Evaluation of DFT Methods to Study
Reactions of Benzene with OH Radical

Steve Scheiner

Department of Chemistry and Biochemistry

Utah State University

Logan, UT 84322-0300, *USA*

steve.scheiner@usu.edu

keywords: addition, H atom abstraction, energy barrier, pre-reaction complex

Abstract

Several DFT methods are applied to two different reaction channels involving $OH\cdot + C_6H_6$, and the results compared to high-level ab initio calculations. The OH· adds directly to one C atom in the first channel, first forming an encounter complex with the OH· poised above the aromatic plane. B3LYP, BH&HLYP, and MPW1K compute an accurate estimate of the overall exothermicity, while M05-2X, PBE0 and PBEPBE, overestimate this quantity to some degree. With the exceptions of PBEPBE and PBE0, the other methods produce an acceptable barrier to addition. All approaches except BH&HLYP correctly predict an exothermic H· abstraction, although PBEPBE is too exothermic. The BH&HLYP barrier to H· abstraction is too high while the MPW1K, PBE0, and B3LYP values are better, and M05-2X the best.

INTRODUCTION

Radicals participate in a whole raft of important chemical processes, from atmospheric and solution chemistry [1-5] to those that are related to catalytic chemical vapor deposition [6]. Further, the interactions of free radicals with biological molecules are essential components to life. As one example, NO· plays a major role in mammalian tissue, e.g. cellular communication [7]. The proper handling of superoxide anion radical is an essential ingredient in maintaining a proper metabolic balance [8]. The reactions of free radicals with peptides and proteins [9,10] are involved in entire classes of enzymes [11-15]. Moreover, reactions of free radicals with amino acids and peptides [16] are of fundamental importance, and indeed ubiquitous. Of many radicals that are present, hydroxyl (OH·) is of especial significance [17,18].

The primary first step of many of these reactions [18-21] is the abstraction of a H atom from a C-H bond, either from the protein backbone, or from an amino acid side chain. Extensive work, carried out over a long time frame [17-20], has shown that the OH radical can remove a H atom not only from the C^α position, but from other sites as well, such as from alkane side chains of certain amino acid residues. In fact, the reaction of side chains with hydroxyl radicals occurs at rates 10 to 1000 times faster [22] than the abstraction of hydrogen from C^α. It was recently pointed out [16] that β and γ positions offer more reactive sites for H abstraction, and that reactivity increases as one moves further from the backbone. This issue was addressed recently by ab initio calculations [23] that rationalized this phenomenon as due to the tendency of strong H-bonding groups of the peptide backbone near the C^αH, such as C=O and NH, to interfere with the H· extraction process by engaging the OH· in nonproductive H-bonds.

While the forgoing work has added to our understanding of the reaction of OH· with the amino acid residues that contain alkyl chains, there are other important classes of amino acids as well. The aromatic amino acids, e.g. His, Phe, and Tyr, are also subject to reaction with OH· [18] and are indeed major targets. In these cases, the OH· tends to favor addition to the aromatic ring, rather than the abstraction of a H· atom. As an example, 81% of the total OH· incorporation occurs in the β position of the histidine ring. Phe shows incorporation only into its β position while 63% of the total occurs in the β position of Tyr, with the remaining 37% contained in the C_3 and C_5 positions. Such preferences can be rather important for the possible reaction channels of proteins, but the reasons remain cloudy.

The reactions of radicals with various aromatics has received some attention from the computational and experimental directions as well, albeit without addressing the aromatic amino acids *per se*. OH· was allowed to react with benzene, for example, using accurate ab initio methods

that yielded good estimates of thermodynamic phenomena [24]. When reacted with OH· [25], benzene preferred addition at low T, and H· abstraction at higher temperature. C-H fission and H· abstraction of methylbenzyl radicals in pyrolysis and oxidation of xylenes was examined [26] and good agreement was achieved with experiment. Both calculations and shock tube/pulsed laser-induced fluorescence methods were applied to the reaction [27] of OH· with benzene and toluene and found a barrier for H· extraction of some 3 kcal/mol, quite similar to the barrier to OH· addition. Reactions of OH· and benzene were examined in 2009 [28] from both experimental and computational perspectives, and more recently with the most accurate calculations to date [29]. The reactions of naphthyl radical with acetylene were studied and it was shown that calculations could reach agreement with experiment [30]. And most recently, both H· and Me· were used to extract a H atom from aromatics, leading to some good benchmarks of bond dissociation energies [31].

With regard to heteroatomic aromatics, the overall rate constants for the reaction of OH· with pyridine and a number of its methylated derivatives, measured [32] using the turbulent flow technique with high-pressure chemical ionization mass spectrometry, led to a structure–reactivity relationship model for parameterizing the OH rate constants based on the type and position of the methyl and ethyl substituents on the pyridine. OH· reactivity with methylpyridine was later studied from both the perspectives of H· abstraction and OH· addition [33] to identify the most reactive channels and found the two processes are of comparable importance.

As computations turn toward larger and larger models of proteins, it will become less tenable to apply high-level correlated ab initio calculations as has been done in the past for the smaller models. It thus becomes important to consider the DFT approach which is less demanding of computer resources, but can be quite accurate nonetheless. Over the years, quite a number of different variants of DFT have appeared in the literature, with varying levels of success. It has also become apparent that a given method can be very accurate for one sort of application, and much less so for a different reaction. In the case of OH· reactions with aromatics, there are two main reaction channels. As indicated above, the radical can either remove a H· atom, or the OH· can add directly to the aromatic ring. The major objective of the present communication is the testing of various different DFT methods for both of these sorts of reactions. A primary goal is the elucidation as to which DFT variants would be most appropriate for consideration of the OH· reactions with aromatics. The criteria involve not only accuracy, but also a balance between the two primary reaction channels, in the sense that a DFT method of choice should not give undue preference to one channel over the other, but should reflect the true competition between these two reactions.

In this work, benzene is taken as the simplest prototype aromatic system which can undergo either H· abstraction or OH· addition, and which also serves as a good model of the specific aromatic system of the amino acid Phe. OH· is allowed to approach the benzene molecule from a number of different angles and the reaction monitored as both reaction channels occur. There are a number of prior very accurate computations of the C_6H_6 + OH· system that establish the benchmarks, as described below. Some of the most popular DFT methods are tested here, and their results compared with the prior accurate data from correlated ab initio calculations.

METHODS OF CALCULATION

Calculations were carried out using the Gaussian 03 and 09 packages [34,35]. DFT methods that were considered were those that have shown some degree of popularity over the years, so have a reasonable track record of performance for a range of different sorts of reactions. They were also limited to those for which there was expectation that they might be accurate for the two reactions being considered here. B3LYP [36-38] has become the most popular functional over the years, used in more calculations than any other. Other functionals tested included BH&HLYP [38-40], PBE0 [41,42] (also known as PBE1PBE), PBEPBE [41], MPW1K [43,44], and M05-2X [45], the newest of this group. For purposes of consistency, all of these DFT functionals were applied to the 6-31+G** basis set.

For each level of calculation, a OH· radical was first placed above the benzene ring as illustrated in Fig 1. From this point, the approaching radical forms a weakly bound π-complex, locating itself above the approximate center of the ring. It then moves toward one of the C atoms, adding to it in an exothermic reaction. The abstraction process (Fig 2) begins as the O atom of OH· approaches one of the CH protons, forming a weak CH···O H-bond. The bridging H atom is abstracted by the OH· forming a molecule of water, and leaving behind a C_6H_5· radical. The C_6H_5···OH_2 complex finally dissociates to isolated monomers. Energetic quantities are defined in Figs 1 and 2 for these two processes. Geometries were optimized separately with each DFT functional, including both minima and transition states.

Unrestricted calculations were checked for spin contamination, which was found to be quite small. In most cases, the eigenvalue of the spin operator S^2 was less than 0.76, very close to the exact value of 0.75. Annihilation of spin contamination brought these values down to 0.75. The only exceptions were the addition channel with the BH&HLYP functional. Eigenvalues were larger, about 0.85, but were then brought down below 0.76 after the contamination was removed.

RESULTS

Benchmarks

As indicated above, there have been a number of studies of both the H· abstraction and the OH· addition process of benzene, using fairly high levels of theory [24,25,27,29,46]. In addition to various specific levels of theory, the results differ also in whether or not zero-point vibrational terms have been added to the electronic energies. As one example of the latter issue, a 2002 set of calculations at the G3 level [24] found that the addition of OH· to benzene was exothermic by 19.4 kcal/mol and that this quantity diminished to 16.4 kcal/mol when ZPE was added. Likewise, the energy barrier to this addition, $E^{\dagger}$, rose from 1.1 to 2.8 kcal/mol upon inclusion of ZPE. In contrast, the exothermicity (ΔE) of the H· abstraction was relatively unaffected by ZPE, changing from -4.0 to -4.2 kcal/mol. There is greater sensitivity of the abstraction barrier, which drops from 7.7 to 5.3 kcal/mol with ZPE. Note that ZPE has the opposite effect upon the barrier to H· abstraction, which is reduced, as compared to OH· addition which rises.

With the forgoing as a caveat, a survey of calculated values for the addition and abstraction processes, including not only G3, but also CBS-QB3 and CCSD(T), leads to the following conclusions. The exothermicity of the addition process falls in the range 12.6-19.4 kcal/mol, prior to ZPE correction, and 16.4-18.3 kcal after this correction. The outlier is a 2008 CBS-QB3 calculation [46] of 10.4 kcal/mol. The barrier for this addition process is clearly less than 5 kcal/mol, but there is significant variation within this range, even some suggesting no barrier at all. There seems to be greater harmony amongst the computations of the H· abstraction process, where the overall exothermicity lies in the 3-6 kcal/mol range. Barrier predictions are more scattered, varying between 3.5 and 7.8 kcal/mol, with a higher outlier of 11.8. The ranges that are derived from the panoply of prior calculations are displayed in the first row of Table 1. In terms of offering a clear target at which to shoot, the previous high-level calculations instead present a rather diffuse and extended bulls-eye. This fact will of course complicate the analysis to a certain extent but still leaves us with some measure of the accuracy of each DFT method.

Overall Reactions

The energetics computed for the addition and abstraction processes are reported in Table 1, as electronic energies without vibrational or other corrections. In both cases, ΔE refers to the entire process from isolated reactants to final products. The barrier $E^{\dagger}$ likewise takes the separated optimized reactant molecules as its base point. Beginning with the addition process, Table 1 indicates that B3LYP, BH&HLYP, and MPW1K all fall into the acceptable range of overall exothermicity; M05-2X is slightly too negative, and PBE0 and PBEPBE a bit more so, particularly

the latter. All of the DFT approaches provide reasonable addition barriers, especially given the wide latitude arising from the assortment of high-level treatments. There is one exception in that PBEPBE does not appear to contain a transition state on its potential energy surface, with the reactants combining in a barrierless process. Also while the B3LYP and PBE0 approaches successfully identify a transition state, this configuration is located nearly 3 kcal/mol below the reactants; likewise for M05-2X, except that the transition state lies at about the same energy as the isolated reactants. Note, however, that the same idea of a transition state that is more stable than isolated reactants is true for some of the high-level calculations as well.

Turning next to the H· abstraction process, BH&HLYP suggests a slightly endothermic process, in contrast to negative values arising from the higher level results. PBEPBE is exothermic but probably too much so; indeed this high exothermicity prevents the identification of a pre-reaction complex or a transition state for the transfer (see below). The total ΔE for the process by which OH· abstracts a H atom from benzene is equivalent to an evaluation of the difference in bond dissociation energies between the CH bond in C_6H_6 and the OH bond in HOH. For example, these two quantities were computed by the B3LYP method to be 118.1 and 122.2 kcal/mol, respectively. The greater stability of the latter bond thus makes for an overall exothermic process by the 4.1 kcal/mol listed in Table 1.

The individual bond dissociation energies are reported in Table 2 for each of the DFT methods, where it may be observed that the smallest C-H BDE of 115.7 kcal/mol is associated with the PBEPBE method, which also yields the largest O-H BDE, which accounts for its prediction of an overly exothermic and barrierless H· abstraction process. The penultimate row of Table 2 lists the same quantities computed by the ROMP2/aug-cc-pVDZ procedure, using geometries obtained with BH&HLYP. (These quantities are essentially unchanged if other optimized geometries are used.) The ROMP2 C-H BDE is smaller than any of the DFT estimates, whereas it falls right within the range of DFT values of the O-H BDE. Regarding the barrier for abstraction, PBEPBE again does not lead to a transition state. The BH&HLYP barrier is too high; the MPW1K value is just barely above the acceptable range and PBE0 and B3LYP slightly below. M05-2X most closely mimics the data obtained with the higher level calculations. The experimental values of the electronic portion of the bond dissociation energies in the last row of Table 2 may be seen to be higher than computed values. More important than the absolute values, however, is the difference of 6 kcal/mol, which expresses the relative strengths of the C-H and O-H bonds. This difference is reproduced reasonably well by B3LYP, PBE0, PBEPBE and ROMP2.

One appealing and efficient prescription by which to study processes of this sort might begin with the optimization of geometries via a DFT method, followed by the application of the MP2 procedure to evaluate the energetics, using a large basis set. In order to analyze the reliability of this approach, ROMP2 calculations were performed with the aug-cc-pVDZ basis set, using geometries obtained from three different DFT methods: BH&HLYP, PBE0, and MPW1K. As indicated in Table 3, the small differences in geometries arising from different DFT functionals have very little effect upon the ROMP2 energies. The addition and abstraction process exothermicities are -18.7 and -7.2 kcal/mol, respectively, regardless of which set of geometries is used. Likewise, a barrier of 2 kcal/mol is obtained for the addition barrier, with the exception of PBE0 for which the transition state located lies below the energy of the reactants, as was also the case in Table 1. There is a fairly high level of inconsistency in the barriers computed for H· abstraction. While the BH&HLYP geometry leads to a ROMP2/aug-cc-pVDZ barrier of 2.3 kcal/mol, closely akin to the BH&HLYP/6-31+G** barrier itself, the PBE0 geometry predicts a barrier of 8.1 kcal/mol, and the MPW1K geometry yields an intermediate value of 5.4 kcal/mol. It would thus appear that the particular geometry can be important when applying the ROMP2 method.

It is natural to wonder then about how the geometries differ. The transition state for H· abstraction is exhibited in Fig 3 where r_C and r_O refer, respectively, to the distance between the transferring H and the C and O atoms. The arrangement is not quite linear with θ(C--H--O) angles between 165º and 170º, as reported in the last column of Table 4. It may be noted that as one progresses from BH&HLYP to MPW1K and then to PBE0, that r_C becomes smaller and r_O larger, consistent with a progressively earlier transition state. This idea is reinforced when the ratio of r_C to the sum of the two X--H segments is computed, as listed in the third column of Table 4. Comparison of these data with the last column of Table 3 suggests that earlier transitions states correlate with a higher abstraction barrier. There is also a trend of diminishing θ, i.e. lesser linearity, as the barrier rises, albeit within the context of small differences in angle.

Individual Reaction Steps

The data reported above refer to the entire process of H· abstraction, from a pair of isolated C_6H_6 and OH· monomers, to C_6H_5· and HOH following abstraction and separation. However, the process occurs by several steps, beginning with the association into the $C_6H_6\cdots$OH complex, the H· transfer within the complex to $C_6H_5\cdots$HOH, and then finally the separation into monomers. As depicted in Fig 2, each step involves a different energetic change. Unfortunately, there has been little study of these individual energetic quantities at high levels of theory. One very recent work, however, has reported values [29] for these quantities, which are listed in the last row of Table 5.

The first column of Table 5 indicates that the association of C_6H_6 with OH· is rather weak, exothermic by roughly 1 kcal/mol. The later dissociation to products C_6H_5 and HOH, E_4, requires a bit more energy, between 2 and 3.5 kcal/mol. The CCSD(T) computations [29] found values of about 3 kcal/mol for both of these complexation energies. The underestimates of the DFT binding energies, particularly that between C_6H_6 and OH·, are likely due at least in part to their failure to properly include dispersion forces. It is in the intermediate steps, involving transition state $C_6H_5\cdots H\cdots OH$, that the various methods differ the most. BH&HLYP indicates the highest barrier of 12.6 kcal/mol from the encounter complex, E_2, with B3LYP predicting the lowest at 3.2 kcal/mol. These values may be compared with the best estimate of this quantity in the literature of 10.1 kcal/mol. (Note that these barriers, going to transition state from encounter complex, differ from the overall energy barriers $E^{\dagger}$ listed in the last column of Table 1, which begin from the fully separated reactants.)

The overall ΔE of the abstraction process, which goes from isolated C_6H_6 with OH· monomers to C_6H_5 plus HOH, has been reported in the penultimate column of Table 1, and represents the difference in C-H and O-H bond energies. One may also inquire about the energy required to go from one well of Fig 2 to the next, from the $C_6H_6\cdots OH$ encounter complex to $C_6H_5\cdots HOH$. This quantity, denoted $\Delta E'$ and equal to E_2+E_3, is listed in the last column of Table 5. It is about 1-2 kcal/mol more negative than the full ΔE in Table 1. This difference is largely due to the stronger binding between products C_6H_5 and HOH than between reactants C_6H_6 and OH. The B3LYP, PBE0, and M05-2X methods all provide values quite similar to one another, between -5.6 and -5.9 kcal/mol, for this quantity, which also mimics the CCSD(T) result in the last row of the table. MPW1K is a little less negative, and BH&HLYP even less so, nearly zero.

Like abstraction, the addition process also passes through an intermediate and transition state. As illustrated in Fig 1, the OH· radical first forms an encounter complex above the approximate center of the benzene plane, with a binding energy of E_1. It then moves down towards one of the C atoms as it adds to that atom and changes its hybridization to sp^3. In doing so, it first passes through a transition state which involves an energy barrier equal to E_2. From this point, the completion of the addition lowers the energy by E_3. As reported in the first column of Table 6, all of the methods predict the initial complexation energy of OH above the benzene plane is between 2.6 and 4.7 kcal/mol, with M05-2X on the high end, possibly a bit inflated. As in the case of abstraction, PBEPBE is anomalous in that the reactants go directly to addition product C_6H_6OH with neither an intermediate nor a transition state. There is a good deal of variability in terms of the barrier E_2. BH&HLYP predicts a high value of 7.1 kcal/mol, MPW1K and M05-2X agree that E_2 is between 4 and 5 kcal/mol, whereas PBE0 and B3LYP lead to an essentially barrierless addition. These values can be compared with the

CCSD(T) estimate of 3.8 kcal/mol. There is near uniformity in the reverse barrier, E_3, in that four of the DFT methods all yield values between 19 and 21 kcal/mol, in agreement with CCSD(T); only B3LYP is in disagreement with a smaller value of 14.4 kcal/mol. This last underestimate is consistent with the lack of a barrier for the addition with B3LYP.

CONCLUSIONS

The various DFT functionals tested here all have certain strengths and weaknesses. B3LYP, BH&HLYP, and MPW1K all handle the addition of OH· to benzene well, falling in the range of exothermicity computed by more accurate ab initio methods. M05-2X is slightly too negative, and PBE0 and PBEPBE more so. Most of these approaches yield acceptable values of the energy barrier to this addition, with the exception of PBEPBE where a transition state is not easily located on the surface; the PBE0 functional identifies a transition state, but this structure lies lower in energy than the isolated reactants. With respect to the other reaction channel, H· abstraction, high-level calculations yield an exothermic process, which is reproduced by most of the DFT methods. The exception here is BH&HLYP which predicts the reaction to be endothermic. On the opposite extreme is the overly exothermic value computed via PBEPBE. The BH&HLYP barrier to H· abstraction is too high while the MPW1K, PBE0, and B3LYP values are better, and M05-2X closest to high-level ab initio calculations. The prescription of applying a correlated ab initio ROMP2 formalism to geometries optimized by DFT is adequate for most quantities, the exception is the H· abstraction barrier which shows a good deal of sensitivity to specific DFT functional optimization

When the individual reaction steps are considered separately, all underestimate the association of OH· with C_6H_6 in the abstraction mode, but do better in the addition channel. With respect to the latter process, the barrier to moving from encounter complex to addition product is rather variable. BH&HLYP predicts the highest barrier, MPW1K and M05-2X somewhat lower, whereas PBE0 and B3LYP predict no barrier. In terms of the abstraction process, the energy needed to separate the HOH and C_6H_5 products is rather uniformly predicted. The barrier that separates the two wells in the abstraction reaction is more sensitive to functional. B3LYP yields the lowest barrier of 3.2 kcal/mol and BH&HLYP the highest, nearly four times greater. The exception is PBEPBE which goes directly to products in either case, with no barrier, and seems ill-suited to study of these processes.

Table 1. Energetics (kcal/mol) calculated for the addition and abstraction processes of benzene with the 6-31+G** basis set.

	addition		abstraction	
	ΔE	$E^{\dagger}$	ΔE	$E^{\dagger}$
high-level[a]	-(13-19)	-1 - +3	-(3-5.5)	3-8
B3LYP	-17.1	-2.7	-4.1	2.5
BH&HLYP	-14.9	4.0	+0.6	11.7
PBE0	-21.3	-2.8	-4.6	2.3
PBEPBE	-24.3	b	-8.4	b
MPW1K	-19.3	1.7[c]	-2.1	8.3
M05-2X	-20.6	-0.1	-3.6	6.2

[a][24,25,27,29,46]
[b]no transition state found
[c]found by series of optimizations

Table 2. Bond dissociation energies (kcal/mol) of C_6H_6 and HOH[a]

	C-H	O-H
B3LYP	118.1	122.2
BH&HLYP	118.0	117.4
PBE0	116.5	121.1
PBEPBE	115.7	124.1
MPW1K	116.7	118.7
M05-2X	119.6	123.1
ROMP2[a]	115.5	122.7
expt[b]	121	127

[a]computed with aug-cc-pVDZ basis set, using BH&HLYP geometries
[b]experimental bond enthalpies of 113 and 119, respectively, for C_6H_6 and HOH [24,28,47], corrected by zero point vibrational energies to estimate electronic contributions

Table 3. Energetics (kcal/mol) calculated for the addition and abstraction processes of benzene by applying ROMP2/aug-cc-pVDZ formalism to geometries obtained with the DFT methods shown.

	addition		abstraction	
geometry	ΔE	$E^{\dagger}$	ΔE	$E^{\dagger}$
BH&HLYP	-18.7	2.0	-7.2	2.3
MPW1K	-18.7	1.9	-7.2	5.4
PBE0	-18.7	a	-7.2	8.1

[a]transition state lies lower in energy than reactants

Table 4. Geometric features of abstraction transition state. See Fig 3 for definitions.

	r_C(C--H), Å	r_O(H--O), Å	$r_C/(r_C+r_O)$	θ(C--H--O), degs
BH&HLYP	1.268	1.200	0.514	169.8
MPW1K	1.244	1.223	0.504	167.2
PBE0	1.222	1.276	0.489	165.9

Table 5. Energetics (kcal/mol) of individual steps of H· abstraction process. See Fig 2 for definition of quantities.

	E_1	E_2	E_3	E_4	$\Delta E'=E_2+E_3$
B3LYP	-0.7	3.2	-8.8	2.3	-5.6
BH&HLYP	-0.9	12.6	-13.0	1.9	-0.4
PBE0	-1.2	3.5	-9.4	2.5	-5.9
PBEPBE	a	a	a	a	a
MPW1K	-0.8	9.2	-12.3	1.9	-3.1
M05-2X	-1.2	7.4	-13.0	3.2	-5.6
high level[b]	-3.6	10.1	-15.7	2.9	-5.6

[a]reactants go to product complex $C_6H_5\cdots HOH$ with no barrier
[b]from [29]

Table 6. Energetics (kcal/mol) of individual steps of H· addition process. See Fig 1 for definition of quantities.

	E_1	E_2	E_3
B3LYP	-2.6	-0.1	-14.4
BH&HLYP	-3.0	7.1	-19.0
PBE0	-3.5	0.8	-18.5
PBEPBE	a	a	a
MPW1K	-3.0	4.7	-21.0
M05-2X	-4.7	4.6	-20.5
high level[b]	-3.6	3.8	-19.6

[a]reactants go to addition complex C_6H_6OH with no barrier
[b]from [29]

REFERENCES

1. Matthews, J.; Sinha, A.; Francisco, J. S. Proc. Nat. Acad. Sci., USA 2005, 102, 7449.
2. Herrmann, H.; Hoffmann, D.; Schaefer, T.; Bräuer, P.; Tilgner, A. Phys. Chem. Chem. Phys. 2010, 11, 3796–3822.
3. Barnes, I.; Solignac, G.; Mellouki, A.; Becker, K. H. Phys. Chem. Chem. Phys. 2010, 11, 3844–3857.
4. Mitroka, S.; Zimmeck, S.; Troya, D.; Tanko, J. M. J. Am. Chem. Soc. 2010, 132, 2907–2913.
5. Christiansen, C. J.; Francisco, J. S. J. Phys. Chem. A 2010, 114, 9163.
6. Wua, S. Y.; Raghunathb, P.; Wua, J. S.; Lin, M. C. J. Phys. Chem. A 2010, 114, 633.
7. Hartung, J. Chem. Rev. 2009, 109, 4500.
8. Dhaouadi, Z.; Nsangou, M.; Garrab, N.; Anouar, E. H.; Marakchi, K.; Lahmar, S. J. Mol. Struct. (Theochem) 2009, 904, 35.
9. Stubbe, J.; van der Donk, W. A. Chem. Rev. 1998, 98, 705.
10. Frey, P. A.; Hegeman, A. D.; Reed, G. H. Chem. Rev. 2006, 106, 3302.
11. Whittaker, J. W. Chem. Rev. 2003, 103, 2347.
12. Grimaldi, S.; Ostermann, T.; Weiden, N.; Mogi, T.; Miyoshi, H.; Ludwig, B.; Michel, H.; Prisner, T. F.; MacMillan, F. Biochem. 2003, 42, 5632
13. Mansoorabadi, S. O.; Seravalli, J.; Furdui, C.; Krymov, V.; Gerfen, G. J.; Begley, T. P.; Melnick, J.; Ragsdale, S. W.; Reed, G. H. Biochem. 2006, 7122
14. Maity, A. N.; Hsieh, C.-P.; Huang, M.-H.; Chen, Y.-H.; Tang, K.-H.; Behshad, E.; Frey, P. A.; Ke, S.-C. J. Phys. Chem. B 2009, 113, 12161.
15. de Visser, S. P.; Shaik, S. J. Am. Chem. Soc. 2003, 125, 7413.
16. Watts, Z. I.; Easton, C. J. J. Am. Chem. Soc. 2009, 131, 11323.
17. Goshe, M. B.; Chen, Y. H.; Anderson, V. E. Biochem. 2000, 39, 1761.
18. Nukuna, B. N.; Goshe, M. B.; Anderson, V. E. J. Am. Chem. Soc. 2001, 123, 1208.
19. Garrison, W. M. Chem. Rev. 1987, 87, 381.
20. Stadtman, E. R. Ann. Rev. Biochem. 1993, 62, 797.
21. Easton, C. J. Chem. Rev. 1997, 97, 53.
22. Takamoto, K.; Chance, M. R. Annu. Rev. Biophys. Biomol. Struct. 2006, 35, 251.
23. Scheiner, S.; Kar, T. J. Am. Chem. Soc. 2010, 132, 16450.
24. Tokmakov, I. V.; Lin, M. C. J. Phys. Chem. A 2002, 106, 11309.
25. Chen, C.-C.; Bozzelli, J. W.; Farrell, J. T. J. Phys. Chem. A 2004, 108, 4632.
26. da Silva, G.; Moore, E. E.; Bozzelli, J. W. J. Phys. Chem. A 2009, 113, 10264.
27. Seta, T.; Nakajima, M.; Miyoshi, A. J. Phys. Chem. A 2006, 110, 5081.
28. Mardyukov, A.; Sanchez-Garcia, E.; Crespo-Otero, R.; Sander, W. Angew. Chem., Int. Ed. Engl. 2009, 48, 4804.
29. Hollman, D. S.; Simmonett, A. C.; Schaefer, H. F. Phys. Chem. Chem. Phys. 2011, 13, 2214.
30. Park, J.; Nguyen, H. M. T.; Xu, Z. F.; Lin, M. C. J. Phys. Chem. A 2009, 113, 12199.
31. Carissan, Y.; Klopper, W. J. Mol. Struct. (Theochem) 2010, 940, 115.
32. Yeung, L. Y.; Elrod, M. J. J. Phys. Chem. A 2003, 107, 4470.
33. Devi, K. J.; Parveen, S.; Chandra, A. K. Chem. Phys. Lett. 2009, 480, 161.
34. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J., J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.;

Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A.; Gaussian, Inc.: Pittsburgh PA, 2003.

35. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; G. E. Scuseria; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; B. Mennucci; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J.; Gaussian, Inc: Wallingford CT, 2009.
36. Becke, A. D. J. Chem. Phys. 1993, 98, 5648.
37. Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. J. Phys. Chem. 1994, 98, 11623–11627.
38. Lee, C.; Yang, W.; Parr, R. G. Phys. Rev. B 1988, 37, 785.
39. Becke, A. D. J. Chem. Phys. 1993, 98, 1372.
40. Becke, A. D. Phys. Rev. A 1988, 38, 3098.
41. Perdew, J. P.; Burke, K.; Ernzerhof, M. Phys. Rev. Lett. 1996, 77, 3865–3868.
42. Adamo, C.; Barone, V. J. Chem. Phys. 1999, 110, 6158.
43. Lynch, B. J.; Fast, P. L.; Harris, M.; Truhlar, D. G. J. Phys. Chem. A 2000, 104, 4811–4815.
44. Lynch, B. J.; Truhlar, D. G. J. Phys. Chem. A 2001, 105, 2936–2941.
45. Zhao, Y.; Schultz, N. E.; Truhlar, D. G. J. Chem. Theory Comput. 2006, 2, 364–382.
46. Uc, V. H.; Alvarez-Idaboy, J. R. l.; Galano, A.; Vivier-Bunge, A. J. Phys. Chem. A 2008, 112, 7608.
47. Blanksby, S. J.; Ellison, G. B. Acc. Chem. Res. 2003, 36, 255.