

Short Note

## One-Pot Synthesis and Crystal Structure of Methyl 5-Hydroxy-1-phenyl-1*H*-pyrazole-3-carboxylate

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**Abstract:** The title compound, Methyl 5-Hydroxy-1-Phenyl-1*H*-Pyrazole-3-Carboxylate (C<sub>11</sub>H<sub>10</sub>N<sub>2</sub>O<sub>3</sub>), was prepared by a one-pot, two-component reaction of an equimolar mixture of phenyl hydrazine and dimethyl acetylene dicarboxylate (DMAD) at reflux temperature for 2 h in a mixture of toluene and dichloromethane as solvent. C<sub>11</sub>H<sub>10</sub>N<sub>2</sub>O<sub>3</sub> was crystallized from an ethanol solution in monoclinic space group *P*2<sub>1</sub>/*c* with unit cell dimensions *a* = 9.5408(16), *b* = 9.5827(16), *c* = 11.580(2) Å, β = 105.838(3)°, *V* = 1018.5(3) Å<sup>3</sup>, *Z* = 4.

**Keywords:** pyrazole; methyl 5-hydroxy-1-phenyl-1*H*-pyrazole-3-carboxylate; crystal structure

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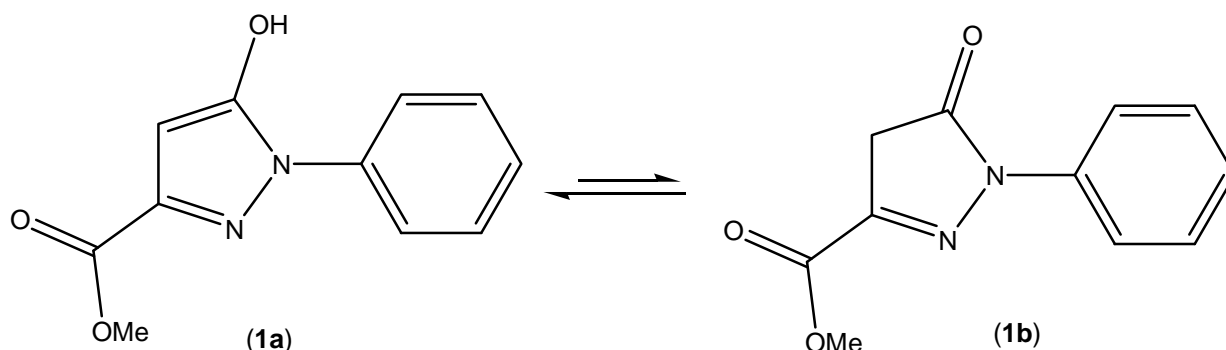
### 1. Introduction

Over the years, pyrazoles have enjoyed a prominent place in heterocyclic chemistry largely due to the wide range of biological activity demonstrated by this class of compounds for uses such as pharmaceuticals and agricultural and veterinary drugs [1–3]. They possess anti-obesity [4], antianxiety [5] and HIV-1 reverse transcriptase inhibitor [6], anti-hyperglycemic, anti-pyretic, analgesic, anti-inflammatory and hypoglycemic activity [7,8]. Their derivatives are used as important intermediates in the preparation of drug molecules, as well as in the laboratory synthesis of natural products. The presence of ester functionality in pyrazoles further offers an attractive method for the generation of derivatives which may possess interesting medicinal and biological properties.

In this paper, we describe a new one pot synthesis and structure of methyl 5-hydroxy-1-phenyl-1*H*-pyrazole-3-carboxylate (**1a**) which is a tautomeric form of methyl 5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazole-3-carboxylate (**1b**) (Figure 1). The tautomeric form **1a** is predominant in a DMSO- $d_6$  solution and this form also crystallizes from ethanol solution.

The structure of the tautomer **1b** is found in the Cambridge database and is an organocatalyst for organic reactions [9].

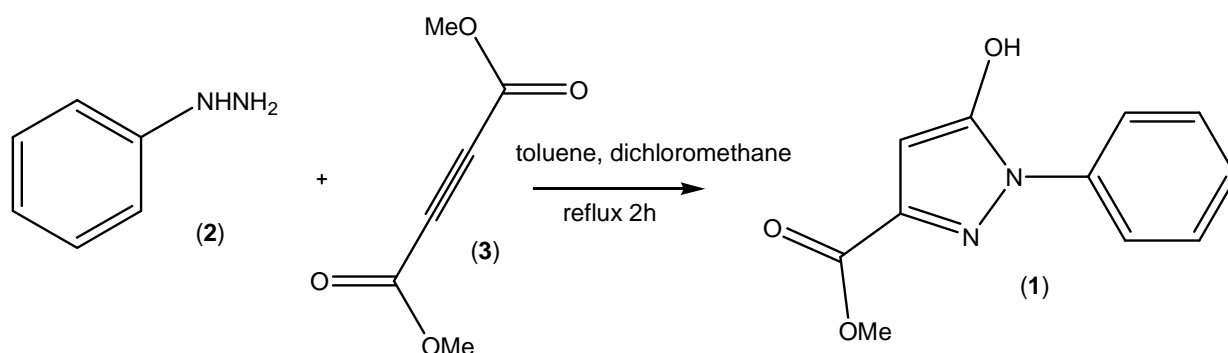
**Figure 1.** Tautomeric forms of methyl 5-hydroxy-1-phenyl-1*H*-pyrazole-3-carboxylate.



## 2. Results and Discussion

Methyl 5-hydroxy-1-phenyl-1*H*-pyrazole-3-carboxylate (**1**) was prepared by refluxing a 1:1 molar ratio of phenyl hydrazine (**2**) and dimethylacetylene dicarboxylate (**3**) for 2 h, in a mixture of toluene and dichloromethane used as a solvent (Figure 2).

**Figure 2.** Synthesis of title compound **1**.



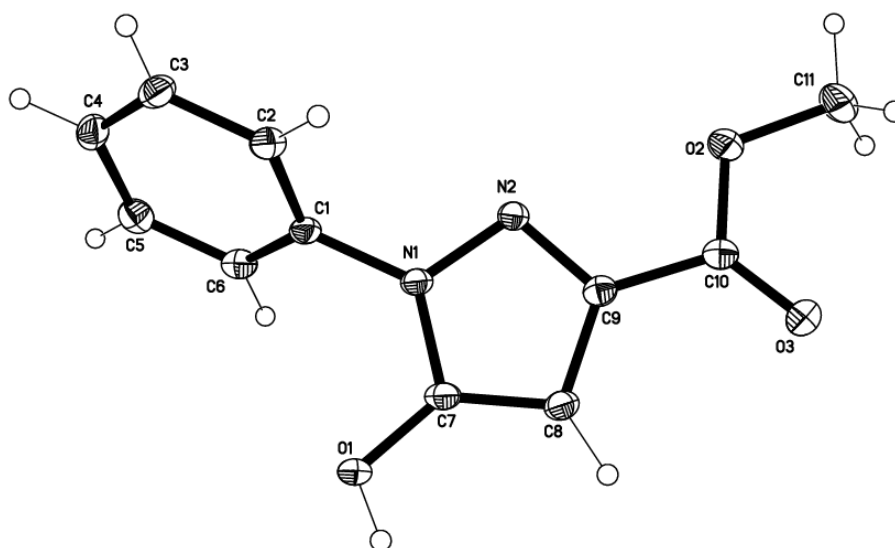
The structure of methyl 5-hydroxy-1-phenyl-1*H*-pyrazole-3-carboxylate was confirmed by  $^1\text{H}$  NMR spectra which revealed the presence of a singlet at  $\delta$  5.98 ppm assignable to 4-pyrazole H. Another singlet in the  $^1\text{H}$  NMR at  $\delta$  3.80 ppm is assigned to three protons of ester methoxy group. A singlet for hydroxyl proton appeared at  $\delta$  12.16 ppm. The FTIR showed peaks at  $3204\text{ cm}^{-1}$  for OH stretching vibrations, and at  $1728\text{ cm}^{-1}$  for the ester carbonyl in addition to other characteristic peaks.

Single crystals suitable for X-ray diffraction were obtained by recrystallization from ethanol. The molecular structure of methyl 5-hydroxy-1-phenyl-1*H*-pyrazole-3-carboxylate is depicted in Figure 3.

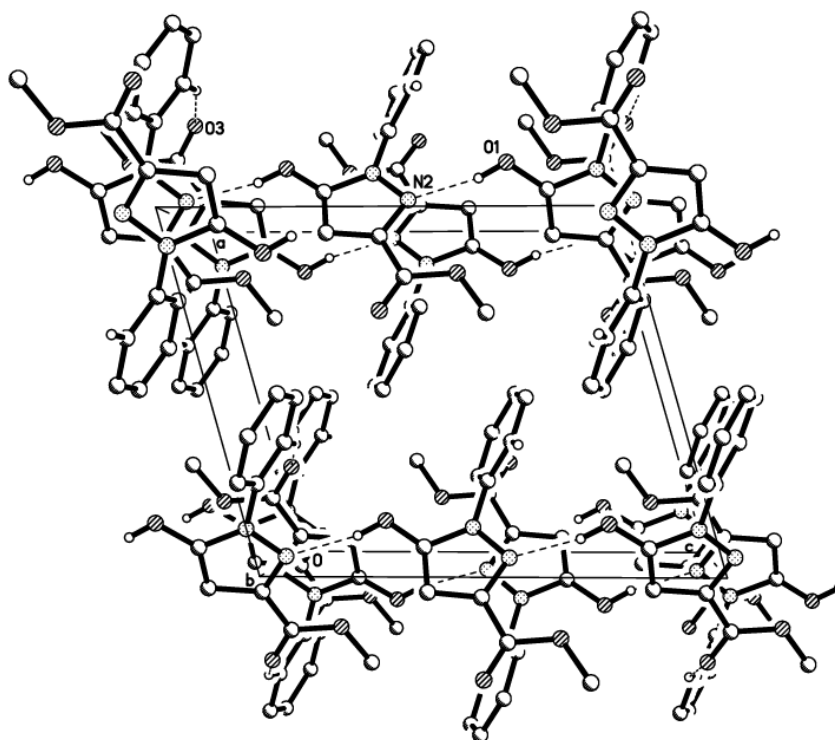
The phenyl and the pyrazole ring planes are inclined at a dihedral angle of  $60.83(5)^\circ$ , the carboxylate group lies in the pyrazole plane with a C8-C9-C10-O2 torsion angle of  $173.0(1)^\circ$ .

There are no unexpected geometric parameters. A closely related molecular structure 3-ethoxycarbonyl-1-phenyl-1H-pyrazol-5-yl 4-chlorobenzoate is known [10] with a 4-chlorobenzoate group replacing the  $-OH$ . Crystal packing shows strong  $O1-H\dots N2$  ( $x, -y + 0.5, z + 0.5$ ) interactions with  $H\dots N2$  1.95 Å and  $O-H\dots N$  167.9° that link the molecules into chains along the  $c$  axis. Weaker  $C2-H\dots O3$  ( $-x + 2, -y + 1, -z$ ) hydrogen bonds with  $H\dots O$  2.42 Å and  $C-H\dots O$  156.3° then connect these chains into centrosymmetric dimers (Figure 4).

**Figure 3.** The molecular structure of methyl 5-hydroxy-1-phenyl-1H-pyrazole-3-carboxylate (**1**). Anisotropic displacement ellipsoids are drawn at the 50% probability level.



**Figure 4.** Crystal packing of **1** viewed along the  $b$ -axis with hydrogen bonding pattern shown as dashed lines. H atoms not involved in bonding are omitted.



### 3. Experimental Section

#### 3.1. General

The melting point was determined on a Stuart SMP3 melting point apparatus and is uncorrected. FT IR spectra were recorded using a Shimadzu IR 460 spectrophotometer by the Attenuated Total Reflectance (ATR) method.  $^1\text{H}$  NMR spectrum was determined as DMSO- $d_6$  solution at 300 MHz using a Bruker AM-300 spectrophotometer. Mass Spectra (EI, 70 eV) were recorded on a GC-MS instrument and the elemental analysis was conducted using a LECO-183 CHNS analyzer.

#### 3.2. Synthesis of Methyl 5-Hydroxy-1-phenyl-1H-pyrazole-3-carboxylate (**1**)

The title compound,  $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}_3$ , was prepared by stirring at reflux a mixture of phenyl hydrazine (0.22 g, 2 mmol) (**2**) and dimethylacetylene dicarboxylate (DMAD) (0.28 g, 2 mmol) (**3**) for 2 h in a 10 mL (1:1) mixture of toluene and DCM. The completion of reaction was monitored by thin layer chromatography. After completion the solvent was evaporated under reduced pressure and the white solid obtained were recrystallized from ethanol. m.p 188 °C.  $^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ )  $\delta$  3.80 (3H, s), 5.98 (1H, s), 7.34–7.74 (5H, m), 12.16 (1H, s); FTIR (ATR): 3204, 1728, 1249  $\text{cm}^{-1}$ . Anal calcd. for  $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}_3$ : C, 60.55; H, 4.62; N, 12.84%; Found C, 60.49; H, 4.67; N, 12.78%.

#### 3.3. X-ray Structure Determination

$\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}_3$ ,  $M_r = 218.2$ , crystal size  $0.21 \times 0.39 \times 0.40 \text{ mm}^3$ , monoclinic, space group  $P2_1/c$ ,  $a = 9.5408(16)$ ,  $b = 9.5827(16)$ ,  $c = 11.580(2) \text{ \AA}$ ,  $\beta = 105.838(3)^\circ$ ,  $V = 1018.5(3) \text{ \AA}^3$ ,  $Z = 4$ ,  $\rho_{\text{calc}} = 1.423 \text{ mg/cm}^3$ ,  $\mu = 0.106 \text{ mm}^{-1}$ ,  $F(000) = 456$ . Data were collected at 130(2) K on a Bruker [11] AXS SMART APEX CCD diffractometer using  $\text{MoK}\alpha$  radiation; 7713 reflections collected  $2.22 < \Theta < 27.88^\circ$ .

The structure was solved by direct methods [12], and refined on  $F^2$  by full-matrix least-squares [12] with 147 parameters and 2402 unique intensities ( $R_{\text{int}} = 0.034$ ). All non-hydrogen atoms were refined anisotropically. All H atom positions were clearly derived from difference Fourier maps and the refined on idealized positions with  $U_{\text{iso}} = 1.2 U_{\text{eq}}(\text{C/O})$  or  $1.5U_{\text{eq}}(\text{C}_{\text{methyl}}, \text{O})$ , C–H distances of 0.95–0.98  $\text{Å}$  and O–H 0.84  $\text{Å}$ . The methyl H atoms were allowed to rotate but not to tip. CCDC-879881.

### 4. Conclusions

A highly efficient synthesis of compound **1** was carried out under mild conditions. The structure assignment as the methyl 5-hydroxy-1-phenyl-1H-3pyrazole-3-carboxylate tautomer was supported by  $^1\text{H}$  NMR data, elementary analysis and the crystallographic studies.

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