

X-ray study of crystal 1-Methyl-5-phenyl-1,3,3a,4,5,5a,11a,11b-hexahydro-2,6-dioxa-1,5-diaza-cyclopenta[a]anthracen-11-one and its weak interactions.

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Abstract: The title compound 1-Methyl-5-phenyl-1,3,3a,4,5,5a,11a,11b-hexahydro-2,6-dioxa-1,5-diaza-cyclopenta[a]anthracen-11-one, crystallizes in the monoclinic space group $P2_1/a$ with the following unit cell parameters: $a=8.111(1)$, $b=23.732(2)$, $c=8.487(1)\text{\AA}$ $\beta=100.20(1)^\circ$, $Z=4$. The crystal structure was solved by direct methods using single crystal X-ray diffraction data, and refined by full matrix least-squares procedures to a final R-value of 0.0378 for 2565 observed reflections. The interaction links the molecules into C-H...O hydrogen bonded dimers. The dimers are packed in layers. Two C-H... π hydrogen bonds are also present. These intermolecular interactions link the molecules within layers.

Key words: X-ray; crystal; direct method.

1. Introduction

Chromone (4H-1-benzopyran-4-one) is a derivative of benzopyran with a substituted keto group on the pyran ring. Most, though not all, chromones are also flavonoids. Several natural and synthetic chromone derivatives are found to exhibit a wide spectrum of biological activities, including spasmolytic, anti-arrhythmic, cardiothonic, antiviral, and alkylating properties¹. Chromone derivatives dilate the heart and are used to treat angina pectoris². Many chromone derivatives show antitumour activity in vivo³⁻⁴ and phosphatase inhibition⁵.

The synthesis of different types of chromones with electron-withdrawing substituents at C-3 has attracted a great deal of attention over the past several years. These chromone derivatives are highly versatile molecules because their reactivity towards nucleophiles provides useful route to preparation of a variety of heterocyclic systems⁶.

In recent years, Aloe chromones (*Aloe vera* and related products) have drawn a great attention from cosmetic, nutraceutical and pharmaceutical industries. In contrast to the reported facile intramolecular 1,3-dipolar cycloadditions of in-situ generated nitrene on heterocyclic systems, reactions of 2-(N-aaryl/crotyl/cinnamyl-anilino)-3-formylchromones with N-phenyl-/methylhydroxylamine under comparable conditions, afford fused isoazolidines only in low to moderate yields; the corresponding amides derived from rearrangement of in situ generated nitrenes are formed as major products. However, when reactions were carried by stirring the reactants at an ice-cold temperature in dichloromethane, highly stereoselective intramolecular 1,3-dipolar cycloaddition lead to novel fused isoxazolidines in high yields (80-90%). The chemical structure of the title compound is shown in Fig. 1. Three dimensional X-ray intensity data were collected on an EnrafNonius CAD-4 diffractometer with graphite monochromated $\text{CuK}\alpha$ radiation (1.5418 \AA) using a crystal of dimensions 0.3 x 0.2 x 0.2 mm. The unit cell parameters were

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obtained from an angular setting of 25 reflections in the range $5 < \theta < 12^\circ$.

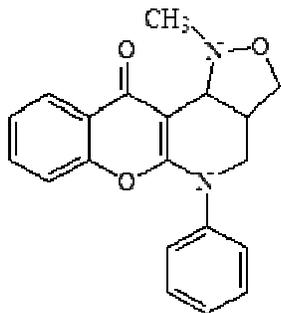


Fig. 1. Chemical structure of 1-Methyl-5-phenyl-1,3,3a,4,5,5a,11a,11b-octahydro-2,6-dioxo-1,5-diazacyclopenta[a]anthracen-11-one.

The intensity data of 3130 reflections were collected ($0 < h < 9$, $0 < k < 28$, $-10 < l < 10$), in $\omega/2\theta$ scan technique for θ ranging from 3.72 to 67.90° and out of these reflections, 2915 were found unique ($R_{int} = 0.0249$). 2565 reflections were treated as observed using ($I > 2\sigma(I)$) as criterion. Two standard reflections were measured after an hour and no significant change in the intensities of these reflections was found throughout data collection. The space group was determined to be $P21/a$ from the systematic absences $h0l : h = 2n + 1$, $0k0 : k = 2n + 1$, $h00 : h = 2n + 1$. Data were corrected for Lorentz-polarization, extinction and ψ -scan-based empirical absorption corrections (transmission factors 0.9376 to 0.9998).

The crystal structure was solved by direct methods using SHELXS97 software. A total of 256 phase sets were refined with the correct phase set having an absolute figure of merit, $M(\text{abs}) = 1.050$ and combined figure of merit $\text{CFOM} = 0.063$. Multisolution tangent refinement was carried out using 745 E-values with $E > 1.2$. All the non-hydrogen atoms of the molecule were obtained from the E-map. The reliability index for the normalized E-values RE comes out to be 0.195. Refinement was carried out by full-matrix least-squares method using SHELXL97 software. Refinement of the positional and isotropic thermal parameters of the non-hydrogen atoms yielded $R = 0.1372$. Four cycles of refinement with anisotropic thermal parameters of non-hydrogen atoms converged the R-index to 0.084. All H atoms were geometrically fixed and allowed to ride on the corresponding non-H atoms with $\text{C-H} = 0.93\text{--}0.98 \text{ \AA}$, and $\text{U}_{iso}(\text{H}) = 1.5 \text{ U}_{eq}(\text{C})$ of the attached C atom for methyl H atoms and 1.2 U_{eq} for other H atoms. The final refinement cycles converged $R = 0.0378$ and $wR(F2) = 0.1052$ for the observed data. The final weighting scheme was $w = 1/[\sigma^2(F_o) + (0.0488P)^2 + 0.5052P]$ where $P = [F_o^2 + 2F_c^2] / 3$. Maximum shift to e.s.d. ratio for all atoms in the final cycle was 0.001 (for U33 O2). The residual electron density in the final difference Fourier map ranges from -0.315 to 0.187 e \AA^{-3} . The crystallographic data are summarized in Table 1. An ORTEP view of the molecule indicating atom numbering scheme is shown in Fig 2.

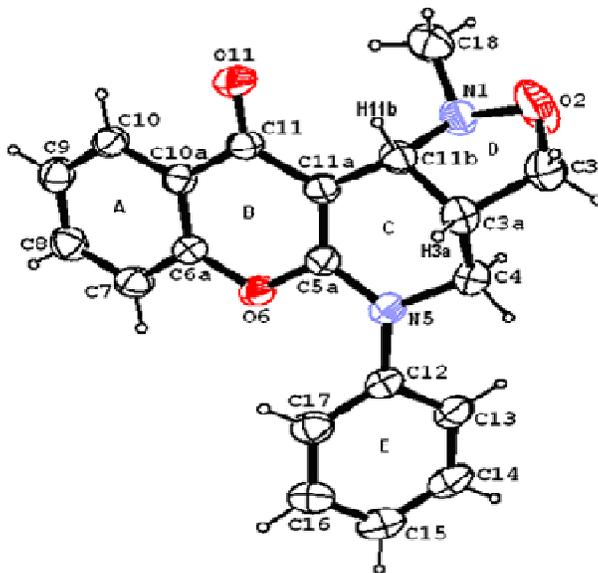


Fig. 2. ORTEP view of the molecule with displacement ellipsoids drawn at 40%. H atoms are shown as small spheres of arbitrary radii.

Table 1. Crystal and experimental data

Crystal description	Light brown irregular
Crystal size	0.3 x 0.2 x 0.2 mm
Empirical formula	C ₂₀ H ₁₈ N ₂ O ₃
Formula weight	334.36
Radiation, Wavelength	Cu K α , 1.5418Å
Unit cell dimensions	a = 8.111(1), b = 23.732(2), c = 8.487(1) Å, β = 100.20(1) $^\circ$
Crystal system	Monoclinic
Space group	P21/a
Unit cell volume	1607.8(3) Å ³
Density (calculated)	1.381 Mg m ⁻³
No. of molecules per unit cell, Z	4
Temperature	293(2) K
Absorption coefficient	0.763 mm ⁻¹
Absorption correction	ψ -scan (T _{min} = 0.9376 and T _{max} = 0.9998)
Extinction coefficient	0.0080(5)
F(000)	704
Refinement of unit cell	25 reflections (5 < θ < 12 $^\circ$)
Scan mode	ω / 2θ
θ range for entire data collection	3.72 < θ < 67.90 $^\circ$
No. of standard reflections	2
Reflections collected / unique	3130 / 2915
Reflections observed [$I > 2\sigma(I)$]	2565
Range of indices	h = 0 to 9, k = 0 to 28, l = -10 to 10
R _{int}	0.0249
R _{sigma}	0.0144
Structure determination	Direct methods
Refinement	Full-matrix least-squares on F ²
No. of parameters refined	227
Final R	0.0378
wR(F ²)	0.1052
Weight	1/[$\sigma^2(F_o^2) + (0.0488P)^2 + 0.5052P$] where P = [$F_o^2 + 2F_c^2$] / 3
Goodness-of-fit	1.025
(Δ / σ) _{max}	0.001 (for U33 O2)
Final residual electron density	-0.315 < $\Delta\rho$ < 0.187 eÅ ⁻³
Measurement	Enraf-Nonius CAD4 diffractometer
Software for structure solution	SHELXL 97 (Sheldrick, 1997)
Software for refinement	SHELXL97 (Sheldrick, 1997)
Software for molecular plotting	ORTEP-3 for Windows (Farrugia, 1997) PLATON (Spek, 2003)
Software for geometrical calculations	PLATON (Spek, 2003); PARST (Nardelli, 1995)

The six C-C bond lengths lie in the range 1.374(2) to 1.398(2)Å [average 1.382(2) Å] for the phenyl ring A and 1.375(3) to 1.393(3) Å [average 1.385(3) Å] for the phenyl ring E. These values agree reasonably well with the literature values⁷. The average value of endocyclic bond angles in both the phenyl rings

A and E is 120.0(1) $^\circ$, which is indicative of a perfect aromatic character.

The hetero atoms, viz. atom O6 in the pyran ring and the oxo substituent O11 at position C11, cause slight variations in the geometric parameters within the ring. The C6a-O6 bond length (Table 6.5-I) agrees with the

literature value [viz. 1.385(3)Å⁸ and 1.383(3)Å⁹]. The anthrone carbonyl C11=O11 distance [1.238(2)Å] is significantly longer than that usually observed for carbonyl bonds [1.192Å⁷], probably because atom O11 is involved in two intra- and intermolecular C-H...O hydrogen bonds (Table 2). The values of the bond angles within the pyran ring are in the range 115.1(1)-123.0(1)°. Similar variations in the geometric parameters of the pyran ring of the benzopyran system have been reported previously¹⁰. The π -electron delocalization of the aromatic rings extends its influence in the adjacent atoms. This is reflected in the bond lengths involving N5 atom of the piperidine ring. The C5a-N5 bond length of 1.360(2) and C12-N5 bond length of 1.433(2) Å are significantly shorter than C4-N5 [1.474(2) Å]; The C-N single bond and C=N double bond distances are 1.48 and 1.28 Å, respectively⁷.

Conformation of the molecule

The phenyl ring A is planar with a maximum deviation of -0.009(2)Å observed for the atom C7. The pyran ring deviates slightly from planarity with a maximum deviation of -0.057(1)Å observed for the atom C11. The benzopyran system is not strictly planar and the dihedral angle formed by the benzene and pyran planes is 5.12(4)°. The piperidine ring C (C11b/C3a/C4/N5/C5a/C11a) adopts 3 $\alpha\alpha$, 4 β -half chair conformation with asymmetry parameter [$\Delta C2$ (C3a-C4) = 0.50]. The conformation of five membered ring D is

intermediate between half chair [$\Delta C2$ (N1-C11b) = 9.64] and envelope [ΔCs (C11b) = 10.34] with pseudorotation parameters $\Delta = -14.96^\circ$ and $\Phi_m = -45.68^{o11}$. The deviation from the half chair conformation is evident from the unequal distances of N1 and C11b from the plane through O2, C3 and C3a ; N1 is 0.193(1)Å over this plane and C11b is -0.513(1) Å below this plane. The phenyl ring E is perfectly planar (maximum deviation 0.009(2)Å for C12) and makes a dihedral angle of 47.64(4)° with the fused ring system.

Crystal packing

Hydrogen H10 on atom C10 forms an intermolecular hydrogen bond with the carbonyl O atom O11 of a neighbouring centrosymmetrically related molecule. This interaction links the molecules into C-H...O hydrogen bonded dimers. Similar feature of formation of hydrogen bonded dimers in anthracenones was reported by Roszak and Engelen, (1990)¹² in 2-acetoxy-10-hydroxy-3-methoxy-10-phenyl-9(10H)-anthra-cenone and by Thamotharan *et al.*, (2003)¹³ in 1,8,10-trihydroxy-10-(prop-2-enyl)-anthracen-9(10H)-one. The dimers are packed in layers (Fig 3). Two C-H... π hydrogen bonds are also present. These intermolecular interactions link the molecules within layers. The three dimensional framework is further stabilized by π - π interactions between rings A and B of the anthracenone system. Details of C-H...O and C-H... π hydrogen bonds, and π - π interactions are given in Table 2 and Table 3, respectively.

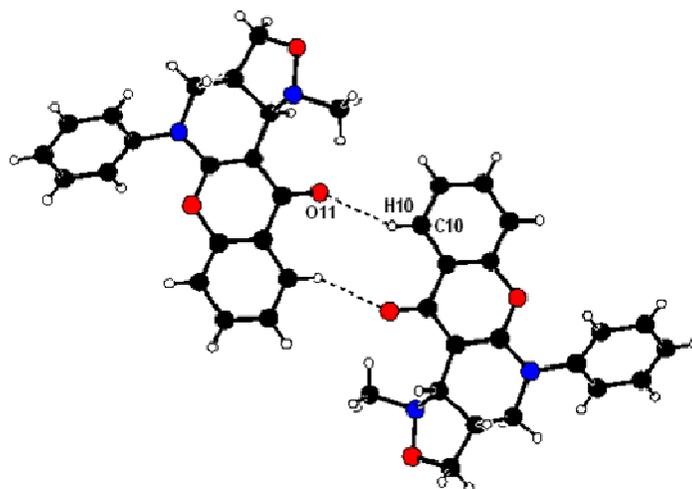


Fig. 3. A plot of two molecules of the title compound showing the formation of dimers by intermolecular C-H...O hydrogen bonds. Atom O11 is at the symmetry position (-1-x, -y, 1-z).

Table 2. Geometry of C-H...O and C-H... π hydrogen bonds. Cg4 and Cg5 represent the center of gravity of the ring A and ring E, respectively.

D-H...A	D-H(Å)	D...A(Å)	H...A(Å)	D-H...A(o)
C18-H18C...O11	0.96	3.154(2)	2.51	124
C10-H10...O11i	0.93	3.259(2)	2.54	134
C16-H16...Cg4ii	0.93	3.781(2)	2.969	146.7
C3-H31...Cg5iii	0.97	3.709(2)	2.870	145.3
Symmetry code:	(i) $-1-x, -y, 1-z$	(ii) $1+x, y, z$	(iii) $x, y, 1+z$	

Table 3. Geometry of π - π interactions. Cg represents the center of gravity of the following rings: Cg2 ring B and Cg4 ring A. CgI...CgJ represents the distance between the ring centroids; CgI...P, the perpendicular distance of the centroid of one ring from the plane of the other. α is the dihedral angle between the planes of rings I and J; β is the angle between normal to the centroid of ring I and the line joining ring centroids; Δ is the displacement of the centroid of ring J relative to the intersection point of the normal to the centroid of ring I and the least-squares plane of ring J.

CgI	CgJ	CgI...CgJ(Å)	CgI...P(Å)	α (o)	β (o)	Δ (Å)
2	2i	3.7862(9)	3.553	0.00	20.23	1.31
2	4i	3.9694(10)	3.540	5.11	22.15	1.80
4	2i	3.9694(10)	3.676	5.11	26.90	1.50
Symmetry code: (i) $-x, -y, 1-z$						

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