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The crystal structure of 2,4-dihydroxybenzoic acid–nicotinamide–methanol (1/1/1), $C_{15}H_{18}N_2O_6$

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	$0.42 \times 0.35 \times 0.27$ mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ :	0.11 mm ^{−1}
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
$\theta_{\max}$, completeness:	25.5°, 99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	5984, 2887, 0.014
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 2225
$N(\text{param})_{\text{refined}}$:	232
Programs:	Bruker [1], SHELX [2, 3], Olex2 [4], Diamond [5]

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Abstract

$C_{15}H_{18}N_2O_6$, triclinic, $P\bar{1}$ (no. 2), $a = 7.4217(18)$ Å, $b = 7.7021(18)$ Å, $c = 15.362(4)$ Å, $\alpha = 79.223(2)^\circ$, $\beta = 82.086(3)^\circ$, $\gamma = 65.182(2)^\circ$, $V = 781.2(3)$ Å³, $Z = 2$, $R_{\text{gt}}(F) = 0.0444$, $wR_{\text{ref}}(F^2) = 0.1341$, $T = 296(2)$ K.

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Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

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Source of material

2,4-Dihydroxybenzoic acid (1 mmol) and nicotinamide (1 mmol) were dissolved in the ethanol (4 mL)-water (2 mL), and this solution was slowly evaporated at room temperature, resulting in colorless block crystals after one week.

Experimental details

The U_{iso} values were set to $1.5U_{\text{eq}}(\text{C})$ hydrogen atoms in hydroxyl and methyl groups, and $1.2U_{\text{eq}}(\text{C or N})$ for the rest. The electron density indicated disorder in ethanol.

Comment

Numerous research regarding co-crystals of nicotinamide molecules have been carried out due to its importance as a pyridine derivative with biological activity and pharmacological property. The pyridine nitrogen atom and the carbonyl oxygen atom of nicotinamide are acceptors, but amide protons are donors, thus affording abundant hydrogen-bond motifs with organic carboxylic acids. For example, malonic acid [6], citric acid [7], pimelic acid [6, 7], succinic acid [8], cycle-carboxylic acids [9] and benzoic acids [6, 10–12] have been used to construct co-crystals with nicotinamide to investigate the stoichiometric variation, proton transfer, polymorphism and phase transition.

The asymmetric unit of the title structure comprises one nicotinamide, one 2,4-dihydroxybenzoic acid molecule and one disordered ethanol molecule (see the Figure). This co-crystal is isostructural to the 2,4-dihydroxybenzoic acid–nicotinamide-methanol co-crystal molecule [6], however, the

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	x	y	z	U _{iso} ^a /U _{eq}
C1	0.8679(3)	0.5277(3)	0.71896(11)	0.0427(4)
H1	0.9264	0.3957	0.7388	0.051*
C2	0.8508(3)	0.6550(3)	0.77568(11)	0.0413(4)
C3	0.7657(3)	0.8516(3)	0.74504(12)	0.0480(4)
H3	0.7501	0.9410	0.7817	0.058*
C4	0.7045(3)	0.9128(3)	0.65966(12)	0.0501(5)
H4A	0.6507	1.0437	0.6372	0.060*
C5	0.7248(3)	0.7761(3)	0.60848(11)	0.0469(4)
H5A	0.6812	0.8179	0.5513	0.056*
C6	0.9141(3)	0.5864(3)	0.86878(11)	0.0475(4)
C7	0.7387(2)	0.3156(2)	0.39116(10)	0.0373(4)
C8	0.6794(2)	0.3947(2)	0.30447(11)	0.0386(4)
C9	0.6861(3)	0.2763(2)	0.24520(11)	0.0424(4)
H9	0.6472	0.3294	0.1878	0.051*
C10	0.7509(3)	0.0789(3)	0.27166(12)	0.0440(4)
C11	0.8093(3)	−0.0019(3)	0.35758(12)	0.0477(4)
H11	0.8524	−0.1344	0.3754	0.057*
C12	0.8025(3)	0.1164(3)	0.41530(12)	0.0441(4)
H12	0.8417	0.0621	0.4726	0.053*
C13	0.7363(2)	0.4415(3)	0.45270(11)	0.0408(4)
C14 ^a	0.7028(9)	0.1979(11)	0.9960(3)	0.141(2)
H14A ^a	0.7093	0.3129	1.0098	0.169*
H14B ^a	0.8375	0.0991	0.9954	0.169*
C14 ^b	0.6282(19)	0.148(2)	0.9723(6)	0.092(4)
H14C ^b	0.5281	0.2674	0.9451	0.110*
H14D ^b	0.6130	0.0418	0.9534	0.110*
C15 ^a	0.6427(11)	0.2394(9)	0.9120(3)	0.138(2)
H15A ^a	0.5635	0.1703	0.9075	0.207*
H15B ^a	0.7572	0.2015	0.8708	0.207*
H15C ^a	0.5651	0.3758	0.8985	0.207*
C15 ^b	0.825(2)	0.142(4)	0.9401(13)	0.181(9)
H15D ^b	0.8747	0.1854	0.9826	0.271*
H15E ^b	0.8158	0.2252	0.8844	0.271*
H15F ^b	0.9142	0.0122	0.9323	0.271*
N1	1.0752(2)	0.4266(2)	0.88331(10)	0.0580(5)
H1A	1.1148	0.3834	0.9362	0.070*
H1B	1.1408	0.3653	0.8399	0.070*
N2	0.8040(2)	0.5862(2)	0.63687(9)	0.0435(4)
O1	0.8151(2)	0.6792(2)	0.92925(8)	0.0694(5)
O2	0.8033(2)	0.35151(19)	0.53040(8)	0.0560(4)
H2	0.7950	0.4307	0.5615	0.084*
O3	0.6785(2)	0.61795(18)	0.43230(8)	0.0526(4)
O4	0.6182(2)	0.58690(17)	0.27520(8)	0.0531(4)
H4	0.6095	0.6438	0.3167	0.080*
O5	0.7605(2)	−0.04366(19)	0.21642(9)	0.0605(4)
H5	0.7058	0.0189	0.1710	0.091*
O6	0.5927(3)	0.1356(3)	1.06639(11)	0.0925(6)
H6	0.4744	0.1931	1.0571	0.139*

^aOccupancy: 0.746(8), ^bOccupancy: 0.254(8).

large difference in structural parameters is still found. For example, the angle of C1–C2–C6–N1 twists more strongly [37.9(3)°]. The lengths of C–O and C–N bonds in the amide group are larger about 0.33 and 0.44 Å compared with its

isostructural compound [6], respectively. The C–O bond lengths of 1.310(2) and 1.232(2) Å for the carboxylic acid group are more typical characteristics of an organic acid, revealing no proton transfer between nicotinamide and 2,4-dihydroxybenzoic acid.

Complex hydrogen bonds are found in this co-crystal. Two nicotinamide molecules construct a dimer by amide–amide hydrogen bonds. This dimer connects two 2,4-dihydroxybenzoic acid with an intra molecular hydrogen bond, through the heteromeric O–H...N hydrogen bonds between the COOH group of acid and the pyridine N of the nicotinamide, to generate a tetramer. Furthermore each 2,4-dihydroxybenzoic acid in this tetramer is connected to one ethanol molecule by its phenol oxygen in the para-position, forming a phenol–alcohol hydrogen bond. More importantly, the two carbonyl oxygen atoms of the amide group form a hydrogen bond with two adjacent ethanol molecules. These intermolecular hydrogen bonds result in a 3-D hydrogen bonded network. In addition, the pyridine and benzene ring further stabilize this crystal by the π – π packing interactions with the Cg–Cg distance of 3.76 Å.

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