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1-Methyl-4′-methoxy-3,5-diiododiphenylamine*

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Abstract. $C_{14}H_{13}ONI_2$, m.p. 125°C, monoclinic, $P2_1/c$, $a=9{\cdot}247$ (3), $b=6{\cdot}292$ (2), $c=25{\cdot}42$ (4) Å, $\beta=94{\cdot}6$ (4)°, $Z=4$, M.W. 464·8, $D_x=2{\cdot}1$, $D_m=2{\cdot}0$ g cm^{-3}, $R=7{\cdot}0$%. The conformation of this molecule is similar to that of numerous thyroid hormones and their analogs. The diphenylamine conformation is defined by the torsional angles ϕ[C(3)–C(4)–N(4)–C(1′)]=89° and ϕ'[C(4)–N(4)–C(1′)–C(6′)]=27°.

Introduction. A 0·08×0·4×0·9 mm crystal was used to measure the lattice parameters and intensities. The data showed systematic absences of $k=2n+1$ for $0k0$, and $l=2n+1$ for $h0l$ indicating the space group $P2_1/c$, and the cell constants were determined by least-squares analysis of the angular settings of 15 reflections [at 20°C; λ(Mo $K\alpha$)=0·7091 Å]. The intensities of 4651 reflections (3384 reflections had $I>2\sigma$) with $2\theta<60°$ were measured on a Nonius CAD-4 automated diffractometer using Mo $K\alpha$ radiation. The linear absorption coefficient $\mu=42{\cdot}7$ cm^{-1}. After the usual Lorentz and polarization corrections had been applied, normalized structure-factor amplitudes were computed, and the structure was solved by application of Patterson and Fourier techniques.

The positional and anisotropic thermal parameters of non-hydrogen atoms located by Fourier difference syntheses were refined by block-diagonal least-squares calculations using all data for which $|F_c|/|F_o|$ was greater than 0·5. The weighting scheme used in the final refinement was $w^{-1}=\sigma(F_o)$, where $\sigma(F_o)$ is defined by Stout & Jensen (1968, equation H.14) and the instability correction was 0·06 rather than 0·01. Refinement was terminated when all shifts were less than $\frac{1}{3}$ of their respective standard deviations. The R index, defined as $\sum(|F_c|-|F_o|)/\sum|F_o|$, had a final value of 7·0% for the 3353 reflections with $I>2\sigma$ and 8·3% for all data (4285 reflections).‡ The final refined

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‡ A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31010 (21 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

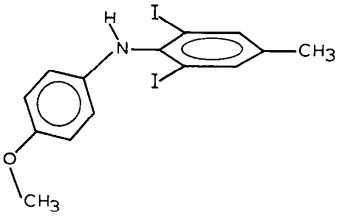

Fig. 1. 1-Methyl-4′-methoxy-3,5-diiododiphenylamine.

Table 1. *Positional and thermal parameters*

	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
I(3)	0·14278 (4)	0·57179 (5)	0·40824 (1)	0·0536 (2)	0·0326 (3)	0·0553 (3)	0·0030 (1)	0·0054 (1)	−0·0082 (1)
I(5)	0·36972 (3)	−0·08723 (5)	0·26068 (1)	0·0337 (1)	0·0410 (1)	0·0563 (3)	0·0038 (1)	0·0125 (1)	−0·0065 (1)
C(1)	−0·0467 (5)	0·0326 (9)	0·3212 (1)	0·027 (2)	0·042 (2)	0·042 (2)	−0·002 (2)	0·002 (2)	−0·002 (2)
C(2)	−0·0245 (5)	0·2172 (8)	0·3511 (1)	0·028 (2)	0·042 (3)	0·047 (3)	0·001 (2)	0·003 (2)	−0·005 (2)
C(3)	0·1119 (5)	0·3140 (7)	0·3560 (1)	0·034 (2)	0·029 (2)	0·040 (2)	0·004 (2)	0·002 (2)	−0·002 (2)
C(4)	0·2274 (4)	0·2342 (7)	0·3301 (1)	0·029 (2)	0·028 (2)	0·040 (2)	−0·002 (2)	0·000 (1)	0·003 (2)
C(5)	0·2012 (5)	0·0541 (7)	0·2991 (1)	0·028 (2)	0·027 (2)	0·043 (2)	0·004 (2)	0·005 (2)	−0·003 (2)
C(6)	0·0670 (5)	−0·0472 (8)	0·2949 (2)	0·030 (2)	0·037 (2)	0·044 (3)	−0·001 (2)	0·000 (2)	−0·004 (2)
C(7)	−0·1918 (6)	−0·0774 (10)	0·3183 (2)	0·028 (2)	0·057 (4)	0·073 (4)	−0·010 (2)	0·005 (2)	−0·004 (3)
N(4′)	0·3669 (4)	0·3348 (6)	0·3344 (1)	0·031 (2)	0·030 (2)	0·048 (2)	−0·006 (1)	0·001 (2)	0·004 (2)
C(1′)	0·4704 (4)	0·2749 (7)	0·3758 (1)	0·025 (2)	0·029 (2)	0·041 (2)	−0·001 (1)	0·005 (2)	−0·005 (2)
C(2′)	0·5756 (5)	0·4207 (7)	0·3926 (2)	0·034 (2)	0·032 (2)	0·049 (3)	−0·003 (2)	0·001 (2)	−0·003 (2)
C(3′)	0·6831 (6)	0·3659 (8)	0·4320 (2)	0·037 (2)	0·035 (2)	0·058 (3)	−0·003 (2)	−0·005 (2)	−0·009 (2)
C(4′)	0·6850 (5)	0·1642 (8)	0·4542 (1)	0·035 (2)	0·035 (2)	0·042 (2)	−0·000 (2)	−0·001 (2)	−0·005 (2)
C(5′)	0·5781 (5)	0·0215 (8)	0·4374 (2)	0·037 (2)	0·032 (2)	0·048 (3)	−0·004 (2)	0·001 (2)	0·000 (2)
C(6′)	0·4723 (5)	0·0746 (7)	0·3988 (2)	0·029 (2)	0·036 (2)	0·044 (2)	−0·008 (2)	0·002 (2)	0·001 (2)
O(4′)1	0·7968 (4)	0·1267 (6)	0·4919 (1)	0·051 (2)	0·041 (2)	0·066 (3)	0·002 (2)	−0·020 (2)	−0·006 (2)
C(4′)2	0·8196 (7)	−0·0912 (11)	0·5084 (3)	0·047 (3)	0·057 (4)	0·077 (4)	0·008 (3)	−0·008 (3)	0·006 (3)

positional and thermal parameters are given in Table 1.

Discussion. In order to study the possible biological effects of nitrogen substitution for the ether oxygen in thyroxine, NH-bridged analogs of thyroxine have been synthesized (Mukherjee & Block, 1971). When tested, these compounds did not show thyroxine-like activity, but some members of the series do possess antimalarial activity. The crystal and molecular

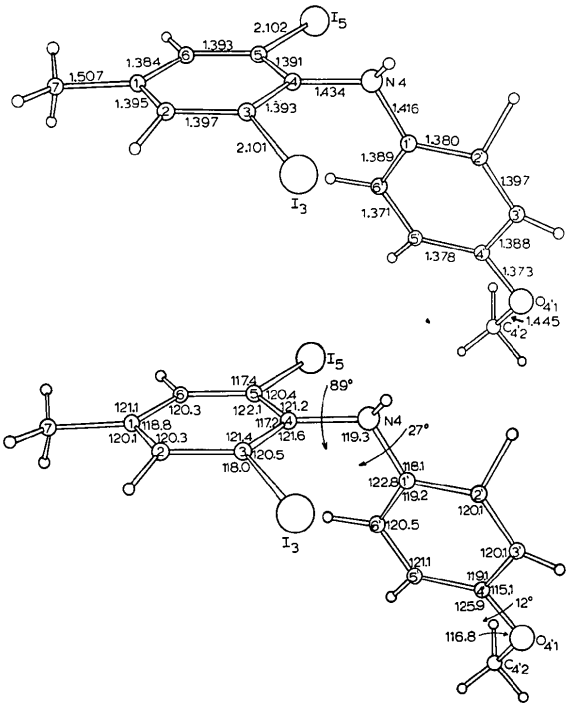

Fig. 2. Bond lengths and bond angles for 1-methyl-4′-methoxy-3,5-diiododiphenylamine.

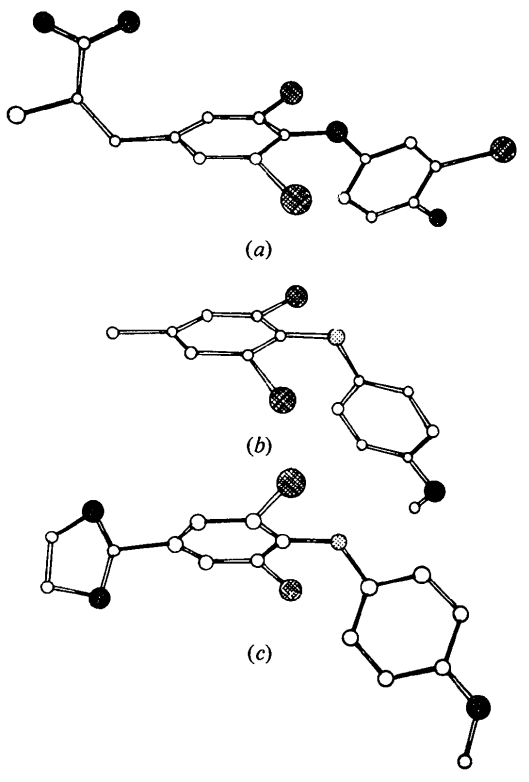

Fig. 3. Comparison of the conformational features of the thyroid hormone T_3 with diiododiphenylamine derivatives. (*a*) 3,5,3′-Triiodo-L-thyronine (T_3). (*b*) 1-Methyl-4′-methoxy-3,5-diiododiphenylamine. (*c*) 1-Acetal-4′-methoxy-3,5-diiododiphenylamine.

Table 2. *Comparison of diphenylamine structures*

φ is the torsional angle C(3)–C(4)–N(4)–C1′. φ' is the torsional angle C(4)–N(4)–C(1′)–C(6′).

Structure	C–X–C	φ	φ'	Reference
1-Methyl-4′-methoxy-3,5-diiododiphenylamine	119°	89°	27°	
1-Acetal-4′-methoxy-3,5-diiododiphenylamine				
Molecule 1	120	−91	−13	Cody, Duax & Norton (1972)
2	128	87	13	
3	116	100	−27	
4	124	−89	−14	
Average diphenylamine	126	44*	30*	†
		−54‡	−28‡	
Average diphenylamine with 3,5-diiodosubstitution	121	88*	20*	†
		−87‡	−18‡	
3,5,3′-Triiodo-L-thyronine	121	116	−21	Cody (1974)
3,5,3′-Triiodo-L-thyronine methyl ester	121	−108	33	Cody (1975)
Average thyroid hormone analog	119	99*	16*	†
		−90‡	−24‡	

* *Transoid.*

† These averages are calculated from the structures: Baggio, Becka, Amzel, Avey & Poljak (1973), Bürgi, Djuric, Dobler & Dunitz (1973), Divjakovic, Nowacki, Edenharter, Engel, Ribar & Halasi (1973), Grison (1949), Hanson (1953), Hlavatá (1971), McConnell (1973), Plieth & Ruban (1961) and Toman & Očenášková (1966).

‡ *Cisoid.*

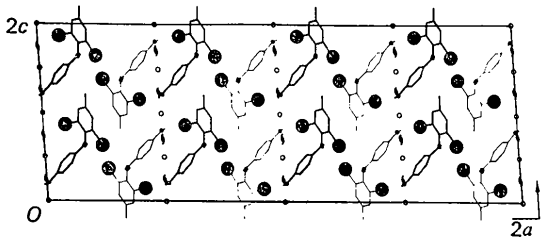

Fig. 4. Packing diagram for 1-methyl-4′-methoxy-3,5-diiododiphenylamine. The dark molecules are above the light ones, the large circles are iodine, the smaller ones oxygen and the squares are nitrogen.

structure of 1-methyl-4′-methoxy-3,5-diiododiphenylamine was undertaken as one in a series of diphenylamine derivatives whose structural features will be compared with those of thyroid hormones (Fig. 1).

The structural formula and the interatomic distances and valency angles among non-hydrogen atoms are given in Fig. 2. The standard deviations of the bond lengths and bond angles range from 0·005 to 0·009 Å and from 0·3 to 0·5°.

The conformations of this molecule, the thyroid hormone T_3 (Cody, 1974), and another diphenylamine derivative (Cody, Duax & Norton, 1972) are compared in Fig. 3. As indicated in Table 2, the magnitudes of the torsional angles, ϕ, and ϕ', about the diphenylamine linkage are comparable with the magnitudes observed for thyroid hormone structures (Cody, 1975). Also, the averages of ϕ and ϕ' for the diphenylamine structures which contain a 3,5-diiodo-substitution agree well with the thyroid hormone data, but differ significantly from other diphenylamine structures. In general, diphenylamines with free 3,5-positions tend to have the planes of the two rings nearly coplanar, while iodo substitution leads to a mutually perpendicular conformation.

Although there are no hydrogen bonds in this structure (Fig. 4) there are short van der Waals contacts of the type I···I (4·02 Å) and I···O (3·19 Å) which are characteristic of many thyroid hormone structures.

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