Supporting Information

Diversity-Oriented Synthesis of 2,4,6-Trisubstituted Piperidines via Type II Anion Relay Chemistry (ARC)

Amos B. Smith, III,* Heeoon Han, Won-Suk Kim

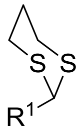
Department of Chemistry, Monell Chemical Senses Center and Laboratory for Research on the Structure of Matter, University of Pennsylvania, Philadelphia, PA 19104, U.S.A.

Table of Contents:

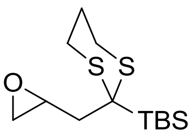
I. Materials and Methods

Reactions were carried out in oven or flame-dried glassware under an argon atmosphere, unless otherwise noted. All solvents were reagent grade. Diethyl ether and THF were obtained from a Pure Solve TM PS-400. Reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with 0.25 mm E. Merck precoated silica gel plates. In aqueous work-up, all organic solutions were dried over sodium sulfate or magnesium sulfate, and filtered prior to rotary evaporation at water aspirator pressure. Flash chromatography was performed with silica gel 60 (particle size 0.040 – 0.062 mm) supplied by Silicycle and Sorbent Technologies. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. t-BuLi (1.7 M in hexane), t-BuOK (1.0 M in THF) were purchased from Aldrich. Infrared spectra were recorded on a Perkin-Elmer Model 283B spectrophotometer or a Jasco Model FT/IR-480 Plus spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX-500 spectrometer. Chemical shifts are reported as δ values relative to the internal chloroform (δ 7.27 ppm for ^{1}H and δ 77.16 ppm for ^{13}C). Optical rotations were measured on a Jasco Perkin-Elmer model 241 polarimeter. High resolution mass spectra were measured at the University of Pennsylvania Mass Spectrometry Service Center on either a VG Micromass 70/70 H or VG ZAB-E spectrometer. Jasco SFC was used for separation of some of the diastereomers using 4.6 mm ϕ × 250 mm CHIRALPAK® IC 5 µm (Eluent: Isocratic CO_2:i-PrOH = 67:33, Flow rate: 4 mL/min).

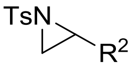
II. Experimental Procedure:



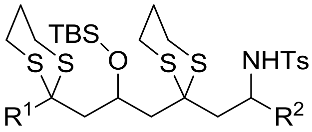
I



II



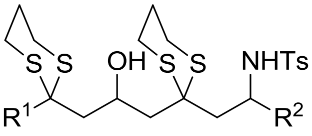
III



TBS-***IV***

1. General procedure for multi-component reaction (Type II ARC): Reactions were carried out on the following scale, unless otherwise noted.

TBS-***IV*** : A solution of dithiane ***I*** (0.050 mL, 0.74 mmol, 1.2 equiv) in THF (2.0 mL) was cooled to –78 °C and treated with a 1.0 M solution of t-BuOK (0.78 mmol, 1.25 equiv) in THF and a 1.7 M solution of t-BuLi (0.78 mmol, 1.3 equiv) in hexane dropwise via syringe, successively. The resulting solution was stirred for 0.5 h. A solution of linchpin ***II*** (0.62 mmol, 1.0 equiv) in THF (2.0 mL) was added dropwise to the reaction mixture at –78 °C via cannula. The resulting solution was stirred for 0.5 h. A solution of aziridine ***III*** (0.81 mmol, 1.3 equiv) in THF (2.0 mL) was added dropwise to the reaction mixture at –78 °C via cannula. Then the reaction was warmed to 0 °C for 2 h with stirring. The resulting mixture was poured into saturated aqueous NH_4Cl (5.0 mL) and extracted with EtOAc (3 X 10 mL). The combined organic layers were washed with brine (5.0 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography on silica gel (hexane/EtOAc = 20/1 to 3/1) provided TBS-***IV*** as a pale yellow oil.

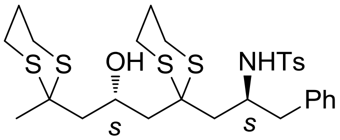


IV

2. General procedure for TBS group removal.

Method A - A solution of TBS-***IV*** in THF was treated with a 1.0 M solution of TBAF in THF (1.5 equiv), and stirred at room temperature for 12 h. The reaction mixture was concentrated in vacuo and flash chromatography on silica gel (hexane/EtOAc = 5/1 to 1/1) provided TBS-***IV***.

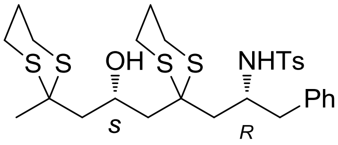
Method B - A solution of TBS-***IV*** in MeOH was treated with a catalytic amount of concentrated HCl, and stirred at room temperature for 12 h. The reaction mixture was concentrated in vacuo and flash chromatography on silica gel (hexane/EtOAc = 5/1 to 1/1) provided ***IV***.



(*S*,*S*)-**4**

TBS-(*S*,*S*)-**4** : Following the general Type II ARC procedure, 2-methyl-1,3-dithiane **1a** (0.54 mL, 4.5 mmol, 1.2 equiv), linchpin (+)-**2** (1.1 g, 3.8 mmol, 1.0 equiv) and aziridine (+)-**3a** (1.4 g, 4.9 mmol, 1.3 equiv) affored TBS-(*S*,*S*)-**4** (2.0 g, 2.8 mmol, 74% yield) as a pale yellow oil.

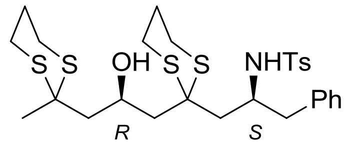
(*S*,*S*)-**4** : Following the general procedure for the TBS group removal (**Method A)**, TBS-(*S*,*S*)-**4** (1.9 g, 2.6 mmol) afforded (*S*,*S*)-**4** (1.4 g, 2.3 mmol, 90% yield) as a pale yellow oil: R_f 0.55 (hexane/EtOAc = 2:1); $[\alpha]^{25}_D$ –2.78 (c 1.00, CHCl$_3$); IR (film) 3179 (m, br), 3025 (w), 2923 (s), 1599 (w), 1494 (w), 1420 (m), 1326 (m), 1157 (s), 1090 (s), 908 (w), 754 (m), 703 (s) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.87 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 7.5 Hz, 2H), 7.22 (d, *J* = 6.9 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 4.38 (t, *J* = 10.0 Hz, 1H), 3.92 – 3.86 (m, 1H), 3.17 (dd, *J* = 6.5, 3.0 Hz, 1H), 3.16 – 3.14 (m, 2H), 3.14 – 3.11 (m, 1H), 3.07 (ddd, *J* = 14.3, 11.4, 2.6 Hz,1H), 2.77 (ddd, *J* = 14.6, 5.4, 3.1 Hz, 2H), 2.62 – 2.51 (m, 2H), 2.48 (dd, *J* = 13.3, 10.7 Hz, 1H), 2.41 (s, 3H), 2.29 (d, *J* = 15.3 Hz, 1H), 2.23 (dd, *J* = 15.6, 9.3 Hz, 1H), 2.16 – 2.09 (m, 1H), 2.07 – 2.02 (m, 1H), 1.90 – 1.85 (m, 1H), 1.85 (dd, *J* = 14.8, 10.5 Hz, 1H), 1.72 – 1.66 (m, 1H), 1.63 – 1.50 (m, 4H), 1.58 (s, 3H), 1.43 (d, *J* = 15.1 Hz, 1H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 143.09, 139.44, 138.57, 130.05, 129.64, 128.59, 127.37, 126.61, 65.62, 53.35, 51.21, 47.34, 47.13, 44.28, 44.20, 38.26, 28.35, 26.93, 26.73, 25.96, 25.22, 24.79, 24.47, 21.66; HRMS (ES) *m/z* 598.1617 [(M+H)$^+$; calcd for C$_{28}$H$_{40}$NO$_3$S$_5$: 598.1612].



(*S*,*R*)-**4**

TBS-(*S*,*R*)-**4** : Following the Type II ARC general procedure, 2-methyl-1,3-dithiane **1a** (0.54 mL, 4.5 mmol, 1.2 equiv), linchpin (+)-**2** (1.1 g, 3.8 mmol, 1.0 equiv) and aziridine (–)-**3a** (1.27g, 4.9 mmol, 1.3 equiv) afforded TBS-(*S*,*R*)-**4** (1.9 g, 2.7 mmol, 69% yield) as a pale yellow oil.

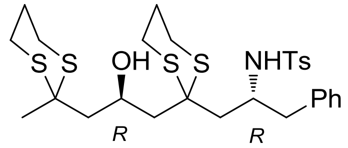
(*S*,*R*)-**4** : Following the general procedure for TBS group removal (Method A), TBS-(*S*,*R*)-**4** (1.7 g, 2.3 mmol) afforded (*S*,*R*)-**4** (1.2 g, 2.0 mmol, 85% yield) as a pale yellow oil: R$_f$ 0.45 (hexane/EtOAc = 2:1); $[\alpha]^{25}_{D}$ –31.21 (c 0.79, CHCl$_3$);); IR (film) 3277 (m, br), 3027 (w), 2923 (s), 1599 (w), 1495 (w), 1420 (m), 1327 (m), 1158 (s), 1091 (s), 908 (w), 737 (m), 666 (s) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.23 (dd, *J* = 8.0, 6.5 Hz, 2H), 7.19 (t, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 6.5 Hz, 2H), 5.44 (d, *J* = 5.0 Hz, 1H), 4.21-4.18 (m, 1H), 3.90 – 3.82 (m, 1H), 3.28 (brs, 1H), 2.97-2.89 (m, 3H), 2.86 – 2.76 (m, 3H), 2.73 – 2.67 (m, 2H), 2.59 (ddd, *J* = 14.0, 7.0, 3.5 Hz,1H), 2.47 (ddd, *J* = 14.0, 8.0, 3.5 Hz, 2H), 2.43 (s, 3H), 2.25 (dd, *J* = 15.5, 4.0 Hz, 1H), 2.17 (dd, *J* = 15.5, 8.5 Hz, 1H), 2.15 (dd, *J* = 15.5, 9.5 Hz, 1H), 2.07 – 2.00 (m, 1H), 1.91 ((dddd, *J* = 105, 10.5, 3.5, 3.5 Hz, 1H), 1.88 – 1.76 (m, 1H), 1.71 (dd, *J* = 15.5, 1.5 Hz, 1H), 1.71 – 1.64 (m, 2H), 1.60 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 143.42, 137.65, 137.47, 130.02, 129.76, 128.54, 127.74, 126.70, 66.07, 57.94, 51.22, 48.42, 47.93, 46.27, 42.79, 42.06, 28.70, 26.92, 26.77, 26.50, 26.08, 24.84, 24.68, 21.74; HRMS (ES) *m/z* 620.1445 [(M+Na)$^+$; calcd for C$_{28}$H$_{39}$NO$_3$S$_5$Na: 620.1431].



(*R*,*S*)-**4**

TBS-(*R*,*S*)-**4** : Following the Type II ARC general procedure, 2-methyl-1,3-dithiane **1a** (0.56 mL, 4.8 mmol, 1.2 equiv), linchpin (–)-**2** (1.17 g, 4.0 mmol, 1.0 equiv) and aziridine (+)-**3a** (1.5 g, 5.2 mmol, 1.3 equiv) afforded TBS-(*S*,*R*)-**4** (2.0g, 2.8 mmol, 69% yield) as a pale yellow oil.

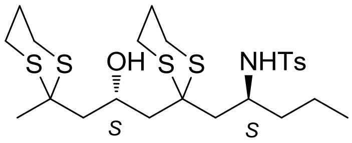
(*R*,*S*)-**4** : Following the general procedure for TBS group removal (Method B), TBS-(*R*,*S*)-**4** (2.0 g, 2.8 mmol) afforded (*R*,*S*)-**4** (1.5 g, 2.4 mmol, 88% yield) as a pale yellow oil: R_f 0.45 (hexane/EtOAc = 2:1); $[\alpha]^{24}_D$ +25.75 (c 0.79, $CHCl_3$); IR, ^{1}H and ^{13}C NMR are identical to those of (*S*,*R*)-**4**; HRMS (ES) m/z 598.1617 [$(M+H)^+$; calcd for $C_{28}H_{39}NO_3S_5$: 598.1612].



(*R*,*R*)-**4**.

TBS-(*R*,*R*)-**4** : Following the Type II ARC general procedure, 2-methyl-1,3-dithiane **1a** (0.578mL, 4.82mmol, 1.10 equiv), linchpin (–)-**2** (1.2 g, 4.0 mmol, 1.0 equiv) and aziridine (–)-**3a** (1.5 g, 5.2 mmol, 1.3 equiv) afforded TBS-(*S*,*R*)-**4** (2.1 g, 3.0 mmol, 74% yield) as a pale yellow oil.

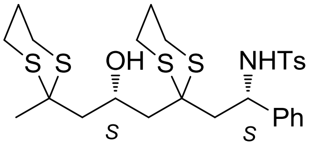
(*R*,*R*)-**4** : Following the general procedure for TBS group removal (Method A), TBS-(*R*,*R*)-**4** (2.0 g, 2.7 mmol) afforded (*R*,*R*)-**4** (1.5 g, 2.5 mmol, 92% yield) as a pale yellow oil: R_f 0.55 (hexane/EtOAc = 2:1); $[\alpha]^{28}_D$ +3.01 (c 1.00, $CHCl_3$); IR, ^{1}H and ^{13}C NMR are identical to those of (*S*,*S*)-**4**; HRMS (ES) m/z 618.1051 [$(M+Cl)^-$; calcd for $C_{27}H_{37}ClNO_3NS_5$: 618.1066].



(*S*,*S*)-**5**.

TBS-(*S*,*S*)-**5** : Following the Type II ARC general procedure, 2-methyl-1,3-dithiane **1a** (0.050 mL, 0.42 mmol, 1.5 equiv), linchpin (+)-**2** (81 mg, 0.28 mmol, 1.0 equiv) and aziridine (+)-**3b** (130 mg, 0.56 mmol, 2.0 equiv) afforded TBS-(*S*,*S*)-**5** (110 mg, 0.17 mmol, 61% yield) as a pale yellow oil.

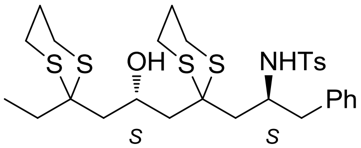
(*S*,*S*)-**5** : Following the general procedure for TBS group removal (Method A), TBS-(*S*,*S*)-**5** (110 mg, 0.16 mmol) afforded (*S*,*S*)-**5** (80 mg, 0.15 mmol, 92% yield) as a pale yellow oil: R_f 0.33 (hexane/EtOAc = 2:1); $[\alpha]^{28}_{D}$ –8.83 (c 0.80, $CHCl_3$); IR (film) 3180 (m, br), 2924 (s), 1599 (w), 1421 (m), 1325 (m), 1157 (s) 1092 (s), 814 (m), 755 (m), 665 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 4.38 (t, *J* = 10.0 Hz, 1H), 3.76 (td, *J* = 9.6, 4.6 Hz, 1H), 3.18 (ddd, *J* = 14.3, 11.6, 2.6 Hz, 1H), 3.10 (ddd, *J* = 14.2, 8.9, 2.6 Hz, 1H), 2.82 -2.68 (m, 6H), 2.65 (dd, *J* = 15.0, 10.0 Hz, 1H), 2.41 (s, 3H), 2.34 (dd, *J* = 15.4, 9.8 Hz, 1H), 2.15 – 2.06 (m, 3H), 1.96 – 1.90 (m, 2H), 1.89 – 1.80 (m, 1H), 1.71 (d, *J* = 15.3 Hz, 1H), 1.63 (dd, *J* = 14.9, 0.9 Hz, 1H), 1.61 (s, 3H), 1.43 – 1.36 (m, 2H), 1.33 – 1.16 (m, 4H), 0.77 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.87, 139.53, 129.48, 127.30, 66.76, 51.62, 50.41, 47.22, 47.18, 42.85, 41.43, 39.27, 28.31, 26.89, 26.70, 26.19, 26.17, 25.44, 24.50, 21.66, 17.76, 14.11; HRMS (ES) *m/z* 572.1418 [$(M+Na)^+$; $C_{24}H_{39}NO_3S_5Na$: 572.1431].



(*S*,*S*)-**6**

TBS-(*S*,*S*)-**6** : Following the Type II ARC general procedure, 2-methyl-1,3-dithiane **1a** (0.050 mL, 0.42 mmol, 1.5 equiv), linchpin (+)-**2** (81 mg, 0.28 mmol, 1.0 equiv) and aziridine (+)-**3c** (190 mg, 0.56 mmol, 2.0 equiv) afforded TBS-(*S*,*S*)-**6** (80 mg, 0.12 mmol, 41% yield) as a pale yellow oil.

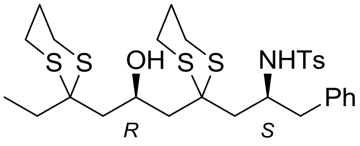
(*S*,*S*)-**6** : Following the general procedure for TBS group removal (Method B), TBS-(*S*,*S*)-**6** (75 mg, 0.11 mmol) afforded (*S*,*S*)-**6** (54 mg, 0.093 mmol, 87% yield) as a pale yellow oil: R_f 0.30 (hexane/EtOAc = 2:1); $[\alpha]^{24}_{D}$ –50.1 (c 2.00, $CHCl_3$); IR (film) 3274 (m, br), 3028 (w), 2920 (m), 1598 (w), 1493 (m), 1420 (m), 1326 (m), 1159 (s), 1091 (m), 813 (w), 756 (m), 701 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.2 Hz, 2H), 7.22 – 7.14 (m, 7H), 6.35 (d, *J* = 3.5 Hz, 1H), 4.76 (ddd, J = 4.10, 4.10, 9.06 Hz 1H), 4.38-4.32 (m, 1H), 3.04 – 2.96 (m, 1H), 2.96 – 2.86 (m, 2H), 2.86 – 2.74 (m, 4H), 2.68 (ddd, *J* = 14.7, 6.4, 3.1 Hz, 1H), 2.62 (dd, *J* = 15.3, 9.1 Hz, 1H), 2.41 (dd, *J* = 15.0, 10.7 Hz, 1H), 2.38 (s, 3H), 2.15 (dd, *J* = 14.9, 9.3 Hz, 1H), 2.09 – 1.96 (m, 2H), 1.93 – 1.80 (m, 2H), 1.70 – 1.64 (m, 3H) 1.63 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.08, 142.34, 137.21, 129.38, 128.44, 127.72, 127.36, 126.90, 65.91, 56.02, 51.20, 48.40, 47.82, 45.84, 45.54, 28.76, 26.86, 26.75, 26.46, 26.21, 24.76, 24.75, 21.63; HRMS (ES) *m/z* 606.1270 [$(M+Na)^+$; $C_{27}H_{39}NO_3S_5Na$: 606.1275].



(*S*,*S*)-**7**

TBS-(*S*,*S*)-**7** : Following the Type II ARC general procedure, 2-methyl-1,3-dithiane **1a** (38 mg, 0.26 mmol, 1.5 equiv), linchpin (+)-**2** (50 mg, 0.17 mmol, 1.0 equiv) and aziridine (+)-**3a** (99 mg, 0.34 mmol, 2.0 equiv) afforded TBS-(*S*,*S*)-**7** (81 mg, 0.11 mmol, 65% yield) as a pale yellow oil.

(*S*,*S*)-**7** : Following the general procedure for removal of TBS group (Method A), TBS-(*S*,*S*)-**7** (81 mg, 0.11 mmol) afforded (*S*,*S*)-**8** (64 mg, 0.11 mmol, 94% yield) as a pale yellow oil: R_f 0.33 (hexane/EtOAc = 2:1); $[\alpha]^{25}_D$ –4.67 (c 0.28, $CHCl_3$); IR (film) 3179 (m, br), 2926 (s), 1419 (m), 1327 (m), 1157 (s), 1091 (s), 813 (m), 754 (m), 667 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 7.4 Hz, 2H), 7.23 (d, *J* = 6.8 Hz, 2H), 7.22 – 7.17 (m, 1H), 4.68 (s, 1H), 4.36 (t, *J* = 9.8 Hz, 1H), 3.88 (app t, *J* = 9.4 Hz, 1H), 3.20 (dd, *J* = 13.2, 3.2 Hz, 1H), 3.13 (ddd, *J* = 13.9, 10.9, 2.7 Hz, 1H), 2.98 (ddd, *J* = 13.9, 10.9, 2.7 Hz, 1H), 2.78 (ddd, *J* = 14.6, 7.5, 4.5 Hz, 1H), 2.57 (ddd, *J* = 13.8, 10.9, 2.7 Hz, 1H), 2.53 – 2.45 (m, 2H), 2.41 (s, 3H), 2.39 ((dd, *J* = 15.0, 10.0 Hz, 1H), 2.29 (d, *J* = 15.4 Hz, 1H), 2.21 (dd, *J* = 15.6, 9.5 Hz, 1H), 2.15 – 2.06 (m, 1H), 2.06 – 1.95 (m, 2H), 1.93 – 1.83 (m, 2H), 1.77 (dd, *J* = 15.1, 10.0 Hz, 1H), 1.71 – 1.65 (m, 2H), 1.61 – 1.53 (m, 1H), 1.53 – 1.45 (m, 1H), 1.40 (d, *J* = 15.0 Hz, 1H), 1.00 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.05, 139.40, 138.62, 130.04, 129.61, 128.57, 127.37, 126.58, 65.10, 53.40, 52.00, 51.14, 44.46, 44.34, 43.85, 37.96, 32.86, 26.55, 25.98, 25.95, 25.18, 24.92, 24.71, 21.65, 8.46; HRMS (ES) *m/z* 634.1599 [$(M+H)^+$; calcd for $C_{29}H_{41}NO_3S_3Na$: 634.1588].

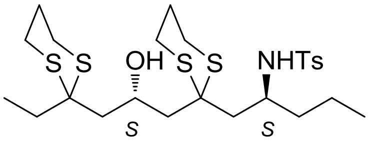


(*R*,*S*)-**7**

TBS-(*R*,*S*)-**7** : Following the Type II ARC general procedure, 2-methyl-1,3-dithiane **1a** (61 mg, 0.41 mmol, 1.5 equiv), linchpin (–)-**2** (80 mg, 0.28 mmol, 1.0 equiv) and aziridine (+)-**3a** (160 mg, 0.55 mmol, 2.0 equiv) afforded TBS-(*R*,*S*)-**7** (120 mg, 0.16 mmol, 59% yield) as a pale yellow oil.

(*R*,*S*)-**7** : Following the general procedure for removal of TBS group (Method B), TBS-(*R*,*S*)-**7** (86 mg, 0.11 mmol) afforded (*R*,*S*)-**7** (70 mg, 0.11 mmol, 97% yield) as a pale yellow oil: R_f 0.31 (hexane/EtOAc = 2:1); $[\alpha]^{28}_D$ +23.64 (c 2.00,

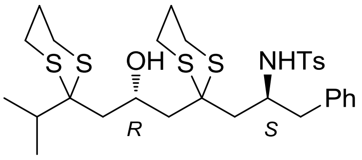
$CHCl_3$); IR (film) 3290 (m, br), 2926 (s), 1598 (w), 1419 (m), 1325 (m), 1157 (s), 1087 (s), 1043 (s), 812 (m), 702 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 7.0 Hz, 2H), 7.19 (dddd, *J* = 8.0, 8.0, 1.0, 1.0 Hz, 1H), 7.14 (d, *J* = 7.0 Hz, 2H), 5.57 (d, *J* = 5.5 Hz, 1H), 4.18 (dddd, *J* = 5.5, 5.5, 3.5, 3.5 Hz, 1H), 3.30 (brs, 1H), 2.95 (dd, *J* = 14.0, 4.5 Hz, 1H), 2.96 – 2.74 (m, 5H), 2.75 – 2.63 (m, 2H), 2.56 (ddd, *J* = 14.5, 7.4, 3.5 Hz, 1H), 2.46 (ddd, *J* = 14.5, 9.0, 3.0 Hz, 1H), 2.42 (s, 3H), 2.24 ((dd, *J* = 15.5, 3.5 Hz, 1H), 2.17 (dd, *J* = 15.0, 8.5 Hz, 1H), 2.08 (dd, *J* = 15.5, 9.5 Hz, 1H), 2.23 – 1.95 (m, 2H), 1.94– 1.85 (m, 2H), 1.85 – 1.73 (m, 2H), 1.66 (dd, *J* = 15.1, 2.0 Hz, 1H), 1.63 (d, *J* = 5.5 Hz, 2H), 0.99 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.31, 137.60, 137.49, 130.02, 129.68, 128.42, 127.70, 126.57, 65.62, 52.90, 52.83, 51.17, 46.31, 44.95, 42.72, 41.83, 32.54, 26.44, 26.36, 26.10, 26.02, 25.06, 24.64, 21.68, 8.88; HRMS (ES) *m/z* 612.1782 [(M+H)$^+$; calcd for $C_{29}H_{42}NO_3S_3$: 612.1768].



(*S*,*S*)-**8**

TBS-(*S*,*S*)-**8** : Following the Type II ARC general procedure, 2-methyl-1,3-dithiane **1a** (6o mg, 0.41 mmol, 1.5 equiv), linchpin (–)-**2** (80 mg, 0.27 mmol, 1.0 equiv) and aziridine (+)-**3a** (130 mg, 0.54 mmol, 2.0 equiv) afforded TBS-(*S*,*S*)-**8** (100 mg, 0.15 mmol, 55% yield) as a pale yellow oil.

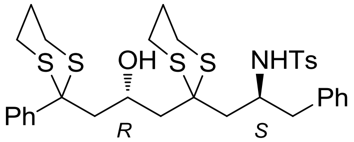
(*S*,*S*)-**8** : Following the general procedure for TBS group removal (Method B), TBS-(*S*,*S*)-**8** (27 mg, 0.040 mmol) afforded (*S*,*S*)-**8** (20 mg, 0.036 mmol, 89% yield) as a pale yellow oil: R_f 0.40 (hexane/EtOAc = 2:1); $[\alpha]^{26}_{D}$ –4.69 (c 1.00, $CHCl_3$); IR (film) 33184 (m, br), 2928 (s), 1598 (w), 1420 (m), 1326 (m), 1158 (s), 1092 (s), 813 (m), 755 (m), 667 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 3.9 Hz, 1H), 4.65 (s, 1H), 4.37 (t, *J* = 9.9 Hz, 1H), 3.78 (sextet, *J* = 4.7 Hz, 1H), 3.19 (ddd, *J* = 14.0, 11.1, 2.6 Hz, 1H), 3.1 (ddd, *J* = 14.0, 11.1, 2.6 Hz, 1H), 2.82 – 2.74 (m, 3H), 2.74 – 2.65 (m, 3H), 2.54 (dd, *J* = 15.2, 10.0 Hz, 1H), 2.41 (s, 3H), 2.34 (dd, *J* = 15.4, 9.9 Hz, 1H), 2.14 – 2.06 (m, 1H), 2.10 (d, 2.03 *J* = 14.4 Hz, 1H), 2.03 (m, 2H), 1.97 – 1.82 (m, 4H), 1.71 (app t, *J* = 13.7 Hz, 2H), 1.45 – 1.39 (m, 2H), 1.36 – 1.26 (m, 1H), 1.26 – 1.16 (m, 1H), 1.03 (t, *J* = 7.4 Hz, 1H), 0.78 (t, *J* = 7.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.82, 139.55, 129.46, 127.31, 66.31, 52.08, 51.61, 50.42, 43.77, 43.02, 41.22, 39.41, 32.87, 26.55, 26.20, 26.14, 25.97, 25.44, 24.98, 21.66, 17.77, 14.12, 8.52; HRMS (ES) *m/z* 586.1584 [(M+Na)$^+$; $C_{25}H_{41}NO_3S_5Na$: 586.1588].



(*R*,*S*)-**9**

TBS-(*R*,*S*)-**9** : Following the Type II ARC general procedure, 2-methyl-1,3-dithiane **1c** (46 mg, 0.28 mmol, 1.5 equiv), linchpin (+)-**2** (55 mg, 0.19 mmol, 1.0 equiv) and aziridine (+)-**3b** (110 mg, 0.38 mmol, 2.0 equiv) afforded TBS-(*R*,*S*)-**9** (78 mg, 0.11 mmol, 56% yield) as a pale yellow oil.

(*R*,*S*)-**9** : Following the general procedure for TBS group removal (Method A), TBS-(*R*,*S*)-**9** (78 mg, 0.110 mmol) afforded (*R*,*S*)-**9** (60 mg, 0.096 mmol, 91% yield) as a pale yellow oil: R_f 0.45 (hexane/EtOAc = 2:1); $[\alpha]^{25}_{D}$ –56.38 (c 1.00, $CHCl_3$); IR (film) 3178 (m, br), 3026 (w), 2926 (s), 1599 (w), 1419 (m), 1328 (m), 1158 (s), 1090 (s), 979 (w), 906 (w), 813 (w), 755 (m), 703 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 3.8 Hz, 1H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.28 (d, *J* = 7.3 Hz, 2H), 7.24 (d, *J* = 6.8 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 4.84 (s, 1H), 4.44 (app t, *J* = 9.9 Hz, 1H), 3.89 (app t, *J* = 9.5 Hz, 1H), 3.21 (dd, *J* = 13.2, 3.3 Hz, 1H), 3.14 (ddd, *J* = 13.9, 8.4, 2.9 Hz, 1H), 2.96 (ddd, *J* = 13.6, 10.4, 2.9 Hz, 1H), 2.84 – 2.76 (m, 2H), 2.57 (ddd, *J* = 14.0, 11.0, 2.7 Hz, 1H), 2.52 – 2.45 (m, 2H), 2.41 (s, 3H), 2.45 – 2.35 (m, 1H), 2.32 – 2.25 (m, 2H), 2.22 (dd, *J* = 15.5, 9.4 Hz, 1H), 2.12-2.06 (m, 1H), 2.02 (m, 1H), 1.92 – 1.83 (m, 1H), 1.78 – 1.71 (m, 2H), 1.71 – 1.64 (m, 1H), 1.59 – 1.52 (m, 1H), 1.51-1.44 (m, 1H), 1.40 (d, *J* = 15.0 Hz, 1H), 1.23 (d, *J* = 6.8 Hz, 2H), 1.00 (d, *J* = 6.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.03, 139.50, 138.71, 130.08, 129.62, 128.59, 127.40, 126.60, 64.77, 56.88, 53.48, 51.20, 44.62, 44.45, 42.14, 37.86, 34.82, 26.41, 25.98, 25.55, 25.24, 25.01, 24.71, 21.68, 18.65, 17.09; HRMS (ES) *m/z* 648.1725 $[(M+Na)^+$; $C_{30}H_{43}NO_3S_5Na$: 648.1744].

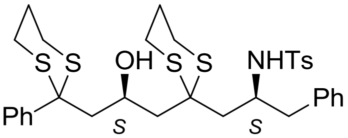


(*R*,*S*)-**10**

TBS-(*R*,*S*)-**10** : Following the Type II ARC general procedure, 2-methyl-1,3-dithiane **1d** (51 mg, 0.26 mmol, 1.5 equiv), linchpin (+)-**2** (50 mg, 0.17 mmol, 1.0 equiv) and aziridine (+)-**3a** (99 mg, 0.34 mmol, 2.0 equiv) afforded TBS-(*R*,*S*)-**10** (69 mg, 0.089 mmol, 52% yield) as a pale yellow oil.

(*R*,*S*)-**10** : Following the general procedure for TBS group removal (Method A), TBS-(*R*,*S*)-**10** (69 mg, 0.089 mmol) afforded (*R*,*S*)-**10** (55 mg, 0.083 mmol, 93% yield) as a pale yellow oil: R_f 0.35 (hexane/EtOAc = 2:1); $[\alpha]^{30}_{D}$ +66.04 (c 1.00,

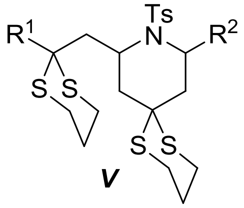
$CHCl_3$); IR (film) 3190 (m, br), 2923 (s), 1597 (w), 1442 (m), 1328 (m), 1158 (s), 1090 (s), 813 (w), 754 (m), 702 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.3 Hz, 2H), 7.83 (d, *J* = 7.5 Hz, 2H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.32 –7.22 (m, 7H), 7.18 (t, *J* = 7.1 Hz, 1H), 4.29 (t, *J* = 9.6 Hz, 1H), 3.83 – 3.77 (m, 1H), 3.24 (dd, *J* = 13.2, 3.2 Hz, 1H), 2.87 (dddd, *J* = 14.0, 14.0, 6.5, 3.0 Hz, 2H), 2.81 – 2.70 (m, 2H), 2.53 (dd, *J* = 13.5, 10.5 Hz, 1H), 2.48 (dd, *J* = 10.6, 3.0 Hz, 1H), 2.44 – 2.38 (m, 1H), 2.39 (s, 2H), 2.27 (dd, *J* = 15.1, 9.3 Hz, 1H), 2.20 (d, *J* = 15.4 Hz, 1H), 2.09 (dd, *J* = 15.6, 9.6 Hz, 1H), 2.07 – 1.97 (m, 2H), 1.99 – 1.90 (m, 1H), 1.87 (d, *J* = 14.9 Hz, 1H), 1.67 – 1.58 (m, 1H), 1.58 – 1.47 (m, 3H), 1.30 (d, *J* = 15.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.06, 141.63, 139.13, 138.59, 130.11, 129.68, 129.13, 128.55, 127.95, 127.89, 127.44, 126.57, 65.55, 56.80, 53.28, 51.11, 44.57, 43.93, 38.16, 28.06, 27.43, 25.92, 25.10, 24.76, 24.63, 21.65; HRMS (ES) *m/z* 682.1603 [$(M+Na)^+$; calcd for $C_{33}H_{41}NO_3S_5Na$: 682.1588].



(*S*,*S*)-**10**

TBS-(*S*,*S*)-**10**: Following the Type II ARC general procedure, 2-methyl-1,3-dithiane **1d** (51 mg, 0.26 mmol, 1.5 equiv), linchpin (–)-**2** (50 mg, 0.17 mmol, 1.0 equiv) and aziridine (+)-**3a** (99 mg, 0.34 mmol, 2.0 equiv) afforded TBS-(*S*,*S*)-**10** (73 mg, 0.094 mmol, 55% yield) as a pale yellow oil.

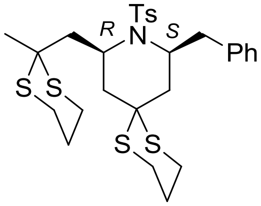
(*S*,*S*)-**10** : Following the general procedure for TBS group removal (Method A), TBS-(*S*,*S*)-**10** (73 mg, 0.094 mmol) afforded (*S*,*S*)-**10** (56 mg, 0.085 mmol, 90% yield) as a pale yellow oil: R_f 0.35 (hexane/EtOAc = 2:1); $[\alpha]^{26}_D$ +14.80 (c 1.00, $CHCl_3$); IR (film) 3282 (m, br), 3025 (w), 2910 (s), 1598 (w), 1422 (m), 1327 (m), 1158 (s), 1089 (s), 814 (w), 753 (m), 702 (s), 665 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 8.4, 1.0 Hz, 2H), 7.77 (d, *J* = 8.3 Hz, 2H), 7.40 (t, *J* = 8.3Hz, 2H), 7.30 – 7.24 (m, 3H), 7.22 (d, *J* = 7.43 Hz, 2H), 7.20 – 7.16 (m, 1H), 7.13 (d, *J* = 7.43 Hz, 2H), 5.29 (d, *J* = 5.4 Hz, 1H), 4.08 – 4.02 (m, 1H), 3.84 – 3.76 (m, 1H), 2.93 (dd, *J* = 13.5, 4.1 Hz, 1H), 2.80 (dd, *J* = 13.5, 7.8 Hz, 1H), 2.74 – 2.68 (m, 4H), 2.62 (d, *J* = 5.7 Hz , 2H), 2.48 (ddd, *J* = 14.5, 6.6, 4.1 Hz, 1H), 2.43 – 2.34 (m, 2H), 2.37 (s, 3H), 2.10 (dd, *J* = 15.4, 3.2 Hz, 1H), 2.08 – 2.03 (m, 1H), 1.99 – 1.91 (m, 3H), 1.80 – 1.76 (m, 1H), 1.78 – 1.69 (m, 2H), 1.42 – 1.39 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.41, 141.95, 137.51, 137.41, 130.08, 129.73, 128.97, 128.58, 128.41, 127.72, 127.49, 126.57, 65.56, 57.74, 52.90, 52.69, 51.04, 45.48, 42.90, 41.61, 27.91, 27.55, 26.36, 25.92, 24.84, 24.59, 21.64; HRMS (ES) *m/z* 694.1383 [$(M+Cl)^-$; calcd for $C_{33}H_{41}ClNO_3S_5$: 694.1379].



V

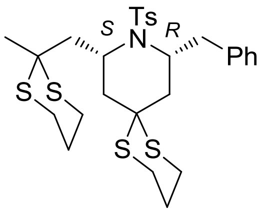
3. General procedure for intramolecular S_N2 cyclization.

V: To a solution of ***IV*** (0.10 mmol, 1.0 equiv) in THF (5.0 mL) were added triethylamine (0.30 mmol, 3.0 equiv) and methanesulfonyl chloride (0.15 mmol, 1.5 equiv) at 0 °C. After being stirred for 5 h, a saturated aqueous NH_4Cl solution (5.0 mL) was added, and the resulting mixture filtered through a short silica gel and rinsed with dry THF (5 x 20mL). The combined organic layers were diluted with THF (100 mL) affording a ~0.5mM solution of the mesylate. This solution was treated with NaH (0.50 mmol, 5.0 equiv) at room temperature, and stirred for 5-12 h. The reaction mixture was quenched with MeOH (5.0 mL) and concentrated in vacuo. Flash chromatography (EtOAc/hexane = 1/10) afforded the fully protected piperidine ***V***.



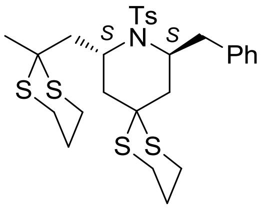
(*R*,*S*)-**11**

(*R*,*S*)-**11**: Following the general procedure for intramolecular S_N2 cyclization, (*S*,*S*)-**4** (1.4 g, 2.3 mmol) afforded (*R*,*S*)-**11** (1.2 mg, 2.1 mmol, 87 % yield) as a pale yellow oil: $[\alpha]^{28}_D$ +21.65 (c 1.00 , $CHCl_3$); IR (film) 2923 (s), 1599 (w), 1493 (w), 1449 (m), 1333 (m), 1159 (s), 1100 (m), 911 (w), 813 (w), 753 (m), 704 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.36 – 7.24 (m, 7H), 4.18 – 4.13 (m, 1H), 4.12 – 4.07 (m, 1H), 3.36 (dd, *J* = 13.2, 3.3 Hz, 1H), 3.22 (dd, *J* = 13.2, 10.2 Hz, 1H), 3.02 (ddd, *J* = 13.8, 10.8, 2.6 Hz, 1H), 2.90 (ddd, *J* = 13.8, 10.8, 2.7 Hz, 1H), 2.84 – 2.67 (m, 5H), 2.61 – 2.52 (m, 2H), 2.41 (s, 3H), 2.23 (dd, *J* = 14.5, 1.6 Hz, 1H), 2.12 (dd, *J* = 15.2, 2.8 Hz, 1H), 2.08 (t, *J* = 7.0 Hz, 2H), 2.06 – 2.01 (m, 1H), 1.92 – 1.78 (m, 2H), 1.71 (dd, *J* = 15.2, 6.3 Hz, 1H), 1.65 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.64, 138.34, 136.81, 129.90, 129.84, 128.68, 127.89, 126.79, 54.47, 50.80, 48.49, 48.31, 44.40, 44.37, 41.38, 37.13, 29.83, 28.52, 27.31, 27.19, 27.05, 26.85, 24.92, 24.74, 21.69; HRMS (ES) *m/z* 580.1509 $[(M+H)^+]$; calcd for $C_{28}H_{38}NO_2S_5$: 580.1506].



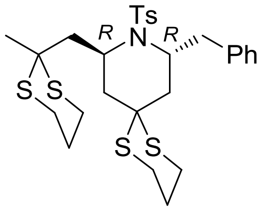
(*S*,*R*)-**11**

(*S*,*R*)-**11**: Following the general procedure for intramolecular S_N2 cyclization, (*R*,*R*)-**4** (1.5 g, 2.5 mmol) afforded (*S*,*R*)-**11** (1.4 g, 2.3 mmol, 85% yield) as a pale yellow oil: $[\alpha]^{26}_{D}$ –24.30 (c 1.00 , $CHCl_3$); IR, 1H and 13C NMR are identical to those of (*R*,*S*)-**11**; HRMS (ES) *m/z* 614.1139 $[(M+Cl)^{-}$; calcd for $C_{28}H_{37}ClNO_2S_5$: 614.1116].



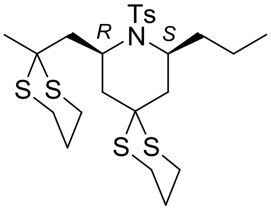
(*S*,*S*)-**11**

(*S*,*S*)-**11**: Following the general procedure for intramolecular S_N2 cyclization, (*R*,*S*)-**4** (0.64 g, 1.1 mmol) affored (*S*,*S*)-**11** (0.36 g, 0.62 mmol, 58% yield) as a pale yellow oil: $[\alpha]^{25}_{D}$ +24.64 (c 0.67 , $CHCl_3$; IR (film) 3026 (w), 2918 (s), 1597 (w), 1495 (w), 1432 (w), 1316 (m), 1150 (s), 1094 (m), 860 (s), 750 (m), 694 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.24 (m, 5H), 7.20 – 7.10 (m, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 4.60 (app brs, 1H), 4.26 – 4.16 (m, 1H), 3.48 (dd, *J* = 13.9, 9.3 Hz, 1H), 3.06 (dd, *J* = 14.0, 6.4 Hz, 1H), 2.92 – 2.83 (m, 2H), 2.83 – 2.75 (m, 1H), 2.70 – 2.63 (m, 1H), 2.60 (d, *J* = 5.4 Hz, 2H), 2.55 (d, *J* = 15.1 Hz, 1H), 2.53 - 2.45 (m, 3H), 2.40 - 2.34 (m, 1H), 2.33 (s, 3H), 2.30 (d, *J* = 4.8 Hz, 2H), 2.26 – 2.23 (m, 1H), 2.02 – 1.88 (m, 2H), 1.80 – 1.69 (m, 2H), 1.50 (s, 3H); 13C NMR (125 MHz, CDCl3) δ 142.67, 141.13, 139.67, 129.65, 129.47, 128.71, 127.11, 126.50, 58.57, 51.60, 49.04, 48.92, 43.72, 43.29, 40.47, 39.90, 27.88, 26.85, 26.47, 26.42, 26.32, 25.24, 24.71, 21.47; HRMS (ES) *m/z* 580.1155 $[(M+H)^{+}$; calcd for $C_{28}H_{38}NO_2S_5$: 580.1506].



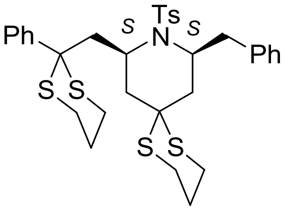
(*R*,*R*)-**11**

(*R*,*R*)-**11**: Following the general procedure for intramolecular S_N2 cyclization, (*S*,*R*)-**4** (0.30g, 0.502 mmol) affored (*R*,*R*)-**11** (0.16 g, 0.276 mmol, 55% yield) as a pale yellow oil: $[\alpha]^{27}_{D}$ –27.54 (c 0.75 , $CHCl_3$); IR, ^1H and ^{13}C NMR are identical to those of (*S*,*S*)-**11**; HRMS (ES) *m/z* 610.1074 [$(M+Cl)^-$; calcd for $C_{28}H_{37}ClNO_2S_5$: 614.1116].



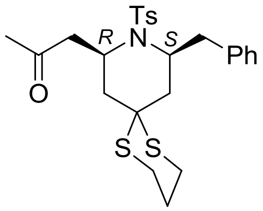
(*R*,*S*)-**12**

(*R*,*S*)-**12**: Following the general procedure for intramolecular S_N2 cyclization, (*S*,*S*)-**5** (80 mg, 0.15 mmol) affored (*R*,*S*)-**12** (69 mg, 0.13 mmol, 89% yield) as a pale yellow oil: $[\alpha]^{31}_{D}$ –31.40 (c 0.51, $CHCl_3$); IR (film) 2956 (s), 2927 (s), 2869 (s), 1597 (w), 1438 (m), 1326 (s), 1161 (s), 1094 (s), 909 (m), 813 (m), 735 (m), 662 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 4.16 (ddd, *J* = 8.7, 6.4, 3.3 Hz, 1H), 3.89 (dq, *J* = 8.2, 6.0 Hz, 1H), 3.07 (ddd, *J* = 14.0, 10.5, 3.0 Hz, 1H), 2.95 (*J* = 14.0, 10.5, 3.0 Hz, 1H), 2.88 – 2.80 (m, 2H), 2.79 – 2.74 (m, 2H), 2.74 – 2.68 (m, 3H), 2.52 (dd, *J* = 14.5, 2.0 Hz, 1H), 2.40 (s, 3H), 2.17 (dd, *J* = 15.1, 4.6 Hz, 1H), 2.08 – 1.96 (m, 5H), 1.93 – 1.85 (m, 3H), 1.80 – 1.71 (m, 1H), 1.69 (s, 3H), 1.46 – 1.36 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.42, 137.24, 129.75, 127.79, 52.85, 50.80, 48.64, 48.38, 44.59, 40.50, 40.45, 38.82, 28.89, 27.24, 27.09, 27.09, 26.92, 24.99, 24.82, 21.68, 19.99, 14.06; HRMS (ES) *m/z* 554.1320 [$(M+Na)^+$; calcd for $C_{24}H_{37}NO_2S_5Na$: 554.1326].



(*S*,*S*)-**13**

(*S*,*S*)-**13**: Following the general procedure for intramolecular S_N2 cyclization, (*R*,*S*)-**10** (0.65 mg, 0.099 mmol) affored (*S*,*S*)-**13** (0.51 mg, 0.080 mmol, 81% yield) as a pale yellow oil: $[\alpha]^{31}_{D}$ –16.86 (c 2.00 , $CHCl_3$); IR (film) 3025 (w), 2908 (s), 1598 (w), 1491 (w), 1442 (m), 1336 (s), 1160 (s), 1100 (s), 908 (m), 814 (m), 753 (s), 702 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.5 Hz, 2H), 7.56 (d, *J* = 8.3 Hz, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.29 (d, *J* = 7.3 Hz, 2H), 7.25 (d, *J* = 6.9 Hz, 1H), 7.23 - 7.17 (m, 3H), 4.14 – 4.05 (m, 1H), 3.96 (dt, *J* = 9.5, 4.8 Hz, 1H), 3.18 (dd, *J* = 13.1, 3.5 Hz, 1H), 3.08 (dd, *J* = 13.1, 10.8 Hz, 1H), 2.84 - 2.77 (m, 2H), 2.77 - 2.67 (m, 5H), 2.64 (ddd, *J* = 14.4, 7.5, 3.5 Hz, 1H), 2.56 (ddd, *J* = 14.2, 8.5, 3.1 Hz, 1H), 2.46 (ddd, *J* = 14.5, 7.5, 3.2 Hz, 1H), 2.37 (s, 3H), 2.03 – 1.92 (m, 1H), 1.90 (dd, *J* = 15.2, 5.7 Hz, 1H), 1.86 – 1.71 (m, 4H), 1.66 (dd, *J* = 15.3, 6.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.28, 141.17, 138.43, 137.04, 129.75, 129.57, 129.06, 128.97, 128.65, 127.73, 127.52, 126.68, 57.59, 54.40, 51.70, 49.68, 44.49, 44.36, 39.77, 36.98, 28.02, 27.75, 27.09, 27.06, 24.90, 24.64, 21.64; HRMS (ES) *m/z* 642.1678 [$(M+H)^+$; calcd for $C_{33}H_{40}NO_2S_5$: 642.1663].



(*R*,*S*)-**14**

(*R*,*S*)-**14**: To a stirred solution of (*R*,*S*)-**11** (130 mg, 0.22 mmol) in THF-H_2O (4:1, 13 mL) were added 2,6-lutidine (180 μL, 1.7 mmol) and $Hg(ClO_4)_2$ (240 mg, 0.60 mmol) at 0 °C. After 30 min, the reaction mixture was filtered through celite and rinsed with EtOAc (3 x 10 mL). The combined organic layers were poured into saturated aqueous NH_4Cl (20 mL) and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (5 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography on silica gel (hexanes/EtOAc, 100/1 to 2/1) provided (*R*,*S*)-**14** (72 mg, 0.15 mmol, 68% yield) as a pale yellow oil: R_f 0.35 (hexane/EtOAc = 4:1); $[\alpha]^{24}_D$ +32.27 (c 0.50, $CHCl_3$); IR (film) 3027 (w), 2922 (s), 1712 (s), 1598 (s), 1473 (w), 1421 (m), 1326 (s), 1160 (s), 1098 (s), 1034 (w), 754 (m), 703 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.3 Hz, 2H), 7.27 – 7.23 (m, 4H), 7.19 (d, *J* = 7.4 Hz, 2H), 7.17 – 7.14 (m, 1H), 4.34 (ddt, *J* = 13.7, 6.9, 3.8 Hz, 1H), 4.13 (ddt, *J* = 10.5, 6.9, 3.4 Hz, 1H), 3.46 (dd, *J* = 17.9, 10.7 Hz, 1H), 3.29 (dd, *J* = 13.0, 11.4 Hz, 1H), 3.14 (dd, *J* = 13.0, 3.5 Hz, 1H), 2.96 (dd, *J* = 17.9, 3.0 Hz, 1H), 2.81 – 2.73 (m, 2H), 2.62 (ddd, *J* = 14.4, 6.6, 3.1 Hz, 1H), 2.51 (ddd, *J* = 14.5, 6.7, 3.0 Hz, 1H), 2.38 (dd, *J* = 15.0, 3.7 Hz, 1H), 2.32 (s, 3H), 2.09 (s, 3H), 1.98 (dd, *J* = 14.9, 2.8 Hz, 1H), 1.86 (dd, *J* = 14.9, 6.1 Hz, 2H), 1.79 – 1.68 (m, 1H), 1.49 (dd, *J* = 15.0, 6.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.88, 143.60, 138.59, 137.22, 129.88, 129.82, 128.74, 127.22, 126.77, 54.58, 50.30, 48.14, 44.84, 44.29, 37.83, 36.82, 30.68, 26.94, 26.90, 24.72, 21.63; HRMS (ES) *m/z* 512.1351 [$(M+Na)^+$; calcd for $C_{25}H_{31}NO_3S_3Na$: 512.1364].

4. Reduction Conditions of (*R*,*S*)-14

A: To a stirred solution of (*R*,*S*)-**14** (8.0 mg, 0.016 mmol) in MeOH (1.0 mL) was added $NaBH_4$ (1.0 mg, 0.026 mmol) at 0 °C. After being stirred for 30 min, the reaction mixture was concentrated in vacuo to provide (*S*,*R*,*S*)-**15** and (*R*,*R*,*S*)-**15** as a

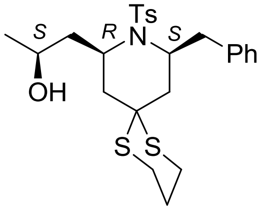
1:2 mixture as determined by crude ^{1}H NMR spectroscopy which were separated by preparatory thin-layer chromatography (hexane/EtOAc = 2/1) affording (*S*,*R*,*S*)-**15** (2.5 mg, 31%) and (*R*,*R*,*S*)-**15** (5.0 mg, 62%) as pale yellow oils.

B: To a stirred solution of (*R*,*S*)-**14** (45 mg, 0.92 mmol) in THF (5.0 mL) was added L-selectride 1.0M in THF (1.3 mL, 1.3 mmol) at – 78 °C. After being stirred for 3 h, the reaction mixture was quenched with MeOH (1.0 mL) and 2N NaOH (5.0 mL). After being stirred at room temperature for 1 h, the reaction mixture was extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with brine and dried over $MgSO_4$, filtered, and concentrated in vacuo to provide (*S*,*R*,*S*)-**15** and (*R*,*R*,*S*)-**15** as a 1:3 mixture as determined by crude ^{1}H NMR spectroscopy which were separated by flash chromatography (hexanes/EtOAc = 2/1) affording (*S*,*R*,*S*)-**15** (13 mg, 28%) and (*R*,*R*,*S*)-**15** (31 mg, 69%) as pale yellow oils.

C: To a stirred solution of (*R*,*S*)-**14** (27 mg, 0.055 mmol) in THF (3.0mL) were added (*S*)-CBS reagent 1.0 M in THF (55 μL, 55 μmol) and BH_3·THF 1.0M in THF (55 μL, 0.055 mmol) at 0 °C. After being stirred for 1 h, the reaction mixture was quenched with MeOH (1.0 mL) and concentrated in vacuo to provide (*S*,*R*,*S*)-**15** and (*R*,*R*,*S*)-**15** as a 1:4 mixture as determined by crude ^{1}H NMR spectroscopy which were separated by flash chromatography (hexane/EtOAc = 2/1) affording (*S*,*R*,*S*)-**15** (4.8 mg, 18%) and (*R*,*R*,*S*)-**15** (20 mg, 74%) as pale yellow oils.

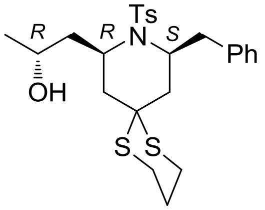
D: To a stirred solution of (*R*,*S*)-**14** (6.0 mg, 0.012 mmol) in THF (3.0 mL) were added (*R*)-CBS reagent 1.0 M in THF (1.2 μL, 1.2 μmol) and BH_3·THF 1.0 M in THF (12 μL, 0.012 mmol) at 0 °C. After being stirred for 1h, the reaction mixture was quenched with MeOH (1.0 mL) and concentrated in vacuo to provide (*S*,*R*,*S*)-**15** and (*R*,*R*,*S*)-**15** as a 20:1 mixture as determined by crude ^{1}H NMR spectroscopy, which was purified by flash chromatography (hexane/EtOAc = 2/1) affording (*S*,*R*,*S*)-**15** (5.8 mg, 0.11 mmol, 93%) as pale yellow oils.

E: To a stirred solution of (*R*,*S*)-**14** (6.0 mg, 0. 012 mmol) in ^{i}PrOH (3.0mL) was treated with $Al(O^iPr)_3$ (25 mg, 0.12 mmol). After heating at reflux for 5 h, the reaction mixture was cooled to room temperature and diluted with Et_2O (10 mL) and treated with 1N HCl. The mixture was extracted with Et_2O (3 x 10 ml) and the combined organic layers were washed with saturated aq. $NaHCO_3$ and brine, and dried over $MgSO_4$. The reaction mixture was filtered through a plug of silica gel and concentrated in vacuo to provide a 1:5 mixture of (*S*,*R*,*S*)-**15** and (*R*,*R*,*S*)-**15** (5.3 mg, 0.011 mmol, 88%) as determined by ^{1}H NMR spectroscopy, as a pale yellow oil.



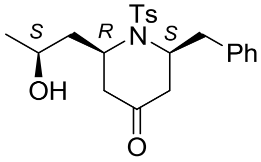
(*S*,*R*,*S*)-**15**

(*S*,*R*,*S*)-**15**: R$_f$ 0.40 (hexane/EtOAc = 2:1); $[\alpha]^{29}_{D}$ +101.0 (c 0.67, $CHCl_3$); IR (film) 3522 (m, br), 3026 (w), 2922 (s), 1596 (w), 1420 (m), 1327 (s), 1157 (s), 1115 (s), 1043 (s), 932 (m), 813 (m), 756 (m), 702 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.36 – 7.32 (m, 4H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.27 – 7.24 (m, 1H), 4.28 - 4.24 (m, 1H), 4.16 – 4.08 (m, 2H), 3.36 (dd, *J* = 13.0, 10.8 Hz, 1H), 3.30 (dd, *J* = 13.0, 3.7 Hz, 1H), 2.82 – 2.72 (m, 2H), 2.66 – 2.57 (m, 2H), 2.41 (s, 3H), 2.32 (t, *J* = 13.4 Hz, 1H), 2.16 (dd, *J* = 14.9, 5.6 Hz, 1H), 2.04 (d, *J* = 15.1 Hz, 1H), 1.93 – 1.78 (m, 2H), 1.72 (dd, *J* = 14.9, 6.3 Hz, 1H), 1.57 (dd, *J* = 15.0, 7.2 Hz, 1H), 1.45 (ddd, *J* = 14.2, 10.6, 3.4 Hz, 1H), 1.22 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.96, 138.58, 136.84, 130.08, 129.76, 128.78, 127.27, 126.84, 63.43, 54.81, 49.81, 46.79, 44.58, 43.95, 40.37, 35.77, 27.09, 27.03, 24.74, 22.99, 21.72; HRMS (ES) *m/z* 492.1688 [(M+H)$^+$; calcd for $C_{25}H_{33}NO_3S_3$: 492.1701].



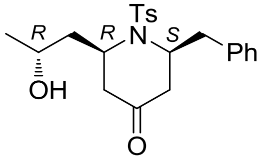
(*R*,*R*,*S*)-**15**

(*R*,*R*,*S*)-**15**: R$_f$ 0.30 (hexane/EtOAc = 2:1); $[\alpha]^{22}_{D}$ +105.6 (c 0.50, $CHCl_3$); IR (film) 3410 (m, br), 3026 (w), 2925 (s), 1599 (w), 1451 (m), 1326 (s), 1159 (s), 1096 (s), 938 (m), 753 (m), 756 (m), 702 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.36 – 7.30 (m, 4H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.26 – 7.22 (m, 1H), 4.25 – 4.14 (m, 2H), 3.98 – 3.90 (m, 1H), 3.34 (dd, J = 13.29, 15.5 Hz, 1H), 3.32 (s, 1H), 2.78 (dd, J = 6.21, 4.99 Hz, 2H), 2.69 – 2.57 (m, 2H), 2.41 (s, 3H), 2.17 (ddd, *J* = 14.9, 10.6, 4.1 Hz, 2H), 2.12 – 1.99 (m, 2H), 1.91 – 1.83 (m, 2H), 1.80 (dd, *J* = 15.0, 6.4 Hz, 2H), 1.74 (dd, *J* = 15.0, 6.7 Hz, 2H), 1.26 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.63, 138.82, 137.20, 129.88, 129.77, 128.73, 127.49, 126.71, 66.42, 54.69, 50.32, 47.17, 44.67, 44.11, 39.08, 36.45, 27.16, 27.05, 24.79, 24.33, 21.69; HRMS (ES) *m/z* 492.1700 [(M+H)$^+$; calcd for $C_{25}H_{34}NO_3S_3$: 492.1701].



(*S*,*R*,*S*)-**16**

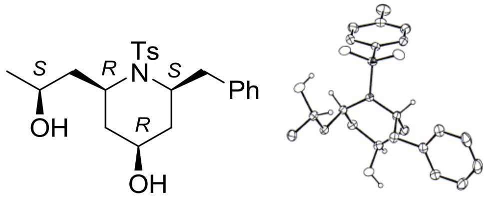
(*S*,*R*,*S*)-**16**: To a stirred solution of (*S*,*R*,*S*)-**15** (43.0 mg, 0.087 mmol) in CH_3CN-H_2O (9:1, 5.0 mL) was added $PhI(O_2CCF_3)_2$ (75 mg, 0.18 mmol) at 0 °C. After 5 min, the reaction mixture was quenched with saturated aq. NH_4Cl (5.0 mL) and extracted with EtOAc (3 x 10 mL) and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. Flash chromatography (hexane/EtOAc = 3:1) afforded (*S*,*R*,*S*)-**16** (30 mg, 0.075 mmol, 86%) as a white solid: R_f 0.45 (hexane/EtOAc = 1:1); $[\alpha]^{20}_D$ +142.0 (c 0.51, $CHCl_3$); IR (film) 3536 (m, br), 3028 (w), 2967 (m), 1719 (s), 1598 (w), 1495 (m), 1453 (m), 1329 (s), 1159 (s), 1105 (s), 927 (m), 855 (m), 700 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 6.0 Hz, 2H), 7.33 (d, *J* = 5.9 Hz, 2H), 7.28 – 7.24 (m, 3H), 4.75 - 4.68 (m, 1H), 4.61 – 4.55 (m, 1H), 4.11 (dt, *J* = 12.3, 5.3 Hz, 1H), 3.44 (d, *J* = 4.2 Hz, 1H), 3.18 (dd, *J* = 12.8, 3.0 Hz, 1H), 2.78 (dd, *J* = 12.8, 11.4 Hz, 1H), 2.44 (s, 3H), 2.23 (ddd, *J* = 14.4, 3.4, 1.6 Hz, 1H), 2.18 (dd, *J* = 14.5, 7.9 Hz, 1H), 2.09 (d, *J* = 14.5 Hz, 1H), 2.05 (dd, *J* = 14.4, 7.6 Hz, 1H), 1.77 (ddd, *J* = 14.3, 12.5, 1.7 Hz, 1H), 1.48 (ddd, *J* = 14.4, 10.5, 3.9 Hz, 1H), 1.21 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.38, 144.52, 137.38, 137.03, 130.51, 129.72, 129.01, 127.25, 126.82, 63.73, 58.12, 53.11, 46.18, 44.35, 44.31, 41.22, 22.73, 21.73; HRMS (ES) *m/z* 402.1721 [$(M+H)^+$; calcd for $C_{22}H_{28}NO_4S$: 402.1739].



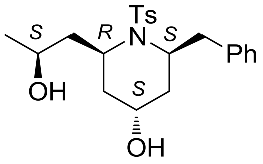
(*R*,*R*,*S*)-**16**

(*R*,*R*,*S*)-**16**: To a stirred solution of (*R*,*R*,*S*)-**15** (30 mg, 0.061 mmol) in CH_3CN-H_2O (9:1, 5.0 mL) was added $PhI(O_2CCF_3)_2$ (53 mg, 0.12 mmol) at 0 °C. After 5 min, the reaction mixture was quenched with saturated aq. NH_4Cl (5.0 mL) and extracted with EtOAc (3 x 10 mL) and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. Flash chromatography (hexane/EtOAc = 3:1) afforded (*R*,*R*,*S*)-**16** (22 mg, 0.054 mmol, 88%) as a white solid: R_f 0.40 (hexane/EtOAc = 1:1); $[\alpha]^{20}_D$ +142.0 (c 0.51, $CHCl_3$); IR (film) 3504 (m, br), 3028 (w), 2967 (m), 1717 (s), 1598 (w), 1494 (m), 1453 (m), 1329 (s), 1160 (s), 1097 (s), 935 (m), 816 (m), 702 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.34 - 7.28 (m, 6H), 7.25 - 7.21 (m, 1H), 4.77 – 4.71 (m, 1H), 4.61 (ddd, *J* = 10.6, 7.1, 3.4 Hz, 1H), 3.88 – 3.81 (m, 1H), 3.19 (dd, *J* = 13.0, 3.2 Hz, 1H), 2.80 (dd, *J* = 12.8, 11.5 Hz, 1H), 2.42 (s, 4H), 2.33 (dd, *J* = 14.6, 7.1 Hz, 1H), 2.30 – 2.24 (m, 2H), 2.18 (dd, *J* = 14.5, 7.3 Hz, 1H), 1.88 (ddd, *J* = 14.1, 9.1, 5.1 Hz, 1H), 1.78 – 1.69 (m, 2H), 1.26 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.06, 144.10, 137.69, 137.41, 130.23, 129.67, 128.91, 127.12, 127.07, 65.50, 57.71, 52.75, 46.52, 44.14, 43.54, 41.76, 24.27, 21.68; HRMS (ES) m/z 402.1733 [$(M+H)^+$; calcd for $C_{22}H_{28}NO_4S$: 402.1739].

4. Reduction Conditions of (*S*,*R*,*S*)-16



(*S*,*R*,*S*,*R*)-**17**



(*S*,*R*,*S*,*S*)-**17**

A: To a stirred solution of (*S*,*R*,*S*)-**16** (6.0 mg, 0.015 mmol) in MeOH (1.0 mL) was treated with $NaBH_4$ (1.0 mg, 0.026 mmol) at 0 °C. After being stirred for 30 min, the reaction mixture was concentrated in vacuo and filtered through a plug of silica affording a 1:5 mixture (*S*,*R*,*S*,*R*)-**17** and (*S*,*R*,*S*,*S*)-**17** (5.6 mg, 0.014 mmol, 93%) as a white solid as determined by crude ^{1}H NMR spectroscopy.

B: To a stirred solution of (*S*,*R*,*S*)-**16** (30 mg, 0.075 mmol) in THF (5.0 mL) was treated with 1.0 M sol of L-Selectride in THF (0.19 mL, 0.19 mmol) at –78 °C. After being stirred for 3 h, the reaction mixture was quenched with MeOH (1.0 mL) and 2N NaOH (5.0 mL) and stirred at room temperature for 1 h. The reaction mixture was extracted with Et_2O (3 x 10 m) and combined organic layers were washed with brine and dried over $MaSO_4$, filtered, and concentrated in vacuo. The residue was filtered through a plug of silica gel affording a 20:1 mixture of (*S*,*R*,*S*,*R*)-**17** and (*S*,*R*,*S*,*S*)-**17** (29 mg, 0.072 mmol, 97%) as a white solid, which was dissolved in CH_2Cl_2 (2.0 mL) and put in a – 20 °C refrigerator affording crystals of (*S*,*R*,*S*,*R*)-**17**.

F: To a stirred solution of (*S*,*R*,*S*)-**16** (6.0 mg, 0.015 mmol) in THF (3.0 mL) was treated with $BH_3{\cdot}THF$ 1.0M in THF (15 μL, 0.015 mmol) at 0 °C and stirred for 1h. The reaction mixture was quenched with MeOH (1.0 mL) and concentrated in vacuo.

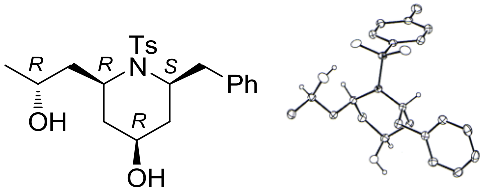
The residue was filtered through short a plug of silica gel affording a 2:1 mixture (5.6 mg, 0.014mmol, 93%) of (*S*,*R*,*S*,*R*)-**17** and (*S*,*R*,*S*,*S*)-**17** as a white solid as determined by crude ^{1}H NMR spectroscopy.

G: To a stirred solution of (*S*,*R*,*S*)-**16** (15 mg, 0.037 mmol) in THF (5.0mL) was added H_2O (40 μL, 0.22 mmol). The solution was cooled to −78 °C and treated with a freshly prepared 0.10 M solution of SmI_2 in THF (1.5 mL, 0.15 mmol). The reaction mixture was slowly warmed to room temperature over 5 h. The reaction mixture was quenched with saturated aq. NH_4Cl (5.0 mL) and extracted with EtOAc (3x10 mL). The combined organic layers were washed with brine and dried over Na_2SO_4, then filtered and concentrated in vacuo to provide as a 2:1 mixture as determined by crude ^{1}H NMR of (*S*,*R*,*S*,*R*)-**17** and (*S*,*R*,*S*,*S*)-**17** which was purified by flash chromatography (hexane/EtOAc, 3:1 to 1:1) affording (*S*,*R*,*S*,*R*)-**17** (8.1 mg, 0.020 mmol, 53%) and (*S*,*R*,*S*,*S*)-**17** (5.3 mg, 0.013 mmol, 35%) as white solids.

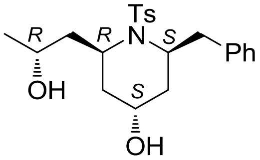
(*S*,*R*,*S*,*R*)-**17**: R_f 0.25 (hexane/EtOAc = 1:1); $[\alpha]^{24}_D$ +62.0 (c 1.00, $CHCl_3$); IR (film) 3430 (s, br), 2922 (s), 1601 (w), 1417 (w), 1316 (m), 1152 (s), 916 (m), 741 (w), 701 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.34 – 7.29 (m, 4H), 7.27 (d, *J* = 8.1 Hz, 2H), 7.25 – 7.20 (m, 1H), 4.34 (ddd, *J* = 10.8, 7.3, 3.2 Hz, 1H), 4.22 – 4.14 (m, 1H), 4.09 (ddd, *J* = 14.9, 7.1, 3.5 Hz, 1H), 3.76 – 3.70 (m, 1H), 3.61 (brs, 1H), 3.31 (t, *J* = 12.0 Hz, 1H), 3.21 (dd, *J* = 12.4, 3.7 Hz, 1H), 2.43 – 2.35 (m, 1H), 2.41 (s, 3H), 1.64 – 1.53 (m, 5H), 1.26 (d, *J* = 6.3 Hz, 3H), 1.15 (ddd, *J* = 14.2, 7.2, 3.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.56, 139.30, 137.91, 130.06, 129.78, 128.71, 126.74, 126.65, 64.55, 63.69, 54.19, 48.61, 47.66, 44.63, 35.15, 30.70, 23.04, 21.66; HRMS (ES) *m/z* 404.1962 [(M+H)$^+$; calcd for $C_{22}H_{29}NO_4S$: 403.1817].

(*S*,*R*,*S*,*S*)-**17**: R_f 0.20 (hexane/EtOAc = 1:1); $[\alpha]^{21}_D$ +98.14 (c 0.30, $CHCl_3$); IR (film) 3409 (s, br), 3027 (w), 2928 (s), 1598 (w), 1494 (w), 1454 (w), 1402 (w), 1324 (m), 1159 (s), 927 (m), 753 (m), 673 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.36 - 7.33 (m, 2H), 7.29 (dd, *J* = 7.9, 5.1 Hz, 2H), 7.27 – 7.24 (m, 3H), 4.50 – 4.43 (m, 1H), 4.33 – 4.27 (m, 1H), 4.18 – 4.10 (m, 2H), 3.74 (d, *J* = 4.0 Hz, 1H), 3.11 (dd, *J* = 12.8, 3.2 Hz, 1H), 2.81 (app t, *J* = 12.3 Hz, 1H), 2.41 (s, 3H), 1.96 (ddd, *J* = 14.2, 12.3, 1.6 Hz, 1H), 1.81 – 1.72 (m, 2H), 1.48 (ddd, *J* = 14.2, 10.5, 3.6 Hz, 1H), 1.31 (brs, 1H), 1.26 (d, *J* = 6.4 Hz, 3H), 1.12 (ddd, *J* = 12.2, 12.2, 6.4 Hz, 1H), 0.75 (ddd, *J* = 12.1, 12.1, 6.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.80, 138.70, 137.79, 130.19, 129.39, 128.94, 127.03, 126.66, 63.60, 61.20, 56.25, 51.10, 45.66, 43.32, 38.37, 33.85, 22.82, 21.68; HRMS (ES) *m/z* 404.1913 [(M+H)$^+$; calcd for $C_{22}H_{29}NO_4S$: 403.1817].

5. Reduction Conditions of (*R*,*R*,*S*)-16



(*R*,*R*,*S*,*R*)-**17**



(*R*,*R*,*S*,*S*)-**17**

B: Following the same reduction conditions **B** of (*S*,*R*,*S*)-**16,** (*R*,*R*,*S*)-**16** (28 mg, 0.070 mmol) afforded 20:1 mixture as determined by crude ^{1}H NMR spectroscopy of (*S*,*R*,*S*,*R*)-**17** and (*S*,*R*,*S*,*S*)-**17** (27 mg, 0.065 mmol, 93%) as white solids, which was dissolved in CH_2Cl_2 (2.0 mL) and put in a –20 °C refrigerator overnight affording crystals of (*S*,*R*,*S*,*R*)-**17**.

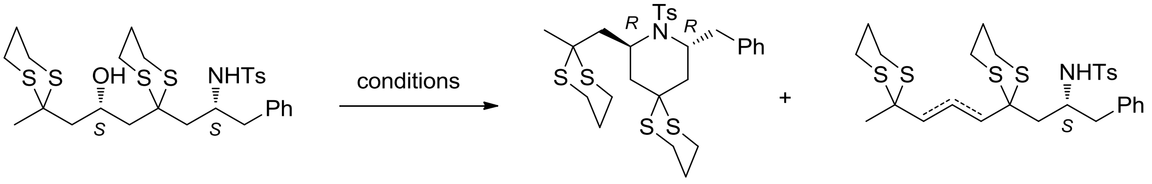
G: Following the same reduction conditions **G** of (*S*,*R*,*S*)-**16,** (*R*,*R*,*S*)-**16** (18 mg, 0.045 mmol) afforded a 1:1.3 mixture of (*R*,*R*,*S*,*R*)-**17** and (*R*,*R*,*S*,*S*)-**17** as determined by crude ^{1}H NMR spectroscopy which were separated by flash chromatography (hexane/EtOAc, 3:1 to 1:1) affording (*R*,*R*,*S*,*R*)-**17** (7.1 mg, 0.018 mmol, 39%) and (*R*,*R*,*S*,*S*)-**17** (9.2 mg, 0.023 mmol, 51%) as white solids.

(*R*,*R*,*S*,*R*)-**17**: R_f 0.40 (hexane/EtOAc = 1:2); $[\alpha]^{29}_D$ +40.3 (c 0.50, $CHCl_3$); IR (film) 3420 (s, br), 2924 (s), 1598 (w), 1495 (w), 1454 (w), 1323 (m), 1159 (s), 934 (m), 814 (w), 751 (m), 668 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.2 Hz, 2H), 7.33 – 7.27 (m, 4H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.24 – 7.19 (m, 1H), 4.29 (td, *J* = 8.5, 2.6 Hz, 1H), 4.15 (ddd, *J* = 15.6, 7.7, 4.0 Hz, 1H), 4.00 – 3.92 (m, 1H), 3.73 (qui, *J* = 4.5 Hz, 1H), 3.34 (dd, *J* = 15.7, 8.4 Hz, 1H), 3.22 (dd, *J* = 12.6, 3.8 Hz, 1H), 2.39 (s, 3H), 2.22 (ddd, *J* = 13.0, 9.0, 3.8 Hz, 1H), 2.09 (ddd, *J* = 14.2, 8.5, 6.0 Hz, 1H), 1.89 (brs, 1H), 1.73 (m, 1H), 1.63 (m, 2H), 1.36 – 1.33 (ddd, *J* = 14.3, 7.5, 3.8 Hz, 1H), 1.29 (d, *J* = 6.2 Hz, 3H), 1.28 - 1.24 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.28, 139.45, 138.07, 129.88, 129.76, 128.62, 126.90, 126.51, 66.25, 64.71, 53.94, 48.85, 47.58, 44.85, 33.99, 31.57, 24.01, 21.63; HRMS (ES) *m/z* 426.1718 [(M+H)$^+$; calcd for $C_{22}H_{29}NO_4SNa$: 426.1715].

(*R*,*R*,*S*,*S*)-**17**: R_f 0.35 (hexane/EtOAc = 1:2); $[\alpha]^{26}_D$ +32.58 (c 1.00, $CHCl_3$); IR (film) 3385 (s, br), 2924 (s), 1599 (w), 1457 (w), 1323 (m), 1160 (s), 929 (m), 755 (m), 671 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.1 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.28 – 7.22 (m, 5H), 4.43 (app q, *J* = 6.2 Hz, 1H), 4.37 – 4.31 (m, 1H), 4.20 – 4.13 (m, 1H), 3.96 – 3.88 (m, 1H), 3.17 (dd, *J* = 12.8, 2.2 Hz, 1H), 2.87 (t, *J* = 12.4 Hz, 1H), 2.40 (s, 3H), 1.97 (ddd, *J* = 14.3, 8.7, 5.7 Hz, 1H), 1.93 – 1.88

(m, 1H), 1.88 – 1.83 (m, 1H), 1.83 – 1.78 (m, 1H), 1.61 (brs, 1H), 1.36 (brs, 1H), 1.30 (d, J = 6.2 Hz,3H), 1.14 (td, J = 12.1, 6.1 Hz, 1H), 0.91 (td, J = 12.1, 6.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.46, 138.98, 138.19, 129.98, 129.39, 128.85, 126.86, 126.81, 66.29, 61.17, 56.03, 51.07, 46.13, 43.35, 37.19, 34.42, 24.34, 21.65; HRMS (ES) *m/z* 426.1707 $[(M+H)^+$; calcd for $C_{22}H_{29}NO_4NaS$: 426.1715].

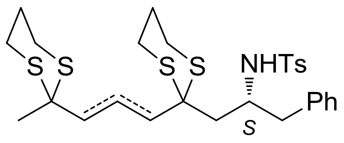
6. Screening Conditions for Intramolecular S_N2 Cyclization.



(*S*,*R*)-**4** (*R*,*R*)-**11** **20**

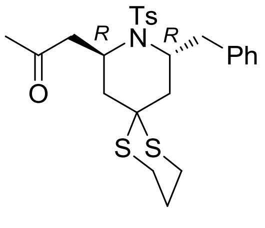
entry	conditions	Ratio of (*S*,*S*)-**11** : **20**	Yield (%)
1	MsCl, TEA, THF, 0 °C; K_2CO_3, MeOH, rt, 12h	**20** only	77
2	MsCl, TEA, THF, 0 °C; tBuOK, DMF, 0 °C-rt, 5h	1:10	77
3	MsCl, TEA, THF, 0 °C; tBuOK, THF, rt, 5h	1:10	74
4	MsCl, TEA, THF, 0 °C; tBuOK, Toluene, 0 °C-rt, 5h	1:7.4	84
5	MsCl, TEA, THF, 0 °C; NaH, THF/HMPA (1:4), rt, 5h	1:5.6	66
6	MsCl, TEA, THF, 0 °C; DBU, DMF, rt, 12h	1:10	84
7	MsCl, TEA, THF, 0 °C; DBU, THF, 12h	1:10	85
8	MsCl, TEA, THF, 0 °C; DBU, $CHCl_3$, 12h	1:10	85

9	MsCl, TEA, THF, 0 °C; DBU, Toluene, 12h	1:7	81
10	MsCl, TEA, THF, 0 °C; NaH, THF, rt, 5h	2:1	82
11	MsCl, TEA, THF, 0 °C; NaH, Toluene, 12h	1:3.5	79
12	Tf_2O, pyr, DCM, 0 °C NaHMDS, THF, 0 °C- rt, 5h	(*R*,*S*)-**4** recovered	>90
13	Tf_2O, pyr, DCM, 0 °C NaH, THF, 0 °C- rt, 5h	(*R*,*S*)-**4** recovered	>90
14	Tf_2O, pyr, DCM, 0 °C DBU, $CHCl_3$, 0 °C- rt, 5h	(*R*,*S*)-**4** recovered	>90
15	DIAD, PPh_3, THF	1:10	77



20

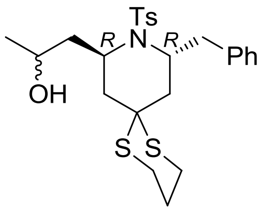
20: HRMS (ES) *m/z* 580.1497 [$(M+H)^+$; calcd for $C_{28}H_{38}NO_2S_5$: 580.1506].



(*R*,*R*)-**14**

(*R*,*R*)-**14**: To a stirred solution of (*R*,*R*)-**11** (60 mg, 0.10 mmol) in THF/H_2O (4:1, 13 mL) were added 2,6-lutidine (66 μL, 0.62 mmol) and $Hg(ClO_4)_2$ (83 mg, 0.21 mmol) at 0 °C. After 30 min, the reaction mixture was filtered through celite and rinsed with EtOAc (3 x 10 mL). The combined organics were poured into saturated aquous NH_4Cl (20 mL) and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (5.0 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography on silica gel (hexanes/EtOAc, 100/1 to 2/1) provided (*R*,*R*)-**14** (31 mg, 0.063 mmol, 61% yield) as a pale yellow oil: R_f 0.37 (hexane/EtOAc = 4:1); $[\alpha]^{21}_{D}$ +4.93 (c 0.86, $CHCl_3$); IR (film) 3027 (w), 2923 (s), 1718 (s), 1305 (s), 1151 (s), 1095 (m), 815 (w), 750 (m), 659 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.3 Hz, 2H), 7.29 – 7.20 (m, 3H), 7.18 – 7.15 (m, 3H), 7.13 (d, *J* = 8.0 Hz, 3H), 4.54 – 4.48 (m, 1H), 4.43 – 4.37 (m, 1H), 3.34 (dd, *J* = 13.7, 7.4 Hz, 1H), 3.16 (dd, *J* = 13.8, 8.3 Hz, 1H), 3.10 (dd, *J* = 18.2, 6.0 Hz, 1H), 3.05 (dd, *J* = 18.5, 8.7 Hz, 1H), 2.99 – 2.87 (m, 1H), 2.74 (ddd, *J* = 14.6, 6.5, 3.1 Hz, 1H), 2.64 ((ddd, *J* = 14.4, 6.9, 3.0 Hz, 1H), 2.38 (s, 3H), 2.35 (dd, *J* = 14.0, 2.7 Hz, 1H), 2.25 (dd, *J* = 14.1, 9.2 Hz, 1H), 2.16 (d, *J* = 4.5 Hz, 3H), 2.05 (s, 1H), 2.02 – 1.95 (m, 1H), 1.93 – 1.85 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.56, 143.21, 139.65, 139.07, 129.65, 129.58, 128.70, 127.25, 126.56, 57.32, 48.73, 48.14, 46.47, 40.80, 39.77, 39.02, 30.46, 26.59, 26.47, 25.15, 21.59; HRMS (ES) m/z 512.1345 $[(M+Na)^+$; calcd for $C_{25}H_{31}NO_3S_3Na$: 512.1364].

7. Screening Conditions for the Reduction of (*R*,*R*)-**14**.

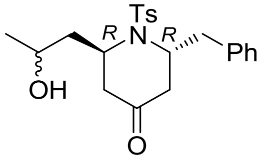


(*S*,*R*,*R*)-**15**/(*R*,*R*,*R*)-**15**

entry	conditions	Ratio of (*S*,*R*,*R*)-**15**:(*R*,*R*,*R*)-**15**	Yield (%)
1	$NaBH_4$, MeOH	2:1	77
2	L-Selectride, THF, -78 °C to rt.	3:1	77
3	$Al(OiPr)_3$, iPrOH, reflux	1.8:1	96
4	$LiHAl(OCEt_3)_3$, THF, -78 °C to rt.	4.5:1	84
5	(*S*)-CBS, BH_3·THF, THF, 0 °C	1:3	66
6	(*R*)-CBS, BH_3·THF, THF, 0 °C	5:1	93

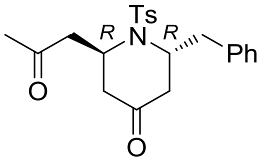
Entry 1: To a stirred solution of (*R*,*R*)-**14** (20 mg, 0.041 mmol) in MeOH (1.0 mL) was treated with $NaBH_4$ (2.3 mg, 0.061 mmol) at 0 °C. After being stirred for 30 min, the reaction mixture was concentrated in vacuo and filtered through a plug of silica gel affording a 1:2 mixture of (*S*,*R*,*R*)-**15** and (*R*,*R*,*R*)-**15** (18 mg, 0.037 mmol, 90%) as a pale yellow oil.

1:2 mixture of (*S*,*R*,*R*)-**15**/(*R*,*R*,*R*)-**15**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.6 Hz, 0.65H), 7.39 (d, *J* = 8.0 Hz, 1.35H), 7.29 (m, 4.30H), 7.18 (d, *J* = 7.1 Hz, 1.35H), 7.14 (d, *J* = 8.2 Hz, 1.35H), 4.43 – 4.33 (m, 1H), 4.28 (dt, *J* = 11.4, 7.2 Hz, 0.68H), 4.16 (m, 0.33 H), 3.85 - 3.76 (m, 0.68H), 3.79 – 3.72 (m, 0.33 H), 3.58 (dd, *J* = 13.8, 6.0 Hz, 0.33H), 3.39 (dd, *J* = 13.7, 7.1 Hz, 0.68H), 3.08 (dd, *J* = 13.7, 8.9 Hz, 0.68H), 3.05 (dd, *J* = 13.9, 9.9 Hz, 0.33H), 2.81 – 2.68 (m, 1.68 H), 2.68 - 2.63 (s, 0.33H), 2.55– 2.48 (m, 1H), 2.41 (s, 1H), 2.38 (s, 2H), 2.28 (dt, *J* = 14.3, 4.8 Hz, 2H), 2.23 – 2.11 (m, 2H), 1.99 – 1.94 (m, 1.35H), 1.93 - 1.87 (m, 1.35H), 1.87 – 1.74 (m, 1H), 1.47 (ddd, *J* = 14.3, 10.0, 3.9 Hz, 0.33H), 1.20 (d, *J* = 6.1 Hz, 2H), 1.15 (d, *J* = 6.2 Hz, 1H); HRMS (ES) *m/z* 492.1676 [$(M+H)^+$; calcd for $C_{25}H_{34}NO_3S_3$: 492.1701].



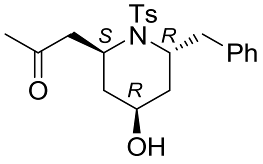
(*S*,*R*,*R*)-**16**/(*R*,*R*,*R*)-**16**

(*S*,*R*,*R*)-**16**/(*R*,*R*,*R*)-**16**: To a stirred solution of a mixture of (*S*,*R*,*R*)-**15** and (*R*,*R*,*R*)-**15** (18 mg, 0.037 mmol) in CH_3CN/H_2O (9:1, 5.0 mL) was added $PhI(O_2CCF_3)_2$ (52 mg, 0.12 mmol) at 0 °C. After 5 min, the reaction mixture was quenched with saturated aquous NH_4Cl (5.0 mL) and extracted with EtOAc (3 x 10 mL) and the combined organics were dried over Na_2SO_4, filtered and concentrated in vacuo. Flash chromatography (hexane:EtOAc=3:1) afforded a 1:2 mixture of (*S*,*R*,*R*)-**16** and (*R*,*R*,*R*)-**16** (13 mg, 0.031 mmol, 84%): HRMS (ES) *m/z* 402.1731 [$(M+H)^+$; calcd for $C_{22}H_{28}NO_4S$: 402.1739].

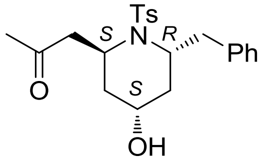


(*R*,*R*)-**18**

(*R*,*R*)-**18**: To a stirred solution of (*R*,*R*)-**11** (120 mg, 0.21 mmol) in CH_3CN/H_2O (4:1, 12 mL) was added the solution of N-chlorosuccinimide (110 mg, 0.83 mmol) and $AgNO_3$ (160 mg, 0.93 mmol) in CH_3CN-H_2O (4:1, 5.0 mL) at 0 °C. After 5 min, the reaction was treated with saturated aquous Na_2SO_3 (1.0mL), saturated aq. $NaHCO_3$ (1.0 mL) and brine (1.0 mL), successively. The reaction mixture was filtered through celite and extracted with Et_2O (3 x 10 mL). The combined organic layers were dried over Na_2SO_4. Flash chromatography (hexane:EtOAc, 6:1 to 2:1) afforded (*R*,*R*)**-18** (73 mg, 0.18 mmol, 88%) as a colorless oil: R_f 0.30 (hexane/EtOAc = 3:1); $[\alpha]^{24}_{D}$ +116.85 (c 0.50, $CHCl_3$); IR (film) 3026 (w), 2923 (m), 1717 (s), 1598 (w), 1495 (w), 1304 (s), 1150 (s), 1095 (s), 1074 (s), 979 (m), 750 (m), 714 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.3 Hz, 2H), 7.30 – 7.23 (m, 3H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.12 – 7.09 (m, 2H), 4.58 (dddd, *J* = 9.4, 6.3, 6.3, 3.1 Hz, 1H), 4.52 (dddd, *J* = 8.5, 8.5, 4.2, 4.2 Hz, 1H), 3.15 (dd, *J* = 18.0, 4.7 Hz, 1H), 3.12 (dd, *J* = 14.1, 5.4 Hz, 1H), 2.70 (dd, *J* = 18.0, 8.4 Hz, 1H), 2.67 – 2.59 (m, 2H), 2.52 (dd, *J* = 15.8, 3.9 Hz, 1H), 2.49 (dd, *J* = 15.9, 3.1 Hz, 1H), 2.40 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.06, 204.66, 143.93, 138.63, 137.21, 129.95, 129.37, 128.92, 127.30, 127.05, 56.72, 49.13, 48.12, 45.55, 43.66, 40.97, 30.31, 21.62; HRMS (ES) *m/z* 400.1579 [$(M+H)^+$; calcd for $C_{22}H_{26}NO_4S$: 400.1583].



(*S*,*R*,*R*)**-19**



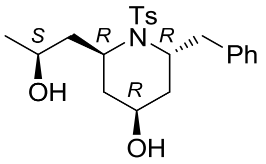
(*S*,*R*,*S*)**-19**

(*S*,*R*,*R*)**-19** and (*S*,*R*,*S*)**-19**: To a stirred solution of (*R*,*R*)**-18** (73 mg, 0.18 mmol) in THF (5.0 mL) was added $LiHAl(OCEt_3)_3$ (0.5 M in THF, 0.44 mL, 0.22 mmol) at −78 °C. The reaction mixture was warmed to room temperature for 3h, quenched with 1N HCl and extracted with Et_2O (3 x 10 m). The combined organic layers were washed with brine and dried over $MgSO_4$. Flash chromatography (hexane:EtOAc, 3:1 to 1:2) afforded (*S*,*R*,*R*)**-19** (16 mg, 0.040mmol, 22%) and (*S*,*R*,*S*)**-19** (27 mg, 0.067mmol, 37%) as colorless oils.

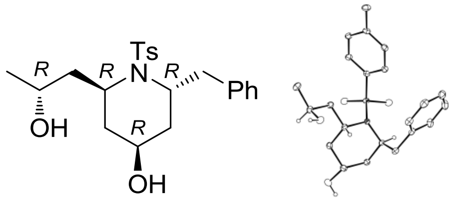
(*S*,*R*,*R*)**-19**: R_f 0.30 (hexane/EtOAc = 1:1); $[\alpha]^{25}_{D}$ +44.92 (c 1.00, $CHCl_3$); IR (film) 3420 (m, br), 3031 (w), 2929 (m), 1717 (s), 1599 (w), 1496 (m), 1455 (m), 1309 (s), 1154 (s), 1095 (s), 985 (m), 863 (m), 700 (m) cm-1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 3H), 7.23 (dd, *J* = 7.6, 1.7 Hz, 2H), 7.15 – 7.11 (m, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 4.54 (qd, *J* = 8.0, 2.5 Hz, 1H), 4.19 – 4.09 (m, 2H), 3.08 – 3.01 (m, 2H), 2.86 (dd, *J* = 9.3, 7.8 Hz, 1H), 2.83 (dd, *J* = 13.8, 7.8 Hz, 1H), 2.36 (s, 3H), 2.02 – 1.96 (m, 1H), 1.98 (s, 3H), 1.93 – 1.88 (m, 1H), 1.71 – 1.63 (m, 2H), 1.62 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.52, 143.15, 139.86, 138.62, 129.63, 129.34, 128.82, 127.17, 126.70, 65.50, 57.30, 49.10, 46.65, 40.01, 38.29, 36.96, 30.46, 21.57; HRMS (ES) *m/z* 402.1727 [$(M+H)^+$; calcd for $C_{22}H_{28}NO_4S$: 402.1739].

(*S*,*R*,*S*)**-19**: R_f 0.30 (hexane/EtOAc = 1:1); $[\alpha]^{25}_{D}$ +43.09 (c 1.35, $CHCl_3$); IR (film) 3412 (m, br), 3062 (w), 3026 (w), 2924 (m), 1713 (s), 1600 (w), 1309 (m), 1152 (s), 1097 (s), 971 (m), 816 (m), 704 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ

7.31 (d, *J* = 8.3 Hz, 2H), 7.27 – 7.21 (m, 3H), 7.17 – 7.13 (m, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 4.63 (ddd, *J* = 9.4, 7.9, 3.2 Hz, 1H), 4.19 (tt, *J* = 7.8, 5.4 Hz, 1H), 4.15 – 4.09 (m, 1H), 3.32 (dd, *J* = 13.6, 7.5 Hz, 1H), 3.03 (dd, *J* = 13.2, 7.7 Hz, 1H), 2.98 (dd, *J* = 17.3, 6.0 Hz, 1H), 2.75 (dd, *J* = 17.5, 8.0 Hz, 1H), 2.37 (s, 2H), 2.08 (ddd, *J* = 13.6, 9.7, 3.8 Hz, 3H), 2.00 (s, 3H), 1.95 (ddd, *J* = 9.5, 7.2, 3.9 Hz, 1H), 1.73 – 1.66 (m, 3H), 1.60 (ddd, *J* = 13.7, 4.9, 3.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.55, 143.10, 139.93, 139.45, 129.63, 129.60, 128.63, 127.22, 126.44, 65.78, 57.07, 46.88, 46.41, 39.95, 38.07, 34.90, 30.37, 21.57; HRMS (ES) *m/z* 401.1717 [(M+H)$^+$; calcd for $C_{22}H_{28}NO_4S$: 402.1739].



(*S*,*R*,*R*,*R*)-**17**

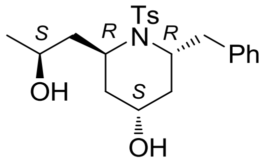


(*R*,*R*,*R*,*R*)-**17**

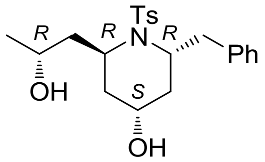
(*S*,*R*,*R*,*R*)-**17**and (*R*,*R*,*R*,*R*)-**17**: To a stirred solution of (*S*,*R*,*R*)-**19** (16 mg, 0.040 mmol) in THF (3.0 mL) was added $BH_3 \cdot THF$ (1.0 M in THF, 50 μL, 0.050 mmol) at 0 °C. After being stirred for 1 h, the reaction mixture was quenched with MeOH (1.0 mL) and concentrated in vacuo, then filtered through a plug of silica gel affording a 1:1 mixture (14 mg, 0.036 mmol, 91%) of (*S*,*R*,*R*,*R*)-**17** and (*R*,*R*,*R*,*R*)-**17** as a white sold, 5.0 mg of which was separated by SFC affording (*S*,*R*,*R*,*R*)-**17** (1.5 mg) as a white solid and (*R*,*R*,*R*,*R*)-**17** (2.1 mg) which was crystalized in Et_2O.

(*S*,*R*,*R*,*R*)-**17**: R_f 0.20 (hexane/EtOAc = 1:1); IR (film) 3389 (s, br), 3061 (w), 2927 (m), 1651 (w), 1600 (w), 1495 (w), 1312 (m), 1147 (s), 1114 (s), 983 (w), 861 (w), 816 (w), 745 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.2 Hz, 2H), 7.32 – 7.26 (m, 3H), 7.20 (d, *J* = 6.7 Hz, 2H), 7.14 (d, *J* = 8.2 Hz, 2H), 4.42 (dddd, *J* = 13.7, 13.0, 8.1, 4.8 Hz, 1H), 4.07 (tt, *J* = 8.2, 4.1 Hz, 1H), 4.01 (dq, *J* = 14.1, 4.4 Hz, 1H), 3.50 (s, 1H), 3.24 (dd, *J* = 13.7, 7.9 Hz, 1H), 2.87 (dd, *J* = 13.8, 8.1 Hz, 1H), 2.38 (s, 3H), 2.29 (ddd, *J* = 14.9, 10.0, 2.2 Hz, 1H), 1.93 **-** 1.88 (m, 2H), 1.81 – 1.74 (m, 1H), 1.75 – 1.67 (m, 1H), 1.63 (ddd, *J* = 12.6, 8.1, 4.5 Hz, 1H), 1.51 (ddd, *J* = 14.6, 9.8, 4.8 Hz, 1H), 1.00 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.16, 140.11, 139.06, 129.61, 129.36, 128.74, 127.33, 126.68, 65.81, 65.01, 55.29, 52.00, 42.76, 39.08, 38.21, 37.08, 24.00, 21.60; HRMS (ES) *m/z* 426.1705 [(M+H)$^+$; calcd for $C_{22}H_{29}NO_4SNa$: 426.1715].

(*R*,*R*,*R*,*R*)-**17**: R_f 0.20 (hexane/EtOAc = 1:1); IR (film) 3398 (s, br), 2926 (m), 1600 (w), 1495 (w), 1452 (m), 1378 (m), 1315 (m), 1097 (s), 862 (w), 813 (w), 742 (m) cm^{-1} ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 3H), 7.21 – 7.15 (m, 4H), 7.06 (d, *J* = 8.1 Hz, 2H), 4.62 (tt, *J* = 9.0, 9.0, 4.5, 4.5 Hz, 1H), 4.13 (dq, *J* = 9.0, 4.5, 4.5, 4.5 Hz, 1H), 3.88 (dddd, *J* = 9.7, 9.7, 4.2, 3.1 Hz, 1H), 3.81 – 3.73 (m, 1H), 3.08 (dd, *J* = 13.7, 8.9 Hz, 1H), 2.85 (dd, *J* = 13.7, 7.4 Hz, 1H), 2.36 (s, 3H), 2.11 (dt, *J* = 13.0, 3.1 Hz, 1H), 2.05 (dt, *J* = 13.4, 3.9 Hz, 1H), 1.93 (ddd, *J* = 13.1, 9.7, 3.1 Hz, 1H), 1.75 – 1.65 (m, 3H), 1.46 (d, *J* = 4.6 Hz, 1H), 1.32 (d, *J* = 4.9 Hz, 1H), 1.14 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 142.84, 140.64, 138.86, 129.48, 129.37, 128.86, 127.08, 126.68, 65.92, 65.52, 56.78, 51.60, 42.29, 38.55, 38.24, 37.77, 24.57, 21.58; HRMS (ES) *m/z* 426.1705 [(M+H)$^+$; calcd for $C_{22}H_{29}NO_4SNa$: 426.1715].



(*S*,*R*,*R*,*S*)-**17**

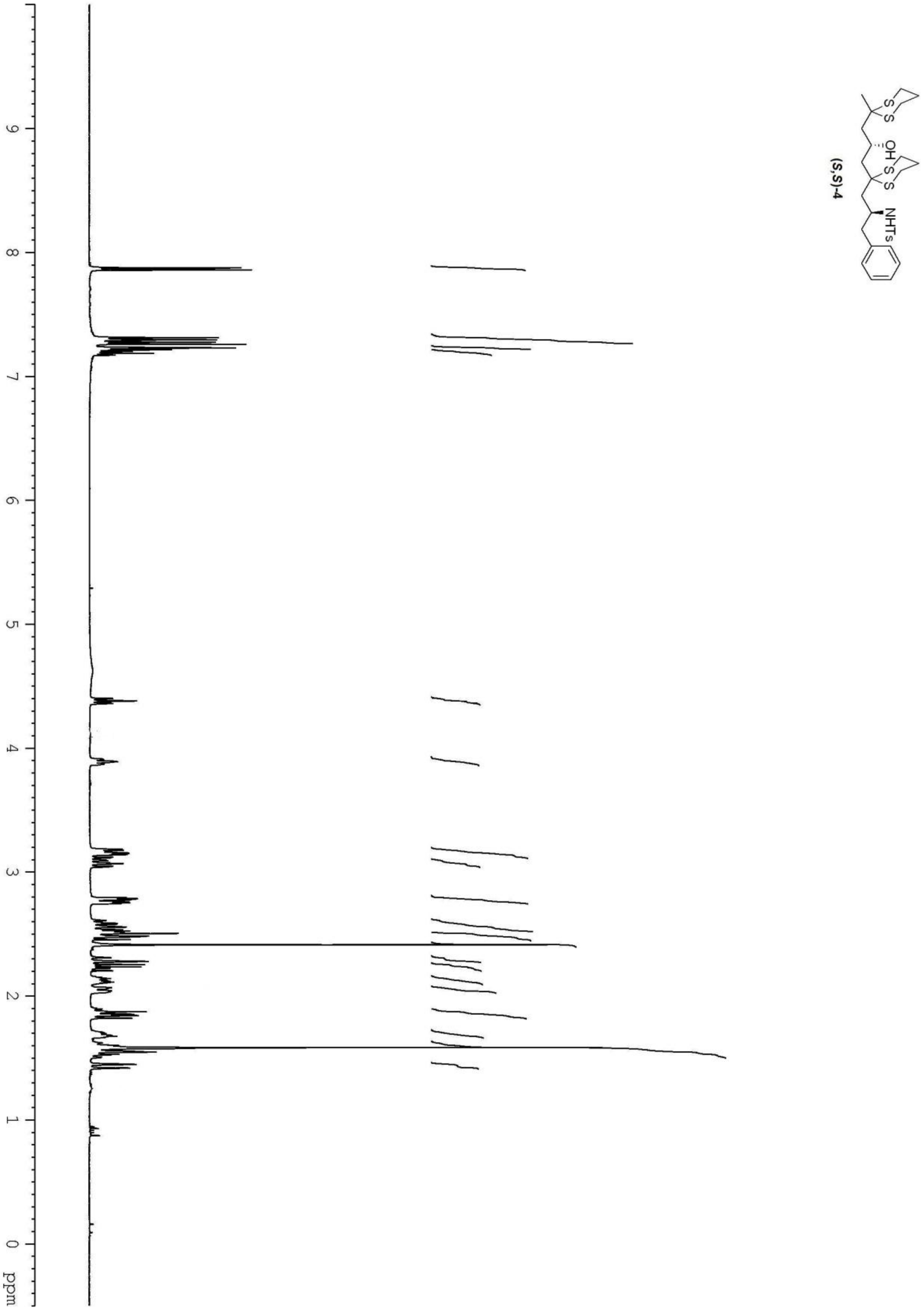


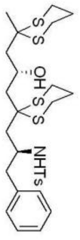
(*R*,*R*,*R*,*S*)-**17**

(*S*,*R*,*R*,*S*)-**17** and (*R*,*R*,*R*,*S*)-**17**: To a stirred solution of (*S*,*R*,*S*)-**19** (27 mg, 0.067 mmol) in THF (4.0 mL) was added BH$_3$·THF (1.0 M in THF, 84 μL, 0.084 mmol) at 0 °C. After being stirred for 1 h, the reaction mixture was quenched with MeOH (1.0 mL) and concentrated in vacuo filtered through a plug of silica gel to afford a1:1 mixture of (*R*,*R*,*R*,*S*)-**17** and (*S*,*R*,*R*,*S*)-**17** (25 mg, 0.062 mmol, 93%) as a white solid, which was separated by SFC affording (*S*,*R*,*R*,*R*)-**17** (12 mg) and (*R*,*R*,*R*,*S*)-**17** (6.7 mg).

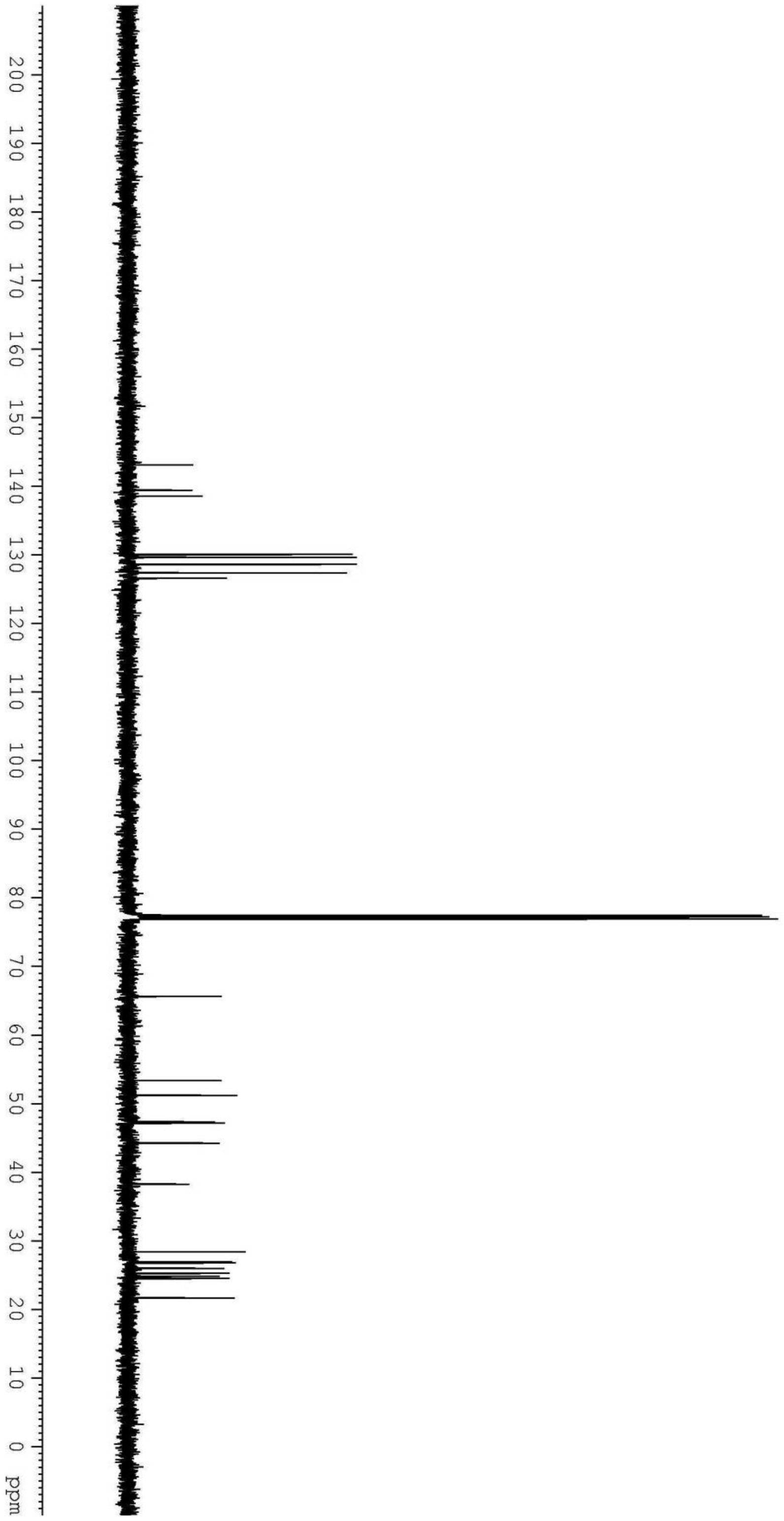
(*S*,*R*,*R*,*S*)-**17**: R$_f$ 0.23 (hexane/EtOAc = 1:1); [α]$^{26}_{D}$ +20.14 (c 0.48, CH$_2$Cl$_2$); IR (film) 3391 (s, br), 3028 (w), 2927 (m), 1600 (w), 1496 (w), 1454 (m), 1317 (s), 1150 (s), 1086 (m), 854 (w), 814 (w), 715 (m) cm^{-1} ; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.62 (d, *J* = 8.2 Hz, 2H), 7.32 – 7.26 (m, 2H), 7.26 – 7.20 (m, 3H), 7.15 (d, *J* = 7.1 Hz, 2H), 4.52 (app dt, *J* = 9.5, 4.4 Hz, 1H), 3.85 – 3.77 (m, 2H), 3.68 **-** 3.62 (m, 1H), 3.59 (dd, *J* = 13.1, 5.3 Hz, 1H), 2.88 (dd, *J* = 13.1, 9.8 Hz, 1H), 2.46 – 2.42 (m, 1H), 2.41 (s, 3H), 2.01 – 1.94 (ddd, *J* = 13.6, 11.2, 2.4 Hz, 1H), 1.90 – 1.81 (m, 2H), 1.46 (ddd, *J* = 11.9, 9.1, 4.6 Hz, 1H), 1.43 – 1.35 (m, 2H), 1.30 (dt, *J* = 12.8, 9.6 Hz, 1H), 1.16 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 143.48, 139.91, 139.29, 129.89, 129.53, 128.74, 127.32, 126.73, 66.01, 64.10, 56.49, 51.97, 41.26, 40.07, 37.83, 37.34, 23.42, 21.66; HRMS (ES) *m/z* 426.1695 [(M+H)$^+$; calcd for $C_{22}H_{29}NO_4SNa$: 426.1715].

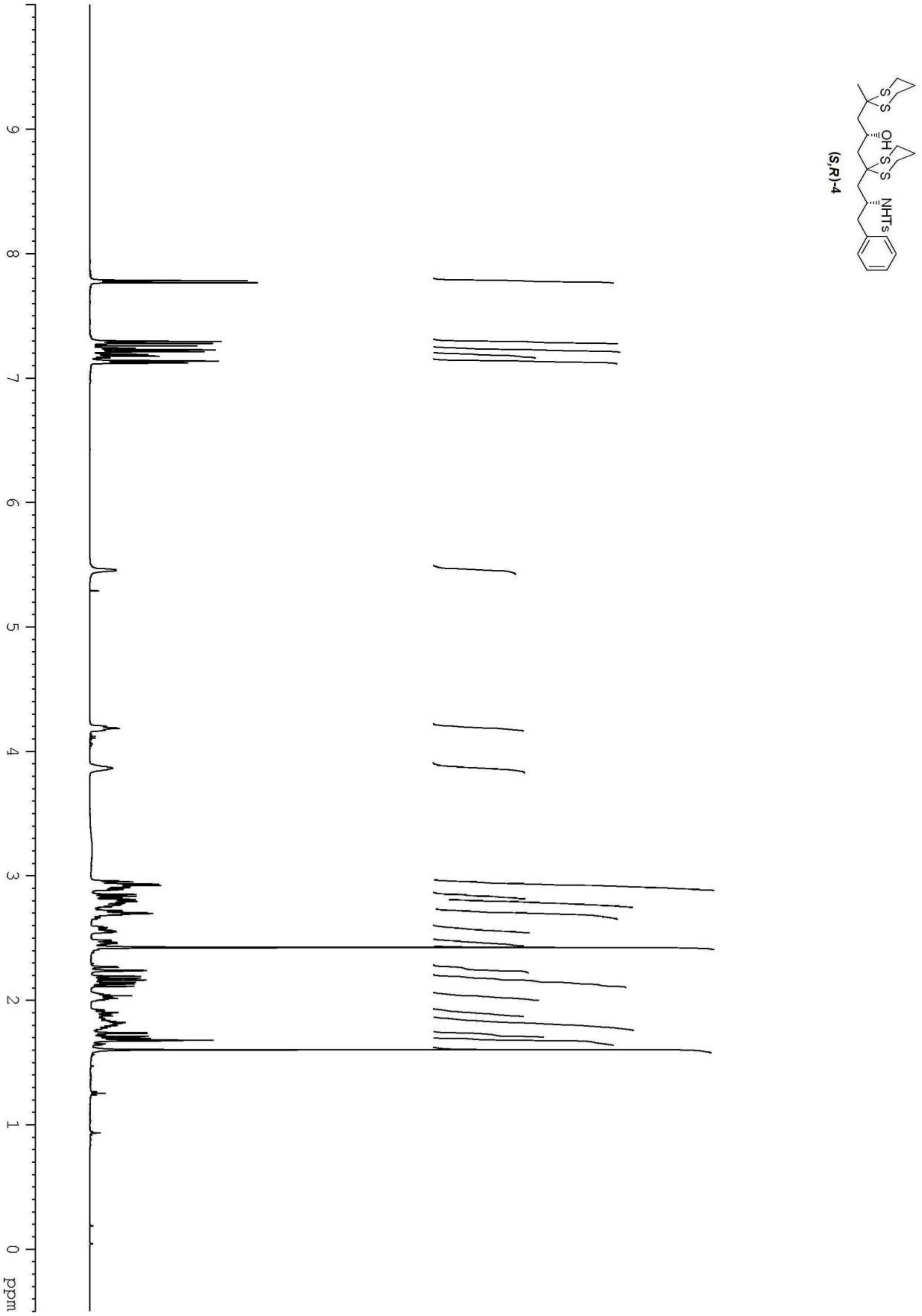
(*R*,*R*,*R*,*S*)-**17**: R$_f$ 0.23 (hexane/EtOAc = 1:1); [α]$^{26}_{D}$ +12.63 (c 0.55, CHCl$_3$); IR (film) 3389 (s, br), 3062 (w), 3025 (w), 2927 (m), 1599 (w), 1316 (m), 1149 (s), 854 (w), 815 (w), 750 (m) cm^{-1} ; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.36 (d, *J* = 8.2 Hz, 2H), 7.29 – 7.20 (m, 3H), 7.13 (t, *J* = 7.1 Hz, 4H), 4.41 – 4.33 (m, 1H), 4.05 (m, 2H), 3.82 (m, 1H), 3.35 (dd, *J* = 13.4, 6.9 Hz, 1H), 2.90 (dd, *J* = 13.4, 8.6 Hz, 1H), 2.55 (brs, 1H), 2.37 (s, 3H), 2.18 (brs, 1H), 2.04 (ddd, *J* = 13.4, 6.8, 4.3 Hz, 1H), 1.97 (dt, *J* = 13.6, 4.1 Hz, 1H), 1.80 – 1.66 (m, 3H), 1.61 (dt, *J* = 13.7, 6.9 Hz, 1H), 1.17 (d, *J* = 6.2 Hz, 2H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 143.06, 140.47, 139.33, 129.60, 129.56, 128.73, 127.13, 126.57, 65.90, 65.55, 56.93, 50.81, 41.67, 39.94, 36.85, 36.78, 24.06, 21.59; HRMS (ES) *m/z* 426.1695 [(M+H)$^+$; calcd for $C_{22}H_{29}NO_4SNa$: 426.1715].


(S,S)-4

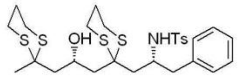


(S,S)-4

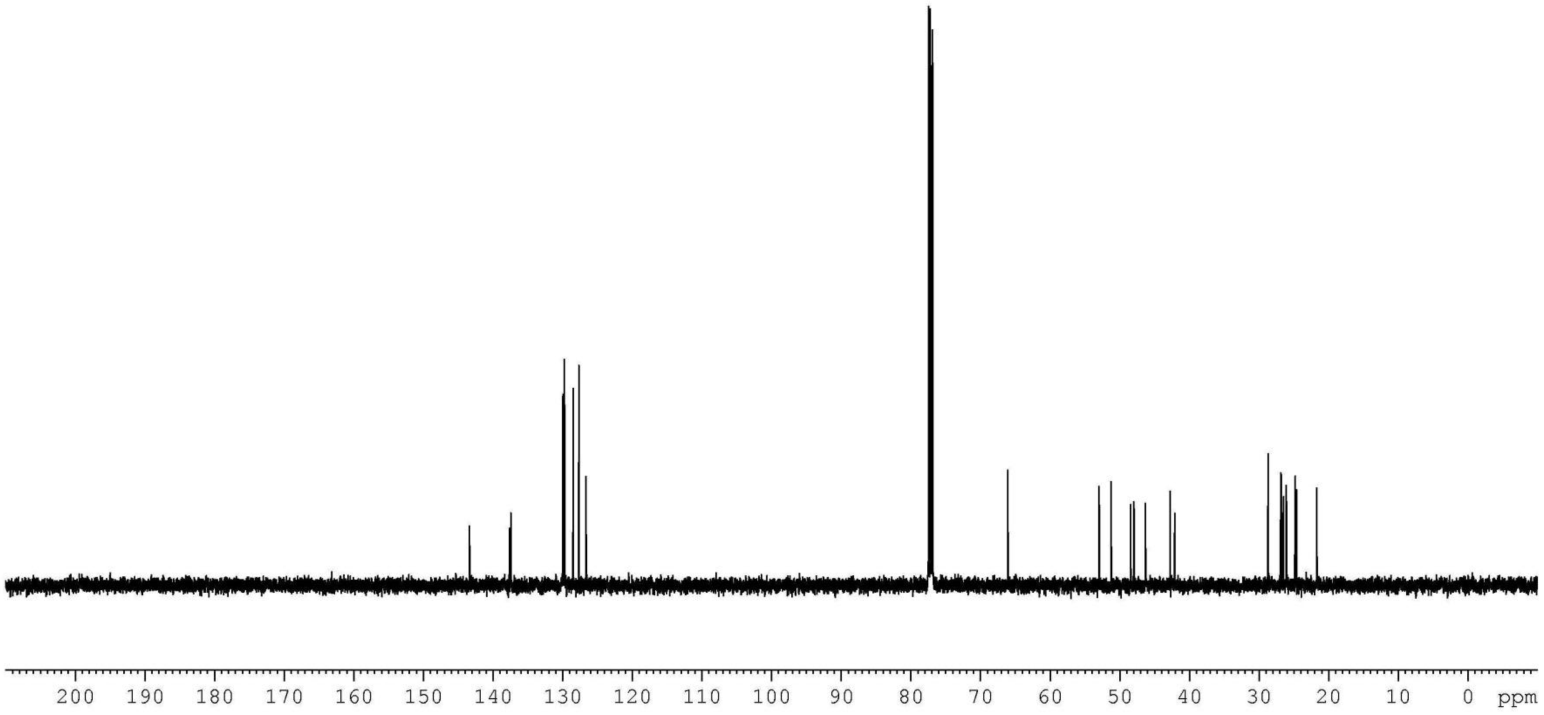

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

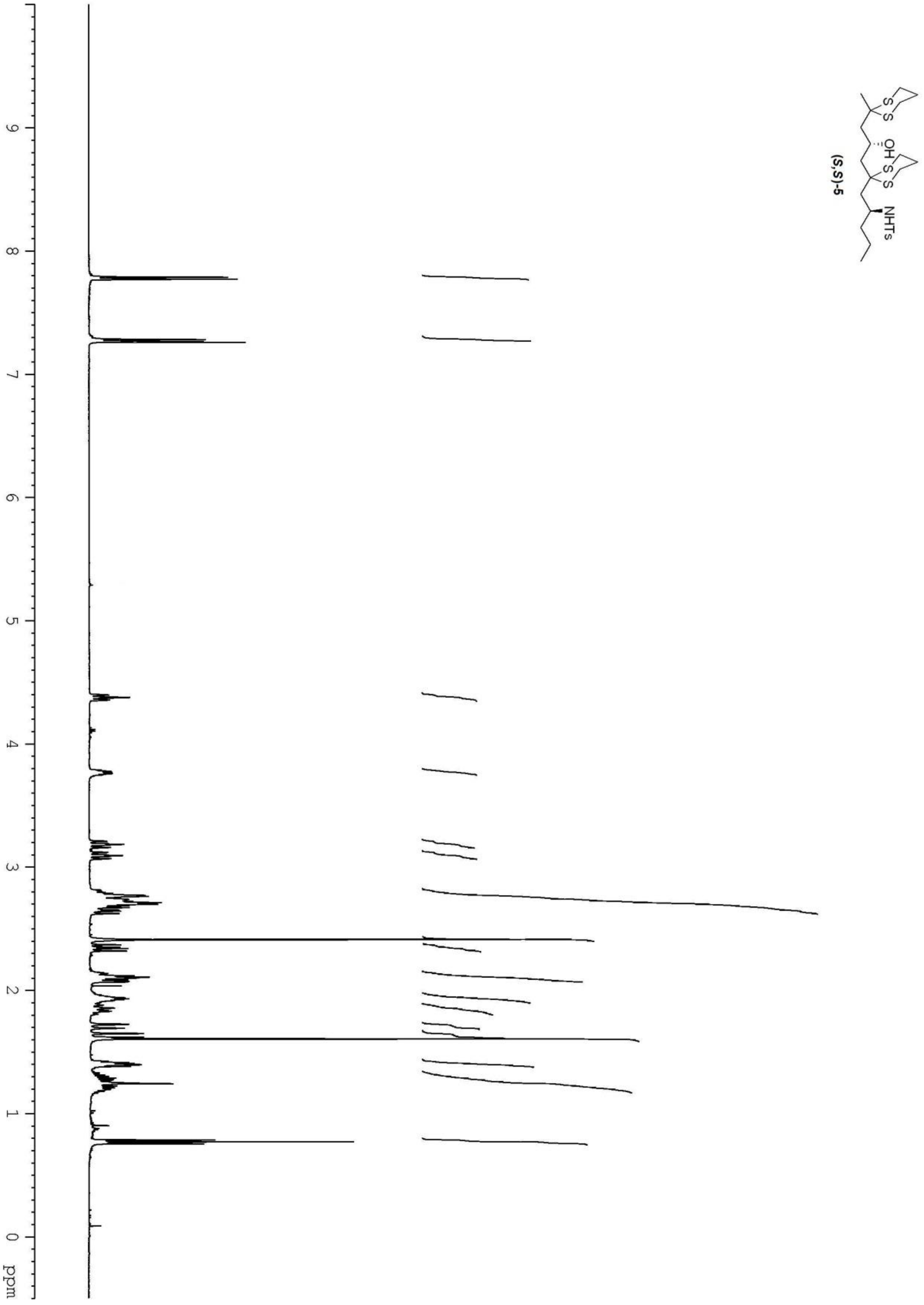


(S,R)-4

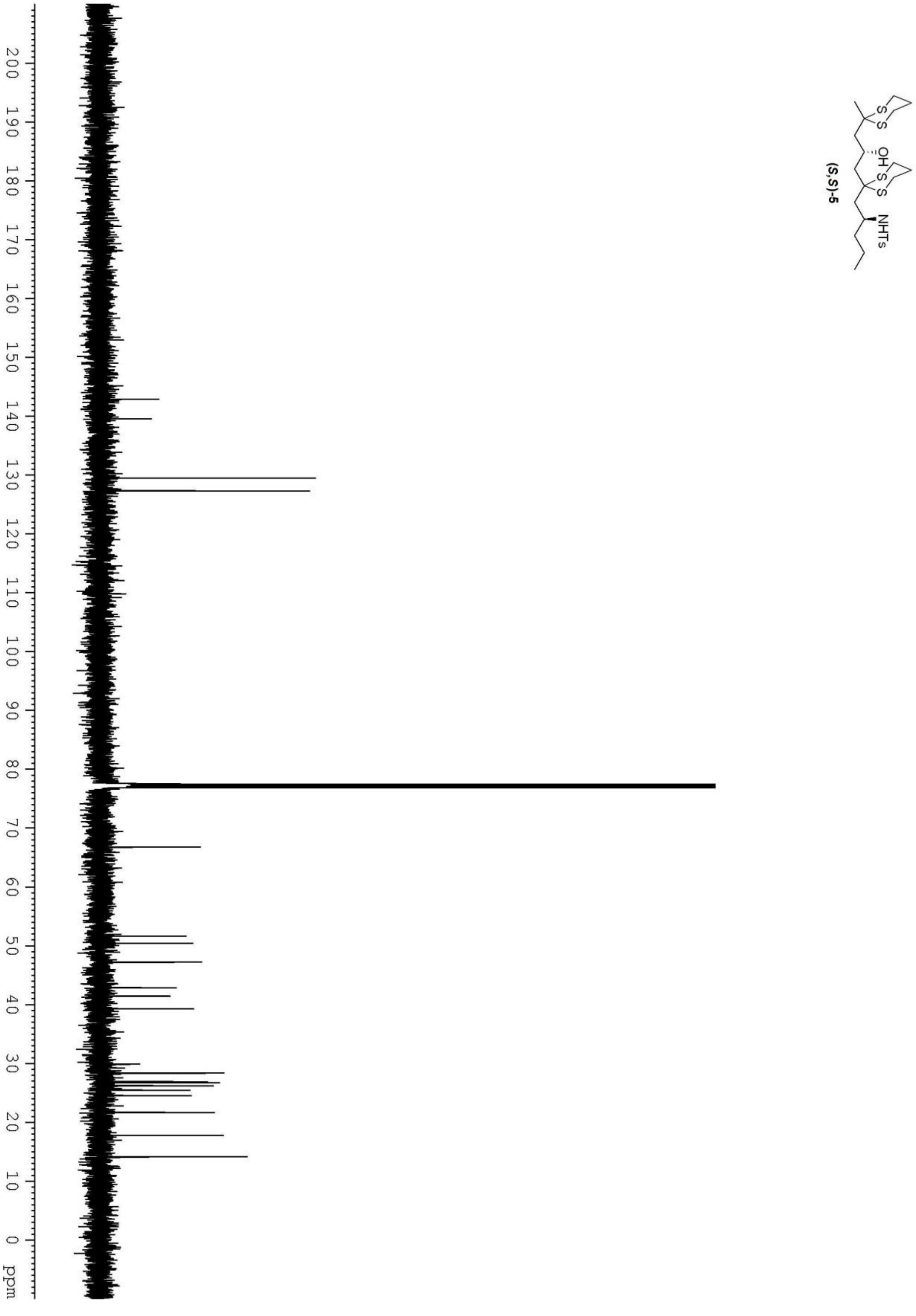

OH
NHTs
S
S

(*S*,*R*)-4

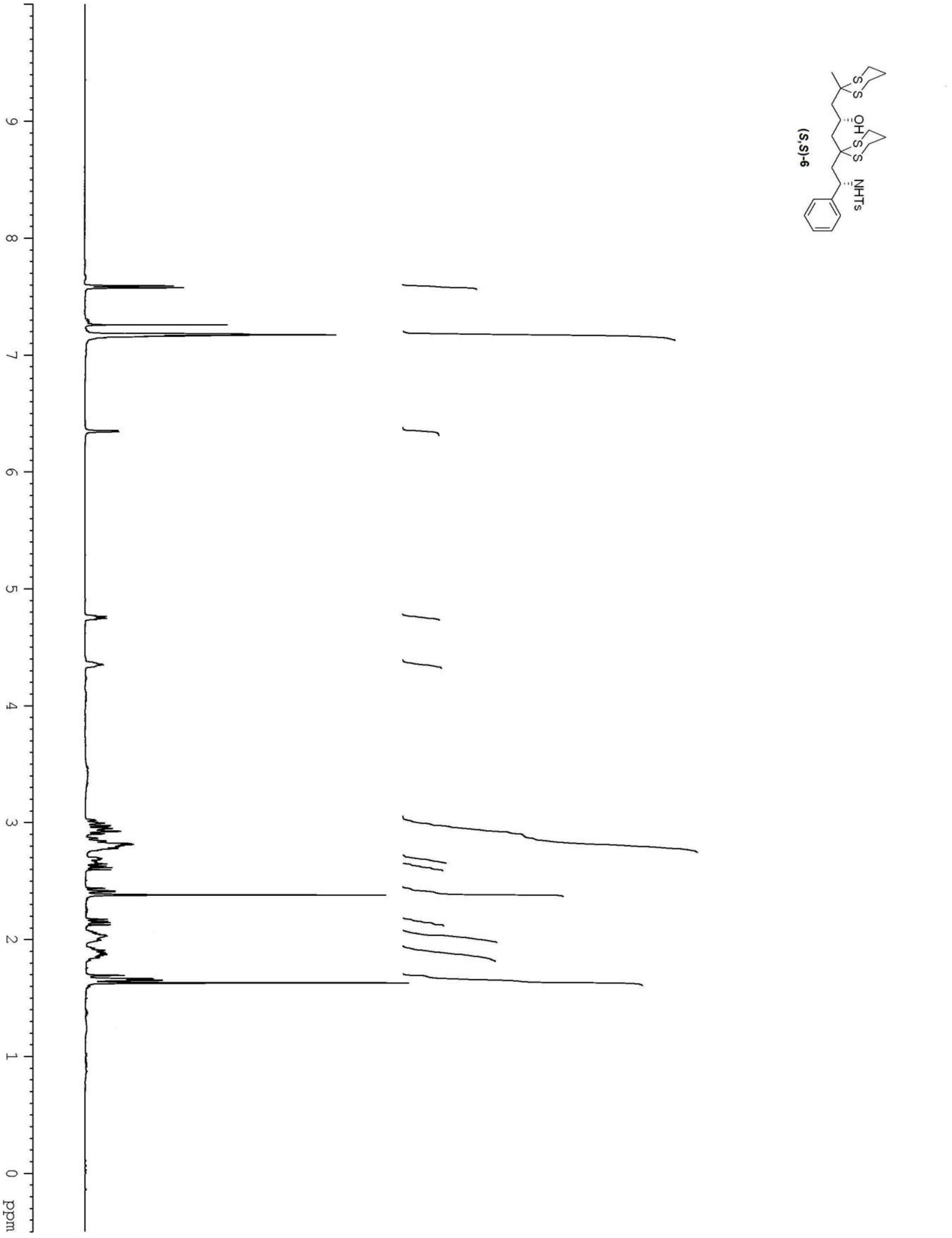

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



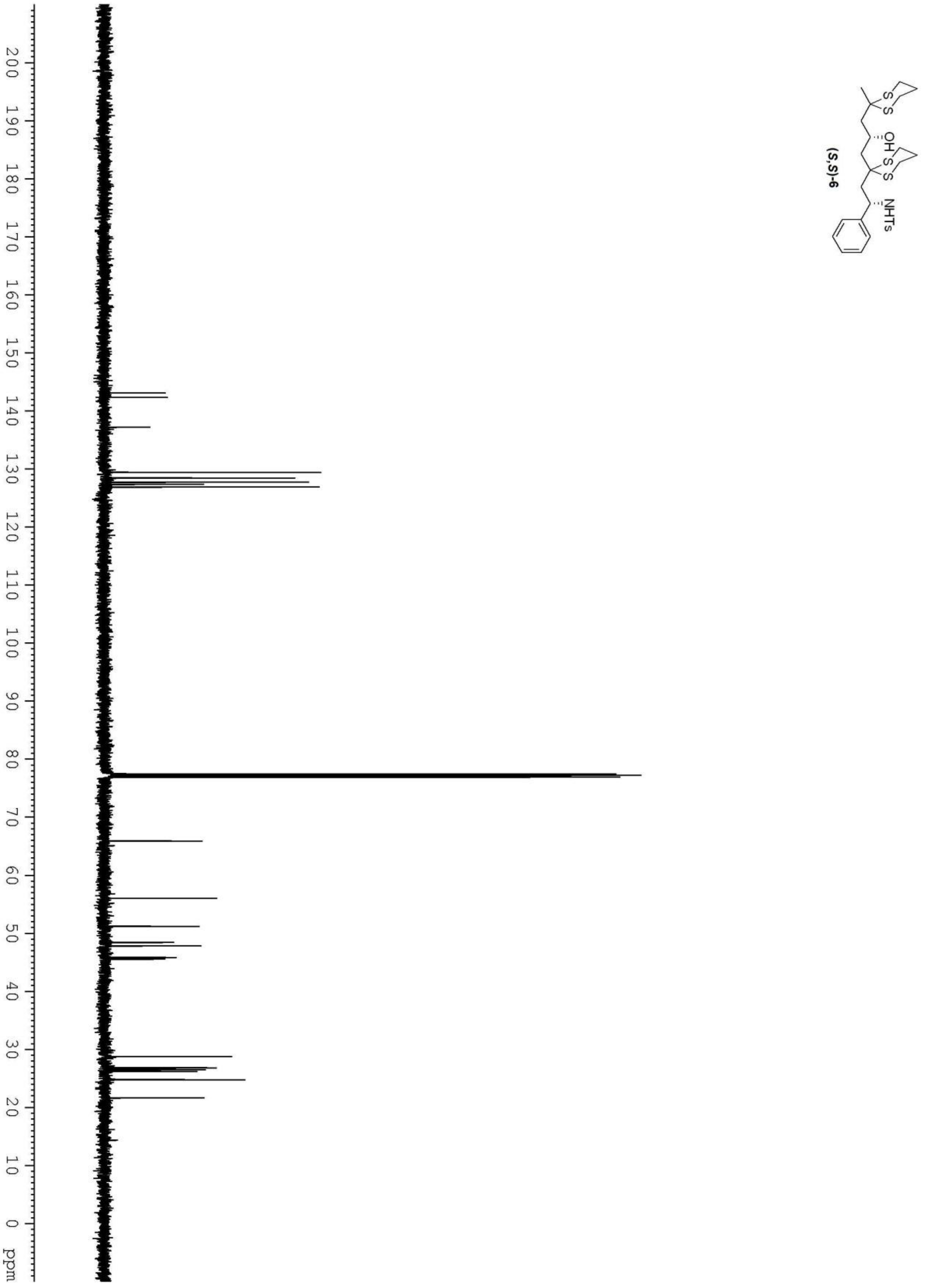
(S,S)-5


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
S
S
OH
S
S
NHTs

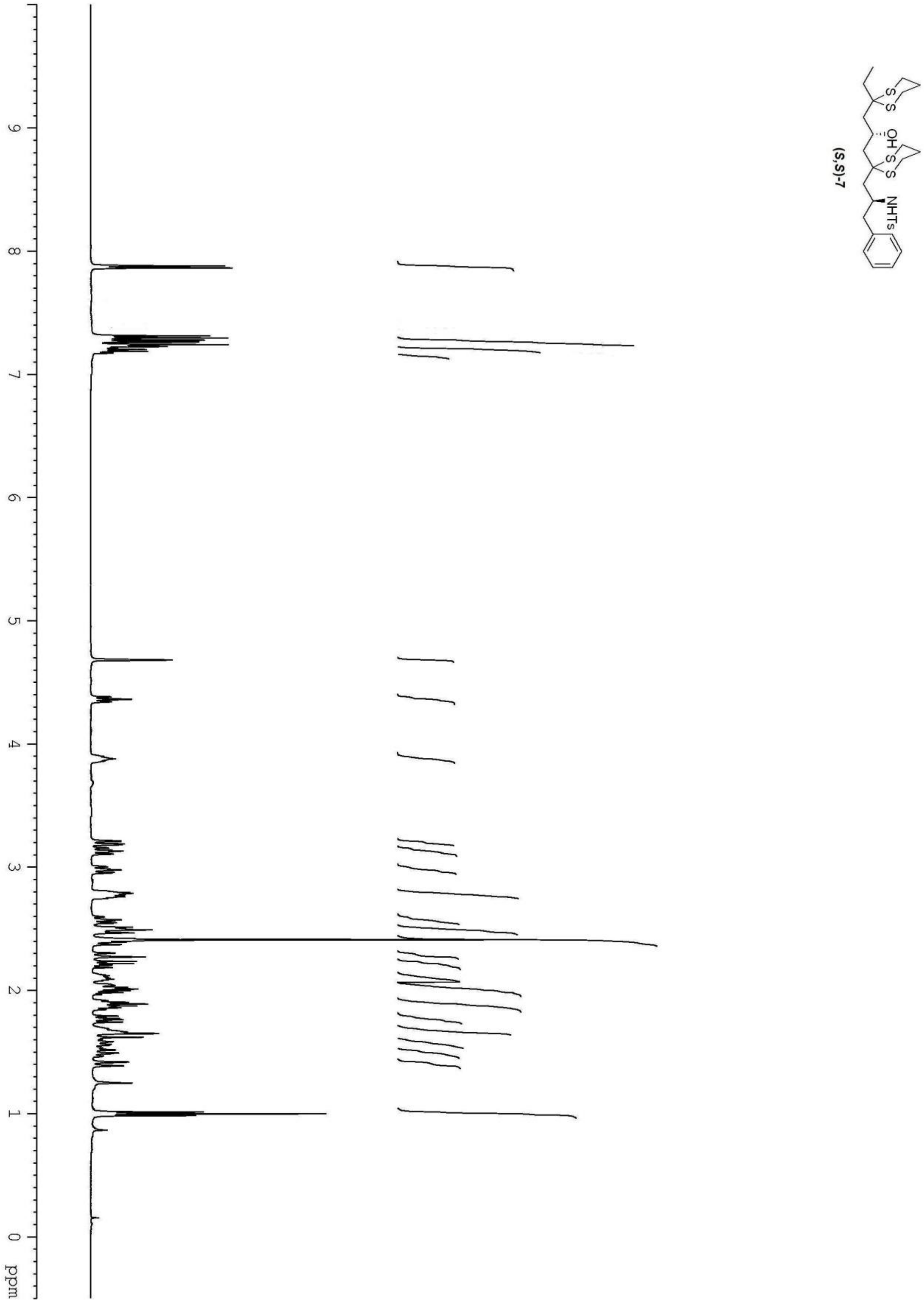
(S,S)-5



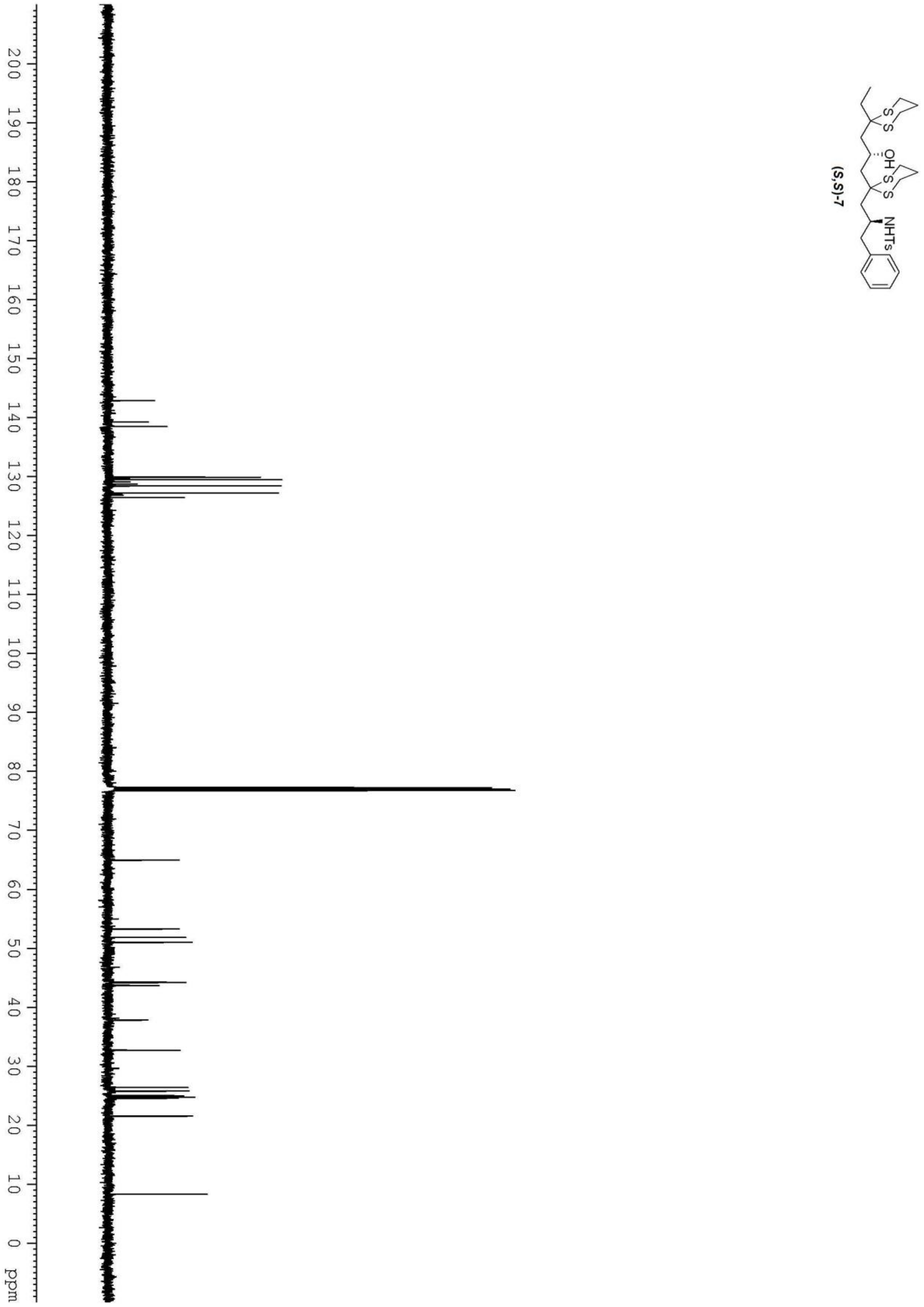
(S,S)-6


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
S
S
OH
S
S
NHTs

(S,S)-6

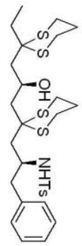


(S,S)-7

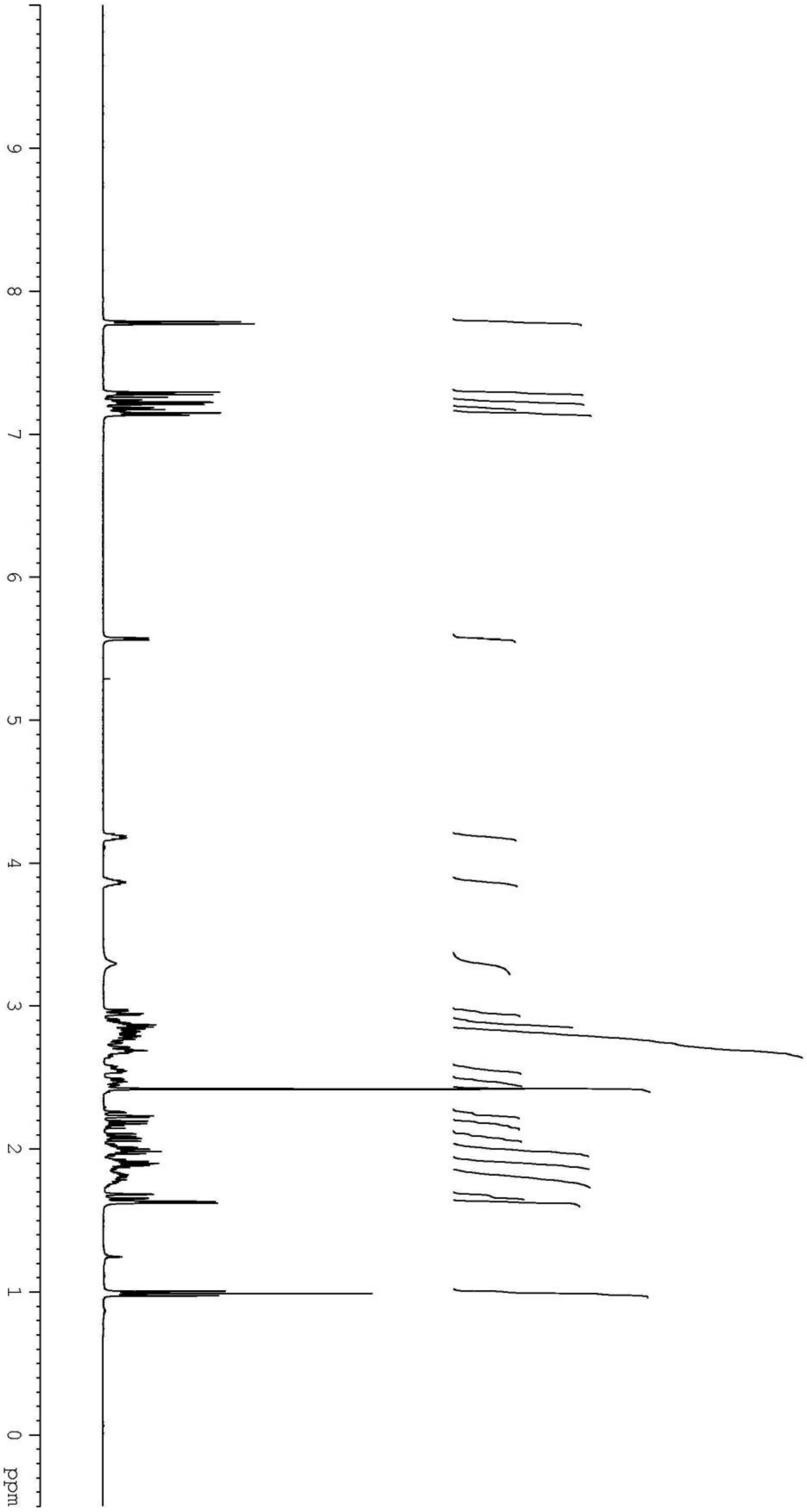


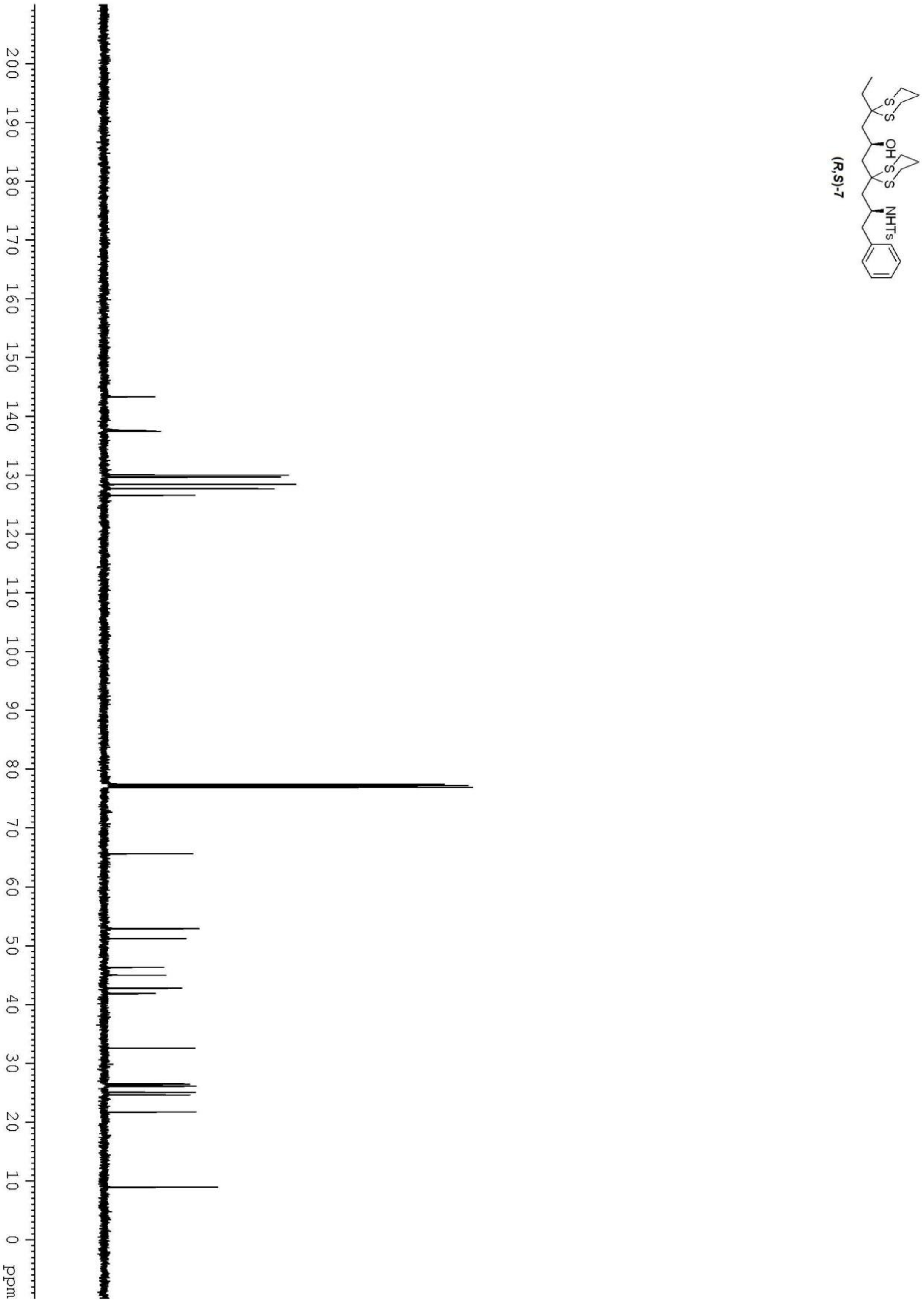
S S
OH
S S
NHTs
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

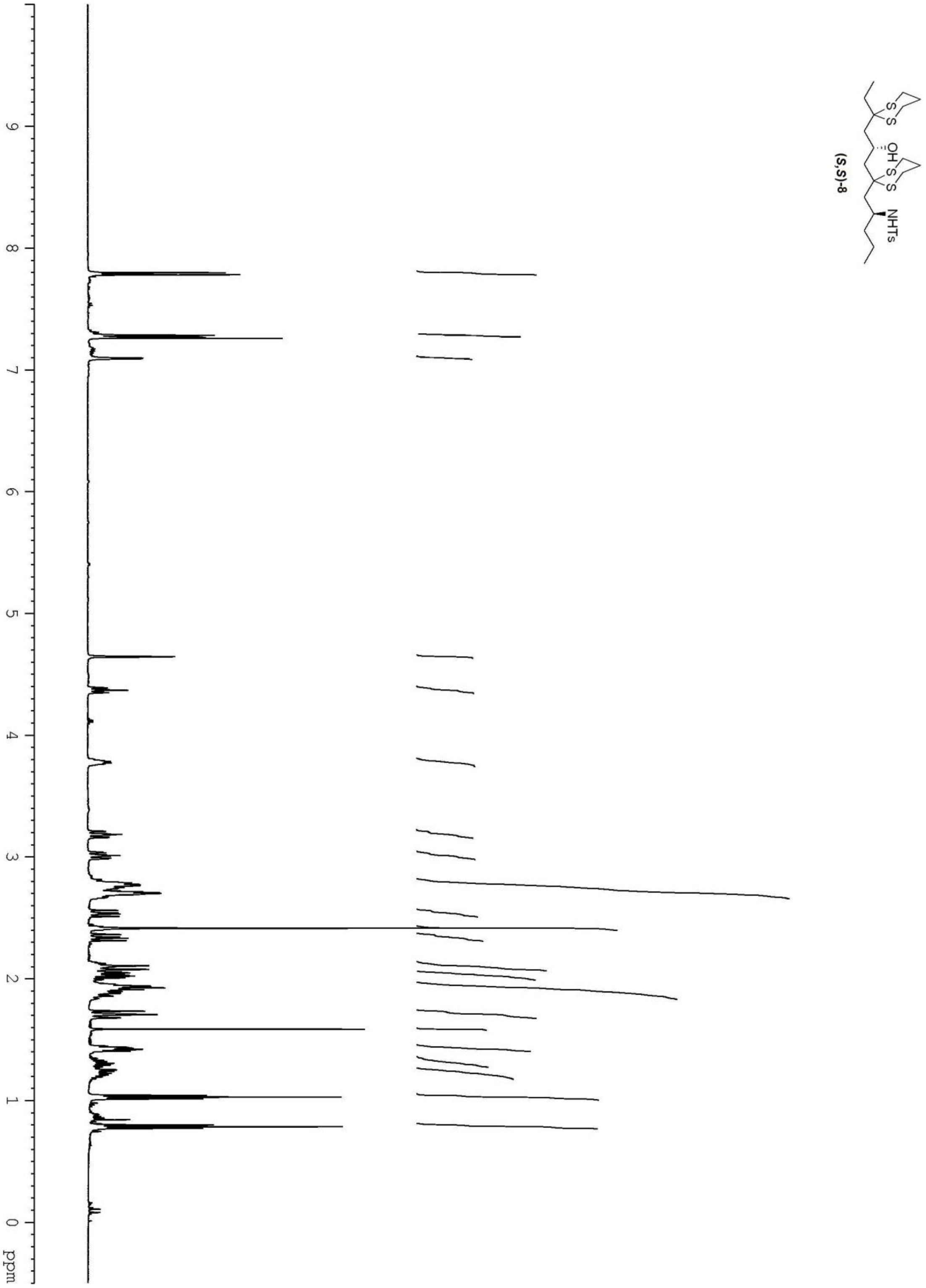
(S,S)-7



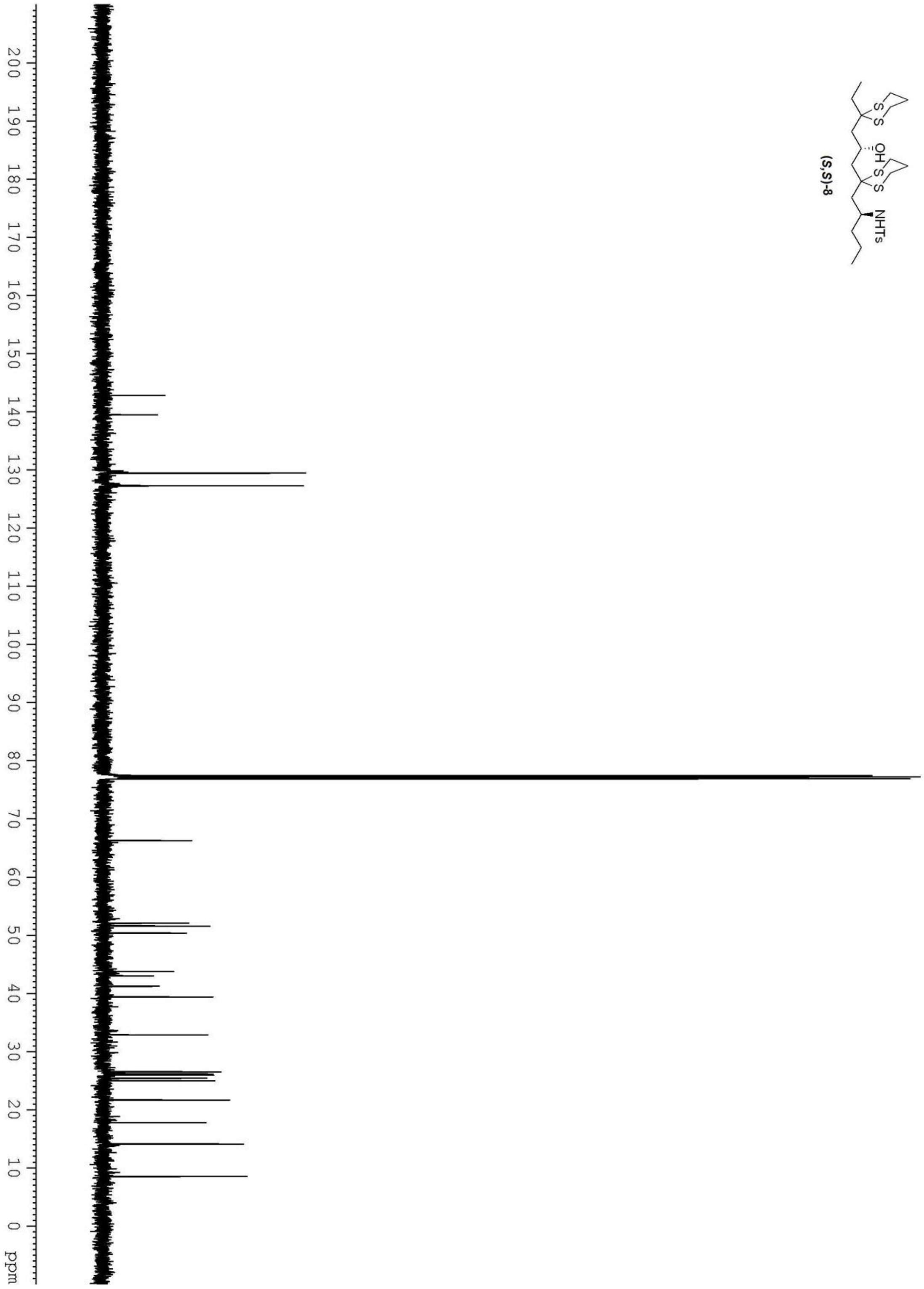
(R,S)-7

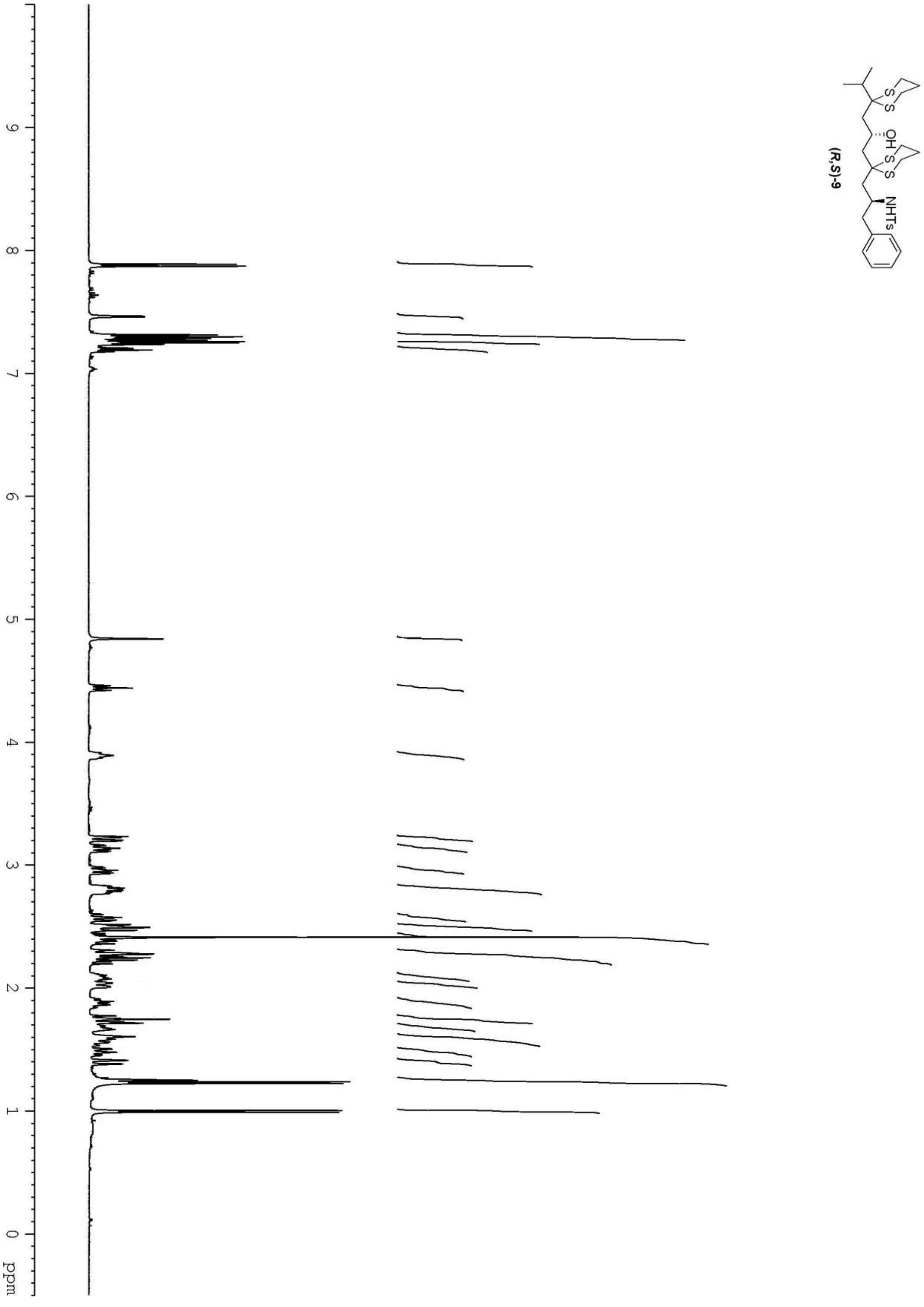



(R,S)-7
NHTs
OH
S S
S S
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

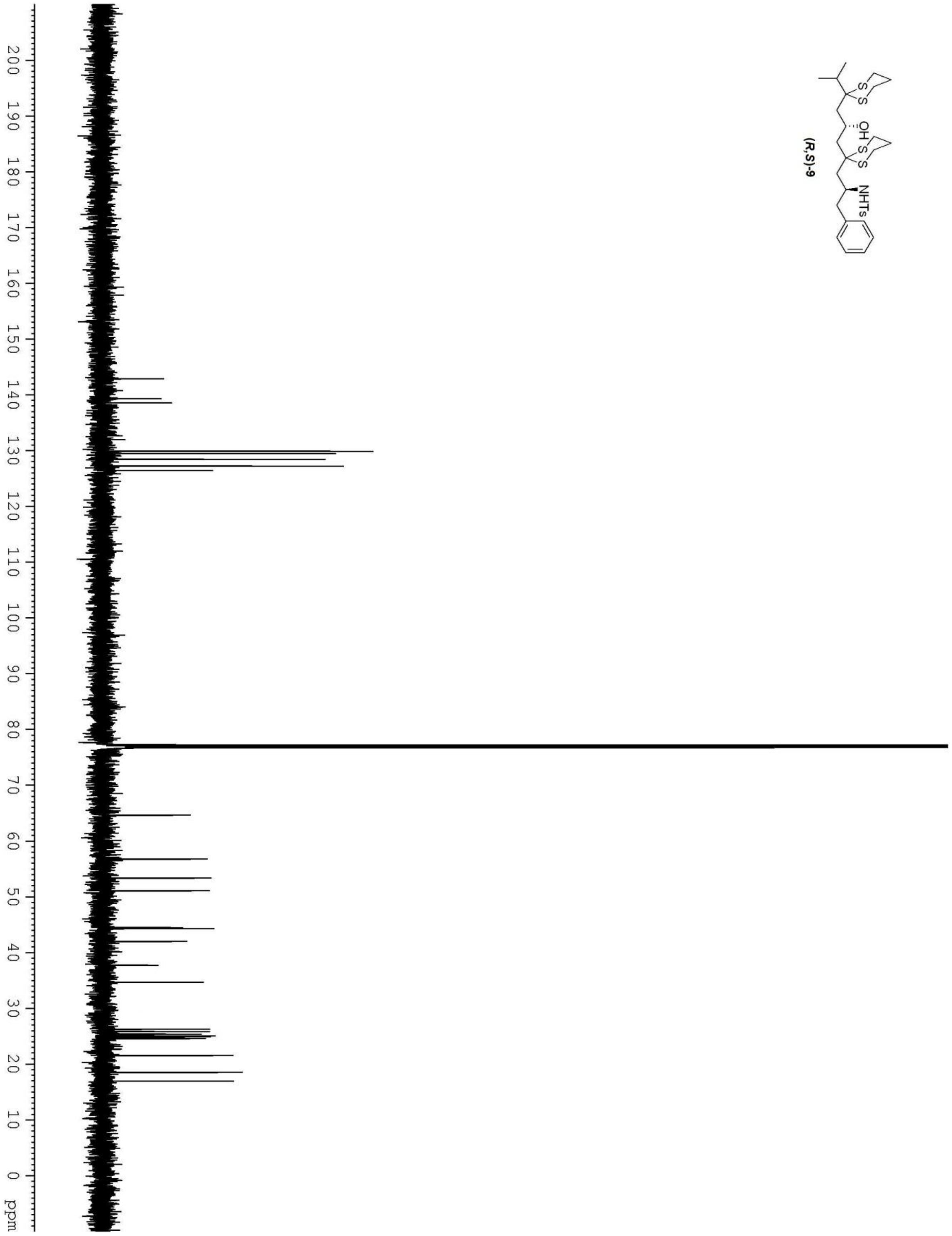


(S,S)-8

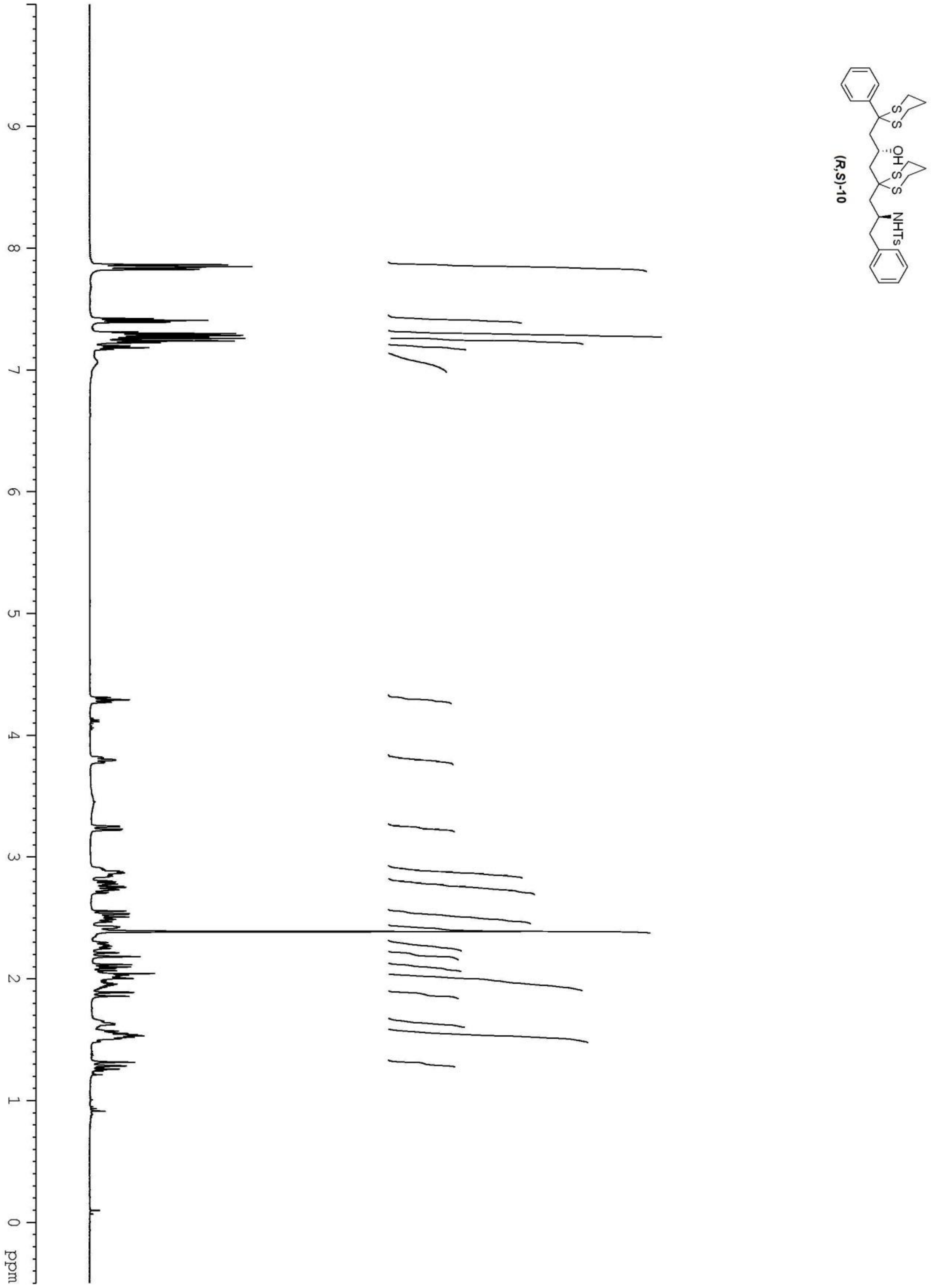

(S,S)-8
S
S
OH
S
S
NHTs
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



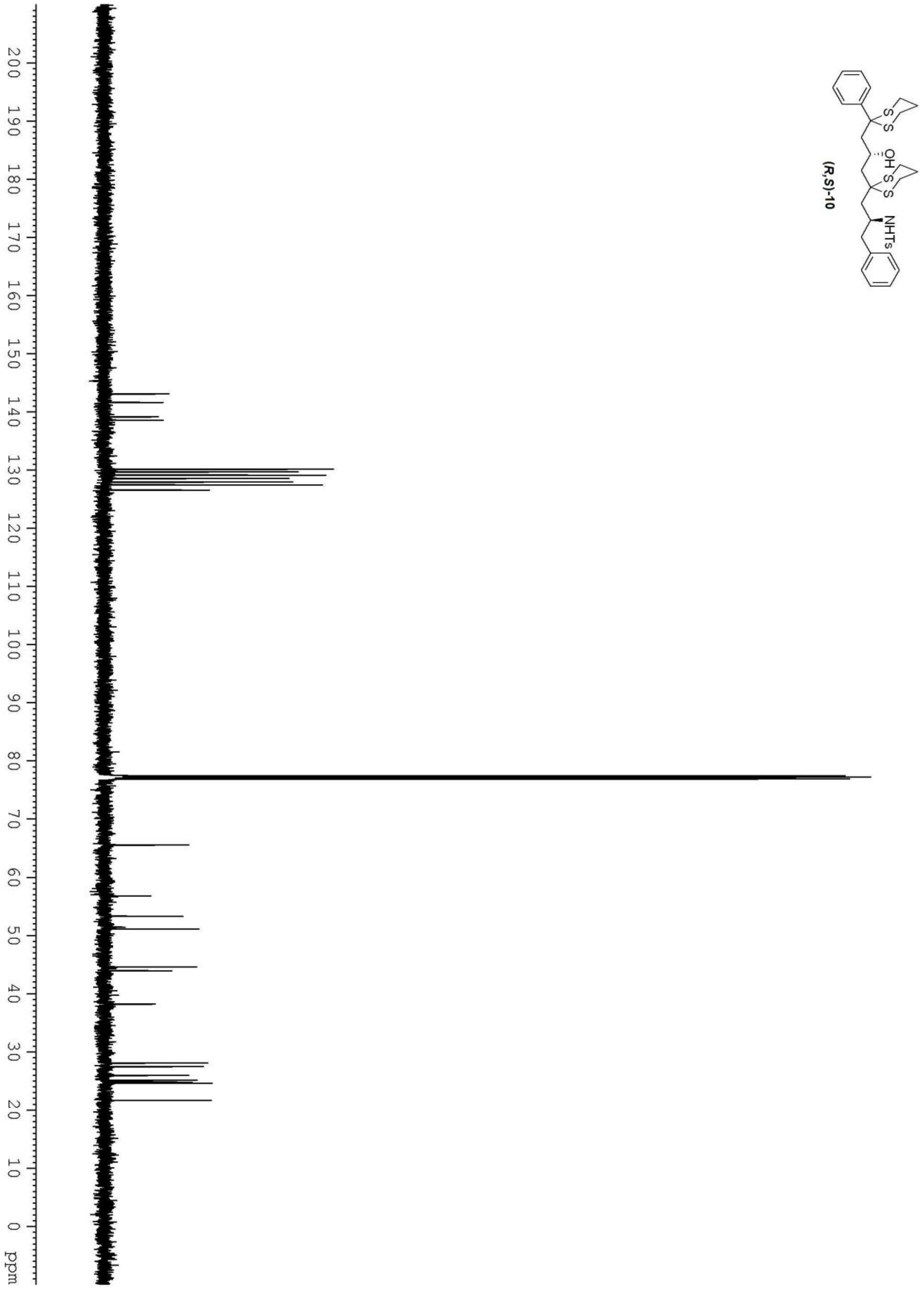
(R,S)-9


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
S S
OH
S S
NHTs

(R,S)-9

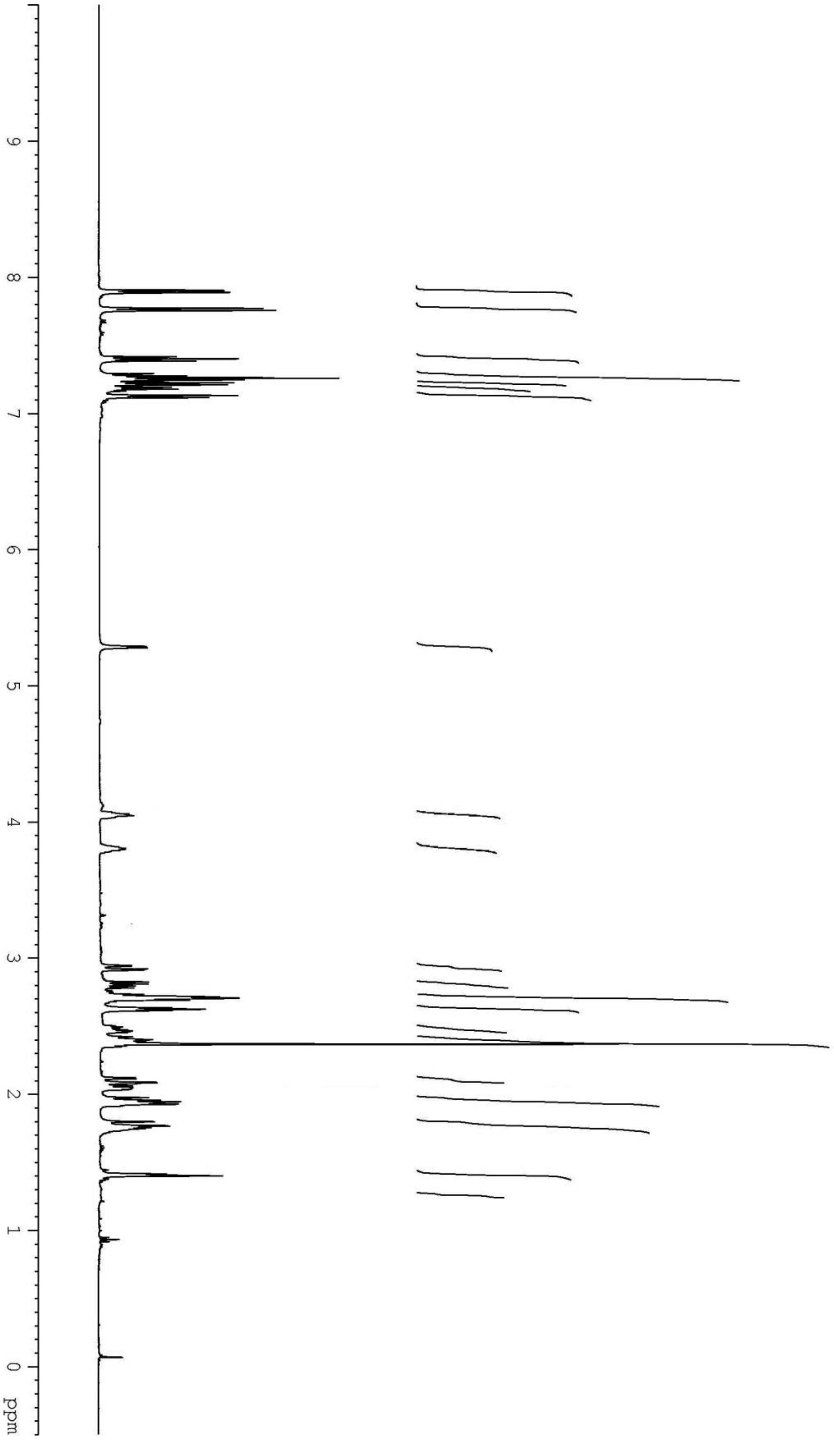


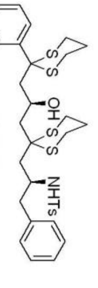
9
8
7
6
5
4
3
2
1
0
ppm
S S
OH S S
NHTs
(R,S)-10



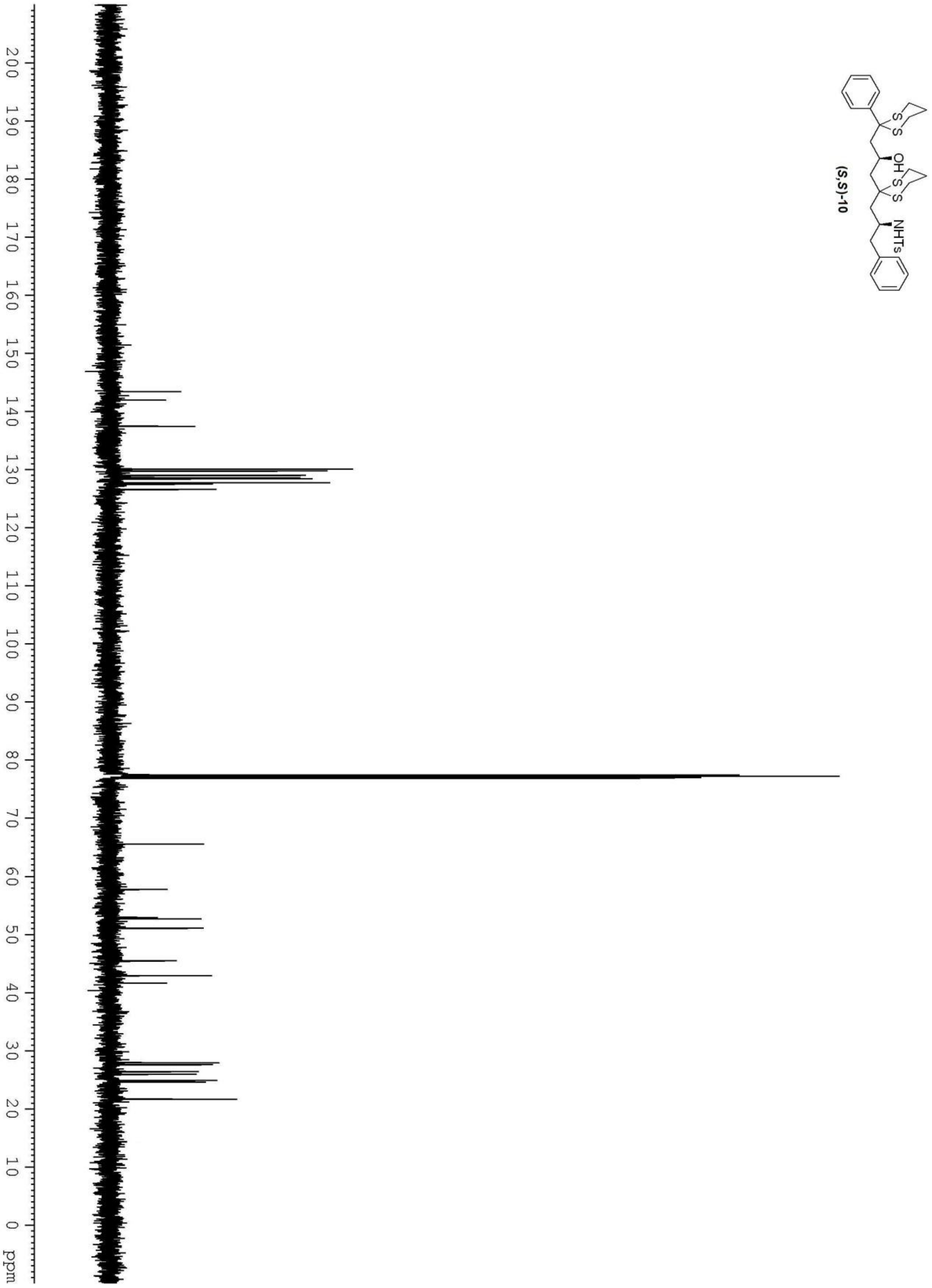
(R,S)-10

S
S
OH
S
S
NHTs
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

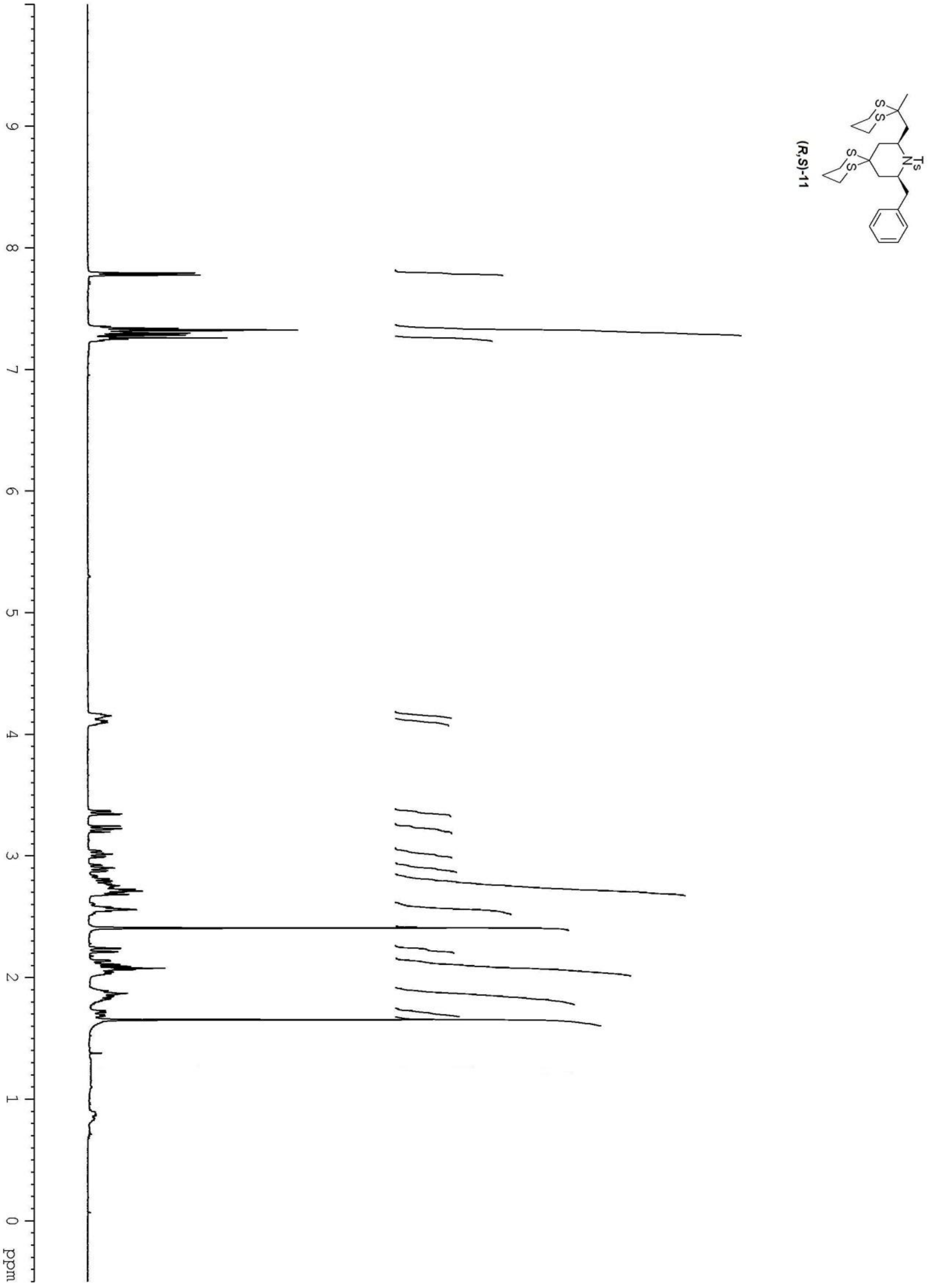




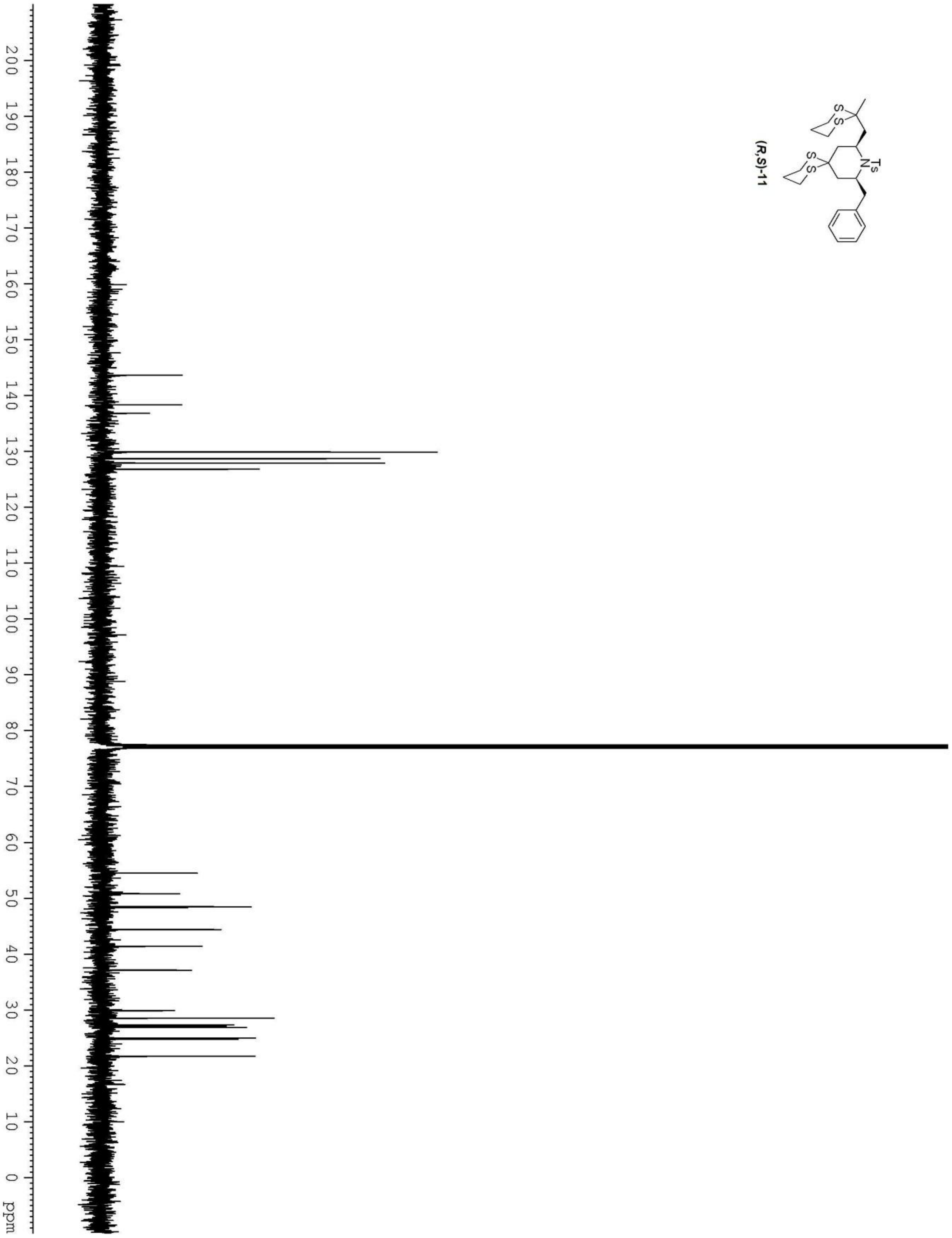
(S,S)-10


(S,S)-10

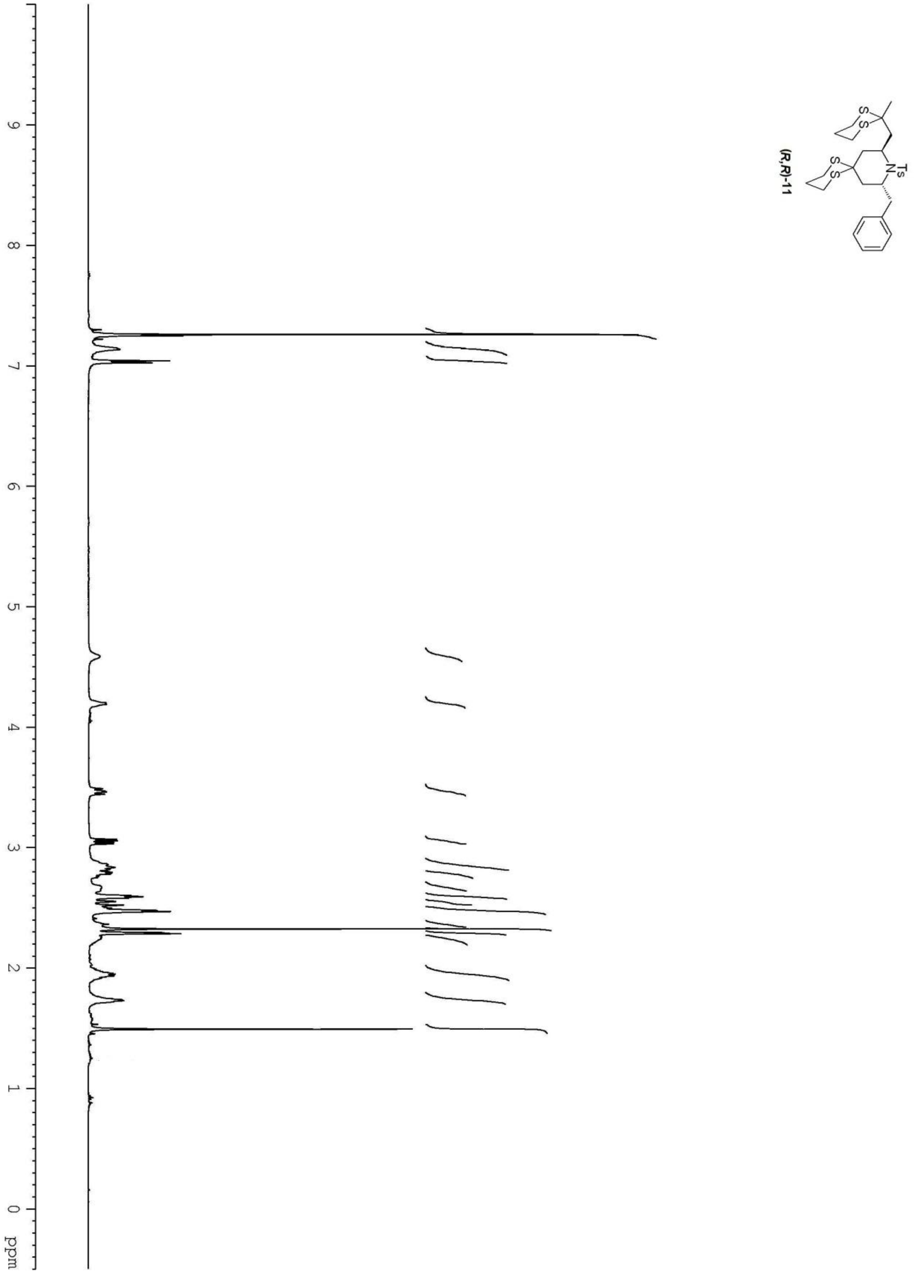
OH
NHTs
S
S
S
S
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



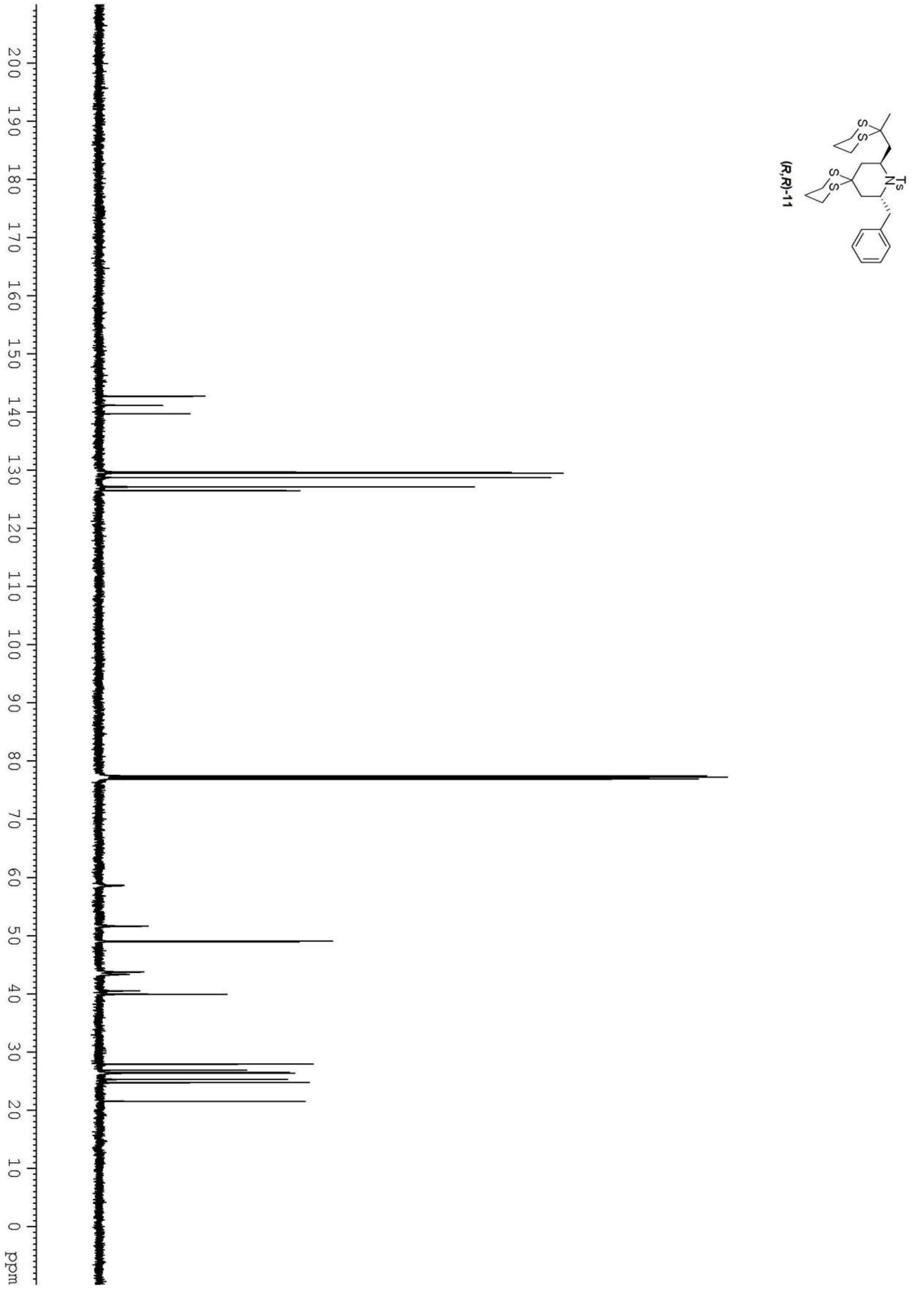
(R,S)-11
Ts
N
S
S
S
S
9
8
7
6
5
4
3
2
1
0
ppm

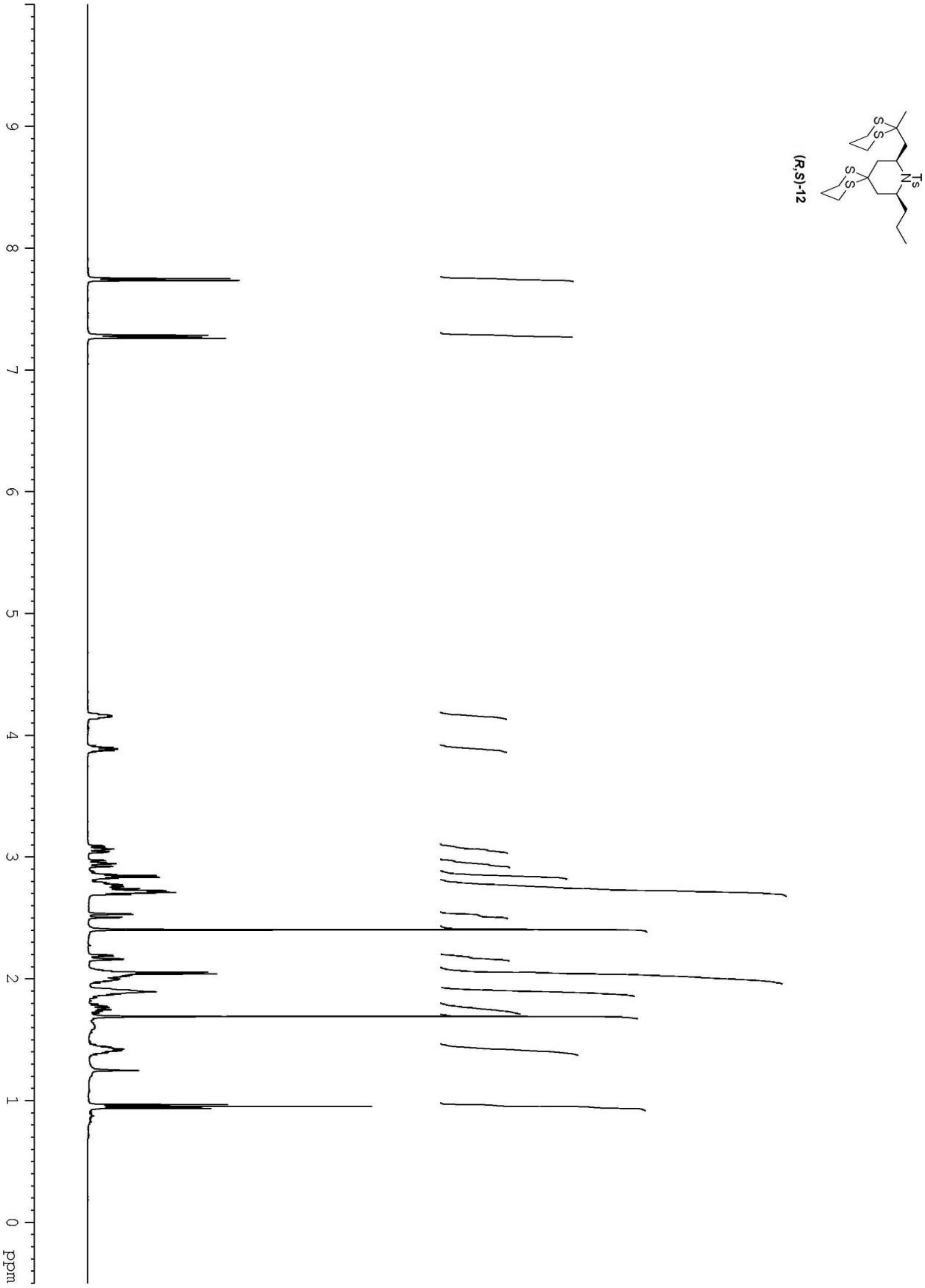

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
Ts
N
S
S
S
S

(R,S)-11

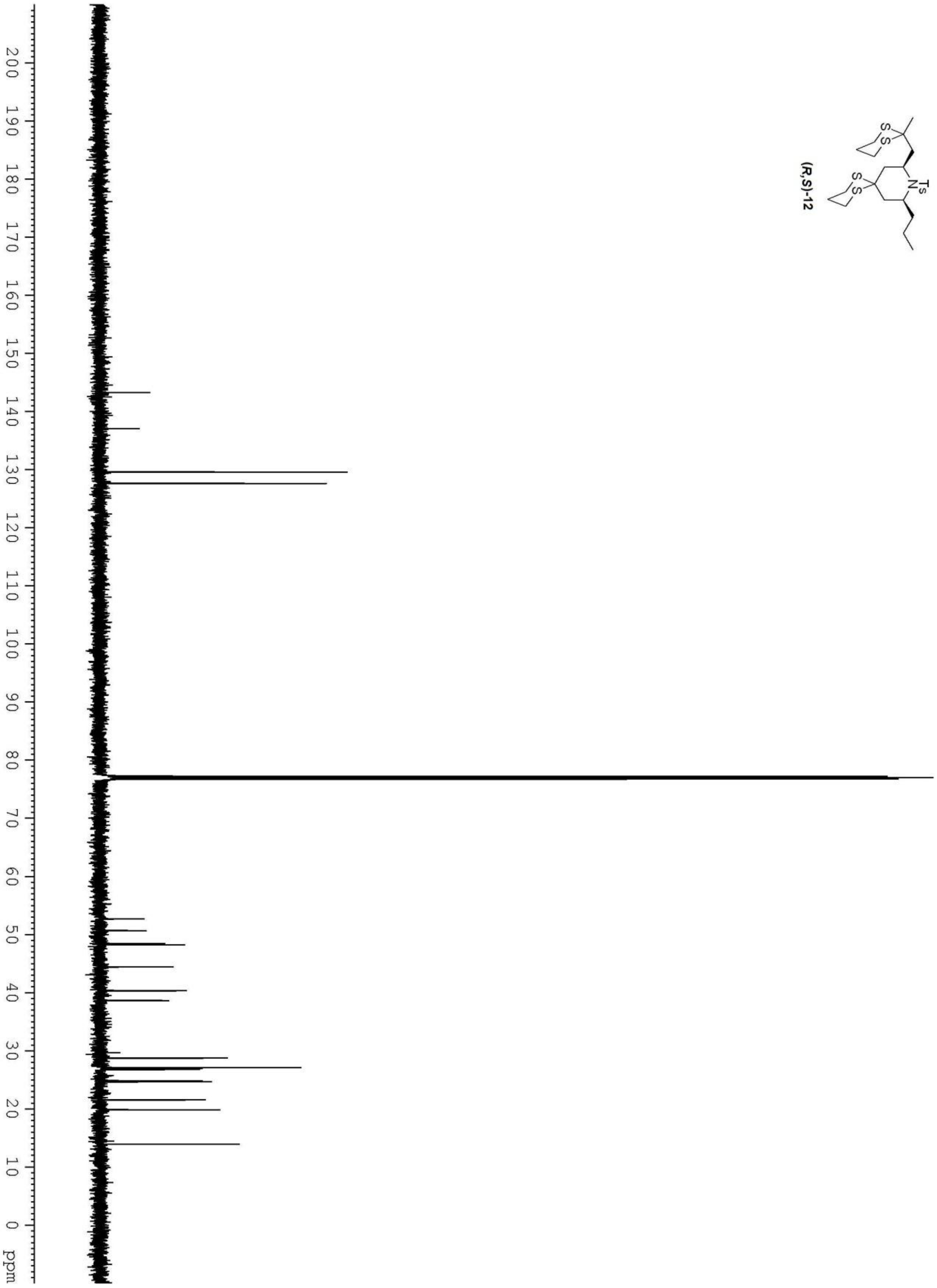


(R,R)-11

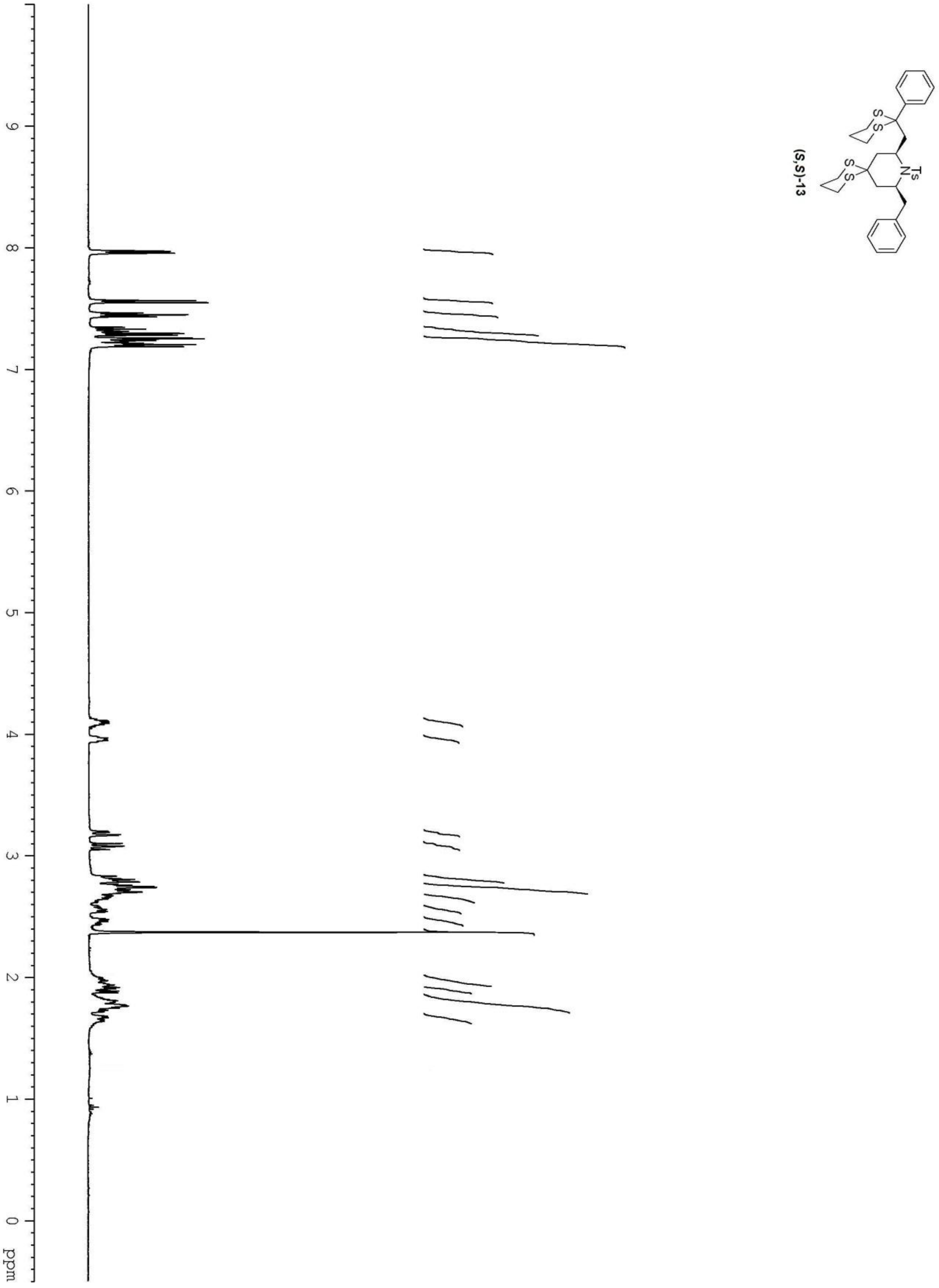
(R,R)-11
Ts
N
S
S
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



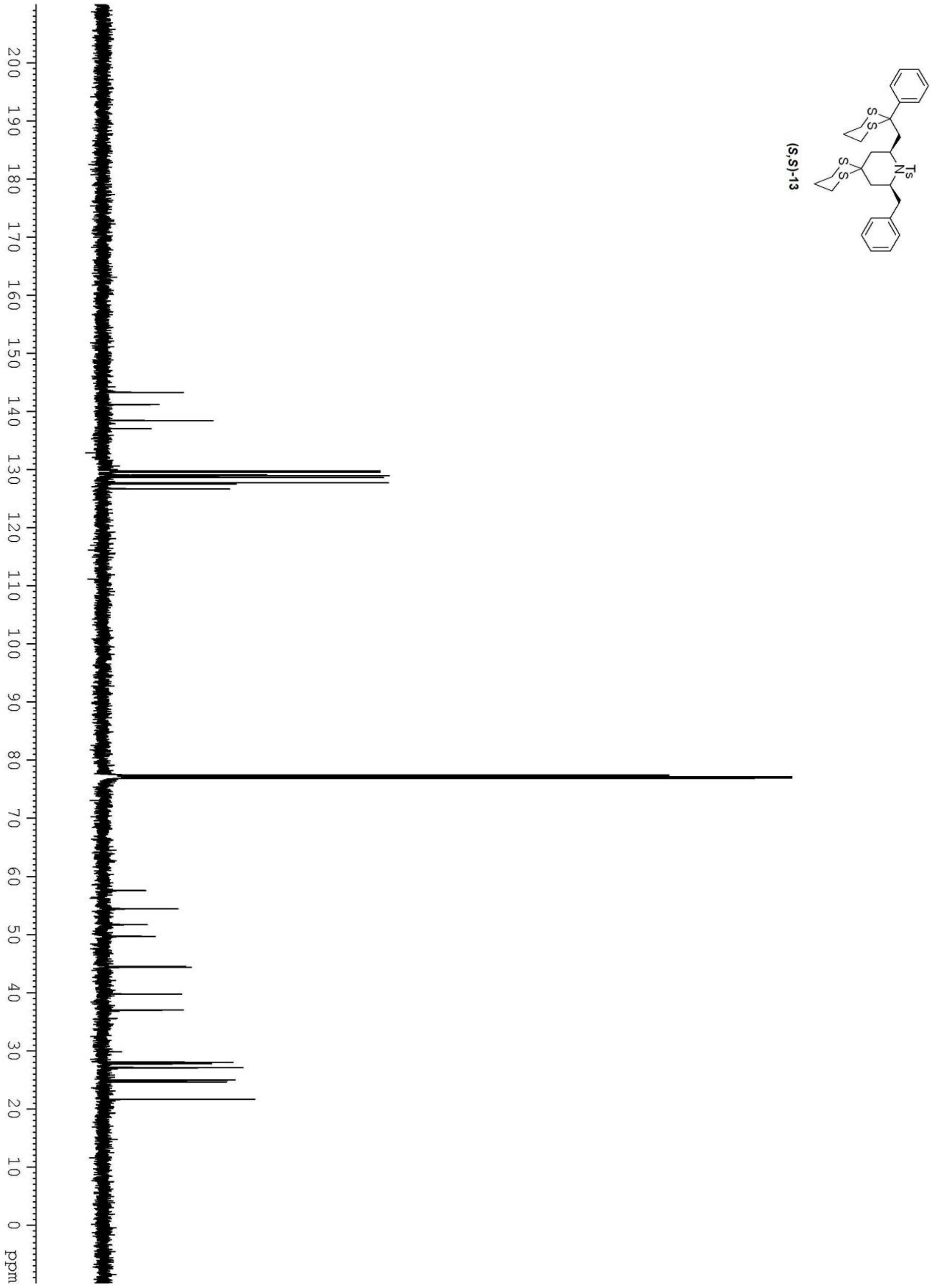
(R,S)-12

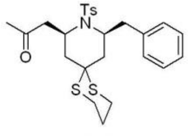

Ts
N
S
S
S
S
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

(*R*,*S*)-12

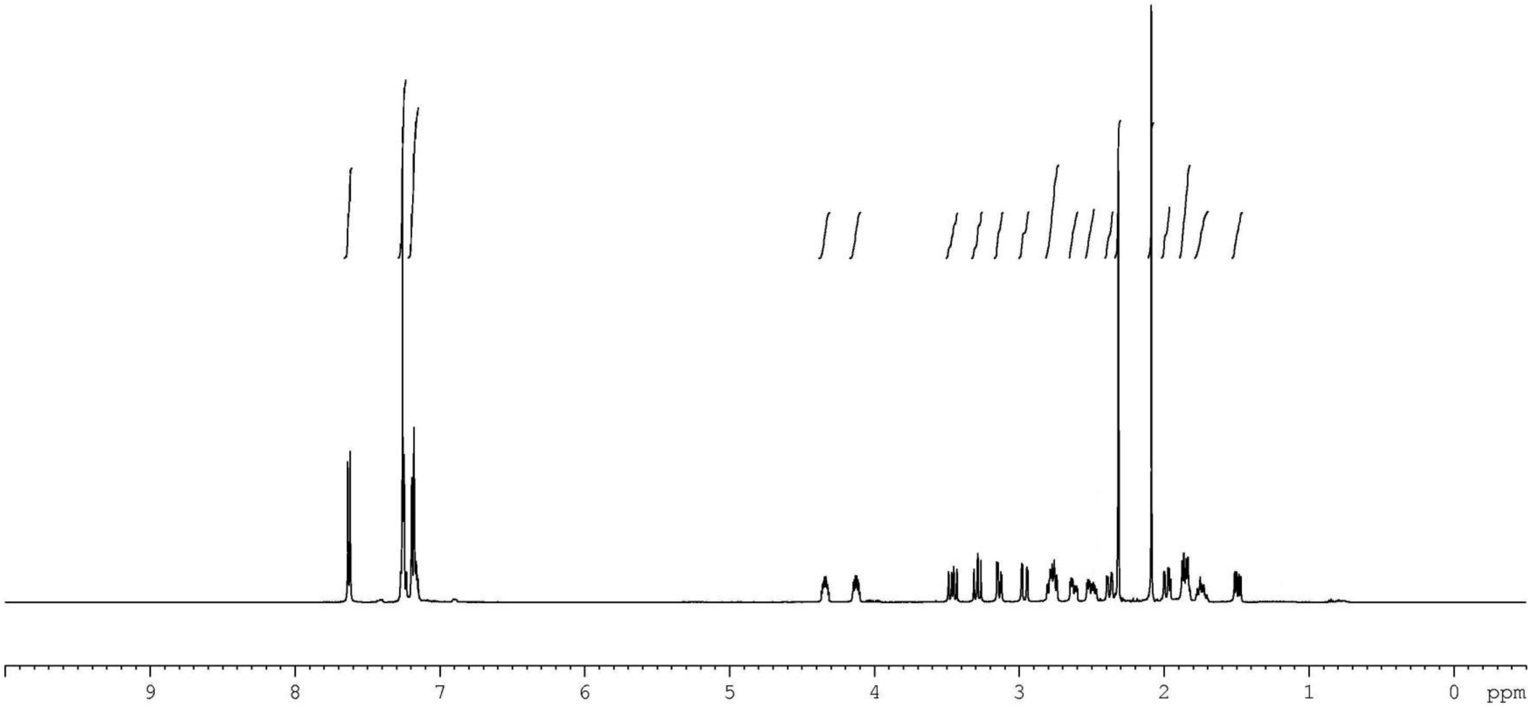


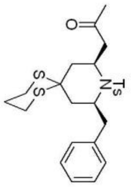
(S,S)-13


(S,S)-13
Ts
N
S
S
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

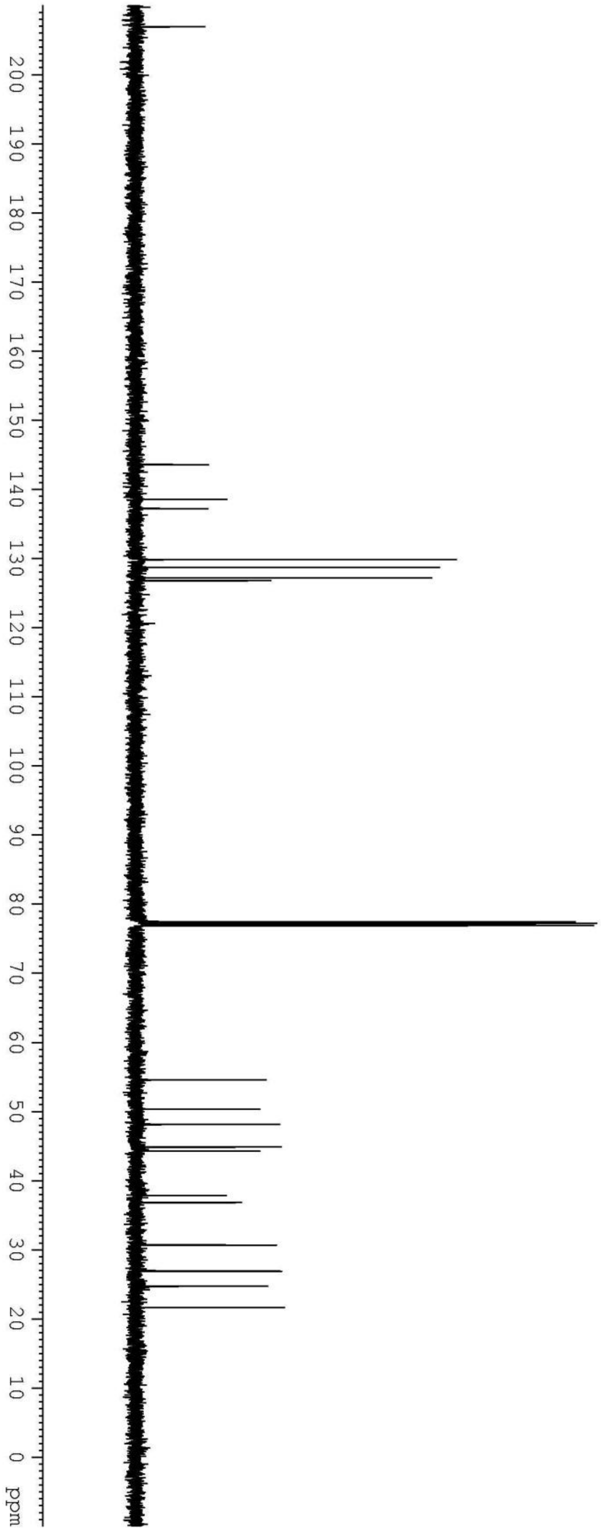


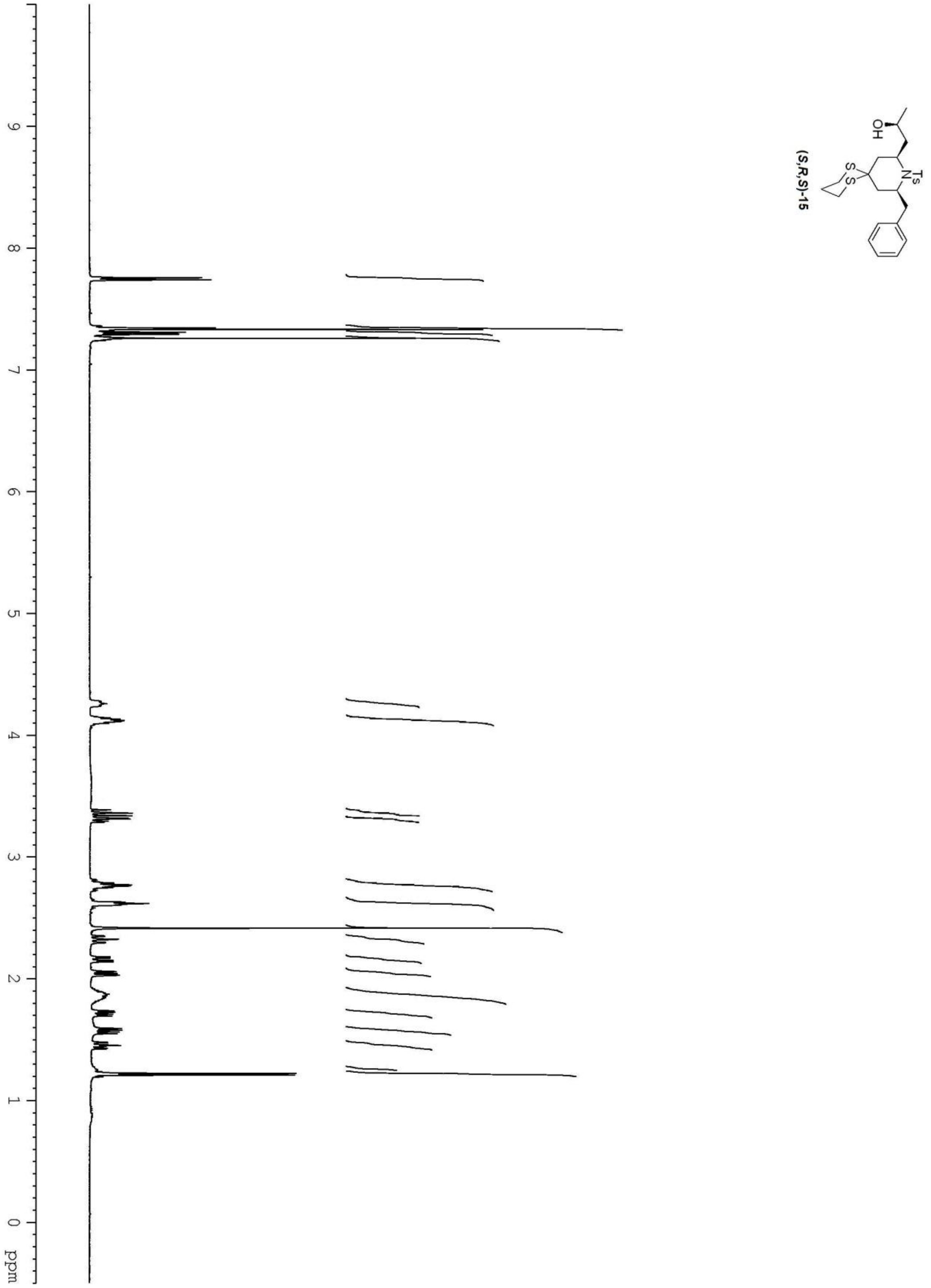
(*R*,*S*)-14

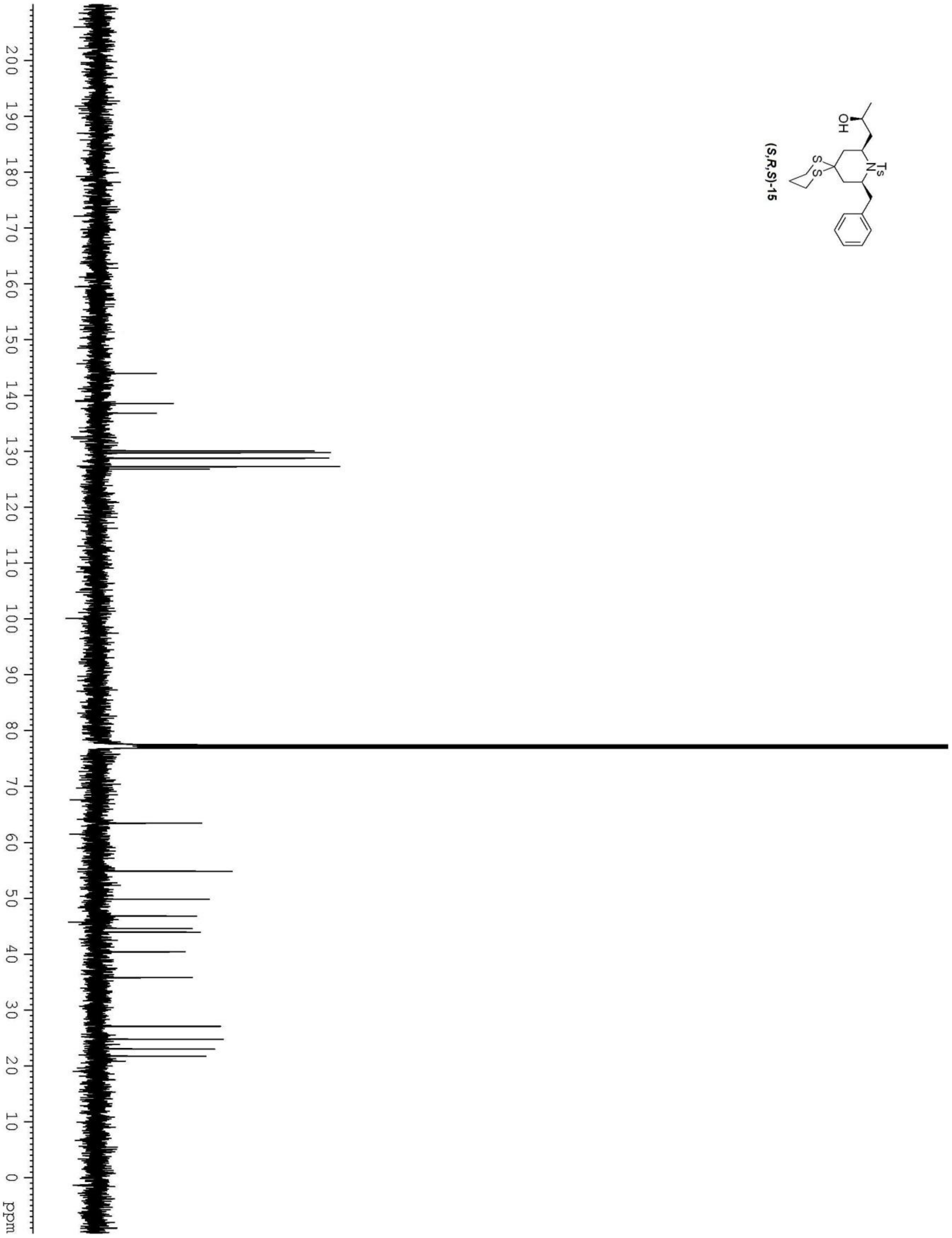



O
Ts
N
S
S

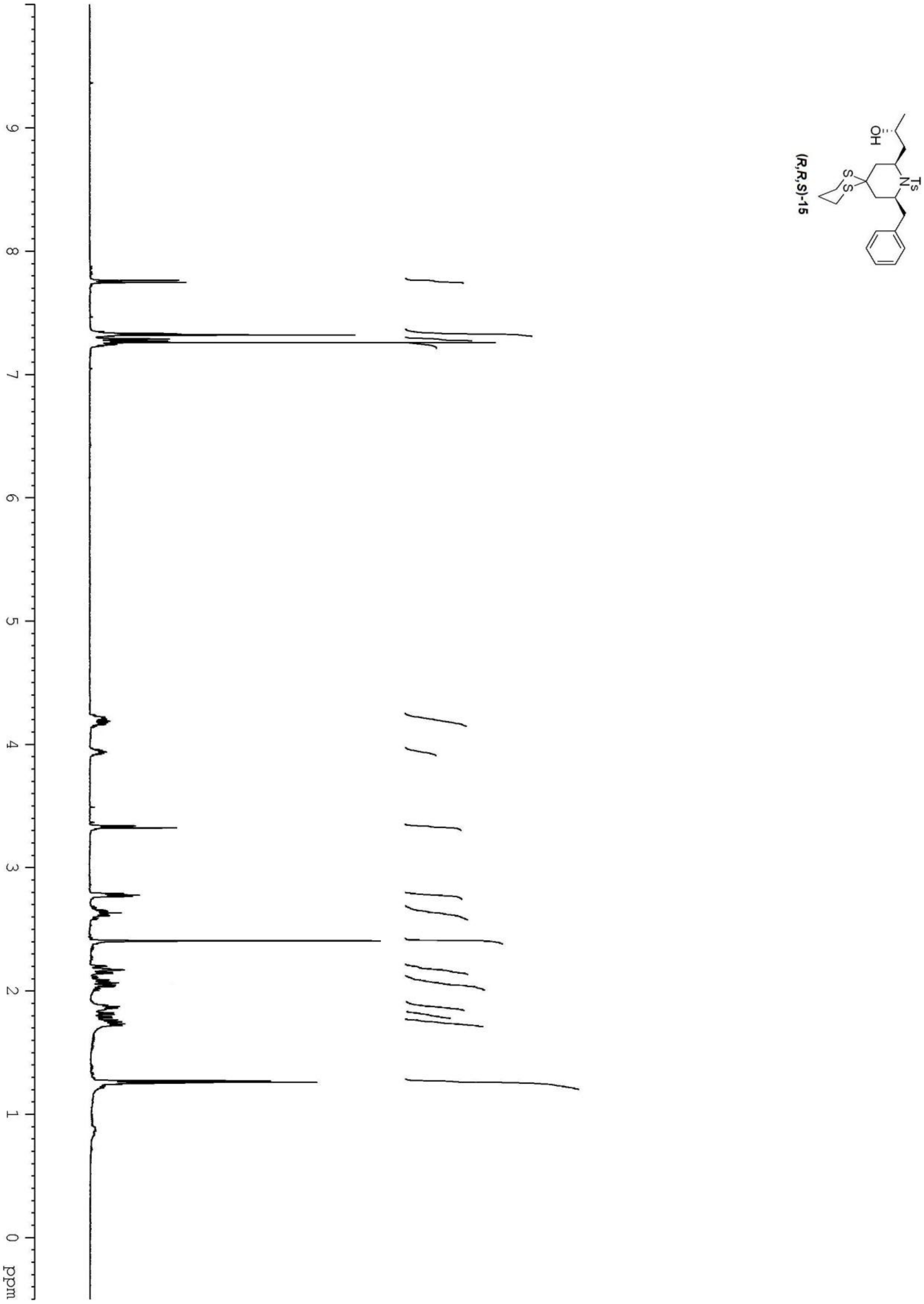
(R,S)-14


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

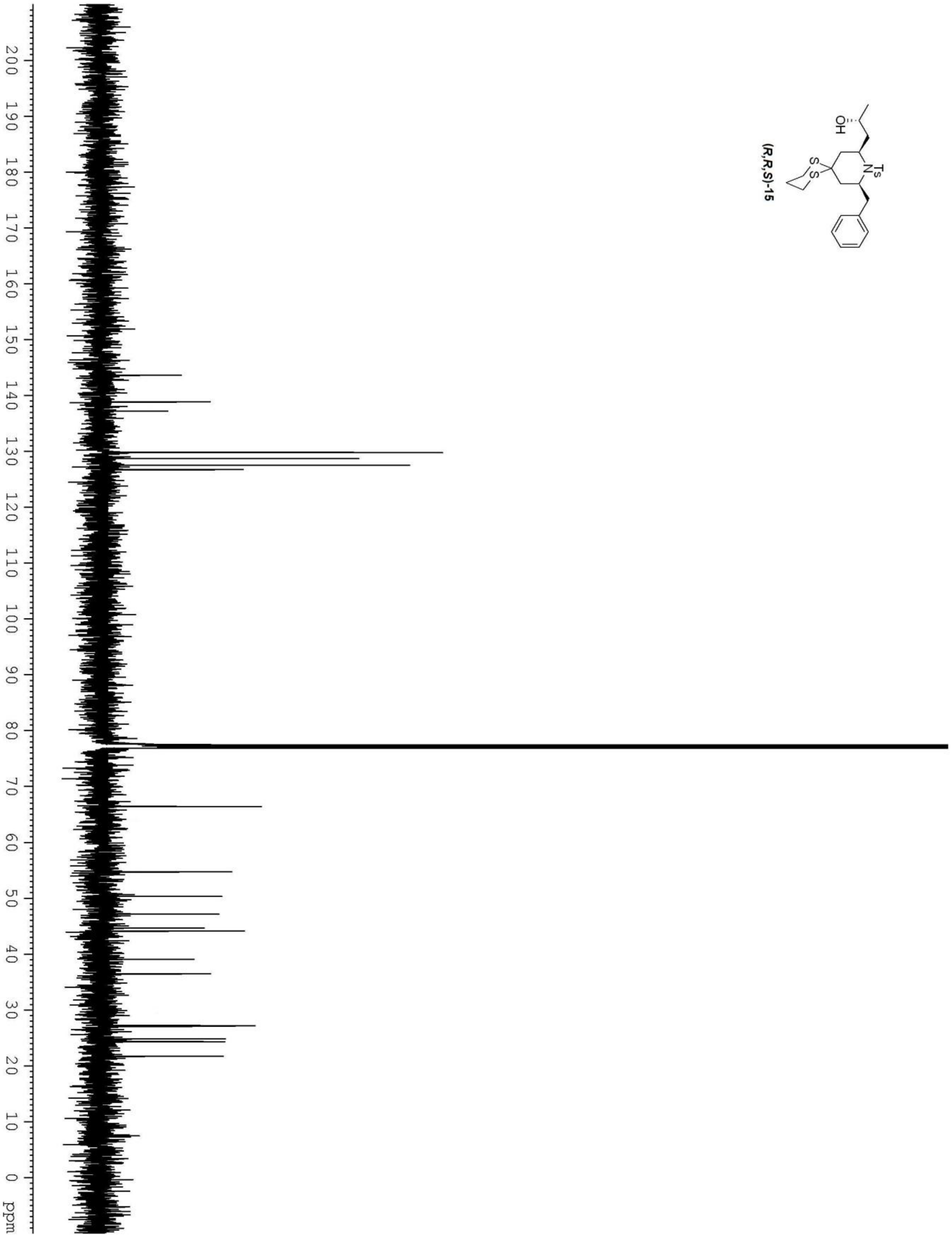

(S,R,S)-15


(S,R,S)-15

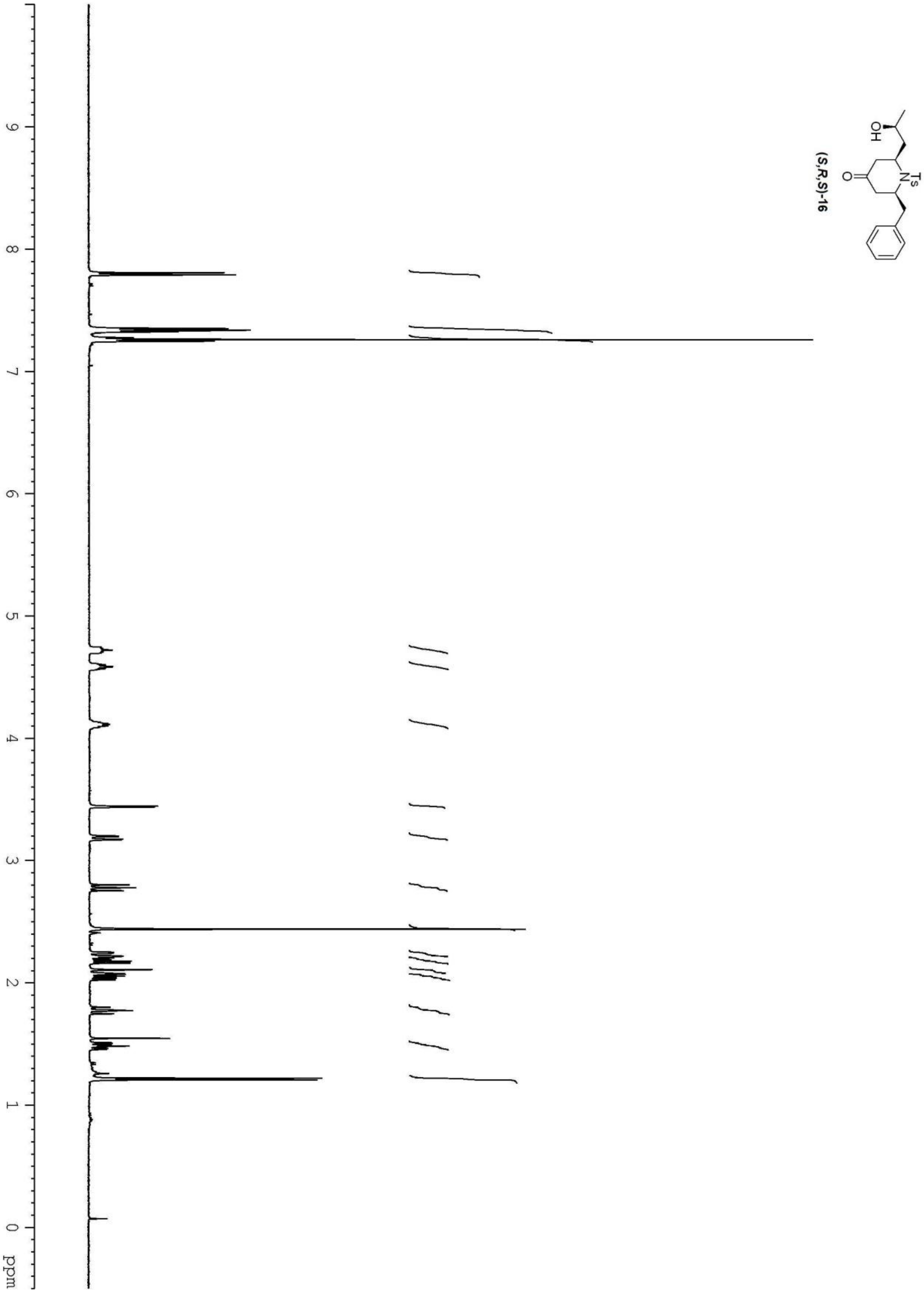
Ts
N
OH
S
S
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



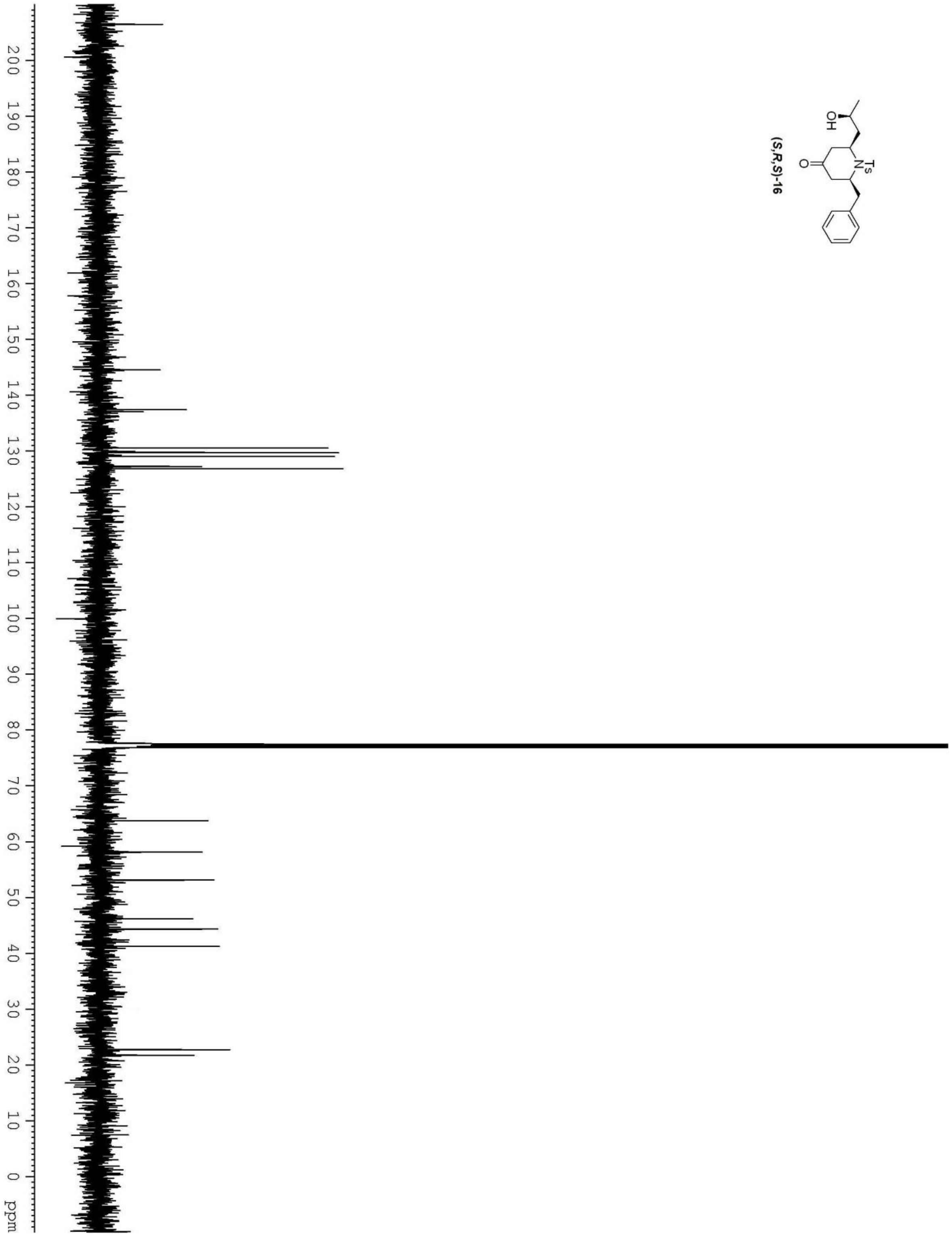
(R,R,S)-15


Ts
N
S
S
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

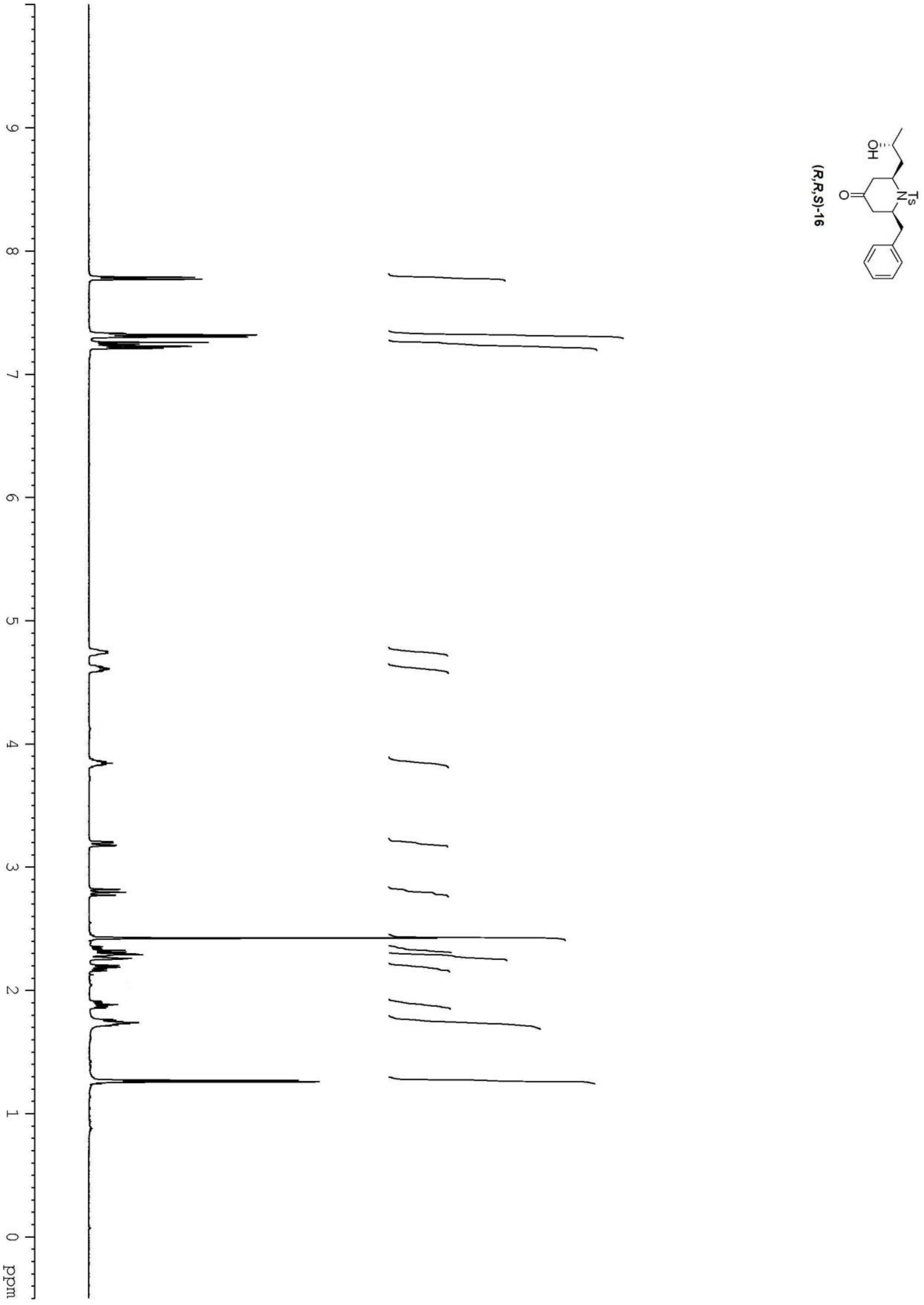
(R,R,S)-15



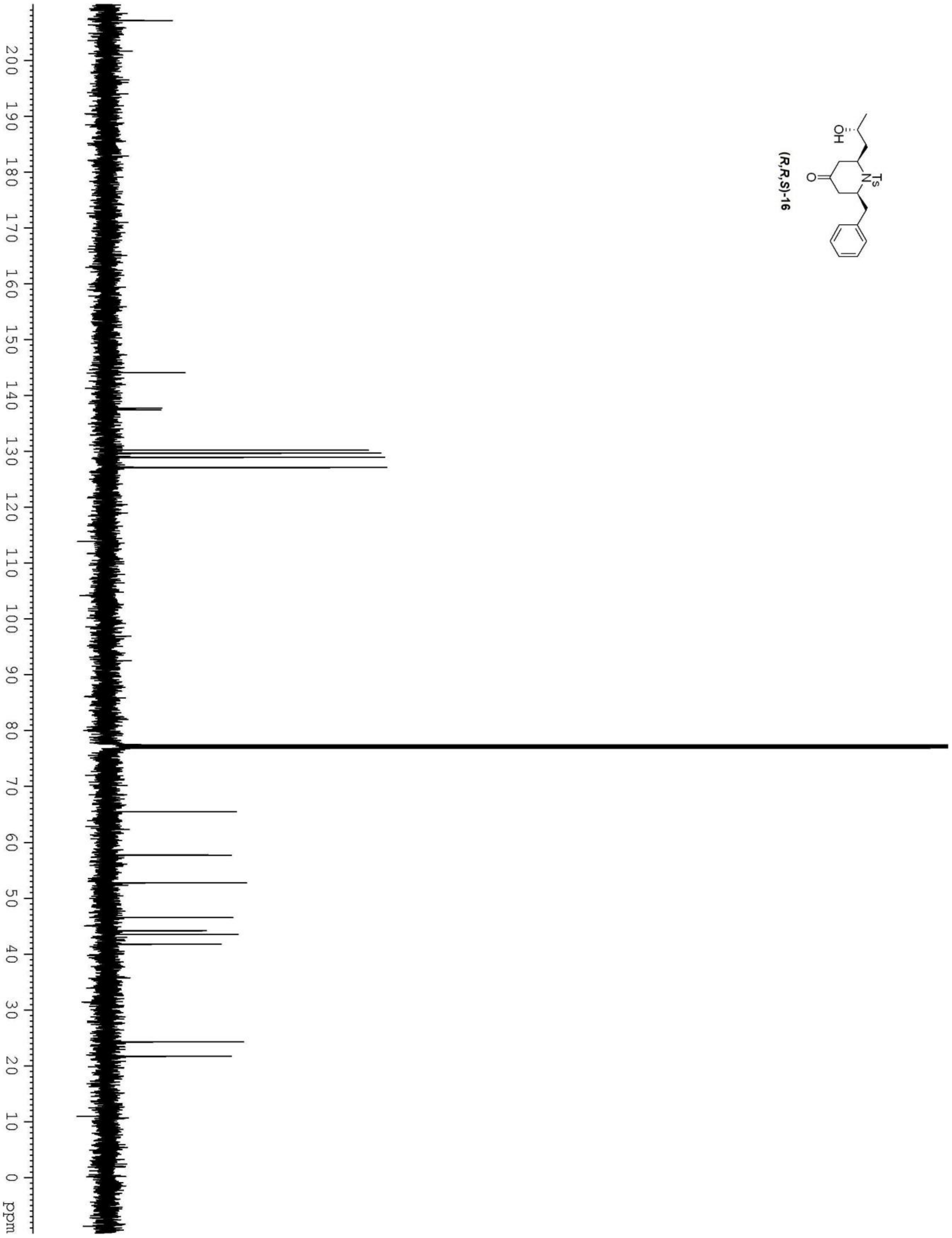
(S,R,S)-16


Ts
N
O
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

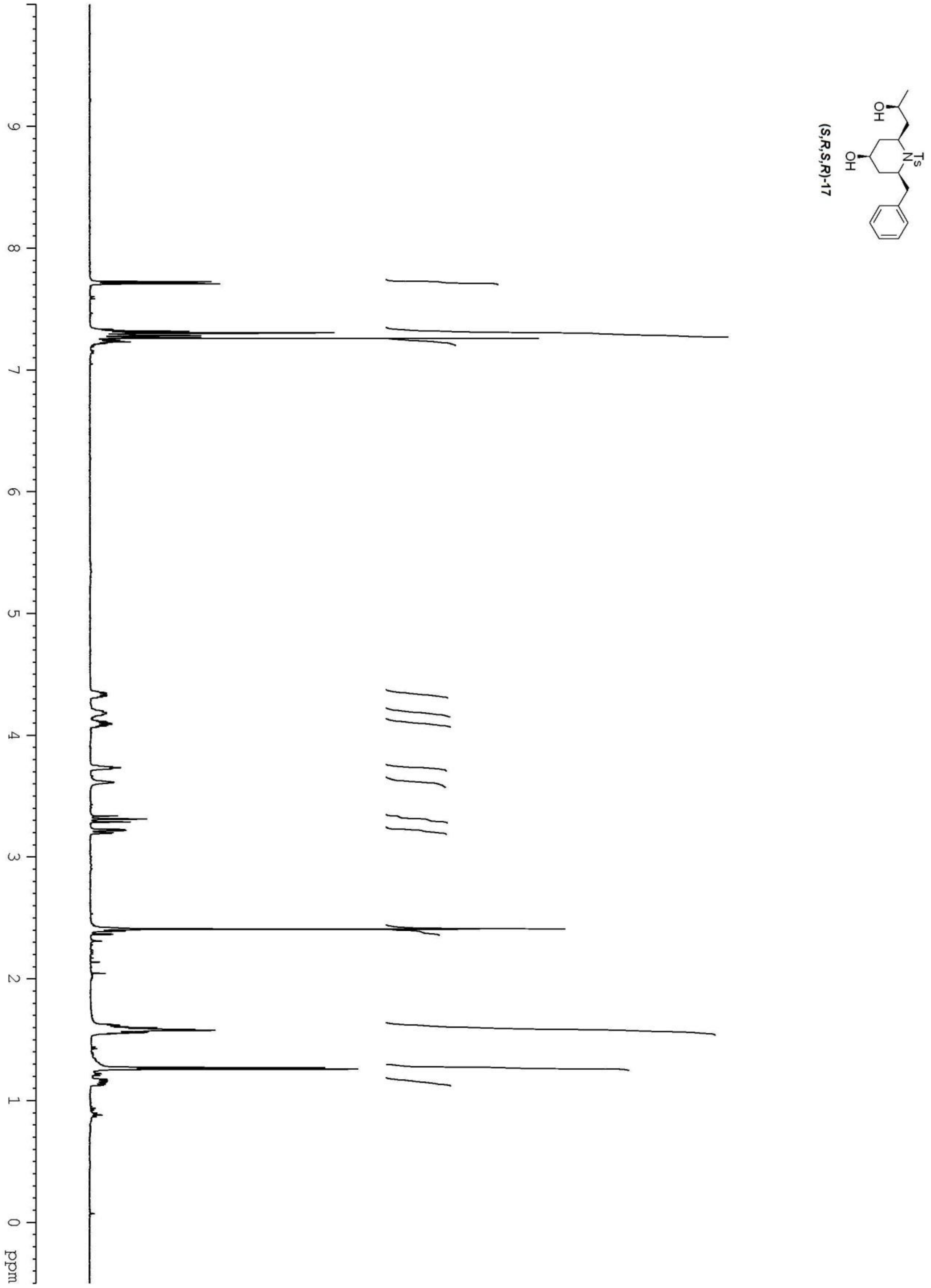
(S,R,S)-16



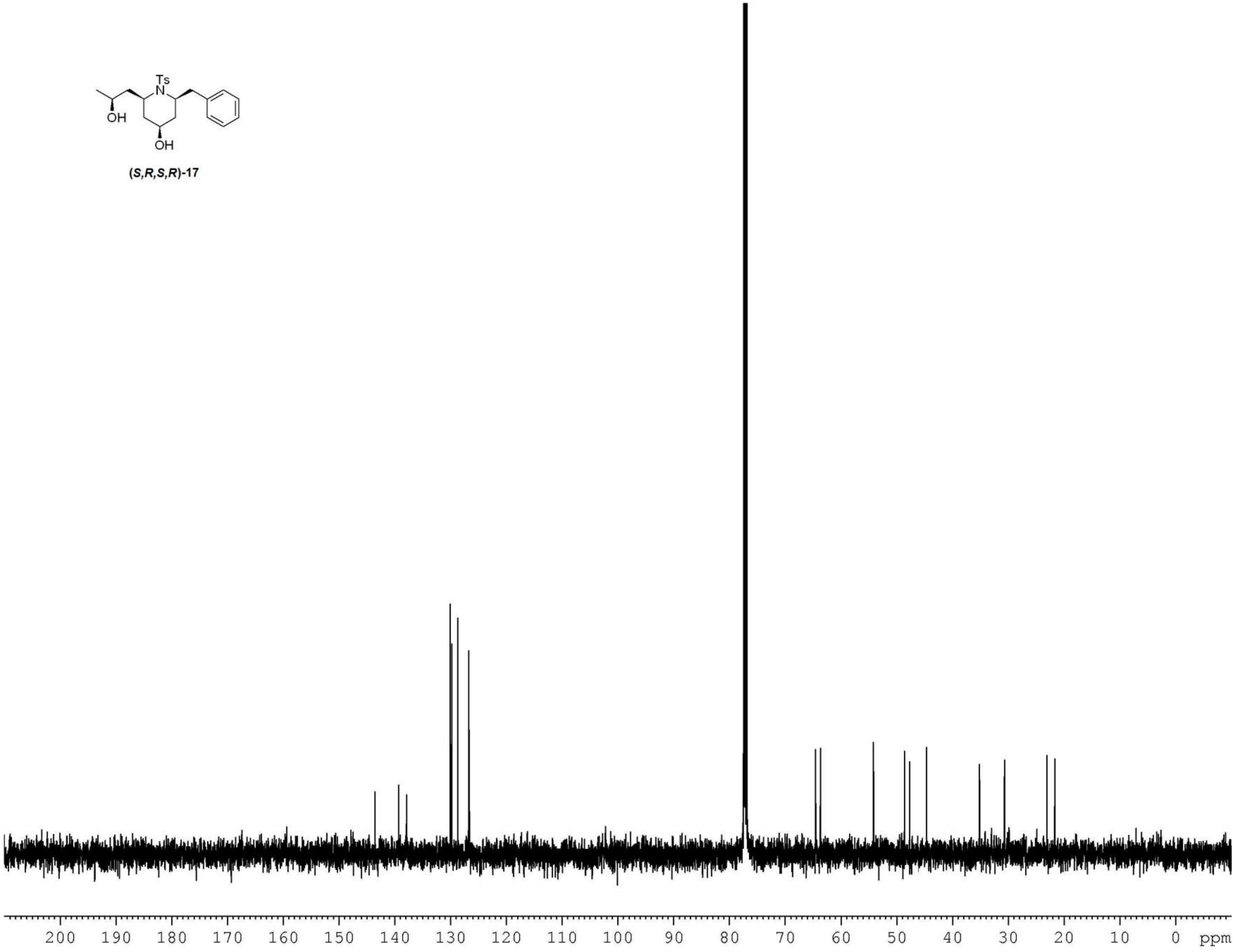
(R,R,S)-16



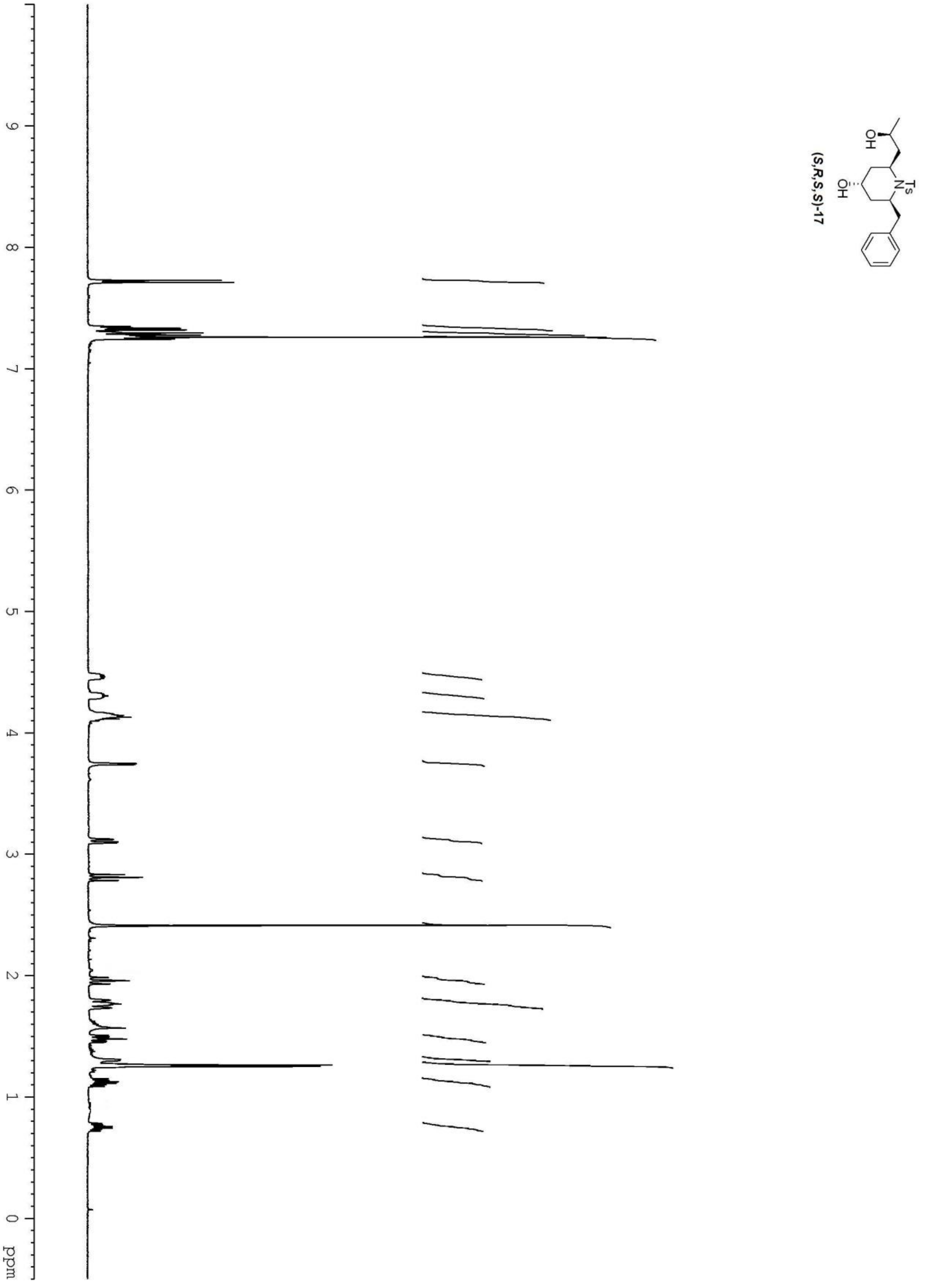
(R,R,S)-16
Ts
N
O
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

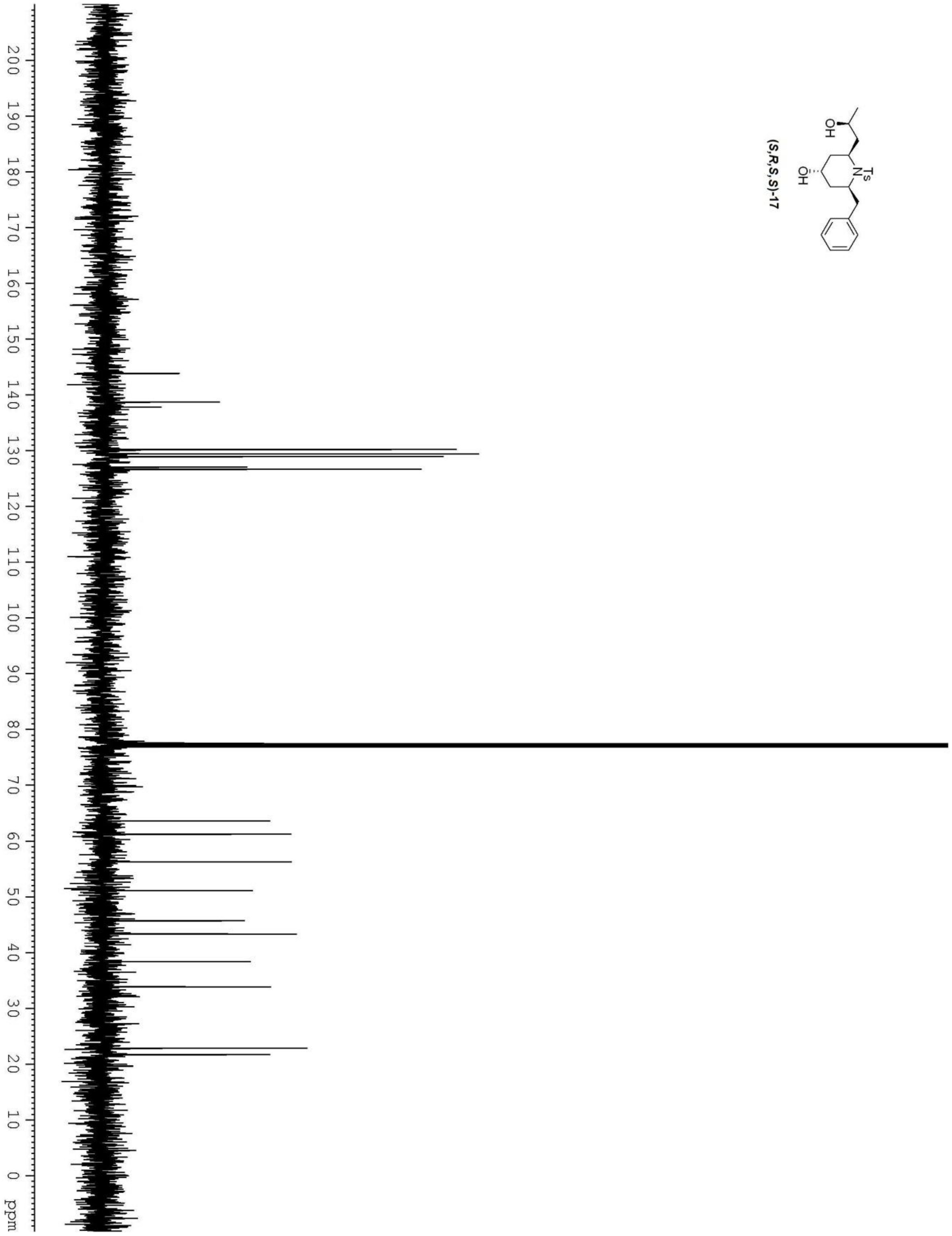


(S,R,S,R)-17

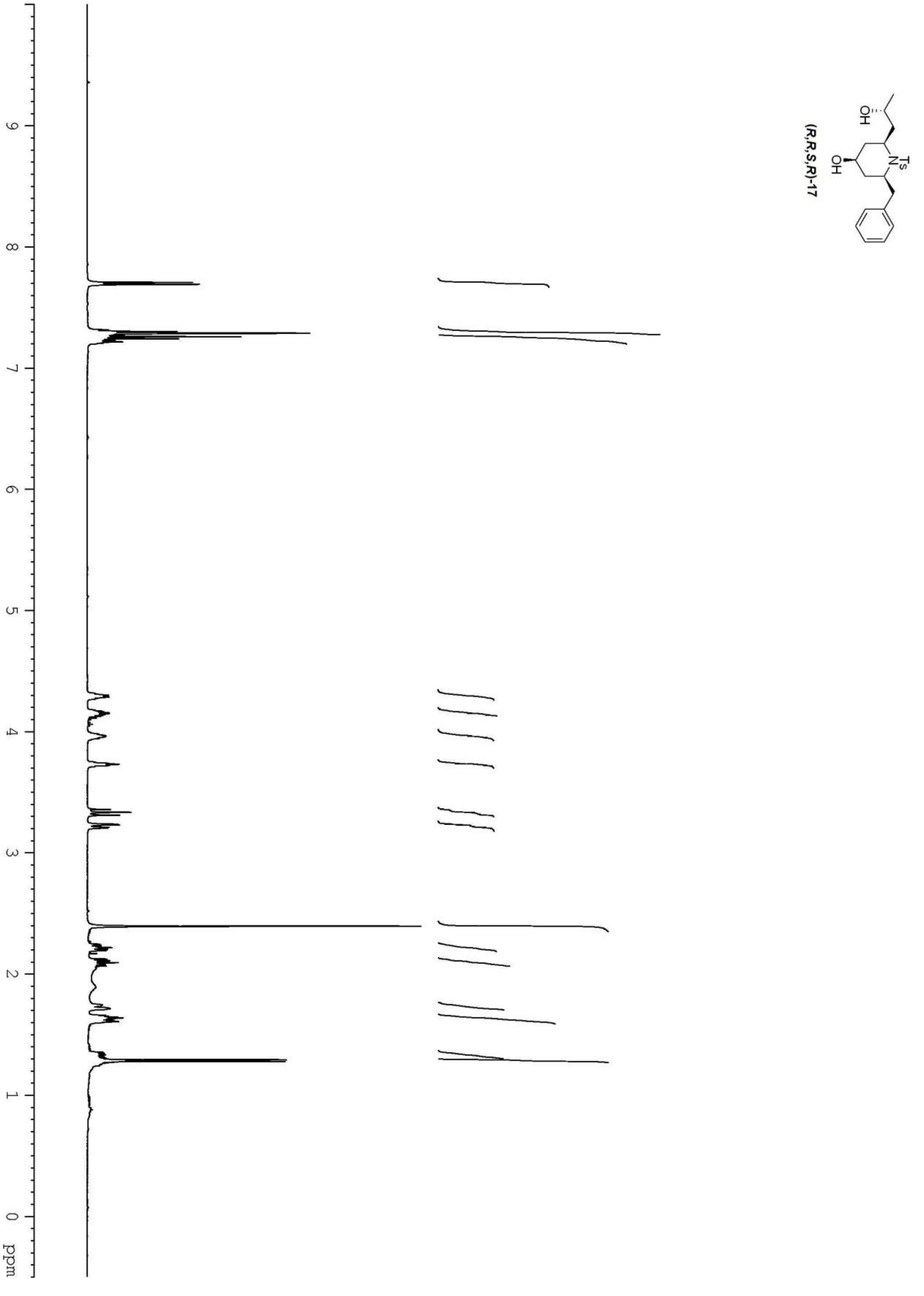
Ts
N
OH
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

(*S*,*R*,*S*,*R*)-**17**

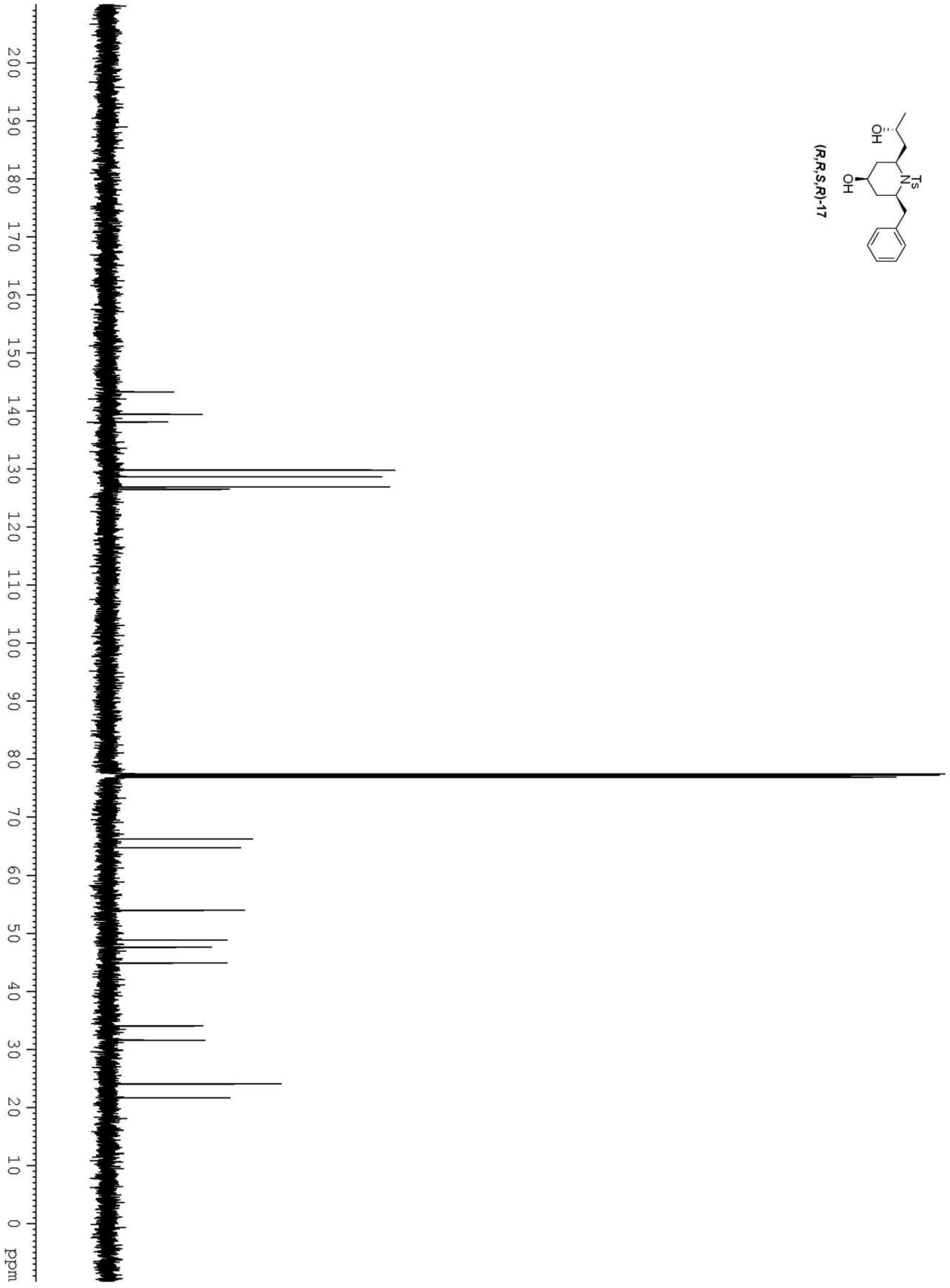

(S,R,S,S)-17

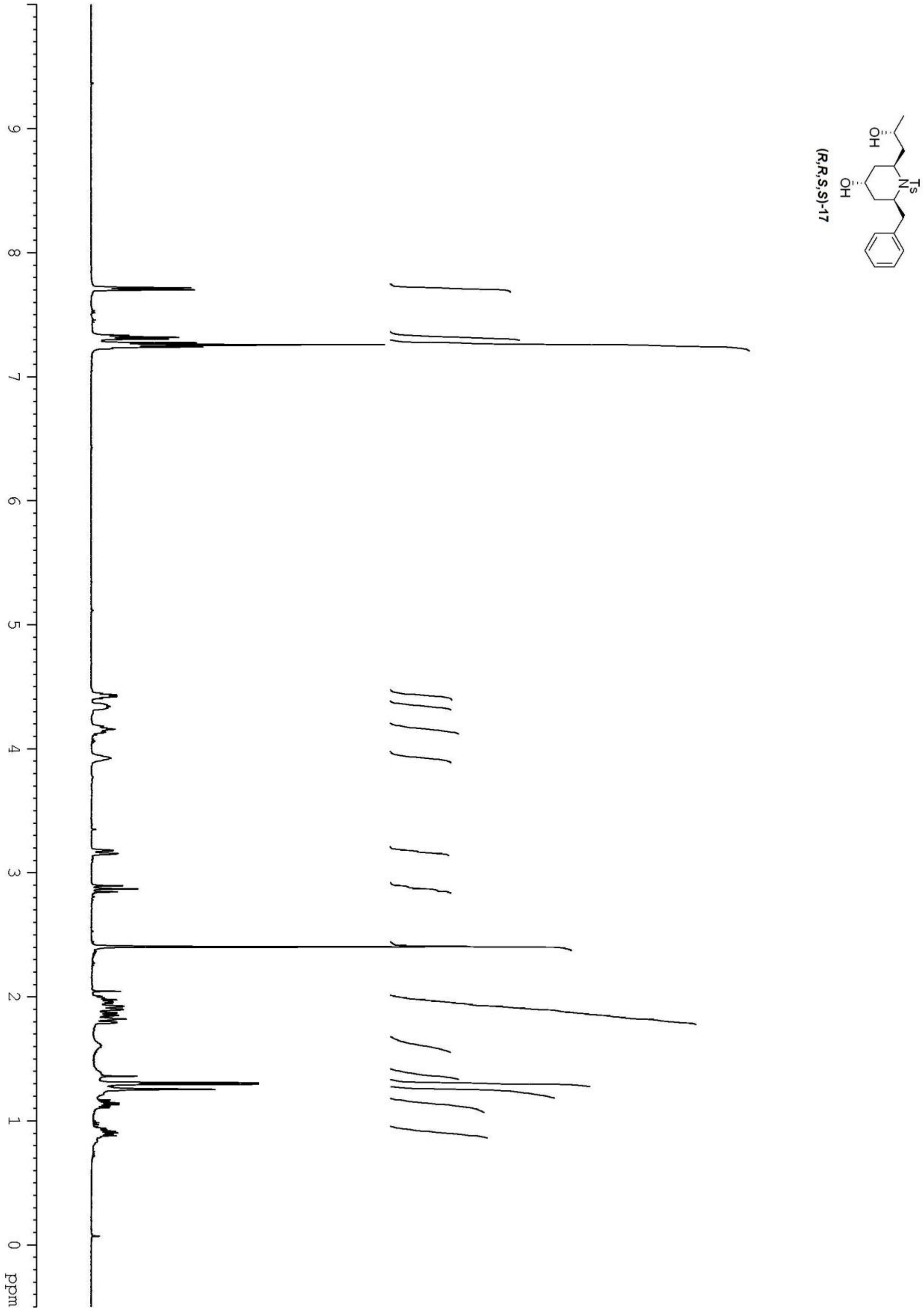

OH
Ts
N
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

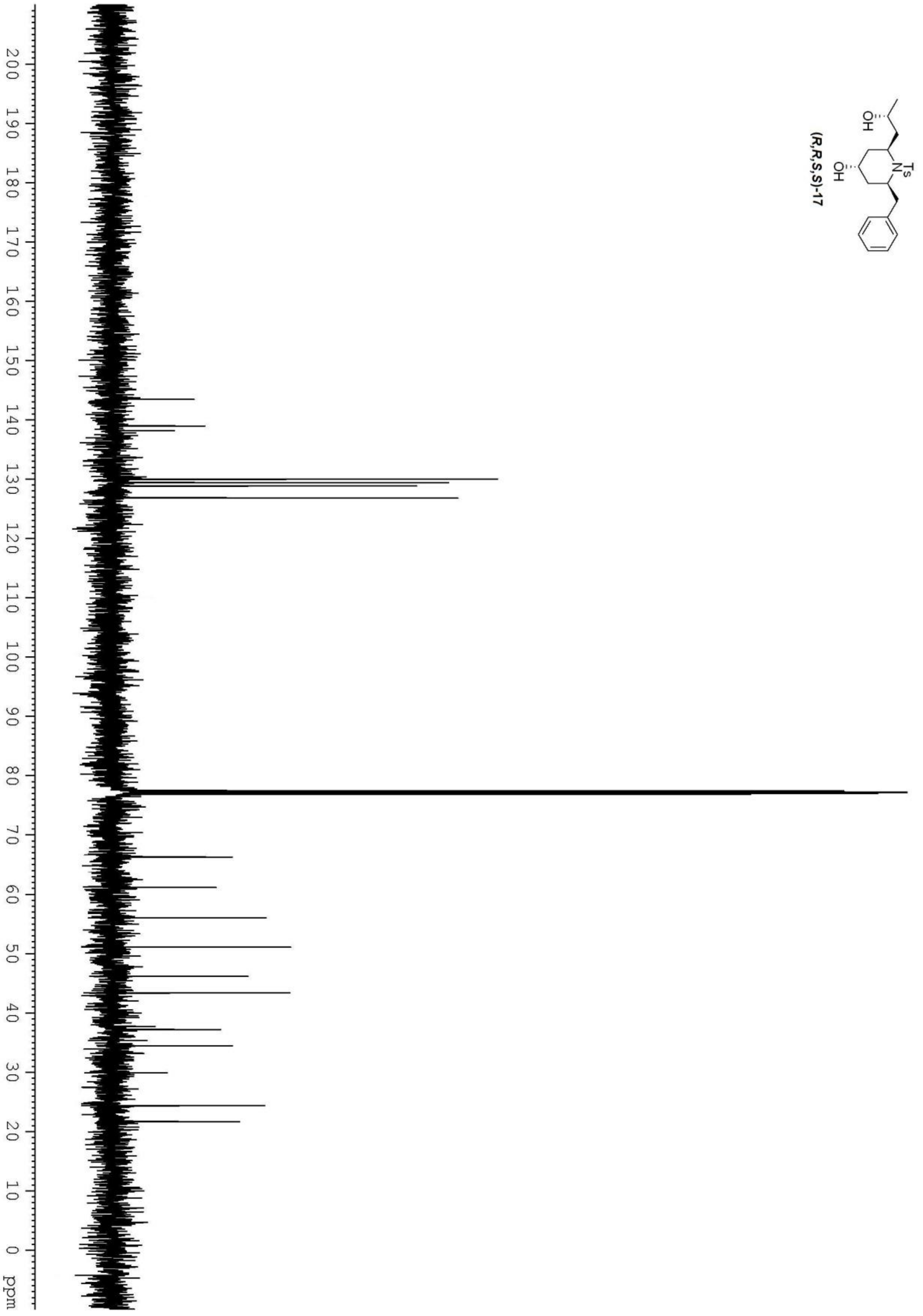
(S,R,S,S)-17



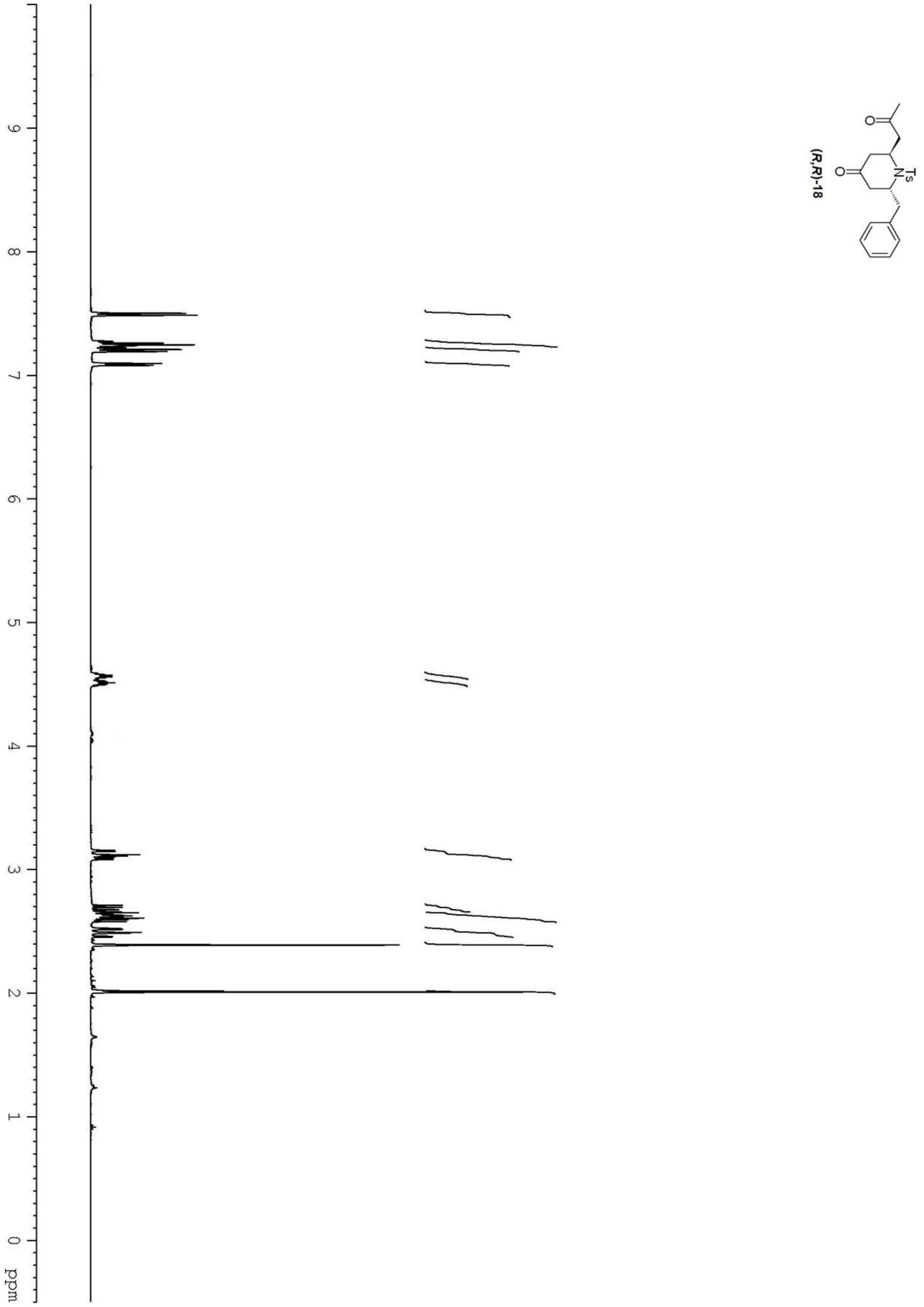
(R,R,S,R)-17


(R,R,S,R)-17
Ts
N
OH
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

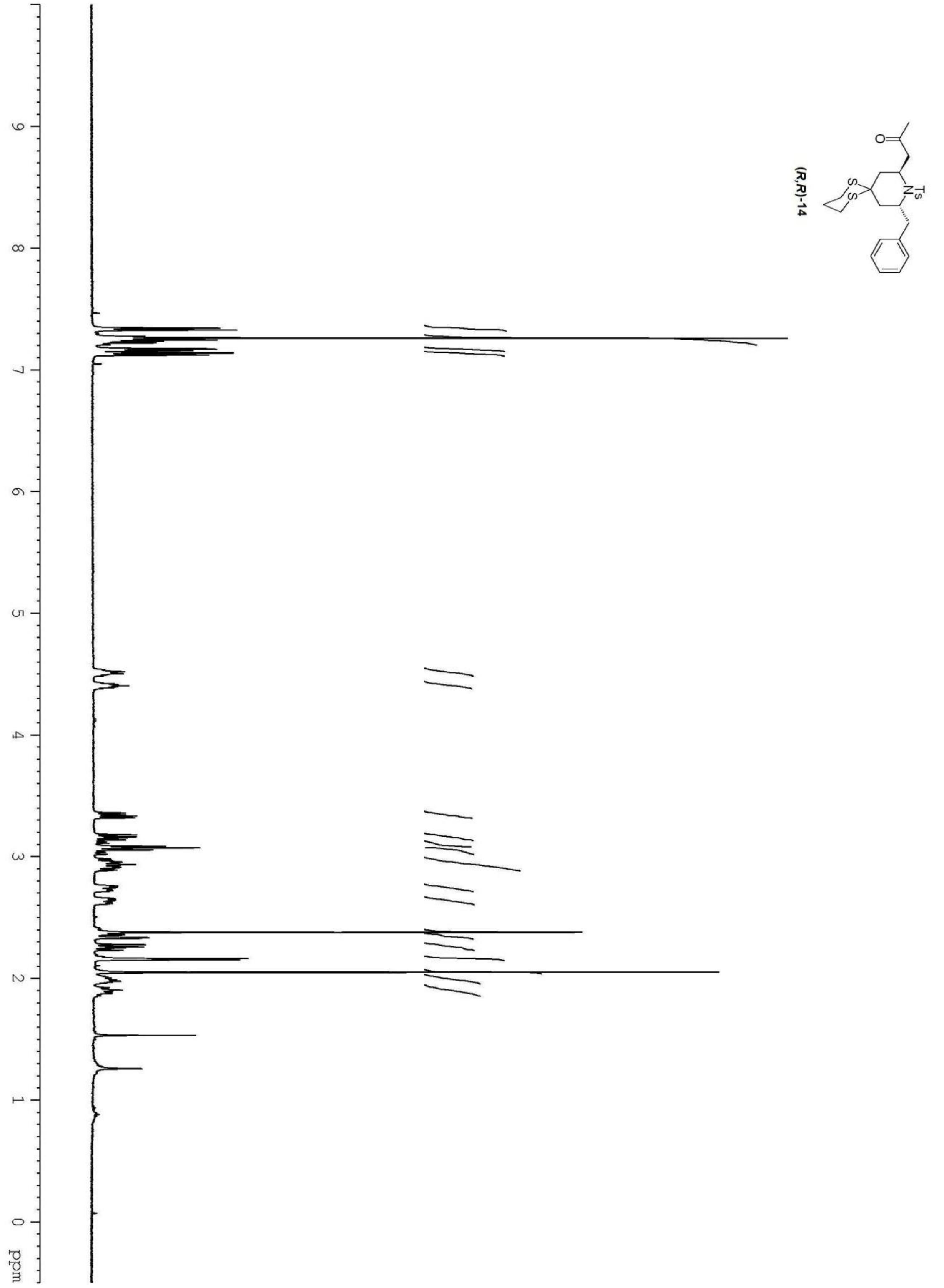

(R,R,S,S)-17


Ts
N
OH
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

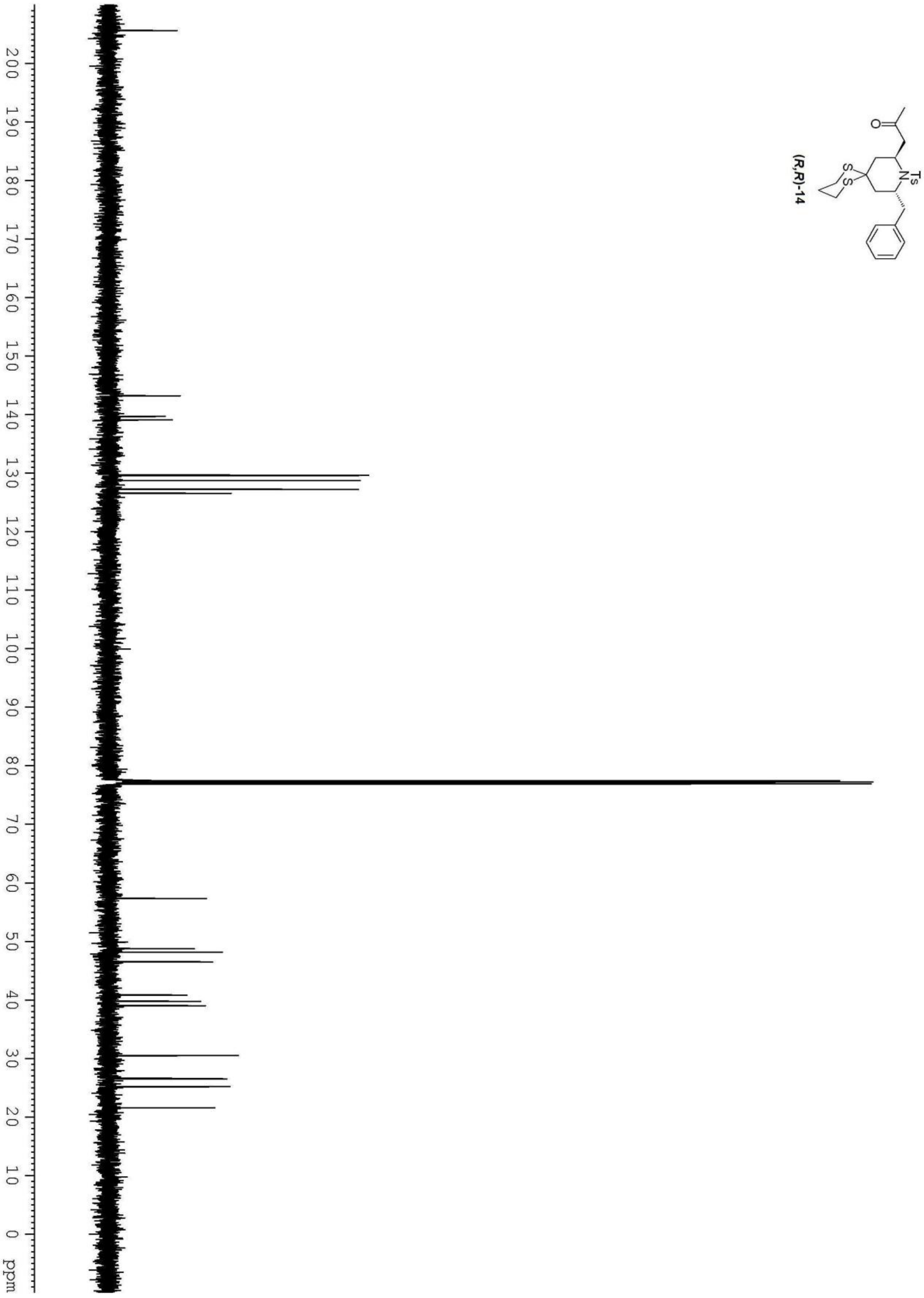
(R,R,S,S)-17



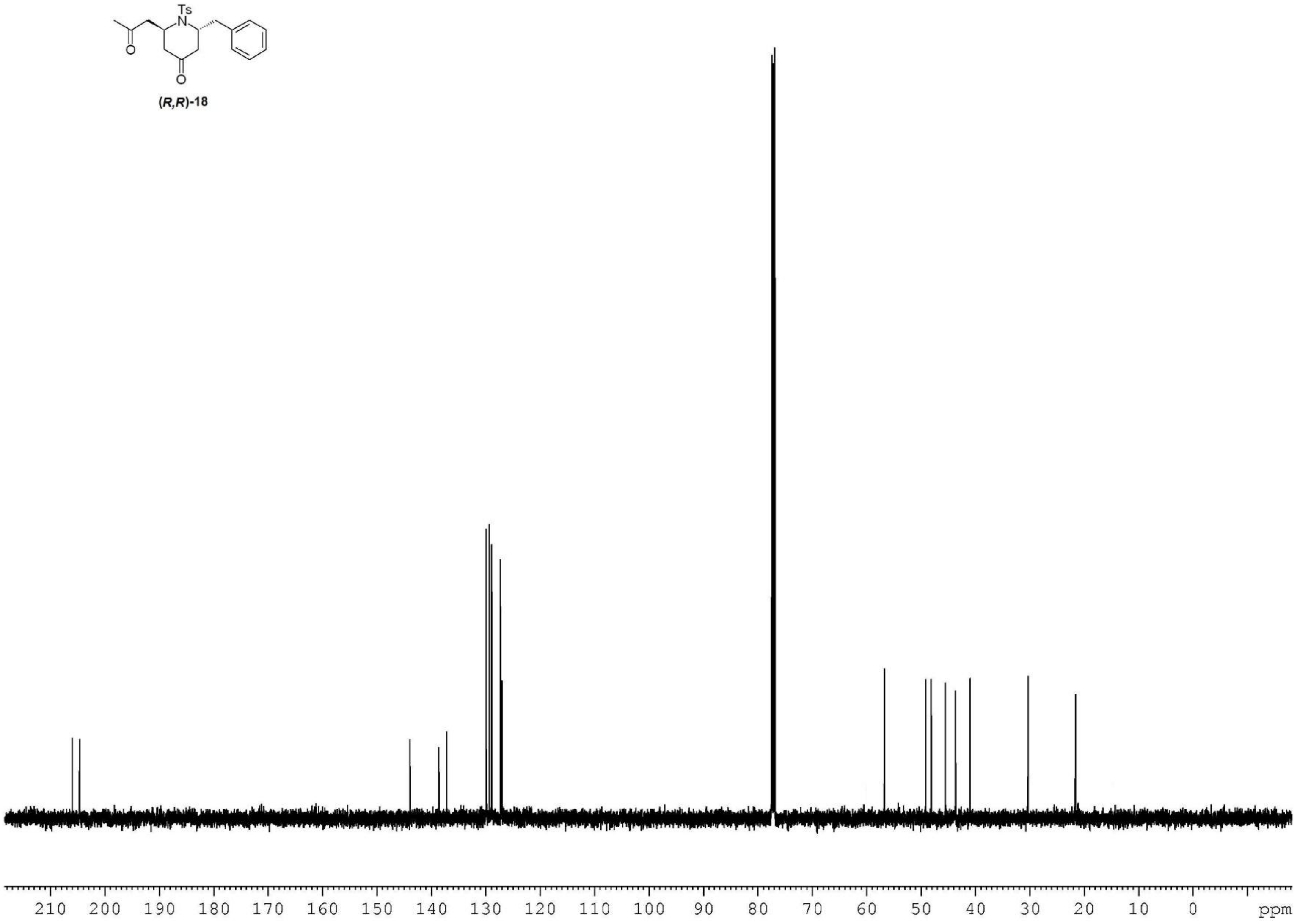
(R,R)-18



(R,R)-14

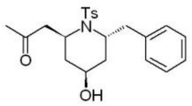

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
Ts
N
S
S
O

(R,R)-14

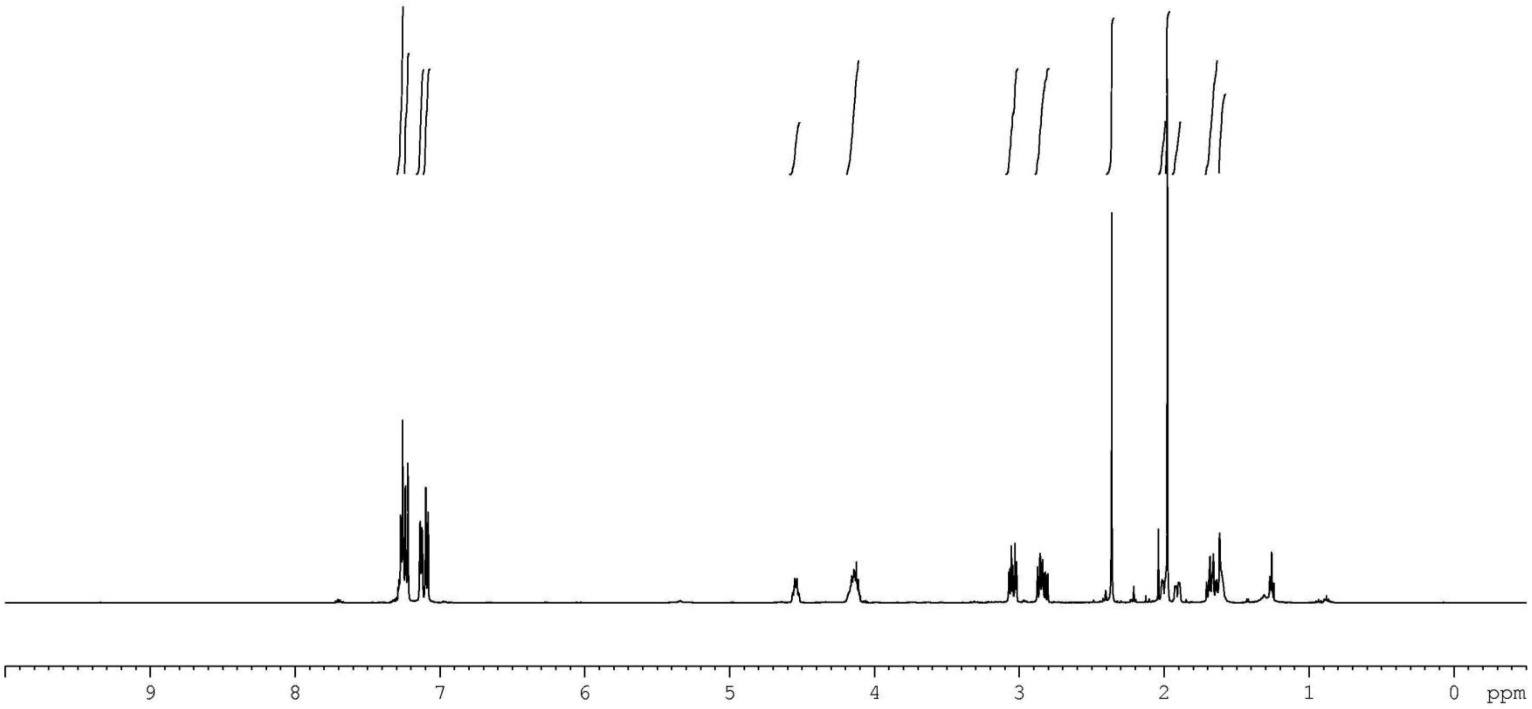


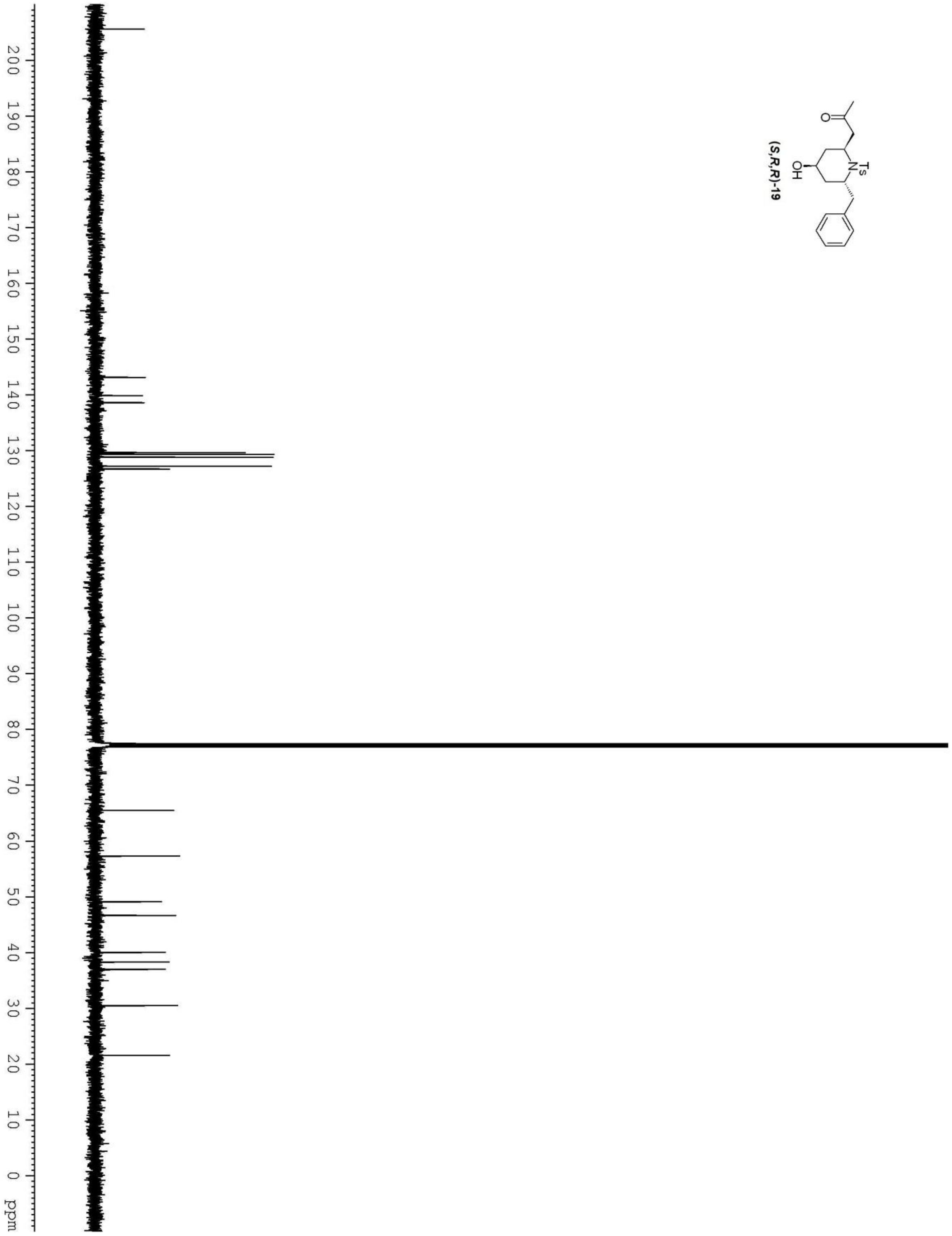
(R,R)-18

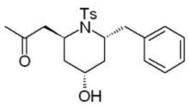
Ts
N
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



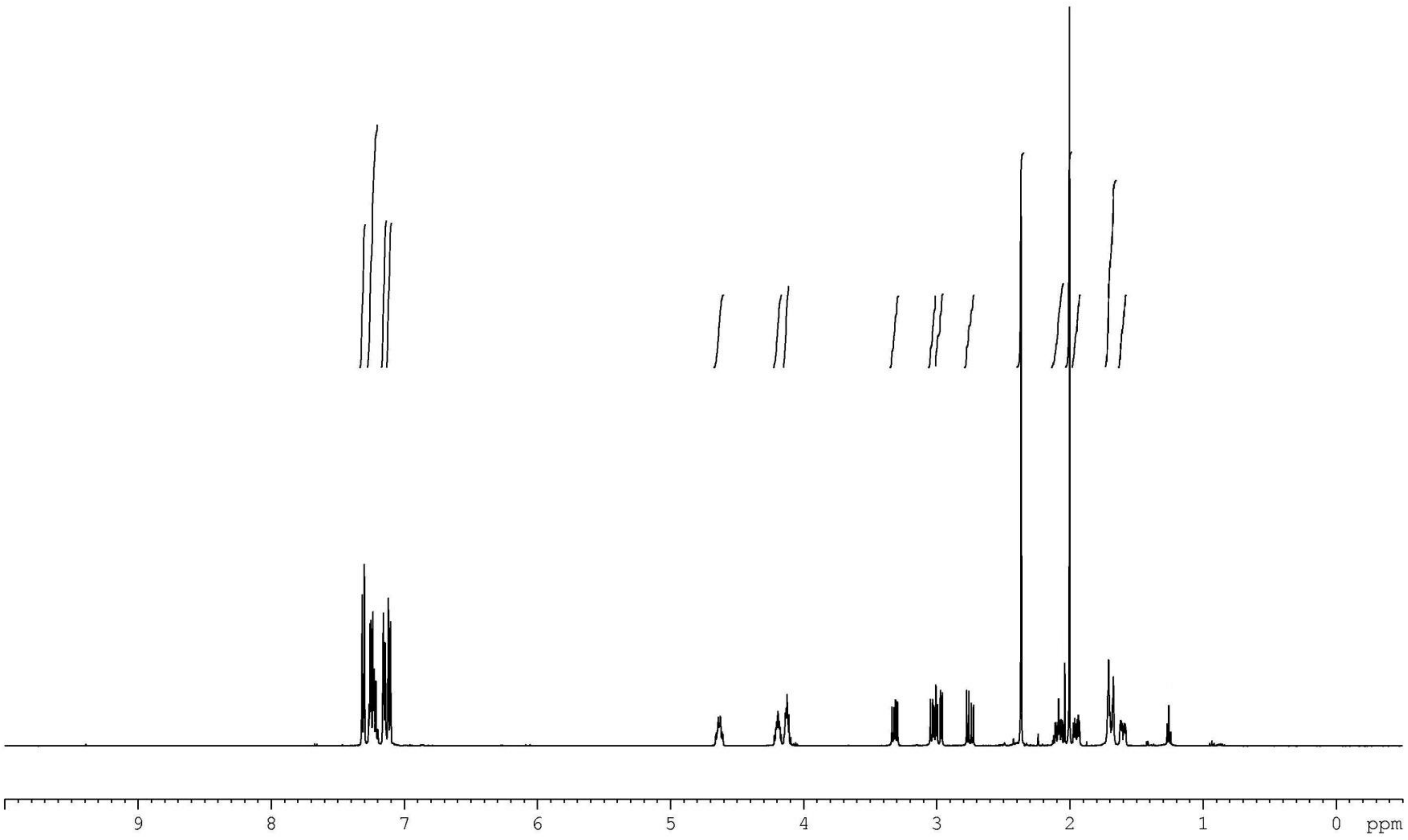
(*S*,*R*,*R*)-19

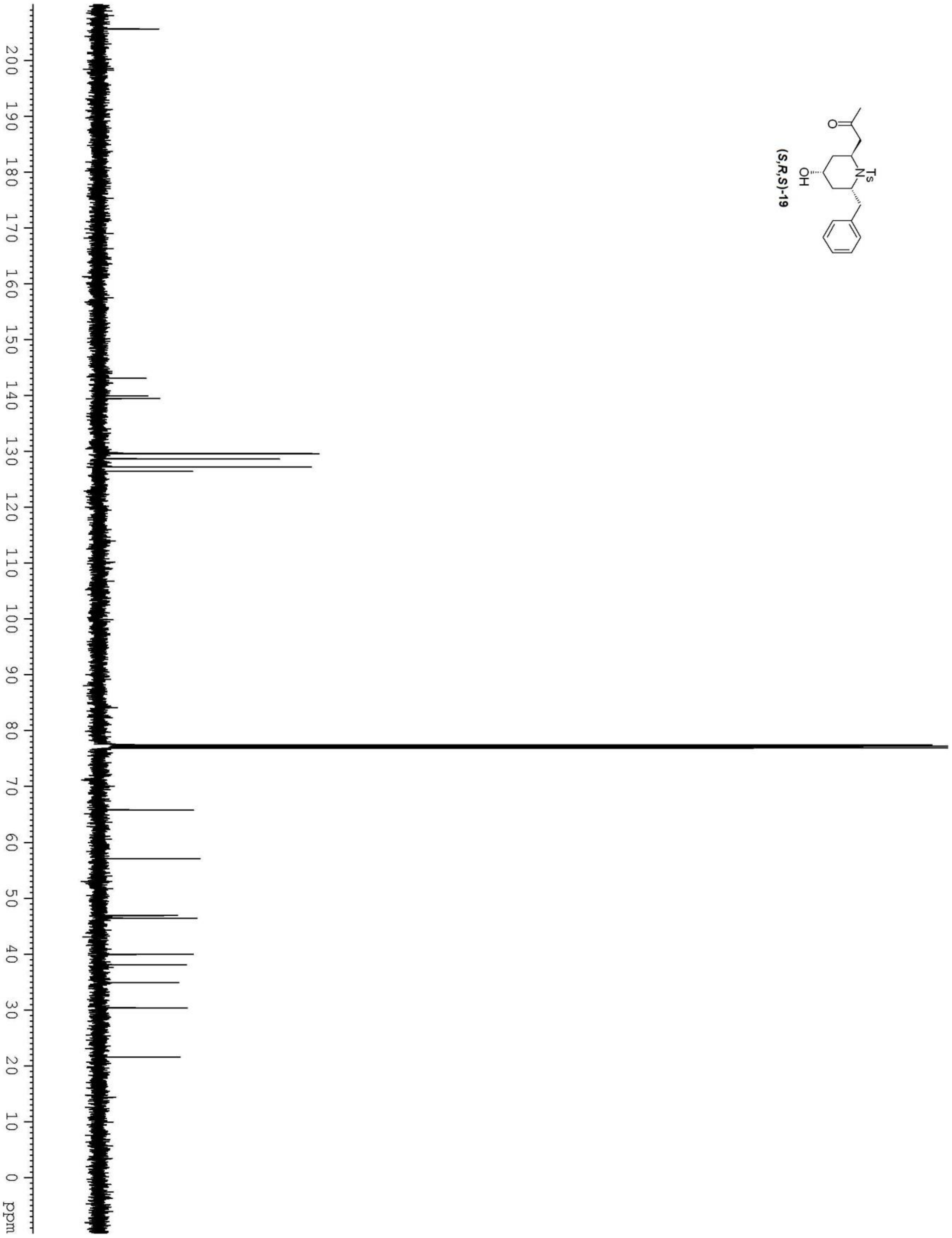



O
Ts
N
OH
(S,R,R)-19
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

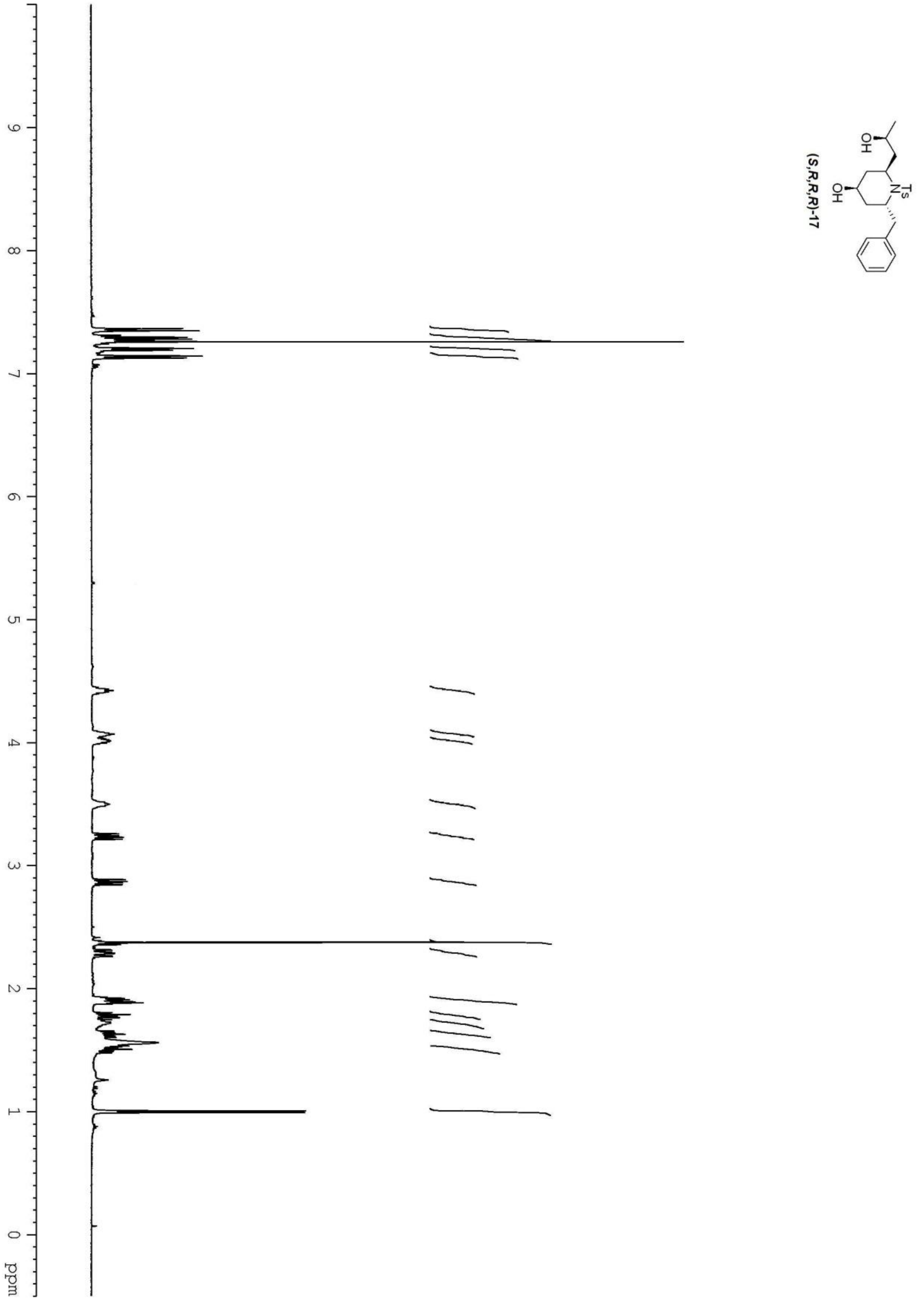


(*S*,*R*,*S*)-19

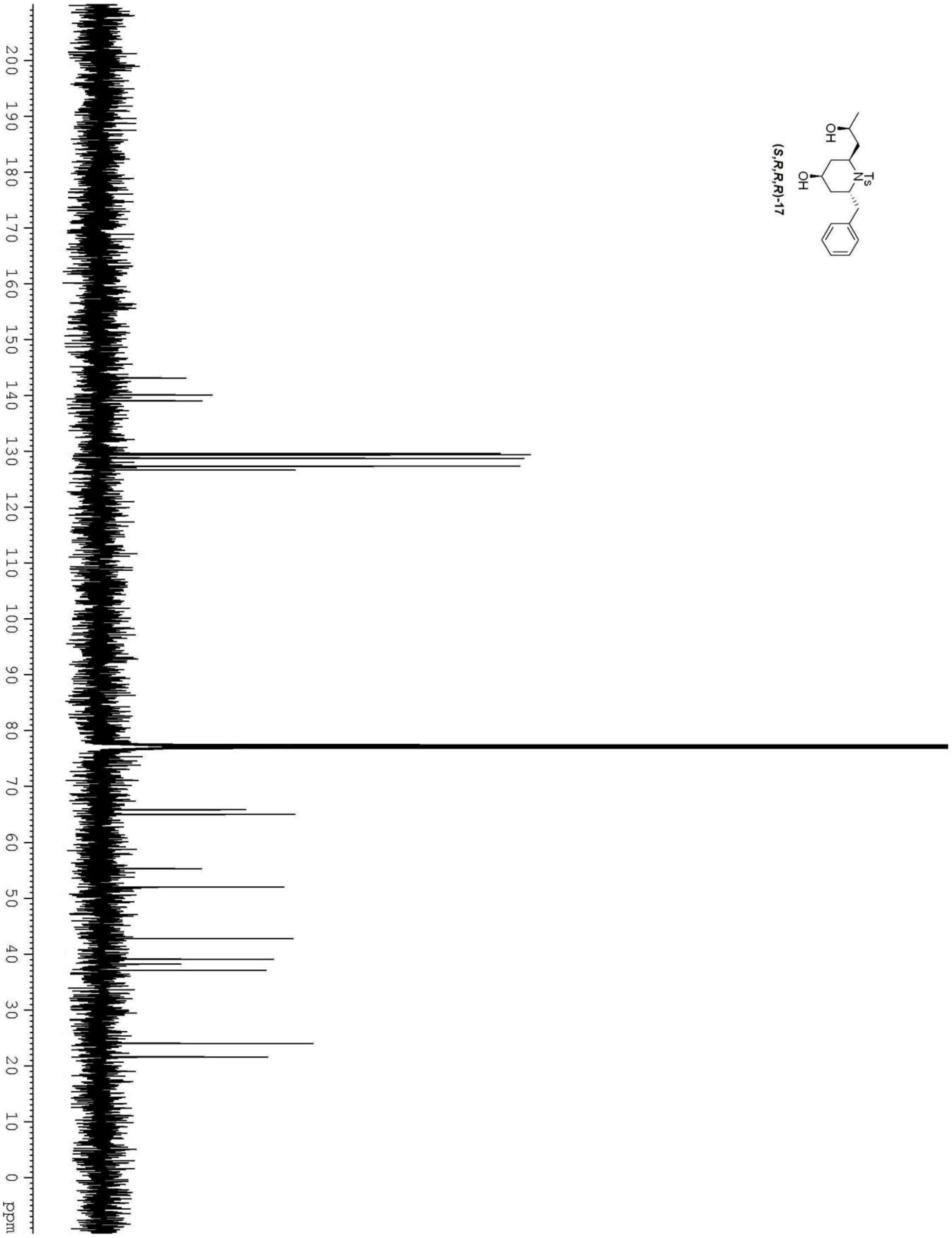



200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
O
Ts
N
OH

(S,R,S)-19

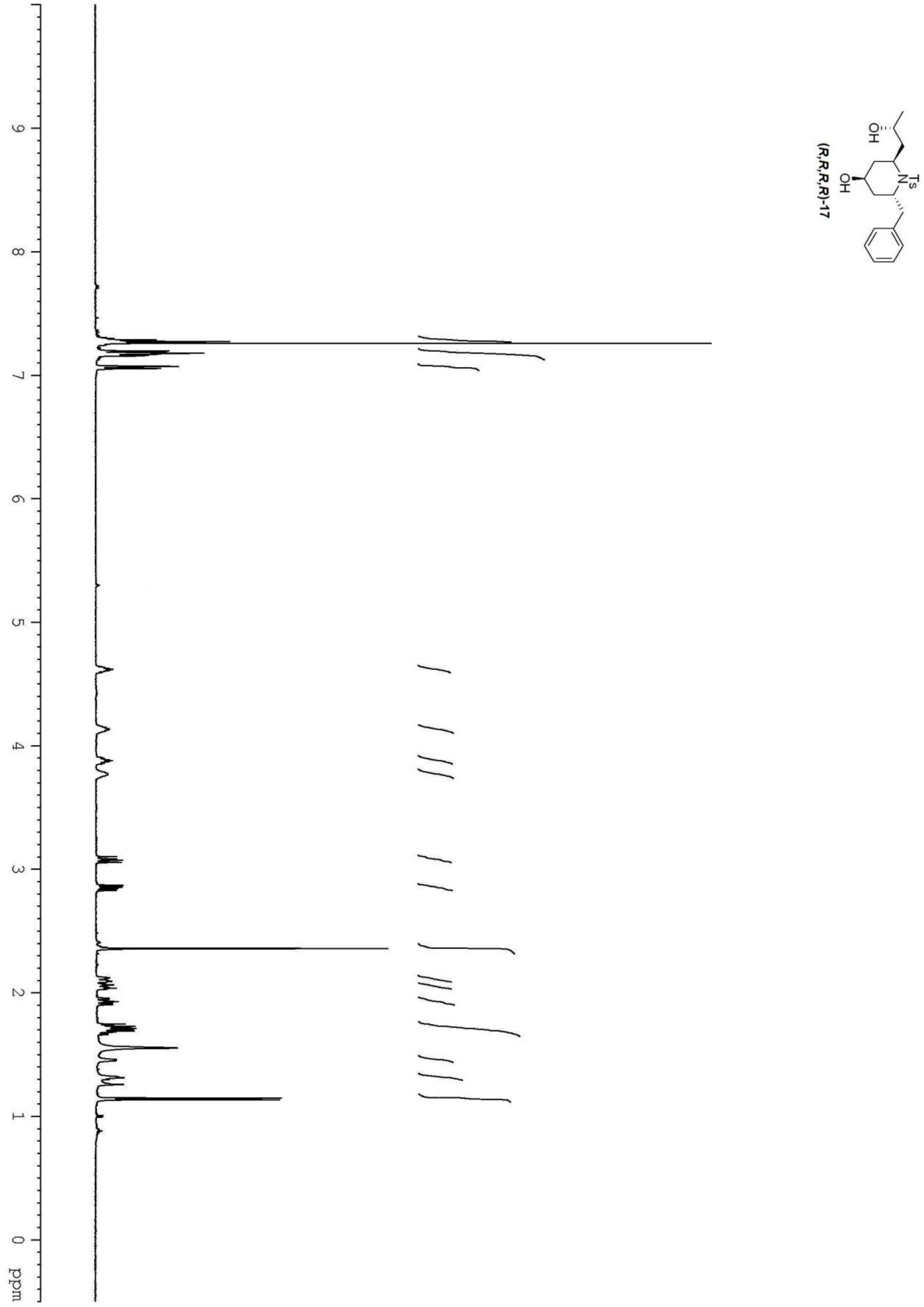


(S,R,R)-17

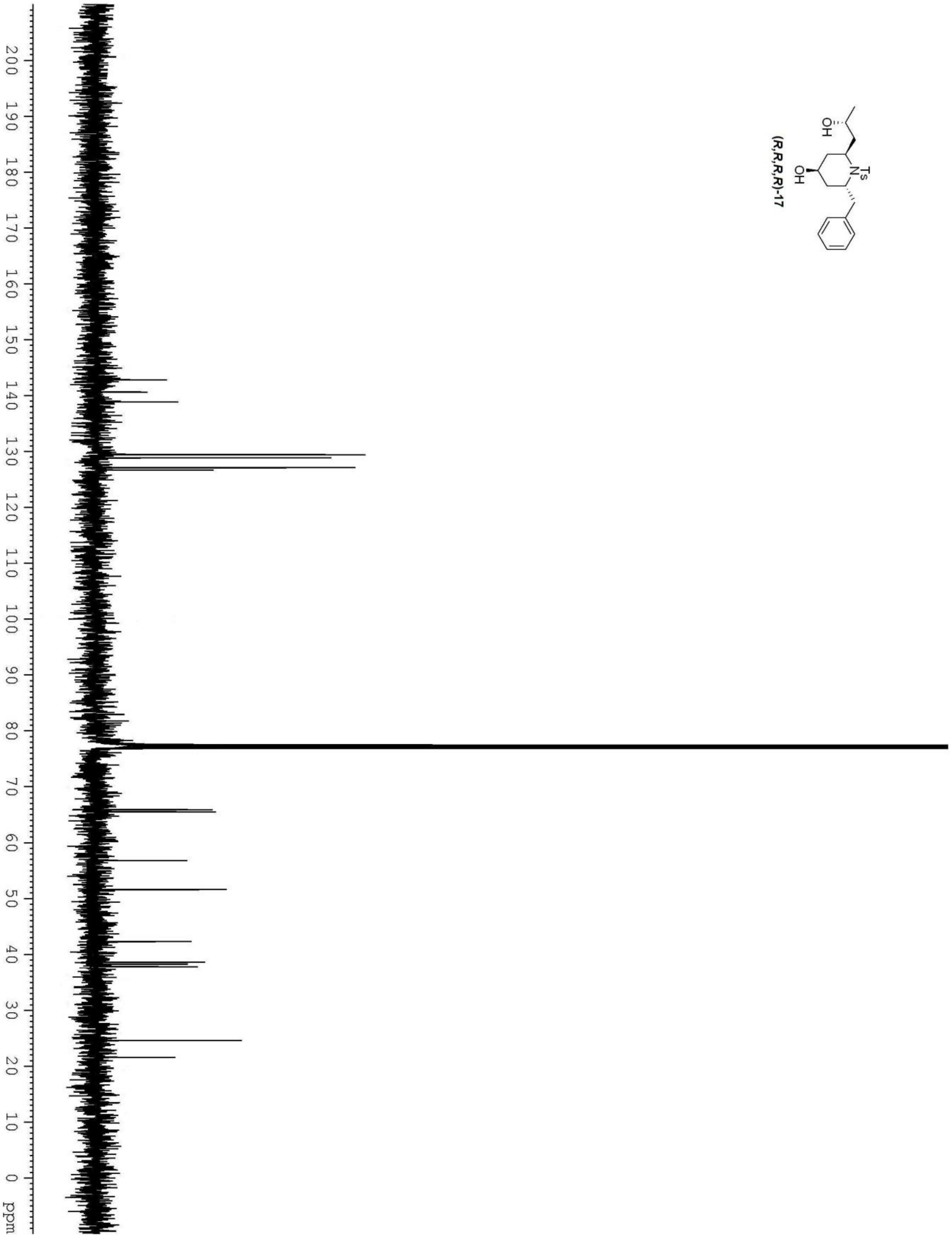


(S,R,R)-17

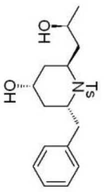
Ts
N
OH
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



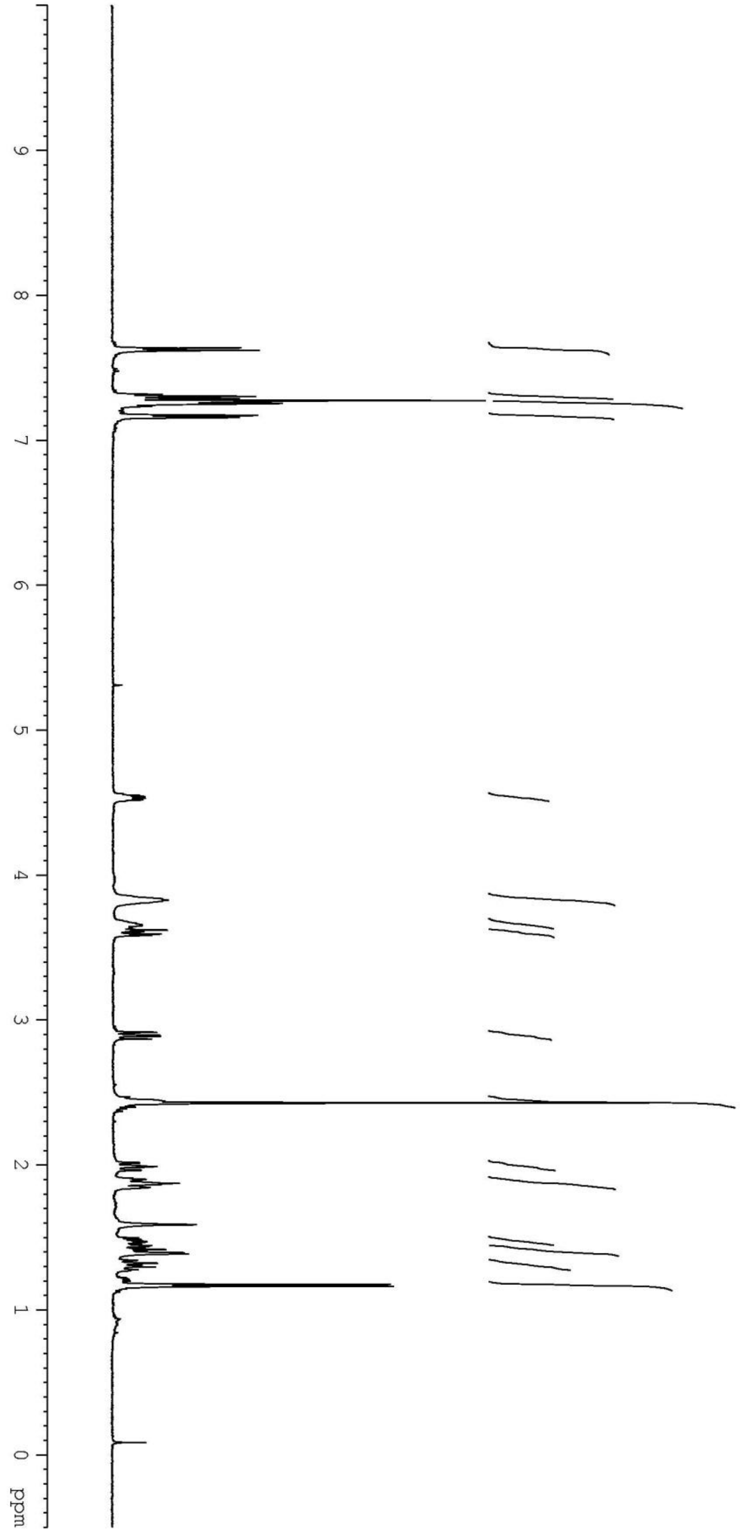
(R,R,R,R)-17

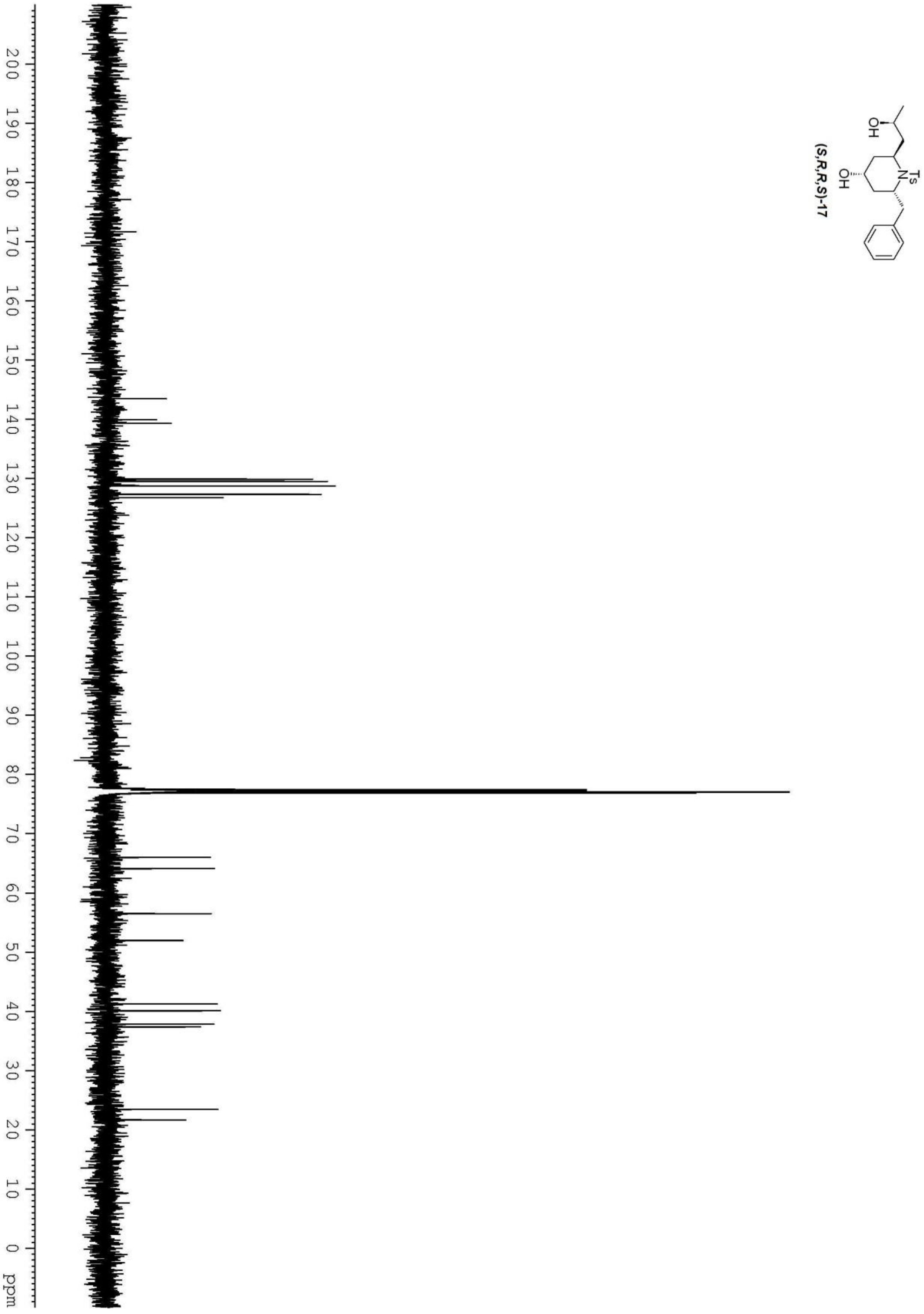
Ts
N
OH
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

(R,R,R,R)-17



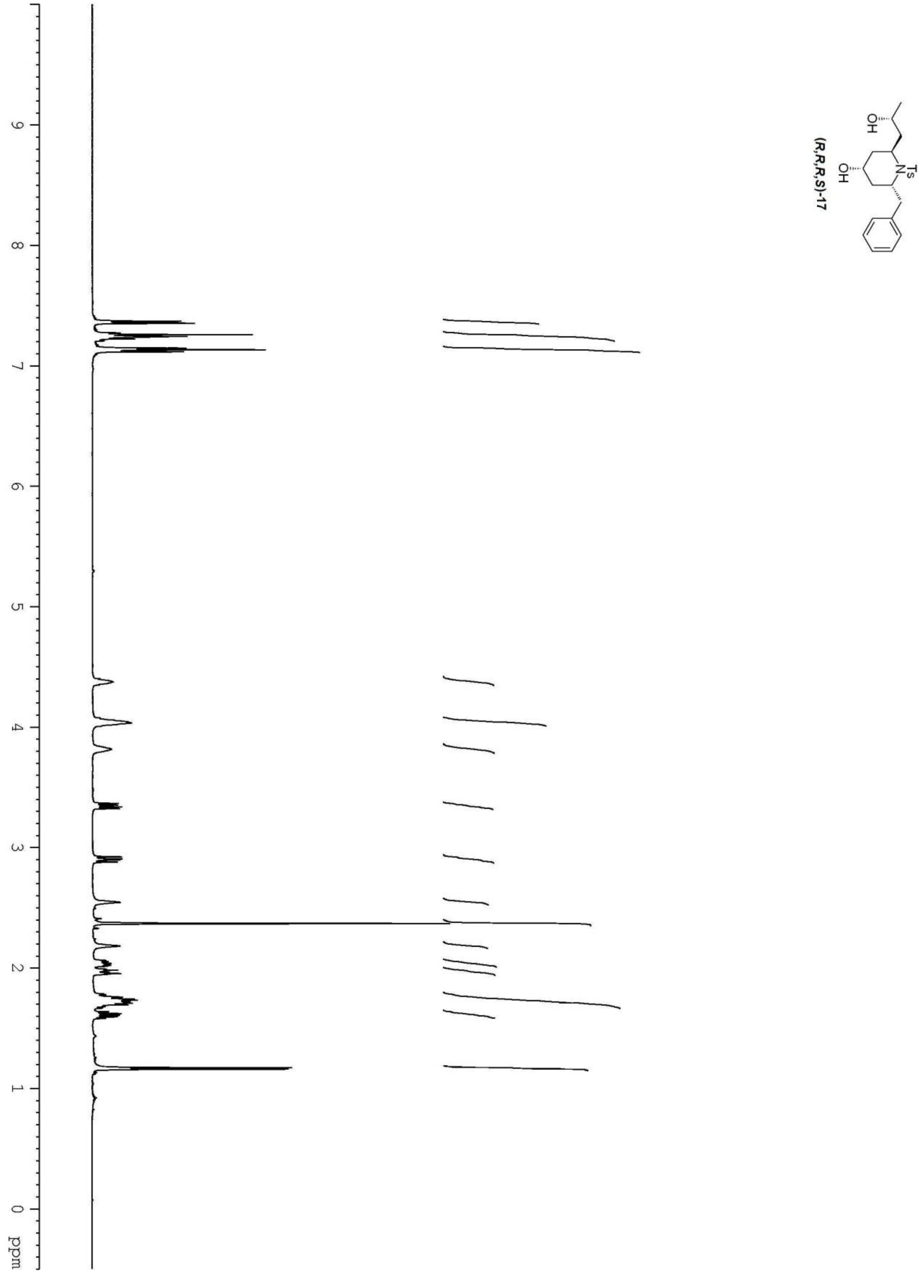
(S,R,R,S)-17



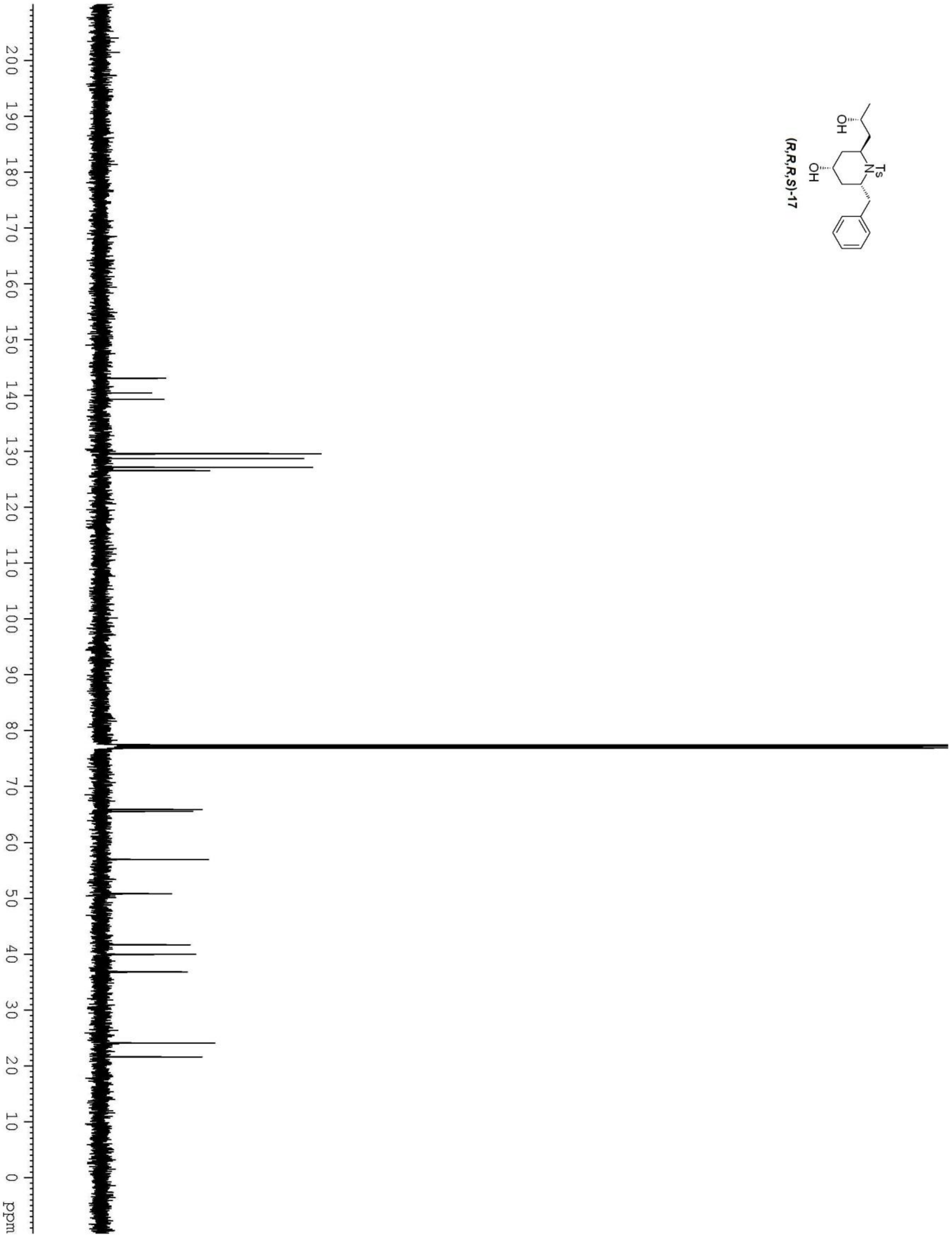


(S,R,R,S)-17

Ts
N
OH
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



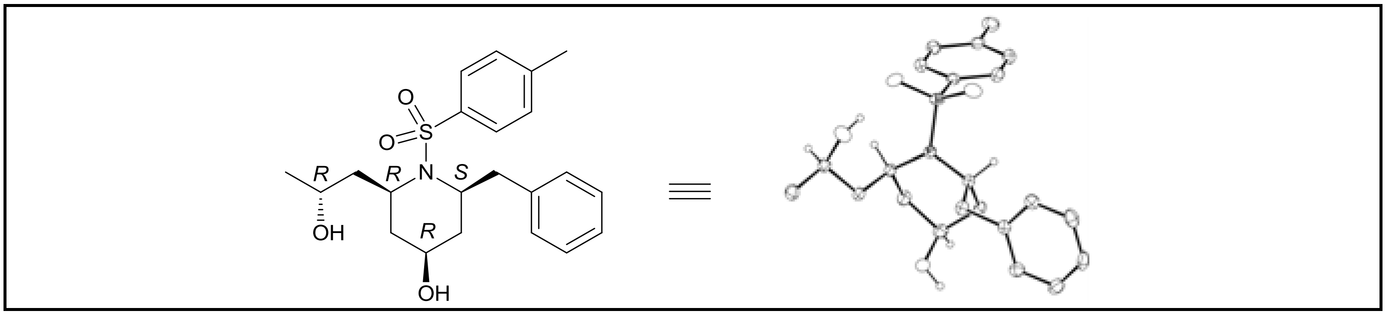
(R,R,R,S)-17



***(R,R,R,S)*-17**

Ts
N
OH
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

X-ray Structure Determination of Compound (*R*,*R*,*S*,*R*)-**17**



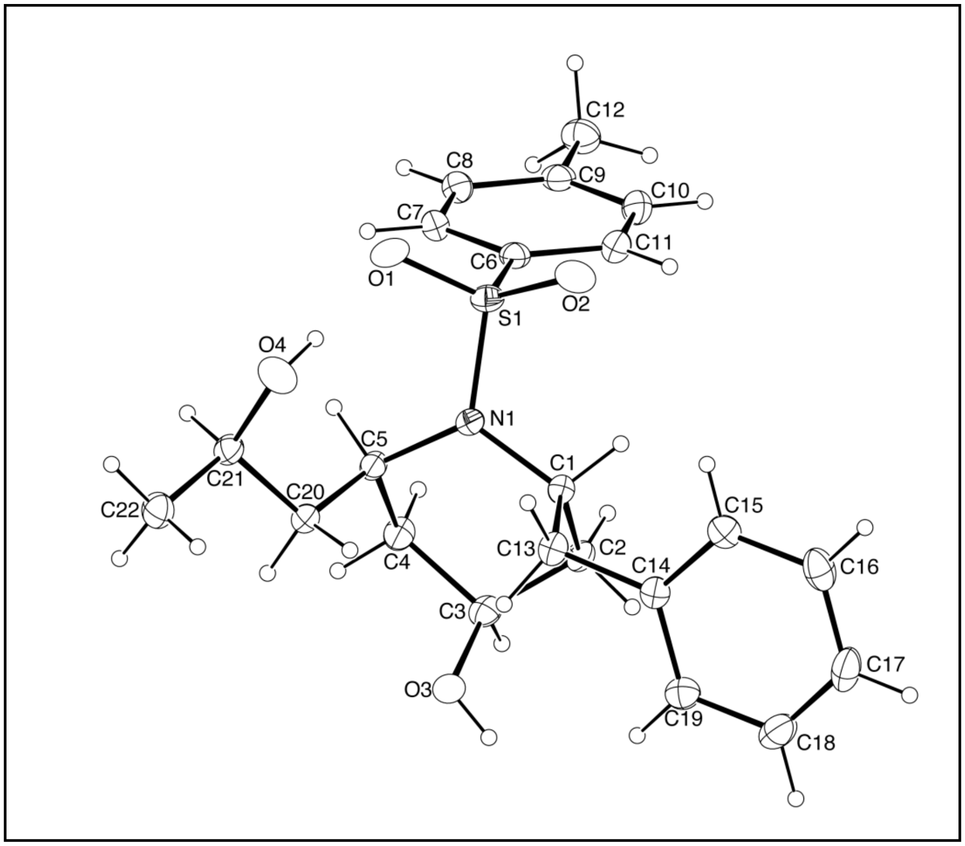


Figure 1. ORTEP drawing of the title compound with 30% probability thermal ellipsoids.

Table 1. Summary of Structure Determination of Compound (*R,R,S,R*)-17

Empirical formula	$C_{22}H_{29}NSO_4$
Formula weight	403.52
Temperature	143(1) K
Wavelength	0.71073 Å
Crystal system	orthorhombic
Space group	$P2_12_12_1$
Cell constants:	
a	8.0248(5) Å
b	12.4438(8) Å
c	20.5847(14) Å
Volume	2055.6(2) $Å^3$
Z	4
Density (calculated)	1.304 Mg/m^3
Absorption coefficient	0.185 mm^{-1}
F(000)	864
Crystal size	0.32 x 0.30 x 0.22 mm^3
Theta range for data collection	2.57 to 25.02°
Index ranges	$-9 \leq h \leq 9, -14 \leq k \leq 14, -24 \leq l \leq 24$
Reflections collected	27757
Independent reflections	3629 [R(int) = 0.0191]
Completeness to theta = 25.02°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.0000 and 0.8654
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3629 / 0 / 258
Goodness-of-fit on F^2	1.068
Final R indices [I>2sigma(I)]	R1 = 0.0292, wR2 = 0.0750
R indices (all data)	R1 = 0.0298, wR2 = 0.0759
Absolute structure parameter	0.02(6)
Largest diff. peak and hole	0.147 and -0.314 e.$Å^{-3}$

Table 2. Refined Positional Parameters for Compound (*R,R,S,R*)-**17**

Atom	x	y	z	U_{eq},Å^2
C1	0.39500(18)	0.51080(12)	0.35065(7)	0.0236(3)
C2	0.24205(19)	0.44020(13)	0.33936(8)	0.0260(3)
C3	0.22873(19)	0.39532(13)	0.27078(8)	0.0288(3)
C4	0.3903(2)	0.33820(13)	0.25287(8)	0.0298(4)
C5	0.54972(18)	0.40537(13)	0.26112(7)	0.0250(3)
C6	0.65640(18)	0.29654(13)	0.41080(7)	0.0263(3)
C7	0.72574(19)	0.20745(14)	0.38061(8)	0.0299(3)
C8	0.7036(2)	0.10657(13)	0.40766(8)	0.0311(3)
C9	0.6138(2)	0.09313(14)	0.46483(8)	0.0306(4)
C10	0.5462(2)	0.18369(15)	0.49450(8)	0.0345(4)
C11	0.5661(2)	0.28515(15)	0.46801(8)	0.0335(4)
C12	0.5904(2)	-0.01704(15)	0.49339(9)	0.0398(4)
C13	0.3816(2)	0.62633(12)	0.32359(8)	0.0280(3)
C14	0.2591(2)	0.69410(12)	0.36123(7)	0.0256(3)
C15	0.3085(2)	0.74481(13)	0.41800(8)	0.0314(3)
C16	0.1976(3)	0.80578(14)	0.45431(8)	0.0406(4)
C17	0.0345(3)	0.81629(16)	0.43391(10)	0.0440(5)
C18	-0.0175(2)	0.76574(15)	0.37735(10)	0.0421(4)
C19	0.0942(2)	0.70523(14)	0.34111(8)	0.0334(4)
C20	0.58273(19)	0.48476(14)	0.20513(7)	0.0277(3)
C21	0.76531(19)	0.50419(14)	0.18764(8)	0.0288(3)
C22	0.7841(2)	0.57317(15)	0.12763(8)	0.0371(4)
N1	0.54971(16)	0.45821(10)	0.32641(6)	0.0249(3)
O1	0.84647(13)	0.41757(10)	0.34275(6)	0.0366(3)
O2	0.68169(16)	0.50106(10)	0.43140(6)	0.0383(3)
O3	0.19728(14)	0.47678(10)	0.22318(5)	0.0332(3)
O4	0.85595(16)	0.55886(11)	0.23798(6)	0.0425(3)
S1	0.69268(5)	0.42613(3)	0.378701(19)	0.02777(11)

$U_{eq}={}^{1}/_{3}[U_{11}(aa^*)^2+U_{22}(bb^*)^2+U_{33}(cc^*)^2+2U_{12}aa^*bb^*\cos\gamma+2U_{13}aa^*cc^*\cos\beta+2U_{23}bb^*cc^*\cos\alpha]$

Table 3. Positional Parameters for Hydrogens in Compound (*R*,*R*,*S*,*R*)-**17**

Atom	x	y	z	U_{iso},Å^2
H1	0.4076	0.5176	0.3978	0.031
H2a	0.2450	0.3807	0.3698	0.035
H2b	0.1428	0.4820	0.3486	0.035
H3	0.1374	0.3431	0.2695	0.038
H4a	0.3829	0.3152	0.2079	0.040
H4b	0.4002	0.2741	0.2794	0.040
H5	0.6429	0.3545	0.2611	0.033
H7	0.7866	0.2154	0.3425	0.040
H8	0.7496	0.0469	0.3873	0.041
H10	0.4864	0.1759	0.5329	0.046
H11	0.5197	0.3449	0.4882	0.045
H12a	0.6900	-0.0381	0.5159	0.060
H12b	0.5677	-0.0675	0.4592	0.060
H12c	0.4986	-0.0159	0.5233	0.060
H13a	0.4905	0.6601	0.3252	0.037
H13b	0.3471	0.6232	0.2785	0.037
H15	0.4181	0.7378	0.4320	0.042
H16	0.2330	0.8394	0.4922	0.054
H17	-0.0404	0.8571	0.4580	0.058
H18	-0.1274	0.7724	0.3637	0.056
H19	0.0588	0.6719	0.3031	0.044
H20a	0.5258	0.4585	0.1667	0.037
H20b	0.5329	0.5533	0.2165	0.037
H21	0.8187	0.4346	0.1796	0.038
H22a	0.7318	0.6415	0.1348	0.056
H22b	0.7321	0.5381	0.0914	0.056
H22c	0.9003	0.5837	0.1186	0.056
H3a	0.1015	0.4988	0.2271	0.050
H4	0.8527	0.5232	0.2714	0.064

Table 4. Refined Thermal Parameters (U's) for Compound (*R*,*R*,*S*,*R*)-17

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	0.0227(7)	0.0246(8)	0.0235(7)	-0.0006(6)	0.0021(6)	0.0002(6)
C2	0.0213(7)	0.0258(8)	0.0310(8)	0.0010(7)	0.0043(6)	-0.0014(6)
C3	0.0213(7)	0.0300(8)	0.0353(8)	-0.0022(7)	-0.0004(6)	-0.0063(6)
C4	0.0265(8)	0.0291(8)	0.0340(8)	-0.0069(6)	0.0010(7)	-0.0034(7)
C5	0.0208(7)	0.0275(8)	0.0267(7)	-0.0049(6)	0.0013(6)	0.0011(6)
C6	0.0219(8)	0.0313(8)	0.0255(7)	0.0019(6)	-0.0038(6)	-0.0009(6)
C7	0.0286(8)	0.0379(8)	0.0230(7)	-0.0009(7)	0.0010(6)	0.0017(7)
C8	0.0320(8)	0.0332(8)	0.0280(8)	-0.0034(7)	-0.0016(7)	0.0028(7)
C9	0.0231(8)	0.0376(9)	0.0310(8)	0.0047(7)	-0.0055(6)	-0.0011(7)
C10	0.0315(9)	0.0420(10)	0.0302(8)	0.0051(8)	0.0063(7)	0.0020(7)
C11	0.0290(8)	0.0397(9)	0.0318(8)	-0.0044(7)	0.0023(7)	0.0055(7)
C12	0.0409(10)	0.0383(10)	0.0402(9)	0.0087(8)	-0.0028(8)	-0.0013(8)
C13	0.0283(8)	0.0242(8)	0.0315(8)	-0.0008(6)	0.0046(7)	-0.0017(6)
C14	0.0296(8)	0.0191(7)	0.0280(8)	0.0028(6)	0.0030(6)	-0.0005(6)
C15	0.0359(9)	0.0271(8)	0.0314(8)	0.0012(6)	-0.0009(7)	-0.0002(7)
C16	0.0619(12)	0.0291(8)	0.0307(9)	-0.0024(7)	0.0061(9)	0.0033(9)
C17	0.0527(12)	0.0359(10)	0.0432(10)	0.0072(8)	0.0215(9)	0.0153(9)
C18	0.0322(9)	0.0433(10)	0.0507(11)	0.0124(9)	0.0058(9)	0.0089(8)
C19	0.0326(9)	0.0325(9)	0.0351(8)	0.0026(7)	-0.0021(7)	0.0000(7)
C20	0.0224(8)	0.0342(9)	0.0265(7)	-0.0019(7)	0.0009(6)	0.0017(7)
C21	0.0224(8)	0.0340(8)	0.0300(8)	-0.0024(7)	0.0014(6)	-0.0018(7)
C22	0.0326(9)	0.0451(10)	0.0336(8)	0.0010(8)	0.0047(7)	-0.0043(8)
N1	0.0211(6)	0.0282(7)	0.0254(7)	-0.0012(5)	-0.0010(5)	0.0026(5)
O1	0.0186(5)	0.0446(7)	0.0466(7)	0.0102(6)	-0.0023(5)	-0.0025(5)
O2	0.0409(7)	0.0347(6)	0.0392(6)	-0.0081(5)	-0.0142(6)	-0.0039(6)
O3	0.0236(5)	0.0445(7)	0.0313(6)	0.0013(5)	-0.0020(5)	0.0004(5)
O4	0.0378(7)	0.0567(8)	0.0330(6)	0.0046(6)	-0.0049(5)	-0.0195(6)
S1	0.02176(18)	0.0300(2)	0.0315(2)	0.00057(16)	-0.00505(15)	-0.00247(15)

The form of the anisotropic displacement parameter is:
$\exp[-2\pi^2(a^{*2}U_{11}h^2+b^{*2}U_{22}k^2+c^{*2}U_{33}l^2+2b^*c^*U_{23}kl+2a^*c^*U_{13}hl+2a^*b^*U_{12}hk)]$

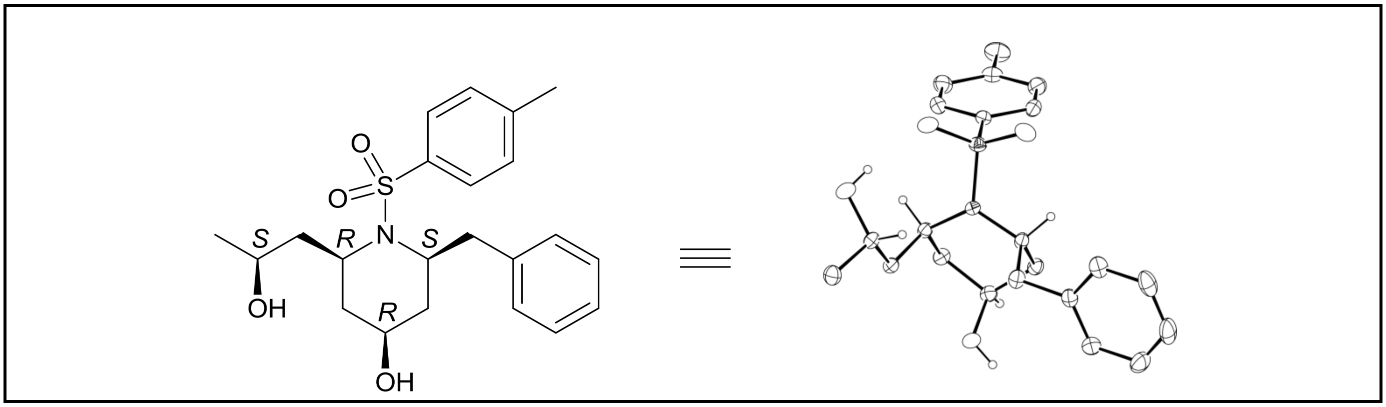
Table 5. Bond Distances in Compound (*R*,*R*,*S*,*R*)-17, Å

C1-N1	1.4895(19)	C1-C2	1.527(2)	C1-C13	1.546(2)
C2-C3	1.522(2)	C3-O3	1.432(2)	C3-C4	1.524(2)
C4-C5	1.538(2)	C5-N1	1.4964(19)	C5-C20	1.541(2)
C6-C7	1.387(2)	C6-C11	1.390(2)	C6-S1	1.7669(16)
C7-C8	1.385(2)	C8-C9	1.390(2)	C9-C10	1.392(3)
C9-C12	1.503(2)	C10-C11	1.385(3)	C13-C14	1.510(2)
C14-C15	1.386(2)	C14-C19	1.393(2)	C15-C16	1.388(2)
C16-C17	1.381(3)	C17-C18	1.387(3)	C18-C19	1.388(3)
C20-C21	1.528(2)	C21-O4	1.437(2)	C21-C22	1.512(2)
N1-S1	1.6230(13)	O1-S1	1.4431(12)	O2-S1	1.4332(12)

Table 6. Bond Angles in Compound (*R*,*R*,*S*,*R*)-17, °

N1-C1-C2	111.48(12)	N1-C1-C13	110.22(12)	C2-C1-C13	115.11(13)
C3-C2-C1	114.13(12)	O3-C3-C2	112.78(13)	O3-C3-C4	108.34(13)
C2-C3-C4	109.62(13)	C3-C4-C5	115.32(12)	N1-C5-C4	109.76(12)
N1-C5-C20	112.96(12)	C4-C5-C20	114.14(13)	C7-C6-C11	120.48(15)
C7-C6-S1	119.71(12)	C11-C6-S1	119.72(13)	C8-C7-C6	119.53(14)
C7-C8-C9	121.06(15)	C8-C9-C10	118.44(15)	C8-C9-C12	120.36(16)
C10-C9-C12	121.21(15)	C11-C10-C9	121.37(15)	C10-C11-C6	119.13(17)
C14-C13-C1	112.32(12)	C15-C14-C19	118.50(16)	C15-C14-C13	120.05(15)
C19-C14-C13	121.43(15)	C14-C15-C16	121.31(17)	C17-C16-C15	119.71(17)
C16-C17-C18	119.80(17)	C17-C18-C19	120.20(18)	C18-C19-C14	120.48(17)
C21-C20-C5	116.26(13)	O4-C21-C22	105.66(13)	O4-C21-C20	112.97(13)
C22-C21-C20	112.20(14)	C1-N1-C5	119.61(12)	C1-N1-S1	118.37(10)
C5-N1-S1	119.18(10)	O2-S1-O1	119.26(8)	O2-S1-N1	107.37(7)
O1-S1-N1	106.41(7)	O2-S1-C6	107.49(7)	O1-S1-C6	105.39(7)
N1-S1-C6	110.86(7)				

X-ray Structure Determination of Compound (*S*,*R*,*S*,*R*)-**17**



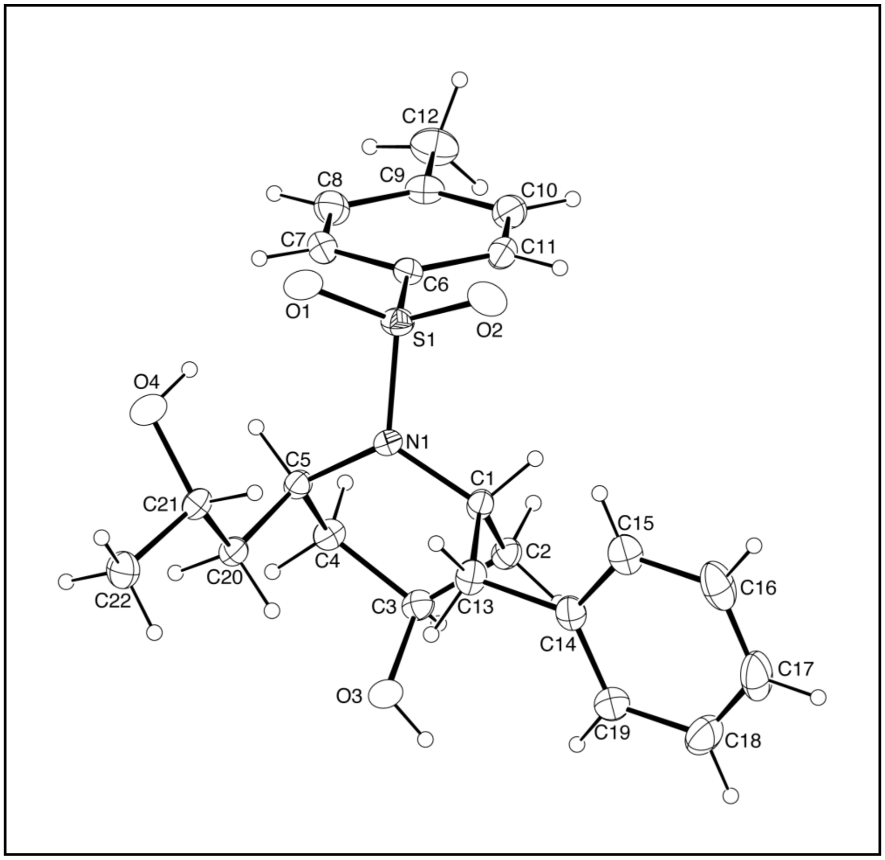


Figure 1. ORTEP drawing of the title compound with 30% probability thermal ellipsoids.

Table 1. Summary of Structure Determination of Compound (*S*,*R*,*S*,*R*)**-17**

Empirical formula	$C_{22}H_{29}NSO_4$
Formula weight	403.52
Temperature	143(1) K
Wavelength	0.71073 Å
Crystal system	orthorhombic
Space group	$P2_12_12_1$
Cell constants:	
a	8.2223(5) Å
b	13.0939(8) Å
c	19.2454(12) Å
Volume	2072.0(2) Å^3
Z	4
Density (calculated)	1.294 Mg/m^3
Absorption coefficient	0.184 mm^{-1}
F(000)	864
Crystal size	0.38 x 0.10 x 0.08 mm^3
Theta range for data collection	2.63 to 25.02°.
Index ranges	$-9 \leq h \leq 9$, $-15 \leq k \leq 13$, $-20 \leq l \leq 22$
Reflections collected	24575
Independent reflections	3651 [R(int) = 0.0309]
Completeness to theta = 25.02°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.0000 and 0.8933
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3651 / 0 / 258
Goodness-of-fit on F^2	1.061
Final R indices [I>2sigma(I)]	R1 = 0.0358, wR2 = 0.0892
R indices (all data)	R1 = 0.0378, wR2 = 0.0915
Absolute structure parameter	0.01(7)
Largest diff. peak and hole	0.157 and -0.298 e.Å^{-3}

Table 2. Refined Positional Parameters for Compound (*S,R,S,R*)-**17**

Atom	x	y	z	U_{eq},Å^2
C1	0.5985(2)	0.49849(14)	0.35228(10)	0.0273(4)
C2	0.7377(2)	0.57286(15)	0.34002(10)	0.0295(4)
C3	0.7348(2)	0.62493(15)	0.26871(10)	0.0296(4)
C4	0.5688(2)	0.67130(14)	0.25486(10)	0.0289(4)
C5	0.4237(2)	0.59894(14)	0.26500(9)	0.0270(4)
C6	0.3341(2)	0.70066(15)	0.41785(9)	0.0274(4)
C7	0.2512(2)	0.77667(16)	0.38252(10)	0.0349(5)
C8	0.2715(3)	0.87794(16)	0.40239(11)	0.0397(5)
C9	0.3703(3)	0.90403(16)	0.45778(11)	0.0357(5)
C10	0.4499(3)	0.82638(16)	0.49328(11)	0.0382(5)
C11	0.4335(3)	0.72473(17)	0.47390(10)	0.0346(5)
C12	0.3931(4)	1.01442(18)	0.47872(13)	0.0516(6)
C13	0.6183(3)	0.39310(14)	0.31727(11)	0.0323(4)
C14	0.7394(3)	0.32593(14)	0.35380(10)	0.0319(5)
C15	0.6913(3)	0.26918(15)	0.41127(11)	0.0414(5)
C16	0.8006(4)	0.20659(17)	0.44617(12)	0.0543(7)
C17	0.9581(4)	0.2000(2)	0.42364(15)	0.0643(9)
C18	1.0089(3)	0.2562(2)	0.36703(14)	0.0618(8)
C19	0.9004(3)	0.31852(19)	0.33230(12)	0.0433(5)
C20	0.3934(2)	0.52806(16)	0.20314(10)	0.0291(4)
C21	0.2467(2)	0.45744(16)	0.20918(10)	0.0328(4)
C22	0.2138(3)	0.40150(17)	0.14241(11)	0.0404(5)
N1	0.43922(19)	0.54411(12)	0.33261(7)	0.0261(3)
O1	0.14971(17)	0.56620(13)	0.36269(7)	0.0406(4)
O2	0.34473(19)	0.50877(11)	0.45221(7)	0.0397(4)
O3	0.77160(16)	0.55680(11)	0.21283(7)	0.0349(3)
O4	0.10194(17)	0.51288(15)	0.22670(8)	0.0474(4)
S1	0.30947(6)	0.57162(4)	0.39335(2)	0.02975(14)

$U_{eq}={}^{1}/_{3}[U_{11}(aa^*)^2+U_{22}(bb^*)^2+U_{33}(cc^*)^2+2U_{12}aa^*bb^*\cos\gamma+2U_{13}aa^*cc^*\cos\beta+2U_{23}bb^*cc^*\cos\alpha]$

Table 3. Positional Parameters for Hydrogens in Compound (*S*,*R*,*S*,*R*)-**17**

Atom	x	y	z	U_{iso},Å^2
H1	0.5942	0.4861	0.4025	0.036
H2a	0.8397	0.5364	0.3449	0.039
H2b	0.7344	0.6251	0.3757	0.039
H3	0.8156	0.6799	0.2687	0.039
H4a	0.5669	0.6964	0.2075	0.038
H4b	0.5548	0.7296	0.2854	0.038
H5	0.3271	0.6424	0.2690	0.036
H7	0.1825	0.7601	0.3458	0.046
H8	0.2177	0.9291	0.3780	0.053
H10	0.5157	0.8428	0.5309	0.051
H11	0.4881	0.6736	0.4980	0.046
H12a	0.3417	1.0261	0.5228	0.077
H12b	0.3450	1.0580	0.4443	0.077
H12c	0.5071	1.0292	0.4824	0.077
H13a	0.5136	0.3589	0.3164	0.043
H13b	0.6530	0.4029	0.2696	0.043
H15	0.5842	0.2732	0.4266	0.055
H16	0.7669	0.1693	0.4847	0.072
H17	1.0312	0.1575	0.4466	0.086
H18	1.1163	0.2521	0.3522	0.082
H19	0.9355	0.3560	0.2941	0.058
H20a	0.3800	0.5698	0.1619	0.039
H20b	0.4896	0.4864	0.1963	0.039
H21	0.2682	0.4072	0.2458	0.044
H22a	0.1205	0.3582	0.1482	0.061
H22b	0.3066	0.3607	0.1304	0.061
H22c	0.1931	0.4500	0.1060	0.061
H3a	0.8696	0.5453	0.2122	0.052
H4	0.1113	0.5371	0.2658	0.071

Table 4. Refined Thermal Parameters (U's) for Compound (*S*,*R*,*S*,*R*)-**17**

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	0.0247(10)	0.0282(9)	0.0289(9)	-0.0009(8)	-0.0049(8)	0.0021(8)
C2	0.0253(10)	0.0297(9)	0.0335(9)	-0.0040(8)	-0.0032(7)	-0.0013(8)
C3	0.0256(10)	0.0292(9)	0.0340(10)	-0.0043(8)	0.0002(8)	-0.0034(8)
C4	0.0289(10)	0.0239(9)	0.0340(10)	0.0034(8)	0.0019(8)	-0.0004(8)
C5	0.0245(10)	0.0279(10)	0.0287(9)	0.0026(8)	0.0001(8)	0.0038(8)
C6	0.0266(10)	0.0321(9)	0.0235(9)	-0.0010(7)	0.0026(7)	0.0006(8)
C7	0.0368(11)	0.0408(11)	0.0271(10)	0.0001(8)	-0.0021(9)	0.0047(9)
C8	0.0484(13)	0.0367(10)	0.0341(11)	0.0054(9)	0.0035(9)	0.0081(10)
C9	0.0355(11)	0.0340(11)	0.0375(10)	-0.0036(9)	0.0107(9)	-0.0023(9)
C10	0.0333(11)	0.0409(11)	0.0403(11)	-0.0125(10)	-0.0042(9)	0.0001(10)
C11	0.0288(10)	0.0399(11)	0.0350(10)	-0.0034(9)	-0.0045(8)	0.0065(9)
C12	0.0636(16)	0.0365(12)	0.0548(14)	-0.0071(11)	0.0132(12)	-0.0033(11)
C13	0.0347(11)	0.0249(9)	0.0373(10)	-0.0021(8)	-0.0065(9)	0.0010(8)
C14	0.0408(12)	0.0242(9)	0.0308(10)	-0.0044(8)	-0.0063(8)	0.0037(8)
C15	0.0516(13)	0.0321(10)	0.0406(11)	-0.0007(9)	-0.0065(10)	0.0000(11)
C16	0.089(2)	0.0348(11)	0.0393(12)	0.0027(10)	-0.0168(14)	0.0072(14)
C17	0.089(2)	0.0520(15)	0.0521(15)	-0.0101(12)	-0.0303(15)	0.0363(16)
C18	0.0516(16)	0.0721(18)	0.0618(17)	-0.0185(15)	-0.0118(13)	0.0305(14)
C19	0.0424(13)	0.0487(13)	0.0387(12)	-0.0040(10)	0.0003(10)	0.0109(11)
C20	0.0245(9)	0.0336(10)	0.0292(9)	0.0021(8)	0.0005(8)	0.0021(8)
C21	0.0217(10)	0.0418(11)	0.0351(10)	-0.0004(8)	-0.0021(8)	0.0008(8)
C22	0.0357(12)	0.0466(12)	0.0389(11)	-0.0041(10)	-0.0060(9)	-0.0046(10)
N1	0.0220(8)	0.0306(8)	0.0256(8)	-0.0004(6)	0.0021(6)	0.0031(7)
O1	0.0237(7)	0.0529(9)	0.0452(8)	-0.0161(7)	0.0048(6)	-0.0070(7)
O2	0.0517(10)	0.0341(7)	0.0332(7)	0.0064(6)	0.0097(7)	-0.0029(7)
O3	0.0236(7)	0.0437(8)	0.0373(7)	-0.0093(6)	0.0023(6)	-0.0001(6)
O4	0.0230(7)	0.0714(11)	0.0479(9)	-0.0194(9)	-0.0013(7)	0.0045(7)
S1	0.0272(2)	0.0322(2)	0.0299(2)	-0.0025(2)	0.00476(19)	-0.0030(2)

The form of the anisotropic displacement parameter is:
$\exp[-2\pi^2(a^{*2}U_{11}h^2+b^{*2}U_{22}k^2+c^{*2}U_{33}l^2+2b^*c^*U_{23}kl+2a^*c^*U_{13}hl+2a^*b^*U_{12}hk)]$

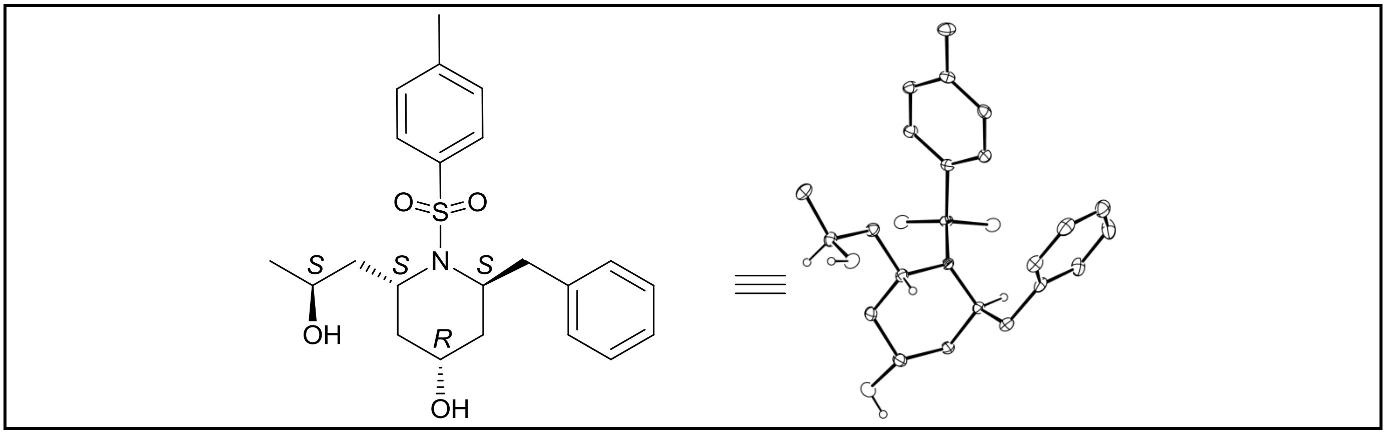
Table 5. Bond Distances in Compound (*S*,*R*,*S*,*R*)-17, Å

C1-N1	1.488(2)	C1-C2	1.522(3)	C1-C13	1.544(3)
C2-C3	1.533(3)	C3-O3	1.430(2)	C3-C4	1.517(3)
C4-C5	1.536(3)	C5-N1	1.492(2)	C5-C20	1.530(3)
C6-C7	1.385(3)	C6-C11	1.389(3)	C6-S1	1.7658(19)
C7-C8	1.390(3)	C8-C9	1.383(3)	C9-C10	1.389(3)
C9-C12	1.512(3)	C10-C11	1.389(3)	C13-C14	1.503(3)
C14-C15	1.390(3)	C14-C19	1.391(3)	C15-C16	1.390(3)
C16-C17	1.369(4)	C17-C18	1.379(4)	C18-C19	1.381(3)
C20-C21	1.524(3)	C21-O4	1.435(2)	C21-C22	1.504(3)
N1-S1	1.6231(15)	O1-S1	1.4417(15)	O2-S1	1.4299(15)

Table 6. Bond Angles in Compound (*S*,*R*,*S*,*R*)-17, °

N1-C1-C2	111.46(15)	N1-C1-C13	109.92(15)	C2-C1-C13	115.14(16)
C1-C2-C3	114.31(15)	O3-C3-C4	107.95(15)	O3-C3-C2	113.12(16)
C4-C3-C2	110.46(15)	C3-C4-C5	115.44(15)	N1-C5-C20	113.62(15)
N1-C5-C4	109.95(15)	C20-C5-C4	113.68(15)	C7-C6-C11	120.50(19)
C7-C6-S1	120.01(15)	C11-C6-S1	119.46(15)	C6-C7-C8	119.43(18)
C9-C8-C7	121.21(19)	C8-C9-C10	118.36(19)	C8-C9-C12	120.9(2)
C10-C9-C12	120.7(2)	C11-C10-C9	121.60(19)	C10-C11-C6	118.9(2)
C14-C13-C1	112.88(16)	C15-C14-C19	118.1(2)	C15-C14-C13	119.8(2)
C19-C14-C13	122.2(2)	C16-C15-C14	121.1(2)	C17-C16-C15	119.8(2)
C16-C17-C18	120.2(2)	C17-C18-C19	120.2(3)	C18-C19-C14	120.8(2)
C21-C20-C5	115.94(16)	O4-C21-C22	107.32(16)	O4-C21-C20	111.57(17)
C22-C21-C20	111.91(17)	C1-N1-C5	119.37(14)	C1-N1-S1	118.97(12)
C5-N1-S1	117.71(12)	O2-S1-O1	118.72(10)	O2-S1-N1	108.03(9)
O1-S1-N1	107.05(8)	O2-S1-C6	108.42(9)	O1-S1-C6	105.13(9)
N1-S1-C6	109.23(9)				

X-ray Structure Determination of Compound (*S*,*S*,*S*,*R*)-**17**



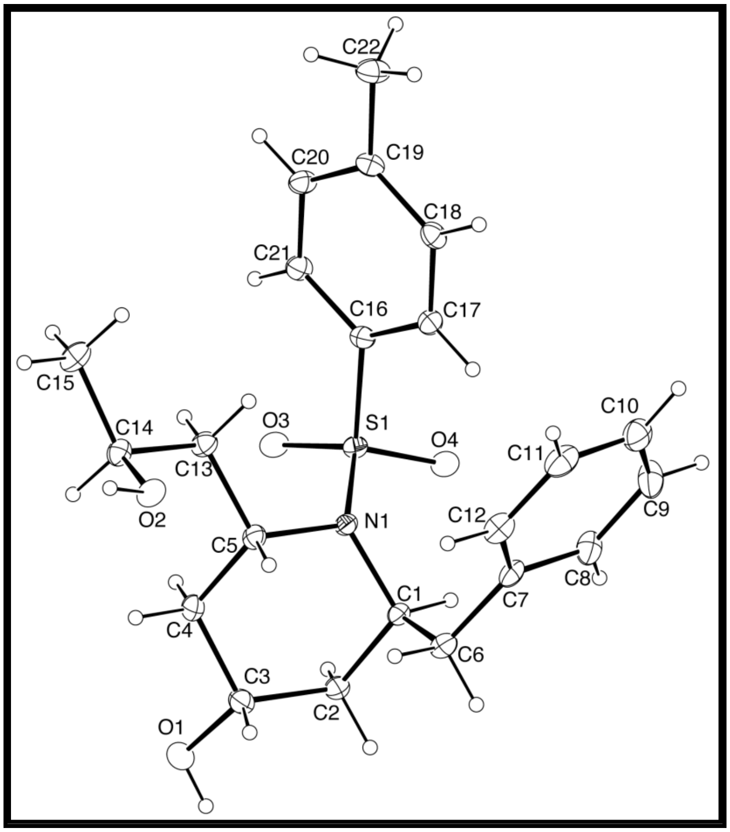


Figure 1. ORTEP drawing of the title compond with 30% probability thermal ellipsoids.

Table 1. Summary of Structure Determination of Compound (*S*,*S*,*S*,*R*)-17

Empirical formula	$C_{22}H_{29}NSO_4$
Formula weight	403.52
Temperature	100(1) K
Wavelength	0.71073 Å
Crystal system	orthorhombic
Space group	$P2_12_12_1$
Cell constants:	
a	13.8629(4) Å
b	16.9650(4) Å
c	17.9277(4) Å
Volume	4216.31(18) $Å^3$
Z	8
Density (calculated)	1.271 Mg/m^3
Absorption coefficient	0.181 mm^{-1}
F(000)	1728
Crystal size	0.35 x 0.18 x 0.06 mm^3
Theta range for data collection	1.65 to 27.55°
Index ranges	$-18 \leq h \leq 18, -22 \leq k \leq 21, -23 \leq l \leq 23$
Reflections collected	87053
Independent reflections	9722 [R(int) = 0.0324]
Completeness to theta = 27.55°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.7022
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9722 / 0 / 514
Goodness-of-fit on F^2	1.006
Final R indices [I>2sigma(I)]	R1 = 0.0290, wR2 = 0.0754
R indices (all data)	R1 = 0.0333, wR2 = 0.0779
Absolute structure parameter	-0.03(3)
Largest diff. peak and hole	0.299 and -0.224 $e.Å^{-3}$

Table 2. Refined Positional Parameters for Compound (*S*,*S*,*S*,*R*)-**17**

Atom	x	y	z	U_{eq}, Å^2
C1	0.37810(10)	0.19794(8)	0.65331(7)	0.0193(3)
C2	0.48323(10)	0.22569(9)	0.64604(8)	0.0223(3)
C3	0.50741(10)	0.26044(10)	0.56978(8)	0.0257(3)
C4	0.43396(10)	0.32256(9)	0.54766(8)	0.0251(3)
C5	0.33030(10)	0.29248(8)	0.55259(7)	0.0205(3)
C6	0.35435(11)	0.12034(9)	0.61372(8)	0.0247(3)
C7	0.25344(11)	0.09292(8)	0.63142(8)	0.0247(3)
C8	0.22771(12)	0.07751(10)	0.70521(9)	0.0313(3)
C9	0.13477(13)	0.05558(11)	0.72385(10)	0.0380(4)
C10	0.06504(13)	0.04726(10)	0.66883(10)	0.0362(4)
C11	0.09035(13)	0.06090(10)	0.59509(11)	0.0355(4)
C12	0.18268(12)	0.08461(9)	0.57699(9)	0.0304(3)
C13	0.25580(11)	0.35298(9)	0.52618(7)	0.0235(3)
C14	0.26478(11)	0.37609(8)	0.44463(8)	0.0237(3)
C15	0.18713(13)	0.43538(10)	0.42377(9)	0.0317(3)
C16	0.14870(10)	0.33778(8)	0.67413(7)	0.0202(3)
C17	0.08613(10)	0.27496(9)	0.66587(8)	0.0233(3)
C18	-0.01026(10)	0.29011(9)	0.64912(8)	0.0241(3)
C19	-0.04349(10)	0.36703(9)	0.64050(8)	0.0236(3)
C20	0.02169(11)	0.42916(9)	0.64915(8)	0.0246(3)
C21	0.11749(10)	0.41504(9)	0.66669(8)	0.0232(3)
C22	-0.14747(11)	0.38373(10)	0.62179(10)	0.0319(3)
N1	0.30963(8)	0.26113(7)	0.62902(6)	0.0185(2)
O1	0.59866(8)	0.29883(7)	0.57015(7)	0.0342(3)
O2	0.25544(8)	0.30510(6)	0.40144(6)	0.0266(2)
O3	0.32001(7)	0.39588(6)	0.69296(6)	0.0250(2)
O4	0.27585(8)	0.27663(6)	0.76314(5)	0.0268(2)
S1	0.27172(2)	0.32091(2)	0.694394(18)	0.01900(7)

$U_{eq}={}^1/_3[U_{11}(aa^*)^2+U_{22}(bb^*)^2+U_{33}(cc^*)^2+2U_{12}aa^*bb^*\cos\gamma+2U_{13}aa^*cc^*\cos\beta+2U_{23}bb^*cc^*\cos\alpha]$

Table 3. Positional Parameters for Hydrogens in Compound (*S*,*S*,*S*,*R*)-17

Atom	x	y	z	U_{iso}, Å^2
H1	0.3664	0.1892	0.7066	0.026
H2a	0.4958	0.2651	0.6840	0.030
H2b	0.5257	0.1813	0.6555	0.030
H3	0.5078	0.2183	0.5324	0.034
H4a	0.4469	0.3395	0.4970	0.033
H4b	0.4411	0.3680	0.5800	0.033
H5	0.3257	0.2476	0.5184	0.027
H6a	0.3607	0.1275	0.5603	0.033
H6b	0.4001	0.0803	0.6291	0.033
H8	0.2739	0.0821	0.7426	0.042
H9	0.1189	0.0463	0.7735	0.051
H10	0.0024	0.0328	0.6812	0.048
H11	0.0448	0.0540	0.5576	0.047
H12	0.1979	0.0952	0.5275	0.040
H13a	0.1918	0.3316	0.5345	0.031
H13b	0.2620	0.4001	0.5565	0.031
H14	0.3285	0.3994	0.4359	0.032
H15a	0.1913	0.4470	0.3714	0.047
H15b	0.1963	0.4829	0.4519	0.047
H15c	0.1248	0.4137	0.4348	0.047
H17	0.1080	0.2235	0.6714	0.031
H18	-0.0530	0.2483	0.6436	0.032
H20	0.0005	0.4808	0.6430	0.033
H21	0.1602	0.4567	0.6734	0.031
H22a	-0.1791	0.4061	0.6645	0.048
H22b	-0.1791	0.3355	0.6081	0.048
H22c	-0.1505	0.4202	0.5809	0.048
H1a	0.6401	0.2681	0.5848	0.051
H2	0.2483	0.3165	0.3573	0.040

Table 4. Refined Thermal Parameters (U's) for Compound (*S,S,S,R*)-17

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	0.0197(6)	0.0191(7)	0.0191(6)	0.0027(5)	-0.0002(5)	0.0031(5)
C2	0.0194(6)	0.0245(7)	0.0231(7)	0.0036(6)	-0.0017(5)	0.0030(6)
C3	0.0202(7)	0.0314(8)	0.0254(7)	0.0046(6)	0.0019(5)	0.0011(6)
C4	0.0243(7)	0.0269(7)	0.0241(7)	0.0082(6)	0.0010(5)	0.0013(6)
C5	0.0239(7)	0.0215(6)	0.0160(6)	0.0016(5)	-0.0004(5)	0.0022(5)
C6	0.0274(7)	0.0209(7)	0.0258(7)	-0.0002(6)	-0.0016(6)	0.0049(6)
C7	0.0299(8)	0.0142(6)	0.0300(7)	0.0017(5)	-0.0043(6)	0.0016(6)
C8	0.0333(8)	0.0296(8)	0.0310(8)	0.0079(6)	-0.0080(7)	-0.0071(7)
C9	0.0401(10)	0.0363(9)	0.0375(9)	0.0114(7)	-0.0031(7)	-0.0123(8)
C10	0.0313(8)	0.0271(8)	0.0501(10)	0.0055(7)	-0.0051(7)	-0.0059(7)
C11	0.0350(9)	0.0271(8)	0.0443(9)	-0.0015(7)	-0.0159(8)	0.0006(7)
C12	0.0370(8)	0.0254(7)	0.0286(7)	-0.0020(6)	-0.0073(6)	0.0030(7)
C13	0.0248(7)	0.0241(7)	0.0216(6)	0.0012(5)	-0.0027(5)	0.0036(6)
C14	0.0257(7)	0.0228(7)	0.0227(6)	0.0029(5)	-0.0033(6)	-0.0002(6)
C15	0.0374(9)	0.0277(8)	0.0299(8)	0.0032(6)	-0.0086(7)	0.0072(7)
C16	0.0174(6)	0.0241(7)	0.0191(6)	-0.0006(5)	0.0002(5)	0.0017(5)
C17	0.0249(7)	0.0192(7)	0.0259(7)	0.0000(6)	0.0026(6)	0.0009(6)
C18	0.0212(7)	0.0242(7)	0.0269(7)	-0.0026(6)	0.0021(5)	-0.0056(6)
C19	0.0199(7)	0.0280(8)	0.0229(7)	-0.0047(6)	0.0027(5)	0.0014(6)
C20	0.0237(7)	0.0219(7)	0.0283(7)	-0.0032(6)	0.0013(6)	0.0043(6)
C21	0.0224(7)	0.0195(7)	0.0276(7)	-0.0045(6)	0.0013(5)	-0.0009(5)
C22	0.0199(7)	0.0324(8)	0.0435(9)	-0.0072(7)	-0.0021(6)	0.0023(6)
N1	0.0202(5)	0.0178(5)	0.0174(5)	0.0014(4)	0.0004(4)	0.0038(4)
O1	0.0203(5)	0.0385(7)	0.0437(7)	0.0121(5)	0.0020(5)	-0.0009(5)
O2	0.0328(6)	0.0268(5)	0.0201(5)	-0.0003(4)	-0.0050(4)	0.0054(4)
O3	0.0219(5)	0.0215(5)	0.0316(5)	-0.0038(4)	-0.0039(4)	-0.0001(4)
O4	0.0290(5)	0.0315(5)	0.0198(5)	0.0020(4)	0.0009(4)	0.0080(5)
S1	0.01822(15)	0.01961(15)	0.01917(15)	-0.00105(12)	-0.00133(12)	0.00166(13)

The form of the anisotropic displacement parameter is:
$\exp[-2\pi^2(a^{*2}U_{11}h^2+b^{*2}U_{22}k^2+c^{*2}U_{33}l^2+2b^*c^*U_{23}kl+2a^*c^*U_{13}hl+2a^*b^*U_{12}hk)]$

Table 5. Bond Distances in Compound (*S*,*S*,*S*,*R*)-**17**, Å

C1-N1	1.4964(17)	C1-C6	1.5314(19)	C1-C2	1.5371(19)
C2-C3	1.5260(19)	C3-O1	1.4229(18)	C3-C4	1.518(2)
C4-C5	1.527(2)	C5-N1	1.4976(16)	C5-C13	1.5311(19)
C6-C7	1.508(2)	C7-C12	1.391(2)	C7-C8	1.395(2)
C8-C9	1.382(2)	C9-C10	1.388(2)	C10-C11	1.387(3)
C11-C12	1.380(3)	C13-C14	1.5189(19)	C14-O2	1.4376(17)
C14-C15	1.520(2)	C16-C17	1.382(2)	C16-C21	1.387(2)
C16-S1	1.7669(14)	C17-C18	1.393(2)	C18-C19	1.392(2)
C19-C20	1.397(2)	C19-C22	1.507(2)	C20-C21	1.386(2)
N1-S1	1.6366(11)	O3-S1	1.4376(10)	O4-S1	1.4445(10)
C1'-N1'	1.4985(17)	C1'-C6'	1.533(2)	C1'-C2'	1.535(2)

Table 6. Bond Angles in Compound (*S*,*S*,*S*,*R*)-**17**, °

N1-C1-C6	110.16(11)	N1-C1-C2	110.94(11)	C6-C1-C2	115.33(12)
C3-C2-C1	113.74(11)	O1-C3-C4	106.24(12)	O1-C3-C2	111.59(12)
C4-C3-C2	110.78(12)	C3-C4-C5	112.58(12)	N1-C5-C4	110.58(11)
N1-C5-C13	113.08(11)	C4-C5-C13	113.13(12)	C7-C6-C1	111.54(12)
C12-C7-C8	117.78(15)	C12-C7-C6	122.54(14)	C8-C7-C6	119.64(13)
C9-C8-C7	121.20(15)	C8-C9-C10	120.31(17)	C9-C10-C11	118.95(16)
C12-C11-C10	120.47(15)	C11-C12-C7	121.24(16)	C14-C13-C5	114.55(12)
O2-C14-C15	110.99(12)	O2-C14-C13	107.14(11)	C15-C14-C13	110.47(12)
C17-C16-C21	121.51(13)	C17-C16-S1	120.20(11)	C21-C16-S1	118.29(11)
C16-C17-C18	118.87(14)	C19-C18-C17	120.93(14)	C18-C19-C20	118.74(13)
C18-C19-C22	121.15(14)	C20-C19-C22	120.10(14)	C21-C20-C19	120.97(14)
C20-C21-C16	118.96(14)	C5-N1-C1	113.53(10)	C5-N1-S1	119.78(9)
C1-N1-S1	116.06(9)	O3-S1-O4	117.19(6)	O3-S1-N1	112.70(6)
O4-S1-N1	106.02(6)	O3-S1-C16	107.61(6)	O4-S1-C16	107.33(6)
N1-S1-C16	105.25(6)	N1'-C1'-C6'	109.87(11)	N1'-C1'-C2'	110.25(12)