Supporting information for

A quantum chemical view of enthalpy-entropy compensation

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3. Comparison of EDA and SAPT values
4. EDA and thermodynamic data for the S66 benchmark set
5. Additional data for the S22 benchmark set
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.

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\(^a\) 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.
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.

<table>
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<th>ES+IND</th>
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\(^a\) 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.
### 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.

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<th></th>
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<th>(\Delta H)</th>
<th>(\Delta G)</th>
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<th>(-T\Delta S_{\text{vib}})</th>
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\(^{[a]}\) 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.\(^{[bc]}\)

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<th>(-T\Delta S_{\text{rot}})</th>
<th>(-T\Delta S_{\text{trans}})</th>
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net contributions per kcal/mol of interaction energy, i.e. \(\frac{X}{\Delta E}\)

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<td>(\frac{S22}{S22+H})</td>
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<td>5.3</td>
<td>3.8</td>
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\(^{[a]}\) 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.

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<th>(\Delta E)</th>
<th>(\Delta H)</th>
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<th>(-T\Delta S_{\text{vib}})</th>
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\(^a\) 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.\(^{[bc]}\)

<table>
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<th>(\Delta H_{\text{ZPVE}})(^d)</th>
<th>(\Delta H_{\text{vib}})</th>
<th>(-T\Delta S_{\text{vib}})</th>
<th>(-T\Delta S_{\text{rot}})</th>
<th>(-T\Delta S_{\text{trans}})</th>
<th>(-T\Delta S)</th>
</tr>
</thead>
<tbody>
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<td>4.4</td>
<td>4.1</td>
<td>10.7</td>
</tr>
<tr>
<td>S22/HB(^f)</td>
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<td>1.8</td>
<td>3.6</td>
<td>4.5</td>
<td>10.6</td>
</tr>
<tr>
<td>S22/D(^g)</td>
<td>1.4</td>
<td>2.4</td>
<td>4.8</td>
<td>4.1</td>
<td>10.7</td>
</tr>
</tbody>
</table>

net contributions per kcal/mol of interaction energy, i.e. \(X/\Delta E\)

| \(S_{22}/D\) \(S_{22}/HB\) | 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.

<table>
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<th>(\Delta E)</th>
<th>(\Delta H)</th>
<th>(\Delta G)</th>
<th>(-T\Delta S)_vib</th>
<th>(-T\Delta S)_rot</th>
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<td>-4.73</td>
<td>5.82</td>
<td>11.18</td>
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</table>

\(^{[a]}\) 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.\(^{[bc]}\)

<table>
<thead>
<tr>
<th></th>
<th>(\Delta H_{ZV PE})(^{[d]})</th>
<th>(\Delta H_{vib})</th>
<th>(-T\Delta S_{vib})</th>
<th>(-T\Delta S_{rot})</th>
<th>(-T\Delta S_{trans})</th>
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<tr>
<td>S22/HB(^{[f]})</td>
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<td>10.6</td>
<td>9.8</td>
<td>-11.6</td>
</tr>
<tr>
<td>S22/D(^{[g]})</td>
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<td>1.9</td>
<td>4.7</td>
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<td>10.5</td>
<td>9.8</td>
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<tr>
<td>S22/D</td>
<td>(\frac{S22}{S22/HB})</td>
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<td>1.1</td>
<td>1.0</td>
<td>1.0</td>
<td>0.2</td>
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\(^{[a]}\) excluding entry 16 and 19, to avoid problems with the RRHO approximation for linear molecules.

\(^{[bc]}\) Vibrational (vib), rotational (rot) and translational (trans) contributions.

\(^{[d]}\) 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 \( \frac{S_{22}^{D}}{S_{22}^{HB}} \) 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 \( \Delta H \) 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 \( \Delta H \) 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 \( \Delta H \) 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.

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Dispersion bound systems

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<td>-11.681</td>
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</table>

Mixed systems

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)\(^{[1]}\) for the S66 benchmark set of non-covalently bound systems, calculated at PBE-D/TZVPP level (using S66 geometries). All values in kcal/mol.

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<th>ER+ES</th>
<th>IND</th>
<th>ER+IND</th>
<th>ES+IND</th>
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\(^{[1]}\) 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\textsuperscript{[a]} benchmark set of non-covalently bound systems, calculated at PBE-D/TZVPP level (using optimized geometries) within the rigid-rotor/harmonic-oscillator (RRHO)\textsuperscript{[b]} approximation. All values in kcal/mol.

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\textsuperscript{[a]} excluding entries 32, 45, 50, 51, 59, 60, and 65, to avoid problems with the RRHO approximation for linear molecules

\textsuperscript{[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.\(^{bc}\)

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Net contributions per kcal/mol of interaction energy, i.e. \(\frac{X}{\Delta E}\):

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\(^a\) excluding entries 32, 45, 50, 51, 59, 60, and 65, to avoid problems with the RRHO approximation for linear molecules.

\(^b\) at PBE-D/TZVP/TZVP 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 \(\Delta H\) 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).

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\(^{[a]}\) 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