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(+)-*N*-{4-[(1*S*,2*S*)-2-(Dimethylamino)-1-(1*H*-imidazol-1-yl)propyl]phenyl}-2-benzothiazolamine

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The metabolism of all-*trans*-retinoic acid is mediated by a cytochrome dependent P-450 system. The title compound, $C_{21}H_{23}N_5S$, is an inhibitor of the P-450 system. Two planar rings connected *via* a central CH group form a dihedral angle of 80.2 (1)°; the planar systems connected through an NH group form a dihedral angle of 37.12 (8)°. The N—H···N hydrogen bonds link the molecules of the title compound into infinite chains stretching along the *c* direction.

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Key indicators

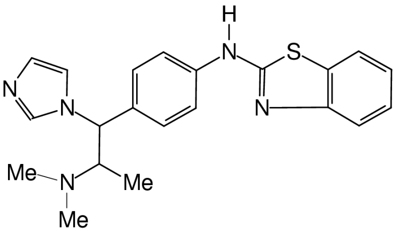
Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.005 Å
R factor = 0.049
wR factor = 0.145
Data-to-parameter ratio = 13.6

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

Comment

All-*trans*-retinoic acid (ATRA) is a metabolite of retinol (Vitamin A) which is involved in growth and epithelial differentiation in mammals. However the potency of ATRA is strongly attenuated by its rapid metabolism involving the stage of hydroxylation, mediated by a cytochrome dependent P-450 system (Leo *et al.*, 1989). The P-450 system is inhibited by the title compound, which leads to increased plasma levels of ATRA.

All four rings in the molecule of the title compound (I) (Fig. 1) are essentially planar. The imidazolyl ring is almost perpendicular to the phenylene ring [dihedral angle 80.2 (1)°]; the phenylene ring and the benzothiazolyl ring are twisted with a dihedral angle of 37.12 (8)°. The secondary amine group is almost coplanar with the benzothiazolyl moiety [dihedral angle 4.3 (2)°] but is twisted with respect to the phenylene ring [dihedral angle 37.3 (3)°]. The degree of coplanarity and conjugation with the π-electron systems of the aromatic rings is reflected in the C—N bond lengths. The C19—N18 bond [1.357 (4) Å] is significantly shorter than the C15—N18 bond [1.411 (4) Å].



(I)

The N18—H18···N9 hydrogen bond [H18···N9^i 2.07 Å, N18···N9^i 2.884 (4) Å, N18—H18···N9^i 158° (D—H distance not normalized); symmetry code (i): $\frac{1}{2}-x, 1-y, z-\frac{1}{2}$] links two molecules related by the 2_1 screw axis parallel to c, thus giving rise to infinite one-dimensional chains stretching along the c axis of the crystal.

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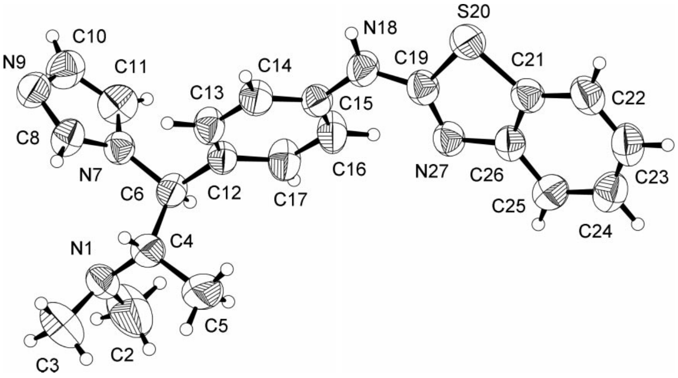

Figure 1
Perspective view of a molecule of the title compound with atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

Experimental

The title compound was obtained from the Janssen Research Foundation, Beerse, Belgium. The synthesis has been described by Venet *et al.* (1997). Single crystals were grown by slow evaporation from a solution in ethanol.

Crystal data

$C_{21}H_{23}N_5S$
$M_r = 377.51$
Orthorhombic, $P2_12_12_1$
$a = 9.4442$ (9) Å
$b = 13.725$ (1) Å
$c = 15.703$ (1) Å
$V = 2035.4$ (3) Å^3
$Z = 4$
$D_x = 1.232$ Mg m^{-3}

Cu *Kα* radiation
Cell parameters from 37 reflections
$\theta = 5.6$–26.6°
$\mu = 1.52$ mm^{-1}
$T = 293$ K
Prism, colourless
0.30 × 0.24 × 0.08 mm

Data collection

Siemens P4 four-circle diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan *XEMP* (Siemens, 1989)
$T_{\min} = 0.625$, $T_{\max} = 0.886$
3908 measured reflections
3370 independent reflections
2912 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.023$
$\theta_{\max} = 69.2°$
$h = -9 \rightarrow 9$
$k = -16 \rightarrow 16$
$l = -19 \rightarrow 19$
3 standard reflections every 100 reflections intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.049$
$wR(F^2) = 0.145$
$S = 1.07$
3370 reflections
248 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0806P)^2 + 0.5545P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} = 0.001$
$\Delta\rho_{\max} = 0.17$ e Å^{-3}
$\Delta\rho_{\min} = -0.18$ e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.0023 (4)
Absolute structure: Flack (1983). 847 Friedel pairs.
Flack parameter = 0.01 (3)

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N18—H18···N9$^{\text{i}}$	0.86	2.07	2.884 (4)	158
C22—H22···N9$^{\text{ii}}$	0.93	2.72	3.503 (5)	142
C23—H23···N1$^{\text{ii}}$	0.93	2.74	3.614 (5)	157

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

After checking their presence in the difference map, H atoms were placed at their geometrically calculated positions (the NH group has a planar environment), except for those of the methyl groups. The latter were found from a circular difference Fourier synthesis. All H atoms were allowed to ride on their parent atom and, for the methyl groups, to rotate around their local threefold axis. The isotropic displacement factors were fixed at 1.25 U_{eq} of their parent atoms.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *DIAMOND* (Bergerhoff, 1996); software used to prepare material for publication: *PARST* (Nardelli, 1983).

References

Altomare, A., Burla, M. C., Camalli, M., Cascarano, G., Giacovazzo, C., Guagliardi, A. & Polidori, G. (1994). *J. Appl. Cryst.* **27**, 435.
Bergerhoff, G. (1996). *DIAMOND*. Bonn, Germany.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Leo, M. A., Lasker, J. M., Raucy, J. L., Kim, C., Black, M. & Lieber, C. L. (1989). *Arch. Biochem. Biophys.* **269**, 305–312.
Nardelli, M. (1983). *Comput. Chem.* **7**, 95–98.
Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.
Siemens (1989). *XEMP*. Siemens Analytical X-ray Instruments, Inc., Madison, Wisconsin, USA.
Siemens (1996). *XSCANS*. Version 2.2. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Venet, M., Mabire, D., Lacrampe, J. & Sanz, G. (1997). Patent No. WO9749704.