Application Note B-SCX1011

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SCX1011 - High-Speed Measurement of a Peptide Drug Using HyPix-Arc 150°

Introduction

“Middle molecule” drugs are a new type of pharmaceutical drugs approximately 0.5 to 5.0 kDa in molecular weight that contain a peptide bond. This group, positioned between small molecule drugs and biopharmaceuticals such as antibody drugs, can possibly solve the disadvantages of those drugs. Of all middle molecule drugs, cyclic peptide pharmaceuticals are considered the “next generation” pharmaceutical drugs to succeed antibody drugs. Rigaku technology allows high-speed and high-accuracy analysis of high molecular weight compound crystals such as cyclic peptides at a level never before accomplished. In this experiment, we combine an ultra-high-intensity microfocus rotating anode X-ray generator and Rigaku’s original HyPix-Arc 150º curved photon counting X-ray detector with a data collection schedule optimized by the CrysAlis^{Pro} all-in-one software package for single crystal X-ray diffraction.

Measurement and results

The previous detector model, HyPix-6000HE, had extremely low noise, a high counting rate, and high spatial resolution, but the maximum angle of detection at the shortest camera length was about 50°. Therefore, with a Cu source, data collection had to be performed on the low-angle side and on the high-angle side separately.

HyPix-Arc 150° has three modules positioned in a curved array, which provides a maximum detection angle of about 150°. This feature enables data collection from low angle to high angle in a short time. Therefore, even data collection of crystals susceptible to damage by X-rays, such as sub-micrometer crystal grains, can be completed before the damage in the crystals progresses.

Data collection and structure analysis results of a micrometer crystal of “Cyclosporine A” (a cyclic peptide drug) (Figure 1) are shown below (Figure 2 and Table 1).

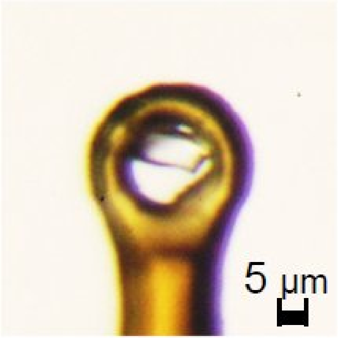

Figure 1: Micrometer crystal of Cyclosporine A

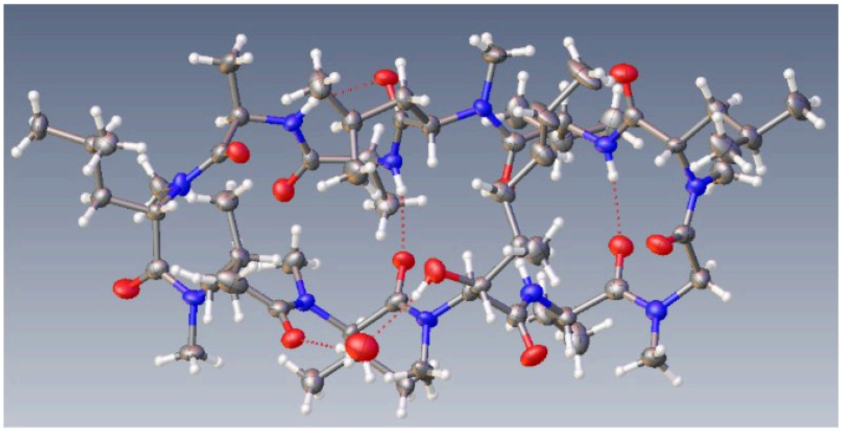

Figure 2: Structure of Cyclosporine A

By using HyPix-Arc 150°, data collection and structure determination were completed in only two hours even with these micrometer-sized crystals and the structure was obtained. The absolute structure could also be determined, since the Flack parameter (which indicates the suitability of an absolute structure) is close to zero and its standard uncertainty is small.

Table 1: Structure analysis result of Cyclosporine A crystal

System	Detector	Total time	I/σ(I)	R_{int} (total / last)	R_1/wR	Flack
XtaLAB Synergy-Custom	HyPix-Arc 150°	1h54m	11.04	12.9% / 72.8%	7.21% / 15.95%	-0.0(2)

Related products

HyPix-Arc 150°

A curved detector based on direct X-ray detection technology with the highest 2θ range at a single position available for the home lab.

XtaLAB SynergyCustom

A bespoke, extremely high-flux diffractometer with custom enclosure and the flexibility to utilize both ports of the rotating anode X-ray source.

XtaLAB Synergy-S

Our most popular diffractometer for Chemical Crystallography and Mineralogy, configured with either single or dual microfocus sealed tube X-ray sources and an extremely low noise direct X-ray detection detector.

XtaLAB Synergy-R

Our most popular diffractometer for Protein Crystallography, configured with a high-flux rotating anode X-ray source and an extremely low noise direct X-ray detection detector.

XtaLAB Synergy-i

An entry-level single crystal X-ray diffractometer for Chemical Crystallography configured with microfocus sealed tube technology and a direct X-ray detection detector.

XtaLAB Synergy-ED

A new and fully integrated electron diffractometer for measuring submicron crystals, utilizing a seamless workflow from data collection to structure determination of crystal structures.

XtaLAB Synergy-DW

Spectacular performance combined with dual wavelength versatility, provides the perfect answer for high-capacity Chemical Crystallography labs or for X-ray facilities that support Chemical Crystallography and Protein Crystallography.

XtaLAB Synergy Flow

Robotic sample changer to provide unattended data acquisition, enhanced productivity and standardized workflow to your research environment.

XtaLAB mini II

A benchtop single crystal X-ray diffractometer ideal for chemical crystallography and teaching.