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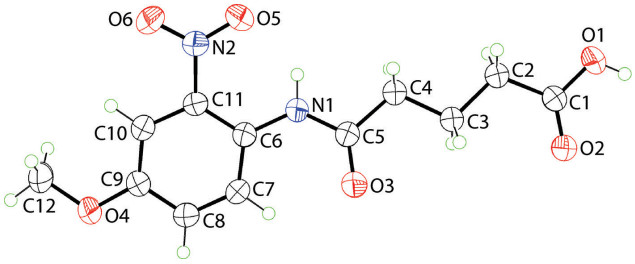
Crystal structure of 4-[(4-methoxy-2-nitrophenyl) carbamoyl]butanoic acid, $C_{12}H_{14}N_2O_6$



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Abstract

$C_{12}H_{14}N_2O_6$, triclinic, $P\bar{1}$ (no. 2), $a = 4.8835(4)$ Å, $b = 9.2111(7)$ Å, $c = 14.6655(7)$ Å, $\alpha = 76.135(5)°$, $\beta = 82.693(6)°$, $\gamma = 87.379(7)°$, $V = 635.19(8)$ Å^3, $Z = 2$, $R_{gt}(F) = 0.0449$, $wR_{ref}(F^2) = 0.1297$, $T = 293(1)$ K.

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The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Source of material

4-Methoxy aniline (Sigma-Aldrich; 0.56 g, 5 mmol) and glutaric anhydride (Sigma-Aldrich; 0.57 g, 5 mmol) were dissolved separately in analytical grade toluene (ca 10–15 mL). The two solutions were then slowly mixed and stirred at room temperature until the appearance of yellow precipitate. The resulting precipitate was washed with a minimum amount of toluene (to remove any unreacted reactants) and then with

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Table 1: Data collection and handling.

Crystal:	Yellow prism
Size:	0.13 × 0.09 × 0.06 mm
Wavelength:	Cu $K\alpha$ radiation (1.54184 Å)
μ:	1.03 mm^{-1}
Diffractometer, scan mode:	XtaLAB Synergy, ω
θ_{max}, completeness:	67.1°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	14803, 2267, 0.041
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma(I_{obs})$, 1969
$N(param)_{refined}$:	188
Programs:	CrysAlis^{PRO} [1], SHELX [2, 3], WinGX/ORTEP [4]

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

Atom	x	y	z	U_{iso}*/U_{eq}
O1	0.7000(3)	0.57969(19)	0.05405(9)	0.0749(5)
H1O	0.799(6)	0.583(4)	0.0032(14)	0.112*
O2	0.9970(3)	0.40397(17)	0.11252(9)	0.0626(4)
O3	0.8601(3)	0.19436(18)	0.47437(9)	0.0675(5)
O4	0.4971(3)	−0.15120(16)	0.90826(9)	0.0632(4)
O5	0.0053(3)	0.33983(16)	0.63309(9)	0.0645(4)
O6	−0.0987(3)	0.27358(19)	0.78196(10)	0.0795(5)
N1	0.4247(3)	0.21163(18)	0.54797(10)	0.0495(4)
H1N	0.269(3)	0.257(2)	0.5398(15)	0.059*
N2	0.0423(3)	0.25956(16)	0.70976(10)	0.0469(4)
C1	0.7882(4)	0.4784(2)	0.12275(11)	0.0461(4)
C2	0.6057(4)	0.4619(2)	0.21419(11)	0.0474(4)
H2A	0.430617	0.421954	0.207848	0.057*
H2B	0.569303	0.560231	0.226627	0.057*
C3	0.7239(3)	0.3617(2)	0.29818(11)	0.0444(4)
H3A	0.761780	0.263015	0.286435	0.053*
H3B	0.896825	0.402060	0.306255	0.053*
C4	0.5254(4)	0.3489(2)	0.38768(11)	0.0481(4)
H4A	0.495603	0.447298	0.400506	0.058*
H4B	0.349208	0.314741	0.377520	0.058*
C5	0.6247(3)	0.2434(2)	0.47306(11)	0.0436(4)
C6	0.4441(3)	0.12560(19)	0.63937(11)	0.0410(4)
C7	0.6483(3)	0.0134(2)	0.65813(12)	0.0442(4)
H7	0.777368	−0.001931	0.608823	0.053*
C8	0.6613(3)	−0.0740(2)	0.74762(12)	0.0461(4)
H8	0.800277	−0.146443	0.757922	0.055*
C9	0.4703(4)	−0.0561(2)	0.82317(12)	0.0456(4)
C10	0.2700(3)	0.0538(2)	0.80762(11)	0.0448(4)
H10	0.141883	0.067954	0.857474	0.054*

Table 2 (continued)

Atom	x	y	z	U_{iso}*/U_{eq}
C11	0.2592(3)	0.14377(18)	0.71717(11)	0.0401(4)
C12	0.2814(5)	−0.1490(3)	0.98342(14)	0.0693(6)
H12A	0.280685	−0.054918	1.000853	0.104*
H12B	0.311520	−0.228699	1.037008	0.104*
H12C	0.106920	−0.161791	0.962920	0.104*

water (to remove any glutaric acid that may have formed during the reaction). After that, the desired compound was air-dried and recrystallised in ethanol:acetone mixture (1:1) to produce yellow crystals. Yield: 82%. **M.pt** (Gallenkamp (UK) electrothermal melting point apparatus): 418–420 K. **FTIR** (FTIR Spectrometer Model Thermo Nicolet iS50; cm^{-1}): 3123 ν(OH); 3348 ν(NH); 1688 ν(amide C=O); 1582 ν(CO_{asym}); 1328 ν(CO_{sym}). **^{1}H NMR** (Bruker Advanced Digital 400 MHz NMR spectrometer, chemical shifts relative to Me_4Si, DMSO-d_6 solution at 298 K; numbering as per the figure): 11.02 (s, 1H, OH), 2.50 (t, 2H, H2, $J = 10.0$ Hz), 1.94 (quin, 2H, H3, $J = 14.7$ Hz), 2.32 (t, 2H, H4, $J = 15$ Hz); 8.58 (s, 1H, NH), 7.38–7.40 (d, 1H, H7, $J = 5$ Hz), 6.75 (d, 1H, H8, $J = 5$ Hz), 6.74 (s, br,1H, H10), 3.70 (s, 3H, H12). **^{13}C{^{1}H} NMR** (as for ^{1}H NMR): 174.3, 32.8, 20.2, 35.9, 170.9, 128.5, 125.3, 121.4, 155.2, 108.4, 140.1, 55.6 for C1–C12, respectively.

Experimental details

The C-bound H atoms were geometrically placed (C—H = 0.93–0.97 Å) and refined as riding with $U_{iso}(H) = 1.2$–$1.5U_{eq}(C)$. The O- and N-bound H atoms were refined with O—H = 0.82 ± 0.01 Å and N—H = 0.86 ± 0.01 Å, and with $U_{iso}(H) = 1.5U_{eq}(O)$ or $1.2U_{eq}(N)$.

Comment

Organotin compounds, including organotin carboxylates, have long been known to possess biological activity, including anti-cancer potential [5, 6]. In continuing studies in this area, recent attention has focussed on the biological activity of organotin carboxylates derived from carboxylic acids incorporating an amide group [7]. Concurrent studies show that these carboxylic acids of the general formula $ArN(H)C(=O)(CH_2)_3C(=O)OH$ also demonstrate potential as anti-cancer and anti-leishmanial agents [8]. In this communication, the crystal and molecular structures of one such carboxylic acid derivative, where Ar = 4-methoxy-2-nitrophenyl, (I), are described.

The molecular structure of (I) is shown in the figure (50% probability displacement ellipsoids) and adopts an extended (all-*trans*) configuration as seen in the sequence of C1—C2—C3—C4 [−179.14(16)°], C2—C3—C4—C5 [176.77(15)°], C3—C4—C5—N1 [−168.45(16)°] and C4—C5—N1—C6 [-176.31(17)°] torsion angles, respectively. A small twist in the chain about the C4—C5 bond is indicated by the deviation of the C3—C4—C5—N1 torsion angle from 180°. The carboxylic acid residue exhibits a significant difference in the C—O bond lengths [C1—O1, O2 = 1.302(2) and 1.216(2) Å] confirming protonation at the O1 atom. This group is twisted out of the plane of the backbone of the molecule as seen in the O2—C1—C2—C3 torsion angle of 9.2(3)°. A far greater twist is noted between the amide group and the appended aryl ring as reflected in the C5—N1—C6—C7 torsion angle of −24.5(3)°. The amide-N—H atom is orientated towards a nitro-O atom to allow the formation of an intramolecular N—H···O hydrogen bond [N1—H1n···O5: H1n···O5 = 2.019(19) Å, N1···O5 = 2.643(2) Å with angle at H1n = 128.8(18)°].

The most closely related compound in the crystallographic literature is the derivative where the Ar group is 4-((methylsulfonyl)amino)-3-phenoxyphenyl. The molecule has a highly twisted conformation in the C_3 chain by contrast to that in (I) [9]. In the molecular packing, an eight-membered $\{\cdots OCOH\}_2$ homosynthon forms as a result of hydroxy-O—H···O(carbonyl) hydrogen bonding [O1—H1o···O2^i: H1o···O2^i = 1.84(2) Å, O1···O2^i = 2.6654(19) Å with angle at H1o = 177(3)° for symmetry operation (i) $2-x, 1-y, -z$]. In addition to the formation of an intramolecular N—H···O interaction, the amide-N—H atom, being bifurcated, forms an intermolecular hydrogen bond with the amide-O atom [N1—H1n···O3^{ii}: H1n···O3^{ii} = 2.470(17) Å, N1···O3^{ii} = 3.110(2) Å with angle at H1n = 132.0(16)° for (ii) $-x, y, z$] to form supramolecular chains to link the aforementioned dimers into a supramolecular tape parallel to (0 −2 −1). The links between tapes to consolidate the three-dimensional packing are weak C—H···O interactions, involving methyl-H and hydroxyl-O1 atoms [C12—H12b..O1^{iii}: H12b···O1^{iii} = 2.53 Å, C12···O1^{iii} = 3.214(3) Å with angle at H12b = 129° for (iii) $x, -1+y, 1+z$] and weaker methylene-C—H···O(nitro) interactions, involving both nitro-O atoms, with a minimum H···O separation of 2.70 Å.

A complementary analysis of the molecular packing of (I) was performed by calculating the Hirshfeld surface and the two-dimensional fingerprint plots employing Crystal Explorer 17 [10] following literature procedures [11]. The analysis confirms the dominance of H···O/O···H contacts to the overall surface, contributing 46.0% of all contacts, and reflecting the hydrogen bonding interactions as well as the numerous weaker interactions. The next most prominent contacts are due to H···H [29.1%], H···C/C···H [11.1%], C···O/O···C [5.5%] and O···O [3.3%] contacts.

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