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Structure of 1-Phenylcyclohexanol*

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Abstract

$C_{12}H_{16}O$, a precursor to the hallucinogenic drug 1-phenylcyclohexylamine, is monoclinic, $P2_1/c$, a = 20·605 (3), b = 10·657 (2), c = 19·683 (3) Å, β = 100·75 (1)°, Z = 16, M_r = 176·26, D_o = 1·101, D_c = 1·103 Mg m^{-3}; R = 0·049 and R_w = 0·052 for 4619 observed reflexions. The cyclohexane ring is in the chair form. The hydroxyl group is axial and the phenyl group equatorial, but the twist of the phenyl ring around the adjoining bond varies through a wide range [~39 (1)°] in the four independent molecules. Four intermolecular O—H···O bonds, forming a closed loop, link the independent molecules into a tetramer while the tetramers are held together only by van der Waals forces. On short exposure to X-rays, the crystals sublime gradually, disappearing completely within a period of two to four days.

Introduction

1-Phenylcyclohexanol is a precursor to the hallucinogenic drug 1-phenylcyclohexylamine, the simplest acyclic-amine analog of phencyclidine (PCP, 'Angel Dust'), a highly potent and widely abused psychotomimetic drug (Garey, Weisberg & Heath, 1977). While PCP itself is governed under provisions of the Canadian Narcotic Control Act, two derivatives of 1-phenylcyclohexylamine, *N*-(1-phenylcyclohexyl)ethylamine and 1-phenyl-*N*-propylcyclohexanamine, are controlled under Schedule *H* of the Canadian Food and Drugs Act. Phencyclidine, an analgesic–anaesthetic drug used in veterinary medicine (Gagné & Pike, 1977), is frequently encountered on the illicit market. 1-Phenylcyclohexanol has been used in the preparation of some illicit drugs (Reed & Kane, 1970) and as an intermediate in the synthesis of 1-phenylcylohexylamine and its derivatives (Bailey & Legault, 1979). The X-ray analysis was undertaken to determine the molecular stereochemistry and examine the possibility of intermolecular OH···π bonding. Such π bonding has been demonstrated by infrared studies (Kleinfelter, 1967).

Large colourless transparent crystals were grown from a mother-liquor concentrate in hexane solution over several months at room temperature. The crystals are stable at room temperature, but once exposed to X-rays they start to sublime and the process continues in a chain reaction, even without further radiation, until they completely disappear. However, the X-ray diffraction spots from the exposed crystals seemed to maintain their relative intensities, and on this basis the data collection from a given crystal was continued until the intensities reached about 50% of their original values. Altogether, four crystals cut to approximate cubes about 0·3 to 0·5 mm in length, were used to collect the full data set.

The space group was determined from precession photographs, and the cell parameters were derived by least squares from the angular settings of eight high-order reflexions (θ = 35 to 40°) measured on a Nonius CAD-4 diffractometer with Ni-filtered Cu radiation, $\lambda(K\alpha_1)$ = 1·5405 Å. The intensities were measured by ω–2θ scans for $\omega = (0{\cdot}8 + 0{\cdot}14 \tan\theta)°$ at a maximum ω speed of 4° min^{-1} for the strong reflexions and at lower speeds for the weaker ones. Each scan was extended by 25% at each end of the scan for measurement of the background. Three reflexions of medium intensity were scanned every 40 min of exposure time for scaling of the data. Data collection was limited to 2θ < 130° where 7226 independent reflexions were scanned. Of these, 4619 with $I > 2\sigma(I)$ were considered observed. The net intensities were corrected for Lorentz and polarization effects, but not for absorption (μ = 0·534 mm^{-1}).

Structure determination

The structure was determined by the direct method of symbolic addition (Karle & Karle, 1963). The starting reflexions consisted of three for origin definition, two with permuted + and − signs, and four symbols. An E map calculated with 878 reflexions ($|E| > 1{\cdot}50$) with phases corresponding to the permutation with the least number of Σ_2 contradictions showed the positions of the 52 independent non-hydrogen atoms. The corresponding R index, with B = 5·0 Å^2, was 0·28. After refinement to R = 0·12, a difference map revealed the

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Table 1. *Fractional atomic coordinates* ($\times 10^4$, $\times 10^3$ *for* H) *and* $B_{\rm eq}$ *values* (B *for* H)

$$B_{\rm eq} = (8\pi^2/3) \sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i . \mathbf{a}_j .$$

	x	y	z	$B_{\rm eq}/B$ (Å^2)		x	y	z	$B_{\rm eq}/B$ (Å^2)
Molecule (I)					Molecule (III)				
C(1)	3113 (1)	1416 (2)	3608 (1)	4·8 (0·1)	C(1)	3880 (1)	5075 (2)	940 (1)	4·1 (0·1)
C(2)	2525 (1)	1546 (3)	3004 (1)	5·6 (0·1)	C(2)	3814 (1)	5993 (2)	1512 (1)	5·3 (0·1)
C(3)	2151 (2)	322 (3)	2846 (1)	6·9 (0·1)	C(3)	3669 (2)	7320 (3)	1244 (2)	7·5 (0·1)
C(4)	2597 (2)	−715 (3)	2693 (2)	8·5 (0·1)	C(4)	4180 (2)	7766 (3)	834 (2)	8·8 (0·1)
C(5)	3177 (2)	−891 (3)	3294 (2)	8·2 (0·1)	C(5)	4217 (2)	6880 (3)	244 (2)	7·5 (0·1)
C(6)	3550 (1)	333 (3)	3470 (1)	6·3 (0·1)	C(6)	4369 (1)	5555 (3)	511 (1)	5·6 (0·1)
C(7)	3502 (1)	2620 (2)	3749 (1)	4·9 (0·1)	C(7)	4073 (1)	3780 (2)	1245 (1)	4·3 (0·1)
C(8)	3791 (1)	2955 (3)	4411 (1)	6·5 (0·1)	C(8)	3635 (1)	2794 (2)	1189 (1)	5·2 (0·1)
C(9)	4147 (2)	4047 (3)	4553 (1)	7·2 (0·1)	C(9)	3818 (1)	1626 (3)	1469 (1)	6·4 (0·1)
C(10)	4235 (2)	4830 (4)	4043 (2)	8·3 (0·1)	C(10)	4446 (2)	1424 (3)	1815 (2)	7·3 (0·1)
C(11)	3972 (3)	4485 (5)	3378 (2)	11·9 (0·2)	C(11)	4891 (2)	2390 (3)	1887 (2)	8·0 (0·1)
C(12)	3614 (2)	3404 (4)	3233 (1)	9·5 (0·1)	C(12)	4708 (1)	3557 (3)	1611 (2)	6·5 (0·1)
O	2838 (1)	1071 (2)	4206 (1)	5·6 (0·1)	O	3246 (1)	5013 (2)	487 (1)	5·0 (0·1)
H(2,1)	270 (1)	182 (2)	259 (1)	3·1 (0·5)	H(2,1)	346 (1)	566 (2)	175 (1)	3·0 (0·5)
H(2,2)	222 (1)	224 (2)	314 (1)	3·8 (0·5)	H(2,2)	426 (1)	600 (2)	184 (1)	3·0 (0·5)
H(3,1)	176 (2)	50 (3)	243 (2)	7·1 (0·8)	H(3,1)	366 (2)	787 (4)	164 (2)	7·8 (0·9)
H(3,2)	193 (1)	9 (3)	325 (1)	5·1 (0·6)	H(3,2)	319 (1)	734 (3)	94 (2)	5·7 (0·7)
H(4,1)	279 (2)	−44 (3)	228 (2)	6·8 (0·8)	H(4,1)	401 (2)	861 (3)	66 (2)	7·3 (0·9)
H(4,2)	230 (2)	−152 (4)	260 (2)	9·1 (1·0)	H(4,2)	466 (2)	782 (3)	115 (2)	7·1 (0·8)
H(5,1)	299 (1)	−119 (3)	372 (2)	5·4 (0·7)	H(5,1)	459 (2)	716 (3)	0 (2)	6·6 (0·8)
H(5,2)	352 (2)	−151 (3)	320 (2)	7·5 (0·9)	H(5,2)	379 (1)	684 (3)	−9 (1)	4·6 (0·6)
H(6,1)	391 (1)	22 (3)	387 (1)	4·4 (0·6)	H(6,1)	437 (1)	491 (3)	14 (1)	4·0 (0·6)
H(6,2)	377 (1)	61 (2)	309 (1)	3·6 (0·5)	H(6,2)	481 (1)	559 (2)	80 (1)	3·7 (0·5)
H(8)	371 (2)	238 (3)	479 (2)	6·3 (0·8)	H(8)	319 (1)	292 (2)	95 (1)	3·9 (0·5)
H(9)	433 (2)	419 (4)	501 (2)	7·4 (0·9)	H(9)	347 (1)	93 (3)	143 (1)	5·2 (0·7)
H(10)	449 (2)	564 (4)	413 (2)	7·9 (0·9)	H(10)	457 (1)	58 (3)	199 (2)	5·7 (0·7)
H(11)	407 (2)	496 (5)	299 (3)	11·9 (1·4)	H(11)	535 (2)	226 (4)	212 (2)	7·8 (0·9)
H(12)	345 (2)	314 (4)	276 (2)	9·0 (1·0)	H(12)	502 (1)	429 (3)	168 (2)	5·4 (0·7)
H(O)	263 (2)	158 (5)	437 (2)	11·1 (1·3)	H(O)	322 (3)	466 (6)	8 (3)	16·0 (1·9)
Molecule (II)					Molecule (IV)				
C(1)	1536 (1)	3487 (2)	4632 (1)	4·4 (0·1)	C(1)	1504 (1)	5326 (2)	873 (1)	4·3 (0·1)
C(2)	1950 (1)	4505 (2)	4377 (1)	5·1 (0·1)	C(2)	1782 (1)	6145 (2)	1492 (1)	5·7 (0·1)
C(3)	2486 (1)	5028 (3)	4945 (2)	6·3 (0·1)	C(3)	1966 (2)	5372 (3)	2159 (1)	7·7 (0·1)
C(4)	2203 (1)	5477 (3)	5554 (2)	6·8 (0·1)	C(4)	1388 (2)	4580 (3)	2288 (2)	8·0 (0·1)
C(5)	1829 (1)	4441 (3)	5834 (1)	6·3 (0·1)	C(5)	1140 (2)	3740 (3)	1684 (2)	7·0 (0·1)
C(6)	1284 (1)	3926 (2)	5272 (1)	5·1 (0·1)	C(6)	942 (1)	4500 (2)	1026 (1)	5·6 (0·1)
C(7)	964 (1)	3102 (2)	4065 (1)	5·2 (0·1)	C(7)	1275 (1)	6120 (2)	231 (1)	4·3 (0·1)
C(8)	919 (2)	1908 (3)	3785 (2)	7·2 (0·1)	C(8)	1611 (2)	6145 (3)	−308 (1)	6·3 (0·1)
C(9)	393 (2)	1608 (4)	3245 (2)	10·0 (0·1)	C(9)	1389 (2)	6867 (3)	−895 (1)	8·0 (0·1)
C(10)	−75 (2)	2475 (5)	3002 (2)	10·4 (0·1)	C(10)	824 (2)	7557 (3)	−945 (1)	7·1 (0·1)
C(11)	−50 (2)	3653 (4)	3282 (2)	9·6 (0·1)	C(11)	495 (1)	7589 (3)	−399 (2)	7·1 (0·1)
C(12)	472 (1)	3963 (3)	3813 (2)	7·2 (0·1)	C(12)	720 (1)	6874 (3)	183 (1)	6·0 (0·1)
O	1972 (1)	2440 (2)	4834 (1)	5·9 (0·1)	O	2015 (1)	4473 (2)	762 (1)	5·3 (0·1)
H(2,1)	164 (1)	520 (2)	420 (1)	3·4 (0·5)	H(2,1)	215 (1)	656 (2)	138 (1)	3·2 (0·5)
H(2,2)	216 (1)	413 (2)	400 (1)	2·7 (0·5)	H(2,2)	144 (1)	678 (3)	154 (1)	4·3 (0·6)
H(3,1)	270 (1)	572 (3)	473 (1)	5·2 (0·7)	H(3,1)	211 (2)	603 (3)	254 (2)	7·3 (0·9)
H(3,2)	280 (1)	432 (3)	510 (1)	5·4 (0·7)	H(3,2)	237 (1)	489 (3)	208 (2)	5·6 (0·7)
H(4,1)	191 (1)	620 (3)	541 (1)	4·2 (0·6)	H(4,1)	154 (2)	403 (4)	272 (2)	7·7 (0·9)
H(4,2)	259 (1)	581 (3)	593 (1)	5·3 (0·7)	H(4,2)	102 (2)	514 (3)	237 (2)	6·1 (0·7)
H(5,1)	162 (1)	477 (2)	619 (1)	3·7 (0·5)	H(5,1)	74 (2)	330 (3)	177 (2)	6·0 (0·7)
H(5,2)	214 (1)	372 (2)	600 (1)	3·7 (0·5)	H(5,2)	150 (1)	310 (3)	160 (1)	5·2 (0·7)
H(6,1)	95 (1)	460 (2)	513 (1)	3·3 (0·5)	H(6,1)	82 (1)	393 (3)	61 (1)	4·5 (0·6)
H(6,2)	105 (1)	323 (2)	544 (1)	3·0 (0·5)	H(6,2)	57 (1)	505 (2)	105 (1)	3·2 (0·5)
H(8)	129 (2)	127 (4)	397 (2)	7·3 (0·9)	H(8)	202 (1)	562 (3)	−30 (1)	4·9 (0·6)
H(9)	46 (2)	72 (4)	312 (2)	8·5 (1·0)	H(9)	169 (2)	690 (3)	−122 (2)	6·5 (0·8)
H(10)	−45 (2)	222 (4)	265 (2)	9·4 (1·1)	H(10)	66 (2)	807 (3)	−136 (2)	6·4 (0·8)
H(11)	−39 (3)	438 (5)	313 (3)	12·0 (1·4)	H(11)	10 (2)	815 (3)	−42 (2)	6·1 (0·8)
H(12)	50 (2)	487 (3)	401 (2)	6·1 (0·7)	H(12)	45 (1)	685 (3)	56 (2)	5·5 (0·7)
H(O)	184 (3)	191 (5)	505 (3)	12·9 (1·5)	H(O)	236 (2)	470 (5)	70 (2)	10·3 (1·2)

positions of 61 of the 64 independent H atoms, and the remaining three were located from a second map at $R = 0·056$.

Refinement was by block-diagonal least-squares calculations on $\sum w(|F_o| - |F_c|)^2$, where $w^{-1} = 1 + [(|F_o| - 20)/25]^2$, and if $\sin^2\theta < 0·3$, $w = w(\sin^2\theta/0·3)$. This weighting scheme was chosen to make $\langle w(F_o - F_c)^2\rangle$ independent of $|F_o|$ and $\sin^2\theta$. Six very strong reflexions affected by extinction and a weak one with possible multiple diffraction, as well as all those unobserved, were excluded from the least-squares summations. In the final cycle, $R = 0·046$ for the 4612 reflexions used in the refinement (0·049 for all the observed reflexions), $R_w = 0·052$, $[\sum w(\Delta F)^2/(m - n)]^{1/2} = 0·71$, and the mean and maximum Δ/σ were 0·1 and 0·4, respectively. Only five of the 2607 unobserved reflexions were calculated higher than 1·5 times their threshold amplitudes. The residual electron density in the final difference map was within −0·14 and 0·19 e Å^{-3}. The refined atomic parameters are listed in Table 1.* All computations were performed with the aid of the NRC System of Programs (Ahmed, Hall, Pippy & Huber, 1973), and the scattering-factor curves for C_{val}, O and H were from *International Tables for X-ray Crystallography* (1974).

Discussion

In the four independent molecules, the cyclohexane ring has the chair conformation with the hydroxyl group axial and the phenyl ring equatorial. The bond lengths and valence angles presented in Fig. 1 are the mean values for the four molecules, and their estimated standard deviations are calculated from the spread in the individual measurements. χ^2 tests on the bond lengths indicate that the estimated standard deviations derived from the block-diagonal least-squares refinement are probably underestimated by about 50%. Increasing the standard deviations by that amount reduces the discrepancies among the four measurements of a given bond to an insignificant level, $P > 0·01$. However, this correction does not eliminate significant differences in some of the valence angles involving C(7), especially C(1)—C(7)—C(12) where one measurement deviates by as much as 1·8 (2)° from the mean value. The C—H distances are 0·92 to 1·07 (5) Å, mean = 0·99 Å, and O—H are 0·78 to 0·88 (5) Å, mean = 0·81 Å.

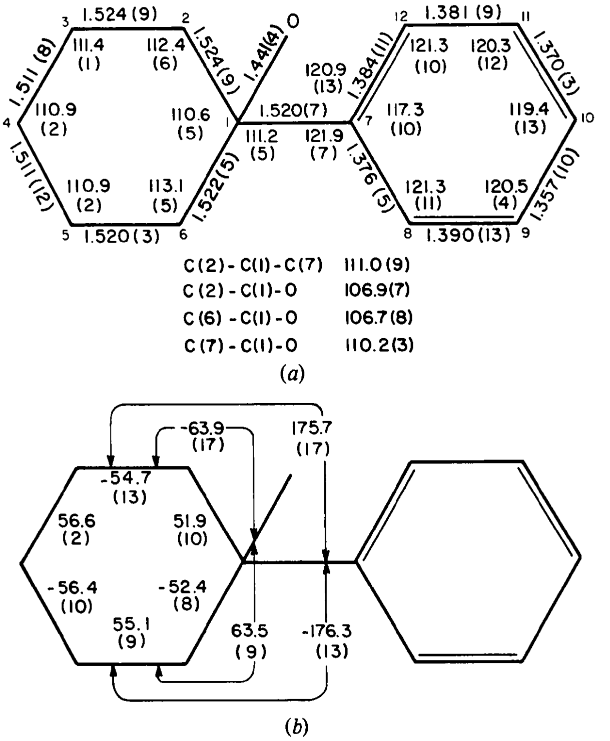

Fig. 1. Schematic drawings showing the average values of (*a*) bond lengths (Å) and valence angles (°), and (*b*) torsion angles (°), with standard deviations depicting the spread in the four independent molecules.

Table 2. *Torsion angles (°) involving the phenyl rings of the four independent molecules (e.s.d.'s ≤ 1·0°)*

	(I)	(II)	(III)	(IV)
O—C(1)—C(7)—C(8)	27·3	−2·8	−11·7	−11·2
O—C(1)—C(7)—C(12)	−155·8	177·7	169·8	170·4
C(2)—C(1)—C(7)—C(8)	145·5	115·1	106·0	108·4
C(2)—C(1)—C(7)—C(12)	−37·6	−64·5	−72·5	−70·0
C(6)—C(1)—C(7)—C(8)	−90·8	−121·8	−130·3	−127·8
C(6)—C(1)—C(7)—C(12)	86·1	58·7	51·2	53·8

The torsion angles shown in Fig. 1(*b*) are the mean values for the four molecules. Their estimated standard deviations, which are based on the actual measurements, show only small differences among the measured values. Each cyclohexane ring is a chair form that is slightly flattened at C(1). The average displacements of C(1) and C(4) are 0·631 (11) and −0·665 (4) Å, respectively, from the mean planes of C(2), C(3), C(5) and C(6). The orientation of the phenyl ring relative to C(1)—OH is quite different in the four molecules as may be seen from the individual torsion angles listed in Table 2. The difference in orientation is also illustrated by the four Newman projections along C(1)—C(7) in Fig. 2, and is as high as 39 (1)° between molecules (I) and (III).

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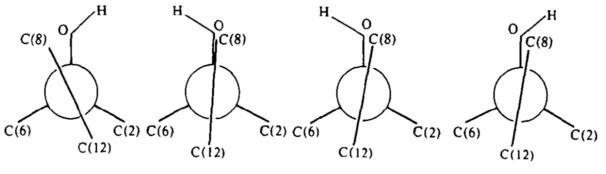
* Lists of structure factors, anisotropic thermal parameters, bond lengths, valence angles and torsion angles of the four independent molecules have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36099 (36 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.



(I) (II) (III) (IV)

Fig. 2. Newman projections along C(7)–C(1) showing the orientations of the phenyl rings relative to OH in the four independent molecules. Corresponding torsion angles are listed in Table 2.

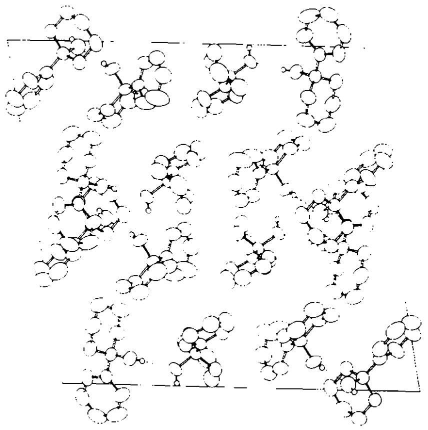


Fig. 3. The [010] projection of the unit-cell contents, with the *a* axis horizontal and the O···H bonds drawn in broken lines.

As shown in the projection in Fig. 3, each group of four independent molecules is interlinked through hydrogen bonds into one tetramer, while the tetramers are held together by normal van der Waals interactions. The intermolecular hydrogen bonds between the OH groups form a closed loop as shown in detail in Fig. 4, which represents a projection on the mean plane of the four O atoms of one tetramer. These O atoms deviate by ±0·32 (1) Å from their mean plane.

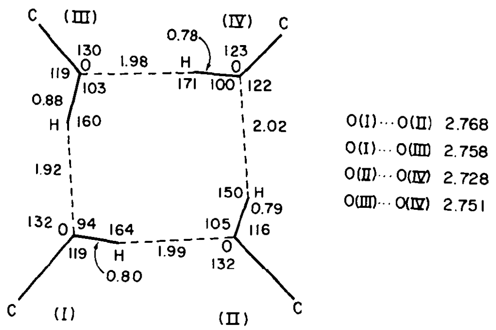


Fig. 4. Geometry of the four-sided loop of intermolecular hydrogen bonds that link each group of four independent molecules into a tetramer.

A careful examination of the intermolecular distances shows no indication of any intermolecular π bonding between OH and the phenyl rings.

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