3·200 (3), N(1)—H(2) = 0·89 (3), H(2)···Cl^- = 2·35 (3) Å, N(1)—H(2)···Cl^- = 160 (3)°] and O(2)—H···Cl^- ($x+\frac{1}{2}$, $y-\frac{1}{2}$, z) [O(2)···Cl^- = 3·143 (3), O(2)—H = 0·81 (3), H···Cl^- = 2·39 (3) Å, O(2)—H···Cl^- = 156 (3)°]. The molecules are thus connected through chloride ions to form sheets perpendicular to the *c* axis. The sheets are held together by van der Waals and dipolar forces acting mainly between the carbamate groups.

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Structure and Absolute Configuration of (−)-3-(*o*-Cyclohexylphenoxy)-1-(isopropylamino)-2-propanol Hydrochloride

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Abstract. $C_{18}H_{30}NO_2^+.Cl^-$, $M_r = 328·0$, orthorhombic, $P2_12_12_1$, $a = 7·224$ (2), $b = 13·961$ (6), $c = 19·424$ (7) Å, $V = 1959·0$ Å^3, $Z = 4$, $D_m = 1·10$, $D_x = 1·11$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, $\mu = 0·55$ mm^{-1}, $F(000) = 712$, $T = 293$ K, final $R = 0·044$ for 927 unique observed reflections. The crystal structure consists of infinite chains along the *a* axis, the molecules within the chains being connected *via* chloride ions by H-bond interactions. Adjacent chains are held together by van der Waals forces. The cyclohexane ring assumes a normal chair conformation with the aromatic ring attached equatorially. The isopropylamino group is oriented −synclinal relative to the 2-hydroxyl group, and the oxymethylene O—CH_2 fragment is approximately coplanar with the aromatic system. A large amount of flexibility in the oxypropanolamine chain of β-blocking drugs arises from rotation about the OCH_2—$CH(OH)CH_2$ bond, and the active (*S*)-enantiomer of the present compound adopts a −synclinal conformation in the crystal.

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Introduction. The racemic mixture of the title compound, hereafter referred to as VUL 111.HCl, was synthesized by Jendrichovský, Rybár, Štibrányi, Dřímal & Jendrichovská (1978). It is a potent cardioselective β-adrenergic blocking agent of the 3-aryloxy-1-(alkylamino)-2-propanol type (Dřímal, Seginko, Gibala & Strižová, 1978). All the drugs in this class exhibit significant differences in pharmacological activity between individual enantiomers, with the (−)-enantiomers being more active. This clearly demonstrates the stereospecifity of the β-receptor binding sites, and emphasizes the need for unequivocal determination of the absolute configuration. The absolute configuration of some of these agents was previously studied by Dukes & Smith (1971) on the basis of experience with the Horeau method and by Nelson & Burke (1978) by interpreting the circular dichroism spectra of oxprenolol isomers; both groups of authors came to the same conclusion that the (−)-enantiomer has an *S* configuration. In order to provide unequivocal evidence for this assignment, the racemic VUL 111 was resolved into its enantiomers and the active (−)-isomer was selected for the X-ray analysis. Another aim of this work was to establish the conformational properties of the flexible oxypropanolamine side chain, which is common to all β-blockers. Knowledge of solid-state conformations of a number of β-blockers could be very valuable in drawing inferences about preferred conformations.

Experimental. Resolution of the (±)-VUL 111 was accomplished through fractional crystallization of the salt formed by the addition of (+)-dibenzoyl-D-tartaric acid monohydrate to a solution of VUL 111 in methanol. Recrystallization from methanol resulted in one of the diastereomeric salts; decomposition of the salt with cold NH_4OH gave the free base, $[\alpha]_D$ −5·6°, m.p. 447–448 K, which was then converted to the HCl salt. Single crystals obtained from ether/acetone solution, colourless prismatic needles, crystal used: 0·40 × 0·10 × 0·05 mm, D_m by flotation; systematic absences $h00$ for h odd, $0k0$ for k odd and $00l$ for l odd, from Weissenberg photographs; Syntex $P2_1$ four-circle diffractometer; accurate unit-cell parameters by least-squares refinement of 11 reflections, $12 < \theta < 45°$; intensity data ($h = 0$ to 7, $k = 0$ to 13, $l = 0$ to 19) collected with Cu $K\alpha$ radiation using θ–2θ scanning mode, each reflection scanned 1° (in 2θ) above and below $K\alpha$ doublet, background-to-scan-time ratio 1·0; two standard reflections measured every 98 reflections, no significant systematic fluctuation; intensities corrected for Lorentz–polarization effects but not for absorption; 1196 unique reflections, $3 < \theta \leq 50°$, 927 with $I \geq 1{\cdot}95\sigma(I)$ considered as observed and included in the refinement; structure solved by heavy-atom techniques and refined by Fourier and block-diagonal least-squares methods, difference electron density map showed positions of all H atoms, refinement continued on all positional parameters, anisotropic thermal parameters for non-H atoms and isotropic thermal parameters for H atoms; in final cycle $R = 0{\cdot}044$, $wR = 0{\cdot}048$ for observed reflections only, max. shift/e.s.d. 0·18, function minimized $\sum w(\Delta F)^2$, where $w = 1$ if $|F_o| < 40$ and $w = 40/|F_o|$ if $|F_o| \geq 40$, max. and min. electron density difference peaks 0·18 and −0·21 e Å^{-3}; utilizing anomalous scattering of the Cl atom, the enantiomeric structure refined under identical conditions to $R = 0{\cdot}052$, $wR = 0{\cdot}056$; scattering factors for neutral atoms and anomalous-scattering corrections for the Cl atom from *International Tables for X-ray Crystallography* (1974); all calculations performed with local version of the *NRC* system (Ahmed, Hall, Pippy & Huber, 1973).

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

$B_{eq} = \frac{4}{3}\sum_i\sum_j \beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	*y*	*z*	B_{eq}(Å²)
C(1)	1276 (9)	−1822 (5)	5716 (3)	4·06
C(2)	64 (11)	−2463 (5)	5431 (4)	4·95
C(3)	136 (11)	−3416 (5)	5644 (4)	5·55
C(4)	1388 (12)	−3703 (5)	6119 (4)	5·94
C(5)	2607 (11)	−3036 (6)	6394 (4)	5·21
C(6)	2610 (9)	−2092 (5)	6200 (3)	3·85
C(7)	3950 (9)	−1331 (5)	6467 (4)	4·22
C(8)	5867 (10)	−1721 (6)	6616 (4)	6·10
C(9)	7157 (12)	−911 (7)	6827 (5)	7·65
C(10)	6465 (13)	−398 (6)	7444 (5)	7·67
C(11)	4500 (14)	−9 (7)	7337 (5)	8·12
C(12)	3195 (11)	−836 (6)	7095 (4)	5·72
C(13)	127 (12)	−547 (5)	5016 (4)	5·35
C(14)	405 (10)	540 (5)	4958 (4)	4·55
C(15)	−350 (10)	996 (5)	5612 (4)	4·73
C(16)	−480 (10)	2509 (5)	6315 (4)	4·99
C(17)	−40 (13)	3569 (5)	6240 (4)	6·53
C(18)	342 (13)	2088 (6)	6964 (4)	7·29
N(1)	297 (7)	2003 (4)	5689 (3)	4·25
O(1)	1302 (7)	−862 (3)	5540 (2)	5·26
O(2)	−552 (10)	822 (4)	4364 (3)	8·38
Cl	4651 (2)	1944 (1)	5728 (1)	5·63

Discussion. Refined positional parameters of non-H atoms and equivalent isotropic B's are listed in Table 1.* Numbering of the atoms is shown in Fig. 1, which also displays configurational and conformational aspects of the molecule. According to Hamilton's (1965) R-factor-ratio test, the hypothesis that the (−)-VUL 111 studied here has an *S* configuration is verified with a significance much better than 0·005, assuming no systematic errors in the data. Thus the coordinates of Table 1 correspond to the correct

* Lists of structure factors, anisotropic thermal parameters, H-atom parameters, best planes and torsion angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51410 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

enantiomorph with almost absolute certainty. This is in agreement with the absolute configuration deduced from CD data (Nelson & Burke, 1978).

Bond lengths and angles involving non-hydrogen atoms (Table 2) have values close to those generally expected. The benzene ring is planar with no atom deviating from the six-atom least-squares plane by more than 0·008 (7) Å; the substituent atoms C(7) and O(1) are displaced from this plane in an opposite direction by 0·015 (5) and 0·048 (7) Å respectively. The cyclohexane ring has an almost ideal chair geometry, as reflected in the small values of the asymmetry parameters (Duax & Norton, 1975), ΔC_s[C(8)] = 1·0, ΔC_2-[C(7), C(8)] = 1·5°.

From the biological point of view the most important structural features of the β-adrenolytics (*i.e.* compounds in which an substituted aromatic ring is linked to an oxypropanolamine chain) are the conformational properties of the oxypropanolamine side chain. In general, the β-antagonists are characterized by three features: (*a*) the alkylamine, (*b*) the 2-hydroxyl, and (*c*) the hydrophobic moiety in the aromatic terminus of the molecule. The three-dimensional disposition of these functional groups, which are assumed to define the interaction with the β-receptor (George, Kier & Hoyland, 1971), depends on the torsion angles τ_1 = C(2)–C(1)–O(1)–C(13), τ_2 = C(1)–O(1)–C(13)–C(14), τ_3 = O(1)–C(13)–C(14)–C(15) and τ_4 = C(13)–C(14)–C(15)–N(1). An examination of literature data on crystal structures of several β-blockers shows that all three staggered conformations about the C(13)–C(14) bond are found in crystals, indicating flexibility of the oxypropanolamine side chain. The

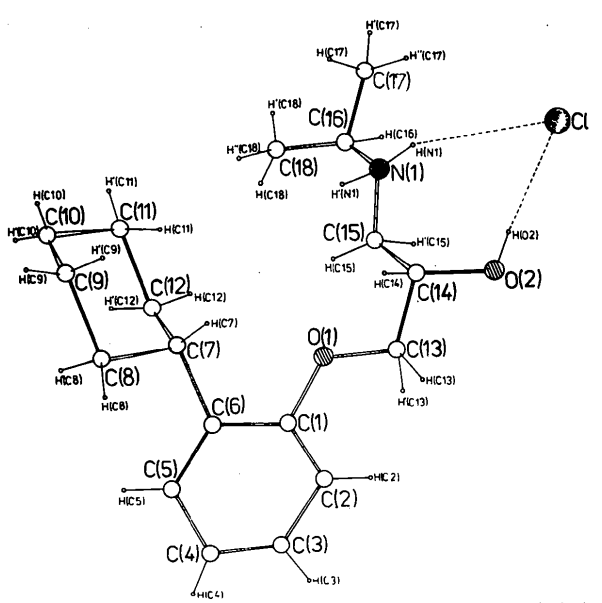

Fig. 1. Perspective view of (−)-VUL 111. HCl molecule showing the numbering of the atoms.

Table 2. *Bond distances* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

C(1)–C(2)	1·37 (1)	C(11)–C(12)	1·56 (1)
C(2)–C(3)	1·39 (1)	C(12)–C(7)	1·50 (1)
C(3)–C(4)	1·35 (1)	C(1)–O(1)	1·38 (1)
C(4)–C(5)	1·39 (1)	O(1)–C(13)	1·40 (1)
C(5)–C(6)	1·37 (1)	C(13)–C(14)	1·54 (1)
C(6)–C(1)	1·40 (1)	C(14)–C(15)	1·52 (1)
C(6)–C(7)	1·53 (1)	C(14)–O(2)	1·40 (1)
C(7)–C(8)	1·52 (1)	C(15)–N(1)	1·49 (1)
C(8)–C(9)	1·52 (1)	N(1)–C(16)	1·51 (1)
C(9)–C(10)	1·48 (1)	C(16)–C(17)	1·52 (1)
C(10)–C(11)	1·53 (1)	C(16)–C(18)	1·51 (1)

C(1)–C(2)–C(3)	118·7 (7)	C(11)–C(12)–C(7)	111·4 (7)
C(2)–C(3)–C(4)	120·7 (7)	C(12)–C(7)–C(8)	109·0 (6)
C(3)–C(4)–C(5)	119·2 (7)	C(2)–C(1)–O(1)	122·9 (6)
C(4)–C(5)–C(6)	122·7 (7)	C(6)–C(1)–O(1)	114·7 (6)
C(5)–C(6)–C(1)	116·3 (6)	C(1)–O(1)–C(13)	118·4 (5)
C(6)–C(1)–C(2)	122·4 (6)	O(1)–C(13)–C(14)	106·5 (6)
C(1)–C(6)–C(7)	118·5 (6)	C(13)–C(14)–C(15)	107·8 (6)
C(5)–C(6)–C(7)	125·2 (6)	C(13)–C(14)–O(2)	105·8 (6)
C(6)–C(7)–C(8)	113·2 (6)	C(15)–C(14)–O(2)	113·2 (6)
C(6)–C(7)–C(12)	111·4 (6)	C(14)–C(15)–N(1)	111·5 (6)
C(7)–C(8)–C(9)	110·1 (7)	C(15)–N(1)–C(16)	113·9 (5)
C(8)–C(9)–C(10)	111·7 (8)	N(1)–C(16)–C(17)	107·4 (6)
C(9)–C(10)–C(11)	111·9 (8)	N(1)–C(16)–C(18)	110·0 (6)
C(10)–C(11)–C(12)	109·7 (7)	C(17)–C(16)–C(18)	112·2 (7)

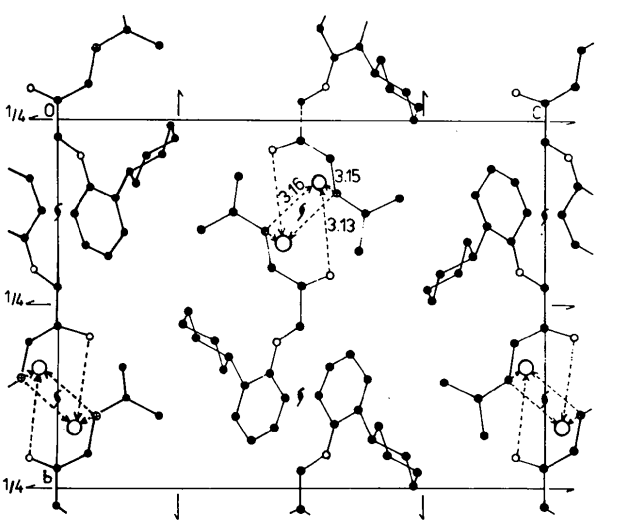

Fig. 2. Molecular packing; C, N and O atoms are represented by filled, crossed and open circles respectively. Chloride ions are larger open circles. Broken lines represent hydrogen bonds (Å) with arrowheads towards the acceptor atom (the chloride ions are slightly displaced for clarity).

conformation around C(13)–C(14) in the present compound is –synclinal [τ_3 = −67·7 (7)°], as in propranolol (Ammon, Howe, Erhardt, Balsamo, Macchia, Macchia & Keefe, 1977), alprenolol (Barrans, Cotrait & Dangoumau, 1973) and betaxolol (Pascard, Huu Dau, Manoury & Mompon, 1984), while in other compounds this conformation is either +synclinal ($\tau_3 \simeq +60°$) or antiperiplanar (*e.g.* Dubost, Leger,

Hickel & Colleter, 1981; Leger, Goursolle & Carpy, 1984; Gadret, Goursolle, Leger & Colleter, 1975; Weber & Petcher, 1977). In contrast to τ_3, the conformations around C(1)–O(1), O(1)–C(13) and C(14)–C(15) are probably strongly preferred as only conformations $\tau_1 \simeq 0$, $\tau_2 \simeq 180$ and $\tau_4 \simeq 180°$ are uniformly found in the crystals; in (–)-VUL 111 $\tau_1 = -4{\cdot}6$ (9), $\tau_2 = 177{\cdot}8$ (6) and $\tau_4 = 164{\cdot}9$ (6)°. The coplanarity of the O(1)–C(13) bond with the adjacent aromatic system, a feature well known from the structures of aromatic alkoxy compounds (Domiano, Nardelli, Balsamo, Macchia & Macchia, 1979), is rationalized on electronic grounds due to some degree of conjugation between the O(1) non-bonding orbital and the aromatic π system. This is further supported by a widening of the C(1)–O(1)–C(13) bond angle [118·4 (5)°], suggesting an essentially sp^2 hybridization state of O(1).

The molecular packing, as can be seen from Fig. 2, is influenced by hydrogen bonding. The (–)-VUL 111 molecules form infinite chains along the screw axes (at $x, \frac{1}{4}, \frac{1}{2}$ and $x, \frac{3}{4}, 0$), the main intrachain interactions being N(1)···Cl$^-$ and O(2)···Cl$^-$ hydrogen bonds. Apart from these hydrogen bonds there are no distances between non-hydrogen atoms shorter than 3·5 Å.

All calculations were performed on a Siemens 4004/150 computer at the Research Computing Centre of Comenius University. We are grateful to Dr J. Soldánová for measurements of X-ray diffraction intensities on a Syntex $P2_1$ diffractometer.

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Structures of 2,6-Bis(benzylidene)cyclohexanone (III) and 3,5-Bis(4-dimethylaminobenzylidene)-1-methyl-4-piperidone (IV)

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Abstract. (III): $C_{20}H_{18}O$, $M_r = 274{\cdot}36$, monoclinic, $P2_1/c$, $a = 10{\cdot}096$ (1), $b = 18{\cdot}393$ (2), $c = 9{\cdot}4731$ (9) Å, $\beta = 121{\cdot}388$ (8)°, $V = 1501{\cdot}79$ Å^3, $Z = 4$, D_m(by flotation) = 1·202, $D_x = 1{\cdot}213$ g cm^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 0{\cdot}57$ cm^{-1}, $F(000) = 584$, $T = 287$ K, $R = 0{\cdot}040$ ($wR = 0{\cdot}044$) for 2580 observed reflections. (IV): $C_{24}H_{29}N_3O$, $M_r = 375{\cdot}52$, monoclinic, $P2_1/n$, $a = 16{\cdot}098$ (2), $b = 6{\cdot}1533$ (6), $c = 20{\cdot}606$ (3) Å, $\beta = 96{\cdot}75$ (1)°, $V = 2027{\cdot}06$ Å^3, $Z = 4$, D_m(by flotation) = 1·233, $D_x = 1{\cdot}230$ g cm^{-3},

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