Enantioselective Total Synthesis and Confirmation of the Absolute and Relative Stereochemistry of Streptorubin B

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Supporting Information

Part 1: Supplemental References

The complete reference for ref. 2b within the manuscript is as follows: Nguyen, M.; Marcellus, R. C.; Roulston, A.; Watson, M.; Serfass, L.; Murthy Madiraju, S. R.; Goulet, D.; Viallet, J.; Be´lec, L.; Billot, X.; Acoca, S.; Purisima, E.; Wiegmans, A.; Cluse, L.; Johnstone, R. W.; Beauparlant, P.; Shore, G. C. *Proc. Natl. Acad. Sci. U. S. A.*, **2007**, *104*, 19512–19517.

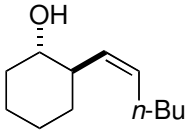
Part 2: General Methods

All reactions were carried out under a nitrogen atmosphere in flame-dried glassware with magnetic stirring unless otherwise stated. THF and CH_2Cl_2 were purified by passage through a bed of activated alumina.[1] Reagents were purified[2] prior to use unless otherwise stated. Purification of reaction products was carried out by flash chromatography using EM Reagent silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and anisaldehyde or potassium permanganate followed by heating. Film infrared spectra were recorded using a BioRad Excalibur and a BioRad FTS-60. Germanium ATR infrared spectra were recorded using a Bruker Tensor 37. ^{1}H-NMR spectra were recorded on a Bruker Advance III 500 (500 MHz), Varian Inova 500 (500 MHz), or Inova 400 (400 MHz) spectrometer and are

1. Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometal.* **1996**, *15*, 1518-1520.
2. Perrin, D. D.; Armarego, W. L. *Purification of Laboratory Chemicals;* 3rd Ed., Pergamon Press, Oxford. 1988

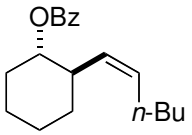
reported in ppm using solvent as an internal standard ($CDCl_3$ at 7.26 ppm) or tetramethylsilane (0.00 ppm). Two-dimensional NMR experiments were run on a Bruker Advance III 500 (500 MHz). Data are reported as (app = apparent, obs = obscured, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, h = hextet, sep = septet, o = octet, m = multiplet, b = broad; integration; coupling constant(s) in Hz. Proton-decoupled ^{13}C-NMR spectra were recorded on a Bruker Advance III 500 (125 MHz), Varian Inova 500 (125 MHz), or Inova 400 (100 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.00 ppm). Mass spectra data were obtained on an Agilent 6210 Time-of-Flight LC/MS and a Thermo Finnegan Mat 900 XL High Resolution Magnetic Sector. X-ray data were collected using a Bruker APEX II detector and processed using an APEX2 from Bruker. Optical rotations were recorded with a Perkin Elmer 341 polarimeter at 589 nm (Na/Hal) at 20°C. Circular dichroism spectra were recorded with a JASCO J-815 circular dichroism spectrophotometer at ambient temperature in $CHCl_3$, using a 2 mm thick cuvette.

Part 3: Experimental Procedures: Synthesis of Streptorubin B



(1*S*,2*R*)-2-((1*Z*)-1-hexen-1-yl)-cyclohexanol (14): To a solution of heptanedial (2.6 g, 20 mmol) in dichloromethane (202 mL) was added (*S*)-proline (232 mg, 2 mmol) at room temperature. The heterogenous mixture was stirred for 12 hours, after which the solution became clear and homogenous. To a suspension of pentyltriphenylphosphonium bromide (10.9 g, 26.3 mmol) in THF (202 mL in a separate flask) at 0 °C was added sodium hexamethyldisilazane (26 mL, 26.3 mmol, 1 M in THF), upon which the solution turned bright orange. The ylide solution was allowed to stir for 1h 20 min prior to addition of aldehyde solution via cannula at 0 °C (total aldol reaction time = 13 h 30 min), upon which the solution turned cloudy and white. After 1h, the reaction mixture was quenched with saturated NH_4Cl (200 mL), and the organic layer separated. The aqueous/halogenated layers were extracted with Et_2O (3 x 200 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash column chromatography (33% Et_2O in hexanes, silica gel) to afford a 10:1:1 mixture of the title compound, the *syn*-diastereomer, and the *E*-isomer, respectively (2.54 g, 69%). When desired, the *syn*-diastereomer was removed by iterative column chromatography (3% MeOH in hexanes, silica gel) to afford the title compound as a 10:1 mixture of *Z* and *E* isomers: **IR** (neat) 3430, 2928, 2856, 1462, 1076 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) 5.58 (dt, 1H, *J* = 10.9, 7.4 Hz), 5.16 (dd, 1H, *J* = 10.9, 10.6 Hz), 3.20 (m, 1H), 2.23 (dddd, 1H, *J* = 10.6 Hz, 10.6 Hz, 9.9 Hz, 3.4 Hz), 2.10 (m, 2H), 2.03 (m, 1H), 1.83 (s, 1H), 1.77 (bm, 1H), 1.64 (bt, 2H, *J* = 10.6, 10.6 Hz), 1.30 (m, 7H), 1.11 (m, 1H), 0.89 (t, 3H, *J* = 6.3 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) 133.4, 131.5, 73.9, 44.9, 33.5, 32.1, 31.4, 27.6, 25.3, 24.9, 22.4, 14.0; **HRMS** (EI): Exact mass calc'd for $C_{12}H_{22}O$ [M^+], 182.1671. Found 182.1665. $[\alpha]_D$ = +38.2 (c = 2.07 g/100 mL, $CHCl_3$).

To determine the enantioselectivity of the aldol-Wittig reaction:

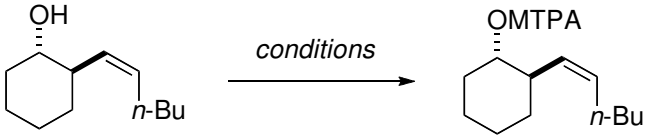


(1*S*,2*R*)-2-((1*Z*)-1-hexen-1-yl)-cyclohexanyl-benzoate: To a stirring solution of **14** (40.0 mg, 0.22 mmol) in DCM (2.2 mL) were added NEt_3 (91 µL, 0.66 mmol), DMAP (3 mg, 0.02 mmol), and benzoyl chloride (77 µL, 0.66 mmol). The solution was stirred for 60 h before being diluted in DCM (10 mL) and poured into H_2O (10 mL). The halogenated layer was washed with sat. $NaHCO_3$ (10 mL), dried

($MgSO_4$), and concentrated in vacuo. The residue was purified via flash chromatography (10% EtOAc in hexanes, silica gel) to afford the title compound as a 10:1 mixture of Z and E isomers (41 mg, 69%): **IR** (neat) 2931, 2857, 1714, 1271 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) 8.00 (dd, 2H, *J* = 8.2, 2.2 Hz), 7.53 (dd, 1H, *J* = 8.2, 7.7 Hz), 7.41 (dd, 2H, 8.2, 7.7 Hz), 5.32 (dt, 1H, *J* = 10.9, 7.0 Hz), 5.19 (dd, 1H, *J* = 10.9, 9.6 Hz), 4.83 (ddd, 1H, 10.7, 10.3, 4.2 Hz), 2.60 (dddd, 1H, 10.3, 10.2, 9.73, 4.0 Hz), 2.07 (m, 3H), 1.83 (m, 1H), 1.73 (m, 2H), 1.44 (m, 2H), 1.27 (m, 6H), 0.85 (t, 3H, *J* = 7.0 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) 166.1, 132.6, 131.4, 131.1, 130.9, 129.6, 128.2, 76.5, 41.6, 32.0, 31.9, 31.6, 27.4, 24.9, 24.6, 22.4, 14.0; **HRMS** (ESI): Exact mass calc'd for $C_{19}H_{27}O_2$ [M+H$^+$], 287.2006. Found 287.2005. $[\alpha]_D$ = +11.8 (c = 0.61 g/100 mL, $CHCl_3$)

The UV-active aromatic ester was used to determine the enantioselectivity of the aldol-Wittig reaction sequence by comparison to the racemic material. Enantioselectivity (97.5:2.5 er) was determined by chiral HPLC analysis: Chiraldex OD-H column (0.46 cm x 25 cm), flow rate of 1.0 mL/min, 0.5% isopropanol in hexanes. Retention times: 7.67 min (+)/10.40 min (–).

Mosher Ester Analysis of (1*S*,2*R*)-2-((1*Z*)-1-hexen-1-yl)-cyclohexanol (14)



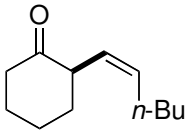
General Procedure for the Preparation of Mosher Esters: To a solution of alcohol **14** (9.4 mg, 0.052 mmol) in dry DCM (0.5 mL) was added DMAP (3.0 mg, 0.025 mmol), *i*Pr_2NEt (14 µL, 0.10 mmol), and (*R*)-(−)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (14 µL, 0.08 mmol). The solution was allowed to stir at room temperature for 12 h before being diluted with Et_2O (3 mL) and quenched with H_2O (1 mL). The aqueous layer was extracted twice with Et_2O (3 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography (20% ethyl acetate in hexanes, silica gel) afforded the (*S*)-Mosher's ester (21 mg, 98%). The same procedure, using (*S*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride, provided the (*R*)-Mosher's ester.

Table S.1 – Mosher-Ester Analysis of Secondary Alcohol

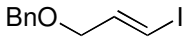
H	δ_S (ppm)	δ_R (ppm)	$\Delta\delta = \delta_S - \delta_R$
C^1-**H_2**	2.011, 1.903	1.905, 1.655	+0.106, +0.248
C^2-**H**	5.435	5.228	+0.207
C^3-**H**	5.234	5.115	+0.119
C^4-**H**	2.543	2.496	+0.047
C^9-**H_2**	1.697, 1.219	1.672, 1.216	+0.025, +0.003
C^6-**H_2**	2.033, 1.322	2.076, 1.495	-0.043, -0.173
C^7-**H_2**	1.771, 1.327	1.811, 1.392	-0.040, -0.065

Based on the model proposed by Mosher,[3] the secondary alcohol was assigned the (1*S*,2*R*) absolute configuration.

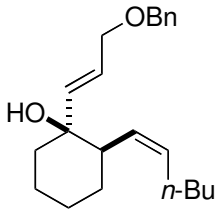
3. Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512–519.



(*R*)-2-((1*Z*)-1-hexen-1-yl)-cyclohexanone (S1): To a solution of freshly distilled oxalyl chloride (199 μL, 2.3 mmol) in DCM (8.8 mL) at -78°C was added dropwise DMSO (192 μL, 2.7 mmol). The solution was stirred for 5 minutes, after which a solution of secondary alcohol **14** (352 mg, 1.93 mmol) in DCM (5.8 mL) was added. The solution was stirred for 20 minutes, followed by the dropwise addition of *i*Pr_2NEt (1.66 mL, 9.65 mmol). The solution was stirred for 10 minutes before being warmed to 0 °C in an ice bath. The solution was further stirred at 0 °C for 30 minutes, then poured into H_2O (30 mL). The organic phase was collected, and the aqueous layer back-extracted with DCM (20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by flash chromatography (10% EtOAc in hexanes, silica gel) afforded the title compound (335 mg, 96%): **IR** (neat) 2958, 2860, 1712, 1126 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) 5.52 (m, 2H), 3.27 (ddd, 1H, *J* = 10.4, 6.9, 6.9 Hz), 2.45 (ddd, 1H, *J* = 13.4, 11.6, 4.9 Hz), 2.31 (m, 1H), 2.00 (m, 4H), 1.87 (m, 1H), 1.73 (m, 2H), 1.61 (m, 2H), 1.31 (m, 4H), 0.88 (t, 3H, *J* = 6.7 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) 211.5, 132.3, 126.4, 49.4, 41.7, 34.9, 31.7, 27.7, 27.3, 24.4, 22.3, 14.0; **HRMS** (ESI): Exact mass calc'd for $C_{12}H_{21}O$ [M+H^+], 181.1587. Found 181.1585. $[\alpha]_D$ = +3.2 (c = 2.64 g/100 mL, $CHCl_3$).



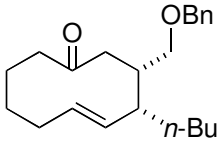
(*E*)-1-benzyloxy-3-iodo-2-propene (S2):[4] To $ZrCp_2Cl_2$ (5.4 g, 19 mmol) under N_2 was added THF (32 mL). The solution was cooled to 0 °C and stirred vigorously as a solution of DIBAL (18.7 mL, 1 M in hexanes) was added slowly. The solution was vigorously stirred for 30 minutes at 0 ºC before addition of benzyl propargyl ether (1.81 g, 12.4 mmol) in THF (6.4 mL). The reaction was warmed to room temperature, and allowed to stir for 3 hours before being cooled to -78 ºC. A homogenous solution of I_2 (5.3 g, 21 mmol) in THF (24 mL) was then added to the black solution, and after 30 minutes at -78 ºC, the solution was raised to 0 ºC, quenched with 1 M aq. HCl (40 mL), extracted with Et_2O (2 x 40 mL). The organic phase was washed with sat. $Na_2S_2O_3$ (20 mL), sat. $NaHCO_3$ (40 mL), and brine (40 mL). The combined organic layers were dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography (10% diethyl ether in hexanes, silica gel) afforded the title compound as a single isomer (2.95 g, 87%): **^{1}H NMR** (500 MHz, $CDCl_3$) 7.45-7.28 (m, 5H), 6.68 (dt, 1H, *J* = 14.4, 5.9 Hz), 6.45 (dt, 1H, *J* = 14.4, 1.5 Hz), 4.54 (s, 2H), 3.98 (dd, *J* = 5.9, 1.5 Hz). Data were identical those those reported in the literature.[4]



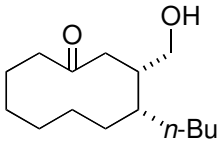
(1*R*,2*R*)-1-((1*E*)-3-benzyloxy-1-propen-1-yl)-2-((1*Z*)-1-hexen-1-yl)-cyclohexanol (13): To a solution of vinyl iodide **S2** (317 mg, 1.16 mmol) in Et_2O (15 mL) at -78 °C was added a solution of *n*-BuLi in hexanes (511 μL, 2.27 M). The mixture was allowed to stir for 1 minute prior to addition of ketone **S1** (123 mg, 0.68 mmol) in Et_2O (7.5 mL) at -78°C. The reaction mixture was allowed to stir for 30 minutes before being warmed to 0 °C and quenched with saturated NH_4Cl solution (15 mL). The organic layer was separated, and the aqueous layer extracted with Et_2O (60 mL). The combined organic layers were washed with H_2O (50 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification by flash chromatography (20% EtOAc in hexanes) afforded the title compound (201 mg, 90%): **IR** (neat) 3473, 2927, 2854, 1453, 946 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) 7.33 (m, 4H), 7.28 (dd, 1H, *J* = 6.3, 2.3, Hz), 5.74

4. Huang, Z.; Negishi, E. *Org. Lett.* **2006**, *8*, 3675–3678

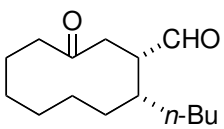
(m, 2H), 5.39 (dt, 1H, 11.0, 7.1 Hz), 5.31 (dd, 1H, *J* = 11.0, 9.8 Hz), 4.48 (d, 2H, *J* = 3.1 Hz), 4.00 (m, 2H), 2.33 (ddd, 1H, *J* = 10.2 Hz, 9.8 Hz, 4.4 Hz), 1.98 (m, 2H), 1.71 (m, 1H), 1.65 (m, 1H), 1.58 (m, 2H), 1.50 (m, 2H), 1.43 (m, 1H), 1.36 (s, 1H), 1.29 (m, 5H), 0.88 (t, 3H, *J* = 7.0 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) 141.1, 138.5, 130.9, 129.7, 128.4, 127.8, 127.6, 123.7, 73.2, 71.9, 70.5, 43.6, 38.1, 31.9, 28.5, 27.6, 25.3, 22.5, 21.4, 14.1; **HRMS** (ESI): Exact mass calc'd for $C_{22}H_{31}O$ (M-OH^-), 311.2369. Found 311.2373. $[\alpha]_D$ = -57.6 (c = 2.43 g/100 mL, $CHCl_3$).
Enantiopurity (97:3 er) was determined by chiral HPLC analysis: Chiraldex OD-H column (0.46 cm x 25 cm), flow rate of 1.0 mL/min, 2% isopropanol in hexanes. Retention times: 10.74 min (–)/12.06 min (+).



(3*S*,4*S*)-3-(benzyloxy-methylene)-4-(*n*-butyl)-5(*E*)-cyclodecenone (12): To a stirring suspension of KH (40 mg, 1.0 mmol) in Et_2O (13 mL) at 0 °C was added hexamethyldisilazane (204 μL, 1.0 mmol). The suspension was stirred for 30 minutes at room temperature prior to addition into a stirring solution of allylic alcohol **13** (170 mg, 0.51 mmol) and 18-crown-6 ether (270 mg, 1.02 mmol) in Et_2O (12 mL) at 0 °C. The resulting yellow solution was stirred for 18 h at room temperature. The reaction was quenched with sat. NH_4Cl solution (1 mL) and poured into H_2O (25 mL). The organic layer was separated, and the aqueous layer was back-extracted with Et_2O (10 mL). The combined organic phases were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by flash chromatography on silica gel (20% EtOAc in hexanes) afforded the title compound (140 mg, 83%): **IR** (neat) 3028, 2951, 1704, 1089, 984 cm^{-1}; (*note: NMR spectra were significantly broadened, presumably due to alkene anisotropy*) **^{1}H NMR** (500 MHz, $CDCl_3$) 7.34 (m, 4H), 7.29 (dd, 1H, *J* = 5.1, 2.4 Hz), 5.22 (br m, 2H), 4.52 (br m, 2H), 3.48 (br m, 2H), 2.33 (br s, 5H), 1.93 (br s, 2H), 1.25 (m, 7H), 1.09 (m, 1H), 0.86 (t, 3H, *J* = 7 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) 128.4, 127.6, 127.5, 33.4, 14.2; **HRMS** (ESI): Exact mass calc'd for $C_{22}H_{33}O_2$ [M+H^+], 329.2475. Found 329.2474. $[\alpha]_D$ = -7.3 (c = 3.77 g/100 mL, $CHCl_3$).
Enantiopurity (97:3 er) was determined by chiral HPLC analysis: Chiraldex OD-H column (0.46 cm x 25 cm), flow rate of 1.0 mL/min, 0.5% isopropanol in hexanes. Retention times: 12.03 min (+)/13.91 min (–).

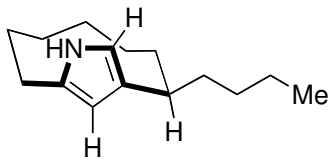


(3*S*,4*R*)-3-(hydroxy-methylene)-4-(*n*-butyl)-cyclodecanone (S3): To a solution of cyclodecanone **12** (116 mg, 0.35 mmol) in dry MeOH (11 mL) was added 10% Pd/C (35 mg). The flask was purged with H_2, and the solution allowed to stir under a balloon of H_2 at room temperature for 19 h. The solution was filtered through celite, eluting with ethyl acetate, and the filtrate concentrated in vacuo. Purification by flash chromatography (50% EtOAc in hexanes) afforded the title compound (81 mg, 95%): **IR** (neat) 3437, 2955, 2931, 2872, 1693, 1266; **^{1}H NMR** (500 MHz, $CDCl_3$) 3.70 (dt, 1H, *J* = 10.4, 4.4 Hz), 3.53 (m, 1H), 2.89 (dd, 1H, *J* = 10.1, 8.7 Hz), 2.57 (ddd, 1H, *J* = 15.2, 10.4, 3.5 Hz), 2.47 (ddd, 1H, *J* = 15.2, 7.7, 3.8 Hz), 2.39 (m, 2H), 2.12 (br s, 1H), 2.05 (m, 1H), 1.70 (m, 1H), 1.64 (app s, 1H), 1.52 (m, 2H), 1.40 (m, 4H), 1.25 (m, 8H), 0.89 (t, 3H, *J* = 7.0 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) 215.9, 64.5, 43.4, 41.9, 40.9, 36.5, 31.6, 30.3, 28.5, 25.7, 25.5, 24.3, 23.9, 22.9, 14.4; **HRMS** (ESI): Exact mass calc'd for $C_{15}H_{29}O_2$ [M+H^+], 241.2162. Found 241.2158. $[\alpha]_D$ = -4.9 (c = 0.45 g/100 mL, $CHCl_3$).



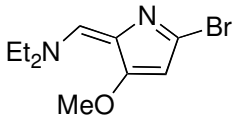
(3*S*,4*R*)-3-(formyl)-4-(*n*-butyl)-cyclodecanone (S4): To a solution of keto-

alcohol **S3** (204 mg, 0.85 mmol) in DCM (28 mL) was added deionized H_2O (15 μL), followed by Dess-Martin periodinane (540 mg, 1.28 mmol). The mixture was allowed to stir for 30 min then diluted with ether, and concentrated to a small volume in vacuo. The residue was taken up in ether and washed with 1:1 0.5 M $Na_2S_2O_3$/sat. $NaHCO_3$ (90 mL), H_2O (30 mL), and brine (30 mL). The aqueous layers were back-extracted with Et_2O (50 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Purification by flash chromatography (20% EtOAc in hexanes, silica gel) afforded the title compound (166 mg, 82%): **IR** (neat) 2929, 2852, 1724, 1702 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) 9.74 (s, 1H), 3.19 (dt, 1H, *J* = 9.7, 3.5 Hz), 2.89 (dd, 1H, 16.2, 9.7 Hz), 2.67 (dd, 1H, 16.2, 3.5 Hz), 2.55 (m, 2H), 2.15 (m, 1H), 2.03 (m, 1H), 1.73 (m, 1H), 1.54-1.18 (br m, 13H), 0.91 (t, 3H, *J* = 7.0 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) 213.2, 203.6, 52.0, 43.1, 37.1, 35.6, 31.8, 29.9, 28.7, 26.1, 25.1, 23.8, 23.4, 22.8, 14.0; **HRMS** (ESI): Exact mass calc'd for $C_{15}H_{27}O_2$ [M+H$^+$], 239.2006. Found 239.2001. $[\alpha]_D$ = +47.7 (c = 0.675 g/100 mL, $CHCl_3$).



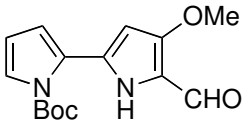
2-butyl-10-azabicyclo[7.2.1]dodeca-1(11),9(12)diene (*syn*-11): To a solution of dicarbonyl **S4** (166 mg, 0.70 mmol) in anhydrous methanol (7 mL) was added dry NH_4OAc (540 mg, 7.0 mmol). The stirred solution was heated at reflux at 65 ºC for 40 minutes then cooled to room temperature. The reaction mixture was diluted in hexanes (75 mL) and filtered through silica gel, eluting with 20% ethyl acetate in hexanes. The crude material was concentrated in vacuo, and the residue was subject to flash chromatography (20% ethyl acetate in hexanes, silica gel) to afford the title compound as a ca. 10:1 mixture of atropisomers (131 mg, 86%): **IR** (neat) 3372, 2924, 2856, 2361, 2336, 1696, 1454 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) 7.70 (br s, 1H), 6.45 (s, 1H), 6.23 (s, 1H), 2.67 (ddd, 1H, *J* = 14.0, 4.6, 2.0 Hz), 2.44 (m, 2H), 1.79-1.62 (m, 5H), 1.55-1.30 (m, 5H), 0.93 (m, 4H), 0.92 (t, 3H, *J* = 7.0 Hz), 0.71 (m, 1H), 0.52 (dd, 1H, *J* = 13.1, 10.8 Hz), -1.89 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) 132.6, 130.0, 114.7, 111.7, 41.8, 41.2, 33.5, 32.6, 30.3, 30.0, 29.8, 29.4, 26.7, 23.0, 14.2; **HRMS** (ESI) Exact mass calc'd for $C_{15}H_{25}N$ [M+H$^+$], 220.2060. Found 220.2057. $[\alpha]_D$ = -32.7 (c = 0.345 g/100 mL, $CHCl_3$).

Enantiopurity (≥97:3 er) was checked by chiral HPLC analysis: Chiraldex OD-H column (0.46 cm x 25 cm), flow rate of 1.0 mL/min, 2% isopropanol in hexanes. Retention times: 6.91 min (–)/9.27 min (+).

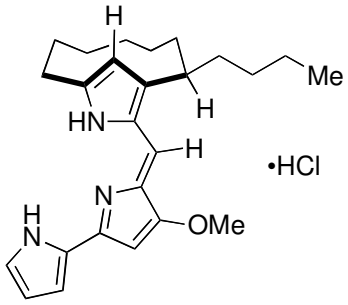


(*E*)-*N*-((5-bromo-3-methoxy-2*H*-pyrrol-2-ylidene)methyl)-*N*-ethylethanamine (S5): To a solution of diethyl formamide (1.54 mL, 13.8 mmol) in DCM (12 mL) at 0 ºC was added dropwise phosphorous oxybromide (4.84 g, 16.8 mmol) in DCM (3 mL) over 15 minutes. The solution was stirred at 0 ºC for 10 minutes before addition of 4-methoxy-3-pyrrolin-2-one (1.0 g, 8.9 mmol) in several portions over 5 minutes. The mixture was stirred for 10 minutes at 0 ºC and then heated to reflux for 3.5 h. The mixture was cooled to 0 ºC and H_2O (1.7 mL) was added dropwise, maintaining the temperature below 20 ºC. The solution was neutralized with 15% aq. NaOH (ca. 20 mL) and extracted with DCM (2 x 20 mL). The organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. Flash chromatography (25% ethyl acetate in hexanes, silica gel) of the residue afforded the title compound (1.27 g, 55%), which was identical in all aspects to that which was previously reported.[5]

5. Dairi, K.; Tripathy, S.; Attardo, G.; Lavaleé, J. F. *Tetrahedron Lett.* **2006**, *47*, 2605–2606.



***tert*-butyl 5'-formyl-4'-methoxy-1*H*,1'*H*-2,2'-bipyrrole-1-carboxylate (21):** To $Pd(OAc)_2$ (30 mg, 0.14 mmol) in toluene (1 mL) was added triphenylphosphine (159 mg, 0.61 mmol). The yellow slurry was stirred for 20 minutes at 70 ºC, followed by the addition of bromoenamine **S5** (350 mg, 1.34 mmol) and *N*-Boc-pyrrole-2-boronic acid (427 mg, 2.0 mmol) in degassed 9:1 dioxane/H_2O (11.5 mL). Na_2CO_3 (429 mg, 4.0 mmol) was added, and the solution was degassed with Ar before heating to 85 ºC for 3.5h. The reaction was cooled to room temperature before being diluted with H_2O (20 mL) and DCM (20 mL). The mixture was stirred vigorously as 2M HCl was added to neutralize the solution. The mixture was extracted with DCM (2 x 20 mL) and the organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. Flash chromatography (15% ethyl acetate in hexanes, silica gel) afforded the title compound as an orange powder (292 mg, 75%), which was identical in all aspects to that which was previously reported.[6]

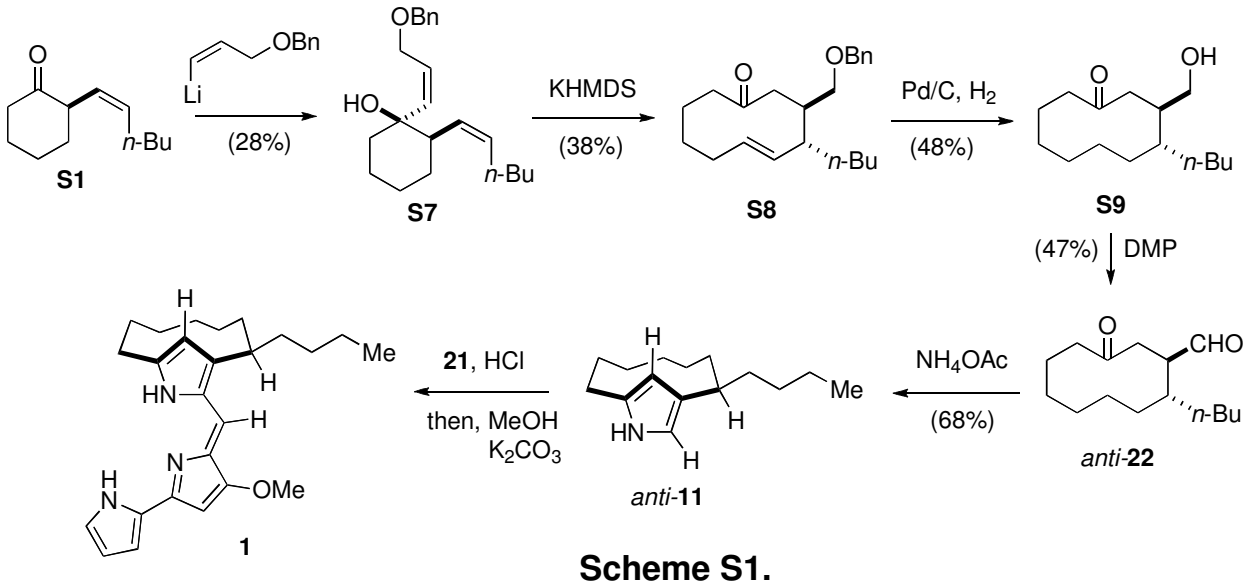


***(R)*-streptorubin B hydrochloride (1):** To pyrrole *syn*-**11** (19 mg, 0.09 mmol) and biaryl aldehyde **21** (31 mg, 0.11 mmol) was added anhydrous MeOH (1.5 mL). The stirred solution was placed in a water bath (18 ºC) and a solution of HCl in MeOH (91 μL, 1 M, freshly generated from AcCl in MeOH) was added, upon which the solution turned brilliant red. The solution was stirred for 1 h 15 min before addition of a suspension of NaOMe in MeOH (910 μL, 0.5 M), upon which the solution turned a dark brown. After 45 min, LCMS showed the reaction to be complete, and the reaction mixture was poured into Et_2O (25 mL) and washed with H_2O (15 mL). The aqueous layer was extracted with Et_2O (15 mL) and the combined organic layers were dried (Na_2SO_4). Two iterations of column chromatography (5% Et_2O and 5% NEt_3 in pentanes, then $CHCl_3$ to 3% MeOH/$CHCl_3$, silica gel) afforded the natural product as the HCl salt, as a ca. 1:1 mixture of atropisomers, which upon standing at room temperature in $CHCl_3$ in a closed vessel equilibrated to a single atropisomer (28 mg, 72%). Single crystals for X-ray diffraction were grown by vapor diffusion of hexanes into a concentrated solution of **1** in ethyl acetate (ca. 5 mg in 0.2 mL solvent). **IR** (neat) 3436, 3371, 3019, 2937, 1764 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) 12.70 (s, 1H), 12.66 (s, 1H), 12.58 (s, 1H), 7.22 (s, 1H), 7.21 (s, 1H), 7.11 (s, 1H), 6.90 (s, 1H), 6.51 (s, 1H), 6.34 (t, 1H, J = 2.7 Hz), 6.09 (s, 1H), 4.02 (s, 3H), 3.33 (m, 1H), 3.10 (m, 1H), 2.53 (dt, 1H, J = 12.3, 5.4 Hz), 1.96-1.68 (m, 5H), 1.55 (m, 2H), 1.37 (m, 5H), 1.14 (m, 2H), 1.24 (m, 3H), 0.91 (m, 5H), 0.78 (m, 1H), -1.55 (dt, 1H, J = 14.1, 8.8 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) 165.4, 154.4, 150.6, 147.0, 126.7, 125.0, 122.4, 120.3, 116.8, 116.6, 112.5, 111.5, 92.8, 58.7, 38.9, 37.5, 31.7, 30.9, 30.4, 30.0, 29.1, 27.7, 25.4, 22.9, 14.2; **HRMS** (ESI) Exact mass calc'd for $C_{25}H_{33}N_3O$ [M+H^+], 392.2696. Found 392.2700.

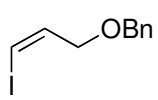
(*S*)-Streptorubin B hydrochloride (*ent*-1): The same procedures used for the synthesis of (*R*)-streptorubin B were employed in the syntheses of (*S*)-streptorubin B and *rac*-streptorubin B, with the exception that (*R*)-proline or *rac*-proline was used instead of (*S*)-proline in the desymmetrizing aldol-Wittig sequence.

6. Aldrich, L. N.; Dawsen, E. S.; Linsley, C. W. *Org. Lett.* **2010**, *12*, 1048–1051.

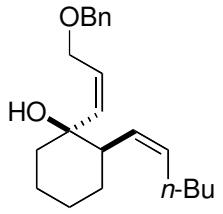
Part 4: Experimental Procedures: Exploration of Pyrrole Atropisomer (Unoptimized)



Scheme S1.

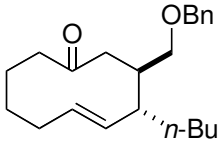


(*Z*)-1-benzyloxy-3-iodo-2-propene (S6): To benzyl propynol (5.0 g, 35 mmol) was added tributyltin hydride (13.0 g, 44.9 mmol). AIBN (57 mg, 0.35 mmol) was added, and the stirring solution was heated at 120 °C for 3 hours. The crude solution was diluted in DCM (340 mL), and a solution of I_2 (11.8 g, 46.6 mmol) in DCM (350 mL) was titrated into the stirring solution via addition funnel. The resulting dark solution was quenched with sat. $Na_2S_2O_3$ (250 mL), washed with 0.5 M aq. NaOH (250 mL), brine (250 mL), and filtered through silica, eluting with DCM. Flash column chromatography (10% diethyl ether in hexanes, silica gel) afforded the title compound in two fractions, the first containing a ~1:1 mixture of the Z and E isomers (3.0 g), the second containing a ~3:2 mixture of Z and E isomers (2.3 g, 56%): **^{1}H NMR** (500 MHz, $CDCl_3$) 7.40-7.28 (m, 5H), 6.50 (dt, 1H, J = 7.6, 5.4 Hz), 6.41 (m, 1H), 4.54 (s, 2H), 4.13 (dd, J = 5.5, 1.5 Hz).

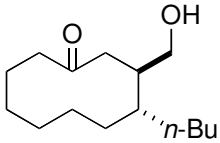


(1*R*,2*R*)-1-((1*Z*)-3-benzyloxy-1-propen-1-yl)-2-((1*Z*)-1-hexen-1-yl)-cyclohexanol (S7): To a solution of a ~3:2 mixture of *Z*:*E* vinyl iodide **S6** (643 mg, 2.35 mmol) in Et_2O (30 mL) at -78 °C was added a solution of *n*-BuLi in hexanes (2.35 mL, 1.0 M). The mixture was allowed to stir for 4 minutes prior to addition of ketone **S1** (249 mg, 1.38 mmol) in Et_2O (16 mL) at -78 °C. The reaction mixture was allowed to stir for 50 minutes before being warmed to 0 °C and quenched with saturated NH_4Cl solution (30 mL). The organic layer was separated, and the aqueous layer extracted with Et_2O (30 mL). The combined organic layers were washed with H_2O (15 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification by flash chromatography (5% EtOAc in hexanes) afforded the title compound (126 mg, 28%), along with the corresponding alkynyl addition product (85 mg, 19%) and the *E*-allylic alcohol **S7** (50 mg, 11%): **IR** (neat) 3457, 3012, 2956, 2858, 1454 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) 7.36-7.27 (m, 5H), 5.57-5.48 (m, 2H), 4.54 (d, 2H, J = 3.84 Hz), 4.25 (app t, 2H, J = 5.4 Hz), 3.06 (s, 1H), 2.30 (m, 1H), 2.07-1.96 (m, 2H), 1.74 (m, 1H), 1.69 (m, 1H), 1.59 (m, 1H), 1.51 (m, 2H), 1.43 (m, 1H), 1.39 (m, 1H), 1.31 (m, 4H), 1.28 (m, 1H), 0.89

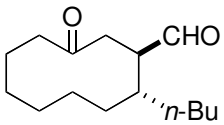
(m, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) 141.2, 130.6, 130.1, 128.4, 127.8, 127.7, 126.5, 124.9, 74.5, 72.5, 66.6, 44.4, 38.4, 32.0, 28.2, 27.5, 25.1, 22.4, 21.1, 14.1; **HRMS** (ESI): Exact mass calc'd for $C_{22}H_{32}O_2Na$ (M+Na^+), 351.2295. Found 351.2296.



(3*R*,4*S*)-3-(benzyloxy-methylene)-4-(*n*-butyl)-5(*E*)-cyclodecenone (S8): To a stirring solution of allylic alcohol **S7** (120 mg, 0.37 mmol) and 18-crown-6 ether (241 mg, 0.91 mmol) in Et_2O (15 mL) at 0 °C was added KHMDS in toluene (0.5 M, 1.83 mL). The resulting yellow solution was stirred for 32 h at room temperature. The reaction was quenched with sat. NH_4Cl solution (5 mL) and poured into H_2O (15 mL). The organic layer was separated, and the aqueous layer was back-extracted with Et_2O (2 x 10 mL). The combined organic phases were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by flash chromatography on silica gel (5% EtOAc in hexanes) afforded the title compound (46 mg, 38%): **IR** (neat) 2952, 2928, 2856, 1707, 1443, 1100 cm^{-1}; (*note: the NMR spectrum did not display the same obscurity observed for the other diastereomer*) **^{1}H NMR** (500 MHz, $CDCl_3$) 7.36-7.26 (m, 5H), 5.30 (ddd, 1H, *J* = 14.6, 11.0, 3.9 Hz), 4.88 (dd, 1H, *J* = 14.6, 10.4 Hz), 4.54 (d, 1H, *J* = 12.1 Hz), 4.43 (d, 1H, *J* = 12.1 Hz), 3.47 (m, 2H), 2.47 (m, 1H), 2.44 (m, 1H), 2.36 (m, 1H), 2.32 (m, 1H), 2.30 (m, 1H), 2.22 (m, 1H), 1.88 (m, 1H), 1.86 (m, 2H), 1.73 (m, 1H), 1.60 (m, 1H), 1.43 (m, 1H), 1.27 (m, 1H), 1.23-1.16 (m, 3H), 1.07 (m, 1H), 0.84 (t, 3H, *J* = 7.2 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) 211.8, 139.5, 138.6, 129.7, 128.4, 127.6, 127.5, 73.0, 71.8, 47.8, 46.7, 45.4, 44.3, 33.5, 31.3, 29.9, 28.8, 22.7, 22.5, 14.1; **HRMS** (ESI): Exact mass calc'd for $C_{22}H_{32}O_2Na$ [M+Na^+], 351.2295. Found 351.2305.

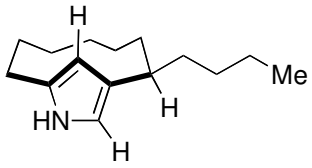


(3*R*,4*R*)-3-(hydroxy-methylene)-4-(*n*-butyl)-cyclodecanone (S9): To a solution of cyclodecanone **S8** (46 mg, 0.14 mmol) in dry MeOH (4 mL) was added 10% Pd/C (14 mg). The flask was purged with H_2, and the solution stirred under a balloon of H_2 at room temperature for 16 h. The solution was filtered through celite, eluting with ethyl acetate, and concentrated in vacuo. Purification by flash chromatography (30% EtOAc in hexanes) afforded the title compound (16 mg, 48%): **IR** (neat) 3305, 2953, 2926, 1694, 1440, 1068; **^{1}H NMR** (500 MHz, $CDCl_3$) 3.74 (dd, 1H, *J* = 10.8, 3.2 Hz), 3.58 (m, 1H), 2.86 (dd, 1H, *J* = 16.2, 3.4 Hz), 2.61 (m, 2H), 2.53 (s, 1H), 2.46 (ddd, 1H, *J* = 14.1, 8.5, 3.4 Hz), 1.99 (m, 1H), 1.86 (m, 1H), 1.75 (m, 1H), 1.56 (m, 1H), 1.50 (m, 1H), 1.43-1.15 (m, 13H), 0.88 (t, 3H, *J* = 7.1 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) 216.4, 65.5, 45.6, 44.6, 42.4, 36.2, 31.9, 28.9, 27.7, 26.2, 25.8, 24.2, 23.7, 23.2, 14.2; **HRMS** (ESI): Exact mass calc'd for $C_{15}H_{28}O_2Na$ [M+Na^+], 263.1982. Found 263.1982.

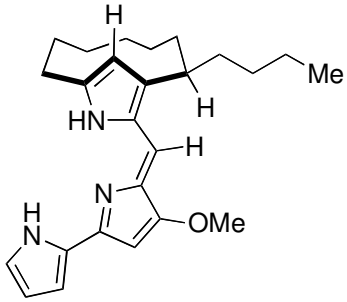


(3*R*,4*R*)-3-(formyl)-4-(*n*-butyl)-cyclodecanone (*anti*-22): To a solution of keto-alcohol **S9** (15 mg, 0.063 mmol) in DCM (2 mL) was added deionized H_2O (~1 μL), followed by Dess-Martin periodinane (40 mg, 0.094 mmol). The solution was allowed to stir for 10 min, then diluted in ether (25 mL) and washed with 1:1 0.5 M $Na_2S_2O_3$/sat. $NaHCO_3$ (25 mL). The aqueous layer was back-extracted with Et_2O (2 x 10 mL) and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Purification by flash chromatography (20% EtOAc in hexanes, silica gel) afforded the title compound (7.0 mg, 47%): **IR** (neat) 2955, 2930, 2859, 1721, 1703, 1455, 1358 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) 9.82 (s, 1H), 2.77 (app s, 3H), 2.63 (ddd, 1H, *J* = 14.3, 9.8, 3.7 Hz), 2.52 (ddd, 1H, 14.3, 8.2, 3.3 Hz), 1.87 (m, 2H), 1.77 (m, 1H), 1.55 (m, 2H), 1.46-1.22 (m, 11H),

0.91 (t, 3H, *J* = 6.9 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) 212.2, 204.3, 52.8, 43.8, 42.0, 36.0, 33.3, 29.2, 26.9, 26.5, 24.9, 23.7, 23.0, 22.9, 14.1; **HRMS** (ESI): Exact mass calc'd for $C_{15}H_{26}O_2Na$ [M+Na^+], 261.1825. Found 261.1825.



2-butyl-10-azabicyclo[7.2.1]dodeca-1(11),9(12)diene (*anti*-11): To a solution of dicarbonyl *anti*-**22** (1.0 mg, 0.004 mmol) in anhydrous methanol (0.5 mL) was added dry NH_4OAc (6 mg, 0.077 mmol). The stirred solution was heated at reflux at 65 ºC for 35 minutes under N_2 and cooled to room temperature. The reaction mixture was diluted in hexanes (2 mL) and the solution was immediately subjected to flash chromatography (10% ethyl acetate in hexanes, silica gel) to afford the title compound as a ca. 5:1 mixture of atropisomers, favoring *anti*-**11** (0.6 mg, 68%): **^{1}H NMR** (500 MHz, $CDCl_3$) 7.62 (s, 1H), 6.47 (s, 1H), 6.26 (s, 1H), 2.79 (m, 1H), 2.63 (ddd, 1H, *J* = 14, 4.7, 1.8 Hz), 2.45 (ddd, 1H, *J* = 14.0, 13.0, 5.0 Hz), 1.80-1.61 (m, 4H), 1.49-1.24 (m, 8H), 1.07-0.82 (m, 4H), 0.89 (t, 3H, *J* = 6.44 Hz), 0.69 (ddd, 1H, *J* = 13.6, 11.7, 7.5 Hz), -1.86 (dt, 1H, *J = 13.4, 8.7 Hz*); **^{13}C NMR** (125 MHz, $CDCl_3$) 133.2, 129.2, 114.5, 111.6, 39.4, 37.3, 32.4, 31.9, 30.7, 29.5, 29.4, 27.3, 26.0, 23.0, 14.3; **HRMS** (ESI) Exact mass calc'd for $C_{15}H_{25}N$ [M+H^+], 220.2060. Found 220.2057.

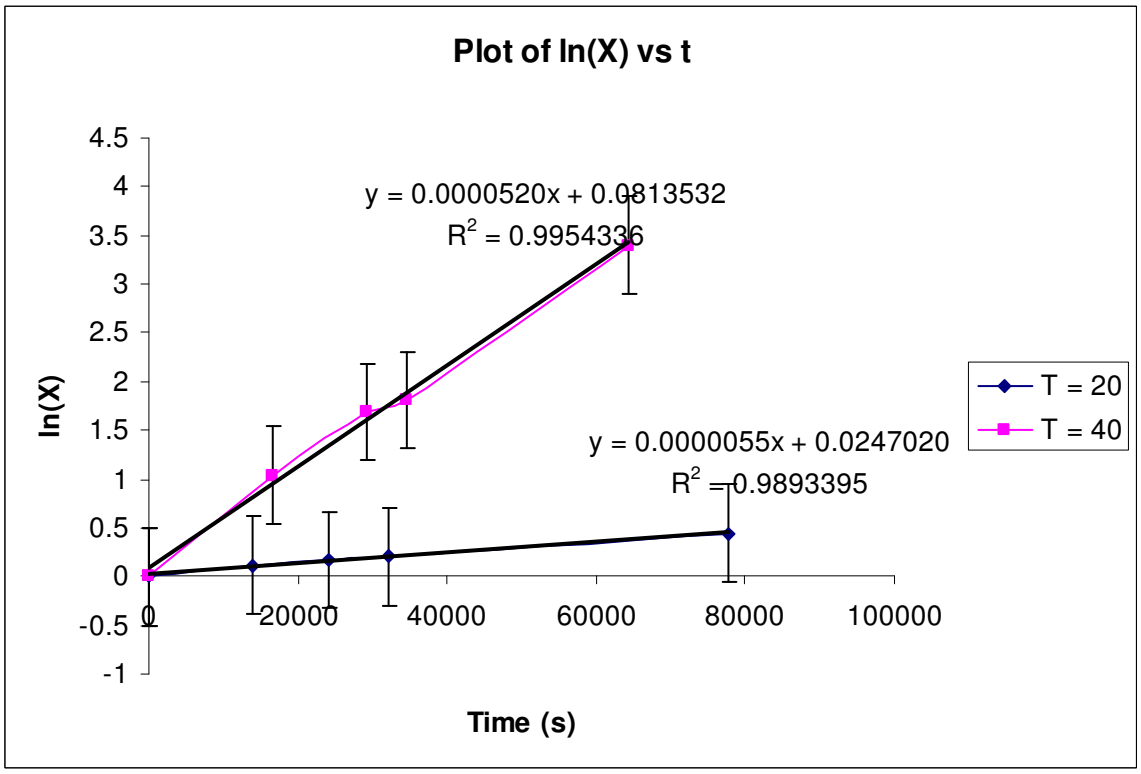


Streptorubin B (1): To the purified *anti*-**11** (0.6 mg, 0.003 mmol) and biaryl aldehyde **21** (2 mg, 0.007 mmol) was added anhydrous MeOH (0.25 mL). To the stirred solution in a water bath (18 ºC) was added a solution of HCl in MeOH (6 µL, 1M, freshly generated from AcCl in MeOH), upon which the solution turned a brilliant pink. The solution was let stir for 1 h 5 min before addition of a suspension of NaOMe in MeOH (120 µL, 0.5 M), upon which the solution turned a bright yellow-orange color. After 45 min, the reaction mixture was poured into Et_2O (10 mL) and washed with H_2O (5 mL). The organic layer was dried (Na_2SO_4) and concentrated in vacuo. The residue was immediately subjected to column chromatography ($CHCl_3$, silica gel), and the fractions containing streptorubin B were concentrated and diluted with hexanes/diethylamine (99.9:0.1), and subject to HPLC analysis (Chiraldex IA column (0.46 cm x 25 cm), flow rate of 1.0 mL/min, 5% isopropanol in 95% hexanes with 0.1% diethylamine. Retention times: 7.30 min ((*S*)-streptorubin B)/8.16 min (*atropdia*-(*R*)-streptorubin B)/9.94 min (*atropdia*-(*S*)-streptorubin B)/26.90 min ((*R*)-streptorubin B). Analysis revealed the selective formation of streptorubin B over the atropisomer.

Part 5: Measurement of Atropisomerism Activation Barrier

Freshly prepared atrop-streptorubin B (2 mg) was dissolved in chloroform (30 mL) and partitioned into two equal fractions. One fraction was let stir in an ambient temperature bath (20 ºC) and the other was let stir in an oil bath at 40 ºC. Fractions (1 mL) were periodically drawn from the two fractions and concentrated. The relative concentrations of the two atropdiastereomers was assayed by HPLC (Chiraldex IA column [(0.46 cm x 25 cm), flow rate of 1.0 mL/min, 5% isopropanol in 95% hexanes with 0.1% diethylamine]. Retention times: 7.30 min (streptorubin B)/9.94 min (atrop-streptorubin B). The relative absorptive efficiency between the two atropdiastereomers was approximately 1:1, as determined by comparison of ^{1}H NMR spectroscopy and HPLC derived data. The activation barrier (~20.5 kcal/mol) was approximated using the Arrhenius equation, assuming first-order equilibration with a rate equation of the form:

$$\ln(X) = \ln(\frac{[S]_0 - [S]_e}{[S]_t - [S]_e}) = (k_1 + k_{-1})t$$



Part 6: CD Spectra

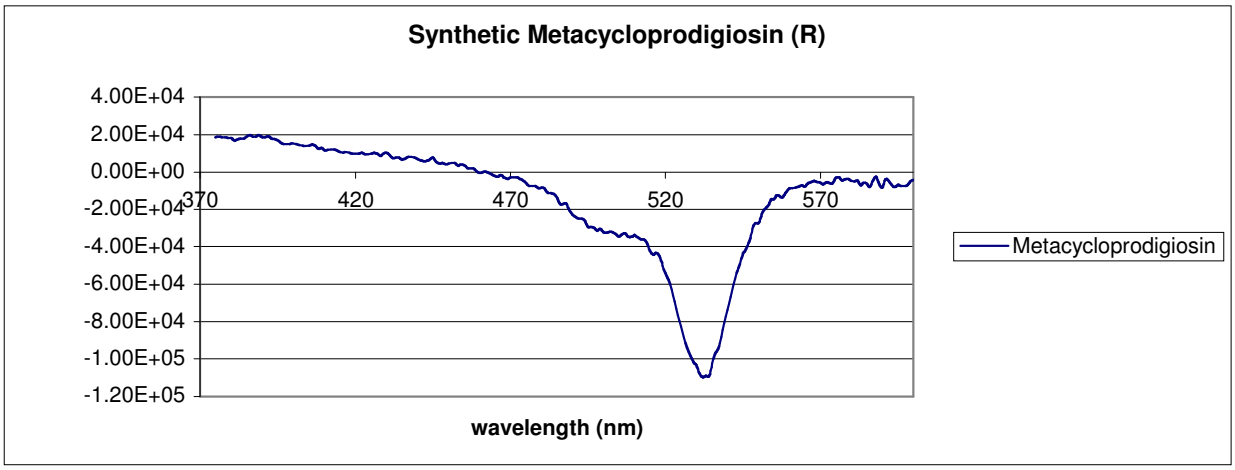


Figure S1. Synthetic Metacycloprodigiosin (R). Prepared according to Clift, M. D.;Thomson R. J., *J. Am. Chem. Soc*, **2009**, *131*, 14579–14583.

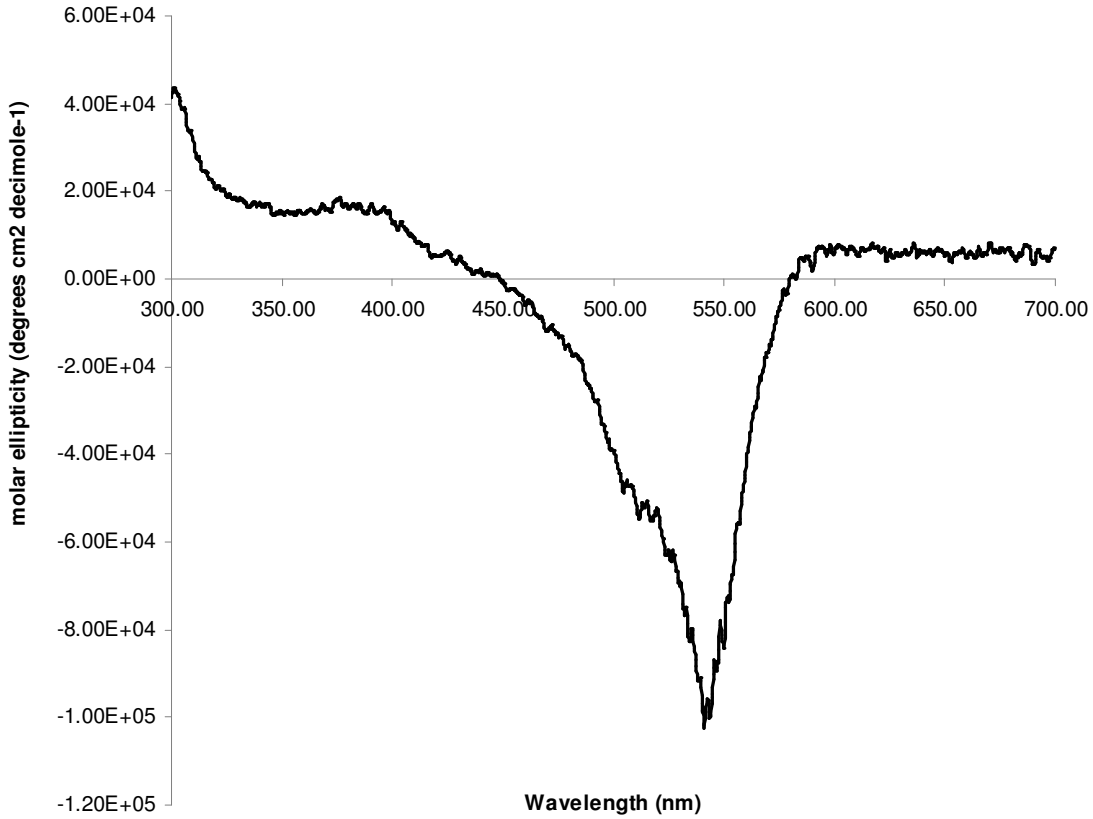


Figure S2. Natural Metacycloprodigiosin (S) isolated from *S. coelicolor* W31 + *mcpG*. Spectrum courtesy of Prof. Gregory Challis, University of Warwick.

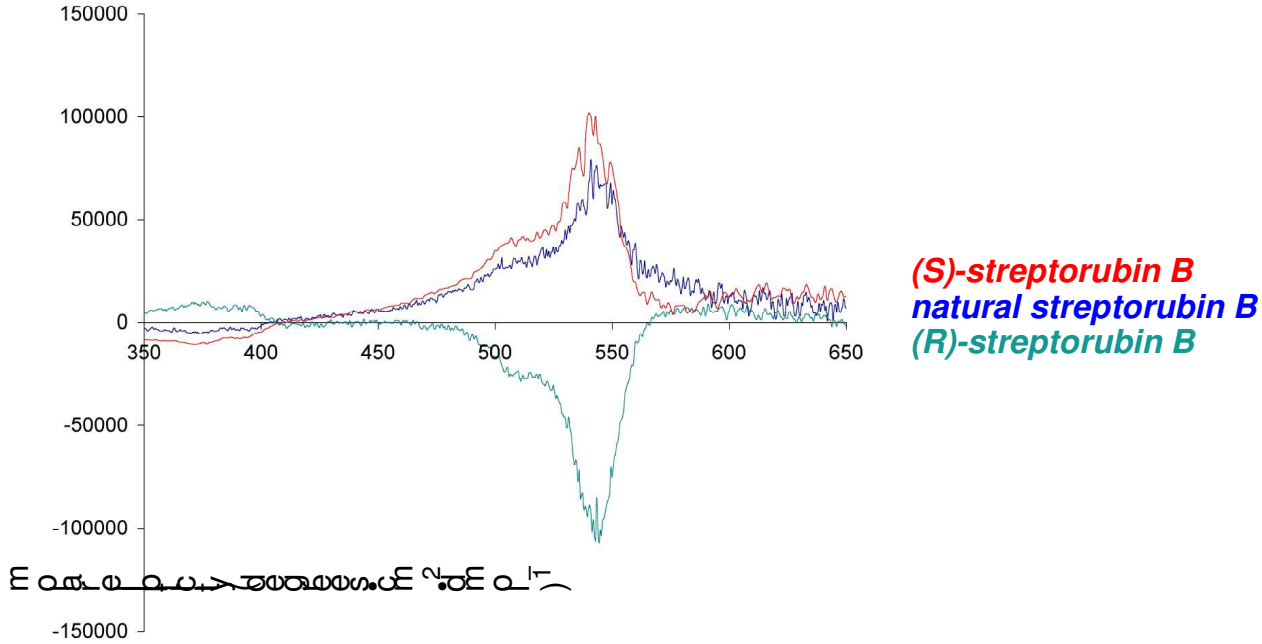
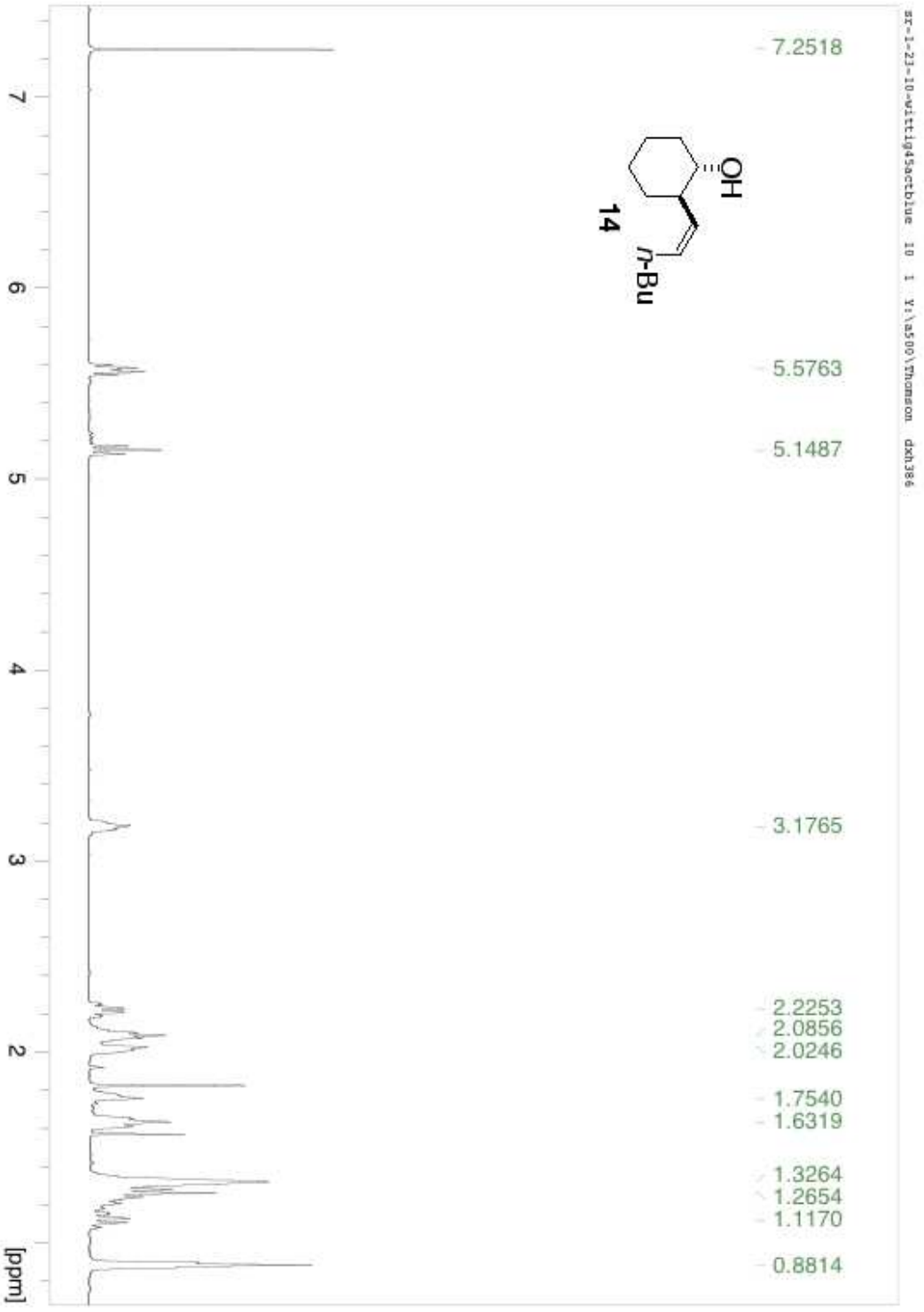
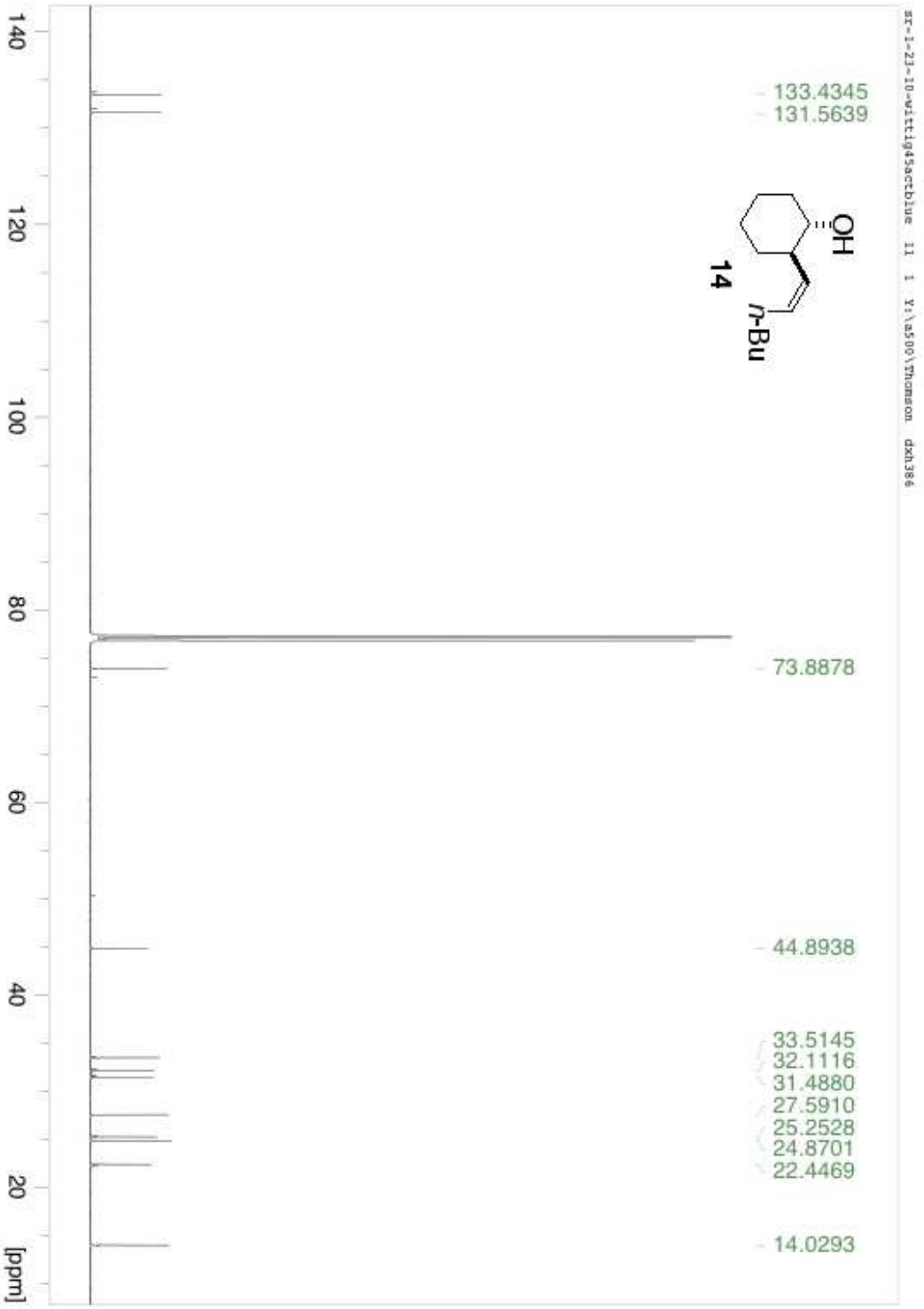
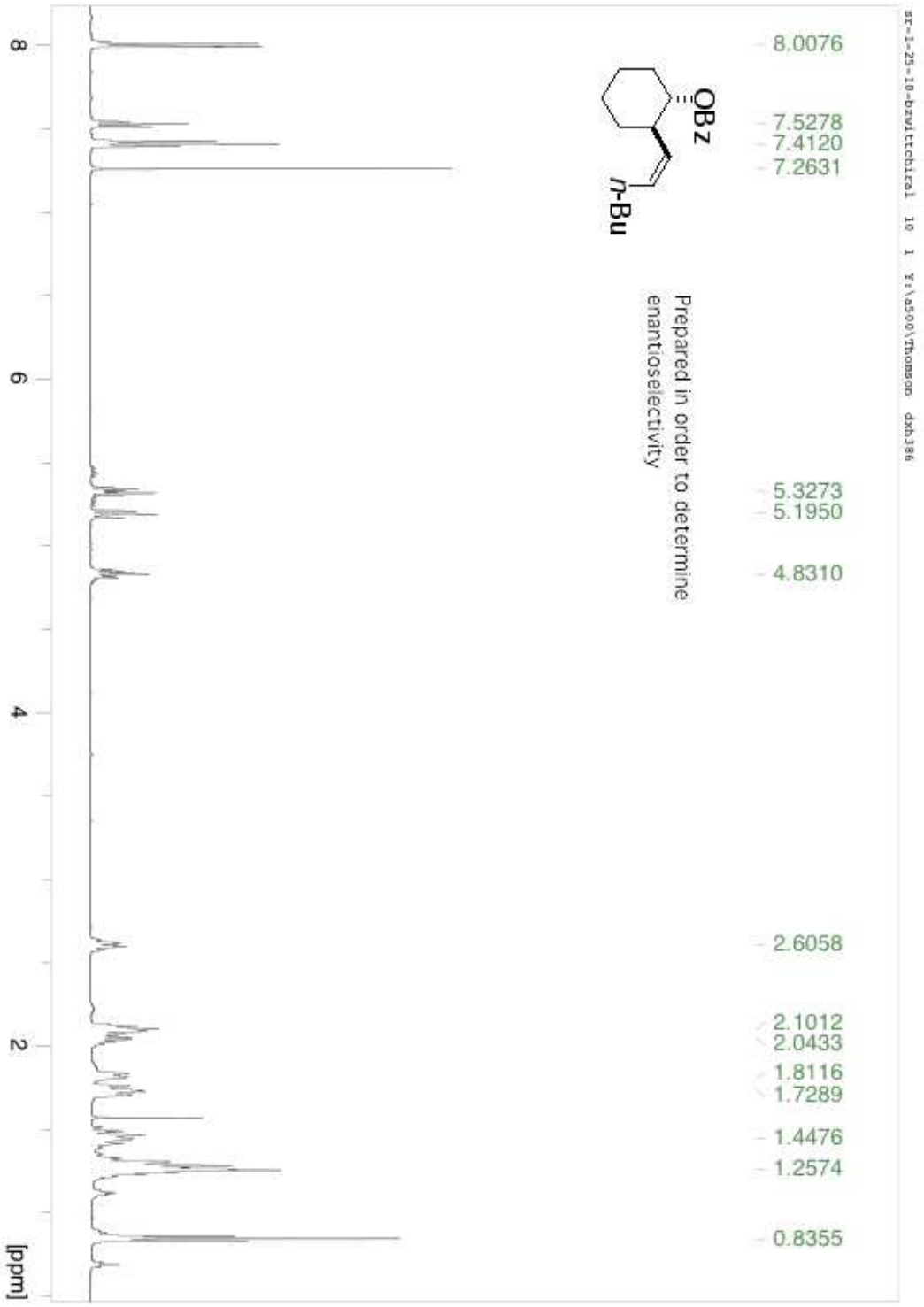


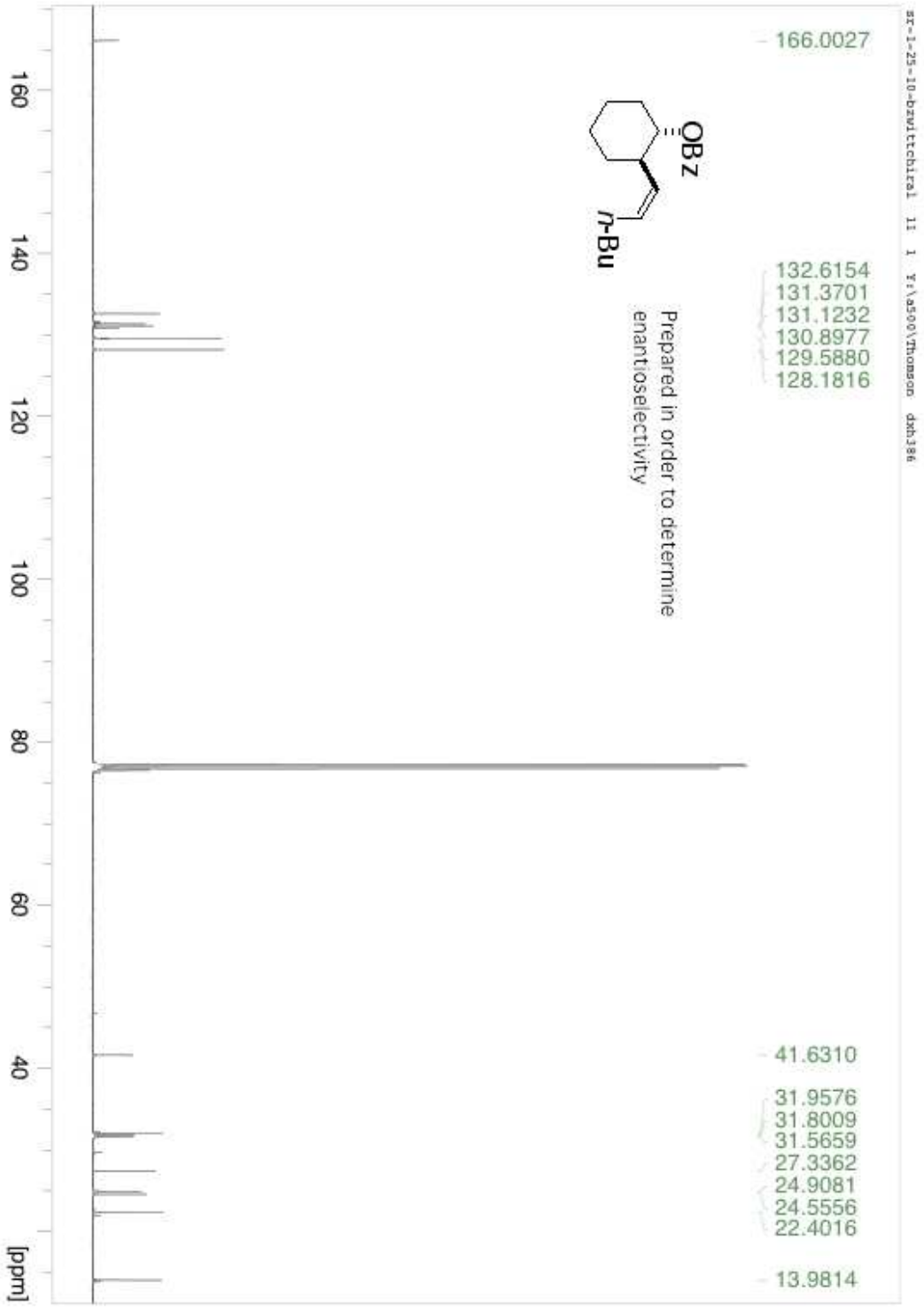
Figure S3. Comparison of synthetic streptorubin B (both enantiomers) with a natural sample isolated from *S. coelicolor* M511 (provided by Prof. Gregory Challis, University of Warwick).

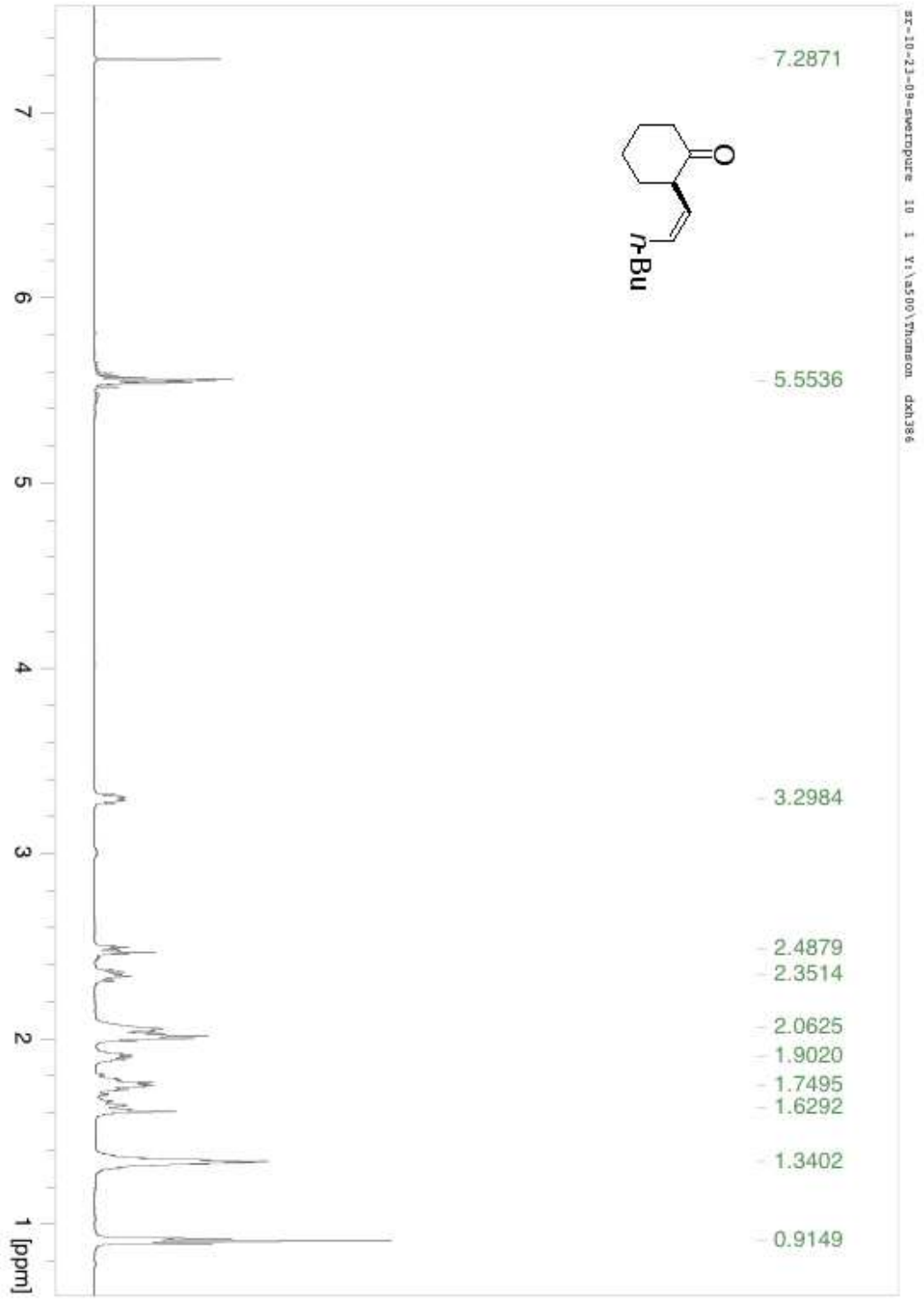
Part 7: 1H and 13C NMR Spectra



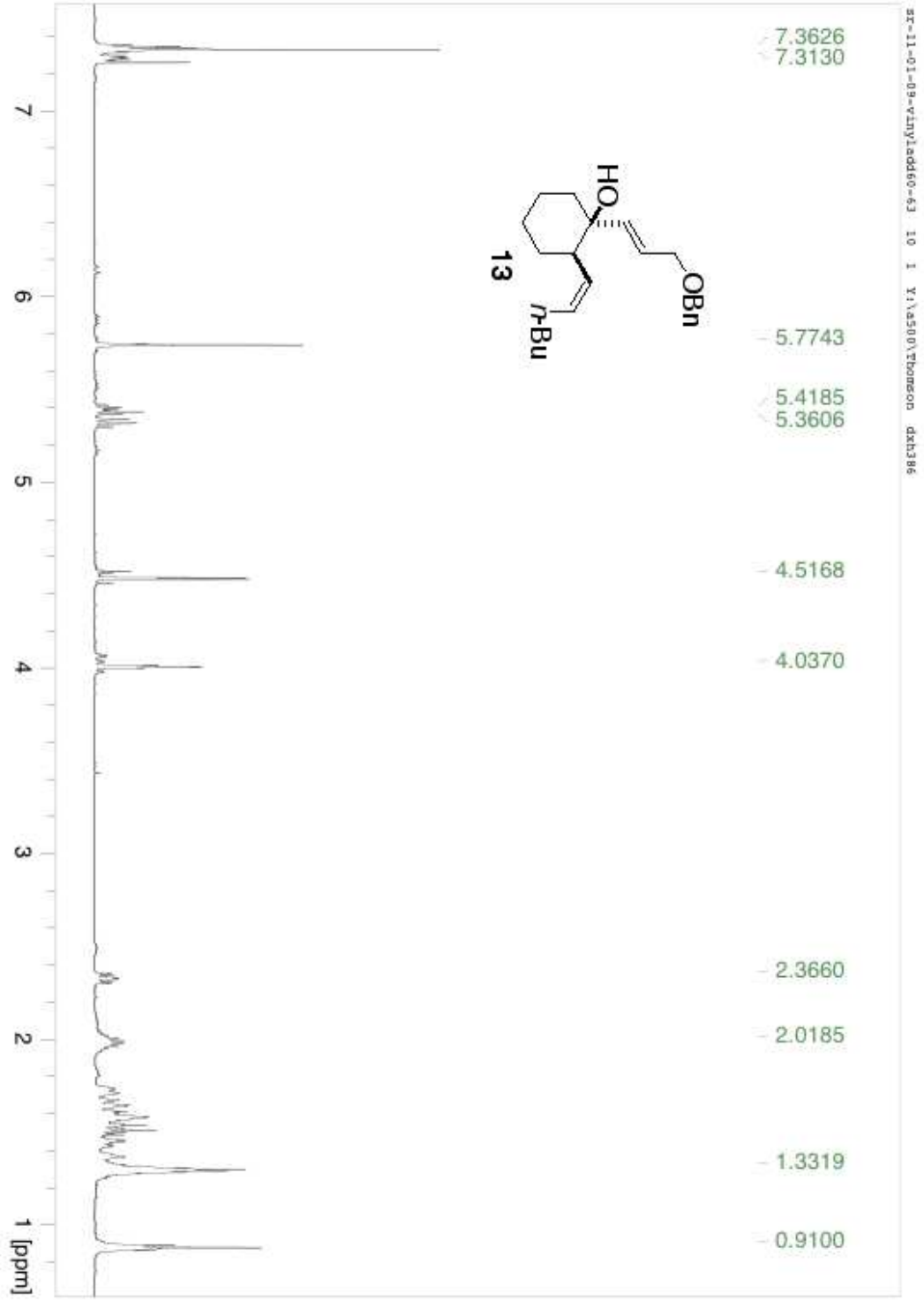

133.4345
131.5639
OH
14
n-Bu
73.8878
44.8938
33.5145
32.1116
31.4880
27.5910
25.2528
24.8701
22.4469
14.0293
140
120
100
80
60
40
20
[ppm]

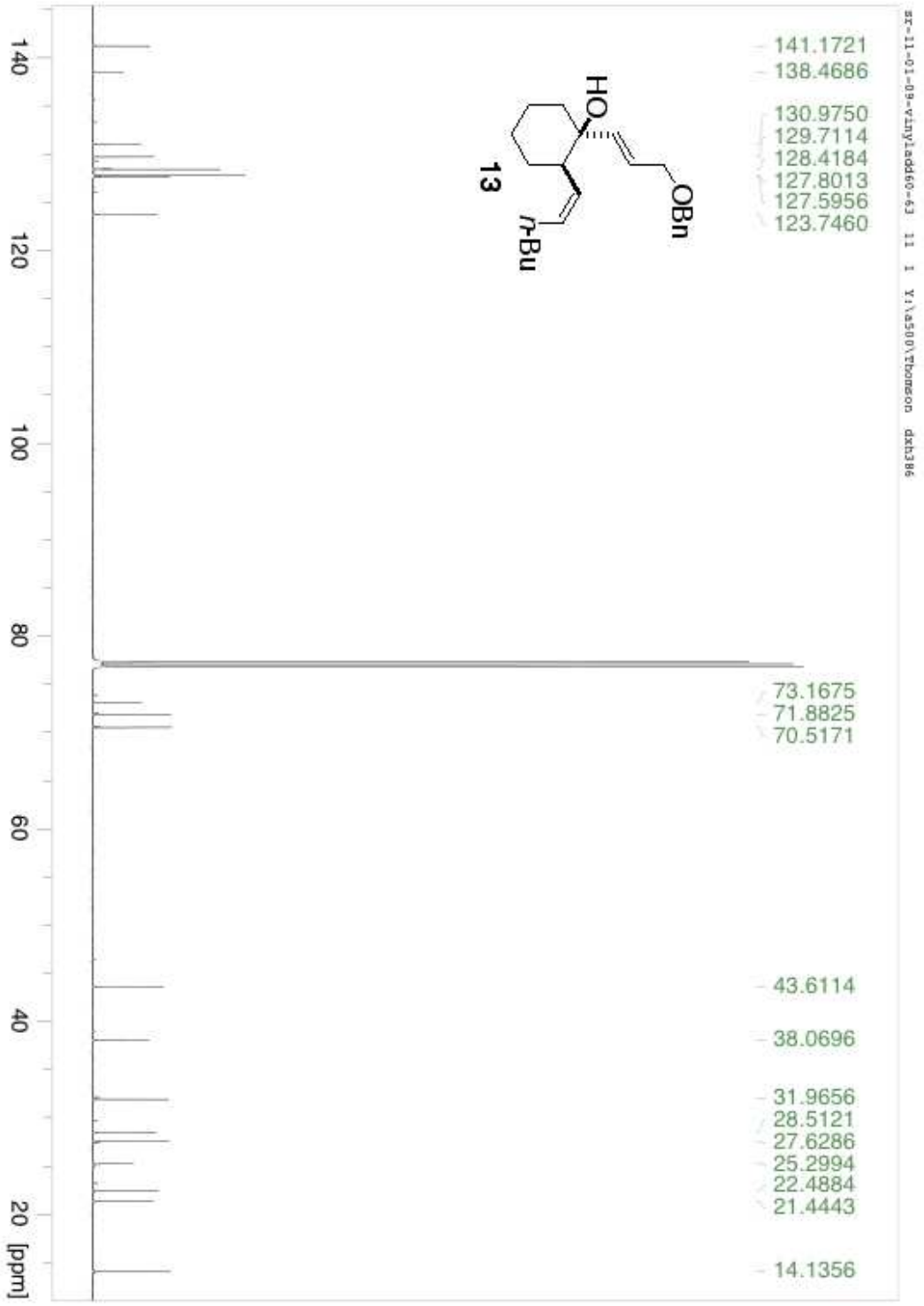

8.0076
7.5278
7.4120
7.2631
5.3273
5.1950
4.8310
2.6058
2.1012
2.0433
1.8116
1.7289
1.4476
1.2574
0.8355
OBz
n-Bu
Prepared in order to determine enantioselectivity
8
6
4
2
[ppm]

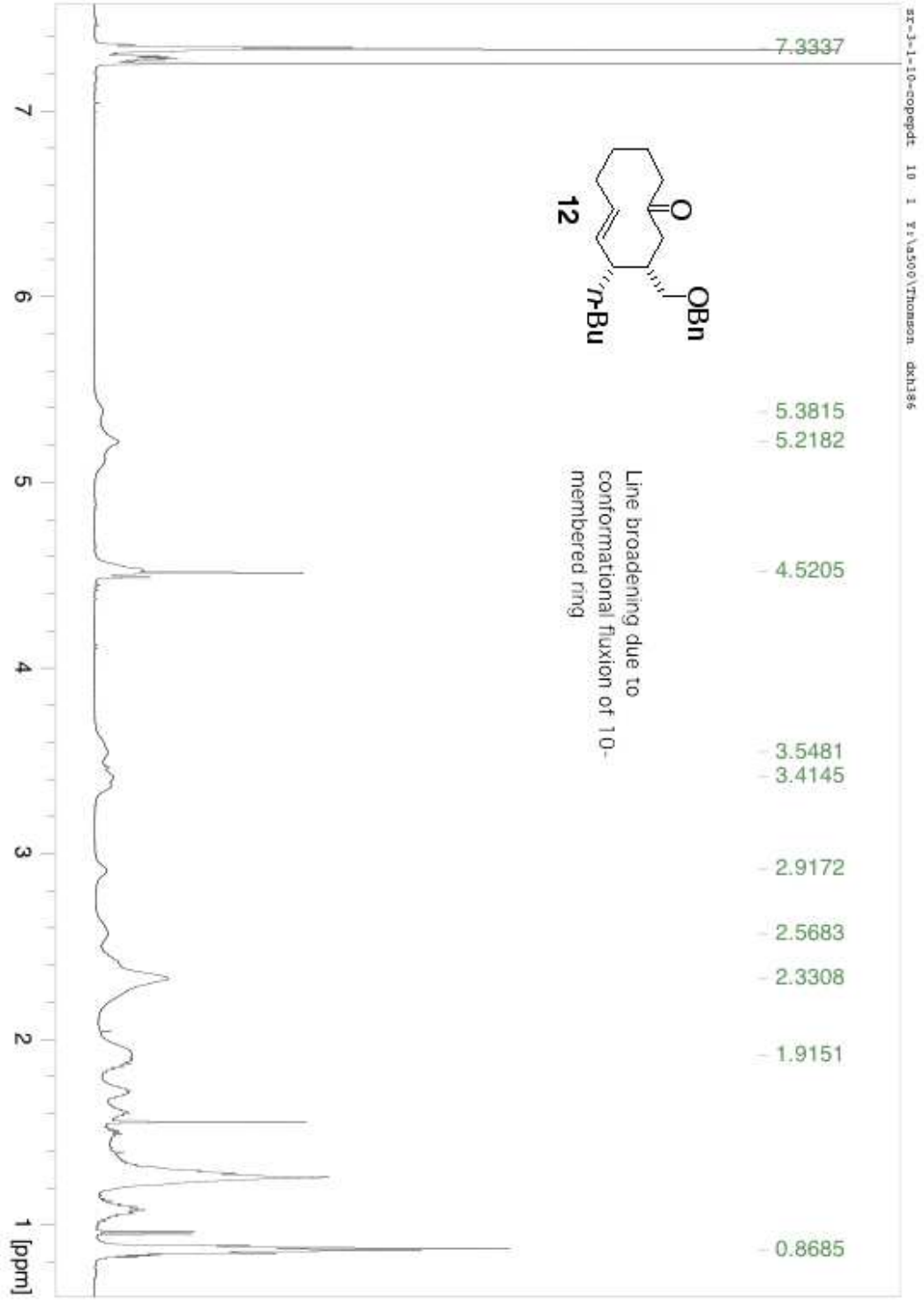

sx-1-25-10-bzwittchiral 11 1 Y:\a500\Thomson dxh386
166.0027
OBz
n-Bu
Prepared in order to determine
enantioselectivity
132.6154
131.3701
131.1232
130.8977
129.5880
128.1816
41.6310
31.9576
31.8009
31.5659
27.3362
24.9081
24.5556
22.4016
13.9814
160
140
120
100
80
60
40
[ppm]

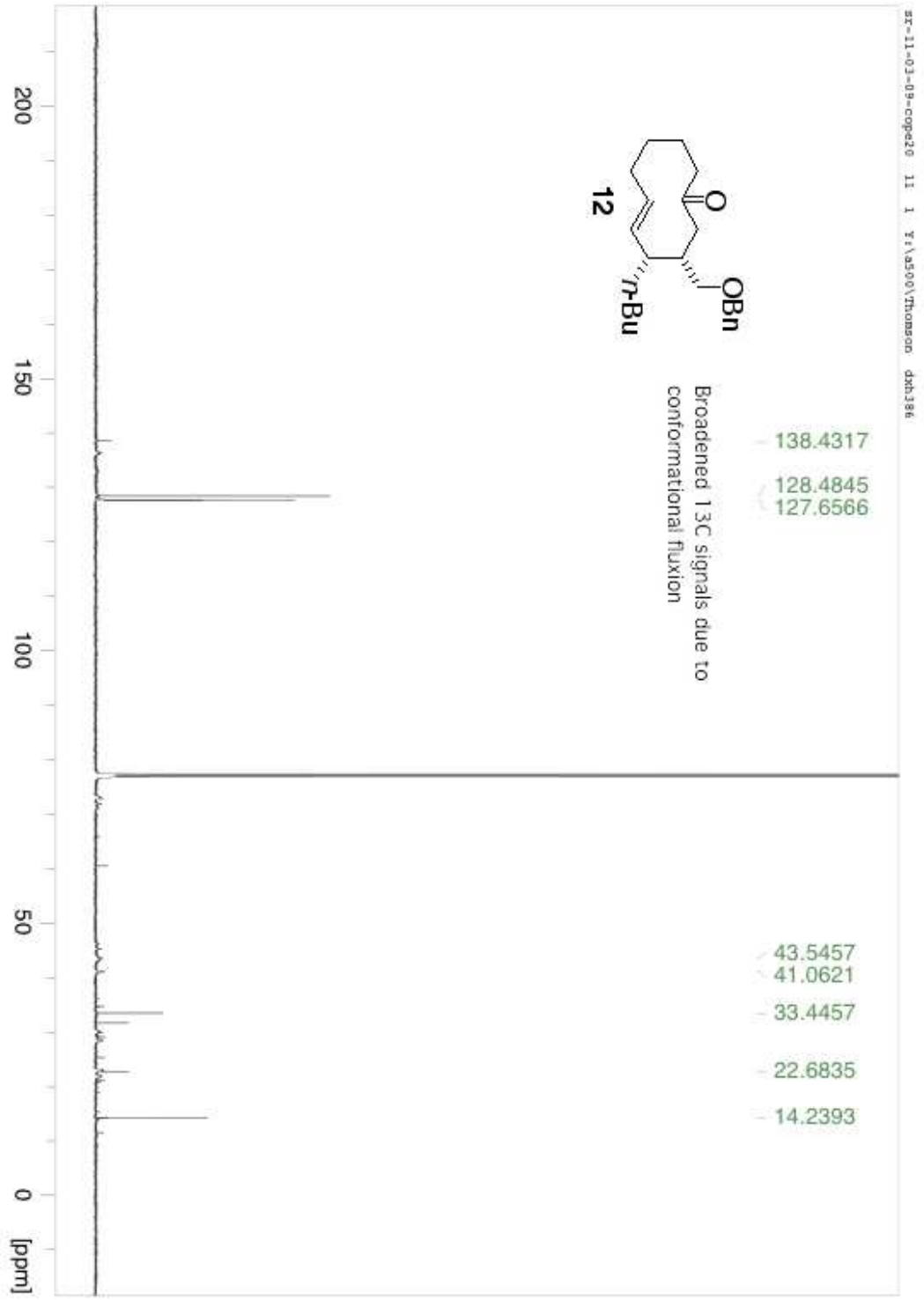

7.2871
5.5536
3.2984
2.4879
2.3514
2.0625
1.9020
1.7495
1.6292
1.3402
0.9149
n-Bu
O
7
6
5
4
3
2
1 [ppm]

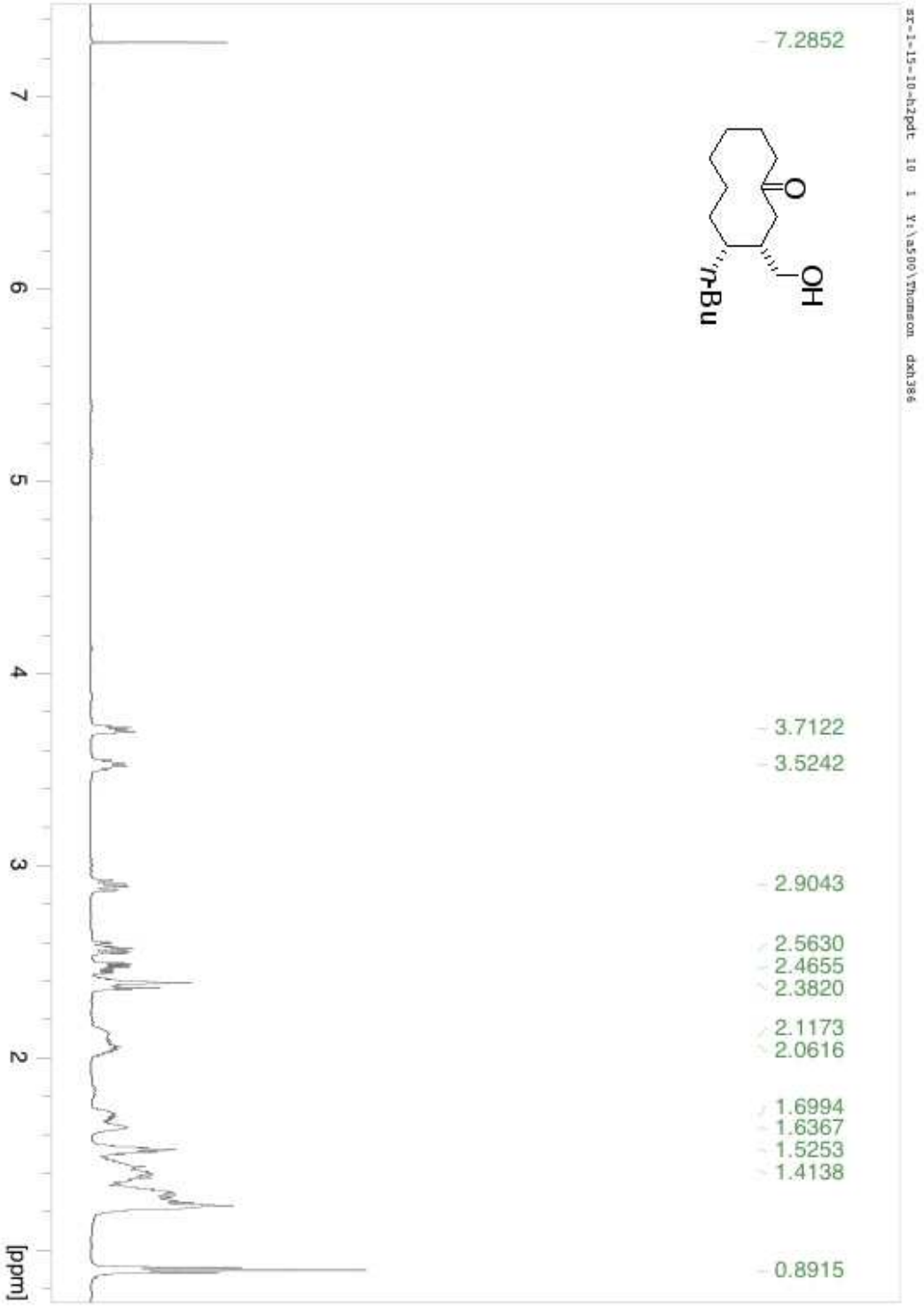

211.5609
132.3395
126.4144
77.2973
77.0426
76.7883
49.4248
41.7783
34.9430
31.7185
27.7590
27.3334
24.4398
22.3646
14.0043
n-Bu
O
200
150
100
50
[ppm]
sx-10-19-09-swernoxpure 12 1 Y:\a500\Thomson dxh386

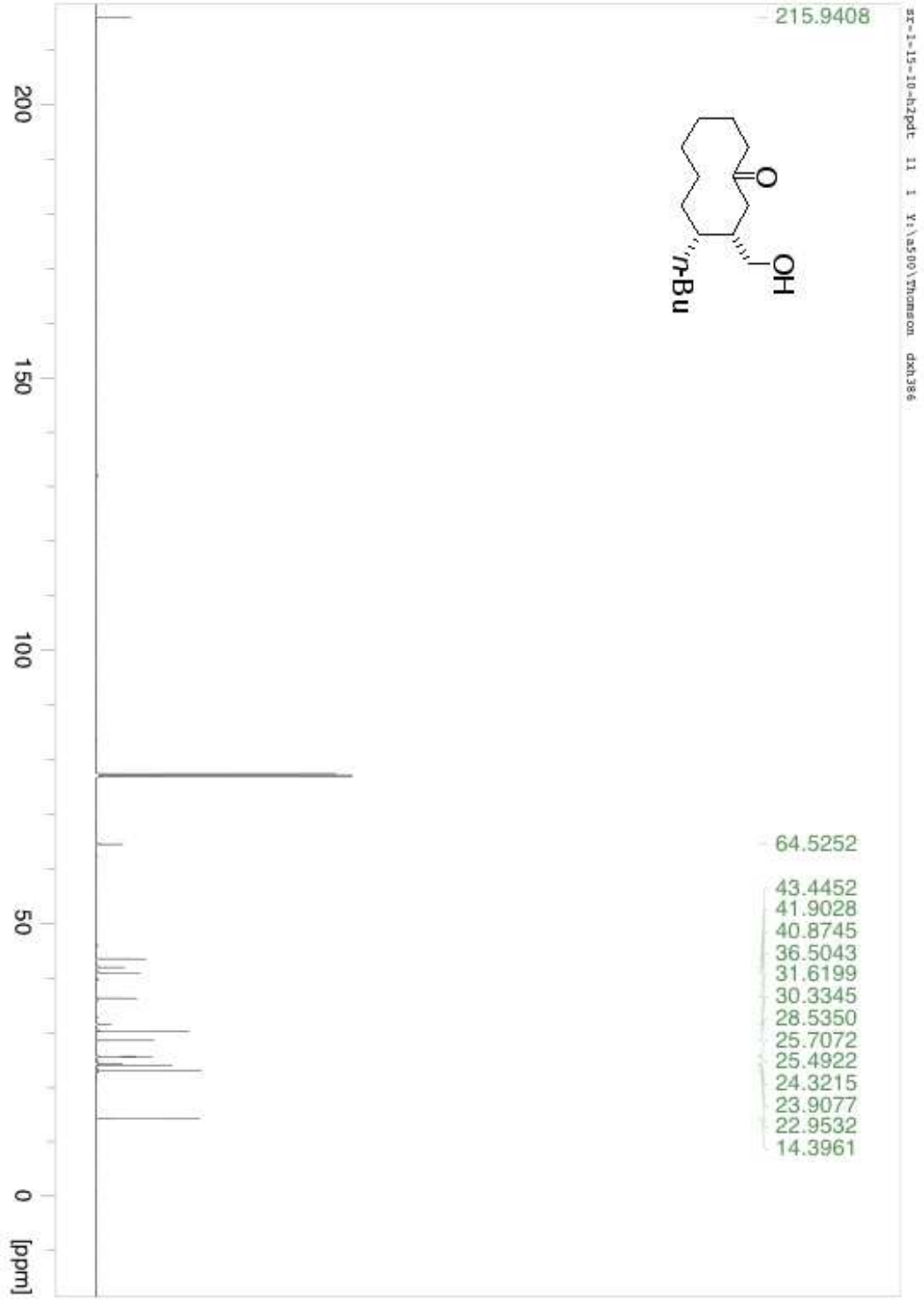

7.3626
7.3130
5.7743
5.4185
5.3606
4.5168
4.0370
2.3660
2.0185
1.3319
0.9100
HO
OBn
n-Bu
13
1 [ppm]

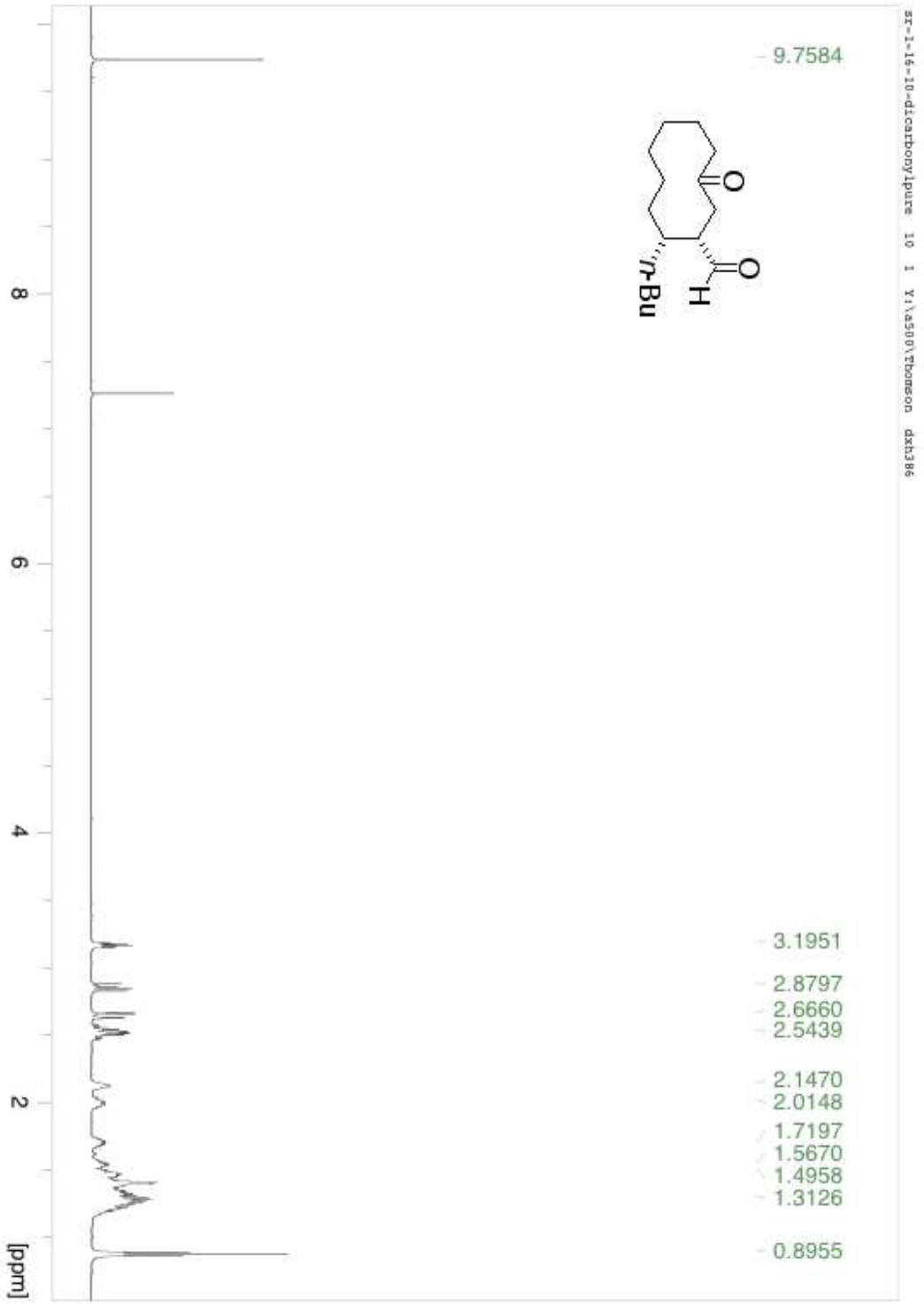

141.1721
138.4686
130.9750
129.7114
128.4184
127.8013
127.5956
123.7460
73.1675
71.8825
70.5171
43.6114
38.0696
31.9656
28.5121
27.6286
25.2994
22.4884
21.4443
14.1356
HO
OBn
n-Bu
13
140
120
100
80
60
40
20
[ppm]

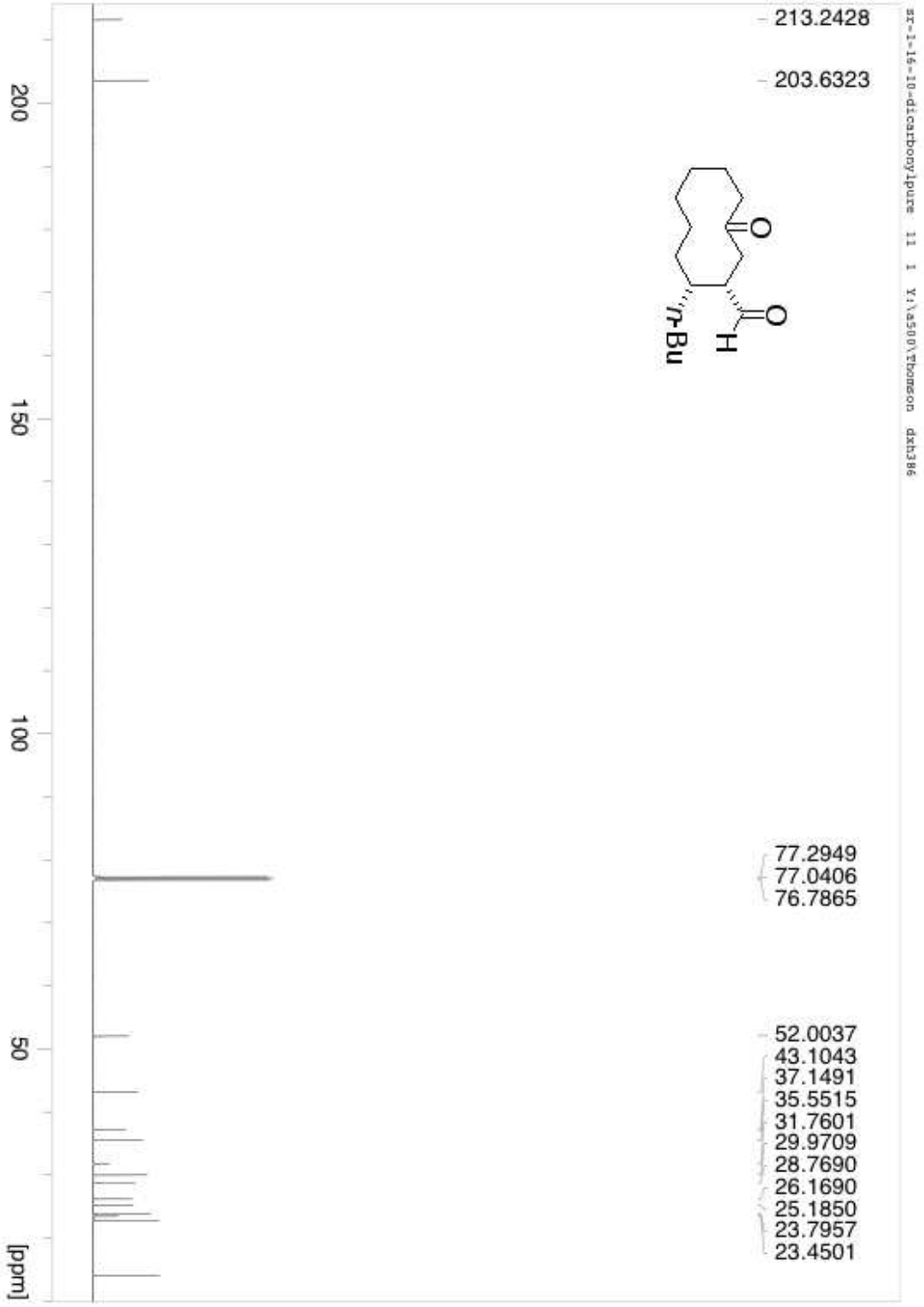

7.3337
5.3815
5.2182
4.5205
3.5481
3.4145
2.9172
2.5683
2.3308
1.9151
0.8685
12
OBn
n-Bu
Line broadening due to conformational fluxion of 10-membered ring
1 [ppm]

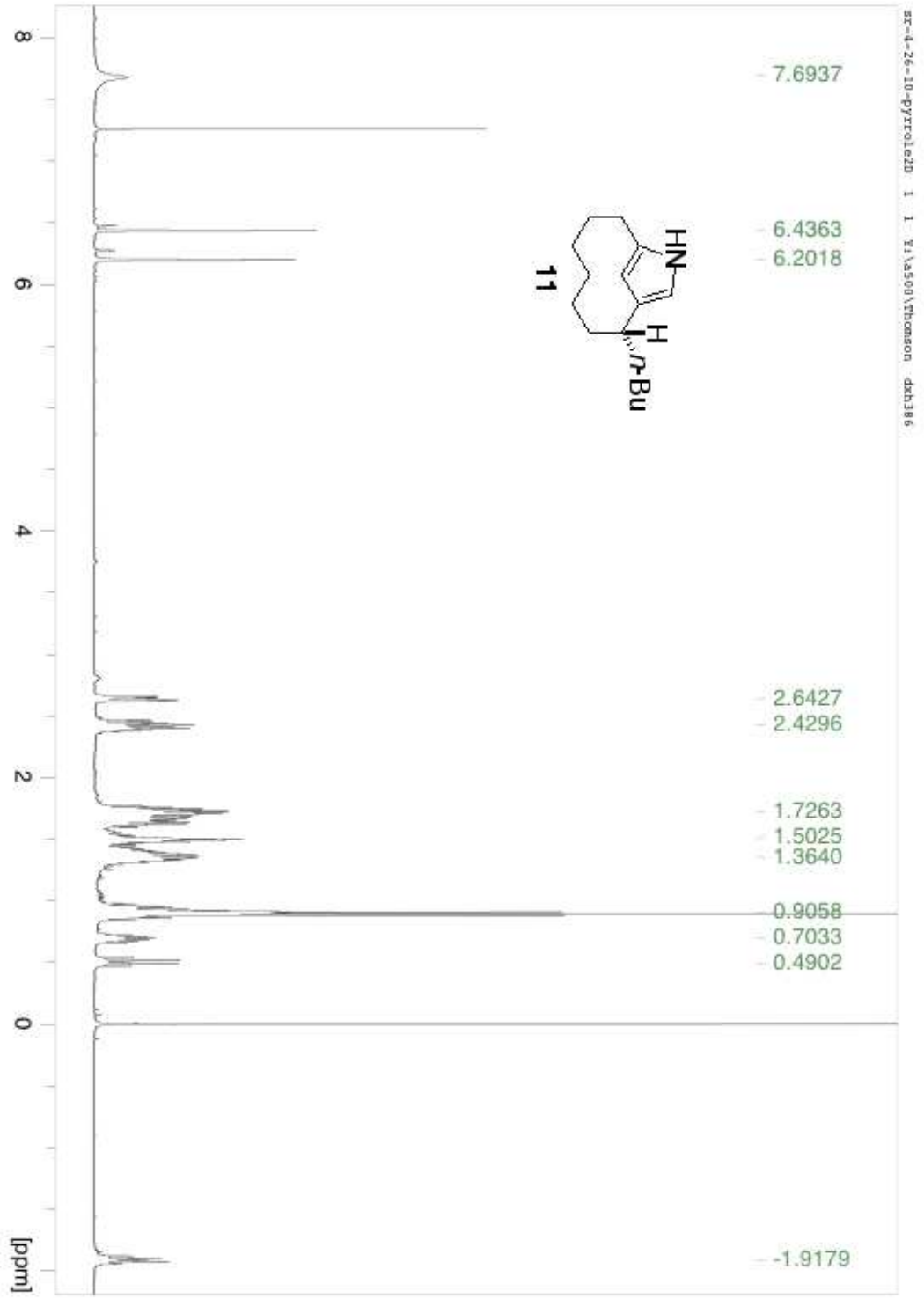

sx-11-03-09-cope20 11 1 Yr\a500\Thomson dxh386
12
OBn
n-Bu
Broadened 13C signals due to conformational fluxion
138.4317
128.4845
127.6566
43.5457
41.0621
33.4457
22.6835
14.2393
200
150
100
50
0
[ppm]

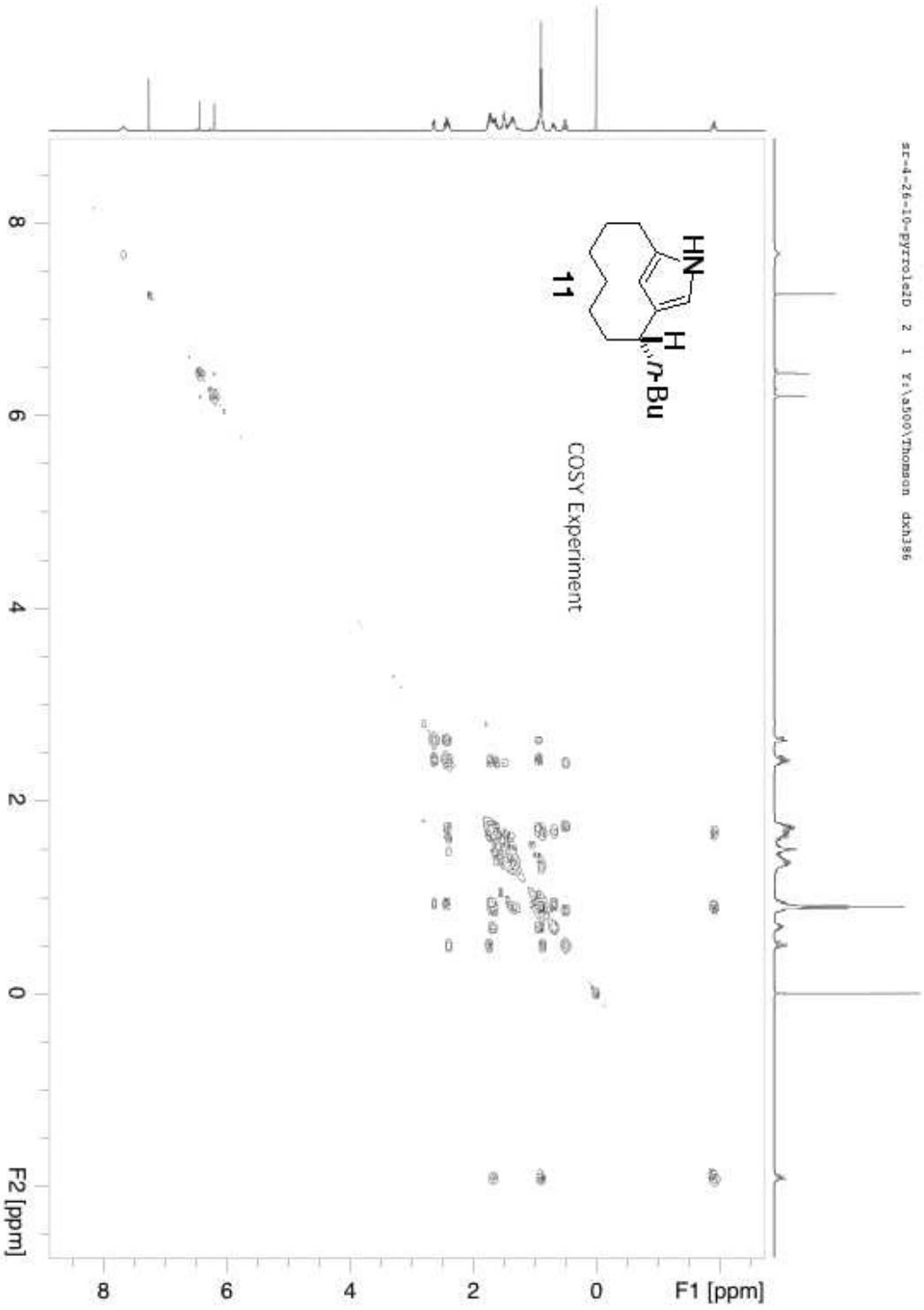

7.2852
3.7122
3.5242
2.9043
2.5630
2.4655
2.3820
2.1173
2.0616
1.6994
1.6367
1.5253
1.4138
0.8915
[ppm]
OH
n-Bu

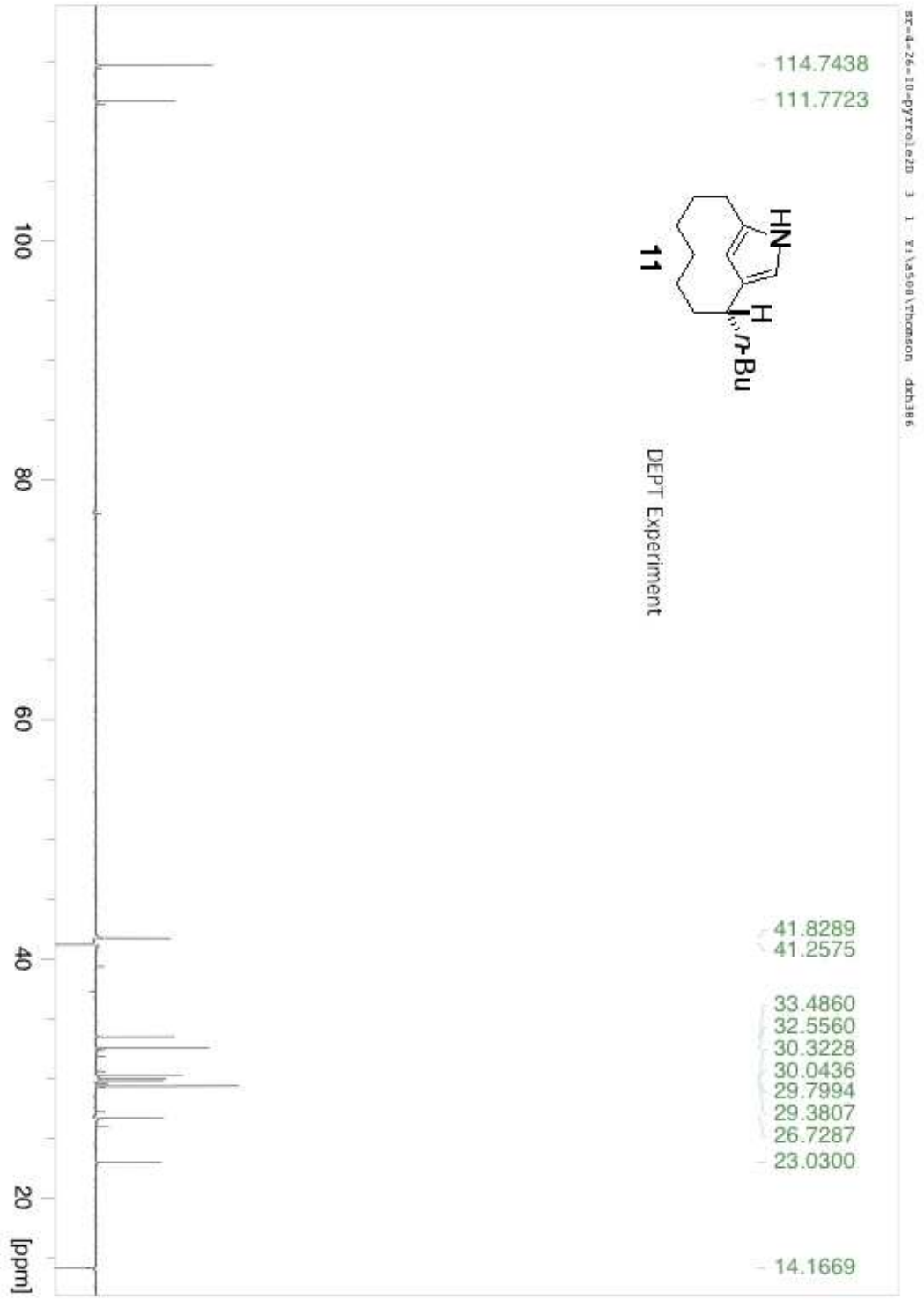

215.9408
64.5252
43.4452
41.9028
40.8745
36.5043
31.6199
30.3345
28.5350
25.7072
25.4922
24.3215
23.9077
22.9532
14.3961
OH
n-Bu
200
150
100
50
0
[ppm]

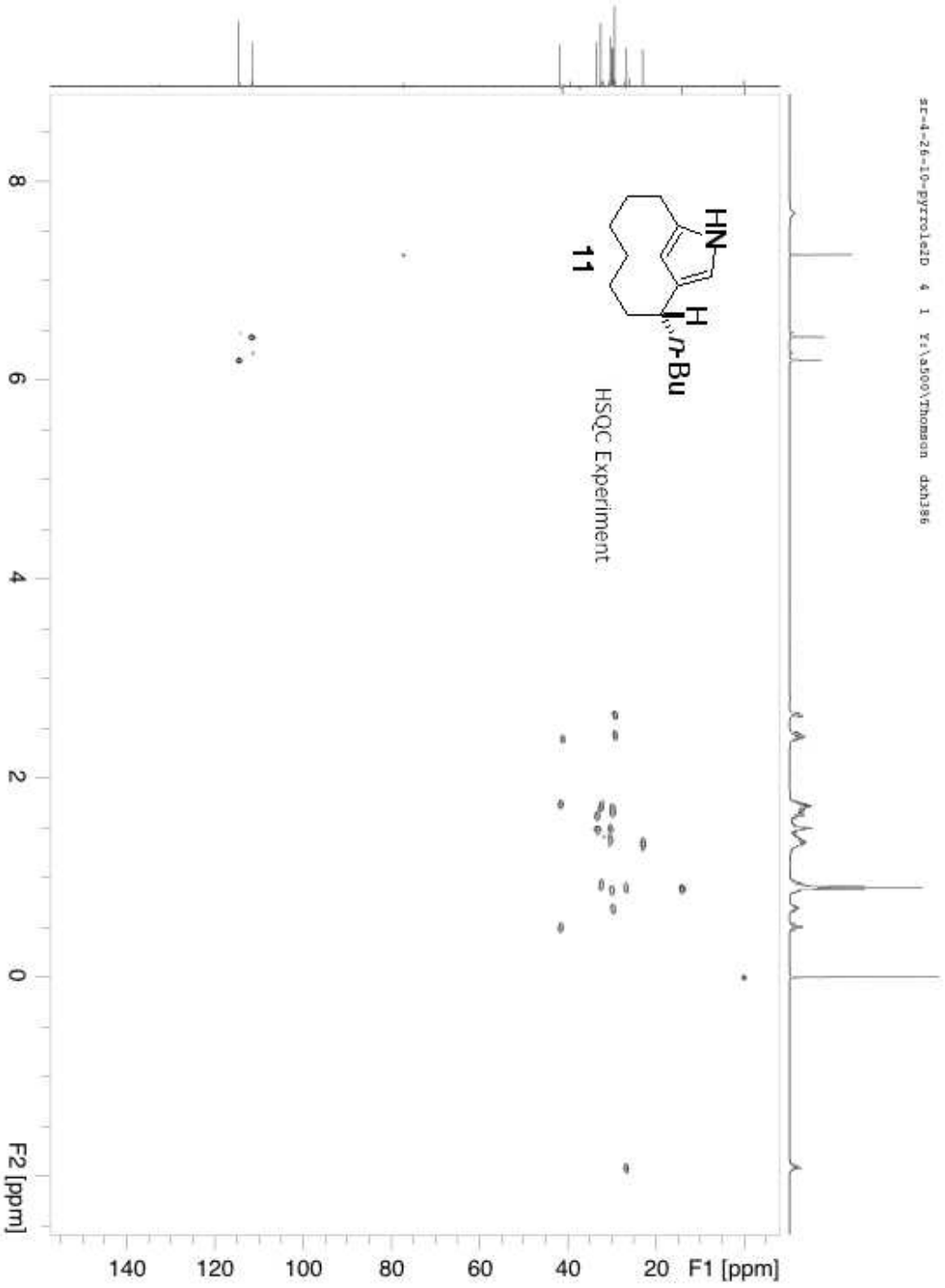

sx-1-16-10-dicarbonylpure 10 1 Y:\s500\thomson dxh386
9.7584
3.1951
2.8797
2.6660
2.5439
2.1470
2.0148
1.7197
1.5670
1.4958
1.3126
0.8955
n-Bu
8
6
4
2
[ppm]

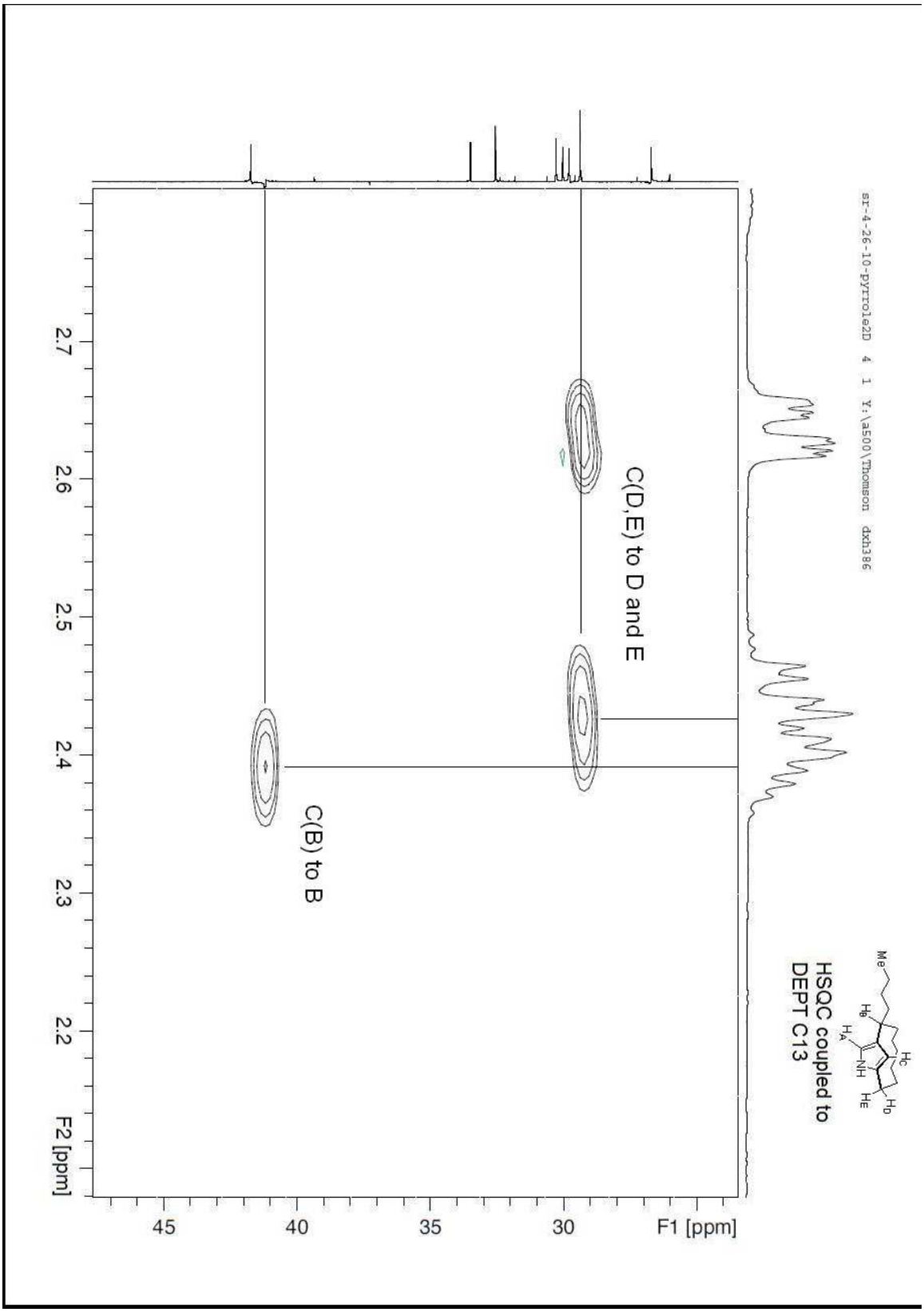

213.2428
203.6323
77.2949
77.0406
76.7865
52.0037
43.1043
37.1491
35.5515
31.7601
29.9709
28.7690
26.1690
25.1850
23.7957
23.4501
200
150
100
50
[ppm]
n-Bu
O
O
H
sx-1-16-10-dicarbonylpure 11 1 Y:\s500\thomson dxh386

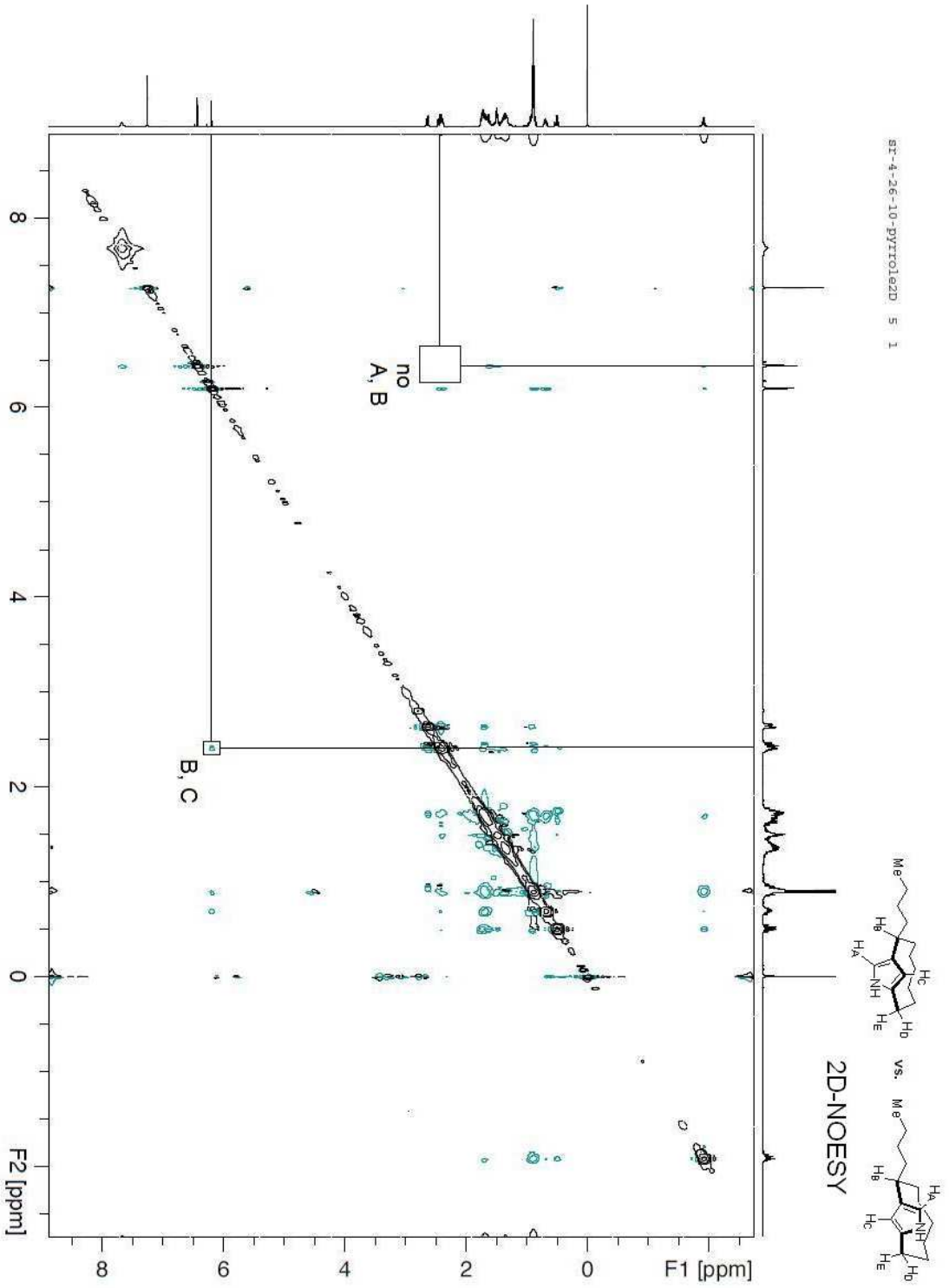

7.6937
6.4363
6.2018
2.6427
2.4296
1.7263
1.5025
1.3640
0.9058
0.7033
0.4902
-1.9179
HN
H
n-Bu
11
8
6
4
2
0
[ppm]

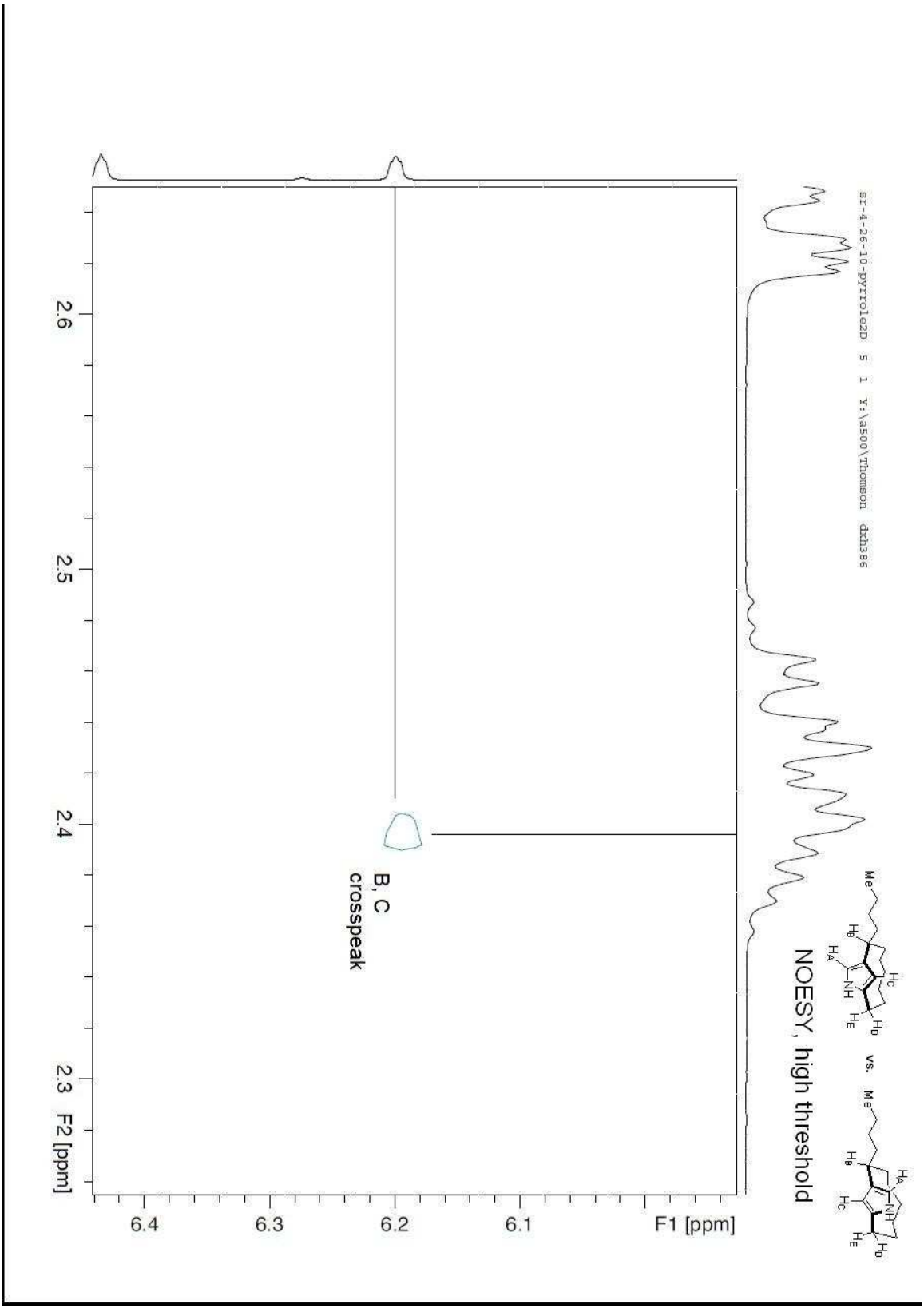

sr-4-26-10-pyrrole2D 2 1 Y:\a500\Thomson dxh386
HN
H
n-Bu
11
COSY Experiment
F2 [ppm]
F1 [ppm]
8
6
4
2
0

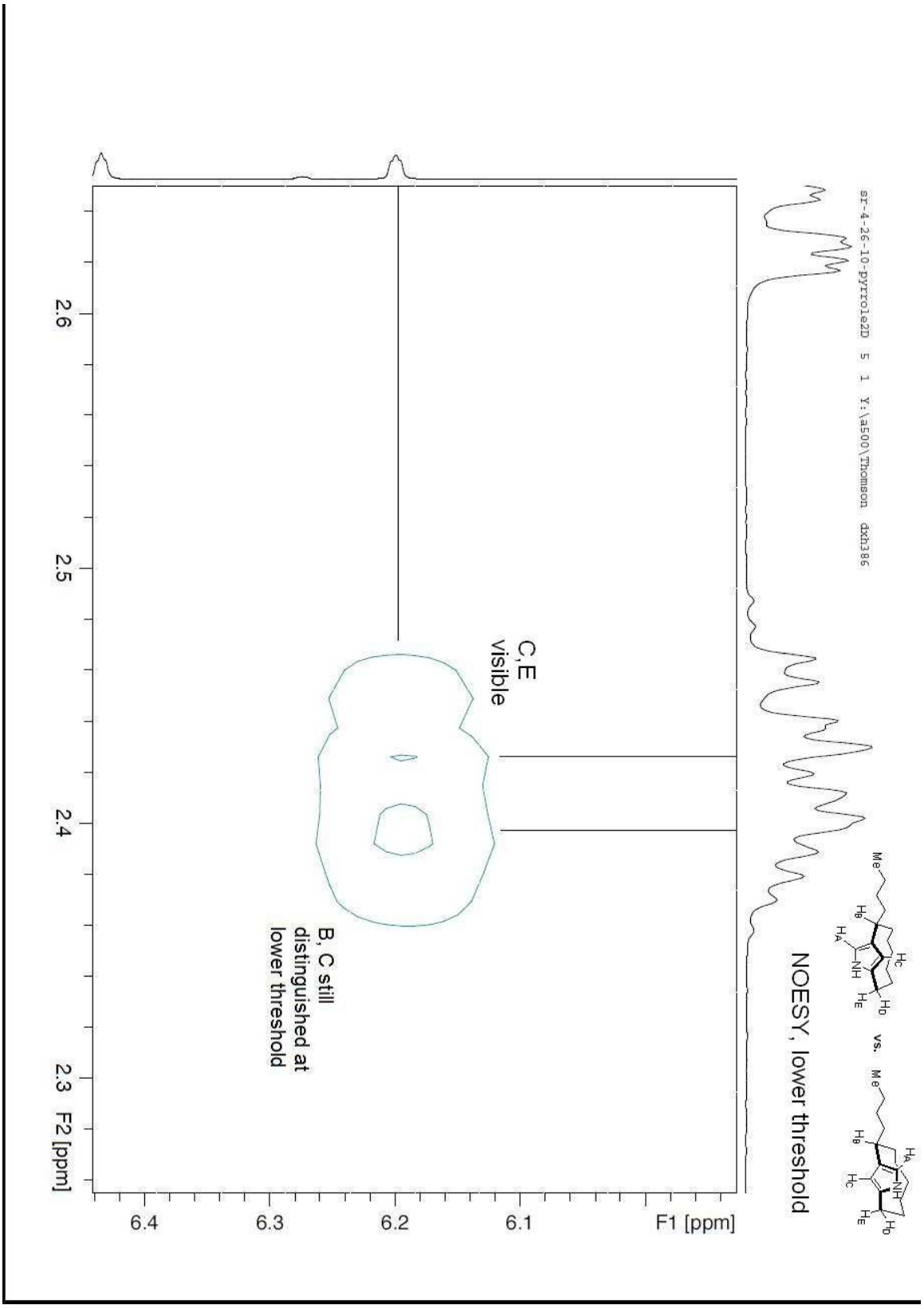

sx-4-26-10-pyrrole2D 3 1 Y:\a500\thomson dxh386
114.7438
111.7723
HN
H
n-Bu
11
DEPT Experiment
41.8289
41.2575
33.4860
32.5560
30.3228
30.0436
29.7994
29.3807
26.7287
23.0300
14.1669
100
80
60
40
20
[ppm]

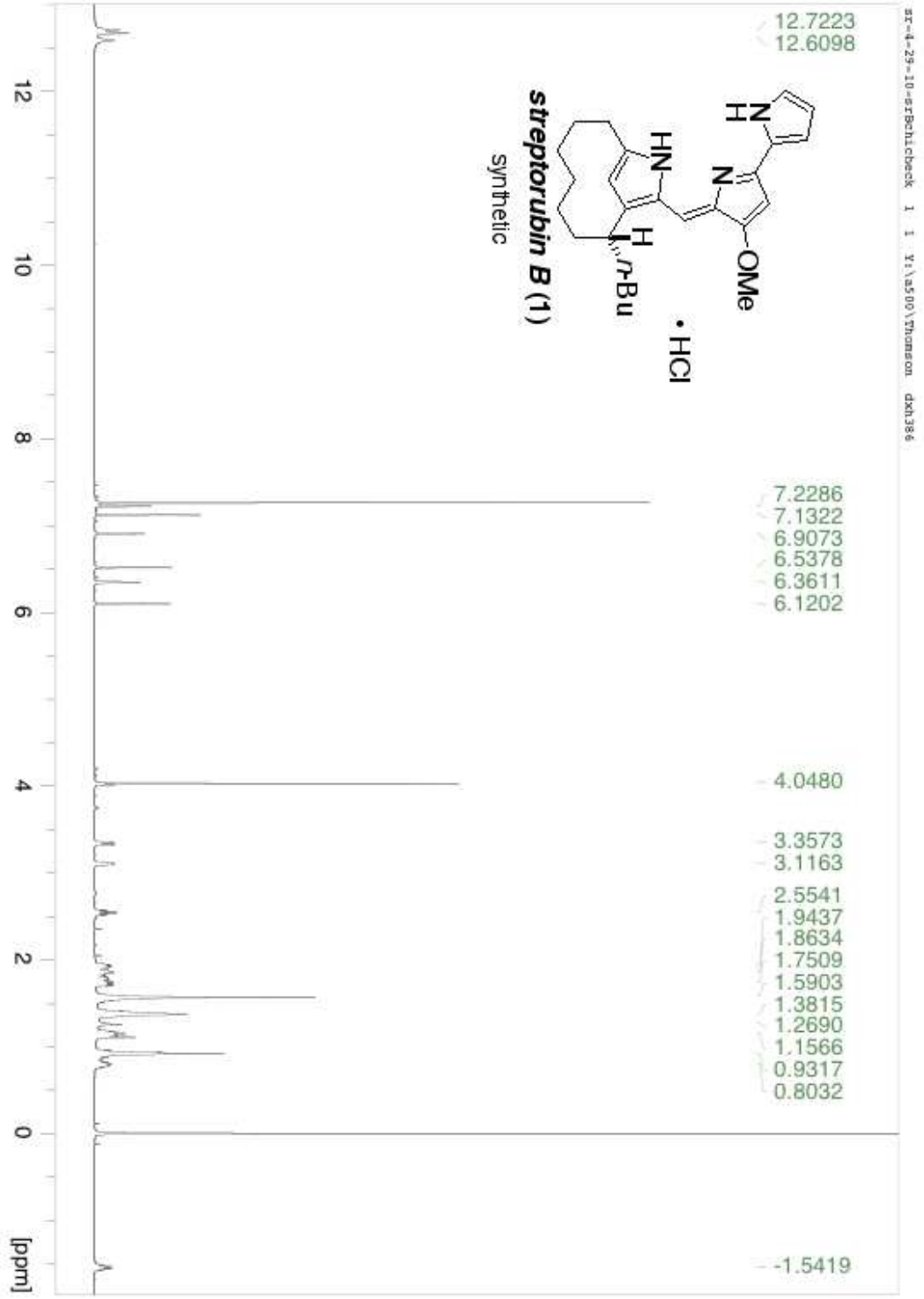

HN
H
n-Bu
11
HSQC Experiment
sr-4-26-10-pyrrole2D 4 1 Y:\a500\Thomson dxh386
F2 [ppm]
F1 [ppm]
8
6
4
2
0
140
120
100
80
60
40
20

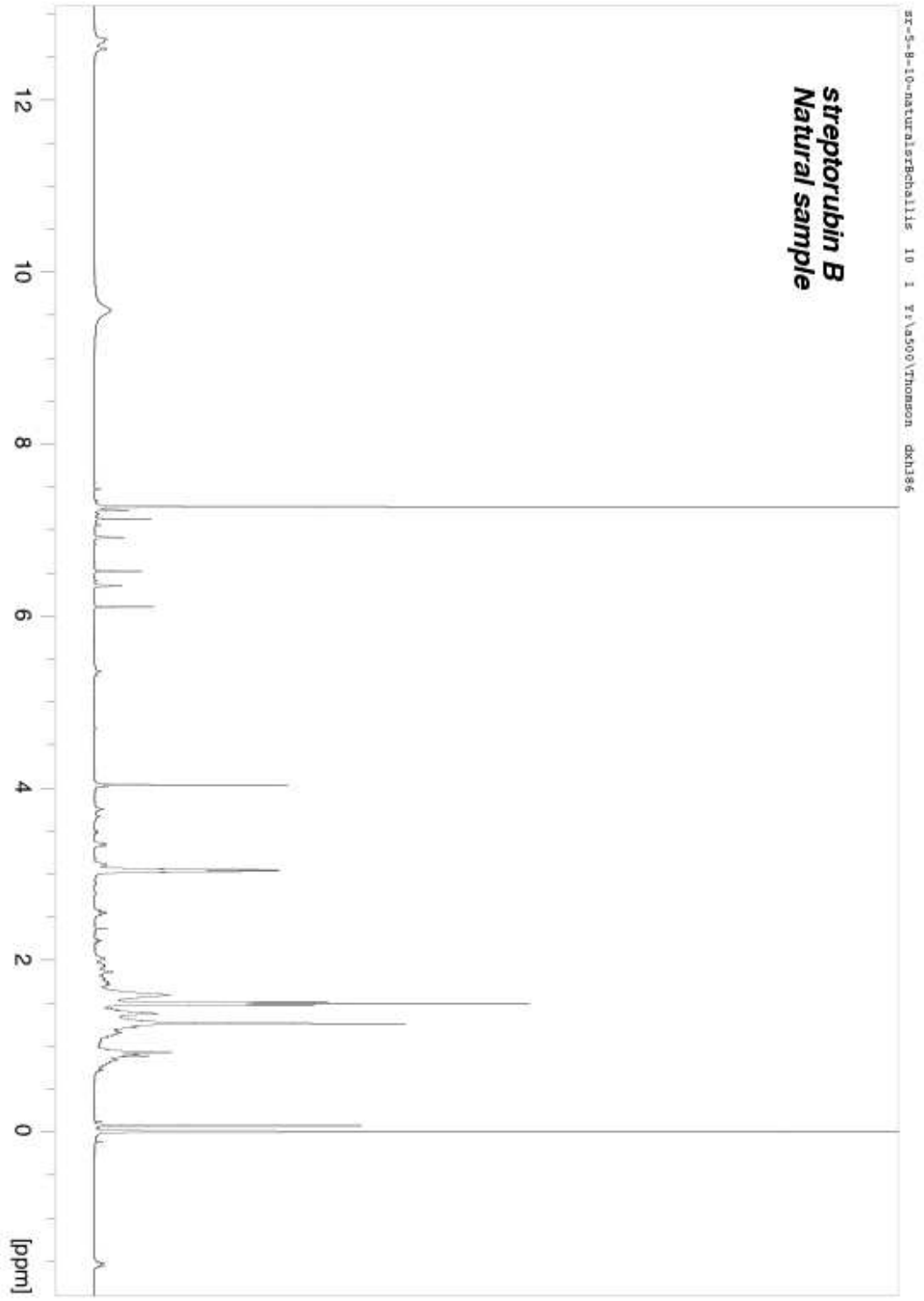

sr-4-26-10-pyrrole2D 4 1 Y:\a500\Thomson dxb186
C(D,E) to D and E
C(B) to B
HSQC coupled to
DEPT C13
F2 [ppm]
F1 [ppm]
2.7
2.6
2.5
2.4
2.3
2.2
45
40
35
30
Me
H_B
H_A
NH
H_C
H_E
H_D

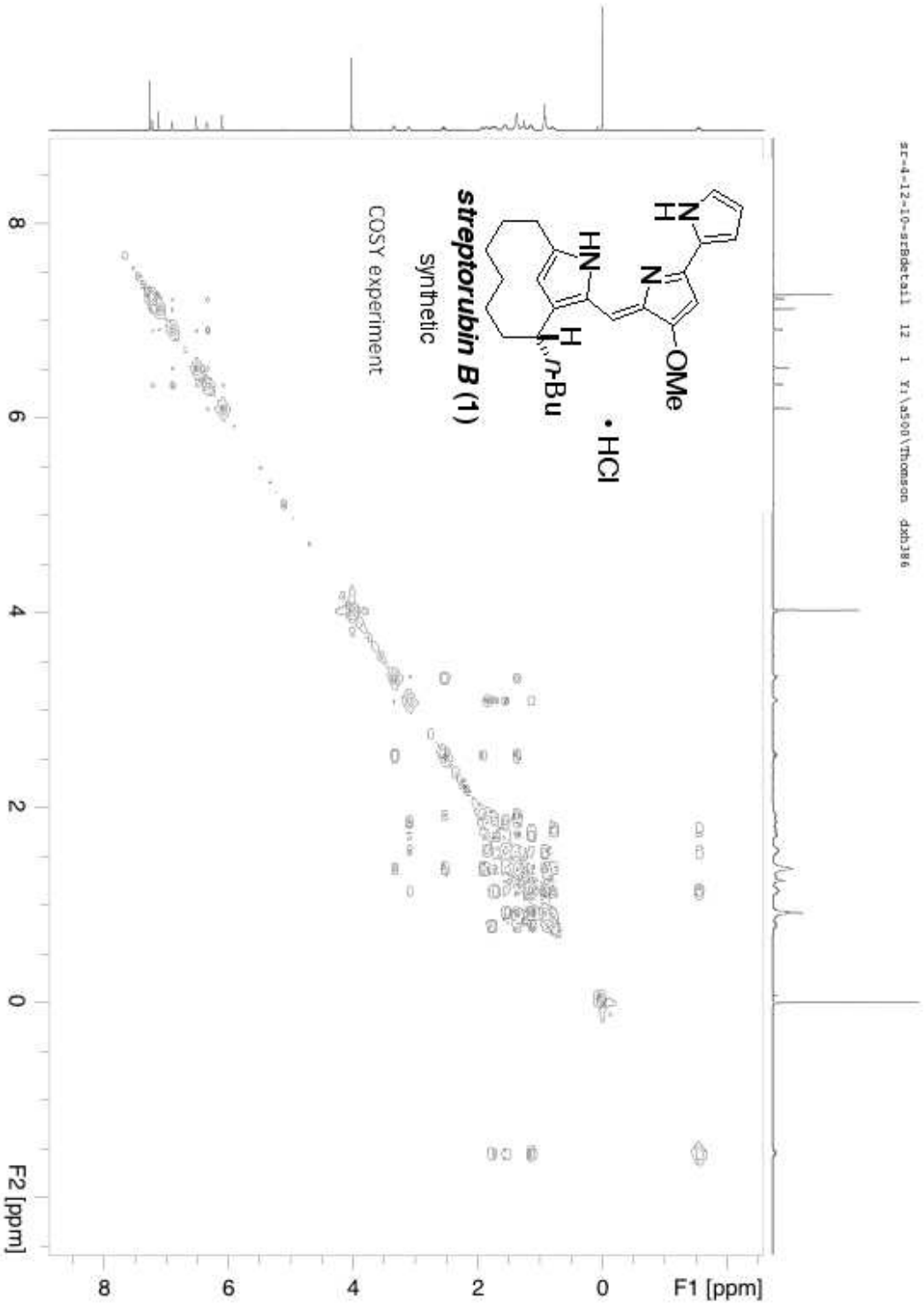

sr-4-26-10-pyrrole2D 5 1
no
A, B
B, C
F2 [ppm]
F1 [ppm]
2D-NOESY
vs.

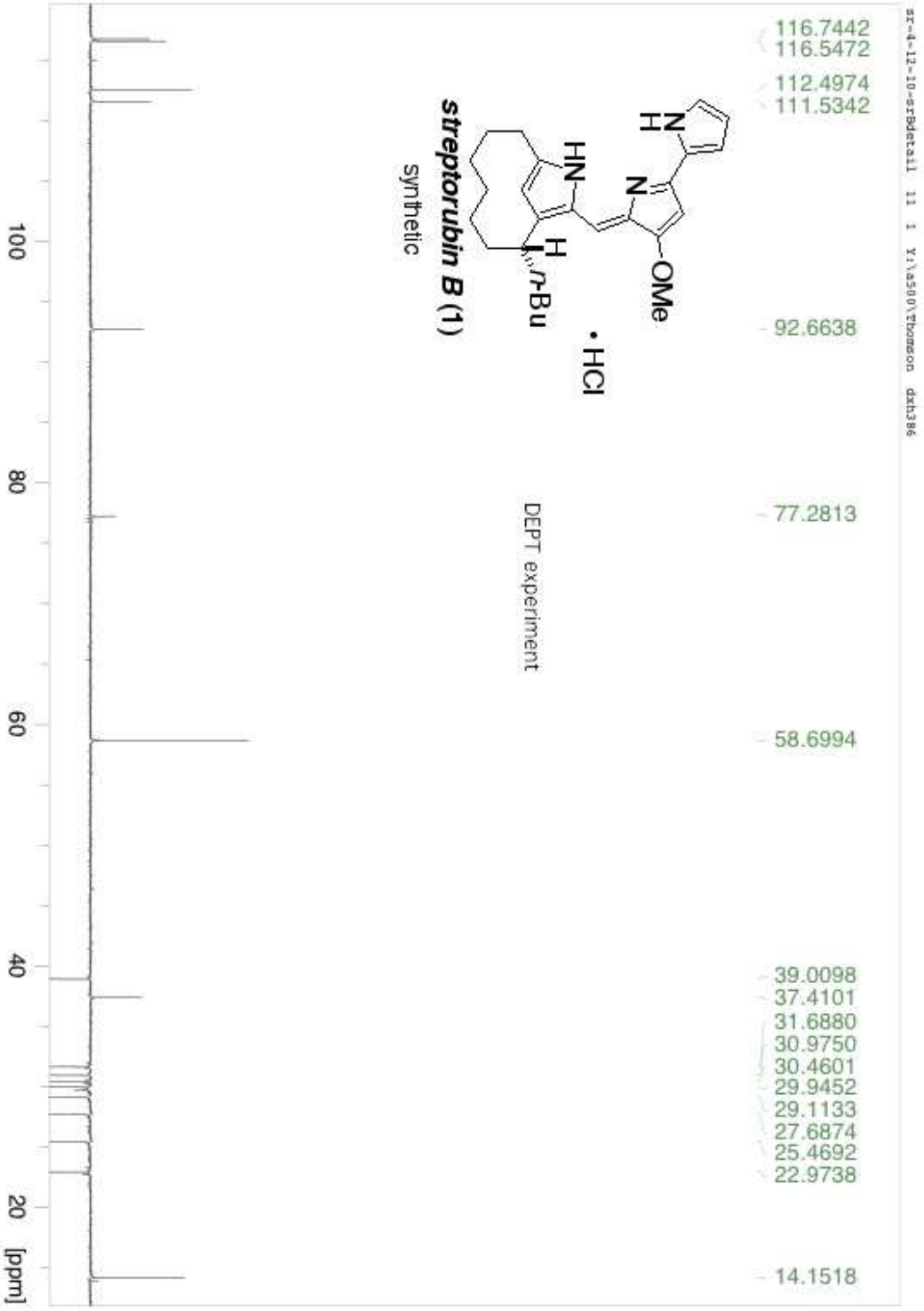

sr-4-26-10-pyrrole2D 5 1 Y:\a500\thomson dxh386
2.6
2.5
2.4
2.3 F2 [ppm]
6.4
6.3
6.2
6.1
F1 [ppm]
B, C
crosspeak
NOESY, high threshold
vs.

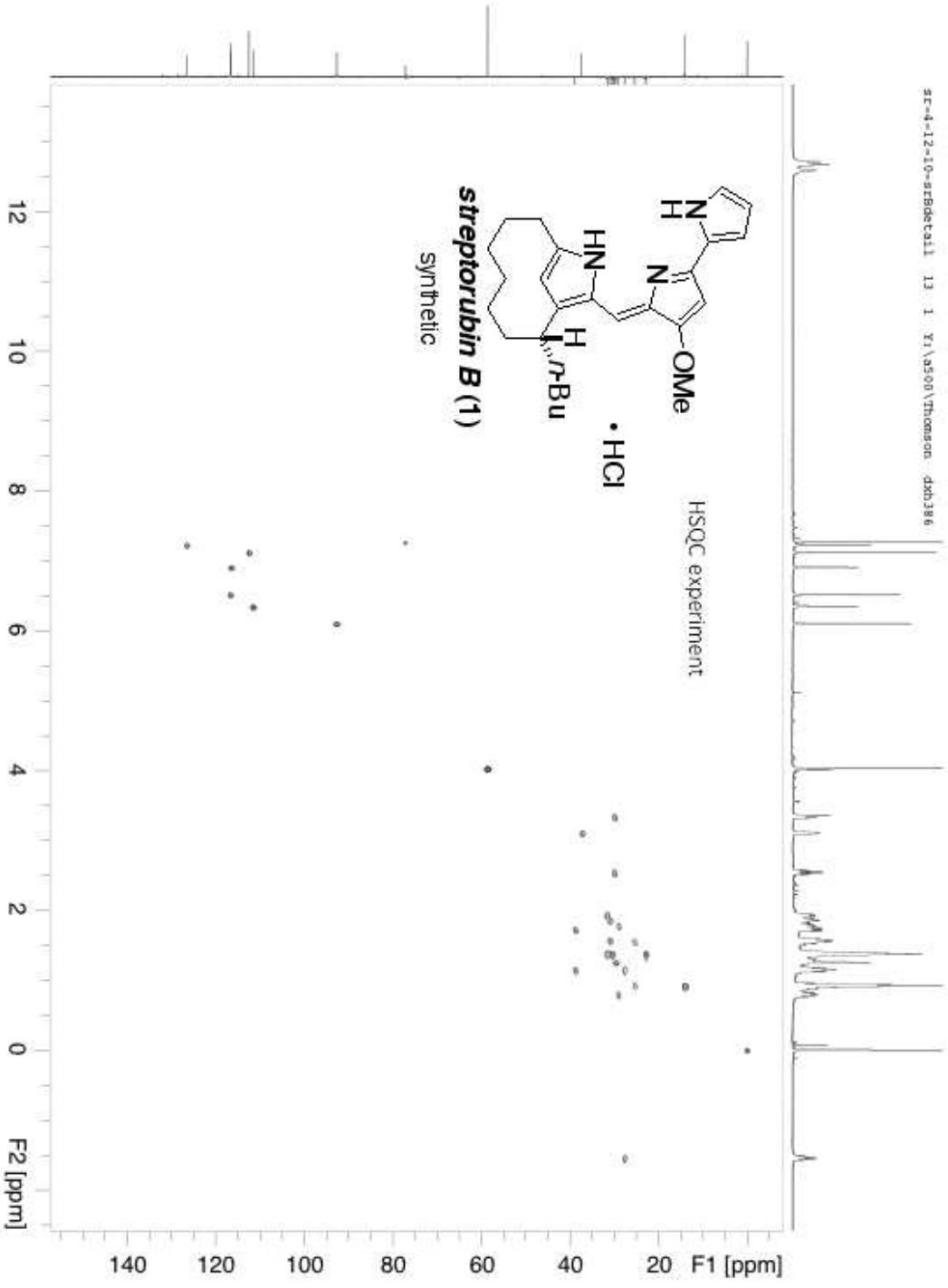

sr-4-26-10-pyrrole2D 5 1 Y:\a500\Thomson dxh386
C,E visible
B, C still distinguished at lower threshold
NOESY, lower threshold
vs.
F1 [ppm]
F2 [ppm]
6.4
6.3
6.2
6.1
2.6
2.5
2.4
2.3

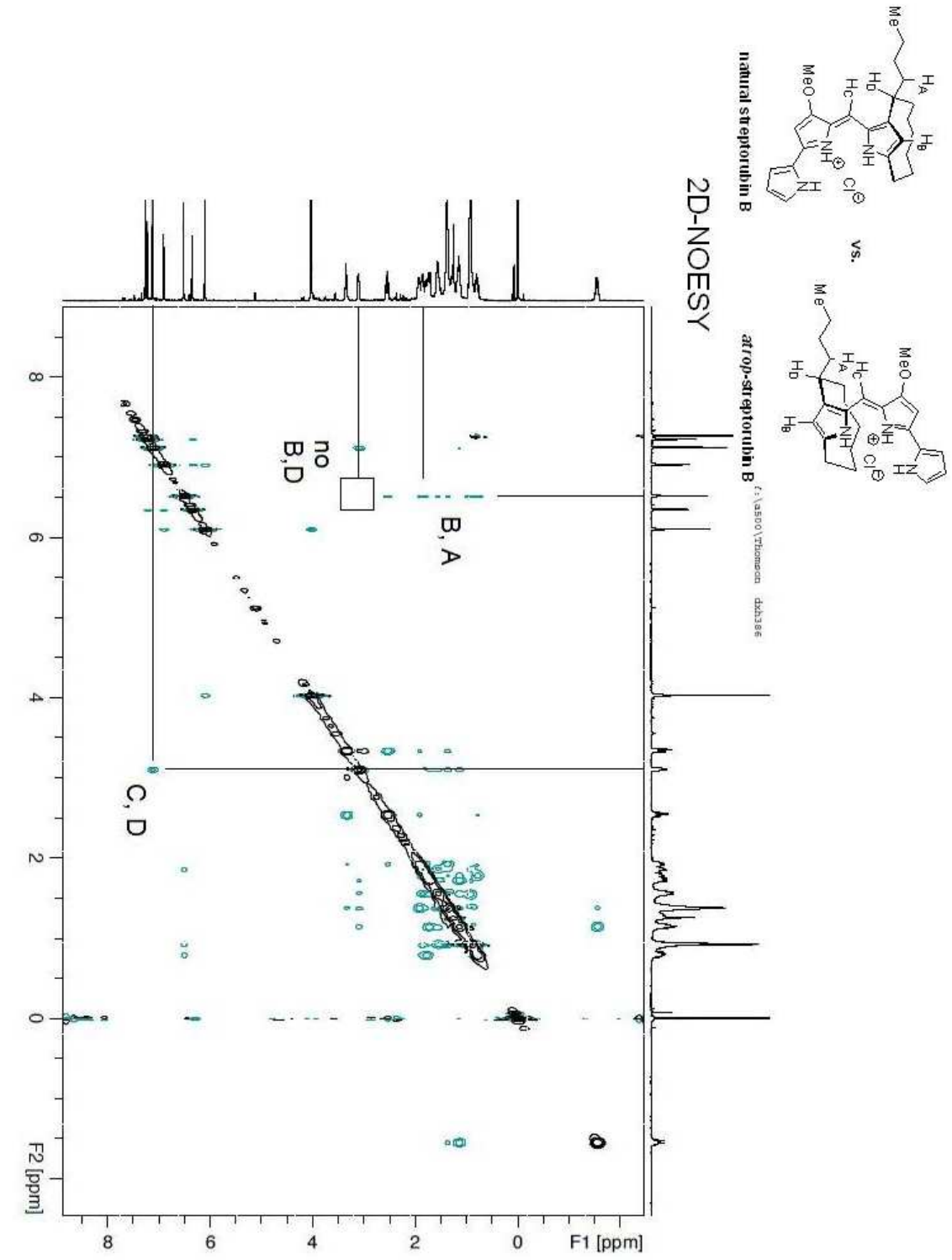

12.7223
12.6098
7.2286
7.1322
6.9073
6.5378
6.3611
6.1202
4.0480
3.3573
3.1163
2.5541
1.9437
1.8634
1.7509
1.5903
1.3815
1.2690
1.1566
0.9317
0.8032
-1.5419
12
10
8
6
4
2
0
[ppm]
streptorubin B (1)
synthetic
HN
H
N
H
N
OMe
n-Bu
• HCl

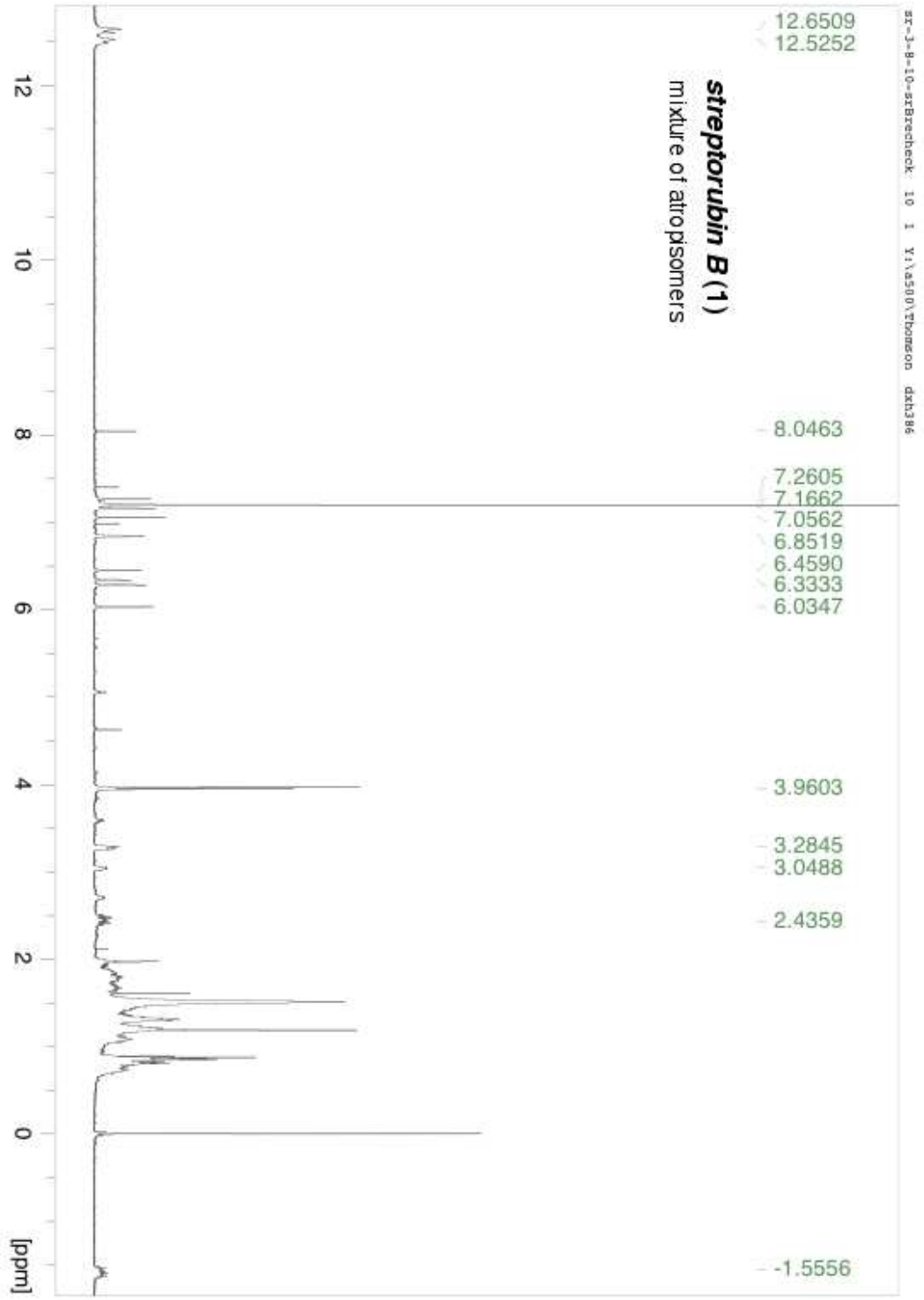

streptorubin B
Natural sample
sr-5-8-10-naturalsrBchalis 10 1 Y:\a500\Thomson dkh386
12
10
8
6
4
2
0
[ppm]

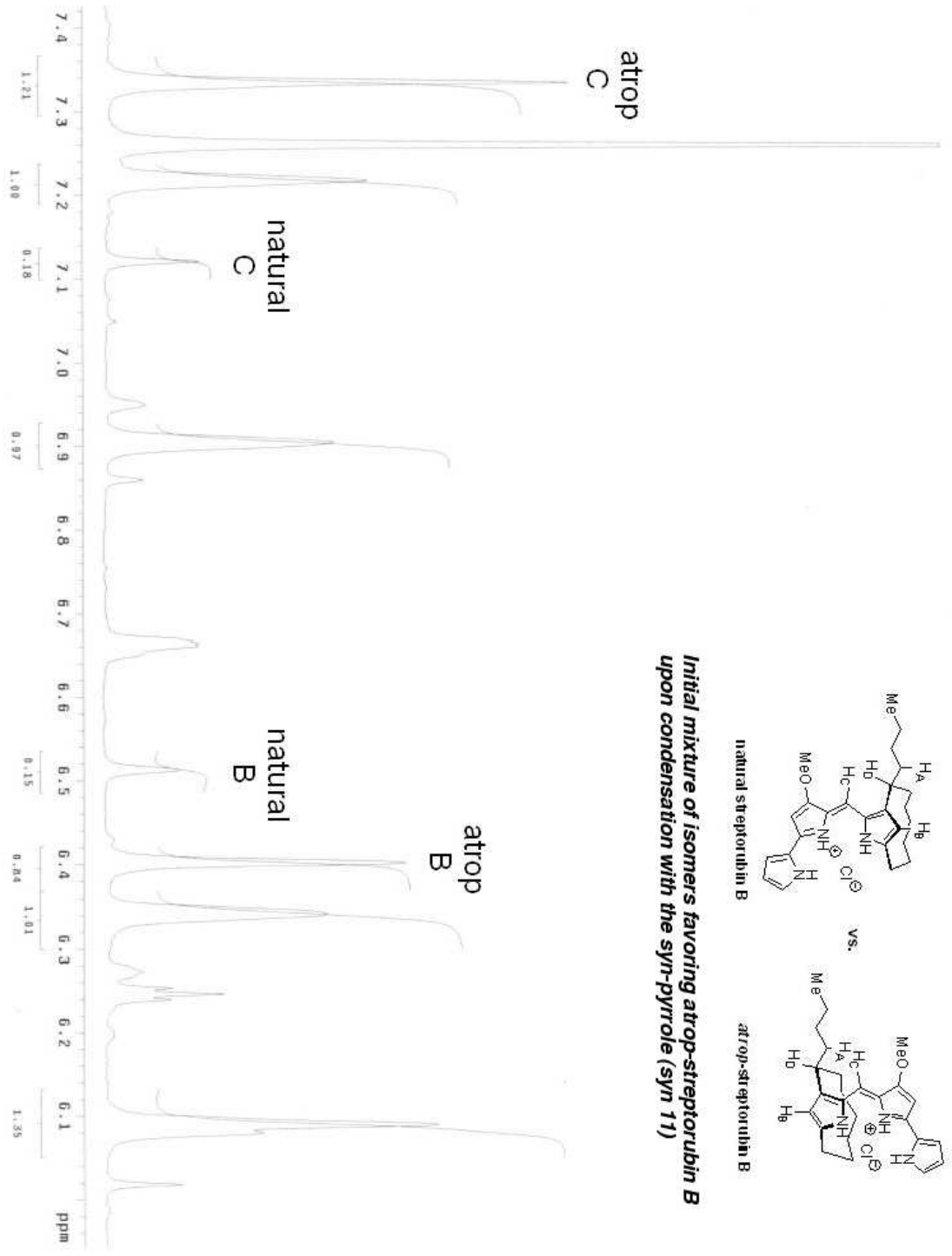

streptorubin B (1)
synthetic
COSY experiment
OMe
HN
N
H
nBu
• HCl
F1 [ppm]
F2 [ppm]
0
2
4
6
8


sx-4-12-10-srBdetail 11 1 Y:\e500\Thomson dxh386
116.7442
116.5472
112.4974
111.5342
92.6638
77.2813
58.6994
39.0098
37.4101
31.6880
30.9750
30.4601
29.9452
29.1133
27.6874
25.4692
22.9738
14.1518
100
80
60
40
20
[ppm]
DEPT experiment
synthetic
streptorubin B (1)
HN
H
n-Bu
N
H
N
OMe
• HCl


sr-4-12-10-srBdetail 13 1 Y:\s500\Thomson dxb386
HSQC experiment
synthetic
streptorubin B (1)
HN
N
H
OMe
H
n-Bu
• HCl
F1 [ppm]
F2 [ppm]
140
120
100
80
60
40
20
0
2
4
6
8
10
12

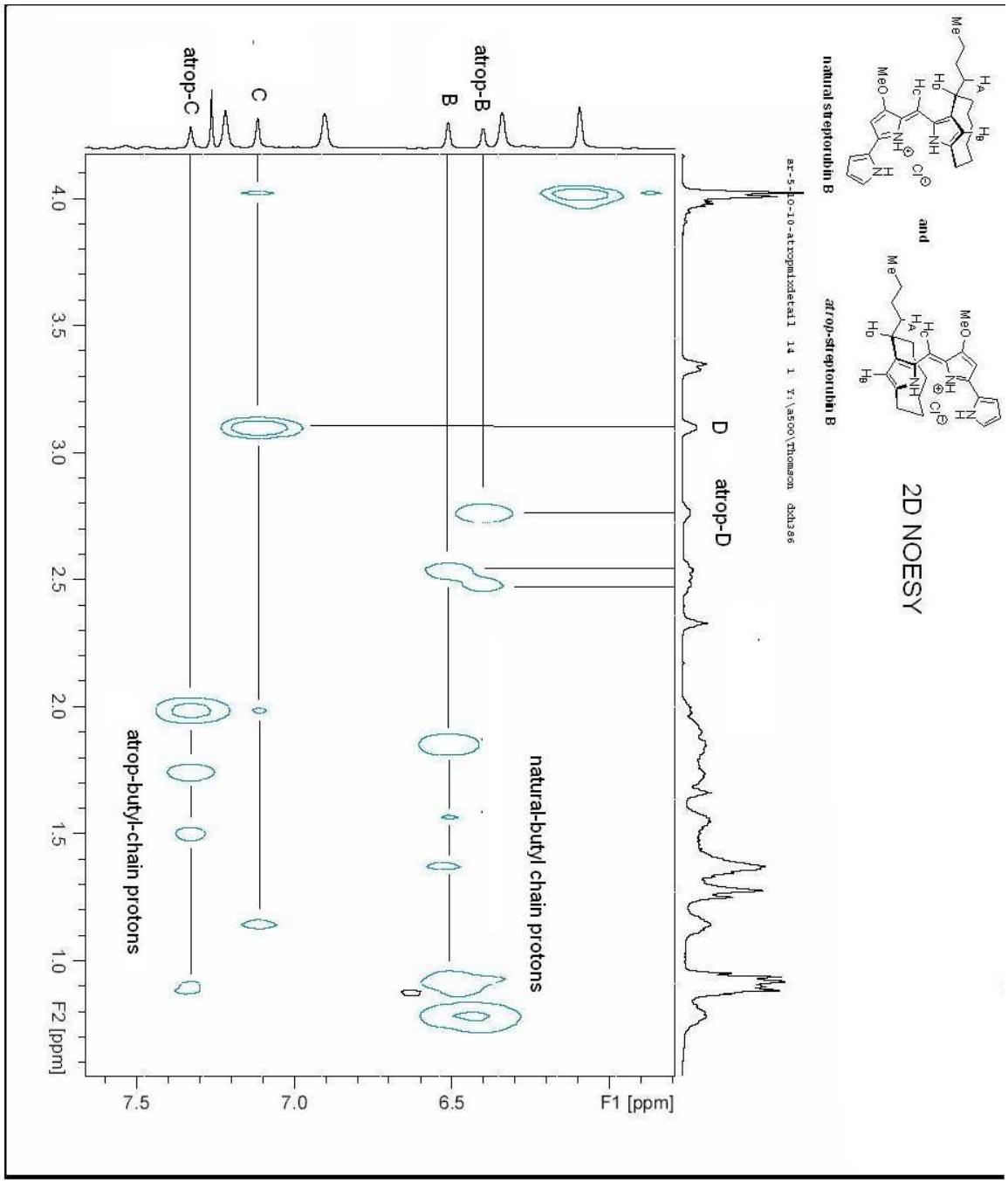

natural streptorubin B
vs.
atrop-streptorubin B
2D-NOESY
B, A
no
B,D
C, D
F2 [ppm]
F1 [ppm]
0
2
4
6
8


12.6509
12.5252
8.0463
7.2605
7.1662
7.0562
6.8519
6.4590
6.3333
6.0347
3.9603
3.2845
3.0488
2.4359
-1.5556
streptorubin B (1)
mixture of atropisomers
sx-3-8-10-srBrecheck 10 1 Y:\a500\Thomson dxh386
12
10
8
6
4
2
0
[ppm]

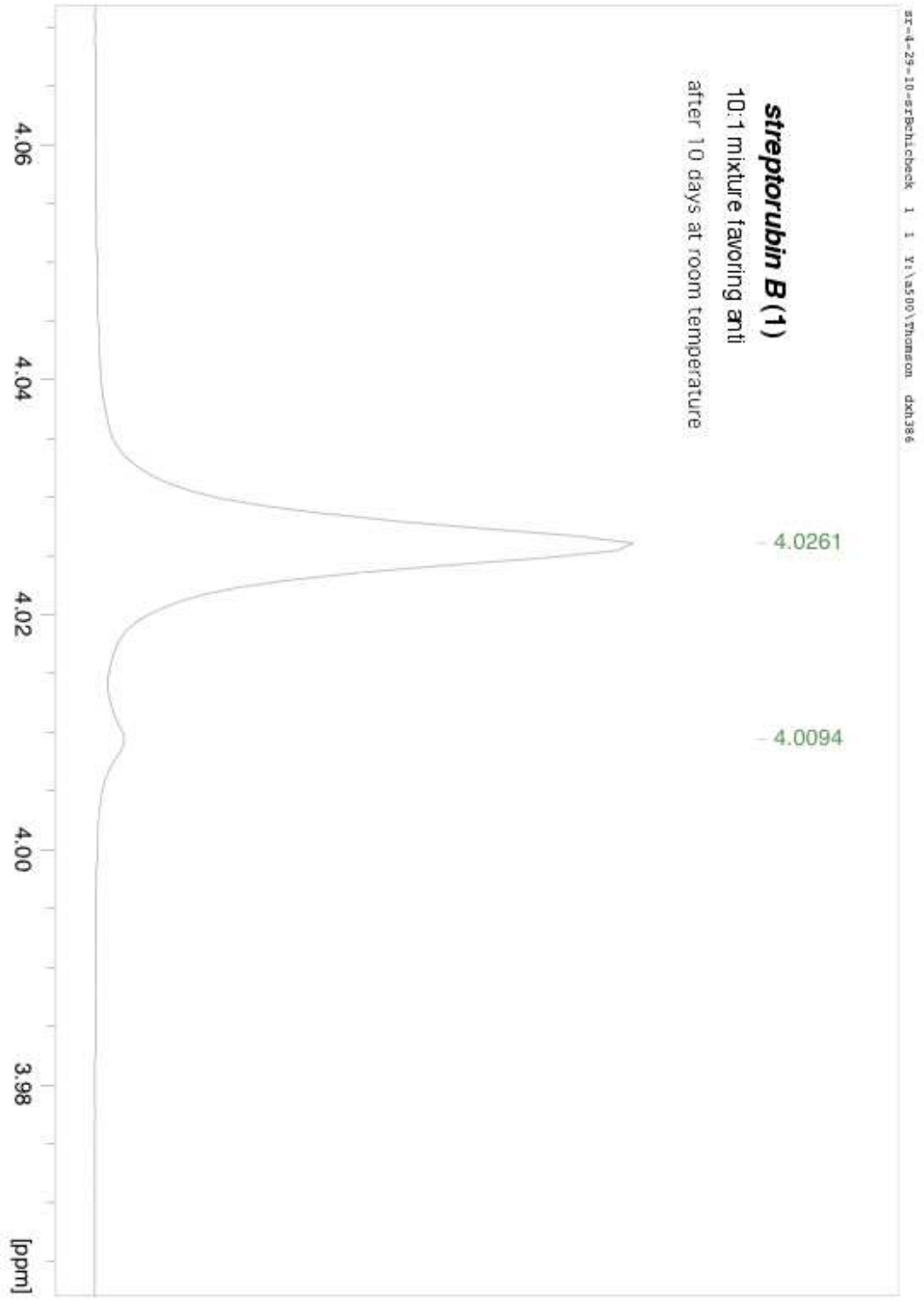


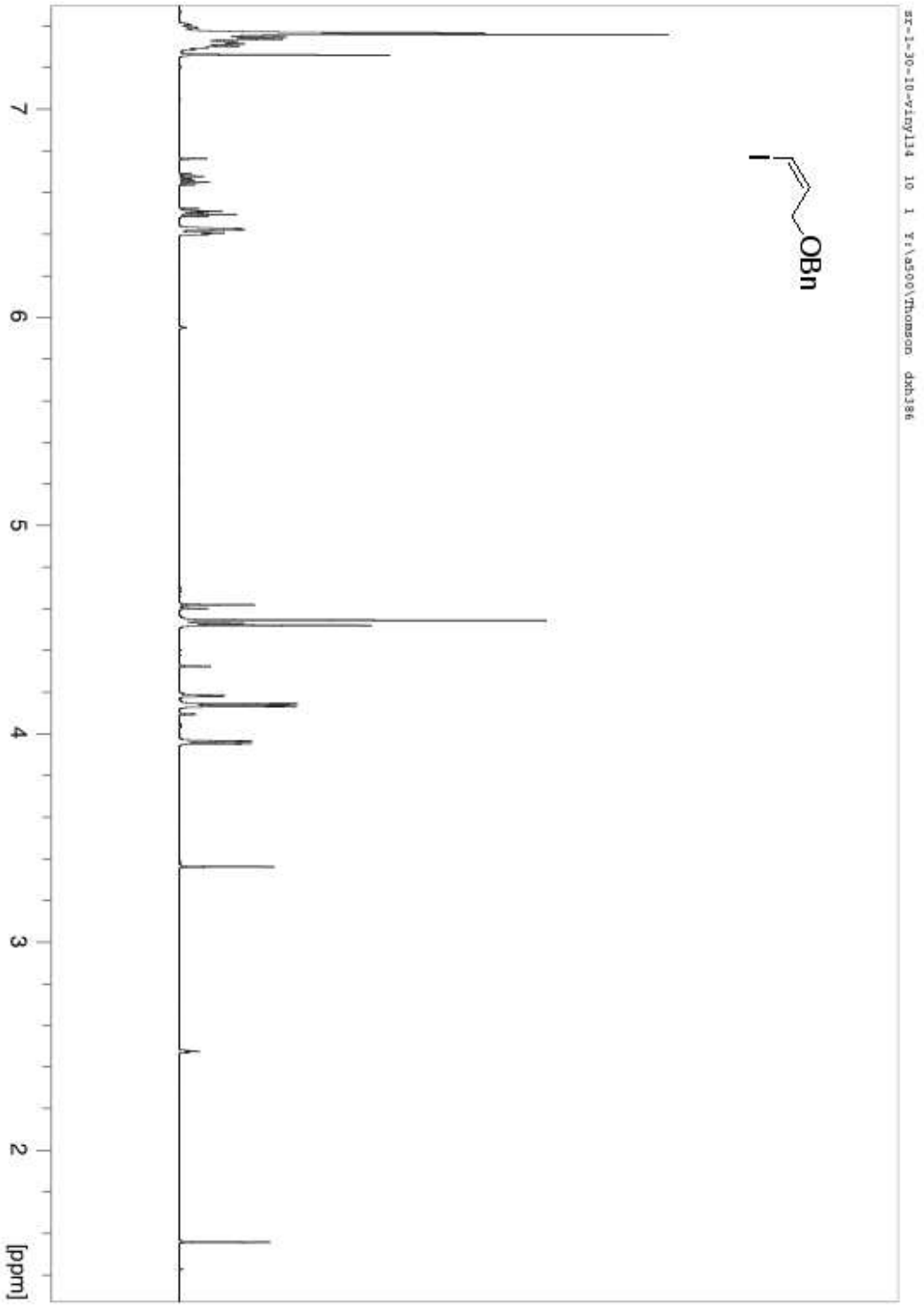
natural streptorubin B vs. *atrop*-streptorubin B

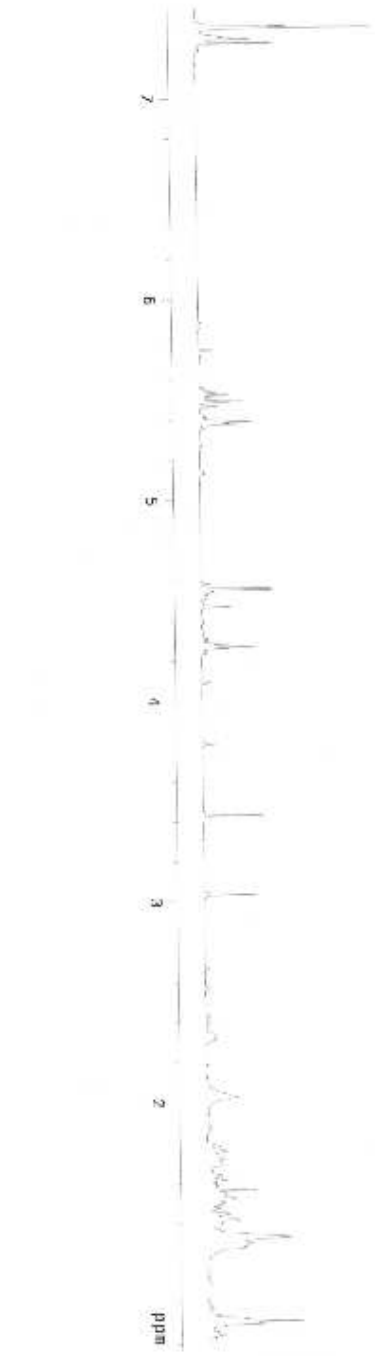
Initial mixture of isomers favoring atrop-streptorubin B upon condensation with the syn-pyrrole (syn 11)

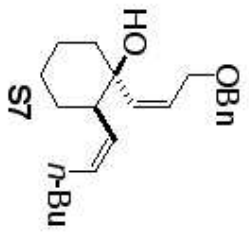

natural streptorubin B
and
atrop-streptorubin B
2D NOESY
atrop-C
C
atrop-B
B
D
atrop-D
natural-butyl chain protons
atrop-butyl-chain protons
F1 [ppm]
F2 [ppm]
7.5
7.0
6.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

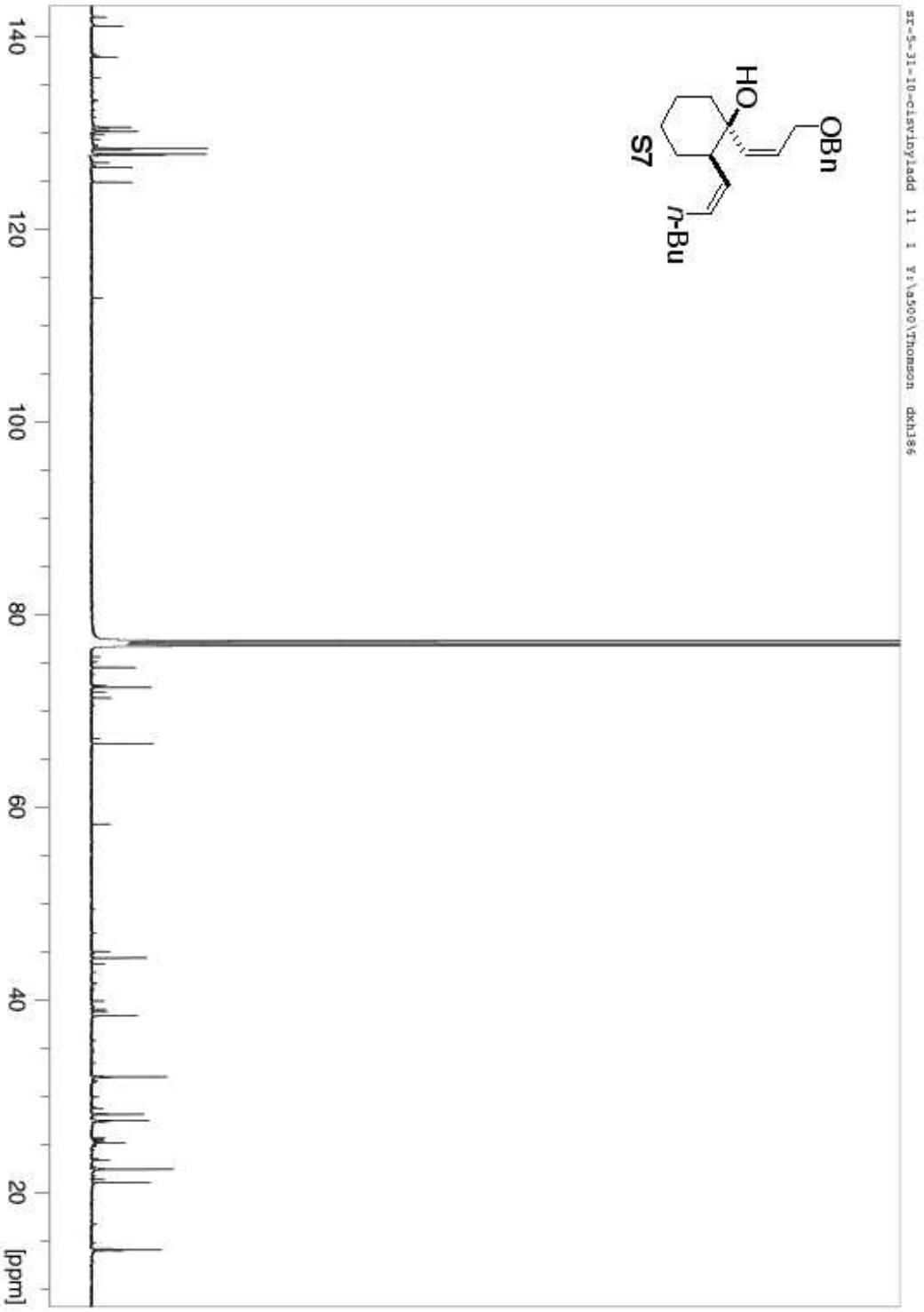

sx-3-8-10-srBrecheck 10 1 Y:\e500\Thomson dxh386
streptorubin B (1)
1:1 mixture of syn and anti
1 day after initial condensation
4.0279
4.0112
4.2
4.1
4.0
3.9
[ppm]

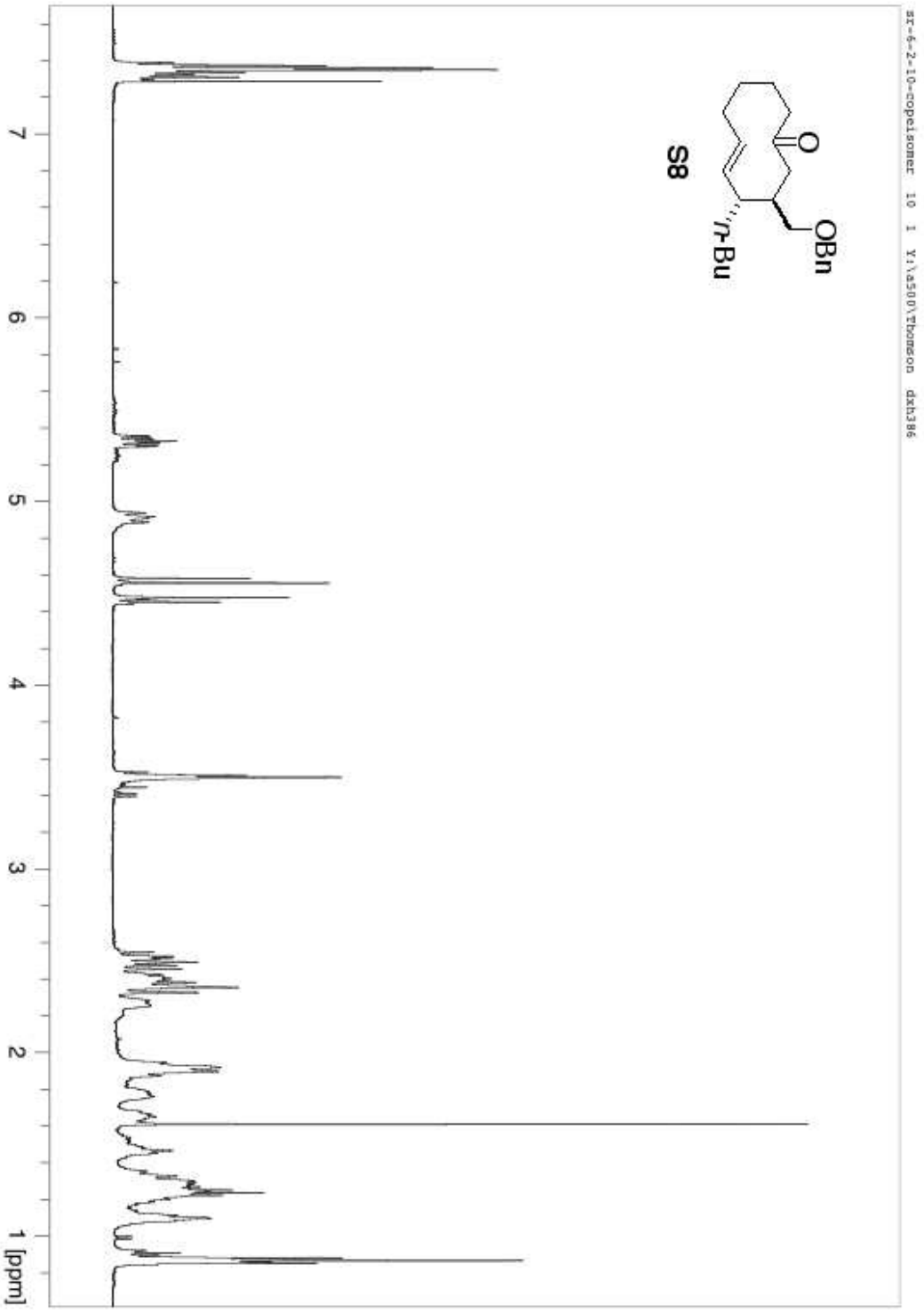

sx-4-29-10-srBchichbck 1 1 Y:\a500\Thomson dxh386
streptorubin B (1)
10:1 mixture favoring anti
after 10 days at room temperature
4.0261
4.0094
4.06
4.04
4.02
4.00
3.98
[ppm]

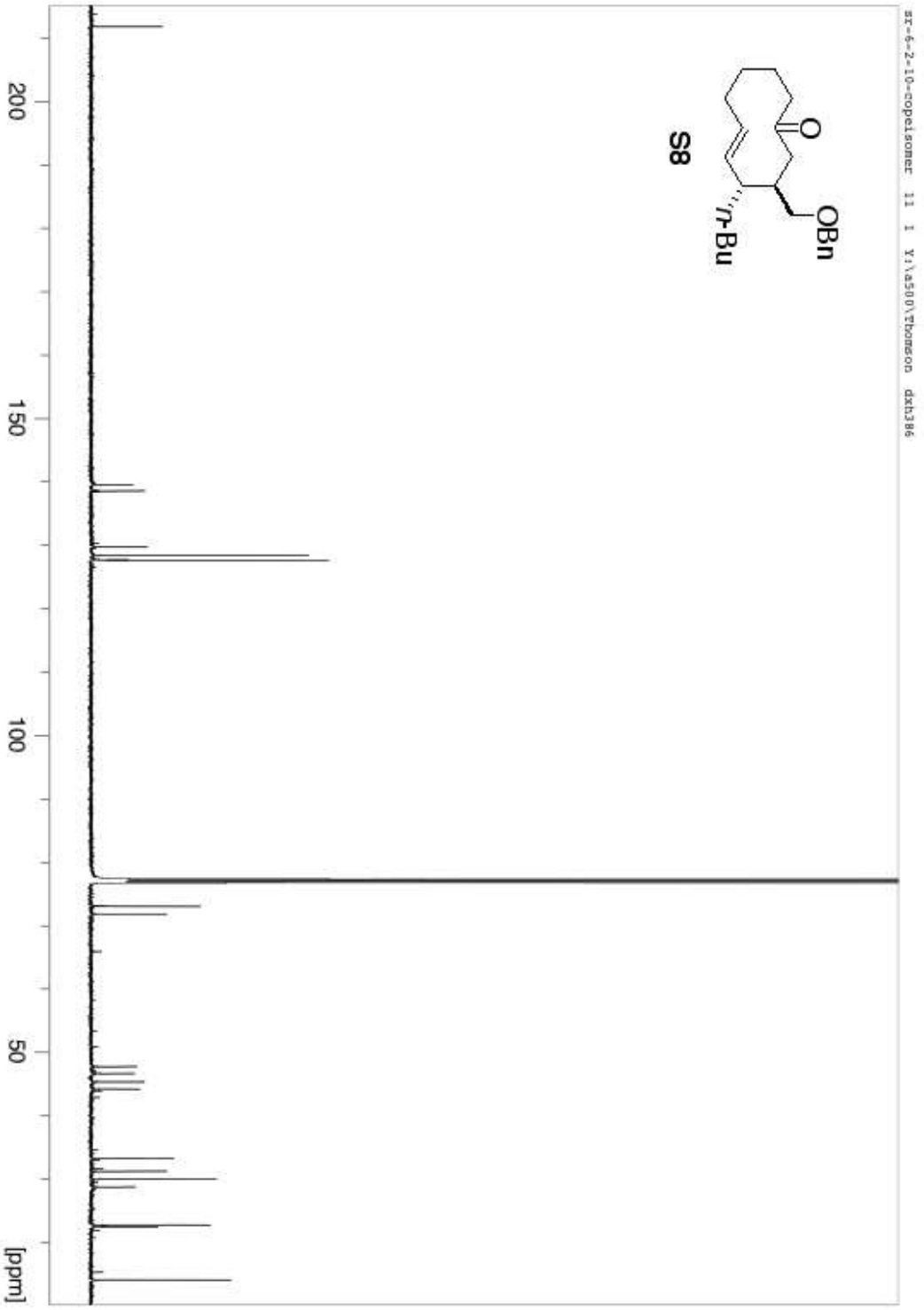

OBn
sx-1-30-10-vinyl14 10 1 Y:\a500\Thomson dmh386
7
6
5
4
3
2
[ppm]

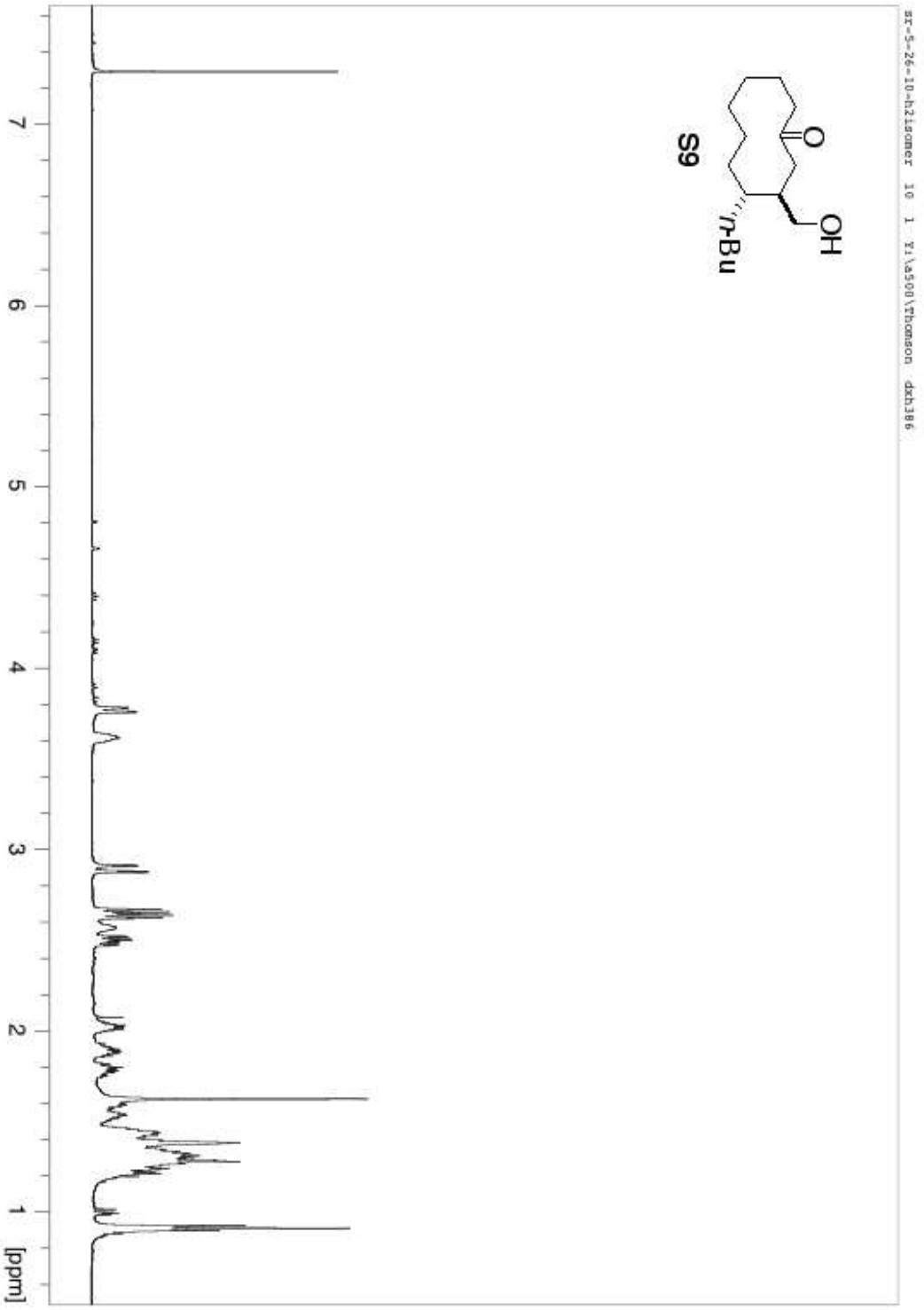

7
6
5
4
3
2
ppm

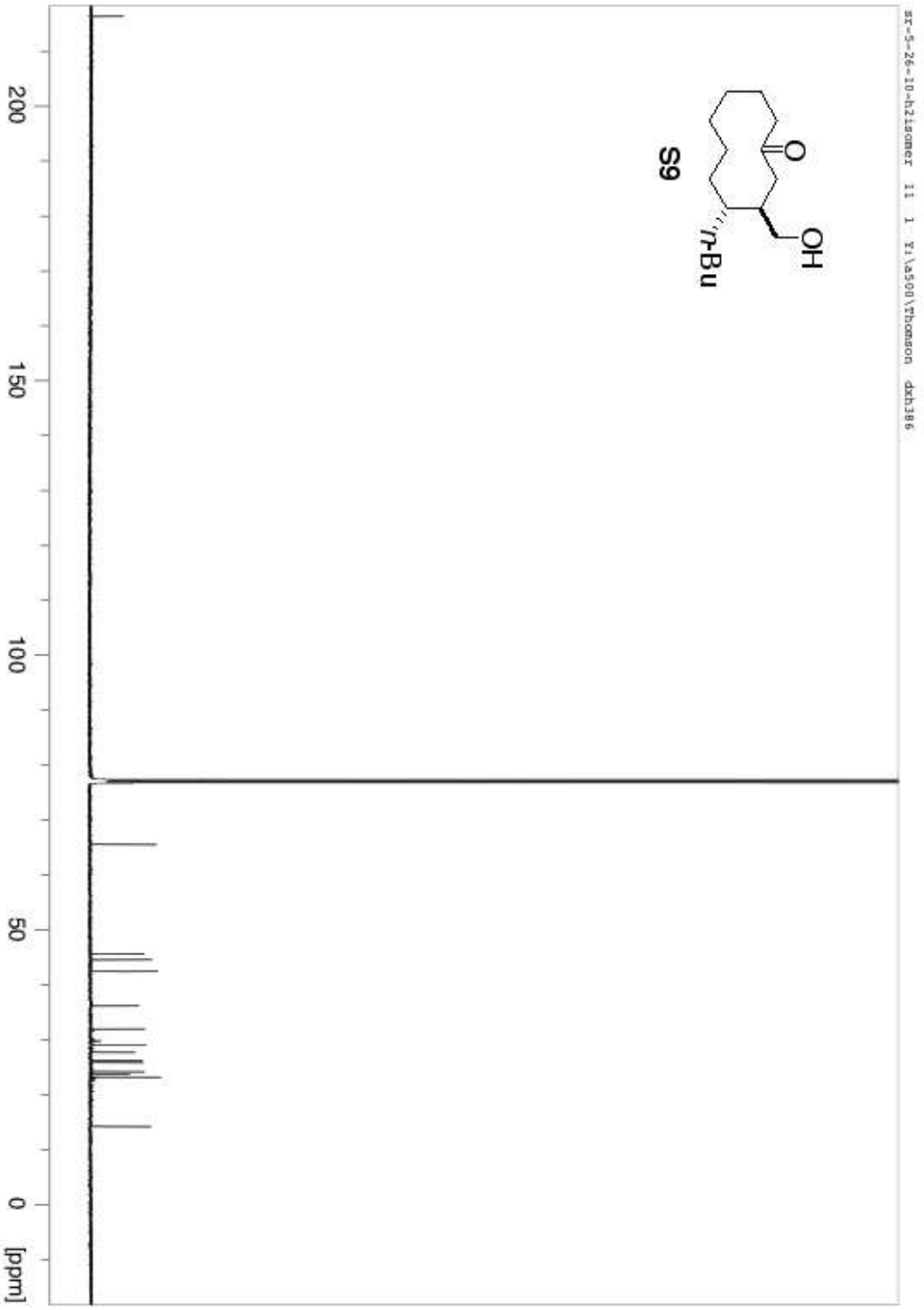

HO
OBn
S7
n-Bu

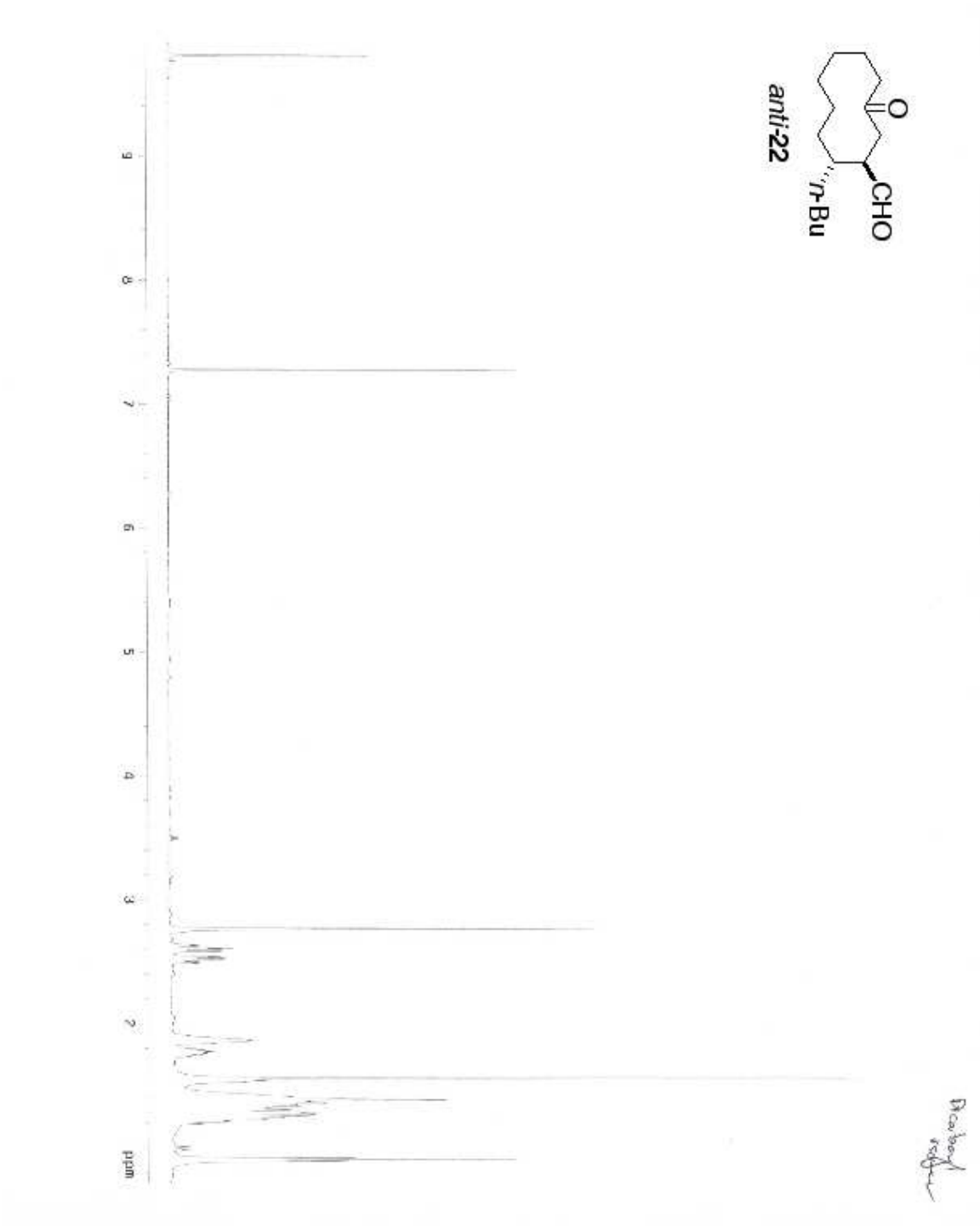

gr-5-31-10-cisvinyladd 11 1 Y:\a500\Thomson dkh186
OBn
HO
S7
n-Bu
140
120
100
80
60
40
20
[ppm]

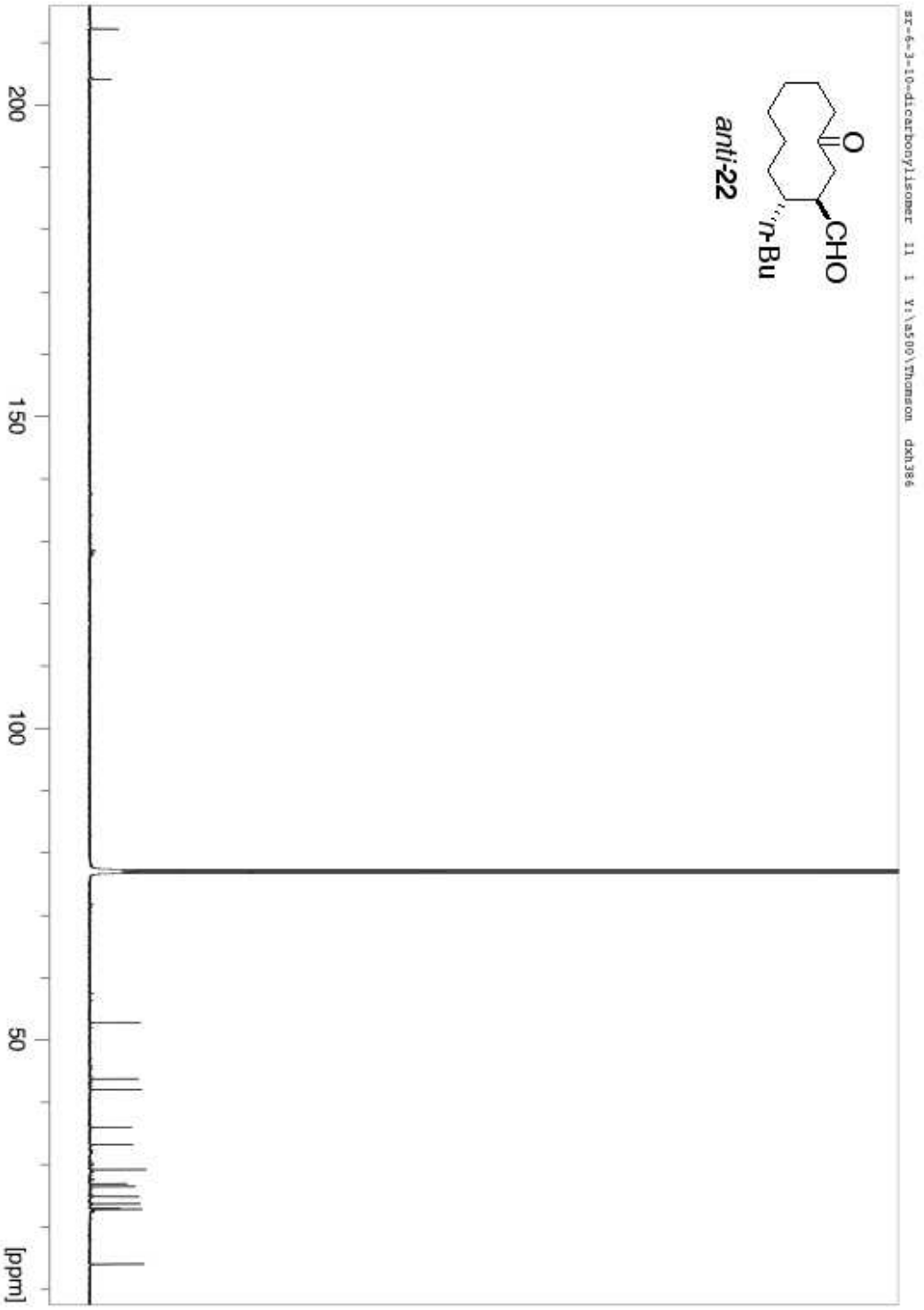

sx-6-2-10-copeisomer 10 1 Y:\a500\Thomson dxh386
S8
OBn
n-Bu
7
6
5
4
3
2
1 [ppm]

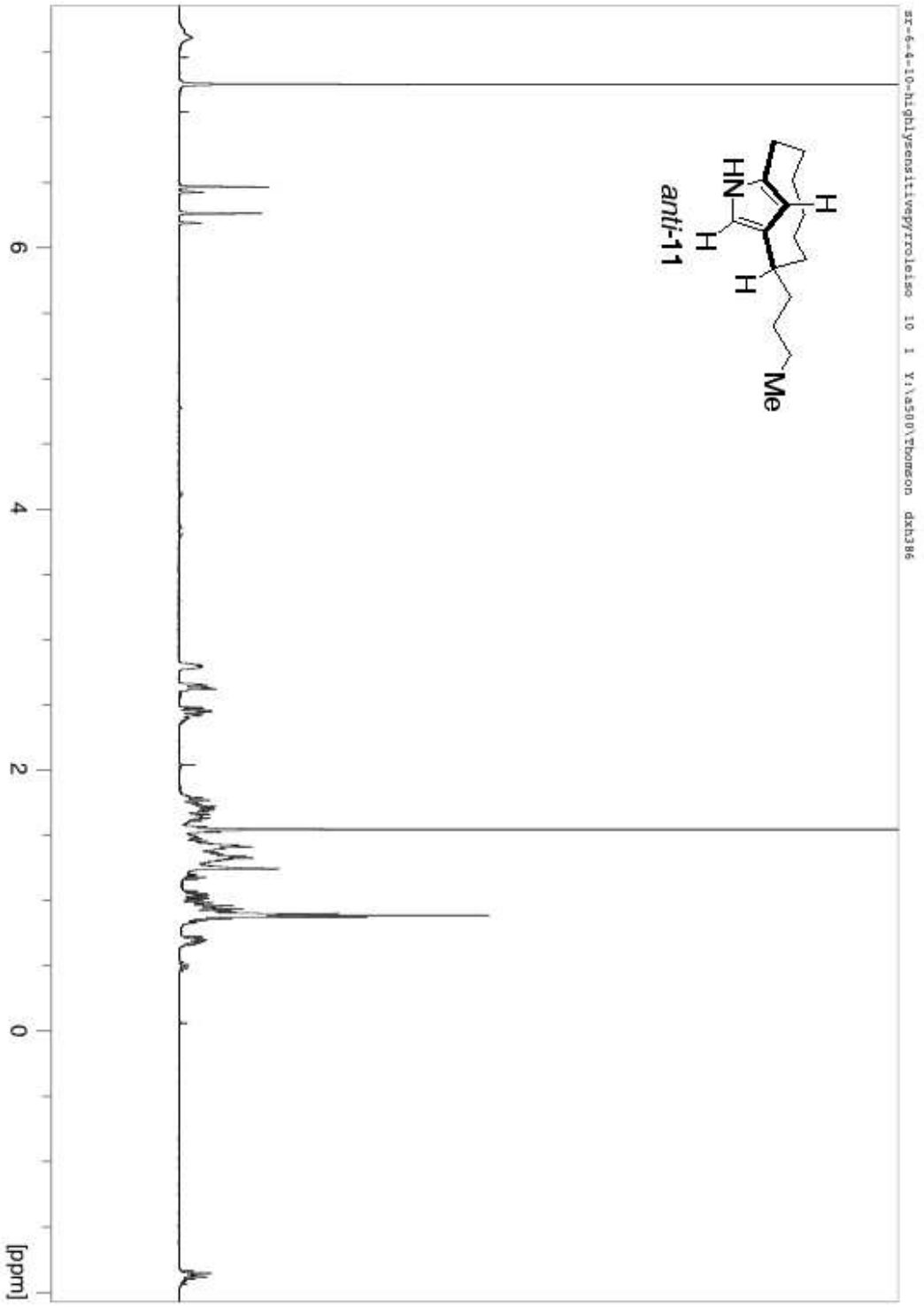

sx-6-2-10-copeisomer 11 1 Y:\a500\Thomson dxh386
S8
OBn
n-Bu
200
150
100
50
[ppm]

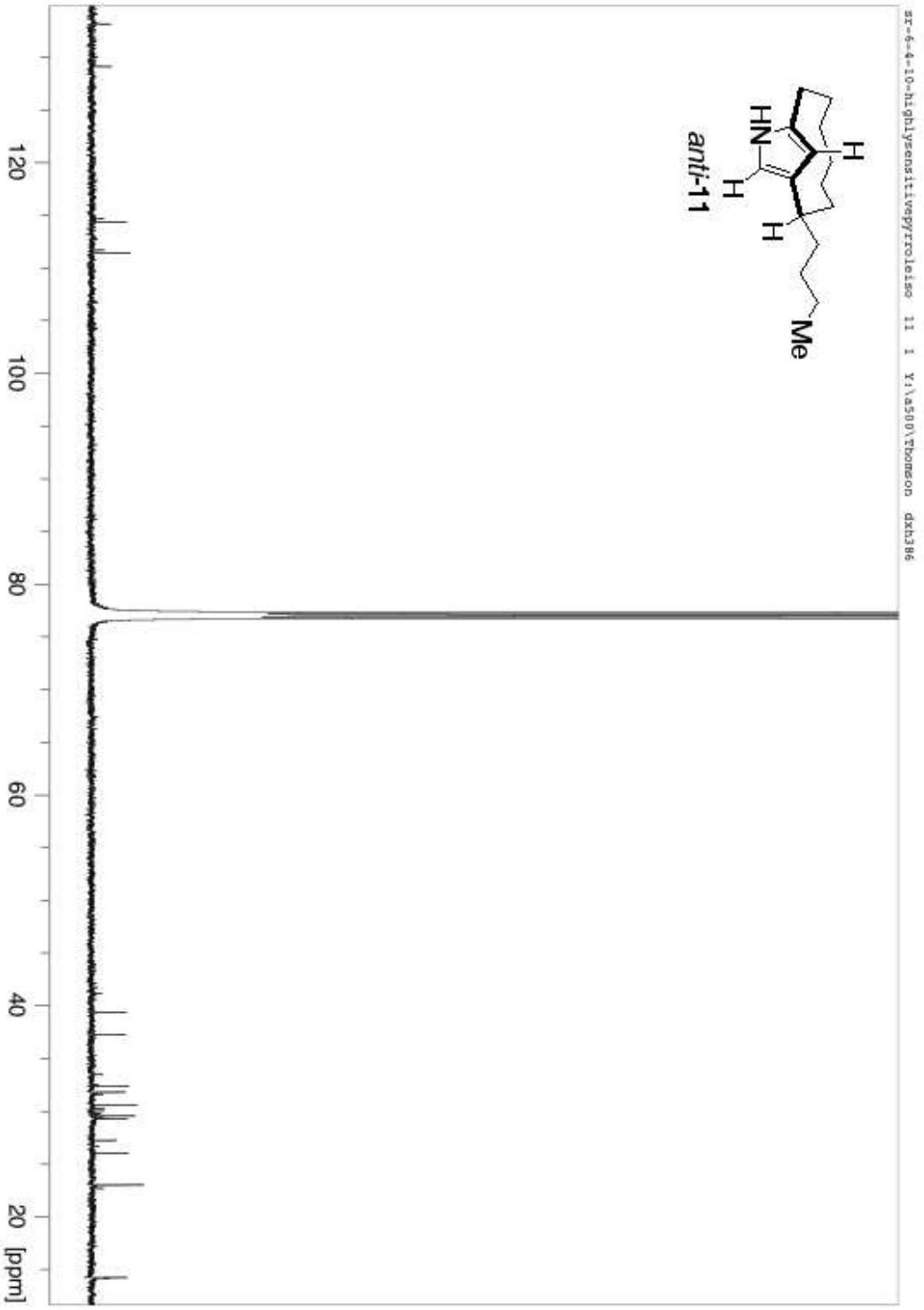

sr-5-26-10-h2isomer 10 1 Y:\a500\thomson dxh386
S9
OH
n-Bu
7
6
5
4
3
2
1
[ppm]


sr-5-26-10-h2isomer 11 1 Y:\a500\thomson dxh386
S9
OH
t-Bu
200
150
100
50
0
[ppm]


anti-22
O
CHO
n-Bu
9
8
7
6
5
4
3
2
ppm


ar-6-3-10-dicarbonylisomer 11 1 Y:\a500\Thomson dxh386
O
CHO
n-Bu
anti-22
200
150
100
50
[ppm]


sx-6-4-10-highlysensitivepyrroleiso 10 1 Y:\e500\Thomson dxh386
H
HN
H
H
Me
anti-11
6
4
2
0
[ppm]


sx-6-4-10-highlysensitivepyrroleiso 11 1 Y:\s500\Thomson dxh386
H
HN
H
H
Me
anti-11
120
100
80
60
40
20 [ppm]