

Ethyl 3,5-dimethyl-4-phenyl-1*H*-pyrrole-2-carboxylateJosé António Paixão,^a Manuela Ramos Silva,^{a*} Ana Matos Beja,^a Abílio J. F. N. Sobral,^b Susana H. Lopes^b and A. M. d'A. Rocha Gonsalves^b^aCEMDRX, Departamento de Física, Faculdade de Ciências e Tecnologia, Universidade de Coimbra, P-3004-516 Coimbra, Portugal, and ^bDepartamento de Química, Faculdade de Ciências e Tecnologia, Universidade de Coimbra, P-3004-535 Coimbra, Portugal

Correspondence e-mail: manuela@pollux.fis.uc.pt

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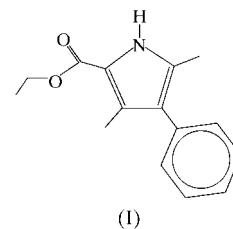
In the title compound, C₁₅H₁₇NO₂, the ethoxycarbonyl group is *anti* with respect to the pyrrole N atom. The angle between the planes of the phenyl and pyrrole rings is 48.26 (9)°. The molecules are joined into dimeric units by a strong hydrogen bonds between pyrrole N—H groups and carbonyl O atoms. The geometry of the isolated molecule was studied by *ab initio* quantum mechanical calculations, employing both molecular orbital Hartree–Fock (MO–HF) and density functional theory (DFT) methods. The minimum energy was achieved for a conformation where the angle between the planes of the phenyl and pyrrole rings is larger, and that between the ethoxycarbonyl and pyrrole planes is smaller than in the solid-state molecule.

Comment

The class of pyrroles includes a large number of important compounds (Chadwick, 1990), usually divided into naturally occurring pyrroles with important biological functions (Battersby & McDonald, 1976), and artificial pyrroles used in the pharmaceutical industry and in the medical (Bonnett, 1995) and materials sciences (Grieve *et al.*, 1994; Smith *et al.*, 1996; Richardson *et al.*, 1998). Following our studies of porphyrin synthesis (Sobral & Rocha Gonsalves, 2001), we have been working on the synthesis and structure determination of several substituted pyrroles (Paixão *et al.*, 2002; Ramos Silva *et al.*, 2000, 2002*a,b,c*), which are intended for incorporation at the β -pyrrole positions of porphyrins. The title compound, (I), was recently synthesized and an X-ray diffraction study undertaken to clarify the conformation of the molecule, the results of which are presented here.

The endocyclic angles of the pyrrole ring of (I) add up to exactly 540°, indicating that the heterocyclic ring is almost perfectly planar. In fact, no atom in the ring deviates by more than 0.005 (1) Å from the least-squares plane. There is a

significant asymmetry between the two N—Csp² bonds [N1—C5 = 1.347 (2) Å and N1—C2 = 1.377 (2) Å]. In addition, the C—C bond opposite to the heteroatom is longer than the others. The asymmetry of the C—N bonds can be explained by the electron-withdrawing character of the ethoxycarbonyl group and by the preferential conjugation of the C6=O1 bond with C2=C3, which leads to a stronger interaction between C4=C5 and the N1 lone pair, resulting in a shortening of the N1—C5 bond. These effects are reproduced in *ab initio* quantum mechanical calculations (see below).



The angle between the planes of the phenyl and pyrrole rings is 48.26 (9)°, which contrasts with the value observed in a similar compound, *viz.* ethyl 4-acetyl-5-methyl-3-phenyl-1*H*-

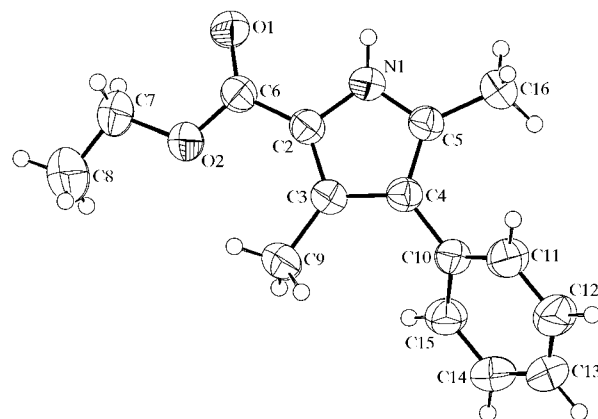


Figure 1

A view of the molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

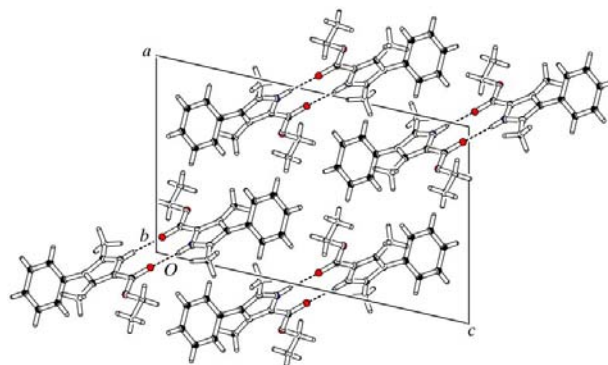


Figure 2

A view down the *b* axis of the unit cell of (I), with the hydrogen bonds shown as dashed lines.

pyrrole-2-carboxylate monohydrate [76.93 (5)^o; Ramos Silva *et al.*, 2002c]. This difference probably occurs because the adjacent methyl substituents in (I) are less sterically hindering than the acetyl and ethoxycarbonyl groups that are adjacent to the phenyl ring in the latter compound.

The ethoxycarbonyl group in (I) adopts an *anti* conformation with respect to the N atom of the heterocyclic ring (Fig. 1). This group is slightly tilted with respect to the pyrrole ring, the C3–C2–C6–O2 torsion angle being –4.8 (3)^o, and is fairly planar, as seen by the C6–O2–C7–C8 torsion angle of 177.7 (2)^o. In this group, the large atomic displacement parameter of atom C8, the short C7–C8 bond, and a nearby peak of residual density (0.57 e Å^{–3}) suggest that the terminal methyl group is disordered. However, attempts to model the disorder were unsuccessful.

A strong hydrogen bond between the pyrrole N–H group and the carbonyl O atom links the molecules of (I) into dimeric units (Fig. 2) in a way similar to that in benzyl 5-carboxy-4-ethyl-3-methyl-pyrrole-2-carboxylate (Ramos Silva *et al.*, 2000). These interactions form rings with a graph-set motif of R₂²(10) (Bernstein *et al.*, 1995).

To investigate the effect of the intermolecular interactions on the conformation of the molecule of (I), we have performed an optimization of the geometry of the isolated molecule by *ab initio* quantum mechanical calculations using the computer program GAMESS (Schmidt *et al.*, 1993), and employing both molecular orbital Hartree–Fock (MO–HF) and density functional theory (DFT) methods. For the latter, a B3LYP functional was chosen and a grid integration method used. In both cases, a standard 6-31G(*d,p*) basis set was employed. The optimization was conducted starting from the experimental crystal structure geometry without imposing any symmetry constraints on the molecule. Each self-consistent field calculation was iterated until a Δρ of less than 10^{–5} bohr^{–3} was achieved. The final equilibrium geometry at the minimum energy had a maximum gradient in internal coordinates of 10^{–5} Hartree bohr^{–1} or Hartree rad^{–1}.

Both HF and DFT calculations closely reproduce the solid-state geometry of the molecule. The C3–C4–C10–C15 torsion angle is calculated to be 60.6 and 50.9^o by HF and DFT, respectively, which is slightly larger than the observed value of 45.9 (3)^o. The most stable conformation of the ethoxycarbonyl group is *anti* and coplanar with the pyrrole ring [C3–C2–C6–O2 = –1.0 (HF) or 0.2^o (DFT)]. The internal distortions of the heterocyclic ring are well reproduced by the calculations. As usually found, the calculated DFT bond lengths are slightly longer than the HF values. The HF values are closer to the experimental values at room temperature, but after correction of the crystal structure model for librational motion, the DFT values become closer. The overall discrepancy is less than 0.011 Å between the zero-motion DFT and the corrected experimental data. The calculated DFT distances for N1–C5 and N1–C2 are 1.357 and 1.380 Å, respectively, compared with the librationaly corrected experimental values of 1.350 and 1.383 Å, respectively. The DFT and experimental values for the pyrrole-ring internal angles differ by less than 0.4^o.

Experimental

The title compound was prepared by a Knorr-type reaction (Paine, 1978) in 70% yield. Small single crystals of (I) (m.p. 418–419 K) were grown from a solution in dichloromethane–ethanol (1:1). Spectroscopic analysis, IR (ν, cm^{–1}): 1651 (C=O), 3302 (N–H); ¹H NMR (CDCl₃, 200 MHz, δ, p.p.m.): 1.3 (*t*, CH₃–CH₂–), 2.2 (*s*, CH₃–), 2.3 (*s*, CH₃–), 4.2 (*q*, CH₃–CH₂–), 7.1 (*m*, –C₆H₅), 8.8 (*m*, –NH–). Elemental analysis, calculated for C₁₅H₁₇NO₂: C 74.05, H 7.04, N 5.76%; found: C 73.66, H 6.93, N 5.83%.

Crystal data

C ₁₅ H ₁₇ NO ₂	D _x = 1.180 Mg m ^{–3}
M _r = 243.30	Cu Kα radiation
Monoclinic, P2 ₁ /c	Cell parameters from 25 reflections
a = 11.3160 (13) Å	θ = 13.3–25.6 ^o
b = 6.744 (2) Å	μ = 0.63 mm ^{–1}
c = 18.4091 (15) Å	T = 293 (2) K
β = 102.887 (8) ^o	Block, colourless
V = 1369.5 (5) Å ³	0.25 × 0.20 × 0.15 mm
Z = 4	

Data collection

Enraf–Nonius MACH3 diffractometer	R _{int} = 0.018
ω/2θ scans	θ _{max} = 72.3 ^o
Absorption correction: ψ scan (North <i>et al.</i> , 1968)	h = –13 → 13
T _{min} = 0.751, T _{max} = 0.911	k = 0 → 7
5053 measured reflections	l = –22 → 22
2606 independent reflections	3 standard reflections
2215 reflections with I > 2σ(I)	frequency: 180 min
	intensity decay: 4%

Refinement

Refinement on F ²	w = 1/[σ ² (F _o ²) + (0.0953P) ² + 0.3261P]
R[F ² > 2σ(F ²)] = 0.054	where P = (F _o ² + 2F _c ²)/3
wR(F ²) = 0.169	(Δ/σ) _{max} < 0.001
S = 1.07	Δρ _{max} = 0.57 e Å ^{–3}
2606 reflections	Δρ _{min} = –0.31 e Å ^{–3}
170 parameters	
H atoms treated by a mixture of independent and constrained refinement	

Table 1

Selected geometric parameters (Å, °).

O1–C6	1.216 (2)	C3–C4	1.416 (3)
O2–C6	1.332 (2)	C4–C5	1.393 (2)
C2–C3	1.387 (2)	C7–C8	1.450 (4)
C5–N1–C2	110.27 (14)	C5–C4–C3	107.56 (15)
N1–C2–C3	107.67 (15)	N1–C5–C4	107.76 (15)
C2–C3–C4	106.73 (15)		

Table 2

Hydrogen-bonding geometry (Å, °).

D–H···A	D–H	H···A	D···A	D–H···A
N1–H1···O1 ⁱ	0.88 (3)	2.02 (3)	2.875 (2)	164 (2)

Symmetry code: (i) –x, 2 – y, –z.

The methyl H atoms were constrained to an ideal geometry (C–H = 0.96 Å), with $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$, but were allowed to rotate freely about the C–C bonds. The positional and atomic displacement parameters of the H atom bonded to the pyrrole N atom were refined freely. All remaining H atoms were placed in geometrically idealized positions (C–H = 0.93–0.97 Å) and constrained to ride on their parent atoms, with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$. Examination of the crystal structure with *PLATON* (Spek, 2002) showed that there were no solvent-accessible voids in the crystal lattice.

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: *SHELXL97*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: LN1155). Services for accessing these data are described at the back of the journal.

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