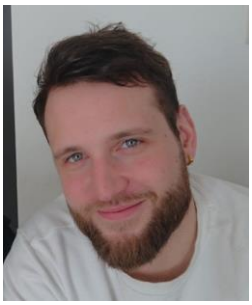
Structural Analysis Revisited by Natural Abundance Deuterium NMR in Weakly Oriented Media: Determination of the Relative Configuration of Bioactive Compounds



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Analytical studies of chiral molecules are of critical importance when dealing with bioactive compounds or in the field of asymmetric synthesis. Several techniques are available to meet the analytical needs, such as chiral chromatographies, chiroptical methods or NMR spectroscopy. The latter is also an invaluable tool for structural elucidation and recent developments involving anisotropic solvents have renewed NMR capabilities in stereochemical characterisation.[1,2]

In contrast to isotropic liquids, any solute in weakly aligning media adopts an orientational order in average, leading to non-null anisotropic NMR interactions. Hence, all (residual) anisotropic NMR interactions can be observed, such as residual ^{13}C-^{1}H dipolar coupling ((^{13}C-^{1}H)-RDC) or residual ^{2}H quadrupolar coupling (^{2}H-RQC). Through the molecular order tensor, these order-sensitive interactions encode 3D geometrical information, making it possible the determination of the relative configuration of multistereocentres compounds.[3,4]

In this work, we will show, first, how the correct relative configuration of Arthemeter, a rigid, complex natural compound with 8 stereogenic centres (256 diastéreoisomers possible), can be robustly selected using ^{2}H-RQC data extracted from the Anisotropic Natural Abundance Deuterium (ANAD) 2D NMR spectrum (@92 MHz). In a second part, an innovative methodological development combining lyotropic "bimesophasic samples" and ANAD 2D NMR will be introduced for the first time.

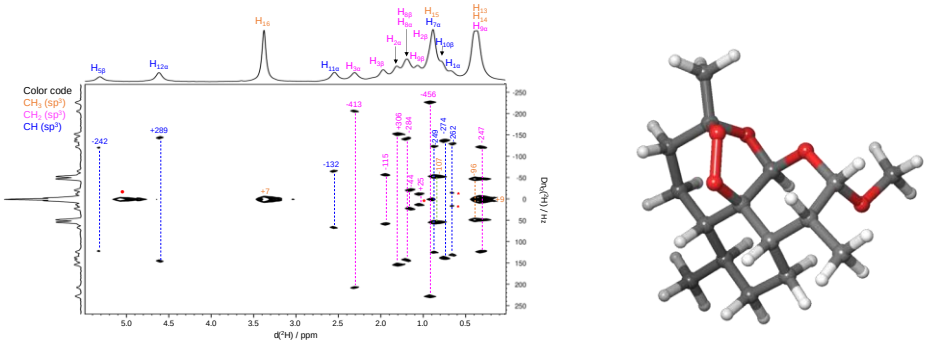

Figure 1 : ANAD 2D *Q*-Resolved spectrum (left) and DFT-optimized structure (right) of Arthemeter

References

1. Lesot, P. et *al*. Prog. *Nucl. Magn. Reson. Spectrosc.* **2020**, *116*, 85–154.
2. Aroulanda, C. et *al*. *Chirality* **2022**, *34* (2), 182–244.
3. Navarro-Vázquez, A. et *al*. *ChemPhysChem* **2017**, *18* (10), 1252–1266.
4. Lesot, P. et *al*. *J. Nat. Prod.* **2020**, *83* (10), 3141–3148.