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Short Note

(*E*)-1-(4-Methoxyphenyl)-5-methyl-4-(1-phenyl-4-((2-(2,4,6-trichlorophenyl)hydrazineylidene)methyl)-1*H*-pyrazol-3-yl)-1*H*-1,2,3-triazole

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Abstract: The reaction of equimolar quantities of 3-(1-(4-methoxyphenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde and (2,4,6-trichlorophenyl)hydrazine in ethanol containing concentrated hydrochloric acid (0.2 mL; 37%) as a catalyst under reflux for 2 h yielded 1-(1-(benzofuran-2-yl)ethylidene)-2-(2,4,6-trichlorophenyl)hydrazine. The crude produced was purified by crystallization using dimethylformamide to provide the title heterocycle in a 95% yield. The structure of the newly synthesized heterocycle was confirmed through X-ray diffraction and spectral analyses.

Keywords: pyrazole-4-carbaldehyde; 1,2,3-triazole; (2,4,6-trichlorophenyl)hydrazine; hydrazone; X-ray diffraction; synthesis

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1. Introduction

Heterocycles based on the 1,2,3-triazole moiety have been utilized in the development of several medicinal scaffolds that demonstrate anti-HIV, antitubercular, antiviral, antibacterial, and anticancer activities [1–5].

Pyrazole is a significant heterocyclic component that possesses a potent pharmacological profile and can be a crucial pharmacophore in the process of drug discovery. A number of commonly used drugs incorporating the pyrazole ring are anti-inflammatory, analgesic, vasodilator, and antidepressant agents. In addition, they can be utilized for cancer treatment, to combat obesity, and to provide cytoprotection [6–10].

Hydrazones have a wide range of biological and pharmacological properties with potential for various applications. They exhibit antimicrobial, anti-inflammatory, analgesic, antifungal, antitubercular, antiviral, anticancer, antiplatelet, antimalarial, anticonvulsant, cardioprotective, antihelmintic, antiprotozoal, antitrypanosomal, and antischistosomiasis properties [11–13]. Moreover, they can be used to create sensor materials that can detect fluoride ions, cyanide ions, heavy metals, and toxic gases [14–19].

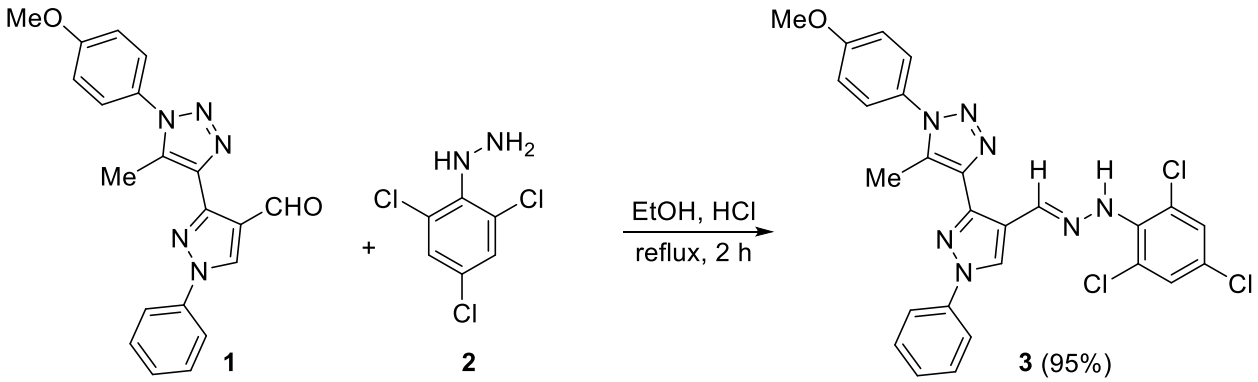
In this study, we present a straightforward method for synthesizing a novel heterocycle containing 1,2,3-triazole, pyrazole, and hydrazone moieties, as well as the determination of the structure.

2. Results and Discussion

2.1. Synthesis of 3

The synthesis of the title heterocycle was performed according to Scheme 1. The method involved the reaction of 3-(1-(4-methoxyphenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde (**1**) and 2,4,6-trichlorophenyl hydrazine (**2**) in ethanol

(EtOH) containing concentrated hydrochloric acid (HCl, 0.2 mL, 37%) in a 1:1 molar ratio. The mixture was stirred in boiling EtOH for 2 h. After cooling, the solid formed was collected and recrystallized from dimethylformamide (DMF). The resulting heterocycle, 1-(1-(benzofuran-2-yl)ethylidene)-2-(2,4,6-trichlorophenyl)hydrazine (**3**), was obtained in a yield of 95%.



Scheme 1. Synthesis of title heterocycle **3**.

2.2. IR and NMR Spectroscopy of **3**

The IR spectrum of **3** showed absorption bands at 3324 cm^{-1} due to the NH group. The absorption bands for the C=C in aromatic moieties appeared at 1670 and 1589 cm^{-1}. The NMR spectra revealed the presence of characteristic singlet signals at 2.59, 3.86, 8.75, and 9.62 ppm, which correspond to the protons of methyl, methoxy, pyrazolyl, and NH groups, respectively. This pattern of chemical shifts suggests that the methyl and methoxy groups are likely attached to an aromatic ring, given their upfield positions. The protons of the 4-methoxyphenyl group appeared as two doublets (J = 8.5 Hz) at 7.17 and 7.97 ppm. The ^{13}C NMR spectrum further supports this structural interpretation, with the carbons of the methyl, methoxy, and CH=N groups appearing at 9.8, 55.6, and 143.0 ppm, respectively. The carbon at the 4-position of the 4-methoxyphenyl group was notably downfield at 160.0 ppm. All the other carbons were observed at chemical shifts that align with the proposed structure.

2.3. Crystal Structure of **3**

The crystal structure of **3** is monoclinic, space group $P2_1/c$, with one molecule in the asymmetric unit (Figure 1). The molecule is composed of six planar fragments, namely the methoxyphenyl (**mphen**, C1–C7, O1), methyltriazolyl (**mtria**, C8–C10, N1–N3), pyrazolyl (**pyraz**, C11–C13, N4, N5), phenyl (**phen**, C14–C19), methanehydrazonoyl (**mhydr**, C20, N6, N7), and trichlorophenyl (**tclphen**, C21–C26, Cl1–Cl3) groups.

The molecule is roughly planar, with the methoxyphenyl group showing the largest deviation from planarity with a **mphen**/**mtria** twist angle of 47.98(7)°. The methyltrazolyl, pyrazolyl, methanehydrazonoyl, and trichlorophenyl groups are essentially coplanar, with twist angles **mtria**/**pyraz**, **pyraz**/**mhydr,** and **mhydr**/**tclphen** of 5.28(14)°, 8.04(27)°, and 8.33(25)°, respectively. The angle twist between the pyrazolyl and the phenyl group (**pyraz**/**phen**) is slightly greater at 18.27(37)°. An intramolecular N–H. . .Cl contact with a N7–H7A. . .Cl1 angle of 114.7° and N7. . .Cl1 distance of 2.896(2) Å occurs in the structure.

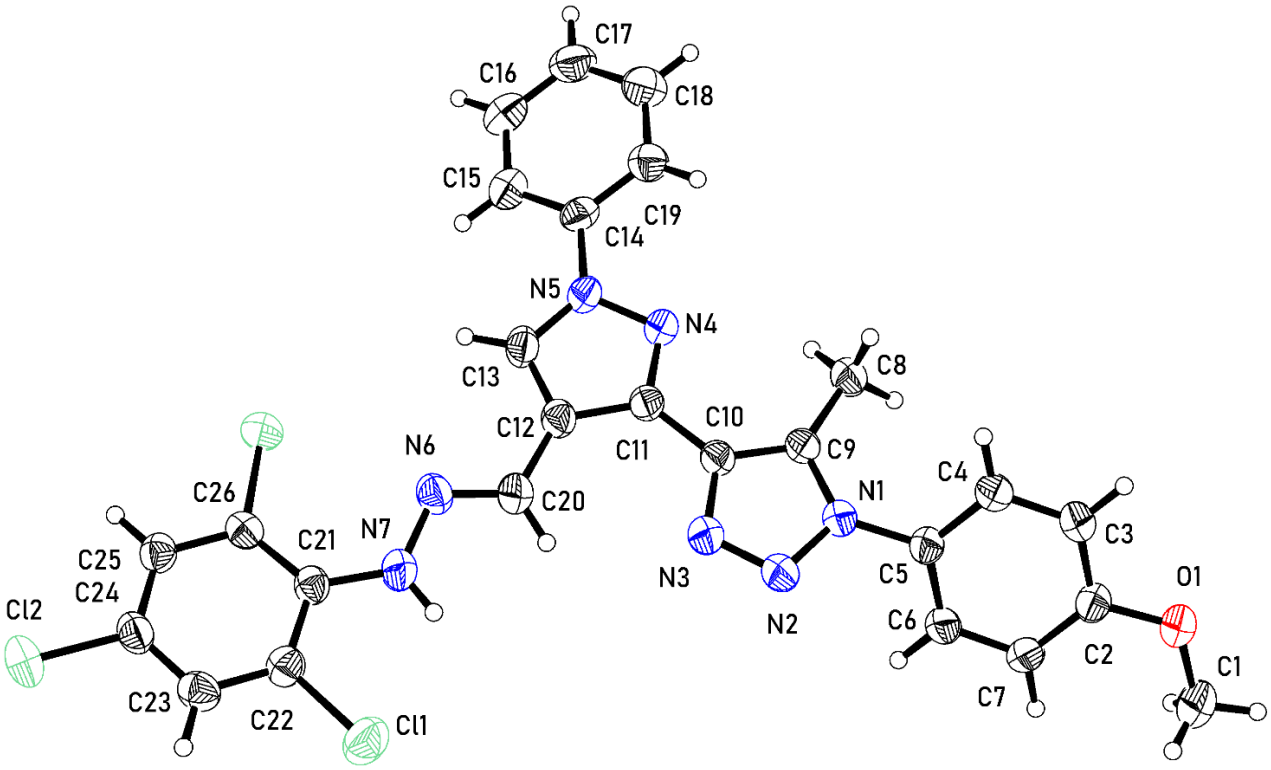


Figure 1. Ortep's representation of the asymmetric unit of **3** displaying the atomic displacement parameters at the 50% probability level.

The effective co-planarity of the methyltriazolyl, pyrazolyl, methanehydrazonoyl, and phenyl groups is also observed in the structures of related compounds 5-(2-(4-fluorophenyl) hydrazono)-4-methyl-2-((3-(5-methyl-1-(4-methylphenyl)-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)methylene)hydrazono)-2,5-dihydrothiazole dimethylformamide monosolvate [20], *N*′-(1-(5-methyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)ethylidene)-2-[(3-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)methylene]hydrazine-1-carbothiohydrazide [21], and 1,2-*bis*((3-(1-(4-fluorophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)methylene)hydrazine [22]. In contrast to **3**, large twist angles (44–65°) are observed between the methanehydrazonoyl and trichlorophenyl groups in (*R*)-4-((*R*)-2-methyl-1-((2,4,6,-trichlorophenyl)hydrazonomethyl)propyl)-2-oxo-3,4-dihydro-2*H*-naphtho(2,1-*e*)(1,3)oxazine-4-carboxylic acid ethyl ester [23], (*E*)-benzaldehyde (2,4,6-trichlorophenyl)hydrazone [24], and 2-((2-(2,4,6-trichlorophenyl)hydrazono)methyl)phenol [25].

The packing in the crystal structure of **3** is shown in Figure 2a. In the crystal structure, interactions of π. . .π type occur between neighboring molecules. One face of the triazolyl group interacts with a pyrazolyl group with a ring centroid-to-centroid distance of 3.483 Å (*i* in Figure 2b). The other face interacts with the trichlorophenyl group with a ring centroid-to-centroid distance of 3.625 Å (*ii* in Figure 2b). The interactions lead to the arrangement of the molecules in pillars aligned parallel to the *c*-axis (Figure 2b). The planes of the molecules within one pilar are parallel. The pillars are related via glide symmetry in the direction of the c-axis, leading to a herringbone arrangement of the molecules in the crystal structure (Figure 2a).

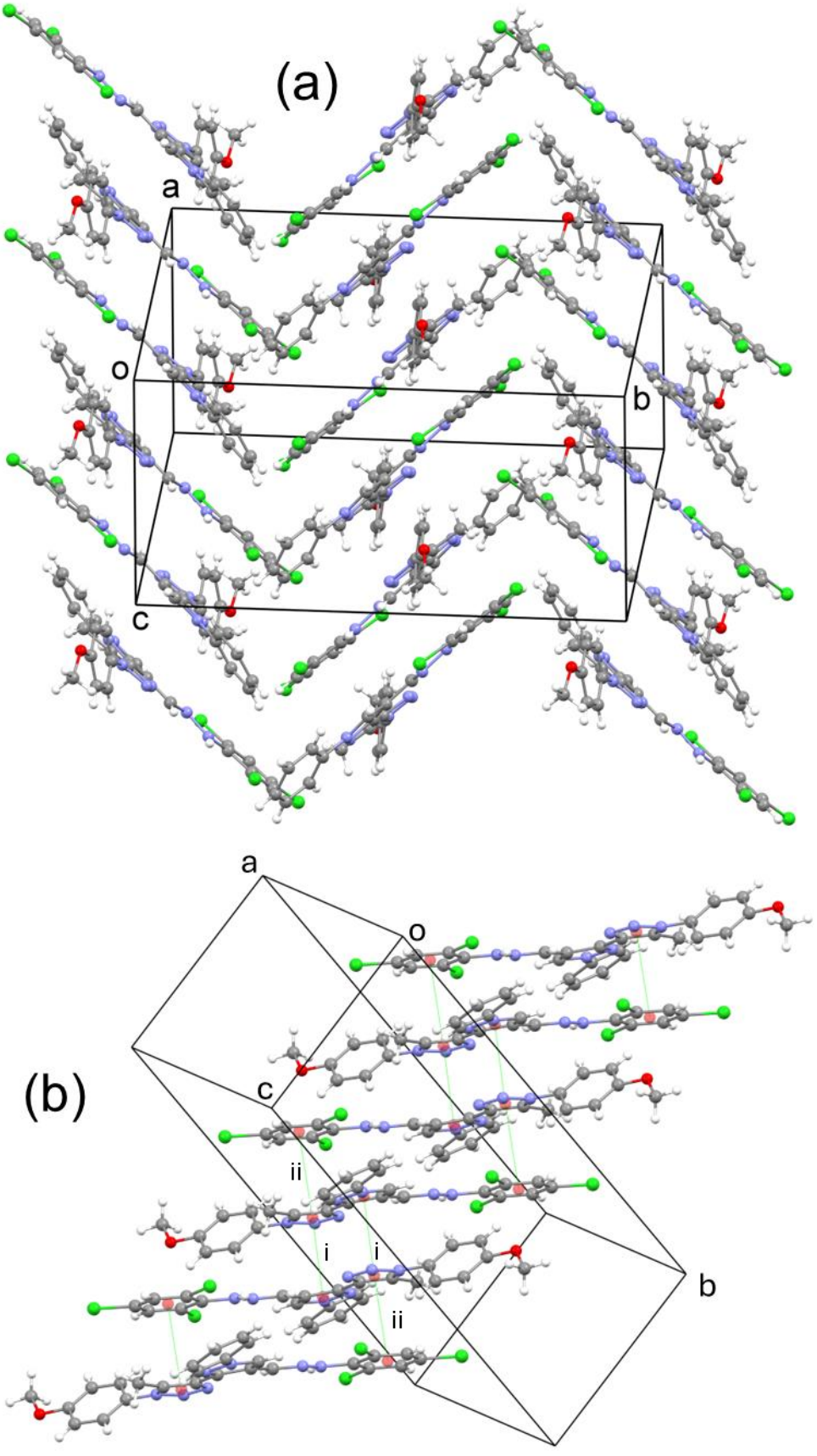


Figure 2. (**a**) Crystal packing in the structure of **3** and (**b**) a segment of the crystal structure showing a column of molecules with π. . .π interactions shown as green dotted lines.

3. Materials and Methods

3.1. General

Merck supplied chemicals, reagents, and solvents. The Bruker Vertex 80 ATR-FTIR spectrometer (Bruker; Tokyo, Japan) was utilized to record the IR spectrum (400–4000 cm^{-1}) of **3**. The NMR spectra of **3** were obtained in deuterated dimethyl sulfoxide (DMSO-d_6) using a Varian Mercury 300 VX spectrometer (Varian, Palo Alto, CA, USA) at 300 MHz for the protons and 75 MHz for the carbons. The chemical shift (δ) was reported in ppm, and the coupling constant (*J*) for the neighboring protons was measured in Hz. The preparation of **1** was based on a reported procedure [26].

3.2. Synthesis of **3**

A mixture of **1** (0.72 g, 2.0 mmol) and **2** (0.42 g, 2.0 mmol) in EtOH (15 mL) containing HCl (0.2 mL; 37%) was refluxed for 2 h. After cooling down to 20 °C, the obtained yellow solid was filtered out and washed with EtOH. The dried solid was recrystallized from DMF to afford **3** in 95% yield. Mp 203–205 °C. IR (KBr): 3324, 2941, 1670, 1598 cm^{-1}. ^{1}H NMR: 2.59 (s, 3H, Me), 3.86 (s, 3H, OMe), 7.17 (d. *J* = 8.5 Hz, 2H, Ar), 7.33 (t, *J* = 7.8 Hz, 1H, Ph), 7.51 (t, *J* = 7.8 Hz, 2H, Ph), 7.57–7.60 (m, 4H, Ar), 7.97 (d. *J* = 8.5 Hz, 2H, Ar), 8.75 (s, 1H, pyrazolyl), 8.80 (d, *J* = 3.0 Hz, 1H, CH=N), 9.62 (s, 1H, NH). ^{13}C NMR: 9.8 (CH_3), 55.6 (CH_3), 114.7 (CH), 118.4 (CH), 119.0 (CH), 124.8 (C_q), 126.6 (C_q), 126.8 (CH), 127.8 (CH), 128.6 (C_q), 128.7 (CH), 129.5 (CH), 132.4 (C_q), 134.4 (C_q), 137.4 (C_q), 137.8 (C_q), 138.0 (C_q), 139.1 (C_q), 143.0 (CH), 160.0 (C_q). Anal. Calcd. for $C_{26}H_{20}Cl_3N_7O$ (551.07): C, 56.49; H, 3.65; N, 17.74. Found C, 56.59; H, 3.83; N, 17.88%.

3.3. Crystal Structure Determination

Data collection was performed at room temperature on an Agilent SuperNova Dual Atlas diffractometer using mirror monochromated MoKα radiation. The structure solution was completed by direct methods using SHELXT [27] and refinement by full-matrix least-squares methods on F^2 using SHELXL [28]. The phenyl group is disordered and was modeled with two components related via a ring twist of 19.88(82)°. MF = $C_{26}H_{20}C_{13}N_7O$, FW = 552.84, T = 293 (2) K, λ = 0.71073 Å, monoclinic, $P2_1/c$, a = 13.0702(6) Å, b = 20.5080(9) Å, c = 9.8479(4) Å, β = 104.377(5)°, V = 2557.0(2) $Å^3$, Z = 4, calculated density = 1.436 Mg/m^3, absorption coefficient = 0.393 mm^{-1}, F (000) = 1136, crystal size = 0.57 × 0.35 × 0.21 mm^3, reflections collected = 23,274, independent reflections = 6483, R (int) = 0.0700, parameters = 379, goodness-of-fit on F^2 = 1.043, R1 = 0.0502, wR2 = 0.1145 for (I > 2sigma (I)), R1 = 0.0856, wR2 = 0.1418 for all data, and largest difference peak and hole = 0.293 and −0.284 e.$Å^{-3}$. The X-ray crystallographic data for heterocycle **3** have been deposited at the Cambridge Crystallographic Data Center with CCDC reference number 2335716.

4. Conclusions

The synthesis of a novel hydrazone containing 1,2,3-triazole and pyrazole moieties has been reported. The procedure used was simple, convenient, and high-yielding. The structure of the newly synthesized heterocycle has been established using nuclear magnetic resonance and X-ray diffraction techniques.

Supplementary Materials: The following are available online: IR, 1H, and 13C NMR spectra, CIFs, and CheckCIF reports for the title heterocycle **3**.

Author Contributions: Conceptualization: B.M.K. and G.A.E.-H.; methodology: B.F.A.-W., B.M.K. and G.A.E.-H.; X-ray crystal structures: B.M.K.; investigation: B.F.A.-W., H.A.M., B.M.K. and G.A.E.-H.; writing—original draft preparation: B.F.A.-W., H.A.M., B.M.K. and G.A.E.-H.; writing—review and editing: B.F.A.-W., H.A.M., 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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