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ORIGINAL PAPER

The Crystal Structure and Conformational Studies of Acridinedione Derivatives

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Abstract Two crystal structures of acridinediones namely, TMHAD and MPHAD were studied by X-ray crystallographic method in view of their occurrence in numerous commercial products including pharmaceuticals, fragrances and dyes. Crystal data of TMHAD are: $C_{17}H_{23}NO_2$, orthorhombic, Fdd2, with cell parameters a = 40.417(6) Å, b = 5.744(1) Å, c = 12.979(2) Å, V = 3013.1(7) Å^3, Z = 8, D_{cal} = 1.205 Mg/m^3, μ = 0.078 mm^{-1}. Crystal data of MPHAD are: $C_{20}H_{18}NO_3$; monoclinic, $P2_1/c$ with cell parameters a = 10.182(9) Å, b = 17.105(14) Å, c = 10.895(9) Å, β = 117.857(1)°, V = 1678(2) Å^3, Z = 4, D_{cal} = 1.268 Mg/m^3, μ = 0.085 mm^{-1}. Both data were collected using λ (MoK_α) = 0.71073 Å. The central ring in the acridinedione moieties tends to be planar while the outer two rings adopt *sofa* conformations. Intermolecular interactions of C–H···O type of hydrogen bond help the molecules to stabilize into the crystal packing. Interestingly, a week forces of C–H···π interactions also helps the molecules for stabilization.

Keywords Crystal structure · Acridinedione · Pyridine · Conformation · Hydrogen bonding

Introduction

Heterocyclic ring system acridinedione is generally considered to be one of the most broadly involved rings in medicinal chemistry field. Also many acridinedione derivatives have been found as potential laser dyes [1–5] due to their strong fluorescence properties. So these are of great potential to be electroluminescence (EL) materials. In addition, most of these derivatives possess photo chemical/physical properties [6–8]. Acridinediones having two keto functional groups at 1st and 8th positions are found to be good antimalarial agents, and the analogue compounds are analyzed as potent anti-malarial activity [10]. Since the acridinedione moiety has the planar conformation, it is expected to have interaction with DNA [9].

The interactions of acridines with nucleic acids [11–14] are generally acknowledged to be responsible for their biological activities. The intercalation hypothesis [15] suggests that the planar aromatic ring system of the acridines becomes inserted (intercalated) in between two adjacent base pairs of a double-stranded nucleic acid. In addition, accridinediones are used as antibacterial agents for wound therapy [16] and as antitumour drugs [17]. Substituted hexahydro acridine-1,8-dione, a novel dihydropyridine molecule resembles K-channel openers, which relaxes KCl precontracted urinary-bladder smooth muscle in vitro [18, 19]. Apart from the above applications, acridinediones also possess photophysical and electrochemical properties [20]. Acridinediones act as laser dyes whose laser activity has been deeply studied by Murugan and others [4]. In view of the above properties, the crystal structure determination of two acridinedione compounds namely, (i) 3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8 (2H, 5H) acridinedione (TMHAD) and (ii) 10-(2-methoxyphenyl)-3,4,7,9,10-hexahydro-1,8 (2H, 5H) acridinedione (MPHAD) were carried out by X-ray crystallographic methods. The chemical diagrams of these molecules are shown in the Scheme 1.

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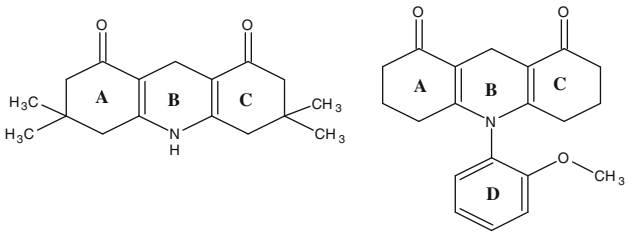


TMHAD MPHAD

Scheme 1 Chemical diagram of the molecules of TMHAD and MPHAD

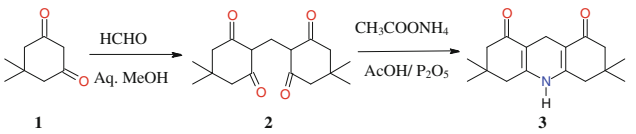
Experimental

Synthesis of Tetraketone

The syntheses of tetraketone compounds 2 and 5 were achieved according to the procedure described in the literature [21]. For that purpose, formaldehyde (25 mmol) was added to the solution of respective cyclohexane-l,3-dione (50 mmol) in aq. methanol (20 mL) and warmed until the solution became cloudy. The tetraketone started to separate out. Then, the reaction mixture was diluted with water to 250 mL and allowed to stand overnight; the tetraketone was collected by filtration and dried and recrystallized from methanol.

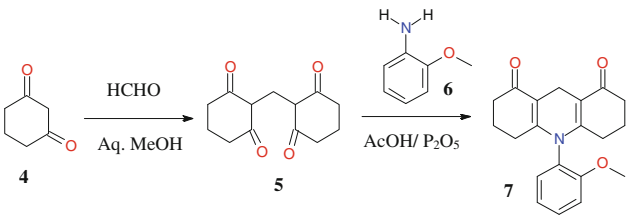
Preparation of TMHAD

The tetraketones (**2**, 0.5 mmol) and excess amount of ammonium acetate (0.7 mmol) were refluxed for 3 h in acetic acid in presence of catalytic amount of P_2O_5. The reaction mixture was cooled and poured into crushed ice. The yellow solid obtained TMHAD (**3**) was filtered, dried and re-crystallized from MeOH: $CHCl_3$ (1:1) ratio.



Preparation of MPHAD

The tetraketones (**5**, 0.5 mmol) and excess amount of anisidine (**6**, 0.7 mmol) were refluxed for 3 h in acetic acid in presence of catalytic amount of P_2O_5. The reaction mixture was cooled and poured into crushed ice. The yellow solid obtained MPHAD (**7**) was filtered, dried and re-crystallized from methanol.



Data Collection, Structure Solution and Refinement

Intensity data were collected on a Siemens SMART CCD area detector diffractometer [22] with graphite monochromated radiation ($\lambda = 0.71073$ Å). The entire data collection was covered over a hemisphere of reciprocal space by a combination of three sets of exposures each having a different ϕ angle (0, 88 and 180°) for the crystal and each exposure time of 10 s. covered 0.3° in ω. The crystal –to-detector distance was 4 cm and the detector swing angle was −35°. MPHAD data was collected up to 28.12° using MoK_α and showed 90% data completeness. But a data collection up to 25° is enough to get the complete information about the structure using MoK_α. MPHAD data completeness will be increased significantly if the data is calculated up to 25°. So the 90% of MPHAD data does not affect the structure quality and is good enough for structure determination.

The structure was solved by direct methods using SHELXS97 [23] and refined by the program SHELXL97 [24]. The non-hydrogen atoms were refined anisotropically and the positions of hydrogen atoms were derived from the difference Fourier map for molecule TMHAD. But for MPHAD molecule, hydrogen atoms were fixed geometrically and allowed to ride over the model on their parent atoms. The final cycle of refinement converged to $R_1 = 0.0672$ & 0.1051 and $wR_2 = 0.1358$ & 0.2791, respectively for TMHAD and MPHAD molecules, based on their observed reflections. The maximum and minimum heights in the final difference Fourier map were found to be 0.205 & −0.204 e. Å^{-3} and 0.314 & −0.243 e. Å^{-3}, respectively. Least-squares planes and asymmetry calculations were done using the program PARST97 [25]. The molecular graphics were drawn for both molecules using the programs ORTEP [26], ZORTEP [27] and PLATON [28]. The crystallographic data and methods of data collection, solution, and refinement are shown in Table 1. All other information relevant to these structures TMHAD and MPHAD are included in the deposited materials (CCDC 771876 & CCDC771875, respectively).

Results and Discussion

The molecule TMHAD shows half molecule symmetry in the crystal structure and molecule MPHAD shows single molecule in the asymmetric unit. The ORTEP and ZORTEP structures are shown in Fig. 1a and b, respectively with 30% probability of thermal ellipsoid levels.

The central ring (B), namely acridinedione moiety adopts planar conformation in both molecules, TMHAD and MPHAD. The fused rings on both sides (A & C) to central ring of acridinedione moiety show *sofa* conformations and

Table 1 Crystal structures data and relevant parameters

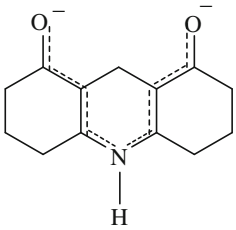
Parameters	TMHAD	MPHAD
CCDC Nos.	CCDC771876	CCDC771875
Empirical formula	$C_{17}H_{23}NO_2$	$C_{20}H_{18}NO_3$
Formula weight	273.36	320.35
Temperature	293(2) K	293(2) K
Wavelength	0.71073 Å	0.71073 Å
Crystal system, space group	Orthorombic, Fdd2	Monoclinic, $P2_1/c$
Unit cell dimensions	a = 40.417(6) Å	a = 10.182(9) Å
	b = 5.744(1) Å	b = 17.105(14) Å
	c = 12.979(2) Å	c = 10.895(9) Å
	–	β = 117.857(1)°
Volume	3013.1(7) $Å^3$	1678(2) $Å^3$
Z, Calculated density	8, 1.205 Mg/m^3	4, 1.268 Mg/m^3
F(000)	1184	676
Crystal size	0.30 × 0.25 × 0.22 mm	0.31 × 0.25 × 0.18 mm
Theta range for data collection	2.02 to 28.33°	2.26 to 28.12°
Limiting indices	$-38 \le h \le 53$	$-13 \le h \le 13$
	$-7 \le k \le 7$	$-22 \le k \le 20$
	$-17 \le l \le 17$	$-13 \le l \le 12$
Reflections collected/unique	4592/1821	9589/3688
Absorption correction	None	None
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	1821/1/138	3688/0/217
Goodness-of-fit on F^2	1.068	1.104
Final R indices [I > 2sigma(I)]	R = 0.0672, wR = 0.1358	R = 0.1051, wR = 0.2791
R indices (all data)	R = 0.1028, wR = 0.1491	R = 0.1900, wR = 0.3223
Largest diff. peak and hole	0.205 and −0.204 e. $Å^{-3}$	0.314 and −0.243 e. $Å^{-3}$

atoms C6 (ring A) & C6a (ring B) in molecule TMHAD and C8 (ring A) & C12 (ring B) in the molecule MPHAD are deviate from the planarity. Maximum deviation from the planarity is −0.304(3) Å for atoms C6 & C6a in TMHAD and atoms C8 & C12 are deviate respectively by −0.242(1) & 0.257(2) Å in MPHAD.

The central C–N–C angles of both molecules are 123.7(3)° and 121.4(4)°, respectively. These angle values support sp^2 hybridization in both molecules of N1 atom. The N1–C15 bond distance in the molecule of MPHAD is 1.437(6) Å, which is in well agreement with C_{phenyl}–$N_{acridine}$ bond length of acridinedione structures [17, 18]. The carbonyl group bond lengths [C4–O1=] 1.242(4) Å in TMHAD and [C14–O1=] 1.220(6) Å & [C10–O2=] 1.214(7) Å in MPHAD are in well agreement with the values observed for related structures [29–31].

The study of plane calculations, torsion angles, bond angles and bond lengths prove that the central ring B shows π-conjugation [O=C–C=C–N–C=C–C=O] which favors strong aromatic character in both the molecules of acridinedione moiety. The possible resonance structure is shown in Scheme 2. This is also seen from the conformational angles of the rings in detail as follows: For TMHAD [N1–C2–C3–C4=] −173.5(2), [C2–C3–C4–O1=] 175.3(3) & [N1–C2–C3–C8=] 5.0(4)° and for MPHAD [N1–C2–C3–C14=] 178.5(5), [N1–C6–C5–C10=] 176.0(5), [C2–C3–C14–O1=] 174.7(5), [C6–C5–C10–O2=] −174.3(5), [N1–C2–C3–C4=] −1.5(8) & [N1–C6–C5–C4=] 0.6(8)°. The planarity of the central ring is further supported by the low value of the puckering amplitude [32] Q_T = 0.108(3), when compared with the values for the other rings A and C of MPHAD for which Q_T = 0.239(1) and 0.3706(1), respectively.

Scheme 2 The possible resonance structure of acridinedione moiety



In the molecule MPHAD, the planar o-methoxy phenyl group is bonded with N1 atom to the central ring. This phenyl ring D is almost perpendicular to the best plane of the central ring, which is evidenced from the dihedral angle of 87.1(2)°. Further study of the torsion angles and least-squares planes

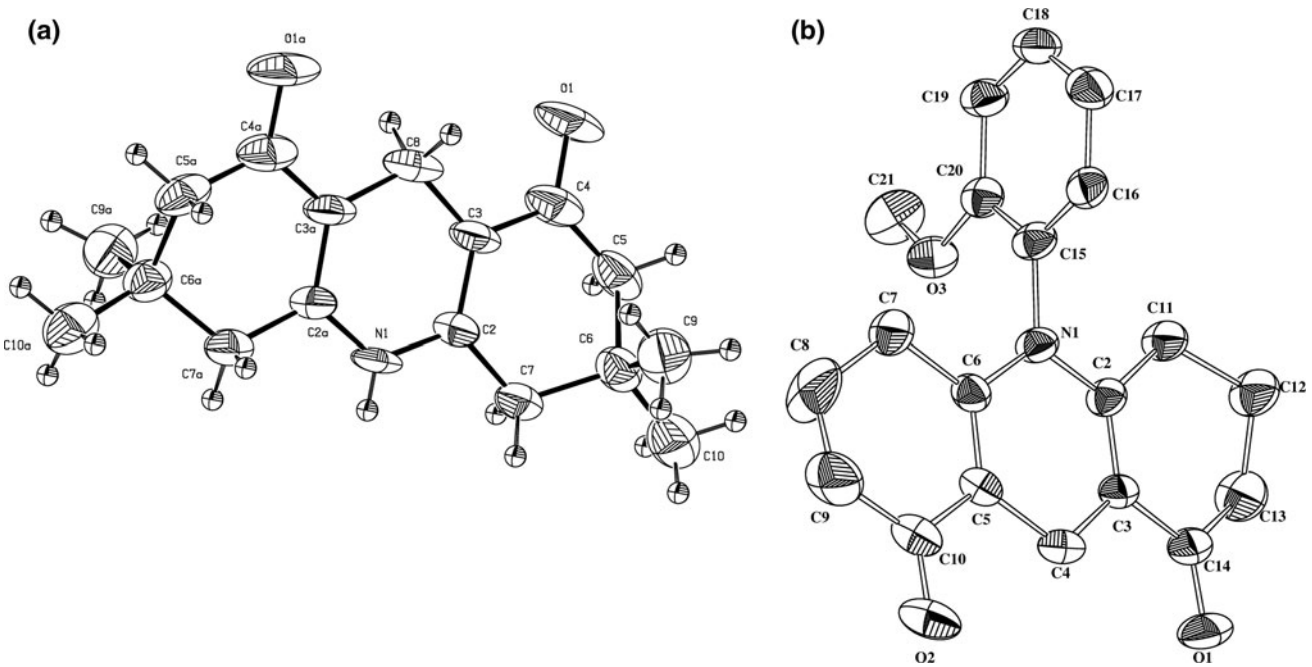


Fig. 1 ORTEP diagram of the molecule TMHAD (**a**) & ZORTEP diagram of the molecule MPHAD (**b**) showing the thermal ellipsoids at 30% probability level. The molecule MPHAD hydrogen atoms are removed for clarity

calculation show that the outer rings A and C adopt *sofa* conformation. The dihedral angles subtended between the rings A & B, B & C and A & C are 5.1(2)°, 3.5(2)° & 8.3(2)°, respectively. The dihedral angle between the rings A and C is supposed to be called as buckling angle and the degree of aromaticity is reflected from these low angle values.

The MPHAD structure is reported with larger R1 and wR2 values due to the higher thermal vibration of some atoms, namely C8, C9, C12 and C13. This is because of either one of the reasons that crystal might have diffracted weakly or might have undergone significant decomposition during data collection which has led to lower data completeness too. Higher thermal motions of these anisotropic ellipsoids of atoms also cast abnormal distances between the bonds (C8–C9 and C12–C13).

Packing Features

The details of hydrogen bonds for both molecules are given in Table 2a and b. The C–H···O and N–H···O types of intermolecular and C–H···O type of intra molecular hydrogen bonds are playing a major role in crystal packing in both molecules. The crystal-packing diagrams of molecules TMHAD and MPHAD are given Fig. 2a and b, respectively. Interestingly, the weak C–H···π intermolecular interactions [33] is also supporting for molecular stability in the unit cell crystal packing of both molecules. All the geometrical details of these hydrogen bonds are presented in the Table 2.

Table 2 Hydrogen bondings and the possible non-bonded interactions (Å, °)

D–H···A	d (D–H)	d (H···A)	d (D···A)	>(D–H···A)
(a) For molecule TMHAD[A]				
C10–H3···O1^{i}	0.956(1)	2.715(3)	3.480(5)	137.6(3)
C7–H10···O1^{ii}	0.968(1)	2.585(3)	3.454(4)	149.4(3)
N1–H15···O1^{ii}	0.736(2)	2.540(2)	3.119(4)	136.9(1)
C5–H8···Cg1^{iii}	1.014	2.796	3.800	171.1
(b) For molecule MPHAD[B]				
C11–H13A···O3^{i}	0.97	2.870(5)	3.417(8)	116.7(4)
C7–H19B···O3^{i}	0.97	2.921(5)	3.607(9)	128.6(4)
C4–H10B···N1^{ii}	0.97	2.928(5)	3.894(8)	173.8(4)
C12–H21B···O2^{ii}	0.97	2.872(6)	3.673(9)	140.5(4)
C19–H11···O2^{iii}	0.93	2.638(5)	3.435(8)	144.1(4)
C4–H10B···Cg2^{iv}	0.97	2.720	3.576	147.4
C8–H24B···Cg2^{v}	0.97	3.330	3.867	116.8

[A] Equivalent positions: (i) x, y − 1/2, z − 1/2; (ii) x, y + 1/2, z − 1/2; (iii) x, 1 + y, z. Cg1 = N1–C2–C3–C8–C3a–C2

[B] Equivalent positions: (i) x, y, z; (ii) −x + 2, −y, −z + 2; (iii) x − 1, −y + 1/2, z − ½; (iv) 2 − x, 1 − y, 1 − z; (v) x, 1/2 − y, −1/2 + z. Cg2 = N1–C2 through C6. Cg is the centroid of the benzene rings

Supplementary Material

Crystallographic data (excluding structure factors) for the structure reported in this article have been deposited with the Cambridge Crystallographic Database Centre as supplementary publication nos. CCDC771876 and

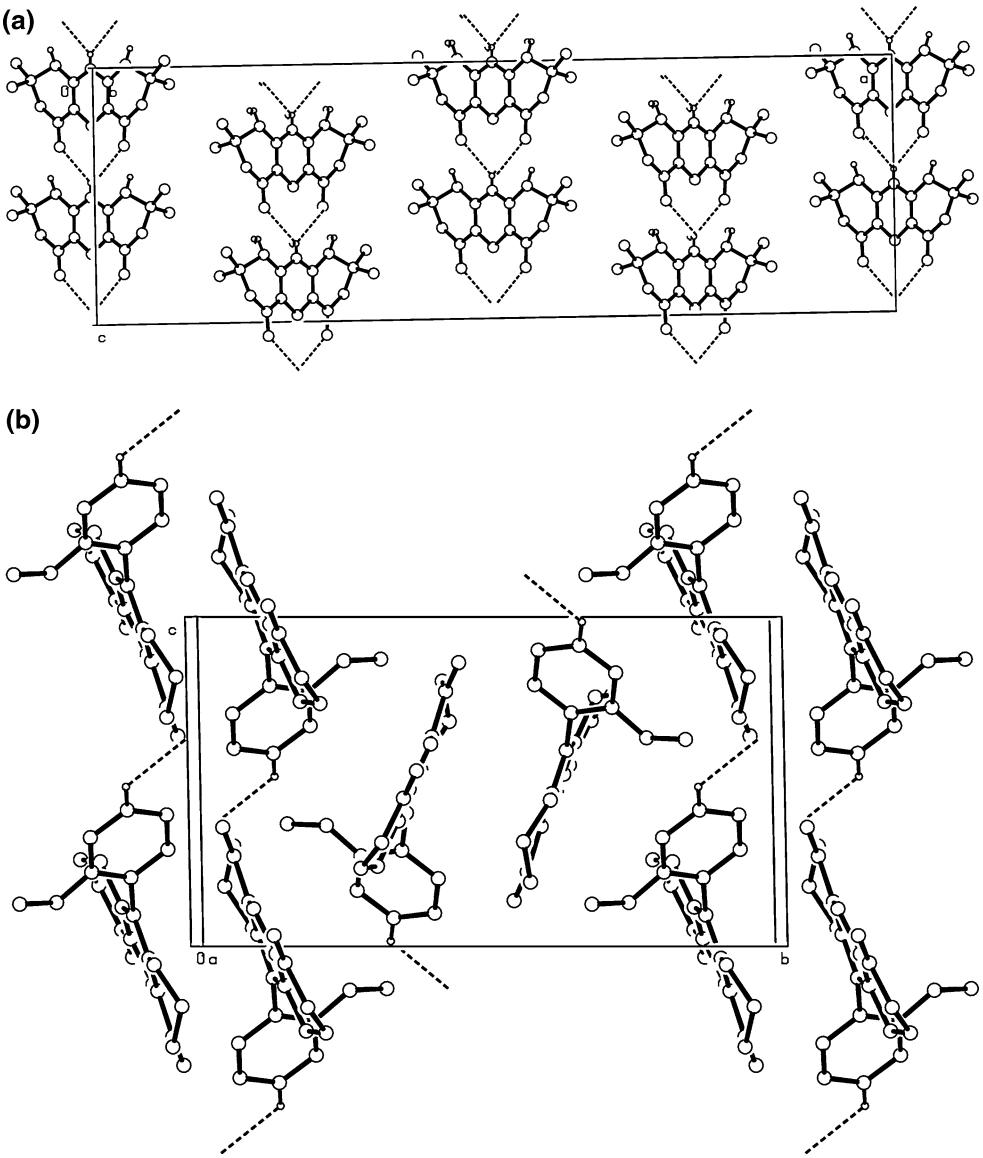


Fig. 2 Packing of the molecules TMHAD (**a**) & MPHAD (**b**) viewed down the b and a-axis, respectively. *Dashed lines* represent hydrogen bonds

CCDC771875 for molecules TMHAD and MPHAD, respectively. Copies of available material can be obtained free of charge at http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223336033; e-mail: deposit@ccdc.cam.ac.uk).

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