Table 4. *Torsion angles* (°) (*average e.s.d.* 2°)

(i) Ring *C*	
C(8)–C(10)–C(11)–N(12)	−38
C(10)–C(11)–N(12)–C(19)	66
C(11)–N(12)–C(19)–C(9)	−57
N(12)–C(19)–C(9)–C(8)	29
C(19)–C(9)–C(8)–C(10)	−2
C(9)–C(8)–C(10)–C(11)	6
(ii) Ring *D*	
N(1)–C(9)–C(19)–C(16)	−30
C(9)–C(19)–C(16)–C(17)	56
C(19)–C(16)–C(17)–C(18)	−65
C(16)–C(17)–C(18)–N(1)	42
C(17)–C(18)–N(1)–C(9)	−10
C(18)–N(1)–C(9)–C(19)	4
(iii) Ring *E*	
N(12)–C(13)–C(14)–C(15)	−59
C(13)–C(14)–C(15)–C(16)	59
C(14)–C(15)–C(16)–C(19)	−53
C(15)–C(16)–C(19)–N(12)	49
C(16)–C(19)–N(12)–C(13)	−51
C(19)–N(12)–C(13)–C(14)	53
(iv) Extra-annular	
C(19)–C(16)–C(20)–C(21)	−171
C(2)–N(1)–C(18)–O(22)	−51
C(2)–N(1)–C(18)–C(23)	70
O(22)–C(18)–C(23)–O(25)	−12
O(22)–C(18)–C(23)–O(24)	173
C(18)–C(23)–O(25)–C(26)	−177
O(24)–C(23)–O(25)–C(26)	−3
(v) Connecting rings *C* and *D*	
C(8)–C(9)–C(19)–C(16)	149
N(1)–C(9)–C(19)–N(12)	−150
(vi) Connecting rings *C* and *E*	
C(9)–C(19)–N(12)–C(13)	70
C(16)–C(19)–N(12)–C(11)	−178
(vii) Connecting rings *D* and *E*	
C(15)–C(16)–C(19)–C(9)	−68
C(17)–C(16)–C(19)–N(12)	173
(viii) α-Oxoglutaric anion	
O(34)–C(27)–C(28)–O(36)	17
O(34)–C(27)–C(28)–C(29)	−163
O(35)–C(27)–C(28)–C(29)	18
C(27)–C(28)–C(29)–C(30)	137
C(28)–C(29)–C(30)–C(31)	−54
C(29)–C(30)–C(31)–O(32)	−4
C(29)–C(30)–C(31)–O(33)	170

Table 5. *Hydrogen-bond geometry*

D = donor, *A* = acceptor.

D–H···*A*	*D*···*A*	*D*–H	H···*A*	∠*DHA*
O(22)H···O(35)	2·67 Å	1·3 Å	1·7 Å	129°
O(33)H···O(34)	2·50	1·0	1·6	143
N(12)H···O(34)	2·73	1·1	1·7	170

would permit a bifurcated H bond between O(22) and O(35), O(25). The other two H bonds present in the oxovinca structure, N(12)H···O(34) and O(33)H···O(34), are detailed in Table 5. The α-oxoglutaric anions link different vincamine cations through H bonds, forming continuous helical chains parallel to **c**. Different chains are also connected through the H bonds between the α-oxoglutaric anions. Fig. 2 shows the packing schematically.

Any structural difference between oxovinca and vincamine could influence the non-hydrolysis of the former. It seems, however, that the proximity of the ester O atom to the hydroxy group, with the possibility of linking by a H bond, could protect the ester O(25) from hydrolysis. Oxovinca from water solution, however, has the methyl ester radical in both positions: with O(25) near O(22) and O(24) near O(22). So the solvent could influence the hydrolysis of the drug.

We thank Professor S. García-Blanco for his support, the JEN of Madrid for the facilities provided on the Univac 1100/80 computer, and ELMU Pharmaceutical Laboratoires of Madrid for supplying the crystals.

References

MAIN, P., WOOLFSON, M. M., LESSINGER, L., GERMAIN, G. & DECLERCQ, J. P. (1977). *MULTAN 77. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.

MONTORO, F., VILAR, A., CALATAYUD, J., DE LA FUENTE, R. & VILA CORO, A. (1978). *International Symposium on Brain Circulation*, Madrid, pp. 166–172. *Excerpta Med.* Spec. Publ.

STEWART, J. M., KUNDELL, F. A. & BALDWIN, J. C. (1970). The XRAY 70 system. Computer Science Center, Univ. of Maryland, College Park, Maryland.

WEBER, H. P. & PETCHER, T. J. (1973). *J. Chem. Soc. Perkin Trans.* 2, pp. 2001–2006.

Acta Cryst. (1981). B**37**, 763–765

4-(α-Hydroxy-4-methoxybenzyl)-3,5-diiodobenzyl Alcohol

BY VIVIAN CODY

Medical Foundation of Buffalo, Inc., 73 High Street, Buffalo, NY 14203, USA

(*Received* 6 *May* 1980; *accepted* 10 *November* 1980)

Abstract. $C_{15}H_{14}I_2O_3$, triclinic, $P\bar{1}$, $a = 9{\cdot}507$ (3), $b = 9{\cdot}735$ (4), $c = 9{\cdot}383$ (2) Å, $\alpha = 99{\cdot}06$ (2), $\beta = 111{\cdot}56$ (3), $\gamma = 84{\cdot}28$ (2)°, $Z = 2$, $M_r = 482{\cdot}06$, $D_c = 2{\cdot}00$ Mg m^{-3}; for 4204 observed data $R = 8{\cdot}2\%$. The conformation of the two phenyl rings is twist-skewed, and the bridging C–C–C angle is 114°.

Introduction. An important feature of the thyroid hormone structure (Fig. 1*a*) is the O bridge linking the two iodophenyl rings. The thyroid hormones are characterized by a bridging angle of 120° and a diphenyl ether conformation which is either skewed (mutually perpendicular and bisecting) or twist-skewed

0567-7408/81/030763-03$01.00

(Cody, Hazel, Langs & Duax, 1977). Originally the bridging O had been thought to act as a quinoid structure permitting electron transfer between rings. However, the observed potency and protein-binding affinity of S- and methylene-bridged analogues disputes this concept and suggests that the role of the bridging atom is to provide the proper stereochemical relationship between the iodophenyl rings. Thus far no methylene- or S-bridged thyroid hormones have been crystallized. In order to determine the effects of O-bridge substitution on thyroid hormone conformation, the crystal structure determinations of several 3,5-diiododiphenyl bridged (C–*X*–C, *X* = C,N) analogues have been carried out (Cody & Mukherjee, 1975; Cody & Hazel, 1976; Cody, Jorgensen & Cheung, 1979). Here is reported the crystal structure of a 3,5-diiododiphenyl C-bridge alcohol (Fig. 1*b*).

Crystals were grown by slow evaporation at room temperature from a solution of ethyl acetate and hexane from a sample provided by Dr Tripp of Ciba-Geigy Corporation. Crystallographic data were measured from a 0·2 × 0·42 × 0·84 mm crystal on a Syntex *P*3 automated diffractometer using Nb-filtered Mo $K\alpha$ radiation. Cell dimensions were obtained by a least-squares refinement based on the 2θ values of 25 reflections with $2\theta > 25°$ using Mo $K\alpha$ radiation. The intensities of 4653 reflections (4204 with $I > 2\sigma$) were measured in the θ–2θ scan mode using a variable scan width to allow for $\alpha_1\alpha_2$ dispersion and a variable scan time to obtain counting errors in the range $0{\cdot}01 \leq \sigma(I)/I \leq 0{\cdot}03$. No significant changes were observed in the intensities of the standard reflections measured after every 94th reflection during data collection. Intensities were corrected for Lorentz and polarization factors and an extinction correction ($g/y = 0{\cdot}199 \times 10^{-4}$) was applied at a later stage, but no absorption correction was made. The structure was solved by heavy-atom techniques.

The positional and anisotropic thermal parameters for all non-hydrogen atoms were refined using full-matrix least-squares procedures on all data. Calculated H positions were included in the structure factor calculations but were not refined. The weights used were the quantities $(1/\sigma_F^2)$ were σ_F is defined by Stout & Jensen (1968), and the instability correction was 0·06.

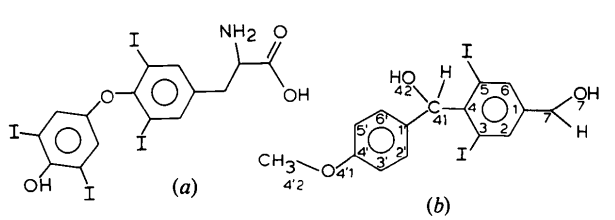


Fig. 1. (*a*) 3,5,3′,5′-Tetraiodo-L-thyronine. (*b*) The title compound with the numbering scheme.

Table 1. *Fractional coordinates* (×10⁴) *and equivalent isotropic thermal parameters, with e.s.d.'s in parentheses*

	x	*y*	*z*	B_{eq} (Å²)*
C(1)	7844 (6)	1506 (5)	153 (6)	358 (10)
C(2)	8092 (6)	1051 (5)	−1224 (5)	362 (10)
C(3)	7964 (5)	−330 (5)	−1840 (5)	338 (9)
C(4)	7566 (5)	−1332 (4)	−1160 (4)	314 (9)
C(5)	7292 (5)	−838 (4)	204 (5)	312 (9)
C(6)	7438 (6)	537 (5)	849 (6)	372 (10)
C(41)	7461 (5)	−2859 (4)	−1853 (6)	359 (10)
C(1′)	5843 (5)	−3317 (4)	−2661 (5)	338 (10)
C(2′)	5502 (6)	−4711 (5)	−2781 (6)	361 (10)
C(3′)	4067 (6)	−5160 (4)	−3653 (6)	365 (10)
C(4′)	2940 (5)	−4234 (5)	−4478 (5)	363 (10)
C(5′)	3263 (6)	−2860 (5)	−4368 (6)	384 (11)
C(6′)	4703 (6)	−2400 (4)	−3447 (6)	371 (11)
O(4′1)	1602 (5)	−4831 (4)	−5377 (5)	481 (11)
C(4′2)	463 (7)	−3911 (7)	−6328 (8)	560 (16)
O(42)	8366 (5)	−3728 (4)	−756 (6)	511 (11)
I(3)	8285 (1)	−832 (1)	−3976 (1)	583 (1)
I(5)	6613 (1)	−2135 (1)	1397 (1)	473 (1)
O(7)	8637 (5)	3783 (4)	168 (6)	525 (12)
C(7)	7920 (7)	2995 (5)	860 (7)	464 (13)

* $B_{eq} = \frac{4}{3}\sum_i \sum_j B_{ij}(\mathbf{a}_i.\mathbf{a}_j)$; taken from Hamilton [1959, equation (18)].

This value increases σ_F for reflections with a large $|F|$ and prevents them from controlling the refinement. The *R* index, $\sum||F_o| - |F_c||/\sum|F_o|$, was 8·2% with 4204 data. The function minimized in the least-squares refinement was $\sum w(|F_o| - |F_c|)^2$. The Fourier and least-squares programs are part of the Nonius crystallographic package for the PDP 11/45 computer. Scattering factors are from *International Tables for X-ray Crystallography* (1974). The final refined positional and isotropic thermal parameters are given in Table 1.*

Discussion. The molecular conformation and geometry of the title compound are illustrated in Figs. 1(*b*) and 2.

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35804 (24 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

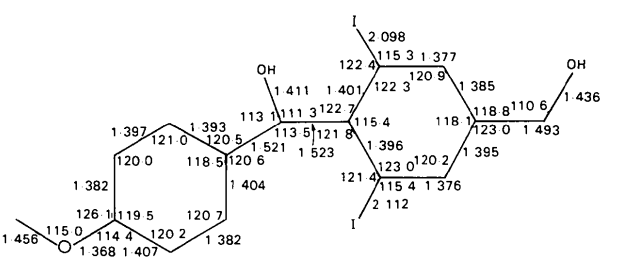
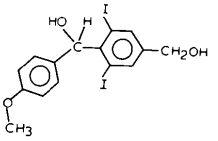
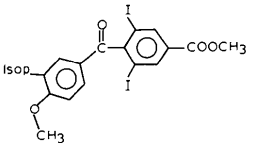
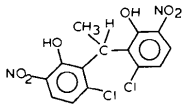
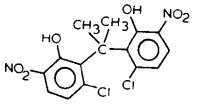
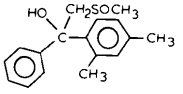
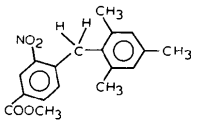
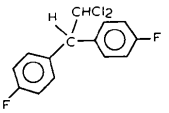


Fig. 2. Bond lengths (Å) and bond angles (°) for the title compound. The e.s.d.'s for bond lengths are 0·007 Å and for angles 0·4°.

Table 2. *Conformations of selected C-bridge diphenyl compounds*

Structure	Bridge angle	Conformation	Reference
	114°	Twist-skewed	This paper
	120	Twist-skewed	Cody, Jorgensen & Cheung (1979)
	113	Twist	Hay & MacKay (1979)
	113	Twist	Hay & MacKay (1979)
	112	Twist-skewed	Tranqui, Richard Vicat & Fillion (1974)
	114	Twist-skewed	van der Heijden, Chandler & Robertson (1975)
	110	Twist	Smith, Kennard & Whitnall (1977)

The two phenyl rings adopt a twist-skewed conformation [C(3)–C(4)–C(41)–C(1′) = −105·3 (5)° and C(4)–C(41)–C(1′)–C(6′) = 34·4 (7)°] as observed in thyroid hormone structures (Cody, Hazel, Langs & Duax, 1977). The 4′-methoxy group is coplanar [2·0 (8)°] with the phenoxy ring, as is the O(7) hydroxyl group [15·4 (8)°] with its ring.

A comparison of this structure with those of other C-bridged diphenyl compounds (Table 2) shows that the bridging angle varies as a function of the bridge-atom substitution – the more fully substituted, the smaller the angle (Gopal, Chandler & Robertson, 1979). Thus the dimethyl derivatives tend toward 112° while the methylene compounds tend toward 117°. This hydroxyl bridge angle is 113·5 (4)°. In addition, there is a wide range in diphenyl conformations with many adopting a twist conformation in which the two

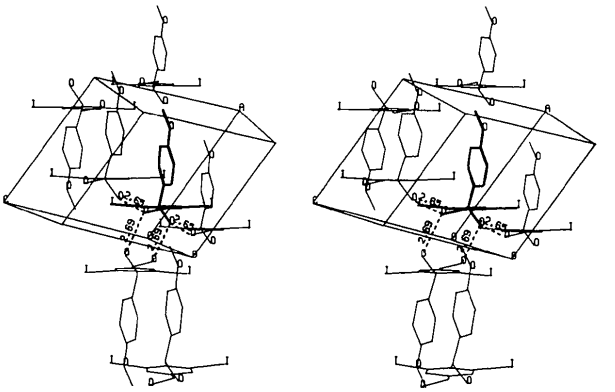


Fig. 3. Stereoview of the crystal packing with hydrogen bonds labelled.

phenyl rings are nearly perpendicular to the plane of the bridging carbons. Thus, as found for the ketone (Cody, Jorgensen & Cheung, 1979), the *ortho* I atoms cause the molecule to adopt the twist-skewed geometry of the thyroid hormones.

There are two hydrogen bonds between the hydroxyl groups [O···O = 2·65 (7), 2·69 (7) Å], forming a layered structure as illustrated in Fig. 3. There are no unusually short I···I or I···O contacts in this structure but there are ring–ring contacts of 3·40 Å (Fig. 3).

The author wishes to thank Dr Tripp of Ciba-Geigy for providing the sample, and Dr R. Blessing, Miss E. DeJarnette and Miss G. Del Bel for able technical assistance. This research was supported in part by Grant No. AM-15051 awarded by the National Institute of Arthritis, Metabolism and Digestive Diseases.

References

CODY, V. & HAZEL, J. P. (1976). *Cryst. Struct. Commun.* **5**, 333–348.

CODY, V., HAZEL, J. P., LANGS, D. A. & DUAX, W. L. (1977). *J. Med. Chem.* **20**, 1628–1631.

CODY, V., JORGENSEN, E. C. & CHEUNG, E. (1979). Am. Crystallogr. Assoc. Meeting. Abstracts, 7(1), p. 23.

CODY, V. & MUKHERJEE, R. (1975). *Acta Cryst.* B**31**, 2168–2170.

GOPAL, R., CHANDLER, W. D. & ROBERTSON, B. E. (1979). *Can. J. Chem.* **57**, 2767–2774.

HAMILTON, W. C. (1959). *Acta Cryst.* **12**, 609–610.

HAY, D. G. & MACKAY, M. F. (1979). *Acta Cryst.* B**35**, 2952–2957.

HEIJDEN, S. P. N. VAN DER, CHANDLER, W. D. & ROBERTSON, B. E. (1975). *Can. J. Chem.* **53**, 2121–2126.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press.

SMITH, G., KENNARD, C. H. L. & WHITNALL, J. (1977). *Cryst. Struct. Commun.* **6**, 131–136.

STOUT, G. H. & JENSEN, L. H. (1968). *X-ray Structure Determination*, p. 457. New York: Macmillan.

TRANQUI, D., RICHARD, P., VICAT, J. & FILLION, H. (1974). *Acta Cryst.* B**30**, 673–679.