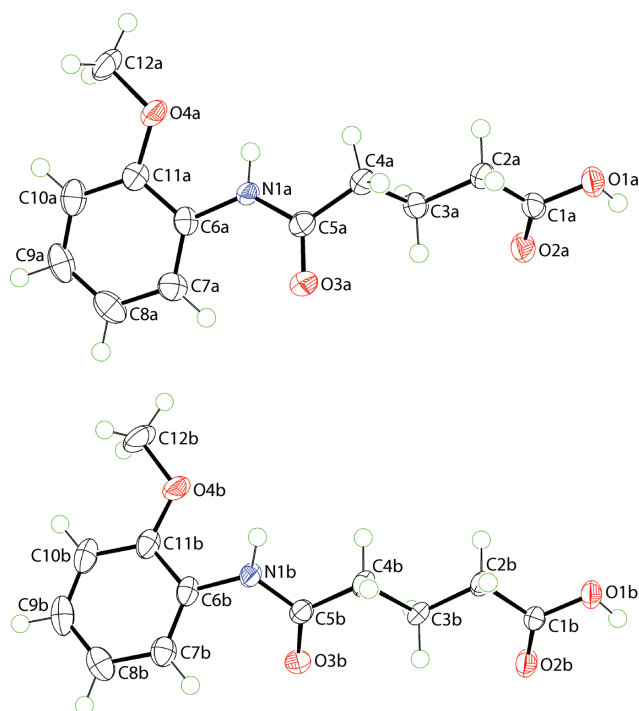


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Crystal structure of 4-[(2-methoxyphenyl) carbamoyl]butanoic acid, $C_{12}H_{15}NO_4$



The molecular structures are 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:	0.16 × 0.10 × 0.05 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%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	28113, 4127, 0.049
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 3630
$N(\text{param})_{\text{refined}}$:	321
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	$U_{\text{iso}}^*/U_{\text{eq}}$
O1A	0.2308(3)	0.1965(3)	0.50223(9)	0.0247(5)
H1O	0.330(4)	0.104(4)	0.5205(14)	0.037*
O2A	0.4827(3)	0.1172(3)	0.43908(9)	0.0250(5)
O3A	0.2060(4)	0.3072(3)	0.23273(9)	0.0284(5)
O4A	-0.0378(3)	1.0023(3)	0.17955(9)	0.0251(5)
N1A	0.1134(4)	0.6416(3)	0.22451(10)	0.0173(5)
H1N	0.057(5)	0.757(3)	0.2420(12)	0.021*
C1A	0.3021(5)	0.2144(4)	0.45195(12)	0.0201(6)
C2A	0.1385(4)	0.3629(4)	0.41285(12)	0.0197(6)
H2A1	0.073038	0.498322	0.429601	0.024*
H2A2	0.031798	0.321223	0.408704	0.024*
C3A	0.2210(4)	0.3785(4)	0.35484(12)	0.0196(6)
H3A1	0.305097	0.240482	0.340555	0.024*
H3A2	0.310940	0.441090	0.358137	0.024*
C4A	0.0493(4)	0.5046(4)	0.31271(12)	0.0207(6)
H4A1	-0.059060	0.464126	0.316168	0.025*
H4A2	-0.012396	0.649928	0.321464	0.025*
C5A	0.1294(4)	0.4753(4)	0.25333(12)	0.0197(6)
C6A	0.1676(4)	0.6556(4)	0.16769(12)	0.0181(6)
C7A	0.2918(5)	0.4919(5)	0.13515(13)	0.0228(6)
H7A	0.348810	0.357487	0.150778	0.027*
C8A	0.3324(5)	0.5256(5)	0.07947(13)	0.0276(7)
H8A	0.417079	0.413486	0.057125	0.033*

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Abstract

$C_{12}H_{15}NO_4$, triclinic, $P\bar{1}$ (no. 2), $a = 7.4325(3)$ Å, $b = 7.5171(3)$ Å, $c = 23.7377(9)$ Å, $\alpha = 87.780(3)^\circ$, $\beta = 89.105(3)^\circ$, $\gamma = 61.299(4)^\circ$, $V = 1162.42(9)$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.0566$, $wR_{\text{ref}}(F^2) = 0.1652$, $T = 100(2)$ K.

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Table 2 (continued)

Atom	x	y	z	U_{iso}^*/U_{eq}
C9A	0.2508(5)	0.7201(5)	0.05640(13)	0.0281(7)
H9A	0.279181	0.740738	0.018262	0.034*
C10A	0.1275(5)	0.8862(5)	0.08845(13)	0.0259(7)
H10A	0.073163	1.020192	0.072676	0.031*
C11A	0.0848(4)	0.8535(4)	0.14394(12)	0.0198(6)
C12A	-0.1178(5)	1.2096(5)	0.16015(14)	0.0296(7)
H12A	-0.004617	1.233212	0.147515	0.044*
H12B	-0.190803	1.299487	0.190986	0.044*
H12C	-0.212671	1.237820	0.128689	0.044*
O1B	0.8088(3)	0.7736(3)	0.00106(8)	0.0235(5)
H2O	0.899(4)	0.683(4)	-0.0185(14)	0.035*
O2B	0.8884(3)	0.5047(3)	0.05900(8)	0.0240(5)
O3B	0.6250(3)	0.5964(3)	0.25787(9)	0.0256(5)
O4B	-0.0286(3)	1.0480(3)	0.31161(9)	0.0303(5)
N1B	0.3567(4)	0.9001(3)	0.28055(10)	0.0188(5)
H2N	0.273(4)	1.022(2)	0.2672(13)	0.023*
C1B	0.7953(4)	0.6873(4)	0.04946(12)	0.0181(6)
C2B	0.6537(4)	0.8357(4)	0.09144(12)	0.0183(6)
H2B1	0.513969	0.910876	0.075137	0.022*
H2B2	0.701067	0.935201	0.098940	0.022*
C3B	0.6460(4)	0.7301(4)	0.14662(11)	0.0180(6)
H3B1	0.787606	0.641092	0.160416	0.022*
H3B2	0.582330	0.643517	0.139855	0.022*
C4B	0.5247(4)	0.8804(4)	0.19162(12)	0.0191(6)
H4B1	0.591711	0.963222	0.199502	0.023*
H4B2	0.384866	0.973154	0.177190	0.023*
C5B	0.5094(4)	0.7759(4)	0.24590(12)	0.0181(6)
C6B	0.3167(5)	0.8494(4)	0.33543(12)	0.0194(6)
C7B	0.4705(5)	0.7256(4)	0.37349(12)	0.0226(6)
H7B	0.610037	0.665540	0.362146	0.027*
C8B	0.4218(5)	0.6889(5)	0.42818(13)	0.0275(7)
H8B	0.527584	0.602795	0.453781	0.033*
C9B	0.2189(5)	0.7783(5)	0.44501(13)	0.0294(7)
H9B	0.186065	0.755437	0.482494	0.035*
C10B	0.0628(5)	0.9013(5)	0.40750(13)	0.0270(7)
H10B	-0.076251	0.962284	0.419257	0.032*
C11B	0.1114(5)	0.9345(4)	0.35266(13)	0.0222(6)
C12B	-0.2421(5)	1.1445(5)	0.32636(16)	0.0364(8)
H12D	-0.281366	1.040751	0.337260	0.055*
H12E	-0.324585	1.225379	0.293882	0.055*
H12F	-0.266034	1.233096	0.358000	0.055*

Source of material

2-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 toluene. The two solutions were then slowly mixed and stirred at room temperature until the appearance of a precipitate. The resulting precipitate was washed with a minimum amount of toluene (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 form yellow crystals.

Yield: 80%. **M.pt.** (Gallenkamp (UK) electrothermal melting point apparatus): 403–405 K. **FTIR** (FTIR Spectrometer Model Thermo Nicolet iS50; cm^{-1}): 3388 $\nu(\text{NH})$, 3270 $\nu(\text{OH})$, 1702 $\nu(\text{amide C=O})$, 1533 $\nu(\text{CO}_{\text{asym}})$, 1322 $\nu(\text{CO}_{\text{sym}})$. **¹H NMR** (Bruker Advanced Digital 400 MHz NMR spectrometer, chemical shifts relative to Me₄Si, CDCl₃ solution at 298 K; numbering as per the figure): 11.10 (1H, OH), 9.50 (1H, NH), 7.87 (1H, H7), 6.68 (1H, H8), 6.56 (1H, H9), 6.68 (1H, H10), 3.50 (3H, H12), 2.14 (2H, H2), 2.04 (2H, H4), 1.65 (2H, H3). **¹³C{¹H} NMR** (as for ¹H NMR): 174.7 (C1), 33.0 (C2), 20.6 (C3), 40.3 (C4), 170.6 (C5), 128.7 (C6), 123.7 (C7), 120.4 (C8), 127.2 (C9), 110.0 (C10), 148.2 (C11), 55.4 (C12).

Experimental details

The C-bound H atoms were geometrically placed (C–H = 0.95–0.99 Å) and refined as riding with $U_{iso}(\text{H}) = 1.2–1.5U_{eq}(\text{C})$. The O- and N-bound H atoms were refined with O–H = 0.84 ± 0.01 Å and N–H = 0.88 ± 0.01 Å, and with $U_{iso}(\text{H}) = 1.5U_{eq}(\text{O})$ or $1.2U_{eq}(\text{N})$. Owing to poor agreement, a number of reflections, i.e. (0 1 0), (–3 4 1), (–2 –1 5), (–2 –4 7) and (–3 –6 11), were omitted from the final cycles of refinement.

Comment

Recently, the crystal structure determination of an ArN(H)C(=O)(CH₂)₃C(=O)OH derivative with Ar = 4-methoxy-2-nitrophenyl was described [5]. The compound was analysed in the context of on-going investigations into the structure and biological activity, i.e. anti-cancer and anti-leishmanial, of these species [6] and their organotin compounds [7]. In continuation of these studies, herein, the crystal and molecular structures of the derivative, where Ar = 2-methoxyphenyl, (I), are described.

Two independent molecules comprise the asymmetric unit of (I) and their molecular structures are shown in the figure (70% probability displacement ellipsoids). The molecules have distinct conformations in their side-chains. This is seen in the sequence of C1–C2–C3–C4 [171.1(2)°], C2–C3–C4–C5 [–165.8(2)], C3–C4–C5–N1 [–117.9(3)°] and C4–C5–N1–C6 [–176.6(3)°] torsion angles for molecule “a”, respectively, compared to the equivalent angles for molecule “b”, i.e. 172.9(2), 177.7(2), –161.8(2) and –174.6(3)°, respectively. Thus, in molecule “a”, there is a significant kink in the side-chain about the C4–C5 bond whereas molecule “b”, to a first approximation adopts an extended (all-trans) configuration. The confirmation of protonation at the O1a and O1b atoms of the carboxylic acid residues is seen in the significant differences in the C–O bond lengths [C1a–O1a, O2a = 1.326(3) and 1.221(4) Å; C1b–O1b, O2b = 1.324(3) and 1.218(4) Å]. The carboxylic acid group is co-planar with the terminal part of the molecule as seen in the O2–C1–C2–C3

torsion angles of 0.6(4) and 1.2(4)° for molecules “a” and “b”, respectively. A twist is noted between the amide group and the appended aryl ring as reflected in the C5–N1–C6–C7 torsion angles of –16.4(5) and 37.3(4)°, respectively. This has the important consequence in that an amide-N–H···O(methoxy) hydrogen bond is formed [N1a–H1n···O4a: H1n···O4a = 2.16(2) Å, N1a···O4a = 2.577(3) Å with angle at H1n = 108(2)°] for molecule “a” but, not for molecule “b”.

Besides the aforementioned Ar = 4-methoxy-2-nitrophenyl derivative [5], which has a conformation close to molecule “b” of (I), the most closely related structure in the literature is one where the Ar group is 4-((methylsulfonyl)amino)-3-phenoxyphenyl [8]. The conformation of this molecule is highly twisted in the C₃ chain and in this way, resembles molecule “a” of (I).

In the crystal, each molecule self-associates about a centre of inversion to form an eight-membered {···OCOH}₂ homosynthon through hydroxy-O–H···O(carbonyl) hydrogen bonding [O1a–H1o···O2aⁱ: H1o···O2aⁱ = 1.82(3) Å, O1a···O2aⁱ = 2.655(3) Å with angle at H1o = 170(3)° and O1b–H2o···O2bⁱⁱ: H2o···O2bⁱⁱ = 1.82(3) Å, O1b···O2bⁱⁱ = 2.661(3) Å with angle at H2o = 175(3)° for symmetry operations (i) 1–x, –y, 1–z and (ii) 2–x, 1–y, –z]. The dimeric aggregates formed by molecules “a” and “b” are connected into a twisted chain along the c-axis by amide-N–H···O(amide) [N1b–H2n···O3aⁱⁱⁱ: H2n···O3aⁱⁱⁱ = 2.089(19) Å, N1b···O3aⁱⁱⁱ = 2.896(3) Å with angle at H2n = 153(3) for (iii) x, 1+y, z] hydrogen bonding. The amide-O atom of molecule “b” accepts two interactions from methylene and methyl donors of molecule “a” [C4a–H4a1···O3b^{iv}: H4a1···O3b^{iv} = 2.48 Å, C4a···O3b^{iv} = 3.176(4) Å with angle at H4a1 = 127° and C12a–H12b···O3b^v: H12b···O3b^v = 2.58 Å, C12a···O3b^v = 3.540(4) Å with angle at H12b = 167° for (iv) –1+x, y, z and (v) –1+x, 1+y, z]. Within this three-dimensional framework, methylene-C–H···π and C=O···π interactions are also noted between the independent molecules with each forming equivalent contacts.

The Hirshfeld surfaces and the two-dimensional fingerprint plots were calculated for each independent molecule with Crystal Explorer 17 [9] and literature procedures [10]. For molecule “a”, H···H contacts dominate the Hirshfeld surface, contributing 48.4% of all contacts. These are followed by H···O/O···H contacts, at 27.1%, and H···C/C···H contacts, at 16.2%. The next most prominent are O···C/C···O contacts, at 4.6%. The same general trends are noted for molecule “b”

where H···H contacts contribute 47.7% to the surface. There is an increase in H···O/O···H contacts, to 30.4%, reflecting the intermolecular hydrogen bond formed by the amide-N–H atom of molecule “b” as opposed to the intramolecular amide-N–H···O(methoxy) interaction formed by molecule “a”. The contribution by H···C/C···H contacts is about the same [15.4%] but, there has been a decrease in O···C/C···O contacts, to 2.3%.

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