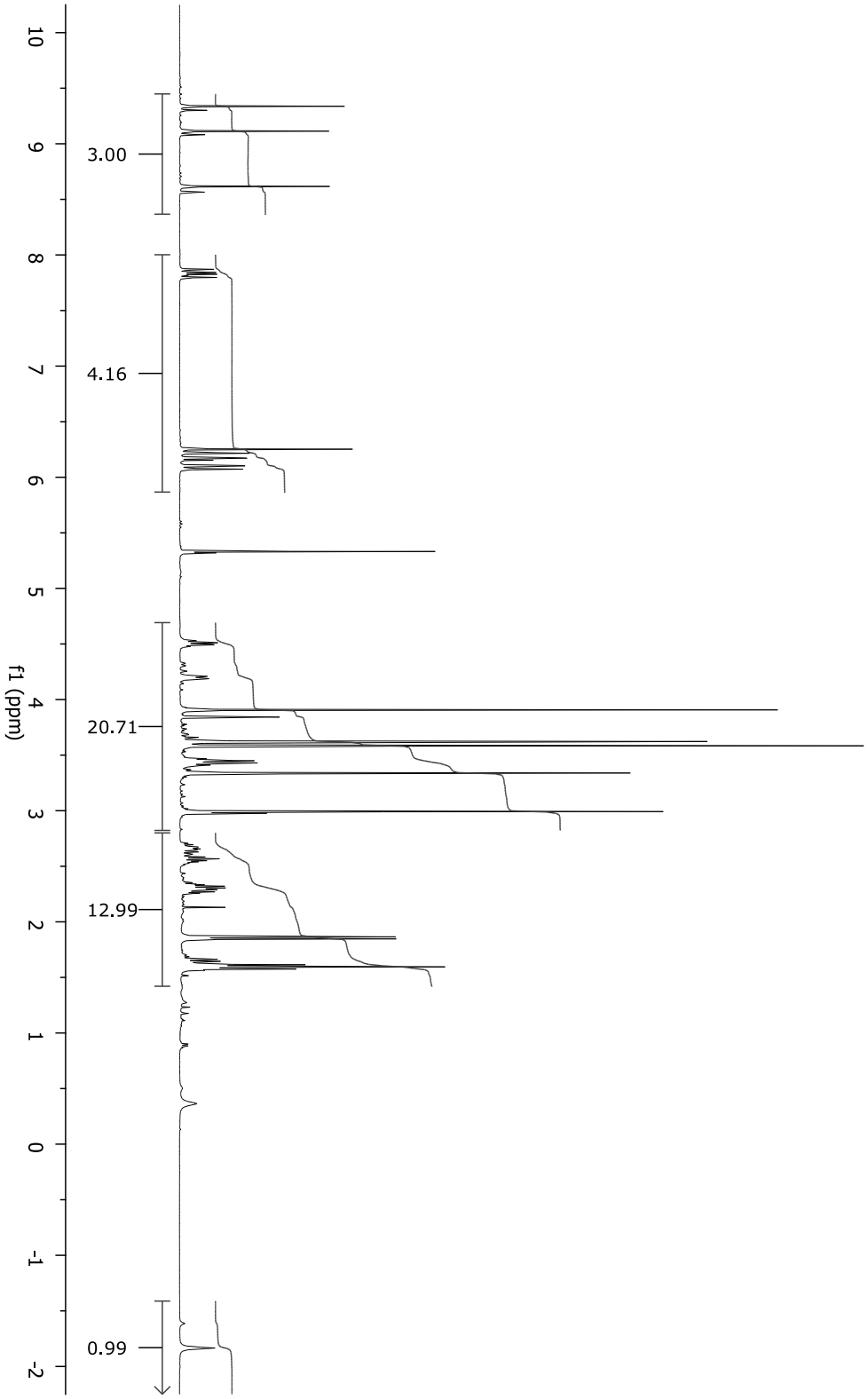
Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Syntheses and Cellular Investigations of Di(aspartate) and Aspartate-lysine Chlorin e_6 Conjugates

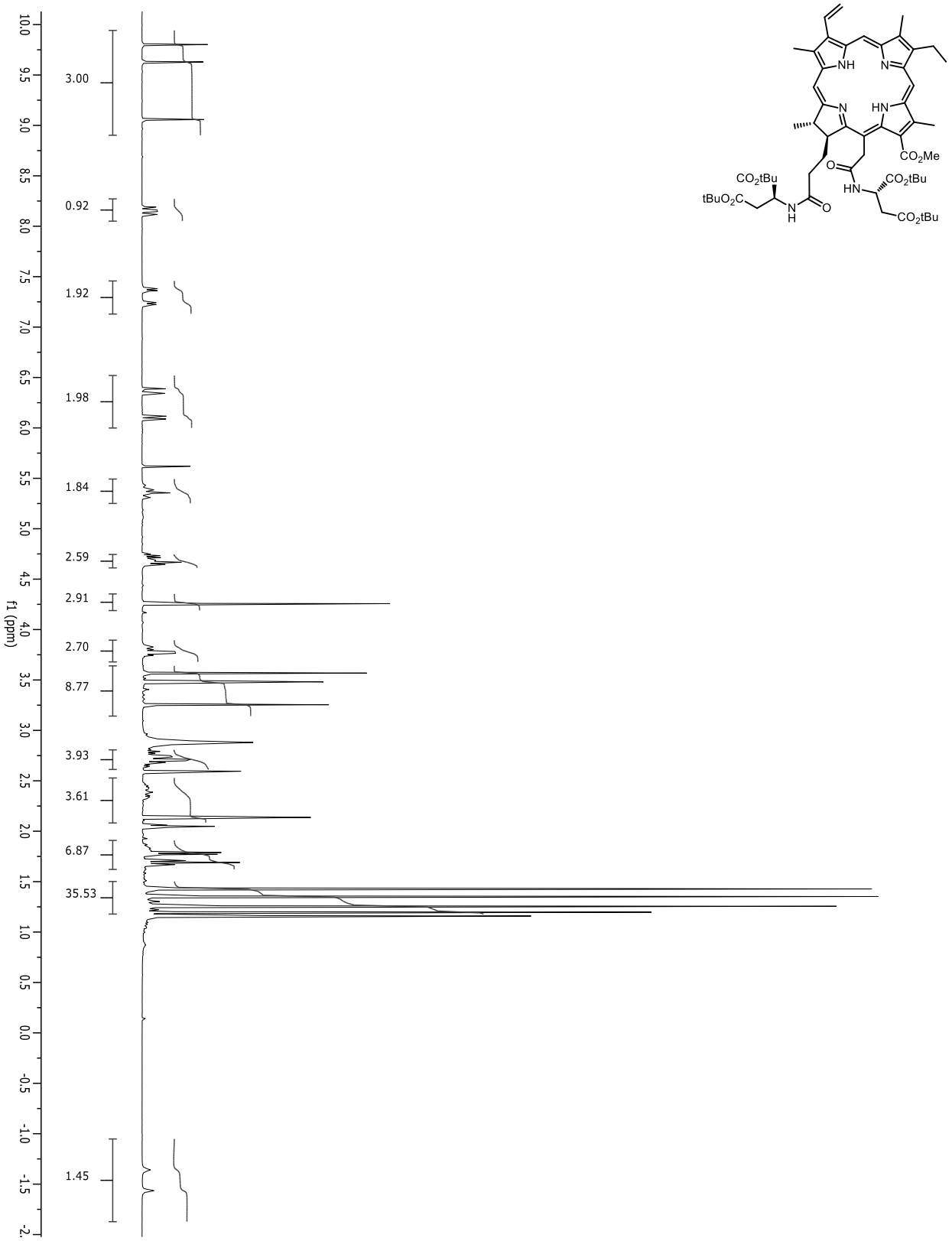
R. G. Waruna Jinadasa, Zehua Zhou, M. Graça H. Vicente and Kevin M. Smith*

ELECTRONIC SUPPLEMENTARY INFORMATION

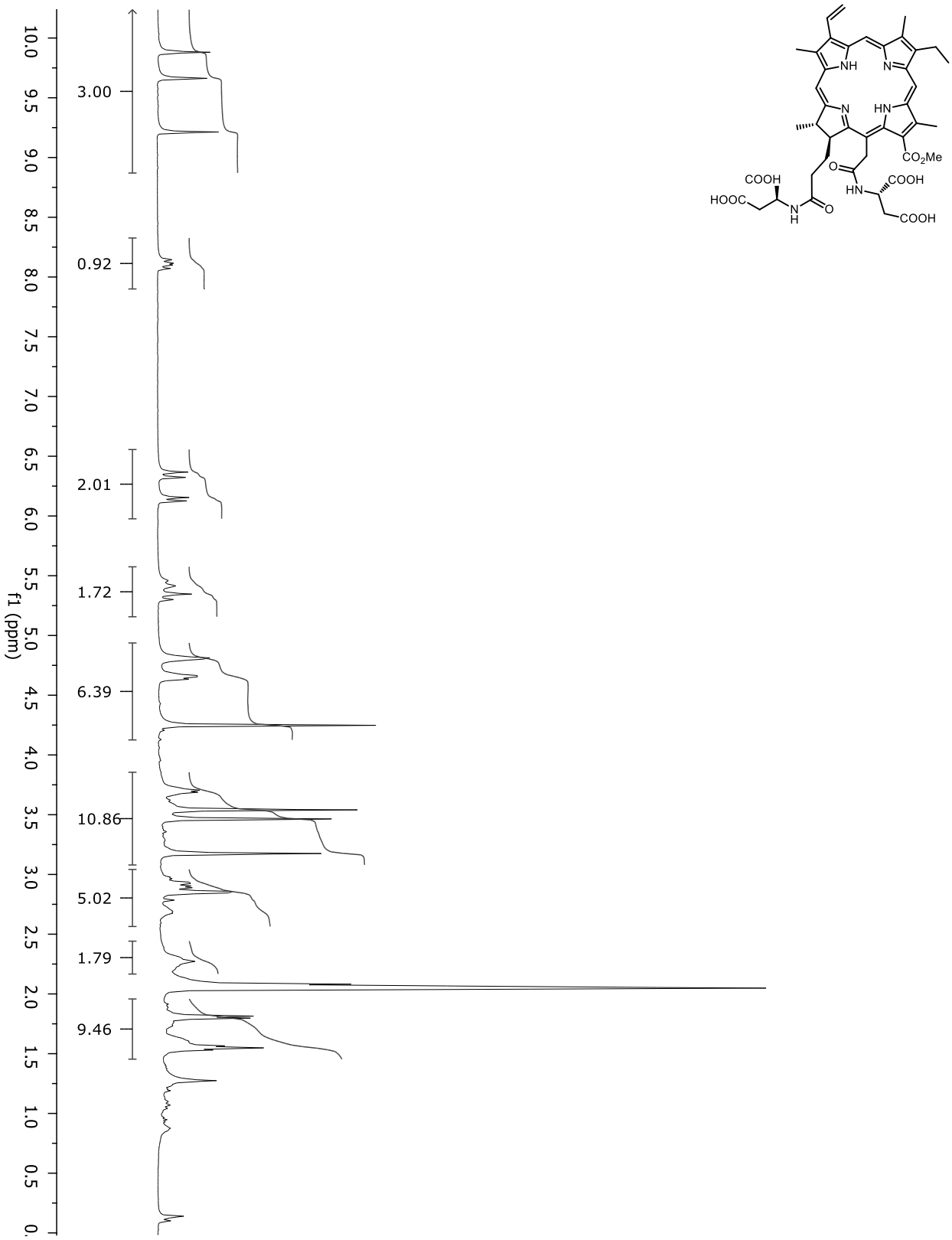
^{1}H NMR spectrum of methyl pheophorbide *a* (**21**) in acetone-d_6 at 400 MHz



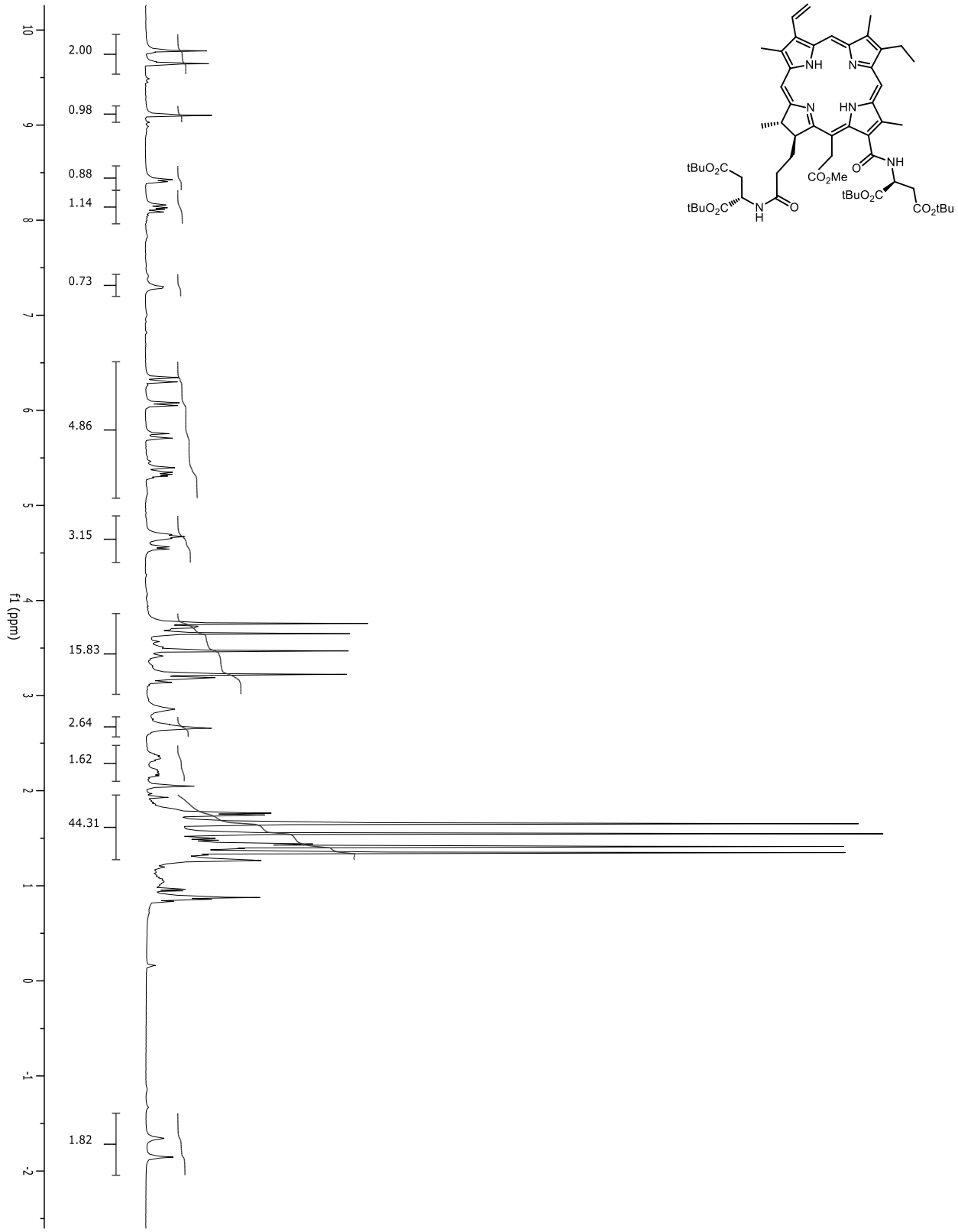
^{1}H NMR spectrum of 15^{2},17^{3}-di(Asp)Ce$_{6}$ *tert*-butyl methyl ester (**11**) in acetone-d_6 at 400 MHz



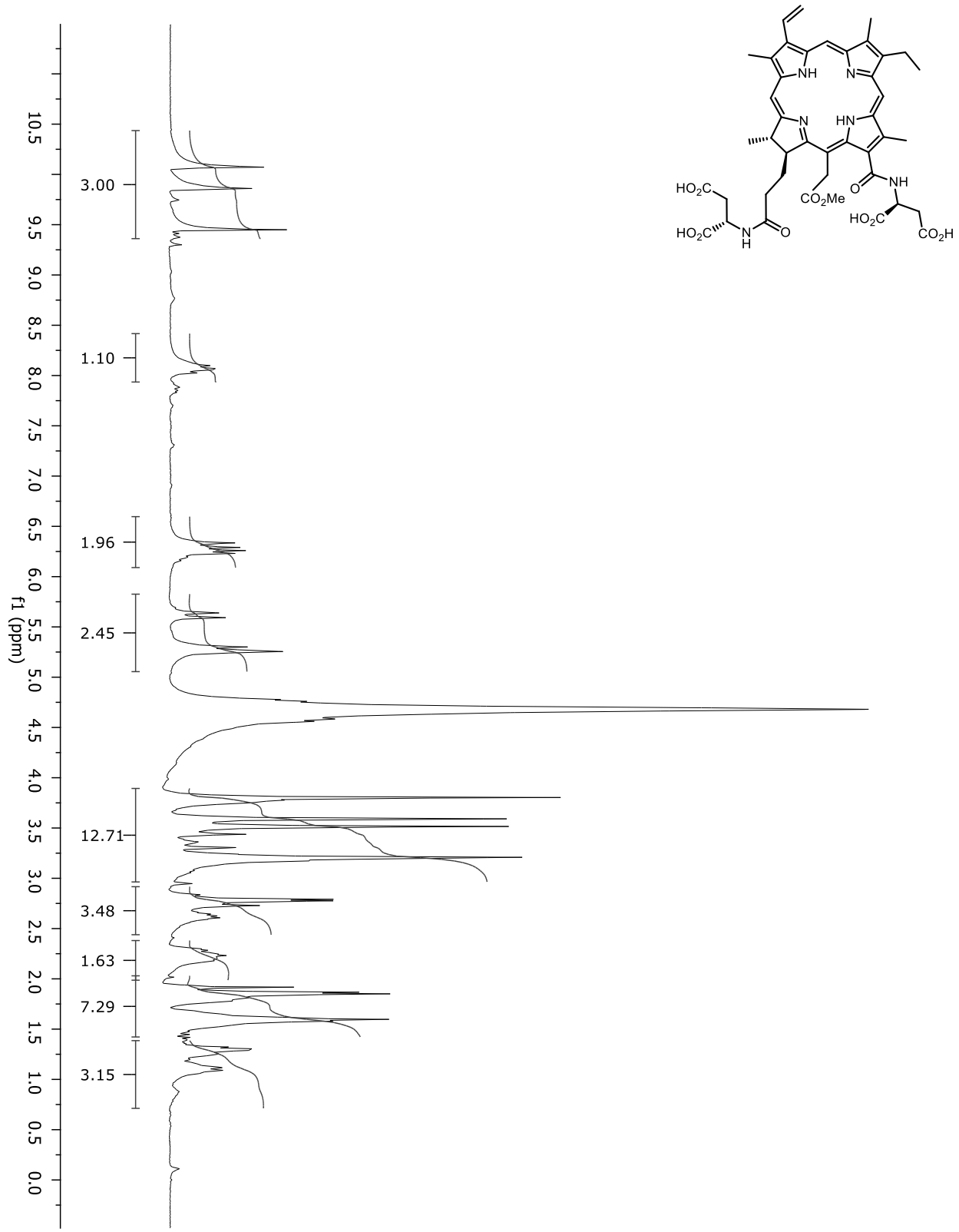
^{1}H NMR spectrum of 15^{2},17^{3}-di(Asp)Ce$_{6}$ methyl ester (**12**) in acetone-d_{6} at 400 MHz



^{1}H NMR spectrum of 13^{1},17^{3}-di(Asp)Ce$_{6}$ *tert*-butyl methyl ester (**20**) in acetone-d_6 at 400 MHz

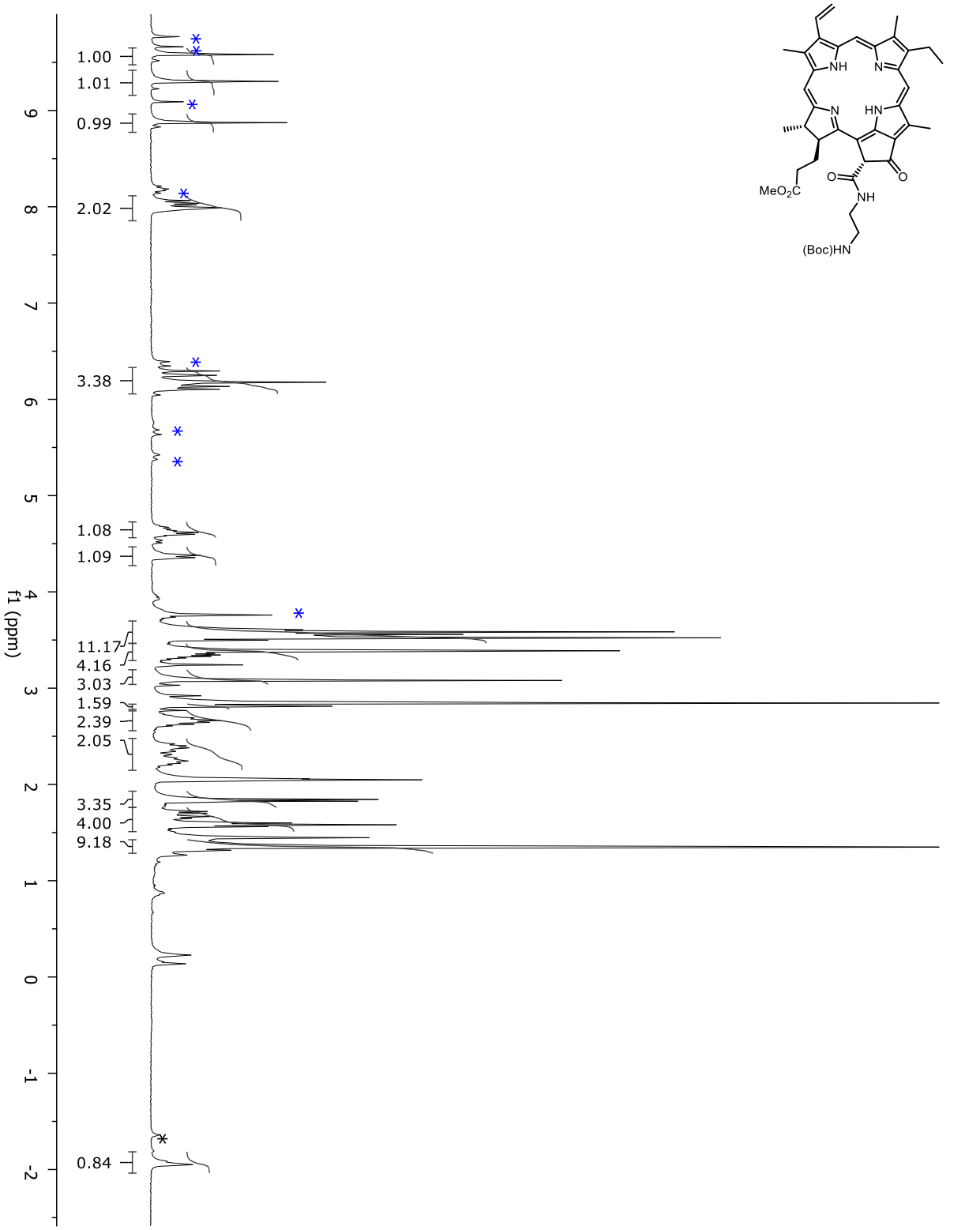


^{1}H NMR spectrum of 13^{1},17^{3}-diaspartylchlorin e$_{6}$ methyl ester (**13**) in MeOD at 400 MHz

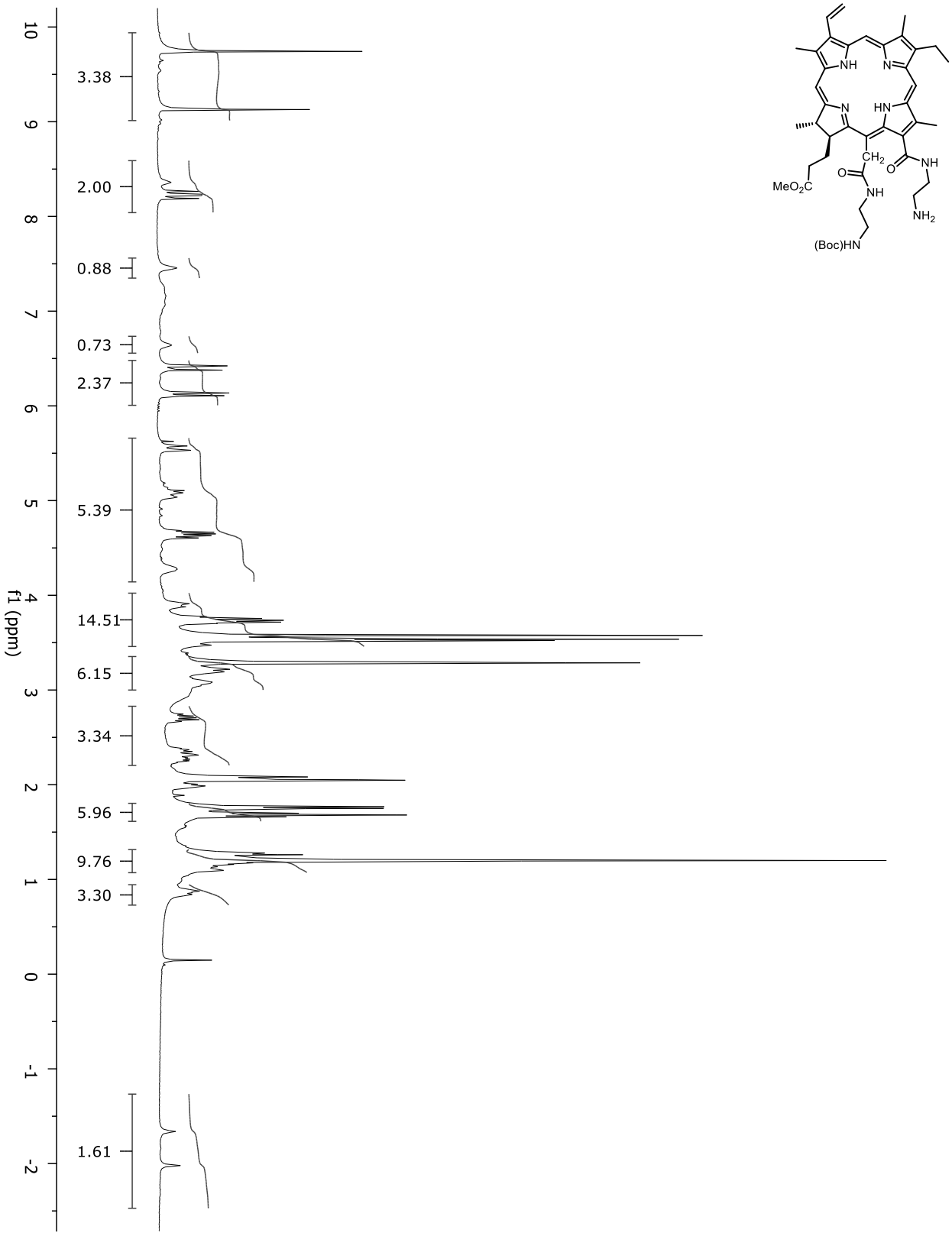


[1]H NMR spectrum of ethylenediaminyl(boc) pheophorbide a (**25**) in acetone-d_6 at 400 MHz

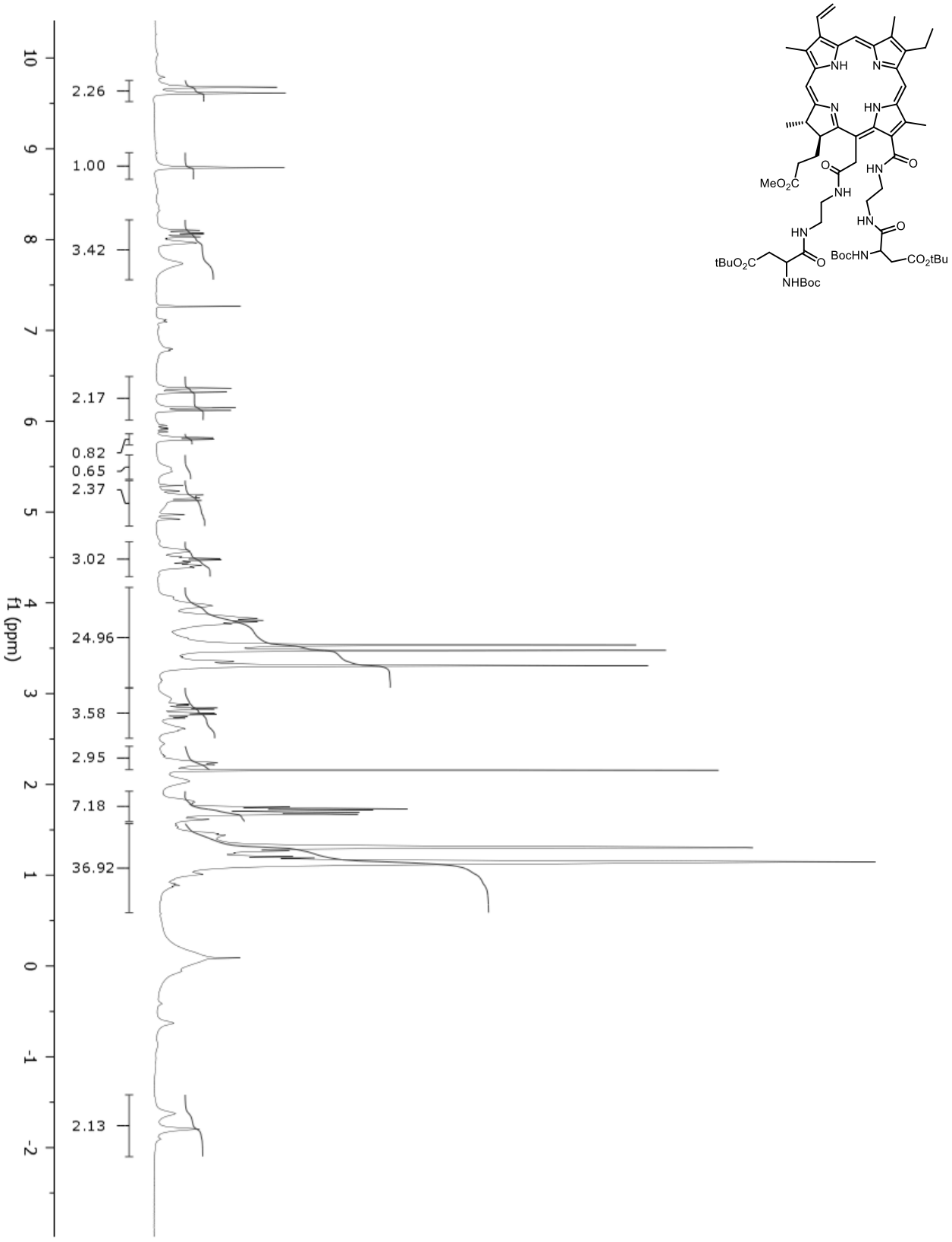
*Contain 10% isocyclic ring opened product **24**



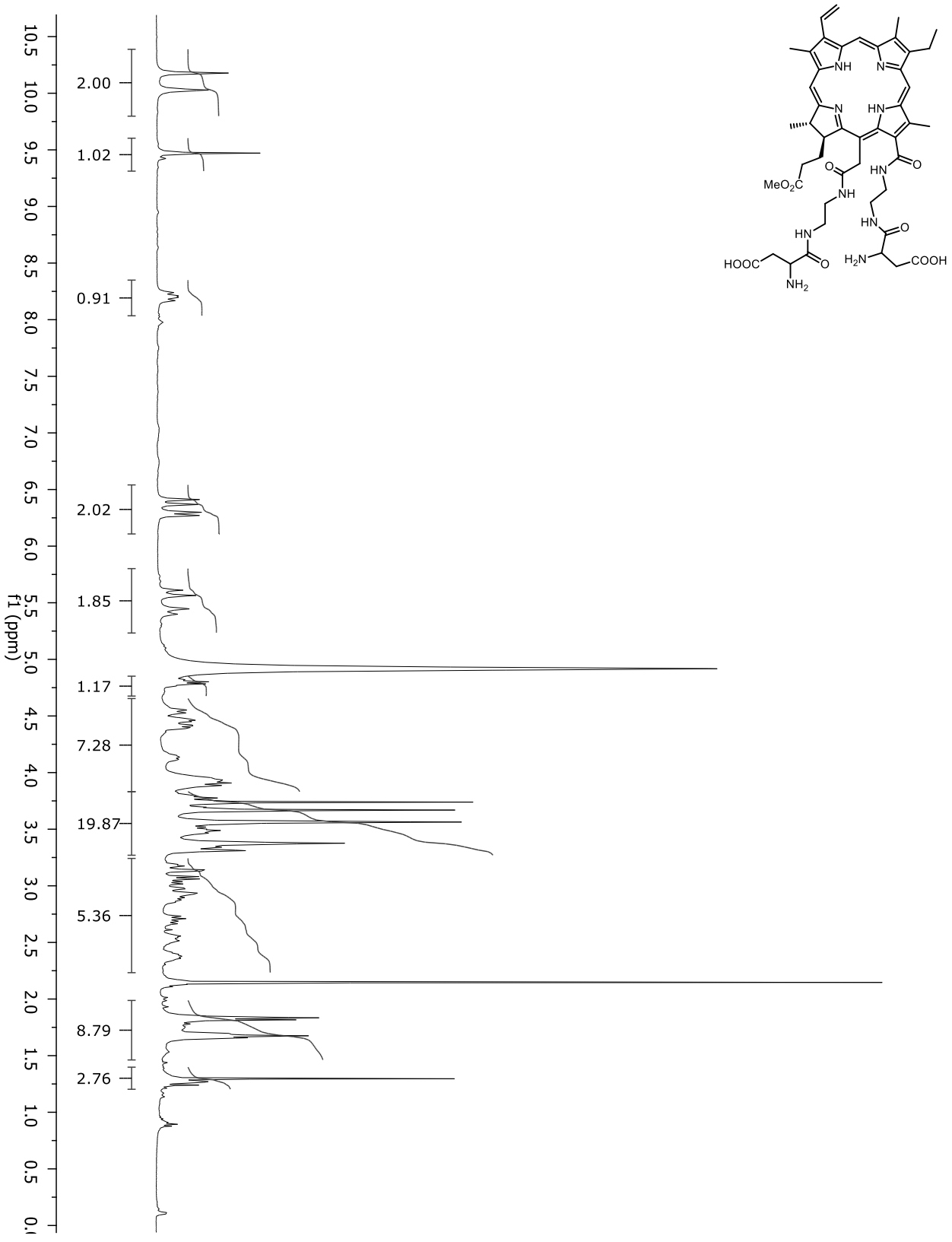
^{1}H NMR spectrum of 13^{1}-ED 15^{2}-ED(boc)Ce$_6$ methyl ester (**26**) in acetone-d_6 at 400 MHz



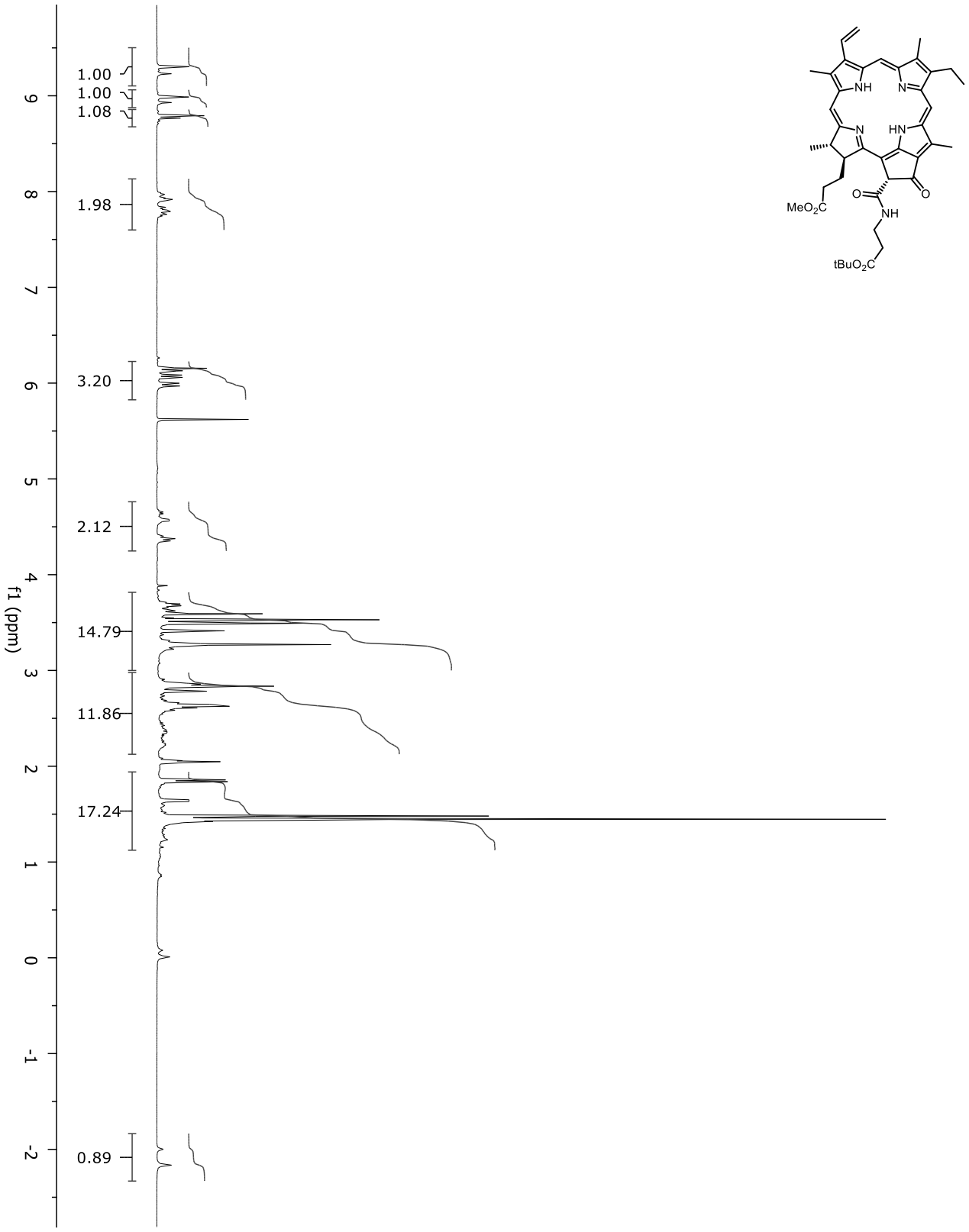
^{1}H NMR spectrum of 13^{1},15^{2}-ED-AspCe$_{6}$ *tert*-butyl boc methyl ester (**28**) in chloroform-*d* at 400 MHz



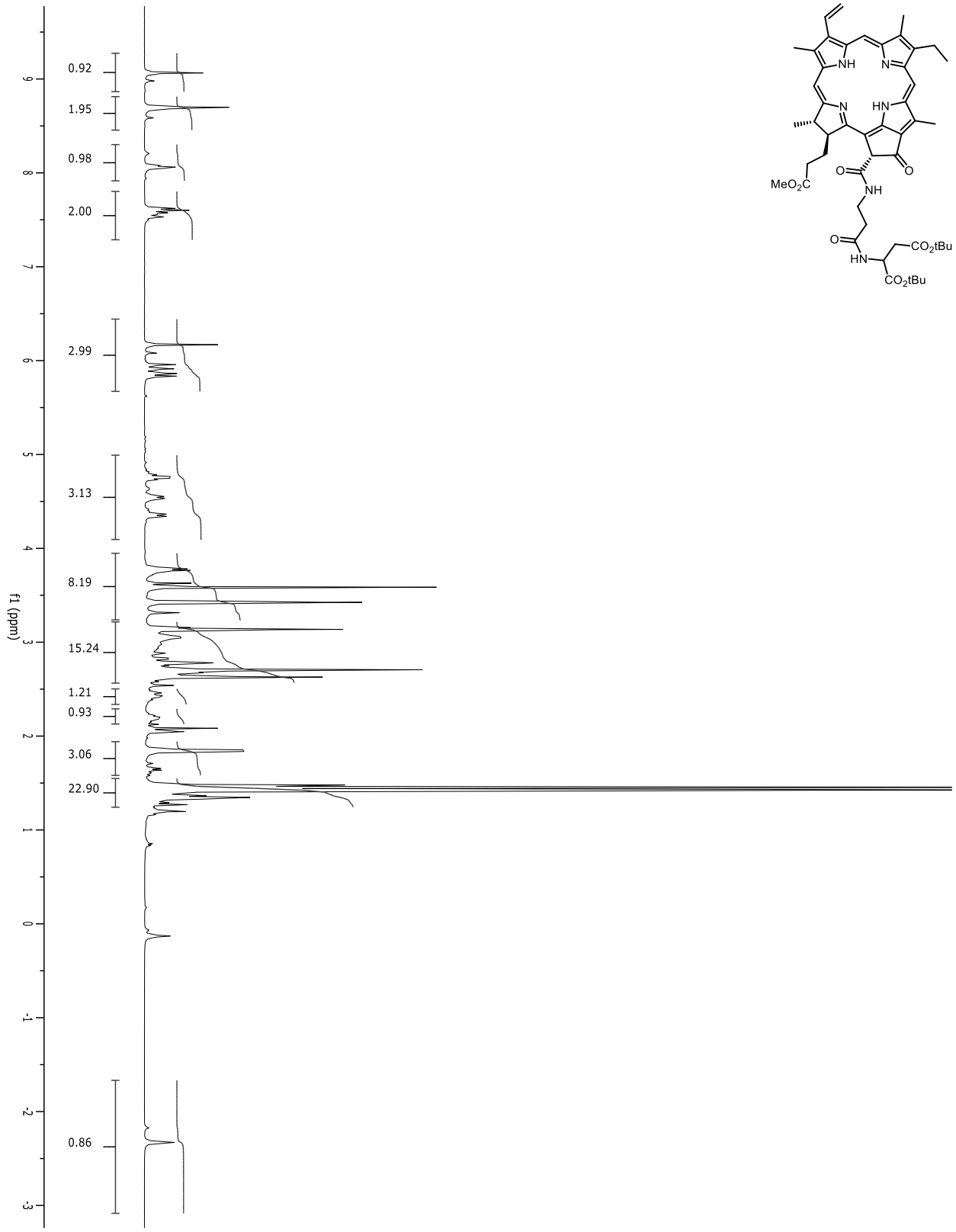
^{1}H NMR spectrum of 13^{1},15^{2}-ED-AspCe$_6$ methyl ester (**29**) in methanol-d_4 at 400 MHz



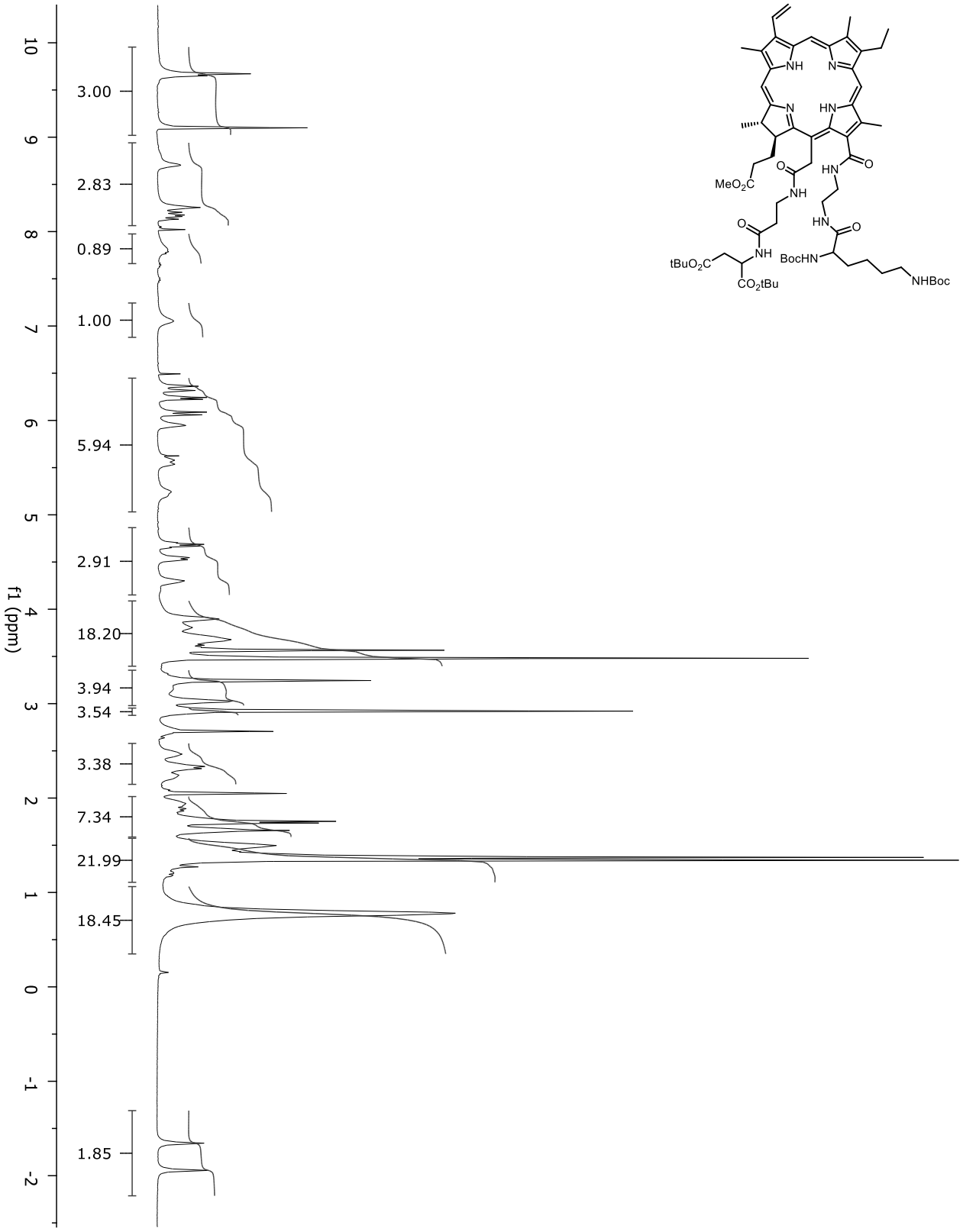
^{1}H NMR spectrum of β-alanylpheoporbide *tert*-butyl methyl ester (**30**) in acetone-d_6 at 400 MHz



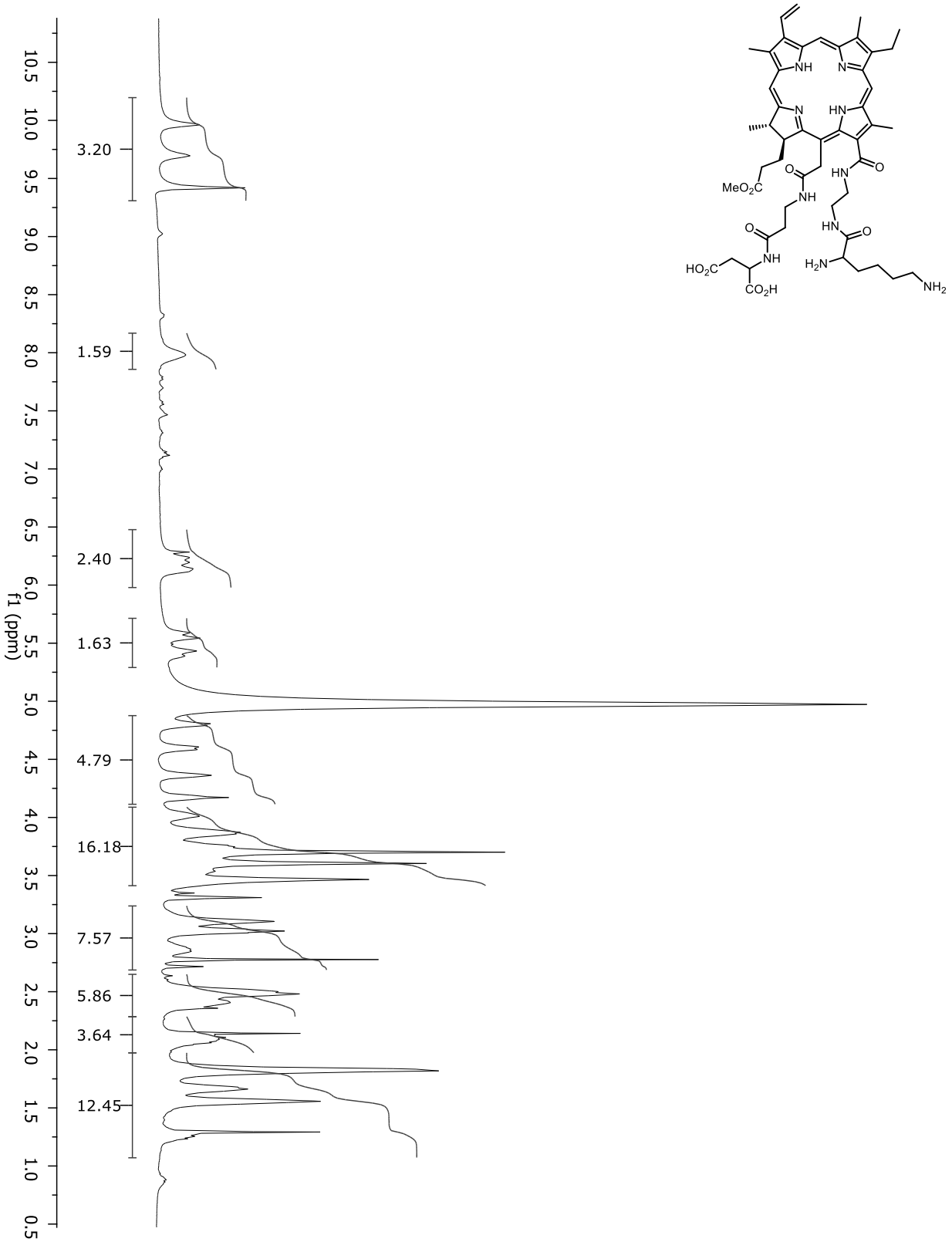
^{1}H NMR spectrum of β-alanylaspartylpheoporbide di-*tert*butyl methyl ester **32** in acetone-d_6 at 400 MHz



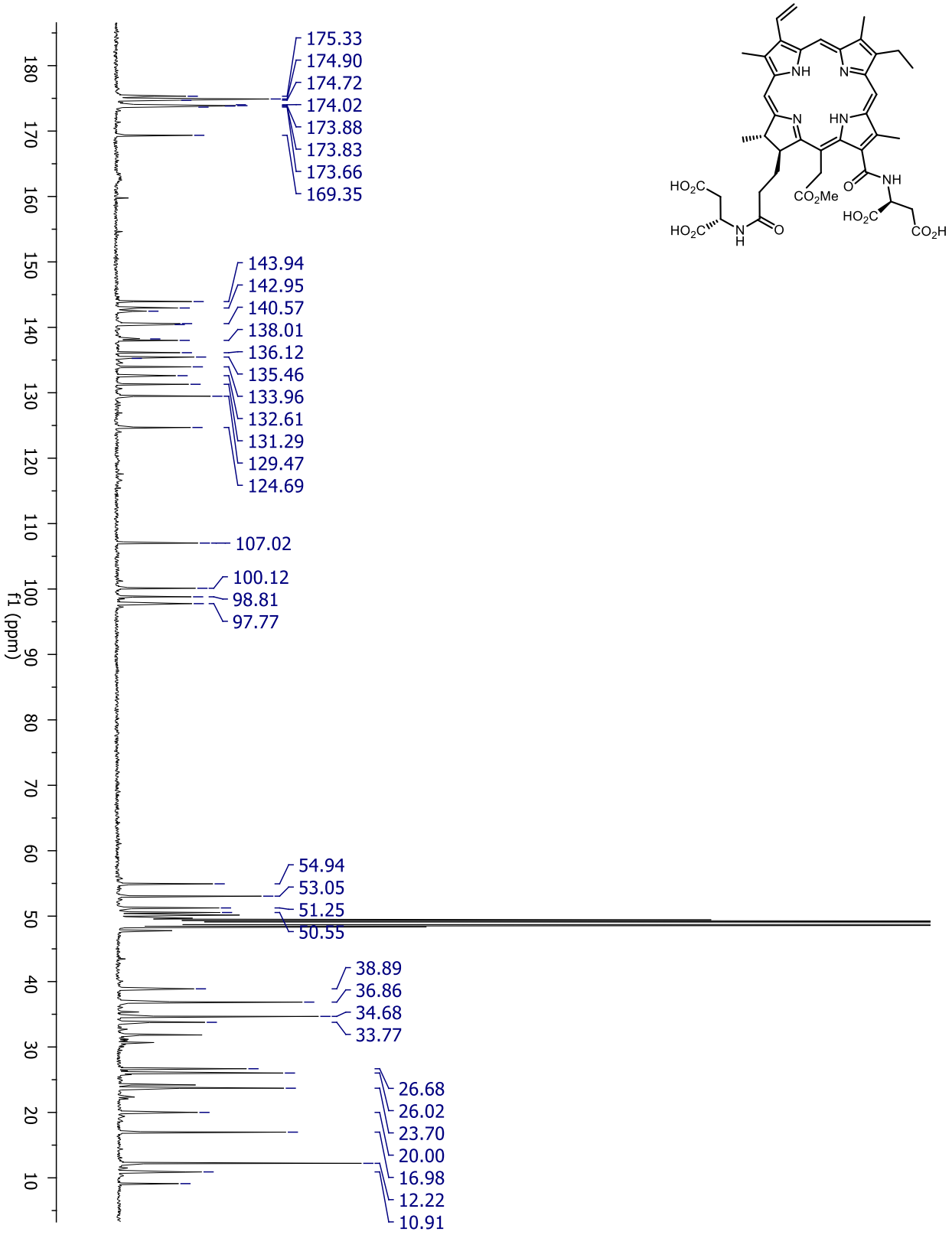
^{1}H NMR spectrum of 13^{2}-EDLys-15^{2}-β-AlaAspCe$_{6}$ *tert*-butyl boc methyl ester in acetone-d_6 at 400 MHz



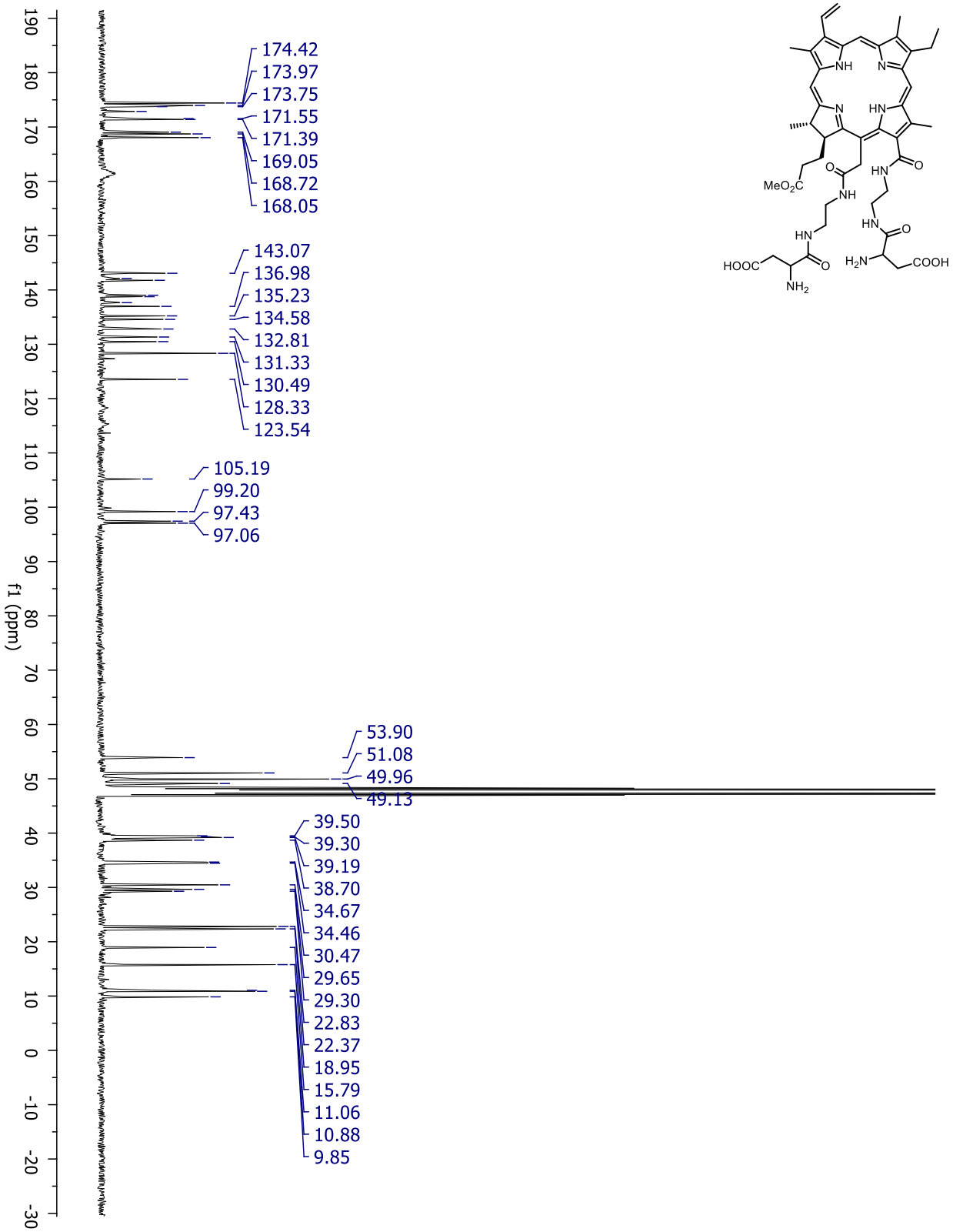
^{1}H NMR spectrum of 13^{2}-EDLys-15^{2}-β-AlaAspCe$_{6}$ methyl ester (**34**) in acetone-d_6 at 400 MHz



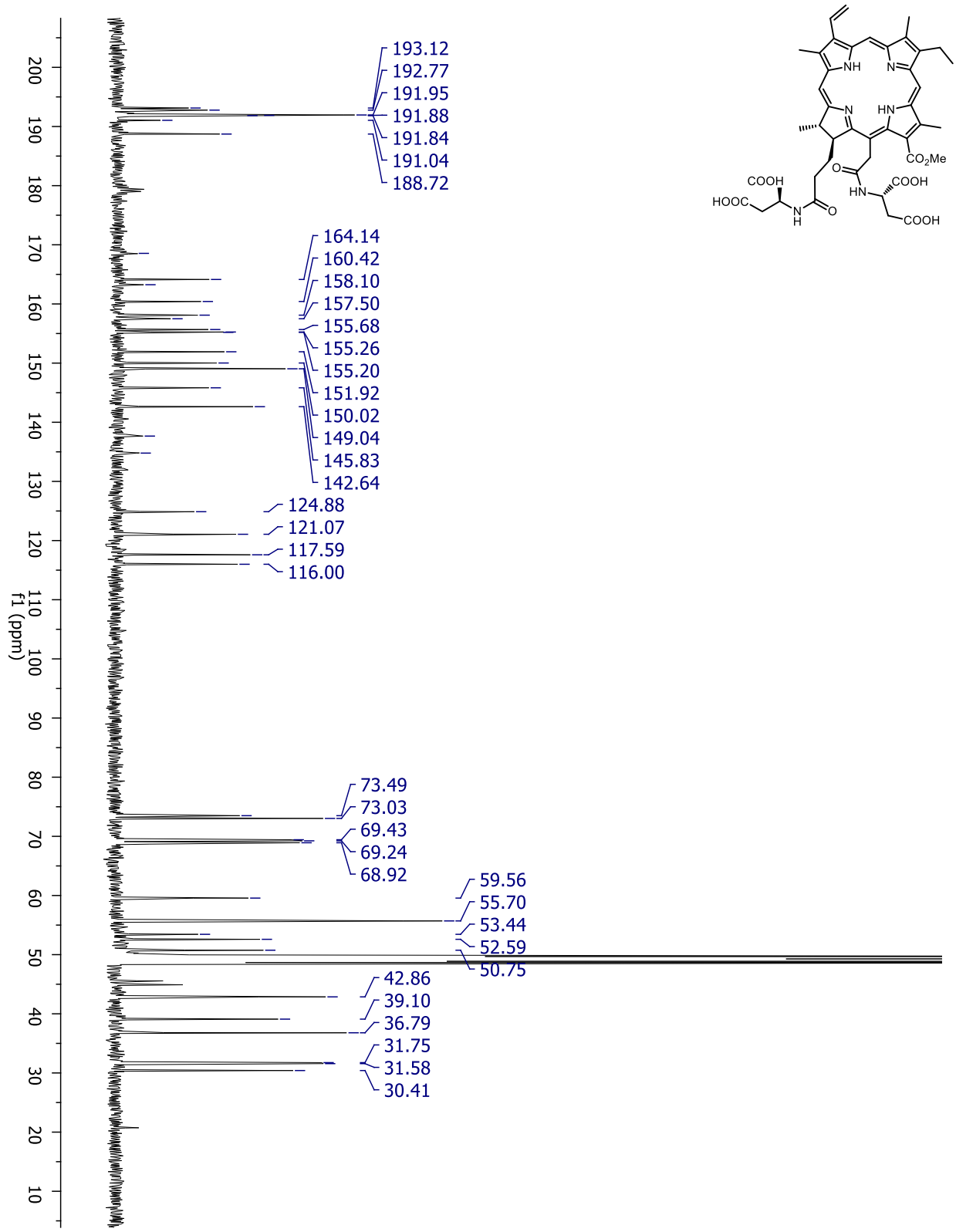
^{1}H NMR spectrum of 13^{1},17^{3}-diaspartylchlorin e$_{6}$ methyl ester (**13**) in MeOD at 400 MHz



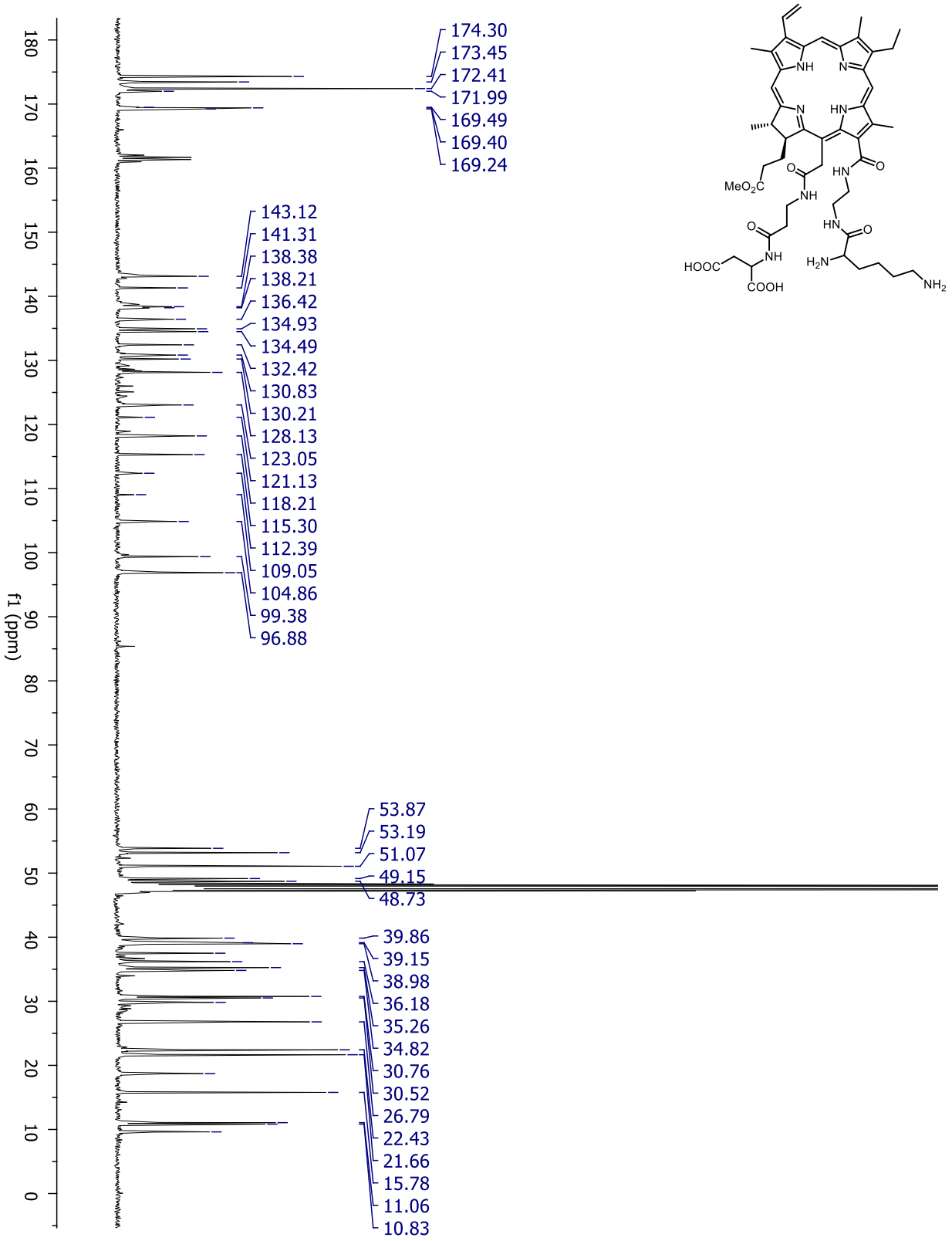
^{13}C NMR spectrum of 13^{1},15^{2}-ED-AspCe$_6$ methyl ester (**29**) in methanol-d_4 at 400 MHz

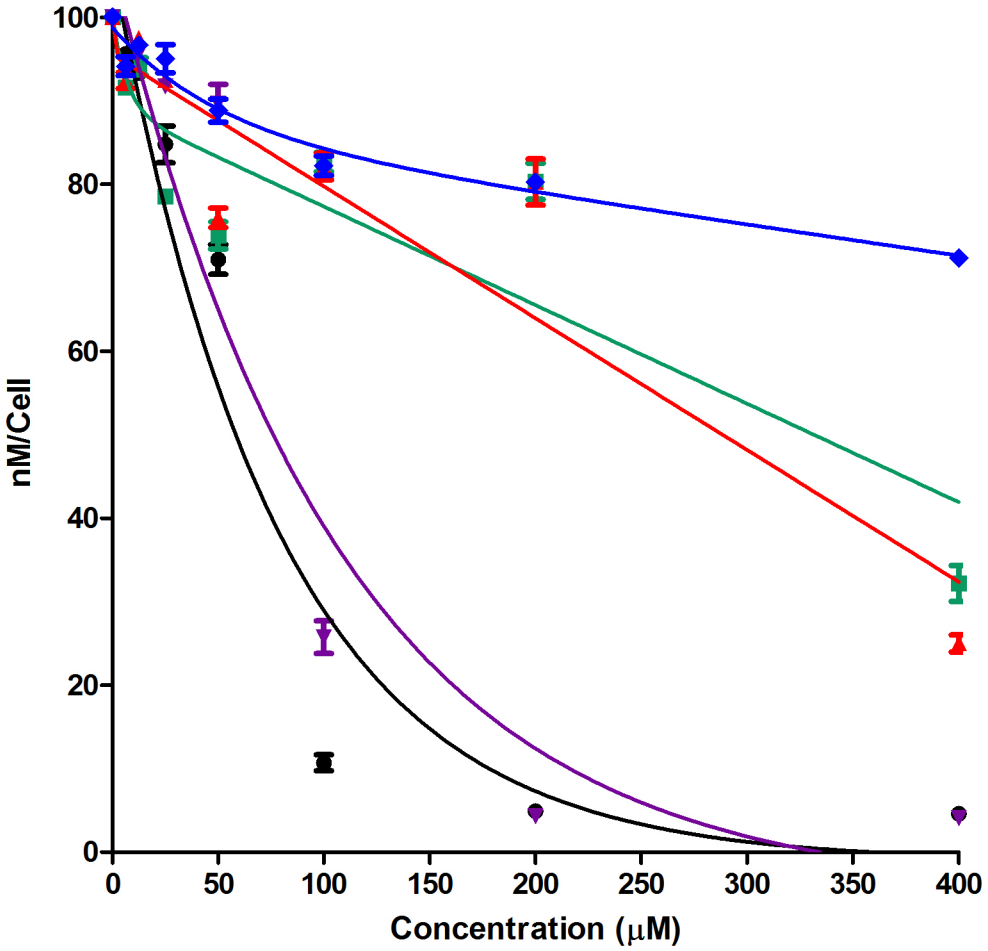


^{13}C NMR spectrum of 15^{2},17^{3}-di(Asp)Ce$_6$ methyl ester (**12**) in methanol-d_4 at 100 MHz

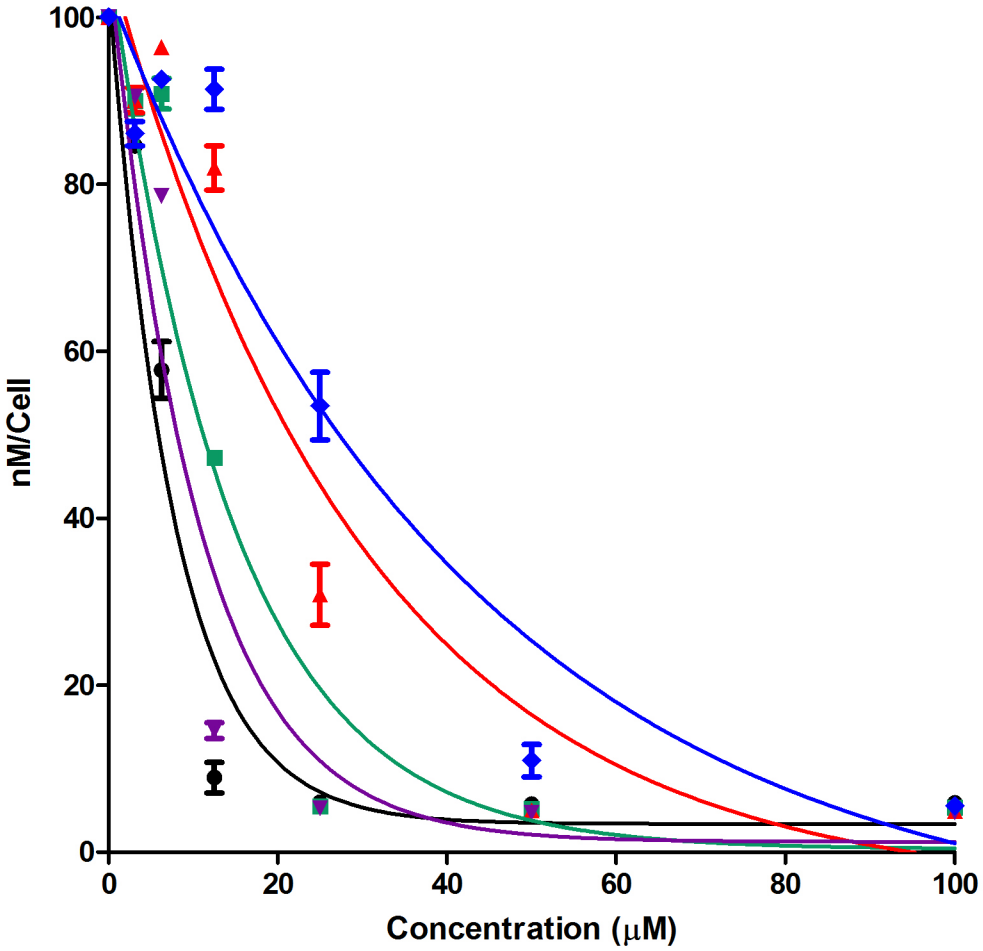


^{13}C NMR spectrum of 13^{2}-EDLys -15^{2}-β-AlaAspCe$_6$ methyl ester (**34**) in methanol-d_4 at 100 MHz

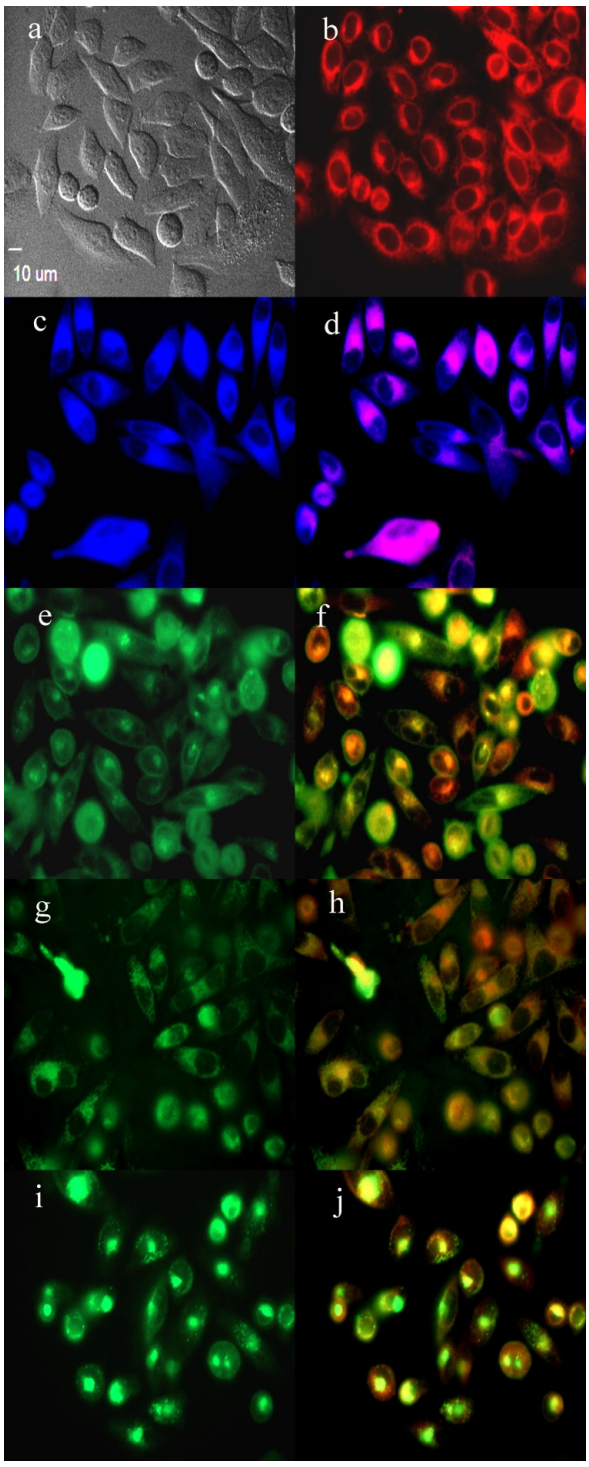




Dark toxicity of chlorin e_6 (**1**, green) and its derivatives 15^2,17^3-di(Asp)Ce_6 MME (**12**, blue), 13^1,17^3-di(Asp)Ce_6 MME (**13**, red), 13^1,15^2-di(EDAsp)Ce_6 MME (**28**, purple) and 13^1-EDLys-15^2-β-AlaAspCe_6 MME (**33**, black), toward HEp2 cells using the Cell Titer Blue assay.



Phototoxicity of chlorin e_6 (**1**, green) and its derivatives 15^2,17^3-di(Asp)Ce_6 MME (**12**, blue), 13^1,17^3-di(Asp)Ce_6 MME (**13**, red), 13^1,15^2-di(EDAsp)Ce_6 MME (**28**, purple) and 13^1-EDLys-15^2-β-AlaAspCe_6 MME (**33**, black), toward HEp2 cells using 1J/cm^2 light dose and the Cell Titer Blue assay.



Subcellular localization of chlorin e_6 in HEp2 cells at 10 μM for 6h, (a) phase contrast, (b) overlay of chlorin e_6 and phase contrast, (c) ER Tracker Blue, (d) overlay of chlorin e_6 and ER Tracker Blue, (e) BODIPY Ceramide, (f) overlay of chlorin e_6 and BODIPY Ceramide, (g) MitoTracker Green, (h) overlay of chlorin e_6 and MitoTracker Green, (i) LysoSensor Green, (j) overlay of chlorin e_6 and LysoSensor Green. Scale bar: 10 μm