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Diverse Confirmations in the Crystal Structures of 2,3-Dihydro-2,2-dimethylquinazolin-4(1*H*)-one Derivatives

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Abstracts The 3-(propan-2-ylideneamino)-2,3-dihydro-2,2-dimethylquinazolin-4(1*H*)-one and 3-(3-nitrobenzy-lideneamino)-2,3-dihydro-2,2-dimethylquinazolin-4(1*H*)-one were synthesized and characterized by IR, ¹H NMR and HRMS. The molecular structures were further confirmed by X-ray diffraction analysis. The former **1**, C₁₃H₁₇ N₃O, is monoclinic, space group *P*2(1)/*c*, *a* = 9.056(2), *b* = 9.439(2), *c* = 14.872(3) Å, β = 133.121(12)°, *Z* = 4, *V* = 1270.9(5) Å³. The latter **2**, C₁₇H₁₆N₄O₃, is also monoclinic, space group *P*2(1)/*c*, *a* = 10.0006(2), *b* = 12.2298(3), *c* = 13.3255(3) Å, β = 96.602(2)°, *Z* = 4, *V* = 1618.97(6) Å³. It is very interesting that the pyrimidine ring in the **1** adopts a half-chair confirmation, while adapting a skew-boat one in the structure of **2**.

Introduction

Quinazolinone derivatives are an important class of molecules with physiological significance and pharmaceutical utility [1-3]. Especially for the 4(3H)-quinazolinone core, is well-known as a "privileged structure" [4, 5] for drug design, which is defined as a class of molecules that are capable of binding to multiple receptors with high affinity [6, 7]. These include anti-inflammatory [8], antihypertensive [9], anticancer [10], antitumor [11] and antibacterial activity [12]. They have recently also been evaluated as antagonists of various biological receptors, such as 5-HT_{5A} related diseases [13], calcitonin gene-related peptide [14] and vasopressin V3 receptors [15]. In this paper, we would like to report the crystal structures of 3-(propan-2-ylideneamino)-2,3-dihydro-2,2-dimethylquinazolin-4(1H)-one (1) and 3-(3-nitrobenzylideneamino)-2,3-dihydro-2, 2-dimethyl quinazolin-4(1H)-one (2), with entirely different confirmations in their pyrimidine cores, this may be indicate different potential activities in bioactive screening.

Experimental

Synthesis of 1 and 2

A dry 50 mL flask was charged with 2-aminobenzohydrazide (0.151 g, 1.0 mmol), acetone (0.232 g, 4.0 mmol) and ionic liquid of [BMIm]Br (BMIm is the abbreviation of 1-butyl-3-methylimidazolium, 2 mL). The reaction mixture was stirred at 50 °C for 10 h, and then 5 mL water was added to the mixture, and the generated yellow solid was filtered off. The crude yellow products were washed with water and purified by recrystallization from 95 % EtOH to give **1** as colorless crystals in 95 % yield, mp 249–251 °C. ¹H NMR (DMSO- d_6 , 400 MHz): $\delta_{\rm H}$ 1.37–1.50 (m, 6H, 2×CH₃), 1.75 (s, 3H, CH₃), 2.08 (s, 3H, CH₃), 6.66–6.71 (m, 2H, ArH), 6.91 (s, 1H, NH), 7.25–7.29 (m, 1H, ArH),

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7.61 (d, J = 7.6 Hz, 1H, ArH). IR (KBr): v 3262, 2998, 2981, 2972, 1629, 1586, 1518, 1488, 1464, 1438, 1382, 1349, 1264, 1189, 1165, 950, 747, 693 cm⁻¹. HRMS (ESI, m/z): Calcd for C₂₆H₃₄N₆O₂Na [2M + Na] ⁺ 485.2635, found 485.2639.

A dry 50 mL flask was charged with 2-aminobenzohydrazide (0.151 g, 1.0 mmol), 3-nitrobenzaldehyde (0.151 g, 1 mmol), and ionic liquid of [BMIm]Br (2 mL). After the reaction mixture was stirred at 0 °C for 2 h, the acetone (0.116 g, 2.0 mmol) was added to the mixture for 6 h at 50 °C. And then a small amount of water (5 mL) was added to the mixture, and the generated yellow solid was filtered off. The crude yellow products were washed with water and purified by recrystallization from 95 % EtOH to give 2 as yellow crystals in 92 % yield, mp 186–188 °C. ¹H NMR (DMSO- d_6 , 400 MHz): δ_H 1.61 (s, 6H, 2CH₃), 6.73-6.77 (m, 2H, ArH), 7.13(s, 1H, NH), 7.32-7.36 (m, 1H, ArH), 7.70 (d, J = 7.6 Hz, 1H, ArH), 7.77–7.81 (m, 1H, ArH), 8.25 (d, J = 8.0 Hz, 1H, ArH), 8.31–8.34 (m, 1H, ArH), 8.60 (s, 1H, ArH), 9.13 (s, 1H, CH). IR(KBr): v 3449, 3103, 3017, 2976, 2936, 1632, 1526, 1489, 1461, 1434, 1385,

 $Table \ 1 \ \ Crystallographic \ data \ for \ 1 \ and \ 2$

1350, 1327, 1285, 1268, 1214, 1181, 1155, 1091, 974, 943, 828, 752, 734, 693 cm⁻¹. HRMS (ESI, *m/z*): Calcd for $C_{17}H_{16}N_4O_3$ [M + Na] ⁺ 347.1120, found, 347.1144.

X-ray Analysis

A summary of the crystallographic data was given in Table 1. The structure was solved by direct method using SHELXTL [16] program and expanded using Fourier technique. The nonhydrogen atoms were refined anisotropically, the hydrogen atoms were positioned geometrically and refined as riding [C-H = 0.93–0.96 Å except for H(1) in **1** and **2**, respectively, and $U_{iso}(H) = 1.2U_{eq}(C)$]. A full-matrix least-squares refinement gave final R = 0.0406 and $\omega R = 0.0993$ (R = 0.0362 and $\omega R = 0.0876$ for **2**) with $\omega = 1/[\sigma^2$ $(F_o^2) + (0.0507P)^2 + 0.2209 P](\omega = 1/[\sigma^2(F_o^2) + (0.0418P)^2 + 0.2894P]$ for **2**), where $P = (F_o^2 + 2F_o^2)/3$.

Analysis

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a TENSOR 27

Compounds	1	2
Empirical formula	C ₁₃ H ₁₇ N ₃ O	C ₁₇ H ₁₆ N ₄ O ₃
CCDC deposit no.	832529	832530
Color/shape	Colorless/block	Yellow/block
Formula weight	231.30	324.34
Temperature	296(2) K	296(2) K
Crystal system	Monoclinic	Monoclinic
Space group	P2(1)/c	P2(1)/c
Unit cell dimensions	$a = 9.056(2) \text{ Å}, \alpha = 90^{\circ}$	$a = 10.0006(2)$ Å, $\alpha = 90^{\circ}$
	$b = 9.439(2) \text{ Å}, \beta = 133.121(12)^{\circ}$	$b = 12.2298(3) \text{ Å}, \beta = 96.602(2)^{\circ}$
	$c = 14.872(3) \text{ Å}, \gamma = 90^{\circ}$	$c = 13.3255(3)$ Å, $\gamma = 90^{\circ}$
Volume	1270.9(5) Å ³	1618.97(6) Å ³
Ζ	4	4
Density (calculated), Mg/m ³	1.209	1.331
Absorption coefficient, mm^{-1}	0.079	0.094
Diffractometer/scan	CCD area detector/ φ and ω	CCD area detector/ φ and ω
<i>F</i> (000)	496	680
Crystal size	$0.293 \times 0.257 \times 0.116 \text{ mm}$	0.271 \times 0.195 \times 0.116 mm
Theta range for data collection	2.56–25.20 °	2.05–25.20 °
Limiting indices	$-10 \le h \le 10, -17 \le k \le 17, -15 \le l \le 15$	$-11 \le h \le 11, -14 \le k \le 14, -15 \le l \le 15$
Reflections collected	15381	12422
Independent reflections	2279 [$R(int) = 0.0304$]	2900 [$R(int) = 0.0278$]
Data/restraints/parameters	2279/1/162	2900/1/224
Goodness-of-fit on F^2	1.044	1.025
Final <i>R</i> indices $[I > 2\sigma (I)]$	$R_1 = 0.0406, wR_2 = 0.0993$	$R_1 = 0.0362, wR_2 = 0.0876$
R indices (all data)	$R_1 = 0.0571, wR_2 = 0.1076$	$R_1 = 0.0532, wR_2 = 0.0979$
Largest diff. peak and hole	0.137 and $-0.167 \text{ e } \text{A}^{-3}$	0.141 and $-0.130 \text{ e } \text{A}^{-3}$

Table 2 Selected bond lengths (Å) and selected bond angles (°) for 1 and 2

Selected Bond Lengths for 1			Selected Bond Lengths for 2				
O(1)–C(1)	1.234(2)	N(3)–C(11)	1.272(2)	N(3)-C(11)	1.266(2)	N(1)-H(1)	0.86(1)
N(1)-C(3)	1.381(2)	C(1)–C(4)	1.465(2)	N(3)–N(2)	1.381(2)	C(12)–C(1)	1.464(2)
N(1)-C(2)	1.455(2)	C(2)-C(10)	1.517(2)	N(2)-C(1)	1.373(2)	C(2)-C(10)	1.518(2)
N(1)-H(1)	0.86(1)	C(2)–C(9)	1.522(3)	N(2)-C(2)	1.497(2)	C(2)–C(9)	1.524(2)
N(2)–C(1)	1.371(2)	C(11)–C(12)	1.483(3)	C(4)–C(1)	1.471(2)	C(16)–N(4)	1.471(2)
N(2)–N(3)	1.429(2)	C(11)–C(13)	1.496(2)	C(1)–O(1)	1.230(2)	O(2)–N(4)	1.214(2)
N(2)-C(2)	1.486(2)			N(1)-C(3)	1.369(2)	N(4)-O(3)	1.221(2)
				N(1)-C(2)	1.449(2)		
Selected Bond Angles for 1			Selected Bond Angles for 2				
C(3)–N(1)–C(2)	119.3(1)	N(2)-C(2)-C(10)	109.6(1)	C(11)–N(3)–N(2)	124.0(1)	C(17)–C(12)–C(11)	121.6(1)
C(3)–N(1)–H(1)	118.2(1)	N(1)-C(2)-C(9)	112.4(1)	C(1)-N(2)-N(3)	125.5(1)	C(13)–C(12)–C(11)	119.4(1)
C(2)–N(1)–H(1)	111.3(1)	N(2)-C(2)-C(9)	109.9(1)	C(1)-N(2)-C(2)	121.5(1)	N(1)-C(2)-N(2)	106.6(1)
C(1)-N(2)-N(3)	117.7(1)	C(10)-C(2)-C(9)	110.8(2)	N(3)-N(2)-C(2)	110.9(1)	N(1)-C(2)-C(10)	107.8(1)
C(1)-N(2)-C(2)	120.7(1)	N(1)-C(3)-C(4)	118.8(1)	C(5)-C(4)-C(1)	120.2(1)	N(2)-C(2)-C(10)	110.5(1)
N(3)–N(2)–C(2)	111.2(1)	N(1)-C(3)-C(8)	122.5(1)	C(3)-C(4)-C(1)	119.7(1)	N(1)-C(2)-C(9)	111.9(1)
C(11)-N(3)-N(2)	114.8(1)	C(5)-C(4)-C(1)	120.3(1)	O(1)-C(1)-N(2)	121.8(1)	N(2)-C(2)-C(9)	108.6(1)
O(1)-C(1)-N(2)	121.7(1)	C(3)–C(4)–C(1)	119.8(1)	O(1)-C(1)-C(4)	122.0(1)	C(10)-C(2)-C(9)	111.4(1)
O(1)–C(1)–C(4)	122.4(1)	N(3)-C(11)-C(12)	127.3(1)	N(2)-C(1)-C(4)	116.2(1)	C(17)-C(16)-N(4)	118.3(2)
N(2)-C(1)-C(4)	115.8(1)	N(3)-C(11)-C(13)	115.4(2)	C(3)-N(1)-C(2)	118.8(1)	C(15)-C(16)-N(4)	119.4(2)
N(1)-C(2)-N(2)	105.5(1)	C(12)-C(11)-C(13)	117.3(2)	C(3)–N(1)–H(1)	116.4(1)	N(3)-C(11)-C(12)	118.9(1)
N(1)-C(2)-C(10)	108.6(1)			C(2)-N(1)-H(1)	112.8(1)	O(2)-N(4)-O(3)	123.5(2)
				N(1)-C(3)-C(4)	118.3(1)	O(2)-N(4)-C(16)	119.0(2)
				N(1)-C(3)-C(8)	122.8(1)	O(3)-N(4)-C(16)	117.6(2)



Fig. 1 The molecular structures of 1 (a) and 2 (b) showing 30% probability displacement ellipsoids

spectrometer in KBr pellet. ¹H NMR spectra were obtained from solution in DMSO-*d*₆ with Me₄Si as internal standard using an Inova-400 spectrometer. HRMS analyses were carried out using a Bruker-micro-TOF-Q-MS analyzer. X-ray diffraction was performed on a Bruker APEX-II area detector diffractometer.

Results and Discussion

In the infrared spectrography of **1**, it was observed a sharp band at 3262 cm⁻¹ (3449 cm⁻¹ for **2**) for the amino group. The carbonyl groups in **1** and **2** exhibit strong bands at 1629 and 1632 cm⁻¹, respectively. In the ¹H NMR



Fig. 2 The packing arrangement in a unit cell of 1 (a) and 2 (b)



$(D-\mathrm{H}\cdots A)$	<i>D</i> –Н (Å)	H…A (Å)	<i>D</i> …A (Å)	<i>D</i> −H··· <i>A</i> (°)
$N(1)-H(1)\cdots O(1)#1$ (1) $N(1)-H(1)\cdots O(1)#2$ (2)	0.86(1) 0.86(1)	2.08(1) 2.06(2)	2.934 (2) 2.914(2)	168(2) 172(2)
$\frac{1}{2} = \frac{1}{2} = \frac{1}$				

spectrum of 1, a singlet is identified as hydrogen on the amino group at 6.91 ppm (7.13 ppm for 2). The other data in IR, ¹H NMR and HRMS are in good agreement with their structures.

The selected bond lengths and bond angles of 1 and 2 are given in Table 2. The structures of 1 and 2, packing arrangement in a unit cell of 1 and 2 are shown in Figs. 1a,b, and Fig. 2a, b respectively. In 1. The atoms N(1)/N(2)/C(1)-C(4) form a new pyrimidine ring, among these atoms, N(1)/N(2)/C(1)/C(3) and C(4) are coplanar, while the atom C(2) deviating from the defined plane by 0.581(2) Å. These data indicate that the above-mentioned pyrimidine ring adopts a half-chair confirmation. It is very interesting that in the structure of 2, the new pyrimidine ring adopts a skew-boat confirmation. The atoms N(1)/C(3)/C(1) and C(4) are on a plane, the atoms C(2) and N(2) deviate from the defined by 0.223(3) and 0.703(3) Å, respectively. The basal plane nearly parallel to the adjacent benzene ring (C(3)-C(8)), forming a dihedral angle of 3.4 (1)° (3.6 (1)° for 1).

The X-ray determination indicates that there are the same classical hydrogen bonds $N-H\cdots O$ in 1 and 2. The hydrogen bonds data are listed in Table 3. The classical hydrogen bonds of $N-H\cdots O$ in 1 and 2 all link the

molecules forming one-dimensional chain structures along b and c, respectively (Fig. 2).

(b)

Supplementary Material

Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-832529 and CCDC-832530. Copies of available material can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-(0)-1223-336033 or e-mail: deposit@ccdc. cam.ac.uk).

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