

## Crystal structure of 3-(4-hydroxy-3-methoxyphenyl)-7,7-dimethyl-7,8-dihydrocinnolin-5(6H)-one

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### ABSTRACT

The title compound 3-(4-hydroxy-3-methoxyphenyl)-7,7-dimethyl-7,8-dihydrocinnolin-5(6H)-one (**3**) was prepared via one-pot three component reaction of 2-(4-hydroxy-3-methoxyphenyl)-2-oxoacetaldehyde with dimedone in the presence of hydrazine hydrate and studied by the single crystal X-ray diffraction method. Its structure was also confirmed by IR, <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy. Compound **3** was crystallized in the monoclinic system, space group *P2<sub>1</sub>/c*, *a* = 7.921(2) Å, *b* = 11.566(4) Å, *c* = 16.986(6) Å, β = 107.338(5)°, *V* = 1485.5(8) Å<sup>3</sup>, *Z* = 4, *R*<sub>1</sub> = 0.0559 and *wR*<sub>2</sub> = 0.1253. The crystal structure of **3** also shows a weak interaction between O3 and N2 atoms.

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## 1. Introduction

Cinnolines and their derivatives exhibit a broad range of biological activity, such as anticancer, fungicidal, bactericidal, and anti-inflammatory properties.<sup>1</sup> Furthermore, compounds containing a cinnoline fragment demonstrate a series of interesting physical characteristics, such as luminescent and nonlinear optical properties.<sup>2</sup> Hence, the synthesis of cinnoline has been studied for many years.<sup>3</sup> Most syntheses of cinnolines involve arenediazonium salts,<sup>4</sup> arylhydrazones,<sup>5</sup> arylhydrazines,<sup>6</sup> and nitriles<sup>7</sup> as their starting materials. Recently, alkynyl-substituted aryltriazene was used as the precursor to prepare cinnoline,<sup>8</sup> however high temperatures or strong acidic conditions were still required. Palladium-catalyzed annulation of alkynes by functionally substituted aryl halides has been demonstrated to be a versatile methodology to construct a wide variety of complicated hetero- and

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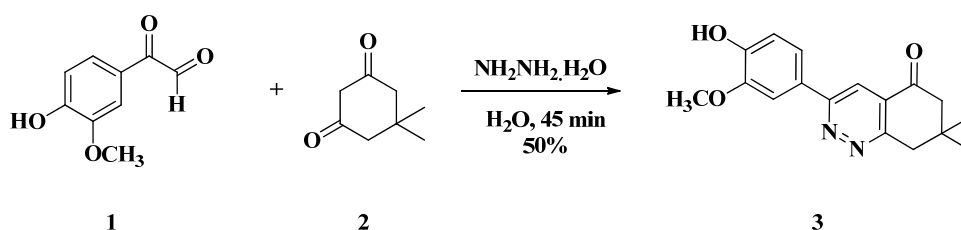
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carbocycles.<sup>9</sup> Cinnoline frameworks have been recently obtained via palladium catalyzed reaction of 2-iodotriazenes with internal alkynes.<sup>10</sup> These procedures often suffer from certain drawbacks such as multi step reactions, harsh reaction conditions and using expensive catalysts. Therefore, these reported annulation reactions prompted us to investigate a single green reaction to prepare cinnoline rings.

In continuation of our recent reports on synthesis of pyridazine derivatives,<sup>11-18</sup> here we report the X-ray crystal structure of 3-(4-hydroxy-3-methoxyphenyl)-7,7-dimethyl-7,8-dihydrocinnolin-5(6*H*)-one prepared by reaction of 2-(4-hydroxy-3-methoxyphenyl)-2-oxoacetaldehyde with dimedone in the presence of hydrazine hydrate.<sup>11</sup>

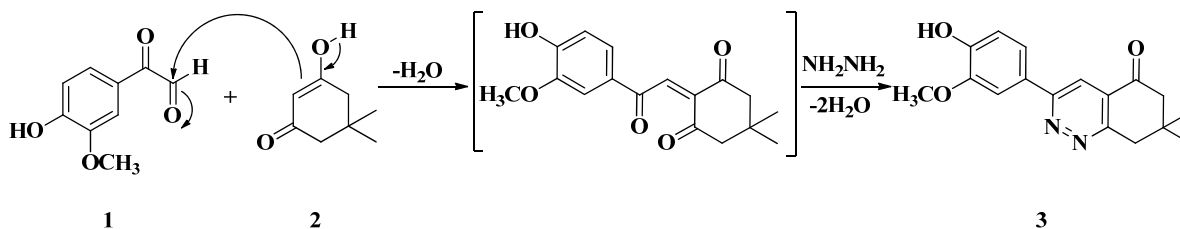
## 2. Results and Discussion

2-(4-Hydroxy-3-methoxyphenyl)-2-oxoacetaldehyde (**1**) was reacted with dimedone (**2**) in the presence of hydrazine hydrate in water at 5-8 °C, which led to form 3-(4-hydroxy-3-methoxyphenyl)-7,7-dimethyl-7,8-dihydrocinnolin-5(6*H*)-one (**3**) (Scheme 1).



**Scheme 1**

The proposed mechanism for the synthesis of final compound (**3**) is shown in Scheme 2.



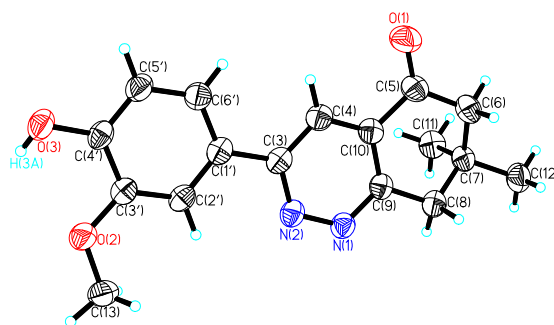
**Scheme 2**

In the <sup>1</sup>H-NMR spectrum of this compound, the CH on pyridazine ring is very deshielded and resonates at low field. The corresponding proton appears at  $\delta = 8.24$  ppm.

### *Crystal structure determination of 3*

The crystal structure of **3** is shown in Fig. 1. Single-crystals of **3** were used for data collection on a Bruker Smart Apex diffractometer using SMART software.<sup>19</sup> Suitable crystals were selected and mounted on a glass fiber using epoxy-based glue. The data sets were collected at room temperature for sample employing a scan of 0.3° in  $\omega$  with an exposure time of 20 s/frame. The cell refinement and data reduction were carried out with SAINT,<sup>20</sup> the program SADABS was used for the absorption correction.<sup>20</sup> The structure was solved by direct methods using SHELXS-97,<sup>21</sup> and difference Fourier syntheses. Full-matrix least-squares refinement against  $|F^2|$  was carried out using the SHELXTL-PLUS,<sup>21</sup> suit of programs. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed geometrically and held in the riding mode during the final refinement. The crystallographic data for structure **3** were deposited to the Cambridge Crystallographic Data Center

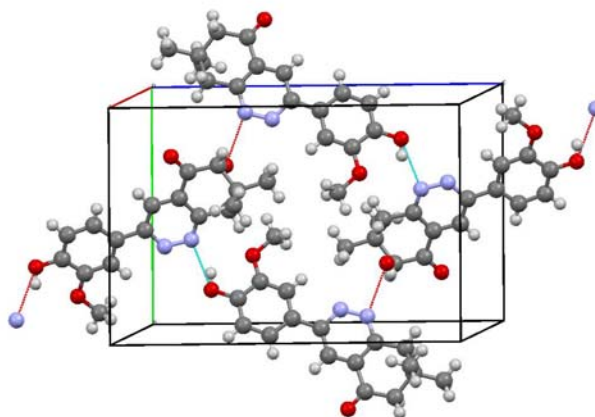
(entry no. CCDC-894314) and are available free of charge upon request to CCDC, 12 Union Road, Cambridge, UK (Fax: +44-1223-336033, e-mail: [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk)).



**Fig. 1.** Crystal structure of compound **3**.

**Table 1.** Crystal data and structure refinement details for **3**.

Empirical formula	C <sub>17</sub> H <sub>18</sub> N <sub>2</sub> O <sub>3</sub>
Formula weight	298.33
Crystal size, mm <sup>3</sup>	0.40×0.20×0.08
Crystal color and form	orange, diamond
Crystal system	monoclinic
Space group	<i>P2<sub>1</sub>/c</i>
<i>a</i> , <i>b</i> , <i>c</i> , Å; β, deg	7.921(2), 11.566(4), 16.986(6), 107.338(5)
<i>V</i> , Å <sup>3</sup>	1485.5(8)
<i>Z</i>	4
<i>D</i> (calc), g.cm <sup>-3</sup>	1.334
<i>μ</i> , mm <sup>-1</sup>	0.092
<i>F</i> (000), e	632
Scan type	ω
θ range, deg	2.16–28.34
Index range	-10< <i>h</i> <10, -15< <i>k</i> <15, -22< <i>l</i> <22
Measured reflections	18028
Independent reflections	3702
Observed refl. <i>I</i> ≥ 2σ( <i>I</i> )	1710
Completeness to θ = 28.34°	99.5
Refinement on	<i>F</i> <sup>2</sup>
Data, restraints, parameters	3702, 0, 199
<i>R</i> ( <i>F</i> <sup>2</sup> > 2σ( <i>F</i> <sup>2</sup> ))	<i>R</i> 1 = 0.0559, <i>wR</i> 2 = 0.1253
<i>R</i> (all data)	<i>R</i> 1 = 0.1326, <i>wR</i> 2 = 0.1584
Goodness-of-fit = <i>S</i>	0.0993
Weighting parameter <i>a/b</i>	0.0416/0.1303
Δρ (max; min), e.Å <sup>-3</sup>	0.9926; 0.9639



**Fig. 2.** Crystal packing diagram of **3** with intermolecular hydrogen bond.

### 3. Description of the crystal 3

The crystal structure of **1** and its crystal packing diagram are shown in Figs. 1 and 2, respectively. A summary of the crystal data and experimental details is given in Table 1. The selected bond lengths and angles for **3** are shown in Table 2. The geometry hydrogen bonds are shown in Table 3. The crystal structure of **3** also shows a weak interaction between O3 and N2 atoms. The dimedone and pyridazine rings moieties are not in the same plane together. The torsion angles of C6–C7–C8–C9, C5–C6–C7–C8 are 50.3° and -55.8°, respectively. The angles of C6–C7–C8, C10–C4–C3 and N1–C9–C8 are 108.12, 118.9 and 117.06° respectively. The carbonyl group in dimedone lies in plane of pyridazine ring. The Bond lengths of N1–N2 and N2–C3 are 1.339 and 1.337 respectively for interaction of O3 with N2. The torsion angles of C9–N1–N2–C3, N2–C3–C1'–C2' equals to 0.5° and 2.8°, respectively.

**Table 2.** Selected bond lengths and angles (Å, °) of **3**.

Bond		Angle	
N(1)–C(9)	1.338(2)	C(9)–N(1)–N(2)	120.47(17)
N(1)–N(2)	1.339(2)	C(3)–N(2)–N(1)	120.69(18)
N(2)–C(3)	1.337(2)	N(2)–C(3)–C(4)	120.60(19)
C(3)–C(1')	1.476(3)	N(2)–C(3)–C(1')	115.72(19)
C(4)–C(10)	1.362(3)	C(10)–C(4)–C(3)	118.9(2)
C(4)–H(4A)	0.93	C(10)–C(4)–H(4A)	120.6
C(5)–O(1)	1.216(2)	O(1)–C(5)–C(10)	120.1(2)
C(5)–C(6)	1.487(3)	C(6)–C(5)–C(10)	116.7(2)
C(5)–C(10)	1.498(3)	C(5)–C(6)–C(7)	114.65(18)
C(6)–C(7)	1.529(3)	C(11)–C(7)–C(12)	110.00(18)
C(6)–H(6A)	0.97	C(11)–C(7)–C(6)	109.94(18)
C(6)–H(6B)	0.97	C(6)–C(7)–C(8)	108.12(17)
C(7)–C(12)	1.528(3)	N(1)–C(9)–C(10)	121.07(19)
C(7)–C(8)	1.531(3)	N(1)–C(9)–C(8)	117.06(18)
C(9)–C(10)	1.397(3)	C(4)–C(10)–C(5)	121.63(19)
C(1')–C(6')	1.381(3)	C(9)–C(10)–C(5)	120.09(19)
C(1')–C(2')	1.400(3)	C(6')–C(1')–C(2')	117.70(19)
C(3')–O(2)	1.373(2)	C(6')–C(1')–C(3)	122.5(2)
C(3')–C(4')	1.388(3)	C(2')–C(3')–O(2)	124.79(19)
C(4')–O(3)	1.351(2)	O(2)–C(3')–C(4')	114.48(18)
C(4')–C(5')	1.377(3)	O(3)–C(4')–C(5')	118.60(19)
C(5')–H(5'A)	0.93	O(3)–C(4')–C(3')	122.9(2)
O(2)–C(13)	1.422(2)	O(2)–C(13)–H(13A)	109.5
O(3)–H(3A)	0.82	C(4')–O(3)–H(3A)	109.5

**Table 3.** Hydrogen bond geometry in **3** (Å, °).

D—H...A	d(D—H)	d(H...A)	d(D...A)	D—H...A
O(3)–H(3A)...N(1)i	0.82	1.99	2.742(2)	151.6
O(3)–H(3A)...N(2)i	0.82	2.64	3.171(2)	123.9

Symmetry codes: (i)  $x, -y+1/2, z+1/2$

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## Experimental

**Materials and Instruments.** Melting point was determined on a digital melting point apparatus (Electrothermal) and remains uncorrected. Infrared spectra were recorded on a Thermo Nicolet (Nexus 670) FT-IR spectrometer, using KBr disks.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded with a Bruker spectrometer at 300 and 75.5 MHz, respectively. The spectra were measured in  $\text{CDCl}_3$  using TMS as the internal standard.

### Synthesis of 3-(4-hydroxy-3-methoxyphenyl)-7,7-dimethyl-7,8-dihydrocinnolin-5(6H)-one (3).

To a mixture of dimedone (1 mmol) and 2-(4-hydroxy-3-methoxyphenyl)-2-oxoacetaldehyde (1 mmol) in water (5 mL), was successively added hydrazine hydrate 100% (3 mmol) at 5-8 °C. The reaction mixture was stirred for 20-40 minutes. The solid was filtered then recrystallized from ethanol to give the title compound as yellow crystals (50%), mp 127 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm): 8.24 (s, 1H, Ar), 7.91 (s, 1H, Ar), 7.57 (d,  $J = 8.4$  Hz, 1H, Ar), 7.06 (d,  $J = 8.4$  Hz, 1H, Ar), 5.96 (bs, 1H, OH), 4.02 (s, 3H,  $\text{OCH}_3$ ), 3.32 (s, 2H,  $\text{CH}_2$ ), 2.65 (s, 2H,  $\text{CH}_2$ ), 1.17 (s, 6H,  $2 \times \text{CH}_3$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm): 197.95, 159.08, 158.55, 148.03, 147.26, 127.92, 127.67, 120.41, 118.22, 114.83, 109.21, 56.15, 52.23, 43.21, 33.07, 28.23. FT-IR  $\nu_{\text{max}}$  3390, 3063, 3008, 2951, 2865, 2631, 1703, 1589, 1514, 1460, 1408, 1335, 1275, 1208, 1128, 1029, 872, 796  $\text{cm}^{-1}$ . Mass spectrum  $m/z$  (%): 298 [ $\text{M}^+$ , 7], 297 (8), 280 (17), 265 (13), 251 (32), 237 (12), 202 (11), 167 (18), 149 (49), 115 (16), 97 (24), 83 (37), 69 (73), 57 (83), 43 (100).

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