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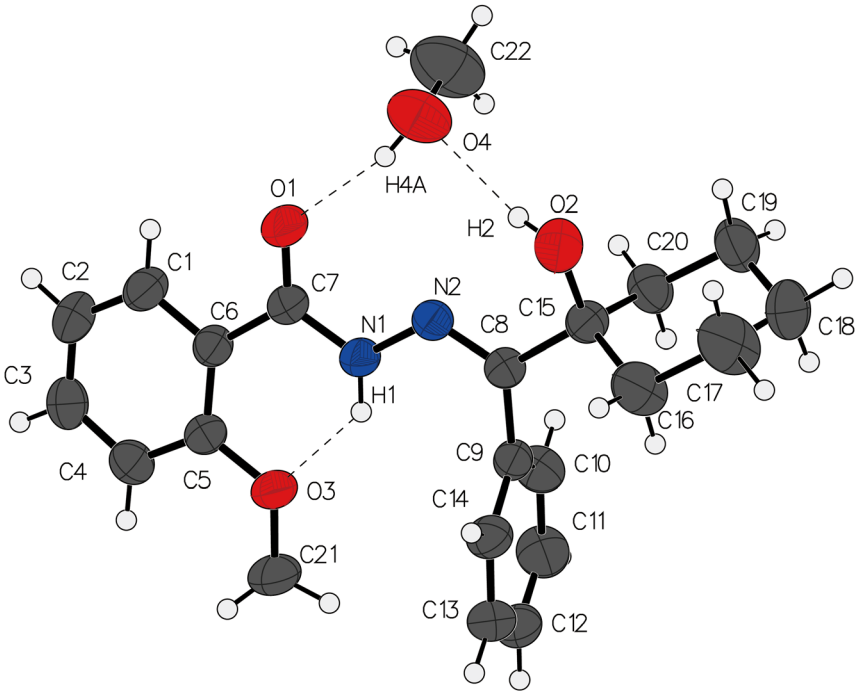
Crystal structure of N′-((1-hydroxycyclohexyl)(phenyl)methyl)-2-methoxybenzohydrazide methanol solvate, $C_{22}H_{28}N_2O_4$



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Abstract

$C_{22}H_{28}N_2O_4$, monoclinic, $P2_1/n$ (no. 14), a = 10.0094(5) Å, b = 17.4999(8) Å, c = 11.9872(6) Å, β = 96.926(2)°, V = 2084.40(18) Å^3, Z = 4, $R_{gt}(F)$ = 0.0542 $wR_{ref}(F^2)$ = 0.1607, T = 296 K.

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The molecular structure is shown in the figure. Table 1 contains the crystallographic data and the list of the atoms including atomic coordinates and displacement parameters can be found in the cif-file attached to this article.

Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.66 × 0.59 × 0.48 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.08 mm^{-1}
Diffractometer, scan mode:	Rigaku SuperNova, ω scans
θ_{max}, completeness:	28.3°, 100 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	77493, 5171, 0.131
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 3827
$N(param)_{refined}$:	257
Programs:	Rigaku,[1] SHELX,[2,3] Olex2[4]

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1 Source of materials

Equimolar amounts (0.5 mmol) of 2-methoxybenzohydrazide (0.083 g) and 1-hydroxycyclohexyl phenyl ketone (0.102 g) were combined in anhydrous ethanol (20 mL) within a 50 mL round-bottom flask. The mixture was acidified with glacial acetic acid (0.25 mL, 5 drops) and heated under reflux at 50 °C with continuous stirring for 3 h. Reaction progression was tracked via TLC analysis using pre-coated silica gel plates (60 F254) with a mixture of ethyl acetate and hexanes (1:3 v/v) as the mobile phase. Upon confirmation of starting material consumption, the system was cooled to room temperature. The resulting solution was concentrated under reduced pressure to afford the crude product as a white powder. A portion (0.05 g) of the crude material was dissolved in methanol (5 mL) for further purification. The resulting solution was transferred to an open crystallization dish and subjected to gradual solvent evaporation under ambient fume hood conditions. Transparent block crystals formed over 72 h through slow volatilization.

2 Experimental details

Diffraction data was acquired at 296 K using a Bruker D8 Venture system with Mo Kα irradiation.[1] Structural determination was initiated via intrinsic phasing (ShelXT[2]), followed by successive full-matrix least-squares refinement (ShelXL[3]) executed through the Olex2 platform.[4] Anisotropic refinement was applied to non-hydrogen atoms, while hydrogen atoms were geometrically constrained and incorporated as riding contributions with fixed isotropic thermal parameters.

3 Comment

Benzohydrazide derivatives have garnered significant interest in structural chemistry due to their diverse biological activities and versatile coordination properties.[5–7] Single-crystal X-ray diffraction (SCXRD) serves as a cornerstone for elucidating their precise molecular conformations, intermolecular interactions, and supramolecular packing motifs of such compounds.[8–11] Such structural insights are critical for rationalizing structure-activity relationships, particularly in pharmaceutical and materials science contexts. The presence of functional groups like methoxy substituents and hydrazide linkages in these compounds often induces distinct hydrogen-bonding networks or π-stacking interactions, which govern crystallization behavior and stability.[12–16] Investigations into solvent-inclusive crystalline forms, such as methanol solvates, further illuminate the role of lattice solvents in modulating crystal packing and physicochemical properties.

In the title compound, as can be seen in the figure, the near-planar arrangement of non-hydrogen atoms within the 2-methoxybenzohydrazide moiety suggests effective π-conjugation across the hydrazide-carbonylic system, a characteristic known to enhance electronic delocalization and stabilize specific tautomeric forms in analogous derivatives. Notably, the cyclohexyl ring adopts a classical chair conformation, with minimal puckering deviations ($\theta < 2°$), consistent with the steric preference for low-energy cyclic alkane geometries.

Distinct C–O bond lengths are observed for hydroxyl (C15–O2: 1.4167(16) Å), acyl (C7–O1: 1.2247(17) Å), and ether (C5–O3: 1.3628(16) Å) functionalities. The shortened acyl C–O bond aligns with partial double-bond character arising from resonance with the adjacent carbonyl group, while the elongated hydroxyl C–O bond likely reflects localized lone-pair electron density at O2. The intermediate ether C–O distance corresponds to typical values for methoxy substituents in aromatic systems.

Crucially, the methanol solvent molecule occupies a central cavity within the crystal lattice, engaging the parent molecule through a robust O4–H4A···O1 hydrogen bond (1.9763(11) Å, 165.1°). The directional preference of this interaction suggests it serves as the primary driving force for methanol inclusion, effectively templating the supramolecular assembly through bifurcated hydrogen-bond networks.

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