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Synthesis and crystal structure (Z)-3-(benzo[d][1,3]dioxol-5-ylamino)-4-(benzo[d][1,3]dioxol-5-ylmethylene)dihydrofuran-2(3H)-one

Sivaranjani.T[1], , KodagalaKameswara Rao[2], , Raja. R[3],Carolina Andrea Monardes Carvajal[4], Steven Andrés Sánchez Varas[4],Musali Krishnaiah, [2, a*], Sakthimurugesan. K[1, a*]

[1,] Department of Physics, Presidency College, Chennai-05, [2,] Department of Physics, Sri Venkateswara Arts College, Tirupati 517501, India, [3]Department of Physics, Thiruthangal Nadar College, Chennai-51, [4]Molecular Biology Laboratory,School of Medicine, University of Atacama, Copayapu - 485, Copiapó, Chile, [2, a*]Department of Physics, Sri Venkateswara University, Tirupati 517 502, India, [1, a*] Department of Physics, Presidency College, Chennai-05, India

Abstract: The asymmetric unit of the title molecule, $C_{38}H_{31}N_2O_{12}$, consists of two molecules differing slightly in conformation and in their intermolecular interactions in the solid. The dihedral angle between the benzene and dioxolane rings is 0.20 (7)° in one molecule and 0.31 (7)° in the other. In the crystal, the two molecules are linked into dimers through pair wise C-H…O hydrogen bonds, with these units being formed into stacks by two different sets of aromatic -stacking interactions. The stacks are connected by N-H…O hydrogen bonds.

Index Terms: *Synthesis; crystal structure; benzodioxolane; oxime; N-H…O; C-H…O; hydrogen bonds; π-stacking; T = 295 K; R factor = 0.0494; wR factor = 0.1403; data-to-parameter ratio = 9.05.*

I. Introduction

It is necessary to investigate the pharmaceutical mechanism of Isodon genus (Lamiaceae), as most species of this family possess a variety of bioactivities such as anti-hypertension, anti-cancer and anti-inflammatory. Besides, Isodonflavidus (Hand. Mazz. Hara.), an important member of this family, is distributed widely in Guizhou province, China. Thus, based on the information mentioned above, we have since discovered the title compound from I. flavidus [1]. Adamantanamine and its derivatives play an important role in pharmaceuticals as well as medicinal chemistry because they possess a broad spectrum of biological activities[2].As a result, a great deal of attention has been paid to the investigation on the structure and property of amantadine and its derivatives. The aim of this study was to further optimize the organic synthesis and structural modification of amantadine amino based materials to design a suitable synthesis route to get novel compounds by a 1–2 steps reaction. To improve bioavailability of 5-FU, the prod rug approach was recently explored for its delivery, notably by chemically modifying with small molecules like glucoside [3], peptide [4], sulfonyl [5], ester [6], and so on, that in most instances improved anticancer potency and therapeutic value of 5-FU. Inspired by the study on linking 5-FU with thiophenecarboxylic acid through esterification reaction as an anticancer photosensitizer [7], we designed the title compound bearing ester of furancarboxylic acid. By multi-step reactions the title compound was obtained with moderate yield.

II. Experimental

The chemical structure of the compound 1is shown in **Figure 1**. The title compound was synthesized using a previously reported procedure [8].

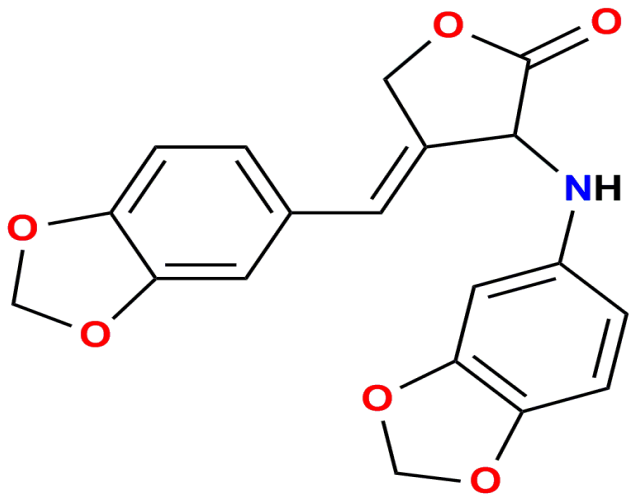

Fig. 1 Scheme diagram of compound 1.

III. Data collection

Data collection: APEX3 (Bruker, 2016)[9]; cell refinement: SAINT (Bruker, 2016); data reduction: SAINT (Bruker, 2016); program(s) used to solve structure: SHELXT (Sheldrick, 2015a)[10]; program(s) used to refine structure: SHELXL2018/3 (Sheldrick, 2015b)[11]; molecular graphics: DIAMOND (Brandenburg & Putz, 2012)[12], PLATON (Spek, 2020)[13]; software used to prepare material for publication: SHELXL2018/3 (Sheldrick, 2015b), PLATON (Spek, 2020) and publCIF (Westrip, 2010)[14].

IV. Refinement

The crystal structure was solved by Direct Methods and refined by full-matrix least-squares methods using the Olex2. All the carbon-bound hydrogen atoms were placed in the calculated positions, with the d(C—H) = 0.93–0.98 Å. The U_{iso}(H) were set to 1.2 U_{eq}(C) and to 1.5 U_{eq}(O).

V. Structural Commentary

There are two crystallographically independent molecules in the asymmetric unit (Fig.2). Both molecules have almost the same geometric parameters. The two aryl rings are linked by a keto group. Additionally, the aminoadamantyl moiety is attached to the second ketone group of the title molecules. The bond distances and angles are in their normal ranges according to the previously reported compounds [6].

All geometrical parameters of the title structure are in the normal ranges. The dioxole ring system adopts a twisted conformation, with the phenyl rings in equatorial orientations with respect to the dioxole ring. The two dioxole rings of the dioxol-5-ylmethylene ring system exhibit a distorted envelope conformation. This title compound is a highly oxygenated lignanoid containing four five-membered rings, two benzene rings and one acetoxyl group. Especially, the epoxy five membered rings A (atoms O3/C1—C2/C4—C5) and B (atoms O7/C1/C5—C6/C8), which is fused to ring A through C1 and C5, are both in half-chair conformations, with atoms C2 and O3 deviating from the best plane through atoms C1/C4/C5 by −0.355 Å and 0.274 Å, respectively, and atoms O7 and C8 deviating from the best plane through atoms C1/C5/C6 by −0.358 Å and 0.267 Å, respectively.

The bond lengths and angles are in the normal ranges. Both the hexacyclic-ring and the pentacyclic-ring in the structure are planar with mean deviation of 0.0022(2) Å and 0.0018(8) Å, respectively, and the dihedral angle between the two rings is 76.59(6)°, indicating they are nearly perpendicular to one another. The benzodioxolane portion of the molecule containing O1 is planar to within 0.0171 (12) Å (r.m.s. deviation of the fitted atoms = 0.0091 Å) with C7 deviating by 0.0171 (12) Å from one side of the mean plane and O1 by 0.0170 (10) Å from the other, indicating a slight twist in the dioxolane ring.

The corresponding portion of the second molecule containing O4 is planar to within 0.0041 (11) Å (r.m.s. deviation of the fitted atoms = 0.0030 Å), indicating a conformational difference, albeit small, between the two molecules. The C6—C1—C8—N1 and C1—C8—N1—O3 torsion angles are, respectively, 3.9 (2)° and -179.96 (11)°, indicating the side chain to be nearly coplanar with the benzodioxolane unit. The corresponding torsion angles in the second molecule are virtually the same as above. The two molecules are connected into dimers through N-H…O and C-H…O hydrogen bonds (Table 3 and Fig. 3), generating $R^2_2(6)$ loops.

VI. Superamolecular features

In the crystal, the dimers are connected into stacks extending along the [101] direction through slipped π-stacking interactions between the six-membered (Cg2: C1–C6 and Cg5: C9– C14) rings. For the C1–C6 rings, the centroid–centroid distance is 3.6024 (11) Å with a slippage of 1.185 Å between molecules at x, y, z and -x, -y + 1,-z. These paired molecules make weak, slipped π-stacking interactions with corresponding pairs at -x + 1, -y + 1, -z + 1 with a centroid– centroid distance of 3.8479 (11) Å and a slippage of 1.947 Å . The C9–C14 ring has slipped π-stacking interactions with its counterparts in molecules at x-1/2, -y + 1 2, z – 1/2 and at x + 1 2, -y + 1/2, z + 1/2 with centroid–centroid distances of 3.8380 (11) Å and dihedral angles of 2.41 (6)° for both. The slippages for these interactions (Fig. 3) are 1.572 Å and 1.662 Å, respectively. These differences in the π-stacking interactions also support the independence of the two molecules in the asymmetric unit. The stacks are associated through C4-H4A…O2, C5-H5A…O1 and C1-H1…O1 hydrogen bonds (Table 3 and Fig. 3).

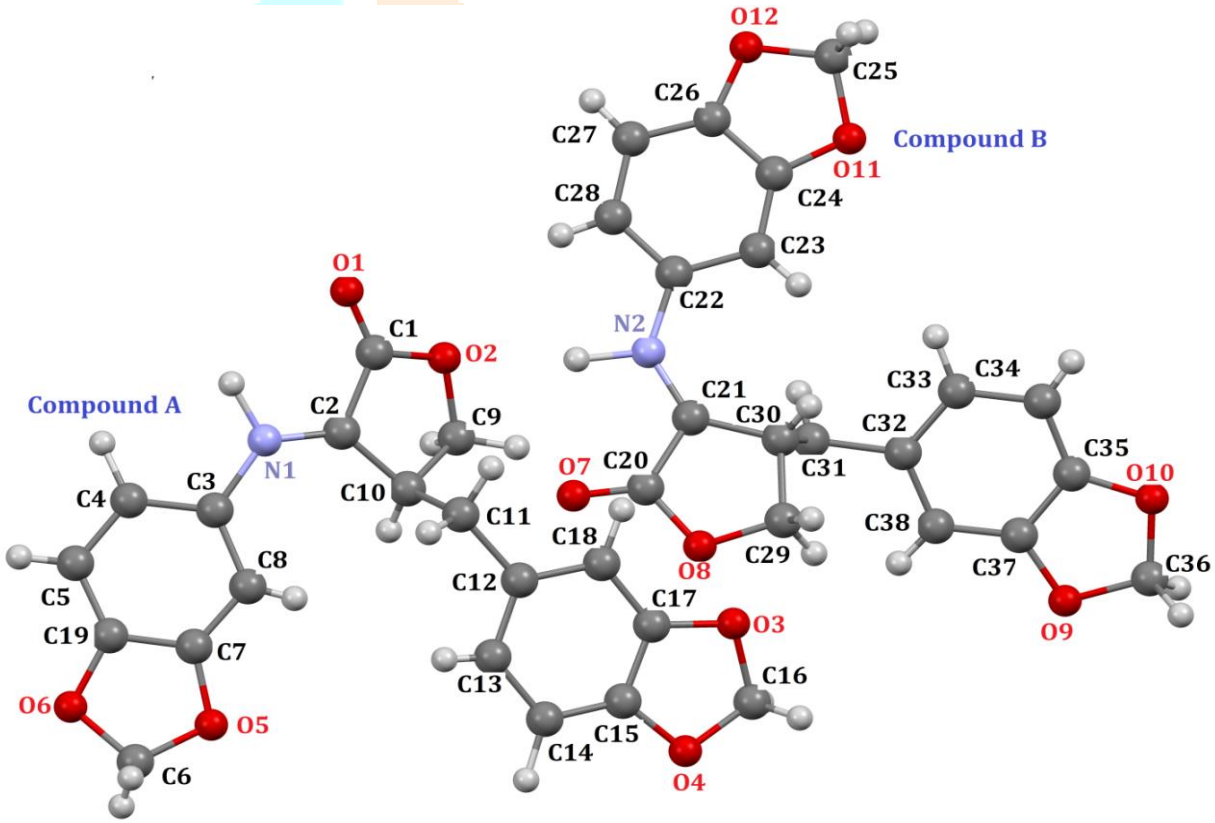

Fig.2. The asymmetric unit with 50% probability ellipsoids.

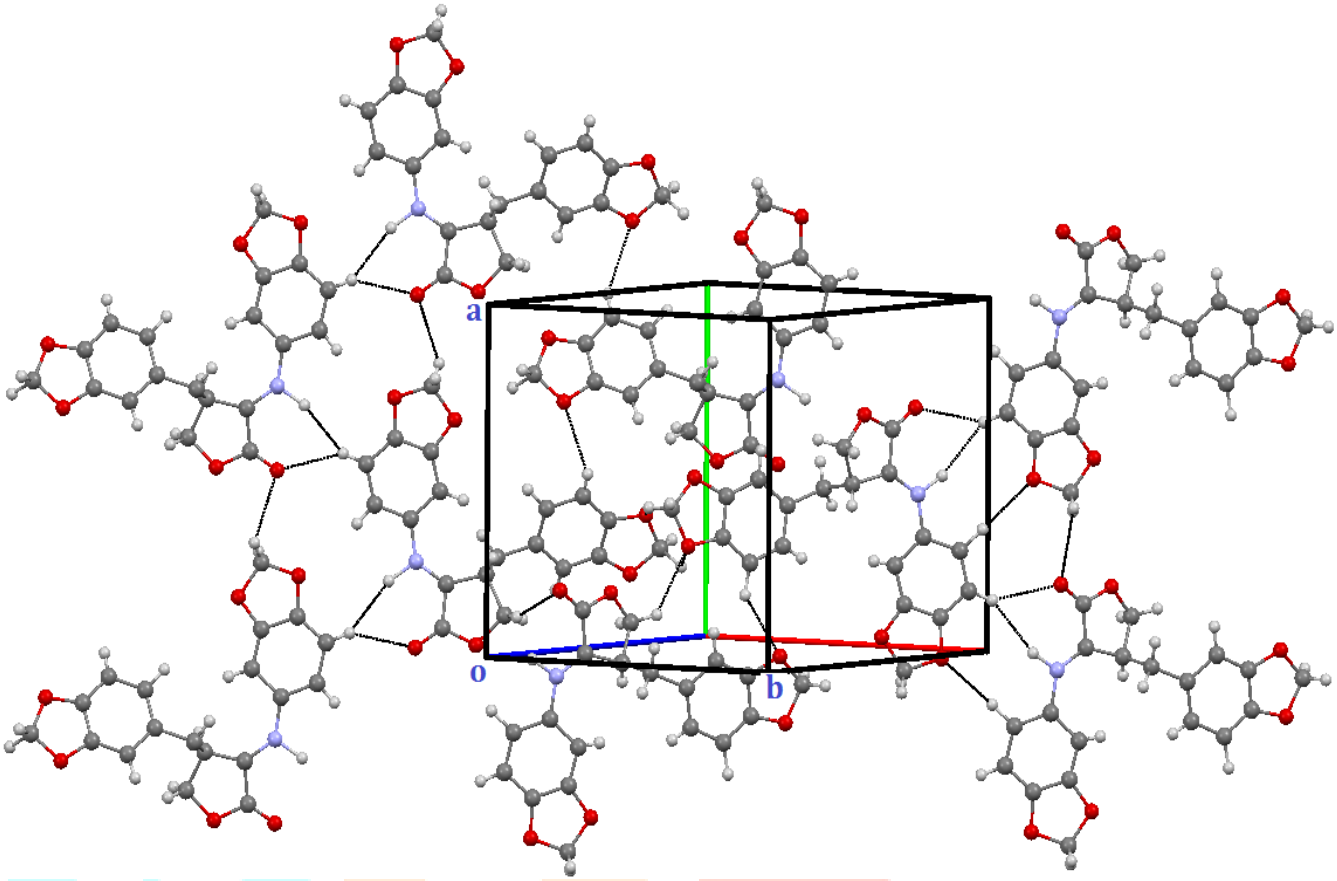

Fig.3 View of the packing seen along the a-axis direction with N-H…O and C-H…O hydrogen bonds interactions depicted, respectively, by light blue, black and orange dashed lines.

VII. Table 1

Selected Bond length and Bond angles (Å, °)

Atom		Length(Å)	Atom	Angles(°)
O1	C1	1.195(3)	C2 - O1 - C1	111.08
O2	C9	1.377(3)	C8 - O5 - C6	105.8
O2	C1	1.439(4)	O3 - C17 - C18	128.0
O3	C16	1.373(3)	N1 - C3 - C4	118.1
O3	C17	1.429(3)	C10 - C11 - C12	111.9
O4	C15	1.437(4)	N1 - C2 - C1	118.35
C13	C12	1.371(3)	N1 - C2 - C9	133.1
O6	C6	1.454(3)	O3 - C16 - O4	108.2
O5	C7	1.353(3)	C6 - O5 - O6	105.96
C8	C3	1.380(3)	C13 - C14- C15	118.6
N1	C2	1.335(3)	O4 - C15 - C14	109.6

VIII. Table 2

Crystal Data and Details of the Structure Determination

Parameters	**Title of compound**
Empirical formula	$C_{38}H_{31}N_2O_{12}$
Formula weight	707.65
Wavelength	0.71073 Å
Crystal system space group	Monoclinic P21
Unit cell dimensions	a = 11.5807(8)Å
	b = 11.8903(8) Å
	c = 12.3268(9) Å
	α = 90°
	β 102.995°
	γ = 90°
Volume	1653.9(2) $Å^3$
Z, Calculated density	2, 1.4210(2)Mg/m^3
Absorption coefficient	0.107 mm^{-1}
F(000)	738
Crystal size	0.15 x 0.20 x 0.25 mm
θ range	1.6 to 25.5°
Index ranges	$-15 \le h \le 15$ $-15 \le k \le 15$ $-12 \le l \le 16$
Reflections collected / unique	14237 / 7214 [R(int) = 0.018]
Completeness to theta	100 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7214/ 0 / 594
Goodness-of-fit on F^2	1.06
Final R indices [I>2sigma(I)]	R1 = 0.0494 wR2 = 0.1403
R indices (all data)	R1 = 0.1083 wR2 = 0.1822
Largest diff. peak and hole	-0.40 and 0.35 $e.Å^{-3}$

IX. Table

Hydrogen-bond geometry (Å ,°).

D-H…A	**D-H**	**H…A**	**D…A**	**D-H…A**
C4-H4A…O2^{i}	0.99	2.52	3.332	131
C5-H5A…O1^{ii}	0.93	2.59	3.410	149
C1-H1…O1^{iii}	0.93	2.59	3.410	142
C2-H2…O2^{iv}	0.92	2.54	3.309	142
C8-H8…O3^{iv}	0.93	2.56	3.241	131
C3-H3A…O3^{v}	1.11	2.56	3.582	152

Symmetry codes: (i) 1-x,-1/2+y,1-z
(ii) 1-x,1/2+y,1-z
(iii) 2-x,-1/2+y,-z
(iv) 1-x,1/2+y,-z
(v) -1+x,y,z

X. ACKNOWLEDGMENT

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XI. References

[1] Sun, H. D.; Huang, S. X.; Han, Q. B. Nat. Prod. Rep. 23 (2006) 673–698.

[2] Leonov H., Astrahan P., Krugliak M. J. Am. Chem. Soc. 2011, 133, 9903–9911.

[3] Ai-WahaibiL.H., AlsfoukA.,Ei-EmamA. A. Acta Crystallogr. 2019, E75, 611–615.

[4] Szymańska-Michalak, A.; Wawrzyniak, D.; Framski, G.; Kujda, M.; Zgola, P.; Stawinski, J.; Barciszewski, J.; Boryski, J.; Kraszewski, A. Euro. J. Med. Chem. 115 (2016) 41–52.

[5] Yin, P.; Hu, M. L.; Yan, X. W.; Wang, S.; Miao, Q.; Chang, X. Q.; Zhao, K. J. Acta Chim. Sinica 66 (2008) 1693–1699.

[6] Li, M. R.; Cai, X. Q.; Zhu, Y. F.; Liu, K. G.; Hu, M. L. Acta Chim. Sinica 69 (2011) 425–430.

[7] Cohen, S. S.; Flaks, J. G.; Barner, H. D.; Loeb, M. R.; Lichtenstein, J. Proc. Natl. Acad. Sci. USA 44 (1958) 1004–1012.

[8] Inorganic Chemistry Communications 134 (2021) 109029, Inorg. Chem. 2020, 59, 17109−17122, Journal of Molecular Structure 1250 (2022) 131782

[9] Bruker (2016). *APEX3* and *SAINT*. Bruker AXS Inc., Madison, Wisconsin, USA.

[10] Sheldrick, G. M. (2015*a*). *Acta Cryst.* A**71**, 3–8.

[11] Sheldrick, G. M. (2015*b*). *Acta Cryst.* C**71**, 3–8.

[12] Brandenburg, K. & Putz, H. (2012). *DIAMOND.* Crystal Impact GbR, Bonn, Germany.

[13] Spek, A. L. (2020). *Acta Cryst.* E**76**, 1–11.

[14] Westrip, S. P. (2010). *J. Appl. Cryst.***43**, 920–925.