

NMR Tools for the Study of Intermolecular Interactions in Fluorous Media.

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The unusual properties of fluorocarbons have been extensively exploited to modulate the physicochemical properties of proteins and to direct the self-assembly of interesting biomolecules¹. However, little is known about the interactions taking place in highly fluorinated solvents, in part because of the lack of solubility of most organic compounds in such media.

We previously described² a new fluorous non-covalent tagging system based on the formation of hydrogen bonds between ureas and perfluoroalkanoic acids, resulting in a dramatic increase of solubility of non-fluorous compounds in perfluorohexane. Herein we use this approach to report the first NMR conformational study of a fluorinated peptidomimetic in C₆F₁₄ in the presence of trifluoroacetic acid. Also, we address the use of PSGE-NMR techniques for the characterization of supramolecular entities in fluorous media.

Both fluorinated and non-fluorinated molecules were selected for our study. The β -turned conformation of a fluorinated β -lactam peptidomimetic in CDCl₃ was established from the determination of temperature coefficients and interproton distances were calculated from 2D-NOESY spectrum. We demonstrate that this conformation was maintained in perfluorohexane upon addition of trifluoroacetic acid.

Diffusion-ordered NMR spectroscopy (DOSY) was used to study the interaction between model compounds and two fluorinated acids (CF₃CO₂H and C₈F₁₇CO₂H, respectively). Association constants in CDCl₃ and C₆F₁₄ were calculated from diffusion data³ and higher values were always obtained in the fluorous solvent.

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