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FeP(Im)–AB Bonding Energies Evaluated with A Large Number of Density Functionals (P = porphine, Im = imidazole, AB = CO, NO, and O₂)

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Abstract

Sixty-four (64) density functionals, ranging from GGA, meta-GGA, hybrid GGA to hybrid meta-GGA, were tested to evaluate the FeP(Im)-AB bonding energies (E_{bond}) in the heme model complexes FeP(Im)(AB) (P = porphine, Im = imidazole, AB = CO, NO, and O₂). The results indicate that an accurate prediction of E_{bond} for the various ligands to heme is difficult with the DFT methods; usually a functional successful for one system does not perform equally well for the other system(s). Relatively satisfactory results for the various FeP(Im)-AB bonding energies are obtained with the meta-GGA functionals BLAP3 and Bm τ 1; they yield E_{bond} values of ca. 1.1, 1.2, and 0.4 eV for AB = CO, NO, and O₂, respectively, which are in reasonable agreement with experimental data (0.78 – 0.85 eV for CO, 0.99 eV for NO, and 0.44 – 0.53 eV for O₂). The other functionals show more or less deficiency for one or two of the systems. The performances of the various functionals in describing the spin-state energetics of the five-coordinate FeP(Im) complex were also examined.

Keywords

Iron porphyrin; diatomic molecules; bonding energies; DFT calculations

1. Introduction

Iron porphyrins (FePors) are biologically very interesting molecules [1] as they serve as the prosthetic group in hemoglobin (Hb) and myoglobin (Mb), as well as other hemoproteins such as peroxidases, catalases, and cytochromes. A major function of iron porphyrin in hemoproteins is the binding of axial ligands. This extra coordination is responsible for attachment of the active iron porphyrin to carrier proteins. The active center of Hb and Mb consists of iron protoporphyrin IX (FePP_{IX}) complex bound through a single, 'proximal', axial histidine (His) to the protein. This FePP_{IX}(His) moiety in Mb/Hb is also called heme. The other side of the porphyrin plane remains free to bind molecular oxygen (O₂) and other ligands. As the respiratory proteins, Hb and Mb must favor the binding of O₂ compared to CO and NO to avoid suffocation; the latter two molecules are ubiquitous in biology. The binding affinity of CO to a *model* heme is 10⁵-fold larger than that of O₂. However, this ratio is reduced by several orders of magnitude when the heme is embedded in the protein matrix. Clearly, the intermolecular interactions by the surrounding protein polypeptide assist in the discrimination against endogenous CO inhibition.

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As the first step to investigate the effects of the protein environment, an examination of independent (or free) heme(AB) molecules ($AB = CO, NO, O_2$) is of great interest. Experimentally, the first heme model is iron tetra($\alpha, \alpha, \alpha, \alpha$ -orthopivalamide)-phenylporphine ligated with 2-methylimidazole, FeTpivPP(2-MeIm), synthesized by Collman and co-workers in the 1970s [2,3]. FeTpivPP is an interesting “picket-fence” compound, having steric shielding on one side of the porphyrin and reversibly oxygenating in solution. On the theoretical side, a simple, unsubstituted iron porphine (FeP) was often adopted to model the basic iron porphyrins; FeP with an axial ligand L such as imidazole (Im), pyridine (Py), or NH_3 was used to mimic the heme. Its AB complex FeP(L)(AB) was therefore used as model for heme(AB). It has been shown that a simple metal porphine (MP) is able to mimic the essential properties of the more complicated FePPIX [4], and unsubstituted imidazole (Im) is a well-simplified model for the histidine residue attached to FePPIX [5].

One of the most important properties of heme(AB) is the heme-AB bonding energies, the magnitudes of which are the key to understanding hemoprotein functions, but they prove to be difficult to predict theoretically. While there are many theoretical studies of FeP(L)(AB) in the literature, relatively few reports were given for the FeP(L)-AB bonding energies [6–10]. Previous theoretical studies are mainly based on density functional theory (DFT), which is an attractive alternative to conventional *ab initio* methods and has become a powerful tool for accurate calculations on large systems. If one wishes to include the protein environment in quantum mechanical (QM) calculations on heme(AB), DFT appears to be the uniquely suitable method among the different quantum chemical methods. However, the accuracy of DFT calculations is dependent on the exchange-correlation (XC) potential used. To show this point, Table 1 provides a comparison of the FeP(Im)-AB bonding energies (E_{bond}) obtained with different DFT methods from the literature [6–10] (for the meanings of the abbreviations BP, OLYP, B3LYP, B3LYP*, and PBE0, see Table 2). High-level *ab initio* CASPT2 calculated results [9] and experimental data [9,11,12] are given for comparison. It is first seen that when more than one reference is cited for the same functional, a different E_{bond} is given for a given AB. Different references may treat E_{bond} differently. In Table 1, the calculated results from refs. [9] and [10] include a correction (Δ_{ZPVE}) for zero-point vibrational energy (ZPVE), while those from refs. [6–8] do not. But the Δ_{ZPVE} contribution to E_{bond} is insignificant, about -0.1 eV or less [9]. On the other hand, the BP functional may give a singlet or triplet ground state for FeP(Im), depending on the program/basis set used. However, the energy difference between the singlet and triplet states obtained with BP is less than 0.05 eV. To understand the origin of the difference of the E_{bond} results obtained with a same functional in two different references, one has to examine the computational details in each reference. Therefore, Table 1 also provides the information about the program package and basis set adopted in each reference. Different programs sometimes imply different approximations are adopted. For example, the CPMD [6] and Jaguar [7] programs use pseudopotentials or effective-core potentials, while the present ADF program employed here uses frozen-core techniques. In ref. [9], all-electron calculations were carried out. The numerical integration method and its accuracy in a program may also influence the accuracy of the calculated results, but such information is usually not provided in the computational details of a paper. Of course, different programs should yield the same results for the same functional if exactly the same settings are used. Examining the results in Table 1, we see that the basis sets employed can be a major source for the differences in the results obtained with the same functional. For example, the Jaguar/B3LYP results from ref. [8] are seen to be very different from those of ref. [10] just because different basis sets were employed in the two references. Large basis-set effects were also found in calculations of ref. [9]. Despite various possible factors within a program that may affect the accuracy of the calculated results, certain conclusions may be drawn based on the results in the table concerning the behaviors of the various functionals. (1) The BP functional overestimates the bonding of each AB, while PBE0, which gives a negative E_{bond} value for $AB = O_2$, severely

underbinds the ligands. (2) The bonding energies obtained with B3LYP are better than those from PBE0, but they are still underestimated as compared to experiment. (3) B3LYP* shows an improvement over B3LYP. (4) The B3LYP, B3LYP*, and PBE0 functionals give the trend in the E_{bond} values from AB = CO to NO which is opposite to the experimental one. (5) OLYP is seemingly the one with the best average performance.

As shown in Table 1, more recent DFT calculations of the FeP(Im)-AB bonding energies were carried out by Siegbahn et al. [10] using the B3LYP and B3LYP* functionals. In fact, these authors also performed additional calculations by including an empirical dispersion correction in DFT in order to improve the B3LYP and B3LYP* results. The so-called DFT + E_{disp} method (it is denoted as DFT-D by these authors) has mainly been applied to noncovalent interactions and shown to give good results [13]. The application of the DFT + E_{disp} model to the covalent systems is a new subject and may need further investigations.

Since future DFT calculations on heme(AB) would preferably include the large protein environment and it is impractical to test a large number of functionals on very large systems, the choice of the best functional becomes especially important for such a case. Through the considerable efforts of many researchers, more and more accurate XC forms have been developed, and numerous DFT methods are now available in the literature. The main shortcoming of DFT is that it is unknown how the functional of the exchange-correlation energy could be improved in a systematic way toward the exact expression. Because all the theoretical models are approximate, there appears to be no direct relation between the sophistication of a model and its usefulness. It is often quite unclear why in some cases, a sophisticated functional produces poorer results than does a simpler one. Nevertheless, some general rules about the behaviors of various functionals may still be deduced, and these will be summarized in the last section (Conclusions and Remarks) based on the present calculated results.

In this work, we examined the performance of a large number (sixty-four) of density functionals, from GGA, meta-GGA, hybrid GGA to hybrid meta-GGA (see Section 2), for calculating the FeP(Im)-AB bonding energies. Radon and Pierloot [9] performed both DFT and *ab initio* calculations on FeP(Im)(AB); the “experimental” heme-AB bonding energies are well reproduced by the CASPT2 method with a large basis set. The high-level *ab initio* calculated result can thus be used here to examine how well present DFT methods treat the various iron heme complexes.

2. Computational Details

All calculations used the Amsterdam Density Functional (ADF) program package – ADF2009.01 [14,15]. The density functionals [16–63] chosen for testing are collected in Table 2, together with a brief description of their formulation. They are given in the order: (1) GGA functionals that contain a generalized gradient approximation (GGA) correction; (2) meta-GGA functionals that contain the electron kinetic energy density $\tau [= \Sigma(\nabla\phi_i)^2]$ (in addition to GGA); (3) hybrid GGA functionals that contain a fraction of the Hartree-Fock (HF) (or exact) exchange; and (4) hybrid meta-GGA functionals that contain both HF exchange and the electron kinetic energy density τ .

In the present version of ADF, certain GGA, meta-GGA, hybrid GGA, and hybrid meta-GGA functionals included in the program are treated in a non-self-consistent (non-SCF) manner. That is, the SCF calculation is performed with a different specific functional; the resulting electron densities are then used as input for energy evaluation with the GGA, meta-GGA or hybrid meta-GGA functional. It has been shown that for calculations of the relative energies (E^{relative}) of spin states in a molecule, the non-SCF and SCF procedures yield very close results [64]. But for calculations of bonding energies (E_{bond}), the non-SCF procedure

could produce a result that is significantly different from the SCF result. This is because E_{bond} is the difference of energies among different species ($AB \rightarrow A + B$) while the E^{relative} values of different spin states are calculated on a same species; there are error cancellations in the non-SCF calculations of E^{relative} , but not in E_{bond} when the non-SCF procedure is adopted. However, the mentioned difference between non-SCF and SCF values of E_{bond} can be reduced greatly when the accuracy of the numerical integration is increased. Thus we set a high level of integration accuracy (accint = 7.0) in the non-SCF calculations of E_{bond} . For the sake of comparison, the SCF results of E_{bond} obtained with a number of functionals are provided.

The STO (Slater-type orbital) basis set used is the standard ADF-TZP, which is triple- ζ for valence orbitals plus one polarization function. The TZP basis set is good or reliable enough for calculations on the present systems [5]. To obtain reliable results, no frozen-core approximation was used; instead, all-electron calculations were carried out here.

Relativistic corrections for the valence electrons were calculated by the quasi-relativistic (QR) method [65]. The calculations for open-shell states were spin unrestricted. Spin contamination in the unrestricted calculations was found to be small, as is shown in other calculations on comparable compounds [52]. Pople et al. [66] argued that spin-contamination was not as significant a problem in DFT as in wave-function theories, and their study suggested that an unrestricted Kohn-Sham (UKS) method should be used as it is able to better reproduce the observed densities in open-shell systems than RKS methods.

3. Results and Discussion

Figure 1 illustrates the molecular structures of FeP, FeP(Im), and FeP(Im)(O₂). When only a single axial ligand (Im) is added to FeP, a significant out-of-plane distortion is expected and in fact observed. The three critical coordination parameters of FeP(Im) are $R_{\text{Ct(N4)}\cdots\text{N(eq)}}$ (distance between the center of the ring and the equatorial, porphinato nitrogen), $R_{\text{Ct(N4)}\cdots\text{Fe}}$ (distance between the center of the ring and Fe), and $R_{\text{Fe-N(ax)}}$ (axial Fe-Im bond length). $R_{\text{Ct(N4)}\cdots\text{N(eq)}}$ is a measure of the porphinato core size and $R_{\text{Ct(N4)}\cdots\text{Fe}}$ represents the displacement of Fe out of the N4-plane toward the Im ligand. Bonding an AB ligand to the five-coordinate complex moves the Fe back into the plane. But $R_{\text{Ct(N4)}\cdots\text{Fe}}$ in FePor(L)(AB), though small, is not zero experimentally and may be different in different compounds [67]. Hence, we have also presented the calculated $R_{\text{Ct(N4)}\cdots\text{Fe}}$ values for each FeP(Im)(AB). The other structural parameters of interest for FeP(Im)(AB) include $R_{\text{Fe-AB}}$ (the axial Fe-AB bond length), $R_{\text{A-B}}$ (the A-B bond length), and $\angle_{\text{FeAB}}$ (the Fe-A-B bond angle). The structure of FeP(Im)(CO) has a straight, upright Fe-C-O unit with the angle $\angle_{\text{FeCO}}$ being 180°. NO or O₂ binds in a bent, end-on fashion, as shown in Figure 1. The calculated FeP(Im)-AB bonding energies in FeP(Im)(AB) are defined as:

$$-E_{\text{bond}} [\text{FeP (Im) - AB}] = E [\text{FeP (Im) (AB)}] - \{E [\text{FeP (Im)}] + E (\text{AB})\}$$

Here $E[\text{FeP(Im)(AB)}]$, $E[\text{FeP(Im)}]$, and $E(\text{AB})$ are total energies of the indicated species, which are optimized independently. Our E_{bond} values do not include corrections for zero-point vibrational energy (ZPVE), which are -0.12 to -0.13 eV for FeP(Im)(CO), -0.09 to -0.11 eV for FeP(Im)(NO), and -0.08 to -0.10 eV for FeP(Im)(O₂) according to our calculations with the BP, revPBE, and RPBE functionals. The results are presented in Table 3. It is impractical to do frequency calculations with every functional tested here. According to the calculations by us and others [9], the ZPVE corrections are similar for different functionals. As mentioned above, the results in Table 1 cited from refs. [9] and [10] were corrected with ZPVE.

As mentioned in Section 2, certain functionals included in ADF are treated in a non-SCF manner. In this case, geometry optimization cannot be efficiently performed with these functionals. According to previous calculations [5], the BP functional gives an excellent description of molecular structure. The changes in the calculated molecular structure by using different functionals are small in most cases; particularly, these changes do not lead to notable errors in the calculated energies. To further support these arguments, we tested five functionals here in the geometry optimizations, namely BP, PBE, revPBE, RPBE, and B3LYP.

The d^6 Fe^{II} ion in $\text{FeP}(\text{Im})$ can exhibit three spin states, namely $S = 0$ (low spin, singlet), $S = 1$ (intermediate spin, triplet), and $S = 2$ (high spin, quintet). The geometry optimization for $\text{FeP}(\text{Im})$ was performed for each spin state. The relationship between the structural parameters and the spin multiplicity has been discussed in a previous paper [5]. Here we focus on a comparison of the structural parameters obtained with different functionals. The electronic structures of $\text{FeP}(\text{Im})(\text{CO})$ and $\text{FeP}(\text{Im})(\text{NO})$ are relatively simple; they are closed-shell singlet and open-shell doublet, respectively. The strong field of the CO or NO ligand makes the six-coordinate system low spin. In the case of $\text{AB} = \text{O}_2$, the ligand field is relatively weak. There is an electron transfer from Fe to O_2 , yielding an $\text{Fe}^{\text{III}}\text{--O}_2^-$ unit in the complex. Therefore, the ground state of $\text{FeP}(\text{Im})(\text{O}_2)$ is either a triplet ($S = 1$) $(d_{xy})^2(d_{xz})^2(d_{yz}\alpha)^1(\text{O}_2-\pi_g^*\alpha)^1$ or an open-shell singlet ($S = 0$) $(d_{xy})^2(d_{xz})^2(d_{yz}\alpha)^1(\text{O}_2-\pi_g^*\beta)^1$. According to our calculations, the triplet is somewhat lower in energy than the open-shell singlet for this complex. The ground state of $\text{FeP}(\text{L})(\text{O}_2)$ is shown to be different with different L [5]; a weaker Fe-L bond more likely leads to an open-shell singlet ground state for the oxy complex.

3.1. Structures of $\text{FeP}(\text{Im})$ and $\text{FeP}(\text{Im})(\text{AB})$ Calculated with the Different Functionals

The calculated structural parameters of $\text{FeP}(\text{Im})$ and $\text{FeP}(\text{Im})(\text{AB})$ with the various functionals are collected in Tables 4 and 5, respectively, together with available X-ray diffraction data on synthetic porphyrins [67–69] and on myoglobins [70–72]. For $\text{FeP}(\text{Im})$, three spin states were considered, while for $\text{FeP}(\text{Im})(\text{AB})$, the results are given only for the calculated ground state.

Examining Table 4, we see that the BP optimized structure of $\text{FeP}(\text{Im})$ in the high-spin state agrees very well with the X-ray diffraction data on the five-coordinate deoxyMb, which is known to be high spin. No X-ray crystal structural data are available in the literature for a comparable, five-coordinate, synthetic $\text{FePor}(\text{Im})$ compound. (Note that the X-ray crystal structural data for the five-coordinate $\text{FeTPP}(2\text{-MeIm})$ and $\text{FeTpivPP}(2\text{-MeIm})$ compounds are available in the literature [67]; Im is most similar to 1-MeIm or 4-EtIm, but rather different from 2-MeIm; see ref. [5] for more details). The structural parameters $R_{\text{Ct}(\text{N4})\cdots\text{N}(\text{eq})}$ and $R_{\text{Ct}(\text{N4})\cdots\text{Fe}}$ that relate to the rigid FeP portion change only slightly (at most 0.02 Å) with a change of functional. But there is a relatively large change in the calculated axial Fe-Im bond length from one functional to another; the $R_{\text{Fe-N}(\text{ax})}$ values obtained with revPBE, RPBE, and B3LYP, which agree well with each other, are more or less (0.03 – 0.08 Å) larger than that with BP, depending on state. The former three functionals tend to give a longer bond than BP.

Concerning $\text{FeP}(\text{Im})(\text{AB})$ (Table 5), we have X-ray structural data on comparable, synthetic $\text{FePor}(\text{L})(\text{AB})$ compounds [67–69]. Except for $\angle\text{FeAB}$, the experimental structural parameters of $\text{FePor}(\text{L})(\text{AB})$ are in general quite close to those measured for the myoglobins (MbAB). The Fe-A-B bond angle is shown to be smaller in MbAB than in $\text{FePor}(\text{L})(\text{AB})$, which may be attributed to the interaction of bound AB with the protein environment in MbAB. A good quantitative agreement is found between the experimental data of $\text{FePor}(\text{L})(\text{AB})$ and the BP optimized structures of $\text{FeP}(\text{Im})(\text{AB})$ for every AB ligand. Again, the

revPBE, RPBE, and B3LYP functionals tend to yield somewhat longer axial Fe-N(ax) and Fe-AB bonds than BP in most cases. In general, RFe-AB varies in the order BP $\approx$ PBE < revPBE $\approx$ RPBE < B3LYP. The structural parameters obtained with PBE are very close to those calculated with BP for every molecule.

According to the $R_{\text{Ct}(\text{N4})\cdots\text{Fe}}$ values, there is a significant out-of-plane displacement of Fe even in the six-coordinate system for AB = CO and NO. $R_{\text{Ct}(\text{N4})\cdots\text{Fe}}$ in FeP(Im)(NO) is as nearly large as -0.1 Å. The negative values just denote that Fe is displaced toward the AB ligand. Fe in FeP(Im)(O₂) can be thought to lie in the porphyrin N4 plane because $R_{\text{Ct}(\text{N4})\cdots\text{Fe}}$ in this complex is less than -0.01 Å. The Ct(N4)⋯Fe distances vary in the order: AB = NO > AB = CO > AB = O₂, a trend which is consistent with the order of the bonding strengths of the AB ligands to Fe (see Table 1).

3.2. Effect of Different Calculated Structure on the FeP(Im)-AB Bonding Energies

Table 6 presents the calculated FeP(Im)-AB bonding energies (E_{bond}) at the BP optimized structure and at the structure optimized with the respective individual functional itself (AB = CO, NO, O₂). It is shown that the E_{bond} values obtained at the different functionals' optimized structures are nearly the same, the difference being at most 0.03 eV. The results support the argument that somewhat changes in the calculated structure do not result in notable errors in the calculated energies. The next calculations of energetics (Sections 3.3 and 3.4) with the large number of functionals are based on the BP optimized structure.

3.3. Spin-State Energetics of FeP(Im) Evaluated with the Large Number of Functionals

We first examined the spin-state energetics of FeP(Im) evaluated with the large number of functionals. The electronic structure of this five-coordinate complex is interesting and has been the subject of many theoretical studies [6,8,9,73–75]. Fe^{II} in FeP(Im) can exhibit three spin states ($S = 0, 1$, and 2 as mentioned above) that are within a narrow energy range. FeP(Im) is thought to have a high-spin ground state ($S = 2$) because deoxyMb is characterized as high spin. Previous DFT calculations [73] with the BP functional predicted a triplet ($S = 1$) state as the ground state for this complex, at odds with the situation for deoxyMb. It has been shown that the ability of DFT to calculate the relative spin-state energies is sensitive to the type of functionals. It would be of interest to see what functionals are able to give the correct ground state for this high-spin system. The calculated relative energies (E^{relative}) for the selected states of FeP(Im) with the large number of functionals are collected in Table 7. The E^{relative} of the triplet is set to zero. A high level of integration accuracy (accint = 7.0) was also set for the calculations of E^{relative} (in addition to the calculations of E_{bond}), and therefore the calculated E^{relative} values here (which should be more accurate) may be slightly different from those in previous calculations with accint = 4.0 [5], where only several functionals were tested.

First looking at the BP results in the GGA category, the triplet and singlet states are predicted to be nearly degenerate, and lie ca. 0.5 eV lower in energy than the high-spin state. Thus, the BP functional greatly overestimates the relative energy of the high spin state. A much better result is obtained with the B88x-BR89c functional, where Perdew's 1986 gradient correction [17] for correlation in BP has been replaced by the Becke-Roussel's 1989 gradient correction [18] for correlation. PW91, mPW, BLYP, PBE, BOP, XLYP, and RGE2 yield results which are similar to those of BP. A revised PBE (mPBE, revPBE, or RPBE) shows some improvement over PBE; the relative energies of the high-spin state show the order of PBE > mPBE > revPBE > RPBE. The dispersion-corrected functionals (BP-D, BLYP-D, PBE-D) predict an even higher E^{relative} for the high-spin state than the original one. KT1 is inferior to BP, but KT2 is a significant improvement over KT1 in calculating the energetics of the high-spin state.

Using the OPTX exchange, the functionals, OPBE, OPBdew, and OLYP, are shown to yield rather different results from those of BP. First, these functionals predict the triplet state to be notably lower than the singlet in energy. Second, the relative energies of the high-spin state are now small, ranging from 0.05 to 0.07 eV. The three functionals are almost equivalent to each other in terms of energy. With VS98, the high-spin state is now favored over the triplet by 0.03 eV; the two states are actually nearly degenerate. In the GGA category, only the HCTH series of functionals (HCTH/93, HCTH/120, HCTH/147, and HCTH/407) favor the high-spin state over the lower-spin states by a clear amount of energy.

In the meta-GGA category, the calculated E^{relative} values are also rather sensitive to the choice of functional. The meta-GGA results do not consistently improve upon those of GGA. A good relative energy for the high-spin state is obtained with τ -HCTH, OLAP3, Becke00, M06-L, or SSB-D. The other meta-GGA functionals greatly overestimate the relative energy of the high-spin state, which ranges from 0.25 to 0.55 eV, depending on functional. It is seen that the modified or revised functionals (KCIS-modified, revTPSS) give results that are improved over the original ones (KCIS-original, TPSS).

The inclusion of some HF (or exact) exchange in the GGA has a large effect on the energetics of the high-spin state. The E^{relative} of the high-spin state decreases by 0.57 eV from BLYP to B3LYP. Compared to the B3LYP result, a higher E^{relative} for $S = 2$ is obtained with B3LYP* that contains 15% HF exchange admixture, whereas the original B3LYP functional has 20% HF exchange. In general, the larger the HF exchange admixture, the lower the resulting E^{relative} for the high-spin state [76]. The calculation with B3LYP* still predicts a triplet ground state for FeP(Im). Again, the dispersion-corrected functionals (B3LYP-D, B97-D) yield higher relative energies for the high-spin state, compared with the original ones (B3LYP, B97). Except for B3LYP*, B3LYP-D, and B97-D, which slightly favor the triplet over the quintet, the other hybrid GGA functionals give the “correct” ground state multiplicity for FeP(Im).

For the hybrid meta-GGAs, all functionals except TPSSh predict a high-spin ground state for FeP(Im). M05-2 $\times$ and M06-2 $\times$, where the HF exchange admixture doubles that in original functionals (M05, M06), give very negative E^{relative} values for $S = 2$. The results obtained with the former two functionals are comparable to each other. But M05 yields results which are rather different from those of M06.

3.4. FeP(Im)-AB Bonding Energies Evaluated with the Large Number of Functionals

The calculated FeP(Im)-AB bonding energies (E_{bond}) (AB = CO, NO, O₂) with the large number of functionals are also collected in Table 7 (on the right-hand side), together with the high-level *ab initio* CASPT2 calculated results [9] and experimental data [9,11,12] for comparison. The latter are actually the measured dissociation barriers for chelated protoheme [11,12] or for Mb, corrected for the absence of the protein environment [9]. The values in parentheses are the results calculated in the SCF manner. We see that the non-SCF and SCF procedures give very close E_{bond} values for all GGA functionals. A relatively large difference between the non-SCF and SCF E_{bond} results is usually found for a hybrid functional, particularly M06-2 $\times$.

First looking at the BP results in the GGA category, the FeP(Im)-AB bonding energies calculated with this functional are 1.74, 1.80, and 0.77 eV for AB = CO, NO, and O₂, respectively. They are larger than the experimental data (CO: 0.78 – 0.85 eV, NO: 0.99 eV, O₂: 0.44 – 0.53 eV) by about 0.9, 0.8, and 0.3 eV, respectively for the three ligands. A significantly better performance is obtained with the B88x-BR89c functional, whose calculated E_{bond} values are smaller than the BP values by 0.38, 0.27 and 0.25 eV, respectively. Therefore, there is a good agreement between the B88x-BR89c calculated

E_{bond} value and the experimental data for $\text{AB} = \text{O}_2$. PW91 and PBE yield poorer results than BP, but the modified or revised functionals (mPW, mPBE, revPBE, RPBE) perform better than the original ones (PW91, PBE); the calculated E_{bond} decreases in the order: $\text{PBE} > \text{mPBE} > \text{revPBE} > \text{RPBE}$. The performance of RPBE is comparable to that of B88x-BR89c. With the BOP functional, E_{bond} amounts to 1.31, 1.44, and 0.52 eV for $\text{AB} = \text{CO}$, NO , and O_2 , respectively. This functional appears to give the best performance overall for the calculations of E_{bond} among the various GGA functionals. The HCTH series of functionals perform better than BOP for $\text{AB} = \text{CO}$ and NO , but they produce too small or even negative E_{bond} for $\text{AB} = \text{O}_2$. HCTH/93 performs very comparably to HCTH/407 and there is no difference in E_{bond} between HCTH/120 and HCTH/147; HCTH/93 surpasses the accuracy of HCTH/120 for $\text{AB} = \text{CO}$ and NO , but the opposite is the case for $\text{AB} = \text{O}_2$. The KT1, KT2, PBESol, and RGE2 functionals all greatly overestimate the FeP(Im)-AB bonding energies, so do the dispersion-corrected ones (BP-D, BLYP-D, PBE-D).

Among the meta-GGAs, BLAP3 and Bm τ 1 give the best results overall. They are also somewhat superior to BOP. The other meta-GGA functionals are more or less inferior to the two functionals for calculations of E_{bond} . KCIS-modified shows better performance than KCIS-original. A good FeP(Im)-O_2 bonding energy can be obtained with the KCIS-modified, PKZB, PKZBx-KCISc, M06-L, and SSB functionals, but they overestimate the FeP(Im)-CO and FeP(Im)-NO bonding energies. This is the situation for several GGA functionals discussed above.

While most GGA and meta-GGA functionals seriously overbind for $\text{AB} = \text{CO}$ and NO , many hybrid functionals provide clearly superior results for the two ligands. For instance, the bonding energies of CO and NO to FeP(Im) improve significantly from BLYP to B3LYP. A good FeP(Im)-CO bonding energy is produced with B3LYP, PBE0, B97, B97-1, O3LYP, and X3LYP, while a good FeP(Im)-NO bonding energy is obtained with the B1LYP, B1PW91, B97-2, and O3LYP functionals. O3LYP appears to be the only good hybrid functional for both the FeP(Im)(CO) and FeP(Im)(NO) systems. However, all these mentioned functionals give too small or even negative bonding energies for $\text{AB} = \text{O}_2$, and so seriously underbind this ligand. Only the dispersion-corrected functionals (B3LYP-D, B97-D) yield reasonable results for $\text{AB} = \text{O}_2$, but they show deficiency when applied to $\text{AB} = \text{CO}$ and NO . Our calculations with B3LYP and PBE0 indicate that the FeP(Im)-CO bonding energy is smaller than the FeP(Im)-NO one, in agreement with the experimental trend, but in contrast to the calculations by other authors [7,9] with the same functionals (see Table 1). In fact, our calculations with the other various hybrid functionals yield the same trend as B3LYP or PBE0.

Concerning the hybrid meta-GGA functionals, their results do not seem to improve upon those of the hybrid GGAs. TPSSh gives good performance for $\text{AB} = \text{O}_2$, but yields poor agreement with experiment for $\text{AB} = \text{CO}$ and NO . Nevertheless, the results of TPSSh are a significant improvement over those of TPSS and revTPSS.

4. Conclusions and Remarks

Accurate prediction of bonding energies for the diatomic ligands (CO , NO , O_2) to heme proves to be a difficult issue in theoretical computations. No universally “best” functional is found for all the three FeP(Im)(AB) systems among the large number of density functionals tested here; a functional successful for one system does not perform equally well for the other system(s). Following conclusions can be drawn from the results obtained.

- (1) In the GGA category, most functionals overbind the ligand greatly for $\text{AB} = \text{CO}$ and NO . Good FeP(Im)-CO and FeP(Im)-NO bonding energies are obtained with HCTH/93 and HCTH/407, which, however, seriously underbind O_2 . A

good FeP(Im)-O₂ bonding energy can be obtained with several GGA functionals, B88x-BR89c, revPBE, RPBE, FT97, and BOP, where BOP performs better than other four functionals for AB = CO and NO.

- (2) The bonding energies of the meta-GGA functionals show some improvement of those of the GGAs. BLAP3 and Bm τ 1 give the best results overall among the meta-GGAs and they are also somewhat superior to BOP; they provide a relatively satisfactory description of the various FeP(Im)-AB bondings.
- (3) The hybrid GGA functionals are a considerable improvement over the GGAs for AB = CO and NO; many hybrid GGA functionals provide excellent bonding energies for the two ligands. But they all seriously underbind O₂ (except the dispersion-corrected hybrid functionals).
- (4) Among the hybrid meta-GGAs, TPSSh shows remarkably high performance for calculating the FeP(Im)-O₂ bonding energy, but it greatly overbinds the CO and NO ligands. The results for other hybrid meta-GGA functionals do not improve upon those of the hybrid GGA.
- (5) The modified or revised functionals usually perform better than the original ones for calculating the spin-state energetics of FeP(Im) as well as the FeP(Im)-AB bonding energies.

From the present results and those in the literature, we can see that even the “best” current DFT functionals rarely deliver a consistently strong performance. This problem can be ascribed to the semiempirical nature of DFT (the PBE functional [22] is the only exception, in which all parameters are fundamental constants). It is a fact that the exact universal functional is unknown and approximations must be introduced. A modern DFT functional always consists of two parts: exchange and correlation, which are obtained by fitting to some experimental data as well as by incorporating some well-known physical constraints. Obviously, the change of the results from one functional to another is a direct consequence

of their different exchange-correlation potentials $\left(\mu_{xc} = \frac{\partial E_{xc}(\rho)}{\partial \rho} = \mu_x + \mu_c\right)$, and so it is useful to examine the differences between those potentials. Studies [55] revealed that the correlation energy E_C (obtained through μ_C) is about 10% of the exchange E_X (obtained through μ_X), and so the accuracy of the exchange μ_X seems to be more important than that of the correlation μ_C for the behavior of a functional. Thus, considerable efforts have been made to design a good exchange. Great progress is made through the introduction of a fraction of the Hartree-Fock (HF) (or exact) exchange in DFT [51]. Here the role of the HF-exchange is to stabilize the high-spin state strongly. This is reason why most hybrid functionals are able to give a correct, high-spin ground state for FeP(Im). Previous studies of Fe(II)-sulfur complexes [52] found a linear relationship between the high-spin/low-spin energy gap and the amount of the HF-exchange. Another role of the HF-exchange is to decrease the bonding energy. While BLYP greatly overbinds the various FeP(Im)-AB molecules, B3LYP results in an almost repulsive interaction for AB = O₂. Reducing the amount of HF-exchange in going from B3LYP (20%) to B3LYP* (15%) gives a quite large increase in the bonding energy. Thus B3LYP* offers a significant improvement over B3LYP for E_{bind} in the case of AB = O₂. But this functional also leads to an overestimation of the FeP(Im)-CO bonding, whereas B3LYP yields a good result. For AB = NO, the amount of HF-exchange needs to be higher than 20% in order to obtain a good bonding energy. Although hybrid functionals perform remarkably well in electronic structure calculations, the fact that the amount of HF-exchange mixing affects different quantities in different ways may be regarded as a disadvantage of the hybrid GGAs.

Meanwhile, great efforts have also been made to obtain optimum GGA functionals. The improvements rely on increasing the number of empirical parameters and generalizing the fitting procedure beyond energetic data. As an example, the OPerdew functional that uses the OPTX correction for exchange is much better than BP (i.e. Becke's exchange + Perdew's correlation) for calculating the high-spin state energetics. OPTX was obtained [29] by refining Becke's exchange to all the first- and second-row atoms, and there is a greater number of parameters in OPTX than in Becke's exchange. Thus, OPTX could lead to improved results in many cases. The same is true for BLYP vs. OLYP. We see that the OPEB, OPerdew, and OLYP functionals which have the same OPTX exchange but different correlation parts, always give close results. This again indicates that in a functional, the accuracy of the exchange is more important than that of the correlation. HCTH is highly parameterized and so it is even better than OPBE, OPerdew, or OLYP for calculating the high-spin state energetics; it possesses a similar accuracy to the hybrid functionals in this aspect. As another example, KT2 is obtained from KT1 by relaxing the uniform electron gas constraint, and the former indeed works better than does the latter in the calculations of the energetics. While the GGA functionals proposed originally (like BP, PW91, BLYP, PBE, etc.) give too high relative energies for the high-spin state and also too large FeP(Im)-AB bonding energies, their modified or revised forms (OPerdew, mPW, OLYP, revPBE, OPBE, etc.) improve the results substantially. Those modifications prove useful with new functionals that display improved prediction capabilities for a variety of properties.

The more recent progress in DFT is the inclusion of the kinetic-energy density ($\tau = \Sigma(\nabla\phi_i)^2$) in the GGA or hybrid GGA. But the role of τ is not obvious for the present calculated results; the meta-GGA functionals possess a similar accuracy to the GGA ones. Tests of the meta-GGAs or hybrid meta-GGAs on the present systems are not enough for a detailed assessment of those functionals.

The difference between results obtained by any two different functionals may not always have a clear explanation, but some general rules about the behaviors of various functionals may still be made according to experiences accumulated, as mentioned above. However, in order to obtain accurate results for some transition metal compounds, there is still a need to test the performance of different functionals. There are various deficiencies in the current, approximate exchange-correlation functionals (e.g. lack of both multireference and van der Waals effects, as pointed out in the literature [10]) despite the remarkable progress in the DFT development. Recently, Goerigk and Grimme [77] assessed 47 density functionals on a large database (GMTKN30) for main group thermochemistry, kinetics, and noncovalent interactions; they also show that the various functionals yield different results for different chemical problems.

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Figure 1.
Molecular structures of iron porphine (FeP), FeP(Im), and FeP(Im)(O₂).

Table 1
Calculated FeP(Im)-AB bonding energies with different functionals from the literature

Functional	$E_{\text{bond}}[\text{FeP(Im)-AB}], \text{ eV}$			Program/Basis set used	ref.
	AB = CO	AB = NO	AB = O ₂		
BP	1.52	1.56	0.65	CPMD/plane wave	[6]
B3LYP	0.73	0.54	0.33	Jaguar/LACV3P**+	[7]
BP	1.57	---	---	Jaguar/6-311G*	[8]
B3LYP	0.78	---	-0.12	Jaguar/6-311G*	[8]
BP	1.76	1.85	1.19	Turbomole5.9/TZVPP	[9] ^d
OLYP	0.75	0.88	0.22	Turbomole5.9/TZVPP	[9] ^d
B3LYP	0.43	0.32	0.16	Turbomole5.9/TZVPP	[9] ^d
PBE0	0.33	0.13	-0.03	Turbomole5.9/TZVPP	[9] ^d
B3LYP	0.47	0.33	0.05	Jaguar/cc-PVTZ(-f)	[10] ^d
B3LYP*	0.72	0.71	0.24	Jaguar/cc-PVTZ(-f)	[10] ^d
CASPT2	0.84	0.94	0.43		[9]
Exptl	0.78 ^a , 0.85 ^c	0.99 ^c	0.53 ^b , 0.44 ^c		

^a Estimated from *b* and relative CO/O₂ dissociation equilibrium constants (refs. [9,11,12]).

^b Dissociation barrier for chelated protoheme (ref. [12]).

^c Dissociation barrier for Mb, corrected for the absence of the protein environment (ref. [9]).

^d The calculated results from these references include a correction ($\Delta ZPVE$) for zero-point vibrational energy (ZPVE).

Table 2**Density functionals used in the Calculations**

GGA Functional	
BP	Becke's 1988 gradient correction for exchange (ref. 16) plus Perdew's 1986 gradient correction for correlation (ref. [17]).
B88x-BR89c	Becke's 1988 gradient correction for exchange plus Becke-Roussel's 1989 gradient correction for correlation (ref. [18]).
PW91	Perdew-Wang's 1991 GGA functional (ref. [19]).
mPW	Modified PW91 functional proposed in 1998 by Adamo and Barone (ref. [20]).
BLYP	Becke's 1988 correction for exchange plus LYP correlation functional (ref. [21]).
PBE	Perdew-Burke-Ernzerhof's 1996 corrections for both exchange and correlation (ref. [22]).
mPBE	Modified PBE functional proposed in 2002 by Adamo and Barone (ref. [23]).
revPBE	Revised PBE functional proposed in 1998 by Zhang and Yang (ref. [24]).
RPBE	Revised PBE functional proposed in 1999 by Hammer, Hansen, and Nørskov (ref. [25]).
FT97	Filatov-Thiel's 1997 correction for both exchange and correlation (ref. [26]).
BOP	Becke's 1988 correction for exchange plus Tsuneda-Suzumura-Hirao's 1999 one-parameter progressive correlation functional (ref. [27]).
VS98	van Voorhis-Scuseria's 1998 GGA functional (ref. [28]).
OPBE	Handy-Cohen's 2001 OPTX correction for exchange (ref. [29]) plus PBE correction for correlation.
OPerdew	OPTX correction for exchange plus Perdew's 1986 gradient correction for correlation.
OLYP	OPTX correction for exchange plus Lee-Yang-Parr's 1988 correlation functional.
HCTH/93	Hamprecht-Cohen-Tozer-Handy's 1998 GGA functional, containing 15 parameters refined against data from a training set of 93 atomic and molecular systems (ref. [30]).
HCTH/120	New HCTH GGA functional, the data of a training set were extended to 120 systems (ref. [31]).
HCTH/147	New HCTH GGA functional, the data of a training set were extended to 147 systems (ref. [31]).
HCTH/407	New HCTH GGA functional, the data of a training set were extended to 470 systems (ref. [32]).
KT1	Keal-Tozer's 2003 GGA functional that was designed specially for use in shielding constant calculations (ref. [33]).
KT2	Modified KT1 functional by relaxing the uniform electron gas constraint (ref. [33]).
XLYP	Extended GGA functional combined with LYP correlation functional (ref. [34]).
PBEsol	Revised PBE functional for solids, proposed in 2008 by Perdew et al. (ref. [35]).
RGE2	Regularized gradient expansion (RGE) approximation density functional proposed in 2009 by Ruzsinszky, Csonka, and Scuseria (ref. [36]).
BP-D	Dispersion-corrected BP functional (ref. [37]).
BLYP-D	Dispersion-corrected BLYP functional (ref. [37]).
PBE-D	Dispersion-corrected PBE functional (ref. [37]).
Meta-GGA functionals	
KCIS-original	Krieger-Chen-Iafrate-Kurth's 1999 exchange-correlation functional that contains the kinetic energy density τ (ref. [38]).
KCIS-modified	Modified KCIS functional (ref. [39]).
mPBEKCIS	Modified PBE exchange functional plus KCIS correlation functional (ref. [40]).
τ -HCTH	The kinetic-energy density τ is included in the HCTH/407 form (ref. [41]).
PKZB	Perdew-Kurth-Zupan-Blaha's 1999 exchange-correlation functional that contains the kinetic energy density τ (ref. [42]).
PKZBx-KCISc	PKZB exchange functional plus KCIS correlation functional (ref. [43]).
BLAP3	Becke's 1988 correction for exchange plus Proynov-Sirois-Salahub's 1997 correlation functional that contains the kinetic energy density τ , the Laplacian of the electron density, and the parallel-spin correlation (ref. [44]).

OLAP3	OPTX correction for exchange plus LAP3 correlation functional.
Bmrl	Becke's 1988 correction for exchange plus Proynov-Chermette-Salahub's 2000 correlation functional that contains the kinetic energy density τ and the Laplacian of the electron density (ref. [45]).
Becke00	Becke's 2000 exchange-correlation functional that contains the kinetic-energy density τ [$=\Sigma(\nabla\phi_i)^2$](ref. [46]).
TPSS	Tao-Perdew-Staroverov-Scuseria's 2003 nonempirical meta-GGA functional (ref. [47]).
revTPSS	Revised TPSS functional proposed in 2009 by Perdew et al. (re. [48])
M06-L	Zhao-Truhlar's 2006 meta-GGA functional (ref. [49]).
TPSS-D	Dispersion-corrected TPSS functional (ref. [37]).
SSB-D	Empirical meta-GGA functional including a dispersion correction, proposed in 2009 by Swart, Sola, and Bickelhaupt (ref. [50]).

 Hybrid GGA functionals

B3LYP	Becke's 1993 three-parameter hybrid functional (ref. [51]) using LYP correlation functional.
B3LYP*	The Hartree-Fock (HF) exchange admixture is reduced from 20% (in original B3LYP) to 15% (ref. [52]).
mPW1PW	One-parameter hybrid functional using modified Perdew-Wang's 1991 exchange and correlation functional (ref. [53]).
B1LYP	One-parameter hybrid functional using Becke's exchange and LYP correlation functional (ref. [54]).
B1PW91	One-parameter hybrid functional using Becke's exchange and Perdew's 1991 correlation functional (ref. [54]).
PBE0	Parameter-free hybrid functional using the PBE model (ref. [55]).
OPBE0	The OPBE functional mixed with 25% Hartree-Fock exchange (ref. [56]).
B97	Becke's 1997 hybrid functional that contains 10 adjustable parameters (ref. [57]).
B97-1	The adjustable parameters in B97 were re-optimized in a self-consistent manner (ref. [30]).
B97-2	Multiplicative potentials are introduced into the B97 functional, and the adjustable parameters were re-optimized by fitting to both thermochemistry and the potentials (ref. [58]).
O3LYP	Cohen-Handy's 2001 three-parameter hybrid functional (ref. [59]) using LYP correlation functional.
X3LYP	Extended hybrid GGA functional combined with LYP correlation functional (ref. [34]).
B3LYP-D	Dispersion-corrected B3LYP functional (ref. [37]).
B97-D	Dispersion-corrected B97 functional (ref. [37]).

 Hybrid meta-GGA functional

τ -HCTH-hyb	HF exchange is introduced into the τ -HCTH functional (ref. [41]).
mPBE0KCIS	Parameter-free hybrid meta-GGA functional, in which exchange (mPBE) and a meta-GGA correlation (KCIS) are integrated (ref. [40]).
mPBE1KCIS	One adjustable parameter is introduced in the above integrated (mPBE)-(KCIS) functional (ref. [40]).
TPSSh	A one-parameter global hybrid version of the TPSS functional (ref. [60]).
M05	Zhao-Schultz-Truhlar's 2005 hybrid meta-GGA functional that contains 28% Hartree-Fock exchange (ref. [61]).
M05-2X	The Hartree-Fock exchange admixture is increased (doubled) from 28% in the original M05 to 56% (ref. [62]).
M06	Zhao-Truhlar's 2006 hybrid meta-GGA functional that contains 27% Hartree-Fock exchange (ref. [63]).
M06-2X	The Hartree-Fock exchange admixture is increased (doubled) from 27% in the original M06 to 54% (ref. [63]).

Table 3

Calculated zero-point vibrational energies (ZPVEs, in eV) and their contributions (Δ_{ZPVE} , in eV) to the FeP(Im)-AB bonding energies

	ZPVE ^a		Δ_{ZPVE} ^b	
	BP	revPBE	RPBE	BP
FeP(Im)CO	9.532	9.500	9.490	-0.12
FeP(Im)NO	9.493	9.458	9.447	-0.09
FeP(Im)O ₂	9.456	9.426	9.415	-0.08
FeP(Im)	9.295	9.234	9.224	
CO	0.131	0.132	0.132	
NO	0.115	0.115	0.115	
O ₂	0.092	0.092	0.092	

^aIt is calculated as sum over all the vibrational frequencies for a system.

^b $\Delta_{\text{ZPVE}} = \{\text{ZPVE}[\text{FeP}(\text{Im})] + \text{ZPVE}(\text{AB})\} - \text{ZPVE}[\text{FeP}(\text{Im})(\text{AB})]$.

Table 4

Calculated structural parameters (distance R in Å) for selected states of FeP(Im) with different functionals

	$R_{\text{Ct(N4)}\cdots\text{N(q)}}$			$R_{\text{Ct(N4)}\cdots\text{Fe}}$			$R_{\text{Fe-N(ax)}}$		
	S = 1	S = 2	S = 0	S = 1	S = 2	S = 0	S = 1	S = 2	S = 0
BP	1.994	2.058	1.984	0.157	0.291	0.150	2.201	2.143	1.906
PBE	1.993	2.058	1.984	0.150	0.284	0.139	2.196	2.141	1.910
revPBE	2.006	2.070	1.998	0.156	0.302	0.159	2.262	2.187	1.931
RPBE	2.011	2.074	2.001	0.155	0.304	0.162	2.278	2.195	1.937
B3LYP	2.017	2.074	2.012	0.151	0.316	0.137	2.250	2.179	1.965
Exptl: deoxyMb ^a		2.036			0.291			2.15	
Exptl: deoxyMb ^b		2.038			0.363			2.14	

^aX-ray crystal structural data on deoxy-Mb (code 1BZP) (ref. [70]).

^bX-ray crystal structural data on deoxy-Mb (code 1A6N) (ref. [71]).

Table 5
Calculated structural parameters (distance R in Å, angle $\angle$ in degree) of FeP(Im)(AB) with different functional

		$R_{\text{Fe-N(eq)}}$	$R_{\text{Ct(N4)} \rightarrow \text{Fe}}$	α	$R_{\text{Fe-N(ax)}}$	$R_{\text{Fe-AB}}$	$R_{\text{A-B}}$	$\angle_{\text{FeAB}}$
AB = CO	BP	2.011	-0.035	2.086	1.748	1.162	180.0	
	PBE	2.011	-0.030	2.085	1.747	1.163	180.0	
	revPBE	2.024	-0.025	2.129	1.751	1.166	180.0	
	RPBE	2.027	-0.023	2.142	1.752	1.167	180.0	
	B3LYP	2.029	-0.048	2.104	1.802	1.146	180.0	
	Exptl: FeP(L)(CO) ^b	2.02	-0.02	2.10	1.77	1.12	179	
	Exptl: MbCO ^c	2.01	-0.02	2.11	1.73	1.13	171.3	
AB = NO	BP	2.016	-0.078	2.168	1.728	1.189	141.2	
	PBE	2.017	-0.072	2.183	1.731	1.188	141.2	
	revPBE	2.029	-0.086	2.298	1.735	1.190	141.9	
	RPBE	2.033	-0.089	2.325	1.736	1.191	141.9	
	B3LYP	2.029	-0.056	2.139	1.787	1.172	141.0	
	Exptl: FeP(L)(NO) ^d	2.008	-0.07	2.180	1.743	1.14	140	
	Exptl: MbNO ^e	2.08	-0.04	2.18	1.89	1.15	112	
AB = O ₂	BP	2.008	-0.008	2.045	1.845	1.287	134.0	
	PBE	2.008	-0.007	2.045	1.846	1.285	134.1	
	revPBE	2.021	-0.006	2.092	1.863	1.289	134.3	
	RPBE	2.025	-0.007	2.107	1.869	1.291	134.2	
	B3LYP	2.025	0.002	2.070	1.922	1.251	136.5	
	Exptl: FeP(L)(O ₂) ^f	1.98	-0.02	2.07	1.75	>1.16	<131	
	Exptl: MbO ₂ ^g	2.01	0.02	2.06	1.81	1.24	123	

^a A negative value denotes an out-of-plane displacement toward the AB ligand.
^b X-ray structural data on FeTPP(Py)(CO) (TPP = tetraphenylporphine, Py = pyridine) (ref. [68]).
^c X-ray structural data on MbCO (code 1BZR) (ref. [70]).
^d X-ray structural data on FeTPP(1-MeIm)(NO) (1-MeIm = 1-methylimidazole) (ref. [69]).

^e_f X-ray structural data on MbNO (code 1HJT) (ref. [72]).

^f_f X-ray structural data on FeTpivPP(1-MeIm)(O₂) [TpivPP = tetra(α,α,α -orthopivalamide)-phenylporphine] (ref. [67]).

^g_f X-ray structural data on MbO₂ (code 1A6M) (ref. [71]).

Table 6

Calculated FeP(Im)–AB bonding energies (eV) at the BP optimized structure and at the structure optimized with the respective individual functional itself

	BP	PBE	revPBE	RPBE	B3LYP	
AB = CO	BP-struct ^a	1.74	1.84	1.48	1.42	0.87
	Indiv-struct ^b		1.84	1.48	1.42	0.85
AB = NO	BP-struct	1.80	1.90	1.55	1.51	1.45
	Indiv-struct		1.90	1.57	1.54	1.44
AB = O ₂	BP-struct	0.77	0.88	0.50	0.46	0.05
	Indiv-struct		0.85	0.50	0.46	0.04

^a At the BP optimized structure.

^b At the structure optimized with the respective individual functional itself.

Table 7

Calculated relative energies (E_{relative}) for the intermediate- ($S = 1$), high- ($S = 2$), and low-spin ($S = 0$) states of $\text{FeP}(\text{Im})$ and calculated $\text{FeP}(\text{Im})\text{-AB}$ bonding energies (E_{bond}) in $\text{FeP}(\text{Im})(\text{AB})$ with various functionals

		$E_{\text{relative}}, \text{eV}$				$E_{\text{bond}}[\text{FeP}(\text{Im})\text{-AB}], \text{eV}$			
		$S = 1$	$S = 2$	$S = 0$		$\text{AB} = \text{CO}$	$\text{AB} = \text{NO}$	$\text{AB} = \text{O}_2$	
GGA	BP	0	0.50	-0.03		1.74	1.80		0.77
	B88x-BR89c	0	0.16	0.17		1.36	1.53		0.52
	PW91	0	0.54	-0.06		1.87 (1.87) ^a	1.92 (1.92) ^a		0.89 (0.89) ^a
	mPW	0	0.51	-0.02		1.73 (1.73)	1.78 (1.78)		0.76 (0.76)
	BLYP	0	0.51	0.01		1.48 (1.47)	1.63 (1.63)		0.74 (0.73)
	PBE	0	0.49	-0.03		1.85 (1.84)	1.90 (1.90)		0.89 (0.88)
	mPBE	0	0.44	0.02		1.76 (1.75)	1.82 (1.81)		0.78 (0.77)
	revPBE	0	0.35	0.10		1.49 (1.48)	1.55 (1.55)		0.51 (0.50)
	RPBE	0	0.31	0.13		1.43 (1.42)	1.51 (1.51)		0.47 (0.46)
	FT97	0	0.46	-0.17		1.74	1.71		0.64
	BOP	0	0.47	0.03		1.31	1.44		0.52
	VS98	0	-0.03	0.17		1.61	1.92		1.00
	OPBE	0	0.05	0.22		1.40 (1.38)	1.37 (1.33)		0.05 (0.04)
	OPerdew	0	0.06	0.21		1.45	1.42		0.17
	OLYP	0	0.07	0.24		1.16 (1.15)	1.23 (1.23)		0.10 (0.10)
	HCTH/93	0	-0.12	0.32		0.96	1.05		-0.10
	HCTH/120	0	-0.13	0.30		1.14	1.27		0.16
	HCTH/147	0	-0.11	0.29		1.16	1.27		0.15
	HCTH/407	0	-0.14	0.37		0.99	1.12		-0.01
	KT1	0	0.63	-0.32		2.05 (2.04)	2.10 (2.10)		1.08 (1.07)
	KT2	0	0.38	-0.19		2.10	2.14		1.03
	XLYP	0	0.49	0.03		1.43	1.60		0.73
	PBEsol	0	0.62	-0.19		2.15	2.13		1.03
	RGE2	0	0.47	-0.06		1.92	1.92		0.79
	BP-D	0	0.56	-0.14		1.99	2.03		1.00
	BLYP-D	0	0.58	-0.13		1.77	1.90		1.00

		E _{relative} , eV			E _{bond} [FeP(Im)-AB], eV		
		S = 1	S = 2	S = 0	AB = CO	AB = NO	AB = O ₂
Meta-GGA	PBE-D	0	0.54	-0.11	2.02	2.06	1.02
	KCIS-modified	0	0.27	0.12	1.35	1.47	0.45
	KCIS-original	0	0.39	0.02	1.60	1.70	0.66
	mPBEKCIS	0	0.48	0.03	1.67	1.74	0.74
	τ-HCTH	0	-0.09	0.24	1.27	1.36	0.22
	PKZB	0	0.30	0.07	1.47	1.60	0.55
	PKZBx-KCISc	0	0.32	0.08	1.45	1.55	0.52
	BLAP3	0	0.28	0.09	1.13	1.28	0.40
	OLAP3	0	-0.16	0.32	0.65	0.72	-0.39
	Bmrl	0	0.25	0.11	1.06	1.23	0.36
Hybrid-GGA	Becke00	0	-0.02	0.18	1.17	1.37	0.31
	TPSS	0	0.48	-0.08	1.70	1.80	0.77
	revTPSS	0	0.43	-0.08	1.74	1.87	0.84
	M06-L	0	-0.09	0.20	1.57	1.74	0.63
	TPSS-D	0	0.55	-0.19	1.93	2.01	0.99
	SSB-D	0	-0.03	0.22	1.65	1.72	0.53
	B3LYP	0	-0.06	0.42	0.81 (0.87)	1.31 (1.45)	-0.14 (0.05)
	B3LYP*	0	0.11	0.28	1.13 (1.01)	1.53 (1.46)	0.21 (0.18)
	mPW1PW	0	-0.24	0.52	0.66	1.16	-0.54
	B1LYP	0	-0.23	0.55	0.41	1.01	-0.56
	B1PW91	0	-0.25	0.53	0.61	1.09	-0.63
	PBE0	0	-0.25	0.51	0.75 (0.76)	1.24 (1.38)	-0.48 (-0.24)
	OPBE0	0	-0.58	0.70	0.06	0.46	-1.43
	B97	0	-0.15	0.41	0.80	1.25	-0.27
	B97-1	0	-0.15	0.40	0.85	1.33	-0.22
	B97-2	0	-0.28	0.47	0.59	1.04	-0.57
	O3LYP	0	-0.19	0.41	0.80	1.05	-0.39
	X3LYP	0	-0.11	0.45	0.76	1.29	-0.20
	B3LYP-D	0	0.01	0.30	1.23	1.71	0.27
B97-D	0	0.06	0.12	1.62	1.73	0.67	

		$E_{\text{relative}}, \text{eV}$			$E_{\text{bond}}[\text{FeP}(\text{Im})-\text{AB}], \text{eV}$		
		S = 1	S = 2	S = 0	AB = CO	AB = NO	AB = O ₂
Hybrid meta-GGA	τ -HCTH-hyb	0	-0.03	0.27	1.24	1.59	0.16
	mPBE0KClS	0	-0.24	0.56	0.58	1.08	-0.59
	mPBE1KClS	0	-0.03	0.40	1.04	1.41	-0.06
	TPSSh	0	0.19	0.14	1.43 (1.44)	1.70 (1.78)	0.41 (0.44)
	M05	0	-0.48	0.75	0.17	0.82	-0.92
	M05-2X	0	-0.99	1.17	-1.19	-0.01	-2.20
Ab Initio	M06	0	-0.28	0.58	0.72 (0.58)	1.28 (1.20)	-0.32 (-0.33)
	M06-2X	0	-1.04	1.20	-1.31 (-0.43)	-0.18 (0.97)	-2.34 (-1.60)
	CASPT2 ^b				0.84	0.94	0.43
	Exptl				0.78 ^c , 0.85 ^e	0.99 ^e	0.53 ^d , 0.44 ^e

^aThe values in parentheses are the results calculated in the SCF procedure

^bCASPT2 calculations with large basis sets (ref. [9]).

^cEstimated from *d* and relative CO/O₂ dissociation equilibrium constants (refs. [9,11,12]).

^dDissociation barrier for chelated protoheme (ref. [12]).

^eDissociation barrier for Mb, corrected for the absence of the protein environment (ref. [9]).