Can we visually predict binding energies?

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Information

A better understanding of weak, non-covalent binding forces is crucial to a large number of biological processes. For example, recognition of substrate by enzyme, antigen by antibody, neurotransmitter by neuroreceptor, etc., all rely on such interactions. Also, many interesting proteins are part of multisubunit and/or multiprotein assemblies, and the same forces are involved in multisubunit recognition and assembly.

While substantial advances continue to be made through direct studies of complex biological systems, small model systems are typically more amenable to detailed, physical investigation. For example, electrostatic potential surfaces have proven to be a very valuable tool in evaluating cation-π interactions.[4] Repeating the study of S. Mecozzi, et al., we look at a collection of representative aromatic systems and compare the qualitative features of the electrostatic potential surface with the calculated binding energy of Na^+ to the ring.

Part 1 Sodium Cation

1. Create a sodium atom. In the calculation options, make sure you set the Charge to 1.

2. Submit a density-fitted Hartree-Fock (DF-HF) computation with a 6-31G** basis set. In the "Job Title" section, type "(yourinitials) Na+ DF-HF/6-31G**" so that you know what job this was.

3. Click the right arrow at the bottom. After the calculation is complete, record the energy (in Hartees and kcal/mol) of the sodium ion.

Part 2 Benzene

4. Open a new job file and do not draw a molecule. Click the "Lookup Molecule" button below the molecular viewer window. Type "benzene" in the dialogue box.

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[4] Mecozzi, S., West, A. P. Jr., & Dougherty, D. A. (1996) *Proc. Natl. Acad. Sci. USA* **93**, 10566-10571

5. Click the forward arrow and select PSI4 as the computational engine. On the options page, provide a title for your job "(yourinitials) Benzene DF-HF/6-31G** MOs". Run a DF-HF ("Method") 6-31G** ("Basis Set") "Molecular Orbitals" calculation.

6. When the computation is complete, select the magnifying glass beside the "Electrostatic potential" line in the "Molecular Orbitals" section of the output page and view the electrostatic potential of the benzene molecule. Make sure to take note of which areas are most electron rich. Record the HF energy from this MO calculation.

Part 3 Aromatic-Sodium Ion Complex

7. Close all previous files and select the benzene job. Below the molecule viewer, click "New Job Using this Geometry".

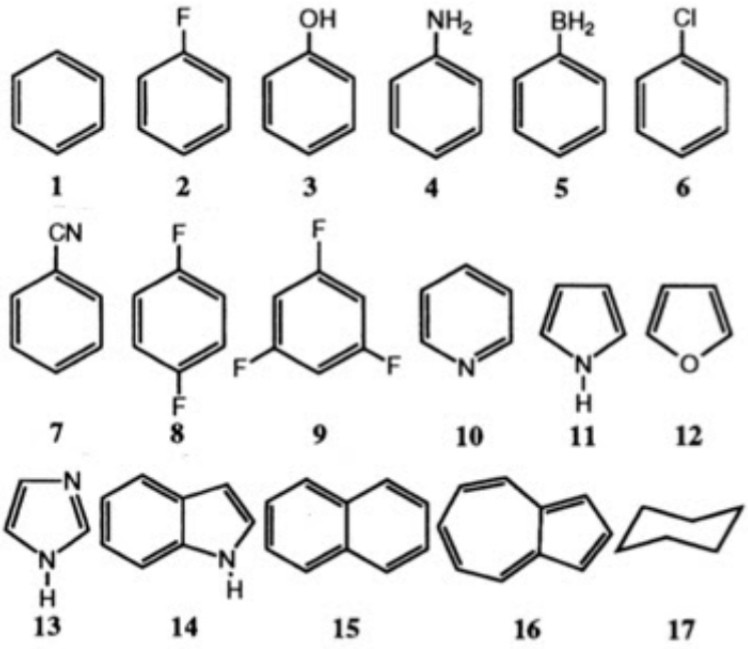
8. Rotate the benzene ring by clicking on the curved arrow icon and then clicking-and-dragging the molecule. Orient it perpendicular to the screen (in other words, with the plane of the molecule perpendicular to the screen). Place an Na^+ atom where you think it will have the most favorable interaction with the benzene ring.

9. Perform a DF-HF/6-31G** "Geometry Optimization" calculation. Make sure that the charge is 1, and give an appropriate title. Click on Submit.

10. Determine the energy of the sodium-benzene complex and calculate the binding energy (in kcal/mol) of sodium ion to benzene. Note: The binding energy is the energy difference between the π-cation complex and the sum of the isolated aromatic ring and sodium ion energies.

11. Determine the binding energy (kcal/mol) utilizing the same procedure (geometry optimization of the molecule, MO plot of the electrostatic potential, and geometry optimization of the complex) for the sodium ion with three other benzene-based aromatic compounds from the following list of structures:

2. flurobenzene	3. phenol	4. aniline	5. phenylborane
6. chlorobenzene	7. benzonitrile	8. 1,4-diflurobenzene	9. 1,3,5-triflurobenzene
10. pyridine	11. 1H-pyrole	12. furan	13. 1H-imidazole
14. 1H-indole	15. naphthalene	16. azulene	17. cyclohexane



12. To create new molecules, simply click “Lookup Molecule” in the molecule viewer, and type the name of the molecule. If the molecule in which you are interested is not available, this will have to be built.

13. To create these molecules, simply add the atoms to the benzene structure you have already created. For example, clicking on the periodic table, selecting “F”, and then clicking one of the hydrogen atoms will replace that H atom with F.

14. To determine if there is a correlation between the binding energy and the electrostatic potential surface of the aromatic structure, open all four electrostatic potential surfaces and select a common color range for display.

15. Rationalize any trends you observe for the electrostatic potential surfaces and the calculated binding energies of your four complexes.

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Name _____ Date _____

Lab Partner _____

Part 1 Na^+ DF-HF/6-31G**

SCF Energy (Hartrees)	
SCF Energy (kcal/mol)	

Part 2 Benzene Ring

Molecule Name:

System (DF-HF/6-31G**)	SCF Energy (Hartrees)	SCF Energy (kcal/mol)	Binding Energy
Benzene			
Benzene – Na^+			

Part 3 Other Aromatics

Molecule Name:

System (DF-HF/6-31G**)	SCF Energy (Hartrees)	SCF Energy (kcal/mol)	Binding Energy
Aromatic			
Aromatic – Na^+			

Molecule Name:

System (DF-HF/6-31G**)	SCF Energy (Hartrees)	SCF Energy (kcal/mol)	Binding Energy
Aromatic			
Aromatic – Na^+			

Molecule Name:

System (DF-HF/6-31G**)	SCF Energy (Hartrees)	SCF Energy (kcal/mol)	Binding Energy
Aromatic			
Aromatic – Na^+			

1. What atoms or functional groups most significantly changed the π-cloud and, hence, location of the sodium cation as compared to benzene? Why? Please use complete and grammatically correct sentences.

2. **Discuss** the trends that you observe between the visual depiction of the electrostatic potentials for your four aromatic compounds and the strength of the binding energies. Please use complete and grammatically correct sentences.