Supporting Information
for

Rational design of a cytotoxic dinuclear Cu_2 complex that binds by molecular recognition at two neighboring phosphates of the DNA backbone

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Figure S1. Thermal ellipsoid plot of **Cu**$_2$(OAc)$_2$ in crystals of **Cu**$_2$(OAc)$_2$·9.75H_2O·CH_3CN. Hydrogen atoms are omitted for clarity; thermal ellipsoids are drawn at the 50 % probability level.

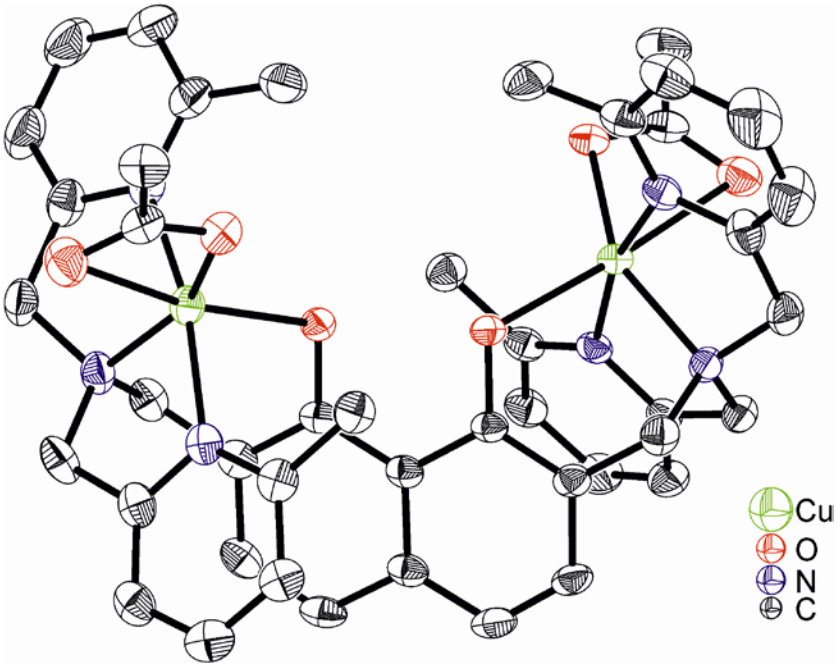


Figure S2. Analysis of plasmid DNA by agarose gel electrophoresis after incubation with **Cu$_2$**(OAc)$_2$. a) Quantification of the fraction of open-circular plasmid DNA. Plasmid DNA incubated with the indicated concentrations of **Cu$_2$**(OAc)$_2$ for 1 h at 37°C was separated by TBE agarose gel electrophoresis, stained with ethidium bromide and viewed under UV light. Note that the $CuCl_2$•$2H_2O$ concentrations were doubled to achieve equimolar copper concentrations. Digital pictures were quantified. Shown are means of four independent experiments, bars indicate standard deviation. **Cu$_2$**(OAc)$_2$ at 5 µM or above increased the open circular form significantly compared to $CuCl_2$•$2H_2O$ ($p<0.01$, unpaired student's t test) indicating that the plasmid DNA was cleaved with low frequency. b) Picture after agarose gel electrophoresis of plasmid DNA incubated with **Cu$_2$**(OAc)$_2$, $CuCl_2$•$2H_2O$ or MOM_2tom^{Me}. The aromatic dye bromphenol blue was present in the loading buffer to monitor the progress of the electrophoresis (arrow). Only in the presence of 100 - 500 µM **Cu$_2^{2+}$** bromphenol blue stayed in the loading pocket together with DNA and **Cu$_2^{2+}$**.

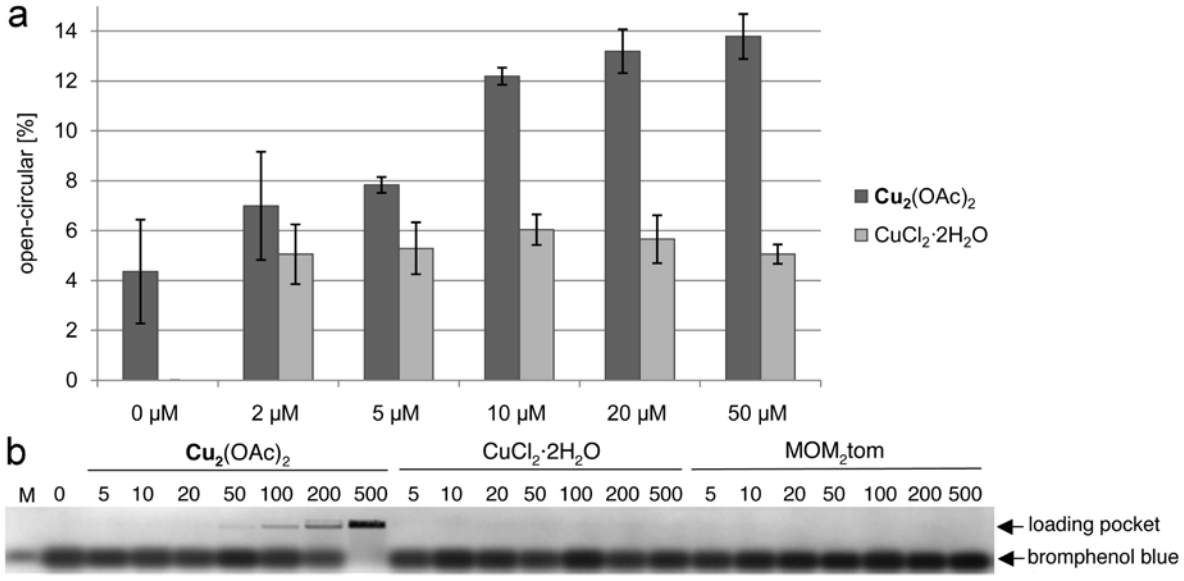
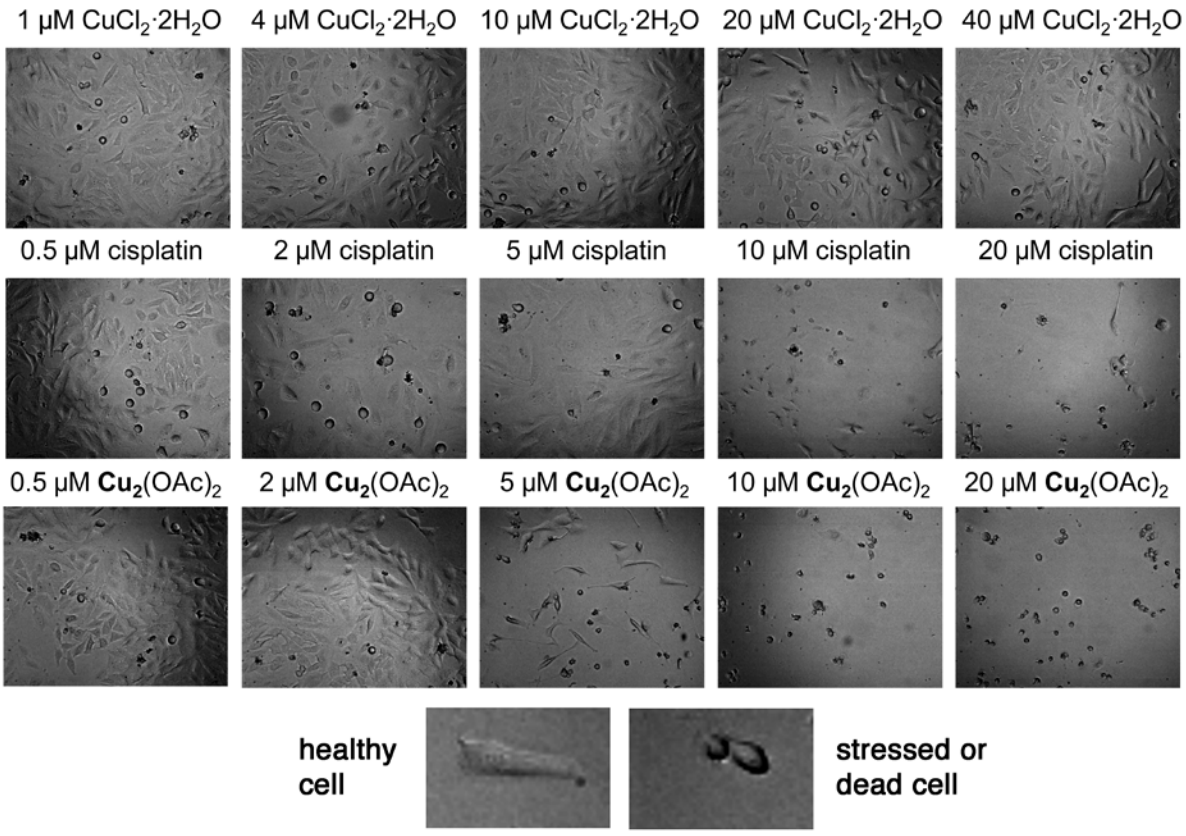


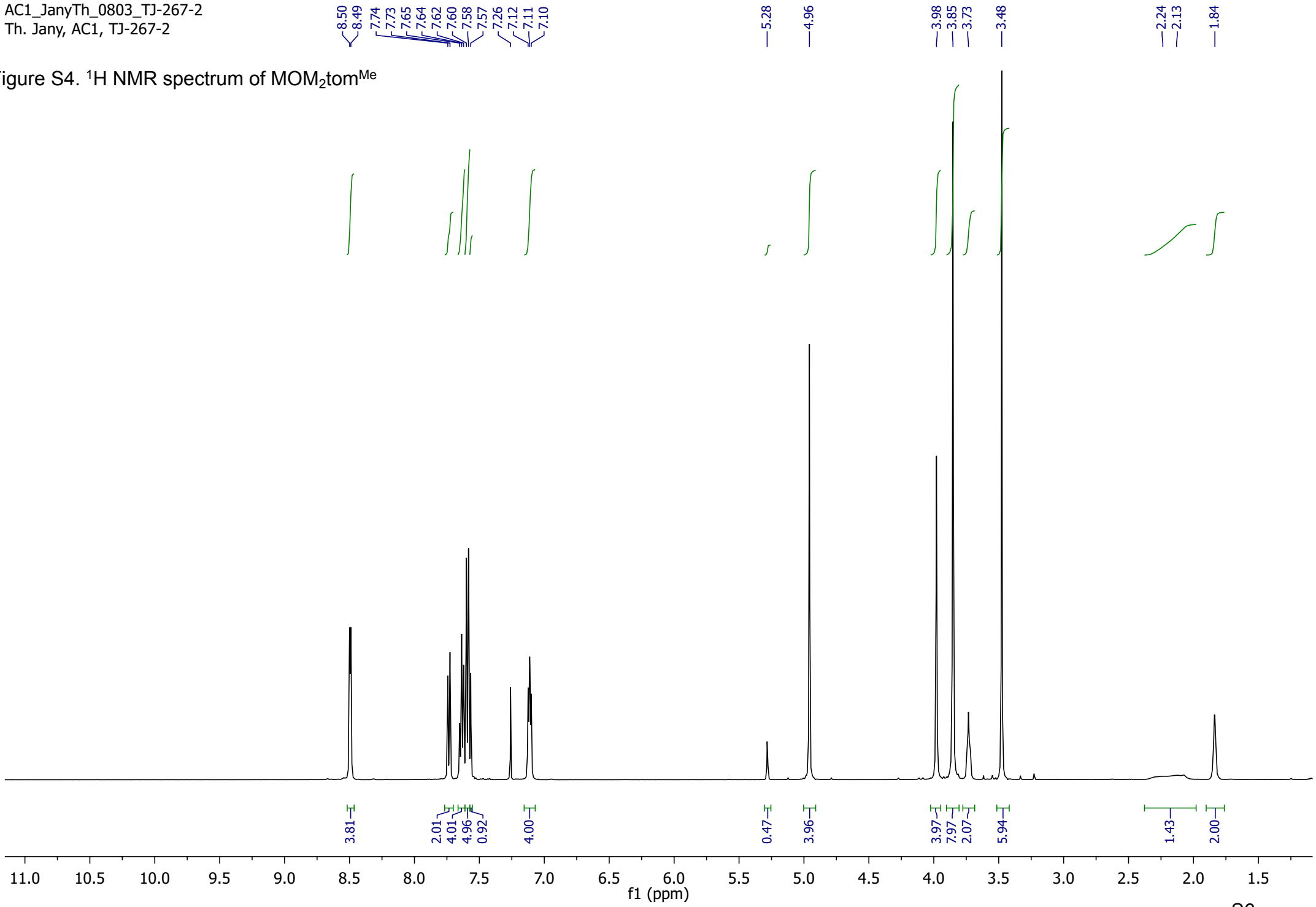
Figure S3. HeLa cells incubated with the indicated additions were analyzed by microscopy after 53 hours. Many healthy, outspread HeLa cells (see small picture) attached to the surface were visible in the presence of $CuCl_2$. Fewer healthy cells, more stressed, spherical cells and more cell debris was observed with increasing concentrations of **Cu**$_2$(OAc)$_2$ or cisplatin.



The following pages contain ^{1}H NMR, ^{13}C NMR, and 2D NMR spectra of MOM_2tom^{Me}.

AC1_JanyTh_0803_TJ-267-2
Th. Jany, AC1, TJ-267-2

Figure S4. ^{1}H NMR spectrum of MOM_2tom^{Me}



AC1_JanyTh_0803_TJ-267-2
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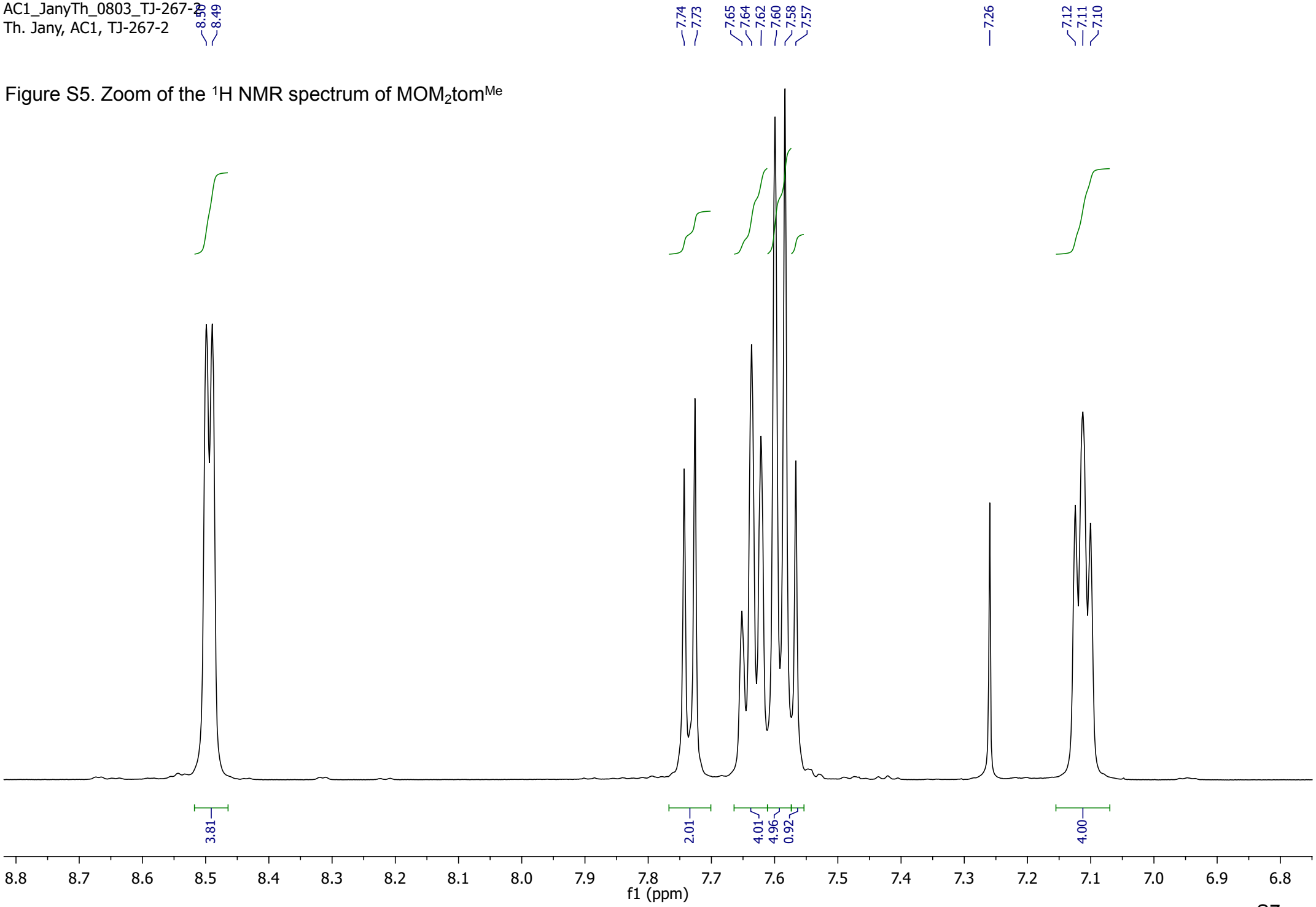
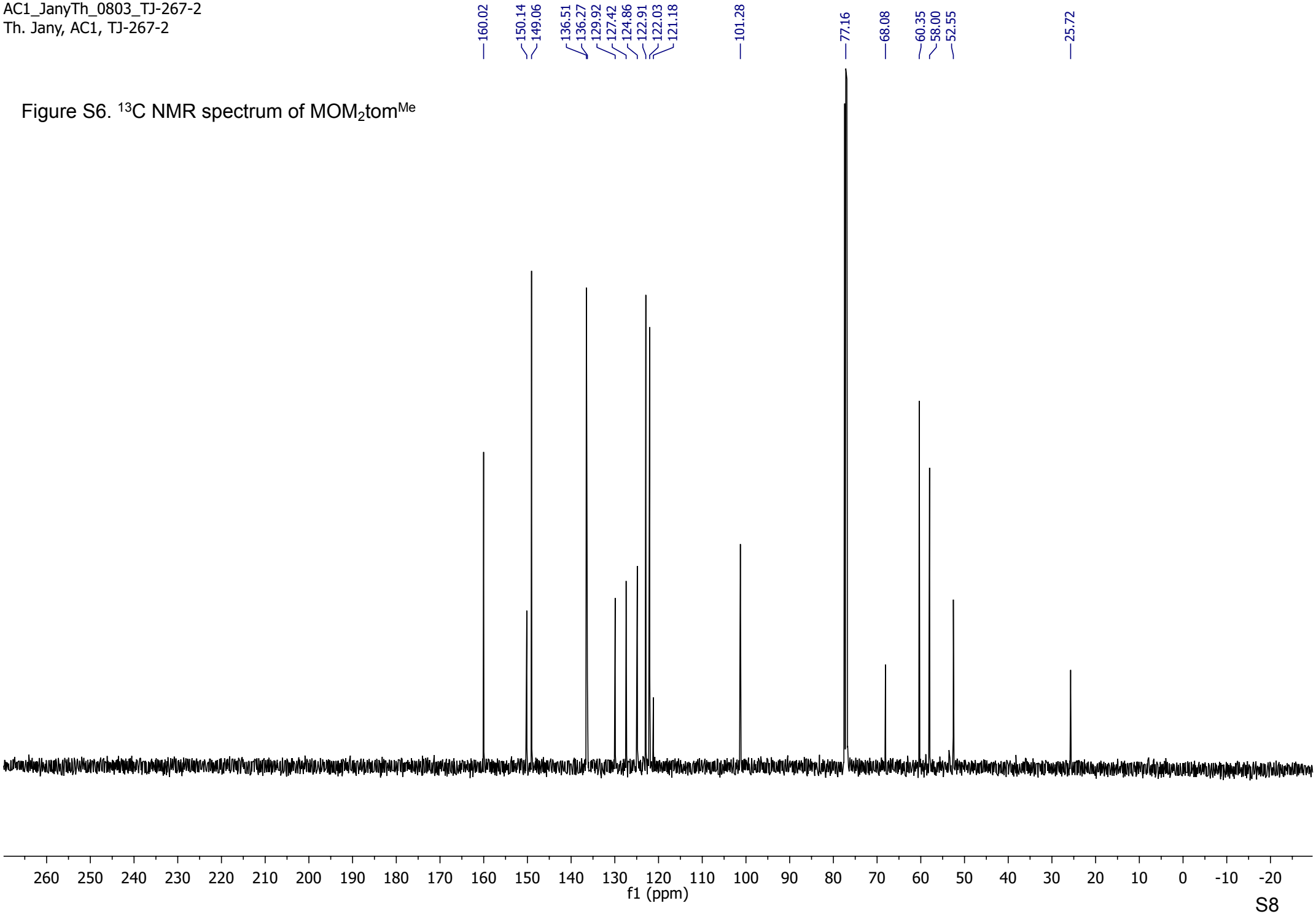
Figure S5. Zoom of the ^{1}H NMR spectrum of MOM_2tom^{Me}



AC1_JanyTh_0803_TJ-267-2
Th. Jany, AC1, TJ-267-2

Figure S6. ^{13}C NMR spectrum of MOM_2tom^{Me}



AC1_JanyTh_0803_TJ-267-2
Th. Jany, AC1, TJ-267-2

Figure S7. Zoom of the ^{13}C NMR spectrum of MOM_2tom^{Me}

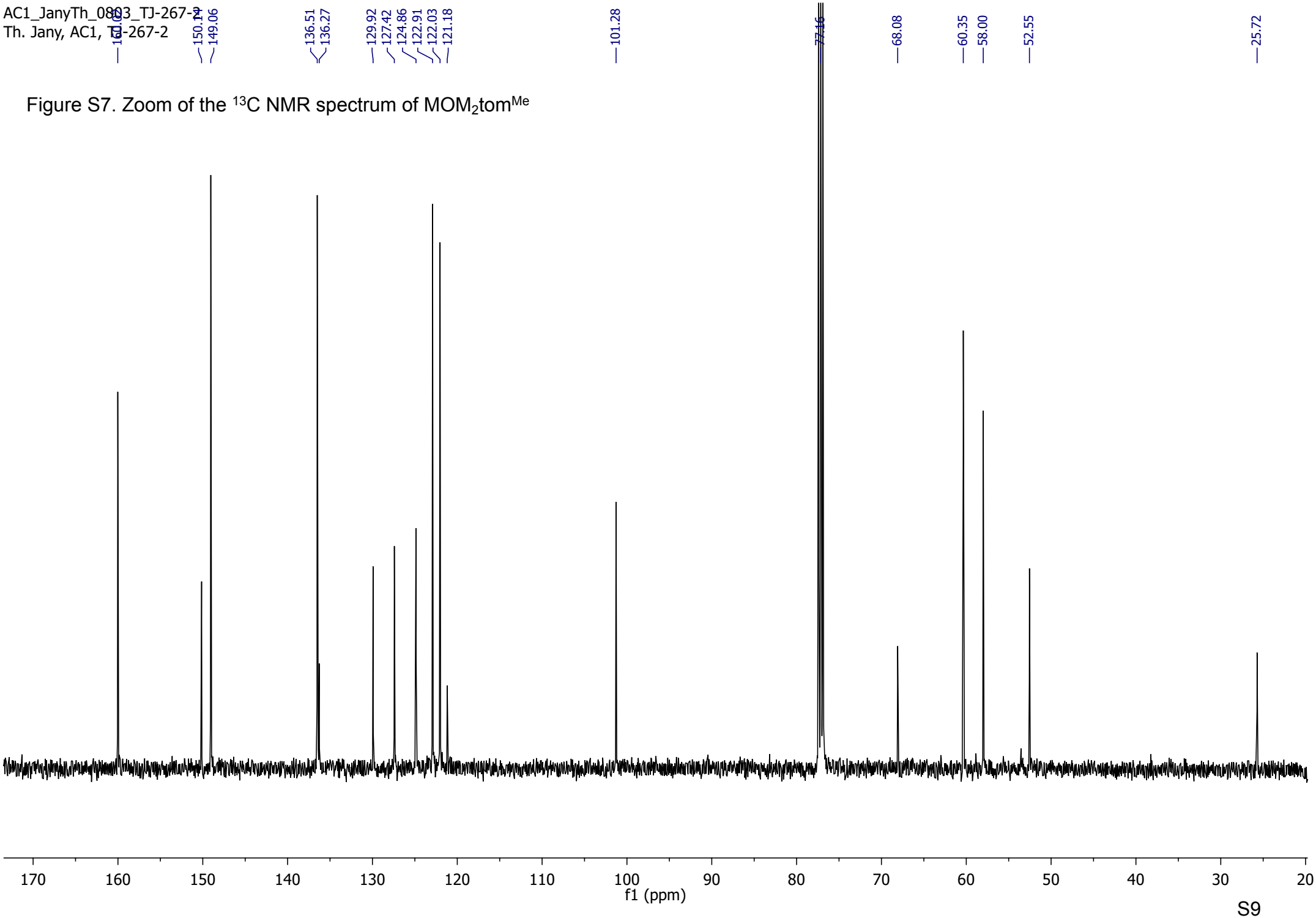


Figure S8. HMBC 2D NMR spectrum of MOM_2tom^{Me}

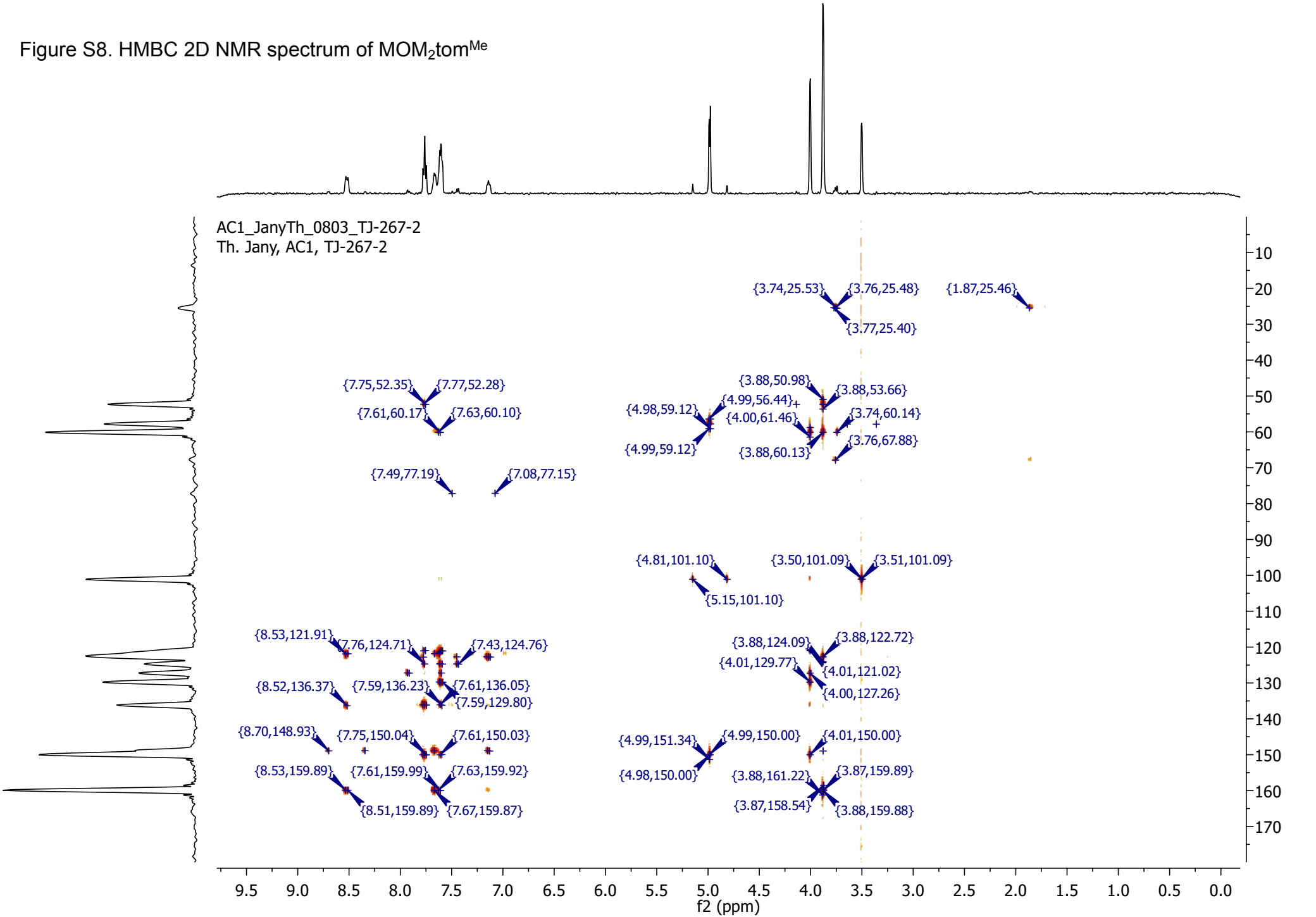


Figure S9. HMQC 2D NMR spectrum of MOM_2tom^{Me}