Research Article

Crystal Structure, Spectral Studies, and Hirshfeld Surfaces Analysis of 5-Methyl-5\(H\)-dibenzo[\(b,f\)]azepine and 5-(4-Methylbenzyl)-5\(H\)-dibenzo[\(b,f\)]azepine

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Received 30 September 2013; Revised 8 December 2013; Accepted 14 February 2014; Published 19 May 2014

Academic Editor: Lúcia R. Gomes

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The compounds, 5-methyl-5\(H\)-dibenzo[\(b,f\)]azepine (1) and 5-(4-methylbenzyl)-5\(H\)-dibenzo[\(b,f\)]azepine (2), were synthesized and characterized by spectral studies, and finally confirmed by single crystal X-ray diffraction method. The compound 1 crystallizes in the orthorhombic crystal system in Pca\(_2\)\(_1\) space group, having cell parameters \(a = 11.5681 (18)\) \(\text{Å}\), \(b = 11.8958 (18)\) \(\text{Å}\), \(c = 8.0342 (13)\) \(\text{Å}\), and \(Z = 4\) and \(V = 1105.6 (3)\) \(\text{Å}^3\). And the compound 2 crystallizes in the orthorhombic crystal system and space group Pbca, with cell parameters \(a = 16.5858 (5)\) \(\text{Å}\), \(b = 8.4947 (2)\) \(\text{Å}\), \(c = 23.1733 (7)\) \(\text{Å}\), and \(Z = 8\) and \(V = 3264.92 (16)\) \(\text{Å}^3\). The azepine ring of both molecules 1 and 2 adopts boat conformation with nitrogen atom showing maximum deviations of 0.483 (2) \(\text{Å}\) and 0.5025 (10) \(\text{Å}\), respectively. The C–H⋯\(H\) short contacts were observed. The dihedral angle between fused benzene rings to the azepine motif is 47.1 (2) \(^\circ\) for compound 1 and 52.59 (6) \(^\circ\) for compound 2, respectively. The short contacts were analyzed and Hirshfeld surfaces computational method for both molecules revealed that the major contribution is from C⋯\(H\) and H⋯\(H\) intercontacts.

1. Introduction

Azepine derivatives have showed to be associated with different pharmacological activities such as antiviral, anticancer, anti-insecticidal, and vasopressin antagonist. Iminostilbene derivatives are found in montainine, coccinine, manthine, and pancracine alkaloids present in Haemanthus and Rhodophiala species [1]. They are the derivatives of drugs, such as carbamazepine [2], opipramol [3], and oxcarbazepine [4], which are used as anticonvulsants and antidepressants and in the treatment of epilepsy and trigeminal neuralgia [5]. Another compound, G32883, an iminostilbene derivative, shows effect on peripheral nerves [6]. Recently, it is reported that carbamazepine with magnesium oxide is used to treat anticonvulsant in albino rats [7]. Lateral dibenzazepine moieties are known to have potential to act as substituents for the binding site of the acetylcholine M\(_2\) receptor [8]. The 11-phenyl-[b,e]-dibenzazepine compounds are proved to be novel antitumor compounds [9].

Synthesis and crystal structures of other iminostilbene derivatives, 5-(prop-2-yn-1-yl)-5\(H\)-dibenzolo[b,f]-azepine, orthorhombic polymorph, and 5-[[4-Benzyl-1H-1,2,3-triazol-1-yl]methyl]-5\(H\)-dibenzolo[b,f]azepine have been reported [10, 11]. As a part of our ongoing research on the synthesis and crystal structures and their importance of iminostilbene derivatives, we report here the synthesis and characterization by spectral studies and crystal structure using single crystal X-ray crystal diffraction of compounds 5-methyl-5\(H\)-dibenzo[b,f]azepine (1) and 5-(4-methylbenzyl)-5\(H\)-dibenzo[b,f]azepine (2). Here, we investigate the role of the main intermolecular interactions on stabilization of the
solid state architecture of the iminostilbene derivatives. And, Hirshfeld surface analysis and fingerprint plots analyzing intermolecular interactions were presented in the same procedure as we reported [12].

2. Material and Methods

2.1. Synthesis of 5-Methyl-5H-dibenzo[b,f]azepine (1). 5H-Dibenzo[b,f]azepine (0.0025 mol) was taken in dimethylformamide (DMF) solvent, and K$_2$CO$_3$ (0.0038 mol) was added at room temperature and stirred for 5 minutes. The reaction mixture was cooled to 0°C, then iodomethane was added (0.0038 mol). After 15 minutes, the resulting reaction mixture was heated at 60°C for 7 hours (Scheme 1). After completion of reaction (monitored by TLC), the reaction mixture was diluted with water (50 mL). The aqueous layer was extracted with ethyl acetate (3 × 20 mL), and the combined ethyl acetate layer was washed with 0.1 N hydrochloric acid (2 × 25 mL), followed by brine solution (2 × 25 mL). Then, the organic layer was dried over anhydrous sodium sulfate and filtered and concentrated under reduced pressure to afford crude product, which was purified by column chromatography over silica gel (9.5:0.5 ratios as eluent). The pure compound was crystallized in ethyl acetate and hexane to obtain yellow hexagonal shaped single crystals.

2.2. Spectral Data

$^1$H NMR (CDCl$_3$, 400 MHz); δ 7.21 (q, $J$ = 4.99 Hz, 2H), 7.01–6.91 (m, 6H), 6.66 (d, $J$ = 7.82 Hz, 2H), and 3.30 (d, $J$ = 7.82 Hz, 2H).

Mass: Calc. 207.27 found: 208.27 (M$^+$ +1).

$^{13}$C NMR (100 MHz, CDCl$_3$); δ 152.28, 132.81, 132.42, 129.21, 128.80, 123.15, 118.82, and 39.30.

MS: $m/z$ = 207.27 (calculated) $m/z$ = 208.27 [M+H]$^+$ (found). Anal. Calcd. for C$_{22}$H$_{19}$N$_2$: C, 86.92; H, 6.32; N, 6.76.

(We also performed DEPT (distortionless enhancement by polarization transfer), which will be given as supplementary data in Supplementary Material available online at http://dx.doi.org/10.1155/2014/862067.)

2.3. Synthesis of 5-(4-Methylbenzyl)-5H-dibenzo[b,f]azepine (2). 5H-Dibenzo[b,f]azepine (0.0025 mol) was taken in a mixture of toluene and water in the ratio of 1:1, and sodium hydroxide (0.029 mol) was added followed by tetra-n-butyrammonium bromide (TBAB) (0.00029 mol) at room temperature. After 15 minutes, 1-(chloromethyl)-4-methylbenzene (0.0031 mol) was added to the reaction mixture at room temperature. Then, the resulting reaction mixture was heated at 60°C for 5 hours (Scheme 2). After completion of reaction (monitored by TLC), the reaction mixture was diluted with water (50 mL). The aqueous layer was extracted with ethyl acetate (3 × 20 mL), and the combined ethyl acetate layer was washed with 0.1 N hydrochloric acid (2 × 25 mL), followed by brine solution (2 × 25 mL). Then, the organic layer was dried over anhydrous sodium sulfate and filtered and concentrated under reduced pressure to afford crude product, which was purified by column chromatography over silica gel (60–120 mesh) using hexane: ethyl acetate mixture in 9.5:0.5 ratios as eluent. The pure
Table 1: Crystal data, data collection, and structure refinement.

<table>
<thead>
<tr>
<th>Compound</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C15 H13 N1</td>
<td>C22 H19 N1</td>
</tr>
<tr>
<td>Formula weight</td>
<td>207.26</td>
<td>297.38</td>
</tr>
<tr>
<td>Temperature (K)</td>
<td>296</td>
<td>100</td>
</tr>
<tr>
<td>Wavelength (Å)</td>
<td>1.54178</td>
<td>1.54178</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Orthorhombic</td>
<td>Orthorhombic</td>
</tr>
<tr>
<td>Space group</td>
<td>Pca2_1</td>
<td>Pba</td>
</tr>
<tr>
<td>Unit cell dimension (Å)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a = 11.5681(18)</td>
<td>A = 16.5858(5)</td>
<td></td>
</tr>
<tr>
<td>b = 11.8958(18)</td>
<td>b = 8.4947(2)</td>
<td></td>
</tr>
<tr>
<td>c = 8.0342(13)</td>
<td>c = 23.1733(7)</td>
<td></td>
</tr>
<tr>
<td>Volume Å³</td>
<td>1105.6(3)</td>
<td>3264.92(16)</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Calculated density g/cm³</td>
<td>1.245</td>
<td>1.210</td>
</tr>
<tr>
<td>Absorption coefficient mm⁻¹</td>
<td>0.554</td>
<td>0.530</td>
</tr>
<tr>
<td>F(000)</td>
<td>440</td>
<td>1264</td>
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<tr>
<td>Crystal size mm³</td>
<td>0.20 x 0.20 x 0.21</td>
<td>0.21 x 0.21 x 0.22</td>
</tr>
<tr>
<td>Theta range for data collection (°)</td>
<td>3.7 to 64.2</td>
<td>6.2 to 64.4</td>
</tr>
<tr>
<td>Limiting indices</td>
<td>-13 ≤ h ≤ 12</td>
<td>-18 ≤ h ≤ 19</td>
</tr>
<tr>
<td>Reflections collected/unique</td>
<td>9156/1417</td>
<td>54177/2696</td>
</tr>
<tr>
<td>R(int) = 0.130</td>
<td>R(int) = 0.034</td>
<td></td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least squares on F²</td>
<td>Full-matrix least squares on F²</td>
</tr>
<tr>
<td>Data/restraints/parameters</td>
<td>1417/1/146</td>
<td>2696/0/209</td>
</tr>
<tr>
<td>Goodness-of-fit on F²</td>
<td>1.16</td>
<td>1.08</td>
</tr>
<tr>
<td>Final R indices [I &gt; 2σ(I)]</td>
<td>R₁ = 0.0786, wR₂ = 0.2070</td>
<td>R₁ = 0.0385, wR₂ = 0.0895</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>-0.32 and 0.28 e Å⁻³</td>
<td>-0.17 and 0.20 e Å⁻³</td>
</tr>
<tr>
<td>CCDC</td>
<td>959827</td>
<td>958853</td>
</tr>
</tbody>
</table>

(compound was crystallized in ethyl acetate and hexane, which yields colorless needle single crystals.

2.4. Spectral Data

\(^1H\) NMR (CDCl₃, 400 MHz); δ 7.31 (d, J = 7.56 Hz, 2H), 7.15 (t, J = 7.78 Hz, 2H), 7.05–6.99 (m, 6H), 6.92 (t, J = 7.34 Hz, 2H), 6.79 (s, 2H), 4.91 (s, 2H), and 2.16 (s, 3H).


\(^13C\) NMR (100 MHz, CDCl₃); δ 150.52, 135.87, 134.51, 133.48, 131.92, 128.87, 128.70, 128.53, 128.28, 128.13, 127.50, 122.90, 120.15, 54.32, and 20.70.


(We also performed DEPT (distortionless enhancement by polarization transfer), which will be given as supplementary data.)

2.5. Single Crystal X-Ray Diffraction Studies. X-ray intensity data were collected for 1 (hexagonal shaped) and 2 (needle shaped) using Bruker X8 Proteum diffractometer at 296 K and 100 K, respectively. Data were collected using CuKα radiation (λ = 1.5418 Å) with the φ and ω scan method [13]. The final unit cell parameters were based on all reflections. Data collections, integration, and scaling of the reflections were performed using the APEX2 program [13].

The structures were solved by direct methods using SHELXS [14] and all of the nonhydrogen atoms were refined anisotropically by full-matrix least-squares on F² using SHELXL [14]. Summary of crystal data, data collection procedures, structure determination methods, and refinement results are summarized in Table 1.

ORTEP (Figures 1 and 2) and packing diagrams (Figures 3 and 4) were generated using MERCURY [15]. And the program Crystal Explorer 3.0 [16] was used to perform Hirshfeld surfaces computational analysis and to quantify the intermolecular interactions in terms of surface contribution and generating graphical representations (Figure 5), plotting 2D fingerprint plots (Figures 6 and 8) [17], and generating
Figure 1: The molecular structure of compound 1 showing the atomic numbering system. Displacement ellipsoids are drawn at the 30% probability.

Figure 2: The crystal packing of compound 1 projected onto bc plane.

electrostatic potential (Figure 5) [18] with TONTO [19]. The electrostatic potential is mapped on Hirshfeld surfaces using Hartree-Fock (STO-3G basis set) theory over the range of $-0.020$ a.u. to $+0.020$ a.u. (Figures 5 and 7). The electrostatic potential surfaces are plotted with red region which is a negative electrostatic potential (hydrogen acceptors) and blue region which is a positive electrostatic potential (hydrogen donor).

Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publications numbers 959827 (1) and 958853 (2).

3. Results and Discussion

The X-ray crystallographic analysis of 1 and 2 was performed, confirming the structures previously established by the NMR data. The crystal structure of each compound presents only one molecule in the asymmetric unit. The ORTEP diagrams of 1 and 2 including the atoms labeled are shown in Figures 1 and 3, respectively. The compounds 1 and 2 crystallize in the centrosymmetric and noncentrosymmetric space groups $Pbca$ and $Pca2_1$, respectively. The structural analysis reveals that all geometric parameters agree well with the expected values reported in the literature, including the iminostilbene...
Figure 3: The molecular structure of compound 2 showing the atomic numbering system. Displacement ellipsoids are drawn at the 50% probability.

Figure 4: The crystal packing of compound 2 projected onto ac plane.
derivatives previously published by us [10, 11]. Overall, both
the molecules adopt butterfly shape and the percentage of
intercontacts of 1 and 2 to the Hirshfeld surface is compared
(Figure 9).

3.1. Compound 1. The fused benzene ring (C1–C5/C15 and
C9–C14) to the azepine motif makes a dihedral angle of
47.1(2)°. Seven-membered (azepine) ring adopts a boat con-
formation with nitrogen atom showing maximum deviations
of 0.483 (2) Å, the puckering parameters $Q_2 = 0.663(5)$ Å,
$\varphi_2 = 182.1(4)^\circ$, $Q_3 = 0.2050(4)$ Å, and $\varphi_3 = 179.7(15)^\circ$,
and the total puckering amplitude $Q_T = 0.6940(4)$ Å [20]. The ORTEP of compound 1 is shown in Figure 1. The
packing (Figure 2) of the molecules is stabilized with the
short contacts C–H···\pi (Table 2), which exist between C12—
H12 and the centroid (Cg(1): C1–C5/C15) of the ring of the
neighboring molecules with a distance of 0.930 Å.

3.2. Hirshfeld Surface Analysis. Here, we estimated the inter-
molecular intercontacts contributing to the Hirshfeld sur-
faces shown in Figures 5 and 9. It shows that the major
contribution is from C–H (39%) (Figures 6(d) and 9) and
H–H (57%) (Figures 6(a) and 9). This is evidence that
van der Waals forces exert an important influence on the
stabilization of the packing in 1. And other intercontacts C–C
(2%) (Figures 6(c) and 9) and N–H (2%) (Figures 6(b) and
9) contribute less to the Hirshfeld surfaces. The mentioned
intercontacts are highlighted by conventional mapping $d_{norm}$
on the molecular Hirshfeld surfaces (Figure 5), where the red
spot areas indicate intercontacts involved in the C–H···\pi
interactions. And the electrostatic potential (Figure 7) shows
the distribution of positive and negative potential over the
Hirshfeld surfaces.

3.3. Compound 2. The fused benzene rings (C1–C6 and C9–
C14) to azepine motif make a dihedral angle of 52.59(6)^\circ. The
terminal benzene ring (C17–C22) makes dihedral angles of
26.66(6)^\circ and 77.06(6)^\circ with benzene rings C1–C6 and
C9–C14, respectively. The ORTEP of the compound 2 is
shown in Figure 3. Seven-membered (azepine) ring adopts
a boat conformation with nitrogen atom showing maxi-

Table 2: Intermolecular interactions geometry [Å, °].

<table>
<thead>
<tr>
<th>D–H···A</th>
<th>D–H (Å)</th>
<th>H–A (Å)</th>
<th>D–A (Å)</th>
<th>D–H···A(°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C12–H12···Cg(1)ii</td>
<td>2.895</td>
<td>0.9300</td>
<td>3.775(12)</td>
<td>166.41</td>
</tr>
<tr>
<td>C3–H3···Cg(1)i</td>
<td>2.990</td>
<td>0.7613</td>
<td>3.7513(15)</td>
<td>141</td>
</tr>
<tr>
<td>C7–H7···Cg(2)ii</td>
<td>2.880</td>
<td>0.8726</td>
<td>3.7526(14)</td>
<td>156</td>
</tr>
<tr>
<td>C8–H8···Cg(1)ii</td>
<td>2.620</td>
<td>0.8787</td>
<td>3.4987(14)</td>
<td>159</td>
</tr>
</tbody>
</table>

$x-1/2$, $y-1/2$, and $z$; $i x-1/2$, $y+1/2$, and $z-1/2$; $ii -x$, $y-2$, and $z-1/2$.
Figure 6: Fingerprint of compound I: (a) C⋯H, (b) N⋯H, (c) C⋯C, and (d) C⋯H. The outline of the full fingerprint is shown in gray. \( d_i \) is the closest internal distance from a given point on the Hirshfeld surface and \( d_e \) is the closest external contacts.

\[ Q_T = 0.7315(12) \text{ Å} \ [20]. \] The packing (Figure 4) of the molecules is stabilized with the short contacts of the type C–H⋯\( \pi \) (Table 2). These short contacts exist between C3–H3⋯Cg(1) with a distance 3.7513 (15) Å (angle 141°), C7–H7⋯Cg(2) with a distance of 3.7526 (14) Å (angle 156°), and C8–H8⋯Cg(1) with a distance 3.4987 (14) Å (angle 159°), with Cg(1): C1–C6; Cg(2): C9–C14.

3.4. Hirshfeld Surface Analysis. The major contribution is from C—H (39%) (Figures 8(b) and 9) and H—H (61%) (Figures 8(a) and 9) intercontacts. The mentioned intercontacts are highlighted by conventional mapping \( d_{norm} \) on the molecular Hirshfeld surfaces (Figure 7). In Figure 7, the red spot areas indicate intercontacts involved in the C–H⋯\( \pi \) interactions. And the electrostatic potential (Figure 7) shows the distribution of positive and negative potential over the Hirshfeld surfaces.

4. Conclusions

Two derivatives, called 5-methyl-5H-dibenzo[b,f]azepine (1) and 5-(4-methylbenzyl)-5H-dibenzo[b,f]azepine (2), were synthesized, characterized by spectral studies (\(^1\)H NMR, \(^13\)C NMR and DEPT) and finally, structural elucidation by...
Figure 7: $d_{	ext{norm}}$ mapped on Hirshfeld surface (b) for visualizing the intercontacts of compound 2. Color scale in between $-0.075$ au (blue) and $1.358$ au (red). Electrostatic potential mapped (c) on Hirshfeld surface (different orientation) with $±0.020$ au. Blue region corresponds to positive electrostatic potential and red region to negative electrostatic potential. The ball and stick model represents the different orientations (front, back, top, and bottom) and correspondingly the Hirshfeld surfaces and their electrostatic potentials are oriented.

Figure 8: Fingerprint of compound 2: (a) C $\cdots$ H and (b) H $\cdots$ H. The outline of the full fingerprint is shown in gray. $di$ is the closest internal distance from a given point on the Hirshfeld surface and $de$ is the closest external contacts.

single crystal X-ray diffraction studies. The azepine rings of compounds 1 and 2 adopt the boat conformation, and, as a whole, molecule assumes butterfly shape. The fused benzene ring to azepine motif makes a dihedral angle of $47.1$ ($2^\circ$ for compound 1 and $52.59$ ($6^\circ$ for compound 2, respectively. Hirshfeld surface analysis of 1 and 2 reveals that H $\cdots$ H and C $\cdots$ H are the most abundant intercontacts. This is evidence that van der Waals forces exert an important influence on the stabilization of the packing in 1 and 2.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.
Figure 9: Hirshfeld surfaces percentage evaluation of short contacts for compound 1 and compound 2. The particular squared colour boxes on the right side represent the type of the intercontact visible at the percentage evaluation boxes.

Acknowledgment

The authors thank Institution of Excellence, University of Mysore, Mysore, for providing single crystal X-ray diffractometer and NMR facility for data collection.

References
