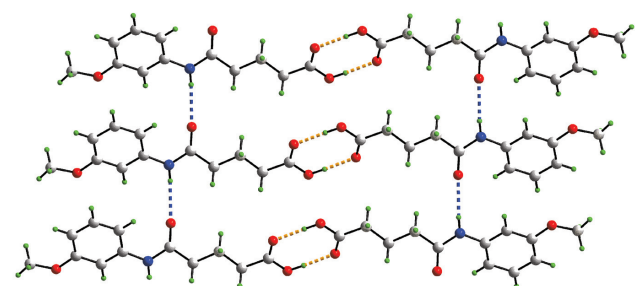
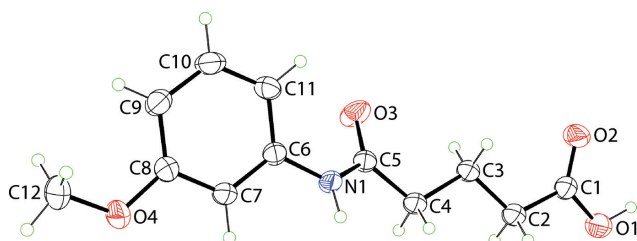


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Crystal structure of 4-[(3-methoxyphenyl) carbamoyl]butanoic acid, $C_{12}H_{15}NO_4$



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Abstract

$C_{12}H_{15}NO_4$, triclinic, $P\bar{1}$ (no. 2), $a = 5.0167(2)$ Å, $b = 7.9264(5)$ Å, $c = 15.2073(7)$ Å, $\alpha = 98.909(4)^\circ$, $\beta = 92.060(4)^\circ$, $\gamma = 101.800(4)^\circ$, $V = 583.36(5)$ Å³, $Z = 2$, $R_{gt}(F) = 0.0403$, $wR_{ref}(F^2) = 0.1179$, $T = 293(2)$ 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.

Table 1: Data collection and handling.

Crystal:	Yellow prism
Size:	0.14 × 0.10 × 0.04 mm
Wavelength:	Cu $K\alpha$ radiation (1.54184 Å)
μ :	0.85 mm ⁻¹
Diffractometer, scan mode:	XtaLAB Synergy, ω
θ_{max} , completeness:	67.1°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int} :	11933, 2063, 0.054
Criterion for I_{obs} , $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 1759
$N(param)_{refined}$:	162
Programs:	CrysAlis ^{PRO} [1], SHELX [2, 3], WinGX/ORTEP [4]

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

Atom	x	y	z	U_{iso}^*/U_{eq}
O1	0.6754(3)	0.3435(2)	0.96977(9)	0.0665(4)
H10	0.791(6)	0.410(4)	1.017(2)	0.100*
O2	0.9810(2)	0.48540(18)	0.89073(8)	0.0625(4)
O3	0.8217(2)	0.2514(2)	0.54362(8)	0.0640(4)
O4	0.0073(2)	0.02065(17)	0.20074(8)	0.0582(4)
N1	0.3876(2)	0.24244(18)	0.49466(9)	0.0419(3)
H1N	0.231(4)	0.234(2)	0.5114(13)	0.050*
C1	0.7638(3)	0.3853(2)	0.89392(11)	0.0448(4)
C2	0.5747(3)	0.2986(2)	0.81469(11)	0.0471(4)
H2A	0.409327	0.344013	0.818760	0.057*
H2B	0.524707	0.174528	0.816865	0.057*
C3	0.6875(3)	0.3218(2)	0.72537(10)	0.0423(4)
H3A	0.851297	0.274892	0.719826	0.051*
H3B	0.736577	0.445392	0.721915	0.051*
C4	0.4793(3)	0.2294(2)	0.64939(10)	0.0420(4)
H4A	0.426713	0.106836	0.654625	0.050*
H4B	0.317493	0.278474	0.654972	0.050*
C5	0.5818(3)	0.2438(2)	0.55819(10)	0.0404(4)
C6	0.4187(3)	0.23759(19)	0.40237(10)	0.0378(4)
C7	0.2087(3)	0.1366(2)	0.34356(10)	0.0413(4)
H7	0.055844	0.073301	0.365534	0.050*
C8	0.2239(3)	0.1290(2)	0.25249(11)	0.0423(4)
C9	0.4497(3)	0.2228(2)	0.21877(12)	0.0484(4)
H9	0.460933	0.218750	0.157603	0.058*

Table 2 (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
C10	0.6586(3)	0.3228(2)	0.27845(12)	0.0526(4)
H10	0.811612	0.385669	0.256300	0.063*
C11	0.6477(3)	0.3325(2)	0.36925(12)	0.0456(4)
H11	0.790496	0.401026	0.407877	0.055*
C12	-0.0053(4)	0.0272(3)	0.10823(12)	0.0664(5)
H12A	-0.006745	0.144315	0.099372	0.100*
H12B	-0.168628	-0.050392	0.079943	0.100*
H12C	0.151080	-0.007909	0.082644	0.100*

Source of material

3-Methoxy aniline (Sigma-Aldrich; 0.56 g, 5 mmol) and glutaric anhydride (Sigma-Aldrich; 0.57 g, 5 mmol) were dissolved separately in about 10–15 mL analytical grade diethyl ether. The two solutions were then slowly mixed and stirred at room temperature until the appearance of a light-brown precipitate. The resulting precipitate was washed with a minimum amount diethyl ether (to remove any unreacted reactants) and then with water (to remove any glutaric acid formed during the reaction). The desired compound was air-dried and recrystallised in an ethanol:acetone mixture (1:1) to isolate yellow crystals.

Yield: 84%. **M. pt** (Gallenkamp (UK) electrothermal melting point apparatus): 409–411 K. **FTIR** (FTIR Spectrometer Model Thermo Nicolet iS50; cm⁻¹): 3196 ν(OH), 3309 ν(NH), 1692 ν(amide C=O), 1547 ν(CO_{asym}), 1313 ν(CO_{sym}). **¹H** (Bruker Advanced Digital 500 MHz NMR spectrometer, chemical shifts relative to Me₄Si, CDCl₃ solution at 298 K; δ in ppm): 12.0 (s, 1H, OH), 2.34 (t, 2H, H2, ³J_{HH} = 15 Hz), 1.80 (dt, 2H, H3, ³J_{HH} = 15, 8 Hz), 2.27 (t, 2H, H4, ³J_{HH} = 14 Hz), 9.80 (s, 1H, NH), 7.11 (d, 1H, H11, ³J_{HH} = 8 Hz), 7.18 (t, 1H, H10, ³J_{HH} = 8 Hz); 6.61 (d, 1H, H9, ³J_{HH} = 8 Hz); 7.30 (s, 1H, H7); 3.72 (s, 3H, H12). **¹³C{¹H} NMR**: C1 (174.6), C2 (33.4), C3 (20.8), C4 (35.9), C5 (171.3), C6 (140.9), C11 (111.8) C10 (129.9), C9 (108.8), C8 (160.0), C7 (105.3), C12 (55.4).

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) = 1.2–1.5*U*_{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) = 1.5*U*_{eq}(O) or 1.2*U*_{eq}(N). A number of reflections were omitted from the final cycles of refinement owing to poor agreement, i.e. (3 –3 11), (3 –4 13), (3 –2 10), (3 –5 12) and (2 –4 14).

Comment

The title 4-[(aryl)carbamoyl]butanoic acid derivative, ArN(H)C(=O)(CH₂)₃C(=O)OH, with Ar = 3-methoxyphenyl, is an isomer of the recently described Ar = 2-methoxyphenyl

species [5], the structure of which complemented a rather small number of related species, i.e. with Ar = 4-((methylsulfonyl)amino)-3-phenoxyphenyl [6], Ar = 3,5-dichlorophenyl [7] and Ar = 4-methoxy-2-nitrophenyl [8]. Over and beyond structural studies, investigations into 4-[(aryl)carbamoyl]butanoic acid derivatives suggest these exhibit anti-cancer potential and activity against leishmaniasis [9]; there are also organotin compounds containing carboxylate ligands derived from these species which exhibit anti-cancer potential [10]. This report describes the synthesis and characterisation of (I) along with the determination of its crystal and molecular structures.

The molecular structure of (I) is shown in the upper part of the figure (35% probability displacement ellipsoids). Consistent with the assignment of a carboxylic acid, there is a difference of 0.10 Å in the C–O bond lengths, i.e. C1–O1 = 1.316(2) Å and C1–O2 = 1.2171(19) Å. There are twists at either end of the molecule, i.e. about the C1–C2 and, in particular, the N1–C6 bonds as seen in the values of the O2–C1–C2–C3 [8.5(3)°] and C5–N1–C6–C7 [141.30(16)°] torsion angles. There is also a twist in the carbon-backbone of the molecule, i.e. about the C4–C5 bond, as seen in the sequence of C1–C2–C3–C4 [–179.78(14)°], C2–C3–C4–C5 [–178.56(13)°], C3–C4–C5–N1 [–149.59(14)°] and C4–C5–N1–C6 [–173.66(14)°] torsion angles. The highly twisted conformation noted for (I) can be compared with the two independent molecules comprising the asymmetric unit in the crystal of the isomeric Ar = 2-methoxyphenyl analogue [5], one of which is also twisted and the other which has an all-*trans* (planar) carbon backbone. The conformational flexibility of these molecules is also apparent in the derivative with Ar = 3,5-dichlorophenyl [7] where a twisted conformation is observed but, when Ar = 4-methoxy-2-nitrophenyl [8], an all-*trans* conformation is noted.

The molecular packing features significant hydrogen bonding interactions. Thus, centrosymmetrically related molecules form hydroxy-O–H···O(carbonyl) hydrogen bonds [O1–H10···O2ⁱ: H10···O2ⁱ = 1.76(3) Å, O1···O2ⁱ = 2.6834(19) Å with angle at H10 = 174(3)° for symmetry operation (i) 2 – *x*, 1 – *y*, 2 – *z*] which generate the well known eight-membered {···OCOH}₂ homosynthon (lower part of the figure). The amide residues also self-associate *via* amide-N–H···O(amide) hydrogen bonds [N1–H1n···O3ⁱⁱ: H1n···O3ⁱⁱ = 2.16(2) Å, N1···O3ⁱⁱ = 2.9727(15) Å with angle at H1n = 169.9(17)° for (ii) –1 + *x*, *y*, *z*] with the result that the dimeric aggregates are connected into a supramolecular tape (along the *a*-axis) as shown in the lower part of the figure. The only identified points of contact to link the tapes into a three-dimensional architecture are weak methylene-C–H···π(phenyl) [C3–H3b···Cg(C6–C11)ⁱⁱⁱ: H3b···Cg(C6–C11)ⁱⁱⁱ = 2.98 Å with angle at H3b = 149°

for (iii) $1 - x$, $1 - y$, $1 - z$] interactions. It is noted that in the crystal of the Ar = 3,5-dichlorophenyl derivative, similar supramolecular tapes are formed [7].

To complete the analysis of the molecular packing, the Hirshfeld surface and the two-dimensional fingerprint plots were calculated using Crystal Explorer 17 [11] and procedures outlined in the literature [12]. The fingerprint plot showed the characteristic sharp spikes due to the O—H...O and N—H...O hydrogen bonding with the contribution from all H...O/O...H contacts being 34.4%, which is still less than the H...H contacts, at 44.7%. The only other major contribution to the Hirshfeld surface is provided by H...C/C...H contacts, at 16.0%. These values may be compared with the surface contacts calculated for the isomeric Ar = 2-methoxyphenyl species [5], i.e. with 48.4% of all contacts due to H...H, 27.1% due to H...O/O...H and 16.2% due to H...C/C...H contacts. The differences occur as a notable contribution was made by O...C/C...O contacts, at 4.6%, compared with 1.4% in (I).

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