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The enol form of nafazatrom

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Key indicators

Single-crystal X-ray study
T = 294 K
Mean σ(C–C) = 0.006 Å
R factor = 0.047
wR factor = 0.176
Data-to-parameter ratio = 12.3

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

In the crystal structure of the title compound, 3-methyl-1-[2-(2-naphthyloxy)ethyl]-1*H*-pyrazol-5-ol (nafazatrom, Bay g 6575), $C_{16}H_{16}N_2O_2$, the enol form is present rather than the keto form. The pyrazole and naphthalene ring systems are planar and the angle between them is 66.76 (12)°. A strong O—H···N hydrogen bond forces the molecules to form ribbons running along the *b* axis. Partial stacking of the naphthalene rings accounts for distinct hydrophilic and hydrophobic regions in the crystal structure.

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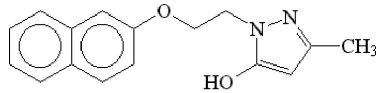
Comment

Bay g 6575 is a lipoxygenase inhibitor which shows antithrombotic properties ten times stronger then acetylsalicylic acid. Although the antithrombotic effect cannot be rationalized by any of the known mechanisms, it has been suggested that its activity results from effects on components of blood vessel walls (Senter *et al.*, 1979), including stimulation of prostacyclin release from vessel walls (Vermylen *et al.*, 1979). There is also evidence that some of the biological effects of nafazatrom may be due to antioxidant activity (Ondrias *et al.*, 1997). The crystal structure of Bay g 6575 was elucidated to provide comparative stereochemical data for antithrombotics. The structure of nafazatrom is presented in Fig. 1.



(I)

Bond distances and angles are consistent with normal values. The naphthalene and pyrazole ring systems are planar and the angle between the planes is 66.76 (12)°. The three

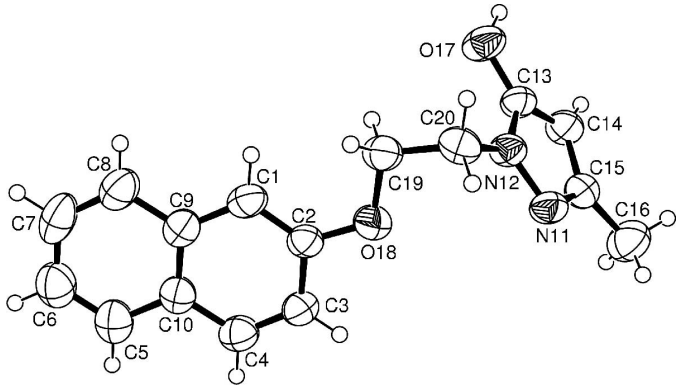


Figure 1
The molecular structure of nafazatrom, showing 50% probability displacement ellipsoids. H atoms are drawn as small circles of arbitrary radii.

atoms of the oxyethylene bridge (O18, C19 and C20) are roughly coplanar with the naphthalene moiety, with the largest deviation being 0.444 (6) Å for atom C20. Atoms C16/O17/C20 and the pyrazole ring are essentially coplanar, with the largest deviation being 0.011 (7) Å for atom C16. The sum of the angles around N12 is 359.9°, indicating sp^2 hybridization. Although the heterocyclic ring is usually depicted in the keto form, it adopts the enol form in this crystal structure. The migration of an H atom from C14 to O17, which transforms the keto into the enol form, is enabled by the stabilizing effects of the π-electron delocalization in the pyrazole ring, and a strong intermolecular hydrogen bond O17—H17···N11 (Table 1) which produces molecular ribbons running parallel to the *b* axis. Due to partial overlapping of the naphthalene rings, distinct hydrophilic and hydrophobic regions perpendicular to the *a* axis are created (Fig. 2). Normal van der Waals interactions also contribute to the crystal packing.

Experimental

To obtain crystals suitable for data collection, nafazatrom was dissolved in methanol and the solution subjected to slow evaporation. Crystals grew in about four weeks. The crystals were very small colorless needles. Attempts to grow bigger crystals proved unsuccessful.

Crystal data

$C_{16}H_{16}N_2O_2$
M_r = 268.31
Orthorhombic, *Pbca*
a = 28.830 (5) Å
b = 10.896 (2) Å
c = 8.879 (2) Å
V = 2789.2 (9) Å^3
Z = 8
D_x = 1.278 Mg m^{-3}
Cu *Kα* radiation
Cell parameters from 32 reflections
θ = 21–42°
μ = 0.69 mm^{-1}
T = 294 (2) K
Needle, colorless
0.25 × 0.06 × 0.01 mm

Data collection

Picker FACS-1 four-circle diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.950, T_{max} = 0.991
2382 measured reflections
2382 independent reflections
1009 reflections with $I > 2\sigma(I)$
θ_{max} = 65.0°
h = 0 → 33
k = 0 → 12
l = 0 → 10
3 standard reflections
every 100 reflections
intensity decay: 3.2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.176
S = 1.13
2382 reflections
193 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0445P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.16 e Å^{-3}
$\Delta\rho_{min}$ = −0.16 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.00063 (18)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O17—H17···N11^{i}	1.13 (6)	1.48 (6)	2.609 (4)	176 (5)

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

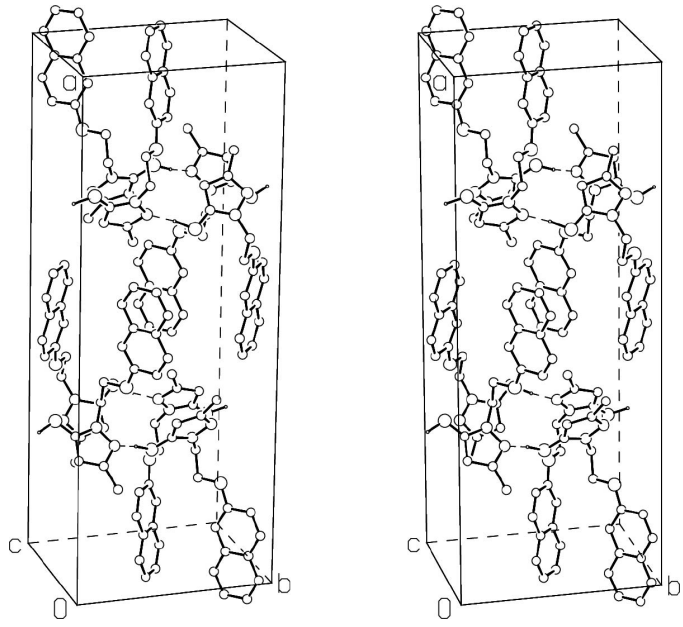


Figure 2
Stereodiagram of the molecular packing and hydrogen-bond scheme (shown as dashed lines between atoms). Atoms are drawn as circles of arbitrary radii. Carbon-bound H atoms have been omitted.

All H atoms, except those at C14 and O17, were positioned geometrically and allowed to ride on their parent atoms. The H atoms were divided into two groups (methyl-group H atoms and the remainder) and the isotropic displacement parameter in each group was refined. The final U_{iso} = 0.139 (13) Å^2 for methyl, and 0.073 (4) Å^2 for the remainder. The H atoms at C14 and O17 were found in a difference map and refined freely with isotropic displacement parameters. Their geometrical parameters are: O17—H17 = 1.13 (6), C14—H14 = 1.02 (5) Å and C13—O17—H17 = 110 (3)°. The long O17—H17 distance can be justified by the strong hydrogen bond O17—H17···N11 (Table 1), in which the H atom is displaced by interaction with atom N11.

Data collection: *Picker Operating Manual* (Picker, 1967); cell refinement: *Picker Operating Manual*; data reduction: *DATRDN* (Stewart, 1976); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

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