ACTA CHEMICA SCANDINAVICA 4 (1950) 1020—1023

Remarks on the Crystal Structure of Asymmetric Molecules. — The β-Phenylglyceric Acids

S. FURBERG and O. HASSEL

Universitetets Kjemiske Institutt, Blindern — Oslo, Norway

Molecules capable of existing in the liquid or gaseous state or in solution in different configurations which do not differ appreciably in internal energy would in general be expected to be able to be present in more than *one* configuration even in a defined crystalline modification. In the crystals of pentaerythritol esters $C(CH_2X)_4$ for example ($X =$ chlorine, bromine or iodine) which have large unit cells containing a great number of molecules it has been suggested[1] that molecules of different configurations are present. In such cases a complete crystal structure determination will in general be very difficult or even impossible with our present means of investigation. It would appear to be of interest, however, to approach such problems even in cases where unit cells and space groups only are being determined.

Amongst the substances which would seem to deserve the attention of the crystallographers a certain class contains molecules which in the gaseous state may exist in *two* relatively stable forms with the same energy, one form being the mirror image of the other. If we assume that the mutual conversion of the two forms do not imply a breaking of chemical bonds and that the activation energy of the process is sufficiently small, the substance will of course always correspond to a "racemic mixture" as long as we are concerned with vapours, liquids or solutions. Examples are provided by amines of the type  $N{\diagup H \atop {-R_1 \atop \diagdown R_2}}$ and certain *cyclo*hexane derivatives[2]. When such substances crystallize we will in general expect the crystals to be of the common "racemic compound" type in which an equal number of *d* and *l* molecules are present. It has been pointed out[2], however, that cases will probably also be found in which substances of the kind just described will yield enantiomorphous crystals, some containing *d* molecules only, others *l* molecules. In order to make such a mixture of crystals thermodynamically more stable than a corresponding "racemic" system, special conditions regarding the lattice energy of the two types of crystals must of course be fulfilled.

In certain cases even molecules considered to be individually "symmetric" (the symmetry corresponding for example to a symmetry plane) may yield enantiomorphous crystals containing either *d* or *l* molecules: According to X-ray analysis β-phloroglucitol crystallizes in the space group $P2_12_12_1$ with four molecules in the unit cell. It seems obvious that the compound must be the *trans* ($\varkappa\varepsilon\varkappa \rightleftharpoons \varepsilon\varkappa\varepsilon$) form of 1,3,5-*cyclo*-hexanetriol[3]. The free rotation about the C—O bonds and the almost self-evident presence of hydrogen bonds in these crystals makes it very probable that the individual molecules are asymmetric in the lattice. If this is so, it follows that only one form (*d* or *l*) is present in one single crystal.

From a chemical point of view it does not appear justified to use expressions like "racemic compounds" or even "racemic crystal" in cases where it would not be possible — at least in principle — to separate *d* and *l* molecules in the liquid or gaseous state (*e. g.* 1,2-*cyclo*hexanediol $\varkappa\varepsilon \rightleftharpoons \varepsilon\varkappa$). Another view expressed by some crystallographers which cannot be accepted by chemists is that *d* and *l* molecules in crystals of true racemic compounds are necessarily related by certain elements of symmetry. We may for instance refer to the crystals of the inactive phenylglyceric acid of m. p. 122° described later on in this paper in which the *d* and *l* molecules are crystallographically independent and probably not true mirror images.

Phenylglyceric acid $C_6H_5CHOH\ CHOH\ COOH$ occurs in two stereoisomeric forms, each of which may be resolved into its two optically active components, and these isomers would appear to provide an interesting object for crystallographic research. Macroscopic examinations have been carried out by Goldschmidt[4] and by Berner[5]. Thanks to the kindness of professor Berner who placed crystals at our disposal we have been able to carry out X-ray examinations of both the inactive and active forms of these two substances.

β-PHENYLGLYCERIC ACID OF M. P. 141°

According to the literature the resolution of the inactive acid has been very difficult to accomplish, but finally Riiber[6] succeeded in resolving it into optical antipodes of m. p. 164°. Goldschmidt[4] carried out a careful crystallographic examination of both the active and the inactive crystals, and was able to prove that the inactive compound of m. p. 141° was no true racemate, but consisted of thin submicroscopic lamellae of alternating *d* and *l* crystals, with (100) as a twin plane.

We have confirmed this conclusion by X-ray examinations of the active and the inactive crystals. In both cases identical cell dimensions were found, namely $a = 12.49$ A, $b = 5.70$ A, $c = 5.90$ A, and $\beta = 94°$. The space group is $P2_1$, and there are two molecules in the unit cell. Weissenberg photographs about the b-axis recording the $h0l$-reflexions show very clearly the relationship between the active and the inactive crystals, the latter giving a diagram which corresponds in all respects to that of a twin crystal of the former, with (100) as a twin plane. Equivalent reflexions from *d* and *l* lamellae have the same intensity, as was to be anticipated.

The original inactive preparation offered us by professor Berner was expected to have a melting point of 141°. As, however, a crystal fragment gave a Weissenberg photograph corresponding to an untwinned crystal, the melting point of the fragment was tested and found to be 164°. In another experiment submicroscopically twinned crystals of m. p. 141° were obtained by rather rapid recrystallisation from water. Professor Berner, who was informed about these results, then performed a very slow crystallisation from water which yielded large single crystals, having dimensions some times as great as 10 × 10 × 3 mm, and which proved to be pure active *d* and *l* crystals of m. p. 164°. The resolution of the inactive acid may thus be performed simply by very slow recrystallisation from water.

The occurence of twinning of the type described above seems to be more frequent than generally expected, and may in certain cases, *e. g.* for orthorhombic crystals belonging to the class 222, escape the attention of the crystallographer.

β-PHENYLGLYCERIC ACID OF M. P. 122°

Berner[5] examined the crystals of the inactive acid, and found that they were monoclinic sphenoidal. We have determined the lattice constants to be as follows: $a = 15.35$ A, $b = 5.81$ A, $c = 10.07$ A and $\beta = 101.5°$. The unit cell contains four molecules. The only systematic absences occur in the $0k0$-reflexions for odd values of k. Using X-ray data only, the space group may be either $P2_1$ or $P2_1/m$, but Berners crystal class determination excludes the latter possibility. The two right-hand molecules in the unit cell are thus crystallographically equivalent, and the same holds for the left-hand molecules. However, the *d* and *l* molecules are crystallographically independent, as mentioned above, and it appears very probable that the configuration of say the *d* molecule is different from the mirror image of the *l* molecule — taking the many "movable" links in the molecule into consideration. A complete crystal structure determination will certainly be extremely difficult.

The *active* forms of this acid have been isolated by Berner and Riiber[7]. We have carried out X-ray measurements of the crystals, and found them to be orthorhombic with the lattice constants $a = 13.58$ A, $b = 5.35$ A and $c = 23.65$ A. The unit cell contains eight molecules, and the space group is $P2_12_12_1$. Two crystallographically inequivalent groups of molecules are present, and it seems reasonable to assume that molecules of one group differ in shape from those of the other.

In his publication Berner[5] favours the view that the crystals are monoclinic with a β angle of 90° 40′. However, the diffraction symmetry and the systematic absences characteristic of the space group $P2_12_12_1$ makes it seem far more probable that the crystals are in fact orthorhombic.

SUMMARY

The geometrical arrangement of non-rigid molecules in crystals has been discussed, special reference being made to the different stereoisomers of β-phenylglyceric acid. For these substances new experimental material has been collected.

We wish to express our sincere gratitude to professor Berner both for his kindness in placing the interesting material at our disposal and for his interest in our experimental work. One of us (S. F.) is indebted to *Norges Teknisk Naturvitenskapelige Forskningsråd* for a grant.

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Received July 6, 1950.