Supporting Data

Jusanin, a new flavonoid from *Artemisia commutata* with an *in silico* inhibitory potential against SARS-CoV-2 main protease

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Content

Method

1. General experimental section

NMR spectra were carried out on a commercial instrument (Bruker Avance 300 and 600 MHz), chemical shifts (δ) are presented in parts per million (ppm) and re-calculated with respect to tetramethylsilane (TMS) (^{1}H) or carbon signals of deuterium solvents (^{13}C). Spin-spin coupling constants (J) are given in hertz (Hz). Refinement of ^{13}C NMR spectra signals was carried out using Dept, HSQC, HMBC NMR spectra. Mass spectra were recorded on an HP5989A instrument (CI and EI, ionization energy 70 eV) with Apollo 300 data, and on a Kratos MS50TC instrument for accurate calculations (reaching by electric shock (ESI), common solvent mixture: CH_2Cl_2-MeOH + NH_4OAc) with MASSLYNX system data. UV spectra were obtained on a Perkin-Elmer Lambda 20 Spectrometer instrument. Melting points were determined on Reichert Thermovar. For column chromatography, silica gel 0.06-0.2 mm (Acros) was used as the stationary phase. Silica gel 32-63 mesh was used for flash column chromatography.

2. Plant material

To study the component composition of *Artemisia commutata* Besser, family *Asteraceae*, the aboveground part of plant is collected in the Eastern-Kazakhstan region (Western Altai Mountains) on July, phase of blooming – beginning of flowering.

Species is identified by botanists of the Altai Botanical Garden (Rider city, eastern Kazakhstan). The herbarium sample is stored in the International Scientific Research Holding «Phytochemistry» Fund. The herbarium sample code is 2007.10.02.02.03.

3. Extraction and isolation

1.04 kg of raw material was placed in a round-bottomed flask and filled with chloroform and heated to the boiling point of solvents. This operation was repeated three times. The solvent was evaporated on a rotary evaporator under the vacuum of a water-jet pump to obtain an extract weighing 20 g, which was used for preparative chromatographic separation by column chromatography on silica gel.

4. Molecular Similarity

Molecular Similarity of the tested compound against the eight co-crystallized ligands of SARS-Cov-2 was carried out calculated using Discovery studio 4.0. At first, the CHARMM force field was applied then the compound was prepared using prepare ligand protocol. Then, the tested compound was used as a reference compound while the co-crystallized ligands were used as a test

set. The protocol was adjusted to give one output. The default molecular properties were applied. The molecular properties include the number of rotatable bonds, number of rings, number of aromatic rings, number of hydrogen bond donors (HBA), number of hydrogen bond acceptors (HBD), partition coefficient (ALog p), molecular weight (M. Wt), and molecular fractional polar surface area (MFPSA).

5. Fingerprint study

A fingerprint study of the tested compound against the eight co-crystallized ligands of SARS-Cov-2 was carried out calculated using Discovery studio 4.0. At first, the CHARMM force field was applied then the compounds were prepared using prepare ligand protocol. Then, the tested compound was used as a reference compound while the co-crystallized ligands was used as a test set. The protocol was adjusted to give the most related co-crystallized ligand s to the tested compound. The default molecular properties were applied. The used fingerprints were based on some parameters related to the type of atoms which may be one of the following: charge, hybridization, H-bond acceptor, H-bond donor, Positive ionizable, Negative ionizable, Halogen, Aromatic, or None of the above. In addition, it includes the ALogP category of atoms.

6. DFT

The DFT parameters (total energy, binding energy, HOMO, LUMO, gap energy, dipole moment, and electrostatic potential) were calculated using Discovery studio software. the tested compounds were prepared using prepare ligand protocol. Then, the prepared compounds were subjected to DFT calculation protocol using the default option

7. Docking studies

Crystal structure of SARS-Cov-2 main protease (PDB ID: 6W63) was obtained from Protein Data Bank. The docking investigation was accomplished using MOE2014 software. At first, the crystal structure of SARS-Cov-2 main protease was prepared by removing water molecules. Only one chain was retained beside the crystallized ligand, **X77,** (N-(4-tert-butylphenyl)-N-[(1R)-2-(cyclohexylamino)-2-oxo-1-(pyridin-3-yl)ethyl]-1H-imidazole-4-carboxamide). Then, the selected chain was protonated and subjected to minimization of energy process. Next, the active site of the target protein was defined.

Structures of the tested compounds and the co-crystallized ligand were drawn using ChemBioDraw Ultra 14.0 and saved as MDL-SD format. Such file was opened using MOE to display the 3D structures which were protonated and subjected to energy minimization. Formerly,

validation of the docking process was performed by docking the co-crystallized ligand against the isolated pocket of the active site. The produced RMSD value indicated the validity of the process. Finally, docking of the tested compounds was done through the dock option inserted in compute window. For each docked molecule, 30 docked poses were produced using ASE for scoring function and force field for refinement. The results of the docking process were then visualized using Discovery Studio 4.0 software.

8. ADMET

ADMET descriptors (absorption, distribution, metabolism, excretion and toxicity) of the compounds were determined using Discovery studio 4.0. At first, the CHARMM force field was applied then the tested compounds were prepared and minimized according to the preparation of small molecule protocol. Then ADMET descriptors protocol was applied to carry out these studies.

9. Toxicity studies

The toxicity parameters of the tested compounds were calculated using Discovery studio 4.0. Indinavir was used as a reference drug. At first, the CHARMM force field was applied then the compounds were prepared and minimized according to the preparation of small molecule protocol. Then different parameters were calculated from the toxicity prediction (extensible) protocol.

10. Molecular dynamics simulations

The system was prepared using the web-based CHARMM-GUI interface with the CHARMM36 force field. All the simulations were done using the NAMD 2.13 package. The TIP3P explicit solvation model was used[78], and the periodic boundary conditions were set with a dimension of the dimensions ---- Å, ----- Å, and ----- Å in x, y, and z, respectively. The parameters for the top docking results were generated using the CHARMM general force field Afterward, the system was neutralized using ---- (Cl^-/Na^+) ions. The MD protocols involved minimization, equilibration, and production. a 2 *fs* time step of integration was chosen for all MD simulations, the equilibration was carried in the canonical (*NVT*) ensemble, while the isothermal–isobaric (*NPT*) ensemble was for the production. Through the 100 *ns* of MD production, the pressure was set at 1 atm using the Nose´–Hoover Langevin piston barostat[80,81] with a Langevin piston decay of 0.05 *ps* and a period of 0.1 *ps*. The temperature was set at 298.15 K using the Langevin thermostat[82]. A distance cutoff of 12.0 Å was applied to short-range nonbonded interactions with

a pair list distance of 16 Å, and Lennard Jones interactions were smoothly truncated at 8.0 Å. Long-range electrostatic interactions were treated using the particle-mesh Ewald (PME) method[83,84], where a grid spacing of 1.0 Å was used for all simulation cells. All covalent bonds involving hydrogen atoms were constrained using the SHAKE algorithm[85]. For consistency, we have applied the same protocol for all MD simulations.

Spectral data

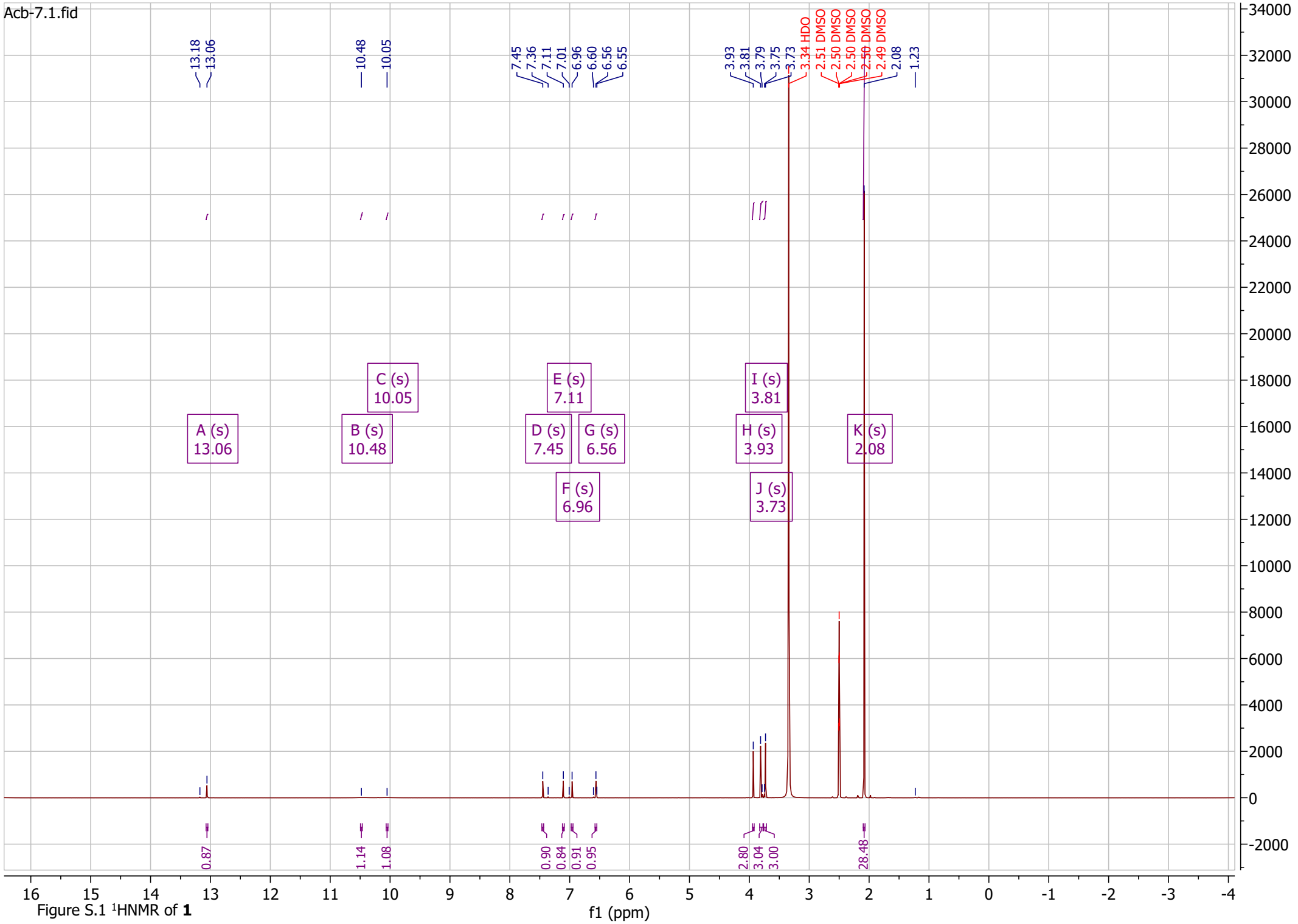


Figure S.1 ^{1}HNMR of **1**

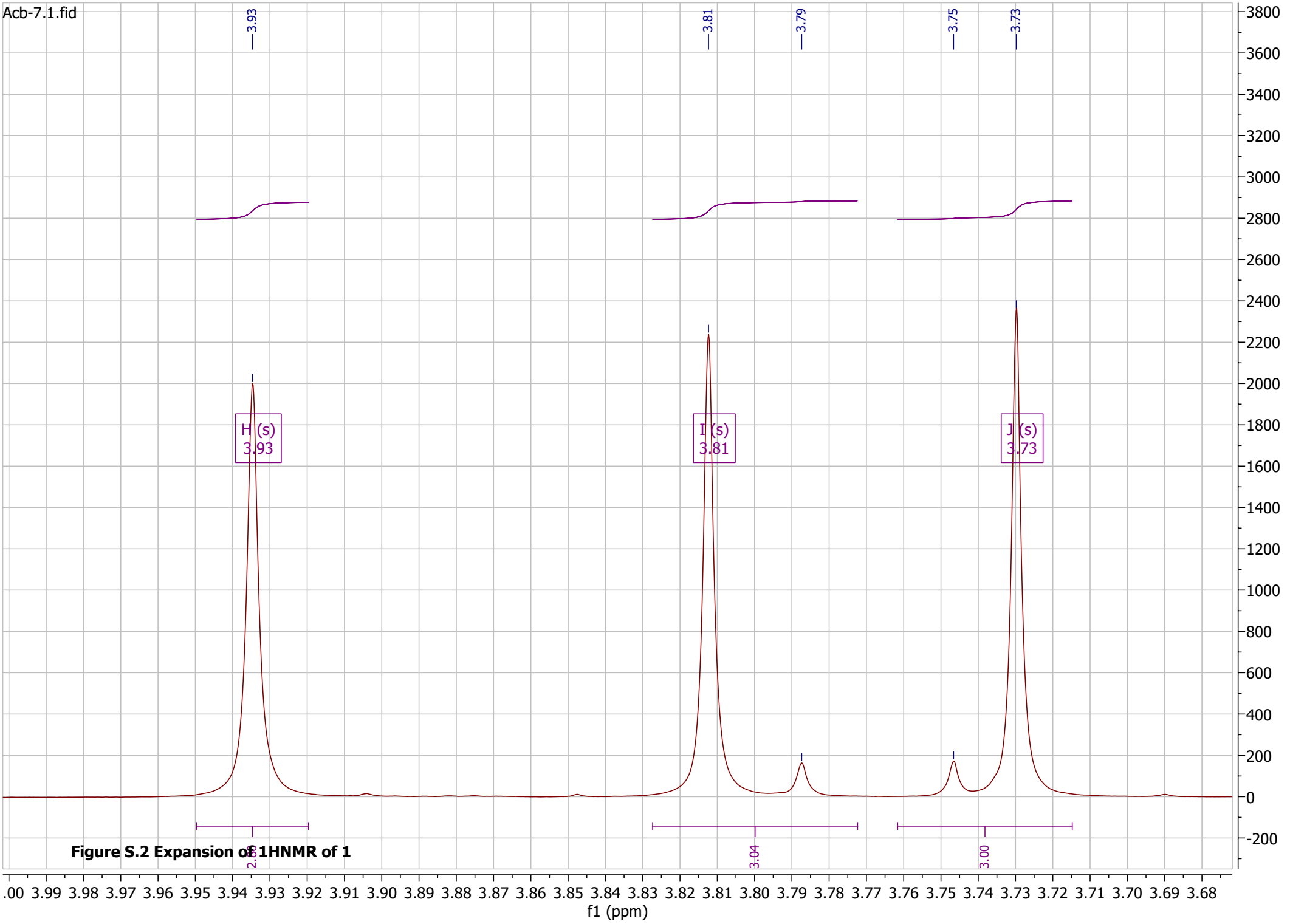


Figure S.2 Expansion of 1HNMR of 1

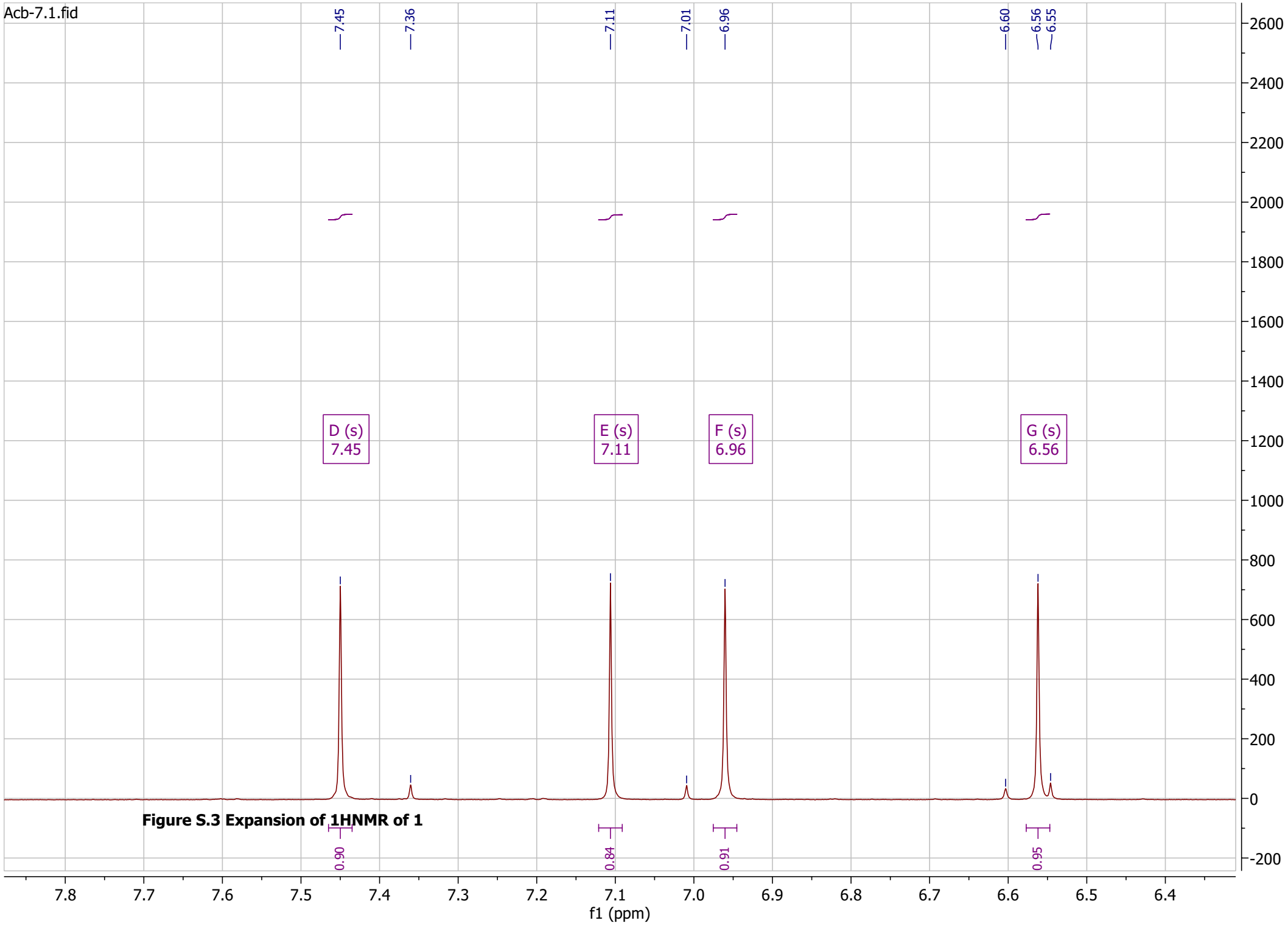


Figure S.3 Expansion of 1HNMR of 1

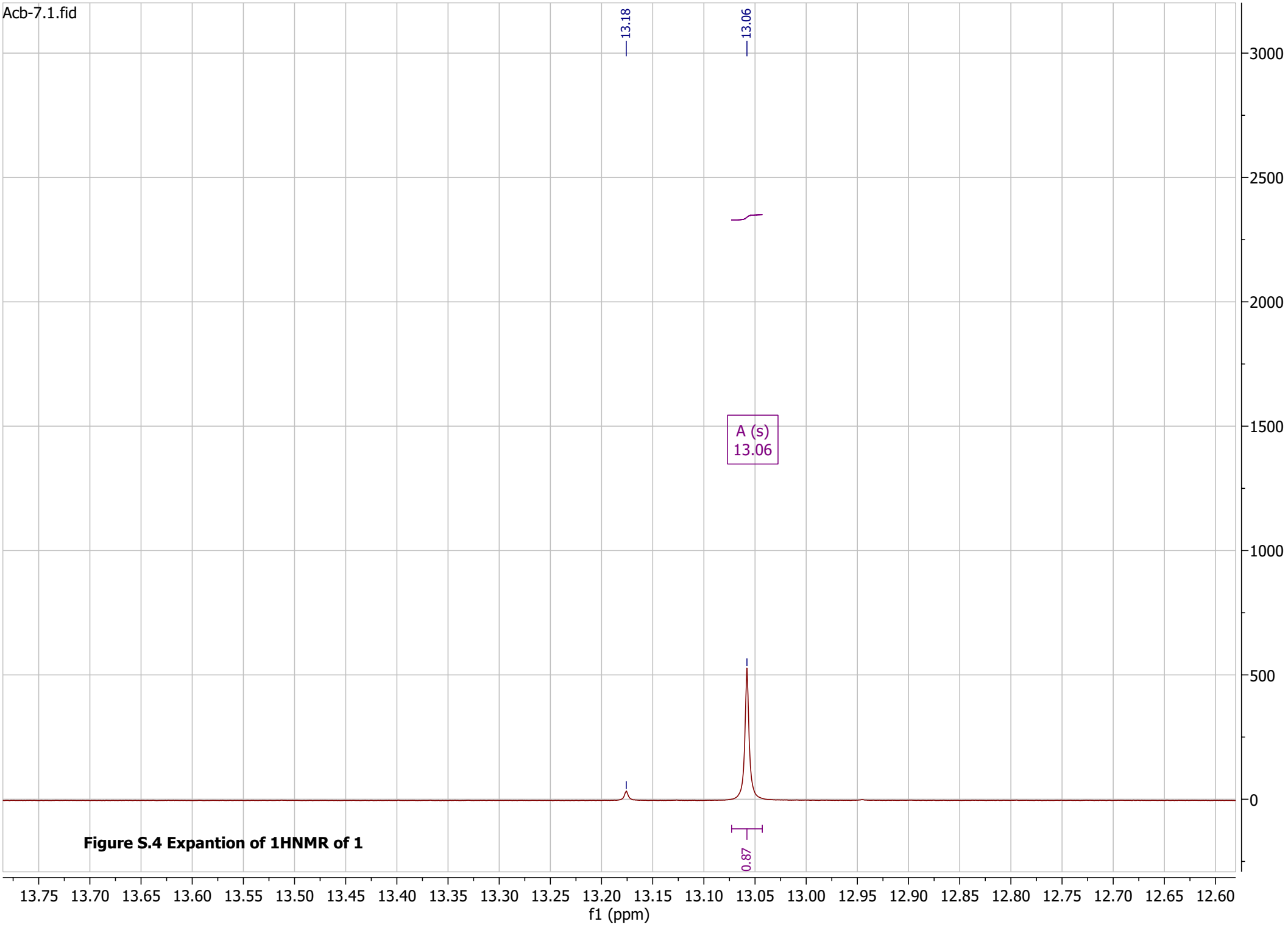


Figure S.4 Expantion of 1HNMR of 1

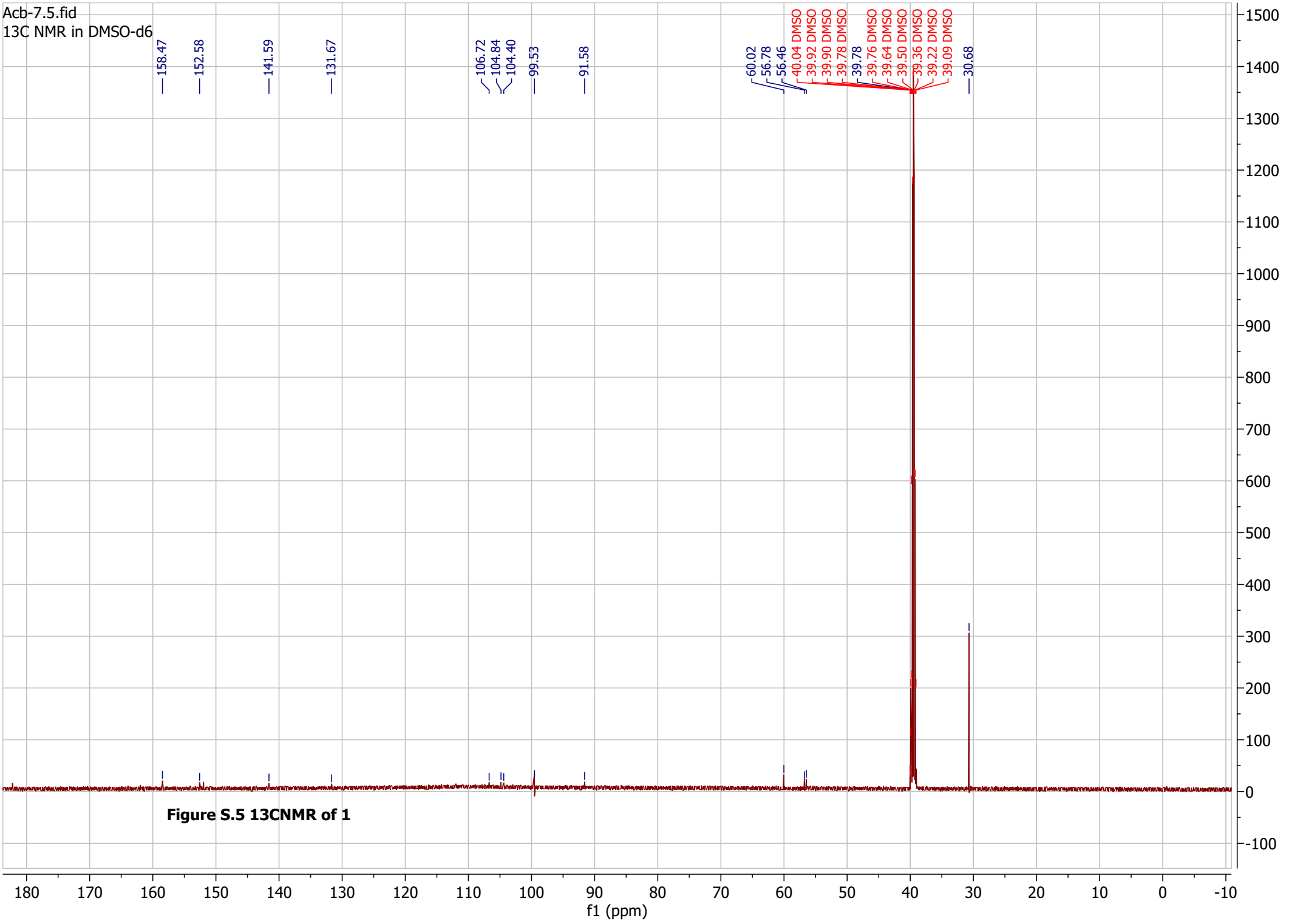


Figure S.5 13CNMR of 1

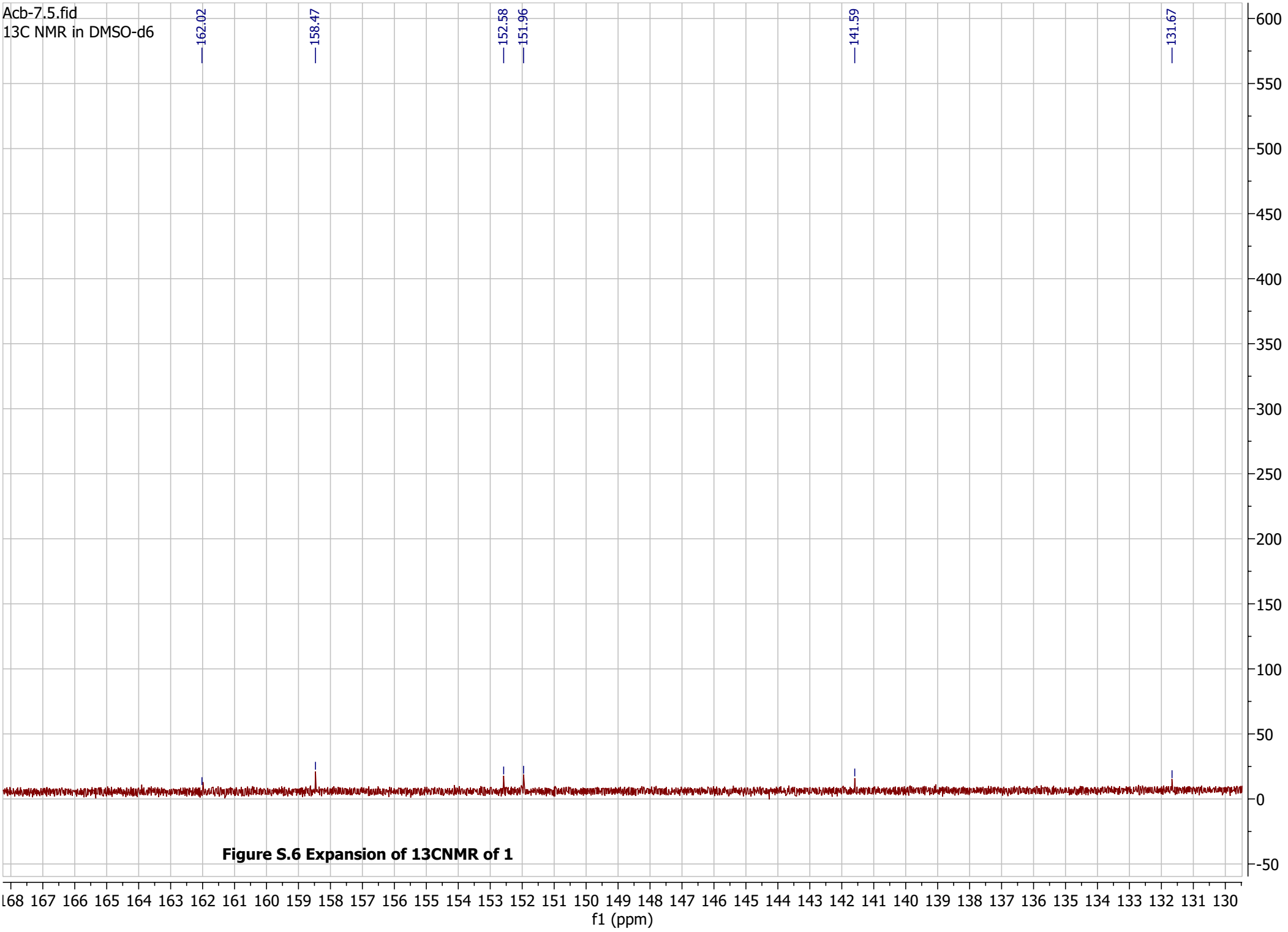


Figure S.6 Expansion of 13CNMR of 1

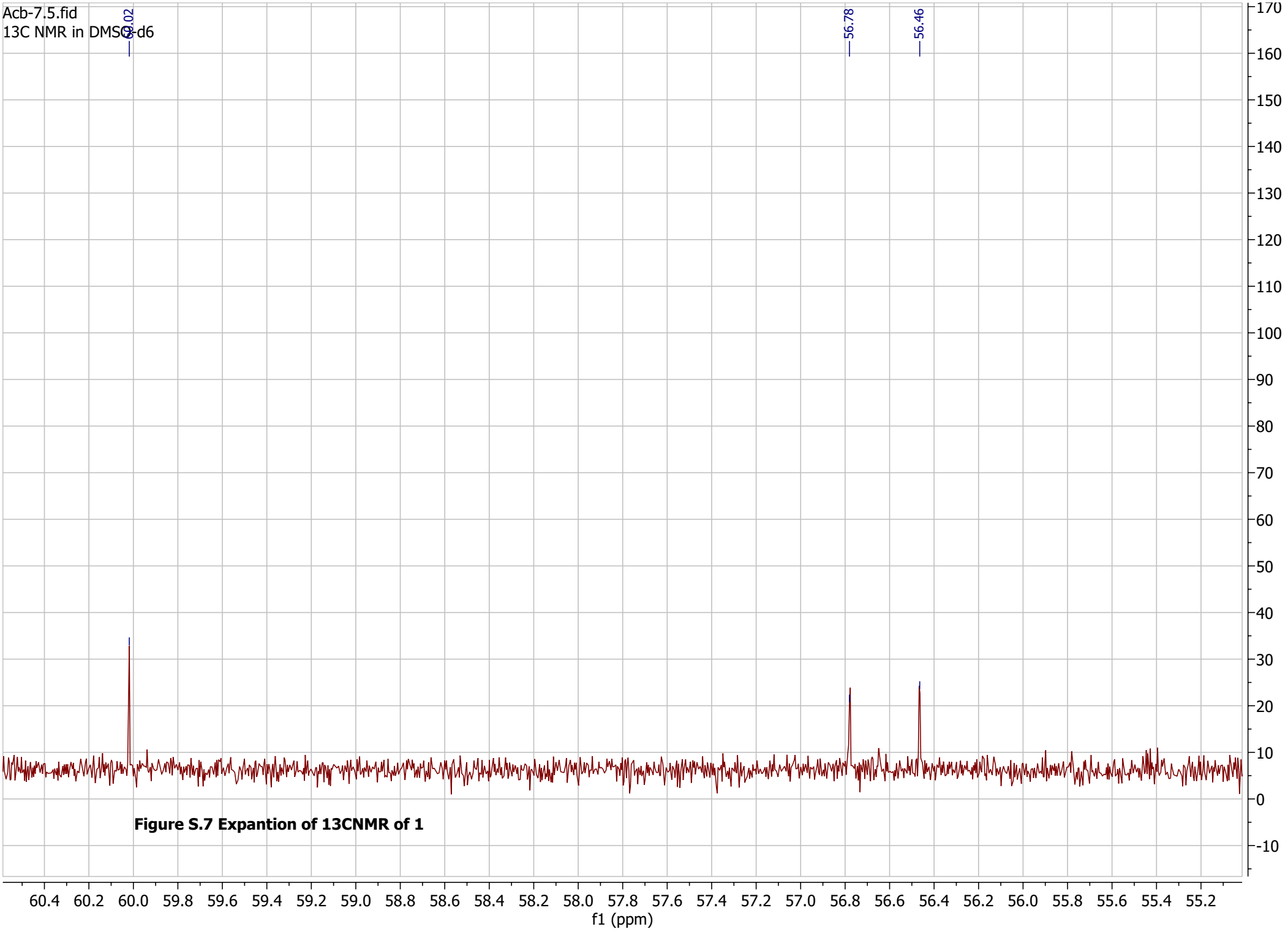


Figure S.7 Expantion of 13CNMR of 1

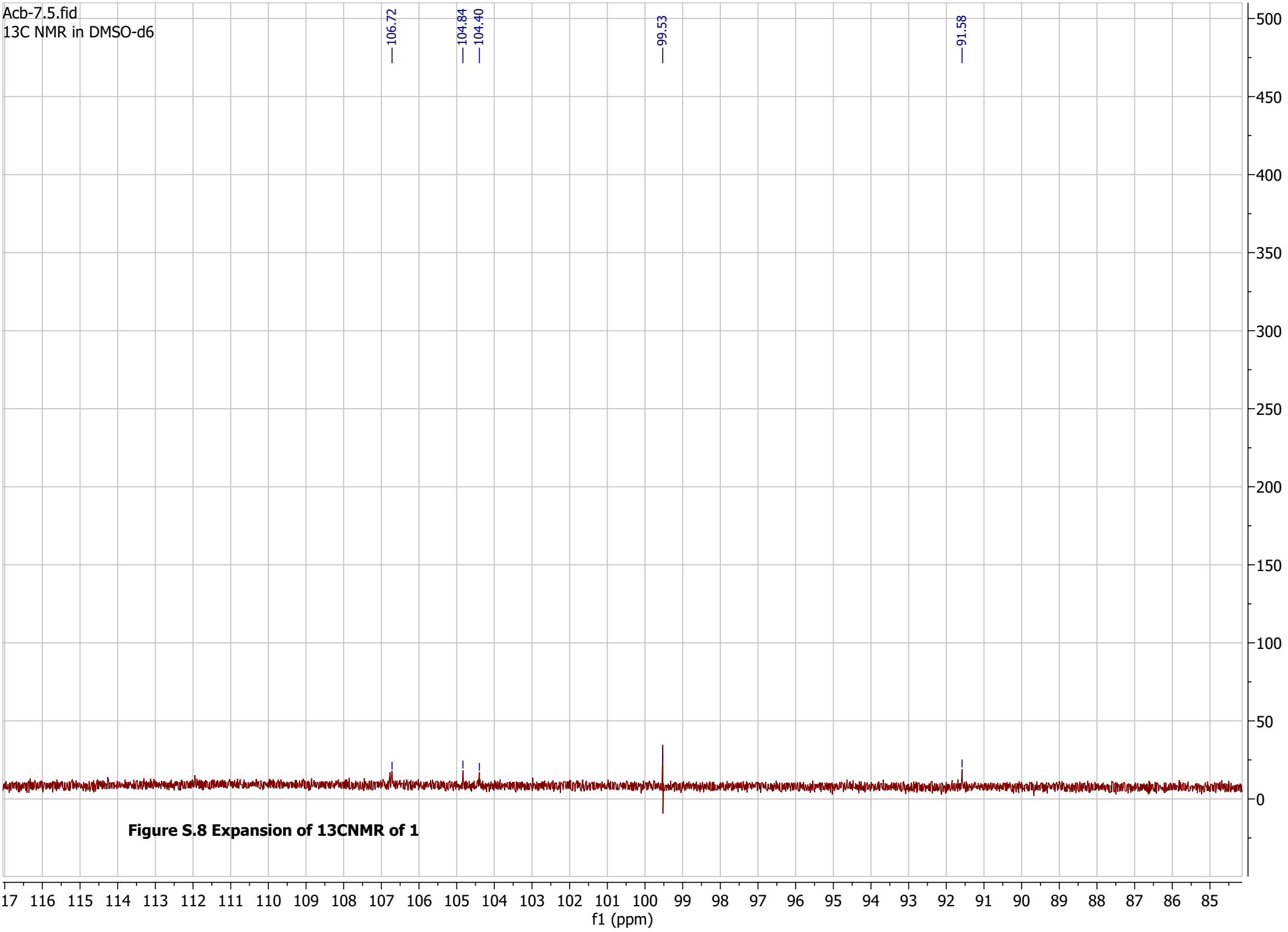


Figure S.8 Expansion of 13CNMR of 1

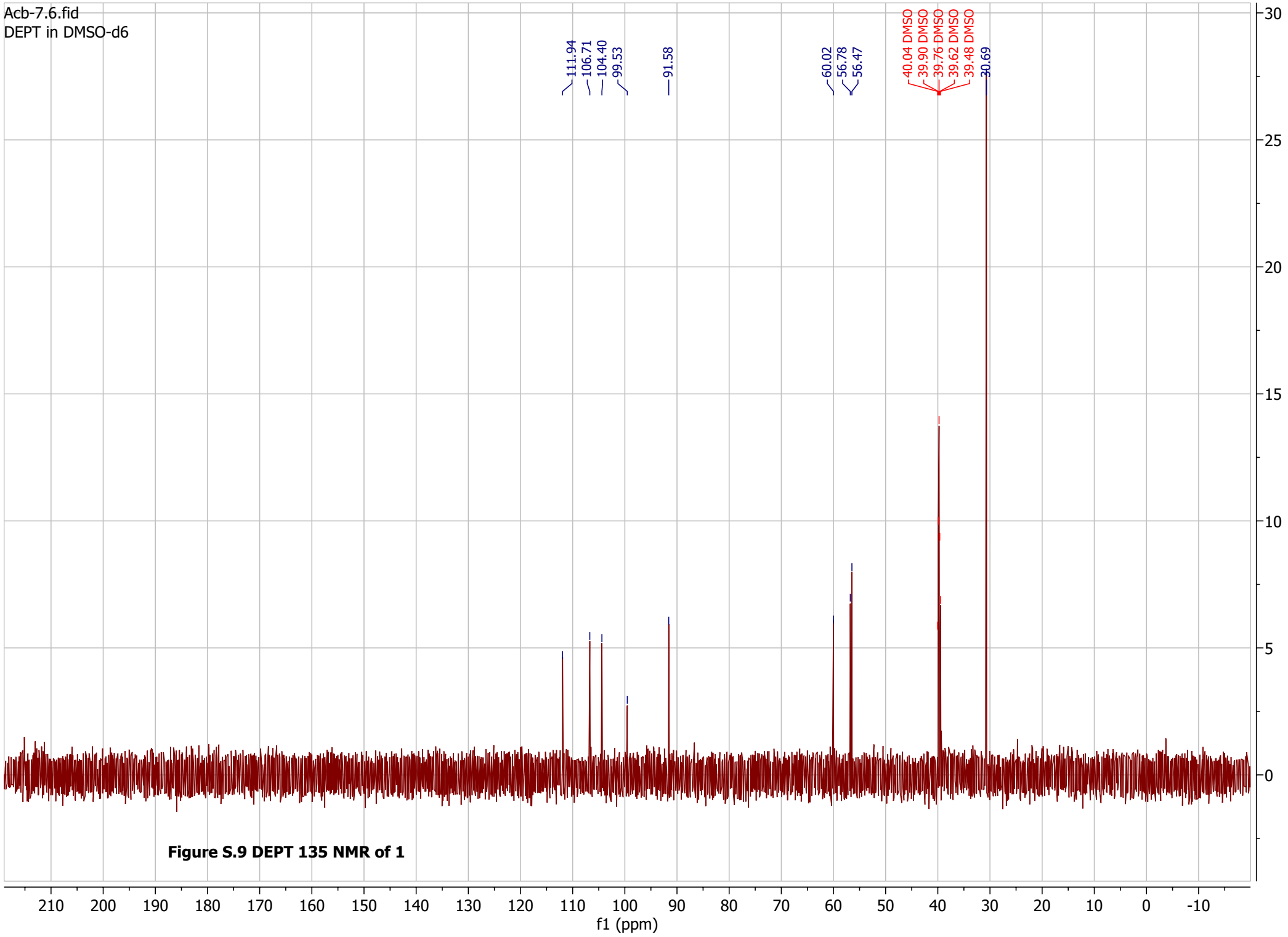


Figure S.9 DEPT 135 NMR of 1

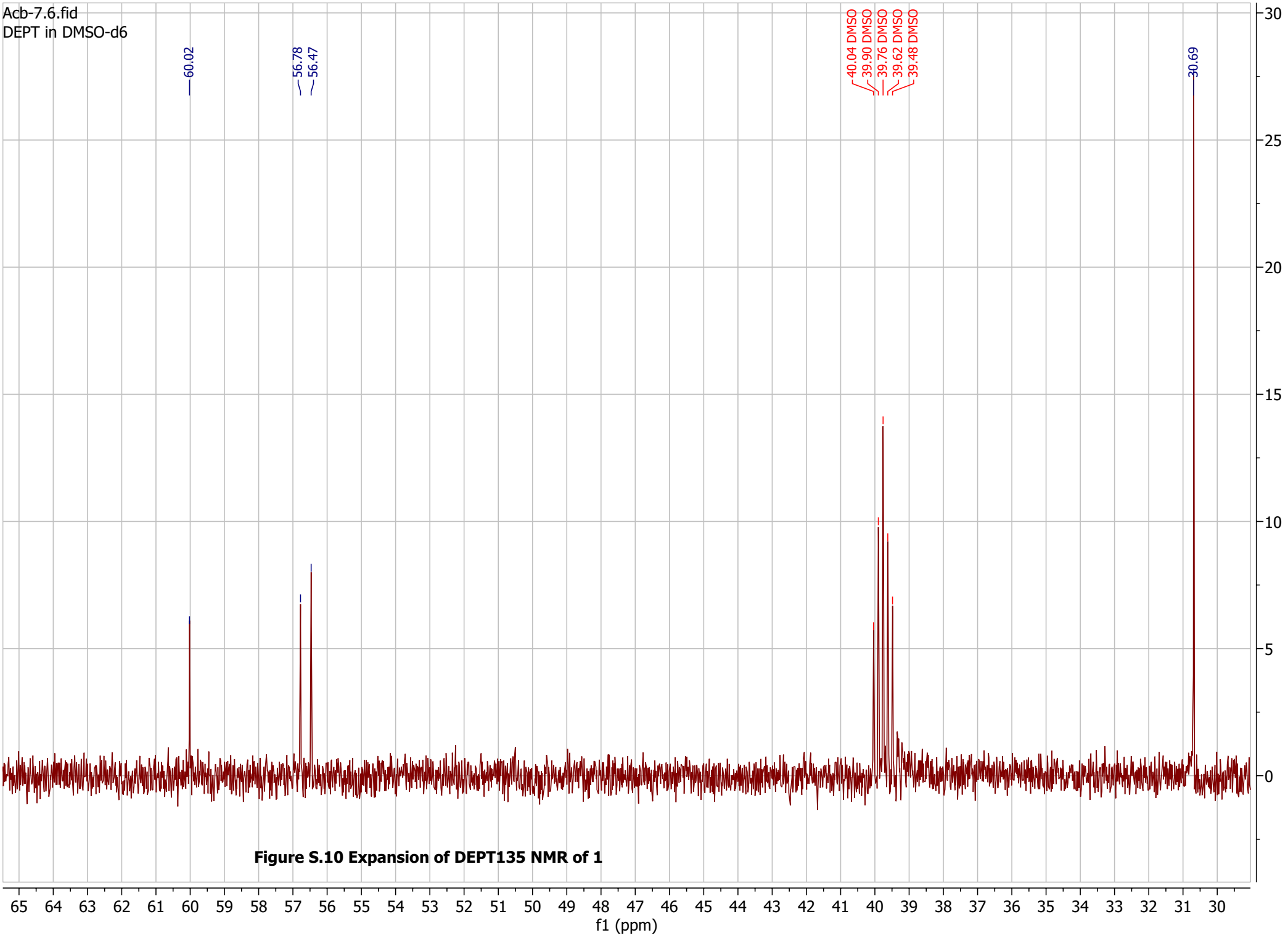


Figure S.10 Expansion of DEPT135 NMR of 1

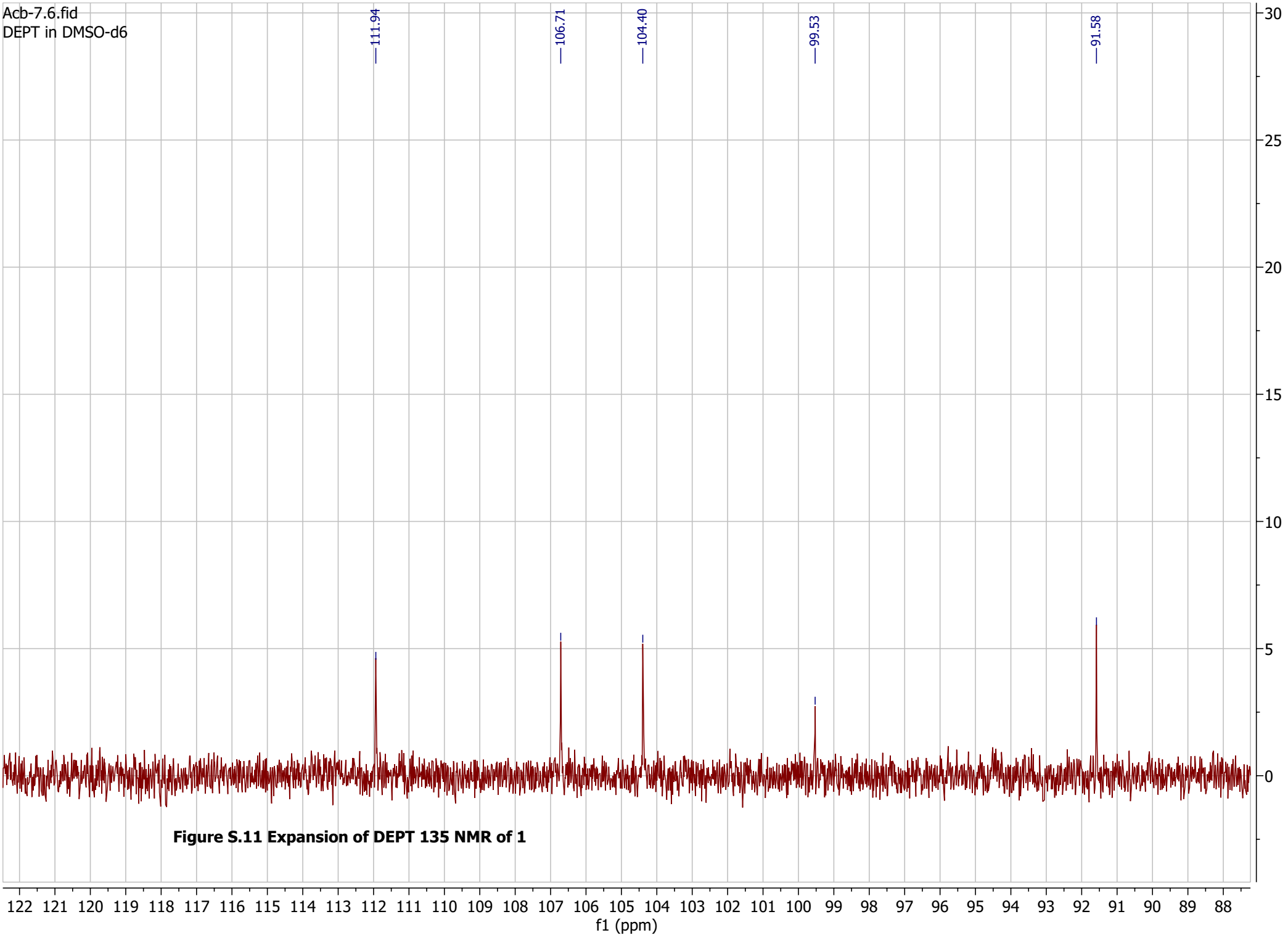


Figure S.11 Expansion of DEPT 135 NMR of 1

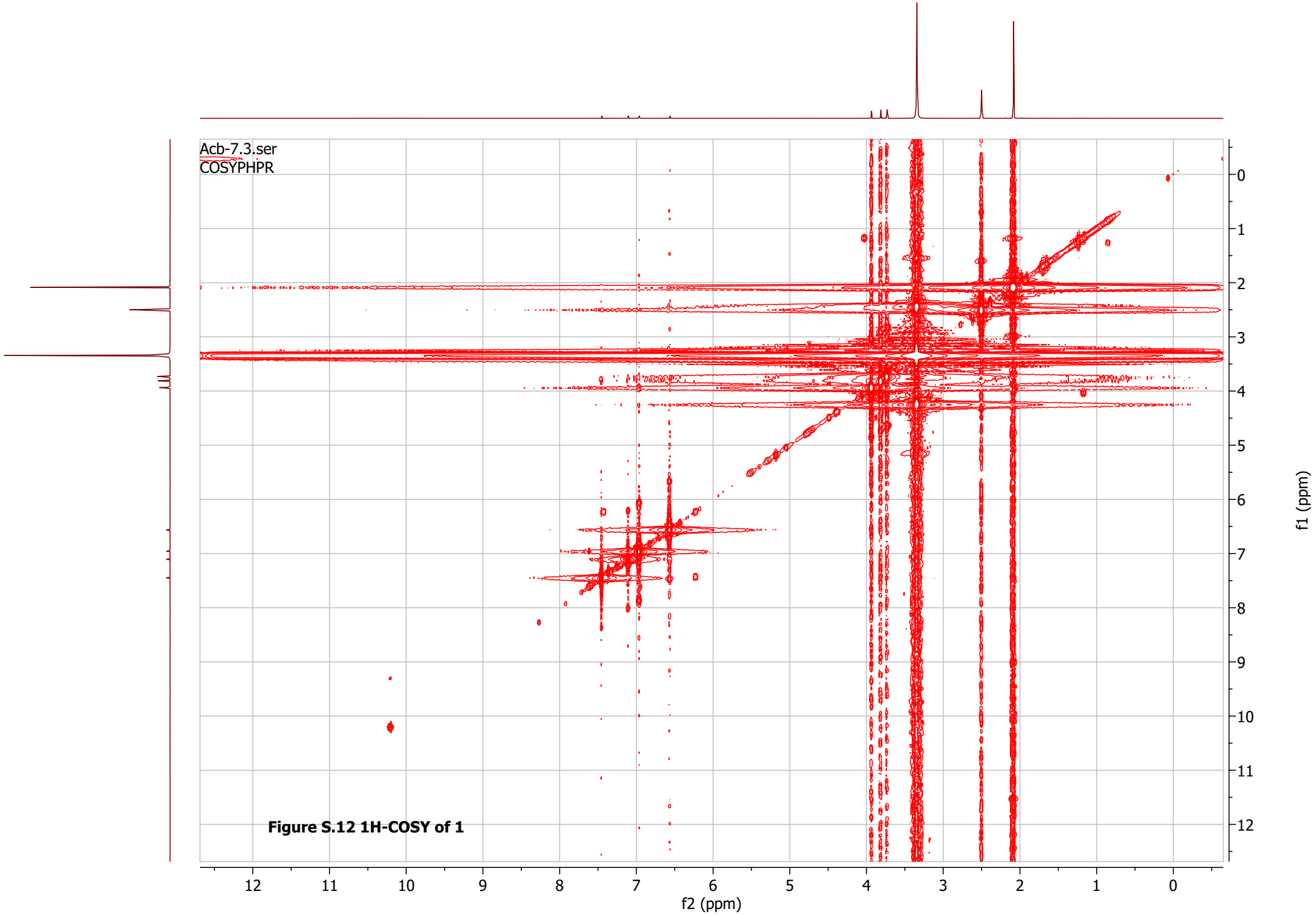


Figure S.12 1H-COSY of 1

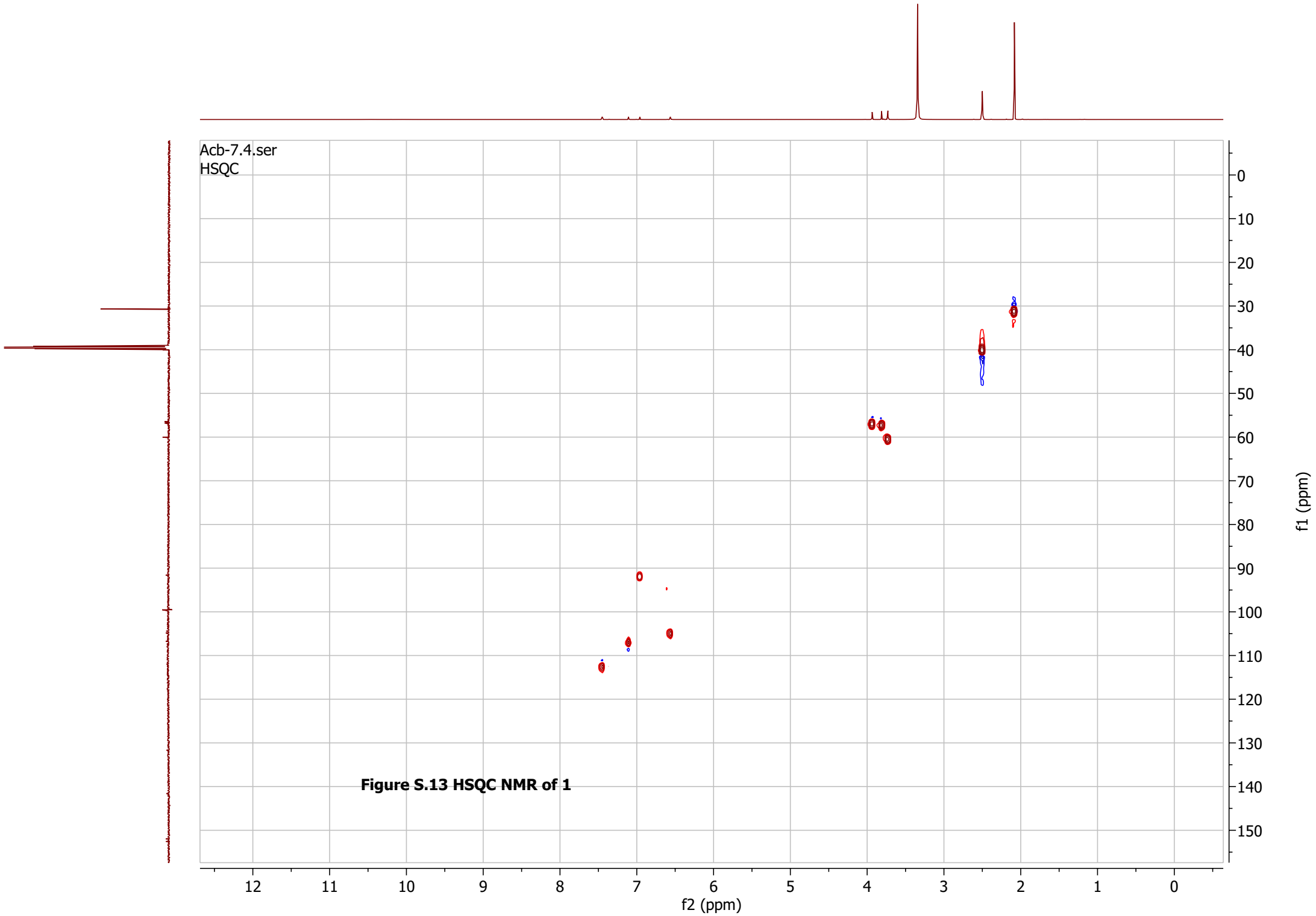


Figure S.13 HSQC NMR of 1

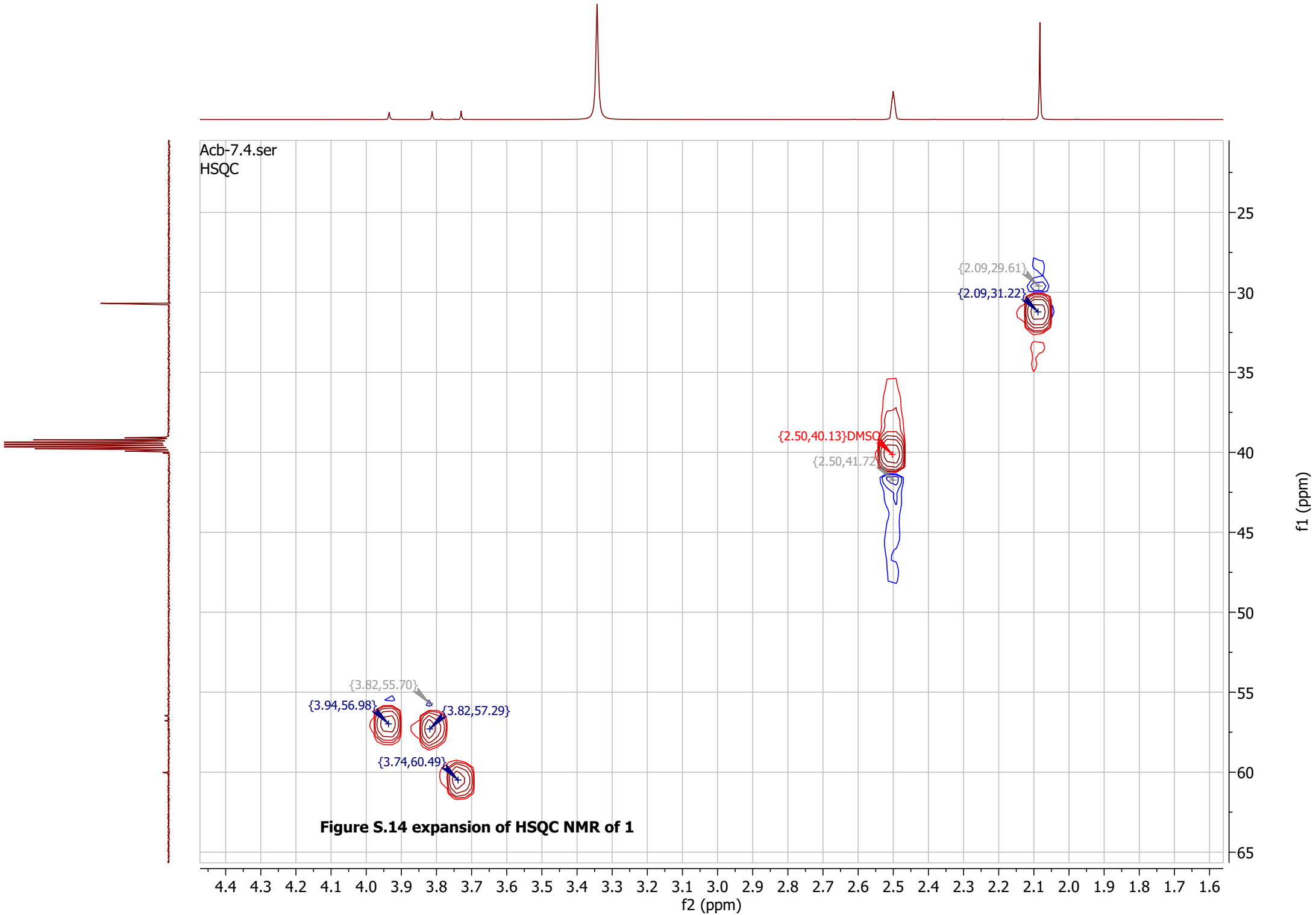


Figure S.14 expansion of HSQC NMR of 1

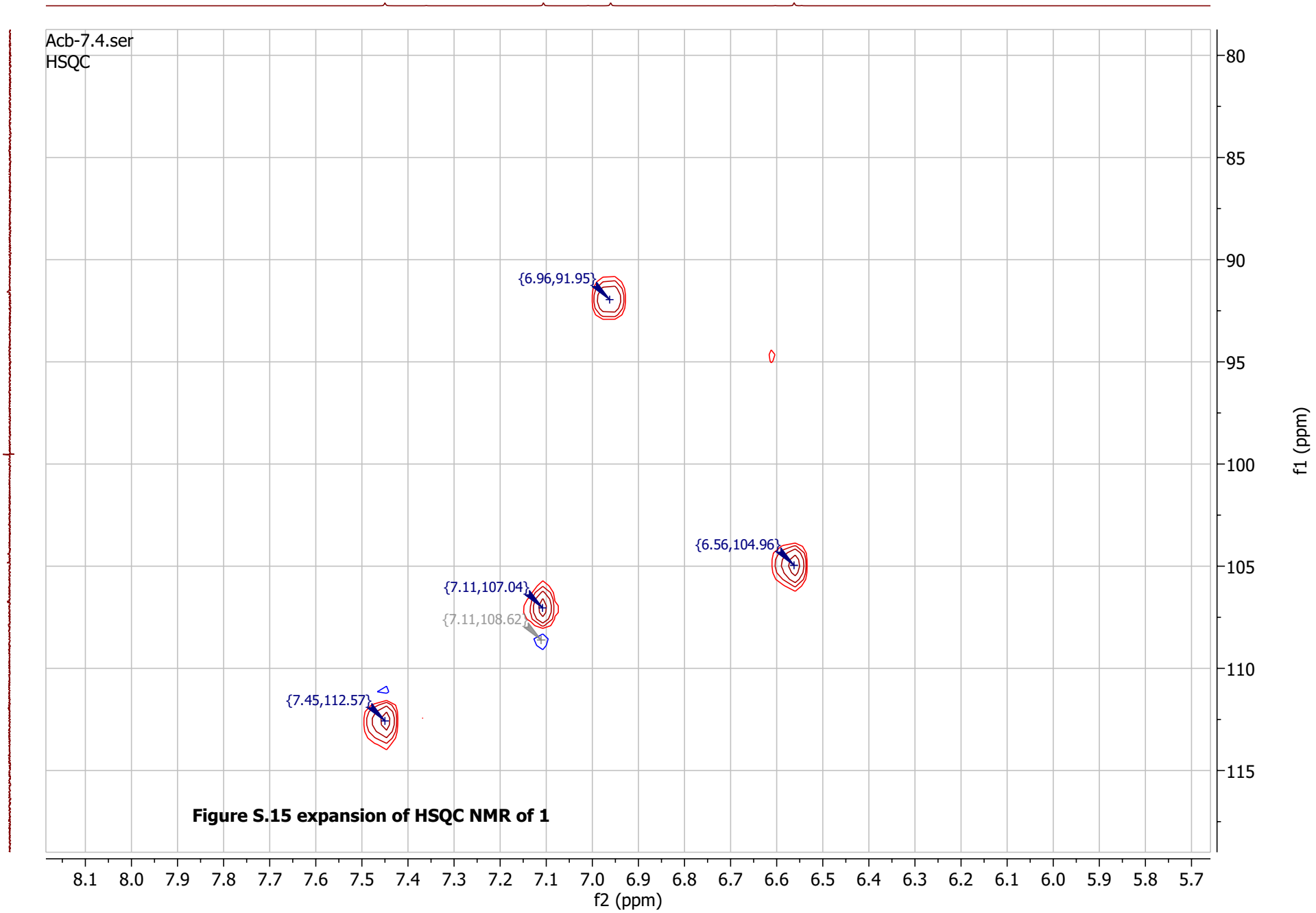


Figure S.15 expansion of HSQC NMR of 1

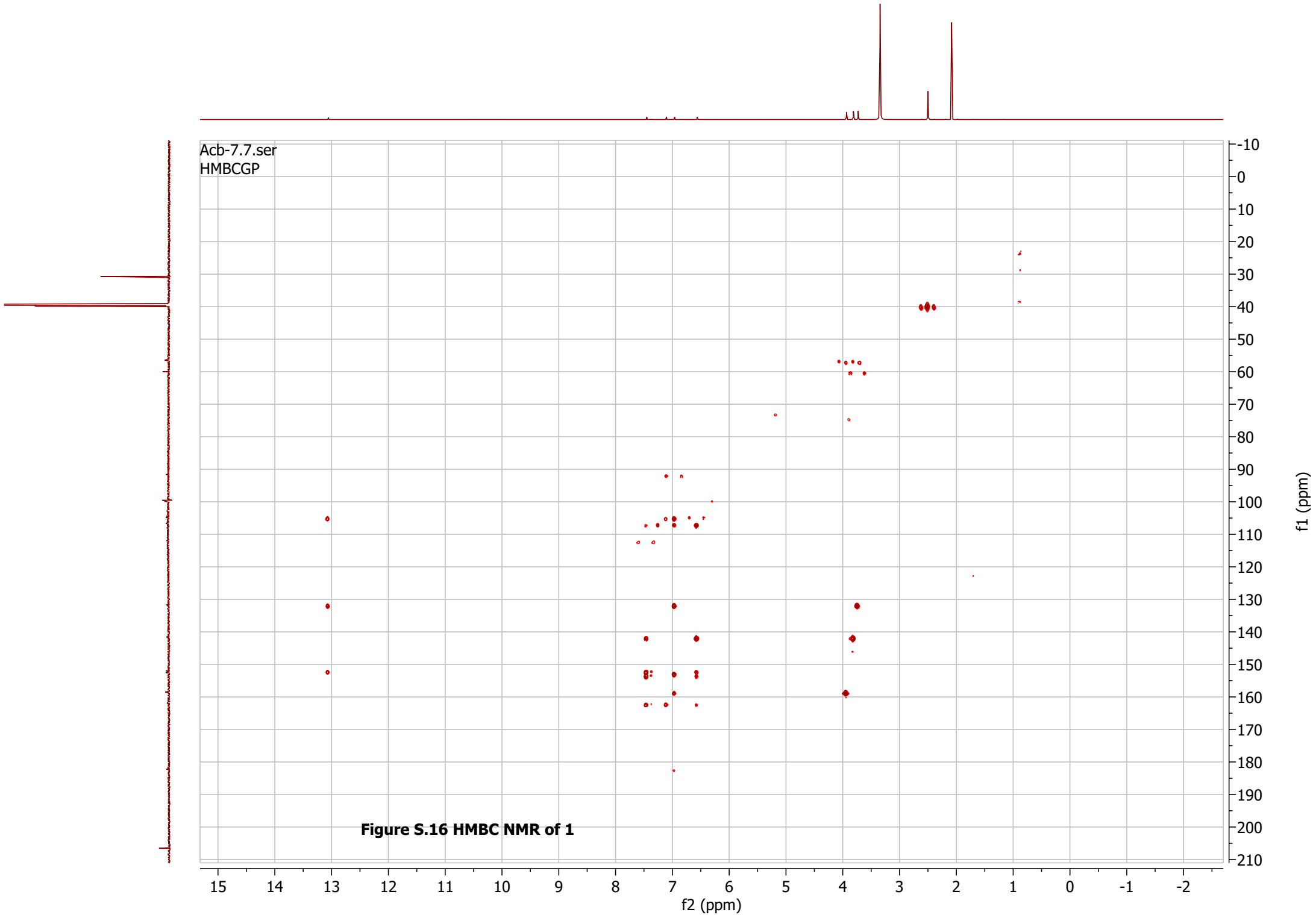


Figure S.16 HMBC NMR of 1

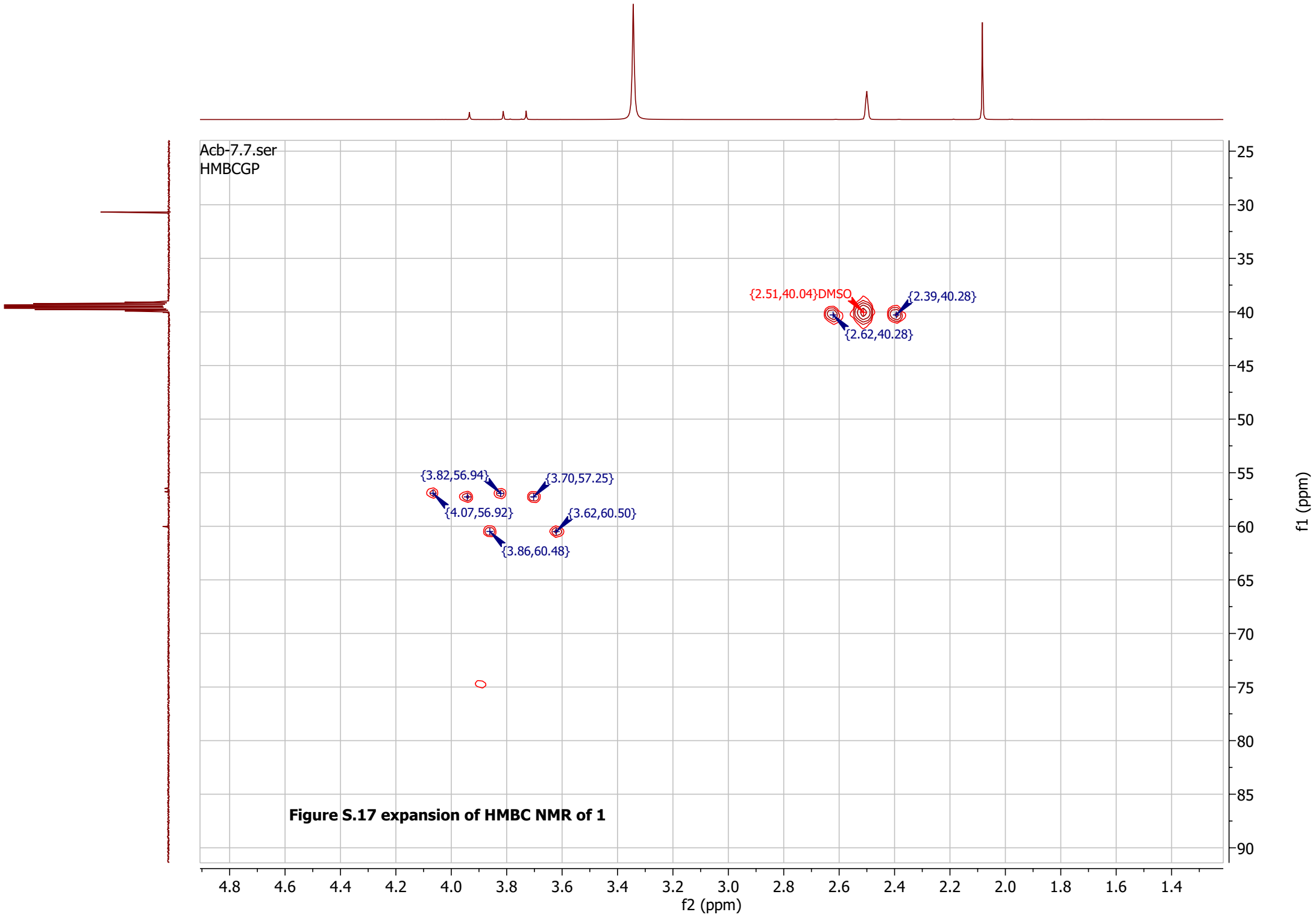


Figure S.17 expansion of HMBC NMR of 1

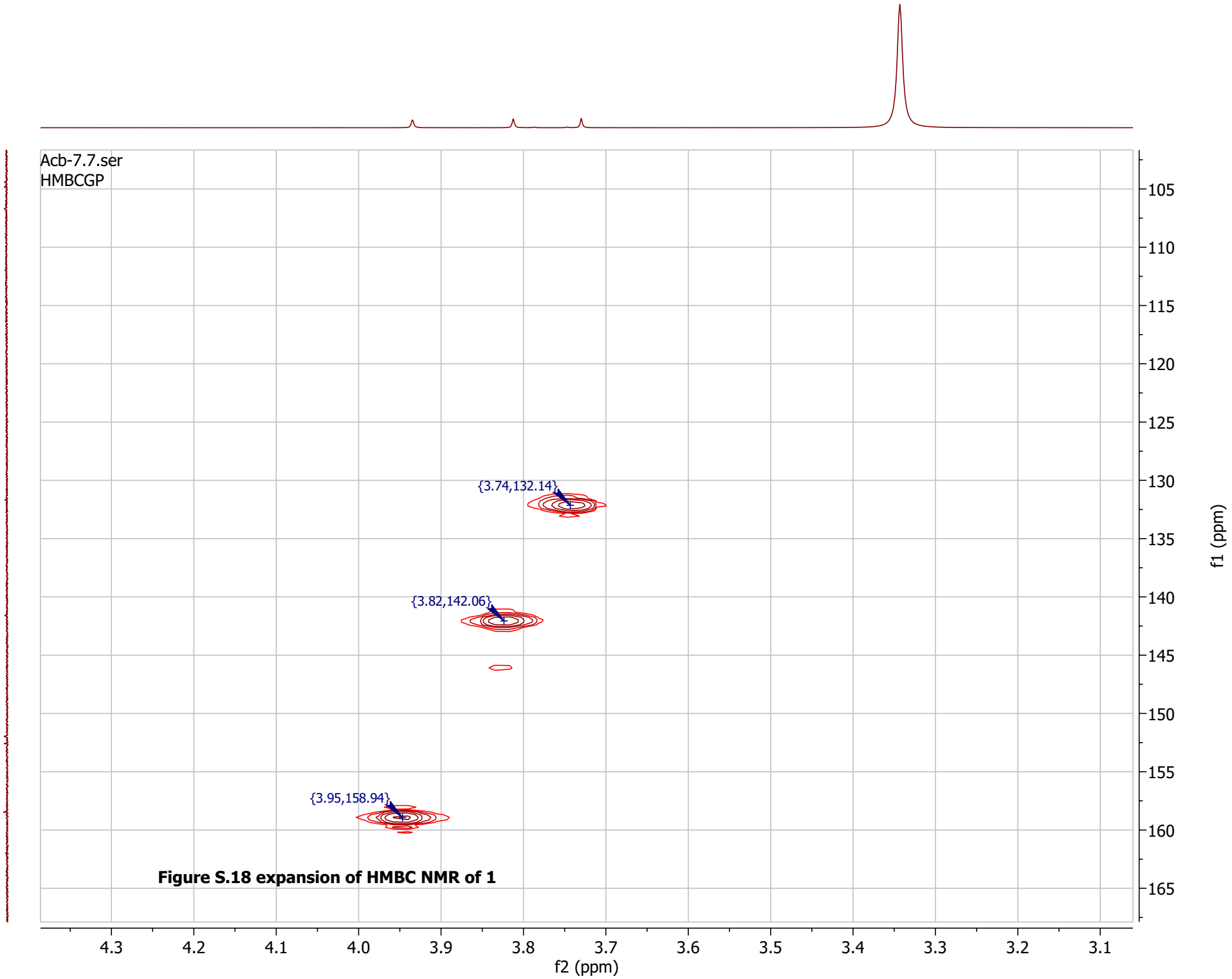


Figure S.18 expansion of HMBC NMR of 1

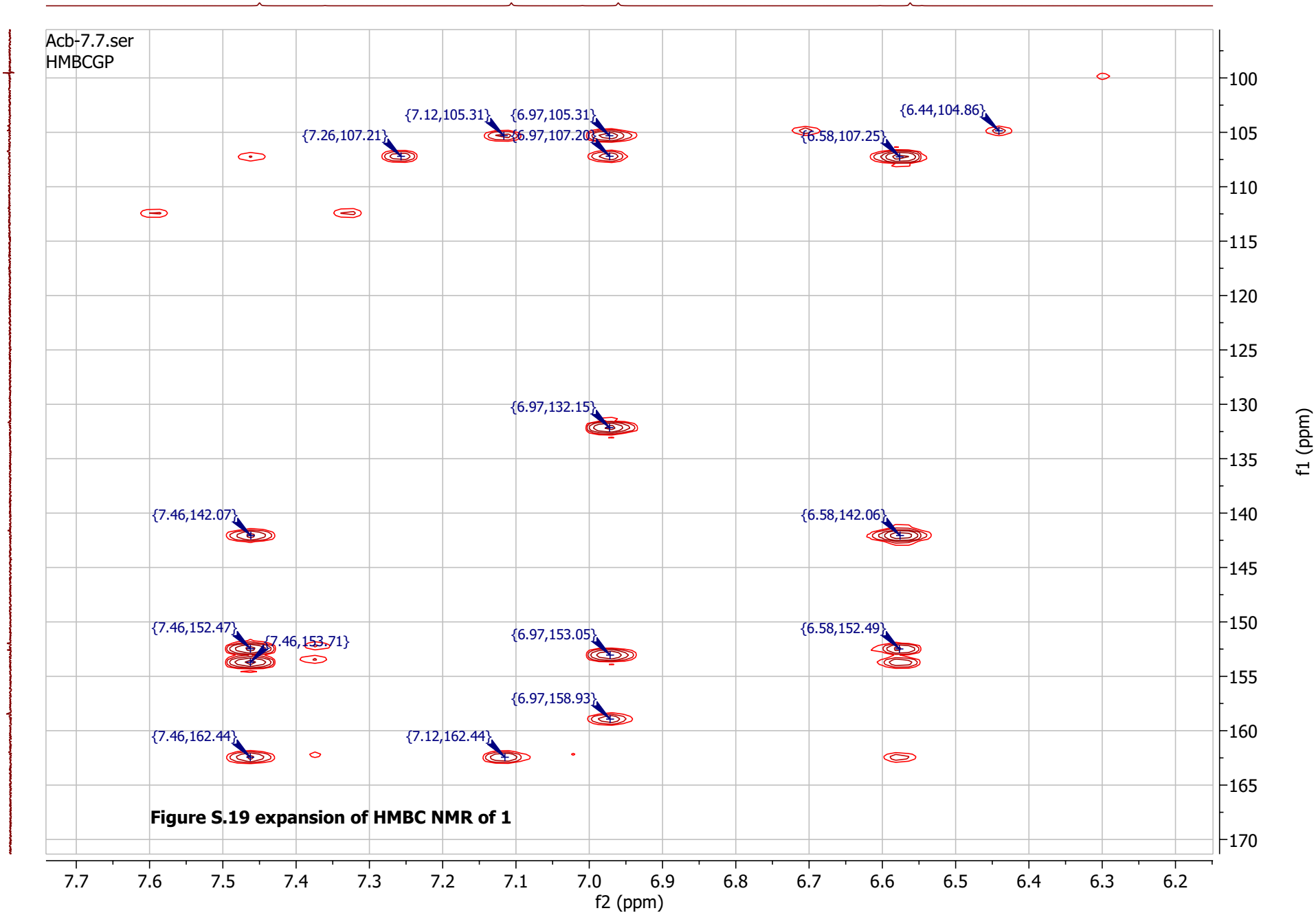


Figure S.19 expansion of HMBC NMR of 1

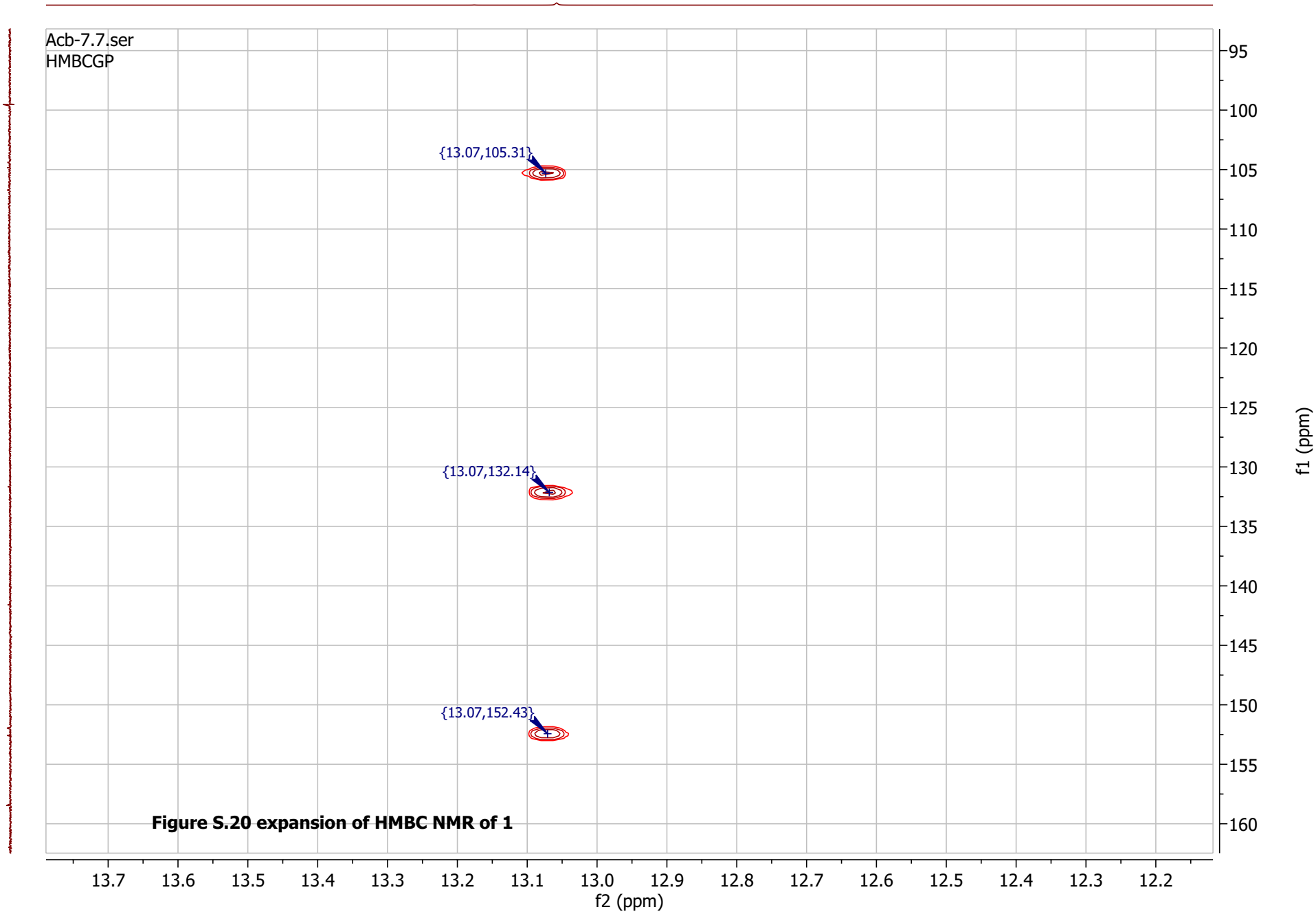
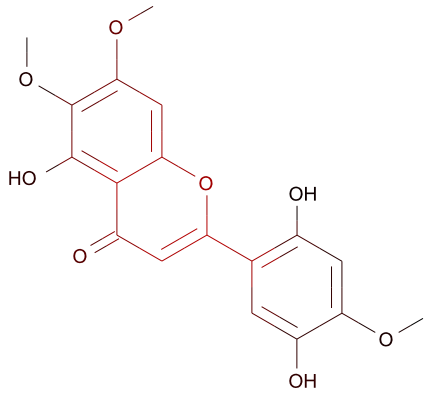


Figure S.20 expansion of HMBC NMR of 1

Toxicity Report

Flavonoid-1



$C_{18}H_{16}O_8$
Molecular Weight: 360.31483
ALogP: 2.361
Rotatable Bonds: 4
Acceptors: 8
Donors: 3

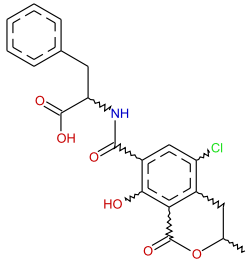
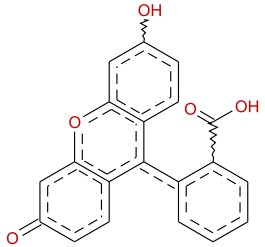
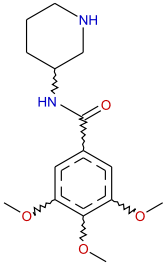
Model Prediction

Prediction: Toxic
Probability: 0.802
Enrichment: 1.52
Bayesian Score: 6.74
Mahalanobis Distance: 11.1
Mahalanobis Distance p-value: 0.000872

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

TOPKAT_Developmental_Toxicity_Potential

Structural Similar Compounds

Name	Ochratoxin a	D&C Yellow 8	N-(3-Piperidyl)3;4;5-trimethoxybenzamide
Structure			
Actual Endpoint	Toxic	Non-Toxic	Toxic
Predicted Endpoint	Toxic	Non-Toxic	Toxic
Distance	0.630	0.708	0.719
Reference	Toxicol Appl Pharmacol 37(2):331-8; 1976	Food Chem Toxicol 24:819-823; 1986	Kiso to Rinsho 18:91-101; 1984

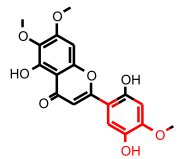
Model Applicability

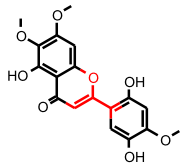
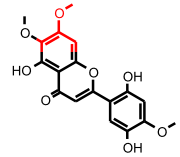
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.

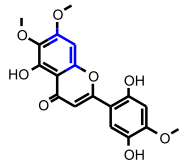
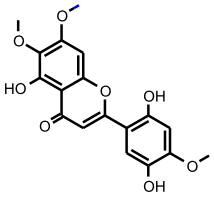
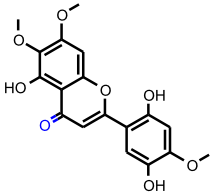
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Toxic in training set
SCFP_6	2116304939	 [*]O[c]1:[cH]:[*]:[c]([*]):[cH]:[c]:1O	0.504	5 out of 5

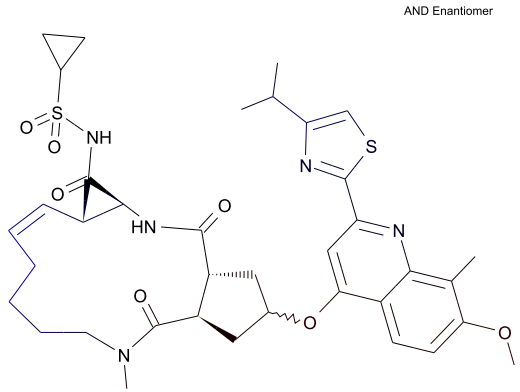
SCFP_6	616636418	 [*]O\C(=C/[*])\[c](:[*]):[*]	0.478	4 out of 4
SCFP_6	591469355	 [*][c](:[*]):[c](OC): [cH]:[*]	0.411	10 out of 12

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Toxic in training set
SCFP_6	-496409612	 [*][c](:[*]):[cH]:[c] ([*]):[*]	0	82 out of 163
SCFP_6	0	 [*]C	0	122 out of 230
SCFP_6	13	 [*]=O	0	81 out of 162

Simeprevir

TOPKAT_Developmental_Toxicity_Potential



$C_{38}H_{47}N_5O_7S_2$

Molecular Weight: 749.93908

ALogP: 4.796

Rotatable Bonds: 8

Acceptors: 9

Donors: 2

Model Prediction

Prediction: Non-Toxic

Probability: 0.438

Enrichment: 0.833

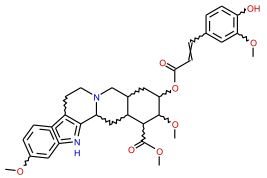
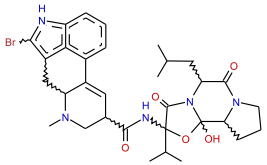
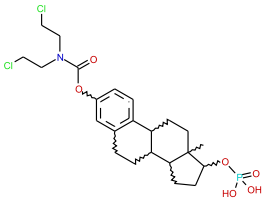
Bayesian Score: -3.14

Mahalanobis Distance: 13.4

Mahalanobis Distance p-value: 9.2e-008

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	Reserpate	Bromocriptine	Estramustine Phosphate Disodium (Free acid form)
Structure			
Actual Endpoint	Toxic	Non-Toxic	Non-Toxic
Predicted Endpoint	Toxic	Non-Toxic	Non-Toxic
Distance	0.675	0.778	0.819
Reference	Oyo Yakuri 18:105-124; 1979	Toxicol Lett 50:189-194; 1990	Oyo Yakuri 20(6):1219-1236; 1980

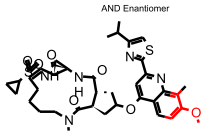
Model Applicability

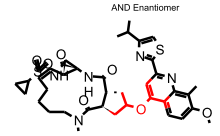
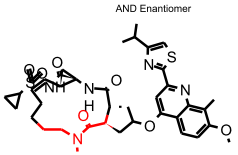
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. OPS PC12 out of range. Value: 3.5244. Training min, max, SD, explained variance: -3.7514, 3.3159, 1.318, 0.0255.

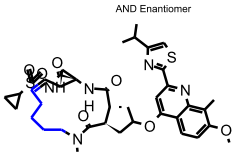
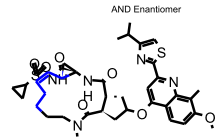
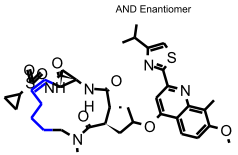
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Toxic in training set
SCFP_6	591469355	 [*][c](:[*]):[c](OC):[cH]:[*]	0.411	10 out of 12

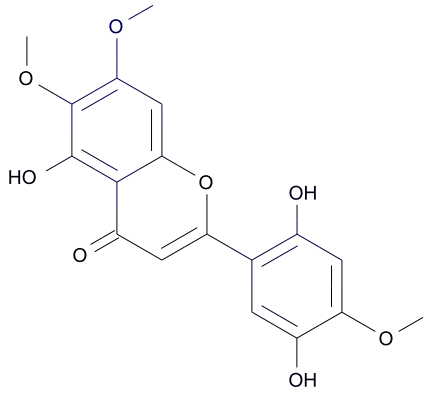
SCFP_6	-395254381	 [*]:[cH]:[c](OC1C[*][*]C1):[c](:[*]):[*]	0.271	1 out of 1
SCFP_6	-109092631	 [*]CCN(C)C(=O)C([*])[*]	0.271	1 out of 1

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Toxic in training set
SCFP_6	-98332825	 [*]CCCCC=[*]	-0.718	0 out of 2
SCFP_6	-1476112164	 [*]CC\C=C/C1[*][*]1	-0.718	0 out of 2
SCFP_6	1260369147	 [*]CCC\C=C/[*]	-0.718	0 out of 2

Flavonoid-1

TOPKAT_Mouse_Female_FDA_None_vs_Carcinogen



$C_{18}H_{16}O_8$

Molecular Weight: 360.31483

ALogP: 2.361

Rotatable Bonds: 4

Acceptors: 8

Donors: 3

Model Prediction

Prediction: Non-Carcinogen

Probability: 0.208

Enrichment: 0.648

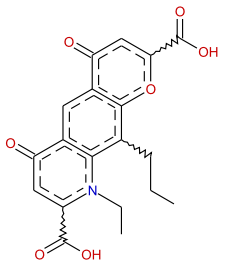
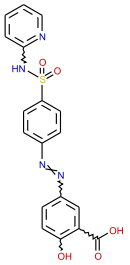
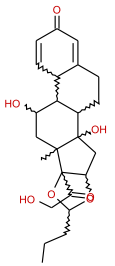
Bayesian Score: -4.85

Mahalanobis Distance: 11.7

Mahalanobis Distance p-value: 0.0252

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	Nedocromil	Sulfasalazine	Budesonide
Structure			
Actual Endpoint	Non-Carcinogen	Carcinogen	Non-Carcinogen
Predicted Endpoint	Non-Carcinogen	Carcinogen	Non-Carcinogen
Distance	0.600	0.669	0.686
Reference	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997

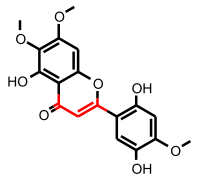
Model Applicability

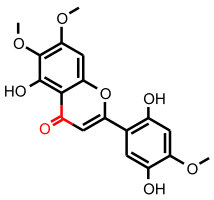
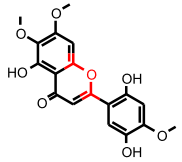
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown ECFP_2 feature: 1573564860: [*]O\C(=C/[*])\[c](:[*]):[*]

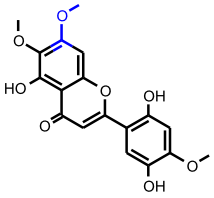
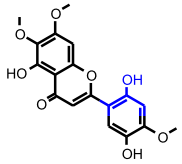
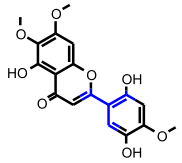
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
ECFP_6	464808839	 [*]C(=CC(=[*])[*])[*]	0.524	8 out of 14

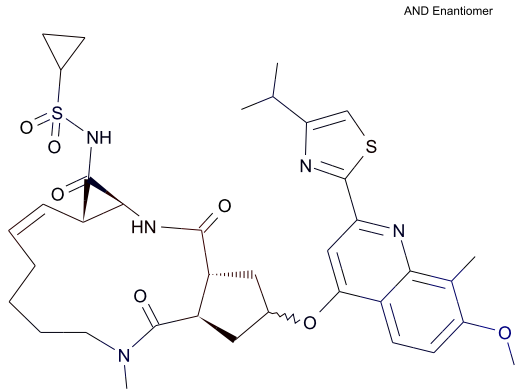
ECFP_6	2106656448	 [*]C(=O)[*]	0.254	31 out of 77
ECFP_6	-560785749	 [*]C(=[*])O[c](:[*]):[*]	0.212	1 out of 2

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
ECFP_6	1307307440	 [*]:[c](:[*])OC	-0.558	4 out of 25
ECFP_6	1334400011	 [*][c](:[*]):[c](O):[cH]:[*]	-0.496	3 out of 18
ECFP_6	-427397688	 [*]C(=[*])[c](:[cH]:[*]):[c]([*]):[*]	-0.476	5 out of 28

Simeprevir

TOPKAT_Mouse_Female_FDA_None_vs_Carcinogen



$C_{38}H_{47}N_5O_7S_2$

Molecular Weight: 749.93908

ALogP: 4.796

Rotatable Bonds: 8

Acceptors: 9

Donors: 2

Model Prediction

Prediction: Non-Carcinogen

Probability: 0.207

Enrichment: 0.646

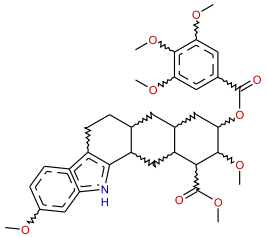
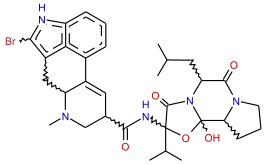
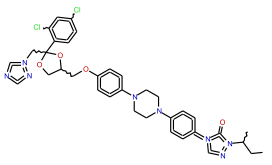
Bayesian Score: -4.97

Mahalanobis Distance: 15.4

Mahalanobis Distance p-value: 4.64e-008

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	Reserpine	Bromocriptine	Itraconazole
Structure			
Actual Endpoint	Carcinogen	Non-Carcinogen	Non-Carcinogen
Predicted Endpoint	Carcinogen	Non-Carcinogen	Non-Carcinogen
Distance	0.783	0.847	0.870
Reference	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997

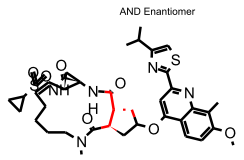
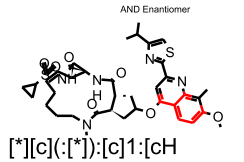
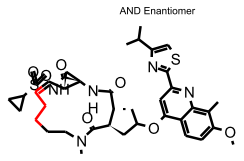
Model Applicability

Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

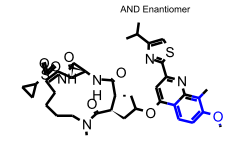
1. OPS PC4 out of range. Value: 5.1697. Training min, max, SD, explained variance: -4.7116, 4.7287, 2.103, 0.0450.
2. OPS PC14 out of range. Value: -3.7168. Training min, max, SD, explained variance: -3.5274, 4.3994, 1.457, 0.0216.
3. OPS PC17 out of range. Value: 3.3515. Training min, max, SD, explained variance: -4.7306, 3.3103, 1.364, 0.0189.
4. Unknown ECFP_2 feature: -309676563: [*]N[C@]1(C[C@H]1[*])C(=[*])[*]
5. Unknown ECFP_2 feature: -1049290660: [*]C1([*])C[C@H]1C=[*]
6. Unknown ECFP_2 feature: 360408239: [*]C\C=C/[*]
7. Unknown ECFP_2 feature: 1616402542: [*]CN(C)C(=[*])[*]
8. Unknown ECFP_2 feature: -1818486371: [*]NC(=O)C1([*])[*][*]1
9. Unknown ECFP_2 feature: 1310940530: [*]C([*])O[c](:[*]):[*]
10. Unknown ECFP_2 feature: -253227249: [*]:[c](:[*])[c]1:n:[*]:[*]:s:1
11. Unknown ECFP_2 feature: 733491677: [*]:[c](:[*])C(C)C
12. Unknown ECFP_2 feature: 2121941848: [*]NS(=O)(=O)C1[*][*]1
13. Unknown ECFP_2 feature: -622223421: [*]S(=[*])(=[*])C1CC1

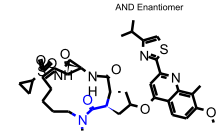
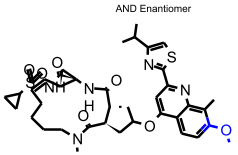
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
ECFP_6	-2095963820	 [*][C@@H]1[*][*]C[C@H]1C(=[*])[*]	0.891	12 out of 14
ECFP_6	2082767335	 [*][c](:[*]):[c]1:[cH]:[cH]:[c]([*]):[*]:[c]:1:[*]	0.617	2 out of 2
ECFP_6	-1331088410	 [*]CCC=[*]	0.442	2 out of 3

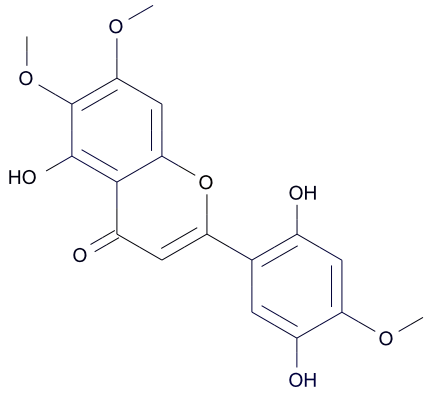
Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
ECFP_6	2077607946	 [*]O[c]1:[cH]:[cH]:[c](:[*]):[*]:[c]:1[*]	-1.15	0 out of 7

ECFP_6	1526862590	 [*]C([*])C(=O)N([*])[*]	-0.638	1 out of 9
ECFP_6	1307307440	 [*]:[c](:[*])OC	-0.558	4 out of 25

Flavonoid-1

TOPKAT_Mouse_Male_FDA_None_vs_Carcinogen



$C_{18}H_{16}O_8$

Molecular Weight: 360.31483

ALogP: 2.361

Rotatable Bonds: 4

Acceptors: 8

Donors: 3

Model Prediction

Prediction: Non-Carcinogen

Probability: 0.217

Enrichment: 0.737

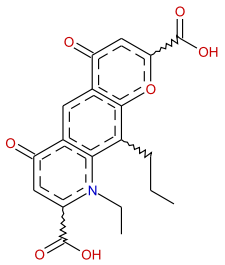
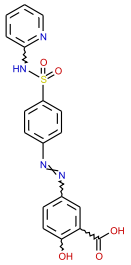
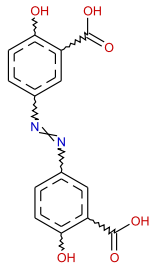
Bayesian Score: -3.97

Mahalanobis Distance: 12

Mahalanobis Distance p-value: 0.00673

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	Nedocromil	Sulfasalazine	Olsalazine
Structure			
Actual Endpoint	Non-Carcinogen	Carcinogen	Non-Carcinogen
Predicted Endpoint	Non-Carcinogen	Carcinogen	Carcinogen
Distance	0.586	0.641	0.691
Reference	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997

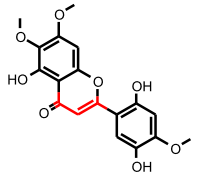
Model Applicability

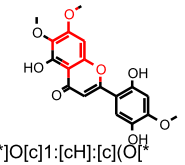
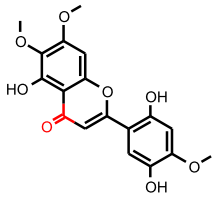
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown FCFP_2 feature: -1678245750: [*]O\C(=C/[*])\[c](:[*]):[*]

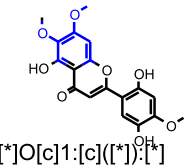
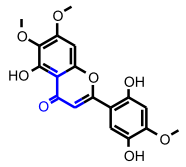
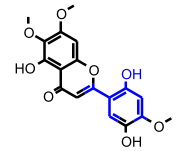
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
FCFP_6	451847724	 [*]C(=CC(=[*])[*])[*]	0.479	21 out of 48

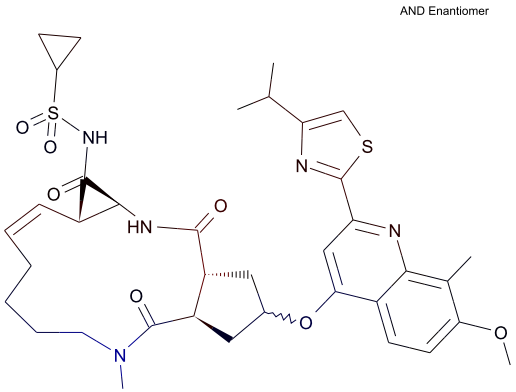
FCFP_6	1679744180	 [*]O[c]1:[cH]:[c](O[*]):[c]([*]):[*]:[c]:1[*]	0.271	1 out of 2
FCFP_6	1872154524	 [*]C(=O)[*]	0.205	69 out of 213

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
FCFP_6	1028934530	 [*]O[c]1:[c]([*]):[*]:[c]([*]):[cH]:[c]:1OC	-0.596	1 out of 10
FCFP_6	-1549192822	 [*]=CC(=O)[c](:[*]):[*]	-0.489	3 out of 21
FCFP_6	-1604301295	 [*]C(=[*])[c]1:[cH]:[*]:[c]([*]):[cH]:[c]:1O	-0.445	2 out of 14

Simeprevir

TOPKAT_Mouse_Male_FDA_None_vs_Carcinogen



$C_{38}H_{47}N_5O_7S_2$

Molecular Weight: 749.93908

ALogP: 4.796

Rotatable Bonds: 8

Acceptors: 9

Donors: 2

Model Prediction

Prediction: Non-Carcinogen

Probability: 0.258

Enrichment: 0.877

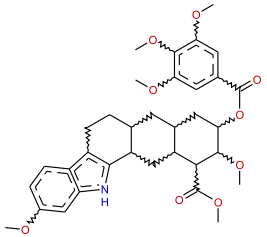
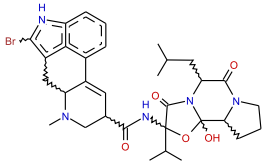
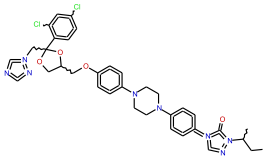
Bayesian Score: -1.92

Mahalanobis Distance: 18.3

Mahalanobis Distance p-value: 6.22e-015

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	Reserpine	Bromocriptine	Itraconazole
Structure			
Actual Endpoint	Carcinogen	Non-Carcinogen	Non-Carcinogen
Predicted Endpoint	Carcinogen	Non-Carcinogen	Non-Carcinogen
Distance	0.775	0.832	0.865
Reference	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997

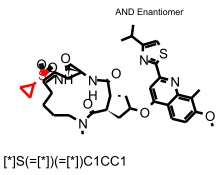
Model Applicability

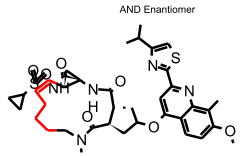
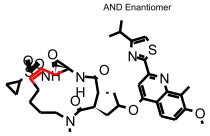
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown FCFP_2 feature: 690481386: [*]:[c](:[*])[c]1:n:[*]:[*]:s:1

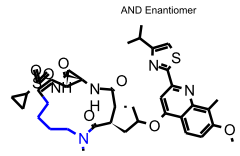
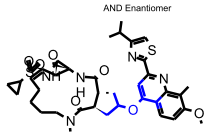
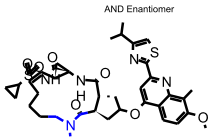
Feature Contribution

Top features for positive contribution

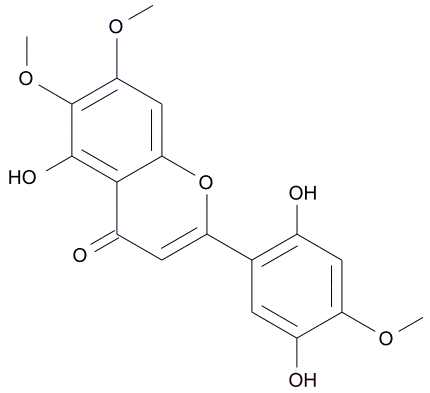
Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
FCFP_6	-55265897	 [*]S(=[*])(=[*])C1CC1	0.594	17 out of 34

FCFP_6	-1289661876	 [*]CCC\C=C/[*]	0.517	2 out of 3
FCFP_6	451847724	 [*]C(=CC(=[*])[*])[*]	0.479	21 out of 48

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
FCFP_6	-98332825	 [*]CCCCN([*])[*]	-0.793	1 out of 13
FCFP_6	-1972798083	 [*]:[cH]:[c](OC1C[*][*]C1):[c](:[*]):[*]	-0.582	0 out of 3
FCFP_6	-1553874037	 [*]CN(C)C(=[*])[*]	-0.45	5 out of 32

Flavonoid-1



$C_{18}H_{16}O_8$

Molecular Weight: 360.31483

ALogP: 2.361

Rotatable Bonds: 4

Acceptors: 8

Donors: 3

Model Prediction

Prediction: Mild

Probability: 0.804

Enrichment: 1.17

Bayesian Score: -0.831

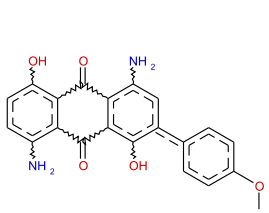
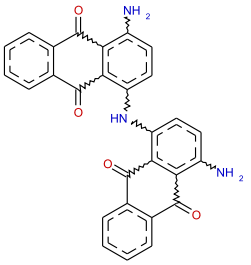
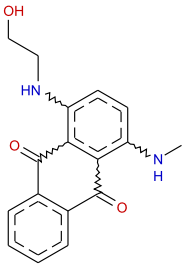
Mahalanobis Distance: 8.69

Mahalanobis Distance p-value: 0.674

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

TOPKAT_Ocular_Irritancy_Mild_vs_Moderate_Severe

Structural Similar Compounds

Name	ANTHRAQUINONE; 1;5-DIAMINO-4;8-DIHYDROXY-3-(p-METHOXYPHENYL)-	4;4'-DIAMINO-1;1'-DIANTHRIMIDE	ANTHRAQUINONE; 1-((2-HYDROXYETHYL)AMINO)-4-(METHYLAMINO)-
Structure			
Actual Endpoint	Mild	Mild	Mild
Predicted Endpoint	Mild	Mild	Mild
Distance	0.709	0.726	0.787
Reference	28ZPAK 245;72	28ZPAK-;125;72	28ZPAK 245;72

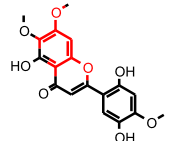
Model Applicability

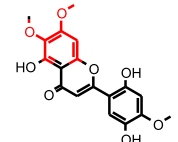
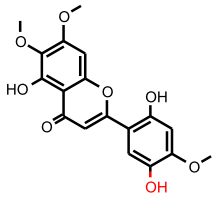
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown FCFP_2 feature: -1678245750: [*]O\C(=C/[*])\[c](:[*]):[*]

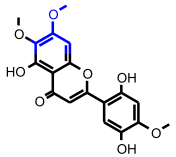
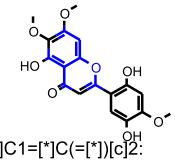
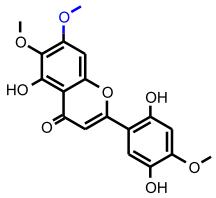
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Moderate_Severe in training set
FCFP_10	1679744180	 [*]O[c]1:[cH]:[c](O[*]):[c]([*]):[*]:[c]:1[*]	0.256	2 out of 2

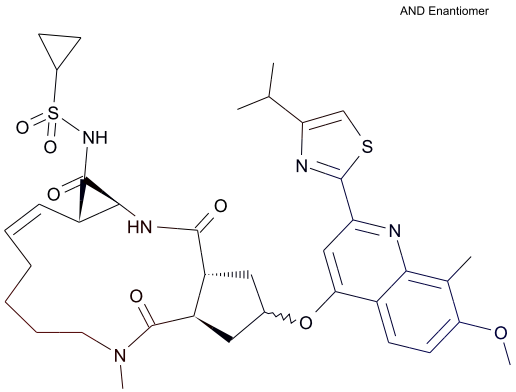
FCFP_10	1028934530	 [*]O[c]1:[c]([*]):[*] :[c]([*]):[cH]:[c]:1 OC	0.256	2 out of 2
FCFP_10	7	 [*]O	0.219	117 out of 142

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Moderate_Severe in training set
FCFP_10	-1977641857	 [*][c](:[*]):[c](OC): [cH]:[*]	-0.78	4 out of 15
FCFP_10	-1099193755	 [*]C1=[*]C(=[*])[c]2: [c]([*]):[*]:[c]([*]):[cH]:[c]:2O1	-0.361	2 out of 5
FCFP_10	136627117	 [*]OC	-0.316	46 out of 96

Simeprevir

TOPKAT_Ocular_Irritancy_Mild_vs_Moderate_Severe



$C_{38}H_{47}N_5O_7S_2$

Molecular Weight: 749.93908

ALogP: 4.796

Rotatable Bonds: 8

Acceptors: 9

Donors: 2

Model Prediction

Prediction: Mild

Probability: 0.777

Enrichment: 1.13

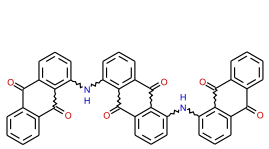
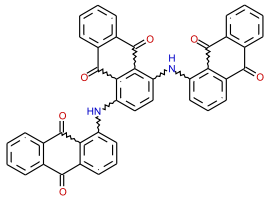
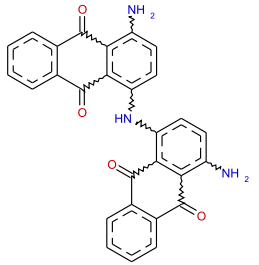
Bayesian Score: -1.77

Mahalanobis Distance: 17.1

Mahalanobis Distance p-value: 9.62e-022

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	Anthraquinone; 1;1'-(anthraquinon-1;5-ylenediimino)di-	Anthraquinone; 1;1'-(anthraquinon-1;4-ylenediimino)di-	4;4'-DIAMINO-1;1'-DIANTHRIMIDE
Structure			
Actual Endpoint	Mild	Mild	Mild
Predicted Endpoint	Mild	Mild	Mild
Distance	0.875	0.875	1.102
Reference	Prehled Prumyslove Toxikologie; Organicke Latky; Marhold; J. pp 736;86	Prehled Prumyslove Toxikologie; Organicke Latky; Marhold; J. pp 736;86	28ZPAK-;125;72

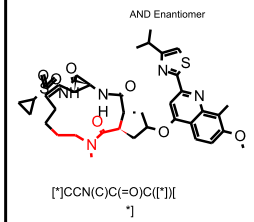
Model Applicability

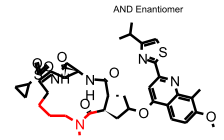
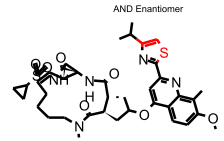
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. OPS PC15 out of range. Value: 5.5683. Training min, max, SD, explained variance: -4.4073, 5.1625, 1.138, 0.0158.

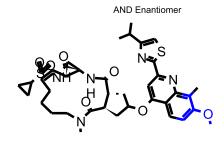
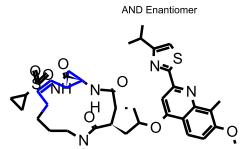
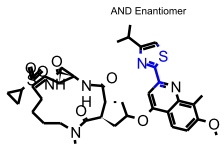
Feature Contribution

Top features for positive contribution

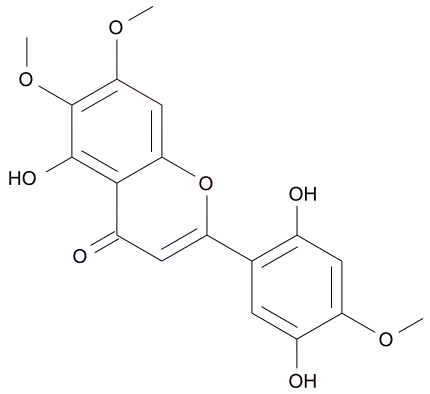
Fingerprint	Bit/Smiles	Feature Structure	Score	Moderate_Severe in training set
FCFP_10	-2015019763	 [*]CCN(C)C(=O)C([*])[*]	0.294	3 out of 3

FCFP_10	-1474971978	 [*]CCCN(C)C(=[*])[*]	0.259	14 out of 16
FCFP_10	-124655670	 [*][c]1:[*]:[*]:s:[cH]:1	0.259	14 out of 16

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Moderate_Severe in training set
FCFP_10	-1977641857	 [*][c](:[*]):[c](OC):[cH]:[*]	-0.78	4 out of 15
FCFP_10	-528918648	 [*]C\C=C/[C@@H]1CC1([*])[*]	-0.651	4 out of 13
FCFP_10	690481386	 [*]:[c](:[*])[c]1:n:[*]:[*]:s:1	-0.6	1 out of 4

Flavonoid-1



$C_{18}H_{16}O_8$

Molecular Weight: 360.31483

ALogP: 2.361

Rotatable Bonds: 4

Acceptors: 8

Donors: 3

Model Prediction

Prediction: Irritant

Probability: 0.976

Enrichment: 1.15

Bayesian Score: 0.256

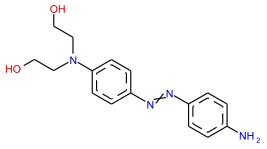
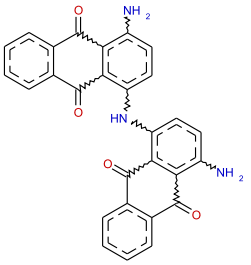
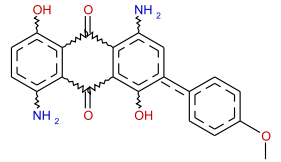
Mahalanobis Distance: 8.37

Mahalanobis Distance p-value: 0.817

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

TOPKAT_Ocular_Irritancy_None_vs_Irritant

Structural Similar Compounds

Name	Disperse Black 9	4;4'-DIAMINO-1;1'-DIANTHRIMIDE	ANTHRAQUINONE; 1;5-DIAMINO-4;8-DIHYDROXY-3-(p-METHOXYPHENYL)-
Structure			
Actual Endpoint	Non-Irritant	Irritant	Irritant
Predicted Endpoint	Non-Irritant	Irritant	Irritant
Distance	0.704	0.708	0.711
Reference	J. Am. Coll. Toxicol. 5(3):205;1986	28ZPAK-;125;72	28ZPAK 245;72

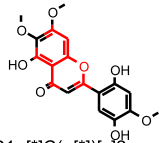
Model Applicability

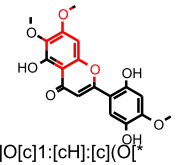
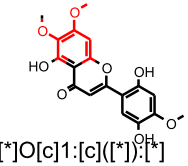
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown FCFP_2 feature: -1678245750: [*]O\C(=C/[*])\[c](:[*]):[*]

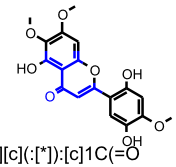
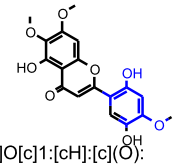
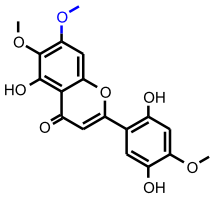
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Irritant in training set
FCFP_12	-1099193755	 [*]C1=[*]C(=[*])[c]2:[c]([*]):[*]:[c]([*]):[cH]:[c]:2O1	0.175	5 out of 5

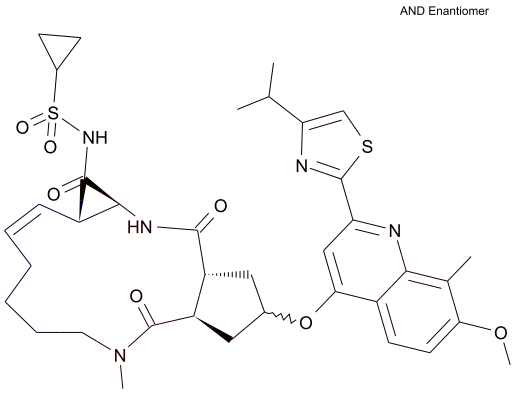
FCFP_12	1679744180	 [*]O[c]1:[cH]:[c](O[*]):[c]([*]):[*]:[c]:1[*]	0.137	2 out of 2
FCFP_12	1028934530	 [*]O[c]1:[c]([*]):[*]:[c]([*]):[cH]:[c]:1OC	0.137	2 out of 2

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Irritant in training set
FCFP_12	1244036906	 [*][c](:[*]):[c]1C(=O)C=C([*])[*][c]:1:[*]	-0.592	0 out of 1
FCFP_12	1673930087	 [*]O[c]1:[cH]:[c](O):[c]([*]):[*]:[c]:1[*]	-0.218	5 out of 8
FCFP_12	136627117	 [*]OC	0	96 out of 113

Simeprevir

TOPKAT_Ocular_Irritancy_None_vs_Irritant



$C_{38}H_{47}N_5O_7S_2$

Molecular Weight: 749.93908

ALogP: 4.796

Rotatable Bonds: 8

Acceptors: 9

Donors: 2

Model Prediction

Prediction: Irritant

Probability: 1

Enrichment: 1.18

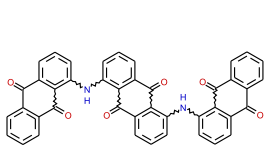
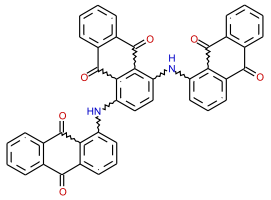
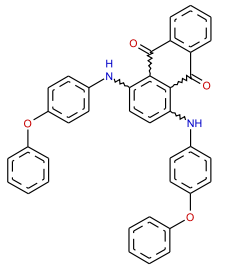
Bayesian Score: 1.81

Mahalanobis Distance: 16.5

Mahalanobis Distance p-value: 1.59e-019

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	Anthraquinone; 1;1'-(anthraquinon-1;5-ylenediimino)di-	Anthraquinone; 1;1'-(anthraquinon-1;4-ylenediimino)di-	ANILINE;N;N'-1;4-ANTHRAQUINONYLENEBIS(4-PHENOXY-
Structure			
Actual Endpoint	Irritant	Irritant	Non-Irritant
Predicted Endpoint	Irritant	Irritant	Non-Irritant
Distance	0.837	0.838	1.053
Reference	Prehled Prumyslove Toxikologie; Organicke Latky; Marhold; J. pp 736;86	Prehled Prumyslove Toxikologie; Organicke Latky; Marhold; J. pp 736;86	28ZPAK-;114;72

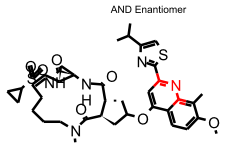
Model Applicability

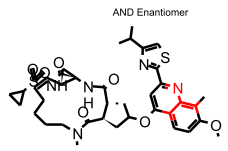
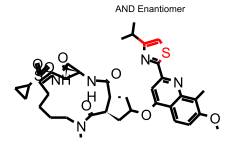
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.

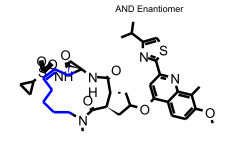
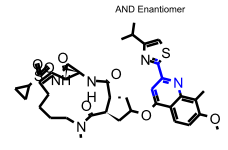
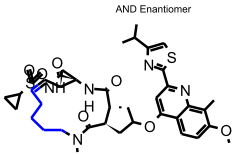
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Irritant in training set
FCFP_12	1747237384	 [*][c](:[*]):n:[c](:[*]):[*]	0.208	44 out of 44

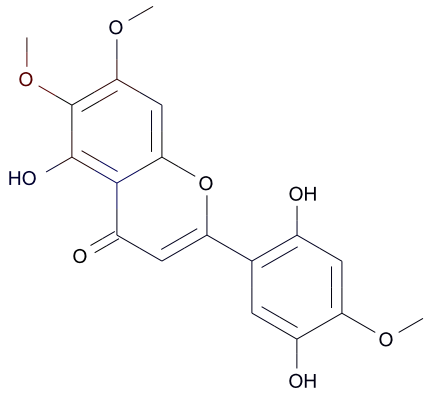
FCFP_12	178336375	 [*][c](:[*]):[c](:n:[*]):[c](:[*]):[*]	0.202	19 out of 19
FCFP_12	-124655670	 [*][c]1:[*]:[*]:s:[cH]:1	0.2	16 out of 16

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Irritant in training set
FCFP_12	-1812846456	 [*]CCCC\C=C/C1[*][*]1	-1.01	2 out of 9
FCFP_12	690511177	 [*]:[cH]:[c](:n:[*])[c](:[*]):[*]	-0.268	1 out of 2
FCFP_12	1175638033	 [*]CCCCC=[*]	-0.133	207 out of 293

Flavonoid-1

TOPKAT_Rat_Female_FDA_None_vs_Carcinogen



$C_{18}H_{16}O_8$

Molecular Weight: 360.31483

ALogP: 2.361

Rotatable Bonds: 4

Acceptors: 8

Donors: 3

Model Prediction

Prediction: Non-Carcinogen

Probability: 0.248

Enrichment: 0.771

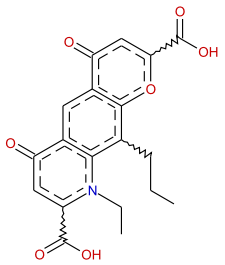
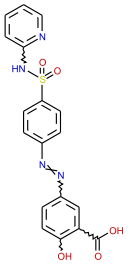
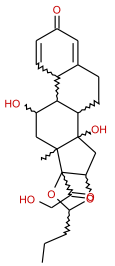
Bayesian Score: -2.89

Mahalanobis Distance: 10.5

Mahalanobis Distance p-value: 0.181

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	Nedocromil	Sulfasalazine	Budesonide
Structure			
Actual Endpoint	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen
Predicted Endpoint	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen
Distance	0.619	0.681	0.700
Reference	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997

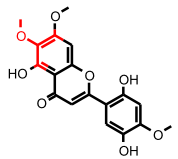
Model Applicability

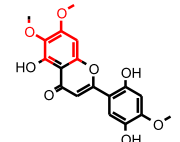
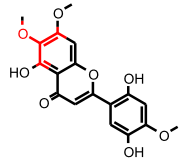
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.

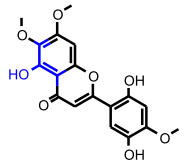
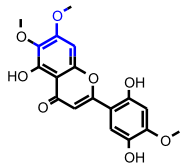
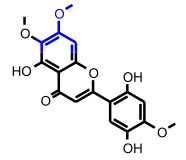
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
ECFP_12	2052151141	 [*][c](:[*]):[c](OC):[c]([*]):[*]	0.668	4 out of 5

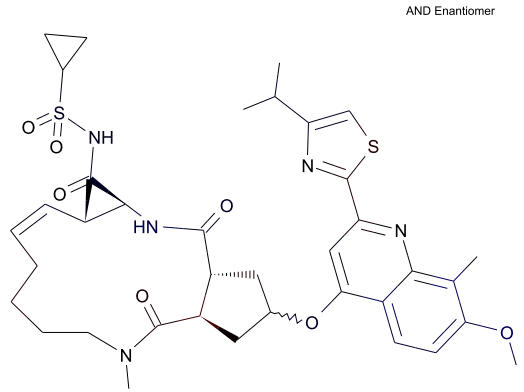
ECFP_12	1151345624	 [*]O[c]1:[c]([*]):[*]:[c]([*]):[cH]:[c]:1OC	0.613	2 out of 2
ECFP_12	-1531301414	 [*]O[c](:[c]([*]):[*]):[c]([*]):[*]	0.454	5 out of 9

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
ECFP_12	-1660913849	 [*][c](:[*]):[c](O):[c]([*]):[*]	-0.941	0 out of 5
ECFP_12	1408898974	 [*]O[c](:[cH]:[*]):[c]([*]):[*]	-0.517	5 out of 29
ECFP_12	1680623188	 [*][c](:[*]):[c](OC):[cH]:[*]	-0.295	3 out of 14

Simeprevir

TOPKAT_Rat_Female_FDA_None_vs_Carcinogen



$C_{38}H_{47}N_5O_7S_2$

Molecular Weight: 749.93908

ALogP: 4.796

Rotatable Bonds: 8

Acceptors: 9

Donors: 2

Model Prediction

Prediction: Non-Carcinogen

Probability: 0.232

Enrichment: 0.719

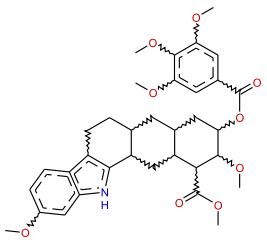
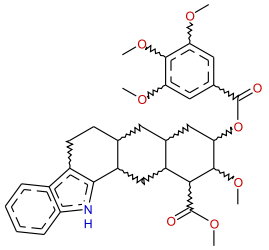
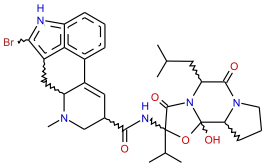
Bayesian Score: -4.13

Mahalanobis Distance: 14.6

Mahalanobis Distance p-value: 1.61e-007

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	Reserpine	Deserpidine	Bromocriptine
Structure			
Actual Endpoint	Carcinogen	Carcinogen	Carcinogen
Predicted Endpoint	Carcinogen	Carcinogen	Carcinogen
Distance	0.807	0.846	0.874
Reference	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997

Model Applicability

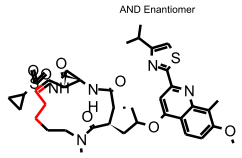
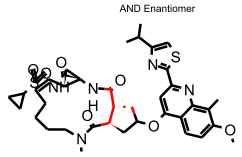
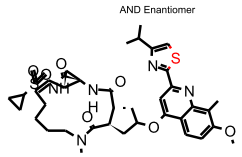
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown ECFP_2 feature: -309676563: [*]N[C@]1(C[C@H]1[*])C(=[*])[*]
3. Unknown ECFP_2 feature: -1049290660: [*]C1([*])C[C@H]1C=[*]
4. Unknown ECFP_2 feature: 1616402542: [*]CN(C)C(=[*])[*]
5. Unknown ECFP_2 feature: -1818486371: [*]NC(=O)C1([*])[*][*]1
6. Unknown ECFP_2 feature: 1310940530: [*]C([*])O[c](:[*]):[*]
7. Unknown ECFP_2 feature: 733491677: [*]:[c](:[*])C(C)C
8. Unknown ECFP_2 feature: 2121941848: [*]NS(=O)(=O)C1[*][*]1
9. Unknown ECFP_2 feature: -622223421: [*]S(=[*])(=[*])C1CC1

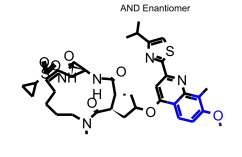
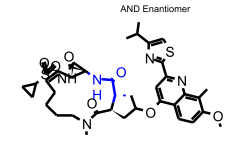
Feature Contribution

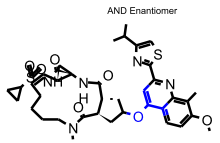
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set

ECFP_12	-1331088410	 [*]CCC=[*]	0.725	3 out of 3
ECFP_12	-2095963820	 [*][C@@H]1[*][*]C[C@H]1C(=[*])[*]	0.722	12 out of 17
ECFP_12	914325265	 [*]:s:[*]	0.516	8 out of 14

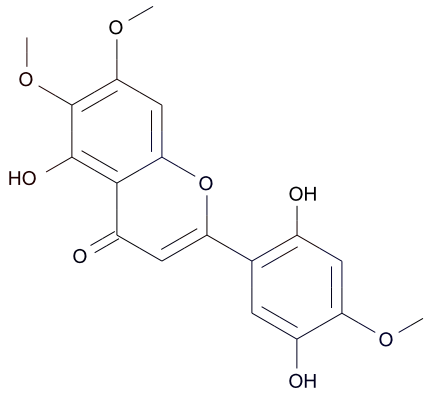
Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
ECFP_12	2077607946	 [*]O[c]1:[cH]:[cH]:[c](:[*]):[*]:[c]:1[*]	-1.25	0 out of 8
ECFP_12	-867777309	 [*]NC(=O)C([*])[*]	-0.661	0 out of 3

ECFP_12	1408898974	AND Enantiomer  [*]O[c](:[cH]:[*]):[c](:[*]):[*]	-0.517	5 out of 29

Flavonoid-1

TOPKAT_Rat_Male_FDA_None_vs_Carcinogen



$C_{18}H_{16}O_8$

Molecular Weight: 360.31483

ALogP: 2.361

Rotatable Bonds: 4

Acceptors: 8

Donors: 3

Model Prediction

Prediction: Non-Carcinogen

Probability: 0.313

Enrichment: 0.938

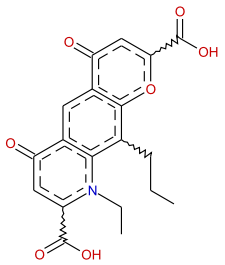
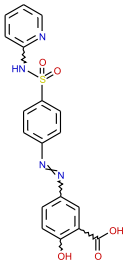
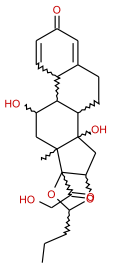
Bayesian Score: -1.58

Mahalanobis Distance: 11.9

Mahalanobis Distance p-value: 0.0324

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	Nedocromil	Sulfasalazine	Budesonide
Structure			
Actual Endpoint	Non-Carcinogen	Carcinogen	Carcinogen
Predicted Endpoint	Non-Carcinogen	Carcinogen	Carcinogen
Distance	0.584	0.649	0.693
Reference	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997

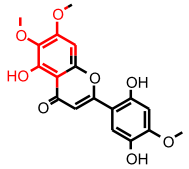
Model Applicability

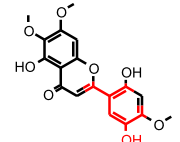
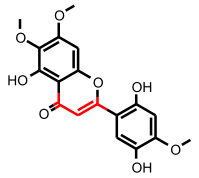
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.

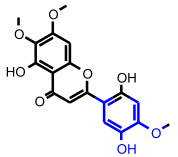
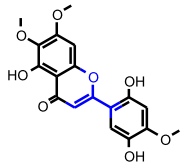
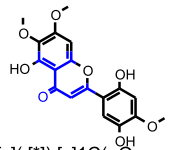
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
SCFP_6	-1547271378	 [*]O[c]1:[cH]:[*]:[c]([*]):[c](O):[c]:1OC	0.603	2 out of 2

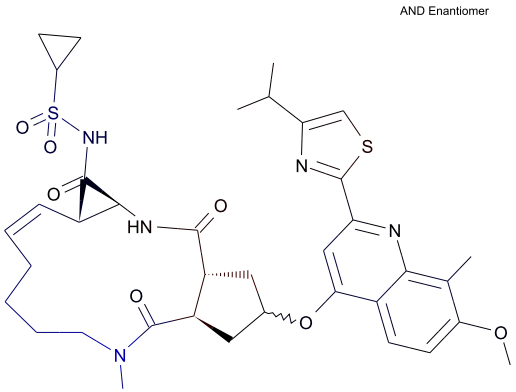
SCFP_6	392579710	 [*]C(=[*])[c]1:[cH]:[c](O):[c]([*]):[*]:[c]:1[*]	0.425	2 out of 3
SCFP_6	-1971196727	 [*]C(=CC(=[*])[*])[*]	0.361	17 out of 36

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
SCFP_6	2116304939	 [*]O[c]1:[cH]:[*]:[c]([*]):[cH]:[c]:1O	-0.825	0 out of 4
SCFP_6	616636418	 [*]O\C(=C/[*])\[c](:[*]):[*]	-0.278	0 out of 1
SCFP_6	-617610981	 [*][c](:[*]):[c]1C(=O)C=C([*])[*][c]:1:[*]	-0.278	0 out of 1

Simeprevir

TOPKAT_Rat_Male_FDA_None_vs_Carcinogen



$C_{38}H_{47}N_5O_7S_2$

Molecular Weight: 749.93908

ALogP: 4.796

Rotatable Bonds: 8

Acceptors: 9

Donors: 2

Model Prediction

Prediction: Non-Carcinogen

Probability: 0.231

Enrichment: 0.69

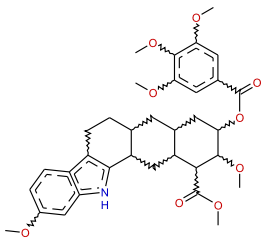
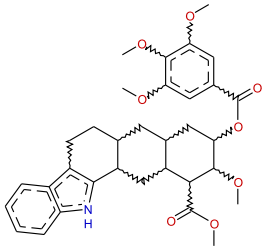
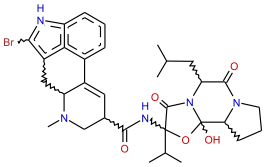
Bayesian Score: -5.43

Mahalanobis Distance: 20.3

Mahalanobis Distance p-value: 1.2e-019

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	Reserpine	Deserpidine	Bromocriptine
Structure			
Actual Endpoint	Carcinogen	Carcinogen	Non-Carcinogen
Predicted Endpoint	Carcinogen	Carcinogen	Non-Carcinogen
Distance	0.771	0.812	0.842
Reference	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997	US FDA (Centre for Drug Eval.& Res./Off. Testing & Res.) Sept. 1997

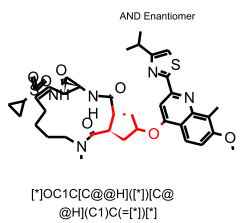
Model Applicability

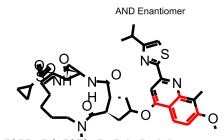
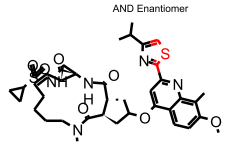
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. OPS PC5 out of range. Value: 7.7766. Training min, max, SD, explained variance: -4.0702, 6.5927, 2.146, 0.0429.
2. OPS PC22 out of range. Value: 3.5288. Training min, max, SD, explained variance: -3.2994, 3.2573, 1.197, 0.0134.

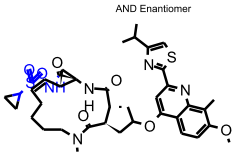
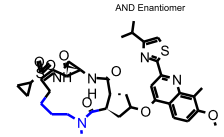
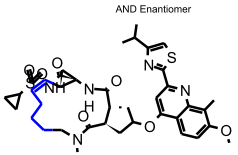
Feature Contribution

Top features for positive contribution

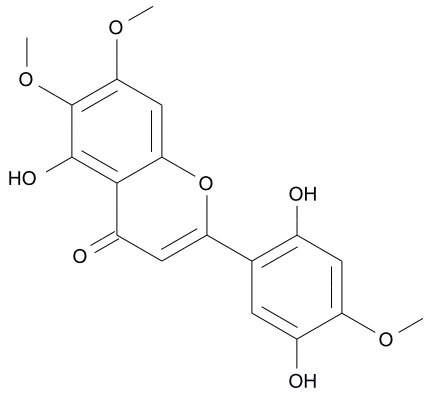
Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
SCFP_6	-1903488337	 [*]OC1C[C@@H]([*])[C@@H](C1)C(=[*])[*]	0.603	2 out of 2

SCFP_6	-1379673609	 [*][c](:[*]):[c]1:[cH]:[cH]:[c]([*]):[*]:[c]:1:[*]	0.526	11 out of 19
SCFP_6	1310748454	 [*][c]1:[*]:[*]:[cH]:s:1	0.437	7 out of 13

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
SCFP_6	182902497	 [*]NS(=O)(=O)C1[*][*]1	-0.825	0 out of 4
SCFP_6	306578635	 [*]CCCN(C)C(=[*])[*]	-0.825	0 out of 4
SCFP_6	1260369147	 [*]CCC\C=C/[*]	-0.674	0 out of 3

Flavonoid-1



$C_{18}H_{16}O_8$

Molecular Weight: 360.31483

ALogP: 2.361

Rotatable Bonds: 4

Acceptors: 8

Donors: 3

Model Prediction

Prediction: Non-Irritant

Probability: 0.968

Enrichment: 1.05

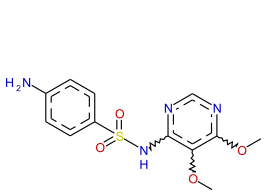
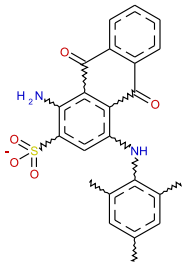
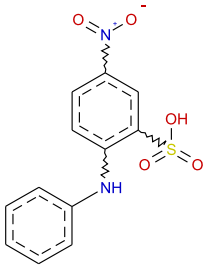
Bayesian Score: -1.14

Mahalanobis Distance: 8.88

Mahalanobis Distance p-value: 0.487

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	Benzenesulfonamide, 4-amino-N-(5,6-dimethoxy-4-pyrimidinyl)-	2-Anthracenesulfonic acid, 1-amino-9,10-dihydro-9,10-dioxo-4-(2,4,6 -trimethylanilino)-, monosodium salt	Benzenesulfonic acid, 2-anilino-5-nitro-
Structure			
Actual Endpoint	Irritant	Irritant	Irritant
Predicted Endpoint	Non-Irritant	Non-Irritant	Non-Irritant
Distance	0.769	0.782	0.828
Reference	FCTXAV 14,307,76	85JCAE "Prehled Prumyslove Toxikologie; Organicke Latky," Marhold, J., Prague , Czechoslovakia, Avicenum, 1986 Volume(issue)/page/year: -,1327,1986	85JCAE "Prehled Prumyslove Toxikologie; Organicke Latky," Marhold, J., Prague , Czechoslovakia, Avicenum, 1986 Volume(issue)/page/year: -,1061,1986

Model Applicability

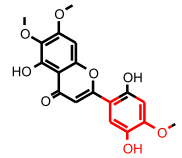
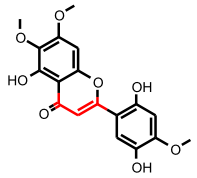
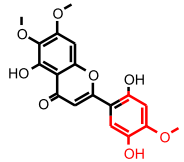
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.

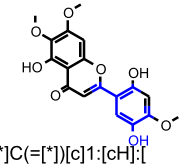
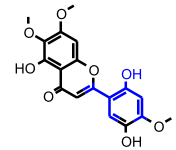
Feature Contribution

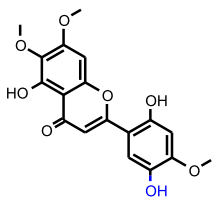
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Irritant in training set

FCFP_12	523826990	 [*]O[c]1:[cH]:[*]:[c]([*]):[cH]:[c]:1O	0.0756	6 out of 6
FCFP_12	451847724	 [*]C(=CC(=[*])[*])[*]	0.0737	270 out of 274
FCFP_12	301073077	 [*][c]1:[*]:[cH]:[c](O):[c](OC):[cH]:1	0.0734	5 out of 5

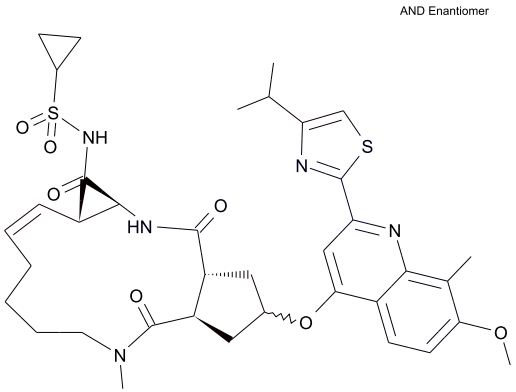
Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Irritant in training set
FCFP_12	949015626	 [*]C(=[*])[c]1:[cH]:[c](O):[c]([*]):[*]:[c]:1[*]	-0.222	2 out of 3
FCFP_12	-1604301295	 [*]C(=[*])[c]1:[cH]:[*]:[c]([*]):[cH]:[c]:1O	-0.18	22 out of 29

FCFP_12	7	 [*]O	-0.118	104 out of 128

Simeprevir

TOPKAT_Skin_Irritancy_None_vs_Irritant



$C_{38}H_{47}N_5O_7S_2$

Molecular Weight: 749.93908

ALogP: 4.796

Rotatable Bonds: 8

Acceptors: 9

Donors: 2

Model Prediction

Prediction: Non-Irritant

Probability: 0.969

Enrichment: 1.05

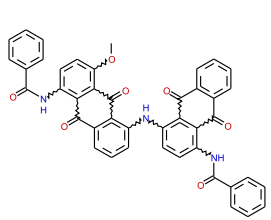
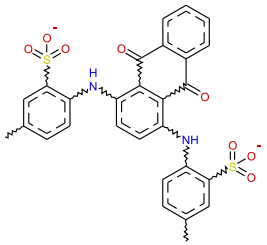
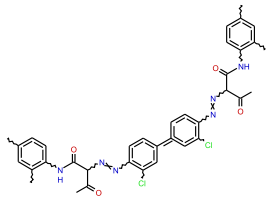
Bayesian Score: -1.05

Mahalanobis Distance: 16.8

Mahalanobis Distance p-value: 1.98e-021

Prediction: Positive if the Bayesian score is above the estimated best cutoff value from minimizing the false positive and false negative rate.
Probability: The esimated probability that the sample is in the positive category. This assumes that the Bayesian score follows a normal distribution and is different from the prediction using a cutoff.
Enrichment: An estimate of enrichment, that is, the increased likelihood (versus random) of this sample being in the category.
Bayesian Score: The standard Laplacian-modified Bayesian score.
Mahalanobis Distance: The Mahalanobis distance (MD) is the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	Anthraquinone, 3-methoxy-5,4'-iminobis(1-benzamido-	Benzenesulfonic acid, 2,2'-(1,4-anthraquinonylenediimino)bis(5-meth yl-, disodium salt	Butanamide, 2,2'-((3,3'-dichloro(1,1'-biphenyl)-4,4'-diyl)bis(azo)) bis(N-(2,4- dimethylphenyl)-3-oxo-
Structure			
Actual Endpoint	Irritant	Irritant	Irritant
Predicted Endpoint	Non-Irritant	Non-Irritant	Non-Irritant
Distance	0.883	1.016	1.027
Reference	28ZPAK "Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku," Marhol d, J.V., Institut Pro Vychovu Vedoucicn Pracovniku Chemickeho Prumyclu Praha, Cz echoslovakia, 1972 Volume(issue)/page/year: -,114,1	85JCAE "Prehled Prumyslove Toxikologie; Organicke Latky," Marhold, J., Prague , Czechoslovakia, Avicenum, 1986 Volume(issue)/page/year: -,1330,1986	NTIS** National Technical Information Service. (Springfield, VA 22161) Forme rly U.S. Clearinghouse for Scientific & Technical Information. Volume(issue)/pag e/year: OTS0555058

Model Applicability

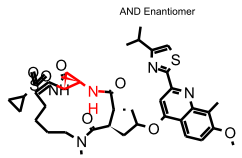
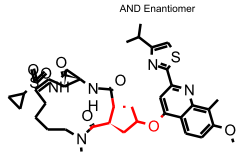
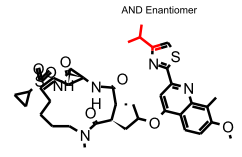
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. OPS PC6 out of range. Value: 7.6964. Training min, max, SD, explained variance: -5.7225, 6.867, 1.786, 0.0403.
2. OPS PC22 out of range. Value: 5.13. Training min, max, SD, explained variance: -2.9568, 3.7845, 1.016, 0.0131.

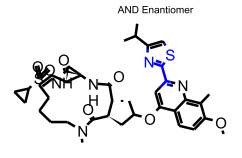
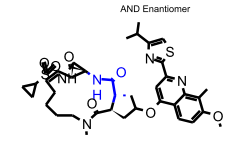
Feature Contribution

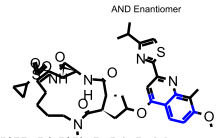
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Irritant in training set

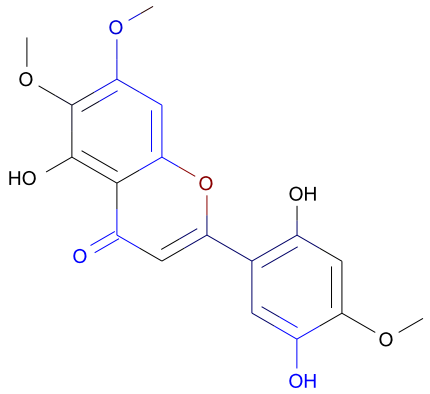
FCFP_12	-415156552	 [*]N[C@]1(C[C@H]1[*])C(=[*])[*]	0.0854	27 out of 27
FCFP_12	-53728878	 [*]OC1C[C@@H]([*])[C@@H](C1)C(=[*])[*]	0.0845	21 out of 21
FCFP_12	1186303932	 [*]:[c](:[*])C(C)C	0.0838	18 out of 18

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Irritant in training set
FCFP_12	690481386	 [*]:[c](:[*])[c]1:n:[*]:[*]:s:1	-0.65	0 out of 1
FCFP_12	566058135	 [*]NC(=O)C([*])[*]	-0.367	13 out of 21

FCFP_12	-1320007763	 [*][c](:[*]):[c]1:[cH]:[cH]:[c]([*]):[*]:[c]:1:[*]	-0.0893	20 out of 24

Flavonoid-1



$C_{18}H_{16}O_8$
Molecular Weight: 360.31483
ALogP: 2.361
Rotatable Bonds: 4
Acceptors: 8
Donors: 3

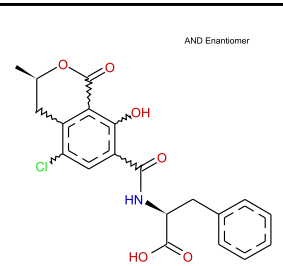
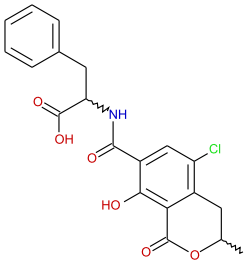
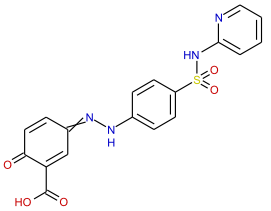
Model Prediction

Prediction: 111
Unit: mg/kg_body_weight/day
Mahalanobis Distance: 10.7
Mahalanobis Distance p-value: 0.00393

Mahalanobis Distance: The Mahalanobis distance (MD) is a generalization of the Euclidean distance that accounts for correlations among the X properties. It is calculated as the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

TOPKAT_Carcinogenic_Potency_TD50_Mouse

Structural Similar Compounds

Name	542	Ochratoxin A	Salicylazosulfapyridine
Structure			
Actual Endpoint (-log C)	4.79932	4.79932	2.5034
Predicted Endpoint (-log C)	3.6353	3.6353	3.54214
Distance	0.621	0.621	0.655
Reference	CPDB	CPDB	CPDB

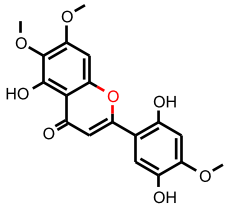
Model Applicability

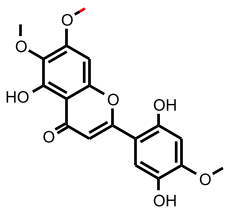
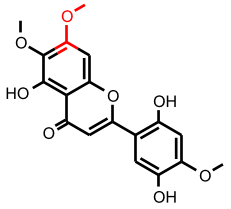
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown ECFP_2 feature: 1573564860: [*]O\C(=C/[*])\[c](:[*]):[*]

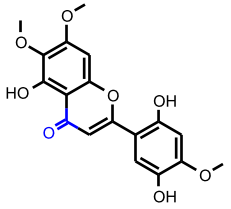
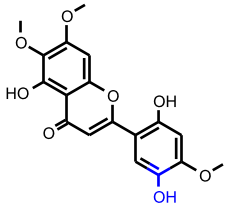
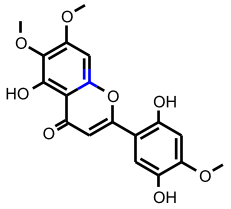
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
ECFP_6	683445015	 [*]O[*]	0.136

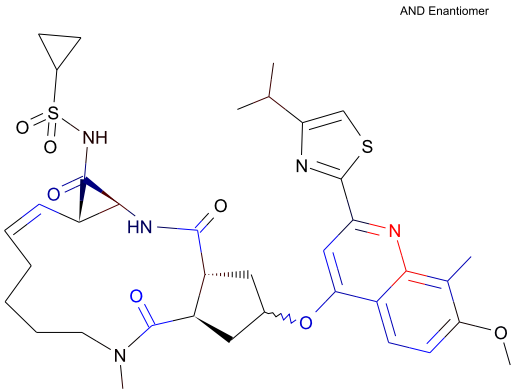
ECFP_6	734603939	 [*]C	0.0424
ECFP_6	1307307440	 [*]:[c](:[*])OC	0.0156

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
ECFP_6	2106656448	 [*]C(=O)[*]	-0.275
ECFP_6	2019062761	 [*]:[c](:[*])O	-0.258
ECFP_6	642810091	 [*][c](:[*]):[*]	-0.247

Simeprevir

TOPKAT_Carcinogenic_Potency_TD50_Mouse



$C_{38}H_{47}N_5O_7S_2$

Molecular Weight: 749.93908

ALogP: 4.796

Rotatable Bonds: 8

Acceptors: 9

Donors: 2

Model Prediction

Prediction: 2.01

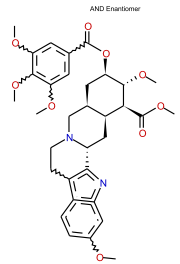
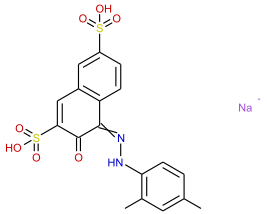
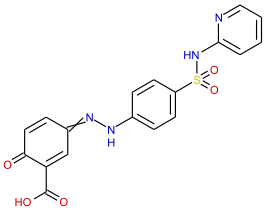
Unit: mg/kg_body_weight/day

Mahalanobis Distance: 16.8

Mahalanobis Distance p-value: 5.81e-019

Mahalanobis Distance: The Mahalanobis distance (MD) is a generalization of the Euclidean distance that accounts for correlations among the X properties. It is calculated as the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	223	D & C red no. 5	Salicylazosulfapyridine
Structure			
Actual Endpoint (-log C)	5.08368	2.80732	2.5034
Predicted Endpoint (-log C)	5.08273	3.78615	3.54214
Distance	0.926	1.173	1.177
Reference	CPDB	CPDB	CPDB

Model Applicability

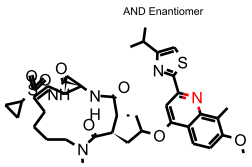
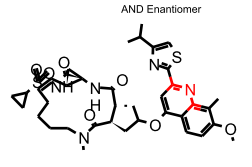
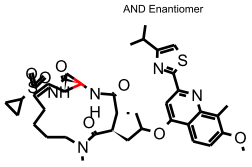
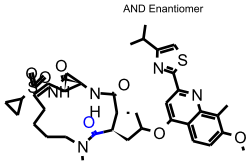
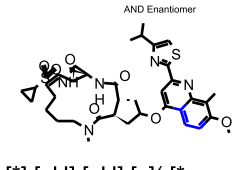
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

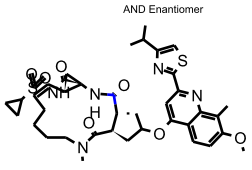
1. OPS PC14 out of range. Value: -4.1139. Training min, max, SD, explained variance: -3.6133, 3.7483, 1.312, 0.0215.
2. OPS PC16 out of range. Value: 4.4468. Training min, max, SD, explained variance: -3.1026, 4.016, 1.245, 0.0193.
3. Unknown ECFP_2 feature: -309676563: [*]N[C@]1(C[C@H]1[*])C(=[*])[*]
4. Unknown ECFP_2 feature: -1049290660: [*]C1([*])C[C@H]1C=[*]
5. Unknown ECFP_2 feature: -1818486371: [*]NC(=O)C1([*])[*][*]1
6. Unknown ECFP_2 feature: 946167604: [*]C(=[*])NS(=[*])(=[*])[*]
7. Unknown ECFP_2 feature: 1310940530: [*]C([*])O[c](:[*]):[*]
8. Unknown ECFP_2 feature: 1411720546: [*]C([*])[c]1:[cH]:[*]:[*]:n:1
9. Unknown ECFP_2 feature: 733491677: [*]:[c](:[*])C(C)C
10. Unknown ECFP_2 feature: 2121941848: [*]NS(=O)(=O)C1[*][*]1
11. Unknown ECFP_2 feature: -622223421: [*]S(=[*])(=[*])C1CC1

Feature Contribution

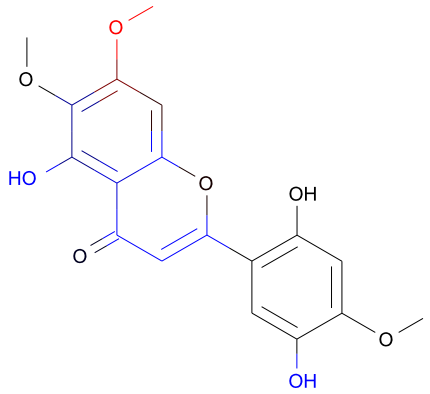
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score

ECFP_6	655739385	 [*]:n:[*]	0.229
ECFP_6	834876373	 [*][c](:[*]):n:[c](:[*]):[*]	0.163
ECFP_6	657586427	 [*]C1([*])[*][*]1	0.0789
Top Features for negative contribution			
Fingerprint	**Bit/Smiles**	**Feature Structure**	**Score**
ECFP_6	2106656448	 [*]C(=O)[*]	-0.275
ECFP_6	1996767644	 [*]:[cH]:[cH]:[c](:[*]):[*]	-0.251

ECFP_6	642810091	AND Enantiomer  [*][c](:[*]):[*]	-0.247

Flavonoid-1



$C_{18}H_{16}O_8$

Molecular Weight: 360.31483

ALogP: 2.361

Rotatable Bonds: 4

Acceptors: 8

Donors: 3

Model Prediction

Prediction: 13.6

Unit: mg/kg_body_weight/day

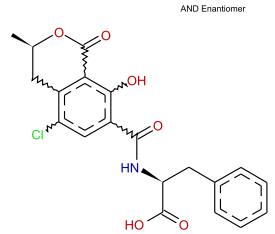
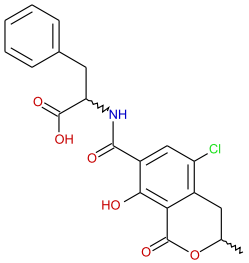
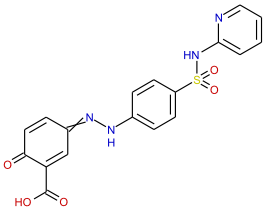
Mahalanobis Distance: 11.7

Mahalanobis Distance p-value: 0.00204

Mahalanobis Distance: The Mahalanobis distance (MD) is a generalization of the Euclidean distance that accounts for correlations among the X properties. It is calculated as the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

TOPKAT_Carcinogenic_Potency_TD50_Rat

Structural Similar Compounds

Name	542	Ochratoxin A	Salicylazosulfapyridine
Structure			
Actual Endpoint (-log C)	6.59334	6.47264	2.39891
Predicted Endpoint (-log C)	5.06501	5.06501	3.17598
Distance	0.601	0.601	0.623
Reference	CPDB	CPDB	CPDB

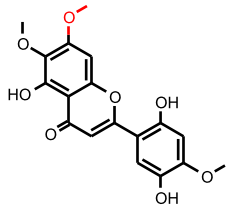
Model Applicability

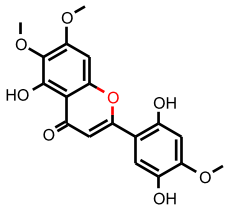
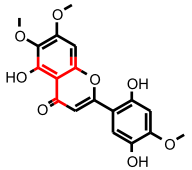
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.

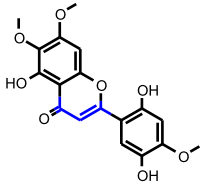
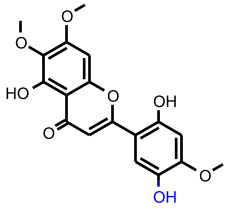
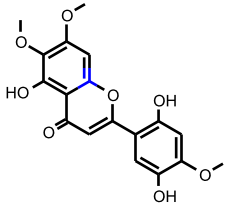
Feature Contribution

Top features for positive contribution

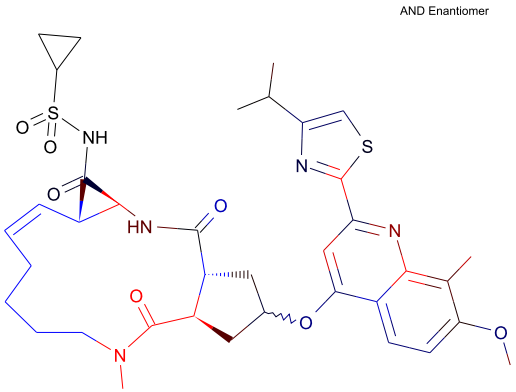
Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_6	136627117	 [*]OC	0.69

FCFP_6	1	 [*]O[*]	0.234
FCFP_6	203677720	 [*]C(=[*])[c](:[c]([*]):[*]):[c]([*]):[*]	0.137

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_6	451847724	 [*]C(=CC(=[*])[*])[*]	-0.436
FCFP_6	7	 [*]O	-0.372
FCFP_6	16	 [*][c](:[*]):[*]	-0.354

Simeprevir



$C_{38}H_{47}N_5O_7S_2$
Molecular Weight: 749.93908
ALogP: 4.796
Rotatable Bonds: 8
Acceptors: 9
Donors: 2

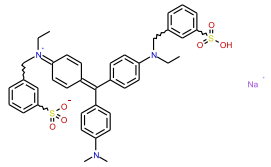
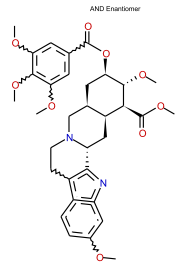
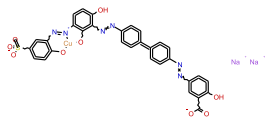
Model Prediction

Prediction: 0.28
Unit: mg/kg_body_weight/day
Mahalanobis Distance: 24.1
Mahalanobis Distance p-value: 1.44e-046

Mahalanobis Distance: The Mahalanobis distance (MD) is a generalization of the Euclidean distance that accounts for correlations among the X properties. It is calculated as the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

TOPKAT_Carcinogenic_Potency_TD50_Rat

Structural Similar Compounds

Name	411	223	188
Structure			
Actual Endpoint (-log C)	3.06566	6.29867	5.5378
Predicted Endpoint (-log C)	4.8672	7.5657	5.71925
Distance	0.846	0.861	0.891
Reference	CPDB	CPDB	CPDB

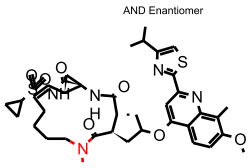
Model Applicability

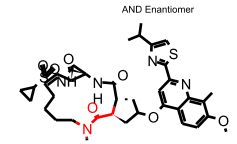
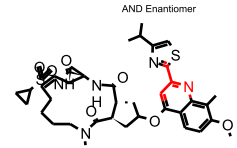
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. OPS PC27 out of range. Value: -3.3094. Training min, max, SD, explained variance: -2.8642, 4.2058, 1.002, 0.0096.

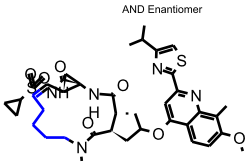
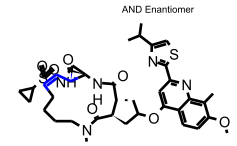
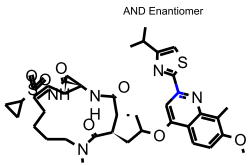
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_6	136627117	 [*]OC	0.69

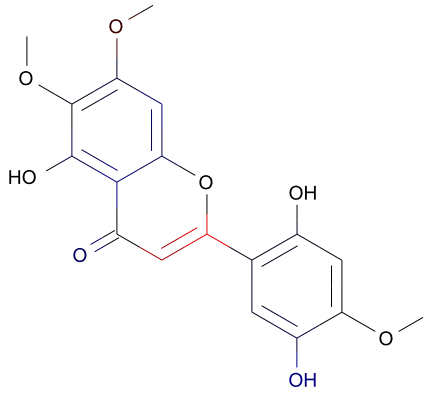
FCFP_6	565998553	 [*]C([*])C(=O)N([*])[*]	0.357
FCFP_6	690511177	 [*]:[cH]:[c](:n:[*])[c](:[*]):[*]	0.293

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_6	1175638033	 [*]CCCCC=[*]	-0.512
FCFP_6	451847724	 [*]C(=CC(=[*])[*])[*]	-0.436
FCFP_6	16	 [*][c](:[*]):[*]	-0.354

Flavonoid-1

TOPKAT_Chronic_LOAEL



$C_{18}H_{16}O_8$

Molecular Weight: 360.31483

ALogP: 2.361

Rotatable Bonds: 4

Acceptors: 8

Donors: 3

Model Prediction

Prediction: 0.0624

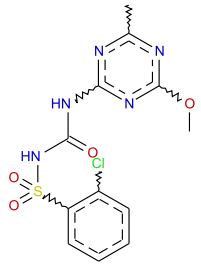
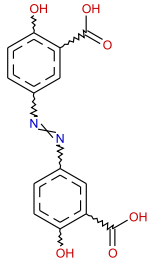
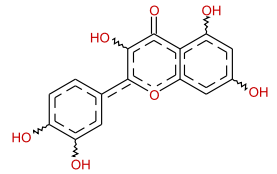
Unit: g/kg_body_weight

Mahalanobis Distance: 24.3

Mahalanobis Distance p-value: 2.58e-014

Mahalanobis Distance: The Mahalanobis distance (MD) is a generalization of the Euclidean distance that accounts for correlations among the X properties. It is calculated as the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	CHLORSULFURON	OLSALAZINE.NA	QUERCETIN
Structure			
Actual Endpoint (-log C)	4.15566	3.17932	2.87829
Predicted Endpoint (-log C)	3.79771	2.89417	3.12498
Distance	0.595	0.618	0.651
Reference	EPA COVER SHEET 0027;880301;(1)	NDA-19715	NTP 409 79

Model Applicability

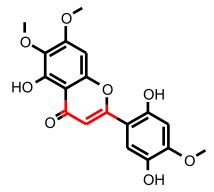
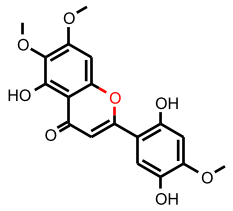
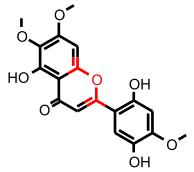
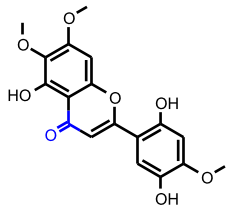
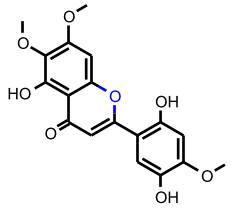
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

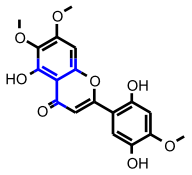
1. All properties and OPS components are within expected ranges.
2. Unknown ECFP_6 feature: -570915357: [*]O[c](:[cH]:[*]):[c]([*]):[*]
3. Unknown ECFP_6 feature: -813997308: [*]C(=[*])[c](:[c]([*]):[*]):[c]([*]):[*]
4. Unknown ECFP_6 feature: -1660913849: [*][c](:[*]):[c](O):[c]([*]):[*]
5. Unknown ECFP_6 feature: -1531301414: [*]O[c](:[c]([*]):[*]):[c]([*]):[*]
6. Unknown ECFP_6 feature: -560785749: [*]C(=[*])O[c](:[*]):[*]
7. Unknown ECFP_6 feature: 1573564860: [*]O\C(=C/[*])\[c](:[*]):[*]
8. Unknown ECFP_6 feature: 1299558496: [*]=CC(=O)[c](:[*]):[*]
9. Unknown ECFP_6 feature: 464808839: [*]C(=CC(=[*])[*])[*]
10. Unknown ECFP_6 feature: 1307307440: [*]:[c](:[*])OC
11. Unknown ECFP_6 feature: 2019062761: [*]:[c](:[*])O

Feature Contribution

Top features for positive contribution

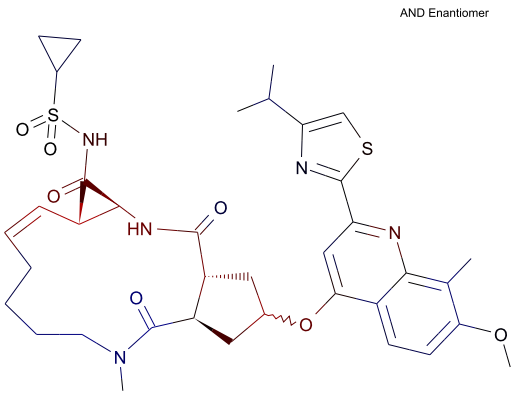
Fingerprint	Bit/Smiles	Feature Structure	Score

FCFP_6	451847724	 [*]C(=CC(=[*])[*])[*]	0.16
ECFP_6	683445015	 [*]O[*]	0.0734
FCFP_6	1036089772	 [*]C(=[*])O[c](:[*]): [*]	0.073
Top Features for negative contribution			
Fingerprint	**Bit/Smiles**	**Feature Structure**	**Score**
ECFP_6	2106656448	 [*]C(=O)[*]	-0.11
FCFP_6	1	 [*]O[*]	-0.102

FCFP_6	203677720	 [*]C(=[*])[c](:[c]([*]):[*]):[c]([*]):[*]	-0.0713

Simeprevir

TOPKAT_Chronic_LOAEL



$C_{38}H_{47}N_5O_7S_2$

Molecular Weight: 749.93908

ALogP: 4.796

Rotatable Bonds: 8

Acceptors: 9

Donors: 2

Model Prediction

Prediction: 0.00211

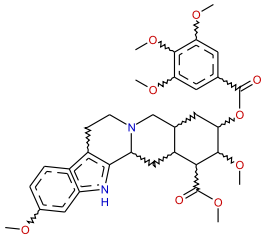
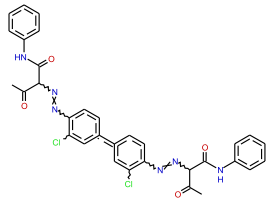
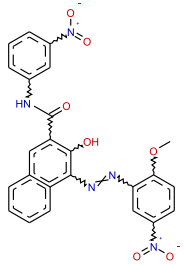
Unit: g/kg_body_weight

Mahalanobis Distance: 55.7

Mahalanobis Distance p-value: 1.58e-065

Mahalanobis Distance: The Mahalanobis distance (MD) is a generalization of the Euclidean distance that accounts for correlations among the X properties. It is calculated as the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	RESERPINE	DIARYLANILIDE YELLOW	C.I.PIGMENT RED 23
Structure			
Actual Endpoint (-log C)	6.38645	2.70208	2.28997
Predicted Endpoint (-log C)	5.548	3.76154	3.52921
Distance	0.885	0.887	0.922
Reference	NTP 193 22	NTP 30 C-4	NTP 411 146

Model Applicability

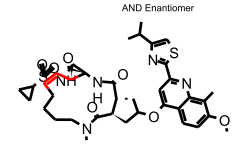
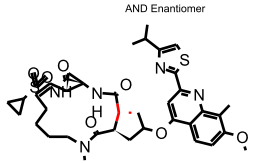
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

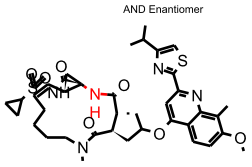
1. OPS PC1 out of range. Value: 18.64. Training min, max, SD, explained variance: -9.2986, 15.594, 5, 0.1094.
2. Unknown FCFP_2 feature: 1018942292: [*]NS(=O)(=O)C1[*][*]1
3. Unknown ECFP_6 feature: -154530762: [*]N[*]
4. Unknown ECFP_6 feature: 914325265: [*]:s:[*]
5. Unknown ECFP_6 feature: -797085356: [*]S(=[*])(=[*])[*]
6. Unknown ECFP_6 feature: -2095963820: [*][C@@H]1[*][*]C[C@H]1C(=[*])[*]
7. Unknown ECFP_6 feature: -867777309: [*]NC(=O)C([*])[*]
8. Unknown ECFP_6 feature: -1338907019: [*]C(=[*])NC1([*])[*][*]1
9. Unknown ECFP_6 feature: -309676563: [*]N[C@]1(C[C@H]1[*])C(=[*])[*]
10. Unknown ECFP_6 feature: 413587124: [*][C@@H]1CC1([*])[*]
11. Unknown ECFP_6 feature: -1049290660: [*]C1([*])C[C@H]1C=[*]
12. Unknown ECFP_6 feature: 890368401: [*]\C=C/C1[*][*]1
13. Unknown ECFP_6 feature: 360408239: [*]C\C=C/[*]
14. Unknown ECFP_6 feature: -1331088410: [*]CCC=[*]
15. Unknown ECFP_6 feature: -1332781180: [*]CCC[*]
16. Unknown ECFP_6 feature: -757679000: [*]CCN([*])[*]
17. Unknown ECFP_6 feature: 1616402542: [*]CN(C)C(=[*])[*]
18. Unknown ECFP_6 feature: 1526862590: [*]C([*])C(=O)N([*])[*]
19. Unknown ECFP_6 feature: -801490360: [*][C@H]1[*][*]C([*])C1

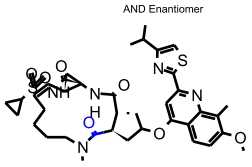
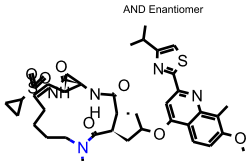
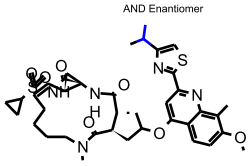
20. Unknown ECFP_6 feature: 1480368712: [*]OC1C[*][*]C1
21. Unknown ECFP_6 feature: -1818486371: [*]NC(=O)C1([*])[*][*]1
22. Unknown ECFP_6 feature: 946167604: [*]C(=[*])NS(=[*])(=[*])[*]
23. Unknown ECFP_6 feature: 866343404: [*]N([*])C
24. Unknown ECFP_6 feature: 1310940530: [*]C([*])O[c](:[*]):[*]
25. Unknown ECFP_6 feature: -428002189: [*]:[cH]:[c](:n:[*])[c](:[*]):[*]
26. Unknown ECFP_6 feature: 1333660716: [*][c](:[*]):[c](:[cH]:[*]):[c](:[*]):[*]
27. Unknown ECFP_6 feature: 1576255326: [*][c](:[*]):[c](C):[c](:[*]):[*]
28. Unknown ECFP_6 feature: 1048320787: [*][c](:[*]):[c](:n:[*]):[c](:[*]):[*]
29. Unknown ECFP_6 feature: -1426923364: [*][c]1:[*]:[*]:[cH]:s:1
30. Unknown ECFP_6 feature: -253227249: [*]:[c](:[*])[c]1:n:[*]:[*]:s:1
31. Unknown ECFP_6 feature: 1411720546: [*]C([*])[c]1:[cH]:[*]:[*]:n:1
32. Unknown ECFP_6 feature: -224638920: [*][c]1:[*]:[*]:s:[cH]:1
33. Unknown ECFP_6 feature: 733491677: [*]:[c](:[*])C(C)C
34. Unknown ECFP_6 feature: 1307307440: [*]:[c](:[*])OC
35. Unknown ECFP_6 feature: 2121941848: [*]NS(=O)(=O)C1[*][*]1
36. Unknown ECFP_6 feature: 2102150379: [*]S(=[*])(=O)[*]
37. Unknown ECFP_6 feature: -622223421: [*]S(=[*])(=[*])C1CC1

Feature Contribution

Top features for positive contribution

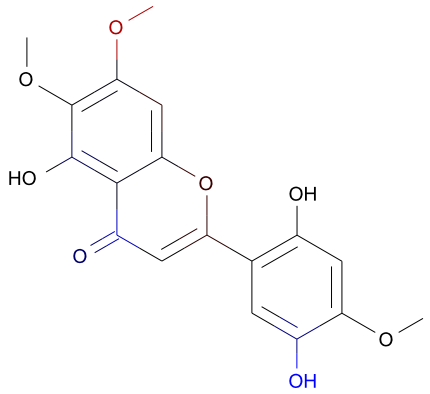
Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_6	451847724	 [*]C(=CC(=[*])[*])[*]	0.16
ECFP_6	-167460056	 [*]C([*])[*]	0.136

FCFP_6	3	 [*]N[*]	0.0924

Top Features for negative contribution			
Fingerprint	**Bit/Smiles**	**Feature Structure**	**Score**
ECFP_6	2106656448	 [*]C(=O)[*]	-0.11
FCFP_6	1	 [*]O[*]	-0.102
FCFP_6	136597326	 [*]C([*])C	-0.0815

Flavonoid-1

TOPKAT_Rat_Maximum_Tolerated_Dose_Feed



$C_{18}H_{16}O_8$

Molecular Weight: 360.31483

ALogP: 2.361

Rotatable Bonds: 4

Acceptors: 8

Donors: 3

Model Prediction

Prediction: 0.35

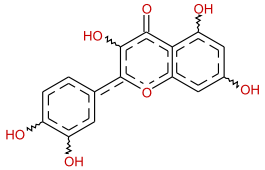
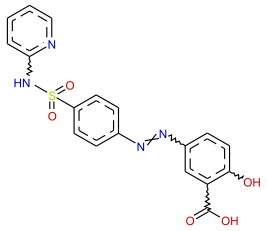
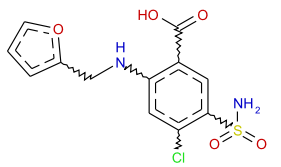
Unit: g/kg_body_weight

Mahalanobis Distance: 5.99

Mahalanobis Distance p-value: 0.645

Mahalanobis Distance: The Mahalanobis distance (MD) is a generalization of the Euclidean distance that accounts for correlations among the X properties. It is calculated as the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	QUERCETIN	SALICYLAZOSULFAPYRIDINE	FUROSEMIDE
Structure			
Actual Endpoint (-log C)	2.2016	3.375	4.04236
Predicted Endpoint (-log C)	2.27782	2.80292	2.8614
Distance	0.513	0.639	0.698
Reference	NCI/NTP TR-409	NCI/NTP TR-457	NCI/NTP TR-356

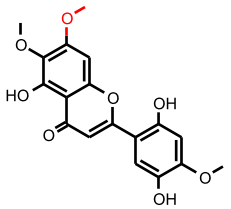
Model Applicability

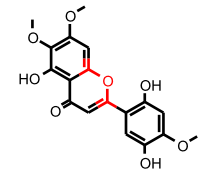
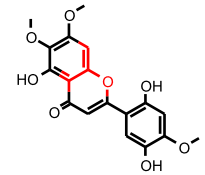
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.

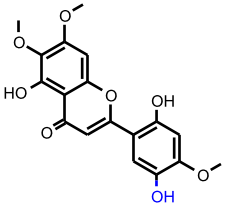
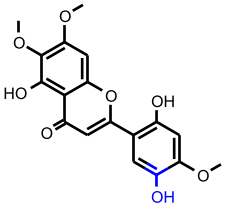
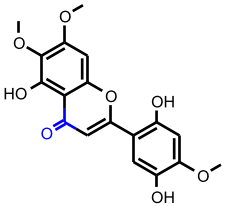
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_2	136627117	 [*]OC	0.173

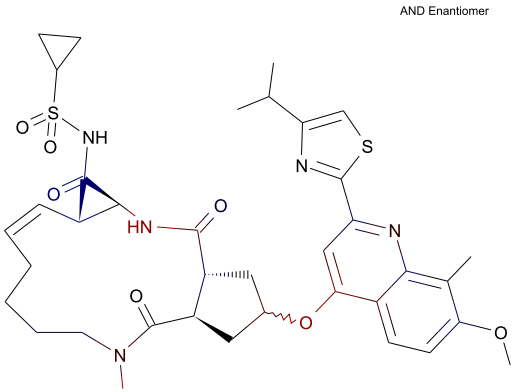
FCFP_2	1036089772	 [*]C(=[*])O[c](:[*]): [*]	0.0749
FCFP_2	332760439	 [*]O[c](:[cH]:[*]):[c]([*]):[*]	0.0611

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_2	7	 [*]O	-0.214
FCFP_2	-549108873	 [*]:[c](:[*])O	-0.127
FCFP_2	1872154524	 [*]C(=O)[*]	-0.105

Simeprevir

TOPKAT_Rat_Maximum_Tolerated_Dose_Feed



$C_{38}H_{47}N_5O_7S_2$

Molecular Weight: 749.93908

ALogP: 4.796

Rotatable Bonds: 8

Acceptors: 9

Donors: 2

Model Prediction

Prediction: 0.00297

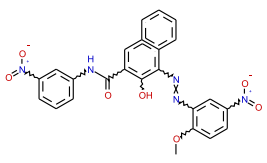
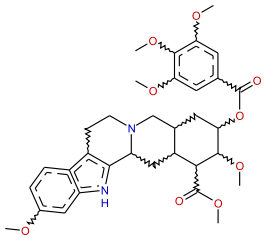
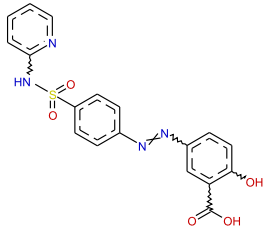
Unit: g/kg_body_weight

Mahalanobis Distance: 14.2

Mahalanobis Distance p-value: 5.46e-013

Mahalanobis Distance: The Mahalanobis distance (MD) is a generalization of the Euclidean distance that accounts for correlations among the X properties. It is calculated as the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	C.I.PIGMENT RED 23	RESERPINE	SALICYLAZOSULFAPYRIDINE
Structure			
Actual Endpoint (-log C)	2.30052	6.13118	3.375
Predicted Endpoint (-log C)	3.55333	4.38304	2.80292
Distance	0.861	0.934	1.035
Reference	NCI/NTP TR-411	NCI/NTP TR-193	NCI/NTP TR-457

Model Applicability

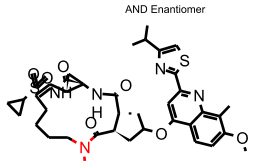
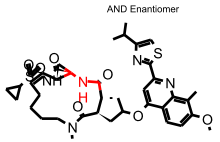
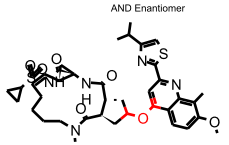
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. Molecular_Weight out of range. Value: 749.94. Training min, max, mean, SD: 74.122, 731.95, 245.25, 106.4.
2. OPS PC9 out of range. Value: 5.11. Training min, max, SD, explained variance: -2.8548, 3.3954, 1.263, 0.0360.
3. OPS PC12 out of range. Value: -3.0299. Training min, max, SD, explained variance: -2.364, 2.9228, 1.079, 0.0263.
4. OPS PC14 out of range. Value: 4.236. Training min, max, SD, explained variance: -2.0656, 3.3808, 1.011, 0.0231.
5. Unknown FCFP_2 feature: 690481386: [*]:[c](:[*])[c]1:n:[*]:[*]:s:1
6. Unknown FCFP_2 feature: 1018942292: [*]NS(=O)(=O)C1[*][*]1

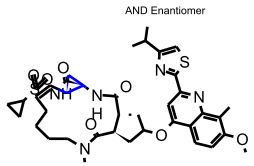
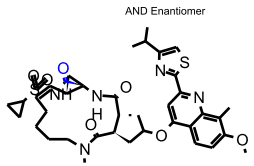
Feature Contribution

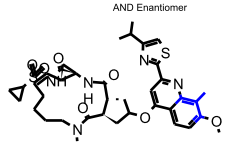
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score

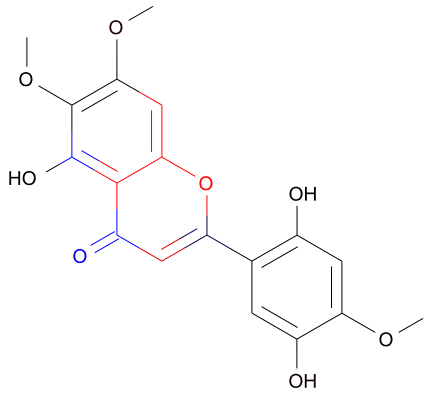
FCFP_2	136627117	 [*]OC	0.173
FCFP_2	-885550502	 [*]C(=[*])NC1([*])[*] [*]1	0.115
FCFP_2	1036089772	 [*]C(=[*])O[c](:[*]): [*]	0.0749

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_2	-1272798659	 [*][C@@H]1CC1([*])[*]	-0.111
FCFP_2	1872154524	 [*]C(=O)[*]	-0.105

FCFP_2	203677720	AND Enantiomer  [*]C(=[*])[c](:[c]([*]):[*]):[c]([*]):[*]	-0.0829

Flavonoid-1



$C_{18}H_{16}O_8$

Molecular Weight: 360.31483

ALogP: 2.361

Rotatable Bonds: 4

Acceptors: 8

Donors: 3

Model Prediction

Prediction: 5.44e-005

Unit: g/kg_body_weight

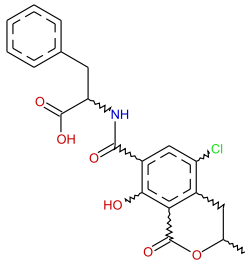
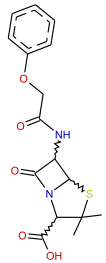
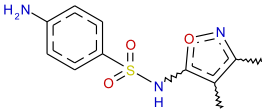
Mahalanobis Distance: 11.3

Mahalanobis Distance p-value: 9.31e-008

Mahalanobis Distance: The Mahalanobis distance (MD) is a generalization of the Euclidean distance that accounts for correlations among the X properties. It is calculated as the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

TOPKAT_Rat_Maximum_Tolerated_Dose_Gavage

Structural Similar Compounds

Name	OCHRATOXIN	PENICILLIN VK	SULFISOOXAZOLE
Structure			
Actual Endpoint (-log C)	6.28396	2.54455	2.82494
Predicted Endpoint (-log C)	5.12358	3.9702	3.0705
Distance	0.613	0.796	0.929
Reference	NCI/NTP TR-358	NCI/NTP TR-336	NCI/NTP TR-138

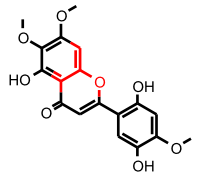
Model Applicability

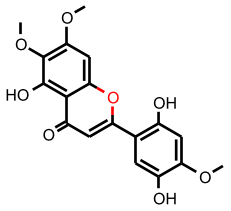
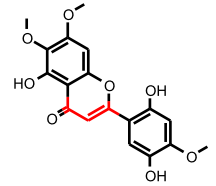
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. Num_H_Acceptors out of range. Value: 8. Training min, max, mean, SD: 0, 6, 1.6146, 1.644.
2. OPS PC9 out of range. Value: 4.6121. Training min, max, SD, explained variance: -2.7086, 2.9267, 1.019, 0.0321.
3. Unknown FCFP_2 feature: -1678245750: [*]O\C(=C/[*])\[c](:[*]):[*]
4. Unknown FCFP_2 feature: -1549192822: [*]=CC(=O)[c](:[*]):[*]

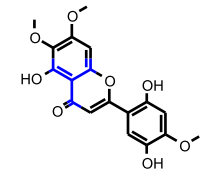
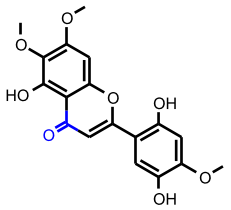
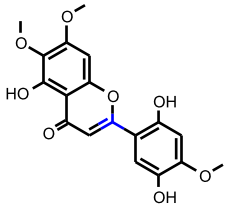
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_2	332760439	 [*]O[c](:[cH]:[*]):[c]([*]):[*]	0.672

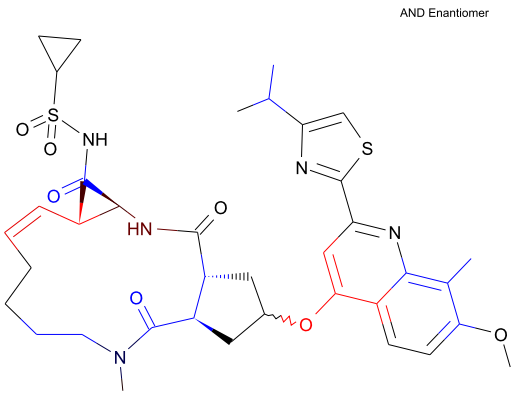
FCFP_2	1	 [*]O[*]	0.511
FCFP_2	451847724	 [*]C(=CC(=[*])[*])[*]	0.225

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_2	203677720	 [*]C(=[*])[c](:[c]([*]):[*]):[c]([*]):[*]	-0.406
FCFP_2	1872154524	 [*]C(=O)[*]	-0.307
FCFP_2	0	 [*]C(=[*])[*]	-0.29

Simeprevir

TOPKAT_Rat_Maximum_Tolerated_Dose_Gavage



$C_{38}H_{47}N_5O_7S_2$

Molecular Weight: 749.93908

ALogP: 4.796

Rotatable Bonds: 8

Acceptors: 9

Donors: 2

Model Prediction

Prediction: 0.000856

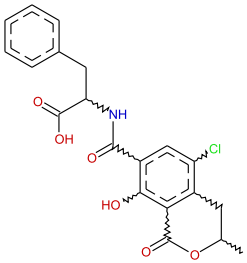
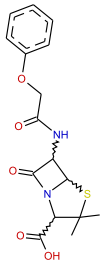
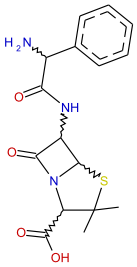
Unit: g/kg_body_weight

Mahalanobis Distance: 16.8

Mahalanobis Distance p-value: 1.77e-015

Mahalanobis Distance: The Mahalanobis distance (MD) is a generalization of the Euclidean distance that accounts for correlations among the X properties. It is calculated as the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Structural Similar Compounds

Name	OCHRATOXIN	PENICILLIN VK	AMPICILLIN TRIHYDRATE
Structure			
Actual Endpoint (-log C)	6.28396	2.54455	2.36724
Predicted Endpoint (-log C)	5.12358	3.9702	2.27651
Distance	1.425	1.545	1.716
Reference	NCI/NTP TR-358	NCI/NTP TR-336	NCI/NTP TR-318

Model Applicability

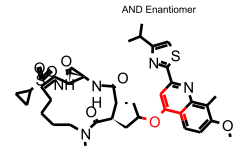
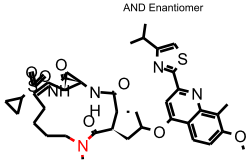
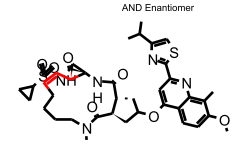
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. Molecular_Weight out of range. Value: 749.94. Training min, max, mean, SD: 68.074, 434.63, 171.13, 85.06.
2. Num_H_Acceptors out of range. Value: 9. Training min, max, mean, SD: 0, 6, 1.6146, 1.644.
3. Num_AromaticRings out of range. Value: 3. Training min, max, mean, SD: 0, 2, 0.5625, 0.693.
4. Molecular_PolarSASA out of range. Value: 272.1. Training min, max, mean, SD: 0, 223.97, 50.816, 55.15.
5. Molecular_PolarSurfaceArea out of range. Value: 193.5. Training min, max, mean, SD: 0, 138.03, 28.978, 32.1.
6. OPS PC1 out of range. Value: 9.6287. Training min, max, SD, explained variance: -4.0008, 7.9165, 2.861, 0.2531.
7. OPS PC6 out of range. Value: -3.4118. Training min, max, SD, explained variance: -2.4321, 2.9885, 1.256, 0.0488.
8. Unknown FCFP_2 feature: -415156552: [*]N[C@]1(C[C@H]1[*])C(=[*])[*]
9. Unknown FCFP_2 feature: 690511177: [*]:[cH]:[c](:n:[*])[c](:[*]):[*]
10. Unknown FCFP_2 feature: 690481386: [*]:[c](:[*])[c]1:n:[*]:[*]:s:1
11. Unknown FCFP_2 feature: 1018942292: [*]NS(=O)(=O)C1[*][*]1

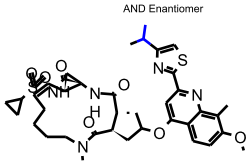
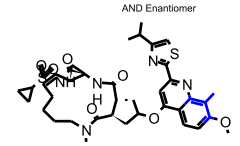
Feature Contribution

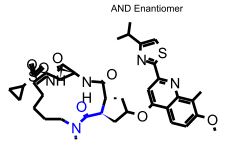
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score

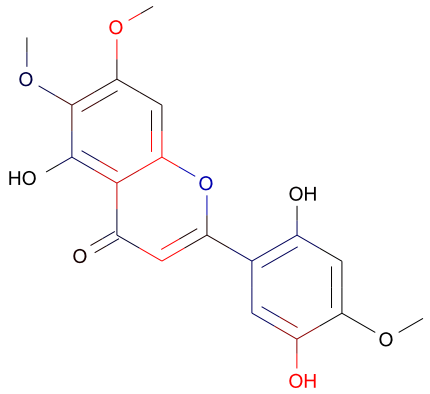
FCFP_2	332760439	 [*]O[c](:[cH]:[*]):[c]([*]):[*]	0.672
FCFP_2	1	 [*]O[*]	0.511
FCFP_2	451847724	 [*]C(=CC(=[*])[*])[*]	0.225

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_2	136597326	 [*]C([*])C	-0.489
FCFP_2	203677720	 [*]C(=[*])[c](:[c]([*]):[*]):[c]([*]):[*]	-0.406

FCFP_2	565998553	AND Enantiomer  [*]C([*])C(=O)N([*])[*]	-0.348

Flavonoid-1



$C_{18}H_{16}O_8$

Molecular Weight: 360.31483

ALogP: 2.361

Rotatable Bonds: 4

Acceptors: 8

Donors: 3

Model Prediction

Prediction: 0.462

Unit: g/kg_body_weight

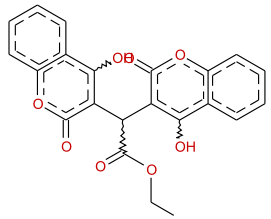
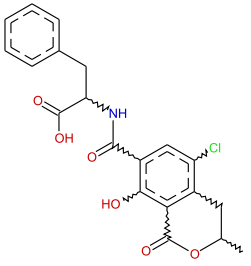
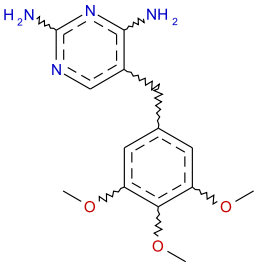
Mahalanobis Distance: 17.2

Mahalanobis Distance p-value: 0.0159

Mahalanobis Distance: The Mahalanobis distance (MD) is a generalization of the Euclidean distance that accounts for correlations among the X properties. It is calculated as the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.
Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

TOPKAT_Rat_Oral_LD50

Structural Similar Compounds

Name	ETHYL-bis-COUMACETATE	OCHRATOXIN A	TRIMETHOPRIM
Structure			
Actual Endpoint (-log C)	2.687	4.305	3.162
Predicted Endpoint (-log C)	2.7054	3.03558	2.44545
Distance	0.555	0.625	0.630
Reference	FEPRA7 10;303;51	FCTXAV 6;479;68	14XBAV -;367;64

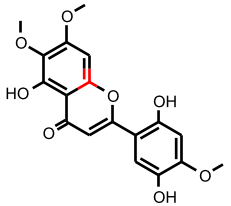
Model Applicability

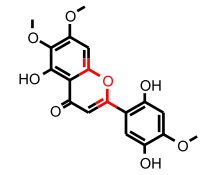
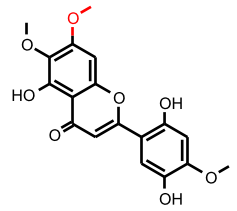
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown FCFP_6 feature: 16: [*][c](:[*]):[*]
3. Unknown FCFP_6 feature: 1618154665: [*][c](:[*]):[cH]:[c]([*]):[*]
4. Unknown FCFP_6 feature: 74595001: [*][c](:[*]):[c](O):[c]([*]):[*]
5. Unknown FCFP_6 feature: -1678245750: [*]O\C(=C/[*])\[c](:[*]):[*]
6. Unknown FCFP_6 feature: -549108873: [*]:[c](:[*])O

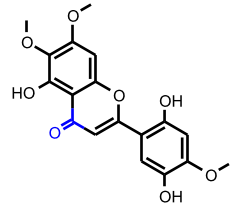
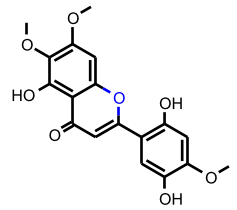
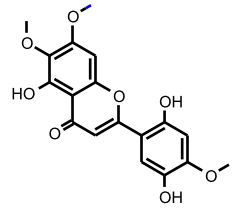
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
ECFP_6	642810091	 [*][c](:[*]):[*]	0.281

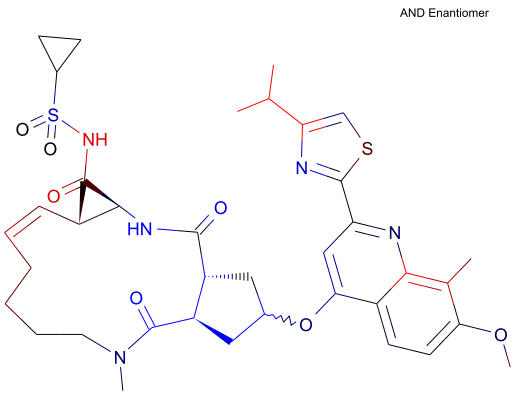
ECFP_6	-560785749	 [*]C(=[*])O[c](:[*]): [*]	0.259
FCFP_6	136627117	 [*]OC	0.17

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
ECFP_6	2106656448	 [*]C(=O)[*]	-0.352
ECFP_6	683445015	 [*]O[*]	-0.266
ECFP_6	734603939	 [*]C	-0.201

Simeprevir

TOPKAT_Rat_Oral_LD50



$C_{38}H_{47}N_5O_7S_2$

Molecular Weight: 749.93908

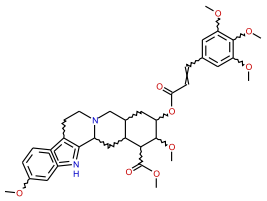
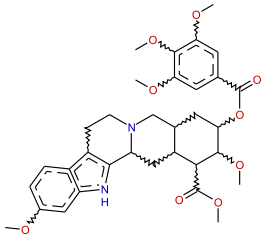
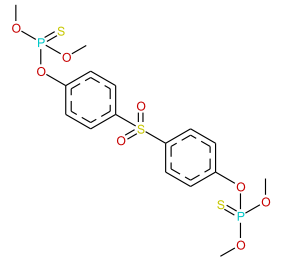
ALogP: 4.796

Rotatable Bonds: 8

Acceptors: 9

Donors: 2

Structural Similar Compounds

Name	ANAPREL	RESERPINE	PHOSPHOROTHIOIC ACID; O;O'-(SULFONYLDI-p-PHENYLENE) O;O;O';O'-TETRAMETHYL ESTER
Structure			
Actual Endpoint (-log C)	2.803	3.161	2.397
Predicted Endpoint (-log C)	2.99154	2.72801	3.8515
Distance	1.032	1.042	1.057
Reference	NIIRDN 6;898;82	PSSCBG 11;555;80	TXAPA9 21;315;72

Model Prediction

Prediction: 0.209

Unit: g/kg_body_weight

Mahalanobis Distance: 37.6

Mahalanobis Distance p-value: 1.1e-129

Mahalanobis Distance: The Mahalanobis distance (MD) is a generalization of the Euclidean distance that accounts for correlations among the X properties. It is calculated as the distance to the center of the training data. The larger the MD, the less trustworthy the prediction.

Mahalanobis Distance p-value: The p-value gives the fraction of training data with an MD greater than or equal to the one for the given sample, assuming normally distributed data. The smaller the p-value, the less trustworthy the prediciton. For highly non-normal X properties (e.g., fingerprints), the MD p-value is wildly inaccurate.

Model Applicability

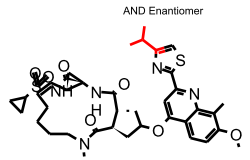
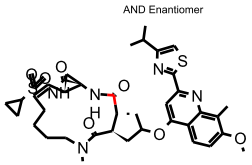
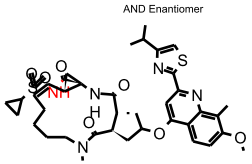
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown ECFP_2 feature: -309676563: [*]N[C@]1(C[C@H]1[*])C(=[*])[*]
3. Unknown ECFP_2 feature: -1049290660: [*]C1([*])C[C@H]1C=[*]
4. Unknown ECFP_2 feature: 2121941848: [*]NS(=O)(=O)C1[*][*]1
5. Unknown FCFP_6 feature: 16: [*][c](:[*]):[*]
6. Unknown FCFP_6 feature: 1747237384: [*][c](:[*]):n:[c](:[*]):[*]
7. Unknown FCFP_6 feature: 690511177: [*]:[cH]:[c](:n:[*])[c](:[*]):[*]
8. Unknown FCFP_6 feature: 1618154665: [*][c](:[*]):[cH]:[c]([*]):[*]
9. Unknown FCFP_6 feature: 690481386: [*]:[c](:[*])[c]1:n:[*]:[*]:s:1
10. Unknown FCFP_6 feature: 1018942292: [*]NS(=O)(=O)C1[*][*]1

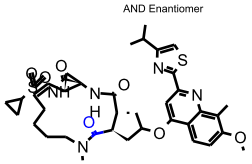
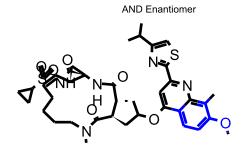
Feature Contribution

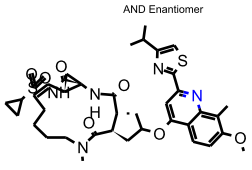
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score

FCFP_6	1186303932	 [*]:[c](:[*])C(C)C	0.375
ECFP_6	642810091	 [*][c](:[*]):[*]	0.281
ECFP_6	-1897341097	 [*]N[*]	0.216

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
ECFP_6	2106656448	 [*]C(=O)[*]	-0.352
ECFP_6	2077607946	 [*]O[c]1:[cH]:[cH]:[c](:[*]):[*]:[c]:1[*]	-0.252

ECFP_6	655739385	AND Enantiomer  [*]:n:[*]	-0.239