

## SINGLE-CRYSTAL X-RAY DIFFRACTION D8 VENTURE with I $\mu$ S DIAMOND II

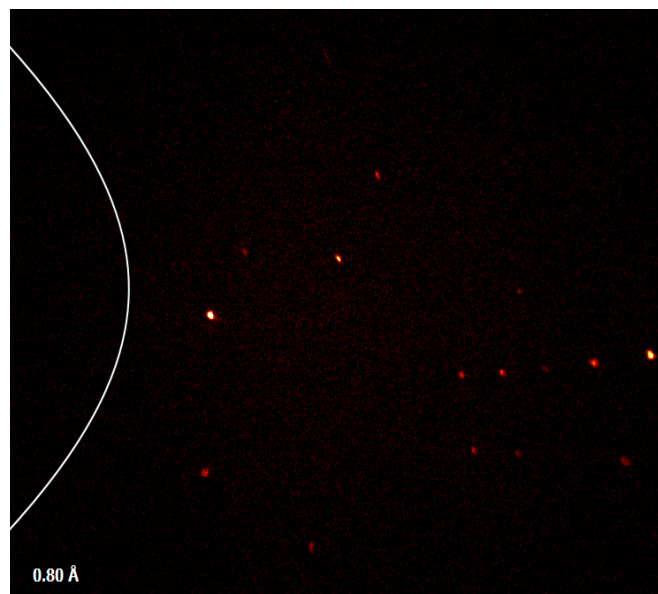
Fast absolute structure determination from a small organic crystal

### The challenge

Absolute structure determination of molecular stereochemistry is essential in the fields of synthetic organic chemistry and drug development, among others. Unambiguous assignment of absolute structure of organic compounds can be particularly challenging when intensity differences between Bijvoet (Friedel) pairs are very small. Measurements of such compounds benefit from the use of a high intensity Cu X-ray sources combined with a large active-area photon-counting detector mounted on a high-precision kappa goniometer – a combination that has only recently become available.

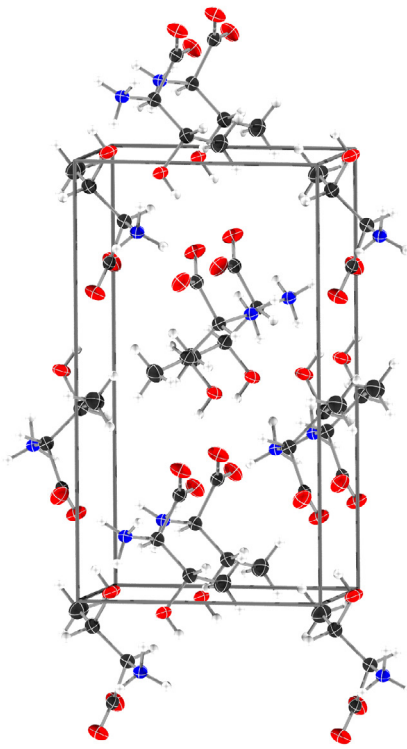
### The new approach

The introduction of the I $\mu$ S DIAMOND II in combination with the PHOTON III lifts SC-XRD instrument performance to a completely new level. This unique combination of unprecedented brilliance with single photon detection allows data to be collected to a quality suitable for absolute structure determination within minutes. To demonstrate the efficiency of the new combination, a small crystal of the amino acid threonine – a pure CHON-organic molecule – is investigated. The absolute structure determination requires the highly accurate measurement of the intensities to precisely determine the extremely small intensity differences in the Friedel pairs.



**Figure 1**

Diffraction image collected with an exposure of 0.2 s/ $^{\circ}$  showing the strong reflection intensities to 0.8 Å.



**Figure 2**  
Structure of the unit cell showing the absolute structure of D-threonine and crystal packing.

**Table 1**

Experimental parameters, data, and refinement statistics of the D-Threonine structure

Experiment time [s]	232
# Runs	7
Frames	584
Resolution [Å]	0.80
Completeness [%]	99.4
Multiplicity	4.0
<i>R</i> (int)	5.86
<i>R</i> (sigma)	3.20
<i>I</i> / $\sigma$	21.1
<i>R</i> <sub>1</sub>	3.60
<i>wR</i> <sub>2</sub>	8.74
Parsons' <i>Q</i>	0.084(177)
RED [Å <sup>3</sup> ]	0.27/-0.18
C-C bond precision [Å]	0.0033

## The sample

D-threonine (C<sub>4</sub>H<sub>9</sub>NO<sub>3</sub>) is a non-proteinogenic amino acid. Although no direct evidence for the presence of free D-threonine in living organisms has been found, indirect evidence was provided by reports of D-threonine linked enzymes. The role and metabolism of D-threonine is still under research. Small crystals of D-threonine present an excellent example to probe the performance and data accuracy of analytical X-ray instruments in the scope of absolute structure determination of organic compounds. Although several structures of L- and the two *allo*-threonine isomers being reported, no structure of D-threonine is reported yet in the CSD database.

## Experiment

A small crystal of enantiopure D-threonine (crystal size 0.055 × 0.060 × 0.080 mm<sup>3</sup>) was measured on a D8 VENTURE equipped with a KAPPA goniometer, PHOTON III 14 detector and I $\mu$ S DIAMOND II microfocus source (Cu-radiation,  $\lambda = 1.54184$  Å) at 100 K. A combination of  $\omega$ - and  $\varphi$ -scans were collected at a detector distance of 37 mm using an exposure time of 0.2 s/ $^\circ$  (Figure 1). Crystal screening, indexing, strategy calculation, data processing and structure refinement were all conducted within the APEX5 software suite.

## Results

The dataset was measured to a resolution of 0.80 Å in less than 4 min. The PHOTON III 14 has a large active area of more than 14 000 mm<sup>2</sup>, which allows for a highly efficient data collection even for Cu-radiation. A complete data set with moderate high multiplicity was obtained in seven scans. Excellent data statistics and model refinement parameters were obtained (Table 1). The dataset allows for the unambiguous determination of the absolute structure as indicated by the low Parsons' *Q*. The experiment definitively proves that the sample does not consist of the natural L- enantiomer of threonine, but of synthetic D-threonine (Figure 2).

## Conclusion

- The absolute structure of the amino acid D-threonine was determined in just under four minutes.
- The D8 VENTURE with I $\mu$ S DIAMOND II, KAPPA goniometer and PHOTON III detector is ideal for quickly collecting high quality data sets from very small crystals.
- APEX5 includes easy to use routines for data collection and processing including absolute structure determination.

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