Can we visually predict binding energies?

Developed by Tricia D. Shepherd[1], Ryan C. Fortenberry[2], Matthew Kennedy [3], and C. David Sherrill[3]

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. Go to the Psi4 submit page. Enter Na in the Search for a molecule box and hit enter to create a sodium atom.

2. Scroll down to "Set Parameters for Quantum Mechanical Calculation and click "Reset Settings to Default

3. Select these options for the computation:

Select your package: PSI4
Name for input file: "Na_your name"
Charge: 1
Basis Set: 6-311G**
DFT Functional: None
The other options should be left at the default values they were set to when you clicked "Reset Settings"

[1] ORCID:0000-0001-6512-8951
[2] ORCID: 0000-0003-4716-8225: Department of Chemistry & Biochemistry, University of Mississippi
[3] ORCID: 0000-0002-5570-7666: Center for Computational Molecular Science and Technology, School of Chemistry and Biochemistry, and School of Computational Science and Engineering, Georgia Institute of Technology
[4] Mecozzi, S., West, A. P. Jr., & Dougherty, D. A. (1996) *Proc. Natl. Acad. Sci. USA* **93**, 10566-10571

4. Click Submit Job. This will take you to the Status page where you can view the results of your job. You should see the output from the job scroll by (there shouldn't be that much output for this simple job).

5. After the calculation is complete, scroll down to the 3D picture of the atom. The electronic energy is located at the top of the 3D window. Record the Electronic Energy in both Hartees and kcal/mol of the sodium ion. Change the Energy Units to "a.u." to see the energy in Hartrees and to "kcal/mol" to see the energy in kcal/mol.

Part 2 Benzene

6. Click the "Submit (Guided)" tab at the very top of the page. Type "benzene" in the Search for a molecule box and click Search.

7. Scroll down to "Set Parameters for Quantum Mechanical Calculation

8. Select these options for the computation:

Select your package: PSI4
Name for input file: "benzene_your name"
Charge: 0
Type: "Geometry Optimization"
Add-Ons: "None"
Basis Set: 6-311G**
DFT Functional: None

9. Click Submit Job. This will take you to the Status page where you can view the results of your job. You should see the output from the job scroll by.

10. When the computation is complete, record the Electronic Energy as before.

11. Click on "Electrostatic potential" to view the electrostatic potential of the benzene molecule. Make sure to take note of which areas are most electron rich (negative values of potential). Take a screenshot of the electrostatic potential because you will compare it later to that of other molecules.

12. Record the electronic energy (top of the 3D box)

Part 3 Aromatic-Sodium Ion Complex

13. Click the "Submit (Guided)" tab at the very top of the page. Type “benzene” in the Search for a molecule box and click Search. Wait for the molecule to minimize and symmetrize. When it’s finished it will appear in the top 2D window.

14. Add a sodium ion to the benzene molecule: Scroll up to "Choose your Molecule"

15. In the 2D window at the right click on the button that says NEW. This will signify that the next atom or molecule you add should not be connected by a bond to the existing benzene.

16. In the 2D window at the right click on the button in the lower left that says X. Enter Na into the Nonstandard atom text box and then click Close.

17. In the 2D window at the right click in the center of the benzene ring. This will place a sodium atom right above the benzene. Click the Transfer button (located below the 2D window) and scroll down to the 3D window. You should see a sodium atom above the benzene.

18. Select these options for the computation:

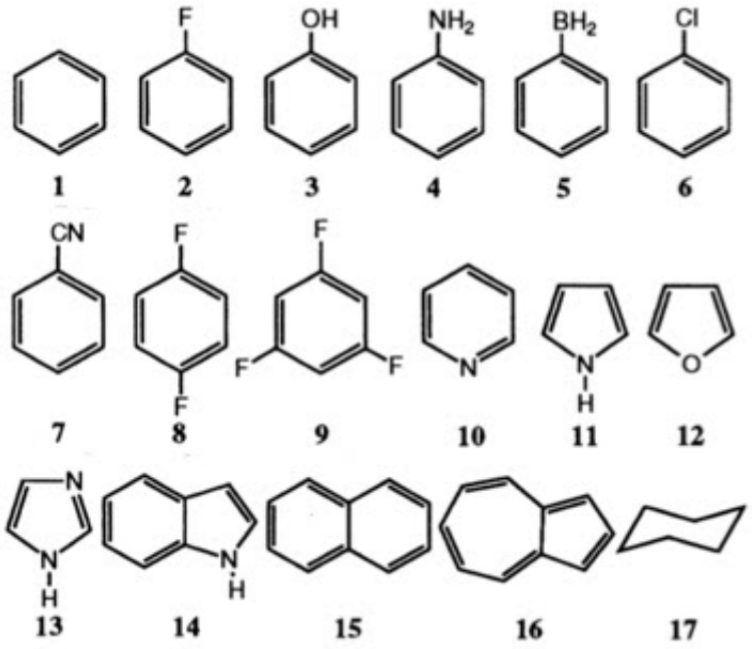
Select your package: PSI4
Name for input file: “benzene_Na_your name”
Charge: 1
Type: “Geometry Optimization”
Add-Ons: “None”
Basis Set: 6-311G**
DFT Functional: None

19. Click Submit Job. This will take you to the Status page where you can view the results of your job. You should see the output from the job scroll by.

20. 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.

21. Determine the binding energy (kcal/mol) utilizing the same procedure (geometry optimization of the molecule, plot 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



22. To create new molecules, simply follow the procedure above for benzene and the benzene-Na+ complex. If the molecule in which you are interested is not available in the database lookup, you will have to build it in the 2D drawing window under Choose your Molecule.

23. Remember to adjust the charge (0 for the lone molecule and 1 for the molecule/Na+ complex)

24. When creating the π-cation complex you may need to adjust the position of the sodium ion to be over the π ring (it may drift over a negatively charged atom). Scroll to the 3D Panel, click Advanced Options, and then click Move atoms by dragging. Drag the Na ion into the π cloud. You may also set its xyz coordinates by clicking Manually alter coordinates instead. **After changing any atom positions click Resymmetrize.**

25. Some molecules may give a "no symmetry found" alert: this is OK, it just means the molecule has no symmetry.

26. To determine if there is a correlation between the binding energy and the electrostatic potential surface of the aromatic structure, visualize all four electrostatic potential surfaces. Screenshots will help you organize your work.

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

Can we visually predict binding energies?

Name _____ Date _____

Lab Partner _____

Part 1 Na^+ HF/6-311G**

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

Part 2 Benzene Ring

Molecule Name:

System (HF/6-311G**)	SCF Energy (Hartrees)	SCF Energy (kcal/mol)	Binding Energy
Benzene			
Benzene – Na^+			

Part 3 Other Aromatics

Molecule Name:

System (HF/6-311G**)	SCF Energy (Hartrees)	SCF Energy (kcal/mol)	Binding Energy
Aromatic			
Aromatic – Na^+			

Molecule Name:

System (HF/6-311G**)	SCF Energy (Hartrees)	SCF Energy (kcal/mol)	Binding Energy
Aromatic			
Aromatic – Na^+			

Molecule Name:

System (HF/6-311G**)	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.