Crystal structure of α-diisopropylaminoethyl-α-phenylpyridine-2-acetamide phosphate, $[C_{21}H_{30}N_3O][H_2PO_4]$

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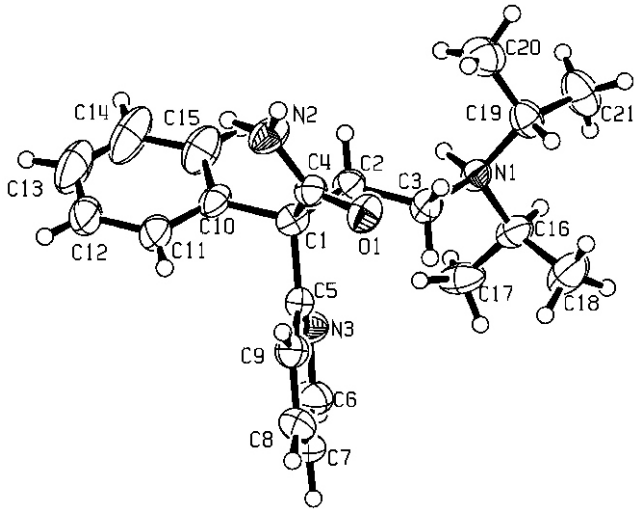

Abstract

$C_{21}H_{32}N_3O_5P$, orthorhombic, $Pna2_1$ (no. 33), a = 8.266(7) Å, b = 12.430(7) Å, c = 20.89(2) Å, V = 2146.4 Å^3, Z = 4, $R_{gt}(F)$ = 0.047, $wR_{ref}(F^2)$ = 0.041, T = 293 K.

Source of material

Disopyramide phosphate was purchased from Sigma-Aldrich Co. The single crystals of the compound were grown from a methanol solution. A colorless platelet crystal was mounted on a glass fiber and used for data collection.

Experimental details

The structure was solved by direct methods and non-H atoms were refined by a full-matrix least squares method with anisotropic displacement factors. Positions of the H atoms attached to the nitrogen atoms and the phosphate oxygen atoms were located from difference Fourier maps. All other H atoms were geometrically calculated. All H atoms were refined applying the riding model. The Flack parameter is 0.08(3), refined using 1792 Friedel pairs.

Discussion

Disopyramide is an antiarrhythmic drug currently applied clinically. It exerts electrophysiological effects very similar to those of quinidine [1]. Although disopyramide has an asymmetric carbon, it is prescribed as a racemate. To disclose the inherent three-dimensional structure of disopyramide, the X-ray analysis of the phosphate salt of the racemate was undertaken.

The chain moiety connecting the phenyl group and the N1 atom is fully extended with the torsion angles of N1–C3–C2–C1 and C3–C2–C1–C10 being –175.8(2)° and 175.3(2)°, respectively. The torsion angle C2–C1–C10–C15 of 6.5(4)° indicates that N1, C3, C2 and C1 atoms are nearly coplanar with the phenyl ring. On the other hand, the pyridine ring is almost perpendicular to the planar part. The dihedral angle between the phenyl and pyridine rings is 97.1(2)°. The torsion angle N2–C4–C1–C10 of 20.3(4)° is significantly smaller than the torsion angle O1–C4–C1–C5 of -44.0(4)°. Owing to this conformation, one of the H atoms attached to the N2 atom points to the center (G) of the phenyl ring with d(H···G) = 3.02 Å and ∠N2–H···G = 127°. This hydrogen atom is not involved in hydrogen bonds. The bonds N3—C5 and C5—C9 are significantly longer than the bonds N3—C6 and C8—C9, respectively. Other bond lengths in the molecule are within the expected ranges. There are intermolecular hydrogen bonds between disopyramide molecules (d(N2···O1; ½+x, ½–y,z) = 2.927(3) Å, d(N2—H29) = 0.83 Å, d(H29···O1) = 2.16 Å, ∠N2–H29···O1 = 156°) and between disopyramide molecules and phosphates (d(N1···O2) = 2.691(3) Å, d(N1—H28) = 0.95 Å, d(H28···O2) = 1.76 Å, ∠N1–H28···O2 = 167°). It is noteworthy that the pyridine nitrogen is not involved in the hydrogen bond. There are two intermolecular hydrogen bonds between phosphates (d(O5···O4; ½+x,¾–y,z) = 2.444(3) Å, d(O5—H31) = 0.81 Å, d(H31···O4) = 1.64 Å, ∠O5–H31···O4 = 173°; d(O3···O2; –½+x,¾–y,z) = 2.491(2) Å, d(O3—H32) = 0.99 Å, d(H32···O2) = 1.51 Å, ∠O3–H32···O2 = 172°). One intramolecular C–H···O bond is observed (d(C3···O1) = 2.934(4) Å, d(C3—H12) = 0.95 Å, d(H12···O1) = 2.34 Å, ∠C9–H12···O1 = 120°). It seems that due to the intramolecular C–H···O bond the O1 atom is fixed between the pyridine ring and the aminoethyl group.

Table 1. Data collection and handling.

Crystal:	colorless platelet, size 0.10 × 0.20 × 0.50 mm
Wavelength:	Cu K_α radiation (1.54187 Å)
μ:	14.61 cm^{-1}
Diffractometer, scan mode:	Rigaku RAXIS-RAPID, ω
$2\theta_{max}$:	136.48°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	16948, 3759
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2484
$N(param)_{refined}$:	304
Programs:	SIR92 [2], ORTEP-3 [3]

Table 2. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{iso}
H(1)	4a	0.2057	0.5429	0.5145	0.063
H(2)	4a	0.1735	0.3994	0.4460	0.057

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Table 2. Continued.

Atom	Site	x	y	z	U_{iso}
H(3)	4*a*	0.3837	0.2758	0.4357	0.058
H(4)	4*a*	0.6148	0.2972	0.4976	0.047
H(5)	4*a*	0.7945	0.4618	0.4659	0.061
H(6)	4*a*	0.9527	0.5868	0.4109	0.086
H(7)	4*a*	1.0205	0.7495	0.4605	0.099
H(8)	4*a*	0.9513	0.7784	0.5639	0.101
H(9)	4*a*	0.7960	0.6559	0.6200	0.070
H(10)	4*a*	0.7207	0.5117	0.6752	0.040
H(11)	4*a*	0.5715	0.5662	0.6439	0.040
H(12)	4*a*	0.5740	0.3572	0.6933	0.042
H(13)	4*a*	0.4260	0.4060	0.6581	0.042
H(14)	4*a*	0.2505	0.5150	0.7879	0.052
H(15)	4*a*	0.3018	0.6031	0.6843	0.075
H(16)	4*a*	0.1244	0.5901	0.7073	0.075
H(17)	4*a*	0.1958	0.5104	0.6576	0.075

Table 2. Continued.

Atom	Site	x	y	z	U_{iso}
H(18)	4*a*	0.1772	0.3493	0.7930	0.081
H(19)	4*a*	0.0885	0.3781	0.7299	0.080
H(20)	4*a*	0.2546	0.3201	0.7276	0.080
H(21)	4*a*	0.5061	0.3336	0.7970	0.056
H(22)	4*a*	0.7355	0.4840	0.8279	0.076
H(23)	4*a*	0.7585	0.3606	0.8215	0.076
H(24)	4*a*	0.7477	0.4318	0.7607	0.076
H(25)	4*a*	0.5355	0.4367	0.8985	0.080
H(26)	4*a*	0.4278	0.5189	0.8624	0.080
H(27)	4*a*	0.3644	0.4034	0.8752	0.080
H(28)	4*a*	0.4985	0.5393	0.7489	0.041
H(29)	4*a*	0.9950	0.3167	0.6037	0.059
H(30)	4*a*	0.9870	0.4087	0.5697	0.059
H(31)	4*a*	0.6379	0.8266	0.8402	0.056
H(32)	4*a*	0.2247	0.8199	0.7598	0.059

Table 3. Atomic coordinates and displacement parameters (in $Å^2$).

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
P(1)	4*a*	0.4391(1)	0.7561(1)	0.80066(6)	0.0258(4)	0.0402(6)	0.0488(5)	0.0029(7)	–0.0026(7)	0.0001(7)
O(1)	4*a*	0.7186(2)	0.2716(2)	0.6115(1)	0.035(2)	0.035(2)	0.064(2)	–0.004(1)	0.003(1)	0.004(2)
O(2)	4*a*	0.5434(2)	0.6741(2)	0.7671(1)	0.020(1)	0.041(2)	0.056(2)	0.000(1)	0.005(1)	–0.016(1)
O(3)	4*a*	0.3410(2)	0.8187(2)	0.7490(1)	0.024(2)	0.068(2)	0.055(2)	0.003(1)	0.005(2)	0.024(2)
O(4)	4*a*	0.3282(2)	0.7079(2)	0.8488(1)	0.025(2)	0.047(2)	0.042(2)	–0.004(1)	0.000(1)	0.011(1)
O(5)	4*a*	0.5461(2)	0.8431(2)	0.8315(1)	0.029(2)	0.041(2)	0.070(2)	–0.002(2)	–0.005(2)	–0.015(1)
N(1)	4*a*	0.4561(3)	0.4684(2)	0.7467(1)	0.037(2)	0.031(2)	0.034(2)	–0.002(2)	0.006(2)	–0.004(2)
N(2)	4*a*	0.9379(3)	0.3696(2)	0.5961(1)	0.040(2)	0.038(2)	0.070(2)	0.010(2)	0.001(2)	0.010(2)
N(3)	4*a*	0.4189(3)	0.5061(2)	0.5471(1)	0.031(2)	0.051(2)	0.045(2)	0.011(2)	–0.008(2)	0.003(2)
C(1)	4*a*	0.6817(4)	0.4587(2)	0.5835(2)	0.036(2)	0.017(2)	0.032(2)	–0.002(2)	0.004(2)	–0.001(2)
C(2)	4*a*	0.6273(3)	0.5001(2)	0.6496(2)	0.029(2)	0.037(2)	0.034(2)	0.004(2)	0.001(2)	0.001(2)
C(3)	4*a*	0.5163(3)	0.4217(2)	0.6846(2)	0.035(2)	0.043(2)	0.028(2)	0.003(2)	0.003(2)	–0.007(2)
C(4)	4*a*	0.7806(4)	0.3557(3)	0.5971(2)	0.026(2)	0.039(2)	0.029(2)	0.005(2)	0.005(2)	–0.007(2)
C(5)	4*a*	0.5352(4)	0.4331(3)	0.5417(2)	0.025(2)	0.044(2)	0.031(2)	–0.012(2)	0.005(2)	–0.001(2)
C(6)	4*a*	0.2904(4)	0.4915(3)	0.5115(2)	0.037(2)	0.067(3)	0.054(3)	0.011(2)	–0.009(2)	0.005(2)
C(7)	4*a*	0.2703(4)	0.4071(3)	0.4701(2)	0.037(2)	0.068(3)	0.036(2)	–0.016(2)	–0.013(2)	0.015(2)
C(8)	4*a*	0.3927(4)	0.3345(3)	0.4646(2)	0.055(3)	0.054(3)	0.036(2)	–0.014(2)	0.002(2)	–0.006(2)
C(9)	4*a*	0.5277(4)	0.3468(3)	0.5006(2)	0.041(2)	0.039(2)	0.037(2)	0.004(2)	–0.002(2)	–0.003(2)
C(10)	4*a*	0.7800(4)	0.5445(3)	0.5492(2)	0.031(2)	0.028(2)	0.047(2)	0.004(2)	–0.004(2)	0.006(2)
C(11)	4*a*	0.8264(4)	0.5265(3)	0.4866(2)	0.033(2)	0.081(3)	0.039(2)	–0.014(2)	–0.014(2)	0.010(2)
C(12)	4*a*	0.9187(5)	0.6010(4)	0.4536(2)	0.042(3)	0.123(5)	0.050(3)	–0.005(3)	–0.001(2)	0.042(3)
C(13)	4*a*	0.9609(6)	0.6965(4)	0.4832(2)	0.071(3)	0.074(4)	0.103(4)	–0.003(3)	0.012(3)	0.050(3)
C(14)	4*a*	0.9182(5)	0.7138(3)	0.5434(2)	0.064(3)	0.058(3)	0.131(4)	–0.016(3)	0.009(4)	0.013(3)
C(15)	4*a*	0.8270(4)	0.6404(3)	0.5772(2)	0.047(2)	0.045(2)	0.084(3)	–0.010(2)	0.011(2)	0.005(2)
C(16)	4*a*	0.2762(4)	0.4796(3)	0.7489(2)	0.029(2)	0.058(3)	0.044(2)	–0.003(2)	0.009(2)	–0.006(2)
C(17)	4*a*	0.2192(3)	0.5527(2)	0.6943(2)	0.024(2)	0.088(3)	0.074(3)	0.008(2)	–0.017(2)	–0.021(2)
C(18)	4*a*	0.1913(4)	0.3717(2)	0.7499(2)	0.057(2)	0.070(3)	0.074(3)	–0.026(2)	0.014(2)	–0.033(2)
C(19)	4*a*	0.5291(4)	0.4079(2)	0.8023(2)	0.070(3)	0.031(2)	0.040(2)	0.004(2)	0.005(3)	0.011(2)
C(20)	4*a*	0.7092(3)	0.4224(3)	0.8031(2)	0.047(2)	0.078(3)	0.064(2)	0.008(2)	–0.018(3)	0.012(2)
C(21)	4*a*	0.4575(4)	0.4452(2)	0.8655(2)	0.093(3)	0.071(3)	0.036(2)	0.011(3)	0.009(2)	0.000(2)

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