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Synthesis and crystal structure of 7,7-dimethyl-2,4-diphenyl-5-oxo-1,4,5,6,7,8-hexahydroquinolin

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The 7,7-dimethyl-2,4-diphenyl-5-oxo-1,4,5,6,7,8-hexahydroquinolin was synthesized and the compound was identified by IR, ^{1}H NMR, elemental analysis and X-ray crystallography. It crystallized in the triclinic space group $P\bar{1}$, with $a = 7.129(2)$ Å, $b = 10.514(3)$ Å, $c = 13.040(3)$ Å, $\alpha = 76.58(2)^\circ$, $\beta = 88.97(2)^\circ$, $\gamma = 79.24(2)^\circ$, and $D_{\mathrm{calc}} = 1.172$ g cm^{-3} for $Z = 2$. X-ray analysis revealed that the atoms C(2), C(3), C(4), C(10), C(9), and N form a six-membered ring that adopts a boat conformation, and another six-membered ring (C(10)–C(9)–C(8)–C(7)–C(6)–C(5)) adopts a half-chair conformation. In addition, there is an intermolecular hydrogen bond (N–H0 $\cdots$ O) in the product molecule.

KEY WORDS: Crystal structure; quinolin; synthesis.

Introduction

1,4-Dihydropyridines (1,4-DHPS) are well-known compounds because of their pharmacological profile as calcium channel modulators.[1] The chemical modifications carried on the DHP ring resulting in the presence of different substituents[2] or heteroatoms[3] have allowed the expansion of the structure–activity relationship and afforded some insight into the molecular interactions at the receptor level. We report here the crystal structure of 7,7-dimethyl-2,4-diphenyl-5-oxo-1,4,5,6,7,8-hexahydroquinolin (**3**).

Experimental

All chemicals were of analytical reagents grade and were used directly without further purification.

Synthesis of 7,7-dimethyl-2,4-diphenyl-5-oxo-1,4,5,6,7,8-hexahydroquinolin

To a solution of 1,3-diphenyl-2-propen-1-one (**1** (2 mmol) in DMF (10 mL), 5,5-dimethyl-1, 3-cyclohexanedione (**2**) (2.5 mmol) and ammonium acetate (5 mmol) were added. The mixture was stirred at 80°C for 1–2 h, and then cooled to room temperature. The mixture was poured into 200-mL water. The yellow solid was filtered off and washed with water. Recrystallization from 95% EtOH gave yellow crystals of **3** in 85% yield. M.p. 206–208°C; IR (KBr, cm^{-1}): 3260, 3030, 2990, 1660, 1630, 1590, 1490, 1450, 770, 760, 695; ^{1}H NMR (DMSO-d_6, δ, ppm): 0.96 (3H, s, CH_3), 1.04 (3H, s, CH_3), 2.00 (1H, d, $J = 16.0$ Hz, C^8—H), 2.18 (1H, d, $J = 16.0$ Hz, C^8—H), 2.48 (2H, s, CH_2), 4.57 (1H, d, $J = 5.6$ Hz, C^4—H), 5.22 (1H, dd, $J = 2.0$ Hz, $J' = 3.6$ Hz, C^3—H), 7.09–7.50 (10H, m, ArH), 8.63 (1H, s, NH); Elemental analysis: found (%): C, 83.93, H, 6.86, N, 4.03; Calcd. for $C_{23}H_{23}NO$: C, 83.85, H, 7.04, N, 4.25.

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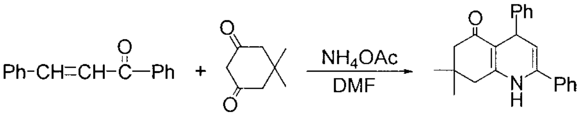

1 **2** **3**

X-ray analysis

A summary of the crystallographic data is given in Table 1. A single crystal with dimensions of 0.44 × 0.38 × 0.32 mm was mounted on a Siemens P4 diffractometer with graphite monochromated Mo $K\alpha$ ($\lambda = 0.71073$ Å) radiation.

The data were collected at the temperature of 295(2) K. Using the ω–2θ scan technique ($3.22^\circ < 2\theta < 50.00^\circ$), 3668 independent reflections were collected, of which 3138 reflections with $I > 2\sigma(I)$ were observed. Corrections for Lp factors were applied. The structure was solved by direct methods using SHELXS97 program and expanded using Fourier technique. The non-hydrogen atoms were refined anisotropically. The hydrogen atoms were determined with theoretical calculations and refined isotropically. A full-matrix least-squares refinement gave final $R = 0.0430$ and $Rw = 0.0982$ $[w = 1/(\sigma^2(F_0^2) + (0.0578P)^2)$, where $P = (F_0^2 + 2F_c{}^2)/3]$. The goodness of fit indicator is 0.868. The maximum peak in the final difference Fourier maps is 0.150 e/Å^3 and the minimum peak is −0.151 e/Å^3. In the final circle refinement the largest parameter shift $(\Delta/\sigma)_{\max}$ is 0.000.

Table 1. Crystallographic Data for **3**

Empirical formula	$C_{23}H_{23}NO$
CCDC deposit no.	CCDC-1003/6146
Color/shape	Pale yellow/block
Formula weight	329.42
Temperature, K	295(2)
Crystal system	Triclinic
Space group	$P\bar{1}$
Unit cell dimensions	$a = 7.129(2)$ Å
	$b = 10.514(3)$ Å
	$c = 13.040(3)$ Å
	$\alpha = 76.58(2)^\circ$
	$\beta = 88.97(2)^\circ$
	$\gamma = 79.24(2)^\circ$
Volume, Å^3	933.7(4)
Z	2
Density (calculated), Mg/m^3	1.172
Absorption coefficient, mm^{-1}	0.071
Diffractometer/scan	Siemens P4/ω–2θ
$F(000)$	352
Crystal size, mm	0.44 × 0.38 × 0.32
θ range for data collection, deg	1.61–25.00
Limiting indices	$0 \le h \le 8$, $-11 \le k \le 12$, $-15 \le l \le 15$
Reflections collected	3668
Independent reflections	3265 [$R_{(\mathrm{int})} = 0.0134$]
Data/restraints/parameters	3265/0/229
Goodness of fit on F^2	0.868
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0430$, $wR_2 = 0.0982$
R indices (all data)	$R_1 = 0.0777$, $wR_2 = 0.1086$
Extinction coefficient	0.027(3)
Largest diff. peak and hole, e/Å^3	0.150 and −0.151

Analysis

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on an FT IR-8101 spectrometer in KBr. ^{1}H NMR spectra were obtained for solution in DMSO-d_6 with Me_4Si as internal standard, using an Inova-400 spectrometer. Elemental analyses were carried out using Carlo Erba 1110 analyzer. X-ray diffraction was measured on a Siemens P4 diffractometer.

Results and discussion

X-ray analysis

Atomic coordinates and equivalent isotropic displacement parameters are listed in Table 2. Interatomic distances and bond angles are given in Table 3. Figure 1 shows the molecular structure of compound **3**. In the product molecule, the atoms C(2), C(3), C(4), C(10), C(9), and N form a six-membered ring, with the interatomic distances 1.336(2) Å for C(2)—C(3) and 1.365(2) Å for C(10)—C(9), which show that they are C=C double bonds. X-ray analysis reveals that the pyridine ring adopts a boat conformation: the

Table 2. Atomic Coordinates (10^4) and Equivalent Isotropic Displacement Parameters (10^3 Å^2)

Atom	*x*	*y*	*z*	*U*(eq)
O	6506(2)	5031(2)	7243(1)	65(1)
N	359(2)	4272(2)	8111(1)	45(1)
C(1)	4843(3)	2026(2)	7666(1)	42(1)
C(2)	1035(2)	3255(2)	8995(1)	40(1)
C(3)	2901(3)	2739(2)	9105(1)	43(1)
C(4)	4304(2)	3115(2)	8275(1)	42(1)
C(5)	4758(2)	5332(2)	7068(1)	43(1)
C(6)	3928(3)	6658(2)	6350(2)	48(1)
C(7)	1948(3)	6760(2)	5875(2)	47(1)
C(8)	677(2)	6232(2)	6765(2)	48(1)
C(9)	1570(2)	4944(2)	7481(1)	38(1)
C(10)	3493(2)	4473(2)	7575(1)	39(1)
C(11)	2101(3)	5967(2)	5028(2)	70(1)
C(12)	1095(3)	8215(2)	5378(2)	75(1)
C(13)	3600(3)	1834(2)	6944(2)	64(1)
C(14)	4079(4)	803(2)	6434(2)	74(1)
C(15)	5783(4)	−50(2)	6633(2)	67(1)
C(16)	7028(4)	125(2)	7341(2)	75(1)
C(17)	6566(3)	1152(2)	7852(2)	63(1)
C(18)	−423(3)	2874(2)	9769(1)	40(1)
C(19)	−1951(3)	3813(2)	9976(2)	48(1)
C(20)	−3323(3)	3425(2)	10678(2)	57(1)
C(21)	−3214(3)	2113(3)	11180(2)	66(1)
C(22)	−1687(4)	1181(2)	11007(2)	70(1)
C(23)	−308(3)	1561(2)	10307(2)	59(1)

Table 3. Selected Bond Lengths (Å) and Selected Bond Angles (deg)

Bond distances			
O—C(5)	1.239(2)	C(10)—C(5)	1.439(2)
N—C(9)	1.361(2)	C(9)—C(8)	1.492(2)
N—C(2)	1.400(2)	C(8)—C(7)	1.525(2)
C(2)—C(3)	1.336(2)	C(7)—C(11)	1.521(3)
C(2)—C(18)	1.480(2)	C(7)—C(6)	1.527(3)
C(3)—C(4)	1.496(3)	C(7)—C(12)	1.529(3)
C(4)—C(10)	1.521(2)	C(6)—C(5)	1.508(3)
C(4)—C(1)	1.527(2)	C(1)—C(17)	1.378(3)
C(10)—C(9)	1.365(2)		
Bond angles			
C(9)—N—C(2)	121.34(15)	C(11)—C(7)—C(8)	111.52(16)
C(3)—C(2)—N	119.45(17)	C(11)—C(7)—C(6)	109.67(16)
C(3)—C(2)—C(18)	124.98(17)	C(8)—C(7)—C(6)	107.93(15)
N—C(2)—C(18)	115.53(15)	C(11)—C(7)—C(12)	109.03(18)
C(2)—C(3)—C(4)	122.84(17)	C(8)—C(7)—C(12)	108.79(16)
C(3)—C(4)—C(10)	109.26(15)	C(6)—C(7)—C(12)	109.89(16)
C(3)—C(4)—C(1)	110.49(15)	C(5)—C(6)—C(7)	115.51(15)
C(10)—C(4)—C(1)	113.48(15)	O—C(5)—C(10)	121.42(18)
C(9)—C(10)—C(5)	118.73(16)	O—C(5)—C(6)	119.28(17)
C(9)—C(10)—C(4)	121.00(16)	C(10)—C(5)—C(6)	119.22(16)
C(5)—C(10)—C(4)	120.07(15)	C(13)—C(1)—C(4)	121.70(17)
N—C(9)—C(10)	120.10(16)	C(17)—C(1)—C(4)	121.27(17)
N—C(9)—C(8)	116.06(15)	C(23)—C(18)—C(2)	120.46(17)
C(10)—C(9)—C(8)	123.70(16)	C(19)—C(18)—C(2)	121.54(17)
C(9)—C(8)—C(7)	114.24(15)		

atoms C(2), C(3), C(10), and C(9) are on one plane (plane 1, the deviations from each atom to the plane are −0.0079, 0.0077, −0.0076, and 0.0077 Å, respectively), while the atom N is away from the plane (0.1373 Å) and the atom C(4) is also away from the plane (0.2941 Å). The dihedral angles between plane 1 and phenyl ring (plane 2, C(1)—C(13)∼C(17)), and between plane 1 phenyl ring (plane 3, C(18)∼C(23)) are 90.87 and 33.39°, respectively. In another six-membered ring (C(5)∼C(10)), the atoms C(10), C(9), C(8), C(6), and C(5) are on another plane (plane 4, mean deviation of 0.0219 Å from the plane), while the atom C(7) is away from the plane (0.6269 Å), which indicates that the ring adopts a half-chair conformation. The deviation from the atom C(8) (0.0151 Å) to this plane is larger than that from the atom C(6) (0.0026 Å) (the torsion angles show the same information: C(9)—C(10)—C(5)—C(6) = −6.9° and C(5)—C(10)—C(9)—C(8) = 8.3°), and so the protons at C(8) are in the different chemical surroundings, which display an AB pattern. The positions of the two methyl groups are different: one methyl (C(11)—CH_3) (the atom C(11) is away from the plane (2.1376 Å)) is in the pseudoaxial site while another methyl (C(12)—CH_3) is in the pseudoequatorial site (the atom C(12) is away from the plane (0.3059 Å). The dihedral angles between plane 4 and plane 1, plane 2, plane 3 are 15.13, 75.75, and 32.83°, respectively. In addition, because of the existence of conjugate system, the distance of C(10)—C(9) (1.365(2) Å) is significantly longer than the normal C=C double bonds;[4] there is corresponding shortening of C(9)—N (1.361(2) Å) and C(2)—N (1.400(2) Å) relative to the normal C(sp^2)—N (1.426 Å) bond,[5] which are in the range of the structures of other similar compounds.[6–8] The distance between atoms N and O, between atoms N

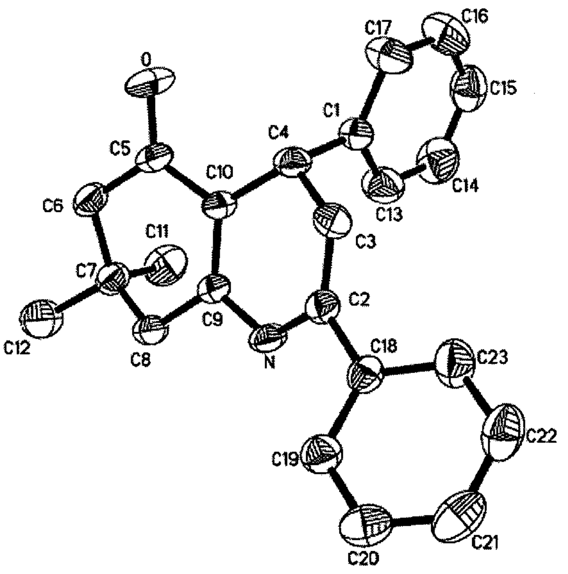

Fig. 1. Structure of compound **3** (50% probability ellipsoids).

and H0 (x: -0.0847, y: 0.4476, z: 0.7963), between atoms O and H0 are 2.887(2), 0.86, and 2.04 Å, respectively, and the angle of N—H0 $\cdots$ O is 166.1°, which indicates the existence of intermolecular hydrogen bond N—H $\cdots$ O (symmetry operation: $-1 + x, y, z$). The packing arrangement in a unit cell of the title molecule is shown in Fig. 2: they are dimers. The molecules are held together by the hydrogen bond.

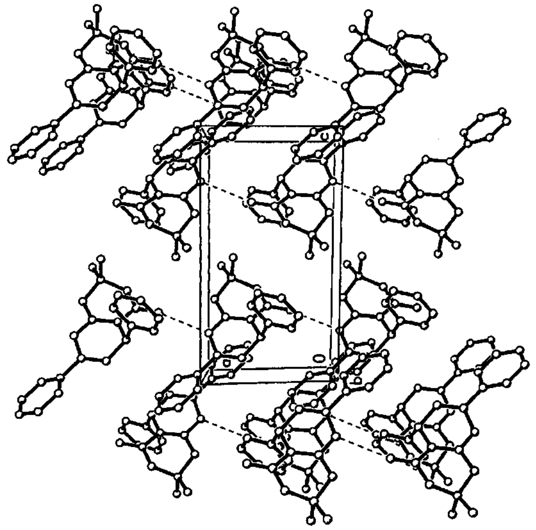

Fig. 2. The packing arrangement in a unit cell of the title molecule.

Spectroscopic analysis

In the infrared spectroscopy of the title compound, the infrared absorption (3260(s) cm^{-1}) is assigned to N—H stretching vibration and the very strong absorption at 1660(vs) cm^{-1} is assigned to $\nu(C{=}O)$. The ^1H NMR data exhibit that the two methyl groups have different chemical shifts (0.96, 1.04 ppm): one methyl ($C(11){-}CH_3$) is in the pseudoaxial site while another methyl ($C(12){-}CH_3$) is in the pseudoequatorial site in the X-ray analysis. The ^1H NMR is partially assigned because of their different shielding degree and coupling constants.

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