A NMR and Theoretical Study of the Aggregates Between Alkyllithium and Chiral Lithium Amides: Control of the Topology Through a Single Asymmetric Center.

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Supporting information

Experimental Part

General Considerations.

^{1}H NMR and ^{13}C NMR spectra for compounds **7**, **8** and **1** were recorded at room temperature on a Bruker DPX300 spectrometer at 300 MHz and 75 MHz respectively and on a Bruker Avance DMX 500 spectrometer at 500 MHz (^{1}H) and 125 MHz (^{13}C). *J* Values are given in Hz. IR spectra were realized on a PERKIN-ELMER 16PC IRTF spectrometer. The mass spectra were obtained on a JEOL AX500 apparatus, under electron impact conditions (EI) at 70 eV ionizing potential; isobutane (*t*-BuH) and ammonia (NH_3) were used for chemical ionization (CI). Melting points were determined using a C. REICHERT microscope apparatus. Thin layer chromatography (TLC) was carried out on Merk 5735 Kieselgel 60 F_{254} fluorescent plates. Flash chromatography was performed with silica gel (Merck Geduran SI 60 Art 11567). Optical rotations, $[\alpha]_D$, were measured in quartz cells (d = 1 dm), using Na and Hg lights, with solvents and concentrations indicated.
Argon was dried and deoxygenated by bubbling through a commercial solution of butyllithium in hexane. Commercial tetrahydrofuran-d_8 was distilled over sodium and benzophenone. ^{6}Li (95%) was purchased from Aldrich and washed in freshly distilled pentane.

N-(*tert*-Butoxycarbonyl)-3-(*R*)-hydroxypyrrolidine 7

A solution of *trans*-4-(*R*)-hydroxy-(L)-proline (5 g, 38,2 mmol) and 2-cyclohexen-1-one (0,5 mL, 5,16 mmol) in cyclohexanol (50 mL) was heated at 160°C for 6 h, until all the solid was dissolved. The resulting red solution was cooled to room temperature and an aqueous solution of acetic acid (20%; 50 mL) and toluene (30 mL) were added. The aqueous layer was washed twice with toluene then potassium carbonate (15 g) was introduced until pH = 9. Dioxane (50 mL) followed by di-*tert*-butyl dicarbonate (8,73 g, 40 mmol) were introduced to the basic resulting solution at 0°C and the reaction mixture was stirred at room temperature for 20 h. The organic materials were extracted twice with ether and the combined organic layers were concentrated. Ethanol (40 mL) was added and the solution was heated under reflux for 20 h. After evaporation of the solvent, the residue was eventually purified by flash chromatography on silica (heptane:ethyl acetate, 30:70) to give **7** as a white solid (6,15 g, 86%): mp 59-61°C (from ethanol); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 1.83-1.89 (m, 2H), 3.25-3.39 (m, 4H), 3.70 (s,1H), 4.34 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.8, 33.8 and 34.2, 43.9 and 44.3, 54.5,70.2 and 71.0, 79.7, 155.2; IR (film, NaCl) υ_{max}/cm^{-1} 1123, 1168, 1412, 1676, 3424; CIMS (200 eV, NH_3) *m/z* (relative intensity) 188 ($M+H^+$, 40), 149 (100); HRMS calcd

for $C_9H_{18}NO_3$ 188.1286, found 188.1284; Anal. Calcd for $C_9H_{17}NO_3$: C, 57.73; H, 9.15; N, 7.48%. Found: C, 57.75; H, 9.45; N, 7.42%. $[\alpha]_D^{26}$ -21.9 (*c* 1.42, CH_2Cl_2).

_N_-(*tert*-Butoxycarbonyl)-3-(*S*)-(1'-(*S*)-phenylethyl) aminopyrrolidine 8e

A solution of di-*iso*-propylethylamine (5.85 mL, 33.58 mmol) in dichloromethane (5 mL) was added to a solution of *N*-(*tert*-butoxycarbonyl)-3-(*R*)-hydroxypyrrolidine **7** (3 g, 16.04 mmol) in cold (-30°C) dichloromethane (22 mL) and placed under nitrogen atmosphere. Trifluoromethanesulfonic anhydride (2.87 mL, 17.1 mmol) was slowly syringed over a period of 25 min, the reaction mixture was then stirred for 45 min at -30°C. A solution of (*S*)-(-)-α-methylbenzylamine (3 mL, 23.2 mmol) in dichloromethane (9 mL) was introduced in 5 min, and the resulting mixture was stirred at room temperature for 20 h. The solution was washed with saturated aqueous potassium hydrogen carbonate (2x30 mL) and brine (1x30 mL). The organic layer was collected, dried ($MgSO_4$), filtered and concentrated. Purification by chromatography on silica (dichloromethane:ethyl acetate, 50:50) gave **8e** as pale yellow oil (2.6 g, 55%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (d, 3H, *J* = 6.4), 1.37 (s, 9H), 1.40 (s, 1H), 1.45-1.60 (m, 1H), 1.75-1.87 (m, 1H), 2.97-3.20 (m,3H), 3.27-3.53 (m, 2H), 3.72 (q, 1H, *J* = 6.4), 7.19-7.26 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.4, 29.2, 32.6 and 33.4, 44.7 and 45.0, 52.0 and 52.6, 55.1 and 56.0, 57.3, 79.8, 127.2, 127.7, 129.2, 146.0, 155.3; IR (film, NaCl) υ_{max}/cm^{-1} 1118, 1164, 1402, 1682, 2972, 3316; CIMS (200 eV, *t*-BuH) *m/z* (relative intensity) 291 (M+H$^+$, 100); HRMS calcd for $C_{17}H_{27}N_2O_2$ 291.2072, found 291.2064; Anal. Calcd for $C_{17}H_{26}N_2O_2$: C, 70.31; H, 9.02; N, 9.65%. Found: C, 70.27; H, 9.22; N, 9.54%. $[\alpha]_D^{25}$ -92.8 (*c* 1.52, $CHCl_3$).

_N_-(*tert*-Butoxycarbonyl)-3-(*S*)-(1'-(*R*)-phenylethyl) aminopyrrolidine 8f

8f was prepared from **7** (2 g, 10.7 mmol) in a similar way to **8e** using (*R*)-(+)-α-methylbenzylamine and led to a pale yellow oil (1.92 g, 62%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (d, 3H, *J* = 6.8), 1.38 (s, 9H), 1.43 (s, 1H), 1.48-1.67 (m, 1H), 1.89-2.04 (m, 1H), 2.80-3.50 (3m,5H), 3.72 (q, 1H, *J* = 6.8), 7.17-7.26 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.2 and 25.3, 29.1, 31.7 and 32.5, 44.6 and 45.1, 52.5 and 52.9, 55.2 and 56.0, 57.0, 79.7 and 79.9, 127.2, 127.8, 129.2, 146.0, 155.2; IR (film, NaCl) υ_{max}/cm^{-1} 1110, 1166, 1412, 1704, 2972, 3307; CIMS (200 eV, *t*-BuH) *m/z* (relative intensity) 291 (M+H$^+$, 100); HRMS calcd for $C_{17}H_{27}N_2O_2$ 291.2072, found 291.2067. $[\alpha]_D^{25}$ +25.4 (*c* 0.885, $CHCl_3$).

_N_-Methyl-3-(*S*)-(1'-(*S*)-phenylethyl) aminopyrrolidine 1e

A solution of *N*-(*tert*-butoxycarbonyl)-3-(*S*)-(1'-(*S*)-phenylethyl) aminopyrrolidine **8e** in dry THF (30 mL) was added for 30 min to a suspension of lithium aluminum hydride (0.21 g, 5.51 mmol) in freshly distilled THF (10 mL), placed under nitrogen atmosphere and cooled to 0°C. The solution was stirred at room temperature for 6h then warmed at 60°C for an hour. After cooling at 0°C, the excess of LAH was hydrolized by successive addition of cold water (0.6 mL), 4N aqueous sodium hydroxide (0.6 mL) and cold water (0.8 mL). The white precipitate was filtered on celite and washed with dichloromethane (10 mL). The filtrate was concentrated and the residue was dissolved in ether (10 mL). 1N aqueous hydrochloric acid (10 mL) was added and the solution was stirred at room temperature for 15 min. The acidic aqueous layer was extracted and sodium hydrogen carbonate was slowly introduced until pH = 9 followed by a few drops of 4N aqueous sodium hydroxide. The medium was then extracted with dichloromethane (3x10mL). The organic layer was collected, dried ($MgSO_4$), filtered and concentrated to give **1e** as a pale yellow oil (0,195 g, 69%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.28 (d, 3H, *J* = 6.6), 1.42-1.46 (m, 1H), 1.97-2.13 (m, 1H), 2.22-2.25 (m, 1H), 2.26 (s, 3H), 2.44-2.46 and 2.55-2.58 (2m,3H), 3.06-3.08 (m, 1H), 3.71 (q, 1H, *J* = 6.6), 7.16-7.25 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.2, 34.0, 42.9, 55.8, 55.9, 57.0, 63.2, 127.4, 127.6, 129.1, 146.1; IR (film, NaCl) υ_{max}/cm^{-1} 1450, 2964, 3386; EIMS (70 eV) *m/z* (relative intensity) 204 ($M^{+\cdot}$, 20), 99 (70), 85 (100); HRMS calcd for $C_{13}H_{20}N_2$ 204.1626, found 204.1631. $[\alpha]_D^{24.5}$ -79.4 (*c* 0.54, $CHCl_3$).

_N_-Methyl-3-(*S*)-(1'-(*R*)-phenylethyl) aminopyrrolidine 1f

1f was prepared from **8f** (0.31 g, 8.26 mmol) in a similar way to **1e** and led to a pale yellow oil (0.218 g, 65%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (d, 3H, *J* = 6.4), 1.40-1.48 (m, 1H), 1.50-1.60 and 1.94-2.05 (2m, 2H), 2.15-2.24 and 2.41-2.47 (2m, 2H), 2.21 (s, 3H), 2.29-2.37 and 2.50-2.58 (2m,2H), 3.05-3.11 (m, 1H), 3.72 (q, 1H, *J* = 6.4), 7.13-7.24 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.1, 33.3, 42.9, 56.0, 57.0, 64.1, 127.4, 127.6, 129.0, 146.2; IR (film, NaCl) υ_{max}/cm^{-1} 1450, 2962, 3306; EIMS (70 eV) *m/z* (relative intensity) 204 ($M^{+\cdot}$, 18); 99 (65), 85 (100); HRMS calcd for $C_{13}H_{20}N_2$ 204.1626, found 204.1635. $[\alpha]_D^{25}$ +65.6 (*c* 0.76, $CHCl_3$).

[^{6}Li] Methyllithium salt-free solution in ether

Finely cut 6-lithium metal ribbon (0.5 g, 83 mmol), 0.5% (weight) of sodium (*ca*. 2,5 mg, 0,11 mmol) and three small pieces of broken glass were introduced in a two necked pear-shaped flask (50 mL) equipped with a glass stopper and a condenser fitted with a balloon of dry argon. The metallic cuttings were covered with octadecane (10 mL) and the solution was heated (reflux of octadecane : 317°C) with a hot air gun while vigorously stirring. When a

maximum amount of the lithium was melted, the flask was placed in a cold bath (- 40°C) allowing the lithium to precipitate as a fine shiny shot. The octadecane was extracted with freshly distilled (over lithium aluminum hydride) heptane (10 mL) using a syringe. After intensive stirring, the heptane was removed and the metal washed twice with this same solvent. Diethylether was syringed and the condenser was quickly replaced by a CO_2 condenser fitted with a balloon of dry argon. Chloromethane (2,3 mL, 41,5 mmol) was condensed directly from the sealed cylinder to a graduated trap at -40°C and then added very slowly (2,3 mL were added over a period of 45 min) connecting the trap to the top of the CO_2 condenser. The formation of a grey salt corresponding to LiCl was observed and the disappearance of the ^{6}Li metal was noticed. After replacing the CO_2 condenser with a septum, the resulting reaction mixture was stirred for 20 h at room temperature under dry argon. The stirring was stopped allowing LiCl to settle. The etheral solution was then pumped off the flask with a syringe and directly inserted into centrifugation tubes placed under dry argon. The residual traces of salt were centrifuged and the clear final solution was collected in a dry flask flushed under dry argon then titrated[1] (1,4 M, 55% yield) and kept until further use.

[^{6}Li] Methyllithium salt-free solution in tetrahydrofuran-*d_8*

A solution of [^{6}Li]-methyllithium in ether prepared above (2,5 mL) was syringed in a tube fitted with a septum and flushed under dry argon. The tube was then placed under vacuum (20 mmHg) for 1 h to evaporate the ether. The resulting white solid was then dissolved in freshly distilled tetrahydrofuran-*d_8* and concentrated under vacuum for 1 h to evaporate the last traces of ether. THF- *d_8* (3 to 3.5 mL) was finally added and the resulting solution was titrated[25] (0.5 to 0.7 M).

[^{6}Li]-Lithium amides 2e or 2f, 2c or 2d

A solution of amine (**1e** (27,9 mg; 0,137 mmol) or **1f** (29,0 mg; 0.142 mmol) in freshly distilled tetrahydrofuran- *d_8* (0,2 mL) was transferred into a dry 5-mm NMR tube fitted with a septum and flushed under argon., 0.5 to 0.7 M [^{6}Li]-Methyllithium (1 eq) in tetrahydrofuran-*d_8* was added dropwise at –78°C with a syringe to the above solution,. The tube was then vigorously shaken and quickly dropped in the pre-cooled (-93°C) NMR probe. All the spectra of the corresponding amide **2e** and **2f** were recorded at this temperature. The lithium amide **2c** and **2d** were prepared following a similar procedure.

[^{6}Li]-Complexes 3c, 3d 3e or 3f

The complexes obtained from amides **2c**, **2d**, **2e** and **2f** with [^{6}Li]-methyllithium in tetrahydrofuran- d_8 were prepared in a similar way to the lithium amides, but using directly an excess of Me^{6}Li/amine (>2eq./**1c**, **1d**, **1e** or **1f**) or adding a second equivalent of Me^{6}Li on **2c**, **2d**, **2e** or **2f**.

Instrumental considerations.

The conformational study of 3AP lithium amides **2c-f** and their complexes with MeLi **3c-f** were achieved by using one and two-dimensional NMR experiments.
All NMR experiments were performed on a Bruker Avance DMX 500 spectrometer, equipped with z-gradient unit and a 5 mm {^{1}H, ^{6}Li, ^{13}C and ^{15}N} quadruple-resonance probe. Measuring frequencies were 500 MHz (^{1}H), 125 MHz (^{13}C), 73 MHz (^{6}Li) and 50 MHz (^{15}N). ^{1}H and ^{13}C chemical shifts were referenced to the solvent THF-d_8 signals at δ 1.73 and δ 25.37 respectively. Lithium spectra were referenced to external 0.3 M ^{6}LiCl in MeOH-d_4 (δ 0.0). Nitrogen spectra were referenced to external 0.1 M ^{15}N urea in DMSO-d_6 (δ 75.9 ppm with respect to NH_3).

1D NMR measurements

The proton and lithium one dimensional experiments were recorded with standard parameters. In order to remove ^{13}C - ^{1}H coupling, the one dimensional ^{13}C spectra were recorded with broad band proton decoupling.

2D NMR measurements

^{6}Li/^{6}Li COSY:[2] The following parameters were used for acquiring and processing the spectra in absolute values: 128 experiments with 1024 data points and 8 scans each were recorded; no proton decoupling was used; one time zero filling in f_1; pure sine bell window function was applied before Fourier Transformation.

^{1}H/^{1}H COSY:[3] The following parameters were used for acquiring and processing the spectra in absolute values: 256 experiments with 2048 data points and 8 scans each were recorded; one time zero filling in f_1; pure sine bell window function was applied before Fourier Transformation.

^{1}H/^{13}C HMQC:[4] The following parameters were used for acquiring and processing the spectra in phase sensitive-sensitive mode: 512 experiments with 2048 data points and 8 scans

each were recorded; pure phase line shapes was obtained by using Time Proportional Phase Incrementation (TPPI) phase cycling[5], one time zero filling in f_1; π / 2 shifted sine square window functions were applied to f_2 and f_1 dimension before Fourier Transformation.

^{1}H/^{1}H NOESY:[6] The following parameters were used for acquiring and processing the spectra in phase sensitive-sensitive mode: 256 experiments with 2048 data points and 16 scans each were recorded; pure phase line shapes was obtained by using Time Proportional Phase Incrementation (TPPI) phase cycling, variable mixing times, depending on the sample, were used; one time zero filling in f_1; π / 2 shifted sine square window functions were applied to f_2 and f_1 dimension before Fourier Transformation.

^{6}Li/^{1}H HOESY:[7] The following parameters were used for acquiring and processing the spectra in phase sensitive-sensitive mode: 128 experiments with 1024 data points and 16 scans each were recorded; pure phase line shapes was obtained by using Time Proportional Phase Incrementation (TPPI) phase cycling; variable mixing times, depending on the sample, were used; one time zero filling in f_1; π / 2 and π / 3 shifted sine square window functions were applied to f_2 and f_1 dimension respectively before Fourier Transformation.

^{6}Li/^{6}Li EXSY:[8] The following parameters were used: 256 experiments with 2048 data points and 8 scans each were recorded; mixing time 4.0 s; pure phase line shapes was obtained by using Time Proportional Phase Incrementation (TPPI) phase cycling; one time zero filling in f_1; π / 2 shifted sine square window functions were applied to f_2 and f_1 dimension before Fourier Transformation.

Processing of NMR data was performed on SGI O2 computer, using the manufacturer's program Xwinnmr2.1 (Bruker).

Computational procedures. The quantum mechanical computations were performed using the 6-31G**, 6-311G**, 6-31++G** and 6-311++G** basis set[9] and the B3P86, B3LYP and B3PW91 hybrid density functional.[10] For all the systems considered, all geometrical parameters were fully optimized. The gas-phase optimizations were obtained from Gaussian98.[11] Those including the dimehtyl ether molecules used as model of THF solvent were carried out with Jaguar 4.1.[12] The nuclear magnetic shielding constants were calculated using the GIAO method,[13] as implemented in Gaussian98.

References:

1. Duhamel, L.; Plaquevent, J.C. *J. Organomet. Chem.* **1993**, *448*, 1-3.
2. Günther, H.; Moskau, D.; Dujardin, R.; Maercker, A. *Tetrahedron Lett.* **1986**, *27*, 2251-2254.
3. Nagayama, K., Kumar, A., Wüthrich, K., Ernst, R. R. *J. Magn. Reson.* **1980**, *40*, 321-334.
4. Bax, A., Griffey, R.H., Hawkins, B.L. *J. Magn. Reson*. **1983**, *55*, 301-315.
5. Marion, D.; Wüthrich, K. *Biochem. Biophys. Res. Comm.* **1983***, 113,* 967-974.
6. States, D.J.; Haberkorn, R.A.; Ruben, D.J. *J. Magn. Reson.* **1982**, *48*, 286-292.
7. Bauer, W.; Schleyer, P.v.R. *Magn. Reson. Chem.* **1988**, *26*, 827-833.
8. a) Meier, B.H.; Ernst R.R. *J. Am. Chem. Soc.* **1979**, *101*, 6441-6442. b) Jeener, J.; Meier, B.H.; Bachman, P.; Ernst, R.R. *J. Chem. Phys*. **1979**, *71*, 4546-4553.
9. Frisch, J. M.; Pople, J. A.; Binkley, J. S. *J. Chem. Phys.* 1984, **80**, 3265-3269.
10. a) Perdew, J. P. *Phys. Rev.* **1986**, *B33*, 8822-8824. b) Becke, A. D. *J. Chem. Phys.* **1989**, *90*, 5648-5652. c) Lee, C.; Yang, W.; Parr, R.G. *Phys. Rev. B* **1988**, *37*, 785-789. d) Miehlich, B.; Savin, A.; Stoll, H.; Preuss, H. *Chem. Phys. Lett.* **1989**, *157*, 200-206. e) Perdew, J.P.; Burke, K.; Wang, Y. *Phys. Rev. B* **1996**, *54*, 16533-16539.
11. GAUSSIAN 98 (Revision A5) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewfki, V. G.; Montgomery, J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, F.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle E. S.; Pople, J. A. **1998**, Gaussian Inc., Pittsburgh PA.
12. a) Jaguar 4.1; Schrödinger Inc., Portland OR, 2000. b) Greeley, B. H.; Russo, T. V.; Mainz, D. T.; Friesner, R. A.; Langlois, J. M.; Goddard, W. A., III; Donnelly, R. E.; Ringalda, M. N. *J. Chem. Phys*. **1994**, *101*, 4028-4041.
13. a) Ditchfield, R. *Mol. Phys.* **1974**, *27*, 789. b) Wolinski, K.; Himton, J. F.; Pulay, P. *J. Am. Chem. Soc.* **1990**, *112*, 8251-8260.

Captions to Figures in Supporting Information.

Fig. 1S: Monodimensional ^{6}Li spectrum of lithium amide **2c** in THF-d_8 at -78°C.

Fig. 2S: Two dimensional ^{1}H/^{1}H COSY contour plot of Me^{6}Li mixed-aggregate **3c** in THF-d_8 solution at -78°C.

Fig. 3S: Two dimensional ^{1}H/^{13}C HMQC contour plot of Me^{6}Li mixed-aggregate **3c** in THF-d_8 solution at -78°C.

Fig. 4S: Monodimensional ^{1}H spectrum of lithium amide **2d** in THF-d_8 solution at -78°C.

Fig. 5S: Monodimensional ^{6}Li spectrum of lithium amide **2d** in THF-d_8 solution at -78°C.

Fig. 6S: Two dimensional ^{1}H/^{1}H COSY contour plot spectrum of Me^{6}Li mixed-aggregate **3d** in THF-d_8 solution at -78°C.

Fig. 7S: Two dimensional ^{1}H/^{13}C HMQC contour plot spectrum of Me^{6}Li mixed-aggregate **3d** in THF-d_8 solution at -78°C.

Fig. 8S: Monodimensional ^{13}C spectrum of Me^{6}Li mixed-aggregate **3d** in THF-d_8 solution at -78°C.

Fig. 9S: Monodimensional ^{1}H spectrum of lithium amide **2e** in THF-d_8 solution at –93°C.

Fig. 10S: Monodimensional ^{6}Li spectrum of lithium amide **2e** in THF-d_8 solution at –93°C.

Fig. 11S: Monodimensional ^{1}H spectrum of lithium amide **3e** in THF-d_8 solution at -93°C.

Fig. 12S: Two dimensional ^{6}Li/^{1}H HOESY contour plot spectrum (τ_m = 1s) of Me^{6}Li mixed-aggregate **3e** in THF-d_8 solution at -93°C.

Fig. 13S: Two dimensional ^{1}H/^{1}H NOESY contour plot spectrum (τ_m = 300ms) of Me^{6}Li mixed-aggregate **3e** in THF-d_8 solution at -93°C.

Fig. 14S: Monodimensional ^{1}H spectrum of lithium amide **2f** in THF-d_8 solution at -93°C.

Fig. 15S: Monodimensional ^{6}Li spectrum of lithium amide **2f** in THF-d_8 solution at -93°C.

Fig. 16S: Monodimensional ^{1}H spectrum of lithium amide **3f** in THF-d_8 solution at -93°C obtained by two successive additions of one equivalent of Me^{6}Li on amine **1e**.

Fig. 17S: Monodimensional ^{1}H spectrum of lithium amide **3f** in THF-d_8 solution at -93°C obtained by the direct addition of 2.3 equivalents of Me^{6}Li on amine **1e**.

Fig. 18S: Two dimensional ^{1}H/^{1}H NOESY contour plot spectrum (τ_m = 300ms) of Me^{6}Li mixed-aggregate **3f** in THF-d_8 solution at -93°C.

Fig. 19S: Two dimensional ^{6}Li /^{1}H HOESY contour plot spectrum (τ_m = 1s) of Me^{6}Li mixed-aggregate **3f** in THF-d_8 solution at -93°C.

Table 1S. Calculated energy values (in a.u.) for the «exo» and «endo» arrangements of the **3e** complex.

Figure 1S

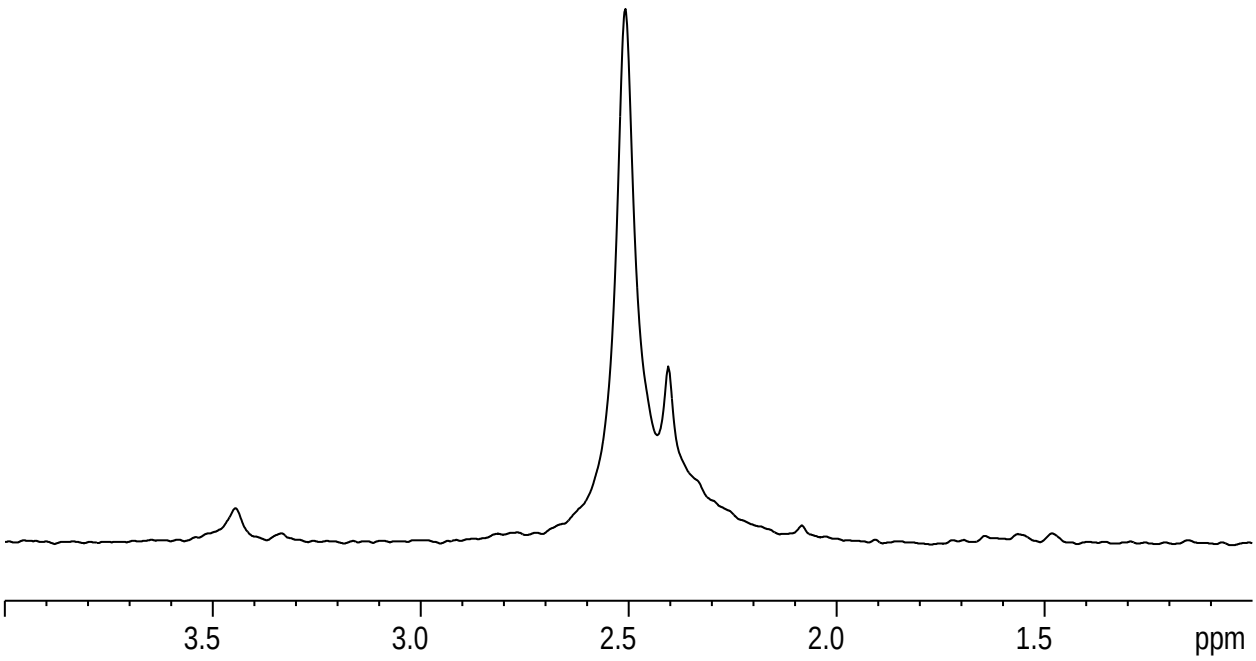

Figure 2S

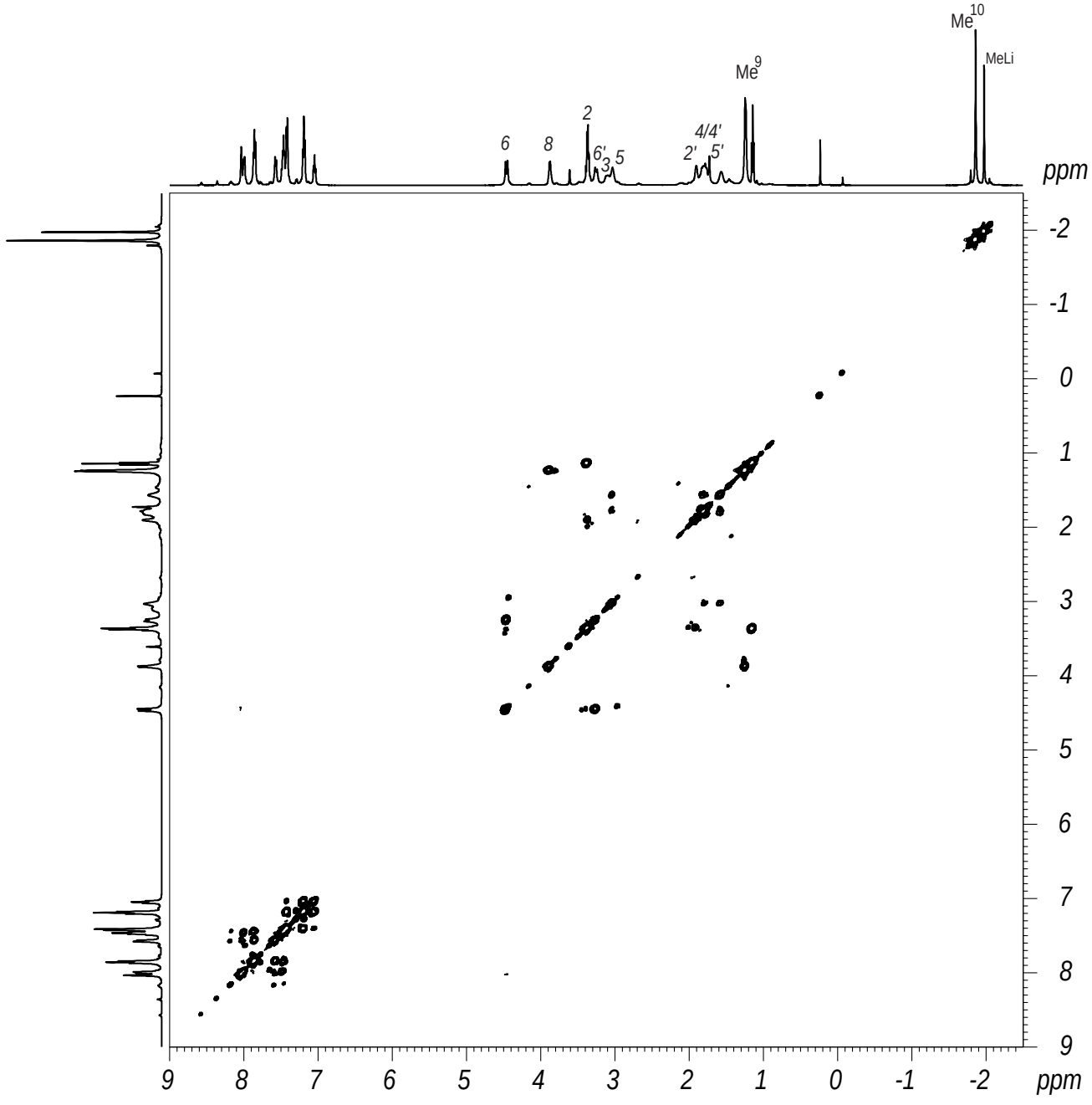
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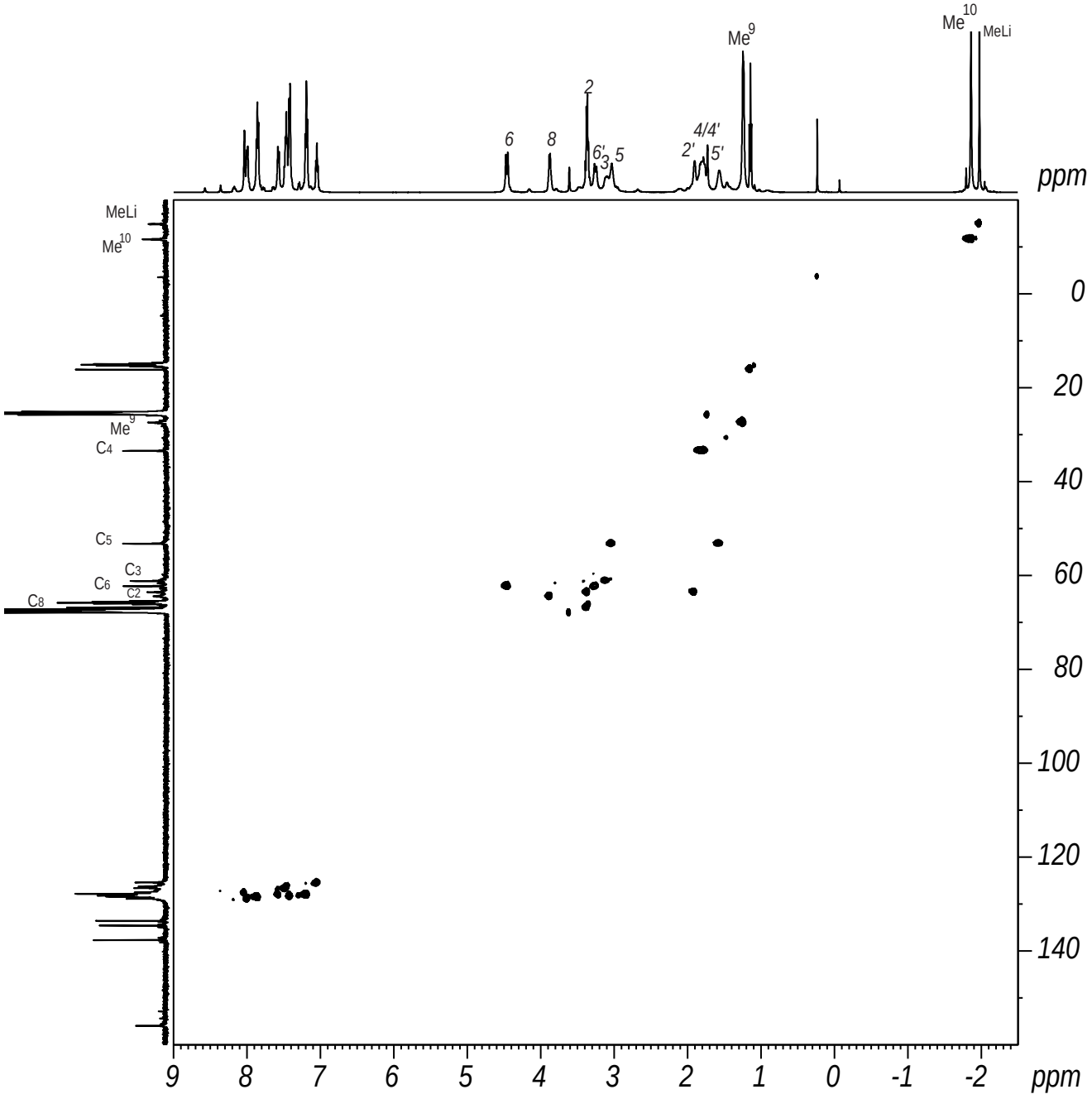
Figure 3S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ppm

Figure 4S

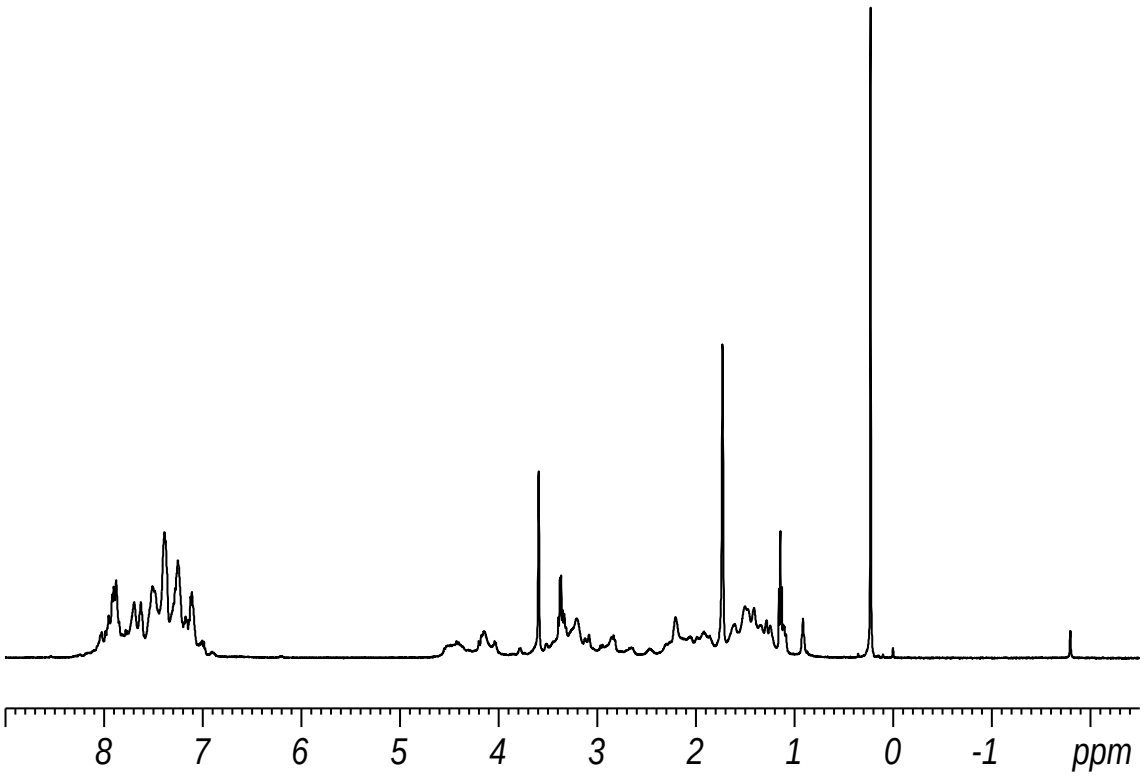

Figure 5S

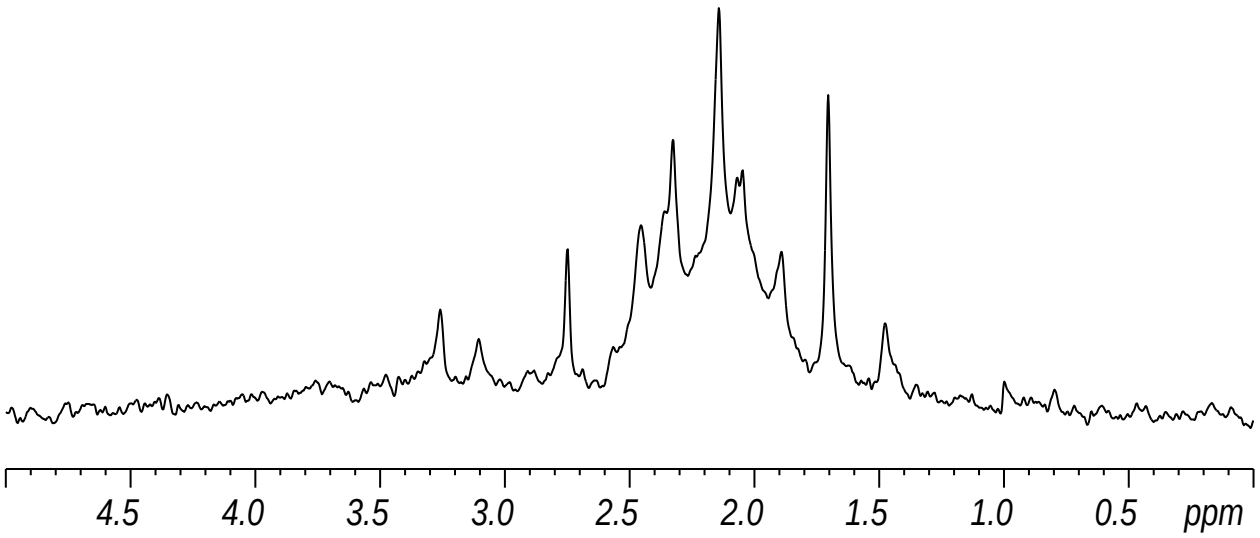

Figure 6S

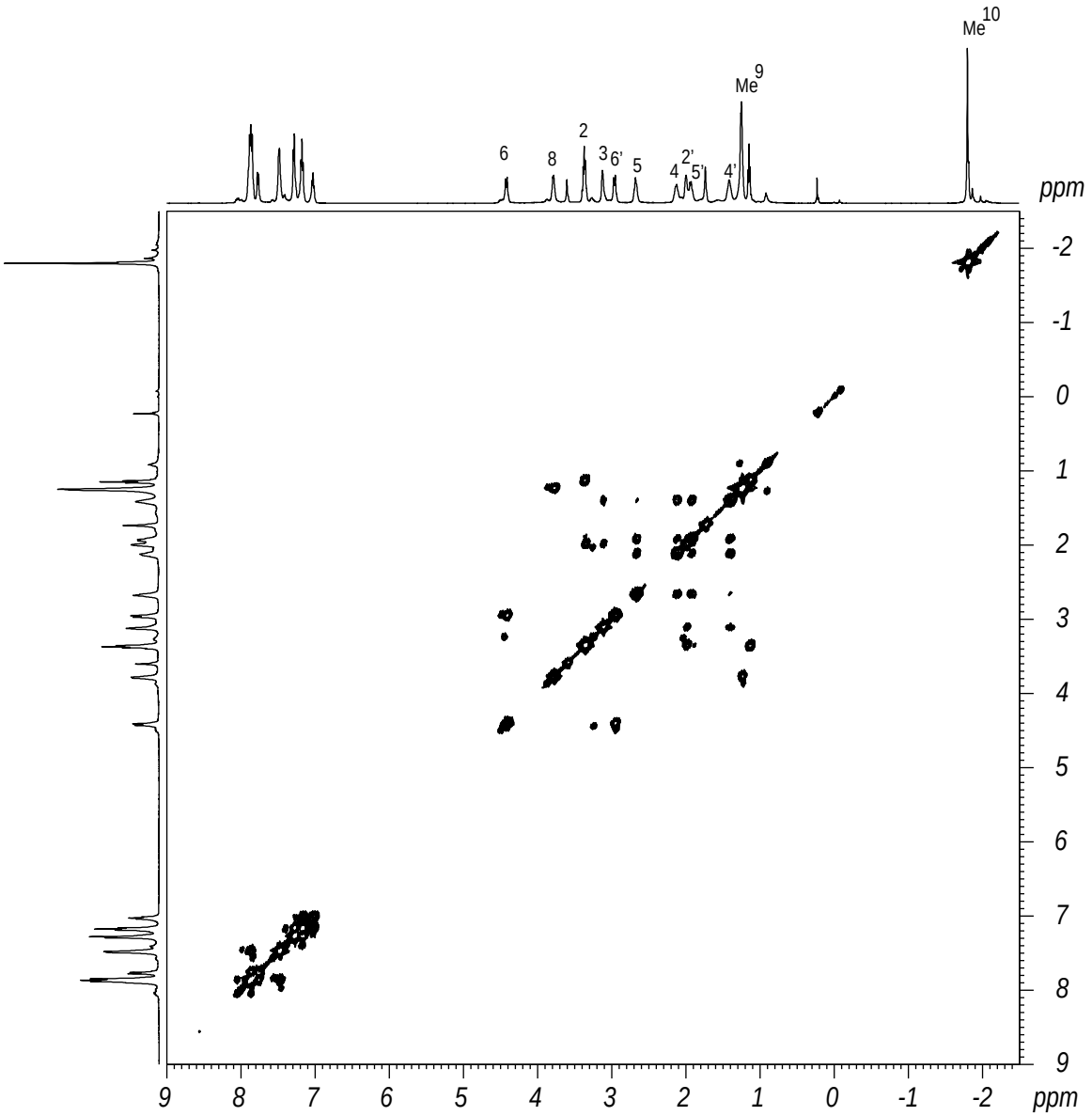

Figure 7S

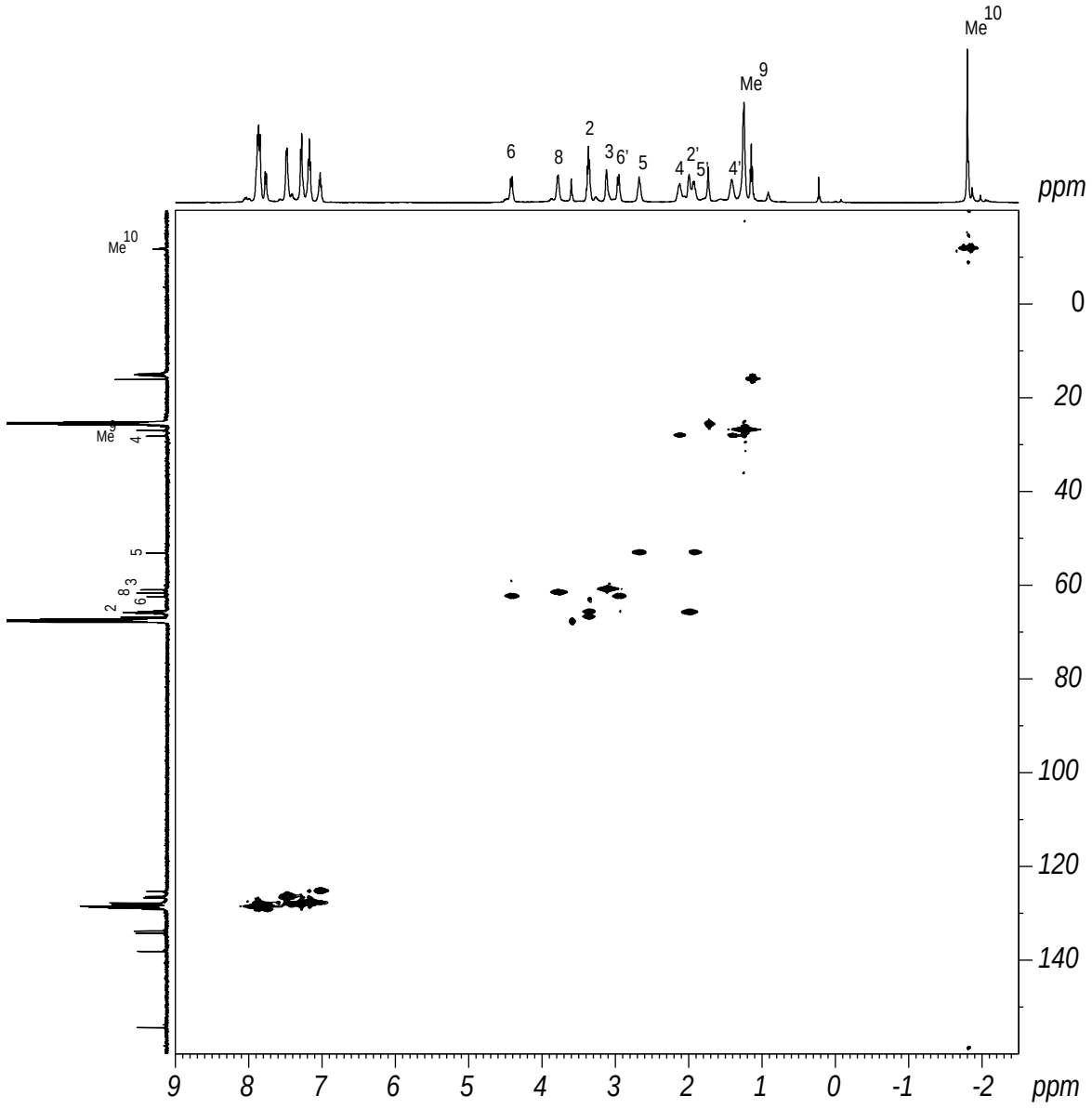
Me10
Me9
2
6
8
3
6'
5
4
2'
5'
4'
ppm
Me10
Me9
4
5
3
8
2
6
0
20
40
60
80
100
120
140
9
8
7
6
5
4
3
2
1
0
-1
-2
ppm

Figure 8S

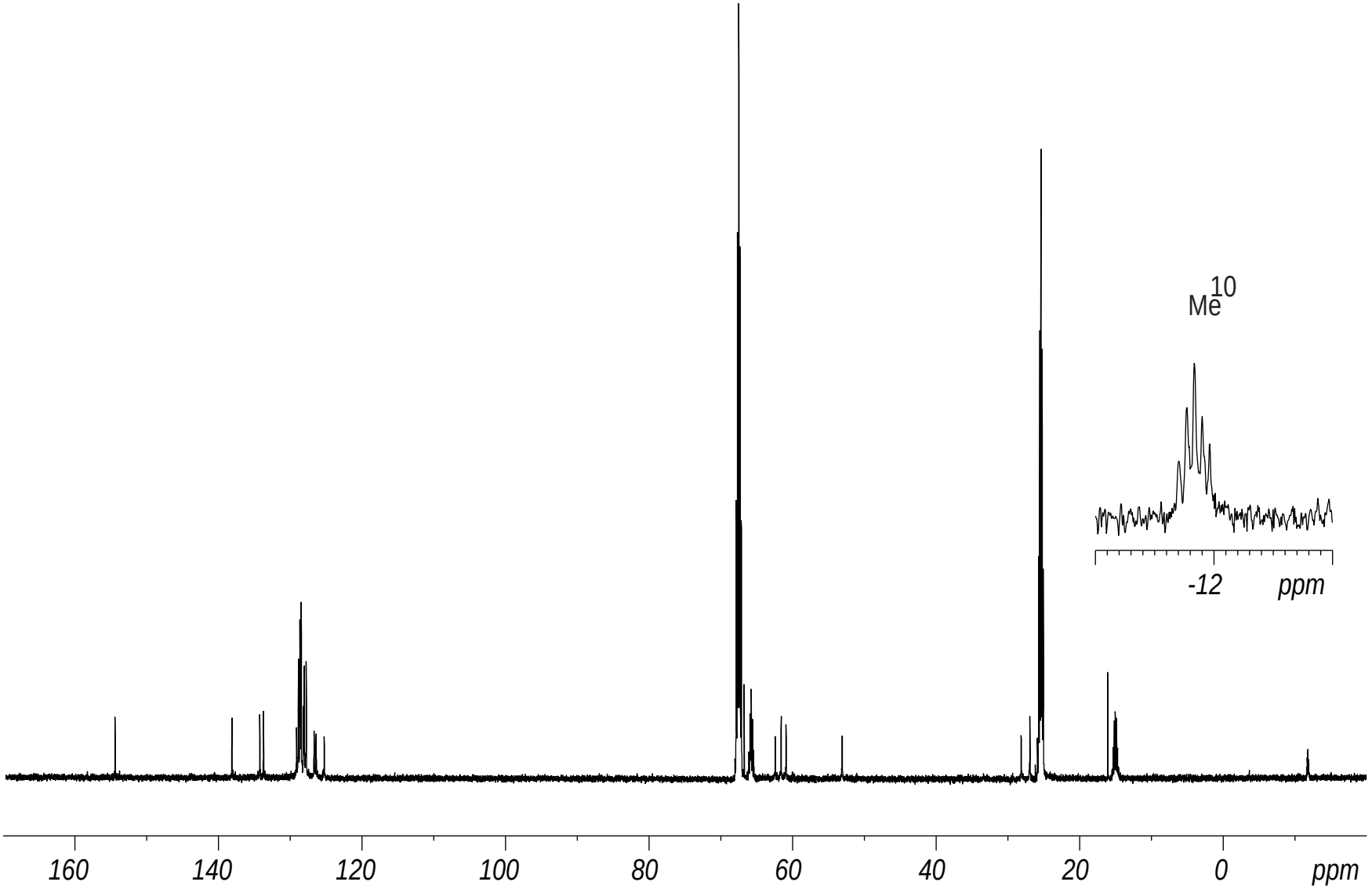

Figure 9S

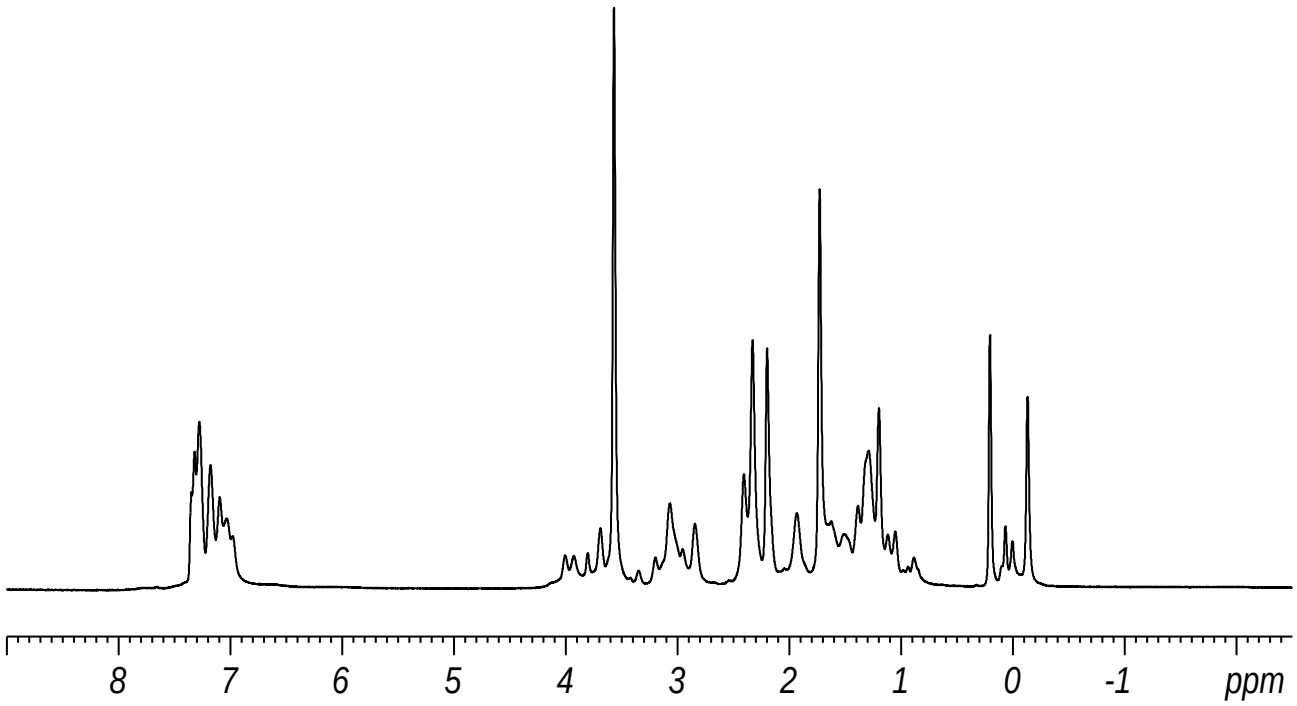

Figure 10S

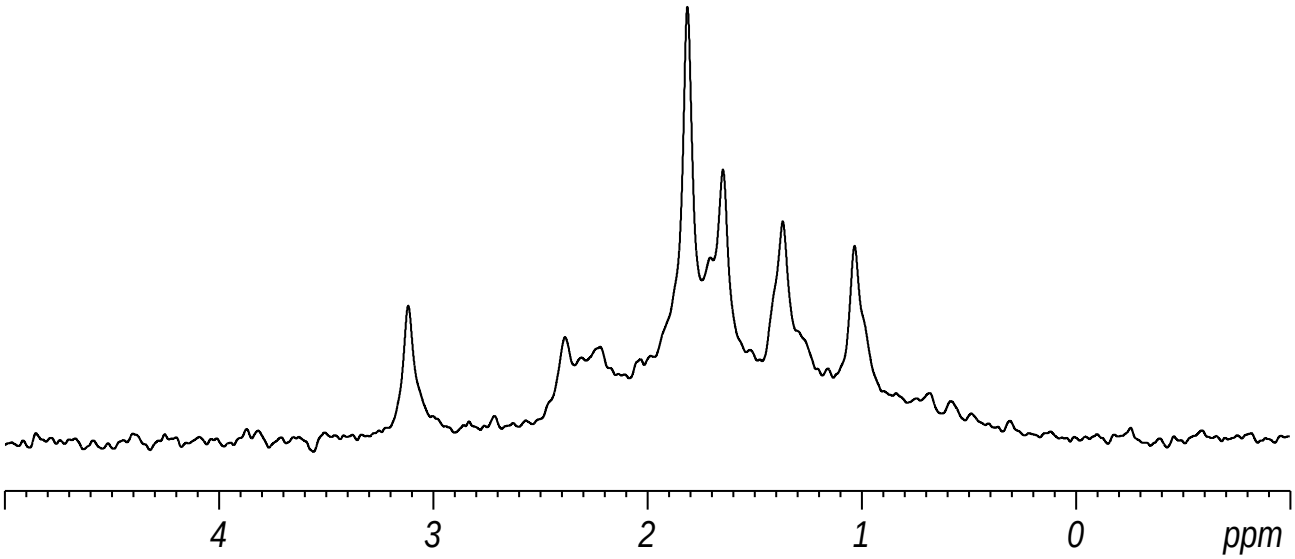

Figure 11S

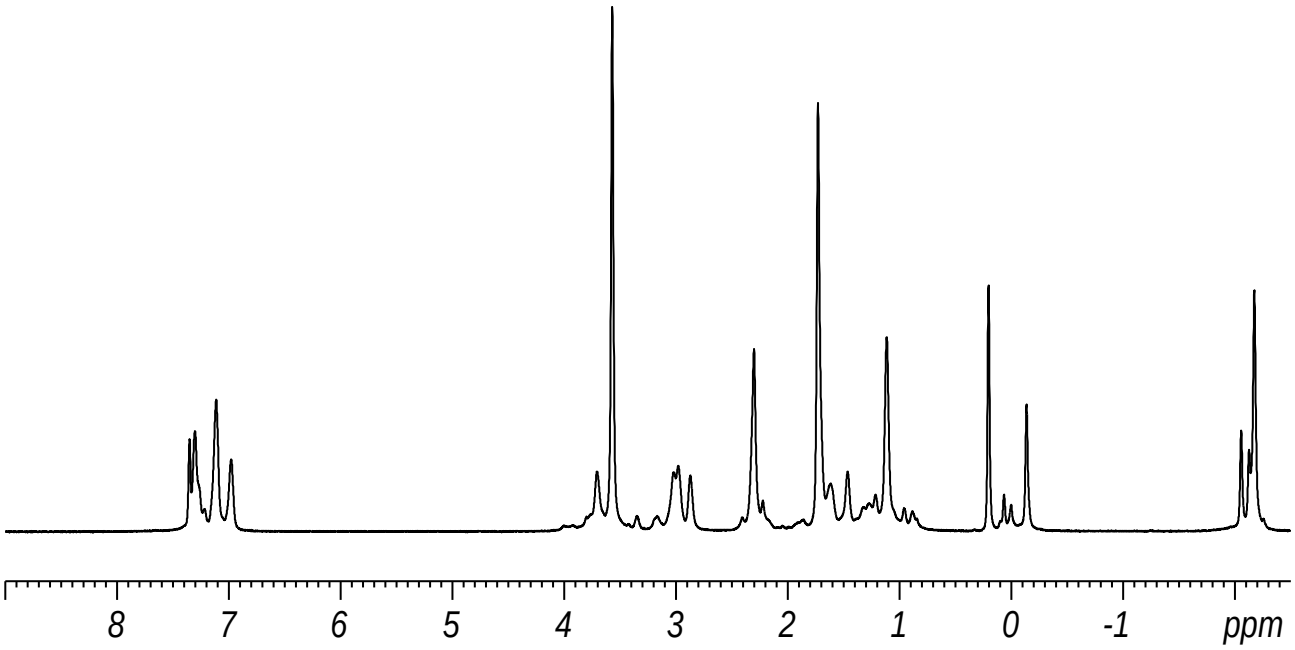

Figure 12S

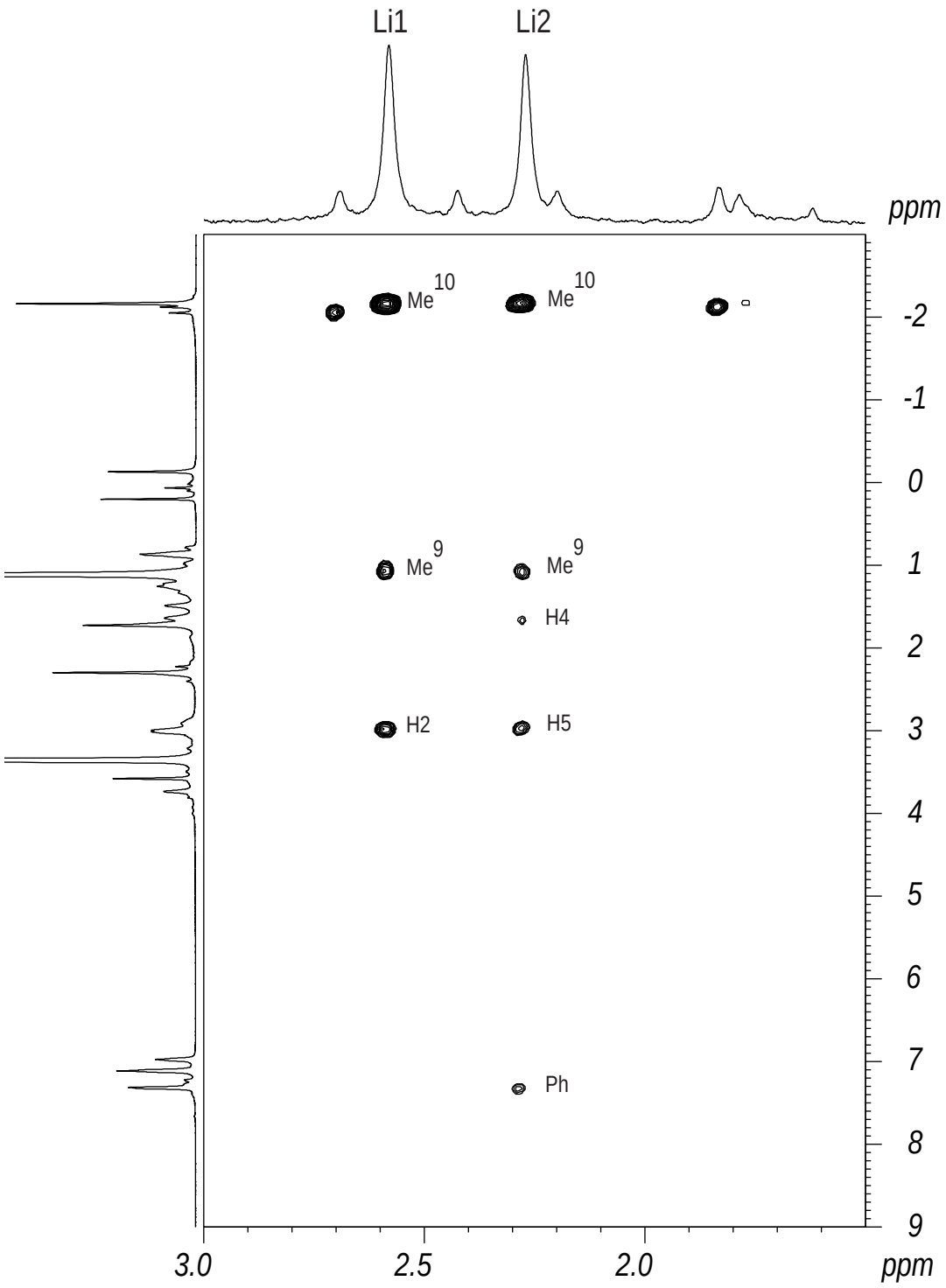
Li1
Li2
ppm
Me10
Me10
Me9
Me9
H4
H2
H5
Ph
-2
-1
0
1
2
3
4
5
6
7
8
9
3.0
2.5
2.0
ppm

Figure 13S

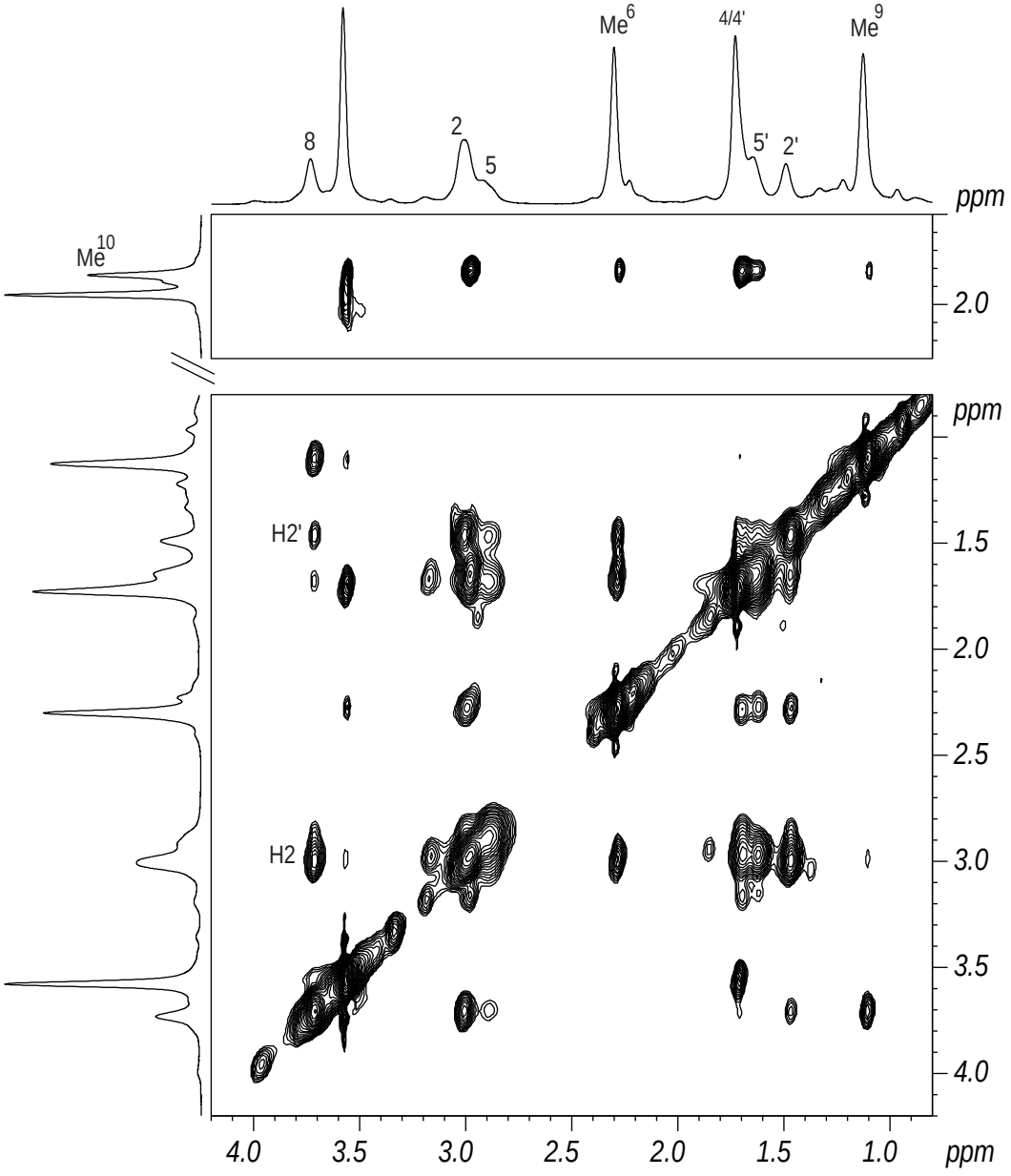
Me6
4/4'
Me9
8
2
5
5'
2'
ppm
Me10
2.0
ppm
H2'
1.5
2.0
2.5
H2
3.0
3.5
4.0
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

Figure 14S

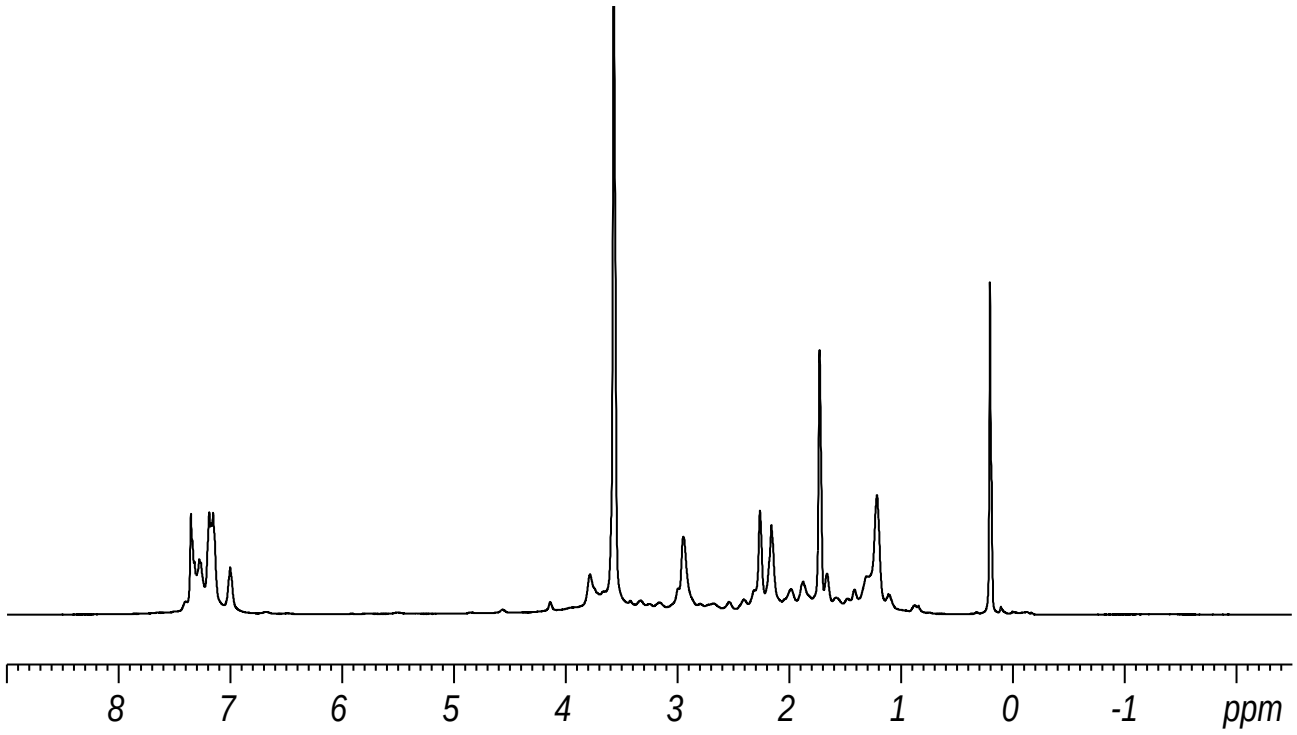

Figure 15S

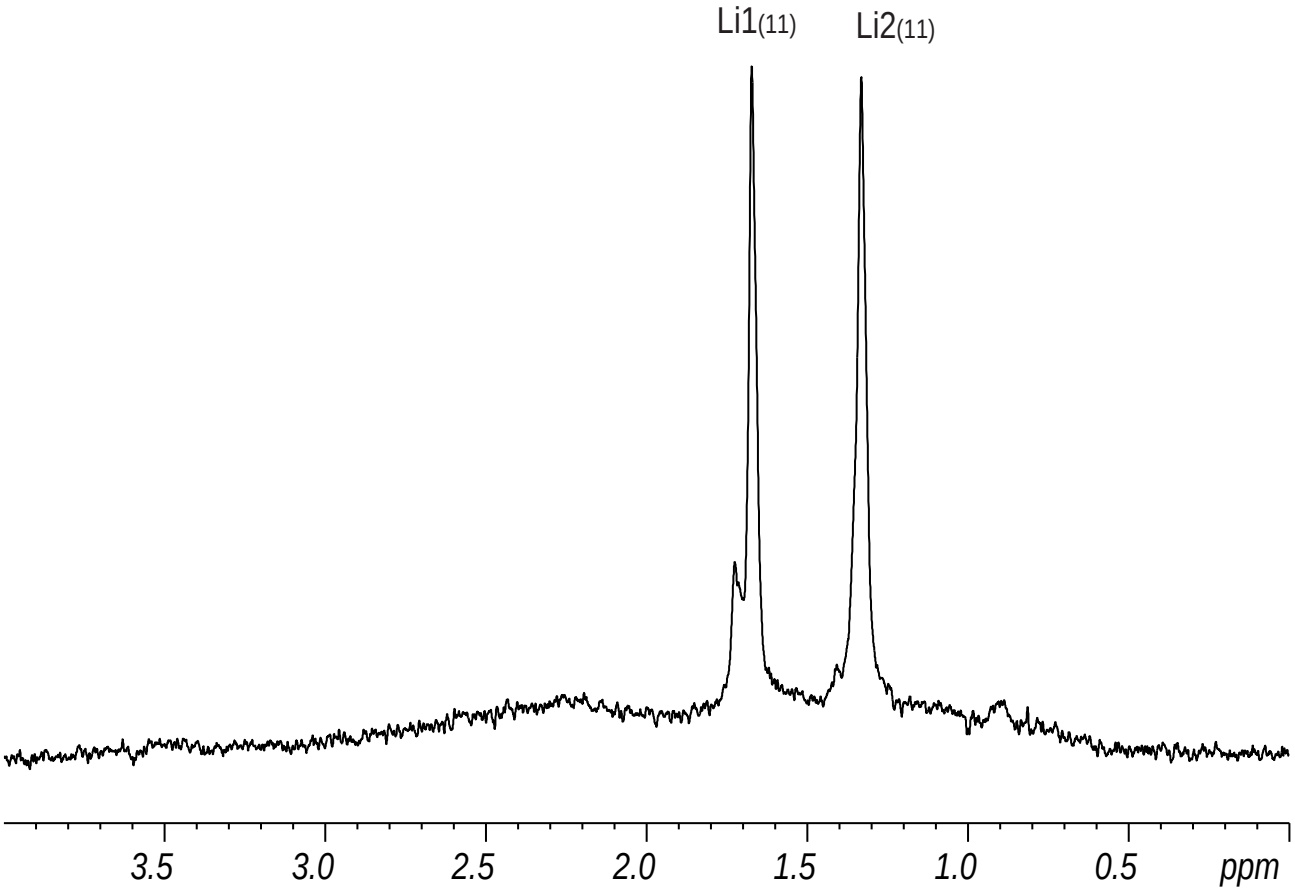

Figure 16S

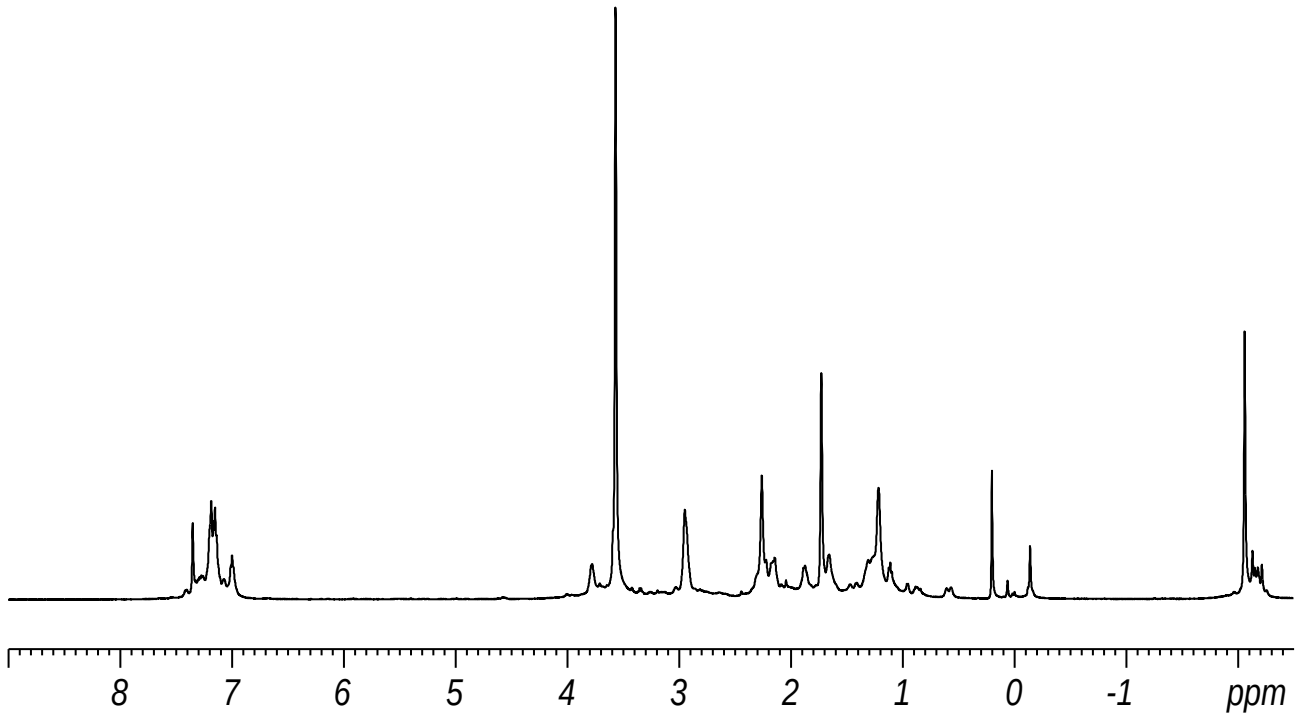

Figure 17S

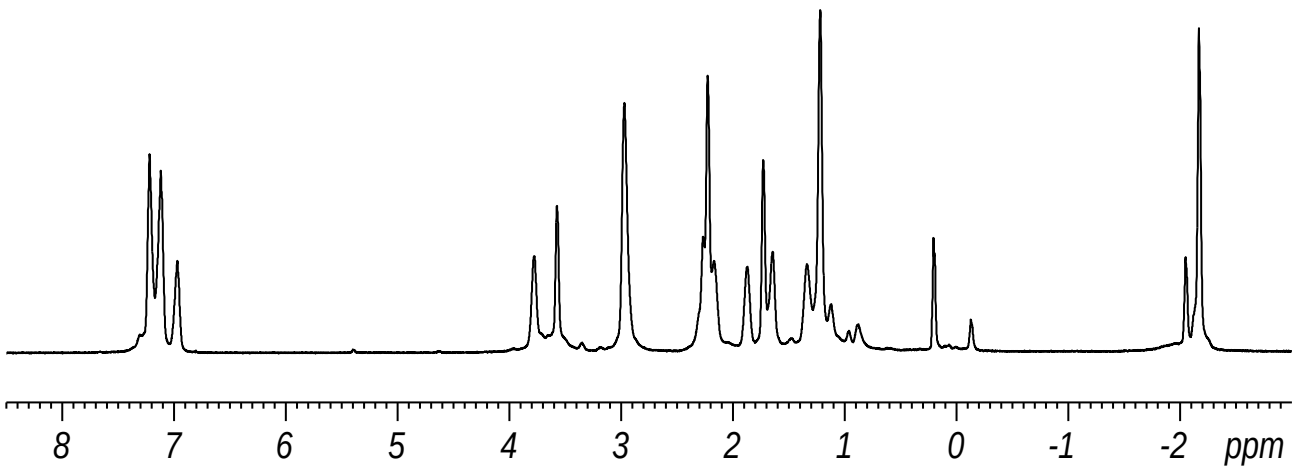

Figure 18S

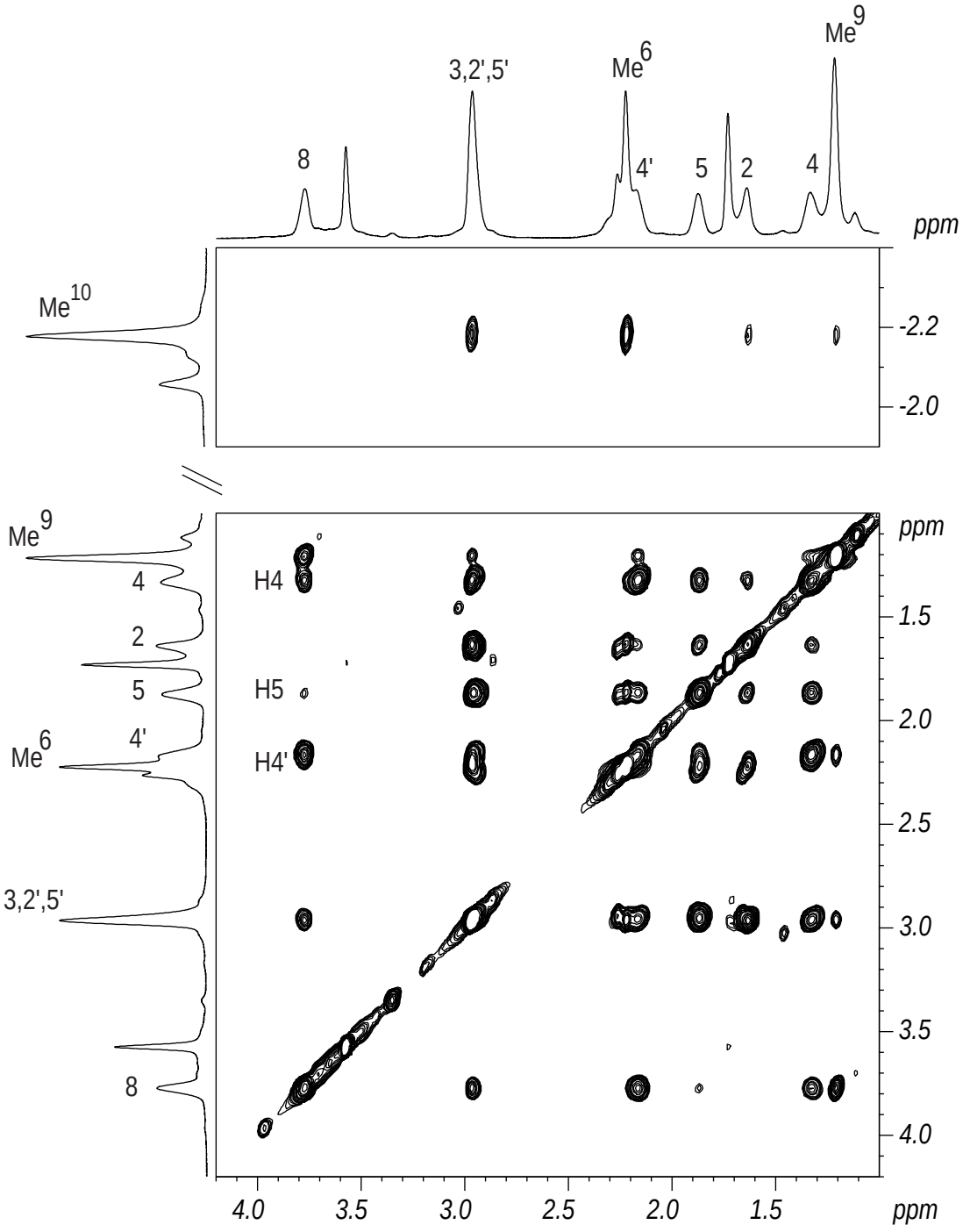
Me9
3,2',5'
Me6
8
4'
5
2
4
ppm
Me10
-2.2
-2.0
Me9
4
2
5
4'
Me6
3,2',5'
8
H4
H5
H4'
ppm
1.5
2.0
2.5
3.0
3.5
4.0
4.0
3.5
3.0
2.5
2.0
1.5
ppm

Figure 19S

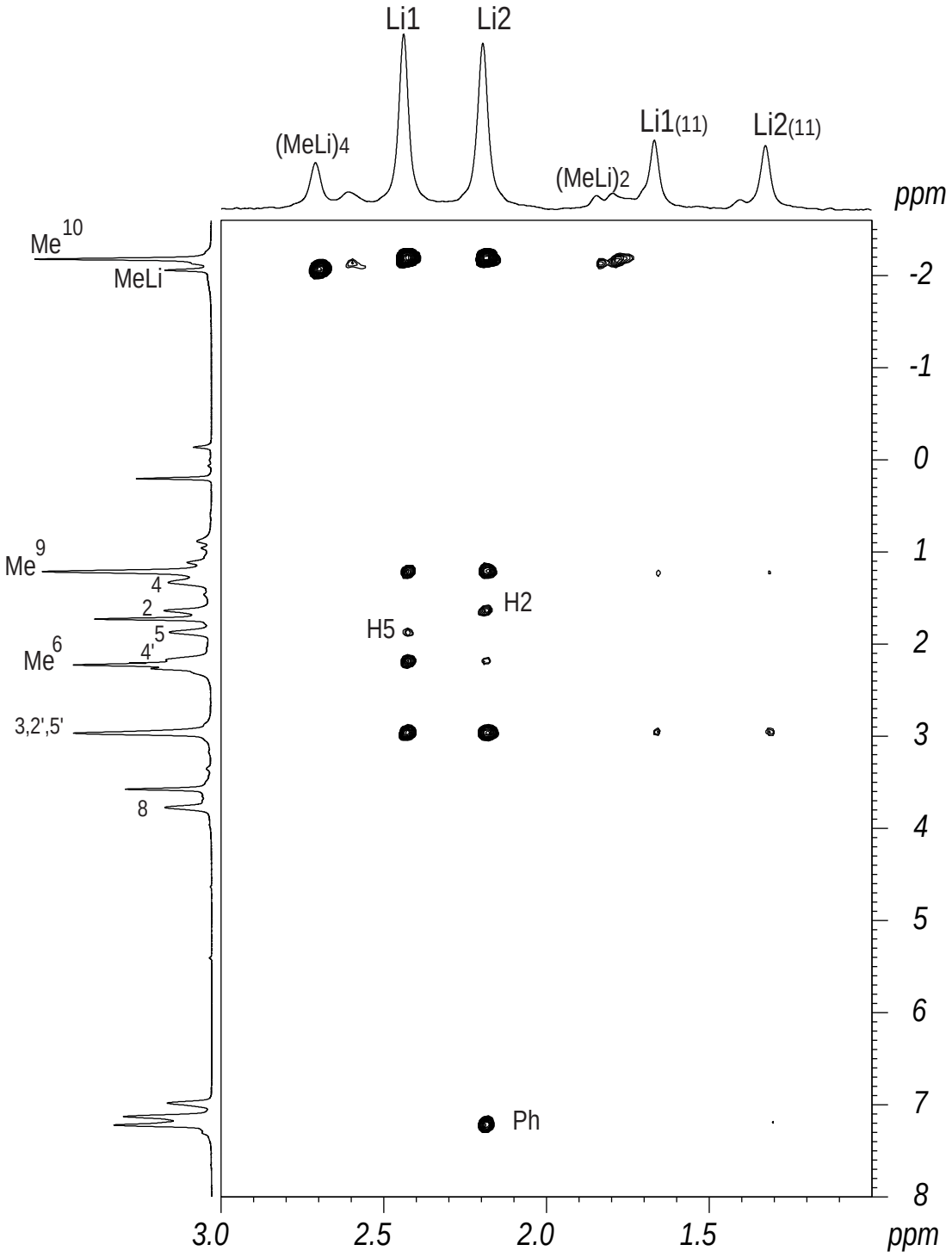
Li1
Li2
(MeLi)4
Li1(11)
Li2(11)
(MeLi)2
ppm
Me10
MeLi
Me9
4
2
5
4'
Me6
3,2',5'
8
H2
H5
Ph
-2
-1
0
1
2
3
4
5
6
7
8
3.0
2.5
2.0
1.5
ppm

Table 1S. Energy values (in a.u.) calculated for the «exo» and «endo» arrangements of complex **3e**. The energy differences are given in kcal/mol.

DFT	**Basis set**	**3e «endo»**	**3e «exo»**	$\mathbf{E_{endo} - E_{exo}}$
B3LYP	6-31G**	-671.3742	-671.3744	0.1
B3LYP	6-311G**	-671.5135	-671.5137	0.1
B3LYP	6-31++G**	-671.3923	-671.3924	0.1
B3P86	6-31G**	-673.6464	-673.6468	0.3
B3PW91	6-31G**	-671.1088	-671.1089	0.1