piperidine ring are comparable with those of dyclonine hydrochloride (Sinha, Vasantha Pattabhi, Nethaji & Gabe, 1987). The bond lengths and angles around the 3,4-methylenedioxyphenyl group are in agreement with the values reported in 7-methoxy-3-methyl-2-(3,4-methylenedioxyphenyl)-5-(prop-1-enyl)-2,3-dihydrobenzo[*b*]furan (Ponnuswamy & Parthasarathy, 1981). The double-bond oxygen O(15) is in a *syn* configuration with respect to the olefinic linkage [C(12)=C(13)]. The piperidine ring takes a chair conformation while the 3,4-methylenedioxyphenyl group is planar within experimental error; atom C(2) deviates by 0·02 Å from the latter. The dihedral angle between the two planes is 45·3 (1)°. In the unit cell the molecules are stabilized solely by van der Waals forces.

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Structure of L-Alprenolol D-Tartrate Monohydrate

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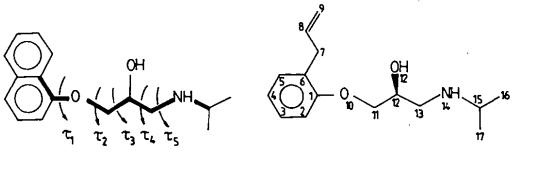
Abstract. L-1-(2-Allylphenoxy)-3-(isopropylamino)-propan-2-ol D-tartrate monohydrate, $C_{15}H_{24}NO_2^+.C_4H_5O_6^-.H_2O$, $M_r = 417{\cdot}46$, monoclinic, $P2_1$, $Z = 2$, $a = 7{\cdot}594$ (7), $b = 8{\cdot}645$ (13), $c = 16{\cdot}575$ (21) Å, $\beta = 93{\cdot}37$ (2)°, $V = 1086$ (2) Å^3, $Z = 2$, $F(000) = 448$, $T = 198$ (5) K, $D_x = 1{\cdot}276$ g cm^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, Ni filter, $\mu = 0{\cdot}863$ cm^{-1}, $R = 0{\cdot}054$, $wR = 0{\cdot}070$, for the 2363 reflections included in the refinement; sample from Sigma Chemical Company (A9389). The propoxinolamine side chain is observed in a conformation that is atypical of β-blocking agents. This conformation may result from the three hydrogen bonds that are formed between the side chain and the tartrate anion and water molecule or may be a result of the extensive hydrogen-bonding pattern between tartrate anions.

Introduction. β-Adrenergic blocking agents are useful in the management of cardiovascular disorders, including hypertension, angina pectoris and cardiac arrhythmias (Weiner, 1985); and, selective drugs function by antagonizing the actions of epinephrine or norepinephrine. Propanolol, the first clinically useful β-adrenergic antagonist, is prototypical of the agents developed to date. Structural similarities, both within each chemical group of β-receptor blocking agents and among the groups, are very close. Proposals for the structural determinants of β-blocking activity (Ammon, Balsamo, Macchia, Macchia, Howe & Keefe, 1975; Macchia *et al.*, 1987) consider the presence of an OH–CH–CH_2–NH–alkyl moiety joined to a planar system to be essential.



Propranolol Alprenolol (active S isomer shown)

Alprenolol belongs to the arylpropoxinolamine class of β-blockers; Leger, Gadret & Carpy (1977) postulate that the affinity of these ligands for the β-adrenoreceptors is related to the relative positions of the aryl moiety, the hydroxyl group [O(12)], and the amine group [N(14)]. Extensive X-ray studies on arylpropoxinolamine β-blockers reveal a uniformity of the conformation of the propoxinolamine chain in the

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crystalline state (Ammon, Howe, Erhardt, Balsamo, Macchia, Macchia & Keefe, 1977; Barrans, Cotrait & Dangoumau, 1973; Carpy, Gadret, Hickel & Leger, 1979; Gadret, Goursolle, Leger & Colleter, 1975*a,b*, 1976*a,b*; Kido, Nakagawa, Fujiwara & Tomita, 1981; Kobelt & Paulus, 1974; Leger, Colleter & Carpy, 1982; Leger *et al.*, 1977; Weber & Petcher, 1977). In general, these studies have been done on the ionic form because the arylpropoxinolamines are extensively protonated in the physiological environment (Sinistri & Villa, 1962); this implies that β-blockers are probably protonated when bound and that they are recognized by an anionic or hydrogen-bonding site. Often such observation of a common conformation for a series of biological molecules would suggest that a single low-energy form exists and represents the conformer bound to the recognition site. In the β-blockers, this common conformation has been observed in a series of crystals which were quite similar in chemical structure and composition; for example, many of the crystals contained the same anion, a chloride ion. Since the chloride ion may dictate the conformation of the drug cation, and since chloride ions are not ideal models for a polypeptide anionic site, the common conformation observed in these crystal structures would be substantiated by further observation in dissimilar environments.

The crystal structure of alprenolol tartrate monohydrate provides an opportunity for studying interactions of the protonated amine with carboxylate or hydroxyl acceptor groups, similar to the acceptor groups present in polypeptides. Accordingly, the crystal structure of this complex was determined to ascertain the molecular conformation of the β-blocker in a carboxylate-containing environment.

Experimental. Colorless crystals were grown by slow evaporation from a 1:1 ethyl acetate:methanol mixture. A crystal of dimensions 0·16 × 0·14 × 0·12 mm was used for data collection on an Enraf–Nonius CAD-4F automated diffractometer. The data were collected over a range of $+h, -k, \pm l$ and to a maximum θ of 75°. The θ range for the 25 reflections that were used to define the cell constants and orientation matrix was 28·2–38·8°. Data were collected at 198 K by cooling the crystal with a stream of cold N_2 gas. The intensities were collected using ω–2θ scans of variable speed to achieve $I > 2{\cdot}5\sigma(I)$ within a maximum measurement time of 200 s. The scan width was defined as $\Delta\omega = 1{\cdot}5\,(0{\cdot}50 + 1{\cdot}4\tan\theta)°$. Three standard reflections (3,0,10, $4\bar{1}\bar{1}$ and $\bar{2}\bar{5}1$) were measured every 2000 s of exposure; the variation in the intensities of these reflections was < 3%. Of the 2386 unique reflections that were measured, 2299 had $I \geq 2{\cdot}5\sigma(I)$ and were taken as observed. The data were corrected for Lorentz and polarization effects; no absorption correction was applied.

The structure was solved with direct methods (*MULTAN*81; Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1981). The initial *E* synthesis revealed the positions of the alprenolol and tartrate ions as well as a molecule of water. After isotropic refinement, peaks in a difference Fourier synthesis indicated that the propylene side chain was disordered; however, separate positions for the alternative conformations of the side chain could not be distinguished. Thus, the two atoms affected, C(08) and C(09), were described with isotropic thermal parameters. The H atoms attached to these disordered atoms were not observed in a difference Fourier synthesis; therefore, the H atoms attached to C(07), C(08) and C(09) were included in the model at calculated positions and were not refined. With the exception of the propylene side chain, the rest of the H atoms were identified in a difference Fourier synthesis and were included in the model at calculated, idealized geometry and refined. The final cycles of refinement included the coordinates of all atoms (except the H atoms bonded to the propylene group), the anisotropic thermal parameters of all of the non-hydrogen atoms except C(08) and C(09), the isotropic thermal parameters of the H atoms, C(08), and C(09), and an isotropic extinction parameter, $g = 5{\cdot}1\,(4) \times 10^{-4}$ (Larson, 1967). The 2363 reflections used in the refinement were the 2299 observed reflections and those unobserved reflections with $|F_c| > 2{\cdot}5\sigma(F_o)$. The function minimized was $\sum w(|F_o| - |F_c|)^2$ where $w^{-1} = |\sigma^2(F_o) + 0{\cdot}0002F_o^2|$. The refinement converged to a maximum shift/e.s.d. = 0·08, $S = 0{\cdot}96$, $R = 0{\cdot}054$, and $wR = 0{\cdot}070$. The maximum peaks in the final difference Fourier synthesis were 1·04 and 0·98 e Å^{-3} which are associated with the disordered atoms C(08) and C(09), respectively.

All calculations except the structure solution were performed with *XRAY*76 (Stewart, 1976). The scattering factors were taken from Cromer & Mann (1968) with the exception of that for the H atom which was taken from Stewart, Davidson & Simpson (1965).

The molecular conformation, atomic labeling scheme, and intermolecular hydrogen-bonding pattern are shown in Fig. 1. The atomic coordinates for the non-hydrogen atoms are given in Table 1 and the bond distances and angles for these atoms are in Table 2.*

Discussion. The conformations found for the propoxinolamine chain in this study and in earlier X-ray studies (Table 3) suggest that there are a limited number of low-energy forms for this chain. Con-

* The anisotropic thermal parameters for the non-hydrogen atoms, the coordinates and thermal parameters for the H atoms and a list of the structure factors have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51644 (19 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

jugation of the lone-pair electrons on the O atom |O(10) in this structure| with the aromatic π system of the ring, coupled with the common presence of an *ortho* substituent on that ring, produces a uniform conformation for the first three atoms of the chain. The torsion angles τ_1 |C(06)–C(01)–O(10)–C(11)| and τ_2 |C(01)–O(10)–C(11)–C(12)| are *trans* in all 14 known crystal structures of alprenolol and propanolol analogues. Another similarity is found for the angle τ_4 |C(11)–C(12)–C(13)–N(14)|; this angle is constrained by the antiperiplanar orientation of the alkylamino and aryloxymethylene groups which results in a *gauche* orientation of the hydroxy substituent in relation to the alkylamino group. The steric preferences for specific conformers around the C(11)–C(12) |τ_3| and C(13)–N(14) |τ_5| bonds are less pronounced, although *trans* conformers are frequently observed. There are only two examples of τ_5 *gauche* (Barrans *et al.*, 1973); but, there are eight examples of *gauche* conformers at τ_3 (Table 3). This uniformity in the conformation of the β-blocker drugs helps to define the relative position of substituents important for protein binding: the amine and the hydroxy groups. The intramolecular separations of the amine and hydroxy groups are constrained to a narrow range of values: between 2·776 (4) and 3·182 (7) Å for O···N.

The orientation of the hydroxyl and amino groups relative to the plane of the aromatic system may show the general arrangement of these three groups when bound to a recognition site. This relative orientation can be defined by the angle between the plane of the

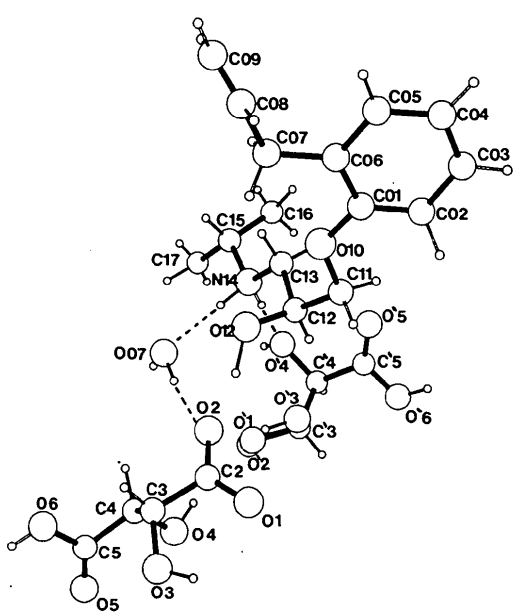


Fig. 1. The molecular conformations of alprenolol cation and tartrate anion. The hydrogen bonds involving alprenolol are shown as dashed lines. The primed tartrate anion is positioned at $1-x, y-\frac{1}{2}, 1-z$. The figure was drawn with the program *PLUTO* (Motherwell, 1979).

Table 1. *Fractional coordinates* ($\times 10^4$) *and* B_{eq} *values* ($\times 10^2$) |*or* B_{iso} *values* ($\times 10^2$) *for* C(08) *and* C(09)| *for the non-hydrogen atoms of alprenolol tartrate hydrate*

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

	x	y	z	B_{eq}(Å^2)
C(01)	5957 (4)	7856 (5)	1327 (2)	242 (13)
C(02)	7690 (5)	7884 (6)	1636 (2)	330 (17)
C(03)	9019 (5)	8236 (8)	1112 (3)	416 (21)
C(04)	8617 (5)	8612 (9)	320 (3)	482 (23)
C(05)	6856 (6)	8594 (8)	23 (2)	435 (21)
C(06)	5501 (5)	8223 (5)	521 (2)	288 (15)
C(07)	3583 (5)	8173 (7)	208 (2)	374 (19)
C(08)	3224 (8)	8898 (9)	−604 (4)	597 (13)
C(09)	2743 (8)	8449 (9)	−1235 (4)	614 (14)
O(10)	4554 (3)	7448 (4)	1766 (1)	257 (10)
C(11)	4858 (4)	7168 (5)	2611 (2)	243 (13)
C(12)	3294 (4)	6267 (5)	2896 (2)	228 (13)
O(12)	1687 (3)	7081 (4)	2756 (1)	273 (11)
C(13)	3134 (5)	4748 (5)	2442 (2)	293 (15)
N(14)	1824 (4)	3706 (4)	2803 (2)	252 (12)
C(15)	1395 (6)	2243 (5)	2319 (2)	325 (16)
C(16)	3055 (8)	1294 (7)	2239 (4)	519 (27)
C(17)	−37 (7)	1361 (7)	2710 (3)	439 (22)
O'(1)	10694 (3)	9742 (3)	4739 (1)	219 (9)
O'(2)	9734 (3)	7647 (3)	4061 (1)	247 (9)
C'(2)	9497 (4)	8848 (4)	4451 (2)	173 (11)
C'(3)	7593 (4)	9295 (4)	4605 (2)	184 (11)
O'(3)	7511 (3)	10569 (3)	5139 (2)	272 (10)
C'(4)	6656 (4)	7921 (4)	4960 (2)	179 (11)
O'(4)	7613 (3)	7384 (3)	5667 (1)	229 (9)
C'(5)	4832 (4)	8428 (4)	5187 (2)	201 (12)
O'(5)	4372 (3)	8529 (4)	5874 (1)	283 (10)
O'(6)	3863 (3)	8796 (3)	4528 (1)	224 (9)
O'(7)	8496 (3)	4895 (4)	3306 (2)	279 (11)

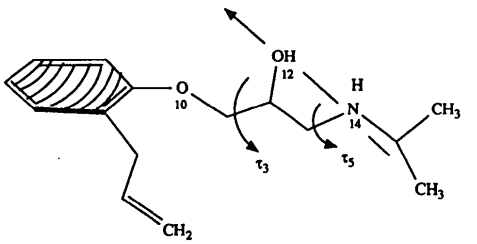
Table 2. *Bond distances* (Å) *and angles* (°) *for the non-hydrogen atoms of alprenolol tartrate hydrate*

C(01)–C(02)	1·383 (6)	C(13)–N(14)	1·493 (6)
C(01)–C(06)	1·397 (5)	N(14)–C(15)	1·522 (6)
C(01)–O(10)	1·371 (6)	C(15)–C(16)	1·517 (8)
C(02)–C(03)	1·403 (7)	C(15)–C(17)	1·505 (8)
C(03)–C(04)	1·370 (7)	O'(1)–C'(2)	1·265 (5)
C(04)–C(05)	1·397 (7)	O'(2)–C'(2)	1·242 (4)
C(05)–C(06)	1·393 (7)	C'(2)–C'(3)	1·532 (4)
C(06)–C(07)	1·518 (6)	C'(3)–O'(3)	1·416 (5)
C(07)–C(08)	1·495 (8)	C'(3)–C'(4)	1·521 (5)
C(08)–C(09)	1·154 (10)	C'(4)–O'(4)	1·420 (6)
O(10)–C(11)	1·428 (4)	C'(4)–C'(5)	1·521 (5)
C(11)–C(12)	1·518 (6)	C'(5)–O'(5)	1·213 (5)
C(12)–O(12)	1·416 (5)	C'(5)–O'(6)	1·320 (6)
C(12)–C(13)	1·515 (6)		

C(02)–C(01)–C(06)	121·8 (3)	C(12)–C(13)–N(14)	111·1 (3)
C(02)–C(01)–O(10)	124·1 (3)	C(13)–N(14)–C(15)	114·6 (3)
C(06)–C(01)–O(10)	114·2 (3)	N(14)–C(15)–C(16)	110·0 (4)
C(01)–C(02)–C(03)	118·6 (3)	N(14)–C(15)–C(17)	109·4 (3)
C(02)–C(03)–C(04)	121·1 (4)	C(16)–C(15)–C(17)	112·9 (4)
C(03)–C(04)–C(05)	119·3 (4)	O'(1)–C'(2)–O'(2)	125·7 (3)
C(04)–C(05)–C(06)	121·3 (4)	O'(1)–C'(2)–C'(3)	116·6 (3)
C(01)–C(06)–C(05)	117·9 (3)	O'(2)–C'(2)–C'(3)	117·7 (3)
C(01)–C(06)–C(07)	119·9 (3)	C'(2)–C'(3)–O'(3)	112·1 (2)
C(05)–C(06)–C(07)	122·2 (3)	C'(2)–C'(3)–C'(4)	109·6 (3)
C(06)–C(07)–C(08)	114·6 (4)	O'(3)–C'(3)–C'(4)	109·1 (3)
C(07)–C(08)–C(09)	134·9 (8)	C'(3)–C'(4)–O'(4)	110·3 (2)
C(01)–O(10)–C(11)	118·5 (2)	C'(3)–C'(4)–C'(5)	108·9 (3)
O(10)–C(11)–C(12)	107·9 (3)	O'(4)–C'(4)–C'(5)	108·6 (2)
C(11)–C(12)–O(12)	112·1 (3)	C'(4)–C'(5)–O'(5)	124·7 (3)
C(11)–C(12)–C(13)	109·4 (3)	C'(4)–C'(5)–O'(6)	109·7 (3)
O(12)–C(12)–C(13)	107·8 (3)	O'(5)–C'(5)–O'(6)	125·6 (3)

Table 3. *Selected intramolecular distances and angles and torsion angles in the arylpropoxinolamine class of β-blockers*

The symbols *g* and *t* indicate *gauche* and *trans* conformations.



Compound	$O_{10}\cdots N$ (Å)	$O_{12}\cdots N$ (Å)	∠Ph,O–N[a] (°)	τ_3	τ_5
Alprenolol class					
alprenolol.$C_4H_6O_6$[b]	4·259 (8)	2·920 (5)	16 (1)	*g*	*t*
alprenolol.HCl[c]	4·13 (12)	2·93 (12)	65 (2)	*g*	*g*
oxprenolol.HCl[d]	4·192 (4)	2·776 (4)	79 (1)	*g*	*t*
penbutolol.HSO_3Me[e]	4·823 (11)	2·788 (11)	77 (2)	*t*	*t*
penbutolol.H_2SO_4	4·810 (5)	2·946 (5)	70 (1)	*t*	*t*
FM24.HCl[g]	4·076 (6)	3·132 (6)	51 (1)	*g*	*t*
acebutolol.HCl[h]	4·218 (4)	2·808 (4)	35 (1)	*g*	*t*
bupranolol.HCl[i]	4·803 (6)	2·996 (6)	36 (1)	*t*	*t*
Propranolol class					
propranolol[j]	4·171 (4)	2·923 (4)	58 (1)	*g*	*t*
propranolol.HCl[c]	4·241 (6)	2·836 (12)	63 (1)	*g*	*g*
propranolol.HCl[k]	4·796 (4)	3·075 (4)	62 (1)	*t*	*t*
pindolol[l]	4·808 (5)	2·816 (5)	67 (1)	*t*	*t*
(OH)benzylpindolol[m]	4·885 (3)	2·832 (3)	63 (1)	*t*	*t*
carteolol.HCl[n]	3·973 (7)	3·182 (7)	72 (1)	*g*	*t*

(*a*) Angle between the plane of the aromatic system (shaded) and the $O_{12}\cdots N_{14}$ line (shown by the arrow); (*b*) this study; (*c*) Barrans *et al.* (1973); (*d*) Leger *et al.* (1977); (*e*) Kobelt & Paulus (1974); (*f*) Gadret *et al.* (1976*b*); (*g*) Leger *et al.* (1982); (*h*) Carpy *et al.* (1979); (*i*) Gadret *et al.* (1975*b*); (*j*) Ammon *et al.* (1977); (*k*) Gadret *et al.* (1975*a*); (*l*) Gadret *et al.* (1976*a*); (*m*) Weber & Petcher (1977); (*n*) Kido *et al.* (1981).

aromatic ring [defined by C(01)–C(06) in this structure] and the line between the hydroxyl oxygen atom [O(12)] and the amino N atom [N(14)]. In the compounds presented in Table 3, the angle is usually in the 50–80° range; in contrast, in this crystal structure, the angle is quite different: 16 (1)°. This exception to the average may be a result of the different chemical composition of this crystal since the anion is a polyoxygenated tartrate with a large number of potential hydrogen-bond donors and acceptors. The hydrogen-bonding pattern for the alprenolol cation is shown in Fig. 1 and all hydrogen bonds are described in Table 4. The hydrogen bonding is dominated by the tartrate ion; one of the bonds from N(14) is formed to the hydroxyl O(4) and the hydrogen bond from O(12) is donated to the carboxylate O(2) atom. N(14) forms a second hydrogen bond to the water molecule. Interestingly, an ion pair interaction, $R_2NH_2^+\cdots{}^-OOC$, is not observed in the structure; this suggests that either multiple hydrogen-bond formation is favored or that spatial matching of the anions in the lattice was more important than an electrostatic interaction. Facilitation of the multiple hydrogen bonds or of the spatial matching may account for the unusual orientation of the side chain relative to the ring.

Table 4. *The geometry of the hydrogen bonds in alprenolol tartrate hydrate*

The equivalent position refers to the hydrogen atom acceptor.

X–H···*Y*	*X*–H (Å)	*X*···*Y* (Å)	H···*Y* (Å)	∠*X*–H···*Y* (°)	Equivalent position
O(12)–H(12)···O(2)	1·12 (7)	2·738 (9)	1·65 (6)	161 (7)	$x-1, y, z$
N(14)–H(141)···O(4)	0·84 (4)	2·791 (5)	1·97 (4)	163 (5)	$1-x, y-\frac{1}{2}, 1-z$
N(14)–H(142)···O(7)	1·02 (5)	2·896 (7)	1·92 (4)	159 (4)	$x-1, y, z$
O(3)–H(3)···O(2)	0·97 (5)	3·006 (8)	2·12 (5)	153 (4)	$2-x, \frac{1}{2}+y, 1-z$
O(4)–H(4)···O(1)	0·94 (5)	2·725 (4)	1·80 (5)	166 (4)	$2-x, y-\frac{1}{2}, 1-z$
O(6)–H(6)···O(1)	0·88 (4)	2·584 (4)	1·70 (4)	176 (4)	$x-1, y, z$
O(7)–H(701)···O(5)	0·77 (6)	2·886 (8)	2·15 (6)	160 (6)	$1-x, y-\frac{1}{2}, 1-z$
O(7)–H(702)···O(2)	0·89 (6)	2·823 (5)	1·95 (6)	165 (5)	x, y, z

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A Neutron Study on the Structure of DL-Aspartic Acid

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Abstract. $C_4H_7NO_4$, $NH_3^+CH(CH_2COOH)COO^-$, M_r = 133·1, monoclinic, $C2/c$, a = 18·96 (1), b = 7·43 (1), c = 9·20 (2) Å, β = 124·1 (1)°, V = 1073 Å^3, Z = 8, D_x = 1·65 g cm^{-3}, neutrons, λ = 1·036 (1) Å, μ = 2·004 cm^{-1}, $F(000)$ = 263 fm, room temperature. For all 648 independent observations with $(\sin\theta)/\lambda \leq 0{\cdot}51$ Å^{-1} $R(F^2)$ is 0·042. The C-atom skeleton is nearly fully extended, with a C—C—C—C torsion angle of 174·2 (2)°. There is a near-perfect staggered conformation across the C—NH_3^+ bond. One of the three N^+—H···O hydrogen bonds is bifurcated with an intramolecular component. The crystal contains chains of aspartic acid molecules in alternately L and D configurations linked through a short and straight O—H···O hydrogen bond between —COOH and —COO^- groups.

Introduction. The present neutron diffraction study on the structure of DL-aspartic acid is part of an ongoing programme aimed at obtaining high-precision data on the H-atom stereochemistry and hydrogen-bonding interactions in amino acids and small peptides [for reviews, see Koetzle & Lehmann (1976) and Ramanadham & Chidambaram (1978)]. A high-precision X-ray study of the structure of DL-aspartic acid was reported earlier by Rao (1973).

Experimental. Tiny crystals of DL-aspartic acid were grown by slow evaporation from an aqueous solution of a commercial grade sample. Large crystals suitable for the neutron experiment were subsequently obtained by seeding a saturated solution with these crystals. A prism-shaped crystal with dimensions 1·8 × 2·3 × 2·9 mm was mounted on the computer-controlled four-circle neutron diffractometer, D4 (Sequeira *et al.*, 1978) at the CIRUS reactor, Trombay, with the prism axis (c axis) coincident with the φ axis of the diffractometer. The cell constants were refined against 2θ values of 30 observations, with $2\theta \leq 26°$, manually centred on the diffractometer. Integrated intensities of 1174 observations with $(\sin\theta)/\lambda \leq 0{\cdot}51$ Å^{-1} were recorded in the θ:2θ (=1:2) step-scan mode with a 2θ step of 0·1°, at a neutron wavelength of 1·036 (1) Å, obtained by using a germanium-(111) monochromator. Two reflections, 400 and 113, were recorded at regular intervals to monitor the consistency of the experimental conditions. The raw data were reduced to a set of F_o^2 values by using the program *TRABS* (Rajagopal & Chidambaram, unpublished), in which absorption corrections were computed by a numerical method (Chidambaram, 1980). Transmission factors were in the range 0·96 to 0·98. The (F_o^2) values were initially computed as $[\sigma^2(\text{count}) + 0{\cdot}04\,|F_o^2|\,|]^{1/2}$. Finally, a set of 648 unique F_o^2 values was obtained by averaging over the repeated ($R_{\text{int}} = 0{\cdot}015$) observations. The ranges of h, k and l for the data set were −19 to 16, 0 to 7 and 0 to 9, respectively.

The X-ray positions of the H atoms were confirmed by relocating them in a neutron F_o Fourier map, phases for which were computed from X-ray positions of the nine non-H atoms. The model, consisting of 16 atoms, was then subjected to full-matrix least-squares refinement, using the Trombay version *TRXFLS* (Rajagopal & Sequeira, unpublished) of the program *ORFLS* (Busing, Martin & Levy, 1962). A scale factor, K, and an isotropic secondary-extinction parameter, G (Zachariasen, 1967), were refined. The quantity minimized was $\sum w(F_o^2 - KF_c^2)^2$, where $w = 1/\sigma^2(F_o^2)$. The neutron scattering lengths used were 6·63 for C, 9·4 for N, 5·75 for O and −3·72 fm for H atoms (*International Tables for X-ray Crystallography*, 1974). All the observations, including the negative F_o^2 values, were considered for inclusion in the refinement. This approach had led earlier to satisfactory results in the refinement of the neutron structure of L-threonine (Ramanadham, Sikka & Chidambaram, 1973). Observations with significantly large ΔF^2 values were carefully excluded at every stage in order to avoid their

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