

## Stacking Interactions at Large Horizontal Displacements—Comparison of Various Ring Types

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**Abstract:** Noncovalent interactions at large distances play an important role in molecular recognition processes, early steps of protein folding or the design of supramolecular structures. Plateaus or even shallow minima can occur at potential energy curves of stacking interactions between certain ring types. Stacking interactions at large horizontal displacements are also frequently found in crystal structures of various rings. In this work, we discuss how horizontal displacement affects stacking interactions on the basis of interaction energy calculations and energy decomposition analysis performed by Symmetry-Adapted Perturbation Theory (SAPT). We compared aromatic/aromatic to aromatic/aliphatic stacking as well as stacking interactions involving resonance-assisted hydrogen bridged (RAHB) rings, including RAHB/RAHB and RAHB/aromatic interactions. Among RAHB rings we observed different behavior of polar and nonpolar RAHB molecules. A comparison of aromatic/aromatic and aromatic/aliphatic systems provides an insight into fundamental differences in the nature between these two interaction types. While comparing stacking involving RAHB rings we can observe the difference between polar and nonpolar RAHB rings.

**Keywords:** stacking at large horizontal displacements, SAPT calculations, RAHB rings

### 1. Introduction

Stacking interactions between aromatic rings in crystal structures are mostly formed at large horizontal displacements. In spite of being disfavoured in dimer systems, stacking at large horizontal displacement is favoured in crystal structures, since it enables the formation of additional interactions with the faces of aromatic rings [1]. Resonance-assisted hydrogen-bridged (RAHB) rings are very interesting molecules useful in synthesis and material design due to synergistic strengthening between intramolecular hydrogen bond and resonance. The stacking of RAHB rings is confirmed by crystal structure analysis and quantum-chemical calculations of interaction energies [2].

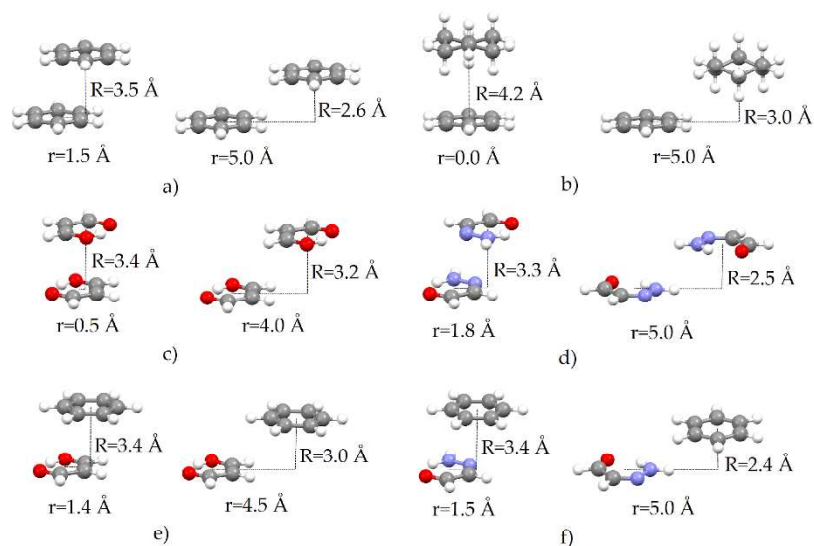
## 2. Methodology

Interaction energies of aromatic/aromatic and aromatic/aliphatic interactions are calculated for the most stable geometries and the horizontally displaced geometries at 5.0 Å (Figure 1a,b) by Symmetry-Adapted Perturbation Theory (SAPT2+3) method at def2-tzvpd level using PSI4 programme [3].

## 3. Results

Stacking interactions between benzene and cyclohexane are somewhat stronger than benzene/benzene interactions [1], however, benzene/benzene interactions preserve a much more significant portion of their strength with increasing horizontal displacements (69.6%) than the benzene/cyclohexane interactions (44.2%) (Table 1). This is the advantage of the aromatic/aromatic interactions since two aromatic rings can recognize each other at a larger range of distances. The electrostatic contribution is the main reason for the observed difference between the two systems (89.7% compared to 28.6% of the electrostatic term is preserved in the two systems, Table 1). The other energy contributions (exchange-repulsion, induction and dispersion terms) are similarly conserved in both systems (31–47%, Table 1). Electrostatic term decreases more in benzene/cyclohexane than in the benzene/benzene systems due to the direction of local C-H dipoles in the large displacement geometries which are orthogonal in benzene/cyclohexane system and antiparallel in benzene/benzene system [1].

Malonaldehyde ( $\text{H}_4\text{C}_3\text{O}_2$ ) and two of its analogues, mononitrogen ( $\text{H}_5\text{C}_3\text{NO}$ ) and dinitrogen ( $\text{H}_4\text{C}_2\text{N}_2\text{O}$ ) are particularly frequent in the Cambridge Structural Database (CSD) [2]. These molecules served as model systems for the calculations of RAHB/RAHB and RAHB/benzene interaction energies. It is interesting that one of these molecules, dinitrogen analogue of malonaldehyde ( $\text{H}_4\text{C}_2\text{N}_2\text{O}$ ), does not have a clearly pronounced dipole moment, which can be visualized from electrostatic potential maps [2]. Hence, we can compare RAHB/RAHB (Figure 1c,d) and RAHB/benzene interactions (Figure 1e,f) in case of a polar and a nonpolar RAHB molecule. The potential energy curves of RAHB/RAHB and RAHB/benzene stacking interactions were calculated along several directions. Plateaus or even shallow minima can occur at potential energy curves at large horizontal displacements, depending on the system and the direction observed [4]. A larger portion of the maximum stacking interaction strength is preserved when shifted to large displacement in the case of the nonpolar RAHB molecule ( $\text{H}_4\text{C}_2\text{N}_2\text{O}$ ) than in the case of the polar RAHB molecule (malonaldehyde), 79.5% and 37.3% respectively for RAHB/RAHB interactions and 86.8% and 51.1% respectively for RAHB/benzene interactions. The main reason is the larger preservation of the electrostatic and induction components in the nonpolar systems than in the polar systems. Namely, the electrostatic and induction terms are more favourable at maximum energy geometries for the polar systems (Table 1) but decrease at large displacements.



**Figure 1.** Model systems for the SAPT calculations with the horizontal displacements ( $r$ ) and distances between the ring planes ( $R$ ) indicated; the left geometry of each system corresponds to the maximum interaction energy, the right geometry is a large displacement one; a) benzene dimer; b) benzene/cyclohexane dimer; c)  $\text{H}_4\text{C}_3\text{O}_2/\text{H}_4\text{C}_3\text{O}_2$  dimer; d)  $\text{H}_4\text{C}_2\text{N}_2\text{O}/\text{H}_4\text{C}_2\text{N}_2\text{O}$  dimer; e)  $\text{H}_4\text{C}_3\text{O}_2/\text{C}_6\text{H}_6$  dimer; f)  $\text{H}_4\text{C}_2\text{N}_2\text{O}/\text{C}_6\text{H}_6$  dimer; large displacement geometries correspond to the plateaus or minima at the potential energy curves for systems c,d,e and f.

**Table 1.** SAPT2+3/def2-tzvpdp energy decomposition analysis of the interactions given in Figure 1. Total interaction energies and its components (ELST, electrostatics; EXCH, exchange-repulsion; IND, induction; DISP, dispersion) are given in kcal/mol.

system	ELST	EXCH	IND	DISP	TOTAL
$\text{C}_6\text{H}_6/\text{C}_6\text{H}_6$ max energy*	-1.51	6.63	-0.71	-7.22	-2.81
$\text{C}_6\text{H}_6/\text{C}_6\text{H}_6$ large displ.*	-1.36	2.85	-0.31	-3.14	-1.96
<b>Conserved (%)</b>	<b>89.7</b>	<b>43.0</b>	<b>43.1</b>	<b>43.5</b>	<b>69.6</b>
$\text{C}_6\text{H}_6/\text{C}_6\text{H}_{12}$ max energy*	-1.87	4.99	-0.63	-5.68	-3.19
$\text{C}_6\text{H}_6/\text{C}_6\text{H}_{12}$ large displ.*	-0.53	2.04	-0.20	-2.72	-1.41
<b>Conserved (%)</b>	<b>28.6</b>	<b>40.9</b>	<b>31.3</b>	<b>47.8</b>	<b>44.2</b>
$\text{H}_4\text{C}_3\text{O}_2/\text{H}_4\text{C}_3\text{O}_2$ max. energy	-3.20	5.18	-0.54	-5.80	-4.35
$\text{H}_4\text{C}_3\text{O}_2/\text{H}_4\text{C}_3\text{O}_2$ large displ.	-1.19	2.36	-0.26	-2.53	-1.63
<b>Conserved (%)</b>	<b>37.2</b>	<b>45.5</b>	<b>49.1</b>	<b>43.6</b>	<b>37.3</b>
$\text{H}_4\text{C}_2\text{N}_2\text{O}/\text{H}_4\text{C}_2\text{N}_2\text{O}$ max. energy	-1.49	5.27	-0.44	-5.61	-2.27
$\text{H}_4\text{C}_2\text{N}_2\text{O}/\text{H}_4\text{C}_2\text{N}_2\text{O}$ large displ.	-1.85	2.34	-0.39	-1.90	-1.80
<b>Conserved (%)</b>	<b>124.8</b>	<b>44.4</b>	<b>88.7</b>	<b>33.8</b>	<b>79.5</b>
$\text{H}_4\text{C}_3\text{O}_2/\text{C}_6\text{H}_6$ max. energy	-2.79	6.72	-0.81	-6.80	-3.68
$\text{H}_4\text{C}_3\text{O}_2/\text{C}_6\text{H}_6$ large displ.	-1.33	2.32	-0.27	-2.61	-1.88
<b>Conserved (%)</b>	<b>47.6</b>	<b>34.6</b>	<b>33.4</b>	<b>38.3</b>	<b>51.1</b>
$\text{H}_4\text{C}_2\text{N}_2\text{O}/\text{C}_6\text{H}_6$ max. energy	-0.81	3.32	-0.39	-4.92	-2.80
$\text{H}_4\text{C}_2\text{N}_2\text{O}/\text{C}_6\text{H}_6$ large displ.	-2.16	2.95	-0.46	-2.75	-2.43
<b>Conserved (%)</b>	<b>268.2</b>	<b>88.8</b>	<b>119.5</b>	<b>55.8</b>	<b>86.8</b>

\*data taken from reference 1

On the other hand, the electrostatic term increases at large displacements of the

H<sub>4</sub>C<sub>2</sub>N<sub>2</sub>O/H<sub>4</sub>C<sub>2</sub>N<sub>2</sub>O dimer since the local N-H dipoles are in antiparallel contact (Figure 1d). The electrostatic term also increases in the H<sub>4</sub>C<sub>2</sub>N<sub>2</sub>O/C<sub>6</sub>H<sub>6</sub> dimer at large displacements due to the interaction of the N-H dipole with the electrostatic potential gradient at the edges of the benzene molecule (Figure 1f). The induction term becomes slightly more favourable at large displacement than at the most stable geometry of the H<sub>4</sub>C<sub>2</sub>N<sub>2</sub>O/C<sub>6</sub>H<sub>6</sub> dimer. Exchange-repulsion term decreases more in the case of H<sub>4</sub>C<sub>3</sub>O<sub>2</sub>/C<sub>6</sub>H<sub>6</sub> than in the case of H<sub>4</sub>C<sub>2</sub>N<sub>2</sub>O/C<sub>6</sub>H<sub>6</sub> dimer. Dispersion term decreases in all systems upon shifting to large displacements due to the smaller contact area of the interacting fragments.

#### 4. Conclusions

Significant stacking interactions occur at large horizontal displacements of certain systems and they sometimes correspond to energy minima or the plateaus on the potential energy curves. Comparing benzene/benzene and benzene/cyclohexane systems the benzene/benzene interaction preserves more of its strength upon horizontal displacement due to the slower decrease of electrostatic term. Both RAHB/RAHB and RAHB/benzene interactions are stronger in the case of a polar RAHB molecule but conserve a smaller portion of their strength at large displacements mostly due to the larger decrease of the electrostatics and induction terms.

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#### References

- [1] D. B. Ninković, J. P. Blagojević Filipović, M. B. Hall, E. N. Brothers, S. D. Zarić, *What Is Special about Aromatic–Aromatic Interactions? Significant Attraction at Large Horizontal Displacement*, ACS Central Science, 6 (2020) 420–425.
- [2] J. P. Blagojević Filipović, M. B. Hall, S. D. Zarić, *Stacking Interactions of Resonance-Assisted Hydrogen-Bridged rings. A Systematic Study of Crystal Structures and Quantum-Chemical Calculations*, Cryst. Growth Des, 19 (2019) 5619–5628.
- [3] R. M. Parrish et al. *PSI4 1.1: An Open-Source Electronic Structure Program Emphasizing Automation, Advanced Libraries, and Interoperability*, J. Chem. Theory Comput. 13 (2017) 3185–3197.
- [4] J. P. Blagojević Filipović, S. D. Zarić, *Significant Stacking Interactions of Resonance-Assisted Hydrogen-Bridged (RAHB) Rings at Large Horizontal Displacements*, Cryst. Growth Des. 21 (2021) 4947–4958.