

ILLUMINATING A SOLVENT-DEPENDENT HIERARCHY FOR AROMATIC CH/ π COMPLEXES WITH DYNAMIC COVALENT GLYCO-BALANCES

Laura Díaz-Casado^a, A. Villacampa^a, F. Corzana^b, J. Jiménez-Barbero^{c-e}, A.M. Gómez^a, A.G. Santana^f, J.L. Asensio^a

^a Instituto de Química Orgánica (IQOG-CSIC), Madrid, Spain
laura.diazcasado@mu.ie

^b Dept. Química y Centro de Investigación en Síntesis Química,
Universidad de La Rioja, Spain

^c Center for Cooperative Research in Biosciences (CIC bioGUNE), Derio, Bizkaia

^d Ikerbasque, Basque Foundation for Science, Bilbao, Spain

^e Centro de Investigación Biomedica En Red de Enfermedades Respiratorias, Madrid, Spain

^f Instituto de Productos Naturales y Agrobiología (IPNA-CSIC), SC Tenerife, Spain

CH/ π interactions are prevalent among aromatic complexes and represent invaluable tools for stabilizing well-defined molecular architectures. Their energy contributions are exceptionally sensitive to various structural and environmental factors, resulting in a context-dependent nature that has led to conflicting findings in the scientific literature. Consequently, a universally accepted hierarchy for aromatic CH/ π interactions has remained elusive. Herein, we present a comprehensive experimental investigation of aromatic CH/ π complexes, employing a novel approach that involves isotopically-labeled glyco-balances generated in situ (*Figure 1*). This innovative strategy not only allows us to uncover thermodynamic insights but also delves into the often less-accessible domain of kinetic information. Our analyses have yielded more than 180 new free energy values, while considering key factors such as solvent properties, the interaction geometry, and the presence and nature of accompanying counterions. Remarkably, the obtained results challenge the conventional wisdom regarding the stability order of common aromatic complexes. While it was believed that cationic CH/ π interactions held the highest strength, followed by polarized CH/ π , non-polarized CH/ π , and finally anionic CH/ π interactions, our study reveals that this hierarchy can be subverted depending on the environment. Indeed, the performance of polarized CH/ π interactions can match, or even outcompete that of cationic CH/ π interactions making them a more reliable stabilization strategy across the entire spectrum of solvent polarity. Overall, our results provide valuable guidelines for the selection of optimal interacting partners in every chemical environment, allowing the design of tailored aromatic complexes with applications in supramolecular chemistry, organocatalysis and/or material sciences.

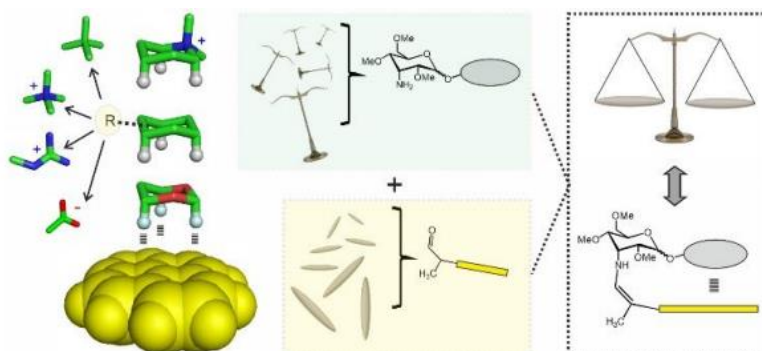


Figure 1. Aromatic X-CH/ π complexes analyzed in this study and schematic representation of the in situ generated glyco-balances employed in this work.

Reference:

1. L. Díaz-Casado, J.L. Asensio, et al. *JACS Au*, **2024**, 4, 2, 476–490.