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Influence of Substituents on the Strength of Aryl C–H···Anion Hydrogen Bonds

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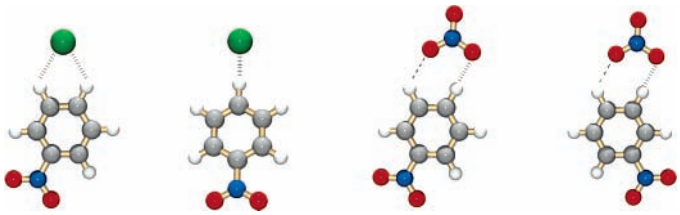
ABSTRACT



When electron-withdrawing substituents are present, aryl C–H groups become powerful hydrogen bond donors, forming stronger complexes than obtained with conventional O–H and N–H groups.

Charge-neutral anion receptors can be constructed by decorating organic scaffolds with hydrogen bond donor groups, X−H, where X is typically an oxygen or a nitrogen atom.[1] The anion-binding affinity of such receptors is moderated by the strength of the hydrogen bonds that are formed. Electronic binding energies, ΔE, computed for complexes formed between hydrogen bond donors and acceptors provide a useful scale to assess the relative strengths of such interactions. For monoanions, such as Cl^- and NO_3^-, the ΔE values for single hydrogen bonds formed with X−H donors range between 10 and 30 kcal mol^{-1}.[2,3] For example, $\Delta E = -15.4$ kcal mol^{-1} for the H_2O-Cl^- complex[2d,3] and $\Delta E = -16.0$ kcal mol^{-1} for the $H_2O-NO_3^-$ complex.[2e,3]

Although not typically considered to be significant donors, there is increasing evidence that C−H groups within an anionophore cavity participate in bonding and lead to enhanced anion-binding affinity.[4] This evidence comes in the form of direct observation of close contacts in crystallographic structures,[5] anion-induced chemical shifts of C−H protons in NMR spectra,[5a,b,6] and theoretical calculations.[3,6e,7] Recent calculations on C_6H_6−anion complexes have shown

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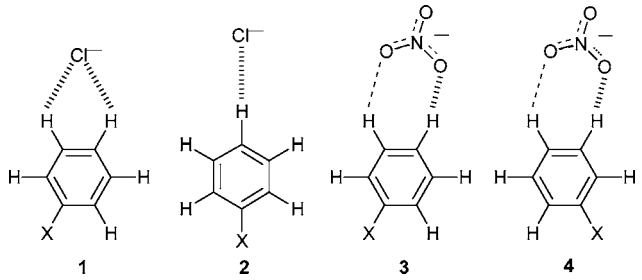

Figure 1. Schematic representation of benzene−anion complexes.

that the aryl C−H group is a surprisingly strong donor, with $\Delta E = -9.0$ kcal mol^{-1} for the C_6H_6−Cl^- complex and $\Delta E = -9.3$ kcal mol^{-1} for the C_6H_6−NO_3^- complex.[3] Comparison of these values with those obtained for H_2O complexes reveals that C−H hydrogen-bonding interactions with C_6H_6 yield 1:1 anion complexes that are ∼60% as stable as the corresponding H_2O complexes.

The strength of an aryl C−H donor group can, in theory, be adjusted through the addition of functional groups on the arene ring. To elucidate the magnitude of such substituent effects, we have carried out further electronic structure calculations on complexes formed between $Cl^-$and NO_3^- with a series of substituted benzenes. In this paper, we report the results of these calculations and provide an example of how this information could be used in anionophore design.

The complexes examined here are illustrated in Figure 1, with both electron-withdrawing (X = NO_2, CN, CF_3, Cl) and -donating (X = CH_3, NH_2) groups added to the benzene ring. Initial geometries for the complexes were generated by adding the substituent X to optimized geometries obtained previously for the C_6H_6−anion complexes.[3] These include global, **1**, and local, **2**, minima for Cl^-, and two forms for NO_3^-, in which the substituent is either para, **3**, or meta, **4**, with respect to the shortest C−H···O contact.[8] All structures were optimized at the MP2/aug-cc-pVDZ level followed by single-point energy calculations at the MP2/aug-cc-pVTZ level.[9]

Tables 1 and 2 summarize the interaction energies and intermolecular distances for **1**−**4**. As is the case for conventional and other C−H hydrogen donors,[10] the addition

Table 1. Electronic Binding Energies[a] (kcal mol^{-1}) for Complexes **1**−**4**

X	**1**	**2**	**3**	**4**
NO_2	−16.76	−16.04	−16.62	−16.35
CN	−16.40	−15.60	−16.21	−16.08
CF_3	−14.18	−13.54	−14.17	−14.03
Cl	−12.45	−11.79	−12.46	−12.47
H	−9.02	−8.60	−9.26	−9.26
CH_3	−8.40	−7.97	−8.66	−8.71
NH_2	−7.53	−7.02	−7.80	−7.99

[a] MP2/aug-cc-pVTZ single-point energies on MP2/aug-cc-pVDZ-optimized geometries.[9]

of electron-withdrawing groups appreciably strengthens the interaction energy and shortens the intermolecular distance to the acceptor. Opposite effects are seen for electron-donating CH_3 and NH_2 groups. Particularly striking is the ability of CN and NO_2 groups to enhance the binding strength, forming complexes that are more stable than those obtained when H_2O is the hydrogen bond donor!

Table 2. Optimized Intermolecular Distances[a] (Å) H···X (X = O, Cl^-) in Complexes **1**−**4**

	1		**2**	**3**		**4**	
R	H_p	H_m	H_p	H_p	H_m	H_p	H_m
NO_2	2.61	2.65	2.29	2.10	2.36	2.32	2.10
CN	2.63	2.65	2.29	2.11	2.36	2.34	2.11
CF_3	2.64	2.67	2.32	2.13	2.38	2.35	2.13
Cl	2.66	2.70	2.34	2.15	2.38	2.39	2.14
H	2.73	2.73	2.39	2.19	2.43	2.43	2.19
CH_3	2.75	2.71	2.39	2.19	2.43	2.45	2.19
NH_2	2.83	2.67	2.41	2.20	2.42	2.49	2.18

[a] Obtained with MP2/aug-cc-pVDZ.[9]

The trend in the ΔE values is consistent with that expected from the Hammett equation. Substituent effects on the strength of the aryl C−H···anion interaction are well described by σ_m substituent constants,[11] with correlation coefficients (R) of ≥0.99 for all complexes (Figure 2). Poorer correlations were obtained with σ_p, suggesting that inductive

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(8) Local minima can be obtained for Cl^- complexes when X is located in an ortho position of **1**. These forms are less stable when X is electron withdrawing and more stable when X is electron donating (X, ΔE in kcal mol^{-1}): NO_2, not stable, reverts to **1**; CN, −15.24; CF_3, −13.58; Cl, −12.09; CH_3, −9.14; NH_2, not stable, forms N−H···Cl bond. Attempts to locate stable geometries in which X is located in a meta position of **2** failed.

(9) Electronic structure calculations were carried out using the NWChem program.[9a] Geometries were optimized at the MP2/aug-cc-pVDZ level followed by single-point energy calculations at the MP2/aug-cc-pVTZ level.[9b,c,d] Control calculations show that this procedure leads to negligible differences in binding energies for benzene− and water−anion complexes (less than 0.03 kcal mol^{-1}) when compared to results obtained after full optimization at the MP2/aug-cc-pVTZ level. (a) Straatsma, T. P. et al. *NWChem, A Computational Chemistry Package for Parallel Computers*, Version 4.6; Pacific Northwest National Laboratory: Richland, WA, 2004. (b) Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618. (c) Dunning, T. H., Jr. *J. Chem. Phys.* **1989**, *90*, *1007*. (d) Kendall, R. A.; Dunning, T. H., Jr.; Harrison, R. J. *J. Chem. Phys.* **1992**, *96*, 6796.

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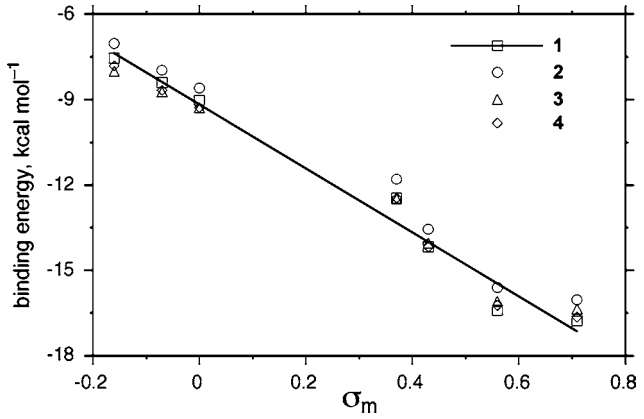

Figure 2. Correlation between binding energy and σ_m for **1**−**4**. For clarity, the line is drawn only through the data for **1**.

effects are more relevant than resonance effects. The small differences in ΔE values for **3** and **4** support this concept. Interestingly, a similar observation has been made previously in studies of the π-cation interaction in C_6H_6···cation complexes.[12]

Further insight on the interaction between substituted arenes and anions is obtained on examining the electrostatic component of the total binding energy for **2**. As shown in Figure 3, a plot of the electrostatic potential at the location

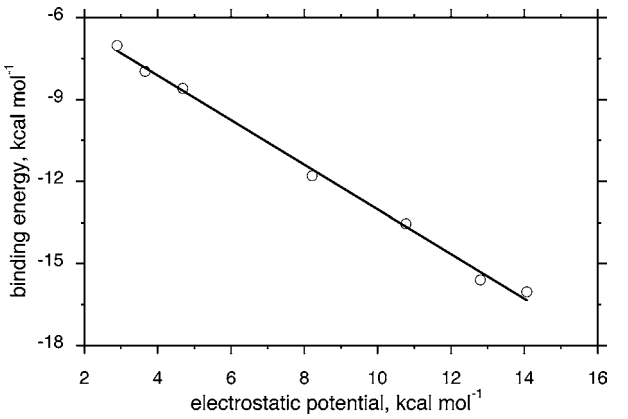

Figure 3. Correlation between binding energy of complex **2** and electrostatic potential[13] for substituted arenes at the points of location of Cl^-.

of the Cl^- anion versus ΔE is linear (R = 0.998).[13] In addition, ΔE values for **2** correlate well (R = 0.997) with projections of MP2/aug-cc-pVTZ dipole moments for the arenes along the direction of the C−H···Cl axis (R = NO_2, 4.30; R = CN, 4.52; R = CF_3, 2.84; R = Cl, 1.70; R = CH_3, −0.38; and R = NH_2, −1.03 D). These correlations are consistent with behavior expected for charge-dipole interactions and indicate the presence of a strong electrostatic contribution to the hydrogen bonding.

To illustrate the utility of aryl C−H binding sites in anionophore design, we consider the series of TREN based ligands, **5**−**9**, shown in Figure 4. Hosts **5**−**7** have been

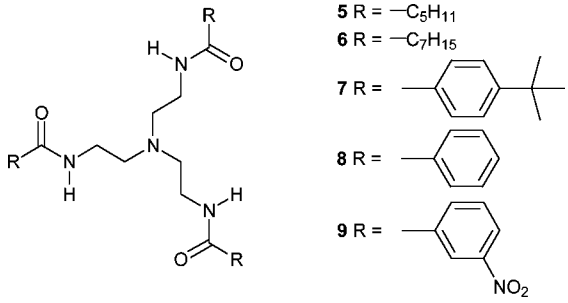

Figure 4. Series of TREN derivatives **5**−**9**.

shown to enhance the extraction of $CsNO_3$ using a dual host strategy.[14] Extraction results suggested that the aryl substituted derivative, **7**, formed the strongest NO_3^- complex of this series. A subsequent study revealed that **7** could also serve as a carrier in a nitrate-selective electrode.[7d] Consistent with these findings, molecular modeling showed that **7** could form a cavity that was complementary for small trigonal anions, such as NO_3^- and ClO_3^-. In addition to the three amide N−H donor groups, each phenyl substituent provided an ortho C−H group that was pointed toward a neighboring nitrate O atom.[7d] The proposed bonding motif is illustrated in Figure 5, where we show an optimized geometry for the NO_3^- complex with the simple analogue, **8**. Although the existence of this binding motif has not been experimentally confirmed, the proposed structure provides an example for demonstrating the extent to which arene substitution can enhance anion-binding affinity.

Prior calculations on C_6H_6···anion complexes[3] suggest that the C−H···O contacts shown in Figure 5 make an important contribution to the complex stability. The current results indicate that this contribution would be enhanced greatly by substituting the arenes with electron-withdrawing groups. Calculations reveal that placing NO_2 groups para with respect to the hydrogen bonding C−H groups, **9**, stabilize the interaction with NO_3^- by 13.5 kcal mol^{-1}, roughly a 33% increase in binding affinity (Table 3). While some of the increased stability likely arises from increased N−H acidity, the change in hydrogen bond distance is greater for the C−H···O contacts than for the N−H···O contacts (Table 3),

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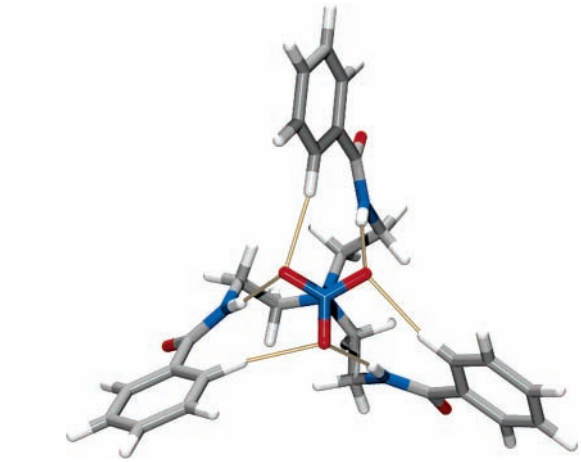

Figure 5. Optimized geometry for the complex of **8** with NO_3^-, obtained at the B3LYP/DZVP2 level of theory.[15]

suggesting that the observed enhancement of binding energy is mainly due to the increased strengths of the C−H···O interactions.

In summary, the aryl C−H group is a strong hydrogen bond donor when electron-withdrawing substituents are present, exibiting hydrogen bond strengths comparable to those obtained with O−H and N−H groups. With respect to anionophore design, substituent effects are consistent with expectations from simple electrostatics and can be predicted by the Hammett relationship using σ_m descriptors.

Table 3. Electronic Binding Energies (kcal mol^{-1}) and Nonbonded H···O Distances (Å) in NO_3^- Complexes with **8** and **9**[a]

host	ΔE	N−H···O	C−H···O
8	−41.03	1.958	2.311
9	−54.56	1.952	2.252

[a] Obtained with B3LYP/DZVP2.[15]

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Supporting Information Available: Cartesian coordinates and absolute energies for optimized structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) Calculations were performed with the NWChem program using density functional theory (DFT).[15a,b] DFT calculations were done with the hybrid B3LYP functional[15c,d] and a polarized double-ζ basis set (DZVP2).[15e] Although this level of theory gives different interaction energies than those reported at the MP2/aug-cc-pVTZ level (Table 1), the differences are not large. For comparison, DFT yields −7.93 kcal mol^{-1} for **3**, X = H (smaller by 1.33 kcal mol^{-1}) and −16.97 kcal mol^{-1} for **3**, X = NO_2 (larger by 0.16 kcal mol^{-1}). (a) Parr, R. G.; Yang, W. In *Density Functional Theory of Atoms and Molecules*; Oxford University Press: Oxford, 1989. (b) *Density Functional Methods in Chemistry*; Labanowski, J. K., Andzelm, J. W., Eds.; Springer-Verlag: New York, 1991. (c) Becke, A. D. *Phys. Rev A* **1988**, *38*, 3098. (d) Lee, C. T.; Yang, W. T.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785. (e) Godbout, N.; Salahub, D. R.; Andzelm, J.; Wimmer, E. *Can. J. Chem.* **1992**, *70*, 560.