Supporting Information

Density Functional Theory (DFT) calculations were carried out to determine the Stark splitting of CO in a variety of environments. Calculations were performed with single and multiple hydrogen bonding groups and CO. In the model system comprising a single hydrogen bonding group with CO, we find that the frequencies tend to be both split and shifted. Hydrogen bonding of the type X-H···O-C tends to have a lower frequency than free CO, while X-H…C-O tends to have a higher frequency. This result is consistent with the vibrational Stark effect if we imagine the X-H dipole to substitute for an externally applied electric field. Clearly, the single-hydrogen bond model does not account for the overall shift of the C-O frequency to lower values than free CO (2143 cm^{-1}) in different media. Polarization effects must be included that provide a model of solvation of CO. The effect of the porphyrin ring and other groups surrounding the CO molecule is likely to shift the average frequency to lower values. The significance of the calculations is that we can systematically study the different interactions, which give rise to the observed Stark splitting.

To this end, we have performed the following studies:
1. Calculation of the vibrational Stark effect on CO
2. X-H···CO and X-H···OC at the equilibrium geometry (X = CH_3, C_6H_5, Im, OH)
3. X-H···CO and X-H···OC as a function of distance (X = CH_3, C_6H_5, Im, OH)
4. X-H···CO···H-Y and X-H···OC···H-Y (X = CH_3, Y = CH_3 and X = Im, Y = CH_3)
5. X-H···CO and X-H···OC (X = CH_3, Im) on a porphine ring

General Considerations

The quality of the density functional theory (DFT) calculation can be gauged by determining the ground state properties of CO. In the following sections, CO will be treated as a test molecule whose frequency is altered depending on the hydrogen bonding geometry or externally applied electric field. The following ground state properties are considered here:
1. Vibrational frequency
2. Anharmonicity
3. Ground state dipole moment
4. Equilibrium bond length

Within the harmonic approximation, the calculated wavenumber of the CO stretching vibration is 2140.4 cm^{-1} with an intensity of 1.51 km/mol. The calculated bond length is d(C-O) = 1.1403 Å. A potential energy surface along the C-O coordinate is plotted in Figure S1. The calculated surface is fitted to a quartic polynomial and the terms in the polynomial are used to generate the anharmonic wavefunctions and energies. For example, when corrected for 15 cm^{-1} anharmonicity, the calculated wavenumber is actually 2125.4 cm^{-1}. If a second polarization function is added to the basis set (38 basis functions for CO instead of 28 basis functions for DNP) the calculated frequency is 2148.0 cm^{-1} and the calculated bond length is d(C-O) = 1.1372 Å. The anharmonicity is essentially unchanged in this calculation so that the corrected wavenumber is 2133 cm^{-1}. Table S1 shows a comparison of the calculated and experimental values for CO. Although the DNPP calculation has better agreement with the experiment, the DNP basis set was used consistently due to the size of constraint of the largest system studied that includes an iron porphine.

Table S1. Calculated and experimental CO stretching wavenumbers, anharmonicities, dipole moments and bond lengths for CO.

	ν_{CO} (cm^{-1})	x_{CO} (cm^{-1})	μ (D)	d(C–O) (Å)
DNP	2125	15	-0.09	1.140
DNPP	2133	15	-0.13	1.137
TN3P	2153	15	-0.20	1.139
Experiment	2143	15	-0.15	1.129

The dipole moment of CO has been used a litmus test for quantum chemical calculations for many years. It is quite small (i.e. –0.15 Debye compared to 1.85 Debye for HF). The experimentally measured dipole moment also has an unexpected polarity, with the negative end being directed towards the carbon rather than the more electronegative element oxygen. The DFT calculation obtains the correct sign for the dipole moment. Significant improvement is observed if an additional polarization function is added (DNPP). The change in dipole moment can be compared in a calculation that includes an electric field term in the hamiltonian (Vibrational Stark effect calculation discussed below). However, the dipole moment cannot be compared in the various models since the dipole moment in a DFT calculation is calculated over the entire electron density. For example, if CO is hydrogen-bonded to water, the calculated dipole moment will be that of the system CO…H-O-H. In other words, it will be a linear combination of the CO dipole moment and the H_2O dipole moment. For this reason, it is helpful to use a charge partitioning method such as the Mulliken charge or Hirschfeld charge in order to compare the effect of an applied electric field or hydrogen bonding, respectively, on the ground state electronic properties of CO.

Qualitatively similar results were obtained for both DNP and DNPP basis sets. The most complete results were obtained using the DNP basis set. The larger TN3P basis set was used as well for CO calculations without improvement of the results. However, full calculations (*e.g.* using a porphine model described below) were not attempted using these larger basis sets DNPP and TN3P.

Calculation of the Vibrational Stark effect on CO

The vibrational Stark effect arises from the sum of electrical and mechanical anharmonicity effects. We have considered both of these effects and report the results to support the conclusions drawn in the manuscript. All calculations are based on the harmonic frequencies obtained using a DNP basis set and the Perdew-Wang GGA exchange functional (1) in the program DMol3 (2,3). The DNP basis set is a double-ζ quality basis set that has been shown to give reasonable agreement for vibrational frequencies (4,5). The vibrational frequencies can be corrected by using the calculated potential energy surface along the normal mode to obtain numerical wave functions using the Numerov-Cooley algorithm (6,7). In this method, both the eigenfunction and eigenvalue (corresponding to the square of the frequency) are obtained. Thus, a correction term can be determined. The potential energy surface and anharmonic wavefunctions for free CO are shown in Figure S1. The anharmonicity is approximately 15 cm^{-1} using the DNP basis set. Anharmonic corrections such as those shown in Figure S1 were calculated for the remaining species; all were within 1 cm^{-1} of 15 cm^{-1}. Thus, differences in the electrical anharmonicity are not responsible for

the observed Stark shifts. We attribute the Stark shifts due to hydrogen bonding to the so-called mechanical anharmonicity. Simply put, the C-O bond length is affected by the interaction of the dipole moment of the respective X-H group.
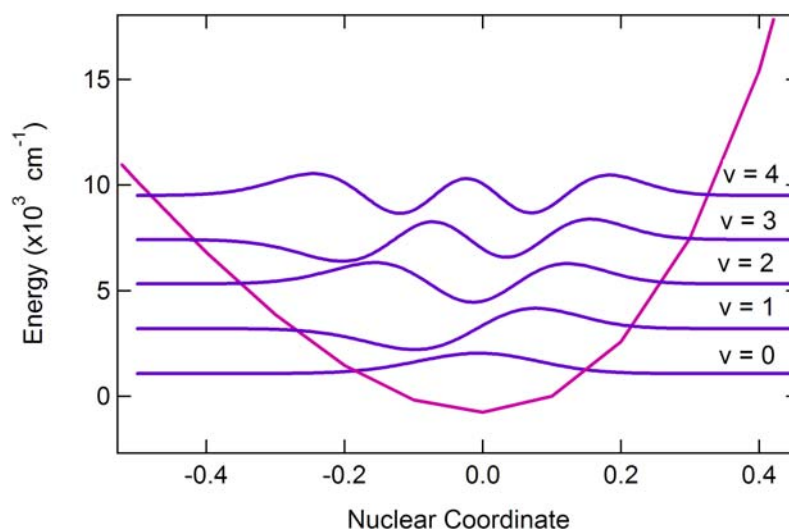

Figure S1. Calculated potential energy surface for the CO stretching vibration and the resulting anharmonic wavefunctions. Their offsets correspond to the energy eigenvalues of the anharmonic oscillator. Wavefunctions and offsets were calculated using the Numerov-Cooley algorithm.

The electrical anharmonicity of the CO oscillator was calculated using DFT methods from the vibrational frequency as a function of applied electric field ranging in field strength from –0.01 to 0.01 in atomic units. This corresponds approximately to $\pm 5.3 \times 10^6$ V/cm. The results are presented in Table S2.

Based on this calculation, we obtain the following correlations:

$$d\ (\text{Å}) = 1.14\ (\pm 0.000102) - F(\text{a.u.}) \cdot 0.33879\ (\pm 0.0169) \tag{S1}$$

and

$$\nu_{CO}\ (\text{cm}^{-1}) = 2143.9 \pm 0.948 + F(\text{a.u.}) \cdot 3180.6 \pm 156. \tag{S2}$$

The correlation between the frequency (actually wavenumber) and the bond length is given in Figure S2. The correlation shown in Figure S2 is represented by the fitted line; the parameters are given in eq. S3.

$$\nu_{CO}\ (\text{cm}^{-1}) = 12840\ (\pm 27.9) - d\ (\text{Å}) \cdot 9382.8\ (\pm 24.5) \tag{S3}$$

Table S2. Calculated values of CO stretching wavenumber, bond length and Mulliken charge at various values of an applied electric field. The applied electric field is given in atomic units. The Mulliken charge is given for carbon [q(C)]; the one for oxygen is equal and opposite in sign.

| Field (au)	v_{CO} (cm^{-1})	d(C-O) (Å)	q(C)
-0.01	2111.3	1.1435	0.145
-0.009	2114.7	1.1431	0.141
-0.008	2118.1	1.1427	0.137
-0.007	2121.5	1.1424	0.133
-0.006	2124.8	1.1420	0.128
-0.005	2128.1	1.1416	0.124
-0.004	2131.4	1.1413	0.12
-0.003	2127.4	1.1417	0.117
-0.002	2134.6	1.1409	0.112
-0.001	2141.9	1.1401	0.107
0	2140.4	1.1403	0.104
0.001	2156.5	1.1386	0.098
0.002	2163.7	1.1378	0.094
0.003	2153.3	1.1389	0.091
0.004	2156.2	1.1386	0.086
0.005	2159.3	1.1383	0.082
0.006	2162.1	1.1380	0.078
0.007	2165	1.1377	0.074
0.008	2167.7	1.1374	0.069
0.009	2170.4	1.1372	0.065
0.01	2173	1.1369	0.061
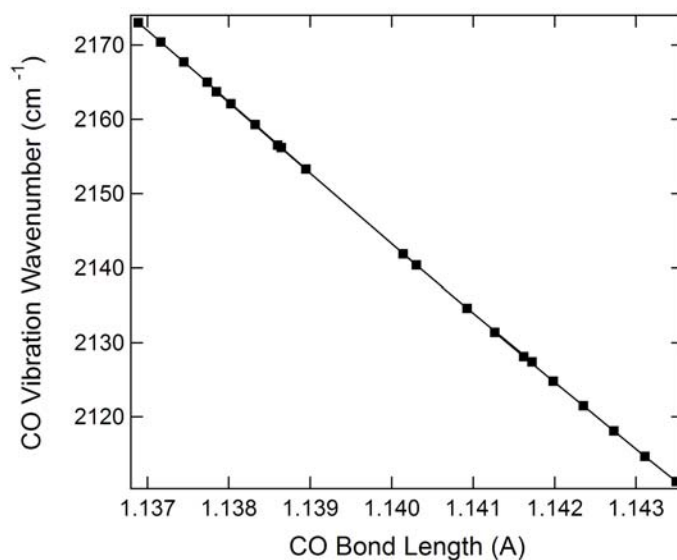
Figure S2. Correlation between CO bond length and wavenumber obtained at different electric field strengths.

Calculations of Geometry-Optimized Hydrogen Bonded Adducts with CO

Geometry optimizations were performed for each hydrogen-bonding adduct with no constraints. The vibrational wavenumbers, C–O bond lengths and hydrogen bonding geometry are compiled in Table S3. From the calculations, we see that the Stark splitting for the two orientations (CO and OC), corresponding conceptually to two polarities of an applied electric field, depend on the chemical identity of the hydrogen bonding group. The magnitude of the splitting decreases in the sequence $H_2O \gg Im > CH_3 > C_6H_6$. According to this calculation, the splitting by imidazole is 6 cm^{-1} whereas that of methane is 5 cm^{-1}.

Table S3. Calculated CO stretching wavenumbers and hydrogen bonding geometries for adducts of a single hydrogen-bonding group with CO. The Mulliken charges are presented in columns 6 and 7.

System	ν_{CO} (cm^{-1})	d(C–O) (Å)	d(H…OC) (Å)	θ(H-O-C) (Å)	q(C)	q(O)
Im-H⋯CO	2151.6	1.1411	3.50	8.2	0.122	-0.103
Im-H⋯OC	2157.5	1.1410	3.49	7.6	0.121	-0.103
CH_3-H⋯CO	2154.9	1.1403	3.76	19.3	0.101	-0.105
CH_3-H⋯OC	2149.9	1.1392	3.84	6.7	0.094	-0.095
HO-H⋯CO	2168.8	1.1372	3.39	7.8	0.110	-0.088
HO-H⋯OC	2150.9	1.1405	3.47	3.2	0.110	-0.106
C_6H_5-H⋯CO	2149.4	1.1403	3.79	15.4	0.111	-0.101
C_6H_5-H⋯OC	2145.4	1.1392	3.77	7.5	0.098	-0.096

The calculated frequency shifts in Table S3 do not agree with the calculation of the CO frequency as a function of distance presented below in Fig. S3 even at comparable distances. These calculations are not the same since the CO…H or OC…H bond distance was fixed in the calculations as a function of distance and these all geometric coordinates were allowed to optimize for calculations carried out in Table S3. For reasons that are not entirely clear the distances are significantly shorter (~0.003 Å) in the constrained calculation for the orientation OC…H compared to the fully optimized geometry. We have not been able to explain this effect and we have used the fully optimized values for comparisons in the manuscript. The rationale is that we do not have a method for arbitrarily choosing the appropriate distance for comparison. Thus, the calculations as a function of distance are included here for completeness sake, but were not applied to the discussion in the manuscript.

Calculations of Hydrogen-Bonded Adducts with CO as a Function of Distance

Calculations were also carried out as a function of hydrogen bonding distance between CO and X-H, with X-H = imidazole, benzene, methane and water. These results are shown in Figure S3. In these calculations, the distance between the hydrogen of X-H and the closest atom of the diatomic (either C or O depending on whether the geometry is X-H···C-O or X-H···O-C) was fixed and the remaining atoms were allowed to geometry optimize.
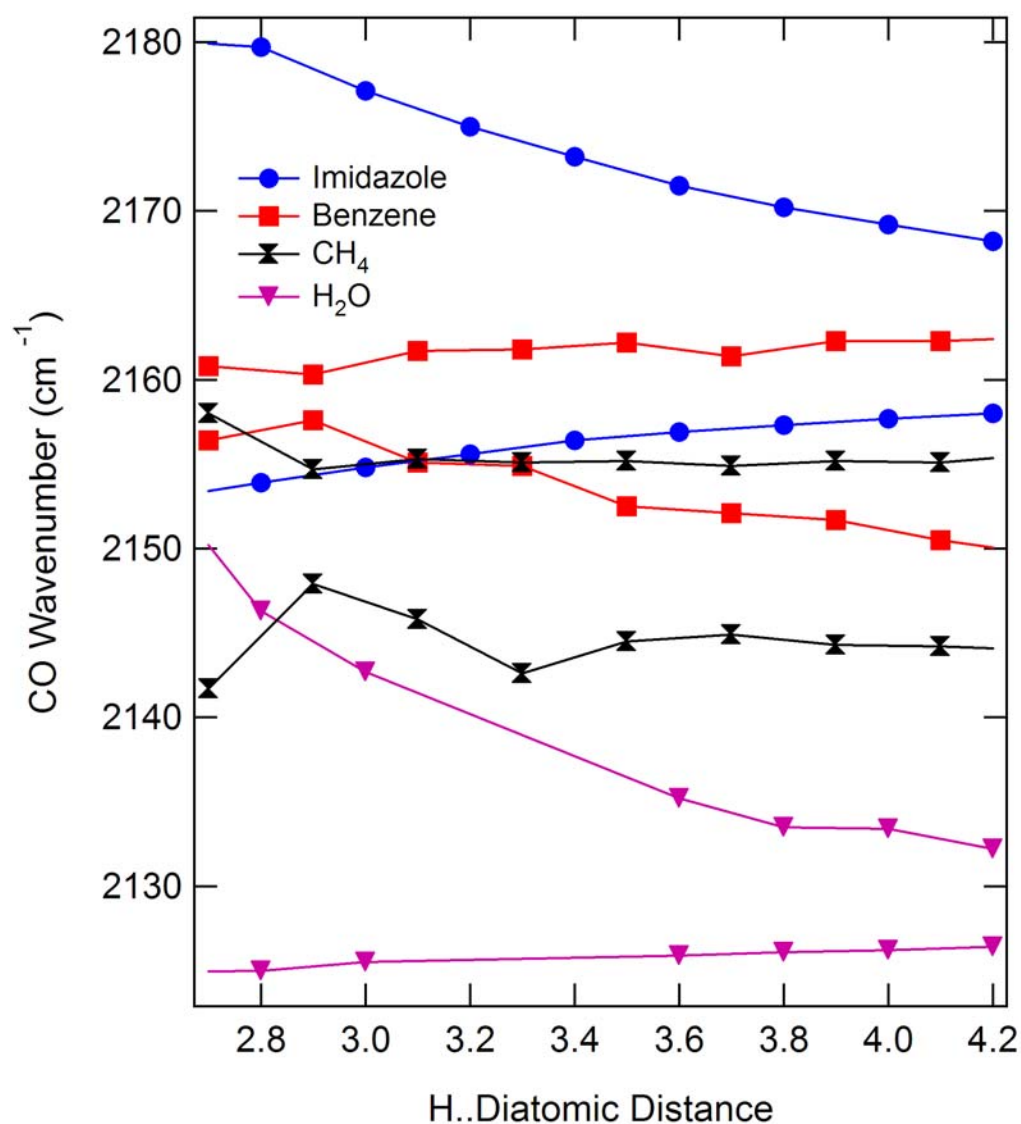

Figure S3. CO stretching frequencies for the X-H – CO and X-H – OC systems as a function of the hydrogen bonding distance (X = H_2O, CH_4, imidazole, benzene). The X-H – CO species always has the higher frequency.

For imidazole, the CO Stark splitting shows significant variation with hydrogen bonding distance, ranging from 28 to 10 cm^{-1} (Figure S4). Similar results are obtained for H_2O hydrogen bonding to CO. On the other hand, CH_4 hydrogen bonding appears to be relatively constant as a function of distance over the range studied. There is significant charge asymmetry in the CO induced by hydrogen bonding. These studies raise the issue of whether the model of a single hydrogen bond suffices for a CO molecule in an environment where multiple hydrogen bonding groups may be present.
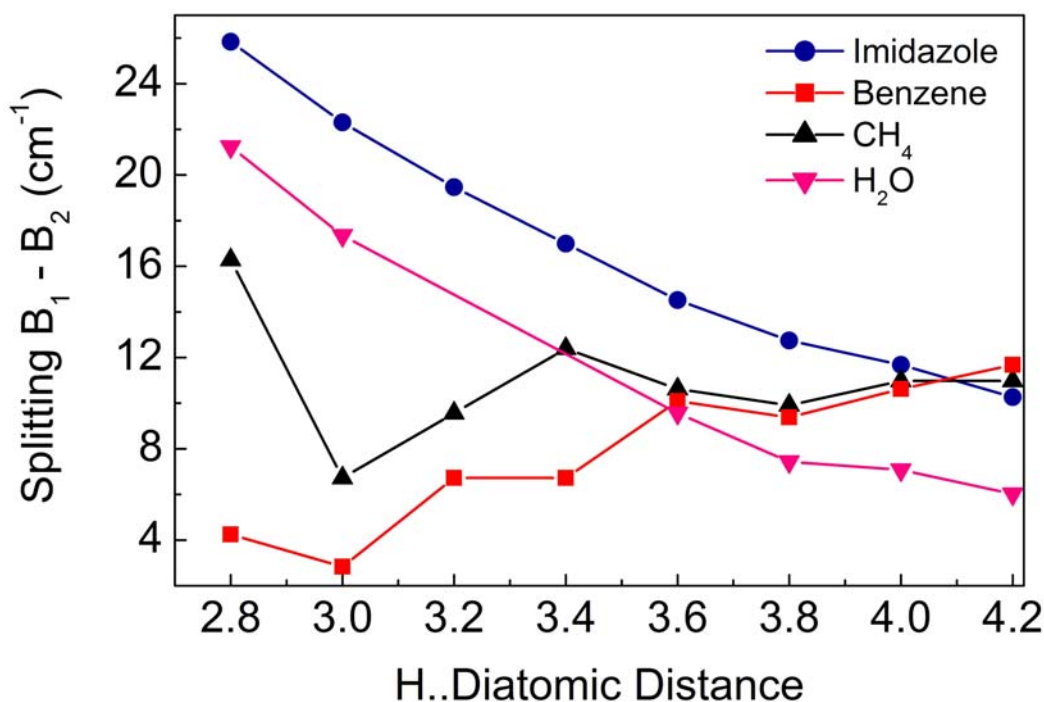
Figure S4: Splitting between the CO stretching bands B_1 and B_2 for all four model systems.

Studies of Double-Hydrogen Bonded Systems

A more realistic model of the hydrogen bonding in the docking site of myoglobin might be obtained by using two hydrogen-bonding groups. The models for this calculation are presented in Table S4.

The ordering of Stark splitting is $Im > H_2O >> C_6H_6$. By symmetry, there is no Stark splitting for the methane system (CH_3-H...CO…H-CH_3). Even the double hydrogen-bonded model system presents issues that need to be resolved. First, the calculated wavenumbers are consistently higher than for free CO. This result is consistent with the bond lengths, which are shorter than that of free CO. Second, there is a significant charge asymmetry. This is an important issue because such a large charge asymmetry indicates that the intensity of the infrared absorption band will be relatively large. Typical values of the transition moment calculated using the above methods range from 80 – 110 km/mol. This is roughly 10 – 20% of the value for CO bound to iron. According to the experiment, the intensity of CO in the docking site is approximately 5% that of bound CO. The resolution to these issues is to consider the role of the porphine.

Table S4. Calculated CO stretching wavenumbers and bond lengths for adducts of two hydrogen-bonding groups with CO. The Mulliken charges q(C) and q(O) are also given.

System	ν_{CO} (cm^{-1})	d(C–O) (Å)	q(C)	q(O)
Im-H···CO···H-CH$_3$	2178.6	1.1382	0.138	-0.078
Im-H···OC···H-CH$_3$	2150.6	1.1409	0.134	-0.099
C$_6$H$_5$-H···CO···H-CH$_3$	2148.6	1.1392	0.119	-0.088
C$_6$H$_5$-H···OC···H-CH$_3$	2147.4	1.1388	0.124	-0.089
HO-H···CO···H-CH$_3$	2147.4	1.1404	0.126	-0.101
HO-H···OC···H-CH$_3$	2124.6	1.1401	0.128	-0.093
CH$_3$-H···CO···H-CH$_3$	2149.6	1.1392	0.120	-0.092

Model Systems that include Porphine

The models that permit comparison had a single hydrogen-bonding group with the CO placed above a porphine ring (see last two sets of model coordinates on p. S12-S16). The effect of hydrogen bonding by imidazole and methane is compared in Table S5. It is clear from the Table that the charge asymmetry is significantly reduced and that the frequency of the vibrations is lower. Moreover, the range of the observed wavenumber for the imidazole model is not extremely far from experiment.

A further test calculation was carried out for high spin iron (S = 2). This calculation required the use of the THERMAL option for DFT. The THERMAL option allows for partial occupancy of electronic levels weighted according to the Grand Canonical Ensemble at a defined electronic temperature (corresponding to 0.02 Ha). The frequencies obtained by this method are shifted by nearly 100 cm^{-1} to lower energy compared to the S = 0 calculation at the same geometry. The origin of this effect arises most likely from the more extended core size of the iron. The electrons occupy the $d_{x^2-y^2}$ and d_{z^2} orbitals. In order to obtain a more realistic model, the iron would have to be permitted to relax out of the plane of the heme. It is well known that the geometry of the heme iron is altered by this relaxation in the deoxy form (S = 2). However, for the present purposes, it suffices to point out that, in spite of the over 100 cm^{-1} shift in energy, the ordering of the shifts for both orientations of the CO is the same as for the S = 0 calculation. In other words, the hypothesis regarding the electrostatic effect of the nitrogen as a hydrogen bonding interaction with free CO is substantiated by this calculation as well.

The N$_\varepsilon$-tautomer of the imidazole ring of histidine was also used in model calculations, as shown in Table S5. In this tautomer, the lone pair (LP) of the imidazole is directed towards the CO rather than the hydrogen in the N-H…CO geometry considered in other models. Although the values of the frequencies are similar to those of the N$_\delta$-tautomer, the ordering of the frequencies is reversed. In other words, the isomer with the oxygen of CO closest to the lone pair (Im-LP…OC) has a lower frequency than the inverted orientation for CO (Im-LP…CO). The ordering of shifts is exactly opposite to that calculated for the hydrogen bonding models, as expected according to the vibrational Stark effect model.

Table S5. Calculated CO stretching wavenumbers and CO bond lengths for adducts of a single hydrogen-bonding group with CO on iron porphine. The Mulliken charge is presented in columns 4 and 5.

System	v_{CO} (cm^{-1})	d(C-O) (Å)	q(C)	q(O)	Spin (S)
Im-H…CO	2023.7	1.1475	---	---	2
Im-H…OC	2019.9	1.1500	---	---	2
Im-LP^a…CO	2120.0	1.1427	---	---	0
Im-LP^a…OC	2132.0	1.1409	---	---	0
Im-H…CO	2129.1	1.1426	0.093	-0.104	0
Im-H…OC	2122.5	1.1414	0.117	-0.117	0
CH$_3$-H…CO	2156.0	1.1409	0.118	-0.113	0
CH$_3$-H…OC	2159.8	1.1406	0.104	-0.103	0

[a] LP is the lone pair in the N_ε-tautomer that interacts with the CO.

A number of other models were tried. There is an inherent problem in the models since constrained geometry optimization must be used. The reason for this is that the CO will simply recombine with the iron if allowed to find the lowest energy structure. The calculations attempt to trap the system in a local minimum. Artificial models that place different hydrogen bonding groups on the porphine ring suffer from the disadvantage the there can be electronic effects between the groups, local maxima (saddle points) and otherwise incorrect features that are not eliminated by the geometry optimization due to the constraint.

Coordinates and Structural Data for Model Systems

The coordinates are listed for the geometry optimized structures used for the calculations of the dependence of the vibrational frequency on the hydrogen bonding geometry.

```
1. Single Hydrogen Bonding Models

CO…Imidazole

C1      1.239092686   -1.643824862    0.000000000 HIS  64    c     C    0.000
H2      1.569027283   -2.677299589    0.000000000 HIS  64    h     H    0.000
N3      2.141108154   -0.603035523    0.000000000 HIS  64    n     N    0.000
C4     -0.053230106   -1.167485513    0.000000000 HIS  64    c     C    0.000
H5     -1.017588838   -1.658549530    0.000000000 HIS  64    h     H    0.000
C6      1.410040890    0.495772401    0.000000000 HIS  64    c     C    0.000
H7      1.787854957    1.512444195    0.000000000 HIS  64    h     H    0.000
N8      0.070931798    0.207398112    0.000000000 HIS  64    n     N    0.000
H9     -0.692178722    0.875596480    0.000000000 HIS  64    h     H    0.000
C56    -3.762953145    2.534207383    0.000000000 CO_   2    c     C    0.000
O57    -2.696805299    2.127497918    0.000000000 CO_   2    o     O    0.000


CO…H₂O

H1      1.853975276   -0.087870656    0.181783821 WAT   1    h     H    0.000
O2      1.284775407   -0.771775581   -0.204575460 WAT   1    o     O    0.000
H3      0.392199173   -0.395216212   -0.155602207 WAT   1    h     H    0.000
C4     -2.845579771    0.858215525   -0.029164753 CO_   2    c     C    0.000
O5     -1.765940888    0.490376213   -0.026916221 CO_   2    o     O    0.000


CO…CH₄

C1      1.225780155    0.004950543    0.100222070 METH  1    c     C    0.000
H2      1.585241823    1.039323310    0.126142795 METH  1    h     H    0.000
H3      1.233159088   -0.409831702    1.113962372 METH  1    h     H    0.000
H4      1.881792919   -0.591540715   -0.542623550 METH  1    h     H    0.000
H5      0.205808467   -0.017723795   -0.295555283 METH  1    c     H    0.000
C6     -3.629074468   -0.007232425   -0.165978131 CO__  2    c     C    0.000
O7     -2.502707986   -0.017945740   -0.336170273 CO__  2    o     O    0.000


CO…Benzene

C1      0.063061082    1.194145210    0.058710504 BENZ  1    c     C    0.000
H2     -0.508676373    2.120903644    0.027518414 BENZ  1    h     H    0.000
C3      1.396377865    1.211008684    0.479927081 BENZ  1    c     C    0.000
H4      1.863063868    2.148591438    0.780415924 BENZ  1    h     H    0.000
C5      2.130033182    0.021388321    0.519079587 BENZ  1    c     C    0.000
H6      3.169304638    0.033320394    0.846450883 BENZ  1    h     H    0.000
C7      1.530700140   -1.183803006    0.140294272 BENZ  1    c     C    0.000
H8      2.103484893   -2.109791428    0.172898633 BENZ  1    h     H    0.000
C9      0.197364009   -1.200394532   -0.280834573 BENZ  1    c     C    0.000
H10    -0.268555082   -2.138841123   -0.580030878 BENZ  1    h     H    0.000
C11    -0.536827779   -0.010891031   -0.320335892 BENZ  1    c     C    0.000
H12    -1.575885770   -0.023071702   -0.644478656 BENZ  1    h     H    0.000
C13    -5.343394225   -0.031059062   -0.504872120 CO__  2    c     C    0.000
O14    -4.220050446   -0.031505334   -0.694742991 CO__  2    o     O    0.000
```

2. Double Hydrogen Bonding Models

CH₄...CO...CH₄
```
C1     -3.140168861     1.514590013    -1.399767311 METH 1      c      C    0.000
H2     -3.213115285     2.545110378    -1.043350136 METH 1      h      H    0.000
H3     -2.086571457     1.250398645    -1.529101644 METH 1      h      H    0.000
H4     -3.610930325     0.845466736    -0.673902178 METH 1      h      H    0.000
H5     -3.655307852     1.422561668    -2.359287475 METH 1      h      H    0.000
C6      2.842800137    -1.754749510     1.799926386 METH 2      c      C    0.000
H7      3.037538724    -1.162564537     2.699212353 METH 2      h      H    0.000
H8      2.034633581    -2.463598908     2.000406127 METH 2      h      H    0.000
H9      3.747138918    -2.301036006     1.516863753 METH 2      h      H    0.000
H10     2.550648007    -1.089177567     0.985358325 METH 2      h      H    0.000
C11     0.465217754     0.906738662    -1.384188401 CO__ 3      c      C    0.000
O12     1.028116658     0.286260426    -0.612169798 CO__ 3      o      O    0.000
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CH₄...CO... Im

```
C1     -3.603640939     3.366044401     2.298981777 METH 1      c      C    0.000
H2     -3.682573503     4.399384783     2.646434603 METH 1      h      H    0.000
H3     -2.549874956     3.094356700     2.195020665 METH 1      h      H    0.000
H4     -4.085546786     2.700084933     3.020394521 METH 1      h      H    0.000
H5     -4.101243569     3.269649427     1.329882486 METH 1      h      H    0.000
C6      1.997624802    -3.310468368    -2.020894841 HIS  64     c      C    0.000
H7      1.836059672    -4.249224118    -2.536761366 HIS  64     h      H    0.000
N8      3.266417914    -2.861480468    -1.732930458 HIS  64     n      N    0.000
C9      1.051974041    -2.425890532    -1.566823150 HIS  64     c      C    0.000
H10    -0.028908607    -2.422119257    -1.599277770 HIS  64     h      H    0.000
C11     3.093756808    -1.713376988    -1.108233775 HIS  64     c      C    0.000
H12     3.878033633    -1.071569551    -0.725776495 HIS  64     h      H    0.000
N13     1.767317448    -1.402095725    -0.982129206 HIS  64     n      N    0.000
H14     1.375794396    -0.576900915    -0.545453745 HIS  64     h      H    0.000
C15    -0.386047847     2.040391572     0.899454400 CO_  2      c      C    0.000
O16     0.170857493     1.163214106     0.428112353 CO_  2      o      O    0.000
```

Im...CO...CH₄

```
C1     -3.603640747     3.366004634     2.298790431 METH 1      c      C    0.000
H2     -3.682559057     4.399164211     2.646400908 METH 1      h      H    0.000
H3     -2.549897723     3.094614199     2.194909657 METH 1      h      H    0.000
H4     -4.085567084     2.700116920     3.020370583 METH 1      h      H    0.000
H5     -4.101239421     3.269813460     1.330236541 METH 1      h      H    0.000
C6      1.997928996    -3.310827385    -2.020938261 HIS  64     c      C    0.000
H7      1.836448723    -4.249355369    -2.536935847 HIS  64     h      H    0.000
N8      3.266761135    -2.862324248    -1.733220484 HIS  64     n      N    0.000
C9      1.052490178    -2.425617634    -1.566525057 HIS  64     c      C    0.000
H10    -0.028823898    -2.421982601    -1.599468881 HIS  64     h      H    0.000
C11     3.092971148    -1.713740092    -1.108222601 HIS  64     c      C    0.000
H12     3.877964786    -1.071540666    -0.726159394 HIS  64     h      H    0.000
N13     1.767892856    -1.402387523    -0.982414469 HIS  64     n      N    0.000
H14     1.374270026    -0.575227625    -0.544072248 HIS  64     h      H    0.000
O15    -0.384913135     2.038998904     0.899463834 CO_  2      o      O    0.000
C16     0.169913250     1.164290817     0.427785291 CO_  2      c      C    0.000
```

Im…Porphine…CH$_4$…CO

C1	3.791516934	0.136178396	0.558642550	HIS	64	c	C	0.000
H2	3.584996047	-0.071462200	1.614356536	HIS	64	h	H	0.000
H3	3.530848549	-0.738539680	-0.045965978	HIS	64	h	H	0.000
H4	3.191854641	0.992633582	0.232936975	HIS	64	h	H	0.000
H5	4.855924082	0.364181847	0.429827499	HIS	64	h	H	0.000
C6	-4.476497682	-0.360384293	-0.520911452	HIS	93	c	C	0.000
H7	-5.436258588	-0.700273669	-0.884976187	HIS	93	h	H	0.000
N8	-4.355346151	0.607172008	0.456011519	HIS	93	n	N	0.000
H9	-5.117404314	1.086439878	0.920686438	HIS	93	h	H	0.000
C10	-3.193805543	-0.714572730	-0.853367451	HIS	93	c	C	0.000
H11	-2.849722467	-1.439574158	-1.578428265	HIS	93	h	H	0.000
C12	-3.032487334	0.815495462	0.690800346	HIS	93	c	C	0.000
H13	-2.644494612	1.525256966	1.408519467	HIS	93	h	H	0.000
N14	-2.307295490	0.024194255	-0.093309257	HIS	93	n	N	0.000
FE15	-0.361393239	-0.035934217	-0.145518334	HEM	1H	Fe	Fe	0.000
C20	-0.290128909	2.364349437	-2.589961686	HEM	1H	c	C	0.000
H21	-0.316601158	3.129524401	-3.365515504	HEM	1H	h	H	0.000
C22	0.093952077	2.387792605	2.238092618	HEM	1H	c	C	0.000
H23	0.228634438	3.154590739	2.999140553	HEM	1H	h	H	0.000
C24	-0.253872899	-2.444771876	2.283526279	HEM	1H	c	C	0.000
H25	-0.257893143	-3.208651897	3.060092545	HEM	1H	h	H	0.000
C26	-0.318597054	-2.481267503	-2.557956913	HEM	1H	c	C	0.000
H27	-0.328230366	-3.256794710	-3.324107677	HEM	1H	h	H	0.000
N28	-0.143759069	1.963020248	-0.169335225	HEM	1H	n	N	0.000
C29	-0.179021522	2.793630659	-1.272848790	HEM	1H	c	C	0.000
C30	-0.045273348	4.172898652	-0.874572722	HEM	1H	c	C	0.000
H31	-0.036849007	5.017924276	-1.557140144	HEM	1H	h	H	0.000
C32	0.082838768	4.180092712	0.484914848	HEM	1H	c	C	0.000
H33	0.220492976	5.030026037	1.146217809	HEM	1H	h	H	0.000
C34	0.015935007	2.804859097	0.914095158	HEM	1H	c	C	0.000
N35	-0.146376464	-0.028983869	1.845574363	HEM	1H	n	N	0.000
C36	0.027871753	1.067546626	2.669654132	HEM	1H	c	C	0.000
C37	0.132795534	0.656478201	4.047668640	HEM	1H	c	C	0.000
H38	0.300302974	1.329413713	4.882845489	HEM	1H	h	H	0.000
C39	0.017258743	-0.703746032	4.061385320	HEM	1H	c	C	0.000
H40	0.071816543	-1.377308627	4.911070176	HEM	1H	h	H	0.000
C41	-0.151130342	-1.120882055	2.692270439	HEM	1H	c	C	0.000
N42	-0.291136167	-2.047359844	-0.139962398	HEM	1H	n	N	0.000
C43	-0.302249534	-2.876354442	0.964058497	HEM	1H	c	C	0.000
C44	-0.333682185	-4.261114878	0.561054926	HEM	1H	c	C	0.000
H45	-0.342182378	-5.105399940	1.244326765	HEM	1H	h	H	0.000
C46	-0.334038712	-4.273509746	-0.803565579	HEM	1H	c	C	0.000
H47	-0.345313033	-5.130427771	-1.471294693	HEM	1H	h	H	0.000
C48	-0.309668524	-2.894897314	-1.230734531	HEM	1H	c	C	0.000
N49	-0.299402326	-0.054863023	-2.157023726	HEM	1H	n	N	0.000
C50	-0.313912928	-1.158578941	-2.988523022	HEM	1H	c	C	0.000
C51	-0.345914152	-0.752429546	-4.372097125	HEM	1H	c	C	0.000
H52	-0.344813367	-1.433863634	-5.218031797	HEM	1H	h	H	0.000
C53	-0.360152680	0.612977406	-4.380293603	HEM	1H	c	C	0.000
H54	-0.373114560	1.282570822	-5.235588319	HEM	1H	h	H	0.000
C55	-0.328212792	1.037345190	-3.001740739	HEM	1H	c	C	0.000
C56	3.179114218	0.101219379	-3.903702150	CO_	2	c	C	0.000
O57	3.088233538	0.037438087	-2.769227807	CO_	2	o	O	0.000
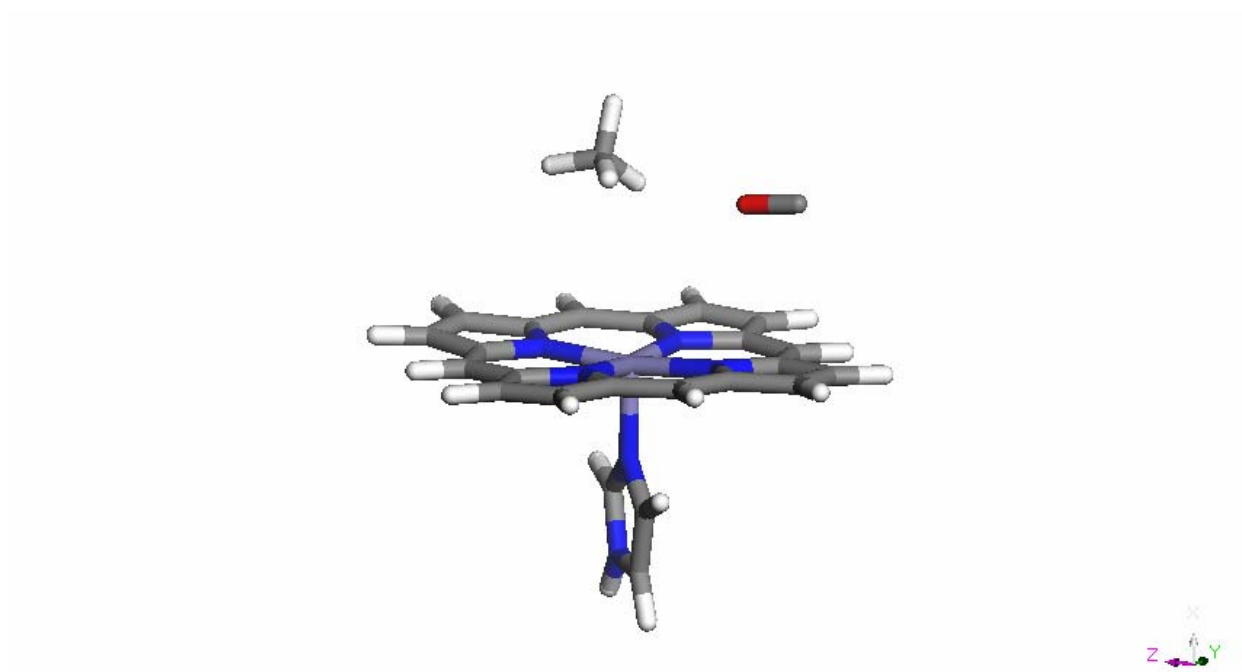
Im…Porphine…Im…CO

C1	4.787083465	-0.154578019	2.479955298	HIS	64	c	C	0.000
H2	5.020909541	-0.333078818	3.522491194	HIS	64	h	H	0.000
N3	5.777236376	0.110547460	1.559783323	HIS	64	n	N	0.000
C4	3.548829470	-0.146610476	1.886720284	HIS	64	c	C	0.000
H5	2.546028108	-0.302404649	2.261933873	HIS	64	h	H	0.000
C6	5.143207949	0.278899667	0.414254651	HIS	64	c	C	0.000
H7	5.601713782	0.504108958	-0.540430251	HIS	64	h	H	0.000
N8	3.791516934	0.136178396	0.558642550	HIS	64	n	N	0.000
H9	3.085566435	0.223089106	-0.186327354	HIS	64	h	H	0.000
C10	-4.471759808	-0.283777122	-0.413280013	HIS	93	c	C	0.000
H11	-5.450335178	-0.610943978	-0.730758430	HIS	93	h	H	0.000
N12	-4.299141925	0.691481146	0.546939351	HIS	93	n	N	0.000
H13	-5.033750939	1.184080386	1.035827304	HIS	93	h	H	0.000
C14	-3.212490879	-0.664067654	-0.789173640	HIS	93	c	C	0.000
H15	-2.899483032	-1.401390048	-1.514816679	HIS	93	h	H	0.000
C16	-2.967182662	0.880208347	0.731279931	HIS	93	c	C	0.000
H17	-2.533608396	1.585224697	1.426764418	HIS	93	h	H	0.000
N18	-2.288819038	0.066383584	-0.069377532	HIS	93	n	N	0.000
FE19	-0.361393239	-0.035934217	-0.145518334	HEM	1H	Fe	Fe	0.000
C20	-0.173501071	2.357482560	-2.582615229	HEM	1H	c	C	0.000
H21	-0.154565082	3.121775435	-3.356792170	HEM	1H	h	H	0.000
C22	0.038117689	2.385208676	2.247682836	HEM	1H	c	C	0.000
H23	0.138375183	3.155141056	3.009426319	HEM	1H	h	H	0.000
C24	-0.271301910	-2.441107581	2.283032774	HEM	1H	c	C	0.000
H25	-0.283264612	-3.204416713	3.058422298	HEM	1H	h	H	0.000
C26	-0.437977235	-2.472573498	-2.546729983	HEM	1H	c	C	0.000
H27	-0.507262407	-3.244282230	-3.310834623	HEM	1H	h	H	0.000
N28	-0.097651283	1.949494070	-0.163981914	HEM	1H	n	N	0.000
C29	-0.082901617	2.782083243	-1.267385958	HEM	1H	c	C	0.000
C30	0.050960751	4.156097419	-0.866476201	HEM	1H	c	C	0.000
H31	0.103728938	4.997017748	-1.549042387	HEM	1H	h	H	0.000

S13

C32	0.118027589	4.165506868	0.492986186	HEM	1H	c	C	0.000
H33	0.229152228	5.015351717	1.156456526	HEM	1H	h	H	0.000
C34	0.019384596	2.795596886	0.922783314	HEM	1H	c	C	0.000
N35	-0.146376464	-0.028983869	1.845574363	HEM	1H	n	N	0.000
C36	-0.031099454	1.068242051	2.679227791	HEM	1H	c	C	0.000
C37	0.018179204	0.656183933	4.058020799	HEM	1H	c	C	0.000
H38	0.119972992	1.329277613	4.902190764	HEM	1H	h	H	0.000
C39	-0.076086607	-0.702840442	4.065290060	HEM	1H	c	C	0.000
H40	-0.062949982	-1.373739755	4.917958791	HEM	1H	h	H	0.000
C41	-0.176931059	-1.120888939	2.692869558	HEM	1H	c	C	0.000
N42	-0.322709970	-2.037841255	-0.135626197	HEM	1H	n	N	0.000
C43	-0.331320492	-2.869102544	0.966831319	HEM	1H	c	C	0.000
C44	-0.402729477	-4.249267999	0.565104980	HEM	1H	c	C	0.000
H45	-0.416999953	-5.093307871	1.246863504	HEM	1H	h	H	0.000
C46	-0.447842566	-4.260841527	-0.794725524	HEM	1H	c	C	0.000
H47	-0.503357185	-5.115928054	-1.459643153	HEM	1H	h	H	0.000
C48	-0.399923717	-2.885722880	-1.223167809	HEM	1H	c	C	0.000
N49	-0.294467198	-0.054308542	-2.145785855	HEM	1H	n	N	0.000
C50	-0.383538862	-1.154016072	-2.977193184	HEM	1H	c	C	0.000
C51	-0.408484048	-0.745714801	-4.357172015	HEM	1H	c	C	0.000
H52	-0.468630461	-1.422452813	-5.202221944	HEM	1H	h	H	0.000
C53	-0.336426684	0.615322287	-4.365906313	HEM	1H	c	C	0.000
H54	-0.325343642	1.281965098	-5.221501537	HEM	1H	h	H	0.000
C55	-0.271332592	1.036629560	-2.992302969	HEM	1H	c	C	0.000
C56	2.892600723	-0.079291489	-3.888552951	CO_	2	c	C	0.000
O57	3.088233538	0.037438087	-2.769227807	CO_	2	o	O	0.000
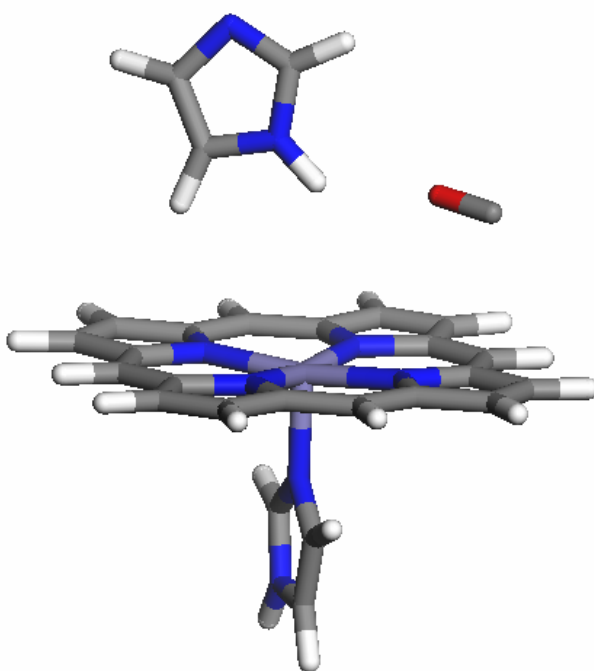
Energy Differences

The energies of the models Im…Porphine…Im…CO are -30283.40 kJ/mol for the Im-N-H…C-O orientation and -30276.79 kJ/mol for the Im-N-H…O-C orientation. This energy difference is consistent with the calculated orientation of the CO dipole as $C(\delta^-)O(\delta^+)$ presented in Table S1. The Lewis acid nature of the carbon end of the molecule is evident in its interaction with the hydrogen atom of the N_ε atom of the imidazole ring.

Basis Sets

```
The DNP basis set is comprised of the basis functions listed below.
Carbon        nbas= 1  z=  6.  7 radial functions,  e_ref= -0.0610950Ha
   n=1  L=0  occ= 2.00 e=     -10.008424Ha      -272.3432eV
   n=2  L=0  occ= 2.00 e=      -0.477668Ha       -12.9980eV
   n=2  L=1  occ= 2.00 e=      -0.162681Ha        -4.4268eV
   n=2  L=0  occ= 0.00 e=      -1.485015Ha       -40.4093eV
   n=2  L=1  occ= 0.00 e=      -1.169296Ha       -31.8182eV
   n=3  L=2  occ= 0.00 e=      -2.722082Ha       -74.0717eV
   n=3  L=2  occ= 0.00 e=      -1.383811Ha       -37.6554eV  eliminated
 Oxygen        nbas= 2  z=  8.  7 radial functions,  e_ref= -0.0607807Ha
   n=1  L=0  occ= 2.00 e=     -18.896548Ha      -514.2014eV
   n=2  L=0  occ= 2.00 e=      -0.868840Ha       -23.6424eV
   n=2  L=1  occ= 4.00 e=      -0.322562Ha        -8.7774eV
   n=2  L=0  occ= 0.00 e=      -2.144678Ha       -58.3597eV
   n=2  L=1  occ= 0.00 e=      -1.593751Ha       -43.3682eV
   n=3  L=2  occ= 0.00 e=      -2.722082Ha       -74.0717eV
   n=3  L=2  occ= 0.00 e=      -1.383811Ha       -37.6554eV  eliminated

total number of valence orbitals:    28


The DNPP basis set is comprised of the basis functions listed below.
Carbon        nbas= 1, z=   6, nrfn= 11, rcut= 20.00, e_ref= -0.046066 Ha
   n=1  L=0  occ= 2.00 e=     -10.053949Ha      -273.5820eV
   n=2  L=0  occ= 2.00 e=      -0.506579Ha       -13.7847eV
   n=2  L=1  occ= 2.00 e=      -0.196458Ha        -5.3459eV
   n=2  L=0  occ= 0.00 e=      -1.461278Ha       -39.7634eV
   n=2  L=1  occ= 0.00 e=      -1.144604Ha       -31.1463eV
   n=3  L=2  occ= 0.00 e=      -2.000000Ha       -54.4228eV
   n=4  L=3  occ= 0.00 e=      -3.125000Ha       -85.0356eV
Oxygen        nbas= 2, z=   8, nrfn= 11, rcut= 20.00, e_ref= -0.055986 Ha
   n=1  L=0  occ= 2.00 e=     -18.913382Ha      -514.6595eV
   n=2  L=0  occ= 2.00 e=      -0.880508Ha       -23.9598eV
   n=2  L=1  occ= 4.00 e=      -0.335081Ha        -9.1180eV
   n=2  L=0  occ= 0.00 e=      -1.462710Ha       -39.8024eV
   n=2  L=1  occ= 0.00 e=      -0.906180Ha       -24.6584eV
   n=3  L=2  occ= 0.00 e=      -2.722222Ha       -74.0755eV
   n=4  L=3  occ= 0.00 e=      -4.500000Ha      -122.4513eV

total number of valence orbitals:    38


The TN3P basis set is comprised of the basis functions listed below.
Carbon        nbas= 1, z=   6, nrfn= 11, rcut= 20.00, e_ref= -0.046066 Ha
   n=1  L=0  occ= 2.00 e=     -10.053949Ha      -273.5820eV
   n=2  L=0  occ= 2.00 e=      -0.506579Ha       -13.7847eV
   n=2  L=1  occ= 2.00 e=      -0.196458Ha        -5.3459eV
```

```
    n=2  L=0  occ= 0.00 e=        -1.461278Ha         -39.7634eV
    n=2  L=1  occ= 0.00 e=        -1.144604Ha         -31.1463eV
    n=3  L=2  occ= 0.00 e=        -2.000000Ha         -54.4228eV
    n=4  L=3  occ= 0.00 e=        -3.125000Ha         -85.0356eV
    n=1  L=0  occ= 0.00 e=       -12.500000Ha        -340.1425eV
    n=2  L=1  occ= 0.00 e=        -3.125000Ha         -85.0356eV
    n=4  L=2  occ= 0.00 e=        -1.531250Ha         -41.6675eV
    n=5  L=3  occ= 0.00 e=        -2.420001Ha         -65.8516eV
Oxygen        nbas=  2, z=    8, nrfn= 11, rcut= 20.00, e_ref= -0.055986 Ha
    n=1  L=0  occ= 2.00 e=       -18.913382Ha        -514.6595eV
    n=2  L=0  occ= 2.00 e=        -0.880508Ha         -23.9598eV
    n=2  L=1  occ= 4.00 e=        -0.335081Ha          -9.1180eV
    n=2  L=0  occ= 0.00 e=        -1.462710Ha         -39.8024eV
    n=2  L=1  occ= 0.00 e=        -0.906180Ha         -24.6584eV
    n=3  L=2  occ= 0.00 e=        -2.722222Ha         -74.0755eV
    n=4  L=3  occ= 0.00 e=        -4.500000Ha        -122.4513eV
    n=1  L=0  occ= 0.00 e=        -4.500000Ha        -122.4513eV
    n=2  L=1  occ= 0.00 e=        -1.125000Ha         -30.6128eV
    n=4  L=2  occ= 0.00 e=        -2.000000Ha         -54.4228eV
    n=5  L=3  occ= 0.00 e=        -2.880001Ha         -78.3688eV

total number of valence orbitals:     74
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