

S66x8 Noncovalent Interactions Revisited: New Benchmark and Performance of Composite Localized Coupled-Cluster Methods

Golokesh Santra,^{a,b} Emmanouil Semidalas,^{a,b} Nisha Mehta,^a Amir Karton,^{c,d} and Jan M.L. Martin^{a*}

^aDepartment of Molecular Chemistry and Materials Science, Weizmann Institute of Science, 7610001 Rehovot, Israel

^bShared first authors.

^cSchool of Molecular Sciences, The University of Western Australia, Perth, WA 6009, Australia

^dSchool of Science and Technology, University of New England, Armidale NSW 2351, Australia

Email: gershom@weizmann.ac.il

Abstract. The S66x8 noncovalent interactions benchmark has been re-evaluated at the “sterling silver” level, using explicitly correlated MP2-F12 near the complete basis set limit, CCSD(F12*)/aug-cc-pVTZ-F12, and a (T) correction from conventional CCSD(T)/sano-V{D,T}Z+ calculations. The revised reference value disagrees by 0.1 kcal/mol RMS with the original Hobza benchmark and its revision by Brauer et al, but by only 0.04 kcal/mol variety from the “bronze” level data in Kesharwani et al., *Aust. J. Chem.* **71**, 238–248 (2018). We then used these to assess the performance of localized-orbital coupled cluster approaches with and without counterpoise corrections, such as PNO-LCCSD(T) as implemented in MOLPRO, DLPNO-CCSD(T₁) as implemented in ORCA, and LNO-CCSD(T) as implemented in MRCC, for their respective “Normal”, “Tight”, and “very Tight” settings. We also considered composite approaches combining different basis sets and cutoffs. Furthermore, in order to isolate basis set convergence from domain truncation error, for the aug-cc-pVTZ basis set we compared PNO, DLPNO, and LNO approaches with canonical CCSD(T). We conclude that LNO-CCSD(T) with veryTight criteria performs very well for “raw” (CP-uncorrected), but struggles to reproduce counterpoise-corrected numbers even for veryveryTight criteria: this means that accurate results can be obtained using either extrapolation from basis sets large enough to quench basis set superposition error (BSSE) such as aug-cc-pV{Q,5}Z, or using a composite scheme such as Tight{T,Q}+1.11[vvTight(T) – Tight(T)]. In contrast, PNO-LCCSD(T) works best with counterpoise, while performance with and without counterpoise is comparable for DLPNO-CCSD(T₁). Among more economical methods, the highest accuracies are seen for dRPA75-D3BJ, ω B97M-V, ω B97M(2), revDSD-PBEP86-D4, and DFT(SAPT) with a TDEXX or ATDEXX kernel.

I. Introduction:

Noncovalent interactions (NCIs) are crucial to several chemical and biological phenomena occurring in the solid, liquid, and gaseous phases.^{1–3} These interactions play a pivotal role in

designing new functional materials,^{4–7} controlling solvation dynamics,^{8–10} protein folding,¹¹ and catalysis^{12,13} with applications in, e.g., liquid-crystal technology,¹⁴ drug delivery,¹⁵ and many more. Over the decades, several experimental studies have been performed (see Refs.^{1,16,17} and references therein). NCIs in the condensed phase are often determined via NMR spectroscopy,^{18–20} while in the gas phase, rotational spectroscopy is a reliable technique for polar molecules; for recent works, see refs.^{21–24}) and still, a significant effort is going on to understand and quantitatively measure different types of noncovalent interactions, present in bulk as well as interfaces. Unfortunately, results from experimentally studied noncovalently-bonded systems often include dynamical and (or) environmental effects, thus inappropriate to use as a reference for developing semi-empirical methods. Hence, accurate wavefunction *ab initio* methods are often essential for obtaining highly precise NCI energies. Over the past few years, several datasets have been proposed^{25–38} for intra- and intermolecular noncovalent interactions involving biologically important organic molecules of different sizes. The strong and weak NCIs in biomolecules are particularly interesting because they often play prominent roles in determining their favorable structures, specific binding sites, and dynamics.¹¹ Hobza’s S66³⁵ and its extended version, S66x8,³⁷ are two such datasets. The S66x8 set comprises equilibrium and angular-displaced nonequilibrium geometries of 66 dimers — built from 14 different monomers. These nonequilibrium structures were generated by multiplying the equilibrium intermonomer distances (r_e) by factors of 0.90, 0.95, 1.00, 1.05, 1.10, 1.25, 1.50, and 2.00, respectively while freezing the other degrees of freedom. All dimers of S66x8 can be categorized into four subsets: hydrogen bonds, π -stacking, London dispersion complexes, and mixed-influence interactions.

It is already well established that even at the complete basis set (CBS) limit, second-order Møller–Plesset perturbation theory (MP2) performs poorly for atomization energies, electron affinities, and barrier heights (see ref.³⁹ and references therein). However, for noncovalent interactions, MP2 with a large basis set can be considered a starting point, which, combined with high-level corrections (e.g., CCSD(T) – MP2 in a smaller basis), can lead to more accurate *ab-initio* energies. [CCSD(T) refers to coupled-cluster theory, including singles, doubles, and perturbative triples^{40,41}].

The original S66x8 NCI reference energies were obtained by adding a [CCSD(T)-MP2]/AVDZ high-level correction (HLC) to the extrapolated MP2/AV{T,Q}Z with full counterpoise (CP) correction. In ref.⁴² Brauer *et al.* improved the reference energies by combining explicitly correlated MP2-F12 energies at the CBS limit with an HLC from [CCSD(T_{sc})-F12b – MP2-F12]/cc-pVDZ-F12. Depending on the *ab initio* methods used for high-level correction, Martin and coworkers⁴³ proposed a hierarchy of revisited standards for NCI energies: gold, silver or sterling silver, and bronze (see section III.A for further details). In practice, the “sterling silver” (i.e., an alloy mix of 92.5% pure silver and 7.5% other metals, usually copper) level NCI energies are a low-cost version of the original “silver” standard. Due to the dominant computational cost, the authors in Ref.⁴³ computed the interaction energies at the “gold” level for only 18 dimers out of 66 present in S66. However, they successfully calculated the “sterling silver” and “bronze” standard energetics of the S66 and S66x8 sets, respectively.

Although canonical CCSD(T) or explicitly correlated CCSD(T)-F12 is often desired for highly accurate NCI energies, the steep cost scaling of these methods with the system size (N) renders them prohibitively expensive for applications on larger systems. Hence, over the past few years, localized coupled-cluster methods, such as PNO-LCCSD(T) [pair natural orbital localized coupled-cluster with singles, doubles, and perturbative triples] approach of the Werner group,⁴⁴ DLPNO-CCSD(T) [domain localized pair natural orbital CCSD(T)] and related methods by the Neese group,^{45,46} and LNO-CCSD(T) [localized natural orbital CCSD(T)] method of Kállay and coworkers^{47–49} have gained considerable attention. These methods' attractive linear scaling behavior allows calculations on systems consisting of hundreds of atoms. Often, with tight accuracy cutoff and large basis sets, they can achieve almost the same accuracy as canonical CCSD(T). Examples of recent use include the energetics of the (H₂O)₂₀ cages using PNO-LCCSD(T)-F12b,⁵⁰ (the F12b suffix refers to explicit correlation⁵¹), the noncovalent interaction energies of seven large dimers (L7 set³²) with LNO-CCSD(T),⁵² the main group thermochemistry, barrier heights, intra-, and intermolecular interaction energies of GMTKN55⁵³ using DLPNO-CCSD(T),⁵⁴ and benchmark studies on the Ru(II) complexes involved in hydroarylation,⁵⁵ highly delocalized polypyrroles (POLYPYR⁵⁶ set), and metal–organic barrier heights (MOBH35, 35 reactions^{57–59}). Despite the linear cost scaling, the accuracy of localized approaches is subject to various predefined cutoffs, and tuned fixed combinations of these cutoffs are often given as keywords in several codes. The available options for DLPNO-CCSD(T) and related methods in ORCA⁶⁰ are `LoosePNO`, `NormalPNO`, `TightPNO`, and `VeryTightPNO` (see Table 1 in Ref.⁶¹ for definitions). The accuracy settings in LNO-CCSD(T) are set to `Normal`, `Tight`, `vTight`, or `vvTight` (see Table 1 in Ref.⁴⁹ for details). In PNO-LCCSD(T), the `Default` and `Tight` (see Tables 1–4 in Ref.⁴⁴ for more information) are the standard settings.

Recently, S66 noncovalent interactions were studied with LNO-CCSD(T) by Kállay and Nagy,⁴⁹ and with eight low-cost LNO-CCSD(T)-based composite schemes by ourselves succinctly in a conference proceeding extended abstract.⁶² Accordingly, both studies showed a smooth error convergence by gradually tightening the accuracy thresholds and increasing the basis set size with respect to the "silver"⁴³ standard reference energies. For our composite schemes, a two-point CBS extrapolation with the same accuracy cutoff was employed, and the effect of a tighter cutoff was estimated as a scaled additivity correction in a relatively small basis set. With half-counterpoise^{63,64} correction (i.e., the average of full counterpoise-corrected and uncorrected results), few low-cost composite LNO-CCSD(T) methods performed very well.

That being said, the main objectives of the present study can be briefly summarized as: (a) climbing one step of the hierarchical ladder of NCI reference energies and the “sterling silver” standard S66x8 interaction energies; (b) evaluating the performance of pure and composite localized coupled-cluster methods based on LNO-CCSD(T), PNO-LCCSD(T), and DLPNO-CCSD(T₁) against the S66x8 set; (c) recommending a localized coupled cluster method which can be used for calculating accurate NCI energies, thus avoiding the expensive canonical coupled-cluster options.

II. Computational Methods:

The Molpro 2021.3⁶⁵ program suite was used for the conventional and explicitly correlated ab initio single-point calculations. The MRCC 2020,⁶⁶ Molpro 2021.3,⁶⁵ and ORCA 5.0.1⁶⁰ packages were employed for the LNO-CCSD(T), PNO-CCSD(T), and DLPNO-CCSD(T₁) calculations, respectively. The reference geometries of the S66x8 dataset were extracted from the Benchmark Energy & Geometry Database website (<http://www.begdb.org/>) and were used without further optimization. All electronic structure calculations were performed jointly on the Faculty of Chemistry’s Linux cluster, ChemFarm at the Weizmann Institute of Science, and the Karton group’s Linux cluster at the University of Western Australia (UWA).

For the explicitly correlated RI-MP2-F12 with the known 3C(FIX) ansatz,^{67,68} we used the correlation-consistent cc-pVnZ-F12 basis sets⁶⁹ for the atom of hydrogen and aug-cc-pVnZ-F12⁷⁰ (n = T, Q) for the nonhydrogen atoms; this expedient is denoted as haVnZ-F12 (n = T, Q) in the present manuscript. The Boys and Bernardi counterpoise correction (CP)⁷¹ was also used for removing the “basis set superposition errors” (BSSE).^{72,73} For the CCSD(F12*)^{74,75} (a.k.a. CCSD-F12c), we used the non-augmented cc-pVTZ-F12⁶⁹ throughout. However, for the conventional CCSD and CCSD(T), we employed the semi-augmented sano-pVnZ+ (n=D,T) atomic natural orbital basis sets of Neese and Valeev.⁷⁶ Appropriate auxiliary basis sets for JKfit⁷⁷ (Coulomb and exchange) and MP2fit^{78,79} (density fitting in MP2) were used across the board. As recommended by Werner and coworkers,⁸⁰ the geminal exponent $\beta = 1.0 \text{ a}_0^{-1}$ was employed for the haVTZ-F12 and haVQZ-F12 basis sets.

For the localized CCSD(T) calculations, haVnZ (n=T,Q, and 5) basis sets together with the corresponding RI fitting basis sets haVnZ-RI^{78,79} (n=T,Q, and 5) were used. Concerning accuracy thresholds, Normal, Tight, vTight, and vvTight were considered for LNO-CCSD(T), whereas for the PNO-LCCSD(T) calculations, we applied the Default and Tight settings. On the other hand, for DLPNO-CCSD(T₁) we employed NormalPNO, TightPNO, and VeryTightPNO (TightPNO with T_{CutMKN}, T_{CutPNO}, and T_{CutPairs} tightened to 10⁻⁴, 10⁻⁸, and 10⁻⁶, respectively).⁸¹ For the detailed description of these cutoff parameters see ref.⁶¹ settings together with RIJCOSX (resolution of the identity in combination with the chain of spheres⁸² algorithm) approximation.

To investigate the dependence of the DLPNO-CCSD(T₁) correlation on the size of the PNO space, we also adjusted the T_{CutPNO} threshold in DLPNO-CCSD(T₁)/Tight from the default value 10⁻⁷ to 10⁻⁶. Two-point PNO extrapolations were also carried out to the complete PNOs space limit (CPS), using the simple two points extrapolation scheme proposed by Altun et al.,⁸³ $E = E^X + [Y^\beta / (Y^\beta - X^\beta)] \times (E^Y - E^X)$, where Y=X+1 and $\beta=5.55$.

Similar to our previous studies,^{62,64,84} in addition to full counterpoise (CP) corrections,⁷¹ we have also considered the average CP or ‘half-CP’ to calculate the dissociation energies of S66x8. A two-point basis set extrapolation was carried out using the following expression from Halkier *et al.*⁸⁵, $E_{\text{CBS}} = E_L + (E_L - E_{L-1}) / [(\frac{L}{L-1})^\alpha - 1]$, where L refers to the basis set cardinal number and α is the basis set extrapolation exponent. For RI-MP2-F12/haV{T,Q}Z-F12, where

haV{T,Q}Z-F12 denotes the extrapolation from haVTZ-F12 and haVQZ-F12 basis sets, we used the same α value of 4.6324 initially obtained for the S66 set.⁴³ Like the W1 and W2 theories,⁸⁶ for the localized CC methods, we employed $\alpha=3$ and 3.22 for the haV{Q,5}Z and haV{T,Q}Z extrapolations, respectively. The optimal values of the linear combination coefficients for the composite localized CC schemes were obtained by minimizing the root mean square deviations (RMSD) for new reference energies.

III. Results and Discussion:

a) *Re-evaluation of reference energies:*

We were able to calculate the RI-MP2-F12/haVTZ-F12 and RI-MP2-F12/haVQZ-F12 level dissociation energies of the S66x8 dimers with and without counterpoise (CP) correction. With respect to the full-CP corrected RI-MP2-F12/haV{T,Q}Z-F12 energies, the RMS error of the counterpoise-uncorrected (i.e., “raw”) and half-CP are 0.005 and 0.002 kcal/mol, respectively. Hence, either full-CP, half-CP, or “raw” MP2-F12/CBS energies can be a starting point for re-evaluating the S66x8 reference NCI energies.

Table 1: Sterling silver^a level S66x8 dissociation energies (kcal/mol). r_e represents the equilibrium distance for each complex.

Dimers		0.90 r_e	0.95 r_e	1.00 r_e	1.05 r_e	1.10 r_e	1.25 r_e	1.50 r_e	2.00 r_e
Hydrogen bonding									
1	Water....Water	4.666	4.954	4.946	4.762	4.480	3.470	2.117	0.874
2	Water....MeOH	5.298	5.629	5.627	5.423	5.106	3.956	2.391	0.954
3	Water....MeNH2	6.606	6.957	6.941	6.695	6.318	4.928	2.980	1.142
4	Water....Peptide	7.739	8.131	8.128	7.878	7.482	5.994	3.830	1.439
5	MeOH....MeOH	5.387	5.771	5.804	5.620	5.312	4.151	2.528	1.011
6	MeOH....MeNH2	7.081	7.554	7.601	7.378	6.994	5.505	3.345	1.273
7	MeOH....Peptide	7.756	8.235	8.289	8.072	7.692	6.188	3.647	1.098
8	MeOH....Water	4.675	5.017	5.045	4.881	4.610	3.598	2.205	0.909
9	MeNH2....MeOH	2.837	3.051	3.037	2.892	2.682	1.971	1.098	0.393
10	MeNH2....MeNH2	3.722	4.104	4.153	4.002	3.742	2.781	1.302	0.385
11	MeNH2....Peptide	4.958	5.354	5.397	5.222	4.923	3.197	1.397	0.455
12	MeNH2....Water	6.861	7.291	7.312	7.077	6.691	5.231	3.155	1.196
13	Peptide....MeOH	5.753	6.165	6.220	6.054	5.759	4.608	2.948	1.307
14	Peptide....MeNH2	6.907	7.411	7.500	7.324	6.986	5.610	3.549	1.488
15	Peptide....Peptide	8.096	8.586	8.659	8.464	8.105	6.649	4.407	1.775
16	Peptide....Water	4.761	5.108	5.150	5.005	4.754	3.799	2.454	1.137
17	Uracil....Uracil (BP)	16.066	17.187	17.405	17.034	16.293	13.190	8.357	3.337
18	Water....Pyridine	6.484	6.870	6.879	6.653	6.289	4.929	3.006	1.184
19	MeOH....Pyridine	6.876	7.374	7.448	7.253	6.897	5.473	3.373	1.328
20	AcOH....AcOH	17.925	19.170	19.397	18.965	18.125	14.635	9.219	3.594
21	AcNH2....AcNH2	15.274	16.299	16.472	16.094	15.380	12.460	8.007	3.008
22	AcOH....Uracil	18.324	19.524	19.759	19.361	18.565	15.198	9.867	4.150
23	AcNH2....Uracil	18.076	19.195	19.432	19.086	18.367	15.265	10.240	4.662
π stack									
24	Benzene....Benzene (π - π)	-0.138	1.791	2.521	2.633	2.450	1.479	0.468	0.059
25	Pyridine....Pyridine (π - π)	0.964	2.891	3.610	3.689	3.452	2.299	0.945	0.233
26	Uracil....Uracil (π - π)	7.593	9.266	9.619	9.256	8.541	5.993	3.071	0.986
27	Benzene....Pyridine (π - π)	0.362	2.413	3.156	3.234	3.001	1.913	0.705	0.143
28	Benzene....Uracil (π - π)	3.178	4.924	5.465	5.351	4.916	3.207	1.334	0.246

29	Pyridine....Uracil (π - π)	3.374	5.878	6.576	6.391	5.820	3.793	1.752	0.529
30	Benzene....Ethene	0.021	0.939	1.269	1.292	1.172	0.651	0.159	-0.013
31	Uracil....Ethene	2.396	3.092	3.257	3.137	2.878	1.949	0.918	0.251
32	Uracil....Ethyne	2.587	3.387	3.587	3.464	3.183	2.159	1.012	0.264
33	Pyridine....Ethene	0.668	1.447	1.721	1.719	1.581	0.985	0.350	0.042
London dispersion complexes									
34	Pentane....Pentane	2.796	3.564	3.723	3.567	3.265	2.211	1.039	0.263
35	Neopentane....Pentane	1.822	2.460	2.580	2.456	2.228	1.479	0.690	0.185
36	Neopentane....Neopentane	1.425	1.705	1.742	1.625	1.502	1.018	0.497	0.132
37	Cyclopentane....Neopentane	1.576	2.217	2.373	2.295	2.111	1.449	0.699	0.189
38	Cyclopentane....Cyclopentane	2.198	2.800	2.956	2.824	2.563	1.693	0.780	0.201
39	Benzene....Cyclopentane	1.969	3.081	3.438	3.364	3.083	2.026	0.884	0.189
40	Benzene....Neopentane	1.712	2.549	2.791	2.721	2.502	1.674	0.762	0.187
41	Uracil....Pentane	3.679	4.560	4.724	4.502	3.999	2.402	0.961	0.212
42	Uracil....Cyclopentane	2.900	3.836	4.019	3.823	3.459	2.249	1.000	0.246
43	Uracil....Neopentane	2.756	3.500	3.613	3.415	3.083	2.013	0.912	0.229
44	Ethene....Pentane	1.597	1.918	1.943	1.822	1.639	1.069	0.481	0.117
45	Ethyne....Pentane	0.992	1.510	1.646	1.589	1.444	0.932	0.400	0.092
46	Peptide....Pentane	3.655	4.115	4.162	3.974	3.665	2.586	1.172	0.282
Mixed influence complexes									
47	Benzene....Benzene (TS)	1.493	2.452	2.762	2.731	2.536	1.734	0.818	0.222
48	Pyridine....Pyridine (TS)	2.402	3.199	3.440	3.375	3.154	2.259	1.168	0.370
49	Benzene....Pyridine (TS)	1.945	2.922	3.226	3.176	2.955	2.068	1.042	0.332
50	Benzene....Ethyne (CH- π)	1.791	2.580	2.810	2.747	2.545	1.772	0.890	0.272
51	Ethyne....Ethyne (TS)	1.170	1.434	1.489	1.431	1.318	0.913	0.452	0.134
52	Benzene....AcOH (OH- π)	3.908	4.525	4.655	4.508	4.213	3.107	1.697	0.554
53	Benzene....AcNH ₂ (NH- π)	3.768	4.242	4.334	4.201	3.945	2.960	1.641	0.481
54	Benzene....Water(OH- π)	2.745	3.161	3.224	3.094	2.870	2.089	1.154	0.417
55	Benzene....MeOH (OH- π)	3.338	3.950	4.106	3.998	3.749	2.774	1.524	0.518
56	Benzene....MeNH ₂ (NH- π)	2.381	2.977	3.139	3.044	2.803	1.922	0.933	0.260
57	Benzene....Peptide (NH- π)	3.595	4.828	5.176	5.059	4.715	3.384	1.799	0.619
58	Pyridine....Pyridine (CH-N)	2.884	3.869	4.166	3.890	3.442	2.173	1.005	0.274
59	Ethyne....Water (CH-O)	2.604	2.865	2.899	2.799	2.628	1.999	1.178	0.461
60	Ethyne....AcOH (OH- π)	4.306	4.787	4.854	4.679	4.371	3.234	1.760	0.556
61	Pentane....AcOH	2.629	2.835	2.820	2.677	2.467	1.757	0.773	0.166
62	Pentane....AcNH ₂	3.074	3.426	3.437	3.259	2.988	2.078	1.025	0.268
63	Benzene....AcOH	2.547	3.444	3.671	3.546	3.253	2.195	1.007	0.259
64	Peptide....Ethene	2.527	2.881	2.928	2.801	2.585	1.828	0.867	0.188
65	Pyridine....Ethyne	3.661	4.008	4.066	3.946	3.724	2.866	1.679	0.618
66	MeNH ₂Pyridine	3.360	3.796	3.893	3.784	3.560	2.677	1.488	0.490

^aSterling silver = MP2-F12/haV{T,Q}Z-F12 full-CP + [CCSD(F12*)-MP2-F12]/VTZ-F12 “raw” + (T)/sano-PV{D,T}Z+ “raw”.

Originally proposed⁴³ for the S66, the four types of HLCs are: (a)gold (employing [CCSD(F12*)-MP2-F12]/cc-pVQZ-F12 half-CP combined with (T)/haV{T,Q}Z half-CP), (b)silver (using [CCSD(F12*)-MP2-F12]/cc-pVTZ-F12 half-CP plus (T)/haV{D,T}Z half-CP), (c)sterling silver (combining [CCSD(F12*)-MP2-F12]/cc-pVTZ-F12 raw and (T)/sano-PV{D,T}Z+ raw), and (d)bronze (employing half-CP CCSD(F12*)(T_{c_{sc}})/cc-pVDZ-F12). In the present study, we adopt the “sterling silver”-level HLC on top of the full-CP corrected RI-MP2-F12/haV{T,Q}Z-F12 noncovalent nitration energies, i.e., RI-MP2-F12/CBS is combined with counterpoise uncorrected [CCSD(F12*)-MP2-F12]/cc-pVTZ-F12, and [CCSD(T)-CCSD]/sano-pV{D,T}Z+. The equation for final energy looks like this,

$$E_{Ref} = E_{MP2-F12/haV\{T,Q\}Z-F12}^{CP} + E_{[CCSD(F12*)-MP2-F12]/VTZ-F12}^{RAW} + E_{[CCSD(T)-CCSD]/sano-pV\{D,T\}Z+}^{RAW}$$

Table 2: Root-mean-square deviations (RMSDs, kcal/mol) of Hobza’s original, Martin’s revised (ref. ⁴²), and “bronze” standard S66x8 dissociation energies evaluated relative to the “sterling silver” reference. Together with full S66x8, we have also included the RMSDs for its four subsets (i.e., hydrogen bonds, π -stacking, London dispersion complexes, and mixed-influence interactions). Heatmapping is from red(worst) via yellow to green (best).

Old reference dissociation energies of S66x8		RMSD (kcal/mol)								
		Full S66x8	Intermolecular Distances							
			0.90r _e	0.95r _e	r _e	1.05r _e	1.10r _e	1.25r _e	1.50r _e	2.00r _e
Hobza ³⁷	Full S66x8	0.103	0.183	0.148	0.118	0.094	0.074	0.035	0.012	0.003
	Hydrogen Bonds	0.111	0.203	0.161	0.125	0.096	0.072	0.027	0.006	0.004
	π -stack	0.168	0.299	0.240	0.192	0.154	0.123	0.062	0.021	0.005
	London Dispersion	0.069	0.109	0.096	0.082	0.071	0.058	0.033	0.012	0.003
	Mixed Influence	0.062	0.104	0.088	0.073	0.061	0.050	0.027	0.009	0.002
Brauer ⁴²	Full S66x8	0.096	0.131	0.125	0.117	0.108	0.098	0.071	0.039	0.014
	Hydrogen Bonds	0.059	0.060	0.064	0.068	0.070	0.071	0.063	0.041	0.015
	π -stack	0.171	0.236	0.225	0.209	0.191	0.172	0.117	0.061	0.022
	London Dispersion	0.102	0.150	0.138	0.124	0.111	0.096	0.064	0.032	0.012
	Mixed Influence	0.072	0.101	0.095	0.087	0.080	0.071	0.049	0.027	0.010
Bronze ⁴³	Full S66x8	0.041	0.054	0.050	0.049	0.047	0.044	0.035	0.020	0.007
	Hydrogen Bonds	0.033	0.062	0.044	0.031	0.023	0.020	0.023	0.018	0.006
	π -stack	0.079	0.089	0.093	0.098	0.097	0.092	0.067	0.036	0.012
	London Dispersion	0.033	0.032	0.039	0.042	0.043	0.039	0.030	0.016	0.006
	Mixed Influence	0.024	0.025	0.027	0.029	0.029	0.029	0.022	0.013	0.005

Our best estimates of the S66x8 dissociation energies are listed in Table 1. Relative to the “sterling silver” standard dissociation energies, the RMS deviation for Hobza’s³⁷ original S66x8 reference is 0.103 kcal/mol, which marginally reduces to 0.096 kcal/mol for the revised reference proposed by Brauer *et al.*⁴² However, the “bronze” quality dissociation energies lately proposed by Kesharwani *et al.*⁴³ have only 0.041 kcal/mol deviation. Among the four subsets, the most significant contribution to the RMS error comes from the π -stack complexes. In general, the error is most prominent for the compressed geometries, which gets dramatically reduced for the relaxed cases (see Table 2).

As the present paper was being finalized for submission, a paper by Nagy, Kállay, and coworkers⁸⁷ was published in which they revisited the S66 reference energies at what they call a “14-karat” [sic] “gold” (14k-gold) level. Their levels of theory through CCSD are nearly identical to those used in the “silver” and “sterling silver” datasets of Ref.⁴³, but their (T) treatment is effectively that of the “gold” level (used only for a subset of 18 systems Ref.⁴³ owing to computational cost), namely CCSD(T)/haV{D,T}Z albeit with a DF approximation.

Essentially all of the discrepancies between “14k-gold” on the one hand and “silver” and “sterling silver” on the other hand can be attributed to the more economical triples corrections in these latter reference standards, namely CCSD(T)/haV{D,T}Z and CCSD(T)/sano-{D,T}Z+, respectively.

For the 18 systems where we were able to obtain “gold” answers in Ref.⁴³, the 14k-gold values of Nagy *et al.*⁸⁷ agree to 0.008 kcal/mol RMS. The “silver” is very close to both, with RMSD of just 0.011 kcal/mol from the “14k-gold” for the whole S66 set, and of just 0.006 kcal/mol from the “gold” for the subset of 18 systems where the latter is available. In contrast, the more

economical “sterling silver” level used for S66x8 in the present study deviates by a somewhat larger 0.027 kcal/mol from “14k-gold” for S66. For the 18-system “gold” subset, we find a not dissimilar 0.024 kcal/mol deviation.

Keeping also in mind residual uncertainties in other components, we conclude from the above that 0.03 kcal/mol RMS is a realistic estimate of the uncertainty in our revised S66x8 data.

a) LNO-CCSD(T)-based methods:

In Ref.⁶² we benchmarked the performance of pure and composite LNO-CCSD(T) methods with respect to the S66 noncovalent interaction energies (“silver” standard⁴³). In the present study, we investigate the performance of LNO-CCSD(T)-based methods for the S66x8 set using different basis sets and accuracy thresholds available.

Like Ref.⁶² here too, we find a consistent improvement of accuracy with the increase of basis set size and tightening of the threshold; counterpoise correction also offers an appreciable improvement (see upper blocks of Table 3). With vTight threshold and half-CP, the LNO-CCSD(T)/haV5Z is the best pick (0.056 kcal/mol) among the single basis set approaches tested here. Except for the “Normal” settings, the RMS deviations with half-CP are marginally better than the full-CP option for all other accuracy thresholds.

Irrespective of the choice of accuracy threshold, a two-point CBS extrapolation improves the RMS error statistics across the board. Among all the LNO-CCSD(T)/CBS methods listed in Table 3, the LNO-CCSD(T, vTight)/haV{T,Q}Z half-CP is the best pick (0.025 kcal/mol) for S66x8 noncovalent interactions. Interestingly, with the Normal setting and “raw” interaction energies, the low-cost LNO-CCSD(T)/haV{T,Q}Z outperforms LNO-CCSD(T)/haV{Q,5}Z, and gradually tightening the accuracy threshold narrows that performance gap. The LNO-CCSD(T)/CBS methods with half-CP always perform better than the full-CP counterparts.

Closer scrutiny of the performance of LNO-CCSD(T)/haVnZ methods for the subsets of S66x8 reveals that employing counterpoise correction makes things worse for the complexes with hydrogen bonds. A Full-CP correction is always preferred for the remaining three subsets. However, the trends are opposite for each subset when considering LNO-CCSD(T)/CBS interaction energies. With CBS extrapolation, the RMS deviations with half-CP are lower than the full-CP alternatives. Using the vTight threshold and half-CP, LNO-CCSD(T)/haV{T,Q}Z is the best pick for all four subsets of S66x8 (see the upper block of Table 3).

Let’s take a closer look at the composite LNO-CCSD(T) schemes (a.k.a, cLNOs⁶²) with different accuracy thresholds and basis sets. Regardless of using CP correction, the RMS deviations of all the cLNO methods are below 0.1 kcal/mol for the complete S66x8 set. With RMS error of 0.024 and 0.028 kcal/mol, respectively, vTight{T,Q} + 0.31[vvTight – vTight]/T half-CP and vTight{Q,5} + 0.71[vvTight – vTight]/T half-CP are the two best picks among eleven cLNOs listed in Table 3. However, the first cLNO scheme is clearly preferred due to the lower computational cost. Either with “raw” or half-CP, the most affordable composite scheme Normal{T,Q} + c₁[vTight – Normal]/T performs similar to the very expensive LNO-CCSD(T, vTight)/haV5Z half-CP.

Table 3: Root-mean-square deviations (RMSDs, kcal/mol) of pure and composite LNO-CCSD(T) methods with respect to the “sterling silver” reference. Heatmapping is from red(worst) via yellow to green (best).

Threshold	Basis set	RMSD (kcal/mol)																	
		Total			Hydrogen bonds			π stack			London Dispersion			Mixed Influence					
		Raw	CP	Half	Raw	CP	Half	Raw	CP	Half	Raw	CP	Half	Raw	CP	Half			
Normal	haVTZ	0.624	0.357	0.391	0.123	0.558	0.300	1.279	0.253	0.731	0.584	0.128	0.331	0.479	0.142	0.248			
	haVQZ	0.337	0.237	0.268	0.108	0.293	0.194	0.700	0.347	0.518	0.297	0.140	0.214	0.244	0.118	0.174			
	haV5Z	0.261	0.209	0.232	0.150	0.199	0.172	0.528	0.371	0.449	0.206	0.150	0.177	0.178	0.123	0.149			
	haV{T,Q}Z	0.169	0.221	0.193	0.133	0.131	0.131	0.328	0.436	0.381	0.127	0.172	0.144	0.101	0.166	0.131			
	haV{Q,5}Z	0.206	0.202	0.198	0.206	0.112	0.155	0.356	0.403	0.378	0.132	0.169	0.146	0.127	0.142	0.130			
Tight	haVTZ	0.515	0.320	0.268	0.111	0.492	0.228	1.030	0.195	0.477	0.501	0.133	0.236	0.408	0.171	0.165			
	haVQZ	0.208	0.150	0.140	0.047	0.231	0.130	0.425	0.111	0.245	0.192	0.066	0.110	0.160	0.061	0.086			
	haV5Z	0.123	0.106	0.104	0.071	0.149	0.109	0.245	0.115	0.174	0.098	0.063	0.072	0.087	0.046	0.061			
	haV{T,Q}Z	0.061	0.087	0.065	0.078	0.067	0.072	0.069	0.151	0.101	0.050	0.068	0.041	0.035	0.071	0.042			
	haV{Q,5}Z	0.085	0.084	0.079	0.118	0.070	0.091	0.085	0.141	0.109	0.068	0.076	0.067	0.037	0.063	0.045			
vTight	haVTZ	0.492	0.297	0.224	0.144	0.441	0.177	0.977	0.191	0.419	0.468	0.160	0.186	0.392	0.181	0.137			
	haVQZ	0.177	0.112	0.092	0.048	0.169	0.071	0.363	0.057	0.179	0.158	0.069	0.070	0.138	0.058	0.056			
	haV5Z	0.081	0.063	0.056	0.017	0.092	0.049	0.171	0.047	0.105	0.065	0.048	0.038	0.064	0.027	0.035			
	haV{T,Q}Z	0.042	0.045	0.025	0.028	0.021	0.019	0.051	0.086	0.029	0.059	0.038	0.037	0.037	0.039	0.018			
	haV{Q,5}Z	0.044	0.044	0.033	0.047	0.025	0.033	0.051	0.082	0.039	0.053	0.039	0.042	0.028	0.038	0.023			
vvTight	haVTZ	0.496	0.281	0.220	0.168	0.418	0.158	0.979	0.178	0.421	0.473	0.148	0.187	0.394	0.173	0.138			
	Coefficients			Composite Methods (cLNO)															
	c ₁																	c ₂	
	Raw	CP	Half																
Normal{T,Q} + c ₁ [vTight – Normal]/T	0.93	1.06	1.02	-----	0.057	0.083	0.059	0.037	0.066	0.044	0.068	0.115	0.077	0.085	0.093	0.078	0.044	0.075	0.048
Normal{Q,5} + c ₁ [vTight – Normal]/T	1.09	0.96	1.03	-----	0.085	0.082	0.068	0.084	0.068	0.055	0.080	0.113	0.078	0.095	0.094	0.083	0.083	0.068	0.066
Tight{T,Q} + c ₁ [vTight – Tight]/T	0.79	1.04	0.95	-----	0.045	0.057	0.037	0.040	0.034	0.030	0.048	0.093	0.046	0.061	0.058	0.049	0.037	0.052	0.030
Tight{T,Q} + c ₁ [vvTight – Tight]/T	0.72	0.78	0.78	-----	0.039	0.061	0.035	0.029	0.042	0.028	0.044	0.106	0.052	0.053	0.047	0.037	0.034	0.056	0.030
Tight{Q,5} + c ₁ [vTight – Tight]/T	1.26	0.84	1.05	-----	0.056	0.065	0.053	0.054	0.038	0.041	0.052	0.094	0.053	0.079	0.093	0.084	0.038	0.048	0.036
Tight{Q,5} + c ₁ [vTight – Tight]/Q	1.14	0.89	1.07	-----	0.060	0.064	0.051	0.061	0.034	0.037	0.052	0.090	0.050	0.083	0.093	0.082	0.040	0.049	0.037
Tight{Q,5} + c ₁ [vvTight – Tight]/T	1.11	0.67	0.9	-----	0.045	0.065	0.047	0.038	0.042	0.034	0.043	0.102	0.055	0.068	0.080	0.070	0.034	0.051	0.035
Tight{Q,5} + c ₁ [vvTight – vTight]/T	3.28	0.68	1.81	-----	0.051	0.080	0.064	0.049	0.060	0.060	0.071	0.139	0.101	0.054	0.070	0.054	0.038	0.065	0.047
Tight{Q,5} + c ₁ [vvTight – vTight]/T + c ₂ [vTight – Tight]/Q	2.45	0.22	0.95	0.59 (Raw) 0.86 (CP) 0.88 (Half)	0.043	0.063	0.046	0.038	0.035	0.034	0.047	0.092	0.054	0.059	0.089	0.068	0.034	0.049	0.036
vTight{T,Q} + c ₁ [vvTight-vTight]/T	0.77	-0.02	0.31	-----	0.039	0.045	0.024	0.019	0.021	0.019	0.052	0.086	0.028	0.053	0.038	0.035	0.036	0.039	0.018
vTight{Q,5} + c ₁ [vvTight-vTight]/T	1.55	0.12	0.71	-----	0.030	0.044	0.028	0.019	0.024	0.023	0.039	0.083	0.035	0.043	0.038	0.035	0.025	0.038	0.023

In special cases, where a counterpoise correction is impossible (e.g., intramolecular or conformer interactions), the composite method, $\text{vTight}\{\text{Q},5\} + 1.55[\text{vvTight} - \text{vTight}]/\text{T}$ offers excellent performance (0.030 kcal/mol). Another low-cost alternative for such situations, is the $\text{Tight}\{\text{T},\text{Q}\} + 0.72[\text{vvTight} - \text{Tight}]/\text{T}$ scheme (0.039 kcal/mol). Without CP corrections, the two-tier scheme, $\text{Tight}\{\text{T},\text{Q}\} + 0.72[\text{vvTight} - \text{Tight}]/\text{T}$ marginally outperforms more expensive three-tier method, $\text{Tight}\{\text{Q},5\} + 2.45[\text{vvTight} - \text{vTight}]/\text{T} + 0.59[\text{vTight} - \text{Tight}]/\text{Q}$, which is contrary to what we observed for S66 in a previous study.⁶² With half-CP, a relatively low-cost method, $\text{Tight}\{\text{T},\text{Q}\} + 0.95[\text{vTight} - \text{Tight}]/\text{T}$ offers very good accuracy (0.037 kcal/mol) when compared to the “sterling silver” level S66x8 interaction energies.

b) PNO-LCCSD(T)-based methods:

The RMS deviations for the pure and composite PNO-LCCSD(T) methods using different basis sets and accuracy thresholds are listed in Table 4.

Overall, the counterpoise uncorrected results indicate a consistent improvement in accuracy with increasing basis set size for any threshold. Among the PNO-LCCSD(T)/haVnZ methods, PNO-LCCSD(T, Tight)/haVQZ offers the best performance (0.071 kcal/mol), followed by PNO-LCCSD(T, Default)/haV5Z (0.075 kcal/mol). Further investigation reveals that the former method is better for the hydrogen-bonded systems and London dispersion complexes, whereas the latter is preferred for the π -stack. Using a full-CP correction worsens performance across the board. However, half-CP can still perform close to the “raw” accuracy with a large basis set. Now, comparing the performance of “raw” and half-CP variants of PNO-LCCSD(T, Tight)/haVQZ for the four subsets of S66x8, we have found that for the hydrogen bonding complexes, half-CP is preferred, but for the π -stack dimers, “raw” variant offers significantly better accuracy than its half-CP counterpart. For the London dispersion and mixed influence dimers, there is very little to choose from these two methods (see Table 4).

Now, what is the effect of CBS extrapolation? Both the $\text{haV}\{\text{T},\text{Q}\}\text{Z}$ and $\text{haV}\{\text{Q},5\}\text{Z}$, in combination with the full-CP and Default threshold, perform remarkably well (0.027 and 0.028 kcal/mol, respectively). Except for the hydrogen bonding subset, the computationally more expensive PNO-LCCSD(T, Default)/ $\text{haV}\{\text{Q},5\}\text{Z}$ is preferred for the remaining three subsets of S66x8. Using a tighter threshold marginally improves the accuracy of PNO-LCCSD(T)/ $\text{haV}\{\text{T},\text{Q}\}\text{Z}$ (0.020 kcal/mol). Hence, irrespective of the choice of accuracy threshold, the standard PNO-LCCSD(T)/CBS methods with full-CP perform similar to the best cLNO schemes.

Table 4: Root-mean-square deviations (RMSDs, kcal/mol) of the pure and composite PNO-LCCSD(T) methods with respect to the “sterling silver” reference. Heatmapping is from red(worst) via yellow to green (best).

Threshold	Basis Set	RMSD (kcal/mol)														
		Total			Hydrogen bonds			π stack			London Dispersion			Mixed Influence		
		Raw	CP	Half	Raw	CP	Half	Raw	CP	Half	Raw	CP	Half	Raw	CP	Half
Default	haVTZ	0.132	0.428	0.258	0.180	0.550	0.363	0.132	0.438	0.197	0.105	0.333	0.204	0.069	0.299	0.150
	haVQZ	0.098	0.175	0.136	0.120	0.225	0.172	0.112	0.183	0.147	0.094	0.139	0.116	0.059	0.115	0.086
	haV5Z	0.075	0.099	0.086	0.089	0.129	0.109	0.095	0.106	0.101	0.064	0.074	0.069	0.046	0.061	0.053
	haV{T,Q}Z	0.131	0.027	0.072	0.085	0.021	0.051	0.236	0.042	0.130	0.118	0.028	0.068	0.105	0.024	0.051
	haV{Q,5}Z	0.056	0.028	0.040	0.063	0.035	0.047	0.083	0.037	0.058	0.040	0.020	0.028	0.037	0.018	0.025
Tight	haVTZ	0.299	0.362	0.163	0.061	0.486	0.237	0.651	0.315	0.172	0.220	0.278	0.091	0.219	0.247	0.055
	haVQZ	0.071	0.143	0.072	0.037	0.190	0.109	0.156	0.137	0.028	0.047	0.111	0.052	0.041	0.094	0.033
	haV{T,Q}Z	0.103	0.020	0.055	0.062	0.015	0.032	0.189	0.032	0.106	0.092	0.021	0.050	0.084	0.019	0.040
	Coefficients (c_i)			Composite Methods (cPNO)												
	Raw	CP	Half													
Default{T,Q} + c_1 [Tight – Default]/T		0.39	0.07	0.34	0.054	0.027	0.035	0.031	0.019	0.021	0.101	0.041	0.066	0.045	0.027	0.031
Default{Q,5} + c_1 [Tight – Default]/T		0.15	0.2	0.16	0.034	0.024	0.027	0.039	0.025	0.030	0.049	0.033	0.039	0.026	0.020	0.022
Default{Q,5} + c_1 [Tight – Default]/Q		0.33	0.47	0.36	0.033	0.024	0.027	0.038	0.024	0.029	0.047	0.031	0.037	0.026	0.021	0.023
Tight{T,Q} + c_1 [Tight – Default]/T		0.3	0.02	0.25	0.049	0.020	0.029	0.029	0.015	0.020	0.090	0.030	0.053	0.043	0.021	0.026
Tight/{T,Q} + c_1 [Tight – Default]/Q		0.66	0.03	0.56	0.049	0.020	0.029	0.030	0.015	0.021	0.088	0.031	0.051	0.044	0.020	0.026

Table 5: Root-mean-square deviations (RMSDs, kcal/mol) of the pure and composite DLPNO-CCSD(T₁) methods with respect to the “sterling silver” reference. Heatmapping is from red(worst) via yellow to green (best).

Threshold	Basis set	T _{Cut} PNO	RMSD (kcal/mol)														
			Total			Hydrogen bonds			π stack			London Dispersion			Mixed Influence		
			Raw	CP	Half	Raw	CP	Half	Raw	CP	Half	Raw	CP	Half	Raw	CP	Half
Normal	haVTZ	default (i.e., 3.33×10^{-7})	0.604	0.515	0.453	0.264	0.799	0.525	1.296	0.318	0.770	0.413	0.263	0.196	0.411	0.218	0.199
	haVQZ		0.368	0.353	0.342	0.309	0.504	0.405	0.737	0.417	0.570	0.186	0.152	0.143	0.205	0.133	0.148
	haV{T,Q}Z		0.267	0.286	0.275	0.345	0.316	0.330	0.392	0.500	0.446	0.133	0.126	0.124	0.106	0.140	0.121
Tight	haVTZ	default (i.e., 1.0×10^{-7})	0.410	0.419	0.217	0.080	0.572	0.290	0.806	0.395	0.263	0.404	0.297	0.134	0.341	0.262	0.115
	haVTZ	1.0×10^{-6}	0.309	0.563	0.283	0.154	0.716	0.428	0.600	0.616	0.181	0.268	0.445	0.163	0.246	0.371	0.139
	haVTZ	CPS or $1.0E-\{6,7\}$	0.501	0.320	0.231	0.136	0.466	0.191	0.964	0.242	0.403	0.511	0.195	0.205	0.417	0.186	0.159
	haVQZ	1.0×10^{-7}	0.124	0.215	0.128	0.085	0.284	0.181	0.213	0.235	0.115	0.114	0.151	0.080	0.106	0.131	0.075
	haV{T,Q}Z	1.0×10^{-7}	0.146	0.095	0.117	0.133	0.100	0.116	0.236	0.141	0.184	0.127	0.068	0.093	0.106	0.075	0.085
	haV{T,Q}Z	CPS or $10E-\{6,7\}$	0.214	0.158	0.184	0.198	0.168	0.183	0.340	0.236	0.286	0.197	0.128	0.160	0.152	0.105	0.126
VeryTight	haVTZ	10×10^{-8}	0.402	0.379	0.176	0.102	0.510	0.232	0.806	0.345	0.243	0.378	0.291	0.093	0.321	0.247	0.073
	Coefficients		Composite Methods (cDLPNO)														
	Raw	CP	Half														
Normal{T,Q} + c_1 [Tight – Normal]/T			0.90	0.94	0.92	0.104	0.091	0.096	0.124	0.101	0.112	0.148	0.134	0.139	0.076	0.073	0.073
Normal/{T,Q} + c_1 [Tight/CPS – Normal]/T			0.90	0.97	0.93	0.076	0.080	0.076	0.052	0.046	0.043	0.101	0.114	0.107	0.096	0.089	0.093
$(T_0)Tight/Q + c_1[(T_0)Tight/Q - (T_0)Tight/T] + c_2[(T_1)Tight/T - (T_0)Tight/T]$			$c_1=0.61$ $c_2=3.33$	$c_1=0.93$ $c_2=1.33$	$c_1=0.95$ $c_2=3.40$	0.079	0.068	0.072	0.094	0.042	0.067	0.094	0.101	0.100	0.055	0.053	0.046
Tight{T,Q} + c_1 [Tight – Normal]/T			-0.11	-0.03	-0.08	0.143	0.097	0.116	0.162	0.110	0.137	0.185	0.131	0.149	0.128	0.067	0.090
Tight{T,Q} + c_1 [vTight – Tight]/T			1.02	1.10	1.11	0.128	0.059	0.090	0.080	0.045	0.059	0.211	0.079	0.142	0.139	0.058	0.097
Tight/{T,Q}/CPS + c_1 [Tight/CPS – Normal]/T			0.16	0.08	0.10	0.151	0.183	0.201	0.113	0.157	0.176	0.286	0.315	0.345	0.115	0.158	0.162

Unlike cLNOs, we have not found any significant improvement in accuracy when PNO-LCCSD(T)-based composite schemes (i.e., cPNOs) are considered instead of the standard PNO-LCCSD(T)/haVnZ or PNO-LCCSD(T)/CBS methods with full-CP. However, for special cases where counterpoise correction is not applicable (in other words using “raw” energies), the composite methods outperform the standard PNO-LCCSD(T) alternatives. With RMS deviations of 0.033 and 0.034 kcal/mol, respectively, $\text{Default}\{Q,5\} + 0.15[\text{Tight} - \text{Default}]/T$ and $\text{Default}\{Q,5\} + 0.33[\text{Tight} - \text{Default}]/Q$ are the two best picks in the counterpoise uncorrected category. In the same vein, comparing the top performers from the “raw” cLNO and cPNO schemes, we have found that for hydrogen bonding and π -stack complexes, cLNOs are preferred, whereas cPNOs offer better accuracy for London dispersion complexes. For the mixed influence subset, there is very little to choose between cLNO and cPNO.

c) DLPNO-CCSD(T₁)-based methods:

Table 5 summarizes the RMSDs of the pure and composite DLPNO-CCSD(T₁) methods for different basis sets, accuracy thresholds, and T_{cutPNO} combinations.

The “raw” results indicate a gradual improvement of accuracy with increasing basis set size and tightening of the thresholds, provided that we use the default T_{cutPNO} (i.e., 3.33×10^{-7} and 1.0×10^{-7} for Normal and TightPNO, respectively). Moving from “raw” to full-CP correction further improves the performance of DLPNO-CCSD(T₁, Normal)/haVTZ, but stays more or less indifferent when haVQZ is employed. However, while using the Tight threshold, the performance of “raw” and full-CP DLPNO-CCSD(T₁)/haVTZ are comparable, but with haVQZ basis set, “raw” performs better.

Interestingly, the strategy of using the threshold $T_{\text{cutPNO}} = 1.0 \times 10^{-6}$ in TightPNO and a haVTZ basis set offers the best performance (0.309 kcal/mol) for “raw” interaction energies. The RMS error counterintuitively increases as the T_{cutPNO} parameter becomes tighter. When CP correction is included, we observe the reverse trend. Irrespective of the choice of T_{cutPNO} , half-CP correction is more beneficial than full-CP. With the same basis set, tightening the accuracy threshold further (i.e., VeryTightPNO) is only beneficial for half-CP. Using a more extensive basis set and default T_{cutPNO} improves accuracy throughout, with and without CP correction. Although “raw” DLPNO-CCSD(T₁, Tight)/haVTZ underperforms “raw” DLPNO-CCSD(T₁, Tight)/haVQZ for π -stacks, London dispersion, and mixed influence subsets, these two methods offer similar performance for H-bonds.

Now, what is the effect of CBS extrapolation? Except for the hydrogen bonding, we noticed an improvement in performance across the board when the Normal threshold is employed. By tightening the accuracy threshold further, we found that CBS extrapolation does more harm than good for “raw” but improves the performance for full and half-CP. With full-CP correction, the DLPNO-CCSD(T₁, Tight)/haV{T,Q}Z (0.095 kcal/mol) is the best pick among the pure methods, followed by its half-CP version (0.117 kcal/mol). The use of DLPNO-CCSD(T₁, Tight)/CPS/haVTZ interaction energies for two-point CBS extrapolation worsen the performance.

Among the counterpoise-uncorrected DLPNO-CCSD(T_1)-based composite schemes, a relatively low-cost composite method, Normal/{T,Q} + 0.90[Tight/CPS – Normal]/T offers the best accuracy (0.076 kcal/mol). The use of counterpoise correction has no additional benefit. However, with full-CP, Tight/{T,Q} + 1.1[vTight – Tight]/T perform marginally better than Normal/{T,Q} + c_1 [Tight/CPS – Normal]/T. With an RMS error of 0.059 kcal/mol, the full CP corrected composite method, Tight/{T,Q} + 1.1[vTight – Tight]/T is the best pick among all the pure and composite DLPNO-CCSD(T_1) listed in Table 5.

DLPNO-CCSD(T_1) is much more demanding in terms of I/O storage and bandwidth requirements than DLPNO-CCSD(T_0), and this will hold especially true for the largest basis sets. It was previously observed by Iron and Janes^{57,58} and by Efremenko and Martin,⁵⁵ both in the context of organometallic catalysis, that the (T_1) – (T_0) difference is relatively insensitive to the basis set; hence, we considered here a two-tier composite method, DLPNO-CCSD(T_0)/haVQZ + c_1 [DLPNO-CCSD(T_0)/haVQZ – DLPNO-CCSD(T_0)/haVTZ] + c_2 [DLPNO-CCSD(T_1)/haVTZ – DLPNO-CCSD(T_0)/haVTZ], where the CBS extrapolation is carried out at the DLPNO-CCSD(T_0) level and the (T_1) – (T_0) difference is evaluated in a smaller basis set. With a root-mean-square error of 0.079 kcal/mol, the performance of this type cDLPNO-scheme is comparable to the best pick in the “raw” category, Normal/{T,Q} + 0.90[Tight/CPS – Normal]/T. While using counterpoise-uncorrected energies, the optimized coefficient for the (T_1) – (T_0) contribution is anomalously large ($c_2=3.33$). However, with full-CP correction, the c_2 is reduced to 1.33, and the RMS error improves to 0.068 kcal/mol, which is not very far from the accuracy of the more expensive DLPNO-CCSD(T_1)-based composite method, Tight/{T,Q} + 1.1[vTight – Tight]/T (see Table 5). These two-tier cDLPNO methods may be an attractive option for larger systems.

d) How far can we go with canonical CCSD(T)?

We could do the canonical CCSD(T) calculations with density fitting and haVnZ (n=D and T) basis set for the whole S66x8 set. Relative to the “sterling silver” reference, DF-CCSD(T)/haVDZ offers RMS deviations of 1.16, 0.90, and 0.53 kcal/mol with “raw”, full-CP, and half-CP correction, respectively. Except for NCIs involving hydrogen bonds, CP correction is beneficial across the board. Using a larger basis set improves RMSDs substantially, and on top of that, a two-point CBS extrapolation (using Schwenke’s⁸⁸ formula) further ameliorates the statistics. With full-CP, DF-CCSD(T)/haV{D,T}Z offers an RMS deviation of 0.11 kcal/mol. For π -stack, London dispersion, and mixed influence subsets, full-CP performs noticeably better than the “raw” and half-CP. The only exceptions are the H-bonded systems, where half-CP wins the race. Compared to the “sterling silver” level HLC, the canonical [CCSD(T)-MP2]/haVTZ energies offer RMS errors of 0.04, 0.05, and 0.07 kcal/mol with “raw”, full, and half CP correction.

Now, let us compare the performance of different localized coupled cluster methods relative to the canonical DF-CCSD(T) interaction energies. LNO-CCSD(T) with vTight and vvTight settings perform remarkably if we do not use any CP correction. Irrespective of the choice of accuracy threshold, full-CP correction is beneficial for the pure PNO-CCSD(T) methods, but they are not even close to “raw” LNO-CCSD(T)/vTight. However, with full CP correction, the PNO-

based composite plan, Tight + A(Tight–Default), offers accuracy similar to “raw” LNO-CCSD(T)/vTight. For DLPNO-CCSD(T₁), it does not make a big difference whether we use counterpoise correction or not (see Table 6).

Table 6: Root-mean-square deviations (RMSDs, kcal/mol) of different localized orbital coupled cluster methods with respect to the canonical DF-CCSD(T)/haVTZ level interaction energies of S66x8. Raw, CP, and half-CP represents the counterpoise uncorrected, full-, and half-CP corrected results. Δ CP represents the size of the counterpoise correction; $\Delta\Delta$ CP is the deviation between Δ CP with this particular localized method and with canonical CCSD(T).

Methods	Coefficient (A)		RMSD(kcal/mol)				
			Total S66x8	Hydrogen bonds	π stack	London Dispersion	Mixed Influence
PNO-CCSD(T)/default		raw	0.504	0.325	0.883	0.533	0.378
		CP	0.136	0.112	0.229	0.120	0.107
		half-CP	0.319	0.218	0.556	0.326	0.242
		$\Delta\Delta$ CP	0.371	0.215	0.655	0.415	0.273
PNO-CCSD(T)/Tight		raw	0.232	0.138	0.344	0.300	0.193
		CP	0.065	0.044	0.111	0.064	0.053
		half-CP	0.147	0.091	0.226	0.182	0.122
		$\Delta\Delta$ CP	0.171	0.096	0.238	0.238	0.143
Tight + A(Tight–Default)	0.605	raw	0.143	0.063	0.237	0.187	0.111
	0.781	CP	0.028	0.020	0.048	0.026	0.023
	0.653	half-CP	0.082	0.035	0.142	0.104	0.063
	0.516	$\Delta\Delta$ CP	0.123	0.059	0.188	0.168	0.098
DLPNO-CCSD(T ₁)/Tight		raw	0.134	0.146	0.195	0.115	0.086
		CP	0.123	0.135	0.190	0.088	0.074
		half-CP	0.128	0.140	0.192	0.100	0.080
		$\Delta\Delta$ CP	0.023	0.018	0.014	0.036	0.022
DLPNO-CCSD(T ₁)/Tight T _{CutPNO} =1.0×10 ^{−6}		raw	0.279	0.282	0.410	0.261	0.190
		CP	0.268	0.279	0.407	0.231	0.176
		half-CP	0.273	0.280	0.408	0.246	0.183
		$\Delta\Delta$ CP	0.022	0.016	0.017	0.035	0.020
DLPNO-CCSD(T ₁)/VeryTight		raw	0.106	0.087	0.161	0.119	0.080
		CP	0.081	0.070	0.137	0.079	0.053
		half-CP	0.093	0.078	0.149	0.099	0.066
		$\Delta\Delta$ CP	0.029	0.018	0.028	0.043	0.029
DLPNO-CCSD(T ₁)/Tight CPS or T _{CutPNO} =1.0E−{6,7}		raw	0.058	0.054	0.085	0.055	0.048
		CP	0.062	0.043	0.088	0.070	0.059
		half-CP	0.059	0.047	0.086	0.060	0.052
		$\Delta\Delta$ CP	0.026	0.022	0.018	0.038	0.024
LNO-CCSD(T)/Normal		raw	0.179	0.167	0.328	0.131	0.093
		CP	0.225	0.138	0.375	0.262	0.175
		half-CP	0.196	0.150	0.351	0.184	0.132
		$\Delta\Delta$ CP	0.111	0.064	0.068	0.193	0.096
LNO-CCSD(T)/Tight		raw	0.068	0.088	0.091	0.043	0.031
		CP	0.102	0.061	0.132	0.154	0.076
		half-CP	0.076	0.072	0.111	0.086	0.050
		$\Delta\Delta$ CP	0.081	0.048	0.051	0.147	0.061
LNO-CCSD(T)/vTight		raw	0.029	0.034	0.033	0.031	0.019
		CP	0.051	0.016	0.065	0.084	0.039
		half-CP	0.029	0.018	0.046	0.035	0.023
		$\Delta\Delta$ CP	0.060	0.039	0.044	0.107	0.042
LNO-CCSD(T)/vvTight		raw	0.015	0.010	0.020	0.021	0.012
		CP	0.056	0.035	0.062	0.090	0.041
		half-CP	0.027	0.017	0.039	0.037	0.021
		$\Delta\Delta$ CP	0.061	0.040	0.048	0.108	0.044
DF-CCSD(T)		Δ CP	0.722	0.585	1.165	0.688	0.581

e) Some remarks on the evaluation of more approximate methods, such as DFT functionals and SAPT(DFT):

The revised reference data prompt the question: to what extent do the revised values affect or modify prior observations (e.g., in Ref.⁴²) on the performance of DFT functionals for the S66x8 dataset.

The easiest way to see this would be to take the Excel workbook in the ESI of the said paper, splice in our now reference data, and compare the published tables in the paper with the dynamic versions in leaf “Summary” of the ESI, particularly for Tables 14 and 15.

Generally speaking, the conclusions from Ref.⁴² are unaffected: for instance, the RMSDs for BLYP-D3BJ and BP86-D3BJ with the def2-QZVP⁸⁹ basis set and full counterpoise change from 0.23 and 0.58 kcal/mol, respectively, to 0.22 and 0.65 kcal/mol, does not affect the superiority of BLYP over BP86 in this context. (The corresponding changes for B3LYP-D3BJ and PBE0-D3BJ are from 0.20 and 0.35 kcal/mol, respectively, to 0.23 and 0.36 kcal/mol.) Among double hybrids, all with haVQZ basis set and half-counterpoise, B2PLYP-D3BJ⁹⁰ and B2GP-PLYP-D3BJ⁹¹ actually improve from 0.19 and 0.22 kcal/mol to 0.15 and 0.18 kcal/mol, respectively, while DSD-PBEP86-D3BJ⁹² deteriorates from 0.20 to 0.26 kcal/mol. However, we previously found the revised version of the latter, revDSD-PBEP86-D3BJ,⁹³ to be an improvement over DSD-PBEP86-D3BJ across the board, and this is also seen here for the new S66x8 reference, RMSD=0.19 kcal/mol. Using the more up-to-date D4⁹⁴ dispersion correction, this latter RMSD drops to 0.17 kcal/mol for revDSD-PBE86-D4. With RMSD of 0.10 kcal/mol, dRPA75⁹⁵ with a custom-fitted⁴² D3BJ correction was the best performer in Ref.⁴² and continues to be so here (0.12 kcal/mol).

As a parenthetical remark, the combinatorially optimized, range-separated hybrid, ω B97M-V⁹⁶ and double hybrid, ω B97M(2)⁹⁷ functionals were not yet available to us when Ref.⁴² was published; we find here 0.15 and 0.14 kcal/mol root-mean-square deviations relative to the new reference, respectively. It means ω B97M-V outperforms all other rung 4 functionals, plus all rung 5 functionals considered in Ref.⁴² other than dRPA75-D3BJ and ω B97M(2).

DFT(SAPT),⁹⁸ i.e., symmetry-adapted perturbation theory⁹⁹ using DFT orbitals, has recently gained some currency as a relatively low-cost/high-accuracy approach for noncovalent interactions. Heßelmann¹⁰⁰ applied such approaches to S66x8, using asymptotically corrected PBE0ac orbitals and three different response kernels, namely ALDA (adiabatic local density approximation), TDEXX (time-dependent exact exchange), and ATDEXX (adiabatic TDEXX). The RMSD between Table 5 of his ESI and the present “sterling silver” reference data is 0.224 kcal/mol using ALDA, but this drops to 0.150 kcal/mol for TDEXX and slightly further to 0.136 kcal/mol for ATDEXX. Most of the improvement results from the π -stacked subset (see Supporting Information for details); suffice to say that both TDEXX and ATDEXX are competitive with the best DFT functionals considered here, and not much inferior to previous wavefunction calculation sets.

IV. Conclusions:

We have successfully calculated the “sterling silver” standard noncovalent interaction energies of the S66x8 set. Analyzing the RMS errors of three other S66x8 reference dissociation energies available in the literature, we can safely conclude that the “sterling silver” reference energies are markedly better than Hobza’s original ones³⁷ as well as the earlier revised version proposed by our group,⁴² but only marginally better than the “bronze”⁴³ level dissociation energies.

Additionally, examining the RMS deviations of a variety of pure and composite localized coupled cluster methods for the new S66x8 reference, we can conclude the following:

- i) With half-CP, LNO-CCSD(T, vTight)/haV{T,Q}Z is among the top performers of all the pure and composite LNO-CCSD(T) methods tested. Although none of the low-cost cLNO methods are as good as the expensive LNO-CCSD(T,vTight)/haV{T,Q}Z half-CP, the $\text{Tight}\{T,Q\} + 0.95[\text{vTight} - \text{Tight}]/T$ half-CP is a viable alternative if someone is restricted to limited computational resources. Especially for London dispersion, the low-cost $\text{Tight}\{T,Q\} + 0.78[\text{vvTight} - \text{Tight}]/T$ half-CP offers accuracy comparable to the more expensive LNO-CCSD(T, vTight)/haV{T,Q}Z half-CP or $\text{vTight}\{T,Q\} + 0.31[\text{vvTight} - \text{vTight}]/T$ half-CP. For the intramolecular interactions, where counterpoise correction is not practical, we can safely recommend the composite method, $\text{vTight}\{T,Q\} + 0.72[\text{vvTight} - \text{vTight}]/T$.
- ii) Even with the Default threshold, PNO-LCCSD(T)/haV{T,Q}Z full-CP performs remarkably sound — which gets even better with a tighter threshold. This remarkable result of the PNO-LCCSD(T, Tight)/haV{T,Q}Z full-CP could be due to the benefits from fortuitous error compensation. Using a composite scheme does not have any added advantage over the pure PNO-LCCSD(T) methods. However, for the intramolecular interactions, the low-cost cPNO method, $\text{Default}\{Q,5\} + 0.15[\text{Tight} - \text{Default}]/T$ still has the edge over the pure methods due to its superiority for the π stack complexes.
- iii) Even with CPS and CBS extrapolation, the pure DLPNO-CCSD(T₁) methods are not up to the mark for S66x8 noncovalent interactions. An RMS deviation of 0.059 kcal/mol is the best accuracy we can achieve by employing a composite scheme, which is well behind the best picks among the PNO or LNO-based composite methods.

Finally, we can safely recommend the low-cost PNO-LCCSD(T, Default)/haV{T,Q}Z full-CP as a viable alternative to canonical CCSD(T). For the special cases where any kind of CP correction is not possible, we recommend the composite cPNO and cLNO methods, $\text{Default}\{Q,5\} + 0.15[\text{Tight} - \text{Default}]/T$ and $\text{Tight}\{T,Q\} + 0.72[\text{vvTight} - \text{Tight}]/T$, respectively.

Among more economical methods, the highest accuracies are seen for dRPA75-D3BJ, ω B97M-V, ω B97M(2), revDSD-PBEP86-D4, and DFT(SAPT) with a TDEXX or ATDEXX kernel.

Conflicts of Interest:

The authors declare no conflicts of interest.

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Supporting Information:

The Supporting Information is available free of charge at <https://doi.org/10.yyyy/xxxxxxx>.

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