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Supporting information for

A quantum chemical view of enthalpy-entropy compensation

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1. EDA data for B97-D/TZVPP and B3LYP-D/TZVPP

a) B97-D/TZVPP

Table 1: Energy decomposition analysis (EDA)[a] for the S22 benchmark set of non-covalently bound systems, calculated at B97-D/TZVPP level (using S22 geometries). All values in kcal/mol.

	ER	ES	ER+ES	IND	ES+IND	ER+ES+IND	D	total
systems dominated by hydrogen-bonds								
01	6.071	-6.231	-0.159	-1.833	-8.064	-1.993	-1.733	-3.726
02	10.402	-11.042	-0.641	-3.457	-14.499	-4.097	-0.970	-5.067
03	54.336	-45.133	9.203	-24.310	-69.443	-15.107	-3.144	-18.251
04	36.102	-33.368	2.734	-14.693	-48.061	-11.959	-3.321	-15.280
05	41.460	-38.819	2.641	-17.920	-56.739	-15.279	-4.168	-19.447
06	41.922	-37.223	4.700	-16.864	-54.087	-12.164	-4.966	-17.130
07	41.452	-36.003	5.449	-16.351	-52.354	-10.903	-5.297	-16.200
dispersion bound systems								
08	1.003	-0.395	0.608	-0.140	-0.534	0.468	-1.033	-0.565
09	3.464	-1.704	1.760	-0.640	-2.344	1.120	-2.672	-1.552
10	3.931	-1.986	1.945	-0.727	-2.713	1.219	-2.725	-1.506
11	11.623	-5.394	6.229	-1.754	-7.148	4.475	-7.147	-2.672
12	12.290	-6.438	5.852	-2.163	-8.601	3.689	-7.762	-4.073
13	15.355	-10.857	4.498	-3.244	-14.101	1.254	-11.268	-10.014
14	17.509	-8.723	8.786	-2.841	-11.564	5.945	-10.666	-4.721
15	24.207	-15.087	9.120	-4.702	-19.789	4.418	-16.526	-12.108
mixed systems								
16	2.821	-2.361	0.460	-0.949	-3.310	-0.489	-1.245	-1.734
17	4.371	-3.412	0.959	-2.172	-5.583	-1.213	-2.924	-4.137
18	3.829	-2.477	1.352	-1.252	-3.729	0.100	-2.848	-2.748
19	6.668	-5.015	1.653	-2.661	-7.676	-1.008	-3.870	-4.878
20	6.700	-3.529	3.171	-1.541	-5.070	1.630	-4.560	-2.930
21	9.586	-5.991	3.595	-3.229	-9.220	0.366	-6.626	-6.260
22	15.169	-11.344	3.825	-5.320	-16.664	-1.496	-5.106	-6.602

[a] exchange-repulsion (ER), electrostatics (first order, ES), induction (second order ES: polarization and/or charge transfer, IND), dispersion (D)

Correlation between these B97-D/TZVPP values and the PBE-D/TZVPP data given in the manuscript is: R=0.99 for ER, R=1.00 for ES, R=1.00 for IND and R=0.99 for D. EX, ES, and IND are about 1.4 times larger for PBE (with the effects of EX and ES canceling each other), D about 0.6 times smaller. Trends are therefore very similar between B97-D/TZVPP values and PBE-D/TZVPP.

b) B3LYP-D/TZVPP

Table 2: Energy decomposition analysis (EDA)[a] for the S22 benchmark set of non-covalently bound systems, calculated at B3LYP-D/TZVPP level (using S22 geometries). All values in kcal/mol.

	ER	ES	ER+ES	IND	ES+IND	ER+ES+IND	D	total
systems dominated by hydrogen-bonds								
01	1.842	-2.766	-0.924	-1.842	-4.608	-2.766	-1.485	-4.251
02	3.957	-5.194	-1.237	-3.957	-9.152	-5.194	-0.991	-6.185
03	31.651	-21.272	10.379	-31.651	-52.923	-21.272	-2.695	-23.967
04	16.866	-15.547	1.319	-16.866	-32.414	-15.547	-2.936	-18.483
05	21.324	-19.464	1.861	-21.324	-40.788	-19.464	-3.721	-23.185
06	22.151	-16.319	5.832	-22.151	-38.469	-16.319	-4.524	-20.843
07	22.062	-14.871	7.191	-22.062	-36.932	-14.871	-4.954	-19.825
dispersion bound systems								
08	0.056	0.385	0.441	-0.056	0.329	0.385	-0.866	-0.481
09	0.734	1.003	1.737	-0.734	0.269	1.003	-2.943	-1.940
10	0.434	0.703	1.137	-0.434	0.269	0.703	-2.271	-1.568
11	1.203	3.509	4.712	-1.203	2.306	3.509	-5.947	-2.438
12	1.465	1.932	3.397	-1.465	0.467	1.932	-6.149	-4.217
13	3.362	-1.768	1.594	-3.362	-5.130	-1.768	-9.917	-11.685
14	1.783	3.151	4.934	-1.783	1.368	3.151	-7.905	-4.754
15	4.024	0.646	4.669	-4.024	-3.378	0.646	-13.982	-13.336
mixed systems								
16	1.079	-0.558	0.520	-1.079	-1.637	-0.558	-1.296	-1.854
17	2.552	-1.244	1.308	-2.552	-3.795	-1.244	-3.467	-4.711
18	1.319	-0.052	1.267	-1.319	-1.370	-0.052	-2.918	-2.970
19	2.341	-2.141	0.201	-2.341	-4.482	-2.141	-3.234	-5.375
20	1.032	0.829	1.861	-1.032	-0.203	0.829	-3.803	-2.974
21	2.603	-0.903	1.701	-2.603	-3.506	-0.903	-5.519	-6.422
22	5.649	-3.643	2.006	-5.649	-9.291	-3.643	-4.463	-8.106

[a] exchange-repulsion (ER), electrostatics (first order, ES), induction (second order ES: polarization and/or charge transfer, IND), dispersion (D)

Correlation between these B3LYP-D/TZVPP values and the PBE-D/TZVPPP data given in the manuscript is: R=0.98 for ER, R=0.94 for ES, R=1.00 for IND and R=1.00 for D. EX and ES are about 2.4 times larger for PBE, but canceling out almost perfectly, so that the sum of first-order contributions is only 2 % larger for PBE. IND is about 8 % larger for PBE, D about 29 % smaller. The biggest difference between Hybrid and GGA DFT methods are thus much smaller values for ES and ER, but these differences cancel out to a large extend when first order contributions are added up.

2. Thermodynamic data for B3LYP-D/TZVPP, MP2/TZVPP and SCS-MP2/TZVPP

a) B3LYP-D/TZVPP

Table 3: Thermodynamic data for the S22[a] benchmark set of non-covalently bound systems, calculated at B3LYP-D/TZVPP level (using optimized geometries) within the rigid-rotor/harmonic-oscillator (RRHO)[b] approximation. All values in kcal/mol.

	ΔE	ΔH	ΔG	-TΔS	-TΔS_{vib}	-TΔS_{rot}	-TΔS_{trans}
			systems dominated by hydrogen-bonds				
01	-4.24	-2.71	2.77	5.48	-4.87	0.71	9.65
02	-6.05	-4.38	1.7	6.08	-3.57	-0.05	9.70
03	-18.16	-16.72	-5.14	11.58	-3.85	4.89	10.53
04	-16.10	-14.23	-2.67	11.56	-3.87	4.90	10.51
05	-19.92	-18.55	-7.14	11.41	-7.12	7.21	11.32
06	-17.38	-16.07	-5.41	10.66	-6.94	6.44	11.17
07	-16.68	-14.75	-4.26	10.49	-8.04	7.08	11.46
			dispersion bound systems				
08	-0.49	0.82	5.17	4.35	-5.52	0.27	9.59
09	-1.95	-0.50	6.92	7.42	-5.32	2.64	10.09
10	-1.58	-0.25	4.88	5.13	-6.44	1.52	10.04
11	-2.47	-1.15	5.47	6.62	-8.06	3.68	11.00
12	-4.27	-2.97	4.86	7.83	-7.70	4.51	11.02
13	-10.35	-8.89	2.51	11.40	-7.46	7.54	11.32
14	-4.68	-3.27	4.79	8.06	-8.29	5.19	11.16
15	-12.60	-10.95	1.4	12.35	-6.58	7.47	11.46
			mixed systems				
17	-4.57	-3.14	1.48	4.62	-6.59	1.08	10.13
18	-2.96	-1.59	3.13	4.72	-6.68	1.31	10.09
20	-2.99	-1.61	2.46	4.07	-10.40	3.47	11.00
21	-6.40	-5.58	3.08	8.66	-7.49	4.99	11.16
22	-7.85	-6.10	3.55	9.65	-8.00	6.49	11.17

[a] excluding entry 16 and 19, to avoid problems with the RRHO approximation for linear molecules
[b] vibrational (vib), rotational (rot) and translational (trans) contributions

Table 4: Average enthalpic and entropic contributions for the S22[a] benchmark set of non-covalently bound systems in kcal/mol.[bc]

	ΔH_{ZVPE}[d]	ΔH_{vib}	$-T\Delta S_{vib}$	$-T\Delta S_{rot}$	$-T\Delta S_{trans}$	$-T\Delta S$	ΔE
			net contributions				
S22	1.2	2.6	6.6	4.1	10.7	8.1	-8.1
S22/HB[f]	1.6	2.3	5.5	4.5	10.6	9.6	-14.1
S22/D[g]	1.0	2.8	6.9	4.1	10.7	7.9	-4.8
$\frac{S22/D}{S22/HB}$	0.6	1.2	1.3	0.9	1.0	0.8	0.3
			net contributions per kcal/mol of interaction energy, i.e. $\frac{X}{\lvert\Delta E\rvert}$				
S22	0.3	0.8	1.9	0.7	3.1	1.8	-
S22/HB[f]	0.2	0.2	0.5	0.3	1.0	0.8	-
S22/D[g]	0.5	1.4	3.3	1.0	5.3	3.0	-
$\frac{S22/D}{S22/HB}$	2.5	7.0	6.6	3.3	5.3	3.8	-

[a] excluding entry 16 and 19, to avoid problems with the RRHO approximation for linear molecules
[b] at B3LYP-D/TZVPP level
[c] within the RRHO approximation: vibrational (vib), rotational (rot) and translational (trans) contributions
[d] zero point vibrational energy (ZVPE) contributions
[e] average number of degrees of freedom (NDF) of the complex systems
[f] subset of systems dominated by hydrogen-bonds, entry 1 to 7
[g] subset of dispersion bound systems, entry 8 to 15

b) MP2/TZVPP

Table 5: Thermodynamic data for the S22[a] benchmark set of non-covalently bound systems, calculated at MP2/TZVPP level (using optimized geometries) within the rigid-rotor/harmonic-oscillator (RRHO)[b] approximation. All values in kcal/mol.

	ΔE	ΔH	ΔG	-TΔS	-TΔS_{vib}	-TΔS_{rot}	-TΔS_{trans}
systems dominated by hydrogen-bonds							
01	-3.44	-1.14	7.17	8.31	-2.04	0.70	9.65
02	-5.37	-2.21	6.15	8.36	-1.27	-0.06	9.70
03	-16.19	-14.66	-2	12.66	-2.76	4.89	10.53
04	-14.87	-12.72	-0.16	12.56	-2.85	4.90	10.51
05	-19.06	-17.68	-4.42	13.26	-5.28	7.21	11.32
06	-16.44	-15.15	-2.72	12.43	-5.18	6.44	11.17
07	-15.71	-14.31	-1.41	12.90	-5.63	7.08	11.46
dispersion bound systems							
08	-0.43	0.98	6.37	5.39	-4.47	0.25	9.59
09	-1.54	0.10	9.05	8.95	-3.74	2.59	10.09
10	-1.89	-0.45	6.35	6.80	-4.76	1.52	10.04
11	-5.36	-4.06	5.26	9.32	-5.38	3.70	11.00
12	-7.08	-5.74	5.06	10.80	-4.77	4.54	11.02
13	-11.59	-10.11	3.38	13.49	-5.38	7.55	11.32
14	-8.90	-7.50	3.68	11.18	-5.22	5.23	11.16
15	-16.08	-14.46	-0.49	13.97	-4.97	7.48	11.46
mixed systems							
17	-4.14	-1.75	6.24	7.99	-3.18	1.05	10.13
18	-2.97	-1.12	6.6	7.72	-3.67	1.30	10.09
20	-4.01	-2.55	6.13	8.68	-5.79	3.49	11.00
21	-7.58	-6.07	4.28	10.35	-5.81	5.00	11.16
22	-8.80	-7.27	5.23	12.50	-5.37	6.70	11.17

[a] excluding entry 16 and 19, to avoid problems with the RRHO approximation for linear molecules
[b] vibrational (vib), rotational (rot) and translational (trans) contributions

Table 6: Average enthalpic and entropic contributions for the S22[a] benchmark set of non-covalently bound systems in kcal/mol.[bc]

	ΔH_{ZVPE}[d]	ΔH_{vib}	$-T\Delta S_{vib}$	$-T\Delta S_{rot}$	$-T\Delta S_{trans}$	$-T\Delta S$	ΔE
net contributions							
S22	1.9	2.1	4.4	4.1	10.7	10.4	-8.5
S22/HB[f]	2.5	1.8	3.6	4.5	10.6	11.5	-13.1
S22/D[g]	1.4	2.4	4.8	4.1	10.7	10.0	-6.6
$\frac{S22/D}{S22/HB}$	0.6	1.3	1.3	0.9	1.0	0.9	0.5
net contributions per kcal/mol of interaction energy, i.e. $\frac{X}{\lvert\Delta E\rvert}$							
S22	0.6	0.7	1.4	0.6	3.2	2.4	-
S22/HB[f]	0.3	0.2	0.3	0.3	1.1	1.1	-
S22/D[g]	0.8	1.2	2.4	0.8	5.4	3.7	-
$\frac{S22/D}{S22/HB}$	2.7	6.0	8.0	2.7	4.9	3.4	-

[a] excluding entry 16 and 19, to avoid problems with the RRHO approximation for linear molecules
[b] at MP2/TZVPP level
[c] within the RRHO approximation: vibrational (vib), rotational (rot) and translational (trans) contributions
[d] zero point vibrational energy (ZVPE) contributions
[e] average number of degrees of freedom (NDF) of the complex systems
[f] subset of systems dominated by hydrogen-bonds, entry 1 to 7
[g] subset of dispersion bound systems, entry 8 to 15

c) SCS-MP2/TZVPP

Table 7: Thermodynamic data for the S22[a] benchmark set of non-covalently bound systems, calculated at SCS-MP2/TZVPP level (using optimized geometries) within the rigid-rotor/harmonic-oscillator (RRHO)[b] approximation. All values in kcal/mol.

	ΔE	ΔH	ΔG	-TΔS	-TΔS_{vib}	-TΔS_{rot}	-TΔS_{trans}
systems dominated by hydrogen-bonds							
01	-3.05	-2.18	4.34	6.52	-4.06	0.93	9.66
02	-4.94	-3.29	2.69	5.98	-3.82	0.10	9.71
03	-14.47	-12.77	-2.56	10.21	-4.14	3.82	10.53
04	-13.48	-10.37	-1.48	8.89	-5.45	3.83	10.51
05	-17.03	-16.21	-4.09	12.12	-5.36	6.14	11.32
06	-14.24	-13.51	-1.94	11.57	-5.39	5.79	11.18
07	-13.73	-13.05	-0.06	12.99	-4.90	6.42	11.46
dispersion bound systems							
08	-0.30	-0.90	5.78	6.68	-4.37	1.45	9.61
09	-1.07	0.20	6.2	6.00	-6.82	2.73	10.09
10	-1.27	-1.86	7.98	9.84	-3.36	3.16	10.05
11	-3.37	-3.39	7.87	11.26	-5.29	5.55	11.00
12	-4.91	-5.00	6.44	11.44	-5.08	5.50	11.02
14	-5.72	-6.35	7.29	13.64	-3.52	5.99	11.16
mixed systems							
17	-3.36	-3.36	4.66	8.02	-4.38	2.27	10.13
18	-2.29	-1.66	4.95	6.61	-6.24	2.75	10.09
20	-2.85	-3.22	9.47	12.69	-3.67	5.36	11.00
21	-5.89	-6.31	6.89	13.20	-3.77	5.81	11.16
22	-6.79	-6.42	5.83	12.25	-4.73	5.82	11.18

[a] excluding entry 16 and 19, to avoid problems with the RRHO approximation for linear molecules, and entry 13 and 15 due to technical problems.
[b] vibrational (vib), rotational (rot) and translational (trans) contributions

Table 8: Average enthalpic and entropic contributions for the S22[a] benchmark set of non-covalently bound systems in kcal/mol.[bc]

	ΔH_{ZVPE}[d]	ΔH_{vib}	$-T\Delta S_{vib}$	$-T\Delta S_{rot}$	$-T\Delta S_{trans}$	$-T\Delta S$	ΔE
net contributions							
S22	0.9	2.0	4.7	4.1	10.6	10.0	-6.6
S22/HB[f]	1.6	2.1	4.7	3.9	10.6	9.8	-11.6
S22/D[g]	0.4	1.9	4.7	4.1	10.5	9.8	-2.8
$\frac{S22/D}{S22/HB}$	0.2	0.9	1.0	1.1	1.0	1.0	0.2
net contributions per kcal/mol of interaction energy, i.e. $\frac{X}{\lvert\Delta E\rvert}$							
S22	0.2	0.8	2.1	1.2	4.5	3.6	-
S22/HB[f]	0.2	0.3	0.5	0.3	1.3	1.0	-
S22/D[g]	0.3	1.7	4.5	2.3	9.5	7.3	-
$\frac{S22/D}{S22/HB}$	1.5	5.7	9.0	7.7	7.3	7.3	-

[a] excluding entry 16 and 19, to avoid problems with the RRHO approximation for linear molecules
[b] at SCS-MP2/TZVPP level
[c] within the RRHO approximation: vibrational (vib), rotational (rot) and translational (trans) contributions
[d] zero point vibrational energy (ZVPE) contributions
[e] average number of degrees of freedom (NDF) of the complex systems
[f] subset of systems dominated by hydrogen-bonds, entry 1 to 7
[g] subset of dispersion bound systems, entry 8 to 15

The ratios for the loss of entropy per unit enthalpy gained are again showing a big difference between Hydrogen-bond and dispersion interaction: We find $\frac{S22/D}{S22/HB}$ ratios for $\frac{-T\Delta S}{|\Delta E|}$ of 3.8, 3.4 and 7.3 for B3LYP-D/TZVPP, MP2/TZVPP, and SCS-MP2/TZVPP, indicating an at least three times higher loss of entropy for dispersion interactions. Correlation between ΔH and $-T\Delta S$ values is R=0.86 for B3LYP, and R=0.97 for the Hydrogen-bond, as well as the dispersion-bound subset. Correlation between ΔH and $-T\Delta S$ values is R=0.92 for MP2/TZVPP, R=0.99 for the Hydrogen-bond, and R=0.94 for the dispersion-bound subset. Correlation between ΔH and $-T\Delta S$ values is R=0.56 for SCS-MP2/TZVPP, R=0.93 for the Hydrogen-bond, and R=0.96 for the dispersion-bound subset. We therefore find a big difference between the trends of Hydrogen-bond and dispersion-bound systems for all methods, with substantially higher correlation factors if the different subsets are treated separately.

3. Comparison of EDA and SAPT values

Table 9: Energy decomposition analysis (EDA)[a] for the S22 benchmark set of non-covalently bound systems, calculated at PBE-D/TZVPP level (using S22 geometries), in comparison to SAPT[b] values from J. Chem. Theory Comput., 2012, 8, 2835 (see main manuscript for citation). All values in kcal/mol.

	EDA					SAPT				
	ER	ES	IND	D	total	ER	ES	IND	D	total
systems dominated by hydrogen-bonds										
01	7.473	-8.858	-2.168	-1.061	-4.614	4.96	-5.07	-0.89	-1.93	-2.92
02	13.529	-14.906	-4.522	-0.708	-6.607	8.37	-8.37	-2.41	-2.20	-4.61
03	74.067	-62.502	-34.155	-1.925	-24.515	41.79	-32.53	-18.28	-9.29	-18.31
04	45.780	-44.066	-18.369	-2.097	-18.752	28.70	-25.60	-11.00	-7.56	-15.46
05	54.221	-51.831	-22.845	-2.658	-23.112	32.57	-29.51	-13.69	-9.20	-19.83
06	60.092	-54.670	-23.843	-3.232	-21.653	32.89	-27.83	-12.27	-9.86	-17.07
07	61.367	-54.560	-23.737	-3.539	-20.469	32.31	-27.11	-11.48	-10.28	-16.57
dispersion bound systems										
08	1.119	-1.144	-0.084	-0.619	-0.729	0.61	-0.19	-0.03	-0.89	-0.49
09	6.178	-5.364	-0.819	-2.102	-2.107	2.46	-1.16	-0.23	-2.35	-1.29
10	4.126	-3.819	-0.441	-1.622	-1.757	2.71	-1.05	-0.31	-2.75	-1.39
11	11.755	-8.870	-1.275	-4.248	-2.638	9.48	-3.13	-0.96	-8.26	-2.86
12	11.391	-9.530	-1.659	-4.392	-4.191	10.19	-4.75	-1.02	-8.87	-4.45
13	19.436	-19.432	-3.727	-7.083	-10.806	12.28	-9.02	-1.76	-11.91	-10.42
14	14.517	-11.681	-1.923	-5.646	-4.733	14.00	-5.22	-1.51	-12.46	-5.19
15	26.182	-23.919	-4.482	-9.987	-12.206	19.15	-11.47	-2.50	-18.08	-12.90
mixed systems										
16	4.538	-4.572	-1.168	-0.926	-2.128	2.31	-1.77	-0.56	-1.34	-1.35
17	8.552	-8.157	-2.934	-2.477	-5.015	3.46	-2.76	-0.99	-2.77	-3.05
18	6.222	-5.844	-1.498	-2.084	-3.204	2.88	-1.81	-0.52	-2.74	-2.20
19	6.965	-7.570	-2.447	-2.310	-5.363	4.71	-3.70	-1.86	-3.58	-4.43
20	6.994	-6.268	-1.059	-2.716	-3.049	4.73	-2.16	-0.68	-4.75	-2.86
21	9.959	-9.622	-2.859	-3.942	-6.464	7.38	-4.45	-1.94	-6.65	-5.66
22	19.816	-18.284	-6.264	-3.188	-7.921	11.71	-8.91	-3.20	-6.61	-7.01

[a] exchange-repulsion (ER), electrostatics (first order, ES), induction (second order ES: polarization and/or charge transfer, IND), dispersion (D)
[b] at SAPT2+(3)/aug-cc-pVTZ level

Correlation between EDA and SAPT values is R=0.99 for ER, R=1.00 for ES, R=0.99 for IND, R=0.88 for D and 0.99 for total. EX and ES are about 50 % smaller for SAPT, but again cancelling out to a large extend. IND is about 50 % smaller for SAPT, D larger by about a factor of 1.8. The biggest difference between EDA and SAPT values is the less perfect correlation between dispersion values, but the differences are not large enough to have a big impact on the ratios for the loss of entropy per unit enthalpy gained (showing the big difference between Hydrogen-bond and dispersion interactions). Nevertheless, using SAPT dispersion terms would likely be an advantage when estimating entropy contributions (see paper for details), but the necessary geometry optimizations and frequency calculations at SAPT level are beyond our resources. DFT-D dispersion estimates are readily available also for larger systems, which might outweigh there presumably lower accuracy when estimating entropic effects.

4. EDA and thermodynamic data for the S66 benchmark set

Table 10: Energy decomposition analysis (EDA)[a] for the S66 benchmark set of non-covalently bound systems, calculated at PBE-D/TZVPP level (using S66 geometries). All values in kcal/mol.

	ER	ES	ER+ES	IND	ES+IND	ER+ES+IND	D	total
systems dominated by hydrogen-bonds								
01	13.520	-14.899	-1.379	-4.520	-19.419	-5.899	-0.708	-6.607
02	15.476	-15.947	-0.471	-5.611	-21.557	-6.082	-1.197	-7.279
03	23.715	-23.704	0.011	-8.330	-32.034	-8.320	-1.272	-9.592
04	20.751	-21.501	-0.750	-7.340	-28.841	-8.090	-1.636	-9.726
05	16.372	-16.725	-0.353	-5.752	-22.477	-6.106	-1.351	-7.457
06	26.247	-25.886	0.361	-8.571	-34.457	-8.210	-1.829	-10.039
07	24.129	-23.698	0.431	-8.507	-32.205	-8.077	-2.377	-10.454
08	14.446	-15.583	-1.137	-4.805	-20.388	-5.942	-0.813	-6.755
09	26.571	-26.014	0.557	-8.984	-34.998	-8.427	-1.872	-10.299
10	13.770	-13.704	0.066	-3.711	-17.415	-3.645	-2.171	-5.816
11	13.960	-14.134	-0.174	-3.669	-17.802	-3.843	-2.894	-6.737
12	23.607	-23.799	-0.192	-8.060	-31.859	-8.252	-1.278	-9.530
13	14.855	-15.496	-0.642	-4.414	-19.910	-5.056	-2.325	-7.381
14	22.753	-22.668	0.085	-7.026	-29.695	-6.941	-2.612	-9.553
15	21.585	-21.605	-0.020	-6.651	-28.256	-6.672	-3.279	-9.951
16	10.478	-12.635	-2.157	-3.162	-15.797	-5.319	-0.967	-6.286
17	52.051	-48.146	3.906	-21.423	-69.568	-17.517	-2.603	-20.120
18	21.552	-21.118	0.434	-8.087	-29.204	-7.652	-1.088	-8.740
19	23.689	-22.792	0.897	-8.750	-31.542	-7.853	-1.511	-9.364
20	77.358	-66.077	11.281	-34.982	-101.059	-23.701	-2.080	-25.781
21	48.543	-46.772	1.771	-19.010	-65.782	-17.239	-2.253	-19.492
22	63.333	-57.363	5.970	-27.582	-84.945	-21.612	-2.319	-23.931
23	52.862	-50.898	1.964	-21.872	-72.770	-19.908	-2.459	-22.367
dispersion bound systems								
24	8.159	-6.222	1.937	-0.952	-7.174	0.985	-3.593	-2.608
25	11.286	-9.441	1.845	-1.364	-10.805	0.481	-4.256	-3.775
26	19.402	-19.426	-0.024	-3.727	-23.153	-3.751	-7.077	-10.828
27	10.301	-8.338	1.963	-1.245	-9.582	0.718	-4.019	-3.301
28	15.165	-12.889	2.275	-2.196	-15.086	0.079	-5.580	-5.501
29	14.804	-13.477	1.327	-2.346	-15.823	-1.019	-5.564	-6.583
30	5.675	-4.342	1.333	-0.708	-5.050	0.625	-2.086	-1.461
31	9.575	-8.522	1.053	-1.413	-9.936	-0.361	-3.187	-3.548
32	14.480	-14.642	-0.162	-4.769	-19.412	-4.932	-1.842	-6.774
33	7.727	-6.304	1.423	-0.925	-7.229	0.498	-2.485	-1.987
34	19.490	-14.568	4.922	-3.015	-17.583	1.907	-7.308	-5.401
35	14.329	-10.934	3.394	-2.191	-13.125	1.203	-5.046	-3.843
36	10.404	-7.784	2.620	-1.718	-9.502	0.902	-3.569	-2.667
37	14.684	-11.304	3.380	-2.066	-13.370	1.314	-5.073	-3.759
38	16.025	-12.410	3.615	-2.284	-14.693	1.332	-5.882	-4.550
39	13.147	-10.703	2.444	-1.732	-12.434	0.713	-4.872	-4.159
40	7.179	-6.447	0.732	-0.858	-7.305	-0.126	-3.109	-3.235
41	17.343	-13.603	3.740	-2.792	-16.395	0.949	-6.765	-5.816
42	14.465	-11.362	3.103	-2.209	-13.571	0.894	-5.854	-4.960
43	11.837	-9.909	1.928	-1.689	-11.597	0.240	-4.608	-4.368
44	10.633	-8.132	2.501	-1.716	-9.848	0.785	-3.753	-2.968
45	4.703	-4.197	0.506	-0.690	-4.887	-0.185	-1.881	-2.066
46	17.370	-13.667	3.703	-3.085	-16.752	0.618	-6.246	-5.628
mixed systems								
47	6.367	-5.808	0.559	-0.963	-6.771	-0.404	-2.703	-3.107
48	9.068	-8.196	0.873	-1.534	-9.730	-0.661	-3.209	-3.870
49	7.493	-6.972	0.522	-1.186	-8.158	-0.664	-2.963	-3.627
50	4.904	-5.124	-0.220	-1.235	-6.359	-1.455	-1.947	-3.402
51	4.283	-4.455	-0.172	-1.093	-5.548	-1.265	-0.827	-2.092
52	9.565	-9.192	0.374	-3.225	-12.417	-2.851	-2.818	-5.669
53	10.799	-10.529	0.270	-2.958	-13.488	-2.688	-2.577	-5.265
54	8.560	-8.150	0.410	-2.955	-11.105	-2.545	-2.459	-5.004
55	9.807	-9.113	0.693	-2.843	-11.956	-2.150	-3.333	-5.483
56	9.317	-8.311	1.006	-1.869	-10.180	-0.862	-3.275	-4.137
57	11.850	-10.948	0.902	-2.706	-13.655	-1.804	-4.360	-6.164
58	9.907	-10.233	-0.326	-2.582	-12.815	-2.907	-1.926	-4.833
59	5.773	-7.366	-1.593	-1.740	-9.106	-3.333	-0.445	-3.778
60	14.302	-14.065	0.237	-4.892	-18.957	-4.655	-1.580	-6.235
61	10.458	-8.460	1.998	-1.873	-10.332	0.125	-4.078	-3.953
62	14.277	-11.470	2.807	-2.706	-14.176	0.101	-4.995	-4.894
63	9.510	-8.623	0.887	-1.562	-10.185	-0.675	-3.505	-4.180
64	8.266	-7.638	0.629	-1.592	-9.230	-0.963	-2.695	-3.658
65	10.759	-11.338	-0.579	-3.492	-14.830	-4.071	-0.924	-4.995
66	11.292	-10.545	0.747	-2.487	-13.031	-1.740	-3.041	-4.781

[a] exchange-repulsion (ER), electrostatics (first order, ES), induction (second order ES: polarization and/or charge transfer, IND), dispersion (D)

Table 11: Thermodynamic data for the S66[a] benchmark set of non-covalently bound systems, calculated at PBE-D/TZVPP level (using optimized geometries) within the rigid-rotor/harmonic-oscillator (RRHO)[b] approximation. All values in kcal/mol.

	ΔE	ΔH	ΔG	-TΔS	-TΔS_{vib}	-TΔS_{rot}	-TΔS_{trans}
systems dominated by hydrogen-bonds							
01	-6.53	-4.91	1.2	6.11	-3.56	-0.02	9.70
02	-7.10	-5.41	2.05	7.46	-4.10	1.65	9.92
03	-9.23	-7.50	0.25	7.75	-3.86	1.71	9.91
04	-9.36	-7.75	0.02	7.77	-4.89	2.55	10.12
05	-7.24	-5.63	2.65	8.28	-5.63	3.70	10.21
06	-9.60	-8.04	0.12	8.16	-5.82	3.78	10.20
07	-9.97	-8.39	1.37	9.76	-5.52	4.78	10.50
08	-6.66	-5.11	1.57	6.68	-4.88	1.64	9.92
09	-9.85	-8.25	0.61	8.86	-5.13	3.80	10.20
10	-5.72	-4.20	4.65	8.85	-5.19	3.85	10.18
11	-6.61	-5.17	4.11	9.28	-6.08	4.88	10.48
12	-9.17	-7.47	-0.27	7.20	-4.42	1.72	9.91
13	-7.06	-5.52	3.14	8.66	-6.57	4.73	10.50
14	-8.93	-7.39	1.6	8.99	-6.32	4.83	10.48
15	-9.57	-8.02	1.87	9.89	-7.12	6.06	10.94
16	-6.20	-5.34	2.18	7.52	-5.02	2.43	10.12
17	-17.77	-16.74	-5.79	10.95	-7.17	6.80	11.32
18	-8.45	-7.42	1.34	8.76	-3.41	2.04	10.13
19	-8.98	-7.48	0.38	7.86	-6.94	4.27	10.52
20	-20.01	-19.14	-7.84	11.30	-5.12	5.65	10.77
21	-17.36	-15.80	-3.96	11.84	-4.55	5.63	10.75
22	-19.89	-18.90	-7.74	11.16	-5.99	6.15	11.00
23	-19.79	-18.46	-6.92	11.54	-5.62	6.16	10.99
dispersion bound systems							
24	-2.58	-1.36	3.83	5.19	-9.06	3.25	11.00
25	-3.75	-2.49	6.02	8.51	-8.28	5.77	11.01
26	-9.63	-8.27	2.8	11.07	-7.80	7.55	11.32
27	-3.27	-2.01	4.9	6.91	-8.40	4.31	11.01
28	-5.37	-4.10	4.05	8.15	-8.19	5.19	11.15
29	-6.43	-5.11	4.38	9.49	-7.90	6.24	11.15
30	-1.45	-0.28	5.18	5.46	-7.79	2.83	10.44
31	-3.48	-2.16	5.62	7.78	-6.93	4.20	10.51
33	-1.98	-0.78	5.91	6.69	-7.23	3.49	10.44
34	-5.38	-3.94	6.92	10.86	-5.98	5.91	10.93
35	-3.81	-2.57	4.61	7.18	-8.04	4.29	10.93
36	-2.68	-1.33	6.44	7.77	-7.38	4.22	10.93
37	-3.69	-2.41	6.01	8.42	-7.08	4.58	10.92
38	-4.54	-3.12	8.28	11.40	-5.48	5.98	10.91
39	-4.13	-2.80	5.2	8.00	-7.57	4.63	10.95
40	-3.19	-2.57	4.42	6.99	-7.14	3.17	10.97
41	-5.72	-4.29	6.56	10.85	-6.96	6.71	11.10
42	-4.88	-3.51	6.94	10.45	-7.15	6.50	11.09
43	-4.21	-3.43	7.46	10.89	-6.74	6.53	11.10
44	-2.96	-1.61	5.71	7.32	-6.51	3.42	10.42
mixed systems							
46	-5.57	-4.18	6.36	10.54	-6.66	6.27	10.94
47	-3.08	-1.78	2.75	4.53	-9.53	3.07	11.00
48	-3.85	-2.53	4.97	7.50	-8.67	5.16	11.01
49	-3.61	-2.28	3.5	5.78	-9.33	4.11	11.01
52	-5.54	-4.91	2.77	7.68	-7.53	4.34	10.88
53	-5.16	-3.80	2.98	6.78	-8.38	4.30	10.87
54	-4.93	-3.58	0.75	4.33	-6.89	1.10	10.13
55	-5.44	-4.16	2.28	6.44	-7.43	3.35	10.52
56	-4.11	-2.81	3.85	6.66	-7.26	3.43	10.50
57	-6.11	-4.75	1.96	6.71	-8.91	4.66	10.97
58	-4.78	-3.36	4.23	7.59	-8.49	5.07	11.01
61	-3.88	-2.56	6.81	9.37	-7.38	5.90	10.85
62	-4.79	-3.44	6.88	10.32	-6.47	5.96	10.84
63	-4.13	-2.84	4.5	7.34	-7.94	4.40	10.88
64	-3.53	-2.24	4.9	7.14	-7.14	3.86	10.42
66	-4.73	-3.35	5.01	8.36	-6.61	4.47	10.50

[a] excluding entries 32, 45, 50, 51, 59, 60, and 65, to avoid problems with the RRHO approximation for linear molecules
[b] vibrational (vib), rotational (rot) and translational (trans) contributions

Table 12: Average enthalpic and entropic contributions for the S66[a] benchmark set of non-covalently bound systems in kcal/mol.[bc]

	ΔH_{ZVPE}[d]	ΔH_{vib}	$-T\Delta S_{vib}$	$-T\Delta S_{rot}$	$-T\Delta S_{trans}$	$-T\Delta S$	ΔE	NDF[e]	mass/a.u.
				net contributions					
S66	1.1	2.6	6.7	4.4	10.7	8.3	-6.6	55.9	126.7
S66/HB[f]	1.5	2.3	5.3	3.9	10.4	8.9	-10.5	40.1	97.7
S66/D[g]	0.8	2.9	7.3	5.0	10.9	8.6	-4.0	72.5	154.3
$\frac{S66/D}{S66/HB}$	0.5	1.3	1.4	1.3	1.0	1.0	0.4	1.8	1.6
				net contributions per kcal/mol of interaction energy, i.e. $\frac{X}{\lvert\Delta E\rvert}$					
S66	0.2	0.6	1.6	0.9	2.3	1.7	-	-	-
S66/HB[f]	0.2	0.3	0.6	0.4	1.1	0.9	-	-	-
S66/D[g]	0.2	0.9	2.4	1.4	3.4	2.5	-	-	-
$\frac{S66/D}{S66/HB}$	1.0	3.0	4.0	3.5	3.1	2.8	-	-	-

[a] excluding entries 32, 45, 50, 51, 59, 60, and 65, to avoid problems with the RRHO approximation for linear molecules
[b] at PBE-D/TZVPP/TZVPP level
[c] within the RRHO approximation: vibrational (vib), rotational (rot) and translational (trans) contributions
[d] zero point vibrational energy (ZVPE) contributions
[e] average number of degrees of freedom (NDF) of the complex systems
[f] subset of systems dominated by hydrogen-bonds, entry 1 to 23
[g] subset of dispersion bound systems, entry 24 to 46

The ratios for the loss of entropy per unit enthalpy gained are again showing a big difference between Hydrogen-bond and dispersion interaction: We find a $\frac{S22/D}{S22/HB}$ ratio for $\frac{-T\Delta S}{|\Delta E|}$ of 2.8, indicating again an about three times higher loss of entropy for dispersion interactions. Correlation between ΔH and $-T\Delta S$ values is R=0.59 for the complete set, R=0.84 for the Hydrogen-bond, and R=0.74 for the dispersion-bound subset. Judging from the ratio of IND over D contributions, subset classifications for the S66 seems less appropriate. For the S22 set, Hydrogen-bonded systems have IND/D ratios between 5 and 15, while this ratio is roughly below 0.5 for dispersion bound ones. Applying this rule to the S66 set, entries 10, 11, 13, 14, and 15 would have to be classified as mixed, not Hydrogen-bonded, and entry 32 again as mixed, not dispersion-bound. This change leads to a much higher correlation value of R=0.93 for the Hydrogen-bond subset, but no improvement for the dispersion-bound one. We therefore find a big difference between the trends of Hydrogen-bond and dispersion-bound systems also for this benchmark set, with substantially higher correlation factors if the different subsets are treated separately (see also figure 1 below). Correlation between calculated and estimated entropic effects (with estimates based on dispersion and non-dispersion energy contributions as done for the S22 set, see main manuscript for details), is R=0.83 for the complete set, R=0.86 for the joint Hydrogen-bond and dispersion-bound subset, and 0.92 for the Hydrogen-bond subset without any refit of the parameters, indicating that the quality of the estimated values somewhat worsens if interactions are more mixed.

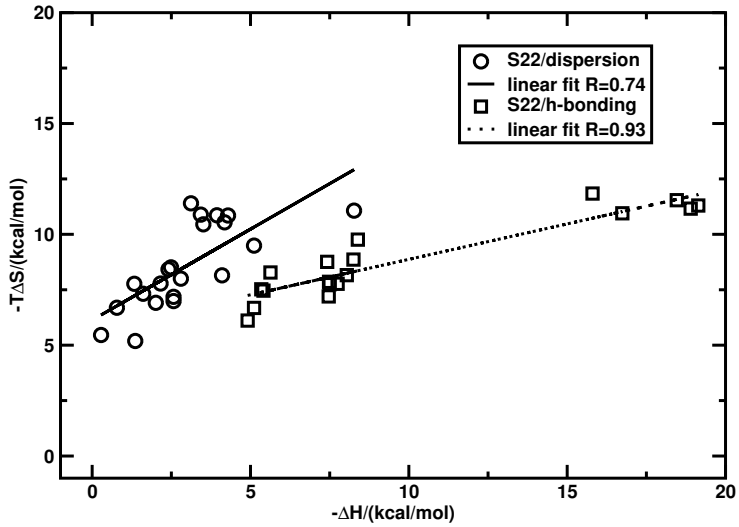

Figure 1: Different enthalpy-entropy compensation for the S66 hydrogen-bond and dispersion subsets (data from table 11, corresponds to figure 2 of the main manuscript for the S22 set).

5. Additional data for the S22 benchmark set

Table 13: Calculated and estimated entropy contributions for the S22[a] benchmark set in kcal/mol[bc], as well the DFT (E_{DFT}) and DFT-D dispersion energy (E_D) values used for the estimation (see main manuscript for details and a graphical presentation of this data in figure 2).

entry	$-T\Delta S_{calculated}$	$-T\Delta S_{estimated}$	ΔE_{DFT}	ΔE_D
1	5.29	5.96	3.78	1.07
2	6.11	6.18	5.65	0.71
3	11.73	10.58	17.68	1.94
4	11.73	9.92	14.84	2.10
5	11.54	11.14	17.66	2.61
6	10.61	11.07	15.46	3.26
7	10.69	10.92	14.17	3.52
8	4.13	4.55	0.11	0.62
9	7.12	5.79	0.08	2.10
10	4.89	5.45	0.31	1.62
11	6.40	7.04	-1.87	4.24
12	7.49	7.68	-0.01	4.39
13	11.07	10.66	2.53	7.08
14	7.74	8.29	-1.64	5.65
15	11.74	12.79	1.44	9.98
17	4.85	6.79	2.52	2.48
18	4.75	6.09	1.22	2.08
20	6.34	6.30	0.04	2.72
21	8.57	7.86	1.94	3.95
22	9.36	7.88	4.30	3.18

[a] excluding entries 16 and 19 to avoid problems with the RRHO approximation for linear molecules
[b] at PBE-D/TZVPP/TZVPP level
[c] within the RRHO approximation: vibrational (vib), rotational (rot) and translational (trans) contributions