




Short Note

Synthesis and Structure Elucidation of *N'*-(4-Methoxybenzylidene)-5-methyl-1-phenyl-1*H*-1,2,3-triazole-4-carbohydrazide

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Abstract: *N'*-(4-Methoxybenzylidene)-5-methyl-1-phenyl-1*H*-1,2,3-triazole-4-carbohydrazide (**3**) was synthesized in a yield of 88% from an acid-catalyzed reaction of 5-methyl-1-phenyl-1*H*-1,2,3-triazole-4-carbohydrazide and 4-methoxybenzaldehyde in ethanol under reflux for 2.5 h. The structure of **3** was confirmed by the data obtained from infrared, nuclear magnetic resonance, mass spectroscopy, single crystal X-ray diffraction, and microanalysis.

Keywords: 1,2,3-triazoles; carbohydrazides; single crystal X-ray diffraction; spectroscopic structural analysis; heterocycles

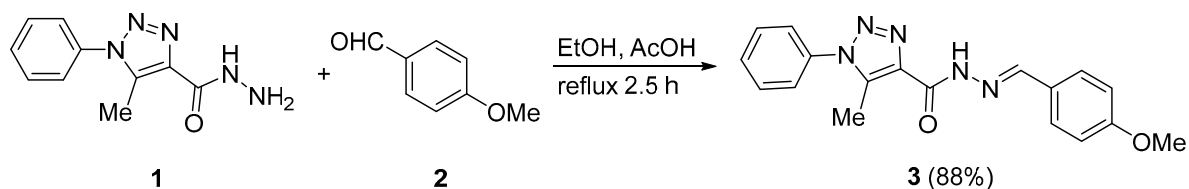
1. Introduction

Arylidene carbohydrazides are remarkable compounds because of their activity as antimicrobial, analgesic, anti-inflammatory, antiproliferative, and antioxidant agents [1–5]. Another interesting group of compounds is 1,2,3-triazoles, which may act as anticancer, antimicrobial, α -glucosidase inhibitors, and cholinesterase inhibitor agents [6–9]. 1,2,3-Triazoles can be synthesized from reactions of azides and calcium carbide, a source of acetylene, in a mixture of acetonitrile and water in the presence of copper iodide [10]; nitroolefins and sodium azide in dimethylformamide in the presence of a catalyst such as *p*-toluenesulfonic acid or Amberlyst-15 [11,12]; alkenyl halides and sodium azide in dioxane or dimethyl sulfoxide in the presence of a palladium catalyst [13]; alkyl bromides and acetylenes in water in the presence of bromotris(triphenylphosphine)copper(I) or copper(I) isonitrile [14,15]; and alkynoic acids, aryl iodides, and azides in a mixture of dimethyl sulfoxide and water in the presence of *L*-proline [16]. Our interest in the synthesis of arylidenes of 1,2,3-triazole emanates from ongoing research in the area of heterocycles [17–22]. In this paper, the synthesis and structure elucidation of *N'*-(4-methoxybenzylidene)-5-methyl-1-phenyl-1*H*-1,2,3-triazole-4-carbohydrazide (**3**) are reported. The synthesis and structure elucidation for similar compounds have been recently published [23].

2. Results and Discussion

2.1. Synthesis of Compound 3

The condensation of 5-methyl-1-phenyl-1*H*-1,2,3-triazole-4-carbohydrazide (**1**) and 4-methoxybenzaldehyde (**2**) in dry ethanol (EtOH) containing glacial acetic acid (AcOH) as a catalyst produced **3** in a yield of 88% (Scheme 1). The chemical structure of **3** was confirmed by the data from microanalysis, infrared (IR), nuclear magnetic resonance (NMR), mass spectroscopy (MS), and single crystal X-ray diffraction (Figure 1).



Scheme 1. Synthetic route to **3**.

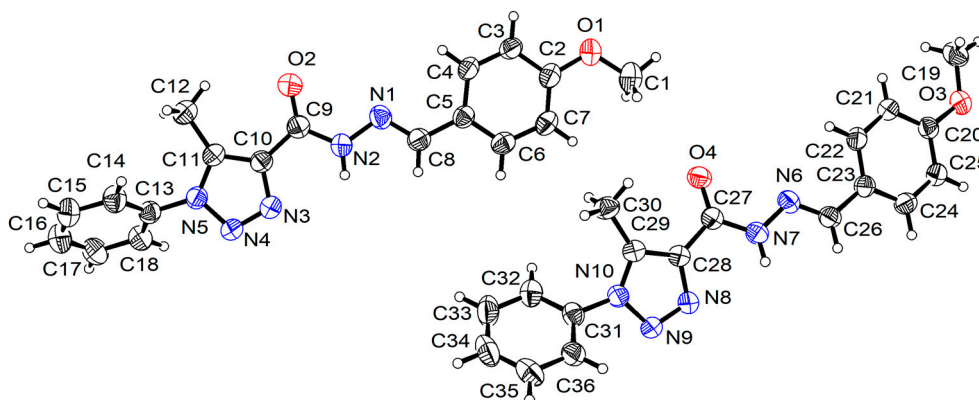


Figure 1. Oak Ridge Thermal Ellipsoid Plot (ORTEP) representation of the asymmetric unit for compound **3** with ellipsoids displayed at the 50% probability level.

2.2. Spectroscopic Structural Analysis

The IR spectrum of **3** showed a strong absorption band at 1680 cm^{-1} (C=O) and a broad absorption band at 3300 cm^{-1} (NH). The ^1H -NMR spectrum of **3** showed an exchangeable singlet corresponding to one proton (NH) that appeared at 12.03 ppm and a singlet that appeared at 8.52 ppm (–CH=N–). It also showed the presence of two singlets each corresponding to three protons that appeared at 2.56 ppm (Me) and 3.80 ppm (OMe). The ^{13}C -NMR spectrum of **3** showed the presence of all expected signals. The carbonyl carbon appeared at 157.1 ppm and the –CH=N– carbon appeared at 147.9 ppm. The methyl and methoxy carbons appeared at 9.4 and 55.3 ppm, respectively. The mass spectrum of **3** showed a molecular ion peak at $m/z = 335$ (2%) and a base peak at $m/z = 84$. See Supplementary Materials for more details.

2.3. X-Ray Structures

The crystal structure of **3** comprises two crystallographically independent molecules (Figure 1). A significant difference between the two independent molecules is the conformation of the methoxy group as indicated by the corresponding torsion angle $\text{C1–O1–C2–C3} = 178.34(67)^\circ$ and $\text{C19–O3–C20–C21} = 6.14(66)^\circ$. The combined methoxybenzylidene-carbohydrazide group (A) is essentially planar in both molecules with maximum atomic deviations from the least-squares planes of $0.100(1)\text{ \AA}$ (for C1) and $0.162(1)\text{ \AA}$ (for O4) for the first molecule (C1–C18) and the second molecule (C19–C36), respectively. The molecules are completed by methyltriazole (B) and phenyl (C) moieties.

The twist angles between the planes through **A** and **B**, and through **B** and **C** are 6.94(18)° and 50.91(13)° for the first molecule and 12.62(19)° and 45.18(20)° for the second molecule.

In the crystal structure, the second type of molecule forms chains parallel to the *c*-axis through N–H...O interactions with geometry: N7–H7A ... O4^a = 159.2° (*a* = *x*, −*y* + 2, *z* + $\frac{1}{2}$) and N ... O = 3.289(6) Å (Figure 2). N–H ... O contacts involving the first type of molecule are weaker (with geometry N2–H2 ... O2^b = 141.6°, N2 ... O2 = 3.522(6) Å, *b* = *x*, −*y* + 1, *z* + $\frac{1}{2}$) but are complemented by C–H ... O contacts (with geometry C8–H8 ... O2^b = 152.0°, C8 ... O2 = 3.289(6) Å) also forming chains parallel to the *c*-axis.

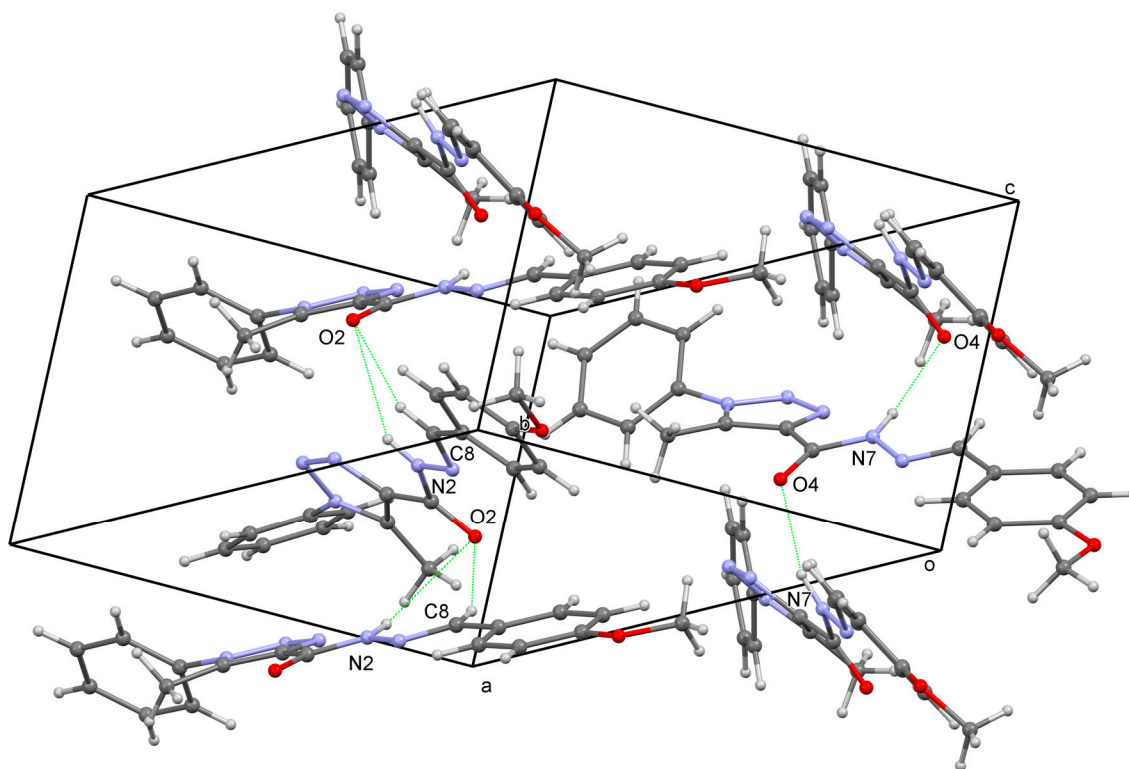


Figure 2. Part of the crystal structure of **3**, showing N–H...O and C–H ... O contacts as green dotted lines.

3. Materials and Method

3.1. General

An Electrothermal IA 9000 melting point apparatus was used to determine the melting point. A FT-IT PerkinElmer Spectrum GX was used to record the IR spectrum (KBr disks). A JOEL-ECA 600 MHz was used to record the NMR spectra in deuterated dimethyl sulfoxide relative to the tetramethylsilane at 600 MHz for ¹H and 150 MHz for ¹³C measurements. The mass spectrum was determined on a GCMS JEOL JMS-Q1050GC Ultra Quad GC/MS (70 eV).

3.2. Synthetic Procedure for Compound 3

A mixture of 5-methyl-1-phenyl-1*H*-1,2,3-triazole-4-carbohydrazide (0.43 g, 2.0 mmol), 4-methoxybenzaldehyde (0.27 g, 2.0 mmol), and glacial AcOH (0.1 mL) in dry EtOH (20 mL) was heated under reflux for 2.5 h. The solid formed was collected by filtration, washed with EtOH, dried and recrystallized from DMF. Mp 231–232 °C. IR(KBr) ν_{max} /cm^{−1}: 1600 (C=C), 1680 (C=O), 3300 (NH). ¹H-NMR: δ 2.56 (s, 3H, Me), 3.80 (s, 3H, OMe), 7.02 (d, *J* = 8.4 Hz, 2H, Ar), 7.62–7.67 (m, 7H, Ar), 8.52 (s, 1H, CH=N), 12.03 (s, exchangeable, 1H, NH). ¹³C-NMR: δ 9.4 (Me), 55.3 (OMe), 114.4 (C-3/C-5 of Ar), 125.5 (C-2/C-6 of Ph), 127.0 (C-1 of Ar), 128.7 (C-3/C-5 of Ph), 129.7 (C-2/C-6 of Ar), 130.1 (C-4 of Ph), 135.3 (C-4 of 1,2,3-triazolyl), 137.4 (C-1 of Ph), 137.8 (C-5 of 1,2,3-triazolyl), 147.9 (CH=N), 157.1 (C=O),

160.8 (C-4 of Ar). MS (EI) m/z (%): 335 (M^+ , 2), 84 (100), 66 (96), 46 (94). Anal. Calcd. for $C_{18}H_{17}N_5O_2$ (335.14): C, 64.47; H, 5.11; N, 20.88. Found: C, 64.86; H, 5.18; N, 20.97%.

Crystal Data: $C_{18}H_{17}N_5O_2$ ($M = 335.36$ g/mol): monoclinic, space group Pc (no. 7), $a = 18.4634(11)$ Å, $b = 12.0289(8)$ Å, $c = 7.7553(5)$ Å, $\beta = 101.401(6)^\circ$, $V = 1688.42(19)$ Å³, $Z = 4$, $T = 296(2)$ K, $\mu(\text{CuK}\alpha) = 0.735$ mm⁻¹, $D_{\text{calc}} = 1.319$ Mg/m³, 16249 reflections measured ($3.67^\circ \leq \theta \leq 74.30^\circ$), 5379 unique ($R_{\text{int}} = 0.0527$, $R_{\text{sigma}} = 0.0502$) which were used in all calculations. The final R_1 was 0.0544 ($I > 2\sigma(I)$) and wR_2 was 0.1478 (all data).

Data Collection and Refinement Details: Diffraction data were collected on a Rigaku SuperNova Dual Atlas diffractometer using mirror monochromated CuK α radiation (1.54184 Å). The structure was solved by direct methods with SHELXS [24] and refined by full-matrix methods on F^2 with SHELXL-2014 [25]. All hydrogen atoms were placed in calculated positions and refined using a riding model. Aromatic C–H distances were set to 0.93 Å and the $U_{\text{iso}}(\text{H})$ set to 1.2 times $U_{\text{eq}}(\text{C})$. Methyl C–H distances were set to 0.96 Å and the $U_{\text{iso}}(\text{H})$ to 1.5 times $U_{\text{eq}}(\text{C})$ with the group allowed to rotate around the C–C bond. Aromatic N–H distances were set to 0.86 Å and the $U_{\text{iso}}(\text{H})$ set to 1.2 times $U_{\text{eq}}(\text{N})$. CCDC 1874941 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html> (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44-1223-336033; E-mail: deposit@ccdc.cam.ac.uk).

Supplementary Materials: The IR, ¹H-NMR, ¹³C-NMR and mass spectra, and the checkCIF file for compound 3 are available online.

Author Contributions: H.M.A. and B.F.A.-W. designed and performed the synthetic work, M.H.A. performed the measurements of IR, NMR and MS, B.M.K. performed the measurements and analysis of the X-ray experiments, A.S.H. and G.A.E.-H. wrote the manuscript.

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Conflicts of Interest: The authors declare no conflict of interest.

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