Poster

The peptoid's path to understand the role of CH···OC and CO···CO interactions in proteins

C. Tedesco[1], G. Pierri[1], N. D'Arminio[1], R. Schettini[1], A. Marabotti[1], F. De Riccardis[1], I. Izzo[1]

[1]*Dept. of Chemistry and Biology "A. Zambelli", University of Salerno, via Giovanni Paolo II 132, 84084 Fisciano (SA) Italy*

ctedesco@unisa.it

Peptoids are *N*-substituted polyglycines with useful biological activities and interesting chemical properties both in solution and in the solid state. The lack of the amide proton prevents the formation of NH···CO hydrogen bonds and makes peptoids the ideal platform for evidencing the influence of CH···OC and CO···OC interactions in stabilizing molecular conformations and the solid state assembly [1].

Our group reported on how inter-annular CH···OC hydrogen bonds can provide face-to-face or side-by-side arrangement of the macrocycles mimicking secondary structure in proteins and forming porous crystalline frameworks [2]. By combining in-situ powder and single crystal X-ray diffraction, thermal analyses, hot-stage optical microscopy we showed how environmental changes (such as temperature, humidity, gas pressure, etc.) may trigger the dynamic behaviour of cyclic peptoids in the solid state [3,4]. By conformational energy and lattice energy calculations we demonstrated the role of intermolecular CH···OC backbone-to-backbone interactions in tightening the peptoid porous framework upon guest release and the role of CH···OC and CH-π host-guest interactions in the framework re-opening [5].

More recently, we highlighted the role of intramolecular backbone-to-backbone CO···CO interactions and CH···OC hydrogen bonds in the stabilization of enantiomorphic right- and left-handed polyproline type I helices in cyclic dodecapeptoids (**Fig. 1**) [6].

The analysis of CO···CO interactions in peptoids evidenced that φ values in the range between -40° and -90° and between 40° and 90° correspond to CO···CO distances below 3.22 Å (Figure 1).

By extending the analysis of CO···CO interactions to different types of beta turns in proteins, we highlighted the role of direct or reciprocal carbonyl-carbonyl in stabilizing the beta turn conformation for each specific type, showing that the occurrence of such interactions could be also advocated to explain from a chemical point of view the diversity of turn types [7].

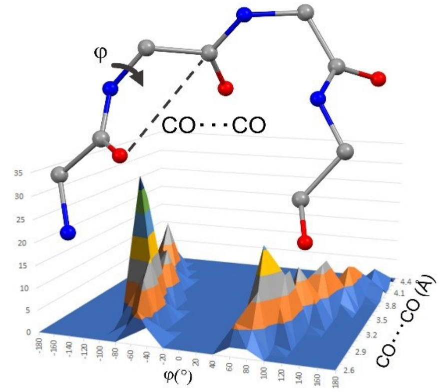

Figure 1. Shortest CO···CO distance (Å) vs φ angle (°) in cyclic peptides, depsipeptides and peptoids for left-handed turns (negative φ values) and right-handed turns (positive φ values), respectively.

[1] Tedesco, C., Erra, L., Izzo, I. & De Riccardis, F. (2014). *CrystEngComm*, **16**, 3667.

[2] Meli, A., Macedi, E., De Riccardis, F., Smith, V. J., Barbour, L. J., Izzo, I. & Tedesco, C. (2016). *Angew. Chem., Int. Ed.*, **55**, 4679.

[3] Macedi, E., Meli, A., De Riccardis, F., Rossi, P., Smith, V. J., Barbour, L. J., Izzo, I. & Tedesco, C. (2017). *CrystEngComm*, **19**, 4704.

[4] Pierri, G., Landi, A., Macedi, E., Izzo, I., De Riccardis, F., Dinnebier R. E. & Tedesco, C. (2020). *Chem. Eur. J.,* **26**, 14320.

[5] Pierri, G., Corno, M., Macedi, E., Voccia, M. & Tedesco, C. (2021). *Cryst. Growth Des.,* **21**, 897.

[6] Pierri, G., Schettini, R., Summa, F. F., De Riccardis, F., Monaco, G., Izzo, I. & Tedesco, C. (2022). *Chem. Comm.*, **58**, 5253.

[7] D'Arminio, N., Ruggiero, V., Pierri, G., Marabotti, A. & Tedesco, C. (2023) *Protein Sci*, DOI: 10.1002/pro.4868

The authors acknowledge FARB funding (University of Salerno) and PRIN 2022 PNRR ID: P2022ZBNC2 (Ministero dell'Università e della Ricerca) for financial support.