Minimally Empirical Double Hybrid Functionals Trained Against the GMTKN55 Database: revDSD-PBEP86-D4, revDOD-PBE-D4, and DOD-SCAN-D4

Golokesh Santra, Nitai Sylvetsky, **Gershon Martin**

Submitted date: 22/05/2019 • Posted date: 22/05/2019

Licence: CC BY-NC-ND 4.0

Citation information: Santra, Golokesh; Sylvetsky, Nitai; Martin, Gershon (2019): Minimally Empirical Double Hybrid Functionals Trained Against the GMTKN55 Database: revDSD-PBEP86-D4, revDOD-PBE-D4, and DOD-SCAN-D4. ChemRxiv. Preprint.

We present a family of minimally empirical double-hybrid DFT functionals parametrized against the very large and diverse GMTKN55 benchmark. The very recently proposed wB97M(2) empirical double hybrid (with 16 empirical parameters) has the lowest WTMAD2 (weighted mean absolute deviation over GMTKN55) ever reported at 2.19 kcal/mol. However, our xrevDSD-PBEP86-D4 functional reaches a statistically equivalent WTMAD2=2.22 kcal/mol, using just a handful of empirical parameters, and the xrevDOD-PBEP86-D4 functional reaches 2.25 kcal/mol with just opposite-spin MP2 correlation, making it amenable to reduced-scaling algorithms. In general, the D4 empirical dispersion correction is clearly superior to D3BJ. If one eschews dispersion corrections of any kind, noDispSD-SCAN offers a viable alternative. Parametrization over the entire GMTKN55 dataset yields substantial improvement over the small training set previously employed in the DSD papers.

File list (2)

revDSD-PBEP86-D4 revision resubmission.pdf (762.64 KiB)

[view on ChemRxiv](#) • [download file](#)

ESI revDSD-PBEP86-D4 revision_submission.pdf (759.63 KiB)

[view on ChemRxiv](#) • [download file](#)

Minimally Empirical Double Hybrid Functionals Trained Against the GMTKN55 Database: revDSD-PBEP86-D4, revDOD-PBE-D4, and DOD-SCAN-D4

Golokesh Santra, Nitai Sylvetsky, and Jan M.L. Martin

Department of Organic Chemistry, Weizmann Institute of Science, 7610001 Rehovot, Israel.

Email: gershom@weizmann.ac.il

Abstract

We present a family of minimally empirical double-hybrid DFT functionals parametrized against the very large and diverse GMTKN55 benchmark. The very recently proposed ω B97M(2) empirical double hybrid (with 16 adjustable parameters) has the lowest WTMAD2 (weighted mean absolute deviation over GMTKN55) ever reported at 2.19 kcal/mol. However, refits of the DSD-BLYP and DSD-PBEP86 spin-component-scaled, dispersion-corrected double hybrids can achieve WTMAD2 values as low as 2.33 with the very recent D4 dispersion correction, (2.42 kcal/mol with the D3(BJ) dispersion term) using just a handful of adjustable parameters. If we use full DFT correlation in the initial orbital evaluation, the xrevDSD-PBEP86-D4 functional reaches WTMAD2=2.23 kcal/mol, statistically indistinguishable from ω B97M(2) but using just four non-arbitrary adjustable parameters (and three semi-arbitrary ones). The changes from the original DSD parametrizations are primarily due to reaction and isomerization energies for large systems, which were undersampled in the original parametrization set. With the new parametrization, same-spin correlation can be eliminated at minimal cost in performance, which permits revDOD-PBEP86-D4 and revDOD-PBE-D4 functionals that scale as N^4 or even N^3 with the size of the system. Dependence of WTMAD2 for DSD functionals on the percentage of HF exchange is roughly quadratic; it is sufficiently weak that any reasonable value in the 64% to 72% range can be chosen semi-arbitrarily. DSD-SCAN and DOD-SCAN double hybrids involving the SCAN non-empirical meta-GGA as the semi-local component have also been considered, and offer a good alternative if one wishes to eliminate either the empirical dispersion correction or the same-spin correlation component. noDispSD-SCAN66 achieves WTMAD2=3.0 kcal/mol, compared to 2.7 kcal/mol for DOD-SCAN66-D4. However, the best performance without dispersion corrections (WTMAD2=2.8 kcal/mol) is reached by rev ω B97X-2, a slight reparametrization of the Chai-Head-Gordon range-separated double hybrid. Finally, in the context of double-hybrid functionals, the very recent D4 dispersion correction is clearly superior over D3(BJ).

Introduction

Large and chemically diverse standardized reference datasets play a crucial role in the validation of new approximate computational chemistry methods (not just density functional methods, but also semi-empirical molecular orbital methods, e.g.,¹, composite wavefunction ab initio schemes,²⁻⁶ and machine learning-assisted approaches⁷).

If these approaches are devoid of empirical parameters (such as the “non-empirical” DFT functionals PBE,⁸ TPSS,⁹ and SCAN,¹⁰ as well as the ccCA,¹¹ W1,^{5,12} and W1-F12⁶ approaches), then the purpose of these datasets is only validation. If the methods include empirical parameters,

however (such as in “empirical” DFT functionals, e.g., B97-1,¹³ HCTH,¹⁴ BMK,¹⁵ M06,¹⁶ MN15,¹⁷ and many others), then such datasets take on the additional role of “training sets” or parametrization sets. In the earliest days, small sets of experimental data were used for this purpose, e.g. for B3LYP¹⁸ and EDF-1;¹⁹ as the practical limitations of this approach became apparent, Handy^{14,20} pioneered the use of high-level wavefunction ab initio data for the same purpose. This approach has perhaps been taken furthest by the Head-Gordon group in their combinatorially optimized ω B97X-V,²¹ B97M-V,²² ω B97M-V,²³ and ω B97M(2)²⁴ functionals.

In Perdew’s “Jacob’s Ladder” metaphor,²⁵ Hartree theory represents the “Earthly vale of tears” and the introduction of each new type of information one more rung on the “Jacob’s Ladder” ascending to the Heaven of chemical accuracy. The first rung corresponds to the local density approximation, where the XC (exchange-correlation) functional only depends on the density ρ . The reduced density gradient is introduced on the second rung, leading to the various GGA (generalized gradient approximation) functionals. The introduction of the Laplacian (or the kinetic energy density, which contains similar information) creates the third rung, the meta-GGAs. The fourth rung introduces dependence on the occupied orbitals:²⁶ the most important special case are the different types of hybrid functionals. Finally, the fifth rung corresponds to dependence on virtual orbitals, such as double-hybrid functionals. The term “doubly hybrid” was first coined to denote the linear combination of GGA correlation and MP2 correlation from HF orbitals,²⁷ but since the landmark paper of Grimme,²⁸ the term “double hybrid” has come to refer exclusively to the admixture of (meta)GGA DFT correlation with GLPT2 (2nd-order Grling-Levy²⁹ perturbation theory) correlation from hybrid (meta)GGA DFT orbitals.

In the first step of a double-hybrid calculation, a Kohn-Sham calculation is carried out for a given semilocal exchange-correlation (XC) functional with a fraction c'_x of Hartree-Fock exchange and $(1-c'_x)$ of XC exchange, plus XC correlation damped by a factor $c'_{c,DFA}$. With the converged Kohn-Sham orbitals at the end, the total energy is then evaluated in the second step as:

$$E = E_{N1e} + c_x E_{x,HF} + (1 - c_x) E_{x,XC} + c_{c,XC} E_{c,XC} + c_{2ab} E_{2ab} + c_{2ss} E_{2ss} + E_{disp} \quad (1)$$

where E_{N1e} stands for the nuclear repulsion and one-electron energy term; $E_{x,HF}$ is the Hartree-Fock exchange energy and c_x the fraction of Hartree-Fock-like exchange energy; $E_{x,XC}$ and $E_{c,XC}$ are the exchange and correlation energies, respectively, for the given semilocal XC functional with the converged density from the first step, and $c_{c,XC}$ the fraction of DFT correlation energy; E_{2ab} and E_{2ss} are the opposite-spin and same-spin MP2-like energies obtained in the basis of Kohn-Sham like orbitals from the first step, and c_{2ab} and c_{2ss} are the linear coefficients for the same; and, finally, E_{disp} is the dispersion energy obtained from a given empirical dispersion model (e.g., D2,³⁰ D3(0),³¹ D3(BJ),^{31,32} or very recently,^{33,34} D4) or nonlocal dispersion functional (such as VV10³⁵), which can itself be dependent on scaling or shaping parameters. In much of the present work, E_{disp} is proportional to a pre-factor s_6 .

In the original Grimme approach,²⁸ $c'_x = c_x$, $c'_{c,XC} = c_{c,XC}$, and $c_{2ab} = c_{2ss}$; the latter constraint in practice restricts^{36,37} the choice of correlation functionals to LYP. In the DSD (dispersion-corrected, spin-component-scaled double hybrid³⁸) functionals of Kozuch and Martin, the constraint $c_{2ab} = c_{2ss}$ is relaxed: this was found^{36,37} to enable a broader variety of exchange-correlation functionals, with DSD-PBEP86 the best performer at that point. In the GMTKN55 benchmark paper, the best two performers were DSD-PBEP86 and DSD-BLYP, followed by B2GP-PLYP.³⁹

In the XYG3 approach of Goddard, Xu, and coworkers,⁴⁰ $c'_{c,xc} = 1 \neq c_{c,xc}$ and c'_x may differ from c_x : the implication of this choice have been discussed at length elsewhere.^{41–43} With two exceptions (namely, ω B97M(2)²⁴ and xrevDSD-PBEP86-D4, see below), functionals of this form are not discussed in this paper. The special case $c'_x = c_x$ in a DSD context has been denoted xDSD.⁴²

Double hybrid DFT has been reviewed by Goerigk and Grimme,⁴⁴ by Sancho-Garcia and Adamo,⁴⁵ and by Xu and coworkers.^{40,46} An extensive comparative study between nonempirical⁴⁷ and semiempirical (e.g., Refs.^{28,36,37,39,48–50}) double hybrids was recently made by Goerigk and coworkers⁵¹, who found semiempirical functionals (at present) to be more accurate and more robust. For some recent perspectives on “the functional zoo” (Perdew’s term), see, e.g., Refs.^{52–54}

Perhaps the two most extensive and chemically diverse validation datasets around are GMTKN55 (General Main-group Thermochemistry, Kinetics, and Noncovalent interactions, 55 problem subsets) of Goerigk, Grimme, and coworkers⁵⁵ — which has about 1,500 nonredundant reaction energies and barrier heights — and the even larger MGCDB84 (Main Group Chemistry DataBase, 84 problem subsets) of Mardirossian and Head-Gordon,⁵³ which has close to 5,000 such nonredundant energy differences. These databases themselves incorporate and extend upon earlier work by these authors themselves (e.g.,^{41,56}), by the Minnesota group (Refs.^{54,57} and references therein), by the Hobza group (particularly for noncovalent interactions^{58–61}) and by the present research team (e.g.,^{39,62–73}.)

Such large and unwieldy reference datasets have themselves inspired the statistical search for representative subsamples that would recover most of the variation in the underlying dataset yet be much easier to handle, particularly as training sets where re-evaluation of the whole dataset at every parameter combination would quickly become unwieldy. To the authors’ knowledge, the first such study was Ref.⁷⁴; the two most recent ones are MG8 by Chan⁷⁵, a 60-reaction subset of MGCDB84 obtained through lasso regularization, and “Diet-GMTKN55” by Gould⁷⁶, the latter of which proposes 30-, 100-, and 150-reaction “Diet” versions of GMTKN55. Aside from “rapid prototyping”, these could in principle serve as training sets for empirical functionals, with the full dataset then used for validation purposes.

Our explorations on the suitability of such reduced training sets for functional development will be discussed elsewhere. In the present paper, we focus instead on the full GMTKN55 benchmark as being sufficiently large and chemically varied that parametrization and validation against it is largely immune to sample bias. To the best of our knowledge, the present work is the first paper in which the full GMTKN55 dataset is used as a training set for DFT functionals, although we are also validating some new functionals not covered in the original GMTKN55 paper (for technical reasons).

We will show below that:

- (a) the most accurate functional that does not entail the fifth rung of Perdew’s “Jacob’s Ladder”²⁵ is the combinatorially optimized, range-separated, hybrid meta-GGA ω B97M-V, again by the Berkeley group,²³
- (b) if the search is widened to fifth-rung options, the combinatorially optimized, range-separated, double hybrid ω B97M(2) by Mardirossian and Head-Gordon²⁴ is at present the most accurate functional available for general main-group chemistry;
- (c) this having been said, reparametrized versions of DSD-BLYP-D3(BJ)³⁸ and DOD-PBEP86-D3(BJ)^{36,37} fitted to GMTKN55 come quite close in performance with just one-third the number of empirical parameters;

- (d) replacing the D3(BJ) dispersion correction by the more modern, partial-charge dependent D4 model significantly enhances performance;
- (e) the xrevDSD-PBEP86-D4 model affords a statistically equivalent WTMAD2 to ω B97M(2), as does its xrevDOD-PBEP86-D4 variant, which is amenable to reduced-scaling MP2 implementations;
- (f) if one eschews empirical dispersion corrections, then the noDispSD-SCAN63 functional proposed in the present work offers the best performance;
- (g) while performance over GMTKN55 is markedly improved from the original versus the refitted DSD functionals, performance for small-molecule atomization energies and barrier heights is barely affected — the improvements are seen in large-molecule isomerization and reaction energies where there is an important dispersion component;
- (h) this presents a cautionary tale about “overfitting” to small and insufficiently diverse reference samples.

Computational Methods

Reference data

As our primary parametrization and validation set, we used the comprehensive GMTKN55 benchmark⁵⁵ of Goerigk, Grimme, and coworkers. This set, itself a further expansion and update of earlier GMTKN⁵⁶ and GMTKN30⁴¹ datasets, is a composite of fifty-five chemical problem types, ranging from small-molecule thermochemistry and barrier heights to large-molecule isomerization energies, noncovalent interactions, conformational equilibria, self-interaction errors, heavy p-block chemistry, ion chemistry, ... intending to cover all aspects of main-group chemistry. Their reference data had been compiled from high-level ab initio benchmark studies in the literature, supplemented by some new benchmark calculations of their own. A detailed breakdown of the 55 subsets (and full source information for the original reference data) can be found in Table S1 in the electronic supporting information (ESI): suffice to say a full evaluation entails 2,459 electronic structure calculations for 1,499 chemical energy differences.

The reference geometries, charge and multiplicity information, and reference data were extracted from the ACCDB database of Morgante and Peverati⁷⁷. While initial runs were made with the help of the Snakemake⁷⁸ workflows defined as part of ACCDB, once we had a full set of input files we elected to use our own scripting. Data analysis was carried out using a Fortran program developed in-house and available on request from the authors.

The primary metric and “objective function” employed is the WTMAD2 (weighted mean absolute deviation, type 2) as defined by Goerigk et al.⁵⁵ It seeks to compensate both for the different energy scales various properties are on and for the different sizes of the various subsets:

$$\text{WTMAD2} = \frac{1}{\sum_i^{55} N_i} \cdot \sum_i^{55} N_i \cdot \frac{56.84 \text{ kcal/mol}}{|\Delta E|_i} \cdot \text{MAD}_i \quad (2)$$

in which $|\Delta E|_i$ is the mean absolute value of all the reference energies for subset i , N_i the number of systems in the subset, and MAD_i represents the mean absolute difference between calculated and reference reaction energies for subset i . We note that MAD is a more “robust statistic”⁷⁹ than the root mean square deviation, in the statistical sense that MAD is less prone to

hypersensitivity to one or a few “outlier” points than the RMSD (root mean square deviation), even as the latter is more useful for spotting “troublemakers” for the exact same reason.

Electronic structure details

Reference geometries were used “as is” and not optimized further. The Weigend-Ahlrichs def2-QZVPP basis set⁸⁰ was used for most systems, except for the subsets WATER27, RG18, IL16, G21EA, and AHB21 where we used the diffuse-function augmented def2-QZVPPD instead,⁸¹ and the large-molecule isomerization subsets C60ISO and UPU23, where we compromised on the def2-TZVPP basis set for reasons of computational cost.⁸⁰

All calculations were carried out using Q-CHEM 5.1.1⁸² running on the ChemFarm HPC cluster of the Weizmann Institute Faculty of Chemistry. For GGAs and double hybrids derived from them, initial calculations employed the SG-2 integration grid,⁸³ which is a pruned (75,302) grid roughly comparable to the (Grid=Fine) in Gaussian; the notation stands for the direct product of a 75-point Euler-Maclaurin radial quadrature^{84,85} and a 302-point Lebedev angular grid (see Ref.⁸⁶ and references therein). For meta-GGAs and double hybrids derived from them, we employed the larger SG-3 grid, which is a pruned (99,590) grid roughly comparable to (Grid=UltraFine) in Gaussian; ultimately, we also recalculated the GGAs and double-hybrid GGAs from them. As can be seen in the Electronic supporting information (Table S12), the switch to an SG-3 grid makes a major difference for the RG18 rare gas complexes subset, and a minor but nontrivial one for the anionic subsets. For the SCAN (strongly constrained and appropriately normed¹⁰) meta-GGA — which exhibits a well-known⁸⁷ integration grid hypersensitivity — after some experimentation we decided on an unpruned (150,590) grid, which for a subset we checked for convergence against an even larger (200,974) grid.

The combinatorially optimized range-separated hybrid (RSH) GGA ω B97X-V,²¹ its RSH meta-GGA successor ω B97M-V²³ (and its meta-GGA ancestor B97M-V²²), and finally its very recent double hybrid spinoff ω B97M(2) were evaluated using their respective implementations in Q-CHEM,²⁴ as was the older range-separated double hybrid GGA ω B97X-2(TQ) of Chai and Head-Gordon.⁸⁸

In the GMTKN55 paper, all electrons were correlated in the MP2-like steps of the double hybrids. While the def2-QZVPP basis set used there and in the present work is not really suitable for core-valence correlation, we have calculated statistics both with and without frozen inner-shell orbitals. In both cases, however, we have elected to correlate the subvalence electrons of the metal and metalloid atoms in subsets MB16-43, HEAVY28, HEAVYSB11, ALK8, and ALKBDE10 sets, as the core-valence gaps with default frozen orbital settings are smaller than 1 hartree. Indeed, for alkali and alkali earth oxides and halides, subvalence (n-1)p orbitals may otherwise intrude into the valence band, and thus result in nonsensical dissociation energies with standard frozen-core settings, as discussed at length in e.g., Refs.^{89,90}

Initially we unfroze all subvalence electrons in HEAVY28 and HAL59. (The importance of subvalence correlation for halogen-bonded species has been shown previously⁶³ for the X40x10 dataset.⁶⁰) However, while the added binding energy from (1s) orbitals of CNOF elements, on the order of 0.3 kcal/mol, might be negligible compared to covalent bond dissociation energies, it represents a nontrivial percentage of the small reaction energies in these sets, which owing to the weighting of subsets by inverse mean absolute reaction energies in WTMAD2 causes an increase of up to 0.15 kcal/mol. (As shown in Ref.³⁸, double hybrid parameters optimized with core correlation have slightly different coefficients to compensate for

the extra correlation energy.) We have hence, in these systems, manually unfrozen the (n-1)s_{pd} orbitals of the heavy elements but not any deeper core orbitals such as the (1s) of first-row elements.

For the sake of comparison and completeness, we also evaluated WTMAD2 in the exact same manner for some additional functionals on rungs 2–4. They were the GGAs PBE,⁸ revPBE,⁹¹ and B97-D3(BJ),³¹ the meta-GGAs TPSS,⁹ revTPSS,⁹² SCAN,¹⁰ the global hybrid GGAs B3LYP,^{18,93} PBE0,⁹⁴ and its analog revPBE0;⁹⁴ the global hybrid meta-GGAs PW6B95,⁹⁵ M06,⁹⁶ M06-2X,⁹⁶ SCAN0,⁹⁷ and MN15.¹⁷ With the exception of M06 and M06-2X, all these functionals were used in conjunction with D3(BJ) corrections: parameters published in Ref.⁵⁵ were used throughout. For M06, D3(0) was used instead as recommended in Ref.⁴¹, where it was found that D3(BJ) parameter optimizations for M06 and M06-2X diverge; for M06, we employed D3(0) instead as per their recommendation, while for M06-2X, we found that D3(0) in fact yields slightly worse WTMAD2 than the uncorrected functional. While the difference is statistically insignificant, we used the uncorrected M06-2X instead according to *lex parsimoniae* (a.k.a. Occam’s Razor).

Optimization details

The BOBYQA (Bound Optimization BY Quadratic Approximation) derivative-free constrained optimizer⁹⁸ by Powell was used as the core of a computer program and collection of shell scripts developed in-house.

A DSD double hybrid, if fully optimized, has six empirical parameters:

- (a) the fraction of HF exchange $c_{X,HF}$. (The fraction of semilocal DFT exchange is always $c_{X,DFT}=1 - c_{X,HF}$.)
- (b) the fraction of semilocal DFT correlation $c_{C,DFT}$;
- (c) the fraction of opposite-spin 2nd-order GLPT correlation energy c_{2ab} ;
- (d) the fraction of same-spin 2nd-order GLPT correlation energy $c_{2ss}=c_{2aa+bb}$;
- (e) the prefactor s_6 for the D3(BJ) empirical dispersion correction^{31,32,99};
- (f) the length scale parameter a_2 for the D3(BJ) damping function. (As in Refs.^{36,37}, we are setting $a_1=0$; we are also setting $s_8=0$ as in Refs.^{36,37}, and in the SCAN-D3(BJ)⁸⁷ paper.)

For a given pair of values for (a,b), it is possible to obtain the optimal group of (c-f) parameters without re-evaluating any electronic structure calculations, simply by extracting individual energy components from the electronic structure calculations, evaluating total energies and hence WTMAD2 for a given combination of $\{c_{2ab}, c_{2ss}, s_6, a_2\}$, and minimizing WTMAD2 with respect to these four parameters using BOBYQA. This could then constitute an inner “microiteration” loop, while the outer “macroiteration” loop consists of varying $\{c_{X,DFT}, c_{C,DFT}\}$ and rerunning all 2,459 calculations with the new parameters. We considered, however, placing one or both variables in the microiteration loop, with the optimum values from the microiterations to be used in the macroiterations, and so forth until “self-consistency” has been reached. While the coupling between (a) and (c,d) proved to strong for this to be viable for $c_{X,DFT}$, we found that for a fixed value of $c_{X,DFT}$, convergence of $c_{C,DFT}$ to two decimal places or better typically does not require more than two macroiterations. Hence, we have adopted the practice of microiterating $\{c_{C,DFT}, c_{2ab}, c_{2ss}, s_6, a_2\}$ at every macroiteration by means of BOBYQA.

The D3(BJ) corrections were computed for a finely spaced grid in a_2 using the standalone DFTD3 program by Grimme and coworkers (<https://www.chemie.uni-bonn.de/pctc/mulliken-center/software/dft-d3/>). Values for intermediate a_2 were obtained by interpolation. We found, however (see below) that if s_6 is part of the microiterations, then the WTMAD2 surface is

sufficiently flat in a_2 that fixing a_2 at semi-arbitrary values both stabilizes the optimization and has negligible effect on the final WTMAD2.

For a DOD double hybrid, $c_{2ss}=0$, leaving just four parameters $\{c_{C,DFT}, c_{2ab}, s_6, a_2\}$ for the microiterations, while for a DSD-noDisp, $s_6=0$ and a_2 is irrelevant, leaving just three parameters $\{c_{C,DFT}, c_{2ab}, c_{2ss}\}$ in the inner loop.

Results and Discussion

WTMAD2 performance metrics over the GMTKN55 dataset are given in Table 1. Results for a large number of GGA, meta-GGAs, and hybrid functionals have been given in the GMTKN55 paper⁵⁵ and will not be repeated here. We have repeated the calculations for B3LYP, PBE0, and ω B97X-V as a sanity check; in addition, we have evaluated the B97M-V and ω B97M-V functionals, which were not considered in the original GMTKN55 paper but were covered in a recent follow-up study by Najibi and Goerigk (NG),¹⁰⁰ and finally the ω B97M(2) double hybrid, for which no GMTKN55 statistics have yet been reported.

As very recently found by NG, the switch from a combinatorially optimized range-separated hybrid GGA (coRSH GGA) in ω B97X-V to a coRSH meta-GGA in ω B97M-V represents a clear improvement over ω B97X-V; we find that WTMAD2 goes down from 3.96 kcal/mol to 3.29 kcal/mol. This latter figure is the lowest WTMAD2 reported thus far for a hybrid functional: ω B97X-V was the previous best contender in the original GMTKN55 paper. Breakdown by components (Table S11) reveals conspicuous accuracy gains for the pericyclic reaction barriers (BHPERI), for bond separation reactions of saturated hydrocarbons (BSR36), and large system reaction energies more generally. By way of data reduction, we may in fact consider the sums of WTMAD2 contributions for each of the five major subcategories in GMTKN55: Thermochemistry, Intermolecular interactions, Conformers, Barrier heights, and Reaction energies for large systems.

Like NG earlier, we find B97M-V and ω B97M-V to be “best in class” on Rungs 3 and 4, respectively, of the Jacob’s Ladder.

It then becomes apparent (Table 2) that the chief gain for ω B97M-V over ω B97X-V is in fact for thermochemistry and large system reaction energies. There is a small improvement for barrier heights, but no change for intermolecular interactions and in fact a slight deterioration for conformers; upon further inspection, the latter can be attributed primarily to the tri- and tetrapeptide conformers (PCONF21). The already excellent statistic for ω B97M-V can be brought down even further to 2.19 kcal/mol with the coRSH mGGA double hybrid ω B97M(2). This improvement is actually seen for all subcategories across the board. The WTMAD2 value for ω B97M(2) is, by some distance, the lowest reported for any functional thus far: the best three performers from the original GMTKN55 paper,⁵⁵ DSD-BLYP-D3(0), DSD-BLYP-D3(BJ), and DSD-PBEP86-D3(BJ), clocked in at 3.00, 3.08, and 3.14 kcal/mol, respectively, while in the followup paper, NG found DSD-PBEP86-NL to be even better at 2.84 kcal/mol. In that same paper, the runners-up were ω B97X-2(TQ)-D3(BJ) and DSD-BLYP-NL at 2.97 and 3.05 kcal/mol, respectively. In the present paper, we found 3.06 for ω B97X-2(TQ)-D3(BJ): detailed analysis revealed that essentially the whole difference can be attributed to the larger def2-QZVPPD basis set used in RG18, which has a disproportionately large weight factor owing to the small average reaction energy in the denominator. (Note that using grids smaller than SG-3 for RG18 causes errors in WTMAD as large as the first decimal place!)

Table1: WTMAD2 values (kcal/mol) for various functionals using the full GMTKN55 database.

Functionals	WTMAD2(kcal/mol)				
	Standard/Original	With Refitted a_2			
		DSD	DOD ($c_{2ss}=0$)	noDispSD ($s_6=0$)	noDispOD ($c_{2ss}=s_6=0$)
PBE-D3(BJ)	10.44				
TPSS-D3(BJ)	9.14				
B97-D3(BJ)	8.61				
revTPSS-D3(BJ)	8.42				
revPBE-D3(BJ)	8.34				
SCAN-D3(BJ)	7.94				
M06-D3(0)	7.75				
SCAN0	7.69				
PBE0-D3(BJ)	6.55				
B3LYP-D3(BJ)	6.50				
B97M-rV	6.38				
B97M-V	6.37				
SCAN0-D3(BJ) ^d	6.23				
MN15-D3(BJ)	5.77				
PW6B95-D3(BJ)	5.49				
revPBE0-D3(BJ)	5.43				
M062X	4.78				
ω B97X-V	3.96				
B2GP-PLYP	3.33				
ω B97M-V	3.29				
Double hybrids without inner-shell correlation					
ω B97M(2)	2.19				
ω B97X-2(TQ)-D3(BJ) ⁸⁸	3.06	2.80	3.71	2.80	
DSD-BLYP-D3(BJ)	3.34	2.48	2.66	4.19	4.89
DSD-PBEP86-D3(BJ)	3.10	2.43	2.45	3.56	4.07
DSD-PBE-D3(BJ)	3.17	2.74	2.75	4.31	
DSD-TPSS-D3(BJ)	3.13	2.95	3.07	4.27	
DSD-PBEP95-D3(BJ)	3.33	2.85	2.91	3.53	3.92
DSD-SCAN0-2-D3(BJ)	4.15 ^a	2.80	2.90	2.97	3.29
DSD-SCAN ₇₄ -D3(BJ)		2.69	2.75	2.94	3.26
DSD-SCAN ₆₉ -D3(BJ)	4.53 ^b	2.66	2.68	2.98	3.23
DSD-SCAN ₆₆ -D3(BJ)		2.66	2.67	3.06	3.41
DSD-SCAN ₆₃ -D3(BJ)		2.69	2.69	3.17	3.51
DSD-SCAN ₅₈ -D3(BJ)		2.79	2.79	3.39	3.69
DSD-SCAN ₅₅ -D3(BJ)		2.89	2.89	3.58	3.86
DSD-SCAN ₅₀ -D3(BJ)	6.11 ^c	3.10	3.10	3.91	4.14
Double hybrids, parameters optimized with inner-shell correlation					
SCAN0-2 [standard]	4.69				
ω B97M(2) [standard]	2.35				
DSD-revPBEP86		2.66			
DSD-BLYP-D3(BJ)		2.47	2.59	3.88	
DSD-PBEP86-D3(BJ)		2.46	2.47	3.35	
DSD-PBE-D3(BJ)		2.72	2.72	4.01	
DSD-PBEP95-D3(BJ)		2.87	2.88	3.38	
DSD-SCAN0-2-D3(BJ)		2.88	2.97	2.93	
DSD-SCAN ₇₄ -D3(BJ)		2.73	2.77	2.83	
DSD-SCAN ₆₉ -D3(BJ)		2.66	2.68	2.83	
DSD-SCAN ₆₆ -D3(BJ)		2.65	2.66	2.88	
DSD-SCAN ₆₃ -D3(BJ)		2.67	2.67	2.97	
DSD-SCAN ₅₈ -D3(BJ)		2.75	2.75	3.16	
DSD-SCAN ₅₅ -D3(BJ)		2.86	2.86	3.35	
DSD-SCAN ₅₀ -D3(BJ)		3.07	3.07	3.68	

* SCAN0-2 can also be written DSD79-SCAN; DSD69-SCAN can also be written as DSD-SCAN-QIDH; DSD55-SCAN as DSD-SCAN-CIDH; (a) SCAN0-2;⁹⁷ (b) SCAN0-QIDH;⁹⁷ (c) SCAN0-DH.⁹⁷ (d) $a_2=7.9042$; $a_1=s_8=0$ (this work)

Table 2: WTMAD2 contribution (kcal/mol) for each of five major subcategories in cases of B97-D3(BJ), B3LYP-D3(BJ), B97M-rV, ω B97X-V, ω B97M-V & ω B97M(2) functionals.

Subcategories	Δ WTMAD2(kcal/mol)					
	B97-D3(BJ)	B3LYP-D3(BJ)	B97M-rV	ω B97X-V	ω B97M-V	ω B97M(2)
Intermolecular interactions (Intermol)	1.238	1.238	0.838	0.578	0.565	0.492
Conformers/Intramolecular (Conformer)	1.542	1.147	1.810	0.729	0.897	0.578
Barrier heights (Barrier)	1.733	1.141	1.008	0.561	0.454	0.258
Thermochemistry (Thermo)	1.817	1.314	1.194	1.02	0.73	0.442
Large-species reaction energies (REAClarge)	2.278	1.662	1.535	1.07	0.64	0.418
Total WTMAD2	8.607	6.503	6.384	3.959	3.286	2.187

ω B97M(2) was parametrized for frozen subvalence orbitals: if correlation from such orbitals were to be included, $c_{2ab}=c_{2ss}$ for this functional would have to be slightly reduced to compensate.³⁸ Indeed, when we evaluated WTMAD2 with all orbitals correlated and original parametrization, we saw an *increase* to 2.36 kcal/mol.

Sensitivity to the percentage of Hartree-Fock exchange: DSD-SCAN as a case study

The costliest parameter to vary in the refit of a DSD functional would be the percentage of Hartree-Fock exchange. As already shown in Figure 1 of Ref.³⁷, only minimal changes in performance statistics result from varying the fraction of HF-like exchange $c_{X,HF}$ of a DSD functional within a fairly broad range—but a relatively small training set was sampled there. Presently, we will consider the case of DSD-SCAN_x-D3(BJ) (where x stands for the percentage of HF exchange) in more detail: for the evaluation points, we have chosen $c_{X,HF}=n^{-1/3}$, where $n=2, 2\frac{1}{2}, 3, 3\frac{1}{2}, 4, 5, 6$, and 8. (In the “nonempirical” double hybrids of Adamo and coworkers, these choices would correspond to $c_{2ab}=c_{2ss}=1/n$, and $c_{C,DFT}=1-1/n$ owing to the putative cubic dependence of the integrand.^{101,102}) For the cases of $n=3, 3\frac{1}{2}$, and 4, this yields values close to percentage points 0.69, 0.66, and 0.63, respectively, and we elected to round off to these latter values.

The WTMAD2 for these trial functionals, with orbitals where $c_{C,DFT}$ was fixed at 0.50 during the iterations (but not during the linear optimization) is depicted in Figure 1.

As can be seen there, these can be fit excellently ($R^2=0.998$ or better) by a simple parabola: for the DSD-SCAN-D3(BJ) curve (black), the minimum is at $c_{X,HF}=0.683$ and the quadratic coefficient is 11.26. The latter implies a remarkably weak sensitivity of WTMAD2 to the percentage of HF exchange: it will vary by just 0.01 kcal/mol from 0.65 to 0.71, by 0.02 kcal/mol over a range from 0.64 to 0.725, and by just 0.05 kcal/mol between 0.62 and 0.750. What this implies is that nonlinear optimization for a specific minimum $c_{X,HF}$ becomes a somewhat academic exercise: one can choose any sensible fixed value in those ranges, such as 0.69 or 0.66 (or, if one prefers, $3^{-1/3}$ or $3.5^{-1/3}$).

Figure 1: dependence on the fraction of HF exchange $x/100$ % of WTMAD2 over the GMTKN55 dataset for the dispersion-corrected, spin-component-scaled, double hybrid DSD-SCAN_x-D3(BJ), as well as the constrained versions DOD (i.e., $c_{2ss}=0$), noDispSD (i.e., $s_6=0$), and noDispOD (i.e., $s_6=c_{2ss}=0$)

Figure 2: dependence on the fraction of HF exchange $x/100$ % of WTMAD2 over the GMTKN55 dataset for the dispersion-corrected, spin-component-scaled, double hybrid DSD-SCAN_x-D3(BJ), as well as of the five major subdivisions thereof and of an objective function similar to Ref.³⁷ (“RMS4”)

The DOD-SCAN-D3(BJ) curve (blue) — where $c_{2ss}=0$ throughout — is only somewhat less flat, with a minimum at $x=0.66$. We note that where $x<0.63$ (the crossing point between DSD and DOD WTMAD2 curves), an unconstrained DSD fit actually has a *negative* c_{2ss} — if c_{2ss} were constrained to be non-negative, then DSD would follow the blue line left of the crossing point. If the empirical dispersion correction is eliminated (which we denote here by noDispSD-SCAN), the curve does become a little steeper and the minimum shifts up to $x=0.75$. If we in addition constrain $c_{2ss}=0$ (the yellow noDispOD-SCAN curve), we pay a relatively modest accuracy premium — but this is specific to the underlying SCAN semilocal functional. We will address this point further below.

Of course, a single global performance metric such as WTMAD2 does not tell the whole story. A breakdown by components is given in Tables S2 through S10. A number of these subsets are essentially indifferent to the fraction of HF exchange (particularly the noncovalent interaction sets), while others prefer small HF exchange (e.g. DC13=thirteen “difficult cases”), yet others (e.g., SIE=self-interaction error) will prefer large HF exchange by design, and a number of the thermochemistry subsets have clearly defined minima.

Following the original GMTKN55 paper and the previous section, we can partition WTMAD2 into the same five primary components. A plot of these as a function of $c_{X,HF}$ is given in Figure 2.

We see there that of these five primary subsets, the two noncovalent interaction sets (intramolecular and intermolecular) display some (opposite) variation, but their average NCI/2 is remarkably insensitive to the percentage of HF exchange. The greatest variation is seen for thermochemistry, where a clear “valley” exists, which is however nearly flat between 0.66 and 0.74. For barrier heights, error goes down slowly but monotonically as $c_{X,HF}$ goes up. Finally, for the large reaction energies, the profile stays fairly flat but error starts increasing for the largest values. The combination of these factors creates something of a “Goldilocks zone” between 0.65 and 0.70, or even between 0.62 and 0.74, as we noted earlier: for instance, while 0.69 yields slightly better thermochemistry and barrier heights than 0.66, this is offset by increased errors in the large system isomerizations.

The GMTKN55 minimum is even more shallow than what we previously found³⁷ in the DSD paper. We do note that instead of weighted MADs, that paper used unweighted RMSDs, which tends to amplify differences; moreover, it focused on a training set with just six subsets. Two of these were transition metal reaction prototypes; the remaining four are identical or similar to the W4-11, BH76, S22, and MB18 subsets from GMTKN55. RMSD4, an average of the latter four’s RMSDs, which should behave quite similarly to the training set used in Ref.³⁷, is displayed as the dot-dashed black line in Figure 2. One indeed sees a much more pronounced variation here, as differences are neither smoothed out by the more robust (in the statistical sense) MAD averaging nor diluted by many noncovalent interaction-driven subsets.

We hence conclude that we may avoid the costly nonlinear optimization of $c_{X,HF}$ for the other DSD-XC functionals, and that we may instead semi-arbitrarily fix $c_{X,HF}$ at either the same value as the original,³⁷ or choose $0.69 \approx 3^{-1/3}$ as a sensible compromise.

The evolution of the parameters in DSD-SCAN_x as a function of $x=c_{X,HF}$ can be seen in Figure S1 in the Supporting Information. Suffice here to say that, for this particular semilocal functional (SCAN) and the DSD form, dependence of all four parameters $c_{C,DFT}$, c_{2ab} , c_{2ss} , and S_6 is remarkably linear over the $0.5 \leq x \leq 0.8$ range. This empirical behavior is somewhat at odds with the cubic dependence argued on theoretical grounds:^{101,103} we will explore this in more detail in a future paper.

DSD double hybrids and refits

Performance statistics for DSD functionals with original parametrization were already given in the GMTKN55 paper: differences with the values reported there are principally due to slight differences in the basis set and choices of frozen-cores. In the present paper, we will use the notation, e.g., DSD-PBEP86-D3(BJ) for the original functional and revDSD-PBEP86-D3(BJ) for the present refit. WTMAD2 statistics can be found in Table 1.

With valence electrons correlated, revDSD-PBE86-D3(BJ) and revDSD-BLYP-D3(BJ) are essentially tied at WTMAD2=2.42 and 2.48 kcal/mol, respectively. While this is still higher than ω B97M(2), it should be kept in mind that DSD-BLYP-D3refit and DSD-PBEP86-D3refit only entail six adjustable parameters rather than sixteen, rendering them less “empirical”. Of these six, $c_{X,HF}$ can be fixed at a semi-arbitrary value; furthermore, we found here that the same is true of the damping function turnover point a_2 of the D3(BJ) dispersion term. In fact, the surface is so flat in a_2 that its inclusion as an optimization parameter leads to poor convergence of WTMAD2: we hence fixed a_2 at semi-arbitrary value of 5.5 for most functionals, 5.2 for short-ranged correlation functionals like LYP and P86, and 5.75 for the longer-ranged SCAN (Table S16).

This leaves us arguably with only four true empirical parameters.

It was previously noted, in the original DSD papers, that “upgrading” the underlying semilocal functional from a GGA to a meta-GGA is not necessarily beneficial, with DSD-TPSS-D3refit for instance being among the poorer performers. At first sight, this observation holds true here as well: it is also notable that DSD-PBE-D3refit does noticeably more poorly than DSD-PBEP86-D3refit and DSD-BLYP-D3refit. What the two best performers have in common are fairly “short-ranged” semilocal correlation functionals, which at long range at least “do no harm” and leave the treatment of dispersion up to the MP2-like correlation and the D3(BJ) correction. In contrast, as noted in Ref.¹⁰⁴, the PBE_c correlation functional exhibits a spurious attraction at long range, and so does TPSS.

The very recent SCAN (strongly constrained and appropriately normed¹⁰) meta-GGA, in contrast, exhibits much better performance in a DSD context than TPSS — second only to DSD-BLYP and DSD-PBEP86.

The great improvement from the original DSD-PBEP86-D3 (WTMAD2=3.10 kcal/mol) to revDSD-PBEP86-D3 serves as a cautionary tale against small and idiosyncratic training sets. All four of the main-group training sets for the DSD functional are part of GMTKN55: if we were to instead consider the sum of the four WTMAD2 contributions for W4-11, RG18, S22, and BH76, we would actually find essentially no improvement from DSD-PBEP86-D3 to revDSD-PBEP86-D3: the large-system subsets are what makes the difference.

Is there any benefit to be gained from correlating the inner-shell orbitals? (We have noted previously³⁸ that DSD-BLYP parameters fitted with and without inner-shell correlation are slightly different.) We have only considered this for a subset of double hybrids. (See also Tables S13 and S14 for sample component breakdowns.) As seen in Table 1, the impact of including inner-shell correlation is quite minor for both DSD and DOD, but for noDisp (see next subsection), where the empirical dispersion correction has been eliminated, including inner-shell correlation systematically improves WTMAD2 by 0.1–0.2 kcal/mol.

The popular simple hybrids B3LYP-D3(BJ) and PBE0-D3(BJ) are nearly tied at WTMAD2=6.5 kcal/mol. Replacing PBE exchange by Weitao Yang’s revision (revPBE⁹¹) leads

to a significant improvement to WTMAD2=5.43 kcal/mol for revPBE0-D3(BJ). (A detailed comparison can be found in Table S15. This functional was not considered in the GMTKN55 paper.) Intriguingly, making a similar substitution in the double hybrid to create DSD-revPBEP86-D3 does *not* yield improved performance (WTMAD2=2.66 kcal/mol, compared to 2.46 for DSD-PBEP86-D3 — both without frozen cores).

At the end of this section, we can report that *and revDSD-PBEP86-D3(BJ) is the best performer, closely followed by revDSD-BLYP-D3.*

Eliminating the semiempirical dispersion correction

The presence of the D3(BJ) dispersion correction^{31,32} in DSD functionals exposes them to the criticism of “mixing DFT with molecular mechanics”. We have earlier considered the option of eliminating D3(BJ) entirely: in practice, this entails an increased percentage of same-spin correlation as compensation.

As can be seen in Table 1, all the DSD-noD3 (or, if you like, noDispSD) functionals exhibit significantly degraded performance compared to their DSD-D3 siblings. In addition, however, the ordering is upended: noDispSD-SCAN now exhibits significantly better performance than the other options. With core-valence correlation included, noDispSD-SCAN-QIDH reaches WTMAD2=2.84 kcal/mol, still significantly better than the original DSD-PBEP86-D3.

Why, in a noDispSD-XC functional, does XC=SCAN outperform all other options? At long range, three scenarios are possible: (a) the functional tapers away quickly (like in BLYP and PBEP86), which at least does no harm but in the absence of a D3(BJ) correction leaves PT2 to handle all the long-range dispersion effects (for which it is inadequate); (b) the functional does not decay quickly but has the wrong behavior, leading to poor performance for noncovalent interactions; (c) the functional can at least partly recover the correct behavior, in which case PT2 may be sufficient to handle the remainder. It appears that (c) is the case for SCAN.

As a proxy for behavior at intermediate distance, we may consider the s_8 coefficient for the r^{-8} term in D3(BJ): for MP2, this was found⁶⁹ to be large and negative, while for DSD double hybrids and functionals like M06, s_8 was found to be zero or statistically insignificantly different from zero. We note in particular that SCAN-D3(BJ), unlike other GGAs and meta-GGA, has a fitted $s_8=0$ in the D3(BJ) correction⁸⁷; in the present work, we also fitted a D3(BJ) correction to the SCAN0 hybrid, and obtained $a_1=0$, $a_2=7.9042$, $s_8=0$.

Somewhat at odds with this argument, however, is ω B97X-2. Upon reoptimizing the prefactor for DFT correlation as well as c2ab and c2ss, we found that WTMAD2=3.06 dropped to 2.80 kcal/mol whether or not the D3(BJ) was included. (The a_1 and a_2 damping function parameters taken from NG place the correction *very* far out in space.) This it becomes our best performer in the absence of a dispersion correction.

Another approach to eliminating the D3(BJ) correction would be to replace it with a nonlocal dispersion functional, such as the Vydrov-Van Voorhis VV10³⁵ (also known as NL¹⁰⁵) employed in the B97M-V and other Berkeley functionals. Najibi and Goerigk found¹⁰⁰ that DSD-PBEP86-NL (using a damping parameter $b=14.2$ as suggested in Ref.¹⁰⁶) yields WTMAD2=2.84 kcal/mol. We obtained VV10 corrections for DSD-PBEP86-NL using $b=12.8$ (as obtained in Ref.⁷¹ for the revised⁷¹ S66x8 noncovalent interactions benchmark,¹⁰⁷ near the basis set limit), then used those to fit a revDSD-PBEP86-NL functional. Its parameters can be found in Table 3: at WTMAD2=2.60 kcal/mol, this is within statistical noise from revDSD-PBEP86-D3(BJ),

illustrating the ability of the DSD refitting process to overcome certain deficiencies in the noncovalent interaction description.

DOD double hybrids and refit

If only opposite-spin MP2 correlation is included, then the cost scaling of the post-KS step can be reduced to $\propto N^4$ formally by means of a Laplace transform algorithm.^{108–110} In fact, Song and Martinez¹¹¹ achieved further reduction to $\propto N^3$ using tensor hypercontraction techniques. In our previous work,³⁷ we have denoted such functionals DOD, short for Dispersion-corrected, Opposite-spin, Double-hybrids.

(As was expected and can be seen in Table 1, the results of trying to eliminate both same-spin correlation and the dispersion correction were dismal for most functionals, with the exception of noDispOD-SCAN₇₄ where WTMAD=3.3 kcal/mol. Still, this is a performance comparable with ω B97M-V, which does not require evaluation of E_{2ab} .)

The tie between revDSD-BLYP and revDSD-PBEP86 is broken in favor of the latter: Inspection reveals that revDSD-PBEP86-D3 functionals has a c_{2ss} coefficient close to zero, which is not the case for revDSD-BLYP. (The latter is plausible when one considers that BLYP does not treat opposite-spin and same-spin correlation on the same footing: in fact, it is easily seen from eq. (2) in Ref.¹¹² that the BLYP correlation energy for a fully polarized uniform electron gas is zero, which is clearly an unphysical answer.) Hence, we see that revDOD-PBEP86-D3 “pulls ahead of” revDOD-BLYP-D3 in the “WTMAD2 race”, at 2.45 vs. 2.66 kcal/mol (Table 1).

revDOD-PBEP86-NL (Table 3) is essentially indistinguishable in performance from revDOD-PBEP86-D3(BJ).

Final recommended D3(BJ) functionals

In light of the above, we only are retaining three exchange-correlation combinations for the semilocal part: BLYP, PBEP86, and SCAN. For PBEP86, both DSD and DOD combinations are given: while DSD represents only a very small improvement over DOD, it comes at zero additional computational expense when using a code that cannot exploit reduced-scaling algorithms for opposite-spin-only MP2. (The most commonly used such codes are Gaussian 09 and Gaussian 16.) Hence, we have elected to recommend both revDSD-PBEP86-D3 and revDOD-PBEP86-D3.

In view of the weak dependence of performance on the percentage of HF exchange, we have elected to retain the original percentages of 71% for DSD-BLYP and 69% for DSD-PBEP86, in order to simplify nonstandard inputs for codes such as Gaussian,¹¹³ ORCA,^{114,115} and Q-CHEM. For DSD-SCAN and DOD-SCAN, we have no such incentive: following inspection of the minima of the parabolic fits to WTMAD2, we have chosen 66% for DOD-SCAN and 69% for noDispSD-SCAN.

Finally, we have noted above that, as long as the dispersion prefactor s_6 is self-consistently optimized with the other parameters, WTMAD2 is only weakly dependent on the chosen turnover parameter a_2 . With a given fixed a_2 , DSD-BLYP has the largest s_6 , followed by DSD-PBEP86: for DSD-SCAN and DOD-SCAN, s_6 is much smaller—this reflects that SCAN is better able to handle long-range effects than the two others. We have hence semi-arbitrarily fixed

a_2 at a “short” value of 5.2 for DSD-BLYP, and at a “longer” values of 5.75 for DSD-SCAN, while for DSD-PBEP86 we chose an intermediate $a_2=5.5$. Comparison with full optimizations including a_2 revealed that WTMAD2 differences are on the order of a few “small” calories per mole: hence fixing these parameters is considered justifiable in light of a more smoothly converging optimization for the remaining ones.

Table 3: Final parameters for revised DSD-D3(BJ) functionals and revDSD-PBEP86-NL. Original parameters, if any, given for comparison

Functionals	$C_{X, HF}$	$C_{C, DFT}$	C_{2ab}	C_{2ss}	S_6	a_1	a_2	WTMAD2 (kcal/mol)
noDispSD-SCAN ₆₉	0.69	0.4409	0.6223	0.26	[0]	—	—	2.98
DOD-SCAN ₆₆ -D3(BJ)	0.66	0.5048	0.6283	[0]	0.3152	[0]	5.75	2.67
revDSD-BLYP-D3(BJ)	0.71	0.5313	0.5477	0.1979	0.5451	[0]	5.2	2.48
revDSD-PBEP86-D3(BJ)	0.69	0.4296	0.5785	0.0799	0.4377	[0]	5.5	2.42
revDSD-PBEP86-NL	0.69	0.435	0.5762	0.0622	0.9921	b=14.2	—	2.44
revDSD-PBEB95-D3(BJ)	0.66	0.4960	0.4935	0.1009	0.3686	[0]	5.5	2.85
revDSD-PBE-D3(BJ)	0.68	0.4528	0.5845	0.0711	0.5746	[0]	5.5	2.72
revDOD-BLYP-D3(BJ)	0.71	0.5911	0.6216	[0]	0.6145	[0]	5.2	2.67
revDOD-PBEP86-D3(BJ)	0.69	0.4449	0.6055	[0]	0.477	[0]	5.5	2.47
revDOD-PBEP86-NL	0.69	0.4445	0.5994	[0]	1.0629	b=14.2	—	2.46
revDOD-PBEB95-D3(BJ)	0.66	0.5225	0.5278	[0]	0.4107	[0]	5.5	2.92
revDOD-PBE-D3(BJ)	0.68	0.4641	0.6134	[0]	0.6067	[0]	5.5	2.73
rev ω B97X-2(TQZ)	(b)	0.9518	0.5123	0.4294	[0]	—	—	2.80
Orig. ³⁷ DSD-BLYP-D3(BJ)	0.71	0.54	0.47	0.4	0.57	[0]	5.4	3.34
Orig. ³⁷ DSD-PBEP86-D3(BJ)	0.69	0.44	0.52	0.22	0.48	[0]	5.6	3.10
Orig. ³⁷ DSD-PBEB95-D3(BJ)	0.66	0.55	0.46	0.09	0.61	[0]	6.2	3.32
Orig. ³⁷ DSD-PBE-D3(BJ)	0.68	0.49	0.55	0.13	0.78	[0]	6.1	3.17
DSD-PBEP86-NL ^(a)	0.69	0.44	0.52	0.22	[1.0]	b=14.2	—	2.60
B2GP-PLYP-D3(BJ) ^{39,55}	0.65	0.64	0.36	0.36	0.56	0.2597	6.333	3.19

(a) calculated using ORCA 4.1,¹¹⁵ this work

(b) short-range 0.6362, long-range 1.0, range separation parameter $\omega=0.3$.

Sample input files for most major codes are given in the ESI. We wish to point out that, while noDispSD-SCAN is inferior to the revDSD offerings, its WTMAD2 is still superior to the original B2GP-PLYP and DSD double hybrids, and this without any empirical dispersion correction and with just three non-arbitrary parameters.

Considering the D4 dispersion correction: Final recommended D4 functionals

As the present manuscript was being prepared for publication, a preprint³⁴ by Grimme and coworkers was posted on ChemRxiv, in which they propose a next-generation D4 dispersion correction (see also Ref.³³). The reader is referred to these references for details; for the purpose of our discussion, the most significant difference between D3(BJ) and D4 is that the latter introduces dependence on atomic partial charges, which (by default) are evaluated using the electronegativity equalization principle.¹¹⁶ (For the general theory, see Refs.^{117,118} and references therein.)

As a first step, we substituted the D4 correction for D3(BJ) in the original DSD functionals from Ref.³⁷ as a “drop-in replacement” using parameters optimized for these functionals and published by Grimme et al.³⁴ The results can be found in the third numerical column of Table 4 and, for individual GMTKN55 subsets, in Table S13. Across the board, the WTMAD2 values are significantly better than those with the original, in the case of DSD-PBE even superior to the refitted revDSD-PBE-D3(BJ)!

We then proceeded to reoptimize the DSD functionals in the presence of D4 and adjusting the latter’s parameters. It quickly became clear that setting s_8 to zero had negligible impact on the WTMAD2: furthermore, that the other parameters settled around $a_1=0.4$ and $a_2=3.6$, and that one could actually choose these ‘semi-arbitrary values’ across the board, leaving the same four adjustable parameters $c_{C,DFT}$, c_{2ab} , c_{2ss} , and s_6 as in the revDSD-XC-D3(BJ) cases.

revDSD-PBEP86-D4 in particular shines, with WTMAD2=2.33 kcal/mol, quite close to the ω B97M(2) functional with its 16 adjustable parameters. But revDSD-SCAN₆₆-D4, revDSD-PBE-D4, and revDSD-PBEP95-D4 all likewise outperform their revDSD-XC-D3(BJ) counterparts, and revDSD-BLYP-D4 marginally bests revDSD-BLYP-D3(BJ).

Three of the refitted functionals have c_{2ss} values close to zero, hence we also performed revDOD-PBE-D4, DOD-SCAN₆₆-D4, and revDOD-PBEP95-D4 fits in case one wants to exploit the reduced-scaling algorithms for opposite-spin-only MP2. For revDOD-BLYP-D4, there is substantial loss in performance, but revDOD-PBEP86-D4, at WTMAD2=2.36 kcal/mol, only sacrifices 0.03 kcal/mol compared to its DSD counterpart. Next in performance is revDOD-PBE-D4 at WTMAD2=2.47 kcal/mol, then followed by DOD-SCAN-D4 at 2.64 kcal/mol.

Inspection of the contributions to WTMAD2 (Table S17) reveals that the improvement from revDSD-PBEP86-D3(BJ) to revDSD-PBEP86-D4 is mostly due to the intermolecular interaction components, and somewhat due to conformers. In DOD-SCAN₆₆-D4, on the other hand, intermolecular interactions and conformers are improved about equally.

While it is easy to rationalize the improvement in WTMAD2 from revDSD-D3(BJ) to revDSD-D4, it is not so obvious why the WTMAD2 of revDSD-PBEP86-D4 would be lower still than that of revDSD-PBEP86-NL. Detailed comparison reveals (Table S13) that four of the 55 subsets account for nearly all the difference: HAL59 (halogen bonding), HEAVY28 (NCI energies involving heavy p-block elements other than halogens), AMINO20X4 (Relative energies in amino acid conformers) and PNICO23 (Interaction energies in pnictogen-containing dimers). All of these have small average reaction energies and thus large weights in the WTMAD2 formula, Eq. (2), which means that small changes in the description of these four subsets have a disproportionately large impact on WTMAD2. (We note that DSD-PBEP86-D4 likewise has a small edge over DSD-PBEP86-NL.) For the remaining 51 subsets, an accuracy gain for NL in the MB16 “mindless benchmark”^{55,119} is offset by a comparable loss in conformer energies for melatonin, leaving the two WTMAD2 totals within 0.10 kcal/mol of each other. While it is clear that both D4 and NL represent substantial improvements over D3(BJ), we have insufficient data to decide whether D4 is superior over NL, or conversely.

Iron and Janes¹²⁰ have very recently examined the performance of hybrid and double-hybrid functionals for their newly developed MOBH35 transition metal barrier heights benchmark as well as for the older MOR41 organometallic reaction energy benchmark.¹²¹ There, the SCAN-based functionals were found to be superior to the others for these applications, even though overall the ω B97M-V functional outperformed all double hybrids except PWPB95.¹²² Detailed inspection of the double-hybrid results revealed a number of outliers for system that exhibit some degree of static correlation: apparently, the PT2 correlation is insufficiently

resilient to that. The use of dRPA (direct random phase approximation) as an alternative, as proposed by Mezei et al.,^{123,124} will be explored in future work. (The use of perturbation theory higher than second order was considered by Chan and Radom¹²⁵ and found to yield essentially no performance benefit.) Results for the ω B97M(2) functional were not given in that paper. For the sake of completeness, we carried out these calculations ourselves using the def2-TZVPP basis set used in Ref.¹²⁰ for the other double hybrids: for MOR41,¹²¹ we obtain MAD=2.8 and RMSD=3.5 kcal/mol, while for MOBH35,¹²⁰ we obtain MAD=2.4 and RMSD=4.0 kcal/mol.

Table 4: Final parameters for revDSD-D4 functionals and comparison of WTMAD2 (kcal/mol) with original double-hybrids (D3(BJ)), ditto with drop-in replacement of D3(BJ) by D4, and revD3(BJ)

Functionals	WTMAD2(kcal/mol)				Parameters							
	D3(BJ)	revD3(BJ)	D4	revD4	C _{X,HF}	C _{C,DFT}	C _{2ab}	C _{2ss}	S ₆	S ₈	a ₁	a ₂
DSD-PBEP86	3.099	2.422	2.649	2.332	0.69	0.4210	0.5922	0.0636	0.5132	0	0.44	3.60
With core corr DSD-PBEP86				2.307	0.69	0.4038	0.5979	0.0571	0.4612	0	0.44	3.60
DSD-PBE	3.170	2.738	2.637	2.461	0.68	0.4403	0.6025	0.0417	0.6706	0	0.4	3.6
DSD-BLYP	3.336	2.484	2.829	2.592	0.71	0.5169	0.5586	0.1972	0.6141	0	0.38	3.52
DSD-SCAN	—	2.662	—	2.635	0.66	0.4855	0.6320	0.0131	0.3203	0	0.4	3.6
DSD-PBEB95	3.325	2.845	3.109	2.700	0.66	0.4549	0.5305	0.0547	0.4707	0	0.42	2.93
xDSD-PBEP86				2.318	0.69	0.4155 ^a	0.6023	0.0514	0.4829	0	0.44	3.60
Ditto, s8≠0				2.302	0.69	0.4135	0.6044	0.0476	0.4158	0.1096	0.44	3.60
With core corr xDSD-PBEP86				2.229	0.69	0.3986 ^a	0.6077	0.0502	0.4200	0	0.44	3.60
With core corr xDOD-PBEP86				2.247	0.69	0.4071 ^a	0.6261	0	0.4561	0	0.44	3.60
DOD-PBEP86				2.363	0.69	0.4323	0.6122	0	0.5552	0	0.44	3.60
DOD-PBE				2.470	0.68	0.4470	0.6181	0	0.6992	0	0.4	3.6
DOD-SCAN				2.637	0.66	0.4914	0.6344	0	0.3270	0	0.4	3.6
DOD-PBEB95				2.714	0.66	0.4653	0.5532	0	0.4915	0	0.42	2.93
DOD-BLYP				2.792	0.71	0.5619	0.6346	0	0.7105	0	0.38	3.52

a. During iterations, C_{C,DFT}=1.00 as for all xDSD functionals

Coming back to GMTKN55: can we improve further over revDSD-PBEP86-D4, at WTMAD2=2.33 kcal/mol? As above, we found a minor improvement over revDSD-PBEP86-D3(BJ) when the frozen-core approximation was not made, we attempted the same here, and found that revDSD-PBEP86-D4(noFC) [where noFC stands for “no frozen cores”] has a slightly lower WTMAD2=2.31 kcal/mol. (See Table S17 for details.)

Then we attempted one more thing that also is present in ω B97M(2): we evaluated the KS orbitals with full DFT correlation, akin to the XYG3 family of functionals⁴⁰. Previously, we have found⁴² for much smaller training sets that (a) typically error metrics go through a minimum when the percentage of HF exchange in the final energy evaluation is at or near that used for determining the orbitals (leading to what we have termed⁴² xDSD functionals); (b) the improvement seen from DSD to xDSD was small and its statistical significance uncertain. Hait and Head-Gordon have discussed some downsides of the xDSD and XYG3 type functionals for nonequilibrium geometries.⁴³ It was argued in Ref.¹²² that the putative success of that approach results not from the effect of the un-throttled DFT correlation on the orbitals but from the smaller orbital gaps appearing in the denominators of the MP2-like terms.

In the present work, we have obtained an xrevDSD-PBEP86-D4(noFC) functional fitted to the GMTKN55 dataset. Parameters are given in Table 4: the WTMAD2 obtained, 2.23 kcal/mol, is the lowest of any functional optimized here, and *is statistically equivalent to the 2.18 kcal/mol of the highly empirical ω B97M(2) functional despite the much smaller number of*

parameters. Detailed inspection of Table S17 reveals that the improvement over the revDSD-PBEP86-D4 functional mostly comes from just one subset, namely, the radical stabilization energies in RSE43. Turning to the five major categories, ω B97M(2) outperforms xrevDSD-PBEP86-D4(noFC) for thermochemistry and is in turn outperformed for conformer energies, while there is little to choose between them for intermolecular interaction energies, barrier heights, and large system reactions.

Can we eliminate the same-spin correlation and thus enable the reduced-scaling MP2 algorithms (as well as eliminate one more empirical parameter)? As seen in Table 4, the WTMAD2 for xrevDOD-PBEP86-D4(noFC) is just 0.02 kcal/mol higher at 2.25 kcal/mol. We have, hence, a functional comparable to ω B97M(2) in quality that is amenable to reduced $O(N^4)$ or $O(N^3)$ MP2 scaling, unlike ω B97M(2) which has $c_{2ab}=c_{2ss}$. This may be relevant in application to larger systems than considered presently. (The largest species in GMTKN55 has ‘only’ 83 atoms.) However, the difference in WTMAD2 between 2.23 for xrev-DSD-PBEP86-D4 and 2.33 for rev-DSD-PBEP86-D4 can be argued to be comparable to the uncertainty in the GMTKN55 reference data, and hence should perhaps not be given excess weight.

Harmonic frequencies as a sanity check

We have previously shown¹²⁶ that for the HFREQ harmonic frequencies benchmark,¹²⁶ the DSD-PBEP86 functional performed exceptionally well (RMSD=9.8 cm⁻¹ with the def-QZVP basis set and a scale factor of 0.9971), unlike earlier double hybrids. As HFREQ samples a different *type* of information than GMTKN55, it can act as a sanity check on revDSD-PBEP86: if RMSD[HFREQ] were substantially higher than for the original DSD-PBEP86, then perhaps the improved performance for GMTKN55 would reflect improved physics not as much as the famous quip attributed to John von Neumann that “with four parameters, I can fit an elephant, and with five, I can make him wiggle his trunk”.

Figure 3: contour plot of RMSD (cm⁻¹) for the HFREQ database for DSD-PBEP86 like forms, as a function of the opposite-spin and same-spin MP2 coefficients c_{2ab} and c_{2ss} , respectively. The square marker indicates the original DSD-PBEP86-D3(BJ) solution, the large round marker revDSD-PBEP86-D3(BJ), and the triangular ones revDSD-PBEP86-D4 on the left and revDOD-PBEP86-D4 on the right. The slanted line only serves to guide the eye.

As one can see in Figure 3, revDSD-PBEP86-D3(BJ) and especially revDSD-PBEP86-D4 in fact show somewhat *improved* performance for harmonic frequencies. If we fit scaling factors for harmonic frequencies in the same manner as in Ref.¹²⁶, we obtain values that are only semantically different from 1.0.

An additional sanity check is afforded by the work of Iron and Janes¹²⁰ on transition metal barrier heights, and of Efremenko and one of us¹²⁷ on a specific organometallic catalysis problem.¹²⁸ In both cases, the revDSD-PBEP86-D3(BJ) and revDSD-PBEP86-D4 functionals came considerably closer to the coupled cluster benchmark data than the original DSD-PBEP86-D3(BJ) parametrization, even though (as noted above) they do not offer the clear added value over ω B97M-V for transition metal systems that they do for main-group systems. Still, our confidence in the reparametrization against GMTKN55 is bolstered by its yielding better performance than the original *both* when sampling a different type of property (energy derivatives) *and* when sampling energetic properties for a different sector of chemical space.

A reviewer inquired about best performers for individual subsets. A sorted, color-shaded table with performance metrics for the five major subsets of WTMAD2, as well as for the total, has been given in the ESI as Table S18, with the top three performers for each subset marked. Said showings are largely a back-and-forth between ω B97M(2) and revDSD-PBEP86-D4. We should point out that revDSD-PBEP86-D3(BJ) entails a small enough loss in performance (much smaller than between ω B97M-V and ω B97M-D3(BJ), for instance) that it remains an attractive option, as it can be carried out with existing codes (including all of Gaussian 16, ORCA, and Q-CHEM) without source code modification and permits analytical first and second derivatives.

Conclusions

Having made an extensive survey of DSD double hybrid (and some other) functionals with the aid of the GMTKN55 dataset, we are in a position to state the following observations:

- the combinatorially optimized ω B97M-V is “best in class” for fourth-rung exchange-correlation functionals, and approaches performance of double hybrids like B2GP-PLYP-D3(BJ);
- the combinatorially optimized ω B97M(2) yields the lowest WTMAD2 metric of any functional in existence, making it best in class for double hybrids;
- in a DSD double hybrid context, the very recent D4 dispersion correction is clearly superior over D3(BJ), presumably owing to the newly introduced partial charge dependence;
- the available data suggest that revDSD-PBEP86-D4 is slightly superior to revDSD-PBEP86-NL;
- while ω B97M(2) has sixteen empirical parameters, refitted revDSD-PBEP86-D3(BJ) comes close in performance, while xrevDSD-PBEP86-D4 and xrevDOD-PBEP86-D4 are essentially equivalent in quality to ω B97M(2). Out of their reduced number of parameters, the percentage of HF exchange $c_{X,HF}$ and the damping function parameters a_1, a_2 can be fixed at semi-arbitrary values (as the WTMAD2 surface is fairly flat in them), leaving just four true optimization parameters for revDSD and three for revDOD. The revDOD option permits the use of reduced-scaling MP2 algorithms, which might prove useful for large systems;
- for the underlying semilocal functional in double hybrids, any good exchange functional appears to work well, while simple correlation functionals that rapidly “get out of the way” at long distances appear to work best (e.g., P86¹²⁹ and LYP¹³⁰);

- if one wishes to avoid the D3 or D4 corrections, however, DSD-SCAN overall appears to work best. Here, the number of empirical parameters is down to four, one of which (the fraction of HF-like exchange) semi-arbitrary. The best performance without dispersion corrections;
- refitting of the DSD functionals to the GMTKN55 database very substantially improves their accuracy particularly for noncovalent interactions and large-system reactions. This serves as a cautionary tale about the use of small, idiosyncratic training sets for empirical functionals.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jpca.9b03157.

Tables S1 through S18 (PDF); Figure S1; sample revDSD-PBEP86-D3BJ inputs for several electronic structure codes.

Acknowledgments

This research was supported by the Israel Science Foundation (grant 1358/15) and by the Minerva Foundation, Munich, Germany, as well as by two internal Weizmann Institute funding sources: the Helen and Martin Kimmel Center for Molecular Design and a research grant from the estate of Emile Mimran. N.S. acknowledges a doctoral fellowship from the Feinberg Graduate School (WIS). The authors would like to thank a referee for helpful comments.

Author Information

Corresponding Author

J. M. L. Martin. E-mail: gershom@weizmann.ac.il. Fax: +972 8 934 3029.

ORCID

Jan M. L. Martin: 0000-0002-0005-5074

Notes

The authors declare no competing financial interest.

References

- (1) Dral, P. O.; Wu, X.; Spörkel, L.; Koslowski, A.; Thiel, W. Semiempirical Quantum-Chemical Orthogonalization-Corrected Methods: Benchmarks for Ground-State Properties. *J. Chem. Theory Comput.* **2016**, *12* (3), 1097–1120. <https://doi.org/10.1021/acs.jctc.5b01047>.
- (2) DeYonker, N. J.; Cundari, T. R.; Wilson, A. K. The Correlation Consistent Composite Approach (CcCA): Efficient and Pan-Periodic Kinetics and Thermodynamics. In *Advances in the Theory of Atomic and Molecular Systems (Progress in Theoretical*

- Chemistry and Physics, Vol. 19*); Piecuch, P., Maruani, J., Delgado-Barrio, G., Wilson, S., Eds.; Progress in Theoretical Chemistry and Physics; Springer Netherlands: Dordrecht, 2009; Vol. 19, pp 197–224. https://doi.org/10.1007/978-90-481-2596-8_9.
- (3) Curtiss, L. A.; Redfern, P. C.; Raghavachari, K. Gaussian-4 Theory. *J. Chem. Phys.* **2007**, *126* (8), 084108. <https://doi.org/10.1063/1.2436888>.
 - (4) Montgomery, J. A.; Frisch, M. J.; Ochterski, J. W.; Petersson, G. A. A Complete Basis Set Model Chemistry. VI. Use of Density Functional Geometries and Frequencies. *J. Chem. Phys.* **1999**, *110* (6), 2822. <https://doi.org/10.1063/1.477924>.
 - (5) Martin, J. M. L.; de Oliveira, G. Towards Standard Methods for Benchmark Quality Ab Initio Thermochemistry—W1 and W2 Theory. *J. Chem. Phys.* **1999**, *111* (5), 1843–1856. <https://doi.org/10.1063/1.479454>.
 - (6) Karton, A.; Martin, J. M. L. Explicitly Correlated Wn Theory: W1-F12 and W2-F12. *J. Chem. Phys.* **2012**, *136* (12), 124114. <https://doi.org/10.1063/1.3697678>.
 - (7) Ramakrishnan, R.; Dral, P. O.; Rupp, M.; von Lilienfeld, O. A. Big Data Meets Quantum Chemistry Approximations: The Δ -Machine Learning Approach. *J. Chem. Theory Comput.* **2015**, *11* (5), 2087–2096. <https://doi.org/10.1021/acs.jctc.5b00099>.
 - (8) Perdew, J. P.; Burke, K.; Ernzerhof, M. Generalized Gradient Approximation Made Simple. *Phys. Rev. Lett.* **1996**, *77* (18), 3865–3868. <https://doi.org/10.1103/PhysRevLett.77.3865>.
 - (9) Tao, J.; Perdew, J. P.; Staroverov, V. N.; Scuseria, G. E. Climbing the Density Functional Ladder: Nonempirical Meta-Generalized Gradient Approximation Designed for Molecules and Solids. *Phys. Rev. Lett.* **2003**, *91* (14), 146401. <https://doi.org/10.1103/PhysRevLett.91.146401>.
 - (10) Sun, J.; Ruzsinszky, A.; Perdew, J. P. Strongly Constrained and Appropriately Normed Semilocal Density Functional. *Phys. Rev. Lett.* **2015**, *115* (3), 036402. <https://doi.org/10.1103/PhysRevLett.115.036402>.
 - (11) DeYonker, N. J.; Cundari, T. R.; Wilson, A. K. The Correlation Consistent Composite Approach (CcCA): An Alternative to the Gaussian-n Methods. *J. Chem. Phys.* **2006**, *124* (11), 114104. <https://doi.org/10.1063/1.2173988>.
 - (12) Martin, J. M. L.; Parthiban, S. W1 and W2 Theories, and Their Variants: Thermochemistry in the KJ/Mol Accuracy Range. In *Quantum-Mechanical Prediction of Thermochemical Data*; Cioslowski, J., Ed.; Understanding Chemical Reactivity; Kluwer Academic Publishers: Dordrecht, 2002; Vol. 22, pp 31–65. https://doi.org/10.1007/0-306-47632-0_2.
 - (13) Becke, A. D. Density-Functional Thermochemistry. V. Systematic Optimization of Exchange-Correlation Functionals. *J. Chem. Phys.* **1997**, *107* (20), 8554–8560. <https://doi.org/10.1063/1.475007>.
 - (14) Hamprecht, F. A.; Cohen, A. J.; Tozer, D. J.; Handy, N. C. Development and Assessment of New Exchange-Correlation Functionals. *J. Chem. Phys.* **1998**, *109* (15), 6264–6271. <https://doi.org/10.1063/1.477267>.
 - (15) Boese, A. D.; Martin, J. M. L. Development of Density Functionals for Thermochemical Kinetics. *J. Chem. Phys.* **2004**, *121* (8), 3405–3416. <https://doi.org/10.1063/1.1774975>.
 - (16) Zhao, Y.; Truhlar, D. G. Density Functionals with Broad Applicability in Chemistry. *Acc. Chem. Res.* **2008**, *41* (2), 157–167. <https://doi.org/10.1021/ar700111a>.
 - (17) Yu, H. S.; He, X.; Li, S. L.; Truhlar, D. G. MN15: A Kohn–Sham Global-Hybrid Exchange–Correlation Density Functional with Broad Accuracy for Multi-Reference and

- Single-Reference Systems and Noncovalent Interactions. *Chem. Sci.* **2016**, 7 (8), 5032–5051. <https://doi.org/10.1039/C6SC00705H>.
- (18) Becke, A. D. Density-functional Thermochemistry. III. The Role of Exact Exchange. *J. Chem. Phys.* **1993**, 98 (7), 5648–5652. <https://doi.org/10.1063/1.464913>.
 - (19) Adamson, R. D.; Gill, P. M. W.; Pople, J. A. Empirical Density Functionals. *Chem. Phys. Lett.* **1998**, 284 (1–2), 6–11. [https://doi.org/10.1016/S0009-2614\(97\)01282-7](https://doi.org/10.1016/S0009-2614(97)01282-7).
 - (20) Boese, A. D.; Handy, N. C. A New Parametrization of Exchange-Correlation Generalized Gradient Approximation Functionals. *J. Chem. Phys.* **2001**, 114 (13), 5497–5503. <https://doi.org/10.1063/1.1347371>.
 - (21) Mardirossian, N.; Head-Gordon, M. Ω B97X-V: A 10-Parameter, Range-Separated Hybrid, Generalized Gradient Approximation Density Functional with Nonlocal Correlation, Designed by a Survival-of-the-Fittest Strategy. *Phys. Chem. Chem. Phys.* **2014**, 16 (21), 9904–9924. <https://doi.org/10.1039/c3cp54374a>.
 - (22) Mardirossian, N.; Head-Gordon, M. Mapping the Genome of Meta-Generalized Gradient Approximation Density Functionals: The Search for B97M-V. *J. Chem. Phys.* **2015**, 142 (7), 074111. <https://doi.org/10.1063/1.4907719>.
 - (23) Mardirossian, N.; Head-Gordon, M. Ω B97M-V: A Combinatorially Optimized, Range-Separated Hybrid, Meta-GGA Density Functional with VV10 Nonlocal Correlation. *J. Chem. Phys.* **2016**, 144 (21), 214110. <https://doi.org/10.1063/1.4952647>.
 - (24) Mardirossian, N.; Head-Gordon, M. Survival of the Most Transferable at the Top of Jacob’s Ladder: Defining and Testing the Ω B97M(2) Double Hybrid Density Functional. *J. Chem. Phys.* **2018**, 148 (24), 241736. <https://doi.org/10.1063/1.5025226>.
 - (25) Perdew, J. P.; Schmidt, K. Jacob’s Ladder of Density Functional Approximations for the Exchange-Correlation Energy. *AIP Conf. Proc.* **2001**, 577 (1), 1–20. <https://doi.org/10.1063/1.1390175>.
 - (26) Kümmel, S.; Kronik, L. Orbital-Dependent Density Functionals: Theory and Applications. *Rev. Mod. Phys.* **2008**, 80 (1), 3–60. <https://doi.org/10.1103/RevModPhys.80.3>.
 - (27) Zhao, Y.; Lynch, B. J.; Truhlar, D. G. Doubly Hybrid Meta DFT: New Multi-Coefficient Correlation and Density Functional Methods for Thermochemistry and Thermochemical Kinetics. *J. Phys. Chem. A* **2004**, 108 (21), 4786–4791. <https://doi.org/10.1021/jp049253v>.
 - (28) Grimme, S. Semiempirical Hybrid Density Functional with Perturbative Second-Order Correlation. *J. Chem. Phys.* **2006**, 124 (3), 034108. <https://doi.org/10.1063/1.2148954>.
 - (29) Görling, A.; Levy, M. Exact Kohn-Sham Scheme Based on Perturbation Theory. *Phys. Rev. A* **1994**, 50 (1), 196–204. <https://doi.org/10.1103/PhysRevA.50.196>.
 - (30) Grimme, S. Semiempirical GGA-Type Density Functional Constructed with a Long-Range Dispersion Correction. *J. Comput. Chem.* **2006**, 27 (15), 1787–1799. <https://doi.org/10.1002/jcc.20495>.
 - (31) Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H. A Consistent and Accurate Ab Initio Parametrization of Density Functional Dispersion Correction (DFT-D) for the 94 Elements H-Pu. *J. Chem. Phys.* **2010**, 132 (15), 154104. <https://doi.org/10.1063/1.3382344>.
 - (32) Grimme, S.; Ehrlich, S.; Goerigk, L. Effect of the Damping Function in Dispersion Corrected Density Functional Theory. *J. Comput. Chem.* **2011**, 32 (7), 1456–1465. <https://doi.org/10.1002/jcc.21759>.
 - (33) Grimme, S.; Bannwarth, C.; Caldeweyher, E.; Pisarek, J.; Hansen, A. A General Intermolecular Force Field Based on Tight-Binding Quantum Chemical Calculations. *J.*

- Chem. Phys.* **2017**, *147* (16), 161708. <https://doi.org/10.1063/1.4991798>.
- (34) Caldeweyher, E.; Ehlert, S.; Hansen, A.; Neugebauer, H.; Spicher, S.; Bannwarth, C.; Grimme, S. A Generally Applicable Atomic-Charge Dependent London Dispersion Correction. *J. Chem. Phys.* **2019**, *150* (15), 154122. <https://doi.org/10.1063/1.5090222>.
 - (35) Vydrov, O. A.; Van Voorhis, T. Nonlocal van Der Waals Density Functional: The Simpler the Better. *J. Chem. Phys.* **2010**, *133* (24), 244103. <https://doi.org/10.1063/1.3521275>.
 - (36) Kozuch, S.; Martin, J. M. L. DSD-PBEP86: In Search of the Best Double-Hybrid DFT with Spin-Component Scaled MP2 and Dispersion Corrections. *Phys. Chem. Chem. Phys.* **2011**, *13* (45), 20104. <https://doi.org/10.1039/c1cp22592h>.
 - (37) Kozuch, S.; Martin, J. M. L. Spin-Component-Scaled Double Hybrids: An Extensive Search for the Best Fifth-Rung Functionals Blending DFT and Perturbation Theory. *J. Comput. Chem.* **2013**, *34* (27), 2327–2344. <https://doi.org/10.1002/jcc.23391>.
 - (38) Kozuch, S.; Gruzman, D.; Martin, J. M. L. DSD-BLYP: A General Purpose Double Hybrid Density Functional Including Spin Component Scaling and Dispersion Correction. *J. Phys. Chem. C* **2010**, *114* (48), 20801–20808. <https://doi.org/10.1021/jp1070852>.
 - (39) Karton, A.; Tarnopolsky, A.; Lamère, J.-F.; Schatz, G. C.; Martin, J. M. L. Highly Accurate First-Principles Benchmark Data Sets for the Parametrization and Validation of Density Functional and Other Approximate Methods. Derivation of a Robust, Generally Applicable, Double-Hybrid Functional for Thermochemistry and Thermochemical . *J. Phys. Chem. A* **2008**, *112* (50), 12868–12886. <https://doi.org/10.1021/jp801805p>.
 - (40) Su, N. Q.; Xu, X. The XYG3 Type of Doubly Hybrid Density Functionals. *Wiley Interdiscip. Rev. Comput. Mol. Sci.* **2016**, *6* (6), 721–747. <https://doi.org/10.1002/wcms.1274>.
 - (41) Goerigk, L.; Grimme, S. A Thorough Benchmark of Density Functional Methods for General Main Group Thermochemistry, Kinetics, and Noncovalent Interactions. *Phys. Chem. Chem. Phys.* **2011**, *13*, 6670–6688. <https://doi.org/10.1039/c0cp02984j>.
 - (42) Kesharwani, M. K.; Kozuch, S.; Martin, J. M. L. Comment on “Doubly Hybrid Density Functional XDH-PBE0 from a Parameter-Free Global Hybrid Model PBE0” [J. Chem. Phys. 136, 174103 (2012)]. *J. Chem. Phys.* **2015**, *143* (18), 187101. <https://doi.org/10.1063/1.4934819>.
 - (43) Hait, D.; Head-Gordon, M. Communication: XDH Double Hybrid Functionals Can Be Qualitatively Incorrect for Non-Equilibrium Geometries: Dipole Moment Inversion and Barriers to Radical-Radical Association Using XYG3 and XYGJ-OS. *J. Chem. Phys.* **2018**, *148* (17), 171102. <https://doi.org/10.1063/1.5031027>.
 - (44) Goerigk, L.; Grimme, S. Double-Hybrid Density Functionals. *Wiley Interdiscip. Rev. Comput. Mol. Sci.* **2014**, *4* (6), 576–600. <https://doi.org/10.1002/wcms.1193>.
 - (45) Sancho-García, J. C.; Adamo, C. Double-Hybrid Density Functionals: Merging Wavefunction and Density Approaches to Get the Best of Both Worlds. *Phys. Chem. Chem. Phys.* **2013**, *15* (35), 14581. <https://doi.org/10.1039/c3cp50907a>.
 - (46) Su, N. Q.; Zhu, Z.; Xu, X. Doubly Hybrid Density Functionals That Correctly Describe Both Density and Energy for Atoms. *Proc. Natl. Acad. Sci. U. S. A.* **2018**, *115* (10), 2287–2292. <https://doi.org/10.1073/pnas.1713047115>.
 - (47) Brémond, E.; Ciofini, I.; Sancho-García, J. C.; Adamo, C. Nonempirical Double-Hybrid Functionals: An Effective Tool for Chemists. *Acc. Chem. Res.* **2016**, *49* (8), 1503–1513. <https://doi.org/10.1021/acs.accounts.6b00232>.
 - (48) Benighaus, T.; Distasio, R.; Lochan, R.; Chai, J.-D.; Head-Gordon, M. Semiempirical

- Double-Hybrid Density Functional with Improved Description of Long-Range Correlation. *J. Phys. Chem. A* **2008**, *112* (12), 2702–2712.
- (49) Graham, D.; Menon, A.; Goerigk, L.; Grimme, S.; Radom, L. Optimization and Basis-Set Dependence of a Restricted-Open-Shell Form of B2-PLYP Double-Hybrid Density Functional Theory. *J. Phys. Chem. A* **2009**, *113* (36), 9861–9873.
- (50) Chan, B.; Radom, L. Accurate Quadruple- ζ Basis-Set Approximation for Double-Hybrid Density Functional Theory with an Order of Magnitude Reduction in Computational Cost. *Theor. Chem. Acc.* **2013**, *133* (2), 1426. <https://doi.org/10.1007/s00214-013-1426-9>.
- (51) Mehta, N.; Casanova-Páez, M.; Goerigk, L. Semi-Empirical or Non-Empirical Double-Hybrid Density Functionals: Which Are More Robust? *Phys. Chem. Chem. Phys.* **2018**, *20* (36), 23175–23194. <https://doi.org/10.1039/C8CP03852J>.
- (52) Goerigk, L.; Mehta, N. A Trip to the Density Functional Theory Zoo: Warnings and Recommendations for the User*. *Aust. J. Chem.* **2019**. <https://doi.org/10.1071/CH19023>.
- (53) Mardirossian, N.; Head-Gordon, M. Thirty Years of Density Functional Theory in Computational Chemistry: An Overview and Extensive Assessment of 200 Density Functionals. *Mol. Phys.* **2017**, *115* (19), 2315–2372. <https://doi.org/10.1080/00268976.2017.1333644>.
- (54) Peverati, R.; Truhlar, D. G. Quest for a Universal Density Functional: The Accuracy of Density Functionals across a Broad Spectrum of Databases in Chemistry and Physics. *Philos. Trans. R. Soc. A Math. Phys. Eng. Sci.* **2014**, *372* (2011), 20120476–20120476. <https://doi.org/10.1098/rsta.2012.0476>.
- (55) Goerigk, L.; Hansen, A.; Bauer, C.; Ehrlich, S.; Najibi, A.; Grimme, S. A Look at the Density Functional Theory Zoo with the Advanced GMTKN55 Database for General Main Group Thermochemistry, Kinetics and Noncovalent Interactions. *Phys. Chem. Chem. Phys.* **2017**, *19* (48), 32184–32215. <https://doi.org/10.1039/C7CP04913G>.
- (56) Goerigk, L.; Grimme, S. A General Database for Main Group Thermochemistry, Kinetics, and Noncovalent Interactions – Assessment of Common and Reparameterized (Meta -)GGA Density Functionals. *J. Chem. Theory Comput.* **2010**, *6* (1), 107–126. <https://doi.org/10.1021/ct900489g>.
- (57) Yu, H. S.; Zhang, W.; Verma, P.; He, X.; Truhlar, D. G. Nonseparable Exchange–Correlation Functional for Molecules, Including Homogeneous Catalysis Involving Transition Metals. *Phys. Chem. Chem. Phys.* **2015**, *17* (18), 12146–12160. <https://doi.org/10.1039/C5CP01425E>.
- (58) Jurecka, P.; Sponer, J.; Cerný, J.; Hobza, P. Benchmark Database of Accurate (MP2 and CCSD(T) Complete Basis Set Limit) Interaction Energies of Small Model Complexes, DNA Base Pairs, and Amino Acid Pairs. *Phys. Chem. Chem. Phys.* **2006**, *8* (17), 1985–1993. <https://doi.org/10.1039/b600027d>.
- (59) Rezáč, J.; Riley, K. E.; Hobza, P. S66: A Well-Balanced Database of Benchmark Interaction Energies Relevant to Biomolecular Structures. *J. Chem. Theory Comput.* **2011**, *7* (8), 2427–2438. <https://doi.org/10.1021/ct2002946>.
- (60) Rezáč, J.; Riley, K. E.; Hobza, P. Benchmark Calculations of Noncovalent Interactions of Halogenated Molecules. *J. Chem. Theory Comput.* **2012**, *8* (11), 4285–4292. <https://doi.org/10.1021/ct300647k>.
- (61) Hobza, P. Calculations on Noncovalent Interactions and Databases of Benchmark Interaction Energies. *Acc. Chem. Res.* **2012**, *45* (4), 663–672. <https://doi.org/10.1021/ar200255p>.

- (62) Karton, A.; Daon, S.; Martin, J. M. L. W4-11: A High-Confidence Benchmark Dataset for Computational Thermochemistry Derived from First-Principles W4 Data. *Chem. Phys. Lett.* **2011**, *510*, 165–178. <https://doi.org/10.1016/j.cplett.2011.05.007>.
- (63) Kesharwani, M. K.; Manna, D.; Sylvetsky, N.; Martin, J. M. L. The X40×10 Halogen Bonding Benchmark Revisited: Surprising Importance of (n – 1)d Subvalence Correlation. *J. Phys. Chem. A* **2018**, *122* (8), 2184–2197. <https://doi.org/10.1021/acs.jpca.7b10958>.
- (64) Fogueri, U. R.; Kozuch, S.; Karton, A.; Martin, J. M. L. The Melatonin Conformer Space: Benchmark and Assessment of Wave Function and DFT Methods for a Paradigmatic Biological and Pharmacological Molecule. *J. Phys. Chem. A* **2013**, *117* (10), 2269–2277. <https://doi.org/10.1021/jp312644t>.
- (65) Kozuch, S.; Martin, J. M. L. Halogen Bonds: Benchmarks and Theoretical Analysis. *J. Chem. Theory Comput.* **2013**, *9*, 1918–1931. <https://doi.org/10.1021/ct301064t>.
- (66) Martin, J. M. L. What Can We Learn About Dispersion from the Conformer Surface of N-Pentane? *J. Phys. Chem. A* **2013**, *117* (14), 3118–3132. <https://doi.org/10.1021/jp401429u>.
- (67) Kozuch, S.; Bachrach, S. M.; Martin, J. M. L. Conformational Equilibria in Butane-1,4-Diol: A Benchmark of a Prototypical System with Strong Intramolecular H-Bonds. *J. Phys. Chem. A* **2014**, *118* (1), 293–303. <https://doi.org/10.1021/jp410723v>.
- (68) Karton, A.; Schreiner, P. R.; Martin, J. M. L. Heats of Formation of Platonic Hydrocarbon Cages by Means of High-Level Thermochemical Procedures. *J. Comput. Chem.* **2016**, *37* (1), 49–58. <https://doi.org/10.1002/jcc.23963>.
- (69) Kesharwani, M. K.; Karton, A.; Martin, J. M. L. Benchmark Ab Initio Conformational Energies for the Proteinogenic Amino Acids through Explicitly Correlated Methods. Assessment of Density Functional Methods. *J. Chem. Theory Comput.* **2016**, *12* (1), 444–454. <https://doi.org/10.1021/acs.jctc.5b01066>.
- (70) Manna, D.; Martin, J. M. L. What Are the Ground State Structures of C₂₀ and C₂₄? An Explicitly Correlated Ab Initio Approach. *J. Phys. Chem. A* **2016**, *120* (1), 153–160. <https://doi.org/10.1021/acs.jpca.5b10266>.
- (71) Brauer, B.; Kesharwani, M. K.; Kozuch, S.; Martin, J. M. L. The S66x8 Benchmark for Noncovalent Interactions Revisited: Explicitly Correlated Ab Initio Methods and Density Functional Theory. *Phys. Chem. Chem. Phys.* **2016**, *18* (31), 20905–20925. <https://doi.org/10.1039/C6CP00688D>.
- (72) Manna, D.; Kesharwani, M. K.; Sylvetsky, N.; Martin, J. M. L. Conventional and Explicitly Correlated Ab Initio Benchmark Study on Water Clusters: Revision of the BEGDB and WATER27 Data Sets. *J. Chem. Theory Comput.* **2017**, *13* (7), 3136–3152. <https://doi.org/10.1021/acs.jctc.6b01046>.
- (73) Karton, A.; Sylvetsky, N.; Martin, J. M. L. W4-17: A Diverse and High-Confidence Dataset of Atomization Energies for Benchmarking High-Level Electronic Structure Methods. *J. Comput. Chem.* **2017**, *38* (24), 2063–2075. <https://doi.org/10.1002/jcc.24854>.
- (74) Lynch, B. J.; Truhlar, D. G. Small Representative Benchmarks for Thermochemical Calculations. *J. Phys. Chem. A* **2003**, *107* (42), 8996–8999. <https://doi.org/10.1021/jp035287b>.
- (75) Chan, B. Formulation of Small Test Sets Using Large Test Sets for Efficient Assessment of Quantum Chemistry Methods. *J. Chem. Theory Comput.* **2018**, *14* (8), 4254–4262. <https://doi.org/10.1021/acs.jctc.8b00514>.
- (76) Gould, T. ‘Diet GMTKN55’ Offers Accelerated Benchmarking through a Representative Subset Approach. *Phys. Chem. Chem. Phys.* **2018**, *20* (44), 27735–27739.

- <https://doi.org/10.1039/C8CP05554H>.
- (77) Morgante, P.; Peverati, R. ACCDB: A Collection of Chemistry Databases for Broad Computational Purposes. *J. Comput. Chem.* **2019**, *40* (6), 839–848. <https://doi.org/10.1002/jcc.25761>.
 - (78) Koster, J.; Rahmann, S. Snakemake--a Scalable Bioinformatics Workflow Engine. *Bioinformatics* **2012**, *28* (19), 2520–2522. <https://doi.org/10.1093/bioinformatics/bts480>.
 - (79) Huber, P. J.; Ronchetti, E. M. *Robust Statistics*; Wiley Series in Probability and Statistics; John Wiley & Sons, Inc.: Hoboken, NJ, USA, 2009. <https://doi.org/10.1002/9780470434697>.
 - (80) Weigend, F.; Ahlrichs, R. Balanced Basis Sets of Split Valence, Triple Zeta Valence and Quadruple Zeta Valence Quality for H to Rn: Design and Assessment of Accuracy. *Phys. Chem. Chem. Phys.* **2005**, *7* (18), 3297–3305. <https://doi.org/10.1039/b508541a>.
 - (81) Rappoport, D.; Furche, F. Property-Optimized Gaussian Basis Sets for Molecular Response Calculations. *J. Chem. Phys.* **2010**, *133* (13), 134105. <https://doi.org/10.1063/1.3484283>.
 - (82) Shao, Y.; Gan, Z.; Epifanovsky, E.; Gilbert, A. T. B.; Wormit, M.; Kussmann, J.; Lange, A. W.; Behn, A.; Deng, J.; Feng, X.; et al. Advances in Molecular Quantum Chemistry Contained in the Q-Chem 4 Program Package. *Mol. Phys.* **2015**, *113* (2), 184–215. <https://doi.org/10.1080/00268976.2014.952696>.
 - (83) Dasgupta, S.; Herbert, J. M. Standard Grids for High-Precision Integration of Modern Density Functionals: SG-2 and SG-3. *J. Comput. Chem.* **2017**, *38* (12), 869–882. <https://doi.org/10.1002/jcc.24761>.
 - (84) Gill, P. M. .; Johnson, B. G.; Pople, J. A. A Standard Grid for Density Functional Calculations. *Chem. Phys. Lett.* **1993**, *209* (5–6), 506–512. [https://doi.org/10.1016/0009-2614\(93\)80125-9](https://doi.org/10.1016/0009-2614(93)80125-9).
 - (85) Murray, C.; Handy, N.; Laming, G. Quadrature Schemes for Integrals of Density Functional Theory. *Mol. Phys.* **1993**, *78* (4), 997–1014. <https://doi.org/10.1080/00268979300100651>.
 - (86) Lebedev, V. I.; Laikov, D. N. A Quadrature Formula for the Sphere of the 131st Algebraic Order of Accuracy. *Dokl. Math.* **1999**, *59* (3), 477–481.
 - (87) Brandenburg, J. G.; Bates, J. E.; Sun, J.; Perdew, J. P. Benchmark Tests of a Strongly Constrained Semilocal Functional with a Long-Range Dispersion Correction. *Phys. Rev. B - Condens. Matter Mater. Phys.* **2016**, *94* (11), 17–19. <https://doi.org/10.1103/PhysRevB.94.115144>.
 - (88) Chai, J.-D.; Head-Gordon, M. Long-Range Corrected Double-Hybrid Density Functionals. *J. Chem. Phys.* **2009**, *131* (17), 174105. <https://doi.org/10.1063/1.3244209>.
 - (89) Sullivan, M. B.; Iron, M. A.; Redfern, P. C.; Martin, J. M. L.; Curtiss, L. A.; Radom, L. Heats of Formation of Alkali Metal and Alkaline Earth Metal Oxides and Hydroxides: Surprisingly Demanding Targets for High-Level Ab Initio Procedures. *J. Phys. Chem. A* **2003**, *107* (29), 5617–5630. <https://doi.org/10.1021/jp034851f>.
 - (90) Haworth, N. L.; Sullivan, M. B.; Wilson, A. K.; Martin, J. M. L.; Radom, L. Structures and Thermochemistry of Calcium-Containing Molecules. *J. Phys. Chem. A* **2005**, *109* (40), 9156–9168. <https://doi.org/10.1021/jp052889h>.
 - (91) Zhang, Y.; Yang, W. Comment on “Generalized Gradient Approximation Made Simple.” *Phys. Rev. Lett.* **1998**, *80* (4), 890–890. <https://doi.org/10.1103/PhysRevLett.80.890>.
 - (92) Perdew, J.; Ruzsinszky, A.; Csonka, G.; Constantin, L.; Sun, J. Workhorse Semilocal

- Density Functional for Condensed Matter Physics and Quantum Chemistry. *Phys. Rev. Lett.* **2009**, *103* (2). <https://doi.org/10.1103/PhysRevLett.103.026403>.
- (93) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. Ab Initio Calculation of Vibrational Absorption and Circular Dichroism Spectra Using Density Functional Force Fields. *J. Phys. Chem.* **1994**, *98* (45), 11623–11627. <https://doi.org/10.1021/j100096a001>.
- (94) Adamo, C.; Barone, V. Toward Reliable Density Functional Methods without Adjustable Parameters: The PBE0 Model. *J. Chem. Phys.* **1999**, *110* (13), 6158–6170. <https://doi.org/10.1063/1.478522>.
- (95) Zhao, Y.; Truhlar, D. G. Design of Density Functionals That Are Broadly Accurate for Thermochemistry, Thermochemical Kinetics, and Nonbonded Interactions. *J. Phys. Chem. A* **2005**, *109* (25), 5656–5667. <https://doi.org/10.1021/jp050536c>.
- (96) Zhao, Y.; Truhlar, D. G. The M06 Suite of Density Functionals for Main Group Thermochemistry, Thermochemical Kinetics, Noncovalent Interactions, Excited States, and Transition Elements: Two New Functionals and Systematic Testing of Four M06-Class Functionals and 12 Other Function. *Theor. Chem. Acc.* **2008**, *120* (1–3), 215–241. <https://doi.org/10.1007/s00214-007-0310-x>.
- (97) Hui, K.; Chai, J.-D. SCAN-Based Hybrid and Double-Hybrid Density Functionals from Models without Fitted Parameters. *J. Chem. Phys.* **2016**, *144* (4), 044114. <https://doi.org/10.1063/1.4940734>.
- (98) Powell, M. J. D. *The BOBYQA Algorithm for Bound Constrained Optimization without Derivatives (DAMPT Report 2009/NA06)*; Department of Applied Mathematics and Theoretical Physics, University of Cambridge, UK, 2009. <https://doi.org/10.1.1.443.7693>.
- (99) Goerigk, L. A Comprehensive Overview of the DFT-D3 London-Dispersion Correction. In *Non-Covalent Interactions in Quantum Chemistry and Physics*; Elsevier, 2017; pp 195–219. <https://doi.org/10.1016/B978-0-12-809835-6.00007-4>.
- (100) Najibi, A.; Goerigk, L. The Nonlocal Kernel in van Der Waals Density Functionals as an Additive Correction: An Extensive Analysis with Special Emphasis on the B97M-V and Ω B97M-V Approaches. *J. Chem. Theory Comput.* **2018**, *14* (11), 5725–5738. <https://doi.org/10.1021/acs.jctc.8b00842>.
- (101) Toulouse, J.; Sharkas, K.; Brémond, E.; Adamo, C. Communication : Rationale for a New Class of Double-Hybrid Approximations in Density-Functional Theory. *J. Chem. Phys.* **2011**, *135*, 101102. <https://doi.org/10.1063/1.3640019>.
- (102) Sharkas, K.; Toulouse, J.; Savin, A. Double-Hybrid Density-Functional Theory Made Rigorous. *J. Chem. Phys.* **2011**, *134* (6), 064113. <https://doi.org/10.1063/1.3544215>.
- (103) Sancho-García, J. C.; Pérez-Jiménez, A. J.; Savarese, M.; Brémond, E.; Adamo, C. Importance of Orbital Optimization for Double-Hybrid Density Functionals: Application of the OO-PBE-QIDH Model for Closed- and Open-Shell Systems. *J. Phys. Chem. A* **2016**, *120* (10), 1756–1762. <https://doi.org/10.1021/acs.jpca.6b00994>.
- (104) Austin, A.; Petersson, G. A.; Frisch, M. J.; Dobek, F. J.; Scalmani, G.; Throssell, K. A Density Functional with Spherical Atom Dispersion Terms. *J. Chem. Theory Comput.* **2012**, *8* (12), 4989–5007.
- (105) Hujo, W.; Grimme, S. Performance of the van Der Waals Density Functional VV10 and (Hybrid)GGA Variants for Thermochemistry and Noncovalent Interactions. *J. Chem. Theory Comput.* **2011**, *7* (12), 3866–3871. <https://doi.org/10.1021/ct200644w>.
- (106) Yu, F. Spin-Component-Scaled Double-Hybrid Density Functionals with Nonlocal van Der Waals Correlations for Noncovalent Interactions. *J. Chem. Theory Comput.* **2014**, *10*,

- 4400–4407. <https://doi.org/10.1021/ct500642x>.
- (107) Řezáč, J.; Riley, K. E.; Hobza, P. Extensions of the S66 Data Set: More Accurate Interaction Energies and Angular-Displaced Nonequilibrium Geometries. *J. Chem. Theory Comput.* **2011**, *7* (11), 3466–3470. <https://doi.org/10.1021/ct200523a>.
 - (108) Almlöf, J. Elimination of Energy Denominators in Møller-Plesset Perturbation Theory by a Laplace Transform Approach. *Chem. Phys. Lett.* **1991**, *181* (4), 319–320. [https://doi.org/10.1016/0009-2614\(91\)80078-C](https://doi.org/10.1016/0009-2614(91)80078-C).
 - (109) Häser, M. Møller-Plesset (MP2) Perturbation Theory for Large Molecules. *Theor. Chim. Acta* **1993**, *87* (1–2), 147–173. <https://doi.org/10.1007/BF01113535>.
 - (110) Häser, M.; Almlöf, J. Laplace Transform Techniques in Møller-Plesset Perturbation Theory. *J. Chem. Phys.* **1992**, *96* (1), 489–494. <https://doi.org/10.1063/1.462485>.
 - (111) Song, C.; Martínez, T. J. Atomic Orbital-Based SOS-MP2 with Tensor Hypercontraction. I. GPU-Based Tensor Construction and Exploiting Sparsity. *J. Chem. Phys.* **2016**, *144* (17), 174111. <https://doi.org/10.1063/1.4948438>.
 - (112) Miehlich, B.; Savin, A.; Stoll, H.; Preuss, H. Results Obtained with the Correlation Energy Density Functionals of Becke and Lee, Yang and Parr. *Chem. Phys. Lett.* **1989**, *157* (3), 200–206. [https://doi.org/10.1016/0009-2614\(89\)87234-3](https://doi.org/10.1016/0009-2614(89)87234-3).
 - (113) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; et al. Gaussian 16 Rev. B01. Gaussian, Inc.: Wallingford, CT 2016.
 - (114) Neese, F. The ORCA Program System. *Wiley Interdiscip. Rev. Comput. Mol. Sci.* **2012**, *2* (1), 73–78. <https://doi.org/10.1002/wcms.81>.
 - (115) Neese, F. Software Update: The ORCA Program System, Version 4.0. *Wiley Interdiscip. Rev. Comput. Mol. Sci.* **2018**, *8* (1), 4–9. <https://doi.org/10.1002/wcms.1327>.
 - (116) Ghasemi, S. A.; Hofstetter, A.; Saha, S.; Goedecker, S. Interatomic Potentials for Ionic Systems with Density Functional Accuracy Based on Charge Densities Obtained by a Neural Network. *Phys. Rev. B - Condens. Matter Mater. Phys.* **2015**, *92* (4), 1–6. <https://doi.org/10.1103/PhysRevB.92.045131>.
 - (117) Rappé, A. K.; Goddard, W. A. Charge Equilibration for Molecular Dynamics Simulations. *J. Phys. Chem.* **1991**, *95* (8), 3358–3363. <https://doi.org/10.1021/j100161a070>.
 - (118) Verstraelen, T.; Van Speybroeck, V.; Waroquier, M. The Electronegativity Equalization Method and the Split Charge Equilibration Applied to Organic Systems: Parametrization, Validation, and Comparison. *J. Chem. Phys.* **2009**, *131* (4), 044127. <https://doi.org/10.1063/1.3187034>.
 - (119) Korth, M.; Grimme, S. “Mindless” DFT Benchmarking. *J. Chem. Theory Comput.* **2009**, *5* (4), 993–1003. <https://doi.org/10.1021/ct800511q>.
 - (120) Iron, M. A.; Janes, T. Evaluating Transition Metal Barrier Heights with the Latest Density Functional Theory Exchange–Correlation Functionals: The MOBH35 Benchmark Database. *J. Phys. Chem. A* **2019**, *123* (17), 3761–3781. <https://doi.org/10.1021/acs.jpca.9b01546>.
 - (121) Dohm, S.; Hansen, A.; Steinmetz, M.; Grimme, S.; Checinski, M. P. Comprehensive Thermochemical Benchmark Set of Realistic Closed-Shell Metal Organic Reactions. *J. Chem. Theory Comput.* **2018**, *14* (5), 2596–2608. <https://doi.org/10.1021/acs.jctc.7b01183>.
 - (122) Goerigk, L.; Grimme, S. Efficient and Accurate Double-Hybrid-Meta-GGA Density Functionals—Evaluation with the Extended GMTKN30 Database for General Main

- Group Thermochemistry, Kinetics, and Noncovalent Interactions. *J. Chem. Theory Comput.* **2011**, 7 (2), 291–309. <https://doi.org/10.1021/ct100466k>.
- (123) Mezei, P. D.; Csonka, G. I.; Ruzsinszky, A.; Kállay, M. Construction and Application of a New Dual-Hybrid Random Phase Approximation. *J. Chem. Theory Comput.* **2015**, 11 (10), 4615–4626. <https://doi.org/10.1021/acs.jctc.5b00420>.
- (124) Mezei, P. D.; Csonka, G. I.; Ruzsinszky, A.; Kállay, M. Construction of a Spin-Component Scaled Dual-Hybrid Random Phase Approximation. *J. Chem. Theory Comput.* **2017**, 13 (2), 796–803. <https://doi.org/10.1021/acs.jctc.6b01140>.
- (125) Chan, B.; Goerigk, L.; Radom, L. On the Inclusion of Post-MP2 Contributions to Double-Hybrid Density Functionals. *J. Comput. Chem.* **2016**, 37 (2), 183–193. <https://doi.org/10.1002/jcc.23972>.
- (126) Kesharwani, M. K.; Brauer, B.; Martin, J. M. L. Frequency and Zero-Point Vibrational Energy Scale Factors for Double-Hybrid Density Functionals (and Other Selected Methods): Can Anharmonic Force Fields Be Avoided? *J. Phys. Chem. A* **2015**, 119, 1701–1714. <https://doi.org/10.1021/jp508422u>.
- (127) Efremenko, I.; Martin, J. M. L. Coupled Cluster Benchmark of New Density Functionals and Domain Pair Natural Orbital Methods: Mechanisms of Hydroarylation and Oxidative Coupling Catalyzed by Ru(II) Chloride Carbonyls. **2019**.
- (128) Weissman, H.; Song, X.; Milstein, D. Ru-Catalyzed Oxidative Coupling of Arenes with Olefins Using O₂. *J. Am. Chem. Soc.* **2001**, 123 (2), 337–338. <https://doi.org/10.1021/ja003361n>.
- (129) Perdew, J. P. Density-Functional Approximation for the Correlation Energy of the Inhomogeneous Electron Gas. *Phys. Rev. B* **1986**, 33 (12), 8822–8824. <https://doi.org/10.1103/PhysRevB.33.8822>.
- (130) Lee, C.; Yang, W.; Parr, R. G. Development of the Colle-Salvetti Correlation-Energy Formula into a Functional of the Electron Density. *Phys. Rev. B* **1988**, 37 (2), 785–789. <https://doi.org/10.1103/PhysRevB.37.785>.

Table of Contents Graphic

revDSD-PBEP86-D4 revision resubmission.pdf (762.64 KiB)

[view on ChemRxiv](#) • [download file](#)

Electronic Supporting Information

Minimally Empirical Double Hybrid Functionals Trained Against the GMTKN55 Database: revDSD-PBEP86-D4, revDOD-PBE-D4, and DOD-SCAN-D4

Golokesh Santra, Nitai Sylvetsky, and Jan M.L. Martin

Department of Organic Chemistry, Weizmann Institute of Science, 7610001 Rehovot, Israel.

Email: gershom@weizmann.ac.il

Table S1: Abbreviations used and their descriptions

Abbreviation	Description
ACONF ¹	Relative energies of alkane conformers
ADIM6 ²	Interaction energies of n-alkane dimers
AHB21 ³	Interaction energies in anion–neutral dimers
AL2X6 ⁴	Dimerisation energies of AlX ₃ compounds
ALK ⁸⁴	Dissociation and other reactions of alkaline compounds
ALKBDE10 ⁵	Dissociation energies in group-1 and -2 diatomics
AMINO20X4 ⁶	Relative energies in amino acid conformers
BH76RC ⁷	Barrier heights of hydrogen transfer, heavy atom transfer, nucleophilic substitution, unimolecular and association reactions
BH76 ^{8,9,7}	Reaction energies of the BH7610,11,23 set
BHDIV10 ⁴	Diverse reaction barrier heights
BHPERI ^{4,10,11,12}	Barrier heights of pericyclic reactions
BHROT27 ⁴	Barrier heights for rotation around single bonds
BSR36 ^{13,14}	Bond-separation reactions of saturated hydrocarbons
BUT14DIOL ¹⁵	Relative energies in butane-1,4-diol conformers
C60ISO ¹⁶	Relative energies between C60 isomers
CARBHB12 ⁴	Hydrogen-bonded complexes between carbene analogues and H ₂ O, NH ₃ , or HCl
CDIE20 ¹⁷	Double-bond isomerisation energies in cyclic systems
CHB6 ³	Interaction energies in cation–neutral dimers
DARC ^{7,18}	Reaction energies of Diels–Alder reactions
DC13 ^{19,7,20,21–29}	13 difficult cases for DFT methods
DIPCS10 ⁴	Double-ionisation potentials of closed-shell systems
FH51 ^{30,31}	Reaction energies in various (in-)organic systems
G21EA ^{7,32}	Adiabatic electron affinities
G21IP ^{7,32}	Adiabatic ionisation potentials
G2RC ^{7,33}	Reaction energies of selected G2/97 systems
HAL59 ^{34,35}	Binding energies in halogenated dimers (incl. halogen bonds)
HEAVY28 ⁹	Noncovalent interaction energies between heavy element hydrides
HEAVYSB11 ⁴	Dissociation energies in heavy-element compounds
ICONF ⁴	Relative energies in conformers of inorganic systems
IDISP ^{7,36–39}	Intramolecular dispersion interactions
IL16 ³	Interaction energies in anion–cation dimers
INV24 ⁴⁰	Inversion/racemisation barrier heights
ISO34 ³⁶	Isomerisation energies of small and medium-sized organic molecules
ISOL24 ⁴¹	Isomerisation energies of large organic molecules
MB16-43 ⁴	Decomposition energies of artificial molecules
MCONF ⁴²	Relative energies in melatonin conformers
NBPRC ^{7,38,43}	Oligomerisations and H ₂ fragmentations of NH ₃ /BH ₃ systems; H ₂ activation reactions with PH ₃ /BH ₃ systems
PA26 ⁴	Adiabatic proton affinities (incl. of amino acids)
PArel ⁴	Relative energies in protonated isomers
PCONF21	Relative energies in tri- and tetrapeptide conformers
PNICO23 ⁴⁴	Interaction energies in pnictogen-containing dimers
PX13 ⁴⁵	Proton-exchange barriers in H ₂ O, NH ₃ , and HF clusters
RC21 ⁴	Fragmentations and rearrangements in radical cations
RG18 ⁴	Interaction energies in rare-gas complexes
RSE43 ⁴⁶	Radical-stabilisation energies
S22 ⁴⁷	Binding energies of noncovalently bound dimers
S66 ⁴⁸	Binding energies of noncovalently bound dimers
SCONF ^{7,49}	Relative energies of sugar conformers
SIE4X ⁵⁰	Self-interaction-error related problems
TAUT15 ⁴	Relative energies in tautomers
UPU23 ⁵¹	Relative energies between RNA-backbone conformers
W4-11 ⁵²	Total atomisation energies

WATER27 ⁵³	Binding energies in (H ₂ O) _n , H ⁺ (H ₂ O) _n and OH ⁻ (H ₂ O) _n
WCPT18 ⁵⁴	Proton-transfer barriers in uncatalysed and water-catalysed reactions
YBDE18 ⁵⁵	Bond-dissociation energies in ylides

Table S2: A breakdown by components of DSD-SCAN₅₀-D3(BJ) taking $C_{x, HF} = 8^{-1/3} = 0.5$

Serial No.	Type	Set Name	No. of Points	MAD	MSD	RSMD	$ \Delta E_{ref} $	$\Delta WTMAD2$	5MAD/4RMSD
1	Conformer	ACONF	15	0.109	0.109	0.127	1.833	0.034	1.081
2	Intermol	ADIM6	6	0.583	-0.583	0.629	3.358	0.040	1.158
3	Intermol	AHB21	21	0.347	-0.290	0.497	22.486	0.012	0.874
4	Thermo	AL2X6	6	0.620	0.620	0.659	35.883	0.004	1.176
5	Thermo	ALK8	8	1.466	1.371	2.209	62.601	0.007	0.829
6	Thermo	ALKBDE10	10	3.596	-2.447	4.258	100.690	0.014	1.056
7	Conformer	AMINO20X4	80	0.128	-0.013	0.160	2.439	0.159	0.997
8	Barrier	BH76RC	30	1.698	-0.110	2.109	21.392	0.090	1.007
9	Thermo	BH76	76	1.956	-1.671	2.346	18.614	0.303	1.042
10	Barrier	BHDIV10	10	1.859	-1.437	2.068	45.333	0.016	1.124
11	Barrier	BHPERI	26	1.595	-1.533	1.724	20.873	0.075	1.156
12	Barrier	BHROT27	27	0.320	0.314	0.427	6.273	0.052	0.935
13	REACLarge	BSR36	36	1.288	-1.288	1.395	16.197	0.109	1.154
14	Conformer	BUT14DIOL	64	0.045	-0.036	0.051	2.800	0.039	1.105
15	REACLarge	C60ISO	9	6.204	-6.100	8.289	98.252	0.022	0.936
16	Intermol	CARBHB12	12	0.404	0.391	0.606	6.036	0.030	0.833
17	REACLarge	CDIE20	20	0.564	0.564	0.632	4.055	0.106	1.115
18	Intermol	CHB6	6	0.822	-0.822	1.008	26.785	0.007	1.019
19	REACLarge	DARC	14	0.780	-0.348	0.975	32.471	0.013	1.001
20	Thermo	DC13	13	2.505	0.465	3.806	54.978	0.023	0.823
21	Thermo	DIPCS10	10	5.008	-5.008	5.666	654.260	0.003	1.105
22	Thermo	FH51	51	1.048	-0.150	1.479	31.011	0.065	0.886
23	Thermo	G21EA	25	3.372	-3.091	3.875	33.624	0.095	1.088
24	Thermo	G21IP	36	2.815	-1.584	3.498	257.610	0.015	1.006
25	Thermo	G2RC	25	2.671	0.166	3.374	51.263	0.049	0.990
26	Intermol	HAL59	59	0.353	0.237	0.544	4.592	0.172	0.812
27	Intermol	HEAVY28	28	0.121	-0.052	0.150	1.241	0.103	1.008
28	Thermo	HEAVYSB11	11	1.628	-1.623	2.045	58.023	0.012	0.995
29	Conformer	ICONF	17	0.106	0.036	0.132	3.266	0.021	1.005
30	Conformer	IDISP	6	1.007	0.658	1.177	14.223	0.016	1.069
31	Intermol	IL16	16	0.402	0.402	0.451	109.045	0.002	1.114
32	Barrier	INV24	24	0.654	0.180	1.027	31.846	0.019	0.797
33	REACLarge	ISO34	34	0.574	-0.196	0.782	14.570	0.051	0.917
34	REACLarge	ISOL24	24	1.504	-0.289	2.145	21.919	0.063	0.877
35	REACLarge	MB16-43	43	5.510	-2.022	7.354	468.394	0.019	0.937
36	Conformer	MCONF	51	0.238	0.187	0.285	4.971	0.093	1.046
37	Thermo	NBPRC	6	0.888	-0.734	1.053	24.683	0.008	1.055
38	Thermo	PA26	26	2.527	2.527	2.998	189.054	0.013	1.054
39	REACLarge	PAREL	20	0.636	0.239	1.058	4.630	0.104	0.751
40	Conformer	PCONF21	18	0.217	0.113	0.277	1.622	0.091	0.979
41	Intermol	PNICO23	23	0.270	0.237	0.443	4.273	0.055	0.762
42	Barrier	PX13	13	2.498	-2.498	2.584	33.362	0.037	1.209
43	Thermo	RC21	21	0.908	0.134	1.191	35.699	0.020	0.953
44	Intermol	RG18	18	0.068	-0.028	0.096	0.580	0.080	0.889
45	REACLarge	RSE43	43	0.600	0.545	0.981	7.602	0.129	0.764

46	Intermol	S22	22	0.207	-0.035	0.280	7.302	0.024	0.927
47	Intermol	S66	66	0.194	-0.082	0.256	5.467	0.089	0.947
48	Conformer	SCONF	17	0.044	0.001	0.066	4.600	0.006	0.824
49	Thermo	SIE4X4	16	7.141	7.141	8.362	33.725	0.129	1.067
50	Thermo	TAUT15	15	0.825	-0.263	0.922	3.046	0.154	1.118
51	Conformer	UPU23	23	0.351	0.144	0.469	5.723	0.054	0.936
52	Thermo	W4-11	140	5.694	-5.654	6.468	306.914	0.099	1.100
53	Intermol	WATER27	27	0.561	0.412	0.678	81.174	0.007	1.033
54	Barrier	WCPT18	18	1.694	-1.694	2.059	34.988	0.033	1.028
55	Thermo	YBDE18	18	1.573	-1.136	1.927	49.276	0.022	1.021

Note: 5MAD/4RMSD should be ≈ 1 for an unbiased normal distribution^{56,57}. The $|\overline{\Delta E_{\text{ref}}}|$ Column has been omitted in subsequent tables.

Table S3: A breakdown by components of DSD-SCAN₅₅-D3(BJ) taking $C_{x,\text{HF}}=6^{-1/3}\approx 0.5503...$

Serial No.	Type	Set Name	No. of Points	MAD	MSD	RSMD	ΔWTMAD2	5MAD/4RMSD
1	Conformer	ACONF	15	0.097	0.097	0.113	0.030	1.066
2	Intermol	ADIM6	6	0.591	-0.591	0.636	0.040	1.161
3	Intermol	AHB21	21	0.334	-0.263	0.470	0.012	0.888
4	Thermo	AL2X6	6	0.498	0.498	0.543	0.003	1.146
5	Thermo	ALK8	8	1.259	1.150	1.937	0.006	0.812
6	Thermo	ALKBDE10	10	3.102	-1.707	3.746	0.012	1.035
7	Conformer	AMINO20X4	80	0.123	-0.018	0.154	0.153	0.997
8	Barrier	BH76RC	30	1.606	-0.150	1.990	0.085	1.009
9	Thermo	BH76	76	1.714	-1.201	2.146	0.265	0.998
10	Barrier	BHDIV10	10	1.610	-1.256	1.824	0.014	1.104
11	Barrier	BHPERI	26	1.520	-1.444	1.647	0.072	1.154
12	Barrier	BHROT27	27	0.275	0.269	0.365	0.045	0.941
13	REACLarge	BSR36	36	1.193	-1.193	1.275	0.101	1.170
14	Conformer	BUT14DIOL	64	0.050	-0.045	0.055	0.044	1.138
15	REACLarge	C60ISO	9	6.549	-6.468	8.693	0.023	0.942
16	Intermol	CARBHB12	12	0.376	0.362	0.560	0.028	0.840
17	REACLarge	CDIE20	20	0.503	0.503	0.566	0.094	1.112
18	Intermol	CHB6	6	0.864	-0.864	1.051	0.007	1.028
19	REACLarge	DARC	14	0.893	-0.704	1.070	0.015	1.044
20	Thermo	DC13	13	2.219	0.214	3.536	0.020	0.784
21	Thermo	DIPCS10	10	4.136	-4.136	4.825	0.002	1.071
22	Thermo	FH51	51	0.972	-0.193	1.341	0.061	0.906
23	Thermo	G21EA	25	2.978	-2.610	3.425	0.084	1.087
24	Thermo	G21IP	36	2.418	-1.091	3.100	0.013	0.975
25	Thermo	G2RC	25	2.445	0.123	3.085	0.045	0.991
26	Intermol	HAL59	59	0.323	0.203	0.489	0.157	0.826
27	Intermol	HEAVY28	28	0.110	-0.044	0.137	0.094	1.003
28	Thermo	HEAVYSB11	11	1.221	-1.081	1.582	0.009	0.965
29	Conformer	ICONF	17	0.093	0.024	0.121	0.018	0.964
30	Conformer	IDISP	6	0.785	0.473	0.865	0.013	1.135
31	Intermol	IL16	16	0.395	0.395	0.437	0.002	1.131
32	Barrier	INV24	24	0.642	0.192	1.031	0.018	0.779
33	REACLarge	ISO34	34	0.539	-0.200	0.690	0.048	0.977
34	REACLarge	ISOL24	24	1.241	-0.171	1.768	0.052	0.878
35	REACLarge	MB16-43	43	4.992	-1.162	6.603	0.017	0.945
36	Conformer	MCONF	51	0.245	0.196	0.288	0.095	1.066
37	Thermo	NBPRC	6	0.831	-0.674	0.980	0.008	1.060
38	Thermo	PA26	26	2.370	2.370	2.782	0.012	1.065
39	REACLarge	PAREL	20	0.606	0.202	0.977	0.099	0.776

40	Conformer	PCONF21	18	0.215	0.110	0.275	0.091	0.978
41	Intermol	PNICO23	23	0.232	0.192	0.382	0.047	0.760
42	Barrier	PX13	13	2.361	-2.361	2.452	0.035	1.204
43	Thermo	RC21	21	0.990	-0.209	1.235	0.022	1.002
44	Intermol	RG18	18	0.066	-0.037	0.099	0.078	0.836
45	REACLarge	RSE43	43	0.757	0.727	1.317	0.162	0.718
46	Intermol	S22	22	0.212	-0.042	0.282	0.024	0.938
47	Intermol	S66	66	0.192	-0.095	0.254	0.088	0.943
48	Conformer	SCONF	17	0.039	0.000	0.059	0.006	0.827
49	Thermo	SIE4X4	16	6.324	6.324	7.433	0.114	1.064
50	Thermo	TAUT15	15	0.760	-0.288	0.864	0.142	1.099
51	Conformer	UPU23	23	0.354	0.153	0.472	0.054	0.937
52	Thermo	W4-11	140	3.663	-3.401	4.437	0.063	1.032
53	Intermol	WATER27	27	0.435	0.191	0.572	0.006	0.951
54	Barrier	WCPT18	18	1.536	-1.536	1.866	0.030	1.029
55	Thermo	YBDE18	18	1.124	-0.299	1.456	0.016	0.965

Table S4: A breakdown by components of DSD-SCAN₅₈-D3(BJ) taking $C_{x, HF} = 5^{-1/3} \approx 0.5848...$

Serial No.	Type	Set Name	No. of Points	MAD	MSD	RSMD	Δ WTMAD2	5MAD/4RMSD
1	Conformer	ACONF	15	0.087	0.087	0.104	0.027	1.045
2	Intermol	ADIM6	6	0.591	-0.591	0.636	0.040	1.161
3	Intermol	AHB21	21	0.329	-0.253	0.457	0.012	0.900
4	Thermo	AL2X6	6	0.499	0.499	0.547	0.003	1.142
5	Thermo	ALK8	8	1.227	1.101	1.821	0.006	0.843
6	Thermo	ALKBDE10	10	2.922	-1.526	3.498	0.011	1.044
7	Conformer	AMINO20X4	80	0.121	-0.020	0.152	0.150	0.991
8	Barrier	BH76RC	30	1.547	-0.184	1.912	0.082	1.011
9	Thermo	BH76	76	1.544	-0.819	2.068	0.239	0.933
10	Barrier	BHDIV10	10	1.427	-1.079	1.610	0.012	1.108
11	Barrier	BHPERI	26	1.425	-1.336	1.562	0.067	1.140
12	Barrier	BHROT27	27	0.254	0.248	0.334	0.041	0.949
13	REACLarge	BSR36	36	1.115	-1.115	1.181	0.094	1.179
14	Conformer	BUT14DIOL	64	0.056	-0.053	0.061	0.049	1.157
15	REACLarge	C60ISO	9	6.456	-6.367	8.601	0.022	0.938
16	Intermol	CARBHB12	12	0.358	0.344	0.528	0.027	0.848
17	REACLarge	CDIE20	20	0.455	0.455	0.517	0.085	1.100
18	Intermol	CHB6	6	0.918	-0.918	1.106	0.008	1.038
19	REACLarge	DARC	14	1.036	-1.030	1.267	0.017	1.022
20	Thermo	DC13	13	2.287	-0.011	3.427	0.021	0.834
21	Thermo	DIPCS10	10	3.747	-3.747	4.473	0.002	1.047
22	Thermo	FH51	51	0.927	-0.264	1.266	0.058	0.915
23	Thermo	G21EA	25	2.866	-2.441	3.315	0.081	1.081
24	Thermo	G21IP	36	2.287	-0.868	2.974	0.012	0.961
25	Thermo	G2RC	25	2.296	0.031	2.893	0.043	0.992
26	Intermol	HAL59	59	0.303	0.177	0.453	0.148	0.837
27	Intermol	HEAVY28	28	0.107	-0.043	0.133	0.091	1.005
28	Thermo	HEAVYSB11	11	1.063	-0.789	1.382	0.008	0.962
29	Conformer	ICONF	17	0.092	0.020	0.117	0.018	0.985
30	Conformer	IDISP	6	0.611	0.330	0.746	0.010	1.025
31	Intermol	IL16	16	0.392	0.392	0.432	0.002	1.136
32	Barrier	INV24	24	0.639	0.244	1.067	0.018	0.749
33	REACLarge	ISO34	34	0.514	-0.189	0.635	0.046	1.012
34	REACLarge	ISOL24	24	1.050	-0.048	1.508	0.044	0.870
35	REACLarge	MB16-43	43	4.826	-0.392	6.347	0.017	0.950
36	Conformer	MCONF	51	0.247	0.200	0.287	0.096	1.078
37	Thermo	NBPRC	6	0.806	-0.658	0.947	0.007	1.065
38	Thermo	PA26	26	2.306	2.306	2.682	0.012	1.075
39	REACLarge	PAREL	20	0.575	0.186	0.911	0.094	0.789

40	Conformer	PCONF21	18	0.212	0.111	0.273	0.089	0.971
41	Intermol	PNICO23	23	0.216	0.170	0.350	0.044	0.771
42	Barrier	PX13	13	2.166	-2.166	2.262	0.032	1.197
43	Thermo	RC21	21	1.127	-0.430	1.351	0.025	1.043
44	Intermol	RG18	18	0.069	-0.043	0.104	0.082	0.834
45	REACLarge	RSE43	43	0.885	0.866	1.558	0.190	0.710
46	Intermol	S22	22	0.211	-0.043	0.280	0.024	0.939
47	Intermol	S66	66	0.190	-0.098	0.252	0.087	0.942
48	Conformer	SCONF	17	0.035	-0.001	0.052	0.005	0.840
49	Thermo	SIE4X4	16	5.678	5.678	6.712	0.102	1.057
50	Thermo	TAUT15	15	0.708	-0.300	0.820	0.132	1.079
51	Conformer	UPU23	23	0.360	0.166	0.478	0.055	0.943
52	Thermo	W4-11	140	3.042	-2.551	3.946	0.053	0.964
53	Intermol	WATER27	27	0.422	0.070	0.576	0.005	0.916
54	Barrier	WCPT18	18	1.338	-1.338	1.670	0.026	1.002
55	Thermo	YBDE18	18	1.017	0.180	1.360	0.014	0.935

Table S5: A breakdown by components of DSD-SCAN₆₃-D3(BJ) taking $C_{x,HF} = 4^{-1/3} \approx 0.6300...$

Serial No.	Type	Set Name	No. of Points	MAD	MSD	RSMD	Δ WTMAD2	5MAD/4RMSD
1	Conformer	ACONF	15	0.080	0.080	0.097	0.025	1.025
2	Intermol	ADIM6	6	0.583	-0.583	0.626	0.040	1.164
3	Intermol	AHB21	21	0.320	-0.229	0.437	0.011	0.916
4	Thermo	AL2X6	6	0.374	0.374	0.430	0.002	1.086
5	Thermo	ALK8	8	1.130	0.908	1.562	0.006	0.904
6	Thermo	ALKBDE10	10	2.734	-1.329	3.231	0.010	1.058
7	Conformer	AMINO20X4	80	0.121	-0.025	0.154	0.151	0.982
8	Barrier	BH76RC	30	1.452	-0.221	1.803	0.077	1.007
9	Thermo	BH76	76	1.431	-0.303	2.113	0.222	0.847
10	Barrier	BHDIV10	10	1.182	-0.829	1.333	0.010	1.109
11	Barrier	BHPERI	26	1.290	-1.185	1.442	0.061	1.119
12	Barrier	BHROT27	27	0.226	0.221	0.296	0.037	0.956
13	REACLarge	BSR36	36	1.012	-1.012	1.057	0.085	1.196
14	Conformer	BUT14DIOL	64	0.065	-0.064	0.071	0.057	1.159
15	REACLarge	C60ISO	9	6.459	-6.364	8.630	0.022	0.936
16	Intermol	CARBHB12	12	0.331	0.315	0.484	0.025	0.855
17	REACLarge	CDIE20	20	0.408	0.408	0.470	0.076	1.087
18	Intermol	CHB6	6	0.965	-0.965	1.154	0.008	1.046
19	REACLarge	DARC	14	1.313	-1.313	1.470	0.022	1.116
20	Thermo	DC13	13	2.377	-0.190	3.356	0.021	0.885
21	Thermo	DIPCS10	10	3.367	-3.367	4.154	0.002	1.013
22	Thermo	FH51	51	0.863	-0.337	1.169	0.054	0.923
23	Thermo	G21EA	25	2.780	-2.258	3.249	0.078	1.070
24	Thermo	G21IP	36	2.154	-0.631	2.906	0.011	0.927
25	Thermo	G2RC	25	2.073	-0.081	2.608	0.038	0.994
26	Intermol	HAL59	59	0.279	0.144	0.405	0.136	0.862
27	Intermol	HEAVY28	28	0.097	-0.035	0.122	0.083	0.995
28	Thermo	HEAVYSB11	11	0.957	-0.517	1.237	0.007	0.968
29	Conformer	ICONF	17	0.092	0.013	0.116	0.018	0.985
30	Conformer	IDISP	6	0.662	0.170	0.815	0.011	1.014
31	Intermol	IL16	16	0.411	0.411	0.445	0.002	1.153
32	Barrier	INV24	24	0.652	0.291	1.115	0.019	0.730
33	REACLarge	ISO34	34	0.487	-0.173	0.590	0.043	1.032
34	REACLarge	ISOL24	24	0.868	0.066	1.257	0.036	0.863
35	REACLarge	MB16-43	43	4.792	0.111	6.190	0.017	0.968

36	Conformer	MCONF	51	0.258	0.211	0.293	0.100	1.101
37	Thermo	NBPRC	6	0.735	-0.594	0.860	0.007	1.068
38	Thermo	PA26	26	2.184	2.184	2.521	0.011	1.083
39	REACLarge	PAREL	20	0.534	0.170	0.832	0.087	0.802
40	Conformer	PCONF21	18	0.214	0.116	0.277	0.090	0.964
41	Intermol	PNICO23	23	0.179	0.130	0.289	0.037	0.775
42	Barrier	PX13	13	1.900	-1.900	2.006	0.028	1.184
43	Thermo	RC21	21	1.347	-0.794	1.619	0.030	1.040
44	Intermol	RG18	18	0.073	-0.050	0.106	0.086	0.862
45	REACLarge	RSE43	43	1.054	1.048	1.884	0.226	0.699
46	Intermol	S22	22	0.214	-0.039	0.285	0.024	0.940
47	Intermol	S66	66	0.186	-0.101	0.247	0.085	0.943
48	Conformer	SCONF	17	0.037	-0.010	0.044	0.005	1.050
49	Thermo	SIE4X4	16	4.831	4.831	5.769	0.087	1.047
50	Thermo	TAUT15	15	0.636	-0.307	0.761	0.119	1.045
51	Conformer	UPU23	23	0.370	0.172	0.486	0.056	0.951
52	Thermo	W4-11	140	2.624	-1.679	3.670	0.045	0.894
53	Intermol	WATER27	27	0.520	-0.182	0.752	0.007	0.865
54	Barrier	WCPT18	18	1.095	-1.079	1.412	0.021	0.969
55	Thermo	YBDE18	18	1.035	0.676	1.449	0.014	0.893

Table S6: A breakdown by components of DSD-SCAN₆₆-D3(BJ) taking $C_{x, \text{HF}} = 3.5^{-1/3} \approx 0.6586...$

Serial No.	Type	Set Name	No. of Points	MAD	MSD	RSMD	Δ WTMAD2	5MAD/4RMSD
1	Conformer	ACONF	15	0.083	0.083	0.101	0.026	1.024
2	Intermol	ADIM6	6	0.594	-0.594	0.636	0.040	1.167
3	Intermol	AHB21	21	0.322	-0.221	0.437	0.011	0.921
4	Thermo	AL2X6	6	0.191	0.174	0.256	0.001	0.933
5	Thermo	ALK8	8	0.990	0.643	1.288	0.005	0.961
6	Thermo	ALKBDE10	10	2.677	-1.202	3.147	0.010	1.063
7	Conformer	AMINO20X4	80	0.122	-0.027	0.155	0.152	0.982
8	Barrier	BH76RC	30	1.372	-0.231	1.688	0.073	1.016
9	Thermo	BH76	76	1.418	0.020	2.214	0.220	0.801
10	Barrier	BHDIV10	10	1.093	-0.711	1.231	0.009	1.110
11	Barrier	BHPERI	26	1.350	-1.243	1.495	0.064	1.129
12	Barrier	BHROT27	27	0.217	0.213	0.284	0.036	0.957
13	REACLarge	BSR36	36	0.871	-0.871	0.899	0.073	1.211
14	Conformer	BUT14DIOL	64	0.068	-0.066	0.074	0.059	1.146
15	REACLarge	C60ISO	9	6.759	-6.670	9.024	0.024	0.936
16	Intermol	CARBHB12	12	0.321	0.302	0.468	0.024	0.857
17	REACLarge	CDIE20	20	0.408	0.408	0.464	0.076	1.098
18	Intermol	CHB6	6	0.962	-0.962	1.150	0.008	1.046
19	REACLarge	DARC	14	1.399	-1.399	1.546	0.023	1.132
20	Thermo	DC13	13	2.488	-0.119	3.384	0.022	0.919
21	Thermo	DIPCS10	10	3.359	-3.359	4.186	0.002	1.003
22	Thermo	FH51	51	0.814	-0.395	1.101	0.051	0.925
23	Thermo	G21EA	25	2.762	-2.211	3.251	0.078	1.062
24	Thermo	G21IP	36	2.112	-0.591	2.912	0.011	0.906
25	Thermo	G2RC	25	1.909	-0.181	2.409	0.035	0.991
26	Intermol	HAL59	59	0.266	0.123	0.381	0.130	0.874
27	Intermol	HEAVY28	28	0.089	-0.032	0.112	0.076	0.992
28	Thermo	HEAVYSB11	11	0.949	-0.468	1.197	0.007	0.992
29	Conformer	ICONF	17	0.094	0.014	0.119	0.019	0.986
30	Conformer	IDISP	6	0.755	0.078	0.949	0.012	0.994
31	Intermol	IL16	16	0.429	0.429	0.459	0.002	1.169
32	Barrier	INV24	24	0.672	0.287	1.133	0.019	0.741
33	REACLarge	ISO34	34	0.486	-0.143	0.577	0.043	1.053
34	REACLarge	ISOL24	24	0.832	0.131	1.191	0.035	0.873

35	REACLarge	MB16-43	43	4.564	0.600	5.951	0.016	0.959
36	Conformer	MCONF	51	0.268	0.220	0.301	0.104	1.112
37	Thermo	NBPRC	6	0.665	-0.517	0.777	0.006	1.069
38	Thermo	PA26	26	1.996	1.996	2.322	0.010	1.074
39	REACLarge	PAREL	20	0.519	0.173	0.795	0.085	0.816
40	Conformer	PCONF21	18	0.212	0.121	0.275	0.089	0.967
41	Intermol	PNICO23	23	0.151	0.096	0.246	0.031	0.764
42	Barrier	PX13	13	1.788	-1.788	1.900	0.026	1.176
43	Thermo	RC21	21	1.561	-1.080	1.889	0.035	1.033
44	Intermol	RG18	18	0.077	-0.056	0.109	0.091	0.882
45	REACLarge	RSE43	43	1.154	1.151	2.086	0.248	0.692
46	Intermol	S22	22	0.217	-0.037	0.289	0.025	0.941
47	Intermol	S66	66	0.189	-0.107	0.250	0.086	0.943
48	Conformer	SCONF	17	0.037	-0.008	0.043	0.005	1.065
49	Thermo	SIE4X4	16	4.273	4.273	5.122	0.077	1.043
50	Thermo	TAUT15	15	0.586	-0.273	0.696	0.109	1.053
51	Conformer	UPU23	23	0.372	0.168	0.488	0.057	0.953
52	Thermo	W4-11	140	2.489	-1.550	3.554	0.043	0.876
53	Intermol	WATER27	27	0.639	-0.362	0.954	0.008	0.837
54	Barrier	WCPT18	18	1.034	-1.003	1.323	0.020	0.978
55	Thermo	YBDE18	18	1.162	0.882	1.599	0.016	0.908

Table S7: A breakdown by components of DSD-SCAN₆₉-D3(BJ) taking $C_{x,HF} = 3^{-1/3} \approx 0.69336...$

Serial No.	Type	Set Name	No. of Points	MAD	MSD	RSMD	Δ WTMAD2	5MAD/4RMSD
1	Conformer	ACONF	15	0.073	0.073	0.093	0.023	0.984
2	Intermol	ADIM6	6	0.590	-0.590	0.632	0.040	1.167
3	Intermol	AHB21	21	0.322	-0.223	0.436	0.011	0.922
4	Thermo	AL2X6	6	0.244	0.244	0.328	0.002	0.929
5	Thermo	ALK8	8	0.968	0.656	1.208	0.005	1.002
6	Thermo	ALKBDE10	10	2.586	-1.163	3.015	0.010	1.072
7	Conformer	AMINO20X4	80	0.120	-0.026	0.154	0.150	0.974
8	Barrier	BH76RC	30	1.333	-0.241	1.612	0.071	1.033
9	Thermo	BH76	76	1.462	0.361	2.397	0.226	0.762
10	Barrier	BHDIV10	10	0.974	-0.584	1.110	0.008	1.098
11	Barrier	BHPERI	26	1.381	-1.266	1.547	0.065	1.115
12	Barrier	BHROT27	27	0.209	0.205	0.271	0.034	0.965
13	REACLarge	BSR36	36	0.699	-0.699	0.721	0.059	1.212
14	Conformer	BUT14DIOL	64	0.070	-0.069	0.076	0.061	1.150
15	REACLarge	C60ISO	9	6.703	-6.600	8.996	0.023	0.931
16	Intermol	CARBHB12	12	0.313	0.294	0.452	0.024	0.866
17	REACLarge	CDIE20	20	0.373	0.373	0.428	0.070	1.090
18	Intermol	CHB6	6	1.010	-1.010	1.200	0.009	1.052
19	REACLarge	DARC	14	1.705	-1.705	1.816	0.028	1.173
20	Thermo	DC13	13	2.717	-0.267	3.514	0.024	0.967
21	Thermo	DIPCS10	10	3.373	-3.358	4.214	0.002	1.001
22	Thermo	FH51	51	0.816	-0.480	1.101	0.051	0.927
23	Thermo	G21EA	25	2.805	-2.216	3.324	0.079	1.055
24	Thermo	G21IP	36	2.079	-0.561	2.948	0.011	0.882
25	Thermo	G2RC	25	1.800	-0.278	2.278	0.033	0.988
26	Intermol	HAL59	59	0.258	0.110	0.369	0.126	0.875
27	Intermol	HEAVY28	28	0.090	-0.036	0.112	0.077	1.004
28	Thermo	HEAVYSB11	11	0.954	-0.248	1.142	0.007	1.045
29	Conformer	ICONF	17	0.093	0.017	0.121	0.018	0.965
30	Conformer	IDISP	6	0.798	-0.051	1.147	0.013	0.870
31	Intermol	IL16	16	0.412	0.412	0.442	0.002	1.164

32	Barrier	INV24	23	0.705	0.351	1.190	0.020	0.740
33	REACLarge	ISO34	34	0.471	-0.110	0.565	0.042	1.043
34	REACLarge	ISOL24	24	0.837	0.281	1.131	0.035	0.926
35	REACLarge	MB16-43	43	4.825	1.929	6.351	0.017	0.950
36	Conformer	MCONF	51	0.274	0.228	0.307	0.107	1.116
37	Thermo	NBPRC	6	0.668	-0.520	0.772	0.006	1.082
38	Thermo	PA26	26	1.928	1.928	2.236	0.010	1.078
39	REACLarge	PAREL	20	0.493	0.169	0.743	0.081	0.829
40	Conformer	PCONF21	18	0.214	0.120	0.277	0.090	0.968
41	Intermol	PNICO23	23	0.150	0.086	0.239	0.031	0.784
42	Barrier	PX13	13	1.606	-1.606	1.724	0.024	1.164
43	Thermo	RC21	21	1.793	-1.303	2.145	0.040	1.045
44	Intermol	RG18	18	0.081	-0.061	0.116	0.095	0.872
45	REACLarge	RSE43	43	1.284	1.283	2.314	0.275	0.694
46	Intermol	S22	22	0.217	-0.028	0.285	0.025	0.953
47	Intermol	S66	66	0.186	-0.104	0.247	0.085	0.941
48	Conformer	SCONF	17	0.029	0.001	0.036	0.004	1.007
49	Thermo	SIE4X4	16	3.687	3.687	4.466	0.066	1.032
50	Thermo	TAUT15	15	0.539	-0.262	0.651	0.101	1.034
51	Conformer	UPU23	23	0.378	0.177	0.491	0.058	0.962
52	Thermo	W4-11	140	2.495	-1.397	3.628	0.043	0.860
53	Intermol	WATER27	27	0.652	-0.394	0.989	0.008	0.824
54	Barrier	WCPT18	18	0.926	-0.853	1.197	0.018	0.967
55	Thermo	YBDE18	18	1.350	1.234	1.826	0.019	0.924

Table S8: A breakdown by components of DSD-SCAN₇₄-D3(BJ) taking $C_{\text{X, HF}} = 2.5^{-1/3} \approx 0.7368...$

Serial No.	Type	Set Name	No. of Points	MAD	MSD	RSMD	ΔWTMAD2	5MAD/4RMSD
1	Conformer	ACONF	15	0.070	0.070	0.092	0.022	0.950
2	Intermol	ADIM6	6	0.593	-0.593	0.633	0.040	1.170
3	Intermol	AHB21	21	0.336	-0.242	0.456	0.012	0.921
4	Thermo	AL2X6	6	0.176	0.130	0.254	0.001	0.864
5	Thermo	ALK8	8	0.827	0.455	0.956	0.004	1.082
6	Thermo	ALKBDE10	10	2.491	-1.108	2.866	0.009	1.087
7	Conformer	AMINO20X4	80	0.120	-0.025	0.155	0.150	0.972
8	Barrier	BH76RC	30	1.256	-0.277	1.530	0.067	1.026
9	Thermo	BH76	76	1.648	0.889	2.765	0.255	0.745
10	Barrier	BHDIV10	10	0.834	-0.382	0.956	0.007	1.090
11	Barrier	BHPERI	26	1.431	-1.305	1.620	0.068	1.104
12	Barrier	BHROT27	27	0.202	0.199	0.262	0.033	0.965
13	REACLarge	BSR36	36	0.490	-0.478	0.529	0.041	1.158
14	Conformer	BUT14DIOL	64	0.071	-0.070	0.078	0.062	1.138
15	REACLarge	C60ISO	9	6.736	-6.615	9.106	0.023	0.925
16	Intermol	CARBHB12	12	0.307	0.288	0.438	0.023	0.876
17	REACLarge	CDIE20	20	0.353	0.353	0.408	0.066	1.082
18	Intermol	CHB6	6	1.055	-1.055	1.244	0.009	1.060
19	REACLarge	DARC	14	2.081	-2.081	2.175	0.034	1.196
20	Thermo	DC13	13	3.056	-0.357	3.781	0.027	1.010
21	Thermo	DIPCS10	10	3.371	-3.249	4.228	0.002	0.997
22	Thermo	FH51	51	0.865	-0.632	1.181	0.054	0.916
23	Thermo	G21EA	25	2.814	-2.167	3.407	0.079	1.032
24	Thermo	G21IP	36	2.010	-0.463	3.014	0.011	0.834
25	Thermo	G2RC	25	1.627	-0.519	2.104	0.030	0.967

26	Intermol	HAL59	59	0.243	0.086	0.348	0.118	0.873
27	Intermol	HEAVY28	28	0.083	-0.031	0.104	0.071	0.998
28	Thermo	HEAVYSB11	11	0.966	-0.079	1.117	0.007	1.081
29	Conformer	ICONF	17	0.095	0.022	0.126	0.019	0.941
30	Conformer	IDISP	6	0.963	-0.237	1.491	0.015	0.807
31	Intermol	IL16	16	0.404	0.404	0.433	0.002	1.165
32	Barrier	INV24	24	0.756	0.400	1.256	0.022	0.753
33	REACLarge	ISO34	34	0.468	-0.058	0.598	0.042	0.979
34	REACLarge	ISOL24	24	0.889	0.462	1.183	0.037	0.939
35	REACLarge	MB16-43	43	5.375	3.496	7.249	0.019	0.927
36	Conformer	MCONF	51	0.288	0.242	0.320	0.112	1.123
37	Thermo	NBPRC	6	0.615	-0.482	0.717	0.006	1.073
38	Thermo	PA26	26	1.714	1.714	2.015	0.009	1.063
39	REACLarge	PAREL	20	0.466	0.180	0.679	0.076	0.858
40	Conformer	PCONF21	18	0.215	0.126	0.276	0.090	0.972
41	Intermol	PNICO23	23	0.133	0.057	0.204	0.027	0.814
42	Barrier	PX13	13	1.393	-1.393	1.529	0.021	1.139
43	Thermo	RC21	21	2.261	-1.686	2.607	0.050	1.084
44	Intermol	RG18	18	0.086	-0.069	0.123	0.102	0.879
45	REACLarge	RSE43	43	1.462	1.462	2.648	0.314	0.690
46	Intermol	S22	22	0.221	-0.012	0.283	0.025	0.976
47	Intermol	S66	66	0.184	-0.100	0.245	0.084	0.940
48	Conformer	SCONF	17	0.028	0.009	0.040	0.004	0.866
49	Thermo	SIE4X4	16	2.784	2.775	3.451	0.050	1.008
50	Thermo	TAUT15	15	0.465	-0.214	0.558	0.087	1.043
51	Conformer	UPU23	23	0.385	0.181	0.497	0.059	0.970
52	Thermo	W4-11	140	2.514	-1.248	3.748	0.044	0.838
53	Intermol	WATER27	27	0.727	-0.490	1.126	0.009	0.808
54	Barrier	WCPT18	18	0.820	-0.668	1.047	0.016	0.980
55	Thermo	YBDE18	18	1.690	1.653	2.188	0.023	0.966

**Table S9: A breakdown by components of DSD-SCAN₇₉-D3(BJ) [DSD-SCAN0-2-D3(BJ)]
taking $C_{x, \text{HF}} = 2^{-1/3} \approx 0.7937...$**

Serial No.	Type	Set Name	No. of Points	MAD	MSD	RSMD	ΔWTMAD2	5MAD/4RMSD
1	Conformer	ACONF	15	0.071	0.071	0.095	0.022	0.934
2	Intermol	ADIM6	6	0.612	-0.612	0.652	0.041	1.172
3	Intermol	AHB21	21	0.359	-0.268	0.493	0.013	0.909
4	Thermo	AL2X6	6	0.222	-0.128	0.236	0.001	1.179
5	Thermo	ALK8	8	0.620	0.098	0.738	0.003	1.050
6	Thermo	ALKBDE10	10	2.339	-1.038	2.708	0.009	1.080
7	Conformer	AMINO20X4	80	0.124	-0.025	0.158	0.154	0.978
8	Barrier	BH76RC	30	1.186	-0.342	1.525	0.063	0.972
9	Thermo	BH76	76	1.996	1.550	3.338	0.309	0.748
10	Barrier	BHDIV10	10	0.708	-0.101	0.800	0.006	1.107
11	Barrier	BHPERI	26	1.424	-1.253	1.628	0.067	1.093
12	Barrier	BHROT27	27	0.193	0.191	0.255	0.032	0.947
13	REACLarge	BSR36	36	0.438	-0.298	0.462	0.037	1.184
14	Conformer	BUT14DIOL	64	0.074	-0.071	0.083	0.064	1.109
15	REACLarge	C60ISO	9	6.691	-6.547	9.132	0.023	0.916
16	Intermol	CARBHB12	12	0.297	0.278	0.419	0.022	0.888
17	REACLarge	CDIE20	20	0.337	0.336	0.398	0.063	1.058
18	Intermol	CHB6	6	1.106	-1.106	1.296	0.009	1.067

19	REACLarge	DARC	14	2.497	-2.497	2.582	0.041	1.209
20	Thermo	DC13	13	3.461	-0.468	4.205	0.031	1.029
21	Thermo	DIPCS10	10	3.230	-2.923	4.156	0.002	0.971
22	Thermo	FH51	51	1.024	-0.824	1.394	0.064	0.919
23	Thermo	G21EA	25	2.808	-2.030	3.509	0.079	1.001
24	Thermo	G21IP	36	1.974	-0.248	3.138	0.011	0.786
25	Thermo	G2RC	25	1.569	-0.860	2.014	0.029	0.974
26	Intermol	HAL59	59	0.237	0.048	0.327	0.116	0.907
27	Intermol	HEAVY28	28	0.072	-0.023	0.091	0.062	0.987
28	Thermo	HEAVYSB11	11	0.977	0.063	1.121	0.007	1.089
29	Conformer	ICONF	17	0.102	0.024	0.137	0.020	0.934
30	Conformer	IDISP	6	1.207	-0.459	1.913	0.019	0.788
31	Intermol	IL16	16	0.413	0.413	0.443	0.002	1.165
32	Barrier	INV24	24	0.817	0.438	1.336	0.023	0.764
33	REACLarge	ISO34	34	0.515	-0.005	0.696	0.046	0.925
34	REACLarge	ISOL24	24	0.996	0.646	1.396	0.041	0.892
35	REACLarge	MB16-43	43	6.629	4.879	8.662	0.023	0.957
36	Conformer	MCONF	51	0.297	0.253	0.329	0.116	1.127
37	Thermo	NBPRC	6	0.512	-0.413	0.623	0.005	1.027
38	Thermo	PA26	26	1.454	1.443	1.762	0.008	1.032
39	REACLarge	PAREL	20	0.446	0.199	0.614	0.073	0.909
40	Conformer	PCONF21	18	0.214	0.137	0.268	0.090	0.995
41	Intermol	PNICO23	23	0.106	0.009	0.150	0.022	0.884
42	Barrier	PX13	13	1.176	-1.140	1.315	0.017	1.118
43	Thermo	RC21	21	2.876	-2.198	3.256	0.064	1.104
44	Intermol	RG18	18	0.093	-0.078	0.131	0.110	0.893
45	REACLarge	RSE43	43	1.678	1.678	3.068	0.360	0.684
46	Intermol	S22	22	0.226	-0.004	0.284	0.026	0.992
47	Intermol	S66	66	0.187	-0.107	0.251	0.086	0.932
48	Conformer	SCONF	17	0.038	0.009	0.059	0.005	0.810
49	Thermo	SIE4X4	16	1.807	1.662	2.285	0.033	0.988
50	Thermo	TAUT15	15	0.385	-0.156	0.450	0.072	1.071
51	Conformer	UPU23	23	0.394	0.190	0.506	0.060	0.973
52	Thermo	W4-11	140	2.668	-0.883	4.024	0.046	0.829
53	Intermol	WATER27	27	0.879	-0.657	1.378	0.011	0.797
54	Barrier	WCPT18	18	0.709	-0.413	0.875	0.014	1.014
55	Thermo	YBDE18	18	2.125	2.125	2.626	0.029	1.011

Table S10: WTMAD2 contribution for each of five major subcategories in cases of DSD-SCAN

Type	$C_{x, HF} = n^{-1/3}$							
	n=8	n=6	n=5	n=4	n=3.5	n=3.0	n=2.5	n=2
Intermol	0.622	0.584	0.570	0.543	0.533	0.533	0.523	0.520
Conformer	0.513	0.503	0.499	0.514	0.522	0.523	0.532	0.550
Barrier	0.534	0.479	0.436	0.252	0.247	0.240	0.233	0.222
Thermo	0.821	0.717	0.671	0.764	0.739	0.735	0.749	0.801
REAClarge	0.613	0.610	0.608	0.617	0.622	0.629	0.652	0.707
Total WTMAD2	3.104	2.893	2.785	2.690	2.662	2.660	2.688	2.800

Table S11: Breakdown by Components for WTMAD2 comparison among above three functionals

Type	Set Name	No. of Points	Δ WTMAD2(kcal/mol)				
			B3LYP-D3(BJ)	PBE0-D3(BJ)	ω B97X-V	ω B97M-V	ω B97M(2)
Conformer	ACONF	15	0.024	0.017	0.008	0.021	0.034
Intermol	ADIM6	6	0.012	0.004	0.009	0.007	0.029
Intermol	AHB21	21	0.017	0.048	0.012	0.007	0.009
Thermo	AL2X6	6	0.016	0.009	0.008	0.008	0.009
Thermo	ALK8	8	0.012	0.023	0.004	0.012	0.010
Thermo	ALKBDE10	10	0.016	0.021	0.015	0.014	0.013
Conformer	AMINO20X4	80	0.258	0.345	0.243	0.231	0.099
Barrier	BH76RC	30	0.117	0.131	0.096	0.061	0.055
Thermo	BH76	76	0.849	0.704	0.286	0.258	0.144
Barrier	BHDIV10	10	0.027	0.040	0.007	0.011	0.006
Barrier	BHPERI	26	0.057	0.153	0.099	0.053	0.024
Barrier	BHROT27	27	0.069	0.095	0.049	0.038	0.027
REACLarge	BSR36	36	0.301	0.294	0.184	0.033	0.054
Conformer	BUT14DIOL	64	0.299	0.210	0.052	0.056	0.040
REACLarge	C60ISO	9	0.008	0.009	0.047	0.041	0.008
Intermol	CARBHB12	12	0.072	0.110	0.027	0.014	0.016
REACLarge	CDIE20	20	0.187	0.231	0.115	0.110	0.041
Intermol	CHB6	6	0.012	0.012	0.008	0.008	0.007
REACLarge	DARC	14	0.127	0.061	0.070	0.012	0.025
Thermo	DC13	13	0.094	0.072	0.059	0.049	0.015
Thermo	DIPCS10	10	0.003	0.002	0.002	0.003	0.001
Thermo	FH51	51	0.159	0.173	0.144	0.067	0.041
Thermo	G21EA	25	0.063	0.083	0.073	0.064	0.042
Thermo	G21IP	36	0.020	0.020	0.016	0.015	0.008
Thermo	G2RC	25	0.051	0.125	0.073	0.038	0.025
Intermol	HAL59	59	0.301	0.299	0.150	0.140	0.131
Intermol	HEAVY28	28	0.312	0.261	0.154	0.156	0.087
Thermo	HEAVYSB11	11	0.022	0.010	0.010	0.019	0.006
Conformer	ICONF	17	0.055	0.056	0.050	0.028	0.024
Conformer	IDISP	6	0.057	0.025	0.041	0.026	0.021
Intermol	IL16	16	0.004	0.002	0.005	0.004	0.001
Barrier	INV24	24	0.029	0.033	0.048	0.038	0.027
REACLarge	ISO34	34	0.155	0.126	0.103	0.055	0.034
REACLarge	ISOL24	24	0.237	0.088	0.123	0.068	0.043
REACLarge	MB16-43	43	0.084	0.055	0.115	0.052	0.047
Conformer	MCONF	51	0.087	0.106	0.090	0.152	0.125
Thermo	NBPRC	6	0.007	0.023	0.010	0.005	0.005
Thermo	PA26	26	0.015	0.015	0.014	0.007	0.006
REACLarge	PAREL	20	0.191	0.197	0.104	0.095	0.070
Conformer	PCONF21	18	0.228	0.382	0.128	0.267	0.138

Intermol	PNICO23	23	0.111	0.196	0.037	0.053	0.043
Barrier	PX13	13	0.065	0.097	0.038	0.029	0.008
Thermo	RC21	21	0.059	0.126	0.079	0.039	0.024
Intermol	RG18	18	0.157	0.106	0.082	0.072	0.080
REACLarge	RSE43	43	0.372	0.309	0.207	0.173	0.095
Intermol	S22	22	0.042	0.059	0.026	0.028	0.016
Intermol	S66	66	0.152	0.171	0.056	0.070	0.067
Conformer	SCONF	17	0.043	0.038	0.021	0.030	0.031
Thermo	SIE4X4	16	0.324	0.259	0.206	0.193	0.094
Thermo	TAUT15	15	0.220	0.211	0.134	0.058	0.050
Conformer	UPU23	23	0.097	0.087	0.097	0.084	0.066
Thermo	W4-11	140	0.056	0.061	0.048	0.036	0.024
Intermol	WATER27	27	0.048	0.067	0.012	0.005	0.008
Barrier	WCPT18	18	0.046	0.085	0.034	0.028	0.021
Thermo	YBDE18	18	0.062	0.013	0.028	0.040	0.014
Total WTMA2			6.502	6.551	3.959	3.286	2.186

Table S12: Integration grid convergence

Serial No.	Set Name	Δ WTMA2(kcal/mol)								
		ω B97X-V		ω B97M-V			B3LYP-D3		DSD-SCAN0-2	
		SG2	SG3	SG2	SG3	grid=150,590	SG2	SG3	SG3	grid=150,590
1	ACONF	0.011	0.008	0.023	0.021	0.018	0.027	0.024	0.026	0.022
2	ADIM6	0.008	0.009	0.005	0.007	0.007	0.010	0.012	0.049	0.041
3	AHB21	0.054	0.012	0.047	0.007	0.008	0.018	0.017	0.013	0.013
4	AL2X6	0.008	0.008	0.008	0.008	0.008	0.016	0.016	0.002	0.001
5	ALK8	0.004	0.004	0.012	0.012	0.012	0.012	0.012	0.003	0.003
6	ALKBDE10	0.015	0.015	0.014	0.014	0.014	0.016	0.016	0.009	0.009
7	AMINO20X4	0.250	0.243	0.239	0.231	0.236	0.276	0.258	0.155	0.154
8	BH76RC	0.096	0.096	0.061	0.061	0.061	0.117	0.117	0.063	0.063
9	BH76	0.285	0.286	0.257	0.258	0.258	0.847	0.849	0.311	0.309
10	BHDIV10	0.007	0.007	0.011	0.011	0.011	0.027	0.027	0.006	0.006
11	BHPERI	0.099	0.099	0.054	0.053	0.053	0.055	0.057	0.064	0.067
12	BHROT27	0.049	0.049	0.037	0.038	0.035	0.075	0.069	0.032	0.032
13	BSR36	0.184	0.184	0.025	0.033	0.043	0.291	0.301	0.044	0.037
14	BUT14DIOL	0.054	0.052	0.039	0.056	0.052	0.288	0.299	0.069	0.064
15	C60ISO	0.047	0.047	0.040	0.041	0.041	0.007	0.008	0.023	0.023
16	CARBHB12	0.027	0.027	0.015	0.014	0.015	0.076	0.072	0.022	0.022
17	CDIE20	0.115	0.115	0.109	0.110	0.111	0.187	0.187	0.063	0.063
18	CHB6	0.008	0.008	0.008	0.008	0.008	0.012	0.012	0.009	0.009
19	DARC	0.071	0.070	0.012	0.012	0.012	0.128	0.127	0.039	0.041
20	DC13	0.067	0.059	0.049	0.049	0.049	0.093	0.094	0.030	0.031
21	DIPCS10	0.002	0.002	0.003	0.003	0.003	0.003	0.003	0.002	0.002
22	FH51	0.144	0.144	0.067	0.067	0.066	0.160	0.159	0.063	0.064
23	G21EA	0.114	0.073	0.111	0.064	0.064	0.065	0.063	0.081	0.079
24	G21IP	0.016	0.016	0.015	0.015	0.015	0.020	0.020	0.011	0.011
25	G2RC	0.073	0.073	0.038	0.038	0.037	0.051	0.051	0.029	0.029
26	HAL59	0.150	0.150	0.140	0.140	0.136	0.332	0.301	0.153	0.116
27	HEAVY28	0.144	0.154	0.149	0.156	0.156	0.334	0.312	0.098	0.062
28	HEAVYSB11	0.010	0.010	0.019	0.019	0.019	0.022	0.022	0.012	0.007
29	ICONF	0.054	0.050	0.03	0.028	0.029	0.063	0.055	0.020	0.020
30	IDISP	0.042	0.041	0.027	0.026	0.026	0.057	0.057	0.018	0.019
31	IL16	0.002	0.005	0.002	0.004	0.004	0.003	0.004	0.003	0.002
32	INV24	0.049	0.048	0.038	0.038	0.038	0.030	0.029	0.021	0.023
33	ISO34	0.103	0.103	0.056	0.055	0.055	0.156	0.155	0.046	0.046
34	ISOL24	0.124	0.123	0.068	0.068	0.067	0.238	0.237	0.040	0.041
35	MB16-43	0.115	0.115	0.053	0.052	0.051	0.084	0.084	0.022	0.023
36	MCONF	0.083	0.090	0.113	0.152	0.149	0.120	0.087	0.093	0.116
37	NBPRC	0.010	0.010	0.006	0.005	0.005	0.007	0.007	0.004	0.005
38	PA26	0.014	0.014	0.007	0.007	0.007	0.015	0.015	0.008	0.008
39	PAREL	0.104	0.104	0.094	0.095	0.098	0.192	0.191	0.072	0.073

40	PCONF21	0.130	0.128	0.275	0.267	0.263	0.229	0.228	0.082	0.090
41	PNICO23	0.042	0.037	0.057	0.053	0.053	0.111	0.111	0.024	0.022
42	PX13	0.038	0.038	0.029	0.029	0.028	0.065	0.065	0.017	0.017
43	RC21	0.079	0.079	0.039	0.039	0.039	0.059	0.059	0.065	0.064
44	RG18	0.299	0.082	0.104	0.072	0.070	0.459	0.157	0.120	0.110
45	RSE43	0.205	0.207	0.174	0.173	0.166	0.367	0.372	0.362	0.360
46	S22	0.027	0.026	0.026	0.028	0.027	0.043	0.042	0.024	0.026
47	S66	0.058	0.056	0.070	0.070	0.066	0.143	0.152	0.105	0.086
48	SCONF	0.020	0.021	0.033	0.030	0.024	0.044	0.043	0.008	0.005
49	SIE4X4	0.206	0.206	0.193	0.193	0.193	0.324	0.324	0.032	0.033
50	TAUT15	0.133	0.134	0.058	0.058	0.062	0.226	0.22	0.072	0.072
51	UPU23	0.081	0.097	0.067	0.084	0.083	0.092	0.097	0.059	0.060
52	W4-11	0.049	0.048	0.036	0.036	0.036	0.056	0.056	0.045	0.046
53	WATER27	0.057	0.012	0.056	0.005	0.007	0.049	0.048	0.013	0.011
54	WCPT18	0.034	0.034	0.028	0.028	0.028	0.045	0.046	0.014	0.014
55	YBDE18	0.028	0.028	0.040	0.040	0.040	0.062	0.062	0.028	0.029

Table S13: Performance Comparison for the WTMAD2 components (kcal/mol) between DSD-PBEP86-D3(BJ), DSD-PBEP86-D4, revDSD-PBEP86-D3(BJ), revDSD-PBE86-noFC (core + valence), and revDSD-PBEP86-D4

Serial No	Subset Name	AWTMAD2(kcal/mol)					
		DSD-PBEP86-D3(BJ)	DSD-PBEP86-D4	revDSD-PBEP86-D3(BJ)	revDSD-PBEP86(noFC)-D3(BJ)	revDSD-PBEP86-NL	revDSD-PBEP86-D4
1	ACONF	0.012	0.039	0.013	0.008	0.012	0.009
2	ADIM6	0.007	0.034	0.021	0.023	0.018	0.019
3	AHB21	0.016	0.011	0.010	0.011	0.010	0.008
4	AL2X6	0.004	0.012	0.003	0.002	0.003	0.011
5	ALK8	0.006	0.009	0.004	0.009	0.005	0.010
6	ALKBDE10	0.011	0.012	0.011	0.011	0.011	0.011
7	AMINO20X4	0.147	0.163	0.153	0.165	0.156	0.135
8	BH76RC	0.049	0.048	0.053	0.051	0.055	0.055
9	BH76	0.197	0.181	0.181	0.177	0.182	0.190
10	BHDIV10	0.014	0.011	0.008	0.008	0.007	0.007
11	BHPERI	0.115	0.065	0.038	0.035	0.032	0.040
12	BHROT27	0.032	0.029	0.020	0.024	0.020	0.016
13	BSR36	0.026	0.137	0.129	0.093	0.131	0.117
14	BUT14DIOL	0.082	0.051	0.045	0.039	0.047	0.050
15	C60ISO	0.023	0.024	0.019	0.019	0.018	0.022
16	CARBHB12	0.052	0.034	0.032	0.030	0.031	0.027
17	CDIE20	0.087	0.101	0.065	0.072	0.062	0.064
18	CHB6	0.011	0.006	0.010	0.009	0.010	0.006
19	DARC	0.024	0.013	0.009	0.010	0.008	0.009
20	DC13	0.022	0.021	0.017	0.030	0.016	0.016
21	DIPCS10	0.003	0.003	0.003	0.003	0.003	0.003
22	FH51	0.052	0.046	0.043	0.043	0.044	0.045
23	G21EA	0.068	0.067	0.074	0.080	0.077	0.072
24	G21IP	0.011	0.011	0.012	0.012	0.012	0.012
25	G2RC	0.036	0.030	0.030	0.030	0.030	0.028
26	HAL59	0.242	0.115	0.141	0.155	0.142	0.100
27	HEAVY28	0.230	0.090	0.116	0.150	0.122	0.097
28	HEAVYSB11	0.007	0.011	0.006	0.008	0.007	0.011
29	ICONF	0.018	0.033	0.019	0.028	0.019	0.021
30	IDISP	0.020	0.014	0.009	0.009	0.008	0.008
31	IL16	0.001	0.003	0.003	0.003	0.004	0.002
32	INV24	0.020	0.019	0.018	0.018	0.018	0.018
33	ISO34	0.035	0.043	0.032	0.031	0.031	0.033
34	ISOL24	0.048	0.057	0.045	0.042	0.044	0.045
35	MB16-43	0.018	0.035	0.027	0.036	0.029	0.051
36	MCONF	0.156	0.044	0.061	0.063	0.064	0.050
37	NBPRC	0.008	0.005	0.004	0.004	0.004	0.004

38	PA26	0.006	0.005	0.009	0.010	0.009	0.007
39	PAREL	0.080	0.077	0.060	0.061	0.057	0.061
40	PCONF21	0.129	0.134	0.082	0.086	0.079	0.058
41	PNICO23	0.099	0.018	0.040	0.031	0.042	0.020
42	PX13	0.036	0.033	0.023	0.019	0.021	0.024
43	RC21	0.033	0.031	0.032	0.032	0.032	0.033
44	RG18	0.085	0.130	0.103	0.091	0.101	0.102
45	RSE43	0.146	0.144	0.169	0.160	0.172	0.176
46	S22	0.048	0.017	0.020	0.020	0.020	0.015
47	S66	0.149	0.095	0.067	0.073	0.064	0.073
48	SCONF	0.020	0.010	0.013	0.013	0.015	0.008
49	SIE4X4	0.092	0.090	0.089	0.088	0.087	0.089
50	TAUT15	0.088	0.084	0.092	0.091	0.096	0.097
51	UPU23	0.065	0.067	0.069	0.072	0.070	0.069
52	W4-11	0.035	0.042	0.042	0.043	0.046	0.042
53	WATER27	0.027	0.009	0.007	0.007	0.007	0.008
54	WCPT18	0.034	0.029	0.019	0.016	0.017	0.019
55	YBDE18	0.020	0.012	0.011	0.011	0.011	0.010
Total WTMAD2		3.100	2.649	2.429	2.463	2.435	2.332

Table S14: Benefit of correlating the inner-shell orbitals for DSD-BLYP: component-wise analysis

Serial No.	Set Name	No. of Points	Δ WTMAD2(kcal/mol)	
			revDSD-BLYP with frozen cores	revDSD-BLYP without frozen cores
1	ACONF	15	0.013	0.010
2	ADIM6	6	0.022	0.026
3	AHB21	21	0.010	0.011
4	AL2X6	6	0.004	0.003
5	ALK8	8	0.011	0.009
6	ALKBDE10	10	0.009	0.009
7	AMINO20X4	80	0.143	0.164
8	BH76RC	30	0.056	0.053
9	BH76	76	0.194	0.186
10	BHDIV10	10	0.008	0.008
11	BHPERI	26	0.037	0.032
12	BHROT27	27	0.030	0.033
13	BSR36	36	0.088	0.056
14	BUT14DIOL	64	0.036	0.035
15	C60ISO	9	0.019	0.019
16	CARBHB12	12	0.027	0.026
17	CDIE20	20	0.065	0.077
18	CHB6	6	0.014	0.012
19	DARC	14	0.029	0.028
20	DC13	13	0.031	0.028
21	DIPCS10	10	0.002	0.002
22	FH51	51	0.049	0.052
23	G21EA	25	0.085	0.088
24	G21IP	36	0.011	0.011
25	G2RC	25	0.017	0.017
26	HAL59	59	0.138	0.147
27	HEAVY28	28	0.077	0.087
28	HEAVYSB11	11	0.009	0.012
29	ICONF	17	0.025	0.027
30	IDISP	6	0.011	0.009
31	IL16	16	0.003	0.003
32	INV24	24	0.023	0.023
33	ISO34	34	0.057	0.054
34	ISOL24	24	0.082	0.077
35	MB16-43	43	0.024	0.036
36	MCONF	51	0.083	0.088
37	NBPRC	6	0.003	0.003
38	PA26	26	0.009	0.009

39	PAREL	20	0.076	0.076
40	PCONF21	18	0.085	0.086
41	PNICO23	23	0.028	0.019
42	PX13	13	0.011	0.008
43	RC21	21	0.038	0.039
44	RG18	18	0.131	0.110
45	RSE43	43	0.142	0.136
46	S22	22	0.017	0.017
47	S66	66	0.074	0.076
48	SCONF	17	0.009	0.011
49	SIE4X4	16	0.094	0.093
50	TAUT15	15	0.080	0.081
51	UPU23	23	0.068	0.071
52	W4-11	140	0.043	0.045
53	WATER27	27	0.010	0.008
54	WCPT18	18	0.015	0.014
55	YBDE18	18	0.013	0.013
WTMAD2			2.484	2.470

Table S15: Comparison of B3LYP-D3(BJ), PBE0-D3(BJ), and revPBE0-D3(BJ) for the WTMAD2 components

Serial No	Type	Set Name	No. of Points	Δ WTMAD2(kcal/mol)		
				B3LYP-D3(BJ)	PBE0-D3(BJ)	revPBE0-D3(BJ)
1	Conformer	ACONF	15	0.024	0.017	0.015
2	Intermol	ADIM6	6	0.012	0.004	0.005
3	Intermol	AHB21	21	0.017	0.048	0.020
4	Thermo	AL2X6	6	0.016	0.009	0.010
5	Thermo	ALK8	8	0.012	0.023	0.024
6	Thermo	ALKBDE10	10	0.016	0.021	0.030
7	Conformer	AMINO20X4	80	0.258	0.345	0.377
8	Thermo	BH76RC	30	0.117	0.131	0.105
9	Barrier	BH76	76	0.849	0.704	0.547
10	Barrier	BHDIV10	10	0.027	0.040	0.035
11	Barrier	BHPERI	26	0.057	0.153	0.151
12	Barrier	BHROT27	27	0.069	0.095	0.076
13	REACLarge	BSR36	36	0.301	0.294	0.187
14	Conformer	BUT14DIOL	64	0.299	0.210	0.203
15	REACLarge	C60ISO	9	0.008	0.009	0.009
16	Intermol	CARBHB12	12	0.072	0.110	0.070
17	REACLarge	CDIE20	20	0.187	0.231	0.202
18	Intermol	CHB6	6	0.012	0.012	0.010
19	REACLarge	DARC	14	0.127	0.061	0.052
20	Thermo	DC13	13	0.094	0.072	0.057
21	Thermo	DIPCS10	10	0.003	0.002	0.002
22	Thermo	FH51	51	0.159	0.173	0.134
23	Thermo	G21EA	25	0.063	0.083	0.105
24	Thermo	G21IP	36	0.020	0.020	0.021
25	Thermo	G2RC	25	0.051	0.125	0.101
26	Intermol	HAL59	59	0.301	0.299	0.238
27	Intermol	HEAVY28	28	0.312	0.261	0.210
28	Thermo	HEAVYSB11	11	0.022	0.010	0.020
29	Conformer	ICONF	17	0.055	0.056	0.046
30	Conformer	IDISP	6	0.057	0.025	0.023
31	Intermol	IL16	16	0.004	0.002	0.004
32	Barrier	INV24	24	0.029	0.033	0.038
33	REACLarge	ISO34	34	0.155	0.126	0.107
34	REACLarge	ISOL24	24	0.237	0.088	0.070
35	REACLarge	MB16-43	43	0.084	0.055	0.056
36	Conformer	MCONF	51	0.087	0.106	0.110
37	Thermo	NBPRC	6	0.007	0.023	0.023
38	Thermo	PA26	26	0.015	0.015	0.026
39	REACLarge	PAREL	20	0.191	0.197	0.159
40	Conformer	PCONF21	18	0.228	0.382	0.235

41	Intermol	PNICO23	23	0.111	0.196	0.149
42	Barrier	PX13	13	0.065	0.097	0.060
43	Thermo	RC21	21	0.059	0.126	0.095
44	Intermol	RG18	18	0.157	0.106	0.054
45	REACLarge	RSE43	43	0.372	0.309	0.212
46	Intermol	S22	22	0.042	0.059	0.032
47	Intermol	S66	66	0.152	0.171	0.083
48	Conformer	SCONF	17	0.043	0.038	0.040
49	Thermo	SIE4X4	16	0.324	0.259	0.254
50	Thermo	TAUT15	15	0.220	0.211	0.172
51	Conformer	UPU23	23	0.097	0.087	0.084
52	Thermo	W4-11	140	0.056	0.061	0.158
53	Intermol	WATER27	27	0.048	0.067	0.038
54	Barrier	WCPT18	18	0.046	0.085	0.055
55	Thermo	YBDE18	18	0.062	0.013	0.031
Total WTMAD2				6.502	6.551	5.429

Table S16: Sensitivity of WTMAD2 to the damping function scale parameter a_2

Functionals	Optimized a_2	Fixed a_2					
		$a_2=5.2$		$a_2=5.5$		$a_2=5.75$	
	WTMAD2	WTMAD2	WTMAD2 difference*	WTMAD2	WTMAD2 difference*	WTMAD2	WTMAD2 difference*
<i>without inner-shell correlation</i>							
DSD-BLYP-D3(BJ)	2.484	2.484	0.000	2.491	0.007	2.508	0.024
DSD-PBEB95-D3(BJ)	2.845	2.840	-0.005	2.846	0.001	2.851	0.006
DSD-PBEP86-D3(BJ)	2.429	2.412	-0.017	2.422	-0.007	2.437	0.008
DSD-PBE-D3(BJ)	2.738	2.716	-0.022	2.722	-0.016	2.737	-0.001
DSD-SCAN ₅₀ -D3(BJ)	3.104	3.168	0.064	3.138	0.034	3.119	0.015
DSD-SCAN ₅₅ -D3(BJ)	2.892	2.944	0.052	2.919	0.027	2.904	0.012
DSD-SCAN ₅₈ -D3(BJ)	2.785	2.820	0.035	2.801	0.016	2.788	0.003
DSD-SCAN ₆₃ -D3(BJ)	2.691	2.717	0.026	2.701	0.010	2.693	0.002
DSD-SCAN ₆₆ -D3(BJ)	2.662	2.684	0.022	2.672	0.010	2.666	0.004
DSD-SCAN ₆₉ -D3(BJ)	2.659	2.672	0.013	2.663	0.004	2.658	-0.001
DSD-SCAN ₇₄ -D3(BJ)	2.688	2.696	0.008	2.689	0.001	2.685	-0.003
DSD-SCAN0-2-D3(BJ)	2.800	2.806	0.006	2.803	0.003	2.800	0.000
DSD-TPSS-D3(BJ)	2.954	2.962	0.008	2.954	0.000	2.957	0.003
<i>with inner-shell correlation</i>							
DSD-BLYP-D3(BJ)	2.470	2.450	-0.020	2.475	0.005	2.504	0.034
DSD-PBEB95-D3(BJ)	2.866	2.851	-0.015	2.865	-0.001	2.873	0.007
DSD-PBE-D3(BJ)	2.718	2.719	0.001	2.735	0.017	2.755	0.037
DSD-PBEP86-D3(BJ)	2.463	2.448	-0.015	2.465	0.002	2.482	0.019
DSD-SCAN ₅₀ -D3(BJ)	3.071	3.112	0.041	3.091	0.020	3.080	0.009
DSD-SCAN ₅₅ -D3(BJ)	2.860	2.890	0.030	2.877	0.017	2.868	0.008
DSD-SCAN ₅₈ -D3(BJ)	2.747	2.769	0.022	2.760	0.013	2.754	0.007
DSD-SCAN ₆₃ -D3(BJ)	2.666	2.675	0.009	2.669	0.003	2.665	-0.001
DSD-SCAN ₆₆ -D3(BJ)	2.649	2.651	0.002	2.651	0.002	2.649	0.000
DSD-SCAN ₆₉ -D3(BJ)	2.660	2.665	0.005	2.662	0.002	2.661	0.001
DSD-SCAN ₇₄ -D3(BJ)	2.727	2.727	0.000	2.727	0.000	2.726	-0.001
DSD-SCAN0-2-D3(BJ)	2.880	2.879	-0.001	2.880	0.000	2.880	0.000

*WTMAD2 difference = (WTMAD2 for fixed a_2 – WTMAD2 for optimized a_2). All WTMAD2 values are in kcal/mol.

Table S17: Comparison of revDSD-PBEP86-D3(BJ), revDSD-PBEP86-D4, revDSD-PBEP86-D4(noFC), and xrevDSD-PBEP86-D4(noFC) for the WTMAD2 components over whole 55 subsets.

Serial No	Type	Subset Name	Δ WTMAD2(kcal/mol)			
			revDSD-PBEP86-D3(BJ)	revDSD-PBEP86-D4	revDSD-PBEP86(noFC)-D4	xrevDSD-PBEP86(noFC)-D4
1	Conformer	ACONF	0.013	0.009	0.005	0.008
2	Intermol	ADIM6	0.021	0.019	0.021	0.018
3	Intermol	AHB21	0.010	0.008	0.010	0.010
4	Thermo	AL2X6	0.003	0.011	0.008	0.006
5	Thermo	ALK8	0.004	0.010	0.007	0.006
6	Thermo	ALKBDE10	0.011	0.011	0.012	0.013
7	Conformer	AMINO20X4	0.153	0.135	0.153	0.145
8	Thermo	BH76RC	0.053	0.055	0.051	0.053
9	Barrier	BH76	0.181	0.190	0.183	0.173
10	Barrier	BHDIV10	0.008	0.007	0.007	0.007
11	Barrier	BHPERI	0.038	0.040	0.033	0.021
12	Barrier	BHROT27	0.020	0.016	0.020	0.020
13	REACLarge	BSR36	0.129	0.117	0.082	0.074
14	Conformer	BUT14DIOL	0.045	0.050	0.037	0.071
15	REACLarge	C60ISO	0.019	0.022	0.022	0.023
16	Intermol	CARBHB12	0.032	0.027	0.024	0.026
17	REACLarge	CDIE20	0.065	0.064	0.071	0.071
18	Intermol	CHB6	0.010	0.006	0.006	0.006
19	REACLarge	DARC	0.009	0.009	0.007	0.008
20	Thermo	DC13	0.017	0.016	0.032	0.017
21	Thermo	DIPCS10	0.003	0.003	0.003	0.003
22	Thermo	FH51	0.043	0.045	0.045	0.045
23	Thermo	G21EA	0.074	0.072	0.080	0.082
24	Thermo	G21IP	0.012	0.012	0.013	0.013
25	Thermo	G2RC	0.030	0.028	0.027	0.029
26	Intermol	HAL59	0.141	0.100	0.112	0.118
27	Intermol	HEAVY28	0.116	0.097	0.090	0.087
28	Thermo	HEAVYSB11	0.006	0.011	0.009	0.010
29	Conformer	ICONF	0.019	0.021	0.033	0.025
30	Conformer	IDISP	0.009	0.008	0.009	0.008
31	Intermol	IL16	0.003	0.002	0.002	0.001
32	Barrier	INV24	0.018	0.018	0.018	0.018
33	REACLarge	ISO34	0.032	0.033	0.032	0.034
34	REACLarge	ISOL24	0.045	0.045	0.044	0.047
35	REACLarge	MB16-43	0.027	0.051	0.062	0.062
36	Conformer	MCONF	0.061	0.050	0.055	0.043
37	Thermo	NBPRC	0.004	0.004	0.003	0.003
38	Thermo	PA26	0.009	0.007	0.008	0.008
39	REACLarge	PAREL	0.060	0.061	0.061	0.062
40	Conformer	PCONF21	0.082	0.058	0.059	0.055
41	Intermol	PNICO23	0.040	0.020	0.017	0.022
42	Barrier	PX13	0.023	0.024	0.019	0.018
43	Thermo	RC21	0.032	0.033	0.034	0.029
44	Intermol	RG18	0.103	0.102	0.086	0.074
45	REACLarge	RSE43	0.169	0.176	0.167	0.108
46	Intermol	S22	0.020	0.015	0.016	0.012
47	Intermol	S66	0.067	0.073	0.071	0.082
48	Conformer	SCONF	0.013	0.008	0.010	0.009
49	Thermo	SIE4X4	0.089	0.089	0.089	0.092
50	Thermo	TAUT15	0.092	0.097	0.098	0.105
51	Conformer	UPU23	0.069	0.069	0.072	0.067
52	Thermo	W4-11	0.042	0.042	0.044	0.042
53	Intermol	WATER27	0.007	0.008	0.007	0.014
54	Barrier	WCPT18	0.019	0.019	0.015	0.015
55	Thermo	YBDE18	0.011	0.010	0.011	0.011
Total WTMAD2			2.429	2.332	2.307	2.229

Table S18: Ranking of performance for WTMAD2 (kcal/mol) of the GMTKN55 dataset and its principal subsets. Heatmapping is from red (worst) via yellow to green (best).^(a)

Functional	WTMAD2 (kcal/mol)	Thermo	Barrier	REAClarge	Conformer	Intermol	NCI ^b
LDA(SPW92)	22.673	4.456	4.051	2.965	5.085	6.116	11.201
PBEsol-D3(BJ)	14.277	2.912	3.108	2.253	3.120	2.884	6.004
PBE-D3(BJ)	10.435	2.094	2.405	2.010	1.881	2.046	3.927
rPBE-D3(BJ)	10.420	2.056	2.295	1.614	1.565	2.890	4.455
TPSS-D3(BJ)	9.141	1.843	2.137	2.024	1.608	1.529	3.137
B97-D3(BJ)	8.608	1.817	1.733	2.278	1.541	1.239	2.780
revTPSS-D3(BJ)	8.424	1.941	2.036	1.771	1.328	1.348	2.676
revPBE-D3(BJ)	8.340	1.774	2.044	1.708	1.545	1.270	2.815
SCAN-D3(BJ)	7.947	1.671	1.950	1.303	1.297	1.726	3.023
M06-D3(0)	7.748	1.146	0.640	1.456	2.978	1.528	4.506
SCAN0	7.685	1.640	1.033	1.317	1.707	1.989	3.696
CAM-QTP-02-D3(BJ)	7.296	1.317	0.918	1.268	1.911	1.883	3.794
CAM-QTP-01-D3(BJ)	6.809	1.256	0.936	1.207	1.808	1.602	3.410
CAM-QTP-00-D3(BJ)	6.479	1.645	1.075	1.276	1.279	1.204	2.483
PBE0-D3(BJ)	6.551	1.376	1.207	1.369	1.264	1.335	2.599
B3LYP-D3(BJ)	6.502	1.314	1.141	1.662	1.147	1.238	2.385
M11	6.417	0.962	0.567	1.098	2.539	1.251	3.790
B97M-V	6.365	1.196	1.003	1.559	1.759	0.848	2.607
SCAN0-D3(BJ)	6.229	1.664	1.091	1.174	1.051	1.250	2.301
MN15-D3(BJ)	5.772	0.999	0.519	1.017	2.126	1.111	3.237
revM11	5.732	1.123	0.761	1.284	1.610	0.954	2.564
PW6B95-D3(BJ)	5.487	1.047	0.789	1.485	1.311	0.855	2.166
LC- ω PBEh-D3(BJ)	5.489	1.324	0.949	1.237	1.134	0.844	1.978
revPBE0-D3(BJ)	5.429	1.367	0.962	1.055	1.134	0.912	2.046
BH&HLYP-D3(BJ)	5.541	1.581	0.819	1.261	0.964	0.916	1.880
CAM-B3LYP-D3(BJ)	5.323	1.129	0.883	1.261	1.236	0.814	2.050
revM06	5.301	1.013	0.523	1.151	1.673	0.940	2.613
M06-2X	4.785	0.858	0.482	1.078	1.224	1.143	2.367
SCAN0-2	4.686	0.975	0.657	1.082	0.945	1.027	1.972
ω B97X-D3(BJ)	4.686	0.975	0.657	1.082	0.945	1.027	1.972
ω B97X-V	3.959	1.020	0.561	1.070	0.730	0.578	1.308
ω B97M-D3(BJ)	3.764	0.737	0.411	0.823	0.893	0.900	1.793
ω B97M-V	3.287	0.729	0.454	0.640	0.897	0.567	1.464
B2GP-PLYP-D3(BJ)	3.187	0.626	0.415	0.662	0.635	0.850	1.485
DSD-PBE-D3(BJ)	3.170	0.657	0.412	0.542	0.730	0.828	1.558
DSD-PBEP86-D3(BJ)	3.099	0.551	0.448	0.486	0.649	0.966	1.615
noDispSD-SCAN69	2.983	0.582	0.524	0.671	0.475	0.731	1.206
rev ω B97X-2	2.804	0.584	0.371	0.582	0.497	0.770	1.267
DSD-BLYP-D4	2.829	0.581	0.379	0.591	0.679	0.598	1.277
revDSD-PBEP86-D4	2.700	0.636	0.310	0.445	0.784	0.524	1.308
DSD-PBEP86-D4	2.649	0.538	0.365	0.631	0.554	0.562	1.116
DSD-PBEP86-NL	2.639	0.583	0.395	0.569	0.535	0.558	1.093
DSD-PBE-D4	2.637	0.612	0.387	0.562	0.532	0.543	1.075
DSD-SCAN-D4	2.635	0.601	0.395	0.624	0.454	0.562	1.016
revDSD-BLYP-D4	2.592	0.568	0.341	0.576	0.483	0.624	1.107
revDSD-PBEP86-D3(BJ)	2.422	0.535	0.310	0.551	0.458	0.568	1.026
revDSD-PBE-D4	2.462	0.646	0.354	0.531	<i>0.433</i>	0.497	<i>0.930</i>
revDSD-PBEP86-NL	2.436	<i>0.546</i>	0.298	0.553	0.470	0.569	1.039
revDOD-PBEP86-D4	2.363	0.591	<i>0.301</i>	0.590	0.406	0.474	0.880
revDSD-PBEP86-D4	2.332	0.556	0.314	0.576	0.409	0.478	0.887
ω B97M(2)	2.186	0.442	0.258	0.418	0.577	<i>0.492</i>	1.069

(a) **Bold underlined** = 1st place; **bold** = 2nd place; *italics* = 3rd place.

(b) NCI= Total Non-Covalent Interaction (Conformer/Intramolecular + Intermolecular)

Figure S1: trends in the parameters c_{2ab} , c_{2ss} , c_{Disp} , and $c_{C,XC}$ for the DSD-SCAN_x-D3(BJ) family as a function of the fraction x of HF-like exchange. Note the remarkably linear behavior over the $x=0.5$ – 0.8 range, as well as the almost perfectly parallel c_{2ab} and c_{2ss} lines

Gaussian sample input files for CO

1. revDSD-BLYP-D3(BJ)

```
$rungauss
%mem=8GB
%nproc=8
#p dsdpbep86/def2TZVPP iop(3/125=0197905477,3/78=0531305313,3/76=0290007100,3/74=0402)
# empiricaldispersion=gd3bj iop(3/174=0545100,3/175=-1,3/176=0,3/177=-1,3/178=5200000)
```

```
0 1
C
O 1 1.1314
```

2. DSD-PBEP86-D3(BJ) (specified manually, for illustration)

```
$rungauss
%mem=8GB
%nproc=8
#p dsdpbep86/def2TZVPP iop(3/125=0220005200,3/78=0440004400,3/76=0310006900,3/74=1004)
# empiricaldispersion=gd3bj iop(3/174=0480000,3/175=-1,3/176=0,3/177=-1,3/178=5600000)
```

```
0 1
C
O 1 1.1314
```

3. revDSD-PBEP86-D3(BJ)

```
$rungauss
%mem=8GB
%nproc=8
#p dsdpbep86/def2TZVPP iop(3/125=0079905785,3/78=0429604296,3/76=0310006900,3/74=1004)
# empiricaldispersion=gd3bj iop(3/174=0437700,3/175=-1,3/176=0,3/177=-1,3/178=5500000)
```

```
0 1
C
O 1 1.1314
```

ORCA sample input files for CO

1. DOD-SCAN-D3(BJ)

```
!PAL8

%MaxCore 2500

! RKS def2-TZVPP def2-tzvpp/c def2/j tightscf rijcosx GRID6 NoPOP d3bj

%method
  Exchange X_SCAN
  Correlation C_SCAN
ScalHFX 0.66
ScalDFX 0.34
ScalGGAC 0.5048
ScalLDAC 0.5048
  ScalMP2C 1.0
  D3S6 0.3152
  D3A2 5.75
  D3S8 0.0
  D3A1 0.0
end
%mp2
DoSCS true
  PS 0.6283
  PT 0.0000
end

*xyz 0 1
  C  0.000000  0.000000  0.000000
  O  0.000000  0.000000  1.131400
*
```

2. noDispSD-SCAN₆₉

```
!PAL8

%MaxCore 2500

! RKS def2-TZVPP def2-tzvpp/c def2/j tightscf rijcosx GRID6 NoPOP

%method
  Exchange X_SCAN
  Correlation C_SCAN
ScalHFX 0.69
ScalDFX 0.31
ScalGGAC 0.4409
ScalLDAC 0.4409
  ScalMP2C 1.0
end

%mp2
DoSCS true
  PS 0.6223
  PT 0.2600
end
```

```
*xyz 0 1
  C  0.000000  0.000000  0.000000
  O  0.000000  0.000000  1.131400
*
```

3. revDSD-PBEP86-D3(BJ)

!PAL8

%MaxCore 2500

! RKS def2-TZVPP def2-tzvpp/c def2/j tightscf rijcosx GRID6 NoPOP d3bj

%method

```
  Exchange X_PBE
  Correlation C_P86
ScalHFX 0.69
ScalDFX 0.31
ScalGGAC 0.4296
ScalLDAC 0.4296
  ScalMP2C 1.0
  D3S6 0.4377
  D3A2 5.5
  D3S8 0.0
  D3A1 0.0
end
```

%mp2

```
DoSCS true
  PS 0.5785
  PT 0.0799
end
```

```
*xyz 0 1
  C  0.000000  0.000000  0.000000
  O  0.000000  0.000000  1.131400
*
```

4. revDSD-BLYP-D3(BJ)

!PAL8

%MaxCore 2500

! RKS def2-TZVPP def2-tzvpp/c def2/j tightscf rijcosx GRID6 NoPOP d3bj

%method

```
  Exchange X_B88
  Correlation C_LYP
ScalHFX 0.71
ScalDFX 0.29
ScalGGAC 0.5313
ScalLDAC 0.5313
  ScalMP2C 1.0
  D3S6 0.5451
  D3A2 5.20
  D3S8 0.0
  D3A1 0.0
```

```

end

%mp2
DoSCS true
  PS 0.5477
  PT 0.1979
end

*xyz 0 1
  C  0.000000  0.000000  0.000000
  O  0.000000  0.000000  1.131400
*
```

5. revDOD-PBEP86-D3(BJ)

```

!PAL8

%MaxCore 2500

! RKS def2-TZVPP def2-tzvpp/c def2/j tightscf rijcosx GRID6 NoPOP d3bj
%method
  Exchange X_PBE
  Correlation C_P86
ScalHFX 0.69
ScalDFX 0.31
ScalGGAC 0.4449
ScalLDAC 0.4449
  ScalMP2C 1.0
  D3S6 0.4770
  D3A2 5.5
  D3S8 0.0
  D3A1 0.0
end

%mp2
DoSCS true
  PS 0.6055
  PT 0.0000
end

*xyz 0 1
  C  0.000000  0.000000  0.000000
  O  0.000000  0.000000  1.131400
*
```


References:

- (1) Gruzman, D.; Karton, A.; Martin, J. M. L. Performance of Ab Initio and Density Functional Methods for Conformational Equilibria of C(n)H(2n+2) Alkane Isomers (n = 4-8). *J. Phys. Chem. A* **2009**, *113* (43), 11974–11983. <https://doi.org/10.1021/jp903640h>.
- (2) Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H. A Consistent and Accurate Ab Initio Parametrization of Density Functional Dispersion Correction (DFT-D) for the 94 Elements H-Pu. *J. Chem. Phys.* **2010**, *132* (15), 154104. <https://doi.org/10.1063/1.3382344>.
- (3) Lao, K. U.; Schäffer, R.; Jansen, G.; Herbert, J. M. Accurate Description of Intermolecular Interactions Involving Ions Using Symmetry-Adapted Perturbation Theory. *J. Chem. Theory Comput.* **2015**, *11* (6), 2473–2486. <https://doi.org/10.1021/ct5010593>.
- (4) Goerigk, L.; Hansen, A.; Bauer, C.; Ehrlich, S.; Najibi, A.; Grimme, S. A Look at the Density Functional Theory Zoo with the Advanced GMTKN55 Database for General Main Group Thermochemistry, Kinetics and Noncovalent Interactions. *Phys. Chem. Chem. Phys.* **2017**, *19* (48), 32184–32215. <https://doi.org/10.1039/C7CP04913G>.
- (5) Yu, H.; Truhlar, D. G. Components of the Bond Energy in Polar Diatomic Molecules, Radicals, and Ions Formed by Group-1 and Group-2 Metal Atoms. *J. Chem. Theory Comput.* **2015**, *11* (7), 2968–2983. <https://doi.org/10.1021/acs.jctc.5b00083>.
- (6) Kesharwani, M. K.; Karton, A.; Martin, J. M. L. Benchmark Ab Initio Conformational Energies for the Proteinogenic Amino Acids through Explicitly Correlated Methods. Assessment of Density Functional Methods. *J. Chem. Theory Comput.* **2016**, *12* (1), 444–454. <https://doi.org/10.1021/acs.jctc.5b01066>.
- (7) Goerigk, L.; Grimme, S. A General Database for Main Group Thermochemistry, Kinetics, and Noncovalent Interactions – Assessment of Common and Reparameterized (Meta-)GGA Density Functionals. *J. Chem. Theory Comput.* **2010**, *6* (1), 107–126. <https://doi.org/10.1021/ct900489g>.
- (8) Zhao, Y.; Lynch, B. J.; Truhlar, D. G. Multi-Coefficient Extrapolated Density Functional Theory for Thermochemistry and Thermochemical Kinetics. *Phys. Chem. Chem. Phys.* **2005**, *7* (1), 43. <https://doi.org/10.1039/b416937a>.
- (9) Zhao, Y.; González-García, N.; Truhlar, D. G. Benchmark Database of Barrier Heights for Heavy Atom Transfer, Nucleophilic Substitution, Association, and Unimolecular Reactions and Its Use to Test Theoretical Methods. *J. Phys. Chem. A* **2005**, *109* (9), 2012–2018. <https://doi.org/10.1021/jp045141s>.
- (10) Guner, V.; Khuong, K. S.; Leach, A. G.; Lee, P. S.; Bartberger, M. D.; Houk, K. N. A Standard Set of Pericyclic Reactions of Hydrocarbons for the Benchmarking of Computational Methods: The Performance of Ab Initio, Density Functional, CASSCF, CASPT2, and CBS-QB3 Methods for the Prediction of Activation Barriers, Reaction Energetics, and. *J. Phys. Chem. A* **2003**, *107* (51), 11445–11459. <https://doi.org/10.1021/jp035501w>.
- (11) Ess, D. H.; Houk, K. N. Activation Energies of Pericyclic Reactions: Performance of DFT, MP2, and CBS-QB3 Methods for the Prediction of Activation Barriers and Reaction Energetics of 1,3-Dipolar Cycloadditions, and Revised Activation Enthalpies for a Standard Set of Hydrocarbon. *J. Phys. Chem. A* **2005**, *109* (42), 9542–9553. <https://doi.org/10.1021/jp052504v>.
- (12) Dinadayalane, T. C.; Vijaya, R.; Smitha, A.; Sastry, G. N. Diels–Alder Reactivity of Butadiene and Cyclic Five-Membered Dienes ((CH)₄X, X = CH₂, SiH₂, O, NH, PH, and S) with Ethylene: A Benchmark Study. *J. Phys. Chem. A* **2002**, *106* (8), 1627–1633. <https://doi.org/10.1021/jp013910r>.
- (13) Steinmann, S. N.; Csonka, G.; Corminboeuf, C. Unified Inter- and Intramolecular Dispersion Correction Formula for Generalized Gradient Approximation Density Functional Theory. *J. Chem. Theory Comput.* **2009**, *5* (11), 2950–2958. <https://doi.org/10.1021/ct9002509>.
- (14) Krieg, H.; Grimme, S. Thermochemical Benchmarking of Hydrocarbon Bond Separation Reaction Energies: Jacob’s Ladder Is Not Reversed! *Mol. Phys.* **2010**, *108* (19–20), 2655–2666. <https://doi.org/10.1080/00268976.2010.519729>.
- (15) Kozuch, S.; Bachrach, S. M.; Martin, J. M. L. Conformational Equilibria in Butane-1,4-Diol: A Benchmark of a Prototypical System with Strong Intramolecular H-Bonds. *J. Phys. Chem. A* **2014**, *118* (1), 293–303. <https://doi.org/10.1021/jp410723v>.
- (16) Sure, R.; Hansen, A.; Schwerdtfeger, P.; Grimme, S. Comprehensive Theoretical Study of All 1812 C₆₀isomers. *Phys. Chem. Chem. Phys.* **2017**, *19* (22), 14296–14305. <https://doi.org/10.1039/c7cp00735c>.
- (17) Yu, L.-J.; Karton, A. Assessment of Theoretical Procedures for a Diverse Set of Isomerization Reactions Involving Double-Bond Migration in Conjugated Dienes. *Chem. Phys.* **2014**, *441*, 166–177. <https://doi.org/10.1016/j.chemphys.2014.07.015>.
- (18) Johnson, E. R.; Mori-Sánchez, P.; Cohen, A. J.; Yang, W. Delocalization Errors in Density Functionals and Implications for Main-Group Thermochemistry. *J. Chem. Phys.* **2008**, *129* (20), 204112. <https://doi.org/10.1063/1.3021474>.
- (19) Zhao, Y.; Truhlar, D. G. The M06 Suite of Density Functionals for Main Group Thermochemistry,

- Thermochemical Kinetics, Noncovalent Interactions, Excited States, and Transition Elements: Two New Functionals and Systematic Testing of Four M06-Class Functionals and 12 Other Function. *Theor. Chem. Acc.* **2008**, *120* (1–3), 215–241. <https://doi.org/10.1007/s00214-007-0310-x>.
- (20) Grimme, S. Semiempirical Hybrid Density Functional with Perturbative Second-Order Correlation. *J. Chem. Phys.* **2006**, *124* (3), 034108. <https://doi.org/10.1063/1.2148954>.
 - (21) Grimme, S.; Mück-Lichtenfeld, C.; Würthwein, E.-U.; Ehlers, A. W.; Goumans, T. P. M.; Lammertsma, K. Consistent Theoretical Description of 1,3-Dipolar Cycloaddition Reactions. *J. Phys. Chem. A* **2006**, *110* (8), 2583–2586. <https://doi.org/10.1021/jp057329x>.
 - (22) Piacenza, M.; Grimme, S. Systematic Quantum Chemical Study of DNA-Base Tautomers. *J. Comput. Chem.* **2004**, *25* (1), 83–99. <https://doi.org/10.1002/jcc.10365>.
 - (23) Woodcock, H. L.; Schaefer, H. F.; Schreiner, P. R. Problematic Energy Differences between Cumulenes and Poly-Ynes: Does This Point to a Systematic Improvement of Density Functional Theory? *J. Phys. Chem. A* **2002**, *106* (49), 11923–11931. <https://doi.org/10.1021/jp0212895>.
 - (24) Schreiner, P. R.; Fokin, A. a; Pascal, R. a; de Meijere, A. Many Density Functional Theory Approaches Fail to Give Reliable Large Hydrocarbon Isomer Energy Differences. *Org. Lett.* **2006**, *8* (17), 3635–3638. <https://doi.org/10.1021/ol0610486>.
 - (25) Lepetit, C.; Chermette, H.; Gicquel, M.; Heully, J.; Chauvin, R. Description of Carbo -Oxocarbons and Assessment of Exchange-Correlation Functionals for the DFT Description of Carbo -Mers. *J. Phys. Chem. A* **2007**, *111* (1), 136–149. <https://doi.org/10.1021/jp064066d>.
 - (26) Lee, J. S. Accurate Ab Initio Binding Energies of Alkaline Earth Metal Clusters. *J. Phys. Chem. A* **2005**, *109* (51), 11927–11932. <https://doi.org/10.1021/jp040705d>.
 - (27) Karton, A.; Martin, J. M. L. Explicitly Correlated Benchmark Calculations on C₈H₈ Isomer Energy Separations: How Accurate Are DFT, Double-Hybrid, and Composite Ab Initio Procedures? *Mol. Phys.* **2012**, *110* (19–20), 2477–2491. <https://doi.org/10.1080/00268976.2012.698316>.
 - (28) Zhao, Y.; Tishchenko, O.; Gour, J. R.; Li, W.; Lutz, J. J.; Piecuch, P.; Truhlar, D. G. Thermochemical Kinetics for Multireference Systems: Addition Reactions of Ozone. *J. Phys. Chem. A* **2009**, *113* (19), 5786–5799. <https://doi.org/10.1021/jp811054n>.
 - (29) Manna, D.; Martin, J. M. L. What Are the Ground State Structures of C₂₀ and C₂₄? An Explicitly Correlated Ab Initio Approach. *J. Phys. Chem. A* **2016**, *120* (1), 153–160. <https://doi.org/10.1021/acs.jpca.5b10266>.
 - (30) Friedrich, J.; Hänchen, J. Incremental CCSD(T)(F12*)|MP2 - A Black Box Method to Obtain Highly Accurate Reaction Energies. *J. Chem. Theory Comput.* **2013**, *13* 1118164711009. <https://doi.org/10.1021/ct4008074>.
 - (31) Friedrich, J. Efficient Calculation of Accurate Reaction Energies - Assessment of Different Models in Electronic Structure Theory. *J. Chem. Theory Comput.* **2015**, *11* (8), 3596–3609. <https://doi.org/10.1021/acs.jctc.5b00087>.
 - (32) Curtiss, L. A.; Raghavachari, K.; Trucks, G. W.; Pople, J. A. Gaussian-2 Theory for Molecular Energies of First- and Second-row Compounds. *J. Chem. Phys.* **1991**, *94* (11), 7221–7230. <https://doi.org/10.1063/1.460205>.
 - (33) Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Pople, J. A. Assessment of Gaussian-2 and Density Functional Theories for the Computation of Enthalpies of Formation. *J. Chem. Phys.* **1997**, *106* (3), 1063–1079. <https://doi.org/10.1063/1.473182>.
 - (34) Kozuch, S.; Martin, J. M. L. Halogen Bonds: Benchmarks and Theoretical Analysis. *J. Chem. Theory Comput.* **2013**, *9*, 1918–1931. <https://doi.org/10.1021/ct301064t>.
 - (35) Řezáč, J.; Riley, K. E.; Hobza, P. Benchmark Calculations of Noncovalent Interactions of Halogenated Molecules. *J. Chem. Theory Comput.* **2012**, *8* (11), 4285–4292. <https://doi.org/10.1021/ct300647k>.
 - (36) Schwabe, T.; Grimme, S. Double-Hybrid Density Functionals with Long-Range Dispersion Corrections: Higher Accuracy and Extended Applicability. *Phys. Chem. Chem. Phys.* **2007**, *9* (26), 3397–3406. <https://doi.org/10.1039/b704725h>.
 - (37) Grimme, S. Seemingly Simple Stereoelectronic Effects in Alkane Isomers and the Implications for Kohn–Sham Density Functional Theory. *Angew. Chemie Int. Ed.* **2006**, *45* (27), 4460–4464. <https://doi.org/10.1002/anie.200600448>.
 - (38) Goerigk, L.; Grimme, S. Efficient and Accurate Double-Hybrid-Meta-GGA Density Functionals—Evaluation with the Extended GMTKN30 Database for General Main Group Thermochemistry, Kinetics, and Noncovalent Interactions. *J. Chem. Theory Comput.* **2011**, *7* (2), 291–309. <https://doi.org/10.1021/ct100466k>.
 - (39) Grimme, S.; Steinmetz, M.; Korth, M. How to Compute Isomerization Energies of Organic Molecules with Quantum Chemical Methods. *J. Org. Chem.* **2007**, *72* (6), 2118–2126. <https://doi.org/10.1021/jo062446p>.
 - (40) Goerigk, L.; Sharma, R. The INV24 Test Set: How Well Do Quantum-Chemical Methods Describe

- Inversion and Racemization Barriers? *Can. J. Chem.* **2016**, *11* (August), cjc-2016-0290. <https://doi.org/10.1139/cjc-2016-0290>.
- (41) Huenerbein, R.; Schirmer, B.; Moellmann, J.; Grimme, S. Effects of London Dispersion on the Isomerization Reactions of Large Organic Molecules: A Density Functional Benchmark Study. *Phys. Chem. Chem. Phys.* **2010**, *12* (26), 6940. <https://doi.org/10.1039/c003951a>.
 - (42) Fogueri, U. R.; Kozuch, S.; Karton, A.; Martin, J. M. L. The Melatonin Conformer Space: Benchmark and Assessment of Wave Function and DFT Methods for a Paradigmatic Biological and Pharmacological Molecule. *J. Phys. Chem. A* **2013**, *117* (10), 2269–2277. <https://doi.org/10.1021/jp312644t>.
 - (43) Grimme, S.; Kruse, H.; Goerigk, L.; Erker, G. The Mechanism of Dihydrogen Activation by Frustrated Lewis Pairs Revisited. *Angew. Chemie Int. Ed.* **2010**, *49* (8), 1402–1405. <https://doi.org/10.1002/anie.200905484>.
 - (44) Setiawan, D.; Kraka, E.; Cremer, D. Strength of the Pnictogen Bond in Complexes Involving Group Va Elements N, P, and As. *J. Phys. Chem. A* **2015**, *119* (9), 1642–1656. <https://doi.org/10.1021/jp508270g>.
 - (45) Karton, A.; O'Reilly, R. J.; Chan, B.; Radom, L. Determination of Barrier Heights for Proton Exchange in Small Water, Ammonia, and Hydrogen Fluoride Clusters with G4(MP2)-Type, MP *n*, and SCS-MP *n* Procedures—A Caveat. *J. Chem. Theory Comput.* **2012**, *8* (9), 3128–3136. <https://doi.org/10.1021/ct3004723>.
 - (46) Neese, F.; Schwabe, T.; Kossmann, S.; Schirmer, B.; Grimme, S. Assessment of Orbital-Optimized, Spin-Component Scaled Second-Order Many-Body Perturbation Theory for Thermochemistry and Kinetics. *J. Chem. Theory Comput.* **2009**, *5*, 3060–3073.
 - (47) Jurečka, P.; Šponer, J.; Černý, J.; Hobza, P. Benchmark Database of Accurate (MP2 and CCSD(T) Complete Basis Set Limit) Interaction Energies of Small Model Complexes, DNA Base Pairs, and Amino Acid Pairs. *Phys. Chem. Chem. Phys.* **2006**, *8* (17), 1985–1993. <https://doi.org/10.1039/B600027D>.
 - (48) Rezáč, J.; Riley, K. E.; Hobza, P. S66: A Well-Balanced Database of Benchmark Interaction Energies Relevant to Biomolecular Structures. *J. Chem. Theory Comput.* **2011**, *7* (8), 2427–2438. <https://doi.org/10.1021/ct2002946>.
 - (49) Csonka, G. I.; French, A. D.; Johnson, G. P.; Stortz, C. A. Evaluation of Density Functionals and Basis Sets for Carbohydrates. *J. Chem. Theory Comput.* **2009**, *5* (4), 679–692. <https://doi.org/10.1021/ct8004479>.
 - (50) Karton, A.; Rabinovich, E.; Martin, J. M. L.; Ruscic, B. W4 Theory for Computational Thermochemistry: In Pursuit of Confident Sub-KJ/Mol Predictions. *J. Chem. Phys.* **2006**, *125* (14), 144108. <https://doi.org/10.1063/1.2348881>.
 - (51) Kruse, H.; Mladek, A.; Gkionis, K.; Hansen, A.; Grimme, S.; Sponer, J. Quantum Chemical Benchmark Study on 46 RNA Backbone Families Using a Dinucleotide Unit. *J. Chem. Theory Comput.* **2015**, *11* (10), 4972–4991. <https://doi.org/10.1021/acs.jctc.5b00515>.
 - (52) Karton, A.; Daon, S.; Martin, J. M. L. W4-11: A High-Confidence Benchmark Dataset for Computational Thermochemistry Derived from First-Principles W4 Data. *Chem. Phys. Lett.* **2011**, *510*, 165–178. <https://doi.org/10.1016/j.cplett.2011.05.007>.
 - (53) Bryantsev, V.; Diallo, M.; van Duin, A.; Goddard, W. Evaluation of B3LYP, X3LYP, and M06-Class Density Functionals for Predicting the Binding Energies of Neutral, Protonated, and Deprotonated Water Clusters. *J. Chem. Theory Comput.* **2009**, *5* (4), 1016–1026.
 - (54) Karton, A.; O'Reilly, R. J.; Radom, L. Assessment of Theoretical Procedures for Calculating Barrier Heights for a Diverse Set of Water-Catalyzed Proton-Transfer Reactions. *J. Phys. Chem. A* **2012**, *116* (16). <https://doi.org/10.1021/jp301499y>.
 - (55) Zhao, Y.; Ng, H. T.; Peverati, R.; Truhlar, D. G. Benchmark Database for Ylidic Bond Dissociation Energies and Its Use for Assessments of Electronic Structure Methods. *J. Chem. Theory Comput.* **2012**, *8* (8), 2824–2834. <https://doi.org/10.1021/ct300457c>.
 - (56) Geary, R. C. The Ratio of the Mean Deviation to the Standard Deviation as a Test of Normality. *Biometrika* **1935**, *27* (3–4), 310–332. <https://doi.org/10.1093/biomet/27.3-4.310>.
 - (57) Geary, R. C. Moments of the Ratio of the Mean Deviation to the Standard Deviation for Normal Samples. *Biometrika* **1936**, *28* (3–4), 295–307. <https://doi.org/10.1093/biomet/28.3-4.295>.

ESI revDSD-PBEP86-D4 revision_submission.pdf (759.63 KiB)

[view on ChemRxiv](#) • [download file](#)