Isolation and In Silico Inhibitory Potential against SARS-CoV-2 RNA Polymerase of the Rare Kaempferol 3-*O*-(6''-*O*-acetyl)-Glucoside from *Calligonum tetrapterum*

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Content

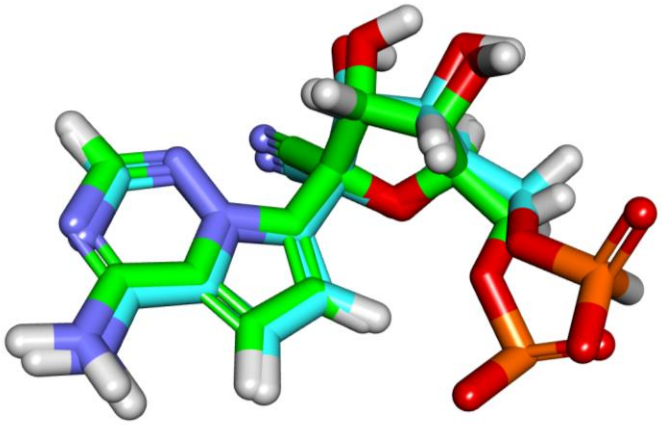
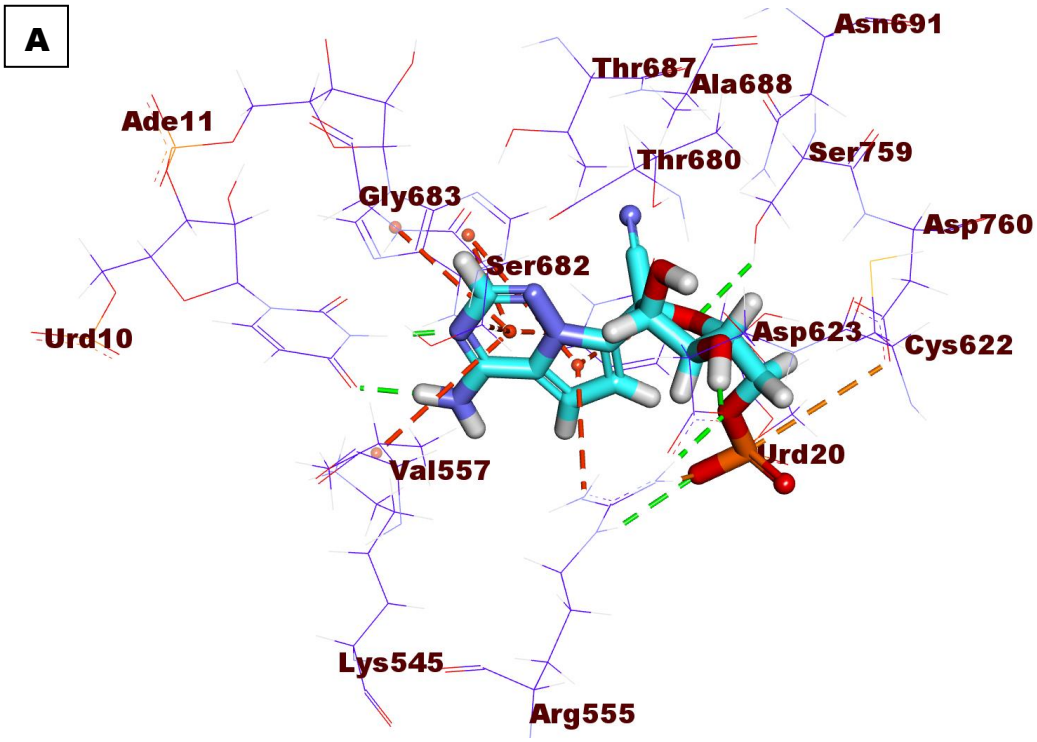


Figure S1. Superimposition of the co-crystallized and the docked pose of Remdesivir (pink and dark green, respectively).



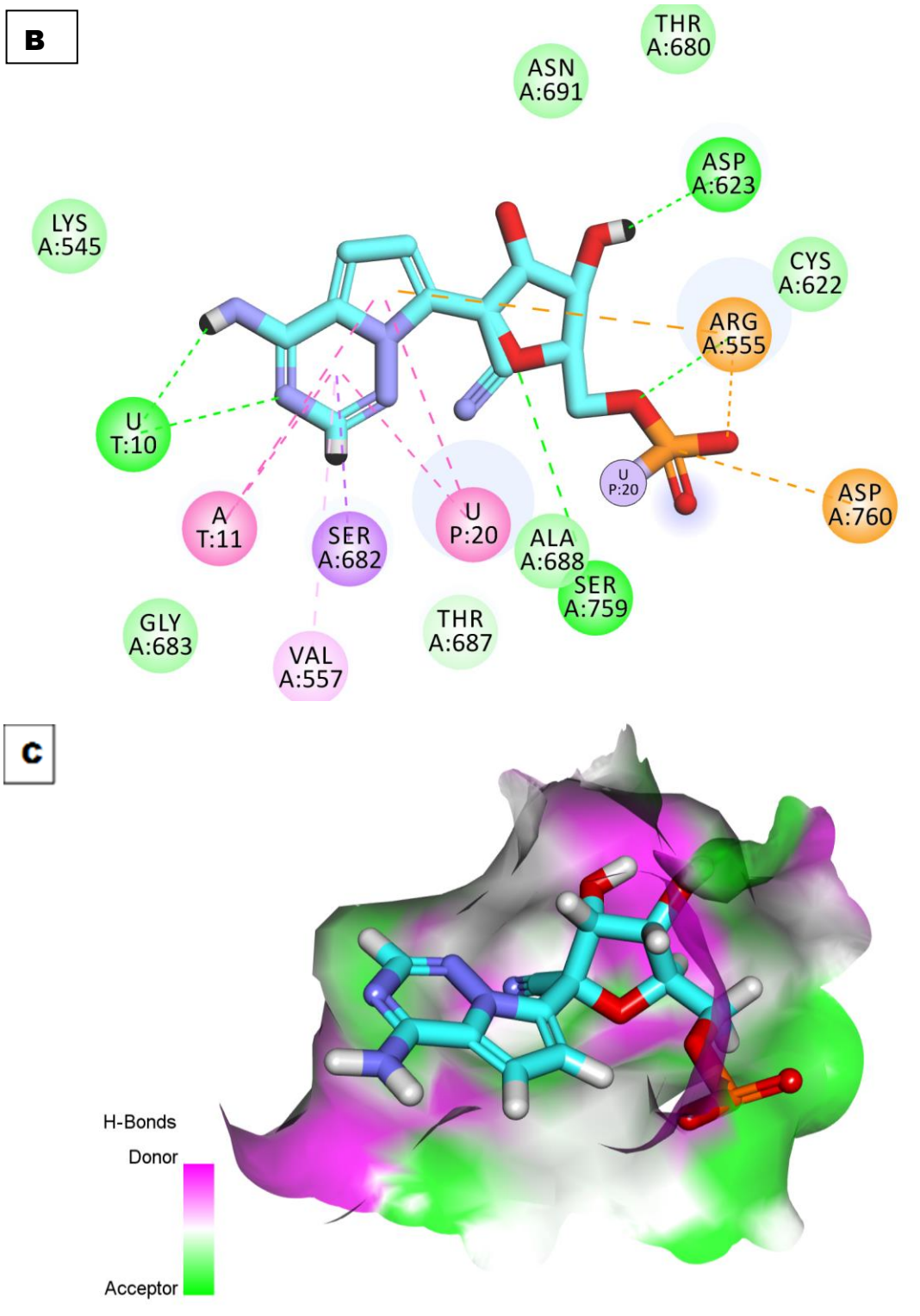
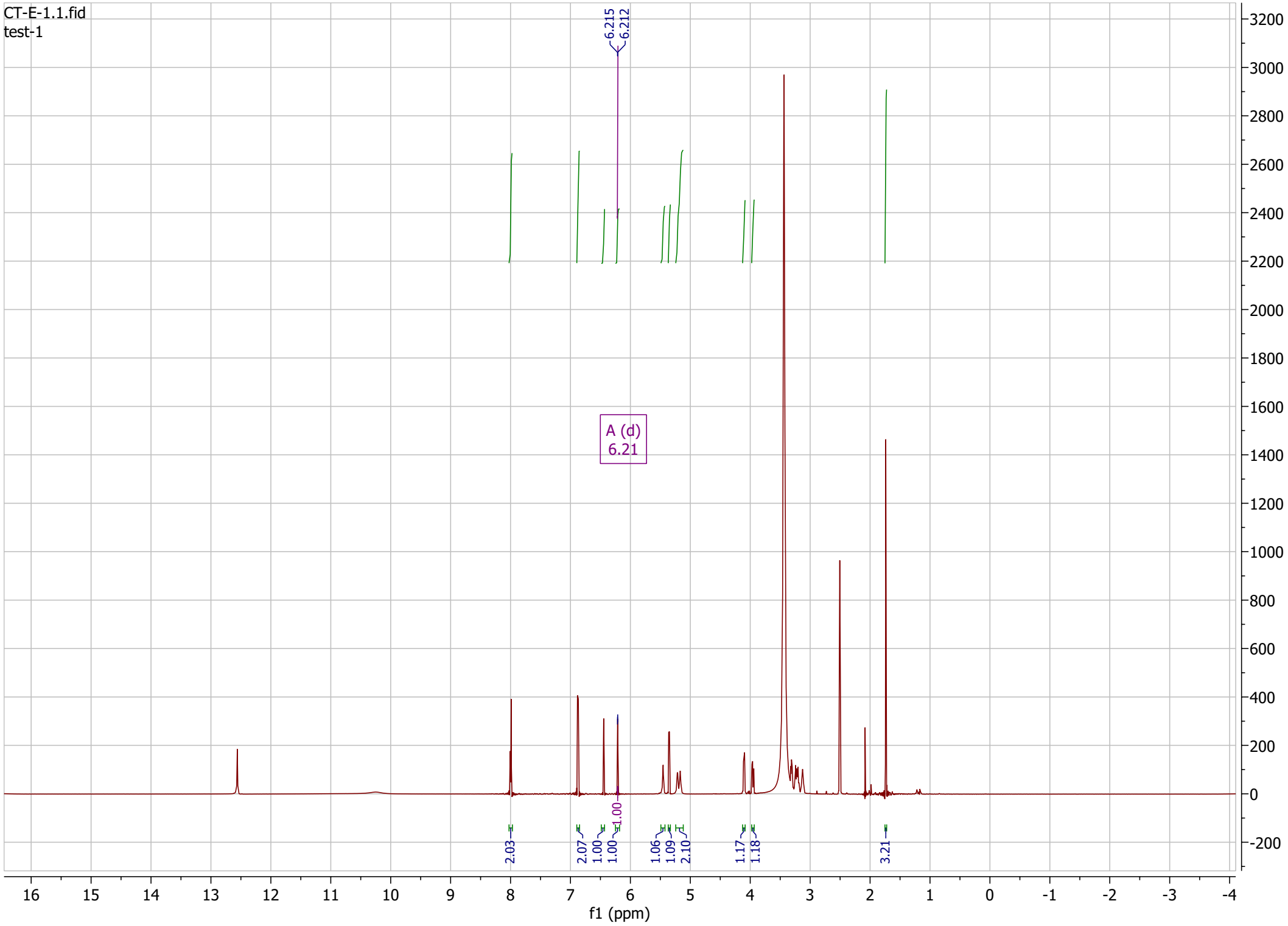


Figure S2 : (**A**) 3D (**B**) 2D and (**C**) Surface mapping of the co-crystallized ligand docked into the active site of SARS-CoV-2 RNA-dependent RNA polymerase.

Spectral data NMR of compound 1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6.212
A (d)
6.21
2.03
2.07
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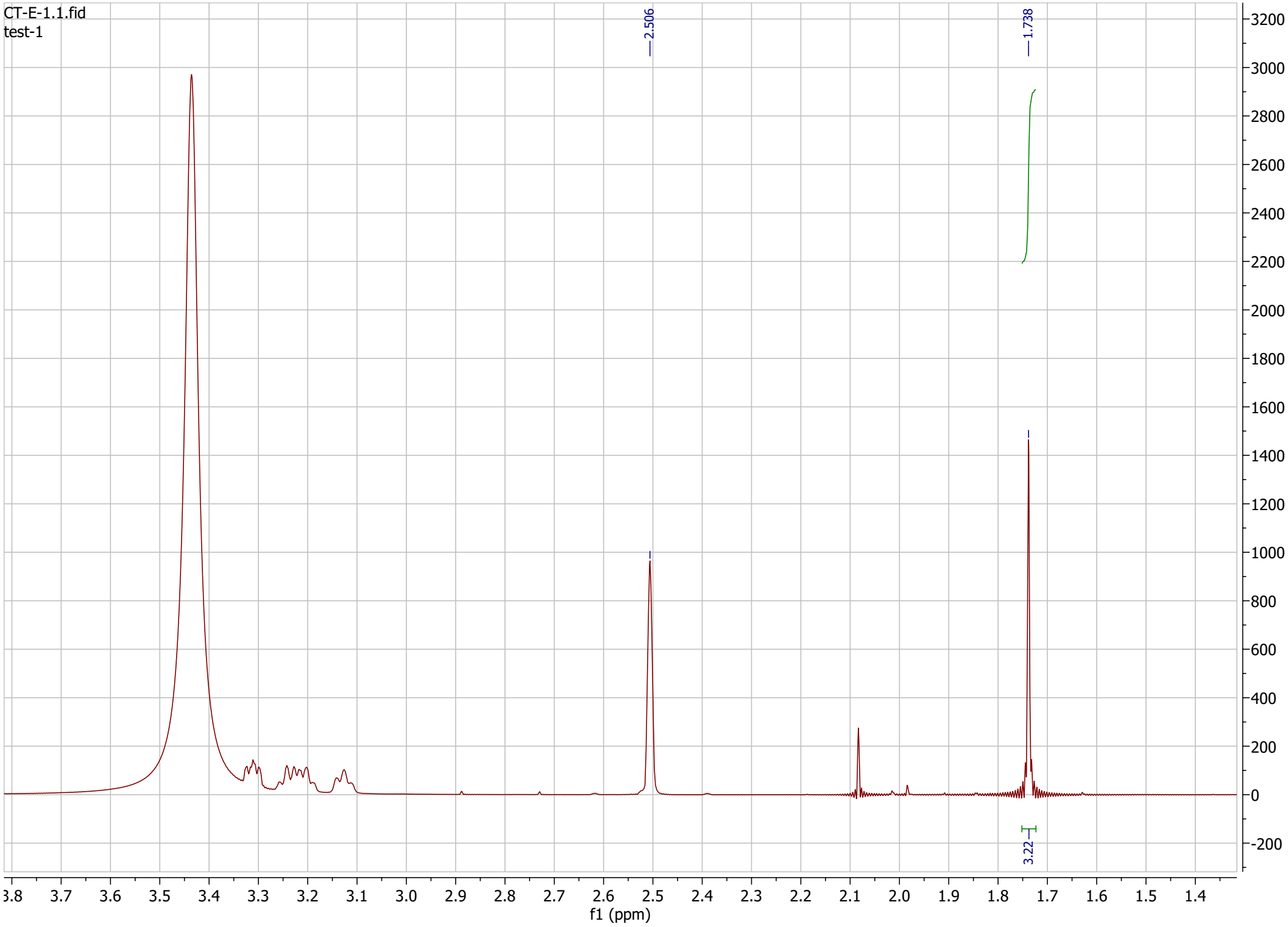
1.00
1.00
1.06
1.09
2.10
1.17
1.18
3.21
f1 (ppm)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1800
1600
1400
1200
1000
800
600
400
200
0
-200
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
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1.8
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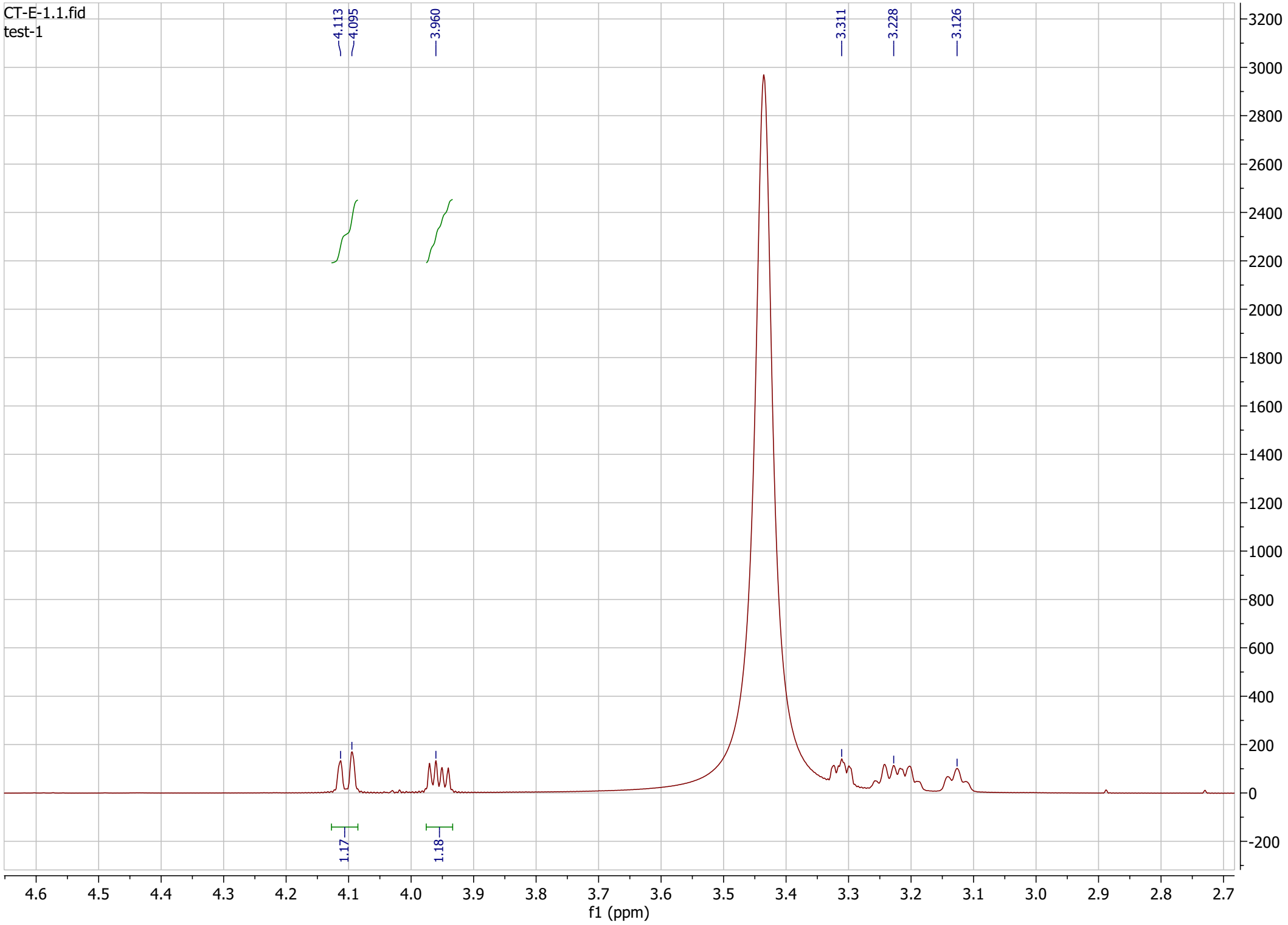
1.6
1.5
1.4
f1 (ppm)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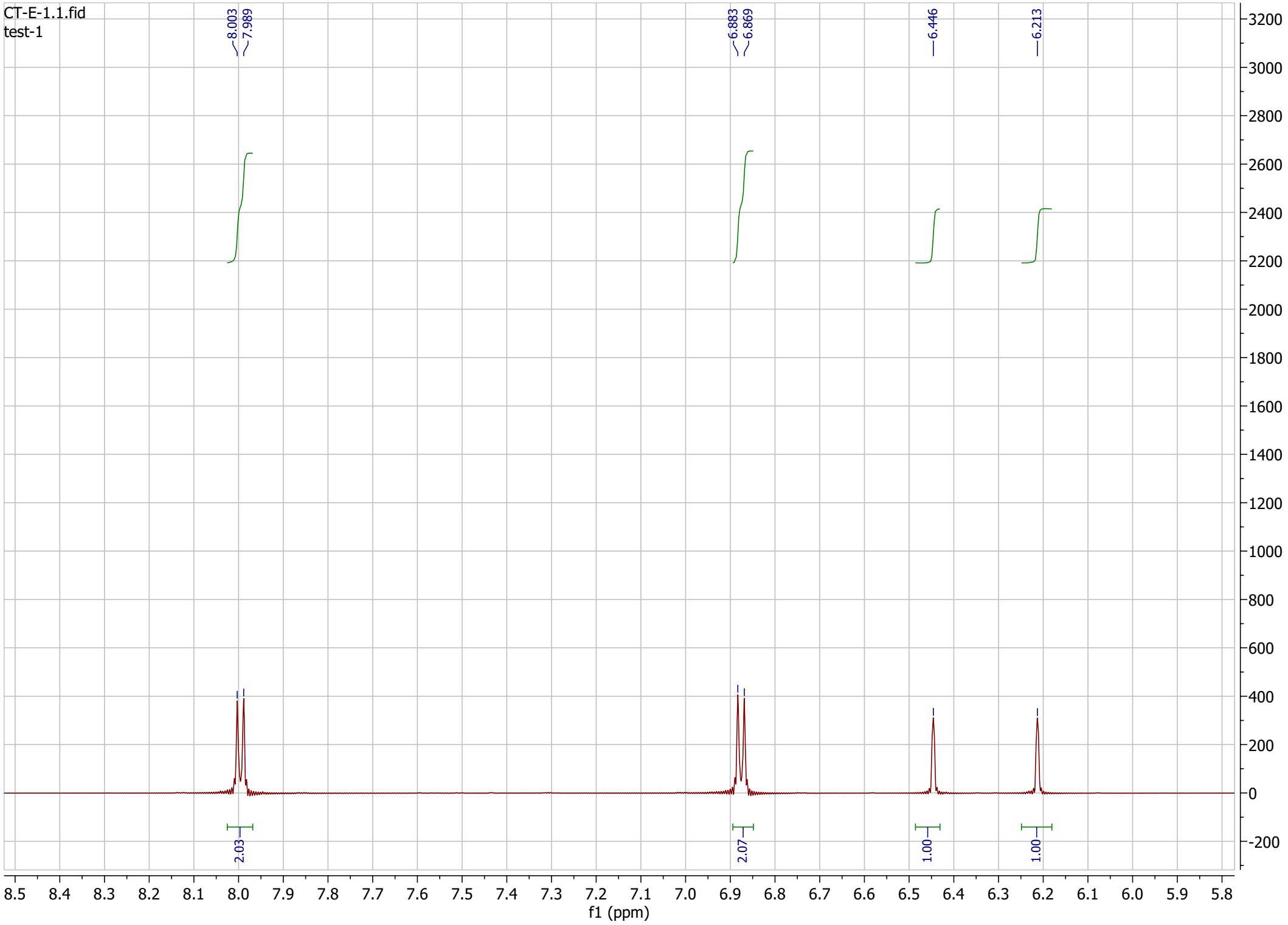
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6.213
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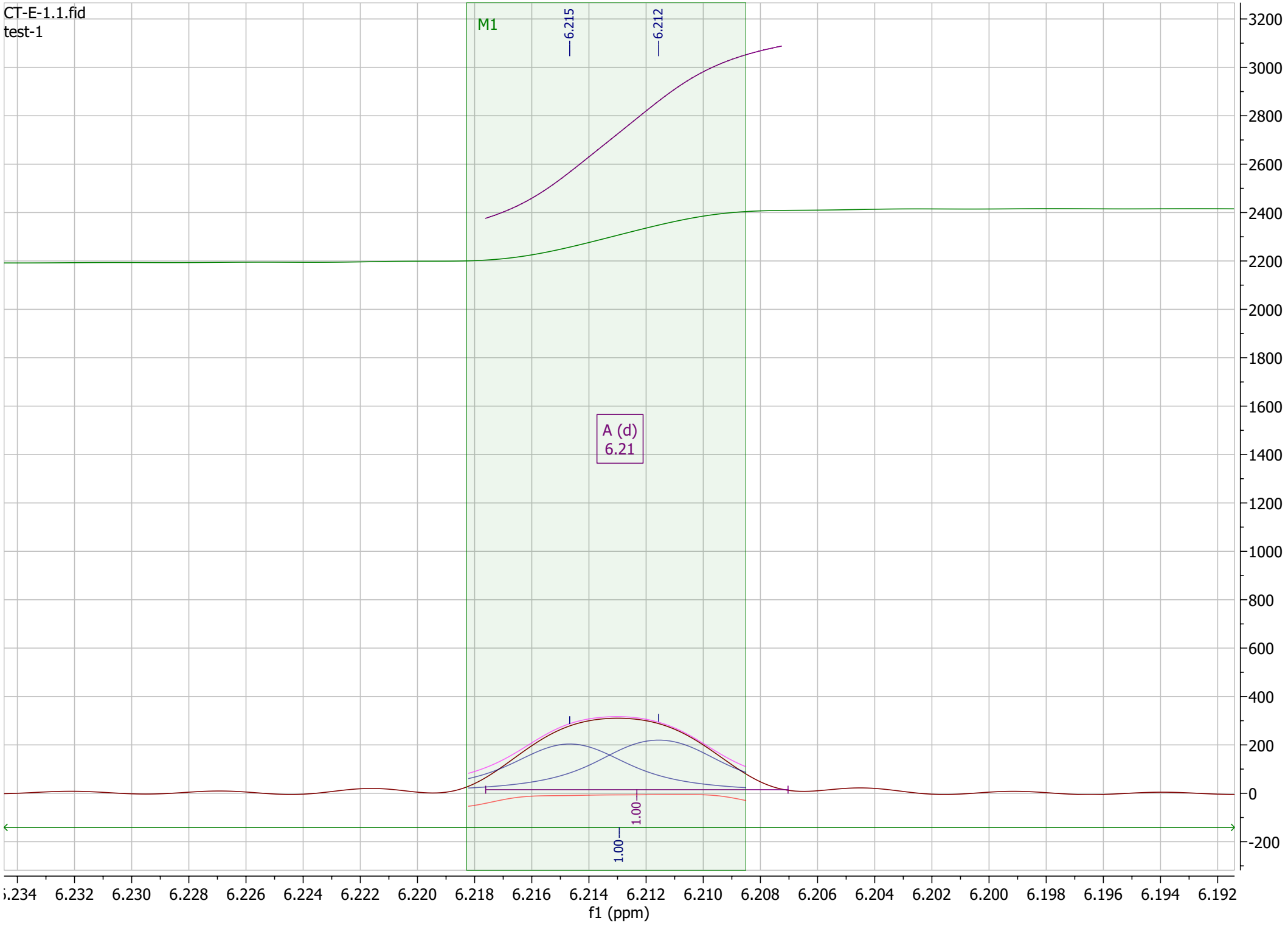
2.07
1.00
1.00
f1 (ppm)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1.00
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3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
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6.232
6.230
6.228
6.226
6.224
6.222
6.220
6.218
6.216
6.214
6.212
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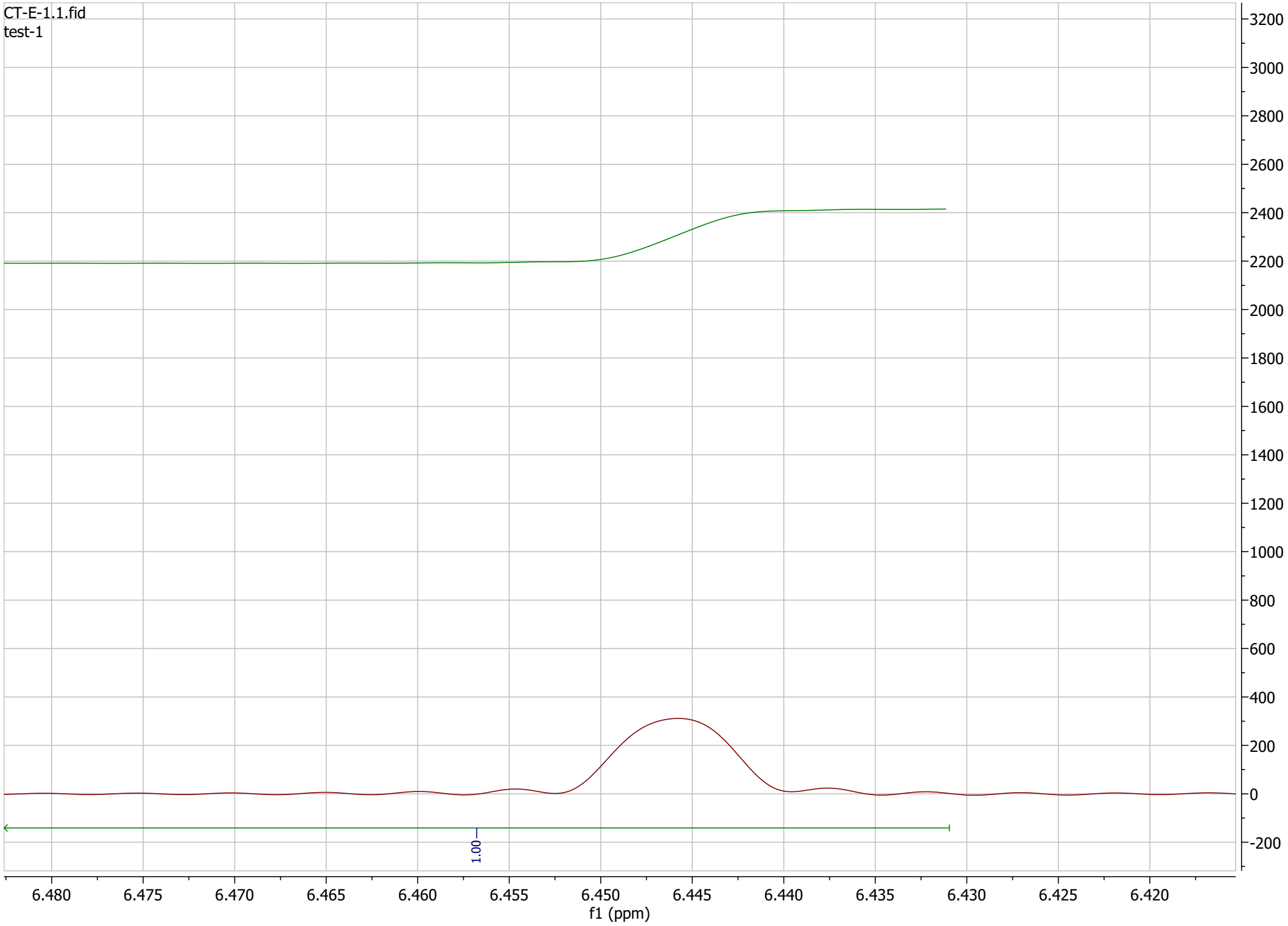
6.196
6.194
6.192
f1 (ppm)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400
200
0
-200
1.00
6.480
6.475
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6.430
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6.420
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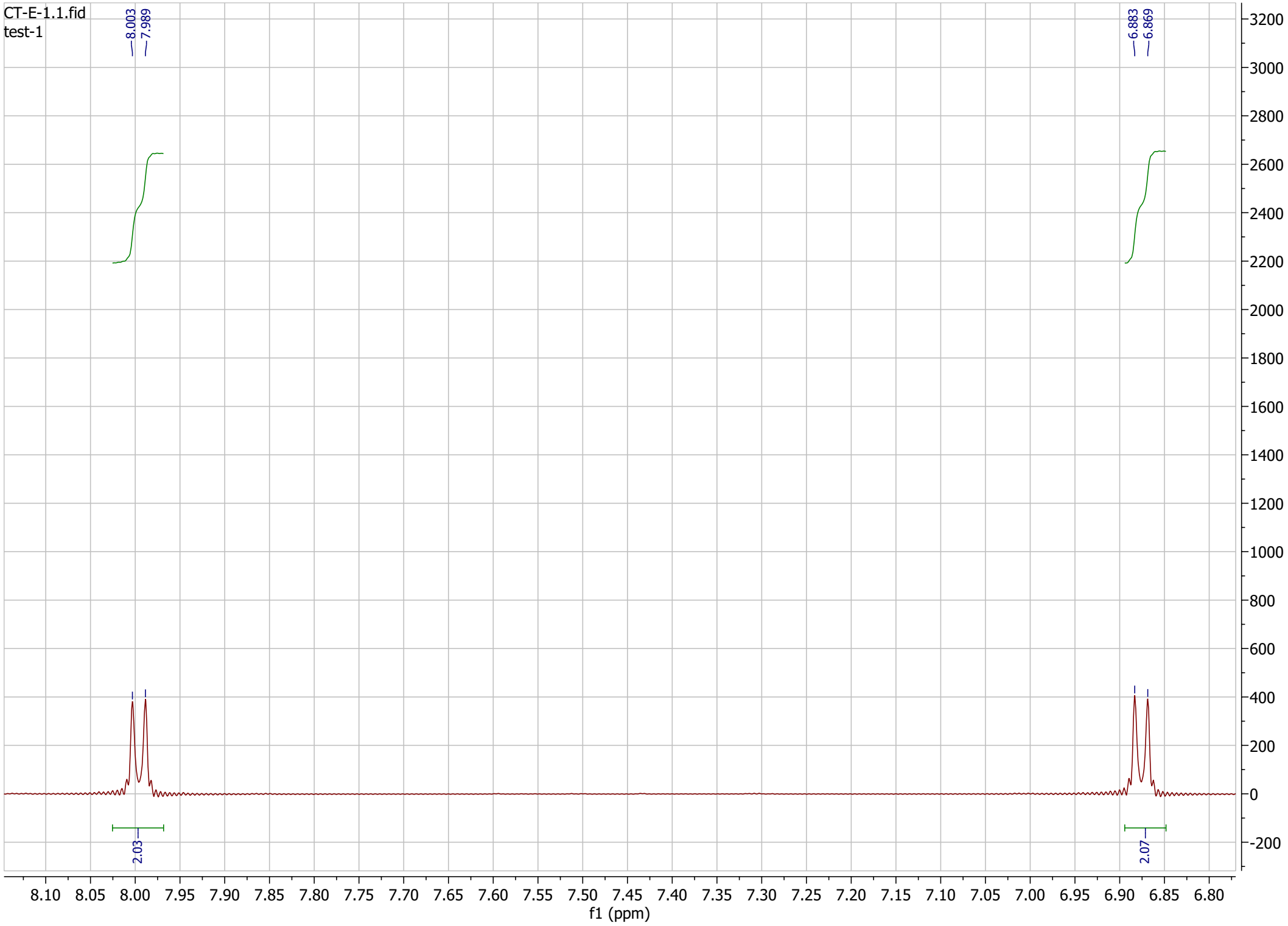
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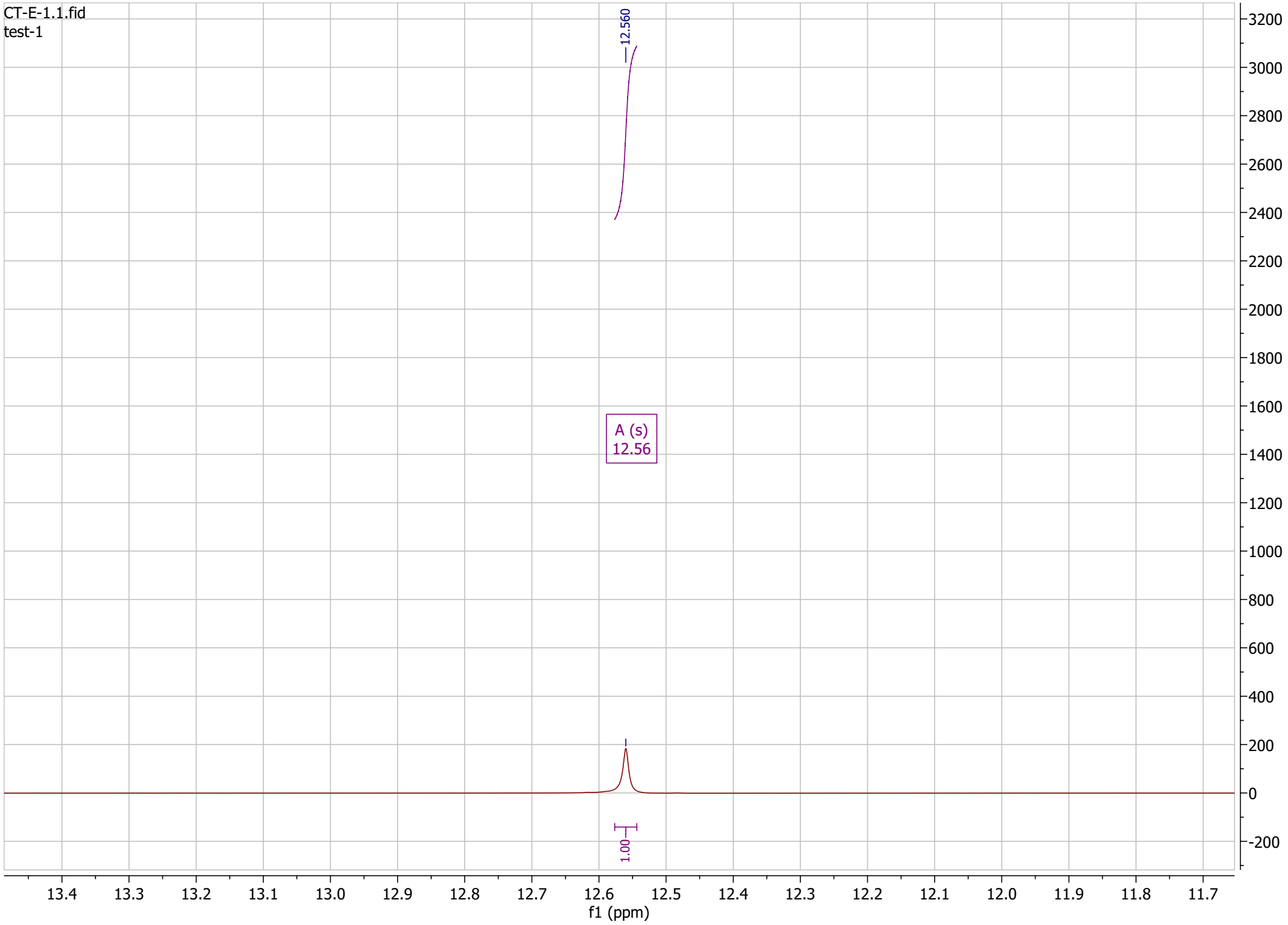
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1800
1600
1400
1200
1000
800
600
400
200
0
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13.4
13.3
13.2
13.1
13.0
12.9
12.8
12.7
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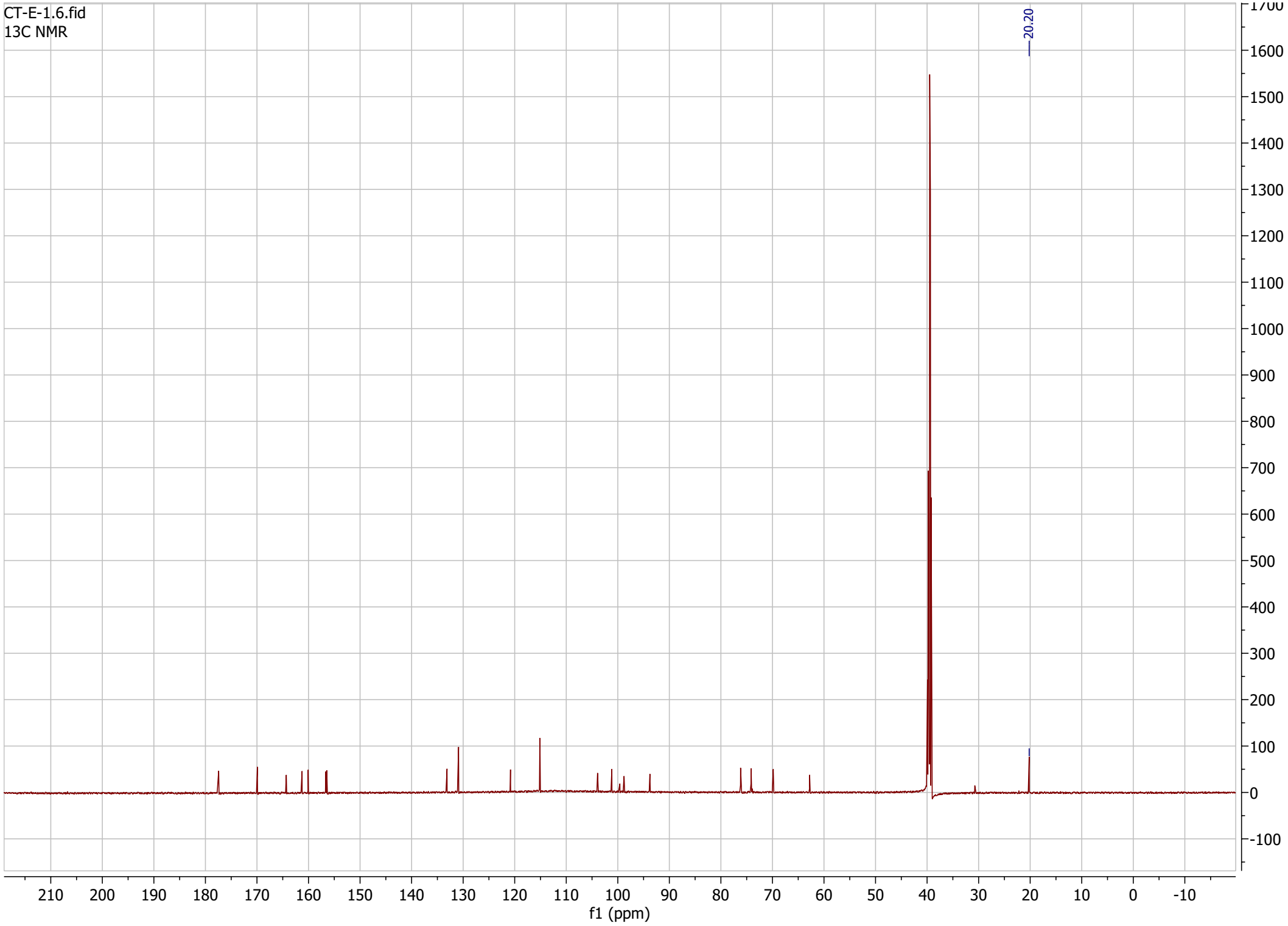
11.9
11.8
11.7
f1 (ppm)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100
0
-100
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200
190
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30
20
10
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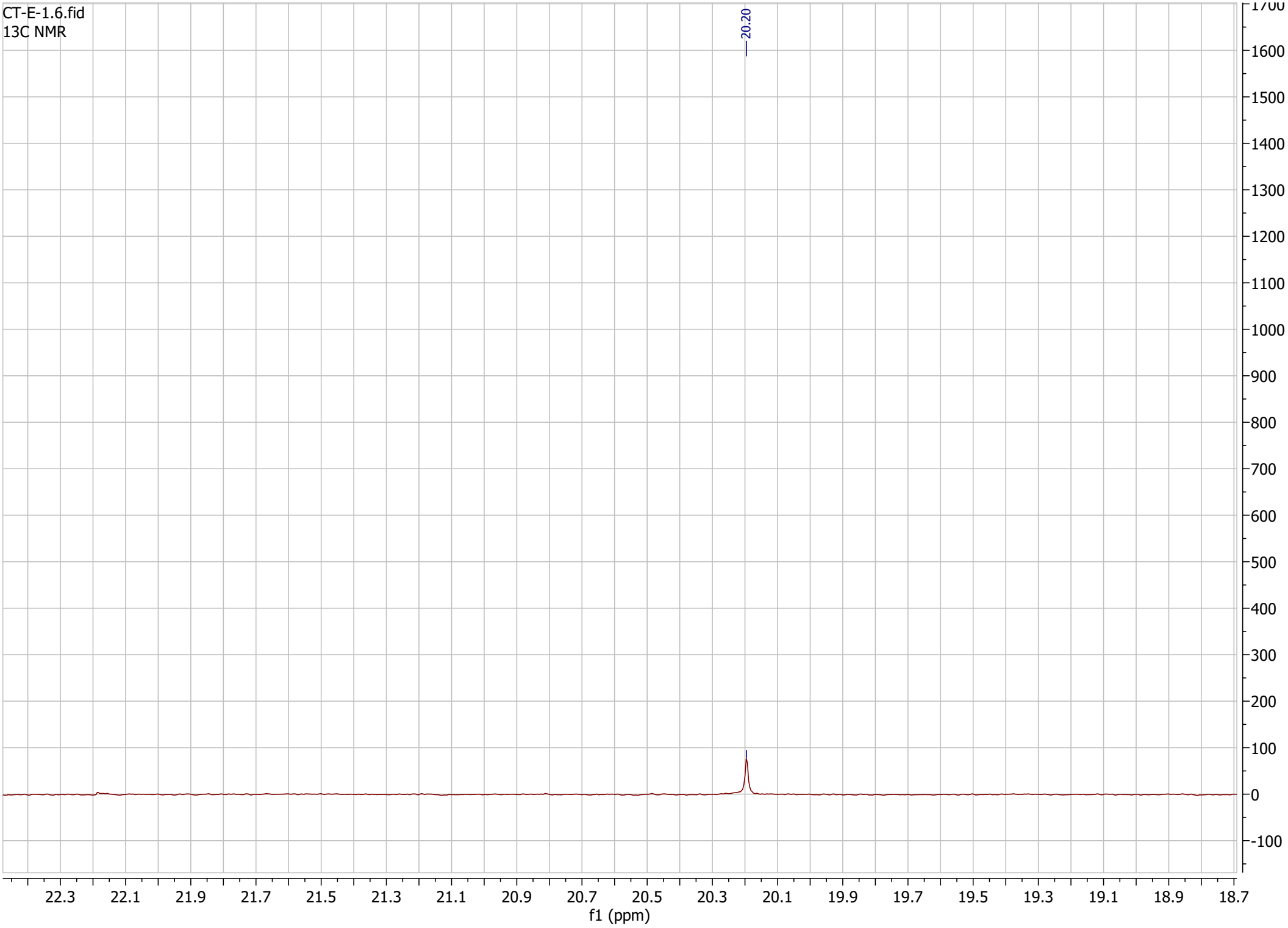
f1 (ppm)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1500
1400
1300
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1100
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900
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500
400
300
200
100
0
-100
22.3
22.1
21.9
21.7
21.5
21.3
21.1
20.9
20.7
20.5
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20.1
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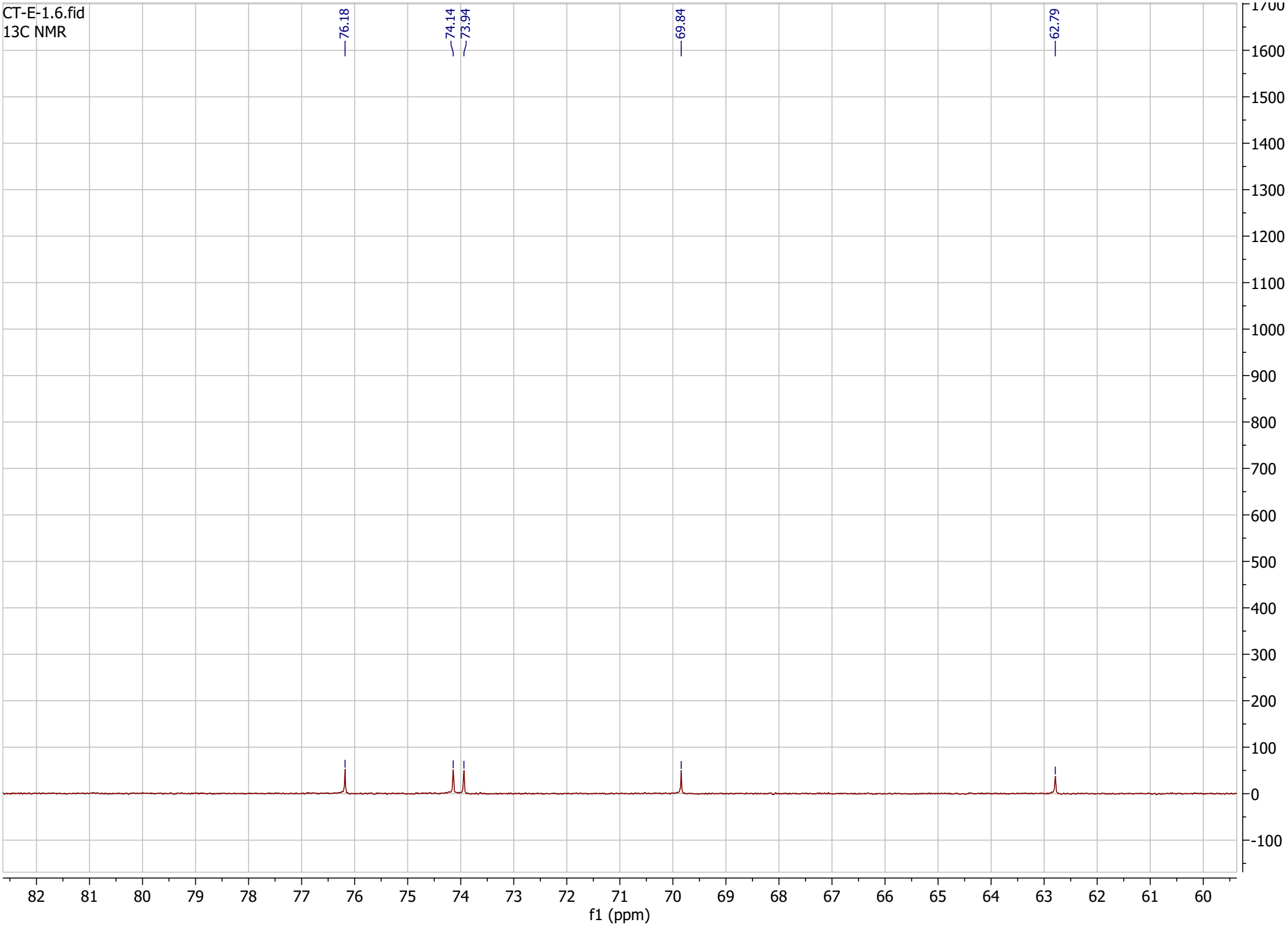
19.3
19.1
18.9
18.7
f1 (ppm)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73.94
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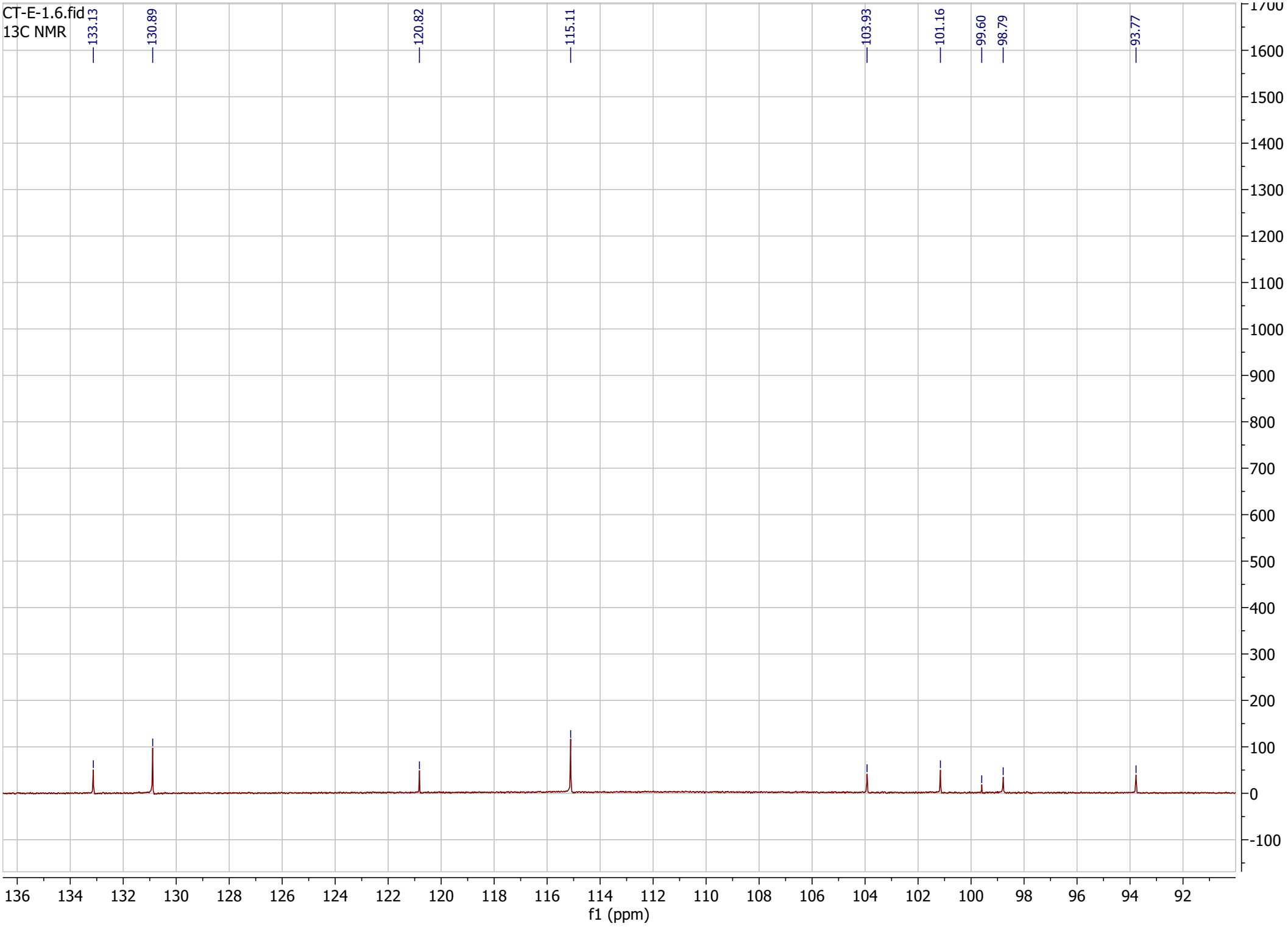
62.79
f1 (ppm)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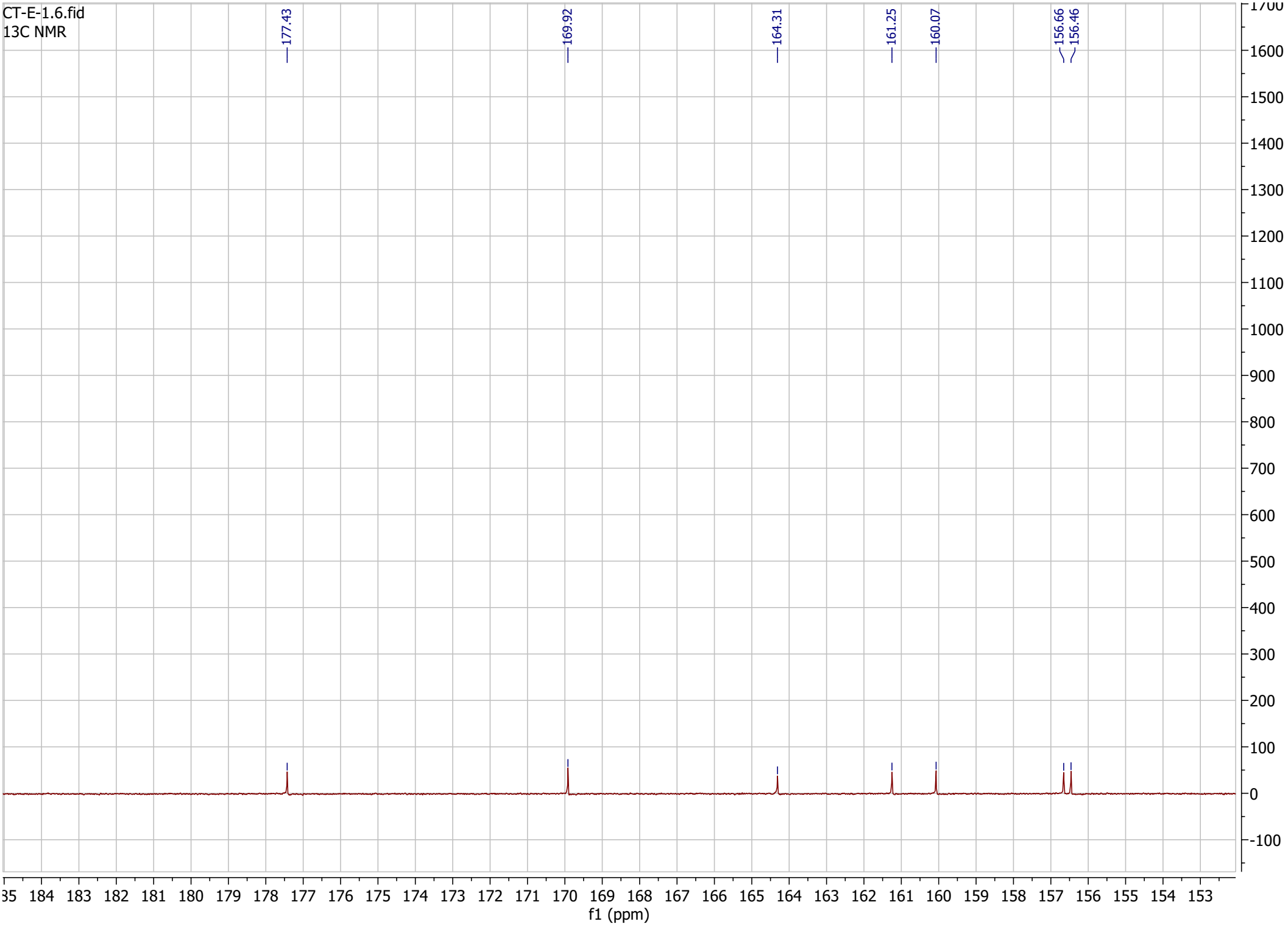
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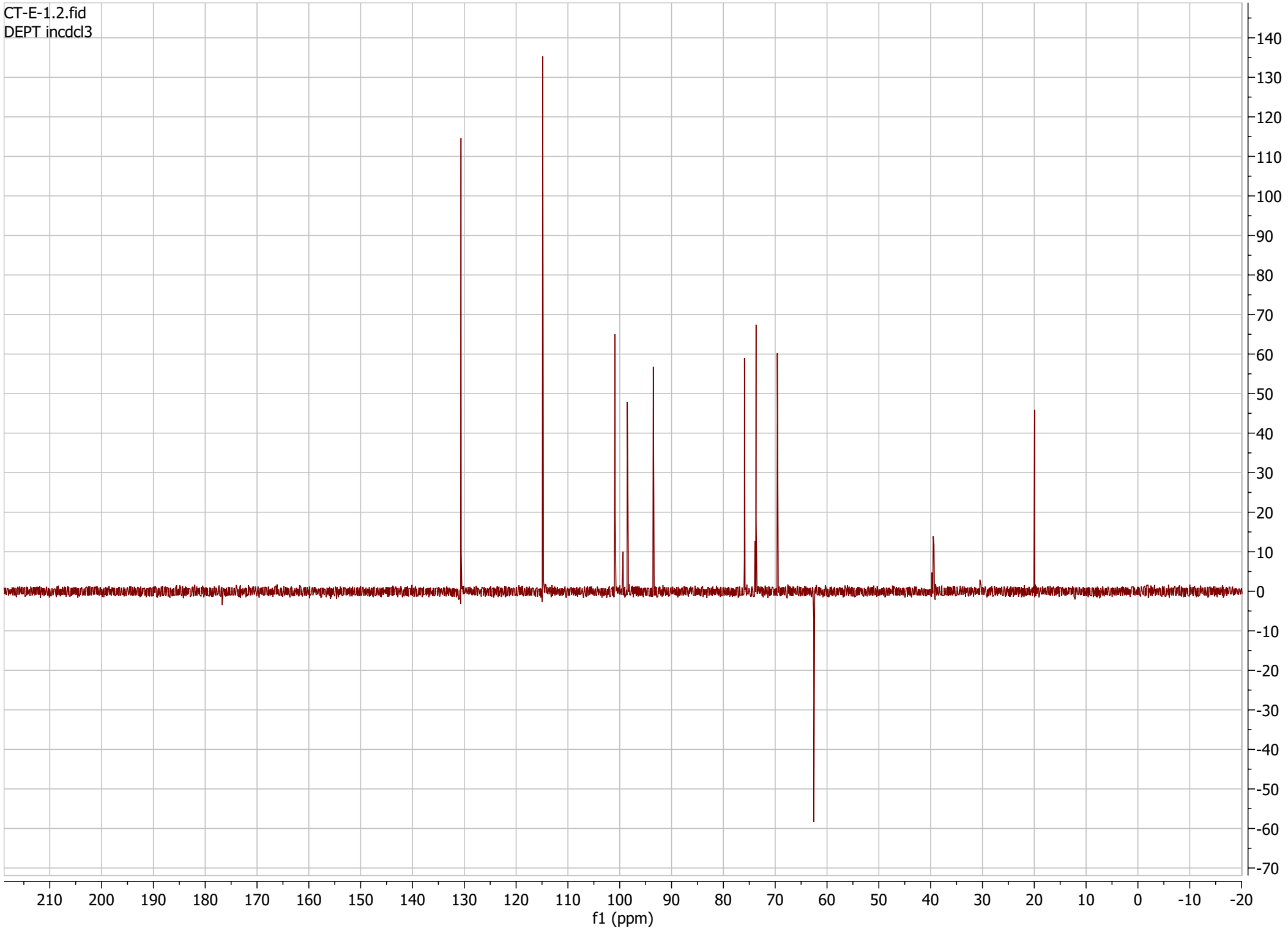
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10
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-10
-20
-30
-40
-50
-60
-70
210
200
190
180
170
160
150
140
130
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90
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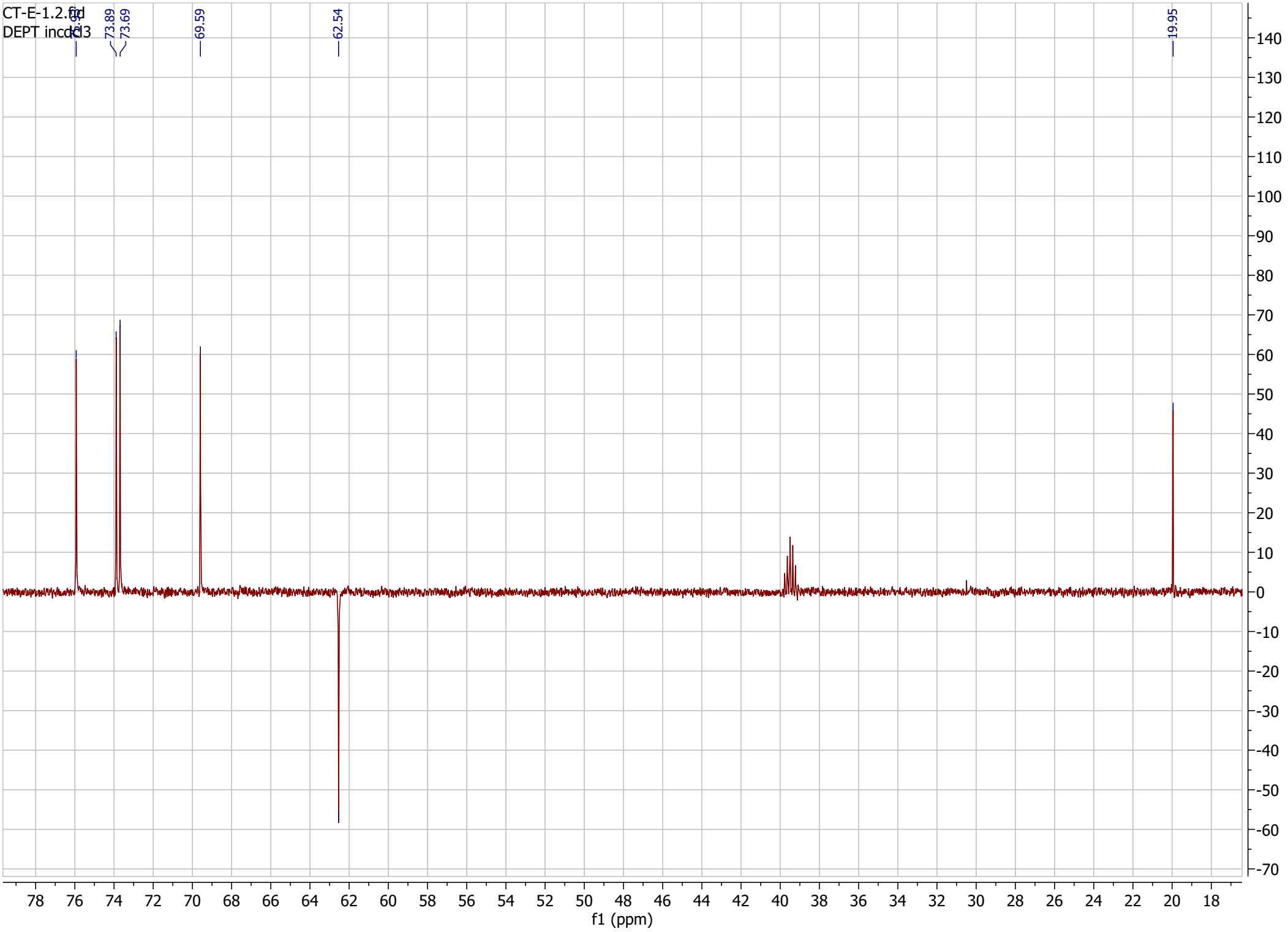
0
-10
-20
f1 (ppm)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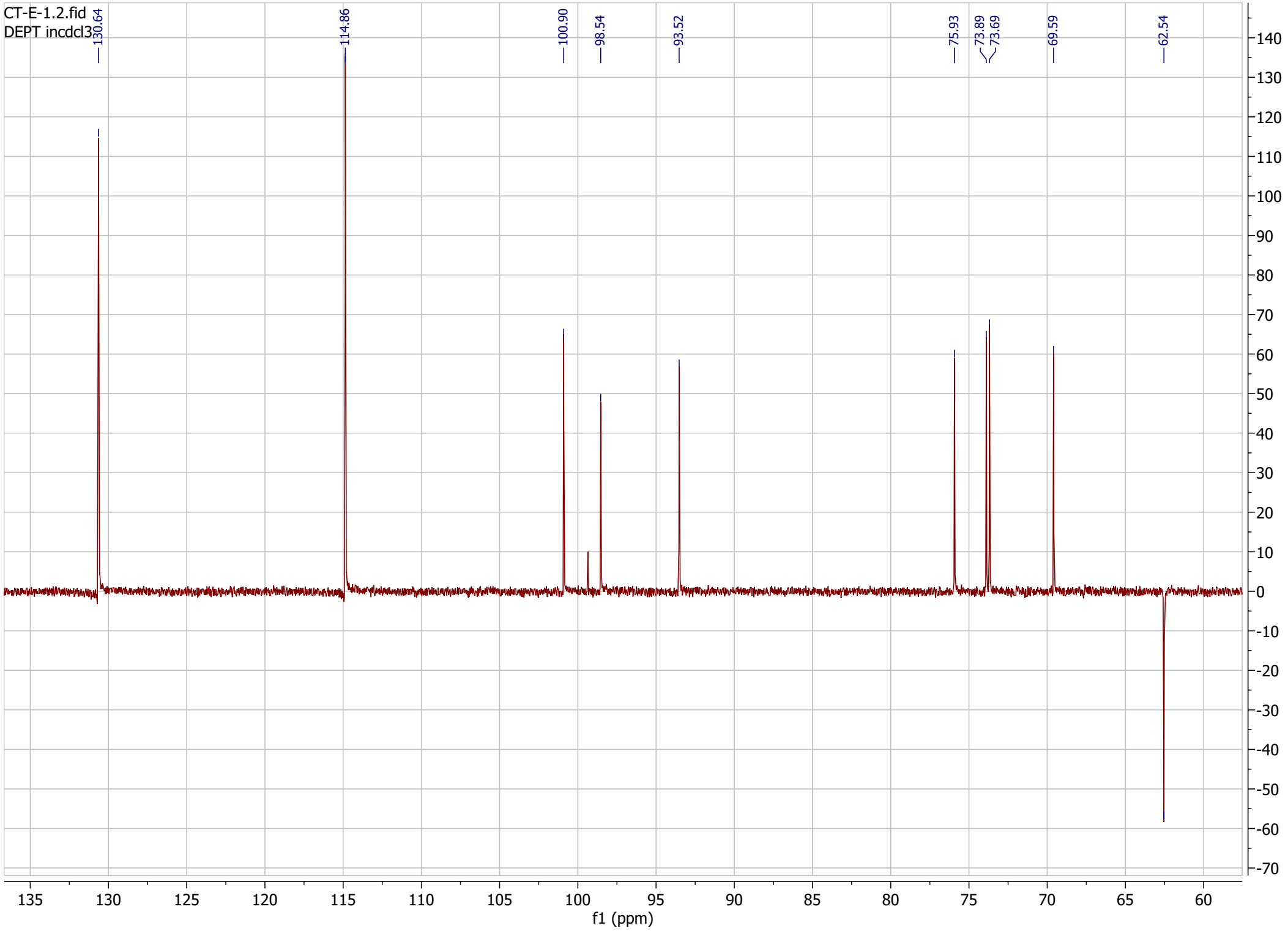
62.54
19.95
f1 (ppm)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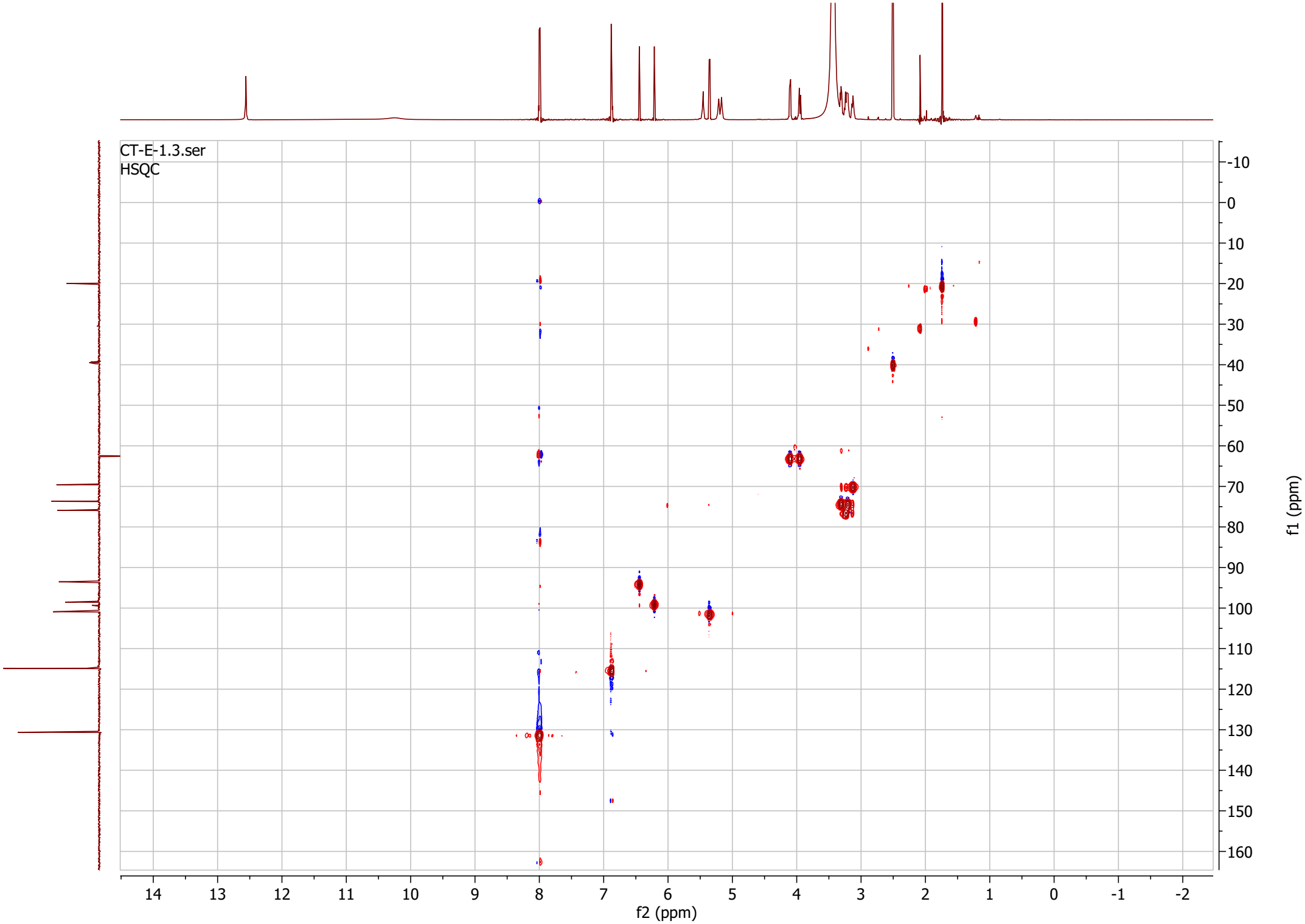
69.59
62.54
f1 (ppm)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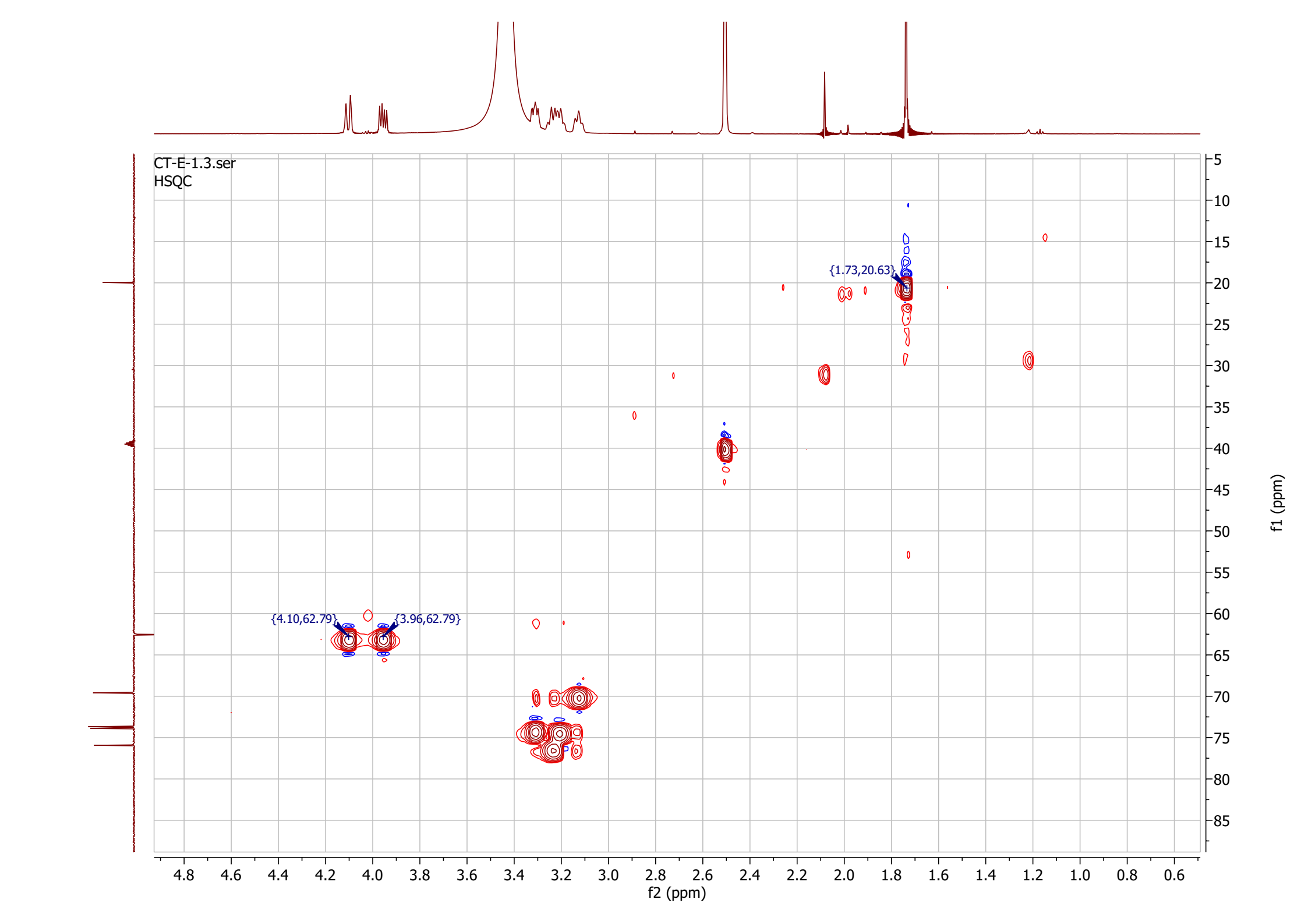
f2 (ppm)
f1 (ppm)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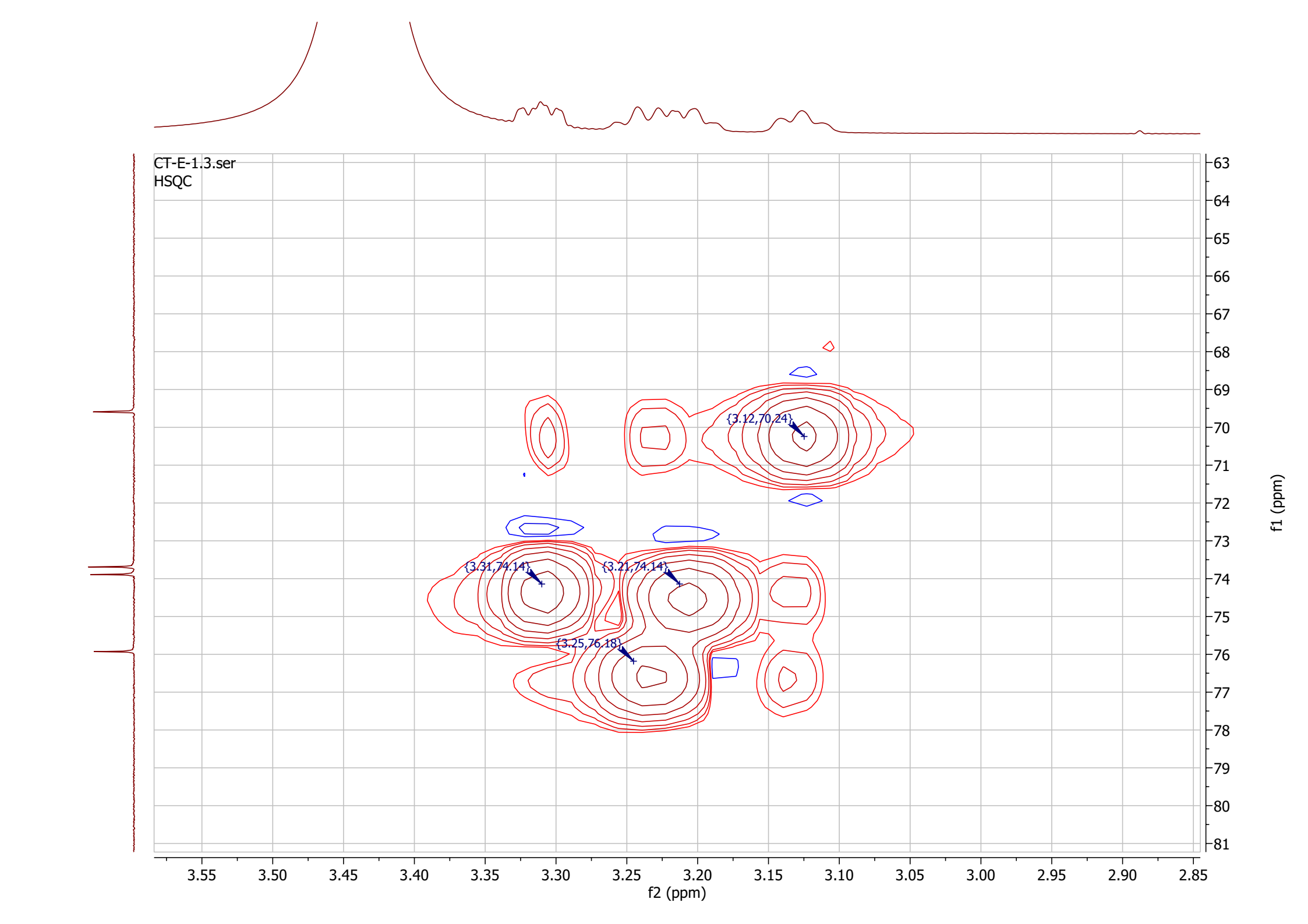
{3.96,62.79}
f2 (ppm)
f1 (ppm)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{3.31,74.14}
{3.21,74.14}
{3.25,76.18}
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
f1 (ppm)
3.55
3.50
3.45
3.40
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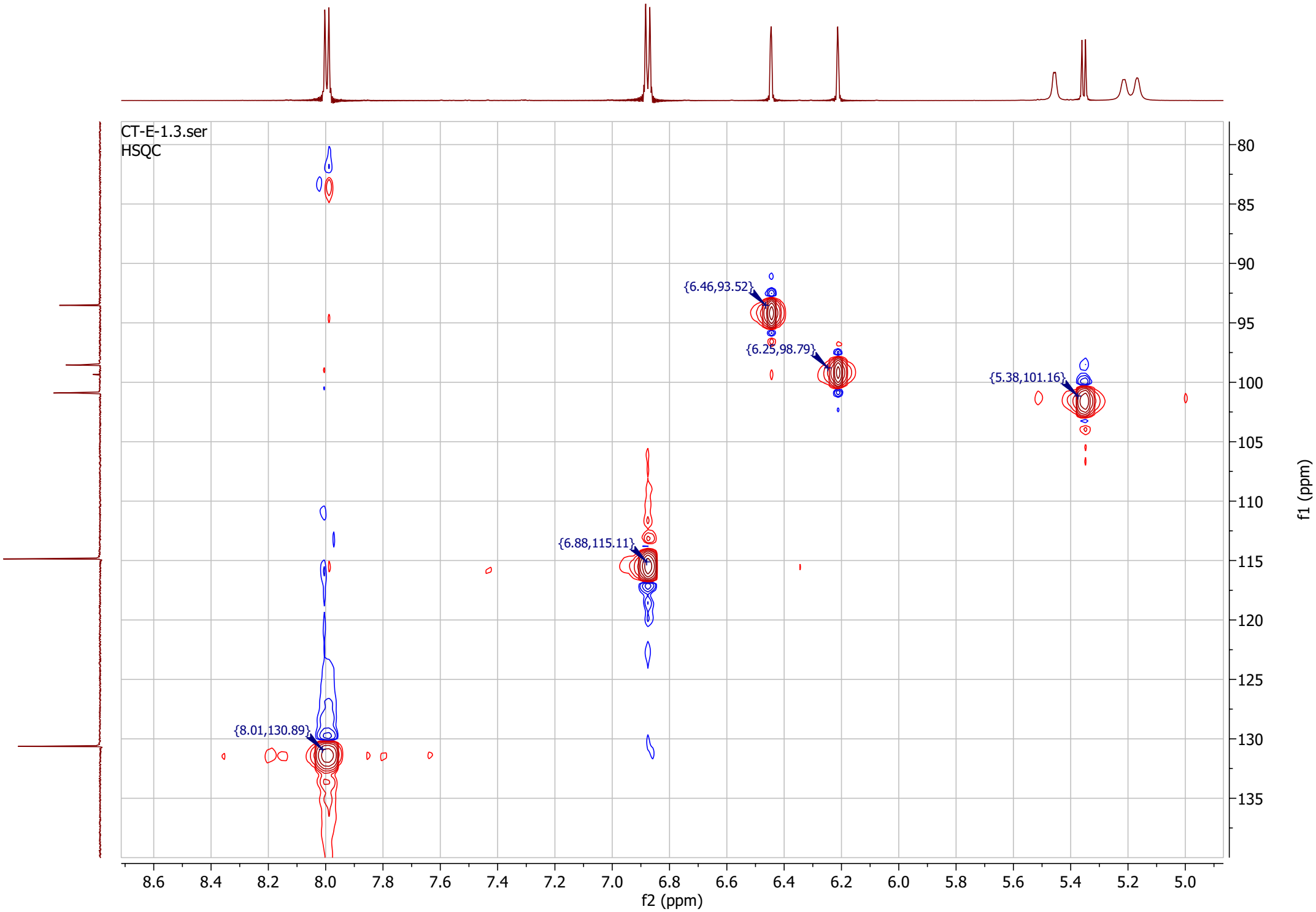
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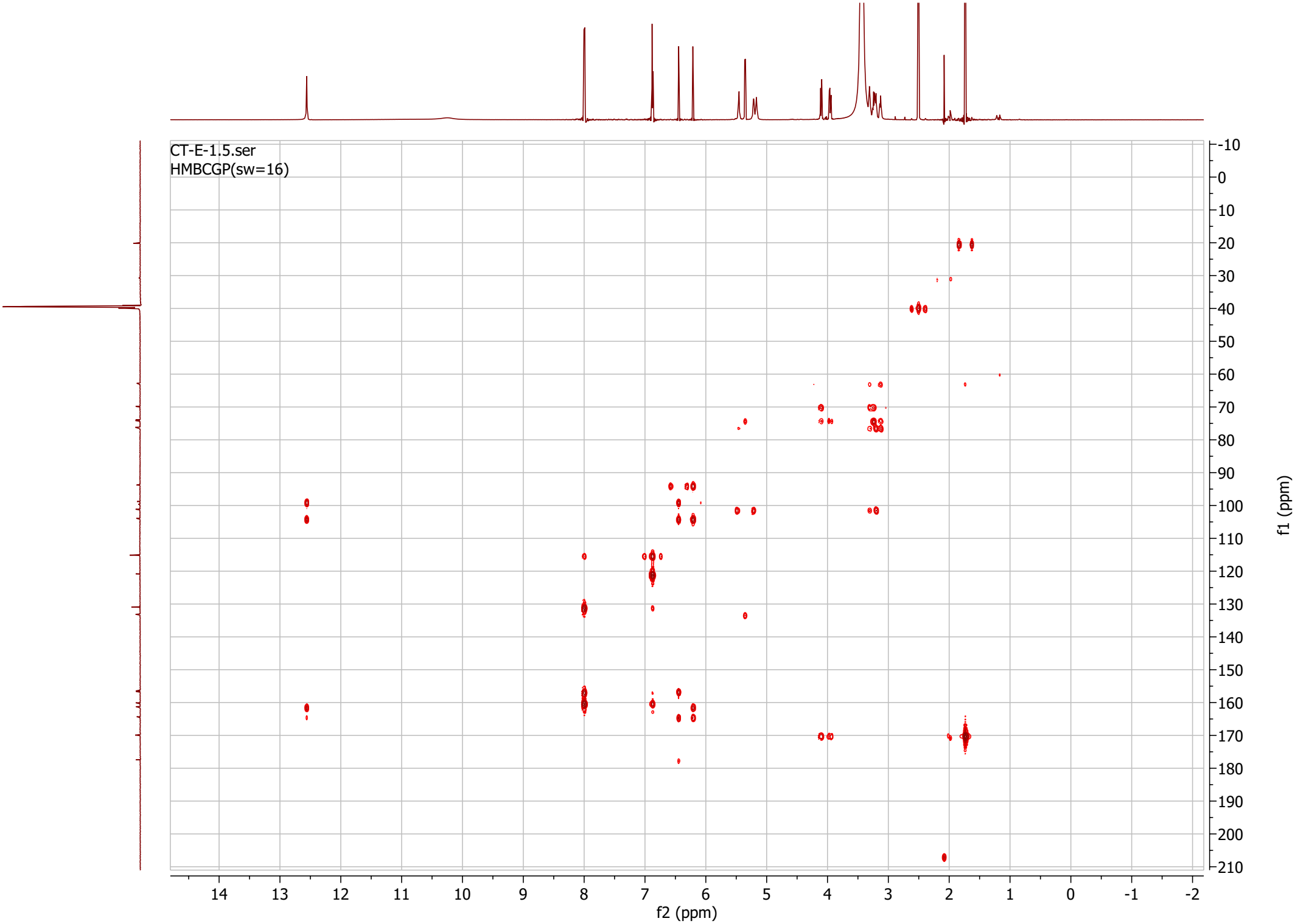
f2 (ppm)
f1 (ppm)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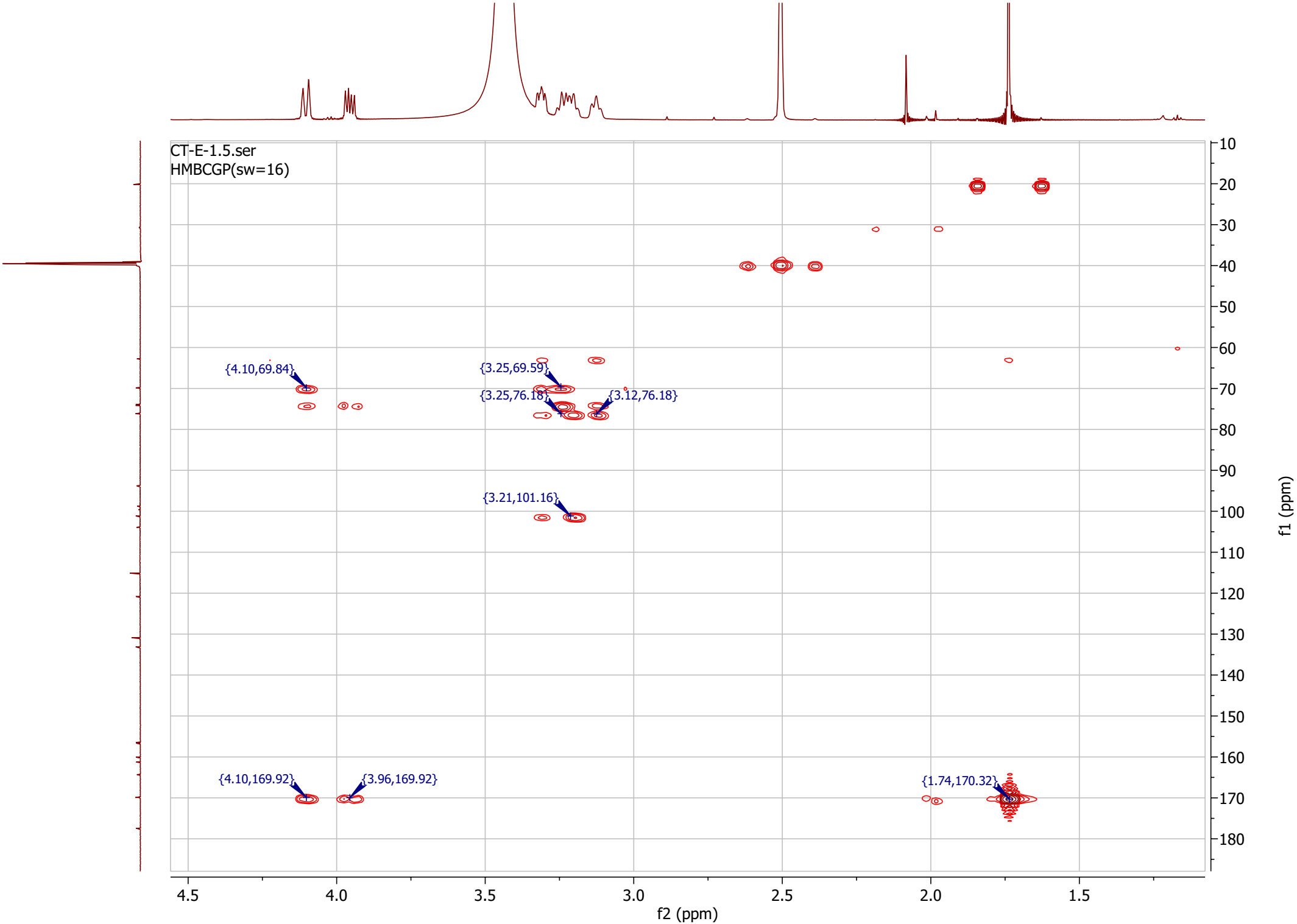
f1 (ppm)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4.5
4.0
3.5
3.0
2.5
2.0
1.5
f2 (ppm)
10
20
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60
70
80
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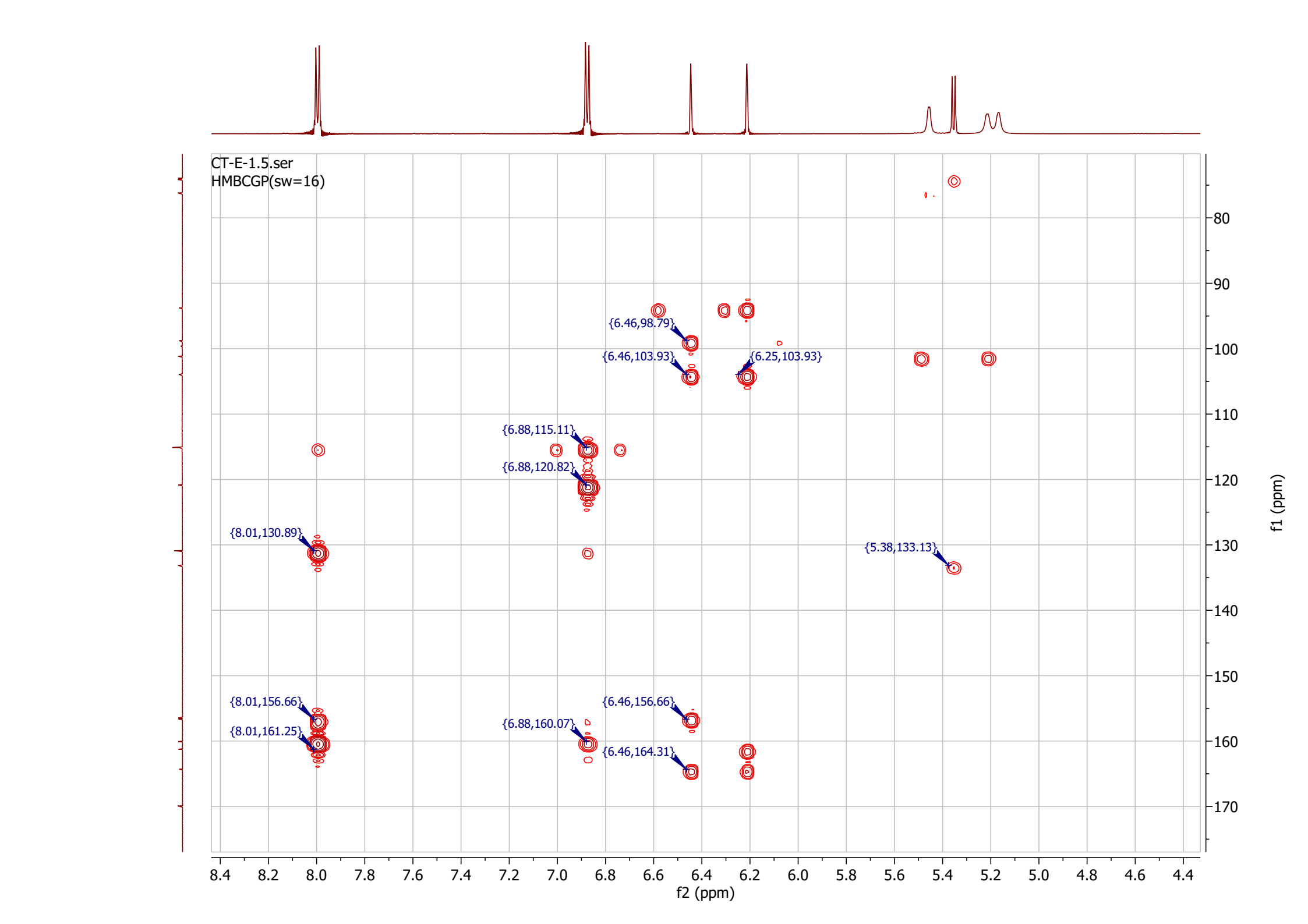
100
110
120
130
140
150
160
170
180
f1 (ppm)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{5.38,133.13}
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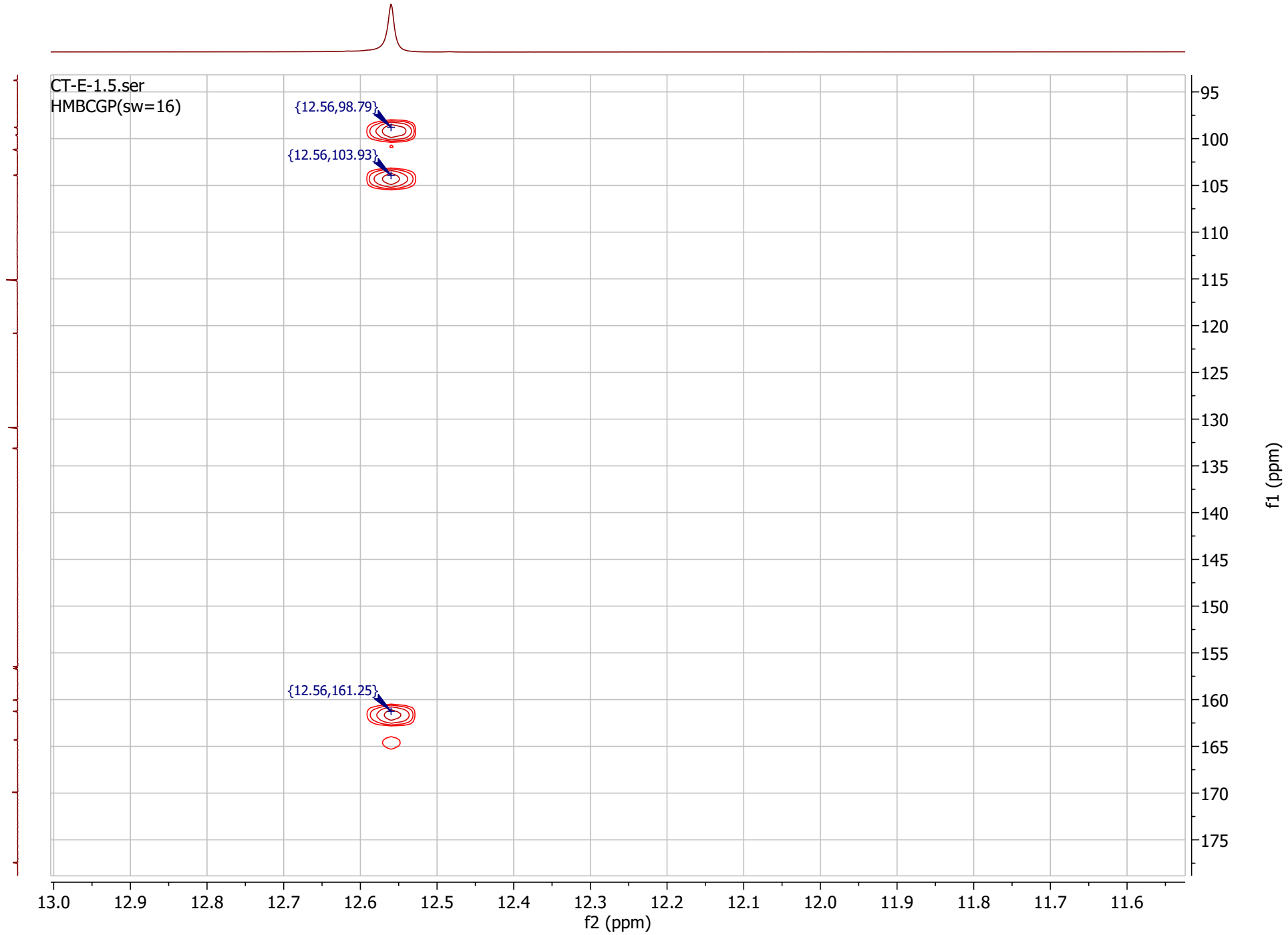
{6.46,164.31}
f2 (ppm)
f1 (ppm)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110
115
120
125
130
135
140
145
150
155
160
165
170
175
f1 (ppm)
13.0
12.9
12.8
12.7
12.6
12.5
12.4
12.3
12.2
12.1
12.0
11.9
11.8
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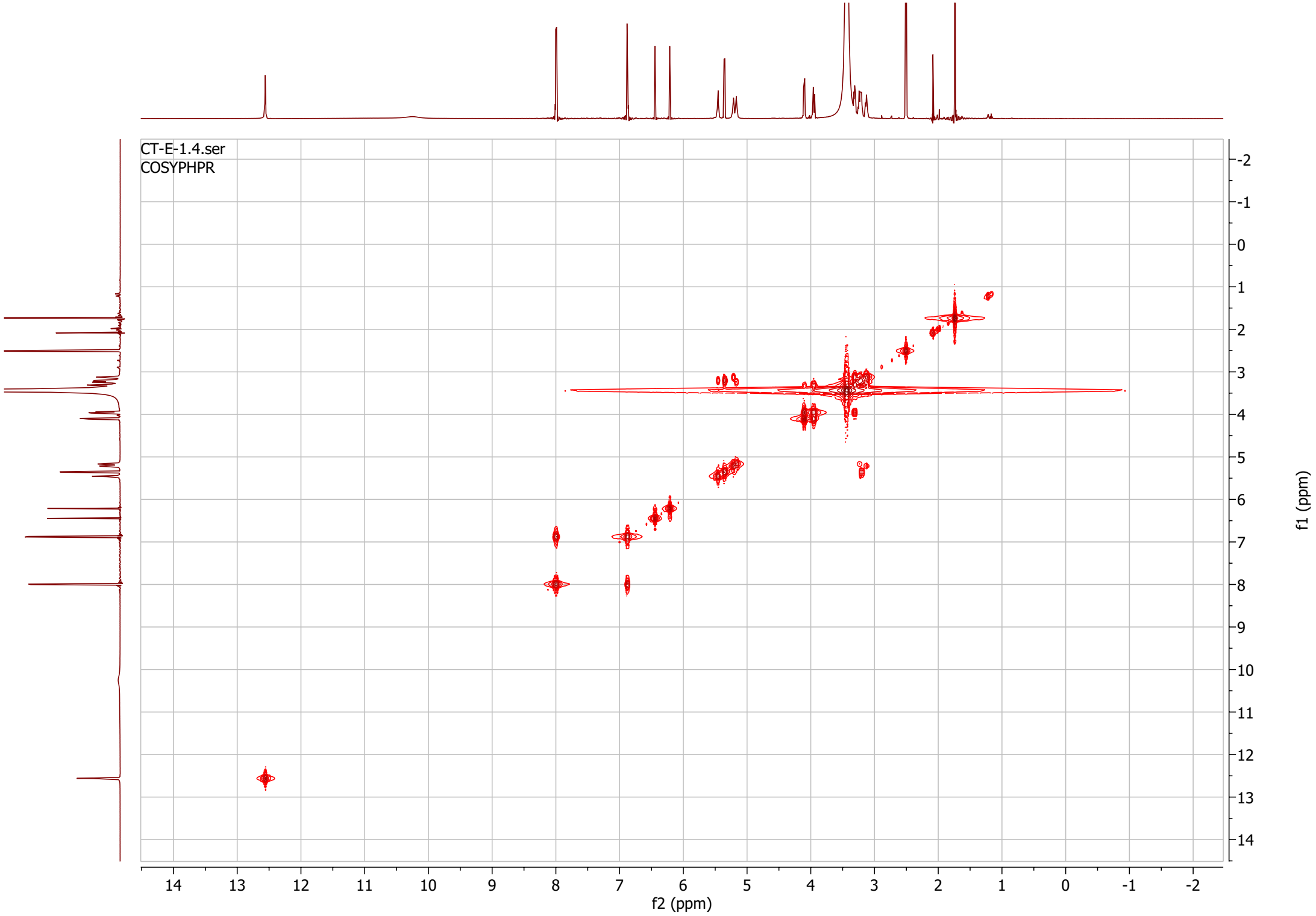
11.6
f2 (ppm)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COSYPHPR
f2 (ppm)
f1 (ppm)

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). 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. Isolation

To study the component composition of *Calligonum tetrapterum*, we used the aboveground part of the raw material (green shots) collected in the vicinity of Sarkand, Almaty region phase fruiting. The specimen is identified by Ishmuratova M.Yu., herbarium sample is located in herbarium fund of Zhezkazgan botanical garden (N2007.09.12.03.01).

Finely raw material *C. tetrapterum* (1 kg) was extracted three times with 70% ethanol by keeping in it at room temperature for 3 days. The extracts were combined, the solvent was evaporated on a rotary evaporator, and the resulting extract was extracted with petroleum ether and ether.

From 10 g of ether extract of 70% alcoholic extract of *C. tetrapterum* raw material by chromatographic separation on silica gel. Fractions of 350 ml were taken and a total of 62 fractions were obtained. By elution with a heptane-ethyl acetate (7:3) system, a compound was isolated, which, according to mass spectral data, so pl. and was identified by ^{1}H NMR as beta-sitosterol **3**.

Compound **2** was isolated by further separation on silica gel by elution with a solvent mixture of heptane-ethyl acetate (1:7). Its structure was determined by ^{1}H and ^{13}C NMR spectroscopy. Compound **2**was obtained in the form of yellow crystals with a melting point of 277-278 °C. Its molecular formula $C_{15}H_{10}O_6$was confirmed by mass spectroscopy, which indicated the peak ion [M+H] _c m/z 287.

According to the data obtained, compound **2** was identified as kaempferol, which was previously isolated from some species of the *Artemisia* family and other plant species. The structure of this compound was also unambiguously established on the basis of mass spectra, ^{1}H and ^{13}C NMR data, UV spectra and their comparison with literature data.

Further elution with a heptane-ethyl acetate (1:100) solvent system gave a white amorphous solid with m.p. 271-275 °C. In accordance with the spectral data, it was proposed the structure of the kaempferol glycoside. Spectral data **1** are presented in Table 1.

kaempferol 3-*O*-(6''-*O*-acetyl)-glucoside (1);

Yellow crystals with so pl. 271-275 °C; UV max (ACN-H_2O) 263, 295 (shoulder) and 350 nm; ^{1}H and ^{13}C NMR (DMSO-d_6) (see Table 1).

Kaempferol (2):

Isolated by elution with a heptane-ethyl acetate system (1:7); Yellow crystals, m.p. 277-278 ºC (lit. 272-275 ºC); Mass spectra: $[M+H]^-$ m/z 287. UV max (ACN-H_2O) 270, 294 (shoulder) and 360 nm;

β-Sitosterol (3):

Isolated by elution with a heptane-ethyl acetate system (7:3). White crystals, m.p. 140-145 ºC; Mass spectra: $[M+H]^+$ c m/z 415

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).

3. 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

4. Docking studies

Protein Preparation: The crystal structure of the employed protein, SARS-CoV-2 RNA-dependent RNA polymerase (PDB ID: 7BV2), was obtained from Protein Data Bank (https://www.rcsb.org). At first, the crystal structure of the SARS-CoV-2 RNA-dependent RNA polymerase (PDB ID: 7BV2) complexed with the remdesivir ligand was prepared by removing crystallographic water molecules. Only one chain was retained besides the co-crystallized ligand (remdesivir). The selected protein chain was protonated using the following setting. The used electrostatic functional form was GB/VI with a distance cut-off of 15 Å. The used value of the dielectric constant was 2 with an 80 dielectric constant of the used solvent. The used Van der Waals functional form was 800R3 with a distance cut-off of 10 Å. Then, the energy of the protein chain was minimized using Hamiltonian AM1 implanted in Molecular Operating Environment (MOE 2019 and MMFF94x (Merck molecular force field) for structural optimization. Next, the

active site of the target protein was defined for ligand docking and redocking (in case of validation of docking protocol). The active site of the protein was identified as the residues that fall within the 5 Å distance from the perimeter of the co-crystallized ligand.

Ligand Preparation: 2D structures of kaempferol 3-*O*-(6"-*O*-acetyl)-glucoside and the standard ligand (remdesivir) were drawn using ChemBioDraw Ultra 14.0 and saved in MDL-SD file format. The 3D structures of the ligands were protonated, and the structures were optimized by energy minimization using MM2 force-field and 10000 iteration steps of 2 fs. The conformationally optimized ligands were used for docking studies.

Docking Setup and Validation of Docking Protocol: The protein-ligand docking studies were carried out using MOE version 2019. Validation of the docking protocol was carried out by redocking the co-crystallized reference ligand (remdesivir) against the isolated pocket of SARSCoV-2 RNA-dependent RNA polymerase (PDB ID: 7BV2). The docking protocol was validated by comparing the heavy atoms RMSD value of the re-docked ligand pose with the corresponding co-crystallized reference ligand structure.

The docking setup for the tested compounds was established according to the protocol followed in the validation step. For each docking run, 30 docked solutions were generated using ASE for scoring function and rigid receptor for refinement. The pose with ideal binding mode was selected for further investigations. The docking results were visualized using Discovery Studio (DS) 4.0. Analysis of the docking results was carried out by comparing the interactions and docking score obtained for the docked ligands with that of the re-docked reference molecul).

5. 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.

6. 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.

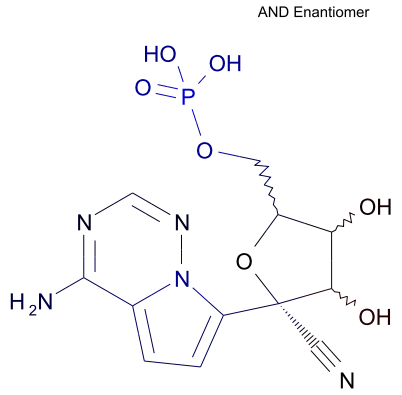
7. Molecular dynamics simulations

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, and the periodic boundary conditions were set with a dimension of the dimensions 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 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. 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, 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. For consistency, we have applied the same protocol for all MD simulations.

Toxicity Report

Remdesivir

TOPKAT_Developmental_Toxicity_Potential



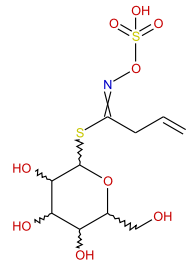
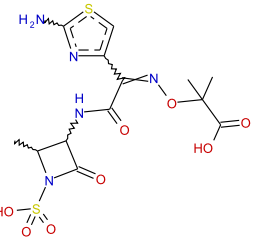
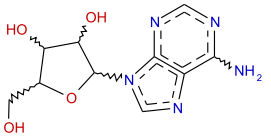
$C_{12}H_{14}N_5O_7P$
Molecular Weight: 371.24262
ALogP: -1.502
Rotatable Bonds: 4
Acceptors: 11
Donors: 5

Model Prediction

Prediction: Non-Toxic
Probability: 0.373
Enrichment: 0.709
Bayesian Score: -5.42
Mahalanobis Distance: 9.05
Mahalanobis Distance p-value: 0.163

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	Sinigrin (Free Acid Form)	Azthreonam	Vidarabine
Structure			
Actual Endpoint	Toxic	Non-Toxic	Non-Toxic
Predicted Endpoint	Toxic	Non-Toxic	Non-Toxic
Distance	0.632	0.707	0.714
Reference	Food Cosmet Toxicol 18(2):159-72; 1980	Chemotherapy 33:203-218; 1985	Teratology 15(3):231-41; 1977

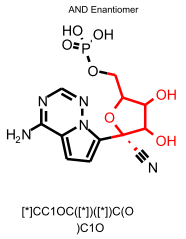
Model Applicability

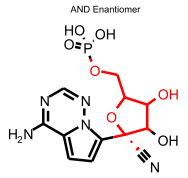
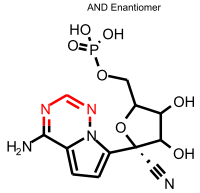
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

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

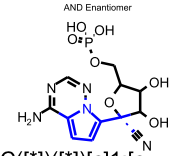
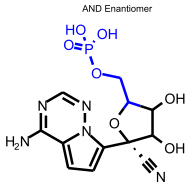
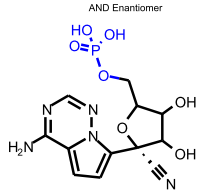
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Toxic in training set
SCFP_6	-1486266146	 [*]CC1OC([*])([*])C(O)C1O	0.431	7 out of 8

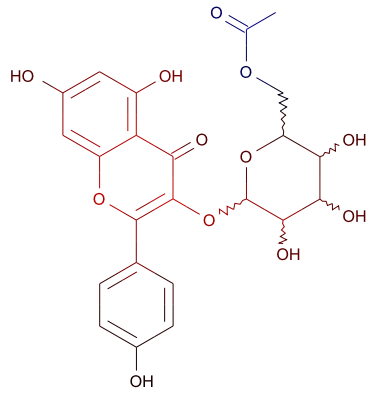
SCFP_6	-1715619483	 [*]OCC1OC([*])([*])C([*])C1O	0.298	6 out of 8
SCFP_6	-1181430618	 [*]:n:[cH]:n:[*]	0.298	6 out of 8

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Toxic in training set
SCFP_6	-1375522316	 [*]C([*])([*])[c]1:[cH]:[cH]:[c](:[*]):n:1:[*]	-0.945	0 out of 3
SCFP_6	2108966103	 [*]C([*])COP(=O)(O)O	-0.945	0 out of 3
SCFP_6	269938867	 [*]OP(=O)(O)O	-0.729	1 out of 6

Flavonoid

TOPKAT_Developmental_Toxicity_Potential



$C_{23}H_{22}O_{12}$

Molecular Weight: 490.41357

ALogP: 0.322

Rotatable Bonds: 6

Acceptors: 12

Donors: 6

Model Prediction

Prediction: Toxic

Probability: 0.808

Enrichment: 1.54

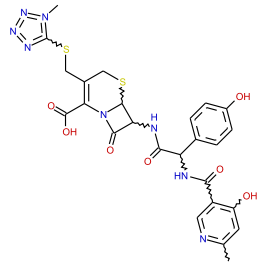
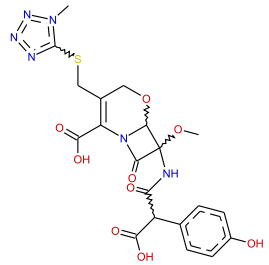
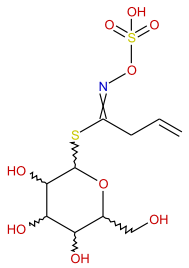
Bayesian Score: 6.94

Mahalanobis Distance: 11.4

Mahalanobis Distance p-value: 0.000317

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	Cefpiramide Sodium (Free acid form)	Latomoxef	Sinigrin (Free Acid Form)
Structure			
Actual Endpoint	Non-Toxic	Toxic	Toxic
Predicted Endpoint	Non-Toxic	Non-Toxic	Toxic
Distance	0.733	0.783	0.804
Reference	Kiso to Rinsho 17:1000-1004; 1983	Chemotherapy 28:1119-1141; 1980	Food Cosmet Toxicol 18(2):159-72; 1980

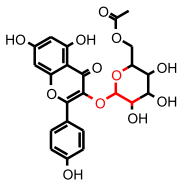
Model Applicability

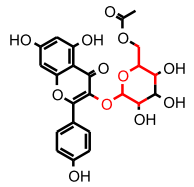
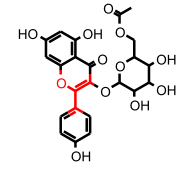
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. OPS PC19 out of range. Value: -2.9432. Training min, max, SD, explained variance: -2.7817, 3.2747, 1.037, 0.0157.

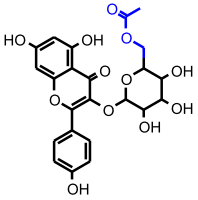
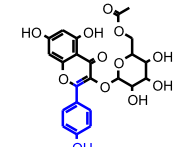
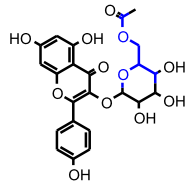
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Toxic in training set
SCFP_6	-2031220028	 [*]OC(O[*])C([*])[*]	0.538	7 out of 7

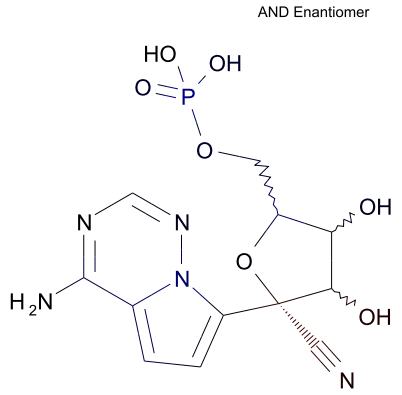
SCFP_6	-37268149	 [*]CC1OC(O[*])C([*])[*]C1[*]	0.523	6 out of 6
SCFP_6	616636418	 [*]OC(=C([*])[*])[c](:[*]):[*]	0.478	4 out of 4

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Toxic in training set
SCFP_6	733985735	 [*]COC(=O)C	-0.945	0 out of 3
SCFP_6	1112262477	 [*]C(=[*])[c]1[cH]:[cH]:[cH]:[c](O):[cH]:[cH]:1	-0.422	0 out of 1
SCFP_6	-183093204	 [*]OC(COC(=[*])[*])C([*])[*]	-0.422	0 out of 1

Remdesivir

TOPKAT_Mouse_Female_FDA_None_vs_Carcinogen



$C_{12}H_{14}N_5O_7P$

Molecular Weight: 371.24262

ALogP: -1.502

Rotatable Bonds: 4

Acceptors: 11

Donors: 5

Model Prediction

Prediction: Non-Carcinogen

Probability: 0.206

Enrichment: 0.642

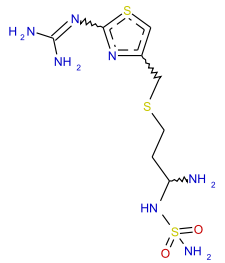
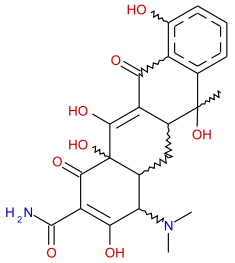
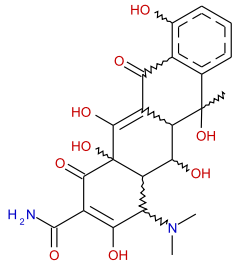
Bayesian Score: -7.17

Mahalanobis Distance: 12.9

Mahalanobis Distance p-value: 0.00074

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	Famotidine	Tetracycline	Oxytetracycline
Structure			
Actual Endpoint	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen
Predicted Endpoint	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen
Distance	0.846	0.848	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

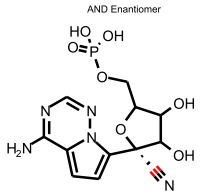
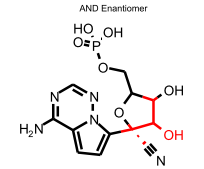
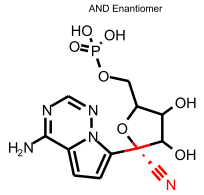
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown ECFP_2 feature: 1126642748: [*]OP(=O)(O)O
3. Unknown ECFP_2 feature: -1250439909: [*]COP(=[*])([*])[*]
4. Unknown ECFP_2 feature: 1258791451: [*]C1[*][*]O[C@]1(C#[*])[c](:[*]):[*]
5. Unknown ECFP_2 feature: -1507082173: [*][c]1:[*]:[*]:[c](:[*]):n:1:n:[*]
6. Unknown ECFP_2 feature: -66263742: [*]C([*])([*])[c]1:[cH]:[*]:[*]:n:1:[*]

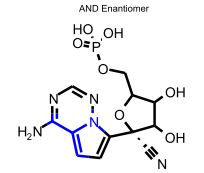
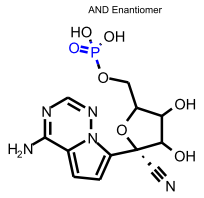
Feature Contribution

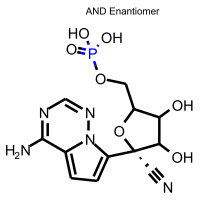
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set

ECFP_6	-1114776580	 [*]C#[*]	0.755	11 out of 15
ECFP_6	-521596699	 [*]C1[*][*]C([*])([*])C1O	0.451	3 out of 5
ECFP_6	-264833661	 [*]C([*])([*])C#N	0.424	1 out of 1

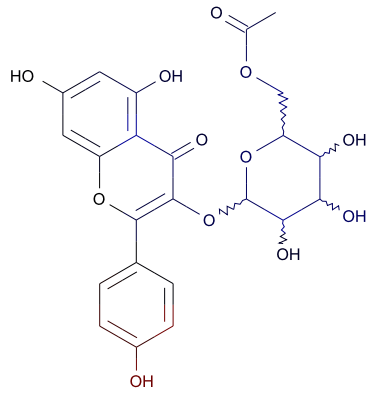
Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
ECFP_6	1334415134	 [*][c](:[*]):[c]1:[cH]:[*]:[*]:n:1:[*]	-0.935	0 out of 5
ECFP_6	2100964382	 [*]P(=O)([*])[*]	-0.935	0 out of 5

ECFP_6	-826638028	 [*]P(=[*])([*])[*]	-0.935	0 out of 5

Flavonoid

TOPKAT_Mouse_Female_FDA_None_vs_Carcinogen



$C_{23}H_{22}O_{12}$

Molecular Weight: 490.41357

ALogP: 0.322

Rotatable Bonds: 6

Acceptors: 12

Donors: 6

Model Prediction

Prediction: Non-Carcinogen

Probability: 0.211

Enrichment: 0.658

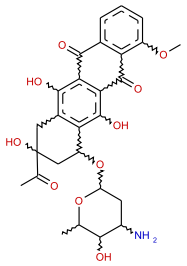
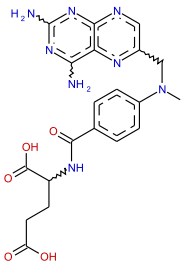
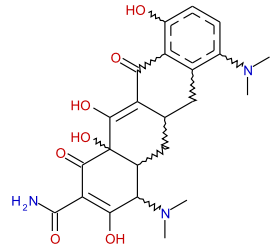
Bayesian Score: -8.44

Mahalanobis Distance: 15.1

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	Daunorubicin	Methotrexate	Minocycline
Structure			
Actual Endpoint	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen
Predicted Endpoint	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen
Distance	0.668	0.712	0.809
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

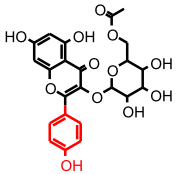
Model Applicability

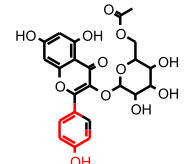
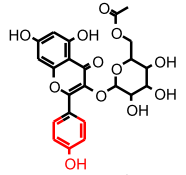
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown ECFP_2 feature: 1310940530: [*]C([*])OC(=[*])[*]
3. Unknown ECFP_2 feature: 1795218697: [*]OC(=C([*])[*])C(=[*])[*]
4. Unknown ECFP_2 feature: 1796421070: [*]OC(=C([*])[*])[c](:[*]):[*]

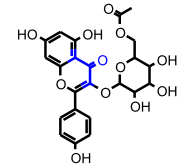
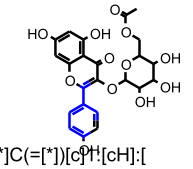
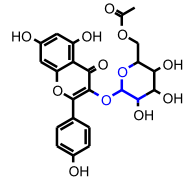
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
ECFP_6	1419645508	 [*][c]1:[cH]:[cH]:[c](O):[cH]:[cH]:1	0.675	4 out of 5

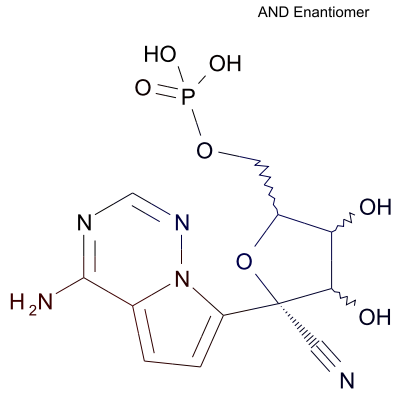
ECFP_6	-790637051	 [*][c]1:[*]:[cH]:[c](O):[cH]:[cH]:1	0.615	6 out of 9
ECFP_6	1740779540	 O[c]1:[cH]:[cH]:[*]:[cH]:[cH]:1	0.56	4 out of 6

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
ECFP_6	1717462980	 [*]C(=[*])C(=O)[c](:[*]):[*]	-1.25	0 out of 8
ECFP_6	-219423964	 [*]C(=[*])[c]1:[cH]:[*]:[c]([*]):[cH]:[cH]:1	-0.935	0 out of 5
ECFP_6	-2060414325	 [*]OC(O[*])C([*])[*]	-0.657	0 out of 3

Remdesivir

TOPKAT_Mouse_Male_FDA_None_vs_Carcinogen



$C_{12}H_{14}N_5O_7P$

Molecular Weight: 371.24262

ALogP: -1.502

Rotatable Bonds: 4

Acceptors: 11

Donors: 5

Model Prediction

Prediction: Non-Carcinogen

Probability: 0.239

Enrichment: 0.812

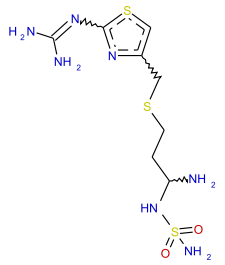
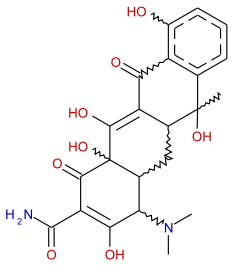
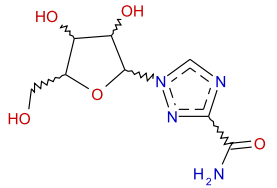
Bayesian Score: -2.82

Mahalanobis Distance: 19.2

Mahalanobis Distance p-value: 7.81e-017

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	Famotidine	Tetracycline	Ribavirin
Structure			
Actual Endpoint	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen
Predicted Endpoint	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen
Distance	0.813	0.843	0.860
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

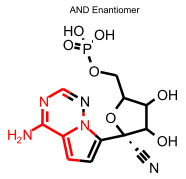
Model Applicability

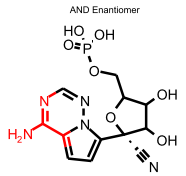
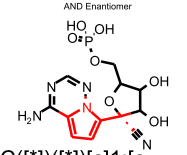
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown FCFP_2 feature: 472180098: [*]OP(=O)(O)O
3. Unknown FCFP_2 feature: -332197802: [*][c]1:[*]:[*]:[c](:[*]):n:1:n:[*]

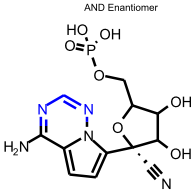
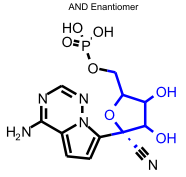
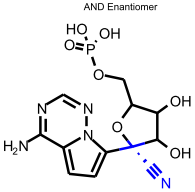
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
FCFP_6	-450797925	 N[c]1:n:[cH]:[*]:n2:[*]:[*]:[cH]:[c]:1:2	0.676	2 out of 2

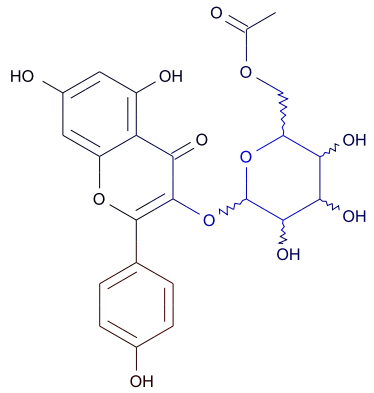
FCFP_6	-1151884458	 [*]:n:[c](N):[c](:[*]):[*]	0.348	6 out of 15
FCFP_6	-1280036918	 [*]C([*])([*])[c]1:[cH]:[cH]:[c](:[*]):n:1:[*]	0.333	7 out of 18

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
FCFP_6	-124685461	 [*]:n:[cH]:n:[*]	-0.731	1 out of 12
FCFP_6	422052003	 [*]CC1OC([*])([*])C(O)C1O	-0.582	0 out of 3
FCFP_6	-1277879912	 [*]C([*])([*])C#N	-0.582	0 out of 3

Flavonoid

TOPKAT_Mouse_Male_FDA_None_vs_Carcinogen



$C_{23}H_{22}O_{12}$

Molecular Weight: 490.41357

ALogP: 0.322

Rotatable Bonds: 6

Acceptors: 12

Donors: 6

Model Prediction

Prediction: Non-Carcinogen

Probability: 0.154

Enrichment: 0.524

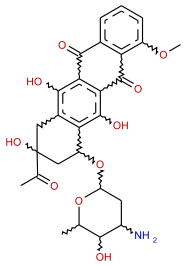
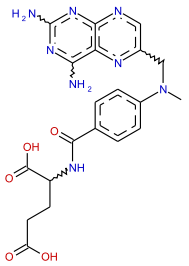
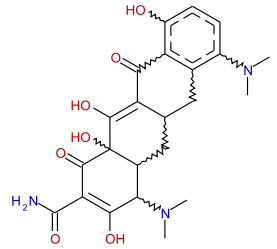
Bayesian Score: -8.56

Mahalanobis Distance: 14

Mahalanobis Distance p-value: 6.73e-006

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	Daunorubicin	Methotrexate	Minocycline
Structure			
Actual Endpoint	Non-Carcinogen	Carcinogen	Non-Carcinogen
Predicted Endpoint	Non-Carcinogen	Carcinogen	Non-Carcinogen
Distance	0.638	0.700	0.797
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

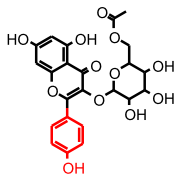
Model Applicability

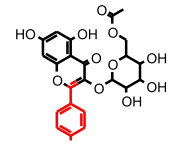
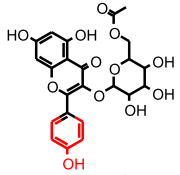
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

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

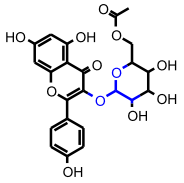
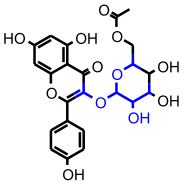
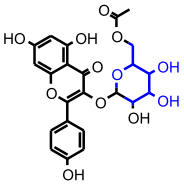
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
FCFP_6	-1066794953	 [*][c]1:[cH]:[cH]:[c](O):[cH]:[cH]:1	0.668	3 out of 4

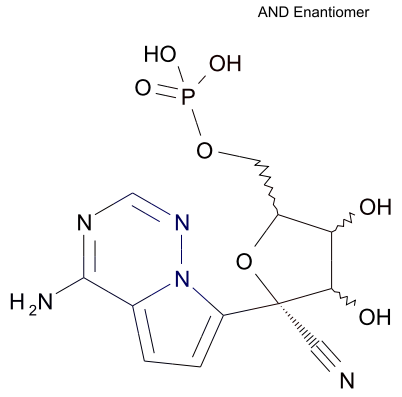
FCFP_6	-1847351220	 [*]C(=[*])[c]1:[cH]:[cH]:[c](O):[cH]:[cH]:1	0.547	3 out of 5
FCFP_6	-158888774	 O[c]1:[cH]:[cH]:[*]:[cH]:[cH]:1	0.367	5 out of 12

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
FCFP_6	699500266	 [*]OC(O[*])C([*])[*]	-0.85	1 out of 14
FCFP_6	-333501072	 [*]C1[*]C([*])C(O)C(OC(=[*])[*])O1	-0.582	0 out of 3
FCFP_6	422052003	 [*]CC1OC([*])([*])C(O)C1O	-0.582	0 out of 3

Remdesivir

TOPKAT_Ocular_Irritancy_Mild_vs_Moderate_Severe



$C_{12}H_{14}N_5O_7P$

Molecular Weight: 371.24262

ALogP: -1.502

Rotatable Bonds: 4

Acceptors: 11

Donors: 5

Model Prediction

Prediction: Mild

Probability: 0.789

Enrichment: 1.15

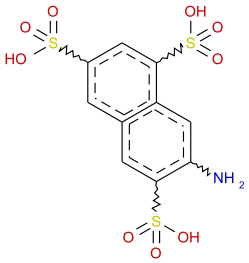
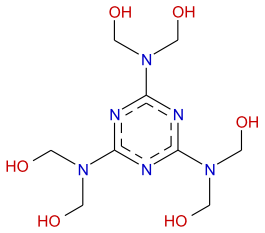
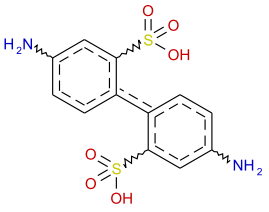
Bayesian Score: -1.39

Mahalanobis Distance: 13.8

Mahalanobis Distance p-value: 1.42e-009

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	1;3;6-NAPHTHALENE TRISULFONIC ACID;7-AMINO-	Methanol; (s-triazine-2;4;6-triyltrinitrilo)hexa-	2;2'-Biphenyldisulfonic acid; 4;4'-diamino-
Structure			
Actual Endpoint	Mild	Moderate_Severe	Mild
Predicted Endpoint	Mild	Moderate_Severe	Mild
Distance	0.776	0.802	0.878
Reference	28ZPAK-;190;72	Prehled Prumyslove Toxikologie; Organicke Latky; Marhold; J. -;876;86	Prehled Prumyslove Toxikologie; Organicke Latky; Marhold; J. pp 1061;86

Model Applicability

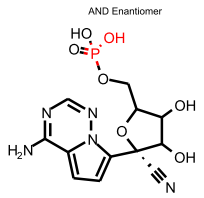
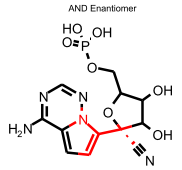
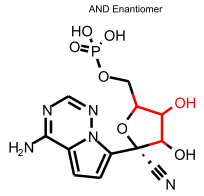
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. OPS PC17 out of range. Value: 4.6782. Training min, max, SD, explained variance: -4.348, 3.9505, 1.094, 0.0146.
2. Unknown FCFP_2 feature: 472180098: [*]OP(=O)(O)O
3. Unknown FCFP_2 feature: -836603894: [*]C1[*][*]O[C@]1(C#[*])[c](:[*]):[*]
4. Unknown FCFP_2 feature: -124685461: [*]:n:[cH]:n:[*]
5. Unknown FCFP_2 feature: -1151884458: [*]:n:[c](N):[c](:[*]):[*]

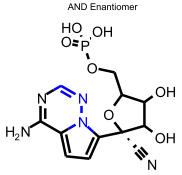
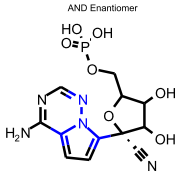
Feature Contribution

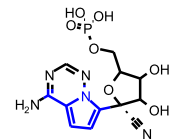
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Moderate_Severe in training set

FCFP_10	1070061035	 [*]P(=[*])([*])O	0.239	284 out of 338
FCFP_10	-1539132615	 [*]C([*])([*])[c]1:[c H]:[*]:[*]:n:1:[*]	0.224	11 out of 13
FCFP_10	-1043250487	 [*]C1[*][*]C([*])C1O	0.22	62 out of 75

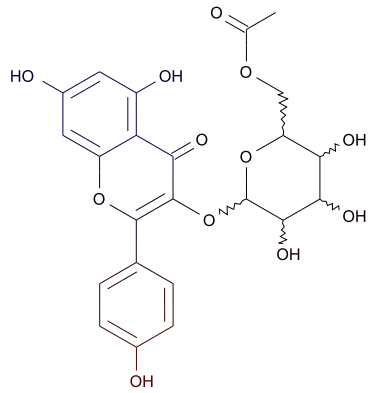
Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Moderate_Severe in training set
FCFP_10	4427049	 [*]:[cH]:n:n(:[*]):[*]	-1.29	0 out of 4
FCFP_10	-332197802	 [*][c]1:[*]:[*]:[c](: [*]):n:1:n:[*]	-0.507	0 out of 1

FCFP_10	713358128	AND Enantiomer  [*][c](:[*]):[c]1:[cH]:[cH]:[c]([*]):n:1:[*]	-0.307	8 out of 17

Flavonoid

TOPKAT_Ocular_Irritancy_Mild_vs_Moderate_Severe



$C_{23}H_{22}O_{12}$

Molecular Weight: 490.41357

ALogP: 0.322

Rotatable Bonds: 6

Acceptors: 12

Donors: 6

Model Prediction

Prediction: Moderate_Severe

Probability: 0.817

Enrichment: 1.19

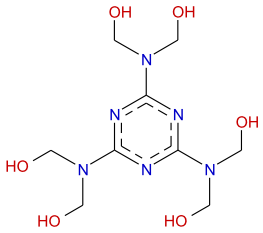
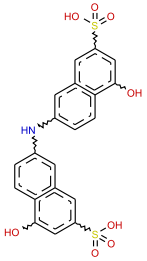
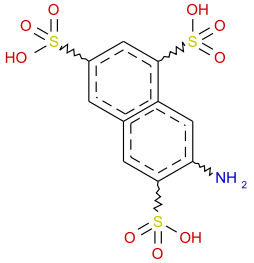
Bayesian Score: -0.257

Mahalanobis Distance: 14

Mahalanobis Distance p-value: 4.67e-010

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	Methanol; (s-triazine-2;4;6-triyltrinitrilo)hexa-	2-Naphthalenesulfonic acid; 5;6'-iminobis(1-hydroxy-	1;3;6-NAPHTHALENE TRISULFONIC ACID;7-AMINO-
Structure			
Actual Endpoint	Moderate_Severe	Mild	Mild
Predicted Endpoint	Moderate_Severe	Mild	Mild
Distance	0.862	0.944	1.115
Reference	Prehled Prumyslove Toxikologie; Organicke Latky; Marhold; J. -;876;86	Prehled Prumyslove Toxikologie; Organicke Latky; Marhold; J. pp 1065;86	28ZPAK-;190;72

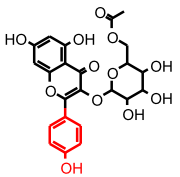
Model Applicability

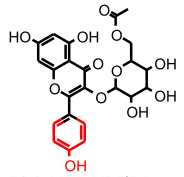
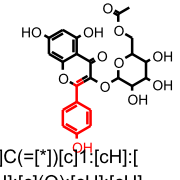
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

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

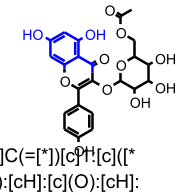
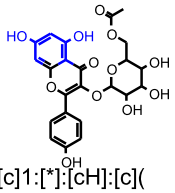
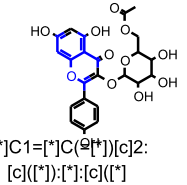
Feature Contribution

Top features for positive contribution

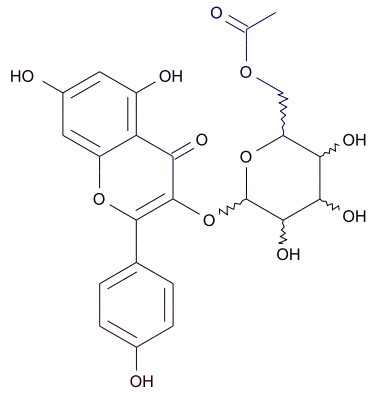
Fingerprint	Bit/Smiles	Feature Structure	Score	Moderate_Severe in training set
FCFP_10	-1066794953	 [*][c]1:[cH]:[cH]:[c](O):[cH]:[cH]:1	0.378	13 out of 13

FCFP_10	-158888774	 O[c]1:[cH]:[cH]:[*]:[cH]:[cH]:1	0.356	24 out of 25
FCFP_10	-1847351220	 [*]C(=[*])[c]1:[cH]:[cH]:[c](O):[cH]:[cH]:1	0.273	9 out of 10

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Moderate_Severe in training set
FCFP_10	115228054	 [*]C(=[*])[c]1:[c]([*]):[cH]:[c](O):[cH]:[c]:1O	-0.507	0 out of 1
FCFP_10	946068634	 [*][c]1:[*]:[cH]:[c](O):[cH]:[c]:1O	-0.4	1 out of 3
FCFP_10	-1099193755	 [*]C1=[*]C(=[*])[c]2:[c]([*]):[*]:[c]([*]):[cH]:[c]:2O1	-0.361	2 out of 5

Flavonoid



$C_{23}H_{22}O_{12}$

Molecular Weight: 490.41357

ALogP: 0.322

Rotatable Bonds: 6

Acceptors: 12

Donors: 6

Model Prediction

Prediction: Moderate

Probability: 0.562

Enrichment: 0.907

Bayesian Score: -3

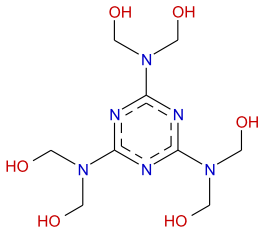
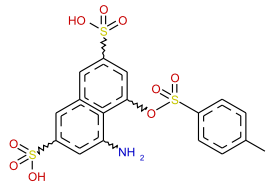
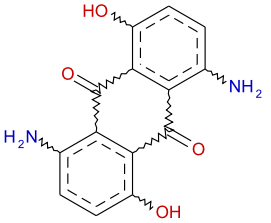
Mahalanobis Distance: 15

Mahalanobis Distance p-value: 4.87e-014

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_Moderate_vs_Severe

Structural Similar Compounds

Name	Methanol; (s-triazine-2;4;6-triyltrinitrilo)hexa-	2;7-NAPHTHALENE DISULFONIC ACID;4-AMINO-5-HYDROXY-;P-TOLUENE SULFONATE (ESTER)	ANTHRAQUINONE;1;5-DIAMINO-4;8-DIHYDROXY-
Structure			
Actual Endpoint	Moderate	Moderate	Moderate
Predicted Endpoint	Moderate	Moderate	Moderate
Distance	0.870	1.251	1.294
Reference	Prehled Prumyslove Toxikologie; Organicke Latky; Marhold; J. -;876;86	28ZPAK-;194;72	28ZPAK-;103;72

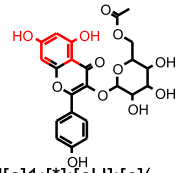
Model Applicability

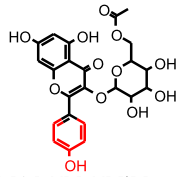
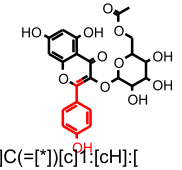
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

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

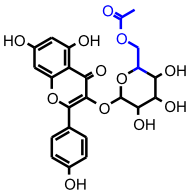
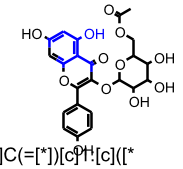
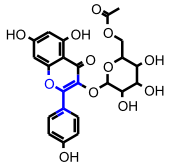
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Severe in training set
SCFP_12	130348166	 [*][c]1:[*]:[cH]:[c](O):[cH]:[c]:1O	0.376	4 out of 4

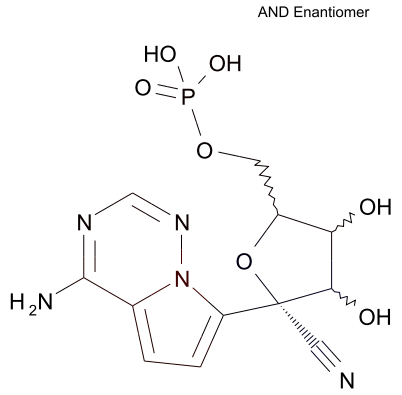
SCFP_12	611156666	 O[c]1:[cH]:[cH]:[*]:[cH]:[cH]:1	0.298	20 out of 24
SCFP_12	1112262477	 [*]C(=[*])[c]1:[cH]:[cH]:[c](O):[cH]:[cH]:1	0.218	1 out of 1

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Severe in training set
SCFP_12	-1031053674	 [*]C([*])COC(=O)C	-0.874	5 out of 22
SCFP_12	860600739	 [*]C(=[*])[c]1:[c]([*]):[*]:[c]([*]):[cH]:[c]:1O	-0.703	1 out of 5
SCFP_12	616636418	 [*]OC(=C([*])[*])[c](:[*]):[*]	-0.475	0 out of 1

Remdesivir

TOPKAT_Ocular_Irritancy_None_vs_Irritant



$C_{12}H_{14}N_5O_7P$

Molecular Weight: 371.24262

ALogP: -1.502

Rotatable Bonds: 4

Acceptors: 11

Donors: 5

Model Prediction

Prediction: Irritant

Probability: 1

Enrichment: 1.18

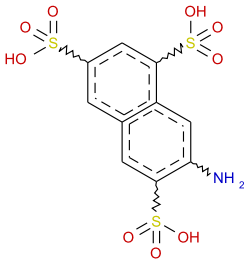
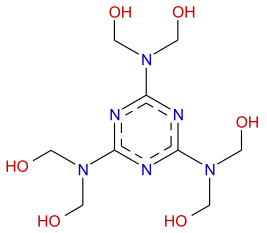
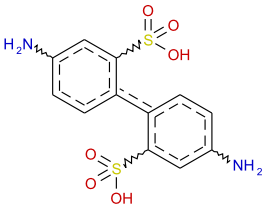
Bayesian Score: 1.33

Mahalanobis Distance: 10.7

Mahalanobis Distance p-value: 0.0147

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	1;3;6-NAPHTHALENE TRISULFONIC ACID;7-AMINO-	Methanol; (s-triazine-2;4;6-triyltrinitrilo)hexa-	2;2'-Biphenyldisulfonic acid; 4;4'-diamino-
Structure			
Actual Endpoint	Irritant	Irritant	Irritant
Predicted Endpoint	Irritant	Irritant	Irritant
Distance	0.766	0.795	0.859
Reference	28ZPAK-;190;72	Prehled Prumyslove Toxikologie; Organicke Latky; Marhold; J. -;876;86	Prehled Prumyslove Toxikologie; Organicke Latky; Marhold; J. pp 1061;86

Model Applicability

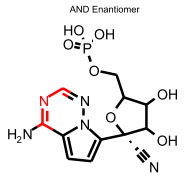
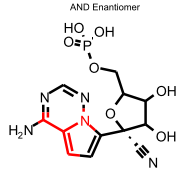
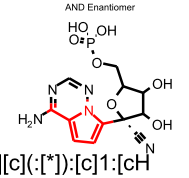
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown FCFP_2 feature: 472180098: [*]OP(=O)(O)O
3. Unknown FCFP_2 feature: -124685461: [*]:n:[cH]:n:[*]
4. Unknown FCFP_2 feature: -1151884458: [*]:n:[c](N):[c](:[*]):[*]

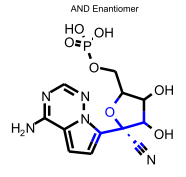
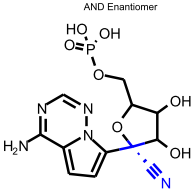
Feature Contribution

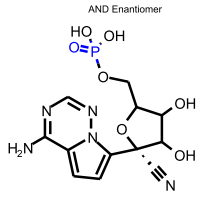
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Irritant in training set

FCFP_12	1747237384	 [*][c](:[*]):n:[cH]:[*]	0.208	44 out of 44
FCFP_12	178336375	 [*][c](:[*]):[c]1:[cH]:[*]:[*]:n:1:[*]	0.202	19 out of 19
FCFP_12	713358128	 [*][c](:[*]):[c]1:[cH]:[cH]:[c]([*]):n:1:[*]	0.2	17 out of 17

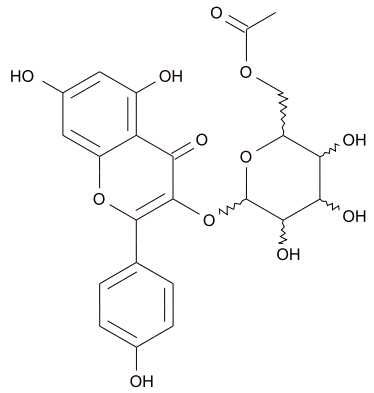
Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Irritant in training set
FCFP_12	-836603894	 [*]C1[*][*]O[C@]1(C#[*])[c](:[*]):[*]	-0.592	0 out of 1
FCFP_12	-1277879912	 [*]C([*])([*])C#N	-0.0939	33 out of 45

FCFP_12	1872154524	 [*]P(=O)([*])[*]	0	563 out of 690

Flavonoid

TOPKAT_Ocular_Irritancy_None_vs_Irritant



$C_{23}H_{22}O_{12}$

Molecular Weight: 490.41357

ALogP: 0.322

Rotatable Bonds: 6

Acceptors: 12

Donors: 6

Model Prediction

Prediction: Irritant

Probability: 1

Enrichment: 1.18

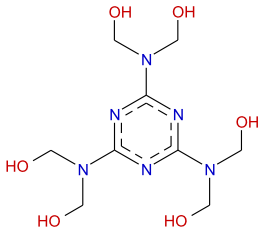
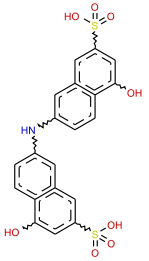
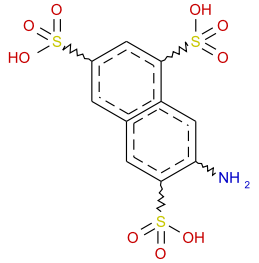
Bayesian Score: 1.54

Mahalanobis Distance: 13.6

Mahalanobis Distance p-value: 3.14e-009

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	Methanol; (s-triazine-2;4;6-triyltrinitrilo)hexa-	2-Naphthalenesulfonic acid; 5;6'-iminobis(1-hydroxy-	1;3;6-NAPHTHALENE TRISULFONIC ACID;7-AMINO-
Structure			
Actual Endpoint	Irritant	Irritant	Irritant
Predicted Endpoint	Irritant	Irritant	Irritant
Distance	0.839	0.915	1.113
Reference	Prehled Prumyslove Toxikologie; Organicke Latky; Marhold; J. -;876;86	Prehled Prumyslove Toxikologie; Organicke Latky; Marhold; J. pp 1065;86	28ZPAK-;190;72

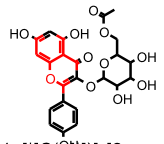
Model Applicability

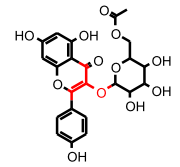
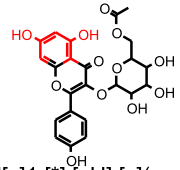
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

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

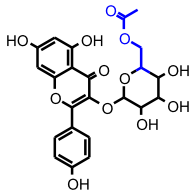
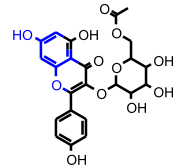
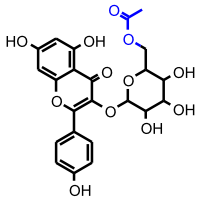
Feature Contribution

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

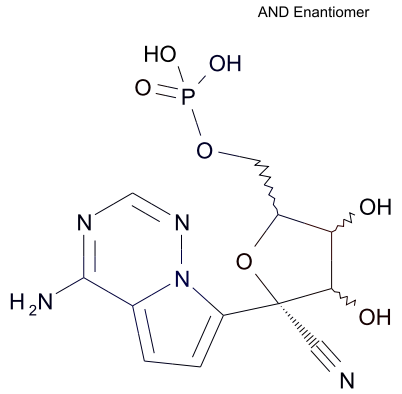
FCFP_12	436915834	 [*]OC(=C([*])[*])C(=[*])[*]	0.167	4 out of 4
FCFP_12	946068634	 [*][c]1:[*]:[cH]:[c](O):[cH]:[c]:1O	0.156	3 out of 3

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Irritant in training set
FCFP_12	-432846198	 [*]C([*])COC(=O)C	-0.229	91 out of 142
FCFP_12	1673930087	 [*]O[c]1:[cH]:[c](O): [cH]:[*]:[c]:1[*]	-0.218	5 out of 8
FCFP_12	565998553	 [*]OC(=O)C	-0.0662	198 out of 262

Remdesivir

TOPKAT_Rat_Female_FDA_None_vs_Carcinogen



$C_{12}H_{14}N_5O_7P$

Molecular Weight: 371.24262

ALogP: -1.502

Rotatable Bonds: 4

Acceptors: 11

Donors: 5

Model Prediction

Prediction: Non-Carcinogen

Probability: 0.243

Enrichment: 0.756

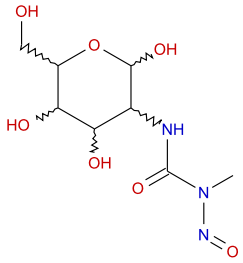
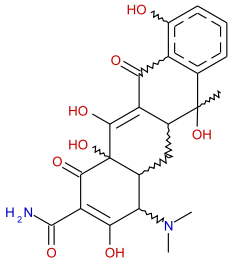
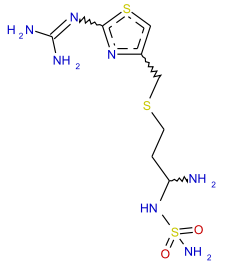
Bayesian Score: -3.24

Mahalanobis Distance: 13.8

Mahalanobis Distance p-value: 5.04e-006

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	Streptozocin	Tetracycline	Famotidine
Structure			
Actual Endpoint	Carcinogen	Non-Carcinogen	Non-Carcinogen
Predicted Endpoint	Carcinogen	Non-Carcinogen	Non-Carcinogen
Distance	0.810	0.858	0.861
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

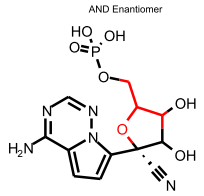
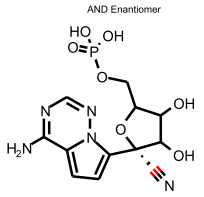
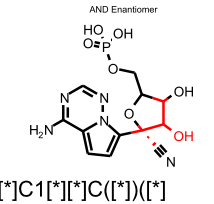
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown ECFP_2 feature: 1126642748: [*]OP(=O)(O)O
3. Unknown ECFP_2 feature: -1250439909: [*]COP(=[*])([*])[*]
4. Unknown ECFP_2 feature: 1258791451: [*]C1[*][*]O[C@]1(C#[*])[c](:[*]):[*]
5. Unknown ECFP_2 feature: -1507082173: [*][c]1:[*]:[*]:[c](:[*]):n:1:n:[*]
6. Unknown ECFP_2 feature: -66263742: [*]C([*])([*])[c]1:[cH]:[*]:[*]:n:1:[*]

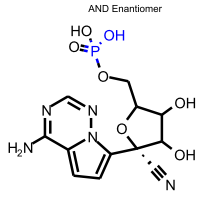
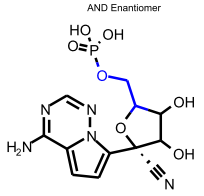
Feature Contribution

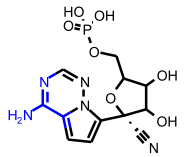
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set

ECFP_12	-553149446	 [*]CC1O[*][*]C1[*]	0.575	3 out of 4
ECFP_12	-1114776580	 [*]C#[*]	0.461	10 out of 19
ECFP_12	-521596699	 [*]C1[*][*]C([*])([*])C1O	0.445	3 out of 5

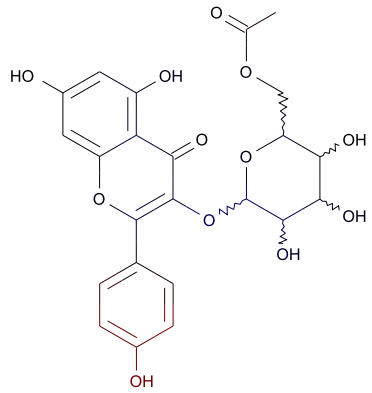
Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
ECFP_12	2024329577	 [*]P(=[*])([*])O	-0.661	0 out of 3
ECFP_12	-1687549011	 [*]OCC([*])[*]	-0.661	0 out of 3

ECFP_12	-1734834311	AND Enantiomer  [*]:n:[c](N):[c](:[*]):[*]	-0.56	1 out of 8

Flavonoid

TOPKAT_Rat_Female_FDA_None_vs_Carcinogen



$C_{23}H_{22}O_{12}$

Molecular Weight: 490.41357

ALogP: 0.322

Rotatable Bonds: 6

Acceptors: 12

Donors: 6

Model Prediction

Prediction: Non-Carcinogen

Probability: 0.247

Enrichment: 0.767

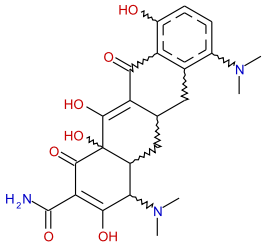
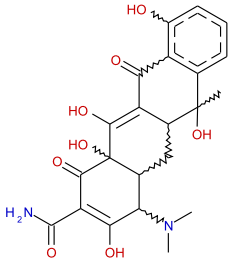
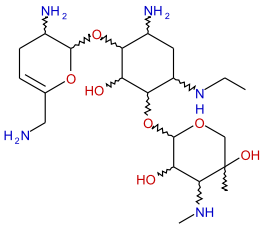
Bayesian Score: -2.98

Mahalanobis Distance: 12.4

Mahalanobis Distance p-value: 0.00147

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	Minocycline	Tetracycline	Netilmicin
Structure			
Actual Endpoint	Carcinogen	Non-Carcinogen	Non-Carcinogen
Predicted Endpoint	Carcinogen	Non-Carcinogen	Non-Carcinogen
Distance	0.838	0.855	0.981
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

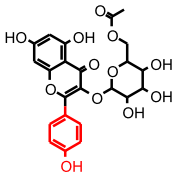
Model Applicability

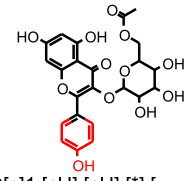
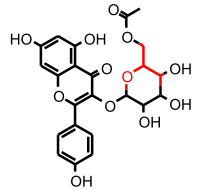
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown ECFP_2 feature: 1310940530: [*]C([*])OC(=[*])[*]
3. Unknown ECFP_2 feature: 1795218697: [*]OC(=C([*])[*])C(=[*])[*]

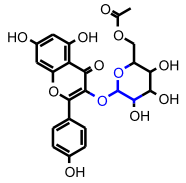
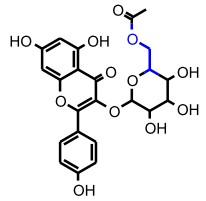
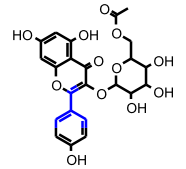
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
ECFP_12	1419645508	 [*][c]1:[cH]:[cH]:[c](O):[cH]:[cH]:1	0.736	5 out of 6

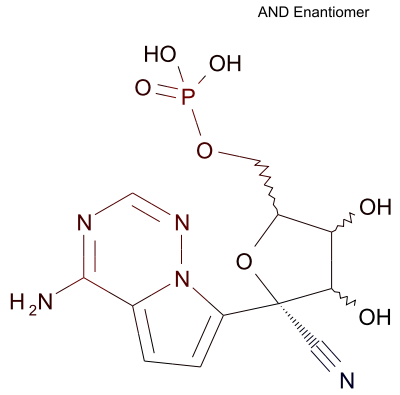
ECFP_12	1740779540	 O[c]1:[cH]:[cH]:[*]:[cH]:[cH]:1	0.633	5 out of 7
ECFP_12	-553149446	 [*]CC1O[*][*]C1[*]	0.575	3 out of 4

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
ECFP_12	-2060414325	 [*]OC(O[*])C([*])[*]	-0.811	0 out of 4
ECFP_12	-1687549011	 [*]OCC([*])[*]	-0.661	0 out of 3
ECFP_12	-181568884	 [*]C(=[*])[c](:[cH]:[*]):[cH]:[*]	-0.505	3 out of 18

Remdesivir

TOPKAT_Rat_Male_FDA_None_vs_Carcinogen



$C_{12}H_{14}N_5O_7P$

Molecular Weight: 371.24262

ALogP: -1.502

Rotatable Bonds: 4

Acceptors: 11

Donors: 5

Model Prediction

Prediction: Carcinogen

Probability: 0.481

Enrichment: 1.44

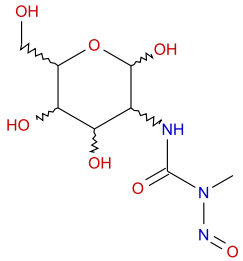
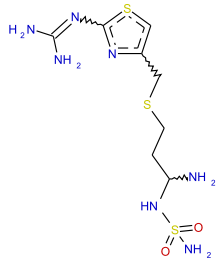
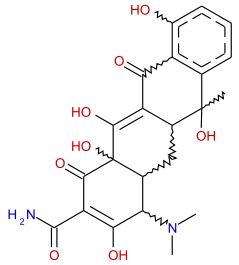
Bayesian Score: 3.82

Mahalanobis Distance: 14.1

Mahalanobis Distance p-value: 3.32e-005

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	Streptozocin	Famotidine	Tetracycline
Structure			
Actual Endpoint	Carcinogen	Non-Carcinogen	Non-Carcinogen
Predicted Endpoint	Carcinogen	Non-Carcinogen	Non-Carcinogen
Distance	0.789	0.850	0.856
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

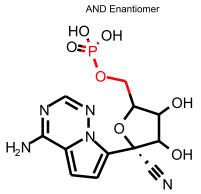
Model Applicability

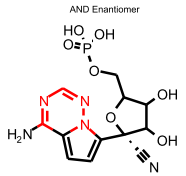
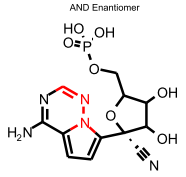
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

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

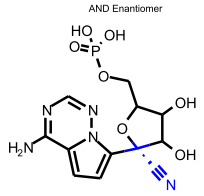
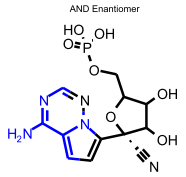
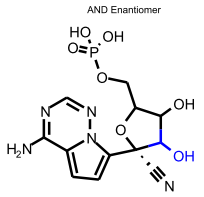
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
SCFP_6	-1029620989	 [*]COP(=[*])([*])[*]	0.712	3 out of 3

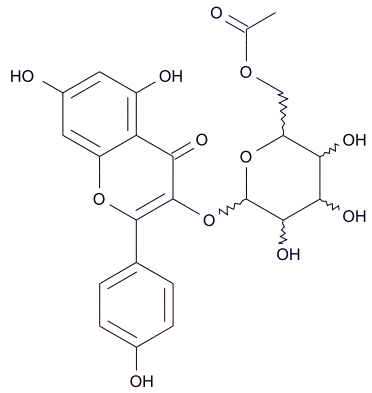
SCFP_6	1245795878	 [*][c]1:[*]:n(:[*]):n :[cH]:n:1	0.603	2 out of 2
SCFP_6	149212520	 [*]:[cH]:n:n(:[*]):[*]	0.543	9 out of 15

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
SCFP_6	-1019297400	 [*]C([*])([*])C#N	-0.674	0 out of 3
SCFP_6	194135988	 N[c]1:n:[cH]:[*]:n2:[*]:[*]:[cH]:[c]:1:2	-0.278	0 out of 1
SCFP_6	-424515134	 [*]C([*])O	-0.157	30 out of 110

Flavonoid

TOPKAT_Rat_Male_FDA_None_vs_Carcinogen



$C_{23}H_{22}O_{12}$

Molecular Weight: 490.41357

ALogP: 0.322

Rotatable Bonds: 6

Acceptors: 12

Donors: 6

Model Prediction

Prediction: Non-Carcinogen

Probability: 0.287

Enrichment: 0.858

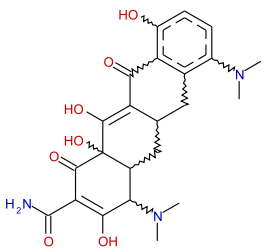
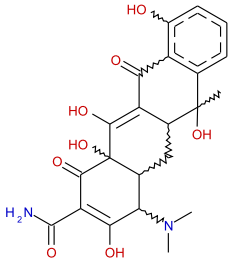
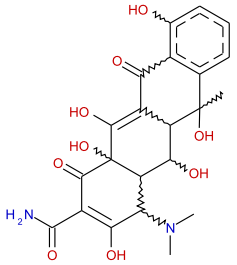
Bayesian Score: -2.69

Mahalanobis Distance: 11.6

Mahalanobis Distance p-value: 0.0665

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	Minocycline	Tetracycline	Oxytetracycline
Structure			
Actual Endpoint	Carcinogen	Non-Carcinogen	Non-Carcinogen
Predicted Endpoint	Carcinogen	Non-Carcinogen	Non-Carcinogen
Distance	0.809	0.826	0.832
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

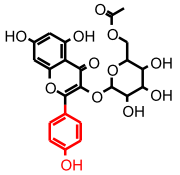
Model Applicability

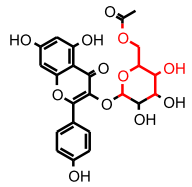
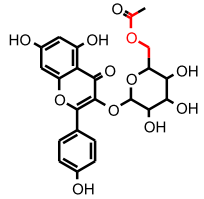
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

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

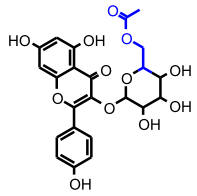
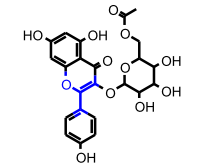
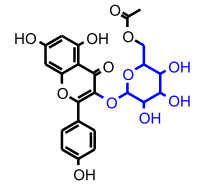
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
SCFP_6	1958008606	 [*][c]1:[cH]:[cH]:[c](O):[cH]:[cH]:1	0.536	4 out of 6

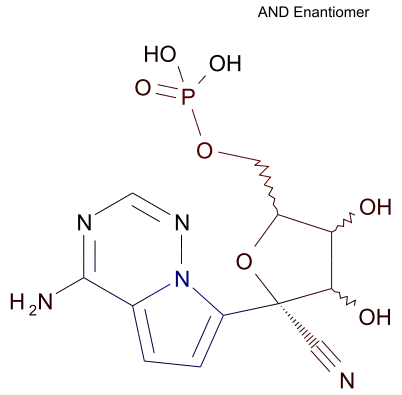
SCFP_6	-1715619483		0.273	2 out of 4
SCFP_6	276223760		0.243	24 out of 58

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Carcinogen in training set
SCFP_6	-1031053674		-0.664	1 out of 9
SCFP_6	616636418		-0.278	0 out of 1
SCFP_6	1433439981		-0.278	0 out of 1

Remdesivir

TOPKAT_Rat_Male_FDA_Single_vs_Multiple



$C_{12}H_{14}N_5O_7P$

Molecular Weight: 371.24262

ALogP: -1.502

Rotatable Bonds: 4

Acceptors: 11

Donors: 5

Model Prediction

Prediction: Multiple-Carcinogen

Probability: 0.556

Enrichment: 1.34

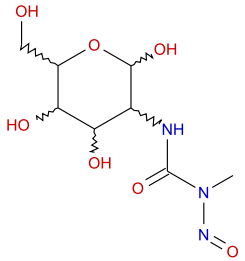
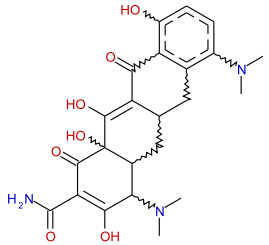
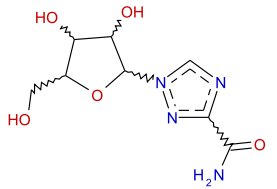
Bayesian Score: 3.52

Mahalanobis Distance: 14

Mahalanobis Distance p-value: 8.72e-005

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	Streptozocin	Minocycline	Ribavirin
Structure			
Actual Endpoint	Multiple-Carcinogen	Single-Carcinogen	Multiple-Carcinogen
Predicted Endpoint	Multiple-Carcinogen	Single-Carcinogen	Multiple-Carcinogen
Distance	0.817	0.908	0.929
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

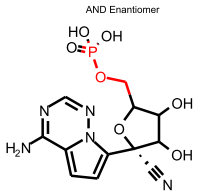
Model Applicability

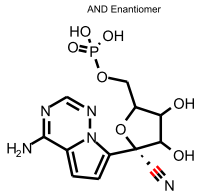
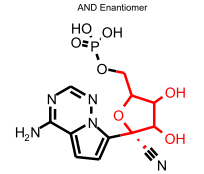
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. Num_H_Acceptors out of range. Value: 11. Training min, max, mean, SD: 0, 9, 3.8906, 2.196.

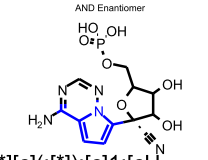
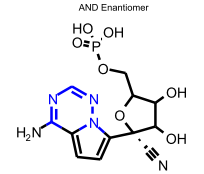
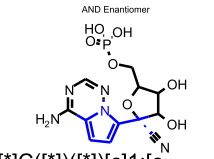
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Multiple-Carcinogen in training set
SCFP_8	-1029620989	 [*]COP(=[*])([*])[*]	0.649	3 out of 3

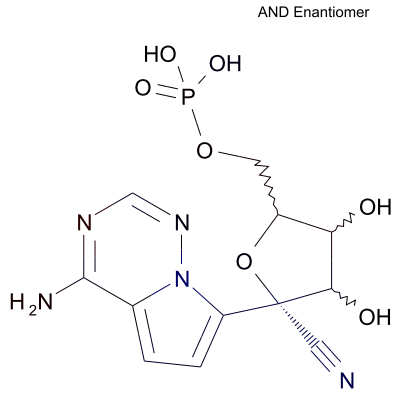
SCFP_8	2	 [*]C#[*]	0.584	6 out of 8
SCFP_8	-1486266146	 [*]CC1OC([*])([*])C(O)C1O	0.553	2 out of 2

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Multiple-Carcinogen in training set
SCFP_8	-1381862798	 [*][c](:[*]):[c]1:[cH]:[cH]:[c]([*]):n:1:[*]	-0.572	1 out of 7
SCFP_8	1245795878	 [*][c]1:[*]:n(:[*]):n:[cH]:n:1	-0.546	0 out of 2
SCFP_8	-1375522316	 [*]C([*])([*])[c]1:[cH]:[cH]:[c](:[*]):n:1:[*]	-0.546	0 out of 2

Remdesivir

TOPKAT_Skin_Irritancy_Mild_vs_Moderate_Severe



$C_{12}H_{14}N_5O_7P$

Molecular Weight: 371.24262

ALogP: -1.502

Rotatable Bonds: 4

Acceptors: 11

Donors: 5

Model Prediction

Prediction: Mild

Probability: 0.0911

Enrichment: 0.247

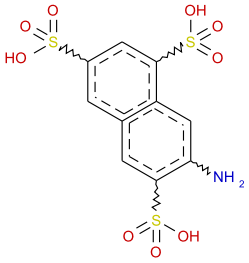
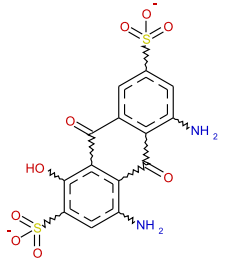
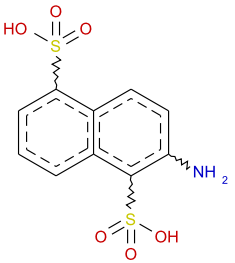
Bayesian Score: -8.73

Mahalanobis Distance: 13.5

Mahalanobis Distance p-value: 1.21e-009

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	1,3,6-Naphthalenetrisulfonic acid, 7-amino-	2,7-Anthracenedisulfonic acid, 9,10-dihydro-4,5-diamino-9,10-dioxo- 1-hydroxy-, disodium salt	1,5-Naphthalenedisulfonic acid, 2-amino-
Structure			
Actual Endpoint	Mild	Mild	Mild
Predicted Endpoint	Mild	Mild	Mild
Distance	0.759	1.033	1.137
Reference	85JCAE "Prehled Prumyslove Toxikologie; Organicke Latky," Marhold, J., Prague , Czechoslovakia, Avicenum, 1986 Volume(issue)/page/year: -,1058,1986	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: -,239,1	85JCAE "Prehled Prumyslove Toxikologie; Organicke Latky," Marhold, J., Prague , Czechoslovakia, Avicenum, 1986 Volume(issue)/page/year: -,1058,1986

Model Applicability

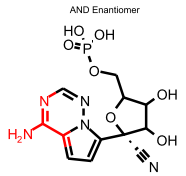
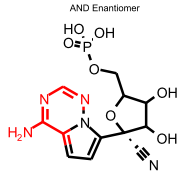
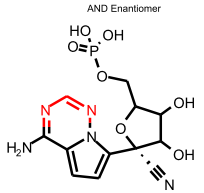
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown FCFP_2 feature: 472180098: [*]OP(=O)(O)O
3. Unknown FCFP_2 feature: -332197802: [*][c]1:[*]:[*]:[c](:[*]):n:1:n:[*]

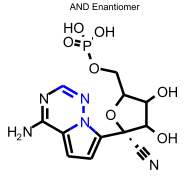
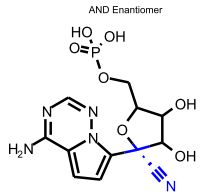
Feature Contribution

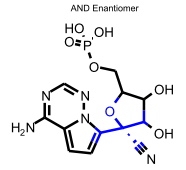
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Moderate_Severe in training set

FCFP_12	-1151884458	 [*]:n:[c](N):[c](:[*]):[*]	0.385	1 out of 1
FCFP_12	76292238	 [*]:[c]1:[*]:n:[cH]:n:[c]:1N	0.385	1 out of 1
FCFP_12	-124685461	 [*]:n:[cH]:n:[*]	0.206	2 out of 4

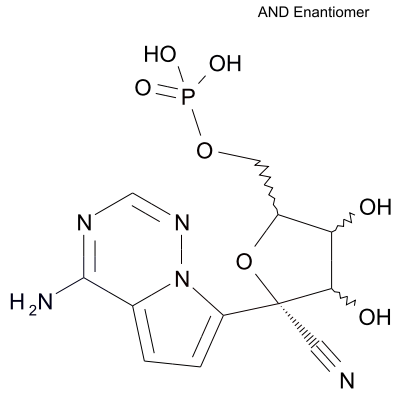
Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Moderate_Severe in training set
FCFP_12	4427049	 [*]:[cH]:n:n(:[*]):[*]	-0.893	0 out of 4
FCFP_12	-1277879912	 [*]C([*])([*])C#N	-0.548	5 out of 26

FCFP_12	-836603894	 [*]C1[*][*]O[C@]1(C#[*])[c](:[*]):[*]	-0.543	0 out of 2

Remdesivir

TOPKAT_Skin_Irritancy_None_vs_Irritant



$C_{12}H_{14}N_5O_7P$

Molecular Weight: 371.24262

ALogP: -1.502

Rotatable Bonds: 4

Acceptors: 11

Donors: 5

Model Prediction

Prediction: Irritant

Probability: 0.976

Enrichment: 1.06

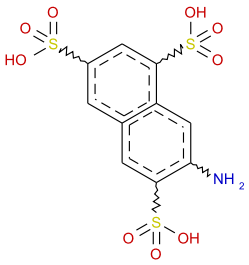
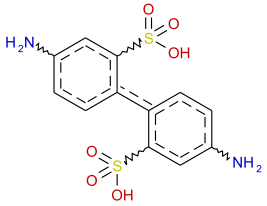
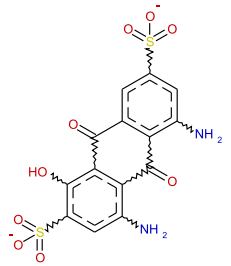
Bayesian Score: -0.492

Mahalanobis Distance: 13.2

Mahalanobis Distance p-value: 3.18e-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	1,3,6-Naphthalenetrisulfonic acid, 7-amino-	2,2'-Benzidine disulfonic acid	2,7-Anthracenedisulfonic acid, 9,10-dihydro-4,5-diamino-9,10-dioxo- 1-hydroxy-, disodium salt
Structure			
Actual Endpoint	Irritant	Non-Irritant	Irritant
Predicted Endpoint	Non-Irritant	Non-Irritant	Non-Irritant
Distance	0.755	0.896	1.025
Reference	85JCAE "Prehled Prumyslove Toxikologie; Organicke Latky," Marhold, J., Prague , Czechoslovakia, Avicenum, 1986 Volume(issue)/page/year: -,1058,1986	28ZPAK -,191,72	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: -,239,1

Model Applicability

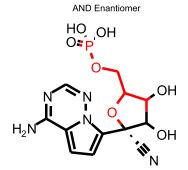
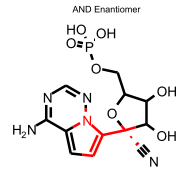
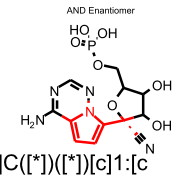
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown FCFP_2 feature: 472180098: [*]OP(=O)(O)O
3. Unknown FCFP_2 feature: -332197802: [*][c]1:[*]:[*]:[c](:[*]):n:1:n:[*]

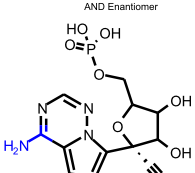
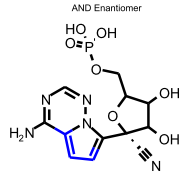
Feature Contribution

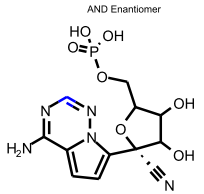
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Irritant in training set

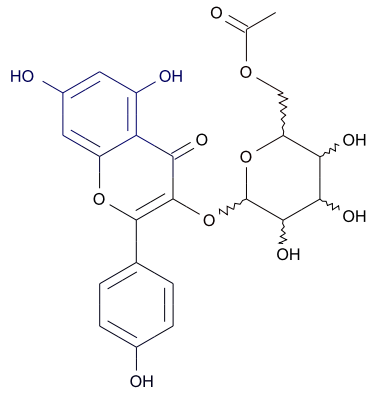
FCFP_12	654335567	 [*]C1[*][*]OC1COP(=[*])([*])[*]	0.0856	29 out of 29
FCFP_12	-1539132615	 [*]C([*])([*])[c]1:[cH]:[*]:[*]:n:1:[*]	0.0795	9 out of 9
FCFP_12	-1280036918	 [*]C([*])([*])[c]1:[cH]:[cH]:[c](:[*]):n:1:[*]	0.0772	7 out of 7

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Irritant in training set
FCFP_12	1069584379	 [*]:[c](:[*])N	-0.439	38 out of 65
FCFP_12	1618154665	 [*]:[c]1:[*]:[*]:[cH]:[cH]:1	-0.0845	412 out of 490

FCFP_12	16	AND Enantiomer  [*]:[cH]:[*]	-0.0843	423 out of 503

Flavonoid



$C_{23}H_{22}O_{12}$

Molecular Weight: 490.41357

ALogP: 0.322

Rotatable Bonds: 6

Acceptors: 12

Donors: 6

Model Prediction

Prediction: Non-Irritant

Probability: 0.892

Enrichment: 0.969

Bayesian Score: -2.84

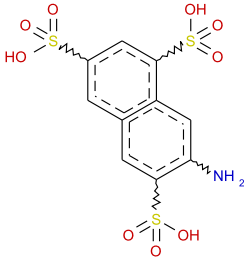
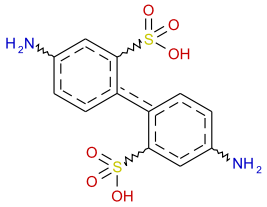
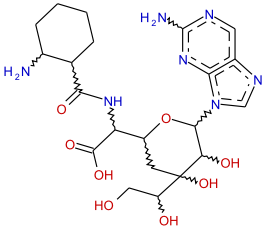
Mahalanobis Distance: 13.3

Mahalanobis Distance p-value: 8.75e-009

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_Skin_Irritancy_None_vs_Irritant

Structural Similar Compounds

Name	1,3,6-Naphthalenetrisulfonic acid, 7-amino-	2,2'-Benzidine disulfonic acid	Amipurimycin, hydrate
Structure			
Actual Endpoint	Irritant	Non-Irritant	Irritant
Predicted Endpoint	Non-Irritant	Non-Irritant	Non-Irritant
Distance	1.105	1.157	1.230
Reference	85JCAE "Prehled Prumyslove Toxikologie; Organicke Latky," Marhold, J., Prague , Czechoslovakia, Avicenum, 1986 Volume(issue)/page/year: -,1058,1986	28ZPAK -,191,72	JANTAJ Journal of Antibiotics. (Japan Antibiotics Research Assoc., 2-20-8 Ka miosaki, Shinagawa-ku, Tokyo, 141, Japan) V.2-5, 1948-52; V.21- 1968- Volume(issue)/page/year: 30,1,1977

Model Applicability

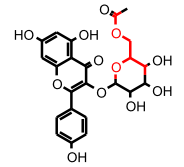
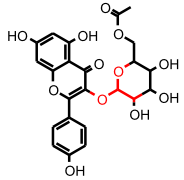
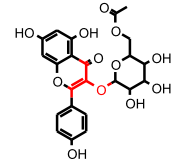
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

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

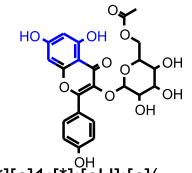
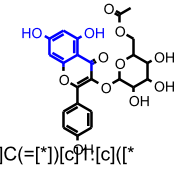
Feature Contribution

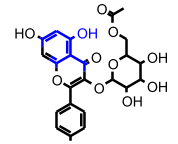
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Irritant in training set

FCFP_12	654335567	 [*]C1[*][*]OC1COP(=[*])([*])[*]	0.0856	29 out of 29
FCFP_12	699500266	 [*]OC(O[*])C([*])[*]	0.0852	25 out of 25
FCFP_12	436915834	 [*]OC(=C([*])[*])C(=[*])[*]	0.0756	6 out of 6

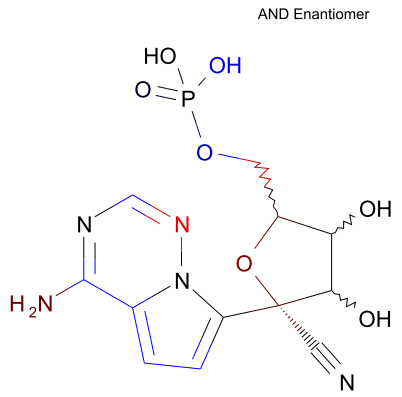
Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score	Irritant in training set
FCFP_12	946068634	 [*][c]1:[*]:[cH]:[c](O):[cH]:[c]:1O	-1.04	0 out of 2
FCFP_12	115228054	 [*]C(=[*])[c]1:[c]([*]):[cH]:[c](O):[cH]: [c]:1O	-0.65	0 out of 1

FCFP_12	-1604301295	 [*]C(=[*])[cH]1[c]([*]):[*]:[c]([*]):[cH] :[c]:1O	-0.18	22 out of 29

Remdesivir

TOPKAT_Carcinogenic_Potency_TD50_Mouse



$C_{12}H_{14}N_5O_7P$

Molecular Weight: 371.24262

ALogP: -1.502

Rotatable Bonds: 4

Acceptors: 11

Donors: 5

Model Prediction

Prediction: 9.25

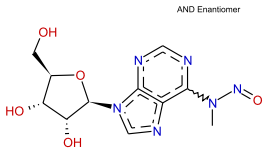
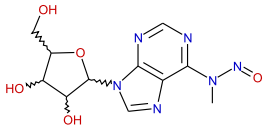
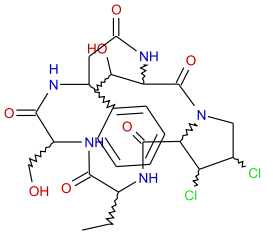
Unit: mg/kg_body_weight/day

Mahalanobis Distance: 14

Mahalanobis Distance p-value: 2.59e-010

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	377	(N-6)-(Methylnitroso)adenosine	338
Structure			
Actual Endpoint (-log C)	4.22928	4.22928	4.39533
Predicted Endpoint (-log C)	5.36013	5.36013	4.31268
Distance	0.852	0.852	0.919
Reference	CPDB	CPDB	CPDB

Model Applicability

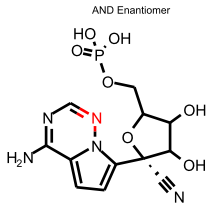
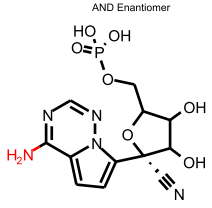
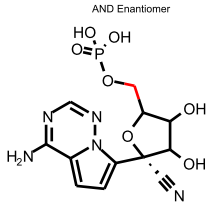
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown ECFP_2 feature: 1126642748: [*]OP(=O)(O)O
3. Unknown ECFP_2 feature: 2024329577: [*]P(=[*])([*])O
4. Unknown ECFP_2 feature: -194719409: [*]C1[*][*]C([*])([*])O1
5. Unknown ECFP_2 feature: 1258791451: [*]C1[*][*]O[C@]1(C#[*])[c](:[*]):[*]
6. Unknown ECFP_2 feature: -264833661: [*]C([*])([*])C#N
7. Unknown ECFP_2 feature: -1507082173: [*][c]1:[*]:[*]:[c](:[*]):n:1:n:[*]
8. Unknown ECFP_2 feature: -676555381: [*]:[cH]:n:n(:[*]):[*]
9. Unknown ECFP_2 feature: -66263742: [*]C([*])([*])[c]1:[cH]:[*]:[*]:n:1:[*]

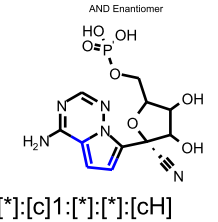
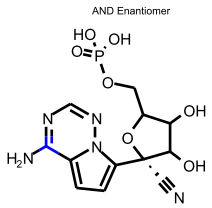
Feature Contribution

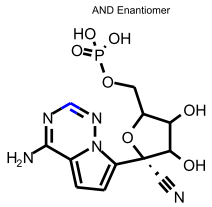
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score

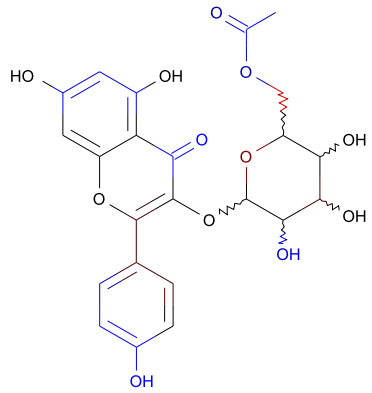
ECFP_6	655739385	 [*]:n:[*]	0.229
ECFP_6	1572579716	 [*]N	0.225
ECFP_6	1559650422	 [*]C[*]	0.203

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
ECFP_6	1996767644	 [*]:[c]1:[*]:[*]:[cH] :[cH]:1	-0.251
ECFP_6	642810091	 [*][c](:[*]):[*]	-0.247

ECFP_6	-182236392	AND Enantiomer  [*]:[cH]:[*]	-0.232

Flavonoid



$C_{23}H_{22}O_{12}$

Molecular Weight: 490.41357

ALogP: 0.322

Rotatable Bonds: 6

Acceptors: 12

Donors: 6

Model Prediction

Prediction: 44.3

Unit: mg/kg_body_weight/day

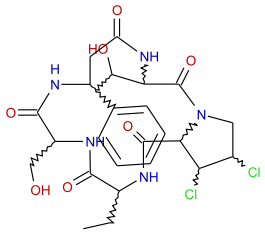
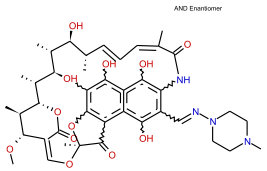
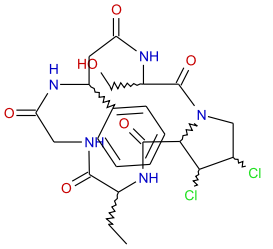
Mahalanobis Distance: 13.3

Mahalanobis Distance p-value: 1.71e-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_Carcinogenic_Potency_TD50_Mouse

Structural Similar Compounds

Name	338	532	Cyclochlorotine
Structure			
Actual Endpoint (-log C)	4.39533	4.38903	4.36142
Predicted Endpoint (-log C)	4.31268	5.60554	4.0834
Distance	0.898	0.966	0.994
Reference	CPDB	CPDB	CPDB

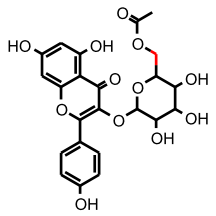
Model Applicability

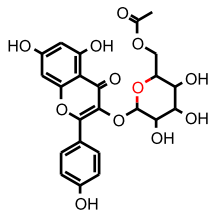
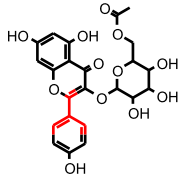
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown ECFP_2 feature: -2060414325: [*]OC(O[*])C([*])[*]
3. Unknown ECFP_2 feature: 1310940530: [*]C([*])OC(=[*])[*]
4. Unknown ECFP_2 feature: 1795218697: [*]OC(=C([*])[*])C(=[*])[*]
5. Unknown ECFP_2 feature: 1796421070: [*]OC(=C([*])[*])[c](:[*]):[*]

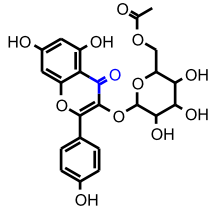
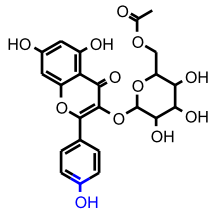
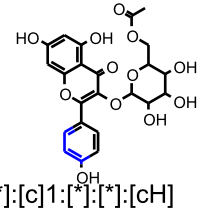
Feature Contribution

Top features for positive contribution

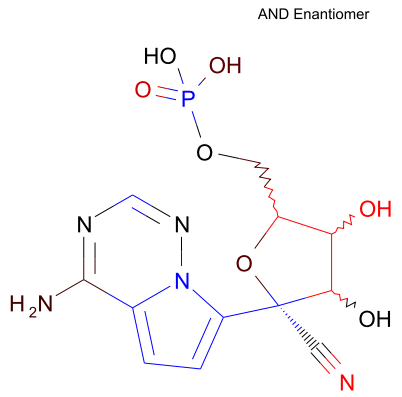
Fingerprint	Bit/Smiles	Feature Structure	Score
ECFP_6	1559650422	 [*]C[*]	0.203

ECFP_6	683445015	 [*]O[*]	0.136
ECFP_6	-181568884	 [*]C(=[*])[c](:[cH]:[*]):[cH]:[*]	0.0725

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	1996767644	 [*]:[c]1:[*]:[*]:[cH]:[cH]:1	-0.251

Remdesivir



$C_{12}H_{14}N_5O_7P$

Molecular Weight: 371.24262

ALogP: -1.502

Rotatable Bonds: 4

Acceptors: 11

Donors: 5

Model Prediction

Prediction: 1.01

Unit: mg/kg_body_weight/day

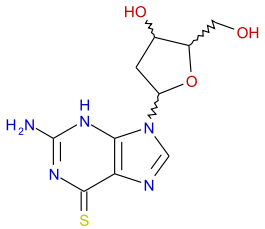
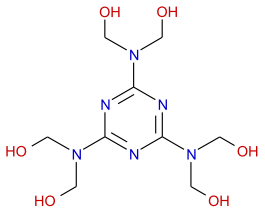
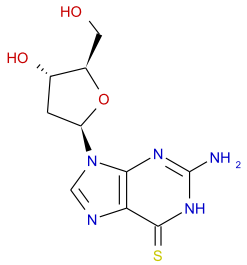
Mahalanobis Distance: 16.2

Mahalanobis Distance p-value: 4.38e-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.

TOPKAT_Carcinogenic_Potency_TD50_Rat

Structural Similar Compounds

Name	b-Thioguanine deoxyriboside	Hexamethylmelamine	604
Structure			
Actual Endpoint (-log C)	5.13004	4.47751	5.13004
Predicted Endpoint (-log C)	4.82552	3.76275	4.96687
Distance	0.805	0.832	0.835
Reference	CPDB	CPDB	CPDB

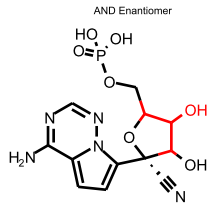
Model Applicability

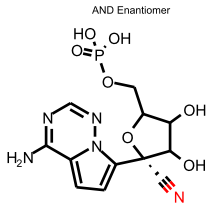
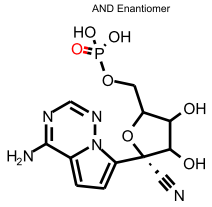
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown FCFP_2 feature: 472180098: [*]OP(=O)(O)O
3. Unknown FCFP_2 feature: -836603894: [*]C1[*][*]O[C@]1(C#[*])[c](:[*]):[*]

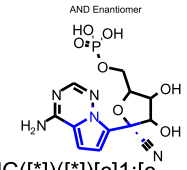
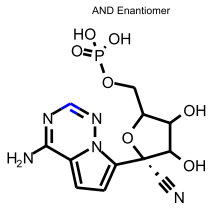
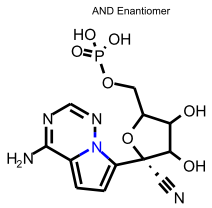
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_6	-1043250487	 [*]C1[*][*]C([*])C1O	1.15

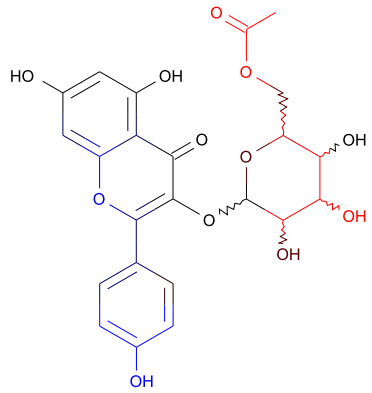
FCFP_6	9	 [*]#N	0.385
FCFP_6	1	 [*]=O	0.234

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_6	-1280036918	 [*]C([*])([*])[c]1:[cH]:[cH]:[c](:[*]):n:1:[*]	-0.363
FCFP_6	16	 [*]:[cH]:[*]	-0.354
FCFP_6	17	 [*]:n(:[*]):[*]	-0.149

Flavonoid

TOPKAT_Carcinogenic_Potency_TD50_Rat



$C_{23}H_{22}O_{12}$

Molecular Weight: 490.41357

ALogP: 0.322

Rotatable Bonds: 6

Acceptors: 12

Donors: 6

Model Prediction

Prediction: 0.544

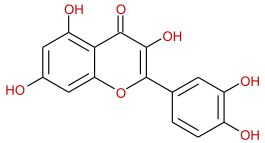
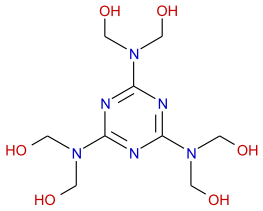
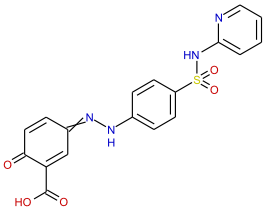
Unit: mg/kg_body_weight/day

Mahalanobis Distance: 12.1

Mahalanobis Distance p-value: 0.000325

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	Hexamethylmelamine	Salicylazosulfapyridine
Structure			
Actual Endpoint (-log C)	4.47602	4.47751	2.39891
Predicted Endpoint (-log C)	3.79194	3.76275	3.17598
Distance	0.891	0.945	0.974
Reference	CPDB	CPDB	CPDB

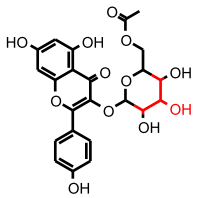
Model Applicability

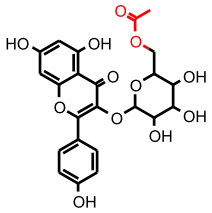
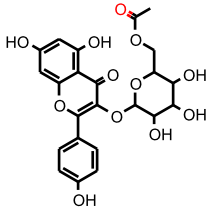
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

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

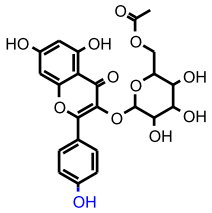
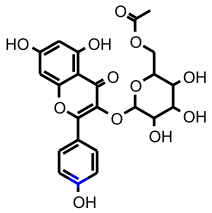
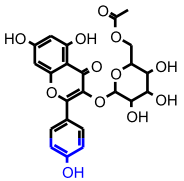
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_6	-1043250487	 [*]C1[*][*]C([*])C1O	1.15

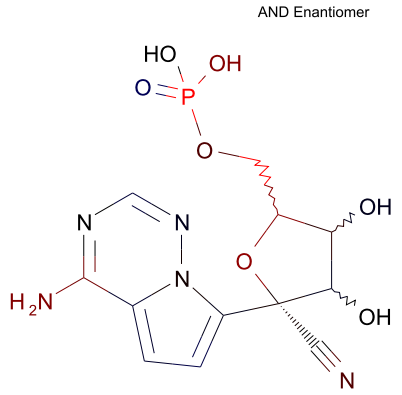
FCFP_6	565998553	 [*]OC(=O)C	0.357
FCFP_6	1	 [*]=O	0.234

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_6	7	 [*]O	-0.372
FCFP_6	16	 [*]:[cH]:[*]	-0.354
FCFP_6	74595001	 [*]:[cH]:[c](O):[cH]:[*]	-0.267

Remdesivir

TOPKAT_Chronic_LOAEL



$C_{12}H_{14}N_5O_7P$

Molecular Weight: 371.24262

ALogP: -1.502

Rotatable Bonds: 4

Acceptors: 11

Donors: 5

Model Prediction

Prediction: 0.00379

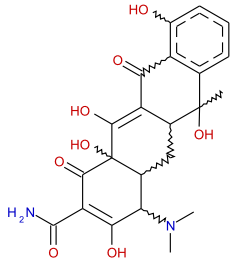
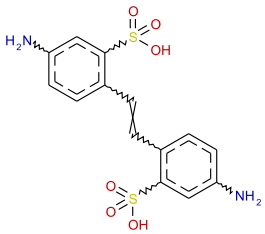
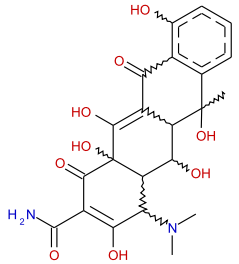
Unit: g/kg_body_weight

Mahalanobis Distance: 47.7

Mahalanobis Distance p-value: 2.93e-054

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	TETRACYCLINE .HCL	4;4'-DIAMINO-2;2'-STILBENEDIS	OXYTETRACYCLINE .HCL
Structure			
Actual Endpoint (-log C)	2.85193	2.47175	2.56626
Predicted Endpoint (-log C)	3.94748	3.53715	3.75581
Distance	0.746	0.746	0.802
Reference	NTP REPORT # 344	NTP 412 82	NTP REPORT # 315

Model Applicability

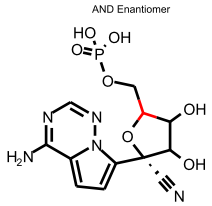
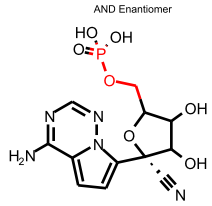
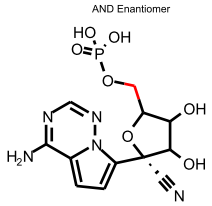
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. All properties and OPS components are within expected ranges.
2. Unknown FCFP_2 feature: 472180098: [*]OP(=O)(O)O
3. Unknown FCFP_2 feature: -332197802: [*][c]1:[*]:[*]:[c](:[*]):n:1:n:[*]
4. Unknown ECFP_6 feature: -1114776580: [*]C#[*]
5. Unknown ECFP_6 feature: -1101847286: [*]#N
6. Unknown ECFP_6 feature: 672362763: [*]:n(:[*]):[*]
7. Unknown ECFP_6 feature: 1126642748: [*]OP(=O)(O)O
8. Unknown ECFP_6 feature: 2100964382: [*]P(=O)([*])[*]
9. Unknown ECFP_6 feature: 2024329577: [*]P(=[*])([*])O
10. Unknown ECFP_6 feature: -1250439909: [*]COP(=[*])([*])[*]
11. Unknown ECFP_6 feature: -1687549011: [*]OCC([*])[*]
12. Unknown ECFP_6 feature: -194719409: [*]C1[*][*]C([*])([*])O1
13. Unknown ECFP_6 feature: -553149446: [*]CC1O[*][*]C1[*]
14. Unknown ECFP_6 feature: 305695353: [*]C1[*][*]C([*])C1O
15. Unknown ECFP_6 feature: -521596699: [*]C1[*][*]C([*])([*])C1O
16. Unknown ECFP_6 feature: 1258791451: [*]C1[*][*]O[C@]1(C#[*])[c](:[*]):[*]
17. Unknown ECFP_6 feature: 2024749573: [*]C([*])O
18. Unknown ECFP_6 feature: -264833661: [*]C([*])([*])C#N
19. Unknown ECFP_6 feature: 1412053881: [*]C#N

20. Unknown ECFP_6 feature: -1507082173: [*][c]1:[*]:[*]:[c](:[*]):n:1:n:[*]
21. Unknown ECFP_6 feature: -676555381: [*]:[cH]:n:n(:[*]):[*]
22. Unknown ECFP_6 feature: -710237522: [*]:n:[cH]:n:[*]
23. Unknown ECFP_6 feature: -677309799: [*][c](:[*]):n:[cH]:[*]
24. Unknown ECFP_6 feature: -1734834311: [*]:n:[c](N):[c](:[*]):[*]
25. Unknown ECFP_6 feature: 1334415134: [*][c](:[*]):[c]1:[cH]:[*]:[*]:n:1:[*]
26. Unknown ECFP_6 feature: -66263742: [*]C([*])([*])[c]1:[cH]:[*]:[*]:n:1:[*]
27. Unknown ECFP_6 feature: -938530932: [*]:[c](:[*])N

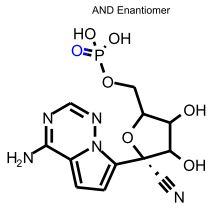
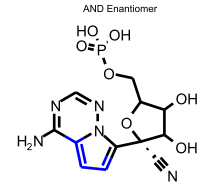
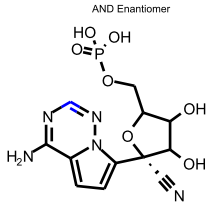
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
ECFP_6	-167460056	 [*]C([*])[*]	0.136
FCFP_6	-1143715940	 [*]COP(=[*])([*])[*]	0.13
ECFP_6	1559650422	 [*]C[*]	0.129

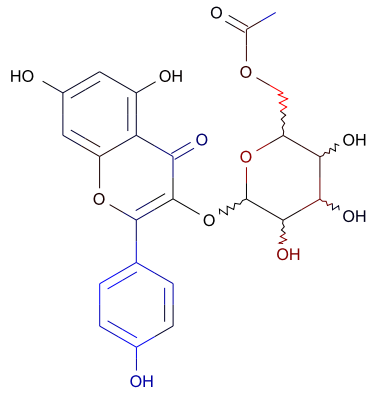
Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score

FCFP_6	1	 [*]=O	-0.102
ECFP_6	1996767644	 [*]:[c]1:[*]:[*]:[cH]:[cH]:1	-0.0497
FCFP_6	16	 [*]:[cH]:[*]	-0.0462

Flavonoid

TOPKAT_Chronic_LOAEL



$C_{23}H_{22}O_{12}$

Molecular Weight: 490.41357

ALogP: 0.322

Rotatable Bonds: 6

Acceptors: 12

Donors: 6

Model Prediction

Prediction: 0.0802

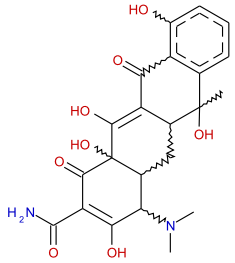
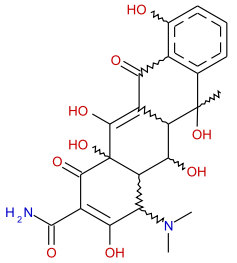
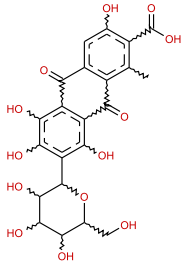
Unit: g/kg_body_weight

Mahalanobis Distance: 29.6

Mahalanobis Distance p-value: 5.79e-024

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	TETRACYCLINE .HCL	OXYTETRACYCLINE .HCL	CARMINE
Structure			
Actual Endpoint (-log C)	2.85193	2.56626	3.5162
Predicted Endpoint (-log C)	3.94748	3.75581	3.66829
Distance	0.748	0.781	0.823
Reference	NTP REPORT # 344	NTP REPORT # 315	FOOD.CHEM.TOXICOL.25.897.1987

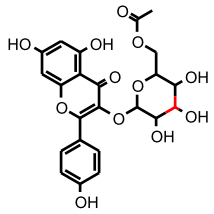
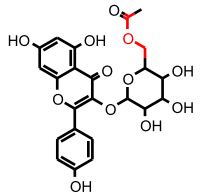
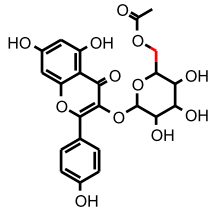
Model Applicability

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

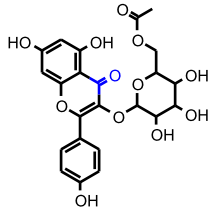
1. All properties and OPS components are within expected ranges.
2. Unknown ECFP_6 feature: -473922720: [*]OC(=O)C
3. Unknown ECFP_6 feature: -1687549011: [*]OCC([*])[*]
4. Unknown ECFP_6 feature: 2024749573: [*]C([*])O
5. Unknown ECFP_6 feature: 305695353: [*]C1[*][*]C([*])C1O
6. Unknown ECFP_6 feature: -2060414325: [*]OC(O[*])C([*])[*]
7. Unknown ECFP_6 feature: -1409796893: [*]C([*])OC([*])[*]
8. Unknown ECFP_6 feature: -553149446: [*]CC1O[*][*]C1[*]
9. Unknown ECFP_6 feature: 2019062761: [*]:[c](:[*])O
10. Unknown ECFP_6 feature: 1310940530: [*]C([*])OC(=[*])[*]
11. Unknown ECFP_6 feature: -177786161: [*]:[cH]:[c](O):[cH]:[*]
12. Unknown ECFP_6 feature: -181568884: [*]C(=[*])[c](:[cH]:[*]):[cH]:[*]
13. Unknown ECFP_6 feature: 1795218697: [*]OC(=C([*])[*])C(=[*])[*]
14. Unknown ECFP_6 feature: 1717462980: [*]C(=[*])C(=O)[c](:[*]):[*]
15. Unknown ECFP_6 feature: 1796421070: [*]OC(=C([*])[*])[c](:[*]):[*]
16. Unknown ECFP_6 feature: -560785749: [*]C(=[*])O[c](:[*]):[*]
17. Unknown ECFP_6 feature: -813997308: [*]C(=[*])[c](:[c]([*]):[*]):[c]([*]):[*]
18. Unknown ECFP_6 feature: -570915357: [*]O[c](:[cH]:[*]):[c]([*]):[*]

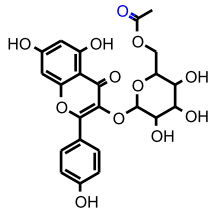
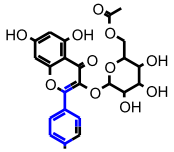
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
ECFP_6	-167460056	 [*]C([*])[*]	0.136
FCFP_6	-1143715940	 [*]COP(=[*])([*])[*]	0.13
ECFP_6	1559650422	 [*]C[*]	0.129

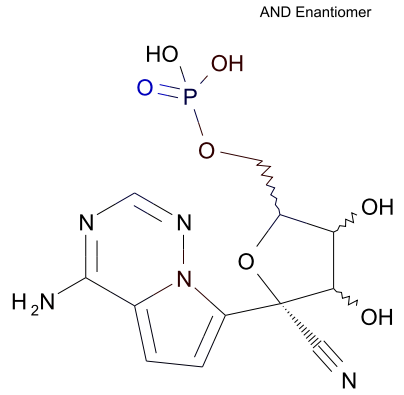
Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
ECFP_6	2106656448	 [*]C(=O)[*]	-0.11

FCFP_6	1	 [*]=O	-0.102
FCFP_6	-453677277	 [*]C(=[*])[c]1:[cH]:[cH]:[*]:[c]([*]):[cH]:[cH]:1	-0.0906

Remdesivir

TOPKAT_Rat_Maximum_Tolerated_Dose_Feed



$C_{12}H_{14}N_5O_7P$

Molecular Weight: 371.24262

ALogP: -1.502

Rotatable Bonds: 4

Acceptors: 11

Donors: 5

Model Prediction

Prediction: 0.235

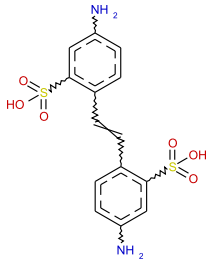
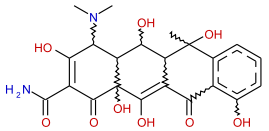
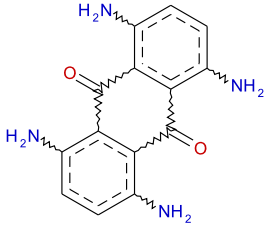
Unit: g/kg_body_weight

Mahalanobis Distance: 9.52

Mahalanobis Distance p-value: 0.000247

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	4,4'-DIAMINO-2,2'-STILBENEDISULFONIC ACID.2NaSALT	OXYTETRACYCLINE	50%1,4,5,8-TETRAAMINOANTHRAQUIONONE + DERIVATIVES
Structure			
Actual Endpoint (-log C)	2.50759	2.36214	3.0764
Predicted Endpoint (-log C)	3.26068	2.77834	3.08142
Distance	0.743	0.818	0.989
Reference	NCI/NTP TR-412	NCI/NTP TR-315	NCI/NTP TR-299

Model Applicability

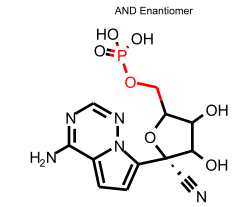
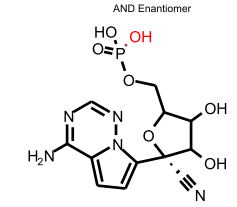
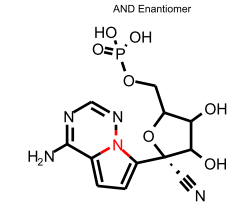
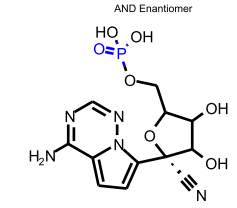
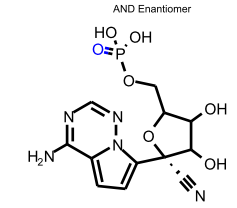
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

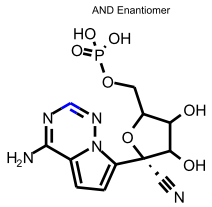
1. Molecular_PolarSurfaceArea out of range. Value: 206.26. Training min, max, mean, SD: 0, 201.84, 63.052, 40.7.
2. Unknown FCFP_2 feature: 472180098: [*]OP(=O)(O)O
3. Unknown FCFP_2 feature: -836603894: [*]C1[*][*]O[C@]1(C#[*])[c](:[*]):[*]
4. Unknown FCFP_2 feature: -1277879912: [*]C([*])([*])C#N
5. Unknown FCFP_2 feature: -332197802: [*][c]1:[*]:[*]:[c](:[*]):n:1:n:[*]
6. Unknown FCFP_2 feature: -124685461: [*]:n:[cH]:n:[*]

Feature Contribution

Top features for positive contribution

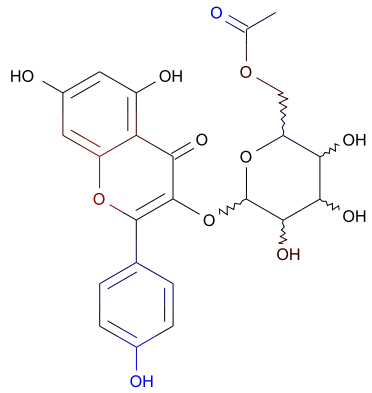
Fingerprint	Bit/Smiles	Feature Structure	Score

FCFP_2	-1143715940	 [*]COP(=[*])([*])[*]	0.095
FCFP_2	3	 [*]O	0.0737
FCFP_2	17	 [*]:n(:[*]):[*]	0.0441
Top Features for negative contribution			
Fingerprint	**Bit/Smiles**	**Feature Structure**	**Score**
FCFP_2	1872154524	 [*]P(=O)([*])[*]	-0.105
FCFP_2	1	 [*]=O	-0.0796

FCFP_2	16	AND Enantiomer  [*]:[cH]:[*]	-0.0512

Flavonoid

TOPKAT_Rat_Maximum_Tolerated_Dose_Feed



$C_{23}H_{22}O_{12}$

Molecular Weight: 490.41357

ALogP: 0.322

Rotatable Bonds: 6

Acceptors: 12

Donors: 6

Model Prediction

Prediction: 0.718

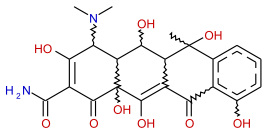
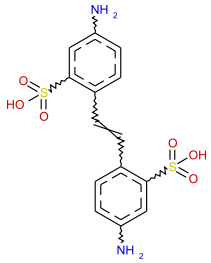
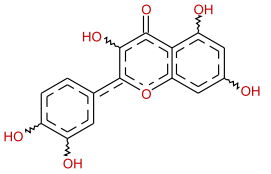
Unit: g/kg_body_weight

Mahalanobis Distance: 10

Mahalanobis Distance p-value: 3.81e-005

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	OXYTETRACYCLINE	4,4'-DIAMINO-2,2'-STILBENEDISULFONIC ACID.2NaSALT	QUERCETIN
Structure			
Actual Endpoint (-log C)	2.36214	2.50759	2.2016
Predicted Endpoint (-log C)	2.77834	3.26068	2.27782
Distance	0.750	0.853	0.947
Reference	NCI/NTP TR-315	NCI/NTP TR-412	NCI/NTP TR-409

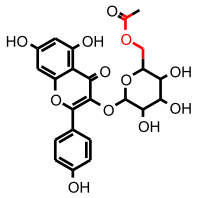
Model Applicability

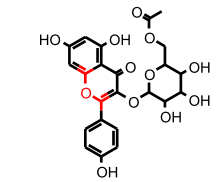
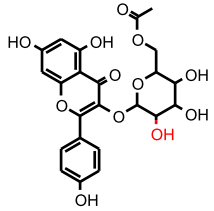
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

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

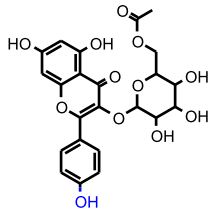
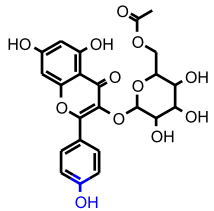
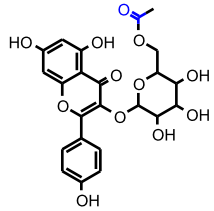
Feature Contribution

Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
FCFP_2	-1143715940	 [*]COP(=[*])([*])[*]	0.095

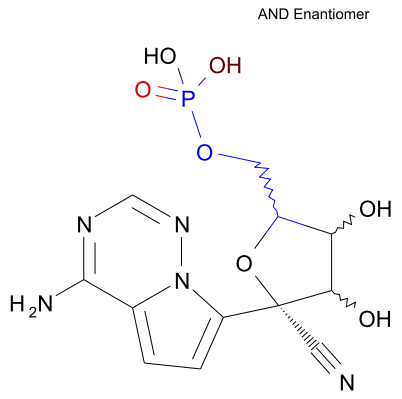
FCFP_2	1036089772	 [*]C(=[*])O[c](:[*]):[*]	0.0749
FCFP_2	3	 [*]O	0.0737

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	 [*]P(=O)([*])[*]	-0.105

Remdesivir

TOPKAT_Rat_Maximum_Tolerated_Dose_Gavage



$C_{12}H_{14}N_5O_7P$

Molecular Weight: 371.24262

ALogP: -1.502

Rotatable Bonds: 4

Acceptors: 11

Donors: 5

Model Prediction

Prediction: 0.000298

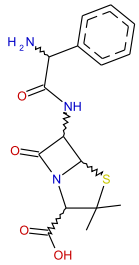
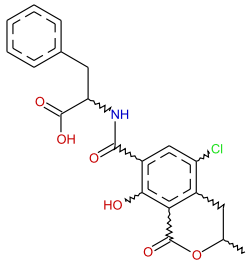
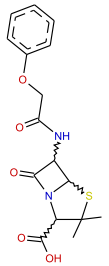
Unit: g/kg_body_weight

Mahalanobis Distance: 17.2

Mahalanobis Distance p-value: 5.05e-016

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

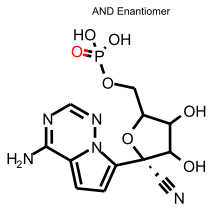
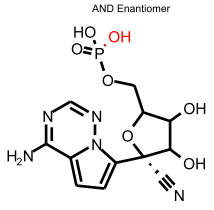
Name	AMPICILLIN TRIHYDRATE	OCHRATOXIN	PENICILLIN VK
Structure			
Actual Endpoint (-log C)	2.36724	6.28396	2.54455
Predicted Endpoint (-log C)	2.27651	5.12358	3.9702
Distance	1.255	1.482	1.498
Reference	NCI/NTP TR-318	NCI/NTP TR-358	NCI/NTP TR-336

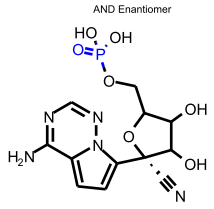
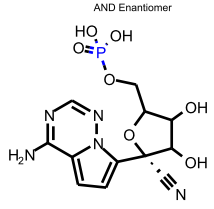
Model Applicability

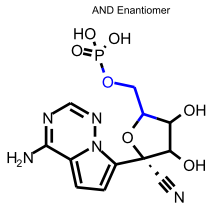
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. Num_H_Donors out of range. Value: 5. Training min, max, mean, SD: 0, 3, 0.4375, 0.8311.
2. Num_H_Acceptors out of range. Value: 11. Training min, max, mean, SD: 0, 6, 1.6146, 1.644.
3. Molecular_PolarSASA out of range. Value: 321.97. Training min, max, mean, SD: 0, 223.97, 50.816, 55.15.
4. Molecular_PolarSurfaceArea out of range. Value: 206.26. Training min, max, mean, SD: 0, 138.03, 28.978, 32.1.
5. OPS PC1 out of range. Value: 9.0116. Training min, max, SD, explained variance: -4.0008, 7.9165, 2.861, 0.2531.
6. OPS PC5 out of range. Value: -4.1876. Training min, max, SD, explained variance: -3.4, 4.1587, 1.489, 0.0686.
7. OPS PC9 out of range. Value: -2.7276. Training min, max, SD, explained variance: -2.7086, 2.9267, 1.019, 0.0321.
8. Unknown FCFP_2 feature: 472180098: [*]OP(=O)(O)O
9. Unknown FCFP_2 feature: -836603894: [*]C1[*][*]O[C@]1(C#[*])[c](:[*]):[*]
10. Unknown FCFP_2 feature: -1277879912: [*]C([*])([*])C#N
11. Unknown FCFP_2 feature: -1362791977: [*]C#N
12. Unknown FCFP_2 feature: -332197802: [*][c]1:[*]:[*]:[c](:[*]):n:1:n:[*]
13. Unknown FCFP_2 feature: -124685461: [*]:n:[cH]:n:[*]

Feature Contribution

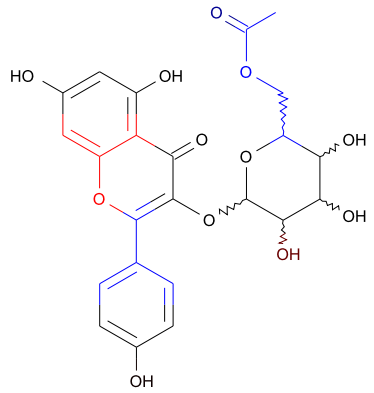
Top features for positive contribution			
Fingerprint	**Bit/Smiles**	**Feature Structure**	**Score**
FCFP_2	1	 [*]=O	0.511
FCFP_2	3	 [*]O	0.104

Top Features for negative contribution			
Fingerprint	**Bit/Smiles**	**Feature Structure**	**Score**
FCFP_2	1872154524	 [*]P(=O)([*])[*]	-0.307
FCFP_2	0	 [*]P(=[*])([*])[*]	-0.29

FCFP_2	-1272768868	AND Enantiomer  [*]OCC([*])[*]	-0.271

Flavonoid

TOPKAT_Rat_Maximum_Tolerated_Dose_Gavage



$C_{23}H_{22}O_{12}$

Molecular Weight: 490.41357

ALogP: 0.322

Rotatable Bonds: 6

Acceptors: 12

Donors: 6

Model Prediction

Prediction: 0.000133

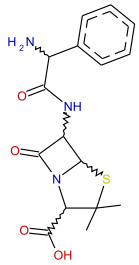
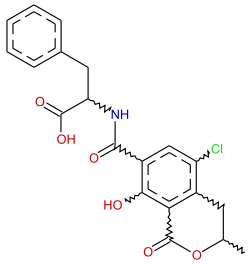
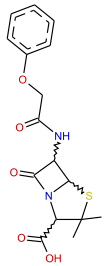
Unit: g/kg_body_weight

Mahalanobis Distance: 15.8

Mahalanobis Distance p-value: 4.48e-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	AMPICILLIN TRIHYDRATE	OCHRATOXIN	PENICILLIN VK
Structure			
Actual Endpoint (-log C)	2.36724	6.28396	2.54455
Predicted Endpoint (-log C)	2.27651	5.12358	3.9702
Distance	1.366	1.426	1.506
Reference	NCI/NTP TR-318	NCI/NTP TR-358	NCI/NTP TR-336

Model Applicability

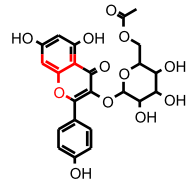
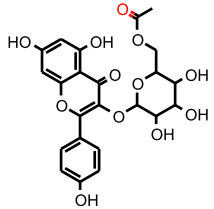
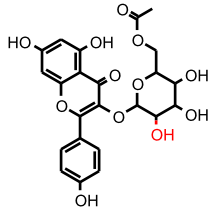
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

1. Molecular_Weight out of range. Value: 490.41. Training min, max, mean, SD: 68.074, 434.63, 171.13, 85.06.
2. Num_H_Donors out of range. Value: 6. Training min, max, mean, SD: 0, 3, 0.4375, 0.8311.
3. Num_H_Acceptors out of range. Value: 12. Training min, max, mean, SD: 0, 6, 1.6146, 1.644.
4. Molecular_PolarSASA out of range. Value: 307.46. Training min, max, mean, SD: 0, 223.97, 50.816, 55.15.
5. Molecular_PolarSurfaceArea out of range. Value: 192.43. Training min, max, mean, SD: 0, 138.03, 28.978, 32.1.
6. OPS PC1 out of range. Value: 12.535. Training min, max, SD, explained variance: -4.0008, 7.9165, 2.861, 0.2531.
7. OPS PC10 out of range. Value: 2.6747. Training min, max, SD, explained variance: -3.9696, 2.3971, 0.982, 0.0298.
8. Unknown FCFP_2 feature: 436915834: [*]OC(=C([*])[*])C(=[*])[*]
9. Unknown FCFP_2 feature: -1549192822: [*]C(=[*])C(=O)[c](:[*]):[*]
10. Unknown FCFP_2 feature: -1678245750: [*]OC(=C([*])[*])[c](:[*]):[*]

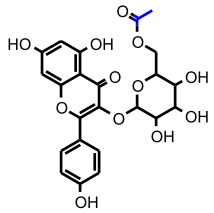
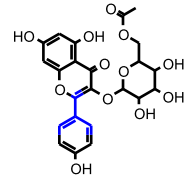
Feature Contribution

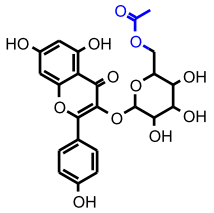
Top features for positive contribution

Fingerprint	Bit/Smiles	Feature Structure	Score

FCFP_2	332760439	 [*]O[c](:[cH]:[*]):[c](:[*]):[*]	0.672
FCFP_2	1	 [*]=O	0.511
FCFP_2	3	 [*]O	0.104

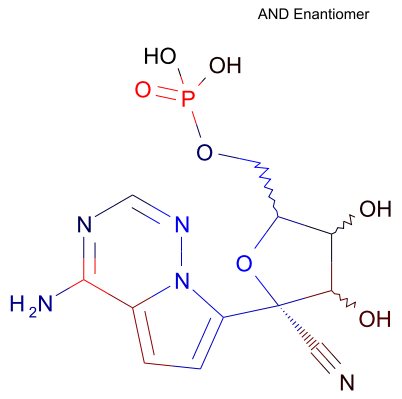
Top Features for negative contribution

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

FCFP_2	565998553	 [*]OC(=O)C	-0.348

Remdesivir

TOPKAT_Rat_Oral_LD50



$C_{12}H_{14}N_5O_7P$

Molecular Weight: 371.24262

ALogP: -1.502

Rotatable Bonds: 4

Acceptors: 11

Donors: 5

Model Prediction

Prediction: 0.309

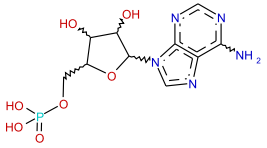
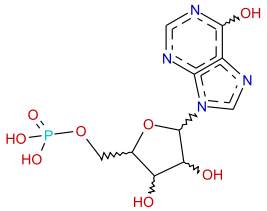
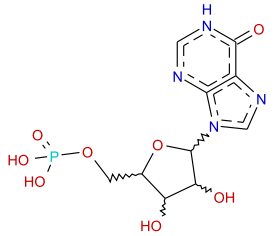
Unit: g/kg_body_weight

Mahalanobis Distance: 29.4

Mahalanobis Distance p-value: 1.72e-059

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	5'-ADENYLIC ACID; POTASSIUM SALT (K STRIPPED)	INOSINATE; DISODIUM SALT (Na STRIPPED)	INOSINE-5'-PHOSPHORIC ACID
Structure			
Actual Endpoint (-log C)	1.49	1.34	1.338
Predicted Endpoint (-log C)	2.45569	2.92201	1.35922
Distance	0.361	0.428	0.592
Reference	OYYAA2 4;689;70	AJINO* -;-;73	ARTODN 47;77;81

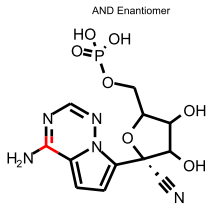
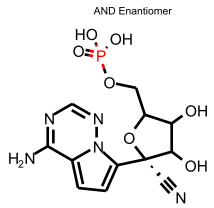
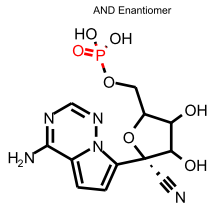
Model Applicability

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

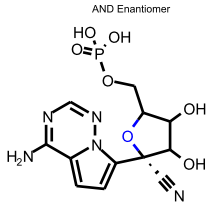
1. OPS PC10 out of range. Value: 15.526. Training min, max, SD, explained variance: -6.0395, 14.892, 2.468, 0.0220.
2. Unknown ECFP_2 feature: 1258791451: [*]C1[*][*]O[C@]1(C#[*])[c](:[*]):[*]
3. Unknown ECFP_2 feature: -264833661: [*]C([*])([*])C#N
4. Unknown ECFP_2 feature: -66263742: [*]C([*])([*])[c]1:[cH]:[*]:[*]:n:1:[*]
5. Unknown FCFP_6 feature: 16: [*]:[cH]:[*]
6. Unknown FCFP_6 feature: 472180098: [*]OP(=O)(O)O
7. Unknown FCFP_6 feature: -836603894: [*]C1[*][*]O[C@]1(C#[*])[c](:[*]):[*]
8. Unknown FCFP_6 feature: -332197802: [*][c]1:[*]:[*]:[c](:[*]):n:1:n:[*]
9. Unknown FCFP_6 feature: 4427049: [*]:[cH]:n:n(:[*]):[*]
10. Unknown FCFP_6 feature: -124685461: [*]:n:[cH]:n:[*]
11. Unknown FCFP_6 feature: 1747237384: [*][c](:[*]):n:[cH]:[*]
12. Unknown FCFP_6 feature: -1151884458: [*]:n:[c](N):[c](:[*]):[*]
13. Unknown FCFP_6 feature: 1618154665: [*]:[c]1:[*]:[*]:[cH]:[cH]:1
14. Unknown FCFP_6 feature: 1069584379: [*]:[c](:[*])N

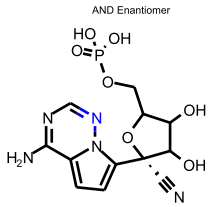
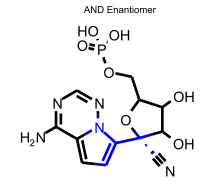
Feature Contribution

Top features for positive contribution

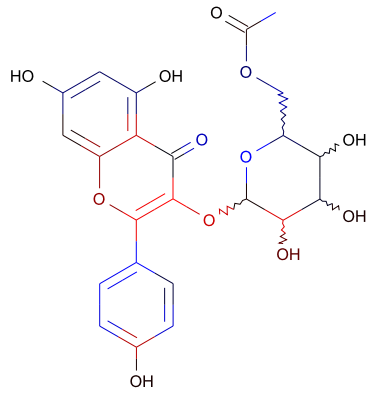
Fingerprint	Bit/Smiles	Feature Structure	Score
ECFP_6	642810091	 [*][c](:[*]):[*]	0.281
ECFP_6	-826638028	 [*]P(=[*])([*])[*]	0.225
ECFP_6	2100964382	 [*]P(=O)([*])[*]	0.166

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
ECFP_6	683445015	 [*]O[*]	-0.266

ECFP_6	655739385	 [*]:n:[*]	-0.239
FCFP_6	-1539132615	 [*]C([*])([*])[c]1:[c H]:[*]:[*]:n:1:[*]	-0.2

Flavonoid



$C_{23}H_{22}O_{12}$

Molecular Weight: 490.41357

ALogP: 0.322

Rotatable Bonds: 6

Acceptors: 12

Donors: 6

Model Prediction

Prediction: 1.04

Unit: g/kg_body_weight

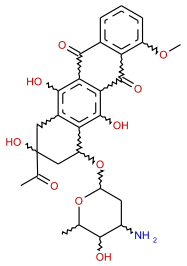
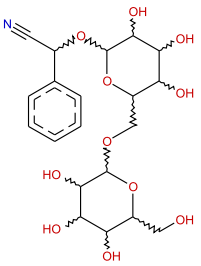
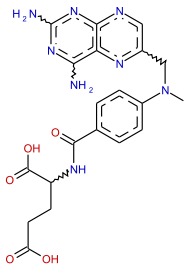
Mahalanobis Distance: 24.3

Mahalanobis Distance p-value: 3.94e-027

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	DAUNOMYCIN	AMYGDALIN (D)	METHOTREXATE
Structure			
Actual Endpoint (-log C)	3.196	2.943	3.527
Predicted Endpoint (-log C)	3.6117	2.51605	2.39978
Distance	0.588	0.728	0.765
Reference	YKYUA6 25;573;74	WJMDA2 134;97;81	NIIRDN 6;841;82

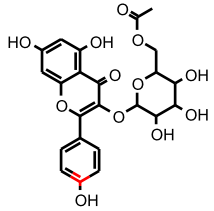
Model Applicability

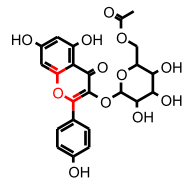
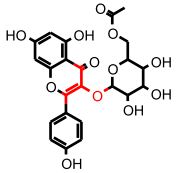
Unknown features are fingerprint features in the query molecule, but not found or appearing too infrequently in the training set.

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

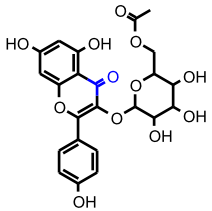
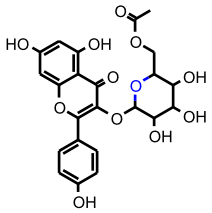
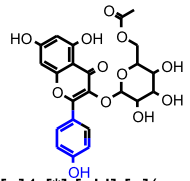
Feature Contribution

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	436915834	 [*]OC(=C([*])[*])C(=[*])[*]	0.184

Top Features for negative contribution

Fingerprint	Bit/Smiles	Feature Structure	Score
ECFP_6	2106656448	 [*]C(=O)[*]	-0.352
ECFP_6	683445015	 [*]O[*]	-0.266
FCFP_6	946589555	 [*][c]1:[*]:[cH]:[c](O):[cH]:[cH]:1	-0.204