

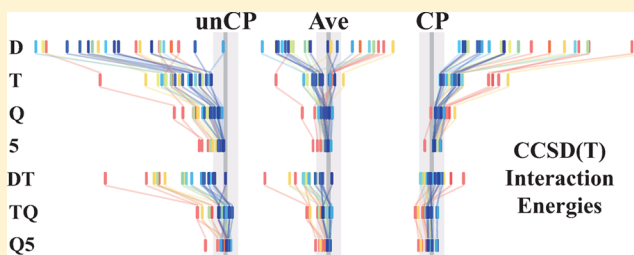
Comparing Counterpoise-Corrected, Uncorrected, and Averaged Binding Energies for Benchmarking Noncovalent Interactions

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S Supporting Information

ABSTRACT: High-quality benchmark computations are critical for the development and assessment of approximate methods to describe noncovalent interactions. Recent advances in the treatment of dispersion by density functional theory and also the development of more efficient wave function techniques to reliably address noncovalent interactions motivate new benchmark computations of increasing accuracy. This work considers focal point approximations to estimate the complete basis set limit of coupled-cluster theory through perturbative triples [CCSD(T)/CBS] and evaluates how this approach is affected by the use or absence of counterpoise (CP) correction or, as has recently gained traction, the average of those values. Current benchmark protocols for interaction energies are computed with all CP procedures and assessed against the A24 and S22B databases and also to highly converged results for formic acid, cyanogen, and benzene dimers. Whether CP correction, no correction, or the average is favored depends upon the theoretical method, basis set, and binding motif. In recent high-quality benchmark studies, interaction energies often use second-order perturbation theory with extrapolated aug-cc-pVTZ (aTZ) and aug-cc-pVQZ (aQZ) basis sets [MP2/aTZ] combined with a “coupled-cluster correction,” $\delta_{\text{MP2}}^{\text{CCSD(T)}}$, evaluated in an aug-cc-pVDZ basis. For such an approach, averaging CP-corrected and uncorrected values for the MP2 component and using CP-corrected $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ values offers errors more balanced among binding motifs and generally more favorable overall. Other combinations of counterpoise correction are not quite as accurate. When employing MP2/aQ5Z extrapolations and an aTZ basis for $\delta_{\text{MP2}}^{\text{CCSD(T)}}$, using CP-corrected or averaged MP2 estimates are about equally effective (and slightly superior to uncorrected MP2 values), but the counterpoise treatment of $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ makes little difference. Focal point estimates at this level achieve benchmark quality results otherwise accessible only with CCSD(T)/aQZ or better.



1. INTRODUCTION

Noncovalent interactions (NCI) are critical to drug binding,^{1–4} biomolecular structure,^{5–9} and crystal packing.^{10–12} Accurate quantum chemical modeling of many types of NCI requires a robust treatment of electron correlation like that supplied by the coupled-cluster theory with single, double, and perturbative triple excitations [CCSD(T)],¹³ which performs so well as to be designated the “gold standard” of computational chemistry. With sufficiently large basis sets, standard CCSD(T) has been shown very reliable for noncovalent interactions.¹⁴ Unfortunately, its steep $O(N^7)$ asymptotic scaling in computational cost (where N is the number of basis functions, a reflection of system size) means CCSD(T) can only be routinely applied to systems of modest size (up to ~ 30 atoms). To extend the range of applicability, focal point analysis^{15,16} is often employed to estimate CCSD(T) in a large basis set

$$E_{\text{CCSD(T)}}^{\text{large}} \approx E_{\text{MP2}}^{\text{large}} + \delta_{\text{MP2}}^{\text{CCSD(T)}} \quad (1)$$

$$\delta_{\text{MP2}}^{\text{CCSD(T)}} = E_{\text{CCSD(T)}}^{\text{small}} - E_{\text{MP2}}^{\text{small}} \quad (2)$$

where subscripts and superscripts on energy terms refer to method and basis set, respectively. Focal point analyses

following this prescription have been applied to NCI in many recent studies.^{4,7,17–28} While this approach has been shown to be reliable, recent work has demonstrated that caution is necessary in selecting the “small” basis set for the $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ term.^{24,26–28}

Counterpoise²⁹ correction (CP) is often employed in NCI computations of interaction energy (IE) to reduce basis set superposition error (BSSE). Often, complexes are overbound in uncorrected (unCP) computations (due to BSSE) and underbound in CP computations. The converged complete basis set (CBS) limit tends to be bounded by CP and unCP values, though convergence of CP results with respect to basis set size is far smoother and more systematic.³⁰ One pragmatic approach then is to average CP and unCP quantities.^{30–35} For example, in a range of basis sets from aug-cc-pVDZ to aug-cc-pV5Z (here abbreviated as aDZ, a5Z, etc.), Halkier and co-workers^{30,36} demonstrated that averaging CP and unCP can yield accurate IE in various small hydrogen-bonded complexes. They found that for the small aDZ basis, unCP was often closer to the CBS

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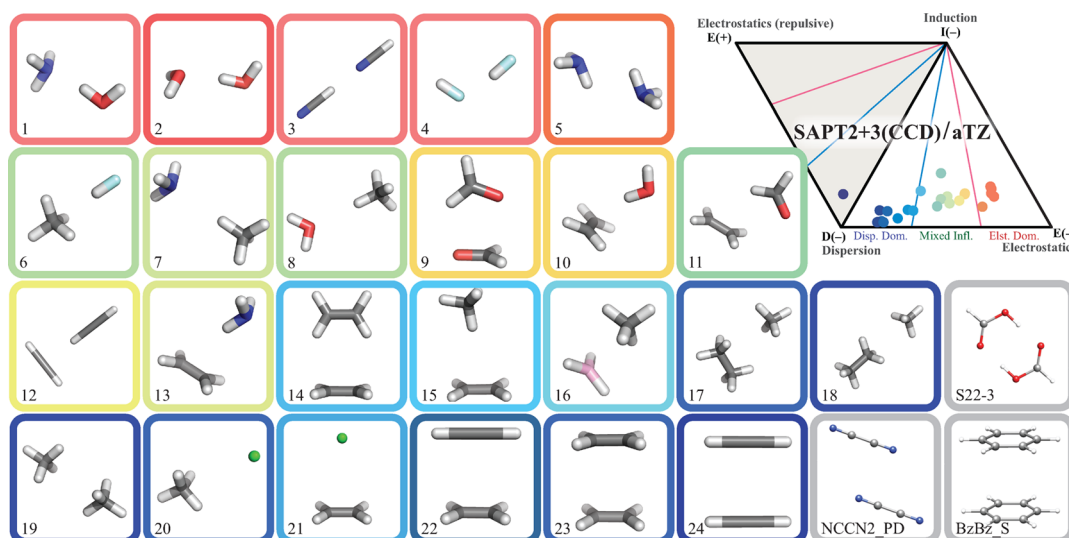


Figure 1. Bimolecular complexes addressed in this work include the A24 database (numbered), formic-acid dimer (S22-3), cyanogen dimer (NCCN2_PD), sandwich benzene dimer (BzBz_S), and the S22 database (not shown). A ternary representation of a SAPT decomposition of the interaction energy (upper right) provides a color index to the bonding motif for A24 members that is used in subsequent figures.

limit than either CP or averaged quantities, but for aTZ and larger bases, averaging was a better approximation. Recently, Mackie and DiLabio³⁷ proposed extending the idea of averaging CP and unCP quantities to focal point methods, as in eqs 1 and 2. In particular, they advocate adding averaged $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ corrections to averaged MP2 interaction energies. Their approach is outlined as

$$E_{\text{Ave-CCSD(T)}}^{\text{large}} \approx E_{\text{Ave-MP2}}^{\text{large}} + \text{Ave-}\delta_{\text{MP2}}^{\text{CCSD(T)}} \quad (3)$$

$$\text{Ave-}\delta_{\text{MP2}}^{\text{CCSD(T)}} = E_{\text{Ave-CCSD(T)}}^{\text{small}} - E_{\text{Ave-MP2}}^{\text{small}} \quad (4)$$

where any quantity with “Ave” is the average of CP and unCP corrected values. In their work and the present work, CP computations use the scheme outlined by Boys and Bernardi.²⁹

The present study compares CP, unCP, and Ave approaches in focal point estimations of CCSD(T)/CBS binding energies in the A24³⁸ and S22⁷ databases. Together, these feature diverse NCI motifs over a range of system sizes, from hydrogen fluoride dimer (4 atoms) to adenine–thymine complexes (30 atoms), and enable basis set convergence properties and error trends to be revealed.

■ COMPUTATIONAL METHODS

To assess various approaches to estimating the CCSD(T)/CBS limit for IEs, we must compare them to reference data of truly high quality. Hence, we examined the A24 database of Hobza and co-workers³⁸ because its bimolecular complexes are small enough to perform large-basis CCSD(T) computations for direct extrapolations to the CBS limit. While geometries were used as published, the existing reference—a power function fit of the aug-cc-pVXZ ($X = \text{T, Q, 5}$) correlation component of the CCSD(T) interaction energy affixed to an aug-cc-pVSZ SCF, all CP-corrected—was revisited (see below) in an effort to formulate an unbiased reference for evaluating unCP, Ave, and CP performance. Members of the A24 database were partitioned by binding type based on SAPT2+3(CCD)/aTZ results, as shown in Figure 1. This resulted in five hydrogen-bonded, nine mixed-influence, and ten dispersion-dominated systems, with the latter two categories reapportioned slightly

from Hobza’s classification. A color map applied to a ternary diagram (upper right of Figure 1) derived from SAPT decompositions of interaction energies yields a quick visual encoding of NCI type (red, hydrogen-bonded; blue, dispersion-dominated; and green, mixed) that is used throughout this work. Analysis of interaction energy errors by category allows one to see if particular methods struggle for certain binding motifs.

We also examined the S22 database of van der Waals complexes,⁷ which includes somewhat larger systems (up to adenine–thymine), although the CCSD(T)/CBS limits are not known quite as accurately as they are for A24. Geometries were used as published, and errors are reported relative to S22B revised interaction energies (all counterpoise corrected).²⁷ S22B reference values for smaller systems are CCSD(T)/aQ5Z or aS6Z extrapolations, where aX(X+1)Z indicates a 2-point Helgaker extrapolation³⁹ of the correlation energy between aXZ and a(X+1)Z basis sets. Reference values for larger systems are commonly $\text{MP2/aQ5Z} + \delta_{\text{MP2}}^{\text{CCSD(T)}}$, where the latter is evaluated at aQZ²⁷ or aTZ + midbond functions.⁴⁰ When a typical S22B reference methodology, $\text{CP-MP2/aQ5Z} + \text{CP-}\delta_{\text{MP2}}^{\text{CCSD(T)}}$ /aQZ, is evaluated against the highly accurate Ave-CCSD(T)/aQ5Z IE for the seven smallest S22 members, mean absolute errors (MAE) are obtained of only 0.02 kcal/mol. In comparison, Mackie and DiLabio’s benchmark approach,³⁷ Ave-CCSD(T)/aTQZ, yields MAE 0.03 kcal/mol. This suggests that benchmarks in both S22B and Mackie and DiLabio’s study are converged to within a few hundredths of a kcal/mol of the CCSD(T)/CBS limit. By comparison, several of the errors analyzed below are on the order of 0.1 kcal/mol or larger. Partitioning of the S22 systems by binding type into hydrogen-bonding, dispersion-dominated, and mixed influence categories is based on SAPT2+ (3)/aTZ results.⁴¹ Color labeling according to NCI character, as described for A24, is also applied to S22.

To examine in detail the basis set convergence behavior of MP2 and CCSD(T) interaction energy components, CCSD(T) results have been obtained (in both CP and unCP) through MOLPRO⁴² 2010.1 with the aXZ ($X = \text{D, T, Q, 5}$) basis sets for all members of A24 and two additional complexes: formic acid dimer (S22-3)⁷ and parallel-displaced cyanogen dimer

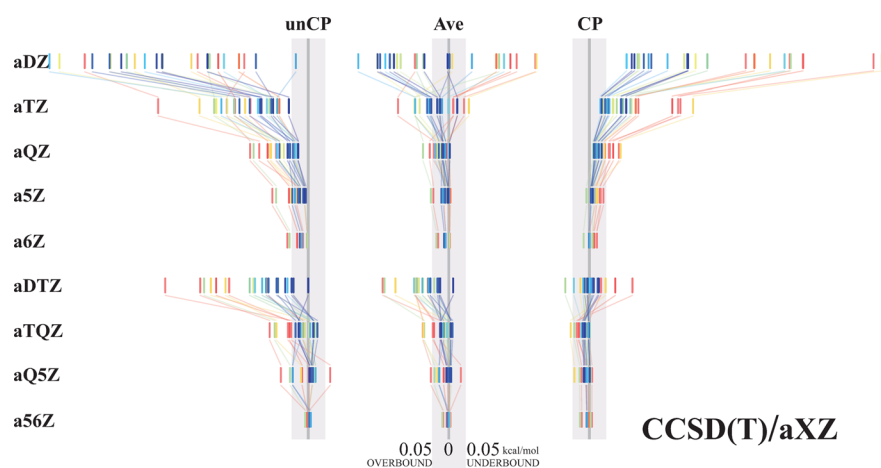


Figure 2. Error in CCSD(T) interaction energy for A24 database members computed with three BSSE treatments: counterpoise corrected (CP), uncorrected (unCP), and averaged (Ave). Threads for each complex show convergence toward the reference across the aug-cc-pVXZ basis set series. Only by using aTQZ or a5Z with Ave or CP procedures are adequate error profiles for benchmark results achieved.

(NCCN2_PD).⁴³ Selected complexes (A24-1, 2, 3, 4, 5, 6, 8, 20, 21) were also computed with the a6Z basis, and the sandwich benzene dimer was obtained through aQZ (NBC10^{27,44} database; BzBz_S at 3.9 Å separation). From these results were extracted CCSD(T) and MP2 interaction energies, $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ terms and various composite interaction energies according to eq 1. All Ave values are literal averages of CP and unCP, both reference and correlation components. For 2-point Helgaker extrapolations of the correlation energy,³⁹ the result is always affixed to the SCF energy in the larger basis, with CP values incorporating purely CP reference and correlation components and unCP incorporating purely unCP components.

RESULTS AND DISCUSSION

CCSD(T) Interaction Energies. In formulating a reference interaction energy from a series of basis set results such as collected here (or in the original A24 publication), there are a number of plausible approaches: Helgaker extrapolation of the dimer and monomer two highest ζ correlation energies then forming an IE, exponential function fit to the dimer and monomer correlation energies then forming an IE, exponential function fit to the correlation IE, power function fit to the correlation IE (Hobza's procedure), or exponential function fit to the total IE. (The aDZ basis is excluded from any of these procedures because in our experience it is too small to be used reliably in extrapolations.) These CBS procedures can be applied in either CP or unCP regimes and within each are stable in their predictions, varying by either less than 0.05 kcal/mol or 2% for all CP and nearly all unCP procedures (5% encompasses all). The exception to this stability is the unCP analog to Hobza's A24 procedure, which would give IEs several kcal/mol too bound in several cases.

We have attempted to avoid bias in reference IEs for the A24 test set by including both CP and unCP information. One could employ procedures like averaging the best Helgaker two-point extrapolations, averaging the exponential fits to the total or correlation IE, or the selection for this work, weighted averaging of the exponential fits to the correlation IE with weights provided by the exponential rate constant. Fortunately, once again, the values by this method are scarcely different to what Hobza chose as the best reference (max difference 0.03, average difference 0.01 kcal/mol) through the power function fitting procedure on aTQ5Z CP. They are also nearly the same

(max difference 0.05, average difference 0.01 kcal/mol) as what our group would ordinarily choose as the best reference, the aQ5Z CP Helgaker-extrapolated procedure. The advantages are simply (1) the use of a value that is neither CP, Ave, nor unCP to judge the relative efficacy of CP, Ave, and unCP and (2) using all reliable information (aTZ and higher, CP and unCP) in proportion to its reliability. That the selected procedure (consult Supporting Information for formulas and reference IE) produces a satisfactory reference can be seen in that curves derived from aTQ5Z fit intersect a6Z values when available (average absolute error 0.003 kcal/mol for CP and 0.019 kcal/mol for unCP over nine species) and by noting that the average BSSE is only 0.02 kcal/mol. This alternate reference was constructed for assessing BSSE schemes, and the authors do not necessarily recommend it replace the original set of reference IE for conventional use. Nevertheless, for clarity, the reference is designated A24A.

The performance of CCSD(T) with respect to the reference is shown in Figure 2 for a progression of basis sets and for unCP, Ave, and CP BSSE treatments. The error in interaction energy (kcal/mol) with respect to the weighted-average reference is represented for each database member as a marker, colored to reflect the bonding character as revealed by SAPT. Tracing a thread from aDZ through to a5Z or a6Z on the CP plot (rightmost in Figure 2) involves a series of shifts in the same direction, indicating that IE are monotonically convergent. In contrast, some members on the unCP plot show nonmonotonic patterns, particularly A24-4, A24-21, and formic acid dimer. Note that a change in reference value for a given system would shift the corresponding thread left or right, not alter the shape of the marker and line assembly. As it can be difficult to pick out individual systems in this plot style, the reader is referred to the Supporting Information, which contains the same information but in an expanded format more suited to following basis set convergence in a given system.

Figure 2 shows that Ave is the preferable BSSE treatment at basis aDZ, being optimal for 19 of the 27 systems considered. Its MAE of 0.145 kcal/mol arises by correcting the worst excesses of unCP (MAE 0.418 kcal/mol) and CP (0.367 kcal/mol), particularly for hydrogen bonding systems in the latter. As BSSE ranges over 0.21–2.73 kcal/mol (A24-21 and formic acid dimer), it is unsurprising that a simple average should be insufficient. The aTZ basis improves errors substantially

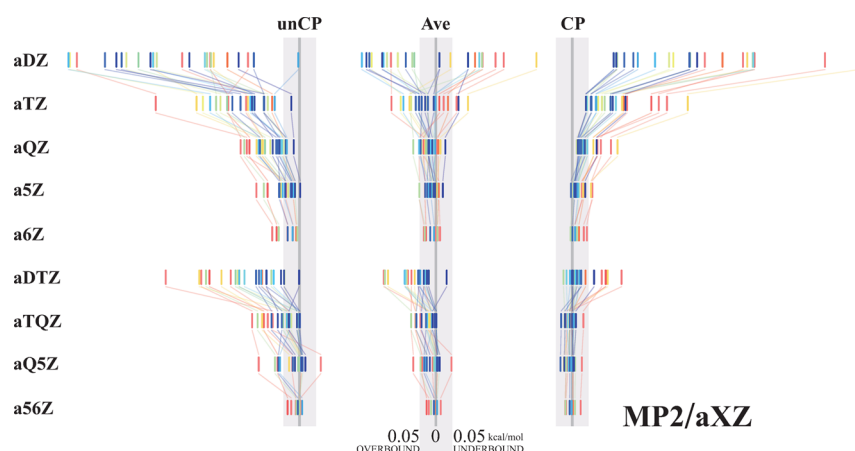


Figure 3. Error in MP2 interaction energy for A24 database members computed with three BSSE treatments: counterpoise corrected (CP), uncorrected (unCP), and averaged (Ave). Threads for each complex show convergence toward the reference across the aug-cc-pVXZ basis set series and the two-basis extrapolation series. Averaging offers clear advantages at smaller basis sets, yet CP is most reliable for the extrapolations routinely employed to construct reference interaction energies.

(BSSE range halved to 0.13–1.48 kcal/mol), but for unCP (MAE 0.185 kcal/mol) and CP (0.110 kcal/mol), members remain reliably overbound and underbound, respectively. Nearly all systems determine Ave (MAE 0.053 kcal/mol) to be the best or nearly best selection. With aQZ and a5Z basis sets, errors reach an acceptable span using Ave and CP treatments. By a5Z, the majority of systems are best represented through counterpoise correction. All errors are within ~ 0.04 kcal/mol, and MAE has reached very low levels: 0.032, 0.011, and 0.013 kcal/mol for unCP, Ave, and CP. Min and max BSSE continue to show a ~ 2 factor of improvement with each zeta level so that by a5Z, the range is 0.01–0.31 kcal/mol. Achieving CCSD(T) interaction energies accurate to ~ 0.05 kcal/mol appears to require computations with aQZ or a5Z basis sets, which are intractable for all but the smallest bimolecular complexes. This work evaluates computational schemes that seek to overcome this barrier. An obvious route is to perform a basis set extrapolation, and CP-CCSD(T)/aDTZ shows promising error statistics with MAE 0.027 kcal/mol. However, extrapolations containing ill-converged quantities, viz. aDZ, can themselves be unreliable and reveal motif-dependent errors, as seen for hydrogen bonding systems (red threads) in CP-CCSD(T)/aDTZ and the divergence of red and blue threads in unCP. In our view, focal point estimates of CCSD(T)/CBS, as in eqs 1 and 2, are more effective in cost/benefit terms, and they are discussed below.

MP2 Interaction Energies. Before considering focal point approaches, separate examination is first made of MP2/CBS values and $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ /CBS corrections to see if averaging CP and unCP is beneficial for either component. Figure 3 presents unCP, Ave, and CP MP2 interaction energies as a function of basis set size (aDZ to a6Z) and corresponding CBS extrapolations (aDTZ to a56Z) for the A24 database. Additional results for the formic acid dimer, parallel-displaced cyanogen dimer, and sandwich benzene dimer are discussed; figures for these are available in the Supporting Information.

Using the relatively small aDZ basis set, Figure 3 shows averaging CP and unCP MP2 interaction energies to be consistently the best approach; MAE for unCP, Ave, and CP are 0.389, 0.137, and 0.364 kcal/mol, respectively. Increasing the basis from aDZ to aTZ reduces the BSSE (difference between CP and unCP values) from 0.20–2.57 to 0.14–1.52 kcal/mol

(largest error in both cases for formic acid dimer). For both aDZ and aTZ, generally unCP is superior to CP for the hydrogen bonded complexes, while CP outclasses unCP for mixed and dispersion-dominated systems. In the aTZ basis, the Ave MAE of 0.052 kcal/mol is clearly superior to 0.181 and 0.126 kcal/mol for unCP and CP.

Using aQZ or a5Z basis sets, CP and Ave continue to surpass unCP (excepting the erratic A24-24), with the better ζ convergence of CP leading to it being increasingly favored with larger basis sets, especially for dispersion-dominated systems. At Ave-MP2/aQZ, most all errors lie within 0.05 kcal/mol of the MP2/CBS reference, as reflected in the MAE value of 0.026 kcal/mol (compare with 0.092 and 0.048 kcal/mol for unCP and CP). By a5Z, advantage is shared between Ave (0.016 kcal/mol) and CP (0.022 kcal/mol), whereas unCP is hampered (0.045 kcal/mol) through slow convergence by the hydrogen-bonded complexes for which it had advantage at smaller basis sets. In the large aQZ basis set, BSSE ranges from 0.06–0.81 kcal/mol, while for a5Z the span is 0.02–0.45 kcal/mol (species for both are A24-19 and formic acid dimer). Although the upper end of this range is perhaps a surprisingly large BSSE for the sizable a5Z, this remains only a modest fraction ($\sim 2.4\%$) of the interaction energy (-18.331 kcal/mol) for the formic acid dimer.

The lower portion of Figure 3 examines the utility of counterpoise averaging in combination with basis set extrapolations of the correlation energy³⁹ through comparison to the estimated CBS limit. There are many cases where unsettled results associated with unCP in small basis sets lead to MP2/aDTZ interaction energies that are inferior to both their aDZ and aTZ ingredients. This same difficulty frequently appears for Ave results (e.g., A24-2 and 16) such that this basis treatment must be considered highly unreliable, even though its BSSE range 0.05–1.24 kcal/mol is better than aTZ. The CP-MP2/aDTZ MAE is 0.036 kcal/mol, which is comparable to Ave-MP2/aQZ, but Figure 3 shows several outliers among hydrogen-bonding systems. Advancing to the very common MP2/aTQZ basis treatment, CP yields the best interactions energies for all 27 cases. Moreover, even at this high ζ extrapolation, some values with Ave (A24-4, 22, formic acid dimer) are worse than their ingredients. MAE statistics are 0.050, 0.027, and 0.010 kcal/mol for unCP, Ave, and CP, the last treatment of which also

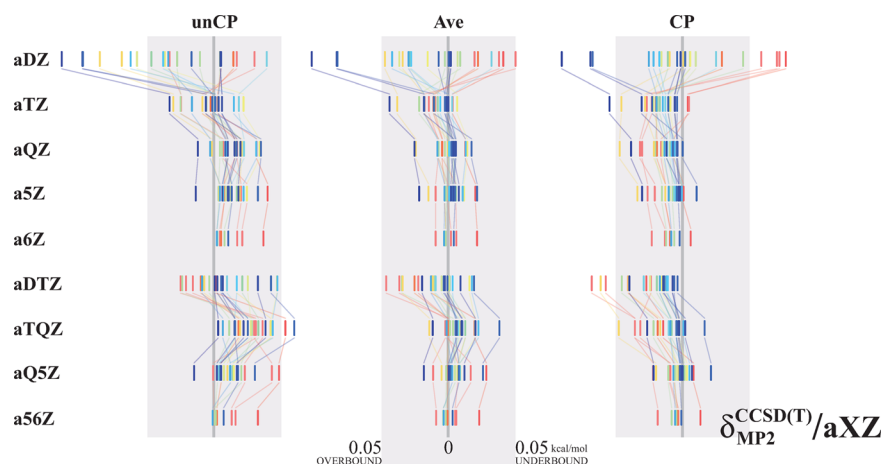


Figure 4. Error in $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ component of interaction energy computed with three BSSE treatments: counterpoise corrected (CP), uncorrected (unCP), and averaged (Ave). Threads for each complex show that for aTZ through a6Z, values are fairly stable with respect to basis set size, whereas the extrapolated series shows greater variation and no advantage in error distribution.

encompasses all member errors within ± 0.035 kcal/mol. BSSE at MP2/aTQZ for formic acid dimer remains large at 0.44 kcal/mol but otherwise is < 0.14 kcal/mol. At MP2/aQ5Z, unCP and Ave continue to improve (MAE 0.026 and 0.018 kcal/mol), but CP is essentially unchanged (0.011 kcal/mol). BSSE yet present is most often < 0.05 kcal/mol, though for formic acid it is 0.16 kcal/mol.

The MP2 results from 27 complexes illustrated in Figure 3 and the Supporting Information support the notion that averaging CP and unCP interaction energies is usually (but not always) beneficial when using a single basis set (no extrapolation). While averaging is particularly useful when employing smaller basis sets like aDZ and aTZ, it is not especially advantageous for the larger basis sets and extrapolations that are routinely used in benchmarking because the remaining BSSE has already been reduced to around 1% of the interaction energy. (It should also be noted that due to the increasing popularity of density-fitting techniques, performing the MP2 computation in a large basis set is not typically the limiting step in benchmark computations.) When using 2-point Helgaker-type extrapolations, CP results are typically the most reliable, followed by Ave results.

$\delta_{\text{MP2}}^{\text{CCSD(T)}}$ Corrections. To investigate the effects of counterpoise correction on the coupled-cluster correction term, errors for each of the unCP, Ave, and CP variants are shown in Figure 4 as a function of basis set size, from aDZ to a6Z; also plotted are Helgaker extrapolations³⁹ for each basis set pair considered. The reference is taken to be the difference in the references from preceding sections (weighted exponential fit to CCSD(T) less weighted exponential fit to MP2). Results are shown in Figure 4 for the A24 database; additionally, the formic acid dimer, parallel-displaced cyanogen dimer, and sandwich benzene dimer are available in the Supporting Information.

The common wisdom that $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ is largely insensitive to the basis set is upheld in the expanded horizontal scale of Figure 4 compared to Figures 2 and 3. Unfortunately, the basis set that has been most commonly employed for benchmark CCSD(T) NCI studies, aDZ, is, among the basis treatments considered here, the one for which that adage is least valid. For aDZ, the maximum BSSE is 0.16 kcal/mol (out of a total correction of -0.185 kcal/mol at the CBS limit) for formic acid dimer (0.10 kcal/mol for A24-4 is maximum within the A24 database). Using aDZ, unCP is best for most hydrogen bonding

complexes, while CP is usually superior for mixed and dispersion-dominated systems. The latter conclusion is consistent with earlier findings by Tschumper and co-workers for the acetylene dimer, cyanogen dimer, and similar systems.²⁸ Though the models for π - π interactions in A24 (22, 23, 24) along with benzene and cyanogen dimers do favor CP, this is only in the sense of least worst choice, as all three BSSE procedures substantially overestimate the coupled-cluster correction compared to larger basis sets. Among A24, maximum absolute errors of ~ 0.1 kcal/mol and average errors of ~ 0.04 kcal/mol are observed regardless of which BSSE scheme is chosen. Hence, there does not appear to be a universal best choice for any particular counterpoise scheme for evaluating $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ in aDZ, unless one wishes to pursue the cumbersome strategy of using uncorrected values for hydrogen-bonded systems and counterpoise-corrected values for other systems.

A few studies have employed for $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ the aTZ basis set^{24–27,37,45} or aDTZ extrapolations.^{4,26,44,46,47} The second row of Figure 4 reveals the substantial improvement concomitant with enlisting aTZ over aDZ; for A24, maximum errors are nearly all within 0.05 kcal/mol, while MAE for unCP, Ave, and CP are 0.010, 0.011, and 0.017 kcal/mol, respectively. The maximum BSSE decreases by two-thirds to 0.05 kcal/mol (benzene dimer). Albeit with small margins, unCP is the best choice by both average and maximum error criteria, and unCP is superior for 17 systems among all binding motifs, compared to 2 for CP and 8 for Ave.

Considering the aDTZ extrapolation, unCP is again best in 13 cases (4 for CP, 10 for Ave). The authors have noted previously²⁷ that CP- $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ /aDTZ is problematic for hydrogen-bonded systems. This is borne out in Figure 4, where for several red threads, the aDTZ extrapolation procedure overshoots, leading to errors substantially larger than plain aTZ CP values. Extrapolating unCP or Ave IE is riskier still because the nonmonotonic convergence of unCP quantities can lead to inferior results even for higher ζ inputs (e.g., A24-7 and 20 with aTQZ). Numerically, aDTZ offers no benefit over aTZ, as it supports broader error ranges and larger MAE values (0.017, 0.015, and 0.025 kcal/mol for unCP, Ave, and CP) for every BSSE treatment. On the basis of these results, the authors continue to advocate the simpler procedure of preferring aTZ values for $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ over aDTZ extrapolations because the extrapolations lead to very little improvement in general and

can occasionally lead to significantly larger errors in hydrogen-bonded systems when using counterpoise correction.

Errors in CP values generally decrease smoothly but slowly with additional improvements in the basis set, while the behavior of unCP values (and to a lesser extent Ave) is more erratic. For the aQZ basis set, Ave is the most preferred BSSE scheme for 18 species, followed by CP for 5, and by unCP for 4. It will be noted that each of the primary basis sets thus far discussed has favored a different counterpoise correction treatment: CP for aDZ, unCP for aTZ, and now Ave for aQZ. This variability speaks to the pattern, clearly apparent in Figure 4, that within a basis unCP/Ave/CP are more alike than different and that beyond aDZ the error profile of $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ changes little. Quantification through MAE values yields 0.016, 0.008, and 0.014 kcal/mol for unCP, Ave, and CP for aQZ, and a5Z produces nearly unchanged results: 0.015, 0.007, and 0.010 kcal/mol. By a5Z, the BSSE preference yet favors Ave, though less dominantly, and at aTQZ, preference has returned to CP, which is unsurprising because these quantities are prominent in defining the reference.

To summarize this section, when computing a coupled-cluster correction, $\delta_{\text{MP2}}^{\text{CCSD(T)}}$, for a noncovalent interaction for which only aDZ quality basis sets are accessible, unCP values appear to be the best choice for hydrogen-bound complexes, while CP values appear best for dispersion-bound and mixed binding motifs. An aTZ basis set is much preferred as errors reduce by half to <0.02 kcal/mol on average; no one BSSE treatment is clearly preferred, though unCP typically best approximates the reference. Progressing to larger basis sets for the evaluation of the focal point correction $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ is generally unhelpful in the sense that errors are not significantly reduced, while computation time grows steeply.

Composite Interaction Energies. While preceding sections analyzed the error profiles of BSSE treatments in MP2 and $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ components of the interaction energy, it remains important to evaluate their overall combination through the focal point approach because of the potential for partial error cancellation. Because composite energy schemes are directed at systems for which coupled-cluster beyond aTZ is intractable, A24 is joined in this analysis by the S22 database, expanding the number and size of complexes considered. It should be noted that because the best set of reference values available, S22B, was extracted from throughout the literature and are often themselves composite energies, it was not feasible to form a reference unbiased toward a given BSSE treatment; S22B, which is entirely counterpoise corrected, is used directly.²⁷ Nevertheless, we expect the S22B results to be converged sufficiently to serve as meaningful reference energies for present purposes. Figure 5 illustrates errors for A24 and S22 interaction energies computed using one of the more popular focal point approaches for small van der Waals complexes, i.e., as the sum of MP2/aTQZ and $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ /aDZ. All combinations of CP, Ave, and unCP for the two components are considered, though the discussion will focus on CP and Ave approaches to the MP2 component as Figure 3 shows unCP-MP2/aTQZ to be inferior for hydrogen-bonding systems.

The CP+CP approach (notation means CP for both MP2 and $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ components) commonly used in benchmark studies has overall MAE of 0.032 and 0.083 kcal/mol for A24 and S22 databases, respectively (consult Table 1 for hydrogen-bonded, mixed-influence, and dispersion-dominated subset statistics). Ave+CP (that is, Ave for MP2 and CP for $\delta_{\text{MP2}}^{\text{CCSD(T)}}$) has MAE of 0.033 and 0.063 kcal/mol, where averaging CP and

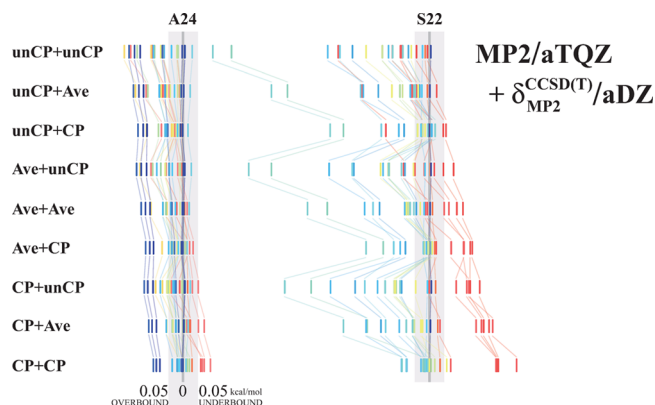


Figure 5. Error in interaction energy computed by MP2 + $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ with coupled-cluster results of double- ζ quality for databases A24 and S22. The label X+Y on each row refers to the counterpoise methods used for the MP2 (X) and $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ (Y) components. Across all combinations of BSSE treatments, threads for each complex show variability according to bonding motif, with Ave+CP presenting a good compromise.

unCP for the MP2 component appreciably improves hydrogen-bonded complexes while not adding much error to the description of dispersion-dominated complexes. Next, averaging CP and unCP for both MP2 and $\delta_{\text{MP2}}^{\text{CCSD(T)}}$, Ave+Ave, yields MAE 0.044 and 0.100 kcal/mol, respectively. While this approach is able to describe hydrogen-bonded complexes quite well, especially in S22, the error incurred for dispersion-dominated systems is notably larger than CP+CP. Ave+unCP produces 0.059 and 0.149 kcal/mol, which is worse for most all subsets relative to the pure Ave approach. Lastly, CP+Ave has MAE of 0.035 and 0.113 kcal/mol again featuring better performance for hydrogen-bonding but worse performance for other motifs relative to pure CP.

Trends with respect to bonding motif are apparent in Figure 5. For both databases, red threads (hydrogen-bonded systems) tend to lie on a diagonal, upper left to lower right, with the result that, fortuitously, there is nearly always one combination of the nine BSSE treatments that hits the reference value. In particular, doubly hydrogen bonded systems (S22-3, 4, 5, 6, 7) cover a greater span of errors (threads have shallower negative slope) than their singly hydrogen bonded counterparts, with formic acid dimer (S22-3) supporting errors between −0.3 kcal/mol for unCP+unCP and +0.3 kcal/mol for CP+CP. The electrostatics-dominated subset of A24 is composed entirely of single hydrogen bonds (and actually includes S22-1 and S22-2 molecules) whose errors vary over the BSSE options by far less (0.05–0.25 kcal/mol). Excluding doubly hydrogen bonded species significantly reduces the propensity to select peculiar BSSE treatments (like unCP+CP, which is actually the best for the hydrogen-bonded subset of S22), and it is clear that any of Ave+CP, CP+unCP, and CP+Ave are satisfactory, with CP+CP scarcely worse. Among dispersion-dominated complexes, π – π contacts versus less-polarizable complexes are another pair of contrasting bonding motifs. The trio of overbound blue threads at the extreme left of Figure 5 are A24 complexes 22, 23, and 24 that were designed to be models for π – π stacking. Their behavior correlates closely with the five S22 members (11–15) featuring that motif and lying at the extreme left of the S22 diagram. These stacked arrangements much favor CP- $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ terms and, less intensely, favor CP-MP2 terms resulting in best models CP+CP > Ave+CP > unCP+CP \approx CP+Ave.

Table 1. Performance of Focal Point Methods for Noncovalent Interaction Classes Hydrogen Bonding (HB), Mixed-Influence (MX), Dispersion Dominated (DD), and Overall (TT)^a

BSSE	HB	MX	DD	TT	HB	MX	DD	TT
aDZ	A24				S22			
unCP+unCP	0.09	0.09	0.08	0.082	0.10	0.28	0.16	0.184
unCP+Ave	0.06	0.06	0.07	0.065	0.06	0.18	0.11	0.121
unCP+CP	0.03	0.04	0.06	0.048	0.04	0.10	0.06	0.066
Ave+unCP	0.04	0.06	0.07	0.059	0.04	0.23	0.16	0.149
Ave+Ave	0.02	0.04	0.06	0.044	0.05	0.14	0.10	0.100
Ave+CP	0.02	0.02	0.05	0.033	0.09	0.05	0.05	0.063
CP+unCP	0.03	0.04	0.05	0.045	0.10	0.19	0.16	0.150
CP+Ave	0.04	0.02	0.04	0.035	0.14	0.10	0.10	0.113
CP+CP	0.06	0.01	0.03	0.032	0.19	0.03	0.04	0.083
aTZ	A24				10/S22			
unCP+unCP	0.06	0.03	0.03	0.033	0.05	0.04	0.02	0.040
unCP+Ave	0.06	0.02	0.03	0.032	0.06	0.02	0.01	0.035
unCP+CP	0.06	0.03	0.03	0.034	0.07	0.01	0.00	0.033
Ave+unCP	0.04	0.02	0.02	0.025	0.02	0.03	0.02	0.023
Ave+Ave	0.04	0.02	0.02	0.024	0.02	0.02	0.01	0.015
Ave+CP	0.04	0.03	0.03	0.029	0.03	0.01	0.00	0.016
CP+unCP	0.02	0.02	0.01	0.016	0.04	0.02	0.01	0.026
CP+Ave	0.02	0.02	0.02	0.017	0.03	0.01	0.00	0.014
CP+CP	0.01	0.03	0.02	0.023	0.02	0.01	0.01	0.012

^aMean absolute energies in kcal/mol are reported for the A24 and S22 databases for MP2/aTZ + $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ /aDZ (upper half) and MP2/aQ5Z + $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ /aTZ (lower half; here, only a subset of S22 is used). The leftmost column indicates the BSSE treatment for the MP2 and coupled-cluster correction portions, respectively. The label X+Y on each row refers to the counterpoise methods used for the MP2 (X) and $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ (Y) components.

Other mixed and dispersion threads in A24 and S22 are adequately described by any BSSE treatment (all MAE < 0.11 kcal/mol), but these, too, favor CP- $\delta_{\text{MP2}}^{\text{CCSD(T)}}$, and Ave+CP and CP+CP achieve MAE < 0.025 kcal/mol. Reconciling these competing trends into a best recommendation will always stint some binding motif. The counsel toward CP+CP for dispersion-dominated cases holds, and percolating reports that jettisoning or averaging counterpoise-correction for many hydrogen-bonded systems simultaneously reduces cost and error hold, too. For a generic system, Ave+CP is the most robust approach, though, it is to be noted, it incurs no cost savings. Compared to direct CCSD(T)/aDZ on the uppermost line of Figure 2, employing $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ /aDZ with a large-basis MP2 extrapolation reduces errors by 3–12-fold, hence the popularity of the focal point scheme. Considering the errors incurred separately by the MP2 and coupled-cluster correction components, composite energies incur error cancellations of ~10–40%.

The corresponding results for balancing MP2 and $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ errors when coupled-cluster is affordable in aTZ are presented in Figure 6 for A24 and a subset of S22. For the latter, only the 10 smallest members are included; this ensures the S22B reference, generally CCSD(T)/aQ5Z or MP2/aQ5Z + $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ /aQZ, is of higher quality than the MP2/aQ5Z + $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ /aTZ focal point results being evaluated here. Overall errors are significantly reduced for the focal point estimates when the basis set for $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ is improved from aDZ to aTZ, whereas the largest absolute errors in Figure 5 (the lower half; Ave+Ave through CP+CP) are 0.15 and 0.50 kcal/mol for A24 and S22, respectively. The corresponding quantities in Figure 6 are <0.08 kcal/mol. Unsurprisingly, those errors belong to A24-4 (hydrogen fluoride dimer) and S22-3 (formic acid dimer), each of which span so wide an error range across the nine BSSE treatments that their respective optimal selections of CP+CP

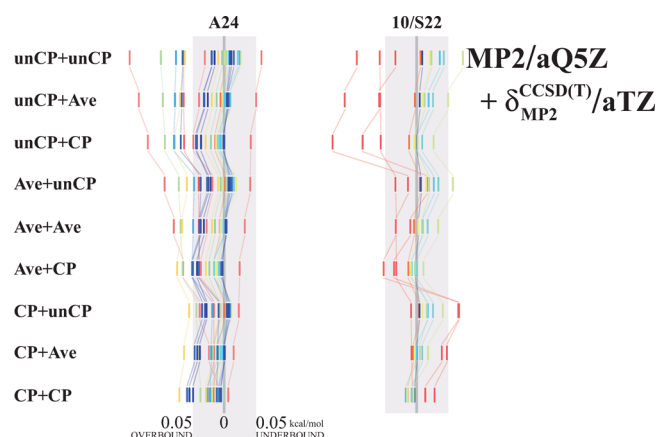


Figure 6. Error in interaction energy computed by MP2 + $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ with coupled-cluster results of triple- ζ quality for databases A24 and the smallest 10 members of S22. The label X+Y on each row refers to the counterpoise methods used for the MP2 (X) and $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ (Y) components. Across all combinations of BSSE treatments, threads for each complex show variability with respect to bonding motif. Any of the lower four approaches well reproduces the error profile desirable for benchmark computations, which through direct CCSD(T) is only achieved through aQZ.

and Ave+unCP can be considered arbitrary. Actual MAE for various BSSE treatments (unCP-MP2 excluded) are so small under MP2/aQ5Z + $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ /aTZ conditions as to be essentially uniform: 0.012–0.029 kcal/mol for both databases. In particular, CP+CP achieves MAE of 0.023 and 0.012 kcal/mol for A24 and S10, respectively, while CP+Ave produces 0.017 and 0.014 kcal/mol. These results are generally consistent with the more detailed analysis of Figure 3, which indicates overall better performance of CP for MP2/aQ5Z. Focal point estimates employing $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ /aTZ are, like the aDZ case, superior to

outright CCSD(T)/aTZ by 2–6-fold in error statistics. Though the CP+CP MAE of 0.023 kcal/mol is about equal to CP-CCSD(T)/aDTZ, the composite approach avoids significant problems for hydrogen-bonding systems when extrapolating with small basis sets and benefits from error cancellation of ~20%.

CONCLUSIONS

The computational chemistry community has long debated the merits of counterpoise corrections in studies of van der Waals clusters. Whether CP, unCP, or an average of the two works best depends on the theoretical method, basis set, and binding motif (hydrogen-bonded systems often behaving differently than other systems).

For both MP2 and CCSD(T) computations, averaging CP and unCP corrected values has merit in avoiding the worst errors incurred by either component method, provided the basis set is aQZ quality or below. For larger basis sets or CBS extrapolations, averaging becomes less useful because the BSSE is often reduced to around 1% or less of the interaction energy; in such cases, CP performs as well as or better than averaging (and both CP and averaging are better than unCP). In the particular case of aTQZ extrapolations commonly employed to estimate the MP2/CBS limit, CP results are best for every one of the 27 test cases considered.

The “coupled-cluster correction,” $\delta_{\text{MP2}}^{\text{CCSD(T)}}$, is relatively insensitive to basis set or to the counterpoise scheme used (CP, unCP, or averaged). For the A24 test set, nearly all values are converged within 0.05 kcal/mol so long as an aTZ basis or larger is used. However, convergence is quite slow after aTZ, so that further improvements in the basis are probably not worth the computational expense in most cases. For the smaller aDZ basis, errors can be somewhat larger (up to a maximum of ~0.1 kcal/mol for the A24 complexes), and they vary significantly with binding motif. unCP results are best for hydrogen-bonded systems, and CP results are best for dispersion-dominated systems.

When MP2/CBS and $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ values are combined in focal point estimates of interaction energies, there is the possibility of error cancellation between the two components, so we also examined errors in the overall interaction energies versus benchmark values for the A24 and S22 databases. When the MP2 component is evaluated by aTQZ extrapolation and aDZ is used for the $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ component (a fairly common procedure in recent high-quality benchmark studies), the results show relatively minor variation with respect to counterpoise treatment for the A24 test set, but larger variations for S22 (whose binding energies are typically larger). The best results overall were obtained when CP or Ave treatments were used for MP2, and CP was used for $\delta_{\text{MP2}}^{\text{CCSD(T)}}$. The recently proposed procedure³⁷ of averaging both MP2 and $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ components typically provides an improvement for hydrogen-bonded systems but worsens predictions overall. When aTZ basis sets can be used for $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ and aQSZ extrapolations are used for MP2, errors are substantially reduced. Once again, CP or Ave are slightly preferred for the MP2 component, while in this case the value of $\delta_{\text{MP2}}^{\text{CCSD(T)}}$ is sufficiently well converged that the counterpoise scheme makes relatively little difference, though CP+Ave has a slight numerical advantage. Mean absolute errors for the two databases are <0.03 kcal/mol for any of these choices.

ASSOCIATED CONTENT

Supporting Information

Expanded representations of the contents of Figures 2, 3, and 4 that portray individual system, along with analogous figures for

formic acid dimer, parallel displaced cyanogen dimer, and sandwich benzene dimer, and details on formulation of the A24 reference and sufficient electronic energies to reproduce all quantities in this work. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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