

## Exercise 2. Halogen bonds versus hydrogen bonds: covalency, dispersion and cooperativity

### Reading material

C. Fonseca Guerra, H. Zijlstra, G. Paragi, F. M. Bickelhaupt, *Chem. Eur. J.* **2011**, *17*, 12612.

L. P. Wolters, F. M. Bickelhaupt, *ChemistryOpen* **2012**, *1*, 96.

L. P. Wolters, N. W. G. Smits, C. Fonseca Guerra, *Phys. Chem. Chem. Phys.* **2015**, *17*, 1585.

### Introduction

The nature of hydrogen bonds has been studied extensively, and it is now generally believed that hydrogen bonds are not purely electrostatic, but also partly covalent in nature (for a detailed overview see e.g. *Chem. Eur. J.* **1999**, *5*, 3581). Halogen bonds, on the other hand, have received considerable less attention. In this exercise, you will study the nature of both bonds by analyzing the following halogen bonded (1) and hydrogen bonded (2) systems:



with D, X, A = F, Cl, Br. The analyses will be carried out within the framework of Kohn-Sham molecular orbital (KS-MO) theory, in combination with a quantitative energy decomposition analysis (EDA) and Voronoi deformation density (VDD) analysis. The main objective is to achieve a detailed understanding of the nature of halogen bonds versus hydrogen bonds. How do they resemble, and how do they differ from one another?

### Step 1. Optimize structures and compute $\Delta E$

Optimize the structures at the BLYP-D3(BJ) / TZ2P level of theory. These computations will give you the electronic bond energy  $\Delta E$  (recall:  $\Delta E = E_{\text{complex}} - E_{\text{reactant1}} - E_{\text{reactant2}}$ ). What trends do you find in bond lengths and energies for the hydrogen-bonded and halogen-bonded systems? Are these trends in line with what you expected?

#### Technical note

An example input file for geometry optimizations is given in the appendix. Make sure you will use the same settings in your other computations (i.e. single point and fragment analyses). The energies of the single atoms can be obtained by running a single point calculation. Do not forget to adjust the charge in your input files.

## Step 2. Using EDA to rationalize trends in $\Delta E$

Next, perform an energy decomposition analysis on each optimized complex to obtain further insight in the interaction energy between the hydrogen donor DH or halogen donor DX (fragment 1) and the acceptor atom  $A^-$  (fragment 2). Do the halogen bonds have a significant covalent component? What happens with the electrostatic interaction  $\Delta V_{\text{elstat}}$ , orbital interaction  $\Delta E_{\text{oi}}$  and dispersion interaction  $\Delta E_{\text{disp}}$  when going from  $A^- = F^-$  to  $Br^-$ ? What is the influence of X and D on the interaction energy components? What are the main resemblances, and what are the main differences between the hydrogen-bonded and halogen-bonded systems?

### Technical note

*Dispersion is a long-range, nonlocal correlation effect. Therefore, the local density functionals (including the formally local GGA functionals) are not capable of describing this interaction component. In the DFT-D3(BJ) method developed by Grimme, the atom pair-wise dispersion interactions are computed in a semiempirical way and added to the total interaction energy. For more information, see Koch and Holthausen, A Chemist's Guide to Density Functional Theory 2<sup>nd</sup> ed. p236-238, and Grimme, Wiley Interdiscip. Rev. Comput. Mol. Sci. **2011**, 1, 211.*

## Step 3. Analyzing the covalent component

In the next step, we want to rationalize the covalent component  $\Delta E_{\text{oi}}$  by doing a KS-MO analysis. First, visualize the orbitals of the separated monomers with ADFview and consider which donor-acceptor interactions might be possible. Next, open the MO diagram of the complex with ADFlevels, and analyze which fragment orbitals participate in HOMO-LUMO interactions. Analyze their mutual overlap and gross populations, and write down their energy difference (HOMO-LUMO gap). Can you explain the differences in orbital interaction strength?

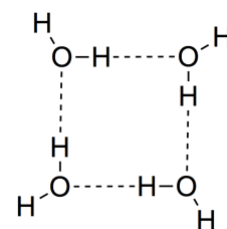
In view of the time, do the analyses on the complexes with one X and D atom of choice (for example:  $F-Cl \cdots A^-$  and  $F-H \cdots A^-$ ,  $A = F, Cl, Br$ ), which gives a total of six different systems only.

## Step 4. Analyzing the electrostatic component

Next, we will study the electrostatic component for the same systems as in the previous step. Use the Voronoi Deformation Density (VDD) charges to explain the trends in  $\Delta V_{\text{elstat}}$ .

## Step 5. Cooperativity in H-bonds and X-bonds

In the final part of this exercise, you will study the cooperativity in a cyclic water tetramer. Optimize the quartet in  $C_{4h}$  symmetry, and determine the amount of cooperativity (see technical notes). For this, you will need to do three fragment analyses:



1. On the optimized quartet in order to obtain  $\Delta E_{\text{int}}$ . In this computation, each water molecule will be a fragment, so you will have four fragments in total.
2. On two hydrogen-bonded water molecules (in the geometry that they have in the interacting quartet) in order to obtain  $\Delta E_{\text{pair}}$
3. On two opposing water molecules (in the geometry that they have in the interacting quartet) in order to obtain  $\Delta E_{\text{diag}}$

Is there a cooperative reinforcement in the water quartet? Is this in line with what you expected, given the cooperativity in (*N*-halo) guanine quartets?

In the next step, we want to trace the actual origin of the cooperativity in the water quartets. This can be done by taking one of the water monomers in the quartet, and stepwise adding the other water monomers (always in the geometry in the quartet), that is  $\text{H}_2\text{O} + \text{H}_2\text{O} = (\text{H}_2\text{O})_2$ ,  $(\text{H}_2\text{O})_2 + \text{H}_2\text{O} = (\text{H}_2\text{O})_3$ , and  $(\text{H}_2\text{O})_3 + \text{H}_2\text{O} = (\text{H}_2\text{O})_4$ . This stepwise approach enables you to examine accurately why and at which point cooperativity begins to show up. Do an energy decomposition analysis on each complexation step. Is the cooperativity mainly caused by  $\Delta V_{\text{elstat}}$ ,  $\Delta E_{\text{oi},\sigma}$  or  $\Delta E_{\text{oi},\pi}$ ? Is this in line with the cooperativity in (*N*-halo) guanine quartets?

**Optional:** rationalize your outcomes by doing an KS-MO and VDD analysis.

### Technical note

The cooperativity  $\Delta E_{\text{syn}}$  in quartets is quantified by comparing the interaction energy  $\Delta E_{\text{int}}$  between the four deformed monomers with the sum  $\Delta E_{\text{sum}}$  of the individual pairwise interactions:

$$\Delta E_{\text{syn}} = \Delta E_{\text{int}} - \Delta E_{\text{sum}}$$

$$\Delta E_{\text{sum}} = 4\Delta E_{\text{pair}} + 2\Delta E_{\text{diag}}$$

More information about cooperativity in hydrogen-bonded and halogen-bonded quartets can be found in the reading material.

## Appendix. Input file geometry optimization

```
#!/bin/bash
export SCM_TMPDIR=/local/datastore0/$USER/$SLURM_JOBID
srun mkdir -p $SCM_TMPDIR
chmod 700 $SCM_TMPDIR
cd $SCM_TMPDIR
export TC_SUBMISSION_DIR=$SLURM_SUBMIT_DIR
```

```
$ADFBIN/adf <<eor>$SLURM_SUBMIT_DIR/.out
```

XC

GGA blyp

DISPERSION Grimme3 BJDAMP

END

BASIS

TYPE TZ2P

CORE none

END

ANALYTICALFREQ

END

SCF

iterations 250

END

Geometry

Iterations 300

Optim Cartesian

Convergence E=1e-4 grad=1e-4

End

SYMMETRY

CHARGE

ZLMFIT

Quality normal

END

BECKEGRID

Quality good

End

ATOMS

END

ENDINPUT

eor

cp TAPE21 \$SLURM\_SUBMIT\_DIR/.t21