Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

Tuning Activity-Based Probe Selectivity for Serine Proteases by On-resin 'Click' Construction of Peptide Diphenyl Phosphonates

Sevnur Serim, Susanne V. Mayer, and Steven H. L. Verhelst*

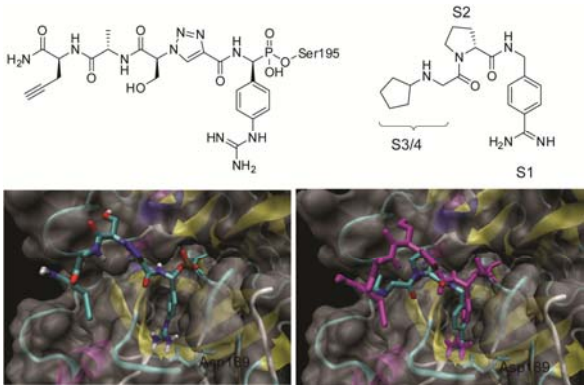
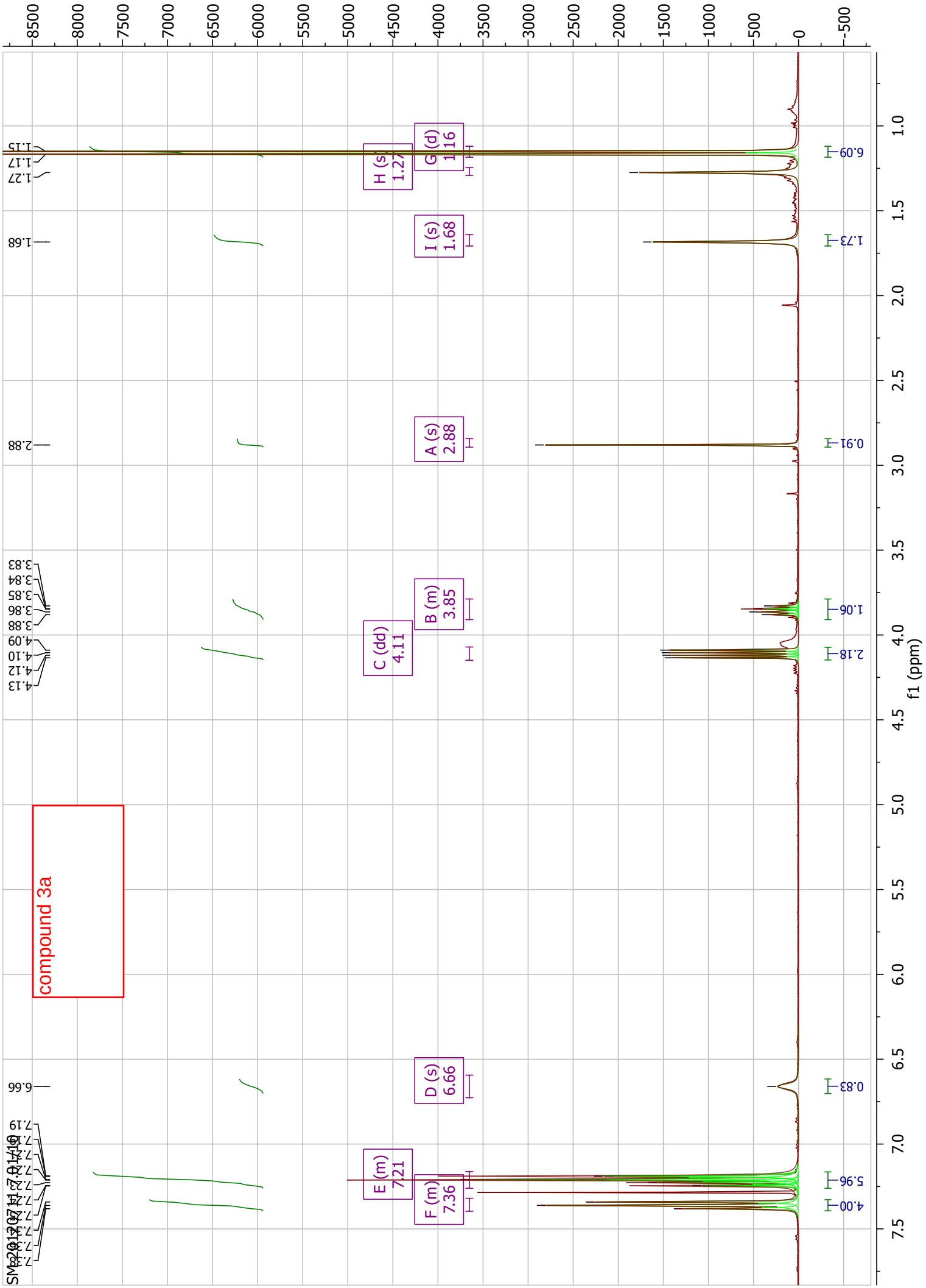
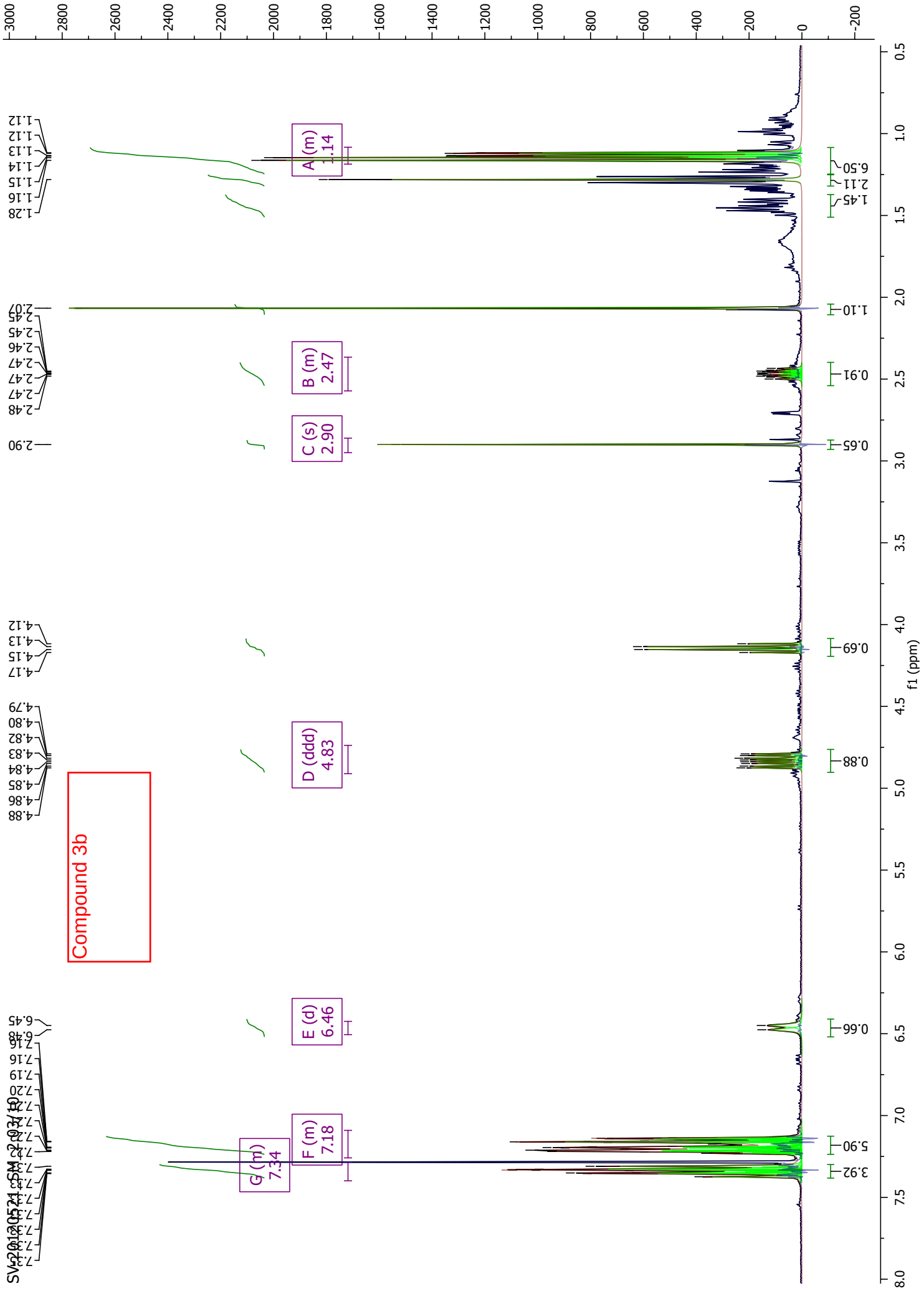
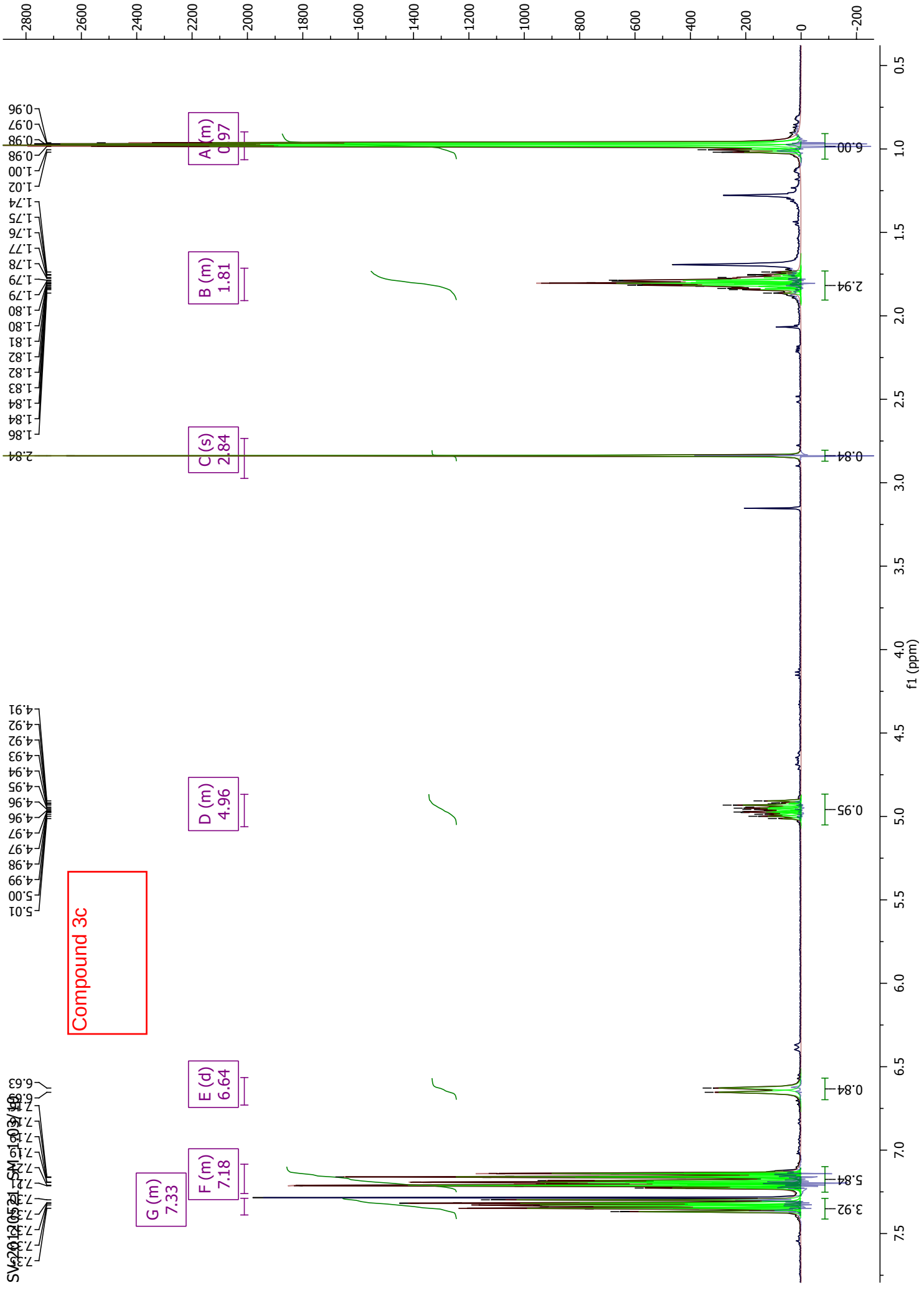
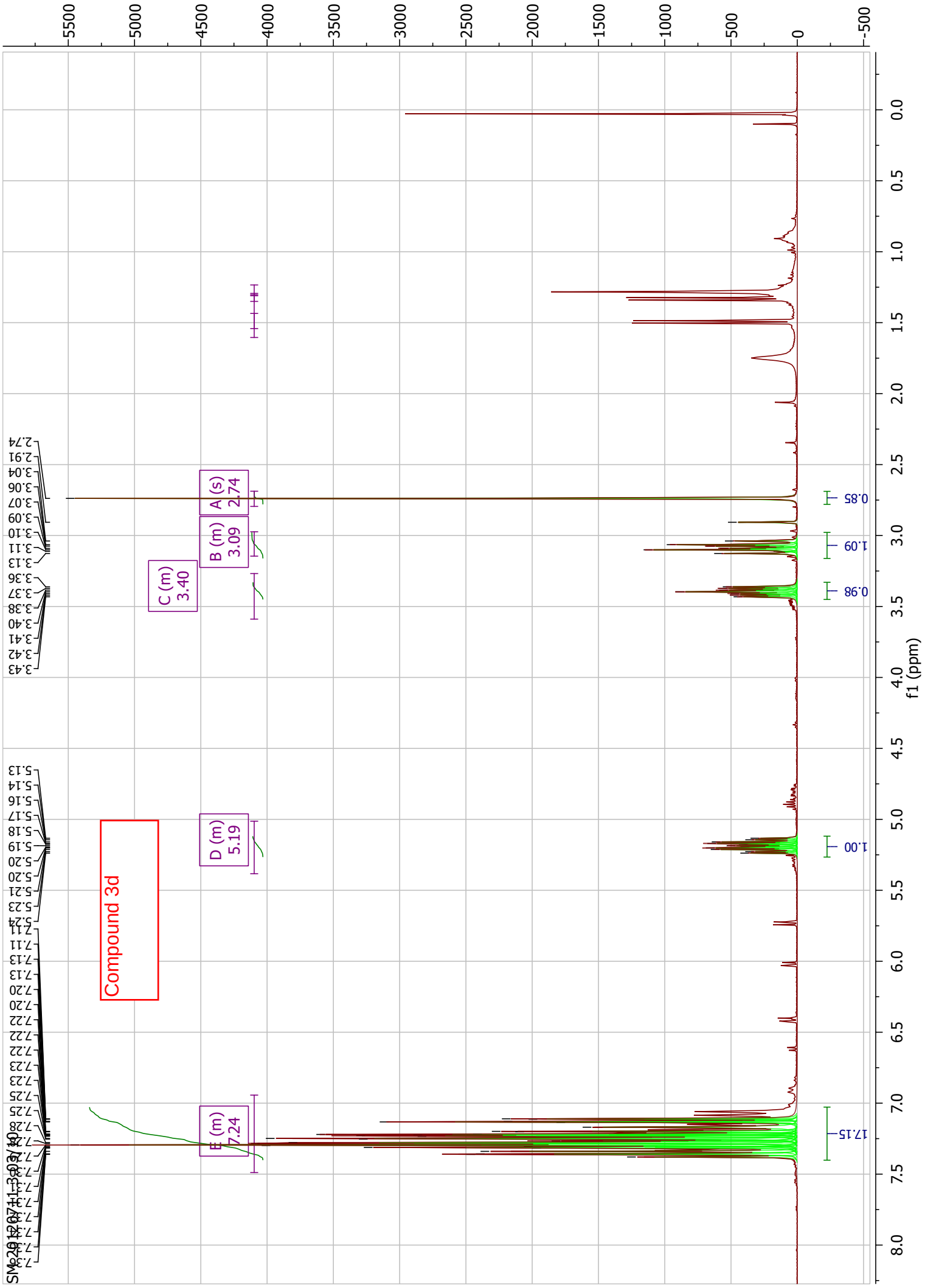


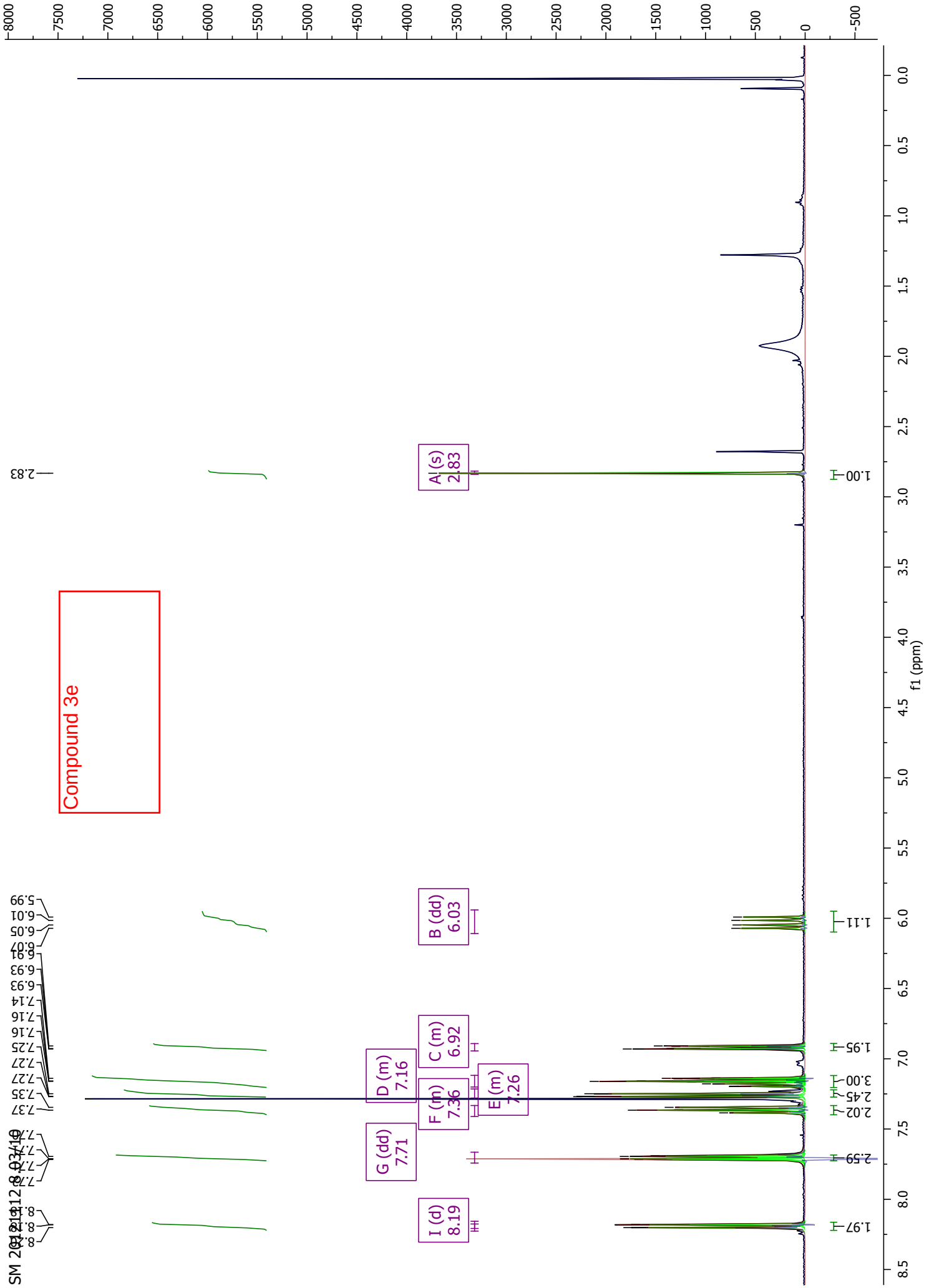
Fig. S1. Graphical representation of probe **10** docked into bovine beta-trypsin. Beta-trypsin is displayed with a transparent surface and a cartoon representation of the backbone. Probe **10** (left: colored by element; right: colored in magenta) and the indicated inhibitor (overlayed with probe **10** in the right panel) are shown as stick models. Asp189, at the bottom of the S1 pocket, also in stick model, forms a salt bridge with the guanidine and amidine, respectively.

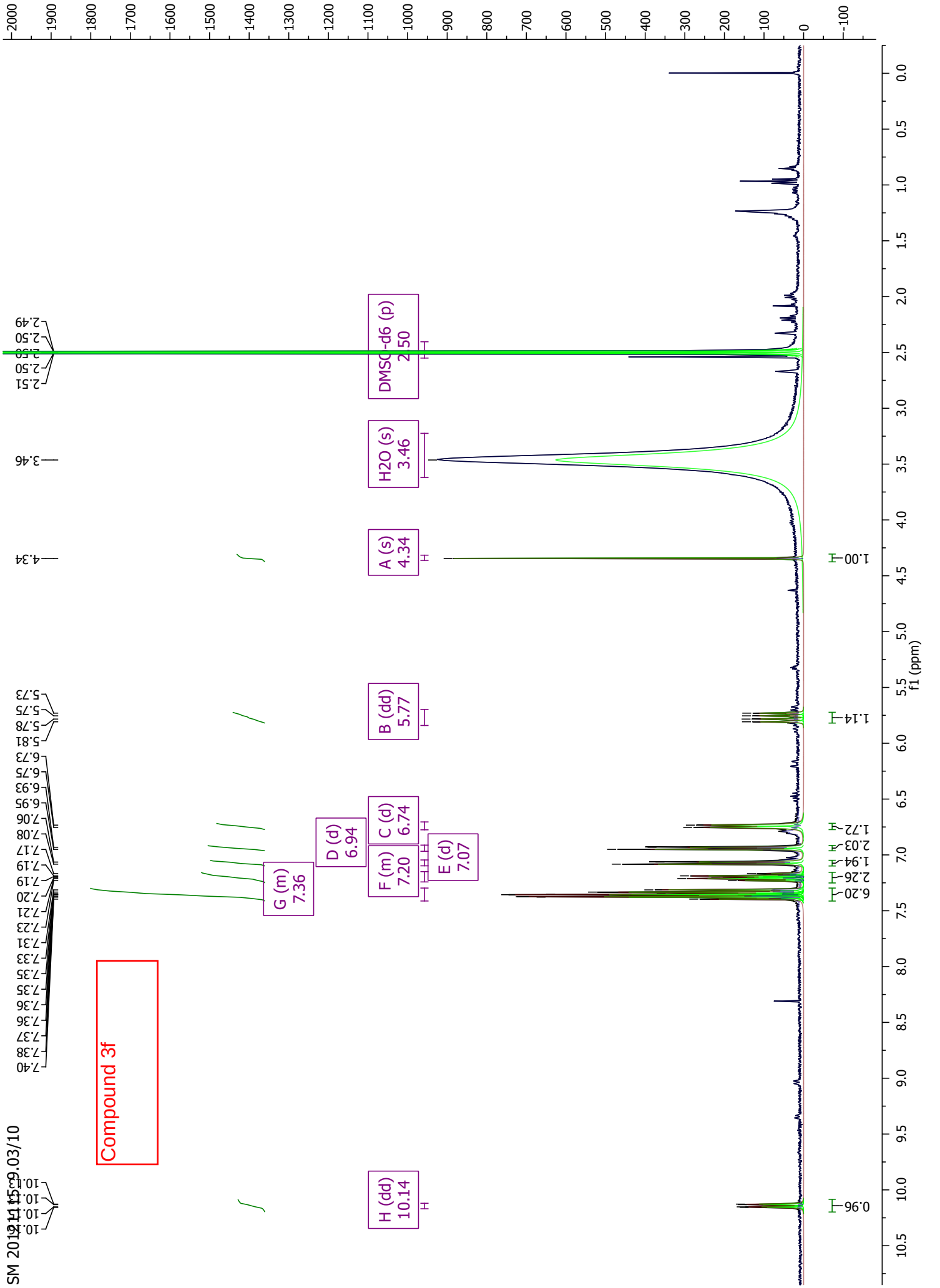


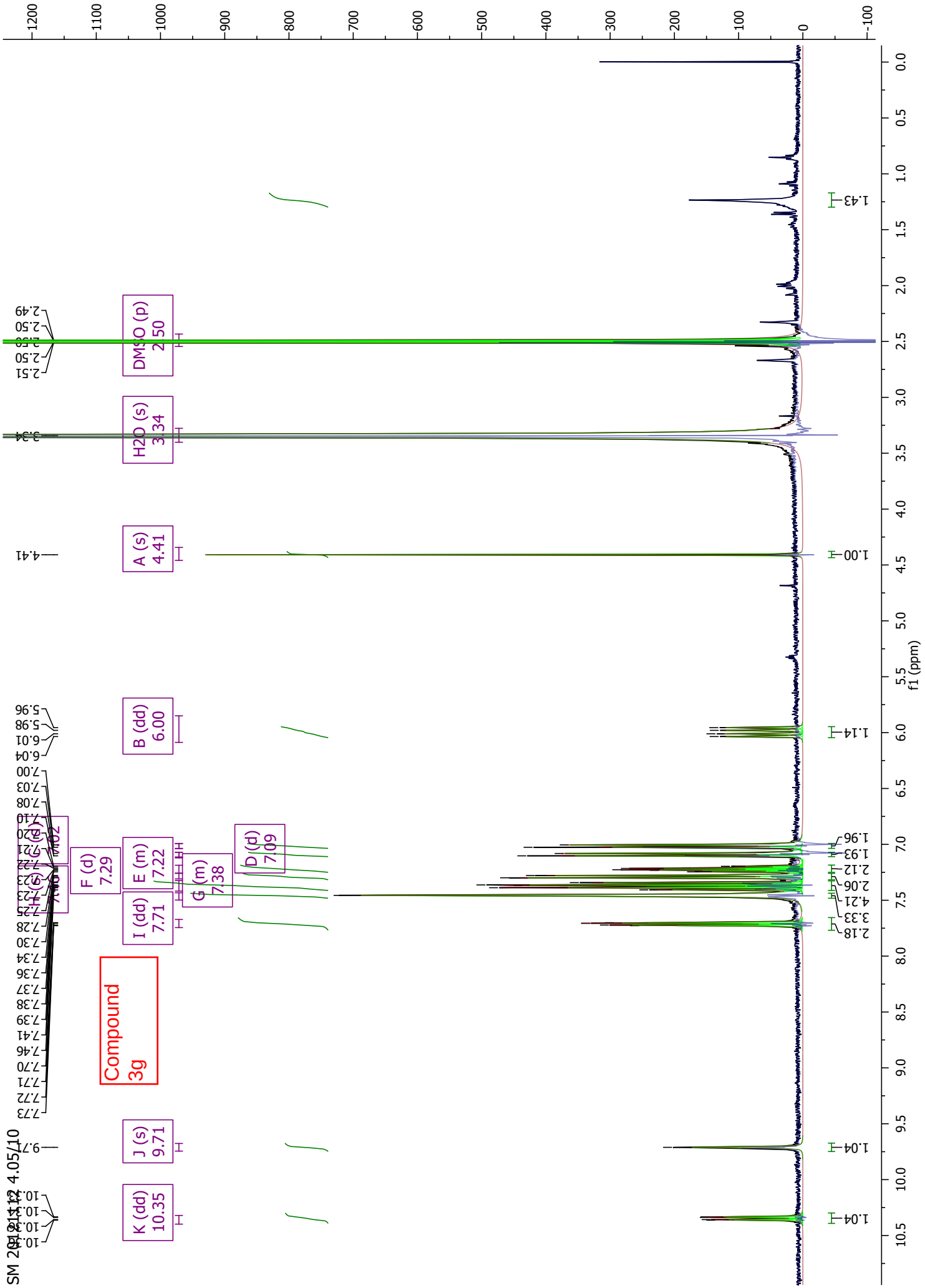






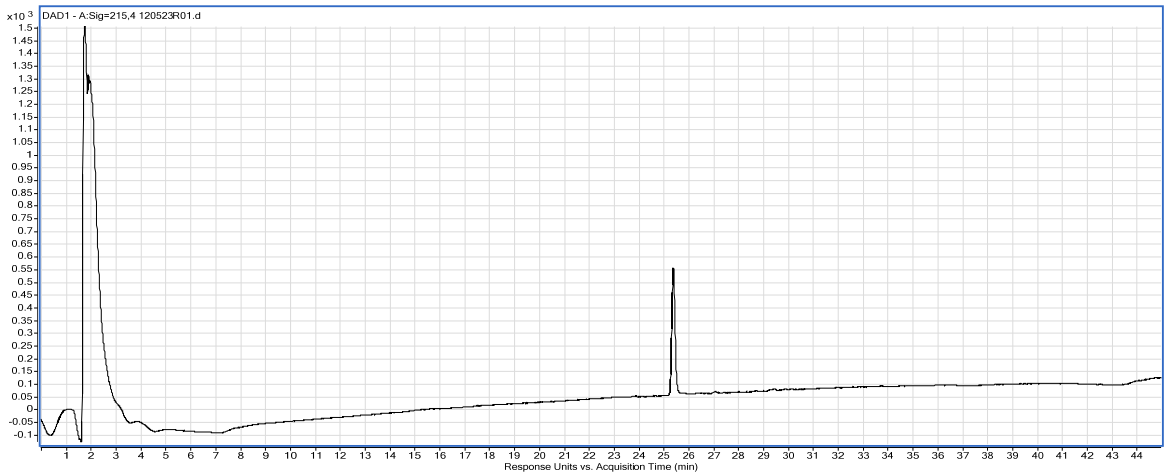




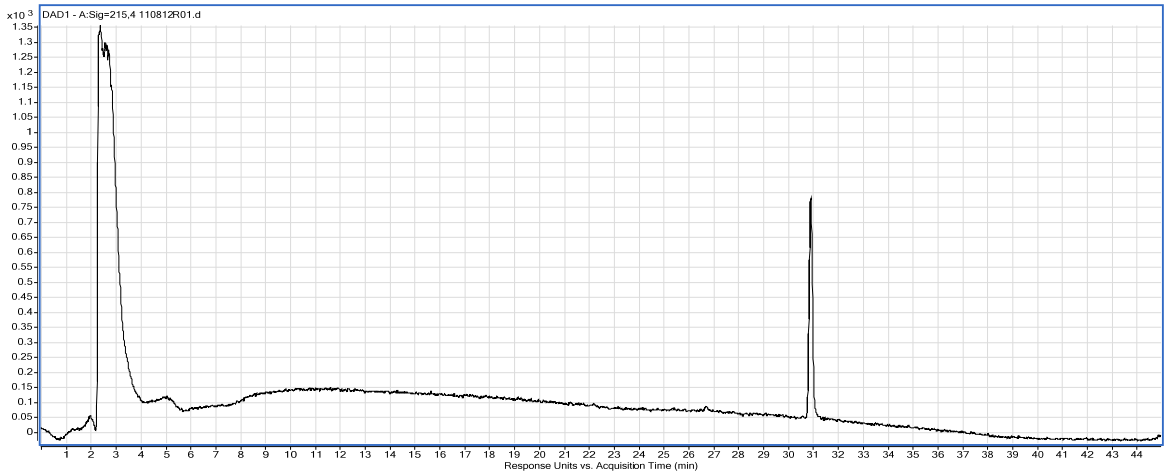


Note that some diastereoisomers of the peptide diphenyl phosphonates do and some do not resolve on reverse phase C18-LC.

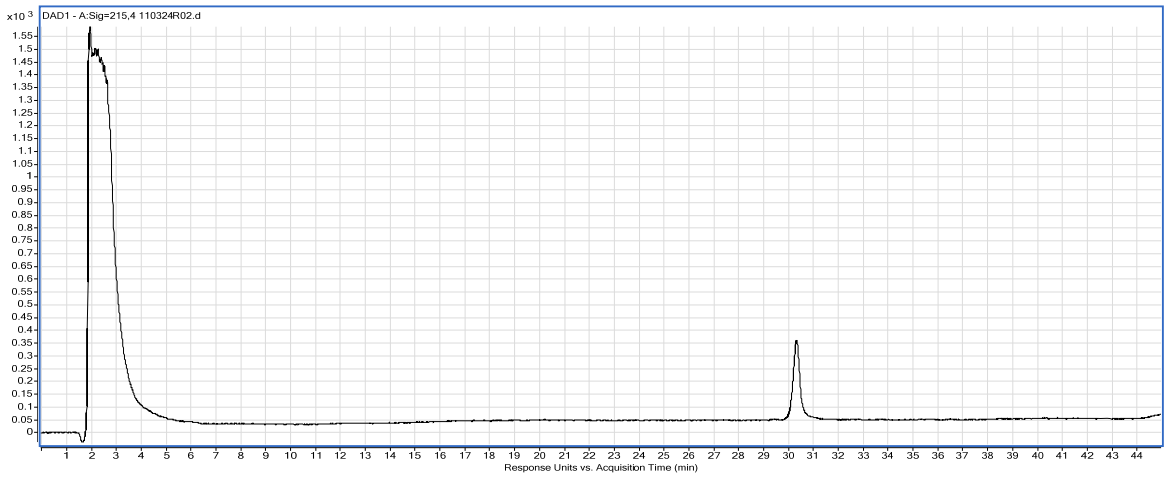
Diphenyl α-*N*-(benzyloxycarbonyl)amino-methylphosphonate (2a)



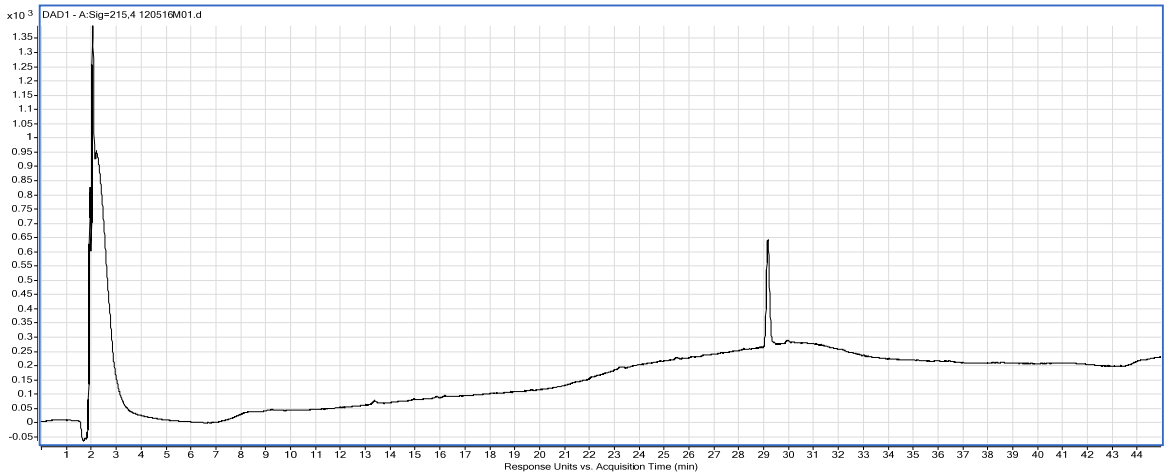
Diphenyl α-*N*-(benzyloxycarbonyl)amino-2-methylpropylphosphonate (2b)



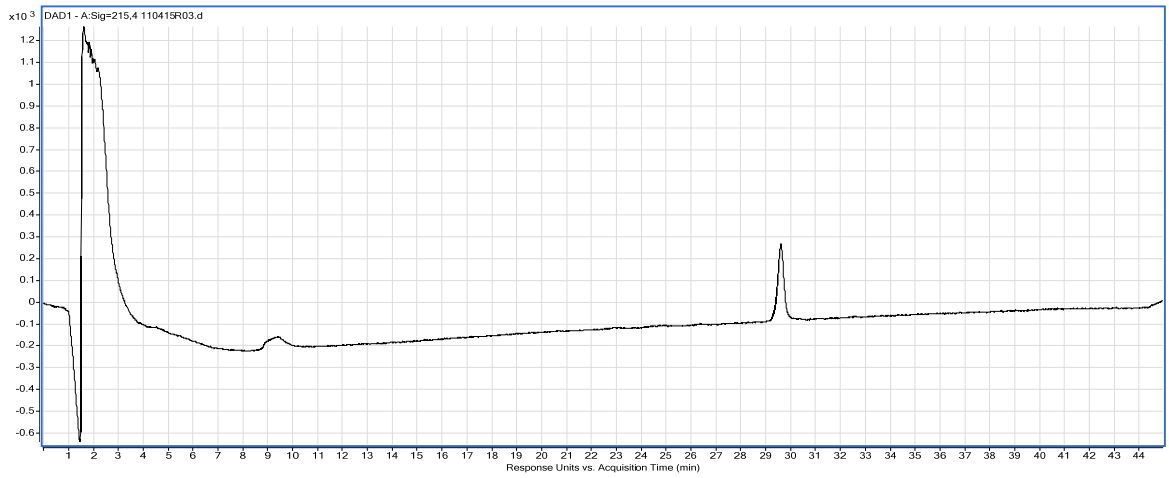
Diphenyl α-*N*-(benzyloxycarbonyl)amino-3-methylbutylphosphonate (2c)



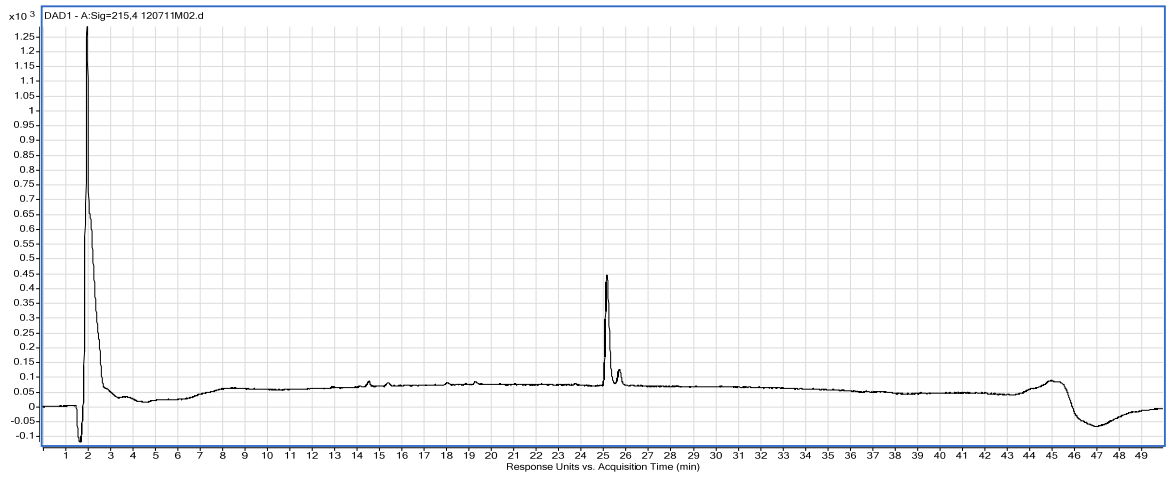
Diphenyl α-*N*-(benzyloxycarbonyl)amino-2-phenylethylphosphonate (2d)



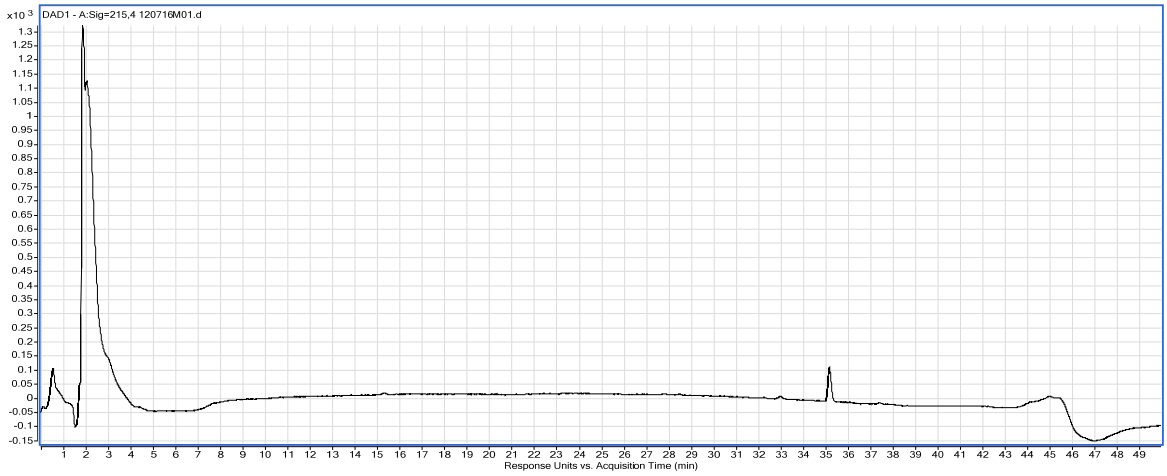
Diphenyl α-*N*-(benzyloxycarbonyl)amino-(4-nitro-phenyl)methanephosphonate (2e)



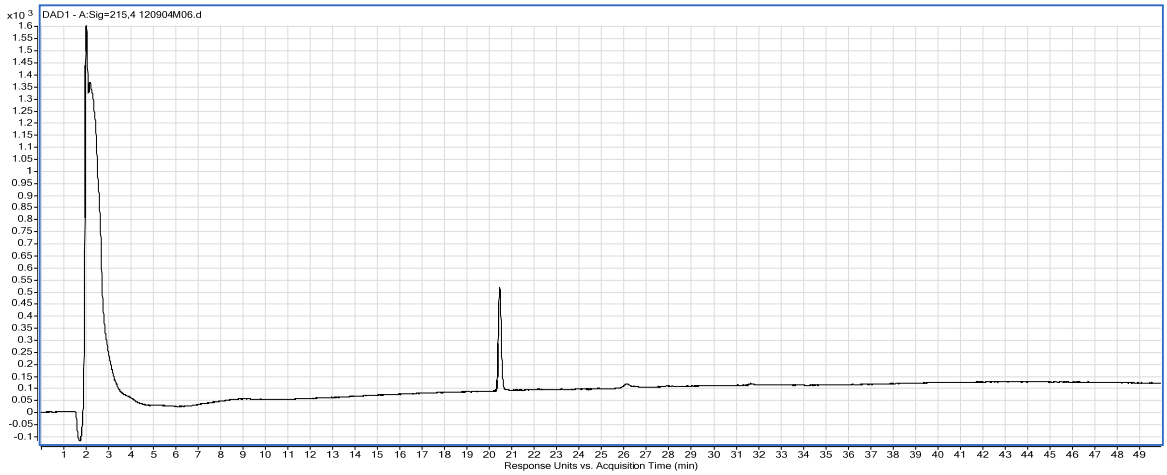
Diphenyl α-*N*-(benzyloxycarbonyl)amino-(4-amino-phenyl)methanephosphonate (2f)



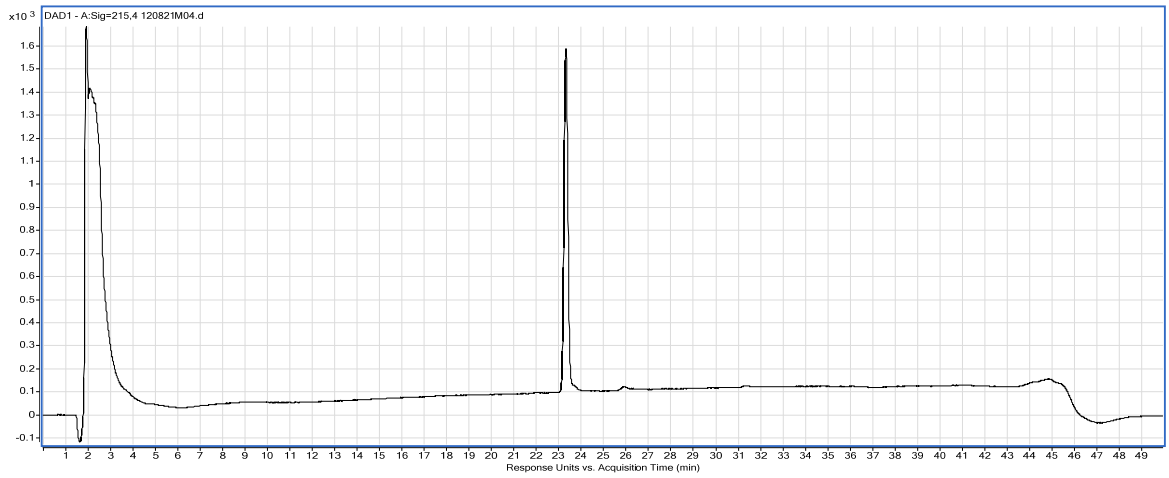
Diphenyl α-*N*-(benzyloxycarbonyl)amino-(4-dibocguanidinium-phenyl)methanephosphonate (2g)



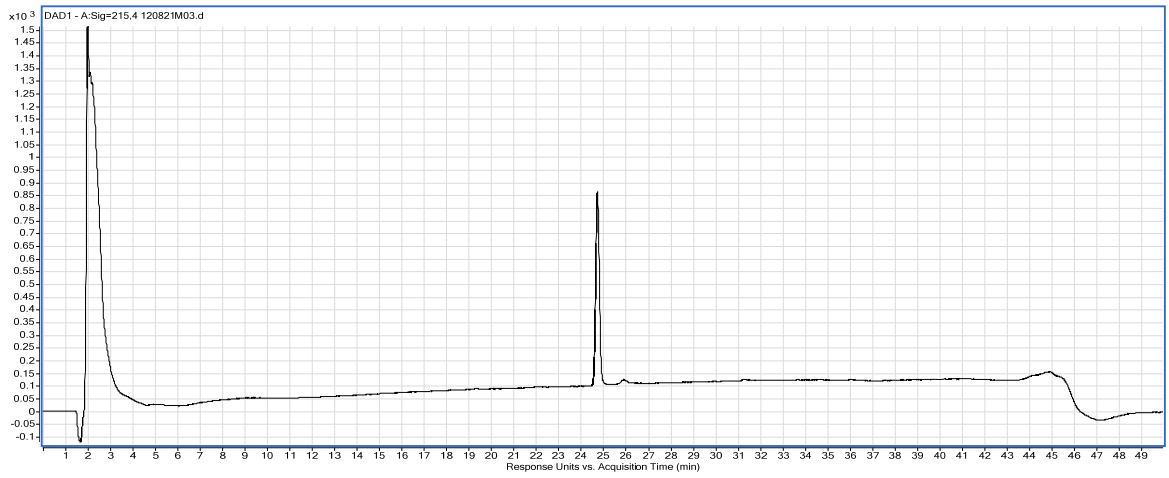
Diphenyl α-*N*-(propiolamido)-methylphosphonate (3a)



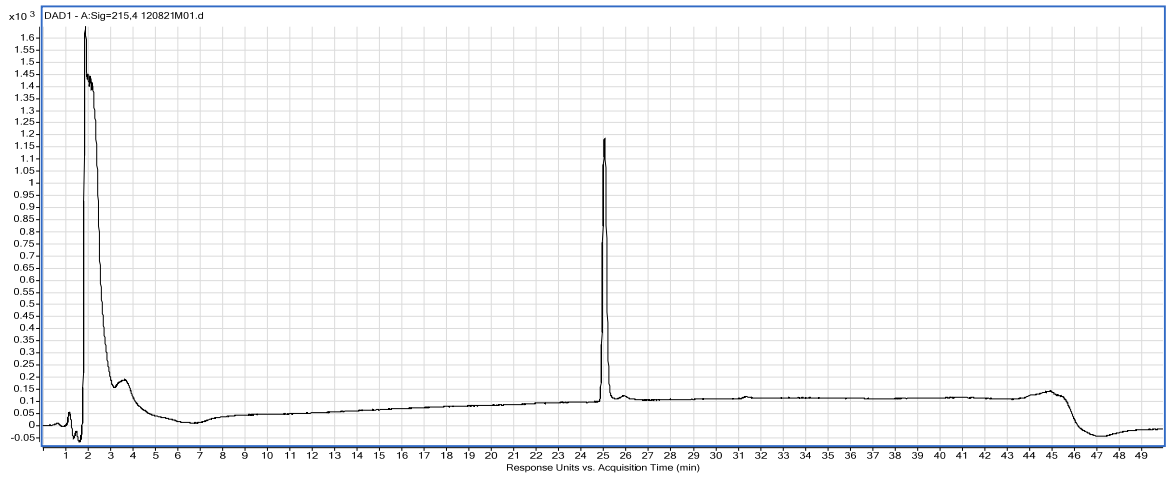
Diphenyl α-*N*-(propiolamido)-2-methylpropylphosphonate (3b)



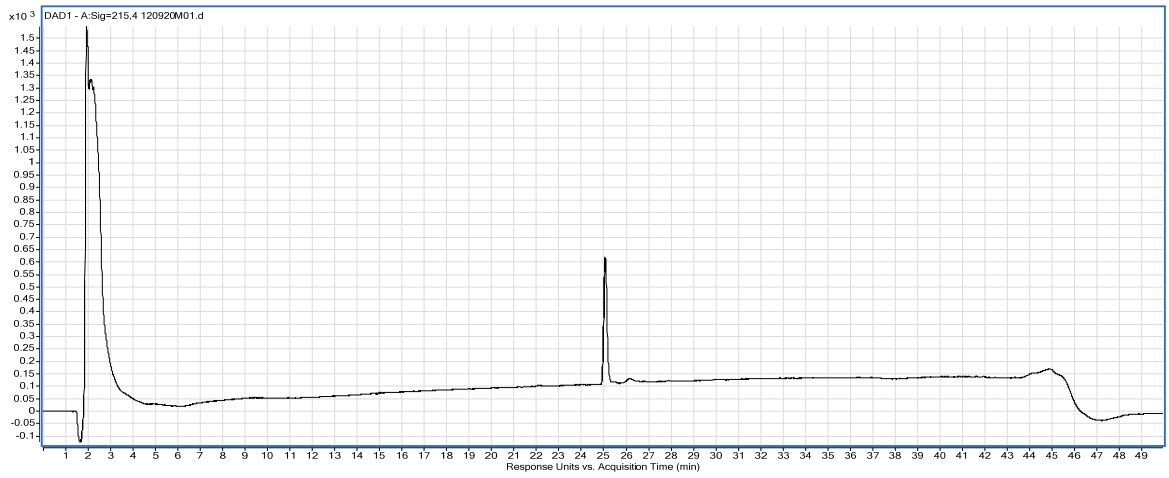
Diphenyl α-*N*-(propiolamido)-3-methylbutylphosphonate (3c)



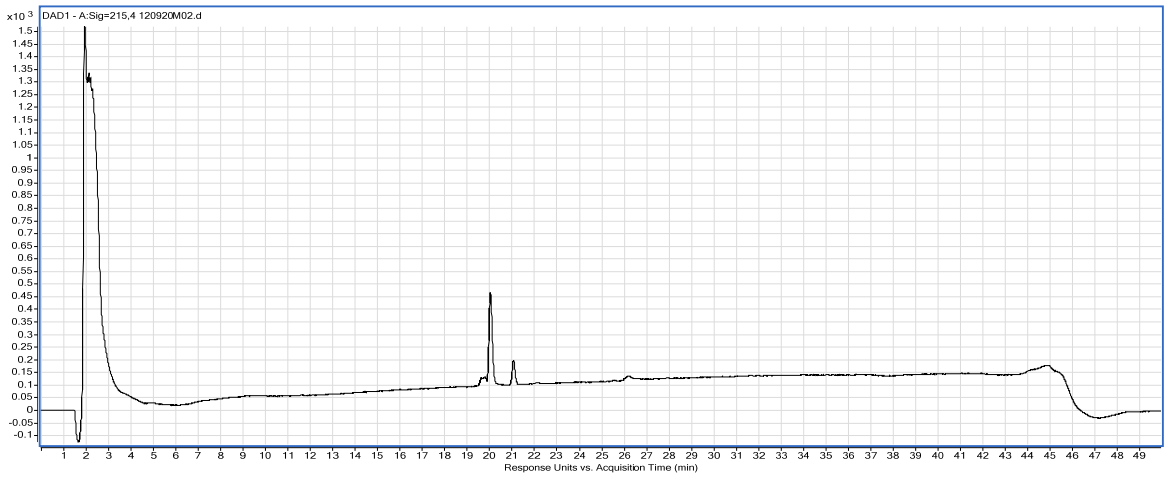
Diphenyl α-*N*-(propiolamido)-2-phenylethylphosphonate (3d)



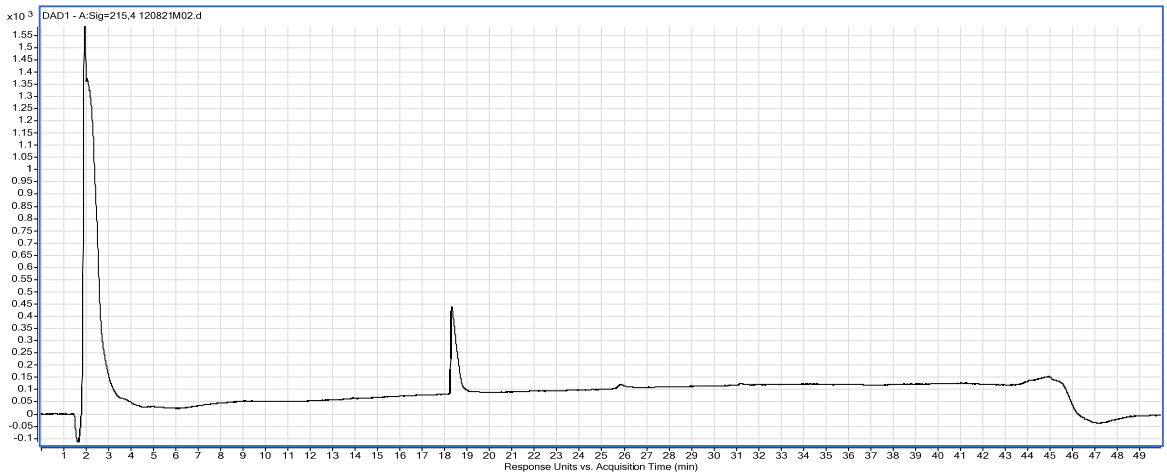
Diphenyl α-*N*-(propiolamido)-(4-nitro-phenyl)methanephosphonate (3e)



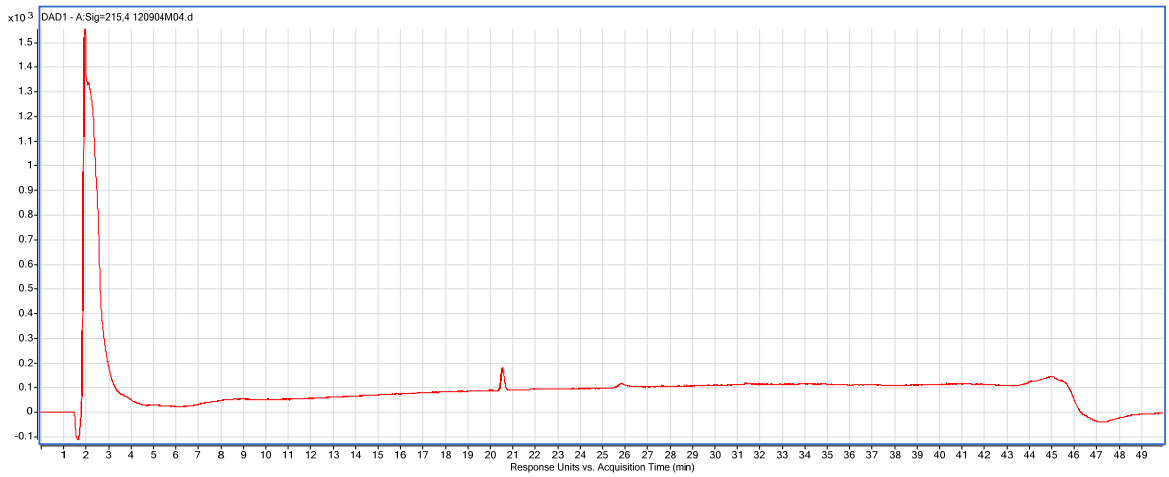
Diphenyl α-*N*-(propiolamido)-(4-amino-phenyl)methanephosphonate (3f)



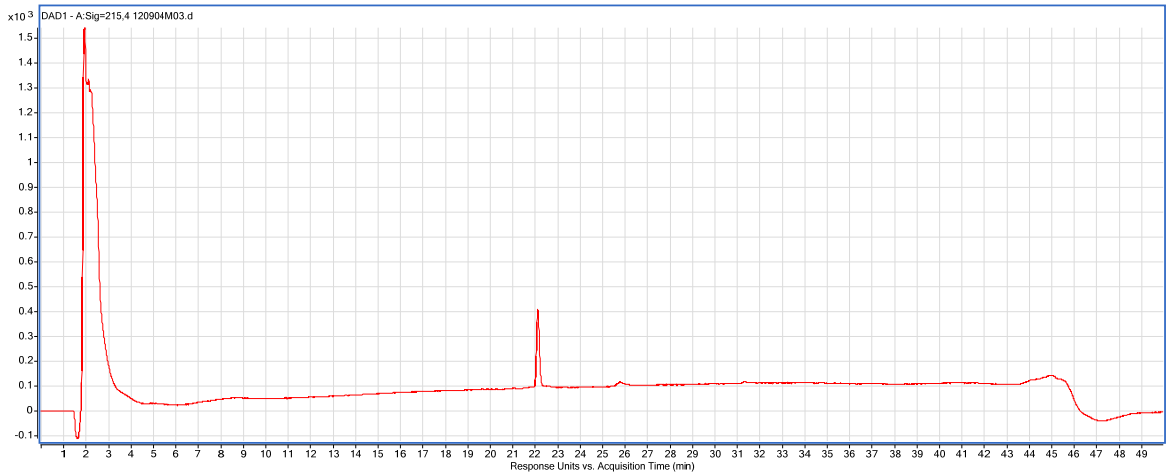
Diphenyl α-*N*-(propiolamido)-(4-guanidinium-phenyl)methanephosphonate (3g)



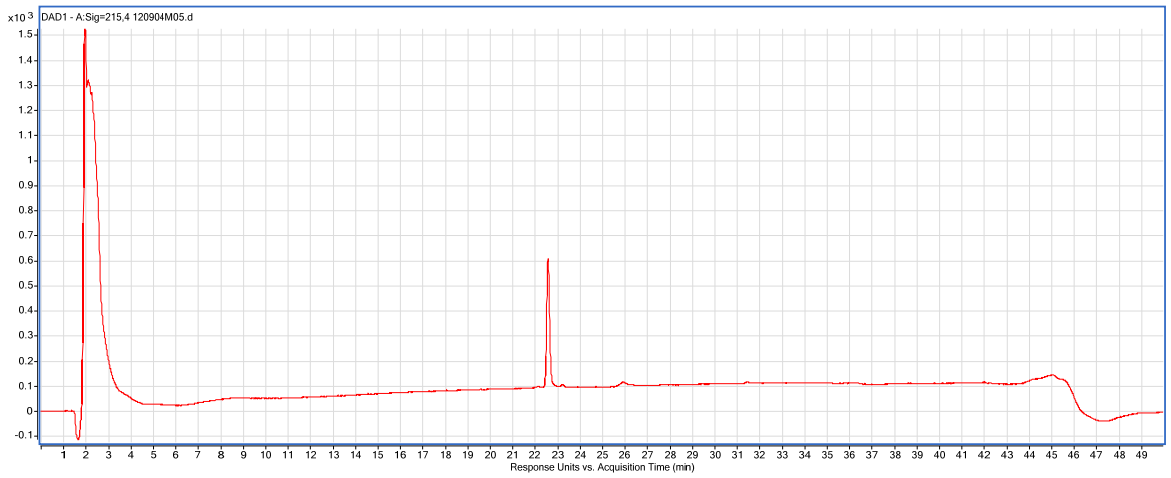
PraAlaGlu(triazole)Val^{P}(OPh)$_2$ (5)



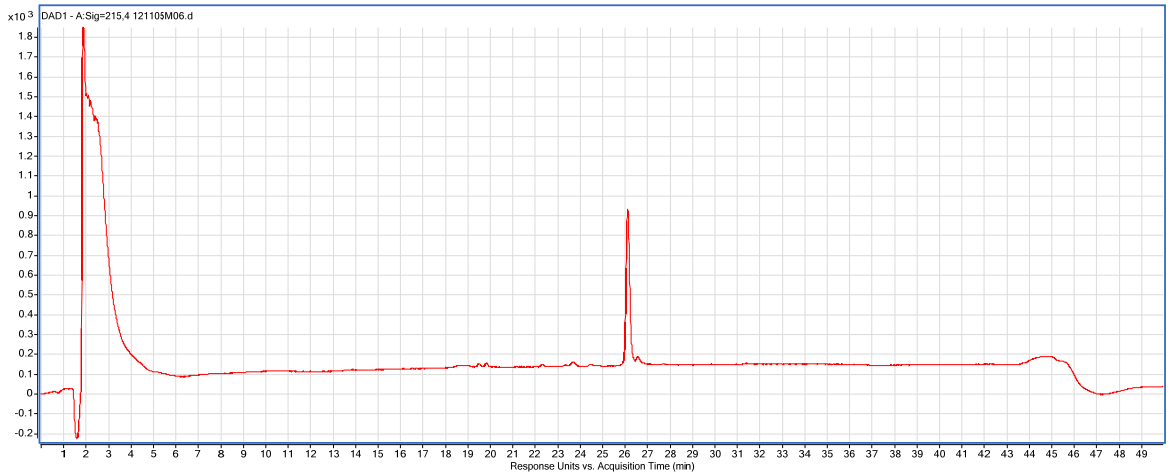
PraAlaAla(triazole)Leu^{P}(OPh)$_2$ (6)



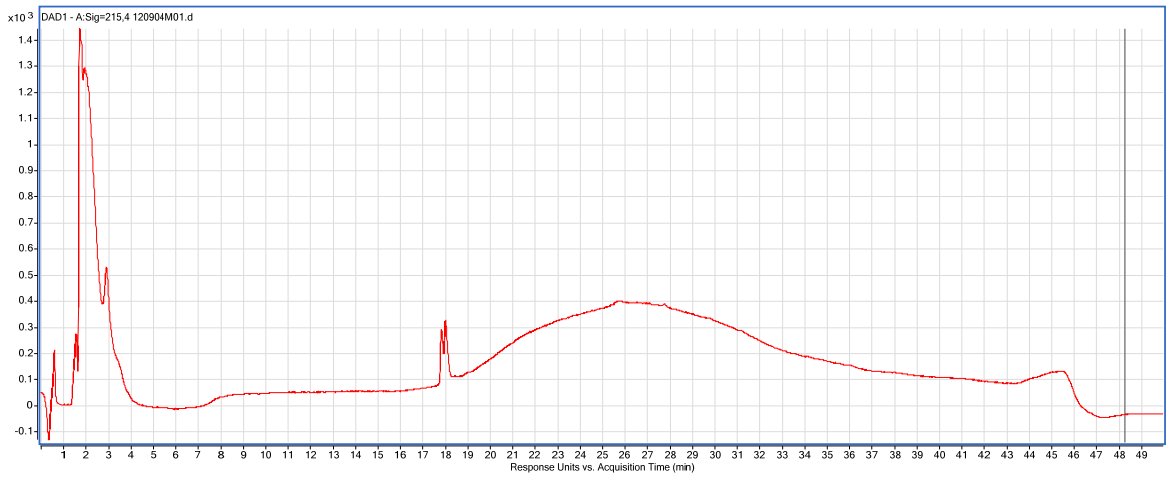
PraAlaAla(triazole)Phe^{P}(OPh)$_2$ (7)



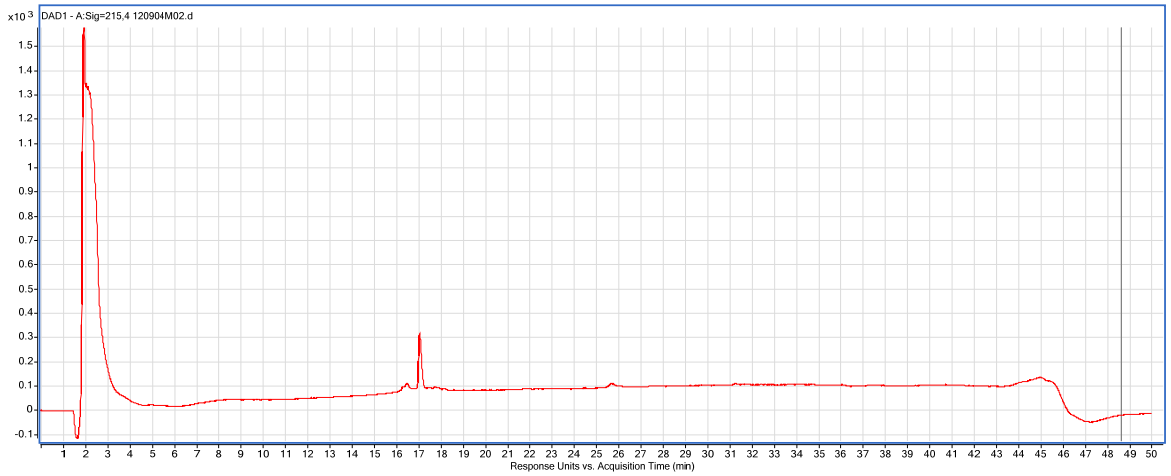
PraMetPhe(triazole)Phe^{P}(OPh)$_2$ (8)



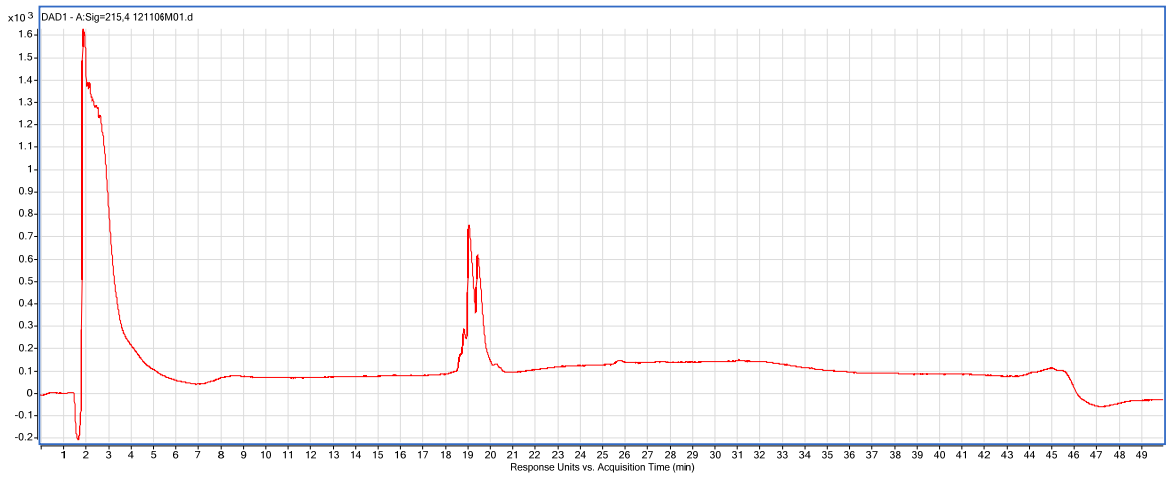
PraAlaAla(triazole)Gua^{P}(OPh)$_2$ (9)



PraAlaSer(triazole)Gua^{P}(OPh)$_2$ (10)



PraNleThr(triazole)Gua^{P}(OPh)$_2$ (11)



PraLeuPhe(triazole)Gua^{P}(OPh)$_2$ (12)