

## MS32-P19 Oleanolic Acid: A Case Study of the Control and Suppression of Solvate Crystals and its Potential for Chiral Resolution

REBECCA YIP<sup>1</sup>, Thanh-ha Nguyen<sup>1</sup>, Yuxin Zhang<sup>1</sup>, Herman H.Y. Sung<sup>1</sup>, Ian D. Williams<sup>1</sup>

1. Hong Kong University of Science and Technology (HKUST)

email: reyip1992@live.co.uk

Oleanolic Acid (OA-H) a natural triterpene of pharmaceutical interest has been found to form solvate crystals from a wide range of solvents.[1][2] The control of solvate versus anhydrous phase formation is demonstrated for a variety of alcohols, with characterization by pXRD, TGA and single-crystal XRD. It appears that the product formation can be correlated to the temperature of crystallization.

OA-H has also demonstrated the ability to form diastereomeric salts with various amines, in particular the formation of diastereomeric salts of OA-H with racemic amines for the purpose of chiral resolutions have been studied. Following on from the solvate phases prepared and the potential of OA-H to form cocrystals with other chiral compounds, the potential of OA-H as a resolving agent for a variety of chiral alcohols has also been explored with promising results.

[1] Tong, H. Y.; Wu, H. B., Zheng, Y., Xi, J., Chow, A. h. I., Chan, C. K. *Int. J. Pharm.* **2008**, *355*, 195-202.

[2] Froelich, A.; Gzella, A. K., *Acta Crystallogr E* **2010**, *66*, o2690.

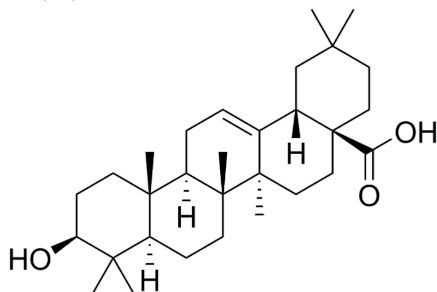


Figure 1. Oleanolic Acid Structure

**Keywords:** Solvates, cocrystals, chiral resolution

## MS32-P20 From 0D to 3D - The structural diversity of polyoxometalate catalysts

Kim D. von Allmen<sup>1,2</sup>, Anthony Linden<sup>1</sup>, Greta R. Patzke<sup>\*1</sup>

1. University of Zurich, Departement of Chemistry

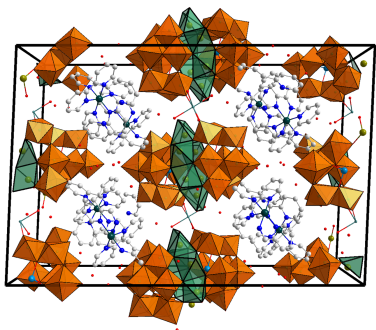
2. Empa Swiss Federal Laboratories for Materials Science and Technology, Center for X-ray Analytics

email: kim.vonallmen@empa.ch

Polyoxometalates (POMs) are metal oxo clusters which are preferably formed by W, Mo and V in their high oxidation states. Among their remarkable spectrum of potential applications, POMs have widely been investigated as homogeneous and heterogeneous catalysts for organic reactions and as catalysts for artificial photosynthesis.[1] It was shown that the extent of Co/W disorder in the transition metal core of Co/Bi-sandwich type POMs based on the lacunary precursor  $\text{Na}_9[\text{B}-\alpha\text{-BiW}_9\text{O}_{33}]$  is a key feature for their activity as water oxidation catalysts (WOCs).[2] In order to understand the origin of the catalytic activity, POMs were prepared from  $\text{Na}_9[\text{B}-\alpha\text{-BiW}_9\text{O}_{33}]$  in the presence of Mn(II), Co(II), and Cu(II) cations. Efforts were made to prepare compounds with a specific composition of the transition metal core. Single crystal X-ray diffraction studies of the new transition metal containing POMs have revealed a large structural diversity of polyanions, which is due to  $\alpha$ - $\beta$  isomerization and partial decomposition of the lacunary precursor. Cross-linking of polyanions via supplementary d- or f-block counter cations resulted in the formation of 1D, 2D, and even 3D networks.[3] The polyanion  $[\text{Cu}_4(\text{H}_2\text{O})_4(\text{B}-\beta\text{-BiW}_{10}\text{O}_{32})]^{10-}$  crystallized with a 2D structure in the presence of  $\text{Na}^+$  and  $\text{K}^+$  cations, while  $\text{Rb}^+$  cations favored the crystallization of the 0D structure  $\text{Na}_6\text{Rb}_4[\text{Cu}_3(\text{H}_2\text{O})_3(\text{B}-\alpha\text{-BiW}_9\text{O}_{33})_2]$  from the same reaction mixture. The importance of the counter cations as structure-directing parameter could thus be highlighted.

The negative charge of polyanions can be exploited to prepare new compounds with interesting properties by introducing of a transition metal complex as the counter cation. Crystals could be grown from  $[\text{Mn}_3(\text{H}_2\text{O})_3\{\text{As}_5\text{W}_{18}\text{O}_{66}\}]^{8-}$  as a potential WOC and the photo-sensitizer cation  $[\text{Ru}(\text{bpy})_3]^{2+}$ . Crystal structure determination confirmed the formation of  $[\text{Ru}(\text{bpy})_3]_4[\text{Mn}_3(\text{H}_2\text{O})_3\{\text{As}_5\text{W}_{18}\text{O}_{66}\}]$  from which crucial structural details could be deduced.

[1] D.-L. Long, R. Tsunashima, L. Cronin, *Angew. Chem. Int. Ed.* **2010**, *49*, 1736. [2] F. Evangelisti, P.-E. Car, O. Blacque, G. R. Patzke, *Catal. Sci. Technol.* **2013**, *3*, 3117. [3] K. von Allmen, H. Grundmann, A. Linden, G. R. Patzke, in preparation for submission.



**Figure 1.** Packing diagram of the POM-PS-complex  $[\text{Ru}(\text{bpy})_3]_2[\text{Mn}_2(\text{H}_2\text{O})_4(\text{As}_2\text{W}_{18}\text{O}_{66})]$ :  $\text{WO}_6$  octahedra (orange), Mn (green), Ru (black).

**Keywords:** Polyoxometalates, Catalysts, Self-Assembling, Multidimensional Structures, Polymorphism

## MS32-P21 Towards understanding solvent-mediated conformational polymorphism

Anikó Udvarhelyi<sup>1</sup>, Grahame Woollam<sup>1</sup>

<sup>1</sup> Novartis Pharma, Basel, Switzerland

email: aniko.udvarhelyi@novartis.com

Polymorphism, the existence of different crystalline forms of the same molecule, represents a major challenge to the pharmaceutical industry. Different polymorphic forms of the same drug substance may significantly impact solubility, dissolution rate, bioavailability, chemical potential and physical/chemical stability. Differences in these properties may be especially pronounced in the case of conformational polymorphs where different molecular conformations of the same chemical species are arranged in the polymorphic lattices. Our aim is to uncover the molecular mechanisms that govern conformational polymorphism of pharmaceutical molecules in order to highlight the risk of polymorphism during drug development and to guide the solvent selection in experimental crystallisation screens.

Here we focus on the conformational changes of the molecule going from the gas to solution phase and ultimately to the crystal phase. The questions of interest to us include what conformational energy penalties are compensated by crystal forces? How is the gas-phase conformational population distribution altered when entering the solution phase? And how is the minimum-energy conformer in a given crystallisation solvent related to the crystal structure?

To tackle these questions we use quantum-chemistry tools and the continuum solvation model COSMO and its extension for real solvents. In COSMO-RS, the pairwise interaction energy between the ideally screened surface patches of contacting molecules is computed within a statistical thermodynamics framework. This framework allows the population prediction of relevant molecule conformations in solvents of interest. We present for the first time a conformation generation and filtering workflow to identify the relevant conformers to be used in the COSMO-RS calculations with an extraordinary example of polymorphism, ritonavir. The weighted conformers in selected solvents are compared to the respective ritonavir polymorphs and its gas-phase conformers.

**Keywords:** molecular conformations, polymorphism, COSMO-RS, solvent effects, computational models