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ÉCOLE CENTRALE PARIS

CENTRALE

Preliminary experimental results on charge density of sulfathizo

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Why sulfathiazole?

- •Sulfathiazole is an antimicrobial agent discovered in 1939. It is no longer widely used among human since less toxic compounds have replaced it.
- •Yet its crystallographic properties have been studied thoroughly, as the molecular structure enables it to form a large variety of hydrogenbonded networks. The polymorphic compound has an extensive family of solvates and adducts. Sulfathiazole can be considered as a model for polymorphism study.

Accurate polymorphism characterization belongs to a wider project "Non Photochemical Light Induced Nucleation".

This compound has been obtained by spontaneous nucleation, NPLIN is in progress.

Polymorphism

•5 polymorphs have been crystallized and identified, where 3 forms share similar crystal packing. The form considered as the most thermodynamically stable is the form IV^[1].

Forn	n Space Group	Unit Cell	Intermolecular H bonds	Remark
I	P2 ₁ /c	a=10.50, b=12.96, c=17.18, α =90, β =107.65, γ =90	dimer $N_{amino}H\cdots N_{imine}$ inter $N_{aniline}H\cdots O_{sulfone}$	centrosymmetri c α dimers
II	P21/c	a=8.190, b=8.532, c=15.45, α=90, β=94.14, γ=90	dimer N _{amino} H…N _{aniline} dimer N _{aniline} H…O _{sulfone} inter N _{aniline} H…O _{sulfone}	β dimers
ш	P2 ₁ /a	a=15.50, b=8.494, c=17.43, α=90, β=112.76, γ=90	$\begin{array}{l} \text{dimer } N_{amino}H \cdots N_{aniline} \\ \text{dimer } N_{aniline}H \cdots O_{sulfone} \\ \text{inter } N_{aniline}H \cdots N_{imine} \end{array}$	β dimers
IV	P2 ₁ /n	a=1.77, b=8.467, c=11.37, α=90, β=91.65, γ=90	dimer N _{amino} H…N _{aniline} dimer N _{aniline} H…O _{sulfone} inter O _{sulfone} …O _{sulfone}	β dimers
v	P2 ₁ /n	a=15.50, b=8.494, c=17.43, α =90, β =112.76, γ =90	inter N _{amino} H…O _{sulfone} inter N _{amino} H…N _{aniline} inter N _{aniline} H…O _{sulfone}	

Experiments and preliminary results

- •In crystal studies, charge density $\rho(\mathbf{r})$ refers to the distribution of charge around and in the molecule. It could be determined theoretically or experimentally.
- •The classical experimental method is through single crystal high resolution X-ray diffraction experiment.
- •To better describe the electron density, the Hansen-Coppens aspherical-atom formalism is widely used^[2].

$$\rho_{at}(\mathbf{r}) = P_c \rho_c(\mathbf{r}) + P_v \kappa^3 \rho_v(\kappa \mathbf{r}) + \sum_{l=0}^{l_{max}} \kappa'^3 R_l(\kappa' \mathbf{r}) \sum_{m=0}^{l} P_{lm\pm} d_{lm\pm}(\theta, \phi)$$
Spherical term
Asoberical term



•Single crystal of sulfathiazole is prepared by slow evaporation of supersaturated 1:1 water-ethanol solution. Due to the energetic similarity, form II, III et IV are crystallized simultaneously. As proved by the following experiment, the tested sample is a form IV crystal.

 The X-ray diffraction experiment is carried out at 100 K $(\lambda = 0.71073 \text{ Å})$, with 13641 independent reflections of 100% completeness. R_{int}=2.01%.

- •The multipole refinement is performed using program package MoPro(Rf = 1.464, wR=1.371, GOF = 0.690).
- Static deformation density of thiazole, phenyl, S=O bond and S-N bond.



The refinement of sulfur parameters is still under process





•The experimental electrostatic potential is shown on the below. EP is generated on molecule surface (0.01eÅ⁻³).



Conclusion and perspective

- •A variety of methods to improve the sulfur density have +•Other improvement during the refinement. been performed: anharmonicity, relativist effect, optimized parameter for sulfur, etc.
- Possible disorder due to the vibration of S=O bond.
- •New sample from NPLIN of sulfathiazole have been prepared for high resolution X-ray diffraction experiment.

Referance: [1] T.N.Drebushchak et al (2008) Zh.Strukt.Khim.(Russ.)(J.Struct.Chem.), 49,90; [2] N. K. Hansen and P. Coppens, Acta Crystallogr., Sect. A: Cryst. Phys., Diffr., Theor. Gen. Crystallogr., 1978, 34, 909–921.