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Crystal and Molecular Structures of 2,2'-Methylenebis(4-chloro-3-methyl-6-isopropylphenol)

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The crystal and molecular structures of 2,2'-methylenebis(4-chloro-3-methyl-6-isopropylphenol) have been determined by single-crystal X-ray diffraction studies. Crystals are monoclinic, space group $P2_1/c$ with unit-cell parameters $a = 11 \cdot 977$ (2), $b = 19 \cdot 035$ (3), $c = 9 \cdot 244$ (4) Å, $\beta = 109 \cdot 25°$ and $Z = 4$. The intensities of 3779 reflections were measured on a Nonius CAD-4 automatic diffractometer. The structure was solved by direct methods and refined by least-squares calculations to an R of $0 \cdot 056$. The structure determination establishes the molecular geometry and shows that the value of the C—C—C valency angle ($118 \cdot 6°$) at the methylene group is appreciably in excess of tetrahedral. Molecules are held together by weak hydrogen bonds ($3 \cdot 05$ Å) forming chains interrelated by van der Waals contacts.

Introduction

This work forms part of a study of phenols with remarkable biological activity; our interest centres on a series of 'bisphenols' with a $C_{Ar}—C_{CH_2}—C_{Ar_2}$ linkage in a position *ortho* to the hydroxyl group; the present paper describes the crystal structure and molecular configuration of 2,2'-methylenebis(4-chloro-3-methyl-6-isopropylphenol).* The only crystal structure determinations of 'bisphenols' with a $C_{Ar}—C_{CH_2}—C_{Ar}$ linkage that have been reported are by Whittaker (1953) and Chaudhuri & Hargreaves (1956); in these compounds the methylene group is in the *para* position relative to the OH group.†

Faith (1952) registered a patent for the title substance. Because of its bactericidal property, it also has a French medicinal patent (1967) No. 4620. It is used under the common name 'Bichlothymol' as a pulmonary antiseptic in a medicine called 'hexapneumine'.
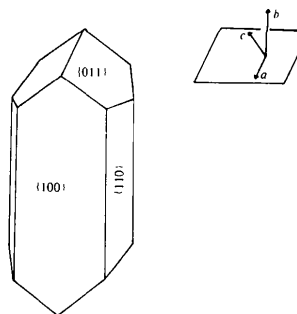

Fig. 1. Crystal morphology.

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* We thank the Doms Establishment of Courbevoie (France) for supplies of this product.

† We thank Professor J. E. Dubois and Mrs Aranda for providing Cambridge Crystallographic Data Centre file compilations.

Experimental

Morphological characteristics

Crystals of 2,2'-methylenebis(4-chloro-3-methyl-6-isopropylphenol) suitable for X-ray work were obtained by recrystallization from saturated solutions in *n*-hexane. The colourless and transparent crystals (Fig. 1) show the pinacoid {100}, the prisms {110} and {011} and sometimes the pinacoid {010}.

Crystal data

A nearly equidimensional crystal was obtained by cleaving and was sealed in a glass capillary. Preliminary X-ray data obtained by rotation and Weissenberg photographs indicated that the crystals are monoclinic with space group $P2_1/c$, systematic extinctions being $0k0$ for $k \neq 2n$ and $h0l$ for $l \neq 2n$. The unit-cell parameters were determined by least-squares methods from 25 accurate 2θ values measured on an automatic diffractometer. The cell parameters and density indicated four molecules per cell, which is compatible with a general position in $P2_1/c$. Table 1 shows crystal data.

Intensity data

The intensities were measured at 20°C by the ω–$x\theta$ scan method on an Enraf–Nonius CAD-4 four-circle automatic diffractometer with Cu $K\alpha$ radiation ($\lambda = 1\cdot54178$ Å). 3779 reflections within the range $1° < \theta < 70°$ were determined: 749 had net counts less than three standard deviations of the total count and were considered to be unobserved. A check reflection was monitored every 1800 s for intensity and after every 100 reflections for orientation. The data were corrected for Lorentz and polarization effects but not for absorption ($\mu r = 0\cdot4$–$0\cdot5$, so the variation of A^* was considered negligible).

Structure determination and refinement

The structure factors were scaled by Wilson's (1942) method and converted to normalized structure factors. The structure was solved with *MULTAN* (Germain, Main & Woolfson, 1971). An initial E map based on 230 reflections ($E > 1\cdot90$) revealed 20 atoms of the molecule: C(1) to C(14), C(20), C(21), O(1), O(2), Cl(1), Cl(2). A Fourier synthesis with these positions

Table 1. *Crystal data*

2,2'-Methylenebis(4-chloro-3-methyl-6-isopropylphenol)
$C_{21}H_{26}Cl_2O_2$; monoclinic $P2_1/c$; $M_r = 381$; m.p. 125 ± 1°C
$a = 11\cdot977$ (2); $b = 19\cdot035$ (3); $c = 9\cdot244$ (4) Å; $\beta = 109\cdot25$ (2)°
$V = 1989\cdot6$ Å³; $Z = 4$; $F(000) = 808$; μ(Cu $K\alpha$) = 30·92 cm⁻¹
$D_m = 1\cdot31$ (flotation in mercury at 20°C); $D_x = 1\cdot27$ g cm⁻³
$(\sin \theta/\lambda)_{max} = 0\cdot61$ Å⁻¹

Table 2. *Final atomic coordinates* ($\times 10^4$), *with corresponding e.s.d.'s in parentheses for non-hydrogen atoms*

	x	y	z
C(1)	2828 (4)	3838 (2)	2900 (6)
C(2)	2703 (4)	4404 (2)	3835 (5)
C(3)	3313 (4)	5038 (2)	3783 (6)
C(4)	3933 (4)	5074 (2)	2781 (6)
C(5)	4033 (4)	4524 (2)	1858 (6)
C(6)	3472 (4)	3882 (2)	1909 (6)
C(7)	3614 (5)	3263 (2)	962 (6)
C(8)	3311 (8)	3460 (4)	−688 (8)
C(9)	4847 (7)	2980 (4)	1532 (10)
C(10)	3266 (5)	5664 (2)	4784 (6)
C(11)	457 (4)	3362 (2)	4716 (5)
C(12)	758 (4)	4025 (2)	4239 (5)
C(13)	−1493 (4)	4404 (2)	3191 (5)
C(14)	−1284 (4)	4123 (2)	2671 (5)
C(15)	−1545 (4)	3474 (2)	3180 (5)
C(16)	−631 (4)	3087 (2)	4210 (5)
C(17)	−918 (5)	2352 (2)	4750 (5)
C(18)	−2195 (5)	2229 (3)	4437 (7)
C(19)	−416 (7)	1772 (3)	3966 (8)
C(20)	97 (6)	5115 (2)	2616 (7)
C(21)	1976 (4)	4308 (2)	4891 (5)
Cl(1)	4698 (1)	5847 (1)	2637 (2)
Cl(2)	−2445 (1)	4571 (1)	1365 (2)
O(1)	2293 (3)	3197 (2)	2963 (4)
O(2)	1433 (3)	3012 (2)	5700 (4)

Table 3. *Final atomic coordinates* ($\times 10^3$) *and isotropic thermal parameters for the hydrogen atoms, with e.s.d.'s in parentheses*

	x	y	z	$B(\text{Å}^2)$
H(11)	145 (4)	329 (2)	296 (5)	4·6 (1)
H(51)	466 (4)	454 (2)	146 (5)	5·0 (1)
H(71)	292 (4)	292 (2)	101 (5)	4·7 (1)
H(81)	256 (5)	357 (3)	−106 (5)	7·2 (1)
H(82)	342 (4)	296 (2)	−131 (5)	6·2 (1)
H(83)	384 (4)	382 (2)	−73 (5)	6·2 (1)
H(91)	561 (5)	336 (3)	168 (6)	9·2 (2)
H(92)	489 (4)	251 (3)	98 (5)	7·1 (1)
H(93)	524 (4)	286 (2)	273 (6)	7·2 (1)
H(101)	243 (4)	591 (2)	435 (5)	5·4 (1)
H(102)	426 (4)	589 (2)	495 (5)	4·9 (1)
H(103)	302 (4)	557 (3)	570 (6)	7·9 (2)
H(111)	98 (5)	272 (3)	587 (6)	7·9 (2)
H(151)	−248 (2)	333 (1)	285 (3)	1·3 (1)
H(171)	−39 (4)	233 (2)	580 (5)	5·1 (1)
H(181)	−239 (5)	177 (3)	433 (6)	8·1 (2)
H(182)	−268 (4)	241 (3)	356 (5)	7·5 (2)
H(183)	−259 (4)	248 (3)	487 (5)	7·6 (2)
H(191)	−105 (5)	170 (2)	299 (6)	7·3 (2)
H(192)	−34 (4)	126 (2)	476 (5)	5·3 (1)
H(193)	42 (4)	184 (2)	391 (5)	5·5 (1)
H(201)	−86 (4)	524 (2)	176 (5)	4·2 (1)
H(202)	89 (4)	504 (2)	243 (6)	7·2 (2)
H(203)	40 (4)	542 (2)	349 (5)	6·5 (1)
H(211)	263 (4)	394 (2)	575 (5)	4·3 (1)
H(212)	189 (3)	469 (2)	530 (4)	4·2 (1)

calculated and with all the reflections showed the structure; the first calculation of the R index gave 0·44.

The atomic coordinates and thermal parameters, first isotropic and then anisotropic, were refined by the least-squares method with a block-diagonal-matrix approximation (Ahmed, Hall, Pippy & Huber, 1966). The weighting scheme employed was: $\sqrt{w} = 1$ if $|F_o| < P_1$; $\sqrt{w} = P_1/|F_o|$ if $|F_o| > P_1$; with $P_1^2/F_{max}^2 = 0·1$. After this refinement, the conventional R value reached 0·091. Theoretical calculations and difference syntheses revealed all the H atoms. The final R, after isotropic refinement of these H atoms, was 0·056. The final atomic positional parameters with their estimated standard deviations are given in Table 2 for non-hydrogen atoms and in Table 3 for H atoms.*

Results and discussion

Molecular geometry

Fig. 2 shows the adopted notation and Fig. 3 the molecular structure with thermal ellipsoids at 50% probability obtained with ORTEP (Johnson, 1965).

Tables 4 and 5, respectively, list the bond distances and bond angles with corresponding estimated standard deviations. The mean bond lengths for the six endo

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* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33136 (20 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.
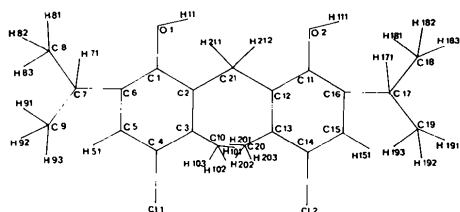
C—C bonds in the benzene ring are 1·395 Å (plane A) and 1·390 Å (plane B); the mean values of the endo bond angles are the same in planes A and B and are equal to 119·98°. The C—O bond distances are greater than the value, 1·36 Å, generally found in the literature [C(1)—O(1) = 1·388; C(11)—O(2) = 1·392 Å] as are the C—Cl bond distances: C(4)—Cl(1) = 1·761, C(14)—Cl(2) = 1·736 Å, literature value 1·70 Å. They are, however, in good agreement with the values found by our group for other phenols (Bavoux, Perrin, Thozet, Bertholon & Perrin, 1976).

The non-ring C—C bond distances are also shorter than the average value 1·54 Å [C(2)—C(21) = 1·517; C(12)—C(21) = 1·484; C(6)—C(7) = 1·510 Å]; however, C(16)—C(17), 1·561 Å, is longer.

Table 4. Bond distances (Å) with their e.s.d.'s in parentheses

C(1)—C(2)	1·419 (6)	O(1)—H(11)	1·023 (51)
C(1)—C(6)	1·382 (7)	C(5)—H(51)	0·939 (46)
C(1)—O(1)	1·388 (6)	C(7)—H(71)	1·069 (46)
C(2)—C(3)	1·419 (6)	C(8)—H(81)	0·874 (56)
C(2)—C(21)	1·517 (7)	C(8)—H(82)	1·144 (47)
C(3)—C(4)	1·368 (7)	C(8)—H(83)	0·936 (50)
C(3)—C(10)	1·520 (7)	C(9)—H(91)	1·145 (59)
C(4)—C(5)	1·381 (7)	C(9)—H(92)	1·045 (50)
C(4)—Cl(1)	1·761 (5)	C(9)—H(93)	1·080 (51)
C(5)—C(6)	1·403 (7)	C(10)—H(101)	1·057 (49)
C(6)—C(7)	1·510 (7)	C(10)—H(102)	1·230 (48)
C(7)—C(8)	1·495 (9)	C(10)—H(103)	1·001 (53)
C(7)—C(9)	1·495 (10)	O(2)—H(111)	0·822 (55)
C(11)—C(12)	1·422 (6)	C(15)—H(151)	1·091 (32)
C(11)—C(16)	1·338 (7)	C(17)—H(171)	0·965 (43)
C(11)—O(2)	1·392 (6)	C(18)—H(181)	0·901 (52)
C(12)—C(13)	1·395 (6)	C(18)—H(182)	0·899 (49)
C(12)—C(21)	1·484 (7)	C(18)—H(183)	0·863 (52)
C(13)—C(14)	1·391 (7)	C(19)—H(191)	0·979 (52)
C(13)—C(20)	1·518 (7)	C(19)—H(192)	1·204 (45)
C(14)—C(15)	1·393 (6)	C(19)—H(193)	1·030 (52)
C(14)—Cl(2)	1·736 (5)	C(20)—H(201)	1·184 (45)
C(15)—C(16)	1·400 (6)	C(20)—H(202)	1·031 (56)
C(16)—C(17)	1·561 (6)	C(20)—H(203)	0·965 (48)
C(17)—C(18)	1·479 (9)	C(21)—H(211)	1·149 (43)
C(17)—C(19)	1·547 (8)	C(21)—H(212)	0·845 (41)

Fig. 2. The $C_{21}H_{26}Cl_2O_2$ molecule showing the atomic numbering.
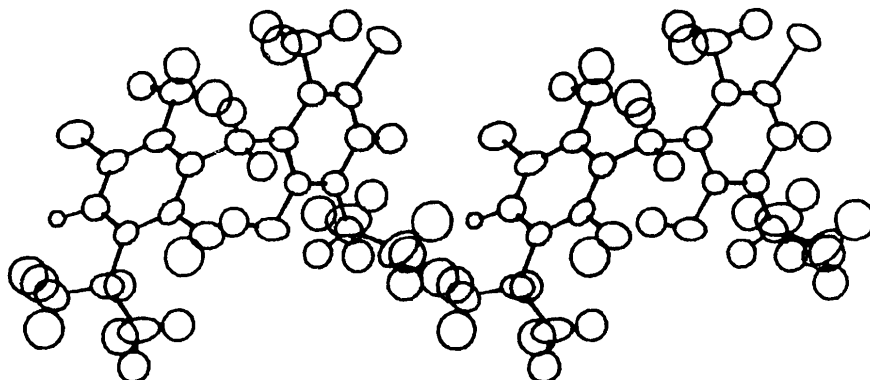
Fig. 3. A stereographic view of the molecule.

Table 5. *Bond angles* (°) *with their e.s.d.'s in parentheses*

C(2)–C(1)–C(6)	123·5 (4)	C(12)–C(13)–C(14)	119·3 (4)	C(7)–C(9)–H(92)	110·2 (29)
C(2)–C(1)–O(1)	119·9 (4)	C(12)–C(13)–C(20)	120·5 (4)	C(7)–C(9)–H(93)	118·8 (28)
C(6)–C(1)–O(1)	116·5 (4)	C(14)–C(13)–C(20)	120·2 (4)	C(3)–C(10)–H(101)	109·8 (26)
C(1)–C(2)–C(3)	117·8 (3)	C(13)–C(14)–C(15)	121·9 (4)	C(3)–C(10)–H(102)	97·4 (21)
C(1)–C(2)–C(21)	119·9 (4)	C(13)–C(14)–Cl(2)	121·2 (4)	C(3)–C(10)–H(103)	117·4 (31)
C(3)–C(2)–C(21)	122·3 (4)	C(15)–C(14)–Cl(2)	117·0 (3)	C(11)–O(2)–H(111)	89·1 (37)
C(2)–C(3)–C(4)	117·8 (4)	C(14)–C(15)–C(16)	118·9 (4)	C(14)–C(15)–H(151)	117·0 (16)
C(2)–C(3)–C(10)	121·5 (4)	C(11)–C(16)–C(15)	119·0 (4)	C(16)–C(15)–H(151)	123·7 (16)
C(4)–C(3)–C(10)	120·6 (4)	C(11)–C(16)–C(17)	122·1 (4)	C(16)–C(17)–H(171)	102·9 (27)
C(3)–C(4)–C(5)	123·8 (5)	C(15)–C(16)–C(17)	118·9 (4)	C(18)–C(17)–H(171)	118·4 (27)
C(3)–C(4)–Cl(1)	120·4 (4)	C(16)–C(17)–C(18)	113·7 (4)	C(19)–C(17)–H(171)	121·9 (7)
C(5)–C(4)–Cl(1)	115·8 (4)	C(16)–C(17)–C(19)	109·2 (4)	C(17)–C(18)–H(181)	112·8 (36)
C(4)–C(5)–C(6)	120·1 (5)	C(18)–C(17)–C(19)	109·4 (5)	C(17)–C(18)–H(182)	115·7 (33)
C(1)–C(6)–C(5)	116·9 (4)	C(2)–C(21)–C(12)	118·6 (4)	C(17)–C(18)–H(183)	120·4 (34)
C(1)–C(6)–C(7)	122·1 (4)	C(1)–O(1)–H(11)	108·1 (26)	C(17)–C(19)–H(191)	102·8 (31)
C(5)–C(6)–C(7)	120·9 (4)	C(4)–C(5)–H(51)	117·2 (27)	C(17)–C(19)–H(192)	104·7 (23)
C(6)–C(7)–C(8)	111·1 (5)	C(6)–C(5)–H(51)	119·8 (27)	C(17)–C(19)–H(193)	117·7 (26)
C(6)–C(7)–C(9)	111·2 (5)	C(6)–C(7)–H(71)	102·5 (21)	C(13)–C(20)–H(201)	98·7 (21)
C(8)–C(7)–C(9)	109·2 (5)	C(8)–C(7)–H(71)	105·3 (24)	C(13)–C(20)–H(202)	103·6 (29)
C(12)–C(11)–C(16)	123·8 (4)	C(9)–C(7)–H(71)	117·1 (24)	C(13)–C(20)–H(203)	107·7 (30)
C(12)–C(11)–O(2)	112·6 (4)	C(7)–C(8)–H(81)	109·3 (35)	C(2)·C(21)·H(211)	96·7 (22)
C(16)–C(11)–O(2)	123·5 (4)	C(7)–C(8)–H(82)	106·0 (25)	C(2)–C(21)–H(212)	111·6 (29)
C(11)–C(12)–C(13)	117·0 (4)	C(7)–C(8)–H(83)	106·4 (30)	C(12)–C(21)–H(211)	114·3 (22)
C(21)–C(12)–C(11)	120·8 (4)	C(7)–C(9)–H(91)	118·3 (29)	C(12)–C(21)–H(212)	104·1 (29)
C(21)–C(12)–C(13)	122·1 (4)				

The *endo* angles around C(1), C(4), C(11), C(14) are greater than 120° and those around C(2), C(6), C(12), C(16) are smaller. This could be connected with the σ-electron withdrawing or releasing character of the substituents.

The equations of characteristic planes and deviations of atoms from them are presented in Table 6 and the dihedral angles between the mean planes in Table 7. The dihedral angle between the two benzene rings (plane A and plane B) is 84·42°. The two rings are linked by a methylene group: the angle C(2)–C(21)–C(12), 118·6°, is larger than expected (109°). Whittaker (1953) and Chaudhuri & Hargreaves (1956) found values of 119° for this same angle in similar compounds: bisphenols with a CH_2 linkage between aromatic rings in the *para* position relative to the OH group.

With a dihedral angle of 87·25°, plane D (the isopropyl group) is nearly perpendicular to plane A and the straight line joining C(8)–C(9) makes an angle of 81° with plane A. On the other side, the dihedral angle between the planes B and E is 66·67° and the angle between C(18)–C(19) and plane B is 46·44°. O(1) and Cl(1) are below plane A, and O(2) and Cl(2) are above plane B. O(2) is 1·5 times further from plane B than O(1) is from plane A. Cl(1) and Cl(2) are about equidistant from planes A and B respectively. O(1) and O(2) are both on the same side of plane C, above which are Cl(1) and Cl(2).

The intramolecular distance O(1)–O(2), 3·05 Å, is a weak intramolecular hydrogen bond.

The torsion angles were calculated. The benzene

Table 6. *Least-squares planes with deviations of atoms* (Å ×10³) *from the planes, with corresponding e.s.d.'s in parentheses*

Asterisks indicate atoms not included in plane calculations.

Plane A: $-0.6079X + 0.3238Y - 0.7250Z + 0.9847 = 0$

C(1)	−6 (5)	C(7)*	−66 (5)
C(2)	15 (5)	C(8)*	1014 (8)
C(3)	−15 (5)	C(9)*	−1393 (9)
C(4)	4 (5)	C(10)*	−42 (6)
C(5)	6 (5)	C(21)*	13 (5)
C(6)	−5 (5)	Cl(1)*	−11 (2)
		O(1)*	−39 (4)

Plane B: $0.4808X - 0.4423Y - 0.7571Z + 6.3714 = 0$

C(11)	−3 (4)	C(17)*	28 (5)
C(12)	−3 (4)	C(18)*	−351 (6)
C(13)	2 (5)	C(19)*	1438 (7)
C(14)	5 (5)	C(20)*	9 (6)
C(15)	−11 (5)	C(21)*	−65 (5)
C(16)	10 (4)	Cl(2)*	13 (1)
		O(2)*	60 (4)

Plane C, through C(2), C(21), C(12):
$$-0.3032X + 0.9298Y - 0.2086Z - 6.4693 = 0$$

C(10)*	1940 (5)	Cl(2)*	2387 (1)
C(20)*	2315 (5)	O(1)*	−1908 (3)
Cl(1)*	1938 (1)	O(2)*	−2170 (3)

Plane D, through C(7), C(8), C(9):
$$-0.2781X - 0.9224Y - 0.2680Z + 7.0761 = 0$$

Plane E, through C(17), C(18), C(19):
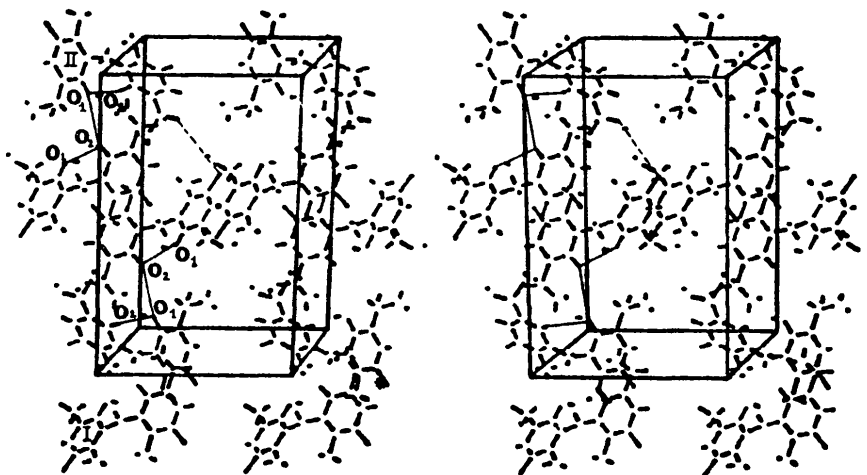$$0.0652X + 0.5614Y - 0.8250Z + 1.0726 = 0$$

Fig. 4. A stereoscopic illustration of the structure seen along [001].

Table 7. *Dihedral angles* (°) *between the mean planes*

Planes	Dihedral angle	Planes	Dihedral angle
A–B	84·42	B–E	66·67
A–C	51·02	B–C	114·78
A–D	87·25		

rings *A* and *B* are not quite planar. The largest deformations occur for plane *A* at the bonds C(1)–C(2) ($\tau = -2 \cdot 48°$), C(2)–C(3) ($\tau = 3 \cdot 19°$) and C(3)–C(4) ($\tau = -2 \cdot 30°$), and for plane *B* at the bonds C(14)–C(15) ($\tau = -1 \cdot 89°$), C(15)–C(16) ($\tau = 2 \cdot 35°$) and C(16)–C(11) ($\tau = -1 \cdot 68°$).

Crystal structure

Hydrogen bonds. In many monophenols, molecules are interlinked by hydrogen bonds forming infinite chains, dimers or tetramers: the O—O distances have values between 2·70 and 2·80 Å in general. For the compound studied here the molecules are linked by a long O—O distance of 3·05 Å forming infinite chains parallel to the (100) plane.

Packing. Different chains are held together by van der Waals interactions. The shortest intermolecular distances with their estimated standard deviations are given in Table 8. Note the contacts between Cl(1) and C(8) of the isopropyl group of molecule VIII (molecule I translated by **a** + **b**) and C(18) of the isopropyl group of molecule II. The table also lists distances less than 4 Å from Cl(1) to C(2), C(3) and C(21) of molecule V (molecule I translated by + **a** + **b** + **c**).

There are also intermolecular van der Waals interactions between Cl(2) and Cl(1), C(4), C(5), C(8) and C(21) of molecule IX (molecule I translated by

+ **b**). Thus, the two Cl atoms seem to play an important part in the interrelation between chains.

Fig. 4 shows an *ORTEP* stereodrawing of the structure.

Conclusion

This structure shows for the first time the geometry of the molecule of a bisphenol where the C_{Ar}–C_{CH_2}–C_{Ar} linkage occurs at the *ortho* position relative to the OH group. Other compounds of the same series with various substituents on the aromatic rings are to be studied by our group in relation to biological properties.

Table 8. *Intermolecular distances less than* 4·0 Å, *with their e.s.d.'s in parentheses*

Symmetry code

(I)	$\bar{x}, \bar{y}, \bar{z}$	(VI)	$\bar{x}, 1 - y, 1 - z$
(II)	$\bar{x}, \frac{1}{2} + y, \frac{1}{2} - z$	(VII)	$-1 + x, y, z$
(III)	$x, \frac{1}{2} - y, \frac{1}{2} + z$	(VIII)	$1 - x, 1 - y, \bar{z}$
(IV)	$x, \frac{1}{2} - y, -\frac{1}{2} + z$	(IX)	$\bar{x}, 1 - y, \bar{z}$
(V)	$1 - x, 1 - y, 1 - z$	(X)	$x, y, 1 + z$

C(10)–C(4^V)	3·649 (8)	Cl(1)–C(8^{VIII})	3·674 (9)
C(10)–C(5^V)	3·689 (8)	Cl(1)–C(18^{II})	3·973 (6)
C(10)–C(14^{VI})	3·876 (8)	Cl(1)–C(21^V)	3·896 (5)
C(10)–C(15^{VI})	3·611 (8)	Cl(1)–Cl(2^{IX})	3·875 (2)
C(17)–C(15^{III})	3·829 (7)	Cl(2)–C(4^{IX})	3·717 (5)
C(18)–C(9^{VII})	3·941 (11)	Cl(2)–C(5^{IX})	3·424 (5)
C(18)–C(14^{III})	3·820 (7)	Cl(2)–C(8^{IX})	3·883 (7)
C(18)–C(15^{III})	3·549 (8)	Cl(2)–C(18^{IV})	3·919 (6)
C(20)–C(11^{VI})	3·999 (7)	Cl(2)–C(21^{IX})	3·945 (5)
C(20)–C(12^{VI})	3·760 (8)	O(1)–C(7^{III})	3·876 (6)
C(20)–C(13^{VI})	3·963 (8)	O(1)–C(8^{III})	3·464 (8)
C(20)–C(19^{II})	3·550 (7)	O(1)–O(2^{IV})	3·052 (5)
Cl(1)–C(2^V)	3·723 (5)	O(2)–C(7^{III})	3·515 (6)
Cl(1)–C(3^V)	3·777 (5)	O(2)–C(8^X)	3·462 (8)

We are very grateful to Mr S. Lecocq for assistance in data collection on the CAD-4 automatic diffractometer.

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Structure Cristalline du Sulfate de Salbutamol [tert-Butylamino-2 (Hydroxy-4 hydroxyméthyl-3 phényl)-1 Ethanol. $\frac{1}{2}$ H₂SO₄]

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The crystal structure of salbutamol sulphate [2-tert-butylamino-1-(4-hydroxy-3-hydroxymethylphenyl)-ethanol.½H₂SO₄] has been determined from X-ray diffraction data. The crystallographic data are $a = 28\cdot069$ (5), $b = 6\cdot183$ (1), $c = 16\cdot914$ (2) Å, $\beta = 81\cdot19$ (1)°. The space group is Cc with two independent molecules and eight molecules in the unit cell. The refinement, carried out by least-squares calculations including anisotropic temperature factors, gave a final R value of $0\cdot067$. Hydrogen bonds are mainly responsible for the crystalline cohesion.

Introduction

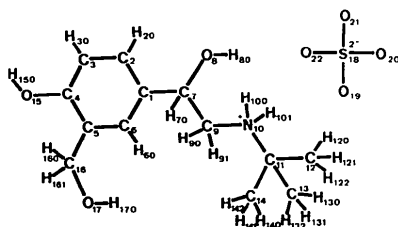Le sulfate de salbutamol est le principe actif de Ventoline, médicament particulièrement utilisé en

Fig. 1. Numération atomique.

pneumologie et en obstétrique. Il exerce une action sélective importante et prolongée sur les récepteurs β_2 adrénergiques qui se traduit par une action inhibitrice prédominante au niveau des muscles lisses bronchiques, utérins et des vaisseaux périphériques. Son action est très faible sur les récepteurs β_1 du muscle cardiaque.

Dans le but de comparer la conformation du salbutamol à celles des dérivés adrénolytiques β-bloquants de synthèse étudiées au laboratoire (Gadret, Goursolle, Leger & Colleter, 1975a,b,c,d, 1976; Gadret, Goursolle, Leger, Colleter & Carpy, 1976; Carpy, Colleter, Gadret, Goursolle & Leger, 1976; Leger, Gadret & Carpy, 1977; Gadret, Leger & Carpy, 1977; Gadret, Leger, Carpy & Berthod, 1978), la détermination de la structure cristalline a été entreprise (Fig. 1).