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Crystal structure of *tert*-butyl 2-(hydroxymethyl)-5-{4-[(methoxycarbonyl)amino]phenyl}-2,5-dihydro-1*H*-pyrrole-1-carboxylate, $C_{18}H_{24}N_2O_5$

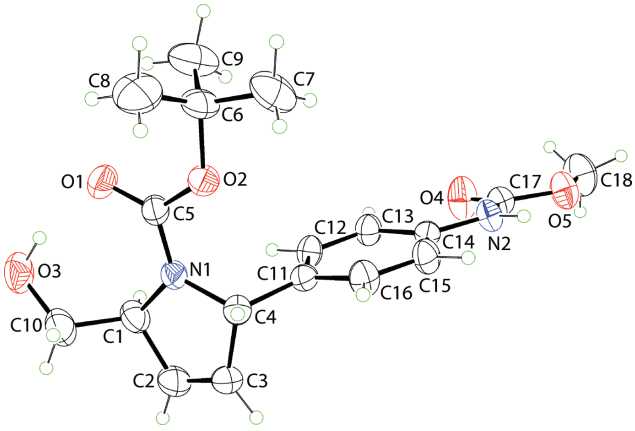

Table 1: Data collection and handling.

Crystal:	Colourless irregular
Size:	0.33 × 0.19 × 0.16 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	0.09 mm^{-1}
Diffractometer, scan mode:	Enraf Nonius TurboCAD4, ω
θ_{max}, completeness:	27.4°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	4328, 4192, 0.029
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 1916
$N(param)_{refined}$:	236
Programs:	CAD4 [1, 2], SIR2014 [3], SHELX [4], WinGX/ORTEP [5]

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Abstract

$C_{18}H_{24}N_2O_5$, monoclinic, $P2_1/c$ (no. 14), $a = 11.4784(7)$ Å, $b = 9.0180(8)$ Å, $c = 17.9483(17)$ Å, $\beta = 92.823(7)°$, $V = 1855.6(3)$ Å^3, $Z = 4$, $R_{gt}(F) = 0.0505$, $wR_{ref}(F^2) = 0.1611$, $T = 293$ 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

The synthesis and characterisation of (I) are as described in ref. [6], with crystals for the X-ray study being obtained from recrystallisation from an ethanol solution of (I).

Experimental details

The C-bound H atoms were geometrically placed (C—H = 0.93–0.98 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

The Heck-Matsuda arylation reaction is a valuable and versatile synthetic procedure for carbon-carbon bond formation, being based on the coupling of an olefin with an arenediazonium salt in the presence of a zerovalent organopalladium species [7]. This technology was employed [6] to synthesise molecules containing an α-aryl heterocyclic framework in the core structure as precursors to pharmacologically-important species such as Schramm's potent antiprotozoan C-azanucleoside [8] and the non-peptide cholecystokinin antagonist (+)-RP 66803 [9]. The title compound (I) was investigated crystallographically in the

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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	0.40740(14)	0.4263(2)	0.89707(10)	0.0718(6)
O2	0.22115(13)	0.49783(19)	0.86865(9)	0.0584(5)
O3	0.57622(14)	0.2889(3)	0.83031(12)	0.0791(6)
H3O	0.534(3)	0.330(4)	0.8605(16)	0.119*
O4	−0.17268(16)	−0.0935(3)	0.95758(12)	0.0842(7)
O5	−0.36070(14)	−0.0287(2)	0.93977(11)	0.0702(6)
N1	0.29677(14)	0.3181(2)	0.80397(11)	0.0480(5)
N2	−0.22909(15)	0.1053(2)	0.88628(12)	0.0521(5)
H2N	−0.2897(15)	0.154(3)	0.8705(13)	0.062*
C1	0.3831(2)	0.2056(3)	0.78279(16)	0.0595(7)
H1	0.391225	0.130030	0.821927	0.071*
C2	0.3208(3)	0.1408(4)	0.71529(17)	0.0740(9)
H2	0.352199	0.066317	0.686530	0.089*
C3	0.2191(2)	0.1984(3)	0.70084(14)	0.0642(8)
H3	0.170939	0.173038	0.659603	0.077*
C4	0.18744(18)	0.3104(3)	0.75792(13)	0.0492(6)
H4	0.172424	0.406278	0.733638	0.059*
C5	0.3154(2)	0.4160(3)	0.85961(14)	0.0503(6)
C6	0.2129(2)	0.6061(3)	0.93005(16)	0.0672(8)
C7	0.0871(3)	0.6531(4)	0.9217(2)	0.0978(11)
H7A	0.070656	0.689850	0.872118	0.147*
H7B	0.072635	0.729743	0.957184	0.147*
H7C	0.037785	0.569528	0.930525	0.147*
C8	0.2918(3)	0.7349(4)	0.9140(2)	0.1128(13)
H8A	0.277816	0.766139	0.863230	0.169*
H8B	0.371696	0.704780	0.921708	0.169*
H8C	0.276038	0.815593	0.946901	0.169*
C9	0.2398(3)	0.5328(4)	1.00428(17)	0.0999(12)
H9A	0.199453	0.439690	1.005960	0.150*
H9B	0.214818	0.595875	1.043518	0.150*
H9C	0.322274	0.516090	1.010698	0.150*
C10	0.5012(2)	0.2641(4)	0.76614(17)	0.0752(9)
H10A	0.538430	0.194200	0.733800	0.090*
H10B	0.491502	0.356683	0.739053	0.090*
C11	0.08093(18)	0.2628(3)	0.79833(13)	0.0451(6)
C12	0.08481(19)	0.1542(3)	0.85220(14)	0.0526(6)
H12	0.156805	0.114735	0.867774	0.063*
C13	−0.01405(18)	0.1017(3)	0.88400(14)	0.0520(6)
H13	−0.008171	0.029924	0.921204	0.062*
C14	−0.12217(18)	0.1567(3)	0.86006(12)	0.0432(6)
C15	−0.12706(19)	0.2691(3)	0.80824(14)	0.0559(7)
H15	−0.198841	0.309918	0.793247	0.067*
C16	−0.0268(2)	0.3222(3)	0.77818(14)	0.0575(7)
H16	−0.031936	0.399319	0.743765	0.069*
C17	−0.2457(2)	−0.0129(3)	0.93032(14)	0.0548(7)
C18	−0.3915(3)	−0.1509(4)	0.9867(2)	0.0932(11)
H18A	−0.388302	−0.241793	0.958990	0.140*
H18B	−0.469038	−0.136582	1.003084	0.140*
H18C	−0.337591	−0.155868	1.029260	0.140*

context of the characterisation of key intermediates of Heck-Matsuda arylation reactions [10, 11].

The molecular structure of (I) is shown in the figure (35% displacement ellipsoids) and is constructed about a tri-substituted, five-membered pyrrole ring. The latter is approximately planar, exhibiting a r.m.s. deviation = 0.0291 Å with maximum deviations to either side of the plane being 0.0391(15) and 0.0387(14) Å for the N1 and C4 atoms, respectively. The dihedral angle between the five-membered ring and the appended carboxylate (CO_2) residue and phenyl rings are 5.1(5) and 85.09(8)°, indicating almost co-planar and orthogonal dispositions, respectively. The O3-hydroxyl group is orientated towards the O1-carbonyl atom enabling the formation of an intramolecular hydroxyl-O3—H···O1(carbonyl) hydrogen bond [O3—H3o···O1: H3o···O1 = 1.84(3) Å, O3···O1 = 2.637(3) Å with angle at H3o = 160(3)°] which closes a S(6) loop. The configurations at the C1 and C4 atoms are each S. However, the centrosymmetric structure contains equal numbers of both enantiomers. Finally, the terminal (methoxycarbonyl)amino residue is planar (r.m.s. deviation for C_2NO_2 = 0.0033 Å) and forms a dihedral angle of 7.46(16)° with the phenyl ring to which it is connected, indicating a small twist between the residues.

There is no direct literature precedent for pyrrole (I) with the most closely related structure being a salt with a N1-bound 6-methylpyridinium substituent and flanked on either side by 2-(1,3-benzodioxol-5-yl) and piperidin-1-ylcarbonyl groups [12]. For the pyrrolidine analogue of (I), the most closely related structure is one where the once double bond of (I) is now saturated with each carbon atom bearing a hydroxyl substituent [13]; the ring is twisted about the C(OH)—C(OH) bond.

The most notable feature of the molecular packing is the presence of amino-N2—H···.O3(hydroxyl) hydrogen bonding [N2—H2n···O3^i: H2n···O3^i = 2.07(2) Å, N2···O3^i = 2.919(3) Å with the angle at H2n = 174(2)° for symmetry operation (i): $-1+x$, y, z] which leads to linear supramolecular chains along the *a*-axis.

In the absence of additional atom-to-atom points of contact between chains, additional insight into the molecular packing of (I) was achieved by an analysis of the calculated Hirshfeld surfaces and of the full and delineated two-dimensional fingerprint plots employing Crystal Explorer 17 [14] and literature procedures [15]. This analysis confirms the dominance of H···H contacts to the surface, contributing 64.8%. Next most prominent are H···O/O···H contacts at 20.2%, with distinctive spikes correlating with the aforementioned hydrogen bonding, and then H···C/C···H contacts at 12.2%. The only other contacts of note are H···N/N···H contacts, at 2.2%.

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