

Accelerate 3D Structure Determination of Organics

● Chaperone Compounds – Versatile Agents for Co-crystallization

Modern instrumentation and processing techniques enable high-quality 3D structure analysis – including absolute structure determination – often in less than an hour, faster and more comprehensively than many spectroscopic methods can even start to achieve. However, large numbers of small or highly flexible organic molecules remain intractable to even the most sophisticated crystallization methods.

Our new set of chemical chaperones for co-crystallization, developed by the University of Stuttgart^[1,2] can significantly increase the probability of

successful crystallization and provide faster access to the absolute 3D structure of an organic analyte^[3]:

- The chaperone method is fast and easy to use
- Structures in hours rather than weeks
- Small quantities of analyte required
- Excellent quality crystals
- Sample screen of 52 organic compounds
 - Diffraction-quality crystals in 88% of cases
 - High resolution X-ray structures in 77% of cases
- The chaperone compounds are highly stable
- 100% analyte occupancy in the crystal guarantees reliable determination of the absolute configuration

Absolute Structures Desperately Needed?

Reliable determination of absolute configuration is one of the key capabilities single crystal X-ray diffraction (SC-XRD) can offer. This makes SC-XRD a *conditio sine qua non* in pharmaceutical research. The success of the method, however, is determined by timely access to suitable crystals. Amongst others, crystals suitable for analysis are characterized suitable by size, diffraction power, and thermal and mechanical properties. Ideally, these samples also do not suffer from major disorder, pseudo-symmetry, twinning or modulation. When these conditions are met, typically a significant anomalous signal can be obtained from non-racemic samples to determine the absolute structure.



Co-crystallization

Co-crystallization is a proven method for growing suitable crystals, even if the given analyte resists even the most sophisticated crystallization attempts. However, finding a chaperoning partner molecule can be a challenge of its own and the number of analytes that can be crystallized with one particular partner molecule is often found to be extremely limited.

Easy as counting 1-2-3...

Fortunately, a high success rate goes along with simplicity in the chaperone application:

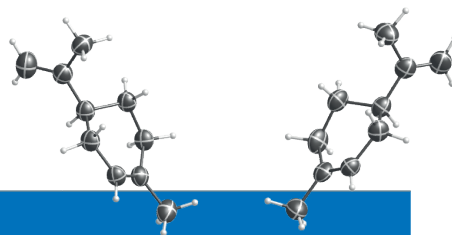
1. In a small glass vial the analyte is added to a few mg of the chaperone.
2. On a small heating plate the mixture is gently warmed until a clear solution is formed.
3. The mixture is allowed to cool down while crystallization occurs.

Outstanding Performance

Our new chaperones are based on molecules exhibiting a ball-shaped body and four flexible substituents, allowing the incorporation of analytes exhibiting a wide spread of different shapes. In an initial study,^[1] as many as 88% of all trials successfully yielded co-crystals. This brings our chaperones to the forefront with respect to the number of successful co-crystallization experiments.

The Perfect Complement to Your D8 Diffractometer

Our third-generation D8 QUEST and D8 VENTURE single crystal diffraction solutions combine the brightest sources and photon counting detectors with the APEX3 software suite to enable the determination of an entire crystal structure in as little as two minutes. The new Chaperone Kit is the ideal accessory to help remove the largest remaining barrier to high throughput structure determination.



Selected Crystallographic Parameters	S-Limonene	R-Limonene
T [K]	100	100
Collection time [h]	2.1	3.4
Resolution [Å]	0.80	0.80
R1 (obs.) [%]	5.67	4.81
wR2 (all) [%]	15.87	13.76
Parson's Q	0.00(17)	0.05(10)

^[1] Angew. Chem. Int. Ed. 2020, 59, 15875–15879.

^[2] We are grateful for the collaboration with Prof. Richert, Institute of Organic Chemistry, Stuttgart and his team.

^[3] Patent pending

● **Bruker AXS GmbH**

info.baxs@bruker.com

www.bruker.com

Worldwide offices

bruker.com/baxs-offices



Online information

bruker.com/sc-xrd

