Structure Determination of Bicalutamide Polymorphic Forms by Powder X-ray Diffraction: Case Studies Using Density Functional Theory Calculations and Rietveld Refinement

Sumitomo Chemical Co., Ltd.
Basic Chemicals Research Laboratory
Masamichi Inui
Fine Chemicals Research Laboratory
Masafumi Ueda

Structure determination from powder X-ray diffraction data (SDPD) has been developing dramatically. A large amount of SDPD work has been reported in the field of crystallography and material science. However, SDPD is not easier than that from single crystal X-ray diffraction data due to intrinsic overlap reflections in powder XRD data. This report describes SDPD of Bicalutamide form-I and form-II performed by Rietveld refinement in combination with density functional theory (DFT) calculations. The effectiveness of the DFT optimization for SDPD is also discussed.

Introduction

Polymorphism of organic compounds is widely known as one of the properties of solid states. In particular, it is extremely important to control the crystal forms of pharmaceutical materials, because the efficacy and the safety of the drugs often vary according to differences in the crystal forms. Polymorphism is strongly related to interactions between water and diluting agents, and to differences in solubility, melting points, stability and other physical and chemical properties. Therefore structure determination is important to understand the essence of polymorphic forms.

Polymorphic forms are distinguished[1] by X-ray diffraction (single crystal diffraction and powder diffraction), thermoanalytical methods (DSC, TG-DTA, calorimetry, etc.) and spectroscopic methods (FT-IR, Raman, solid state NMR, etc.). Of these, crystal structure is normally determined by single crystal X-ray diffraction. Single crystal methods are superior methods that determine crystal structures with high precision and accuracy. In particular, since it has become possible to utilize ultra-bright X-rays and experiments for anomalous dispersion effects at synchrotron radiation facilities, landmark progress has been made in determining microcrystal forms on the order of several microns in a short period of time.[2]

In order to understand the physical and chemical properties of polymorphic forms, it is desirable to obtain the crystal structures, so that information such as molecular bonding and molecular conformation can be simultaneously evaluated in a multifaceted manner, both visually and numerically. In particular, three-dimensional information that can only be obtained from crystal structures is valuable, and it is superior for attaining an intuitive understanding of the structures. However, since organic compounds that cannot provide single crystals of a suitable size for determination can only be classified and categorized as polymorphic forms using other analytical methods, the crystal structures are still unknown.

In the field of pharmaceuticals, information on crystal structure greatly contributes to generating new business by being patented when developed products not only have a new crystal structure but also have remarkable changes in strength. Therefore, leading pharmaceutical companies that have been already placing patented products on the market have the risk of succumbing to market competition before they recover development costs for their patented products, even

before the patents expire. Furthermore, when leading pharmaceutical companies' patents expire, their business is limited by new patent holders who have done the follow-on development.

Even if organic compounds do not have a suitable size for the single crystal method, they often give sufficient quality data from powder X-ray diffraction. Therefore, there has been a need for SDPD. It can be seen that reports of SDPD started around 1940.[3] In 1998[4] and 2002[5] contests for SDPD were held as SDPD Round Robins. In one of the reports[4] from these, Le Bail et al., stated that, "The conclusion from this 1998 Round Robin is that solving structures 'on demand' from powder diffraction is non-routine and non-trivial, requiring much skill and tenacity on the part of practitioners." This can be understood as saying that even though some problems still exist, it is sufficiently possible to carry out SDPD. In fact, there is a report by Kenneth et al.[6] of successfully determining crystal structures in some organic compounds by SDPD, using a laboratory powder X-ray diffractometer. In other words, if there are good-quality powder samples, it is possible to determine crystal structures in the laboratory.

We introduced a conventional powder X-ray diffractometer under monochromatic Cu Kα1 radiation with the aim of carrying out Rietveld refinement and SDPD for organic compounds. In around 2005 we carried out SDPD of the organic compound bicalutamide, for which single crystal growth could not be achieved and which has two racemic forms (form-I and form-Ⅱ). Sample information for bicalutamide is shown in **Table 1**.

Bicalutamide is a useful compound with an antiandrogenic activity, and it is mainly used in medical applications as an anticancer drug. Bicalutamide is supplied to the market as a tablet, but the quality must be strictly managed for stable effectiveness of the compound. In particular, the crystal form, grain size and specific surface area are important because they have a big influence on the drug efficacy and on side effects.

We were already successful in SDPD of the two racemic forms (form-I and form-Ⅱ), and we were able to obtain crystal structure data for these forms. Recently, Vega et al.[7] have reported on crystal structure data[8] for the two racemic forms (form-I and form-Ⅱ) obtained by a single crystal method. When we compared our crystal structures to the crystal structures reported by Vega et al., the lattice constants and space group were the same for both, but it was apparent that parts of the molecular conformation were different and the positions of terminal groups were also different. It was very interesting to speculate as to whether there was a difference in the original substances or if there was a problem with our manner of SDPD.

In this work, we will report on a method for verifying the crystal structure by SDPD of form-I and form-Ⅱ bicalutamide polymorphic forms with asymmetric carbon. Typical SDPD procedures are cited in the references[2), 3), 6), 9)–13)], focusing on crystal structure determination for organic compounds. See the references for detailed descriptions.

Table 1 Sample information

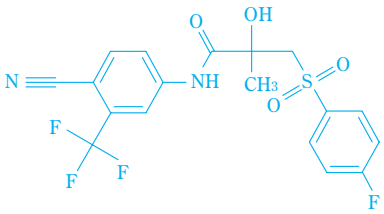
Compound name	Bicalutamide
Chemical name	(*RS*)-*N*-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methylpropanamide
Structure formula	
Molecular formula	$C_{18}H_{14}F_4N_2O_4S$
Molecular weight	430.37
CAS No.	90357-06-5

Table 2 Experimental data of Bicalutamide form-I

Compound name	Bicalutamide form-I
Wavelength λ/Å	1.540593 (Cu Kα1)
Specimen	capillary 1.0 mm
Absorption coefficient μ	0.67
Rotation speed	60 r.p.m
2θ range /°	3.0000 – 70.0157
Step size (2θ) /°	0.0016696
Time per step /sec	723

Table 3 Experimental data of Bicalutamide form-Ⅱ

Compound name	Bicalutamide form-Ⅱ
Wavelength λ/Å	1.540593 (Cu Kα1)
Specimen	capillary 1.0 mm
Absorption coefficient μ	1.15
Rotation speed	60 r.p.m
2θ range /°	3.00 – 79.9962
Step size (2θ) /°	0.016696
Time per step /sec	723

Experiments and Discussion

1. Measurement

Two types of powder sample were sealed in 1.0 mm diameter borosilicate glass tubes. Conventional characteristic X-ray powder diffraction data was collected at room temperature on a D8 ADVANCE with a Vαrio-1 diffractometer with a modified Debye–Scherrer geometry using monochromatic Cu Kα1 radiation (λ = 1.540593 Å, Cu Kα1) and a VÅNTEC-1 high-speed 1D position sensitive detector (PSD). Details of the measurement conditions are shown in **Tables 2** and **3**.

Moreover, the linear absorption coefficient was calculated from the following equation.

$$I_x = I_0 \exp(-\mu t)$$

where μ is the linear absorption coefficient, t is the sample thickness, I_x is the X-ray intensity through the sample and I_0 is the incident X-ray intensity.

2. Indexing and Initial Structure Determination

(1) Bicalutamide form-I

Indexing was carried out by the DICVOL91[14] program using the 35 peaks and the space group was determined on $P\,2_1/c$ by the extinction rule. The mol-file was created from a plane or molecular model using ChemSketch[15] software, and initial structure determination was carried out by a direct space method using the DASH[16] program package. The DASH[16] program package employed a simulated annealing (SA) method for the structure search. Integrated intensity in the range of $d \geq 2.8$ Å was extracted from measurement data using the Pawley refinement method. Then, the crystal structure with the lowest profile chi-square value in several SA runs was set as the initial structure model.

(2) Bicalutamide form-Ⅱ

Indexing was carried out by the DICVOL04[17] program using the 20 peaks as well as form-I. Zero correction for the angle 2θ and the consideration of impurity peaks from DICVOL04 were useful in this indexing. As a result, the crystal system was determined on a triclinic system, but we could not make a judgment about the presence of a symmetrical center because of the principles of powder diffraction. Therefore we assumed space group $P\,\bar{1}$, which conveniently had a symmetrical center. Initial structure determination was carried out using a SA method as well as form-I. Pawley refinement was performed in the range of $d \geq 2.5$ Å.

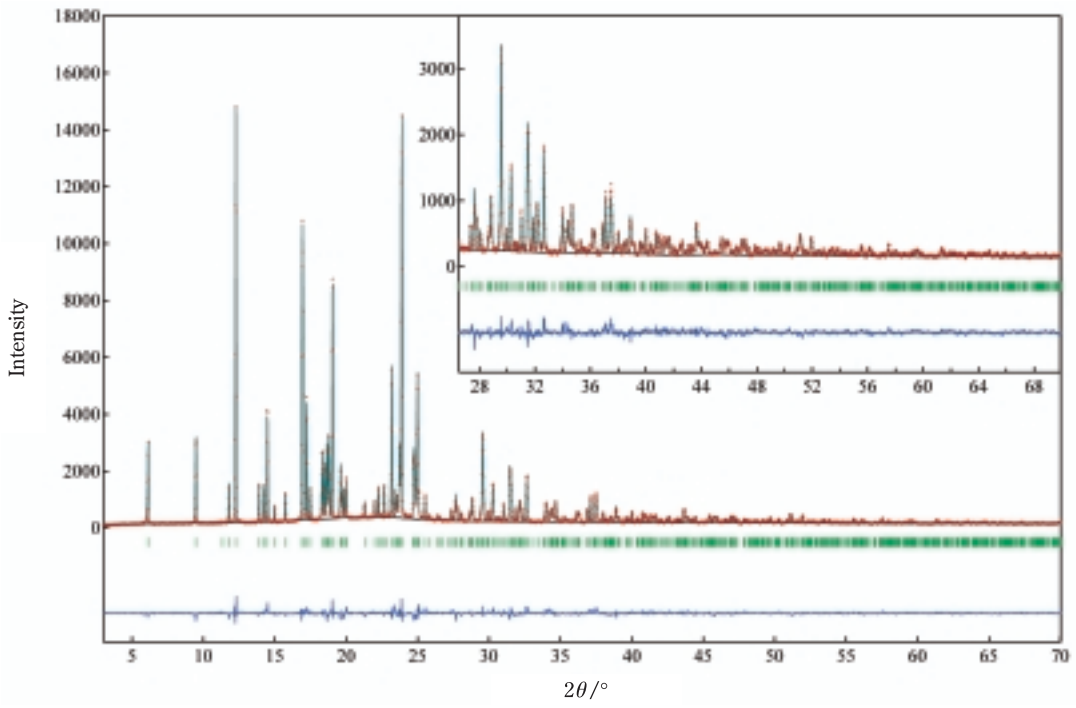


Fig. 1 Difference plots of Bicalutamide form-I (±*syn*–*clinal*) after the Rietveld refinement.
The observed diffraction intensities are represented by plus (+) marks (red), and the calculated pattern by the solid line (blue). The curve (dark blue) at the bottom represents the weighted difference, $Y_{io}-Y_{ic}$, where Y_{io} and Y_{ic} are the observed and calculated intensities of the i th point, respectively. Short vertical bars (green) below the observed and calculated patterns indicate the positions of allowed Bragg reflections.

3. Rietveld Refinement

Rietveld refinement was carried out using the RIETAN-FP[18] program package. The linear absorption coefficient was considered to improve precision of Rietveld refinement because of transmission geometry with long wavelengths. A small bump of around $2\theta = 24°$ observed in the background was attributed to the presence of the capillary tube composed of amorphous borosilicate. A composite background function between the 11th-order Legendre polynomial and the preliminary background data is particularly useful for the Debye-Scherrer geometry. The preliminary background data was approximated using the PowderX[19] program. A modified split pseudo-Voigt function was used to model the peak profiles. The VESTA[20] program was used for visualization of the structural model. The Rietveld refinement results for form-I and form-Ⅱ are given in **Table 4** and **Fig. 1–4**.

Table 4
Structure refinement of Bicalutamide form-I and form-Ⅱ

Compound name	Bicalutamide form-I (±*syn* – *clinal*)	Bicalutamide form-Ⅱ (*m*1)
R_{wp}	0.0798	0.1609
R_B	0.0244	0.0608
R_F	0.0211	0.0451

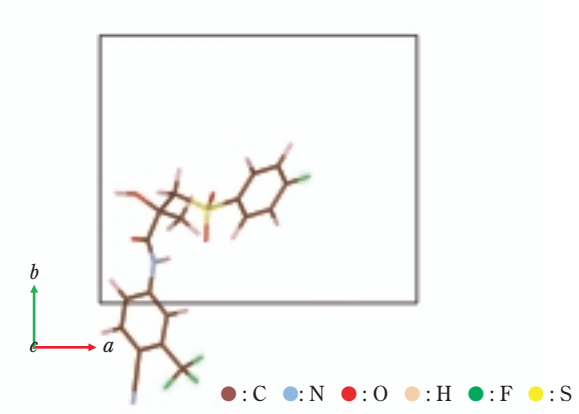


Fig. 2
A single molecule diagram of Bicalutamide form-I (±*syn* – *clinal*)

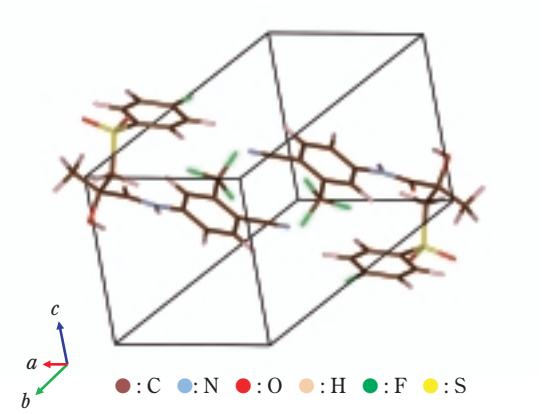


Fig. 4
Packing diagram of Bicalutamide form-Ⅱ (*m*1, See **4.** (2))

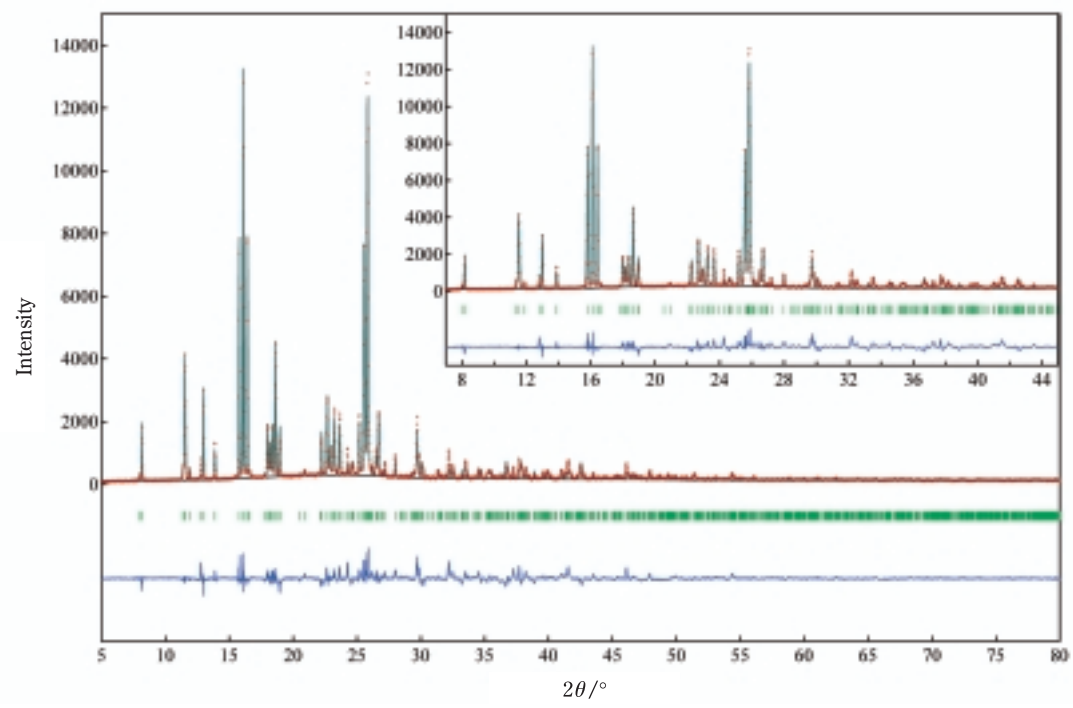


Fig. 3 Difference plots of Bicalutamide form-Ⅱ (*m*1, See **4.** (2)) after the Rietveld refinement

4. Crystal Structure Verification

(1) Bicalutamide form-I

Decreasing the reliability factors R_{wp}, R_B and R_F in the Rietveld refinement somewhat improves the reliability of the crystal structure. Furthermore, more investigation is necessary to confirm whether values such as the bond distances, bonding angles and torsion angles are expected values. In particular, the ratio of the number of the observed reflections to the number of refinement parameters is small in the case of powder diffraction, so the problem of local minima occurs easily in a nonlinear least square calculation,[3] and verification of the crystal structure is necessary.

It is effective to use a crystal structure database to verify parameters such as the bond distances, bonding angles and torsion angles, however this verification alone may not be sufficient. In particular, we examined the fact that in bicalutamide form-I, which has asymmetric carbon, there could be two stereoisomers. If the other stereoisomer having the same molecular structure was found first in the SA run, this convergence structure model was unfortunately led to the false structure model. Since they are stereoisomers that have the same molecular structure, it is difficult to distinguish between the false crystal structure and true crystal structure without more careful verification of the bond distances, bonding angles and torsion angles. Of course, this can be determined by carrying out a total search such as a grid search[3] using high resolution data, however, the required calculation time would not be practical. For example, we could also consider greatly increasing the number of SA runs (seeds) and using sufficient time with parallel tempering.[21]

Since Pawley refinement was performed in the range of $d \geq 2.8$ Å because of the limitations of peaks that could be treated by the program in this time, the integrated intensity did not contain sufficient structural information to differentiate between –OH and –CH_3, and it was difficult to distinguish between true and false crystal structures. Kenneth et al.[22] reported their investigations into this data resolution in detail. Furthermore, the number of electrons for –OH and –CH_3 with interposed asymmetric centers for the stereoisomers was the same, at 9. The diffracted waves due to the number of electrons and the spread of electrons are used as observed values in X-ray diffraction, so when there are almost no differences in the number of electrons, it is difficult to discriminate between true and false crystal structures in the sequence of operations from the SA method to Rietveld refinement.

In this example we already know that two stereoisomers are present (**Fig. 5**). Therefore, based on the crystal structures refined using Rietveld refinement, we substituted –OH and –CH_3 and created another stereoisomer. To distinguish between –OH and –CH_3, we compared the two stereoisomers using measurement data in the range of $d \geq 1.3$ Å ($2\theta = 70°$). At this time the isotropic atomic displacement parameter for H atoms was kept at a fixed value.

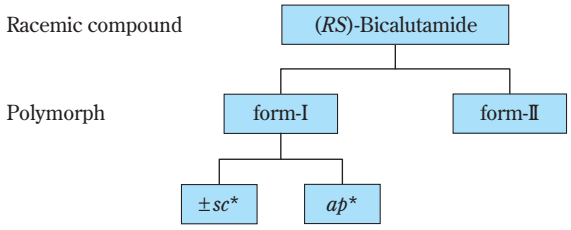


Fig. 5
Tree diagram of stereoisomer in Bicalutamide crystal (*See **4.** (1))

We used a Klyne-Prelog notation of conformation to distinguish between the crystal structures of the two stereoisomers. The molecular model determined by SA is called a *±syn–clinal* form (*±sc*-form) with the torsion angle for O–C–C=O being ±86.82°. Conversely, the stereoisomer model with –OH and –CH_3 interchanged and with a torsion angle for O–C–C=O of ±156.01° (**Fig. 6**) is called an *anti–preplanar* form (*ap*-form).

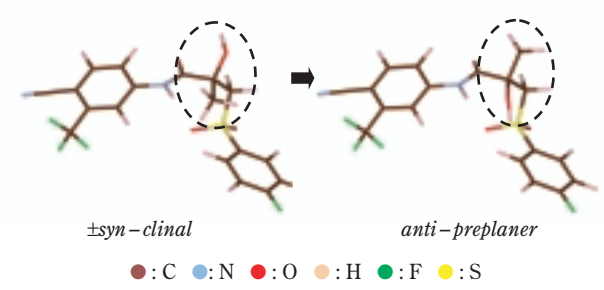


Fig. 6
A single molecule diagram of Bicalutamide form-I
left : *±syn – clinal*, right : *anti – preplaner*

Reliability factors for the *ap*-form using Rietveld refinement were lower values of $R_{wp} = 0.0690$, $R_B = 0.0188$ and $R_F = 0.0167$ for the *ap*-form than for the *±sc* form (**Fig. 7**, **Fig. 8**). Consequently, we could determine that the true crystal structure was *ap*-form. This

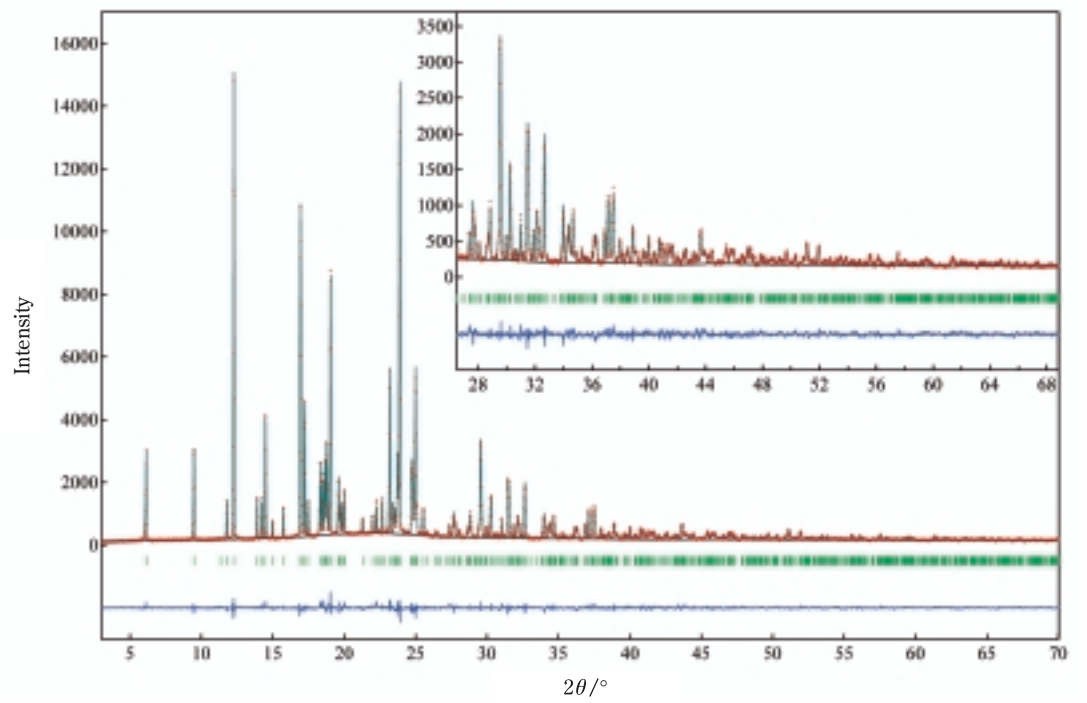


Fig. 7 Difference plots of Bicalutamide form-I (*anti – preplaner*) after the Rietveld refinement

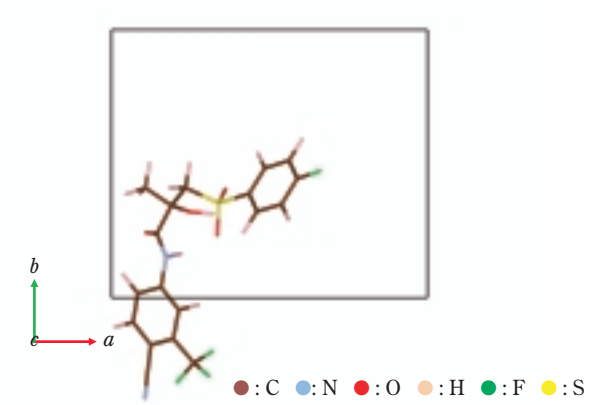


Fig. 8
A single molecule diagram of Bicalutamide form-I (*anti – preplaner*)

ap-form crystal structure was equivalent to the crystal structure reported by Vega et al. (**Table 5**).

(2) Bicalutamide form-Ⅱ

The reliability factor $R_F = 0.0451$ may be a comparatively good value from the Rietveld refinement, however the other reliability factor $R_{wp} = 0.1609$ was hardly a good value (letting this crystal model be *m*1; see **Fig. 4**).

Therefore, the *m*1 crystal structure was refined again using Rietveld refinement under weak constraint conditions for the atomic distances and bonding angles in comparison to the previous Rietveld refinement. In this second refinement, we adopted the conjugation direction method for nonlinear least square calculation mounted on RIETAN-FP, which method made it possible to escape from local minima easily and automatically. Consequently, the *m*1 crystal structure had changed into a new crystal structure (*m*2) where the conformation had partial variations in comparison to the *m*1 crystal structure (**Fig. 9**).

Furthermore, geometry optimization of the *m*2 crystal structural was carried out using DFT calculation to correct the distorted atomic distances, bonding angles and torsion angles (see **5**) and this corrected crystal structure was refined again using Rietveld refinement.

Table 5
Crystallographic data of Bicalutamide form-I

Compound name	Bicalutamide form-I (*anti – preplaner*)
Chemical formula	$C_{18}H_{14}F_4N_2O_4S$
Space group	$P2_1/c$ (No. 14, setting 1)
a / Å	14.9064 (4)
b / Å	12.2234 (3)
c / Å	10.4876 (3)
β / °	104.7790 (14)
Unit-cell volume / Å^3	1847.7 (7)
Formula unit *Z*	4
Rietveld analysis	
R_{wp}	0.0690
R_B	0.0188
R_F	0.0167
S	1.4061

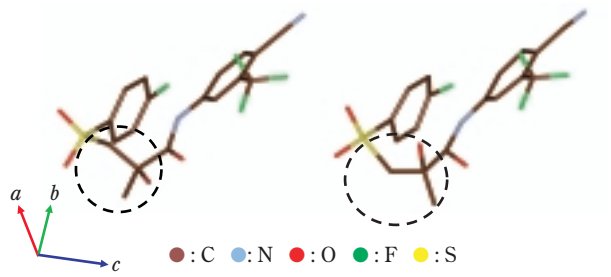


Fig. 9
A single molecule diagram of Bicalutamide form-Ⅱ
left : *m*1 (exclusion of H atom), right : *m*2

Table 6
Crystallographic data of Bicalutamide form-Ⅱ

Compound name	Bicalutamide form-Ⅱ (Rietveld refinement of *m*2)
Chemical formula	$C_{18}H_{14}F_4N_2O_4S$
Space group	*P*-1 (No. 2)
a / Å	7.7875 (3)
b / Å	11.0355 (4)
c / Å	11.2888 (5)
α / °	87.968 (3)
β / °	77.050 (3)
γ / °	78.012 (6)
Unit-cell volume / Å^3	924.8 (8)
Formula unit *Z*	2
Rietveld analysis	
R_{wp}	0.0872
R_B	0.0198
R_F	0.0197
S	1.6705

Consequently, the reliability factors $R_{wp}=0.0872$, $R_B=0.0198$ and $R_F=0.0197$ were remarkably decreased (**Table 6**, **Fig. 10**). And now the *m*2 crystal structure was equivalent to the crystal structure reported by Vega et al.

5. Usefulness of Density-functional-theory (DFT) Calculations

H. R. Karfunkel et al.[23] were successful in predicting the crystal structure of organic compounds using both semiempirical molecular orbital methods and DFT calculations on the basis of X-ray powder patterns, and this predict crystal structures were refined by Rietveld refinement. On the other hand, Honda et al. indicate that there are problems with current computational chemistry and that it is not easy to determine the crystal structures from organic molecules alone.[2] Because the computational chemistry approach is able to evaluate the crystal structure energy when the conformations differ for the same molecules in the crystal structure determination sequence from the SA method to Rietveld refinement, we expect it to be a suitable method for determining whether the crystal structure is true or false. Here, the crystal structure energy in both cases where the asymmetric carbon functional groups –OH and –CH_3 were exchanged for form-I were calculated, and the crystal structure energy of the *m*1 and the *m*2 for form-Ⅱ were

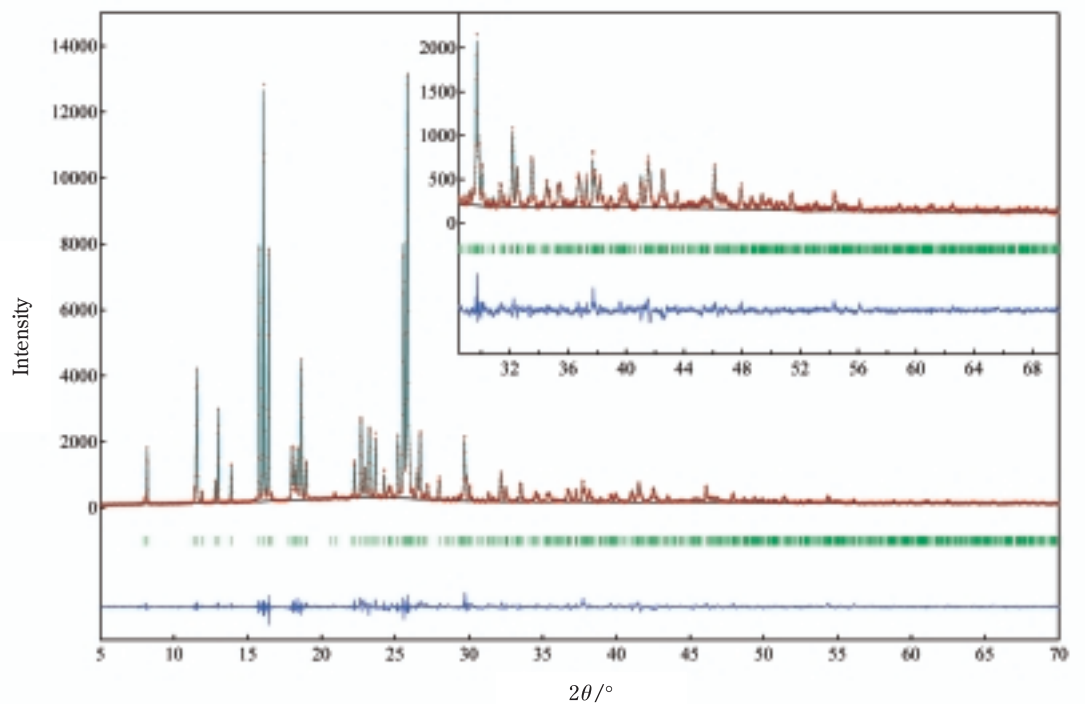


Fig. 10 Difference plots of Bicalutamide form-Ⅱ (*m*2) after the Rietveld refinement

calculated, respectively. Especially, we focused on the energy stability of each of the molecular conformations for form-I, and focused on the interaction energy between molecules for form-II.

The DFT calculation was performed by the DMol^3 program implemented in the Materials Studio[24] program package. For geometry optimization calculation, a double numerical basis set with a polarization function (DNP) equivalent to the 6-31G* basis set was applied to the numerical base function, and a Perdew-Burke-Ernzerhof (PBE) functional using generalized-gradient approximation was applied to the exchange-correlation interaction. All of the calculations were carried out with 3.3 Å as the *R*-cutoff value for all atoms.

In conformation of form-I (±*sc*-form) using DFT calculations, there was an energy convergence value of –7604.3481872 Ha (Ha = 2625.4986 kJ/*mol*) without altering the ±*sc*-form refined by Rietveld refinement. On the other hand, in conformation of form-I (*ap*-form) using DFT calculations, there was an energy convergence value of –7604.4178405 Ha without altering the *ap*-form refined by Rietveld refinement. The energy difference between the ±*sc*-form and the *ap*-form was large with Δ0.0697 Ha (= 182.99725242 kJ/*mol*), and we concluded that the form-I (*ap*-form) was more stable in terms of energy. This is consistent with the results of the Rietveld refinement, and a true crystal structure was also apparent from the DFT calculation.

In the case of form-II, when the *m*1 crystal structure refined by Rietveld refinement under the strong constraint conditions of atomic distances and bonding angles and the *m*2 crystal structure refined under weak constraint conditions by Rietveld refinement were compared, we expected there to be a difference in the energy conversion values because of partial differences in structure.

The energy convergence value of the *m*1 crystal structure was –3802.1855665 Ha without altering the *m*1 crystal structure refined by Rietveld refinement. The energy convergence value of the *m*2 crystal structure was –3802.1990037 Ha without altering the *m*2 crystal structure refined by Rietveld refinement. The correct crystal structure *m*2 could not be predicted by DFT calculations from the *m*1 crystal structure, however, the energy difference between *m*1 and the *m*2 was Δ0.0134372 Ha (= 35.2793417256 kJ/*mol*). We concluded that *m*2 was somewhat more stable in terms of energy under these calculation conditions. We found a clear difference with Rietveld refinement, but even though there was consistency in the results of Rietveld refinement, there was only a slight difference between the energy convergence values for the two models using DFT calculations. This would be caused by the force of molecular interactions being underestimated in DFT. Essential problems such as the underestimation of molecular interactions in the DFT calculation and the fact that the most energy stable structure is not always the correct structure as discussed by Honda et al.[2] still remain. However, when stereoisomers are found because of asymmetric carbon such as form-I, a clear difference is seen with the energy calculations using DFT calculation even though there is little difference in the Rietveld refinement. DFT calculation is useful to evaluate the conformation of molecules.

Conclusion

We have reported that crystal structure verifications using geometry optimization with a combination of Rietveld refinement and DFT calculation is effective in cases of evaluating the SDPD for bicalutamide form-I and form-II, which have asymmetric carbon.

SDPD program packages using the direct space method, e.g. DASH, can progress semi-automatically in the same way as a single crystal method, if the powder diffraction data is provided with good quality. It is possible to obtain comparatively close crystal structures, excluding the details with just the click of a mouse. However, SDPD still has some problems in reaching the same accuracy in the determination of crystal structure as the single crystal method, including crystal structure verification from SDPD overviewed by Le Bail. Single crystal method and powder diffraction method are just a difference in the method of crystal structure determination, and the certainty of results is not desirable to be different. When researchers make the effort to understand substances well and actively use other analysis methods, the crystal structure from SDPD will be closer to a correct solution.

Single crystal X-ray diffraction data where measurement points (Laue spots) have copious reciprocal space information for three dimensions are extremely superior to powder X-ray diffraction data (Debye ring) that can only give one-dimensional overlapping reciprocal space information. Therefore, it is mathematically clear that the single crystal method is superior in the determination of crystal structures. It is not appropriate

to select SDPD in the first place, simply because of the ease of reducing the work in making single crystals for samples. It is best to attempt structure determination from single crystals first.

However, there are many materials for which it is difficult to form single crystals, and crystal structure determination of a powder (polycrystalline) compound is necessary. In such cases, SDPD is the only method for crystal structure determination. Recently, there have been great strides in measurement equipment and programs for SDPD in research fields. The suitable use of SDPD with an understanding of its merits and shortcomings will improves the reliability of SDPD and will promote dissemination of information. We hope that this report will be a contribution to the technical development of SDPD and to the development of materials.

Acknowledgments

We held discussions with Midori Goto of the National Institute of Advanced Industrial Science and Technology (AIST) Center on isomeric structures and crystal chemistry for organic compounds and, in addition, had technical discussions and received helpful advice from Dr. Takuji Ikeda, a researcher at the Research Center for Compact Chemical Process of the AIST. Here we would like to express our gratitude to them.

References

1) Kazuhide Ashizawa (Ed.), "Iyakuhin no Takeigensyo to Syouseki no Kagaku", MARUZEN PLANET Co., LTD. (2002).
2) Hachiro Nakanishi (Ed.), "Recent Advance in Research and Development of Organic Crystalline Materials", CMC Publishing Co., LTD. (2005).
3) William I.F. David, Kenneth Shankland, Lynne B. McCusker and Christian Baerlocher (Ed.), "Structure Determination from powder Diffraction Data", Oxford Science publications (2002).
4) Armel Le Bail and L M D Cranswick, *Commission on Powder Diffraction, IUCr Newslett.,* No.**25**, 7 (2001).
5) http://sdpd.univ-lemans.fr/sdpdrr2/results/index.html
6) Kenneth Shankland, Anders J. Markvardsen and William I. F. David, *Z. Kristallogr.* **219**, 857 (2004).
7) Daniel R. Vega, Griselda Polla, Andrea Martinez, Elsa Mendioroz and María Reinoso, *Int. J. Pharm.* **328**, 112 (2007).
8) http://www.ccdc.cam.ac.uk/
9) Izumi Nakai, Fujio Izumi (Ed.), "Funmatsu Xsen Kaiseki no Jissai", Asakura Publishing Co., LTD. (2002).
10) Jörg Bergmann, Armel Le Bail, Robin Shieley and Victor Zlokazov, *Z. Kristallogr.* **219**, 783 (2004).
11) Angela Altomare, Rocco Caliandro, Mercedes Camalli, Corrad Cuocci, Carmelo Giacovazzo, Anna Grazia, Guiseppina Moliterni, Rosanna Rizzi, Riccardo Spagna and Javier Gonzalez–Platas, *Z. Kristallogr.* **219**, 833 (2004).
12) Kenneth D. M. Harris, Scott Haberrshon, Eugen Y. Cheung and Roy L. Jphnston, *Z. Kristallogr.* **219**, 838 (2004).
13) Vincent Favre–Nicolin and Radovan Černý, *Z. Kristallogr.* **219**, 847 (2004).
14) Ali Boultif and Daniel Louër, *J. Appl. Cryst.* **24**, 987 (1991).
15) http://www.acdlabs.com
16) http://www.ccdc.cam.ac.uk/products/powder_diffraction/dash/
17) Ali Boultif and Daniel Louër, *J. Appl. Cryst.* **37**, 724 (2004).
18) Fujio Izumi and Koichi Momma, *Solid. State Phenom.,* **130**, 15 (2007).
19) Cheng Dong, *J. Appl. Crystallogr.* **32**, 838 (1999).
20) K. Momma and F. Izumi, *J. Appl. Crystallogr.* **41**, 653 (2008).
21) Marco Falcioni and Michael W. Deem, *J. Chem. Phys.*, **110**, 1754 (1999).
22) Kenneth Shankland, Lorraine McBride, William I. F. David, Norman Shankland and Gerald Steele, *J. Appl. Crystallogr.* **35**, 443 (2002).
23) H. R. Karfunkel, Z. J. Wu, A. Burkhard, G. Rihs, D. Sinnreich, H. M. Buerger and J. Stanek, *Acta Crystallogr., Sect. B: Struct. Sci.* **B52**, 555 (1996).
24) http://www.accelrys.com/products/mstudio/

PROFILE

Masamichi Inui

Sumitomo Chemical Co., Ltd.
Basic Chemicals Research Laboratory
Research Associate

Masafumi Ueda

Sumitomo Chemical Co., Ltd.
Fine Chemicals Research Laboratory
Senior Research Associate