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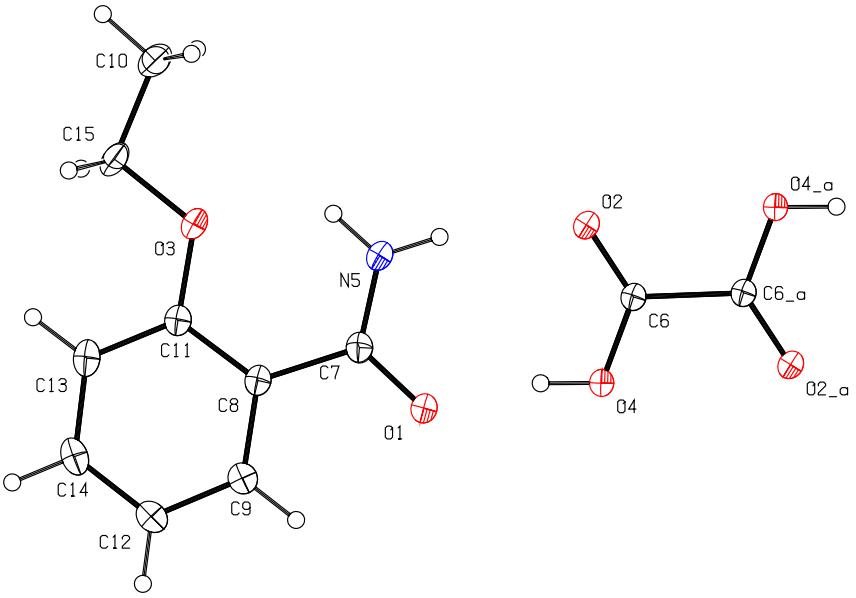
The crystal structure of oxalic acid – 2-ethoxybenzamide (2/1), $C_{20}H_{24}N_2O_8$



https://doi.org/10.1515/ncrs-2022-0493
Received October 7, 2022; accepted October 27, 2022;
published online December 1, 2022

Abstract

$C_{20}H_{24}N_2O_8$, monoclinic, $P2_1/n$ (no. 14), a = 3.8981(3) Å, b = 16.0675(11) Å, c = 16.2908(10) Å, β = 94.537(3)°, V = 1017.14(12) Å^3, Z = 2, $R_{gt}(F)$ = 0.0634, $wR_{ref}(F^2)$ = 0.1746, T = 170 K.

CCDC no.: 2209328

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

Table 1: Data collection and handling.

Crystal:	Colourless needle
Size:	0.12 × 0.03 × 0.02 mm
Wavelength:	Ga *K*α radiation (1.34138 Å)
μ:	0.58 mm^{-1}
Diffractometer, scan mode:	Bruker D8 Venture, φ and ω
θ_{max}, completeness:	61.2°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	9587, 2322, 0.040
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 1879
$N(param)_{refined}$:	140
Programs:	Bruker [1], Olex2 [2], SHELX [3, 4]

Source of materials

A mixture of ethenzamide (165.2 mg, 1 mmol) and oxalic acid (90.0 mg, 1 mmol) was dissolved in 3 mL of ethyl acetate solution, and the resulting mixture was stirred and dissolved at 60 °C to obtain a clear solution, which was filtered and placed in a 5 mL glass vial. Crystals of the title compound were obtained after two days.

Experimental details

Absorption corrections were applied by using multi-scan program [1]. Using Olex2 [2], the structure was solved with the ShelXT [3] structure solution program and refined with the ShelXL [4] refinement package.

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
O1	0.2516 (5)	0.76162 (10)	0.55529 (10)	0.0406 (4)
O2	0.2852 (5)	0.97356 (10)	0.58366 (11)	0.0447 (5)
O3	0.8657 (4)	0.71675 (10)	0.76926 (10)	0.0375 (4)
O4	−0.0123 (5)	0.89223 (10)	0.49207 (10)	0.0384 (4)
N5	0.5659 (6)	0.82041 (13)	0.66029 (12)	0.0401 (5)
H5A	0.503969	0.870566	0.643227	0.048*
H5B	0.705555	0.814310	0.705035	0.048*
C6	0.0845 (6)	0.96279 (13)	0.52385 (13)	0.0305 (5)
C7	0.4494 (6)	0.75428 (14)	0.61873 (14)	0.0322 (5)
C8	0.5512 (6)	0.66881 (14)	0.64758 (14)	0.0326 (5)
C9	0.4326 (7)	0.60262 (15)	0.59799 (16)	0.0392 (6)
H9	0.299623	0.613955	0.547845	0.047*
C10	1.1576 (7)	0.78427 (17)	0.88286 (15)	0.0425 (6)
H10A	1.286298	0.815349	0.843616	0.064*
H10B	1.301918	0.776627	0.934342	0.064*
H10C	0.949867	0.815338	0.893906	0.064*
C11	0.7451 (6)	0.65044 (15)	0.72178 (14)	0.0336 (5)
C12	0.5032 (8)	0.52072 (16)	0.61975 (18)	0.0479 (7)
H12	0.423417	0.476491	0.584545	0.057*
C13	0.8115 (7)	0.56859 (16)	0.74503 (17)	0.0443 (6)
H13	0.938123	0.556486	0.795862	0.053*
C14	0.6907 (9)	0.50435 (17)	0.69312 (19)	0.0525 (8)
H14	0.738509	0.448286	0.708616	0.063*
C15	1.0576 (6)	0.70077 (17)	0.84717 (14)	0.0373 (6)
H15A	1.265090	0.667213	0.838915	0.045*
H15B	0.914008	0.670077	0.884486	0.045*
H4	0.091 (8)	0.8522 (16)	0.5185 (18)	0.056*

Comment

Ethenzamide is an API from the non-steroidal antiinflammatory (NSAID) group of drugs which shows analgesic and antipyretic activity. It is a poorly-water soluble drug used for treatment of moderate and mild pain [5]. That feature makes a great challenge to enhance ethenzamide solubility and one of the best method is cocrystallization [6]. Cocrystals of pyrazinamide were obtained with flufenamic acid (CCDC:1448786, FAQXAZ) [7], ferulic acid (CCDC:1448786, FAQXAZ) [8], 2,6-dihydroxybenzoic acid (CCDC:891074, GEQXEH), 3,5−dichlorobenzoic acid (CCDC:891075, GEQXIL) [9], 2-chloro-4-nitrobenzoic acid (CCDC:752481, REHSEE), 4−hydroxy-3-methoxybenzoic acid (CCDC:752482, REHSII), 4-aminobenzoic acid (CCDC:752483, REHSOO), 4-hydroxybenzoic acid (CCDC:752484, REHSUU), fumaric acid (CCDC:896104, REHTAB) [10], pentanedioic acid (CCDC:1854255, TIWPIB), (2Z)-but-2-enedioic acid (CCDC:1854256, TIWPOH), propanedioic acid (CCDC:1854257, TIWPUN) [11], ethylmalonic acid (CCDC:752465, VAKTOS) [12], Saccharin (CCDC:711674, VUHFIO) [13] and so on. Among them, some studies found that the solubility of the cocrystal formed by ethenzamide and oxalic acid at a stoichiometric ratio of 2:1 was 2.0 and 2.5 times of that of ethenzamide raw material in phosphate buffer solution and simulated gastric juice, respectively, but the perfect crystal was not cultivated [14].

In the unit cell of the title co-crystal, the predominant force is the formation of intermolecular hydrogen bonds between the amide group of the ethenzamide and the carboxyl group on the oxalic acid (see the figure). On the one hand, the O2 atom on the carboxyl group of the oxalic acid molecule is a hydrogen bond acceptor, and the H5A atom on the amide group (N5−H5) of the ethenzamide molecule is a hydrogen bond donor, forming an intermolecular hydrogen bond N5−H5A···O2 [length 2.932(3) Å, angle 166.8°]; on the other hand, the O1 atom on the amide group of the ethenzamide molecule is a hydrogen bond acceptor, and the H4 atom on the carboxyl group (O4−H4) of the oxalic acid molecule is a hydrogen bond donor, forming intermolecular hydrogen bonds O4−H4···O1 [length 2.521(2) Å, angle 168(3)°].

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Research funding: This work was funded by Zhejiang Province Basic Public Welfare Research Project (LGJ20B060001).

Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

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