0.014 mmol, 0.1 equiv). The resulting mixture was allowed to stir at 23 °C. After 12 h, the reaction was quenched with saturated aqueous NH_4Cl (5 mL) and diluted with EtOAc (10 mL). The organic layer was separated, and then the organic layer was washed with brine (50 mL), and dried over Na_2SO_4. Evaporation under reduced pressure afforded the crude product, which was purified by flash chromatography (4:1 Hexane:EtOAc) to afford known silylether **14** (118.5 mg, 90% yield over two steps) as a white solid. Silylether **14**: Mp = 192-195 °C; R_f 0.65 (1:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.05 (br s, 1H), 7.08 (t, J = 7.9, 1H), 6.91 (d, J = 8.0, 1H), 6.89 (s, 1H), 6.52 (d, J = 7.7, 1H), 6.19 (br s, 1H), 4.38 (d, J = 10.2, 1H), 4.24 (d, J = 3.9, 1H), 3.65 (dd, J = 10.1, 4.3, 1H), 3.48 (t, J = 9.5, 1H), 3.17 (d, J = 17.4, 1H), 2.95–2.88 (m, 4H), 2.65–2.61 (m, 1H), 0.94 (d, J = 6.4, 3H), 0.91 (s, 3H), 0.89 (s, 9H), 0.64 (d, J = 6.7, 3H), 0.06 (s, 3H) 0.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.1, 148.0, 139.5, 123.0, 121.4, 118.1, 114.7, 106.4, 104.0, 71.3, 65.5, 55.2, 34.2, 33.0, 28.7, 26.0, 21.7, 19.6, 18.4, -5.2, -5.3; IR (film): 3320, 2928, 1643, 1251 cm^{-1}; HRMS-ESI (*m/z*) [M + Na]$^+$ calculated for $C_{23}H_{37}N_3O_2SiNa$, 438.2553; found, 438.2554; $[\alpha]^{20}_D$ –124.00° (c 0.10 CH_2Cl_2).

B. Cross-coupling to introduce the C7 sp^2–sp^3 linkage



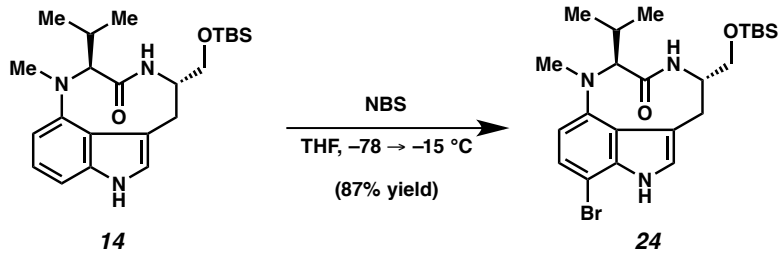
15 *21* *16b*

Ester 16b. Ester **16b** was prepared following the general coupling protocol described by Hartwig for the cross-coupling of silyl ketene acetals with aryl bromides, with modifications.[10] A flame-dried vial under N_2, containing 7-bromoskatol (**15**)[11] (9.9 mg, 0.047 mmol), was transferred to a glovebox. A magnetic stir bar was added, followed by P(*t*Bu)$_3$ (4.7 µl, 4.7 µmol, 0.1 equiv), ZnF_2 (2.5 mg, 0.025 mmol, 0.5 equiv), and a solution of Pd(dba)$_2$ (1.4 mg, 2.4 µmol, 0.05 equiv) in DMF (0.47 mL). Trimethylsilyldimethylketene (**21**) (14.4 µl, 0.071 mmol, 1.5 equiv) was added and the vial was sealed with a teflon-coated cap and removed from the glovebox. The reaction was stirred at 80 °C for 12 h, cooled to 23 °C, and then filtered over silica (100% EtOAc eluent) and concentrated in vacuo. The crude residue was purified by preparative thin layer chromatography (3:1:1 Hexanes:CH_2Cl_2:EtO_2) to afford ester **16b** (9.9 mg, 91%) as an amorphous tan solid. Ester **16b**: R_f 0.6 (3:1:1 Hexanes:CH_2Cl_2: EtO_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.63 (br s, 1H), 7.52 (ddd, *J* = 7.8, 1.0, 1.0, 1H), 7.19 (dd, *J* = 7.5, 1.0 1H), 7.12 (dd, *J* = 7.8, 7.5 1H), 6.96 (ddd, *J* = 1.0, 1.0, 1.0, 1H), 3.61 (s, 3H), 2.32 (d, *J* = 1.0, 3H), 1.71 (s, 6H),; ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.7, 134.1, 129.2, 126.5, 121.9, 119.2, 118.4, 117.9, 111.4, 52.8, 45.3, 25.2, 9.8; IR (film): 3428, 2950, 1713, 1434, 1264, 1152 cm^{-1}; HRMS-ESI (*m/z*) [M + H]$^+$ calculated for $C_{14}H_{18}NO_2$, 232.1332; found, 232.1328.



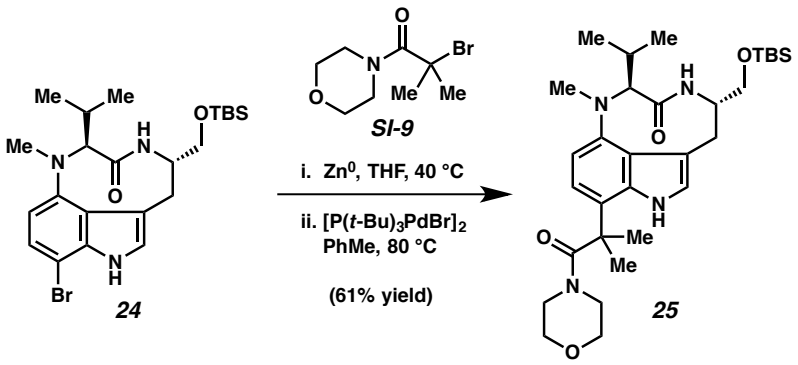
Morpholine amide 16c. Amide **16c** was prepared following the general protocol for the cross-coupling of α-bromoamides with aryl bromides described by Hartwig, with modifications.[12] Inside a glove box, a vial was charged with morpholine amide **SI-9** (390.0 mg, 1.65 mmol, 5 equiv), activated zinc dust (112.0 mg, 1.71 mmol, 5.2 equiv) and THF (1.4 mL). The vial was sealed and placed into a heating block maintained at 40 °C for 4 h. This heterogeneous solution was removed from the heat and immediately added to a solution of 7-bromoskatol **15**[11] (69.0 mg, 0.33 mmol) and $[P(t\text{-Bu})_3PdBr]_2$ (38.3 mg, 0.05 mmol, 0.15 equiv) in toluene (3.2 mL). The resulting solution was stirred at 80 °C for 12 h. After cooling to 23 °C, the reaction mixture was loaded directly onto a silica gel column and separated by flash chromatography (5:1 Hexane:EtOAc) to afford morpholine amide **16c** (50.3 mg, 53% yield) as a clear oil. Morpholine Amide **16c**: R_f 0.08 (5:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.35 (br s, 1H), 7.51–7.46 (m, 1H), 7.12–7.08 (m, 2H), 6.95–6.93 (m, 1H), 3.89–2.45 (br m, 8H), 2.32 (d, J = 1.1, 3H), 1.67 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.2, 133.7, 129.3, 128.1, 121.9, 119.6, 118.0, 116.1, 111.6, 67.1, 65.8, 47.5, 45.3, 43.7, 9.8; IR (film): 3365, 2920, 1619, 1426, 1245, 1112 cm^{-1}; HRMS-ESI (*m/z*) $[M - H]^-$ calculated for $C_{17}H_{21}N_2O_2$, 285.1609; found, 285.1610.

C. Total synthesis of (–)-pendolmycin (2)

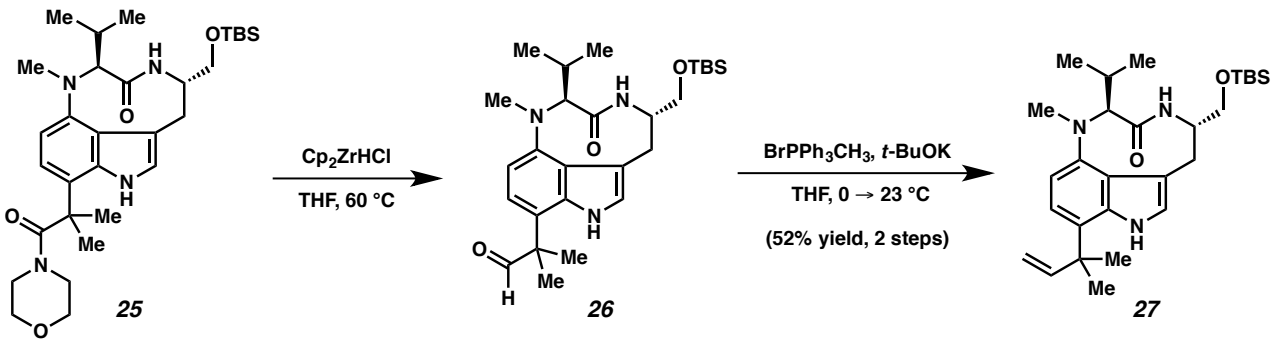


14 ***24***

Bromoindole 24. Silylether **14** was functionalized following the general protocol described by Kishi, with modification.[13] To a stirred solution of silylether **14** (9.5 mg, 0.023 mmol) in THF (2.3 mL) at –78 °C was added *N*-bromosuccinimide (4.1 mg, 0.023 mmol, 1.0 equiv) in THF (2.3 mL). After 10 min, the reaction warmed to –15 °C and stirred for an additional 10 min. The reaction was quenched with water (1 mL), diluted with EtOAc (10 mL) and then washed sequentially with water (10 mL), and brine (5 mL). The organic layers were combined and dried over Na_2SO_4. Evaporation under reduced pressure afforded the crude product, which was purified by flash chromatography (3:1 Hexane:EtOAc) to afford bromoindole **24** (6.8 mg, 87% yield) as a white solid. Bromoindole **24**: Mp: 188–190 °C; R_f 0.6 (2:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20 (br s, 1H), 7.18 (d, J = 8.3, 1H), 6.94 (t, J = 1.8, 1H), 6.41 (d, J = 8.3, 1H), 6.16 (s, 1H), 4.30 (d, J = 10.2, 1H), 4.18–4.14 (m, 1H), 3.65 (dd, J = 10.2, 4.4, 1H), 3.48 (dd, J = 10.0, 9.1 1H), 3.17–3.10 (m, 1H), 2.93–2.87 (m, 4H), 2.66–2.55 (m, 1H) 0.93 (d, J = 6.3, 3H), 0.90–0.88 (m, 9H), 0.62 (d, J = 6.8, 3H), 0.04 (d, J = 11.9, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.7, 147.6, 137.3, 125.1, 121.8, 119.1, 116.1, 107.6, 95.9, 71.5, 65.4, 55.0, 34.1, 33.0, 28.7, 26.0, 21.7, 19.7, 18.4, -5.2, -5.3; IR (film): 3369, 3325, 2928, 2857, 1647, 1502, 1251, 1104 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{23}H_{36}BrN_3O_2SiNa$, 516.1658; found, 516.1659; $[\alpha]^{20}_D$ –384.00° (c 0.10 CH_2Cl_2).



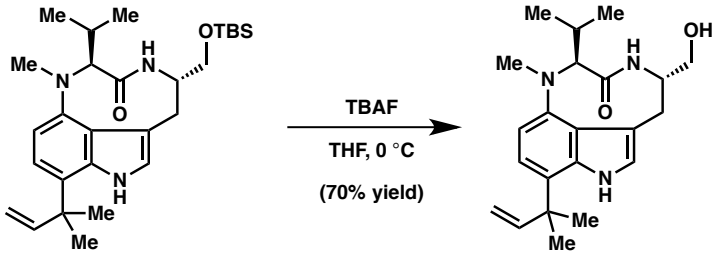
Morpholine amide 25. Amide **25** was prepared following the general protocol described by Hartwig for the cross-coupling of α-bromoamides with aryl bromides, with modifications.[12] Inside a glove box, a vial was charged with morpholine amide **SI-9** (19.1 mg, 0.081 mmol, 10.0 equiv), activated zinc dust (5.5 mg, 0.084 mmol, 10.4 equiv) and THF (0.3 mL). The vial was sealed and placed into a heating block maintained at 40 °C for 4 h. This heterogeneous solution was removed from the heat and immediately added to a solution of bromoindole **24** (4.0 mg, 8 μmol) and $[P(t\text{-Bu})_3PdBr]_2$ (0.9 mg, 1 μmol, 15 mol%) in toluene (0.2 mL). The resulting solution was stirred at 80 °C for 12 h. After cooling to 23 °C, the reaction mixture was loaded directly onto a silica gel column and separated by flash chromatography (1:1 Hexane:EtOAc) to afford morpholine amide **25** (2.8 mg, 61% yield) as a light yellow oil. Morpholine amide **25**: R_f 0.4 (1:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (br s, 1H), 6.96 (d, J = 8.0, 1H), 6.86 (s, 1H), 6.49 (d, J = 8.0, 1H), 6.16 (br s, 1H), 4.33 (d, J = 10.0, 1H), 4.25–4.16 (m, 1H), 3.70–3.56 (m, 4H), 3.47 (t, J = 10.0, 1H), 3.39–3.20 (m, 3H), 3.14 (d, J =17.4, 3H), 2.66–2.55 (m, 1H), 1.70 (s, 3H), 1.42 (s, 3H), 1.10 (d, J = 6.6, 3H), 0.93 (d, J = 6.6, 4H), 0.88 (s, 9H), 0.55 (d, J = 6.6, 3H), 0.05 (d, J = 12.5, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.6, 172.9, 170.9, 147.0, 136.7, 122.0, 120.5, 118.7, 117.2, 114.3, 106.3, 71.2, 65.5, 56.7, 55.0, 44.8, 36.4, 34.1, 32.9, 28.7, 26.0, 23.4, 21.7, 20.7, 19.7, 18.4 -5.2, -5.3; IR (film): 3375, 2956, 2928, 2857, 1665, 1620, 1508 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{31}H_{50}N_4O_4SiNa$, 593.3498; found, 593.3499; $[\alpha]^{22}_D$ 317.80° (c 0.10 CH_2Cl_2).



Olefin 27. Aldehyde **26** was prepared following the general protocol described by Georg for the reduction of tertiary amides, with modifications.[14] Inside a glove box, Cp_2ZrHCl (33.9 mg, 0.131 mmol, 5 equiv) and THF (0.7 mL) were added to a vial containing **25** (15.0 mg, 0.026 mmol). The reaction vessel was placed in an aluminum block maintained at 60 °C. After stirring for 2 h, the vial was transferred out of the glove box and the reaction mixture was quenched with H_2O (5 mL) and EtOAc (5 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with brine (15 mL) and dried over Na_2SO_4. Evaporation under reduced pressure afforded the crude product, which was used in the subsequent step without further purification. Aldehyde **26**: R_f 0.8 (1:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.33 (s, 1H), 8.39 (br s, 1H), 7.07 (d, J = 8.2, 1H), 6.85 (s, 1H), 6.56 (d, J = 8.2, 1H), 6.15 (s, 1H), 4.33 (d, J = 10.1, 1H), 4.21–4.12 (m, 1H), 3.62 (dd, J = 10.1, 4.2, 1H), 3.45 (t, J = 10.1, 1H), 3.17–3.10 (m, 1H), 2.92 (s, 3H), 2.90–2.86 (m, 1H), 2.66–2.57 (m, 1H) 1.56 (s, 3H), 0.93 (d, J = 6.3, 3H), 0.87 (s, 9H), 0.62 (d, J = 6.7, 3H), 0.09–0.0 (m, 9H).

To a solution of methyl triphenylphosphonium bromide (48.8 mg, 0.137 mmol, 12 equiv) in THF (0.29 mL) at 0 °C was added potassium *tert*-butoxide (15.3 mg, 0.137 mmol, 12 equiv). The resulting mixture was stirred at 0 °C for 30 min then warmed 23 °C. After 30 min the vial was cooled to 0 °C and a solution of aldehyde **26** (5.5 mg, 0.011 mmol) in THF (0.29 mL) was added. After 1 h, the reaction was warmed to 23 °C for 2 h. The reaction is quenched with water (5 mL) and diluted with EtOAc (10 mL). The layers were separated, and then the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (5 mL) and dried over $MgSO_4$. Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (4:1 Hexanes:EtOAc + 2% Et_3N) to provide olefin **27** (2.9 mg, 52% yield) as a light yellow oil. Olefin **27**: R_f 0.3 (5:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): 8.47 (br s, 1H), 7.01 (d, J = 8.0, 1H), 6.85–6.79 (m, 1H), 6.53–6.46 (m,

1H), 6.24–6.10 (m, 2H), 5.33 (dd, *J* = 17.8, 1.2, 1H), 5.22 (dd, *J* = 10.5, 1.2 1H), 4.32 (d, *J* = 10.5, 1H) 4.29–4.21 (m, 1H) 3.63 (dd, *J* = 10.5, 4.2, 1H), 3.49–3.41 (m, 1H), 3.15 (app d, *J* = 17.8, 1H), 2.91 (s, 3H), 2.89–2.72 (m, 1H), 2.68–2.57 (m, 1H), 1.51 (s, 3H), 1.48 (s, 3H), 0.95–0.90 (m, 3H), 0.87 (s, 9H), 0.65 (d, *J* = 6.5, 3H), 0.05 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.2, 149.8, 146.8, 137.6, 122.8, 121.2, 119.2, 118.8, 114.3, 111.4, 106.5, 71.3, 65.5, 55.1, 40.3, 34.1, 33.1, 28.7, 27.4, 26.9, 26.0, 21.7, 19.7, 18.4, -5.2, -5.3; IR (film): 3452, 3380, 2956, 2929, 2858, 1656, 1507 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{28}H_{45}N_3O_2SiNa$, 506.3179; found, 506.3182; $[\alpha]^{20}_D$ –126.00° (c 0.10 CH_2Cl_2).

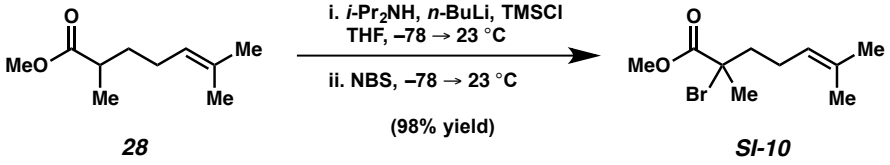


27 ***pendolmycin (2)***

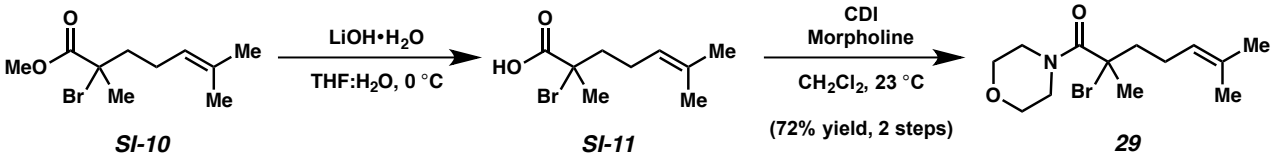
Pendolmycin (2). To a solution of olefin **27** (6.7 mg, 0.014 mmol) in THF (0.276 mL) at 0 °C was added a solution of TBAF in THF (1.0 M, 138 μL, 0.138 mmol, 10 equiv) dropwise over 3 min. The solution was stirred for 15 min, and then quenched with H_2O (2 mL). The biphasic mixture was further diluted with EtOAc (10 mL) and H_2O (5 mL). The layers were separated, and then the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over $MgSO_4$. Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (5:1 CH_2Cl_2:CH_3OH) to provide pendolmycin (**2**) (3.6 mg, 70% yield) as a viscous oil. Spectral data for synthetic **2** was consistent with literature reports.[15] Pendolmycin (**2**): R_f 0.2 (5:1 CH_2Cl_2:CH_3OH); ^{1}H NMR (500 MHz, $CDCl_3$): Major conformer: δ 8.48 (br s, 1H), 7.01 (d, *J* = 8.0, 1H), 6.86–6.82 (m, 1H), 6.48 (d, *J* = 8.0, 1H), 6.19 (dd, *J* = 17.8, 10.5, 1H), 5.32 (dd, *J* = 17.8, 1.4, 1H), 5.21 (dd, *J* = 10.5, 1.0, 1H), 4.34 (d, *J* = 10.0, 1H), 4.36–4.29 (m, 1H), 3.74 (app d, *J* = 12.0, 1H), 3.62–3.39 (m, 2H), 3.39–3.32 (m, 1H), 3.17 (app d, *J* = 17.0, 1H), 3.08 (dd, *J* = 17.0, 4.0, 1H), 2.9 (s, 3H), 2.65–2.55 (m, 1H) 1.51 (s, 3H), 1.48 (s, 3H), 0.92 (d, *J* = 7.0, 3H), 0.64 (d, *J* = 7.0, 3H); Minor conformer [26/31 protons were discernable]: δ 8.72 (br s, 1H), 7.12 (d, *J* = 7.8, 1H), 7.02 (d, *J* = 7.8, 1H), 6.97 (d, *J* = 2.0,

1H), 6.21 (dd, 17.8, 10.5, 1H), 5.37 (dd, J =17.8, 1.4, 1H), 5.27 (dd, J =10.5, 1.4, 1H), 4.48–4.39 (m, 1H), 3.43 (app d, J =7.2, 1H), 3.44–3.39 (dd, J =1.8, 1.4, 1H), 2.99 (d, J =10.5, 1.4, 1H), 2.80 (dd, J = 15.0, 2.0, 1H), 2.73 (s, 3H), 2.44–2.31 (m, 1H), 1.53 (s, 3H), 1.52 (s, 3H), 1.25 (d, J =6.7, 1H), 0.94 (d, J =6.7, 3H).

D. Total syntheses of (–)-lyngbyatoxin A (3) and (–)-teleocidin A-2 (4)

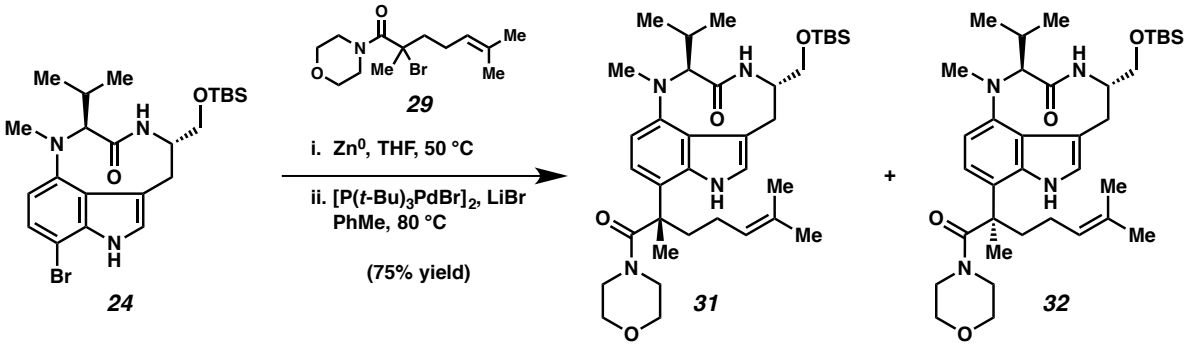


Bromo ester SI-10. α-Bromo methyl ester **SI-10** was prepared following the known protocol described by Webber for the α-bromination of esters, with modifications.[16] A flask containing THF (33.4 mL) and diisopropylamine (2.81 mL, 20.03 mmol, 2.4 equiv) was cooled to –78 °C and then a solution of *n*-BuLi (8.8 mL, 2.55 M in hexanes, 2.7 equiv) was added dropwise over 5 min. The reaction was stirred for an additional 10 min at –78 °C and then warmed to 23 °C over 1 h. The mixture was cooled to –78 °C and TMSCl (2.8 mL, 21.8 mmol, 2.61 equiv) was added dropwise over 5 min. To the resulting clear solution was added ester **28** (1.42 g, 8.35 mmol) as a solution in THF (41.7 mL) over 10 min. The resulting yellow solution was stirred at –78 °C for 20 min and *N*-bromosuccinamide (3.86 g, 21.7 mmol, 2.6 equiv) was added quickly under a stream of nitrogen. The flask was purged with nitrogen for 1 min and allowed to warm to 23 °C in the absence of light over 2.5 h. The reaction was quenched with saturated aqueous NH_4Cl (30 mL) and further diluted with water (200 mL) and Et_2O (200 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 × 200 mL). The organics were combined, washed with brine (50 mL), and dried over $MgSO_4$. Evaporation under reduced pressure provided a crude light yellow oil, which was purified by flash chromatography (60:1 Hexane:Et_2O) to afford bromo ester **SI-10** (2.03 g, 98% yield) as a yellow oil. Bromo ester **SI-10**: ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.12–5.06 (m, 1H), 3.78 (s, 3H), 2.18–1.96 (m, 4H), 1.91 (s, 3H), 1.68 (s, 3H), 1.61 (s, 3H).



α-Bromo amide 29. Carboxylic acid **SI-11** was prepared following the general protocol by Xia for the saponification of methyl esters, with modifications.[17] To a stirred solution of α-bromo methyl ester **SI-10** (12.50 g, 50.1 mmol) in THF (157 mL) at –15 °C was added a solution of lithium hydroxide monohydrate (3.13 g, 74.6 mmol, 1.4 equiv) in H_2O (133 mL) dropwise via syringe pump. After 7 h, the reaction was quenched with 1 M HCl (100 mL) and then diluted with EtOAc (100 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 100 mL). The combined organic layers were dried over $MgSO_4$. Evaporation of the solvent under reduced pressure afforded crude **SI-11**, which was used in the subsequent step without further purification.

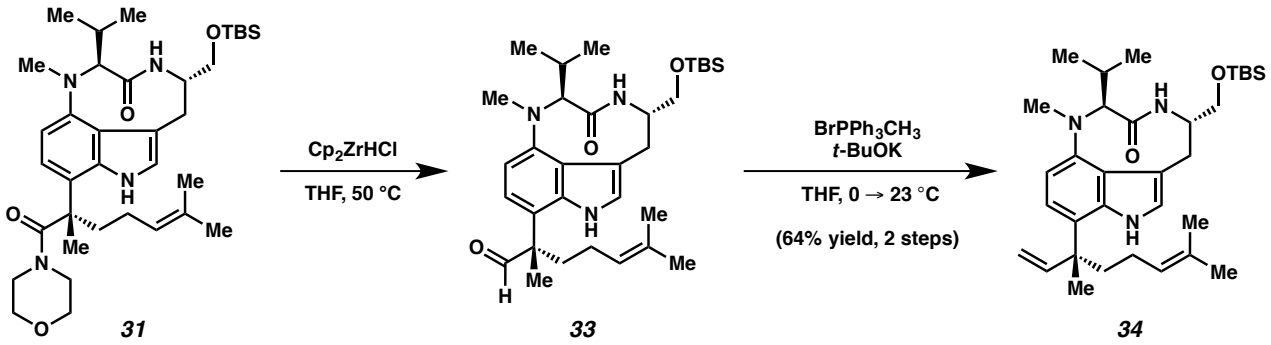
Amide **29** was prepared from crude **SI-11** following a general protocol for the coupling of esters to amines using 1,1'-carbonyldiimidazole, with modifications.[18] To a solution of crude **SI-11** in CH_2Cl_2 (250 mL) was added 1,1'-carbonyldiimidazole (12.99 g, 80.16 mmol, 1.6 equiv). After stirring for 15 min, morpholine (10.83 mL, 125.25 mmol, 2.5 equiv) was added and the reaction was allowed to stir for 6 h. The reaction was quenched with 5% citric acid (400 mL), concentrated in vacuo, and then diluted with H_2O (150 mL) and Et_2O (150 mL). The organic layer was separated, washed with brine (50 mL), and then dried over $MgSO_4$. Evaporation under reduced pressure afforded the crude product, which was purified by flash chromatography (5:1 Hexanes:EtOAc) to afford α-bromo amide **29** (11.0 g, 72% yield, over two steps) as a yellow oil. α-Bromo amide **29**: R_f 0.7 (1:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.11–5.05 (m, 1H), 4.00–3.66 (m, 8H), 2.30–1.90 (m, 7H), 1.68 (s, 3H), 1.61 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.6, 133.1, 122.3, 66.6, 61.4, 43.0, 30.5, 25.7, 24.7, 17.7; IR (neat): 2967, 2916, 2855, 1635, 1418 cm^{-1}; HRMS-ESI (*m/z*) $[M + H]^+$ calculated for $C_{13}H_{22}BrNO_2$, 304.0907; found, 304.0901.



Morpholine amides 31 and 32. Amides **31** and **32** were prepared following the general protocol described by Hartwig for the cross-coupling of α-bromoamides with aryl bromides, with modifications.[12] Inside a glove box, a vial was charged with a magnetic stir bar, α-bromo amide **29** (41.2 mg, 0.135 mmol, 10 equiv), activated zinc dust (8.8 mg, 0.134 mmol, 9.9 equiv), and THF (0.32 mL). The vial was sealed and placed into a heating block maintained at 50 °C for 12 h. This clear, pale yellow solution was removed from the heat and immediately added to a solution of bromoindole **24** (6.7 mg, 0.0135 mmol), LiBr (1.2 mg, 0.0135 mmol, 1.0 equiv) and [P(*t*-Bu)$_3$PdBr]$_2$ (1.6 mg, 2 μmol, 15 mmol%) in toluene (0.2 mL). The resulting solution was stirred at 80 °C for 12 h. The reaction mixture was passed through a silica gel plug (EtOAc eluent) and concentrated in vacuo. The crude residue was separated by preparatory thin layer chromatography (2:1 Hexane:EtOAc) to afford two separate diastereomeric amides **31** (1.8 mg, 43% yield) and **32** (2.4 mg, 32% yield) as light yellow viscous oils. Morpholine amide **31**: R_f 0.7 (2:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (br s, 1H), 6.89 (d, J = 8.2, 1H), 6.82 (br s, 1H), 6.46 (d, J = 8.2, 1H), 6.13 (br s, 1H), 4.40–4.00 (m, 1H), 4.31 (d, J = 10.2, 1H), 4.28–4.20 (m, 1H), 3.65 (dd, J = 10.2, 4.3, 2H), 3.48 (t, J = 9.9, 1H), 3.39–2.70 (m, 14H), 2.69–2.50 (m, 1H), 2.45–1.66 (m, 10H), 0.94–0.91 (m, 4H), 0.88 (s, 9H), 0.54 (br s, 3H), 0.04 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.9, 146.9, 136.8, 124.5, 121.8, 118.7, 114.1, 106.2, 71.3, 67.2, 65.9, 65.6, 61.6, 55.1, 54.5, 47.5, 46.0, 43.7, 38.8, 34.1, 32.9, 29.9, 28.7, 26.0, 25.8, 23.2, 21.7, 20.3, 19.7, 17.6, -5.2, -5.3; IR (film): 3383, 2928, 1664, 1508, 1115 cm^{-1}; HRMS-ESI (*m/z*) $[M + H]^+$ calculated for $C_{36}H_{59}N_4O_4Si$, 639.4305; found, 639.4301; $[\alpha]^{22}_D$ –108.00 (c 0.10 CH_2Cl_2). Morpholine amide **32**: R_f 0.7 (2:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.53 (br s, 1H), 6.95 (d, J = 8.2, 1H), 6.84 (br s, 1H), 6.46 (d, J = 8.2, 1H), 6.14 (br s, 1H), 5.25–5.00 (m, 1H), 4.32 (d, J = 10.0, 1H), 4.24–4.16 (br m, 1H), 3.70–3.42 (m, 1H) 3.64 (dd, J = 10.0, 4.1, 2H), 3.46 (t, J = 9.9, 1H), 3.40–3.0 (m, 6H), 2.90 (dd, J = 17.9, 4.1, 1H) 2.90 (s, 3H), 2.66–

2.51 (m, 1H), 2.35–1.81 (m, 5H), 1.79–1.58 (m, 8H), 0.96–0.89 (m, 4H), 0.87 (s, 9H), 0.52 (d, *J* = 6.6, 3H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) [28/36 carbons were discernable]: δ 175.5, 172.9, 171.3, 147.0, 136.6, 118.7, 114.2, 106.2, 71.2, 67.2, 65.9, 65.5, 60.6, 55.0, 47.5, 34.2, 32.9, 29.8, 29.4, 28.8, 26.0, 21.7, 21.2, 19.7, 18.4, 14.4, -5.2, -5.3; IR (film): 3375, 2928, 1666, 1508, 1115 cm^{-1}; HRMS-ESI (*m/z*) $[M - H]^-$ calculated for $C_{36}H_{57}N_4O_4Si$, 637.4149; found, 637.4147; $[\alpha]^{22}_D$ –106.00 (c 0.10 CH_2Cl_2).

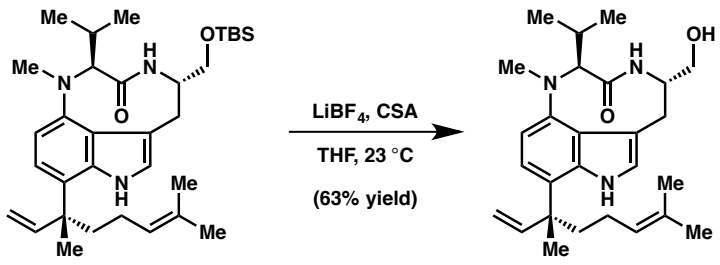
Note: ^{1}H NMR and ^{13}C NMR integrations and peaks were complicated by the presence of major and minor conformers.[19] Empirical data is therefore reported for compounds **31**–**34**, **SI-12** and **SI-13**. Absolute stereochemical configuration for amides **31** and **32** were determined by subjecting each compound to the subsequent synthetic steps and matching each resulting compound to known spectral data for the natural products **3** and **4.**



Olefin 34. Aldehyde **33** was prepared following the general protocol described by Georg for the reduction of tertiary amides, with modifications.[14] Inside a glove box, Cp_2ZrHCl (7.3 mg, 0.03 mmol, 10 equiv) and THF (0.3 mL) were added to a vial containing **31** (1.8 mg, 3 μmol). The reaction vessel was placed into an aluminum block maintained at 50 °C. After stirring for 12 h, the vial was transferred out of the glove box. The reaction mixture was quenched with silica gel (10.0 mg) and EtOAc with 2% Et_3N (1.0 mL), and then stirred for 1 h. The mixture was eluted through a plug of silica gel (EtOAc with 2% Et_3N eluent). Evaporation under reduced pressure afforded crude **33**, which was used in the subsequent step without further purification. Aldehyde **33**: R_f 0.9 (1:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.33 (s, 1H), 8.5 (br s, 1H), 7.05 (d, *J* = 8.2, 1H), 6.83 (b s, 1H), 6.55 (d, *J* = 8.2, 1H), 6.16 (s, 1H), 5.18–5.01 (m, 1H), 4.33 (d, *J* = 9.9, 1H), 4.26–4.08 (m, 1H), 3.78–3.68 (m, 1H), 3.63 (dd, *J* = 10.9, 4.8, 1H), 3.45 (t, *J* = 9.9,

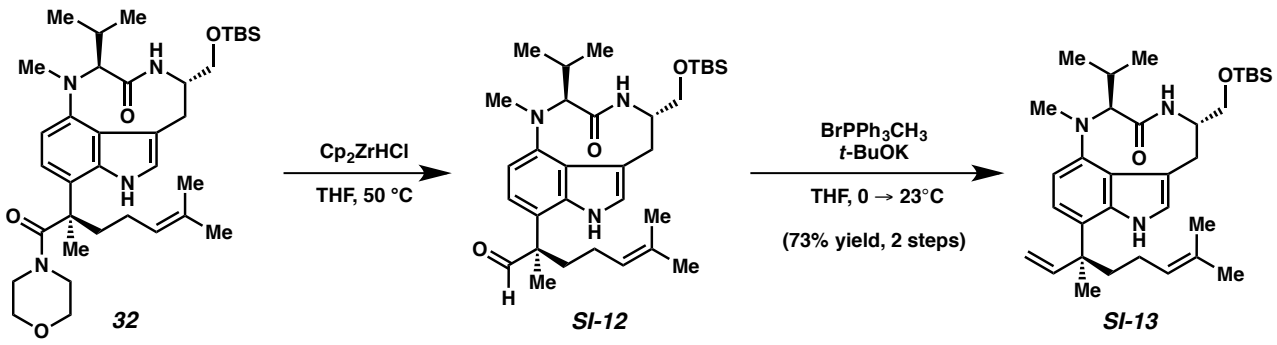
1H), 3.11–3.06 (m, 1H), 2.91 (s, 3H), 2.79–2.49 (m, 2H), 2.43–1.76 (m, 5H), 1.65 (s, 2H), 1.63 (s, 2H), 1.42–1.40 (m, 1H), 0.94–0.88 (m, 9H), 0.86–0.80 (m, 3H), 0.82 (dd, J = 9.9, 6.7, 2H) 0.58 (d, J = 6.7, 3H), 0.05 (s, 3H), 0.02 (s, 3H).

A vial was charged with methyl triphenylphosphonium bromide (266.5 mg, 0.746 mmol, 265 equiv) and placed in a 0 °C bath. To this vial was added a solution of potassium *tert*-butoxide (79.0 mg, 0.704 mmol, 250 equiv) in THF (1.0 mL) dropwise over 2 min, and the resulting yellow mixture was allowed to warm to 23 °C over 30 min. After 1 h, an aliquot of the resulting ylide stock solution (20.0 µl, 5 equiv) was added dropwise to a solution of aldehyde **33** (3 µmol) in THF (0.3 mL) at 0 °C. After 1 h, the reaction was warmed up to 23 °C and stirred for 12 h. The reaction was quenched with water (1 mL) and EtOAc (1 mL). The layers were separated, and then the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over $MgSO_4$. Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (1:199 Acetone:Benzene) to provide olefin **34** (1.0 mg, 64% yield over two steps) as a viscous light yellow oil. Olefin **34**: R_f 0.5 (5:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.54–8.47 (m, 1H), 6.97 (d, J = 8.1, 1H), 6.80 (br s, 1H), 6.48 (d, J = 8.1, 1H), 6.17 (dd, J = 17.6, 10.6, 1H), 6.15 (br s, 1H), 5.36–5.23 (m, 3H), 5.13–5.03 (m, 1H), 4.31 (d, J = 10.0, 1H), 4.24 (dd, J = 10.0, 3.6, 1H), 3.63 (dd, J = 10.0, 3.6, 1H), 3.46 (t, J = 10.0, 1H), 3.13 (d, J = 17.6, 1H), 3.00–2.85 (s, 5H), 2.85–2.73 (m, 1H), 2.65–2.57 (m, 1H), 2.55–1.73 (m, 5H), 1.65 (app s, 2H), 1.49–1.44 (m, 6H), 0.88 (s, 9H), 0.64 (d, J = 6.8, 3H), 0.05 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.3, 148.6, 146.7, 137.7, 131.6, 124.8, 121.6, 121.0 120.1, 118.9, 114.2, 112.6, 106.5, 71.3, 65.5, 55.1, 43.4, 39.8, 38.7, 34.1, 33.0, 32.1, 28.7, 26.0, 24.2, 23.2, 21.7, 19.7, 18.4, 17.7, 14.3, -5.2, -5.3; IR (film): 2927, 2856, 1662, 1508, 1105 cm^{-1}; HRMS-ESI (*m/z*) [M – H]$^-$ calculated for $C_{33}H_{52}N_3O_2Si$, 550.38233; found, 550.38368; $[\alpha]^{20}_D$ –98.00 (c 0.10 CH_2Cl_2).



34 ***lyngbyatoxin A (3)***

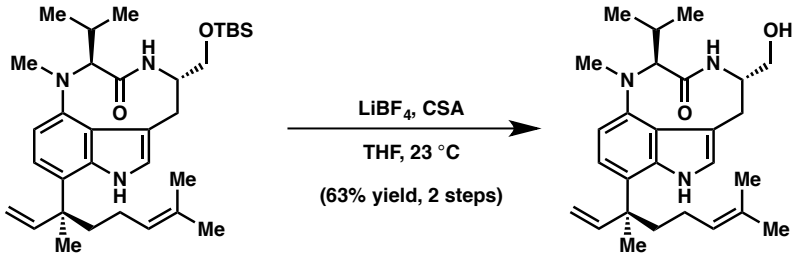
Lyngbyatoxin A (3). Lyngbyatoxin A (**3**) was prepared following the general protocol for desilylation described by Kishi, with modifications.[9] A vial was charged with lithium tetrafluoroborate (85.0 mg, 0.91 mmol, 500 equiv) and CH_3CN (0.91 mL). An aliquot of the resulting mixture (1.0 M, 9 μL, 9 μmol, 5 equiv) was added dropwise to a solution of **34** (1.0 mg, 1.8 μmol) in THF (0.25 mL) over 1 min. After the solution was stirred for 20 min, (±)-camphorsulfonic acid (2.1 mg, 9 μmol, 5 equiv) was added and the reaction was stirred for 24 h at 23 °C. The mixture was diluted with EtOAc (1 mL) and H_2O (1 mL). The layers were separated, and then the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over $MgSO_4$. Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (17:2:1 Hexanes:$CHCl_3$:*i*PrOH) to provide lyngbyatoxin A (**3**) (0.5 mg, 63% yield) as a viscous light yellow oil. Lyngbyatoxin A (**3**): R_f 0.6 (100% EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ (major conformer) 8.52 (br s, 1H), 6.97 (d, *J* = 8.2, 1H), 6.83–6.77 (m, 1H), 6.48 (d, *J* = 8.2, 1H), 6.34 (s, 1H), 6.18 (dd, *J* = 18.0, 10.5, 1H), 5.32 (d, *J* = 18.0, 1H), 5.28 (d, *J* = 10.5, 1H), 5.12–5.02 (m, 1H), 4.30 (d, *J* = 10.0, 1H), 4.29– 4.20 (m, 1H), 3.75 (dd, *J* = 10.7, 4.2 1H), 3.54–3.50 (m, 1H), 3.18 (br d, *J* = 17.0, 1H), 2.99 (dd, *J* = 15.0, 11.0, 1H), 2.91 (s, 3H), 2.58 (dqq, *J* = 10.7, 6.5, 6.5, 1H), 2.04–2.16 (m, 5H), 1.65 (s, 3H), 1.47 (s, 3H), 1.44 (s, 3H) 0.92 (d, *J* = 6.5, 3H), 0.64 (d, *J* = 6.5, 3H); δ (minor conformer) [27/39 protons were discernable] 8.76 (br s, 1H), 7.10 (d, *J* = 8.0, 1H), 7.01 (d, *J* = 8.0, 1H), 5.34 (d, *J* = 18.0, 1H), 4.46–4.40 (m, 1H), 3.46 (dd, *J* = 11.0, 6.7, 1H), 3.38 (dd, *J* = 11.0, 6.7, 1H), 2.80 (dd, *J* = 15.0, 1.5, 1H), 2.74 (s, 3H), 2.39 (dqq, *J* = 10.8, 6.5, 6.5, 1H), 1.63 (s, 3H), 1.50 (s, 3H), 1.49 (s, 3H), 1.25 (d, *J* = 6.5, 3H), 0.97 (d, *J* = 6.5, 3H).



Olefin SI-13. Aldehyde **SI-12** was prepared following the general protocol described by Georg for the reduction of tertiary amides, with modifications.[14] Inside a glove box, Cp_2ZrHCl (7.7 mg, 0.03 mmol, 10 equiv) and THF (0.3 mL) were added to a vial containing **32** (1.9 mg, 3 μmol). The reaction vessel was placed into an aluminum block maintained at 50 °C. After stirring for 12 h, the vial was transferred out of the glove box. The reaction mixture was quenched with silica gel (10.0 mg) and EtOAc with 2% Et_3N (1.0 mL), and then stirred for 1 h. The mixture was eluted through a plug of silica gel (EtOAc with 2% Et_3N eluent). Evaporation under reduced pressure afforded crude **SI-12**, which was used in the subsequent step without further purification. Aldehyde **SI-12**: R_f 0.9 (1:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.33 (s, 1H), 8.5 (br s, 1H), 7.04 (d, J = 8.4, 1H), 6.84 (m, 1H), 6.55 (d, J = 8.4, 1H), 6.16 (s, 1H), 5.15–4.98 (m, 1H), 4.47–3.97 (m, 2H), 4.43 (d, J = 10.0, 1H), 3.78–3.68 (m, 1H), 3.61 (dd, J = 10.0, 4.3, 2H), 3.44 (t, J = 10.0, 1H), 3.17–3.10 (m, 2H), 2.91 (s, 3H), 2.79–2.54 (m, 3H), 2.23–1.81 (m, 5H), 1.41 (s, 3H), 0.87 (m, 9H), 0.77 (dd, J = 10.0, 6.7, 3H) 0.57 (d, J = 6.7, 3H), 0.05 (s, 3H), 0.02 (s, 3H).

A vial was charged with methyl triphenylphosphonium bromide (117.0 mg, 0.328 mmol, 110 equiv) and placed in a 0 °C bath. To this vial was added a solution of potassium *tert*-butoxide (33.3 mg, 0.297 mmol, 100 equiv) in THF (1.0 mL) dropwise over 2 min and the resulting yellow mixture was allowed to warm to 23 °C over 30 min. After 1 h, an aliquot of the resulting ylide stock solution (50.0 μl, 5 equiv) was added dropwise to a solution of aldehyde **SI-12** (3 μmol) in THF (0.3 mL) at 0 °C. After 1 h, the reaction was warmed up to 23 °C and stirred for 12 h. The reaction was quenched with water (1 mL) and EtOAc (1 mL). The layers were separated, and then the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over $MgSO_4$. Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (1:199 Acetone:Benzene) to

provide olefin **SI-13** (1.2 mg, 73% yield over two steps) as a viscous light yellow oil. Olefin **SI-13**: R_f 0.5 (5:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.54 (br m, 1H), 6.98 (d, J = 8.1, 1H), 6.82 (br s, 1H), 6.49 (d, J = 8.1, 1H), 6.21 (dd, J = 17.6, 10.6, 1H), 6.15 (br s, 1H), 5.32–5.22 (m, 2H), 5.13–5.01 (m, 1H), 4.31 (d, J = 10.1, 1H), 4.25 (m, 1H), 3.63 (dd, J = 10.1, 4.5, 1H), 3.45 (t, J = 10.1, 1H), 3.13 (d, J = 17.7, 1H), 2.91 (s, 3H), 2.88–2.74 (m, 2H), 2.66–2.54 (m, 1H), 2.10–1.70 (m, 3H), 1.65–1.61 (m, 2H), 1.45 (s, 2H), 1.43 (s, 1H), 1.38 (s, 2H), 0.88 (s, 9H), 0.85 (dd, J = 6.8, 4.5, 2H), 0.83–0.78 (m, 1H), 0.75 (dd, J = 4.5, 6.8, 2H), 0.60 (d, J = 6.8, 3H), 0.05 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.2, 149.3, 146.7, 137.6, 131.6, 124.7, 121.2, 120.4, 118.7, 114.1, 112.2, 106.0, 71.3, 65.5, 55.0, 43.5, 39.6, 38.1, 34.2, 32.9, 32.1, 28.7, 26.0, 24.9, 23.3, 22.7, 21.8, 19.6, 18.4, 17.5, 14.3, -5.2, -5.3; IR (film): 2927, 2854, 1662, 1466, 1105 cm^{-1}; HRMS-ESI (*m/z*) [M – H]$^-$ calculated for $C_{33}H_{52}N_3O_2Si$, 550.38233; found, 550.38371; $[\alpha]^{20}_D$ –136.00 (c 0.10 CH_2Cl_2).



SI-13 ***teleocidin A-2 (4)***

Teleocidin A-2 (4). Teleocidin A-2 (**4**) was prepared following the general protocol for desilylation described by Kishi, with modifications.[9] A vial was charged with lithium tetrafluoroborate (63.7 mg, 0.68 mmol, 250 equiv) and CH_3CN (0.68 mL). An aliquot of the resulting mixture (1.0 M, 14 μL, 14 μmol, 5 equiv) was added dropwise to a solution of **SI-13** (1.5 mg, 3 μmol) in THF (0.25 mL) over 1 min. After the solution was stirred for 20 min, (±)-camphorsulfonic acid (3.2 mg, 14 μmol, 5 equiv) was added and the reaction was stirred for 24 h at 23 °C. The mixture was diluted with EtOAc (1 mL) and H_2O (1 mL). The layers were separated, and then the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over $MgSO_4$. Evaporation under reduced pressure afforded the crude product, which was further purified by flash chromatography (17:2:1 Hexanes:$CHCl_3$:*i*PrOH) to provide teleocidin A-2 (**4**) (0.5 mg, 63% yield) as a viscous light yellow oil. Teleocidin A-2 (**4**):

R_f 0.6 (100% EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ (major conformer) 8.53 (br s, 1H), 6.98 (d, *J* = 8.1, 1H), 6.83–6.80 (m, 1H), 6.49 (d, *J* = 8.1, 1H), 6.20 (dd, *J* = 18.0, 10.5, 1H), 5.30 (d, *J* = 18.0, 1H), 5.26 (d, *J* = 10.5, 1H), 5.10–5.05 (m, 1H), 4.34 (d, *J* = 10.5, 1H), 4.37– 4.30 (m, 1H), 3.72 (dd, *J* = 10.8, 4.0 1H), 3.54–3.44 (m, 1H), 3.18 (br d, *J* = 17.0, 1H), 2.96 (dd, *J* = 17.0, 4.0 1H), 2.92 (s, 3H) 2.60 (dqq, *J* = 10.8, 6.5, 6.5, 1H), 2.51–1.69 (m, 6H), 1.62 (s, 3H), 1.45 (s, 3H), 1.39 (s, 3H) 0.92 (d, *J* = 6.5, 3H), 0.60 (d, *J* = 6.5, 3H); δ (minor conformer) [31/39 protons were discernable] 8.75 (br s, 1H), 7.09 (d, *J* = 8.0, 1H), 7.01 (d, *J* = 8.0, 1H), 6.97 (s, 1H), 6.22 (dd, *J* = 17.9, 10.3, 1H), 5.35 (*J* = 17.9, 1H), 5.33 (d, *J* = 11.0, 1H), 5.12–5.02 (m, 1H) 4.48–4.39 (m, 1H), 3.46 (dd, *J* = 11.0, 6.5, 1H), 3.39 (dd, *J* = 11.0, 6.5, 1H), 2.80 (dd, *J* = 15.0, 1.5, 1H), 2.73 (s, 3H), 2.39 (dqq, *J* = 11.0, 6.5, 6.5, 1H), 1.65 (s, 3H), 1.47 (s, 3H), 1.42 (s, 3H), 1.25 (d, *J* = 6.5, 3H), 0.94 (d, *J* = 6.5, 3H).

References

[1] Im, G-Y. J.; Bronner, S. M.; Goetz, A. E.; Paton, R. S.; Cheong, P.H.-Y.; Houk, K. N.; Garg, N. K. *J. Am. Chem. Soc.* **2010**, *132*, 1267–1269.

[2] Igarashi, Y.; Yanagisawa, E.; Ohshima, T.; Takeda, S.; Aburada, M.; Miyamoto, K. *Chem. Pharm. Bull.* **2007**, *55*, 328–333.

[3] Kauch, M.; Hoppe, D. *Can. J. Chem.* **2001**, *79*, 1736–1746.

[4] Kauch, M.; Snieckus, V.; Hoppe, D. *J. Org. Chem.* **2005**, *70*, 7149–7158.

[5] Griffen, E. J.; Roe, D. G.; Snieckus, V. *J. Org. Chem.* **1995**, *60*, 1484–1485.

[6] Bronner, S. M.; Goetz, A. E.; Garg, N. K. *J. Am. Chem. Soc.* **2011**, *133*, 3832–3835.

[7] Angelini, E.; Balsamini, C.; Bartoccini, F.; Lucarini, S.; Piersanti, G. *J. Org. Chem.* **2008**, *73*, 5654–5657.

[8] Masuda, T.; Nakatsuka, S.-i.; Goto, T. *Agric. Biol. Chem.* **1989**, *53*, 2257–2260.

[9] Moreno, O. A.; Kishi, Y. *Bioorg. Med. Chem.* **1998**, *6*, 1243–1254.

[10] (a) Hama, T.; Liu, X.; Culkin, D. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 11176–11177. (b) Liu, X.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 5182–5191.

[11] Dobbs, A. *J. Org. Chem.* **2001**, *66*, 638–641.

[12] Hama, T.; Culkin, D. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 4976–2985.

[13] Moreno, O. A.; Kishi, Y. *J. Am. Chem. Soc.* **1996**, *118*, 8180–8181.

[14] Georg, G.; White, J.; Tunoori, A. *J. Am. Chem. Soc.* **2000**, *122*, 11995–11996.

[15] (a) Muratake, H.; Natsume, M.; Okabe, K. *Tetrahedron* **1990**, *46*, 5113–5120. (b) Okabe, K.; Natsume, M. *Tetrahedron* **1991**, *47*, 7615–7624.

[16] Webber, M. J.; Weston, M.; Grainger, D. M.; Lloyd, S.; Warren, S. A.; Powell, W. L.; Alanine, A.; Stonehouse, J. P., Frampton, C. S.; White, A. J. P.; Spivey, A. C. *Synlett* **2011**, *18*, 2693–2696.

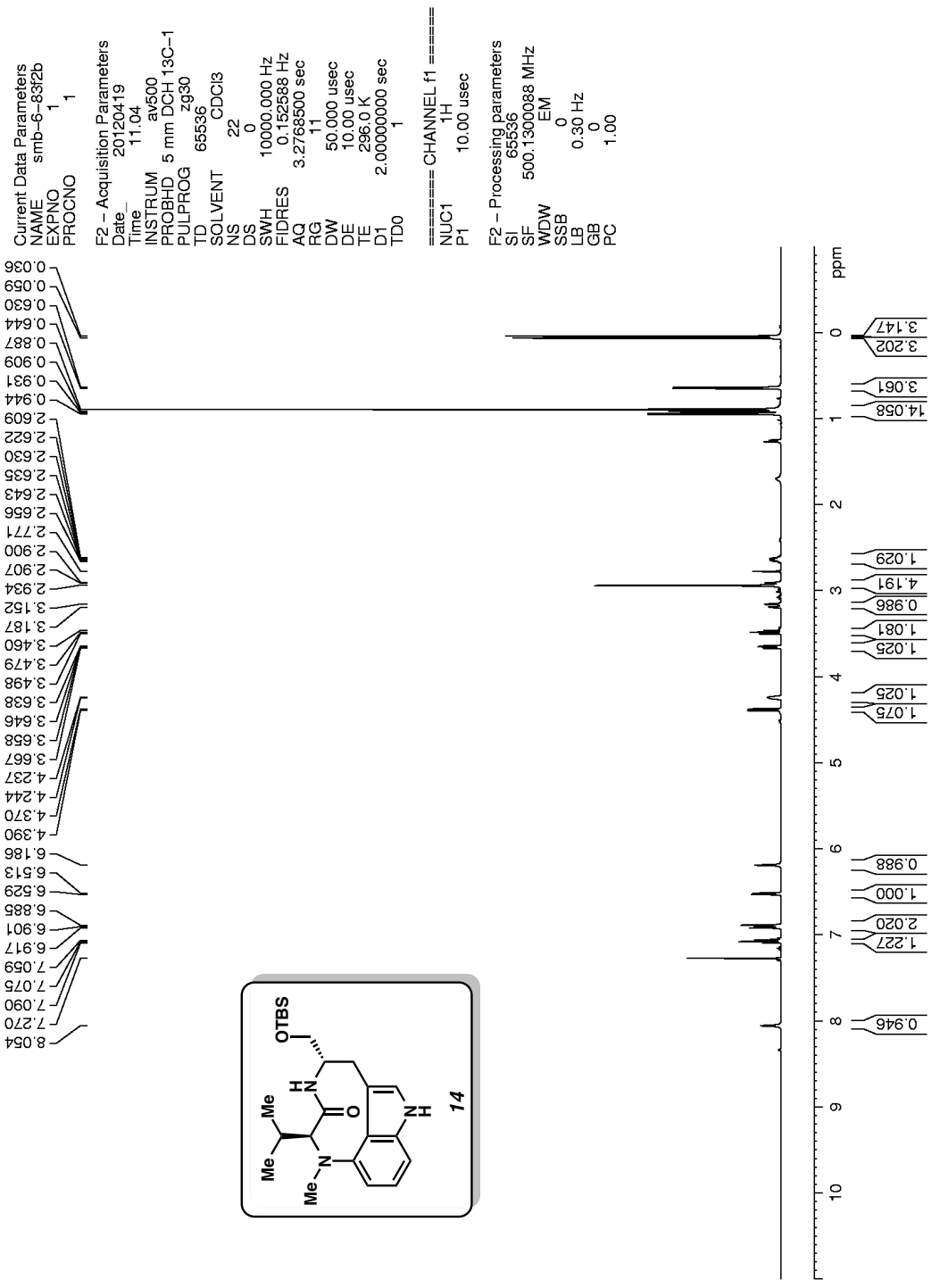
[17] Jelf, C. P.; Salmon, R. (Syngenta LTD, USA). Quinolin-, isoquinolin-, and quinazolin-oxyalkylamides and their use as fungicides. US Patent 0,072,884, March 29, 2007.

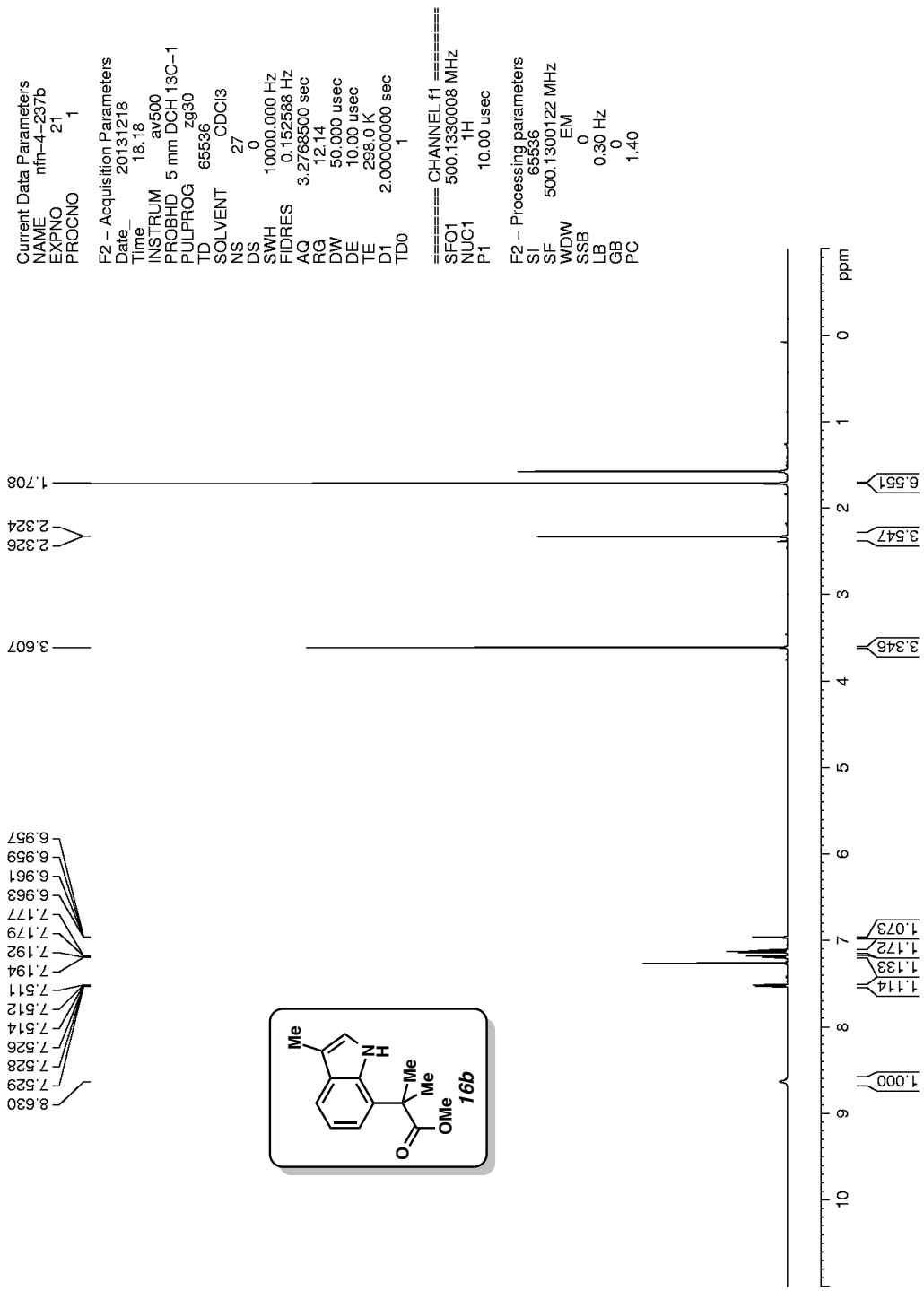
[18] Garg, N. K.; Caspi, D. D.; Stoltz, B. M. *J. Am. Chem. Soc.* **2005**, *127*, 5970–5978.

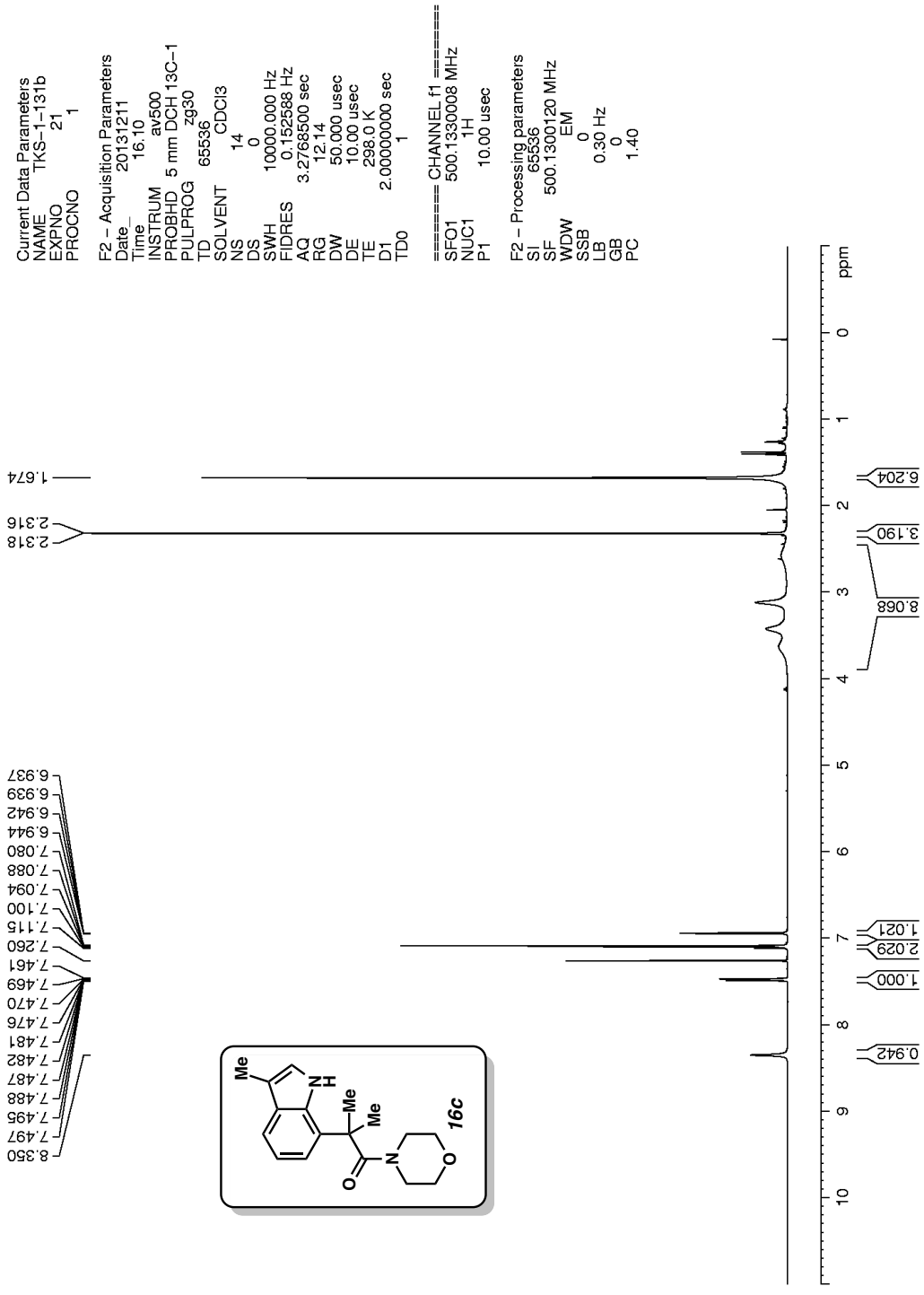
[19] For a discussion on conformational analysis of indolactam alkaloids, see: (a) Endo, Y.; Hasegawa, M.; Itai, A.; Shudo, K.; Tori, M.; Asakawa, Y.; Sakai, S.-i. *Tetrahedron Lett.* **1985**,

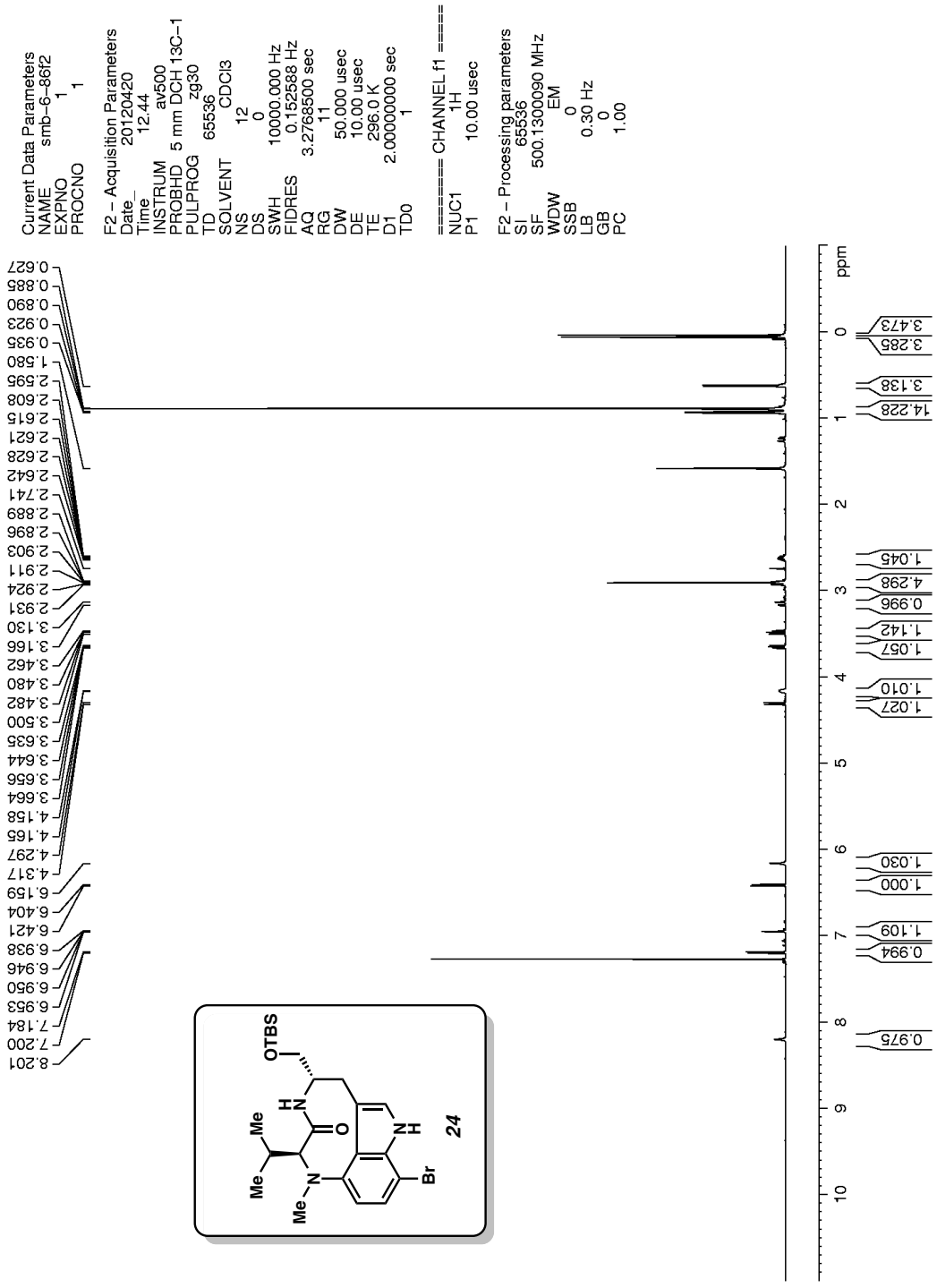
26, 1069–1072. (b) Kawai, T.; Ichinose, T.; Endo, Y.; Shudo, K.; Itai, A. *J. Med. Chem.* **1992**, *35*, 2248–2253.

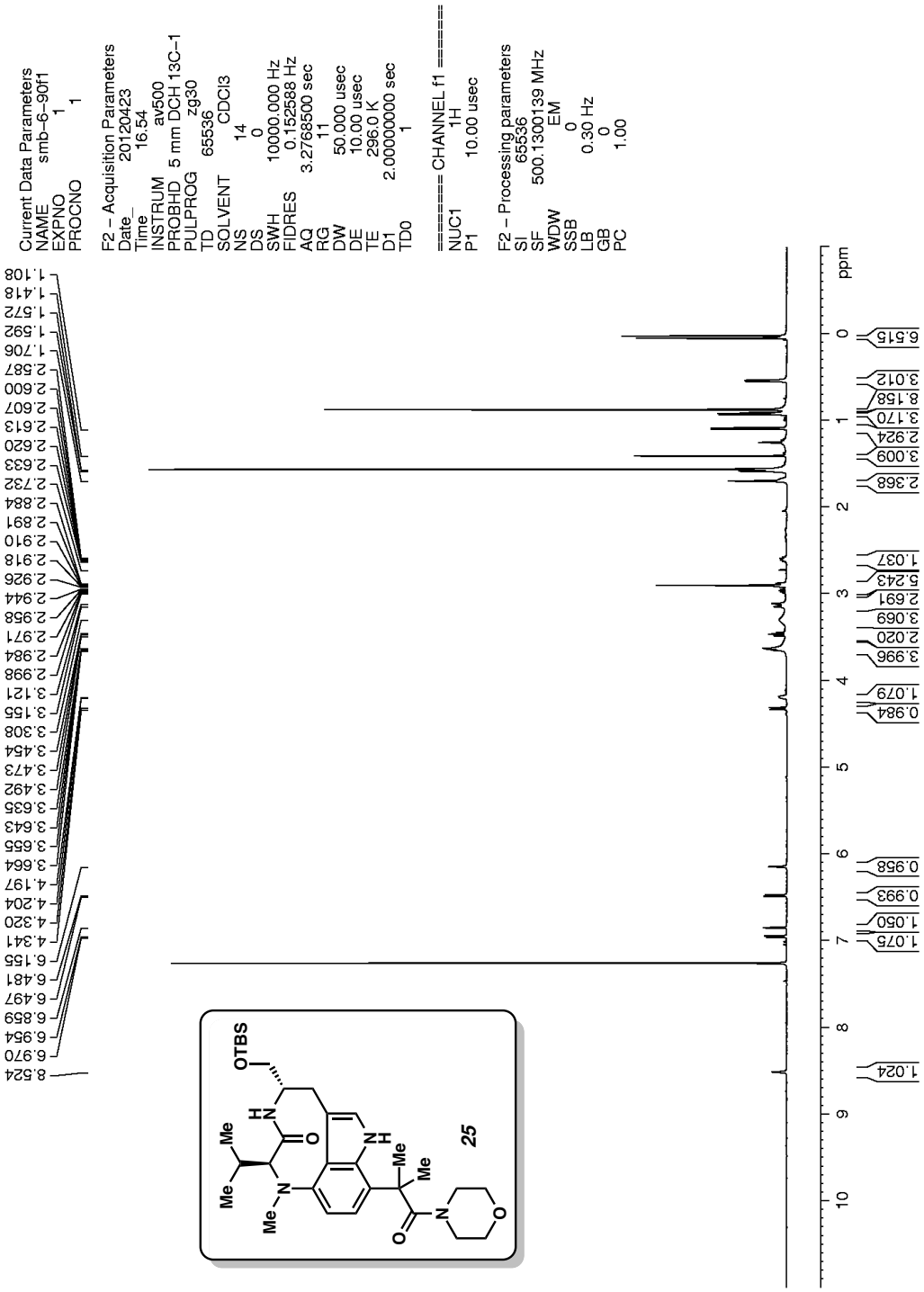
^{1}H NMR Spectra:

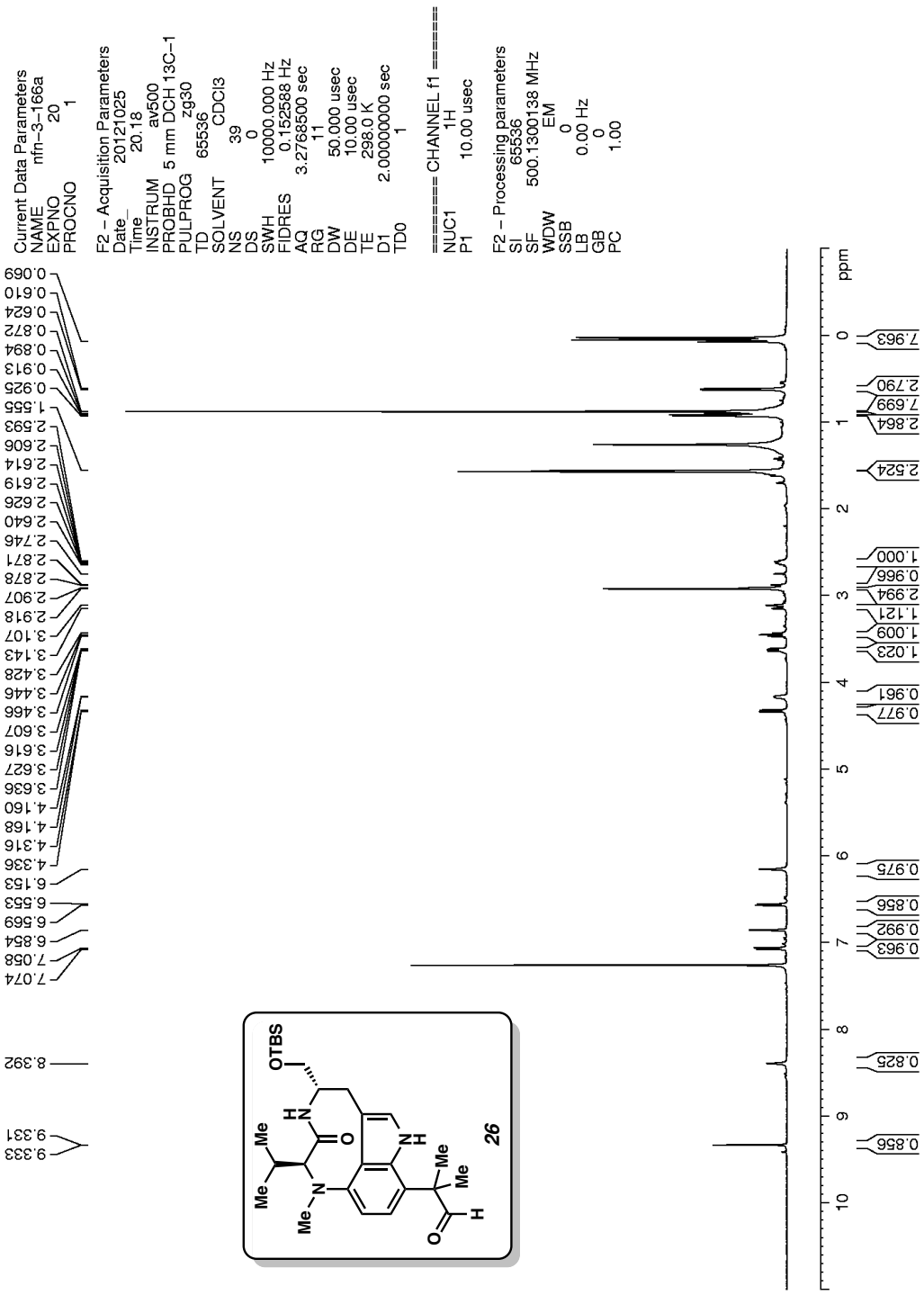

Current Data Parameters
NAME smb-6-83f2b
EXPNO 1
PROCNO 1
F2 – Acquisition Parameters
Date_ 20120419
Time 11.04
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 22
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 11
DW 50.000 usec
DE 10.00 usec
TE 296.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 10.00 usec
F2 – Processing parameters
SI 65536
SF 500.1300088 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OTBS
Me
Me
Me
N
H
N
O
H
N
14
ppm
3.147
3.202
14.058
3.061
1.029
4.191
0.986
1.081
1.025
1.075
1.025
0.988
1.000
2.020
1.227
0.946

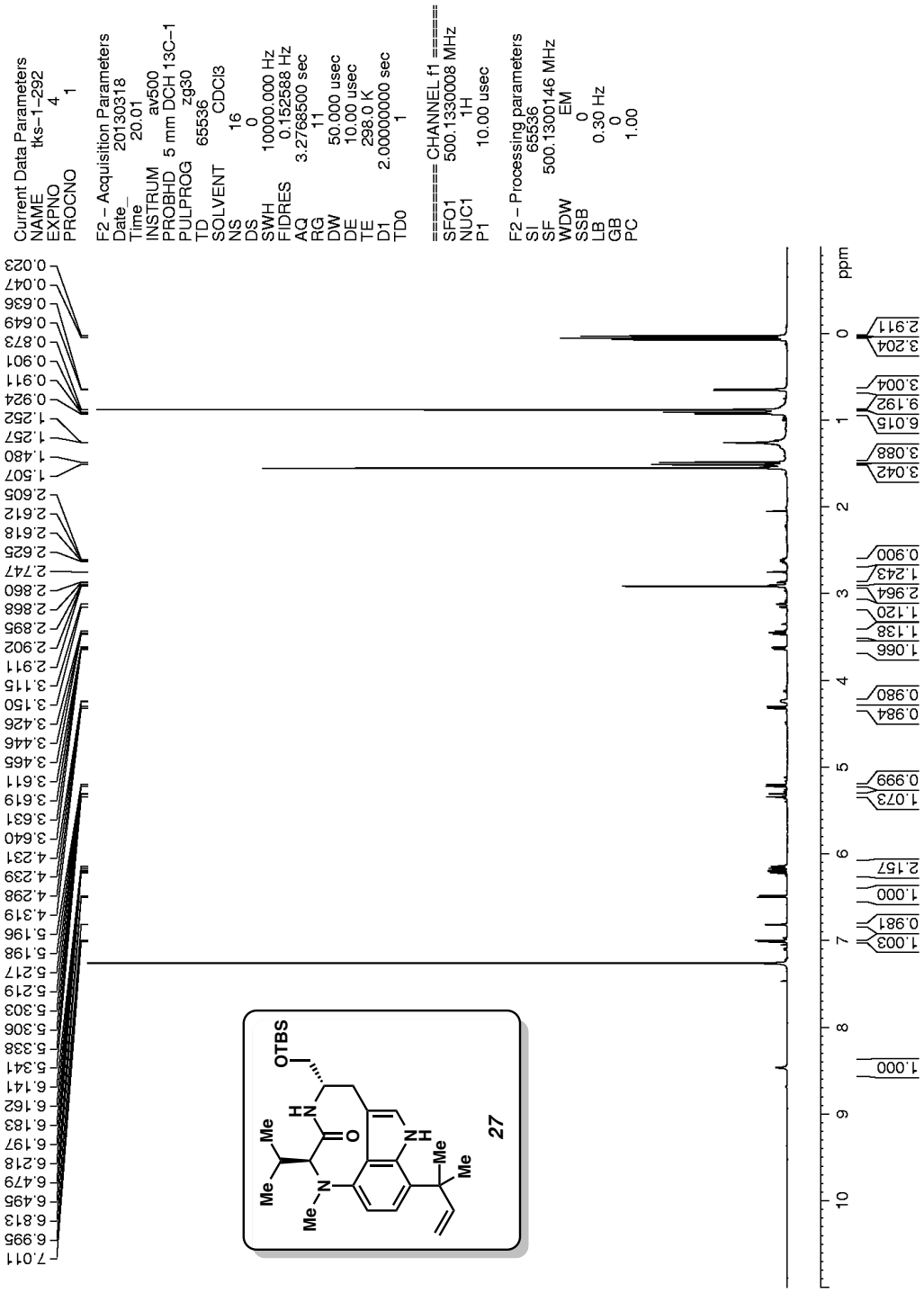

Current Data Parameters
NAME nfn-4-237b
EXPNO 21
PROCNO 1
F2 – Acquisition Parameters
Date_ 20131218
Time 18.18
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 27
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 12.14
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
F2 – Processing parameters
SI 65536
SF 500.1300122 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
1.708
2.324
2.326
3.607
6.957
6.959
6.961
6.963
7.177
7.179
7.192
7.194
7.511
7.512
7.514
7.526
7.528
7.529
8.630
Me
N
H
Me
Me
OMe
O
16b
6.551
3.547
3.346
1.073
1.172
1.133
1.114
1.000
ppm

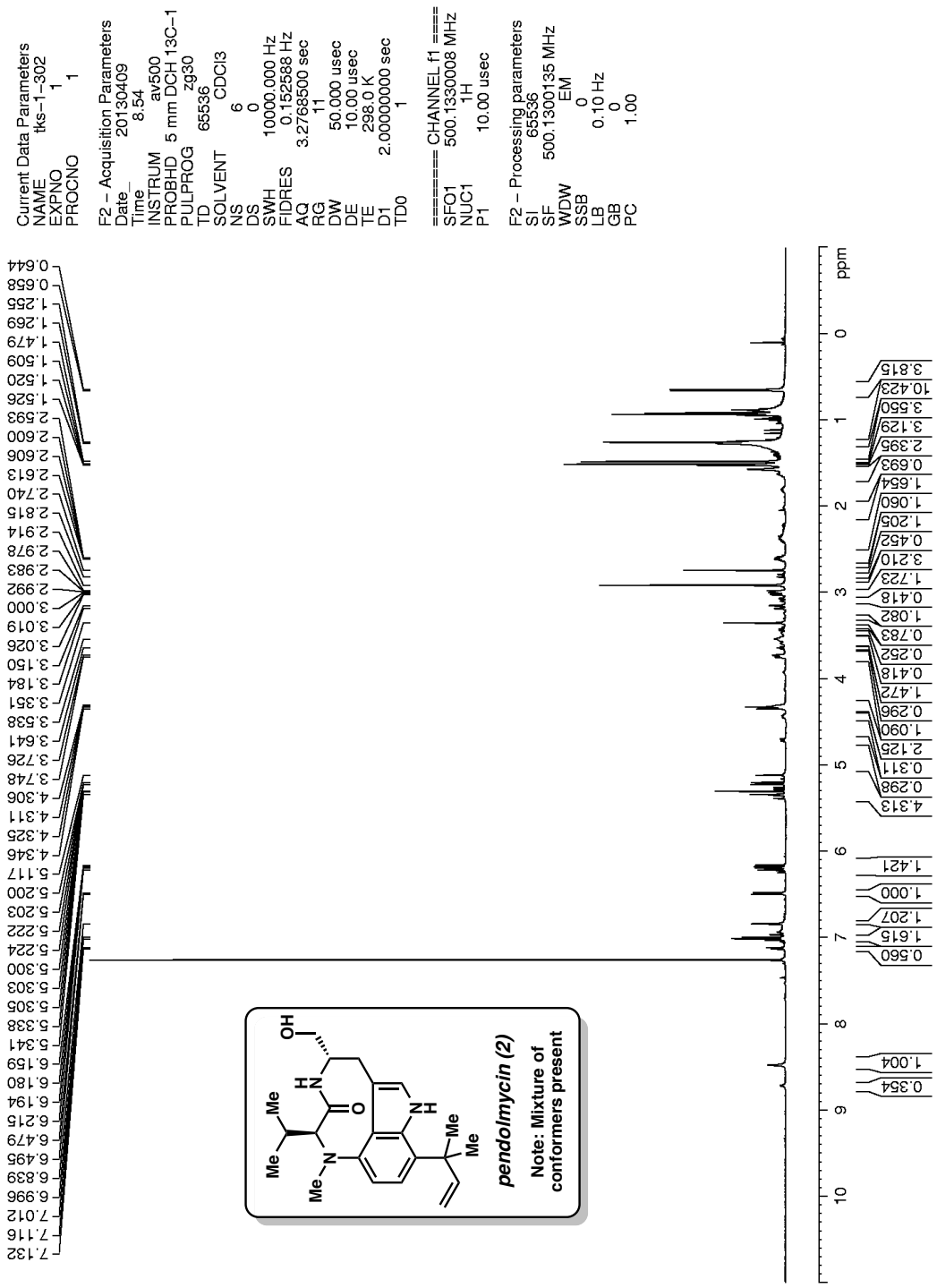

Current Data Parameters
NAME TKS-1-131b
EXPNO 21
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131211
Time 16.10
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 14
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 12.14
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
F2 - Processing parameters
SI 65536
SF 500.1300120 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
1.674
2.316
2.318
6.937
6.939
6.942
6.944
7.080
7.088
7.094
7.100
7.115
7.260
7.461
7.469
7.470
7.476
7.481
7.482
7.487
7.488
7.495
7.497
8.350
Me
N
H
Me
Me
O
N
O
16c
6.204
3.190
8.068
1.021
2.029
1.000
0.942
ppm

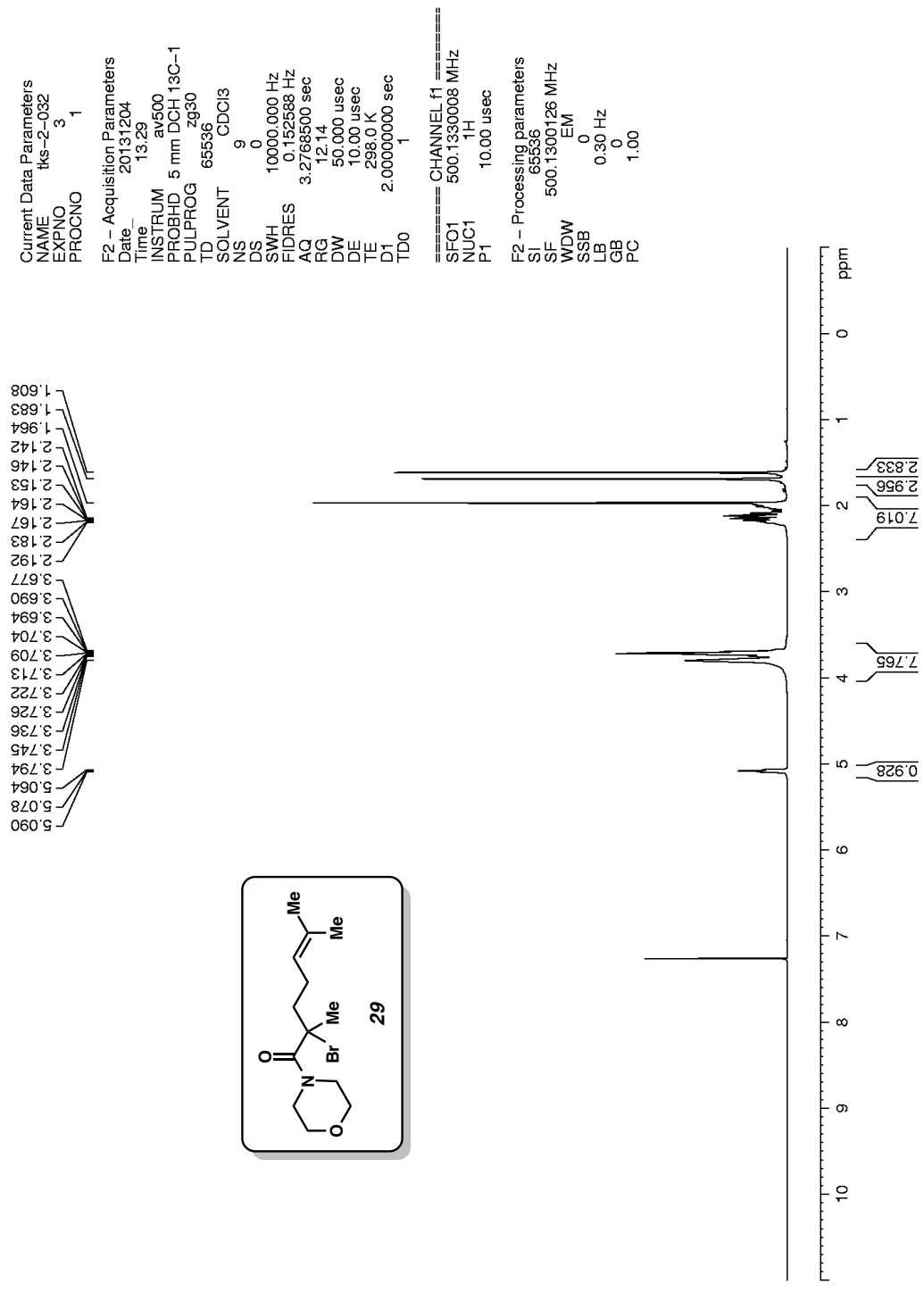

Current Data Parameters
NAME smb–6–86f2
EXPNO 1
PROCNO 1
F2 – Acquisition Parameters
Date_ 20120420
Time 12.44
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 12
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 11
DW 50.000 usec
DE 10.00 usec
TE 296.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 10.00 usec
F2 – Processing parameters
SI 65536
SF 500.1300090 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.201
7.200
7.184
6.953
6.950
6.946
6.938
6.421
6.404
6.159
4.317
4.297
4.165
4.158
3.664
3.656
3.644
3.635
3.500
3.482
3.480
3.462
3.166
3.130
2.931
2.924
2.911
2.903
2.896
2.889
2.741
2.642
2.628
2.621
2.615
2.608
2.595
1.580
0.935
0.923
0.890
0.885
0.627
OTBS
H
N
O
N
H
Me
Me
Me
N
Br
24
ppm
0
1
2
3
4
5
6
7
8
9
10
3.473
3.285
3.138
14.228
1.045
4.298
0.996
1.142
1.057
1.010
1.027
1.030
1.000
1.109
0.994
0.975

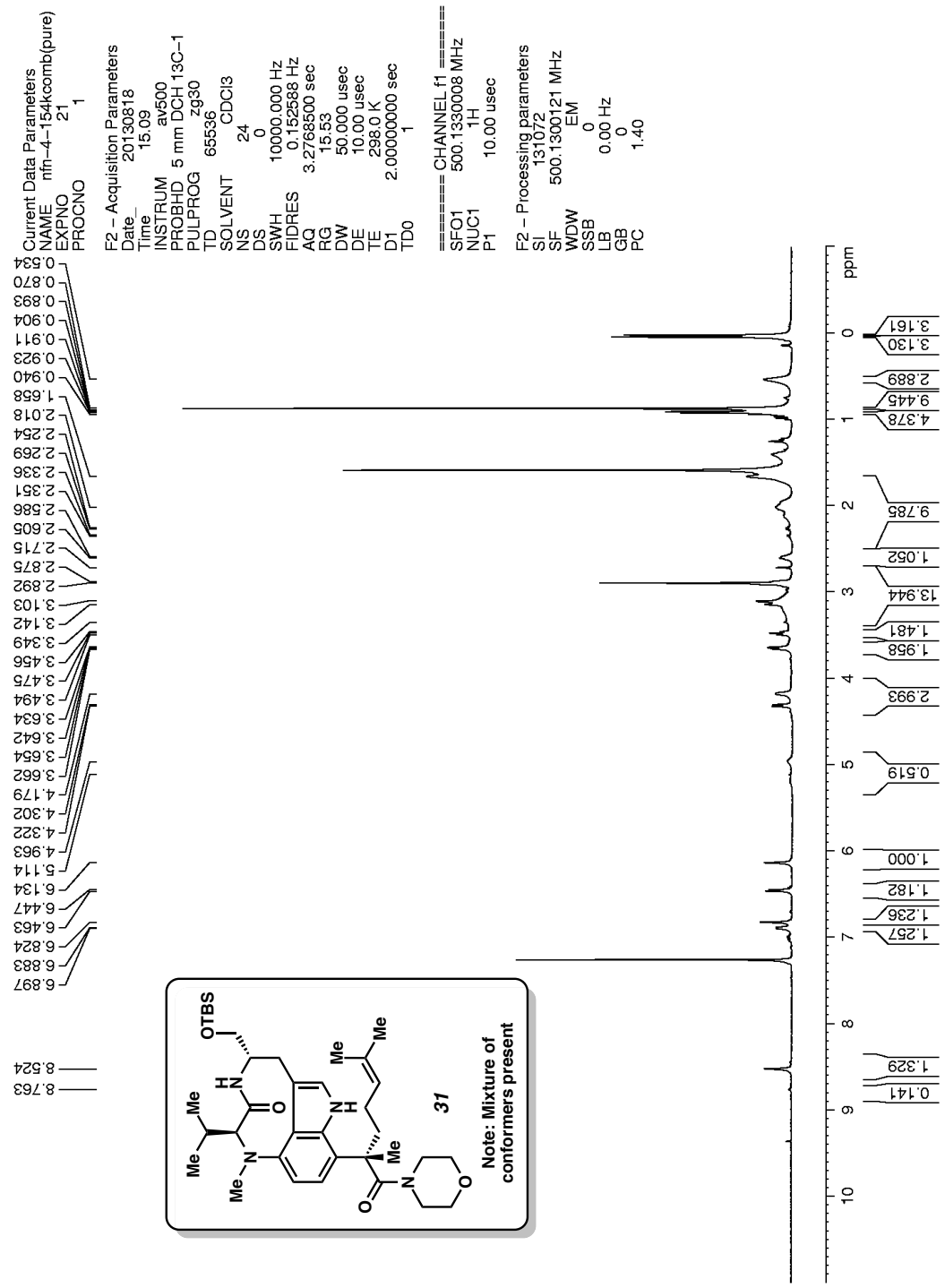

Current Data Parameters
NAME smb-6-90f1
EXPNO 1
PROCNO 1
F2 – Acquisition Parameters
Date_ 20120423
Time_ 16.54
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 14
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 11
DW 50.000 usec
DE 10.00 usec
TE 296.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 10.00 usec
F2 – Processing parameters
SI 65536
SF 500.1300139 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OTBS
Me
Me
Me
Me
Me
25
ppm
6.515
3.012
8.158
3.170
2.924
3.009
2.368
1.037
5.243
2.691
3.069
2.020
3.996
0.984
1.079
0.958
0.993
1.050
1.075
1.024

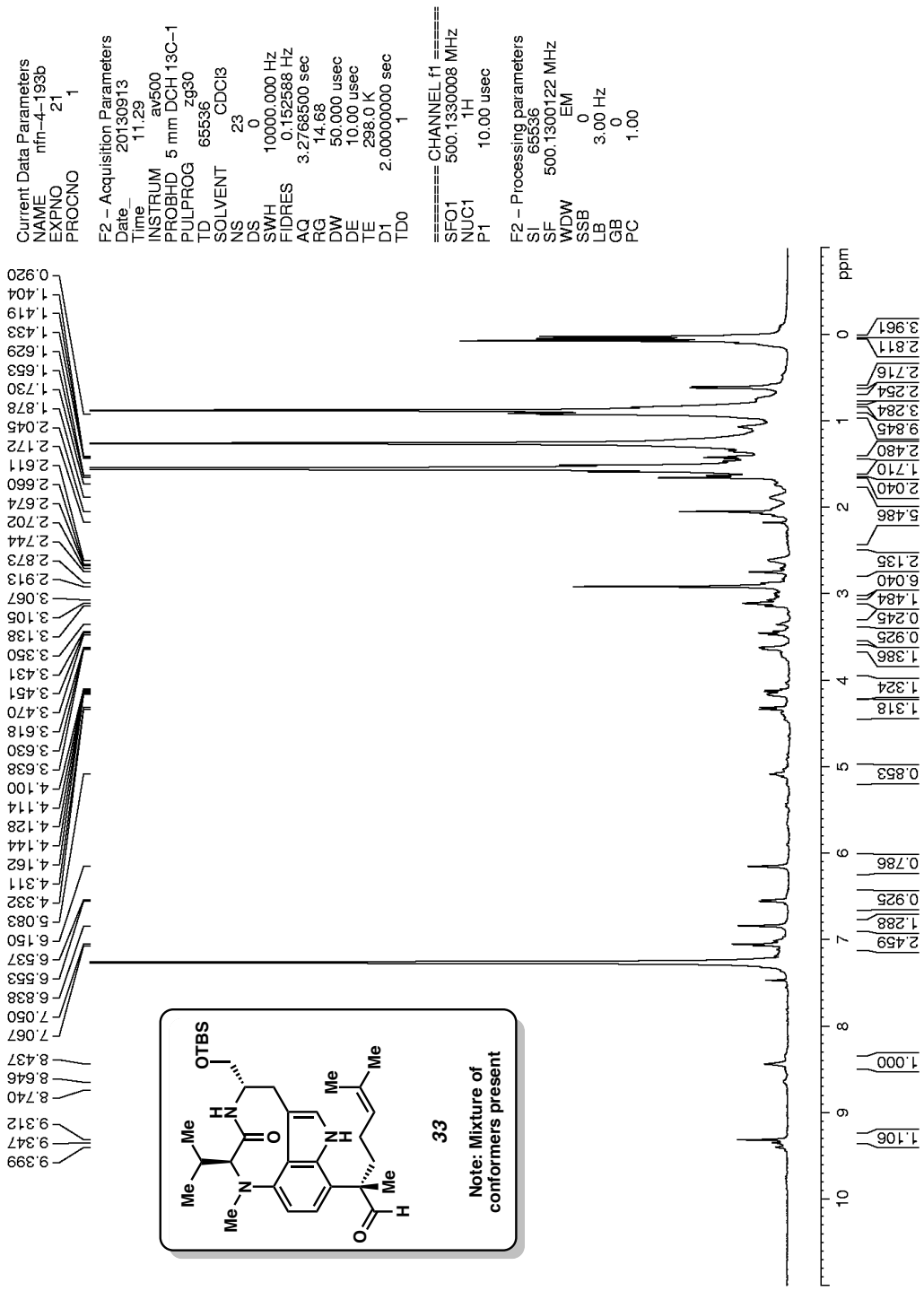

Current Data Parameters
NAME nfn-3-166a
EXPNO 20
PROCNO 1
F2 – Acquisition Parameters
Date_ 20121025
Time 20.18
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 39
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 11
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 10.00 usec
F2 – Processing parameters
SI 65536
SF 500.1300138 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
OTBS
Me
Me
Me
Me
H
N
O
N
H
O
H
26
ppm

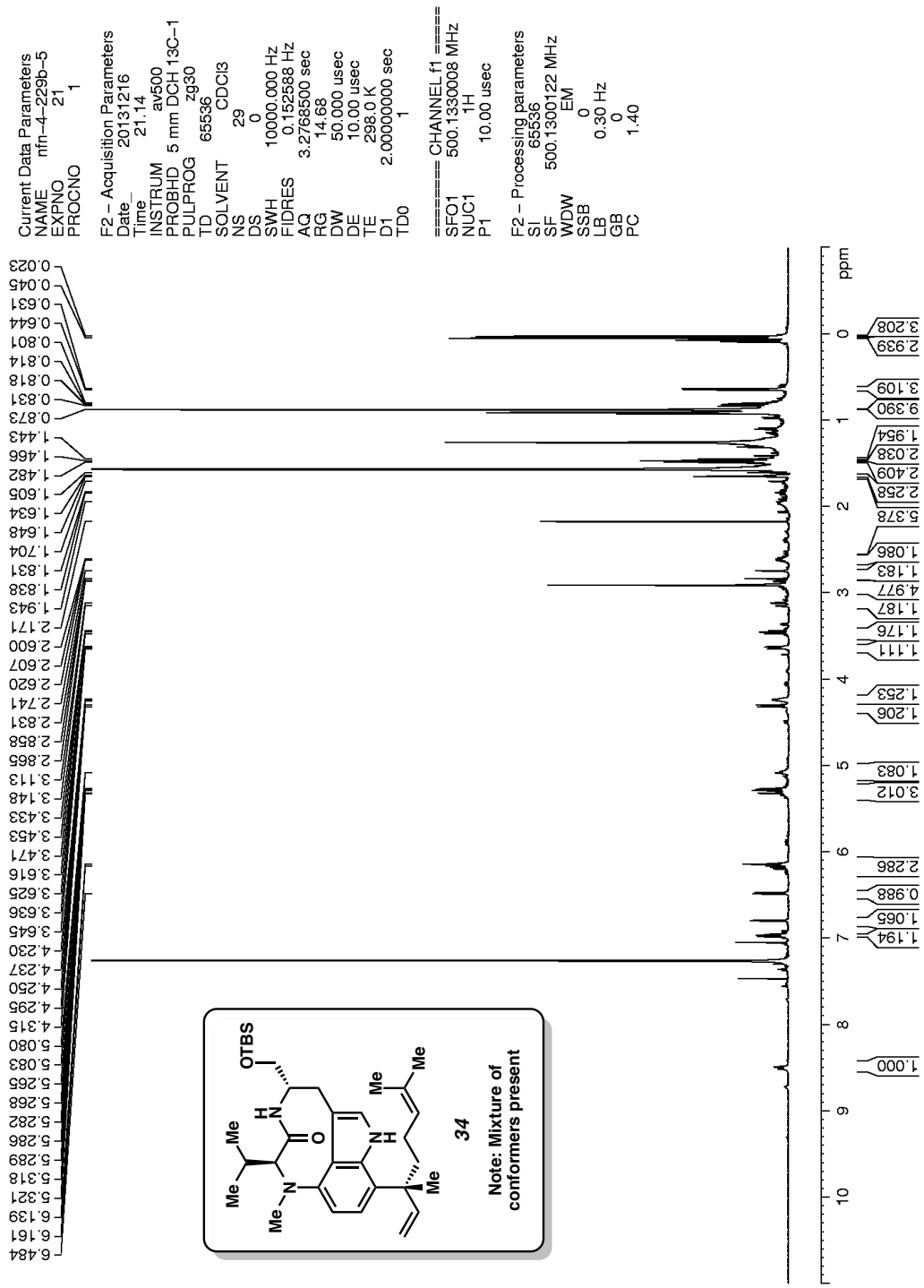

Current Data Parameters
NAME tks–1–292
EXPNO 4
PROCNO 1
F2 – Acquisition Parameters
Date_ 20130318
Time 20.01
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 11
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ======
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
F2 – Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OTBS
Me
Me
Me
Me
Me
27
ppm

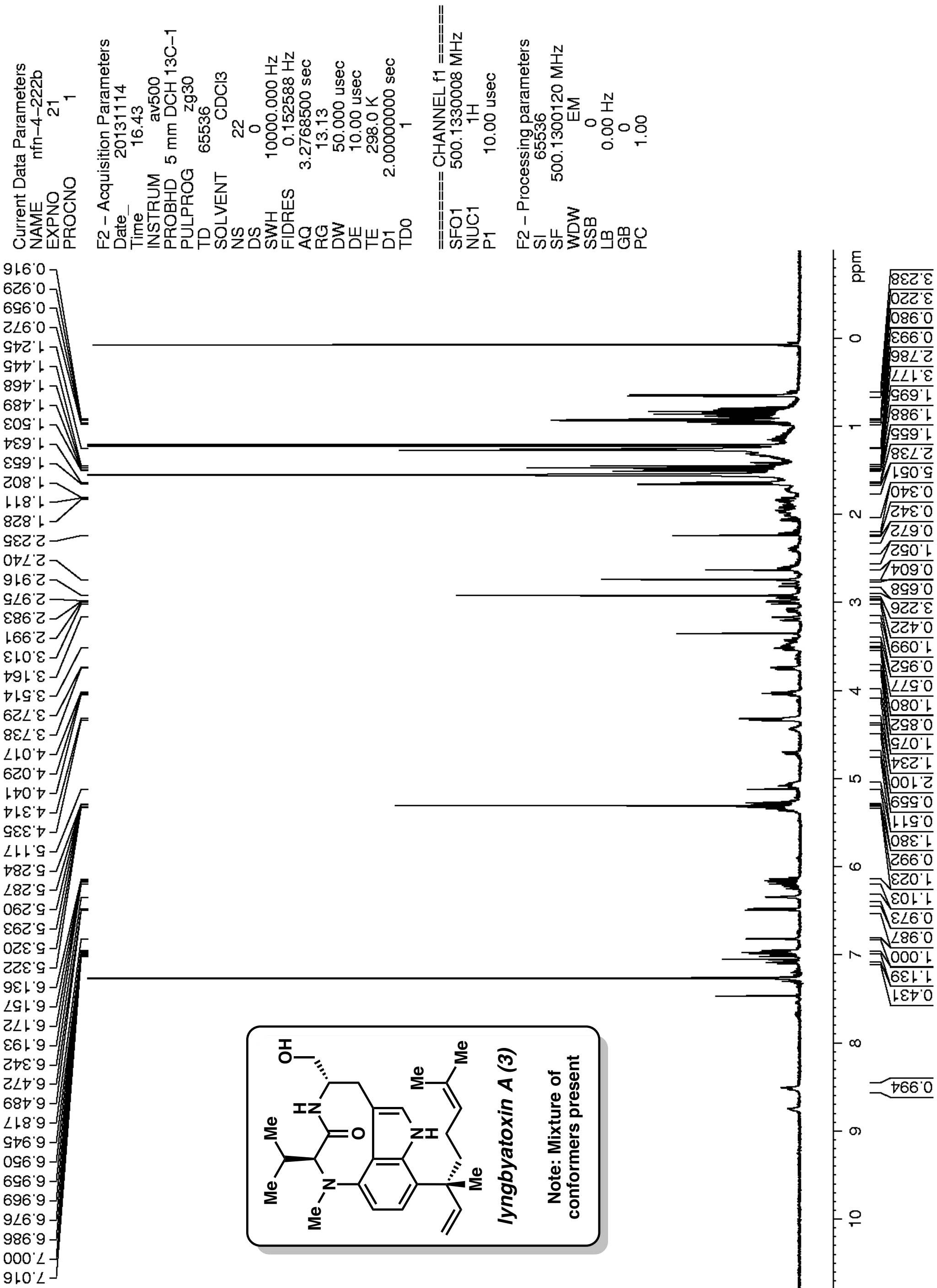

Current Data Parameters
NAME tks–1–302
EXPNO 1
PROCNO 1
F2 – Acquisition Parameters
Date_ 20130409
Time 8.54
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 6
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 11
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ====
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
F2 – Processing parameters
SI 65536
SF 500.1300135 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00
pendolmycin (2)
Note: Mixture of conformers present
ppm

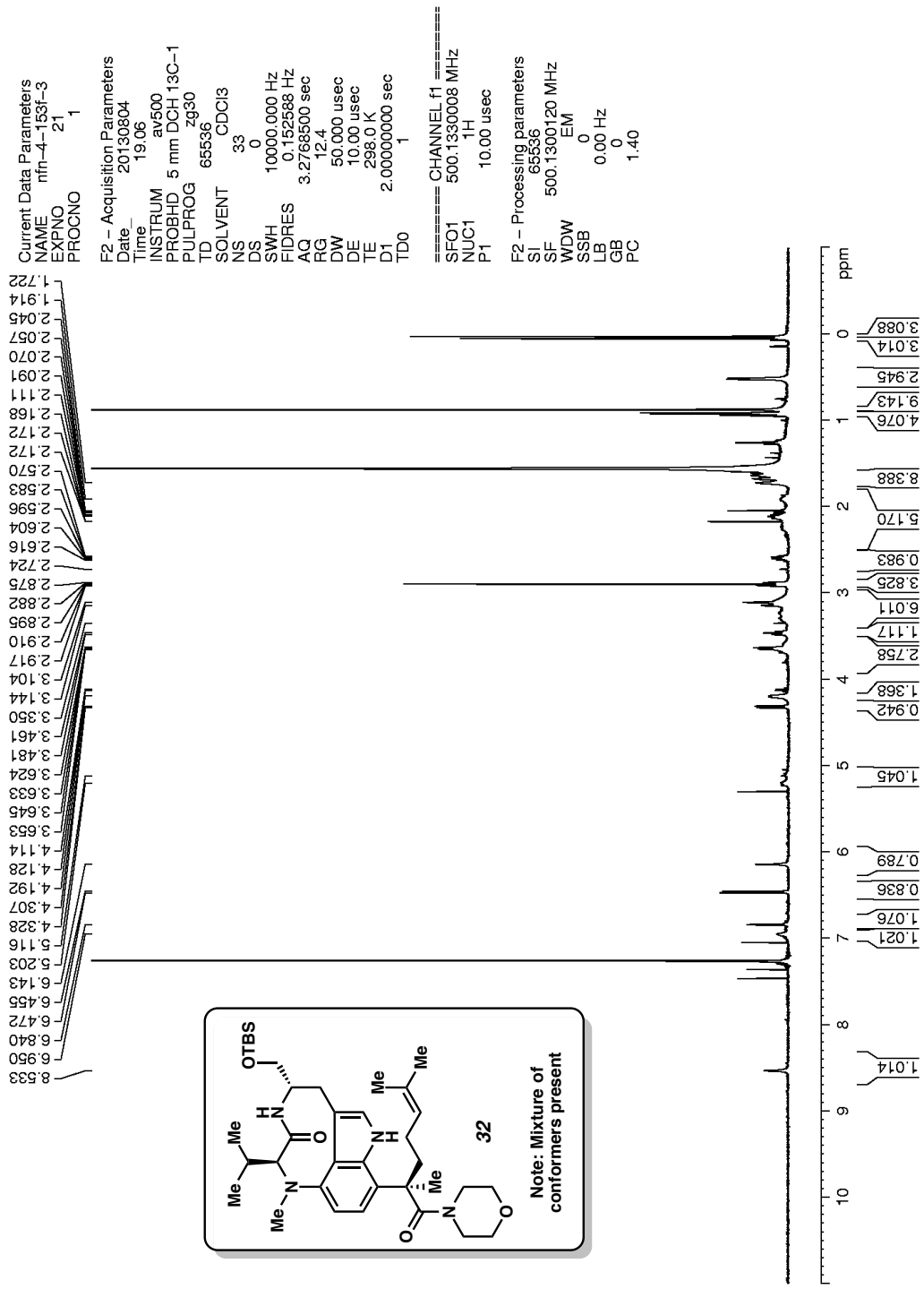

Current Data Parameters
NAME tks-2-032
EXPNO 3
PROCNO 1
F2 – Acquisition Parameters
Date_ 20131204
Time 13.29
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 9
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 12.14
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
F2 – Processing parameters
SI 65536
SF 500.1300126 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
5.090
5.078
5.064
3.794
3.745
3.736
3.726
3.722
3.713
3.709
3.704
3.694
3.690
3.677
2.192
2.183
2.167
2.164
2.153
2.146
2.142
1.964
1.683
1.608
0.928
7.765
7.019
2.956
2.833
ppm
Me
Me
Me
Br
O
N
O
29

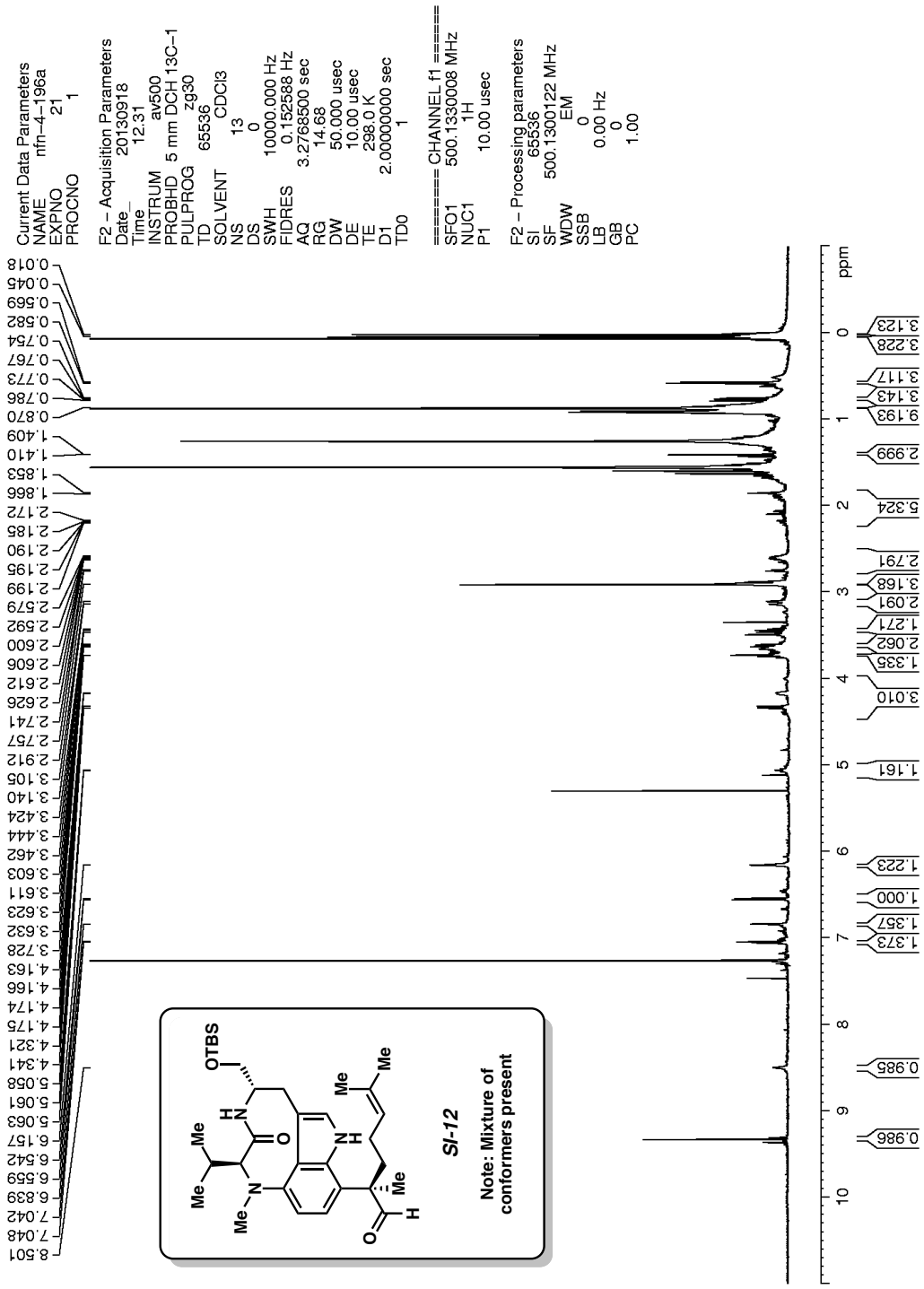

Current Data Parameters
NAME nfn–4–154kcomb(pure)
EXPNO 21
PROCNO 1
F2 – Acquisition Parameters
Date_ 20130818
Time 15.09
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 24
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 15.53
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
F2 – Processing parameters
SI 131072
SF 500.1300121 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
OTBS
Me
Me
Me
Me
Me
Me
31
Note: Mixture of conformers present
ppm

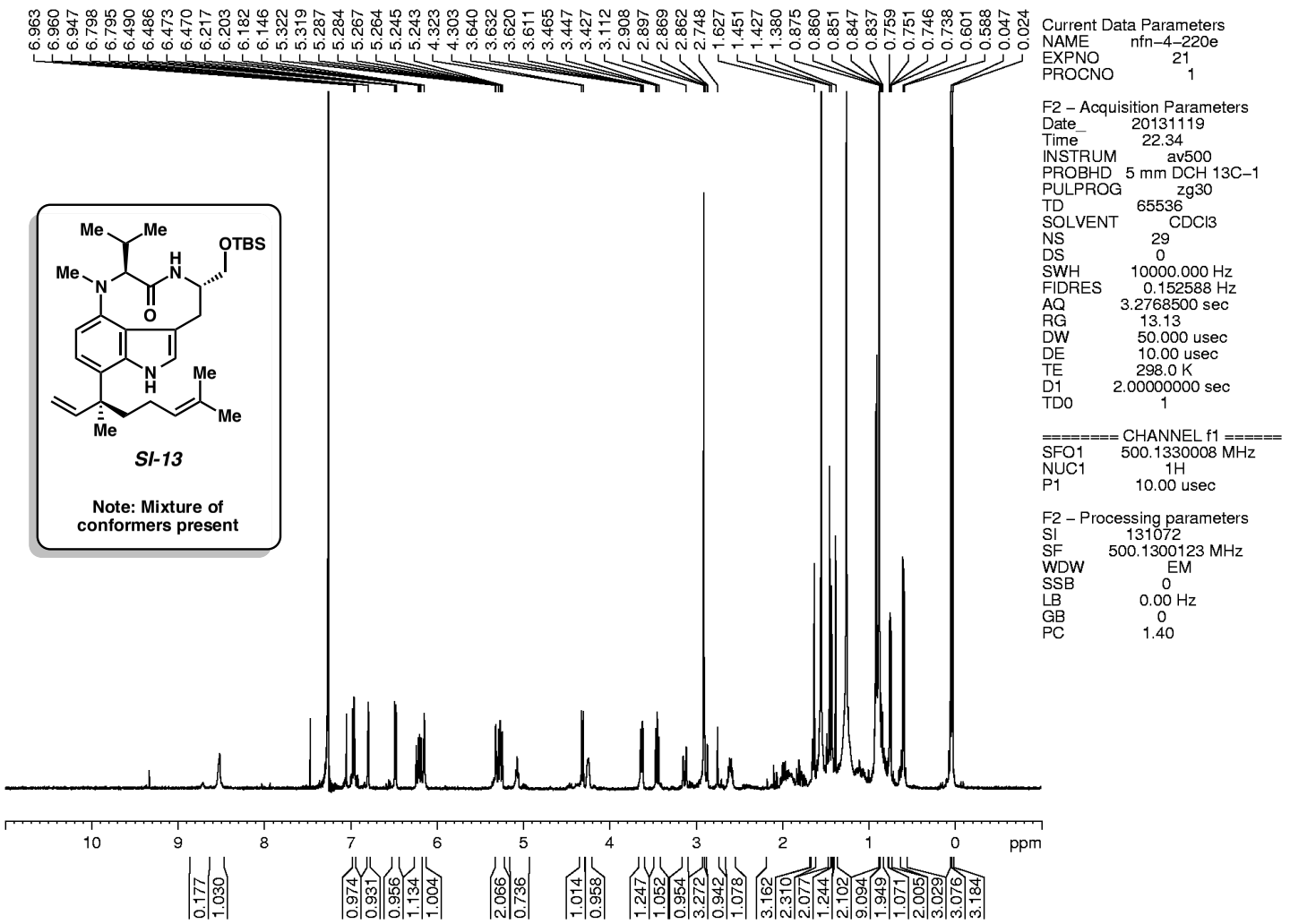

Current Data Parameters
NAME nfn–4–193b
EXPNO 21
PROCNO 1
F2 – Acquisition Parameters
Date_ 20130913
Time 11.29
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 23
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 14.68
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ======
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
F2 – Processing parameters
SI 65536
SF 500.1300122 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
OTBS
Me
Me
Me
Me
Me
H
N
N
H
O
O
H
33
Note: Mixture of conformers present
ppm


Current Data Parameters
NAME nfn-4-229b-5
EXPNO 21
PROCNO 1
F2 – Acquisition Parameters
Date_ 20131216
Time 21.14
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 29
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 14.68
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ======
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
F2 – Processing parameters
SI 65536
SF 500.1300122 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
OTBS
Me
Me
Me
Me
Me
Me
34
Note: Mixture of conformers present
ppm


Current Data Parameters
NAME nfn-4-222b
EXPNO 21
PROCNO 1
F2 – Acquisition Parameters
Date_ 20131114
Time 16.43
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 22
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 13.13
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
F2 – Processing parameters
SI 65536
SF 500.1300120 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
0.916
0.929
0.959
0.972
1.245
1.445
1.468
1.489
1.503
1.634
1.653
1.802
1.811
1.828
2.235
2.740
2.916
2.975
2.983
2.991
3.013
3.164
3.514
3.729
3.738
4.017
4.029
4.041
4.314
4.335
5.117
5.284
5.287
5.290
5.293
5.320
5.322
6.136
6.157
6.172
6.193
6.342
6.472
6.489
6.817
6.945
6.950
6.959
6.969
6.976
6.986
7.000
7.016
ppm
0
1
2
3
4
5
6
7
8
9
10
3.238
3.220
0.980
0.993
2.786
3.177
1.695
1.988
1.655
2.738
5.051
0.340
0.342
0.672
1.052
0.604
0.658
3.226
0.422
1.099
0.952
0.577
1.080
0.852
1.075
1.234
2.100
0.559
0.511
1.380
0.992
1.023
1.103
0.973
0.987
1.000
1.139
0.431
0.994
OH
H
N
O
Me
Me
Me
N
N
H
Me
Me
Me
lyngbyatoxin A (3)
Note: Mixture of conformers present


Current Data Parameters
NAME nfn-4-153f-3
EXPNO 21
PROCNO 1
F2 – Acquisition Parameters
Date_ 20130804
Time 19.06
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 33
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 12.4
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
F2 – Processing parameters
SI 65536
SF 500.1300120 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
OTBS
Me
Me
Me
Me
Me
32
Note: Mixture of conformers present
ppm


Current Data Parameters
NAME nfn–4–196a
EXPNO 21
PROCNO 1
F2 – Acquisition Parameters
Date_ 20130918
Time 12.31
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 13
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 14.68
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ======
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
F2 – Processing parameters
SI 65536
SF 500.1300122 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
OTBS
Me
Me
Me
Me
Me
H
O
N
H
N
O
H
SI-12
Note: Mixture of conformers present
ppm

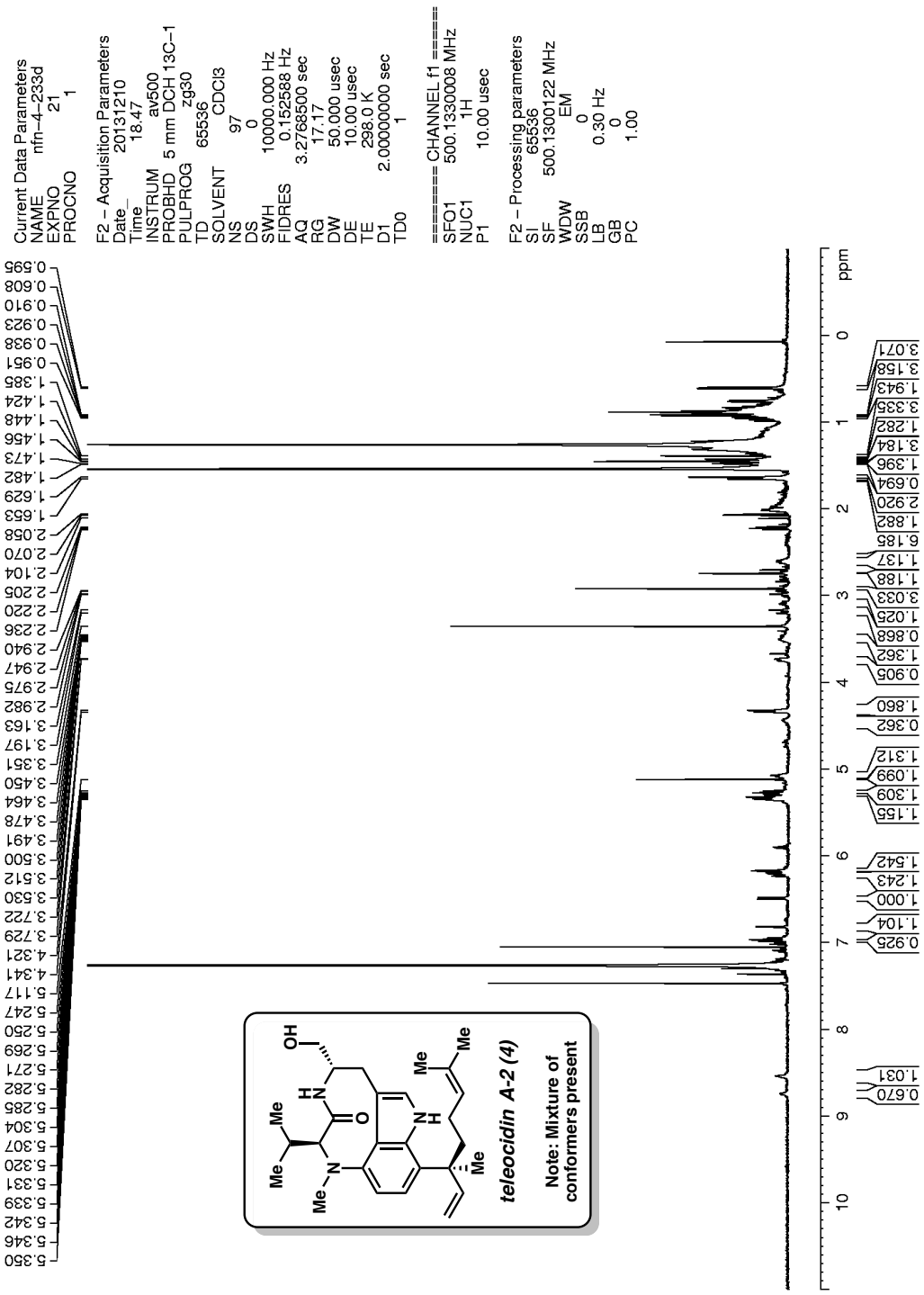


Current Data Parameters
NAME nfn–4–220e
EXPNO 21
PROCNO 1

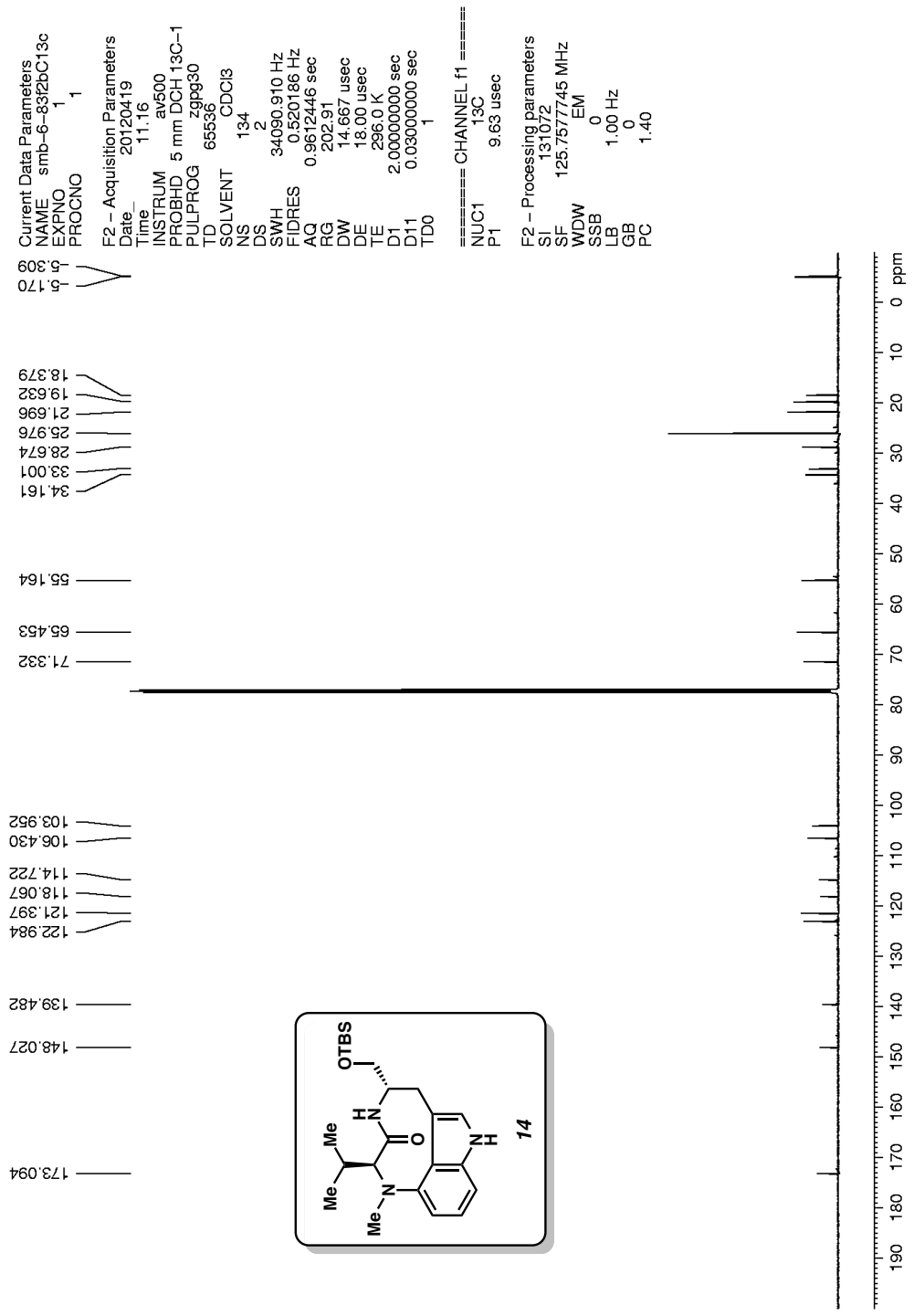
F2 – Acquisition Parameters
Date_ 20131119
Time 22.34
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 29
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 13.13
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1

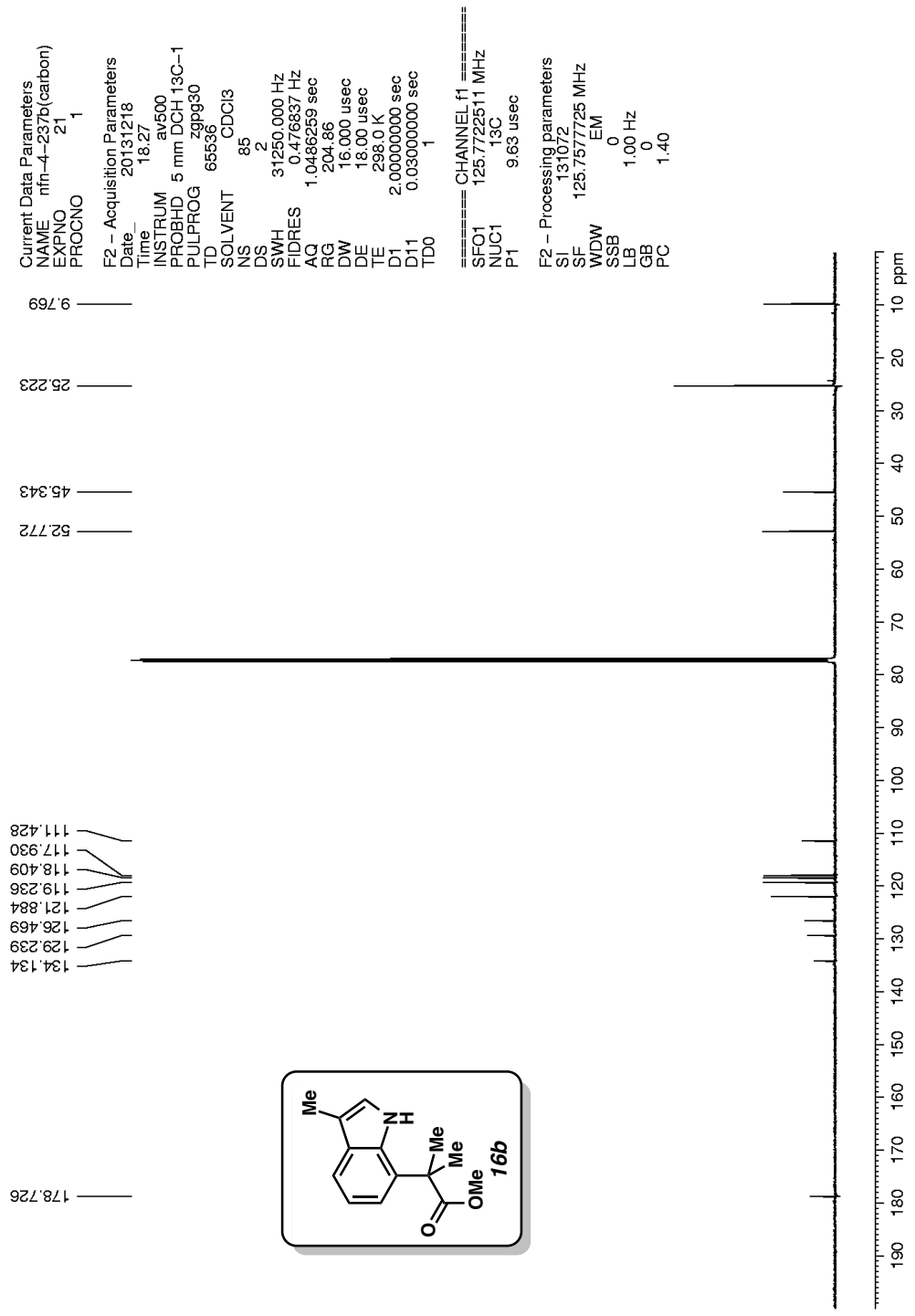
======== CHANNEL f1 ======
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec

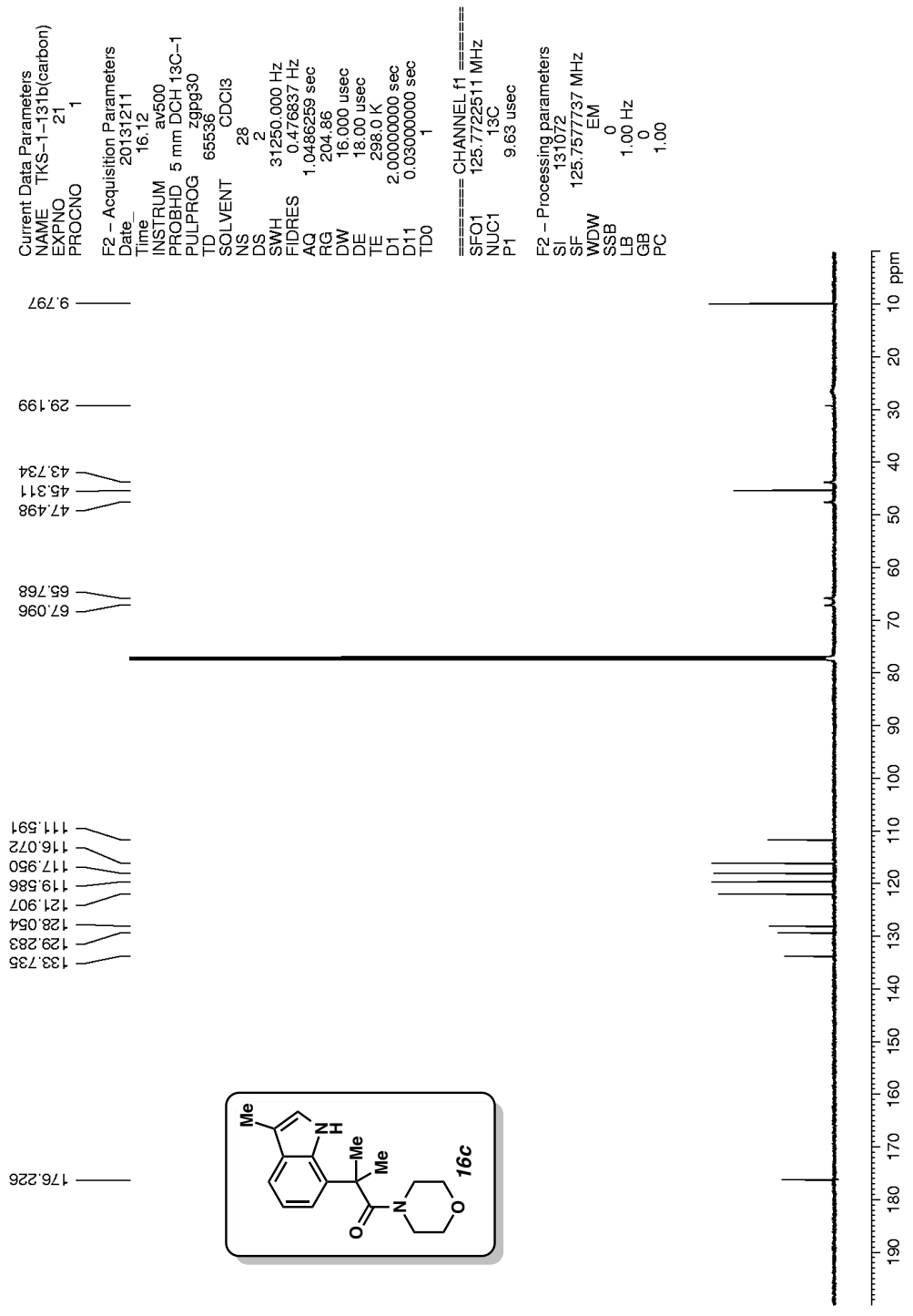
F2 – Processing parameters
SI 131072
SF 500.1300123 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.40

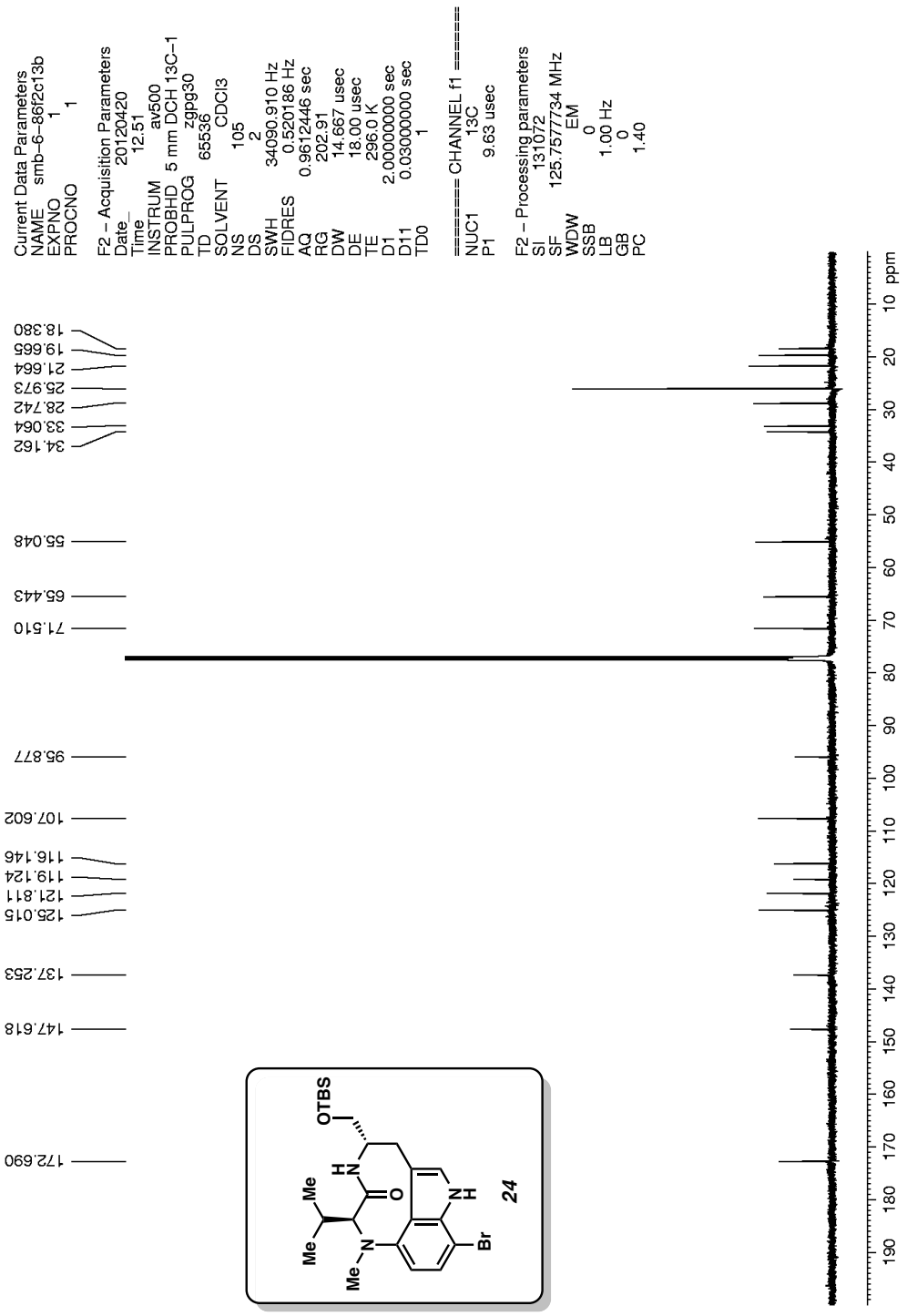

Current Data Parameters
NAME nfn–4–233d
EXPNO 21
PROCNO 1
F2 – Acquisition Parameters
Date_ 20131210
Time 18.47
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 97
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 17.17
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ======
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
F2 – Processing parameters
SI 65536
SF 500.1300122 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
teleocidin A-2 (4)
Note: Mixture of conformers present

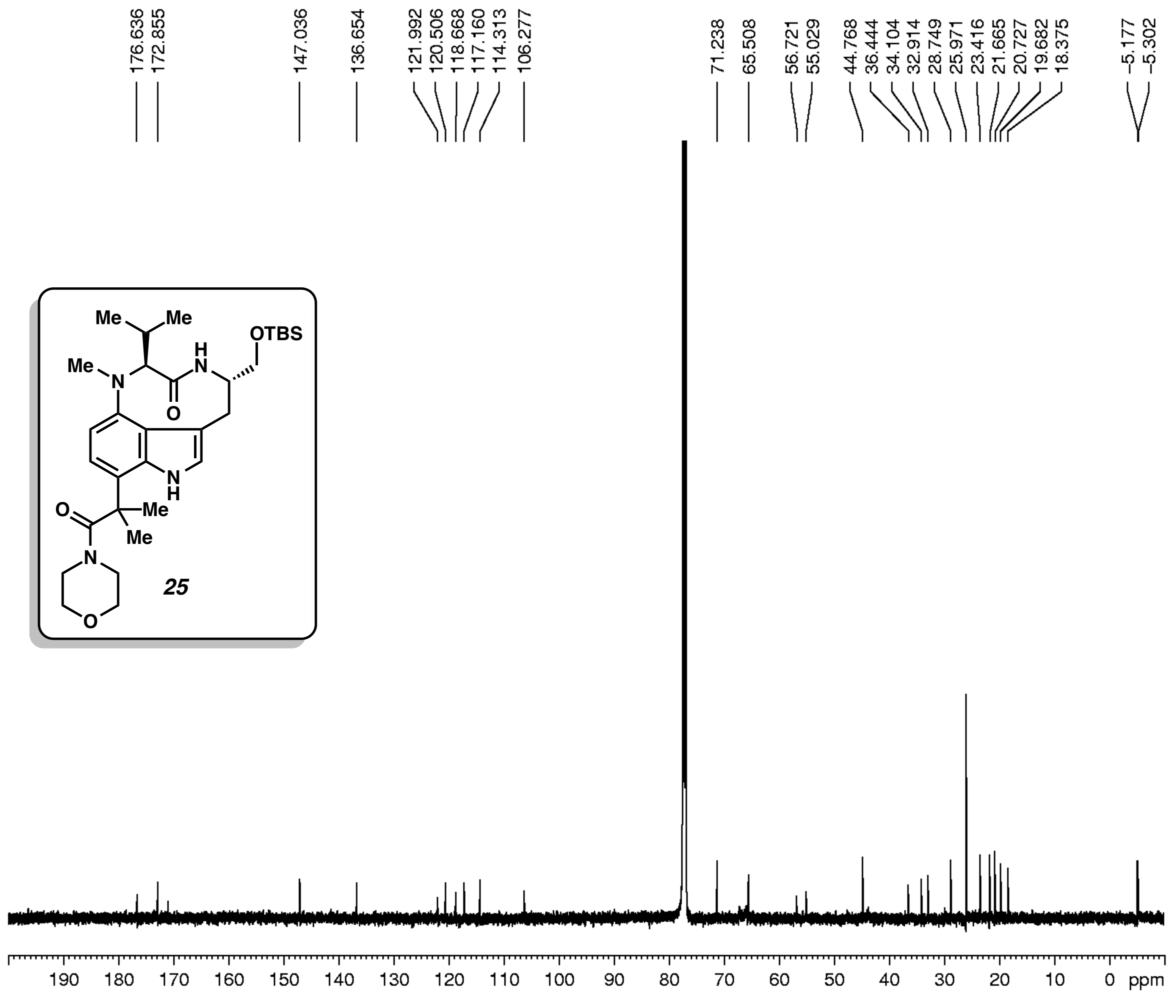
^{13}C NMR Spectra:


Current Data Parameters
NAME smb–6–83f2bC13c
EXPNO 1
PROCNO 1
F2 – Acquisition Parameters
Date_ 20120419
Time 11.16
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 134
DS 2
SWH 34090.910 Hz
FIDRES 0.520186 Hz
AQ 0.9612446 sec
RG 202.91
DW 14.667 usec
DE 18.00 usec
TE 296.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 9.63 usec
F2 – Processing parameters
SI 131072
SF 125.7577745 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
173.094
148.027
139.482
122.984
121.397
118.067
114.722
106.430
103.952
71.332
65.453
55.164
34.161
33.001
28.674
25.976
21.696
19.632
18.379
15.309
15.170
OTBS
Me
Me
Me
N
H
N
O
N
H
14
0 ppm


Current Data Parameters
NAME nfn–4–237b(carbon)
EXPNO 21
PROCNO 1
F2 – Acquisition Parameters
Date_ 20131218
Time 18.27
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 85
DS 2
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0486259 sec
RG 204.86
DW 16.000 usec
DE 18.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7722511 MHz
NUC1 13C
P1 9.63 usec
F2 – Processing parameters
SI 131072
SF 125.7577725 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
178.726
134.134
129.239
126.469
121.884
119.236
118.409
117.930
111.428
52.772
45.343
25.223
9.769
Me
N
H
Me
Me
OMe
O
16b
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


Current Data Parameters
NAME TKS–1–131b(carbon)
EXPNO 21
PROCNO 1
F2 – Acquisition Parameters
Date_ 20131211
Time 16.12
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 28
DS 2
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0486259 sec
RG 204.86
DW 16.000 usec
DE 18.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7722511 MHz
NUC1 13C
P1 9.63 usec
F2 – Processing parameters
SI 131072
SF 125.7577737 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00
176.226
133.735
129.283
128.054
121.907
119.586
117.950
116.072
111.591
67.096
65.768
47.498
45.311
43.734
29.199
9.797
Me
N
H
Me
Me
O
N
O
16c
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


Current Data Parameters
NAME smb–6–86f2c13b
EXPNO 1
PROCNO 1
F2 – Acquisition Parameters
Date_ 20120420
Time 12.51
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 105
DS 2
SWH 34090.910 Hz
FIDRES 0.520186 Hz
AQ 0.9612446 sec
RG 202.91
DW 14.667 usec
DE 18.00 usec
TE 296.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.63 usec
F2 – Processing parameters
SI 131072
SF 125.7577734 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
18.380
19.665
21.664
25.973
28.742
33.064
34.162
55.048
65.443
71.510
95.877
107.602
116.146
119.124
121.811
125.015
137.253
147.618
172.690
OTBS
Me
Me
Me
N
H
N
O
N
H
Br
24
10 ppm

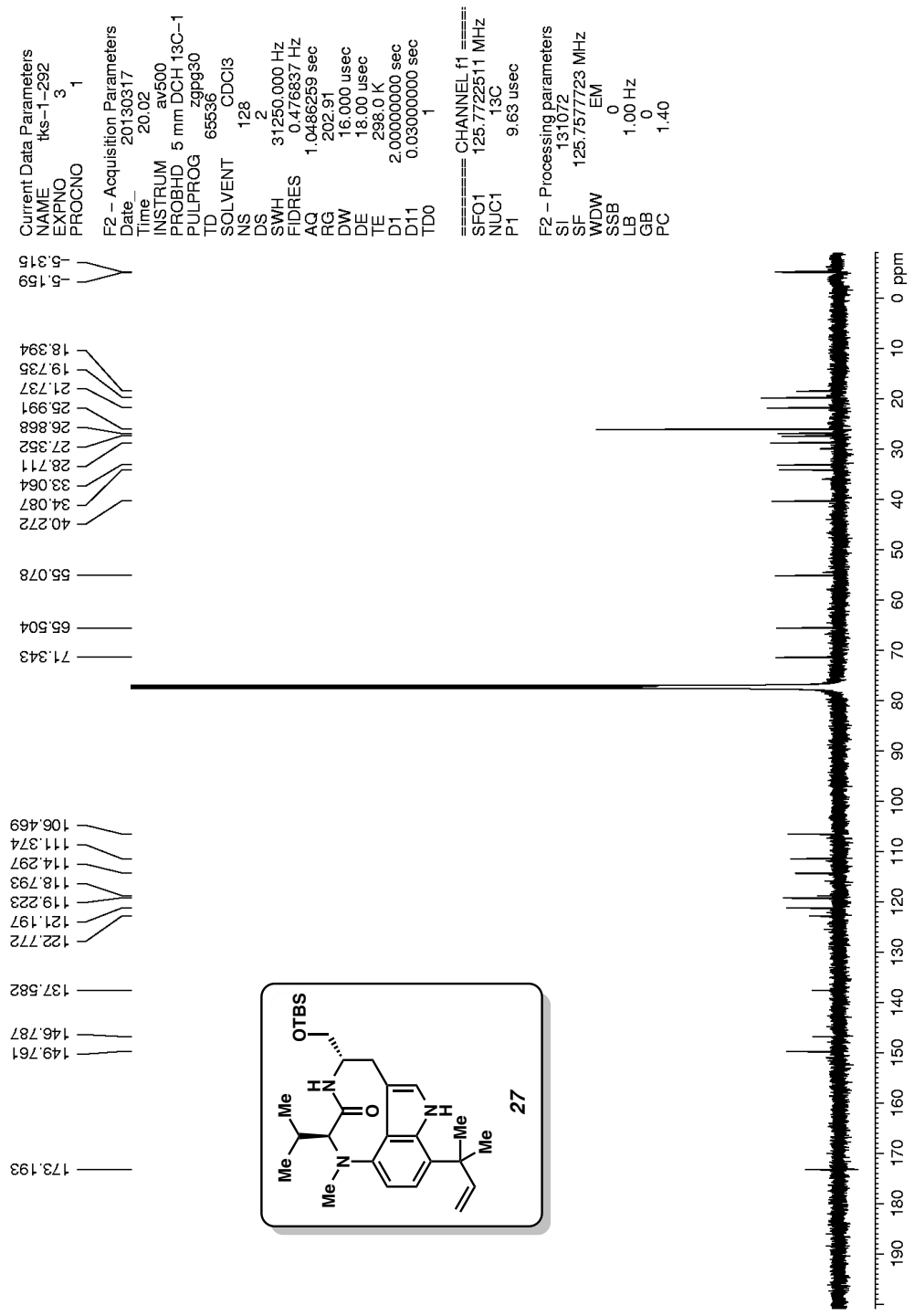


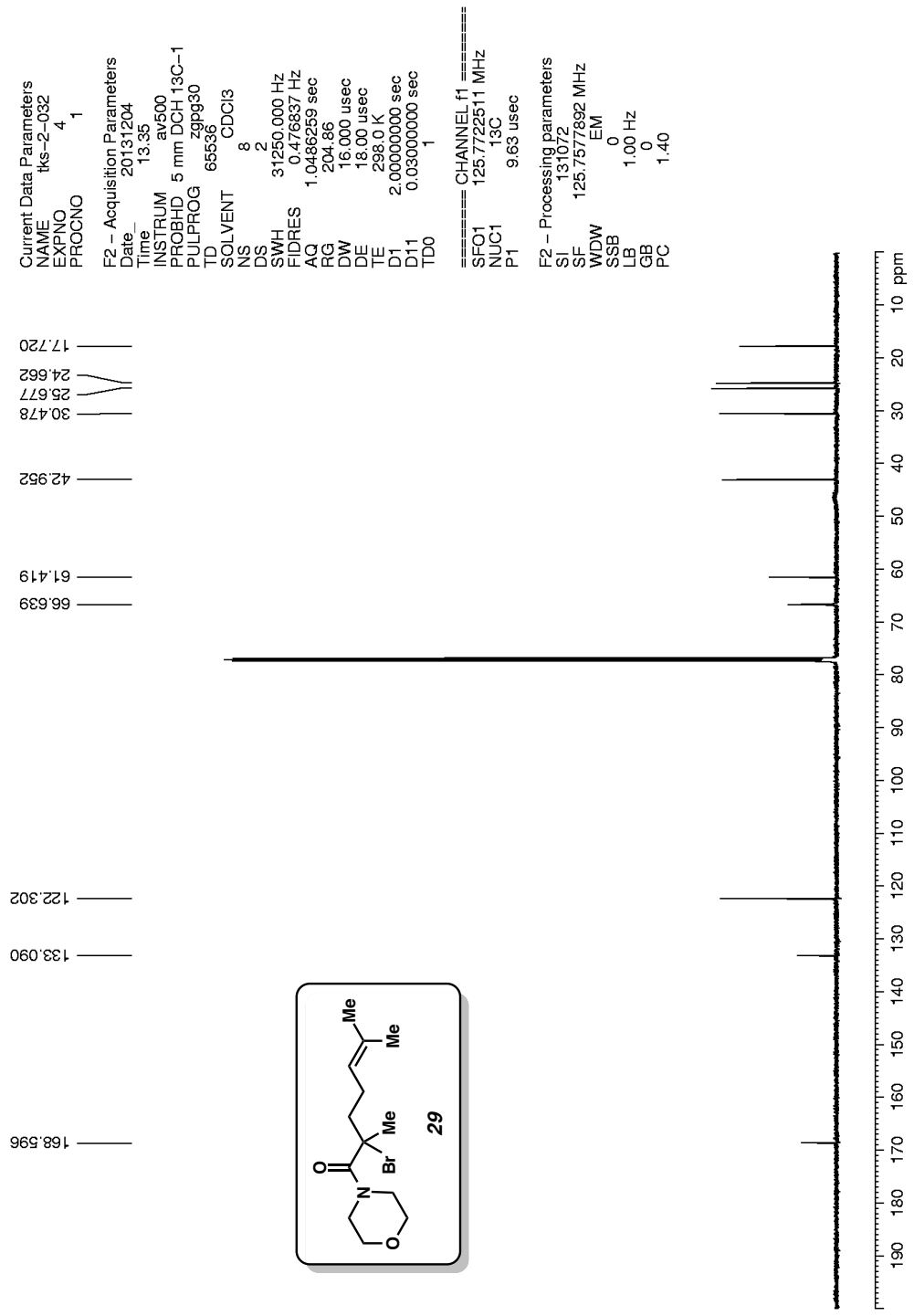
Current Data Parameters
NAME smb–6–90f1C13
EXPNO 1
PROCNO 1

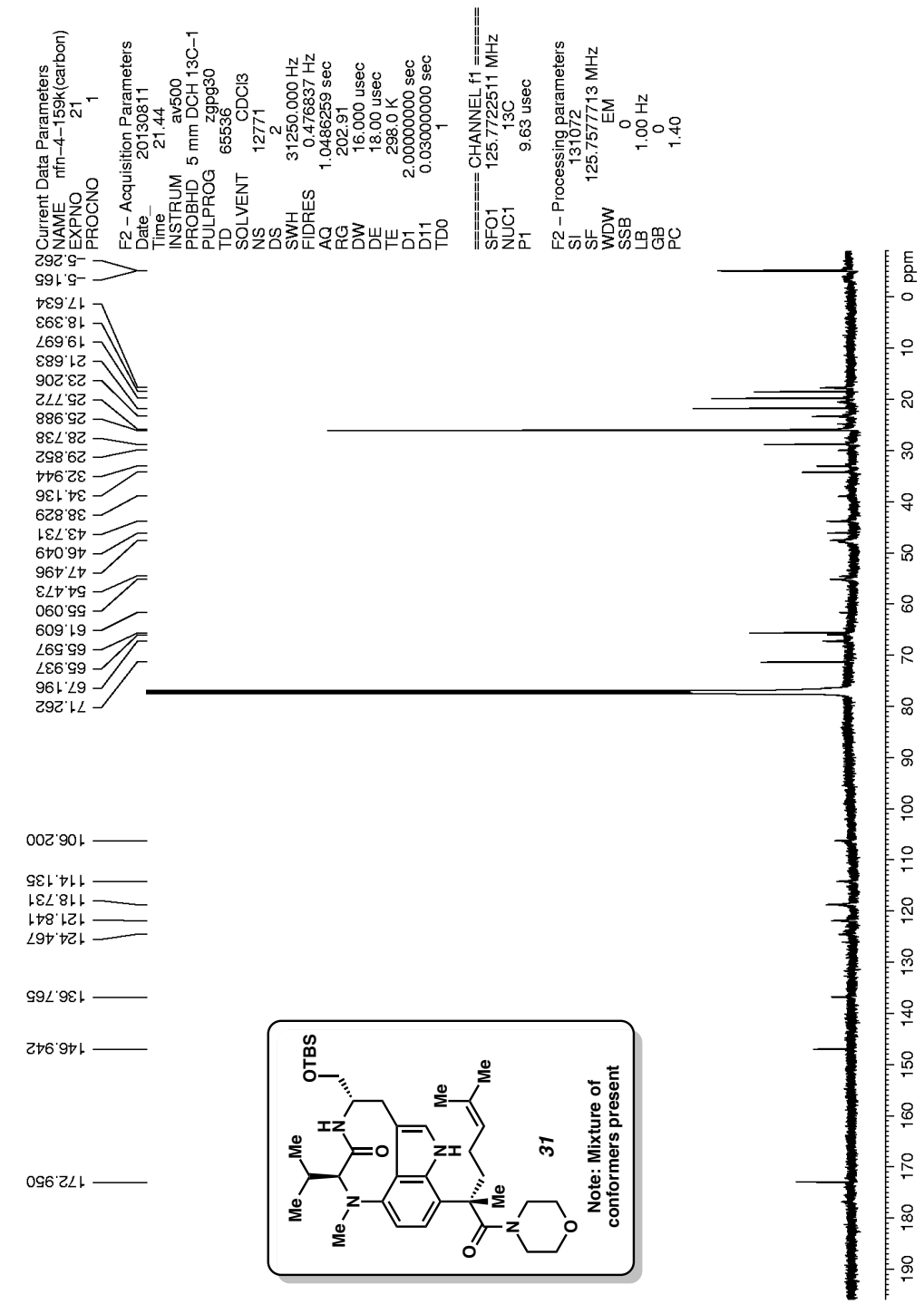
F2 – Acquisition Parameters
Date_ 20120423
Time 17.01
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 376
DS 2
SWH 34090.910 Hz
FIDRES 0.520186 Hz
AQ 0.9612446 sec
RG 202.91
DW 14.667 usec
DE 18.00 usec
TE 296.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

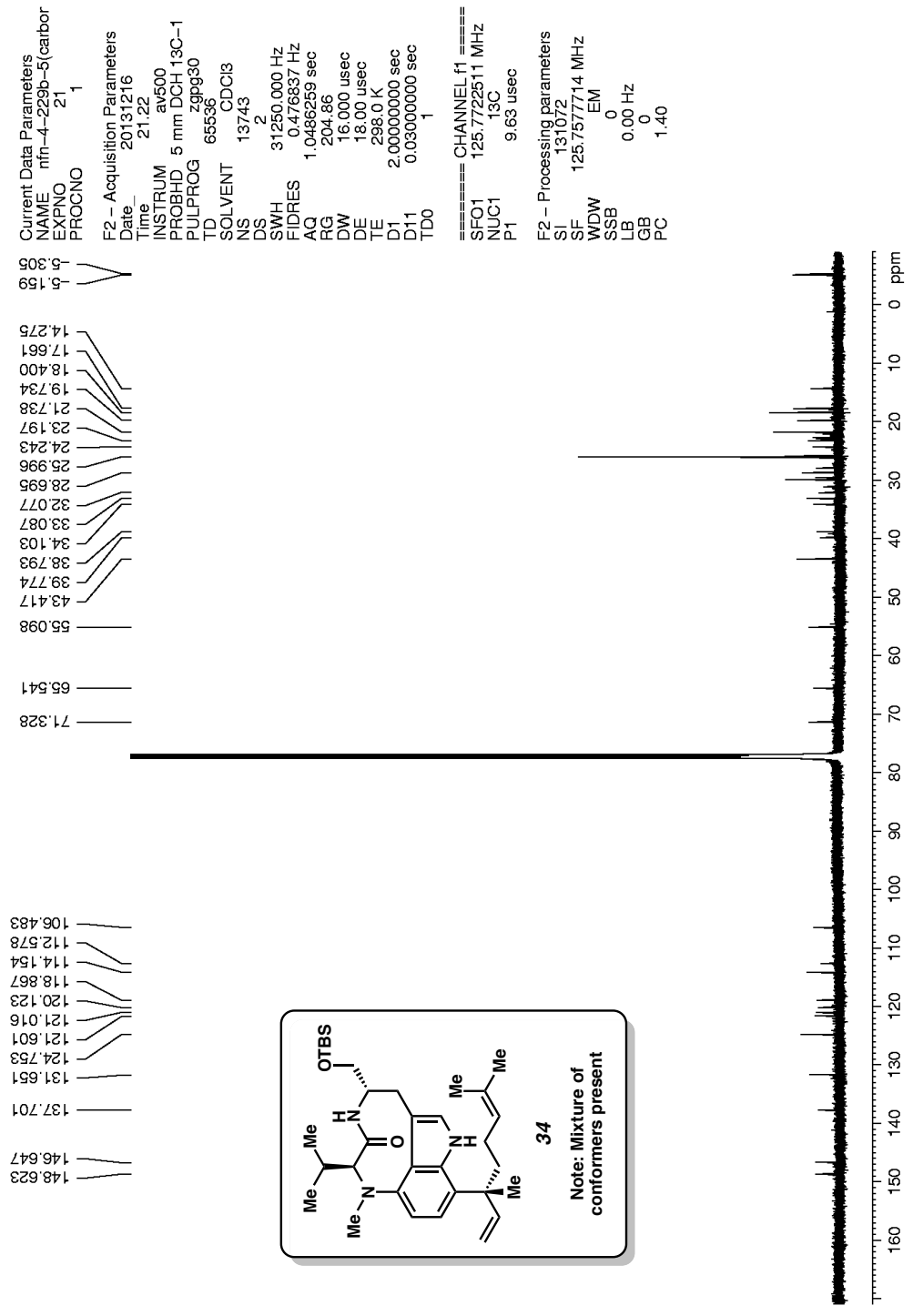
======== CHANNEL f1 =====
NUC1 13C
P1 9.63 usec

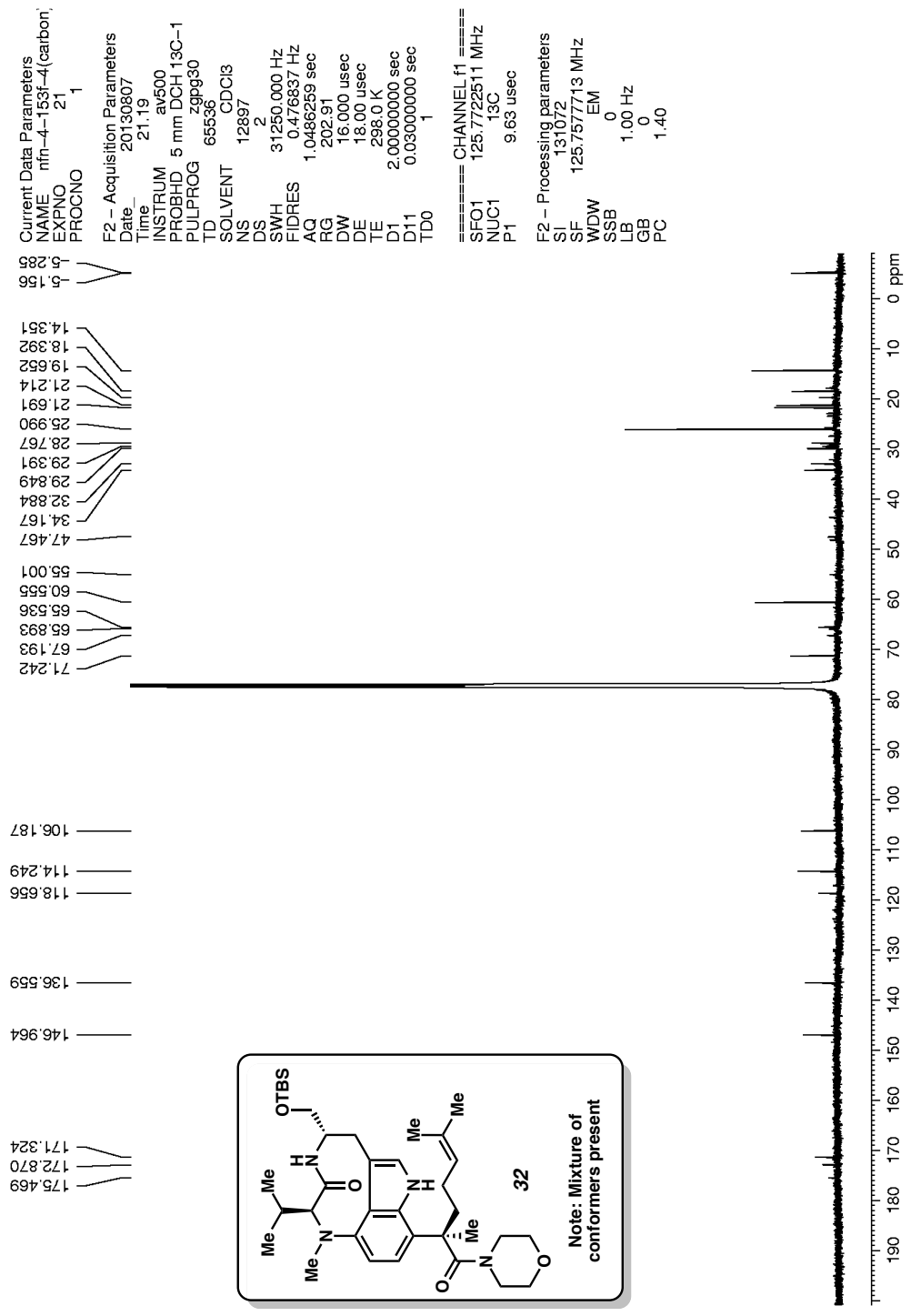
F2 – Processing parameters
SI 131072
SF 125.7577743 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

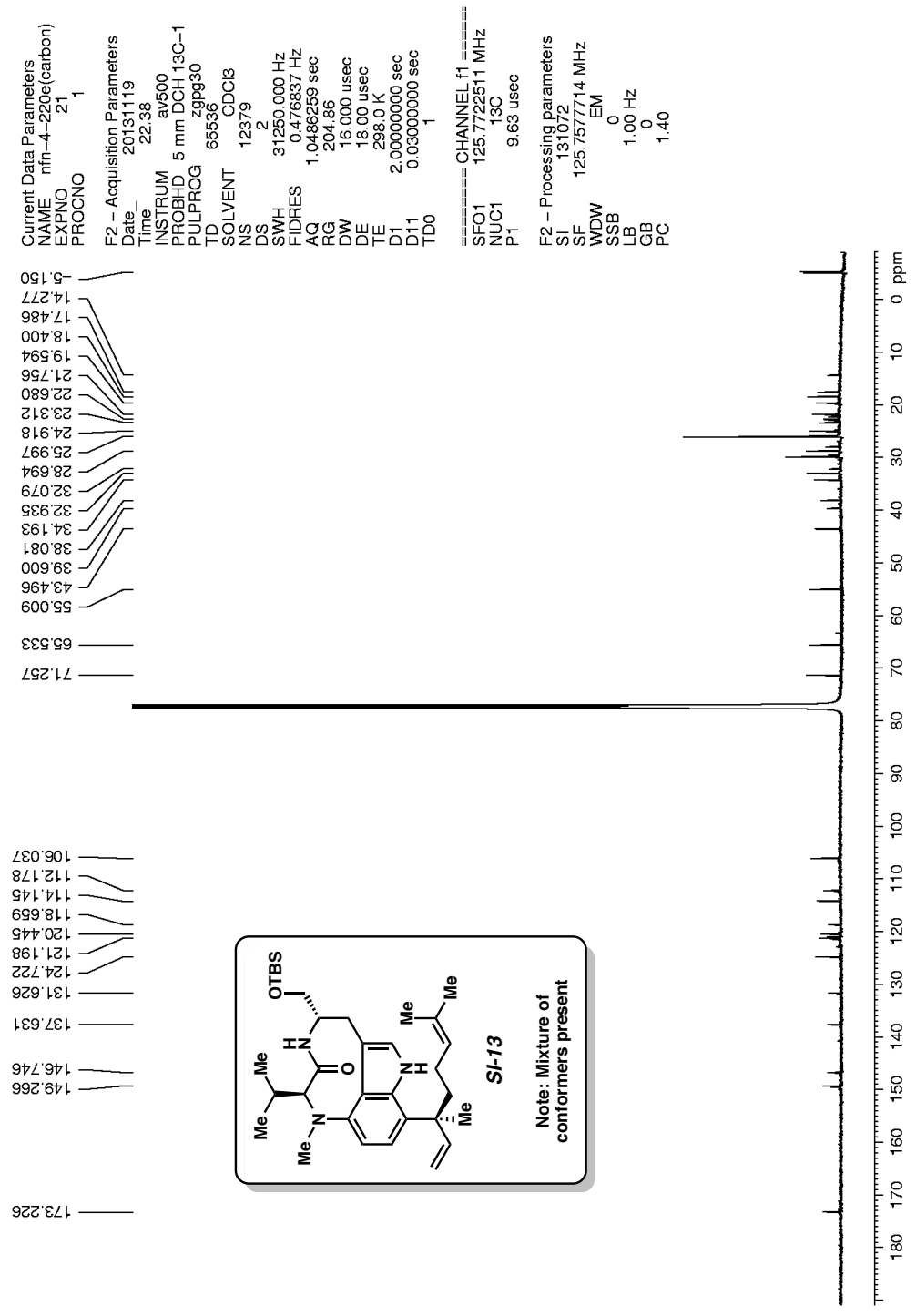

Current Data Parameters
NAME tks–1–292
EXPNO 3
PROCNO 1
F2 – Acquisition Parameters
Date_ 20130317
Time 20.02
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 128
DS 2
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0486259 sec
RG 202.91
DW 16.000 usec
DE 18.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7722511 MHz
NUC1 13C
P1 9.63 usec
F2 – Processing parameters
SI 131072
SF 125.7577723 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
OTBS
Me
Me
Me
Me
27
0 ppm


Current Data Parameters
NAME tks--2--032
EXPNO 4
PROCNO 1
F2 – Acquisition Parameters
Date_ 20131204
Time 13.35
INSTRUM av500
PROBHD 5 mm DCH 13C--1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0486259 sec
RG 204.86
DW 16.000 usec
DE 18.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7722511 MHz
NUC1 13C
P1 9.63 usec
F2 – Processing parameters
SI 131072
SF 125.7577892 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
168.596
133.090
122.302
66.639
61.419
42.952
30.478
25.677
24.662
17.720
Me
Me
Me
Br
O
N
O
29
10 ppm


Current Data Parameters
NAME mfn-4-159k(carbon)
EXPNO 21
PROCNO 1
F2 – Acquisition Parameters
Date_ 20130811
Time 21.44
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 12771
DS 2
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0486259 sec
RG 202.91
DW 16.000 usec
DE 18.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ======
SFO1 125.7722511 MHz
NUC1 13C
P1 9.63 usec
F2 – Processing parameters
SI 131072
SF 125.7577713 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
OTBS
Me
Me
Me
H
N
O
N
H
Me
Me
Me
N
O
O
31
Note: Mixture of conformers present
ppm


Current Data Parameters
NAME nfn–4–229b–5(carbor
EXPNO 21
PROCNO 1
F2 – Acquisition Parameters
Date_ 20131216
Time 21.22
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 13743
DS 2
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0486259 sec
RG 204.86
DW 16.000 usec
DE 18.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ======
SFO1 125.7722511 MHz
NUC1 13C
P1 9.63 usec
F2 – Processing parameters
SI 131072
SF 125.7577714 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
OTBS
Me
Me
Me
Me
Me
34
Note: Mixture of conformers present
ppm


Current Data Parameters
NAME nfn–4–153f–4(carbon)
EXPNO 21
PROCNO 1
F2 – Acquisition Parameters
Date_ 20130807
Time 21.19
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 12897
DS 2
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0486259 sec
RG 202.91
DW 16.000 usec
DE 18.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ======
SFO1 125.7722511 MHz
NUC1 13C
P1 9.63 usec
F2 – Processing parameters
SI 131072
SF 125.7577713 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
175.469
172.870
171.324
146.964
136.559
118.656
114.249
106.187
71.242
67.193
65.893
65.536
60.555
55.001
47.467
34.167
32.884
29.849
29.391
28.767
25.990
21.691
21.214
19.652
18.392
14.351
5.156
5.285
OTBS
Me
Me
Me
Me
Me
32
Note: Mixture of conformers present
ppm


Current Data Parameters
NAME nfn–4–220e(carbon)
EXPNO 21
PROCNO 1
F2 – Acquisition Parameters
Date_ 20131119
Time 22.38
INSTRUM av500
PROBHD 5 mm DCH 13C–1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 12379
DS 2
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0486259 sec
RG 204.86
DW 16.000 usec
DE 18.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ======
SFO1 125.7722511 MHz
NUC1 13C
P1 9.63 usec
F2 – Processing parameters
SI 131072
SF 125.7577714 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
OTBS
Me
Me
Me
Me
Me
Me
Si-13
Note: Mixture of conformers present
ppm