CROSS TOKAI Experimental Report J-PARC	承認日Date of Approval 2016/1/18 承認者Approver Takashi Ohhara 提出日Date of Report 2016/1/15
実験課題番号 Project No. 2014P0905 実験課題名 Title of experiment Structure and dynamics of proton, ionic functional materials 実験責任者名 Name of principal investigator Ryoji Kiyanagi 所属 Affiliation J-PARC neutron science section	装置責任者 Name of responsible person Takashi Ohhara 装置名 Name of Instrument/（BL No.） SENJU/BL18 利用期間 Dates of experiments 2014/12/5-2014/12/8 2015/3/22-2015/3/24

1．研究成果概要（試料の名称、組成、物理的・化学的性状を明記するとともに、実験方法、利用の結果得られた主なデータ、考察、結論、図表等を記述してください。

Outline of experimental results (experimental method and results should be reported including sample information such as composition, physical and/or chemical characteristics.

[1] Determination of hydrogen positions in Levofloxacin-oxalate

Exploration of various forms of active pharmaceutical ingredient (API) is essential for expanding the functionalities of pure APIs, and crystal structure is one of the most important information for characterizing these forms. Levofloxacin is known as a broad spectrum fluoroquinolone antibiotic drug and a new anhydrous form of Levofloxacin, Levofloxacin-oxalate, has recently been reported. An X-ray diffraction study has been conducted to study the structure of this material, but determination of the positions of hydrogen atoms has not been successful. Here, a neutron diffraction experiment was carried out on a single crystal of Levofloxacin-oxalate in order to determine the positions of the hydrogen atoms.

Single-crystal neutron diffraction data were collected at room-temperature using the quasi-Laue neutron single crystal diffractometer SENJU (BL18). A box shape single-crystal of 1 mm^3 size was coated by Apiezon-grease to prevent the desorption of crystalline water molecules, and mounted to an aluminum rod (Fig. 1). The diffraction patterns were measured in 15 different crystal orientations, spending 51 hours. As a total, 30737 reflections were measured. Figure 2 shows the diffraction image obtained in one crystal orientation.

The Space group was *P1* and the cell parameters were determined to be a = 10.056(5) Å, b = 17.40(1) Å, c = 19.06(1) Å, α = 67.77(3)˚, β = 86.13(5)˚ and γ = 77.19(3)˚. The observed reflections were corrected for the incident spectrum and the Lorentz corrections. The structure analysis was carried out with the program JANA2006[1] using the observed reflections. The determined frameworks of the molecules showed good agreement with the ones obtained from a previous X-ray diffraction study. More detailed and thorough analysis is underway in order to determine the hydrogen positions.

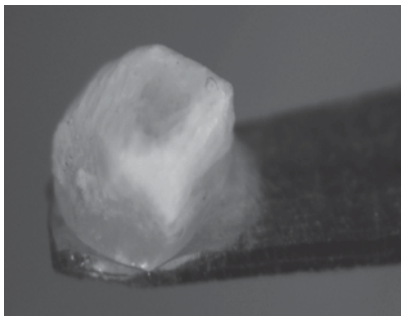

Fig. 1 single crystal of Levofloxacin-oxalate

1．研究成果概要（つづき） Outline of experimental results (continued).

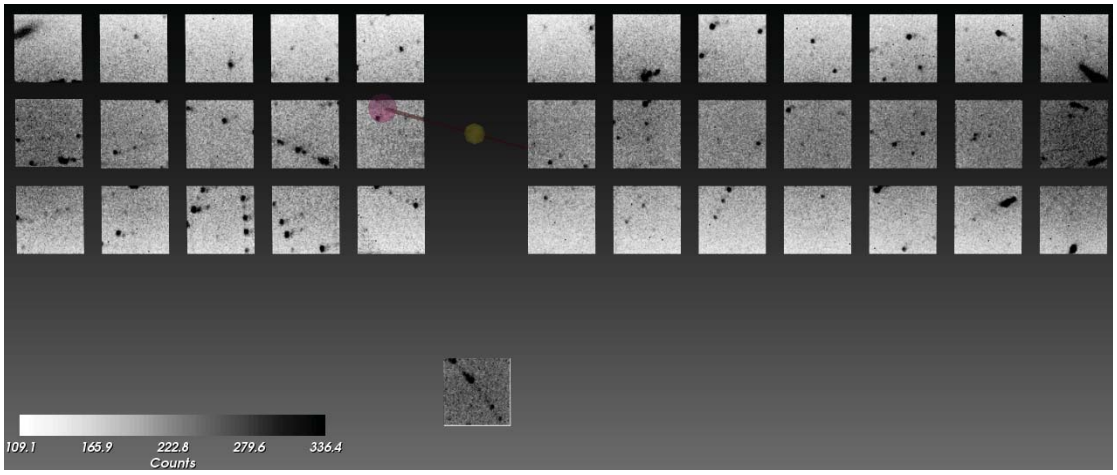

Fig. 2 Observed Laue-type diffraction pattern of Levofloxacin-oxalate.

[2] Neutron photo-crystallographic study of a photo-functional 2-(2'-hydroxyphenyl)benzimidazole crystal

A fluorescent molecular compound, 2-(2'-hydroxyphenyl)benzimidazole (HPBI: Fig. 1), has been drawing much attention as a candidate of new photo-functional molecular materials because photo-induced excited state intramolecular proton transfer (ESIPT) occurs both in solution and crystalline state in this molecule, and consequently solution, film and crystal of this molecule shows an unique fluorescent property. In this experiment, the author and co-workers tried to observe the photo-induced proton transfer by single crystal neutron structure analyses of a HPBI crystal by using a single crystal neutron diffractometer SENJU and a cryostat for photo-crystallography.

HPBI

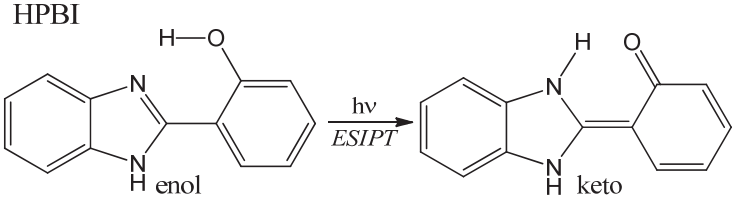

Fig. 1 HPBI molecule (enol- and keto-form)

The cryostat for photo-crystallography is composed of a 4K pulse-tube refrigerator, a fixed-χ type 2-axes goniometer using piezo-rotators and an optic fiber light guide. There are several service ports at the interface between the vacuum part and atmospheric part, and a vacuum connector in which the light guide is embedded is set on one of the service ports. The forefront of the light guide is covered with super-insulation film and fixed on an optical port of the 4K radiation shield beside the goniometer. Visible light is led into the vacuum part of the cryostat through this light guide and applied to the sample crystal. The Xe light source for the cryostat, MAX-303 (ASAHI SPECTRA Co.), has some wavelength selecting filters and the optimum wavelength region for each experiment can be chosen. The lowest temperature at the sample position was 8 K without photo-irradiation, 11 K with a 400 nm band-path filter, 18 K with a 400 nm long-cut filter and 66 K with no filter.

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A single crystal of HPBI with 4.0 x 2.0 x 0.2 mm^3 size was obtained by slow evaporation of ethanol-water solution of the commercially available HPBI. Single crystal neutron diffraction measurements were carried out by using SENJU (BL18). The crystal was mounted on the cryostat for photo-crystallography and visible light of which wavelength was shorter than 400nm was applied to the sample as shown in figure 2. The measurement temperature was 20K. The Space group was $P2_1$ and the cell parameters were a = 3.7602(3) Å, b = 22.016(1) Å, c = 5.7707(3) Å and β = 94.230(5)°. Measurement time and number of measured reflections were 52 hours (13 orientations x 4 hours) and 13181, respectively.

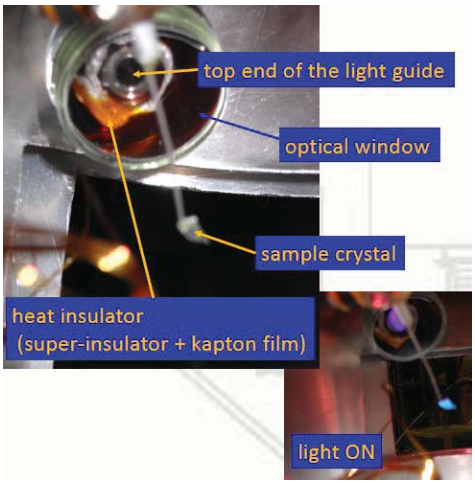

Fig. 2 Sample position of the cryostat for photo-crystallography.

Structure refinement is now in progress by using program JANA2006 [1]. Bragg reflections of which intensities are larger than 3σ are used in the refinements. The minimum value of d-spacing is 0.4 Å. The appearance of the photo-exposed HPBI single crystal suggests some kind of reaction occurred by the photo-exposure. Thus, we are now carrying out the structure analysis carefully to detect the structural change of the HPBI molecule by the photo-exposure.

References

[1] V. Petricek, *et al.*, *Z. Kristallogr.*, **229,** 345 (2014).