X-Ray and NMR structural analysis of a sulfonamide

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Introduction

Sulfamethoxazole is an antibiotic of the sulfonamide family. The pharmacological activities of sulfonamides are well known in literature. Indeed, this antibiotic is already used for treating burns on humans or animals. However, antibiotics alone are becoming less and less efficient against bacteria which are more and more resistant. Therefore, mixture of antibiotics are tested in order to increase their activities, in particular for the treatments of nosocomial infections. Another chemical pathway is possible: the synthesis of sulphonamides complex with antiseptic metals. A major step before this synthesis is the condensation of the sulfamethoxazole. This step is used to increase the coordination sites. This study will present the modification of a sulfamethoxazole and the characterization of this molecule by NMR and X-Ray diffraction.

Synthesis

The NH2 group of our molecule was modified to an enaminone moities by adding of trifluoromethyl ether. This condensation reaction (figure 1) allows increasing the number of coordination sites.

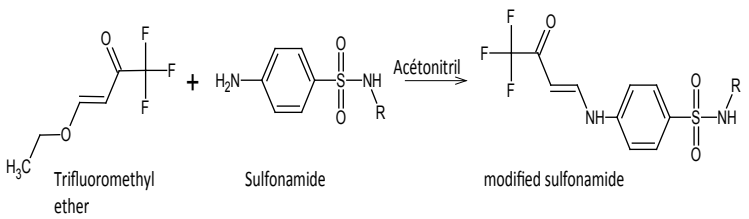

Figure 1: Condensation reaction of sulfamethoxazole

Results and discussion

• **X-Ray diffraction**

X-ray diffraction was used to determine the chemical structure of the synthesized product (figure 2) even though the main difficulty was to obtain single-crystals available for analysis.

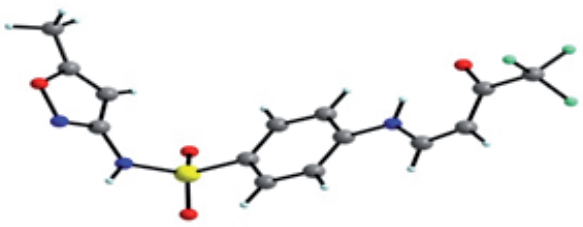

Figure 2: Modified sulfamethoxazole structure where Oxygen is shown in red, Nitrogen in blue, Carbon in grey, Sulphur in yellow.

• **NMR**

NMR provides structural information of the molecule in a solution. Therefore, we can verify the purity of the product. It can be seen in figure 4 that the NH2 group disappeared in the 1H NMR spectrum (doublet initially at 6.1ppm in sulfamethoxazole spectrum). Similarly, we can distinguish the "CH=CH moities" at 8.2ppm/8.4ppm and 5.7ppm/5.9ppm. This chemical displacement characterizes the group "trifluoromethyl ether enaminone". Moreover, it is apparent from the data in figure 3 that the reaction was successful. Finally, the synthesized product was presented in two isomers cis and trans with the relative ratio 20/80.

The spectrum 1H NMR was obtained using a spectrometer BRUKER of 400MHZ equipped with a probe BBI.

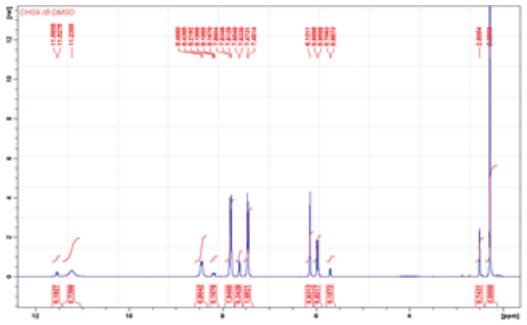

Figure 3: 1H_ NMR spectrum of sulfamethoxazole modified in DMSO d6. DMSO peak is at 2.5ppm.

Conclusion

The sulfamethoxazole condensation was successful. This modified antibiotic was characterized by X-ray diffraction and 1H NMR methods. Two isomers are obtained from this synthesis: Cis and Trans forms. This discovery is very important in view of the molecule pharmacological properties.

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