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tert-Butyl 4-[2-(methoxycarbonyl)ethyl]-3,5-dimethyl-1*H*-pyrrole-2-carboxylate

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.003 Å
R factor = 0.043
wR factor = 0.130
Data-to-parameter ratio = 15.2

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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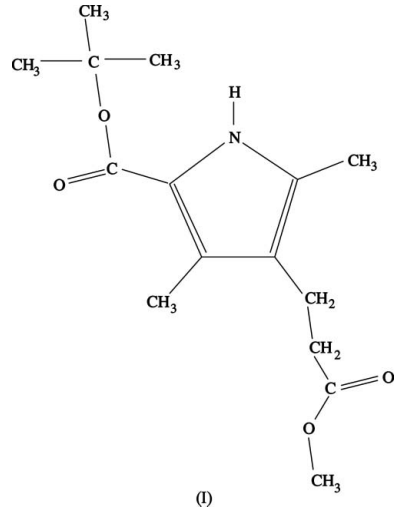
In the solid state, the title compound, $C_{15}H_{23}NO_4$, forms centrosymmetric dimers in which individual molecules are linked by intermolecular N—H···O hydrogen bonds. The pyrrole ring is planar within 0.004 (9) Å.

Comment

The importance of pyrroles in nature is well known (Spencer & Jordan, 1994; Scott, 1994). Therefore, they have been widely utilized, *e.g.* in the pharmaceutical sciences as antibiotics (Palermo *et al.*, 1996), enzyme inhibitors (Corsini *et al.*, 1999; Holub *et al.*, 2004) or as potent cytotoxics against a variety of tumour models (Gupton *et al.*, 1999; Holub *et al.*, 2004).



(I)

Among the synthetic routes to pyrroles, the cyclization reaction of α-aminoketones with carbonylic compounds with a β-diketone or β-ketoester, known as the Knorr synthesis, is one of the most widely used reactions (Bean, 1990). Using that process, we prepared the title compound, (I). The heterocyclic ring is almost perfectly planar; no atom in the ring deviates more than 0.004 (9) Å from the least-squares plane. As seen in similar pyrrole compounds (Ramos Silva *et al.*, 2002; Paixão *et al.*, 2002), the two N—Csp^2 bonds are asymmetric [N—C5 = 1.354 (2) Å and N—C2 = 1.375 (2) Å]. The molecule adopts a staggered conformation, when viewed along the O2—C7 bond, C6 is *anti* to C10 and C7 and C9 are *gauche* to C6 with torsion angles of 64.8 (2) and −60.4 (2)°, respectively. When viewed along C2—C6, the conformation is almost eclipsed (torsion angle approximately 10°). If the molecule is viewed along C13—C14, C12 is *gauche* to O3 [dihedral angle = −27.9 (3)°]. A strong hydrogen bond between the pyrrole N atom and the carbonyl O atom links the molecules of the title

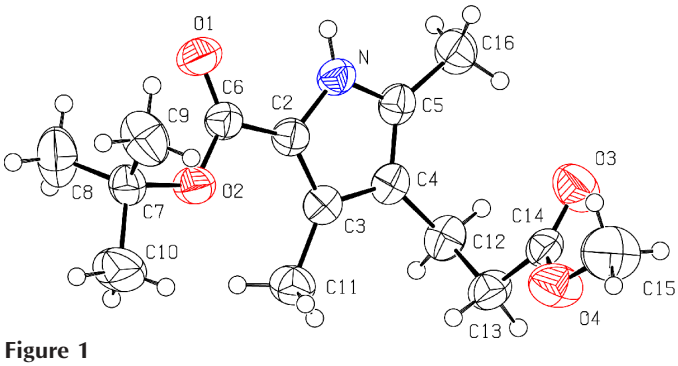


Figure 1
ORTEPII plot (Johnson, 1976) of the title compound. Displacement ellipsoids are drawn at the 50% probability level.

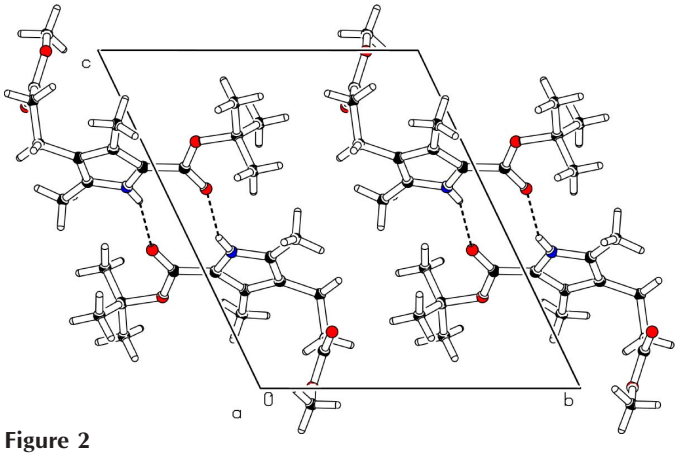


Figure 2
View of the packing, with hydrogen-bonding interactions shown as dashed lines.

compound into dimeric units (Fig. 2), forming ten-membered rings.

Experimental

A mixture of methyl 4-acethyl-5-oxohexanoate (9.30 g, 0.050 mol), zinc dust (7.00 g, 0,107 mol) and glacial acetic acid (50 ml) was placed in a 500-ml round-bottomed flask fitted with a reflux condenser and a silica guard tube. After dissolution of all the reactants at 353 K, the oxime *tert*-butyl 2-hydroxyimino-3-oxo-butyrate was slowly added; the oxime was prepared by dropwise treatment of an acid acetic solution (20 ml) of *tert*-butyl acetoacetate (7.90 g, 0.050 mol) with aqueous sodium nitrite (3.70 g, 0.054 mol) in water (12.5 ml) and then stirred for 2 h at < 283 K. This mixture was kept overnight at room temperature. The mixture was stirred and heated under reflux for 2.5 h. The hot reaction mixture was decanted from the zinc sludge before zinc acetate or the product crystallized. To promote crystallization, several volumes of water were slowly added to the reaction. After a few hours, the product was filtered off and washed thoroughly with water. Since the pyrrole was not sufficiently pure, it was immediately purified by column chromatography using a mixture of hexane and ethyl acetoacetate (first 4:1 and then 2:1 to separate the pyrrole) as eluant. The product was obtained in 8.5% yield. Its mass was verified by GC–MS ($C_{15}H_{23}O_4N$ corresponds to 281, found by FAB+, M^+: m/z = 281) and recrystallized from dichloromethane/ethanol as small transparent crystals.

Crystal data

$C_{15}H_{23}NO_4$
M_r = 281.34
Triclinic, $P\overline{1}$
a = 6.1468 (13) Å
b = 11.261 (2) Å
c = 12.9983 (7) Å
α = 114.775 (10)°
β = 92.134 (11)°
γ = 100.408 (10)°
V = 797.0 (2) Å^3
Z = 2
D_x = 1.172 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 9.7–15.8°
μ = 0.08 mm^{-1}
T = 293 (2) K
Plate, colourless
0.34 × 0.25 × 0.09 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
Profile data from ω–2θ scans
Absorption correction: none
3470 measured reflections
2836 independent reflections
2418 reflections with $I > 2\sigma(I)$
R_{int} = 0.009
θ_{max} = 25.1°
$h = -6 \rightarrow 7$
$k = -13 \rightarrow 13$
$l = -15 \rightarrow 15$
3 standard reflections
frequency: 180 min
intensity decay: 0.5%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.130
S = 1.06
2836 reflections
187 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0678P)^2 + 0.194P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.19 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N—H···O1^{i}	0.86	2.10	2.9142 (18)	157

Symmetry code: (i) $1-x, -y, 1-z$.

H atoms were treated as riding in idealized positions [N—H = 0.86, C— H = 0.96–0.97 Å and U_{iso}(H) = 1.2U_{eq}(N) and 1.2 or 1.5 times U_{eq}(C)], with torsional freedom for the methyl group. Examination of the crystal structure with *PLATON* (Spek, 2003) showed that there are no solvent-accessible voids.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *HELENA* (Spek, 1997); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL*97.

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