A CRYSTALLOGRAPHIC STUDY OF CRYSTALLINE PENICILLIN G. SODIUM

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Many studies on the production[1)2)] and medical application of Penicillin (hereafter abbreviated as Pc.) have been published in recent years, but the property of crystalline Pc. has not yet been made clear though its chemical structural formula has already been determined.

This study has no direct relation with the production and the medical use of Pc. and has remained a subject which most doctors are not interested. It can, however, not be denied that a knowledge of the optical property has an important significance in examining and determining the purity and different internal structures of crystalline Pc.

I have been making observations on crystalline Pc. G. Na by means of a polarizing-microscope,[5)6)] and as the result of these observations and experiments, I obtained the following crystallo-graphic data. The present paper is a report of studies made on the chemico-physical properties of crystalline Pc.

MATERIALS AND APPLIANCE

i) Materials

Pc's used in the experiment were Penicillium G. sodium Crystallium and Penicillinum G. Potassicum Crystallinum (both manufactured in Japan). The solvents used for recrystallization were redistilled water, 25% ethanol, 98% ethanol, aceton, etc. When, however. Pc. G. Pot. cryst, is crystallized between mineral slide and coverglass, the thin pieces of the cystall will, whatever the solvent used, have the crystal habitus that only (100) those optically parallel to the optic axis develop (the straight extinction position), and other faces will never be found.

Consequently the use of Pc. K for observation by means of a polarizing-microscope is very incovenient and makes it impossible for investigating certain optical properties. So in this experiment I was obliged to use Pc. Na only.

Of the solvents used for recrystallization, redistilled water was most ideal for the recrystallization of Pc. Na. As for ethanol and aceton, they could be used crystallographically with the same result as when H_2O was used, but the thickness of the crystal pieces obtained were not favorable for the microscopic observations.

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ii) Appliance

In order to observe the shape of the crystals and their optical property, I used a biological microscope and Polarizing microscope manufactured by E. Leitz and Leichert.

As light source, I used white light thrown through tetra-ammin cupric sulphate solution. In some cases when precise measurments were needed, I used Natrium monochromatic light and read the interfacial angles by rotating the stage of a microscope.

EXPERIMENTAL RESULT AND DISCUSSION

i) Observations on the shapes of crystals by means of a biological microscope

The crystalline Pc. Na seperated from redistilled water by recrystallization is somewhat brownish and transparent and its shape varied as shown in Fig. 1.

The shape (1) in Fig. 1 is most frequently observed, and the long axes lie in straight lines and at both ends there are triaingular-shaped fence pickets. Shape (4) which is a fully developed crystal is seldom observed.

Most of the crystals exist as a single crystal with a distinct edge. The number of crystals adhering or clinging to one another is comparatively few. The crystal taces are seen in Fig. 1.

The developement of (100) is especially remarkable.

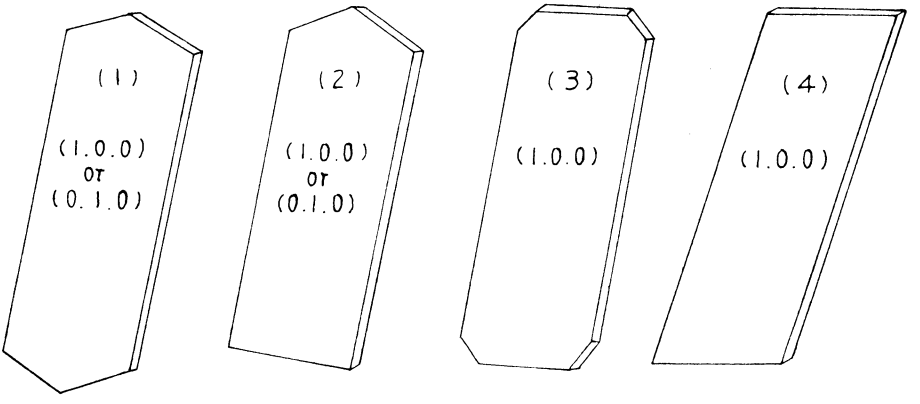


FIG. 1. The crystal shapes and faces of Pc. Na.

ii) Observations by means of a polarizing-micro-scope

1) The determination of the crystal system

Next I intended to determine the crystal system of Pc. Na. When, with an orthoscope, observations are made on the thin pieces of the crystals shown in Fig. 1 and 2 (produced between a slide glass and a cover glass) placed on the rotating stage of a microscope, some crystals show straight extinctions on a distinctly developed direction P-P' and others show oblique extinctions.

Next, when the conoscopig figures of some thin pieces which show obligue extinctions are observed under illumination of white light and by inserting the

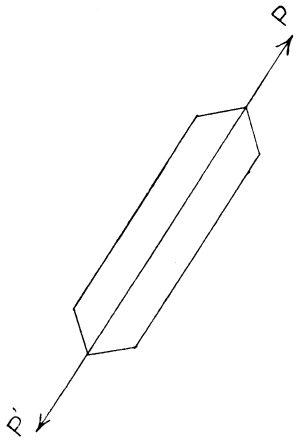


FIG. 2

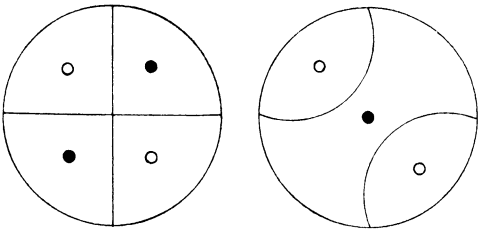


FIG. 3. Extinctionctionposition diagonalposition Addition and substraction Phenomena of the thin pieces. Showing oblique extinction in case of the insertin of Gips Red I test-plate.
○ Addition ● Substraction

upper Nicol, the ring of interference color and melatopes peculiar to an optically bixial crystal can be found. In order to make clear whether these thin pieces are perpendicular to the optic elasticity axis "X" or "Z", I adopted the method of Gips Red I test-plate. As the result of this experiment, there appear, as shown in Fig. 3, the phenomenon of addition and blue color and that of substraction and yellow color at extinction positions and diagonal positions. Therefore it can be proved that this interference figureis "$\perp X$". On the other hand, when the thin pieces showing straight extinctions are set for the conoscope at extinction positions, the ring of concentric circles with a dark cross in its visual center appears in every case, but as it moves gradually from extinction position to diagonal position by rotating the stage, this isogre of the dark cross changes from two parts of a hyperbole to guadrants (see Fig. 4) and then forms a characteristic flash figure which continues to expand beyond the range of a microscope.

That is to say, it is clear that all the thin pieces at straight extinction positions are parallel to the optic axial plane are in the direction of the optic elasticity axis "Y".

The retardation in Fig. 4 is in the order of $1<2<3$. Again, under illumination of white light the thin pieces at straight extinction positions are observed with an orthoscope by inserting Gips Red 1 test-plate.

These thin pieces show the substraction phenomenon when they are brought to diagonal positions by rotating the stage 45°, and show the addition phenomenon by rotating 90° to the left from the previous

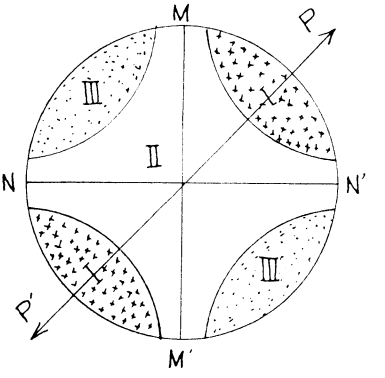


FIG. 4. Interference figures at right diagonal position of a crystal at straight extinction position.
MM' and *NN'* are the vibration directions of the upper and the lower nicol respectively.

position.

The vibration directions of the faster light wave against a Gips Red 1 test-plate (X') and that of the slower one (Z') are showen in Fig. 5.

So the direction P-P' indicates the vibration of the faster light wave while the direction perpendicular to P-P' the vibration direction of the slower light wave.

The results of the observations seem to show that Pc. Na is an optically biaxial crystal and belongs to the monoclinic system. By giving the crystallographic axes "a", "b", and "c" to the monoclinic system, the optical orientation can be determined as follows.

In Fig. 6 are shown a stereographic projection and a model of the monoclinic system.

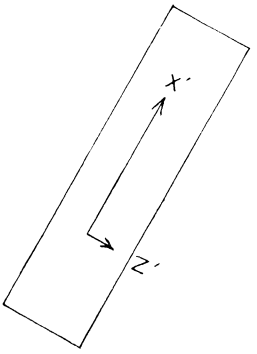
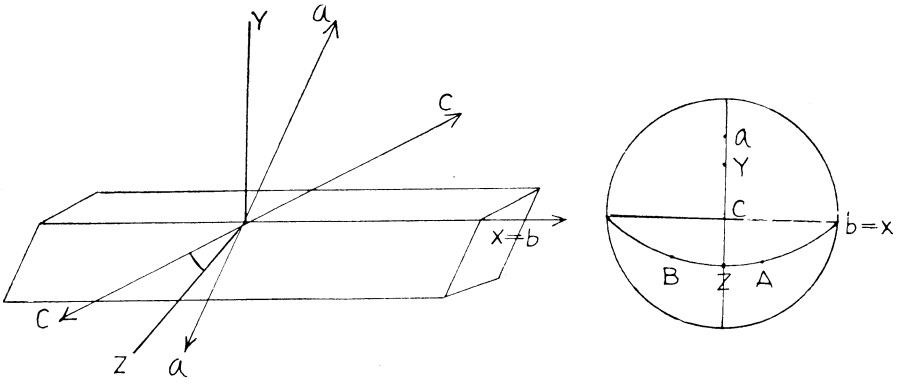


FIG. 5. Vibration direction to two light wave against Gips Red 1 test-plate.



A model of monoclinic system of Pc, Na. Stereographic projection of Pc, Na.

FIG. 6

$b=X$ plane of optic axis $\perp 010$.
c is on the direction of "Z" axis
a is on the direction of "Y" axis

It is noted that a remarkable developement is seen in the direction of "b".

2) Extinction angle

Pc. Na., when parallel to (100), shows straight extinctions and, when parallel to (010), shows maximum extinction angle, which is the same as the angle that the axis "C" makes with the optic elasticity axis "Z" on the (010).

As for the monoclinic system concerned, the degrees of the extinction angle represent the character of the crystal.

When the angle CZ is measured for many crystal powders, its statistic value shows that CZ is equal to 32°20′ (<the obtuse angle β).

3) Optical axial angle value and optical character

The angle ($2\,\Omega$ or $180°-2\,\Omega$ respectively) between optic axis AA' and BB' and optic elasticity axis X and Z are regarded as the apparent optical angle from the interference figure of a polarizing-microsope. Then the following formula makes it possible to compute the value of the angle between optic axis and elasticity axis.

$$D = K \sin x.$$

K is Mallard's constant for each combination of microscope lenses. D is the distance between the center of the conoscopic figure and the two melatopes A and B.

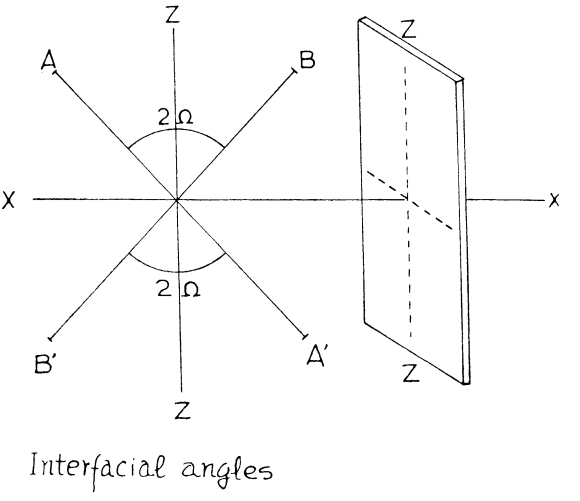


FIG. 7

If the optical angle computed from the above formula is equal to $2\,\Omega$ ($2\,\Omega < 90°$), the optical character of the crystal is positive.

If it is equal to $180°-2\,\Omega$ (in this case $2\,\Omega > 90°$), the optical character is negative.

Now I will decide Mallard's constant and then find out the value of the apparent optical angle $2\,E$ from the interference figure of the thin pieces of $\perp X$ Pc. Na.

Mallard's constant K can be measured from the fact that in calcite $2\,E$ is equal to 63° and from the distance, between the center of the interference figure and melatopes A and B, which is easily measured by using an eyeglass with a micrometer, in both cases of calcite and the thin pieces of $\perp X$ Pc. Na.

The results are as follows: for Pc. Na, D it is equal to 8 mm, for calcite, D is equal to 7 mm. The apparent optical angle is determined by substituting these values in the formula $D = K \sin x$.

Mallard's constant: $7 = K \sin 31°30' \quad \therefore \; K = 13.4126$
Apparent angle: $8 = 13.4126 \sin x \quad \therefore \; x = 42°13'$

$$2E = 180° - 84°26'$$

On the other hand, when F. E. Wrights method[7] is used for deciding the optical angle $2V$, it is found that V is equal to $90° \fallingdotseq 37°$. Consequently, as 2Ω is wider than 90°, Pc, Na is a bixial negative crystal.

X is an acute bisectrix
Z is an obtuse bisectrix.

4) Dispersion

As for Pc, Na the dispersion[8] of optic orientation is remarkable. By dispersion a rather red than blue colour is seen in the neighborhood of the melatope of the interference figure.

$$\rho < \Omega$$

Axial colours and pleochroism can not be observed.

5) The determination of an interfacial angle

As for the shape of Pc, Na., a crystal with a full developed edge as seen in the model of the monoclinic system (Fig. 6) is seldom found. There are seen various shapes as shown in Fig. 1. That is to say, the shape is not invariable. Accordingly it is quite diffcult and almost impossible to decide which interfacial angle is proper and peculiar to Pc, Na.

In some literature on the same subject it is stated that the shape (1) in Fig. 1, where one side is straight and both ends resemble a fence picket with an equilateral triangle, should be beheied to be the proper shape of crystalline Pc, Na. The results of statisitical measurements of these interfacial angles are shown below.

6) Twin and hemi-morphy

These were not found. The principal refractive index of Pc, Na could not be measured.

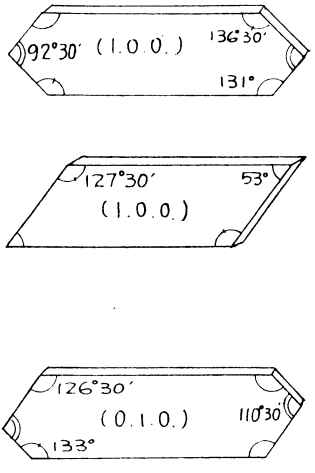


FIG. 1

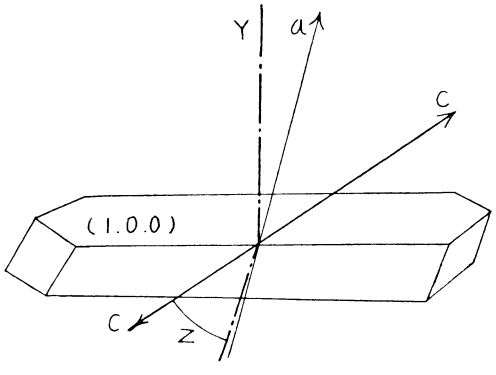


FIG. 2

The reason is that Pc. is easily solable in various substances and at the same time has great hygroscopicity. Sodium is deliquescent in two or three minutes when left alone in the air.

As for the refractive index, it was impossible to measure by using materials enclosed in a glass. It is regrettable that measurement of the refractive index has to remain a study for the future.

CONCLUSIONS

The present study was made to observe the shape and optical property of Pc, G, Na, cryst. As a result, the following facts have been made clear.

Shape: In most cases the direction of the long axis is straight and both ends have a triangular fence picket shape. In rare cases we can find a crystal with fully developed edges as seen in a model of the monoclinic system. As for the crystal face, (100) and (010) appear most frequently.

The crystals usually exist singly and crystals adhering or clinging to one another are rarely found. (c.f. Fig. 1)

Crystal system: Monoclinic system.

Optic orientation: $b=X$

Y is in the direction of a
Z is in the direction of c

A remarkable developement is seen in the direction of b.

X is the (first) acute bisectrix.
Z is the (second) obtuse bisectrix.

Optical character: biaxial negative crystal

Extinction angle: maximum extinction angle

$CZ=32°20'$ ($<$an obtuse angle β)
Straight extinction in case of (100)

Apparent optical angle: $2E=180°-84°26'$

Dispersion: $\rho > \Omega$

Pleochroism and Axial colours: not found.

Twin and Hemimorphy: not found.

Optical elongation: Positive or negative.

(Interfacial angle: C.f. the same item).

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