

Supplementary

α -Glucosidase Inhibition and Molecular Docking Studies of Natural Brominated Metabolites from Marine Macro Brown Alga *Dictyopteris hoytii*

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Nadiya Al-Saady ⁴, Abdullah Hilal Al-Balushi ⁴, Haitham Khamis Al-Busaidi ⁴ and
Ahmed Al-Harrasi ^{1,*}

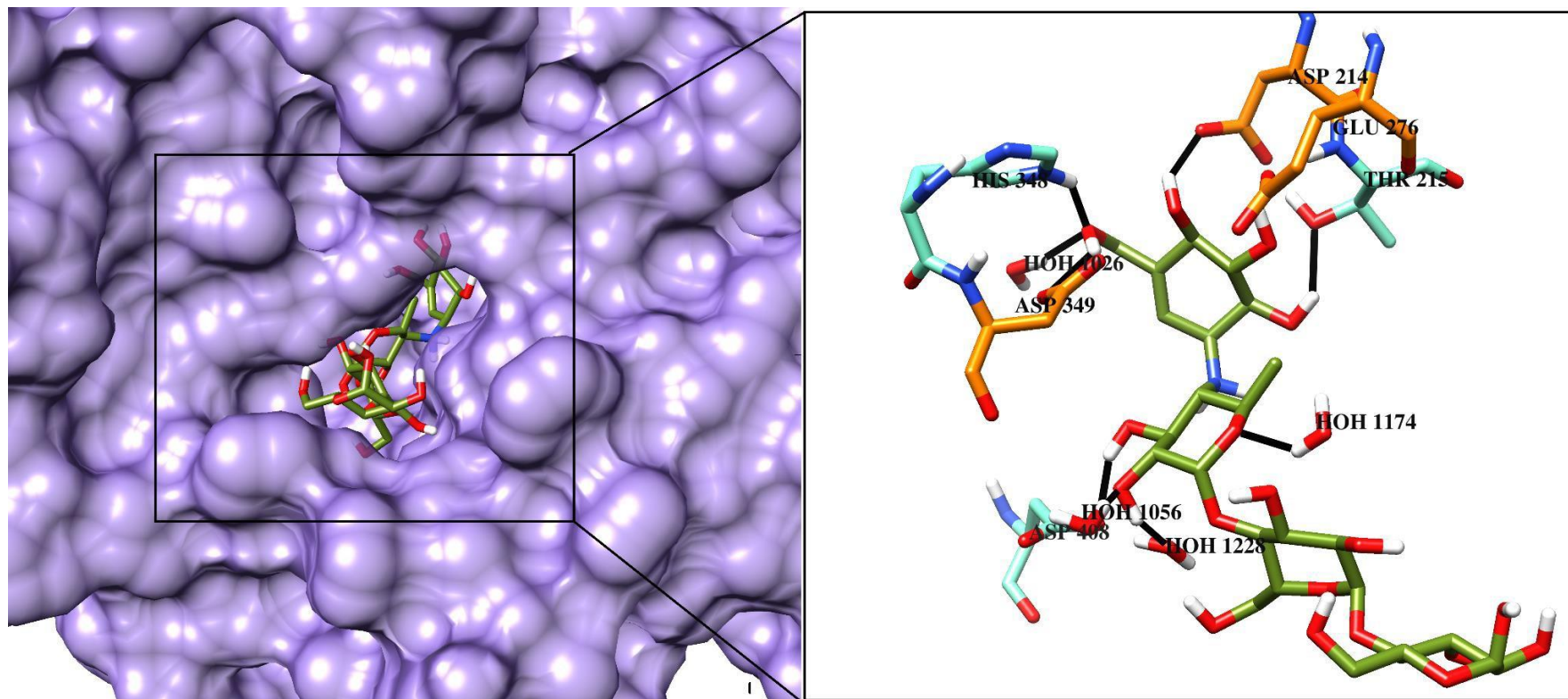


Figure S1. Docked view of known inhibitor Acarbose in the active site of *S. cerevisiae* α -glucosidase enzyme. The binding interactions are highlighted in box. Catalytic residues are shown in orange stick model, Hydrogen bonds are depicted in black lines. Acarbose is shown in olive green stick model.

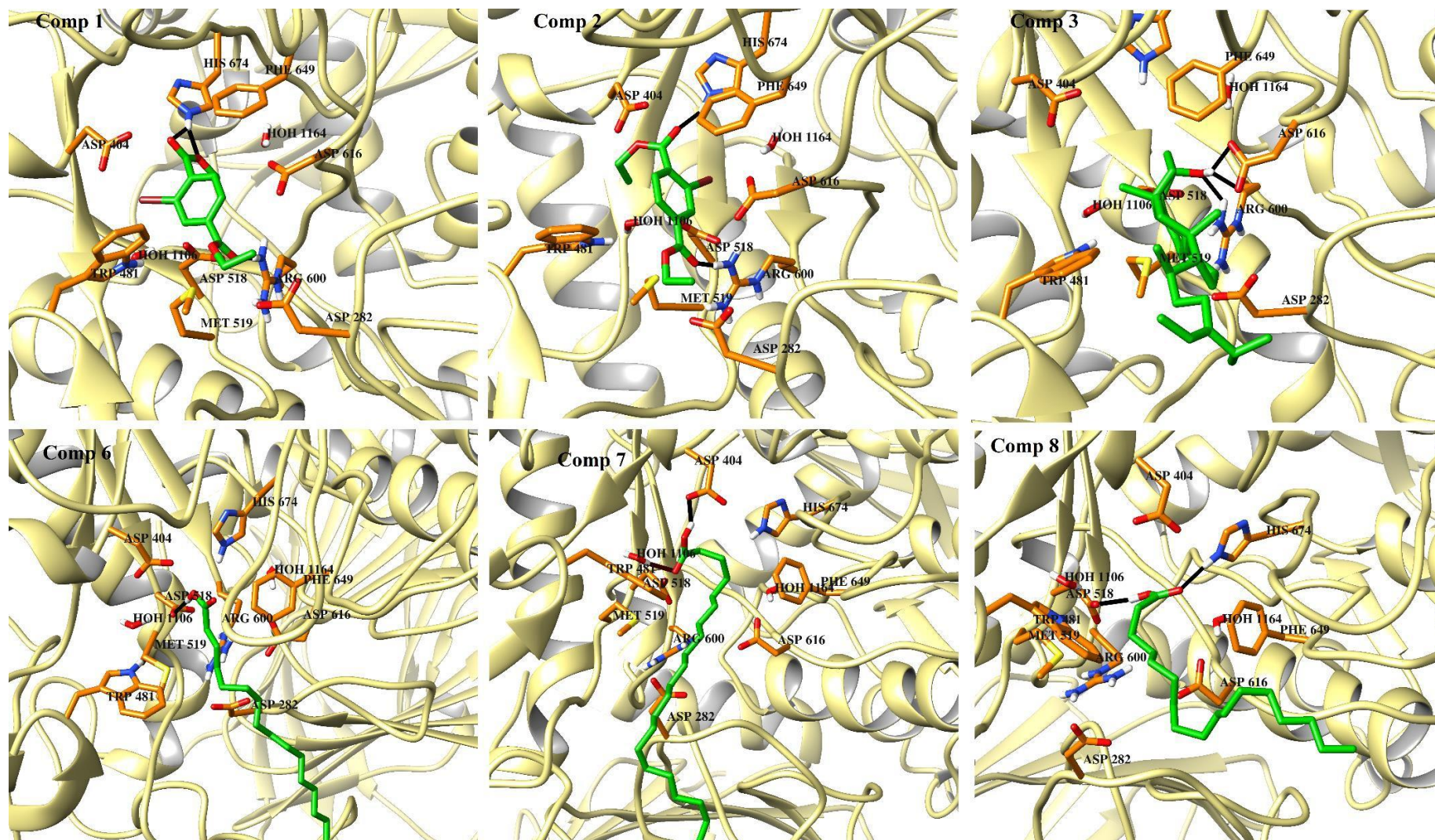


Figure S2. Docked view of compounds 1-3 and 6-8 in the active site of human α -glucosidase enzyme. The ligands are shown in green stick model, interacting residues are shown in orange stick model, and Hydrogen bonds are depicted in black lines.

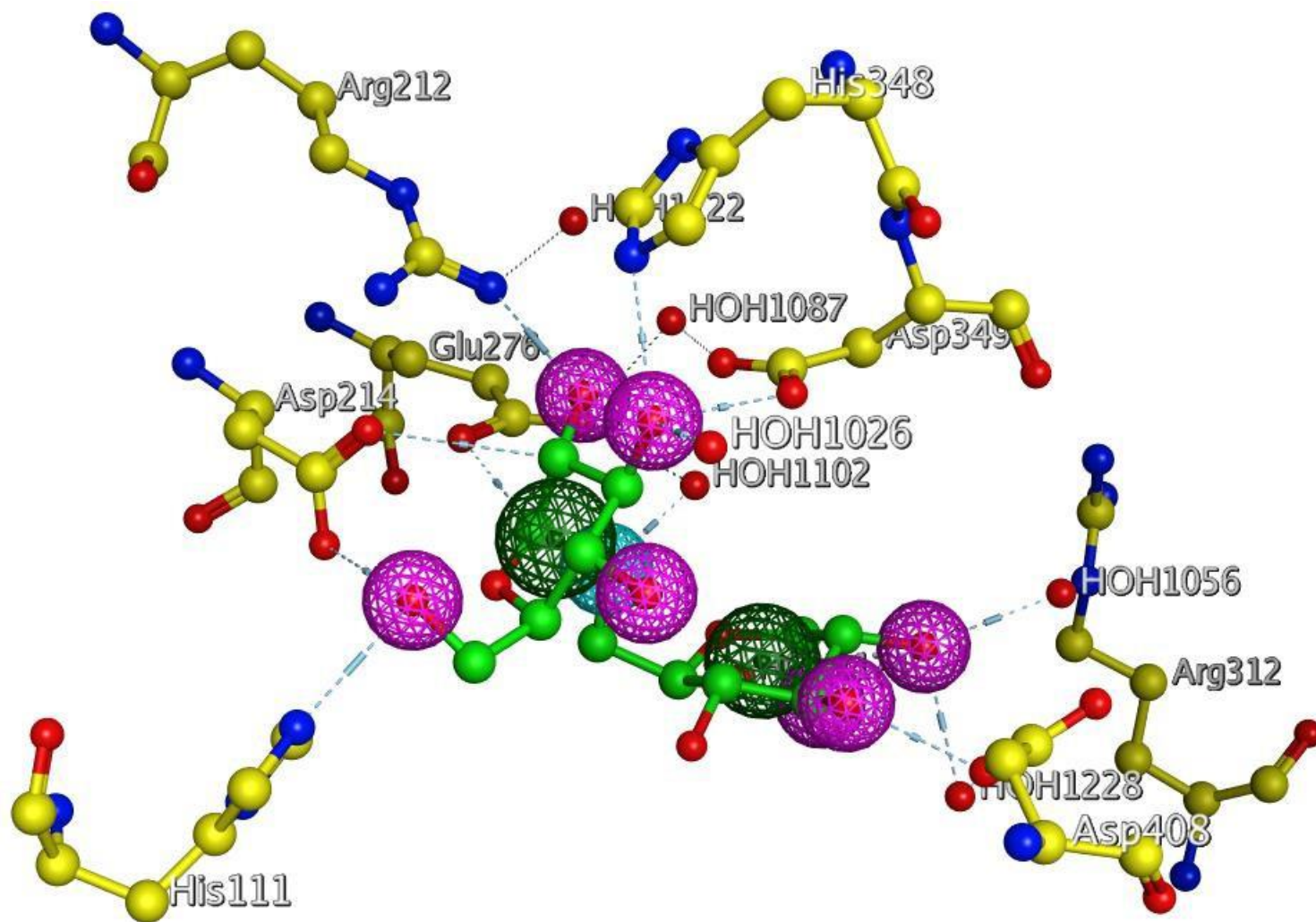


Figure S3. Structure-based pharmacophore model (called Ph-1) generated by *S. cerevisiae* α -glucosidase enzyme in complex with isomaltose (substrate). Substrate is shown in green stick model, interacting residues are shown in yellow stick model. Water molecules are shown in red ball. Hydrogen bonds are depicted in cyan dotted lines. Seven H-bond donor/Acceptor (Don/Acc) features are presented in magenta spheres. Hydrophobic features are shown in dark green spheres. One H-bond Acceptor feature is presented in cyan (Acc) sphere.

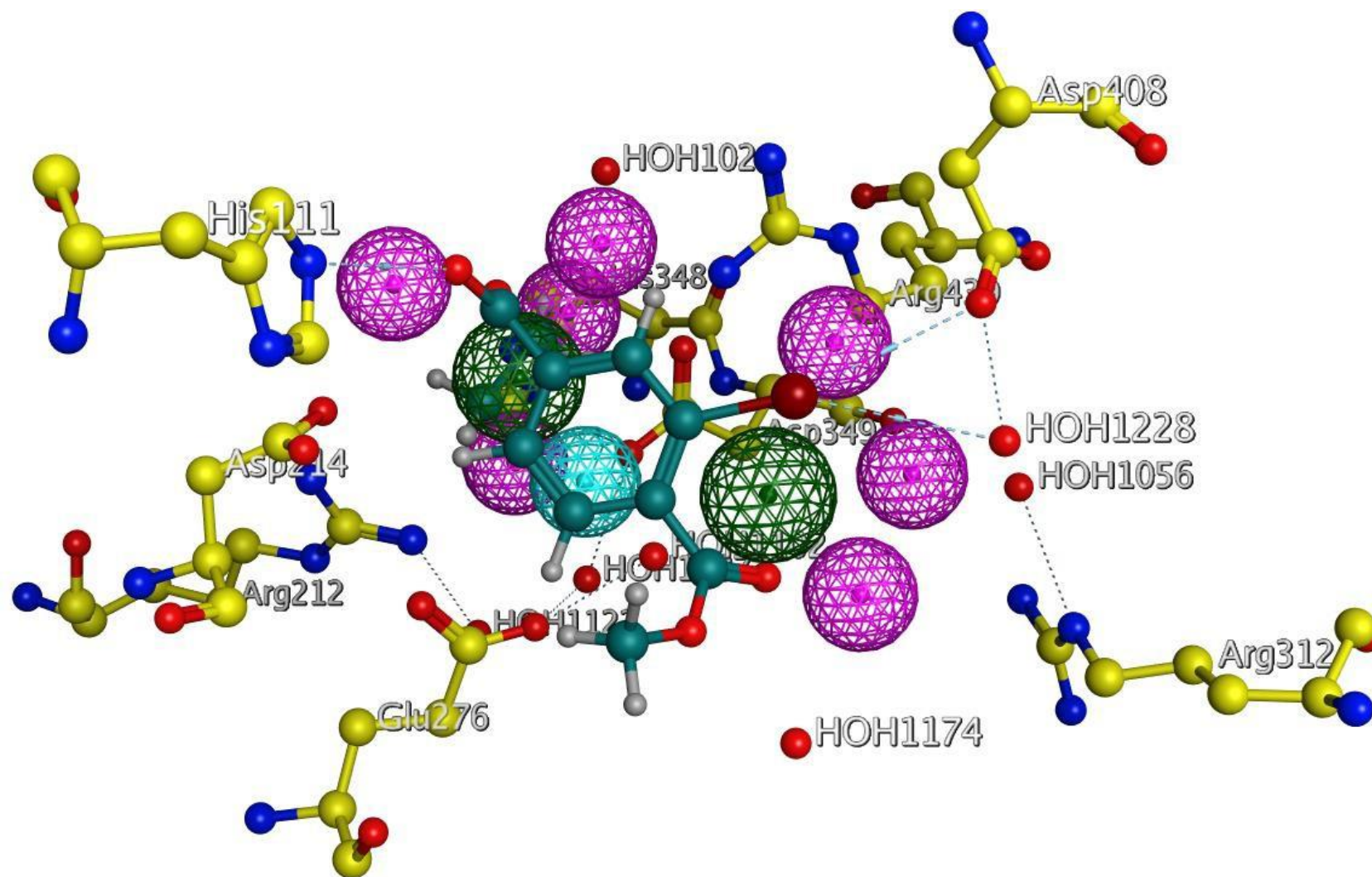


Figure S4. Superimposed view of Compound 1 on Ph-1. Ligand is shown in green stick model, interacting residues are shown in yellow stick model. Water molecules are shown in red ball. Hydrogen bonds are depicted in cyan dotted lines. H-bond Don/Acc Hydrophobic features, H-bond Acceptor feature are presented in magenta spheres, dark green spheres and cyan sphere, respectively

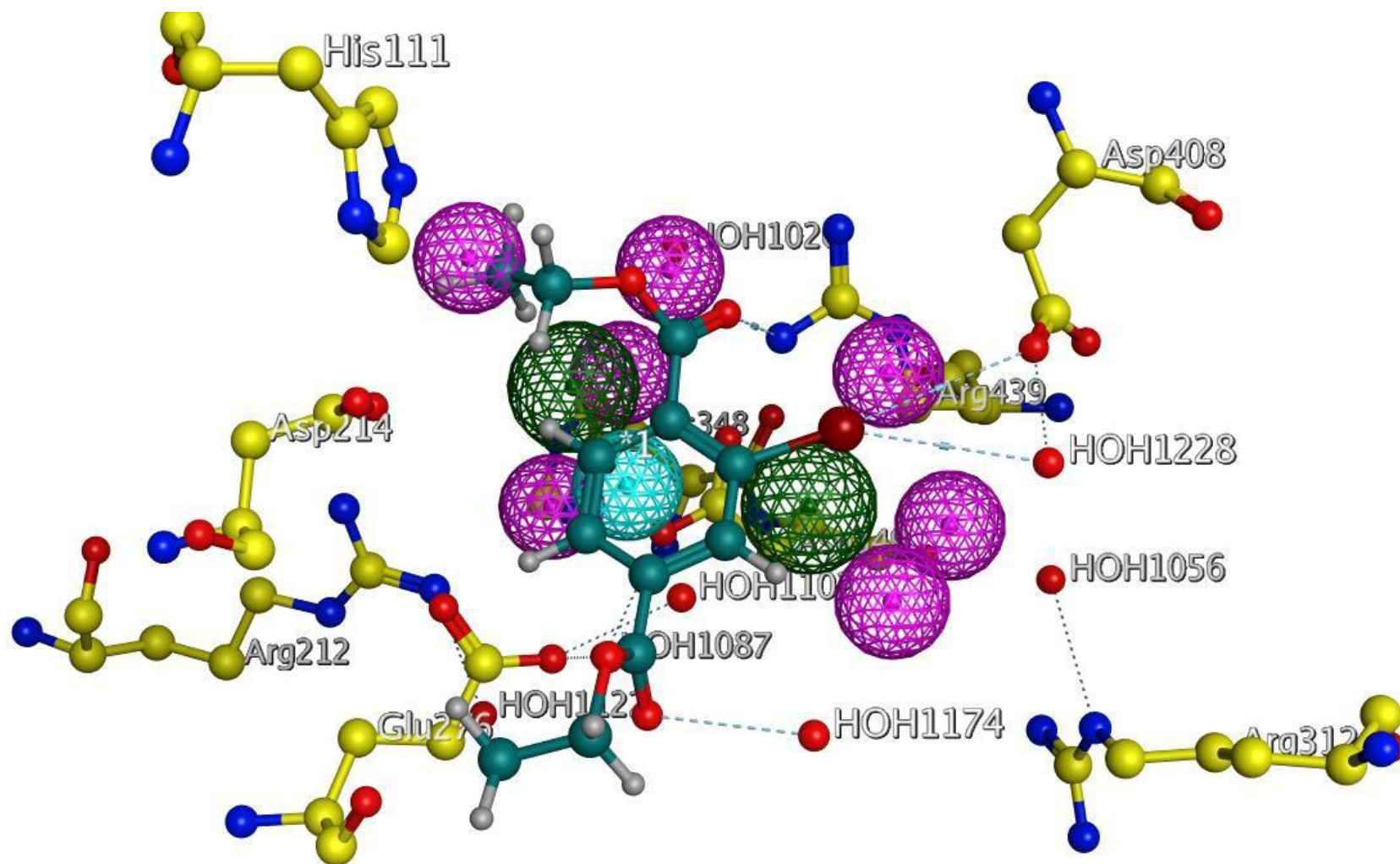


Figure S5. Superimposed view of Compound 2 on Ph-1. Ligand is shown in green stick model, interacting residues are shown in yellow stick model. Water molecules are shown in red ball. Hydrogen bonds are depicted in cyan dotted lines. H-bond Don/Acc Hydrophobic features, H-bond Acceptor feature are presented in magenta spheres, dark green spheres and cyan sphere, respectively

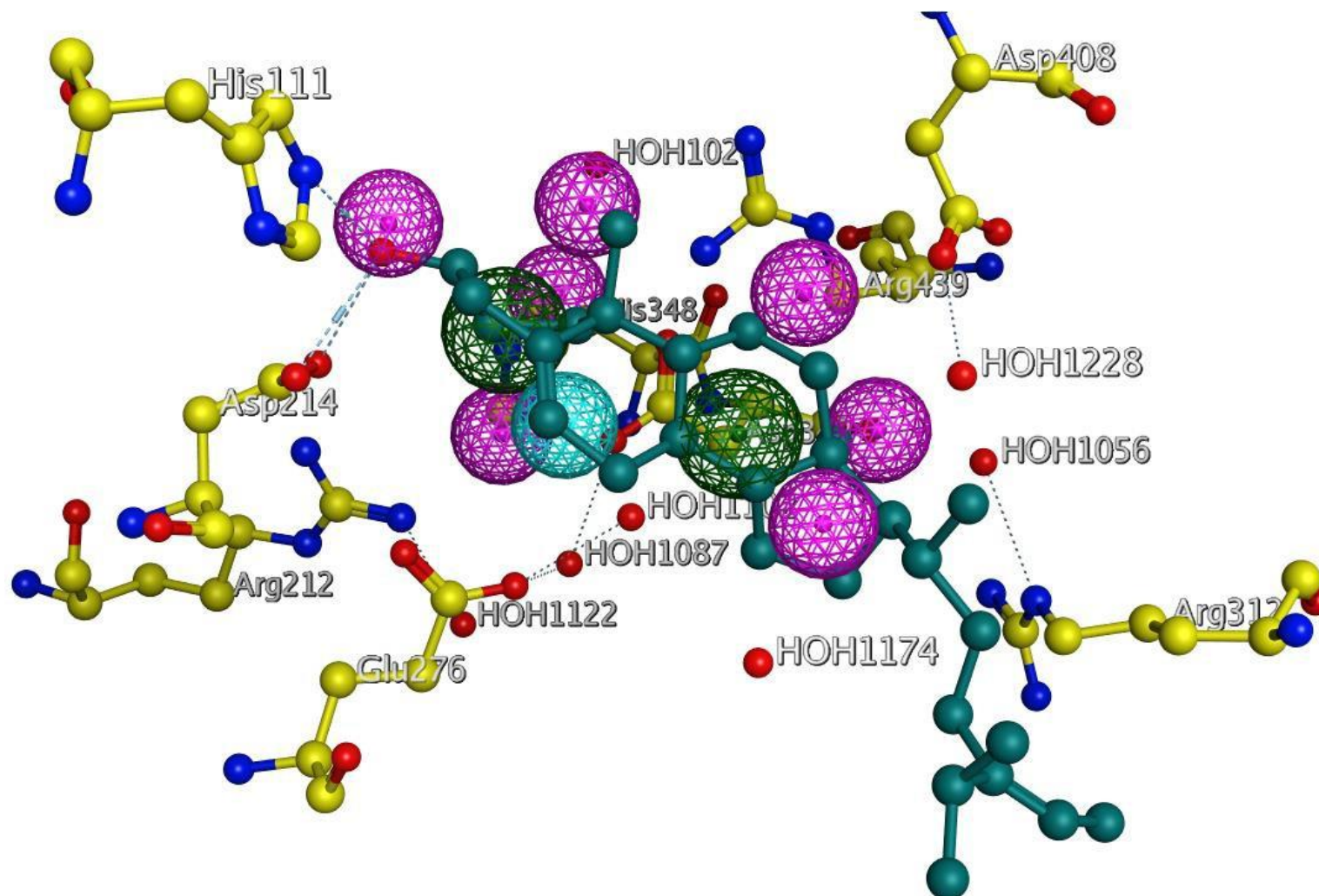


Figure S6. Superimposed view of Compound 3 on Ph-1. Ligand is shown in green stick model, interacting residues are shown in yellow stick model. Water molecules are shown in red ball. Hydrogen bonds are depicted in cyan dotted lines. H-bond Don/Acc Hydrophobic features, H-bond Acceptor feature are presented in magenta spheres, dark green spheres and cyan sphere, respectively

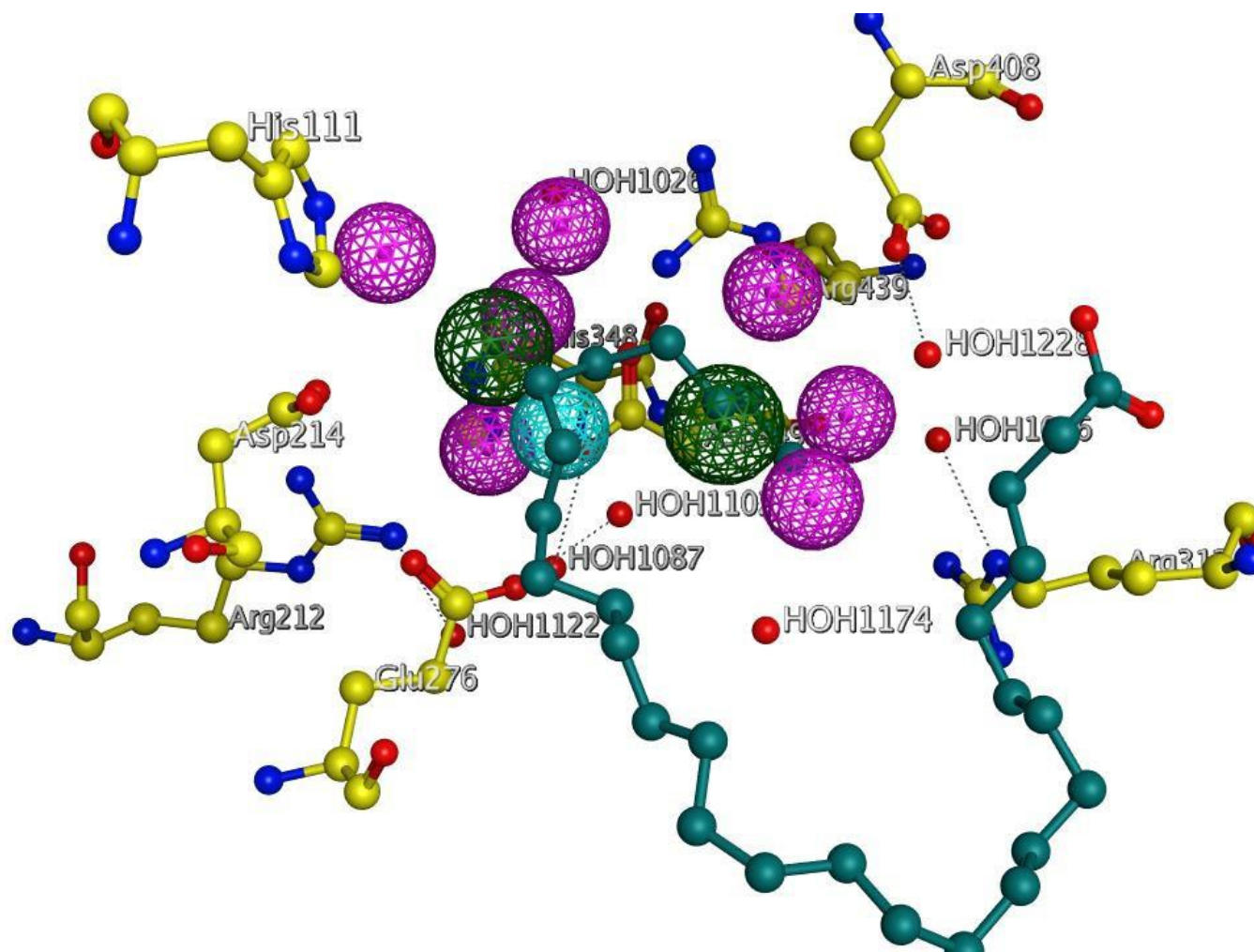


Figure S7. Superimposed view of Compound 6 on Ph-1. Ligand is shown in green stick model, interacting residues are shown in yellow stick model. Water molecules are shown in red ball. Hydrogen bonds are depicted in cyan dotted lines. H-bond Don/Acc Hydrophobic features, H-bond Acceptor feature are presented in magenta spheres, dark green spheres and cyan sphere, respectively

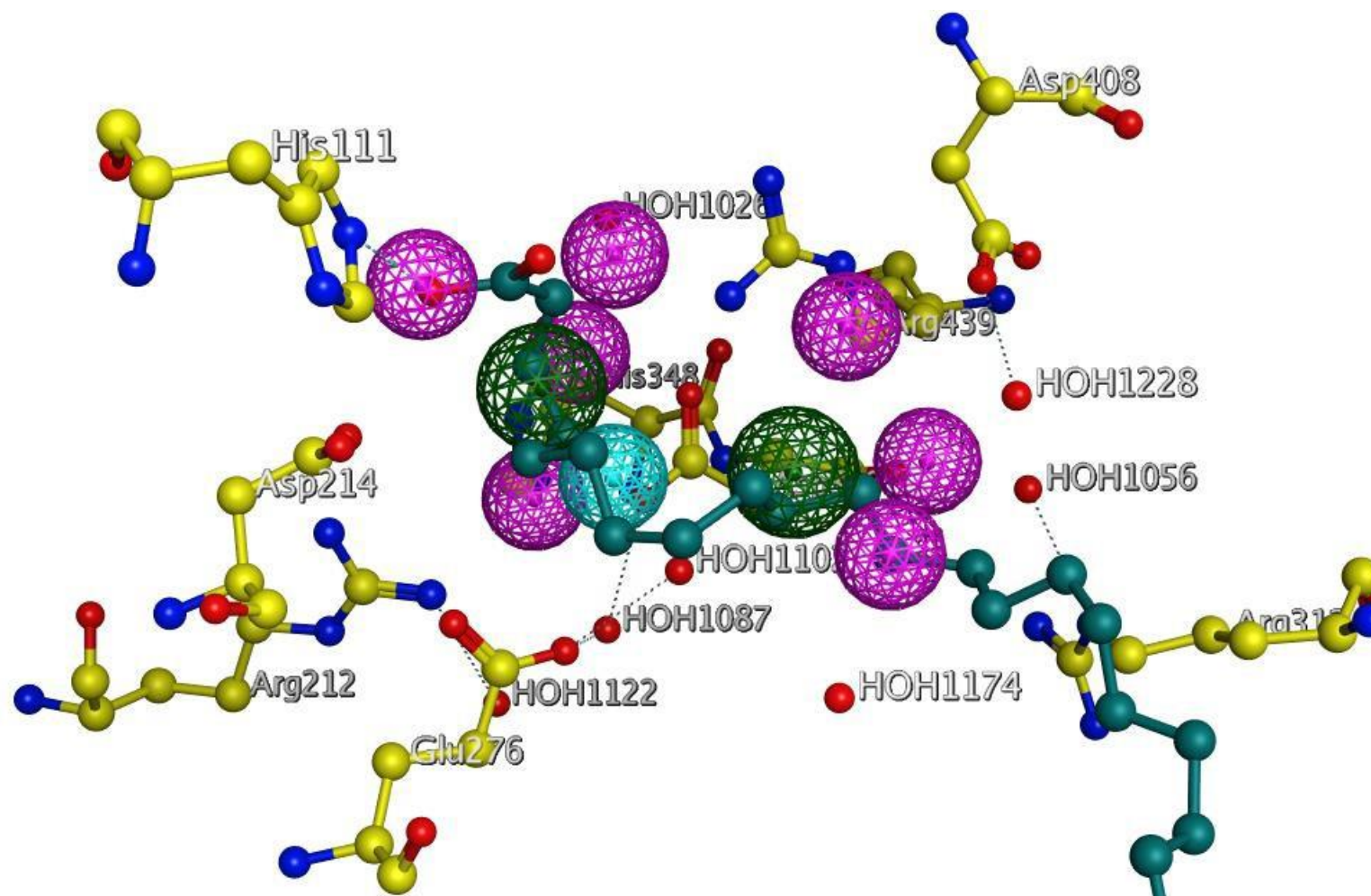


Figure S8. Superimposed view of Compound 7 on Ph-1. Ligand is shown in green stick model, interacting residues are shown in yellow stick model. Water molecules are shown in red ball. Hydrogen bonds are depicted in cyan dotted lines. H-bond Don/Acc Hydrophobic features, H-bond Acceptor feature are presented in magenta spheres, dark green spheres and cyan sphere, respectively

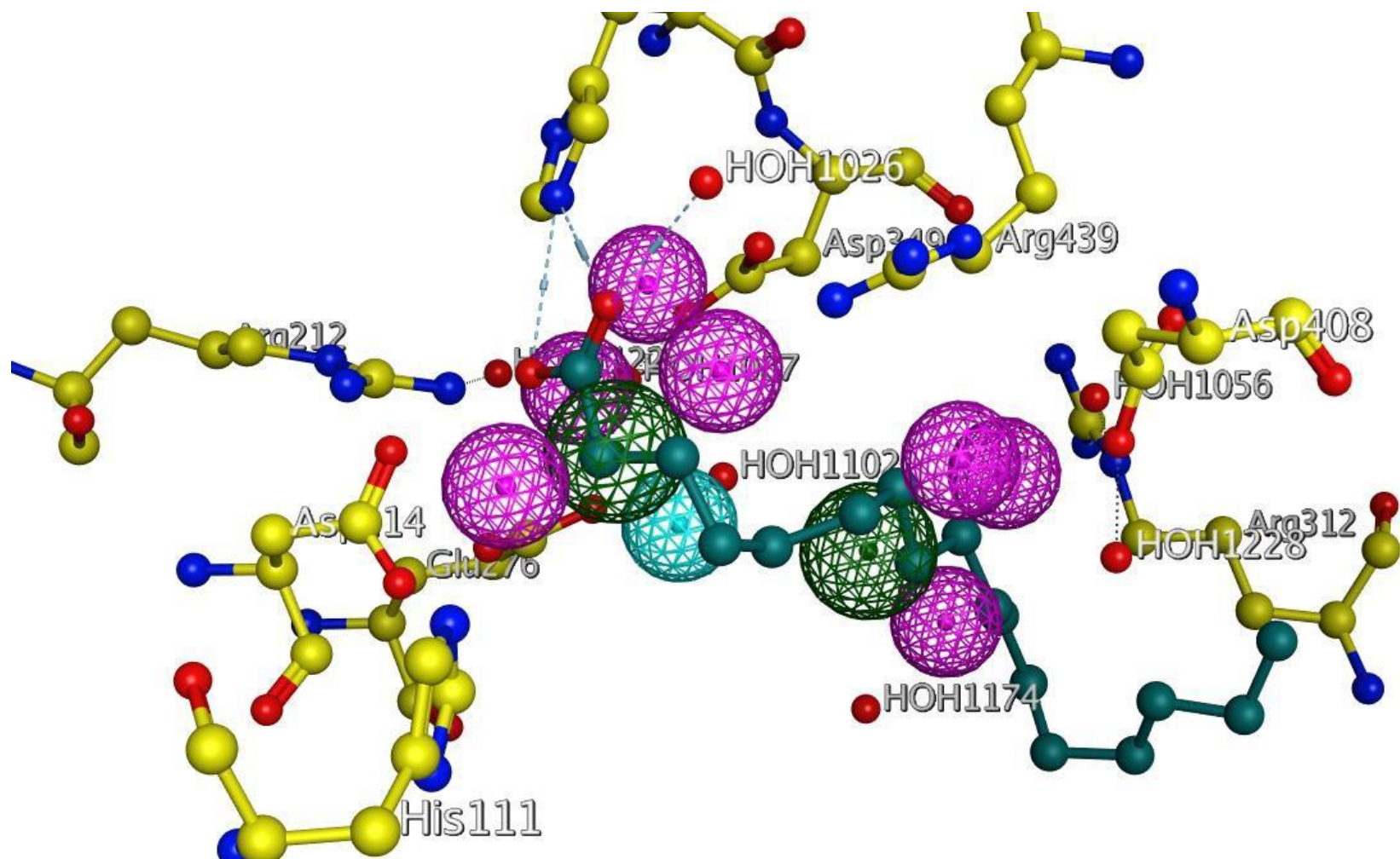


Figure S9. Superimposed view of Compound 8 on Ph-1. Ligand is shown in green stick model, interacting residues are shown in yellow stick model. Water molecules are shown in red ball. Hydrogen bonds are depicted in cyan dotted lines. H-bond Don/Acc Hydrophobic features, H-bond Acceptor feature are presented in magenta spheres, dark green spheres and cyan sphere, respectively

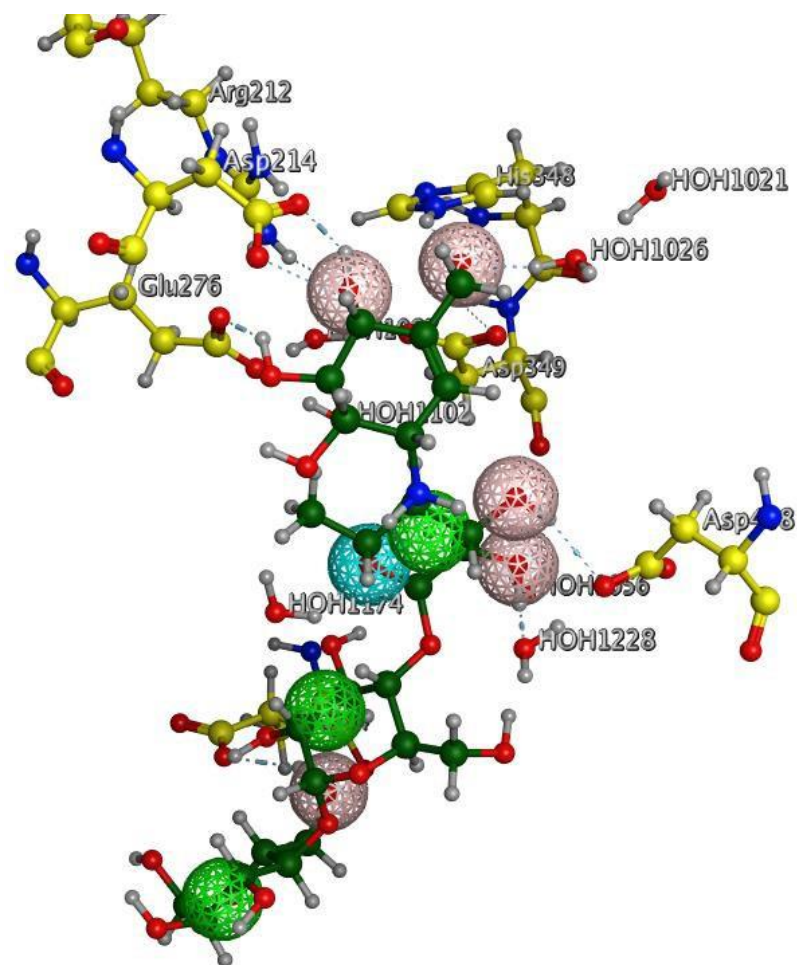


Figure S10. Structure-based pharmacophore model (called Ph-2) generated by *S. cerevisiae* α -glucosidase enzyme in complex with Acarbose (inhibitor). Acarbose is shown in green stick model, interacting residues are shown in yellow stick model. Water molecules are shown in red ball. Hydrogen bonds are depicted in cyan dotted lines. Five H-bond donor/Acceptor (Don/Acc) features are presented in light pink spheres. Hydrophobic features are shown in dark green spheres. One H-bond Acceptor (Acc) feature is presented in cyan sphere.

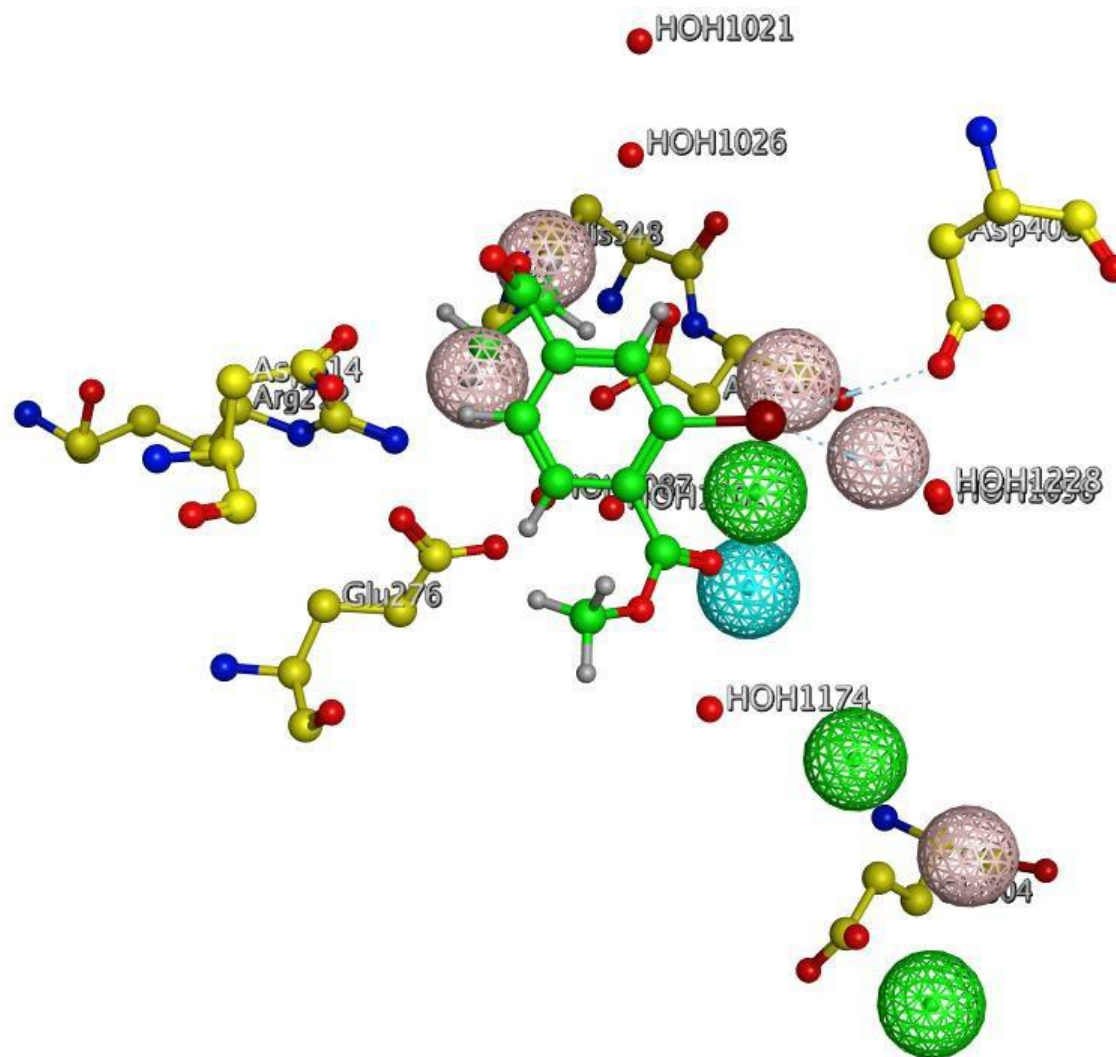


Figure S11. Superimposed view of Compound 1 on Ph-2. Ligand is shown in green stick model, interacting residues are shown in yellow stick model. Water molecules are shown in red ball. Hydrogen bonds are depicted in cyan dotted lines. H-bond Don/Acc Hydrophobic features, H-bond Acceptor feature are presented in light pink spheres, dark green spheres and cyan sphere, respectively

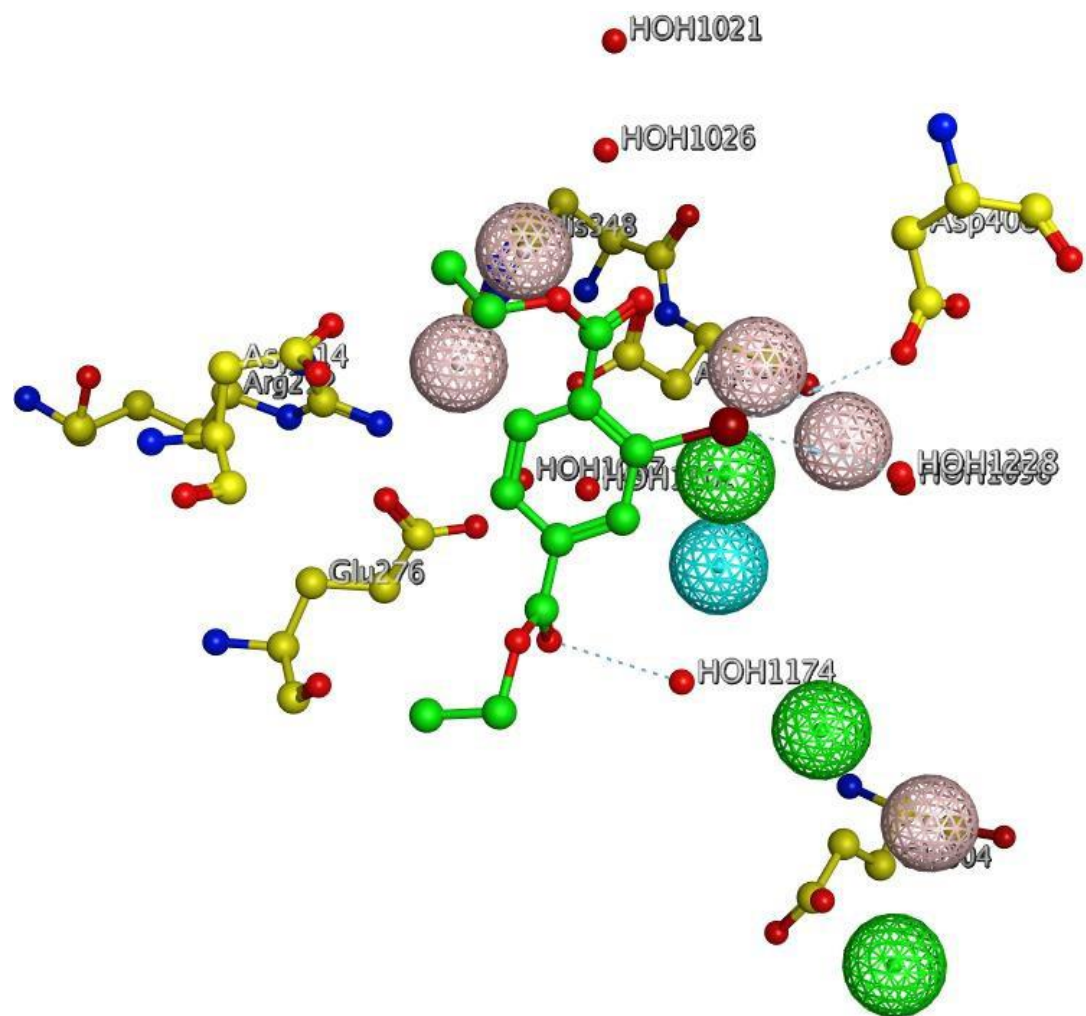


Figure S12. Superimposed view of Compound 2 on Ph-2. Ligand is shown in green stick model, interacting residues are shown in yellow stick model. Water molecules are shown in red ball. Hydrogen bonds are depicted in cyan dotted lines. H-bond Don/Acc Hydrophobic features, H-bond Acceptor feature are presented in light pink spheres, dark green spheres and cyan sphere, respectively

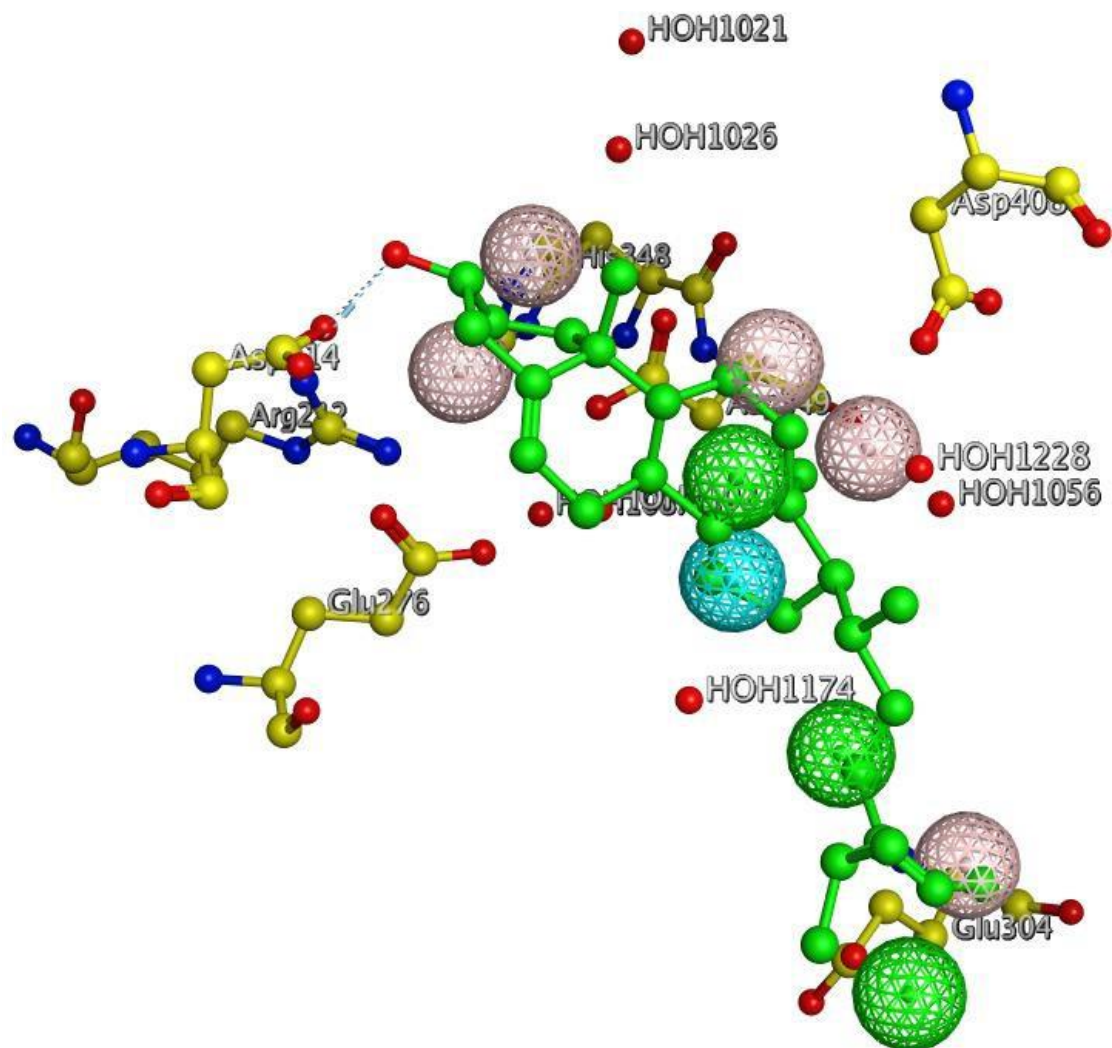


Figure S13 Superimposed view of Compound 3 on Ph-2. Ligand is shown in green stick model, interacting residues are shown in yellow stick model. Water molecules are shown in red ball. Hydrogen bonds are depicted in cyan dotted lines. H-bond Don/Acc Hydrophobic features, H-bond Acceptor feature are presented in light pink spheres, dark green spheres and cyan sphere, respectively

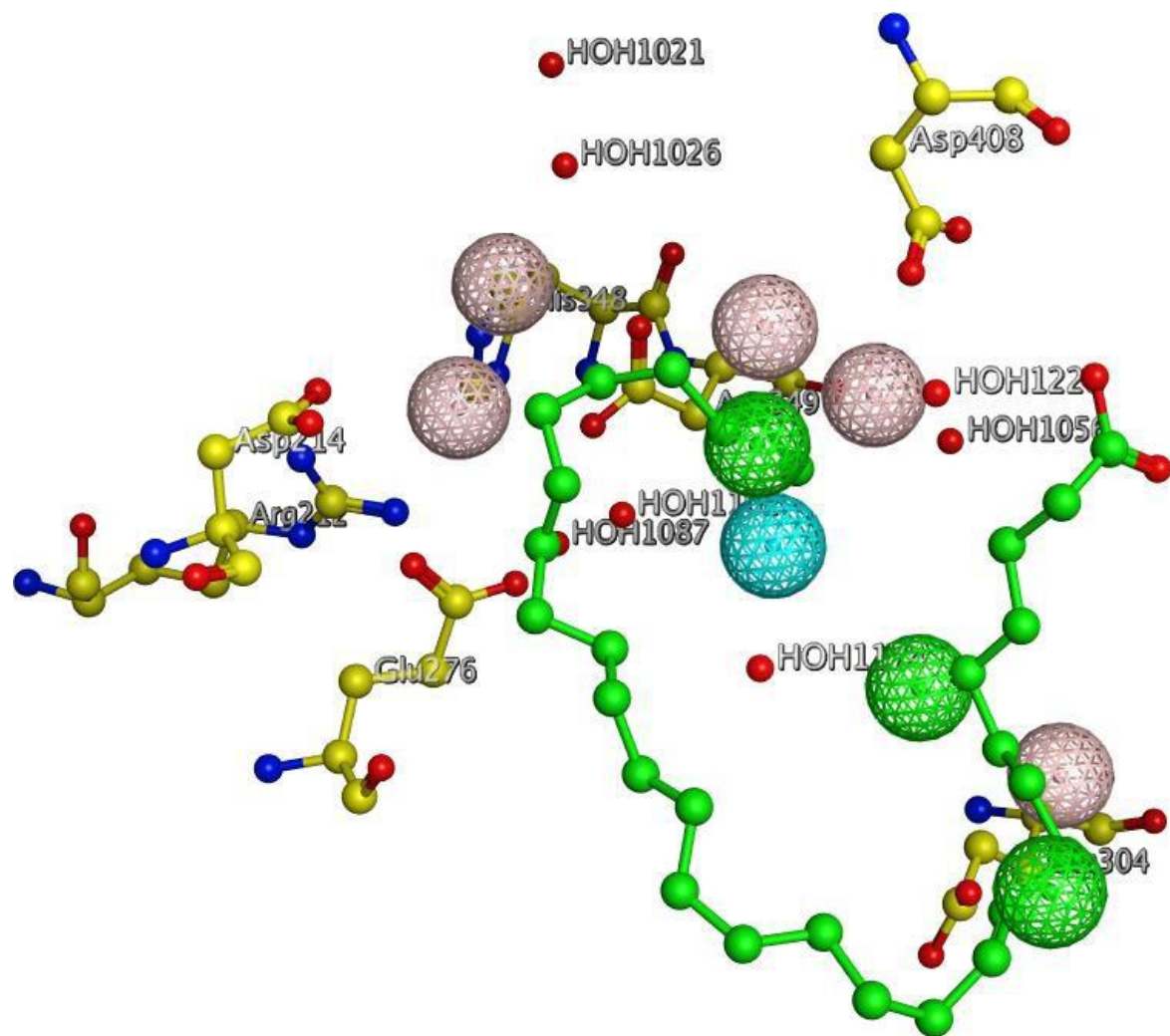


Figure S14. Superimposed view of Compound 6 on Ph-2. Ligand is shown in green stick model, interacting residues are shown in yellow stick model. Water molecules are shown in red ball. Hydrogen bonds are depicted in cyan dotted lines. H-bond Don/Acc Hydrophobic features, H-bond Acceptor feature are presented in light pink spheres, dark green spheres and cyan sphere, respectively

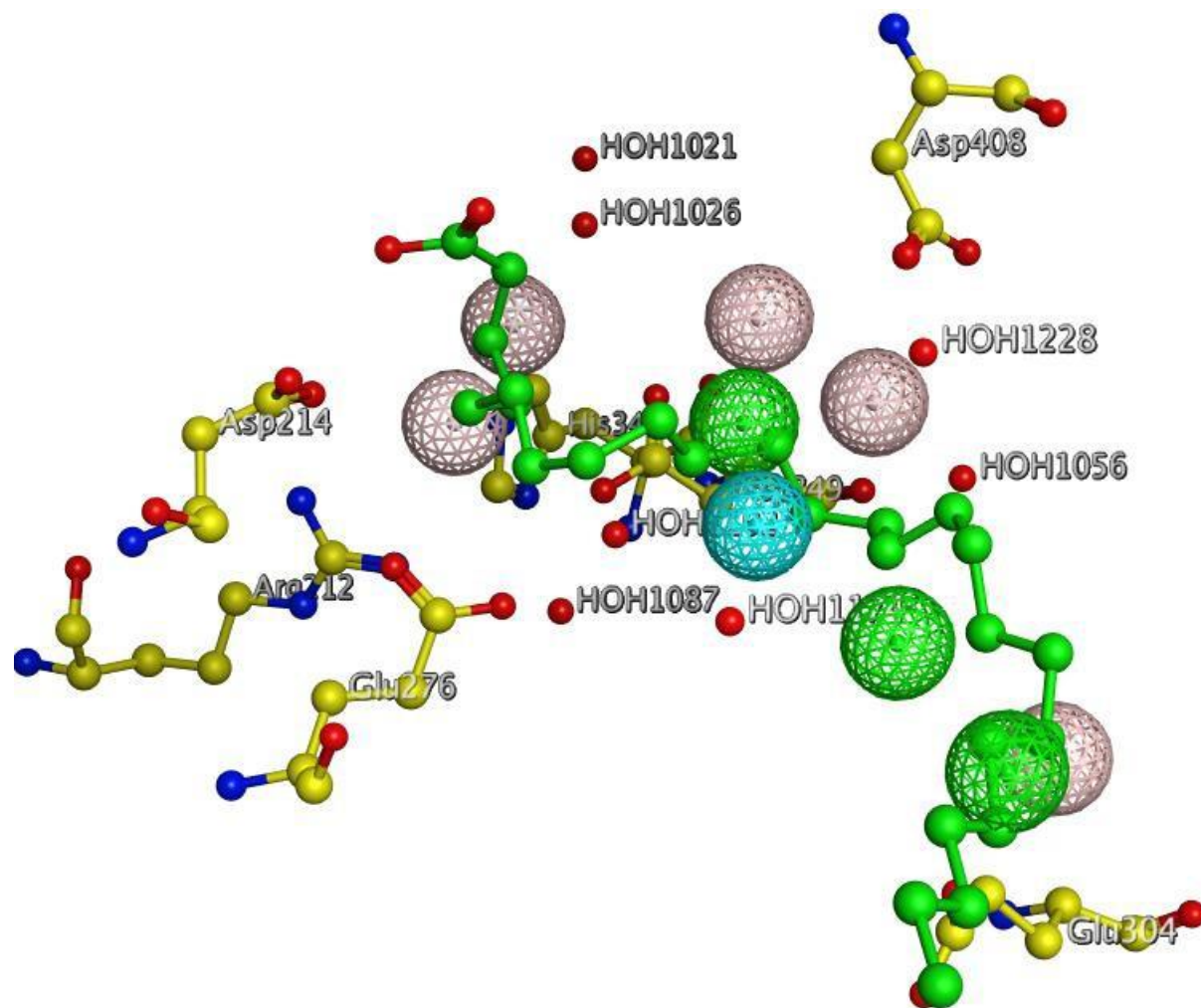


Figure S15. Superimposed view of Compound 7 on Ph-2. Ligand is shown in green stick model, interacting residues are shown in yellow stick model. Water molecules are shown in red ball. Hydrogen bonds are depicted in cyan dotted lines. H-bond Don/Acc Hydrophobic features, H-bond Acceptor feature are presented in light pink spheres, dark green spheres and cyan sphere, respectively

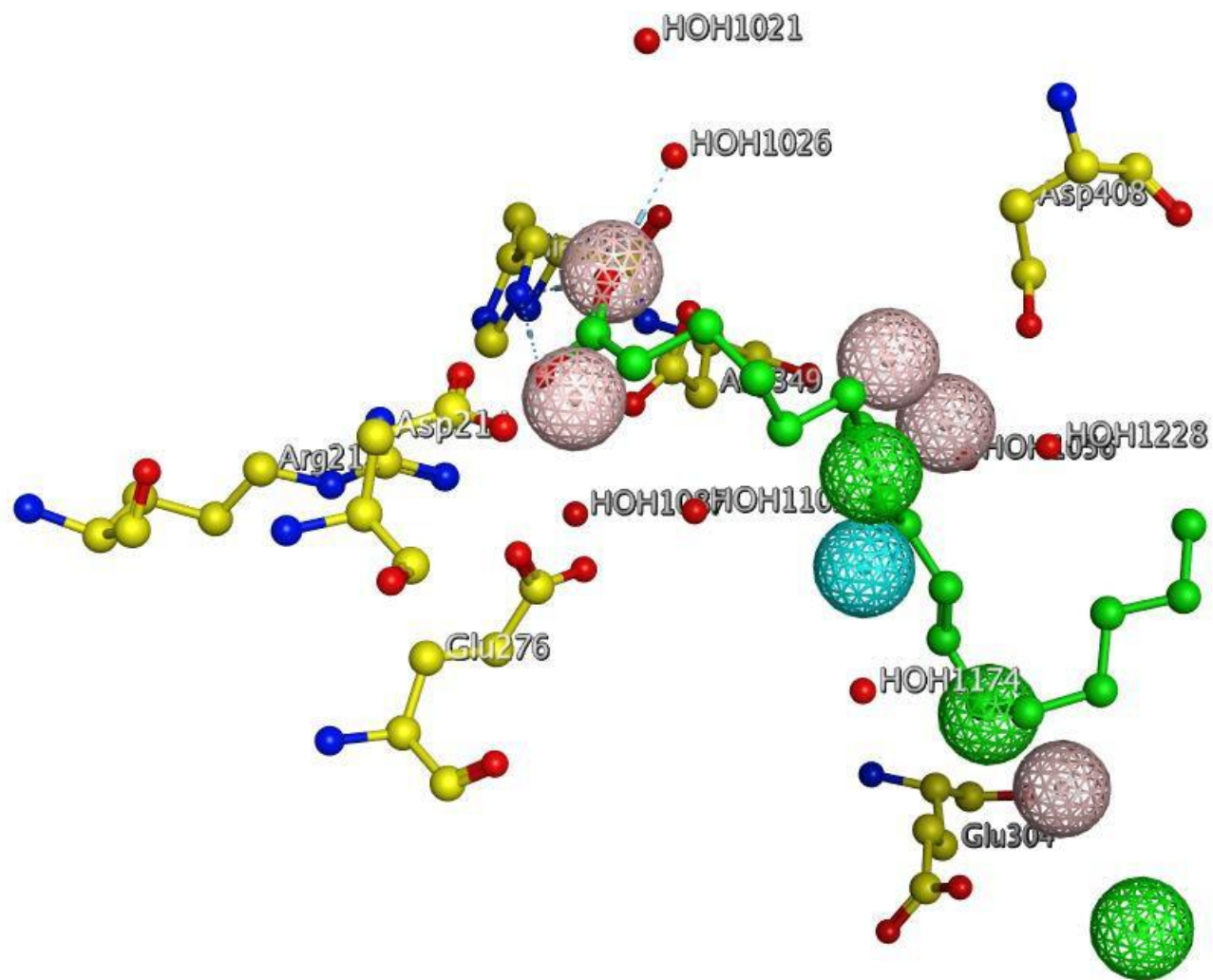


Figure S16. Superimposed view of Compound 8 on Ph-2. Ligand is shown in green stick model, interacting residues are shown in yellow stick model. Water molecules are shown in red ball. Hydrogen bonds are depicted in cyan dotted lines. H-bond Don/Acc Hydrophobic features, H-bond Acceptor feature are presented in light pink spheres, dark green spheres and cyan sphere, respectively.

NMR Spectra and HRMS of the Isolated Compounds

Figure S17. ¹H-NMR (600 MHz, CDCl₃) of compound 1

Figure S18. ¹³C-NMR (150 MHz, CDCl₃) Spectrum of Compound 1

Figure S19. DEPT 135 of compound 1

Figure S20. DEPT 90 of compound 1

Figure S20. HRMS (ESI+) of compound 1

Figure S22. ¹H-NMR (600 MHz, CDCl₃) of compound 2

Figure S23. ¹³C-NMR (150 MHz, CDCl₃) of compound 2

Figure S24. DEPT 135 of compound 2

Figure S25. DEPT 90 of compound 2

Figure S26. HRMS (ESI+) of compound 2

Figure S27. ¹H-NMR (600 MHz, CDCl₃) of compound 3

Figure S28. ¹³C-NMR (150 MHz, CDCl₃) of compound 3

Figure S29. HRMS (ESI+) of compound 3

Figure S30. ¹H-NMR (600 MHz, CDCl₃) of compound 4

Figure S31. ¹³C-NMR (150 MHz, CDCl₃) of compound **4**

Figure S32. HRMS (ESI+) of compound **4**

Figure S33. ¹H-NMR (600 MHz, CDCl₃) of compound **5**

Figure S34. ¹³C-NMR (150 MHz, CDCl₃) of compound **5**

Figure S35. HRMS (ESI+) of compound **5**

Figure S36. ¹H-NMR (600 MHz, CDCl₃) of compound **6**

Figure S37. ¹³C-NMR (150 MHz, CDCl₃) of compound **6**

Figure S38. HRMS (ESI+) of compound **6**

Figure S39. ¹H-NMR (600 MHz, CDCl₃) of compound **7**

Figure S40. ¹³C-NMR (150 MHz, CDCl₃) of compound **7**

Figure S41. HRMS (ESI+) of compound **7**

Figure S42. ¹H-NMR (600 MHz, CDCl₃) of compound **8**

Figure S43. ¹³C-NMR (150 MHz, CDCl₃) of compound **8**

Figure S44. HRMS (ESI+) of compound **8**

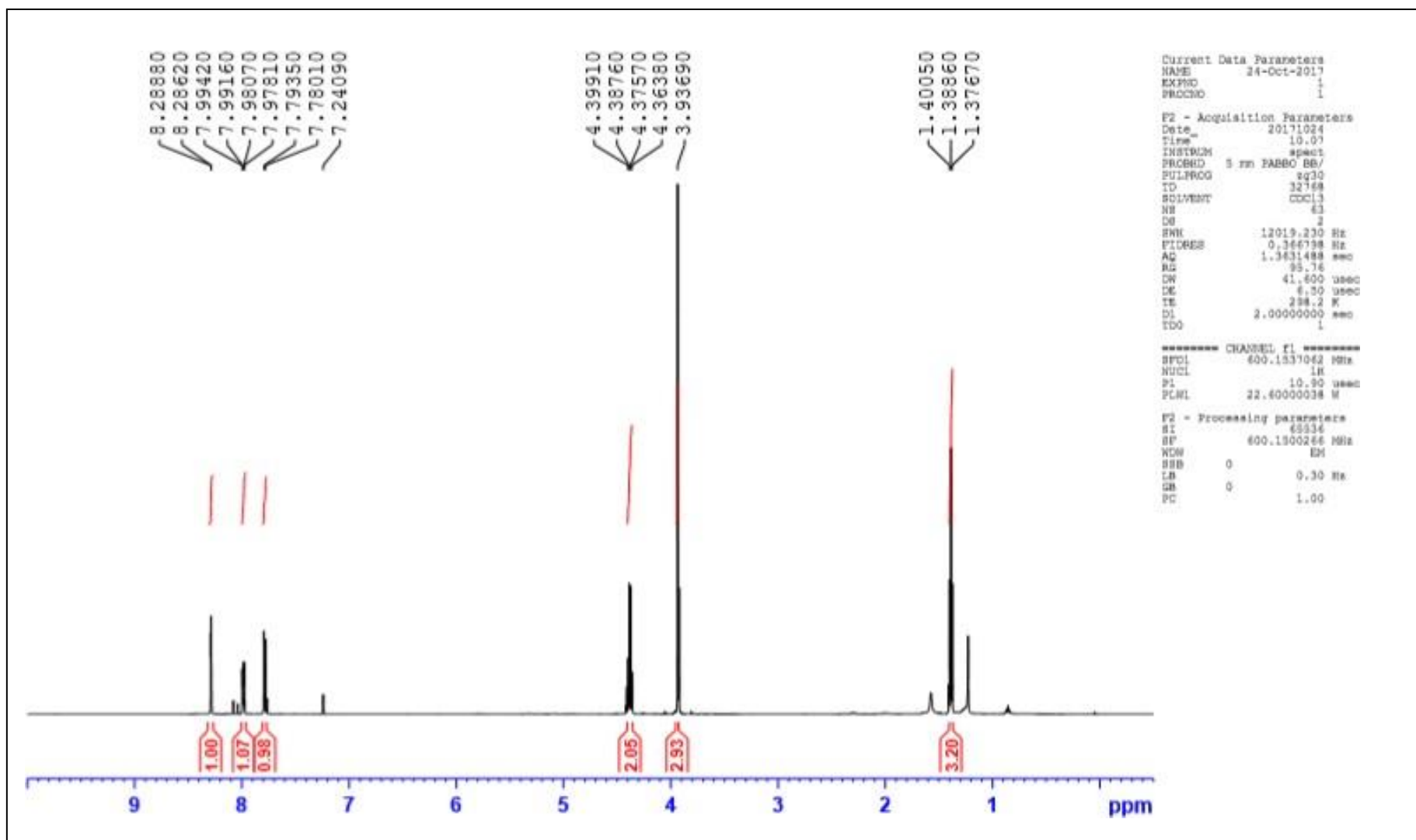


Figure S17. $^1\text{H-NMR}$ (600 MHz, CDCl_3) of compound 1

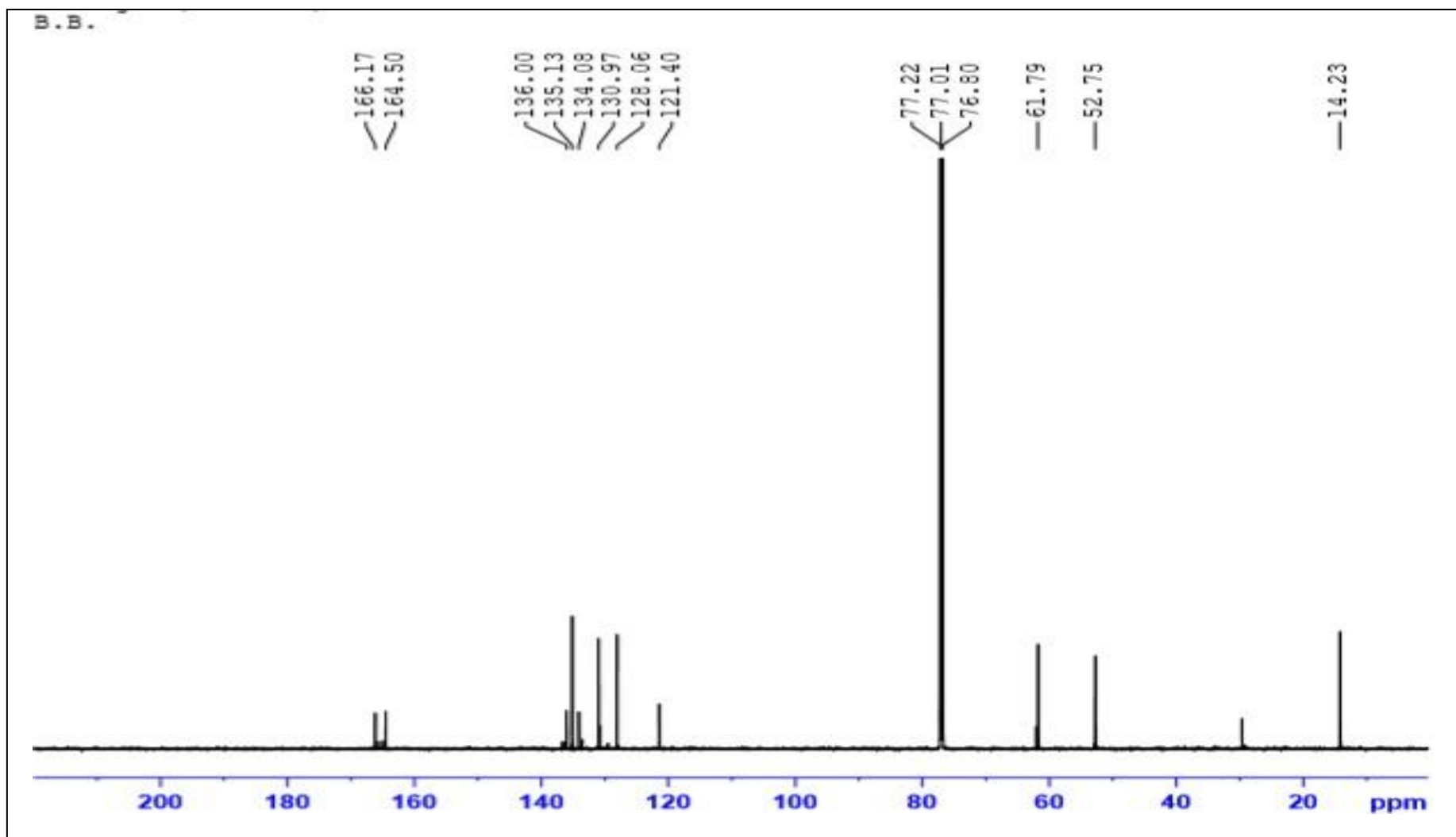


Figure S18. ^{13}C -NMR (150 MHz, CDCl_3) of compound 1

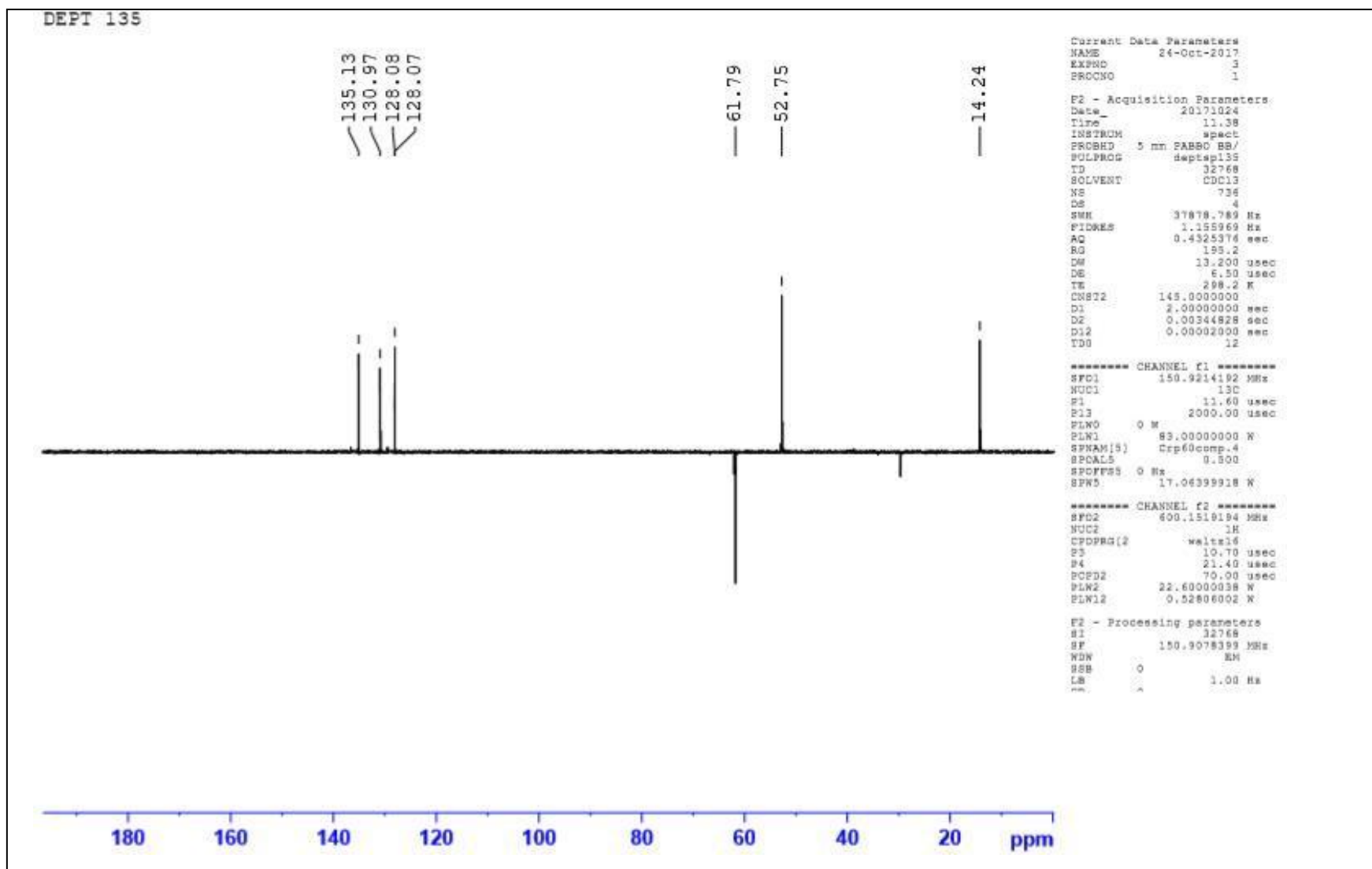


Figure S19. DEPT 135 of compound 1

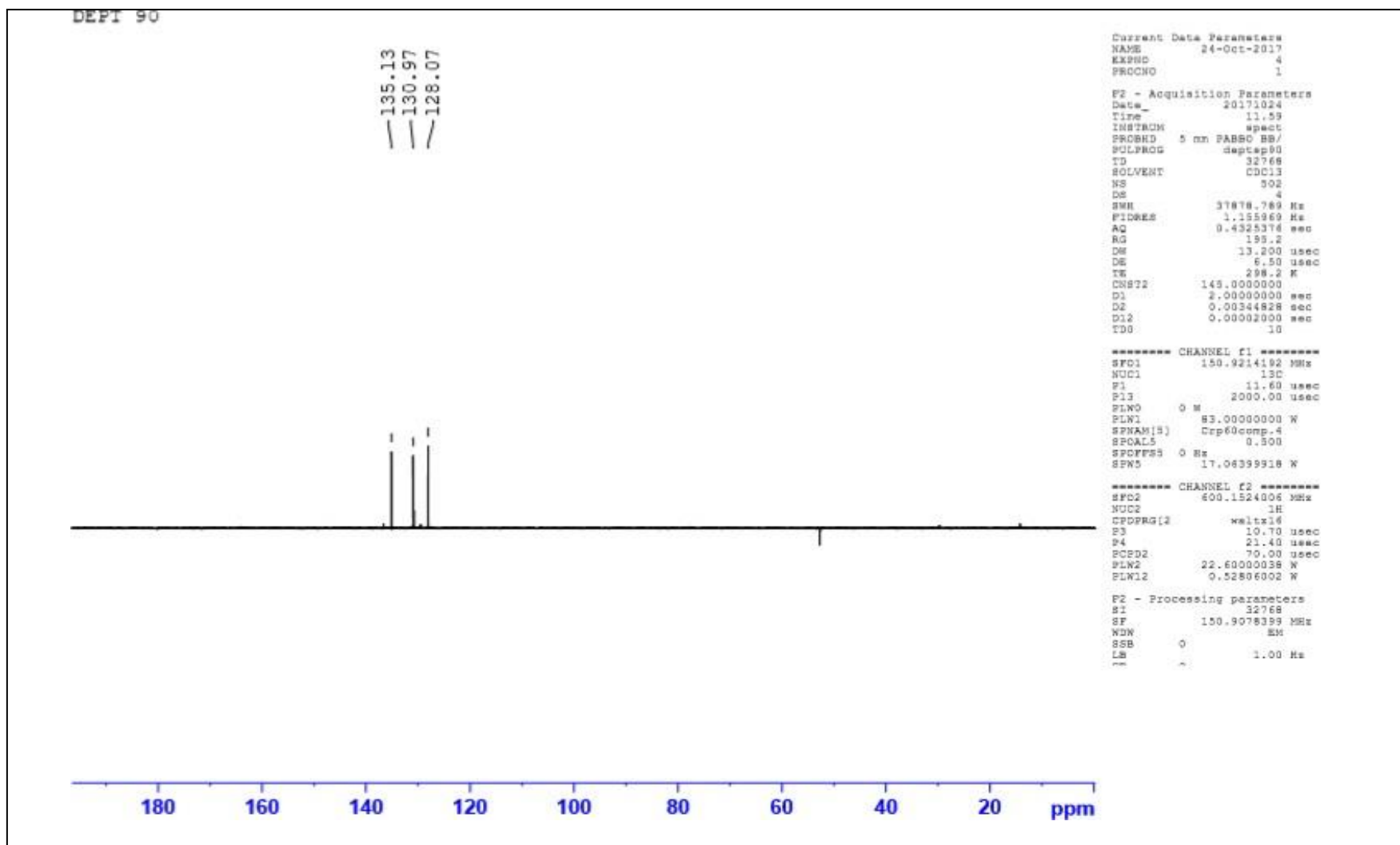


Figure S20. DEPT 90 of compound 1

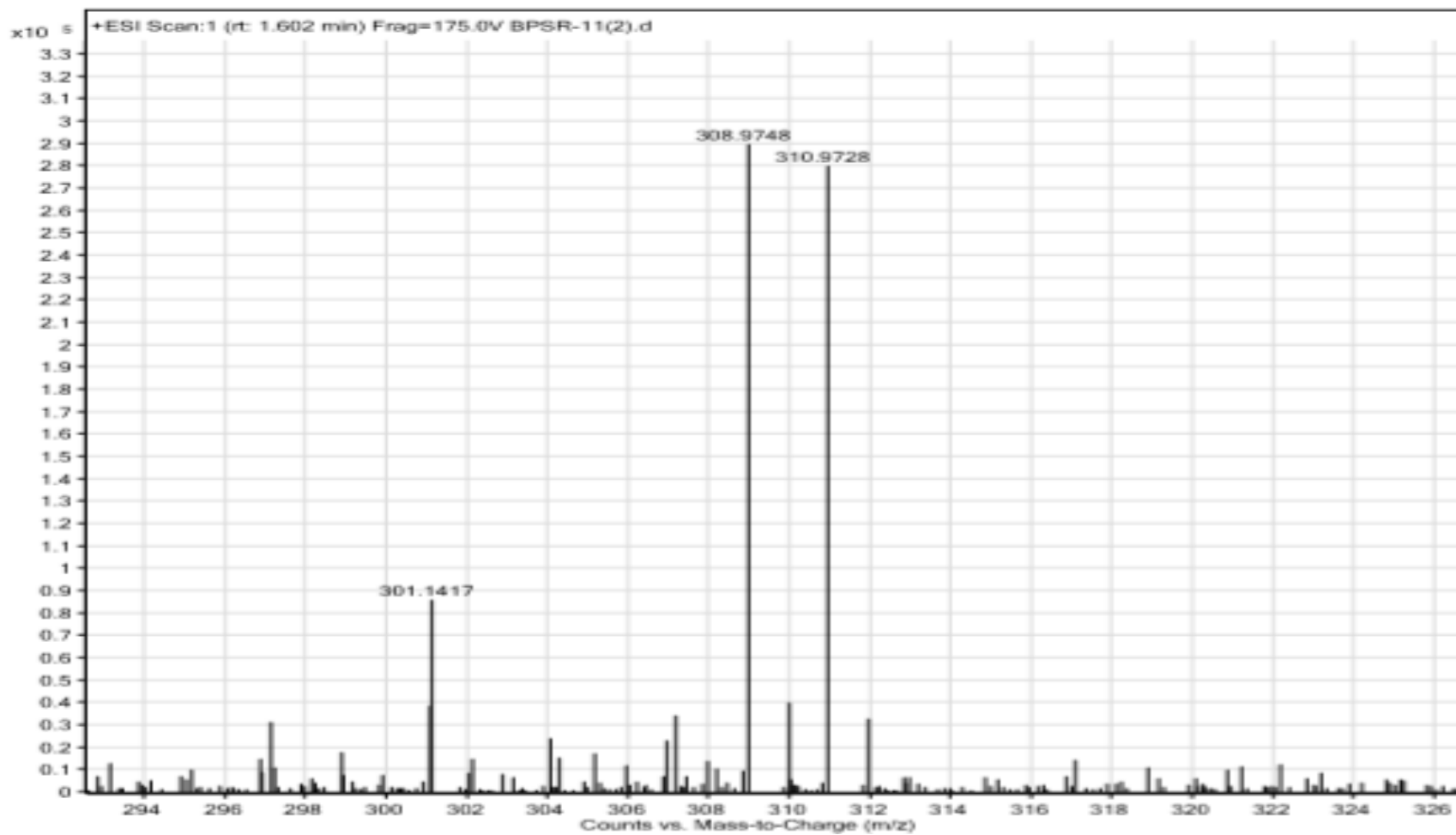


Figure S21. HRMS (ESI+) of compound 1

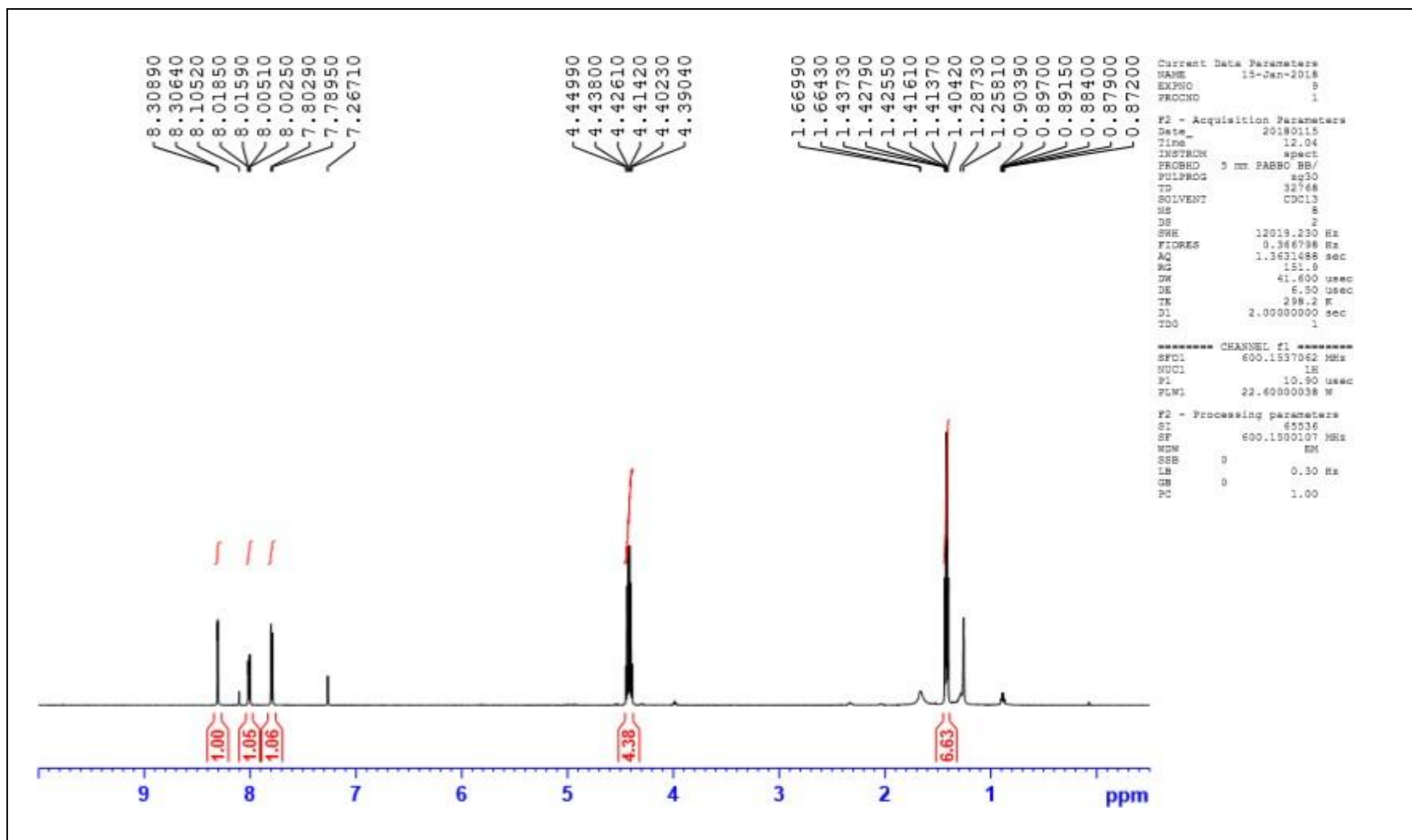


Figure S22. $^1\text{H-NMR}$ (600 MHz, CDCl_3) of compound 2

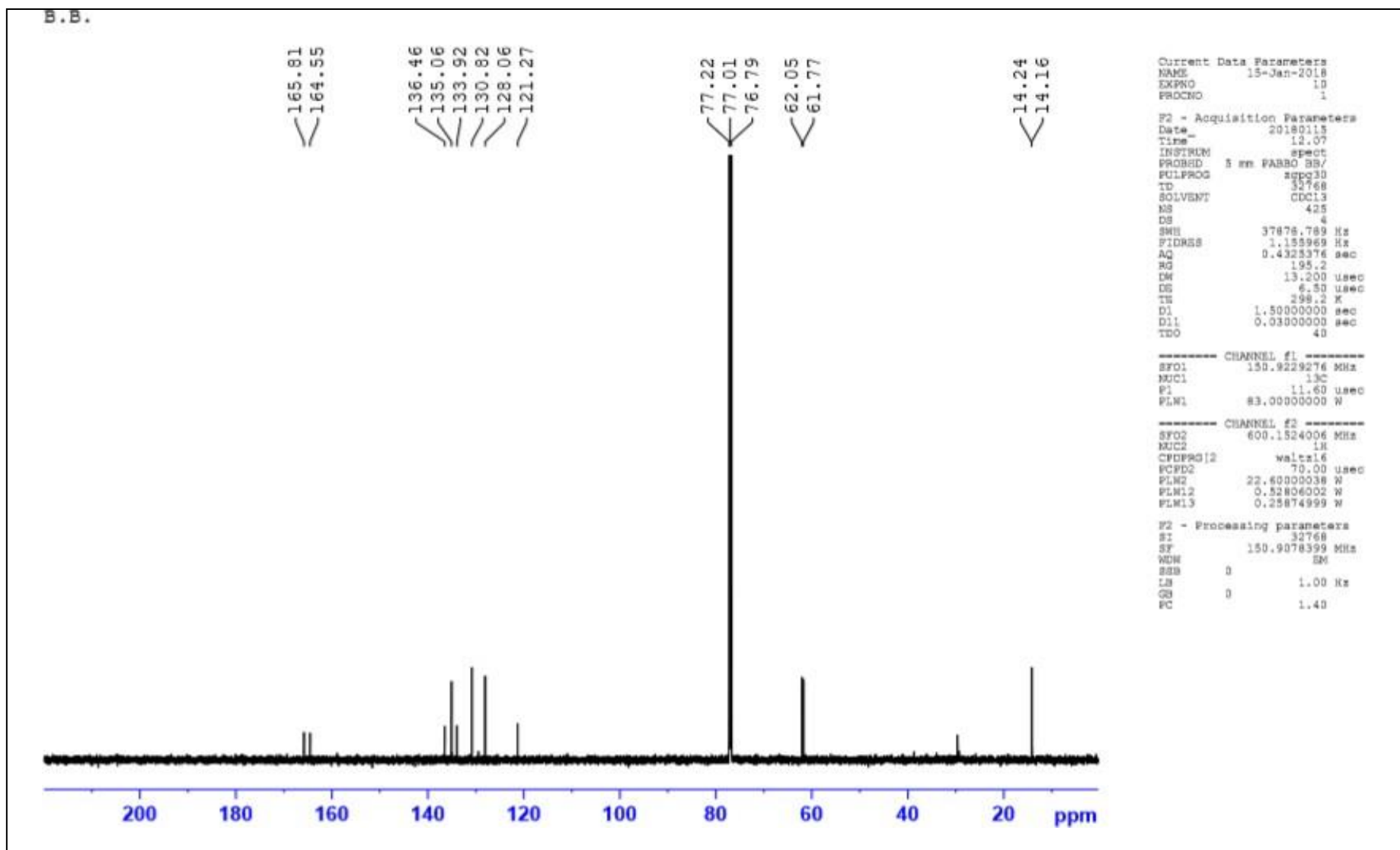


Figure S23. ^{13}C -NMR (150 MHz, CDCl_3) of compound 2

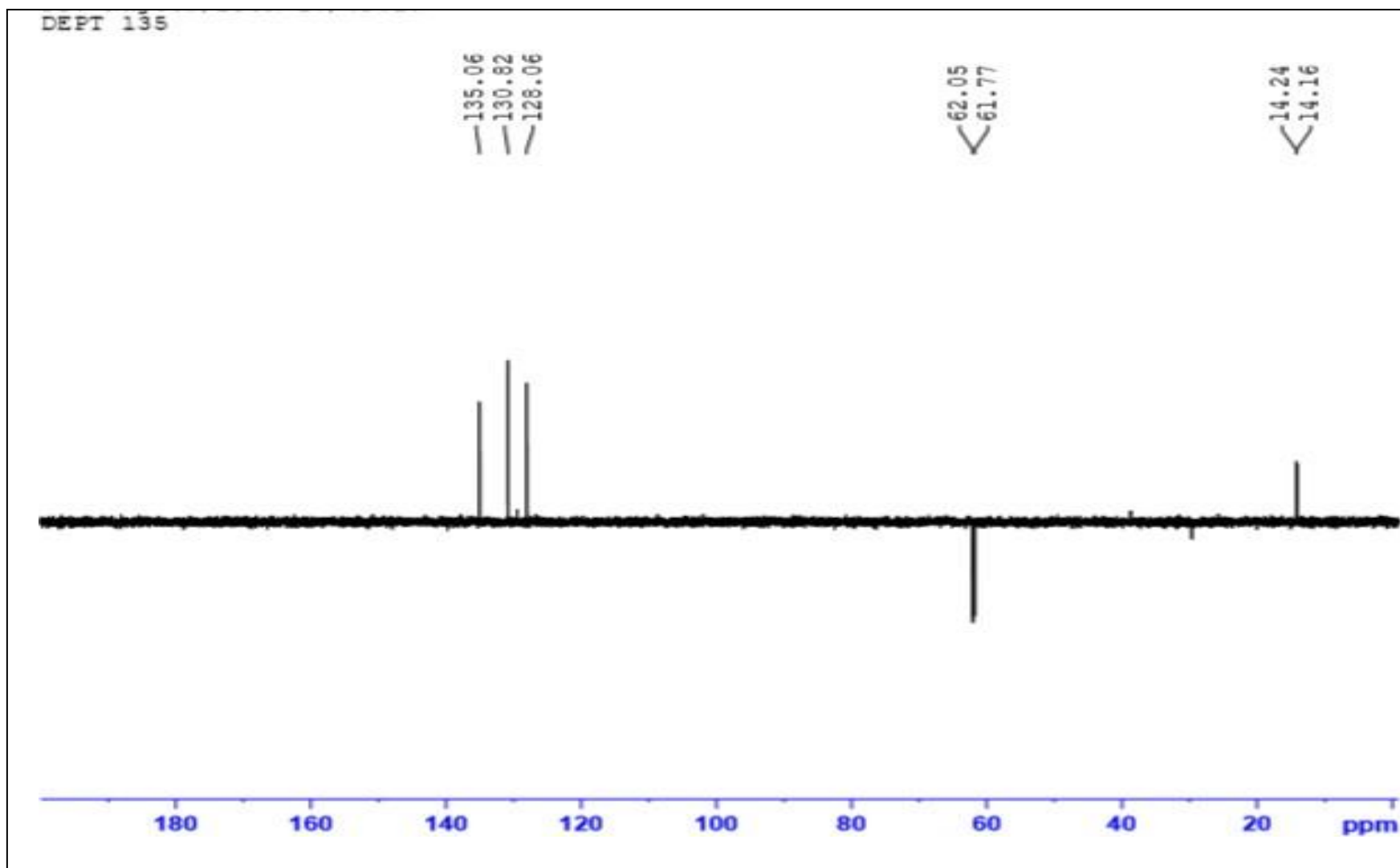


Figure S24. DEPT 135 of compound 2

Dr. Najeeb/BPSR-10/CDC13
DEPT 90



135.06
130.82
128.06

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EXPNO     12
PROCNO    1

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SWH        1.355969 Hz
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AQ         193.2
RG         33.200 usec
DE         6.50 usec
TE        298.2 K
CDSF2     145.0000000
D1         2.0000000 sec
D2         0.00344828 sec
D12        0.00002000 sec
TD         3

----- CHANNEL f1 -----
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P1         11.80 usec
P13        2000.00 usec
P1M0       0 W
P1M1      83.00000000 W
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----- CHANNEL f2 -----
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NUC2       1H
CPOFFS[2]  waltz16
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PCPD2     70.00 usec
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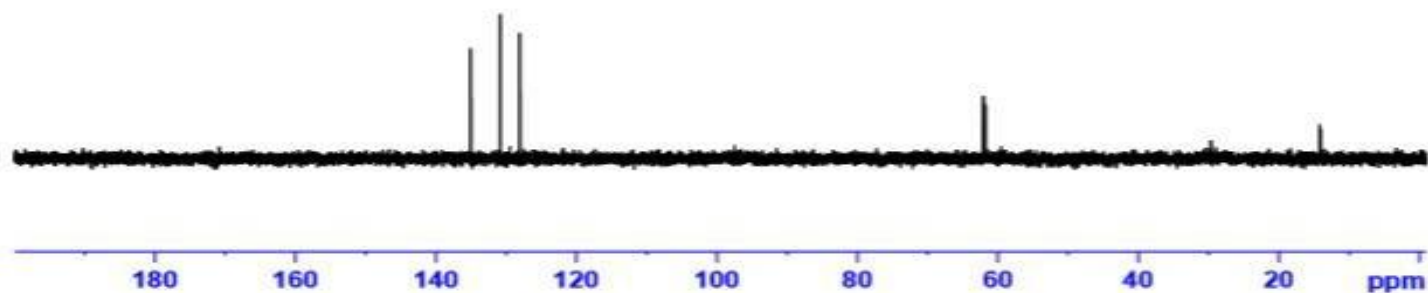


Figure S25. DEPT 90 of compound 2

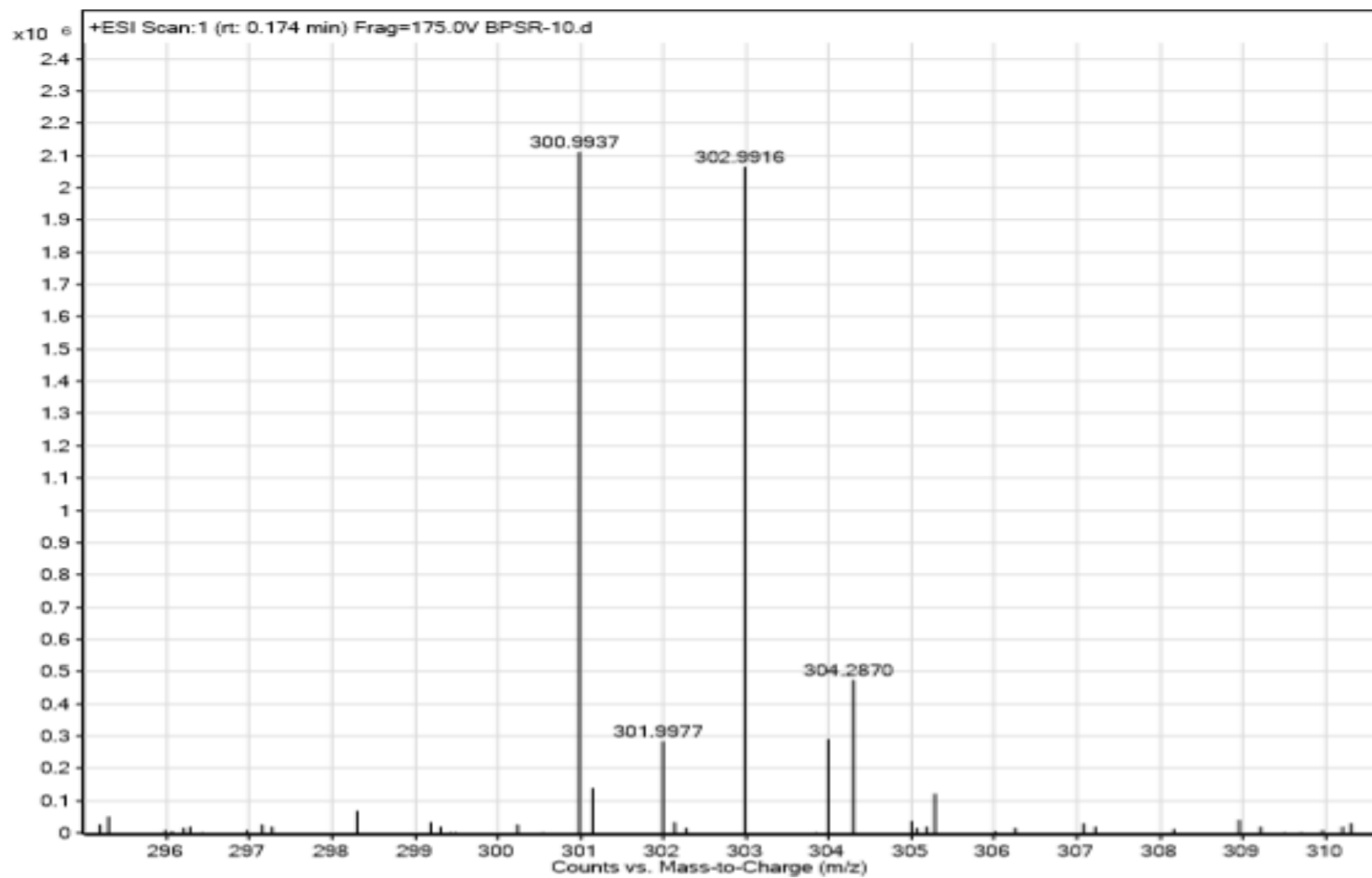


Figure S26. HRMS (ESI+) of compound 2

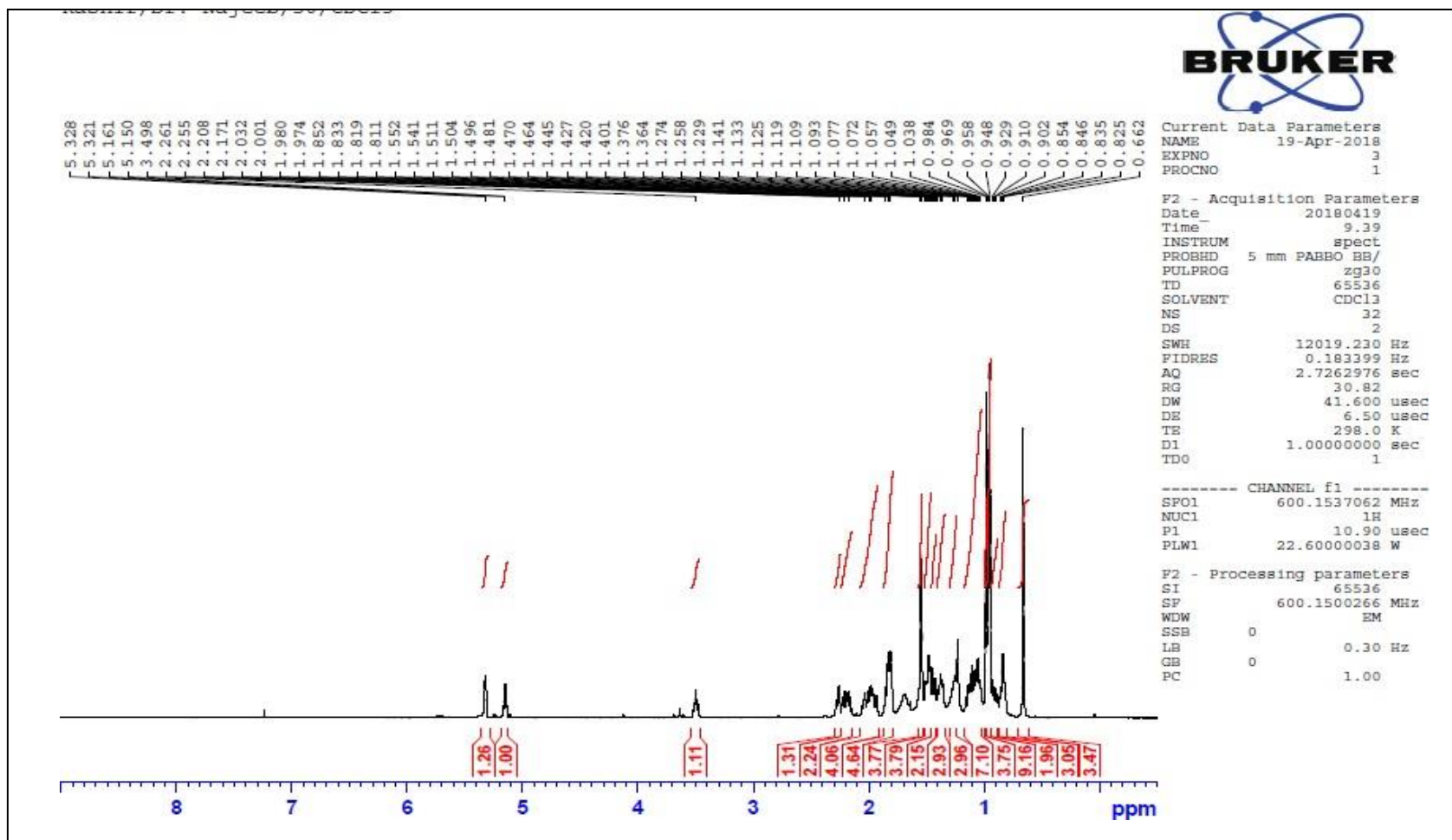


Figure S30. $^1\text{H-NMR}$ (600 MHz, CDCl_3) of compound **3**

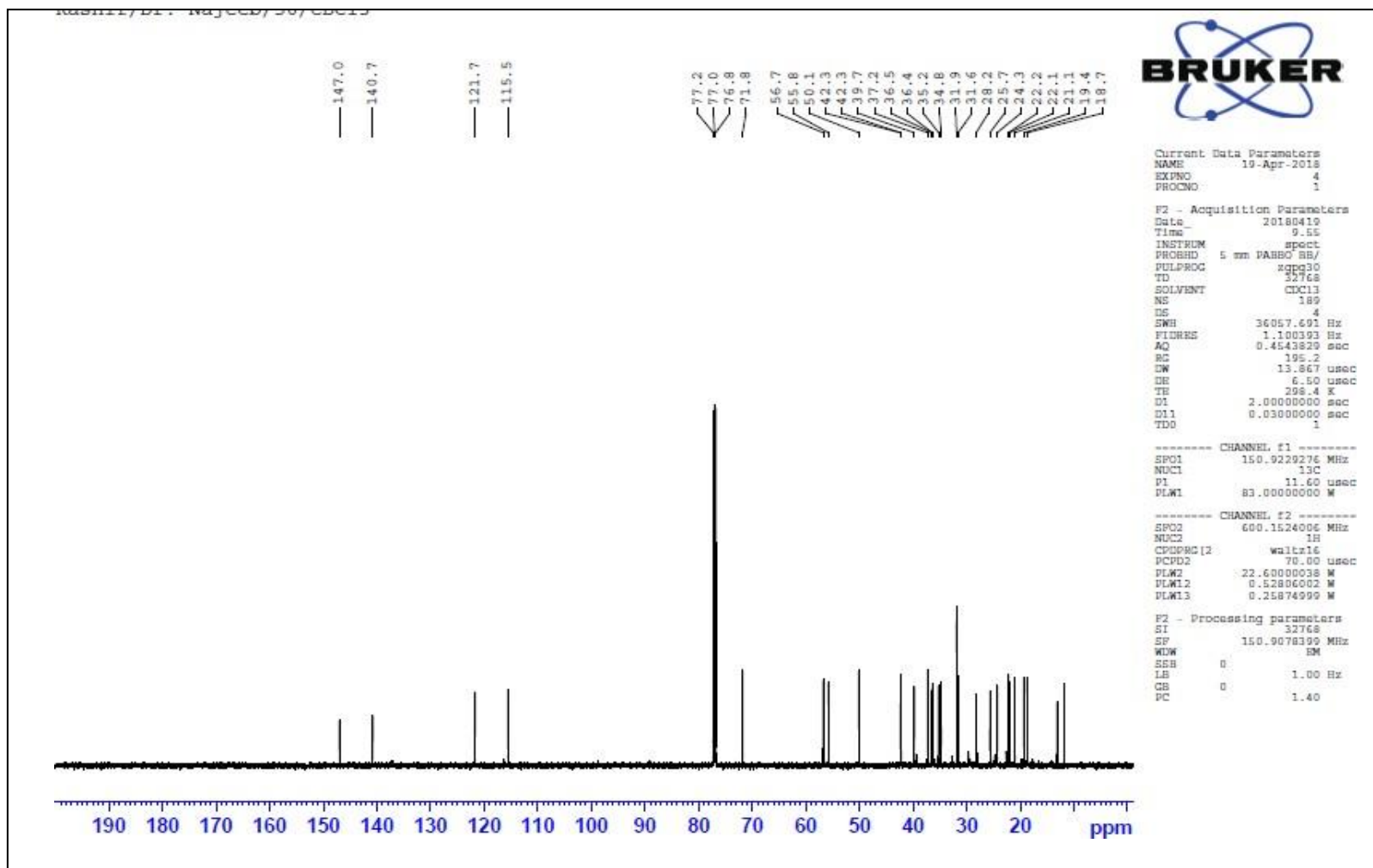


Figure S31. ^{13}C -NMR (150 MHz, CDCl_3) of compound 3

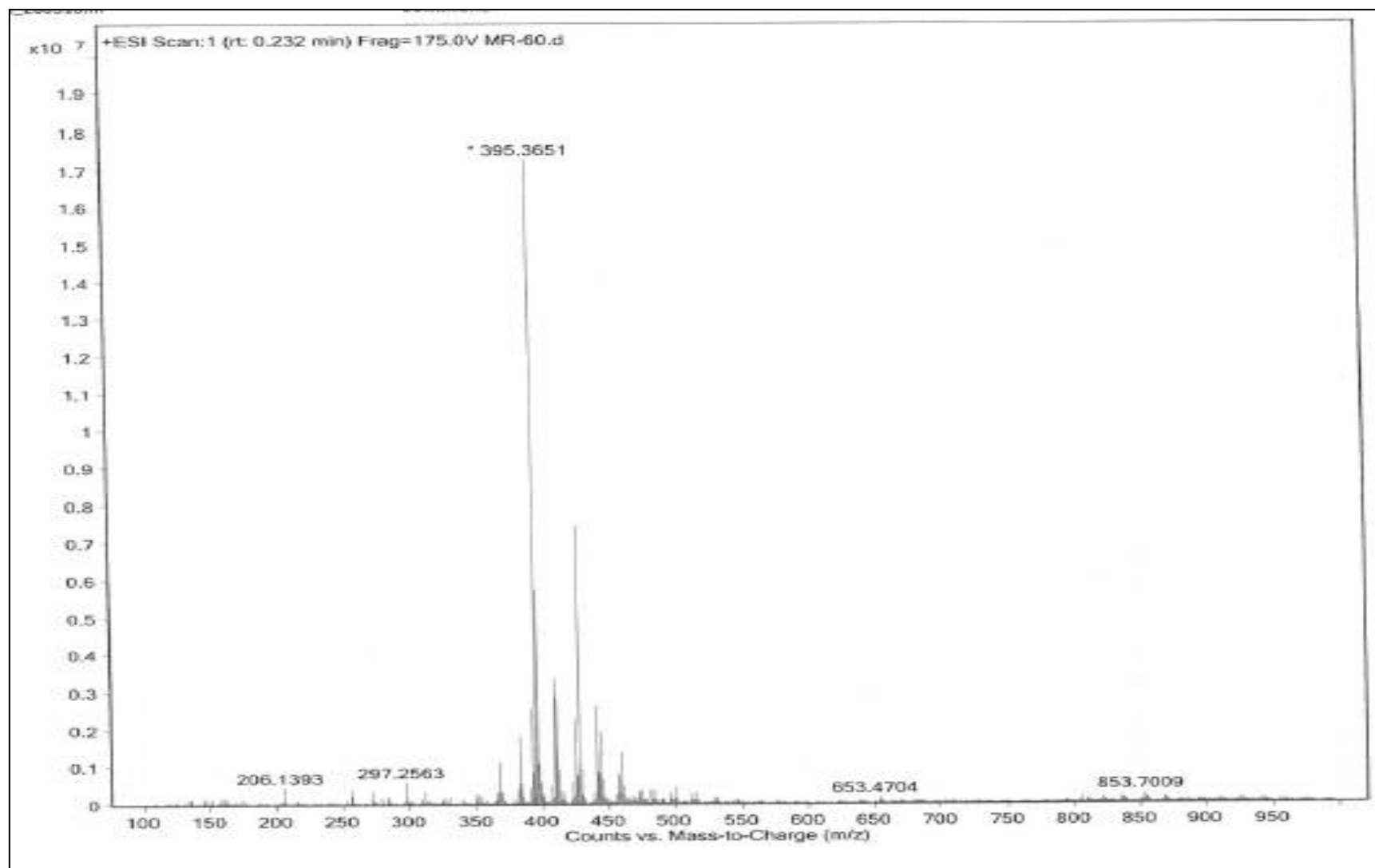


Figure S32. HRMS (ESI+) of compound 3

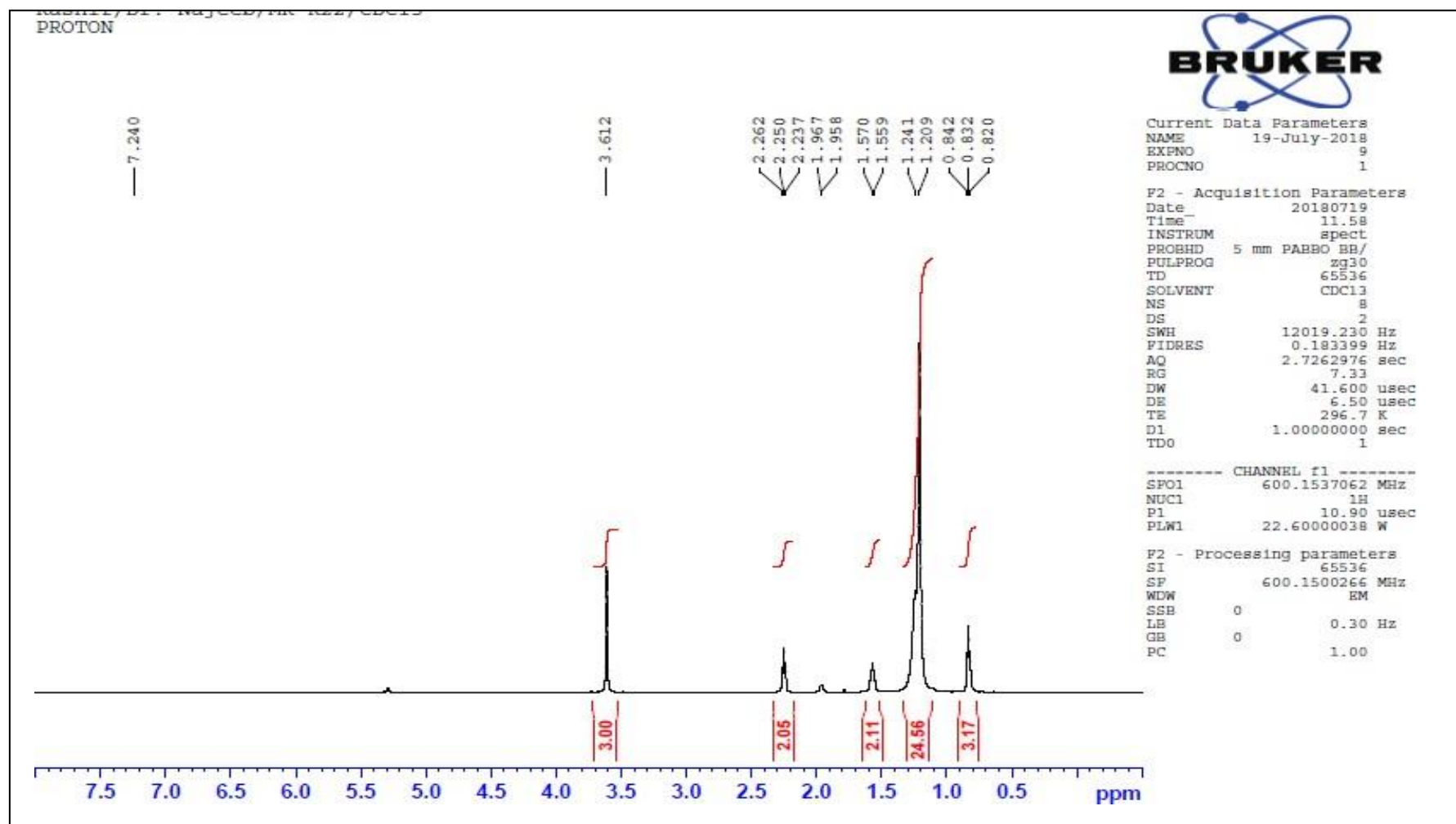


Figure S33. ¹H-NMR (600 MHz, CDCl₃) of compound 4

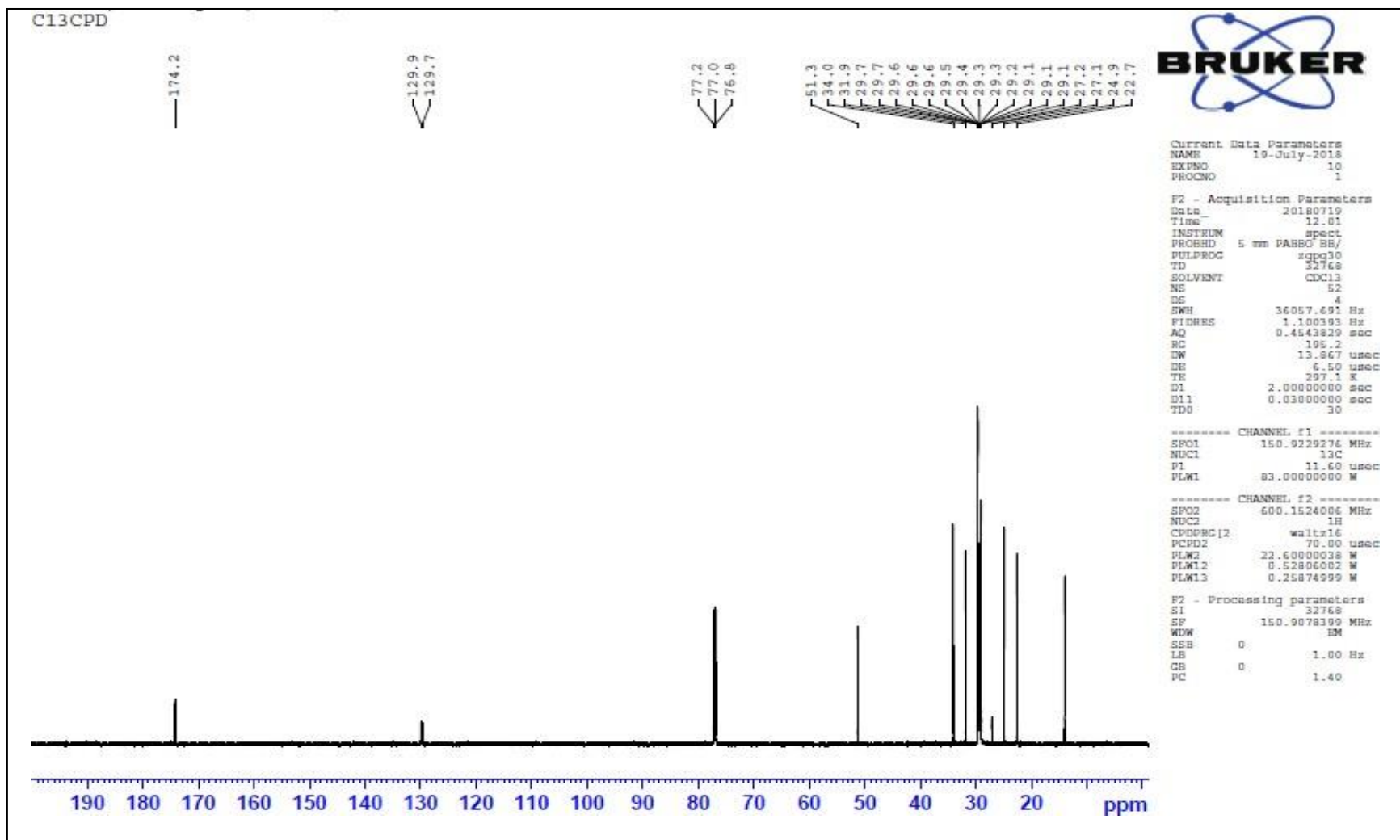


Figure S34. ^{13}C -NMR (150 MHz, CDCl_3) of compound 4

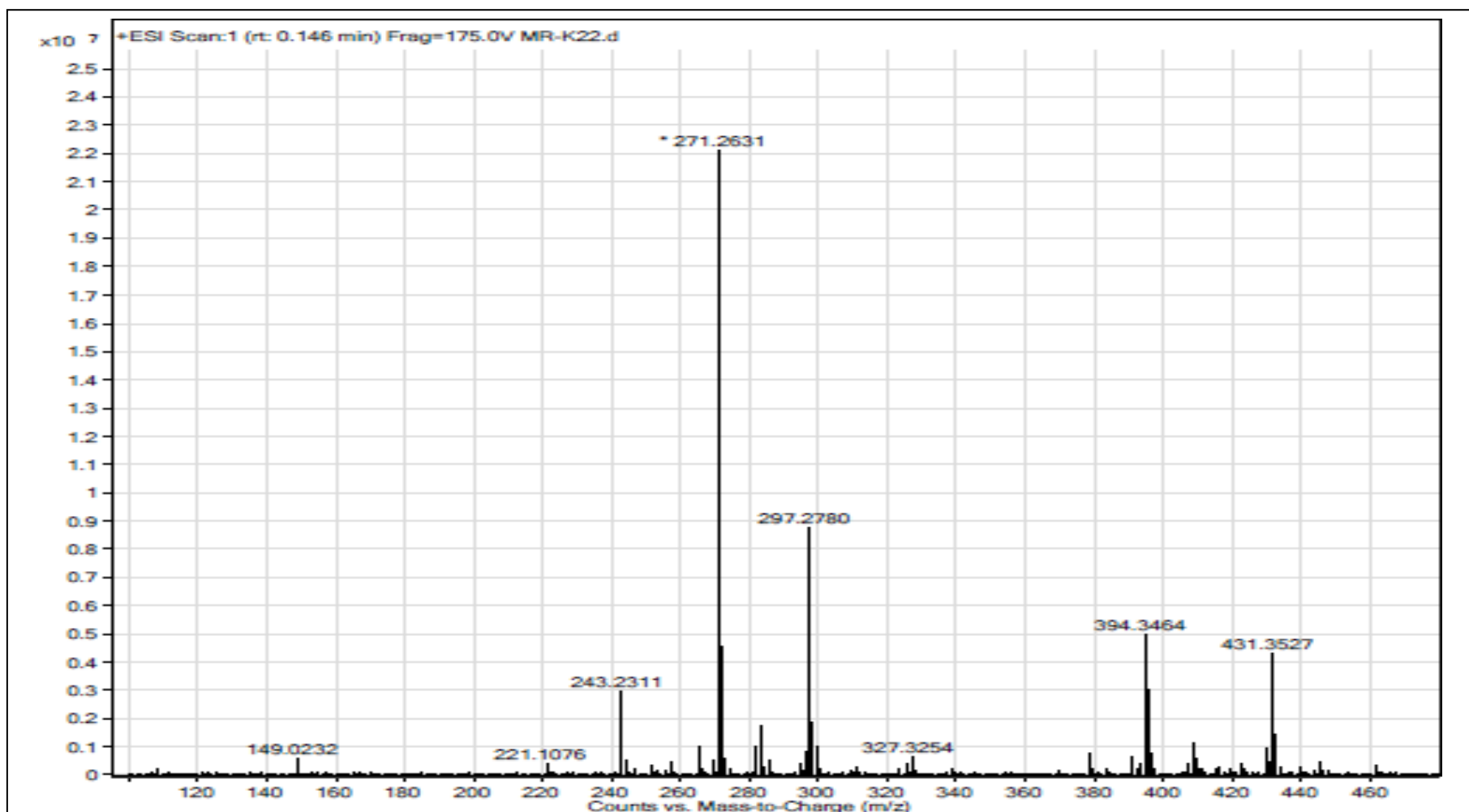


Figure S35. HRMS (ESI+) of compound 4

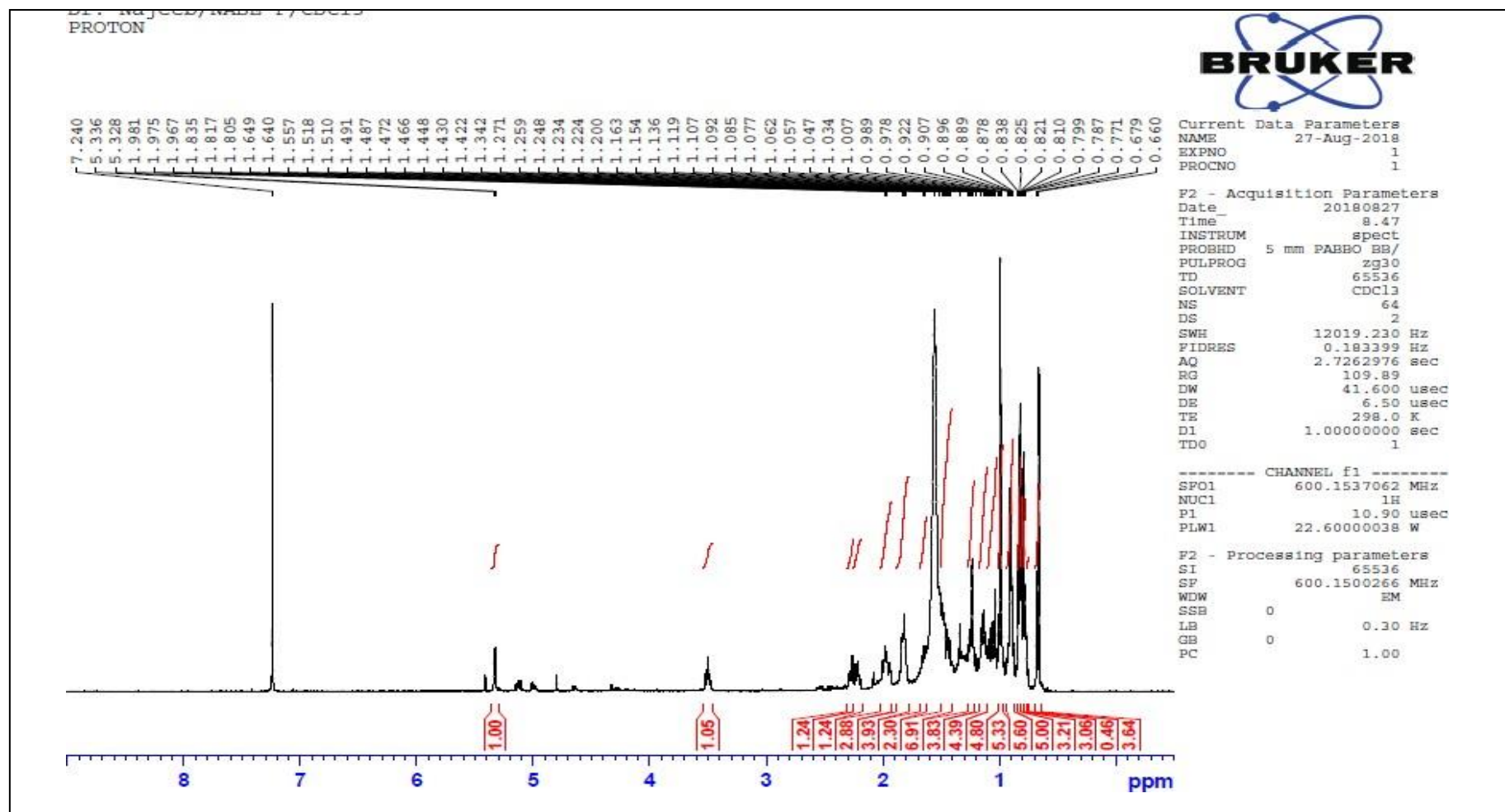


Figure S27. $^1\text{H-NMR}$ (600 MHz, CDCl_3) of compound 5

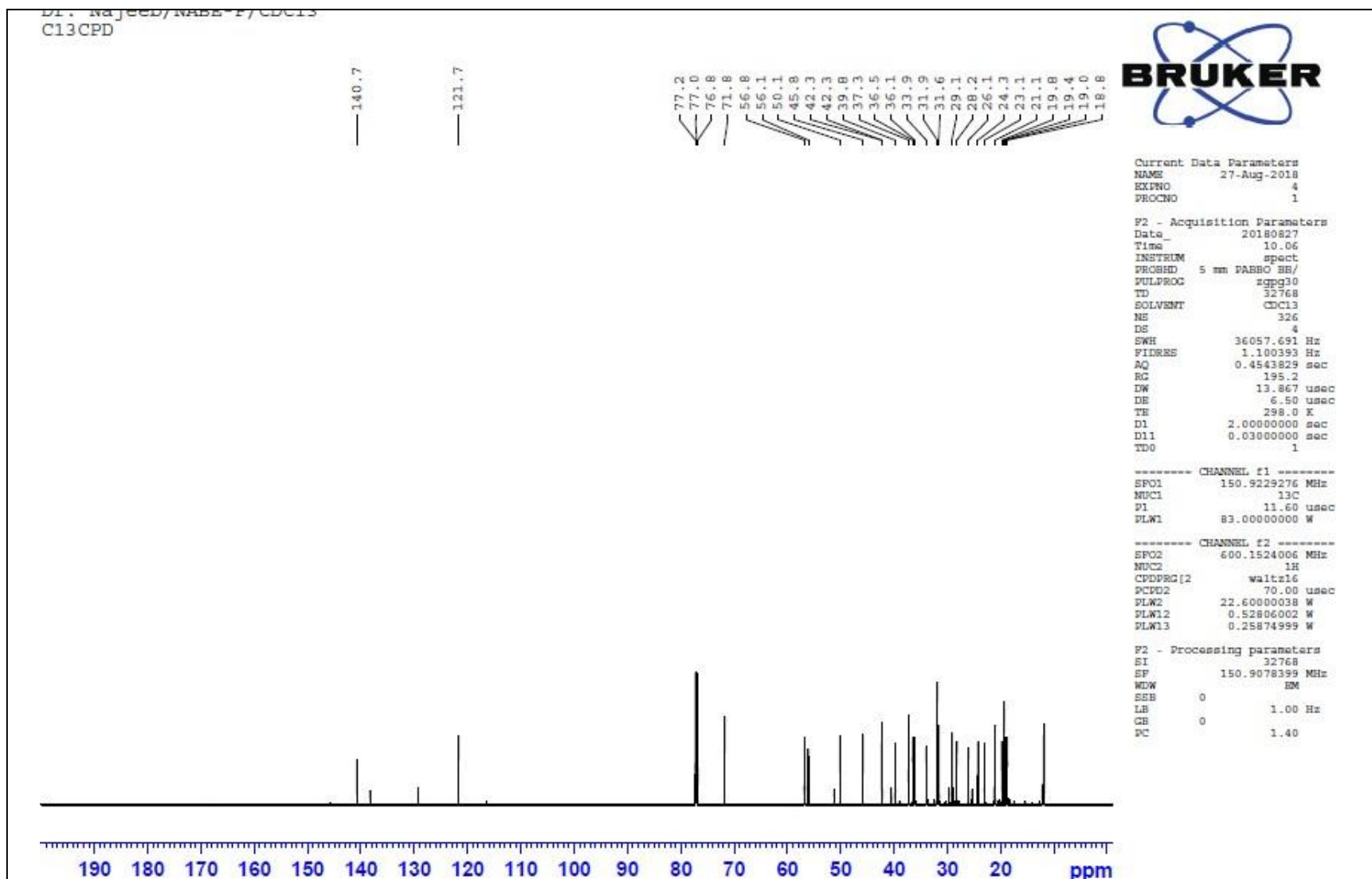


Figure S28. ^{13}C -NMR (150 MHz, CDCl_3) of compound 5

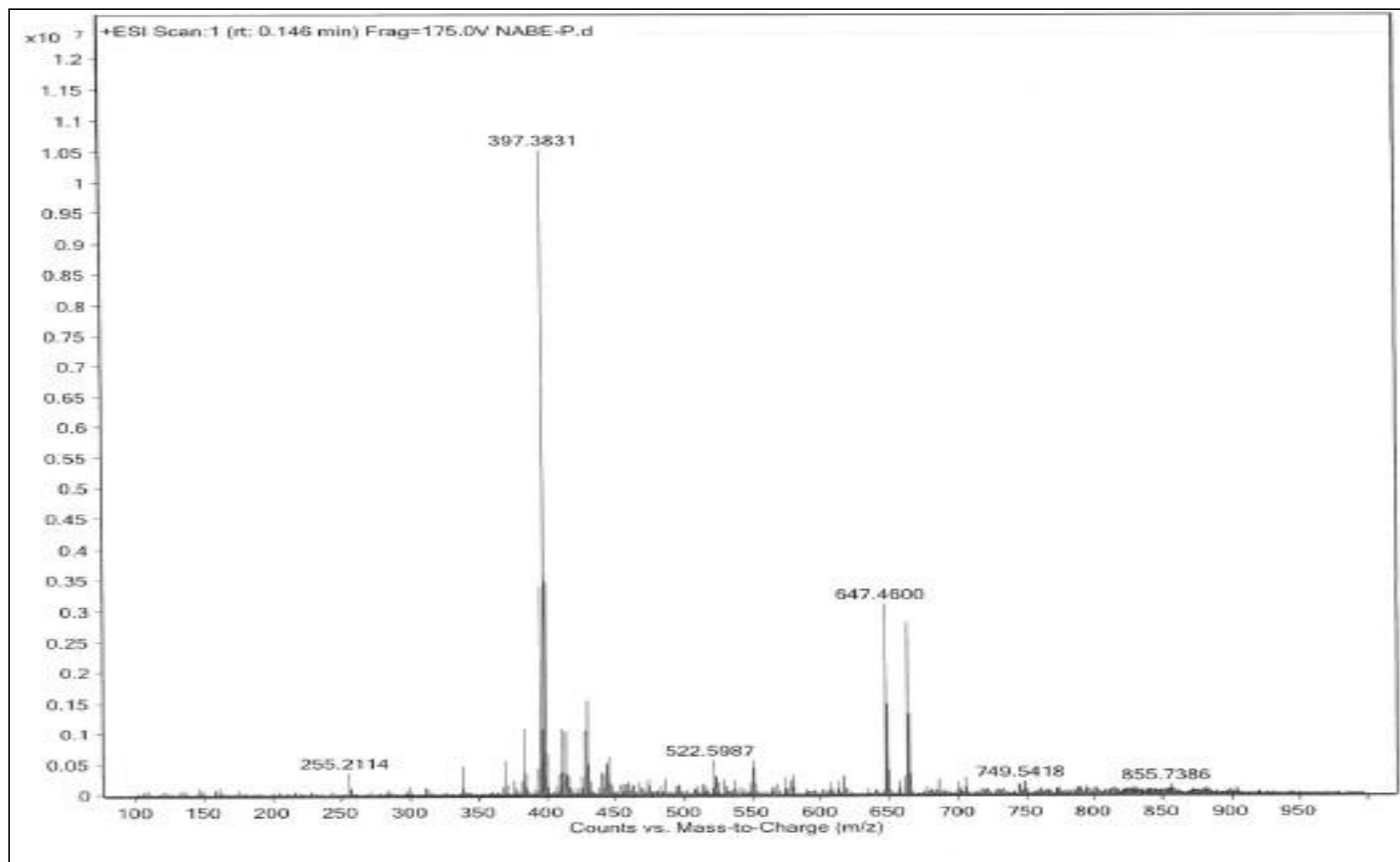


Figure S29. HRMS (ESI+) of compound 5

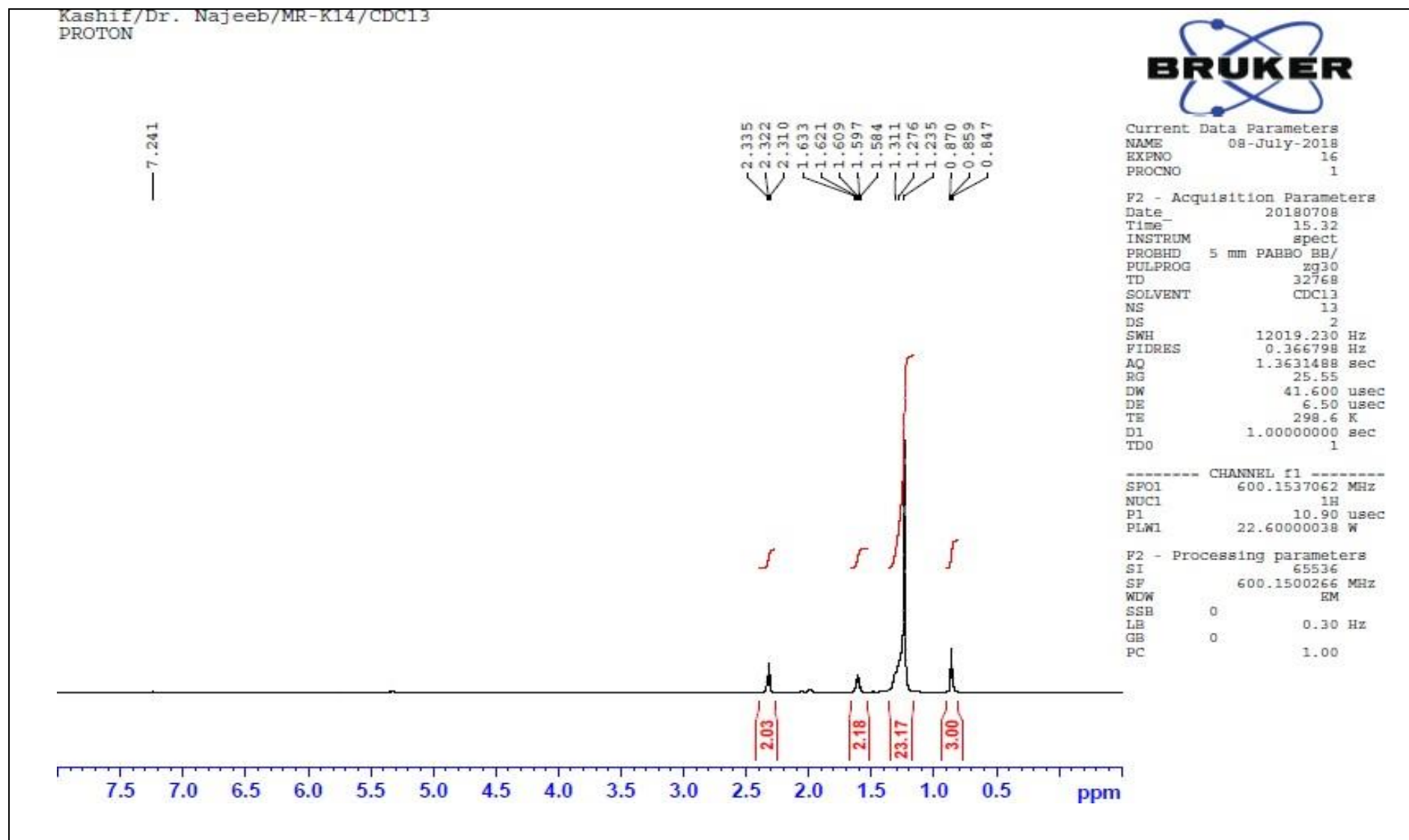


Figure S39. ¹H-NMR (600 MHz, CDCl₃) of compound 6

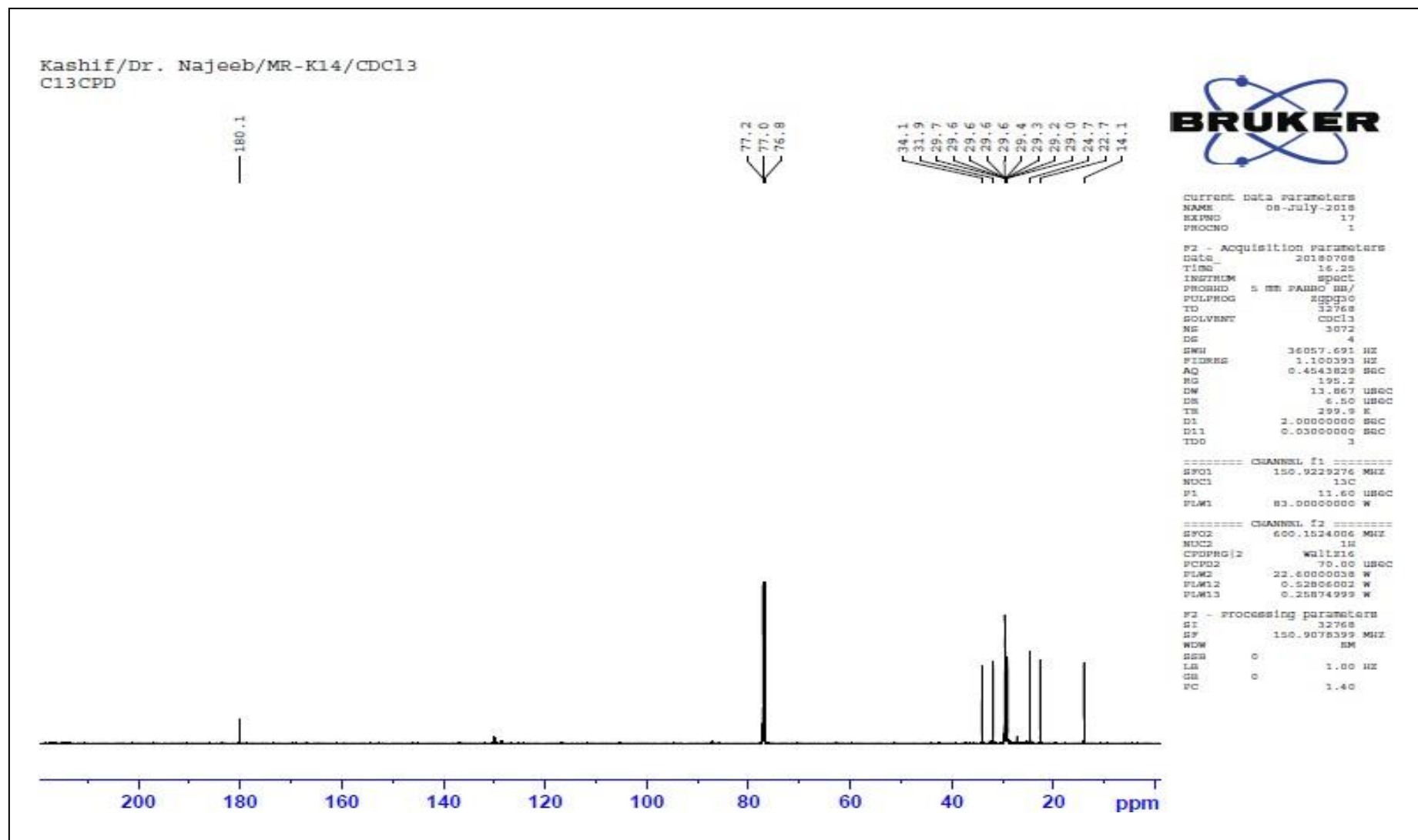


Figure S40. ¹³C-NMR (150 MHz, CDCl₃) of compound 6

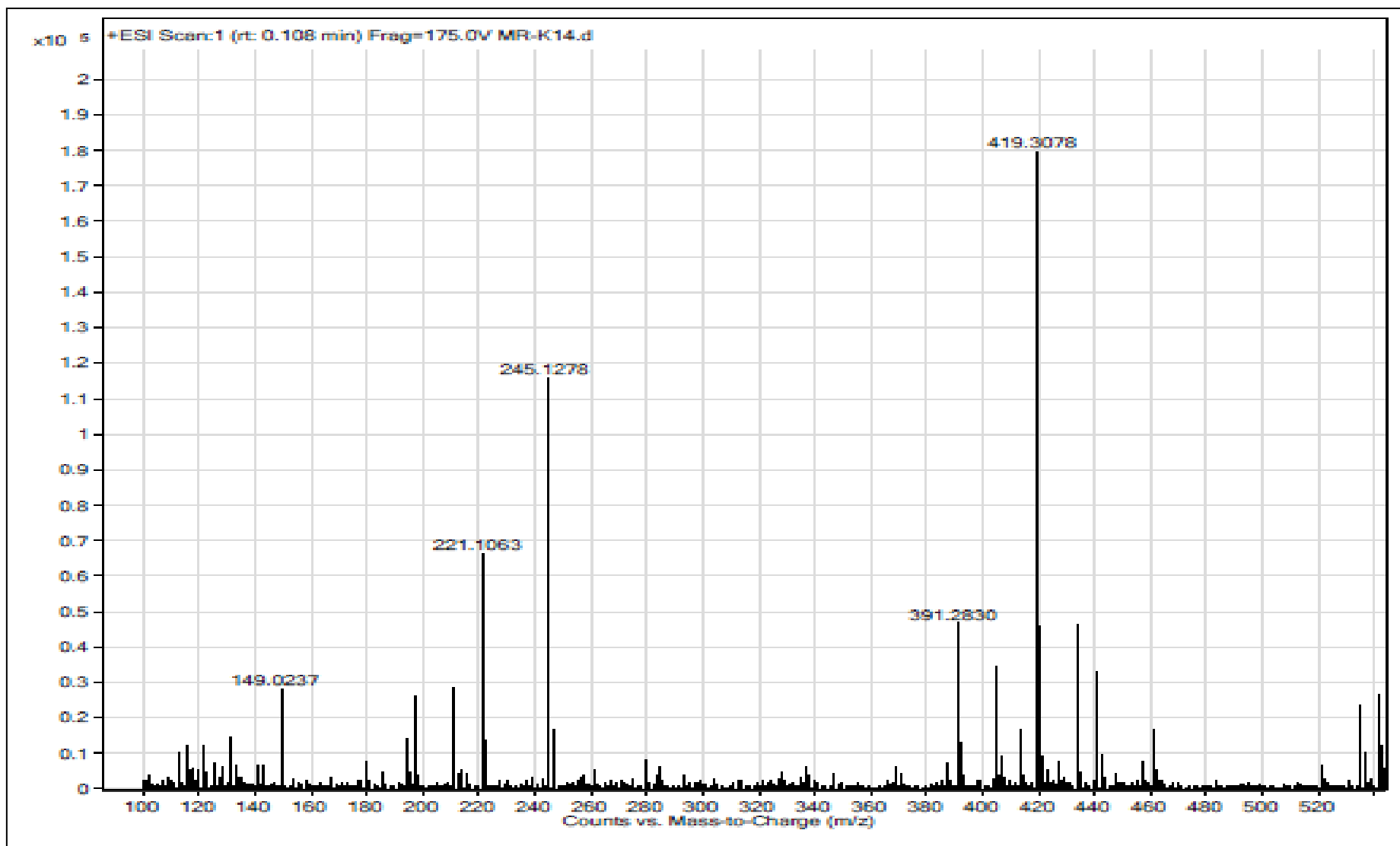


Figure S41. HRMS (ESI+) of compound 6

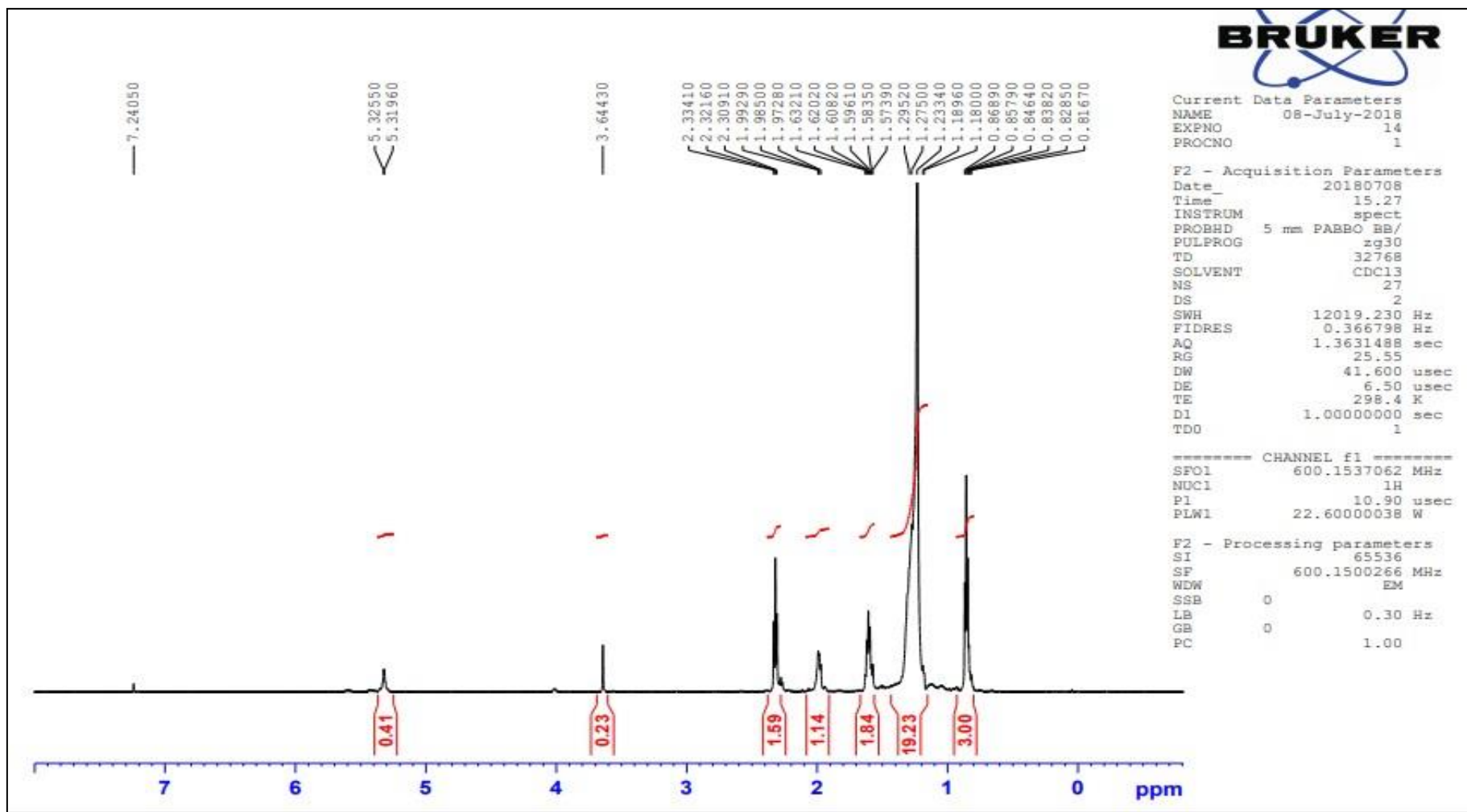


Figure S36. $^1\text{H-NMR}$ (600 MHz, CDCl_3) of compound 7

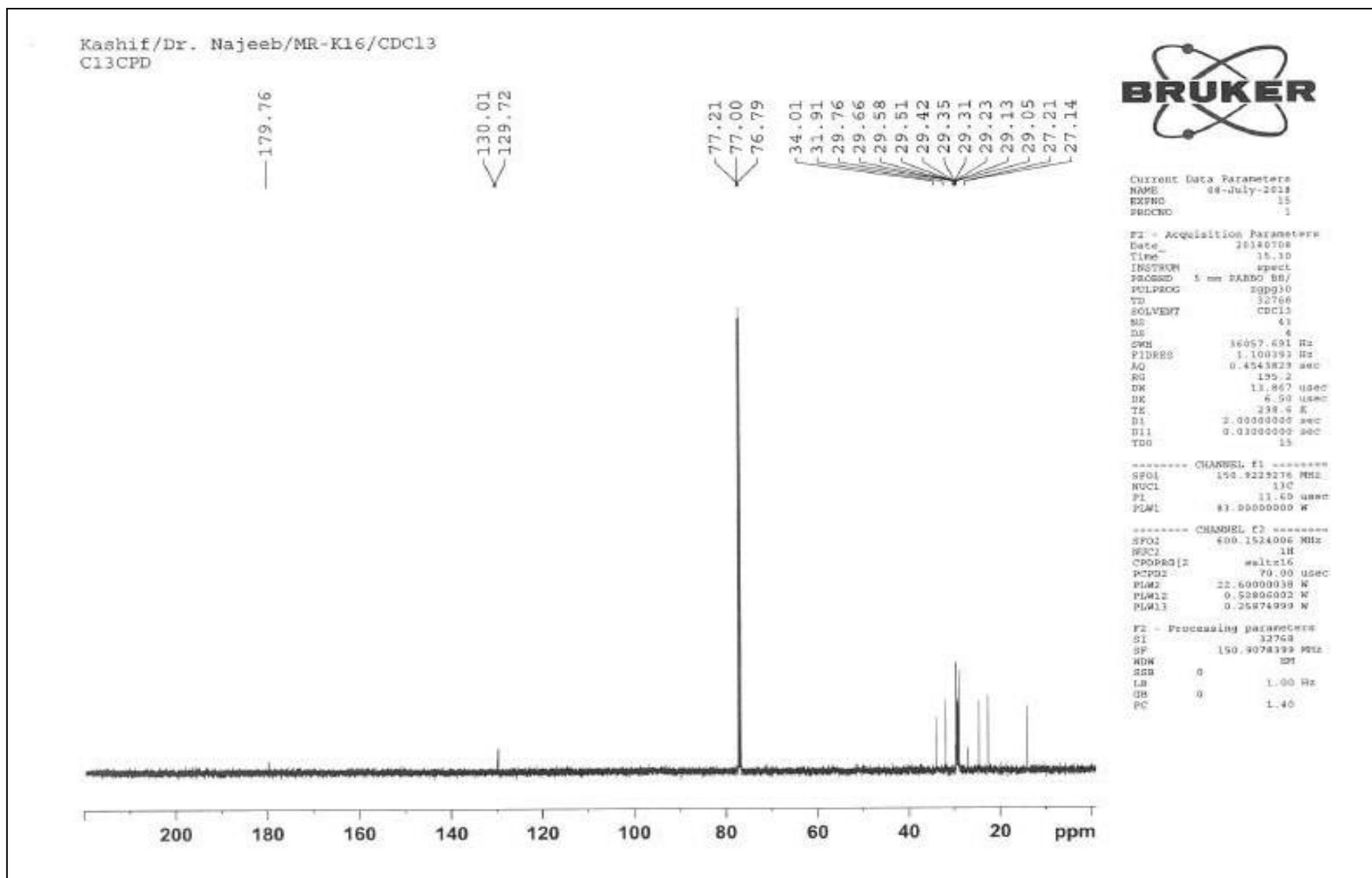


Figure S37. ¹³C-NMR (150 MHz, CDCl₃) of compound 7

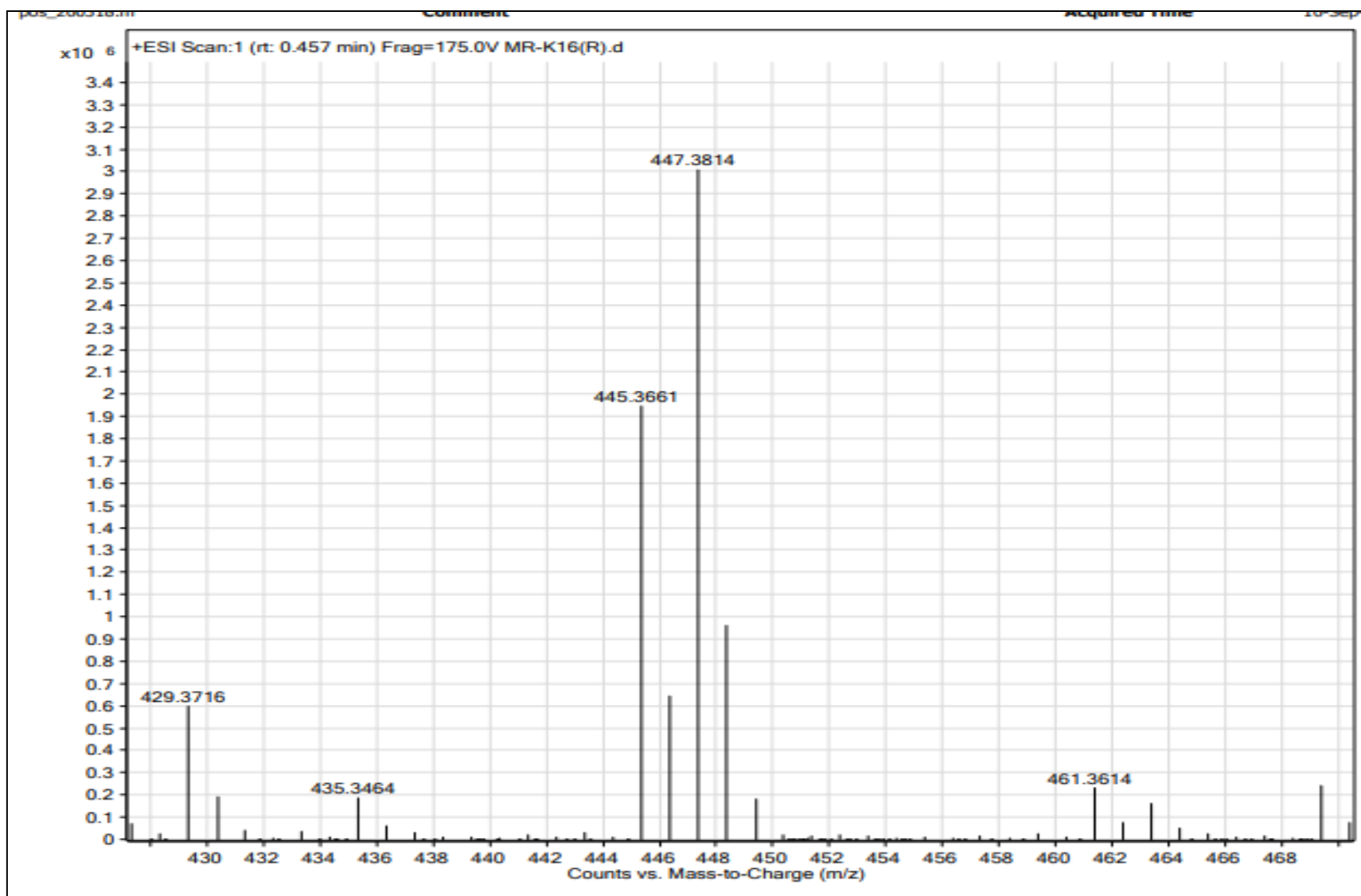


Figure S38. HRMS (ESI+) of compound 7

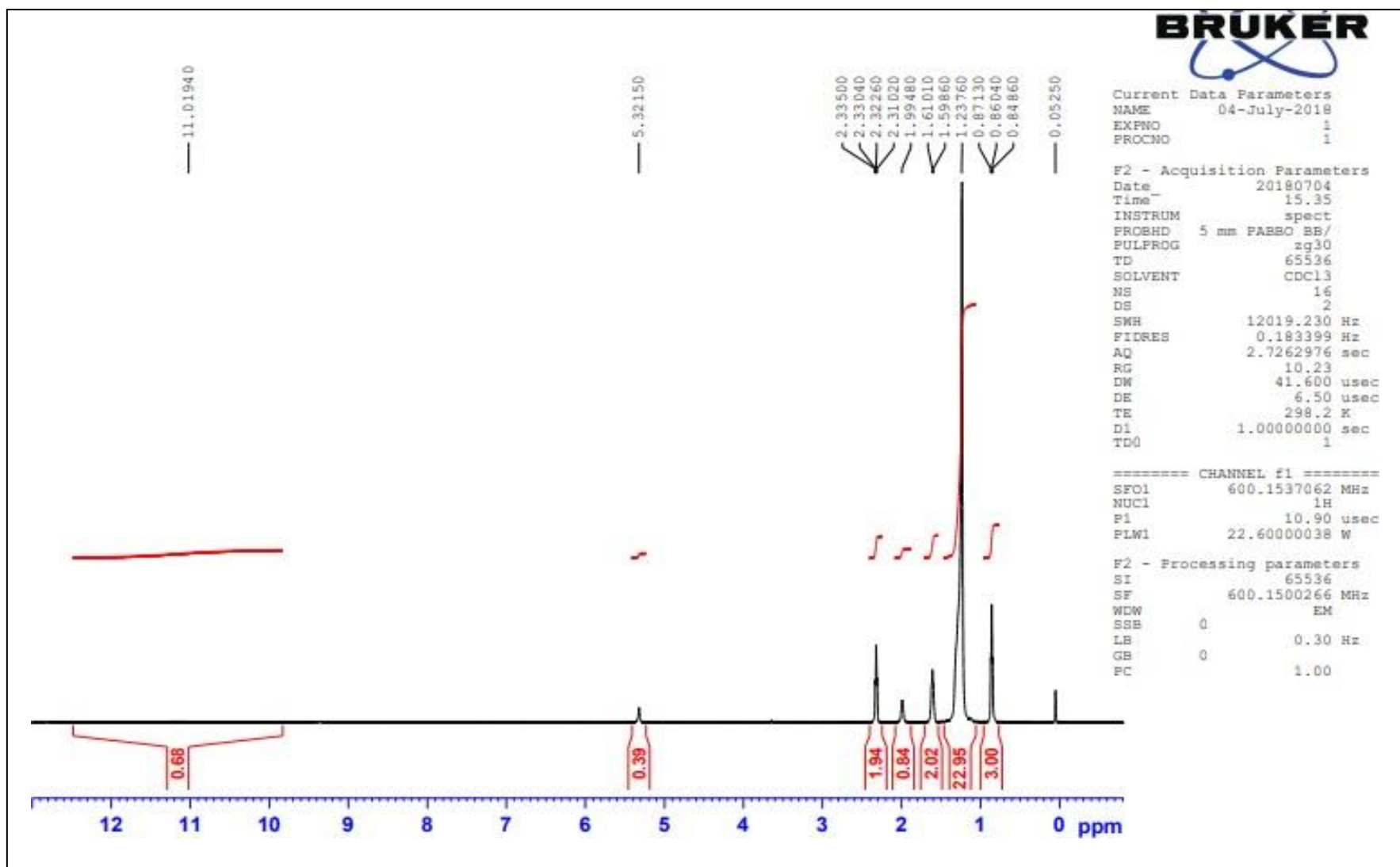


Figure S42. ¹H-NMR (600 MHz, CDCl₃) of compound 8

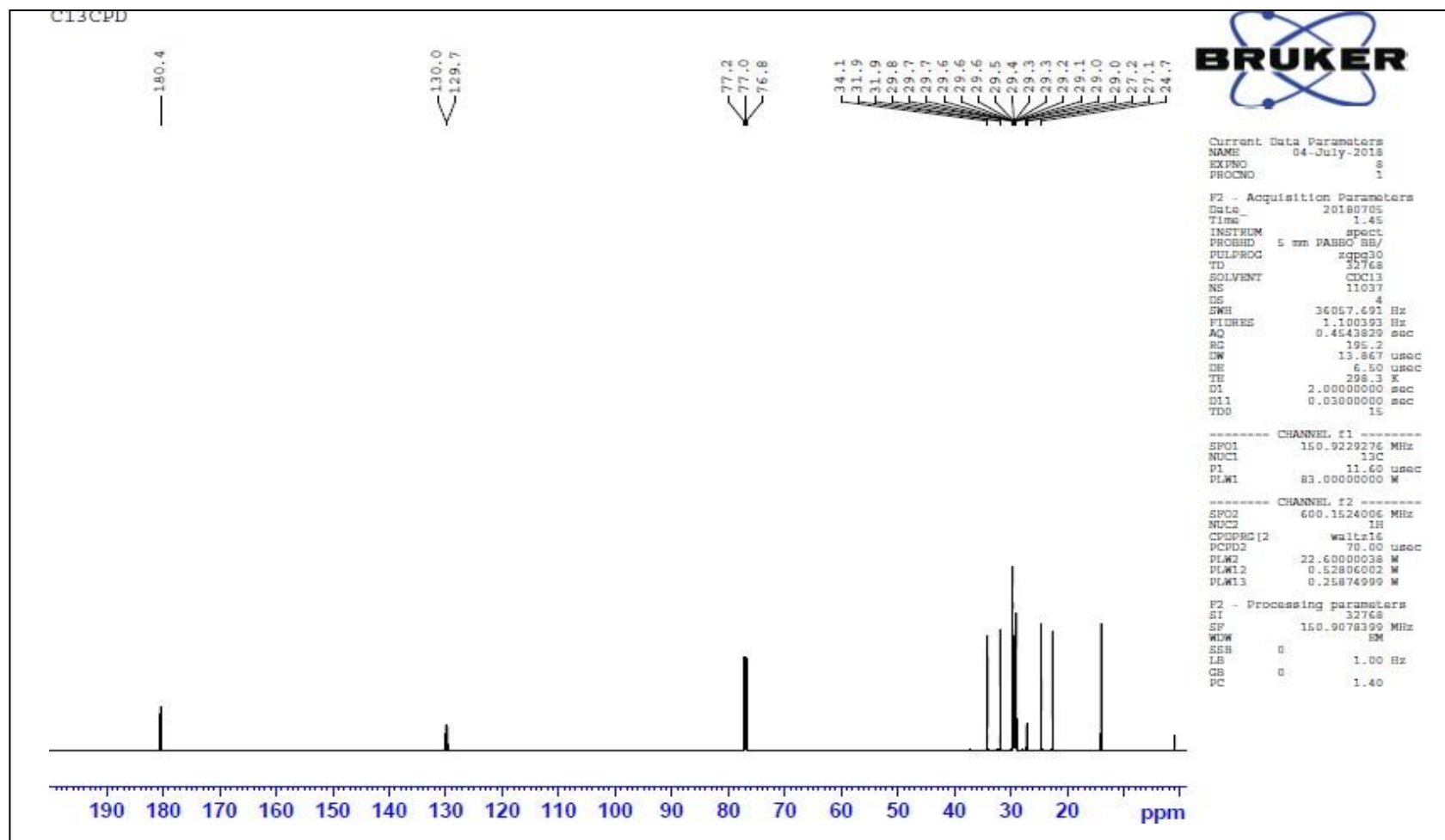


Figure S43. ^{13}C -NMR (150 MHz, CDCl_3) of compound 8

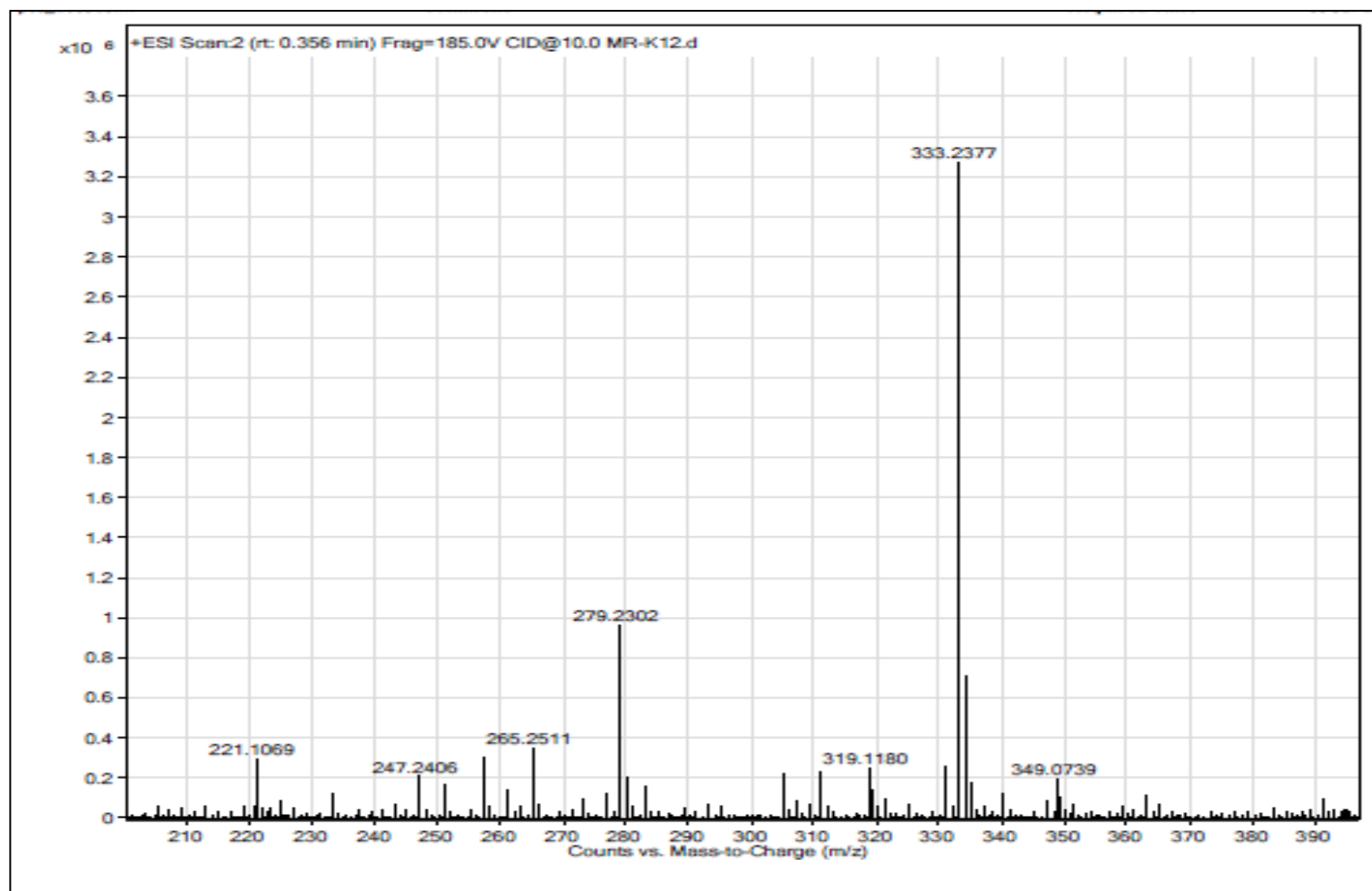


Figure S44. HRMS (ESI+) of compound 8