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Structure and Absolute Configuration of (*R*)-*N*-Chloroacetyl-(+)-3,3,3-trifluoro-2-aminoisobutyric acid,* $C_6H_7ClF_3NO_3$

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Abstract. $M_r = 233{\cdot}57$, monoclinic, $P2_1$, $a = 10{\cdot}258$ (3), $b = 8{\cdot}357$ (3), $c = 5{\cdot}749$ (3) Å, $\beta = 96{\cdot}45$ (3)°, $V = 489{\cdot}8$ (3) Å^3, $Z = 2$, $D_x = 1{\cdot}58$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71073 Å, $\mu = 4{\cdot}3$ cm^{-1}, $F(000) = 236$, $T = 296$ K. Final $R = 0{\cdot}042$ for 1407 observed reflections. The R absolute configuration was determined by least-squares refinement of 545 Friedel pairs including the parameter η as a multiplier of f''. The title compound is a heavy-atom derivative of (+)-3,3,3-trifluoro-2-aminoisobutyric acid, a potent irreversible inhibitor of *Pseudomonas cepacia* dialkylamino acid transaminase.

Introduction. *Pseudomonas cepacia* dialkylamino acid transaminase catalyzes simultaneous decarboxylation and transamination of various dialkylamino acids, such as 2-aminoisobutyric acid (Lamartiniere, Itoh & Dempsey, 1971; Sato, Honma & Shimomura, 1978). A fluorinated substrate analog, racemic 3,3,3-trifluoro-2-aminoisobutyric acid, has been shown to be an irreversible inhibitor of this enzyme (Keller & O'Leary, 1979). Recently this compound has been resolved and the (+)-isomer shown to be more active against the enzyme than the racemate (Keller, 1982). The present X-ray study was undertaken so that configurational and structural comparisons between the inhibitor isomers and substrate molecules can be made.

Experimental. Crystals of the title compound suitable for X-ray diffraction studies were grown from water. A rectangular parallelepiped-shaped crystal, 0·90 × 0·45 × 0·30 mm, mounted with its longest dimension parallel to the φ axis of a computer-controlled Nicolet $P\bar{1}$ autodiffractometer, graphite monochromator, 15 reflections used for measuring lattice parameters, 1783 independent reflections having $2\theta_{MoK\bar{\alpha}} < 63{\cdot}7°$ ($-14 \le h \le 15, 0 \le k \le 12, 0 \le l \le 8$) measured with ω scan for each reflection between ω settings 0·50° above and below the calculated $K\bar{\alpha}$ doublet value, background counts measured at ω settings 1·0° above and below the calculated $K\bar{\alpha}$ doublet value for each reflection; six standard reflections showed no intensity variation; intensities reduced without an absorption correction to relative squared amplitudes, $|F_o|^2$, by means of standard Lorentz and polarization corrections; structure solved by direct methods with Nicolet *SHELXTL* (Sheldrick, 1981) software; the 14 non-H atoms in the R configuration were located in an E-map calculated from a trial set of phases; isotropic least-squares refinement of the structural parameters for these 14 non-H atoms gave R_1 (unweighted, based on F) = 0·122 and R_2 (weighted, based on F) = 0·140 for 595 independent reflections having $2\theta_{MoK\alpha} < 43°$ and $I > 3\sigma(I)$; anisotropic refinement converged to $R_1 = 0{\cdot}049$ and $R_2 = 0{\cdot}052$. These and all subsequent structure-factor calculations employed recent tabulations of atomic form factors and an anomalous-dispersion correction (*International Tables for X-ray Crystallography*, 1974) to the scattering factors of the Cl and F atoms. Blocked cascade least-squares techniques (with a maximum block size of 103 variables/cycle) and weights derived from counting statistics were used for all refinement cycles, $w = 1/\sigma_F^2$ where $\sigma_F = \{[\sigma(F_o)]^2 + (0{\cdot}01|F_o|)^2\}^{-1/2}$. A difference Fourier synthesis calculated at this point contained peaks which corresponded to chemically anticipated positions for the seven H atoms. All additional least-squares cycles refined H atoms with isotropic thermal parameters and non-H atoms with anisotropic thermal parameters. The final refinement employed the more complete data set [$2\theta_{MoK\bar{\alpha}} < 63{\cdot}7°$, $I > 3\sigma(I)$, 1407 independent (non-Friedel pair) reflections] and a variable extinction correction and converged to $R_1 = 0{\cdot}042$ and $R_2 = 0{\cdot}043$; max. shift for all parameters 0·02 σ, no peaks in final difference Fourier map above the noise level (0·32 e Å^{-3}).

The correctness of the R enantiomeric description was checked in two ways with a separate set of 545 Friedel pairs (1090 total reflections) having $2\theta_{MoK\bar{\alpha}} < 43°$ and $I > 3\sigma(I)$. The η multiplier of f'' (Rogers, 1981; Sheldrick, 1981) was first included as a variable

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in the least-squares refinement with these Friedel pairs and refined to a value of 1·13 (22). Then η was fixed at 1·00 and both enantiomers were refined; the R configuration gave $R_1 = 0{\cdot}027$ and $R_2 = 0{\cdot}028$ while the S configuration gave $R_1 = 0{\cdot}029$ and $R_2 = 0{\cdot}030$.

Table 1. *Atomic coordinates* ($\times 10^4$) *and equivalent isotropic thermal parameters* ($\times 10^3$) *for the non*-H *atoms with e.s.d.'s in the last significant digit in parentheses*

Atoms are labeled in agreement with Fig. 1.

	x	y	z	B_{eq}*(Å^2)
Cl	3330 (2)	0 †	−304 (3)	94 (1)
F(1)	1488 (2)	2659 (3)	5463 (3)	45 (1)
F(2)	345 (2)	4781 (3)	5597 (3)	48 (1)
F(3)	84 (2)	3273 (3)	2567 (3)	53 (1)
O(1)	3004 (2)	5488 (3)	6931 (3)	36 (1)
O(2)	4002 (2)	6161 (4)	3816 (3)	41 (1)
O(1′)	4001 (2)	2592 (4)	3946 (3)	39 (1)
N	2567 (2)	3832 (4)	1323 (3)	25 (1)
C(1)	3072 (2)	5495 (4)	4853 (4)	26 (1)
C(2)	2002 (2)	4838 (4)	3014 (4)	23 (1)
C(3)	981 (3)	3881 (4)	4184 (5)	32 (1)
C(4)	1314 (3)	6254 (5)	1692 (5)	37 (1)
C(1′)	3548 (2)	2799 (4)	1908 (4)	27 (1)
C(2′)	4040 (3)	1899 (4)	−96 (5)	36 (1)

* Defined as one third of the trace of the orthogonalized $\mathbf{B}_{ij}$ tensor.

† This parameter was used to define the origin of the unit cell along the b axis and is listed without an e.s.d.

Table 2. *Intramolecular bond distances* (Å) *and angles* (°) *between non*-H *atoms with e.s.d.'s in parentheses*

C(1)–O(1)	1·205 (3)	C(1′)–O(1′)	1·223 (3)
C(1)–O(2)	1·305 (4)	C(1′)–C(2′)	1·510 (4)
C(1)–C(2)	1·537 (3)	C(2′)–Cl	1·745 (3)
C(2)–C(3)	1·531 (4)	C(3)–F(1)	1·330 (4)
C(2)–C(4)	1·535 (4)	C(3)–F(2)	1·330 (4)
C(2)–N	1·454 (3)	C(3)–F(3)	1·333 (3)
N–C(1′)	1·340 (4)		
C(2)–C(1)–O(1)	124·3 (2)	C(2)–C(3)–F(1)	113·6 (2)
C(2)–C(1)–O(2)	109·9 (2)	C(2)–C(3)–F(2)	112·3 (3)
O(1)–C(1)–O(2)	125·6 (2)	C(2)–C(3)–F(3)	110·2 (2)
C(1)–C(2)–C(3)	110·8 (2)	F(1)–C(3)–F(2)	106·5 (2)
C(1)–C(2)–C(4)	108·6 (3)	F(1)–C(3)–F(3)	106·8 (3)
C(3)–C(2)–C(4)	108·7 (2)	F(2)–C(3)–F(3)	107·1 (2)
C(1)–C(2)–N	111·0 (2)	C(2′)–C(1′)–O(1′)	122·5 (3)
C(3)–C(2)–N	109·6 (3)	C(2′)–C(1′)–N	115·8 (3)
C(4)–C(2)–N	108·1 (2)	O(1′)–C(1′)–N	115·8 (2)
		C(1′)–C(2′)–Cl	109·4 (2)
		C(2)–N–C(1′)	123·3 (2)

Discussion. Positional and thermal parameters are presented in Table 1 and selected bond lengths and bond angles are presented in Table 2. An *ORTEP* drawing (Johnson, 1976) of the molecule is shown in Fig. 1. Close intermolecular contacts involving H are listed in Table 3.*

The observed structure differs in some respects from the reported structures of *N*-chloroacetyl-DL-alanine (Cole, 1970) and (*R*)-*N*-chloroacetylisovaline (Bosch, Bruckner, Jung & Winter, 1982). For example, in the title structure the backbone angle at C(2) [C(1)–C(2)–N = 111°] is close to the usual value of 110° (Pauling, 1960) whereas the same angle in (*R*)-*N*-chloroacetylisovaline is about 104° (Bosch *et al.*, 1982). Also, both Bosch *et al.* (1982) and Cole (1970) report Cl atoms and carboxylate carbonyl O atoms aligned for close approach to the amide H. Bosch *et al.* (1982) interpret this conformation as due to intramolecular bifurcated hydrogen bonds with N as donor and carbonyl O and Cl as acceptors. In the present structure such an intramolecular hydrogen bond is impossible, since the carboxylate group is on the opposite side of the molecule from the N–H bond and the C(2)–Cl bond is orthogonal to the N–H bond. In

* Tables containing structure-factor amplitudes for 1407 reflections, anisotropic thermal parameters for non-H atoms, dihedral angles, positional and thermal parameters of H atoms, and bond angles involving H atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39299 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

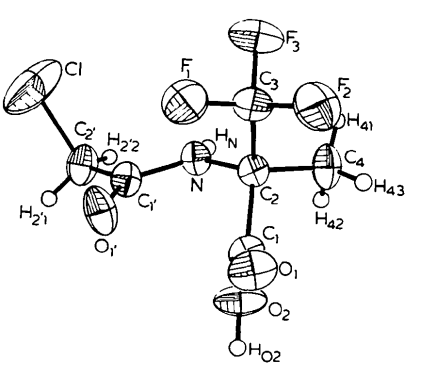

Fig. 1. *ORTEP* drawing of (*R*)-*N*-chloroacetyl-(+)-3,3,3-trifluoro-2-aminoisobutyric acid.

Table 3. *Close contacts involving* H *atoms*

The numbers in parentheses are the e.s.d.'s in the last significant digit.

*D**	*A*	*D*···*A*	H···*A*	*D*–H···*A*	H–*D*···*A*	H···*A*–*C*†	Asymmetric unit of *A*
O(2)–H(O2)	O(1′)	2·586 (3) Å	1·75 (3) Å	159 (2)°	14 (2)°	131 (2)°	$1-x, \frac{1}{2}+y, 1-z$
N–H(N)	O(1)	2·957 (3)	2·26 (3)	146 (2)	26 (2)	145 (2)	$x, y, z-1$

* The H atom involved in the interaction is also indicated.

† The symbol *C* is used to denote the C atoms which are covalently bonded to the acceptor O atoms.

fact, as indicated in Table 3, each molecule in the crystal participates in two intermolecular hydrogen bonds: one with carboxylate as donor and chloroacetyl O of an adjacent molecule as acceptor and a second with N as donor and the carboxylate carbonyl O of a different adjacent molecule as acceptor. A similar intermolecular hydrogen-bonding network has been observed in crystalline *N*-acetylglycine (Levy, Peterson & Schomaker, 1957).

The observed *R* configuration of *N*-chloroacetyl-(+)-3,3,3-trifluoro-2-aminoisobutyric acid places the parent amino acid in the same stereochemical family as D-alanine, since both molecules have the same configuration of methyl, amino and carboxylate groups. This is relevant to the finding of Bailey, Chotamangsa & Vuttivej (1970) that D- and L-alanine are both substrates for the *P. cepacia* dialkylamino acid transaminase but are processed differently by the enzyme: D-alanine is decarboxylated and transaminated to acetaldehyde, but L-alanine is transaminated to pyruvate. Stereospecificity has also been observed in the reaction of the transaminase with the 3,3,3-trifluoro-2-aminoisobutyric acid enantiomers: the (+)-isomer (here shown to have the *R* configuration) causes rapid irreversible inactivation of the transaminase but the (−)-isomer (*S*) inactivates slowly or not at all (Keller, 1982). Also, inactivation of the transaminase by the racemic trifluoroamino acid is accompanied by decarboxylation (Keller & O'Leary, 1979). These facts suggest a similar mode of binding and processing for D-alanine and the *R* isomer of 3,3,3-trifluoro-2-aminoisobutyric acid by the dialkylamino acid transaminase.

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Structures of 3-(*p*-Ethoxyphenyl)sydnone (1), $C_{10}H_{10}N_2O_3$, and 3-(*p*-Tolyl)sydnone (2), $C_9H_8N_2O_2$

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Abstract. (1) $M_r = 206$, monoclinic, $P2_1/n$, $a = 7{\cdot}609$ (1), $b = 7{\cdot}350$ (1), $c = 17{\cdot}567$ (4) Å, $\beta = 94{\cdot}93$ (1)°, $V = 979{\cdot}02$ Å^3, $Z = 4$, $D_m = 1{\cdot}4$, $D_x = 1{\cdot}399$ g cm^{-3}, λ(Mo $K\alpha$) = 0·7093 Å, μ(Mo $K\alpha$) = 0·985 cm^{-1}, $F(000) = 431{\cdot}92$, $T = 298$ K, final $R = 0{\cdot}051$ for 1391 observed reflections. (2) $M_r = 176$, monoclinic, $P2_1/c$, $a = 3{\cdot}853$ (2), $b = 11{\cdot}819$ (3), $c = 18{\cdot}249$ (3) Å, $\beta = 92{\cdot}22$ (3)°, $V = 830{\cdot}286$ Å^3, $Z = 4$, $D_m = 1{\cdot}4$, $D_x = 1{\cdot}41$ g cm^{-3}, μ(Mo $K\alpha$) = 0·958 cm^{-1}, $F(000) = 367{\cdot}92$, $T = 298$ K, final $R =$

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