Acta Cryst. (1987). C**43**, 1010–1011

Structure of an Antisickling Agent, L-Phenylalanyl-3-aminopyridinium Dichloride Monohydrate

BY S. K. BURLEY

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA 02139, *USA and Harvard Medical School (Health and Sciences and Technology Division), 25 Shattuck Street, Boston, MA* 02115, *USA*

AND A. H.-J. WANG

Department of Biology, Massachusetts Institute of Technology, Cambridge, MA 02139, *USA*

(*Received* 27 *September* 1986; *accepted* 23 *December* 1986)

Abstract. L-Phenylalanyl-3-aminopyridinium dichloride monohydrate, $C_{14}H_{17}N_3O^{2+}.2Cl^-.H_2O$, $M_r = 332{\cdot}2$, orthorhombic, $P2_12_12_1$, $a = 7{\cdot}335\ (2)$, $b = 18{\cdot}824\ (4)$, $c = 11{\cdot}685\ (4)$ Å, $V = 1613{\cdot}4\ (2)$ Å^3, $Z = 4$, $D_x = 1{\cdot}367$ g cm^{-3}, $\lambda(\text{Cu } K\alpha) = 1{\cdot}5418$ Å, $\mu = 35{\cdot}49$ cm^{-1}, $F(000) = 706$, $T = 283$ K, $R = 0{\cdot}033$ for 996 unique observed reflections. The molecule adopts an extended conformation. Peptide torsion angles: L-Phe: $\psi = 164{\cdot}8\ (5)$, $\omega = 173{\cdot}7\ (5)$, $\chi^1 = -62{\cdot}4\ (6)$, $\chi^{2,1} = -78{\cdot}9\ (7)°$. Aminopyridinium: C(L-Phe)—N(aminopyridinium)—C(3)(aminopyridinium)—C(2)(aminopyridinium) = 13·9 (6)°. Intermolecular hydrogen bonds: N(L-Phe)—H···O(*W*) = 2·711 (7), N(L-Phe)—H···Cl(2) = 3·196 (5), N(L-Phe)—H···Cl(2′) = 3·259 (5), N(amino)—H···Cl(1) = 3·092 (5), N(1)-(pyridinium)—H···Cl(2) = 3·073 (5), O(*W*)—H···Cl(1) = 3·065 (6), O(*W*)—H···Cl(2) = 3·229 (6) Å. Finally, there is a 'hydrogen bond' between O(L-Phe) and C(6)(pyridinium) [C(6)(pyridinium)—H···O(L-Phe) = 3·155 (6) Å].

Experimental. Rectangular crystal from aqueous solution by evaporation, 0·3 × 0·3 × 0·6 mm, Nicolet *P*3 diffractometer, Ni-filtered radiation, ω-scan method, $(\sin\theta)/\lambda < 0{\cdot}58$ Å^{-1}, lattice parameters from the 2θ values of 10 reflections with $41 < 2\theta < 58°$, no absorption corrections, $h = 0$ to 10, $k = 0$ to 30, $l = 0$ to 20, reflections 0,10,0, 026 and 361 as intensity standards, intensity variation <2%. 1344 unique reflections measured, 348 excluded during refinement [$F < 3\sigma(F)$]. Structure solved by heavy-atom phasing from two chlorides, first *F* map revealed the positions of all non-hydrogen atoms, least-squares refinement using *SHELX*76 (Sheldrick, 1976), *F* magnitudes, unit weights; isotropic and then anisotropic temperature factors gave $R = 0{\cdot}033$ and $S = 1{\cdot}01$ with H atoms at positions calculated or located by difference synthesis. 193 parameters varied: *x*, *y*, *z*, U_{ij} for non-H atoms and three single *U*'s, one each for all phenyl and pyridine-ring H atoms, for all backbone H atoms, and for the three amino terminal protons, respectively. In final

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

$U_{eq} = \frac{1}{3}(U_{11} + U_{22} + U_{33})$.

	x	*y*	*z*	U_{eq}(Å^2)
Cl(1)	0·5948 (3)	0·32906 (8)	0·93875 (14)	0·055
Cl(2)	0·8508 (2)	0·15540 (7)	0·48964 (12)	0·045
N(*F*1)	0·9745 (7)	−0·2295 (2)	0·8418 (4)	0·038
C*A*(*F*1)	0·9142 (8)	−0·2449 (3)	0·7223 (5)	0·036
C*B*(*F*1)	0·7270 (8)	−0·2807 (3)	0·7216 (5)	0·037
C*G*(*F*1)	0·7268 (8)	−0·3520 (3)	0·7818 (5)	0·038
C*D*1(*F*1)	0·6554 (10)	−0·3591 (3)	0·8911 (5)	0·053
C*E*1(*F*1)	0·6454 (12)	−0·4247 (4)	0·9439 (6)	0·064
C*Z*(*F*1)	0·7096 (11)	−0·4838 (4)	0·8874 (7)	0·068
C*E*2(*F*1)	0·7819 (10)	−0·4781 (3)	0·7789 (7)	0·062
C*D*2(*F*1)	0·7930 (9)	−0·4118 (3)	0·7278 (6)	0·049
C(*F*1)	0·9030 (8)	−0·1722 (3)	0·6632 (5)	0·037
O(*F*1)	0·8978 (6)	−0·11734 (19)	0·7153 (3)	0·046
N(*A*2)	0·8939 (6)	−0·1790 (2)	0·5462 (4)	0·039
C3(*P*2)	0·8652 (9)	−0·1222 (3)	0·4706 (5)	0·036
C2(*P*2)	0·8797 (9)	−0·0521 (3)	0·5008 (5)	0·047
N1(*P*2)	0·8492 (8)	−0·0020 (2)	0·4201 (5)	0·051
C6(*P*2)	0·8116 (10)	−0·0164 (3)	0·3109 (6)	0·053
C5(*P*2)	0·7983 (9)	−0·0861 (3)	0·2775 (6)	0·049
C4(*P*2)	0·8267 (8)	−0·1390 (3)	0·3564 (5)	0·041
O(*W*)	0·1920 (6)	0·1694 (3)	0·3163 (4)	0·080

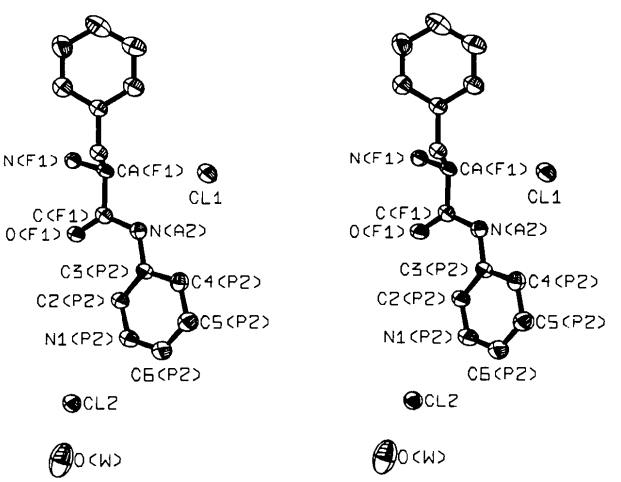

Fig. 1. Stereodrawing of the molecular structure showing the numbering scheme. The thermal ellipsoids are drawn at the 50% level.

0108-2701/87/051010–02$01.50

cycle $(\Delta/\sigma)_{max} = 0.033$. Final difference synthesis $(\Delta\rho)_{max} = 0.26$, $(\Delta\rho)_{min} = -0.25$ e Å^{-3}. Scattering factors from *International Tables for X-ray Crystallography* (1974). Table 1* gives the atom parameters. Fig. 1 shows the molecular structure and the atomic numbering scheme drawn by *ORTEP*II (Johnson, 1976).

Related literature. The compound was synthesized according to Altman, Gorecki, Wilchek, Votano & Rich (1983). Votano, Altman, Wilchek, Gorecki & Rich (1984) have described the effect of this compound on erythrocytes containing deoxyhemoglobin S.

We thank Professor G. A. Petsko for his useful discussion. One of us (SKB) was supported by a Natural Sciences and Engineering Research Council of Canada postdoctoral fellowship.

* Lists of structure-factor amplitudes, anisotropic thermal parameters, bond lengths and bond angles, and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43676 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

ALTMAN, J., GORECKI, M., WILCHEK, M., VOTANO, J. R. & RICH, A. (1983). *J. Med. Chem.* **27**, 596–600.

International Tables for X-ray Crystallography (1974). Vol. IV, pp. 72–75. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)

JOHNSON, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee.

SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.

VOTANO, J. R., ALTMAN, J., WILCHEK, M., GORECKI, M. & RICH, A. (1984). *Proc. Natl Acad. Sci. USA*, **81**, 3190–3194.

Acta Cryst. (1987). C**43**, 1011–1012

The Structure of an Antisickling Agent, L-Phenylalanine Benzyl Ester Monochloride

BY A. H.-J. WANG

Department of Biology, Massachusetts Institute of Technology, Cambridge, MA 02139, *USA*

AND S. K. BURLEY

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA 02139, *USA and Harvard Medical School (Health and Sciences and Technology Division), 25 Shattuck Street, Boston, MA* 02115, *USA*

(*Received* 27 *August* 1986; *accepted* 23 *December* 1986)

Abstract. L-Phenylalanine benzyl ester monochloride, $C_{16}H_{18}NO_2^+.Cl^-$, $M_r = 291.8$, orthorhombic, $P2_12_12_1$, $a = 5.221$ (1), $b = 8.674$ (1), $c = 33.880$ (3) Å, $V = 1534.7$ (1) Å^3, $Z = 4$, $D_x = 1.262$ g cm^{-3} λ(Cu $K\alpha$) $= 1.5418$ Å, $\mu = 20.8$ cm^{-1}, $F(000) = 616$, $T = 283$ K, $R = 0.052$ for 1247 unique observed reflections. The molecule adopts a compact and amphipathic conformation. Peptide torsion angles: L-Phe: $\psi_{T'} = 37.5$ (4), Cα(L-Phe)–C(L-Phe)–O(benzyl)–C(benzyl) $= -176.5$ (5), $\chi^1 = -171.4$ (6), $\chi^{2,1} = 65.9$ (8)°; benzyl: C(L-Phe)–O(benzyl)–C(benzyl)–C(1)(benzyl) $= -153.2$ (7), O(benzyl)–C(benzyl)–C(1)(benzyl)–C(2)(benzyl) $= -47.5$ (8)°. Intramolecular edge-to-face interaction between phenyl rings: phenyl(L-Phe)–phenyl(benzyl) centroid separation = 5.07 (1) Å and dihedral angle = 79.7 (8)°. Intermolecular hydrogen bonds: N(L-Phe)–H···O(L-Phe′) = 2.839 (6), N(L-Phe)–H···Cl = 3.252 (4) and N(L-Phe)–H···Cl′ = 3.080 (4) Å. Intermolecular edge-to-face interaction between phenyl rings: phenyl(L-Phe)–phenyl(benzyl′) $d = 5.00$ (1) Å and dihedral angle = 79.7 (8)°.

Experimental. Rectangular crystal by evaporation from aqueous solution at neutral pH, 0.1 × 0.2 × 0.6 mm, Nicolet *P*3 diffractometer, Ni-filtered radiation, ω-scan method, $(\sin\theta)/\lambda < 0.58$ Å^{-1}, lattice parameters from the 2θ values of 15 reflections with $40.40 < 2\theta < 49.54°$, no absorption correction, $h = 0$ to 10, $k = 0$ to 10, $l = 0$ to 40, reflections 0,0,16, 020 and 400 as intensity standards, intensity variation < 2%. 1550 unique reflections measured, 303 excluded during refinement [$F < 2\sigma(F)$], chloride counterion position from Patterson function, other non-H atoms from Fourier syntheses based on phases defined by chloride counterion; least-squares refinement using *SHELX*76 (Sheldrick, 1976), *F* magnitudes, unit weights; isotropic and then anisotropic temperature factors gave $R = 0.052$ and $S = 0.86$ with H atoms at positions

0108-2701/87/051011–02$01.50