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Crystal Structures of Nadifloxacin Anhydride and Its Hemihydrate

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The crystal structures of nadifloxacin [9-fluoro-6,7-dihydro-8-(4-hydroxy-1-piperidyl)-5-methyl-1-oxo-1*H*,5*H*-benzo[*i*,*j*]quinolizine-2-carboxylic acid, OPC-7251]anhydride and its hemihydrate were determined by X-ray analysis. In both crystals, two crystallographically independent molecules (A and B) are contained in an asymmetric unit. Two of molecule A and two of molecule B are tightly bound by hydrogen bonds around a center of symmetry. The structural features of nadifloxacin molecules in the two crystals are very similar to each other.

Keywords nadifloxacin; OPC-7251; antibacterial agent; X-ray analysis; 4-oxoquinolinone-3-carboxylic acid; *Propionibacterium acnes*

Since nalidixic acid (**2**)[1] was found as the first synthetic quinolone antibacterial drug, many new quinolone antibacterial agents have been synthesized and used for chemotherapy.[2] The structure–activity relationships have been discussed,[3] and the structures of some compounds have been determined by X-ray analysis.[4]

Nadifloxacin [9-fluoro-6,7-dihydro-8-(4-hydroxy-1-piperidyl)-5-methyl-1-oxo-1*H*,5*H*-benzo[*i*,*j*]quinolizine-2-carboxylic acid, OPC-7251] (**1**)[5] shows characteristically potent activity against *Propionibacterium acnes*, the causative agent of acne vulgaris.[6] It forms different crystal structures depending on the solvent used for recrystallization. One of the crystal structures is assigned as the anhydride, and the other as the hemihydrate. We have performed X-ray analyses of both crystals to elucidate the structural features of the compound.

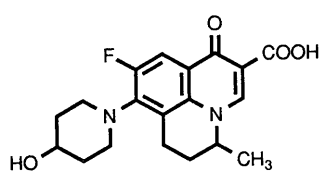
Results and Discussion

The crystals of nadifloxacin anhydride were obtained from acetonitrile solution as colorless cubic crystals which contain two nadifloxacin molecules in an asymmetric unit. The crystals of nadifloxacin hemihydrate were obtained as prism crystals from EtOH aqueous solution: the asymmetric unit consists of two nadifloxacin molecules and one water molecule.

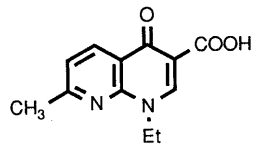
Perspective views of the asymmetric unit with the atomic numbering scheme for both anhydride and hemihydrate crystals are presented in Figs. 1a and 1b, respectively. Bond distances and angles are listed in Tables I and II, respectively, together with their estimated standard deviations in parentheses. No abnormal bond lengths or angles were found in these structures. The four independent molecules in the two crystal forms can be

TABLE I. Bond Lengths (Å) for Nadifloxacin Anhydride and Hemihydrate with Their e.s.d.'s in Parentheses

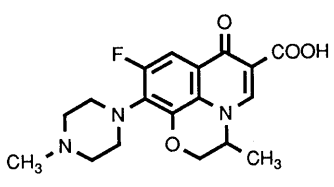
Atom	Atom	Anhydride		Hemihydrate	
		Mol. A Distance	Mol. B Distance	Mol. A Distance	Mol. B Distance
F(1)	C(6)	1.369 (6)	1.363 (6)	1.352 (4)	1.365 (4)
O(1)	C(14)	1.210 (7)	1.203 (6)	1.215 (5)	1.214 (5)
O(2)	C(14)	1.324 (7)	1.332 (6)	1.327 (5)	1.329 (6)
O(3)	C(3)	1.262 (6)	1.268 (6)	1.265 (5)	1.260 (5)
O(4)	C(17)	1.437 (7)	1.422 (8)	1.436 (5)	1.424 (6)
N(1)	C(1)	1.343 (7)	1.332 (7)	1.333 (5)	1.331 (5)
N(1)	C(9)	1.392 (6)	1.391 (6)	1.403 (5)	1.397 (5)
N(1)	C(10)	1.495 (6)	1.509 (6)	1.491 (5)	1.489 (6)
N(2)	C(7)	1.407 (6)	1.395 (7)	1.408 (5)	1.412 (5)
N(2)	C(15)	1.446 (7)	1.461 (8)	1.461 (6)	1.453 (6)
N(2)	C(19)	1.466 (8)	1.476 (8)	1.468 (5)	1.458 (6)
C(1)	C(2)	1.379 (7)	1.374 (7)	1.363 (6)	1.358 (6)
C(2)	C(3)	1.411 (7)	1.410 (7)	1.410 (6)	1.417 (6)
C(2)	C(14)	1.474 (7)	1.472 (7)	1.485 (6)	1.482 (6)
C(3)	C(4)	1.456 (7)	1.450 (8)	1.449 (6)	1.450 (6)
C(4)	C(5)	1.385 (7)	1.396 (8)	1.392 (6)	1.394 (6)
C(4)	C(9)	1.431 (7)	1.427 (7)	1.402 (6)	1.411 (6)
C(5)	C(6)	1.344 (8)	1.338 (8)	1.350 (6)	1.354 (6)
C(6)	C(7)	1.411 (7)	1.429 (7)	1.407 (6)	1.399 (6)
C(7)	C(8)	1.394 (7)	1.394 (7)	1.392 (6)	1.393 (6)
C(8)	C(9)	1.407 (7)	1.409 (7)	1.406 (5)	1.412 (6)
C(8)	C(12)	1.508 (7)	1.517 (8)	1.514 (6)	1.508 (6)
C(10)	C(11)	1.509 (8)	1.515 (8)	1.515 (7)	1.518 (7)
C(10)	C(13)	1.504 (9)	1.51 (1)	1.496 (8)	1.494 (8)
C(11)	C(12)	1.524 (8)	1.504 (9)	1.518 (7)	1.545 (7)
C(15)	C(16)	1.513 (8)	1.51 (1)	1.517 (7)	1.517 (8)
C(16)	C(17)	1.51 (1)	1.530 (9)	1.512 (7)	1.515 (7)
C(17)	C(18)	1.52 (1)	1.528 (9)	1.503 (7)	1.497 (7)
C(18)	C(19)	1.508 (9)	1.52 (1)	1.509 (6)	1.515 (7)



nadifloxacin (1)



nalidixic acid (2)



ofloxacin (3)

Chart 1

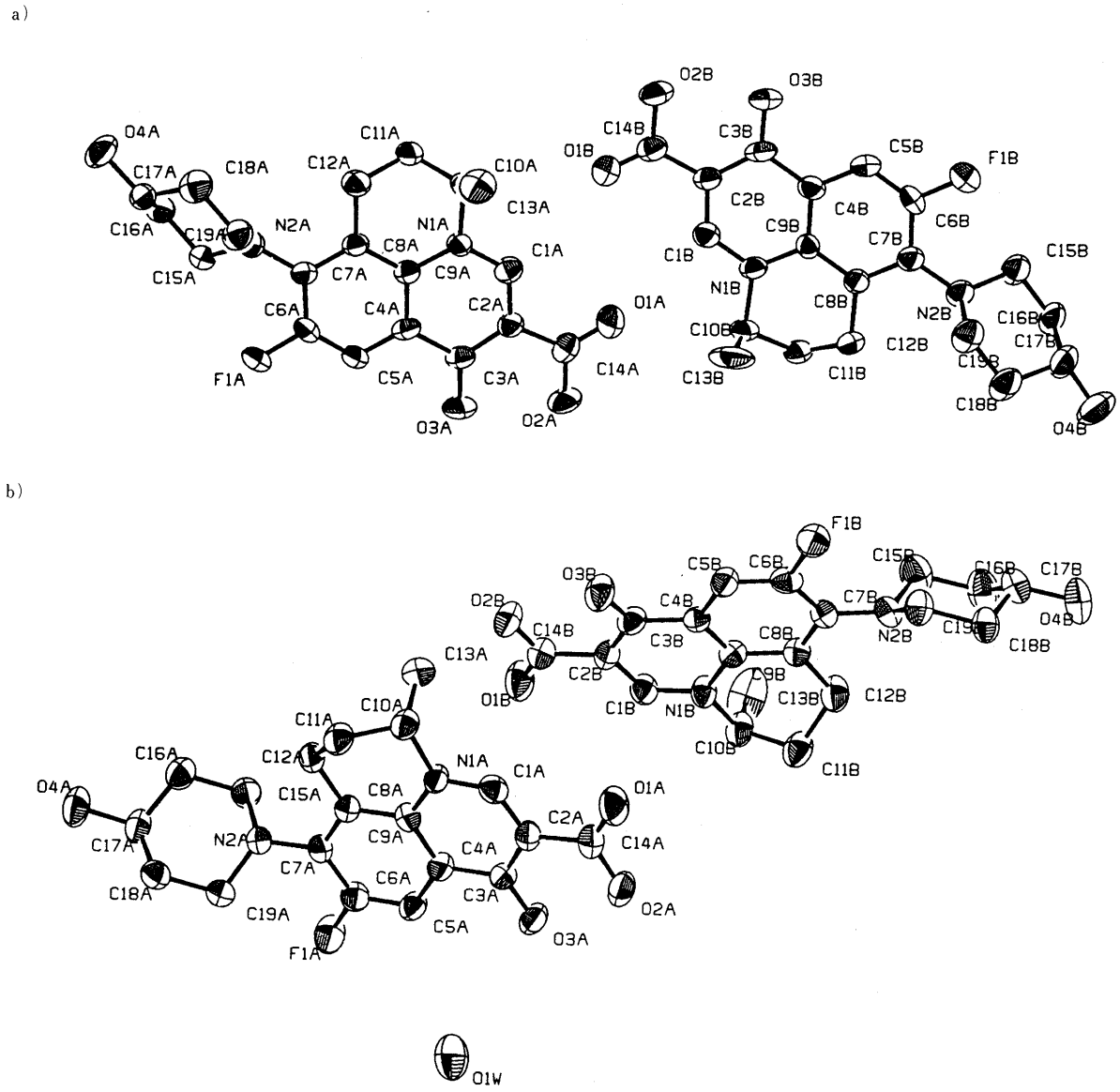


Fig. 1. ORTEP View of the Molecular Structure with Numbering System

Thermal ellipsoids are drawn at 50% probability; H atoms are not shown. a) nadifloxacin anhydride, b) nadifloxacin hemihydrate.

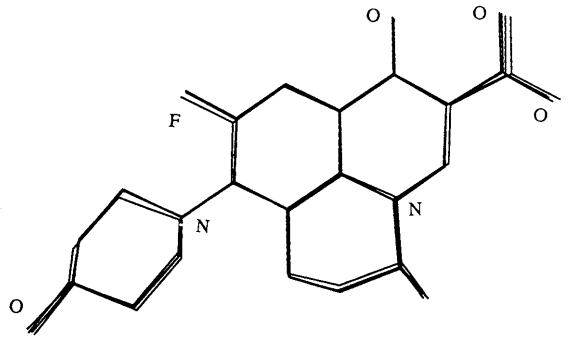


Fig. 2. The Four Molecular Structures Superposed upon One Another by the Least-Squares Method (Non-H Atoms, Only)

superposed well upon one another (Fig. 2). The structural features of these molecules are very similar to each other.

The equations of the least-squares planes of the 4-oxoquinolinone moiety of the four independent molecules in the two crystals and deviations of individual atoms from them are given in Table III. The molecules exhibit *anti* conformation, and the C(11) and C(13) atoms are located at opposite sides of the plane. The C(13) atom is almost perpendicular to the 4-oxoquinolinone moiety with dihedral angles about C(10)–N(1) of $\pm 86°$ and $\pm 85°$ for nadifloxacin anhydride, and $\pm 86°$ and $\pm 80°$ for nadifloxacin hemihydrate. This is consistent with the suggestion by Sato and Mitsuhashi[7] that the corresponding dihedral angle in the oxazine ring of ofloxacin (**3**) is in the ranges of 30° to 90° or −30° to −90°.

The four piperidine rings in the two crystals have typical chair conformations. The N(2) and C(17) atoms deviate by 0.65 to 0.68 and −0.65 to −0.70 Å from the respective mean plane through C(15), C(16), C(18) and C(19). The C(14)–O(2) distances in the four molecules were 1.324 Å to 1.332 Å, and the C(14)–O(1) distances were 1.203 Å to 1.215 Å. Intramolecular distances between O(2) and O(3) of 2.520 to 2.546 Å suggested that an intramolecular hydrogen bond exists between the oxygen atoms.

TABLE II. Bond Angles (°) for Nadifloxacin Anhydride and Hemihydrate with Their e.s.d.'s in Parentheses

Atom	Atom	Atom	Anhydride		Hemihydrate	
			Mol. A Angle	Mol. B Angle	Mol. A Angle	Mol. B Angle
C(1)	N(1)	C(9)	121.2 (4)	121.2 (4)	120.0 (4)	119.7 (4)
C(1)	N(1)	C(10)	117.1 (5)	117.3 (5)	119.3 (4)	119.2 (4)
C(9)	N(1)	C(10)	121.6 (5)	121.4 (5)	120.6 (4)	120.7 (4)
C(7)	N(2)	C(15)	119.0 (5)	120.7 (5)	116.1 (4)	115.3 (4)
C(7)	N(2)	C(19)	116.3 (5)	117.5 (6)	119.3 (4)	118.8 (4)
C(15)	N(2)	C(19)	112.6 (6)	110.9 (6)	112.2 (4)	112.4 (4)
N(1)	C(1)	C(2)	123.2 (6)	124.0 (6)	124.6 (4)	124.7 (4)
C(1)	C(2)	C(3)	120.2 (6)	119.0 (6)	119.2 (4)	119.5 (4)
C(1)	C(2)	C(14)	118.8 (5)	117.8 (6)	118.5 (4)	118.8 (4)
C(3)	C(2)	C(14)	121.0 (5)	123.3 (5)	122.3 (4)	121.7 (4)
O(3)	C(3)	C(2)	123.3 (6)	122.5 (6)	122.3 (4)	122.9 (4)
O(3)	C(3)	C(4)	119.8 (5)	120.7 (6)	120.6 (4)	120.7 (4)
C(2)	C(3)	C(4)	116.9 (5)	116.8 (5)	117.1 (4)	116.3 (4)
C(3)	C(4)	C(5)	120.4 (5)	120.8 (5)	119.8 (4)	119.6 (4)
C(3)	C(4)	C(9)	120.0 (5)	121.7 (5)	120.8 (4)	120.7 (4)
C(5)	C(4)	C(9)	119.5 (6)	117.4 (6)	119.4 (4)	119.7 (4)
C(4)	C(5)	C(6)	119.2 (5)	120.2 (6)	118.8 (4)	118.0 (4)
F(1)	C(6)	C(5)	117.6 (5)	118.6 (5)	117.8 (4)	117.5 (4)
F(1)	C(6)	C(7)	118.2 (6)	117.2 (6)	118.4 (4)	117.7 (3)
C(5)	C(6)	C(7)	124.2 (6)	124.2 (6)	123.8 (4)	124.8 (4)
N(2)	C(7)	C(6)	123.3 (5)	123.5 (5)	122.8 (4)	124.2 (4)
N(2)	C(7)	C(8)	119.2 (5)	120.2 (5)	119.4 (4)	118.0 (4)
C(6)	C(7)	C(8)	117.5 (6)	116.2 (6)	117.8 (4)	117.8 (4)
C(7)	C(8)	C(9)	119.3 (5)	120.0 (5)	119.2 (4)	118.9 (4)
C(7)	C(8)	C(12)	120.6 (6)	120.2 (6)	120.6 (4)	120.5 (4)
C(9)	C(8)	C(12)	119.9 (5)	119.7 (6)	120.2 (4)	120.5 (4)
N(1)	C(9)	C(4)	118.4 (6)	117.2 (5)	118.4 (4)	118.5 (4)
N(1)	C(9)	C(8)	121.5 (4)	121.0 (4)	120.7 (4)	120.6 (4)
C(4)	C(9)	C(8)	120.1 (5)	121.9 (5)	120.9 (4)	120.8 (4)
N(1)	C(10)	C(11)	108.5 (5)	107.7 (5)	108.7 (4)	109.2 (4)
N(1)	C(10)	C(13)	109.0 (5)	106.0 (5)	110.1 (4)	109.1 (5)
C(11)	C(10)	C(13)	115.5 (6)	115.1 (7)	115.1 (5)	115.9 (5)
C(10)	C(11)	C(12)	112.1 (5)	111.1 (6)	110.2 (5)	109.0 (5)
C(8)	C(12)	C(11)	110.6 (6)	110.7 (6)	110.7 (4)	110.0 (4)
O(1)	C(14)	O(2)	120.8 (7)	120.8 (7)	120.7 (4)	121.6 (5)
O(1)	C(14)	C(2)	123.7 (5)	124.8 (5)	123.6 (5)	122.9 (5)
O(2)	C(14)	C(2)	115.5 (5)	114.4 (6)	115.8 (4)	115.6 (4)
N(2)	C(15)	C(16)	109.1 (5)	108.3 (5)	109.9 (4)	110.2 (5)
C(15)	C(16)	C(17)	111.7 (6)	109.1 (6)	111.2 (5)	110.2 (5)
O(4)	C(17)	C(16)	113.2 (6)	110.0 (6)	110.2 (4)	107.5 (5)
O(4)	C(17)	C(18)	112.6 (6)	107.9 (6)	112.0 (4)	113.5 (5)
C(16)	C(17)	C(18)	110.1 (8)	107.4 (7)	110.5 (4)	109.0 (5)
C(17)	C(18)	C(19)	110.6 (6)	110.1 (6)	110.7 (4)	110.3 (5)
N(2)	C(19)	C(18)	110.6 (6)	110.7 (6)	108.4 (4)	109.9 (4)

TABLE III. The Deviations (Å) of Atoms from the Least-Squares Planes

	Anhydride		Hemihydrate	
	Mol. A[a]	Mol. B[b]	Mol. A[c]	Mol. B[d]
C(4)[e]	0.01	0.01	0.00	0.00
C(5)[e]	0.01	−0.00	0.00	0.01
C(6)[e]	−0.02	−0.00	−0.00	−0.01
C(7)[e]	0.01	0.00	−0.00	0.00
C(8)[e]	0.00	0.00	0.01	0.01
C(9)[e]	−0.00	−0.01	−0.00	−0.01
N(1)	0.03	−0.06	0.02	−0.02
C(1)	0.12	−0.10	0.07	−0.15
C(2)	0.12	−0.02	0.07	−0.20
C(3)	0.05	−0.05	0.02	−0.04
C(10)	0.01	−0.06	−0.06	−0.02
C(11)	0.70	0.69	0.68	0.77
C(12)	0.08	0.07	0.07	0.12
C(13)	−1.41	−1.51	−1.49	−1.44

a) $-0.68599x+0.72759y+0.00616z=-0.32100$. *b*) $-0.80064x+0.57601y+0.16489z=-0.66126$. *c*) $0.15749x-0.98645y+0.04607z=-1.29958$. *d*) $-0.19464x-0.97928y+0.05590z=-2.04405$. *e*) The atoms indicated were included in the calculation of the least-squares planes.

TABLE IV. Significant Hydrogen-Bonding (Å)

	D–H	A	Distance	Symmetry code
Anhydride:				
	O(2)A–H	O(3)A	2.520 (7)	x, y, z
	O(2)B–H	O(3)B	2.546 (6)	x, y, z
	O(4)A–H	O(3)B	2.847 (6)	$1-x, 1-y, -z$
	O(4)B–H	O(4)A	2.833 (8)	$-1+x, -1+y, 1+z$
Hemihydrate:				
	O(2)A–H	O(3)A	2.544 (5)	x, y, z
	O(2)B–H	O(3)B	2.543 (5)	x, y, z
	O(4)A–H	O(3)A	2.800 (5)	$1+x, y, z$
	O(1W)–H	O(3)B	2.943 (5)	$1-x, -y, 1-z$
	O(1W)–H	O(4)A	2.797 (5)	$-1+x, y, z$
	O(4)B–H	O(1W)	2.812 (5)	$-1+x, y, -1+z$

The main features of the two crystal structures are caused by hydrogen bonding interactions (Fig. 3). In the anhydride crystal, O(4) A (hydroxy group of a piperidine ring of molecule A) bridges two molecules B related by a center of symmetry through O(4)A$\cdots$H-O(4)B and O(4)A-H$\cdots$O(3)B hydrogen bonds. In the hemihydrate crystal, occupying the position corresponding to O(4)A of the anhydride crystal, a water molecule shifts molecule A by a hydrogen bonding distance along the molecular axis. In both crystals two molecules A and two molecules B are tightly bound by the hydrogen bonds around a center of symmetry (Table IV). Each crystal structure is mainly stabilized by the hydrogen bonds and usual van der Waals contacts among these neighboring molecules.

Experimental

X-Ray Analysis of Nadifloxacin Anhydride The cubic crystal used for the X-ray study was obtained from acetonitrile solution and had dimensions of approximately $0.3\times0.3\times0.3$ mm. Crystal data: $C_{19}H_{21}FN_2O_4$, $M_r=360.38$, triclinic, $a=11.238(9)$, $b=16.31(1)$, $c=10.178(4)$ Å, $\alpha=101.62(5)$, $\beta=105.69(5)$, $\gamma=80.30(6)°$, $V=1746(2)$ Å^3, space group $P\bar{1}$, $Z=4$, $D_x=1.371$ g/cm^3, $F(000)=760$, and $\mu(MoK_\alpha)=0.97$ cm^{-1}. Intensity data were collected at room temperature on a Rigaku AFC5S diffractometer with monochromated MoK_α radiation, in the ω–2θ scan mode. In total, 4489 independent reflections with $2\theta<45°$ were measured. Lorentz and polarization corrections were applied, but no absorption correction. Finally, 2389 reflections with $I>3\sigma(I)$ were used for structure determination and refinement. The stucture was solved by the direct method using the TEXSAN crystallographic software package.[8]

Atomic parameters were refined by the full-matrix least-squares procedure. All of the H atoms were readily located on the difference Fourier map. In the further refinement, anisotropic and isotropic thermal parameters were employed for the non-H and H atoms, respectively. The refinement converged to $R=0.052$ and $R_w=0.058$. Atomic scattering factors were taken from "International Tables for X-ray Crystallography."[9] The final positional parameters of non-H atoms are given in Table V.[10]

X-Ray Analysis of Nadifloxacin Hemihydrate The prism crystal used for the X-ray study was obtained from EtOH aqueous solution and had dimensions of approximately $0.5\times0.5\times0.5$ mm. Data collection, reduction and refinement were as described for nadifloxacin anhydride crystal. Crystal data: $(C_{19}H_{21}FN_2O_4)_2\cdot H_2O$, $M_r=738.78$, monoclinic, $a=10.722(5)$, $b=17.336(3)$, $c=18.893(2)$ Å, $\beta=91.58(2)°$, $V=3510(1)$ Å^3, space group $P2_1/n$, $Z=4$, $D_x=1.398$ g/cm^3, $F(000)=1560$, and $\mu(MoK_\alpha)=1.00$ cm^{-1}. In total, 6469 independent reflections were

TABLE V. Positional Parameters for the Non-H Atoms of Nadifloxacin Anhydride with Their e.s.d.'s in Parentheses

Atom	Molecule A			Molecule B		
	x	y	z	x	y	z
F(1)	1.0392 (3)	0.7311 (2)	0.5622 (3)	0.1529 (3)	−0.0611 (2)	0.3780 (3)
O(1)	0.5742 (4)	0.4032 (3)	0.6429 (4)	0.4632 (4)	0.3404 (3)	0.2540 (4)
O(2)	0.6950 (4)	0.4746 (3)	0.8205 (4)	0.3389 (4)	0.2657 (3)	0.0837 (4)
O(3)	0.8369 (4)	0.5671 (3)	0.7824 (4)	0.2359 (4)	0.1530 (3)	0.1374 (4)
O(4)	1.0235 (4)	0.8076 (3)	−0.0239 (4)	0.2503 (4)	−0.1339 (3)	0.9886 (5)
N(1)	0.7069 (4)	0.4971 (3)	0.3653 (4)	0.4144 (4)	0.2125 (3)	0.5437 (4)
N(2)	0.9410 (4)	0.6945 (3)	0.2727 (4)	0.2651 (4)	−0.0187 (3)	0.6633 (4)
C(1)	0.6658 (5)	0.4663 (4)	0.4556 (5)	0.4239 (5)	0.2555 (4)	0.4494 (6)
C(2)	0.7066 (5)	0.4878 (3)	0.5971 (5)	0.3699 (5)	0.2368 (3)	0.3104 (5)
C(3)	0.7953 (5)	0.5452 (3)	0.6539 (5)	0.2942 (5)	0.1709 (4)	0.2629 (5)
C(4)	0.8363 (5)	0.5812 (3)	0.5562 (5)	0.2854 (5)	0.1227 (4)	0.3644 (5)
C(5)	0.9181 (5)	0.6415 (4)	0.6032 (6)	0.2193 (6)	0.0530 (4)	0.3259 (6)
C(6)	0.9545 (5)	0.6742 (4)	0.5114 (5)	0.2146 (5)	0.0084 (4)	0.4210 (6)
C(7)	0.9097 (5)	0.6543 (3)	0.3666 (5)	0.2744 (5)	0.0268 (3)	0.5648 (5)
C(8)	0.8283 (5)	0.5931 (3)	0.3163 (5)	0.3418 (5)	0.0958 (3)	0.6055 (5)
C(9)	0.7913 (5)	0.5563 (3)	0.4102 (5)	0.3480 (5)	0.1432 (3)	0.5066 (5)
C(10)	0.6561 (6)	0.4668 (4)	0.2147 (5)	0.4863 (6)	0.2376 (4)	0.6910 (5)
C(11)	0.6485 (6)	0.5376 (4)	0.1363 (6)	0.4174 (7)	0.2160 (4)	0.7861 (6)
C(12)	0.7737 (6)	0.5703 (4)	0.1630 (5)	0.4040 (6)	0.1234 (4)	0.7566 (6)
C(13)	0.7328 (8)	0.3862 (5)	0.1707 (8)	0.6178 (7)	0.1942 (7)	0.7040 (9)
C(14)	0.6517 (6)	0.4517 (4)	0.6857 (6)	0.3951 (5)	0.2862 (4)	0.2169 (6)
C(15)	0.9617 (7)	0.7822 (4)	0.3118 (6)	0.1524 (6)	−0.0570 (6)	0.6464 (8)
C(16)	0.9454 (7)	0.8199 (5)	0.1830 (6)	0.1427 (6)	−0.0688 (5)	0.7867 (8)
C(17)	1.0335 (7)	0.7724 (5)	0.0978 (7)	0.2550 (6)	−0.1267 (5)	0.8532 (7)
C(18)	1.0171 (7)	0.6793 (5)	0.0648 (7)	0.3726 (7)	−0.0879 (6)	0.8639 (8)
C(19)	1.0294 (6)	0.6451 (5)	0.1955 (7)	0.3772 (6)	−0.0734 (5)	0.7229 (8)

TABLE VI. Positional Parameters for the Non-H Atoms of Nadifloxacin Hemihydrate with Their e.s.d.'s in Parentheses

Atom	Molecule A			Molecule B		
	x	y	z	x	y	z
F(1)	0.7817 (2)	0.1088 (2)	0.8445 (1)	0.1425 (2)	0.1080 (2)	0.0004 (1)
O(1)	0.3324 (3)	0.0759 (2)	0.4763 (2)	0.6042 (3)	0.1075 (2)	0.3629 (2)
O(2)	0.2582 (3)	0.0594 (2)	0.5832 (2)	0.6759 (3)	0.0822 (2)	0.2563 (1)
O(3)	0.4032 (3)	0.0790 (2)	0.6906 (2)	0.5210 (3)	0.0640 (2)	0.1533 (1)
O(4)	1.3605 (3)	0.1523 (2)	0.8197 (2)	−0.4208 (3)	0.1874 (2)	0.0200 (2)
N(1)	0.6909 (3)	0.1119 (2)	0.5573 (2)	0.2395 (3)	0.1116 (2)	0.2871 (2)
N(2)	0.9863 (3)	0.1291 (2)	0.7563 (2)	−0.0586 (3)	0.1343 (2)	0.0908 (2)
C(1)	0.5749 (4)	0.0990 (3)	0.5330 (3)	0.3576 (4)	0.1062 (3)	0.3102 (2)
C(2)	0.4750 (4)	0.0869 (2)	0.5747 (2)	0.4564 (4)	0.0943 (2)	0.2680 (2)
C(3)	0.4927 (4)	0.0875 (2)	0.6490 (2)	0.4355 (4)	0.0827 (3)	0.1944 (2)
C(4)	0.6187 (4)	0.0992 (2)	0.6764 (2)	0.3087 (4)	0.0937 (2)	0.1677 (2)
C(5)	0.6428 (4)	0.0977 (3)	0.7492 (2)	0.2833 (4)	0.0916 (3)	0.0950 (2)
C(6)	0.7612 (4)	0.1082 (3)	0.7736 (2)	0.1648 (4)	0.1056 (3)	0.0718 (2)
C(7)	0.8631 (4)	0.1207 (2)	0.7297 (2)	0.0646 (4)	0.1203 (2)	0.1157 (2)
C(8)	0.8400 (4)	0.1220 (2)	0.6569 (2)	0.0884 (4)	0.1218 (2)	0.1885 (2)
C(9)	0.7172 (4)	0.1121 (2)	0.6305 (2)	0.2116 (4)	0.1097 (2)	0.2144 (2)
C(10)	0.7906 (4)	0.1294 (3)	0.5063 (2)	0.1403 (4)	0.1277 (4)	0.3387 (3)
C(11)	0.9127 (5)	0.0964 (4)	0.5349 (3)	0.0177 (5)	0.0941 (4)	0.3110 (3)
C(12)	0.9461 (5)	0.1316 (4)	0.6064 (3)	−0.0168 (5)	0.1318 (4)	0.2391 (3)
C(13)	0.7926 (6)	0.2139 (4)	0.4905 (4)	0.1394 (7)	0.2120 (4)	0.3550 (4)
C(14)	0.3507 (4)	0.0743 (3)	0.5400 (3)	0.5838 (4)	0.0949 (3)	0.3005 (3)
C(15)	1.0366 (5)	0.2074 (3)	0.7566 (3)	−0.0940 (5)	0.2151 (3)	0.0861 (4)
C(16)	1.1781 (5)	0.2047 (3)	0.7588 (3)	−0.2350 (6)	0.2228 (4)	0.0828 (4)
C(17)	1.2268 (4)	0.1569 (3)	0.8205 (3)	−0.2890 (5)	0.1772 (3)	0.0207 (3)
C(18)	1.1670 (4)	0.0784 (3)	0.8197 (3)	−0.2493 (4)	0.0948 (3)	0.0281 (3)
C(19)	1.0267 (4)	0.0853 (3)	0.8194 (3)	−0.1082 (3)	0.0891 (3)	0.0314 (3)
O(1W)	0.4588 (3)	0.0731 (2)	0.9375 (2)			

measured with $2\theta < 50°$, among which 3262 reflections ($I > 2\sigma(I)$) were regarded as observed. The resulting E map revealed the positions of all non-H atoms. Of the 44H atoms, 42 (excluding the two H atoms of the water molecule) were located near the expected positions on the difference Fourier maps. In the refinement, anisotropic and isotropic thermal parameters were employed for the non-H and H aroms, respectively. The refinement converged to $R = 0.059$ and $R_w = 0.066$. The final positional parameters of non-H atoms are given in Table VI.[10]

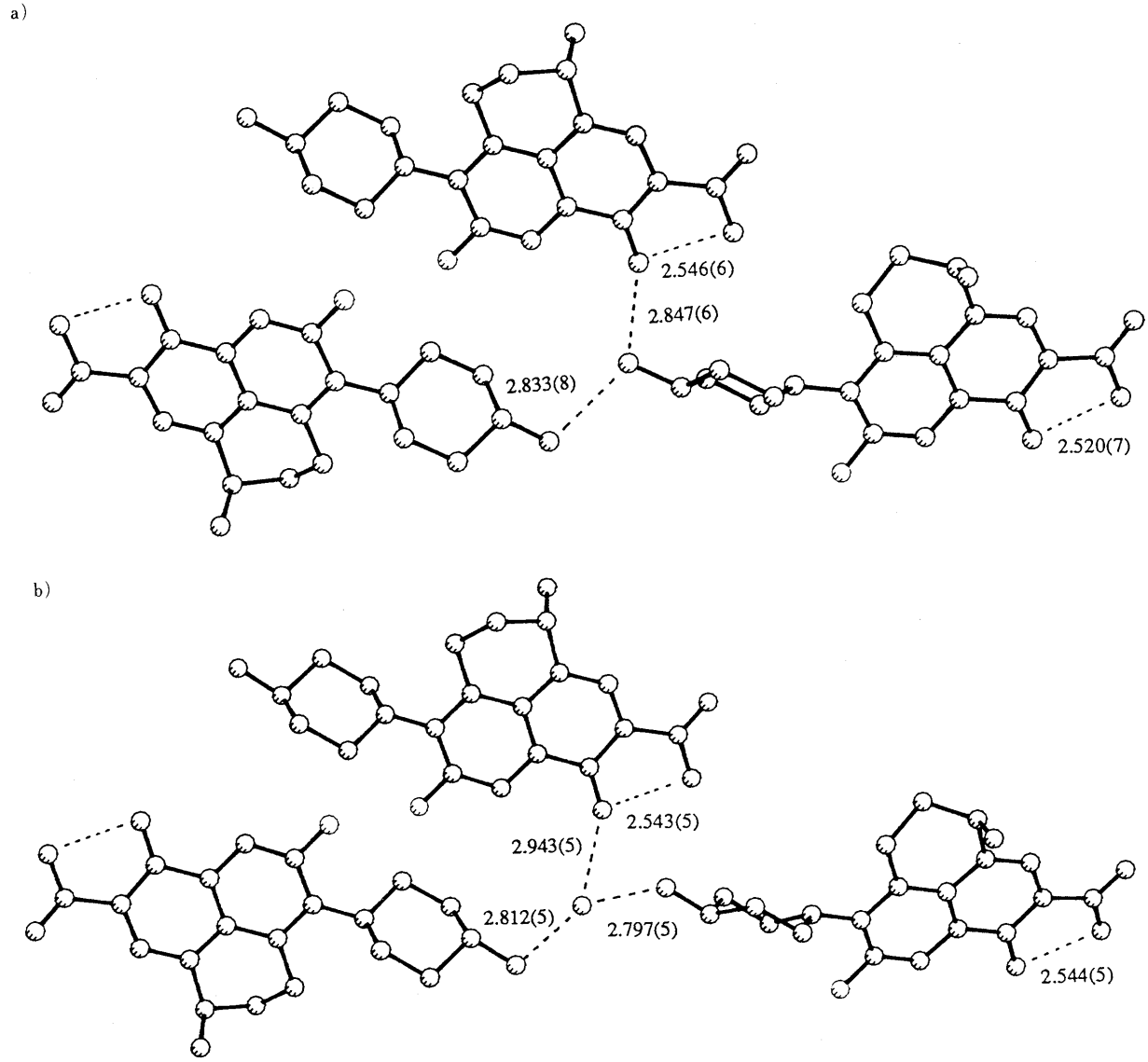


Fig. 3. Hydrogen-Bonding Network

Hydrogen bond distances (Å) with their e.s.d.'s in parentheses are shown as ○---○ in the figure. a) nadifloxacin anhydride, b) nadifloxacin hemihydrate.

References and Notes

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10) Tables of the anisotropic temperature factors for non-H atoms, the atomic coordinates and isotropic temperature factors for H atoms are available from the authors on request.