ANAD 2D-NMR Spectroscopy: Explore new Horizons in the Determination of the Relative Configuration Analysis of Natural Products

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Résumé

Determination of the configuration (and preferred conformation) of complex organic molecules (natural or synthetic substances) is still a challenging task for chemists, with various implications in pharmaceutical sciences, in particular whether these compounds possess specific bioactivities. NMR in aligning media, either lyotropic liquid crystals (LLC) or polymer gels, in combination with molecular modelling is a unique framework to solve complex structural problems whose analytical wealth lies in the detection of anisotropic NMR data and establishment of non-local structural correlations [1].
As an alternative to two well-established anisotropic NMR parameters, the RDCs (residual dipolar couplings) and RCSAs (residual chemical shift anisotropies), it is possible to exploit the potential of deuterium residual quadrupolar couplings (2H-RQCs) extracted from anisotropic 2H 2D-NMR spectra recorded at natural abundance level (ANAD NMR) in polypeptide-based LLCs [1]. These 2H-RQCs specific to spin $I > 1/2$ can be successfully used to solve non-trivial molecular structural problems, in combination with an integrated computational protocol adapted to quadrupolar nuclei [2].

In this work, we demonstrate that the 3D structure/relative configuration of complex bioactive molecules can be unambiguously established using only 2H-RQCs, being in this case at 2H natural abundance. The performance and scope of this promising analytical approach is examined for two natural chiral compounds of pharmaceutical interest: strychnine and artemisinin [3].

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