

## CAN LONDON DISPERSION OVERRIDE CATION- $\pi$ INTERACTIONS?

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We report an evaluation of the importance of London dispersion in moderately large (up to 32 heavy atoms) organic molecules by means of a molecular torsion balance<sup>a</sup> whose conformations “weigh” London forces against cation- $\pi$ (aryl) in the absence of solvent. The experimental gas-phase study is performed using cryogenic ion vibrational predissociation (CIVP) spectroscopy covering both the N-H and the effectively “deperturbed” N-D<sup>b</sup> stretching modes, taking into account possible perturbation due to the tag molecule.<sup>c</sup> The gas-phase data is supported by solid-state FT-IR spectroscopy, single-crystal x-ray crystallography, and is accompanied by DFT calculations, including an extensive search and analysis of the accessible conformations. We begin with the unsubstituted molecular torsion balance, and then step up the complexity systematically by adding alkyl groups incrementally as dispersion energy donors (DEDs) to achieve a degree of chemical complexity comparable to what is typically found in transition states for many regio- and stereoselective reaction in organic and organometallic chemistry. We find clear evidence for the small attractive contribution by DEDs, as had been reported in other studies, but we also find that small individual contributions by London dispersion, when they operate in opposition to other weak non-covalent interactions, produce composite effects on the structure that are difficult to predict intuitively, or by modern quantum chemical calculations. The experimentally observed structures, together with a reasonable value for a reference cation- $\pi$  interaction, indicate that the pairwise interaction between two *tert*-butyl groups, in the best case, is modest. Moreover, the visualization of the conformational space, and comparison to spectroscopic indicators of structure, as one steps up the complexity of the manifold of non-covalent interactions, makes clear that *in silico* predictive ability for the structure of moderately large, flexible, organic molecules falters sooner than one might have expected.<sup>d</sup>

<sup>a</sup>Tsybizova $\ddagger$ , A.; Fritshe $\ddagger$ , L.; Gorbachev $\ddagger$ , V.; Miloglyadova, L.; Chen, P. *J. Chem. Phys.* **2019**, *151*, 234304

<sup>b</sup>Gorbachev, V.; Miloglyadova, L.; Tsybizova, A.; Chen, P. *Rev. Sci. Instrum.* **2021**, *92*, 083002

<sup>c</sup>Tsybizova, A.; Paenurk, E.; Gorbachev, V.; Chen, P. *J. Phys. Chem. A* **2020**, *124*, 41, 8519, 234304

<sup>d</sup>Gorbachev, V.; Tsybizova, A.; Miloglyadova, L.; Chen, P. *J. Am. Chem. Soc.* **2022**, *submitted*