Machine Learning and Neural Network Models

The advent of machine learning (ML) or neural network (NN) approaches offers the possibility of a new class of computational models that afford both high reliability and quality as well as low (computational) cost. A series of *seven* neural network models is currently implemented in ***Spartan'24***. These models were developed for specific (fundamental) computational tasks, to: (**i**) improve conformer energy differences provided by MMFF94[1-4] molecular mechanics, (**ii**) accurately estimate ωB97X-D/6-31G*[5-7] equilibrium geometries starting from MMFF geometries, (**iii**) accurately estimate total energies from:

ωB97X-V[8]/6-311+G(2df,2p)[11,12]//ωB97X-D/6-31G*
ωB97M-V[9]/6-311+G(2df,2p)[11,12]//ωB97X-D/6-31G*
ωB97M(2)[10]/6-311+G(2df,2p)[11,12]//ωB97X-D/6-31G*

models starting from *either* ωB97X-D/6-31G* equilibrium geometries and energies or from *estimated* ωB97X-D/6-31G* equilibrium geometries (neural network model) and ωB97X-D/6-31G* (single point) energies, and (**iv**) provide fast and accurate ^{1}H and ^{13}C chemical shifts, trained to reproduce results from the empirically corrected[13] ωB97X-D/6-31G* model. All machine learning models are supported for closed shell uncharged molecules comprising the elements: H, C, N, O, F, S, Cl and Br (only)[†]. Continued neural network development is underway; additional models will almost certainly find their way into future ***Spartan*** releases.

With some customizations, the published SpookyNet[14] learning forcefield approach has been used to generate each neural network model. A training set of more than ***140k molecules*** with more than ***1.8 million total conformers*** obtained from ωB97X-V/6-311+G(2df,2p)[6-311G*]//MMFF calculations for the **Corrected MMFF** neural net, ≈***120,000 molecules*** each with both equilibrium geometries and 50 distorted geometries ***(>6 million structures***) obtained from ωB97X-D/6-31G* calculations for the **Est. Density Functional ωB97X-D/6-31G* geometry** neural net, ≈***295,000 molecules*** from ωB97X-V/6-311+G(2df,2p)//ωB97X-D/6-31G* calculations for the **Est. ωB97X-V/6-311+G(2df,2p) energy** neural net, ≈***289,000 molecules*** from ωB97M-V/6-311+G(2df,2p)//ωB97X-D/6-31G* calculations for the **Est. ωB97M-V/6-311+G(2df,2p) energy** neural net, and ≈***289,000 molecules*** from ωB97M(2)/6-311+G(2df,2p)//ωB97X-D/6-31G* calculations for the **Est.**

† NMR shift networks available for proton and ^{13}C only (at present).

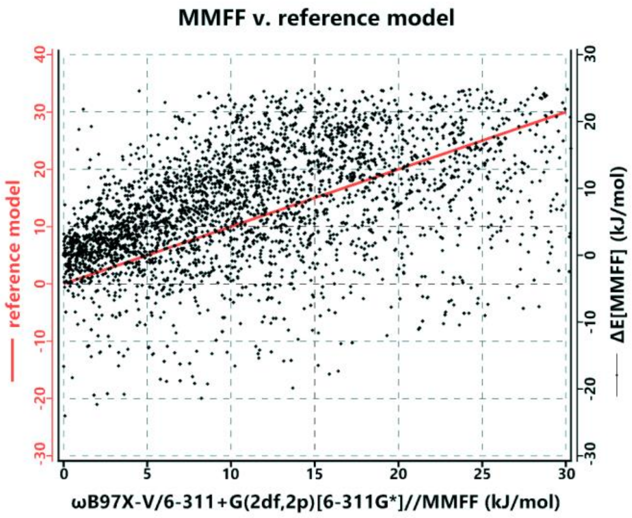
ωB97M(2)/6-311+G(2df,2p) energy neural net. The NMR neural network training sets include ≈2.2 million molecules with more than 44 million calculated ^{1}H and 33 million calculated ^{13}C chemical shifts from ωB97X-D/6-31G*.

Improving MMFF94 Molecular Mechanics (Corrected MMFF)[15]

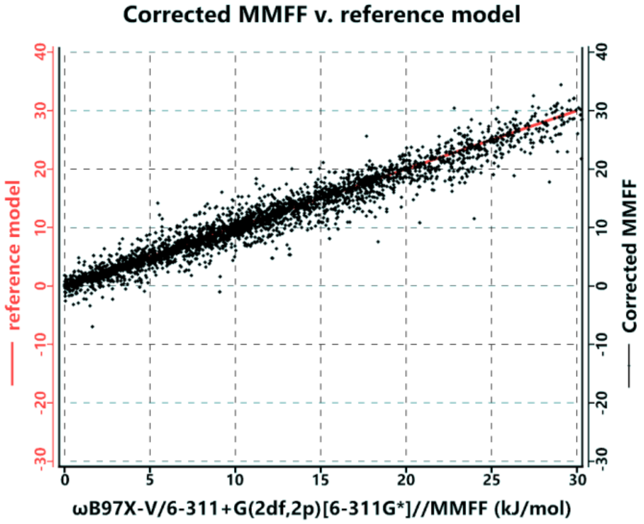
Molecular mechanics is perhaps the only class of methods that is routinely practical for calculations of conformer energy differences for flexible molecules with several degrees of conformational freedom. All accessible conformers (or at the very least a representative sample of these conformers) need to be identified and ranked based on energy. Assuming three-fold rotors, two and three degrees of freedom lead to only 9 and 27 conformers, respectively, whereas a molecule with 9 degrees of freedom (not at all unusual in natural products) leads to nearly 20,000 conformers. While only a relatively few conformers are likely to seriously contribute to calculated molecular properties, all must be examined to determine *which* few.

The MMFF94 approach has been shown to closely reproduce experimental conformational energy differences for small molecules with a single degree of conformational freedom. However, as suggested from the plot below, for a diverse series of moderately sized organic molecules with multiple degrees of conformational freedom, MMFF is not satisfactory. As experimental data are completely lacking, the reference energy is ωB97X-V/6-311+G(2df,2p)[6-311G*] density functional energy using MMFF equilibrium geometries, the same quantum chemical model used to train the neural net.

MMFF structures *corrected by neural net energies* provide a far better accounting with only a modest (*factor of two*) increase in computer time. The overall RMS error reduces from ***10.2*** **kJ/mol** for MMFF to ***1.8*** **kJ/mol** with the neural net correction. In conformer searching, ***Spartan's*** MMFF implementation is quite fast (typically no more than a second per conformer, and most of that is CPU overhead, not actual computational time). Adding a second or less (per conformer), to substantively improve the quality of conformational energy differences is time well spent, as it requires far fewer conformers calculated with more accurate (and time consuming) quantum chemical computational approaches to establish an accurate Boltzmann distribution.



Comparison of Conformational Energy Differences Obtained from MMFF and ωB97X-V/6-311+G(2df,2p)[6-311G*] Calculations



Comparison of Conformational Energy Differences Obtained from Neural Net and ωB97X-V/6-311+G(2df,2p)[6-311G*] Calculations

Estimating ωB97X-D/6-31G* Equilibrium Geometries[16]

Two considerations generally dictate model selection, quality of results and computation time. It is generally accepted that density functional models provide more consistent and more accurate results than Hartree-Fock molecular orbital models, but are also more time consuming, sometimes significantly so. The ωB97X-

D/6-31G* density functional model is among the most used quantum chemical models for geometry calculation. It is both accurate and reliable, properly accounting for the geometries of molecules that are often poorly dealt with using Hartree-Fock models. Additionally, it has been recognized as a standout for NMR shift prediction among several dozen functionals surveyed[17]. While it is generally not sufficiently accurate for use in determining reaction energies, or energy differences among conformers, structures from ωB97X-D/6-31G* provide a good foundation for energy calculations with more rigorous functionals and larger (more complete) basis sets.

The neural net fit to ωB97X-D/6-31G* incorporated into ***Spartan'24*** is orders of magnitude faster than the underlying density functional model. Structures that previously required hours of computer time may now be closely approximated in seconds (at most a few minutes). It should be emphasized that each one of these neural network calculations is unique and specific to the underlying computational model (and particular property, or properties) it is trained to reproduce, from a *specific* functional, and with a *specific* basis set. A neural net constructed to reproduce equilibrium geometries from the popular B3LYP-D3/6-31G* model (for example) will be distinct from that directed at ωB97X-D/6-31G* structures. Also acknowledged: different training sets and different convergence criteria (as well as different starting geometries) will ultimately lead to different neural network definitions. The hope is that subtle differences in training sets will lead to nearly the same final (or very similar) equilibrium geometries.

To assess how well the geometry neural network performs, a test set comprising 430 natural products with molecular weights ranging from ≈ 200 to 700 amu (with a mean of 447 amu) was established. None of molecules in the test set were used in training or validation. We chose three criteria for assessment: structure, energy, and NMR chemical shifts.

The most obvious criterion is structure (itself): *bond lengths*, *bond angles*, and *dihedral angles* [excluding those involving hydrogen(s)]. The performance was substantive, with only 14 molecules showing bond lengths that deviate from ωB97X-D/6-31G* values by more than 0.02 Å. Similar results were observed in bond angles; only 4 and 7 molecules incorporate a bond angle that differs by more than **10º** and **5º**, respectively. Less than a quarter of the molecules show individual bond-angle deviations of more than **2º**.

Dihedral angles are perhaps the most important structural parameter in that large deviations may result in molecular shapes that differ greatly from those obtained using ωB97X-D/6-31G* (the training model). Of additional concern is that further calculation of NMR chemical shifts, which are sensitive to medium to long-range interactions, might be impacted. Only two molecules show very large (>50°) deviations; 34 (8%) show deviations >20; 30% of molecules show deviations of >10°.

The second criterion involves differences in energies resulting from use of neural net equilibrium geometries in lieu of ωB97X-D/6-31G* geometries. The RMS error for the neural net is 8 kJ/mol and the energies of only 11 molecules deviate from ωB97X-D/6-31G* by more than 20 kJ/mol, the largest of which is 42 kJ/mol. Fifty-four (54) molecules deviate by more than 10 kJ/mol.

Perhaps the most important metric is the effect of equilibrium geometry on ^{1}H and especially ^{13}C NMR chemical shifts. This is because geometry calculation is key in any effort to realize an accurate rapid procedure to calculate chemical shifts of conformationally flexible organic molecules, natural products among them, and to distinguish among stereoisomers that closely reproduce the results of the accurate (but time consuming) QM-based multi-step protocols available since ***Spartan'18***. Only 4 and 29 molecules exhibit individual proton shift deviations greater than 1 and 0.5 ppm, respectively, more than a third of the molecules have one or more protons with chemical shifts that deviate from ωB97X-D/6-31G* values by more than 0.2 ppm.

Statistics for ^{13}C chemical shifts mimic those for proton shifts. Only one molecule exhibits an individual deviation >10 ppm and only 11 exhibit individual deviations >5 ppm. Roughly a third of the molecules based on neural net geometries show at least one individual deviation >2 ppm. The overall RMS (all carbons) and the RMS of the maximum individual ^{13}C shift errors (per molecule) from the neural net geometries are 0.8 ppm and 2.3 ppm, respectively.

Improved Reaction and Conformer Energy Calculations

Reaction energies and conformer energies differences are among the most important quantities obtained from quantum chemical calculations. Organic chemists (synthetic and natural products chemists in particular) will benefit from calculations able to identify the dominant stereoisomer arising from a chemical reaction, and from determination of conformer energy differences, providing Boltzmann weights and with these, accurate prediction of NMR shifts of flexible molecules.

The "gold standard" CCSD(T)/CBS calculations[18] scale formally as the seventh power of the number of basis functions, and can take many hours (even days) to complete. Reducing computational cost while achieving CCSD(T) accuracy has been the primary motivation for development of many density functional models. In previous versions of ***Spartan***, the primary focus has been on the Head-Gordon functionals: ωB97X-V, ωB97M-V and ωB97M(2), all with the 6-311+G(2df,2p) basis set and all starting from ωB97X-D/6-31G* geometries. The CCSD(T)[19] procedure is superior to these three functionals, and while the 6-311+G(2df,2p) basis set is moderately large and diverse, the recipe developed to yield a "complete basis set" (CBS) ensures that further additions will at most have modest impact on the energy. Finally, in our case, the geometry is different from that used in CCSD(T) calculations (MP2/aug-cc-pVDZ basis set vs. ωB97X-D/6-31G*).

The two models ωB97X-V/6-311+G(2df,2p)//ωB97X-D/6-31G* and (to a lesser extent) ωB97M-V/6-311+G(2df,2p)//ωB97X-D/6-31G* are practical for routine calculations on rigid molecules (or those with only a few degrees of conformational freedom) up to molecular weights <400 amu, although they may require tens of minutes to several hours to complete. They are clearly impractical, at least routinely so, for significantly larger systems, or for molecules with multiple degrees of conformational freedom. The ωB97M(2)/6-311+G(2df,2p)//ωB97X-D/6-31G* is more computationally costly and practical ranges are even smaller.

Spartan'24 provides neural networks providing Est. DFT energies[20] trained to these three density functional models. These require an ωB97X-D/6-31G* geometry (or an estimated geometry from the Est. ωB97X-D/6-31G* neural network along with a single point ωB97X-D/6-31G* energy). Because of these requirements, application of these neural nets is not "instantaneous" (unlike the two previous described machine learning models, these three are not devoid of quantum chemical calculations as input). This said, the overall performance is easily an *order of magnitude faster* utilizing these neural networks to provide energies (compared to the corresponding quantum chemical energy calculations). As quality conformer energy differences are needed to establish accurate **Conformer Distributions** (as well as Boltzmann weighted NMR shifts), these energy-focused neural networks provide significant computational savings in tasks featuring conformational searching, offering the hope of an analogous machine learning option to the QM-heavy multi-step **NMR Spectrum** task (the protocol established for determining accurate ^{13}C and ^{1}H Chemical Shifts for conformationally flexible molecules)**11**. Although the routine desire for quality energies (alone) suggests that the three **Est. Density Functional energy** models will have ample opportunity for application in conjunction with standard equilibrium geometry calculations.

Estimating accurate Proton and ^{13}C NMR Chemical Shifts

The challenging task of assigning molecular structure for novel synthetic and/or novel natural product molecules has, in recent years, been supported by density functional calculations (typically GIAO-based). Calculations have become a useful tool to aid or challenge structural assignments[21-33]. ***Spartan's*** multi-step protocol is often successfully applied in support of confirming structural assignment[34-39]. The major limiting factor to more routine application of the multi-step protocol remains the unfortunately long calculation times (many hours to days). While the original ***Spartan'20*** protocol remains an option, beginning in ***Spartan'24***, we have introduced (by default) the ***Corrected MMFF*** model as an additional filter between MMFF94 optimized structures and further DFT optimization and energy calculation. This step adds only a small fraction of overall computational time, and allows a reduction of the energy window (above "best" conformation) from 40 kJ/mol to 20 kJ/mol, as well as a reduction in the maximum total number of conformers passed on to further quantum chemical calculations (from 200 to 100). This allows for a factor of 2 to 5 faster results (compared to the *Spartan'20* protocol). While an improvement, the QM-heavy protocol often remains time consuming, a recent sample of conformationally flexible (mean of ≈ 280,000 conformers) natural products molecules (with a mean molecular weight of 447.8 amu) required an average of 319 minutes computational time (per isomer) to provide Boltzmann weighted Chemical Shifts (per isomer), sufficient to compare with experimental shifts and assign structure.

To be routinely applicable, improved computational time is highly desired. Two independently trained neural network models providing ^{1}H and ^{13}C chemical shifts (only), have been implemented beginning with ***Spartan'24 1.3.0***. Trained on > 2.7 million equilibrium geometry calculations (over 44 million ^{1}H and 33 million ^{13}C chemical shifts) from ωB97X-D/6-31G* density functional and the Est. ωB97X-D/6-31G* machine learning model (trained to reproduce the former). These NMR chemical shift machine learning models perform consistently well when applied to organic systems outside of the formidable training set. An assessment of 601 molecules from the Marine Natural Product Database[40], ranging in weight from 111 to 693 amu (with an average weight of 290 amu) has been made. Results from the ^{1}H and ^{13}C chemical shift neural networks from two equilibrium geometry input sources (ωB97X-D/6-31G* density functional the est. ωB97X-D/6-31G* machine learning model) were compared with chemical shift results from direct calculation with quantum chemical (empirically corrected) GIAO density functional ωB97X-D/6-31G* calculations. The NMR neural net models performed equally well when using structures (equilibrium geometries) from ωB97X-D/6-31G* density functional and the Est. ωB97X-D/6-31G* machine learning model, with RMS errors for chemical shifts of .05 ppm for ^{1}H and .73 ppm^{13}C from QM geometries and .09 ppm and 1.02 ppm from machine learning geometries. Summarized in **Table 1**:

Table 1. **RMS and Max. Absolute Errors for ^{1}H and ^{13}C Chemical Shifts (ppm)**

Equilibrium Geometry model:	**ωB97X-D/6-31G***		**Est. ωB97X-D/6-31G***	
signal	^{1}H	^{13}C	^{1}H	^{13}C
RMS (ppm)	0.05	0.73	0.09	1.02
Max error (ppm)	0.62	5.79	2.10	10.48

Table 1 – Neural Network chemical shifts compared with those from corrected ωB97X-D/6-31G* (GIAO-based) density functional calculations for a series of 601 rigid marine natural product molecules.

Results are quite close to the underlying QM shifts, at essentially a few seconds per molecule. In the case of the original multi-step protocol (with no machine learning steps), calculations complete in multiple hours to days. ***Spartan'24's*** default ***Density Functional*** protocol (with *one* machine learning step) performs on a time scale of hours. The default ***Est. Density Functional*** protocol (with *five* different machine learning models) performs on a time scale of minutes. A representative sampling of flexible natural products molecules (with a mean of ≈280k conformers) from the Natural Products Database[41] (a collection included with ***Spartan'24***) indicate the *est. density functional* protocol (maximum use of machine learning models) is on the order of **30** times faster than the *density functional* protocol (with a single machine learning model step) when performing the same Boltzmann weighted NMR spectrum (^{1}H and ^{13}C shifts).

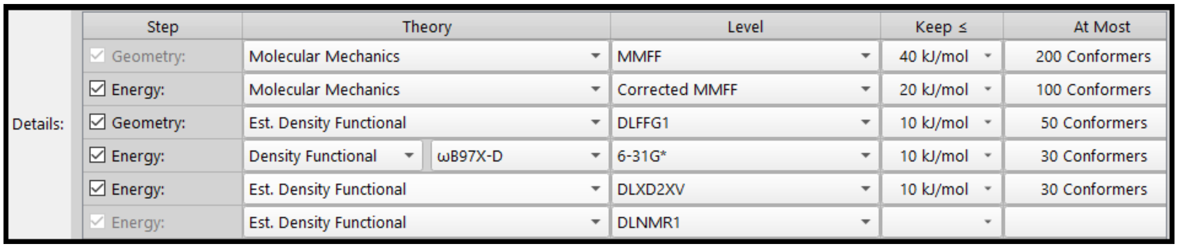
Table 2, below, provides an example of performance along with breakdown of molecular weight, conformers identified, and computational times (in minutes) for both the **Est. Density functional** protocol (machine-learning) and the **Density functional** protocol (quantum-chemical). Assessment compares times for a set of eighteen natural products molecules. The machine learning protocol performance is impressive.

Table 2. Flexible Natural Products Examples. Boltzmann Weighted NMR Spectrum task Machine Learning (NN) vs. Density Functional (QM) computational times.

molecule	conformers	Formula	Wt. (amu)	NN*	QM*	factor of
coodeanone A	78,732	$C_{23}H_{32}O_5$	388.5	13.6	459.8	33.8
bromophycolide R	1,417,176	$C_{27}H_{35}BrO_4$	503.5	3.3	164.8	49.9
psiguadial C	11,664	$C_{20}H_{24}O_{10}$	490.6	3.0	97.1	32.4
lythrine	2	$C_{26}H_{29}NO_5$	435.5	2.2	82.7	37.6
angustilongine A	68,024,448	$C_{43}H_{54}N_4O_5$	706.9	35.2	1277.8	36.3
ternifolide A	209,952	$C_{22}H_{28}O_7$	404.5	4.2	78.7	18.7
tonantzitlolone A	6,377,292	$C_{26}H_{40}O_7$	464.6	17.1	308.7	18.1
prunifoline D	576	$C_{21}H_{24}N_2O_4$	368.4	8.5	212.9	25.0
kopsonoline	4	$C_{19}H_{22}N_2O$	294.4	1.2	37.2	31.0
ciliatonoid A	128	$C_{26}H_{32}O_5$	424.5	7.3	161.3	22.1
epoxyresibufogenin…	1,728	$C_{25}H_{32}O_6$	428.5	3.8	102.8	27.1
achillinin B	13,122	$C_{31}H_{38}O_8$	538.6	20.7	652	31.5
lycopodine	3,888	$C_{16}H_{25}NO$	247.4	1.2	25.1	20.9
caesalappanin G	39,366	$C_{22}H_{30}O_7$	406.5	6.4	124.6	19.5
stauntonine	17,496	$C_{21}H_{28}O_7$	392.5	14.9	310.5	20.8
flueggine B	12	$C_{24}H_{28}N_2O_5$	424.5	2.4	82.6	34.4
shearinine I	2,592	$C_{37}H_{45}NO_7$	615.8	8.2	371.9	45.4
saroclide A	708,588	$C_{25}H_{32}N_2O_5$	440.5	13.5	969.5	71.8
mean	4,272,598		443.1	**9.3**	**306.7**	**30.2**

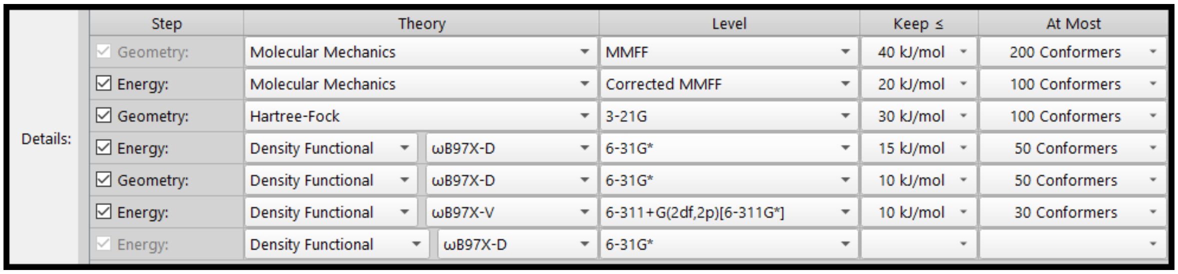
*Time in minutes. Calculations performed on a one of three different Intel systems: 12-core Intel i7 (Win 11), 10-core Intel i9 (Ubuntu 22.04 LTS), 24-core Intel i9 (Win 11). At the low end, improvement from the Neural Network protocol offers more than an order of magnitude faster results than the Quantum Chemical protocol. This dataset is available from neural network folder in the Tutorials directory "NMR-Spectrum-Timing.spartan." Average RMS against experimental ^{13}C Shifts is 1.27 ppm for the density functional calculations and 1.55 ppm for the neural network models.

From the user’s perspective, the only change in the details of the Calculations dialog is changing the selection from **Density Functional** to **Est. Density Functional** for the “with” menu in the **NMR Spectrum** task. ***Spartan*** configures all details, which are exposed if one *clicks* on the **Details** checkbox:



	Step	Theory	Level	Keep ≤	At Most
Details:	☑ Geometry:	Molecular Mechanics	MMFF	40 kJ/mol	200 Conformers
	☑ Energy:	Molecular Mechanics	Corrected MMFF	20 kJ/mol	100 Conformers
	☑ Geometry:	Est. Density Functional	DLFFG1	10 kJ/mol	50 Conformers
	☑ Energy:	Density Functional ωB97X-D	6-31G*	10 kJ/mol	30 Conformers
	☑ Energy:	Est. Density Functional	DLXD2XV	10 kJ/mol	30 Conformers
	☑ Energy:	Est. Density Functional	DLNMR1		

For comparison, the details of the **Density Functional** protocol for the **NMR Spectrum** are provided below:



	Step	Theory	Level	Keep ≤	At Most
Details:	☑ Geometry:	Molecular Mechanics	MMFF	40 kJ/mol	200 Conformers
	☑ Energy:	Molecular Mechanics	Corrected MMFF	20 kJ/mol	100 Conformers
	☑ Geometry:	Hartree-Fock	3-21G	30 kJ/mol	100 Conformers
	☑ Energy:	Density Functional ωB97X-D	6-31G*	15 kJ/mol	50 Conformers
	☑ Geometry:	Density Functional ωB97X-D	6-31G*	10 kJ/mol	50 Conformers
	☑ Energy:	Density Functional ωB97X-V	6-311+G(2df,2p)[6-311G*]	10 kJ/mol	30 Conformers
	☑ Energy:	Density Functional ωB97X-D	6-31G*		

Both approaches begin with the same 2 steps: **MMFF94** is used to establish an initial conformer distribution and MMFF energies are improved by the **Corrected MMFF** model trained to ωB97X-V/6-311+G(2df,2p)[6-311G*]. The procedures fork beyond this point. The **Density Functional** protocol goes on to perform as many as 300+ additional quantum chemical calculations, some potentially quite time consuming. Final chemical shift data is obtained from density functional GIAO-based ωB97X-D/6-31G* calculations, including empirically corrected chemical shifts. Whereas in the **Est. Density Functional** protocol with only a single quantum chemical calculation (with a modest basis set), machine learning models provide the energies for Boltzmann weighting as well as ^{13}C and ^{1}H chemical shifts (one neural network per center). The combination of comparable accuracy to the QM-heavy protocol and the remarkably fast performance suggests the new ML protocol is positioned to play a substantive role in assisting practicing chemists with structure assignment of novel organic molecules.

References:

1. *J. Comput. Chem.* **1996**, 33, 490.
2. *J. Comput. Chem.* **1996**, 33, 520.
3. *J. Comput. Chem.* **1996**, 33, 553.
4. *J. Comput. Chem.* **1996**, 33, 587.
5. *Phys. Chem. Chem. Phys.* **2008**, 10, 6615-6620.
6. ***Ab Initio Molecular Orbital Theory***, Wiley, New York, 1985. ISBN: 978-0-471-81241-8
7. *J. Chem. Phys.* **1989**, 90, 1007-1023.
8. *Phys. Chem. Chem. Phys.* **2014**, 16, 9904-9924.
9. *J. Chem. Phys.* **2016**, 144, 214110.
10. *J. Chem. Phys.* **2018**, 148(24), 241736.
11. *J. Chem. Phys.* **1980**, 72, 650-654.
12. *J. Comp. Chem.* **1983**, 4 (3), 294-301.
13. *J. Nat. Prod.* **2019,** 82(8), 2299-2306.
14. *Nat. Commun.* **2021**, 12(1) 7273. (SpookyNet).
15. *J. Comp. Chem.* **2025**, 46(1), 70016. (CorrectedMMFFEnergies).
16. *J. Chem. Inf. Model.* **2025**, 65(5), 2314-2321. (EstimatedDFTGeometries).
17. *Molecules.* **2023**, 28(6), 2449.
18. *J. Chem. Theory. Comput.* **2013**, 9(5) 2151-2155.
19. *Chem. Phys. Lett.* **1997**, 281, 130-134.
20. *J. Comp. Chem.* **2025,** 46(12), 700129. (EstimatedDFTEnergies).
21. *J. Am. Chem. Soc.* **1990**, 112, 23, 8251–8260.
22. *J. Phys. Chem. A* **1999**, 103, 36, 7357–7363.
23. *Chem. Rev.* **1999**, 99, 1, 293–352.
24. *Angew. Chem.* **2004**, 116 4585-4589.
25. *Chem. A Eur. J.* **2006**, 12, 5514–5525.
26. *Chem. Rev.* **2012**, 112, 1839–1862.
27. *Nat. Protoc.* **2014**, 9, 643–660.
28. *J. Nat. Prod.* **2015**, 78, 7, 1505–1510.
29. *Chem. Eur. J.* **2016**, 22, 12246–12261.
30. *Molecules*. **2017**, 22(4), 521-526.
31. *Acc. Chem. Res.* **2020**, 53, 9, 1922–1932.
32. *Org. Chem. Front.* **2021**, 8, 2019-2058.
33. *Molecules.* **2024**, 29(2), 336.
34. *J. Phys. Chem. A* **2021**, 125, 28, 6029–6041.
35. *Chem. Lett.* **2022**, 51(11), 1080-1082.
36. *J. Nat. Prod.* **2023**, 86, 10, 2294–2303.
37. *J. Agric. Food Chem.* **2023**, 71, 36, 13338–13345.
38. *Biomolecules.* **2024**, 14(7), 780.
39. *J. Am. Chem. Soc.* **2025**, 147, 1, 498–509.
40. *Nucleic Acids Res.* **2022**, 50, d665-d667.
41. *NPD.* ***Spartan'24 v.1.3.0*** **2025**, Wavefunction, Inc., Irvine, CA USA.

Updated May 2025