

Structure of naphazoline nitrate¹

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2-(1-Naphthylmethyl)-2-imidazoline nitrate, C₁₄H₁₅N₃O₃, $M_r = 273.29$, orthorhombic, *Pbca*, $a = 12.033(4)$, $b = 14.387(4)$, $c = 15.913(4)$ Å, $V = 2754.9(4)$ Å³, $Z = 8$, $D_m = 1.32(3)$ (floatation), $D_x = 1.318$ Mg m⁻³, (Cu Kα) = 1.5418 Å, $\mu = 7.45$ cm⁻¹, $F(000) = 1152$, $T = 296$ K, final $R = 0.078$, $wR = 0.058$ for 1397 reflections with $I > 2\sigma(I)$. The naphthalene ring exhibits orientational disorder. The N—H ··· O hydrogen bonds involving both the nitrogen atoms of the imidazoline ring serve to form infinite chains of alternating naphazoline cations and nitrate anions.

Introduction

Naphazoline compounds are sympathomimetic drugs having α -agonistic activity and are similar to epinephrine and phenylethyl amines (Bowman and Rand, 1980; Weiner, 1980). The present work describes the X-ray crystal structure of the title compound.

Experimental

Pale yellow colored crystals from methanol, 0.30 × 0.40 × 0.20 mm, D_m by flotation, Enraf-Nonius CAD-4 graphite monochromatized single-crystal diffractometer, cell dimensions from 25 accurately centered reflections, $30 \leq 2\theta \leq 60$, $w/2\theta$ scan, Cu Kα radiation, three standard reflections monitored for every 100 reflections showed the change in intensity to be less than 3%, with $0 \leq h \leq 13$, $0 \leq k \leq 16$, $0 \leq l \leq 17$, 1626 unique reflections, $R_{\text{int}} = 0.03$, 1397 reflections with $I > 2\sigma(I)$ used in the least squares refinement; $2\theta_{\text{max}} = 120^\circ$. Data corrected for Lorentz and polarization effects but no absorption correction. Structure solution was by direct methods. The final Fourier map revealed two orientations of the naphthalene ring. The atoms in the naphthalene ring were given half occupancy. All attempts to refine this occupancy did not improve the R factor. All hydrogen positions except that

of the hydrogen attached to N1 and also those of the naphthalene rings were obtained from ΔF map; hydrogens of the naphthalene ring as well as atom HN1 were fixed and not refined. A full matrix least squares refinement was carried out on F_o , with anisotropic temperature factors for all nonhydrogen atoms except those of the naphthalene ring. The positional as well as thermal parameters of those hydrogen atoms found from the ΔF map were refined isotropically. The atoms of the naphthalene ring were refined isotropically; final R factor 0.078, $wR = 0.058$, $w = 1/[\sigma^2(F_o) + 0.04 F_o^2]$, $S = 1.49$, the final ΔF map was featureless, $(\Delta/\sigma)_{\text{max}} = 0.14$, final $(\Delta\rho)$ excursions are from -0.20 to $+0.34$ e Å⁻³. The high value for the R factor is likely due to the effects of disorder. No correction for secondary extinction was made. All calculations including geometric parameters were performed using the SDP (Frenz, 1978) on VAX 11/730 computing system. Scattering factors were those incorporated in the SDP package.

Discussion

The final atomic positional parameters of nonhydrogens are given in Table 1 and interatomic distances and angles in Table 2 and Table 3. The conformation of the molecule (program PLUTO, Motherwell and Clegg, 1978) is given in Fig. 1.

The present compound is an analog of the hydrochloride derivative (Podder *et al.*, 1983). Here, the naphthalene ring has an orientational disorder and the

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Table 1. Positional parameters of nonhydrogens and their estimated standard deviations

Atom	x	y	z	B(Å ²)	Atom	x	y	z	B(Å ²)
N1	0.1443(3)	0.0751(3)	0.0460(2)	6.8(1)	C10	0.0824(8)	-0.0328(6)	-0.3291(6)	6.4(2) ^a
C1	0.0846(4)	0.0264(4)	0.1135(3)	8.1(1)	C11	0.1177(9)	-0.1256(7)	-0.3240(7)	7.6(3) ^a
C2	0.1326(4)	-0.0707(4)	0.1099(3)	7.9(1)	C12	0.180(1)	-0.1545(8)	-0.2493(8)	9.3(3) ^a
N2	0.2142(3)	-0.0641(3)	0.0413(2)	6.5(1)	C13	0.2126(8)	-0.0867(7)	-0.1927(6)	6.8(2) ^a
C3	0.2143(3)	0.0188(3)	0.0094(2)	5.3(1)	C14	0.1803(6)	0.0084(5)	-0.1992(5)	4.5(2) ^a
C4	0.2862(3)	0.0499(4)	-0.0632(3)	6.3(1)	C5'	0.2348(7)	0.0093(6)	-0.1449(5)	5.0(2) ^a
N3	0.0514(3)	0.2956(3)	0.0066(3)	7.8(1)	C6'	0.2537(9)	-0.0797(7)	-0.1692(6)	7.0(2) ^a
O1	0.0320(3)	0.3754(3)	-0.0171(3)	10.1(1)	C7'	0.2056(8)	-0.1212(7)	-0.2445(7)	7.2(2) ^a
O2	0.1503(3)	0.2731(3)	0.0202(3)	9.3(1)	C8'	0.1350(9)	-0.0681(7)	-0.2911(6)	7.5(2) ^a
O3	-0.0240(3)	0.2403(3)	0.0178(3)	10.8(1)	C9'	0.1128(3)	0.0298(3)	-0.2682(3)	6.0(1) ^a
C5	0.2145(7)	0.0767(6)	-0.1401(5)	4.9(2) ^a	C10'	0.0412(8)	0.0847(7)	-0.3122(6)	6.6(2) ^a
C6	0.1792(9)	0.1682(7)	-0.1492(7)	7.8(3) ^a	C11'	0.0158(9)	0.1720(8)	-0.2911(7)	8.3(3) ^a
C7	0.1081(8)	0.1894(7)	-0.2187(6)	7.2(2) ^a	C12'	0.0667(9)	0.2140(7)	-0.2194(6)	7.8(3) ^a
C8	0.0745(9)	0.1294(7)	-0.2766(6)	7.7(3) ^a	C13'	0.1413(7)	0.1602(6)	-0.1715(5)	5.4(2) ^a
C9	0.1128(3)	0.0298(3)	-0.2682(3)	6.0(1) ^a	C14'	0.1633(7)	0.0678(6)	-0.1909(5)	4.8(2) ^a

^aAtoms were refined isotropically. Anisotropically refined atoms are given in the form of the isotropic equivalent displacement parameter defined as: $(4/3) * [a^{*2}B(1,1) + b^{*2}B(2,2) + c^{*2}B(3,3)]$.

Table 2. Bond distances of nonhydrogens in angstroms

Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance
N1	C1	1.471(6) ^a	C5	C6	1.391(3)	C5'	C6'	1.356(2)
N1	C3	1.306(6)	C5	C14	1.421(1)	C5'	C14'	1.409(1)
C1	C2	1.513(8)	C6	C7	1.431(4)	C6'	C7'	1.459(3)
C2	N2	1.471(6)	C7	C8	1.326(4)	C7'	C8'	1.362(4)
N2	C3	1.296(6)	C9	C8	1.511(1)	C9'	C8'	1.478(1)
C3	C4	1.510(6)	C9	C10	1.371(1)	C9'	C10'	1.362(1)
C4	C5	1.546(9)	C9	C14	1.400(9)	C9'	C14'	1.477(9)
C4	C5'	1.554(9)	C10	C11	1.403(3)	C10'	C11'	1.336(4)
N3	O1	1.231(6)	C11	C12	1.465(6)	C11'	C12'	1.429(4)
N3	O2	1.253(5)	C12	C13	1.385(5)	C12'	C13'	1.409(3)
N3	O3	1.219(6)	C13	C14	1.426(2)	C13'	C14'	1.389(1)

^aNumbers in parentheses are estimated standard deviations in the least significant digits.

Table 3. Bond angles of nonhydrogens in degrees

Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle
C1	N1	C3	110.2(4) ^a	O2	N3	O3	120.8(4)	C5	C14	C13	122.4(7)
N1	C1	C2	103.1(4)	C4	C5	C6	119.3(7)	C9	C14	C5	122.4(7)
C1	C2	N2	102.9(4)	C4	C5	C14	120.9(6)	C9	C14	C13	115.2(7)
C2	N2	C3	110.6(4)	C6	C5	C14	119.8(8)	C4	C5'	C6'	121.7(7)
N1	C3	N2	113.3(4)	C5	C6	C7	117.7(9)	C4	C5'	C14'	117.0(7)
N1	C3	C4	121.8(4)	C6	C7	C8	125.4(9)	C6'	C5'	C14'	121.3(8)
N2	C3	C4	124.9(4)	C9	C8	C7	117.6(8)	C5'	C6'	C7'	123.6(9)
C3	C4	C5	111.0(4)	C8'	C9'	C10'	122.7(7)	C6'	C7'	C8'	117.7(9)
C3	C4	C5'	107.5(4)	C8'	C9'	C14'	118.9(6)	C9'	C8'	C7'	120.9(8)
C8	C9	C10	118.6(6)	C10'	C9'	C14'	118.2(6)	C9'	C10'	C11'	124.1(9)
C8	C9	C14	117.0(6)	C9	C10	C11	120.2(8)	C10'	C11'	C12'	120.1(9)
C10	C9	C14	124.3(6)	C10	C11	C12	118.1(9)	C11'	C12'	C13'	118.1(9)
O1	N3	O2	118.3(4)	C11	C12	C13	118.3(9)	C12'	C13'	C14'	121.8(8)
O1	N3	O3	120.8(4)	C12	C13	C14	123.4(9)	C9'	C14'	C5'	117.5(6)
C9'	14'	C13'	117.5(7)	C5'	C14'	C13'	124.9(7)				

^aNumbers in parentheses are estimated standard deviations in the least significant digits.

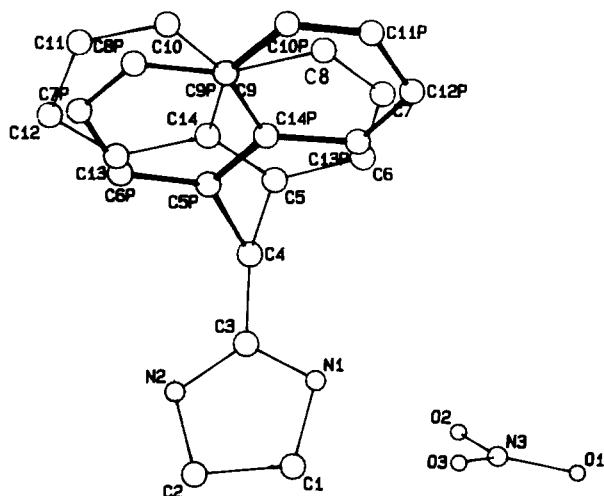


Fig. 1. Conformation of molecule.

angle between the two orientations of the naphthalene ring is $173.2(2)^\circ$. A similar kind of disorder of a portion of the molecule has been reported earlier (Weber *et al.*, 1983). The imidazoline ring and the naphthalene rings

are individually almost planar ($\chi^2 = 3, 106$ and 91 , respectively). The angle between the least squares plane of the imidazoline ring and the two orientations of the naphthalene rings are $106.5(1)$ and $105.6(1)^\circ$, respectively.

The conformation of the ring systems have been compared to those of the naphazoline hydrochloride compound. The bond lengths and bond angles agree well with those of the hydrochloride compound, except for the C3—C4 bond length (numbering scheme as in Fig. 1). The discrepancy may be a function of the rotational disorder of the naphthyl group in the title compound.

Both the nitrogens of the imidazoline ring are protonated in the cation and form hydrogen bonds with O2 ($N1 \cdots O2$ and $N2 \cdots O2$ are $2.879(6)$ and $2.874(6)$ Å, respectively). The hydrogen bonds result in the formation of infinite chains of alternating cations and nitrate anions parallel to the cell edge "b". It is of interest in this context that among the $N \cdots O$ distances in the nitrate anion, N3—O2 ($1.252(5)$ Å) is appreciably longer than either N3—O1 or N3—O3 ($1.231(6)$ and $1.220(6)$, respectively).

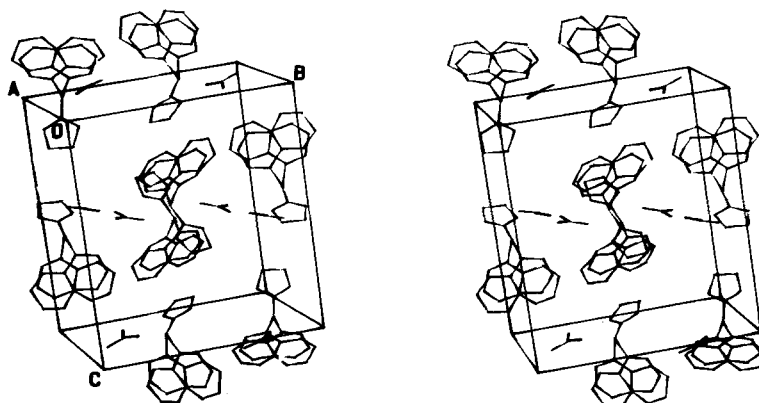
As pointed out by Podder *et al.* (1983), naphazo-

Table 4. A comparison of important torsion angles

Illustrations	Torsion Angles ($^\circ$)		
1. Expected for Phenethylamines ^a	C14—C5—C4—C3	C5—C4—C3—N1	C5—C4—C3—N2
	± 90.0		± 180.0
2. Naphazoline Hydrochloride ^b			
		$-176.8(6)$	$+85.4(6)$
3. Present study	C14—C5—C4—C3	C5—C4—C3—N1	C5—C4—C3—N2
One orientation	$-86.5(7)$	$-63.7(5)$	$115.8(5)$
Other orientation	C14'—C5'—C4—C3	C5'—C4—C3—N1	C5'—C4—C3—N2
	$96.1(8)$	$-103.6(5)$	$75.8(5)$

^aCarlstrom *et al.* (1973), Hebert (1979), Duax (1978).

^bPodder *et al.* (1983).

Fig. 2. Stereo packing diagram of the unit cell viewed down the *a*-axis.

line can be considered in terms of a phenyl-ethylamine skeleton [(C5 to C14)/(C5' to C14')] as the phenyl ring and [(C5—C4—C3—N)/C5'—C4—C3—N] as the side chain. The conformation of a portion of the molecule along with those of other phenethylamines (Carlstrom *et al.*, 1973; Hebert, 1979; Duax, 1978) is tabulated in Table 4. Comparison of the molecular conformation of the present compound with other active phenethylamines has revealed the fact that the present compound neither adopts an extended *trans* conformation nor is in the folded form observed in naphazoline hydrochloride (Aloka *et al.*, 1983). The naphazoline nitrate takes up an altogether different conformation and has no preferred conformation of sympathomimetic compounds.

Figure 2 shows the stereo packing diagram of the contents of the unit cell down *a*-axis, with the molecule in both the orientations.

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List of structure factor amplitudes, anisotropic thermal parameters, torsion angles, least squares plane calculation, hydrogen atom positions and bond lengths and bond angles involving hydrogen atoms have been deposited with the British Library, Boston Spa, Wetherby, West Yorkshire, UK as supplementary publication no. 63284 (24 pages).