Discussion. Bond lengths, bond angles and torsion angles are given in Table 2; an *ORTEP* (Johnson, 1965) drawing is shown in Fig. 1. The molecule is a diammonium carboxylate. The two ammonium cations are involved in a total of seven hydrogen bonds (Table 3, Fig. 2). H3 and H4 on the α-NH$_3^+$ participate in three H bonds to carboxylate O atoms; these interactions are listed on the first three lines in Table 3. Although these data and the packing diagram of Fig. 2 suggest that H4 forms a bifurcated hydrogen bond, the N1—H4···O1 contact is especially weak with an H···O distance of 2·50 (3) Å. The H4 bifurcation geometry is close to planar with a sum of 351·6 (4)° for the three angles at H4. The third H atom, H2, is linked to a chloride ion with a N···Cl$^-$ distance of 3·365 (3) Å. Each of the three ε-NH$_3^+$ group H atoms participates in an N—H···Cl$^-$ interaction. Each chloride ion is linked to four N-bonded H atoms in an approximately tetrahedral arrangement; the six H···Cl$^-$···H angles range from 94 to 124°.

It was expected that the C2···C5 distance in thialysine would be larger than the corresponding separation in lysine [L-lysine monohydrochloride dihydrate, (II); Koetzle, Lehmann, Verbist & Hamilton (1972)] because of C—S vs C—C bond-length differences: in (I), C—S = 1·816 (3) and 1·811 (3) Å; in (II), C—C = 1·529 and 1·535 Å. However, the observed C2···C5 distances in the two molecules are reversed with 4·209 (5) Å in thialysine and 5·118 Å in L-lysine. This apparent discrepancy may be accounted for by differences in the side-chain torsion angles. In thialysine, the C2—C3—S—C4 and C3—S—C4—C5 torsion angles are 76·7 (2) and 67·8 (3)°, compared to the corresponding C—C—C—C values of −175·1 nd 173·1° in lysine. A survey of the Cambridge Structural Database (1990) for the open-chain fragment CH—CH$_2$—S—CH$_2$—CH$_2$ was made to determine if there is a conformational preference for the C—C—S—C—C

unit. Values of the torsion angles corresponding to C2—C3—S—C4 and C3—S—C4—C5 were found to occur in two groups. Sixteen were in one group with a range of 59·2–87·0° (average = 77·3°) and four fell into a second group with a range of 152·0–177·4° (average = 170·2°). The corresponding C2···C5 distances were 3·71–4·77 Å (average = 4·30 Å) for the first group and 4·77–5·28 Å (average = 4·95 Å) in the second, a difference of about 0·6 Å. Thialysine can be seen to belong to the more common first group and lysine to the less common second group. Given these differences, one cannot predict with any level of confidence the C2···C5 separation of a thialysine residue in a macromolecule or the effect of the residue on the conformations in the local environment.

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Structure of Nortriptyline Hydrochloride

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Abstract. C$_{19}$H$_{22}$N$^+$.Cl$^-$, $M_r = 299\cdot84$, monoclinic, $P2_1/c$, $a = 5\cdot070$ (2), $b = 34\cdot088$ (5), $c = 9\cdot976$ (1) Å, $\beta = 90\cdot74$ (2)°, $V = 1724\cdot0$ Å^3, $Z = 4$, $D_x = 1\cdot16$ g cm^{-3}, λ(Mo $K\alpha_1$) = 0·70930 Å, $\mu = 2\cdot2$ cm^{-1}, $F(000) = 640$, $T = 295$ K, final $R = 0\cdot046$ for 1381 observed reflections. The nortriptyline molecule crys-

tallized with a 'butterfly' fold angle of 124·3 (2)° and an extended propylamino side chain. The amino nitrogen is involved in hydrogen bonds to two different chloride ions.

Introduction. Nortriptyline, 3-(10,11-dihydro-5*H*-dibenzo[*a*,*d*]cyclohepten-5-ylidene)-*N*-methyl-1-propanamine (I), is the active metabolite of amitriptyline, a dibenzocycloheptene derivative tricyclic antidepressant drug. Pharmacological studies indicate that it inhibits the activity of histamine and acetylcholine and that it interferes with the transport, release and storage of catecholamines. In order to better understand the pharmacological activity of other classes of tricyclic compounds (phenothiazines), we have been studying the structural characteristics of a series of chemically similar molecules (Klein & Conrad, 1986; Southall, Malmstrom & Klein, 1987; Harris & Klein, 1987).

(I)
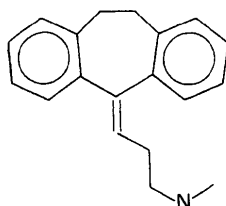
Experimental. The title compound was purchased from Sigma Chemical Company and recrystallized from ethanol to give a colorless crystal with approximate dimensions 0·25 × 0·35 × 0·40 mm. Enraf–Nonius CAD-4 diffractometer with graphite-crystal-monochromatized Mo $K\alpha$ radiation. Unit-cell dimensions and systematic absences ($h0l$), $l = 2n + 1$ and $0k0$, $k = 2n + 1$ uniquely determined the space group as $P2_1/c$. Unit-cell dimensions were determined by least-squaares fit of 25 reflections with $22 < 2\theta < 41°$ measured on diffractometer. Three-dimensional intensity data collected in $\omega:2\theta$ scan mode; total of 2249 independent reflections, 1381 observed with $I > 3\sigma(I)$; $1 < 2\theta < 40°$; $(\sin\theta/\lambda)_{max} = 0·48 \text{ Å}^{-1}$; $-4 \le h \le 4$, $0 \le k \le 32$, $0 \le l \le 10$. Data corrected for Lorentz and polarization effects. Three standard reflections measured every 2 h during data collection (122, 200, 002) showed no significant change in intensity. Absorption as a function of ψ minimal. Symmetry-equivalent reflections averaged, $R_{int} = 0·017$. Structure solved by direct methods using $MULTAN11/82$ (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1982). Hydrogen atoms located on Fourier difference map. Full-matrix least-squares refinement on F of 21 anisotropic non-hydrogen atoms and 22 isotropic hydrogen atoms (278 variables). No extinction correction. Final $R = 0·046$, $wR = 0·055$ where $w = 1/\sigma(F)^2$,

Table 1. *Positional parameters and equivalent isotropic thermal parameters with e.s.d.'s in parentheses*

Anisotropically refined atoms are given in the form of the equivalent isotropic displacement parameter defined as: $(4/3)[a^2\beta(1,1) + b^2\beta(2,2) + c^2\beta(3,3) + ab(\cos\gamma)\beta(1,2) + ac(\cos\beta)\beta(1,3) + bc(\cos\alpha)\beta(2,3)]$.

	x	y	z	$B(\text{Å}^2)$
Cl(1)	0·2286 (2)	0·23903 (5)	0·1487 (1)	6·40 (3)
N(1)	−0·1119 (7)	0·25606 (9)	−0·1007 (3)	4·10 (8)
C(1)	−0·253 (1)	0·0656 (1)	0·1501 (5)	5·9 (1)
C(2)	−0·390 (1)	0·0870 (2)	0·2425 (5)	6·4 (1)
C(3)	−0·533 (1)	0·1195 (1)	0·2025 (4)	5·7 (1)
C(4)	−0·5299 (9)	0·1305 (1)	0·0695 (4)	4·7 (1)
C(5)	−0·3897 (8)	0·1097 (1)	−0·0241 (4)	3·57 (9)
C(6)	−0·2520 (9)	0·0764 (1)	0·0152 (4)	4·5 (1)
C(7)	−0·1121 (9)	0·0529 (1)	−0·0886 (5)	5·7 (1)
C(8)	−0·302 (1)	0·0307 (1)	−0·1812 (5)	6·2 (1)
C(9)	−0·4861 (9)	0·0539 (1)	−0·2704 (4)	4·8 (1)
C(10)	−0·629 (1)	0·0335 (1)	−0·3696 (5)	6·4 (1)
C(11)	−0·799 (1)	0·0501 (1)	−0·4572 (5)	7·1 (1)
C(12)	−0·837 (1)	0·0895 (2)	−0·4516 (5)	6·0 (1)
C(13)	−0·6975 (9)	0·1111 (1)	−0·3583 (4)	5·4 (1)
C(14)	−0·5227 (8)	0·0946 (1)	−0·2668 (4)	4·1 (1)
C(15)	−0·3879 (8)	0·1206 (1)	−0·1684 (4)	3·61 (9)
C(16)	−0·2755 (8)	0·1537 (1)	−0·2110 (4)	3·80 (9)
C(17)	−0·1340 (8)	0·1839 (1)	−0·1292 (4)	4·11 (9)
C(18)	−0·2859 (8)	0·2220 (1)	−0·1287 (4)	4·0 (1)
C(19)	−0·258 (1)	0·2932 (1)	−0·0883 (5)	6·5 (1)

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

N(1)—C(18)	1·482 (4)		C(5)—C(15)	1·486 (4)
N(1)—C(19)	1·472 (4)		C(6)—C(7)	1·494 (4)
C(1)—C(2)	1·373 (5)		C(7)—C(8)	1·526 (5)
C(1)—C(6)	1·395 (4)		C(8)—C(9)	1·507 (5)
C(2)—C(3)	1·380 (5)		C(9)—C(10)	1·403 (5)
C(3)—C(4)	1·379 (4)		C(9)—C(14)	1·400 (4)
C(4)—C(5)	1·377 (4)		C(10)—C(11)	1·347 (6)
C(5)—C(6)	1·388 (4)		C(11)—C(12)	1·358 (5)
C(12)—C(13)	1·375 (5)		C(15)—C(16)	1·335 (4)
C(13)—C(14)	1·383 (5)		C(16)—C(17)	1·493 (4)
C(14)—C(15)	1·482 (4)		C(17)—C(18)	1·511 (4)

C(18)—N(1)—C(19)	113·0 (3)		C(5)—C(6)—C(7)	119·0 (3)
C(2)—C(1)—C(6)	121·0 (4)		C(6)—C(7)—C(8)	112·6 (3)
C(1)—C(2)—C(3)	120·1 (4)		C(7)—C(8)—C(9)	118·5 (3)
C(2)—C(3)—C(4)	119·0 (4)		C(8)—C(9)—C(10)	117·7 (4)
C(3)—C(4)—C(5)	121·7 (3)		C(8)—C(9)—C(14)	125·9 (3)
C(4)—C(5)—C(6)	119·5 (3)		C(10)—C(9)—C(14)	116·3 (4)
C(4)—C(5)—C(15)	122·6 (3)		C(9)—C(10)—C(11)	124·7 (4)
C(6)—C(5)—C(15)	117·9 (3)		C(10)—C(11)—C(12)	118·6 (4)
C(1)—C(6)—C(5)	118·7 (3)		C(11)—C(12)—C(13)	119·1 (4)
C(1)—C(6)—C(7)	122·3 (3)		C(12)—C(13)—C(14)	123·3 (4)
C(9)—C(14)—C(13)	118·0 (3)		C(14)—C(15)—C(16)	119·3 (3)
C(9)—C(14)—C(15)	123·3 (3)		C(15)—C(16)—C(17)	127·8 (3)
C(13)—C(14)—C(15)	118·7 (3)		C(16)—C(17)—C(18)	110·7 (3)
C(5)—C(15)—C(14)	118·9 (2)		N(1)—C(18)—C(17)	111·8 (3)
C(5)—C(15)—C(16)	121·8 (3)			

$\sigma(F)^2 = [\sigma(I)_{cs}^2 + (0·02)^2(F^2)^2]$ and cs means from counting statistics, $S = 2·60$. In final least-squares cycle $(\Delta/\sigma)_{max} < 0·1$. Maximum and minimum peaks in the difference Fourier map were 0·248 and $-0·247 \text{ e Å}^{-3}$, respectively. Scattering factors, taken from *International Tables for X-ray Crystallography* (1974, Vol. IV, pp. 71–151), were corrected for anomalous-scattering contributions. CAD-4 *SDP* programs used (Frenz, 1978).

Discussion. Final fractional coordinates for the non-hydrogen atoms are given in Table 1.* The numbering system for the molecule is shown in Fig. 1. Bond lengths and angles are in Table 2. The title compound crystallizes as the HCl salt with one molecule in the asymmetric unit and the N-methylpropylamine nitrogen atom [N(1)] protonated. There is a hydrogen bond between the protonated propylamine nitrogen atom and the chloride ion [N(1)···Cl(1) 3·066 (3) Å; N(1)—H···Cl(1) 176·9 (27)°]. There is another hydrogen bond between the nitrogen atom and the chloride ion in an equivalent position (x, ½ − y, ½ + z) [N(1)···Cl(1) 3·061 (3) Å; N(1)—H···Cl(1) 170·2 (28)°]. Each of these hydrogen bonds involves
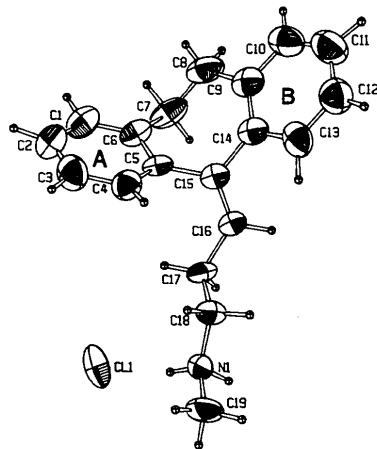

Fig. 1. Molecular structure and numbering system for one molecule of nortriptyline hydrochloride. The thermal ellipsoids of non-hydrogen atoms are drawn at 50% probability levels.
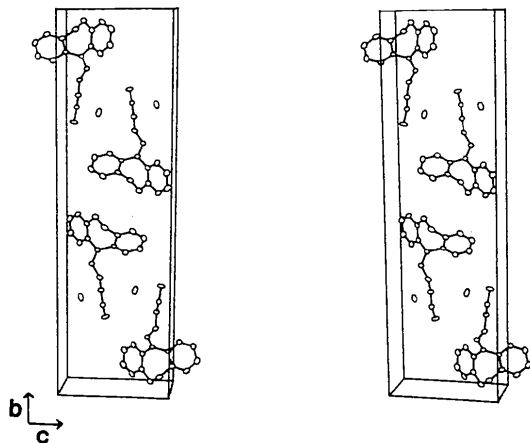

Fig. 2. Stereoscopic packing diagram of the contents of the unit cell looking down the a axis.

a different hydrogen atom on the same nitrogen. The propylamino side chain is in an extended conformation. A stereoscopic packing diagram can be found in Fig. 2.

The tricyclic ring system consists of two aromatic rings separated by a seven-membered ring with a fold angle of 124·3 (2)° between the least-squares planes through the aromatic rings. Ring A includes C(1), C(2), C(3), C(4), C(5) and C(6) and ring B includes C(9), C(10), C(11), C(12), C(13) and C(14). The amount of 'twist' in the ring system is reflected in the angles between the aromatic ring planes and the C(7)–C(8)–C(15) plane. These are 116·8 (2) and 9·1 (13)° for rings A and B, respectively. These values are similar in magnitude to those obtained from some dibenz[b,f]azepines and related molecules (Post & Horn, 1977). In solution, these tricyclic molecules are known to undergo a hetero-ring inversion and ethano-bridge flip [by rotation about the bond equivalent of C(7)—C(8)] to give an equilibrium state of conformational isomers (Abraham, Kricka & Ledwith, 1974; Ellefson, Swenton, Bible & Green, 1976). One should keep in mind, therefore, that the solid-state conformation of nortriptyline hydrochloride reported here is only one of two equilibrium conformations.

A parameter which has been previously reported in describing the spatial requirements for dopamine receptor blockade by neuroleptic drug molecules is the distance between aromatic ring centers and the amine nitrogen atom (Horn, Post & Kennard, 1975). In this case the N(1)···ring A distance is 5·96 Å and N(1)···ring B is 7·33 Å.

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