

Narrative report for “**Variable temperature NMR study of proton-bound dimers. role of dispersion in solvatophobic effects on bond strengths,**”

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As mentioned in the previous report, the PRF-funded project has produced a comprehensive paper on the effects of dispersion on the bond dissociation energy of proton-bound dimers, both in the gas phase and in dichloromethane solution.

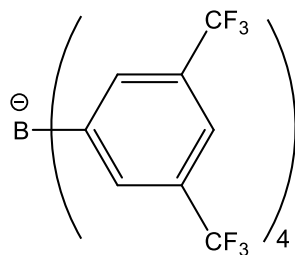
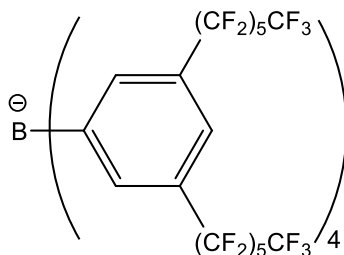
“Attenuation of London Dispersion in Dichloromethane Solutions,” R. Pollice, M. Bot, I.J. Kobylanski, I. Shenderovich, P. Chen, *J. Am. Chem. Soc.* **2017**, 139(37), 13126–13140. DOI:10.1021/jacs.7b06997.

The work is a direct output of the ACS-PRF funding. In comparison to the proposal, we investigated a much larger set of proton-bound dimers of pyridines, tertiary amines, and quinolines, 36 in all, and, in addition to the proposed variable temperature NMR work, we executed isothermal calorimetric measurements to ensure that the measured equilibrium constants were correct. Repeating again the conclusion of the paper, as in the report last year:

In this work we report an extensive study of bond dissociation equilibria of a wide variety of proton-bound dimers in the gas-phase and in solution by T-CID measurements, computational methods and NMR studies. We conclude that London dispersion becomes very significant for medium-to-large molecules in the gas-phase, which was observed directly by experiment, and is always accompanied by significant contribution of repulsive Pauli exchange, which, however, does not fully compensate the attractive contribution of dispersion. The significant attractive contribution of dispersion, despite being attenuated by about 70%, still transfers into dichloromethane solution temperatures that are relevant for chemical reactions, at least for the chosen test systems, showing that altering London dispersion can indeed be a useful design principle to tune molecular stability for chemical processes in solution. Furthermore, currently employed implicit solvent models are shown to describe attenuation of dispersion in solution inadequately, especially when the corresponding contribution becomes large, showing that alternative theoretical approaches and models are required in that regard for a proper estimation of energies. While we have chosen a specific test system for this study, our results and conclusions are not specific to that type of system. The contribution of dispersion to the gas-phase bond dissociation energies in molecular complexes decorated with increasingly large interacting hydrocarbon substituents is expected to become large for any molecular complex. Additionally, the observation that intermolecular London dispersion, while largely attenuated, still transfers into a polar organic solvent like CH₂Cl₂ is likely more general, as well, and we expect a very similar trend for other comparable organic solvents. Furthermore, the spectacular failure of implicit solvent models to predict the Gibbs free energy of dissociation in solution, suggests that these models are inadequate to describe dispersive solute-solvent interactions. Again, this is expected to be applicable not only to our test system, but in general to molecular complexes having sufficiently large interacting hydrocarbon substituents. Considering these points, and the wide variety of systems for which a DFT+PCM or a DFT+COSMO computational approach has been applied to in literature, we claim that our conclusions are widely applicable to homogeneous catalysis and supramolecular chemistry in polar organic solvents. Further work continuing gas-phase measurements using T-CID, investigating proton-bound dimer equilibria in different solvents and exploring alternative theoretical approaches to estimate Gibbs free energies of solvation are underway in our group.

For the second year of PRF financing, we had indicated that the acquired fluorine lock would be installed, and then used to repeat the series of variable temperature NMR experiments on the set of 36 proton-bound dimers, but this time in a fluorous solvent. Our expectation was that the expected weaker fluorous-

hydrocarbon interactions would mean a less complete cancelation of dispersion forces going from the gas phase into solution, and, hence, significantly larger bond dissociation energies. We envisioned a solution to the technical problem of solubility of the non-fluorous proton-bound dimer cations in the fluorous solvent. We proposed to use a fluorous BArF anion, previously reported in the literature.

BArF₂₄

van den Broeke, J.; Deelman, B. -J.; van Koten, G.
Tet. Lett. **2001**, 42, 8085-8087.

Ghosh, S. K.; Sullivan Ojeda, A.; Guerrero-Leal, J.;
Bhuvanesh, N.; Gladysz, J. A.
Inorg. Chem. **2013**, 52, 9369-9378.

For this second year of PRF financing, we can report that we have indeed prepared the fluorous BArF salts of all 36 cations in our test set, and that they did indeed display the desired solubility in the fluorous solvent, at least in mM concentrations. We have completed the variable temperature NMR studies on the association constants, and the qualitative expectation of significantly stronger binding is fulfilled. We have also completed a measurement campaign of the same set of 36 proton-bound dimers in bromobenzene as the solvent, as a strongly dispersive comparison to the weakly dispersive fluorocarbons. These results will be published within the next several months. Nevertheless, the individual variations in bond dissociation energies proved to be surprising, so we have also embarked on a theoretical investigation of the fluorous effect and its relation to dispersion interactions. The extensive benchmarking study and the surprising conclusion about the origin of the fluorous effect is being prepared for submission within the next one month, with the title, *Origin of the Immiscibility of Alkanes and Perfluoroalkanes*. We intend to submit it to JACS.