Synthesis and Structural Studies of (*R*)-(+)-1-[(1-Methylpyrrol-2-yl)acetyl]-4-(1-phenylethyl)semicarbazide

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The title compound, C₁₆H₂₀N₄O₂, was synthesized and characterized by X-ray diffraction analysis. The compound crystallizes in the monoclinic system, space group *P*2₁ with *a* = 10.883(3) Å, *b* = 4.663(1) Å, *c* = 15.785(3) Å, β = 103.09(2)° and *Z* = 2. It exists in the *keto* form and adopts the *Z* conformation in the solid state. The dihedral angles between the almost planar semicarbazide moiety and the pyrrole and phenyl rings are 82.1(1) and 50.0(2)°, respectively. In the crystal structure, molecules are linked by N-H...O and C-H...O intermolecular interactions into infinite chains parallel to the *b* axis.

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The semicarbazides are important organic intermediates for the synthesis of many heterocyclic compounds. The cyclization of these derivatives have been shown to be an excellent strategy for the synthesis of triazoles and pyrazolones.^{1,2} Apart from their chemical significance, semicarbazides are also known for their antinociceptive and anticonvulsant properties.³ Additionally, derivatives having the pyrrole ring show good activity against *Bacillus cereus* and *Micrococcus luteus*.⁴ The title compound **1** was synthesized to investigate its possible anticancer and antiproliferative activities. The structure of semicarbazide is similar to those of previously reported thiosemicarbazides.⁵ Therefore, theoretically it can exist in three possible tautomeric forms (Scheme 1). An X-ray analysis of the compound **1** was undertaken to establish the structure. Determining the structure was considered to be potentially useful for future work aimed at understanding its biological activity.

A mixture of 1-methylpyrrol-2-ylacetohydrazide (0.01 mol) and (*R*)-(+)-1-phenylethylisocyanate (0.01 mol) was dissolved in 10 ml anhydrous diethyl ether and kept for 24 h at room temperature. Then the formed compound was filtered off, washed with diethyl ether and recrystallized from ethanol. Yield 71%; m.p.: 155 – 157°C. Found %: C, 63.87; H, 6.78; N, 18.59 (Calculated for C₁₆H₂₀N₄O₂ %: C, 63.98; H, 6.71; N 18.65).

An orange crystal of **1**, having approximate dimensions of

0.52 × 0.35 × 0.09 mm, was selected for X-ray diffraction studies. Details of the crystal data, X-ray data collection and refinement are given in Table 1. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms bonded to N2, N3 and N4 atoms were located from a difference Fourier map and were not refined. The remaining hydrogen atoms were positioned geometrically and allowed to ride on their parent atoms, with C-H = 0.93 – 0.98 Å and *U*_{iso}(H) = 1.2 *U*_{eq}(C). The absolute configuration was assigned based on the known configuration of the asymmetric carbon in the molecule. The final atomic coordinates and the equivalent isotropic displacement parameters for the nonhydrogen atoms

Table 1 Crystal and experimental data

Formula: C ₁₆ H ₂₀ N ₄ O ₂	
Formula weight: 300.36	
Temperature = 294(3)K	
Crystal system: monoclinic	
Space group: <i>P</i> 2 ₁	<i>Z</i> = 2
<i>a</i> = 10.833(3) Å	
<i>b</i> = 4.663(1) Å	β = 103.09(2)°
<i>c</i> = 15.785(3) Å	
<i>V</i> = 780.5(3) Å ³	
<i>D</i> _x = 1.553 g cm ⁻³	
Absorption coefficient: 0.087 mm ⁻¹	
No. of reflections used = 3585	
2 θ _{max} = 27.55° with Mo <i>K</i> α	
<i>R</i> ₁ = 0.0568	
<i>wR</i> ₂ = 0.1247	
Flack parameter: 0.0(2)	
(Δ / σ) _{max} = 0.008	
($\Delta\rho$) _{max} = 0.14 e Å ⁻³	
($\Delta\rho$) _{min} = -0.14 e Å ⁻³	
Measurements: Oxford Diffraction Xcalibur	
Program system: CRYSLIS CCD (Oxford Diffraction, 2005)	
Structure determination: direct methods (SHELXS97)	
Refinement: full matrix least-squares (SHELXS97)	
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Scheme 1 Three possible tautomeric structures of the title compound

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Fig. 1 The molecular structure of the title compound with the atom labeling scheme. The displacement ellipsoids are drawn at the 30% probability level.

Table 2 Atomic coordinates and equivalent isotropic displacement parameters for the trace of the non-hydrogen atoms

Atom	x	y	z	U(eq)
N1	0.5048(3)	0.2048(6)	-0.3219(2)	0.071(1)
C2	0.4220(3)	0.1373(7)	-0.2721(2)	0.054(1)
C3	0.3382(4)	-0.0499(8)	-0.3174(3)	0.081(1)
C4	0.3706(6)	-0.0987(11)	-0.3969(3)	0.112(2)
C5	0.4714(5)	0.0622(11)	-0.3985(3)	0.101(2)
C1m	0.6093(3)	0.4015(10)	-0.2978(3)	0.100(1)
C6	0.4321(3)	0.2588(7)	-0.1840(2)	0.055(1)
C7	0.5360(3)	0.1288(6)	-0.1161(2)	0.051(1)
O1	0.5539(3)	-0.1311(5)	-0.1108(2)	0.092(1)
N2	0.6060(3)	0.3004(5)	-0.0606(2)	0.060(1)
N3	0.7000(3)	0.1834(5)	0.0047(2)	0.073(1)
C8	0.7860(3)	0.3446(6)	0.0566(2)	0.044(1)
O2	0.7830(2)	0.6076(4)	0.0538(1)	0.057(1)
N4	0.8720(2)	0.1902(5)	0.1123(2)	0.059(1)
C9	0.9858(3)	0.3130(7)	0.1660(2)	0.058(1)
C2m	1.0963(4)	0.2671(12)	0.1234(2)	0.106(2)
C10	1.0117(3)	0.2010(7)	0.2577(2)	0.047(1)
C11	0.9348(3)	0.0073(8)	0.2853(2)	0.064(1)
C12	0.9602(4)	-0.0915(8)	0.3702(2)	0.080(1)
C13	1.0635(4)	0.0032(10)	0.4280(2)	0.076(1)
C14	1.1414(4)	0.1959(10)	0.4030(2)	0.081(1)
C15	1.1155(3)	0.2972(9)	0.3183(2)	0.072(1)

$$U_{eq} = (1/3)\sum_i \sum_j U_{ij}(a_i^* a_j^*)(a_i a_j)$$

Table 3 Selected bond distances [Å] and torsion angles [°]

N1–C5	1.355(5)	C7–O1	1.227(3)
N1–C2	1.360(4)	C7–N2	1.299(4)
C2–C3	1.345(4)	N2–N3	1.389(3)
C3–C4	1.397(6)	N3–C8	1.329(4)
C4–C5	1.335(7)	C8–O2	1.227(3)
N1–C1m	1.444(3)	C8–N4	1.340(4)
C2–C6	1.482(4)	N4–C9	1.451(4)
C6–C7	1.499(4)		
C2–C6–C7–N2	136.6(3)	N2–N3–C8–N4	-176.8(3)
C6–C7–N2–N3	177.8(3)	N2–N3–C8–O2	4.8(5)
O1–C7–N2–N3	-0.6(5)	N3–C8–N4–C9	170.2(3)
C7–N2–N3–C8	170.9(3)		

are listed in Table 2.

The molecular structure of **1** with the atom numbering scheme is shown in Fig. 1. The selected bond lengths and torsion angles are given in Table 3. The central semicarbazide moiety in the title compound, comprising atoms N2, N3, C8, O2 and N4, is almost planar, with a maximum mean plane deviation of 0.030(3) Å for atom N3. A torsion angle of 4.8(5)°

Fig. 2 Hydrogen-bonded chains, in view along the *a* axis, formed by compound **1** in the solid state (symmetry code: (a) *x*, *y*+1, *z*).

corresponding to the O2–C8–N3–N2 moiety implies a *cis* alignment of the carbonyl O2 atom with respect to the hydrazine N2 atom. The C8–O2 bond length of 1.227(3) Å, which is in good agreement with that of the C=O double bond,⁶ shows that compound exists in the solid state in the *keto* tautomeric form. Moreover, the C8–N3 (1.329(4)) and C8–N4 (1.340(4)) Å bond distances, which are intermediate between those of single and double C–N bonds, as well as the N2–N3 (1.389(3)) Å distance, indicate conjugation of the semicarbazide part.

The molecule **1** adopts a *cis-cis* configuration with respect to the position of the (1-methylpyrrole)acetamide and phenylethyl functionalities, relative to the carbonyl O2 atom across the C8–N3 and C8–N4 bonds. The five atoms in the pyrrole ring are planar with deviation less than 0.008 Å, but are not coplanar with the central N2/N3/C8/O2/N4 moiety; the dihedral angle between their planes is 82.1(2)°. At the same time the semicarbazide part forms a dihedral angle of 50.0(1)° with the phenyl C10–C15 ring.

As can be seen in Fig. 2, in the solid state, compound **1** forms, hydrogen-bonded chains through urea-urea and acetamide-acetamide N/C–H...O intermolecular interactions with N...O distances of N3...O2ⁱ 2.883(3), N4...O2ⁱ 2.961(4), N2...O1ⁱⁱ 2.788(4) Å and N–H...O bond angles of 145, 149, 148°, respectively, and with a C...O distance of C6...O1ⁱⁱ 3.239(4) Å and a C–H...O bond angle of 146° (symmetry codes: (i) *x*, *y*–1, *z*; (ii) *x*, *y*+1, *z*).

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