Br2′*a*—C2′—Br2′*b*	111.4 (6)	C2′—C3′—C4′	121 (1)
Br2′*a*—C2′—C1′	115.5 (7)	C2′—C3′—C7′	123 (1)
Br2′*a*—C2′—C3′	115.6 (8)	C4′—C3′—C7′	108 (1)
Br2′*b*—C2′—C1′	123.8 (8)	C3′—C4′—C5′	105 (1)
Br2′*b*—C2′—C3′	120.8 (8)	C4′—C5′—C6′	106 (1)
C1′—C2′—C3′	61.6 (7)	C5′—C6′—C7′	106 (1)
C1—C2—C3	122 (1)	C3′—C7′—C6′	105 (1)

The θ-scan width used was (1.40 + 0.30tanθ)° at a speed of 16° min^{-1} (in ω). The weak reflections were rescanned a maximum of four times and the counts accumulated to ensure good counting statistics. Stationary background counts were made on each side of the reflection with a 2:1 ratio of peak to background counting time. H atoms were located from difference maps and then fixed at ideal positions with C—H = 0.96 Å and U_{iso} = 1.2U_{eq}(C). A linear correction factor was applied to account for substantial crystal decay. The structure was solved by Patterson methods using the program *PATTY* (Beurskens *et al.*, 1992) and expanded using Fourier techniques (*DIRDIF*; Beurskens *et al.*, 1992). Refinement was carried out using full-matrix least-squares techniques. All calculations were performed using *TEXSAN* (Molecular Structure Corporation, 1995).

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1993). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN*. Program(s) used to refine structure: *TEXSAN*. Software used to prepare material for publication: *TEXSAN*.

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Lists of atomic coordinates, displacement parameters, structure factors and complete geometry have been deposited with the IUCr (Reference: OA1016). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Antazoline

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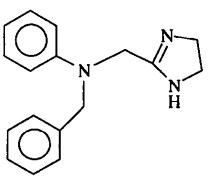
Abstract

The crystal structure of the title compound, 4,5-dihydro-*N*-phenyl-*N*-(phenylmethyl)-1*H*-imidazole-2-methanamine, $C_{17}H_{19}N_3$, is composed of independent molecules of the free base with normal molecular dimensions. There is an intermolecular N—H···N hydrogen bond between the imidazole ring N atoms linking the molecules into a chain structure [N···N 2.965 (4) Å].

Comment

The crystal structures of antazoline hydrochloride (Bertolasi, Borea & Gilli, 1982) and bis(antazoline)dichlorozinc(II) (Parvez & Rusiewick, 1995) have been reported. The crystal structure of the free base, antazoline, (1), which is an anti-allergic drug effective on H1 receptors is reported in this paper.



(1)

The phenyl rings were constrained to be regular hexagons, with C—$C_{aromatic}$ 1.395 Å and C—C—C 120.0°. The remaining molecular dimensions in (1) are normal and are identical within 3σ values to the dimensions reported for its hydrochloride salt (Bertolasi, Borea & Gilli, 1982), except the N3—C15 distance of 1.351 (4) Å in (1) which is clearly a C_{sp^2}—N single bond.

The imidazole ring in (1) is essentially planar [maximum deviation 0.033 (3) Å] and lies at angles of 79.47 (14) and 113.29 (14)° with respect to the planes of the C1–C6 and C8–C13 phenyl rings, respectively; the mean-planes angle between the two phenyl rings is 95.72 (13)°. The corresponding mean-planes angles in the Zn complex are 92.4 (9), 47.7 (12) and 86.6 (11)° in one half and 84.9 (9), 89.7 (10) and 99.5 (12)° in the other half of the molecule. The mean-planes angles in (1) are also different from the corresponding

angles in the hydrochloride structure, with values of 69.3, 85.0 and 102.5°. The molecules of antazoline are linked through hydrogen bonds between imidazole rings of the adjacent molecules with an N2···N3 separation of 2.965 (4) Å.

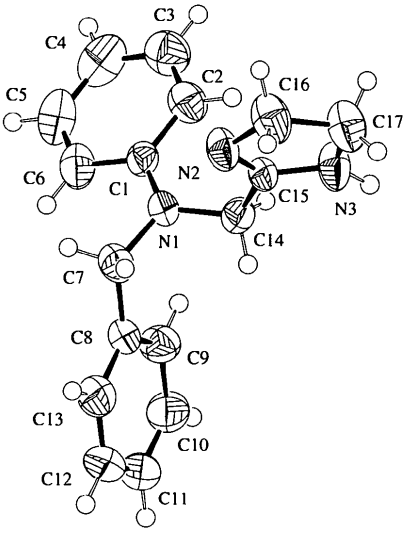


Fig. 1. *ORTEP*II (Johnson, 1976) drawing of antazoline with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms have been assigned arbitrary radii.

Experimental

An aqueous solution of antazoline hydrochloride (Sigma Inc.) was treated with an aqueous solution of NaOH. The free base was extracted with CCl_4, dried over $MgSO_4$ and allowed to crystallize at room temperature.

Crystal data

$C_{17}H_{19}N_3$
M_r = 265.36
Orthorhombic
Pbca
a = 19.670 (6) Å
b = 15.904 (3) Å
c = 9.485 (6) Å
V = 2967 (2) Å^3
Z = 8
D_x = 1.188 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 22 reflections
θ = 10.0–15.0°
μ = 0.072 mm^{-1}
T = 295 (1) K
Prism
0.50 × 0.50 × 0.20 mm
Colourless

Data collection

Rigaku AFC-6*S* diffractometer
$\omega/2\theta$ scans
Absorption correction: none
2618 measured reflections
2618 independent reflections
973 reflections with $F > 4\sigma(F)$

θ_{max} = 25.0°
$h = 0 \rightarrow 23$
$k = 0 \rightarrow 18$
$l = -11 \rightarrow 0$
3 standard reflections every 200 reflections
intensity decay: 1.42%

Refinement

Refinement on F^2
$R(F)$ = 0.0493
$wR(F^2)$ = 0.1289
S = 1.136
2596 reflections
158 parameters
H atoms riding, with C—H and N—H = 0.95 Å

$w = 1/[\sigma^2(F_o^2) + (0.0708P)^2 + 1.094P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.032
$\Delta\rho_{max}$ = 0.180 e Å^{-3}
$\Delta\rho_{min}$ = −0.177 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °) and hydrogen-bonding geometry (Å, °)*

N1—C1	1.405 (4)	N2—C16	1.473 (5)
N1—C14	1.444 (4)	N3—C15	1.351 (4)
N1—C7	1.451 (4)	N3—C17	1.443 (5)
N2—C15	1.288 (4)		
C1—N1—C14	119.7 (3)	C15—N2—C16	105.9 (3)
C1—N1—C7	123.0 (3)	C15—N3—C17	108.6 (3)
C14—N1—C7	116.1 (3)		

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3—H3···N2^i	0.95	2.22	2.965 (4)	135

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

The space group *Pbca* was determined uniquely from the systematic absences of $0kl$, $k = 2n + 1$, $h0l$, $l = 2n + 1$, and $hk0$, $h = 2n + 1$.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1994). Program(s) used to solve structure: *SAPI*91 (Fan, 1991). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *SHELXL*93.

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Lists of atomic coordinates, displacement parameters, structure factors and complete geometry have been deposited with the IUCr (Reference: FG1252). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Disorder in 13-*cis*-Retinoic Acid

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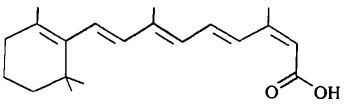
Abstract

13-*cis*-Retinoic acid [(2*Z*,4*E*,6*E*,8*E*)-3,7-dimethyl-9-(2,6,6-trimethylcyclohex-1-enyl)-2,4,6,8-nonatetraenoic acid, $C_{20}H_{28}O_2$] was found to adopt the 6-*s*-*trans* conformation, with the ring double bond and all the C atoms of the polyene chain coplanar. The plane of the double-bond system is coincident with a crystallographic mirror plane. The crystal displays crystallographic symmetry arising from disorder, indeed the cyclohexene ring, in a half-chair conformation, is present in two equally occupied conformations related to one another by the mirror plane. The carboxylic acid group is also disordered, lying on opposite sides of the plane of the double-bond system. In the crystal, the molecules form dimers connected by hydrogen bonds involving the carboxylic acid groups, and the dimers pack in parallel layers.

Comment

It has been well established that, of the naturally occurring isomeric vitamin A acids (Zechmeister, 1962), 13-*cis*-retinoic acid (isotretinoin) is of relevant practical importance due to its outstanding pharmacological activities (Bollag, 1981). The material is synthetically available by regioselective isomerization of the 11-double bond of 11,13-di-*cis*-retinoic acid obtained in a C-15 + C-5 Wittig condensation (Pattenden & Weedon, 1968), using either Pd^0 chemistry (US Patent 4 556 518) or photochemical methods (Mag Laboratories, 1997). A major drawback of 13-*cis*-retinoic acid is its apparent intrinsic instability and its remarkable aptitude to react with oxygen of the air. Although numerous related compounds have been characterized by X-ray diffraction, until now there has been no structural information in the literature for isotretinoin, (I). The X-ray analysis of this compound has been undertaken and its molecular conformation and crystal structure are reported here.



(I)

The perspective view of 13-*cis*-retinoic acid is shown in Fig. 1. The molecule is found to have a 6-*s*-*trans* conformation, so that the double-bond system from C5 to C14 has an all-*trans* conformation and is perfectly planar, its plane being coincident with a crystallographic mirror plane. The ring adopts an almost half-chair conformation; atoms C1 and C2 are located at distances of 0.22 (2) and 0.537 (5) Å, respectively, from the double-bond plane and C3 on the other side of the plane is located at a distance of 0.36 (7) Å. The molecule shows disorder both of the cyclohexene ring and of the carboxylic O atoms. The most interesting feature of the disorder is that the atoms involved, *i.e.* C1, C2, C3, C16 and C17, O1, O2, flip over two symmetrical and equally occupied positions on opposite sides of the plane of the double-bond system. As a result, the disorder allows the two alternative half-chair conformers of the cyclohexene ring to co-exist in the crystal structure as a 1:1 mixture; in accordance, the methyl groups (C16 and C17) also assume alternative positions (Fig. 2).

Conformational disorder of the cyclohexene ring was found or supposed to exist in crystal structures of a number of vitamin A retinal-related compounds and carotenoids. The evidence for this is as follows: (i) the unusually short C2—C3 bond length as found in the triclinic modification of the vitamin A acid (Stam, 1972), in the 6-*s*-*cis* conformer of 13-*cis*-retinal (Simmons, Liu, Denny & Seff, 1981), in a 9-*cis*-retinal derivative (Simmons, Asato, Denny & Liu, 1986) and in all-*trans* retinal (Hamanaka, Mitsui, Ashida & Kakudo, 1972); (ii) the unexpected planarity of the cyclohexene ring, as found in 2,6-di-*cis*-4-hydroxy-retinoic acid γ-lactone (Thackeray & Gafner, 1974); (iii) the presence of residual peaks in the final $\Delta\rho$ map in the vicinity of C_{sp^3} ring atoms and the presence of very large displacement parameters for these atoms, as commonly observed in the above-mentioned class of compounds. The disorder has been interpreted either as static and ascribed to the co-existence of the two alternative half-chair conformers in a variable reciprocal ratio, or as dynamic and attributed to high thermal motion of some of the ring atoms. In isotretinoin, the attribution of the two equally occupied conformations to the cyclohexene ring allows good ring geometry (see Table 2) and is also consistent with the molecular packing. The distance between the two half-occupied