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A comparison studies of Dibenzoazepine derivatives and their Hirshfeld surface analysis

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Abstract
In the crystal structures of dibenzoazepine derivatives 5-Methyl-5H-dibenzo[b,f]azepine (a), 5-(4-Methylbenzyl)-5H-dibenzo[b,f]azepine (b), 5-[(1-Benzyl-1H-1,2,3-triazol-4-yl)meth-yl]-5H-dibenzo[b,f] azepine (c) and 5-(Prop-2-yn-1-yl)-5H-dibenzo[b,f]azepine (d), the azepine ring exhibits the boat conformation. The molecules are connected through common short contacts of the type C—H…π. The short contacts for the first time for molecules b and d are quantized using computational Hirshfeld surfaces method and compared with molecules (a and b).

*Keywords*Dibenzoazepine, Intermolecular contacts, Hirshfeld surfaces.

Introduction

The chemical compounds are vital for many process ranging from living and non-living things. Heterocycles are the chemical compounds found abundantly in nature and involved in metabolism of the living cells. One of the group of heterocyclic compounds are azepines having seven membered ring (carbon atoms) with a nitrogen replacing a carbon at one position. They are found to be associated with diverse pharmacological activities such as antiviral, anticancer, anticonvulsant, antidepressant, anti-insecticidal, vasopressin antagonist activity. One of them dibenzoazepine (iminostilbene) is a chemical compound with two benzene rings fused to an azepine group (Figure 1) [1].

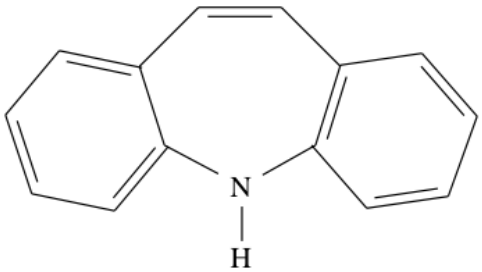

Figure 1. Schematic diagram of the dibenzoazepine molecule.

In nature, Montanine, Coccinine, Manthine, Pancracine are the only alkaloids known to possess the morphanthridine (dibenzoazepine) ring system present in *Haemanthus* and *Rhodophiala* species [2]. Dibenzoazepine are important and valuable compounds in medicinal chemistry. Previous studies indicated that, changing the polarity (incorporation of hydrophilic or hydrophobic groups) at N-position play an important role to enhance the biological activity [3,4]. Also, reported to be as antioxidant and sirtuin-2 inhibitory activity [5,6]). The naturally occurring pyrrolo benzodiazepines from streptomyces species are used as antitumor and

antibiotics [7]. The synthesis of tricyclic azepine moiety tethered with piperazine and 1,2,3-triazole moiety shows anticancer activity [8]. Dibenzoazepine derivative, 5H-dibenzo[b,f]azepine is a common basic fused tricyclic amine and used as an intermediate for the synthesis of the registered anticonvulsant drug oxcarbazepine [9,10]. In addition, reported as having antiallergic activity, specifically antihistaminic, spasmolytic, serotonin antagonistic, anticonvulsive, antiemetic, antiepileptic, anti-inflammatory, sedative and fungicidal action [11]. Some dibenzo[b,f]azepine derivatives with piperazine skeleton are reported as effective anticancer agents and piperazinyl dibenzazepines are also reported to have sedative and antidepressant activities [12,13].

The number of crystal structures of 5H-dibenzo[b,f]azepine derivatives; (a) 5-Methyl-5H-dibenzo[b,f]azepine [14], (b) 5-(4-Methylbenzyl)-5H-dibenzo[b,f]azepine [14], (c) 5-[(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl]-5H-dibenzo[b,f]azepine [15] and one polymorph (d) 5-(Prop-2-yn-1-yl)-5H-dibenzo[b,f]azepine [16] and thier synthesis has been reported. The intermolecular contacts are involved in crystal structure stabilization and have been analysed using Hirshfeld surfaces analysis [17].

2. Materials and methods

2.1. Softwares and Databases

The crystal structures are retrieved from the CCDC through reported literatures [14-16] and the software used to compute intercontacts over Hirshfeld surfaces is Crystal Explorer [17]. The 2D fingerprint plots were generated using the method described [22].

3. Results and discussion

3.1. Crystal structure comparison

The crystal structures of molecules a, b, c and d are reported earlier [14-16] and they are compared in the table 1. The molecules a, b and d crystallizes in the crystal system orthorhombic and space groups *Pca*21, *Pbca* and *Iba*2, respectively. The molecule c crystallizes in monoclinic space group with the space group *P*21/*c*. In all the crystal structures, azepine ring is puckered and adopts a boat configuration. The fused benzene rings to azepine moiety show dihedral angles of 47.1^0 (a), 52.9^0 (b), 49.40^0 (c) and 55.99^0 (d). In the crystal packing, the short contacts C—H…π is observed in all the compounds. Compound c, shows an additional π...π interaction, which is absent in other compounds (a,b and d). The bond lengths and bond angles in all the molecules are in good agreement with the standard values [18, 19].

Table 1: Comparison of crystal structure parameters and molecular structure parameters.

	(a)	(b)	(c)	(d)
Empirical formula	C15H13N	C22H19N	C24H20N4	C17H13N
Crystal system	Orthorhombic	Orthorhombic	Monoclinic	Orthorhombic
Space group	Pca21	Pbca	P21/c	Iba2
Conformation of azepine ring	boat	boat	boat	boat
Dihedral angle between fused benzene ring to the azepine moiety (^{0})	47.1	52.9	49.40	55.99
Intermolecular contacts (intermolecular hydrogen bond)	C—H…π	C—H…π	C—H…π, π...π and C—H..N	C—H…π

3.2. Hirshfeld surfaces analysis

The intermolecular interactions of the compounds (a,b, c and d), over Hirshfeld surfaces are analysed using the computational methods implemented in program Crystal Explorer [20,21]. The parameters used for calculating the surfaces are *de* and *di*, where *de* is the distance external to the surface, which measures the distance from the surface to the nearest nucleus in another molecule and *di* is the internal distance to the surface. The intercontacts that contribute to the total Hirshfeld surface area are estimated and listed in Table 2.

The molecules c shows the C...C (2 %), C...H (32 %), H...H (52 %), N...H (13 %) and C...N (1 %) intercontacts. In molecule d, C...C (3 %), C...H (44 %), H...H (51 %) and N...H (2 %) intercontacts are observed. The Hirshfeld surfaces of the intercontacts are highlighted by conventional mapping of *dnorm* on molecular Hirshfeld surfaces. In addition, the fingerprint plots [22-24] are also plotted and shown in Figures 2. The major intercontacts of dibenzoazepine derivatives a to d, the Hirshfeld surfaces are found to be C...H and H...H, whereas the percentage of contribution of other intercontacts is comparatively less.

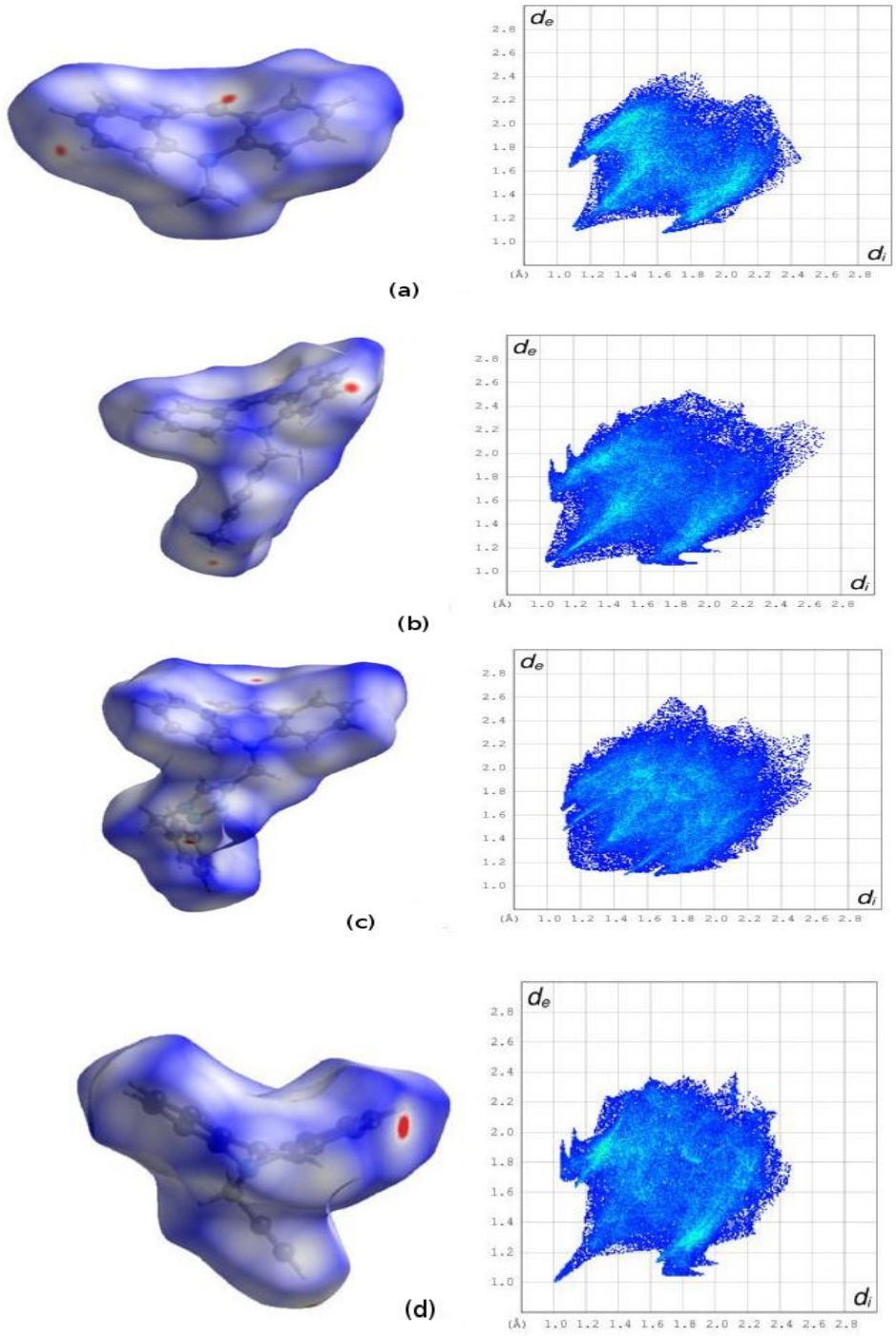

Figure 2: d_{norm} mapped on Hirshfeld surface for visualizing the intercontacts of the molecules, 1 to 4 (left side). Color scale in between -0.050 au (blue) to 1.100 au (red). Fingerprint plot of the molecules, 1 to 4 are shown (right side).

Table 2**:** Percentage of intercontacts in dibenzoazepine derivatives (a,b,c and d).

Molecule	C...C	C...H	H...H	N...H	C...N
a	1	39	57	3	-
b	-	39	61	-	-
c	2	32	52	13	1
d	3	44	51	2	-

Conclusion

The crystal and molecular structures of four dibenzoazepine derivatives are compared. In all the molecular structure, azepine moiety adopts boat configuration. In the crystal structure, the molecules are stabilized majorly from the C—H…π interactions. The short contacts are analysed using computational Hishfeld surfaces analysis and intercontacts (C...H and H...H) are having major contribution for the Hirshfeld surfaces.

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