Acta Cryst. (1951). **4**, 283

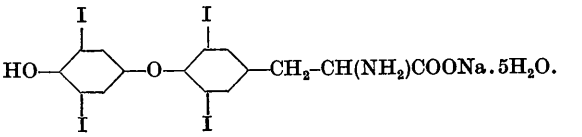
On the crystal structure of thyroxine.

By N. JOEL* and F. G. CANEPA,† *Birkbeck College Research Laboratory, 21 Torrington Square, London W.C. 1, England*

(*Received* 31 *January* 1951)

The presence of four iodine atoms in the molecule of thyroxine directed our attention to the problem of determining its crystal structure.

Samples of thyroxine and sodium thyroxine were kindly supplied by Dr A. B. Hems of Glaxo Laboratories, Greenford, Middlesex. As the DL-sodium salt was found to crystallize more readily and to form better crystals, it was decided to start work on that compound. Its chemical formula is



The crystals are triclinic, flat and very thin (0·03 mm. or less) in habit. The most developed face is (100); other faces less frequently present are (011) and (01$\bar{1}$). In general, the contour of the flat crystals is quite irregular. They are colourless, but after a very prolonged over-exposure to X-rays they acquire a brown colour, suggesting the breakdown of the molecule with formation of molecular iodine.

X-ray diffraction photographs (Cu $K\alpha_1 = 1{\cdot}5405$ A.) gave:

$$a = 15{\cdot}81 \pm 0{\cdot}02, \quad b = 9{\cdot}53 \pm 0{\cdot}01, \quad c = 8{\cdot}33 \pm 0{\cdot}01 \text{ A.},$$
$$\alpha = 94{\cdot}8 \pm 0{\cdot}1°, \quad \beta = 84{\cdot}1 \pm 0{\cdot}1°, \quad \gamma = 95{\cdot}5 \pm 0{\cdot}1°.$$

Corrections have been made for deformation of the film during processing and washing.

Optical measurements were made, during the course of which a quick method was developed for determining the indicatrix of uniaxial and highly birefringent biaxial crystals and for referring it to the unit cell (Joel, 1950, 1951).

The refractive indices are

$$\alpha = 1{\cdot}65, \quad \beta = 1{\cdot}69, \quad \gamma = 1{\cdot}79,$$

with $2V = 67°$. The crystal is strongly positive, and the Z axis of its indicatrix is nearly parallel to the plane $23\bar{2}$ (Fig. 1). This was found by X-ray diffraction photographs of the sample studied optically.

The specific gravity of the crystals at room temperature was found to be $2{\cdot}381 \pm 0{\cdot}002$, referred to water at 4° C., whence: (i) $z = 2$, and (ii) the number of molecules of water per molecule of sodium thyroxine is $4{\cdot}9 \pm 0{\cdot}2$, i.e. 5.

The substance being a DL-compound, the unit cell is most likely to contain a centre of symmetry. Pyro- and piezo-electricity tests were carried out and gave a negative result, which, without being a proof, at least does not rule out the presence of a centre of symmetry. The space group is, hence, $P\bar{1}$.

Stereochemical considerations would suggest that the planes of the two benzene rings are nearly perpendicular to each other, but no further assumption is made.

Weissenberg photographs about the b and c axes were taken; about 110 and 130 reflexions respectively were recorded on the two zero layers (the highest value of ξ was about 1·5). From the c-axis Patterson projection (Fig. 2) the x and y co-ordinates of the eight iodine atoms in the unit cell have been determined. These are:

	I_1	I_2	I_3	I_4
$x=$	0·00	0·16	0·47	0·16
$y=$	0·24	0·10	0·42	0·68

and the four centro-symmetric ones. There are plausible values for the z co-ordinates of these atoms, but they still need confirmation.

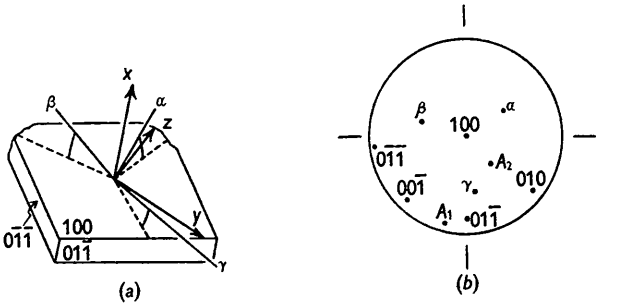


Fig. 1. (*a*) The axes of the indicatrix (α, β, γ) and of the unit cell (x, y, z) in a crystal of DL-sodium thyroxine. (*b*) Stereographic projection on the (100) face. α, β and γ represent the axes of the indicatrix; A_1 and A_2 are the directions of the optic axes.

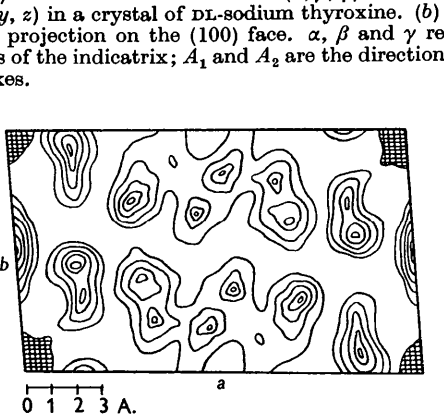


Fig. 2. The Patterson projection of DL-sodium thyroxine along the c axis drawn on (001).

At this stage, work on the structure determination has been momentarily interrupted owing to the authors' return to Chile, but will be continued there as soon as possible.

We are highly indebted to Prof. J. D. Bernal and Dr C. H. Carlisle for supervising our work.

References

JOEL, N. (1950). *Miner. Mag.* **29**, 206.
JOEL, N. (1951). *Miner. Mag.* (To appear in June.)

* Now at Instituto Pedagógico, Universidad de Chile, Casilla 147, Santiago, Chile.
† Now at Escuela de Ingeniería Química, Universidad de Concepción, Casilla 783, Concepción, Chile.