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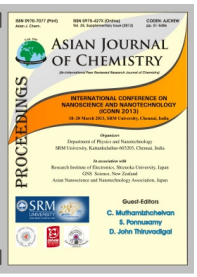

Synthesis and Crystal Structure of Methyl 9-(4-Methoxyphenyl)-8a,9,9a,10,11,12,13,14a-octa hydro-8*H*-benzo[f]chromeno[3,4-*b*]indolizine-8a-carboxylate†

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The crystal structure of methyl 9-(4-methoxyphenyl)- 8a,9,9a,10,11,12,13,14a-octa hydro-8*H*-benzo[f]chromeno[3,4-*b*]indolizine-8a-carboxylate has been determined by means of X-Ray diffraction. The compound crystallizes in the monoclinic space group $P2_1/c$ with a = 11.288(11) Å, b = 23.760(2) Å, c = 9.202(8) Å and β = 112.292(3)º. The pyrrolidine ring adopts an envelope conformation and the piperidine ring exhibits a chair conformation. The mean plane of the naphthalene ring system makes a dihedral angle of 55.90 (6)º with the methyl benzene ring. The naphthalene ring and tetrahydro pyran ring is almost planar and the dihedral angle between these rings is 9.43 (5)º. The molecular structure of the compound is stabilized by weak intramolecular C–H···N interaction and the crystal packing of the compound is controlled by weak intermolecular C–H···O and C–H···π interactions.

Key Words: Single-crystal X-ray study, Indolizine, Weak interaction, R factor = 0.039.

INTRODUCTION

Heterocycles are involved in a wide range of biologically important chemical reactions in living organisms and therefore they form one of the most important and well investigated classes of organic compounds. One group of heterocycles, indolizines, has received much scientific attention during the recent years[1-3]. Organic compounds containing two condensed rings (5- and 6-membered) and a bridging nitrogen atom are known as indolizines[4]. Indolizines are electron-rich heterocycles with very low oxidation potential. This system and its aza-derivatives are isoelectronic with naphthalene or indole and represent a group of heterocyclic compounds structurally related to purines. Therefore, indolizines can be considered as a 10-π electron system, a combination of π-excessive and π-deficient rings[5]. The synthesis of biologically active indolizine derivatives continues to attract the attention of organic chemists, because of their wide spectrum of biological activity. Indolizines are natural structures, which are remarkable in its diversity and efficacy. Many substituted indolizines, like azaindolizines and poliazaindolizines, as both unsaturated and saturated systems, are subject of extensive research due to biological, medical, photographic and other useful applications[6-8]. In addition, indolizines and their derivatives are important in the field of material science owing to their unique photophysical properties. Functionalized indolizines are common substructures found in biologically important natural products and synthetic pharmaceuticals[1-3]. Polycyclic indolizine derivatives are found to have high-efficiency long-wavelength fluorescence quantum yield[9] and these derivatives have recently attracted much research interest in the search for new opto-electric materials[10]. Several polyhydroxylated indolizines are interesting as inhibitors of glycosides[11].

EXPERIMENTAL

A mixture of (Z)-methyl 2-[(1-formylnaphthalen-2-yloxy) methyl]-3-(4-methoxy phenylacrylate) (20 mmol) and piperidine-2-carboxylic acid (30 mmol) were refluxed in benzene for 20 h and the solvent was removed under reduced pressure. The crude product was subjected to column chromatography to get the pure product. Chloroform and methanol (1:1) solvent mixture was used for the crystallization under slow evaporation method.

X-Ray structure determination: Single crystal X-ray diffraction data for the compound at room temperature was collected by Bruker Kappa diffractometer with MoK_α radiation using ω/2θ scan mode. SMART APEX2 CCD area detector with MoK_α radiation and ω scan mode was applied to obtain

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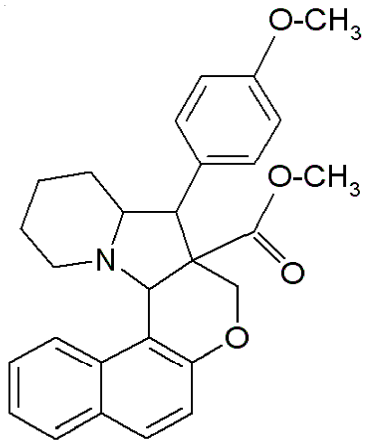
an accurate unit cell parameters and orientation matrix within the least-square fit of several high angle reflections in the ranges 2.13° < θ < 23.75°. Cell refinement and data reduction were carried out using SAINT. A total of 13998 reflections were collected, resulting in 3466 independent reflections of which 2542 had I > 2σ(I). The intensities for Lorentz and polarization effects and absorption corrections were corrected by using SADABS[12]. The structure of compound was solved by direct method procedure as implemented in SHELXS97[13] program. The full matrix least squares refinement using SHELXL97 program was used to include the position of all non hydrogen atoms. The thermal parameters for each atom were assigned a value of 0.05 (U's) in the initial stage and refinement was followed. The initial scale factor was pegged at 1.0. Thereafter the anisotropic refinement for a few cycles of full matrix least square was continued. At this stage the positions of all hydrogen's were geometrically fixed at calculated positions and they were allowed to ride on the corresponding non-hydrogen atoms. The minimum and maximum value of residual electron density was -0.14, 0.15 e.Å^{-3} and the final R-factor was 0.039.



Structure of the title compound

In this compound, the terminal methoxy group is disordered over two positions. The site occupancy factors of disordered C atom was redefined as C28 = 0.72 (3) and C28A = 0.28 (3) and the same of O atom was redefined as O2 = 0.72 (3) and O2A = 0.28 (3) during anisotropic refinement. The O2-C28 and O2A-C28A bond distances were restrained to be 1.450 (1) Å. The components of the anisotropic displacements in the direction of the bond O2 and C28 were restrained to be equal with an effective deviation of 0.001 using the DELU command in SHELXL. Crystallographic data of the compound is summarized in Table-1.

TABLE-1
CRYSTAL DATA, DATA COLLECTION AND STRUCTURE REFINEMENT

Formula	$C_{28}H_{29}NO_4$
Formula weight	443.52
Crystal system	Monoclinic
Space group	$P2_1/c$
T (K)	295(2)
a (Å)	11.289(11)
b (Å)	23.760(2)
c (Å)	9.202(8)
β(°)	112.292(3)
V (Å^3)	2283.7(4)
Z	4
D_x (g cm^{-3})	1.290
F(000)	944
μ (mm^{-1})	0.09
Crystal size (mm)	0.20 × 0.20 × 0.15
θ range (°)	2.13-23.75
hkl range	-12 ≤ h ≤ 12
	-23 ≤ k ≤ 26
	-10 ≤ l ≤ 8
Reflections	
Collected	13994
Unique (R_{int})	3464 (0.036)
With [I>2σ(I)]	2542
Number of parameters	321
R(F) [I>2σ(I)]	0.039
wR(F^2) [I>2σ(I)]	0.105
R(F) [all data]	0.064
wR(F^2) [all data]	0.096
Goodness of fit	1.02
Max/min Δρ (e Å^{-3})	0.15/-0.14
CCDC NO	848737

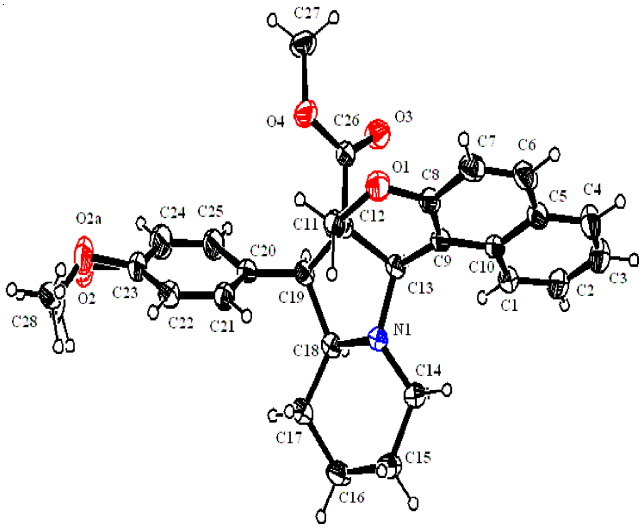


Fig. 1. ORTEP plot of the compound drawn at 30 % probability

RESULTS AND DISCUSSION

Fig. 1 shows the ORTEP plot of the molecule drawn at 30 % probability ellipsoid level with atom numbering scheme. Fig. 2 shows the packing of compound viewed down 'a' axis. The structure contains pyrrolidine ring fused with piperidine ring to form an indolizine system. The dihedral angle between these two rings is 10.35(7)°. The pyrrolidine ring adopts an envelope conformation with envelope on C13 with an asymmetry parameter[14] Cs (C9) = 11.09 (3) and with puckering parameters[15] q2 = 0.4931 (3) Å and φ2 = 208.56 (1)°. The piperidine ring exhibits a chair conformation with asymmetry parameters Cs (N1) =2.91 (1)/(C16) = 2.91 (1) and with puckering parameters Q = 0.5831 (2) Å, Θ = 4.53 (3)° and φ = 322.36 (8)°. In this compound the terminal methoxy group is disordered over two positions with site occupancies of O2 and C28 are 0.72(3) and O2A and C28A are 0.28(3) respectively. Table-2 summarizes the selected geometrical parameters of the compound.

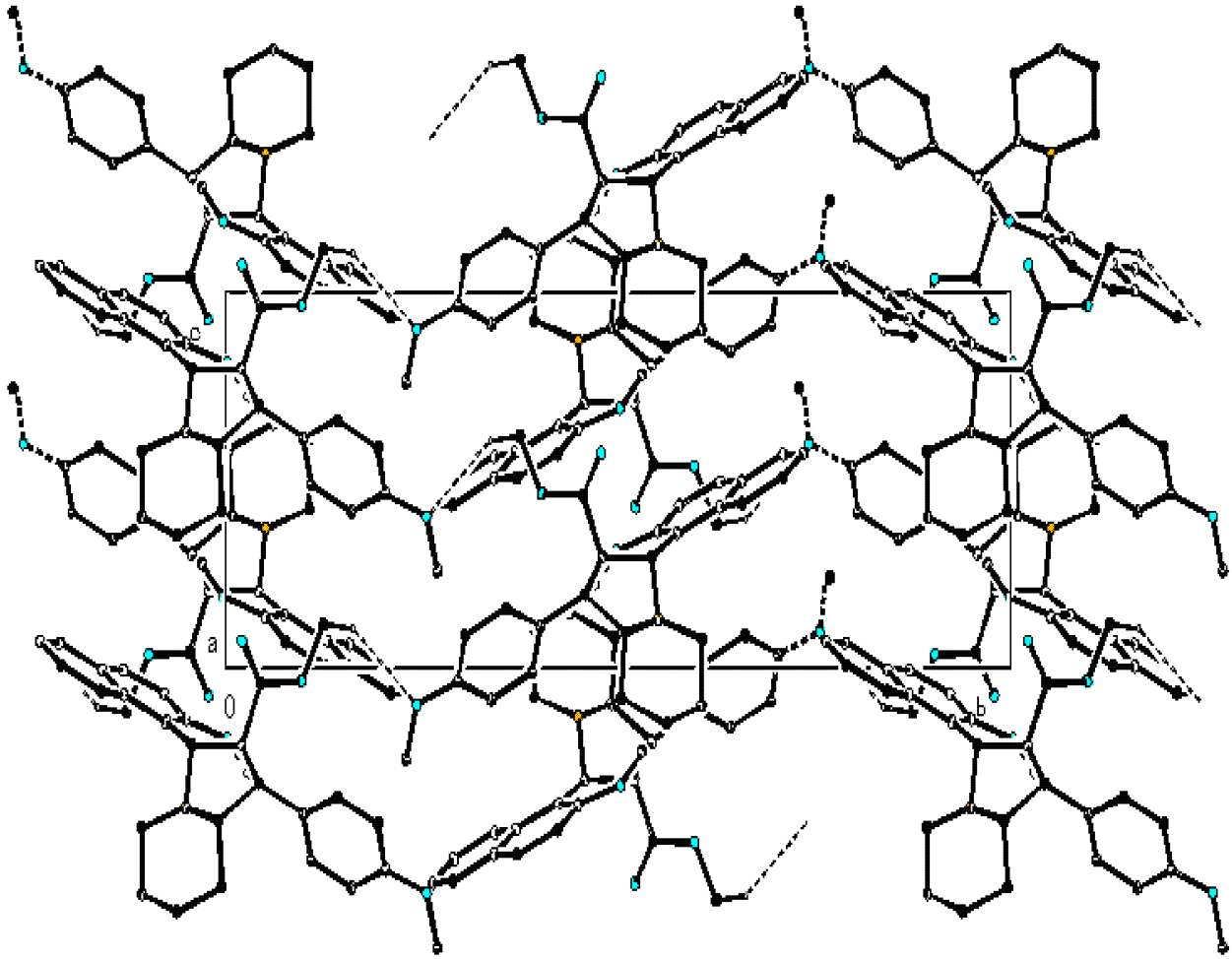


Fig. 2. Packing of the compound viewed down 'a' axis. Hydrogen bonds are shown as dashed lines

TABLE-2
SELECTED GEOMETRICAL PARAMETERS (Å, º)
WITH su's IN PARENTHESES

C8-O1	1.368(2)	C14-N1-C18	111.8(1)
C11-O1	1.433(2)	C14-N1-C13	118.1(1)
C13-N1	1.471(2)	C18-N1-C13	104.3(1)
C14-N1	1.453(3)	C24-C23-O2	109.1(1)
C18-N1	1.464(2)	C22-C23-O2	128.4(1)
C26-O3	1.187(2)	C24-C23-O2A	127.9(1)
C26-O4	1.331(2)	C22-C23-O2A	110.2(2)
C27-O4	1.445(2)	O2-C23-O2A	26.7(1)
C23-O2	1.387(2)	C23-O2-C28	110.8(1)
C23-O2A	1.420(2)	C28A-O2A-C23	120.5(2)
O2-C28	1.450(1)	N1-C13-C9	116.0(2)
O2A-C28A	1.450(1)	N1-C13-C12	99.5(1)
		N1-C14-C15	109.3(2)
		N1-C18-C17	109.4(2)
		N1-C18-C19	104.2(1)

The mean plane of the naphthalene ring system makes a dihedral angle of 55.90 (6)º with the methyl benzene ring. The naphthalene ring and tetrahydro pyran ring is almost planar and the dihedral angle between these rings is 9.43 (5)º. The N1- C14 and N1-C18 bond distances are 1.450 (3) Å, 1.464 (2) Å respectively are comparable to the literature value of 1.4530 (18) Å and 1.4730(18) Å[1-3]. The sum of bond angles around N1 [333. 12(10)º] indicates the sp^3 hybridized state of atoms N1 in the molecule. The similar pyramidalization behaviour is also observed in related indolizines[1-3,16]. The molecular structure is stabilized by weak C–H···N type of intramolecular interaction. The N1 atom in the indolizine system acts as potent acceptor for C11-H11B···N1 hydrogen bond in which atom C11 donates a proton. The crystal packing of compound is controlled by weak intermolecular C–H···O [C27–H27B···O2 distance of 3.360 (2) Å] and C–H···π [C16–H16B···Cg5 distance of 3.818 (2) Å, C22–H22···Cg5 distance of 3.711 (2) Å and C28A-H28E…Cg6 distance of 3.646 (2) Å] interactions. Table-3 gives the Hydrogen bond data of the compound.

TABLE-3
NON-BONDED INTERACTIONS AND
POSSIBLE HYDROGEN BONDS (Å, º)

D–H···A	D–H	H···A	D···A	DHA
C11-H11B...N1	0.97	2.49	2.840(3)	100.9
C27-H27B...O2i	0.96	2.58	3.359(2)	138.1
C16-H16B...Cg5ii	0.97	2.95	3.818(2)	150.0
C22-H22...Cg5iii	0.93	2.96	3.711(2)	139.0
C28A-H28E...Cg6iv	0.96	2.91	3.646(2)	134.0

Cg 5 and Cg 6 are the centroid of the rings defined by the atoms C5-C10 & C20-C25 respectively.

Conclusion

Heterocycles are involved in a wide range of biologically important chemical reactions in living organisms and therefore

they form one of the most important and well investigated classes of organic compounds. The structure contains central pyrrolidine ring fused with piperidine ring to form an indolizine system. In this compound, the terminal methoxy group is disordered. The molecular structure is stabilized by weak C–H···N type of intramolecular interaction. The crystal packing of the compound is controlled by weak intermolecular C–H···O and C–H···π interactions.

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