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(1*S*)-*tert*-Butyl [3-chloro-1-(3,5-difluorophenyl)-propyl]carbamate: structure and absolute configuration

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Key indicators

Single-crystal X-ray study
T = 200 K
Mean σ(C–C) = 0.004 Å
R factor = 0.038
wR factor = 0.091
Data-to-parameter ratio = 17.6

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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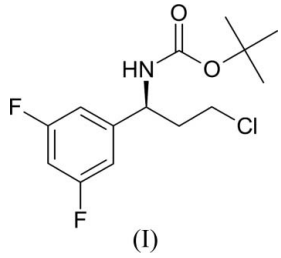
The title compound, $C_{14}H_{18}ClF_2NO_2$, crystallizes as a single enantiomer, and the absolute configuration for the chiral C atom was confirmed as *S*. The molecules are efficiently stacked, with no residual void for solvent inclusion.

Comment

The title compound, (I), is an intermediate in the synthesis of compounds exhibiting antagonistic properties against the CCR5 receptor, a member of the class of G-protein-coupled receptors, believed to be important, for example, in inflammation processes (Moore & Brown, 2006). The present X-ray investigation was undertaken in order to confirm the absolute stereochemistry of the carbamate intermediate made in the course of the synthesis of chiral amides.



(I)

The molecular conformation and absolute configuration of (I) are presented in Fig. 1 and selected geometric parameters are given in Table 1. The molecule has six heteroatoms, only one of which bears an H atom, namely the N atom. This potential hydrogen-bond donor participates in intermolecular hydrogen-bond interactions (Table 2), linking the molecules into infinite one-dimensional chains by N—H···O(carbamate) interactions, with an N···O distance of 3.051 (3) Å, along the [100] direction (Fig. 2).

The molecules are efficiently stacked, with no residual void for solvent inclusion (Fig. 3). The packing coefficient of (I), calculated by *PLATON*, is 0.688 (Kitaigorodskij, 1973; Spek, 2003), reflecting a fairly efficient molecular packing arrangement.

Experimental

The synthesis of (I) is to be described in a paper to be published by Moore & Brown (2006). Needle-shaped crystals suitable for single-crystal X-ray diffraction were grown from a diethyl ether–hexane mixture (1:3) at AstraZeneca Research and Development, Mereside, Alderley Park, Macclesfield, UK. The structure determination was performed at AstraZeneca Research and Development, Södertälje, Sweden.

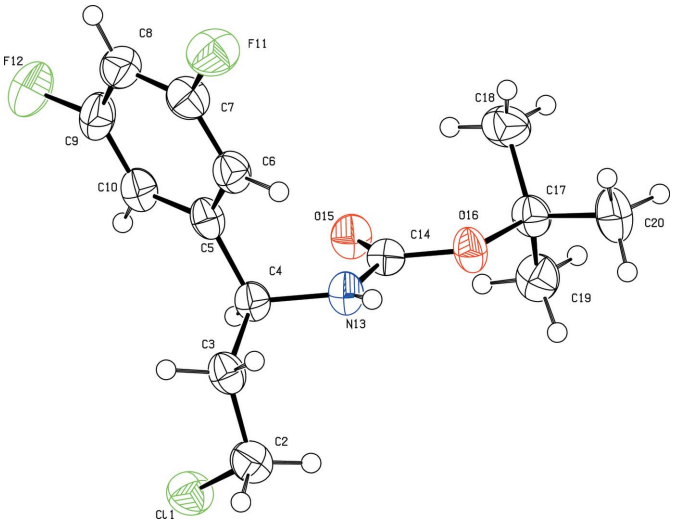


Figure 1
A view of the title compound, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.

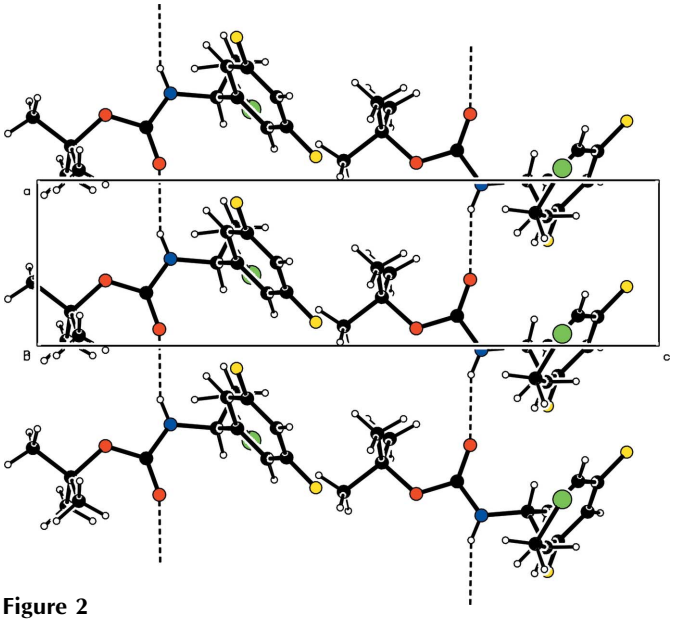


Figure 2
Part of the molecular hydrogen-bonding scheme of (I), with the molecules joined as chains containing equivalent symmetry-translated units along the [100] direction. Dotted lines indicate hydrogen-bond interactions. The view is along the [010] direction.

Crystal data

$C_{14}H_{18}ClF_2NO_2$
M_r = 305.74
Orthorhombic, $P2_12_12_1$
a = 5.2216 (2) Å
b = 14.3035 (6) Å
c = 19.6163 (8) Å
V = 1465.09 (10) Å^3
Z = 4
D_x = 1.386 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.28 mm^{-1}
T = 200 (2) K
Needle, colourless
0.60 × 0.03 × 0.03 mm

Data collection

Nonius KappaCCD area-detector diffractometer
φ and ω scans with κ offsets
Absorption correction: none
17273 measured reflections
3178 independent reflections
1724 reflections with $I > 2\sigma(I)$
R_{int} = 0.055
θ_{max} = 27.5°

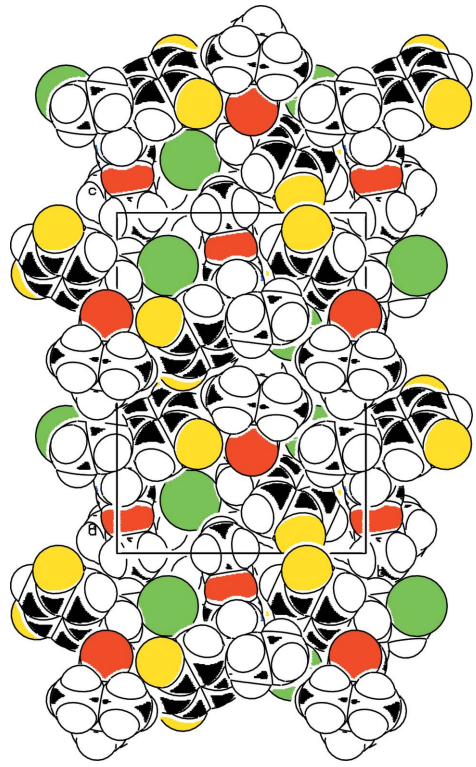


Figure 3
CPK space-filling diagram of the molecules, along the [100] direction.

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.039
$wR(F^2)$ = 0.091
S = 0.85
3178 reflections
181 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0453P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.15 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}
Absolute structure: Flack (1983), with 1268 Friedel pairs
Flack parameter: −0.06 (8)

Table 1
Selected geometric parameters (Å, °).

Cl1—C2	1.802 (3)	O15—C14	1.224 (4)
F11—C7	1.359 (3)	O16—C14	1.350 (3)
F12—C9	1.361 (3)	N13—C14	1.349 (4)
C14—O16—C17	121.1 (2)	N13—C4—C5	113.2 (2)
C4—N13—C14	120.6 (2)	O15—C14—O16	125.9 (3)
Cl1—C2—C3	111.1 (2)	O16—C14—N13	109.2 (2)

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N13—H13···O15^{i}	0.85	2.25	3.051 (3)	158
C3—H3B···O15^{i}	0.96	2.54	3.376 (3)	146
C18—H18C···O15	0.96	2.35	2.972 (3)	122
C19—H19B···O15	0.96	2.51	3.102 (3)	120

Symmetry code: (i) $x + 1, y, z$.

Although present in late difference maps, the aromatic and Csp^3-bonded H atoms were placed in calculated positions, due to poor bond angles, and constrained to ideal positions, with C—H = 0.96 Å. Atom H13, found in a difference map, was constrained in the final refinement stages to 0.85 Å from its parent atom N13. All H atoms were refined with U_{iso}(H) = 1.2U_{eq}(carrier atom).

Data collection: *COLLECT* and *KappaCCD Server Software* (Nonius, 1997–2000); cell refinement: *DENZO-SMN* (Otwinowski & Minor, 1997); data reduction: *DENZO-SMN* and *SCALEPACK* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976) and *PLATON* (Spek, 2003); software used to prepare material for publication: *PLATON* and *ACD/Labs* (Advanced Chemistry Development, 1994–2004).

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References

Advanced Chemistry Development (1994–2004). *ACD/Labs*. Release 8.00, product version 8.05. Advanced Chemistry Development Inc., Toronto, Ontario, Canada.

Altomare, A., Burla, M. C., Camalli, M., Cascarano, G., Giacovazzo, C., Guagliardi, A., Moliterni, A. G. G., Polidori, G. & Spagna, R. (1999). *J. Appl. Cryst.* **32**, 115–119.

Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.

Johnson, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

Kitaigorodskij, A. I. (1973). *Molecular Crystals and Molecules*. New York: Academic Press.

Moore, P. R. & Brown, D. S. (2006). *Tetrahedron Lett.* In the press.

Nonius (1997–2000). *COLLECT* and *KappaCCD Server Software*. Nonius BV, Delft, The Netherlands.

Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.

Sheldrick, G. M. (1997). *SHELXL97*. University of Göttingen, Germany.

Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.