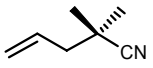
Supplementary Material (ESI) for Chemical Communications

Base catalysed asymmetric hydroamination/cyclisation of aminoalkenes utilising a dimeric chiral diamidobinaphthyl dilithium salt

Patricia Horrillo Martínez, Kai C. Hultzsch* and Frank Hampel

Experimental Section

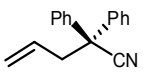
General Considerations. All operations were performed under an inert atmosphere of nitrogen or argon using standard Schlenk-line or glovebox techniques. After drying over KOH, THF and diethyl ether were distilled from sodium benzophenone ketyl. After drying over CaH_2, hexanes was purified by distillation from sodium/triglyme/benzophenone ketyl. Deuterated benzene was dried with sodium benzophenone ketyl and distilled *in vacuo*. Boc-*L*-proline (>99% ee, Fluka), diphenylacetonitrile (Aldrich), cyclohexanecarbonitrile (Aldrich) and 1-naphthylamine (Aldrich) were used as received. (*R*)-(+)-α-Methoxy-α-trifluoro-methylphenylacetic acid (>99% ee, from Reuter Chemische Apparatebau KG (RCA), Freiburg, Germany) was transformed to its acid chloride using oxalyl chloride/DMF in hexanes.[1] *rac*-Diaminobinaphthyl (DABN)[2] was synthesized as described in the literature. The substrates were distilled from finely powdered CaH_2 and stored over molecular sieves. Enantiomerically pure (*R*)-DABN was prepared via its *D*-(+)-camphersulfonic acid salt.[2a] All other chemicals were commercially available and were used as received. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on Bruker Avance 300 or Avance 400 spectrometer. Enantiomeric excess of the hydroamination products were determined by ^{19}F NMR of their Mosher amides at 60-80°C (*vide infra*). ^{7}Li NMR was recorded on a Jeol Alpha 500. Mass Spectra were recorded on a Finnigan MAT 95XP instrument (EI). Preparative HPLC was performed on a Varian Prostar instrument with a Dynamax Column 250 × 41.4 mm, Microsorb 100-8 Si.



2,2-Dimethyl-pent-4-enenitrile. A solution of *n*-BuLi (58.0 mL, 151 mmol, 2.6 M in hexanes) was added dropwise to a solution of diisopropylamine (15.20 g, 150 mmol) in THF (250 mL) at –78 °C. The resulting slight yellow solution was warmed to 0 °C, stirred for 1 h at this temperature and was then cooled again to –78 °C. Then isobutyronitrile (10.40 g, 150.5 mmol) was added dropwise and the reaction mixture was allowed to warm to 0 °C and was stirred for 2.5 h at this temperature. After cooling back to –78 °C, allyl

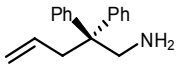
bromide (19.70 g, 162.8 mmol) was added. The reaction mixture was slowly warmed to room temperature and stirred overnight. Then, water (5 mL) was added and the solvent carefully removed under reduced pressure (40 °C, 130 mbar). The residue was dissolved in Et_2O (200 mL) and was washed with brine (2 × 50 mL) and water (10 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was carefully removed under reduced pressure (40 °C, 130 mbar) to give 16.10 g (98%) of 2,2-diphenyl-pent-4-enenitrile as a slight yellow oil, which was sufficiently pure according to NMR spectroscopy and was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.83 (m, 1H, CH_2=C*H*), 5.17 (m, 2H, C*H*$_2$=CH), 2.25 (d, $^3J_{H,H}$ = 7.3 Hz, 2H, =CHC*H*$_2$), 1.31 (s, 6H, C(C*H*$_3$)$_2$); ^{13}C {^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 132.2 (*C*H=CH$_2$), 124.7 (CN), 119.9 (CH=*C*H$_2$), 45.0 (=CH*C*H$_2$), 32.1 (*C*(CH$_3$)$_2$), 25.6 (C(*C*H$_3$)$_2$).

2,2-Dimethyl-pent-4-enylamine (5).[3] A solution of 2,2-dimethyl-pent-4-enenitrile (16.10 g, 147.5 mmol) in Et_2O (100 mL) was added dropwise to a suspension of $LiAlH_4$ (5.80 g, 152.8 mmol) in Et_2O (200 mL). The suspension was refluxed for 4 h and then stirred at room temperature overnight. The reaction mixture was cooled to 0 °C and treated carefully with water (6 mL), 15% NaOH (6 mL) and again water (20 mL). The ether layer was decanted from the white precipitate and the precipitate was extracted with Et_2O again (3 × 100 mL). The organic layers were combined, dried over $MgSO_4$, filtered and the solvent was carefully removed under reduced pressure (40 °C, 150 mbar). Residual ether was removed by dissolving the crude product in pentane and careful evaporation of the solvent under reduced pressure. The crude product was purified by distillation (b.p. 130–133.5 °C) to give 11.24 g (67%) of **5** as a colourless oil. ^{1}H NMR (400 MHz, C_6D_6): δ 5.73 (m, 1H, *CH*=CH$_2$), 5.00 (m, 2H, CH=*CH*$_2$), 2.26 (s, 2H, NH$_2$*CH*$_2$), 1.88 (dt, $^3J_{H,H}$ = 7.5 Hz, $^4J_{H,H}$ = 1.0 Hz, 2H, =CH*CH*$_2$), 0.74 (s, 6H, C(*CH*$_3$)$_2$), 0.46 (br s, 2H, NH$_2$); ^{13}C {^{1}H} NMR (100.6 MHz, C_6D_6): δ 136.0 (*CH*=CH$_2$), 116.7 (CH=*C*H$_2$), 52.7 (NH$_2$*C*H$_2$), 44.2 (=CH*C*H$_2$), 35.0 (*C*(CH$_3$)$_2$), 24.7 (C(*C*H$_3$)$_2$).

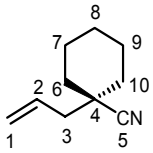


2,2-Diphenyl-pent-4-enenitrile.[4] A solution of *n*-BuLi (17.6 mL, 44.1 mmol, 2.5 M in hexanes) was added dropwise to a solution of diisopropylamine (4.553 g, 44.99 mmol) in THF (20 mL) at –78 °C. The resulting slight yellow solution was warmed to 0 °C and cooled again to –78 °C. Then diphenylacetonitrile (8.116 g, 42.00 mmol) in THF (20 mL) was added

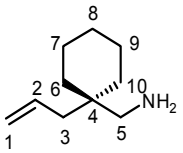
dropwise and the reaction mixture was stirred at –78 °C for 2 h. Allyl bromide (5.081 g, 42.0 mmol) was added and the reaction mixture slowly warmed to room temperature. Then, the reaction mixture was washed with 10% NH_4Cl aqueous solution (40 mL) and extracted with Et_2O (2 × 40 mL). The organic layers were combined, dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure to give 9.750 g (99%) of crude 2,2-diphenyl-pent-4-enenitrile as a slight yellow oil, which was sufficiently pure according to NMR spectroscopy and was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (m, 10H, aryl-H), 5.70 (m, 1H, C*H*=CH_2), 5.17 (m, 2H, CH=C*H*$_2$), 3.12 (d, $^3J_{H,H}$ = 7.0 Hz, 2H, =CHC*H*$_2$); ^{13}C {^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 139.7 (*C*H=CH_2), 131.7, 128.8, 127.9, 127.0 (aryl), 121.9 (CN), 120.4 (CH=*C*H_2), 51.7 (*C*Ph_2), 43.9 (=CH*C*H_2); MS (FAB, 3-NBA), m/z = 234 ($[M+1]^+$, 64%), 207 ($[M-CN]^+$, 100%).



2,2-Diphenyl-pent-4-enylamine (7).[4] A solution of 2,2-diphenylpent-4-ene (9.750 g, 41.8 mmol) in Et_2O (20 mL) was added dropwise to a suspension of $LiAlH_4$ (7.930 g, 208.9 mmol) in Et_2O (150 mL). The suspension was stirred at room temperature for 48 h and then refluxed for additional 4 h. The reaction mixture was diluted with Et_2O (50 mL) and treated carefully with water (ice-water bath). The ether layer was decanted from the white precipitate and the precipitate extracted with Et_2O again (2 × 40 mL). The organic layers were combined and the hydrochloride salt of the crude product was precipitated by addition of conc. HCl (8 mL). The organic layer was separated and discarded. The ammonium salt was taken up in water (10 mL) and Et_2O (50 mL). The mixture was cooled to 0 °C and cold 50% KOH (18 mL) was added to generate the free amine. The aqueous layer was extracted with Et_2O (2 × 40 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. Vacuum distillation (118–120 °C, 0.1 mbar) gave 7.609 g (77% yield) of **7** as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (m, 4H, aryl-H), 7.18 (m, 6H, aryl-H), 5.37 (m, 1H, C*H*=CH_2), 5.00 (m, 2H, CH=C*H*$_2$), 3.32 (s, 2H, NH_2C*H*$_2$), 2.91 (d, $^3J_{H,H}$ = 7.06 Hz, 2H, C*H*$_2$), 0.85 (br s, 2H, NH_2); ^{13}C {^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 146.2 (aryl), 134.6 (*C*H=CH_2), 128.2, 128.0, 126.0 (aryl), 117.6 (CH=*C*H_2), 51.3 (*C*Ph_2), 48.6 (NH_2*C*H_2), 41.1 (=CH*C*H_2); HRMS (EI), m/z calcd for $C_{17}H_{19}N$: 237.1512; found: 237.1507.

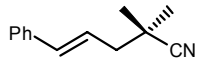


1-Allyl-cyclohexanecarbonitrile.[5] A solution of *n*-BuLi (33.6 mL, 84.0 mmol, 2.5 M in hexanes) was added dropwise to a solution of diisopropylamine (8.904 g, 87.99 mmol) in THF (20 mL) at –78 °C. The resulting slight yellow solution was warmed to 0 °C and cooled again to –78 °C. Then cyclohexanecarbonitrile (8.734 g, 80.00 mmol) in THF (20 mL) was added dropwise and the reaction mixture was stirred at –78 °C for 2 h. Allyl bromide (9.678 g, 80.00 mmol) was added dropwise to the reaction mixture at this temperature and the reaction mixture was allowed to warm to room temperature. Then, the reaction mixture was washed with 10% NH_4Cl aqueous solution (40 mL) and was extracted with diethyl ether (2 × 40 mL). The organic layers were combined, dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was distilled under vacuum (15–20 mbar, b.p. 90 °C) to give 8.66 g (73%) of a colourless oil which was used without further purifications. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.85 (m, 1H, H_2), 5.15 (m, 2H, H_1), 2.25 (d, $^3J_{H,H}$ = 7.34 Hz, 2H, H_3), 1.93 (m, 2H, $H_{6,10}$), 1.59 (m, 6H, $H_{6,10}$, $H_{7,9}$), 1.21 (m, 2H, H_8); ^{13}C {^{1}H} NMR (75.5 MHz, $CDCl_3$): δ 131.9 (C_2), 123.3 (CN), 119.6 (C_1), 44.6 (C_3), 38.8 (C_4), 35.3 ($C_{6,10}$), 25.2 (C_8), 23.0 ($C_{7,9}$).

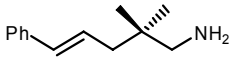


***C*-(1-allyl-cyclohexyl)-methylamine (9).**[5] A solution of 1-allyl-cyclohexanecarbonitrile (8.660 g, 58.03 mmol) in Et_2O (20 mL) was added dropwise to a suspension of $LiAlH_4$ (5.064 g, 133.4 mmol) in Et_2O (150 mL) at 0 °C. The suspension was stirred at room temperature overnight and then refluxed for additional 6 h. The reaction mixture was diluted with Et_2O (50 mL) and treated carefully with water, 15% NaOH aqueous solution and water again (ice-water bath). The ether phase was decanted from the white precipitate and the precipitate extracted with Et_2O again (2 × 40 mL). The organic layers were combined, dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure to give 9.912 g of slightly yellow oil as a crude product which was distilled *in vacuo* (12 mbar, b.p.119–125 °C). The product was treated at 0 °C with 2N HCl to form the ammonium salt. After 30 min, the suspension was brought to room temperature and the solvent was removed *in vacuo*. The white precipitate was washed with Et_2O (2 × 50 mL), followed by addition of 50% KOH to form the free

amine again. The aqueous layer was extracted with Et_2O (3 × 50 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure to give 2.433 g of **9** (27%) as a colourless oil. ^{1}H NMR (400 MHz, C_6D_6): δ 5.73 (m, 1H, H_2), 5.00 (m, 2H, H_1), 2.36 (s, 2H, H_5), 2.00 (d, $^3J_{H,H}$ = 7.52 Hz, 2H, H_3), 1.29 (m, 6H, $H_{6,10}$, $H_{7,9}$), 1.15 (m, 4H, $H_{6,10}$, H_8), 0.46 (br s, 2H, NH_2); ^{13}C {^{1}H} NMR (100.6 MHz, C_6D_6): δ 135.7 (C_2), 116.6 (C_1), 48.8 (C_5), 40.1 (C_3), 37.3 (C_4), 33.4 ($C_{6,10}$), 26.8 (C_8), 21.9 ($C_{7,9}$); HRMS (EI), m/z calcd for $C_{10}H_{18}N^+$: 152.1434; found: 152.1429.

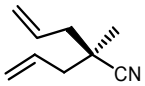


(4*E*)-2,2-Dimethyl-5-phenylpent-4-enenitrile.[6] THF (100 mL) was cooled to –78 °C and *n*-BuLi (40 mL, 2.5 M in hexanes, 100 mmol) was added, followed by addition of diisopropylamine (14.4 mL, 10.3 g, 102 mmol) at –78 °C. The resulting solution was allowed to warm to –30 °C and was then cooled back to –78 °C. Isobutyronitrile (9.1 mL, 6.91 g, 100 mmol) was added dropwise to this solution. The reaction mixture was stirred at –50 °C and was then treated with a solution of *trans*-cinnamyl bromide (19.7 g, 100.0 mmol) in THF (20 mL). The reaction mixture was allowed to reach room temperature and was stirred at this temperature for additional 4 h. The solvent was removed by rotary evaporation and the residue was treated with CH_2Cl_2 (150 mL) and water (100 mL). The organic layer was separated, dried over Na_2SO_4 and concentrated by rotary evaporation. The crude material was distilled (bp 95–101 °C, 0.1 mbar) to give 11.7 g (63% yield) of a colourless liquid of (4*E*)-2,2-dimethyl-5-phenylpent-4-enenitrile, which solidified within a few hours to give a white crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (m, 2H, aryl-H), 7.31 (m, 2H, aryl-H), 7.24 (m, 1H, aryl-H), 6.51 (d, $^3J_{H,H}$ = 15.7 Hz, 1H, PhC*H*=), 6.25 (m, 1H, =C*H*CH_2), 2.43 (dd, $^3J_{H,H}$ = 7.5 Hz, $^4J_{H,H}$ = 1.1 Hz, 2H, =CHC*H*$_2$), 1.37 (s, 6H, C(C*H*$_3$)$_2$); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 136.7, 134.8, 128.5, 127.6, 126.3 (aryl and vinyl), 124.7 (C≡N), 123.5, 44.3 (=CH*C*H$_2$), 32.5 (*C*(CH$_3$)$_2$), 26.3 (C(*C*H$_3$)$_2$).

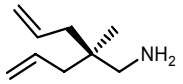


(4*E*)-2,2-Dimethyl-5-phenylpent-4-enylamine (11).[6] To a suspension of $LiAlH_4$ (2.30 g, 60.7 mmol) in Et_2O (100 mL) was added a solution of (4*E*)-2,2-dimethyl-5-phenylpent-4-enenitrile (7.41 g, 40.0 mmol) in Et_2O (20 mL) at 0 °C. The reaction mixture was stirred at room temperature overnight, was then cooled back to 0 °C and treated carefully with 15% NaOH (15 mL). The ether layer was decanted off from the white precipitate and the

precipitate was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over KOH and concentrated by rotary evaporation. The residue was distilled (80–85 °C, 0.1 mbar) to give 6.40 g (85% yield) of **11** as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (m, 2H, aryl-H), 7.28 (m, 2H, aryl-H), 7.18 (m, 1H, aryl-H), 6.38 (d, $^3J_{H,H}$ = 15.7 Hz, 1H, PhC*H*=), 6.22 (m, 1H, =C*H*CH_2), 2.48 (s, 2H, C*H*$_2NH_2$), 2.11 (d, $^3J_{H,H}$ = 7.5 Hz, 2H, =CHC*H*$_2$), 0.96 (br s, 2H, NH_2), 0.89 (s, 6H, C(CH_3)$_2$); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 137.7, 132.1, 128.4, 127.3, 126.9, 125.9 (aryl and vinyl), 52.7 (CH_2N), 43.1 (=CH*C*H_2), 35.6 (*C*(CH_3)$_2$), 24.7 (C(*C*H_3)$_2$).

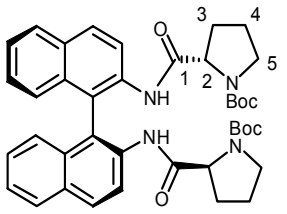


2-Allyl-2-methylpent-4-enenitrile.[7] A solution of *n*-BuLi (40.0 mL, 100.0 mmol, 2.5 M solution in hexanes) was added dropwise to a solution of diisopropylamine (10.38 g, 102.6 mmol) in THF (45 mL) at –78 °C. The resulting light yellow solution was stirred for 90 min at 0 °C. 49 mL of this solution of lithium diisopropylamide (LDA) was transferred to a dropping funnel and was added slowly dropwise to a solution of propionitrile (2.89 g, 52.5 mmol) in THF (40 mL) at –78 °C. The solution was stirred for 90 min at this temperature and was then treated with allyl bromide (5.99 g, 49.5 mmol) dropwise. The solution was stirred for another 30 min at –78 °C and was then allowed to warm to room temperature. After 1 h, the solution was cooled back to –78 °C, and the second part of LDA was added over 30 min. The solution was allowed to warm to 0 °C and was stirred for 30 min. After cooling back to –78 °C the solution was treated with allyl bromide (7.30 g, 60.3 mmol). The reaction mixture was allowed to warm slowly to room temperature and stirred overnight. The reaction was quenched by addition of water (3 mL), and the solvent was removed *in vacuo* (40 °C, 300 mbar). The residue was taken up with Et_2O (200 mL), washed with brine (2 × 30 mL) and water (10 mL), dried over $MgSO_4$. Concentration *in vacuo* (40 °C, 150 mbar) gave 6.91 g (97% yield) of a yellow oil, which was shown to be sufficiently clean by NMR spectroscopy and was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.85 (m, 2H, C*H*=CH_2), 5.18 (m, 4H, CH=C*H*$_2$), 2.27 (m, 4H, =CHC*H*$_2$), 1.27 (s, 3H, C(C*H*$_3$)); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 131.9 (*C*H=CH_2), 123.6 (CN), 120.1 (CH=*C*H_2), 43.0 (=CH*C*H_2), 36.3 (*C*(CH_3)), 23.4 (C(*C*H_3)).



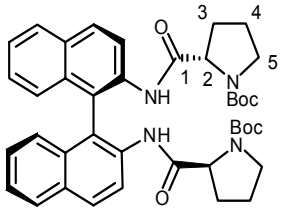
2-Allyl-2-methylpent-4-enylamine (13).[7] A solution of 2-allyl-2-methylpent-4-enenitrile (6.91 g, 51.1 mmol) in Et_2O (50 mL) was added dropwise to a suspension of $LiAlH_4$ (2.15 g, 56.7 mmol) in Et_2O (50 mL). The suspension was heated at reflux for 2 h and was stirred at room temperature overnight. The suspension was diluted with Et_2O (100 mL) and treated carefully with water (2.2 mL), 15% NaOH (2.2 mL) and then again with water (7.4 mL). The ether phase was decanted from the white precipitate, and the precipitate was extracted with Et_2O (3 × 60 mL). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo* (40 °C, 100 mbar) to give 6.50 g (91%) of a yellow oil. The crude product was stirred over calcium hydride for several days and was then distilled *in vacuo*. ^{1}H NMR (400 MHz, C_6D_6): δ 5.74 (m, 2H, C*H*=CH_2), 4.99 (m, 4H, CH=C*H*$_2$), 2.29 (s, 2H, C*H*$_2$$NH_2$), 1.92 (d, $^3J_{H,H}$ = 7.6 Hz, 4H, =CHC*H*$_2$), 0.72 (s, 3H, C(C*H*$_3$)), 0.47 (br s, 2H, NH_2); ^{13}C{1H} NMR (100.6 MHz, C_6D_6): δ 135.6 (*C*H=CH_2), 117.0 (CH=*C*H_2), 50.0 (*C*$H_2$$NH_2$), 42.0 (=CH*C*$H_2$), 37.9 (*C*($CH_3$)), 22.3 (C(*C*$H_3$)).

(*rac*)-DABN(BocProlin)$_2$ (*rac*-1). A solution of 2.152 g Boc-*L*-proline (10.00 mmol) in dry THF (50 mL) was cooled to -15 °C. Then Et_3N (1.113 g, 11.00 mmol) was added followed by dropwise addition of $ClCO_2Et$ (1.085 g, 10.00 mmol). The white suspension was stirred for 1 h at this temperature and was then treated dropwise with a –15 °C cold solution of *rac*-DABN (1.422 g, 5.00 mmol) in dry THF (30 mL) over 60 min. The mixture was slowly warmed to RT and stirred overnight. The solvent was removed *in vacuo* and the residue was taken up in ethyl acetate (100 mL). The organic layer was washed with 0.5 M HCl (3 × 80 mL), saturated aqueous $NaHCO_3$ (2 × 80 mL) and brine (1 × 100 mL). Then, the organic layer was dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to give 3.645 g of a orange brown wax as crude product. The (*R,S,S*)- and (*S,S,S*)-diastereomers were separated by column chromatography or preparative HPLC (hexanes/EtOAc 1:1) to give 1.507 g (45%) of (*S,S,S*)-**1** (R_f = 0.20, R_t = 9.14 min) as a brown-orange solid and 1.163 g (34%) of (*R,S,S*)-**1** (R_f = 0.11, R_t = 12.97 min) as a brown-orange solid (79% overall yield).



(*S*,*S*,*S*)-**1**

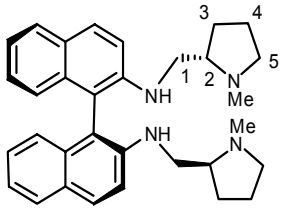
(*S*,*S*,*S*)-**1** ^{1}H NMR (400 MHz, $CDCl_3$, 60 °C): δ 8.63 (d, $^{3}J_{H,H}$ = 9.0 Hz, 2H, aryl-H), 7.96 (d, $^{3}J_{H,H}$ = 8.8 Hz, 2H, aryl-H), 7.83 (d, $^{3}J_{H,H}$ = 8.1 Hz, 2H, aryl-H), 7.69 (br s, 2H, NH), 7.31 (t, $^{3}J_{H,H}$ = 6.8 Hz, 2H, aryl-H), 7.15 (t, $^{3}J_{H,H}$ = 6.8 Hz, 2H, aryl-H), 7.00 (d, $^{3}J_{H,H}$ = 8.6 Hz, 2H, aryl-H), 3.96 (m, 2H, H_2), 2.77 (m, 2H, H_5), 1.93-1.89 (m, 2H, H_5), 1.70 (m, 4H, H_3, H_4), 1.30 (m, 2H, H_3), 1.20 (s, 18H, $C(CH_3)_3$), 0.93 (m, 2H, H_4); $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$, 60 °C): δ 171.2, 154.5 (C=O), 135.4, 132.3, 131.4, 130.1, 128.5, 127.3, 125.4, 125.0, 121.0, 119.6 (aryl), 80.5 ($C(CH_3)_3$), 61.7 (C_2), 46.5 (C_5), 28.3 ($C(CH_3)_3$, C_3), 23.6 (C_4). Anal. Calcd. for $C_{40}H_{46}N_4O_6$: C, 70.77; H, 6.83; N, 8.25. Found: C, 70.96; H, 6.90; N, 7.69.



(*R*,*S*,*S*)-**1**

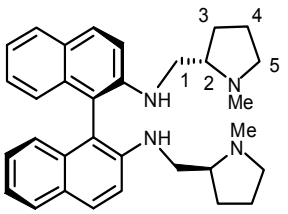
(*R*,*S*,*S*)-**1** ^{1}H NMR (400 MHz, 60 °C, $CDCl_3$): δ 8.48 (d, $^{3}J_{H,H}$ = 8.8 Hz, 2H, aryl-H), 8.03 (d, $^{3}J_{H,H}$ = 9.0 Hz, 2H, aryl-H), 7.93 (d, $^{3}J_{H,H}$ = 8.1 Hz, 2H, aryl-H), 7.54 (br s, 2H, NH), 7.43 (t, $^{3}J_{H,H}$ = 7.8 Hz, 2H, aryl-H), 7.25 (t, $^{3}J_{H,H}$ = 7.6 Hz, 2H, aryl-H), 7.08 (d, $^{3}J_{H,H}$ = 7.8 Hz, 2H, aryl-H), 4.04 (dd, $^{3}J_{H,H}$ = 8.6 Hz, $^{3}J_{H,H}$ = 3.1 Hz, 2H, H_2), 3.02 (m, 2H, H_5), 2.50 (m, 2H, H_5), 1.82 (m, 2H, H_3), 1.69 (br s, 2H, H_3), 1.56 (m, 2H, H_4), 1.29 (m, 2H, H_4), 1.19 (s, 18H, $C(CH_3)_3$); $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$, 60 °C): δ 171.2, 154.3 (C=O), 134.8, 132.5, 131.5, 129.7, 128.4, 127.6, 125.7, 124.8, 121.6, 121.5 (aryl), 80.1 ($C(CH_3)_3$), 61.8 (C_2), 46.6 (C_5), 28.2 ($C(CH_3)_3$, C_3), 23.7 (C_4). Anal. Calcd. for $C_{40}H_{46}N_4O_6$: C, 70.77; H, 6.83; N, 8.25. Found: C, 70.60; H, 6.97; N, 8.17.

The identity of (*R*,*S*,*S*)-**1** was verified independently by preparation starting from enantiopure (*R*)-DABN.



(*S*,*S*,*S*)-**2**

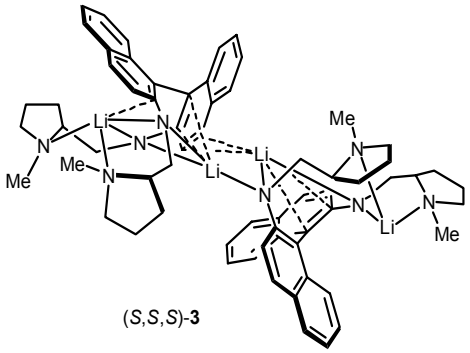
(*S*,*S*,*S*)-2. A solution of (*S*,*S*,*S*)-**1** (1.565 g, 2.30 mmol) in Et_2O (15 mL) was added dropwise to a suspension of $LiAlH_4$ (0.875 g, 23.0 mmol) in Et_2O (55 mL) at 0 °C. The suspension was heated to reflux for 7 h and was then stirred at room temperature overnight. The reaction mixture was diluted with Et_2O (30 mL) and treated carefully with water (ice-water bath), NaOH (15% aqueous solution) and again water, until full consumption of the excess of $LiAlH_4$. The ether phase was decanted from the white precipitate and the precipitate was extracted with Et_2O again (2 × 40 mL). The combined organic layers were dried over $MgSO_4$ and filtered. The solvent from the filtrate was removed under reduced pressure to give a brown solid as a crude product which was purified by column chromatography (EtOAc/MeOH 10:1, R_f = 0.2) to give 0.930 g (84%) of an off-white foam of (*S*,*S*,*S*)-**2**. ^{1}H NMR (400 MHz, C_6D_6, 60 °C): δ 7.83 (d, $^3J_{H,H}$ = 8.8 Hz, 2H, aryl-H), 7.75 (d, $^3J_{H,H}$ = 7.8 Hz, 2H, aryl-H), 7.33 (d, $^3J_{H,H}$ = 8.3 Hz, 2H, aryl-H), 7.16 (m, 2H, aryl-H, overlapped by solvent signal), 7.10 (pt, $^3J_{H,H}$ = 7.1 Hz, 2H, aryl-H), 7.04 (pt, $^3J_{H,H}$ = 7.0 Hz, 2H, aryl-H), 4.30 (br d, 2H, NH), 3.04 (m, 2H, H_1), 2.88 (m, 2H, H_1), 2.52 (t, $^3J_{H,H}$ = 7.8 Hz, 2H, H_5), 1.96 (br s, 8H, NCH_3 and H_2), 1.74 (m, 2H, H_5), 1.35 (m, 2H, H_3), 1.22 (m, 2H, H_4), 1.10 (m, 2H, H_3), 0.86 (m, 2H, H_4); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, 60 °C): δ 144.9, 134.2, 129.5, 128.0, 127.8, 126.5, 124.1, 121.7, 114.1, 112.5 (aryl), 65.1 (C_2), 57.1 (C_5), 46.8 (C_1), 40.6 (NCH_3), 29.3 (C_3), 22.5 (C_4). MS (FAB, 3-NBA), m/z = 480 ($[M+H]^+$, 100%), 394 ($[M-C_5H_{10}N]^+$, 32%], 280 ($[M-2\ C_6H_{12}N]^+$, 24%).



(*R*,*S*,*S*)-**2**

(*R*,*S*,*S*)-2. (*R*,*S*,*S*)-**1** (1.104 g, 1.63 mmol) was reduced with $LiAlH_4$ (0.617 g, 16.3 mmol) in a procedure similar to that for (*S*,*S*,*S*)-**2**. The crude product (0.732 g) was purified by column chromatography (EtOAc/MeOH 10:1, R_f = 0.03) to give 0.344 g (44%) of a white foam of (*R*,*S*,*S*)-**2**. ^{1}H NMR (400 MHz, $CDCl_3$, 60 °C): δ 7.86 (d, $^3J_{H,H}$ = 8.9 Hz, 2H, aryl-H), 7.75 (d,

$^3J_{H,H}$ = 7.0 Hz, 2H, aryl-H), 7.22 (d, $^3J_{H,H}$ = 8.9 Hz, 2H, aryl-H), 7.14 (m, 4H, aryl-H), 7.01 (d, $^3J_{H,H}$ = 8.3 Hz, 2H, aryl-H), 3.90 (m, 4H, NH and H_2), 3.34 (m, 2H, H_1), 3.00 (m, 2H, H_1), 2.77 (m, 2H, H_5), 2.25 (m, 2H, H_5), 2.04 (m, 8H, NCH_3 and H_2), 1.68 (m, 2H, H_3 and H_4), 1.48, (m, 4H, H_3 and H_4), 1.37 (m, 2H, H_3 and H_4); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, 60 °C): δ 144.7, 133.9, 129.4, 128.0, 127.5, 126.5, 123.7, 121.6, 114.1, 112.3 (aryl), 64.5 (C_2), 57.1 (C_5), 47.0 (C_1), 40.4 (NCH_3), 29.1 (C_3), 22.5 (C_4). MS (FAB, 3-NBA), m/z = 480 ($[M+H]^+$, 100%), 394 ($[M-C_5H_{10}N]^+$, 20%], 280 ($[M-2(C_6H_{12}N)]^+$, 20%).

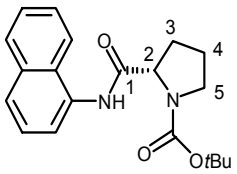


(*S*,*S*,*S*)-**3**

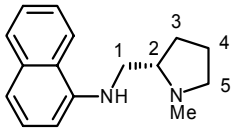
(*S*,*S*,*S*)-3. (*S*,*S*,*S*)-**2** (0.900 g, 1.88 mmol) was dissolved in dry hexanes (15 mL) and benzene (5 mL) and the solution was cooled to 0 °C. Then *n*-BuLi (1.58 mL, 3.95 mmol, 2.5 M in hexanes) was added dropwise. After 15 min stirring at 0 °C the solution was allowed to warm to room temperature and stirred for 1 h. The suspension was then filtered and the remaining yellow solid dried *in vacuo* for 10 min. to give 480 mg (52%) of (*S*,*S*,*S*)-**3**. ^1H NMR (400 MHz, C_6D_6, 60 °C): δ 7.75 (d, $^3J_{H,H}$ = 9.1 Hz, 2H, aryl-H), 7.63 (br m, 2H, aryl-H), 7.26 (d, $^3J_{H,H}$ = 8.8 Hz, 2H, aryl-H), 7.01 (br m, 2H, aryl-H), 6.86 (m, 4H, aryl-H), 3.41 (br d, $^3J_{H,H}$ = 12.4 Hz, 2H, H_1), 3.28 (br d, $^3J_{HH}$ = 12.9 Hz, 2H, H_1), 2.10 (br m, 4H, H_2, H_5), 1.83 (s, 6H, NCH_3), 1.54 (m, 4H, H_5, H_3), 1.30 (m, 2H, H_3), 0.99 (br m, 2H, H_4), 0.53 (br m, 2H, H_4); $^{13}C\{^1H\}$ NMR (100.6 MHz, C_6D_6, 60 °C): δ 156.6, 129.3, 128.6, 128.5, 127.9, 126.3, 125.4, 125.3, 118.7, 116.4 (aryl), 70.9 (C_2), 57.2 (C_5), 48.7 (C_1), 40.0 (CH_3), 27.2 (C_3), 22.0 (C_4); ^7Li NMR (194.5 MHz, 60 °C, C_6D_6): δ -0.116 (s).

(*S*,*S*,*S*)-3×4THF. (*S*,*S*,*S*)-**2** (107 mg, 0.224 mmol) was dissolved in dry hexanes (5 mL) and the solution was cooled to 0 °C. Then, *n*-BuLi (0.18 mL, 0.45 mmol, 2.5 M in hexanes) was added dropwise. The orange solution turned yellow and a precipitate was formed. The suspension was allowed to warm to room temperature and stirred overnight. Then the solvent was removed *in vacuo* to give a brown-orange powder which was dried *in vacuo*. The powder was redissolved in dry hexanes and heated to reflux. Then, 4 equiv. of dry THF (65 μL, 0.90

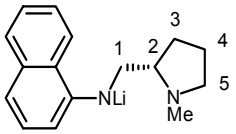
mmol) were added. The volume was concentrated to approximately half volume, and the flask was cooled to –30 °C for crystallization. After filtration and drying *in vacuo* 60 mg (42%) of a fine orange powder of (*S*,*S*,*S*)-**3**×2THF was obtained. ^{1}H NMR (300 MHz, C_6D_6, 60 °C): δ 7.75 (d, $^{3}J_{H,H}$ = 8.9 Hz, 2H, aryl-H), 7.66 (m, 2H, aryl-H), 7.33 (d, $^{3}J_{H,H}$ = 8.9 Hz, 2H, aryl-H), 7.08 (m, 2H, aryl-H), 6.87 (m, 4H, aryl-H), 3.44 (br s, 2H, H_2), 3.33 (br m, 4H, THF), 3.23 (br m, 4H, THF), 2.27 (t, $^{3}J_{H,H}$ = 7.4 Hz, 2H, H_1), 2.10 (br m, 2H, H_1), 1.87 (s, 6H, NCH_3), 1.75–1.56 (m, 4H, H_5), 1.40–1.27 (m, 10H, THF and H_3), 1.08 (m, 2H, H_3), 0.85 (m, 2H, H_4), 0.74 (m, 2H, H_4).



2-(Naphthalen-1-ylcarbamoyl)-pyrrolidine-1-carboxylic acid tert-butyl ester. A solution of 2.162 g (10.00 mmol) of Boc-*L*-proline in THF (60 mL) was cooled to –20 °C. Then Et_3N (1.113 g, 11.00 mmol) was added, followed by dropwise addition of $ClCO_2Et$ (1.112 g, 10.20 mmol). The white suspension was stirred for 2 h at this temperature and was then treated dropwise with a –20 °C cold solution of 1-naphthylamine (1.432, 10.00 mmol) in THF (40 mL) over approximately 60 min. The mixture was slowly warmed to room temperature and stirred for 21 h. The solvent was then removed *in vacuo*. The residue was taken up in EtOAc (100 mL) and the organic layer was washed with 0.5 M HCl (2 × 100 mL), saturated $NaHCO_3$ (2 × 100 mL), and brine (100 mL). The organic layer was then dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to give 3.252 g (96%) of a slightly pink solid as a crude product which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$, 60 °C): δ 9.35 (br s, 1H, NH), 8.13 (d, $^{3}J_{H,H}$ = 7.3 Hz, 1H, aryl-H), 8.02 (br d, 1H, aryl-H), 7.82 (m, 1H, aryl-H), 7.63 (d, $^{3}J_{H,H}$ = 8.1 Hz, 1H, aryl-H), 7.46 (m, 3H, aryl-H), 4.60 (br m, 1H, H_2), 3.49 (br m, 2H, H_5), 2.59 (br s, 1H, H_3), 2.08–1.92 (m, 3H, H_3, H_4), 1.54 (s, 9H, CH_3); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, 60 °C): δ 170.7, 170.4 (C=O), 134.3, 133.2, 133.1, 128.6, 126.7, 126.1, 125.8, 124.9, 121.0, 119.2 (aryl), 81.1 ($C(CH_3)_3$), 61.2 (C_2), 47.4 (C_5), 28.6 (CH_3, C_3), 24.6 (C_4). MS (FAB, 3-NBA), m/z = 340 ($[M]^+$, 63%], 285 ($[M-C_4H_8]^+$, 32%), 241 ($[M-C_5H_9O_2]^+$, 100%).



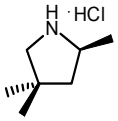
(*S*)-1-Methyl-2-[(*N*-1-naphthylamino)methyl]pyrrolidine. Following a procedure reported by Kobayashi and coworkers,[8] a solution of (*S*)-**4a** (3.214 g, 9.44 mmol) in dry Et_2O (40 mL) was added dropwise to a suspension of $LiAlH_4$ (1.876 g, 47.21 mmol) in Et_2O (100 mL). The suspension was stirred at room temperature for 48 h and heated to reflux for additional 4 h. The reaction mixture was diluted with Et_2O (50 mL) and treated carefully with water (ice-water bath), NaOH (15% aqueous solution) and again water, until full consumption of the excess of $LiAlH_4$. The ether phase was decanted from the white precipitate and the precipitate was extracted with Et_2O (2 × 40 mL). The organic layers were combined, dried over $MgSO_4$ and filtered. The solvent was removed from the filtrate under reduced pressure and the product dried *in vacuo* for several hours to give 2.078 g (92%) of a lilac-violet oil of the desired product. ^{1}H NMR (400 MHz, $CDCl_3$, 60 °C): δ 7.83 (m, 1H, aryl-H), 7.76 (m, 1H, aryl-H), 7.41 (m, 2H, aryl-H), 7.32 (t, $^3J_{H,H}$ = 7.9 Hz, 1H, aryl-H), 7.19 (d, $^3J_{H,H}$ = 8.1 Hz, 1H, aryl-H), 6.58 (d, $^3J_{H,H}$ = 7.6 Hz, 1H, aryl-H), 5.03 (br s, 1H, NH), 3.30 (m, 2H, H_1), 3.18 (m, 1H, H_5), 2.62 (m, 1H, H_5), 2.38 (s, 3H, CH_3), 1.99 (m, 1H, H_2), 1.95–1.70 (m, 4H, H_3, H_4); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, 60 °C): δ 144.4, 134.6, 128.5, 126.7, 125.6, 124.4, 124.0, 120.2, 116.9, 104.2 (aryl), 64.6 (C_2), 57.6 (C_5), 45.2 (C_2), 40.5 (NCH_3), 29.2 (C_3), 23.1 (C_4). MS (FAB, 3-NBA), m/z = 241 ($[M+H]^+$, 100%).



(*S*)-4. (*S*)-1-Methyl-2-[(*N*-1-naphthylamino)methyl]pyrrolidine (1.898 g, 7.90 mmol) was dissolved in dry hexanes (30 mL) and the solution was cooled to 0 °C. Then *n*-BuLi (4.17 mL, 10.43 mmol, 2.5 M in hexanes) was added dropwise. The lilac-violet solution turned yellow and a precipitate formed. The suspension was allowed to warm to room temperature and stirred overnight. Then, the solvent was removed *in vacuo*, the yellow powder was washed with hexanes (3 × 10 mL) and dried *in vacuo* for a few hours to give 1.683 g (86%) of a yellow fine powder of **(*S*)-4**. ^{1}H NMR (300 MHz, C_6D_6): δ 9.39 (d, $^3J_{H,H}$ = 8.2 Hz, 1H, aryl-H), 7.73 (m, 2H, aryl-H), 7.42 (t, $^3J_{H,H}$ = 7.9 Hz, 1H, aryl-H), 7.23 (t, $^3J_{H,H}$ = 7.4 Hz, 1H, aryl-H), 7.02 (d, $^3J_{H,H}$ = 7.9 Hz, 1H, aryl-H), 6.45 (d, $^3J_{H,H}$ = 7.9 Hz, 1H, aryl-H), 3.72 (m, 1H, H_2), 3.00 (m, 2H, H_1), 1.49–1.43 (m, 2H, H_5), 1.30–1.24 (m, 2H, H_5), 1.08 (m, 2H, H_3), 0.99 (s,

3H, CH_3), 0.84 (m, 2H, H_4); $^{13}C\{^1H\}$ NMR (100.6 MHz, C_6D_6): δ 155.4, 136.8, 130.0, 129.3, 126.7, 125.9, 125.0, 118.2, 110.4, 102.4 (aryl), 60.0 (C_2), 56.5 (C_5), 43.5 (NCH_3), 29.4 (C_3), 25.5 (C_1), 22.7 (C_4).

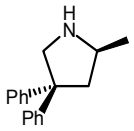
General procedure for NMR-scale catalytic hydroamination/cyclisation reactions. In the glove box, a screw cap NMR tube was charged with (*S*,*S*,*S*)-**3** (14.7 mg, 15 μmol), ferrocene (6.0 mg, 32.3 μmol), C_6D_6 (0.5 mL) and the substrate (0.30 mmol) in that order. The conversion was monitored by ^1H NMR spectroscopy by following the disappearance of the olefinic signals of the substrate relative to the internal standard ferrocene. The final NMR yield relative to the ferrocene standard was determined by ^1H NMR spectroscopy.



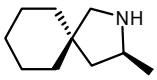
Preparative-scale procedure for 2,4,4-trimethylpyrrolidine hydrochloride (6·HCl). In the glovebox, a flask was fitted with a stirring bar and was charged with (*S*,*S*,*S*)-**3** (21 mg, 21.4 μmol), C_6D_6 (1.5 mL), and **5** (90 mg, 0.79 mmol) in that order. The solution was then stirred at 23 °C for 42 h. All volatiles were then vacuum transferred, diluted with Et_2O (2 mL), and treated with hydrochloric acid (1.59 mL, 0.5 M, 0.81 mmol) at 0 °C. After 30 min, the suspension was brought to room temperature and the solvent was removed *in vacuo*. The white precipitate was washed with diethyl ether and then dried in air to give 102 mg (86%) of **6·HCl** as a white powder. ^1H NMR ($CDCl_3$, 25 °C): δ 9.87 (br s, 1H, NH_2Cl), 9.47 (br s, 1H, NH_2Cl), 3,79 (m, 1H, C*H*(CH_3)NH_2Cl), 3.07 (m, 1H, C*H*$_2$$NH_2Cl$), 2.95 (m, 1H, C*H*$_2$$NH_2Cl$), 1.87 (dd, 1H, $^2J_{HH}$ = 12.9 Hz, $^3J_{HH}$ = 6.5 Hz, C*H*$_2$CH(CH_3)NH_2Cl), 1.53 (dd, 1H, $^2J_{HH}$ = 12.9 Hz, $^3J_{HH}$ = 11.2 Hz, C*H*$_2$CH(CH_3)NH_2Cl), 1.48 (d, $^3J_{HH}$ = 6.5 Hz, CH(C*H*$_3$)NH_2Cl), 1.16 (s, 3H, C(CH_3)$_2$), 1.11 (s, 3H, C(CH_3)$_2$); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 25 °C): δ 56.3 (CH_2NH_2Cl), 55.3 (*C*H(CH_3)NH_2Cl), 46.9 (*C*H_2CH(CH_3)NH_2Cl), 38.7 (*C*(CH_3)$_2$), 27.22 (C(*C*H_3)$_2$), 27.19 (C(*C*H_3)$_2$), 18.0 (CH(*C*H_3).

The spectroscopic Data of the free base is given for additional reference: **2,4,4-Trimethyl-pyrrolidine (6).**[9] ^1H NMR (400 MHz, C_6D_6): δ 3.07 (m, 1H, *CH*(CH_3)NH), 2.62 (d, $^2J_{H,H}$ = 10.1 Hz, 1H, *CH*$_2$NH), 2.47 (d, $^2J_{H,H}$ = 10.1 Hz, 1H, *CH*$_2$NH), 1.47 (dd, $^2J_{H,H}$ = 12.1 Hz, $^3J_{H,H}$ = 6.9 Hz, 1H, *CH*$_2$CH(CH_3)NH), 1.25 (br s, 1H, NH), 1.04 (d, $^3J_{H,H}$ = 6.2 Hz, 3H, CH*CH*$_3$), 0.97 (s, 3H, C(*CH*$_3$)$_2$), 0.93 (m, 1H, *CH*$_2$CH(CH_3)NH, obscured by other signal), 0.91 (s, 3H,

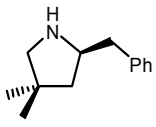
C(CH_3)$_2$); ^{13}C {^{1}H} NMR (100.6 MHz, C_6D_6): δ 61.5 (CH_2NH), 54.5 (*C*H(CH_3)NH), 50.0 (*C*H_2CH(CH_3)NH), 39.7 (*C*(CH_3)$_2$), 29.2 (C(*C*H_3)$_2$), 28.2 (C(*C*H_3)$_2$), 22.4 (CH*C*H_3).



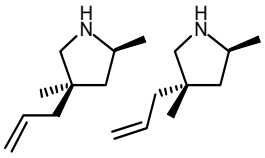
2-Methyl-4,4-diphenylpyrrolidine (8).[4] ^{1}H NMR (400 MHz, C_6D_6): δ 7.21 (d, $^3J_{H,H}$ = 7.6 Hz, 2H, aryl-H), 7.10 (m, 6H, aryl-H), 7.00 (t, $^3J_{H,H}$ = 7.01 Hz, 2H, aryl-H), 3.51 (d, $^3J_{H,H}$ = 10.9 Hz, 1H, *C*H_2NH), 3.34 (d, $^3J_{H,H}$ = 10.8 Hz, 1H, *C*H_2NH), 3.14 (m, 1H, *C*H(CH_3)NH), 2.38 (m, 1H, *C*H_2CH(CH_3)NH), 1.80 (m, 1H, *C*H_2CH(CH_3)NH), 1.27 (br s, 1H, NH), 1.00 (d, $^3J_{H,H}$ = 6.3 Hz, 3H, CH*C*H_3); ^{13}C {^{1}H} NMR (100.6 MHz, C_6D_6): δ 148.8, 148.2, 128.4, 127.6, 127.5, 126.0, 126.0 (aryl), 58.7 (*C*H_2NH), 57.3 (*C*Ph_2), 53.1 (*C*H(CH_3)NH), 47.6 (*C*H_2CH(CH_3)NH), 22.5 (CH(*C*H_3)NH).



Preparative-scale procedure for 3-methyl-2-aza-spiro[4.5]decane.[10] In the glovebox, a flask was fitted with a stirring bar and was charged with (*S*,*S*,*S*)-**3** (25.0 mg, 25.5 μmol), toluene (2.5 mL), and **9** (151 mg, 0.985 mmol) in that order. The solution was stirred at 20 °C for 2 h. All volatiles were then transferred under high vacuum. The solvent was removed under reduced pressure to give 124 mg (82%) of a colourless liquid. ^{1}H NMR (400 MHz, C_6D_6): δ 3.00 (m, 1H, *C*H(CH_3)NH), 2.73 (d, $^2J_{H,H}$ =10.4 Hz, 1H, *C*H_2NH), 2.50 (d, $^2J_{H,H}$ = 10.4 Hz, 1 H, *C*H_2NH), 1.55 (dd, $^2J_{H,H}$ = 12.3 Hz, $^3J_{H,H}$ = 6.6 Hz, 1H, CH(CH_3)CH_2), 1.29 (br m, 10H, CH_2), 1.06 (d, $^3J_{H,H}$ = 6.2 Hz, 3H, CH(*C*H_3)NH), 1.06 (br s, 1H, NH, obscured by other signal), 0.88 (dd, $^2J_{H,H}$ = 12.3 Hz, $^3J_{H,H}$ = 9.1 Hz, 1H, CH(CH_3)CH_2); ^{13}C NMR (100.6 MHz, C_6D_6): δ 59.7 (CH_2NH), 54.1 (*C*H(CH_3)NH), 47.8 (*C*H_2CH(CH_3)NH), 43.9 (*C*$_{quart}$), 39.0 (CH_2), 37.6 (CH_2), 26.5 (CH_2), 24.2 (CH_2), 24.1 (CH_2), 22.0 (CH(*C*H_3)NH).



2-Benzyl-4,4-dimethylpyrrolidine (12).[6b] ^{1}H NMR (300 MHz, C_6D_6): δ 7.21−7.05 (m, 5H, aryl-H), 3.20 (m, 1H, *C*H(CH_3)NH), 2.69−2.53 (m, 3H, PhCH_2 and *C*H_2NH), 2.37 (m, 1H, PhCH_2), 1.49 (m, 1H, CH(CH_3)CH_2), 1.20 (br m, 1H, NH), 1.11 (m, 1H, CH(CH_3)CH_2), 0.99 (s, 3H, CH_3), 0.85 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (75.5 MHz, C_6D_6): δ 141.0, 129.5, 128.5, 126.2 (aryl), 60.7, 60.5, 47.4, 43.9, 38.9 (C(CH_3)$_2$), 29.0, 28.0 (CH_3).



14a **14b**

Preparative-scale procedure for 4-allyl-2,4-dimethyl-pyrrolidine (14).[9] In the glovebox, a flask was fitted with a stirring bar and was charged with (*S*,*S*,*S*)-**3** (25.0 mg, 25.5 μmol), C_6D_6 (2.5 mL), and **13** (69.5 mg, 0.499 mmol) in that order. The solution was then stirred at 22 °C for 2 h. The solution was then diluted with Et_2O (10 mL) and filtered through a pad of silica gel. The solvent was removed under reduced pressure to give 55.0 mg (79%) of **14** (**14a**:**14b** = 1.2:1) as a colourless liquid. Isomer **a**: ^{1}H NMR (400 MHz, C_6D_6): δ 5.72 (m, 1H, C*H*=CH_2), 4.99 (m, 2H, CH=C*H*$_2$), 3.03 (m, 1H, C*H*(CH_3)NH), 2.73 (d, $^2J_{H,H}$ = 10.4 Hz, 1 H, C*H*$_2$NH), 2.42 (d, $^2J_{H,H}$ = 10.4 Hz, 1 H, C*H*$_2$NH), 1.99 (d, $^3J_{H,H}$ = 7.3 Hz, 2 H, C*H*$_2$CH=CH_2), 1.39 (dd, $^2J_{H,H}$ = 12.3 Hz, $^3J_{H,H}$ = 6.5 Hz, 1 H, C*H*$_2$CH(CH_3)), 1.16 (br s, 1H, NH), 1.03 (d, $^3J_{H,H}$ = 6.2 Hz, 3H, CH(C*H*$_3$)NH), 1.01 (dd, $^2J_{H,H}$ = 12.3 Hz, $^3J_{H,H}$ = 9.2 Hz, 1 H, C*H*$_2$CH(CH_3)), 0.88 (s, 3H, C(C*H*$_3$)); ^{13}C{^{1}H} NMR (100.6 MHz, C_6D_6): δ 136.4 (*C*H=CH_2), 116.8 (CH=*C*H_2), 59.7 (CH_2NH), 54.2 (*C*H(CH_3)NH), 48.1 (*C*H_2CH(CH_3)), 46.8 (*C*H_2CH=CH_2), 42.9 (*C*(CH_3)), 25.9 (C(*C*H_3)), 21.9 (CH(*C*H_3)). Isomer **b**: ^{1}H NMR (400 MHz, C_6D_6): δ 5.72 (m, 1H, C*H*=CH_2), 4.99 (m, 2H, CH=C*H*$_2$), 3.03 (m, 1H, C*H*(CH_3)NH), 2.56 (s, 2 H, C*H*$_2$NH), 1.95 (d, $^3J_{H,H}$ = 7.4 Hz, 2 H, C*H*$_2$CH=CH_2), 1.62 (dd, $^2J_{H,H}$ = 12.5 Hz, $^3J_{H,H}$ = 7.1 Hz, 1 H, C*H*$_2$CH(CH_3)), 1.16 (br s, 1H, NH), 1.03 (d, $^3J_{H,H}$ = 6.2 Hz, 3H, CH(C*H*$_3$)NH), 0.95 (s, 3H, C(C*H*$_3$)), 0.85 (dd, $^2J_{H,H}$ = 12.5 Hz, $^3J_{H,H}$ = 8.6 Hz, 1 H, C*H*$_2$CH(CH_3)); ^{13}C{^{1}H} NMR (100.6 MHz, C_6D_6): δ 136.3 (*C*H=CH_2), 116.8 (CH=*C*H_2), 59.8 (*C*H_2NH), 54.5 (*C*H(CH_3)NH), 47.7 (*C*H_2CH(CH_3)), 45.6 (*C*H_2CH=CH_2), 42.9 (*C*(CH_3)), 27.0 (C(*C*H_3)), 22.3 (CH(*C*H_3)).

exo,*exo*-**15**

***Exo*,*exo*-2,4,6-dimethyl-1-aza-bicyclo[2.2.1]heptane (*exo*,*exo*-15).**[9] ^{1}H NMR (400 MHz, C_6D_6): δ 2.57 (m, 2H, C*H*(CH_3)), 2.05 (s, 2H, bridging CH_2), 1.13 (m, 2H, C*H*$_2$CH(CH_3)), 1.03 – 1.10 (m, 9H, CH_3), 0.74 (m, 2H, C*H*$_2$CH(CH_3)); ^{13}C{^{1}H} NMR (100.6 MHz, C_6D_6): δ 62.7 (*C*HCH_3), 57.6 (bridging CH_2), 46.9 (*C*(CH_3)), 45.7 (*C*H_2CH(CH_3)), 23.1 (C(*C*H_3), 17.1 (CH(*C*H_3)).

General procedure for preparation of Mosher amides. The amine (0.08–0.1 mmol) was dissolved in $CDCl_3$ or C_6D_6 (0.5 mL) in a NMR tube. Hünig's base (1.5 eq. with respect to the amine) and (R)-(+)-α-methoxy-α-trifluoro-methylphenylacetic acid chloride (1.2 eq. with respect to the amine) were added. Enantiomeric excess was then determined by ^{19}F NMR at 60–80 °C.

Excess of Mosher acid chloride was transformed into its methyl ester by addition of methanol in cases where the signal of the acid chloride interfered with the determination of the enantiomeric excess.

2,4,4-Trimethyl-pyrrolidine (6): ^{19}F NMR ($CDCl_3$, 60 °C): δ –69.7, –70.6.

2-Methyl-4,4-diphenylpyrrolidine (8): ^{19}F NMR ($CDCl_3$, 60 °C): δ –69.5, –70.6.

3-Methyl-2-aza-spiro[4.5]decane (10):: ^{19}F NMR ($CDCl_3$, 60 °C): δ –70.0, –70.9.

2-Benzyl-4,4-dimethylpyrrolidine (12): ^{19}F NMR (C_6D_6, 60 °C): δ –69.9, –70.9.

4-Allyl-2,4-dimethyl-pyrrolidine (14): ^{19}F NMR ($CDCl_3$, 80 °C): δ –69.95 (minor isomer **b**), –70.05 (major isomer **a**), –70.7 (minor isomer **b**), –70.9 (major isomer **a**).

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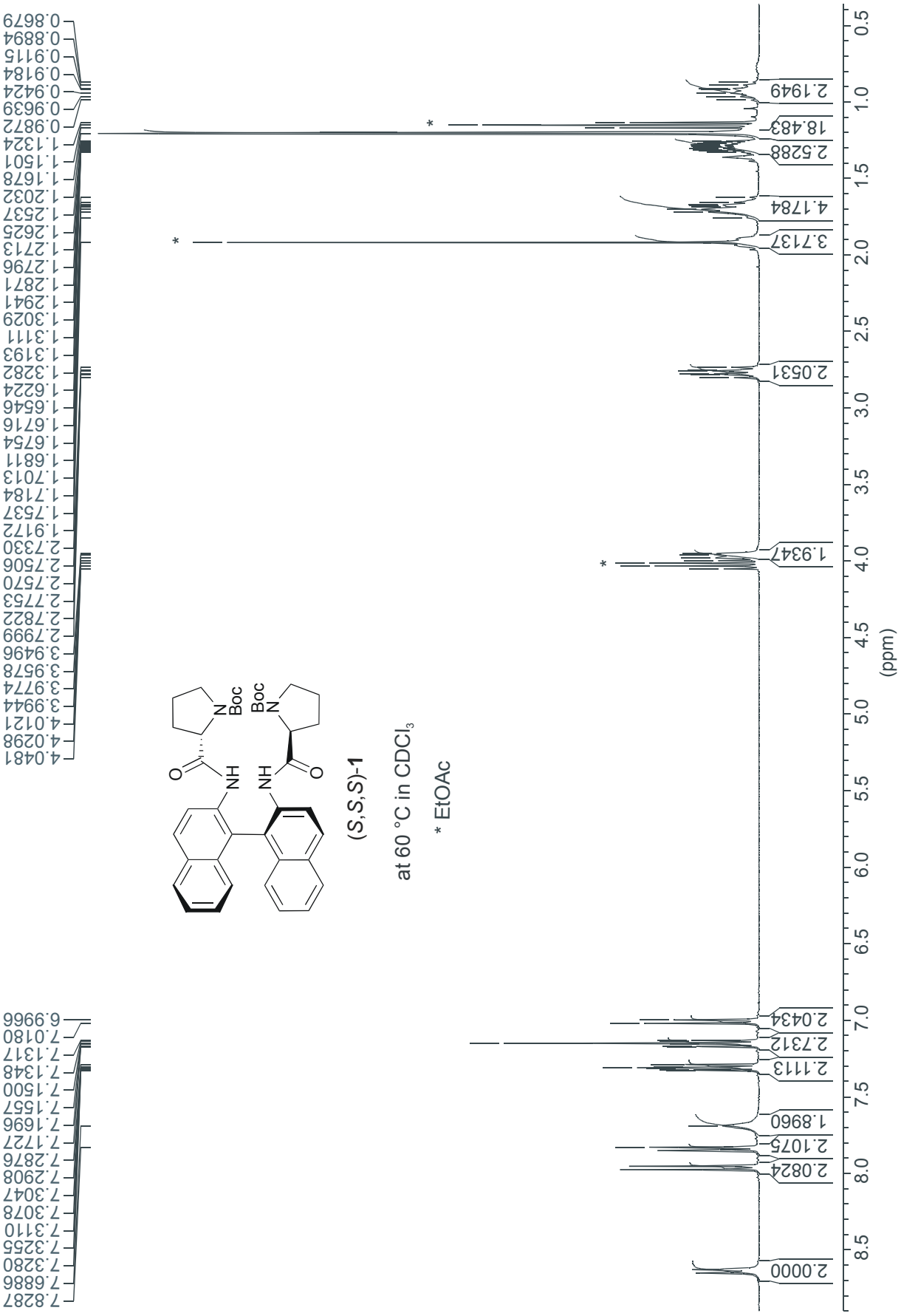
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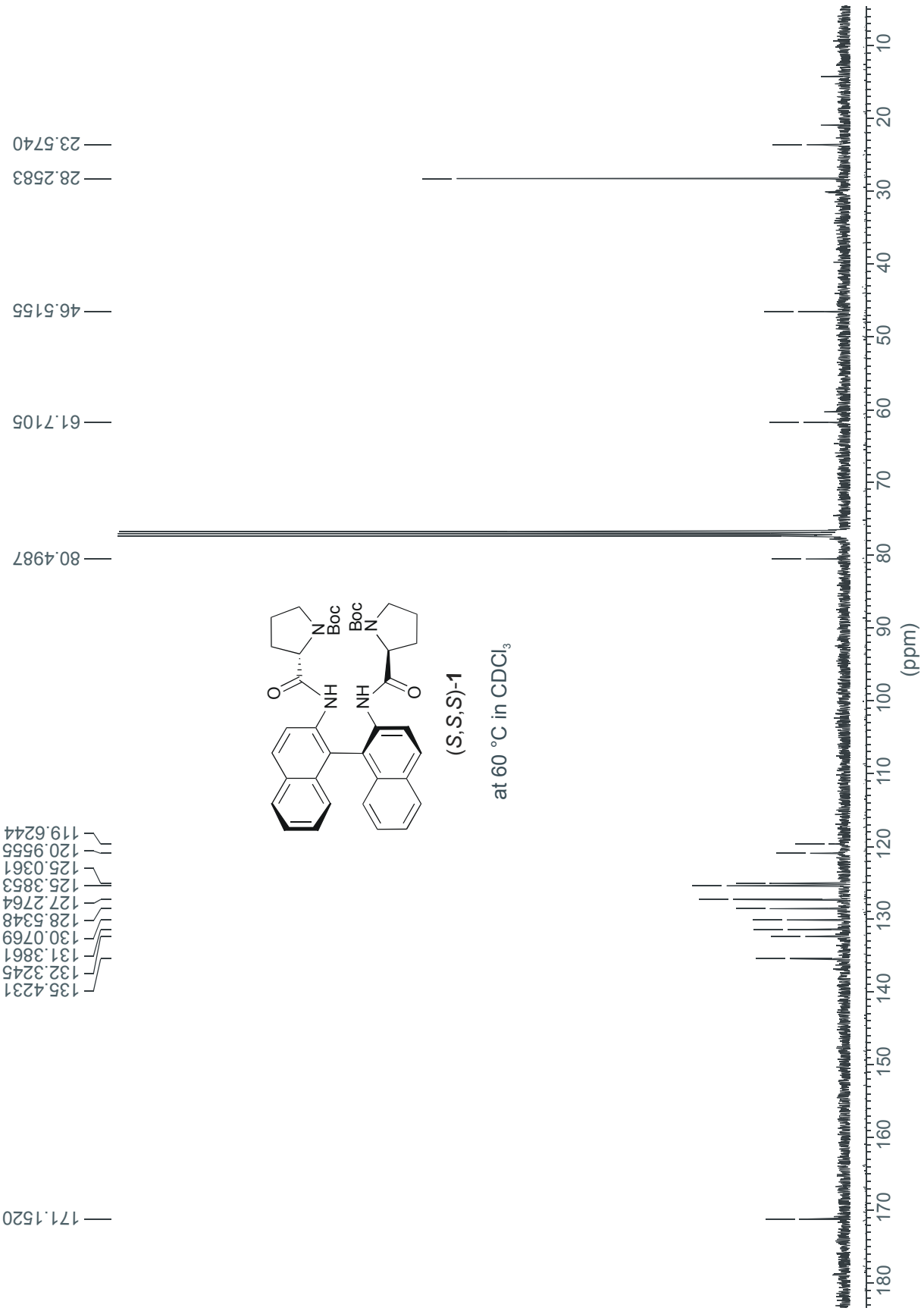
N
NH
NH
O
O
(ppm)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125.3853
127.2764
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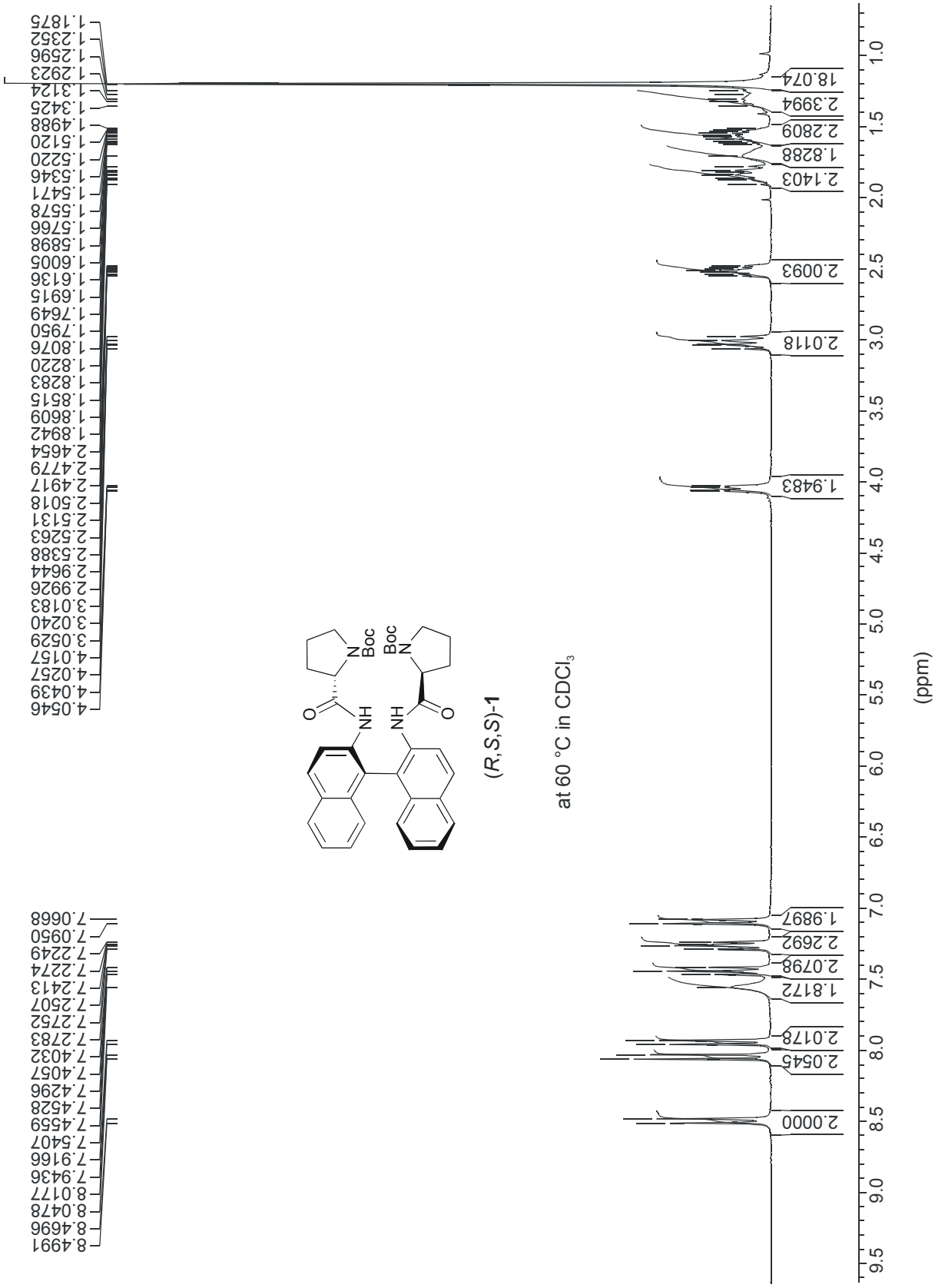
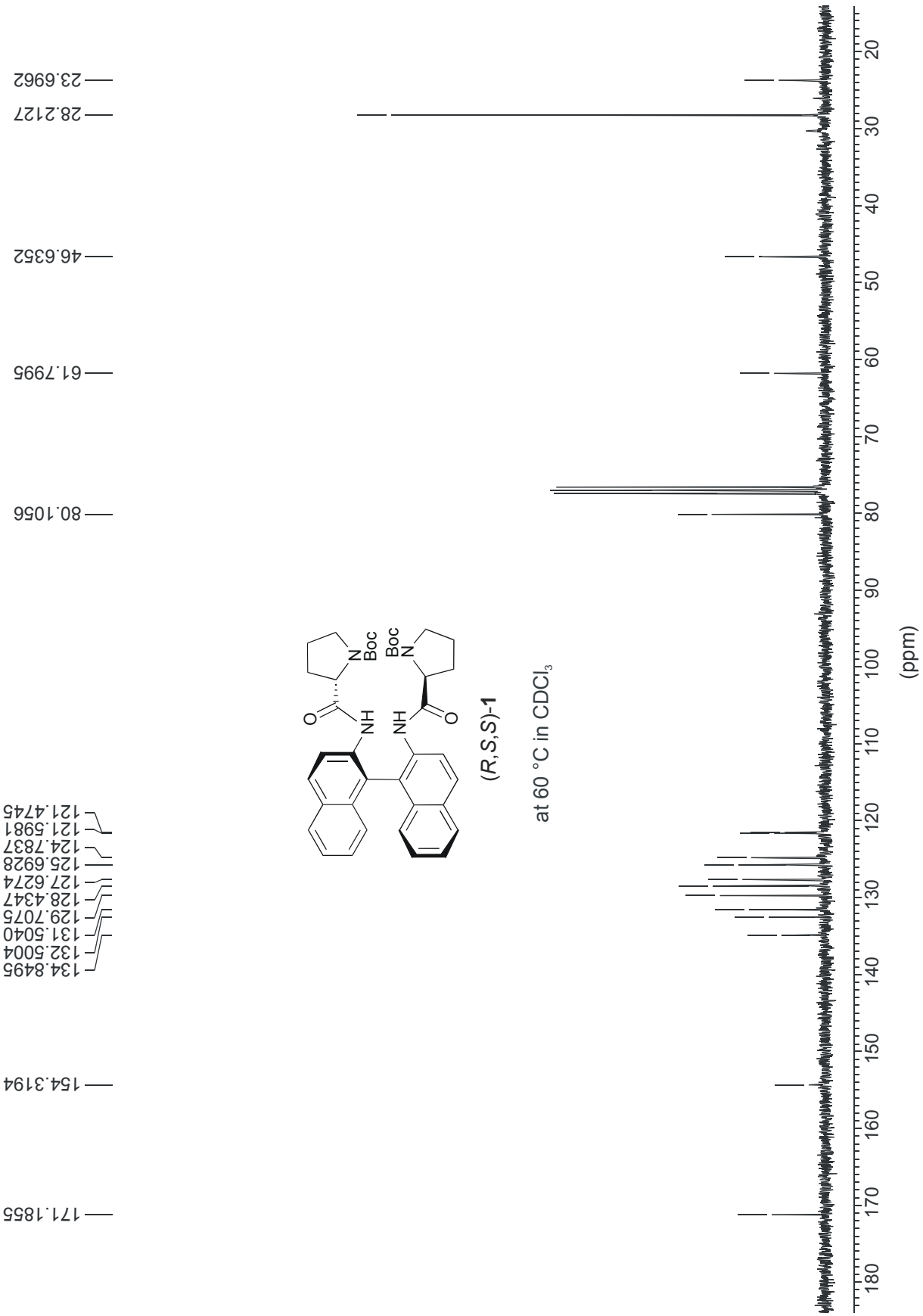
131.3861
132.3245
135.4231
171.1520
(S,S,S)-1
at 60 °C in CDCl3
(ppm)


(R,S,S)-1
at 60 °C in CDCl3
(ppm)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121.5981
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128.4347
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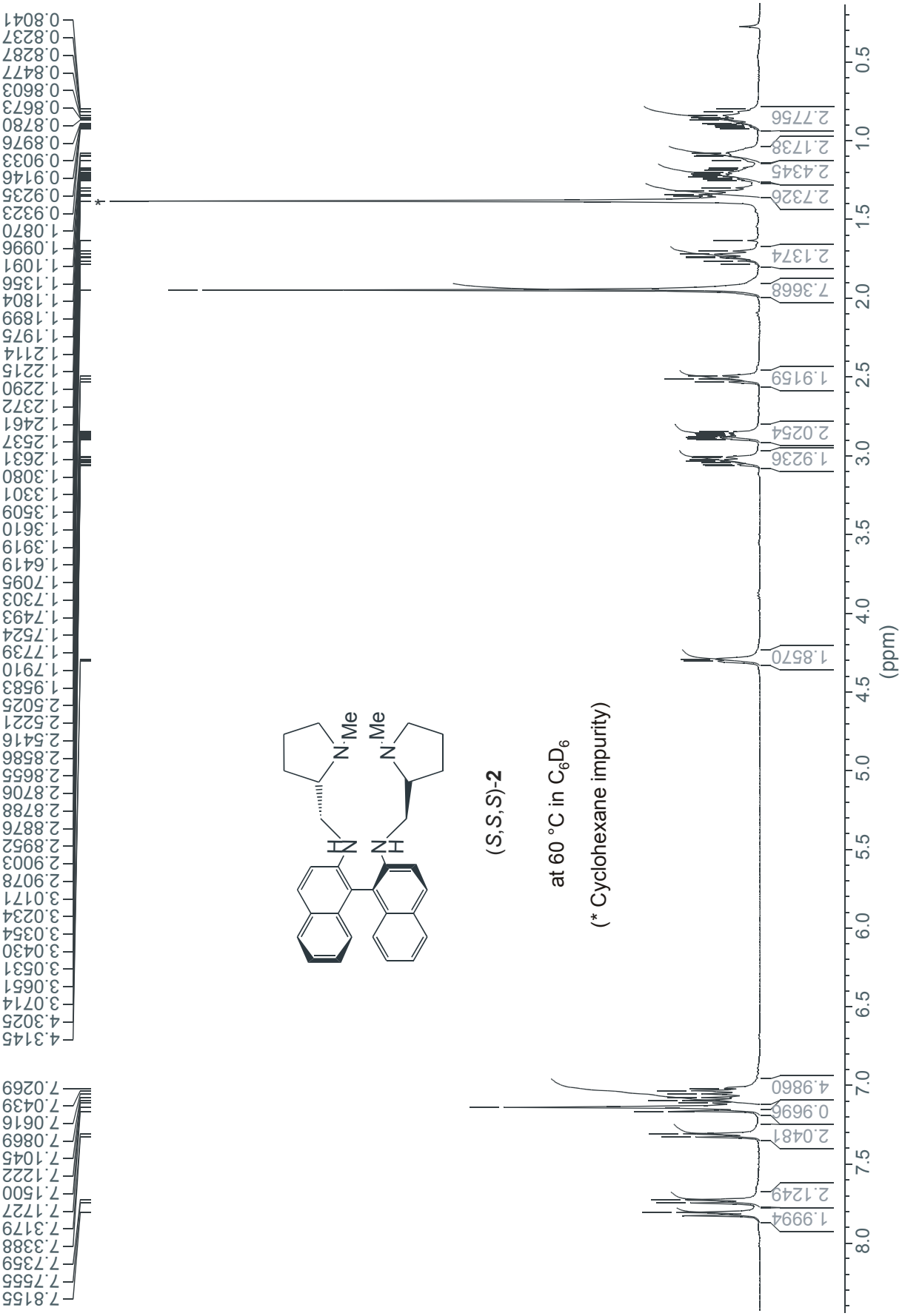
154.3194
171.1855
(R,S,S)-1
at 60 °C in CDCl3
(ppm)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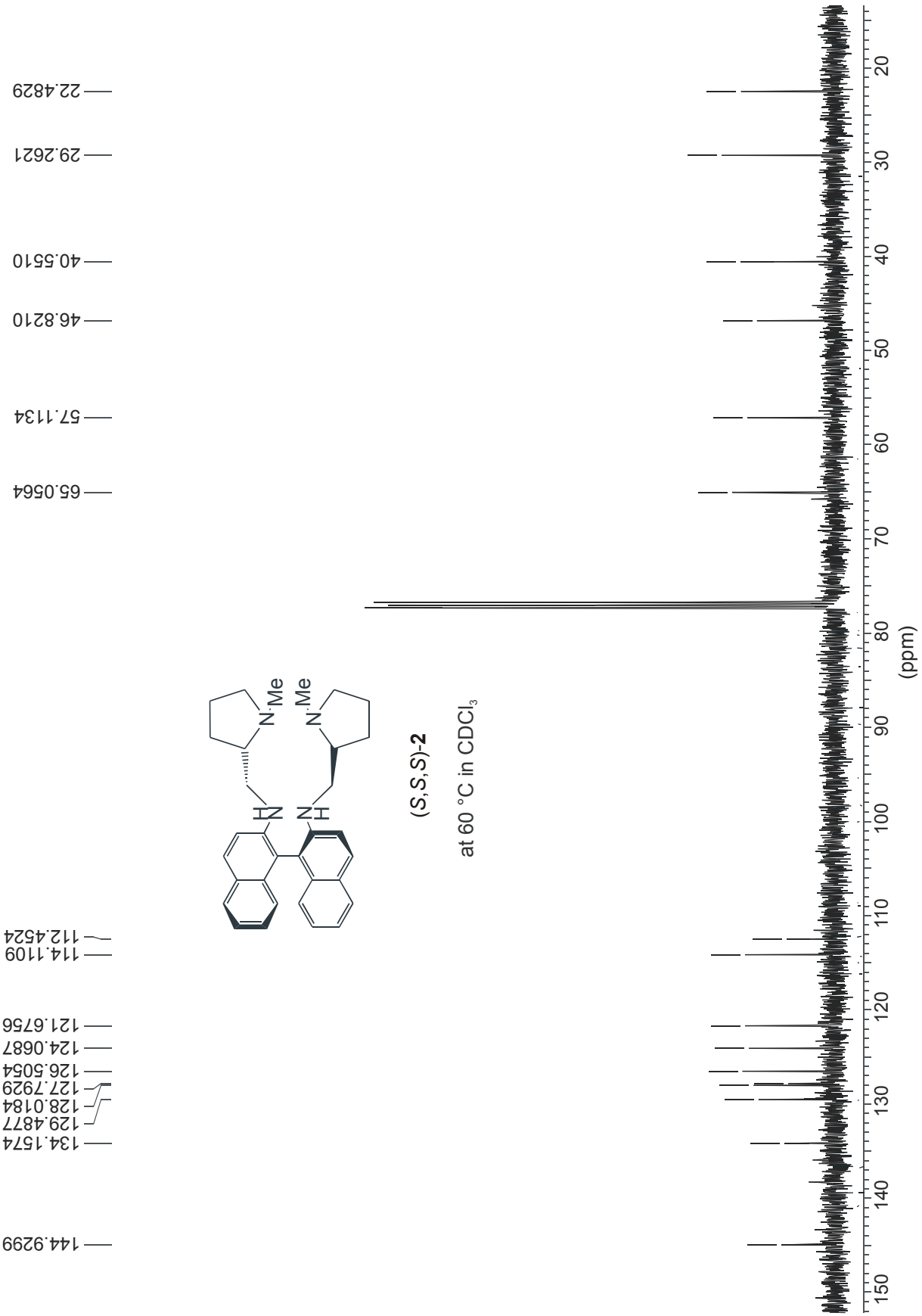
at 60 °C in C6D6
(* Cyclohexane impurity)
(ppm)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126.5054
127.7929
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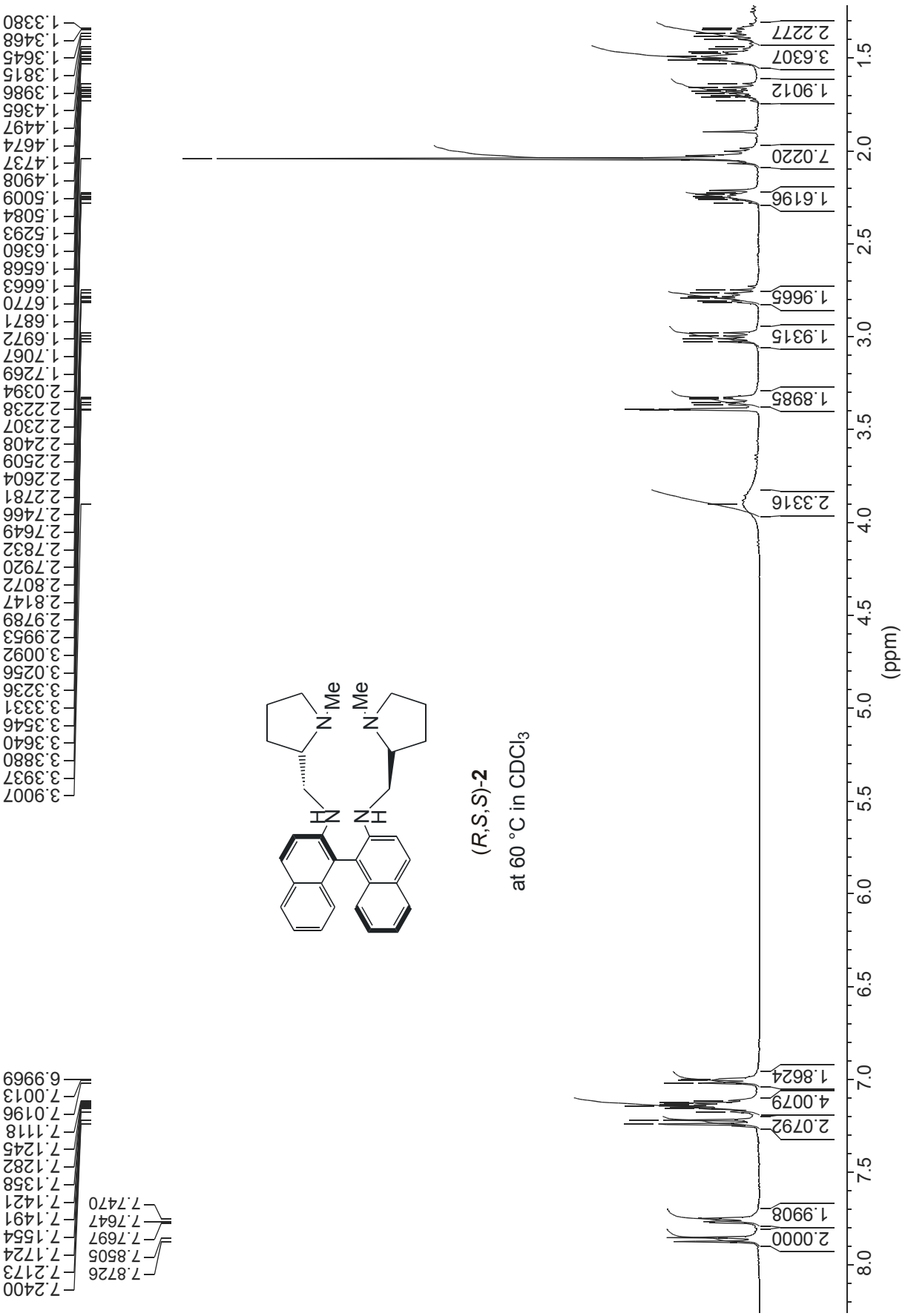
(S,S,S)-2
at 60 °C in CDCl3
N
Me
H
(ppm)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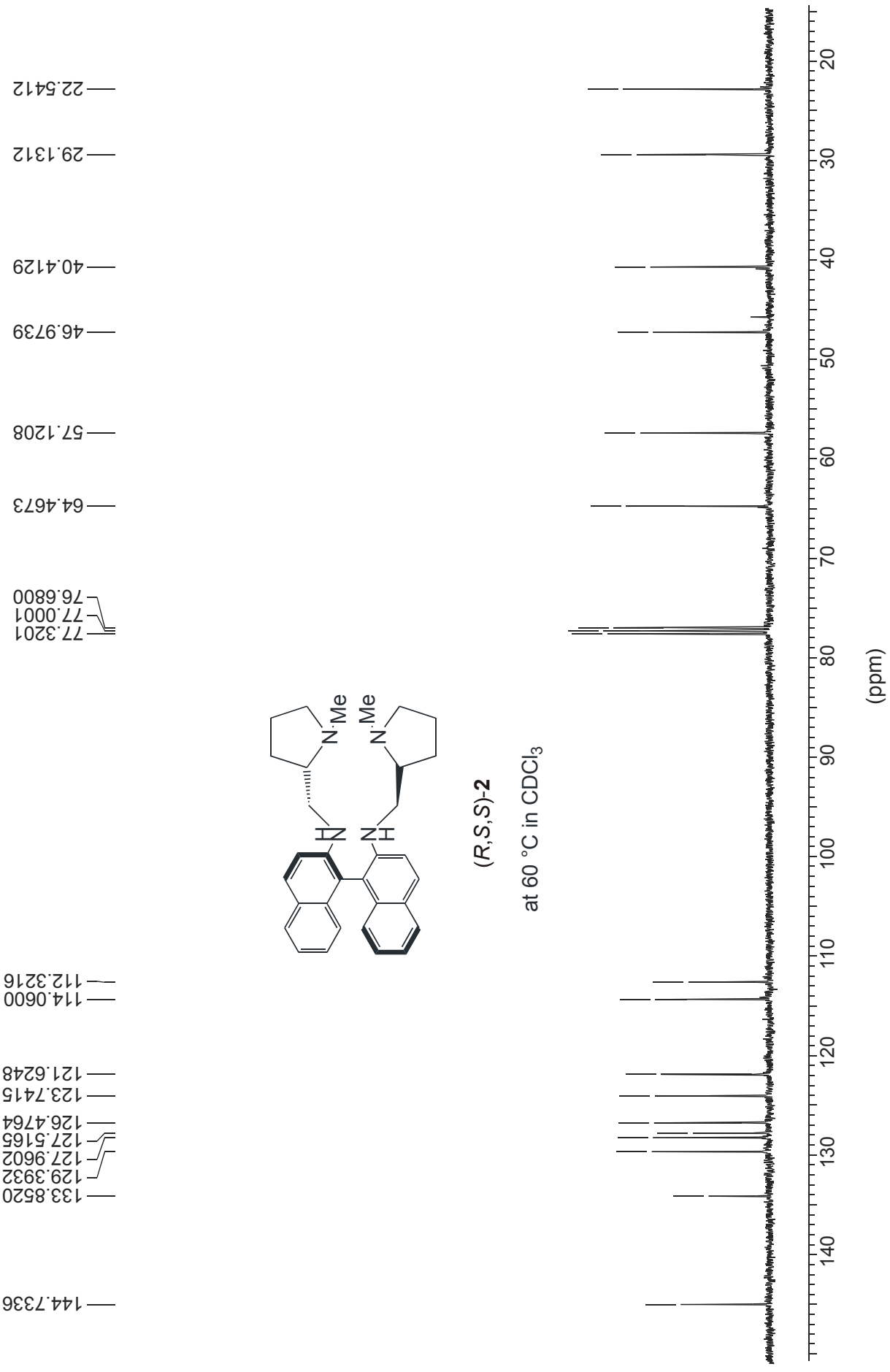
at 60 °C in CDCl3
N
Me
H
(ppm)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114.0600
121.6248
123.7415
126.4764
127.5165
127.9602
129.3932
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144.7336
(R,S,S)-2
at 60 °C in CDCl3
N
Me
H
20
30
40
50
60
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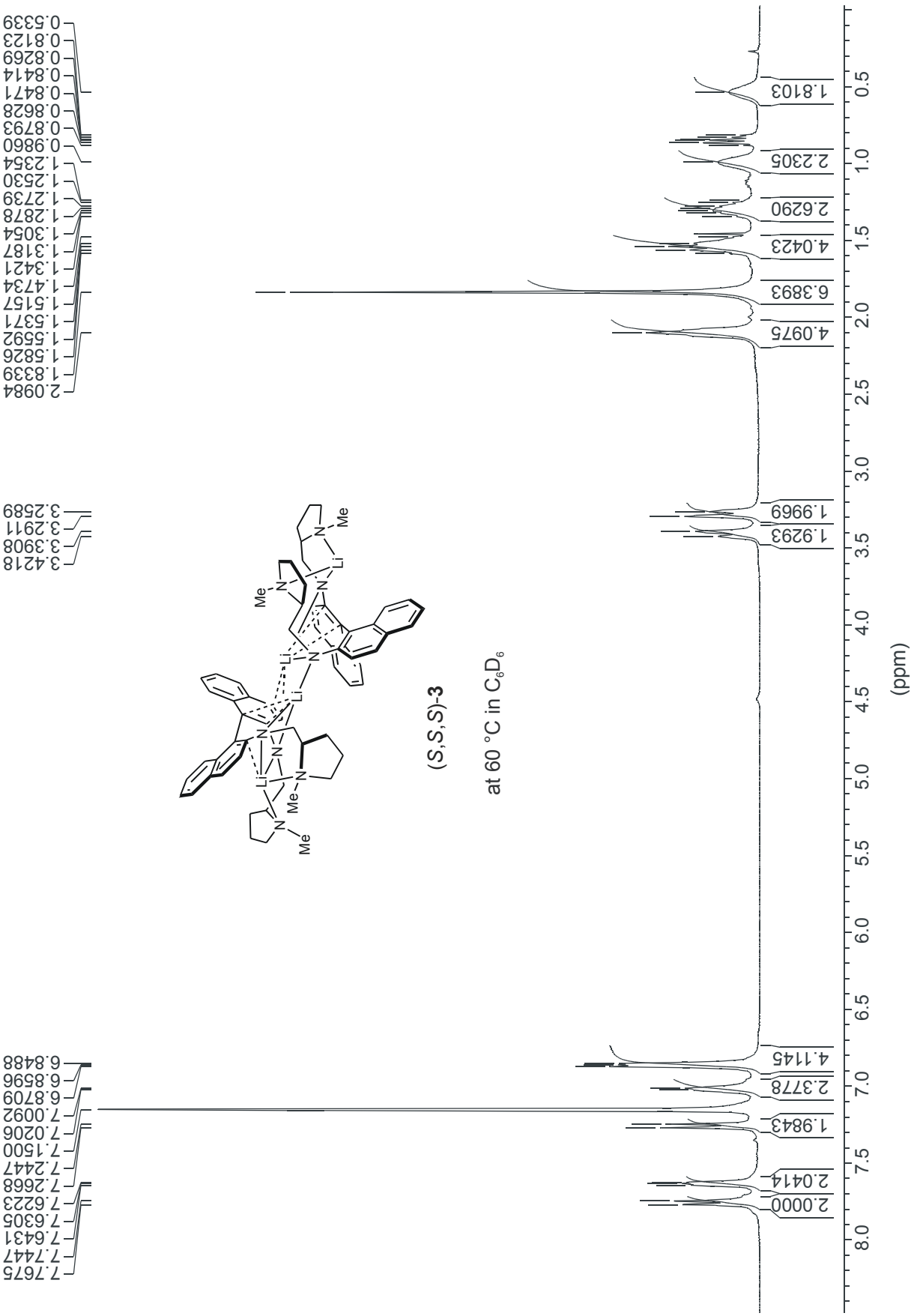
80
90
100
110
120
130
140
(ppm)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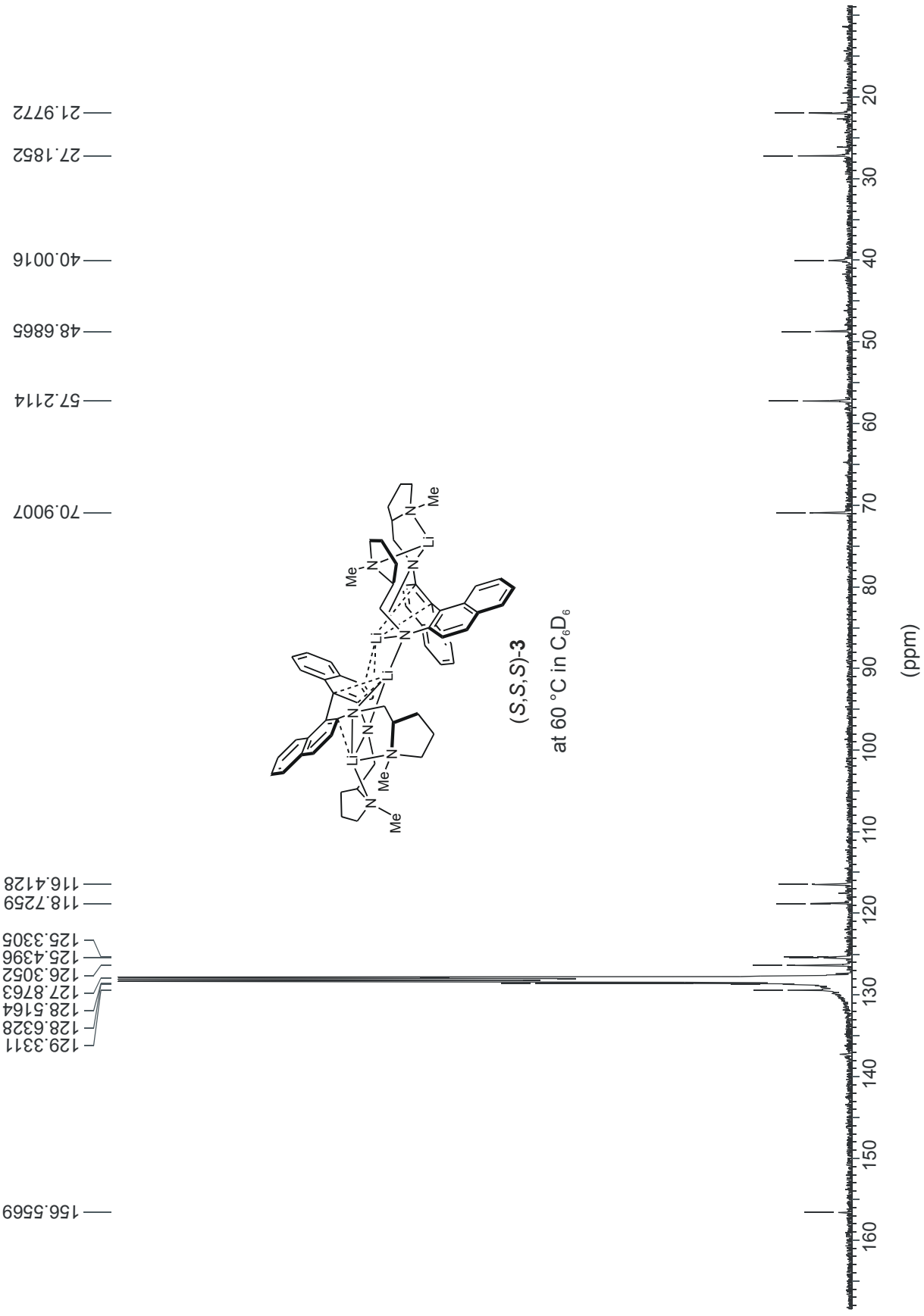
at 60 °C in C6D6
(ppm)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129.3311
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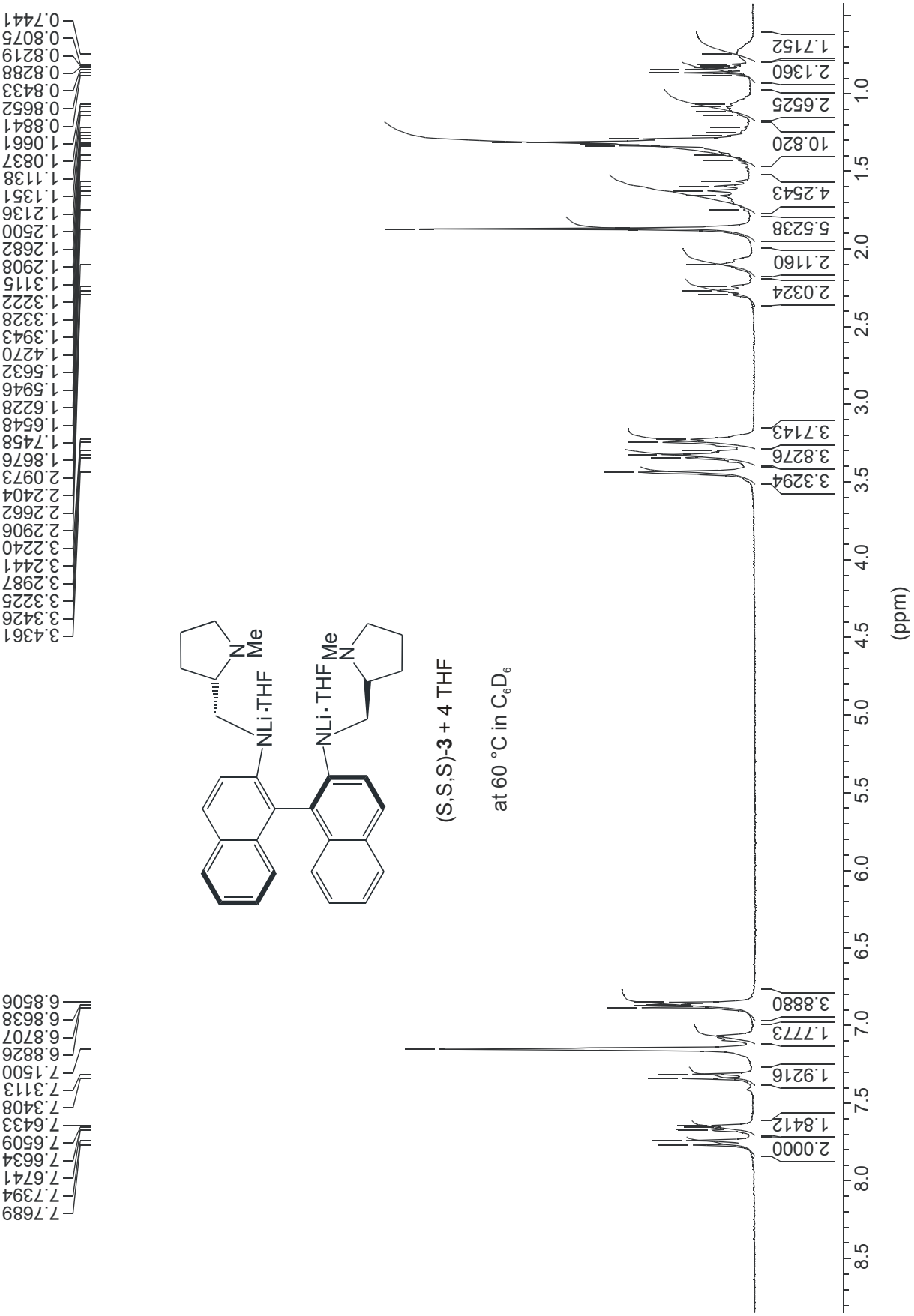
at 60 °C in C6D6
(ppm)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1.8412
2.0000
N
Me
NLi·THF
NLi·THF
Me
N
(S,S,S)-3 + 4 THF
at 60 °C in C6D6
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
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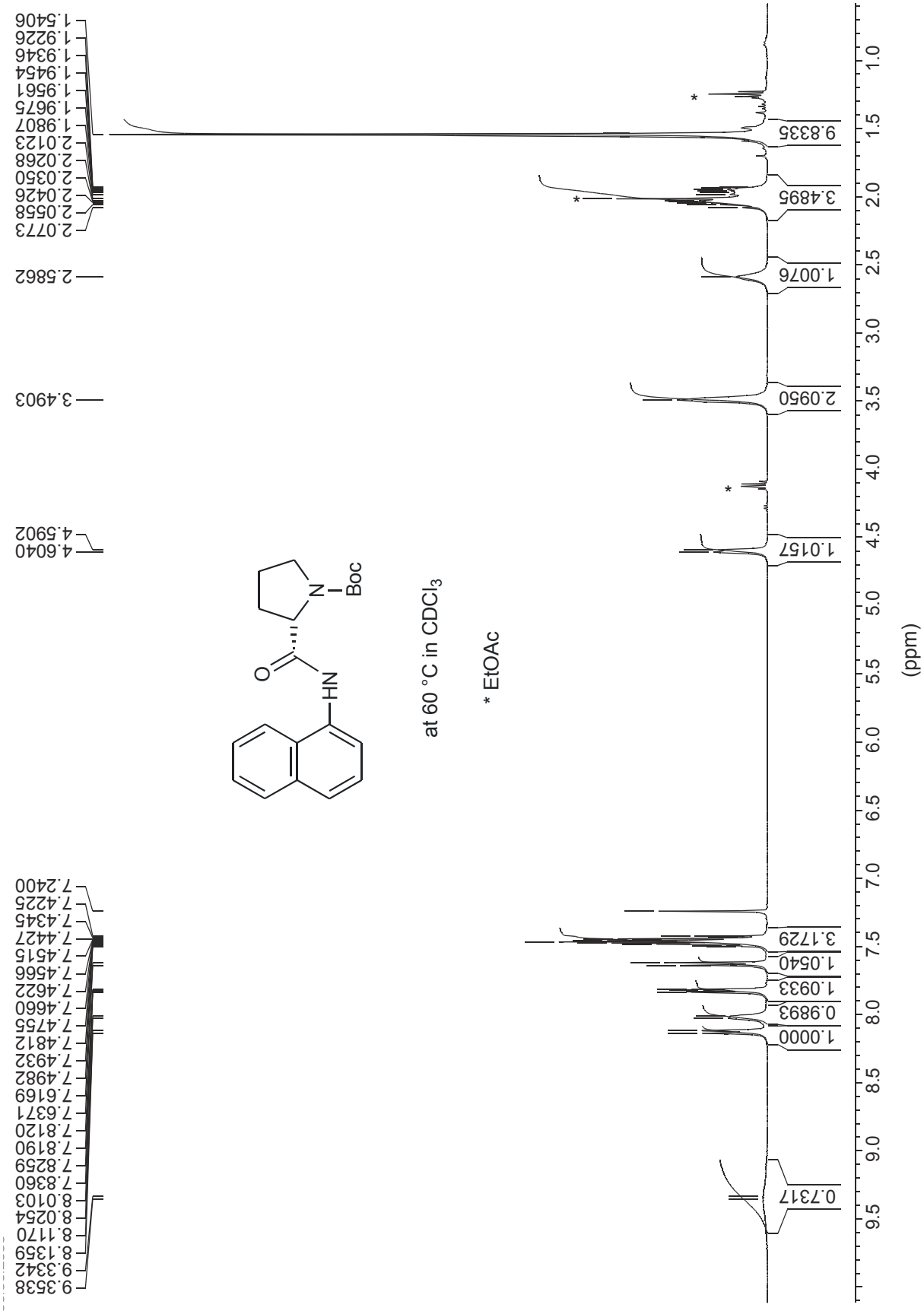
3.5
3.0
2.5
2.0
1.5
1.0
(ppm)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7.8360
8.0103
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Boc
N
O
HN
at 60 °C in CDCl3
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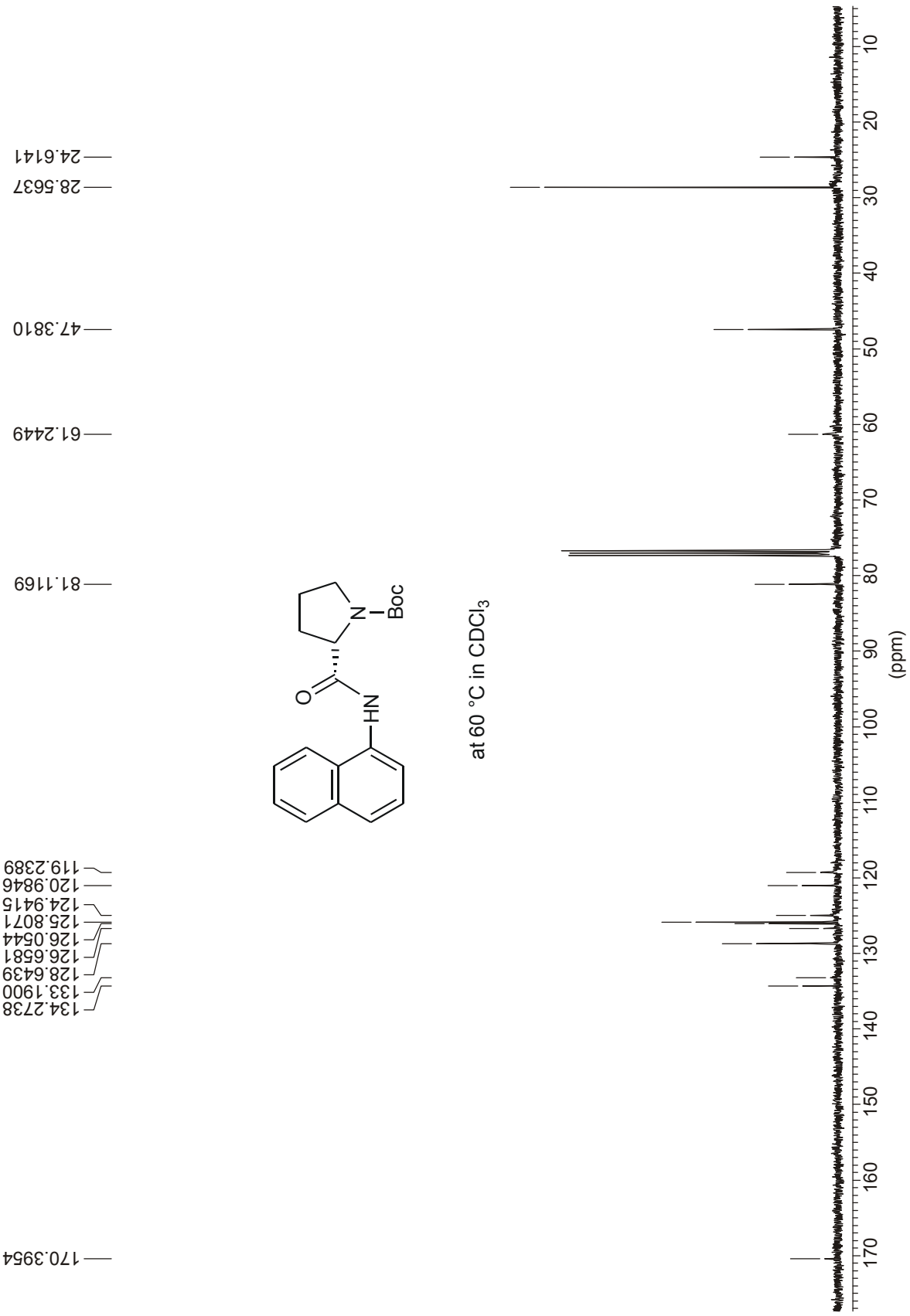
(ppm)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Boc
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O
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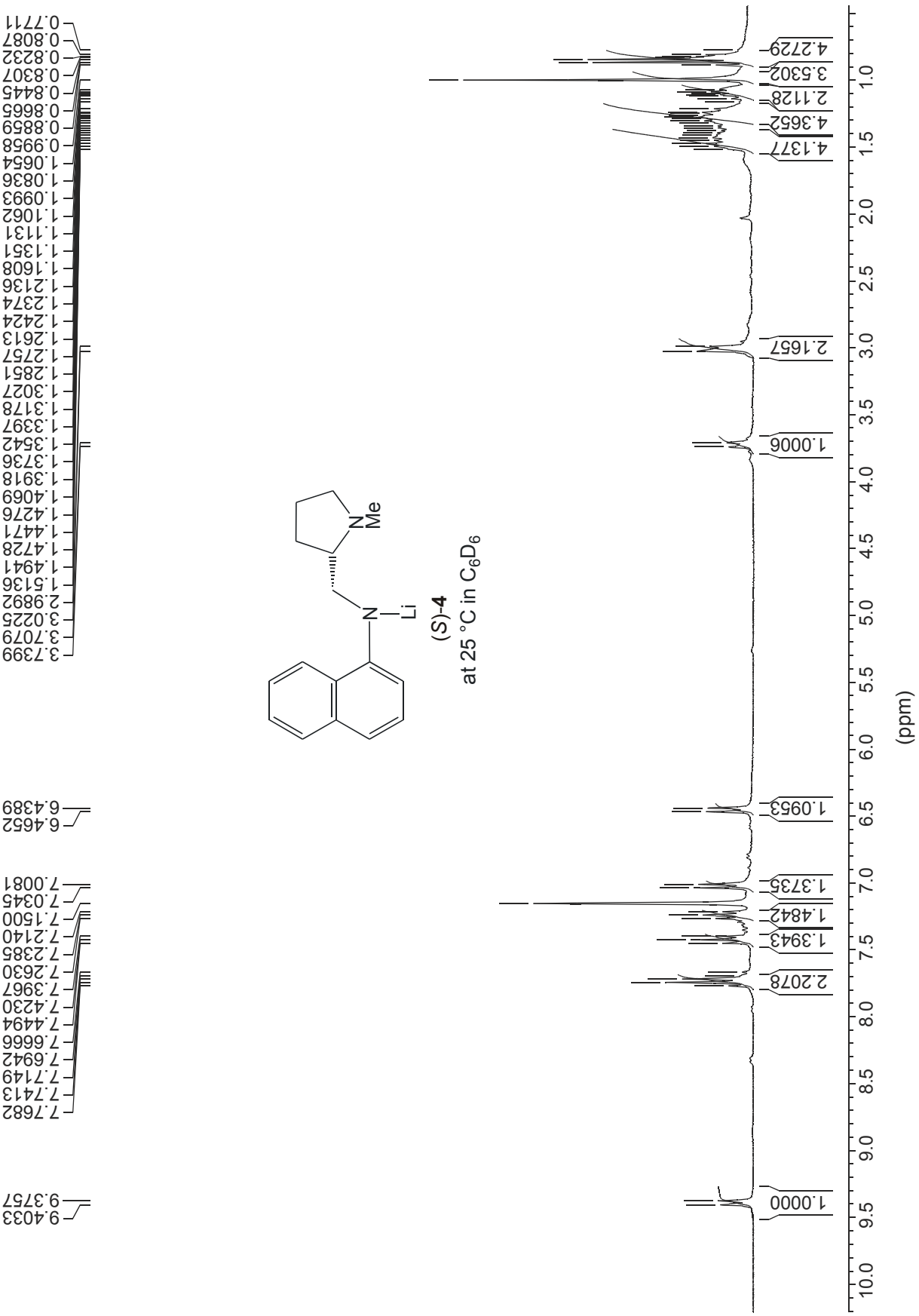
(ppm)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Me
N
Li
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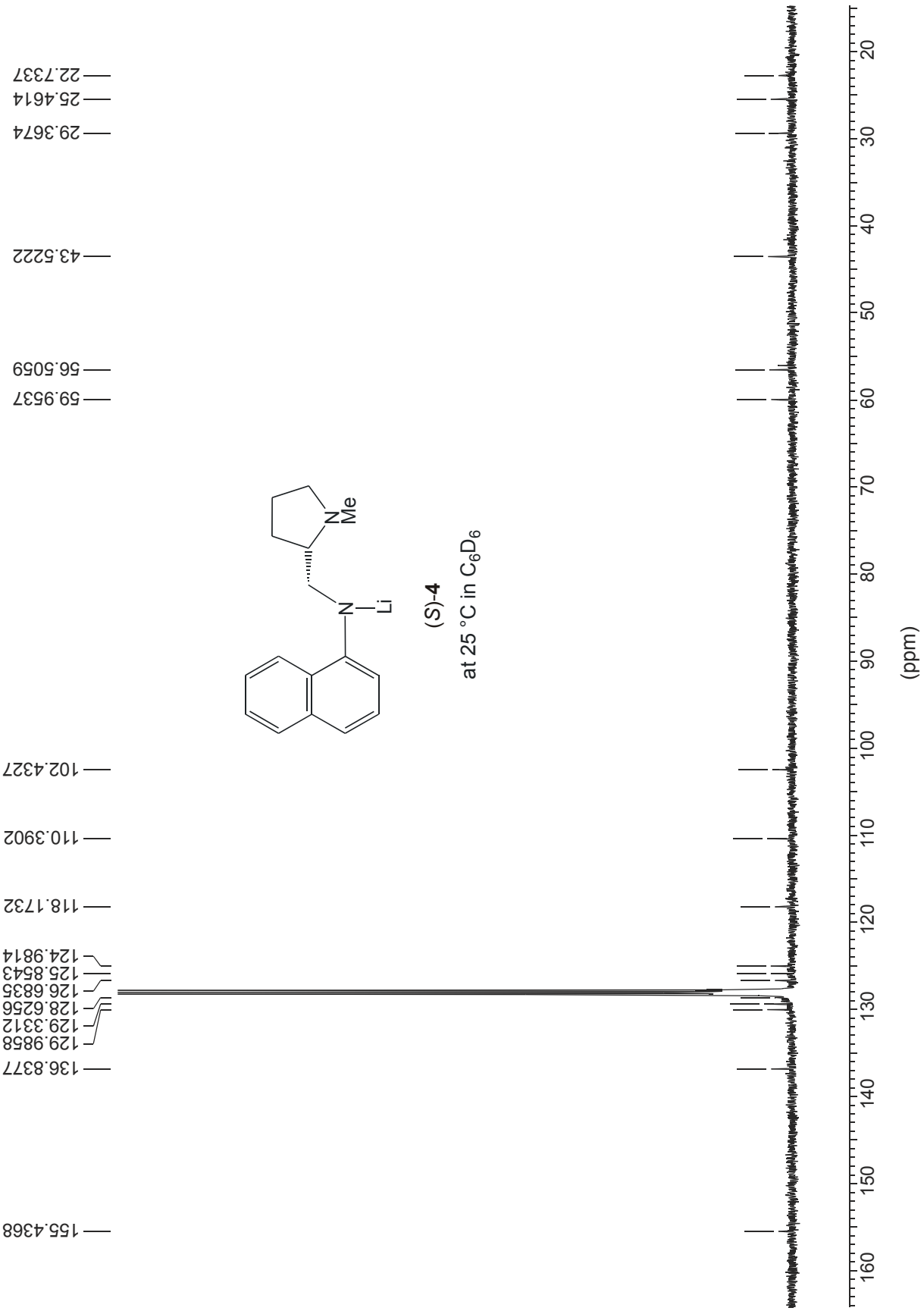
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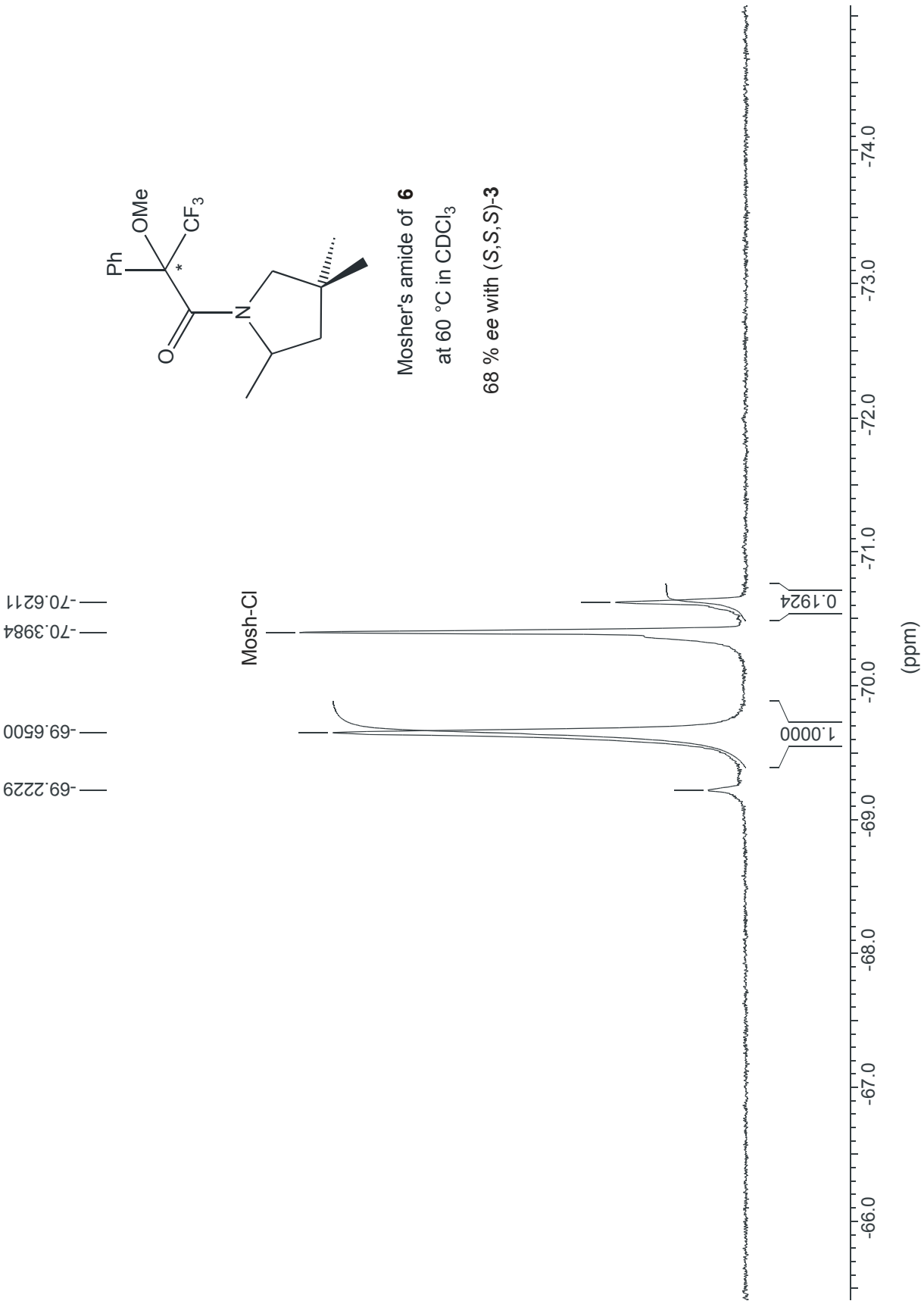
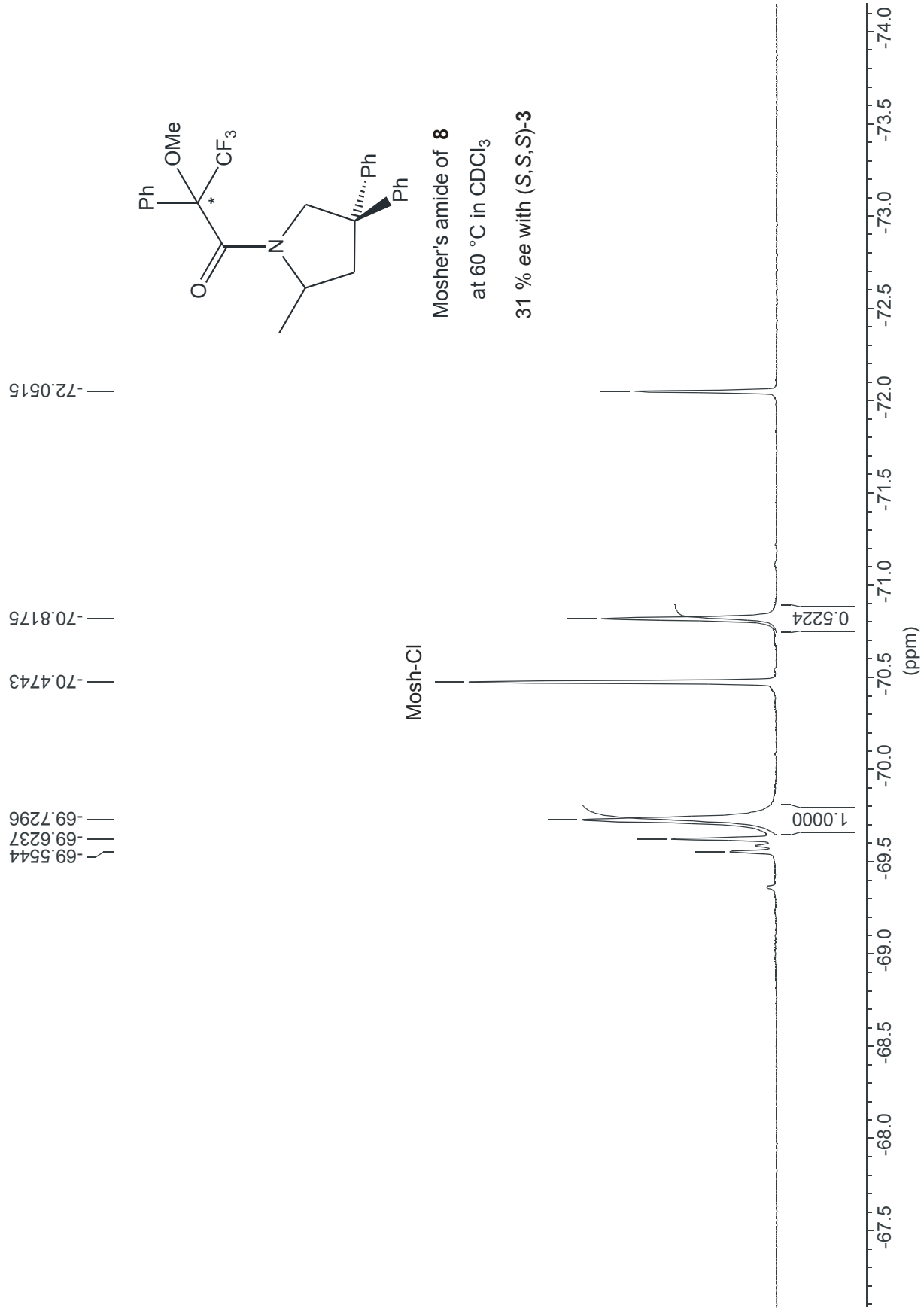
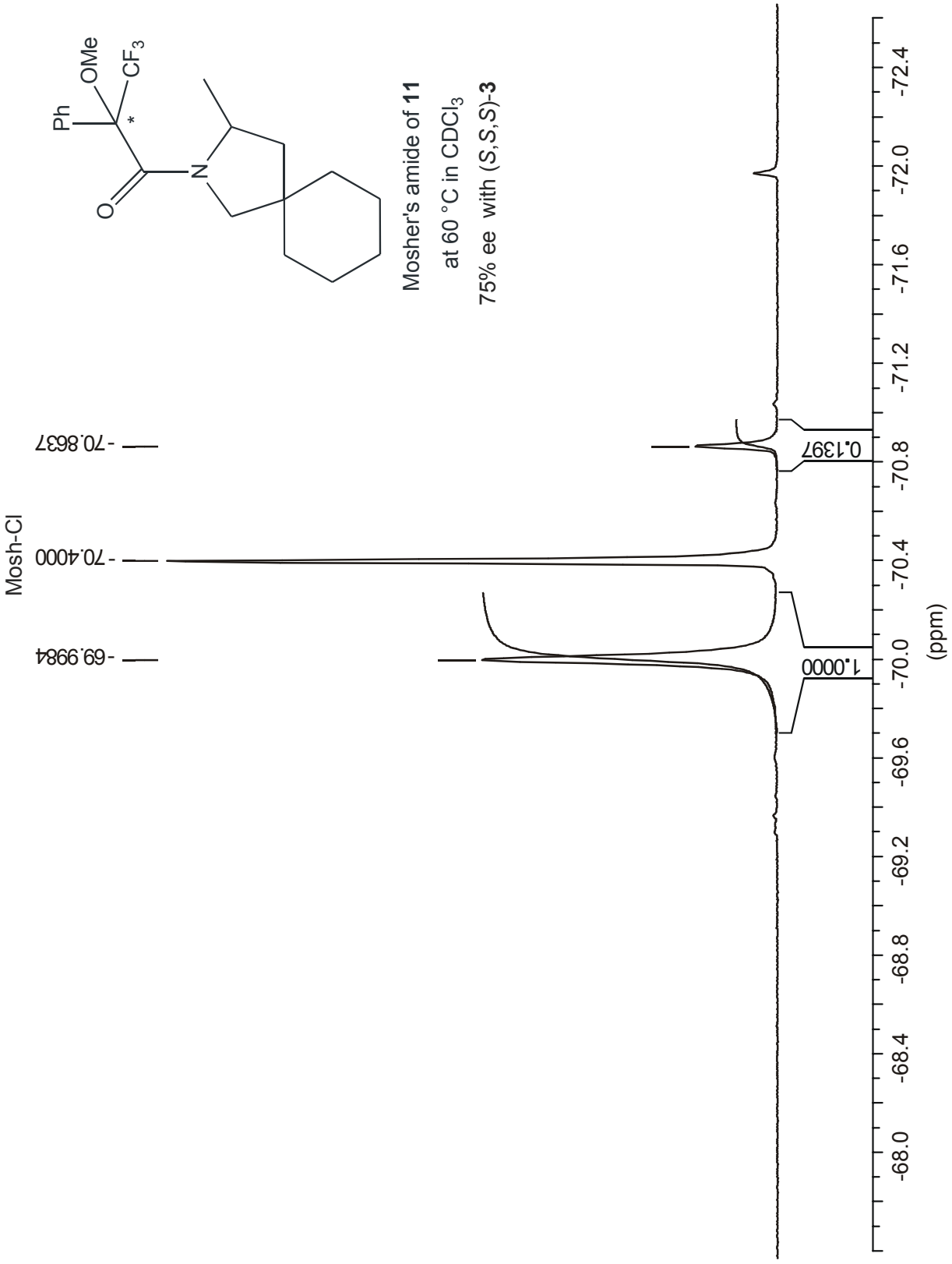
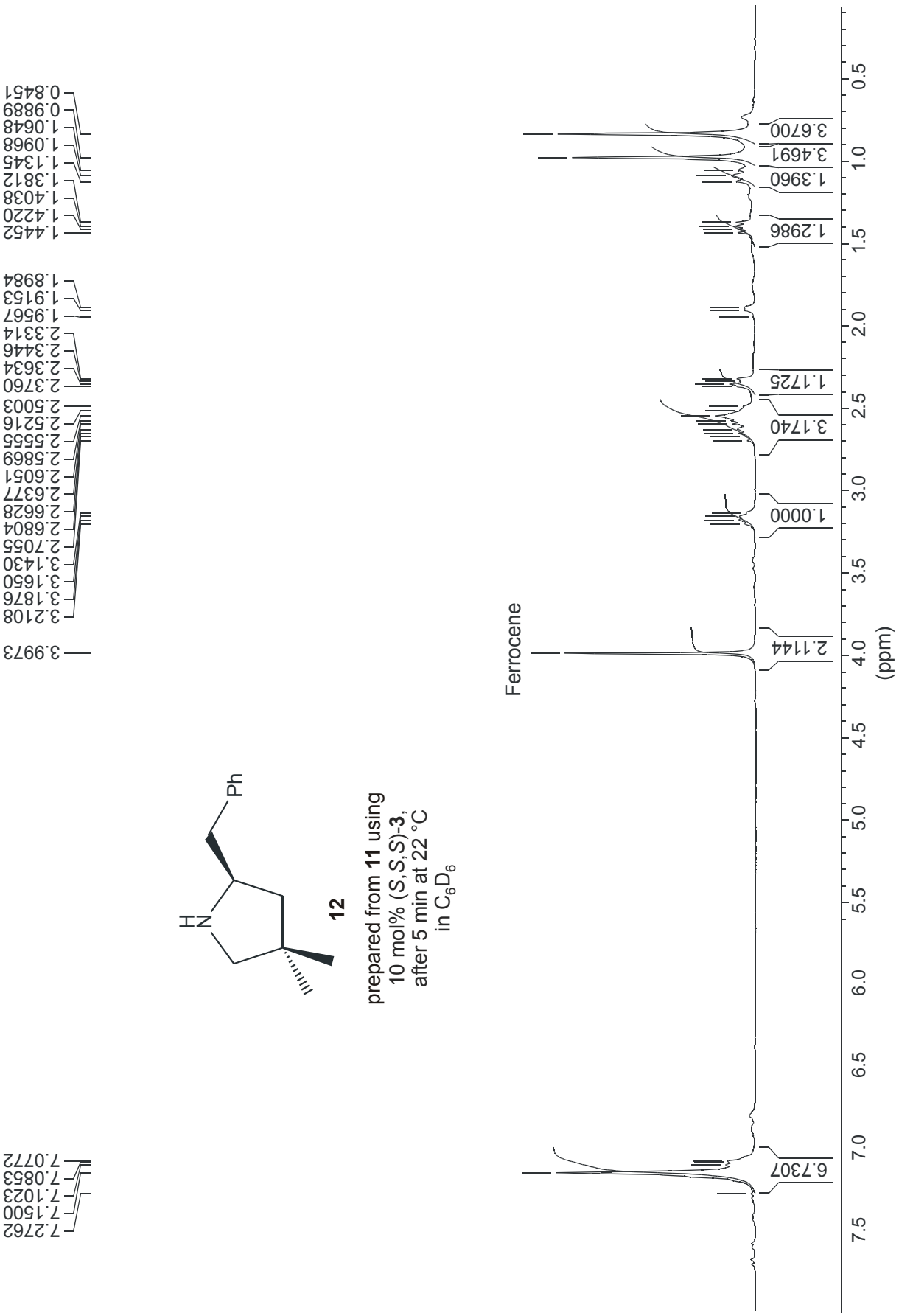
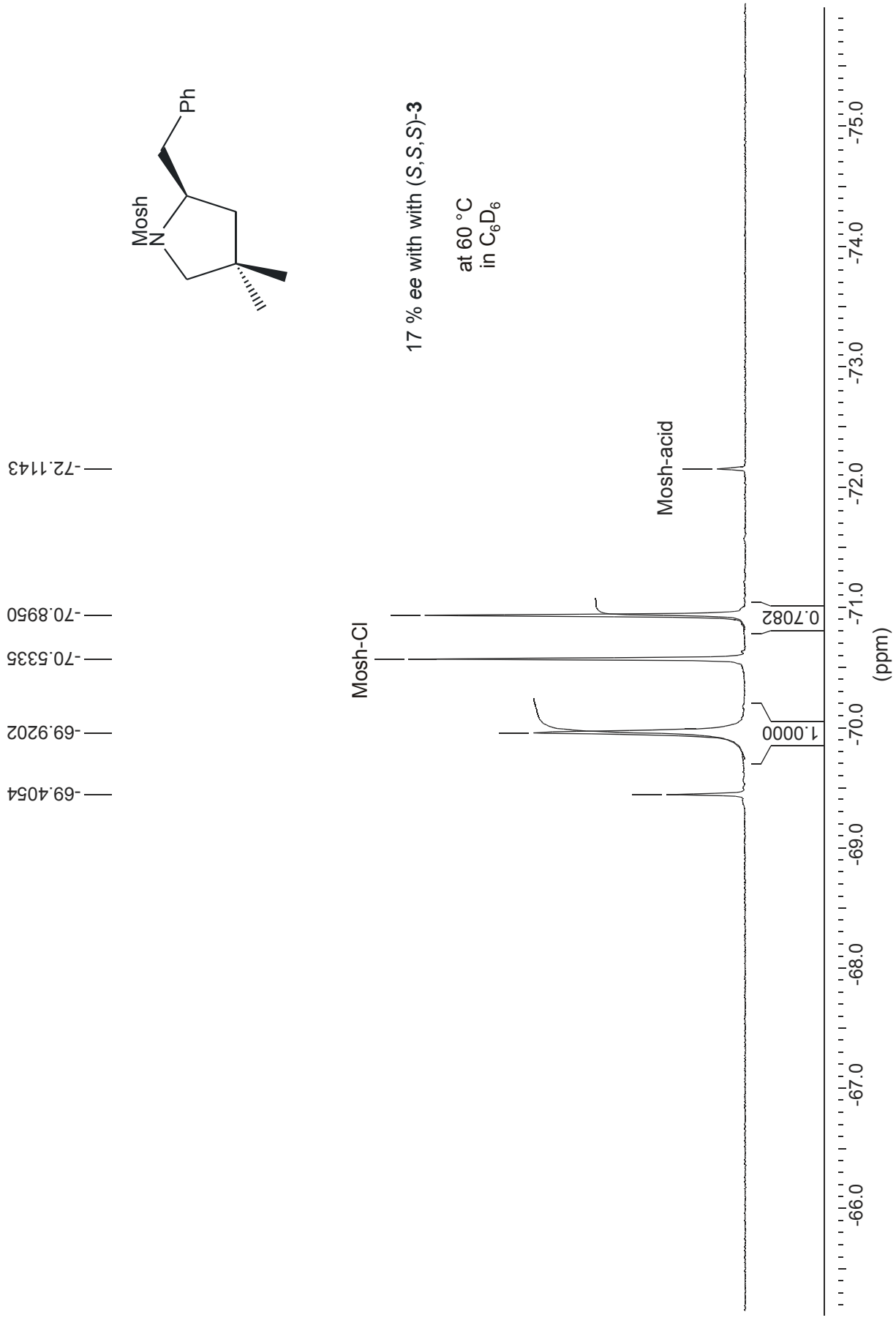
124.9814
125.8543
126.6835
128.6256
129.3312
129.9858
136.8377
155.4368
N
Me
N
Li
(S)-4
at 25 °C in C6D6
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
(ppm)

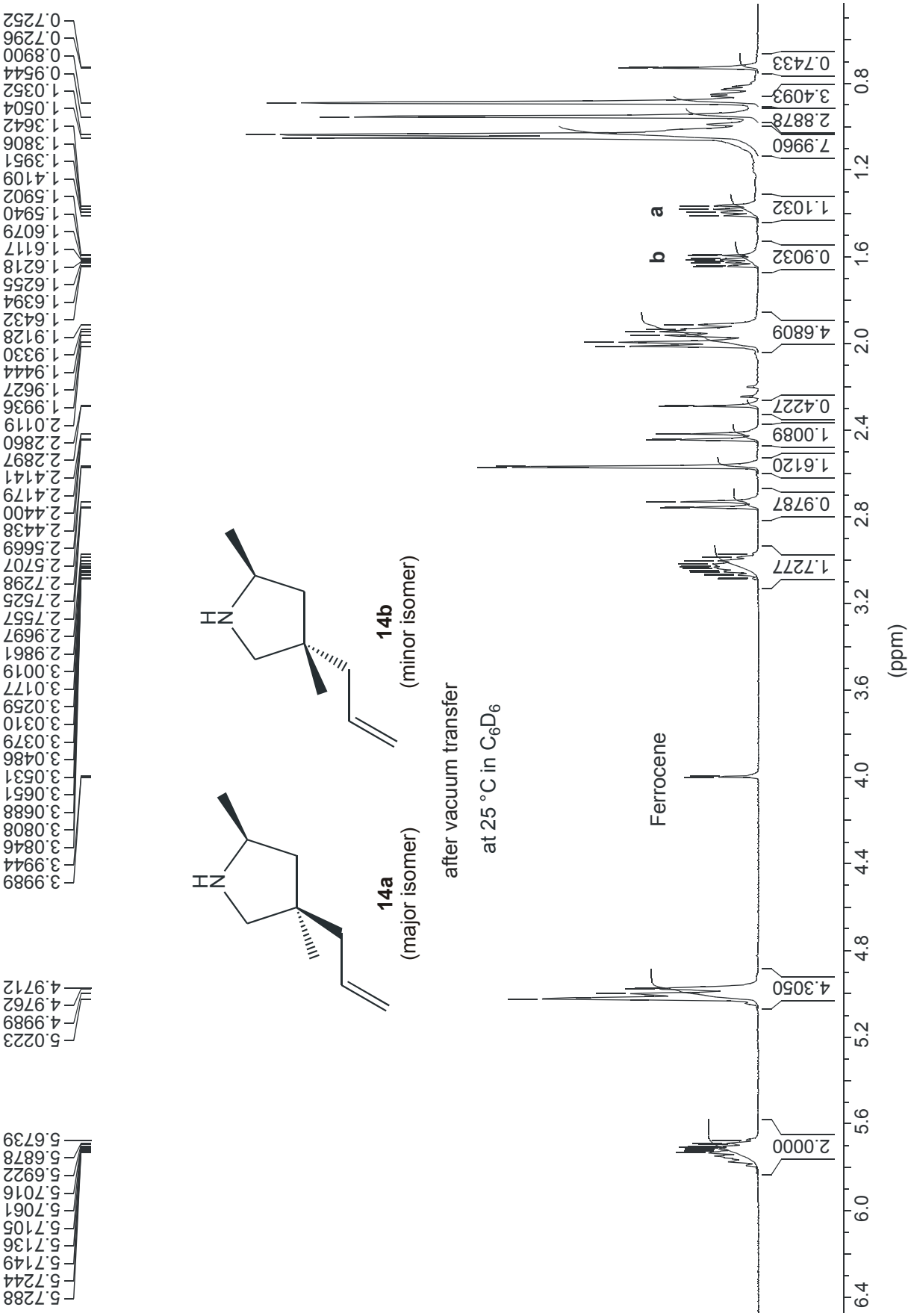

Ph
OMe
CF3
*
O
N
Mosher's amide of 6
at 60 °C in CDCl3
68 % ee with (S,S,S)-3
Mosh-Cl
-70.6211
-70.3984
-69.6500
-69.2229
0.1924
1.0000
-66.0
-67.0
-68.0
-69.0
-70.0
-71.0
-72.0
-73.0
-74.0
(ppm)

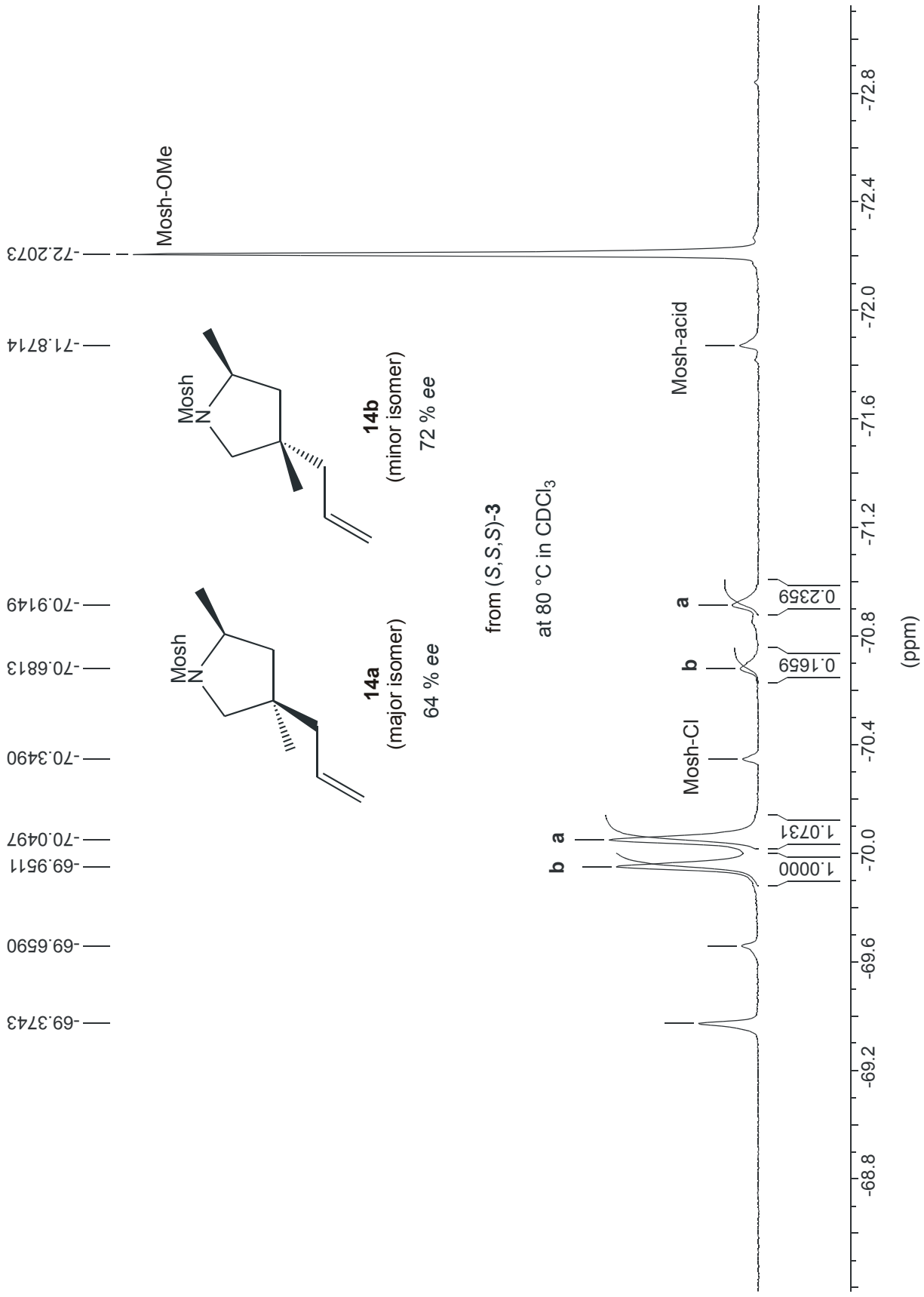

Mosher's amide of 8
at 60 °C in CDCl3
31 % ee with (S,S,S)-3
Ph
OMe
CF3
Ph
Ph
O
N
-72.0515
-70.8175
-70.4743
-69.7296
-69.6237
-69.5544
Mosh-Cl
0.5224
1.0000
-74.0
-73.5
-73.0
-72.5
-72.0
-71.5
-71.0
-70.5
-70.0
-69.5
-69.0
-68.5
-68.0
-67.5
(ppm)


Ph
OMe
CF3
*
O
N
Mosher's amide of 11
at 60 °C in CDCl3
75% ee with (S,S,S)-3
Mosh-Cl
-70.8637
-70.4000
-69.9984
0.1397
1.0000
-72.4
-72.0
-71.6
-71.2
-70.8
-70.4
-70.0
-69.6
-69.2
-68.8
-68.4
-68.0
(ppm)


Ferrocene
3.6700
3.4691
1.3960
1.2986
1.1725
3.1740
1.0000
2.1144
6.7307
(ppm)
prepared from 11 using
10 mol% (S,S,S)-3,
after 5 min at 22 °C
in C6D6
12
Ph
N
H


Ph
Mosh
N
17 % ee with with (S,S,S)-3
at 60 °C
in C6D6
Mosh-acid
Mosh-Cl
-72.1143
-70.8950
-70.5335
-69.9202
-69.4054
0.7082
1.0000
-66.0
-67.0
-68.0
-69.0
-70.0
-71.0
-72.0
-73.0
-74.0
-75.0
(ppm)


14b
(minor isomer)
14a
(major isomer)
after vacuum transfer
at 25 °C in C6D6
Ferrocene
a
b
(ppm)


Mosh-OMe
Mosh-acid
Mosh-Cl
Mosh
N
14b
(minor isomer)
72 % ee
14a
(major isomer)
64 % ee
from (S,S,S)-3
at 80 °C in CDCl3
a
b
0.2359
0.1659
1.0731
1.0000
-72.2073
-71.8714
-70.9149
-70.6813
-70.3490
-70.0497
-69.9511
-69.6590
-69.3743
-72.8
-72.4
-72.0
-71.6
-71.2
-70.8
-70.4
-70.0
-69.6
-69.2
-68.8
(ppm)