Supporting Information

Accurate Treatment of Large Supramolecular Complexes by Double-Hybrid Density Functionals Coupled with Nonlocal van der Waals Corrections

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The L7 test set proposed by Sedlak *et al.*[1] contains seven supramolecular complexes intentionally selected to be mostly dispersion-dominated (aliphatic-aliphatic and π–π interactions) and their size ranges from 48 to 112 atoms (Figure S1). The dataset contains the following supramolecular complexes: **CBH**, the octadecane dimer in a stacked parallel conformation with closest contacts between the hydrogen atoms of 2.42 Å (aliphatic dispersion-dominated interaction); **GGG**, a stacked guanine trimer positioned as in the DNA chain (aromatic stacking π–π dispersion interaction); **GCGC**, a stacked Watson-Crick H-bonded guanine-cytosine dimer arranged as in DNA (strong aromatic dispersion interaction with implicit H-bonding-stacking, the binding energy between the two G–C pairs is evaluated); **PHE**, an amyloid fragment consisting in three phenylalanine residues in mixed H-bonded-stacked conformation ("mixed-character" interaction: H-bond and π–π dispersion forces); **C3A**, a stacked circumcoronene–adenine dimer (strong aromatic dispersion interaction); **C3GC**, a stacked circumcoronene and Watson-Crick hydrogen-bonded guanine–cytosine dimer (strong aromatic dispersion interaction with implicit H-bonding-stacking, the binding energy between the circumcoronene and the G–C pair is evaluated); and **C2C2PD**, a parallel-displaced stacked coronene dimer (strong aromatic dispersion interaction). The geometry of the different supramolecular dimers were obtained from Ref. 1.

The S12L dataset proposed by Grimme *et al.*[2] includes twelve supramolecular complexes (involving both neutral and charged species) dominated by non-polar, π–stacking, H-bonding, and electrostatic cation-dipolar interactions (Figure S2). The supramolecular complexes included in this test set range from 86 to 177 atoms and are classified as follows: **2a** and **2b**,[3] a tweezer-like host that bears tetracyanoquinodimethane (TCNQ) and 1,4-dicyanobenzene, respectively (governed by non-polar dispersion interactions); **3a** and **3b**,[4] two pincer-like complexes of organic π systems (π–π dispersion interaction); **4a** and **4b**,[5] the so-called buckycatcher hosting fullerene C_{60} and C_{70}, respectively (π–π dispersion forces); **5a** and **5b**,[6] an amide macrocycle that binds benzoquinone (BQ) and glycine anhydride, respectively (H-bond interaction); **6a** and **6b**,[7] the cucurbit[6]uril (CB6) cation complexes of butylammonium (BuNH4) and propylammonium (PrNH4), respectively (cation-dipolar interaction); **7a**,[8] the cucurbit[7]uril host forming an extremely stable inclusion complex with the dicationic ferrocene derivative bis(trimethylammoniomethyl)ferrocene (FECP, cation-dipolar interaction); and **7b**,[8] the cucurbit[7]uril host with 1-hydroxyadamantane (ADOH) as guest (H-bond interaction).

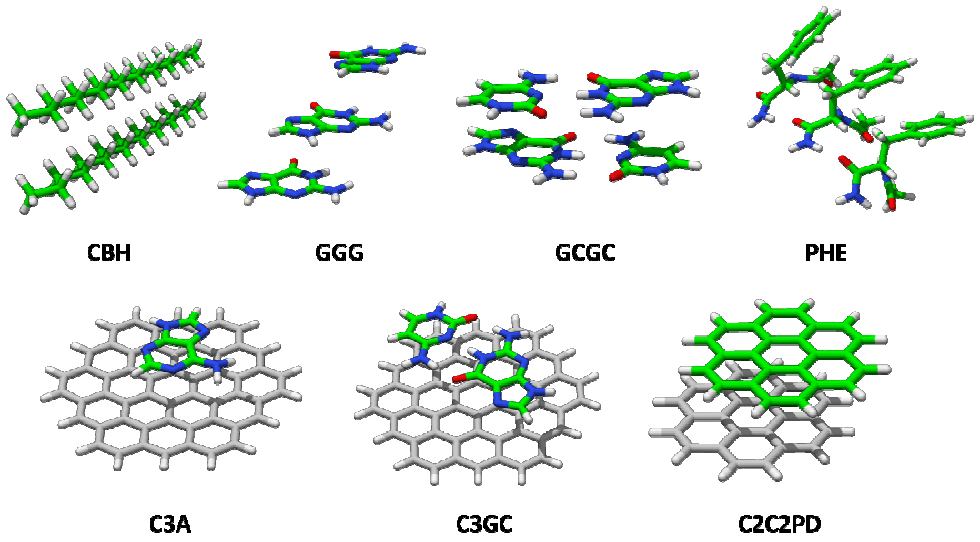


Figure S1. Structures of the supramolecular complexes constituting the L7 dataset. Color code: C in green, H in white, N in blue and O in red. Graphene-like C sheets are colored in gray for best viewing.

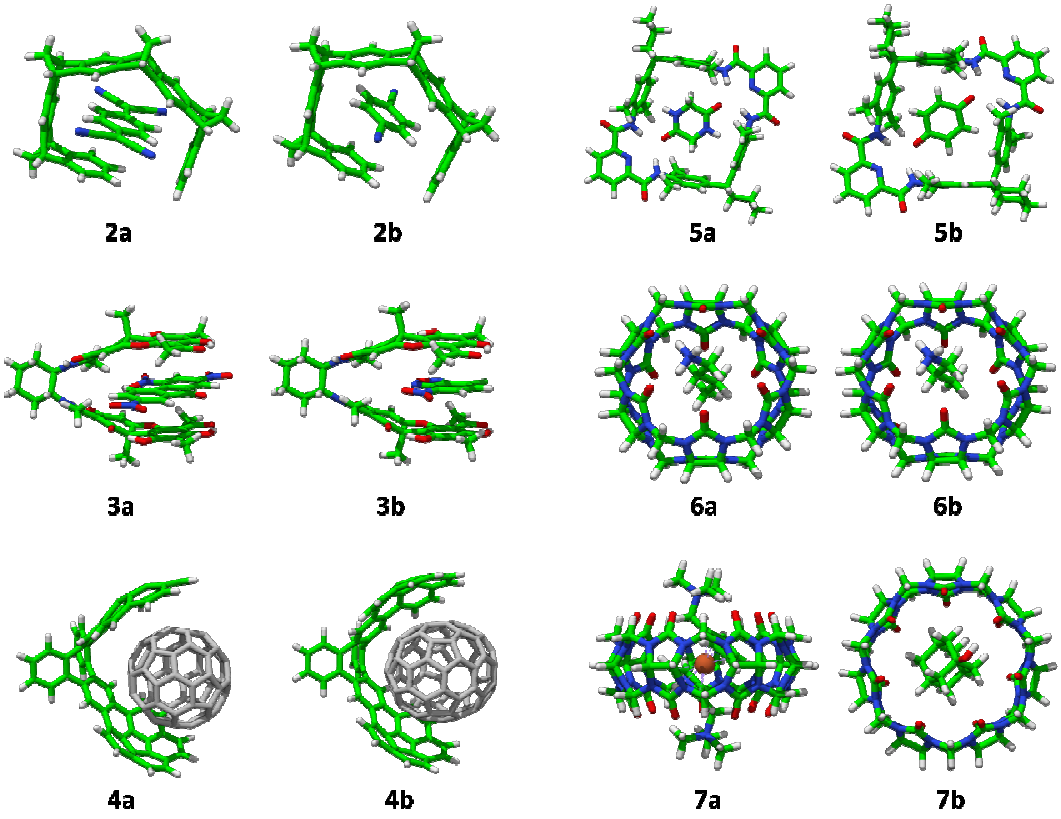


Figure S2. Structures of the supramolecular complexes constituting the S12L dataset. Color code: C in green, H in white, N in blue, O in red and Fe in orange. Fullerene C atoms are colored in gray for best viewing.

The basis set superposition error (BSSE) arises when calculating weak interacting systems due to the fact that finite basis sets are used. In a dimer *AB*, the monomer *A* benefits from the basis functions of monomer *B* and *vice versa*. The wavefunction of each monomer separately, however, is expanded in much less basis functions than the wavefunction of the complex, obtaining interaction energies that are biased towards the dimer formation due to basis set effects. BSSE can be counterpoise (CP) corrected by using the Boys and Bernardi procedure:[9]

$$\Delta E_{bin}^{CP}(AB) = [E_{AB}^{AB}(AB) - E_{AB}^{AB}(A) - E_{AB}^{AB}(B)] + [E_{A}^{AB}(A) - E_{A}^{A}(A) + E_{B}^{AB}(B) - E_{B}^{B}(B)] = E_{\text{int}}^{CP}(AB) + E_{\text{def}} \quad \text{(S1)}$$

In this expression, $E_X^Y(Z)$ is the energy of the fragment *Z* calculated at the geometry of fragment *Y* with the basis set of fragment *X*. Note that the CP-corrected binding energy ΔE_{bind}^{CP} can be expressed as a combination of two terms: the CP-corrected interaction energy of the complex *AB*, $E_{\text{int}}^{CP}(AB) = E_{AB}^{AB}(AB) - E_{AB}^{AB}(A) - E_{AB}^{AB}(B)$, and the deformation energy, $E_{\text{def}} = E_{\text{def}}^{A} + E_{\text{def}}^{B} = E_{A}^{AB}(A) - E_{A}^{A}(A) + E_{B}^{AB}(B) - E_{B}^{B}(B)$, which quantifies the energy change of the monomers due to the geometry change in forming the complex. In case of small geometrical changes moving from the isolated monomers to the dimer, ΔE_{bind}^{CP} can be approximated to E_{int}^{CP}; however, when large geometrical deformations take place, E_{def} can no longer be neglected.

Table S1. Comparison of the counterpoise-uncorrected (No-CP) and counterpoise-corrected (CP) interaction energies (in kcal/mol) computed for complex **C3GC** at MP2 by using the cc-pVDZ, cc-pVTZ, and cc-pVQZ basis sets and the corresponding extrapolation schemes CBS(cc-pVDZ/cc-pVTZ) and CBS(cc-pVTZ/cc-pVQZ) as indicated in Eq. 2 and 3 (main text).

Basis Set	No-CP	CP
cc-pVDZ	-54.66	-45.18
cc-pVTZ	-64.72	-57.49
cc-pVQZ	-64.71	-61.00
CBS(cc-pVDZ/cc-pVTZ)	-70.60	-64.69
CBS(cc-pVDZ/cc-pVTZ)	-64.70	-63.50

Table S2.CP-uncorrected (No-CP) and CP-corrected (CP) interaction energies (in kcal/mol) computed at MP2/CBS(cc-pVDZ/cc-pVTZ).

	No-CP[a]	CP[b]	BSSE[c]
C2C2PD	-44.42	-40.75	3.67
C3A	-31.98	-29.07	2.91
C3GC	-54.70	-48.26	6.44
CBH	-12.88	-13.67	-0.79
GCGC	-24.82	-19.79	5.03
GGG	-6.11	-4.24	1.87
PHE	-28.03	-26.62	1.41
2a	-53.63	-48.44	5.19
2b	-36.97	-32.98	3.99
3a	-47.35	-35.29	12.06
3b	-33.18	-24.56	8.62
5a	-45.54	-41.06	4.48
5b	-33.83	-29.98	3.85
6a	-91.96	-88.45	3.51
6b	-87.28	-84.52	2.76
7a	-163.12	-160.17	2.95
7b	-39.97	-35.28	4.69

[a] No-CP interaction energies were calculated as $E^{No-CP} = E_{AB}^{AB}(AB) - E_{A}^{A}(A) - E_{B}^{B}(B)$. [b] CP interaction energies were calculated according to expression S1. The BSSE energy is defined as $E^{BSSE} = E_{A}^{AB}(A) - E_{AB}^{AB}(A) + E_{B}^{AB}(B) - E_{AB}^{AB}(B)$.

Table S3. Deformation energies (in kcal/mol) computed at MP2/CBS and SCS-MP2/CBS for the S12L data set.

	MP2/CBS	SCS-MP2/CBS
2a	4.13	3.00
2b	2.89	1.76
3a	25.30	17.95
3b	23.02	15.78
4a	2.43	0.63
4b	4.59	2.59
5a	9.78	7.22
5b	8.35	5.68
6a	6.34	4.19
6b	6.48	4.64
7a	0.74	2.72
7b	3.04	0.80

Table S4. MP2/CBS interaction, SCS-MP2/CBS deformation and $\Delta E_{corr}^{DLPNO\text{-}CCSD(T)/def2\text{-}TZVPP}$ correlation energy terms, and final DLPNO-CCSD(T)/CBS interaction energies computed for L7 and S12L. All energies are given in kcal/mol.

	$E_{int}^{MP2/CBS}$	$E_{def}^{SCS\text{-}MP2/CBS}$	$\Delta E_{corr}^{DLPNO\text{-}CCSD(T)}$	$E^{DLPNO\text{-}CCSD(T)/CBS}$
C2C2PD	-40.75	-	15.94	-24.81
C3A	-29.07	-	11.09	-17.98
C3GC	-48.26	-	18.40	-29.86
CBH	-13.67	-	2.03	-11.64
GCGC	-19.79	-	6.58	-13.21
GGG	-4.24	-	2.56	-1.68
PHE	-26.62	-	3.81	-22.81
2a	-52.57	3.00	18.92	-30.65
2b	-35.87	1.76	11.07	-23.04
3a	-60.59	17.95	18.96	-23.68
3b	-47.58	15.78	8.72	-23.08
5a	-50.84	7.22	10.22	-33.40
5b	-38.33	5.68	9.67	-22.98
6a	-94.79	4.19	10.81	-79.79
6b	-91.00	4.64	8.54	-77.82
7a	-160.91	2.72	34.30	-123.89
7b	-38.32	0.80	14.78	-22.74

Table S5. Mean errors (ME), mean absolute errors (MAE) (in kcal/mol), and mean absolute relative errors (MARE in percentage) computed for the interaction energies of the L7 data set compared with the reference DLPNO-CCSD(T)/CBS values. The maximum absolute deviation (MAX) and the system affected by that deviation are indicated in the last column.

	ME	MAE	MARE	MAX	
revPBE-NL	-1.91	1.91	16.0	4.14	**C3GC**
revPBE-NL+E_{ABC}	-0.85	1.26	10.5	2.34	**GCGC**
revPBE0-NL	-0.76	1.22	6.8	2.16	**PHE**
revPBE0-NL+E_{ABC}	0.30	1.07	7.9	3.18	**C2C2PD**
revPBE0-DH-NL	-0.65	1.25	8.9	2.32	**C3GC**
revPBE0-DH-NL+E_{ABC}	0.40	1.01	9.8	2.49	**C2C2PD**
BLYP-NL	-0.77	1.50	8.5	2.64	**PHE**
BLYP-NL+E_{ABC}	0.29	1.49	8.9	4.15	**C2C2PD**
B3LYP-NL	-0.50	1.62	10.2	3.60	**PHE**
B3LYP-NL+E_{ABC}	0.55	1.88	12.3	4.90	**C2C2PD**
B2PLYP-NL	-0.88	1.17	6.7	2.60	**C3GC**
B2PLYP-NL+E_{ABC}	0.18	0.88	7.3	2.05	**C2C2PD**
B2PLYP-D3	0.26	0.69	9.2	1.36	**CBH**
B2PLYP-D3+E_{ABC}	1.31	1.54	15.5	2.75	**C2C2PD**

Table S6. Mean errors (ME), mean absolute errors (MAE) (in kcal/mol), and mean absolute relative errors (MARE in percentage) computed for the interaction energies of the S12L data set (excluding complexes **4a** and **4b**) compared with the reference DLPNO-CCSD(T)/CBS values. The maximum absolute deviation (MAX) and the system affected by that deviation are indicated in the last column.

	ME	MAE	MARE	MAX	
revPBE-NL	-6.32	6.41	16.5	18.91	**7a**
revPBE-NL+E_{ABC}	-4.38	4.62	11.9	14.31	**7a**
revPBE0-NL	-6.26	6.42	15.4	19.90	**7a**
revPBE0-NL+E_{ABC}	-4.32	4.75	11.4	15.30	**7a**
revPBE0-DH-NL	-4.47	4.71	13.6	10.57	**7b**
revPBE0-DH-NL+E_{ABC}	-2.53	3.01	9.4	7.31	**7b**
BLYP-NL	-5.86	6.44	15.6	19.74	**7a**
BLYP-NL+E_{ABC}	-3.92	4.88	12.1	15.14	**7a**
B3LYP-NL	-6.70	7.16	16.5	22.30	**7a**
B3LYP-NL+E_{ABC}	-4.76	5.61	13.0	17.71	**7a**
B2PLYP-NL	-5.40	5.95	13.5	21.51	**7a**
B2PLYP-NL+E_{ABC}	-3.46	4.39	10.0	16.92	**7a**
B2PLYP-D3	-1.33	2.49	7.2	4.63	**7b**
B2PLYP-D3+E_{ABC}	0.61	1.81	5.9	5.07	**3b**

Table S7. Mean errors (ME), mean absolute errors (MAE) (in kcal/mol), and mean absolute relative errors (MARE in percentage) computed for the interaction energies of the two L7 and S12L data sets (excluding complexes **4a** and **4b**) considered as one compared with the reference DLPNO-CCSD(T)/CBS values. The maximum absolute deviation (MAX) and the system affected by that deviation are indicated in the last column.

	ME	MAE	MARE	MAX	
revPBE-NL	-4.50	4.56	16.3	18.91	**7a**
revPBE-NL+E_{ABC}	-2.93	3.24	11.3	14.31	**7a**
revPBE0-NL	-4.00	4.28	11.9	19.90	**7a**
revPBE0-NL+E_{ABC}	-2.42	3.23	9.9	15.30	**7a**
revPBE0-DH-NL	-2.90	3.29	11.7	10.57	**7b**
revPBE0-DH-NL+E_{ABC}	-1.32	2.19	9.6	7.31	**7b**
BLYP-NL	-3.76	4.40	12.7	19.74	**7a**
BLYP-NL+E_{ABC}	-2.19	3.49	10.8	15.14	**7a**
B3LYP-NL	-4.15	4.88	13.9	22.30	**7a**
B3LYP-NL+E_{ABC}	-2.57	4.07	12.7	17.71	**7a**
B2PLYP-NL	-3.54	3.98	10.7	21.51	**7a**
B2PLYP-NL+E_{ABC}	-1.96	2.95	8.9	16.92	**7a**
B2PLYP-D3	-0.67	1.75	8.0	4.63	**7b**
B2PLYP-D3+E_{ABC}	0.90	1.70	9.9	5.07	**3b**

Table S8. Mean errors (ME), mean absolute errors (MAE) (in kcal/mol), and mean absolute relative errors (MARE in percentage) computed for the interaction energies of the L7 data set compared with the published reference values.[1] The maximum absolute deviation (MAX) and the system affected by that deviation are indicated in the last column.

	ME	MAE	MARE	MAX	
revPBE-NL	-1.14	1.56	9.0	2.75	**C3GC**
revPBE-NL+E_{ABC}	-0.08	0.96	7.0	1.86	**GCGC**
revPBE0-NL	0.01	0.75	8.3	1.07	**C2C2PD**
revPBE0-NL+E_{ABC}	1.07	1.11	10.3	2.73	**C2C2PD**
revPBE0-DH-NL	0.12	0.59	8.3	1.05	**GGG**
revPBE0-DH-NL+E_{ABC}	1.17	1.17	12.7	2.05	**C2C2PD**
BLYP-NL	0.00	0.95	9.3	2.04	**C2C2PD**
BLYP-NL+E_{ABC}	1.06	1.46	11.8	3.70	**C2C2PD**
B3LYP-NL	0.27	1.18	11.4	2.79	**C2C2PD**
B3LYP-NL+E_{ABC}	1.32	1.69	14.0	4.45	**C2C2PD**
B2PLYP-NL	-0.11	0.53	6.8	1.21	**C3GC**
B2PLYP-NL+E_{ABC}	0.95	0.95	10.4	1.60	**C2C2PD**
B2PLYP-D3	1.03	1.03	12.7	1.75	**PHE**
B2PLYP-D3+E_{ABC}	2.09	2.09	19.1	3.30	**C3GC**

Table S9. Mean errors (ME), mean absolute errors (MAE) (in kcal/mol), and mean absolute relative errors (MARE in percentage) computed for the interaction energies of the S12L data set (excluding complexes **4a** and **4b**) compared with the published reference values.[10] The maximum absolute deviation (MAX) and the system affected by that deviation are indicated in the last column.

	ME	MAE	MARE	MAX	
revPBE-NL	-6.46	6.46	18.9	13.86	**7b**
revPBE-NL+E_{ABC}	-4.52	4.52	13.6	10.60	**7b**
revPBE0-NL	-6.40	6.40	17.6	12.28	**7a**
revPBE0-NL+E_{ABC}	-4.46	4.46	12.2	8.88	**7b**
revPBE0-DH-NL	-4.61	5.07	15.8	10.71	**7b**
revPBE0-DH-NL+E_{ABC}	-2.67	4.05	11.2	7.74	**6a**
BLYP-NL	-6.00	6.00	15.8	12.75	**7b**
BLYP-NL+E_{ABC}	-4.06	4.14	10.9	9.49	**7b**
B3LYP-NL	-6.84	6.84	17.3	14.69	**7a**
B3LYP-NL+E_{ABC}	-4.90	4.92	12.0	10.90	**7a**
B2PLYP-NL	-5.54	5.54	13.9	13.90	**7a**
B2PLYP-NL+E_{ABC}	-3.60	3.60	8.5	9.30	**7a**
B2PLYP-D3	-1.46	3.04	8.0	7.01	**6a**
B2PLYP-D3+E_{ABC}	0.48	2.76	6.2	9.57	**7a**

Table S10. Mean errors (ME), mean absolute errors (MAE) (in kcal/mol), and mean absolute relative errors (MARE in percentage) computed for the interaction energies of the two L7 and S12L data sets (excluding complexes **4a** and **4b**) considered as one compared with the published reference values.[1,10] The maximum absolute deviation (MAX) and the system affected by that deviation are indicated in the last column.

	ME	MAE	MARE	MAX	
revPBE-NL	-4.27	4.44	14.8	13.86	**7a**
revPBE-NL+E_{ABC}	-2.69	3.05	10.9	10.60	**7a**
revPBE0-NL	-3.76	4.07	13.7	12.28	**7a**
revPBE0-NL+E_{ABC}	-2.18	3.08	11.4	8.88	**7a**
revPBE0-DH-NL	-2.66	3.23	12.7	10.71	**7b**
revPBE0-DH-NL+E_{ABC}	-1.09	2.87	11.8	7.74	**7b**
BLYP-NL	-3.53	3.92	13.1	12.75	**7a**
BLYP-NL+E_{ABC}	-1.95	3.04	11.3	9.49	**7a**
B3LYP-NL	-3.91	4.51	14.9	14.69	**7a**
B3LYP-NL+E_{ABC}	-2.34	3.59	12.8	10.90	**7a**
B2PLYP-NL	-3.30	3.48	10.9	13.90	**7a**
B2PLYP-NL+E_{ABC}	-1.73	2.51	9.3	9.30	**7a**
B2PLYP-D3	-0.44	2.21	9.9	7.01	**7b**
B2PLYP-D3+E_{ABC}	1.14	2.48	11.5	9.57	**3a**

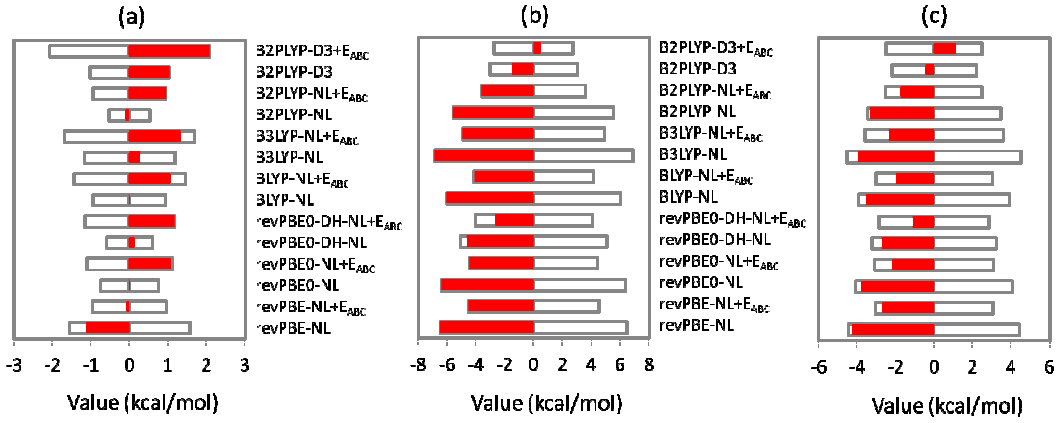


Figure S3. ME (red bar) and MAE (grey-border bar) computed for the different DFs coupled to the NL approach (the B2PLYP-D3 method is included for comparison purposes) for L7 (a), S12L (b), and considering both sets as one (c). The interaction energies reported in Ref. 1 for L7 and Ref. 10 for S12L (excluding complexes **4a** and **4b**) are used as a reference. Note that MAD (grey-border bar) has been mirrored.

Table S11. Interactions energies (in kcal/mol) computed for the L7 and S12L datasets with the revised Perdew-Burke-Ernzerhof family of DFs coupled to the NL approach. The def2-TZVP basis set is employed for the calculations.

	revPBE-NL	revPBE0-NL	revPBE0-DH-NL
C2C2PD	-25.05	-23.29	-23.98
C3A	-19.68	-18.51	-18.88
C3GC	-34.00	-31.91	-32.18
CBH	-13.40	-11.90	-10.72
GCGC	-16.53	-15.13	-14.40
GGG	-2.37	-1.59	-1.35
PHE	-24.30	-24.97	-25.05
2a	-36.98	-36.28	-36.77
2b	-24.22	-23.63	-23.80
3a	-30.84	-29.29	-28.49
3b	-22.62	-22.31	-21.88
4a	-47.86	-45.28	-48.78
4b	-49.98	-46.74	-50.36
5a	-36.40	-37.49	-37.59
5b	-24.69	-24.71	-25.00
6a	-86.83	-87.89	-87.36
6b	-82.43	-83.59	-82.42
7a	-142.79	-143.78	-129.17
7b	-36.46	-34.75	-33.31

Table S12. Interactions energies (in kcal/mol) computed for the L7 and S12L datasets with the revised Perdew-Burke-Ernzerhof family of DFs coupled to the NL approach and including the three-body dispersion correction. The def2-TZVP basis set is employed for the calculations.

	revPBE-NL+E_{ABC}	revPBE0-NL+E_{ABC}	revPBE0-DH-NL+E_{ABC}
C2C2PD	-23.39	-21.63	-22.31
C3A	-18.49	-17.32	-17.69
C3GC	-31.78	-29.69	-29.96
CBH	-12.70	-11.21	-10.03
GCGC	-15.55	-14.14	-13.41
GGG	-2.13	-1.35	-1.12
PHE	-23.90	-24.57	-24.65
2[a]	-35.22	-34.52	-35.01
2b	-23.01	-22.41	-22.58
3[a]	-29.03	-27.48	-26.68
3b	-21.90	-21.59	-21.17
4[a]	-44.68	-42.10	-45.60
4b	-46.50	-43.26	-46.87
5[a]	-35.40	-36.49	-36.58
5b	-23.71	-23.72	-24.02
6[a]	-84.61	-85.67	-85.14
6b	-80.60	-81.76	-80.59
7[a]	-138.20	-139.19	-124.58
7b	-33.20	-31.48	-30.05

Table S13. Interactions energies (in kcal/mol) computed for the L7 and S12L datasets with the Becke-Lee-Yang-Parr family of DFs coupled to the NL approach. The def2-TZVP basis set is employed for the calculations.

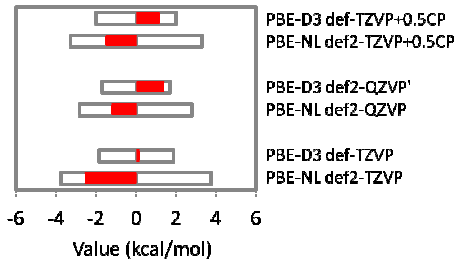
	BLYP-NL	B3LYP-NL	B2PLYP-NL	B2PLYP-D3
C2C2PD	-22.32	-21.57	-24.42	-23.72
C3A	-17.90	-17.50	-19.07	-17.82
C3GC	-31.47	-30.57	-32.46	-30.17
CBH	-12.88	-12.78	-11.14	-10.28
GCGC	-15.63	-15.21	-14.36	-13.19
GGG	-1.73	-1.47	-1.56	-0.99
PHE	-25.45	-26.41	-25.12	-24.01
2a	-33.10	-33.47	-34.56	-33.49
2b	-21.31	-21.60	-22.18	-21.55
3a	-29.04	-28.48	-27.28	-23.77
3b	-21.94	-22.23	-21.22	-18.72
4a	-40.84	-39.59	-48.99	-43.76
4b	-43.00	-41.23	-51.20	-45.62
5a	-36.76	-38.32	-36.24	-34.08
5b	-25.90	-26.43	-25.41	-23.65
6a	-88.73	-90.52	-87.24	-84.41
6b	-83.91	-85.65	-82.99	-80.76
7a	-143.62	-146.19	-145.40	-126.52
7b	-35.35	-35.19	-32.56	-27.37

Table S14. Interactions energies (in kcal/mol) computed for the L7 and S12L datasets with the Becke-Lee-Yang-Parr family of DFs coupled to the NL approach and including the three-body dispersion correction. The def2-TZVP basis set is employed for the calculations.

	BLYP-NL+E_{ABC}	B3LYP-NL+E_{ABC}	B2PLYP-NL+E_{ABC}	B2PLYP-D3+E_{ABC}
C2C2PD	-20.66	-19.91	-22.76	-22.05
C3A	-16.71	-16.31	-17.89	-16.63
C3GC	-29.24	-28.35	-30.24	-27.95
CBH	-12.19	-12.08	-10.44	-9.59
GCGC	-14.64	-14.23	-13.37	-12.20
GGG	-1.49	-1.23	-1.33	-0.76
PHE	-25.05	-26.01	-24.72	-23.61
2a	-31.34	-31.71	-32.80	-31.73
2b	-20.09	-20.38	-20.96	-20.34
3a	-27.23	-26.67	-25.47	-21.96
3b	-21.23	-21.52	-20.51	-18.01
4a	-37.65	-36.40	-45.80	-40.58
4b	-39.51	-37.75	-47.71	-42.13
5a	-35.75	-37.31	-35.23	-33.07
5b	-24.91	-25.44	-24.43	-22.66
6a	-86.51	-88.30	-85.02	-82.19
6b	-82.09	-83.82	-81.16	-78.93
7a	-139.03	-141.59	-140.80	-121.93
7b	-32.09	-31.93	-29.30	-24.11

Table S14. Mean error (ME, red bar) and mean absolute error (MAE, grey-border bar) (in kcal/mol) computed for the interaction energies of the S12L dataset (excluding complexes **4a** and **4b**) reported in Ref. 2 with respect to the DLPNO-CCSD(T)/CBS reference values computed in this work. Note that MAE (grey-border bar) has been mirrored in the adjacent Figure.

	ME	MAE	Max.	
PBE-NL+E_{ABC}/def2-TZVP	-2.52	3.76	10.71	**7a**
PBE-D3+E_{ABC}/def2-TZVP	0.16	1.87	4.14	**2b**
PBE-NL+E_{ABC}/def2-QZVP	-1.22	2.81	7.61	**7a**
PBE-D3+E_{ABC}/def2-QZVP'	1.36	1.69	3.84	**2b**
PBE-NL+E_{ABC}/def2-TZVP + 0.5CP	-1.51	3.29	9.21	**7a**
PBE-D3+E_{ABC}/def2-TZVP + 0.5CP	1.17	2.00	4.88	**3b**



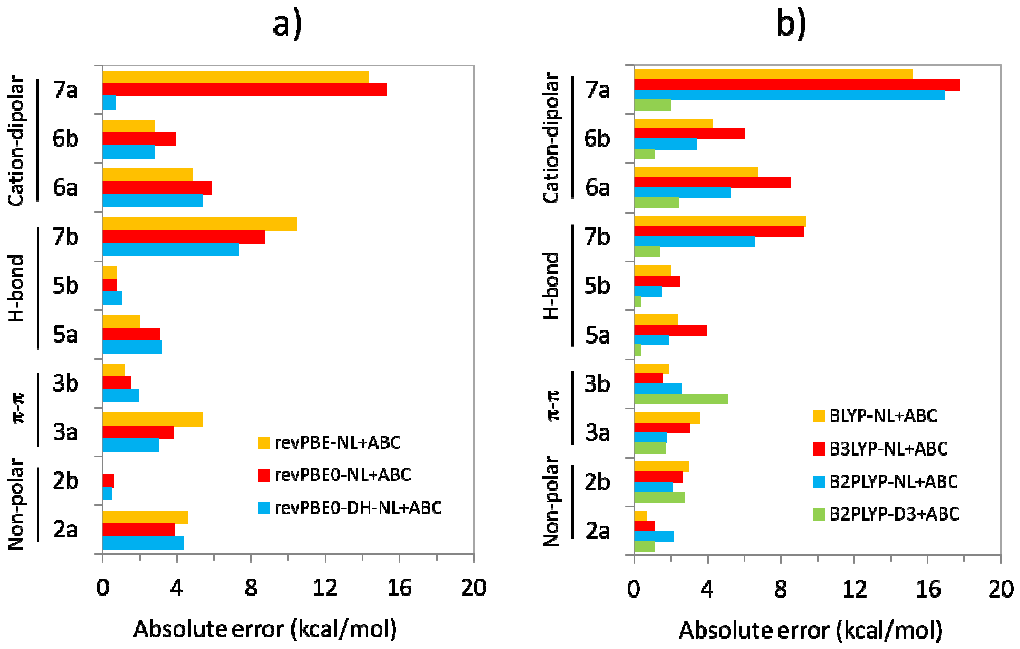


Figure S4. Absolute errors computed for all the supramolecular complexes in S12L ordered by interacting nature in the revPBE (a) and BLYP (b) functional families: Non-polar interaction (**2a** and **2b**), π-π stacking (**3a** and **3b**), H-bonding (**5a**, **5b** and **7b**), and Cation-dipolar interaction (**6a**, **6b** and **7a**).

References

(1) Sedlak, R.; Janowski, T.; Pitoňák, M.; Řezáč, J.; Pulay, P.; Hobza, P. Accuracy of Quantum Chemical Methods for Large Noncovalent Complexes. *J. Chem. Theory Comput.* **2013,** *9*, 3364-3374.

(2) Risthaus, T.; Grimme, S. Benchmarking of London Dispersion-Accounting Density Functional Theory Methods on Very Large Molecular Complexes. *J. Chem. Theory Comput.* **2013,** *9*, 1580-1591.

(3) Kamieth, M.; Burkert, U.; Corbin, P. S.; Dell, S. J.; Zimmerman, S. C.; Klärner, F.-G. Molecular Tweezers as Synthetic Receptors: Molecular Recognition of Electron-Deficient Aromatic Substrates by Chemically Bonded Stationary Phases. *Eur. J. Org. Chem.* **1999,** *1999*, 2741-2749.

(4) Graton, J.; Le Questel, J.-Y.; Legouin, B.; Uriac, P.; van de Weghe, P.; Jacquemin, D. A DFT-D evaluation of the complexation of a molecular tweezer with small aromatic molecules. *Chem. Phys. Lett.* **2012,** *522*, 11-16.

(5) Muck-Lichtenfeld, C.; Grimme, S.; Kobryn, L.; Sygula, A. Inclusion complexes of buckycatcher with C60 and C70. *Phys. Chem. Chem. Phys.* **2010,** *12*, 7091-7097.

(6) Allott, C.; Adams, H.; A. Hunter, C.; A. Thomas, J.; L. Bernad Jr, P.; Rotger, C. Hydrogen-bond recognition of cyclic dipeptides in water. *Chem. Commun.* **1998**, 2449-2450.

(7) Mock, W. L.; Shih, N. Y. Dynamics of molecular recognition involving cucurbituril. *J. Am. Chem. Soc.* **1989,** *111*, 2697-2699.

(8) Moghaddam, S.; Yang, C.; Rekharsky, M.; Ko, Y. H.; Kim, K.; Inoue, Y.; Gilson, M. K. New Ultrahigh Affinity Host−Guest Complexes of Cucurbit[7]uril with Bicyclo[2.2.2]octane and Adamantane Guests: Thermodynamic Analysis and Evaluation of M2 Affinity Calculations. *J. Am. Chem. Soc.* **2011,** *133*, 3570-3581.
(9) Boys, S. F.; Bernardi, F. The calculation of small molecular interactions by the differences of separate total energies. Some procedures with reduced errors. *Mol. Phys.* **1970,** *19*, 553-566.
(10) Grimme, S. Supramolecular Binding Thermodynamics by Dispersion-Corrected Density Functional Theory. *Chem. Eur. J.* **2012,** *18*, 9955-9964.