Crystals and Co-crystals of Chlorpropamide

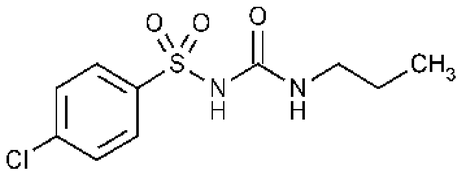
Shamarri Riddle and Cheryl L. Klein Stevens

Department of Chemistry, Xavier University of Louisiana, New Orleans, LA 70125

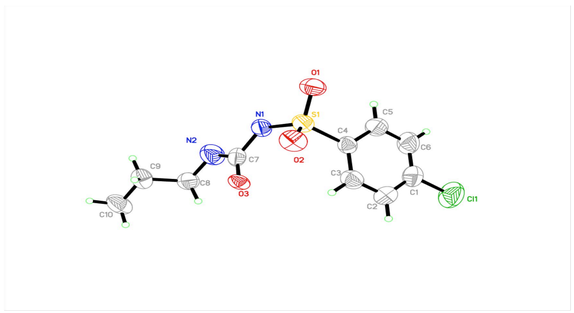
Abstract

Polymorphism is the ability of a substance to exist in more than one distinct crystalline form. This is an important consideration for characterizing the properties of drug candidates. Chlorpropamide is a compound that is known to treat type 2 diabetes. However, I haven't successfully identified any of the crystals or co-crystals that have been made. So far I have gotten crystals for chlorpropamide with methanol, ethanol, tetrahydrofuran, 1-propanol, 2-propanol, and methyl, ethyl ketone. I have also made co-crystals of chlorpropamide and salicylic acid with ethanol, ethyl acetate, methyl ethyl ketone, and 2-propanol . A comparison of the structural features of the title compounds at 170 K will be reported.

Below is the structure of chlorpropamide.

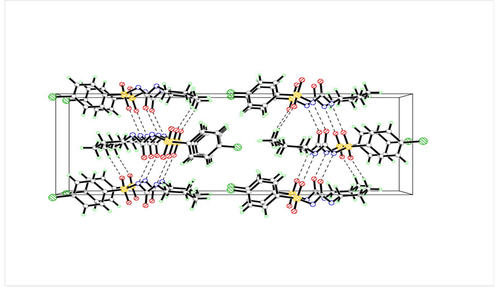


Structure of Chlorpropamide Crystallized

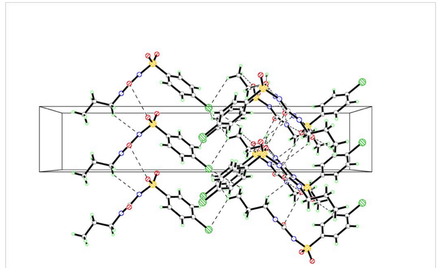


Packing Diagrams

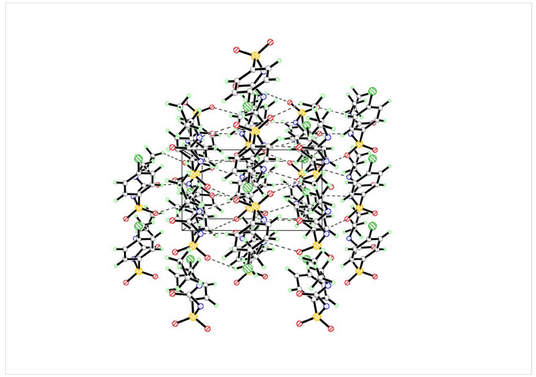
Chlorpropamide



Projected down a axis



Projected down b axis



Projected down c axis

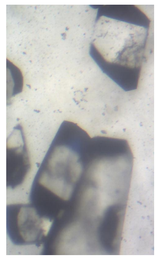
ACKNOWLEDGEMENTS

Support of this research from the NSF-PREM (DMR-0934111) , NIH-RISE (2R25GM060926) and NIH-RCMI (1G12RR026260) programs is gratefully acknowledged.

Experimental

All chlorpropamide crystals were prepared by slow evaporation from a saturated solution of chlorpropamide, either salicylic acid or caffeine and a solvent. Mixtures were allowed to stand at room temperature for a few days or weeks after mixing. Single crystals were collected from the evaporation mixtures and allowed to air dry. The crystals for each form of Chlorpropamide were analyzed using X-ray Crystallography at 170 K on a Bruker SMART X2S automated diffractometer. Data has not yet been collected. This means that the crystal structures have not yet been determined. Eventually they will be determined by direct methods and refined using the Bruker ApexII software package.

Picture



Chlorpropamide with propanol crystals

	Chlorpropamide
Solvent	propanol
Space Group	P 21 21 21
a (Å) b (Å) c (Å) β°	5.2268(16) 9.078(3) 26.586(8) 90(3)
V (Å^3)	1261.5(7)
Z	4
R (I>4σ(I))	6.23%
S	1.060

Results and Conclusions

1. Chlorpropamide crystallizes better with less polar solvents.
2. Chlorpropamide takes approximately one month to crystallize when using the slow evaporation method.
3. The more solute you use, the faster the crystals will form.
4. Future studies will involve growing co-crystals of chlorpropamide and a cofactor.