

Communication

Synthesis and Structure Determination of 1-(4-Methoxyphenyl)-5-methyl-*N'*-(2-oxoindolin-3-ylidene)-1*H*-1,2,3-triazole-4-carbohydrazide

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Abstract: A reaction of equimolar equivalents of 1-(4-methoxyphenyl)-5-methyl-1*H*-1,2,3-triazole-4-carbohydrazide (**1**) and indoline-2,3-dione (**2**) in boiling ethanol for 4 h under acidic conditions gave 1-(4-methoxyphenyl)-5-methyl-*N'*-(2-oxoindolin-3-ylidene)-1*H*-1,2,3-triazole-4-carbohydrazide (**3**) in 88% yield. The structure of **3** was ascertained by NMR spectroscopy and single-crystal X-ray diffraction.

Keywords: synthesis; 1,2,3-triazole; X-ray crystal structure; heterocycles; carbohydrazide; indoline-2,3-dione



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1. Introduction

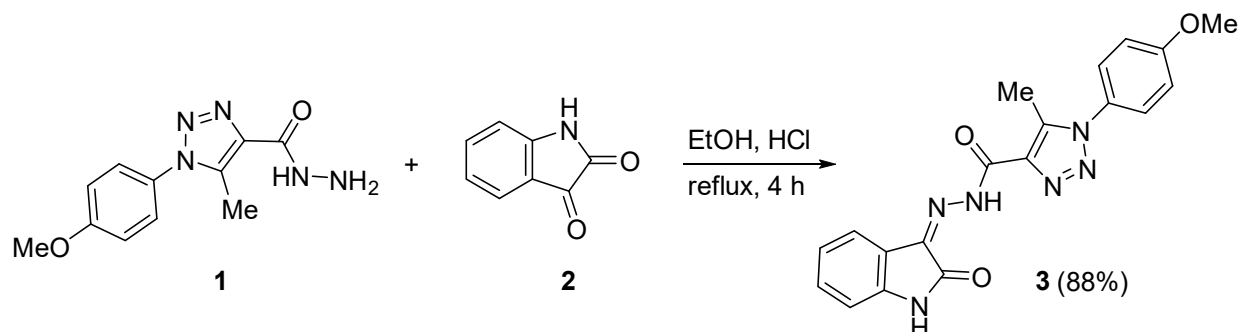
Heterocycles containing nitrogen are versatile in synthetic chemistry and have a wide range of prospective medicinal applications [1–3]. Heterocycles containing the 1,2,3-triazole moiety are known to display significant biological activities [4–7]. Indeed, several medications such as tazobactam and carboxyamidotriazole contain the 1,2,3-triazole unit in their skeletons [8]. In addition, 1,2,3-triazoles have excellent metabolic and thermal stability and have been used in diverse applications [9–11]. The synthetic procedures of 1,2,3-triazoles through click chemistry are simple and high yielding to produce many substituted derivatives [8]. 1,3-Cycloaddition of aryl azides and substituted nitriles containing an active methylene group is a straightforward procedure for the production of 1,2,3-triazoles [12,13]. 1,2,3-Triazoles can also be synthesized from reactions of diazo compounds and carbodiimides [14]; amines, enolizable ketones, and azides [15]; and azides and alkynes in the presence of a catalyst [16–18]. Additionally, compounds containing the isatin ring system showed a variety of biological activities [19–21]. Accordingly, the synthesis of molecules containing both 1,2,3-triazole and isatin moieties could generate materials with hybrid properties, for example. The current work reports the synthesis and structural characterization of a heterocycle containing 1,3-dihydro-2*H*-indol-2-one and 1,2,3-triazole ring systems. The synthesis and structure determination of numerous other related heterocycles have been reported [22–25].

2. Results and Discussion

2.1. Synthesis of **3**

Reaction of equimolar equivalents of 1-(4-methoxyphenyl)-5-methyl-1*H*-1,2,3-triazole-4-carbohydrazide (**1**) and indoline-2,3-dione (**2**) in boiling ethanol (EtOH) for 4 h in the pres-

ence of concentrated hydrochloric acid (HCl) produced 1-(4-methoxyphenyl)-5-methyl-*N'*-(2-oxoindolin-3-ylidene)-1*H*-1,2,3-triazole-4-carbohydrazide (**3**) with 88% yield (Scheme 1). The structure of **3** was confirmed using NMR spectroscopy (see Section 3.2. for details) and single-crystal X-ray diffraction (Figure 1).



Scheme 1. Synthesis of **3**.

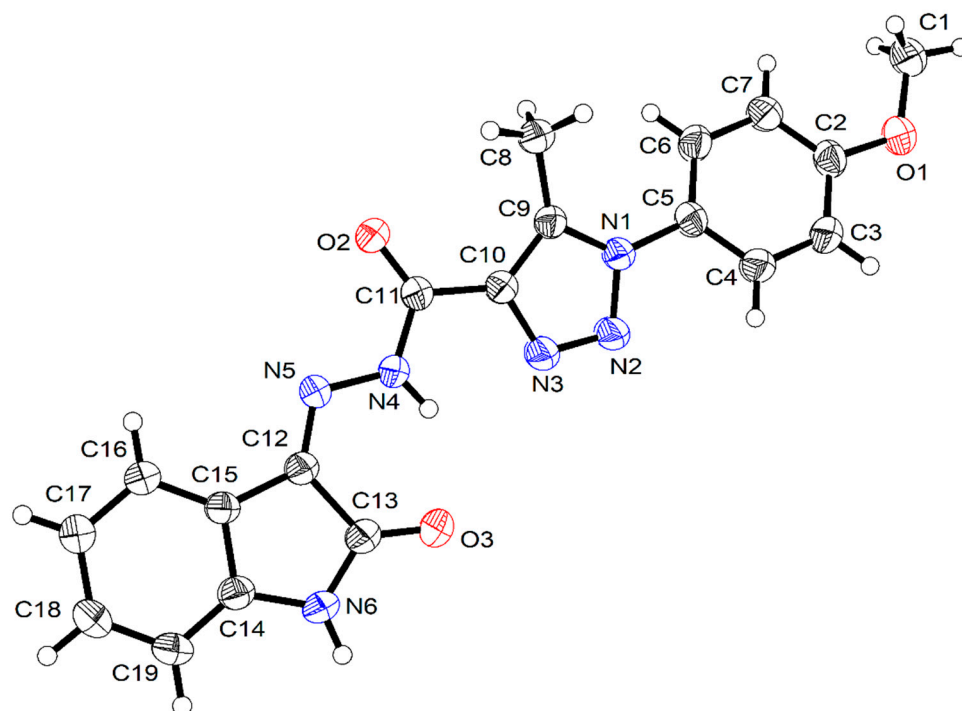


Figure 1. A molecule of **3** with atomic displacement ellipsoids represented at 50% probability.

2.2. NMR Spectroscopy

The ^1H NMR spectrum of **3** contains two singlets (three protons each) upfield at 2.47 and 3.83 ppm, which correspond to the methyl and methoxy protons, respectively. In addition, there are two exchangeable singlets at 14.24 and 11.29 ppm corresponding to the two NH protons. The ^1H NMR spectrum of **3** indicates the presence of 8 aromatic protons. The ^{13}C NMR spectrum of **3** shows signals corresponding to 17 different carbons with the methyl (Me) and methoxy (OMe) carbons appearing at 9.9 and 56.2 ppm, respectively. In addition, the two carbonyl carbons ($\text{C}=\text{O}$) appear downfield at 158.0 and 163.2 ppm and the aryl carbon attached to the methoxy group appears at 160.9 ppm. The ^1H and ^{13}C NMR spectra of **3** are included in the Supplementary Material.

2.3. X-ray Structure

The asymmetric unit of the crystal structure consists of one molecule of **3**. The molecule comprises methoxyphenyl (A [C1–C7, O1]), methyltriazolyl (B [C8–C10, N1–N3]), and oxoindolinyldenyl (D [C12–C19, O1]) rings systems and the carbohydrazine moiety (C [C11, O2, N4, N5]). The molecule is almost planar, as indicated by the twist angles between the following groups: A/B = 24.28(7)°, B/C = 10.48(9)°, C/D = 6.35(11)°. Intramolecular N–H···O hydrogen bonding occurs in the molecule with the following geometry: N4···O3 = 2.6952(19) Å, N4–H4A···O3 = 137.1° (Figure 2). The hydrogen bonding contact may play a role in the stabilization of the Z-configuration of the C = N bond.

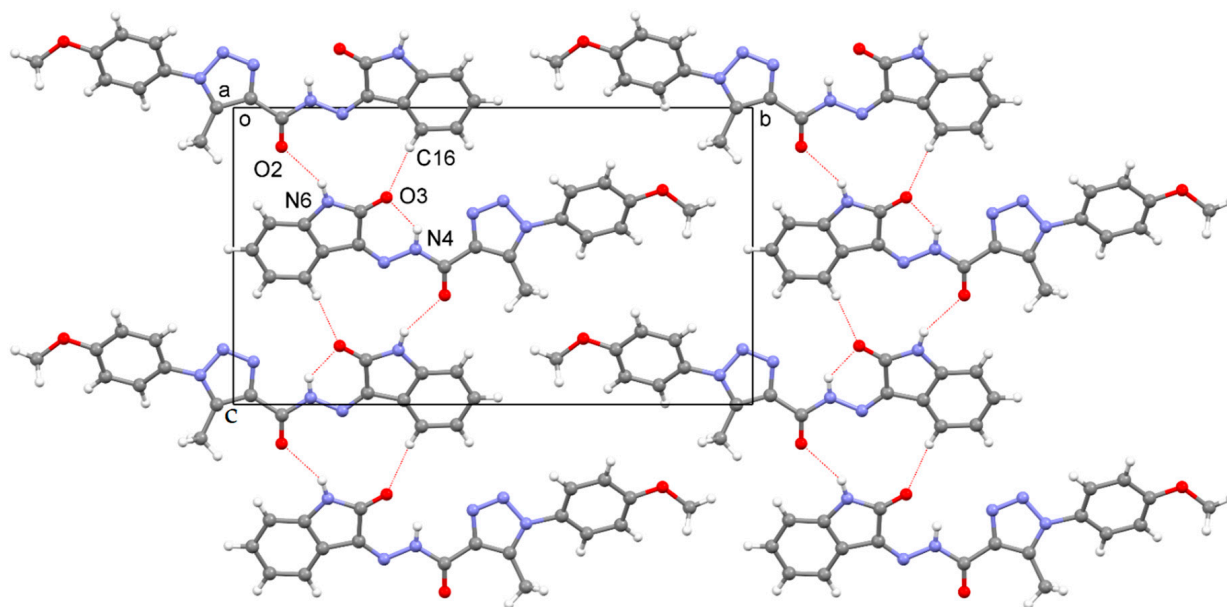


Figure 2. A segment of the crystal structure of **3**, viewed down the *a*, axis, showing a layer with contacts shown as red dotted lines.

Close contacts between pairs of neighboring molecules with geometry C16···O3 = 3.127(2) Å, C16–H16···O3 165.8° and N6···O2 = 2.9401(19) Å, and N6–H6A···O2 146.3° form R(12)₂² rings in the crystal. These result in the formation of molecular ribbons in the [101] direction in the crystal. Interdigitation of the methoxy-phenyl groups on either side of the ribbons form essentially flat sheets of molecules parallel to the (10–1) plane. In the structure, the sheets are stacked in the [10–1] direction with adjacent sheets being related by inversion symmetry.

3. Materials and Methods

3.1. General

The melting point was determined using an electrothermal melting point apparatus. The IR spectrum of **3** was recorded on a JASCO FT/IR-4600 spectrometer. The NMR spectra were recorded on a JEOLNMR 500 MHz spectrometer at 500 MHz for the ¹H and 125 MHz for the ¹³C NMR. The coupling constant (*J*) was measured in Hz and the chemical shift (δ) was measured in ppm. The elemental analyses of compound **3** were determined at the microanalytical unit, Cairo University. Compound **1** was produced based on a literature procedure [26].

3.2. Synthesis of 3

A mixture of **1** (0.49 g, 2.0 mmol) and **2** (0.29 g, 2.0 mmol) in absolute ethanol (10 mL) containing concentrated HCl acid (0.2 mL) was refluxed for 4 h. The solid obtained on cooling was collected, filtered, washed with cold water, dried, and recrystallized from dimethylformamide to obtain yellow crystals of **3**. Yield 88%, mp 289–290 °C. IR (KBr):

3518 (NH), 3240 (NH), 1709 (C = O), 1678 (C = O), 1566 (C = N) cm^{-1} . ^1H NMR ($\text{DMSO}-d_6$): 2.47 (s, 3H, Me), 3.83 (s, 3H, OMe), 6.91 (d, $J = 7.7$ Hz, 1H, H7 of 2-oxoindolin-3-ylideneyl), 7.08 (t, $J = 7.7$ Hz, 1H, H5 of 2-oxoindolin-3-ylideneyl), 7.15 (d, $J = 9.5$ Hz, 2H, H3/H5 of 4-methoxyphenyl), 7.36 (t, $J = 7.7$ Hz, 1H, H6 of 2-oxoindolin-3-ylideneyl), 7.55–7.58 (m, 3H, H2/H6 of 4-methoxyphenyl and H4 of 2-oxoindolin-3-ylideneyl), 11.29 (s, exch., 1H, NH), 14.24 (s, exch., 1H, NH). ^{13}C NMR ($\text{DMSO}-d_6$): 9.9 (C1), 56.2 (C8), 111.7 (C15), 115.3 (C3 and C7), 120.5 (C19), 121.5 (C17), 123.1 (C16), 127.5 (C4 and C6), 128.4 (C5), 132.2 (C18), 136.9 (C10), 138.4 (C12), 139.6 (C9), 143.1 (C14), 158.0 (C2), 160.9 (C11), 163.2 (C13). Anal. Calcd. for $\text{C}_{19}\text{H}_{16}\text{N}_6\text{O}_3$ (367.38): C, 60.63; H, 4.29; N, 22.33%. Found: C, 60.77; H, 4.34; N, 22.56%.

3.3. Data Collection and Refinement Details

The diffraction data were collected on an Agilent SuperNova Dual Atlas diffractometer using mirror monochromated $\text{CuK}\alpha$ radiation ($\lambda = 1.54184$ Å). The structure of **3** was solved by direct methods using SHELXS [27] and refined by full-matrix least squares methods on F^2 with SHELXL–2014 [28]. Crystal Data: $\text{C}_{19}\text{H}_{16}\text{N}_6\text{O}_3$ ($M = 367.38$ g/mol), monoclinic, space group $\text{P2}_1/\text{n}$, $0.26 \times 0.17 \times 0.10$ mm^3 , $a = 7.3166$ (3) Å, $b = 20.3011$ (11) Å, $c = 11.6776$ (5) Å, $\beta = 97.266$ (4)°, $V = 1720.60$ (14) Å³, $Z = 4$, $T = 298$ K, μ ($\text{Cu K}\alpha$) = 0.10 mm^{-1} , $D_{\text{calc}} = 1.453$ Mg m^{-3} , 15,227 reflections measured ($\theta = 3.7$ – 29.4 °), 3144 unique $R_{\text{int}} = 0.031$, $R1 = 0.0494$ and $wR2 = 0.1244$ for $I > 2 \sigma(I)$, $R1 = 0.0665$, $wR2 = 0.1354$ for all data. The X-ray crystallographic data for compound **3** have been deposited at the Cambridge Crystallographic Data Center with CCDC reference number 2169899.

4. Conclusions

1-(4-Methoxyphenyl)-5-methyl- N' -(2-oxoindolin-3-ylidene)-1*H*-1,2,3-triazole-4-carbohydrazide was synthesized in high yield using a convenient and efficient procedure and its structure was confirmed using NMR spectroscopy and single-crystal X-ray diffraction.

Supplementary Materials: The following are available online—IR, ^1H and ^{13}C NMR spectra, CIFs and checkcif report for compound **3**.

Author Contributions: Conceptualization, B.M.K. and G.A.E.-H.; methodology, B.M.K., B.F.A.-W. and G.A.E.-H.; X-ray crystal structures, B.M.K.; investigation, B.M.K., B.F.A.-W., A.A.F. and G.A.E.-H.; writing—original draft preparation, B.M.K., B.F.A.-W., A.A.F. and G.A.E.-H.; writing—review and editing, B.M.K. and G.A.E.-H. All authors have read and agreed to the published version of the manuscript.

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

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