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Structure of the Thyroid Hormone Metabolite 3-Iodo-L-thyronine Hydrochloride Dihydrate, $C_{15}H_{15}INO_4^+.Cl^-.2H_2O$

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Abstract. $M_r = 471{\cdot}7$, monoclinic, $P2_1$, $a = 10{\cdot}296$ (5), $b = 11{\cdot}883$ (4), $c = 14{\cdot}869$ (5) Å, $\beta = 91{\cdot}20$ (4)°, $V = 1818{\cdot}8$ (12) Å^3, $Z = 4$, $D_m = 1{\cdot}67$, $D_x = 1{\cdot}722$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 15{\cdot}7$ mm^{-1}, $F(000) = 936$, $T = 293$ K, final $R = 0{\cdot}098$ for 1267 reflections. Two conformers, (I) and (II), are present in an asymmetric unit. Both conformers show overall *transoid* conformations, but their 3-iodo atoms are located on opposite sides. There is a hydrogen-bonding network involving the 3-iodo-L-thyronine molecules, water molecules and Cl^- ions.

Introduction. The molecular conformations of about twenty thyroid hormones and their analogues are characterized by a skewed or a twist-skewed diphenyl ether conformation (Cody, 1980). These conformations have been considered an important requirement for thyromimetic activity. To further structural understanding of the hormone action and its metabolism, the thyroid hormone metabolite 3-iodo-L-thyronine has been synthesized and its crystal structure determined.

Experimental. 3-Iodo-L-thyronine ($3\text{-}T_1$) was synthesized from 3,5-diiodo-L-thyronine ($3,5\text{-}T_2$) by modifying the photodeiodination method (Sorimachi & Ui, 1975) and was crystallized from 0·1 *M* HCl–ethanol (1:1) as $3\text{-}T_1.HCl.2H_2O$. Crystal 0·10 × 0·15 × 0·20 mm. D_m by flotation in benzene/ethylene dibromide. Rigaku AFC-5 automated four-circle diffractometer, graphite monochromator, Cu $K\alpha$ radiation. Cell dimensions by least-squares methods from 2θ values of 19 reflections with $12 < 2\theta < 30°$. Intensity data: $2\theta \leq 125°$, h −11 to 11, k 0 to 13, l 0 to 7, $2\theta/\omega$ scan, scan speed 2° min^{-1}, scan width ($\Delta\omega$) $(1{\cdot}2 + 0{\cdot}15\tan\theta)°$ at 40 kV and 30 mA. Three standard reflections every 50 reflections, variation <4%. Accuracy of measurement was low owing to poor crystallinity: half-value width of the reflection curve 0·16° (no peak splitting). 3060 independent reflections measured. Of 1066 in the range $100° < 2\theta \leq 125°$ only 141 had $|F_o| > 3\sigma(|F_o|)$. Total of 1267 intensities with $|F_o| > 3\sigma(|F_o|)$ used for structure determination. Corrections for Lorentz and polarization factors, and for absorption (max. and min. values of transmission factor 0·2710 and 0·1897 respectively). Structure solved by Patterson and Fourier methods, refined by block-diagonal least squares with anisotropic thermal parameters and anomalous-dispersion corrections for I and Cl atoms. H positions calculated and included in the refinement. $\sum w(|F_o| - |F_c|)^2$ minimized, $w = 0{\cdot}0$ for $F_o = 0$ and $w = 1{\cdot}0$ for $F_o \neq 0$. Final $R = 0{\cdot}098$, $R_w = 0{\cdot}109$, $S = 7{\cdot}09$. $(\Delta/\sigma)_{\text{ave}} = 0{\cdot}15$, $(\Delta/\sigma)_{\max} = 0{\cdot}32$. Final $\Delta\rho$ excursions −1·46 to 1·46 e Å^{-3}. No correction for secondary extinction. Atomic scattering factors and anomalous-dispersion coefficients from *International Tables for X-ray Crystallography* (1974). Programs *MFPA* (Yasuoka & Tanaka, 1979), *SFFR* and *HBLSV* (Ashida, 1979), *MOLCON* (Fujii, 1979), *ACACA* (Wuensch & Prewitt, 1965) and *ORTEP* (Johnson, 1976). All numerical calculations performed at the Crystallographic Research Center, Institute for Protein Research, Osaka University.

Discussion. The final positional and isotropic thermal parameters are given in Table 1.* The bond lengths and angles of the conformers are given in Fig. 1. Perspective views of the conformers are shown in Fig. 2. The overall conformations of the conformers (I) and (II) are described as *transoid* in which the alanine moiety and the outer ring lie on the opposite sides of the inner-ring plane. As shown in the stereoscopic views of the conformers (Fig. 2), the significant conformational difference between these conformers involves the positions of the 3-iodo atoms, which are located on opposite sides. The diphenyl ether conformations characterized by the torsion angles

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* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39502 (8 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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φ[C(5)—C(4)—O(4)—C(1′)] and φ'[C(4)—O(4)—C(1′)—C(6′)] are 50 and 54° for conformer (I) and −63 and −33° for conformer (II), respectively. These conformations are nearly midway between a skewed conformation ($\varphi = 90°/\varphi' = 0°$) and an anti-skewed one ($\varphi = 0°/\varphi' = 90°$). The outer phenyl ring of the conformers swings largely about the C(4)—O(4) axis as compared with the thyroid hormone analogues, in which the swing motion of the outer ring is restricted by the substituents (I or Br atoms at both 3 and 5 positions). The direction of the swing of the outer ring of the conformers is opposite to the side with the I atom at the 3 position. This is similar to 3,3′,5′-triiodo-L-thyronine (r-T_3) (Okabe, Fujiwara, Yamagata & Tomita, 1982), in which the outer ring is located exactly opposite to the side with the I atom at position 3, in an anti-skewed conformation ($\varphi = 8°/\varphi' = 86°$ or $\varphi =$

Table 1. *Final atomic parameters with e.s.d.'s in parentheses and isotropic temperature factors*

For Cl and I atoms $B_{\rm eq} = \frac{4}{3}\sum_i\sum_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	$B_{\rm eq}$ or $B_{\rm iso}$(Å^2)
Conformer (I)				
I(3)	0·8699 (4)	0·7495	0·6466 (3)	4·0 (1)
C(1)	0·846 (5)	0·395 (4)	0·718 (3)	2·2 (10)
C(2)	0·832 (4)	0·518 (4)	0·706 (3)	1·8 (9)
C(3)	0·901 (4)	0·573 (4)	0·657 (3)	2·1 (9)
C(4)	0·972 (4)	0·525 (4)	0·595 (3)	1·7 (9)
C(5)	0·989 (5)	0·405 (5)	0·594 (4)	3·6 (12)
C(6)	0·932 (5)	0·343 (4)	0·663 (4)	2·9 (11)
C(7)	0·765 (5)	0·331 (4)	0·774 (4)	2·8 (10)
C(8)	0·756 (5)	0·367 (4)	0·874 (4)	3·1 (11)
C(9)	0·668 (5)	0·291 (4)	0·928 (3)	2·6 (10)
C(1′)	1·072 (4)	0·563 (4)	0·452 (3)	2·3 (10)
C(2′)	1·193 (5)	0·559 (4)	0·413 (4)	3·2 (11)
C(3′)	1·199 (5)	0·542 (5)	0·322 (4)	3·5 (12)
C(4′)	1·085 (5)	0·539 (5)	0·267 (4)	3·4 (12)
C(5′)	0·963 (5)	0·551 (4)	0·314 (3)	2·5 (10)
C(6′)	0·955 (5)	0·549 (4)	0·398 (3)	2·7 (10)
O(4)	1·055 (3)	0·595 (3)	0·549 (2)	3·1 (7)
O(4′)	1·083 (4)	0·523 (3)	0·176 (3)	5·0 (9)
O(9)	0·540 (4)	0·298 (3)	0·904 (3)	4·6 (9)
O(10)	0·700 (3)	0·216 (3)	0·981 (2)	4·0 (8)
N(8)	0·884 (5)	0·365 (4)	0·921 (3)	4·8 (12)
Conformer (II)				
I(3)	0·5672 (4)	0·6254 (4)	0·3556 (3)	4·7 (1)
C(1)	0·679 (4)	0·968 (4)	0·303 (3)	1·8 (9)
C(2)	0·676 (5)	0·851 (4)	0·300 (4)	3·2 (11)
C(3)	0·566 (5)	0·798 (4)	0·355 (3)	2·1 (9)
C(4)	0·482 (4)	0·869 (4)	0·387 (3)	2·0 (9)
C(5)	0·490 (4)	0·982 (4)	0·388 (3)	2·1 (9)
C(6)	0·593 (4)	1·032 (4)	0·347 (3)	2·4 (10)
C(7)	0·790 (5)	1·027 (4)	0·252 (3)	2·4 (10)
C(8)	0·753 (4)	1·062 (4)	0·153 (3)	2·2 (9)
C(9)	0·882 (4)	1·105 (4)	0·118 (3)	2·0 (9)
C(1′)	0·381 (4)	0·828 (3)	0·538 (3)	1·3 (8)
C(2′)	0·261 (4)	0·818 (4)	0·574 (3)	2·1 (9)
C(3′)	0·256 (4)	0·819 (4)	0·654 (3)	1·6 (9)
C(4′)	0·383 (4)	0·842 (3)	0·716 (3)	1·4 (8)
C(5′)	0·492 (5)	0·849 (4)	0·676 (4)	2·8 (11)
C(6′)	0·501 (5)	0·832 (4)	0·580 (3)	2·2 (9)
O(4)	0·385 (3)	0·819 (3)	0·440 (2)	3·3 (7)
O(4′)	0·372 (4)	0·838 (3)	0·811 (3)	3·9 (8)
O(9)	0·942 (4)	1·051 (3)	0·062 (3)	4·0 (8)
O(10)	0·925 (3)	1·198 (3)	0·142 (2)	3·3 (7)
N(8)	0·698 (4)	0·976 (4)	0·100 (3)	3·7 (10)
Cl(1)	0·6318 (19)	0·9357 (21)	0·8903 (10)	6·9 (7)
Cl(2)	0·8528 (15)	0·7428 (16)	0·1168 (11)	5·7 (5)
O(*W*1)	0·842 (4)	0·733 (4)	0·908 (3)	5·2 (9)
O(*W*2)	0·591 (4)	0·605 (4)	0·060 (3)	6·1 (10)
O(*W*3)	0·567 (4)	0·597 (3)	0·867 (3)	5·0 (9)
O(*W*4)	0·839 (4)	0·450 (3)	0·081 (2)	4·0 (8)

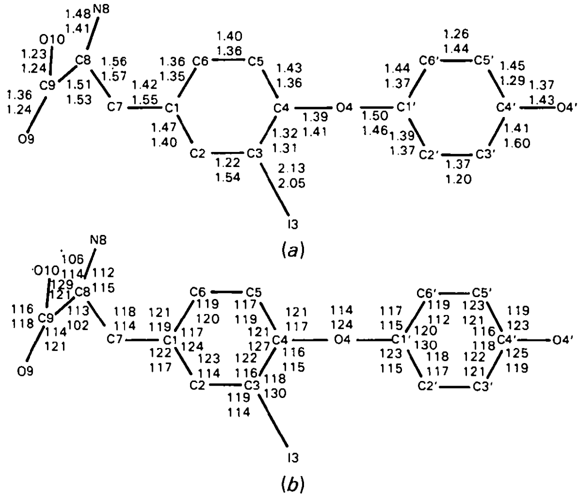

Fig. 1. (*a*) Bond lengths (Å) and (*b*) bond angles (°) in conformer (I) (upper numbers) and conformer (II) (lower numbers). The e.s.d.'s are 0·07 Å for bond lengths and 4·17° for bond angles.

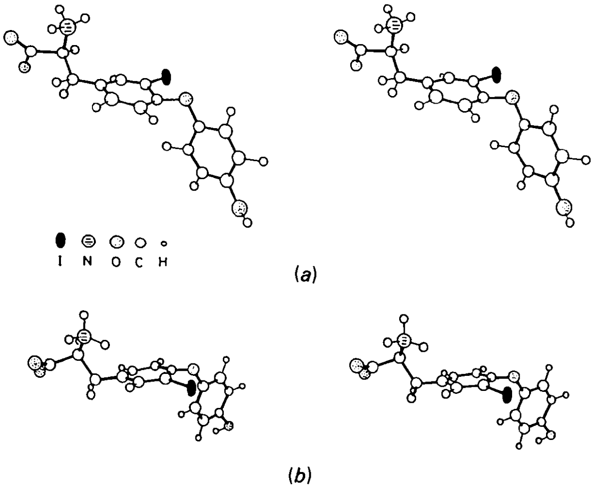

Fig. 2. Stereoscopic view of (*a*) conformer (I) and (*b*) conformer (II).

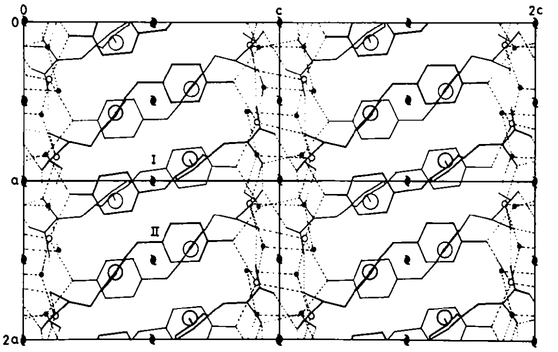

Fig. 3. Packing of the molecules viewed down the *b* axis. The dark molecules are above the light ones. The large and small open circles indicate the I atom and the Cl⁻ ion, respectively. The filled circle indicates the water molecule.

$-6^\circ/\varphi' = 87^\circ$). The outer-ring orientation of both 3-T_1 and *r*-T_3 is different from that of the intramolecular charge-transfer complex model (Lehmann, 1972), in which the outer-ring plane interacts with the I atom on the inner ring. The φ and φ' values of the thyroinactive 3-T_1 and *r*-T_3 as well as L-thyronine (T_0) ($\varphi = -37^\circ/\varphi' = -67^\circ$) (Camerman & Camerman, 1974) are clearly different from those of the thyroactive compounds of the skewed or the twist-skewed conformation (near $\varphi = 108^\circ/\varphi' = -28^\circ$ or $\varphi = -108^\circ/\varphi' = 28^\circ$) (Cody, 1980). This result may reinforce the existence of a permissible region of φ and φ' angles for protein-binding ability to produce effective thyromimetic activity. The alanine side-chain conformation is described by torsion angles χ^1[C(1)—C(7)—C(8)—N(8)], χ^2[C(2)—C(1)—C(7)—C(8)] and ψ[N(8)—C(8)—C(9)—O(10)]. χ^1, χ^2 and ψ values of the 3-T_1 conformers are −59, −55 and −21° for conformer (I) and −51, 94 and 161° for conformer (II). There are no characteristics in the alanine side-chain conformations indicative of thyroactive or inactive compounds. The intermolecular interactions are indicated in the crystal packing shown in Fig. 3, in which the molecular arrangement is projected along the *b* axis. The 3-T_1 molecule is joined to neighboring molecules by the hydrogen-bond network involving carboxyl, amino and phenolic groups of 3-T_1, water molecules and Cl^- ions.

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Structure of the 2,4-Dinitrophenylhydrazine Adduct of Pyrroloquinolinequinone (PQQ) Dimethyl Ethyl Triester,* $C_{24}H_{18}N_6O_{11}$

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Abstract. $M_r = 566{\cdot}44$, triclinic, $P\bar{1}$, $a = 11{\cdot}018$ (3), $b = 15{\cdot}451$ (3), $c = 7{\cdot}507$ (2), $\alpha = 92{\cdot}68$ (3), $\beta = 104{\cdot}69$ (3), $\gamma = 86{\cdot}83$ (3)°, $V = 1233{\cdot}6$ (10) Å^3, $Z = 2$, $D_x = 1{\cdot}530$ Mg m^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å, $\mu = 0{\cdot}15$ mm^{-1}, $F(000) = 584$, $T = 293$ K, final $R = 0{\cdot}053$ for 2238 observed data. The keto atom at C(5) in PQQ triester is substituted by dinitrophenylhydrazine *via* a hydrazone bond. The fused-ring system of PQQ is coplanar with the phenylhydrazine moiety of the molecule because of an intramolecular bifurcated hydrogen bond. The structure analysis proves that the enzyme plasma amine oxidase contains a prosthetic group in which the basic structure of PQQ is retained.

Introduction. Compound (I), 4,5-dioxo-1*H*-pyrrolo[2,3-*f*]quinoline-2,7,9-tricarboxylic acid is known in the biochemical literature as pyrroloquinolinequinone (abbreviated to PQQ) (Duine, Frank & Verwiel, 1980) and

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* IUPAC name: 2-ethyl 7,9-dimethyl 4,5-dihydro-5-(2,4-dinitrophenylhydrazono)-4-oxo-1*H*-pyrrolo[2,3-*f*]quinoline-2,7,9-tricarboxylate.

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