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Crystal and Molecular Structures of Atropisomeric *N*-Aryl-1,2,3,4-tetrahydro-3,3-dimethyl-2,4-quinolinediones

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ABSTRACT: *The crystal structures of N-aryl-1,2,3,4-tetrahydro-3,3-dimethyl-2,4-quinolinediones bearing methoxy- (**1**), methyl- (**2**), and chloro- (**3**) substituents in 2′-position of the phenyl ring have been determined by X-ray crystal structure analysis. The heterocyclic ring in **1–3** adopts an envelope conformation, with the smallest ring puckering in the ortho-chloro derivative **3**. The N-aryl ring is almost perpendicular with respect to the quinoline-2,4-dione ring. The corresponding dihedral angle values are 83.2(1)°, 80.0(9)°, and 83.4(2)° in **1**, **2** and **3**, respectively. The hydrogen bond of C—H···O type joins the molecules of the ortho-methoxy derivative **1** into dimers. The supramolecular structure also contains two C—H···π interactions that link the hydrogen-bonded dimers into sheets. In ortho-methyl derivative **2**, one C—H···π interaction generates infinite chains, whereas two C—H···O hydrogen bonds and three C—H···π interactions in the ortho-chloro derivative **3** form three-dimensional framework.* Heteroatom Chem 19:325–331, 2008; DOI 10.1002/hc.20436

INTRODUCTION

This work is related to our studies on separation of enantiomers (*P*) and (*M*) and the determination of barriers to racemization of the chiral *N*-aryl-2(1*H*)-quinolones [1] and *N*-aryl-1,2,3,4-tetrahydro-3,3-dimethyl-2,4-quinolinediones [2]. There are two possible transition states for rotation about the C(sp^2)—N(sp^2) bond of *N*-aryl-quinoline-2,4-diones: the ortho-aryl substituent passing either near the carbonyl group or the benzo ring (cf. Scheme 1). The preferred pathway, corresponding to less steric hindrance and, accordingly, to lower free enthalpy of activation, is that in which the bulky ortho-substituent of the aryl ring passes the carbonyl group rather than the benzo ring. This mechanism has been corroborated by molecular-mechanics calculations for the ground and possible transition states of the closely related *N*-aryl-2(1*H*)-quinolones, having the same sterical arrangement around the C—N bond [3].

The present study deals with the molecular and crystal structures of atropisomeric *N*-aryl-quinoline-

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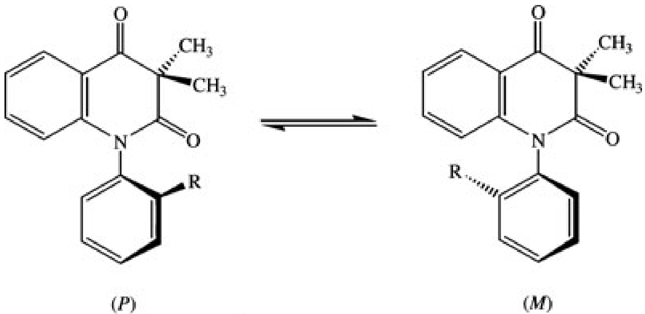


	(1)	(2)	(3)
R	OCH_3	CH_3	Cl

SCHEME 1 (*P*) and (*M*) enantiomers of atropisomeric *N*-aryl-1,2,3,4-tetrahydro-3,3-dimethyl-2,4-quinolinediones.

2,4-diones **1–3**, and it was undertaken primarily to determine their exact stereostructures, particularly deviation from the planarity of this molecules in the ground state and to compare those structural data with barriers to racemization (cf. Scheme 1). Besides, since the formation of identical packing motifs can be expected for the structures with such small differences in their surface, that is, they can exhibit isostructurality or homostructurality [4,5], we analyzed also their supramolecular assembling. Our special attention was directed toward the crystal structures of the compounds **2** and **3**, since the closeness of the van der Waals radii of chlorine and methyl group permits the isostructurality [4].

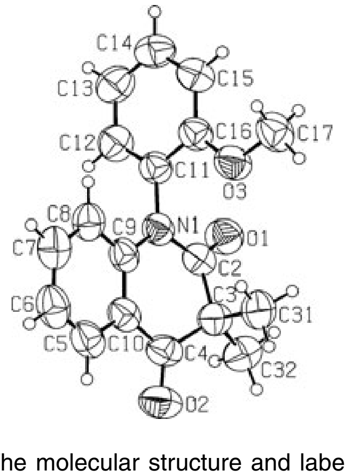


FIGURE 1 The molecular structure and labeling of **1**. Displacement ellipsoids are drawn at the 40% probability level, and hydrogen atoms are shown as small spheres of arbitrary radii.

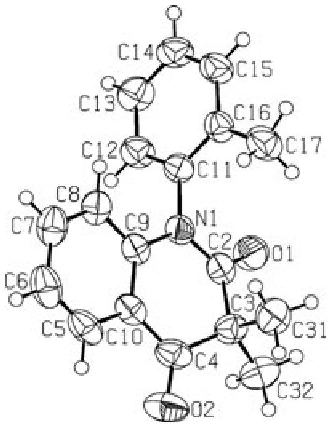


FIGURE 2 The molecular structure and labeling of **2**. Displacement ellipsoids are drawn at the 50% probability level, and hydrogen atoms are shown as small spheres of arbitrary radii.

EXPERIMENTAL

Preparation of N-Aryl-quinoline-2,4-diones **1–3**

The synthesis of the racemic compounds **1–3** has been described previously [2]. The single crystals were obtained at room temperature by slow evaporation of a very diluted ethanol–water solution (96:4, v/v).

X-Ray Crystal Structure Determination

For compound **1**, the intensities were collected at 295 K on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromated Mo K_α radiation. The intensities for **2** and **3** were collected at 295 K on a Philips PW1100 diffractometer updated by Stoe & Cie [6,7] with graphite-monochromated Mo K_α radiation for **2** and Cu K_α radiation for **3**. The intensities

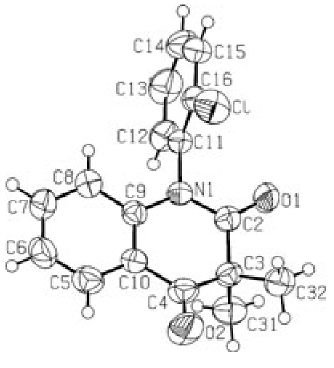


FIGURE 3 The molecular structure and labeling of **3**. Displacement ellipsoids are drawn at the 50% probability level, and hydrogen atoms are shown as small spheres of arbitrary radii.

TABLE 1 Crystal Data and Summary of Data Collection and Refinement for **1–3**

Compound	**1**	**2**	**3**
Formula	$C_{18}H_{17}NO_3$	$C_{18}H_{17}NO_2$	$C_{17}H_{14}ClNO_2$
Formula weight	295.33	279.33	299.74
Temperature (K)	293(2)	293(2)	293(2)
Radiation (Å)	0.71073 (Mo K_α)	0.71073 (Mo K_α)	1.54178 (Cu K_α)
Crystal size (mm)	0.27 × 0.20 × 0.13	0.45 × 0.27 × 0.08	0.30 × 0.15 × 0.12
Crystal color, shape	Colorless, prismatic		
Crystal system, space group	Monoclinic, $P2_1/c$ (No. 14)		
Unit cell dimensions			
a (Å)	13.3865(13)	12.985(5)	6.236(1)
b (Å)	15.741(2)	15.649(4)	20.914(2)
c (Å)	7.3405(5)	7.406(2)	12.549(2)
β (°)	101.970(6)	104.79(2)	115.79(1)
V (Å^3)	1513.1(3)	1455.1(8)	1473.6(4)
Z	4	4	4
$D_{\text{calc.}}$ (g cm^{-3})	1.296	1.275	1.351
Absorption coefficient μ (mm^{-1})	0.088	0.083	2.323
$F(000)$	624	592	624
Scan-mode	$\theta/2\theta$	ω/θ	$\omega/2\theta$
θ Range for data collection (°)	3.92–27.92	2.08–28.00	4.23–63.21
Index ranges	$-17 \leq h \leq 16$	$0 \leq h \leq 17$	$-7 \leq h \leq 7$
	$0 \leq k \leq 19$	$0 \leq k \leq 20$	$-24 \leq k \leq 0$
	$0 \leq l \leq 9$	$-9 \leq l \leq 9$	$-7 \leq l \leq 14$
Collected reflections	2217	3979	2624
Independent reflections/$R_{int.}$	2015/0.0624	3498/0.0909	2396/0.0442
Reflection number $I \geq 2\sigma(I)$	1580	1454	1280
Data/restraints/parameters	2015/0/202	3498/0/193	2396/0/192
Weighting parameters a, b^a	0.1257, 0.0000	0.0810, 0.0000	0.1007, 0.0000
Goodness-of-fit on F^2	0.957	0.834	0.911
$R\,[I \geq 2\sigma(I)]$	0.0704	0.0490	0.0502
$wR\,[I \geq 2\sigma(I)]$	0.1636	0.1245	0.1359
Max./min. electron density (e Å^{-3})	0.279/−0.235	0.254/−0.215	0.370/−0.345

^{a}w $= 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$, where $P = (F_o^2 + 2F_c^2)/3$.

were corrected for Lorentz and polarization effects. Crystal data and details of data collection and refinement are listed in Table 1.

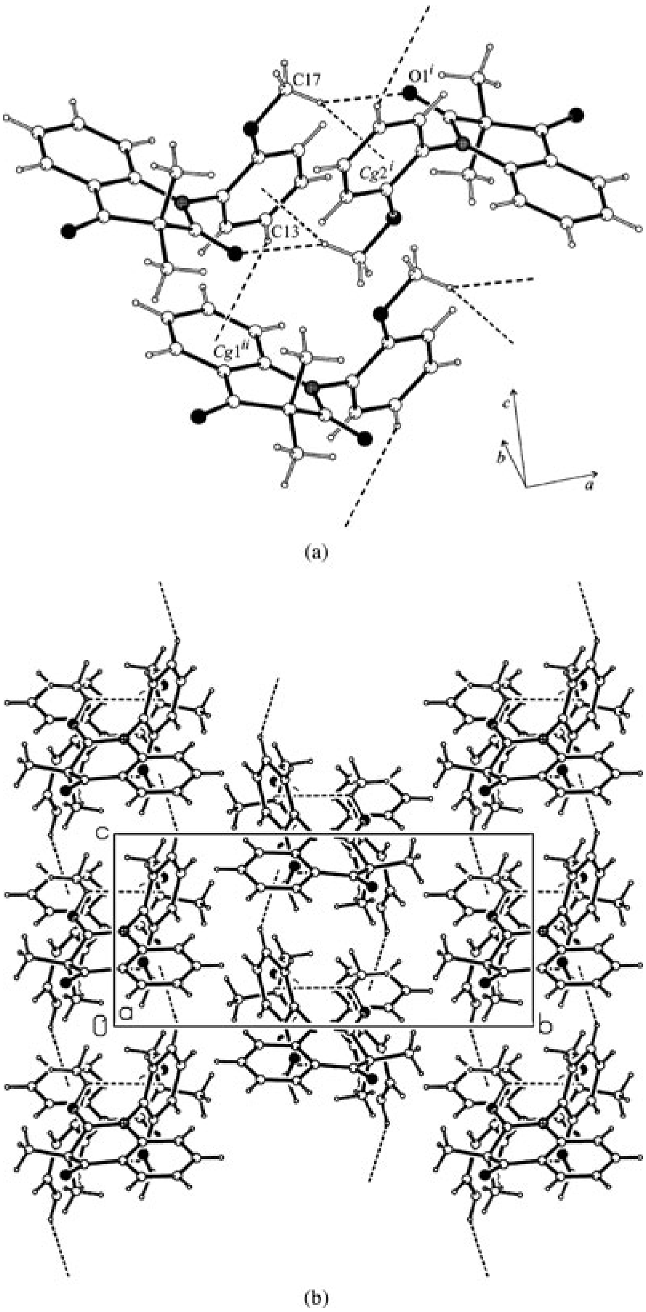
The crystal structures were solved by direct methods. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares calculations based on F^2. All hydrogen atoms were included in calculated positions as riding atoms, with C—H distances of 0.93 Å for aromatic and 0.96 Å for methyl hydrogen atoms. Programs used for structure solution, refinement, and analysis include SHELXS97 [8], SHELXL97 [9], and PLATON [10]. The molecular and crystal structure drawings were prepared by PLATON program [10]. CCDC 266435–266437 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

RESULTS AND DISCUSSION

Molecular Structures

N-aryl-quinoline-2,4-diones **1–3** crystallize in the same space group, $P2_1/c$ (Table 1). Their molecular structures with the atom-numbering scheme are shown in Figs. 1–3, and selected bond lengths and angles are given in Table 2.

The molecules **1–3** consist of two ring systems, an aryl ring attached at the N1 atom of the quinoline-2,4-dione ring. The *N*-aryl rings and the benzo moieties of the quinoline-2,4-dione rings are almost planar in all structures. The largest deviation of one of the ring atoms from the rings mean plane in **1–3** is 0.016(3) Å for the C9 atom in the benzo ring of **3**. On the other hand, the heterocyclic ring (N1/C2/C3/C4/C10/C9) is puckered and adopts an envelope conformation. The C3 atom is disposed of the mean plane of the other ring atoms by 0.451(2) and 0.431(2) Å in **1** and **2**, respectively. The puckering is considerably smaller in **3** as illustrated by the C3



(a)

(b)

FIGURE 4 (a) Part of the crystal structure of **1**, showing the C17—H17B···O1^i hydrogen bond that forms $R_2^2(16)$ rings, as well as the C13—H13···*Cg*1^{ii} and C17—H17B···*Cg*2^i interactions (*Cg*1 and *Cg*2 are the C5–C10 and C11–C16 ring centroids). Hydrogen bond and C—H···π interactions are indicated by dashed lines, and the unit-cell box has been omitted for clarity. Symmetry codes: (*i*) $-x + 1, -y + 1, -z + 2$; (*ii*) $x, y, z - 1$. (b) A crystal packing diagram of **1**, viewed along the *a* axis, showing sheets generated by C—H···O hydrogen bond and C—H···π interactions. Hydrogen bond and C—H···π interactions are indicated by dashed lines.

atom displacement of 0.224(3) Å. Accordingly, the bond angle C2–C3–C4 in **1** and **2** is smaller than in **3** (Table 2). The other bond lengths and angles in **1–3** are very similar, and they agree with the corresponding ones in quinoline-2,4-diones [11,12].

The sum of the bond angles around the N1 atom is nearly 360° in all structures (Table 2), indicating that the nitrogen atom possesses a planar sp^2 arrangement. However, the aryl ring in **2** and **3** is slightly out of the plane of the quinoline-2,4-dione ring. The dihedral angle between the bond line N1–C11 and the mean plane of the heterocyclic-ring atoms that lie in the same plane (N1/C2/C4/C9/C10) is 6.1(1) and 4.7(2)° in **2** and **3**, respectively. The corresponding dihedral angle value in **1** is 0.5(2)°. Furthermore, the aryl C11–C16 ring is almost perpendicular with respect to the quinoline-2,4-dione ring; the dihedral angle between the mean planes of the N1/C2/C4/C9/C10 atoms and the aryl ring amounts to 83.2(1)°, 80.0(1)°, and 83.4(2)° in **1, 2** and **3**, respectively.

Comparison of Structural Data with Barriers to Racemization

The $\Delta G^{\neq}$ value for restricted rotation about the C—N bond is slightly higher for the ortho-methyl derivative **2** [(0.8 kJ mol^{-1})] than the ortho-chloro derivative **3** at practically the same temperatures [2]. Thus, the greater C11—C16—C17 bond angle in **2** (Table 2) with respect to the corresponding one in **3** [(C11–C16–Cl)] is a consequence of greater steric hindrance between the carbonyl and methyl groups in **2** than the carbonyl group and chlorine atom in **3**. This is also corroborated with the slightly higher dihedral angle between the mean plane of the C11—C17 atoms and the plane of the N1/C2/O1 atoms in **2** [86.7(2)°] with respect to the angle between the mean plane of the C11–C16/Cl atoms and the plane of the N1/C2/O1 atoms in **3** [82.4(4)°].

Crystal Structures

The molecules of **1** and **3** are joined by intermolecular hydrogen bonds of C—H···O type [13,14], and in both structures a carbonyl oxygen O1 atom participates as a proton acceptor (Table 3). The supramolecular aggregation of **1** and **3** is augmented by weak C—H···π interactions [15,16]. In **2**, the molecules are linked only by one C—H···π interaction (Table 3).

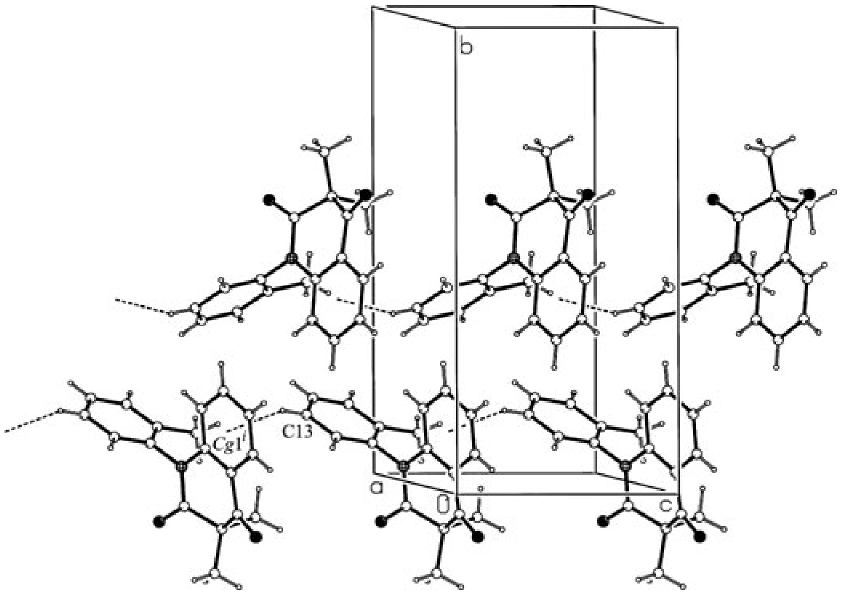


FIGURE 5 A crystal-packing diagram of **2**, showing the C13—H13···*Cg*1^i interaction (*Cg*1 is the C5–C10 ring centroid), which forms infinite chains parallel to the *c* axis. C—H···π interaction is indicated by dashed lines. Symmetry code: (*i*) *x*, *y*, *z* − 1.

In **1**, the pairs of C17···O1 hydrogen bond connect the molecules into dimers (Fig. 4a), thus forming 16-membered rings defined by the graph-set notation as $R_2^2(16)$ [17]. The geometry centers of the rings coincide with the crystallographic center of inversion. The same methyl-group hydrogen atom, H17B, participates in the C—H···π interaction (Table 3), in which the aryl C11–C16 ring of the same neighboring molecule is involved (C17—H17B···*Cg*2; Fig. 4a). The second C—H···π interaction, C13—H13···*Cg*1, links the hydrogen-bonded dimers into sheets (Fig. 4b).

Thus, in **2**, the position of the aryl-ring hydrogen atom H13 with respect to the benzo ring in adjacent molecule enables the C—H···π interaction that links the molecules into infinite chains parallel to the *c* axis (Fig. 5; Table 3).

The C8···O1 hydrogen bond in **3** forms a *C*(6) [17] chain motif, as well as C15···O2 hydrogen bond that links the molecules parallel to the *b* axis (Fig. 6a). The combination of these two chain motifs forms $R_4^4(26)$ rings and leads to a (4,4) net [18]. In addition, three C—H···π interactions (Table 3) link hydrogen-bonded nets into three-dimensional framework (Fig. 6b).

TABLE 2 Selected Bond Lengths (Å) and Angles (°) for **1–3**

Bond Lengths	**1**	**2**	**3**	*Bond Angles*	**1**	**2**	**3**
N1—C2	1.380(3)	1.377(2)	1.387(4)	C2—N1—C11	116.6(2)	117.5(1)	115.7(2)
N1—C9	1.411(3)	1.419(2)	1.402(3)	C9—N1—C11	120.0(2)	119.3(1)	120.0(2)
N1—C11	1.438(3)	1.447(2)	1.442(3)	C2—N1—C9	123.0(2)	122.9(1)	124.1(2)
C2—O1	1.211(3)	1.212(2)	1.214(3)	N1—C2—O1	120.7(2)	120.8(2)	120.4(3)
C2—C3	1.521(4)	1.528(2)	1.525(4)	N1—C2—C3	117.6(2)	117.5(2)	117.9(2)
C3—C31	1.559(4)	1.553(2)	1.552(4)	O1—C2—C3	121.5(2)	121.6(2)	121.6(3)
C3—C32	1.518(4)	1.518(3)	1.528(4)	C2—C3—C4	112.8(2)	112.6(1)	115.9(2)
C3—C4	1.521(4)	1.522(3)	1.503(4)	O2—C4—C3	121.2(3)	121.1(2)	120.8(3)
C4—O2	1.212(3)	1.219(2)	1.209(3)	C3—C4—C10	115.9(2)	116.5(2)	117.5(2)
C4—C10	1.472(4)	1.466(3)	1.481(4)	O2—C4—C10	122.7(3)	122.2(2)	121.6(3)
C9—C10	1.398(4)	1.400(2)	1.384(4)	C4—C10—C9	120.1(2)	120.9(2)	120.4(3)
C16—O3	1.357(3)	–	–	C10—C9—N1	120.3(2)	120.0(2)	121.1(3)
O3—C17	1.410(4)	–	–	C11—C16—O3	115.2(2)	–	–
C16—C17	–	1.497(3)	–	C16—O3—C17	119.1(2)	–	–
C16—Cl	–	–	1.721(3)	C11—C16—C17	–	122.2(2)	–
				C11—C16—Cl	–	–	119.5(2)

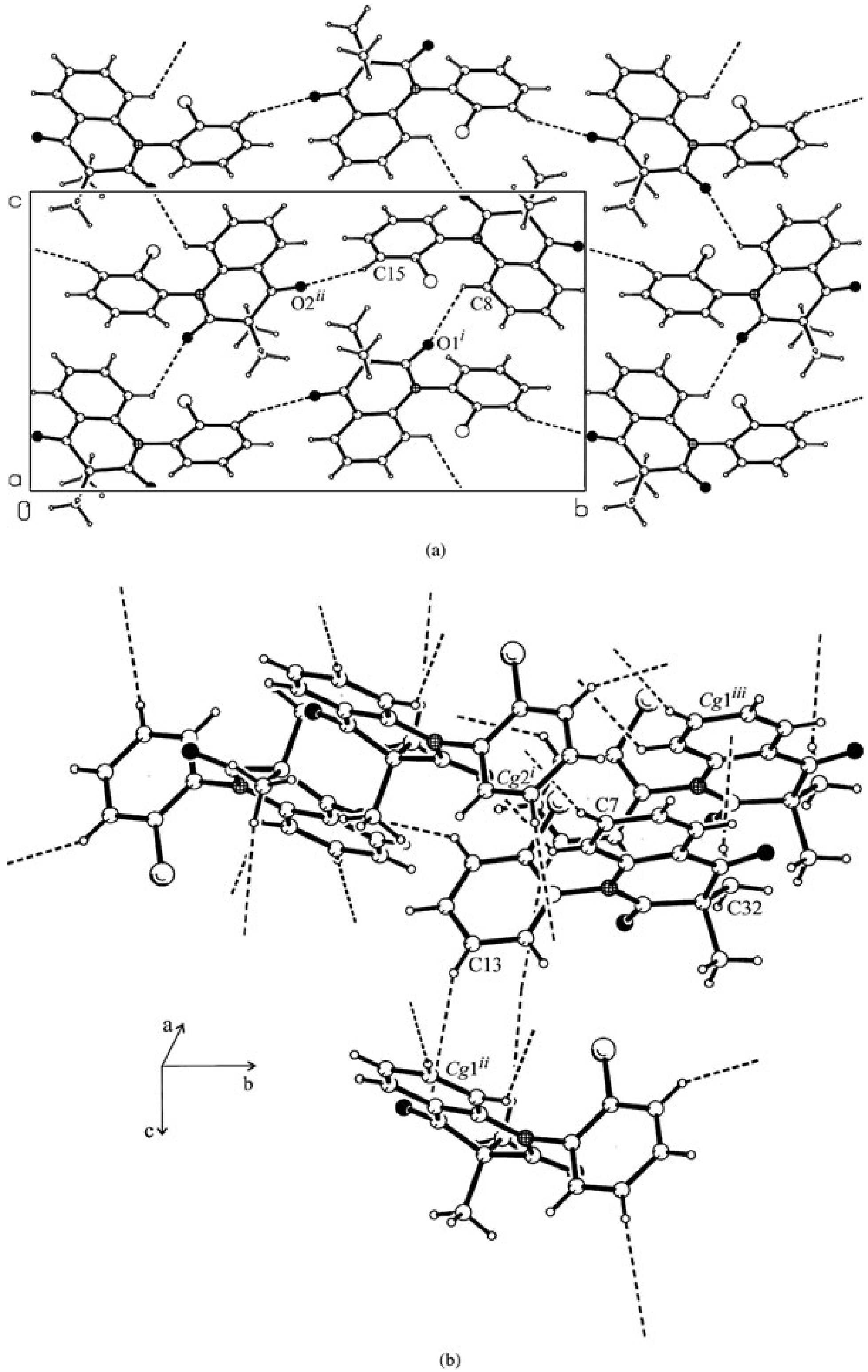


FIGURE 6 (a) A crystal-packing diagram of **3**, viewed along the *a* axis, showing the C8—H8···O1^{i} and C15—H15···O2^{ii} hydrogen bonds that generate a (4,4) net of R_4^4 (26) rings. Hydrogen bonds are indicated by dashed lines. Symmetry codes: (*i*) $x - 1, -y + 3/2, z - 1/2$; (*ii*) $-x, y - 1/2, -z + 3/2$. (b) Part of the crystal structure of **3**, showing C—H···O hydrogen bonds and the C7—H7···*Cg*2^{i}, C13—H13···*Cg*1^{ii}, and C32—H32A···*Cg*1^{iii} interactions (*Cg*1 and *Cg*2 are the C5–C10 and C11–C16 ring centroids) that link a (4,4) net into a three-dimensional framework. Hydrogen bonds and C—H···π interactions are indicated by dashed lines, and the unit-cell box has been omitted for clarity. Symmetry codes: (*i*) $x - 1, -y + 3/2, z - 1/2$; (*ii*) $x, -y + 3/2, z + 1/2$; (*iii*) $x + 1, y, z$.

TABLE 3 Hydrogen-Bonding Geometry for **1–3**

	D—H···A	*D—H (Å)*	*H···A (Å)*	*D···A (Å)*	*D—H···A (°)*	*Symmetry Codes*
1	C17—H17B···O1	0.96	2.47	3.297(4)	145	$-x+1, -y+1, -z+2$
	C13—H13···*Cg*1[a]	0.93	3.10	3.827(4)	137	$x, y, z-1$
	C17—H17B···*Cg*2[b]	0.96	3.16	3.882(3)	134	$-x+1, -y+1, -z+2$
2	C13—H13···*Cg*1[a]	0.93	2.71	3.550(2)	152	$x, y, z-1$
3	C8—H8···O1	0.93	2.59	3.168(4)	121	$x-1, -y+3/2, z-1/2$
	C15—H15···O2	0.93	2.48	3.241(4)	138	$-x, y-1/2, -z+3/2$
	C7—H7···*Cg*2[b]	0.93	2.78	3.672(4)	161	$x-1, -y+3/2, z-1/2$
	C13—H13···*Cg*1[a]	0.93	3.03	3.856(4)	149	$x, -y+3/2, z+1/2$
	C32—H32A···*Cg*1[a]	0.96	2.90	3.831(4)	165	$x+1, y, z$

[a] *Cg*1 is the C5–C10 ring centroid.
[b] *Cg*2 is the C11–C16 ring centroid.

In conclusion, the analysis of the X-ray crystal structure data of **1–3** shows that the *N*-aryl and quinoline-2,4-dione rings are almost perpendicular to each other. The bond angles C11—C16—C17 in ortho-methyl derivative **2** and C11–C16–Cl in ortho-chloro derivative **3**, indicating the steric hindrance for rotation around the C—N bond, are consistent with their barriers to racemization. Although these structures differ only in the aryl ring substituent, their crystal-packing motifs are quite different, so that they are neither isostructural nor homostructural.

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