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# *N*-[4-Cyano-3-(trifluoromethyl)phenyl]-2-methyloxirane-2-carboxamide: a bicalutamide intermediate

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In the title compound, $C_{12}H_9F_3N_2O_2$, the O atoms participate in hydrogen-bonding interactions with both the NH group and also the CH groups of adjoining molecules.

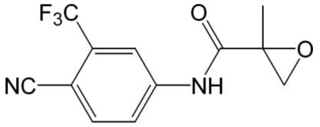
**Key indicators**

Single-crystal X-ray study
*T* = 298 K
Mean $\sigma$(C–C) = 0.002 Å
Disorder in main residue
*R* factor = 0.038
*wR* factor = 0.107
Data-to-parameter ratio = 11.5

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

## Comment

The title compound, (I), is a bicalutamide intermediate. Bicalutamide is an oral non-steroidal anti-androgen for prostate cancer. It is thought to prevent the growth of prostate cancer by blocking the effects of androgens on the cancer cells (Bohl *et al.*, 2005; Tucker *et al.*, 1988). It blocks the effect of testosterone which is a male sex hormone. Bicalutamide is often used with another drug that lowers testosterone levels in the body. Bicalutamide is an antineoplastic hormonal agent, which is a pure, non-steroidal anti-androgen with affinity for androgen receptors (but not for progestogen, estrogen, or glucocorticoid receptors). Consequently, bicalutamide blocks the action of androgens of adrenal and testicular origin which stimulate the growth of normal and malignant prostatic tissue. Prostate cancer is mostly androgen-dependent and can be treated with surgical or chemical castration. The mechanism of action of bicalutamide competes with androgen for the binding of androgen receptors, consequently blocking the action of androgens of adrenal and testicular origin which stimulate the growth of normal and malignant prostatic tissue (Masiello *et al.*, 2002; Schellhammer, 2002; Schellhammer & Davis, 2004). The crystal structures of related compounds have been recently reported (Hu & Gu, 2005; Tang & Gu, 2005). In view of the importance of the title compound and to confirm the structure, a crystal structure of (I) is reported (Fig. 1).



(I)

The C—O distances in the oxirane unit [1.4346 (17) and 1.447 (2) Å] are within the normal range observed for these groups (Cambridge Structural Database, Version 5.27; Allen, 2002). The trifluoromethyl group is disordered, as is typically found for these groups even in structures determined at low temperatures. The benzene ring and the carboxamide group are nearly coplanar [dihedral angle = 6.6 (1)°]; intramolecular C6—H6···O1 and N1—H1*N*···O2 interactions contribute to their coplanarity. As shown in Fig. 2, there are extensive intermolecular interactions between the O atoms and the NH group and also CH groups of adjoining molecules (Table 2). These link the molecules into hydrogen-bonded dimers by

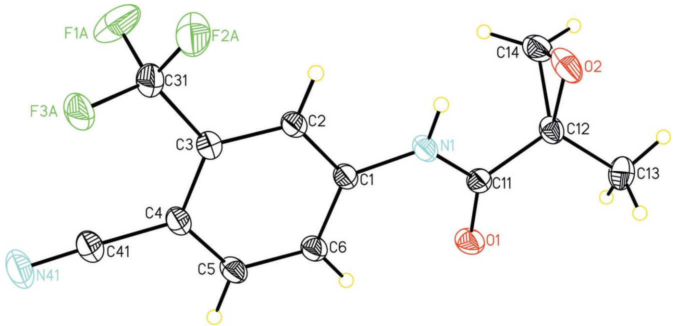


**Figure 1**
The molecular structure of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 20% probability level. Only the major conformer of the disordered trifluoromethyl group is shown.

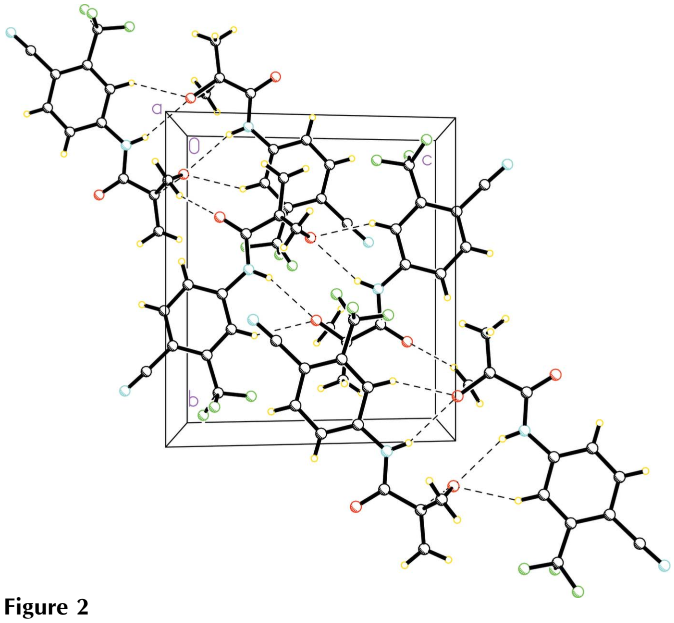


**Figure 2**
The molecular packing for (I), viewed down the *a* axis. Only the major conformer of the disordered trifluoromethyl group is shown. Hydrogen bonds are indicated by dashed lines.

forming two C—H···O and two N—H···O interactions involving the oxirane O atom (Fig. 2). These dimers are also linked to adjoining molecules by weak C—H···O interactions involving the carbonyl O atom of the carboxamide group.

## Experimental

The title compound was obtained as a gift sample from CIPLA, Mumbai, India. The compound was used without further purification. Recrystallization from ethanol yielded X-ray diffraction quality crystals (m.p. 422 K).

*Crystal data*

$C_{12}H_9F_3N_2O_2$
$M_r = 270.21$
Monoclinic, $P2_1/n$
$a = 10.2636\ (5)$ Å
$b = 11.5179\ (6)$ Å
$c = 10.4182\ (5)$ Å
$\beta = 102.944\ (1)^\circ$
$V = 1200.29\ (10)$ Å$^3$
$Z = 4$
$D_x = 1.495$ Mg m$^{-3}$
Mo $K\alpha$ radiation
$\mu = 0.13$ mm$^{-1}$
$T = 298\ (2)$ K
Block, colorless
$0.48 \times 0.37 \times 0.18$ mm

*Data collection*

Bruker APEX-2 CCD area-detector diffractometer
$\varphi$ and $\omega$ scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{\min} = 0.914$, $T_{\max} = 0.966$
10248 measured reflections
2352 independent reflections
2043 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.015$
$\theta_{\max} = 26.0^\circ$

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.038$
$wR(F^2) = 0.107$
$S = 1.05$
2352 reflections
205 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0522P)^2 + 0.266P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.18$ e Å$^{-3}$
$\Delta\rho_{\min} = -0.17$ e Å$^{-3}$

**Table 1**
Selected geometric parameters (Å, °).

| | | | |
|---|---|---|---|
| O1—C11 | 1.2098 (16) | N1—C1 | 1.3972 (16) |
| O2—C12 | 1.4346 (17) | C12—C14 | 1.464 (2) |
| O2—C14 | 1.447 (2) | C4—C41 | 1.4419 (19) |
| N1—C11 | 1.3595 (18) | C41—N41 | 1.136 (2) |
| | | | |
| C12—O2—C14 | 61.07 (10) | N1—C11—C12 | 114.20 (11) |
| O1—C11—N1 | 124.90 (13) | O2—C12—C14 | 59.89 (10) |
| O1—C11—C12 | 120.86 (12) | N41—C41—C4 | 178.03 (18) |

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

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| N1—H1*N*···O2$^{\rm i}$ | 0.84 (2) | 2.48 (2) | 3.243 (2) | 151 (1) |
| C2—H2*A*···O2$^{\rm i}$ | 0.93 | 2.46 | 3.264 (2) | 145 |
| C14—H14*A*···O1$^{\rm ii}$ | 0.97 | 2.44 | 3.375 (2) | 161 |
| C6—H6*A*···O1 | 0.93 | 2.30 | 2.889 (2) | 121 |
| N1—H1*N*···O2 | 0.84 (2) | 2.20 (2) | 2.673 (2) | 116 (2) |

Symmetry codes: (i) $-x, -y+2, -z$; (ii) $x-\frac{1}{2}, -y+\frac{3}{2}, z-\frac{1}{2}$.

The trifluoromethyl group was disordered over two conformations and occupancy factors refined to 0.540 (17) and 0.460 (17). In the refinement process a common C—F distance was refined to a value of 1.3076 (14) Å. All H atoms were initially located in a difference Fourier map. The methyl H atoms were then constrained to an ideal geometry, with C—H distances of 0.98 Å and $U_{\rm iso}({\rm H}) = 1.5U_{\rm eq}({\rm C})$, but each group was allowed to rotate freely about its C—C bond. All other carbon-bound H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms, with C—H distances in the range 0.95–1.00 Å and $U_{\rm iso}({\rm H}) = 1.2U_{\rm eq}({\rm C})$. The positional parameters for the amine H atom were refined with $U_{\rm iso}({\rm H}) = 1.2U_{\rm eq}({\rm N})$.

Data collection: *APEX2* (Bruker, 2006); cell refinement: *SAINT* (Bruker, 2004); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 2003); software used to prepare material for publication: *SHELXTL*.

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## References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.

Bohl, C. E., Gao, W.-Q., Miller, D. D., Bell, C. E. & Dalton, J. T. (2005). *Pharmacology*, **102**, 6201–6206.

Bruker (2003). *SHELXTL*. Version 6.14. Bruker AXS Inc., Madison, Wisconsin, USA.

Bruker (2004). *SAINT*. Version 7.23A. Bruker AXS Inc., Madison, Wisconsin, USA.

Bruker (2006). *APEX2*. Version 2.0-2. Bruker AXS Inc., Madison, Wisconsin, USA.

Hu, X.-R. & Gu, J.-M. (2005). *Acta Cryst.* E**61**, o3897–o3898.

Masiello, D., Cheng, S., Bubley, G. J., Lu, M. L. & Balk, S. P. (2002). *J. Biol. Chem.* **277**, 26321–26326.

Schellhammer, P. F. (2002). *Exp. Opin. Pharmacother.* **3**, 1313–1328.

Schellhammer, P. F. & Davis, J. W. (2004). *Clin. Prostate Cancer*, **2**, 213–219.

Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.

Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.

Tang, G.-P. & Gu, J.-M. (2005). *Acta Cryst.* E**61**, o3184–o3186.

Tucker, H., Crook, J. W. & Chesterson, G. J. (1988). *J. Med. Chem.* **31**, 954–959.

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